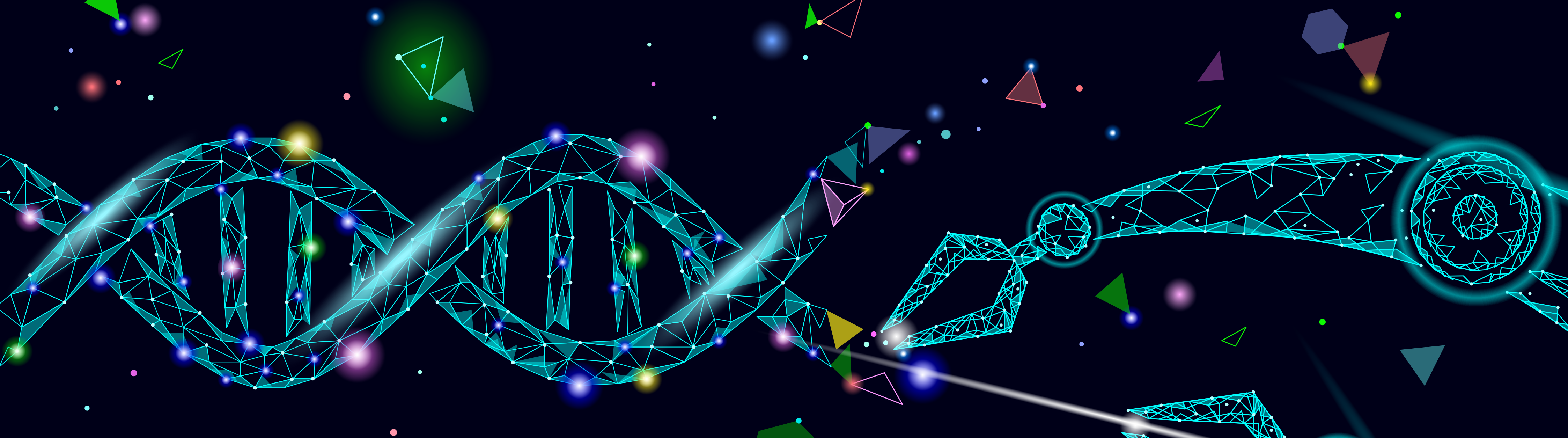

RAND EUROPE

Machine Learning and gene editing at the helm of a societal evolution

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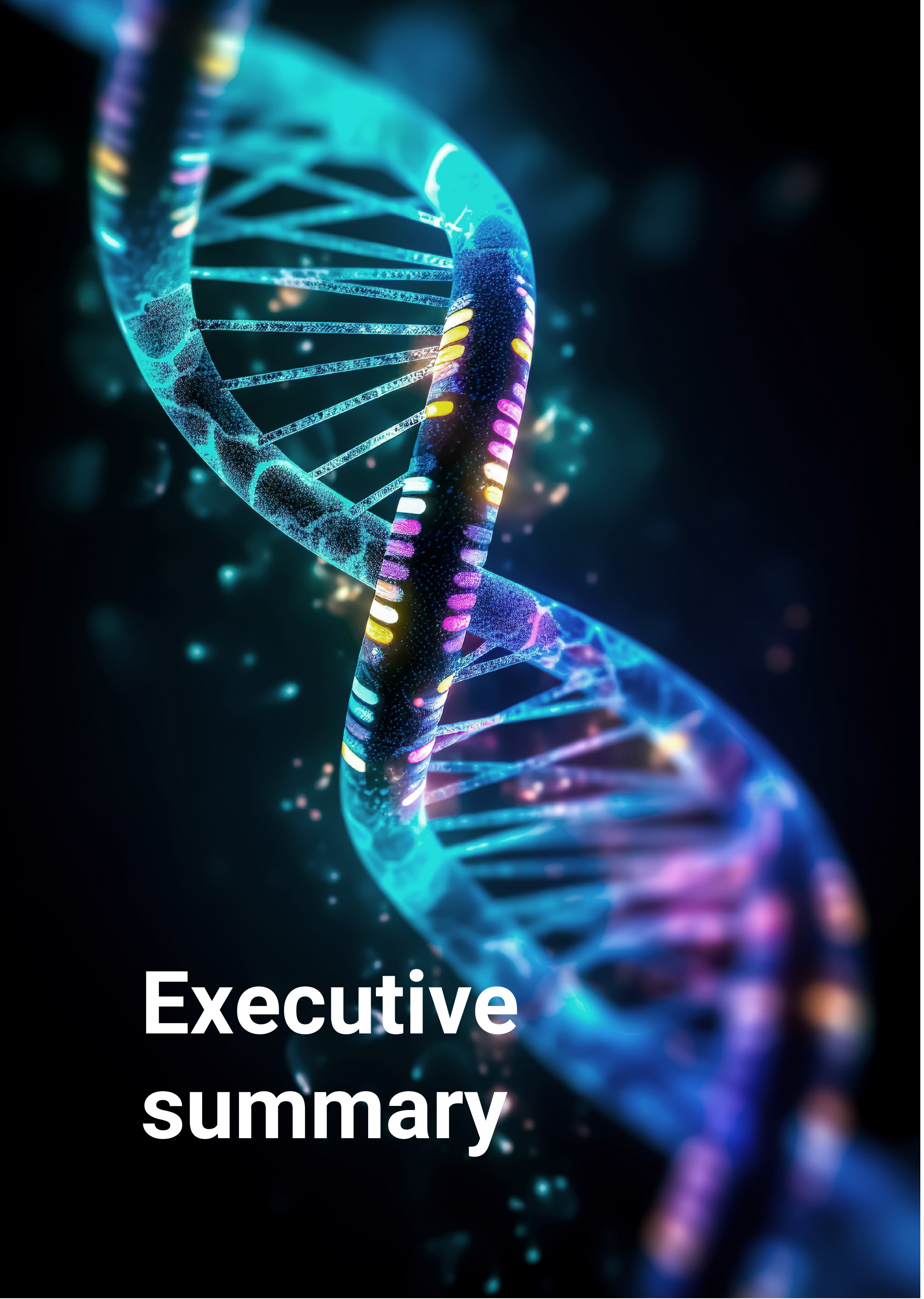


Executive summary

As the impact of machine learning (ML) and gene editing (GE) expands, forward looking policy is needed to mitigate risks and leverage opportunities. The two technologies have increasing significance, the complexity of which magnifies when they integrate. Consideration of technology advancements and policies in different geographic regions, and involvement of multiple organisations, further confound this complexity. Thus, this study explores the technological and policy implications of the intersection of ML and GE, with a focus on the United States (US), the United Kingdom (UK), China and the European Union (EU). Analysis of technical and policy developments over time and an assessment of their current state have informed policy recommendations that can help manage beneficial use of technologies and their convergence. The proposed approach can be applied to a variety of technologies and sectors. This report is intended for policymakers to prompt reflection and consideration of how to approach the convergence of the two technologies most effectively. Technical experts and practitioners may also find it valuable as a resource when considering the type of information and policy stakeholders to engage with on technological development.

Recommendations: implement nimble policy, focus on data, and incentivise collaboration

Policymakers should **analyse the trajectory of both policy and technology development concurrently in multiple countries**, to foster better understanding and planning of international cooperation and/or competition.

To accommodate the fast pace of technology advances and the uncertainty with international relationships, **policy must be anticipatory, participatory, and nimble and follow a policy lifecycle**, oscillating between policy approaches, to mirror technology maturity levels.

State governments and scientific communities should **incentivise international collaboration and coordination** by publicising potential national/international stakeholders; leveraging existing international brokers, which have a history of independently setting policy where there previously has been none; and encouraging the technical community to communicate more frequently to non-technical audiences.

Governments and international brokers should **develop and use international standards to foster international agreements**.

National policymakers should **create frameworks and opportunities to support more public education and deliberative dialogue**.

Governments should **develop centralised workforce development plans** that target the interface of ML and GE and all levels of education.

Governments and national policymakers should **adopt both upstream (prior to the application of the technology) and downstream (pertaining to applications) regulation**.

Policymakers should focus on **regulating the accessibility and distribution of underlying data**.

Governments should **establish a knowledge bank about biosecurity measures, technology standards and frameworks**.

Motivation: integrated technologies require proactive management to leverage benefits and mitigate risks

The integration of artificial intelligence (AI) and biotechnology, while in its infancy, presents significant opportunities and risks, and proactive policy is needed to manage these emerging technologies. While AI continues to have significant and broad impact, its relevance and complexity magnify when integrated with other emerging technologies. The confluence of AI with GE in particular can foster substantial benefits as well as daunting risks that range from lack of ethical considerations to national security. These complex technologies have implications for multiple sectors, ranging from agriculture and medicine to economic competition and national security. And this complexity expands with the number of organisations, government departments and countries involved in collaboration and/or competition.

Application of ML (as one aspect of AI) to GE and its underpinning bioinformatics platforms will catapult the revolutionary potential of GE from 'hypothetical' to imminent. This poses specific risks like potential weaponisation and bioterrorism and opportunities like improved health and wellbeing. Given the pace of technology advancement and convergence, there is an impetus to track and assess advanced technologies while increasing the focus on policy development and societal debate. This combined field has not yet been adequately studied from a policy perspective.

It is critical for policymakers to take stock of advancements and assess where the combined technology could progress. Furthermore, the public requires improved understanding of the state of the art of ML and GE capabilities to comprehend societal implications and to contribute to policy discussions. However, the policy frameworks and parameters that exist today may no longer be fit for purpose.

Approach: literature review and historical analysis to inform a table-top game

Our study entailed a landscape analysis which led to a futures assessment to identify prevalent risks and opportunities. We explored the current state of ML and GE technologies and policies, used historical analysis to project potential future risks and opportunities, and surfaced risks and opportunities of technology alongside potential policy interventions with a future focussed table-top exercise.

The **landscape assessment** consisted of software-assisted horizon scanning to summarise the state of the art of ML and GE capabilities as well as the integrated applications of these capabilities. We categorised these capabilities and applications based on their technology readiness levels (TRLs), their potential impact and the current barriers to further progress. We complemented this analysis with a desk-based review of the key policies that predate and/or follow GE and ML advancement, to assess their interplay and connectedness. We supplemented this assessment with interviews of subject matter experts on risks and opportunities. This analysis resulted in timelines of primary policy and technical developments across the United States, the United Kingdom, China and the European Union. These timelines were in turn used to extract past trends, extrapolate potential future trends, and compare policies and technologies between regions.

The **futures assessment** built on outputs from the landscape assessment and provided a deeper analysis of international relationships and more extensive policy actions. This led to the identification of primary drivers of change with regards to the convergence of these technologies, based on proposed future scenarios looking towards 2045. The scenarios were used in a discursive seminar game to develop potential policy actions to minimise harm and maximise opportunities across the United States, the United Kingdom, China and the European Union.

Results: significant advances with a need to manage the convergence of technologies and assimilate cultures

ML is accelerating advances in biology, primarily by enabling faster processes with efficiencies.

The integration of GE and ML has substantial **practical implications, but much of the underlying technology still requires development**.

One of the **most significant risks with these technologies is their dual-use nature** – the capability for improving lives while simultaneously being used to create bioweapons, deadly compounds, malware and misinformation.

Technology is advancing faster than associated policies, with little to no policy development at the intersection of ML and GE.

Technology and policy developments are often interconnected across the global stage, highlighting the need for international policies and for supranational organisations.

There are significant **differences in the progress of technology and policy development for AI and GE**. The domino effect of national AI plans across the international stage highlights the reactionary nature of recent policy actions regarding AI, which are underpinned by geopolitics rather than technological progress. Alternatively, GE involves constant iteration of technology and policy development adopting the precautionary approach. Furthermore, while key GE milestones in policy spread out over time and focused on regulation, AI and ML landmark policies are concentrated in a few clusters with past policies focused on innovation and current topical activity focused on regulation.

ML and GE are set to revolutionise multiple sectors, but **public engagement and perception are crucial** to consider in future policymaking.

International brokers can help fill a vacuum of agile and responsive policymakers.

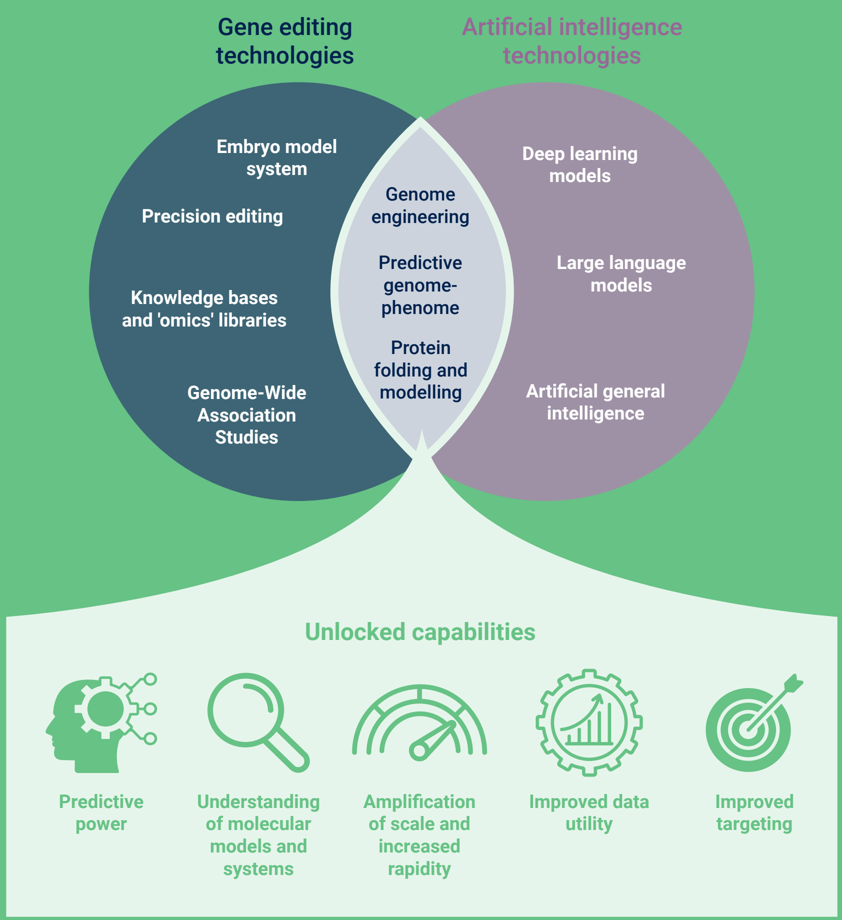
The culture gap between the ML and GE communities must be bridged to enact policies that address both communities and their concerns.

Education and engagement of both the public and policymakers are crucial to policymaking but must be undertaken with a focus on the applications rather than on debating the technical aspects.

Managing access to data could be central to effective policy development but related political and ethical issues must be addressed.

