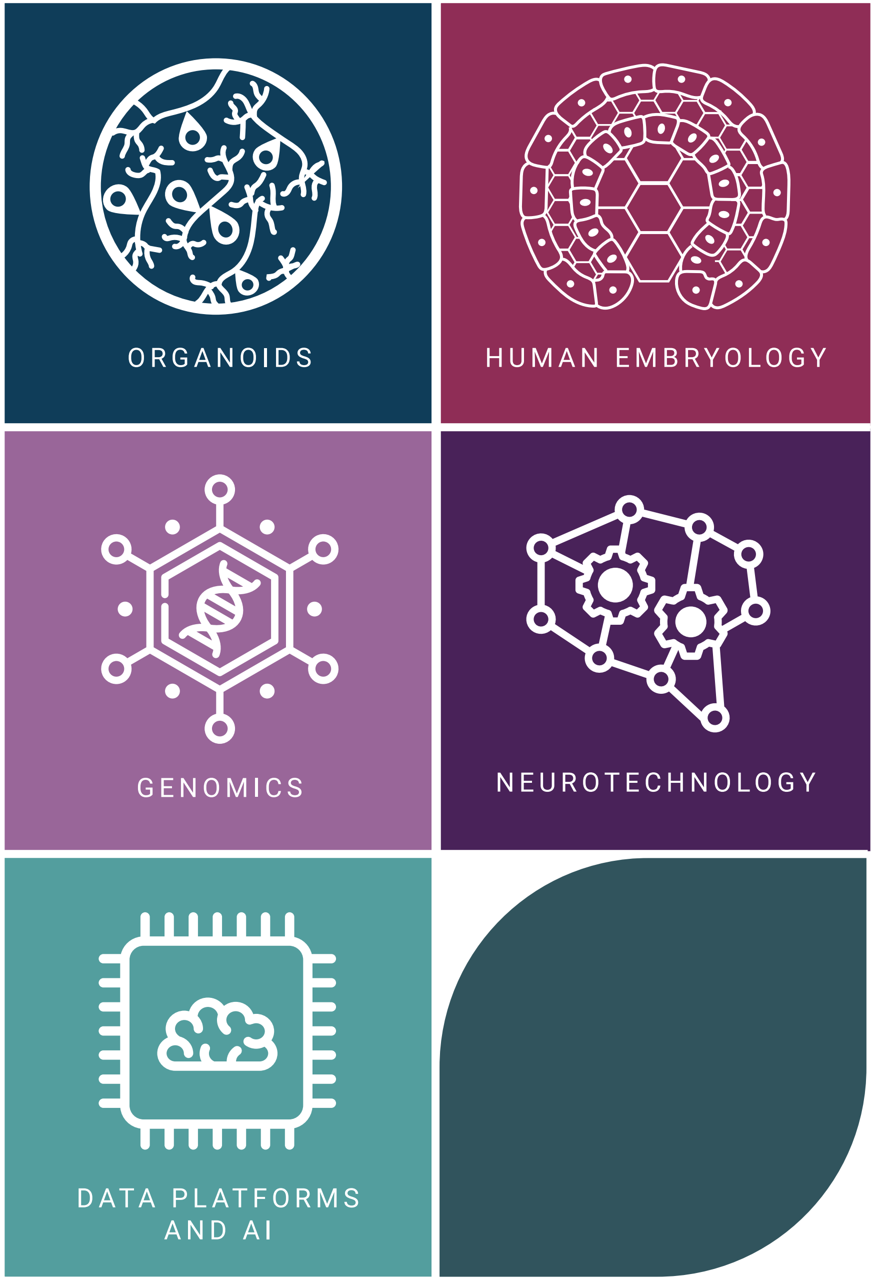

RAND EUROPE

State-of-play and future trends on the development of oversight frameworks for emerging technologies

Part 1. Global landscape review of emerging technology areas

Sana Zakaria, Ioli Howard, Eva Coringrato, Anna-Louise Todsen, Imogen Wade, Devika Kapoor, Alec Ross, Katarina Pisani, Chryssa Politi, Martin Szomszor and Salil Gunashekar

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Acronyms and abbreviations

AI	Artificial intelligence
ANN	Artificial neural networks
BCI	Brain–computer interface
BMI	Brain–machine interface
CAD	Computer-aided design
CNN	Convolutional neural networks
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
DL	Deep learning
DNN	Deep neural network
EEG	Electroencephalogram
EU	European Union
FDA	Food and Drug Administration
FL	Federated learning
GDPR	General Data Protection Regulation
GWAS	Genome-Wide Association Study
HDS	Health Data Space
hESC	Human embryonic stem cells
HFEA	Human Fertilisation and Embryology Authority
HI	High income
IRB	Institutional review board
ISSCR	International Society for Stem Cell Research
IVF	In vitro fertilisation
LI	Low income
LLM	Large language model
LMIC	Low- or middle-income countries
LMM	Large multi-modal models
ML	Machine learning
MRI	Magnetic resonance imaging
NEWG	Neuroethics Working Group
NLP	Natural Language Processing
OECD	Organisation for Economic Co-operation and Development
OI	Organoid intelligence
ONN	Organoid neural network
RHC	Regulatory Horizons Council
SCBEM	Stem cell-based embryo model
TRE	Trusted research environment
UKRI	UK Research and Innovation
UNESCO	United Nations Educational, Scientific and Cultural Organization
VR	Virtual reality
WGS	Whole genome sequencing
WHO	World Health Organization
WP	Work packages

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For more information about RAND Europe or this document, please contact:

Salil Gunashekar (Deputy Director, Science and Emerging Technology Research Group)
RAND Europe
Eastbrook House, Shaftesbury Road, Cambridge CB2 8DR
United Kingdom
Email: sgunashe@randeurope.org

Sana Zakaria (Research Leader, Science and Emerging Technology Research Group)
RAND Europe
Eastbrook House, Shaftesbury Road, Cambridge CB2 8DR
United Kingdom
Email: szakaria@randeurope.org

Chapter 1

Research snapshot

Wellcome commissioned RAND Europe to undertake a study on the state-of-play and future trends on the development of oversight frameworks for emerging technologies. The specific objective of the study is to identify and analyse a suite of oversight frameworks and mechanisms (including associated emerging trends and novel approaches) that are in use, in development or under debate in different jurisdictions across the globe for a set of emerging technologies. The technologies of interest include genomics (specifically engineering biology), embryology, organoids, neurotechnology, Artificial Intelligence (AI) (specifically its application and use as a research tool) and data platforms.

The study findings are presented in two related documents: the global technology landscape review report (this document) and the technology oversight report. The two reports should be read alongside each other. This report presents a comprehensive landscape review of the technology areas. It examines the trends, opportunities, challenges and prevalent oversight mechanisms across these technology areas, drawing on a mixed-methods approach that combined desk research, scientometric analysis and expert consultations. The desk research involved reviewing literature to identify the trends, opportunities and challenges associated with the emerging technologies in terms of investment, advancement and application. The scientometric analysis quantitatively assessed research and innovation activities globally using indicators such as publications, patents and policy documents. An expert advisory panel provided insights on the key oversight discussions that are emerging in the context of technological advancement.

This report underscores the transformative potential of emerging technologies, while highlighting the associated ethical, regulatory and societal challenges. Effective oversight mechanisms that encompass a range of informal (i.e. not legally binding) and formal and legally binding approaches are crucial for harnessing the benefits of these technologies and at the same time mitigating risks. Many such instruments are either in place or in development. These instruments fill critical gaps, as well as expose others, and are the focus of the accompanying report on technology oversight mechanisms.

Key takeaways:
Data platforms and AI

Data platforms and AI are crucial, cross-cutting technologies that impact various domains, including genomics, embryology, organoids and neurotechnology. The two technologies are interconnected and lend increasing maturity, as well as complexity, to the other technology areas discussed in this report. Highlights from data platforms and AI are as follows:

Exemplar trends: There are significant advancements taking place in AI algorithmic maturity, machine learning model development and data analytics capabilities.

Exemplar opportunities: These areas have the potential to revolutionise medical research, personalised medicine and data-driven decision making based on further leveraging omics[1] datasets.

Exemplar challenges: Ethical concerns on algorithmic transparency, data use and privacy, algorithmic biases, and a fragmented governance landscape are seen as some of the critical challenges in this field.

Exemplar oversight mechanisms: A mix of hard laws such as the General Data Protection Regulation (GDPR) and the European Union (EU) AI act, ethical guidelines, and self-regulatory frameworks are in place or under development.

1 Omics refers to the totality of specific factors within a cell, tissue or organism, and primarily refers to genomics, transcriptomics, proteomics and metabolomics.

GENOMICS

Key takeaways:
Genomics

Genomics (focusing on engineering biology) is a field of biology that focuses on the study of an organism's complete set of DNA. Engineering biology applies the tools and techniques of engineering to biology, enabling novel biological system design, or redesign of existing systems.

Exemplar trends: There has been a rapid growth of engineering biology infrastructure, research and applications that span biomanufacturing, net-zero and climate mitigation, and agriculture security.

Exemplar opportunities: Innovations in healthcare, agriculture and industrial biotechnology are leading to sustainable solutions and new bio-based products.

Exemplar challenges: These include biosafety concerns given the dual-use nature of biological tools and outputs, ethical implications of synthetic organisms, and public acceptance.

Exemplar oversight mechanisms: Given its varied applications, diverse policies, laws and frameworks govern this field, such as biosafety standards and public contracts, as well as international conventions such as the Biological Weapons Convention (BWC).

Key takeaways:
Organoids

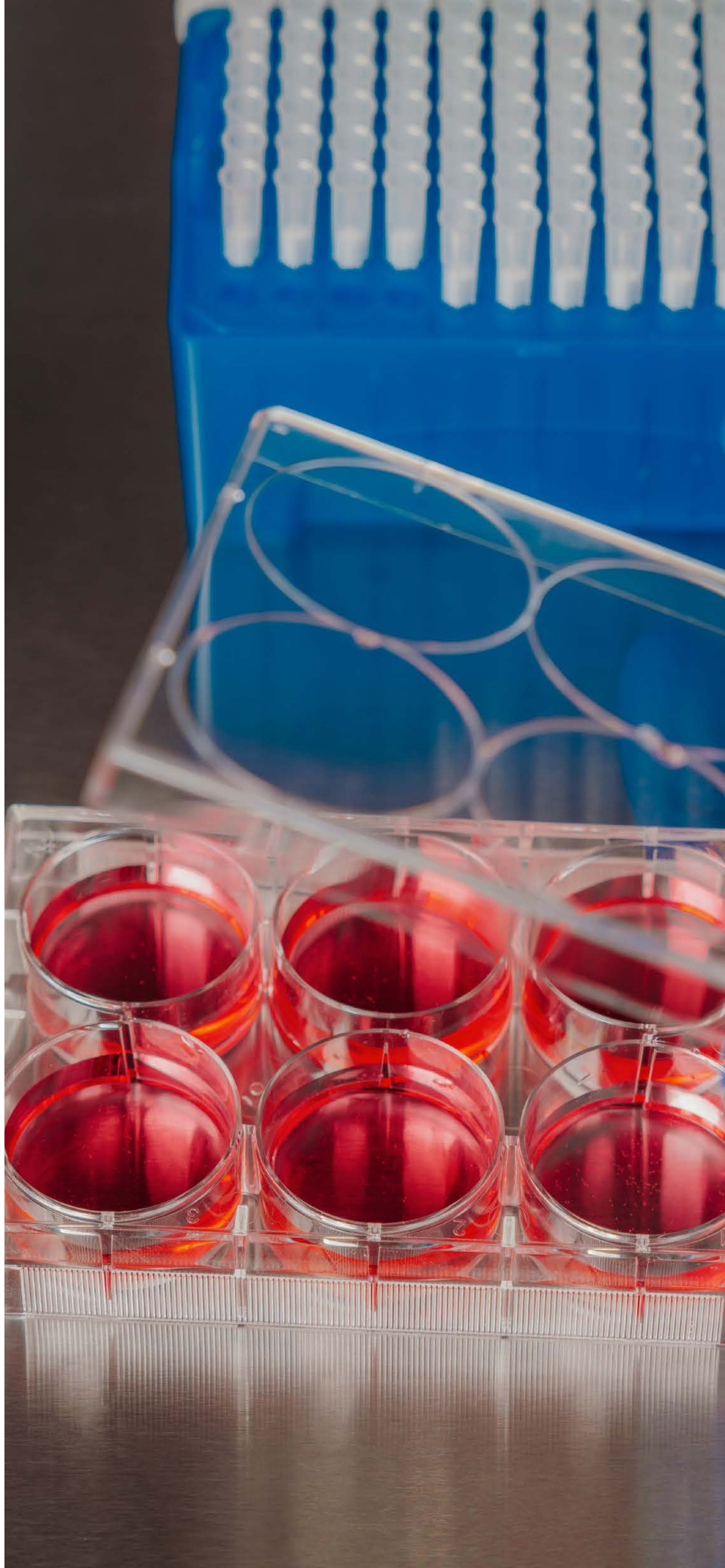
Organoids are three-dimensional structures derived from stem cells and capable of self-organising into structures that mimic the key functional, structural and biological complexity of an organ.

Exemplar trends: There are rapid developments in organoid technology, with applications in disease modelling and drug testing.

Exemplar opportunities: These include advancements in personalised medicine, better understanding of human development and novel therapeutic strategies.

Exemplar challenges: Ethical issues regarding the use of human tissues, technical limitations in replicating complex organ systems, and standardisation of protocols are some of the barriers to further progress.

Exemplar oversight mechanisms: There are emerging guidelines on ethical use, data sharing policies and international collaborations to standardise practices.



Key takeaways:
Human embryology

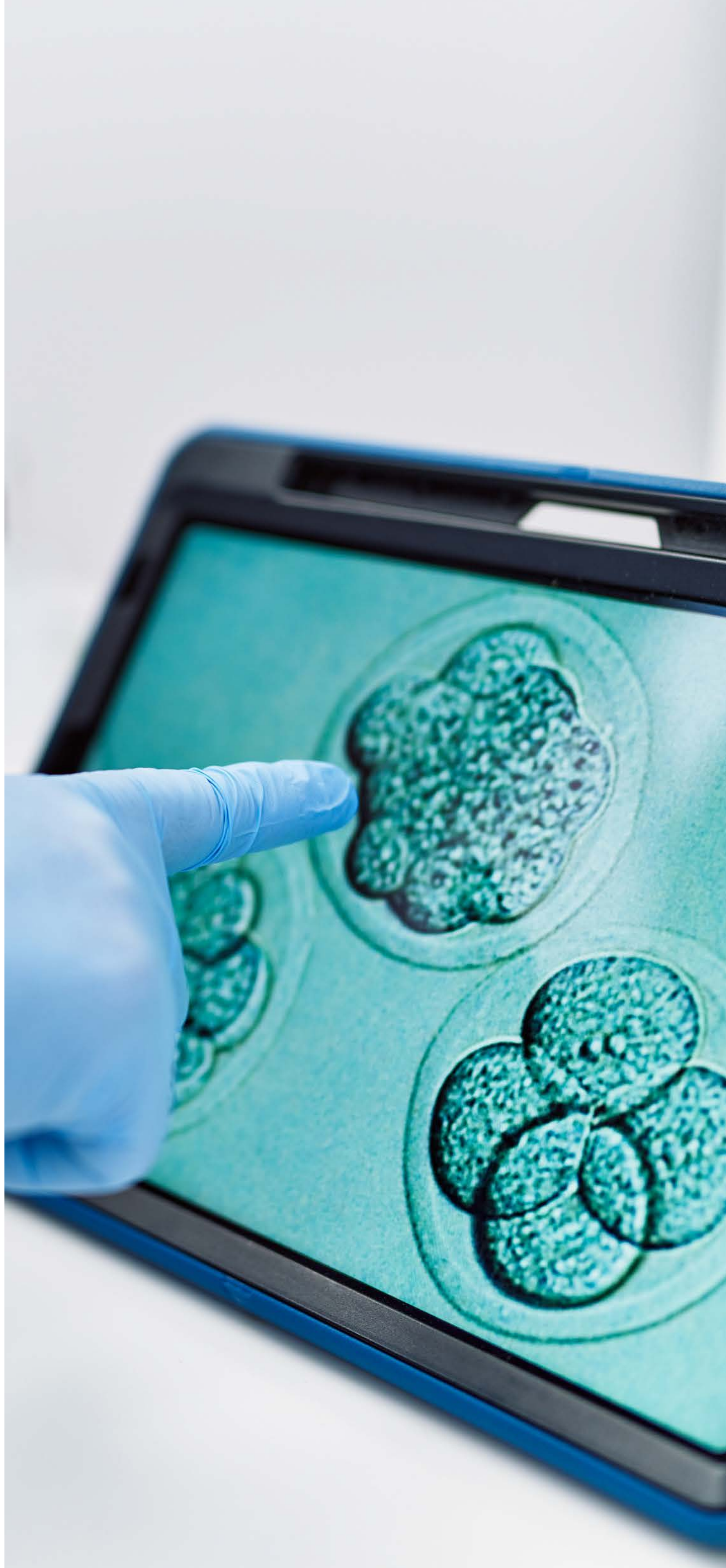
Human embryology is a sub-field of developmental biology that concerns human development from fertilisation to birth and involves the study of human embryos from fertilisation onward.

Exemplar trends: Advances in embryo research, genomic editing and in vitro fertilisation (IVF) technologies are exemplified by milestone discoveries such as the development of stem cell-based embryo model systems (SCBEMs).

Exemplar opportunities: Improvements in reproductive health and the potential to correct inherited genetic disorders are being progressed.

Exemplar challenges: These include ethical and moral considerations and their variation in a global context, regulatory loopholes, and the potential misuse of gene-editing technologies.

Exemplar oversight mechanisms: Legally binding regulatory frameworks such as the Oviedo Convention, international guidelines such as the 14-day rule, and ethical codes such as the SCBEM code of practice to govern embryo research and clinical applications are under review or development.



Key takeaways:
Neurotechnology

Neurotechnology is a rapidly evolving field that consists of devices and procedures used to access, monitor, investigate, assess, manipulate and emulate the structure and function of the neural systems of animals or human beings.

Exemplar trends: Progress in brain–computer interfaces, neural prosthetics and cognitive enhancement technologies is ongoing, with huge investments seen in both the United States and China.

Exemplar opportunities: The potential to treat neurological disorders, improve mental health and enhance cognitive abilities in a medical setting is being progressed, while non-medical use cases such as immersive gaming and meditation are emerging.

Exemplar challenges: Ethical issues related to cognitive enhancement, privacy concerns, agency and autonomy, and the need for long-term safety studies are some of the many challenges in this complex field.

Exemplar oversight mechanisms: Ethical guidelines, consumer protection laws, and medically relevant acts and frameworks are some of the diverse ways this technology is overseen, with new models emerging such as dynamic consent and neurorights law.

Chapter 2
Background and introduction

Developments in technology are transforming our world, creating an uncertain future with potential for both benefits and risks. As technologies become more pervasive and form a critical aspect of our societal infrastructure, governance and wider oversight mechanisms have a key role to play in ensuring that benefits from technology are maximised and risks are managed proactively. In a 2019 report, Wellcome recommended that the UK government 'seize the opportunity to set out its vision and a package of reforms to make the UK the world-leader in the regulatory oversight of emerging science and technologies' (Clift 2019). The UK's Science and Technology Framework published in March 2023 sets out the UK government's goals and vision for science and technology until 2030 (UK Government 2024a). This framework identifies a portfolio of five critical technologies: 1) AI; 2) engineering biology; 3) future telecommunications; 4) semiconductors; and 5) quantum technologies. It also discusses regulation and standards that could promote the oversight of digital technologies, green technologies and life sciences initially, followed by the creative industries and advanced manufacturing. While these activities exemplify developments taking place in the UK context, they also signify a trend of activities occurring on a global scale in relation to the oversight of new and emerging technologies.[2]

At the same time as these developments there is evidence of technology acceleration, with multiple technologies converging to enhance capabilities, such as a machine learning (ML)[3] based tool that has accurately predicted the structure of over 200 million proteins (Callaway 2022). Scientific advancements are also taking place that challenge existing oversight mechanisms, for instance the development of embryo model systems from stem cells that fall outside the legal definition of human embryos in many parts of the world (Zernicka-Goetz 2023). A clear understanding of current and future oversight mechanisms in emerging science and technology across the globe is essential for effective research and innovation. Appropriate oversight can also ensure that technology advancements provide benefits to society. It is therefore critical to proactively identify oversight practices that can support the use of emerging technologies in a transparent and ethical manner (Gunashekar et al. 2019).

Against this backdrop, Wellcome commissioned RAND Europe to undertake a study on the state-of-play and future trends on the

2 For examples see: *UN Secretary-General's Strategy on New Technologies* (United Nations 2018); 'A Europe Fit for the Digital Age' (European Commission 2024a); and 'Regulators Are Taking on Global Technology Trends' (Economist Impact 2024).

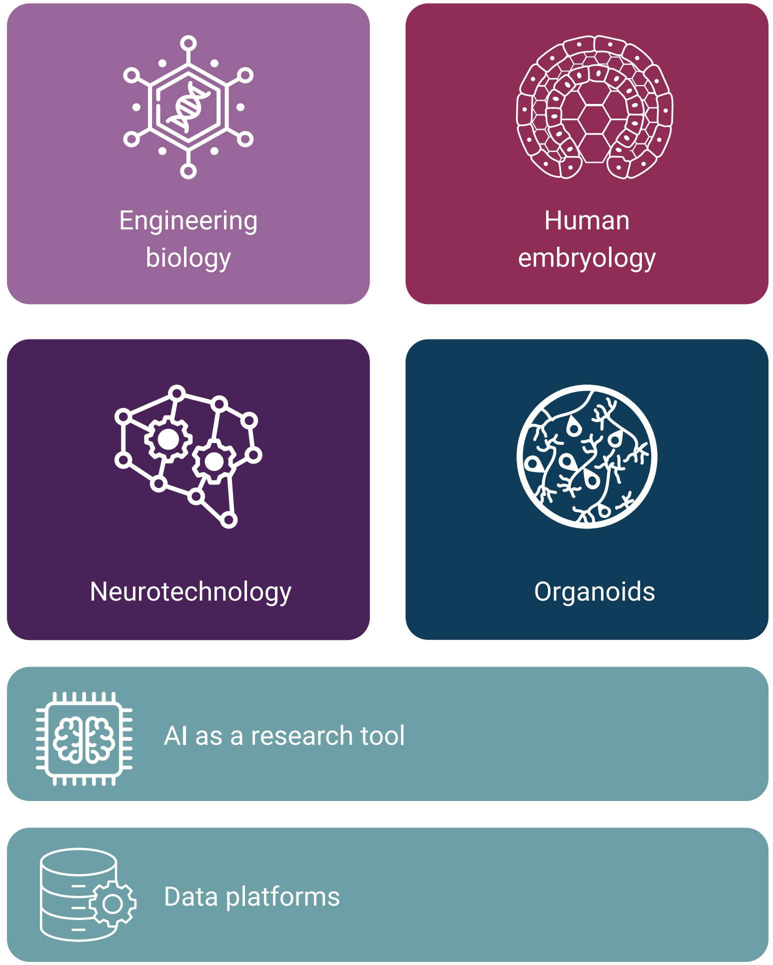
3 Machine learning is a branch of AI that focuses on the development of algorithms that allow computers to learn from data and improve with experience.

development of oversight frameworks for emerging technologies. The specific objective of the study is to identify and analyse a suite of oversight frameworks and mechanisms (including associated emerging trends and novel approaches) that are in use, in development or under debate in different jurisdictions across the globe for a set of emerging technologies. The technologies of interest include genomics (specifically engineering biology), embryology, organoids, neurotechnology, AI (specifically its application and use as a research tool) and data platforms. Each of these technology areas are defined in the relevant sections of the report. The study findings are presented in two related documents: the global technology landscape review report (this document) and the technology oversight report (Zakaria et al. 2024). The global technology landscape review report provides an in-depth analysis of global research and innovation (R&I) developments occurring within each technology area, identifying key trends, challenges and opportunities. The technology oversight report examines notable oversight mechanisms that are either established or under development across a selection of global jurisdictions and offers key learning and insights that could inform future technology oversight discussions. The two reports should be read alongside each other.

2.1. A note about data platforms and AI

AI and data platforms are two crucial technology areas that are relevant to a wide range of domains and applications. They are also interconnected. Based on previous analysis and discussions with Wellcome, this report addresses the technologies together and as 'transversal' to the other four technology areas (Figure 1).

Figure 1. Technology areas covered by this study



Source: RAND Europe analysis.

This study uses an expansive interpretation of technology oversight or governance, as conceptualised in a previous study (Gunashekar et al. 2019). For each technology area, the accompanying technology oversight report maps and examines a variety of oversight frameworks, covering a spectrum of options with differing levels of accountability, obligation and enforcement. These range from mechanisms such as legislation, regulations and treaties to non-regulatory standards, ethical guidance, codes of conduct and self-regulatory frameworks created by professional/industry bodies, industry or the research community (see Figure 2).

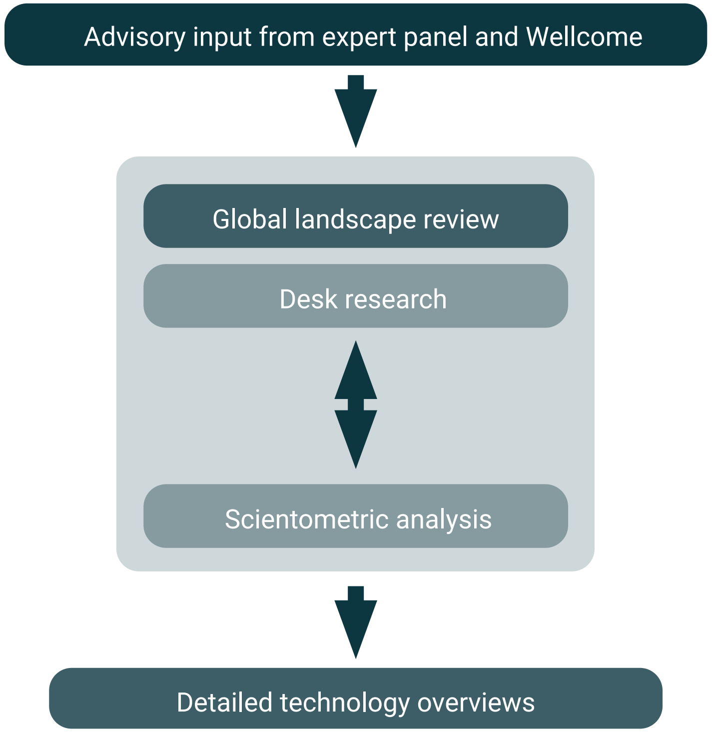
Figure 2. Spectrum of oversight approaches

Source: RAND Europe analysis.

Chapter 3
Overview of research approach

This chapter presents a summary of the research methods, encompassing a global landscape review for the different technology areas, as illustrated in Figure 3. Each step is briefly described in the research process in the following sections, with a more detailed explanation of the methodology provided in Annex A.

Figure 3. Overview of research approach



Source: RAND Europe analysis.

3.1. Global landscape review

The global landscape review for the technology areas consisted of desk research and a comprehensive scientometric analysis.

3.1.1. Desk research

A detailed literature review was undertaken to support the global landscape review for each technology area. The literature searches focused on identifying notable scientific and industry trends in each technology area, which yielded further insights into the opportunities and challenges they present with their maturity. The desk research also helped identify a selection of key oversight mechanisms associated with each technology area, as well as corresponding jurisdictions of interest (these are discussed in the accompanying technology oversight report (Zakaria et al. 2024)).

The search terms developed were generic in the first instance (e.g. ‘engineering biology trends’, ‘engineering biology and genomics definitions', 'investment trends in engineering biology', 'challenges in engineering biology') to identify influential papers in the field. Based on a review of the top 15 papers from the last five years, a snowballing approach[4] was used to identify further documents of interest and assimilate information on trends, opportunities, challenges and key oversight discussions. The analysis drew on scientific articles, reports, and relevant data repositories and observatories associated with each technology area. The research team also consulted members of the expert advisory panel and Wellcome during the desk research phase to obtain their insights into the areas of research.[5]

3.1.2. Scientometric analysis

The scientometric analysis was focused on developing a quantitative understanding of how each technology area is developing across the globe based on various input and output indicators of associated R&I activities. The research team used a range of data including publications, patents, companies and policy documents (Table 1).

Table 1. Scientometric data sources

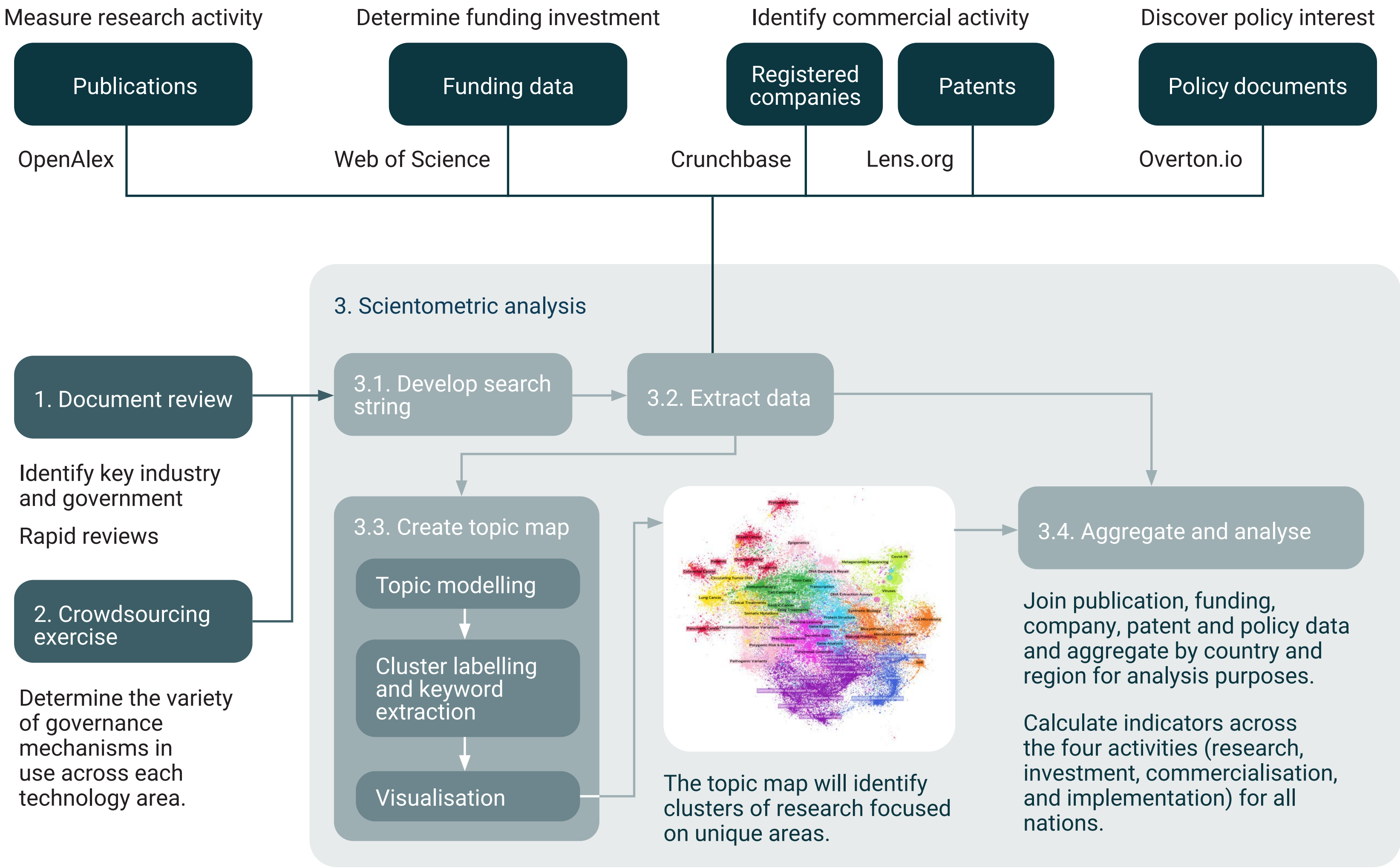
R&I activity	Type of data	Data source (2019–23)
Research activity	Publications (i.e. knowledge production/research outputs)	OpenAlex
Funding investment	Funded publications	Funding acknowledgements recorded in the Web of Science*
Commercial activity	Registered companies	Crunchbase
	Patents	Lens.org
Policy interest	Policy documents	Overton

*Note: * Web of Science data is preferred over OpenAlex for funder acknowledgements due to much higher levels of coverage. Web of Science examines the text in acknowledgement sections of the paper to determine funders, whereas OpenAlex only contains links made public through Crossref.*

Source: RAND Europe analysis.

4 Snowballing, also known as citation chaining, is the process of searching the references and/or the citations of a list of articles to identify other relevant material.
5 An expert advisory panel was convened at the project inception stage consisting of six subject matter, policy and legal experts across the technology areas.

Figure 4. High-level depiction of the scientometric analysis



Source: RAND Europe analysis.

Figure 4 shows the flow of data and the data processing steps used in the scientometric analysis. The various data sources are shown at the top (green boxes). A custom search string was developed for each technology area and used to interrogate each data source for relevant records, such as publications, patents granted or policy documents published. Given the diverse and multidisciplinary nature of the technology areas, an important step in the scientometric analysis was to determine the topical makeup of each area, providing a visual map of the research landscape and a mechanism to identify and measure trends in research. To achieve this the research team used topic modelling, a natural language processing technique that determines clusters of keywords frequently used together, tailoring the number of topics for each technology based on volume and variety.

Following data extraction and topic modelling, the various datasets were combined and a range of indicators were calculated to measure various aspects of research intensity (e.g. publication volume, relative publication share), research impact (e.g. citations), amount of investment (e.g. funder acknowledgements), intellectual property claims (e.g. patent count), commercial uptake (e.g. active companies) and early signs of governance discussions (e.g. policy documents). For each data source, outputs were aggregated by country and region to support various analyses. This wide-ranging and inclusive approach fed into the jurisdiction selection.

3.2. Expert panel input

At project inception an expert advisory panel consisting of subject matter (e.g. neurotechnology, embryology, genomics, data, ethics and systemic risk), policy and legal experts across the technology areas was convened. The research team engaged the experts throughout all key phases of the research design and output development, and their inputs fed into validating the findings.

Chapter 4
Enabling technologies: Data platforms and AI

This chapter presents insights and trends related to data platforms and AI, with a particular emphasis on their cross-cutting aspects. Key developments associated with the intersection of AI/data platforms and each of the four core technology areas are described in Chapters 5-8.

KEY TAKEAWAYS FROM THE GLOBAL LANDSCAPE REVIEW FOR DATA PLATFORMS AND AI

- 'Data platforms' is a catch-all term referring to many data-centred capabilities.
- Innovations in laboratory and clinic technologies and techniques have accelerated the volume of data collected across the life sciences sectors.
- There is growing interest in migrating research and clinical data from siloed institutional platforms to centralised data repositories and cloud-based platforms.
- Integrated data platforms are supporting innovation across sectors.

Centralised data platforms widen data access, promoting discovery, enabling inclusion and improving the representativeness and relevance of research findings.

Federated architecture is emerging as a promising way of enabling data integration and sharing, while complying with varied institutional, national and international data governance mechanisms.

Data platforms face many pervasive issues related to data use issues, including consent, maintenance of de-identification and anonymity.

Data oversight has tiers of mechanisms in place ranging from hard law to high-level principles.

Critical debates about AI are focused on safety and reliability.

As analytical capabilities improve, there is growing interest in powering data platforms with emerging analytical tools.

Lack of standardisation and poor interoperability hinder data integration and aggregation efforts.

A disjointed international governance landscape is a barrier for international cooperation and data sharing.

AI is an umbrella term encompassing multiple technologies that exhibit advanced capabilities.

AI oversight is an area of active development, with nations adopting varied stances.

Source: RAND Europe analysis.

4.1. Data platforms as an enabling infrastructure

‘Data platforms’ is a catch-all term referring to many data-centred capabilities

The term ‘data platforms’ refers to an infrastructure that houses data. Depending on the structure and purpose of the platform, it may possess various capabilities including storage, management and analysis. While many digital technologies can serve these functions, a data platform is distinctive as its main purpose is to unify a set of data in a common operating environment, organised by an overarching structure that allows for repeatable data extraction and storage (Goddard 2023).

Data platforms do not have a clear or consistent definition in academic literature or in legislative or policy documents. A variety of terminology is used to refer to technologies with similar capabilities including ‘data management platforms and computing platforms’. The term ‘data platforms’ is commonly used as a catch-all term to refer to specific types of data storage and analysis environments, including data lakes, data warehouses, and extract, transform, load (ETL) tools, each of which have technical definitions (Goddard 2023).

As data underpins many aspects of modern life, data platforms are increasingly recognised as a type of critical infrastructure (Wollacott 2023). Several countries and trading blocs, including the United Kingdom, the EU and Singapore, have amended or are considering amending regulations to include data platforms and centres as critical or essential infrastructure alongside traditional utilities such as electricity and water, offering greater resources for security and maintenance (Wollacott 2023; Butler 2023).

Innovations in laboratory and clinic technologies and techniques have accelerated the volume of data collected across the life sciences sectors

One of the most significant developments affecting data platforms has been the sheer volume of data generated from scientific research and clinical practice in the last decade. This has facilitated scientific discovery but placed new demands on data platforms. (Blay et al. 2020).

For example, next generation sequencing, commonly used in genetics and genomics research, can sequence genes or even an entire genome in a matter of hours or days, amounting to a 100–1,000 factor increase in sequencing capacity compared to other techniques, leading to significant cost savings (Qin 2019; Goodwin 2016). Various high-throughput techniques have supported broad scientific discovery, enabling the identification of novel drug candidates, facilitating rapid responses to infectious pathogens, and contributing to comprehensive efforts such as the 1,000 Genomes Project, the Cancer Genome Atlas and the 100,000 Genomes Project.

Outside of the laboratory, technological innovations in direct-to-consumer wearable devices are increasingly being adopted, adding to the growing volume of data. While the data generated by these products is generally seen as being of insufficient quality for use in research or clinical practice, the technologies are improving (Smuck et al. 2021; Fuller et al. 2020) and the data generated is increasingly of interest to scientists, clinicians and other practitioners, particularly for their application in personalised and precision medicine approaches (Powell and Godfrey 2023; Seneviratne et al. 2023).

There is growing interest in migrating research and clinical data from siloed institutional platforms to centralised data repositories and cloud-based platforms

Across fields there is growing interest in the development and widespread use of centralised data repositories and storage environments, as well as cloud-based platforms. Proliferating research and clinical data is placing increasing demands on data platforms in terms of storing, managing and transferring/sharing large quantities of data and associated computational capabilities. In this context, many institutional data platforms are failing to keep pace with the increasing volume of data and the growing need for integrated analytical capabilities. Furthermore, institutional platforms are increasingly seen as siloed, inhibiting research collaboration and data sharing and increasing the likelihood of duplication of research efforts, particularly in data-intensive fields such as genomics (Hinkson et al. 2017; Thorogood et al. 2021). In response, there is a growing movement towards centralised data repositories, data networks and global biobanking, which are seen as better for enabling data aggregation and research collaboration, reducing redundancy, enabling data reuse, and promoting values related to open science and transparency (Harris et al. 2012; Koutkias 2019; Tenopir et al. 2020). Notable examples of such centralised systems include the European Health Data and Evidence Network (EHDEN 2024) and the Human Cell Atlas (Human Cell Atlas 2024).

In tandem with centralised data repositories there is increased interest in cloud-based data storage environments for research and clinical data. Cloud-based platforms are seen as advantageous as they enable data storage and analysis at the scale necessary for rapidly increasing volumes of data, while also allowing for the integration of a variety of analytical tools (Hinkson et al. 2017; Abernathey et al. 2021). While there is growing interest in migrating research and clinical data to cloud-based storage environments, appetite for and adoption of this approach varies across disciplines and sectors, with prominent adoption in genomics, cell biology and related disciplines producing platforms such as the Open Science Data Cloud (OSDC 2024) and the US National Cancer Institute Genomic Data Commons (NCI GDC 2024).

Integrated data platforms are supporting innovation across sectors

In the health sector, integrated health data platforms have facilitated advancements in clinical support tools. For example, developments in such platforms have enhanced clinical decision support systems (CDSS) software and predictive analytics, supporting evidence-based practice and enabling prevention and early intervention efforts (Sutton et al. 2020). Data platform integration has also expanded health data access points, facilitating individual engagement and control over health data through patient- and consumer-focused tools (Singh et al. 2019). Finally, integrated data platforms, including health information exchange (HEI) capabilities, have allowed for enhanced and often real-time biosurveillance (Hulme et al. 2023). This is particularly useful for emergency and pandemic preparedness, as well as for monitoring health trends (Blauer et al. 2023).

Centralised data platforms widen data access, promoting discovery, enabling inclusion and improving the representativeness and relevance of research findings

Large, collaborative research and clinical data repositories and cloud-based storage environments have enabled access to a variety of data sources and supported emerging areas of research. The increasing amount of data produced is expected to have a positive impact on research through enabling scientific discovery, enhancing rigour and facilitating reproducibility (Jwa and Poldrack 2022). Notably, large, collaborative datasets support new areas of scientific discovery, particularly those previously limited by data scarcity challenges. For example, reducing institutional data silos and moving away from proprietary databases is expected to support drug discovery, particularly for rare diseases where insufficient data has historically limited advancement (Denton et al. 2021). Furthermore, as data platforms grow and move towards general, field-agnostic repositories, there are growing opportunities for interdisciplinary research (Aguilar Gómez and Bernal 2023; Grossman et al. 2016). For example, health data integrated with environmental data allows researchers to investigate interdisciplinary research questions, such as how environmental conditions affect disease prevalence and severity.

As these platforms support wide data aggregation, they allow for expanded opportunities for data access and inclusion. This includes making data accessible to a wider community of researchers and stakeholders (for example, citizen data reporting), which presents increasing opportunities for inter-institutional and international research collaboration and supports the participation and inclusion of researchers from underrepresented geographies, including low- or middle-income countries (LMICs).

As analytical capabilities improve, there is growing interest in powering data platforms with emerging analytical tools

As analytical tools improve, alongside increasing capabilities to integrate these tools into data platforms, there is broad interest in integrating emerging analytical tools into data platforms. There is particular interest in integrating data science capabilities, notably ML tools and AI networks, especially given rapid recent improvements in functionality. Although AI and ML have been used to analyse research and clinical data for many years, facilitating important scientific discovery, the potential to integrate these technologies into data storage environments represents a new frontier. For example, in step with the general public's interest in AI and ML, and following the demonstrated utility of AI for life sciences (e.g. AlphaFold), there is increasing interest in incorporating AI and ML tools into genomics data platforms (Infante 2023). The ability and potential to analyse large volumes of genomic data is spurring interest in data-intensive sub-fields of genomics such as the 'dark genome'[6] (Parida and Haferlach 2019). There is also growing interest in integrating blockchain technologies, which provide a non-modifiable means of cataloguing and tracking information within and across data environments, providing persistent identification capabilities. Blockchain technologies show promise in managing healthcare data (Yaqoob et al. 2022) and cataloguing biological specimens, and are increasingly considered for biobanking approaches (Ortiz-Lizcano et al. 2023). For example, blockchain ledgers are emerging

6 The 'dark genome' is used to refer to regions of the genome that have not been well characterised or understood in terms of their function.

as an effective means of cataloguing, matching and tracking embryological specimens such as eggs and embryos.

Integrating AI and ML capabilities into data platforms has supported the development and improvement of predictive analytics, and has catalysed a boom in 'precision' applications across sectors, notably medicine, education and agriculture. For example, the precision health market was estimated to have a global market size of US$578 billion in 2023 and is projected to grow to US$1,233 billion by 2033 (Precedence Research 2024).

Federated architecture is emerging as a promising way of enabling data integration and sharing, while complying with varied institutional, national and international data governance mechanisms

As data access and integration capabilities improve, persistent governance challenges continue to inhibit data access and sharing. A notable advancement in this area are federated data platforms, which are a form of data platform architecture that allow for information sharing within and between organisations, while allowing data to remain with the jurisdictional boundaries of the organisation (Alvarellos et al. 2023; Palchuk et al. 2023). Federated systems are being integrated into national and multi-national datasets, particularly in genomics, in Australia (Stark et al. 2019), Canada (Dursi et al. 2021) and Europe (Blomberg and Lauer 2020). Efforts to implement federated systems are also underway by the Common Infrastructure for National Cohorts in Europe, Canada and Africa (CINECA) (Dursi et al. 2021) and within NHS England (NHS England 2024).

Lack of standardisation and poor interoperability hinder data integration and aggregation efforts

While efforts to integrate and aggregate data continue, there are notable challenges to realising visions of broad data repositories and agile data platforms, such as data standardisation (Kush et al. 2020; Lehne et al. 2019). Many fields in science and medicine struggle to standardise data collection and reporting mechanisms, which limits the potential for data aggregation (Lehne et al. 2019). This challenge is particularly acute for new methods, experimental techniques and technologies that are sufficiently novel to lack broad consensus around standardisation, and that may face challenges when integrating with historical data formats (Marx 2023).

Interoperability, the ability for diverse data to be merged or aggregated in meaningful ways (NIH 2024), is another significant challenge for data integration and aggregation. There are various forms of interoperability, for example, syntactic interoperability refers to the compatibility of data formats and structures (Lehne et al. 2019), and semantic interoperability refers to the meaning of the data or the shared understanding of what is being measured (Lehne et al. 2019).

Data platforms face many pervasive issues related to data use issues, including consent, maintenance of de-identification and anonymity

The proliferation of integrated data platforms with advanced analytic capabilities raises concerns about various issues related to data use, including reuse, ownership and privacy; appropriate consent processes for ongoing, secondary and follow-on use; integration with public data; and notification procedures for incidental findings. Debates in this area generally centre on who provides consent and how consent is maintained. Some believe that consent should be obtained individually each time the use of the data is expanded, whereas others believe that consent should be managed by an ethics board or data trusts (Maloy and Bass 2020). Three types of access are often built into platforms: 1) open access; 2) controlled access; and 3) registered access. A major player in genomics data governance, the Global Alliance for Genomics and Health, has supported a registered access approach through its Passports and Authentication and Authorization Infrastructure specifications, which act as a means of authenticating digital identity and automating access (GA4GH 2019). This approach allows for continued engagement with data for reuse while maintaining data security.

As the realm of devices that collect data expand, along with the growing number of data platforms and the linkages between them, there are increasing concerns regarding maintaining privacy and the de-identification of data. Privacy is a particularly strong concern for the integration of data from multiple devices into border data platforms (Canali et al. 2022). Protecting privacy often centres on the de-identification of data, anonymisation and pseudonymisation. Some data platforms address this challenge by limiting data linking, either through the functionality of the platform or through its terms of service. Others resort to only storing summary data and statistics. However, the loss of detail when using summary data can render the information useless, particularly for research or clinical use (O'Doherty et al. 2021).

A disjointed international governance landscape is a barrier for international cooperation and data sharing

A notable challenge affecting data collection, management and sharing is the disjointed landscape of data governance. Data governance varies across many dimensions including data type, sector and geography. In addition, data governance mechanisms are developed and enforced by many actors including governments, industry and interest groups and funders, posing a layered and complex set of obligations and recommendations for international research collaboration and data sharing. This fragmented landscape can be a prominent challenge for research collaboration, creating barriers to data sharing and transfer, and a lack of clarity when navigating multiple jurisdictions, particularly with the increasing adoption of cloud-based platforms that transcend geographic boundaries (British Academy/The Royal Society 2017). Furthermore, as funders and research sponsors often adopt existing general data governance principles, such as the EU GDPR and the US Health Insurance Portability and Accountability Act (HIPAA), researchers frequently need to comply with these practices as well as with field-specific norms and common practices (Eke et al. 2022). While most hard law mechanisms for data governance prioritise privacy, many scientific fields are strongly aligned with open science values, meaning that these various governance mechanisms are often in tension.

Data oversight has tiers of mechanisms in place ranging from hard law to high-level principles

Hard law data governance mechanisms, notably GDPR, have a primary focus on data privacy. As data has become ubiquitous in all aspects of life there are growing efforts to develop comprehensive laws and regulations for data governance. In this respect, the EU took the first steps with GDPR, which given its timing and the position of the EU on the global stage had a strong influence on existing and emerging data governance policies worldwide (Mercer 2020). As GDPR has a strong focus on privacy, privacy and data protection have been the primary focus of hard law data governance mechanisms in most countries.

Many nations have looked to the EU and GDPR as a testing ground for data regulation, and have subsequently created new laws or updated existing data laws. One of the most direct examples of this is Brazil's *Lei Geral de Proteçao de Dados*, implemented in 2020, which is directly modelled on GDPR and has similar scope and applicability, albeit less harsh financial penalties (Government of Brazil 2024). Similarly, in 2023 India passed its Digital Person Data Protection (DPDP) Act, which includes many terms similar to those in GDPR (Burman 2023). The 2019 Nigeria Data Protection Regulation (NDPR) and South Africa's 2020 Protection of Personal Information Act (POPIA) also share similarities with GDPR (Simmons, n.d.). Furthermore, GDPR appears to have spurred many nations to revisit and revise their existing data protection policies. For example, Australia, China and Singapore have revised their data protection legislation, largely in the direction of further protecting privacy and increasing penalties for privacy violations (A&O Shearman 2023).

Given the lack of comprehensive hard law mechanisms to govern data in research, medicine and related fields, there has been a proliferation of researcher- and funder-led bodies producing principles and guidance for self-regulation. Most commonly adopted in the research community are the findability, accessibility, interoperability, and reusability (FAIR) principles, which state that data should be findable, accessible, interoperable and reusable. The use of the FAIR principles has been further encouraged and normalised by prominent funding bodies such as Horizon Europe, which usually requires organisations awarded funding to follow the FAIR principles (European Commission 2024b).

In addition to general principles for research data, various groups have emerged across fields and geographies to address specific aspects of research data governance. Many of these soft law principles and recommendations, in contrast to hard law mechanisms, place greater focus on open science and data sharing, in addition to privacy protection. For example, ELIXIR, a European intergovernmental organisation of life and computer scientists and support staff, provides participating member states with resources and infrastructure to manage growing volumes and complexities of research data in order to support innovation and industry usage (ELIXIR 2024). Similar efforts are underway at a global scale. Building on previous efforts from the Global Life Science Data Resources Working group, the Global Biodata Coalition works at the funder level to strategise and share resources around data management, use and infrastructure (Global Biodata Coalition 2024).

Many principles and guidance for health data, such as the Organisation for Economic Co-operation and Development's (OECD) Recommendation on Health Data Governance, attempt to strike a balance between privacy and access, acknowledging the sensitivity of health data while recognising the potential benefits of data sharing in appropriate contexts such as healthcare delivery and sometimes research (OECD 2022). However other frameworks, such as the World Health Organization (WHO) Data Principles (WHO 2024a) and the European Health Data Space (European Commission 2024c), place greater emphasis on enabling data sharing and data access than on protecting privacy. By contrast, frameworks such as the Health Data Governance Principles emphasise human rights and equity above all other considerations (Health Data Governance Principles 2024).

In addition to the proliferation of soft law principles and practices developed by alliances and interest groups, research funders and academic journals exert a strong normative influence on data governance (Chawinga and Zinn 2019; Reeves et al. 2022). Increasingly, funders require detailed data management plans and other requirements around data availability and sharing at the conclusion of a funded project (Reeves et al. 2022). Similarly, academic journals influence data management and sharing through their publishing policies (Chawinga and Zinn 2019). While norms around data accessibility and sharing are tending towards open access across fields, there remain issues related to ideological hegemony and the lack of inclusion of diverse perspectives and worldviews in these policies, particularly as the landscape of prominent funders and academic journals is dominated by Western, English-speaking scientists (Kaye et al. 2018; Reeves et al. 2022). There is growing recognition that current norms and soft law governance mechanisms may not be inclusive or representative of all viewpoints, particularly indigenous and non-Western perspectives (Kaye et al. 2018; Yoshizawa et al. 2014; Reeves et al. 2022). In response, movements around data sovereignty are placing emphasis on local or national autonomy on if and how data is used, or for human subject data that emphasise participant benefit and control over data (Reeves et al. 2022). This perspective has been embodied in the increasingly adopted CARE principles, which stand for collective benefit, authority over control, responsibility and ethics (GIDA 2024).

Given the cross-cutting nature of data platforms and how they underpin multiple sectors and technologies, the remaining chapters examine data platforms as an enabling infrastructure applied to the four core technology areas of interest, identifying trends, opportunities, challenges and governance debates at the intersection of data/data platforms and each technology.

4.2. Artificial intelligence (AI) as an enabling general purpose technology

AI is an umbrella term encompassing multiple technologies that exhibit advanced capabilities

AI is an umbrella term that encompasses a range of technologies that use machines to process targeted data inputs, generating specific outputs (European Commission 2021; OECD 2024a). Some definitions of AI specify that the technology is adaptable and autonomous (Gajjar 2024). AI is a rapidly evolving field of strategic importance and has developed significantly in recent years. Generative AI[7] is a rapidly evolving sub-field that involves the use of AI systems to generate new content such as images, videos, audio and text. Generative AI also encompasses foundation models[8] that have seen rapid advancements in their capabilities based on their ability to perform a range of general tasks. These models are producing increasingly sophisticated outputs and are developed through training large volumes of data. Large language models (LLMs) are a subset of foundation models that are trained on vast volumes of text data.

The field of AI has catalysed research productivity, filling in research gaps across multiple sectors. For example, AI has been used for environmental monitoring in climate science. The healthcare sector has received the most private investment of any AI-enabled sector, totalling US$6.1 billion globally between 2017 and 2022, concentrated in the United States (Stanford University 2023), with a steep upward trend in venture capital investments in recent years (360 Nautica 2024).

7 Generative AI 'encompasses AI systems that create new and original content (text, image, video, audio) based on user inputs such as text prompts' (Hicks et al. 2023).
8 Foundation models: 'systems that use machine learning models trained on large and broad data sets' (Hicks et al. 2023).

A great deal of literature describes the developments of AI in the healthcare context, covering data processing (imaging and textual data), administrative tasks and organisation, and patient diagnosis, treatment and monitoring (Ali et al. 2023). AI has also been used in collecting health data, with federated learning (FL) emerging as a key development in the healthcare ecosystem.[9] The use of FL in health research is enabling models to be trained on a wider set of data than other models (as heterogeneous data from multiple hospitals and research centres can be accessed), thus improving the use of AI in medical imaging. In research, supervised learning[10] and anomaly detection[11] methods are regularly used forms of AI, while deep learning (DL)[12] has been used to handle unstructured data, often in medical imaging (OECD 2023). Other common applications include using AI to summarise research in peer review processes and improving data interpretability.

Critical debates about AI are focused on safety and reliability

The main debates about AI are broadly focused on mitigating the risks posed by its dual-use nature and reliability. Debates on oversight have ranged from limiting computational power to having guardrails for the use of AI on protection of rights, intellectual property, litigation and privacy (Taddeo et al. 2021). Given the maturity and appetite for AI use in healthcare and life sciences, more specific risks have emerged related to patient safety and privacy, data accuracy, and ownership (Caudai et al. 2021; Holland et al. 2024; Dias and Torkamani 2019). In particular:

- Governance issues regarding data imputation,[13] denoising[14] and integration.
- Difficulty in choosing the right model due to a lack of explainability and interpretability of DL and other forms of AI.
- Liability and reliability concerns in relation to data sharing and privacy, and use of open-source databases.
- Wider societal issues including ethical, legal and sustainability challenges (e.g. environmental and biodiversity risks).

AI oversight is an area of active development, with nations adopting varied stances

Given the breadth of available AI technologies and the varied contexts within which they are being used, it is challenging to implement a single, universal oversight mechanism, and governments have had to respond rapidly to rising concerns (European Parliament 2023). To date, relatively little national-level legislation has been put in place to govern AI, but several countries have published strategies

9 Federated learning (FL): a decentralised machine learning technique where multiple devices collaboratively train a shared model by keeping the data localised and without exchanging raw data (Khan et al. 2023).

10 Supervised learning: a model is trained with existing, formatted data to predict future data.

11 For example, searching for anomalies in medical imaging.

12 Deep learning (DL) uses multiple, layered artificial neural networks to model and analyse complex data (Gajjar 2024). Artificial neural networks (ANN) are brain-inspired networks of interconnected computational units which exchange data across units and layers. Outputs of one layer are used as the inputs for the next layer (Gajjar 2024). Other types of neural network include deep neural networks (DNN), which are more than three layers of ANN, and convolutional neural networks (CNN).

13 Data imputation is a statistical method used to fill in missing values in a dataset with estimated values.

14 Data denoising is the process of removing noise from a signal or dataset. Noise refers to random variations in the data that are not of interest or are unwanted.

and frameworks (BowerGroupAsia 2023; OECD 2024b), such as Singapore and Japan's National AI Strategy that was published in 2019 and updated in 2022 (Ling 2024). Notably, the EU became the first jurisdiction to adopt a comprehensive framework – the EU AI Act – to regulate the deployment of AI in the European Union (European Commission 2021). The EU AI Act entered into force on 1 August 2024 (European Commission 2024d). Initial responses to the draft versions of the Act called for further clarification of the scope and definition of AI in order to appropriately consider the intersection of AI with technologies such as genomics (Botes 2023). The EU is also currently negotiating a Draft AI Liability Directive to reduce legal fragmentation and uncertainty around issues of liability associated with the use of AI, particularly when working across borders (European Commission 2022). There are existing AI regulations in China; however, they are specific to generative AI (Cyberspace Administration of China 2023). In 2023, the United States issued the Executive Order on Safe, Secure and Trustworthy Development and Use of AI that focuses on standards for safe AI (White House 2023).

In recent years, the UK government has been adopting a 'pro-innovation approach to AI regulation' that aimed to develop safe AI through investments in R&I and ensuring that regulators apply existing technology-agnostic regulations to AI (UK Government 2023a). AI-specific regulations were not foreseen in the short term (Gallo and Nair 2024), with individual government departments outlining their own AI strategies (Shepley and Gill 2023). Since assuming office in July 2024, the new UK government has expressed its intention to 'establish the appropriate legislation to place requirements on those working to develop the most powerful artificial intelligence models' (UK Government 2024b). It has also commissioned an action plan to explore the potential of AI in stimulating economic growth and improving outcomes for UK citizens (UK Government 2024c).

Despite the relative lack of AI infrastructure in Africa, the African Union is taking a preventative approach when drafting and accepting an AI strategy to avoid negative impacts (e.g. bias, human rights, and wages) and ensure positive socioeconomic development (Musoni 2024; Tsanni 2024). The white paper includes actions on innovation and skills, data privacy regulation, and funding mechanisms to support innovation. It also recommends an AU-wide consortium to promote collaboration and partnerships (AUDA-NEDAP 2023).

A number of jurisdictions have taken a soft law approach to AI oversight, providing advice, tools and guidelines to oversee specific aspects of AI, including ethical concerns. This information may be through observatories and advisory groups, or directly from governments.

At the international level a range of initiatives have been noted; the United Nations hosts the Global AI Ethics and Governance Observatory (UNESCO 2024) and the Inter-Agency Working Group on AI (United Nations 2024). These initiatives and others have produced various guidelines for example:

- Ethical Impact Assessment tool by UNESCO (UNESCO 2023a).
- WHO's healthcare-specific guidance on the ethics and governance of large multi-modal models (WHO 2024b).
- The Association of Southeast Asian Nations' (ASEAN) voluntary guidance on ethics of AI (ASEAN 2024).
- Australia's voluntary AI Ethics Principles (Australian Government 2019).

- EU's assessment list for trustworthy AI (ALTAI), which is a checklist to help action the seven requirements of trustworthy AI[15] defined by the Ethics Guidelines for Trustworthy AI (European Commission 2020).
- Singapore's Model Governance Framework for Generative AI (IMDA 2024).
- ASEAN's ethics guidance also includes a framework on AI governance (ASEAN 2024).
- EU's Health Data Space (HDS) to foster a trustworthy environment and ecosystem for health data use in AI. The HDS has established rules, standards and practices, and a governance framework (OECD 2023).

Given the cross-cutting nature of this technology, and how AI tools are being utilised across multiple sectors, the remaining chapters examine AI as an enabling technology applied to the four core technology areas of interest, identifying trends, opportunities, challenges and governance debates of note at the intersection of AI and each technology.

15 1) human agency and oversight; 2) technical robustness and safety; 3) privacy and data governance; 4) transparency; 5) diversity, non-discrimination and fairness; 6) environmental and societal well-being; and 7) accountability.

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Chapter 5
Global landscape review for genomics (focusing on engineering biology)

This chapter presents the findings of the global landscape review for genomics based on desk research and a comprehensive scientometric analysis. It first provides some context and defines what is meant by genomics in the context of this study, specifying a focus on engineering biology for follow-on analysis from the scientometrics. The key trends, challenges and opportunities associated with global engineering biology research and innovation are then highlighted. The chapter concludes with reflections on oversight mechanisms associated with engineering biology (oversight mechanisms and their implications are examined in depth in the accompanying technology oversight report (Zakaria et al. 2024).[16]

16 As noted in Chapter 2, given the cross-cutting nature of AI and data platforms, and how they underpin multiple sectors and technologies, these two areas are examined as cross-cutting technologies applied to genomics (and specifically engineering biology). Where relevant, the research team has identified a selection of notable trends, opportunities, challenges and governance debates at the intersection of AI/data platforms and genomics.

KEY TAKEAWAYS FROM THE GLOBAL LANDSCAPE REVIEW FOR GENOMICS (FOCUSING ON ENGINEERING BIOLOGY)

Trends in genomics and engineering biology:

- Genomics is a large and active area of research globally, with research activity mostly focused in the fields of biochemistry, molecular biology and medicine.
- The United States and China are the largest contributors to research in genomics (46% of global output), with European countries producing research with the highest citation impact.
- Evidence of commercial applications of genomics is greatest in the United States, the United Kingdom, China, India and Canada.
- Governments across the globe are increasingly investing in engineering biology research and innovation.
- Research on disease-specific and treatment-related topics are increasing most rapidly in terms of relative global output.
- Genomics research is mostly conducted through collaboration between researchers across multiple locations.
- Policy documents published relating to genomics are mainly from the United States, the United Kingdom, intergovernmental organisations (IGOs), the EU and Australia.
- Cheaper genome sequencing is making the technology and its outputs more accessible.
- Bioconvergence in engineering biology has yielded benefits across various sectors.

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Opportunities associated with engineering biology:

Precision health research has particularly flourished due to engineering biology breakthroughs.

Engineering biology tools have unlocked future opportunities for climate change mitigation and adaptation.

Engineering biology could be a core enabler of food security and sustainability.

Challenges associated with engineering biology:

Dual-use engineering biology developments can carry biosecurity threats.

Lack of diversity in genomic datasets can hamper progress in precision research.

Sceptical public attitudes towards engineering biology can be a barrier to widespread adoption.

Scaling and translation are seen as significant bottlenecks for utilising engineering biology outputs.

Key developments associated with the intersection of AI/data platforms and genomics and engineering biology:

AI has unlocked a multitude of capabilities in genomics and engineering biology research.

AI tools have opened up new avenues of research, such as the study of biological systems and demographics

Progress is hampered by a lack of access to genomic data, impacting training algorithms and producing biased results.

AI-enabled developments in engineering biology pose a national security concern.

Key developments in AI algorithms applied in genomics could serve as a leading example for other technologies.

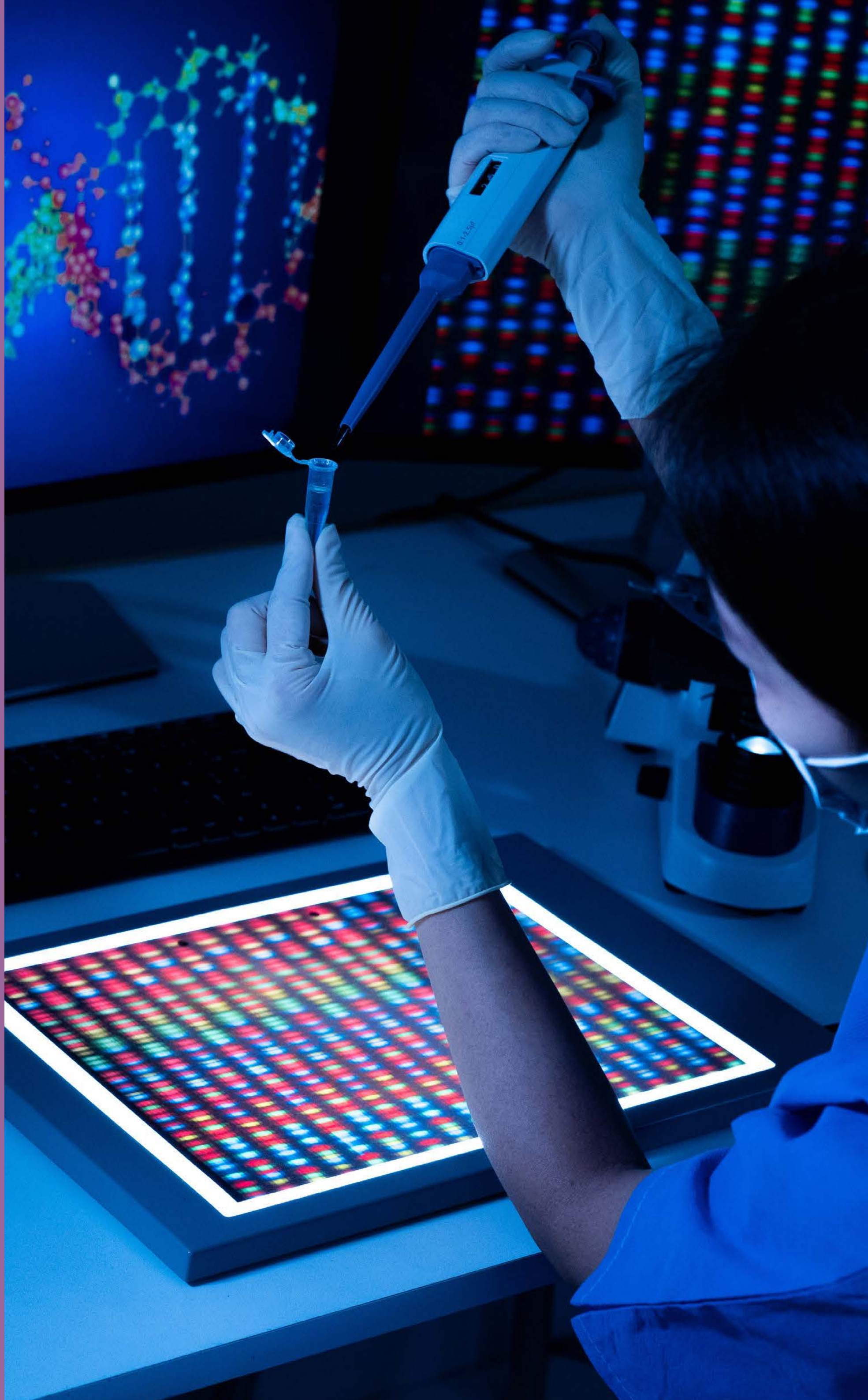
A key debate at the nexus of AI and engineering biology tools is whether access to biological data for training should be restricted.