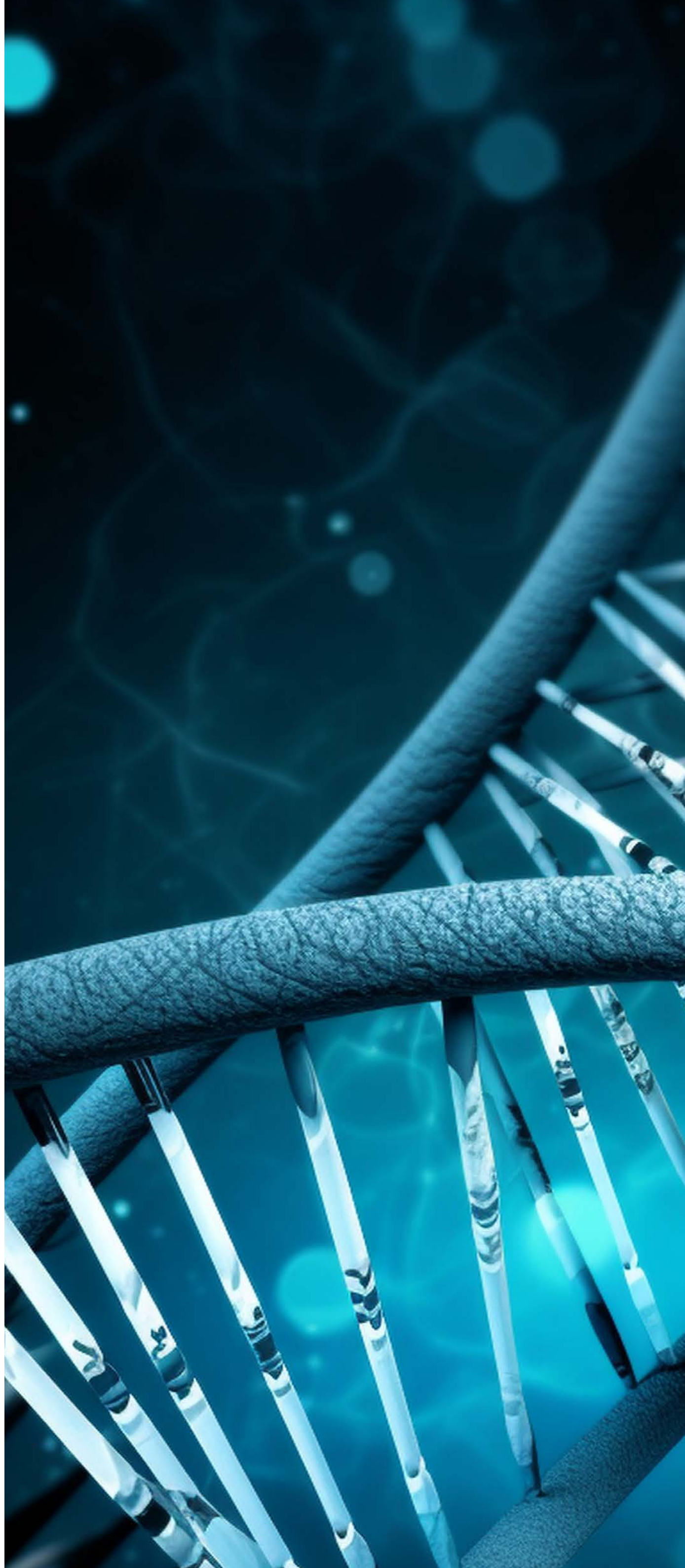
An **approach to policymaking is needed that is both reactive to unanticipated changes, and proactive with respect to anticipated risks and benefits**.

Figure ES1. Intersection of technology and unlocked capabilities



Source: RAND analysis 2023

Table of contents



Figures

Tables

Abbreviations

AI	Artificial intelligence
ChatGPT	Chat Generative Pre-trained Transformer
CRISPR	Clustered regularly interspaced short palindromic repeats
DARPA	The US Defence Advanced Research Projects Agency
DDBJ	DNA Data Bank of Japan
DNA	Deoxyribonucleic acid
ENA	European Nucleotide Archive
EPA	The US Environmental Protection Agency
ESMFold	Evolutionary Scale Modeling
EU	European Union
FDA	The US Food and Drug Administration
GE	Genome editing or gene editing
GM	Genetically modified
GMO	Genetically modified organism
GPT	Generative Pre-trained Transformer
GPU	Graphics processing unit
HFEA	The UK Human Fertilisation and Embryology Agency
HIPAA	US Health Insurance Portability and Accountability Act of 1996
INSDC	International Nucleotide Sequence Database Collaboration
IP	Intellectual property
ISSCR	International Society for Stem Cell Research
ML	Machine learning
NLP	Natural language processing
OECD	Organisation for Economic Co-operation and Development
RNA	Ribonucleic acid
TRL	Technology readiness level
UK	United Kingdom
UN	United Nations
UNESCO	United Nations Educational, Scientific and Cultural Organization
UNIDIR	United Nations Institute for Disarmament Research
US	United States
USDA	United States Department of Agriculture
WHO	World Health Organization
WWII	World War II

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Chapter 1

Introduction

1.1. Rationale for the study

Recent headlines outline the enormous leaps made in technology, especially in the field of artificial intelligence (AI), engineering biology and, more broadly, gene editing (GE). The developments are being met with both excitement and concern for the future because of the opportunities these technologies can unlock. For instance, the demonstrable use of Chat Generative Pre-trained Transformer (ChatGPT) in writing grant proposals,[1] to passing the law qualification exam[2] and generating biological weapons[3] poses challenges as well as opportunities for society. Developments in GE are also presenting similar challenges and opportunities with the innovative uses of gene modification tools like clustered regularly interspaced short palindromic repeats (CRISPR),[4] the development of a model embryo system in a lab without the use of human sperm or egg,[5] and the catalysation of the field of engineering biology.[6]

1 Najafali et al. (2023).
2 Koetsier (2023).
3 Urbina et al. (2022).
4 CRISPR/Cas9 edits genes by precisely cutting DNA and then letting natural DNA repair processes to take over. The system consists of two parts: the Cas9 enzyme and a guide RNA. As of 15 September 2023: https://crisprtx.com/gene-editing/crispr-cas9
5 Weatherbee et al. (2023).
6 Voigt et al. (2020).

While the advancement of technology in GE and AI has been revolutionary for society, it is the convergence of these technologies, and more specifically application of machine learning (ML) to GE, where opportunities for innovation and societal progress are further enabled, and challenges further compounded. Many political and academic actors are now becoming more aware of the yet untapped potential and risk of this convergence, demonstrated through opinion pieces highlighting ‘biology as the new frontier for large language models’[7] and the ‘new dawn for humanity’.[8] Given the pace of technology advancement and convergence[9] there is an impetus to track and assess advanced technologies while increasing the focus on policy development and societal debate. Yet this combined sector has not been adequately studied from a policy perspective.

It is noteworthy that these are complex technologies that have implications for multiple sectors ranging from agriculture and medicine to economic competition and national security.[10] [11] This complexity is further compounded by the number of organisations, government departments and countries involved in collaboration and competition.

As these technologies continue to mature and accelerate, it is critical for policymakers to take stock of advancement and assess where the combined technology could be headed over the next few decades. Practitioners as well as the general public require a better understanding of the state-of-the-art technologies to understand societal implication and to contribute to policy developments. The policy frameworks and parameters that exist today may no longer be fit for purpose, as we are currently witnessing in the case of large language models, which have enabled outfits like GPT-3 and GPT-4 to be used in detrimental ways with a negative impact on technology acceptance.[12] [13] This illustrates the importance of being future focused in technology policy development with an anticipatory lens on potential value and trade-offs of technology.

> 'In this small-scale pilot study, we have considered the history of technology and policy advancement in the United States (US), the United Kingdom (UK), China and the European Union (EU) to learn from and deliberate over the future of technology convergence (ML and GE) and its policy implications.'

7 Toews (2023).
8 Naughton (2023).
9 Marr (2018).
10 Harding & Ghoorhoo (2023).
11 Häyry & Lehto (2023).
12 McCallum (2023).
13 Herman (2023).

This study is intended to increase awareness of the scientific progress that has occurred to date and explore the opportunities, risks and policy gaps associated with the convergence of ML and GE technologies as it becomes accessible and part of everyday life. The intended audience for this analysis includes supranational organisations like the World Health Organization (WHO), the International Society for Stem Cell Research (ISSCR) and the United Nations (UN), as well as national policymakers in the United States and Europe. The report is intended to enable them to take stock of advances in the technologies, and use a future-focused framework to take a proactive and anticipatory approach to develop proportionate policies that can support progress, while predicting risks and proposing mitigation strategies.

1.2. Scope and definitions

This pilot study is intended to provide a foundation for additional analysis. The scope of this study is limited to GE and ML in geographies with large-scale investment in these technologies, with political and institutional agendas that are relevant to both, so the United States, the United Kingdom, China and the European Union are the regions of focus of this proof-of-concept study. Moreover, we have focused our efforts on discussing landmark and representative technology and policy developments in these sectors. We do not cover these in depth or exhaustively and such an analysis could be the subject of a follow-on study conducted at scale.

Box 1, overleaf, lists the most prevalent definitions of concepts that reflect the scope for this analysis.

Box 1. Key terms and definitions

Artificial intelligence

A branch of computer science dealing with the simulation of intelligent behaviour.[14] The capability of a machine to imitate intelligent human behaviour.

Bioeconomy

Based on products, services and processes derived from biological resources.[15]

Biotechnology

The manipulation (as through genetic engineering) of living organisms or their components to produce useful usually commercial products (such as pest resistant crops, new bacterial strains or novel pharmaceuticals).[16] Technology based on biology.[17]

Gene editing

Alteration of the genetic material of a living organism by inserting, replacing or deleting a deoxyribonucleic acid (DNA) sequence, typically with the aim of improving some characteristic of a crop or farm animal, or correcting a genetic disorder.[18] Intended as a catch all term including advancements in **engineering biology**, for the purpose of this study

Machine learning

A branch of artificial intelligence focussed on analysing and learning from data.[19]

Synthetic biology

Field of scientific research that applies engineering principles to living organisms and living systems.[20] Field of science that involves redesigning organisms for useful purposes by engineering them to have new abilities.[21]

Source: RAND 2023

14 Marr (2018).
15 Gallo (2022).
16 Merriam-Webster (2023).
17 Biotechnology Innovation Organization (2023).
18 Oxford English Dictionary (2023).
19 Center for a New American Security (2017).
20 Hanczyc (2020).
21 National Human Genome Research Institute (2023a).

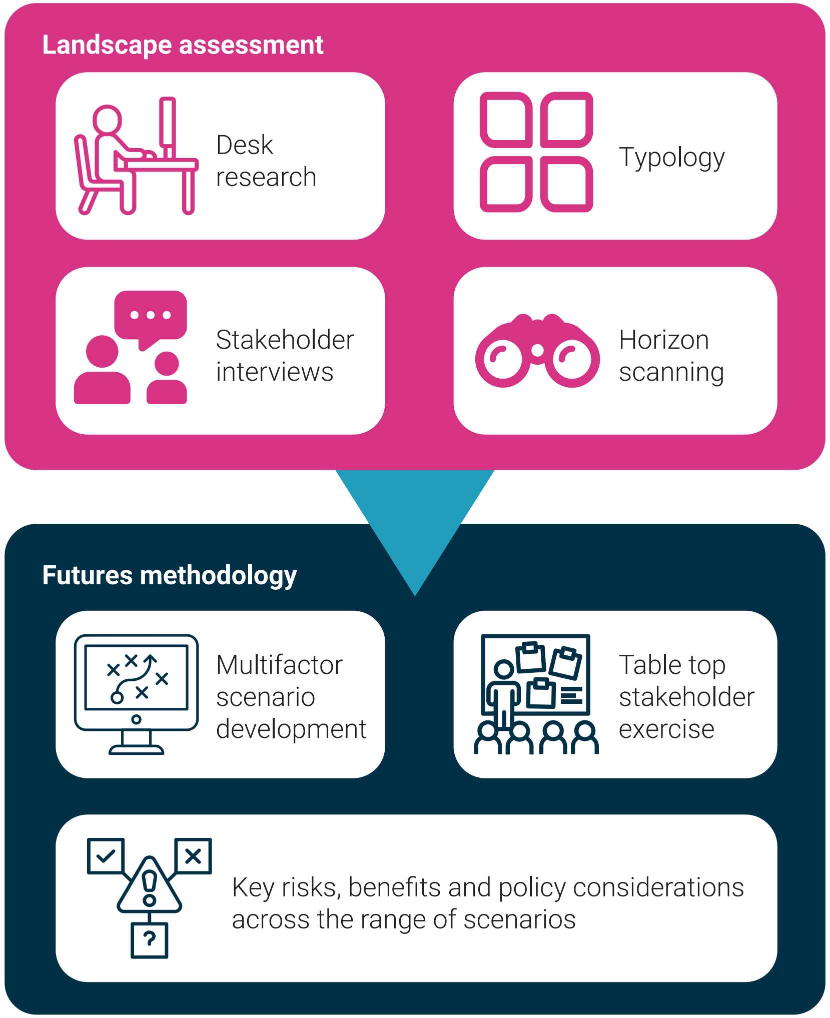
1.3. Study approach

The overarching approach of the study consisted of a landscape assessment which underpinned the futures assessment as illustrated in Figure 1, below. The landscape assessment consisted of desk research to seek past technology and policy trends in AI and GE, and a horizon scan which identified the current state-of-the-art developments in each technology domain as well as at their intersection. This assessment was supplemented by interviews with subject matter experts and synthesised to develop policy and technology timelines, which illustrate policy and technology interconnectedness and the geographic interplay across this technology ecosystem.

The historic technology progress was grouped into loosely defined 'eras of progress' and state-of-the-art technologies were assessed by using technology readiness levels (TRLs) as indicators for maturity, and were mapped with their applications, and potential impact and barriers. The policies were parsed using a policy style framework. By policy styles, we do not refer to the substance of these policies (fiscal, regulatory, industrial etc.) but rather the manner in which they were brought about in relation to the technology (reactively, pre-emptively etc.). To aid in this assessment we developed a categorisation framework, retrospectively, based on prevalent trends observed in the literature. These styles are pre-emptive, proactive, reactionary and legacy, and are described in Table 1, overleaf. The policy styles are not mutually exclusive, and a single region or country does not necessarily use just one style. In many cases, these styles overlap, are context dependent, and can be used for regulating separate components of GE or ML or their application.

Each technology sector (ML and GE) was characterised and discussed alongside its interconnected policy landscape to understand the distinct cultures and policy stances prevalent in these sectors before delving into a discussion on their convergence. A detailed methodology for the landscape analysis can be found in Annex A.

Figure 1. Landscape and futures assessment



Source: RAND 2023

Table 1. Policy classification framework

Style	Description	Key assumptions or outcomes
Pre-emptive	Policy approach that provides highly restrictive or prohibitive regulations that seek to prevent perceived potential impacts even if those impacts have yet to be realised.	Innovations in GE or ML may be harmful to human health and the environment.
Proactive	Provides specific regulations regarding GE or ML by considering not just their potential negative impacts, but positive impacts as well.	Results in constant discourse between policymakers and scientists and leads to iterative cycles of policies and their implementation.
Reactionary	Formulates regulation and policies as a response to incidents in GE or ML innovation that have caused controversy.	Results in short-term bans that in the long term could slow down innovation and technological progress.
Legacy	Relies on *a priori* existing regulations or guidelines from other domains and apply them to GE or ML technologies.	Existing regulations might be sufficient to apply for a new setting or technological advancement.

Source: RAND analysis 2023

The landscape assessment informed the development of three future scenarios in 2045 which were used to conduct a table-top game. The table-top game involved key subject matter experts and policymakers, who assumed the roles of US, Chinese, EU and UK decision makers, and developed policy actions to minimise harm and maximise opportunities across all three future scenarios. The policy actions were assessed through the lens of geopolitical cooperation and competition, identifying reactive dynamism in policymaking at the intersection of technologies. A detailed outline of the futures methodology can be found in Annex C on futures methodology.