Multi-omics data generation is challenging current concepts of consent due to the potential for personal identification and data reuse.

Oversight mechanisms associated with engineering biology:

- International recommendations have set the global stage for discussions on engineering biology powered genome editing.
- There are different schools of thought on whether to regulate the tools or their outputs.
- Experimental approaches to the regulation of engineering biology, such as regulatory sandboxes, are emerging.
- Genomics data is increasingly considered a critical infrastructure.
- Multiple AI-genomics focused advisory boards and consortia are generating insights into non-legal mechanisms of oversight.

Source: RAND Europe analysis.



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5.1. What do we mean by genomics and engineering biology?

Genomics is a sub-field of biology that involves studying the entire genome of a living organism, with the genome considered the organism's 'operating manual' (NIH 2022). A widely recognised definition of genomics characterises it as a field that aims to understand how genes operate and interact with each other and with the external environment. The field encompasses a diverse set of techniques and tools (NHS England 2024).

Since the Human Genome Project first successfully sequenced 92% of the human genome in 2003 and made the information freely available in public databases, genomics has transformed healthcare through numerous applications such as non-invasive prenatal genetic testing, DNA-based forensics, genetic disease diagnostics, personalised healthcare treatments and Covid-19 surveillance (UK Parliament 2023). It also has applications in other diverse fields such as agriculture, biomanufacturing and environmental science. For instance, the United Kingdom passed the Precision Breeding Act in March 2023 to facilitate use of new gene-editing techniques for increasing food resilience (UK Government 2023b).

Genomics has rapidly evolved over the last decade due to advancements in nucleic acid sequencing and synthesis, as well as convergence with AI and machine learning (Zakaria et al. 2023). One particular field associated with genomics is engineering biology, which has gained particular interest over the past decade due to its many applications. Engineering biology (sometimes used interchangeably with synthetic biology)[17] applies the tools and techniques of engineering to biology, and has great potential to enable scientists to create novel biological systems, or redesign existing systems enabled by genomics tools . As a transformative platform technology there are many potential applications across health, food and materials (UK Government 2023c), with many governments and companies across the world investing significantly in this growing field.

A focus on engineering biology

This study focuses on engineering biology for three main reasons. First, governments and companies across the globe are paying increasing strategic attention and investing more in the technology; for instance, the United Kingdom recognised engineering biology as one of five critical technologies in 2023 (UK Government 2023d). Second, there is a rapid and widespread increase in computational tools being deployed in engineering biology to help address the challenges faced in the areas of health, agriculture and environment. Third, notable technological breakthroughs such as CRISPR-Cas9[18] genetic editing techniques have further advanced the potential of engineering biology. In addition, given the vastness of the field of genomics, the focus on engineering biology for the desk research component of the study was deemed appropriate to surface more meaningful and focused insights.

17 Engineering biology and synthetic biology are often considered synonymous (Sheets et al. 2023). However, synthetic biology has been around longer as a label and is narrower in scope, typically used to refer to the generation of new and synthetic products. Engineering biology or biological engineering is broader in scope, more interdisciplinary and refers to the application of engineering principles to study biological systems and includes the commercialisation aspects of the technology. For a useful overview that discusses the similarities and differences between these two terms, see (Nerlich 2020).

18 As mentioned in Chapter 6, clustered regularly interspaced palindromic repeats (CRISPR-Cas9) is a gene-editing technology that uses RNA as a guide to make precise edits in the genome. It is cheaper, faster and more accurate than previously discovered tools.

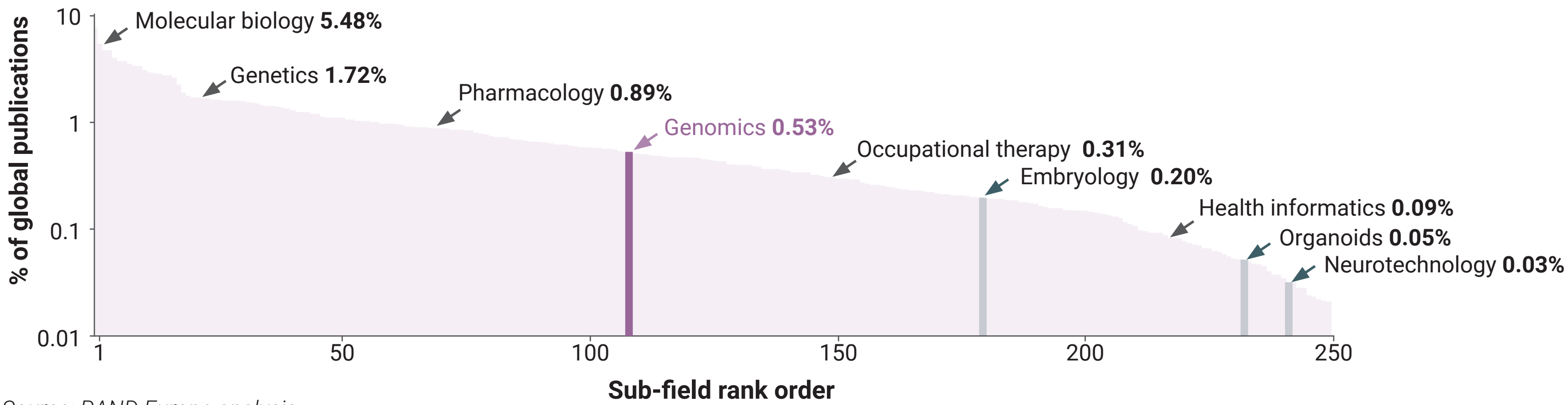
5.2. What are the emerging trends in genomics and engineering biology research and innovation?

Genomics is a large and active area of research globally, with research activity mostly focused in the fields of biochemistry, genetics, molecular biology and medicine

Genomics is a large technology area, with 264,721 publications released between 2019 and 2023 covering sub-fields[19] such as biochemistry, genetics, molecular biology and medicine. Genomics represents 0.53% of the global publication share, and is ranked 109 when compared to all sub-fields (Figure 5). Genomics global publication share ranked against all sub-fields). Of the four technology areas focused on in this study, genomics is the largest and fastest growing research area, with +0.19% increase in global publication share between 2020 and 2023.

Figure 6 shows the topic map for genomics. It reveals a range of topics covering treatments for cancers (red, yellow and dark green clusters), data and the use of AI (violet), population and plant genomics (purple and pink), synthetic biology (orange), and genetics (cyan and pink).

Figure 5. Genomics global publication share ranked against all sub-fields of biological research



Source: RAND Europe analysis.

19 The OpenAlex classification assigns publications to topics based on titles, abstracts, journals and citations. They are aggregated into 252 sub-fields (OpenAlex 2024a).

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Figure 6. Genomics topic map (publications between 2019 and 2023)

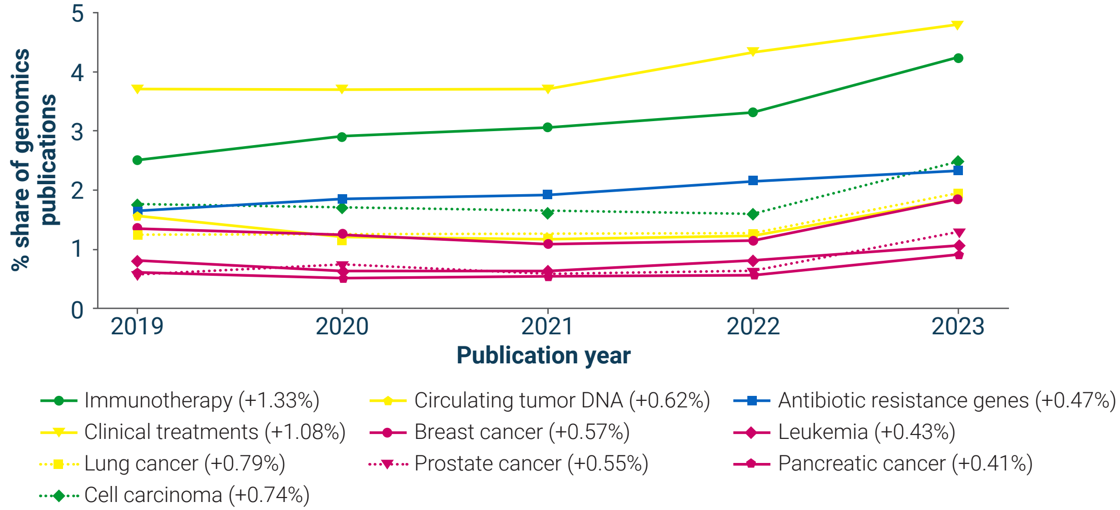
Source: RAND Europe analysis.

Research on disease-specific and treatment-related topics are increasing most rapidly in terms of relative global output

When comparing the relative share of publications in genomics across the 50 topics shown in Figure 6, the largest increases are in immunotherapy (+1.3%), clinical treatments (+1.1%) and lung cancer (+0.8%). Of the top ten topics (ranked by increase in share between 2020 and 2023), nine are related to cancer treatment, except for antibiotic resistance genes. Figure 7 shows the relative volume of publications for the ten topics with the highest growth between 2020 and 2023. The colours match those used in the topic map (Figure 6) to facilitate cross reference.

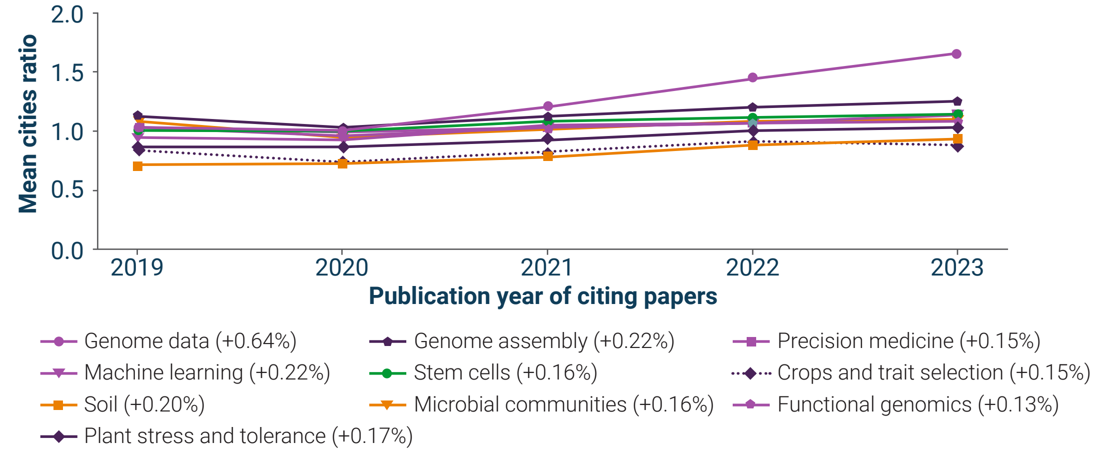
Topics can be compared over the same period according to variation in citation rate, giving insights into relative changes in attention (i.e. papers cited) and an indication of which topics are underpinning the most recent genomics research. The highest ranked topics according to change in the average number of publication citations per year are genomics data (relative increase of +0.64 between 2020 and 2023), machine learning (+0.22) and genome assembly (+0.22) (Figure 8). This substantial increase reveals the growing use of genomics data, particularly in the application of AI and ML.

Figure 7. Top ten fastest growing genomics topics (relative publication share 2019–23)



Source: RAND Europe analysis.

Figure 8. Top ten fastest growing genomics topics (mean cites ratio 2019–23)



Source: RAND Europe analysis.

The United States and China are the largest contributors to research in genomics (46% of global output), with European countries producing research with the highest citation impact

In terms of the relative share of genomics publications, the leading nations are the United States (31.8%), China (17.0%), the United Kingdom (8.1%), Germany (5.8%) and France (4.4%). The map shown in Figure 9 a typical global spread of research concentrated in high-income countries, with the notable exceptions of China, India, Brazil and Russia. In South America, Brazil produces the most genomics research (2.3% of global genomics publications) – more than the combined output of all other South American countries. In Africa, no country produces more than 1% of global output and only ten produce more than 0.1%: South Africa (0.8%), Egypt (0.5%), Nigeria (0.3%), Kenya (0.3%), Ethiopia (0.2%), Ghana (0.1%), Morocco (0.1%), Tanzania (0.1%), Tunisia (0.1%), and Uganda (0.1%). In Asia, only four countries produce more than 1% of global output (China, India, Japan and Korea), and seven produce more than 0.5% (Israel, Singapore, Iran, Taiwan, Saudi Arabia, Turkey and Pakistan). A full table containing all indicators relating to publications, patents, funding acknowledgements, commercial companies and grey literature publications can be found in Annex C.

Citation impact, as measured by mean citation percentile, is highest in European nations (see column mean citation percentile in Table 2). The top five countries producing at least 1% of global output are Denmark (76.7), Sweden (76.4), Belgium (76.2), the Netherlands (75.8) and Germany (75.0). This reveals a notable difference in the citation impact achieved by some European countries when compared to other parts of the world, except Australia, which performs at a similar level.

Although research volume and citation performance are useful indicators when benchmarking national publication output, it is also valuable to examine the relative focus of outputs with respect to overall national output (see column % of national publication output in Table 2) For genomics, the top five countries are Denmark (1.7%), Sweden (1.5%), Australia (1.4%), Finland (1.4%), and Switzerland (1.3%). Norway is also ranked highly by this measure (1.2%), revealing a strong focus in Nordic countries.

In terms of funding investment, national comparisons are difficult as global data on grants awarded does not adequately cover many of the countries profiled. However, it is possible to examine the funders acknowledged in publications to understand the relative investments by different countries. According to figures from the Web of Science (representing 76.5% of indexed articles), the highest relative share is for funders in the United States (55.8%), China (41.1%), the United Kingdom (12.0%), Japan (7.5%) and Canada (5.2%).

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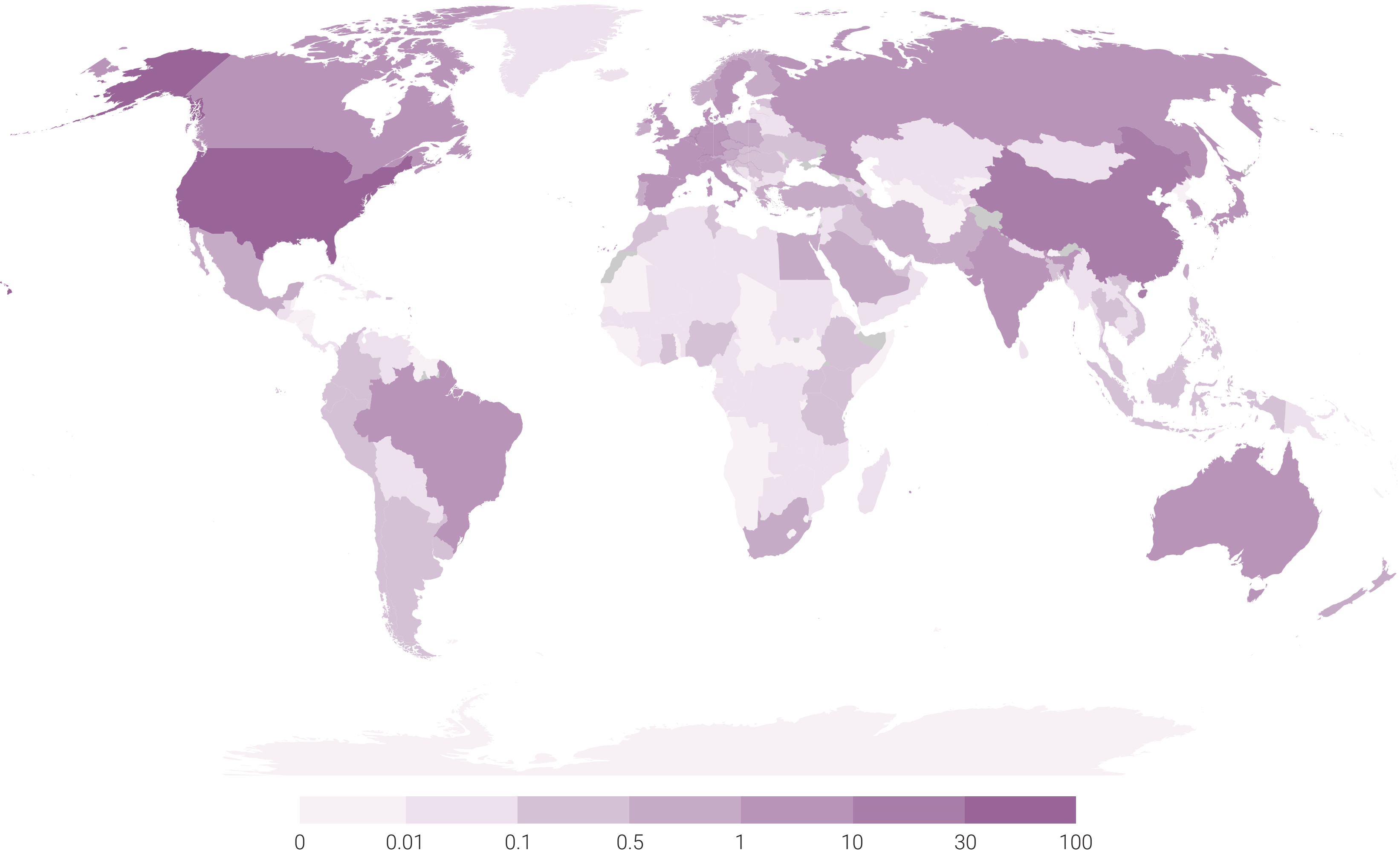
Figure 9. Global map showing the share of genomics publications by author country



Source: RAND Europe analysis.

Table 2. Publication metrics for countries producing more than 1% of global output in genomics research

Continent	Country	% of global genomics publications	% of national publication output	Mean citation percentile
Asia	China	17.0	0.9	73.4
Asia	India	4.2	0.7	67.9
Asia	Japan	3.5	0.9	71.5
Asia	Korea	2.0	0.9	73.7
Europe	Belgium	1.2	1.1	76.2
Europe	Denmark	1.5	1.7	76.7
Europe	Finland	0.8	1.4	71.4
Europe	France	4.4	1.0	73.4
Europe	Germany	5.8	1.0	75.0
Europe	Italy	3.8	1.1	74.8
Europe	Netherlands	2.4	1.3	75.8
Europe	Norway	0.9	1.2	75.4
Europe	Russia	1.3	0.4	69.7
Europe	Spain	3.4	1.1	74.2
Europe	Sweden	1.8	1.5	76.4
Europe	Switzerland	2.0	1.3	74.9
Europe	United Kingdom	8.1	1.3	73.2
North America	Canada	4.2	1.3	72.8
North America	United States	31.8	1.3	70.2
Oceania	Australia	4.0	1.4	74.6
South America	Brazil	2.3	0.6	73.0

Source: RAND Europe analysis.

Genomics research is mostly conducted through collaboration between researchers across multiple locations

A great deal of published academic literature does not originate from a single country, but from collaboration between researchers across multiple locations. This aspect of research is important to consider in any scientometric analysis as collaboration can increase opportunities for researchers, especially in the understanding of how research applies to those in different economies. Although 62% of the global output relating to genomics is produced by high-income countries, insights can be gained by measuring how much they collaborate with different income groups.

For each publication in the study dataset, collaborations were determined by examining the countries listed in author affiliations. When more than one country is listed (i.e. there is collaboration), the collaborator income group is determined based on the World Bank classification (World Bank 2024a). This data is summarised in Figure 10, where two plots are shown (based on countries producing more

Figure 10. Rates of genomics research collaboration with upper and lower middle-income countries

Source: RAND Europe analysis.

than 0.5% of global publications): on the left, the top 15 countries are ranked by the number of papers produced with collaborators from upper middle-income countries, and on the right they are ranked by the amount of papers produced with lower middle-income countries. It is apparent from the distribution that many countries have similar collaboration rates of around 20% with upper middle-income countries and around 10% with lower middle-income countries. However, some collaboration rates are notably higher: for collaboration with upper middle-income countries, rates in Pakistan (36.9%), Singapore (26.5%) and Denmark (25.3%) are highest, and for collaboration with lower middle-income countries, rates in Saudi Arabia (41.8%), South Africa (18.8%), Egypt (15.9%), Pakistan (14.9%), and Turkey (14.0%) are highest.

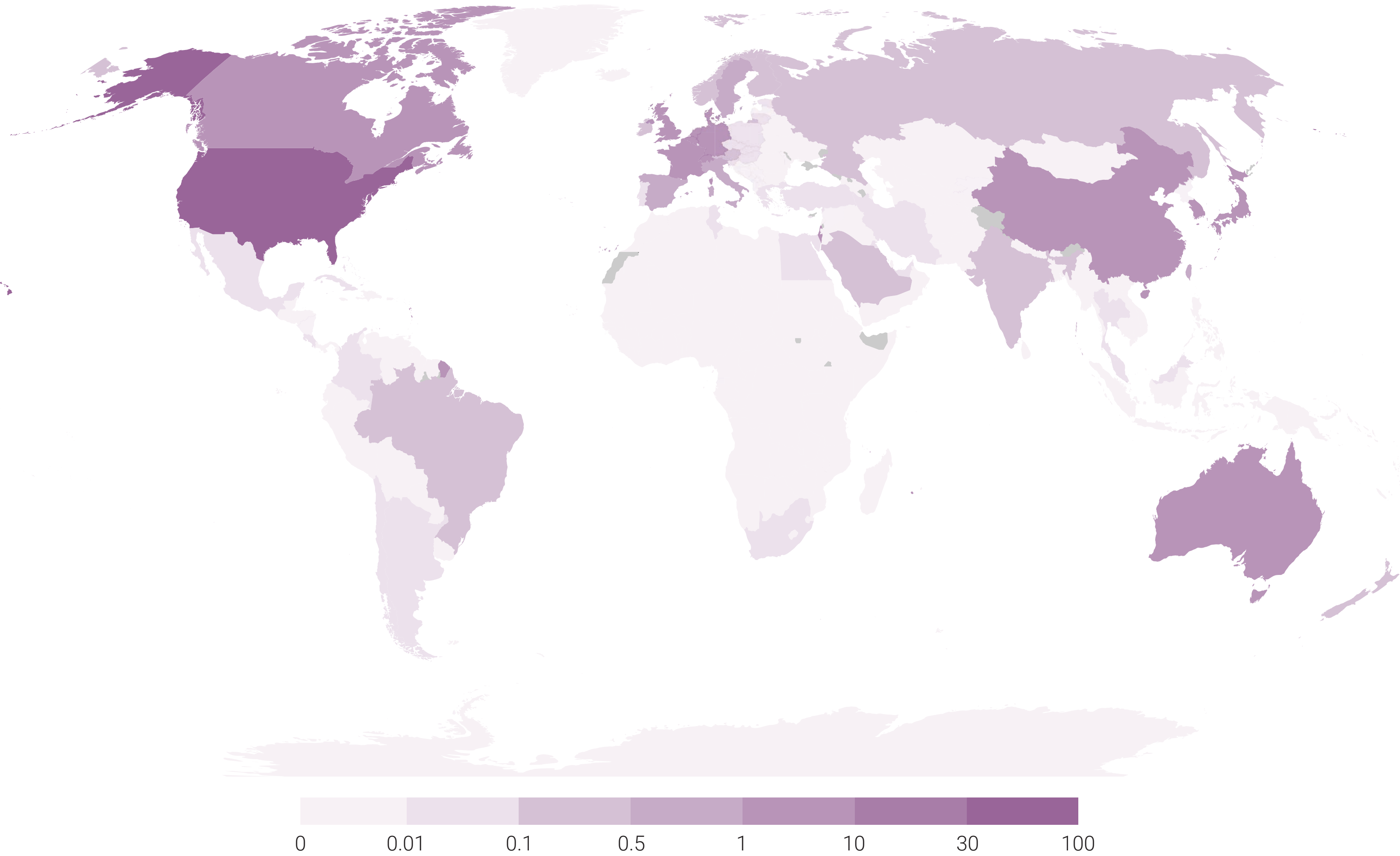
Evidence of commercial applications of genomics is greatest in the United States, the United Kingdom, China, India and Canada

Two data sources are used to shed light on the amount of commercial activity in each study area: patent activity (patents granted after 1 January 2019 according to lens.org) and the number of registered companies (according to Crunchbase). The map in Figure 11 shows the relative share of extended patent families[20] granted to each country. As with the distribution of publications (Figure 9), activity is mostly found in high-income countries – of the top 20 countries (ranked by volume), only China is not classified as high income. When ranked by share of global patents granted, the top five countries are the United States (65.9%), Germany (4.4%), Japan (3.8%), Switzerland (3.3%), the United Kingdom (3.2%) and China (3.1%).
In South America, only Brazil (0.15%) produced more than 0.1% of global patents, approximately the same as Argentina and Chile combined. There is very little patent activity in Africa, only South Africa (0.1%) was granted more than ten patents in the study period. In Asia, four countries own more than 1% of global patents: Japan (3.8%), China (3.1%), Korea (2.4%) and Israel (1.2%), with another five owning more than 0.1%: Taiwan (0.7%), Singapore (0.5%), India (0.4%), Hong Kong (0.2%) and Saudi Arabia (0.2%).

The top five countries in terms of the number of genomics-related companies registered are the United States (1,256), the United Kingdom (164), China (142), India (83) and Canada (76), strongly reflecting the distribution seen in patents granted. Table 3 provides summary indicators for patents and companies registered for countries with more than 0.5% of global patents. As with the publication analysis, it is useful to examine the relative percentage of a nation's patenting activity to highlight countries with the largest proportion of patenting output. By this metric (column % of national patents in Table 3), Denmark has the highest focus, with 6.1% of national patents in genomics, a trend similar to that observed in number of publications, where Denmark was also the highest.

20 Individual patents are often grouped into families when they relate to the same technology or invention but have been filed separately, for example to cover different jurisdictions or ownerships.

Figure 11. Global map showing the share of genomics patents by applicant country



Source: RAND Europe analysis.

Table 3. Commercialisation indicators for countries registering more than 0.5% of global patents on genomics research

Continent	Country	% of global genomics patents	% of national patents	Crunchbase companies
Asia	China	3.1	0.8	142
Asia	Israel	1.2	3.5	34
Asia	Japan	3.8	0.4	50
Asia	Korea	2.4	0.3	40
Asia	Singapore	0.5	1.8	26
Asia	Taiwan	0.7	0.3	15
Europe	Belgium	1.3	4.3	10
Europe	Denmark	1.7	6.1	20
Europe	France	2.7	1.1	59
Europe	Germany	4.4	0.8	58
Europe	Italy	0.8	1.1	27
Europe	Netherlands	2.0	1.9	24
Europe	Spain	0.7	2.5	46
Europe	Sweden	0.7	0.9	19
Europe	Switzerland	3.3	2.9	32
Europe	United Kingdom	3.2	2.4	164
North America	Canada	1.9	2.3	76
North America	United States	65.9	3.3	1,256
Oceania	Australia	1.1	3.8	24

Source: RAND Europe analysis.

Policy documents published relating to genomics are mainly from the United States, the United Kingdom, IGOs, the EU and Australia

To measure the amount of activity recorded in the grey literature (i.e. published reports, white papers, guidelines), Overton was searched for documents relating to genomics. Overton indexes publications by government departments, IGOs, think tanks and charities, and can be used to measure attention from policymakers. Although Overton links publications to the country of origin, a significant proportion of the database is not attributed to a single country but to IGOs (e.g. United Nations, World Health Organization, World Bank) or EU institutions.

Table 4 provides policy document indicators for the top 15 countries (ranked by document count), along with IGOs and the EU. The top five producers of policy documents on genomics are the United States (26.6% of global output), the United Kingdom (16.8%), IGOs (12.5%), the EU (11.1%) and Australia (5.0%). Ireland (1.2%) and the United Kingdom (1.1%) have the highest percentage of genomics policy documents with respect to all national policy documents.

Table 4. Genomics policy document indicators for the top 15 countries (ranked by document count)

Continent	Country	Policy document count	% of global genomics policy documents	% of national policy documents
North America	United States	5,731	26.6	0.4
Europe	United Kingdom	3,611	16.8	1.1
Global	IGO	2,682	12.5	0.8
Europe	EU	2,398	11.1	1.3
Oceania	Australia	1,071	5.0	0.9
Europe	France	741	3.4	0.8
North America	Canada	618	2.9	0.5
Europe	Spain	539	2.5	0.2
Asia	Japan	383	1.8	0.2
Europe	Italy	373	1.7	0.8
Europe	Ireland	363	1.7	1.2
Europe	Germany	293	1.4	0.2
Europe	Belgium	293	1.4	0.9
Europe	Netherlands	270	1.3	0.3
Europe	Sweden	190	0.9	0.1
North America	Mexico	165	0.8	0.5
Oceania	New Zealand	160	0.7	0.9

Source: RAND Europe analysis.

Governments across the globe are increasingly investing in engineering biology research and innovation

A growing number of countries are investing heavily in engineering biology and its applications in biomanufacturing and the development of novel bio-products as they recognise the potential of this technology across diverse sectors. The United States, the United Kingdom, China, Europe (notably Denmark, France and Germany), Israel, Japan and Singapore are leading the field (The White House 2022; UK Government 2023e; Dorfan et al. 2023; Ong 2018; Innovate UK 2018; Zhang, Xu et al. 2022).

At a high-level summit on biotechnology and biomanufacturing in September 2022, the US federal government announced more than $2 billion of new funding to kickstart President Biden's National Biotechnology and Biomanufacturing Initiative. The funding is intended to be spent on policies including: biotechnologies in diverse supply chains, domestic biomanufacturing, bringing bio-products to markets, strengthening biotechnology talent, regulatory innovation to make biotechnology products more accessible, measurements and standards for the bioeconomy, reducing risks via investing in biosecurity innovations, and supporting data infrastructure to make it easier to share data that advance the bioeconomy (The White House 2022).

In December 2023, the UK government announced an extra £2 billion for engineering biology over the next ten years. This funding builds on the £100 million invested through the UK Research and Innovation's (UKRI) Synthetic Biology for Growth programme, as well as the £73 million invested in a network of Engineering Biology Missions Hubs and Mission Awards to build the UK's reputation as a hub of innovation in the field. All these investments are anticipated to help strengthen the existing engineering biology clusters located across the country (UK Government 2023e).

Israel and Singapore have also increased their state support for engineering biology through financial investment and strategic leadership. This is reflected in the growing number of engineering biology firms located in Israel and Singapore, creating more competition for firms in China, the EU and the United States. The government of Israel, particularly the Israeli Innovation Authority and Department of Defence, started supporting the growing field of synthetic biology because of its potential benefits for the economy and defence. Notably, in 2020 the Israeli Innovation Authority launched a large-scale funding programme totalling $3.9 million to support the commercialisation of bioconvergence research and development – a new multidisciplinary field that combines biology, AI and genetic engineering to address health challenges (Solomon, Shoshanna 2020). Israeli state support for engineering biology builds on decades-long research strengths in Israeli academia and industry (Dorfan et al. 2023).

The government of Singapore has also increased support for synthetic/engineering biology over the last decade. A task force set up by the government in 2012 noted the commercial potential of engineering biology and its links with the country's research capabilities in biomedicine. In January 2018 a five-year Synthetic Biology Research and Development Programme was launched that will disburse 25 million Singapore dollars (approx. US$19 million) in grants to research projects via the National Research Foundation Singapore, with three areas prioritised: 1) the development of synthetic cannabinoids; 2) production of rare fatty acids that can be used in pharmaceuticals; and 3) the development of new strains of micro-organisms that can be used to make products for industry (Ong 2018; Innovate UK 2018). In addition, the Synthetic Biology for Clinical

& Technological Innovation (SynCTI) programme at the National University of Singapore (NUS) hosts the Singapore Biofoundry, an integrated facility to make the 'Design–Build–Test–Learn' cycle more efficient by using the latest automation techniques. The Singapore Biofoundry also cofounded the Global Biofoundry Alliance in 2019, a global initiative to develop the sustainable bioeconomy globally (NUS news 2019; Biotech Connection Singapore 2020).

In February 2023, India launched a new biomanufacturing and biofoundry funded by the national government. This facility will be oriented towards sustainability and green growth by producing biodegradable polymers, biopharmaceuticals and agricultural inputs. It aims to help the country become one of the top five countries globally for global biomanufacturing hubs by 2025, building on and boosting its booming national bioeconomy sector, which grew from US$10 billion in 2014 to US$80 billion in 2024 (Thaker 2024).

There is a critical mass of engineering biology companies emerging worldwide, including in the United States, the United Kingdom and India, collectively valued at several billion US dollars. These represent immense potential for engineered biomanufacturing (Meng and Ellis 2020).

Cheaper genome sequencing is making the technology and its outputs more accessible

Technological progress has made whole genome sequencing (WGS) much faster and cheaper, which means that the technology and its outputs are more accessible to scientists, researchers and the general public. The cost has fallen by six times from just under $100 million in 2001 to $525 in 2022 (current US dollar prices) (Roser et al 2023). Another source reports that the cost of WGS was as low as $300 in 2020 (The IQVIA Institute 2020). It is possible to buy 'do-it-yourself' WGS kits online for less than $200 (The ODIN n.d.).

Making WGS so much cheaper and faster has implications for healthcare, disease detection and treatments. For example, NHS England now offers WGS as a specific service (UK Government 2022a).

Bioconvergence in engineering biology has yielded benefits across various sectors

Engineering biology has existed as a research topic for nearly 25 years, with significant research papers contributing to new techniques and ways of working (Meng and Ellis 2020). However, by 2010 some criticisms had begun to emerge about stalled progress in technological developments, as highlighted in a seminal article that linked slow progress with not meeting the promised reliability, standardisation and automated design celebrated as the benefits of the field (Kwok 2010). Between 2010 and 2020, more technical work was undertaken to focus on the design elements of engineering biology (for instance leading to the breakthrough of Cello, an end-to-end computer-aided design system for logic circuit construction in the group of bacteria called 'E. coli') and to bring together developments such as CRISPR-Cas9-based gene editing and high-throughput screening (Kwok 2010).

Bioconvergence, which refers to the interface of biotechnology, software and engineering, has shown the potential of the field in diverse areas of societal and global importance, including health and medicine, environmental biotechnology (climate change, bioremediation), food and agriculture, energy, industrial biotechnology (e.g. materials, chemicals), and national security (RHC 2022; Sheets et al. 2023), as further highlighted in the sections below.

5.3. What are the opportunities in engineering biology?

Precision health research has particularly flourished due to engineering biology breakthroughs

Advancements in engineering biology have had a profound impact across multiple sectors, with developments in one sector also having potential to be transferable to others. For example, researchers at the UK's Laboratory of Molecular Biology in Cambridge recently made a pioneering breakthrough: they were able to genetically engineer microbes (bacterial cells) into 'miniature factories' that can synthesise new substances (Dunkelmann et al. 2024). The researchers forecast many commercial applications from this new technique that can be used for drugs, household plastics and antibiotics, and the Medical Research Council has filed a patent application in anticipation (Peel and Cookson 2024).

New technological developments can also have impacts in healthcare, specifically in how cancers are detected, monitored and treated. Researchers at Johns Hopkins University in the United States have used an ML technique called Artemis to study repeats of genetic code sequences ('junk DNA'[21] or dark matter), which had never been examined before. This new knowledge is significant because it leads to better understanding of how cancerous tumours develop, and is expected to lead to new cancer treatments and screening techniques (Peel and Cookson 2024). Personalised and precision medicine and 3D bioprinting are other areas where applications of engineering biology have immense potential. Engineering personalised medicine technologies include wearable devices to analyse sweat or blood, and diagnostics to detect circulating tumour cells. Novel engineering precision medicine technologies include genome-guided medicine (e.g. pharmacogenomics) and devices such as single cell/biopsy analysis (Ho et al. 2020).

The role of non-commercial biofoundries increased during the Covid-19 pandemic as they were used to address bottlenecks in testing capability (Crone et al. 2020). In the last decade, various countries, including the United States, the United Kingdom, China, Singapore, Australia and India, have established biofoundries to boost their capabilities in biotechnology. The aim of biofoundries is to 'accelerate and enhance both academic and translational research in engineering biology by promoting and enabling the beneficial use of automation and high-throughput equipment including process scale-up, computer-aided design software, and other new workflows and tools' (Hillson et al. 2019). The Global Biofoundry Alliance (GBA), formed in 2019, brings together 15 non-commercial biofoundries to exchange knowledge and experience and share resources. The GBA is well-placed to expand cooperation between its members to address global challenges such as those covered in the United Nations' Sustainable Development Goals.

21 'Junk DNA' is a term historically used to describe regions of the genome that do not code for proteins and were thought to have no functional significance.

Engineering biology tools have unlocked future opportunities for climate change mitigation and adaptation

The Engineering Biology Research Consortium, a US-based, non-profit public–private partnership, published its fifth technical roadmap in September 2022, highlighting engineering biology technologies and capabilities that have potential to help the world reduce greenhouse gases, decrease and remove pollution, and increase biodiversity and the conservation of ecosystems. Some of these developments and opportunities include the ability to engineer microbes, plants and algae to sequester and store carbon in soils and other long-term carbon sinks, and to engineer microbes to sequester and degrade problematic pollutants such as plastic waste. Genetically engineering key marine and freshwater species so that they become more resistant to environmental stressors is another example of how the technology could help marine and coastal ecosystems adapt to rising ocean water temperatures and acidification. To help forests grow back after wildfires, which have become more intense and frequent with global warming, scientists could engineer fungi, microbes and microbial communities that are tolerant to heat-stress and drought (EBRC 2022). To protect fragile coral reef ecosystems, a group of researchers have engineered symbiotic microbes that can colonise coral to facilitate reactive oxygen species scavenging, which should help corals tolerate higher heat and lower pH levels (Quigley et al. 2021). The roadmap also identifies more sustainable solutions in the food and agriculture sector, materials and industrial processes, and transportation and energy sectors. (Aurand et al. 2024; EBRC 2022).

Engineering biology could be a core enabler of food security and sustainability

Recent developments in engineering biology have the potential to address global food insecurity, nutrition and health problems and help countries worldwide adapt to climate change. For example, it is possible to engineer crops that are tolerant of high temperatures by intervening in the protein metabolism of plants to minimise the accumulation of damaged proteins (Singh and Grover 2008). This is a significant development as average temperatures are rising in many parts of the world due to global warming. In plant genomics, drought- and disease-resistant crops have been developed that do not need to be sprayed with highly carbon-intensive pesticides, as can be seen in the work undertaken at the Roslin Institute, University of Edinburgh (UK Parliament 2023).

The UK's Advanced Research and Invention Agency (ARIA)[22] is investigating programmable plants. These are technology platforms focused on plants that aim to find solutions for the world's most pressing problems such as food insecurity, climate change and environmental degradation (ARIA 2024).

22 ARIA was formally set up as a non-departmental body under the sponsorship of the Department for Science, Innovation and Technology in January 2023. Like its US equivalent the Defense Advanced Research Projects Agency (DARPA) – upon which it is modelled – its mandate is to fund high-risk and high-reward research. It has the organisational autonomy from the UKRI to disburse its own funding in the form of rapid 'seed' funding, large grants and bonuses to achieve research goals.

5.4. What are the challenges associated with engineering biology?

Dual-use engineering biology developments can have biosecurity threats

As with organoids (see Chapter 6), engineering biology developments can potentially have dual-use applications, including the development of bioweapons. Various governments and weapons proliferation watchdogs have been warning of likely bioweapon attacks by nefarious actors for several years, citing engineering biology developments that can create lethal bacteria, viruses, bacteria or other germs that can be released in targeted ways (Delcker 2018; Pilkington and Oladipo 2022). Advances in synthetic biology and biotechnology mean that it is now possible to engineer pathogens such as those causing smallpox and the plague in a laboratory (Nelson 2019). If leaked by accident or on purpose, such pathogens could cause a pandemic. DNA-based surveillance is another biosecurity threat posed by engineering biology technologies, with commercial DNA databases at risk of becoming the next frontier of 'surveillance capitalism' (Engineering and Technology 2021). In a report published in November 2023, the Engineering Biology Research Consortium (EBRC) highlighted de novo biological design[23] as one of the three technological areas that need to be monitored due to potential security threats if used by actors with malicious intents, along with closed-loop autonomous labs[24] and large language models.[25] The report also noted that it is hard to assess how much of a risk these technologies pose and difficult to reach agreement on ways to stop or mitigate the risks (Johnson et al. 2023).

Lack of diversity in genomic datasets can hamper progress in precision research

Many global genomics datasets are not representative of African and Asian genetic diversity due to the lack of inclusion of these communities in research and the communities' lack of trust in enrolling in research (Fatumo et al. 2022). This is a challenge for engineering biology because if the genomic datasets that engineering biology tools and techniques rely on do not incorporate the world's genetic diversity, then engineering technology-based treatments and drug screening will not be relevant to people with diverse genetic makeups, causing significant inequalities in health access and treatments (Koch 2024). Several efforts are attempting to address this issue and better reflect the world's populations in genetic datasets. For instance, a recent study funded by the Wellcome Sanger Institute, and others, is aiming to develop quantum computing algorithms to speed up the production and analysis of pangenomes[26] and build a more diverse reference dataset.

23 De novo biological design refers to the process of creating novel biological systems, molecules or organisms from scratch.
24 Closed-loop autonomous labs are advanced laboratory systems that integrate automation, robotics, artificial intelligence and data analytics.
25 Large language models are artificial intelligence models that are trained on vast amounts of text data to understand and generate human language.
26 Pangenomes are representations of DNA sequences that capture population diversity.

Sceptical public attitudes towards engineering biology can be a barrier to widespread adoption

Two reports published in January 2024 by the British Science Association in its role as member of the Sciencewise consortium (a public dialogue programme delivered by UKRI) note that members of the public are more likely to be upbeat about the potential of engineering biology in solving global and relevant challenges when they have more knowledge and awareness about engineering biology, as well as more trust in science overall. However, people in the United Kingdom are concerned about engineering biology and its safety, inequitable access (especially in health applications), misuse, and blurring the boundary between natural and artificial. Moreover, sceptical attitudes towards genetically modified foods in the past may make government, research and civil society stakeholders think that people will similarly be mistrustful of newer biotechnologies (Sciencewise 2024). In Africa, a 2021 survey of seven countries conducted by the forum SynBio Africa found that while popular perceptions of synthetic biology were generally positive, members of the public expressed concern that synthetic biology could be exploited for harmful actions such as bioweapon production (Otim et al. 2023).

Scaling and translation are seen as significant bottlenecks for utilising engineering biology outputs

As a mature field that emerged 20 years ago, engineering biology now faces new challenges. The successes it has spawned over the last two decades have led to innovations in bioeconomy and biotechnology. Today, engineering biology must find new ways to scale past successes and translate the accumulated research strengths and capabilities and emerging applications into economic and societal impacts. For example, tools to automate the design–build–test–learn (DBTL) cycle are already operational in biofoundries and big companies. In addition, there are repositories of characterised parts, which together with computer-aided design (CAD) tools help select parts and design genetic constructs. Going forward, the challenge will be to link up such tools into flexible and efficient pipelines so that engineering biology solutions can be found more quickly (Gallup et al. 2021).

Scaling challenges are also evident in designing whole-cell simulations. Early research to understand the behaviour of genes and proteins in the bacterium *Mycoplasma genitalium*, which has a relatively small genome of only around 500 genes, enabled researchers to come up with a way to integrate these models into a dynamic simulation of a cell cycle. The challenge now is to scale this work by using the large amounts of omics[27] data available online to carry out whole-cell simulations as a design tool for commonly engineered model organisms such as Baker's yeast or human cell lines. Scientists are close to developing a whole-cell simulation of the group of bacteria called E. coli. Such simulations can build on the tools of genome-scale metabolic modelling, which are now

27 Omics refers to the totality of specific factors within a cell, tissue or organism and primarily refer to genomics, transcriptomics, proteomics and metabolomics.

regularly used to advance biosynthesis cell engineering projects in many microbial systems. The potential of whole-cell simulations lies in the scope for the approach to be applied beyond metabolic engineering projects and in more complex synthetic biology projects such as applications of logic circuits (Gallup et al. 2021).

The role of governments will be critical to overcome the hurdles of scale and translation. Examples of policies that could address these challenges include speeding up the commercialisation of research, nurturing start-ups with most potential to grow, and increasing the trust and confidence in engineering biology technologies among businesses, investors and consumers (UK Government 2023c).

The role of biofoundries and big companies in achieving scale and translation is also significant. The most rapid work to address the challenges of scaling is being undertaken in around 12 biofoundries and well-resourced companies (e.g. Ginkgo Bioworks, a leading horizontal platform company, and Microsoft's Station B) that have the financial resources and integration infrastructure for automation work using high-throughput equipment. Some biofoundries and companies are acting as 'cloud labs', offering their skills and software to partners and researchers who lack synthetic biology capabilities to speed up the iterative DBTL cycle and reduce development times (Gallup et al. 2021; Hillson et al. 2019).

5.5. What are some of the key developments associated with the intersection of AI/data platforms and engineering biology?

AI has unlocked a multitude of capabilities in engineering biology research

A recent global study highlighted the vast range of capabilities and tools that have emerged at the intersection of AI and gene editing, ranging from protein structure prediction to the processing of large datasets to generate links between the genome and phenome (Zakaria et al. 2023).[28]

The UK-based Ada Lovelace Institute project, DNA.I, has demonstrated notable growth in research and private investment in AI-genomics, in particular around 'data collection, drug discovery and precision medicine' (Farmer 2023). In particular, AI offers considerable benefits to address the challenges often faced in genomics research, including automation of collection and processing of phenotypic data, increasing efficiency of analysis through genomic data modelling, and rapid and facile pattern identification (Farmer 2023).

Deep-learning techniques in ML have driven significant progress in analysing the outputs of WGS, providing a way to process large volumes of complex data in a non-labour-intensive way (Lin and Ngiam 2023; Alharbi and Rashid 2022). These advancements are being used in genome-wide association studies (GWAS) to aid the detection and identification of disease variants and disorders, the prediction of disease progression, and diagnosis and treatment (NIH 2022). Given the developments mentioned above, AI is a valuable tool

28 The phenome refers to the full set of phenotypes (observable characteristics) across the whole genome, i.e. a person's physical attributes.

for enabling disease detection through the identification of specific biomarkers in genomic data, leading to early diagnosis, treatment and prognosis, as well as further study of at-risk populations (Vilhekar and Rawekar 2024).

Recently, AI has also been used to enhance engineering biology, coupling AI/ML algorithms and robotics to digitise and automate the sector. AI-enabled engineering biology (AI-EB) uses AI in the prediction of biological systems, automated research and analysis (Holland et al. 2024; NIH 2022). Specific examples of where AI-EB has been used are in metabolic engineering (Lawson et al. 2021) and genome editing, where AI has helped CRISPR-Cas9 to correct mutated gene sequences or identify targets for gene editing (Dixit et al. 2024). The research is still in a very early phase, and Frontiers is currently accepting journal article submissions on the research topic of 'Artificial Intelligence for Metabolic Engineering' (Frontiers 2024).

AI tools have opened up new avenues of research, such as the study of biological systems and demographics

AI can be used to study the interaction of genomics with the wider biological ecosystem. Also known as multi-omics, functional genomics describes where genomics interact with the wider biological environment including proteins and metabolites to determine how a particular phenotype is produced (Caudai et al. 2021). Multi-view learning has been applied to this research, analysing and combining multiple data sources and types to get a general picture of functional genomics (Wang et al. 2024; Lin and Ngiam 2023). Studies of at-risk populations using AI-enabled genomics is an opportunity to implement preventative measures and ensure targeted treatment (Vilhekar and Rawekar 2024).

Conventional techniques used in AI-genomics research include employing DNN, ML and Natural Language Processing (NLP) to diagnose and treat diseases (Guo et al. 2023). Research has already extended to transfer learning[29] to improve disease prediction and early detection through the processing of large, complex datasets (Theodoris et al. 2023; Saad Alatrany et al. 2023; Lin and Ngiam 2023). Technical developments in this sector can pave the way for learning in other areas of biotechnology, including AI-driven organoid research, gene editing with CRISPR-Cas9 and the use of new AI tools to enhance data analysis while safeguarding privacy (Dixit et al. 2024).

Progress is hampered by a lack of access to genomic data, impacting training algorithms and producing biased results

Genomics research is still limited by data sharing, the reliability of open-source data and explainability due to issues with dataset variance (Caudai et al. 2021). Reliable and diverse datasets are necessary when training AI algorithms to avoid bias and ensure that the analysis is reproducible. The general lack of transparent AI tools also poses risks to reproducible and interpretable data and analysis (Farmer 2023).

29 Transfer learning is defined as 'a technique of training a deep learning model on a large dataset and then using the pre-trained model to perform similar tasks that may be in a different domain on another dataset' (Lin and Ngiam 2023).

AI-enabled developments in engineering biology pose a national security concern

AI can lower the technical and knowledge barrier relating to genomics research, and inform the public about materials and targets, as well as synthesis methods (Moon and Ghionis 2024). As a result, access to technologies such as ChatGPT are enabling the public to engage with information on the misuse of biological research, such as engineering suitable viruses that could lead to pandemics (Matthews 2023). Although previous RAND research has shown this information is limited, and step-by-step instructions are not provided to the user (Mouton et al. 2023), without proper oversight this open-access format could lead to unintended consequences (Egan and Rosenbach 2023; Kuilken 2023).

Key developments in AI algorithms applied in genomics could serve as a leading example for other technologies

FL is an emerging area with the potential to balance privacy and data concerns with progress in research. As noted in Chapter 4, FL is a decentralised machine learning technique where multiple devices collaboratively train a shared model by keeping the data localised and without exchanging raw data (Khan et al. 2023). Some of the features of FL such as decentralised training and scalability provide a possible solution to cybersecurity and privacy challenges, which are particular risks in the biotechnology sector (OECD 2023). Homomorphic encryption is a form of encryption that allows computations to be performed on encrypted data without needing to decrypt it first, meaning that data can remain secure and private while still being processed (Sarkar 2023). For this reason it is noted to be a particularly useful method to encrypt genomic data (Ogburn et al. 2013), with datasets able to be encrypted at-source, prior to collection and compilation from different sources. Data privacy can alternatively be maintained through secure multi-party computation, where individual parties perform computation on their own datasets to avoid data sharing (Williamson and Prybutok 2024). The United Kingdom revealed intentions to implement a FL infrastructure to manage genomics data through Genome UK and the Genome Strategy (UK Government 2022b). This has culminated in a Genomics England Trusted Research Environment (TRE) that can engage with other organisational TREs to facilitate the use of FL models, as exemplified in the case of Cambridge Biomedical Research Centre.

A key debate at the nexus of AI and engineering biology tools is whether access to biological data for training should be restricted

Data misuse and uncontrolled access to DNA sequences could amplify risks to biosafety and security. A ‘structured access’ approach, where AI tools/data are restricted to specific users, could prevent users acquiring the tools themselves. Instead, the developer maintains control over modifications to and uses of the model (Kuilken 2023). This oversight approach could apply a universal oversight mechanism across all research and development stages in AI-powered biological tools development or may need to consider tools at different technology readiness levels on a case-by-case basis. For example, there are WHO guidelines specific to large multi-modal models (LMMs)[30] and that emphasise their use in genomics (WHO 2024b).

Multi-omics data generation is challenging current concepts of consent due to the potential for personal identification and data reuse

The pace of genetic research has grown rapidly in the past decade with the advent of key technologies that allow for faster data collection and, critically, for experiments to be run in parallel. The advent of high-throughput screening and whole genome/next generation sequencing, along with improved computational and methodological capabilities to integrate and map genomic data types, have led to the development of emerging areas of study within genomics, notably multi-omics (or omics), which integrates biological data from multiple sources including the genome, proteome, metabolome and epigenome (Hasin et al. 2017); and transcriptomics, which studies all RNA molecules within an organism (the transcriptome) (Liu et al. 2022).

The growing ease of genetic sequencing has also garnered significant commercial interest. The last decade has seen a proliferation of direct-to-consumer genetic testing tools that have further contributed to the abundance of genetic data, although the data generated from these tools is generally less accessible and often subject to less stringent governance due to control by private companies (Laestadius et al. 2017; Hendricks-Sturrup and Lu 2019). There is now a great deal of genomics and broader omics data, and while norms and values are generally still aligned to promote open science and data sharing, these are slowly shifting in response to a landscape that looks very different from when genetics research began.

As with other forms of health and personal data, omics data is personal and identifiable, warranting additional measures to protect privacy and maintain confidentiality and anonymity, particularly with respect to data sharing and linkage. There are also notable concerns over consent and data reuse (Johnson et al. 2020). Concerns specific to genomics data include the fact that in addition to being personally identifiable, such data are reasonably identifiable for blood relatives, widening the sphere of those with legitimate interest in genomics data governance beyond the individual and the researcher or clinician (Johnson et al. 2020). Establishing and maintaining anonymised and de-identified genomics data has become increasingly difficult in recent years due to advancements in genomics data analysis tools, including AI and ML integration, which have allowed for the synthesis of complex and increasingly diverse data sources. These forms of analysis now have sufficient pattern recognition capabilities to effectively re-identify information previously seen and governed as being de-identified (Rocher et al. 2019). As such, these advancements have posed significant challenges for data sharing and reuse, as well as complicating historical and future consent processes.

Consent has proven a challenge in genomics data collection, management and governance given many of the special features and capabilities of genomics data. As the broad sequencing of genomes has become more common, so too has the potential for incidental findings (Krier and Green 2013). Various consent processes have attempted to address preferences on notifications for incidental findings, but these mechanisms generally do not cover all possible

30 LMMs: The WHO uses this term interchangeably with 'general-purpose FMs' (foundation models). In the guidelines, LMMs are a broad category that include LLMs, but output data is not limited to the type of input data and can therefore, in theory, be used in multiple applications (WHO 2024b).

scenarios, creating ethical dilemmas over the reporting and sharing of findings. There are also notable challenges related to data reuse and authority overuse. With data sharing norms dominating the field there has been a strong push for data aggregation and reuse (Lorenzo et al. 2023). However, consent forms must adequately describe and provide information on the potential uses of data, providing challenges to obtaining appropriately informed consent in genomics. Several consent models have attempted to address this, including processes of re-consent, where consent is obtained for each subsequent use of the data, and broad consent processes, which cover many possibilities for future use (Fisher and Layman 2018; Goodman et al. 2016). However, these processes are generally insufficiently comprehensive to address all ethical concerns on consent, particularly given fuzzy boundaries around what is considered 'new use' and technological developments that cannot be foreseen under broad consent processes (Fredriksson 2021; Mc Cartney et al. 2022). Related to consent challenges are issues of extractive practices in the field, and concerns about the benefits of genetic discoveries being appropriately shared with the source of the information, whether that be a person, or in the case of plant and animal genetics, the place in which the information originated (Fredriksson 2021; Mc Cartney et al. 2022).

5.6. What are some of the developments associated with the oversight of engineering biology research and innovation?

There are a range of mechanisms across the globe that provide oversight for genomics and by extension for engineering biology research and its applications. These range from informal non-binding agreements such as international ethical guidelines on genome editing to nationally binding laws such as the UK's Genetic Technology Act. Latest advancements in the field are challenging many of the legacy frameworks of oversight. This section highlights a range of examples of oversight from across the globe and lays the foundations for a more comprehensive analysis on oversight mechanisms underpinning engineering biology research and use that can be found in the accompanying technology oversight report.

International recommendations have set the global stage for discussions on engineering biology powered genome editing

Two companion reports released on 12 July 2021 by the WHO contained the first global recommendations to help establish human genome editing as a tool for public health, with an emphasis on safety, effectiveness and ethics. One report focused on recommendations on the governance and oversight of human genome editing in nine discrete areas, including human genome editing registries; international research and medical travel; illegal, unregistered, unethical or unsafe research; intellectual property; and education, engagement and empowerment (WHO 2021a). The second WHO report draws on good practices in the governance of emerging technologies and applies them specifically to human genome editing. It offers recommendations on global, national, regional and governance mechanisms for human genome editing (WHO 2021b).

The Third International Summit on Human Genome Editing hosted in London in March 2023 was a high-level global forum for discussions about somatic and germline human genome editing convened by several national scientific academies. The key themes discussed included developments in clinical trials and genome editing tools such as CRISPR-Cas9, as well as the ethical, social and accessibility issues brought about by these scientific developments. It concluded that governance mechanisms for human genome editing must be put in place to safeguard legitimate research and ban individuals or health clinics from offering interventions that are not evidence based. The forum also advised that heritable human genome editing should be banned until it fulfils appropriate standards for safety and efficacy (The Royal Society 2023). Developments due to engineering biology were a feature of the debate on whether heritable editing may become viable sooner rather than later.

There are different schools of thought on whether to regulate the tools or their outputs

A group of scientists in the Global Observatory for Genome Editing have cautioned against setting up an international regulatory commission on human germline genome editing convened by scientific academies. Instead, they have called for a new global mechanism to enable active and ongoing reflections by scientists about their own work. This dialogue should happen with scholars from diverse disciplines and with representatives of the public who come from different social, political and religious backgrounds (Jasanoff et al. 2019). These efforts are focused on the tools and processes used in engineering biology and genome editing more largely.

A contrasting approach to oversight comes from the UK's Regulatory Horizons Council (RHC), an independent expert committee that recommends regulating the product rather than the second-generation of genetic technologies themselves (i.e. synthetic biology, engineering biology, genome editing) (RHC 2022). The RHC proposes that regulations should focus on the nature of the products ready for market and the associated benefits and risks, and should pay less attention to the technologies used to make these products. However, similar to the scientists from the Global Observatory for Genome Editing, the RHC also proposes that standards, guidelines, policy and technology initiatives should be used as alternatives to formal legislation as they take less time yet can still enable careful product development (RHC 2022).

Experimental approaches to the regulation of engineering biology, such as regulatory sandboxes, are emerging

The idea of regulatory sandboxes has been popular in different technology areas for several years and has recently been applied to engineering biology. A regulatory sandbox is a contained environment that enables the live testing of regulatory innovations, tools and mechanisms with interaction and supervision from regulatory bodies. An Engineering Biology Sandbox Fund was announced in early March 2024 in the United Kingdom. It is conceived as a 'safe' experimental place where the engineering biology industry and regulator will maintain dialogue to share information on which regulation(s) would be good, or not, when implementing an innovation (UK Government 2024d).

In Singapore there is a combination of civil society and legal approaches for the oversight of engineering biology (Bohua et al. 2023). Nigeria is also developing mechanisms specific to engineering biology following the development of the National Biosafety Management Agency (NBMA 2024).

Genomics data is increasingly considered a critical infrastructure

In a move away from the general approaches focused on open science seen in life sciences, some nations are taking a more protectionist approach to the governance of genomics and wider omics data. Notably, the United States recently classified omics data as a protected asset, thereby subjecting it to more stringent restrictions on sharing and increasing penalties for non-compliance (The White House 2024). The move was made in conjunction with efforts to protect privacy and secure national autonomy over other kinds of data, and was prompted by concerns about the improved capabilities of AI and other technologies to use these data sources as threats against individuals. The reclassification is largely targeted at preventing data sharing with 'countries of concern' given the potential for personal genomics and wider omics data to enable targeted attacks.

The government of India has recently set up a National Biodiversity Authority to regulate the use of biological resources and associated modern genetic engineering and synthetic biology tools. These efforts are also focused on the enabling aspects like data access and sharing and are active areas of oversight development and debate.

The African Union's Convention on Cybersecurity and Personal Data Protection specifies that any sharing of personal genetic data is authorised by national authorities and processed according to African Union guidelines (African Union 2014; WHO 2024b). Complementing the convention, the African Union's Digital Transformation Strategy further requires that African Union members 'have adequate regulation; particularly around data governance and digital platforms, to ensure that trust is preserved in the digitalization'.

The Nagoya Protocol, which came into force in 2014, is an interesting example of an international convention that seeks to address issues of data sovereignty related to genetic data, including issues related to consent, authority overuse and reuse, traditional knowledge, and equitable benefits sharing for non-human genetic material (Buck and Hamilton 2011). The Protocol has established consent procedures indicating that before genetic data can be taken across geographies, consent and appropriate agreement about benefits arising from the information, including monetary and non-monetary benefits, as well as intellectual property, must be made with individuals from the place of its origin (Buck and Hamilton 2011). There were proposals in in 2022 to extend the scope of the Protocol to include digital sequence information (DSI), which broadly includes the genomic sequence and related digital data (Klünker and Richter 2022). This proposition received mixed views in the scientific community. Those concerned about the inclusion of DSI in the Protocol generally believe that it will hinder data sharing and therefore scientific progress, noting the existing complexities of open data sources used in genomics and the consequent challenges of tracing use and appropriately sharing benefits (Watanabe 2019). However, others note that the opposite could occur and that inclusion of DSI could promote data sharing and facilitate research efforts through improving equitable collaboration processes and preventing exploitation, which are more likely to foster long-term collaboration (Ambler et al. 2021).

Multiple AI-genomics focused advisory boards and consortia are generating insights into non-legal mechanisms of oversight

One mechanism for responsible research include Ethical, Legal and Social Implications (ELSI) advisory boards, piloted by the Human Genome Project (Human Genome Project 2012). ELSI groups can advise on ethical and social issues to provide oversight (SPHN 2024). They comprise experts across bioethics, life sciences, law and social sciences, as well as representatives from medical councils and satellite groups. The convergence of experts across relevant disciplines has led to a number of reports that present policy recommendations and options on carrying out research.

Another example of group-led oversight is the UKRI Artificial Intelligence for Engineering Biology (AI-4-EB) Consortium in the United Kingdom, which aims to develop a strategy to address challenges arising from the convergence of the two technologies (Imperial 2024). A UK-based workshop brought experts together to discuss the role of AI in the 'design and implementation of biological systems' (IBioIC 2023). The United States has an equivalent organisation: the Engineering Biology Research Consortium (EBRC 2024).

Chapter 6
Global landscape review for organoids

This chapter presents the findings of the global landscape review for organoids based on desk research and a comprehensive scientometric analysis. It first provides some context and defines what is meant by organoids in this study. It then highlights the key trends, challenges and opportunities associated with global organoid research and innovation, with the final section reflecting on some of the oversight mechanisms associated with organoids (oversight mechanisms and their implications are examined in depth in the accompanying technology oversight report (Zakaria et al. 2024).[31]

KEY TAKEAWAYS FROM THE GLOBAL LANDSCAPE REVIEW FOR ORGANOIDS

Trends in organoid research and innovation:

Organoids that integrate multiple cell types are being developed, highlighting the scientific acceleration of the field.

31 As noted in Chapter 2, given the cross-cutting nature of AI and data platforms, and how they underpin multiple sectors and technologies, these two areas are examined as cross-cutting technologies applied to organoids. Where relevant, the team has identified a selection of notable trends, opportunities, challenges and governance debates at the intersection of AI/data platforms and organoids.

The vascularisation of organoids is expanding their use in cases such as drug discovery and improved disease modelling.

3D bioprinting is enabling the development of more complex and functional organoids.

Organoids is a relatively small technology area, with most research undertaken in the fields of medicine, biochemistry, genetics and molecular biology.

The United States and China are the largest contributors to organoid research.

Evidence of the commercial application of organoid research is scarce, with only the United States, China, Japan and Korea showing any significant activity.

Organoids-on-chip are allowing researchers increasing control over cells in organoids, closely mirroring human physiological conditions.

Advances in organoid development have led to the creation of brain organoids, signalling a new frontier for neural research.

Patient-derived organoids and cancer are the fastest growing areas for organoid research.

Organoid research is concentrated in high-income countries, which contribute to 71% of global output.

The volume of policy documents published relating to organoids is low and largely from the EU (21.3%), United States (17.3%), Spain (11.8%), United Kingdom (8.3%) and Germany (5.8%).