Collectively, these methodologies and their outputs have informed the formulation of high-level recommendations for national and supranational policymakers to catalyse further research and societal deliberation at the convergence of ML and GE and other converging technology sectors.

1.4. Outline of the report

This report is split into three parts. Part 1 discusses the results of the landscape assessment; Part 2 discusses the outputs of the futures assessment; and Part 3 synthesises the key primary themes and recommendations. In Part 1, chapters 2 and 3 discuss the developments in GE technology and trace its interconnected policy landscape. In a comparable fashion, chapters 4 and 5 address ML. Chapter 6 discusses practical implications and applications stemming from the application of ML to GE. In Part 2, Chapter 7 discusses the outputs of the futures assessment. Finally, in Part 3, Chapter 8 summarises novel contributions, discusses pervasive themes, and summarises high-level findings and recommendations.

Part 1. Landscape assessment: **Race between technology and policy developments**

This section highlights the technology landscape that has emerged in GE, ML and at their intersection. The focus is on key landmark advances in these sectors analysed against landmark regulations and policies brought in over time. The section concludes with the comparative assessment of policymaking styles across GE, ML and their combined use; and proposing risks, benefits and policy implications that should be considered in future.

Chapter 2.

State of the art and history of gene editing

Key findings

The state of the art of GE involves a wide variety of effort and potential applications. Especially with respect to public perception, GE may be much more relevant and significant than the non-practitioner or policymaker may realise.

GE developments and discoveries have progressed substantially over the decades with milestones such as sequencing of the entire human genome, cloning of the first mammal, cloning Dolly the sheep, and discovery of CRISPR-based GE methods.

These developments underpinned an era of therapeutics and agriculture applications to treat cancers and inherited diseases, and development of pest and climate adaptive crops.

The current focus of GE technology continues to be on therapeutic applications with growing applications in energy, climate change and agriculture. These applications continue to leverage and improve on CRISPR-based editing mechanisms.

Many barriers to advancement exist, including lack of diversity in genome data, which can often perpetuate or exacerbate inequities and bias, false positives in disease and genome association studies, and unintended mutations.

This chapter highlights latest technological advancements in GE with historic progress categorised into loosely defined eras based on the focus of the technology at a given point in time. This history provides a foundation for the state-of-the-art, cross-border analysis, and exploration of potential future developments. Figure 2, below, illustrates the key technology eras across the United States, the United Kingdom, China and the European Union. We also note that historic developments charted as well as state-of-the-art technologies presented here are not exhaustive and focus on prevalent technologies and/or significant milestone technologies.

2.1. State of the art: GE today

There have been significant improvements to GE capabilities in recent years. These include improved and more accurate sequencing, greater precision in editing, and an increased understanding of gene association and expression in relation to physical traits and ailments. The sections below summarise some of the main capabilities that have been advanced with examples provided for each. Note that these are exemplars, rather than comprehensive details of all the latest advancements in the field, demonstrating the diverse impact that GE technology can have.

Precision GE

Since CRISPR technology was first used, scientists have worked to improve its capability. Novel approaches using CRISPR have expanded the GE toolbox, enabling the development of potentially curative therapies for diseases with complex drivers.[22]

CRISPR has enabled precision in GE. One example is the development of a genome editing tool called PASTE.[23] PASTE builds on CRISPR by combining the precise targeting of CRISPR-Cas9 with enzymes called integrases.[24] In doing so, PASTE expands the capabilities of genome editing by allowing the insertion of large pieces of DNA without double-stranded DNA breaks which can lead to random mutations.[25] This modified CRISPR technique has been used to modify normal human body cells, which can then target specific cancer cells in the body, opening up a huge advancement in hard-to-treat diseases.[26]

CRISPR has also been coupled with something called 'transposon-based editing' to insert large gene segments in patient cells, which is game changing given that this has not been possible at this scale before.[27] CRISPR-mediated disruption of long non-coding ribonucleic acids (RNAs) is being studied in a lab setting in cancer to reduce cell growth and overcome metastasis.[28]

22 Chavez et al. (2022).
23 Programmable addition via site-specific targeting elements (PASTE)
24 Yarnall et al. (2022).
25 LeMieux (2022); Yarnall et al. (2022).
26 LeMieux (2022).
27 SynBioBeta (2019).
28 Chavez et al. (2022).

Another CRISPR modification and application includes CRISPR-Clear, which can detect organisms that have been modified with a gene drive. The technique uses a battery powered device with naked-eye visualisation of the results, opening the innovation to non-specialists.[29] This has implications for use in surveillance and security settings.[30] Other notable advances using CRISPR tools include base editing and prime editing.[31]

Knowledge bases and libraries

As technical developments have progressed, there are ongoing efforts to curate and disseminate databases containing DNA and RNA sequences. Sequence databases include GenBank, European Nucleotide Archive (ENA), DNA Data Bank of Japan (DDBJ) and China National GeneBank. Daily data exchange occurs between GenBank, the ENA and the DDBJ as part of the International Nucleotide Sequence Database Collaboration (INSDC), an international initiative established to consolidate nucleotide sequences.[32] A description of what these databases encompass is listed in Table 2, opposite.

Table 2. Examples of sequence databases

Name	Description	Part of the INSDC?
China National GeneBank	A unified platform built for biological big data sharing and application services to the research community; based on the big data and cloud computing technologies, it provides data services such as archive, analysis, knowledge search, management authorisation and visualisation[33]	No
DDBJ	The DDBJ Center collects nucleotide sequence data as a member of INSDC and provides freely available nucleotide sequence data and supercomputer system, to support research activities in life science[34]	Yes
ENA	A comprehensive record of the world's nucleotide sequencing information, covering raw sequencing data, sequence assembly information and functional annotation[35]	Yes
GenBank	A comprehensive, public database that contains 19.6 trillion base pairs from over 2.9 billion nucleotide sequences for 504,000 formally described species[36]	Yes

Source: RAND analysis 2023

29 Nieuwenweg et al. (2019).
30 Nieuwenweg et al. (2019).
31 Kantor et al. (2020).
32 International Nucleotide Sequence Database Collaboration (2023).
33 China National GeneBank DataBase (2023).
34 DDBJ Center (2023).
35 EMBL European Bioinformatics Institute (2023).
36 Sayers et al. (2023).

Another such database is UniProt, which seeks to provide the scientific community with a comprehensive, high quality and freely accessible resource of protein sequence and functional information.[37] The volume of genetic sequence information in such databases has grown by a factor of 100 in the last 20 years, as sequencing technology has evolved.[38] These have generated some datasets that are classified as 'big data' and also generated datasets for open and wider consumption for academics and commercial organisations. This type of data is central to the use of AI in biotechnology.

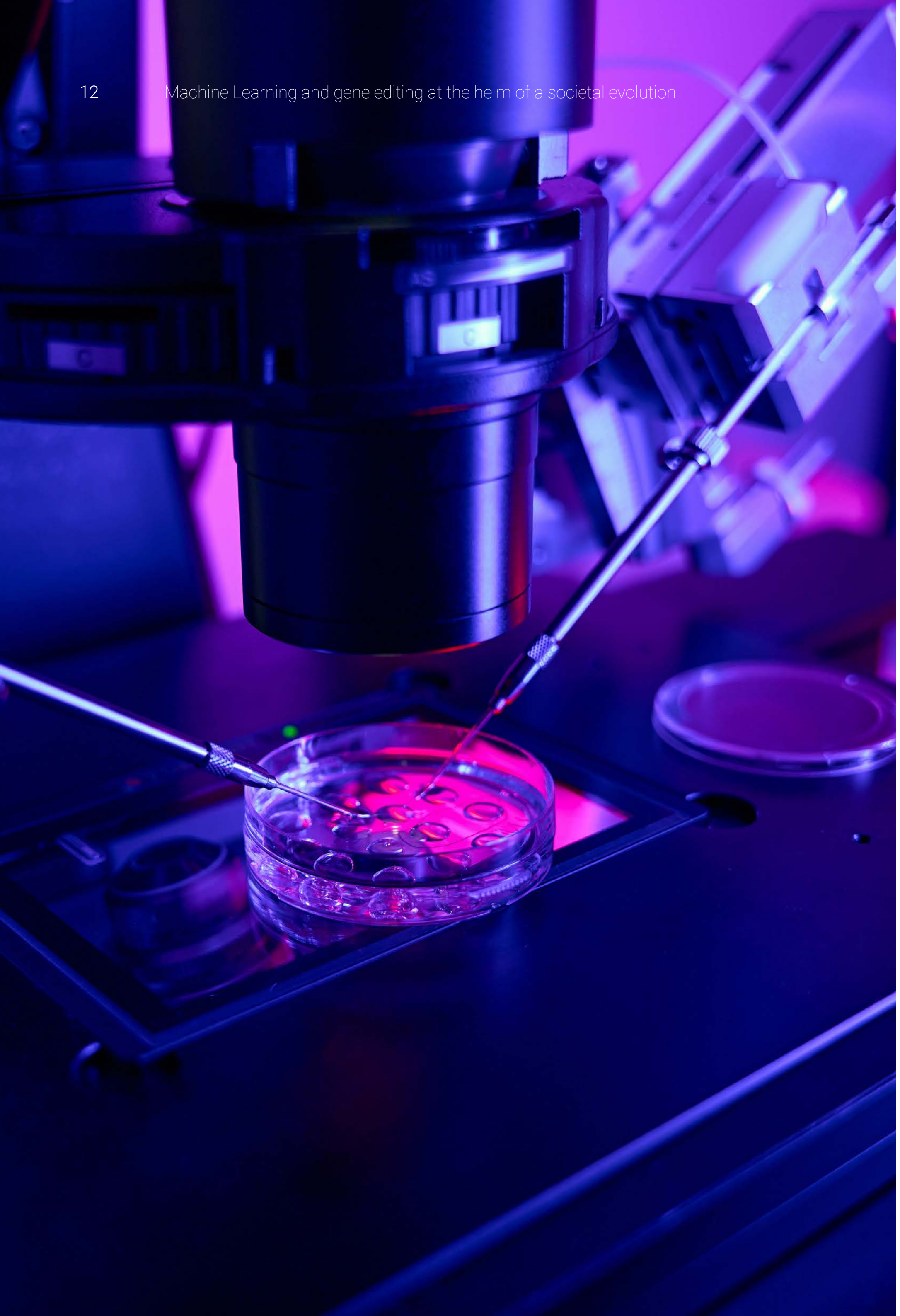
Genome-wide association studies

Another key area of development following the Human Genome Project and other genome sequencing efforts has been the drive to study associations between segments of the genome and how they play out into other attributes. This includes, for instance, genetic variants linked to height,[39] cardiovascular disease[40] and even musical beat synchronisation.[41] Genome-wide association studies have been enabled by several key developments – notably the completion of the Human Genome Project in 2003 and the International HapMap Project in 2005, which provided researchers with the tools to find genetic contributions to common diseases.[42]

Challenges and barriers in state-of-the-art GE

Despite the advances highlighted above, there are many barriers that exist for further advancement of GE. For instance, CRISPR-based editing comes with challenges of off-targets effects, whereby unintended changes may spontaneously occur in the genome being edited, causing unanticipated adverse effects.[43] Challenges of false positives, lack of diverse datasets, replication of association findings, population stratification and sample size have prevented progress in many clinical areas of genome-wide studies.[44] The development of databases also comes with challenges. For instance, the INSDC databases have been accused of lacking global accountability and transparency, as they have been operated by a small number of high-income countries.[45]

37 EMBL European Bioinformatics Institute (2023).
38 Kuiken (2023).
39 Broad Institute (2022).
40 Walsh et al. (2023, 2039–2055).
41 Niarchouet et al. (2022).
42 National Human Genome Research Institute (2019).
43 Guo et al. (2023).
44 Peter & Seddon (2010).
45 Johnson et al. (2022).



2.2. Technology history: the developmental eras of GE

We briefly highlight five key technology eras of GE which have contributed to the current state of technology in the field. The main purpose of this charting of development is to discuss it further below in the context of policy and the interconnectedness of how policies can heavily impact technological progress in a field, and vice versa. This has implications for how the policy landscape could impact the convergence of ML and GE. Figure 2 below illustrates the key eras of progress, not including the state of the art discussed above.

Turning point for GE

The 1980s was a turning point for GE technologies where we saw developments such as DNA microinjections[46] for creating genetically modified (GM) animals and synthetic insulin.[47] The discovery of zinc finger nucleases[48] in the United Kingdom is most noteworthy for our study as it became one of the most predominantly used techniques to alter genes.

46 Shen et al. (1982, 1145–54).
47 Vecchio et al. (2018).
48 Klug (2010, 1–21).

Decoding the genome

In the 1990s the Human Genome Project, spearheaded by the United States, began with the ambition to sequence and decode the entire human genome.[49] This period also included discoveries in the European Union studying GE mechanisms like zinc finger fusion machinery that could potentially edit genes.[50] [51]

The dawn of therapeutic applications

This decade saw the first gene-targeted therapy (treatment in which cells from an individual are modified and then inserted back into their body); Glivec was approved to treat chronic myelogenous leukaemia in the United States and the European Union,[52] which paved the way for other breakthroughs in therapies for cancer, such as melanoma.[53] GE technology was also used to develop vaccines for the first time.[54]

The seminal step of cloning Dolly the sheep in the United Kingdom ushered in new possibilities around cloning, as she was the first mammal to be cloned from adult cells that were reprogrammed.[55] On the agricultural front, the first ever GM crop for pest control, 'bt corn', was widely adopted in the United States and became a staple commodity.[56]

49 National Human Genome Research Institute (2023b).
50 van Soolingen et al. (1993, 1987–1995).
51 Jansen et al. (2002, 1565–75).
52 Capdeville et al. (2002, 493–502).
53 Daley (2020).
54 Lages et al. (2022, 9957).
55 Dolly 20 Years (2023).
56 Watters (2018).

The CRISPR revolution

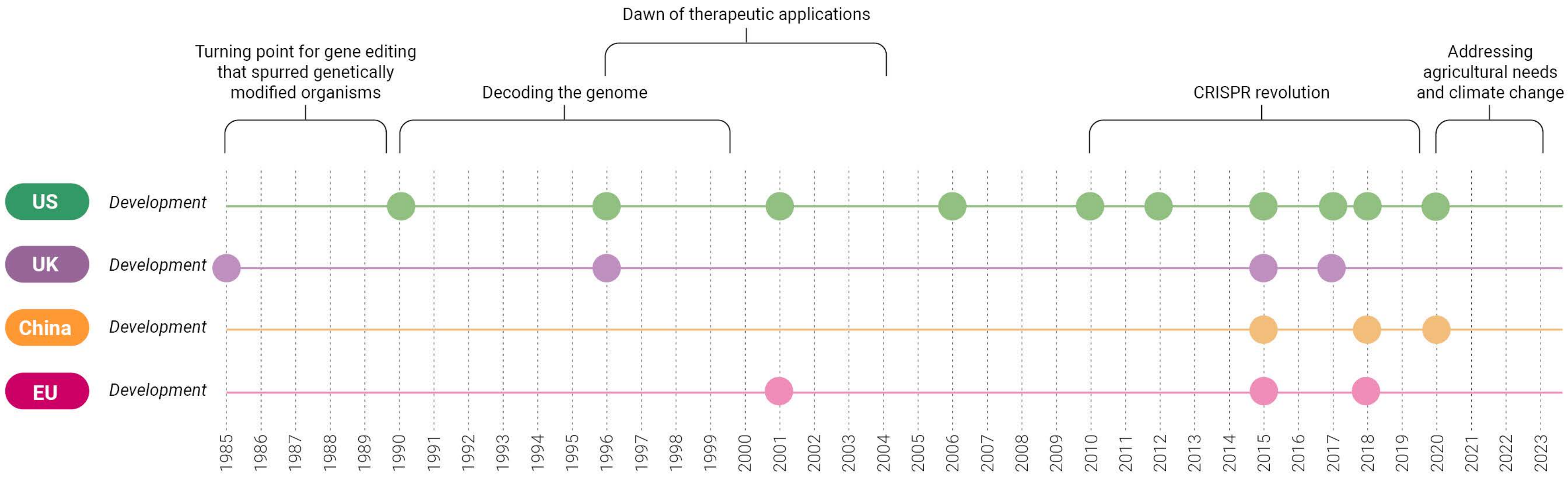
As GE techniques further advanced into the 2010s, American and French scientists discovered the GE use cases of CRISPR-Cas9 system, which led them to winning the 2020 Nobel Prize.[57] The discovery of CRISPR catalysed large amounts of GE and modification practices in agriculture and animal husbandry in the United States, China and the European Union. Examples include modifying various types of livestock to grow more muscle for meat[58] or to increase disease resistance,[59] [60] weather and blight resistant and higher yielding crops,[61] [62] and healthier produce.[63] [64] CRISPR has also led to a rise in the use of gene drives, a technique that selectively propagates genes through a given population. Gene drives, particularly in the United States and the European Union, are often used to control pests in the interest of public health, such as malaria-resistant[65] or dengue-resistant[66] mosquitos. The 2010s faced a controversial turning point in 2018 when a Chinese scientist brought GM embryos to term and was confronted with a global outcry.[67]

Addressing agricultural needs and climate change

In more recent years (2020 onward) this trajectory of innovations revolving around agriculture and animal husbandry has continued. For instance, researchers have made significant headway developing crops that can withstand the various challenges brought on by climate change, such as warmer weather, more saline water sources,[68] and more exposure to pests. China in particular has increased its innovations in agriculture with the aim of securing a resilient food supply.[69]

57 United Nations Educational, Scientific and Cultural Organization (2023).
58 Khalil et al. (2017).
59 Pullman (2016).
60 Le Page (2020).
61 Shan et al. (2013, 686–88).
62 Van Eijck (2023).
63 Demorest et al. (2016, 1–8).
64 Waltz (2018, 6–7).
65 Gantz et al. (2015, E6736–43).
66 Scudellari (2019, 160–62).
67 Cyranoski & Ledford (2018, 607–8).
68 European Commission (2002).
69 Oliva et al. (2019, 1344–50).

Figure 2. GE technology development timeline



United States

1990	*Human Genome Project begins*
1996	*First genetically modified crop, corn, adopted in the US*
2001	*First gene targeted therapy is developed (for chronic myelogenous leukaemia)*
2006	*Human papillomavirus vaccine Gardasil is developed using GE breakthrough*
2010	*Creation of first synthetic life form*
2010	*The GE function of transcription activator-like nucleases first discovered*
2012	*Cas9 engineered to find and cut DNA target specified by guide RNA (2020 Nobel Prize winner)*
2015	*Gene drives for malaria resistant mosquitos is developed*
2017	*First time a US-based group edited human embryos*
2018	*CRISPR gene drives tested in mammals for first time*
2020	*Stem cell therapy for diabetes*

United Kingdom

1985	*Zinc finger nucleases are discovered for targeted genetic engineering*
1996	*Dolly the sheep is successfully cloned*
2015	*Gene therapy clinical trials completed for various types of cancer, e.g., head and neck, liver, ovarian, prostate, breast, colorectal, cervical, melanoma and non-Hodgkin's lymphoma*
2015	*Chimeric antigen receptor T-cell therapy clinical trials (using patients' own immune cells to treat their cancer) completed for various types of cancer including leukaemia, head and neck cancer and melanoma*
2017	*Mitochondrial replacement therapy becomes possible*

China

2015	*At least 11 clinical trials testing CRISPR gene therapies for cancer treatment (e.g., oesophageal); Anhui Kedgene Biotechnology start-up involved in most trials*
2015	*CRISPR on germline editing in human embryos*
2018	*Global outcry when scientist carries GM human embryos to term*
2020	*Herbicide-resistant soy is developed*

European Union

2001	*CRISPR coined to describe clustered regularly interspaced short palindromic repeats*
2015	*Gene drives to lessen spread of malaria via mosquitos is developed*
2015	*First stem cell therapy developed in Europe to treat eye burns*
2018	*GM pigs used as human models*

Source: RAND analysis 2023

Chapter 3.
Trends in gene editing policies

Key findings

Technology and policy developments are often interconnected across the global stage, highlighting the need for international policies and for supranational organisations like the UN and WHO to spearhead collaboration and cooperation at the convergence of technologies.

The United States, the United Kingdom, China and the European Union have adopted a primarily pre-emptive style of policymaking with highly regulated or prohibitive legislations over GE. Nonetheless, policy for GE has followed a variety of strategies, reflecting a somewhat ad hoc approach to policymaking. The United States, the United Kingdom, China and the European Union have varying levels of permissiveness and risk aversion when regulating GE technologies, which can make collaboration challenging.

The US provides a stark contrast in the agricultural space, with its relaxed approach to GM crops, and China provides a contrast with its slightly less prohibitive measures in the human health domain.

In the earlier decades of GE progress, policies have tended to predate technology development, with a reliance on legacy frameworks, thus giving rise to reactionary regimes as the policy becomes out of date against the pace of technology development. As a result reactionary practices are emerging in response to novel developments such as embryo model systems which challenge the traditional doctrine of biology. A more proactive approach to policymaking is only found at the supra/international level, where a primary focus has been on ethics and the public good.

International brokers can help fill a vacuum of agile ad responsive policymakers. They can discuss the complexities of emerging GE technologies and the longer term ethical and humanitarian implications of such innovations because they are not national level policymakers who may have shorter term agendas with accountability to their constituents.

This chapter presents milestone policies in the United States, the United Kingdom, China and the European Union in relation to technology progress and categorises the styles of policymaking based on the framework presented in Table 1. As mentioned previously, it is worth noting that we use policy as a catch all term including regulation and other types of policies. However, we have focused on just a subset of the most prevalent and relevant policies in GE, which have culminated in a heavy focus on regulation and the maintenance of the precautionary principle[70] in relation to GE.

The timelines in Annex B (Figures of timelines for GE and AI/ML) (figures 13–14) provide additional detail on the multitude of policies and acts that have predated and followed on from the technical progress in GE spanning the 1980s to 2000s.

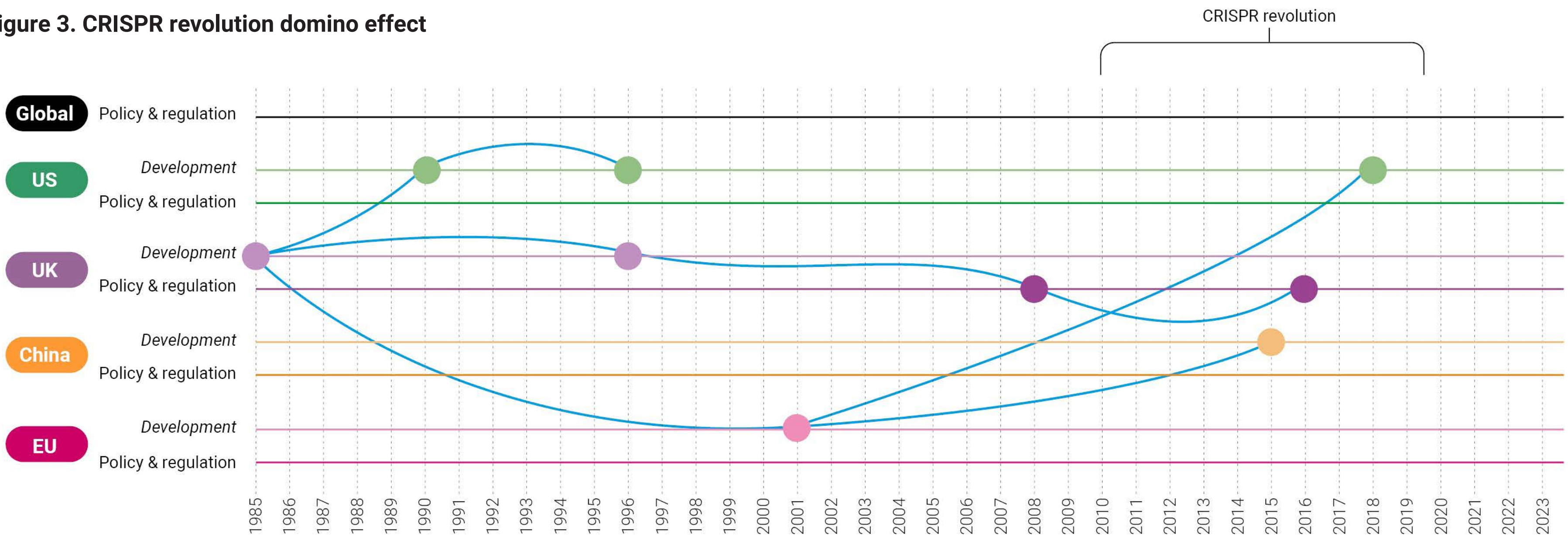
3.1. Policy and technology domino effect

The milestones in GE technology and policy development are interconnected with impact across geographies, highlighting the global chain of events that often follows technology advancements and national policies. While the cause and effect of some of this chain of events is nebulous, some present a clear domino effect across countries.

Hence the need for considering technical and policy developments across borders can be seen in the case of CRISPR development (see Figure 3 below) where the interconnectedness and global nature of technology and policies impact one another. Figure 3 highlights how GE developments in the United Kingdom spurred US counterparts and culminated in the discovery of CRISPR in the European Union in 2001, albeit its potential had not been realised. As a reaction to these technical developments, the United Kingdom passed the Human Fertilisation and Embryology Act,[71] which enabled researchers to obtain a Human Fertilisation and Embryology Agency (HFEA) research licence to edit human embryos, in 2008. Then followed the use of CRISPR in China in 2015 with the United Kingdom approving CRISPR GE technology in 2016. The chain reaction that followed from the initial progress of zinc finger nucleases in the United Kingdom could be seen as the catalyst for the competition-based advancements and the resulting regulations which have spanned multiple geographies. This is just one example that demonstrates how critical it is to consider both technical and policy developments across borders. This in turn illustrates the need for transparency and international cooperation, and for supranational organisations to foster this.

70 Think Tank: European Parliament (2015).
71 Expert Participation (2023).

Figure 3. CRISPR revolution domino effect



United States

1990 *Human Genome Project begins*
1996 *First genetically modified crop, corn, adopted in the US*
2018 *CRISPR gene drives tested in mammals for first time*

United Kingdom

1985 *Zinc finger nucleases are discovered for targeted genetic engineering*
1996 *Dolly the sheep is successfully cloned*
2008 Human Fertilisation and Embryology Act enables researchers to obtain HFEA research licence to edit human embryos
2016 HFEA approves CRISPR GE

China

2015 *At least 11 clinical trials testing CRISPR gene therapies for cancer treatment (e.g., oesophageal); Anhui Kedgene Biotechnology start-up involved in most trials*
2015 *CRISPR on germline editing in human embryos*

European Union

2001 *CRISPR coined to describe clustered regularly interspaced short palindromic repeats*

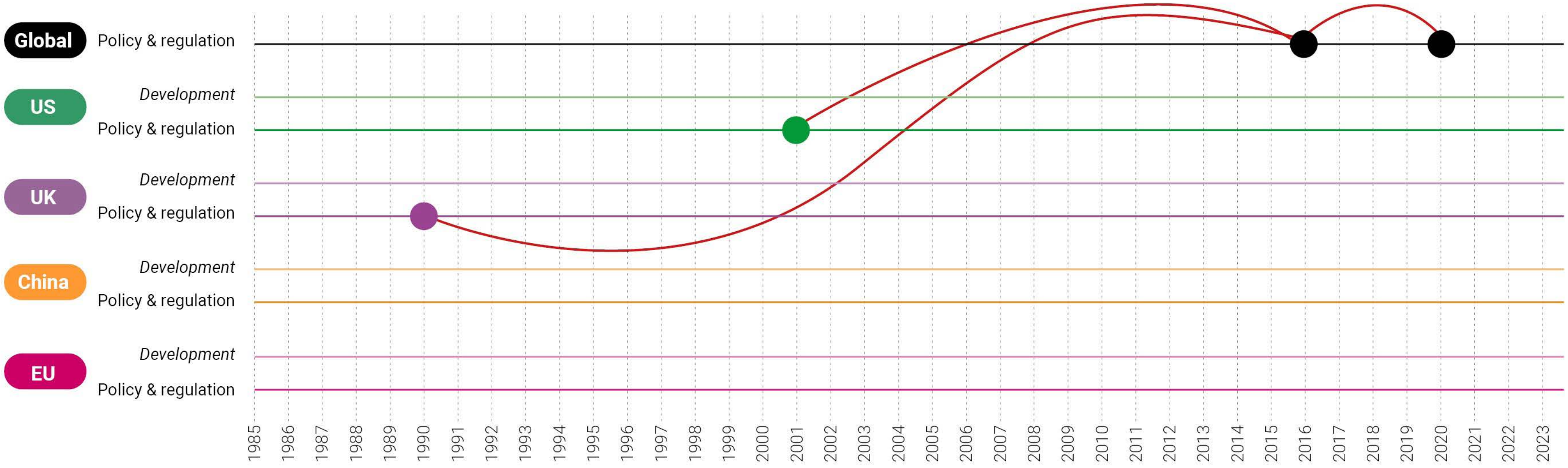
Source: RAND analysis 2023

Another example of interactions across national borders is the way the ISSCR became the standard bearer for ethical guidelines for conducting research using stem cells (see Figure 4 below). Initially, with the pre-emptive policy style taken up by the United Kingdom in 1990 with the HFEA[72] to regulate human germline editing and the United States' 2001 ban on funding for embryonic stem cell research, there was little

72 Expert Participation (2023).

room or incentive for researchers to conduct research using stem cells. This spurred the creation of the ISSCR, a global collective of researchers, and the publication of its 2016 guidelines on ethical stem cell research. Because this document filled the vacuum on guidelines for conducting research in this space, it quickly became the standard for scientists in the United States, the United Kingdom, China and the European Union, with the latest iteration of the guidelines recently updated in 2021.