Opportunities associated with organoids:

Organoids can enable more sophisticated disease modelling.

Organoids can improve the efficiency and accuracy of vaccine and drug development.

Organoids can potentially contribute to developing personalised medicine approaches.

Organoids can inform new methods of computing.

Challenges associated with organoids:

- Organoid research brings challenges in terms of informed consent and the privacy of genetic information.
- Ethical implications of brain organoids include concepts of agency and human identity, which challenge oversight mechanisms.
- Current organoid technology faces limitations in terms of scalability and reproducibility.
- There are barriers to the translation of organoid research into clinical applications due to the lack of reproducibility and scalability of organoids.
- Dual-use organoid research can lead to biosecurity threats.

Key developments associated with the intersection of AI and/or data platforms and organoids:

- AI has facilitated disease detection and diagnosis through improved organoid characterisation.
- Major trends in AI-enabled organoid research centre around brainoids.
- AI-enabled organoid research is spurring developments in brain–computer interfaces and clinical imaging applications.
- The challenge of poor data conformity and quality hinders the full potential of AI in organoid research.
- Organoid research is rapidly producing large quantities of interconnected data.
- Technical developments are posing challenges related to data privacy for organoids containing human-derived cells.
- Some areas of organoid research are adopting a biobanking approach, with implications for organoid data governance.

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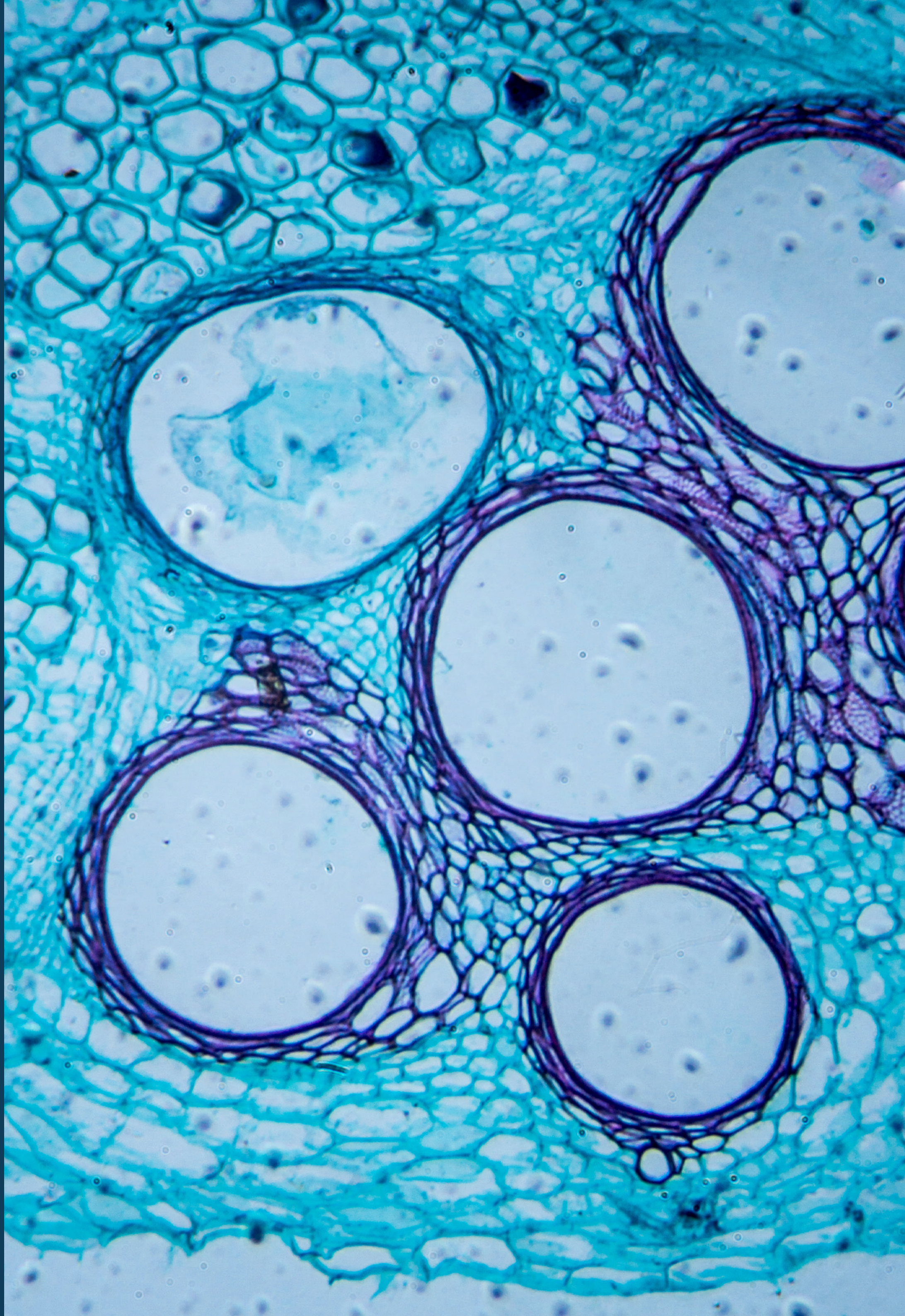
Oversight mechanisms associated with organoids:

- International guidelines provide an ethical framework for organoid research.
- Common research ethics processes are broadly used for conducting organoid research.
- National and regional regulatory frameworks for biomedical research influence organoid research.
- Data protection and privacy oversight heavily impacts organoid research.
- Patent and intellectual property laws also govern organoid research.
- A variety of soft oversight mechanisms are being developed to enhance organoid research and its clinical translation.
- Public engagement is increasingly playing a role in the development of oversight mechanisms.

Source: RAND Europe analysis.



6.1. What do we mean by organoids?

Organoids are three-dimensional structures that are derived from stem cells and are capable of self-organising into structures that mimic the key functional, structural and biological complexity of an organ (Zhao et al. 2022). They are created by culturing stem cells in a specialised environment that mimics the conditions found in the body. The term 'organoid' was first coined to describe three-dimensional structures derived from intestinal stem cells (Sato et al. 2009). Since then, the technology has rapidly advanced, and organoids can now be derived from a wide range of tissues.

Organoids have the potential to revolutionise the understanding of human development and disease as they allow for an improved means of studying organs in controlled laboratory settings. They have the potential to be used in a wide range of applications, to model a wide range of diseases, to test the efficacy and safety of new drugs, and to be used in personalised medicine as they can be derived from a patient's own cells (Li et al. 2020).

6.2. What are the emerging trends in organoid research and innovation?

Organoids that integrate multiple cell types are being developed, highlighting the scientific acceleration of the field

A significant trend in organoid technological advancement is the integration of multiple cell types that allows for better replication of the complexity of natural organs (Vogt 2021; Kim et al. 2020). Initially, organoids were composed of a single cell type, but advances in tissue engineering have facilitated the development of organoids that integrate multiple cell types. Some initial studies focused on developing organoids composed of multiple cell types from the same organ (Birey et al. 2017), whereas more recent developments have allowed for the creation of organoids composed of multiple cell types from different organs (Yang et al. 2023).

The integration of multiple cell types in organoids represents advantages for disease modelling, drug development and regenerative medicine as it facilitates a more accurate modelling of interactions within tissues and allows for better understanding of cellular dynamics and tissue behaviour. This enables the study of cell interactions that are important in organ development and function, and shows how interactions between different tissues give rise to new cellular properties. An example of this is the development of a lung organoid through the use of respiratory epithelial cells, endothelial cells and immune cells (Dye et al. 2015). The organoid was able to replicate the structure and function of the human lung and thus allow for a more accurate modelling of lung development and diseases such as cystic fibrosis. The use of organoids with different cell types is also increasingly used in infectious disease research. For example, by combining brain organoids with spinal organoids and muscular organoids, Han et al. (2021) modelled how SARS-CoV-2 affects the central nervous system.

The United States and Canada have been at the forefront of integrating various cell types into organoids to model diseases more accurately and test drug responses. Substantial funding from public agencies such as the National Institutes of Health (NIH) and private foundations has driven these advancements in organoid models (HSC 2017). In Europe, the Netherlands has been leading the development of intestinal organoids that incorporate various cell types, and houses the largest biobank of patient-derived organoids (Foundation Hubrecht Organoid Biobank 2024). Research groups in the United Kingdom have also made significant contributions to brain and intestinal organoid research (Coleman 2023). While research on the integration of multiple cell types in organoids is currently concentrated in high-income countries, there have also been some developments in LMICs such as Egypt and South Africa.

The vascularisation of organoids is expanding their use in cases such as drug discovery and improved disease modelling

The vascularisation of organoids involves the development of blood vessel networks within organoids (i.e. the vasculature), which facilitates the exchange of nutrients and oxygen to the cells within the organoid (Naderi-Meshkin et al. 2023). This represents an important development, as organoids without vascularisation are limited in terms of long-term growth in laboratories, functional complexities and size (Liu et al. 2023).

Vascularised organoids can be used to study diseases that affect the network of blood vessels. An example of this is the study of cancer, as tumour growth and metastasis[32] are dependent on the formation of new blood vessels. Vascularised organoids have been used to model this process and study the interactions between cancer cells and blood vessels, providing insights into the mechanisms underlying tumour growth and blood vessel formation (Rennert et al. 2016). Vascularised organoids can also be used to test the efficacy and toxicity of drugs more accurately and efficiently than conventional two-dimensional cell cultures as these do not provide three-dimensional spatial and functional information. For example, vascularised liver organoids used to test the toxicity of chemotherapy drugs were more accurate in predicting the effect of the drug than two-dimensional cell cultures, and could identify a potential new drug target (Nguyen et al. 2021). Most recent advancements in the vascularisation of organoids have focused on improving the efficiency and reproducibility of the process, allowing for the vascularisation of an increasing range of organoid types (Sun et al. 2022).

Research on vascularised organoids across global regions has focused on different aspects of the technology. In the United States, researchers have made progress in developing vascularised organoids for a variety of organs, including the liver, kidney and heart. The same has been studied in Asia through investments from governments and the region's strong biotechnology sector (Lee et al. 2021). LMICs are less represented in this area of organoid research as the cost of developing and maintaining vascularised organoids can be expensive, and the resources required to develop these models may be less available (Aguilera et al. 2020). However, due to recent efforts to improve the efficiency and reproducibility of vascularised organoids, including research into low-cost methods for creating vascularised organoids such as using 3D printing technology, this can be expected to change in coming years.

Organoids-on-chip are allowing researchers increasing control over cells in organoids, closely mirroring human physiological conditions

While the development of organoids-on-chip is still in its infancy, studies have shown promising results, and interest in the area is growing. An organoid-on-chip is a small-scale device that can precisely control the flow of fluids (Park et al. 2019). The technology

32 Metastasis is the spread of cancer cells from the original tumour to other parts of the body.

allows researchers enhanced control of the cellular environment of organoids and allows for a more accurate simulation of physiological conditions. As a result, the development of organoid-on-chip technology is closely linked with the development of other organoid innovations, such as vascularisation (Garreta et al. 2021).

Organoids-on-chip can be customised to replicate the specific microenvironment of different organs, and can thus allow for the study of organ-specific diseases and drug responses. For example, organoid-on-chip models of the human intestine have enabled analysis of how individual cellular, chemical and physical control parameters affect the human microbiome, which would not be possible with conventional organoid systems (Bein et al. 2018). Organoids-on-chip can also be used to study the effects of mechanical forces such as fluid flow and shear stress on organoid behaviour, which is important for understanding the behaviour of organs in the body (Hu et al. 2024).

European researchers are at the forefront of developing organoid-on-chip and microfluid devices. For example, the Max Planck Institute in Germany has led the development of microfluid platforms of liver organoids, which is one of the largest areas of organoid research (Prior et al. 2019). The Netherlands has also emerged as a leader in organoid-on-chip technology, combining organoid and microfluidics[33] technology to create 'organs-on-chips' (Utrecht University 2021). High-income countries in Asia, in particular Singapore, have also contributed significantly to the development of microfluid devices for organoids (Yu et al. 2019).

3D bioprinting is enabling the development of more complex and functional organoids

With recent advancements in 3D bioprinting techniques, the 3D printing of organoids is a rapidly growing area of research. By combining 3D printing with organoid technology researchers can create more complex and functional organoids that can be used for a variety of applications, and that are often more easily reproducible and less costly to produce in bulk. These techniques allow for the precise positioning of cell types within the organoid structure, improving the functional and structural resemblance to natural organs (Ren et al. 2021).

An example of the application of 3D printing of organoids is in the field of tissue engineering, where 3D printing has been used to create liver organoids that can perform liver functions such as drug metabolism and bile secretion. The 3D printed organoids were found to be more functional than conventional liver organoids, and it has been suggested that as the technology develops it could be used to create functional liver tissue for transplantation (Wu et al. 2020).

The United States, Europe and Japan are currently at the forefront of research in 3D bioprinting. In the United States, there has been significant research on the use of 3D-printed organoids, with a focus on personalised medicine. Researchers in Europe are exploring a wide range of applications for 3D-printed organoids, including tissue engineering, drug testing and disease modelling (Ren et al. 2021). In Asia, there has been increasing interest in the 3D printing of organoids, with several research institutions and companies developing new applications for the technology. The RIKEN Centre in Japan is at the forefront of these efforts (RIKEN 2022). There is also research

33 Microfluidics are miniaturised systems that manipulate and control fluids at the microscale level.

happening in LMICs such as Brazil and India and upper-middle income countries like China. However, the amount of research activity in these countries is generally lower than in high-income countries.

Advances in organoid development have led to the creation of brain organoids, signalling a new frontier for neural research

Brain organoids, or 'brainoids', contain complex neural structures of human origin that can model human cognition and cellular activity similar to human neural activity. They are typically created by culturing stem cells in a specialised environment that mimics the microenvironment of the developing brain (Qian, Song, and Ming 2019). Over time, the stem cells differentiate into different types of brain cells, including neurons and glial cells, and form complex networks that resemble the structure of the human brain. This has been made possible due to recent advances in other areas of organoid technology, including the integration of different cell types, vascularisation and the use of microfluid devices (Song et al. 2022).

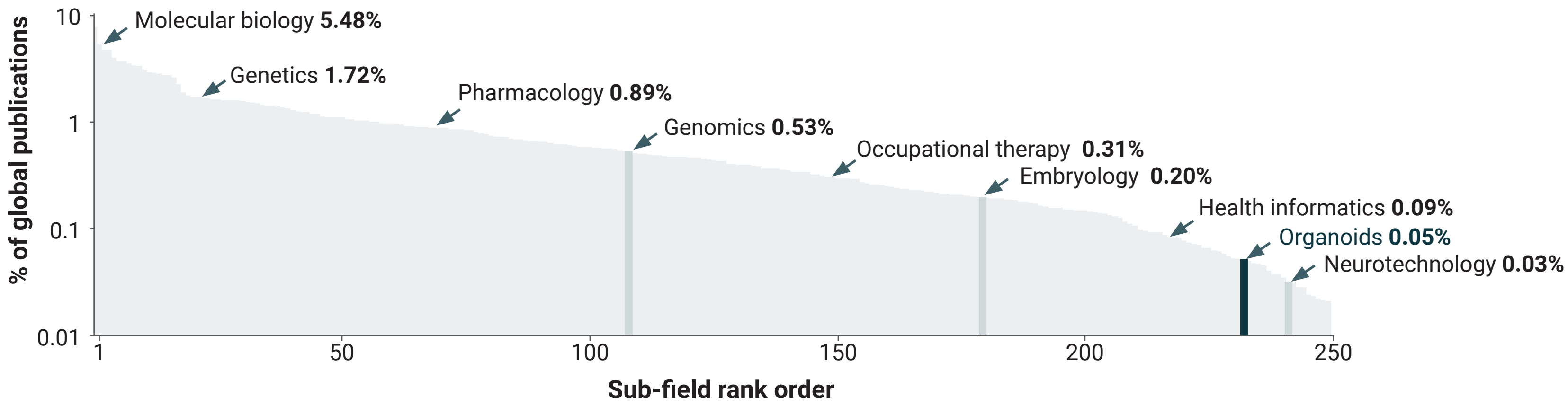
Brain organoids have a wide range of applications in neuroscience research, including in the study of brain development, disease modelling and drug testing. For example, they have been used in relation to neurological neurodegenerative disorders to study the effects of genetic mutations associated with autism. Brain organoids accurately replicated the effects of these mutations on brain development and allowed for the identification of several potential drug targets for these disorders (Schafer et al. 2019). By integrating different types of cells into brain study, researchers have also been able to model aspects of spinal cord development and make progress on research on Amyotrophic Lateral Sclerosis (ALS) (Vieira de Sá et al. 2021). Brain organoids have also been used in the study of infectious diseases, for example to study the effects of the Zika virus on brain development (Watanabe et al. 2017). The researchers found that the brain organoids accurately replicated the effects of the virus on brain development, and identified several potential drug targets.

The current state of research on brain organoids varies around the world, and developments in this area are closely linked to how brain cells and neural activity in organoids are categorised and regulated, such as consent on use of cells, storage and further use of organoids (Hyun et al. 2020). In the United States and Europe there has been significant research on brain organoids, with several universities and research institutions developing new techniques and applications for the technology. There are also rapid developments taking place in Asia, largely due to the region's growing biotech sector (Corrò et al. 2020).

Organoids is a relatively small technology area, with most research undertaken in the fields of medicine, biochemistry, genetics and molecular biology

The area of organoid research is relatively small compared to the other technology areas covered in this study. The 25,514 articles published between 2019 and 2023 make up 0.05% of global publications, and the topic is ranked 231 against all sub-fields of biological research. Figure 12 illustrates the relative volume of organoid research (highlighted red) against all sub-fields (light grey) and the other technology areas in this study (dark grey).

Figure 12. Organoids global publication share ranked against all sub-fields of biological research



Source: RAND Europe analysis.

The topic map of the 25,514 publications (Figure 13) reveals a range of research topics, many of which are focused on specific cancers (orange, dark blue and red clusters), particular organs or diseases (yellow, violet and green), brain organoids (cyan), and organoid engineering (purple).

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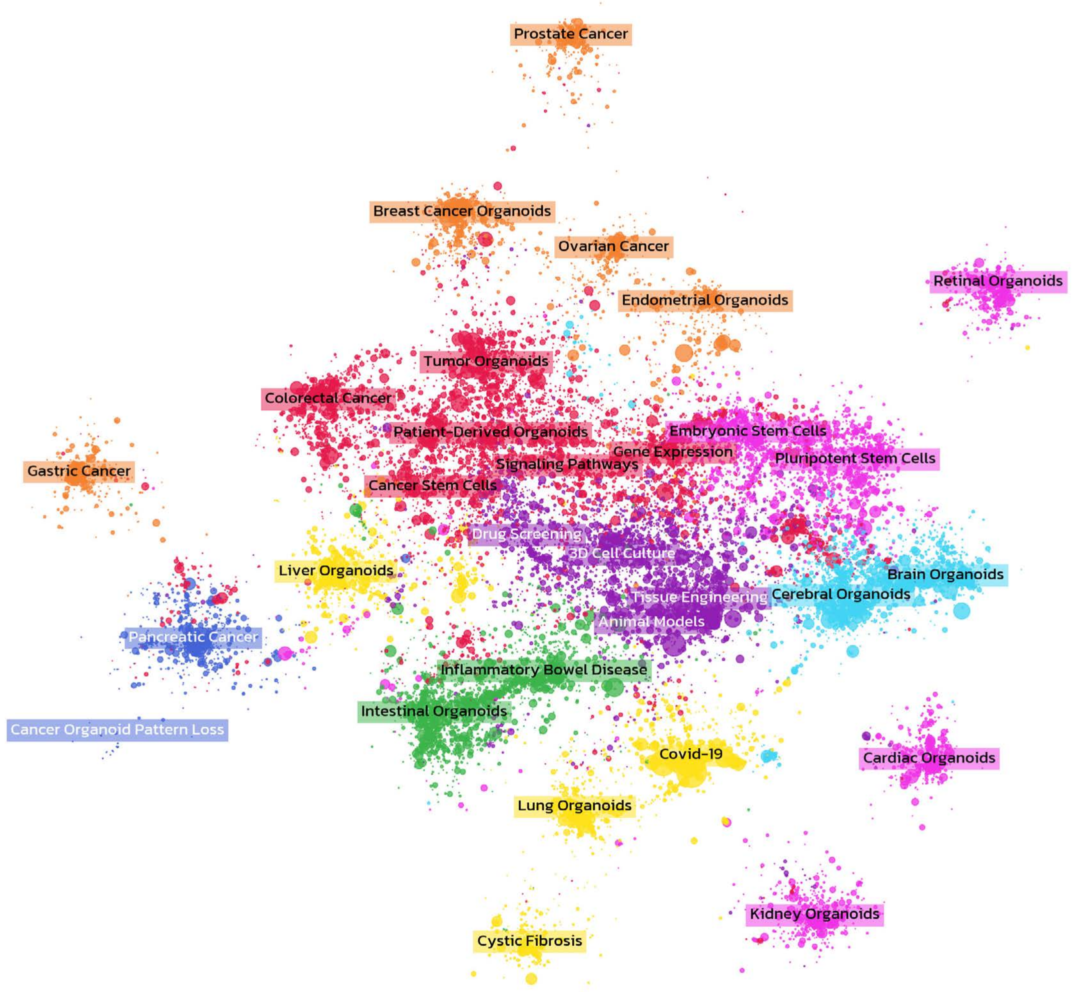
Figure 13. Organoids topic map (publications between 2019 and 2023)



Note: Paper titles and abstracts (where available) were used to generate topic models for each technology area. Topic maps show a visual representation of the distribution of publications across topics. Points on the topic map are individual publications and the point size is proportional to citation count. Indicative labels are shown for each topic in the map (the topic labels were created based on high frequency terms, either manually or via a large language model). The topics are grouped by colour into related clusters.

Source: RAND Europe analysis.

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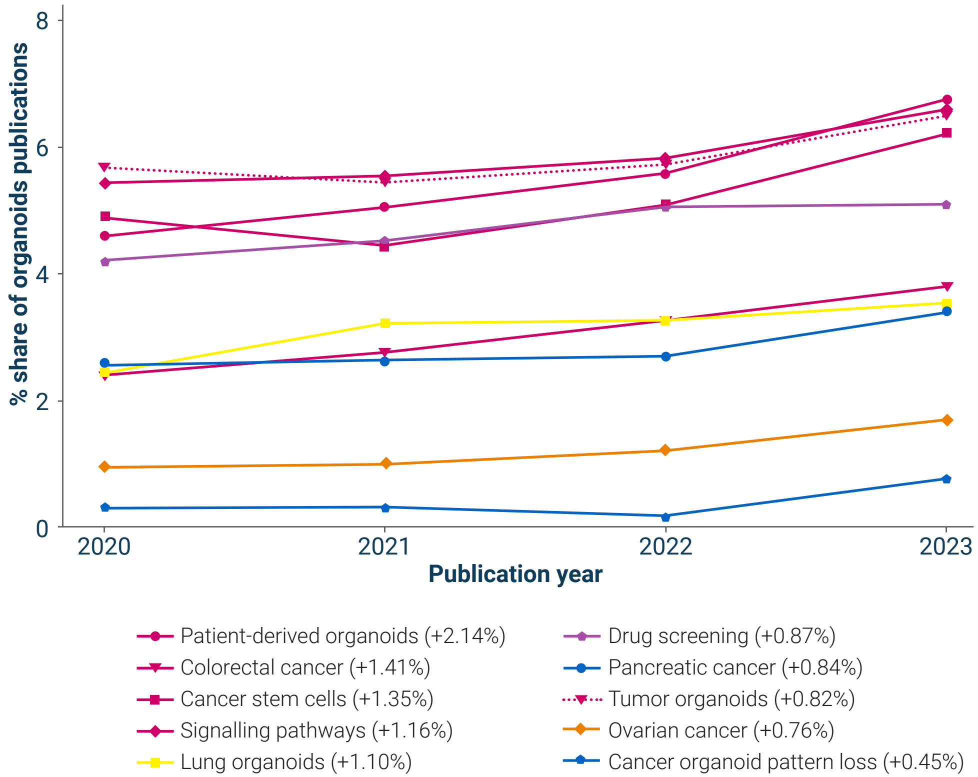
Patient-derived organoids and cancer are the fastest growth areas in organoid research

The top three topics in terms of growth in relative share of publications since 2020 are patient-derived organoids (+2.1%), colorectal cancer (+1.4%) and cancer stem cells (+1.3%). Figure 14 shows the time series plots for the top ten topics when ranked by increase in share from 2020 to 2023, revealing strong growth across topics relating to cancer treatment.

Table 5 shows the number of citations of organoid research in policy documents, with topics ranked from one to ten according to the mean number of citations per paper (to account for variation in topic size). Most topics have attracted little attention from policy sources, with only four topics gathering more than 0.03 cites per paper: 1) Covid-19 (0.13 cites per paper); 2) animal models (0.06 cites per paper); 3) cystic fibrosis (0.05 cites per paper); and 4) brain organoids (0.03 cites per paper).

Figure 14. Top ten fastest growing organoid topics (relative publication share 2020–23)



Source: RAND Europe analysis.

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Table 5. Top ten organoid topics (ranked by mean Overton cites per paper)

Topic	Publication count	Total Overton cites	Mean cites per paper
Covid-19	974	124	0.13
Animal models	542	30	0.06
Cystic fibrosis	334	17	0.05
Brain organoids	1,468	37	0.03
Drug screening	1,764	42	0.02
Patient-derived organoids	2,033	40	0.02
Tissue engineering	1,776	33	0.02
Intestinal organoids	1,997	36	0.02
Pluripotent stem cells	2,165	39	0.02
Gene expression	2,573	42	0.02

Source: RAND Europe analysis.

The United States and China are the largest contributors to organoid research

The leading nations producing publications on organoid research are the United States (34.7%), China (12.6%), Germany (8.4%), the United Kingdom (7.8%) and Japan (5.8%). Figure 15 shows the relative share of global publications for each country, highlighting the concentration of research in high-income economies. In South America, Brazil has the largest share of publications (0.87%), followed by Argentina (0.15%) and Chile (0.18%). Only two countries in Africa produce more than 0.1% of global output: Egypt (0.31%) and South Africa (0.19%). In Asia, five countries produce more than 1% of global output: China (12.6%), Japan (5.8%), Korea (3.3%), India (1.6%) and Singapore (1.1%).

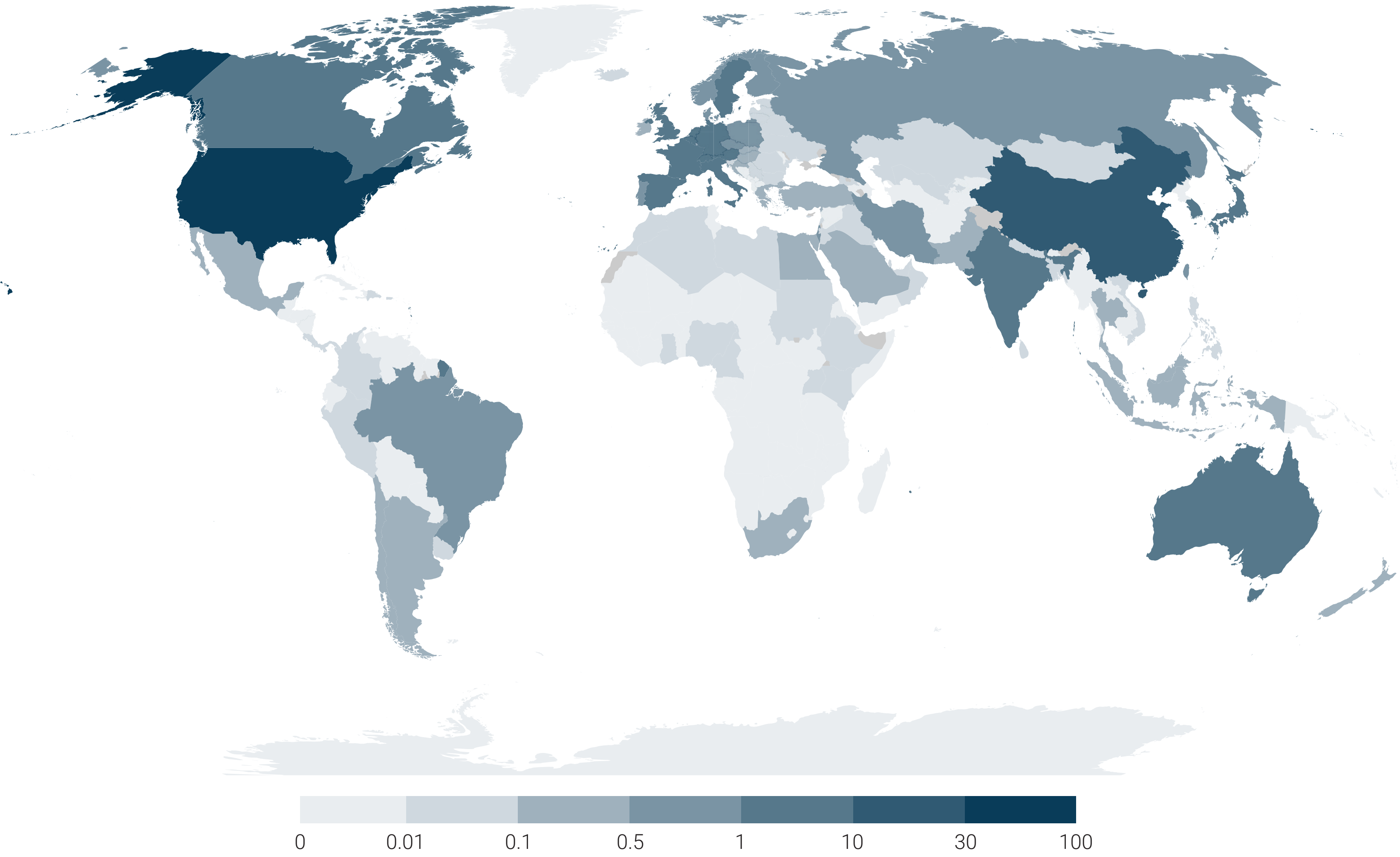
Normalised citation percentiles[34] for nations producing at least 1% of global output are highest for Austria (78.8), Sweden (77.1), Italy (76.6), Australia (76.6) and Singapore (76.2%) (Table 6). Although the United States produces the most research on this technology area, it is ranked lowest out of these top producing nations in terms of mean citation percentile.

As Table 6 shows, countries with the highest proportion of national publication output in organoids are the Netherlands (0.32%), Switzerland (0.19%), Singapore (0.18%), Japan (0.16%) and Austria (0.16%).

In terms of funders acknowledged in published works (representing 74.5% of the indexed articles), the highest relative share is for funders in the United States (75.7%), China (36.5%), Japan (16.3%), the United Kingdom (13.6%) and Germany (9.0%).

34 Normalised indicators were used to measure the overall citation performance of a group of papers, i.e. they have been adjusted to compare like for like. This is calculated by taking all papers with the same subject area, document type (article, conference paper, book chapter, etc), and publication year and assigning each paper a percentile rank. An aggregated count was used for the share of papers in the top 1%.

Figure 15. Global map showing the share of organoid publications by author country



Source: RAND Europe analysis.

Table 6. Publication metrics for countries producing more than 1% of global output in organoid research

Continent	Country	% of global organoid publications	% of national publication output	Mean citation percentile
Asia	China	12.6	0.07	75.4
Asia	India	1.6	0.03	71.4
Asia	Japan	5.8	0.16	74.1
Asia	Korea	3.3	0.15	72.5
Asia	Singapore	1.1	0.18	76.2
Europe	Austria	1.3	0.16	78.8
Europe	Belgium	1.6	0.15	75.3
Europe	France	3.5	0.08	71.8
Europe	Germany	8.4	0.15	74.6
Europe	Italy	3.9	0.11	76.6
Europe	Netherlands	5.7	0.32	75.7
Europe	Spain	2.4	0.08	73.5
Europe	Sweden	1.5	0.13	77.1
Europe	Switzerland	2.8	0.19	74.8
Europe	United Kingdom	7.8	0.13	73.2
North America	Canada	3.8	0.12	71.6
North America	United States	34.7	0.15	70.7
Oceania	Australia	2.8	0.10	76.6

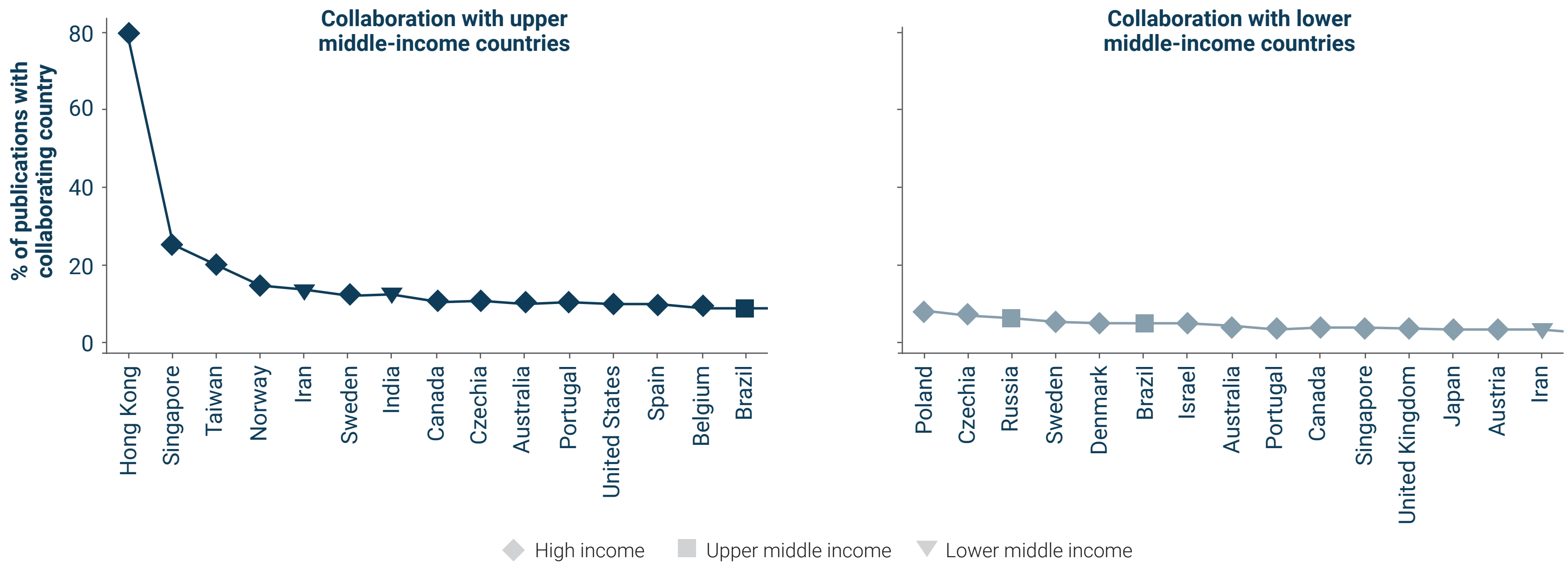
Source: RAND Europe analysis.

Organoid research is concentrated in high-income countries, which contribute to 71% of global output

The plots in Figure 16 (based on countries producing more than 0.5% of global publications) show the top 15 countries ranked by number of papers produced with collaborators from upper middle-income countries (left), and the top 15 countries ranked by the number of papers produced with LMIC collaborators (right). Of the countries producing more than 0.5% of global publications, those with the highest collaboration rate with upper middle-income countries are Hong Kong (79.5%), Singapore (25.4%), Taiwan (20.5%), Norway (14.9%) and Iran (13.0%). In Europe, the top countries collaborating with LMICs are Norway (14.9%), Sweden (12.6%), Czechia (11.0%), Portugal (10.5%) and Spain (9.8%).

Collaboration with LMICs is much lower than with upper middle-income countries (on average 5.5% versus 11.9%). Countries with the highest rates of collaboration with LMICs are Poland (8.8%), Czechia (7.4%), Russia (6.6%), Sweden (5.2%) and Denmark (5.1%).

Figure 16. Rates of organoid research collaboration with upper and lower middle-income countries



Source: RAND Europe analysis.

Evidence of the commercial application of organoid research shows limited activity, with only the United States, China, Japan and Korea showing any significant activity

The number of patents granted relating to organoids is small compared to the other technology areas covered by this study, with only the United States, Japan and Korea holding more than 100 patents. Figure 17 shows the global share of extended patent families granted for each country, and is visibly skewed to high-income countries. The leading nations are the United States (56.7%), Japan (5.9%), Korea (5.6%), Germany (2.0%) and China (1.3%).

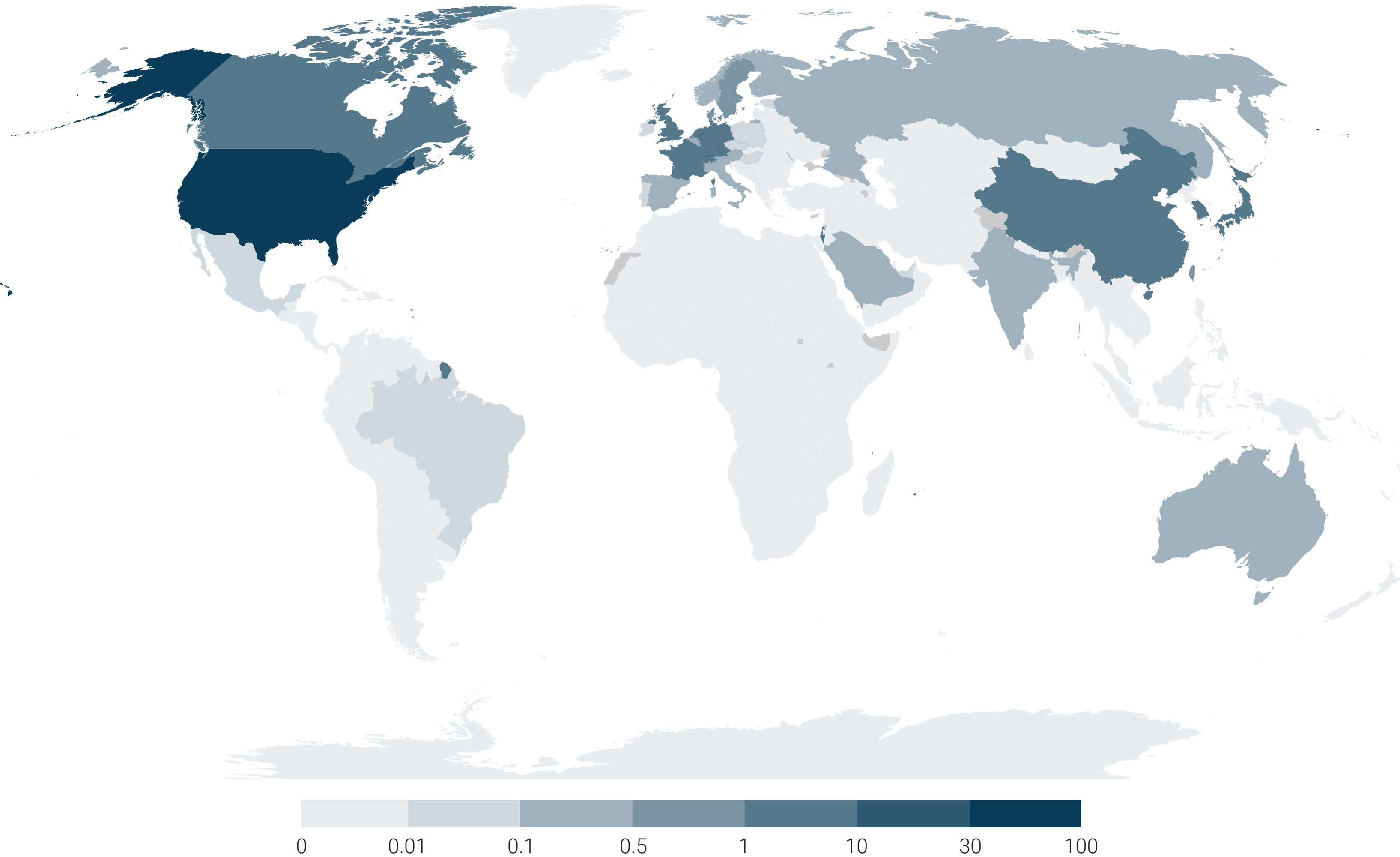
Only the United States and China have more than ten companies with descriptions directly relating to organoids in the Crunchbase database. The top five countries are the United States (19), China (11), Japan (3), Korea (3) and the Netherlands (3) (Table 7).

Table 7. Commercialisation indicators for countries registering more than 0.5% of global patents on organoids

Continent	Country	% of global organoid patents	% of national patents	Crunchbase companies
Asia	China	1.3	0.03	11
Asia	Israel	1.3	0.31	0
Asia	Japan	5.9	0.05	3
Asia	Korea	5.6	0.06	3
Asia	Singapore	0.7	0.19	0
Asia	Taiwan	0.6	0.02	1
Europe	Denmark	0.5	0.14	0
Europe	France	1.1	0.04	1
Europe	Germany	2.0	0.03	1
Europe	Netherlands	1.3	0.10	3
Europe	Sweden	0.7	0.07	0
Europe	Switzerland	1.2	0.09	3
Europe	United Kingdom	1.8	0.11	2
North America	Canada	1.4	0.14	1
North America	United States	56.7	0.23	19

Source: RAND Europe analysis.

Figure 17. Global map showing the share of organoid patents by applicant country



Source: RAND Europe analysis.

The volume of policy documents published relating to organoids is low and largely from the EU (21.3%), United States (17.3%), Spain (11.8%), United Kingdom (8.3%) and Germany (5.8%)

The amount of grey literature directly related to organoids is summarised in Table 8 for the top 15 countries (ranked by policy document count). The EU and Singapore has the highest percentage of their total output relating to organoids, each with 0.07%. Although IGOs rank higher in all other technology areas included in this study, for organoids they produce one of the lowest number of national policy documents, and rank only eighth.

Table 8. Organoid policy document indicators for the top 15 countries (ranked by document count)

Region	Country	Policy document count	% of global organoid policy documents	% of national policy documents
Europe	EU	121	21.3	0.07
North America	United States	98	17.3	0.01
Europe	Spain	67	11.8	0.02
Europe	United Kingdom	47	8.3	0.01
Europe	Germany	33	5.8	0.03
Europe	Netherlands	28	4.9	0.03
Oceania	Australia	27	4.8	0.02
Global	IGO	26	4.6	0.01
Asia	Singapore	17	3.0	0.07
Europe	Italy	16	2.8	0.04
Asia	Japan	14	2.5	0.01
Europe	Switzerland	9	1.6	0.03
Europe	Austria	8	1.4	0.05
Europe	Sweden	8	1.4	0.01
Europe	France	7	1.2	0.01
Europe	Belgium	6	1.1	0.02
North America	Canada	5	0.9	0.00

Source: RAND Europe analysis.

6.3. What are the opportunities associated with organoids?

Organoids can enable more sophisticated disease modelling

The advancements in organoid development described above have been transformative for organoid-based research. In particular, they have enabled new methods for organoid-based disease modelling (Garreta et al. 2021; Nature Materials 2021). Disease modelling that uses organoids with new technologies involving multiple cell types and vascularisation allows researchers to recreate and study the progression of various diseases. This is crucial for understanding underlying mechanisms, identifying biomarkers and testing potential therapeutic interventions, and shows promise for modelling different types of disease.

Organoids have emerged as an effective tool for infectious disease modelling as they facilitate investigation of the interaction between pathogens and host tissues, and thereby provide insights into how they start, spread and can be treated. One of the key examples of this application is the use of human small-intestinal organoids to model norovirus infection and propagation (Chia et al. 2022). Norovirus has been notoriously difficult to study due to the lack of physiologically relevant *in vitro* culture systems, and because it does not infect the animals commonly used to model infectious disease (Hosmillo et al. 2020). The development of human organoids has provided a significant breakthrough in this area as it has provided valuable insights into the life cycle of norovirus and its interaction with the host. Organoids are also increasingly being employed for a wide range of studies involving various infectious agents. For instance, lung organoid models derived from human stem cells have been used for drug screening for SARS-CoV-2 pathogenesis (Han et al. 2021). The use of organoids in infectious disease modelling represents a significant advancement in the field, offering a more sophisticated and physiologically relevant system for studying host–pathogen interactions.

Innovations in organoid development are also enabling new opportunities for cancer modelling. In particular, they offer advantages over conventional methods for studying cancer as they can be created from tumour cells and maintain features of the tumour of origin, and therefore capture the intratumor cell heterogeneity, which is associated with metastasis, relapse and therapy resistance in cancers (Xu et al. 2022). This means they have great potential in predicting the therapeutic response, investigating treatment resistance-related mechanisms, optimising treatment strategies and exploring potential therapies.

Organoids also show promise for modelling genetic disorders as they can keep genetic stability over time. The modelling of genetic disorders in organoids is facilitated by combining organoid and gene-editing technologies (Teriyapirom et al. 2021). For example, researchers have used brain organoids with functional neural networks to model the developing human brain and study autism spectrum disorder (ASD) related genes (Santos et al. 2023). This has been done by introducing genetic mutations into the brain organoids and observing the resulting changes in neuronal connectivity and synaptic function.

Organoids can improve the efficiency and accuracy of vaccine and drug development

Innovative organoid development represents new opportunities in vaccine development (Wagar 2023). By infecting organoids with viruses it is possible to gain insights into the infection process and identify potential vaccine targets. For example, organoids were used to study the effects of SARS-CoV-2 infection on lung tissue (Lamers et al. 2020). The researchers found that the virus was able to infect and replicate in the lung organoids, and that the organoids accurately replicated the immune response to the virus seen in human patients. This study provided important insights into the pathogenesis of SARS-CoV-2 and identified potential vaccine targets, which contributed to the development of the SARS-CoV-2 vaccine (Lamers et al. 2020).

Organoids also bring new opportunities for drug development by providing a platform to assess drug efficacy. They can therefore also be useful for screening drugs in preclinical trials, improving safety (Tang et al. 2022).

Organoids can potentially contribute to developing personalised medicine approaches

Organoids can be derived from individual patient's stem cells, and therefore offer an opportunity to create models tailored to the patient-specific genetic and environmental factors. This can inform a personalised medicine approach to drug development that has the potential to give more accurate predictions of drug efficacy and toxicity, and that can help to identify new therapeutic targets for a wide range of diseases (Li et al. 2020).

For example, organoids derived from patient tumour samples have been used to test the efficacy of chemotherapy drugs for treating gastrointestinal cancers (Vlachogiannis et al. 2018). Such organoids can be used to predict the response of a patient's tumours to chemotherapy, and to test the efficacy of several chemotherapy drugs on the organoids. This approach provides a more personalised model of cancer treatment than traditional cell culture systems, thus facilitating clinical decision making and aiding the development of treatment plans that are specific to each patient. This can ultimately improve treatment outcomes and reduce the risk of side effects for a wide range of diseases (Li et al. 2020).

Organoids can inform new methods of computing

Innovations in organoid technology also offer opportunities beyond health research. For example, brain organoids can inform new approaches to biologically inspired computing and organoid intelligence (OI)[35] (Smirnova, Caffo, Gracias et al. 2023). Advancements in organoid technology also allow for more understanding of self-organisation, adaptive learning, optimisation of energy usage, and networks and connectivity in cellular systems, which are informing novel computing technologies (Shi et al. 2024). While this aspect of brain organoid development is still in its infancy, it is attracting interest and investment worldwide, and is likely to grow in coming years.

35 Organoid intelligence is an emerging field within biology and computer science that develops and studies biological computing using brain organoids to model human cognition.

6.4. What are the challenges associated with organoids?

Organoid research brings challenges in terms of informed consent and the privacy of genetic information

Informed consent is essential in ethical biomedical research that involves stem cells, and individuals must be fully informed of how their biological samples will be used. However, the complexity of organoid research introduces several challenges to consent due to the wide range of applications. For example, with fast-paced developments in the field it is possible to develop complex structures or mimic human physiology more closely than anticipated at the time of consent, and therefore the ownership of organoids once an individual's cells are donated and transformed must be determined. The implications of this for informed consent is an area gaining attention from researchers and research ethics regulatory bodies, and has been highlighted as presenting particular challenges within the area of brain organoids (MacDuffie et al. 2023).

Securing donor confidentiality is another challenge related to informed consent. Human-derived cells and data are commonly 'de-identified' so that they cannot be traced back to the donor patient. This means that they are no longer subject to regulations on human participants in research (Boers and Bredenoord 2018). However, new sophisticated genomic sequencing techniques can allow for the reidentification of cells. Although new methods of obscuring sequence variants in DNA have been developed to address this, with ongoing developments in the field it is likely that new regulations relating to privacy and the reidentification of specimens will be needed in the future (National Academies of Sciences, Engineering, and Medicine et al. 2021).

Ethical implications of brain organoids include concepts of agency and human identity, which challenge oversight mechanisms

The creation of organ-like structures *in vitro* poses ethical questions related to human identity, especially as organoid technology advances towards more complex and functional organ models. This challenge is particularly present within the context of brain organoids, as these can contain complex neural structures that can model human cognition and neural activity (Hyun et al. 2020). The potential for brain organoids to exhibit neural activity also prompts re-evaluation of their moral and legal status. Currently, organoids are not given the same ethical considerations as human subjects in research. However, as the technology evolves, ethical frameworks will need to adapt to consider the moral significance of organoids' human-derived nature and their potential for complex neural activity (National Academies of Sciences, Engineering, and Medicine et al. 2021). This underscores the need for ethical guidelines to navigate the potential for organoids to develop features associated with consciousness.

Current organoid technology faces limitations in terms of scalability and reproducibility

As the field of organoid research progresses, significant challenges are being encountered in terms of scalability and reproducibility (Bock et al. 2021). Organoid growth is resource intensive as organoids require specialist equipment and involve manual processes. This makes them costly to produce, which poses limitations to their scalability across settings with fewer resources. Organoids also require specific conditions, including oxygen levels, nutrients and mechanical forces, to develop properly. Scaling these conditions, while maintaining the exact requirements for each organoid type, is technically demanding (Zhang, Li, et al. 2022). Standardised and documented processes on organoid generation are also important. Different laboratories may use varying methods for stem cell isolation, differentiation and organoid culture, leading to inconsistencies in organoid quality and structure across studies (Glass et al. 2023). One of the most significant challenges to the reproducibility of organoids is the inherent biological variability of stem cells, which can lead to differences in organoid size, shape and cellular composition.

To overcome these scalability and reproducibility challenges there is a growing interest in the development of automated systems and devices that have higher levels of control over the microenvironment and that can reduce the labour costs associated with organoids. These are related to several of the trends identified in this review, including organoids-on-chips, which represent opportunities for overcoming some of these issues (Chakradhar 2016).

There are barriers to the translation of organoid research into clinical applications due to the lack of reproducibility and scalability of organoids

The reproducibility and scalability of organoids described above is one of the main technical challenges in the translation of organoid research into clinical applications. This variability introduces challenges in standardising protocols, which are necessary for clinical application (Nguyen et al. 2020).

Related to this, safety and efficacy standards when applying organoids to regenerative medicine and transplantation are another barrier to clinical applications. There are regulatory questions regarding the safety and efficacy of using organoids relating to the sourcing of stem cells and the long-term integration of organoids into human tissue (Sawai et al. 2022).

In some areas of organoid research, academics are debating whether studies should be categorised as research or as clinical care. For example, there is an ongoing debate on whether personalised drug testing should be treated as research rather than care, where different oversight frameworks would apply depending on the categorisation. This demonstrates that current regulatory frameworks are not sufficient, and that new guidelines and ethical oversight bodies are needed in this area (de Jongh et al. 2022).

Dual-use organoid research can lead to biosecurity threats

Organoid research can potentially have dual-use applications,[36] including commercialisation and the development of bioweapons. While this risk affects much biomedical research, it is particularly pronounced within organoid research due to the new opportunities for disease modelling, and in particular the study of infectious disease in human tissue. As a result, organisations such as the WHO and the Biological Weapons Convention (BWC) provide related guidelines and recommendations.

36 Dual-use refers to anything that can be used for both benefit and harm. It has recently been used in the context of weaponisation and use of technology and applications by nefarious actors. Historically the term was used to indicate technology that has both military and civilian uses.

6.5. What are some of the key developments associated with the intersection of AI/data platforms and organoids?

AI has facilitated disease detection and diagnosis through improved organoid characterisation

Supervised and unsupervised ML methods are used in organoid research to classify data and recognise patterns (Shi et al. 2024). Sophisticated algorithms such as DL algorithms have been used to track dynamic changes in the structure of organoids, validated using imaging from carcinoma organoids (Matthews et al. 2022). This dynamic tracking of the organoid structural changes over time enables predictions of drug responses. Other ML methods have been used to identify structure–function correlations and patterns in cardiac organoids (Maramraju et al. 2024).

Major trends in AI-enabled organoid research centre around brainoids

The convergence of AI and organoids has led to organoid intelligence (OI), which is 'redefining our understanding of developmental biology, disease mechanisms, and therapeutic strategies' (Shi et al. 2024). Another notable development centred around brainoids and AI is reservoir computing, which mimics brain function through an organoid neural network (ONN), in contrast to some biocomputers where biological systems mimic computational technology. The plasticity and diversity of brainoids' 'reservoir' enables them to receive and respond to signals with unsupervised learning, including electrical stimuli (Cai et al. 2023). The responses can be recorded and analysed with integrated algorithms (Smirnova, Caffo and Johnson 2023). This technology has been applied to speech recognition and is being actively explored further.

AI-enabled organoid research is spurring developments in brain–computer interfaces and clinical imaging applications

Emerging applications for AI-enabled organoid research include gene editing, magnetic resonance imaging (MRI) and electroencephalography (EEG). In MRI, for example, convolutional and deep neural networks (CNN[37] and DNN[38]) have been used in research to investigate brainoid structure and biomarkers to detect neurological diseases, using algorithms that identify and classify imaging features (Badai et al. 2020).

There are also cross-cutting opportunities between AI-enabled organoids and neurotechnology, for example through brain–computer interfaces (BCI) and EEG. The use of AI in organoid research has been noted to surpass human capabilities regarding the analysis of complex data, particularly in the detection of early-stage diseases in medical imaging and the study of neural connectivity (Maramraju et al. 2024; Ballav et al. 2024). This is especially relevant for BCI and reservoir computing based on organoids (Hartung, Pantoja and Smirnova 2024). It is possible to interface brainoids with BCIs, as BCIs can process output signals from organoids and provide feedback loops to input signals, with ML providing prediction analysis (Zheng, Feng, et al. 2022). BCIs are discussed further in Chapter 8.

37 Convolutional neural networks (CNNs) are a type of deep learning algorithm often used for analysing visual imagery. They are designed to automatically learn spatial hierarchies of features from the input data.

38 Deep neural networks (DNNs) are a type of artificial neural network that consists of multiple layers of interconnected nodes. They have more than one hidden layer between the input and output layers.

Enhanced reservoir computing using brainoids can lead to positive impacts on ethics and sustainability. The use of brainoids in AI chips and reservoir computing such as Brainoware has reportedly lowered energy consumption and is highly adaptive (Cai et al. 2023). This can open up new avenues for sustainable and efficient research, and mitigate the negative impacts of energy-intensive AI computing.

The challenge of poor data conformity and quality hinders the full potential of AI in organoid research

The variability in brainoid cultures and the lack of large datasets used in this type of research poses a notable challenge to the analysis of organoids with AI (Hartung, Pantoja and Smirnova 2024). Training of AI algorithms requires high-quality, varied and trustworthy datasets. Organoid cultures can be inconsistent, which can compromise the integrity of the datasets used in training and lead to unreliable analysis that varies between algorithms depending on the data they have been trained on (Maramraju et al. 2024). This is pertinent for DNN use in MRI diagnoses and the detection of brainoids, where data availability limits model optimisation steps (Badai et al. 2020).

Organoid research is rapidly producing large quantities of interconnected data

Organoid research, in step with other areas of science, is experiencing a rapid increase in the volume of experimental data due to improved technologies. Consequently, a priority in the field is exploring the means of collecting and aggregating data to promote research collaboration, amass larger datasets and reduce the duplication of research efforts (Park et al. 2019). Relatedly, there is the need to relate various data points to each other (cell-to-cell alignment) (Park et al. 2019; Bock et al. 2021). Understanding the alignment and interconnections of cells requires the integration of many data sources along spatial dimensions, providing a comprehensive 'map' of organs and primary tissues (Bock et al. 2021). This effort requires significant data aggregation and integration. To this end, large organoid data repositories are emerging, such as the Organoid Cell Atlas. These repositories aim to contribute to a comprehensive reference of all human cells to support improved understanding of health and to better model, diagnose, monitor and treat disease (Bock et al. 2021).

Technical developments are posing challenges related to data privacy for organoids containing human-derived cells

Technical developments in genomic sequencing and analysis have allowed for easier re-identification of individuals from whom the organoids were derived, particularly when data sources are linked (Boers and Bredenoord 2018). As this kind of re-identification was previously not possible, most oversight of human-derived cells has been based on defining these cells as 'de-identified' and therefore not subject to human subject protections. This capability to re-identify cells poses challenges for human-cell derived organoids, particularly for individuals modelled for rare diseases or genetic mutations, who may find themselves most easily identifiable (de Jongh et al. 2022). While de-identification is a common process in many fields to enable responsible data reuse, there is debate in the field of organoids on the extent to which de-identification is supportive of the goals of field. Specifically, some scientists argue that de-identification in organoid research is actually undesirable as it limits the extent to which data can be linked, thus limiting the possibility of studying complete biological systems (de Jongh et al. 2022). De-identification also limits the extent to which relevant research can be returned to the donor, and limits potential utility for precision medicine applications (de Jongh et al. 2022). As such,

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processes of de-identification and the risk of re-identification will require careful consideration in organoid research.

Some areas of organoid research are adopting a biobanking approach, with implications for organoid data governance

As organoid research involves physical specimens, some areas of research are adopting biobank approaches that allow for the storing and cataloguing of specimens (Boers and Bredenoord 2018). This approach to collecting and aggregating specimens, and the data collected from them, has enabled research advancements, particularly with respect to drug discovery (Jin et al. 2024). Organoid biobanks are emerging rapidly. Some are organ or disease specific, while others, including biobanks at the Hubrecht Institute, Utrecht University Medical Center and the Royal Netherlands Academy of Arts and Sciences, are collecting broad organoid specimens (Xie et al. 2023). The biobank maintains long-term cultures that are cryopreserved to allow for long-term use in experiments and testing (Foundation Hubrecht Organoid Biobank 2024). While the biobanking approach shows promise, it also creates data oversight issues common to other types of biobank including the long-term sustainability of data, managing access, and implementing appropriate consent processes that allow for a variety of future uses and account for the varied relationships donors will have with their organoid specimens (Lewis and Holm 2022). In addition to these concerns, challenges specific to the biobanking of organoids may arise from the long-term use of human-derived specimens. Specifically, as these specimens are likely to be used in the development of drugs and medical therapies, there remain open questions as to whether donors should be compensated when their specimens are used to test and model therapies that are ultimately commercialised (Boers et al. 2016). Given that biobanks are likely to be managed by both public and private institutions, suitable governance mechanisms will be critical for ensuring that approaches use appropriate benefit sharing.

6.6. What are some of the developments associated with the oversight of organoid research and innovation?

There are a range of mechanisms across the globe that provide oversight for organoid research and its applications. These span from informal non-binding agreements such as international ethical guidelines to nationally binding laws such as the EU Tissue and Cells Directive. This section highlights a range of examples of oversight from across the globe and lays the foundations for a more comprehensive analysis of oversight mechanisms underpinning organoid research and use, which can be found in the accompanying technology oversight report.

International guidelines provide an ethical framework for organoid research

International guidelines and declarations provide a framework for the ethical conduct of research involving human tissues and stem cells that are relevant to organoid research. These influence the conduct of organoid research globally and include guidelines for biomedical research such as the Declaration of Helsinki (WMA 2024), the International Ethical Guidelines for Health-related Research Involving Humans (van Delden and van der Graaf 2017), and the International Society for Stem Cell Research (ISSCR) Guidelines for Stem Cell Research and Clinical Translation (Lovell-Badge et al. 2021). More recently the Baltimore Declaration for oversight of OI has also emerged (Hartung et al. 2023). Although not legal instruments, compliance with these guidelines can be important for obtaining ethical approval by institutional review boards and ethics committees, and

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they therefore play an important role in shaping the ethical conduct of organoid research.

Common research ethics processes are broadly used for conducting organoid research

Institutional review boards (IRBs) and ethics committees occupy a central position in the oversight of organoid research, ensuring that studies are conducted in accordance with established ethical standards and regulatory requirements (Mehta et al. 2023). The primary function of IRBs is to review and approve research proposals before studies commence, and to monitor ongoing approved studies. This includes monitoring compliance with approved protocols and ensuring that ethical considerations are continuously addressed throughout the research lifecycle. They therefore play a crucial role in the oversight of organoid research. The role of IRBs and ethics committees may differ across settings due to variations in regulatory frameworks and organisational structures.

National and regional regulatory frameworks for biomedical research influence organoid research

Regulatory frameworks for biomedical research significantly shape organoid research. Across jurisdictions, the presence of regulatory mechanisms is shaped by the approach to organoid research. For instance, regulatory mechanisms in China are designed to support innovation and may allow for higher levels of risk, potentially overlooking internationally recognised ethical concerns. This reflects the country's substantial investment in biomedical research and its ambition to establish leadership in the field (Mallapaty 2018). In contrast, Germany has stringent regulations designed to address ethical concerns and risks more comprehensively (EuroStemCell 2024). High-income countries might also have more resources to invest in ethical oversight mechanisms than LMICs, where limited resources can constrain the capacity for oversight monitoring and investment.

The regulatory landscape for organoid research in Europe is multifaceted, including EU-wide regulations and national legislation that reflects each country's specific stance on ethical considerations in biomedical research. EU-wide regulations are stringent and play an important role in setting overarching standards for organoid research across member states. For example, the EU Tissues and Cells Directives establish standards for the quality and safety of human tissues and cells, including those used in organoid research (European Commission 2024e). These directives set stringent standards for the procurement, testing, processing, preservation, storage and distribution of human tissues and cells intended for use in humans. They also encompass the use of stem cells, which are essential components of organoid research. National regulations complement these EU-wide regulatory frameworks.

In North America, the regulatory landscape of organoid research is shaped by a combination of federal regulations in the United States and national regulations in Canada. In the United States, the Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research oversees the regulation of cellular and gene therapy products, including those derived from organoids (Center for Biologics Evaluation and Research (CBER) 2024). Individual US states can also have specific regulations related to stem cell research that may influence organoid research. In Canada, Health Canada regulates the use of organoids within the broader framework of cell and gene therapies, and provides guidance on the development, testing and approval of cellular products (Government of Canada 2023).

In Asia, regulatory frameworks reflect that several countries in the region have established themselves as leaders in the field. For example, the environment in Japan is generally supportive of stem cell research and is considered more permissive than regulatory bodies in other regions (Nagai and Ozawa 2017). China is also investing more in the field of organoid research, with its regulations generally as perceived as less stringent than Western regions (Fedaseyeu and Yu 2022). This can lead to faster advancement, but also increased ethical concerns.

In Latin America, organoid research is an emerging and rapidly evolving field. While the stage of organoid research differs across countries, there is an interest in growing this area. This has prompted increased attention on regulatory considerations and an emphasis on collaboration between regulatory authorities and researchers. Currently, research on organoids is primarily regulated by national regulations on general biomedical research, such as the National Health Council's regulation in Brazil (Novoa 2014).

In Africa, national and regional regulatory frameworks reflect the varying stages of development in biomedical research infrastructure. The growing interest in the potential of organoid research means that African countries are developing new frameworks or adapting existing regulatory frameworks to accommodate the unique challenges of organoid research. Initiatives such as the African Academy of Sciences (AAS) and the African Union's Scientific, Technical and Research Commission (AU-STRC), and networks such as the African Research Ethics Review Association (AFRERA), aim to promote ethical research practices and could play a role in shaping the regulatory landscape for emerging technologies such as organoids.

In Oceania, Australia and New Zealand are producing prominent organoid research. In Australia, the Therapeutic Goods Administration ensures compliance with the regulatory requirements of organoid research, with New Zealand's Health and Disability Ethics Committees (HDEC) playing a similar role (Australian Government 2024).

Data protection and privacy oversight heavily impacts organoid research

Beyond regulations that directly address biomedical research and organoids, broader regulatory regimes also impact organoid research. Given the potential for organoids to contain genetic information about the donor, regulations on data protection and privacy strongly influence organoid research. Regulations such as the EU GDPR provide frameworks for handling and protecting personal data, including genetic information. Similar regulations on data privacy are found in other jurisdictions; however, these are typically not as stringent as GDPR (Thales 2021).

Challenges relating to consent and the changing use of tissue, as previously mentioned, are also being addressed through new governance structures. An ongoing approach to gaining consent from donors of tissue is the use of a 'consent to governance' approach instead of individual consent for each study using biospecimens (Boers and Bredenoord 2018). This has been developed to address the challenges relating to informed consent and the changing use of biospecimens in organoid research where the future uses of human data or cells are uncertain. Instead of giving consent for individual studies, donors give consent for the biobank in which their specimens are stored to govern how they are used in research. However, this approach has limitations, with some arguing that specific consent is still needed due to the unique moral characteristics of these areas of research. This debate suggests that rather than using the 'consent or anonymise' mechanism, where consent is not needed if data is anonymised, consent should be requested alongside privacy enhancing measures (Boers and Bredenoord 2018).

Patent and intellectual property laws also govern organoid research

Patent and intellectual property laws regulate the ownership, use and commercialisation of organoid technologies, ensuring that they are developed and used in ways consistent with public interest and ethical standards. These laws can also function as safeguarding mechanisms that protect organoid research from being subject to inappropriate dual-use concerns (Heus et al. 2017).

A variety of soft oversight mechanisms are being developed to enhance organoid research and its clinical translation

As identified above, there are challenges for researchers translating organoid research into clinical application. Regulatory frameworks for the approval of organoid-based therapies are still in their infancy, and there is a lack of clear guidelines that address the unique characteristics and challenges of organoids. This uncertainty can slow the progress of organoid therapies through the clinical trial and approval process. To address this, some jurisdictions are developing oversight mechanisms to facilitate this process.

In the Netherlands, institutions have been key in establishing organoid biobanks and promoting the standardisation of organoid protocols to facilitate their use in research and clinical settings (Foundation Hubrecht Organoid Biobank 2024). Japan has been a pioneer in regenerative medicine, including organoid research, significantly influenced by its regulatory environment, including the Act on the Safety of Regenerative Medicine and the Pharmaceuticals and Medical Devices Act (Ikka et al. 2023). These facilitate the rapid translation of stem cell research into clinical applications, including organoid-based therapies. The framework differentiates between research, clinical research and clinical applications, which streamlines the approval process. This regulatory agility has positioned Japan as a global leader in the field as it encourages innovation while ensuring safety and ethical compliance. In the United Kingdom, the Imperial BRC Organoid Facility serves as a multidisciplinary research and training hub to decrease barriers to accessing stem cell and organoid-related methods, supporting organoid work and developing complex disease models with multi-omics[39] readouts (NIHR 2024). The Nuffield Council of Bioethics has also recently published ethical considerations for research on neural organoids (Nuffield Council on Bioethics 2024).

Public engagement is increasingly playing a role in the development of oversight mechanisms

Given the ethical and cultural concerns influencing how organoid research is perceived, which impact donors' ethical consent, there is a growing interest in public engagements such as citizen juries, public consultations and stakeholder dialogues (Aiyegbusi et al. 2023). Public involvement can ensure that oversight mechanisms are more effective and represent public interest by incorporating societal values, concerns and expectations. This approach has been used within the development of ethical guidelines, as well as within institutional review board and ethics committee approval processes. However, there are growing calls to further include public involvement within the development of regulatory mechanisms for biomedical research, including organoid research (Erikainen et al. 2021).

39 Multi-omics refers to the integration and analysis of multiple types of omics data, such as genomics, transcriptomics, proteomics, metabolomics and epigenomics.

HUMAN EMBRYOLOGY

Chapter 7
Global landscape review for human embryology

This chapter presents the findings of the global landscape review for embryology based on desk research and a comprehensive scientometric analysis. It first provides some context and defines what is meant by embryology in the context of this study, and then highlights the key trends, challenges and opportunities associated with global embryology research and innovation. The chapter concludes with reflections on some of the oversight mechanisms associated with embryology (oversight mechanisms and their implications are examined in depth in the accompanying technology oversight report (Zakaria et al. 2024)).[40]

40 As noted in Chapter 2, given the cross-cutting nature of AI and data platforms, and how they underpin multiple sectors and technologies, these two areas are examined as cross-cutting technologies applied to human embryology. Where relevant, the team has identified a selection of notable trends, opportunities, challenges and governance debates at the intersection of AI/data platforms and human embryology.

BOX 4: KEY TAKEAWAYS FROM THE GLOBAL LANDSCAPE REVIEW FOR HUMAN EMBRYOLOGY

Trends in human embryology research and innovation:

- Stem cell research has led to major breakthroughs in embryology research.
- Major advancements have been noted in assisted reproductive technology.
- Research on the use of embryology in human fertility has grown moderately since 2020.
- Embryology research is concentrated in high-income countries (60% of global output), although many of these collaborate with middle-income countries.
- Policy documents published relating to embryology are largely from the United States (28.0%), United Kingdom (20.7%), IGOs (12.0%), Canada (7.9%) and the EU (5.5%).
- Breakthroughs in gene-editing technology have spurred developments in correcting inherited disorders in embryos.
- Embryology is a relatively large technology area, with research focused mostly in the fields of biochemistry, genetics, molecular biology and medicine.
- The United States and China are the largest contributors to research in embryology (41% of global output), with European countries producing research with the highest citation impact.
- Commercial applications of embryology are present in the United States, Japan, Germany, Switzerland, India, United Kingdom, Australia, Spain and Israel.

Opportunities associated with human embryology:

- New technologies could substantially improve the clinical outcomes of in vitro fertilisation (IVF).
- New technologies are deepening understanding of inherited diseases.

Challenges associated with human embryology:

- Gene editing of embryos poses significant ethical challenges.
- There are challenges in establishing a common definition of an embryo.

Key developments associated with the intersection of AI/ data platforms and human embryology:

- There has been a significant upward trend in the use of AI-enabled IVF, with applications seen in embryo screening, ranking and selection.
- The use of AI in IVF research requires further clarity and transparency.
- There is an increased need for governance of AI–embryology research, particularly on the transparency of algorithmic decision making.
- Comprehensive IVF datasets are integral to producing reliable AI models for IVF embryo selection.
- Global IVF data repositories will require governance approaches that centre on trustworthiness.

Oversight mechanisms associated with human embryology:

- Guidelines concerning the use of human embryos in research vary greatly globally, and reaching a universal agreement is challenging.
- The ability to use surplus embryos in research varies across jurisdictions.
- Embryo and stem cell research are underpinned by complex oversight structures and mechanisms.
- Gaps in oversight of stem cell-based embryo model systems (SCBEMs) are being addressed by codes of conduct.
- Developments in gene editing have reanimated oversight debates on heritable genome editing.

Source: RAND Europe analysis.

7.1. What do we mean by embryology?

Human embryology is a sub-field of developmental biology that concerns human development from fertilisation to birth and involves the study of human embryos from fertilisation onwards. It is a crucial field for understanding evolution, disease progression and aetiology, the development of treatments for inherited diseases, and to support reproductive technologies (Rivron et al. 2023).

An embryo, biologically defined as a group of cells that may form a foetus, is usually the result of fertilisation, the process where an oocyte merges with a sperm cell to form a zygote (Rivron et al. 2023). However, the legal definition of an embryo varies across the world (Rivron et al. 2023). Following technological advancements, such as the development of stem cell-based embryo model systems (SCBEMs) that bypass human fertilisation, it has been proposed that an updated definition of the embryo is required (Ball 2023). Embryology has been shaped by politics, religion and societal values, with ongoing ethical debates about the study of human embryos. This topic has regained prominence due to the growth of research on human embryonic stem cells and SCBEMs (Brivanlou and Gleicher 2021).

7.2. What are the emerging trends in human embryology research and innovation?

Stem cell research has led to major breakthroughs in embryology research

In 2023, embryology saw a major breakthrough with the development of SCBEMs, which use adult stem cells to bypass the need for fertilisation. This development could hold great promise for studying human development outside of the body and conducting further research into inherited diseases and fertility challenges (Oldak et al. 2023). SCBEMs are seen by some as enabling scientists to research the early stages of human development without the ethical concerns associated with human embryos (Piotrowska 2021). In 2020, lab-grown embryonic cells developed into structures partly similar to a 19-day human embryo, but without the brain seed or the placenta tissues. Embryo models have been described as 'a tremendous tool' that could allow us to understand what is considered the 'black box' of human development: the stage when different organs begin to form (Ansede 2023). Stem cells, in particular induced-pluripotent stem cells (iPSC),[41] have also advanced embryology and fertility research significantly, with iPSCs taken from women with fertility disorders aiding the understanding of pathogenesis that underpin the various disorders (Wang et al. 2019).

41 Induced-pluripotent stem cells (iPSC) are a type of stem cell that can be generated from adult cells through reprogramming techniques.

Breakthroughs in gene-editing technology have spurred developments in correcting inherited disorders in embryos

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR-Cas9)[42] is a gene-editing tool that uses a guide ribonucleic acid to target the exact desired sequence of interest to allow modifications to a genome (Redman et al. 2016). This method has the potential to treat hereditary or developmental neurological disorders such as fragile X syndrome and Down syndrome to improve the quality of life for those affected (Wong et al. 2021). In 2017, CRISPR-Cas9 was used to successfully correct a genetic mutation in human embryos in a laboratory setting, with corrections made to the mutation that causes hypertrophic cardiomyopathy, which can result in sudden cardiac arrest and often death, particularly in young people. This development has critical implications for the correction of a wide range of inherited genetic conditions. While the advent of sophisticated tools such as CRISPR-Cas9 has advanced precision and efficacy, there are considerable safety considerations, and gene editing in human embryos taken to term is therefore not yet permitted (Wong et al. 2021).

Major advancements have been noted in assisted reproductive technology

Artificial wombs are an emerging technology that could change reproductive treatments. They facilitate embryo growth outside of the womb to reduce risks from IVF and reduce the death rate of preterm birth in newborns (Kozlov 2023). Given the 44% increase in the rate of preterm births observed globally over the last 20 years, artificial wombs are a critical technological advancement. Artificial placentas are another technology closely connected to the artificial womb that aims to support preterm birth. Both technologies are advancing rapidly, and it is speculated that there will soon be clinical trials with humans involved (Kukora, Mychaliska, and Weiss 2023).

Mitochondrial replacement therapy (MRT) is a state-of-the-art technique that prevents mutations in the mother's mitochondria from being passed onto the child. There are multiple ways of replacing the mother's mitochondria that is carrying mutations with a donor's mitochondria during the stages of fertilisation. As a result, the child born from the procedure has 99.9% of the parents' DNA, without inheriting any harmful mitochondrial mutations (European Parliament. Directorate General for Parliamentary Research Services 2022). The technique was first trialled and regulated in the United Kingdom for patients with serious genetic conditions, and the first UK baby to benefit from this technique was born in May 2023 (Sample 2023).

42 CRISPR is a gene-editing technology that allows scientists to make precise changes to DNA.

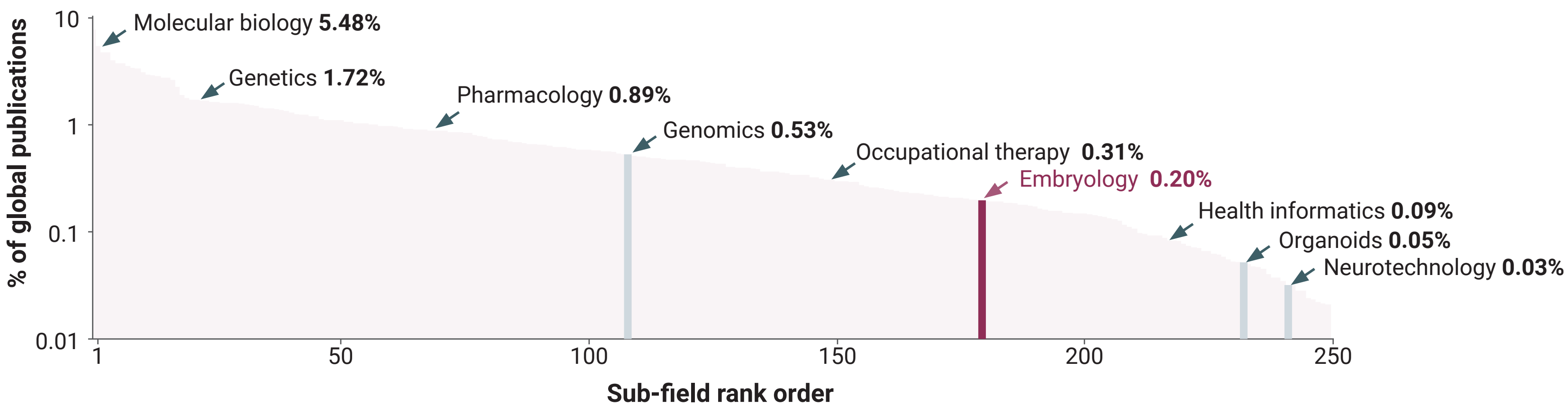
Embryology is a relatively large technology area, with research focused mostly in the fields of biochemistry, genetics, molecular biology and medicine

Embryology is a relatively large technology area compared to the other areas in this study, with 99,652 publications published between 2019 and 2023 spanning several sub-fields of biological science including biochemistry, genetics, molecular biology and medicine.

Embryology makes up 0.20% of global publications, and is ranked 179 when compared to all sub-fields (Figure 18).

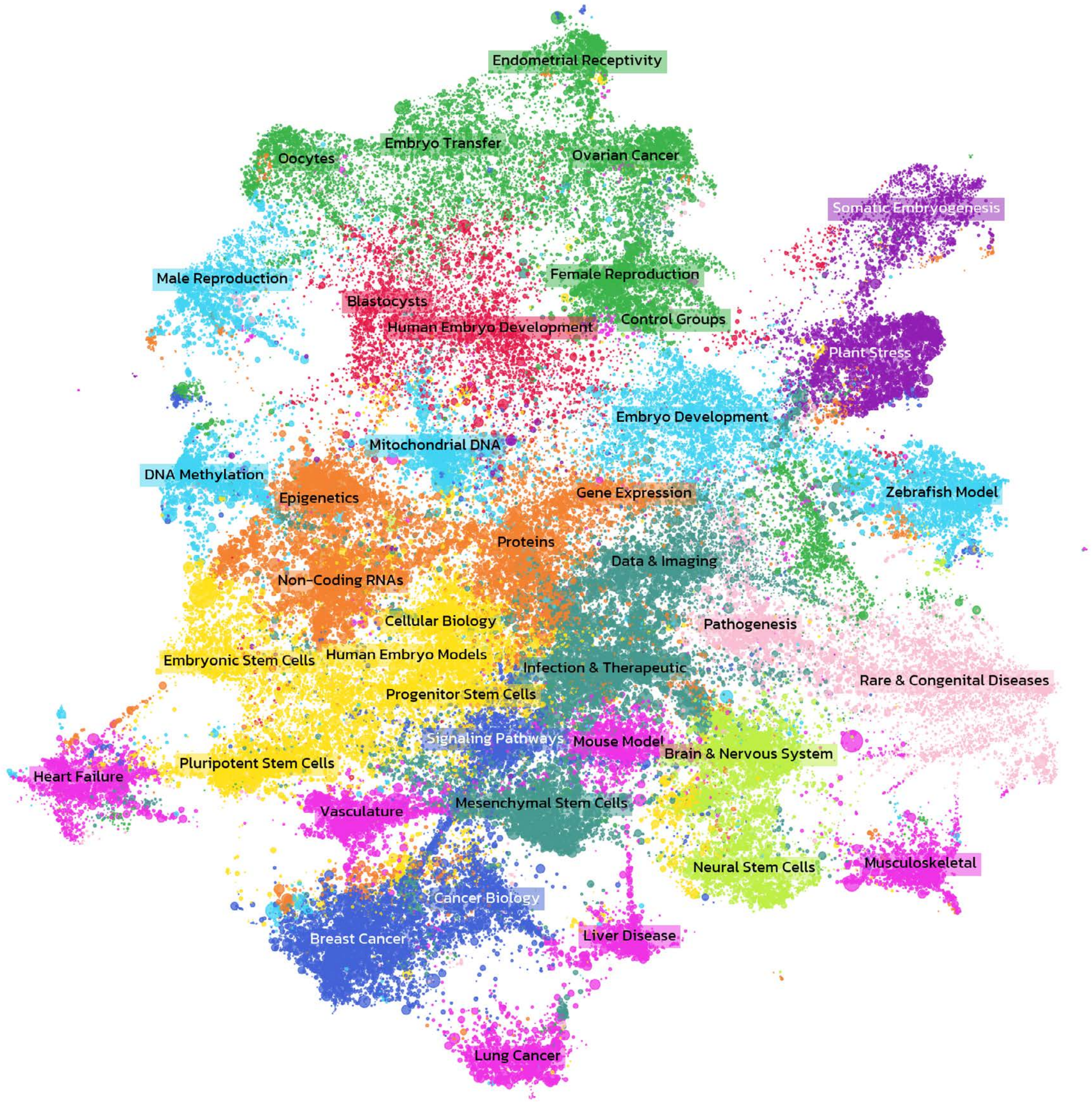
The topic map for embryology presented in Figure 19 shows a wide range of research topics covering reproduction (green cluster), stem cells (yellow), disease-specific topics (violet), cancer (dark blue), molecular biology (cyan), genetics (orange) and human embryo development (red).

Figure 18. Embryology global publication share ranked against all sub-fields of biological research



Source: RAND Europe analysis.

Figure 19. Embryology topic map (publications between 2019 and 2023)



Source: RAND Europe analysis.

HUMAN EMBRYOLOGY

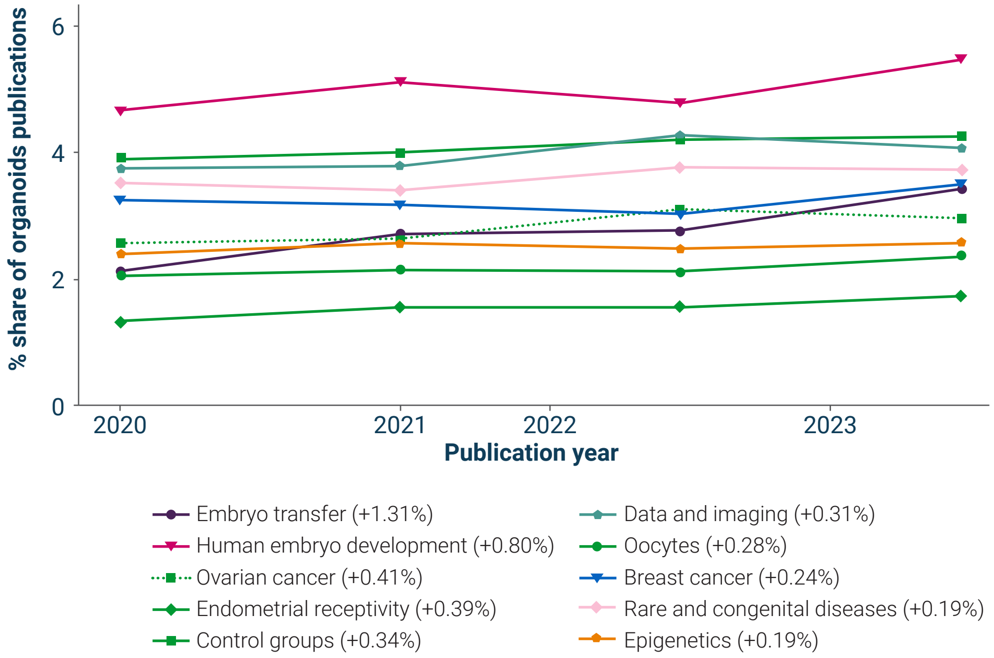
Research on the use of embryology in human fertility has grown moderately since 2020

Based on analysis of the relative share of embryology publications between 2020 and 2023, the topics with the largest growth are embryo transfer (+1.3%), human embryo development (+0.8%) and ovarian cancer (+0.4%). Of the top ten topics (ranked by increase in share between 2020 and 2023), five are related to reproduction in humans (Figure 20).

The United States and China are the largest contributors to research in embryology (41% of global output), with European countries producing research with the highest citation impact

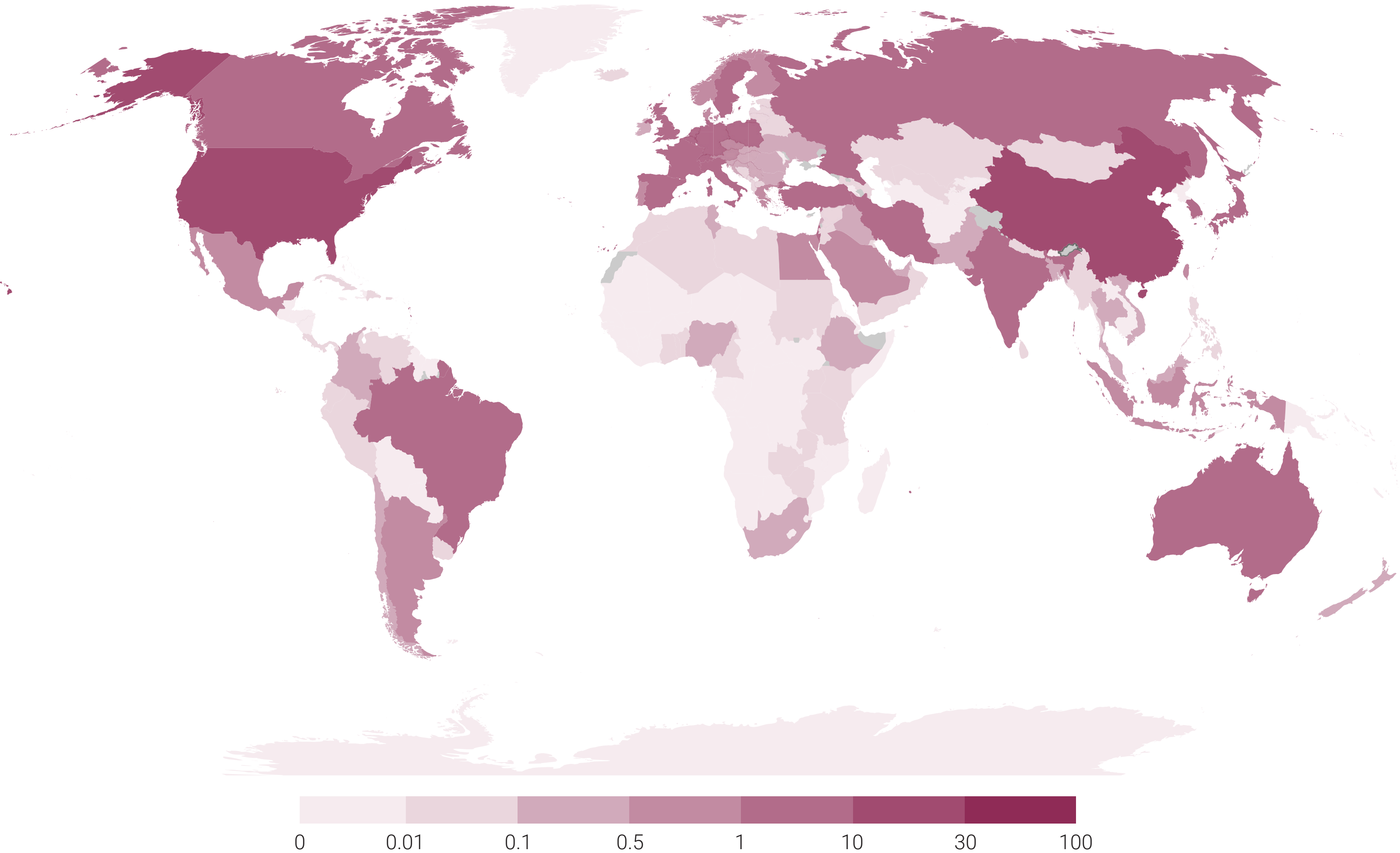
In terms of relative share of publications, the leading nations are the United States (24.5%), China (18.9%), United Kingdom (6.7%), Germany (5.5%) and Japan (4.7%). As the map in Figure 21 illustrates, research is most intensive in high-income countries – of the top 20 ranked by publication volume, 15 are high income, 3 are upper middle income (China, Brazil and Russia) and 2 are lower middle income (India and Iran). In South America, Brazil produces the most publications (2.6% of global output), followed by Argentina (0.6%), Chile (0.4%) and Colombia (0.2%). In Africa, no country produces more than 1% of global output, although Egypt is close with 0.9%, and only five produce more than 0.1%: South Africa (0.3%), Nigeria (0.2%), Ethiopia and Tunisia (both 0.1%). In Asia, six countries produce more than 1% of global output: China (18.9%), Japan (4.7%), India (3.2%), Korea (2.4%), Iran (1.5%), Turkey (1.2%) and Israel (1.1%).

Figure 20. Top ten fastest growing embryology topics (relative publication share 2020–23)



Source: RAND Europe analysis.

Figure 21. Global map showing the share of embryology publications by author country



Source: RAND Europe analysis.

Normalised citation percentiles for nations producing at least 1% of global output are highest for Sweden (79.5), the Netherlands (79.3), Italy (79.2), Germany (78.8) and Poland (78.5), as shown in Table 9 (mean citation percentile column). Of the top ten countries ranked by mean citation percentile, eight are from Europe, along with Australia and China.

Of the countries with more than 0.1% of global publication output in all topics, those with the highest proportion of output in embryology are Israel (0.6%), Belgium (0.5%), Czechia (0.5%), Japan (0.5%) and Spain (0.5%). There is little variation in this rate across countries in Europe, except for Russia, which has a significantly lower rate (0.2%).

Based on funder acknowledgement data from the Web of Science (representing 74.5% of indexed articles), the highest relative share is for funders in China (42.8%), the United States (36.7%), Japan (11.6%), United Kingdom (9.7%) and Spain (5.0%).

Table 9. Publication metrics for countries producing more than 1% of global output in embryology research

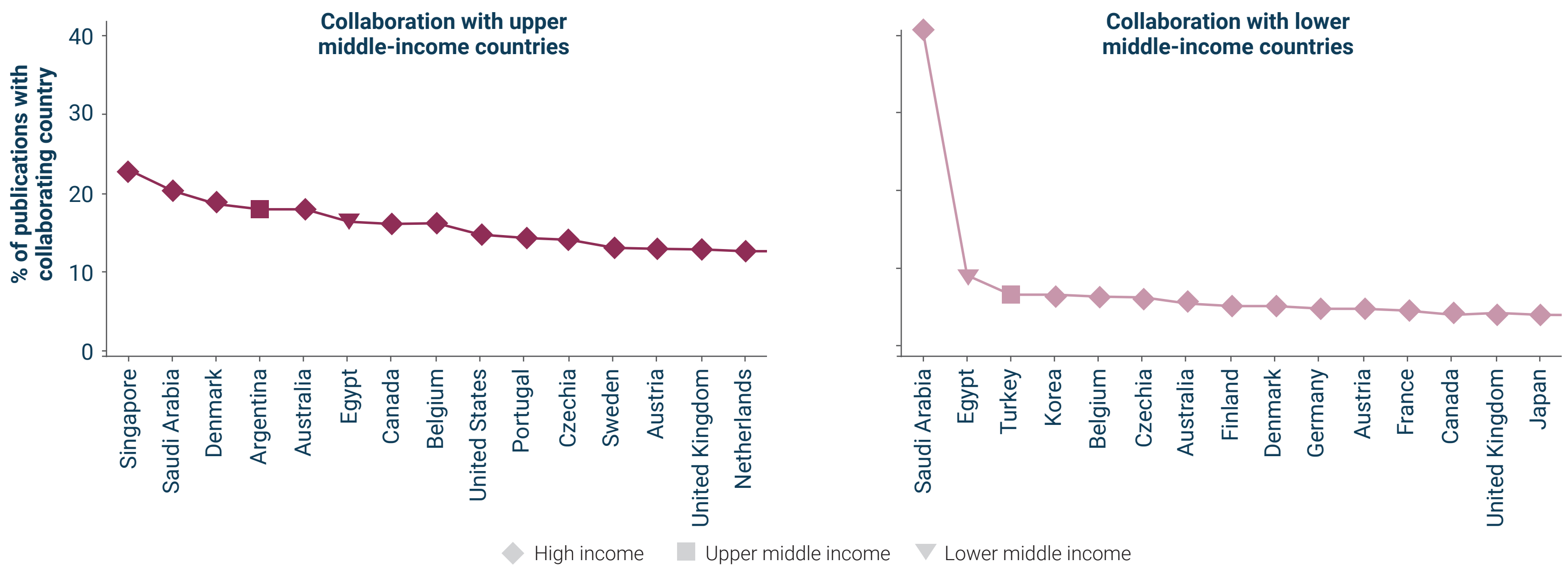
Continent	Country	% of global embryology publications	% of national publication output	Mean citation percentile
Asia	China	18.9	0.4	77.1
Asia	India	3.2	0.2	67.0
Asia	Iran	1.5	0.3	74.8
Asia	Israel	1.1	0.6	75.8
Asia	Japan	4.7	0.5	74.4
Asia	Korea	2.4	0.4	76.9
Asia	Turkey	1.2	0.2	66.7
Europe	Belgium	1.4	0.5	76.9
Europe	France	4.0	0.4	76.9
Europe	Germany	5.5	0.4	78.8
Europe	Italy	4.2	0.5	79.2
Europe	Netherlands	2.1	0.5	79.3
Europe	Poland	1.6	0.4	78.5
Europe	Russia	1.5	0.2	69.3
Europe	Spain	3.8	0.5	74.6
Europe	Sweden	1.4	0.5	79.5
Europe	Switzerland	1.6	0.4	78.1
Europe	United Kingdom	6.7	0.4	76.5
North America	Canada	3.2	0.4	76.2
North America	United States	24.5	0.4	73.5
Oceania	Australia	2.7	0.4	77.9
South America	Brazil	2.6	0.3	71.5

Source: RAND Europe analysis.

Embryology research is concentrated in high-income countries (60% of global output), although many of these collaborate with middle-income countries

Similar to trends seen in genomics research (see Chapter 5), embryology research in high-income countries is often in collaboration with middle-income countries. Figure 22 has two plots based on countries producing more than 0.5% of global publications: on the left, the top 15 countries are ranked by the number of papers produced with collaborators from upper middle-income countries, and on the right, the top 15 countries are ranked by the amount of papers produced with lower middle-income collaborators. The collaboration rate with upper middle-income countries (ranging between 12% and 22% for the top 15 countries) is highest for Singapore (22.7%), Saudi Arabia (20.5%), Denmark (18.8%), Argentina (18.2%) and Australia (18.1%). Collaboration with lower middle-income countries is substantially higher for Saudi Arabia (40.8%) than for any other country.

Figure 22. Rates of embryology research collaboration with upper and lower middle-income countries

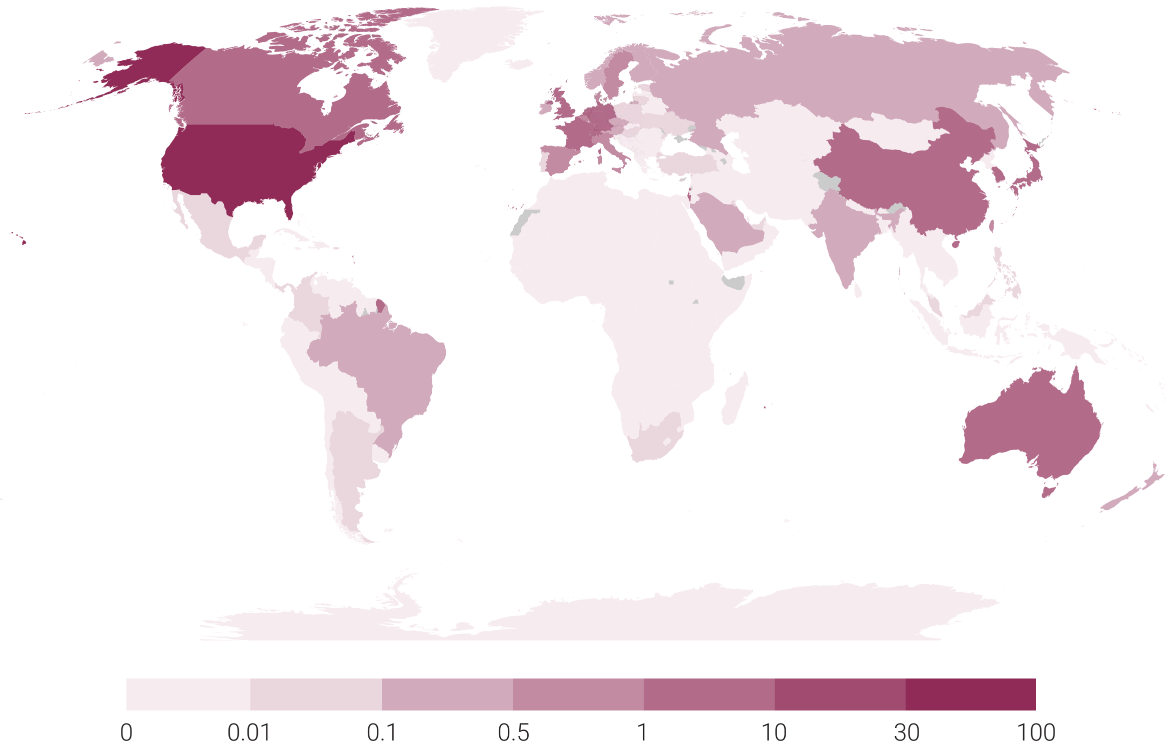


Source: RAND Europe analysis.

Commercial applications of embryology are present in the United States, Japan, Germany, Switzerland, India, United Kingdom, Australia, Spain and Israel

The global distribution of patent share in embryology is particularly skewed to high-income countries, as Figure 23 reveals. The highest producing countries are the United States (59.2%), Japan (5.9%), Germany (3.9%), Switzerland (3.4%) and the United Kingdom (2.9%). No countries in South America produced more than 0.5% of global patents, with Brazil producing the most at 0.14%. Only three countries in Africa have granted any patents: South Africa with three, and Tunisia and Sierra Leone both with one. There are six countries in Asia that have more than 0.5% of the global share of patents: Japan (5.9%), Korea (2.6%), China (2.5%), Israel (1.6), Taiwan (0.8%) and Singapore (0.8%).

Figure 23. Global map showing the share of embryology patents by applicant country



Source: RAND Europe analysis.

Table 10. Commercialisation indicators for countries registering more than 0.5% of global patents on embryology

Continent	Country	% of global embryology patents	% of national patents	Crunchbase companies
Asia	China	2.5	0.2	33
Asia	Israel	1.6	1.4	22
Asia	Japan	5.9	0.2	6
Asia	Korea	2.6	0.1	3
Asia	Singapore	0.8	0.8	3
Asia	Taiwan	0.8	0.1	2
Europe	Belgium	1.0	1.0	4
Europe	Denmark	0.6	0.7	11
Europe	France	2.5	0.3	8
Europe	Germany	3.9	0.2	14
Europe	Italy	0.8	0.4	4
Europe	Netherlands	1.3	0.4	5
Europe	Spain	0.8	0.9	41
Europe	Sweden	0.6	0.2	6
Europe	Switzerland	3.4	0.9	5
Europe	United Kingdom	2.9	0.7	44
North America	Canada	1.5	0.5	21
North America	United States	59.2	0.9	335
Oceania	Australia	1.3	1.4	43

Source: RAND Europe analysis.

Policy documents published relating to embryology are largely from the United States, United Kingdom, IGOs, Canada and the EU

The publication of grey literature documents (e.g. reports, white papers, guidelines) is highest in the United States (28.0% of global output), the United Kingdom (20.7%), IGOs (12.0%), Canada (7.9%) and the EU (5.5%). Countries with the largest proportion of national output in embryology are Canada (0.7%), the United Kingdom (0.6%) and Indonesia (0.5%) (Table 11).

Table 11. Embryology policy document indicators for the top 15 countries (ranked by document count)

Continent	Country	Policy document count	% of global embryology policy documents	% of national policy documents
North America	United States	2,916	28.0	0.2
Europe	United Kingdom	2,153	20.7	0.6
Global	IGO	1,252	12.0	0.4
North America	Canada	825	7.9	0.7
Europe	EU	568	5.5	0.3
Oceania	Australia	392	3.8	0.3
Europe	France	283	2.7	0.3
Europe	Spain	142	1.4	0.1
Asia	Japan	139	1.3	0.1
Europe	Netherlands	132	1.3	0.1
Asia	Indonesia	126	1.2	0.5
Europe	Finland	112	1.1	0.3
Europe	Sweden	103	1.0	0.1
Europe	Belgium	96	0.9	0.3
Europe	Germany	94	0.9	0.1
Europe	Ireland	92	0.9	0.3
Asia	Philippines	91	0.9	0.2

Source: RAND Europe analysis.

7.3. What are the opportunities associated with human embryology research?

New technologies may substantially improve the clinical outcomes of IVF

In 2021, more than 1.3 million IVF cycles had been delivered in the United Kingdom, highlighting the progress made in the field of embryology at large. Technological advancements will continue to offer an immense number of opportunities and challenges that will redefine embryo research and reproduction in the years to come. There are multiple emerging developments that point to this trend; for instance, metabolomic profiling[43] could address the multiple pregnancy rate and improve the success rate of IVF by streamlining the embryo selection process (Motiei et al. 2020). Another notable development may emerge from the IVF lab-on-a-chip concept, which could automate the IVF process within a single system through microfluidics, reducing costs and the need for human intervention (Weng 2019; Kushnir et al. 2022). Lastly, another groundbreaking development is in vitro gametogenesis (IVG), which is the process of creating 'gametes outside the body' using somatic cells to create either an oocyte or sperm cell in the laboratory that is then combined with gametes of the opposite biological sex, resulting in an embryo. This treatment may be significant for those who have had cancer and who wish to preserve their fertility through IVF (Wesevich et al. 2023).

New technologies are deepening understanding of inherited diseases

Epigenome[44] editing-based therapies have the potential to treat genetic diseases by controlling the relevant epigenome with very little, if any, change to the genomic DNA, which could open up opportunities for use on human embryos (Ueda, Yamazaki, and Funakoshi 2023).

AI is also set to play a key role in embryology in terms of personalising infertility treatment, particularly in regard to drug selection and dosing, cycle monitoring, and selecting embryos with the highest success rate (Hanassab et al. 2024). For instance, Repro-AI, a tool at the intersection of reproductive medicine and mathematical science, aims to improve the diagnosis and treatment of infertility. IVF cycles supported by Repro-AI may be feasible in the next few years (Sadeghi 2022).

7.4. What are the challenges associated with human embryology research?

Gene editing of embryos poses significant ethical challenges

Embryology's future holds both possibilities and challenges, with advancements in technology offering opportunities to significantly improve people's lives, while also presenting risks of misuse and ethical concerns. For example, although CRISPR-Cas9

43 Metabolomic profiling is a technique used in the field of metabolomics to identify and quantify small molecules in a biological sample.

44 The epigenome refers to a collection of chemical compounds and modifications that can influence the activity of genes within a cell.

can be used to correct genetic mutations, it could also be used to give embryos subjectively defined 'desirable' characteristics (McKie 2023).

Social and economic circumstances may mean that many people will be unable to use technological advancements due to cost or lack of access, which could further increase inequities, with some likening it to choosing a private school over a state school (Devlin 2019). There are also safety considerations given that most techniques come with an unquantified degree of risk (Devlin 2019; McKie 2023). The scientific community has also warned about the ethical boundaries and the safety standards needed by highlighting the case in China where CRISPR-Cas9 was used to genetically modify the embryos of twin girls to develop HIV resistance. It is unclear how this procedure will affect the girls later in life and whether they will be more vulnerable to other viruses (Cyranoski 2019). There is considerable progress to be made both on safety and ethical boundaries before CRISPR-Cas9 can be used in embryos (Wong et al. 2021).

There are challenges in establishing a common definition of an embryo

The legal definition of an embryo varies across the world. In a study of 22 countries, only 13 (Australia, Belgium, Canada, Germany, India, Japan, the Netherlands, South Korea, Spain, Switzerland, Taiwan, the United Kingdom and the United States) were found to define an embryo within their laws and guidelines. Austria, Russia, China and Sweden do not define an embryo, even though their laws mention similar terms or include stem cell research (Xue and Shang 2022; Matthews and Moralí 2020).

In February 2024, the Alabama Supreme Court discussed the lack of clarity surrounding the definition of an embryo after an accident at a fertility clinic destroyed the embryos of three couples. Through this ruling, questions emerged as to whether fertilisation entails 'personhood'. The court ruled that embryos are 'children' even if kept outside the womb (Chesak 2024).

It has been argued that given technological advancements a new definition of embryo is needed that includes embryo models that could potentially develop into a foetus (Rivron et al. 2023). Human stem cells can imitate early embryo development and include cells that can be found in the uterus and the placenta. However, embryo models have not been included in definitions of the embryo and thus are not protected by embryo research regulations (Ball 2023). It is anticipated that embryo models, specifically SCBEMs, may in the future reach a point where ethical distinctions with an embryo no longer apply, signalling a new frontier in the study of embryology (Ball 2023).

7.5. What are some of the key developments associated with the intersection of AI/data platforms and human embryology?

There has been a significant upward trend in the use of AI-enabled IVF, with applications seen in embryo screening, ranking and selection

The viability of embryos is traditionally assessed through imaging, whereby specific biomarkers are annotated (VerMilyea et al. 2020; Zaninovic et al. 2024). The annotated embryos are then ranked prior to selection for IVF. This process is extremely variable and subject to bias and human errors in annotation (Bormann et al. 2020). To avoid this, DL and 'AI-driven decision support systems' have been applied to embryo assessments where automated annotation and embryo ranking is possible (Lee et al. 2024a). Alternative embryo selection strategies, for example Preimplantation Genetic Testing for Aneuploidies (PGT-A), can be enhanced by DL-based convolutional neural networks (CNN) such as iDAScore v1.0, which can offer more objective and reproducible analysis (Cimadomo et al. 2023). iDAScore was used in a large, randomised control trial held across Australia, Denmark and Ireland (Vitrus Health 2020).

The prediction of ploidy status (number of chromosomes in an organism) is essential to prioritise and select embryos for implantation. For example, STORK-A, a DL algorithm, predicts embryo ploidy to improve the study of implantation potential (Digital Health Global 2023). The Embryo Ranking Intelligent Classification Algorithm (ERICA) uses ML to recognise patterns in embryo images to predict ploidy (Chavez-Badiola et al. 2020). AI/ML has also been able to predict the potential of embryo implantation with 100% accuracy using customised artificial neural networks (ANN) (Cheredath et al. 2023).

Using AI analysis of embryonic images is non-invasive, enabling assessments of blastocyst formation and quality of embryos (Jiang and Bormann 2023; Curchoe 2023). This improved embryo screening and selection can benefit IVF embryo transfer by decreasing risks in pregnancy, and can reduce costs by predicting pregnancy losses and other outcomes (Wen et al. 2022; Chavez-Badiola et al. 2024).

The use of AI in IVF research requires further clarity and transparency

Due to the high ethical implications of AI-assisted embryology there has been an upsurge in researchers calling for clarity and standards in research findings (Curchoe 2023). Such standards should consider issues such as the validation and verification of databases used, and sample sizes (Salih et al. 2023). There is a call to move away from the 'black box' AI model to more interpretable and transparent AI in IVF. Researchers have noted that using ML models in embryo ranking in a transparent and reproducible manner could improve the interpretability and explainability of AI-driven analysis (Afnan et al. 2021).

To date, nearly all AI algorithms (including DL) used in embryology exist in a 'black box', where the algorithms are not interpretable (Afnan et al. 2021), and the verification of AI models through randomised control trials has not yet been conducted (Lee et al. 2024a). A key challenge linked to uninterpretable AI is the potential generalisation of populations resulting from poor or limited algorithm training leading to increased research bias and impacts on trust (Afnan et al. 2021). The black box models often used in these settings are also limited by the datasets they are trained on creating further challenges of adapting the models to clinical settings.

Despite numerous studies and reviews on AI-assisted embryo selection and ranking, further validation in a clinical setting, for example through randomised control trials, is needed before the technology becomes widespread (Cimadomo et al. 2023). One review noted that the studies included in the review 'did not show any intent to take the developed technology to a clinical trial stage' (Salih et al. 2023). The low uptake in clinical settings can also be attributed to the fact that AI-enabled predictions of ongoing pregnancies is of greater clinical importance than the prediction of implantation (Salih et al. 2023).

There is a need for increased governance of AI–embryology research, particularly on the transparency of algorithmic decision making

Embryologists have called for human dignity and rights to be prioritised in the oversight of AI–embryology technologies. This is particularly relevant to data privacy and protection, where models and research should be operated with maximum transparency. Researchers have noted that international consensus on research guidelines and best practices is key to achieve this (Medenica et al. 2022).

Proceedings from the first AI Fertility World Conference suggest that a working group on AI in embryology would be the best way to generate guidelines or a checklist for responsible reporting (Curchoe 2023). It was noted that this could include a checklist of whether specific data annotations or embryos were present, the quality of data and description, and the risk of bias to ensure consistent and clear reporting across publications. The 2022 conference led to the creation of the international AI Fertility Society, which includes sub-committees addressing regulation, ethics and transparency, and responsible innovation ('AI Fertility Society', n.d.). However, their activities since the conference in 2022 are unclear.

Although there are guidelines and tools to avoid bias and ensure transparency in research, they are not widespread or common practice. Examples include the PROBAST tool, which assesses the risk of bias (Moons et al. 2019), and the TRIPOD tool, which provides guidelines for transparent reporting (Collins et al. 2015). A classification system for embryo selection was proposed in early 2024 to provide clarity and consistency in the selection process with regards to 'subjectivity, explainability and interpretability' (Lee et al. 2024b). In 2023, the first study ranking embryo quality against eight different algorithms was published. This study brought together embryologists to come to an agreement on embryo quality between AI (Cimadomo et al. 2023; Zaninovic et al. 2024). The work was led by researchers from Argentina, Denmark, Italy, Spain, Sweden, the United Kingdom and the United States.

Comprehensive IVF datasets are integral to producing reliable AI models for IVF embryo selection

The training of AI models and the testing of data are key to improving and validating AI models, including those used for embryo selection (Afnan et al. 2022; Hickman et al. 2020). For AI models, access to sufficient and diverse data is critical for limiting bias and overfitting – a phenomenon whereby AI is overly attuned to its training data resulting in poorer performance on new data (Kragh and Karstoft 2021; Afnan et al. 2022). In the context of IVF, access to ample and diverse data is not always straightforward.

As with many data-heavy fields, IVF data faces challenges of aggregation and interoperability, posing hurdles to amassing sufficient quantities of accurate and usable data. In particular, inter-clinic variations in definitions, thresholds and collection of patient demographic information, as well as differences in clinical and laboratory processes, pose interoperability challenges and threaten the reliability of AI training data (Hickman et al. 2020). In addition, IVF data, including data on the embryo, the patient and the ultimate outcome of the IVF treatment, are personal and identifying, making them subject to stricter human subject protections and limiting data sharing and access (van Panuis et al. 2014). Furthermore, as IVF data concerns personhood, infertility and family life, and are therefore socially, emotionally and politically charged, their governance is often subject to stronger privacy protections than other personal or health data, limiting potential for data linkage and reuse in research (Carson et al. 2019). These issues are further complicated by existing practices around data use and consent in assisted reproductive technologies and IVF, where consent frequently does not include permissions for data reuse. In addition, most routinely collected IVF data is for regulatory purposes and is aggregated at the national scale in summary form, limiting its potential use for AI training and validation (Hickman et al. 2020). Finally, most IVF clinics around the globe still rely on paper records, and as such a mass digitisation effort would be necessary to create the large, comprehensive global datasets needed for reliable and generalisable results from AI models (Hickman et al. 2020). Data access, sharing and aggregation are therefore formidable hurdles to the continued development and improvement of AI models for embryo selection.

Global IVF data repositories will require governance approaches that centre on trustworthiness

In order to support IVF research, including the development of AI models, there are growing calls for an open access and comprehensive data repository of embryo images and data (Afnan et al. 2022). Such a repository would enable data aggregation at the scale necessary to develop AI models that are trained and validated on sufficiently diverse data. Establishing a data repository of this nature would require action and cooperation from governing bodies such as the UK's Human Fertilisation and Embryology Authority, and from professional and academic bodies such as the Academy of Clinical Embryologists (Afnan et al. 2022). Governance mechanisms that appropriately protect privacy, enable access and promote inclusion will be essential in the establishment of an IVF data repository. To this end, data solidarity principles have been suggested as a means of governance (Afnan et al. 2022). Data solidarity refers to 'an approach to the collection, use, and sharing of health data and data for health that safeguards individual human rights while building a culture of data justice and equity, and ensuring that the value of data is harnessed for public good' (Kickbusch et al. 2021). These principles look at health data governance through the lens of a social contract, where there is a balance of personal and collective needs and responsibilities, and an interest in where these overlap (Kickbusch et al. 2021). Data solidarity emphasises non-extractive approaches to data collection, use and sharing, promoting trustworthiness and harnessing the value of the data for public good (Kickbusch et al. 2021). Developing these principles requires involvement and input from affected groups and multisectoral partners, as well as investment and efforts towards consensus building (Lancet Digital Health 2021). As such, the development of a global repository and implementation of necessary data governance mechanisms will be a concerted international effort that, if successful, may be a significant advancement in the field of IVF.

7.6. What are some of the developments associated with the oversight of human embryology research and innovation?

There are a range of mechanisms across the globe that provide oversight for embryology research and its applications. These span from informal non-binding agreements such as international guidelines to nationally binding laws such as the Oviedo Convention. This section highlights a range of examples of oversight from across the globe and lays the foundations for a more comprehensive analysis on oversight mechanisms underpinning embryology research and use, which can be found in the accompanying technology oversight report.

Many of the key challenges in this area relate to the ethics and safety of technology use. While the oversight of some of these developments are dictated by existing legal frameworks, some are being called into question due to patient demand, changing concepts of ethics and agency, and the evolution of technologies themselves. Technological advances have also created scenarios where existing legal frameworks no longer apply, creating new debates on appropriate oversight.

Guidelines concerning the use of human embryos vary greatly globally, and reaching a universal agreement is challenging

The ISSCR provides guidelines on using embryos for research with its '14-day rule', which limits the amount of time that human embryos can be allowed to develop in a research setting. This is an internationally recognised, and in many cases nationally enforced, guideline. However, the most recent release of the guidelines states that this limit could be extended or even abolished to allow research on some crucial stages of embryo development, which may include the main causes for miscarriages and birth defects (Foreman et al. 2023). These guidelines do not represent global consensus, with opinions varied in different countries. For example, in February 2020 a new bill by the French Senate was proposed to allow embryos to be developed for up to 21 days; however, it was ultimately rejected (Fabbri et al. 2023). The definition of an embryo itself varies across many jurisdictions, as previously discussed, which impacts embryo research and the 14-day limit (Foreman et al. 2023).

China has implemented a combination of legislative measures and ethical guidelines that include sanctions and a specified 14-day limit, as outlined by its national human embryonic stem cells guidelines. However, a religious-centric view of the embryo is not common in China and as a result there is no firm opposition to the extension of the 14-day rule (Xue and Shang 2022). China follows the ethical priority principle, which means that oversight for prevention and precaution is needed if research has not attained social ethical consensus and may have technological or moral risks. However, because of the case mentioned previously involving CRISPR-Cas9 and twin babies,[45] policymakers have taken a 'people-centred' approach, and bioethics were included in national strategic goals. In 2020, Article 1009 of the Civil Code stated that medical and scientific research that involves human DNA and embryos must comply with the relevant laws and regulations and must not threaten human health, ethics and public interest. It was also stated that scientists who do not comply with legal requirements would face sanctions and the incident would be recorded in the database of serious breaches of trust in scientific research integrity (Xue and Shang 2022).

Switzerland is the only country to have a seven-day limit for embryos used for research or for the development of human embryonic stem cells (hESC), and only allows the use of hESC derivatives after day seven (Matthews and Moralí 2020). The United Kingdom is still considering its stance on the 14-day limit, with a paper in the British Medical Journal suggesting that this rule is now too limiting (McCully 2021). The Human Fertilisation and Embryology Authority (HFEA) highlights the importance of a clear time limit for embryo research, as well as a mechanism that guarantees consensus on the new limit (HFEA 2023). At the same time, the Health Council of Netherlands has recommended that the Dutch Embryo Act (the Netherlands) extends its 14-day rule to 28 days (Health Council of the Netherlands 2023).

Although the United States was the first to suggest the 14-day limit, it was never passed as a federal law (Matthews and Moralí 2020). Similarly, Brazil's laws on hESC research do not mention a limit or

45 A scientist in China used CRISPR-Cas9 to edit embryos during IVF to infer HIV resistance and brought the embryos to term. This was deemed illegal and led to a global outcry.

any restrictions on the development of human embryos in a research setting (Matthews and Moralí 2020; Health Council of the Netherlands 2023). Even though there have been discussions though the European Court and the ISSCR, due to lack of political and societal support the 14-day limit has not yet been extended by any country (Health Council of the Netherlands 2023).

The ability to use surplus embryos in research varies across jurisdictions

Surplus embryos are the unused embryos from an IVF cycle that have received consent for use in research. Germany's Embryo Protection Act[46] bans all basic research on human embryos (Xue and Shang 2022). In certain cases, permission may be granted for the import and use of embryonic stem cells for research if the cells are derived from surplus embryos obtained before May 2007, if they are no longer needed to induce pregnancy, and if no payment is involved. The law also requires that such research serves significant scientific goals and cannot be achieved using other types of cells (Understanding Stem Cells 2017; Gärditz 2023). The scientific community supports the position that embryos are crucial to research (Leopoldina 2021), and Germany is calling for a review of this act to enable scientists to make discoveries in embryology by using embryos in research. The United States, Israel, Sweden, the United Kingdom, France, and Japan, among others, pose no restrictions on the use of surplus embryos in research (Matthews and Moralí 2020).

Embryo and stem cell research are underpinned by complex oversight structures and mechanisms

Regulatory oversight of embryonic stem cell research is underpinned by diverse mechanisms that lack a globally agreed approach. Oversight in the United States is decentralised, with an analysis of 50 states finding that based on plain text interpretation, laws did not directly discuss embryonic stem cell research, as the majority of laws were created to address other matters such as abortion and reproductive cloning. Eighteen states allow human embryo research, 21 do not have any related laws and 11 have prohibitive laws (Abelman, Lopes, and O'Rourke 2015). It is worth noting that definitions may vary substantially, and thus researchers need to carefully consider state laws and local politics to engage in embryo and stem cell research (Matthews and Moralí 2022).

In the United Kingdom, policies focus on legal and regulatory measures for human embryos, while the definition does not expand into characterisation of the embryo itself or its moral status. The HFEA regulates human embryo and stem cell research, with its remit passing over to the Human Tissue Authority once the embryo is no longer involved. The Human Fertilisation and Embryo Act was updated in 2008 and is currently undergoing another update to consider emerging developments in the field.

In Japan, a combination of laws and guidelines applied by various organisational bodies make up the oversight landscape concerning human embryo research, human tissue research, derivation of embryonic stem cells and utilisation of embryonic stem cells. The rules applied depend on the specific characteristics of each study,

46 Germany's Embryo Protection Act (Embryonenschutzgesetz) is a law that regulates the use of human embryos in scientific research and medical practice.

which has been cited as a confusing and fractured landscape to navigate (Yui et al. 2022).

Gaps in oversight of stem cell-based embryo model systems (SCBEMs) are being addressed by codes of conduct

Recent advancements such as SCBEMs are not included in the legal definition of an embryo for many countries, and as such work is underway to address the gaps in oversight with regards to the use and modification of SCBEMs in a laboratory setting. The United Kingdom is leading developments in terms of SCBEM governance with a project called Governance of Stem Cell-Based Embryo Models (G-SCBEM). The project, cofounded by the University of Cambridge in partnership with the Progress Educational Trust, aims to establish the first governance framework for SCBEM research. It will examine the challenges and opportunities in this field and set the foundations for ongoing dialogue with the public and various stakeholders (University of Cambridge 2023).

Developments in gene editing have reanimated oversight debates on heritable genome editing

Breakthroughs in genetic editing tools are creating newly energised debates on the oversight of heritable genome editing.[47] While heritable genome editing is currently prohibited across the world, advancements in treating diseases such as cystic fibrosis and sickle cell disease, where current therapies do not hold huge amounts of promise, have spurred the debate between policymakers, academics, parents and clinicians on access to heritable genome editing (Zarghamian, Klermund, and Cathomen 2023). In Europe, national laws on genome editing have been largely influenced by the Oviedo Convention, which discusses bioethics and forbids heritable human genome editing. Its impact on national laws varies across countries as some have not signed or ratified the convention. For example, in Spain, which has signed the convention, it is prohibited to create ‘embryos for experimental purposes’. However, it has been argued by scientists that if new genetic material is not introduced and it does not aim to change the human genome, germline modification is allowed. Italy has not ratified the convention; however, it follows the 2004 Act on Medically Assisted Reproduction, which prohibits any type of embryo selection or efforts to predetermine genetic characteristics unless there is a diagnostic and therapeutic purpose. Italian legislation currently allows very limited interventions (National Academies of Sciences, Engineering, and Medicine/Policy and Global Affairs 2023).

In 2023 the United Kingdom hosted the Third International Summit on Human Genome Editing, where a consensus emerged that research is still needed to broaden the treatments offered and to mitigate its risks, before genome editing can safely be used in human embryos. The organising committee called for a continuing dialogue and international collaboration regarding the governance and regulation of heritable human genome editing technologies (National Academies of Sciences, Engineering, and Medicine/Policy and Global Affairs 2023). In China, implantation of a genetically edited or cloned embryo may face sanctions, such as up to seven years imprisonment or a fine (Xue and Shang 2022). As research in embryology progresses, it is speculated that ethical debates will focus on utilitarian arguments for heritable genome editing in the context of health (Brivanlou, Rivron, and Gleicher 2021).

47 Heritable genome editing involves making intentional changes to the DNA of germ cells or embryos.

Chapter 8
Global landscape review for neurotechnology

This chapter present the findings of the global landscape review for neurotechnology based on desk research and a comprehensive scientometric analysis. It first provides some context and defines is meant by neurotechnology in the context of this study, and then highlights the key trends, challenges and opportunities associated with global neurotechnology research and innovation. The chapter concludes with reflections on some of the oversight mechanisms associated with neurotechnology (oversight mechanisms and their implications are examined in depth in the accompanying technology oversight report (Zakaria et al. 2024).[48]

48 As noted in Chapter 2, given the cross-cutting nature of AI and data platforms, and how they underpin multiple sectors and technologies, these two areas are examined as cross-cutting technologies applied to neurotechnology. Where relevant, the research team has identified a selection of trends, opportunities, challenges and governance debates of note at the intersection of AI/data platforms and neurotechnology.

BOX 5: KEY TAKEAWAYS FROM THE GLOBAL LANDSCAPE REVIEW FOR NEUROTECHNOLOGY

Trends in neurotechnology research and innovation:

- Brain–computer interfaces (BCIs) are becoming increasingly prominent and powerful.
- Neuromodulation therapies are evolving with the development of novel techniques.
- Neurotechnology research is being spurred by an increasing burden of neurological diseases globally, as well as commercial interests.
- Research on the use of artificial intelligence in neurotechnology has grown significantly since 2020.
- Research is concentrated in high-income countries (50% of global output), although many collaborate with middle-income countries.
- Policy documents published relating to neurotechnology are largely from the EU (36.9%), IGOs (30.0%), the United States (21.7%) and the United Kingdom (7.0%).
- Emerging developments in neuroinformatics are driving innovation by leveraging computational methods, data analytics and advanced technologies to enhance understanding of the brain.
- Wearable neurotechnologies are rapidly evolving and encompassing a wide range of devices, with multiple possible use cases.
- Neurotechnology is a relatively small technology area, with most research in the fields of neuroscience, engineering and computer science.
- The United States and China are the largest contributors to research in neurotechnology, responsible for 37% of global output
- Commercial applications of neurotechnology are present in the United States, China, Canada, the United Kingdom, France, Korea, Australia and Israel.

Opportunities associated with neurotechnology:

- Virtual reality holds promise to become increasingly integrated with brain–computer interfaces (BCIs).
- Technological and research developments in neurotechnology hold significant promise for advancing drug delivery methods.
- Ongoing investments in neurotechnology research and innovation highlight its diverse impacts in both health and commercial settings.

Challenges associated with neurotechnology:

- Research and technological challenges need to be overcome for the advancement of neurotechnology.
- Neurotechnology advancements create risks ranging from brain hijacking to infringement of privacy.
- Greater understanding is needed of the complexities and nuances of how current and future neurotechnologies could infringe upon specific rights, and of the necessary governance and regulation priorities and approaches.

Key developments associated with the intersection of AI/data platforms neurotechnology:

- AI-powered brain–computer interfaces are on the rise and investments are rapidly increasing.
- AI-driven neurotechnology has led to the development of a new subcategory: neuroethics.
- Data collection efforts in neurotechnology are growing, but there are risks related to its storage and use.
- Maintaining privacy and agency, especially at the intersection of AI and neurotechnology, are critical challenges.

Oversight mechanisms associated with neurotechnology:

Current data governance mechanisms may be insufficient to address the challenges of neurodata, and new consent mechanisms are emerging.

Globally emerging oversight developments in the sector are spearheaded by a few prominent international institutions and reflect the normative debates surrounding neurotechnologies.

Across the globe, nations and supranational entities are governing neurotechnologies in a variety of ways, which could need coordination and consensus in the future.

The AI–neurotechnology nexus is primarily governed through advisory bodies, groups and consortia, with a focus on neuroethics.

Source: RAND Europe analysis.

8.1. What do we mean by neurotechnology?

Neurotechnology is a rapidly evolving field that consists of devices and procedures used to access, monitor, investigate, assess, manipulate and emulate the structure and function of the neural systems of animals or human beings (UNESCO 2023b). Broadly speaking, neurotechnology uses neural interfaces to read or write information into the nervous system via invasive or non-invasive mechanisms.

Non-invasive technologies are applied to the scalp/skin and include electroencephalography (EEG), functional magnetic resonance imaging (fMRI) and transcranial magnetic stimulation (TMS) (ICO 2023). Invasive technologies are implanted in the brain and include deep brain stimulation (DBS), electrocorticography (ECoG) or cortical implants directly implanted into the cortex to stimulate neuroactivity (Collins and Klein 2023).

Within neurotechnology, brain–computer interfaces (BCIs) and brain–machine interfaces (BMIs) enable direct communication between the brain and external devices. Although sometimes used interchangeably, there are some differences in their scope, invasiveness and application methods. BCIs refer to any technology that enables communication between the brain and an electronic device, whereas BMIs are the actual interfaces between nervous system tissue and devices, typically requiring surgical implantation of electrodes. While BCIs emphasise the computational aspect, focusing on the 'computer' in the brain–device interface, BMIs stress the 'interface' itself, dealing with the direct connection between the nervous system and external devices (Andrews and Koehler 2023).

8.2. What are the emerging trends in neurotechnology research and innovation?

Brain–computer interfaces are becoming increasingly prominent and powerful

BCIs are systems that enable direct communication between the brain and external devices, bypassing traditional neuromuscular pathways. They typically consist of hardware and software components that record, interpret and translate brain signals into commands that control devices or applications. This is done through a complex chain of events, beginning with signal acquisition, whereby BCIs use methods such as EEG, magnetoencephalography (MEG) and fMRI, as well as invasive techniques such as implanted electrodes to acquire signals from the brain. These signals are then processed to extract relevant information through filtering, amplifying and analysing the signals to identify patterns or features that correspond to specific mental states or intentions. Thereafter, pattern recognition techniques or ML algorithms are applied to classify the extracted features, enabling an increasingly complex analysis of the user's brain activity. The distinctive feature of BCIs is that classified signals can be translated into control signals that can be used to interact with external devices such as computers, prosthetic limbs or even mobile applications (Shih et al. 2012).

In the current landscape, advances in signal processing (Wu et al. 2023) and ML (Ahn et al. 2022; Pawan and Dhiman 2023) have improved the accuracy and reliability of non-invasive BCIs, particularly EEG-based systems. For instance, advancements in deep learning, fed by large-scale datasets and greater computational power, have led researchers in many recent studies to adopt deep neural networks (DNNs) to extract features from brain signals and decode brain states (Hossain et al. 2023). Researchers are thus increasingly exploring new electrode designs, signal processing techniques and machine learning algorithms to enhance the performance of non-invasive BCIs.

Another interesting development in the field of BCI research is the growing promise of 'hybrid' BCIs that simultaneously combine multiple methods of imaging to boost performance and accuracy (Almajidy et al. 2023; Li et al. 2023).

There have also been developments in implantable BCIs, which use electrodes implanted directly into the brain to offer high spatial resolution and signal fidelity. Researchers are developing implantable devices with improved biocompatibility, longevity and wireless connectivity to enable long-term, real-world applications such as neural prosthetics and assistive technology. These advances have been spurred on by developments in electrode technologies (Vansteensel et al. 2023), enabling higher resolution and precision in recording and stimulating brain activity. Developments in BCI wireless connectivity (Brown University 2021; Simeral et al. 2021) are reducing the need for external hardware, and removing the risk of infections associated with wired connections. Closed-loop BCIs have also emerged as an important category of implantable BCIs. These systems integrate real-time neural signal processing with responsive feedback, and have shown promise in improving the efficacy of treatments for neurological disorders such as epilepsy, Parkinson's disease and depression (Belkacem et al. 2023; Widge et al. 2018).

Implantable BCIs are increasingly being used for neurorehabilitation.[49] They hold great promise in this regard by facilitating neural plasticity and restoring lost motor or sensory functions in individuals who have experienced spinal cord injuries, stroke or other neurological disorders (Young et al. 2021). Emerging approaches combine BCI technologies with neurofeedback training, virtual reality environments and assistive robotics to promote functional recovery and enhance quality of life.