Figure 4. ISSCR guidelines movement



United States

2001 Federal ban on funding for embryonic stem cell research

United Kingdom

1990 Human Fertilisation and Embryology Act regulates human germline editing

Global

2016 ISSCR publishes guidelines, becomes default standard bearer

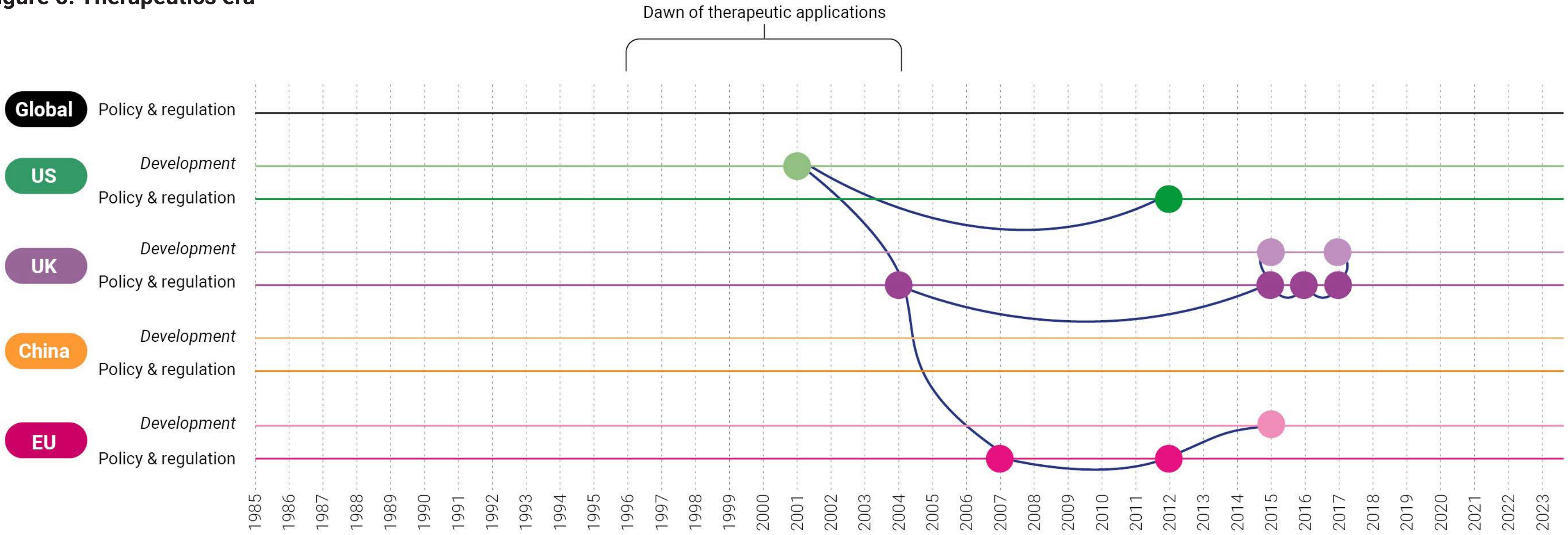
2020 A committee of ten countries concludes technology is not ready for use in human embryos destined for implantation

Source: RAND analysis 2023

The development of therapeutic applications is an important example of reactive policies that enabled innovation and competition (see Figure 5 below) while outlining the dynamics between GE technology development and regulation across the United States, the United Kingdom, China and the European Union. In 2001 the United States developed the first gene-targeted therapy for chronic myelogenous leukaemia,[73] with the United Kingdom in 2004 providing regulatory guidance for gene therapy clinical trials in 2004.[74] The EU Commission responded to these developments by outlining guidance for gene therapies in 2007,[75] which was followed by the US Food and Drug Administration (FDA) streamlining development to breakthrough drugs in 2012.[76] These regulatory regimes paved the way for the European Union to approve its first gene therapy in 2012,[77] followed by the European Union's first stem cell therapy to treat eye burns in 2015.[78] Due to the UK's regulatory approval for gene therapy trials, many of these were completed for various types of cancer by 2015,[79] and thus mitochondrial replacement therapy was made possible by 2017, with the HFEA providing the first licence for such a therapy in the same year.[80]

73 Dana-Faber Cancer Institute (2019).
74 King's Printer of Acts of Parliament (2023b).
75 European Medicines Agency (2023).
76 Maxmen (2017).
77 Gallagher (2012).
78 Knapton (2014).
79 Gilham et al. (2015, 276–285).
80 Sample (2017).

Figure 5. Therapeutics era



United States

2001 *First gene targeted therapy is developed (for chronic myelogenous leukaemia)*
2012 FDA streamlines development of breakthrough drugs, with breakthrough therapy designation

United Kingdom

2004 Medicines for Human Regulations provide guidance for gene therapy clinical trials
2015 Human Fertilisation and Embryology Regulations enable mitochondrial therapy
2015 *Gene therapy clinical trials completed for various types of cancer, e.g., head and neck, liver, ovarian, prostate, breast, colorectal, cervical, melanoma and non-Hodgkin's lymphoma*
2015 *CAR T-cell therapy clinical trials (using patients' own immune cells to treat their cancer) completed for various types of cancer including leukaemia, head and neck cancer and melanoma*
2016 HFEA approves CRISPR GE
2017 HFEA provides first licence for mitochondrial replacement therapy
2017 *Mitochondrial replacement therapy becomes possible*

European Union

2007 Commission outlines guidance for approving gene therapies
2012 A gene therapy is approved for first time
2015 *First stem cell therapy developed in Europe to treat eye burns*

Source: RAND analysis 2023

Finally, reactionary policies can be seen in the case of GE in human embryos when, in 2018, a scientist in China carried GM human embryos to term, which is illegal, and prompted a temporary ban on all human GE in China immediately,[81] but also led to a call for a global framework to police germline (heritable) editing.[82] A 2020 committee of ten countries concluded that the technology was not ready for use in human embryos for germline editing.[83] In 2021, a WHO outline of a governance framework was developed to oversee research on the human genome.[84] This illustrates how one highly controversial study in one geography can prompt regulatory reaction across the globe.

3.2. Varying styles of policymaking in GE

Varying styles of policymaking, primarily focused on the domain of regulation, are observed in GE developments. The strict regulation of genetically edited and modified organisms in the European Union[85] and their ban by many EU countries,[86] as well as the ban of federal funding for embryonic research in the United States,[87] exemplify **pre-emptive styles** of regulating GE. The European Genetically Modified Organism directive, for instance, requires environmental risk assessments, traceability, labelling and post-market environmental monitoring obligations that are onerous and cumbersome.[88] This speaks to the precautionary principle-based approach[89] that underpins almost all GE technologies and applications.

Similarly, in the United States, the regulatory regime around embryonic stem cells assumes that research on stem cells would lead to human embryos being genetically altered, created and destroyed in ways that have ethical implications. This led to the Dickey-Wicker Amendment being passed in 1996, which prevents federal funding to any research involving human embryos, an amendment that keeps being renewed,[90] with further executive bans on federal funding for research in new embryonic stem cells.[91] This creates a barrier to innovation, with alternative sources of funding being relied on.

The quintessential example of **proactive approach** to regulating or providing oversight of GE is the ISSCR's ethical guidelines for using

81 Harney (2018).
82 Lander et al. (2019).
83 Ledford (2020).
84 Health Ethics & Governance (2021).
85 European Parliament, Council of the European Union (2001).
86 European Parliament (2020a).
87 National Institutes of Health (2023).
88 EUR-Lex (2016).
89 EUR-Lex (2023).
90 Subbaraman (2020).
91 The Unified Website for Biotechnology Regulation (2023).

human stem cells in research, which have become default guidelines for scientists across the globe.[92] Section 3.4, below, on the role of international brokers in policymaking provides more detail about the proactive approach of international organisations.

An example of a **reactionary approach** is discussed in Section 3.1 (above) in the context of how one controversial study in China, where CRISPR edited babies were brought to term, elicited global policies to curtail the technology and monitor it more closely.[93]

An example of a **legacy regime** in GE is shown by the US Environmental Protection Agency (EPA); the 1910 Federal Insecticide, Fungicide and Rodenticide Act and the 1976 Toxic Substances Control Act specify that any innovations that involve genetic modification in plants to produce pesticides or that may prove toxic to human health will be under the purview of the EPA.[94] [95] The EPA uses these guidelines now to regulate gene drives, a newer technology, that can function as pest control.

It is evident from our literature review that in the earlier decades of GE progress, policies have tended to predate technology development with a reliance on legacy frameworks focused on the precautionary principle, thus giving rise to reactionary regimes as the policy becomes outdated against the pace of technology development. Currently, nuancing of legacy policies and reactionary practices are emerging in response to new developments, such as embryo model systems.

3.3. Permissive versus risk-management-based policymaking

The United States, the United Kingdom, China and the European Union have varying levels of permissiveness and risk-management based approaches when regulating GE technologies. The level of risk acceptability and permissiveness can depend on whether the GE is applied to human health, gene drive technology per se, or agriculture. Data from the Genetic Literacy Project,[96] which scores how regulated each of these domains are in various countries, is outlined in Table 3, below, highlighting the permissiveness or risk aversion of the United States, the United Kingdom, China and the European Union over GE policies.

92 International Society for Stem Cell Research (2022).
93 XinhuaNet (2019).
94 United States Environmental Protection Agency (2023a).
95 United States Environmental Protection Agency (2023b).
96 Global Gene Editing Regulation Tracker (2023).

Table 3. Risk-based regulation matrix of policymaking regimes in the United States, the United Kingdom, China and the European Union

Region	GE domain		
	Human health	Gene drive technology	Agriculture
United States	Highly regulated	Highly regulated	No unique regulations
UK	Highly regulated	Mostly prohibited	Mostly prohibited
China	No unique regulations	Limited research	Regulations in development
EU	Highly regulated	Prohibited	Mostly prohibited

Source: RAND 2023

Among the three main domains of GE, countries of interest seem to deploy the most risk-management-based approaches to gene drives. While the United States highly regulates gene drives, the EU and the United Kingdom outright prohibits them, and in China there is not enough gene drive research yet to have a policy specific to it. This policy stance is likely because gene drives have a direct impact on the environment as the genes pass through a given population with many unknown long-term effects on the environment.[97]

Bar China, countries tend to be risk-management focused over GE in human health. China uses legacy frameworks for GE in human health, leaving regulation to the discretion of the committees instead of codified national law.[98] There has been some activity of note recently in China, at the national level, with calls for ethical committees to have more explicit national-level oversight via a national registrar of review committees, though this is currently at draft stage.[99]

Meanwhile, the United States, the United Kingdom and the European Union have not prohibited GE for human health but have highly regulated it. The most permissive regime has been the United States in the way it regulates GE in the domain of agriculture, which is the opposite end of the spectrum of the European regime. The United States operates legacy regulations enforced by the US Department of Agriculture to GM crops; these tend to treat GM crops as any other crops, whereas the EU has a pre-emptive style of policy towards GE, effectively banning the use of GM crops (much of which has been done without scientific justification and primarily motivated by public sentiment).[100]

97 European Parliament (2020).
98 Huanhuan et al. (2021).
99 Interesse (2023).
100 Halford (2019).

3.4. The role of international brokers

Scientists at the forefront of GE and other emerging technologies have not always been able to rely on their country's national-level policies to support or guide their innovations or research, because policy has not caught up to the rapid pace of innovation.[101] They default to developing standards, guidelines and principles that they put in place in lieu of relying on policymakers.[102] This in and of itself is noteworthy – scientists taking the initiative to act as policymakers for lack of leadership in the broader sector of emerging technologies. International and supranational organisations such as the WHO, UN, ISSCR, Gates Foundation etc. often play a significant role at this stage, outlining best practices and ethical guidelines surrounding GE to support scientific endeavours.[103] For instance, Europe's Oviedo Convention is the only international convention that oversees the ethics of human GE and is employed by the European Union to push the agenda on its member states to highly regulate the use of GE on human DNA.[104]

While there is a vast body of literature on the normative processes associated with the development of policies with the involvement of multiple national and international stakeholders, here we simply refer to the types of organisations that have played the role of convening scientific and public policy communities and developed ethics centric frameworks and guidelines. These types of international organisations can have the bandwidth and resources to be important conveners of multiple stakeholders when developing complex policies and building cooperation.[105] Their members can discuss the complexities of emerging technologies and the longer term ethical and humanitarian implications of such innovations without the restriction of jurisdiction, political appointment terms and lack of accountability to a group of constituents.

ISSCR

ISSCR has become a broker in the field of GE, because by providing relevant guidelines for stem cell research it fulfilled a need that governments did not meet, and did so by consulting and comprising key stakeholders themselves.[106] The experts and scientists, bio-ethicists and so on who helped develop the guidelines of the ISSCR have discussed the policy needs and implications of the field in a way that policymakers in the United States, the United Kingdom, China and the European Union have not been able to.

101 Jasanoff & Hurlbut (2018).
102 Kleiderman & Ogbogu (2019, 257–64).
103 Zhang et al. (2020, 1651–1669).
104 De Wert et al. (2018, 450–70).
105 Molnár-Gábor(2018, 33–49).
106 International Society for Stem Cell Research (2023).

Chapter 4.
State of the art and history of machine learning technology

Key findings

The current state-of-the-art technology is focused on deep learning models, large language models and artificial general intelligence, with key barriers to advancement including the algorithmic black box, poor data quality and access to materials to develop requisite compute power.

The early developments in AI in the 1960s and 1970s had been funded and spearheaded primarily by the US via defence funding.

Due to progress not deemed appropriate nor aligned to the defence strategy, significant AI funding cuts were made and the sector experienced an 'AI winter'.

In the 1980s and 1990s there was a renaissance in AI through milestones in expert systems (e.g., IBM's first PC) and robotics, which excited governments and industry and attracted significant investments.

The 2010s ushered in an era of big data when other players beyond the United States, like the United Kingdom, the European Union and most importantly China, rose in prominence in the field of ML, as China became one of the key players in AI development in its academic output, capital market size and technological developments.

In this chapter we present the state of the art in ML followed by a brief discussion of the milestone technology developments that have led to the current state of progress. We categorise the progress into loosely defined eras that describe key moments of funding, turning points in epistemological approaches, or focus on specific applications. As with GE, these trends in technology development provide the foundation for further discussions on the interplay between technology and policy and their interconnectedness across our geographies of interest for this study. We also note that historic developments charted as well as state-of-the-art technologies presented are not exhaustive but rather refer to prevalent technologies and/or significant milestone technologies.

4.4. State of the art: ML today

To understand the state of AI and more specifically ML, it is important to look at the technological advancements that have facilitated its development, as discussed in sections below. Despite the field's statistical foundations being decades old, the algorithmic advances, increase in compute power, and increased access to data have catalysed the developments in this field. In 2017, studies approximated that 90 per cent of the world's data had been generated in the preceding five years.[107] This access to data has facilitated training of algorithms and testing environments that had not been accessible before.

The development of a new graphics processing unit (GPU)-based architecture has enabled an increase in computer processing speed, which has been an important enabler in the current state of the art in AI. GPUs have been central to training large language models, such as ChatGPT.[108] The Chinese company ByteDance, for example, has ordered $1 billion of NVIDIA GPUs in 2023.[109]

We focus here on game-changing state-of-the-art developments in ML that are being deployed today with examples discussed below.

Deep learning models

Some of the most significant recent developments in AI have been in deep learning models. Deep learning is distinguished from classical ML by the type of data that it works with and the methods with which it learns.[110] Deep learning algorithms can process unstructured data, such as text and images, and automate feature extraction, removing some of the dependency on human experts.[111] Deep learning methods have been outperforming other ML techniques in numerous scientific fields, such as chemistry, physics, biology and materials science.[112]

Numerous deep learning models have been created to generate images from natural language descriptions, such as DALL·E and Midjourney. These have demonstrated the capacity for AI-generated content to capture the public attention, to be indistinguishable from real images, and have

107 The Royal Society (2017).
108 Olcott (2023).
109 Liang & Lu (2023).
110 IBM Corporation (2023c).
111 IBM Corporation (2023c).
112 Choudhary et al. (2022).

been shown to have significant real-world implications. An AI-generated image of an explosion near the Pentagon complex was linked to a brief dip in the stock market.[113] This highlights the potential significance of public perception and understanding with technology development and deployment, especially as R&D funding tends to shift from governments to the private sector, thus responding to market demands.