Emerging developments in neuroinformatics are driving innovation by leveraging computational methods, data analytics and advanced technologies to enhance understanding of the brain

Neuroinformatics involves the analysis and integration of large-scale neuroscience data, and is crucial for understanding complex brain functions and disorders. Notable efforts include the Human Connectome Project and the BRAIN Initiative in the United States, as well as collaborative projects in Europe such as the Human Brain Project (Dipietro et al. 2023). Developments in this field are being spurred by technological advancements and hold great promise for creating a greater understanding of the brain and promoting innovation in use cases and applications. These facilitating drivers include the surge of big data and data integration, with neuroinformatics benefiting from the accumulation of large-scale datasets from sources such as neuroimaging, electrophysiology, genetics and clinical records. Advanced data integration techniques such as data fusion, machine learning and network analysis enable researchers to integrate heterogeneous data types and extract meaningful insights into brain structure, function and dysfunction across different scales of organisation (Dipietro et al. 2023).

49 Neurorehabilitation is a medical process that aims to aid recovery from a nervous system injury and minimise and/or compensate for any resulting functional alterations.

Advancements in neuroimaging and connectomics[50] are also contributing to the greater sophistication of neuroinformatics. High-resolution neuroimaging techniques such as fMRI, diffusion tensor imaging (DTI) and MEG are generating vast amounts of data on brain activity and connectivity patterns. Neuroinformatics tools and pipelines are being developed to process, analyse and visualise neuroimaging data, allowing researchers to map brain networks, identify biomarkers of neurological disorders, and investigate the neural basis of cognition and behaviour (Xia and He 2023; Tavakol et al. 2019).

Neuroinformatics efforts focus on creating comprehensive brain atlases and computational models that provide detailed anatomical and functional information about the brain across different species and developmental stages. With greater innovation, these atlases are enabling comparative analyses and predictive modelling of brain structure and function, and have applications for stroke management (Nowinski 2020), surgical planning and drug targeting (Nowinski 2021).

Neuromodulation therapies are evolving with the development of novel techniques

Neuromodulation involves the use of electrical or magnetic stimulation to modulate neural activity, offering promising treatments for neurological and psychiatric disorders such as Parkinson's disease and depression. Non-invasive neuromodulation techniques continue to be refined and expanded for therapeutic applications, with researchers investigating new stimulation parameters, target locations and treatment protocols to enhance the efficacy, specificity and durability of such therapies for conditions such as depression (Guo et al. 2023), chronic pain (Knotkova et al. 2021) and movement disorders (Mitchell and Starr 2020).

Novel methods and techniques enabling more effective neuromodulation are also emerging. For example, optogenetic and chemogenetic techniques enable the precise control of neural activity using light (for optogenetic) or designer (for chemogenetic) receptors that are engineered to fit therapeutic purposes. Researchers are exploring the therapeutic potential of optogenetic (Mickle et al. 2019) and chemogenetic neuromodulation approaches for modulating neural circuits implicated in neurological and neuropsychiatric disorders such as epilepsy, Parkinson's disease, and addiction, with high spatial and temporal precision (Song et al. 2022).

Bioelectronic medicines, which involve interfacing with the peripheral nervous system to regulate organ function and treat diseases, represent an emerging frontier in neuromodulation research. Researchers are developing implantable devices and neural interfaces to modulate the neural circuits involved in regulating cardiovascular, respiratory, metabolic and immune functions (Berggren 2022), with the potential to revolutionise the treatment of chronic diseases and metabolic disorders (Donati and Indiveri 2023).

Wearable neurotechnologies are rapidly evolving and encompassing a wide range of devices, with multiple possible use cases

The integration of neurotechnology into wearable devices is rapidly expanding, allowing for the continuous monitoring of brain activity and behaviour outside of laboratory settings. Applications range from brain–computer interfaces for gaming and entertainment to mental

50 Connectomics is a field of study within neuroscience that focuses on mapping and analysing the connections between neurons in the brain, known as the connectome.

health monitoring and stress management tools. However, ensuring the sustainability of these products remains a challenge, particularly regarding data privacy, cybersecurity, and long-term support for hardware and software updates.

There are a few key emerging drivers of the current and future proliferation of neurotechnology. For example, EEG headsets are becoming increasingly popular, with the latest headsets featuring dry electrodes, flexible sensors and wireless connectivity, enabling users to record EEG signals with minimal setup and without the need for conductive gels or cumbersome wiring. These devices are used for applications such as neurofeedback training, cognitive enhancement and mental health monitoring, and are promisingly also being delivered in low-cost settings (Muhammad et al. 2022; Lau-Zhu et al. 2019).

Functional near-infrared spectroscopy (fNIRS) devices are another key emerging driver. These wearable devices use near-infrared light to measure changes in the brain, providing insights into neural activation patterns during cognitive tasks, emotional responses and neurorehabilitation interventions. Advances in fNIRS technology have led to portable and wireless devices that offer real-time monitoring of brain function in various environments (Pinti et al. 2018), including classrooms (Bulgarelli et al. 2023), workplaces (Varandas et al. 2022) and home settings (Uchitel et al. 2021).

Wearable neurotechnologies are also being used for sleep monitoring and can provide insights into sleep stages and sleep quality, helping users track and optimise their sleep. For instance, the EU has funded a Horizon 2020 project on wearable technologies for sleep quality improvement (European Commission 2023), and neurotechnology start-ups such as Elemind, which focus specifically on sleep, are gaining traction and attracting increasing investment (Takahashi 2024).

Neurotechnology research is being spurred by an increasing burden of neurological diseases globally, as well as commercial interests

The anticipated increase in the prevalence of neurological conditions globally is set to drive the growth of the neurotechnology market in the coming years (Perez et al. 2023). Neurological conditions encompass various disorders or diseases affecting the brain, including Alzheimer's disease, Parkinson's disease, epilepsy and migraine. The American Heart Association has projected that Alzheimer's disease and related dementias will impact approximately 9.3 million people in the United States by 2060 (Alzheimer's Association 2022), and the WHO has stated that an estimated 5 million people worldwide are expected to be diagnosed with epilepsy annually (WHO 2024c). Neurotechnology is playing a crucial role in diagnosing and treating these conditions through methods such as brain imaging, neurostimulation, neurofeedback and brain–computer interfaces.

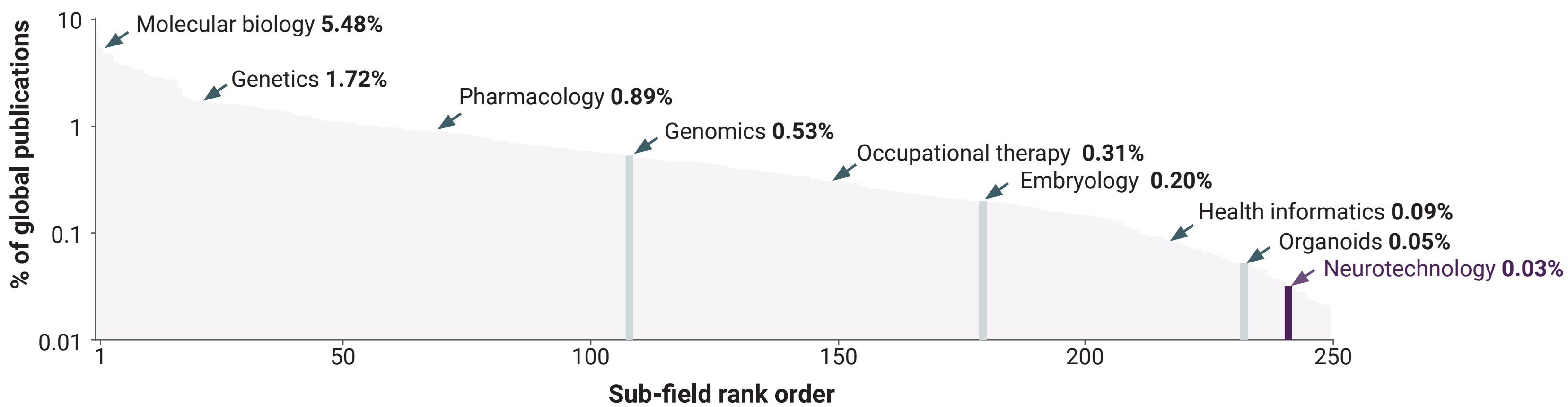
These drivers and global health imperatives have and are increasingly translating to interest and investment in neurotechnologies, including from the private sector. Commercial technological advancements represent a significant trend driving research and innovation, with companies adopting innovative technologies to maintain their market positions (Garden et al. 2019). The 2022 launch of Neuralace by Blackrock Neurotech is a case in point. Resembling a lace thinner than an eyelash, Neuralace can cover large areas of the brain's surface, providing insights into the technology powering future brain–computer interfaces. The system helps patients regain tactile function, limb and prosthetic movement, and the ability to control digital devices.

Neurotechnology is a relatively small technology area, with most research in the fields of neuroscience, engineering and computer science

Between 2019 and 2023, 16,178 articles were published relating to neurotechnology, mostly in the fields of neuroscience, engineering and computer science. Neurotechnology is responsible for only 0.03% of the global publication share, ranking it 239 when compared to all sub-fields (Figure 24).

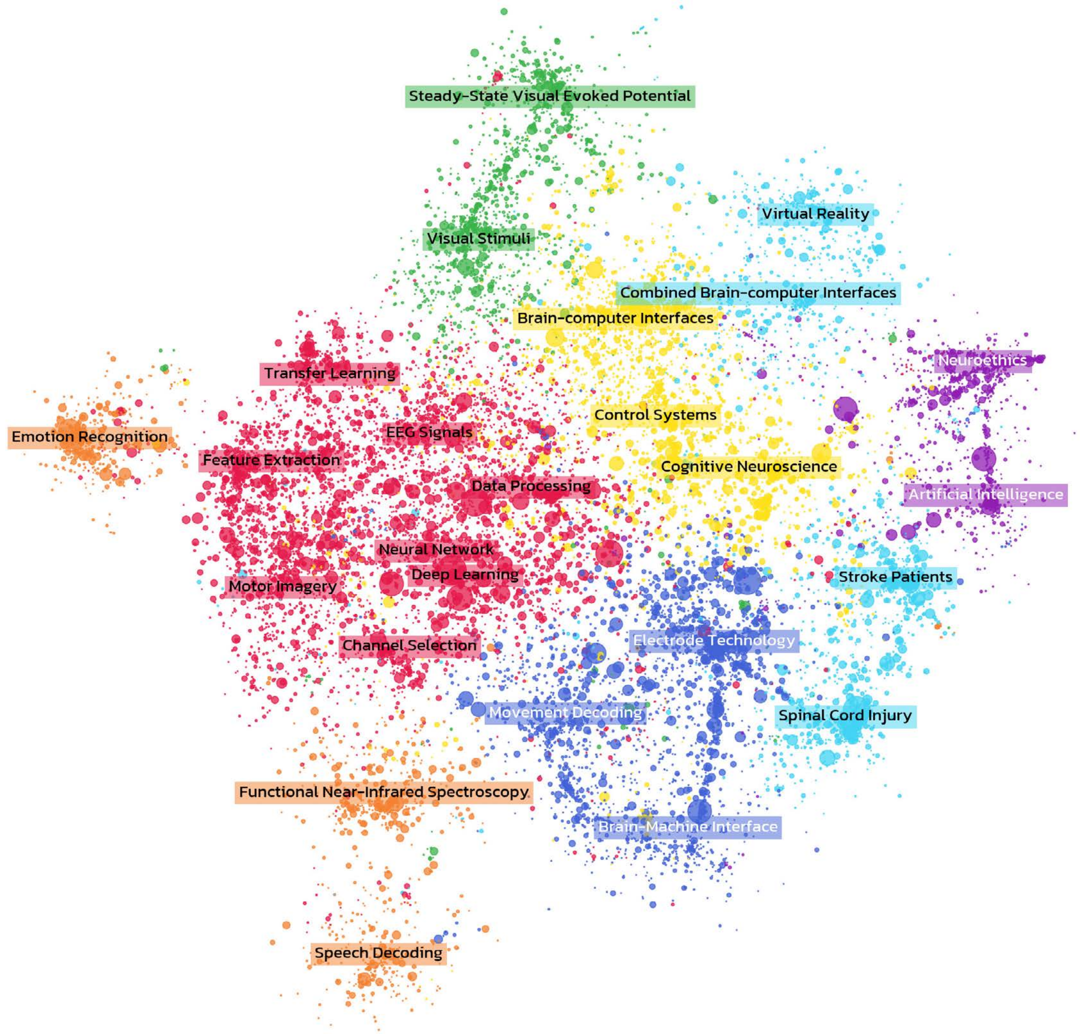
Topic modelling reveals a range of research topics. As the topic map presented in Figure 25 shows, much research is focused on data and signal processing (red, orange and green clusters), in particular EEG signals. There are also clusters of research on engineering aspects (dark blue and yellow), medical application (light blue) and societal impacts (purple). It is interesting to note that two separate, but similar, keyword phrases were identified in topics: brain–computer interface (yellow) and brain–machine interface (blue). It is not possible to determine whether this is because different terminology is favoured in different fields or applications, whether they are used as synonyms, or if there is a more fundamental difference in use.

Figure 24. Neurotechnology global publication share ranked against all sub-fields of biological research



Source: RAND Europe analysis.

Figure 25. Neurotechnology topic map (publications between 2019 and 2023)



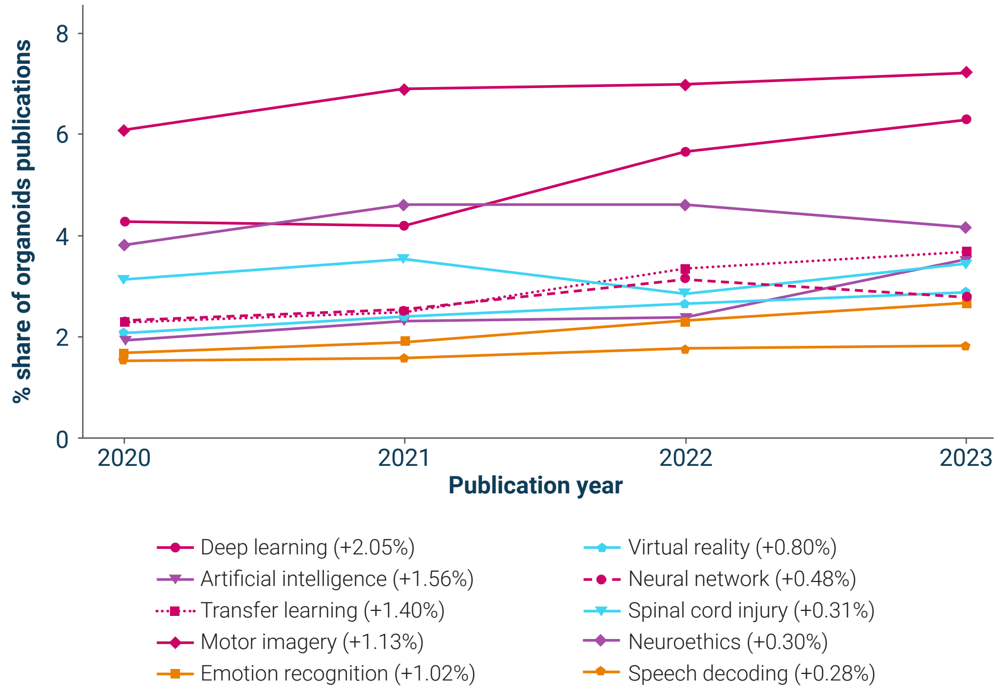
Source: RAND Europe analysis.

Research on the use of artificial intelligence in neurotechnology has grown significantly since 2020

The top three topics in terms of growth in relative share of publications since 2020 are deep learning (+2.0%), AI (+1.6%) and transfer learning (+1.4%), the last of which is defined as the reuse of existing machine learning models in new and domains (Figure 26).

The volume of citations of neurotechnology in grey literature sources is low and mostly focused on the topic of neuroethics. The top ten topics (ranked by the average number of citations per paper) are listed in Table 12. The only medical topic with any significant policy attention is spinal cord injury.

Figure 26. Top ten fastest growing neurotechnology topics (relative publication share 2019–23)



Source: RAND Europe analysis.

Table 12. Top ten neurotechnology topics (ranked by mean Overton cites per paper)

Topic	Publication count	Total Overton Cites	Mean cites per paper
Neuroethics	972	199	0.20
Artificial intelligence	529	30	0.06
Cognitive neuroscience	752	31	0.04
Spinal cord injury	772	29	0.04
Combined brain–computer interfaces	598	12	0.02
Speech decoding	331	6	0.02
Brain–computer interfaces	1,826	33	0.02
Data processing	1,023	17	0.02
Electrode technology	1,301	21	0.02
Stroke patients	645	9	0.01

Source: RAND Europe analysis.

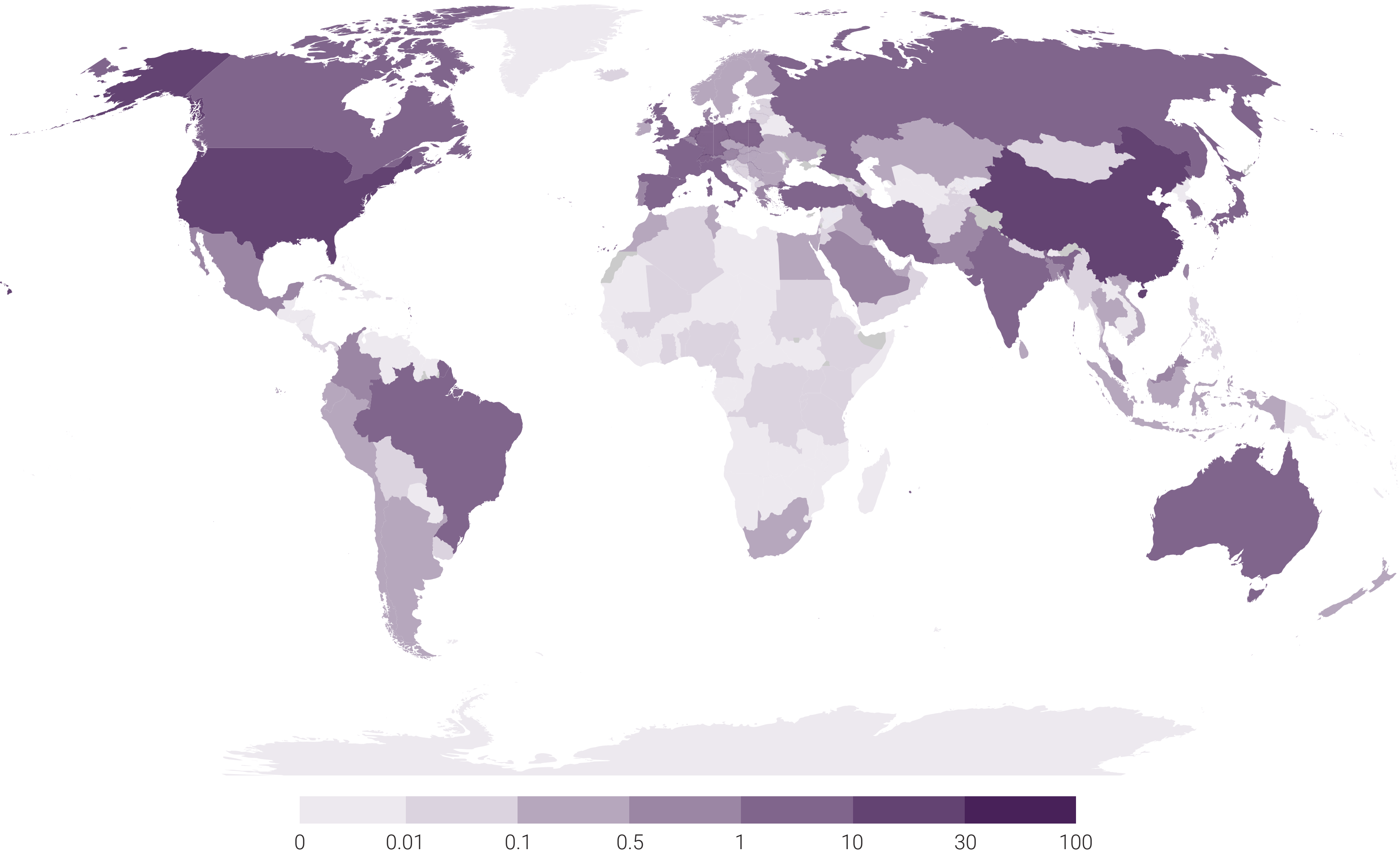
The United States and China are the largest contributors to research in neurotechnology, responsible for 37% of global output

In terms of relative share of all neurotechnology publications, the leading nations are China (19.8%), the United States (18.8%), India (6.3%), the United Kingdom (5.9%) and Germany (4.3%). The global map (Figure 27) shows a more balanced distribution than seen for organoids – of all countries producing more than 1% of global output, six are middle-income compared to only two in organoids. In South America, countries with the highest publication outputs are Brazil (1.4%), Colombia (0.5%) and Argentina (0.4%). In Africa, four countries produce more than 0.1% of neurotechnology publications: Egypt (0.3%), South Africa (0.2%), Morocco (0.2%) and Tunisia (0.1%). Six countries in Asia produce more than 1% of publications: China (19.8%), India (6.3%), Korea (3.5%), Japan (3.1%), Iran (1.7%), Singapore and Turkey (both 1.2%).

Summary publication indicators for countries producing at least 1% of global output are listed in Table 13. Unlike the other technology areas in this study, citation impact for neurotechnology (see mean citation percentile column) is not highest only in Europe, with Singapore (79.2), Switzerland (78.7), Australia (75.9), Korea (75.5) and Germany (74.8) the leading countries.

As Table 13 shows, countries producing the highest proportion of their national publication output in neurotechnology are Singapore (0.13%), Korea (0.1%), Switzerland (0.08%), China (0.07%) and India (0.07%).

Figure 27. Global map showing the share of neurotechnology publications by author country



Source: RAND Europe analysis.

Table 13. Publication metrics for countries producing more than 1% of global output in neurotechnology research

Continent	Country	% of global neurotechnology publications	% of national publication output	Mean citation percentile
Asia	China	19.8	0.07	72.5
Asia	India	6.3	0.07	65.6
Asia	Iran	1.7	0.06	70.6
Asia	Japan	3.1	0.06	67.2
Asia	Korea	3.5	0.10	75.5
Asia	Singapore	1.2	0.13	79.2
Asia	Turkey	1.2	0.04	69.2
Europe	France	2.8	0.04	69.4
Europe	Germany	4.3	0.05	74.8
Europe	Italy	3.4	0.06	74.7
Europe	Netherlands	1.5	0.05	74.6
Europe	Poland	1.2	0.05	73.5
Europe	Russia	2.5	0.05	63.7
Europe	Spain	2.6	0.05	71.3
Europe	Switzerland	1.8	0.08	78.7
Europe	United Kingdom	5.9	0.06	73.9
North America	Canada	3.3	0.07	73.7
North America	United States	18.8	0.05	72.3
Oceania	Australia	2.5	0.06	75.9
South America	Brazil	1.4	0.02	65.6

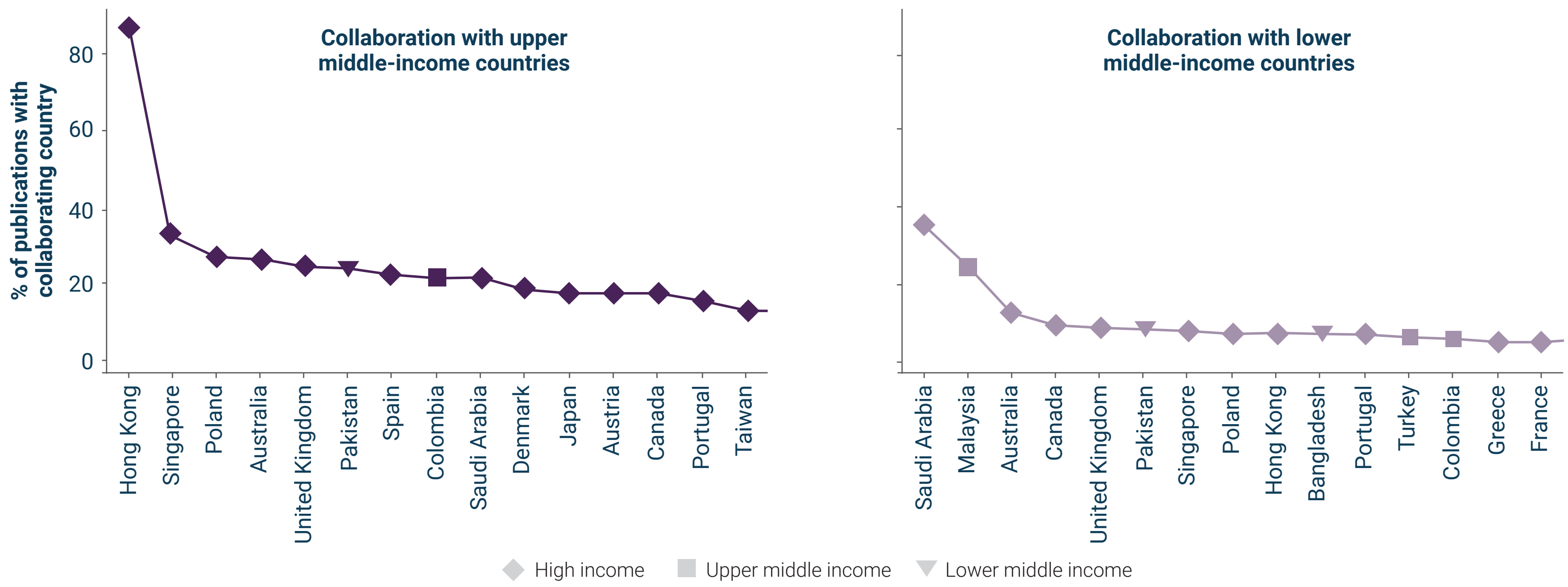
Source: RAND Europe analysis.

In terms of funders acknowledged in published works (representing 67.7% of the indexed articles), the highest relative share is for funders in China (58.4%), the United States (26.3%), Korea (9.7%), Japan (5.8%) and the United Kingdom (4.3%).

Research is concentrated in high-income countries (50% of global output), although many collaborate with middle-income countries

Figure 28 illustrates the collaboration of high-income countries with middle-income countries on neurotechnology research. The two plots (based on countries producing more than 0.5% of global publications) show collaboration rates with upper middle-income countries on the left and with lower middle-income countries on the right. Countries with the highest collaboration rate with upper middle-income countries are Hong Kong (87.0%), Singapore (33.3%), Poland (27.7%), Australia (26.1%) and the United Kingdom (24.9%). In terms of collaboration with lower middle-income countries, the highest rates are in Saudi Arabia (35.3%), Malaysia (24.3%), Australia (12.3%), Canada (9.0%), the United Kingdom (8.6%) and Singapore (8.0%).

Figure 28. Rates of neurotechnology research collaboration with upper and lower middle-income countries



Source: RAND Europe analysis.

Commercial applications of neurotechnology are present in the United States, China, Canada, the United Kingdom, France, Korea, Australia and Israel

The global distribution of patent share in neurotechnology (in terms of extended patent families) is particularly skewed to high-income countries (Figure 29): of the top 20 countries by volume, only China and India are not high-income economies. Countries that produce the most patents are the United States (62.5%), Korea (3.0%), Australia (2.7%), Canada (2.2%) and Israel (2.1%). There is little patent activity in South America (only Brazil has any) and none in Africa. In Asia, four countries have more than 1% of global patents: Korea (3.0%), Japan (2.0%), Israel (1.7%) and China (1.0%).

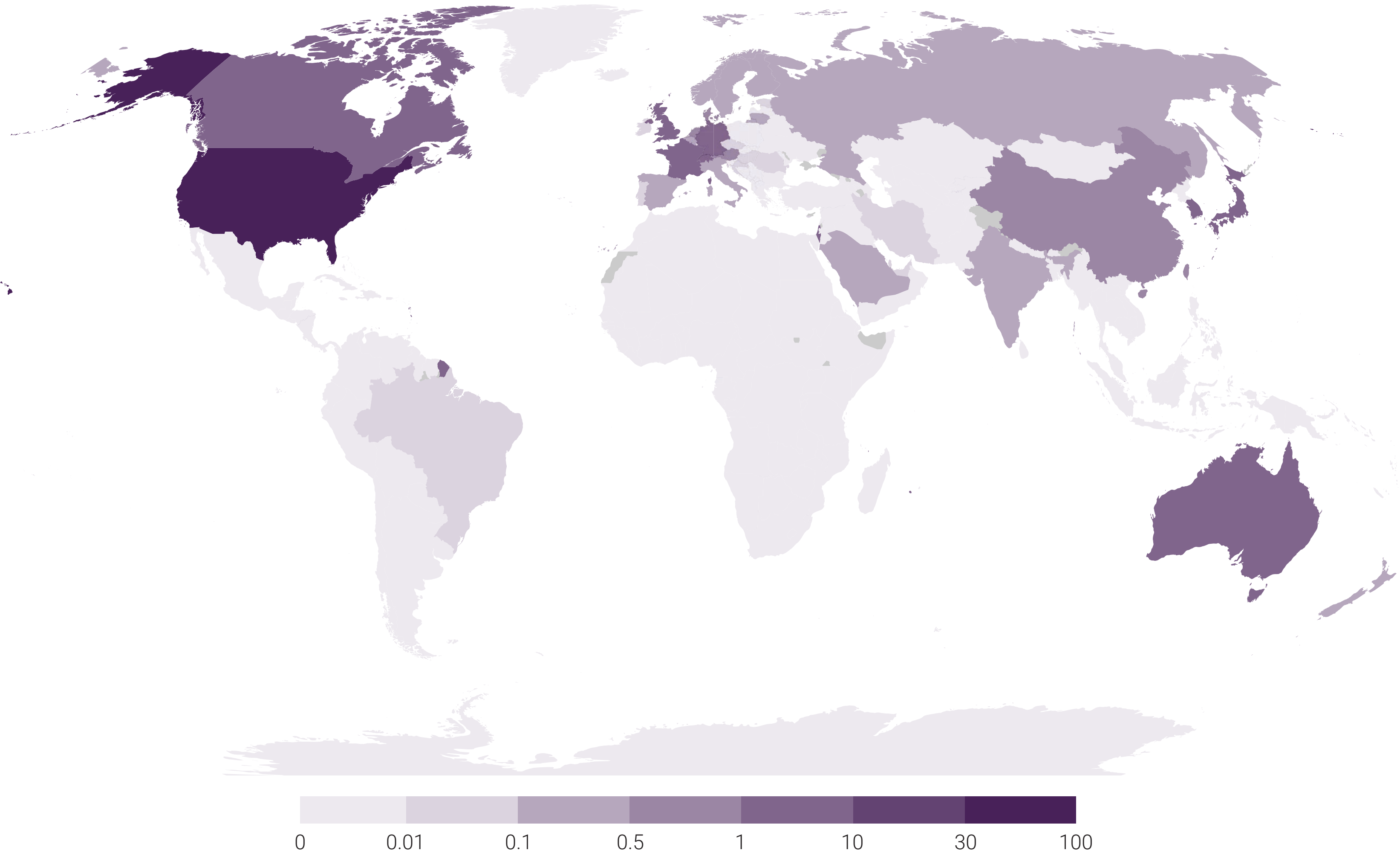
Table 14 provides summary indicators for patents and companies registered in countries that have more than 0.1% of global patents. Nations with the highest number of neurotechnology companies indexed in Crunchbase are the United States (247), China (16), Canada (15), France and the United Kingdom (14). In terms of relative share of national patent output (see % of national patents column in Table 14), Australia (0.64%), Israel (0.39%) and the United States (0.23%) have registered the highest proportion of their national patent output in neurotechnology.

Table 14. Commercialisation indicators for countries registering more than 0.5% of global patents on neurotechnology research

Continent	Country	% of global neurotechnology patents	% of national patents	Crunchbase companies
Asia	China	1.0	0.02	16
Asia	Israel	1.7	0.39	11
Asia	Japan	2.0	0.02	5
Asia	Korea	4.0	0.04	5
Asia	Taiwan	0.5	0.02	1
Europe	Austria	0.6	0.11	2
Europe	Denmark	0.5	0.14	1
Europe	France	1.4	0.04	14
Europe	Germany	1.5	0.02	13
Europe	Netherlands	1.0	0.08	8
Europe	Switzerland	1.1	0.08	12
Europe	United Kingdom	1.3	0.08	14
North America	Canada	1.6	0.16	15
North America	United States	57.6	0.23	247
Oceania	Australia	2.3	0.64	7

Source: RAND Europe analysis.

Figure 29. Global map showing the share of neurotechnology patents by applicant country



Source: RAND Europe analysis.

Policy documents published relating to neurotechnology are largely from the EU (36.9%), IGOs (30.0%), the United States (21.7%) and the United Kingdom (7.0%)

The amount of published grey literature directly related to neurotechnology is summarised in Table 15 for the top 15 countries (ranked by policy document count). It is notable that IGOs have the highest proportion of their output in neurotechnology (0.07%), more than any country or the EU.

Table 15. Neurotechnology policy document indicators for the top 15 countries (ranked by document count)

Continent	Country	Policy document count	% of global neurotechnology policy documents	% of national policy documents
Global	IGOs	231	30.0	0.07
North America	United States	167	21.7	0.01
Europe	EU	83	10.8	0.05
Europe	United Kingdom	54	7.0	0.02
Asia	Japan	30	3.9	0.01
Europe	Spain	23	3.0	0.01
Oceania	Australia	20	2.6	0.02
Europe	Germany	18	2.3	0.01
Europe	Italy	14	1.8	0.03
Europe	Sweden	13	1.7	0.01
Europe	France	12	1.6	0.01
Europe	Belgium	12	1.6	0.04
North America	Canada	11	1.4	0.01
Europe	Netherlands	11	1.4	0.01
Asia	Indonesia	10	1.3	0.04
Asia	Singapore	10	1.3	0.04
Europe	Switzerland	5	0.6	0.02

Source: RAND Europe analysis.

8.3. What are the opportunities associated with neurotechnology?

Virtual reality holds promise to become increasingly integrated with brain–computer interfaces

Neuroadaptive virtual reality (VR) environments based on real-time analysis of the user's neural signals are becoming possible. These systems could use BCIs to monitor the user's cognitive state, emotions and preferences, and adapt the VR experience accordingly to enhance immersion, engagement and overall user experience (Baker and Fairclough 2022). By providing interactive and engaging VR environments coupled with real-time neural feedback, BCI–VR systems can promote motor learning, cognitive function rehabilitation and emotional regulation in individuals with neurological disorders or cognitive impairments (Leeb and Pérez-Marcos 2020).

BCIs combined with VR technology have the potential to facilitate telepresence and social interaction by enabling real-time communication and collaboration between individuals in virtual environments. BCIs integrated with VR gaming platforms also offer new opportunities for immersive gaming experiences. Users could game environments using their brain signals, and VR–BCI systems could adapt game difficulty levels or content based on the user's cognitive load, engagement level or emotional responses, enhancing gameplay experiences (Khan 2020).

Technological and research developments in neurotechnology hold significant promise for advancing drug delivery methods

Progress in the field of nanotechnology and microfluidic technologies is creating opportunities in the development of programmable drug delivery platforms in the form of implantable probes (Yoon et al. 2022; Luo et al. 2023). The most advanced systems support the precise temporal control of multiple drugs that are infused independently over long periods of time with minimal damage to the tissues. The design of these systems allows for studies of animals behaving naturally (Ma et al. 2022).

Ongoing investments in neurotechnology research and innovation highlight its diverse impacts in both health and commercial settings

Advancements in neurotechnologies are expected to evolve possible medical treatments and create new applications beyond medicine that could become widely used in, for instance, the gaming fitness and well-being industries, which have emerged as areas of commercial, non-invasive neurotechnology innovation (Research and Markets 2023).

The opportunities and drivers that could make myriad, effective and large-scale use of life changing neurotechnologies include the sector's potential to reap widespread benefits for future funders – including the government and private corporations. Investment in neural interfaces is a growing proportion of medical research that is expected to grow further in the coming years (ICO 2023). Moreover, the likelihood of devices such as EEG headsets becoming widely available, accessible and popular, and the promise of dramatic products and services that could enable 'typing by the brain' (Willett et al. 2021) becoming a reality, could potentially drive further investment in next generation innovation.

8.4. What are the challenges associated with neurotechnology?

Research and technological challenges need to be overcome for the advancement of neurotechnology

Despite advancements in interpreting and simulating parts of the nervous system, researchers face many obstacles in developing more complex and sophisticated applications. For instance, creating biocompatible materials that can be easily fitted and accepted by the human brain, while lasting sustainably and ensuring scalability, remains a challenge (Fekete et al. 2023). Moreover, capturing and decoding the brain's complex electrical signals need advancements in high-resolution signal recording and stimulation. Similarly, advanced algorithms and computational techniques to meaningfully interpret these complex and non-linear neural signals will need to be developed (Saha et al. 2021).

Current neural implants mostly engage precise small populations of neurons or use a 'scatter gun' approach to record or stimulate neurons randomly. More effective interfaces need to be able to engage larger number of neurons in a sophisticated manner (Lancet 2019). Challenges of scalability, power consumption, high manufacturing and development costs, as well as regulatory hurdles, will need to be overcome as the technology progresses further (Chen and Pesaran 2021)

Neurotechnology advancements create risks ranging from brain hijacking to infringement of privacy

The collection and analysis of neural data raise concerns about privacy and data security. Unauthorised access to sensitive brain-related information could lead to identity theft, manipulation or discrimination, with several ramifications for individual autonomy (Jwa and Poldrack 2022). Ongoing debates on these important concerns around individual and collective human rights are reflected in the various emerging governance mechanisms that cover the innovation and regulation of neurotechnologies. In recent years, evidence has emerged of the greater potential of malicious actors to hack into networked devices, including brain implants. In addition to information theft, these attacks have tremendous potential to cause bodily harm such as stopping implant stimulus, interfering with device batteries and even inducing tissue damage through 'brainjacking' (Pycroft et al. 2016).

The current and potential dual-use nature of neurotechnologies raises several ethical, societal and security implications, including on the nature of informed consent. For example, neurotechnologies could be misused for surveillance and control, which could at a micro scale hamper privacy and individual autonomy (Moreno et al. 2017). When potentially used by global actors, including governments, corporations and hostile third-party stakeholders at a much larger scale, these technologies could in the long term be misused to disrupt global ideas of democracy and transparency, and diminish public trust in institutions (Ienca et al. 2018).

Powerful state and non-state actors could also potentially weaponise neurotechnologies to harm individuals or groups of individuals and violate human rights by inducing pain, altering cognitive function and manipulating behaviour at a large scale (Hassan et al. 2023). Ethical and humanitarian concerns could arise from such a scenario, and could exacerbate global inequality and suffering, especially in conflict ridden areas of the world.

Greater understanding is needed of the complexities and nuances of how current and future neurotechnologies could infringe upon specific rights, and of the necessary governance and regulation priorities and approaches

The convergence of neurotechnologies and other emerging technologies with AI is creating further complexities in an already complex and disruptive field (Mantellassi 2022), making their impact even more unpredictable, disruptive and complex. A recent report from the United Nations Educational, Scientific and Cultural Organization (UNESCO) highlighted that neurotechnologies have the potential to decode and influence behaviour, cognition and memory. This has led to calls for specialist 'neurorights' that would encompass the concepts of mental privacy[51] and cognitive liberty.[52]

Scientists and bioethicists have called for a new international legal and human rights framework that can be understood as a new set of human rights for the brain, offering individuals enhanced legal safeguards that go beyond current laws and regulations (Ochang et al. 2023). The path to implementing these rights is the subject of much debate, with concerns around the dilution of existing human rights, the challenges of governing a rapidly changing technology, and the need to incorporate diverse interpretations of neurorights shaped by people's cultural, economic and political contexts.

Related to this, ascertaining what informed consent means in practice in the case of neurotechnologies is also a tricky and challenging task that governments and global stakeholders will have to grapple with in the near future, especially when dealing with vulnerable populations or those unable to provide consent, including patients and children (for instance, there are already many cases of neurotechnology being used in educational settings).

Governments and corporations must also manage the ethical implications of using neurotechnologies for enhancement, treatment or research; consider questions of fairness, justice and equity; and explore the potential ramifications of altering human cognition or behaviour (Bhidayasiri 2024).

Ensuring global equity in future neurotechnology innovation is also a potential challenge. At an individual and micro level debates concern the potential exacerbation of socioeconomic disparities if neuroenhancement becomes available only to privileged individuals or populations. At a societal and global level, with the ever-greater generation and use of neurodata there is an emerging issue of whether the data is representative and inclusive. Neurorights advocates and data-ethicists from the developing world have steadily pointed out how current developments in the field are reliant on the use of global population datasets, with a notable lack of local datasets and brain imaging data from LMICs. This has potential ramifications for the inclusivity of neurotechnology innovation and design practices, and may lead to biases in insights generated (Bhidayasiri 2024).

51 Mental privacy proposes that individuals should have control over access to their neural data and to information about their mental processes and states that can be obtained by analysing it.

52 The freedom of an individual to control their own mental processes, cognition and consciousness (UNESCO 2023c).

Another layer of complexity in ascertaining what the future of neurotechnologies should look like is the issue of abandonment. This concept deals with the legal and ethical ramifications that arise when makers of neural implants 'abandon' their projects, whether due to commercial or regulatory bottlenecks. A leading example is the closure of ATI (a company treating cluster headaches through their implants) after failing to get FDA approval in the United States (Drew 2022). The issue of abandonment is related to congruent debates on the sustainability of neural devices, as well as patients' right to repair. It is becoming an increasingly pressing issue with the rapidly blurring line between what differentiates medical and consumer neurotechnology. While neurotechnology has been approved and used in the management of neurological disorders for decades, there is now also rapid development in the consumer sector, and the use of neurodata for personal well-being, sports, marketing and even workforce monitoring is leading to the proliferation of these technologies beyond the medical world and into our daily existence. This compounds and further complicates the task at hand for governance (Drew 2022).

8.5. What are some of the key developments associated with the intersection of AI/data platforms and neurotechnology?

AI-powered brain–computer interfaces are on the rise, and investments are rapidly increasing

Investments in AI-driven neurotechnology have surged in recent years, reaching $30 billion in August 2023, with notable investments in wearable neurotechnology. Investments were led by the United States (accounting for 45% of investments) and the EU (23%), followed by the United Kingdom and Asia (10% each) (Neurotech.com 2023). The main trend in AI-driven neurotechnology concerns the application of AI to control systems in neural implants, using brain–computer interfaces. AI is prime for use in BCI and BMI,[53] specifically in signal processing and the control of algorithms using DL and DNN (Rainey and Erden 2020; Jaber et al. 2024). AI-powered BCIs can enhance disease detection using their ability to track changes in neural activity for medical diagnosis and monitoring, for example monitoring the progression of neurodegenerative disorders such as Alzheimer's (Sudharson et al. 2023). The development of AI-driven BCI's – also known as brain-AI interfaces – can advance cognitive enhancement and neuroprediction, with applications ranging from prosthetic control to audio and visual sensing (Zhang et al. 2020).

Brain activity can also be monitored through EEG and MRI. AI and ML algorithms have used DL to monitor brain activity in EEG and MRI and processed EEG images to classify data and detect/diagnose disease (Singh et al. 2023).

53 BMIs are a subset of BCIs that use brain activity to control machines external to the brain (Graceshalini, Rathnamala, and Prabhanantha Kumar 2023).

AI-driven neurotechnology has led to the development of a new subcategory: neuroethics

Ethical considerations are much more pervasive in neurotechnology than other biotechnology subsectors due to the risks of collecting neural data through implants and overwriting information into nervous systems. These risks are not detectable given the unconscious nature of nervous systems and can lead to adverse impacts on mental privacy, agency, autonomy and identity (Berger and Rossi 2023). While the concepts of fairness, accuracy, security and transparency are common across biotechnologies, integrity and ethics challenges in AI–neurotechnology also cover mental privacy, well-being, and human identity and agency (Eaton 2023). This is due to the additional considerations of consent versus non-consent in an unconscious nervous system (Berger and Rossi 2021).

The UNESCO International Bioethics Committee has expressed concern about the potential for AI to imitate human cognition, language and reasoning in neurotechnology (UNESCO 2021). These issues can aggregate during the rapid and unregulated commercialisation of products.

An unregulated brain–computer connection may also be at further risk regarding bioweapons, hacking of neural implants and cognitive enhancement. The hacking of neural implants and neurotechnologies is referred to as 'biohacking', and could lead to sensitive data being stolen or exploited, cognition being influenced, and inequalities being exacerbated (Doya et al. 2022).

As such, a new field of study called 'neurocomputational ethics' is emerging to address the ethical challenges associated with AI-driven neurotechnology, building on existing neuroethics concepts. There is a research group dedicated to the topic (NC State University 2024), and it has been discussed in recent consortia events.

Data collection efforts in neurotechnology are growing, but there are risks related to its storage and use

As neurotechnologies for research and clinical use continue to develop at a rapid rate, so does the quantity of neurodata (Jwa and Poldrack 2022). The proliferation of direct-to-consumer neurotechnologies including BCIs, neurostimulation devices, VR systems and other wearables also contribute to vast amounts of neurodata (Kreitmair 2019). The integration of AI and ML into neuroscience technologies have advanced the processing and analysis of neuroscience data, contributing to scientific advancements in understanding brain health and disease. It has also highlighted the burgeoning future for predictive and precision neurotechnologies, which have received substantial commercial interest.

The scale of data produced from these varied sources and advancements in analytical capabilities through AI and ML integration are expected to continue having a positive impact in research through enhancing rigour and reproducibility, and increasing capabilities to understand the inherent complexities of the brain (Jwa and Poldrack 2022). However, these benefits do not come without the related challenges of privacy, autonomy and consent. While these concerns pervade all fields that collect human subject data, there are heightened concerns regarding neurodata, which may face more barriers to privacy and anonymisation and which are often viewed as having greater sensitivity than other types of personal data (Jwa and Poldrack 2022).

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Maintaining privacy and agency, especially at the intersection of AI and neurotechnology, are critical challenges

Technological developments including BCIs and neuromodulators are expected to continue to improve the diagnosis and treatment of neurological diseases and mental illness; however, as these technologies mature and gain capabilities, there are also concerns that they will develop the capacity to alter individual agency (Goering et al. 2021). Furthermore, some researchers anticipate that AI integration with neuroscience data will facilitate 'AI neuroprediction', which may soon have powerful predictive capabilities, including anticipating the risk of developing neurological disorders such as Alzheimer's Disease (Young et al. 2020). Others believe that neuroscience data will have the capacity to predict future behaviours, including criminal behaviour, raising concerns about the potential for bias, discrimination, coercion and self-fulfilling prophesies (Tortora et al. 2020). Future possibilities around neurotechnologies, including neuroprediction, neuromarketing and pervasive neurotechnologies, are also spurring interest in pre-emptive neuroscience data governance mechanisms (Eke et al. 2022)

Issues related to privacy and the need to anonymise data, particularly for sharing and reuse, as needed for most applications involving AL and ML, are key concerns for neurodata governance. With certain types of neurodata, in particular various types of brain imaging data, issues around privacy are much more challenging as brain folding structures imaged through MRIs are sufficiently unique as to be identifying (Jwa and Poldrack 2022). These images also frequently include features of the face or skull, providing further identifying information (Jwa and Poldrack 2022). There are also notable concerns about the potential of de-anonymisation from data linkage, as recent research indicates that when images are integrated with other data sources, such as brain activation patterns, they may be identifying. For example, it has recently been shown that 'functional connectomes' are unique to individuals (Ravindra, Drineas and Grama 2021).

Neurodata are frequently characterised as being more sensitive than other types of health data, with some describing it as being 'more proximal to personhood' and having strong ties to individual identity (Jwa and Poldrack 2022). As mentioned previously, there is a growing movement in scholarship around the concept of neurorights, which are being championed using existing human rights frameworks as a model (Jwa and Poldrack 2022). Neurorights are proposed as an addition to the Universal Declaration of Human Rights (Yuste et al. 2017). Neuroethicists share broad concerns in this domain including protection of 'cognitive liberty' and concerns about the 'commodification of brain data' (Mineo 2023).

8.6. What are some of the developments associated with the oversight of neurotechnology research and innovation?

There are a range of mechanisms across the globe that provide oversight for neurotechnology research and its applications. These mechanisms appear to be distributed across multiple sectors such as consumer goods, healthcare and research settings. This section highlights some examples of oversight from across the globe and lays the foundations of a comprehensive analysis on oversight mechanisms underpinning neurotechnology research and use that can be found in the accompanying technology oversight report.

Current data governance mechanisms may be insufficient to address the challenges of neurodata, and new consent mechanisms are emerging

There is ongoing debate as to whether current data protection and health data protection mechanisms can be modified to cover areas specific to neuroscience data, or whether the concerns around neuroscience data are sufficiently particular (i.e. complexity, scale and association with personhood and identity) to warrant specialised governance mechanisms (Eke et al. 2022). Some believe that the perceived need for specialised governance of neuroscience data due to its sensitive and intimate character may be a philosophical rather than technical assessment, as other types of data such as GPS and internet usage can be just as intimate and identifying (Jwa and Poldrack 2022). Some have argued that neuroscience data should have a more granular consent process than other types of health data, as this would give individuals greater control over their personal data throughout the research process and in subsequent research activities (Goering et al. 2021). However, a more granular consent process would also be expected to slow research activities and provide a significant hurdle for secondary research (Jwa and Poldrack 2022).

To address this, several novel consent approaches have been suggested, such as dynamic consent[54] (Kaye et al. 2015) and data trusts[55] (including those that use blockchain ledgers) (Lomotey, Kumi and Deters 2022). Some organisations pursue broad consent, which provides generic consent for open data sharing. For example, the international initiative Open Brain seeks to facilitate sharing of brain imaging data while maintaining privacy. It supplies consent tools and guidance for developing consent processes that grant broad permissions for data reuse, while minimising the risk of reidentification (Bannier et al. 2021).

Following the Genetic Information Non-discrimination Act (GINA), which was developed through acknowledgement of the 'specialness' of genetic data (i.e. how general data protection legislation does not offer sufficient protection of genetic information given that it is inherently identifying) and its implications for regulation and policy, some US scholars have proposed the Neuroscience Information Non-discrimination Act (NINA). This act would consider the particularities of neuroscience data and information, with an explicit focus on preventing harms from data misuse (Jwa and Poldrack 2022). The act would seek to balance the promotion of open science values with proactively protecting against the potential harms of neurodata-based discrimination (Jwa and Poldrack 2022). While

54 Dynamic consent is an approach to informed consent in research that allows participants to engage in an ongoing and interactive process of providing and managing their consent preferences.

55 Data trusts are legal frameworks that govern the collection, storage, management and sharing of data in a trustworthy and responsible manner.

such an act has only been discussed and is far from enactment or implementation, it provides an interesting look into the potential future of neurodata governance.

Globally emerging oversight developments in the sector are spearheaded by a few prominent international institutions and reflect the normative debates surrounding neurotechnologies

The OECD Recommendation on Responsible Innovation in Neurotechnology offers normative guidance and is a notable example of one of the first soft law instruments to govern the sector. The OECD is calling for an international standard on responsible innovation, particularly with the convergence of AI and neurotechnology (OECD 2019).

Global initiatives that aim to address the governance of neurotechnologies from a human rights perspective include those spearheaded by UNESCO, such as the 2021 report by its International Bioethics Committee on the ethical issues related to neurotechnologies, and the 2023 International Conference on Ethics of Neurotechnology, which called for the development of a global normative instrument and ethical framework similar to UNESCO's recommendation on the Ethics of Artificial Intelligence.

UNESCO's development of an ethical framework also includes a focus on AI-enhanced neurotechnology (UNESCO 2023d). Section II.4 of a recent UNESCO International Bioethics Committee report on the ethical issues of neurotechnology refers specifically to AI in neurotechnology, particularly around the potential for AI to imitate human cognition, impacting sensing, language and reasoning, among other cognitive functions (UNESCO 2021).

The human rights approach is mirrored in the Council of Europe's Strategic Action Plan on Human Rights and Technologies in Biomedicine in 2020, and the Organization of American States' adoption of the Inter-American Declaration of Principles Regarding Neuroscience, Neurotechnologies, and Human Rights in 2023.

Across the globe, nations and supranational entities are governing neurotechnologies in a variety of ways, which could need coordination and consensus in the future

National governments have engaged with neurotechnology governance in varying ways. A leading example of a hard law approach is the 2021 constitutional reform in Chile, which legally protects mental privacy and free will and gives personal brain data the same status as an organ so that it cannot be bought or sold, trafficked or manipulated (Cornejo-Plaza et al. 2024).

Some governments have taken a softer approach that is influenced by global debates, including those led by international organisations. Examples of such developments include the 2021 Digital Rights Charter in Spain, aimed to be used as a reference guide for future action, and the 2022 Neurorights charter in France, which called for responsible innovation, international cooperation, and the use of neurotechnologies for 'healing and repair' (Leger 2024).

Multiple regulatory frameworks in nations also govern a range of current neurotechnologies, and might potentially require further coordination. Examples of these include oversight by agencies such as the FDA in the United States, the European Medicines Agency in Europe, and regulatory bodies in emerging economies such as India and Brazil. These frameworks aim to ensure the safety, efficacy and ethical use of neurotechnological interventions. In addition, ethics committees and guidelines have been created by the leading medical research bodies of some nations, for example the National Institutes of Health (NIH) in the United States and the National Research Ethics Service (NRES) in the United Kingdom provide ethical guidance for neuroscience research.

Nations are also responding in a similar way to the confluence of neurotechnologies and AI. For instance, in Japan, guidelines from the Japanese Society for Artificial Intelligence's ethics committee propose that AI should be treated as a 'quasi-member of society', with Article 9 stipulating that AI must comply with the ethical guidelines to address issues stemming from unsupervised autonomy (Doya et al. 2022). In contrast, Chile, as outlined earlier, is taking a regulatory 'neurolaw' approach to this confluence (Perelló 2022), with the regulation outlining consent in AI–neurotechnology and requiring any technology to be reversible.

The AI–neurotechnology nexus is primarily governed through advisory bodies, groups and consortia, with a focus on neuroethics

There are a number of institutions and working groups in the field of neuroethics that will have potential impacts on computational ethics relating to the convergence of AI-driven neurotechnology. For example, the Neuroethics Working Group (NEWG) is an international group hosted by the NIH Brain Initiative (Neuroethics Working Group 2022). Similarly, the International Neuroethics Society (INS) hosts the Affinity Group on Neurotechnology and Artificial Intelligence. The activities of this group specifically pertain to the discussion of needs in 'neurocomputational ethics' (International Neuroethics Society, n.d.).

The NIH Brain Initiative and NEWG, partnered with the INS, host the annual Global Neuroethics Summit. Previous discussions at these summits have highlighted the emerging need to incorporate AI considerations into neuroethics (Neuroethics Working Group 2022). The upcoming 2024 INS Annual Meeting on Neuroethics session, 'The Challenges of Neuroenhancement: Comparative Legal Perspectives from US, EU and Japan', is anticipated to discuss the permeation of AI into neurotechnology from a governance perspective and consider the impacts and mechanisms to address these issues, with at least one expert speaker working at the interface of AI and security policy (International Neuroethics Society 2024).

The US National Academy of Sciences, Engineering, and Medicine hosted a workshop on 25–26 March 2024, to 'convene a diverse group of leaders and experts across sectors within the neuroscience and AI ecosystems to further the conversation on current and potential use of AI in neuroscience and strategies to enhance public and regulatory understanding and implications of AI utilization' (National Academies of Sciences, Engineering, and Medicine 2023). The fifth session specifically addressed policy, regulation and advocacy (US-focused), with objectives to 'review the current and proposed regulatory frameworks governing the use of AI in neuroscience' and 'discuss the key role of neuroscience in equipping regulators and policymakers with knowledge and resources for the responsible use of AI in research, clinical, and general applications'. The University of Lausanne (Switzerland), the Federation of European Neuroscience Societies (FENS), the Chen Institute and NeuroLéman are set to run a summer school in August 2024, with sessions on explainable, transparent ML analysis of behaviour, and standards and good governance practices related to ethics (FENS 2024).

Bibliography

360 Nautica. 2024. "AI and the Venture Capital Landscape in 2024: Predictions and Trends." As of 18 November 2024: https://www.linkedin.com/pulse/ai-venture-capital-landscape-2024-predictions-gepdc/

A&O Shearman. 2023. "How Has GDPR Influenced the Evolution of Data Protection in APAC?" As of 15 August 2024: https://www.aoshearman.com/en/insights/how-has-gdpr-influenced-the-evolution-of-data-protection-in-apac

Abelman, Melina, Melissa Lopes, and P. Pearl O'Rourke. 2015. "Chapter 12 - Human Embryonic Stem Cell Research Oversight: A Confluence of Voluntary Self-Regulation and Shifting Policy Initiatives." In *Research Regulatory Compliance*, edited by Mark A. Suckow and Bill J. Yates, 297–320. Academic Press. As of 29 November 2024: https://doi.org/10.1016/B978-0-12-420058-6.00012-5

Abernathey, Ryan P., Tom Augspurger, Anderson Banihirwe, Charles C. Blackmon-Luca, Timothy J. Crone, Chelle L. Gentemann, Joseph J. Hamman, et al. 2021. "Cloud-Native Repositories for Big Scientific Data." *Computing in Science & Engineering* 23 (2): 26–35. As of 18 November 2024: https://doi.org/10.1109/MCSE.2021.3059437

Afnan, Masoud, Michael A.M. Afnan, Yanhe Liu, Julian Savulescu, Abhishek Mishra, Vincent Conitzer, and Cynthia Rudin. 2022. "Data Solidarity for Machine Learning for Embryo Selection: A Call for the Creation of an Open Access Repository of Embryo Data." *Reproductive BioMedicine Online* 45 (1): 10–13. As of 18 November 2024: https://doi.org/10.1016/j.rbmo.2022.03.015

Afnan, Michael A. M., Yanhe Liu, Vincent Conitzer, Cynthia Rudin, Abhishek Mishra, Julian Savulescu, and Masoud Afnan. 2021. "Interpretable, not black-box, artificial intelligence should be used for embryo selection." *Human Reproduction Open* 2021 (4): hoab040. As of 29 November 2024: https://doi.org/10.1093/hropen/hoab040

African Union. 2014. "African Union Convention on Cyber Security and Personal Data Protection | African Union." As of 18 November 2024: https://au.int/en/treaties/african-union-convention-cyber-security-and-personal-data-protection

Aguilar Gómez, Fernando, and Isabel Bernal. 2023. "FAIR EVA: Bringing Institutional Multidisciplinary Repositories into the FAIR Picture." *Scientific Data* 10 (1): 764. As of 18 November 2024: https://doi.org/10.1038/s41597-023-02652-8

Aguilera, Bernardo, David DeGrazia, and Annette Rid. 2020. "Regulating International Clinical Research: An Ethical Framework for Policy-Makers." *BMJ Global Health* 5 (5). As of 18 November 2024: https://doi.org/10.1136/bmjgh-2020-002287

Alzheimer's Association. 2022. "2022 Alzheimer's Disease Facts and Figures." *Alzheimer's & Dementia: The Journal of the Alzheimer's Association* 18 (4): 700–789. As of 18 November 2024: https://doi.org/10.1002/alz.12638

Ahn, Minkyu, Sung Chan Jun, Hong Gi Yeom, and Hohyun Cho. 2022. "Editorial: Deep Learning in Brain-Computer Interface." *Frontiers in Human Neuroscience* 16 (May). As of 18 November 2024: https://doi.org/10.3389/fnhum.2022.927567

AI Fertility Society. n.d. "AI Fertility Society." As of 10 April 2024: https://aifertility.org/

Aiyegbusi, Olalekan Lee, Samantha Cruz Rivera, Kathy Oliver, Elaine Manna, Phil Collis, Bellinda L. King-Kallimanis, Vishal Bhatnagar, et al. 2023. "The Opportunity for Greater Patient and Public Involvement and Engagement in Drug Development and Regulation." *Nature Reviews Drug Discovery* 22 (5): 337–38. As of 18 November 2024: https://doi.org/10.1038/d41573-023-00031-x

Alharbi, Wardah S., and Mamoon Rashid. 2022. "A Review of Deep Learning Applications in Human Genomics Using Next-Generation Sequencing Data." *Human Genomics* 16 (July): 26. As of 18 November 2024: https://doi.org/10.1186/s40246-022-00396-x

Ali, Omar, Wiem Abdelbaki, Anup Shrestha, Ersin Elbasi, Mohammad Abdallah Ali Alryalat, and Yogesh K Dwivedi. 2023. "A Systematic Literature Review of Artificial Intelligence in the Healthcare Sector: Benefits, Challenges, Methodologies, and Functionalities." *Journal of Innovation & Knowledge* 8 (1): 100333. As of 18 November 2024: https://doi.org/10.1016/j.jik.2023.100333

Almajidy, Rand Kasim, Soheil Mottaghi, Asmaa A. Ajwad, Yacine Boudria, Kunal Mankodiya, Walter Besio, and Ulrich G. Hofmann. 2023. "A Case for Hybrid BCIs: Combining Optical and Electrical Modalities Improves Accuracy." *Frontiers in Human Neuroscience* 17 (June). As of 18 November 2024: https://doi.org/10.3389/fnhum.2023.1162712

Alvarellos, Maria, Hadley E. Sheppard, Ingrid Knarston, Craig Davison, Nathaniel Raine, Thorben Seeger, Pablo Prieto Barja, and Maria Chatzou Dunford. 2023. "Democratizing Clinical-Genomic Data: How Federated Platforms Can Promote Benefits Sharing in Genomics." *Frontiers in Genetics* 13 (January): 1045450. As of 18 November 2024: https://doi.org/10.3389/fgene.2022.1045450

Ambler, Jon, Alpha Ahmadou Diallo, Peter K. Dearden, Phil Wilcox, Maui Hudson, and Nicki Tiffin. 2021. "Including Digital Sequence Data in the Nagoya Protocol Can Promote Data Sharing." *Trends in Biotechnology* 39 (2): 116–25. As of 18 November 2024: https://doi.org/10.1016/j.tibtech.2020.06.009

Andrews, Russell J, and Peter J Koehler. 2023. "Neurotechnology: Brain-Computer and Brain-Machine Interfaces." MedLink Neurology. 2023. As of 18 November 2024: https://www.medlink.com/articles/neurotechnology-brain-computer-and-brain-machine-interfaces

Ansede, Manuel. 2023. "New 14-day embryo model sheds light on the biggest enigma of human development." *EL PAÍS English*, 15 June. As of 29 November 2024: https://english.elpais.com/science-tech/2023-06-15/new-14-day-embryo-model-sheds-light-on-the-biggest-enigma-of-human-development.html

ARIA. 2024. "What We're Working On." Advanced Research & Invention Agency. As of 14 August 2024: https://www.aria.org.uk/what-were-working-on/

ASEAN. 2024. "ASEAN Guide on AI Governance and Ethics." As of 18 November 2024: https://asean.org/book/asean-guide-on-ai-governance-and-ethics/

AUDA-NEDAP. 2023. *White Paper: Regulation and Responsible Adoption of AI for African Towards Achievement of AU Agenda 2063. African Union Development Agency.* African Union Development Agency.