Large language models

One of the most impactful ways in which deep learning models have entered the public consciousness is with large language models. An example of this is OpenAI's Generative Pre-trained Transformer 3 (GPT-3) and GPT-4, large language models that use deep learning to produce, in seconds, text[114] such as poems, essays, musical lyrics and other genres of outputs that were often seen as only within the purview of human creativity and analytical ability. ChatGPT, a chatbot based on GPT-3.5 and GPT-4, became the fastest growing consumer application in history, reaching 100 million users over just two months after its launch in 2023.[115]

Multimodality and artificial general intelligence

There have been developments in the creation of general-purpose AI systems that have a wide range of uses, both intended and unintended by the developers, and which can be applied to many different tasks across a range of fields without significant need for modification or fine-tuning.[116] One such example is Gato, a general-purpose system capable of performing 600 different tasks, including playing Atari, captioning images, and stacking blocks with a real robot arm.[117] General-purpose AI systems, such as ClinicalBERT and C5T5, are increasingly used for powerful applications in medicine and healthcare, as well as in the life sciences and chemistry.[118] This proliferation in general-purpose AI systems goes to the heart of a key debate in AI and philosophy about whether AI can accomplish any intellectual task a human can, or can surpass human capabilities, in what is known as artificial general intelligence.[119]

Challenges and barriers in state-of-the-art AI

There are several challenges and barriers associated with further maturity and scalability of the state of the art in AI. Deep learning methods have disadvantages, with one of the most significant being their 'black box' nature, which may hinder physical insights into the phenomena under examination.[120] Truly understanding why a ML algorithm arrived at a particular result requires understanding many underlying parameters, which can be complex and intractable, especially for less technical users. There are several other technological barriers associated with the further maturity and scalability of these tools. These include barriers in

113 Clayton (2023).
114 OpenAI (2023).
115 Hu (2023).
116 Future of Life Institute (2022).
117 Google DeepMind (2023).
118 Alsentzeret al. (2019); Rothchild et al. (2021).
119 Shevlin et al. (2019).
120 Choudhary et al. (2022).

miniaturisation (the death of Moore's Law),[121] power usage efficiency, and poor data quality with training.

4.2. Technology history: the developmental eras of ML

This section summarises the key eras defined as per this study, charting the technological progress in AI, focusing on ML components where relevant. These have provided the foundations for where ML technology is today. Figure 6, below, illustrates the main eras of AI development, which are discussed below.

The symbolic systems era and the waxing and waning of government support

The 1960s to the mid-1970s was a 'symbolic systems' era in which a plethora of well-funded AI-specific labs[122] [123] [124] were initiated, particularly in the United States where natural language processing (NLP) and reasoning were at the forefront of AI development. This was an era of many firsts in AI functioning symbolically (in logic that is comprehensible to humans) through programming languages like Lisp,[125] industrial robots like Unimate,[126] and chatbots like ELIZA.[127]

This flourishing in the 1960s and 1970s was also a product of state interest and major funding, primarily via US military funding, including significant US Defence Advanced Research Projects Agency (DARPA) investments.[128] It is through such funding that milestones in expert systems[129] and mobile robotics[130] became possible.

AI winter

Development in AI and ML was abruptly followed by an era of decreased government interest and subsequent cuts in funding. This 'AI winter' was experienced during the 1970s and early 1980s, driven by a steep decrease in support for any basic scientific research in AI that was not linked to the US Department of Defense's missions at that time.[131]

121 Andrei (2022).
122 Stanford Artificial Intelligence Lab (2023).
123 Ehrenfeucht (1957, 61–79).
124 Vadapalli (2020).
125 Two-Bit History (2018).
126 Automate (2023).
127 Landsteiner (2005).
128 Lefkowitz (2019).
129 Copeland (2008).
130 ETHW (2017).
131 National Science Board (2023a).

AI renaissance led by expert systems and robotics

The 1980s ushered in a decade of investment in AI, with a focus on designing systems that could compete with the decision-making faculties of a human expert.[132] A key development during this period was Moravec's paradox, which argued that learning through sensorimotor and perceptual cognition could be more important in reasoning and learning than computational cognition.[133] Conceptual advancements like this led to the 'robotics era' of AI development that started in the late 1980s and continued well into the 1990s, seeing the likes of MIT's Kismet, the first robot able to express emotions.[134]

The rise of intelligent agents

Overlapping with the robotics era, the 1990s also saw the rise of intelligent and autonomous agents,[135] an era that lasted until around 2012. This was a time in which AI development revolved around autonomous entities that could react to and learn from their environments by using sensors, a culmination of the past development in AI and evidence of Moore's Law coming to fruition in real time.[136] Indeed, in this era DARPA re-invested in AI mainly by incentivising developments in autonomous vehicles,[137] the Google app on iPhone allowed for voice recognition,[138] and Apple released Siri.[139] Beyond these milestones, the extent of intelligent agents' capabilities had reached a notable level of competency, demonstrated through IBM's Deep Blue defeating champion chess players[140] and IBM's Watson defeating Jeopardy champions.[141]

The shift to big data

Between 1990 and 2012 intelligence itself was being redefined as data. Data collection, quality, and the sheer breadth and volume of data can be the deciding factors in how useful AI and ML is and will be.[142] Since the 2010s, big data has underpinned major commercial developments such as Amazon's voice activated system Alexa,[143] and Google's AlphaGo, which beat world champions in Go.[144]

132 Hooper (1988).
133 Moravec (1988).
134 Robots Team (2023).
135 JavatPoint (2023).
136 Hughes (2022).
137 Chow (2014).
138 Markoff (2008).
139 Apple (2023).
140 IBM Corporation (2023a).
141 IBM Corporation. (2023b).
142 Oracle United Kingdom (2023).
143 Amazon (2023).
144 BBC News (2016).

While early era developments were mainly spearheaded in the United States, this period ushered in major developments in the United Kingdom and the European Union, with more investment in AI labs[145] and in innovations in a variety of applications such as e-commerce,[146] transportation,[147] insurance,[148] manufacturing,[149] visual robotics[150] and parsing centuries of library data.[151]

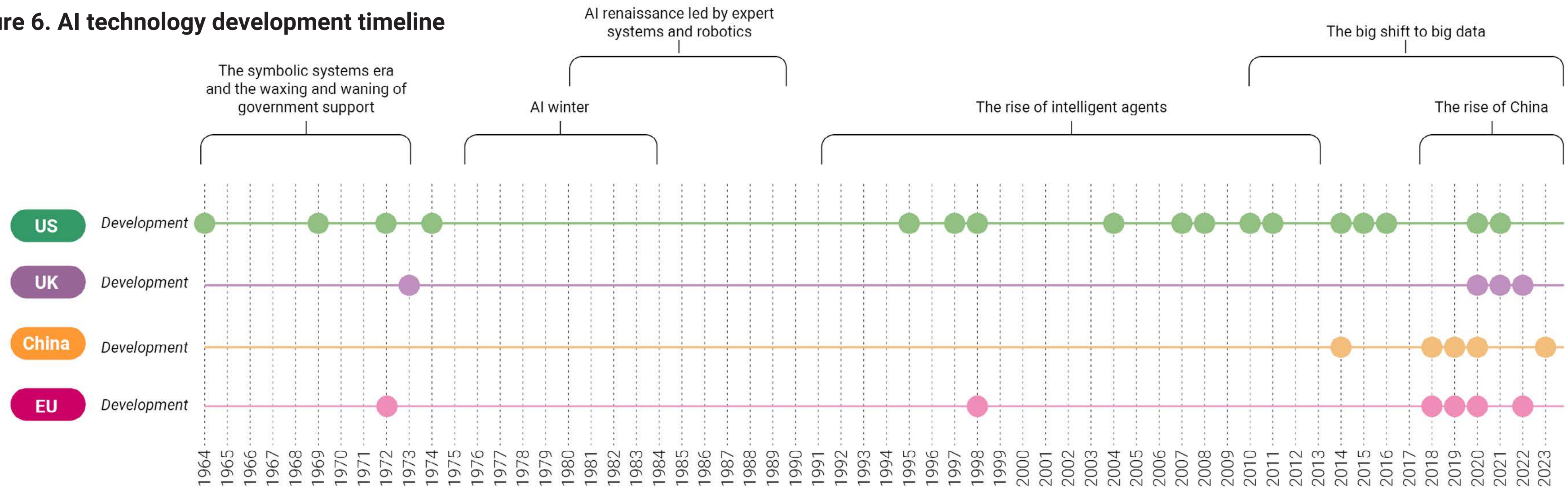
The rise of China

During the big data era China's role in AI development rose suddenly. In 2012 there was a surge in computer start-ups and products in China's security market, such as Megvii, which capitalised on the international interest in automation.[152] In 2014, the Chinese government announced a bold seven-year plan to have a social credit scoring system using AI,[153] and SenseTime, one of the world's most highly valued AI start-ups, was founded.[154] By the late 2010s, Chinese companies had reached many milestones in NLP and computation. There were significant advancements in China with the application and investment in facial recognition technology for its mass surveillance systems,[155] and a program was designed at the Beijing Institute of Technology that recruited children to be trained in a defence and AI programme.[156]

> 'Most significantly, it is during this era of big data that China became the top publisher of AI-related papers and one of the most cited in AI related papers.'
>
> 'By 2020, China heralded an age where it is a key player in AI development, as it has the largest capital market for AI start-ups in the world.'

145 ELLIS Unit Cambridge (2023).
146 Ecommerce News (2017).
147 Marr (2017).
148 Allianz UK (2019).
149 ASSEMBLY (2023).
150 PROPHESEE (2023).
151 West (2023).
152 Chen (2021).
153 Yang (2022).
154 Knight (2017).
155 Jiaquan (2018).
156 Chen (2018).
157 Schoenick (2019).
158 Westerheide (2020).

Figure 6. AI technology development timeline



United States

1964	*Joseph Weizenbaum invents first chatbot, ELIZA*
1969	*Marvin Minsky releases Perceptrons, a publication about artificial neural networks*
1972	*Stanford Research Institute's Artificial Intelligence Center develops Shakey, a mobile intelligent robot*
1974	*Paul Werbos lays the foundation for backpropagation, designed to aid in teaching neural networks how to recognise patterns*
1995	*Richard Wallace presents A.L.I.C.E., a chatbot inspired by ELIZA but with enhanced NLP*
1997	*IBM's Deep Blue chess-playing computer beats human world champion chess player Garry Kasparov*
1998	*MIT designs Kismet, the first robot able to express emotions*
2004	*DARPA initiates Grand Challenge to develop autonomous vehicles*
2007	*Nvidia releases Compute Unified Device Architecture*
2008	*Google app on iPhone allows for voice recognition*
2010	*Initial release of ImageNet*
2011	*Apple releases Siri as voice activated virtual assistant*
2011	*Google Brain founded to focus on AI*
2014	*Amazon releases Alexa, a voice activated virtual assistant*
2014	*Meta's DeepFace outperforms humans in performing the "Faces in the Wild" test, ushering in an era of deepfake and facial recognition applications*
2015	*Initial release of TensorFlow as an open-source tool is what triggered the current renaissance*
2016	*AlphaGo beats Lee Seidol*
2020	*OpenAI release GPT-3, a natural language model using deep learning to produce human-like responses*
2021	*Initial release of Dall-E by OpenAI*
2021	*Midjourney*

United Kingdom

1973	*University of Edinburgh builds Freddy robot, which is able to use visual perception to build models*
2020	*DeepMind's AlphaStar is Grandmaster level in the game StarCraft II*
2021	*Stable Diffusion (Stability AI)*
2022	*DeepMind releases Gato, first generalist AI*

China

2014	*Government announced seven-year plan to have a social credit scoring system using AI*
2014	*SenseTime, one of the world's most highly valued AI start ups is founded*
2018	*China implements facial recognition in its mass surveillance system*
2018	*Beijing Institute of Technology opens first ever course in military AI geared toward children*
2019	*China is top publisher of AI-related papers*
2020	*China has biggest capital market for AI start-ups*
2023	*China's investment (via ByteDance) in buying hardware from NVIDIA (hardware)*

European Union

1972	*Prolog language developed by Alain Colmerauer with Philippe Roussel*
1998	*First Environment and AI Workshop in Europe held*
2018	*European Lab for Learning and Intelligent Systems is established to compete with China and US AI investment and efforts*
2019	*Allianz Insurance first to use AI to completely automate injury claims*
2020	*BMW integrates AI applications throughout its production process, maximising efficiency and productivity*
2022	*French AI firm Prophesee designs near-human level vision for robotics*

Source: RAND analysis 2023

Chapter 5.
Trends in machine learning policies

Key findings

The AI winter experienced in the 1970s and 1980s was a direct result of US policies that led to funding being cut from AI basic research programmes.

Reactionary policies are prevalent in this sector and have primarily spurred investment and progress in AI/ML, as exemplified through the US reignition of DARPA funding, UK development of the Alvey project, and the latest CHIPS and Science Act in the US.

China's 2017 AI national action plan spurred the United States, the United Kingdom and the European Union to draft their own plans, and the EU was the first to publish a regulation on AI as the EU AI Act.

Less policy development is apparent in AI/ML than in GE, with a heavy focus on legacy frameworks or reactionary policy. This is likely due to the fear of causing irreversible harm to humans and the environment.

As seen for GE, international organisations have demonstrated thought leadership in developing AI principles and ethics.

This chapter presents milestone policies in the United States, the United Kingdom, China and the European Union, in relation to technology progress, and has categorised the styles of policymaking based on the framework presented in Table 1. The policies discussed here are not exhaustive and present key moments in time, which highlight the interconnectedness of policy and technology and the wider global stage. The full policy timeline, developed in July 2023, can be found in Annex B (Figures of timelines for GE and AI/ML); it does not capture the latest developments afoot in ML and AI regulation.