Aurand, Emily R., Tae Seok Moon., Nicole R. Buan, Kevin V. Solomon, Michael Köpke & EBRC Technical Roadmapping Working Group. 2024. "Addressing the climate crisis through engineering biology." *npj Climate Action* 3 (9): 1-4. As of 5 December 2024: https://doi.org/10.1038/s44168-023-00089-8

Australian Government. 2019. A*ustralia's Artificial Intelligence Ethics Framework*. Department of Industry, Science and Resources. As of 12 August 2024: https://www.industry.gov.au/publications/australias-artificial-intelligence-ethics-framework

Australian Government. 2024. "About Health and Medical Research in Australia." Australian Government Department of Health and Aged Care. As of 12 August 2024: https://www.health.gov.au/topics/health-data-and-medical-research/about-health-and-medical-research

Badai, Jiayidaer, Qian Bu, and Le Zhang. 2020. "Review of Artificial Intelligence Applications and Algorithms for Brain Organoid Research." *Interdisciplinary Sciences: Computational Life Sciences* 12 (4): 383–94. As of 18 November 2024: https://doi.org/10.1007/s12539-020-00386-4

Baker, Christopher, and Stephen H. Fairclough. 2022. "Chapter 9 – Adaptive Virtual Reality." In Current Research in Neuroadaptive Technology, edited by Stephen H. Fairclough and Thorsten O. Zander, 159–176. As of 12 August 2024: https://doi.org/10.1016/B978-0-12-821413-8.00014-2

Ball, Philip. 2023. "What is an embryo? Scientists say definition needs to change." *Nature*, 18 August. As of 29 November 2024: https://www.nature.com/articles/d41586-023-02641-2

Ballav, Sangeeta, Amit Ranjan, Shubhayan Sur, Soumya Basu, and Amit Ranjan. 2024. "Organoid Intelligence: Bridging Artificial Intelligence for Biological Computing and Neurological Insights." In *Technologies in Cell Culture - A Journey From Basics to Advanced Applications*, edited by Soumya Basu, Amit Ranjan, and Subhayan Sur. IntechOpen. As of 18 November 2024: https://doi.org/10.5772/intechopen.114304

Bannier, Elise, et al. 2021. "The Open Brain Consent: Informing research participants and obtaining consent to share brain imaging data." *Human Brain Mapping*, 42 (7): 1945–1951. As of 29 November 2024: https://doi.org/10.1002/hbm.25351

Bein, Amir, Woojung Shin, Sasan Jalili-Firoozinezhad, Min Hee Park, Alexandra Sontheimer-Phelps, Alessio Tovaglieri, Angeliki Chalkiadaki, Hyun Jung Kim, and Ingber De. 2018. "Microfluidic Organ-on-a-Chip Models of Human Intestine." *Cellular and Molecular Gastroenterology and Hepatology* 5 (4). As of 18 November 2024: https://doi.org/10.1016/j.jcmgh.2017.12.010

Belkacem, Abdelkader Nasreddine, Nuraini Jamil, Sumayya Khalid, and Fady Alnajjar. 2023. "On Closed-Loop Brain Stimulation Systems for Improving the Quality of Life of Patients with Neurological Disorders." Frontiers in Human Neuroscience 17: 1085173. As of 12 August 2024: https://doi.org/10.3389/fnhum.2023.1085173

Berger, Sara, and Francesca Rossi. 2021. "The Future of AI Ethics and the Role of Neurotechnology." As of 19 November 2024: https://research.ibm.com/publications/the-future-of-ai-ethics-and-the-role-of-neurotechnology

Berger, Sara, and Francesca Rossi. 2023. "AI and Neurotechnology: Learning from AI Ethics to Address an Expanded Ethics Landscape." Communications of the ACM, 1 March 2023. As of 12 August 2024: https://cacm.acm.org/research/ai-and-neurotechnology/

Berggren, Magnus, Eric D. Głowacki, Daniel T. Simon, Eleni Stavrinidou, and Klas Tybrandt. 2022. "In Vivo Organic Bioelectronics for Neuromodulation." Chemical Reviews 122 (4). As of 15 August 2024: https://pubs.acs.org/doi/10.1021/acs.chemrev.1c00390

Bhidayasiri, Roongroj. 2024. "The grand challenge at the frontiers of neurotechnology and its emerging clinical applications." Frontiers in Neurotechnology 15. As of 17 August 2024: https://doi.org/10.3389/fneur.2024.1314477

Birey, Fikri, Jimena Andersen, Christopher D. Makinson, Saiful Islam, Wu Wei, Nina Huber, H. Christina Fan, et al. 2017. "Assembly of Functionally Integrated Human Forebrain Spheroids." *Nature* 545 (7652): 54–59. As of 18 November 2024: https://doi.org/10.1038/nature22330

Blauer, Beth, John S. Brownstein, Lauren Gardner, Moritz U.G. Kraemer, Zoila Beatriz Leiva Rioja, Edouard Mathieu, Isabel Redies, and Oliver W. Morgan. 2023. "Innovative Platforms for Data Aggregation, Linkage and Analysis in the Context of Pandemic and Epidemic Intelligence." *Eurosurveillance* 28 (24): 2200860. As of 18 November 2024: https://doi.org/10.2807/1560-7917.ES.2023.28.24.2200860

Blay, Vincent, Bhairavi Tolani, Sunita P. Ho, and Michelle R. Arkin. 2020. "High-Throughput Screening: today's biochemical and cell-based approaches." Drug Discovery Today 25 (10): 1807–21. As of 29 November 2024: https://doi.org/10.1016/j.drudis.2020.07.024

Blomberg, Niklas, and Katharina B. Lauer. 2020. "Connecting Data, Tools and People across Europe: ELIXIR's Response to the COVID-19 Pandemic." *European Journal of Human Genetics* 28 (6): 719–23. As of 18 November 2024: https://doi.org/10.1038/s41431-020-0637-5

Bock, Christoph, Michael Boutros, J. Gray Camp, Laura Clarke, Hans Clevers, Juergen A. Knoblich, Prisca Liberali, et al. 2021. "The Organoid Cell Atlas." *Nature Biotechnology* 39 (1): 13–17. As of 18 November 2024: https://doi.org/10.1038/s41587-020-00762-x

Boers, Sarah N., and Annelien L. Bredenoord. 2018. "Consent for Governance in the Ethical Use of Organoids." *Nature Cell Biology* 20 (6): 642–45. As of 18 November 2024: https://doi.org/10.1038/s41556-018-0112-5

Boers, Sarah N., Johannes J.M. van Delden, Hans Clevers, and Annelien L. Bredenoord. 2016. "Organoid Biobanking: Identifying the Ethics." *EMBO Reports* 17 (7): 938–41. As of 18 November 2024: https://doi.org/10.15252/embr.201642613

Bohua, Liao, Wang Yuexin, Ou Yakun, Zuo Kunlan, Liu Huan, and Lei Ruipeng. 2023. "Ethical Framework on Risk Governance of Synthetic Biology." *Journal of Biosafety and Biosecurity* 5 (2): 45–56. As of 18 November 2024: https://doi.org/10.1016/j.jobb.2023.03.002

Botes, Marietjie. 2023. "Regulating Scientific and Technological Uncertainty: The Precautionary Principle in the Context of Human Genomics and AI." *South African Journal of Science* 119 (5/6). As of 18 November 2024: https://doi.org/10.17159/sajs.2023/15037

Bormann, Charles L., Prudhvi Thirumalaraju, Manoj K. Kanakasabapathy, Hemanth Kandula, Irene Souter, Irene Dimitriadis, Raghav Gupta, Rohan P. Pooniwala, and Hadi Shafiee. 2020. "Consistency and objectivity of automated embryo assessments using deep neural networks." Fertility and Sterility 113 (4): 781-787.e1. As of 29 November 2024: https://doi.org/10.1016/j.fertnstert.2019.12.004

BowerGroupAsia. 2023. "AI Policy and Regulatory Frameworks Take Shape in APAC." As of 18 November 2024: https://bowergroupasia.com/ai-policy-and-regulatory-frameworks-take-shape-in-apac/

Brivanlou, Ali H., and Norbert Gleicher. 2021. "The evolution of our understanding of human development over the last 10 years." Nature Communications 12 (1): 4615. As of 29 November 2024: https://doi.org/10.1038/s41467-021-24793-3

Brivanlou, Ali H., Nicolas Rivron, and Norbert Gleicher. 2021. 'How will our understanding of human development evolve over the next 10 years'. *Nature Communications* 12 (1): 4614. As of 5 December 2024: https://www.nature.com/articles/s41467-021-24794-2

British Academy, and the Royal Society. 2017. *Data Management and Use: Governance in the 21st Century.* As of 17 August 2024: https://www.thebritishacademy.ac.uk/documents/105/Data_management_and_use_-_Governance_in_the_21st_century.pdf

Brown University. 2021. "Researchers Demonstrate First Human Use of High-Bandwidth Wireless Brain-Computer Interface." 31 March. As of 16 August 2024: https://www.brown.edu/news/2021-03-31/braingate-wireless

Buck, Matthias, and Clare Hamilton. 2011. "The Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from Their Utilization to the Convention on Biological Diversity." *Review of European Community & International Environmental Law* 20 (1): 47–61. As of 18 November 2024: https://doi.org/10.1111/j.1467-9388.2011.00703.x

Bulgarelli, Chiara, Paola Pinti, Nadine Aburumman, and Emily J.H. Jones. 2023. "Combining Wearable fNIRS and Immersive Virtual Reality to Study Preschoolers' Social Development: A Proof-of-Principle Study on Preschoolers' Social Preference." *Oxford Open Neuroscience* 2 (February): kvad012. As of 18 November 2024: https://doi.org/10.1093/oons/kvad012

Burman, Anirudh. 2023. "Understanding India's New Data Protection Law." Carnegie India. 3 October. As of 18 November 2024: https://carnegieindia.org/2023/10/03/understanding-india-s-new-data-protection-law-pub-90624

Butler, Georgia. 2023. "Singapore Could Make Data Centers and Clouds 'Critical Infrastructure.'" Data Center Dynamics. 21 December. As of 18 November 2024: https://www.datacenterdynamics.com/en/news/singapore-could-make-data-centers-and-clouds-critical-infrastructure/

Cai, Hongwei, Zheng Ao, Chunhui Tian, Zhuhao Wu, Hongcheng Liu, Jason Tchieu, Mingxia Gu, Ken Mackie, and Feng Guo. 2023. "Brain Organoid Reservoir Computing for Artificial Intelligence." *Nature Electronics* 6 (12): 1032–39. As of 18 November 2024: https://doi.org/10.1038/s41928-023-01069-w

Callaway, Ewen. 2022. "'The Entire Protein Universe': AI Predicts Shape of Nearly Every Known Protein." *Nature* 608 (7921): 15–16. https://doi.org/10.1038/d41586-022-02083-2

Canali, Stefano, Viola Schiaffonati, and Andrea Aliverti. 2022. "Challenges and Recommendations for Wearable Devices in Digital Health: Data Quality, Interoperability, Health Equity, Fairness." *PLOS Digital Health* 1 (10): e0000104. As of 18 November 2024: https://doi.org/10.1371/journal.pdig.0000104

Care, Australian Government Department of Health and Aged. 2024. "About Health and Medical Research in Australia." 4 March. As of 18 November 2024: https://www.health.gov.au/topics/health-data-and-medical-research/about-health-and-medical-research

Carson, Claire, Lisa Hinton, Jenny Kurinczuk, and Maria Quigley. 2019. "'I Haven't Met Them, I Don't Have Any Trust in Them. It Just Feels like a Big Unknown': A Qualitative Study Exploring the Determinants of Consent to Use Human Fertilisation and Embryology Authority Registry Data in Research." *BMJ Open* 9 (5): e026469. As of 18 November 2024: https://doi.org/10.1136/bmjopen-2018-026469

Caudai, Claudia, Antonella Galizia, Filippo Geraci, Loredana Le Pera, Veronica Morea, Emanuele Salerno, Allegra Via, and Teresa Colombo. 2021. "AI Applications in Functional Genomics." *Computational and Structural Biotechnology Journal* 19 (January): 5762–90. As of 18 November 2024: https://doi.org/10.1016/j.csbj.2021.10.009

Center for Biologics Evaluation and Research. 2024. "Center for Biologics Evaluation and Research (CBER)." FDA. 19 March. As of 18 November 2024: https://www.fda.gov/about-fda/fda-organization/center-biologics-evaluation-and-research-cber

Chakradhar, Shraddha. 2016. "New Company Aims to Broaden Researchers' Access to Organoids." *Nature Medicine* 22 (4): 338. As of 18 November 2024: https://doi.org/10.1038/nm0416-338

ChatGPT. 2024. "Homepage." As of 12 August 2024: https://chat.openai.com

Chavez-Badiola, Alejandro, Adolfo Flores-Saiffe-Farías, Gerardo Mendizabal-Ruiz, Andrew J. Drakeley, and Jacques Cohen. 2020. "Embryo Ranking Intelligent Classification Algorithm (ERICA): Artificial intelligence clinical assistant predicting embryo ploidy and implantation." *Reproductive Biomedicine Online* 41 (4): 585–93. As of 29 November 2024: https://doi.org/10.1016/j.rbmo.2020.07.003

Chawinga, Winner Dominic, and Sandy Zinn. 2019. "Global Perspectives of Research Data Sharing: A Systematic Literature Review." *Library & Information Science Research* 41 (2): 109–22. As of 18 November 2024: https://doi.org/10.1016/j.lisr.2019.04.004

Chen, Zhe Sage, and Bijan Pesaran. 2021. "Improving Scalability in Systems Neuroscience." *Neuron* 109 (11): 1776–90. As of 18 November 2024: https://doi.org/10.1016/j.neuron.2021.03.025

Cheredath, Aswathi, Shubhashree Uppangala, Asha C. S., Ameya Jijo, Vani Lakshimi R., Pratap Kumar, David Joseph, Nagana Gowda G. A., Guruprasad Kalthur, and Satish Kumar Adiga. 2023. "Combining Machine Learning with Metabolomic and Embryologic Data Improves Embryo Implantation Prediction." Reproductive Sciences 30: 984–994. As if 29 November 2024: https://doi.org/10.1007/s43032-022-01071-1

Chesak, Jennifer. 2024. "Global perspectives on the Alabama ruling, IVF and when cells become a person." As of 12 April 2024: https://www.bbc.com/future/article/20240226-what-is-an-embryo-global-medical-definition-of-personhood-ivf-ruling

Chia, Shirley Pei Shan, Sharleen Li Ying Kong, Jeremy Kah Sheng Pang, and Boon-Seng Soh. 2022. "3D Human Organoids: The Next 'Viral' Model for the Molecular Basis of Infectious Diseases." *Biomedicines* 10 (7): 1541. As of 18 November 2024: https://doi.org/10.3390/biomedicines10071541

Cimadomo, Danilo, et al. 2023. "Towards Automation in IVF: Pre-Clinical Validation of a Deep Learning-Based Embryo Grading System during PGT-A Cycles." Journal of Clinical Medicine 12 (5): 1806. As of 29 November 2024: https://doi.org/10.3390/jcm12051806

Clift, Joseph. 2019. *A Blueprint for the Oversight of Emerging Science and Technologies*. Wellcome. As of 12 August 2024: https://wellcome.org/reports/blueprint-oversight-emerging-science-and-technologies

Coleman, Benjie. 2023. "New Organoid Facility for Cutting-Edge Disease Modelling and Precision Medicine." Imperial College London, 19 June. As of 17 August 2024: https://www.imperial.ac.uk/news/245454/new-organoid-facility-cutting-edge-disease-modelling/

Collins, Benjamin, and Eran Klein. 2023. "Invasive Neurotechnology: A Study of the Concept of Invasiveness in Neuroethics." *Neuroethics* 16 (1): 11. As of 18 November 2024: https://doi.org/10.1007/s12152-023-09518-1

Collins, Gary S., Johannes B. Reitsma, Douglas G. Altman, and Karel G.M. Moons. 2015. "Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD Statement." BMC Medicine 13: 1. As of 29 November 2024: https://doi.org/10.1186/s12916-014-0241-z

Cornejo-Plaza, María Isabel, Roberto Cippitani, and Vincenzo Pasquino. 2024. "Chilean Supreme Court Ruling on the Protection of Brain Activity: Neurorights, Personal Data Protection, and Neurodata." Frontiers in Psychology 15. As of 17 August 2024: https://doi.org/10.3389/fpsyg.2024.1330439

Corrò, Claudia, Laura Novellasdemunt, and Vivian S.W. Li. 2020. "A Brief History of Organoids." *American Journal of Physiology - Cell Physiology* 319 (1): C151–65. As of 18 November 2024: https://doi.org/10.1152/ajpcell.00120.2020

Crone, Michael A., Miles Priestman, Marta Ciechonska, Kirsten Jensen, David J. Sharp, Arthi Anand, Paul Randell, Marko Storch, and Paul S. Freemont. 2020. "A Role for Biofoundries in Rapid Development and Validation of Automated SARS-CoV-2 Clinical Diagnostics." *Nature Communications* 11 (1): 4464. As of 18 November 2024: https://doi.org/10.1038/s41467-020-18130-3

Curchoe, Carol L. 2023. "Proceedings of the first world conference on AI in fertility." *Journal of Assisted Reproduction and Genetics* 40 (2): 215–222. As of 29 November 2024: https://doi.org/10.1007/s10815-022-02704-9

Cyberspace Administration of China. 2023. "Interim Measures for the Management of Generative AI Services." As of 15 August 2024: https://www.cac.gov.cn/2023-07/13/c_1690898327029107.htm

Cyranoski, David 2019. “The CRISPR-baby scandal: What’s next for human gene-editing.” Nature 566 (7745): 440–442. As of 29 November 2024: https://doi.org/10.1038/d41586-019-00673-1

de Jongh, Dide, Emma K. Massey, VANGUARD consortium, and Eline M. Bunnik. 2022. “Organoids: A Systematic Review of Ethical Issues.” *Stem Cell Research & Therapy* 13 (1): 337. As of 18 November 2024: https://doi.org/10.1186/s13287-022-02950-9

Delcker, Janosch. 2018. “Risk of Bioweapon Attack Growing, Dutch Defense Minister Says.” *POLITICO*, 18 February. As of 12 August 2024: https://www.politico.eu/article/ank-bijleveld-bioweapon-risk-attack-growing-dutch-defense-minister-says/

Delden, Johannes J. M. van, and Rieke van der Graaf. 2017. “Revised CIOMS International Ethical Guidelines for Health-Related Research Involving Humans.” *JAMA* 317 (2): 135–36. As of 18 November 2024: https://doi.org/10.1001/jama.2016.18977

Denton, Nathan, Monique Molloy, Samantha Charleston, Craig Lipset, Jonathan Hirsch, Andrew E. Mulberg, Paul Howard, and Eric D. Marsh. 2021. “Data Silos Are Undermining Drug Development and Failing Rare Disease Patients.” *Orphanet Journal of Rare Diseases* 16 (1): 161. As of 18 November 2024: https://doi.org/10.1186/s13023-021-01806-4

Devlin, Hannah. 2019. “IVF couples could be able to choose the ‘smartest’ embryo.” Guardian, 24 May. As of 29 November 2024: https://www.theguardian.com/society/2019/may/24/ivf-couples-could-be-able-to-choose-the-smartest-embryo

Dias, Raquel, and Ali Torkamani. 2019. “Artificial Intelligence in Clinical and Genomic Diagnostics.” *Genome Medicine* 11 (1): 70. As of 18 November 2024: https://doi.org/10.1186/s13073-019-0689-8

Digital Health Global. 2023. “STORK-A: Using Artificial Intelligence to Predict Ploidy Status of Embryos for Improved Implantation Potential.” 10 March. As of 13 August 2024: https://www.digitalhealthglobal.com/stork-a-using-artificial-intelligence-to-predict-ploidy-status-of-embryos-for-improved-implantation-potential/

Dipietro, Laura, Paola Gonzalez-Mego, Ciro Ramos-Estebanez, Lauren Hana Zukowski, Rahul Mikkilineni, Richard Jarrett Rushmore, and Timothy Wagner. 2023. “The Evolution of Big Data in Neuroscience and Neurology.” *Journal of Big Data* 10 (116). As of 15 August 2024: https://journalofbigdata.springeropen.com/articles/10.1186/s40537-023-00751-2

Dixit, Shriniket, Anant Kumar, Kathiravan Srinivasan, P. M. Durai Raj Vincent, and Nadesh Ramu Krishnan. 2024. “Advancing Genome Editing with Artificial Intelligence: Opportunities, Challenges, and Future Directions.” *Frontiers in Bioengineering and Biotechnology* 11 (January): 1335901. As of 18 November 2024: https://doi.org/10.3389/fbioe.2023.1335901

Donati, Elisa, and Giacomo Indiveri. 2023. “Neuromorphic Bioelectronic Medicine for Nervous System Interfaces: From Neural Computational Primitives to Medical Applications - IOPscience.” As of 18 November 2024: https://iopscience.iop.org/article/10.1088/2516-1091/acb51c/meta

Dorfan, Yuval, Aviv Zeevi, Gita Reinitz, Magi Mualem, and Yosi Shacham-Diamand. 2023. “Israel and the Global Synthetic Biology Ecosystem.” Engineering Biology 7 (1–4): 18–28. As of 12 August 2024: https://doi.org/10.1049/enb2.12027

Doya, Kenji, Arisa Ema, Hiroaki Kitano, Masamichi Sakagami, and Stuart Russell. 2022. “Social Impact and Governance of AI and Neurotechnologies.” *Neural Networks* 152 (August): 542–54. As of 18 November 2024: https://doi.org/10.1016/j.neunet.2022.05.012

Drew, Liam. 2022. "Abandoned: The Human Cost of Neurotechnology Failure." *Nature*, December. As of 18 November 2024: https://doi.org/10.1038/d41586-022-03810-5

DSIT. 2024. "A Pro-Innovation Approach to AI Regulation." CP 1019. Department for Science, Innovation and Technology. As of 18 November 2024: https://www.gov.uk/government/publications/ai-regulation-a-pro-innovation-approach/white-paper

Dunkelmann, Daniel L., Carlos Piedrafita, Alexandre Dickson, Kim C. Liu, Thomas S. Elliott, Marc Fiedler, Dom Bellini, Andrew Zhou, Daniele Cervettini, and Jason W. Chin. 2024. "Adding α,α-disubstituted and β-linked monomers to the genetic code of an organism." *Nature*, 625 (7995): 603–10. As of 29 November 2024: https://doi.org/10.1038/s41586-023-06897-6

Dursi, L. Jonathan, Zoltan Bozoky, Richard de Borja, Haoyuan Li, David Bujold, Adam Lipski, Shaikh Farhan Rashid, et al. 2021. "CanDIG: Federated Network across Canada for Multi-Omic and Health Data Discovery and Analysis." *Cell Genomics* 1 (2): 100033. As of 18 November 2024: https://doi.org/10.1016/j.xgen.2021.100033

Dye, Briana R., David R. Hill, Michael A.H. Ferguson, Yu-Hwai Tsai, Melinda S. Nagy, Rachel Dyal, James M. Wells, et al. 2015. "In Vitro Generation of Human Pluripotent Stem Cell Derived Lung Organoids." *eLife* 4 (March). As of 18 November 2024: https://doi.org/10.7554/eLife.05098

Eaton, Sarah E. 2023. "Postplagiarism: Transdisciplinary ethics and integrity in the age of artificial intelligence and neurotechnology." *International Journal for Educational Integrity* 19 (1): 23. As of 29 November 2024: https://doi.org/10.1007/s40979-023-00144-1

EBRC. 2022. "Engineering Biology for Climate & Sustainability Executive Summary | EBRC Research Roadmap." As of 18 November 2024: https://roadmap.ebrc.org/executive-summary/

———. 2024. "Engineering Biology Research Consortium." As of 18 November 2024: https://ebrc.org/

Economist Impact. 2024. "Regulators are taking on global technology trends." As of 17 August 2024: https://impact.economist.com/projects/the-next-ten/emerging-tech/

Egan, Janet, and Eric Rosenbach. 2023. "Biosecurity in the Age of AI: What's the Risk? | Belfer Center for Science and International Affairs." As of 18 November 2024: https://www.belfercenter.org/publication/biosecurity-age-ai-whats-risk

EHDEN. 2024. "Homepage." European Health Data Evidence Network. As of 15 August 2024: https://www.ehden.eu/

Eke, Damian O., Amy Bernard, Jan G. Bjaalie, Ricardo Chavarriaga, Takashi Hanakawa, Anthony J. Hannan, Sean L. Hill, et al. 2022. "International Data Governance for Neuroscience." *Neuron* 110 (4): 600–612. As of 18 November 2024: https://doi.org/10.1016/j.neuron.2021.11.017

ELIXIR. n.d. "ELIXIR." As of 18 November 2024: https://elixir-europe.org/

Engineering and Technology. 2021. "Bioengineering Threats Rated as a Top Biosecurity Risk." Engineering and Technology Magazine, 3 February. As of 14 August 2024: https://eandt.theiet.org/2021/02/03/bioengineering-threats-rated-top-biosecurity-risk

Erikainen, Sonja, Phoebe Friesen, Leah Rand, Karin Jongsma, Michael Dunn, Annie Sorbie, Matthew McCoy, et al. 2021. "Public Involvement in the Governance of Population-Level Biomedical Research: Unresolved Questions and Future Directions." *Journal of Medical Ethics* 47 (7): 522–25. As of 18 November 2024: https://doi.org/10.1136/medethics-2020-106530

European Commission. 2020. *Assessment List for Trustworthy Artificial Intelligence (ALTAI) for Self-Assessment.* Shaping Europe's Digital Future. As of 15 August 2024: https://digital-strategy.ec.europa.eu/en/library/assessment-list-trustworthy-artificial-intelligence-altai-self-assessment

———. 2021. *Proposal for a Regulation of the of the European Parliament and of the Council Laying Down Harmonised Rules on Artificial Intelligence (Artificial Intelligence Act) and Amending Certain Union Legislative Acts.* As of 18 November 2024: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A52021PC0206

———. 2022. "Liability Rules for Artificial Intelligence." As of 15 August 2024: https://commission.europa.eu/business-economy-euro/doing-business-eu/contract-rules/digital-contracts/liability-rules-artificial-intelligence_en

———. 2023. "Wearable Neurotechnology for Sleep Quality Improvement." As of 16 August 2024: https://cordis.europa.eu/project/id/957095

———. 2024a. "A Europe fit for the digital age." As of 17 August 2024: https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/europe-fit-digital-age_en

———. 2024b. "Open Data, Software and Code Guidelines." Open Research Europe. As of 14 August 2024: https://open-research-europe.ec.europa.eu/for-authors/data-guidelines

———. 2024c. "European Health Data Space." As of 15 August 2024: https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en

———. 2024d. "Regulation (EU) 2024/1689 of the European Parliament and of the Council of 13 June 2024 laying down harmonised rules on artificial intelligence and amending Regulations (EC) No 300/2008, (EU) No 167/2013, (EU) No 168/2013, (EU) 2018/858, (EU) 2018/1139 and (EU) 2019/2144 and Directives 2014/90/EU, (EU) 2016/797 and (EU) 2020/1828 (Artificial Intelligence Act) (Text with EEA relevance)." As of 17 August 2024: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L_202401689

———. 2024e. "Tissues and Cells." As of 17 August 2024: https://health.ec.europa.eu/blood-tissues-cells-and-organs/tissues-and-cells_en

European Parliament. 2023. "Artificial Intelligence Act: Briefing." As of 18 November 2024: https://www.europarl.europa.eu/RegData/etudes/BRIE/2021/698792/EPRS_BRI(2021)698792_EN.pdf

European Parliament. Directorate General for Parliamentary Research Services. 2022. *Genome editing in humans: A survey of law, regulation and governance principles.* As of 29 November 2024: https://data.europa.eu/doi/10.2861/07058

EuroStemCell. 2024. "Regulation of Stem Cell Research in Germany." As of 17 August 2024: https://www.eurostemcell.org/regulation-stem-cell-research-germany

Fabbri, Morris, Margaret Ginoza, Lars Assen, Karin Jongsma, and Rosario Isasi. 2023. "Modeling policy development: Examining national governance of stem cell-based embryo models." *Regenerative Medicine* 18 (2): 155–68. As of 29 November 2024: https://doi.org/10.2217/rme-2022-0136

Farmer, Harry. 2023. "DNA.I. - Early Findings and Emerging Questions on the Use of AI in Genomics." As of 18 November 2024: https://www.adalovelaceinstitute.org/report/dna-ai-genomics/

Fatumo, Segun, Tinashe Chikowore, Ananyo Choudhury, Muhammad Ayub, Alicia R. Martin, and Karoline Kuchenbäcker. 2022. "Diversity in Genomic Studies: A Roadmap to Address the Imbalance." *Nature Medicine* 28 (2): 243–50. As of 14 August 2025: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7614889/

Fedaseyeu, Viktar, and Adam Yu. 2022. "How to Read China's Unwritten Rules and Regulations." *Diplomat*, 3 October. As of 15 August 2024: https://thediplomat.com/2022/10/how-to-read-chinas-unwritten-rules-and-regulations/

Fekete, Zoltan, Anita Zátonyi, Attila Kaszás, Miklós Madarász, and Andrea Slézia. 2023. "Transparent Neural Interfaces: Challenges and Solutions of Microengineered Multimodal Implants Designed to Measure Intact Neuronal Populations Using High-Resolution Electrophysiology and Microscopy Simultaneously." *Microsystems & Nanoengineering* 9 (1): 1–30. As of 18 November 2024: https://doi.org/10.1038/s41378-023-00519-x

FENS. 2024. "FENS – Chen Institute – NeuroLéman Summer School on Monitoring and manipulating the affective state: new perspectives on neurotechnologies and AI tools." Federation of European Neuroscience Societies. As of 17 August 2024: https://www.fens.org/news-activities/fens-and-societies-calendar/training-event/fens-chen-institute-neuroleman-summer-school-2024

Fisher, Celia B., and Deborah M. Layman. 2018. "Genomics, Big Data, and Broad Consent: A New Ethics Frontier for Prevention Science." *Prevention Science* 19 (7): 871–79. As of 18 November 2024: https://doi.org/10.1007/s11121-018-0944-z

Foreman, Amy L., Kathleen Liddell, Sarah Franklin, Emily Jackson, Christina Rozeik, and Kathy K. Niakan. 2023. "Human embryo models: The importance of national policy and governance review." Current Opinion in Genetics & Development 82: 102103. As of 29 November 2024: https://doi.org/10.1016/j.gde.2023.102103

Foundation Hubrecht Organoid Biobank. 2024. "Homepage." As of 15 August 2024: https://www.hubrechtorganoidbiobank.org/

Fredriksson, Martin. 2021. "Dilemmas of Protection: Decolonising the Regulation of Genetic Resources as Cultural Heritage." *International Journal of Heritage Studies* 27 (7): 720–33. https://doi.org/10.1080/13527258.2020.1852295

Frontiers. 2024. "Artificial Intelligence for Metabolic Engineering: Research Topic." As of 18 November 2024: https://www.frontiersin.org/research-topics/62529/artificial-intelligence-for-metabolic-engineering

Fuller, Daniel, Emily Colwell, Jonathan Low, Kassia Orychock, Melissa Ann Tobin, Bo Simango, Richard Buote, et al. 2020. "Reliability and Validity of Commercially Available Wearable Devices for Measuring Steps, Energy Expenditure, and Heart Rate: Systematic Review." *JMIR mHealth and uHealth* 8 (9): e18694. As of 18 November 2024: https://doi.org/10.2196/18694

GA4GH. 2019. "GA4GH Passports and the Authorization & Authentication Infrastructure." Global Alliance for Genomics & Health. 17 December. As of 17 August 2024: https://www.ga4gh.org/news_item/ga4gh-passports-and-the-authorization-and-authentication-infrastructure/

Gajjar, Devyani. 2024. "Artificial Intelligence (AI) Glossary." UK Parliamentary Office of Science and Technology (POST). As of 18 November 2024: https://post.parliament.uk/artificial-intelligence-ai-glossary/

Gallo, Valeria, and Suchitra Nair. n.d. "The UK's Framework for AI Regulation." Deloitte. As of 18 November 2024: https://www2.deloitte.com/uk/en/blog/emea-centre-for-regulatory-strategy/2024/the-uks-framework-for-ai-regulation.html

Gallup, Olivia, Hia Ming, and Tom Ellis. 2021. "Ten Future Challenges for Synthetic Biology." Engineering Biology 5 (3): 51–59. As of 14 August 2024: https://doi.org/10.1049/enb2.12011

Garden, Hermann, et al. 2019. "Responsible innovation in neurotechnology enterprises." *OECD Science, Technology and Industry Working Papers 2019/05*. Paris: OECD Publishing. As of 16 August 2024: https://doi.org/10.1787/9685e4fd-en

Gärditz, Klaus Ferdinand. 2023. "Work with Embryonic Stem Cells – Legal Considerations." *Journal of Perinatal Medicine* 51 (6): 763–68. As of 18 November 2024: https://doi.org/10.1515/jpm-2022-0511

Garreta, Elena, Roger D. Kamm, Susana M. Chuva de Sousa Lopes, Madeline A. Lancaster, Ron Weiss, Xavier Trepat, Insoo Hyun, and Nuria Montserrat. 2021. "Rethinking Organoid Technology through Bioengineering." *Nature Materials* 20 (2): 145–55. As of 18 November 2024: https://doi.org/10.1038/s41563-020-00804-4

GIDA. 2024. "CARE Principles for Indigenous Data Governance." Global Indigenous Data Alliance. As of 12 August 2024: https://www.gida-global.org/care

Glass, Madison R., Elisa A. Waxman, Satoshi Yamashita, Michael Lafferty, Alvaro Beltran, Tala Farah, Niyanta K. Patel, et al. 2023. "Cross-Site Reproducibility of Human Cortical Organoids Reveals Consistent Cell Type Composition and Architecture." *bioRxiv: The Preprint Server for Biology*, July, 2023.07.28.550873. As of 18 November 2024: https://doi.org/10.1101/2023.07.28.550873

Global Biodata Coalition. 2024. "Homepage." As of 15 August 2024: https://globalbiodata.org/

Goddard, Nick. 2023. "Unravelling the Difference: Modern Data Platform vs. Data Mesh." A-Team Chronicles. 27 June. As of 18 November 2024: https://blogs.oracle.com/ateam/post/unravelling-the-difference-modern-data-platform-vs-data-mesh

Goering, Sara, et al. 2021. "Recommendations for Responsible Development and Application of Neurotechnologies." *Neuroethics* 14 (3): 365–386. As of 29 November 2024: https://doi.org/10.1007/s12152-021-09468-6

Goodman, Deborah, Catherine O. Johnson, Lari Wenzel, Deborah Bowen, Celeste Condit, and Karen L. Edwards. 2016. "Consent Issues in Genetic Research: Views of Research Participants." *Public Health Genomics* 19 (4): 220–28. As of 18 November 2024: https://doi.org/10.1159/000447346

Goodwin, Sara, John D. McPherson, and W. Richard McCombie. 2016. "Coming of Age: Ten Years of next-Generation Sequencing Technologies." *Nature Reviews Genetics* 17 (6): 333–51. As of 18 November 2024: https://doi.org/10.1038/nrg.2016.49

Government of Brazil. 2024. "Lei Geral de Proteção de Dados Pessoais (LGPD) [General Personal Data Protection Law]." As of 15 August 2024: https://www.gov.br/esporte/pt-br/acesso-a-informacao/lgpd/lei-geral-de-protecao-de-dados-pessoais-lgpd

Government of Canada, Interagency Advisory Panel on Research Ethics. 2023. "Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2 (2022)." 11 January. As of 18 November 2024: https://ethics.gc.ca/eng/policy-politique_tcps2-eptc2_2022.html

Grossman, Robert L., Allison Heath, Mark Murphy, Maria Patterson, and Walt Wells. 2016. "A Case for Data Commons: Toward Data Science as a Service." *Computing in Science & Engineering* 18 (5): 10–20. As of 18 November 2024: https://doi.org/10.1109/MCSE.2016.92

Gunashekar, Salil, Sarah Parks, Joe Francombe, Camilla d'Angelo, Gemma-Claire Ali, Pamina Smith, Daniela Rodriguez-Rincon, Marlene Altenhofer, and Gordon R. McInroy. 2019. *Oversight of Emerging Science and Technology: Learning from Past and Present Efforts around the World*. Santa Monica, Calif.: RAND Corporation. RR-2921-WT. As of 18 November 2024: https://www.rand.org/pubs/research_reports/RR2921.html

Guo, Kairui, Mengjia Wu, Zelia Soo, Yue Yang, Yi Zhang, Qian Zhang, Hua Lin, et al. 2023. "Artificial Intelligence-Driven Biomedical Genomics." *Knowledge-Based Systems* 279 (November): 110937. As of 18 November 2024: https://doi.org/10.1016/j.knosys.2023.110937

Han, Yuling, Xiaohua Duan, Liuliu Yang, Benjamin E. Nilsson-Payant, Pengfei Wang, Fuyu Duan, Xuming Tang, et al. 2021. "Identification of SARS-CoV-2 Inhibitors Using Lung and Colonic Organoids." *Nature* 589 (7841): 270–75. As of 18 November 2024: https://doi.org/10.1038/s41586-020-2901-9

Hanassab, Simon, Ali Abbara, Arthur C. Yeung, Margaritis Voliotis, Krasimira Tsaneva-Atanasova, Tom W. Kelsey, Geoffrey H. Trew, Scott M. Nelson, Thomas Heinis, and Waljit S. Dhillo. 2024. "The prospect of artificial intelligence to personalize assisted reproductive technology." Npj Digital Medicine 7(1): 1–19. As of 29 November 2024: https://doi.org/10.1038/s41746-024-01006-x

Harris, Jennifer R., Paul Burton, Bartha Maria Knoppers, Klaus Lindpaintner, Marianna Bledsoe, Anthony J. Brookes, Isabelle Budin-Ljøsne, et al. 2012. "Toward a Roadmap in Global Biobanking for Health." *European Journal of Human Genetics* 20 (11): 1105–11. As of 18 November 2024: https://doi.org/10.1038/ejhg.2012.96

Hartung, Thomas, Itzy E. Morales Pantoja, and Lena Smirnova. 2024. "Brain Organoids and Organoid Intelligence from Ethical, Legal, and Social Points of View." *Frontiers in Artificial Intelligence* 6 (January). As of 18 November 2024: https://doi.org/10.3389/frai.2023.1307613

Hartung, Thomas, Lena Smirnova, Itzy Erin Morales Pantoja, Akwasi Akwaboah, Dowlette-Mary Din, Cynthia Berlinicke, J. Boyd, et al. 2023. "The Baltimore Declaration toward the Exploration of Organoid Intelligence." *Frontiers in Science* 1 (February): 1068159. As of 18 November 2024: https://doi.org/10.3389/fsci.2023.1068159

Hasin, Yehudit, Marcus Seldin, and Aldons Lusis. 2017. "Multi-Omics Approaches to Disease." *Genome Biology* 18 (1): 1–15. As of 14 August 2024: https://doi.org/10.1186/s13059-017-1215-1

Hassan, Mofor, Garibaldi, and Abadia. 2023. "A Comprehensive Analysis of Neurotechnologies in the Context of Human Rights: Consequences, Challenges, and Successes." OHCHR. As of 18 November 2024: https://www.ohchr.org/sites/default/files/documents/hrbodies/hrcouncil/advisorycommittee/neurotechnology/03-ngos/ac-submission-cso-icure.pdf

Health Council of the Netherlands. 2023. "The 14-Day Rule in the Dutch Embryo Act." As of 13 August 2024: https://www.healthcouncil.nl/documents/advisory-reports/2023/10/31/the-14-day-rule-in-the-dutch-embryo-act

Health Data Governance Principles. 2024. "Homepage." As of 14 August 2024: https://healthdataprinciples.org

Hendricks-Sturrup, Rachele M., and Christine Y. Lu. 2019. "Direct-to-Consumer Genetic Testing Data Privacy: Key Concerns and Recommendations Based on Consumer Perspectives." *Journal of Personalized Medicine* 9 (2): 25. As of 18 November 2024: https://doi.org/10.3390/jpm9020025

Heus, Joris J., Elmar S. de Pauw, Leloux Mirjam, Morpurgo Margherita, Hamblin Michael R, and Heger Michal. 2017. "Importance of Intellectual Property Generated by Biomedical Research at Universities and Academic Hospitals." *Journal of Clinical and Translational Research* 3 (2): 250–59.

HFEA. 2023. *Modernising Fertility Law: Recommendations from the Human Fertilisation and Embryology Authority (HFEA) for changes to the Human Fertilisation and Embryology Act 1990 (as amended).* Human Fertilisation & Embryology Authority. As of 13 August 2024: https://www.hfea.gov.uk/about-us/modernising-the-regulation-of-fertility-treatment-and-research-involving-human-embryos/modernising-fertility-law/

Hickman, Cristina Fontes Lindemann, Hoor Alshubbar, Jerome Chambost, Celine Jacques, Chris-Alexandre Pena, Andrew Drakeley, and Thomas Freour. 2020. "Data Sharing: Using Blockchain and Decentralized Data Technologies to Unlock the Potential of Artificial Intelligence: What Can Assisted Reproduction Learn from Other Areas of Medicine?" *Fertility and Sterility* 114 (5): 927–33. As of 18 November 2024: https://doi.org/10.1016/j.fertnstert.2020.09.160

Hicks, Marie-Laure, Ella Guest, Jess Whittlestone, Jacob Ohrvik-Stott, Sana Zakaria, Cecilia Ang, Chryssa Politi, Imogen Wade, and Salil Gunashekar. 2023. *Exploring Red Teaming to Identify New and Emerging Risks from AI Foundation Models.* Santa Monica, Calif.: RAND Corporation. CF-A3031-1. As of 18 November 2024: https://www.rand.org/pubs/conf_proceedings/CFA3031-1.html

Hillson, Nathan, Mark Caddick, Yizhi Cai, Jose A. Carrasco, Matthew Wook Chang, Natalie C. Curach, David J. Bell, et al. 2019. "Building a Global Alliance of Biofoundries." Nature Communications 10 (1): 2040. As of 14 August 2024: https://doi.org/10.1038/s41467-019-10079-2

Hinkson, Izumi V., Tanja M. Davidsen, Juli D. Klemm, Ishwar Chandramouliswaran, Anthony R. Kerlavage, and Warren A. Kibbe. 2017. "A Comprehensive Infrastructure for Big Data in Cancer Research: Accelerating Cancer Research and Precision Medicine." *Frontiers in Cell and Developmental Biology* 5 (September): 291496. As of 18 November 2024: https://doi.org/10.3389/fcell.2017.00083

Ho, Dean, et al. 2020. "Enabling technologies for personalized and precision medicine." *Trends in Biotechnology* 38 (5): 497. As of 29 November 2024: https://doi.org/10.1016/j.tibtech.2019.12.021

Holland, Claire, Adam McCarthy, Priscila Ferri, and Philip Shapira. 2024. "Innovation Intermediaries at the Convergence of Digital Technologies, Sustainability, and Governance: A Case Study of AI-Enabled Engineering Biology." *Technovation* 129 (January): 102875. As of 18 November 2024: https://doi.org/10.1016/j.technovation.2023.102875

Hosmillo, Myra, Yasmin Chaudhry, Komal Nayak, Frederic Sorgeloos, Bon-Kyoung Koo, Alessandra Merenda, Reidun Lillestol, Lydia Drumright, Matthias Zilbauer, and Ian Goodfellow. 2020. "Norovirus Replication in Human Intestinal Epithelial Cells Is Restricted by the Interferon-Induced JAK/STAT Signaling Pathway and RNA Polymerase II-Mediated Transcriptional Responses." *mBio* 11 (2). As of 18 November 2024: https://doi.org/10.1128/mBio.00215-20

Hossain, Khondoker Murad, Md Ariful Islam, Shahera Hossain, Anton Nijholt, and Md Atiqur Rahman Ahad. 2023. "Status of Deep Learning for EEG-Based Brain–Computer Interface Applications." *Frontiers in Computational Neuroscience* 16 (January). As of 18 November 2024: https://doi.org/10.3389/fncom.2022.1006763

HSC. 2017. "Organoids: A New Window into Disease, Development and Discovery." Harvard Stem Cell Institute. 7 November. As of 17 August 2024: https://hsci.harvard.edu/organoids

Hu, Chengyu, Sheng Yang, Tianyi Zhang, Yiling Ge, Zaozao Chen, Juan Zhang, Yuepu Pu, and Geyu Liang. 2024. "Organoids and Organoids-on-a-Chip as the New Testing Strategies for Environmental Toxicology-Applications & Advantages." *Environment International* 184 (February): 108415. As of 18 November 2024: https://doi.org/10.1016/j.envint.2024.108415

Hulme, Philip E., Jacqueline R. Beggs, Rachelle N. Binny, Jonathan P. Bray, Naomi Cogger, Manpreet K. Dhami, Susanna C. Finlay-Smits, et al. 2023. "Emerging Advances in Biosecurity to Underpin Human, Animal, Plant, and Ecosystem Health." *iScience* 26 (9): 107462. As of 18 November 2024: https://doi.org/10.1016/j.isci.2023.107462

Human Cell Atlas. 2024. "Homepage." As of 15 August 2024: https://www.humancellatlas.org/

Human Genome Project. 2021. "ELSI Planning and Evaluation History." National Human Genome Research Institute. As of 18 November 2024: https://www.genome.gov/10001754/elsi-planning-and-evaluation-history

Hyun, Insoo, J.C. Scharf-Deering, and Jeantine E. Lunshof. 2020. "Ethical Issues Related to Brain Organoid Research." *Brain Research* 1732 (April): 146653. As of 18 November 2024: https://doi.org/10.1016/j.brainres.2020.146653

IBioIC. 2023. "AI, Engineering Biology & Beyond." As of 12 August 2024: https://www.ibioic.com/events-database/ai-engineering-biology-amp-beyond

ICO. 2023. "ICO Tech Futures: Neurotechnology." As of 18 November 2024: https://ico.org.uk/about-the-ico/research-reports-impact-and-evaluation/research-and-reports/technology-and-innovation/ico-tech-futures-neurotechnology/

Ienca, Marcello, Fabrice Jotterand, and Bernice S. Elger. 2018. "From Healthcare to Warfare and Reverse: How Should We Regulate Dual-Use Neurotechnology?" *Neuron* 97 (2): 269–74. As of 18 November 2024: https://doi.org/10.1016/j.neuron.2017.12.017

Ikka, Tsunakuni, Taichi Hatta, Yoko Saito, and Misao Fujita. 2023. "Does the Act on the Safety of Regenerative Medicine in Japan Ensure 'Safety'?: Implications of Low Adverse Event Reporting." *Stem Cell Reports* 18 (12): 2297–99. As of 18 November 2024: https://doi.org/10.1016/j.stemcr.2023.10.012

IMDA. 2024. "Singapore Proposes Framework to Foster Trusted Generative AI Development." Infocomm Media Development Authority. 16 January. As of 17 August 2024: https://www.imda.gov.sg/resources/press-releases-factsheets-and-speeches/press-releases/2024/public-consult-model-ai-governance-framework-genai

Imperial. 2024. "UKRI Artificial Intelligence for Engineering Biology Consortium." Imperial College London. As of 15 August 2024: https://www.imperial.ac.uk/ukri-ai-engineering/

Infante, Deliana. 2023. "AI-Powered Genomic Analysis: Revolutionizing the Detection of Genetic Mutations." News-Medical. 8 November. As of 18 November 2024: https://www.news-medical.net/health/AI-Powered-Genomic-Analysis-Revolutionizing-the-Detection-of-Genetic-Mutations.aspx

Innovate UK. 2018. "Singapore Launches National S$25 Million, 5-Year Synthetic Biology R&D Programme - Innovate UK Business Connect."" 23 January. As of 15 August 2024: https://iuk.ktn-uk.org/news/singapore-launches-national-s25-million-5-year-synthetic-biology-rd-programme/

International Neuroethics Society. N.d. "AI and Consciousness Affinity Group." As of 9 April 2024: https://www.neuroethicssociety.org/ai-consciousness-group

IQVIA Institute. 2020. Understanding the Global Landscape of Genomic Initiatives: Progress and Promise. The IQVIA Institute. As of 29 November 2024: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/understanding-the-global-landscape-of-genomic-initiatives

Jaber, Wassim, Hussein A.H. Jaber, Ramzi Jaber, and Zahraa Saleh. 2024. "The Convergence of AI and BCIs: A New Era of Brain-Machine Interfaces." In Artificial Intelligence in the Age of Nanotechnology, 98–113. IGI Global. As of 29 November 2024: https://doi.org/10.4018/979-8-3693-0368-9.ch006

Jasanoff, Sheila, J. Benjamin Hurlbut, and Krishanu Saha. 2019. "Democratic Governance of Human Germline Genome Editing." *CRISPR Journal* 2 (5): 266–71. As of 18 November 2024: https://doi.org/10.1089/crispr.2019.0047

Jiang, Victoria S., and Charles L. Bormann. 2023. "Noninvasive genetic screening: Current advances in artificial intelligence for embryo ploidy prediction." *Fertility and Sterility* 120 (2), 228–234. As of 29 November 2024: https://doi.org/10.1016/j.fertnstert.2023.06.025

Jin, Haojie, Zhen Sun, and René Bernards. 2024. "LICOB: A Powerful Organoid Platform for Drug Discovery." *Cell Research* 34 (1): 11–12. As of 18 November 2024: https://doi.org/10.1038/s41422-023-00878-0

Johnson, Charlie D., Wilson Sinclair, and Rebecca Mackelprang. 2023. *Security Considerations at the Intersection of Engineering Biology and Artificial Intelligence.* Engineering Biology Research Consortium. As of 14 August 2024: https://doi.org/10.25498/E4J017

Johnson, Stephanie B., Ingrid Slade, Alberto Giubilini, and Mackenzie Graham. 2020. "Rethinking the Ethical Principles of Genomic Medicine Services." *European Journal of Human Genetics* 28 (2): 147–54. As of 18 November 2024: https://doi.org/10.1038/s41431-019-0507-1

Jwa, Anita S., and Russell A. Poldrack. 2022. "Addressing Privacy Risk in Neuroscience Data: From Data Protection to Harm Prevention." *Journal of Law and the Biosciences* 9 (2): lsac025. As of 18 November 2024: https://doi.org/10.1093/jlb/lsac025

Kaye, Jane, Edgar A. Whitley, David Lund, Michael Morrison, Harriet Teare, and Karen Melham. 2015. "Dynamic consent: A patient interface for twenty-first century research networks." *European Journal of Human Genetics* 23 (2): 141–146. As of 29 November 2024: https://doi.org/10.1038/ejhg.2014.71

Kaye, Jane, Sharon F. Terry, Eric Juengst, Sarah Coy, Jennifer R. Harris, Don Chalmers, Edward S. Dove, et al. 2018. "Including All Voices in International Data-Sharing Governance." *Human Genomics* 12 (1): 13. As of 18 November 2024: https://doi.org/10.1186/s40246-018-0143-9

Khan, Ahnaaf. 2020. "Playing With Your Thoughts: How VR and BCIs Can Make You Sound Not Crazy." Medium, 22 November. As of 16 August 2024: https://ahnaafk.medium.com/playing-with-your-thoughts-how-vr-and-bcis-can-make-you-sound-not-crazy-522cb730f7bf

Khan, Mashal, Frank G. Glavin, and Matthias Nickles. 2023. "Federated Learning as a Privacy Solution - An Overview." *Procedia Computer Science*, 4th International Conference on Industry 4.0 and Smart Manufacturing 217 (January): 316–25. As of 18 November 2024: https://doi.org/10.1016/j.procs.2022.12.227

Kickbusch, Ilona, Dario Piselli, Anurag Agrawal, Ran Balicer, Olivia Banner, Michael Adelhardt, Emanuele Capobianco, et al. 2021. "The Lancet and Financial Times Commission on Governing Health Futures 2030: Growing up in a Digital World." *Lancet* 398 (10312): 1727–76. As of 18 November 2024: https://doi.org/10.1016/S0140-6736(21)01824-9

Kim, Jihoon, Bon-Kyoung Koo, and Juergen A. Knoblich. 2020. "Human Organoids: Model Systems for Human Biology and Medicine." *Nature Reviews Molecular Cell Biology* 21 (10): 571–84. As of 18 November 2024: https://doi.org/10.1038/s41580-020-0259-3

Klünker, Irma, and Heiko Richter. 2022. "Digital Sequence Information between Benefit-Sharing and Open Data." *Journal of Law and the Biosciences* 9 (2): lsac035. As of 18 November 2024: https://doi.org/10.1093/jlb/lsac035

Knotkova, Helena, Clement Hamani, Eellan Sivanesan, María Francisca Elgueta Le Beuffe, Jee Youn Moon, Steven P. Cohen, and Marc A. Huntoon. 2021. "Neuromodulation for Chronic Pain." *Lancet* 397 (10289): 2111–24. As of 18 November 2024: https://doi.org/10.1016/S0140-6736(21)00794-7

Koch, Linda. 2024. "Global Genomic Diversity for All of Us." Nature Reviews Genetics 25. As of 14 August 2024: https://doi.org/10.1038/s41576-024-00727-9

Koutkias, Vassilis. 2019. "From Data Silos to Standardized, Linked, and FAIR Data for Pharmacovigilance: Current Advances and Challenges with Observational Healthcare Data." *Drug Safety* 42 (5): 583–86. As of 18 November 2024: https://doi.org/10.1007/s40264-018-00793-z

Kozlov, Max 2023. “Human trials of artificial wombs could start soon. Here’s what you need to know.” Nature 621 (7979): 458–460. As of 29 November 2024: https://doi.org/10.1038/d41586-023-02901-1

Kragh, Mikkel Fly, and Henrik Karstoft. 2021. “Embryo Selection with Artificial Intelligence: How to Evaluate and Compare Methods?” *Journal of Assisted Reproduction and Genetics* 38 (7): 1675–89. As of 18 November 2024: https://doi.org/10.1007/s10815-021-02254-6

Kreitmair, Karola V. 2019. “Dimensions of Ethical Direct-to-Consumer Neurotechnologies.” *AJOB Neuroscience* 10 (4): 152–66. As of 18 November 2024: https://doi.org/10.1080/21507740.2019.1665120

Krier, Joel B., and Robert C. Green. 2013. “Management of Incidental Findings in Clinical Genomic Sequencing.” *Current Protocols in Human Genetics* 0 9: Unit9.23. As of 18 November 2024: https://doi.org/10.1002/0471142905.hg0923s77

Kuilken, Todd. 2023. “Artificial Intelligence in the Biological Sciences: Uses, Safety, Security, and Oversight.” R47849. Congressional Research Service. As of 18 November 2024: https://crsreports.congress.gov/product/details?prodcode=R47849

Kukora, Stephanie, George B. Mychaliska, and Elliott M. Weiss. 2023. “Ethical challenges in first-in-human trials of the artificial placenta and artificial womb: Not all technologies are created equally, ethically.” Journal of Perinatology 43 (11): 1337–1342. As of 29 November 2024: https://doi.org/10.1038/s41372-023-01713-5

Kush, R. D., D. Warzel, M. A. Kush, A. Sherman, E. A. Navarro, R. Fitzmartin, F. Pétavy, et al. 2020. “FAIR Data Sharing: The Roles of Common Data Elements and Harmonization.” *Journal of Biomedical Informatics* 107 (July):103421. As of 18 November 2024: https://doi.org/10.1016/j.jbi.2020.103421

Kushnir, Vitaly A., Gary D. Smith, and Eli Y. Adashi. 2022. “The Future of IVF: The New Normal in Human Reproduction.” *Reproductive Sciences* 29 (3): 849–56. As of 18 November 2024: https://doi.org/10.1007/s43032-021-00829-3

Kwok, Roberta. 2010. “Five Hard Truths for Synthetic Biology.” *Nature* 463 (7279): 288–90. As of 18 November 2024: https://doi.org/10.1038/463288a

Laestadius, Linnea I., Jennifer R. Rich, and Paul L. Auer. 2017. “All Your Data (Effectively) Belong to Us: Data Practices among Direct-to-Consumer Genetic Testing Firms.” *Genetics in Medicine* 19 (5): 513–20. As of 18 November 2024: https://doi.org/10.1038/gim.2016.136

Lamers, Mart M., Joep Beumer, Jelte van der Vaart, Kèvin Knoops, Jens Puschhof, Tim I. Breugem, Raimond B.G. Ravelli, et al. 2020. “SARS-CoV-2 Productively Infects Human Gut Enterocytes.” *Science* 369 (6499): 50–54. As of 18 November 2024: https://doi.org/10.1126/science.abc1669

Lancet. 2019. “iHuman: A Futuristic Vision for the Human Experience.” *Lancet* 394 (10203): 979. As of 18 November 2024: https://doi.org/10.1016/S0140-6736(19)32141-5

Lancet Digital Health. 2021. “Digital Technologies: A New Determinant of Health.” *Lancet Digital Health* 3 (11): e684. As of 18 November 2024: https://doi.org/10.1016/S2589-7500(21)00238-7

Lau-Zhu, Alex, Michael P.H. Lau, and Gráinne McLoughlin. 2019. “Mobile EEG in Research on Neurodevelopmental Disorders: Opportunities and Challenges.” Developmental Cognitive Neuroscience 36 (April): 100635. As of 14 August 2024: https://doi.org/10.1016/j.dcn.2019.100635

Lawson, Christopher E., Jose Manuel Martí, Tijana Radivojevic, Sai Vamshi R. Jonnalagadda, Reinhard Gentz, Nathan J. Hillson, Sean Peisert, et al. 2021. “Machine Learning for Metabolic Engineering: A Review.” *Metabolic Engineering* 63 (January): 34–60. As of 18 November 2024: https://doi.org/10.1016/j.ymben.2020.10.005

Lee, Hanbyeol, Jeong Suk Im, Da Bin Choi, and Dong-Hun Woo. 2021. “Trends in the Global Organoid Technology and Industry: From Organogenesis in a Dish to the Commercialization of Organoids.” *Organoid* 1 (July). As of 18 November 2024: https://doi.org/10.51335/organoid.2021.1.e11

Lee, Tammy, Jay Natalwala, Vincent Chapple, and Yanhe Liu, Y. 2024. "A brief history of artificial intelligence embryo selection: From black-box to glass-box." Human Reproduction 39 (2): 285–292. As of 29 November 2024: https://doi.org/10.1093/humrep/dead254

Leeb, Robert, and Daniel Pérez-Marcos. 2020. "Brain-Computer Interfaces and Virtual Reality for Neurorehabilitation." *Handbook of Clinical Neurology* 168: 183–97. As of 18 November 2024: https://doi.org/10.1016/B978-0-444-63934-9.00014-7

Leger, Laura. 2024. "Neurorights in Europe: Striking a Balance between Ethical Regulation and Competitiveness." Centre for European Progression. 16 January. As of 18 November 2024: https://c4ep.eu/neurorights-in-europe-striking-a-balance-between-ethical-regulation-and-competitiveness/

Lehne, Moritz, Julian Sass, Andrea Essenwanger, Josef Schepers, and Sylvia Thun. 2019. "Why Digital Medicine Depends on Interoperability." *Npj Digital Medicine* 2 (1): 1–5. As of 18 November 2024: https://doi.org/10.1038/s41746-019-0158-1

Leopoldina. 2021. "Ethical Aspects and a New Set of Regulations." As of 13 August 2024: https://www.leopoldina.org/en/topics/embryo-research/ethical-aspects-and-a-new-set-of-regulations/

Lewis, Jonathan, and Søren Holm. 2022. "Organoid Biobanking, Autonomy and the Limits of Consent." *Bioethics* 36 (7): 742–56. As of 18 November 2024: https://doi.org/10.1111/bioe.13047

Li, Xiang, Jingjing Chen, Nanlin Shi, Chen Yang, Puze Gao, Xiaogang Chen, Yijun Wang, Shangkai Gao, and Xiaorong Gao. 2023. "A Hybrid Steady-State Visual Evoked Response-Based Brain-Computer Interface with MEG and EEG." *Expert Systems with Applications* 223: 119736. As of 18 August 2024: https://doi.org/10.1016/j.eswa.2023.119736

Li, Yaqi, Peiyuan Tang, Sanjun Cai, Junjie Peng, and Guoqiang Hua. 2020. "Organoid Based Personalized Medicine: From Bench to Bedside." *Cell Regeneration* 9 (November): 21. As of 18 November 2024: https://doi.org/10.1186/s13619-020-00059-z

Lim, Cheng Kai, Ning Mao and Lee Hui Ling. 2020. "The Burgeoning Impact of Synthetic Biology". *Biotech Connection Singapore*, 3 June. As of 5 December 2024: https://www.biotechconnection-sg.org/the-burgeoning-impact-of-synthetic-biology/

Lin, Jing, and Kee Yuan Ngiam. 2023. "How Data Science and AI-Based Technologies Impact Genomics." *Singapore Medical Journal* 64 (1): 59–66. As of 18 November 2024: https://doi.org/10.4103/singaporemedj.SMJ-2021-438

Ling, Ho 2024. "AI: The evolving legal landscape in Asia Pacific." Clifford Chance, 31 January. As of 12 August 2024: https://www.cliffordchance.com/content/cliffordchance/insights/thought_leadership/ai-and-tech/ai-the-evolving-legal-landscape-in-apac.html

Liu, Haitao, Xu Zhang, Jiayue Liu, and Jianhua Qin. 2023. "Vascularization of Engineered Organoids." *BMEMat* 1 (3): e12031. As of 18 November 2024: https://doi.org/10.1002/bmm2.12031

Liu, Xu, Jialu Zhao, Liting Xue, Tian Zhao, Wei Ding, Yuying Han, and Haihong Ye. 2022. "A Comparison of Transcriptome Analysis Methods with Reference Genome." *BMC Genomics* 23 (1): 1–15. As of 18 November 2024: https://doi.org/10.1186/s12864-022-08465-0

Lomotey, Richard K., Sandra Kumi, and Ralph Deters. 2022. "Data Trusts as a Service: Providing a platform for multi-party data sharing." International Journal of Information Management Data Insights 2(1): 100075. As of 29 November 2024: https://doi.org/10.1016/j.jjimei.2022.100075

Lorenzo, David, Montse Esquerda, Margarita Bofarull, Victoria Cusi, Helena Roig, Joan Bertran, Joan Carrera, et al. 2023. "The Reuse of Genetic Information in Research and Informed Consent." *European Journal of Human Genetics* 31 (12): 1393–97. As of 18 November 2024: https://doi.org/10.1038/s41431-023-01457-y

Lovell-Badge, Robin, Eric Anthony, Roger A. Barker, Tania Bubela, Ali H. Brivanlou, Melissa Carpenter, R. Alta Charo, et al. 2021. "ISSCR Guidelines for Stem Cell Research and Clinical Translation: The 2021 Update." *Stem Cell Reports* 16 (6): 1398–1408. As of 18 November 2024: https://doi.org/10.1016/j.stemcr.2021.05.012

Luo, Tao, Lican Zheng, Dongyang Chen, Chen Zhang, Sirui Liu, Chongjie Jiang, Yu Xie, Dan Du, and Wei Zhou. 2023. "Implantable Microfluidics: Methods and Applications." Analyst 148 (19): 4637–54. As of 18 August 2024: https://doi.org/10.1039/D3AN00981E

Ma, Zhiyun, Baicheng Li, Jie Peng, and Dan Gao. 2022. "Recent Development of Drug Delivery Systems through Microfluidics: From Synthesis to Evaluation." As of 18 November 2024: https://www.mdpi.com/1999-4923/14/2/434

MacDuffie, Katherine E., Jason L. Stein, Dan Doherty, Suman Jayadev, Jessica B. Girault, Katherine A. Emmons, Madison Rose Glass, et al. 2023. "Donor Perspectives on Informed Consent and Use of Biospecimens for Brain Organoid Research." *Stem Cell Reports* 18 (7): 1389–93. As of 18 November 2024: https://doi.org/10.1016/j.stemcr.2023.05.019

Mallapaty, Smriti. 2018. "Engineering a Biomedical Revolution." *Nature* 564 (7735): S66–68. As of 18 November 2024: https://doi.org/10.1038/d41586-018-07692-4

Maloy, John W., and Pat F. Bass. 2020. "Understanding Broad Consent." *Ochsner Journal* 20 (1): 81–86. As of 18 November 2024: https://doi.org/10.31486/toj.19.0088

Mantellassi, Federico. 2022. "In Focus: The Challenges of Neurotechnology." Geneva Centre for Security Policy. As of 17 August 2024: https://www.gcsp.ch/global-insights/focus-challenges-neurotechnology

Maramraju, Sudhiksha, Andrew Kowalczewski, Anirudh Kaza, Xiyuan Liu, Jathin Pranav Singaraju, Mark V. Albert, Zhen Ma, and Huaxiao Yang. 2024. "AI-Organoid Integrated Systems for Biomedical Studies and Applications." *Bioengineering & Translational Medicine* 9 (2): e10641. As of 18 November 2024: https://doi.org/10.1002/btm2.10641

Marx, Vivien. 2023. "To Share Is to Be a Scientist." *Nature Methods* 20 (7): 984–89. As of 18 November 2024: https://doi.org/10.1038/s41592-023-01927-7

Matthews, David. 2023. "Scientists Grapple with Risk of Artificial Intelligence-Created Pandemics." *Science|Business*, 5 September. As of 18 November 2024: https://sciencebusiness.net/news/ai/scientists-grapple-risk-artificial-intelligence-created-pandemics

Matthews, Jonathan M., Brooke Schuster, Sara Saheb Kashaf, Ping Liu, Rakefet Ben-Yishay, Dana Ishay-Ronen, Evgeny Izumchenko, et al. 2022. "OrganoID: A Versatile Deep Learning Platform for Tracking and Analysis of Single-Organoid Dynamics." *PLOS Computational Biology* 18 (11): e1010584. As of 18 November 2024: https://doi.org/10.1371/journal.pcbi.1010584

Matthews, Kirstin R.W., and Daniel Moralí. 2020. "National Human Embryo and Embryoid Research Policies: A Survey of 22 Top Research-Intensive Countries." *Regenerative Medicine* 15 (7): 1905–17. As of 18 November 2024: https://doi.org/10.2217/rme-2019-0138

Mc Cartney, Ann M., Jane Anderson, Libby Liggins, Maui L. Hudson, Matthew Z. Anderson, Ben TeAika, Janis Geary, Robert Cook-Deegan, Hardip R. Patel, and Adam M. Phillippy. 2022. "Balancing Openness with Indigenous Data Sovereignty: An Opportunity to Leave No One behind in the Journey to Sequence All of Life." *Proceedings of the National Academy of Sciences* 119 (4): e2115860119. As of 18 November 2024: https://doi.org/10.1073/pnas.2115860119

McCully, Sophia. 2021. "The Time Has Come to Extend the 14-Day Limit." *Journal of Medical Ethics* 47 (12): e66. As of 18 November 2024: https://doi.org/10.1136/medethics-2020-106406

McKie, Robin. 2023. "How far should we go with gene editing in pursuit of the 'perfect' human?" *Observer,* 5 February. As of 29 November 2024: https://www.theguardian.com/science/2023/feb/05/how-far-should-we-go-with-gene-editing-in-pursuit-of-the-perfect-human

Medenica, Sanja, Dusan Zivanovic, Ljubica Batkoska, Susanna Marinelli, Giuseppe Basile, Antonio Perino, Gaspare Cucinella, Giuseppe Gullo, and Simona Zaami. 2022. "The Future Is Coming: Artificial Intelligence in the Treatment of Infertility Could Improve Assisted Reproduction Outcomes—The Value of Regulatory Frameworks." *Diagnostics* 12 (12): 2979. As of 29 November 2024: https://doi.org/10.3390/diagnostics12122979

Mehta, Dhvani D., Angela Praecht, Heather B. Ward, Marcos Sanches, Maryam Sorkhou, Victor M. Tang, Vaughn R. Steele, Colleen A. Hanlon, and Tony P. George. 2023. "A Systematic Review and Meta-Analysis of Neuromodulation Therapies for Substance Use Disorders." *Neuropsychopharmacology* (December): 1–32. As of 18 November 2024: https://doi.org/10.1038/s41386-023-01776-0