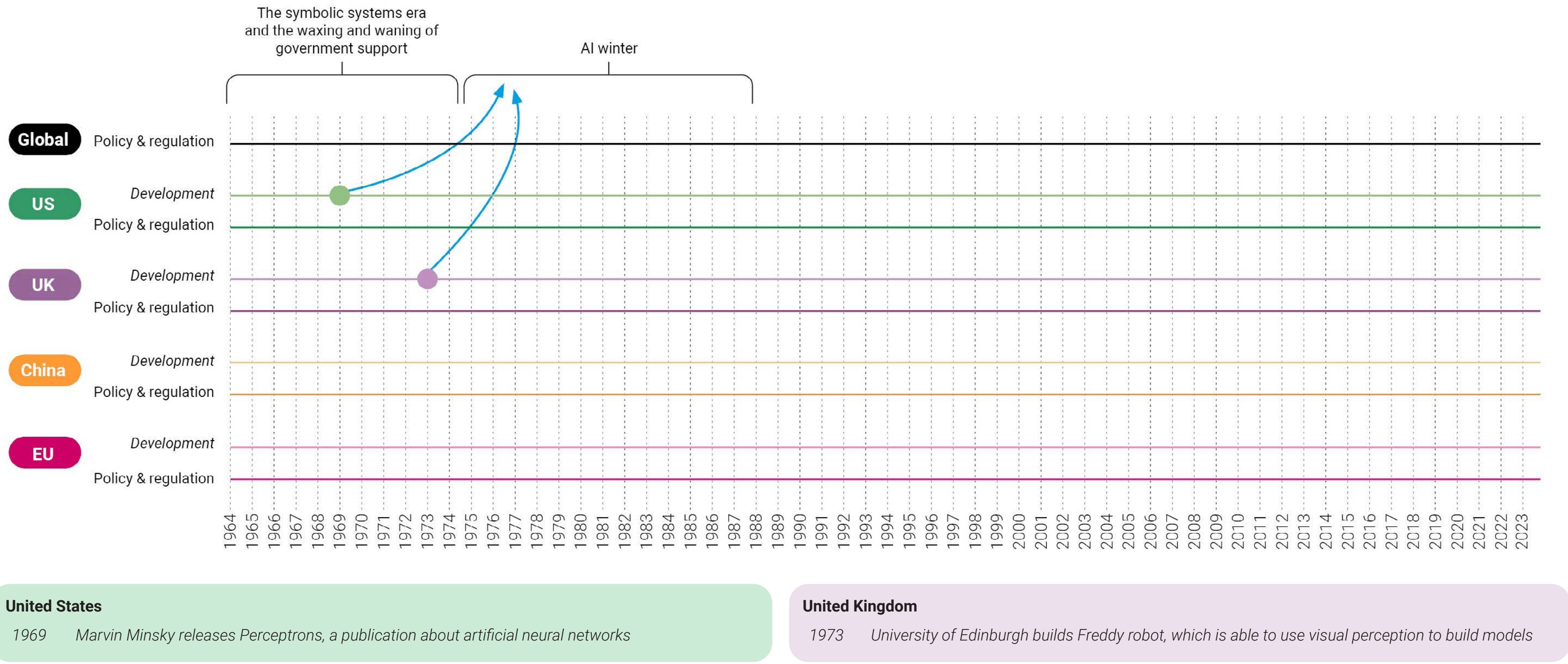
As mentioned before, we use policy as a catch all term that includes regulation and other types of policies. However, we have focused on just a subset of the most prevalent and relevant policies in ML, which have culminated in a heavy focus on economic growth and innovation in contrast to GE, where the focus was regulation policy. Any comparisons of policies themselves are limited to the policymaking styles rather than their substance. As mentioned previously, it is pertinent to chart and assess the technology and policy developments in AI and GE, especially taking note of their interconnectedness in order to deliberate over how policies today could influence the convergence of ML and GE sectors.

5.1. Interplay of ML and AI technology and policy

As is the case for GE, the interconnected nature of technological developments and wider policies can be seen on many occasions through the history of developments charted earlier. For instance, significant public investment was made largely in the United States via DARPA, which spurred many of the early developments in ML symbolic systems;[159] however, it was taken away in 1969 through the Mansfield Amendment,[160] as promises of AI were perceived by the public and politicians as not coming to fruition, initiating a period of decreased research and investment in AI across the United States and United Kingdom[161] (see Figure 7 below).

159 Knight (2006).
160 National Science Board (2023b).
161 Zenil (2011).

Figure 7. DARPA influence and the AI winter



Source: RAND analysis 2023

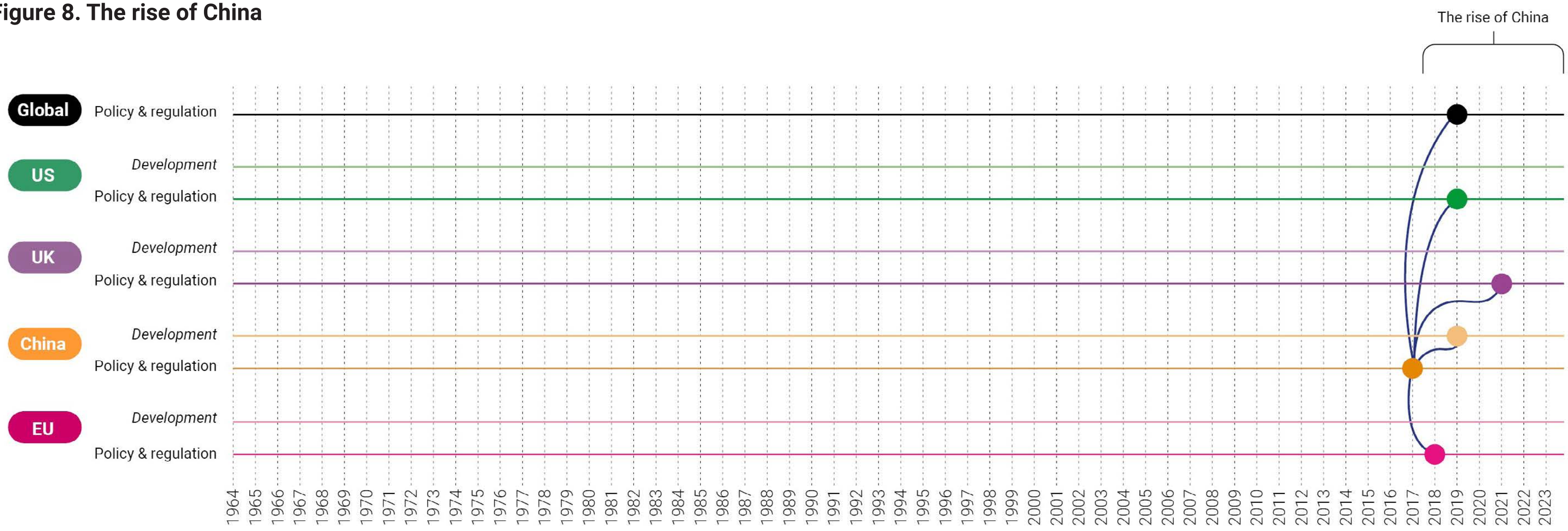
Another example of the interplay between technology and policy is where China's 2017 National AI 2030 Strategy,[162] the first one of its kind on the global stage, eventually manifested in quick returns, with China becoming the top publisher of AI-related peer-reviewed papers in 2019,[163] highlighting the volume of work afoot. The European Union reacted to China's action plan (see Figure 8 below) by publishing its

162 State Council (2017).
163 Schoenick (2019).

Coordinated Plan on AI in 2018.[164] The United States also reacted by publishing its own national AI strategy in 2019,[165] and at the international level, the Organisation for Economic Co-operation and Development (OECD) published its AI principles.[166] The ripple effect of the creation of China's national AI strategy on others is further seen in the United Kingdom with the publication of a national AI strategy in 2021.[167] The domino effect of national AI plans being drawn up across the international stage highlights the reactionary nature of recent policy actions within AI, which are underpinned by geopolitics rather than technological progress. These trends contrast with developments in GE, where constant iteration of technology development and policy is most likely to be caused by the nature of human intervention, whereas there were less obvious use cases of AI systems impacting humans. This has changed with the rise of large language models; however our study does not cover these developments in policy and regulation.

164 European Commission (2021).
165 Executive Office of the President (2019).
166 OECD AI (2019).
167 Department for Science, Innovation and Technology (2022).

Figure 8. The rise of China



United States

2019 US national AI strategy: executive order on maintaining American leadership in AI

United Kingdom

2021 Government releases national AI strategy

China

2017 Government sets ambitious AI 2030 strategy

2019 China is top publisher of AI-related papers

European Union

2018 Commission establishes the AI Alliance initiative to encourage experts to collaborate and promote dialogue across academia and industry

Global

2019 Beijing Consensus

Source: RAND analysis 2023

5.2. Various styles of policymaking in ML and AI

Despite the immense strides in AI and ML development since the early 1900s, in the United States AI research was decommissioned in the 1960s and 1970s due to the **reactionary policy** brought in through the 1969 Mansfield Amendment, which required that all federally funded research must have a 'mission-oriented' and explicit outcome.[168] This reactionary policy was a direct response to the failed promises of AI. In 1973, the United Kingdom faced a similar backlash against the unrealised promises of AI.[169]

Other examples of a **reactionary** style leading to the catalysation of innovation in AI regulation are the US–UK declaration of AI R&D cooperation[170] and the US–EU Trade and Technology Council,[171] which have put AI atop the agenda in US, UK and EU-level policymaking, and have resulted in the drafting of specific AI strategies in various US government departments,[172] UK ministries[173] and EU funding frameworks.[174] The European Union, though, has since 2021 taken a step further towards implementing a **proactive** policy style, with its EU AI Act, the first

> 'The reactive regime in AI was focused on propelling research further whereas the reactive regimes in GE have been regulation focused to curtail technological progress and avoid further harm.'

regulation on AI,[175] which pulled together many sector experts to consult on comprehensive factors that can characterise AI applications as posing varying levels of risk.

Another example of a positive reactionary stance in policy, is the CHIPS and Science Act,[176] a US federal statute enacted in 2022 that poured hundreds of billions of dollars into domestic US semiconductor manufacturing and R&D to boost United States presence in this highly competitive space, and to level China's growing advantage.

In recent times the most palpable surge in AI-related policymaking activity and development has happened as a result of China's **proactive** 2017 AI

168 National Science Board (2023).
169 Zenil, Hector (2011).
170 United States Department of State (2012).
171 White House (2021).
172 Department of Defense (2018).
173 King's Printer of Acts of Parliament (2023a).
174 The AI Data Robotics Association (2023).
175 European Parliament (2023).
176 PricewaterhouseCoopers (2023).

2030 strategy[177] as well as the increasing real-world realisation of the use of AI and ML, as highlighted in the technology sections. However, the study does not cover the plethora of AI- and ML-policy-focused activity afoot since June 2023.

The United States, the United Kingdom and the European Union adopted a **reactionary** approach to their pro-innovation and national security focused policymaking in response to China's **proactive** AI policy style focused on economic growth. The European Commission's Coordinated Plan on AI[178] and the United States' national AI strategy[179] (which led to the National AI Initiative Act[180]) came shortly after China's 2017 strategy (in 2018 and 2019 respectively). After officially leaving the European Union in 2020, the United Kingdom released its own AI national action plan.[181]

Other reactionary policy responses included establishing AI-specific committees to facilitate AI-specific policies, such as the UK's Senior AI Council, created in 2019 as an advisory board on adopting AI,[182] and most recently the Office for AI and the Foundation Models Taskforce. The European Union established AI Watch to monitor the Coordinated Plan on AI.[183]

This flurry of regulatory and policymaking developments are intricately linked to the strides made in ML and the opportunities it has unlocked for society. This is in stark contrast to earlier decades where policy was innovation and funding focused with little regard for ethics, safety and security given there were no use cases for such concerns.

5.3. The role of international brokers

As with GE, international organisations can play a significant role in AI and ML policymaking. They provide a space where deep debate about complex ethical issues and the long-term humanitarian impact of AI and ML has led to standards and guidelines that can be used by researchers and policymakers in the field. Of note is the work spearheaded by the United Nations Institute for Disarmament Research (UNIDIR) building awareness and international coordination with regards to weaponisation of autonomous systems and creating transparency around the black box issue of ML, for instance.[184]

The OECD has also published value-based principles in AI,[185] which consider not just inclusive and equitable development, but the role of AI in sustainability, fairness, transparency, safety and security, and accountability – all a result of complex ethical debates and discussions by techno-ethicists, intellectual property (IP) experts, academics and a plethora of other relevant stakeholders.

177 State Council (2017).
178 European Commission (2021).
179 Executive Office of the President (2019).
180 Congress of the United States (2022).
181 Department for Science, Innovation and Technology (2022).
182 GOV.UK (2023).
183 European Commission (2023).
184 United Nations Institute for Disarmament Research (2023).
185 OECD AI (2019).

Most importantly, the OECD's principles also provide clear recommendations for policymakers at the state level, which include swathes of frameworks they can use when investing in AI R&D, incentivising a digital ecosystem that can enable AI, preparing a labour market for AI, and so forth. The OECD also provides constantly updated data about various countries' legal frameworks, funding, etc., all of which provides a resource and benchmarking tool by national-level policymakers as well.

Another example of international organisations possessing the thought leadership and oversight of AI principles and ethics is the World Economic forum tools for AI procurement,[186] which has been adopted and used in some EU countries, the United Kingdom and various other countries. UNESCO's Beijing Consensus[187] also exemplifies the proactive style to AI policy, as it sets guidelines on how UNESCO member states should use AI technology in education.

In both the GE and AI and ML policy context, the **proactive** approach to regulation tends to stem from efforts at the supranational and international level, where ethical, long-term considerations are discussed in an international setting. The latest instance of this can be seen by the globally coordinated calls to halt unchecked and unregulated progress in large language model development and deployment with increased focus on accountability and transparency.[188]

186 World Economic Forum (2020).
187 United Nations Educational, Scientific and Cultural Organization (2019).
188 Future of Life (2023).

Chapter 6.
Convergence of technologies

Key findings

STATE OF THE ART

- In general, ML is accelerating advances in biology, primarily by enabling faster processes with efficiencies. When applied to GE, ML has catalysed technological advancements at scale and pace, with novel technologies emerging in genome-wide engineering and synthetic design, predictive genome studies, and protein modelling and manipulation. This has resulted in key capabilities being unlocked, such as improved predictive power in medicine, improved understanding of biological systems, more precision in genome engineering, improved use of existing data and, most importantly, an increase in pace and scale of activity due to automation and increased compute power.
- While the integration of GE and ML has substantial practical implications, much of the underlying technology still requires more development.
- Applications of technologies at this intersection are primarily being trialed in the health sector, with emerging applications in climate and agriculture as well as military and defence.
- There are still multiple barriers to further advancements of these technologies, primarily the transition from in silico experimentation to real world environments. Other barriers include but are not limited to computation capacity plateauing, ethical barriers and a dwindling skills pipeline.

POLICY

- Platform technologies like ML and GE are set to revolutionise multiple sectors, but public engagement and perception are crucial to consider in future policymaking.
- There was limited evidence of policymaking found at the intersection of these technologies, beyond the longstanding challenges of considering software as a medical device, which can offer some insight for future consideration.
- A fundamental difference between GE and ML reactionary policies has been that GE reactionary measures have focused on mitigating against controversies and harm, and halting unchecked progress, whereas reactionary measures in ML have spurred competition and innovation.
- The domino effect of national AI plans across the international stage highlights the reactionary nature of recent policy actions within AI, which are underpinned by geopolitics rather than technological progress. These trends contrast with developments in GE, where constant iteration of technology development and policy is seen. Furthermore, while the GE timelines illustrate key milestones in policy that spread out over time, AI/ML landmark policies are concentrated in a few clusters with currently topical activity.