Meng, Fankang, and Tom Ellis. 2020. "The second decade of synthetic biology: 2010–2020." Nature Communica-tions 11 (1): 5174. https://doi.org/10.1038/s41467-020-19092-2

Mercer, Shannon Togawa. 2020. "The Limitations of European Data Protection As A Model for Global Privacy Regulation" 114 (January): 20–25. As of 18 November 2024: https://doi.org/10.1017/aju.2019.83

Mickle, Aaron D., Sang Min Won, Kyung Nim Noh, Jangyeol Yoon, Kathleen W. Meacham, Yeguang Xue, Lisa A. McIlvried, et al. 2019. "A Wireless Closed-Loop System for Optogenetic Peripheral Neuromodulation." *Nature* 565 (7739): 361–65. As of 18 November 2024: https://doi.org/10.1038/s41586-018-0823-6

Mineo, Liz. 2023. "We should be fighting for our cognitive liberty, says ethics expert." Harvard Gazette, 26 April. As of 29 November 2024: https://news.harvard.edu/gazette/story/2023/04/we-should-be-fighting-for-our-cognitive-liberty-says-ethics-expert/

Mitchell, Kyle T., and Philip A. Starr. 2020. "Chapter 12 - Smart Neuromodulation in Movement Disorders." In *Handbook of Clinical Neurology*, edited by Nick F. Ramsey and José del R. Millán 168: 153–61. Brain-Computer Interfaces. Elsevier. As of 18 November 2024: https://doi.org/10.1016/B978-0-444-63934-9.00012-3

Moon, Joshua, and Alexander Ghionis. 2024. "AI-Anxieties: Framing the Artificial Intelligence Challenge within the CBW Prohibition Regimes." Report. University of Sussex. As of 18 November 2024: https://sussex.figshare.com/articles/report/AI-Anxieties_framing_the_artificial_intelligence_challenge_within_the_CBW_prohibition_regimes/25027769/1

Moons, Karel G. M., Robert F. Wolff, Richard D. Riley, Penny F. Whiting, Marie Westwood, Gary S. Collins, Johannes B. Reitsma, Jos Kleijnen, and Sue Mallett. 2019. "PROBAST: A Tool to Assess Risk of Bias and Applicability of Prediction Model Studies: Explanation and Elaboration." Annals of Internal Medicine 170 (1): W1–W33. As of 29 November 2024: https://doi.org/10.7326/M18-1377

Moreno, Jonathan D., Michael N. Tennison, and James Giordano. 2017. “Security Threat versus Aggregated Truths: Ethical Issues in the Use of Neuroscience and Neurotechnology for National Security.” In *Neuroethics: Anticipating the Future*, edited by Judy Illes. Oxford: Oxford University Press. As of 18 November 2024: https://doi.org/10.1093/oso/9780198786832.003.0027

Motiei, Marjan, Katerina Vaculikova, Andrea Cela, Katerina Tvrdonova, Reza Khalili, David Rumpik, Tatana Rumpikova, Zdenek Glatz, and Tomas Saha. 2020. “Non-Invasive Human Embryo Metabolic Assessment as a Devel-opmental Criterion.” Journal of Clinical Medicine 9 (12): 4094. As of 29 November 2024: https://doi.org/10.3390/jcm9124094

Mouton, Christopher A., Caleb Lucas, and Ella Guest. 2023. The Operational Risks of AI in Large-Scale Biological Attacks: A Red-Team Approach. Santa Monica, Calif.: RAND Corporation. RR-A2977-1. As of 14 August 2024: https://www.rand.org/pubs/research_reports/RRA2977-1.html

Muhammad, Riaz, Ahmed Ali, M. Anwar, Toufique Soomro, Omar AlShorman, Adel Alshahrani, Mahmoud Masadeh, et al. 2022. “Design and Development of Low-Cost Wearable Electroencephalograms (EEG) Headset.” *Intelligent Automation & Soft Computing* 35 (3): 2821–35. As of 18 November 2024: https://doi.org/10.32604/iasc.2023.026279

Musoni, Melody. 2024. “Envisioning Africa’s AI Governance Landscape in 2024.” *Policy Brief* 177. EDDPM. As of 18 November 2024: https://ecdpm.org/work/envisioning-africas-ai-governance-landscape-2024

Naderi-Meshkin, Hojjat, Victoria A. Cornelius, Magdalini Eleftheriadou, Koray Niels Potel, Wiwit Ananda Wahyu Setyaningsih, and Andriana Margariti. 2023. “Vascular Organoids: Unveiling Advantages, Applications, Challenges, and Disease Modelling Strategies.” *Stem Cell Research & Therapy* 14 (1): 292. As of 18 November 2024: https://doi.org/10.1186/s13287-023-03521-2

Nagai, Sumimasa, and Keiya Ozawa. 2017. “New Japanese Regulatory Frameworks for Clinical Research and Marketing Authorization of Gene Therapy and Cellular Therapy Products.” *Current Gene Therapy* 17 (1): 17–28. As of 18 November 2024: https://doi.org/10.2174/1566523217666170406123231

National Academies of Sciences, Engineering, Policy and Global Affairs, Technology Committee on Science, and Legal Committee on Ethical. 2021. “Oversight and Governance.” In *The Emerging Field of Human Neural Organoids, Transplants, and Chimeras: Science, Ethics, and Governance*. Washington (DC): National Academies Press (US). As of 18 November 2024: https://www.ncbi.nlm.nih.gov/books/NBK572233/

National Academies of Sciences, Engineering, and Medicine; Policy and Global Affairs. 2023. *Third International Summit on Human Genome Editing: Expanding Capabilities, Participation, and Access: Proceedings of a Workshop—in Brief*. Edited by Steve Olson. The National Academies Collection: Reports Funded by National Institutes of Health. Washington (DC): National Academies Press (US). As of 18 November 2024: http://www.ncbi.nlm.nih.gov/books/NBK593530/

Nature Materials. 2021. ‘The Promise of Organoids and Embryoids’. *Nature Materials* 20 (2): 121–121. As of 5 December 2024: https://doi.org/10.1038/s41563-021-00926-3

NBMA. n.d. “Our Guidelines – NBMA.” As of 18 November 2024: https://nbma.gov.ng/our-guidelines/

NC State University. 2024. “Team Members.” NeuroComputational Ethics Research Group. As of 17 August 2024: https://sites.google.com/view/neuroethics-group/team-members

NCI GDC. 2024. “National Cancer Institute Genomic Data Commons.” As of 12 August 2024: https://gdc.cancer.gov/

Nelson, Cassidy. 2019. “Engineered Pathogens: The Opportunities, Risks and Challenges.” *Biochem* 41 (3): 34–39. As of 18 November 2024: https://doi.org/10.1042/BIO04103034

Nerlich, Brigitte. 2020. "Synthetic biology, engineering biology and responsible innovation." Making Science Public. As of 29 November 2024: https://blogs.nottingham.ac.uk/makingsciencepublic/2020/10/16/synthetic-biology-engineering-biology-and-responsible-innovation/

Neuroethics Working Group. 2022. "Brain Research Through Advancing Innovative Neurotechnologies (BRAIN): Neuroethics Working Group Meeting." International Brain Initiative. As of 29 November 2024: https://braininitiative.nih.gov/sites/default/files/documents/nih_brain_newg_meeting_summary_aug_23_2022_final_508c.pdf

Neurotech.com. 2023. "Unlocking Insights for AI in NeuroTech 2023." September 27, 2023. As of 18 November 2024: https://www.linkedin.com/pulse/unlocking-insights-ai-neurotech-2023-new-report-platform/

Nguyen, Romario, Sarah Da Won Bae, Gang Zhou, Scott A. Read, Golo Ahlenstiel, Jacob George, and Liang Qiao. 2020. "Application of Organoids in Translational Research of Human Diseases with a Particular Focus on Gastrointestinal Cancers." *Biochimica et Biophysica Acta (BBA) - Reviews on Cancer* 1873 (2): 188350. As of 18 November 2024: https://doi.org/10.1016/j.bbcan.2020.188350

Nguyen, Romario, Sarah Da Won Bae, Liang Qiao, and Jacob George. 2021. "Developing Liver Organoids from Induced Pluripotent Stem Cells (iPSCs): An Alternative Source of Organoid Generation for Liver Cancer Research." *Cancer Letters* 508 (June):13–17. As of 18 November 2024: https://doi.org/10.1016/j.canlet.2021.03.017

NHS England. 2024. "Federated Data Platform – improving and connecting our health information." As of 14 August 2024: https://www.england.nhs.uk/long-read/federated-data-platform-improving-and-connecting-our-health-information/

NIH. 2022. "Artificial Intelligence, Machine Learning and Genomics." As of 18 November 2024: https://www.genome.gov/about-genomics/educational-resources/fact-sheets/artificial-intelligence-machine-learning-and-genomics

———. 2024. "Data Interoperability." Network of the National Library of Medicine. As of 12 August 2024: https://www.nnlm.gov/guides/data-glossary/data-interoperability

NIHR. 2024. "Organoid Facility." NIHR Imperial Biomedical Research Centre. As of 17 August 2024: https://imperialbrc.nihr.ac.uk/facilities/organoid-facility/

Novoa, Patricia Correia Rodrigues. 2014. "What Changes in Research Ethics in Brazil: Resolution No. 466/12 of the National Health Council." Einstein 12 (1). As of 15 August 2024: https://doi.org/10.1590/S1679-45082014ED3077

Nowinski, Wieslaw L. 2020. "Human Brain Atlases in Stroke Management." *Neuroinformatics* 18 (4): 549–67. As of 18 November 2024: https://doi.org/10.1007/s12021-020-09462-y

———. 2021. "Evolution of Human Brain Atlases in Terms of Content, Applications, Functionality, and Availability." *Neuroinformatics* 19 (1): 1–22. As of 18 November 2024: https://doi.org/10.1007/s12021-020-09481-9

Nuffield Council on Bioethics. 2024. "Neural Organoids in Research." As of 18 November 2024: https://www.nuffieldbioethics.org/publications/neural-organoids-in-research

NUS News. 2019. "NUS SynCTI cofounds the Global BioFoundry Alliance." 27 June. As of 29 November 2024: https://news.nus.edu.sg/nus-syncti-cofounds-the-global-biofoundry-alliance/

Ochang, Paschal, Damian Eke, and Bernd Carsten Stahl. 2023. "Towards an Understanding of Global Brain Data Governance: Ethical Positions That Underpin Global Brain Data Governance Discourse." *Frontiers in Big Data* 6 (November):1240660. As of 20 November 2024: https://doi.org/10.3389/fdata.2023.1240660

ODIN. N.d. “DIY Bacterial Gene Engineering CRISPR Kit.” The ODIN. As 11 April 2024: https://www.the-odin.com/diy-crispr-kit/

O’Doherty, Kieran C., Mahsa Shabani, Edward S. Dove, Heidi Beate Bentzen, Pascal Borry, Michael M. Burgess, Don Chalmers, et al. 2021. “Towards Better Governance of Human Genomic Data.” *Nature Genetics* 53 (1): 2–8. As of 18 November 2024: https://doi.org/10.1038/s41588-020-00742-6

OECD. 2019. “Recommendation of the Council on Responsible Innovation in Neurotechnology.” Paris: OECD. As of 18 August 2024: https://legalinstruments.oecd.org/en/instruments/OECD-LEGAL-0457

———. 2022. H*ealth Data Governance for the Digital Age: Implementing the OECD Recommendation on Health Data Governance*. Paris: OECD. As of 15 August 2024: https://www.oecd.org/health/health-data-governance-for-the-digital-age-68b60796-en.htm

———. 2023. *Artificial Intelligence in Science: Challenges, Opportunities and the Future of Research*. Paris: OECD Publishing. As of 18 November 2024: https://doi.org/10.1787/a8d820bd-en

———. 2024a. *Recommendation of the Council on Artificial Intelligence [OECD/LEGAL/0449]*. As of 18 November 2024: https://legalinstruments.oecd.org/en/instruments/OECD-LEGAL-0449

———. 2024b. “AI in Japan.” OECD.AI Policy Observatory. As of 17 August 2024: https://oecd.ai/en/dashboards/countries/Japan

Ogburn, Monique, Claude Turner, and Pushkar Dahal. 2013. “Homomorphic Encryption.” *Procedia Computer Science* 20 (January): 502–9. As of 18 November 2024: https://doi.org/10.1016/j.procs.2013.09.310

Oldak, Bernardo, et al. 2023. “Complete human day 14 post-implantation embryo models from naive ES cells.” *Nature* 622 (7983): 562–573. As of 29 November 2024: https://doi.org/10.1038/s41586-023-06604-5

Ong, Sandy. 2018. “Singapore Bets Big on Synthetic Biology.” *Nature*, 25 April. As of 18 August 2024: https://doi.org/10.1038/d41586-018-04123-2

OpenAlex. 2024a. “Topics.” As of 14 August 2024: https://docs.openalex.org/api-entities/topics

———. 2024b. “Search Works.” As of 16 August 2024: https://docs.openalex.org/api-entities/works/search-works

Ortiz-Lizcano, María Isabel, Enrique Arias-Antunez, Ángel Hernández Bravo, María Blanca Caminero, Tomás Rojo Guillen, and Syong Hyun Nam Cha. 2023. “Increasing the Security and Traceability of Biological Samples in Biobanks by Blockchain Technology.” *Computer Methods and Programs in Biomedicine* 231 (April): 107379. As of 18 November 2024: https://doi.org/10.1016/j.cmpb.2023.107379

OSDC. 2024. “Open Science Data Cloud.” As of 12 August 2024: https://www.opensciencedatacloud.org/

Otim, Geoffrey, Sandra Matinyi, Erikan Baluku, Ivy S. G. Chimulwa, George P. Magoola, Alex Katumba, Stephen Mukuze, Alex Kyabarongo, and Stephen O. Opiyo. 2023. “SynBio Africa’s Story from the Grassroots, the Present, and the Future.” *Biotechnology Notes* 4 (January): 1–6. As of 18 November 2024: https://doi.org/10.1016/j.biotno.2022.11.003

Palchuk, Matvey B., Jack W. London, David Perez-Rey, Zuzanna J. Drebert, Jessamine P. Winer-Jones, Courtney N. Thompson, John Esposito, and Brecht Claerhout. 2023. “A Global Federated Real-World Data and Analytics Platform for Research.” *JAMIA Open* 6 (2): ooad035. As of 18 November 2024: https://doi.org/10.1093/jamiaopen/ooad035

Panhuis, Willem G. van, Proma Paul, Claudia Emerson, John Grefenstette, Richard Wilder, Abraham J. Herbst, David Heymann, and Donald S. Burke. 2014. “A Systematic Review of Barriers to Data Sharing in Public Health.” *BMC Public Health* 14 (1): 1144. As of 18 November 2024: https://doi.org/10.1186/1471-2458-14-1144

Park, Sunghee Estelle, Andrei Georgescu, and Dongeun Huh. 2019. “Organoids-on-a-Chip.” *Science* 364 (6444): 960–65. As of 18 November 2024: https://doi.org/10.1126/science.aaw7894

Parida, Laxmi, and Torsten Haferlach. 2019. “Dark Matter Matters: AI Makes DNA Dark Matter Useful.” IBM Research Blog, 12 September. As of 12 August 2024: https://research.ibm.com/blog/ai-makes-dna-dark-matter-useful

Pawan, and Rohtash Dhiman. 2023. “Machine Learning Techniques for Electroencephalogram Based Brain-Computer Interface: A Systematic Literature Review.” *Measurement: Sensors* 28 (August): 100823. As of 18 November 2024: https://doi.org/10.1016/j.measen.2023.100823

Peel, Michael, and Cookson, Clive. 2024. “Scientists reprogramme microbes in quest to create new materials.” *Financial Times*, 11 January. As of 29 November 2024: https://www.ft.com/content/19989e64-6f52-49ff-bcb6-124c7e41ca7f

Perelló, Carlos. 2022. “Natural and Artificial Neural Networks: The Chilean Legal Framework.” *Journal of Civil Law Studies* 14 (1). As of 18 November 2024: https://digitalcommons.law.lsu.edu/jcls/vol14/iss1/11

Perez, Alvaro Nuno, Jose Suarez, and Michel Le Bars. 2023. “Sizing the Brain: Segmentation and growth factors of the global neuroscience market.” Deloitte Insights, 14 February. As of 16 August 2024: https://www2.deloitte.com/us/en/insights/industry/health-care/global-neuroscience-market-investment-report.html

Pilkington, Ed, and Gloria Oladipo. 2022. “What Are Russia’s Biological Weapons Claims and What’s Actually Happening?” *Guardian*, 22 March. As of 14 August 2024: https://www.theguardian.com/world/2022/mar/11/russia-biological-weapon-claim-us-un-ukraine-bio-labs-explainer

Pinti, Paola, Clarisse Aichelburg, Sam Gilbert, Antonia Hamilton, Joy Hirsch, Paul Burgess, and Ilias Tachtsidis. 2018. “A Review on the Use of Wearable Functional Near-Infrared Spectroscopy in Naturalistic Environments.” *Japanese Psychological Research* 60 (4): 347–73. As of 18 November 2024: https://doi.org/10.1111/jpr.12206

Piotrowska, Monika. 2021. “Research guidelines for embryoids.” *Journal of Medical Ethics* 47 (12): e67. As of 29 November 2024: https://doi.org/10.1136/medethics-2020-106493

Powell, Dylan, and Alan Godfrey. 2023. “Considerations for Integrating Wearables into the Everyday Healthcare Practice.” *Npj Digital Medicine* 6 (1): 1–3. As of 18 November 2024: https://doi.org/10.1038/s41746-023-00820-z

Precedence Research. 2024. “Personalized Medicine Market Size to Hit USD 1,233.23 Billion by 2033.” As of 14 August 2024: https://www.precedenceresearch.com/personalized-medicine-market

Prior, Nicole, Patricia Inacio, and Meritxell Huch. 2019. “Liver Organoids: From Basic Research to Therapeutic Applications.” *Gut* 68 (12): 2228–37. As of 18 November 2024: https://doi.org/10.1136/gutjnl-2019-319256

Pycroft, Laurie, Sandra G. Boccard, Sarah L. F. Owen, John F. Stein, James J. Fitzgerald, Alexander L. Green, and Tipu Z. Aziz. 2016. “Brainjacking: Implant Security Issues in Invasive Neuromodulation.” *World Neurosurgery* 92 (August): 454–62. As of 18 November 2024: https://doi.org/10.1016/j.wneu.2016.05.010

Qian, Xuyu, Hongjun Song, and Guo-li Ming. 2019. “Brain organoids: Advances, applications and challenges.” *Development* 146 (8): dev166074. As of 29 November 2024: https://doi.org/10.1242/dev.166074

Qin, Dahui. 2019. “Next-Generation Sequencing and Its Clinical Application.” *Cancer Biology & Medicine* 16 (1): 4. As of 18 November 2024: https://doi.org/10.20892/j.issn.2095-3941.2018.0055

Quigley, Kate M., Carlos Alvarez-Roa, Victor H. Beltran, Bill Leggat, and Bette L. Willis. 2021. "Experimental Evolution of the Coral Algal Endosymbiont, Cladocopium Goreaui: Lessons Learnt across a Decade of Stress Experiments to Enhance Coral Heat Tolerance." *Restoration Ecology* 29 (3). As of 18 November 2024: https://doi.org/10.1111/rec.13342

Rainey, Stephen, and Yasemin J. Erden. 2020. "Correcting the Brain? The Convergence of Neuroscience, Neurotechnology, Psychiatry, and Artificial Intelligence." *Science and Engineering Ethics* 26 (5): 2439–54. As of 29 November 2024: https://doi.org/10.1007/s11948-020-00240-2

Ravindra, Vikram, Petros Drineas, and Ananth Grama. 2021. "Constructing Compact Signatures for Individual Fingerprinting of Brain Connectomes." *Frontiers in Neuroscience* 15. As of 29 November 2024: https://doi.org/10.3389/fnins.2021.549322

Reeves, Jane, Gareth J. Treharne, Reremoana Theodore (Ngāpuhi and Te Arawa), Ngāruahine Edwards (Taranaki Iwi Tāngahoe, Pakakohi, Ngāti Ruanui) ,Will, Mihi Ratima (Whakatōhea and Ngāti Awa), and Richie Poulton. 2022. "Understanding the Data-Sharing Debate in the Context of Aotearoa/New Zealand: A Narrative Review on the Perspectives of Funders, Publishers/Journals, Researchers, Participants and Māori Collectives." *Kōtuitui: New Zealand Journal of Social Sciences Online* 17 (1): 1–23. As of 18 November 2024: https://doi.org/10.1080/1177083X.2021.1922465

Redman, Melody, Andrew King, Caroline Watson, and David King. 2016. "What is CRISPR/Cas9? Archives of Dis-ease in Childhood." *Education and Practice Edition* 101 (4): 213–215. As of 29 November 2024: https://doi.org/10.1136/archdischild-2016-310459

Ren, Ya, Xue Yang, Zhengjiang Ma, Xin Sun, Yuxin Zhang, Wentao Li, Han Yang, et al. 2021. "Developments and Opportunities for 3D Bioprinted Organoids." *International Journal of Bioprinting* 7 (3): 364. As of 18 November 2024: https://doi.org/10.18063/ijb.v7i3.364

Rennert, Robert C., Michael Januszyk, Michael Sorkin, Melanie Rodrigues, Zeshaan N. Maan, Dominik Duscher, Alexander J. Whittam, et al. 2016. "Microfluidic Single-Cell Transcriptional Analysis Rationally Identifies Novel Surface Marker Profiles to Enhance Cell-Based Therapies." *Nature Communications* 7 (1): 1–9. As of 18 November 2024: https://doi.org/10.1038/ncomms11945

Research and Markets. 2023. "Neuro-Gaming Technology Market - Growth, Trends, COVID-19 Impact, and Forecasts (2023 - 2028)." 2023. As of 18 November 2024: https://www.researchandmarkets.com/reports/5239515/neuro-gaming-technology-market-growth-trends

RHC. 2022. *Regulatory Horizons Council Report on Genetic Technologies.* Regulatory Horizons Council. As of 14 August 2024: https://www.gov.uk/government/publications/regulatory-horizons-council-report-on-genetic-technologies

RIKEN. 2022. "The next Milestones in Generating Artificial Organs." As of 15 August 2024: https://www.riken.jp/en/news_pubs/research_news/rr/20221221_1/index.html

Rivron, Nicolas C., Alfonso Martinez Arias, Martin F. Pera, Naomi Moris, and Hafez Ismaili M'hamdi. 2023. "An ethical framework for human embryology with embryo models." *Cell* 186 (17): 3548–57. As of 29 November 2024: https://doi.org/10.1016/j.cell.2023.07.028

Rocher, Luc, Julien M. Hendrickx, and Yves-Alexandre de Montjoye. 2019. "Estimating the Success of Re-Identifications in Incomplete Datasets Using Generative Models." *Nature Communications* 10 (1): 3069. As of 14 August 2024: https://doi.org/10.1038/s41467-019-10933-3

Roser, Max, Hannah Ritchie, and Edouard Mathieu. 2023. "Cost of sequencing a full human genome." Our World in Data. As of 29 November 2024: https://ourworldindata.org/grapher/cost-of-sequencing-a-full-human-genome

Royal Society. 2023. “Third International Human Genome Editing Summit.” As of 15 August 2024: https://royalsociety.org/science-events-and-lectures/2023/03/2023-human-genome-editing-summit/

Saad Alatrany, Abbas, Wasiq Khan, Abir J. Hussain, Jamila Mustafina, and Dhiya Al-Jumeily. 2023. “Transfer Learning for Classification of Alzheimer’s Disease Based on Genome Wide Data.” *IEEE Journals & Magazine* 20 (5): 2700–2711. As of 18 November 2024: https://doi.org/10.1109/TCBB.2022.3233869

Sadeghi, Mohammad R. 2022. “Will Artificial Intelligence Change the Future of IVF?” Journal of Reproduction & Infertility 23 (3): 139–140. As of 29 November 2024: https://doi.org/10.18502/jri.v23i3.10003

Saha, Simanto, Khondaker A. Mamun, Khawza Ahmed, Raqibul Mostafa, Ganesh R. Naik, Sam Darvishi, Ahsan H. Khandoker, and Mathias Baumert. 2021. “Progress in Brain Computer Interface: Challenges and Opportunities.” *Frontiers in Systems Neuroscience* 15 (February): 578875. As of 18 November 2024: https://doi.org/10.3389/fnsys.2021.578875

Salih, Mohamed, et al. 2023. “Embryo selection through artificial intelligence versus embryologists: A systematic review.” H*uman Reproduction Open* 2023 (3): hoad031. As of 29 November 2024: https://doi.org/10.1093/hropen/hoad031

Sample, Ian. 2023. “First UK Baby with DNA from Three People Born after New IVF Procedure.” *Guardian*. 9 May. As of 18 November 2024: https://www.theguardian.com/science/2023/may/09/first-uk-baby-with-dna-from-three-people-born-after-new-ivf-procedure

Santos, John Lenon de Souza, Cecília de Almeida Araújo, Clarissa Araújo Gurgel Rocha, Zaquer Suzana Munhoz Costa-Ferro, and Bruno Solano de Freitas Souza. 2023. “Modeling Autism Spectrum Disorders with Induced Pluripotent Stem Cell-Derived Brain Organoids.” *Biomolecules* 13 (2): 260. As of 18 November 2024: https://doi.org/10.3390/biom13020260

Sarkar, Esha, Eduardo Chielle, Gamze Gursoy, Leo Chen, Mark Gerstein, and Michail Maniatakos. 2023. “Privacy-preserving cancer type prediction with homomorphic encryption.” *Nature* 13. As of 14 August 2024: https://www.nature.com/articles/s41598-023-28481-8

Sato, Toshiro, Robert G. Vries, Hugo J. Snippert, Marc van de Wetering, Nick Barker, Daniel E. Stange, Johan H. van Es, et al. 2009. “Single Lgr5 Stem Cells Build Crypt-Villus Structures in Vitro without a Mesenchymal Niche.” *Nature* 459 (7244): 262–65. As of 18 November 2024: https://doi.org/10.1038/nature07935

Sawai, Tsutomu, Yoshiyuki Hayashi, Takuya Niikawa, Joshua Shepherd, Elizabeth Thomas, Tsung-Ling Lee, Alexandre Erler, Momoko Watanabe, and Hideya Sakaguchi. 2022. “Mapping the Ethical Issues of Brain Organoid Research and Application.” *AJOB Neuroscience* 13 (2): 81–94. As of 18 November 2024: https://doi.org/10.1080/21507740.2021.1896603

Schafer, Simon T., Apua C.M. Paquola, Shani Stern, David Gosselin, Manching Ku, Monique Pena, Thomas J.M. Kuret, et al. 2019. “Pathological Priming Causes Developmental Gene Network Heterochronicity in Autistic Subject-Derived Neurons.” *Nature Neuroscience* 22 (2). As of 18 November 2024: https://doi.org/10.1038/s41593-018-0295-x

Sciencewise. 2024. *Public Perceptions of Engineering Biology – Part 2: Food Applications*. As of 17 August 2024: https://sciencewise.org.uk/2024/04/public-perceptions-of-engineering-biology-food/

Seneviratne, Martin G., Susan B. Connolly, Seth S. Martin, and Kapil Parakh. 2023. “Grains of Sand to Clinical Pearls: Realizing the Potential of Wearable Data.” *American Journal of Medicine* 136 (2): 136–42. As of 18 November 2024: https://doi.org/10.1016/j.amjmed.2022.10.006

Sheets, Michael B., Joshua T. Atkinson, Mark P. Styczynski, and Emily R. Aurand. 2023. “Introduction to Engineer-ing Biology: A Conceptual Framework for Teaching Synthetic Biology.” *ACS Synthetic Biology* 12 (6): 1574–8. As of 29 November 2024: https://doi.org/10.1021/acssynbio.3c00194

Shepley, Paul, and Matthew Gill. 2023. “Artificial Intelligence: How Is the Government Approaching Regulation?” Institute for Government, 27 October. As of 12 August 2024: https://www.instituteforgovernment.org.uk/explainer/artificial-intelligence-regulation

Shi, Huaiyu, Andrew Kowalczewski, Danny Vu, Xiyuan Liu, Asif Salekin, Huaxiao Yang, and Zhen Ma. 2024. “Organoid Intelligence: Integration of Organoid Technology and Artificial Intelligence in the New Era of in Vitro Models.” *Medicine in Novel Technology and Devices* 21 (March): 100276. As of 18 November 2024: https://doi.org/10.1016/j.medntd.2023.100276

Shih, Jerry J., Dean J. Krusienski, and Jonathan R. Wolpawc. 2012. “Brain-Computer Interfaces in Medicine.” *Mayo Clinic Proceedings* 87 (3): 268–279. As of 12 August 2024: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3497935/

Simmons, Dan. n.d. “17 Countries with GDPR-like Data Privacy Laws.” As of 18 November 2024: https://insights.comforte.com/countries-with-gdpr-like-data-privacy-laws

Simeral, John D., Thomas Hosman, Jad Saab, Sharlene N. Flesher, Marco Vilela, Brian Franco, Jessica Kelemen, et al. 2021. “Home Use of a Percutaneous Wireless Intracortical Brain-Computer Interface by Individuals With Tetraplegia.” *IEEE Transactions on Bio-Medical Engineering* 68 (7): 2313–25. As of 18 August 2024: https://doi.org/10.1109/TBME.2021.3069119

Singh, Amanjot, and Anil Grover. 2008. “Genetic Engineering for Heat Tolerance in Plants.” *Physiology and Molecular Biology of Plants: An International Journal of Functional Plant Biology* 14 (1–2): 155–66. As of 14 August 2024: https://doi.org/10.1007/s12298-008-0014-2

Singh, Arihant, Vivek R Velagala, Tanishq Kumar, Rajoshee R Dutta, and Tushar Sontakke. 2023. “The Application of Deep Learning to Electroencephalograms, Magnetic Resonance Imaging, and Implants for the Detection of Epileptic Seizures: A Narrative Review.” *Cureus* 15 (7): e42460. As of 18 November 2024: https://doi.org/10.7759/cureus.42460

Singh, Karandeep, Sean R. Meyer, and John M. Westfall. 2019. “Consumer-Facing Data, Information, And Tools: Self-Management Of Health In The Digital Age.” *Health Affairs* 38 (3): 352–58. As of 18 November 2024: https://doi.org/10.1377/hlthaff.2018.05404

Smirnova, Lena, Brian Caffo, and Erik C. Johnson. 2023. “Reservoir Computing with Brain Organoids.” *Nature Electronics* 6 (12): 943–44. As of 18 November 2024: https://doi.org/10.1038/s41928-023-01096-7

Smirnova, Lena, Brian S. Caffo, David H. Gracias, Qi Huang, Itzy E. Morales Pantoja, Bohao Tang, Donald J. Zack, et al. 2023. “Organoid Intelligence (OI): The New Frontier in Biocomputing and Intelligence-in-a-Dish.” *Frontiers in Science* 1. As of 18 November 2024: https://www.frontiersin.org/journals/science/articles/10.3389/fsci.2023.1017235

Smuck, Matthew, Charles A. Odonkor, Jonathan K. Wilt, Nicolas Schmidt, and Michael A. Swiernik. 2021. “The Emerging Clinical Role of Wearables: Factors for Successful Implementation in Healthcare.” *Npj Digital Medicine* 4 (1): 1–8. As of 18 November 2024: https://doi.org/10.1038/s41746-021-00418-3

Solomon, Shoshanna. 2020. “Israel seeks edge at intersection of biology with engineering, AI.” *Times of Israel*, 12 July. As of 29 November 2024: https://www.timesofisrael.com/israel-seeks-edge-at-intersection-of-biology-with-engineering-ai/

Song, Jingwei, Ruchit V. Patel, Massoud Sharif, Anagha Ashokan, and Michael Michaelides. 2022. “Chemogenetics as a Neuromodulatory Approach to Treating Neuropsychiatric Diseases and Disorders.” *Molecular Therapy* 30 (3): 990–1005. As of 18 November 2024: https://doi.org/10.1016/j.ymthe.2021.11.019

Song, Jiyoung, Seokyoung Bang, Nakwon Choi, and Hong Nam Kim. 2022. "Brain Organoid-on-a-Chip: A next-Generation Human Brain Avatar for Recapitulating Human Brain Physiology and Pathology." *Biomicrofluidics* 16 (6): 061301. As of 18 November 2024: https://doi.org/10.1063/5.0121476

SPHN. 2024. "ELSI Advisory Group (ELSIag)." Swiss Personalized Health Network. As of 15 August 2024: https://sphn.ch/organization/governance/elsi-advisory-group/

Stanford University. 2023. Artificial Intelligence Index Report 2023. As of 12 August 2024: https://aiindex.stanford.edu/wp-content/uploads/2023/04/HAI_AI-Index-Report_2023.pdf

Stark, Zornitza, Lena Dolman, Teri A Manolio, Brad Ozenberger, Sue L. Hill, Mark J. Caulfied, Yves Levy, David Glazer, Julia Wilson, and Mark Lawler. 2019. "Integrating Genomics into Healthcare: A Global Responsibility." *American Journal of Human Genetics* 104 (1): 13–20.

Sudharson, N. A., M. Joseph, N. Kurian, K. G. Varghese, S. Wadhwa, and H. A. Thomas. 2023. "AI-Powered Neural Implants." *British Dental Journal* 234 (6): 359–60. As of 18 November 2024: https://doi.org/10.1038/s41415-023-5698-8

Sun, Xin-Yao, Xiang-Chun Ju, Yang Li, Peng-Ming Zeng, Jian Wu, Ying-Ying Zhou, Li-Bing Shen, Jian Dong, Yue-Jun Chen, and Zhen-Ge Luo. 2022. "Generation of Vascularized Brain Organoids to Study Neurovascular Interactions." *eLife* 11:e76707. As of 18 November 2024: https://doi.org/10.7554/eLife.76707

Sutton, Reed T., David Pincock, Daniel C. Baumgart, Daniel C. Sadowski, Richard N. Fedorak, and Karen I. Kroeker. 2020. "An Overview of Clinical Decision Support Systems: Benefits, Risks, and Strategies for Success." *Npj Digital Medicine* 3 (1): 1–10. As of 18 November 2024: https://doi.org/10.1038/s41746-020-0221-y

Taddeo, Mariarosaria, Andreas Tsamados, Josh Cowls, and Luciano Floridi. 2021. "Artificial Intelligence and the Climate Emergency: Opportunities, Challenges, and Recommendations." *One Earth* 4 (6): 776–79. As of 18 November 2024: https://doi.org/10.1016/j.oneear.2021.05.018

Takahashi, Dean. 2024. "Elemind Raises $12M for Neurotech Wearable That Can Help Your Brain and Let You Sleep Better." VentureBeat. 6 February. As of 18 November 2024: https://venturebeat.com/ai/elemind-raises-12m-for-neurotech-wearable-that-can-help-your-brain-and-let-you-sleep-better/

Tang, Xiao-Yan, Shanshan Wu, Da Wang, Chu Chu, Yuan Hong, Mengdan Tao, Hao Hu, Min Xu, Xing Guo, and Yan Liu. 2022. "Human Organoids in Basic Research and Clinical Applications." *Signal Transduction and Targeted Therapy* 7 (1): 1–17. As of 18 November 2024: https://doi.org/10.1038/s41392-022-01024-9

Tavakol, Shahin, Jessica Royer, Alexander J. Lowe, Leonardo Bonilha, Joseph I. Tracy, Graeme D. Jackson, John S. Duncan, Andrea Bernasconi, Neda Bernasconi, and Boris C. Bernhardt. 2019. "Neuroimaging and Connectomics of Drug-Resistant Epilepsy at Multiple Scales: From Focal Lesions to Macroscale Networks." *Epilepsia* 60 (4): 593–604. As of 15 August 2024: https://doi.org/10.1111/epi.14688

Tenopir, Carol, Natalie M. Rice, Suzie Allard, Lynn Baird, Josh Borycz, Lisa Christian, Bruce Grant, Robert Olendorf, and Robert J. Sandusky. 2020. "Data Sharing, Management, Use, and Reuse: Practices and Perceptions of Scientists Worldwide." *PLOS ONE* 15 (3): e0229003. As of 18 November 2024: https://doi.org/10.1371/journal.pone.0229003

Teriyapirom, Isaree, Andreia S. Batista-Rocha, and Bon-Kyoung Koo. 2021. "Genetic Engineering in Organoids." *Journal of Molecular Medicine* 99 (4): 555. As of 18 November 2024: https://doi.org/10.1007/s00109-020-02029-z

Thaker, Naini. 2024. “Budget 2024: Sitharaman Announces Launch Of A New Bio-Manufacturing And Bio-Foundry Scheme.” *Forbes India*, 1 February. As of 14 August 2024: https://www.forbesindia.com/article/news/budget-2024-sitharaman-announces-launch-of-a-new-biomanufacturing-and-biofoundry-scheme/91179/1

Thales. 2021. “Beyond GDPR: Data Protection Regulation around the World.” As of 12 August 2024: https://www.thalesgroup.com/en/markets/digital-identity-and-security/government/magazine/beyond-gdpr-data-protection-around-world

Theodoris, Christina V., Ling Xiao, Anant Chopra, Mark D. Chaffin, Zeina R. Al Sayed, Matthew C. Hill, Helene Mantineo, et al. 2023. “Transfer Learning Enables Predictions in Network Biology.” *Nature* 618 (7965): 616–24. As of 18 November 2024: https://doi.org/10.1038/s41586-023-06139-9

Thorogood, Adrian, Heidi L. Rehm, Peter Goodhand, Angela J. H. Page, Yann Joly, Michael Baudis, Jordi Rambla, et al. 2021. “International Federation of Genomic Medicine Databases Using GA4GH Standards.” *Cell Genomics* 1 (2): 100032. As of 18 November 2024: https://doi.org/10.1016/j.xgen.2021.100032

Tortora, Leda, Gerben Meynen, Johannes Bijlsma, Enrico Tronci, and Stefano Ferracuti, S. 2020. “Neuroprediction and A.I. in Forensic Psychiatry and Criminal Justice: A Neurolaw Perspective.” *Frontiers in Psychology* 11. As of 29 November 2024: https://doi.org/10.3389/fpsyg.2020.00220

Tsanni, Abdullahi. 2024. “Africa’s Push to Regulate AI Starts Now.” MIT Technology Review. 15 March. As of 18 November 2024: https://www.technologyreview.com/2024/03/15/1089844/africa-ai-artificial-intelligence-regulation-au-policy/

Uchitel, Julie, Ernesto E. Vidal-Rosas, Robert J. Cooper, and Hubin Zhao. 2021. “Wearable, Integrated EEG–fNIRS Technologies: A Review.” *Sensors* 21 (18): 6106. As of 18 November 2024: https://doi.org/10.3390/s21186106

Ueda, Jun, Taiga Yamazaki, and Hiroshi Funakoshi. 2023. “Toward the Development of Epigenome Editing-Based Therapeutics: Potentials and Challenges.” *International Journal of Molecular Sciences* 24 (5): 4778. As of 29 November 2024: https://doi.org/10.3390/ijms24054778

UK Government. 2022a. *Genome UK: 2022 to 2025 Implementation Plan for England.* As of 14 August 2024: https://www.gov.uk/government/publications/genome-uk-2022-to-2025-implementation-plan-for-england

———. 2022b. *Genome UK: Shared Commitments for UK-Wide Implementation 2022 to 2025.* As of 14 August 2024: https://www.gov.uk/government/publications/genome-uk-shared-commitments-for-uk-wide-implementation-2022-to-2025/genome-uk-shared-commitments-for-uk-wide-implementation-2022-to-2025

———. 2023a. A *Pro-Innovation Approach to AI Regulation. Department for Science, Innovation and Technology.* As of 12 August 2024: https://www.gov.uk/government/publications/ai-regulation-a-pro-innovation-approach/white-paper

———. 2023b. “Genetic Technology Act key tool for UK food security.” 23 March. As of 14 August 2024: https://www.gov.uk/government/news/genetic-technology-act-key-tool-for-uk-food-security

———. 2023c. “Report on Engineering Biology: Opportunities for the UK Economy and National Goals.” As of 14 August 2024: https://www.gov.uk/government/publications/advice-on-engineering-biology/report-on-engineering-biology-opportunities-for-the-uk-economy-and-national-goals-html

———. 2023d. *The UK's International Technology Strategy.* As of 14 August 2024:
https://www.gov.uk/government/publications/uk-international-technology-strategy/the-uks-international-technology-strategy

———. 2023e. "Government Publishes £2 Billion Vision for Engineering Biology to Revolutionise Medicine, Food and Environmental Protection." 5 December. As of 14 August 2024:
https://www.gov.uk/government/news/government-publishes-2-billion-vision-for-engineering-biology-to-revolutionise-medicine-food-and-environmental-protection

———. 2024a. "UK Science and Technology Framework." As of 17 August 2024:
https://www.gov.uk/government/publications/uk-science-and-technology-framework

———. 2024b. "Oral Statement to Parliament: The King's Speech 2024." As of 17 August 2024:
https://www.gov.uk/government/speeches/the-kings-speech-2024

———. 2024c. "AI Expert to Lead Action Plan to Ensure UK Reaps the Benefits of Artificial Intelligence." 26 July. As of 17 August 2024:
https://www.gov.uk/government/news/ai-expert-to-lead-action-plan-to-ensure-uk-reaps-the-benefits-of-artificial-intelligence

———. 2024d. "Engineering Biology Sandbox Fund: Clarification Questions." As of 15 August 2024:
https://www.gov.uk/government/publications/engineering-biology-sandbox-fund/engineering-biology-sandbox-fund-clarification-questions

UK Parliament. 2023. "Genomics and National Security." Volume 729: debated on 8 March. As of 14 August 2024:
https://hansard.parliament.uk/commons/2023-03-08/debates/3F7E5903-596F-492A-B130-A4503928CA7F/GenomicsAndNationalSecurity

UMAP. 2024. "Uniform Manifold Approximation and Projection for Dimension Reduction." As of 15 August 2024:
https://umap-learn.readthedocs.io/en/latest/

Understanding Stem Cells. "Legal Basics." 2017. March. As of 18 November 2024:
https://www.understanding-stemcells.info/ethics/legalbasics.aspx

UNESCO. 2021. Ethical Issues of Neurotechnology. Report of the International Bioethics Committee of UNESCO (IBC), United Nations Educational, Scientific and Cultural Organization. As of 17 August 2024:
https://unesdoc.unesco.org/ark:/48223/pf0000378724

———. 2023a. Ethical Impact Assessment: A Tool of the Recommendation on the Ethics of Artificial Intelligence. United Nations Educational, Scientific and Cultural Organization. As of 15 August 2024:
https://www.unesco.org/en/articles/ethical-impact-assessment-tool-recommendation-ethics-artificial-intelligence

———. 2023b. Unveiling the Neurotechnology Landscape: Scientific Advancements Innovations and Major Trends. United Nations Educational, Scientific and Cultural Organization. As of 15 August 2024:
https://unesdoc.unesco.org/ark:/48223/pf0000386137/PDF/386137eng.pdf.multi

———. 2023c. The Risks and Challenges of Neurotechnologies for Human Rights. United Nations Educational, Scientific and Cultural Organization. As of 17 August 2024:
https://unesdoc.unesco.org/ark:/48223/pf0000384185

———. 2023d. "UNESCO to Lead Global Dialogue on the Ethics of Neurotechnology." United Nations Educational, Scientific and Cultural Organization. 6 June. As of 17 August 2024:
https://www.unesco.org/en/articles/unesco-lead-global-dialogue-ethics-neurotechnology

———. 2024. “Global AI Ethics and Governance Observatory.” United Nations Educational, Scientific and Cultural Organization. As of 15 August 2024: https://www.unesco.org/ethics-ai/en

United Nations. 2018. *UN Secretary-General’s Strategy on New Technologies*. As of 17 August 2024: https://www.un.org/en/newtechnologies/images/pdf/SGs-Strategy-on-New-Technologies.pdf

———. 2024. “Inter-Agency Working Group on Artificial Intelligence.” As of 18 August 2024: https://unsceb.org/inter-agency-working-group-artificial-intelligence

University of Cambridge. 2023. “Project Launched to Provide Guidance on Research Using Human Stem Cell-Based Embryo Models.” 16 June. As of 13 August 2024: https://www.cam.ac.uk/research/news/project-launched-to-provide-guidance-on-research-using-human-stem-cell-based-embryo-models

Utrecht University. 2021. “To Be or Not to Be: An Organoid.” 6 May. As of 17 August 2024: https://www.uu.nl/en/news/to-be-or-not-to-be-an-organoid

van Delden, Johannes J.M., and Rieke van der Graaf. 2017. “Revised CIOMS International Ethical Guidelines for Health-Related Research Involving Humans.” *JAMA* 317 (2): 135–36. As of 12 August 2024: https://doi.org/10.1001/jama.2016.18977

Vansteensel, Mariska J., Eran Klein, Ghislaine van Thiel, Michael Gaytant, Zachary Simmons, Jonathan R. Wolpaw, and Theresa M. Vaughan. 2023. “Towards Clinical Application of Implantable Brain–Computer Interfaces for People with Late-Stage ALS: Medical and Ethical Considerations.” *Journal of Neurology* 270 (3): 1323–36. As of 18 November 2024: https://doi.org/10.1007/s00415-022-11464-6

Varandas, Rui, Rodrigo Lima, Sergi Bermúdez I Badia, Hugo Silva, and Hugo Gamboa. 2022. “Automatic Cognitive Fatigue Detection Using Wearable fNIRS and Machine Learning.” *Sensors* 22 (11): 4010. As of 18 November 2024: https://doi.org/10.3390/s22114010

VerMilyea, M., J.M.M. Hall, S.M. Diakiw, A. Johnston, T. Nguyen, D. Perugini, A. Miller, A. Picou, A.P. Murphy, and M. Perugini. 2020. “Development of an artificial intelligence-based assessment model for prediction of embryo viability using static images captured by optical light microscopy during IVF.” *Human Reproduction* 35 (4): 770–784. As of 2 December 2024: https://doi.org/10.1093/humrep/deaa013

Vieira de Sá, Renata, Marta Cañizares Luna, and R. Jeroen Pasterkamp. 2021. “Advances in Central Nervous System Organoids: A Focus on Organoid-Based Models for Motor Neuron Disease.” *Tissue Engineering. Part C, Methods* 27 (3): 213–24. As of 18 November 2024: https://doi.org/10.1089/ten.TEC.2020.0337

Vilhekar, Rohit S, and Alka Rawekar. 2024. “Artificial Intelligence in Genetics.” *Cureus* 16 (1): e52035. As of 18 November 2024: https://doi.org/10.7759/cureus.52035

Virtus Health. 2020. “Australian-first trial using the power of AI begins and welcomes back hopeful IVF parents.” Virtus Health, 15 May. As of 2 December 2024: https://www.virtushealth.com.au/investor-centre/asx-announcements/australian-first-trial-using-the-power-of-ai-begins-and-welcomes-back-hopeful-ivf-parents

Vlachogiannis, Georgios, Somaieh Hedayat, Alexandra Vatsiou, Yann Jamin, Javier Fernández-Mateos, Khurum Khan, Andrea Lampis, et al. 2018. “Patient-Derived Organoids Model Treatment Response of Metastatic Gastrointestinal Cancers.” *Science* 359 (6378): 920–926. As of 18 November 2024: https://doi.org/10.1126/science.aao2774

Vogt, Nina. 2021. “Assembloids.” *Nature Methods* 18 (1): 27–27. As of 18 November 2024: https://doi.org/10.1038/s41592-020-01026-x

Wagar, Lisa E. 2023. “Human Immune Organoids: A Tool to Study Vaccine Responses.” *Nature Reviews. Immunology* 23 (11): 699. As of 18 November 2024: https://doi.org/10.1038/s41577-023-00956-9

Wang, Hengkang, Han Lu, Ju Sun, and Sandra E. Safo. 2024. "Interpretable Deep Learning Methods for Multiview Learning." *BMC Bioinformatics* 25 (1): 69. As of 18 November 2024: https://doi.org/10.1186/s12859-024-05679-9

Wang, Jing, Chi Liu, Masayuki Fujino, Guoqing Tong, Qinxiu Zhang, Xiao-Kang Li, and Hua Yan. 2019. "Stem Cells as a Resource for Treatment of Infertility-related Diseases." *Current Molecular Medicine* 19 (8): 519–546. As of 2 December 2024: https://doi.org/10.2174/1566524019666190709172636

Watanabe, Momoko, Jessie E. Buth, Neda Vishlaghi, Luis de la Torre-Ubieta, Jiannis Taxidis, Baljit S. Khakh, Giovanni Coppola, et al. 2017. "Self-Organized Cerebral Organoids with Human-Specific Features Predict Effective Drugs to Combat Zika Virus Infection." *Cell Reports* 21 (2): 517–32. As of 18 November 2024: https://doi.org/10.1016/j.celrep.2017.09.047

Watanabe, Myrna E. 2019. "The Nagoya Protocol: The Conundrum of Defining Digital Sequence Information." *BioScience* 69 (6): 480. As of 18 November 2024: https://doi.org/10.1093/biosci/biz034

Wen, Jen-Yu, Chung-Fen Liu, Ming-Ting Chung, and Yung-Chieh Tsai. 2022. "Artificial intelligence model to predict pregnancy and multiple pregnancy risk following in vitro fertilization-embryo transfer (IVF-ET)." Taiwanese Journal of Obstetrics and Gynecology 61 (5): 837–846. As of 2 December 2024: https://doi.org/10.1016/j.tjog.2021.11.038

Weng, Lindong. 2019. "IVF-on-a-Chip: Recent Advances in Microfluidics Technology for In Vitro Fertilization." *SLAS Technology* 24 (4): 373–85. As of 18 November 2024: https://doi.org/10.1177/2472630319851765

Wesevich, Victoria G., Christopher Arkfeld, and David B. Seifer. 2023. "In Vitro Gametogenesis in Oncofertility: A Review of Its Potential Use and Present-Day Challenges in Moving toward Fertility Preservation and Restoration." *Journal of Clinical Medicine* 12 (9): 3305. As of 18 November 2024: https://doi.org/10.3390/jcm12093305

White House. 2022. "FACT SHEET: The United States Announces New Investments and Resources to Advance President Biden's National Biotechnology and Biomanufacturing Initiative." Briefing Room, statements and releases, 14 September. As of 14 August 2024: https://www.whitehouse.gov/briefing-room/statements-releases/2022/09/14/fact-sheet-the-united-states-announces-new-investments-and-resources-to-advance-president-bidens-national-biotechnology-and-biomanufacturing-initiative/

———. 2023. "FACT SHEET: President Biden Issues Executive Order on Safe, Secure, and Trustworthy Artificial Intelligence." Briefing Room, statements and releases, 30 October. As of 14 August 2024: https://www.whitehouse.gov/briefing-room/statements-releases/2023/10/30/fact-sheet-president-biden-issues-executive-order-on-safe-secure-and-trustworthy-artificial-intelligence/

———. 2024. "Executive Order on Preventing Access to Americans' Bulk Sensitive Personal Data and United States Government-Related Data by Countries of Concern." Briefing Room, presidential actions. As of 14 August 2024: https://www.whitehouse.gov/briefing-room/presidential-actions/2024/02/28/executive-order-on-preventing-access-to-americans-bulk-sensitive-personal-data-and-united-states-government-related-data-by-countries-of-concern/

WHO. 2021a. *Human Genome Editing: Recommendations.* World Health Organization. As of 15 August 2024: https://www.who.int/publications-detail-redirect/9789240030381

———. 2021b. *Human Genome Editing: A Framework for Governance.* World Health Organization. As of 15 August 2024: https://www.who.int/publications-detail-redirect/9789240030060

———. 2024a. "WHO Data Principles." World Health Organization. As of 14 August 2024: https://www.who.int/data/principles

———. 2024b. *Ethics and Governance of Artificial Intelligence for Health: Guidance on Large Multi-Modal Models*. World Health Organization. As of 14 August 2024: https://www.who.int/publications-detail-redirect/9789240084759

———. 2024c. "Epilepsy." 2024. As of 18 November 2024: https://www.who.int/news-room/fact-sheets/detail/epilepsy

Widge, Alik S., Donald A. Malone, and Darin D. Dougherty. 2018. "Closing the Loop on Deep Brain Stimulation for Treatment-Resistant Depression." *Frontiers in Neuroscience* 21 (12): 175. As of 12 August 2024: https://pubmed.ncbi.nlm.nih.gov/29618967/

Willett, Francis R., Donald T. Avansino, Leigh R. Hochberg, Jaimie M. Henderson, and Krishna V. Shenoy. 2021. "High-Performance Brain-to-Text Communication via Handwriting." *Nature* 593 (7858): 249–54. As of 18 November 2024: https://doi.org/10.1038/s41586-021-03506-2

Williamson, Steven M., and Victor Prybutok. 2024. "Balancing Privacy and Progress: A Review of Privacy Challenges, Systemic Oversight, and Patient Perceptions in AI-Driven Healthcare." *Applied Sciences* 14 (2): 675. As of 18 November 2024: https://doi.org/10.3390/app14020675

WMA. 2024. "Declaration of Helsinki." World Medical Association. As of 14 August 2024: https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/

Wollacott, Emma. 2023. "UK Data Centers to Be Classed as Critical Infrastructure under New Gov Proposals." ITPro. 15 December. As of 18 November 2024: https://www.itpro.com/infrastructure/data-centres/uk-data-centers-to-be-classed-as-critical-infrastructure-under-new-gov-proposals

Wong, Poh Kuan, Fook Choe Cheah, Saiful Effendi Syafruddin, M. Aiman Mohtar, Norazrina Azmi, Pei Yuen Ng, and Eng Wee Chua. 2021. "CRISPR Gene-Editing Models Geared Toward Therapy for Hereditary and Developmental Neurological Disorders." *Frontiers in Pediatrics* 9: 592571. As of 2 December 2024: https://doi.org/10.3389/fped.2021.592571

World Bank. 2024a. "World Bank Country and Lending Groups." As of 14 August 2024: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups

———. 2024b. "Country Classification by Income." As of 16 August 2024: https://wfh.org/wp-content/uploads/2023/08/country-classifications-by-income-2024.pdf

Wu, Le, Aiping Liu, Rabab K. Ward, Z. Jane Wang, and Xun Chen. 2023. "Signal Processing for Brain–Computer Interfaces: A Review and Current Perspectives." *IEEE Signal Processing Magazine* 40 (5): 80–91. As of 18 November 2024: https://doi.org/10.1109/MSP.2023.3278074

Wu, Yun, Andrew Wenger, Hossein Golzar, and Xiaowu (Shirley) Tang. 2020. "3D Bioprinting of Bicellular Liver Lobule-Mimetic Structures via Microextrusion of Cellulose Nanocrystal-Incorporated Shear-Thinning Bioink." *Scientific Reports* 10 (1): 20648. As of 18 November 2024: https://doi.org/10.1038/s41598-020-77146-3

Xia, Mingrui, and Yong He. 2023. "Connectomics Reconciles Seemingly Irreconcilable Neuroimaging Findings." *Trends in Cognitive Sciences* 27 (6): 512–13. As of 18 November 2024: https://doi.org/10.1016/j.tics.2023.04.005

Xie, Xuexue, Xinyu Li, and Wei Song. 2023. "Tumor Organoid Biobank-New Platform for Medical Research." *Scientific Reports* 13 (1): 1819. As of 18 November 2024: https://doi.org/10.1038/s41598-023-29065-2

Xu, Hanxiao, Dechao Jiao, Aiguo Liu, and Kongming Wu. 2022. "Tumor Organoids: Applications in Cancer Modeling and Potentials in Precision Medicine." *Journal of Hematology & Oncology* 15 (1): 58. As of 18 November 2024: https://doi.org/10.1186/s13045-022-01278-4

Xue, Yang, and Lijun Shang. 2022. "Are we ready for the revision of the 14-day rule? Implications from Chinese legislations guiding human embryo and embryoid research." *Frontiers in Cell and Developmental Biology* 10: 1016988. As of 2 December 2024: https://doi.org/10.3389/fcell.2022.1016988

Yang, Siqi, Haijie Hu, Hengchung Kung, Ruiqi Zou, Yushi Dai, Yafei Hu, Tiantian Wang, Tianrun Lv, Jun Yu, and Fuyu Li. 2023. "Organoids: The Current Status and Biomedical Applications." *MedComm* 4 (3): e274. As of 18 November 2024: https://doi.org/10.1002/mco2.274

Yaqoob, Ibrar, Khaled Salah, Raja Jayaraman, and Yousof Al-Hammadi. 2022. "Blockchain for Healthcare Data Management: Opportunities, Challenges, and Future Recommendations." *Neural Computing and Applications* 34 (14): 11475–90. As of 18 November 2024: https://doi.org/10.1007/s00521-020-05519-w

Yoon, Yousang, Hyogeun Shin, Donghak Byun, Jiwan Woo, Yakdol Cho, Nakwon Choi, and Il-Joo Cho. 2022. "Neural Probe System for Behavioral Neuropharmacology by Bi-Directional Wireless Drug Delivery and Electrophysiology in Socially Interacting Mice." *Nature Communications* 13 (September):5521. As of 18 November 2024: https://doi.org/10.1038/s41467-022-33296-8

Yoshizawa, Go, Calvin Wai-Loon Ho, Wei Zhu, Chingli Hu, Yoni Syukriani, Ilhak Lee, Hannah Kim, Daniel Fu Chang Tsai, Jusaku Minari, and Kazuto Kato. 2014. "ELSI Practices in Genomic Research in East Asia: Implications for Research Collaboration and Public Participation." *Genome Medicine* 6 (5): 39. As of 18 November 2024: https://doi.org/10.1186/gm556

Young, Michael J., David J. Lin, and Leigh R. Hochberg. 2021. "Brain-Computer Interfaces in Neurorecovery and Neurorehabilitation." *Seminars in Neurology* 41 (2): 206–16. As of 18 November 2024: https://doi.org/10.1055/s-0041-1725137

Young, Peter N.E., et al. 2020. "Imaging biomarkers in neurodegeneration: Current and future practices". *Alzheimer's Research & Therapy* 12 (1): 49. As of 2 December 2024: https://doi.org/10.1186/s13195-020-00612-7

Yu, Fang, Walter Hunziker, and Deepak Choudhury. 2019. "Engineering Microfluidic Organoid-on-a-Chip Platforms." *Micromachines* 10 (3): 165. As of 18 November 2024: https://doi.org/10.3390/mi10030165

Yui, Hideki, Kaori Muto, Yoshimi Yashiro, Saori Watanabe, Yukitaka Kiya, Ayako Kamisato, Yusuke Inoue, and Zentaro Yamagata. 2022. "Comparison of the 2021 International Society for Stem Cell Research (ISSCR) Guidelines for 'Laboratory-Based Human Stem Cell Research, Embryo Research, and Related Research Activities' and the Corresponding Japanese Regulations." *Regenerative Therapy* 21 (December): 46–51. As of 18 November 2024: https://doi.org/10.1016/j.reth.2022.05.002

Yuste, Rafael. 2017. "Four ethical priorities for neurotechnologies and AI." Nature 551 (7679): 159–163. As of 2 December 2024: https://doi.org/10.1038/551159a

Zakaria, Sana, Timothy Marler, Mark Cabling, Suzanne Genc, Artur Honich, Mann Virdee, and Sam Stockwell. 2023. "Machine Learning and Gene Editing at the Helm of a Societal Evolution." Santa Monica, Calif.: RAND Corporation. RR-A2838-1. As of 18 November 2024: https://www.rand.org/pubs/research_reports/RRA2838-1.html

Zakaria, Sana, Ioli Howard, Eva Coringrato, Anna-Louise Todsen, Alec Ross, Imogen Wade, Katarina Pisani, Devika Kapoor, Martin Szomzor, and Salil Gunashekar. 2024. State-of-play and future trends on oversight mechanisms for emerging technologies: Oversight report. Santa Monica, Calif.: RAND Corporation. RR-A3215-2. As of 16 December 2024: http://www.rand.org/pubs/research_reports/RRA3215-2

Zaninovic, Nikica, Jose T. Sierra, Jonas E. Malmsten, and Zev Rosenwaks. 2024. 'Embryo Ranking Agreement between Embryologists and Artificial Intelligence Algorithms'. *F&S Science* 5 (1): 50–57. As of 5 December 2024: https://doi.org/10.1016/j.xfss.2023.10.002

Zarghamian, Parinaz, Julia Klermund, and Toni Cathomen. 2023. "Clinical genome editing to treat sickle cell disease—A brief update." *Frontiers in Medicine* 9: 1065377. As of 2 December 2024: https://doi.org/10.3389/fmed.2022.1065377

Zernicka-Goetz, Magdalena. 2023. "The Evolution of Embryo Models." *Nature Methods* 20 (12): 1844–48. As of 18 November 2024: https://doi.org/10.1038/s41592-023-02077-6

Zhang, Weijie, Jiawei Li, Jiaqi Zhou, Abhay Rastogi, and Shaohua Ma. 2022. "Translational Organoid Technology – the Convergence of Chemical, Mechanical, and Computational Biology." *Trends in Biotechnology* 40 (9): 1121–35. As of 18 November 2024: https://doi.org/10.1016/j.tibtech.2022.03.003

Zhang, Xiayin, Ziyue Ma, Huaijin Zheng, Tongkeng Li, Kexin Chen, Xun Wang, Chenting Liu, et al. 2020. "The Combination of Brain-Computer Interfaces and Artificial Intelligence: Applications and Challenges." *Annals of Translational Medicine* 8 (11): 712. As of 18 November 2024: https://doi.org/10.21037/atm.2019.11.109

Zhang, Xu, Cuihuan Zhao, Ming-Wei Shao, Yi-Ling Chen, Puyuan Liu, and Guo-Qiang Chen. 2022. "The Roadmap of Bioeconomy in China." Engineering Biology 6 (4): 71–81. As of 18 August 2024: https://doi.org/10.1049/enb2.12026

Zhao, Zixuan, Xinyi Chen, Anna M. Dowbaj, Aleksandra Sljukic, Kaitlin Bratlie, Luda Lin, Eliza Li Shan Fong, et al. 2022. "Organoids." *Nature Reviews Methods Primers* 2 (1): 1–21. As of 18 November 2024: https://doi.org/10.1038/s43586-022-00174-y

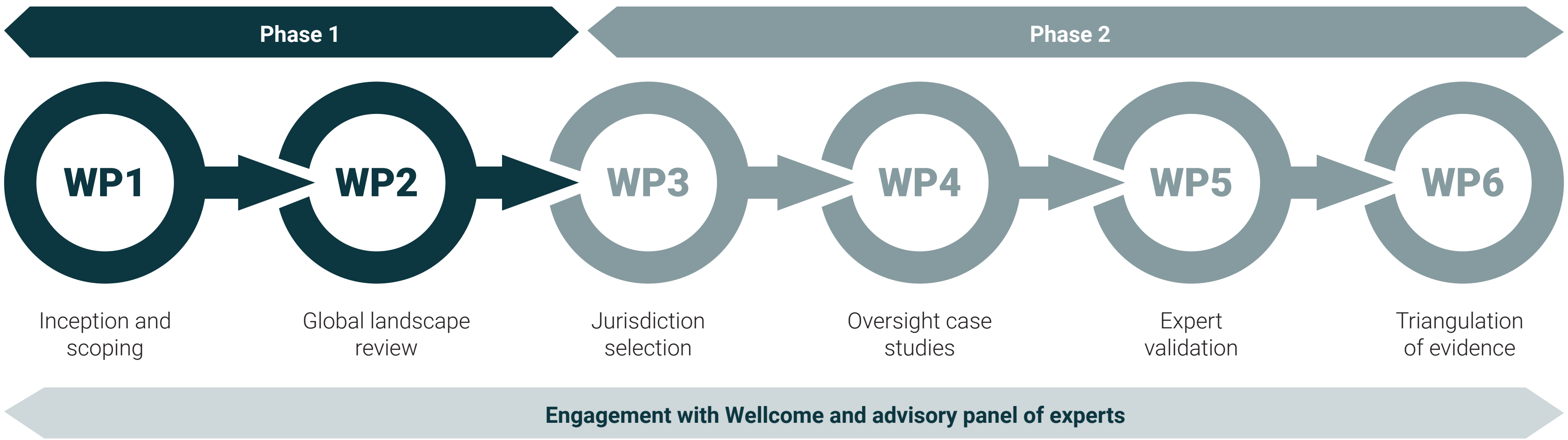
Zheng, Honghui, Yilin Feng, Jiyuan Tang, and Shaohua Ma. 2022. "Interfacing Brain Organoids with Precision Medicine and Machine Learning." *Cell Reports Physical Science* 3 (7): 100974. As of 18 November 2024: https://doi.org/10.1016/j.xcrp.2022.100974

Annex A

Detailed description of the methodology

This study takes a staged approach encompassing six work packages (WPs) spread over two phases, as shown in Figure 30. This annex details the methods used in Phase 1 of the project, the outputs of which are described in this report.

Figure 30. Research approach: Phases and work packages



Note: This report concerns Phase 1, encompassing WP1 and 2. Phase 2 of the research is described in the accompanying technology oversight report (Zakaria et al. 2024).

Source: RAND Europe analysis.

A.1. WP1: Inception and scoping

Following a kick-off meeting with Wellcome, WP1 encompassed a rapid background scoping exercise, serving as a preliminary review of the technology areas (genomics (focussing on engineering biology), human embryology, neurotechnology, organoids, AI and data platforms). The exercise aimed to:

- Assess recent technical developments in the field.
- Identify key applications and use cases across sectors.
- Examine some of the notable ongoing oversight debates in the technologies.
- Propose a comprehensive definition of each technology area to take forward throughout the study.

The scoping was conducted using generic terms associated with the technology area. These search terms evolved throughout the scoping and fed into search terms used in the WP2 on the global landscape review (Figure 30). Examples of early search terms include ‘neurotechnology *and* recent developments’, ‘embryology *and* applications’, ‘AI best practices *or* standards’, and ‘genomics *and* governance *or* oversight mechanisms’. These search terms identified secondary data sources such as systematic reviews, industry perspectives and policy positions relevant to the technologies. The results of the initial technology scoping were also reviewed by the expert advisory panel[56] for their respective areas, and their advice was sought on the focus of the WP2 global landscape review (discussed below).

In tandem to identifying publications, the study identified a list of additional sources such as global observatories, data repositories and other similar aggregator data platforms associated with each technology area that could inform the scientometrics aspect of the global landscape review. The study attempted to cover a wide range of jurisdictions to get an appropriate global overview.

Including this step prior to the global landscape review served as an opportunity to outline a clear aim and scope for the final review, identifying potential areas of technology development that were relevant to Wellcome’s strategic priorities. The findings of this scoping exercise were discussed with Wellcome to finalise the global landscape review approach and scope of the technology areas. Due to the cross-cutting nature of AI and data platforms, these two technologies were addressed together and as ‘transversal’ to the other four technology areas

A.2. WP2: Global landscape review

The global landscape review consisted of a rapid document/ data review and a comprehensive scientometric analysis. The two facets of the landscape review provided both a qualitative and quantitative perspective to the research, and were complemented by consultations with the expert advisory panel. For example, rapid desk research was conducted to support the qualitative aspect of the landscape review, identifying prevalent areas of discussion relating to the oversight of technologies in order to address the challenges noted and seize the opportunities identified. Jurisdictions that provided examples of current or novel activity were also captured in the desk

56 The study assembled a group of six senior experts with knowledge and expertise in the various technology areas to offer advice and critical feedback on the team’s research.

research exercise to complement the quantitative review of research and policy outputs across the technologies.

A.2.1. Rapid document review

Drawing on the refined technology scope agreed in WP1, the document/data review surfaced more in-depth examples of technology development and maturity, information about relevant investment and science policy ecosystems, as well as technology oversight mechanisms in use and/or development at a high level. The review was primarily jurisdiction-agnostic and focused on niche and innovative examples of oversight discussions and international or cross-continent developments. This enabled a ground-up view of relevant oversight debates of interest in the technology sectors, and provided a refined scope for aspects of technology oversight that were a valuable focus of research. Moreover, it enabled the research team to uncover developments in LMICs that have been underreported in scientometric databases.

Searches across each technology were focused on identifying notable scientific and industry trends in a given technology field, which yielded further insights into the opportunities and challenges in the sector. The search terms developed were generic in the first instance and became more focused as the landscape review progressed into more specific and niche areas. Search strings for the AI and data platforms topics varied compared to the other four technology areas given the cross-cutting nature and availability of data. For example, in some instances the technology convergence between AI/data platforms and biotechnology was too nascent to provide useful outputs based on generic searches of (e.g.) 'data platforms *and* embryology', so a more targeted approach using keywords specific to data platforms was used. Table 16 highlights example search strings used to identify seminal papers in each field.

Table 16. Search strings used to identify relevant research and developments across the technologies

Technologies	Search string examples
Genomics, neurotechnology, embryology, organoids	'[technology] *and* trends or recent developments'; '[sub-technology] *and* key trends'; '[technology] *and* literature reviews'; 'engineering biology* *and* definitions'; 'investment trends in [technology]'; 'challenges in [technology]'; '[technology] *and* innovation'; '[technology] *and* regulation or ethics'
AI + technologies	'AI and [technology] *and* key trends or recent developments'; 'AI *and* [technology] *and* investments'; 'AI *and* [technology] *and* governance'; 'deep learning* *and* [technology] *and* recent developments or trends'
Data platforms + technologies	'[technology] *and* big data'; '[technology] *and* interoperability'; '[technology] *and* data governance'; '[technology] *and* privacy or consent'

*Note: *Similar searches were applied to other fields of study across the technologies.*
Source: RAND Europe analysis.

Through desk research and using this targeted search approach, the research team identified an updated list of key publications (n=5–10 per technology) that provided a holistic description of the technology area. This included systematic reviews and key reports from the grey literature, and drew on some of the sources identified in WP1. Where possible, examples of papers and reports that covered oversight and governance debates were included in this list. Due to the increased focus on emerging technology areas in WP2, extra focus was placed on surfacing publications released within the last three-to-five years, depending on the technology (for example, AI is a rapidly growing and evolving area and therefore publications from the last two years were prioritised).

Based on the review of the top 15 initial papers, a snowballing approach was used to identify further documents of interest and gather the information on trends, opportunities, challenges and key oversight discussions at play within each technology (within the agreed scope) over the last five years. To complement the more quantitative scientometric assessment of publication and patent trends, the landscape review looked to identify particular trends that had developed over an extended period of time. 'Trends' focused on the current state-of-play in terms of sector trends, industry and major investments, and provided an indication of the potential direction of future research and investments. 'Opportunities' often overlapped with the trends but were less established, highlighting what might happen in the future based on current developments. 'Challenges' highlighted issues the technologies were facing that prevented further development. Finally, the landscape review surfaced both current and planned oversight mechanisms and processes, ranging from hard to soft law mechanisms. These included:

- Topics under debate and challenges to be addressed where oversight is warranted.
- Different mechanisms being proposed or discussed, or that are in place already.
- Different forums and countries involved in development efforts, or where very different stances/schools of thought on oversight exist.

In some cases, the emerging nature of the technology or sub-technology meant that there were no tangible examples of governance oversight being implemented. In this case, governance needs and potential mechanisms were highlighted.

Across all technologies, notable oversight examples were surfaced through the search strings defined above, with additional examples found through: 1) targeted searches including 'AI *and* governance *and* Asia', 'AI *and* governance *and* India'[57]; 2) discussions with the advisory panel (described below); and 3) searching global observatories and data repositories for countries involved in each sector.

A.2.2. Scientometric analysis

The scientometric analysis focused on developing a quantitative understanding of the technology areas across the globe based on various input and output indicators of associated R&I activities. Specifically, different indicators of R&I activity for the technology areas were examined, drawing on a range of data including publications, patents, companies and policy documents (see Chapter 3 and Annex B). Data sources identified in the initial scoping exercise and in conjunction with the advisory panel (comprising recent and relevant literature reviews, policy documents, and global observatories) were used as an initial basis for the analysis. Using these sources, the research team developed targeted search strings for the scientometric analysis, extracting data over the last three-to-five years. Full details of scientometric outputs are provided in Annex B.

A.2.3. Expert panel consultations

An expert advisory panel was convened in the project inception stage (WP1) consisting of six experts across the six technology areas of interest, as well as those from industry and academia with additional expertise in emerging technology law and regulation, biotechnology governance, and bioethics. The experts were consulted in parallel to the desk research and scientometric

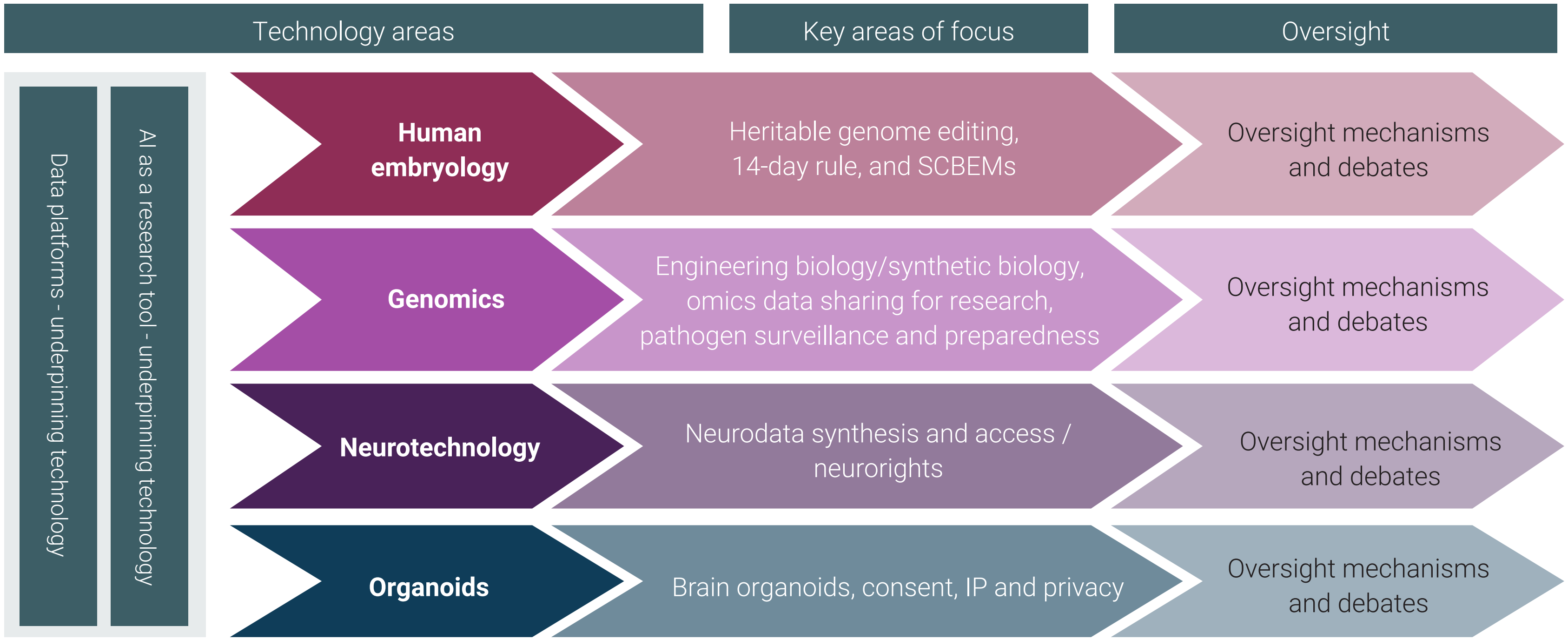
57 Or other jurisdictions.

assessment to provide on-the-ground insights on key oversight discussions of interest, and information on notable jurisdictions that are active or developing a novel aspect of oversight. In particular, the panel was consulted following the initial scoping exercise and provided relevant resources to review and additional guidance on particular areas of interest. Their input in this way enabled a more targeted landscape review.

Information from the experts alongside the desk research was brought together to develop a long list of notable jurisdictions and oversight activities for all the of the key technology areas. These activities were cross referenced against the scientometric trends to ensure that the proposed value judgements on jurisdiction shortlisting aligned with the patterns of activity noted across the R&I indicators.

The landscape review looked at each technology impact area individually, focusing on key areas identified during the scoping exercise and through consultations with the expert panel (Figure 31).

Figure 31. Summary findings from the landscape review



Source: RAND Europe analysis.

Annex B
Supplementary evidence associated with the scientometric analyses

B.1. Scientometric analysis

This annex provides details on the methodology used in the scientometric analysis.

B.1.1. Search string development

The first step in the scientometric analysis was to develop search strings for each of the technology areas. Searches were developed based on inputs from the desk research (see Chapter 3 and Annex A) to identify publications, patents, grey literature documents and companies relevant to each technology area. Searches and data collection were carried out in early March and April 2024. Information regarding the data extraction method, search types used and filters applied are listed for each source in Table 17.

Table 17. Scientometric data sources and extraction summary

Type	Source	Method	Search fields	Filters
Publications	OpenAlex	API	The default.search* parameter was used that searches titles, abstracts and full-text (where available)	publication_year:>=2019
Funding data	Web of Science (Core Collection)	Website – extract as CSV	Topic search (TS=) was used which searches titles, abstracts and author keywords	Publication years 2019, 2020, 2021, 2022, 2023, 2024
Patents	Lens.org	Website – extract as CSV	All fields	Granted date >= 2019-01-01 (implicitly excludes patents not granted)
Grey literature	Overton	Website and data dump	Document titles, summaries and full-text	Publication year >=2019
Companies	Crunchbase	Website – extract as CSV	Description keywords**	

*Note: *See OpenAlex (2024b); **Searches keywords across an organisation's associated full description, industries, industry groups, headquarter location and region.*

Source: RAND Europe analysis.

The search strings for each technology area are detailed below. The same search strings provided consistent results for publications, funding data, patents and grey literature. However, the research team found that company searches using the same search strings did not yield results that aligned well with reviews from desk research, leaving out many companies that were active in the technology area. Further investigation revealed that this was because terms used in company descriptions relating to the application of the technology were more specific than those listed in the search. For example, in embryology, many companies active in assisted reproduction did not list embryo terms in their descriptions. Therefore, an additional step was included when creating a Crunchbase search whereby topic modelling outcomes were reviewed to select other relevant terms that would be an indicator of relevance to the technology area.

It should be noted that while patents and the number of active companies are a good proxy for measuring commercialisation, there are significant differences in how patenting is used across different countries, as well as variation in the coverage of patents indexed. While Crunchbase seeks to provide international coverage, data is collected via self-reporting from around 3,500 investment firms, as well as community entrepreneurs and executives, resulting in gaps across many countries and regions. Hence, careful interpretation of the data is required, only comparing across certain countries and indicators where appropriate.

Search strategy for genomics

Publications, funding data, patents and grey literature search: (genomic* OR metagenomic* OR epigenomic* OR proteogenomic* OR 'synthetic biology' OR 'engineering biology'). Use of an asterisk indicates a wildcard search, matching any word that contains the search term directly followed by any other character(s).

Additional terms added to the companies search and the source are listed in Table 18.

Table 18. Genomics companies search terms

Search term	Source
Genomic	Bibliometric search
Metagenomic	Bibliometric search
Epigenomic	Bibliometric search
Proteogenomic	Bibliometric search
'synthetic biology'	Bibliometric search
'engineering biology'	Bibliometric search
Genomics	Plural form bibliometric search
Metagenomics	Plural form bibliometric search
Epigenomics	Plural form bibliometric search
Proteogenomics	Plural form bibliometric search
'DNA detection'	Topic model
'Next generation sequencing'	Topic model
Genome	Topic model
Genomes	Topic model
Epigenetic	Topic model
Epigenetics	Topic model
'DNA replication'	Topic model
'Gene sequencing'	Topic model
'RNA sequencing'	Topic model
'lncrna'	Topic model
'Microrna'	Topic model
'Micrornas'	Topic model

Source: RAND Europe analysis.

Search strategy for organoids

Publications, funding data, patents and grey literature search: (organoid* OR embryoid* OR brainoid*).

Additional terms added to the companies search and their source are listed in Table 19.

Table 19. Organoids companies search terms

Search term	Source
Organoid	Bibliometric search
Organoids	Plural form bibliometric search
Embryoid	Bibliometric search
Embryoids	Plural form bibliometric search
Brainoid	Bibliometric search
Brainoids	Plural form bibliometric search

Source: RAND Europe analysis.

Search strategy for embryology

Publications, funding data, patents and grey literature search: (embryology OR 'embryonic development' OR 'embryo development' OR embryogenesis OR 'embryonic morphogenesis' OR 'embryonic stem cells' OR 'embryo model systems' OR 'blastocyst*' OR 'stem cell-based embryo models' OR 'stem cell-derived embryo models').

Additional terms added to the companies search and their source are listed in Table 20.

Table 20. Embryology companies search terms

Search term	Source
Embryology	Bibliometric search
'Embryonic development'	Bibliometric search
'Embryo development'	Bibliometric search
Embryogenesis	Bibliometric search
'Embryonic morphogenesis'	Bibliometric search
'Embryonic stem cell'	Bibliometric search
'Embryonic stem cells'	Plural form bibliometric search
'Embryo model systems'	Bibliometric search
Blastocyst	Bibliometric search
Blastocysts	Plural form bibliometric search
'Stem cell-based embryo'	Bibliometric search
'Stem cell-derived embryo'	Bibliometric search
'Reproductive technology'	Topic model
'In vitro fertilization'	Topic model
Embryos	Topic model
'Assisted reproduction'	Topic model
'Assisted reproductive'	Topic model
'Preimplantation genetic'	Topic model
'Fertility clinic'	Topic model
'IVF'	Topic model

Source: RAND Europe analysis.

Search strategy for neurotechnology

Publications, funding data, patents and grey literature search: (neurotechnology OR 'brain computer interface' OR 'brain machine interface' OR 'neuroinformatics' OR 'neural engineering').

Additional terms added to the companies search and their source are listed in Table 21.

Table 21. Neurotechnology companies search terms

Search Term	Source
Neurotechnology	Bibliometric search
'Brain computer interface'	Bibliometric search
'Brain machine interface'	Bibliometric search
'Neuroinformatics'	Bibliometric search
'Neural engineering'	Bibliometric search
Neuroethics	Topic model
Neuropharmacology	Topic model
Neurostimulation	Topic model
Neurofeedback	Topic model
Neuroimaging	Topic model
Neuroprosthetics	Topic model

Source: RAND Europe analysis.

A summary of the record counts for each search and source are provided in Table 22.

Table 22. Search result counts for each technology area

Type	Genomics	Embryology	Organoids	Neurotechnology
Publications	264,721	99,652	25,514	16,178
Funding data	173,102	35,521	14,615	7,412
Patents	36,358	11,170	2,971	2,946
Grey literature	21,536	2,907	568	771
Companies	2,706	924	56	439

Source: RAND Europe analysis.

B.1.2. Topic modelling

Topic modelling is a natural language processing technique that determines how to use specific clusters of related words (topics) to categorise underlying data. Because it is data-driven, results are derived from the data itself and are thus independent of existing categorical systems (such as journal categories). This study used topic modelling to classify publications based on the text contained in the titles and abstracts.

The research team implemented topic modelling using Python and the open-source libraries Scikit-learn[58] and the Natural Language Toolkit (NLTK).[59] Publication texts (titles and abstracts) were filtered using the automatic language detection library 'pycld2'[60] to select only fragments in English. Various keyword searches were also used to remove other irrelevant metadata, such as links

58 https://scikit-learn.org/
59 https://www.nltk.org/
60 https://github.com/aboSamoor/pycld2

to Crossref, Mendeley, Google Scholar and Scopus. Publication texts were normalised using the following steps: lowercasing, replacing diacritic characters with ASCII equivalents, removing punctuation characters and normalising URLs (i.e. replacing full URLs with the associated domain name). Trigrams (up to three-word sequences) were extracted for each publication text, with the team subsequently removing common stop-words, short words and digits with only one or two characters. Words appearing in more than 50% of documents or fewer than five individual publications were also removed. The top 100,000 most frequently used trigrams were retained and weighted using TF-IDF.[61]

After text processing, the research team used nonnegative matrix factorisation (NMF) to create topic models for each technology area using a range of target topics (between 10 and 100). Each were reviewed and one was selected to be used in the study based on providing reasonable sized clusters (between 1,000 and 10,000 as the primary topic) and sufficient detail to support the jurisdiction selection process. Up to three topics were chosen for each publication. The primary topic had the largest weight, along with optional secondary and tertiary topics if their weight exceeded a minimum threshold (higher than 95% of all weights).

For each topic model, indicative labels were created for each topic based on the top 20 most highly weighted words, using manual review and the results from ChatGPT (ChatGPT 2024) queries.[62] In addition, related topics were grouped into clusters (as shown in the topic maps using different colours) based on Ward similarity of the resulting topic-token matrix.

Topic maps were produced using Uniform Manifold Approximation and Projection for Dimension Reduction (UMAP) via the Python library umap-learn (UMAP 2024). The doc-topic weight matrix was used as input to the algorithm, along with the following parameter values: n_neighbors=50, min_dist=0.2 and metric='cosine'. The result of the algorithm was a mapping of each publication to an x,y coordinate. Indicative topic labels were positioned based on the mean value of all coordinates allocated to publications on the topic.

B.1.3. Metrics and indicators

Throughout the study, various metrics and indicators were used to highlight trends in research and commercialisation across countries and topics. The following definitions are provided:

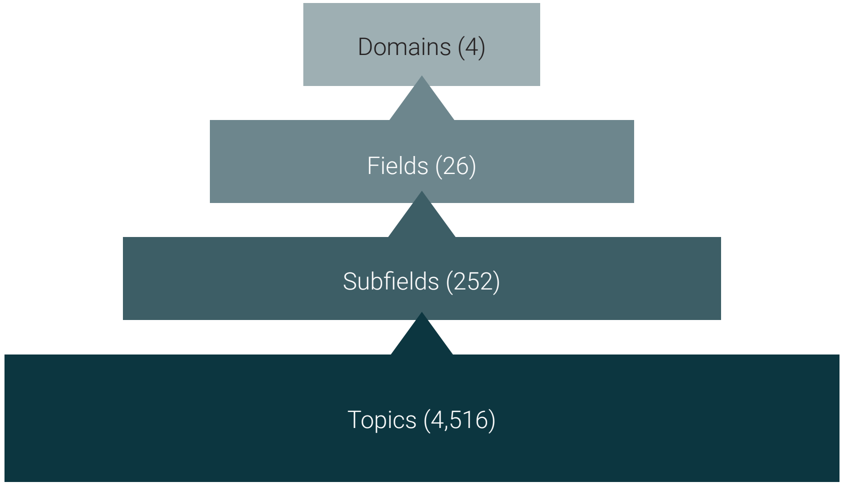
Sub-fields

Publication data were categorised using OpenAlex topics data. OpenAlex is an automated system that takes into account the available information about a work, including title, abstract, source (journal) name and citations. There are around 4,500 topics that are grouped into sub-fields, which are grouped into fields, which are grouped into top-level domains, as shown in Figure 32.

61 https://en.wikipedia.org/wiki/Tf%E2%80%93idf

62 GPT3.5 with the prompt: 'What are the following top keywords about [list of keywords]?'

Figure 32. OpenAlex subject classification hierarchy



Source: OpenAlex (2024a).

Global publication share

For each technology area, the global publication share is reported. This is the percentage of all published works indexed by OpenAlex that were returned by the search during the same period.

Relative share

In the case of publications, patents and grey literature (policy documents), the volume of output for a specific country is reported according to relative share (e.g. % of genomics publications in Table 2, % of genomics patents in Table 3, % of genomics policy documents in Table 4). This makes it possible to compare nations across technology areas even when there are significant differences in volume. For this indicator, the number of outputs attributed to the country was divided by the total number of outputs collected for technology area, multiplied by 100.

National focus

The output of a particular country is also reported as a percentage of national share (e.g. % of national publication output in Table 2, % of national patents in Table 3, % of national policy documents in Table 4). This indicator highlights countries that may have a relatively low volume of the share, but have invested a significant proportion of their national output in a particular technology area.

Mean citation percentile

Citation percentiles are used to report academic impact. This is in preference to raw citation counts as these vary across disciplines and are correlated with the age of publication (older publications have had longer to accumulate citations). Citation percentiles were calculated by ranking the citation count of each publication alongside all other publications from the same year and field. Zero citations corresponds to the minimum percentile value, the highest number of citations receives the percentile score of 100.

Annex C. Supplementary scientometric data

C.1. Data description

The following subsections list scientometric indicators for each technology area. In each case, countries with at least 0.1% of the publication share are listed. Column headers are:

- Continent – Geographic continent for the country.
- Income group – Income group assigned by the World Bank[63] abbreviated to HI (high income), UMI (upper middle income), LMI (lower middle income) and LI (low income).
- Country name – Country name.
- Pub count – Count of publications returned from OpenAlex where an author lists the country in their affiliation.
- Pub share % – Percentage of publications attributed to the country as a fraction of global publications in the technology area.
- Pub focus % – Percentage of all publications attributed to the country that were in the technology area.
- Mean citation percentile – Mean citation percentile assigned to publications returned from OpenAlex.
- % collab with HI – Percentage of publications where a collaborating author lists a high-income country in their affiliation.
- % collab with UMI – As above for upper middle-income countries.
- % collab with LMI – As above for lower middle-income counties.
- % collab with LI – As above for low-income countries.
- Patent count – Total number of extended patent families granted to applicants from the country.
- Patent share % – Percentage of patents attributed to the country as a fraction of global patent output in the technology area.

63 The World Bank's Country Classification by Income (World Bank 2024b).

- Patent focus % – Percentage of all patents attributed to the country that were in the technology area.
- Overton count – Number of documents indexed in Overton from sources in the country.
- Overton share % – Percentage of all documents attributed to the country as a fraction of the global output.
- Overton focus % – Percentage of all documents attributed to the country in the technology area.
- Pubs cited in Overton – Number of publications that were cited by documents indexed by Overton.
- WOS funding % – Percentage of funder acknowledgements to funders in the country as a fraction of all funder acknowledgements (Web of Science).
- Crunchbase company count – Number of companies with descriptions indicating activity in the technology area.

C.1.1. Genomics – country indicators table

Table 23. Genomics country indicators

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Africa	LMI	Egypt	1,261	0.5	0.49	73.6	58.8	21.2	15.9	3.6	4	0	4.7	2	0	0.12	1	0.1	2
Africa	LI	Ethiopia	417	0.2	0.68	71.2	73.1	37.6	37.6	14.6	0	0	0	18	0.1	1.67	0	0	0
Africa	LMI	Ghana	347	0.1	0.89	71.5	75.2	34.9	47.6	27.4	0	0	0	7	0	0.44	0	0	1
Africa	LMI	Kenya	722	0.3	1.69	73.5	69.5	42.1	32.3	25.6	0	0	0	51	0.2	1.4	5	0	0
Africa	LMI	Morocco	310	0.1	0.43	71.6	64.2	20	35.5	14.5	1	0	0.2	4	0	0.08	0	0	0
Africa	LMI	Nigeria	855	0.3	0.58	66.7	54	30.6	27.1	12.9	2	0	22.2	11	0.1	0.77	1	0	1
Africa	UMI	South Africa	2,016	0.8	1.05	75.3	63.2	18.8	22.8	10	36	0.1	1.2	57	0.3	0.22	5	0.8	4

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Africa	LMI	Tanzania	247	0.1	1.17	73.7	80.6	29.6	40.9	29.1	0	0	0	21	0.1	0.09	1	0	0
Africa	LMI	Tunisia	298	0.1	0.49	73.2	68.1	18.1	21.5	9.1	4	0	13.3	0	0	0	0	0	0
Africa	LI	Uganda	325	0.1	1.53	71.2	83.1	33.8	42.8	18.2	0	0	0	8	0	0.27	0	0	0
Asia	LMI	Bangladesh	764	0.3	0.81	72	60.7	24.2	18.5	2.4	2	0	12.5	3	0	0.08	0	0.1	0
Asia	UMI	China	41,640	17	0.93	73.4	28.1	2.8	3.8	0.3	1,138	3.1	0.8	49	0.2	0.17	2	41.1	142
Asia	HI	Hong Kong	936	0.4	0.74	76.1	49.4	78.1	4.9	0.7	74	0.2	1.4	0	0	0	0	0	8
Asia	LMI	India	10,274	4.2	0.68	67.9	29.7	8.9	5.4	0.9	130	0.4	1.6	84	0.4	0.51	35	3.6	83
Asia	UMI	Indonesia	763	0.3	0.06	61.6	37.5	16.1	10.4	2.4	1	0	1.7	65	0.3	0.25	29	0.1	2
Asia	LMI	Iran	2,035	0.8	0.45	70.4	36.6	11.9	6.6	0.9	4	0	1	2	0	0.06	0	0.5	1
Asia	UMI	Iraq	256	0.1	0.25	59.3	27	12.9	23	2.3	0	0	0	0	0	0	0	0	0
Asia	HI	Israel	2,146	0.9	1.32	74.8	65.1	15.3	6.2	0.9	451	1.2	3.5	13	0.1	0.29	6	0.5	34
Asia	HI	Japan	8,523	3.5	0.94	71.5	34.4	13.2	5.9	0.6	1,381	3.8	0.4	383	1.8	0.16	113	7.5	50
Asia	HI	Korea	4,969	2	0.88	73.7	33	11.5	8.2	1.1	889	2.4	0.3	17	0.1	1.3	1	3.9	40
Asia	UMI	Malaysia	1,066	0.4	0.45	71.6	52.7	27.7	20.4	2.7	27	0.1	0.6	19	0.1	0.45	8	0.3	7
Asia	LMI	Pakistan	1,597	0.7	0.71	70.4	46.8	36.9	14.8	2.3	1	0	1.3	9	0	0.81	0	0.2	3
Asia	LMI	Philippines	410	0.2	0.81	70	66.3	33.4	24.1	2.4	2	0	1.4	119	0.6	0.32	9	0.1	3
Asia	HI	Qatar	317	0.1	0.87	74.7	72.2	15.8	20.8	1.3	1	0	0.6	4	0	0.55	0	0.1	0
Asia	HI	Saudi Arabia	1,657	0.7	0.65	75.3	54.7	21.7	41.8	3.6	56	0.2	0.9	13	0.1	1.22	2	0.4	5
Asia	HI	Singapore	2,078	0.8	1.3	69.6	65.7	26.5	8.6	0.9	198	0.5	1.8	134	0.6	0.54	28	0.7	26
Asia	HI	Taiwan	2,003	0.8	0.83	72.7	39.6	20.4	6.7	0.4	253	0.7	0.3	18	0.1	0.07	2	1.4	15

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Asia	UMI	Thailand	1,143	0.5	0.91	73.9	59.3	22.5	13.4	2.1	11	0	2.1	24	0.1	0.11	6	0.4	2
Asia	UMI	Turkey	1,630	0.7	0.31	70.4	45.6	13.4	14	1.2	6	0	0.2	48	0.2	0.18	17	0.3	7
Asia	HI	United Arab Emirates	521	0.2	0.7	73.5	74.9	16.7	26.5	3.5	7	0	0.9	4	0	1.23	0	0.2	4
Asia	LMI	Viet Nam	543	0.2	0.55	70.8	68.7	21.7	17.5	4.4	0	0	0	0	0	0	0	0.1	1
Europe	HI	Austria	2,284	0.9	1.12	76.5	77.8	19	7.4	1.2	121	0.3	0.8	28	0.1	0.19	14	0.6	6
Europe	HI	Belgium	2,943	1.2	1.1	76.2	74.3	19.8	8.6	3.4	457	1.3	4.3	293	1.4	0.92	119	0.7	10
Europe	HI	Croatia	359	0.1	0.61	74.9	65.7	26.2	7.5	1.1	2	0	1.7	7	0	0.25	1	0.1	1
Europe	HI	Czechia	1,974	0.8	1.28	69.9	73	22.1	9	1.9	31	0.1	0.9	27	0.1	0.15	6	1.1	2
Europe	HI	Denmark	3,636	1.5	1.73	76.7	74.5	25.3	6.4	1.2	631	1.7	6.1	37	0.2	0.09	43	1.4	20
Europe	HI	Estonia	406	0.2	1.68	78.3	86	27.8	14.8	2	10	0	3.4	10	0	0.2	6	0.1	1
Europe	HI	Finland	2,080	0.8	1.35	71.4	79.8	16.1	7.6	1.1	86	0.2	0.7	94	0.4	0.28	110	1	7
Europe	HI	France	10,898	4.4	1.02	73.4	60	15.2	8.6	1.8	987	2.7	1.1	741	3.4	0.78	716	5	59
Europe	HI	Germany	14,284	5.8	1.01	75	66.2	17.1	6.4	1	1,603	4.4	0.8	293	1.4	0.24	315	5	58
Europe	HI	Greece	1,279	0.5	0.84	73.2	63.5	14.1	5.1	1	11	0	0.6	3	0	0.04	0	0.2	1
Europe	HI	Hungary	1,059	0.4	1.08	64.7	67.9	13.8	6.1	0.3	36	0.1	3.5	3	0	0.13	0	0.4	2
Europe	HI	Ireland	1,485	0.6	1.2	74.6	70.2	17.6	6.1	1.6	137	0.4	1.7	363	1.7	1.2	115	0.6	8
Europe	HI	Italy	9,251	3.8	1.05	74.8	57.2	13	6	0.7	277	0.8	1.1	373	1.7	0.84	64	2.1	27
Europe	HI	Netherlands	5,912	2.4	1.3	75.8	74.6	17.1	5.5	1.3	740	2	1.9	270	1.3	0.3	208	1.4	24
Europe	HI	Norway	2,148	0.9	1.21	75.4	79.1	19.1	5.2	1.4	98	0.3	1.5	61	0.3	0.7	55	0.9	4
Europe	HI	Poland	2,039	0.8	0.55	74.5	56	15.1	7.5	0.8	34	0.1	0.2	2	0	0.04	0	0.6	6

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Europe	HI	Portugal	1,819	0.7	0.81	74.7	64.3	21.7	7.8	2.9	27	0.1	1.9	46	0.2	0.16	51	0.7	6
Europe	HI	Romania	387	0.2	0.35	70.9	56.1	20.7	11.4	0.8	0	0	0	33	0.2	0.15	7	0	1
Europe	UMI	Russian Federation	3,083	1.3	0.39	69.7	43.1	14.5	7.5	0.8	104	0.3	0.2	1	0	0.03	24	1.2	7
Europe	UMI	Serbia	291	0.1	0.52	72.8	66.3	34	13.4	2.1	3	0	1.1	7	0	0.17	0	0.1	0
Europe	HI	Slovakia	461	0.2	0.88	58	79.8	10.8	6.3	0.7	5	0	0.8	35	0.2	0.32	14	0.1	0
Europe	HI	Slovenia	413	0.2	0.88	75.8	65.6	22	5.8	0.2	9	0	0.7	14	0.1	0.11	8	0.1	3
Europe	HI	Spain	8,237	3.4	1.07	74.2	62.5	16.8	5	0.9	259	0.7	2.5	539	2.5	0.19	659	4.7	46
Europe	HI	Sweden	4,412	1.8	1.51	76.4	77.4	20.6	7.6	1.3	246	0.7	0.9	190	0.9	0.15	110	2.4	19
Europe	HI	Switzerland	4,906	2	1.35	74.9	75.1	14.6	7.2	1.4	1,191	3.3	2.9	125	0.6	0.46	227	1.6	32
Europe	LMI	Ukraine	269	0.1	0.15	64.6	54.3	27.5	13.8	1.9	2	0	0.4	4	0	0.05	1	0	3
Europe	HI	United Kingdom	19,958	8.1	1.29	73.2	64.9	17.8	8.9	2.4	1,149	3.2	2.4	3,611	16.8	1.07	929	12	164
North America	HI	Canada	10,312	4.2	1.27	72.8	60.2	16.9	6.2	0.8	681	1.9	2.3	618	2.9	0.54	269	5.2	76
North America	UMI	Mexico	2,256	0.9	0.89	72.9	57.4	19.4	10	1.3	25	0.1	2	165	0.8	0.48	171	0.8	13
North America	HI	Puerto Rico	260	0.1	1.91	64.2	79.2	18.1	6.2	3.8	2	0	0.3	0	0	0	0	0	0
North America	HI	United States	77,914	31.8	1.33	70.2	32.2	14.9	4.9	0.7	23,958	65.9	3.3	5,731	26.6	0.38	1,866	55.8	1,256
Oceania	HI	Australia	9,841	4	1.37	74.6	57.8	20.3	10.2	1.3	396	1.1	3.8	1,071	5	0.88	499	3.8	24
Oceania	HI	New Zealand	1,373	0.6	1.25	75	70.3	19.6	7.9	1.2	48	0.1	2.6	160	0.7	0.93	125	0.5	11

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
South America	UMI	Argentina	1,047	0.4	0.76	72.4	65.1	23.8	5.8	0.6	34	0.1	8.7	2	0	0.02	1	0.4	8
South America	UMI	Brazil	5,556	2.3	0.56	73	55.8	13.9	5.4	1	53	0.1	0.6	33	0.2	0.08	14	4.5	29
South America	HI	Chile	1,063	0.4	0.86	74.8	67	33.4	4.8	0.8	20	0.1	4.3	17	0.1	0.12	0	0.6	2
South America	UMI	Colombia	884	0.4	0.65	71.6	69.1	30.5	10	2.4	8	0	3.3	4	0	0.01	2	0.2	2
South America	UMI	Ecuador	263	0.1	0.38	70.6	77.6	34.2	10.3	0.8	0	0	0	0	0	0	0	0	0
South America	UMI	Peru	412	0.2	0.59	70.4	71.4	44.9	14.8	5.1	1	0	2.1	4	0	0.01	2	0	2
South America	HI	Uruguay	292	0.1	1.49	74.7	63.4	46.2	8.9	0.7	3	0	4.5	17	0.1	0.06	5	0.1	

Source: RAND Europe analysis.

C.1.2. Organoids – country indicators table

Table 24. Organoids country indicators

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Africa	LMI	Egypt	80	0.3	0.0	81.1	88.8	11.3	3.8	0.0	0	0.0	0.0	0	0.0	0.0	0	0.0	0
Africa	UMI	South Africa	49	0.2	0.0	75.1	65.3	10.2	12.2	0.0	0	0.0	0.0	0	0.0	0.0	0	0.3	0
Asia	UMI	China	3,220	12.6	0.1	75.4	35.4	1.4	1.6	0.0	40	1.3	0.03	4	0.7	0.01	0	36.5	11
Asia	HI	Hong Kong	161	0.6	0.1	77.6	39.1	79.5	2.5	0.0	3	0.1	0.06	0	0.0	0.0	0	0.0	0
Asia	LMI	India	396	1.6	0.0	71.4	48.2	12.4	2.3	0.0	4	0.1	0.05	0	0.0	0.0	0	1.1	0
Asia	UMI	Indonesia	43	0.2	0.0	62.9	60.5	7.0	7.0	0.0	0	0.0	0.0	0	0.0	0.0	0	0.1	0
Asia	LMI	Iran	153	0.6	0.0	75.8	45.8	13.1	3.3	0.0	0	0.0	0.0	0	0.0	0.0	0	0.6	0
Asia	HI	Israel	202	0.8	0.1	73.1	67.3	7.9	5.0	0.0	40	1.3	0.31	0	0.0	0.0	0	0.5	0
Asia	HI	Japan	1,471	5.8	0.2	74.1	33.8	6.6	3.5	0.0	174	5.9	0.05	14	2.5	0.01	16	16.3	3
Asia	HI	Korea	830	3.3	0.1	72.5	29.9	5.4	1.4	1.1	167	5.6	0.06	0	0.0	0.0	1	8.2	3
Asia	HI	Macao	38	0.1	0.2	73.6	55.3	84.2	0.0	0.0	0	0.0	0.0	0	0.0	0.0	0	0.0	0
Asia	UMI	Malaysia	42	0.2	0.0	67.2	47.6	16.7	16.7	0.0	0	0.0	0.0	0	0.0	0.0	0	0.1	0
Asia	LMI	Pakistan	28	0.1	0.0	74.0	75.0	7.1	7.1	0.0	0	0.0	0.0	0	0.0	0.0	0	0.1	0
Asia	HI	Saudi Arabia	69	0.3	0.0	75.6	76.8	20.3	31.9	0.0	3	0.1	0.05	0	0.0	0.0	0	0.1	0
Asia	HI	Singapore	284	1.1	0.2	76.2	66.2	25.4	3.9	0.0	21	0.7	0.19	17	3.0	0.07	2	1.4	0
Asia	HI	Taiwan	185	0.7	0.1	76.2	50.3	20.5	1.6	0.5	17	0.6	0.02	2	0.4	0.01	1	1.2	1
Asia	UMI	Thailand	78	0.3	0.1	73.8	60.3	9.0	5.1	0.0	0	0.0	0.0	0	0.0	0.0	0	0.4	0

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Asia	UMI	Turkey	112	0.4	0.0	70.9	56.3	17.0	8.9	0.0	0	0.0	0.0	0	0.0	0.0	2	0.3	0
Europe	HI	Austria	322	1.3	0.2	78.8	68.3	6.5	3.4	0.0	10	0.3	0.06	8	1.4	0.05	6	1.2	2
Europe	HI	Belgium	409	1.6	0.2	75.3	66.5	9.3	3.2	0.0	14	0.5	0.13	6	1.1	0.02	22	1.4	0
Europe	HI	Croatia	30	0.1	0.1	69.2	80.0	10.0	16.7	0.0	0	0.0	0.0	0	0.0	0.0	0	0.0	0
Europe	HI	Czechia	136	0.5	0.1	72.8	69.9	11.0	7.4	0.0	1	0.0	0.03	3	0.5	0.02	0	1.1	0
Europe	HI	Denmark	255	1.0	0.1	75.9	71.8	6.3	5.1	0.0	15	0.5	0.14	1	0.2	0.00	4	1.5	0
Europe	HI	Finland	179	0.7	0.1	74.2	74.3	5.6	2.2	0.0	5	0.2	0.04	4	0.7	0.01	0	1.1	0
Europe	HI	France	895	3.5	0.1	71.8	55.9	8.5	2.1	0.1	34	1.1	0.04	7	1.2	0.01	23	4.6	1
Europe	HI	Germany	2,131	8.4	0.2	74.6	58.8	8.1	2.6	0.2	60	2.0	0.03	33	5.8	0.03	21	9.0	1
Europe	HI	Greece	84	0.3	0.1	81.0	69.0	7.1	0.0	0.0	0	0.0	0.0	0	0.0	0.0	0	0.2	0
Europe	HI	Hungary	84	0.3	0.1	63.1	56.0	4.8	1.2	0.0	1	0.0	0.10	0	0.0	0.0	0	0.6	0
Europe	HI	Ireland	121	0.5	0.1	72.7	62.8	14.0	3.3	0.8	1	0.0	0.01	1	0.2	0.00	1	0.5	1
Europe	HI	Italy	1,006	3.9	0.1	76.6	57.9	7.8	2.9	0.0	9	0.3	0.03	16	2.8	0.04	1	3.6	1
Europe	HI	Luxembourg	90	0.4	0.4	69.5	82.2	6.7	1.1	0.0	4	0.1	0.11	0	0.0	0.0	2	0.4	1
Europe	HI	Netherlands	1,466	5.7	0.3	75.7	56.3	8.7	2.1	0.1	39	1.3	0.10	28	4.9	0.03	18	5.4	3
Europe	HI	Norway	195	0.8	0.1	72.5	70.3	14.9	2.6	0.0	6	0.2	0.09	3	0.5	0.03	2	0.9	0
Europe	HI	Poland	136	0.5	0.0	77.7	64.7	8.8	8.1	0.0	1	0.0	0.01	0	0.0	0.0	0	0.5	0
Europe	HI	Portugal	153	0.6	0.1	78.4	58.8	10.5	3.9	0.0	2	0.1	0.14	4	0.7	0.01	5	0.7	0
Europe	UMI	Russia	182	0.7	0.0	69.4	36.8	6.6	6.0	0.0	4	0.1	0.01	0	0.0	0.0	0	0.6	0
Europe	HI	Slovakia	33	0.1	0.1	65.4	75.8	18.2	24.2	0.0	0	0.0	0.0	1	0.2	0.01	0	0.1	0

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Europe	HI	Spain	625	2.4	0.1	73.5	61.0	9.8	2.1	0.2	8	0.3	0.08	67	11.8	0.02	43	5.5	0
Europe	HI	Sweden	388	1.5	0.1	77.1	78.6	12.6	5.2	0.3	21	0.7	0.07	8	1.4	0.01	15	2.6	0
Europe	HI	Switzerland	709	2.8	0.2	74.8	71.7	8.5	2.4	0.4	37	1.2	0.09	9	1.6	0.03	19	2.5	3
Europe	HI	United Kingdom	1,979	7.8	0.1	73.2	60.1	8.6	3.7	0.2	53	1.8	0.11	47	8.3	0.01	48	13.6	2
North America	HI	Canada	970	3.8	0.1	71.6	53.8	11.0	3.9	0.1	41	1.4	0.14	5	0.9	0.00	9	5.3	1
North America	UMI	Mexico	70	0.3	0.0	69.1	64.3	7.1	0.0	0.0	2	0.1	0.16	0	0.0	0.0	0	0.3	0
North America	HI	United States	8,843	34.7	0.2	70.7	30.5	10.0	2.5	0.0	1,684	56.7	0.23	98	17.3	0.01	145	75.7	19
Oceania	HI	Australia	705	2.8	0.1	76.6	47.9	10.8	4.3	0.1	12	0.4	0.12	27	4.8	0.02	30	4.6	0
Oceania	HI	New Zealand	65	0.3	0.1	72.5	64.6	7.7	3.1	0.0	0	0.0	0.0	2	0.4	0.01	1	0.3	0
South America	UMI	Argentina	38	0.1	0.0	67.6	60.5	13.2	2.6	0.0	0	0.0	0.0	1	0.2	0.01	0	0.1	0
South America	UMI	Brazil	222	0.9	0.0	75.9	59.0	9.0	5.0	0.5	2	0.1	0.02	1	0.2	0.00	0	1.8	0
South America	HI	Chile	35	0.1	0.0	74.0	62.9	20.0	2.9	0.0	0	0.0	0.0	0	0.0	0.0	0	0.1	0

Source: RAND Europe analysis.

C.1.3. Embryology – country indicators table

Table 25. Embryology country indicators

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Africa	LMI	Egypt	913	0.9	0.35	68.9	45.8	16.4	9.7	1.2	0	0	0	2	0	0.12	0	0.1	0
Africa	LI	Ethiopia	116	0.1	0.19	71.9	38.8	10.3	17.2	1.7	0	0	0	6	0.1	0.56	0	0	0
Africa	LMI	Nigeria	163	0.2	0.11	65.5	36.2	30.1	13.5	8	0	0	0	7	0.1	0.49	0	0	3
Africa	UMI	South Africa	335	0.3	0.18	76.6	57.3	16.4	22.4	2.1	3	0	0.1	22	0.2	0.08	0	0.3	0
Africa	LMI	Tunisia	111	0.1	0.18	68.8	56.8	13.5	6.3	0	1	0	3.33	1	0	0.05	0	0	0
Asia	LMI	Bangladesh	167	0.2	0.18	69.2	56.9	15	14.4	1.2	1	0	6.25	0	0	0	0	0.1	0
Asia	UMI	China	18,836	18.9	0.42	77.1	23	1.5	2.2	0.1	280	2.5	0.19	20	0.2	0.07	0	42.8	33
Asia	HI	Hong Kong	435	0.4	0.34	79.6	34.9	81.1	6	0.2	23	0.2	0.45	0	0	0	0	0	2
Asia	LMI	India	3,177	3.2	0.21	67	27.7	6.8	3.1	0.6	25	0.2	0.3	15	0.1	0.09	2	3.1	167
Asia	UMI	Indonesia	586	0.6	0.04	52.2	15.2	6.8	4.1	0.7	0	0	0	126	1.2	0.48	7	0.1	4
Asia	LMI	Iran	1,473	1.5	0.32	74.8	30.6	8.9	3.7	0.5	0	0	0	2	0	0.06	0	1.2	1
Asia	UMI	Iraq	169	0.2	0.17	58.9	26.6	11.2	17.8	3.6	0	0	0	0	0	0	0	0	0
Asia	HI	Israel	1,048	1.1	0.64	75.8	54	9.6	3.4	0	184	1.6	1.43	2	0	0.04	0	0.6	22
Asia	HI	Japan	4,658	4.7	0.51	74.4	29.4	9	4.6	0.2	654	5.9	0.21	139	1.3	0.06	25	11.6	6
Asia	HI	Korea	2,344	2.4	0.42	76.9	21.9	7.6	7.1	1.2	294	2.6	0.1	20	0.2	1.53	0	4.5	3
Asia	LMI	Lebanon	102	0.1	0.34	77.4	58.8	9.8	10.8	2	1	0	1.18	3	0	0.08	0	0.1	2
Asia	UMI	Malaysia	451	0.5	0.19	72.9	37.9	15.5	15.5	0.4	2	0	0.04	22	0.2	0.52	0	0.3	1
Asia	LMI	Pakistan	431	0.4	0.19	72.1	45.2	39.2	16	2.6	1	0	1.32	0	0	0	0	0.1	0

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Asia	HI	Qatar	151	0.2	0.41	82.2	72.2	18.5	23.8	0.7	0	0	0	2	0	0.28	1	0.1	0
Asia	HI	Saudi Arabia	566	0.6	0.22	76.5	53	20.5	40.8	3.5	20	0.2	0.32	6	0.1	0.56	0	0.3	1
Asia	HI	Singapore	677	0.7	0.42	79.2	63.4	22.7	4.1	0.1	87	0.8	0.8	61	0.6	0.24	3	0.7	3
Asia	HI	Taiwan	920	0.9	0.38	78	30.9	12.2	3.8	0.2	93	0.8	0.09	7	0.1	0.03	0	1.1	2
Asia	UMI	Thailand	303	0.3	0.24	73.8	40.9	18.8	8.9	0	0	0	0	11	0.1	0.05	0	0.2	6
Asia	UMI	Turkey	1,203	1.2	0.23	66.7	31.3	7.1	7.4	0.7	10	0.1	0.42	56	0.5	0.21	2	0.5	7
Asia	HI	United Arab Emirates	251	0.3	0.34	71.1	58.6	23.5	21.5	0.4	2	0	0.27	3	0	0.93	0	0.2	9
Asia	LMI	Viet Nam	194	0.2	0.2	67.2	56.2	19.6	4.6	0.5	0	0	0	0	0	0	0	0.1	1
Europe	HI	Austria	898	0.9	0.44	78.2	70.7	13.3	5.5	0.3	22	0.2	0.14	24	0.2	0.16	2	0.5	0
Europe	HI	Belgium	1,380	1.4	0.52	76.9	66	16.2	6.9	0.8	110	1	1.03	96	0.9	0.3	19	0.9	4
Europe	UMI	Bulgaria	146	0.1	0.35	66.2	47.9	21.2	3.4	0	1	0	0.11	0	0	0	0	0.7	2
Europe	HI	Croatia	168	0.2	0.29	78.3	61.9	23.8	6.5	0	1	0	0.86	2	0	0.07	0	0.1	0
Europe	HI	Czechia	836	0.8	0.54	77.1	59.8	14.2	6.8	0.1	14	0.1	0.43	11	0.1	0.06	0	1.2	3
Europe	HI	Denmark	989	1	0.47	77.7	67.4	18.8	5.8	0.6	68	0.6	0.65	10	0.1	0.02	10	0.8	11
Europe	HI	Finland	570	0.6	0.37	80.6	70.5	11.4	5.8	0.2	18	0.2	0.15	112	1.1	0.33	8	0.7	0
Europe	HI	France	3,974	4	0.37	76.9	53.2	11.5	5.1	0.4	279	2.5	0.3	283	2.7	0.3	93	5	8
Europe	HI	Germany	5,499	5.5	0.39	78.8	57.2	12.5	5.5	0.2	439	3.9	0.22	94	0.9	0.08	47	3.9	14
Europe	HI	Greece	629	0.6	0.41	75.4	51.7	7.9	4.3	0	1	0	0.05	1	0	0.01	0	0.1	7
Europe	HI	Hungary	413	0.4	0.42	73.3	51.3	11.1	4.4	0.2	9	0.1	0.88	3	0	0.13	0	0.4	3

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Europe	HI	Ireland	355	0.4	0.29	76.3	61.7	12.7	4.8	0.8	40	0.4	0.49	92	0.9	0.31	8	0.2	8
Europe	HI	Italy	4,164	4.2	0.47	79.2	46.4	9.7	4.3	0.2	94	0.8	0.36	34	0.3	0.08	2	1.9	4
Europe	HI	Netherlands	2,085	2.1	0.46	79.3	62.3	12.7	3	0.3	145	1.3	0.38	132	1.3	0.15	24	1.1	5
Europe	HI	Norway	534	0.5	0.3	78.9	71	11.4	4.3	0.6	17	0.2	0.26	38	0.4	0.44	7	0.5	
Europe	HI	Poland	1,554	1.6	0.42	78.5	35.8	7.6	3.5	0	6	0.1	0.04	0	0	0	0	1.2	3
Europe	HI	Portugal	831	0.8	0.37	79.3	51.1	14.6	3.4	0.2	9	0.1	0.62	61	0.6	0.22	14	0.7	1
Europe	HI	Romania	280	0.3	0.25	76.5	34.3	9.6	5.7	0.4	0	0	0	2	0	0.01	0	0.1	1
Europe	UMI	Russia	1,487	1.5	0.19	69.3	30.4	7.6	4.4	0.2	36	0.3	0.06	0	0	0	0	1.5	2
Europe	UMI	Serbia	138	0.1	0.25	71.1	30.4	19.6	3.6	0.7	1	0	0.36	7	0.1	0.17	0	0.1	1
Europe	HI	Slovakia	214	0.2	0.41	75.5	59.3	13.6	13.1	0.5	0	0	0	2	0	0.02	2	0.2	0
Europe	HI	Slovenia	138	0.1	0.29	79.2	54.3	8.7	5.1	0	0	0	0	0	0	0	9	0.1	0
Europe	HI	Spain	3,830	3.8	0.5	74.6	52.2	11.3	2.4	0.1	92	0.8	0.89	142	1.4	0.05	62	5.1	41
Europe	HI	Sweden	1,401	1.4	0.48	79.5	69.7	13.3	4.1	0.3	68	0.6	0.24	103	1	0.08	19	2.2	6
Europe	HI	Switzerland	1,616	1.6	0.44	78.1	66.8	9.8	3.9	0.2	377	3.4	0.91	53	0.5	0.2	20	1.4	5
Europe	LMI	Ukraine	304	0.3	0.17	55.6	22.7	6.3	1	0	5	0	1.02	2	0	0.03		0	3
Europe	HI	United Kingdom	6,713	6.7	0.43	76.5	57.6	13.1	4.9	0.5	322	2.9	0.67	2153	20.7	0.64	88	9.7	44
North America	HI	Canada	3,177	3.2	0.39	76.2	48.3	16.3	5	0.2	163	1.5	0.55	825	7.9	0.72	28	3.4	21
North America	UMI	Mexico	913	0.9	0.36	71	39.4	12.4	3.9	0.3	7	0.1	0.55	38	0.4	0.11	2	1	9

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
North America	HI	United States	24,407	24.5	0.42	73.5	29.4	14.9	3.5	0.2	6,610	59.2	0.91	2916	28	0.19	239	36.7	335
Oceania	HI	Australia	2,673	2.7	0.37	77.9	49	18.1	6.5	0.3	142	1.3	1.37	392	3.8	0.32	52	2.4	43
Oceania	HI	New Zealand	342	0.3	0.31	78.3	54.7	18.1	5.3	0	14	0.1	0.76	88	0.8	0.51	1	0.3	0
South America	UMI	Argentina	617	0.6	0.45	71.5	48.5	18.2	2.1	0.2	2	0	0.51	8	0.1	0.09	0	0.7	3
South America	UMI	Brazil	2,584	2.6	0.26	71.5	38.8	8.2	2.4	0.1	16	0.1	0.17	15	0.1	0.04	0	5.1	21
South America	HI	Chile	396	0.4	0.32	75.7	52.3	27.3	4.3	0.3	1	0	0.22	5	0	0.04	1	0.5	0
South America	UMI	Colombia	248	0.2	0.18	70.2	53.2	22.6	8.1	0	2	0	0.84	3	0	0.01	0	0.1	1

Source: RAND Europe analysis.

C.1.4. Neurotechnology – country indicators table

Table 26. Neurotechnology country indicators

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Africa	LMI	Egypt	49	0.3	0.02	69.6	26.5	12.2	6.1	0	0	0	0	0	0	0	0	0.1	0
Africa	LMI	Morocco	28	0.2	0.04	68.8	17.9	10.7	7.1	3.6	0	0	0	0	0	0	0	0.1	0
Africa	UMI	South Africa	33	0.2	0.02	70.5	39.4	24.2	24.2	0	0	0	0	2	0.3	0.01	1	0.1	1
Africa	LMI	Tunisia	21	0.1	0.03	70	66.7	28.6	9.5	0	0	0	0	0	0	0	0	0	0
Asia	LMI	Bangladesh	114	0.7	0.12	71.8	33.3	8.8	7	0	0	0	0	0	0	0	0	0.2	0
Asia	UMI	China	3,205	19.8	0.07	72.5	26	2.6	1.7	0	28	1	0.02	1	0.1	0	0	58.4	16
Asia	HI	Hong Kong	108	0.7	0.09	72.5	34.3	87	7.4	0	3	0.1	0.06	0	0	0	0	0	3
Asia	LMI	India	1,020	6.3	0.07	65.6	15.8	5	2.4	0.6	13	0.4	0.16	5	0.6	0.03	3	1.9	7
Asia	UMI	Indonesia	79	0.5	0.01	58.9	10.1	5.1	2.5	0	0	0	0	10	1.3	0.04	0	0.2	0
Asia	LMI	Iran	277	1.7	0.06	70.6	28.5	5.4	3.2	0.4	1	0	0.25	0	0	0	0	0.4	0
Asia	UMI	Iraq	52	0.3	0.05	67.3	28.8	25	11.5	0	0	0	0	0	0	0	0	0.1	0
Asia	HI	Israel	77	0.5	0.05	72.1	51.9	5.2	1.3	1.3	50	1.7	0.39	0	0	0	0	0.4	11
Asia	HI	Japan	507	3.1	0.06	67.2	33.1	17.8	5.1	0.2	59	2	0.02	30	3.9	0.01	5	5.8	5
Asia	UMI	Kazakhstan	37	0.2	0.09	76.7	35.1	2.7	2.7	0	0	0	0	0	0	0	0	0	0
Asia	HI	Korea	568	3.5	0.1	75.5	23.9	7.6	4.4	0.5	119	4	0.04	1	0.1	0.08	0	9.7	5
Asia	HI	Macao	49	0.3	0.19	74.7	44.9	69.4	8.2	0	1	0	0.51	0	0	0	0	0	0
Asia	UMI	Malaysia	140	0.9	0.06	68.8	25	11.4	24.3	4.3	0	0	0	3	0.4	0.07	0	0.9	1
Asia	LMI	Pakistan	133	0.8	0.06	74.9	51.1	24.1	8.3	0.8	0	0	0	0	0	0	0	0.2	0

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Asia	HI	Saudi Arabia	116	0.7	0.05	76.9	41.4	21.6	35.3	2.6	3	0.1	0.05	0	0	0	0	0.8	0
Asia	HI	Singapore	201	1.2	0.13	79.2	41.3	33.3	8	0.5	10	0.3	0.09	10	1.3	0.04	2	0.9	2
Asia	LMI	Sri Lanka	25	0.2	0.08	64.2	56	8	8	0	0	0	0	1	0.1	0.02	0	0	0
Asia	HI	Taiwan	152	0.9	0.06	73	34.9	13.2	4.6	0	16	0.5	0.02	0	0	0	0	1.6	1
Asia	UMI	Thailand	46	0.3	0.04	66.7	17.4	6.5	4.3	0	0	0	0	1	0.1	0	0	0.3	0
Asia	UMI	Turkey	187	1.2	0.04	69.2	22.5	5.3	5.9	0	0	0	0	0	0	0	0	0.5	0
Asia	HI	United Arab Emirates	65	0.4	0.09	75.9	58.5	24.6	23.1	0	1	0	0.13	0	0	0	0	0.3	0
Asia	LMI	Viet Nam	28	0.2	0.03	66	25	10.7	7.1	0	0	0	0	0	0	0	0	0	0
Europe	HI	Austria	158	1	0.08	74	70.3	17.7	1.3	0.6	17	0.6	0.11	4	0.5	0.03	7	0.2	2
Europe	HI	Belgium	113	0.7	0.04	78.4	67.3	8	0.9	0.9	8	0.3	0.08	12	1.6	0.04	2	0.6	4
Europe	UMI	Bulgaria	28	0.2	0.07	58.9	28.6	7.1	21.4	0	0	0	0	0	0	0	0	0.4	0
Europe	HI	Czechia	40	0.2	0.03	69	40	22.5	15	2.5	1	0	0.03	1	0.1	0.01	0	0.5	1
Europe	HI	Denmark	122	0.8	0.06	76.8	63.1	18.9	4.9	0	15	0.5	0.14	0	0	0	3	0.1	1
Europe	HI	Finland	78	0.5	0.05	78.1	60.3	24.4	7.7	0	3	0.1	0.02	2	0.3	0.01	4	0.3	1
Europe	HI	France	459	2.8	0.04	69.4	53.8	8.1	5.2	1.1	40	1.4	0.04	12	1.6	0.01	2	2.1	14
Europe	HI	Germany	697	4.3	0.05	74.8	54.4	12.9	2.3	0.1	45	1.5	0.02	18	2.3	0.01	29	3	13
Europe	HI	Greece	94	0.6	0.06	73.8	39.4	11.7	5.3	0	0	0	0	0	0	0	0	0.1	0
Europe	HI	Hungary	20	0.1	0.02	78.5	40	0	0	0	2	0.1	0.2	0	0	0	0	0.2	0
Europe	HI	Ireland	79	0.5	0.06	71.2	70.9	5.1	7.6	0	2	0.1	0.02	2	0.3	0.01	4	0.5	2
Europe	HI	Italy	552	3.4	0.06	74.7	48.2	9.6	4.3	0.7	13	0.4	0.05	14	1.8	0.03	1	1.2	4

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Europe	HI	Netherlands	243	1.5	0.05	74.6	59.3	5.3	4.1	0	29	1	0.08	11	1.4	0.01	7	0.5	8
Europe	HI	Norway	65	0.4	0.04	73.1	50.8	26.2	20	0	3	0.1	0.05	2	0.3	0.02	0	0.1	0
Europe	HI	Poland	202	1.2	0.05	73.5	43.6	27.7	7.4	0	0	0	0	0	0	0	0	0.7	0
Europe	HI	Portugal	104	0.6	0.05	71.3	55.8	15.4	6.7	1	2	0.1	0.14	2	0.3	0.01	0	0.5	0
Europe	HI	Romania	76	0.5	0.07	59.1	21.1	3.9	3.9	0	1	0	0.05	1	0.1	0	0	0	0
Europe	UMI	Russia	406	2.5	0.05	63.7	27.6	11.3	2.2	0	7	0.2	0.01	1	0.1	0.03	0	1.2	0
Europe	UMI	Serbia	18	0.1	0.03	75.8	83.3	16.7	0	0	0	0	0	0	0	0	0	0.1	0
Europe	HI	Slovakia	24	0.1	0.05	64.4	41.7	12.5	4.2	0	0	0	0	0	0	0	0	0.1	0
Europe	HI	Spain	420	2.6	0.05	71.3	48.8	22.4	3.6	0	9	0.3	0.09	23	3	0.01	5	3	6
Europe	HI	Sweden	77	0.5	0.03	73.9	53.2	23.4	11.7	0	11	0.4	0.04	13	1.7	0.01	2	0.4	3
Europe	HI	Switzerland	299	1.8	0.08	78.7	72.9	11.4	2.3	0.3	33	1.1	0.08	5	0.6	0.02	2	1.4	12
Europe	LMI	Ukraine	33	0.2	0.02	60.8	30.3	15.2	6.1	0	0	0	0	0	0	0	0	0	0
Europe	HI	United	949	5.9	0.06	73.9	51.5	24.9	8.6	0.4	39	1.3	0.08	54	7	0.02	50	4.3	14
North America	HI	Canada	535	3.3	0.07	73.7	40.7	17.4	9	0.4	47	1.6	0.16	11	1.4	0.01	7	3.2	15
North America	UMI	Cuba	20	0.1	0.06	67.6	65	70	5	0	0	0	0	0	0	0	0	0.1	0
North America	UMI	Mexico	156	1	0.06	67.2	18.6	8.3	1.9	1.3	0	0	0	1	0.1	0	1	0.6	1
North America	HI	United States	3,044	18.8	0.05	72.3	30	12.7	4.2	0.2	1,696	57.6	0.23	167	21.7	0.01	70	26.3	247
Oceania	HI	Australia	398	2.5	0.06	75.9	47.7	26.1	12.3	0	67	2.3	0.64	20	2.6	0.02	8	1.7	7

Continent	Income group	Country name	Pub count	Pub share %	Pub focus %	Mean citation percentile	% Collab with HI	% Collab with UMI	% Collab with LMI	% Collab with LI	Patent count	Patent share %	Patent focus %	Overton count	Overton share %	Overton focus %	Pubs cited in Overton	WOS funding %	Crunchbase company count
Oceania	HI	New Zealand	40	0.2	0.04	75	60	15	22.5	0	3	0.1	0.16	2	0.3	0.01	0	0.1	1
South America	UMI	Argentina	58	0.4	0.04	68.6	51.7	20.7	3.4	0	0	0	0	0	0	0	1	0.2	1
South America	UMI	Brazil	228	1.4	0.02	65.6	34.2	12.3	3.1	0	1	0	0.01	1	0.1	0	1	2.4	5
South America	HI	Chile	29	0.2	0.02	66.6	72.4	34.5	0	0	0	0	0	1	0.1	0.01	0	0.2	0
South America	UMI	Colombia	87	0.5	0.06	64.9	28.7	21.8	5.7	0	0	0	0	0	0	0	1	0.3	0
South America	UMI	Ecuador	29	0.2	0.04	61.8	51.7	20.7	6.9	0	0	0	0	0	0	0	0	0.1	0
South America	UMI	Peru	24	0.1	0.03	66.2	45.8	12.5	16.7	0	0	0	0	0	0	0	0	0.1	0

Source: RAND Europe analysis.