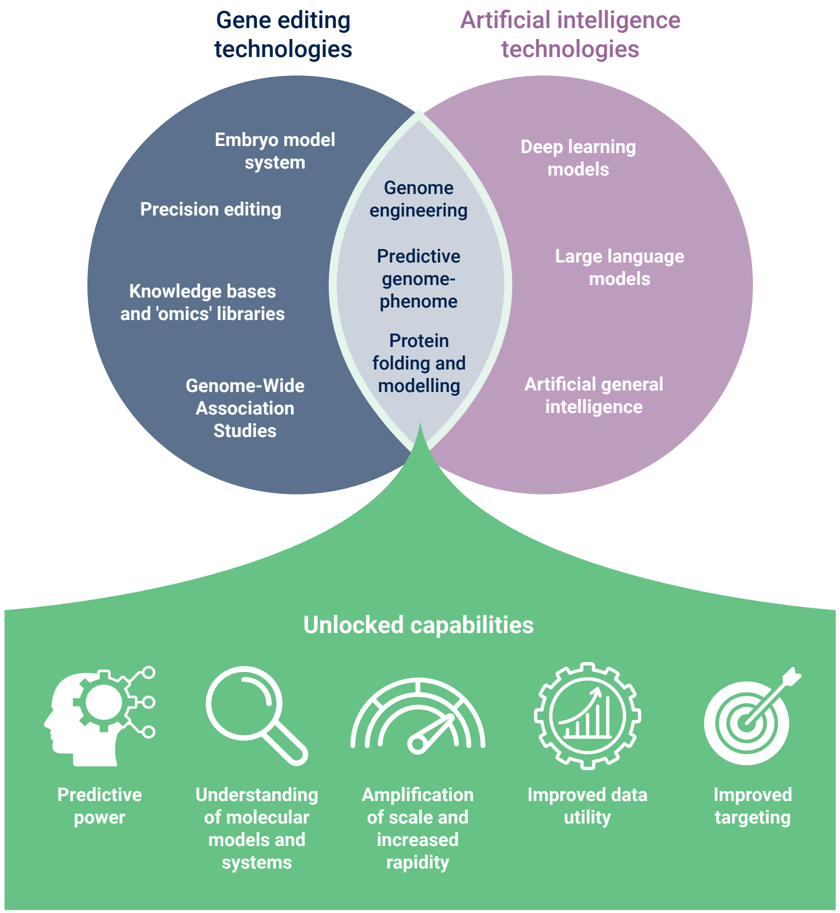
This chapter highlights and discusses some of the key technological developments enabled through the convergence of ML and GE. While we have discussed the developments in ML and GE independently thus far, their convergence highlights how ML has the potential to truly unlock GE capabilities and use in everyday life. We then focus on the barriers to further progress at this convergence and the policy landscape that currently relates to these advancements.

There have been significant strides in technical advancements in GE and ML in their own rights. However, in the last 5 years we are seeing an era of the convergence of ML and GE technologies, to create a new platform technology, providing the foundation of multiple applications. The impact of this convergence continues to unfold and create a seismic shift in society, influencing the way we think about fertility and being a human, and how we cultivate food and consume energy. In fact, this is just one example of how the integration of multiple quickly emerging technologies can have significant implications and thus deserves thorough analysis.

A platform technology is a group of technologies that are used as a base on which other applications, processes or technologies are developed.[189]

Figure 9 opposite illustrates the key technical advances that have emerged through the convergence of these technologies, and it highlights primary capabilities that have been unlocked as a result. The sections in the rest of this chapter further elaborate on these developments and their implications.

Figure 9. Intersection of technology and unlocked capabilities



Source: RAND analysis 2023

189 Rouse (2020).

6.1. Technology advancements at the convergence of ML and GE

The convergence of AI and GE has led to substantive technological advancements; the experts we interviewed specifically noted protein design, synthetic engineering and use of more *in silico* working models as key among them. The technology examples chosen below reflect the most prevalent outputs of the horizon scanning and expert interviews.

We categorised the technologies using the TRLs framework used by the Science and Technologies Facilities Council.[190] TRL 1 represents technology that has displayed some basic principles as per a given hypothesis prior to comprehensive lab testing, and a TRL 9 represents technology that is proven, operational and commercially viable in its intended environment. Our analysis of the 66 technologies we characterised at the intersection of GE and ML produced an average TRL score of 4.4, with a range observe of TRL 2–6. TRLs 4 and 5 refer to 'technology validated in a lab' and 'technology validated in its relevant/ application-based environment', respectively. This score represents an early stage of technology maturity and is further discussed in Section 6.3 on barriers to advancements.

Here, we focus on a few exemplar innovations – genome engineering and synthetic design, predictive genome-phenome studies, and protein folding and modelling – to highlight the progress in this rapidly advancing field, and discuss what it means for society at present.

Genome engineering and synthetic design

Technology description: Understanding what genes encode and mean has been fundamental to using the outputs of the Human Genome Project. This understanding has aided progress in the field of engineering biology to engineer and manipulate genes and genomes. More significantly, it is ML models that have catalysed this process where detailed mechanistic knowledge of biological systems is not required and the ability to manipulate genes and assess derivative products is much more rapid through use of ML models.

Example use case: The Automated Recommendation Tool has been developed to systematically engineer, underpinned by probabilistic predictions, the ability to synthesise new biofuels, beer, fatty acids etc. among a multitude of applications.[191] Algorithms have been used to create new species of bacteria and viruses *in silico*.[192] Most experts interviewed considered this advancement a major breakthrough.[193]

Future considerations: The further advancement of this technology and its application depends on multiple factors such as engineering biology infrastructure investments, commercial competitiveness and permissive policies. These aspects are further discussed in the sections below.

190 UK Research and Innovation (2023).
191 Radivojević et al. (2020).
192 ScienceDaily (2019).
193 INT_01, _03, _04, _05, _06, _07, _10, _11, _12

Predictive genome-phenome studies

Technology description: The vast array of data on the genomic code has been underused owing to the lack of ability to assess how it translates to a person's physical attributes (phenome). There have been many genome-wide association studies looking at the effects of one gene on another and linking it to the phenome, but scaling this has been a challenge because of the immense volume of data involved and the lack of predictive abilities. This is where use of ML computational models has revolutionised the studies in terms of what is now possible.

Example use case: In 2022, researchers at Google introduced DeepNull, a deep neural network to model the relationship linking effects on phenotypes and genome and improve genome-wide association studies outputs.[194] This has led to a wide range of disease risk assessments and predictions, such as prediction of the risk of an individual sensitivity to radiotherapy, Parkinson's disease and Type 1 diabetes to name a few.[195]

Future considerations: Access to appropriate computational power and the transparency of ML models in this space are some of the critical factors that will dictate the extent to which the outputs of this development can be used in clinical settings.

Protein folding and modelling

Technology description: One of the quintessential challenges in biology has been the lack of ability to understand and predict how proteins form 3-D structures and fold in their natural environment. Application of ML models to predict protein folding accurately and structured in 3-D has revolutionised molecular biology and the field of GE.

Example use case: AlphaFold, a deep learning model, has accurately predicted the 3-D structure of more than 200 million proteins, which is almost all that are currently known to exist.[196] These capabilities have opened the floodgates for medical researchers to develop countless drugs and vaccines and to understand the genome to protein translation mechanisms better.[197] Following this development, a variety of other protein folding models have been released; Meta AI's launch of Evolutionary Scale Modeling (ESMFold) became one of the biggest competitors to AlphaFold and is reported to be 60 times faster though less accurate.[198] RoseTTAFold, a deep neural network model, can predict structure of multiple protein complexes, marking a massive shift in this sector given other ML models are restricted to single proteins.[199]

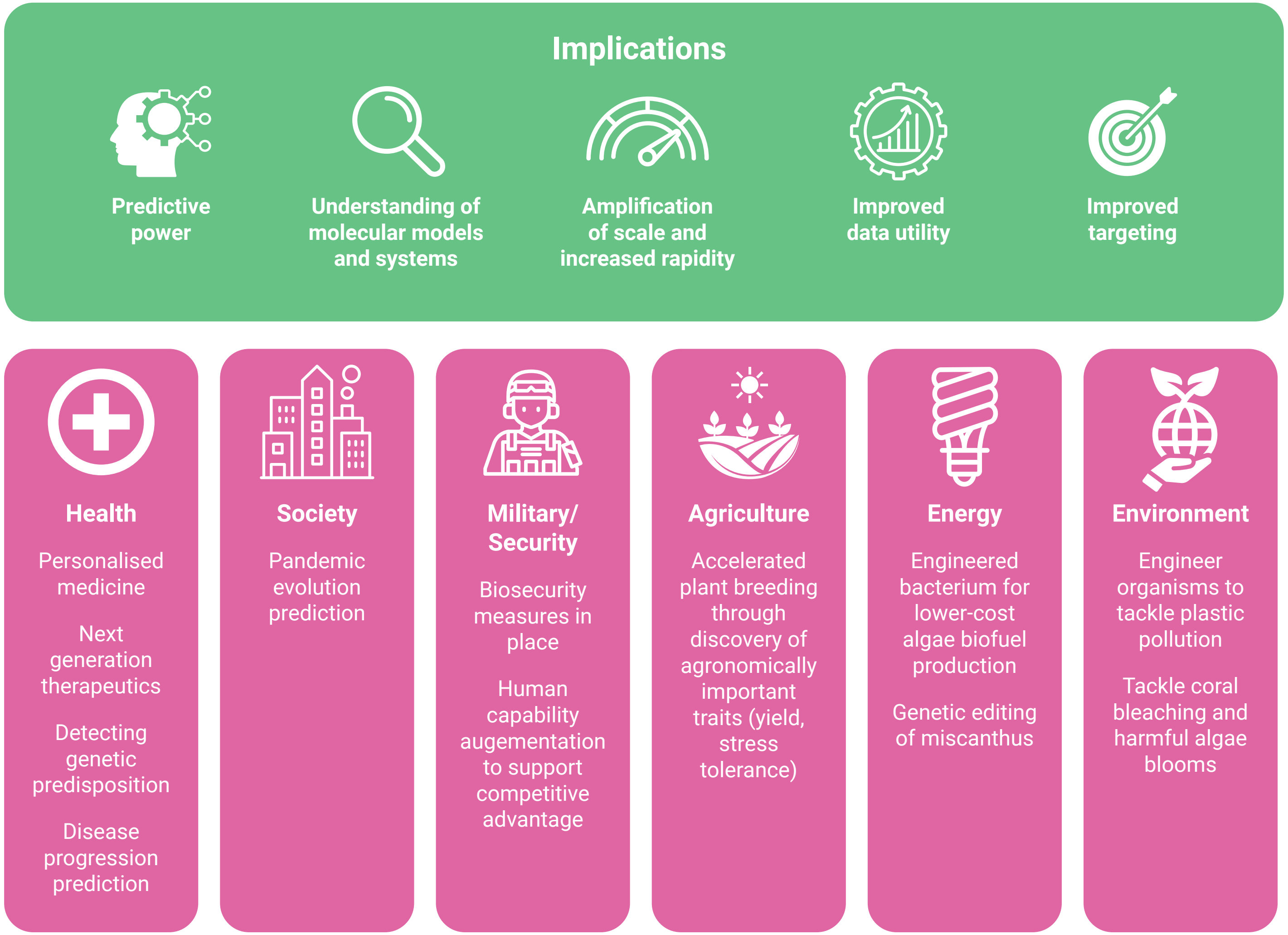
Future considerations: The commercial competitiveness and policies underpinning the challenges of the dual use of this technology will determine how the capabilities are used.

194 McCaw et al. (2022); Ansari (2022).
195 Enoma et al. (2022, 101847).
196 Tewari (2022).
197 Tewari (2022).
198 Jackson (2023).
199 Drake et al. (2022).

6.2. Capabilities unlocked from technology advancements

Technological advancements at the intersection of GE and ML have unlocked crucial capabilities that have implications on the lives of people in multiple sectors of society, as illustrated in Figure 10, opposite. In the sections below, we describe the most relevant thematic capabilities that emerged as an output of key technology advancements in our horizon scan.

Figure 10. Capabilities unlocked at the intersections of technologies



Source: RAND analysis 2023

Improved predictive power

The ability for inference and prediction has been beneficial for the field of GE where functional projections of how genes, proteins and cellular/ molecular systems will behave and what the likely impact of genetic manipulations has been possible, which otherwise would have been extremely time consuming if not impossible to conduct. Predictive capabilities offered through AI/ML have led to vaccine and drug development and more precise gene edits.[200] For example, NLP has been used to predict viral evolution and escape;[201] a tree ensemble ML model has been used to predict the interaction of complex systems in the gut;[202] and a deep learning model has been used to predict gene expression from large regulatory sequence datasets.[203]

Improved understanding of molecular and cellular models and systems

Multiple studies using ML models have provided insight into spatial mapping of molecular components and have provided data concerning the interaction between genes, proteins and other molecular machinery/ fragments. These novel insights into biological functions could not be studied or predicted previously. Some of the experts interviewed cited examples of where wet lab work has been replaced by *in silico* work to help conduct more biological experimentation with less deep knowledge.[204] For example, BioNeMo uses a biomolecular large language model to predict protein structures and properties,[205] and PenLight uses a graph neural network for protein structural and functional annotations.[206]

Amplification of scale and increased rapidity

Given the substantial volume of data generated in the genomics and GE fields, ML has been particularly helpful in canvassing large datasets and generating novel insights into biological functions, disease mechanisms and drug targets. Editing has been enabled not just at a small scale but rather with engineering capabilities that can be deployed at scale to generate new hypothetical species of viruses and bacteria. In fact, experts indicated that the ability to identify and map proteins and genes is happening at an unparalleled pace.[207] Meta AI's ESMFold, while not as accurate as its rival AlphaFold, is reported to be 60 times faster at predicting protein structures for short sequences, which allows researchers to scale structure prediction to larger databases.[208]

200 Subject matter expert interviews
201 Hie et al. (2019, 284–88).
202 Ruaud et al. (2022).
203 Ding et al. (2023).
204 INT_03, _06, _07
205 NVIDIA.DEVELOPER (2022).
206 Luo & Luo (2022).
207 INT_01, _03, _04, _05, _07, _08, _10, _11
208 Callaway (2022).

Improved data utility

ML models have allowed missing data in the genome to be generated and thus inform functional links between molecular components. Given the rise of knowledge libraries and genomics data, deploying ML models and training them on these large datasets has provided novel information to progress applications in drug development, clean energy and climate adaptation, none of which would have occurred at pace without the use of algorithms canvassing and analysing large volumes of data. For instance, a recent study reported AI picking up disease causing variation in the human DNA by studying large volumes of genetic data across a population set.[209] One expert concurred that this is paving the way to applications in the medical sector such as polygenic risk scoring.[210] AI has also enabled noise in datasets to be filtered. For example, researchers have presented a neural network approach to develop a gene expression recovery framework to recover missing expressions, which previously would have led to inaccurate gene counts and hindered downstream analysis.[211] Moreover, new algorithms have been developed to infer species information from gene trees with high proportions of missing data that has been synthetically engineered.[212]

Improved targeting

ML and its ability to characterise the genome and its proteins has allowed extremely precise targeting of genetic components for drug delivery and design. Experts have stated that drug discovery is indeed accelerating due to *in silico* experimentation.[213] For example, algorithms to predict CRISPR target sites can help identify genomic sites with genetic sequences or epigenetic features that increase the efficiency of editing with minimal off-target activity.[214] In addition, ML has been used to discover potential therapeutic targets for conditions such as fibrotic diseases, using large-scale human-based data.[215]

All experts interviewed agreed with the premise that ML is accelerating advances in biology primarily by enabling faster processes with efficiencies. ML applied to biotechnology is enabling for controlled and predictable processes in ways that were not possible prior to its application.

Capability use

Sectors where these joint technological capabilities have been used vary from energy, to agriculture, to health (Figure 10). However, the current predominant applications are focused on the health and medical sector. Experts highlighted medically relevant examples of progress, but some suggested that the more innovative and risky approaches will be trialled to develop more resilient crops and livestock considering challenges

209 Johnson (2023).
210 INT_08
211 Islam et al. (2022).
212 Morel et al. (2023).
213 INT_08, _10
214 Bhandari et al. (2022).
215 Pfizer (2023).

and demand from the energy and climate sectors.[216] Nonetheless, new capabilities have implications for other sectors as well, like military, security and human augmentation. In fact, experts are concerned about the capabilities in creating synthetic compounds that could cause disease, avoid detection and vetting, and potentially create pandemics or global bioterrorism events.[217] This has been the prevalent debate in national security focused policy dialogues as of late.

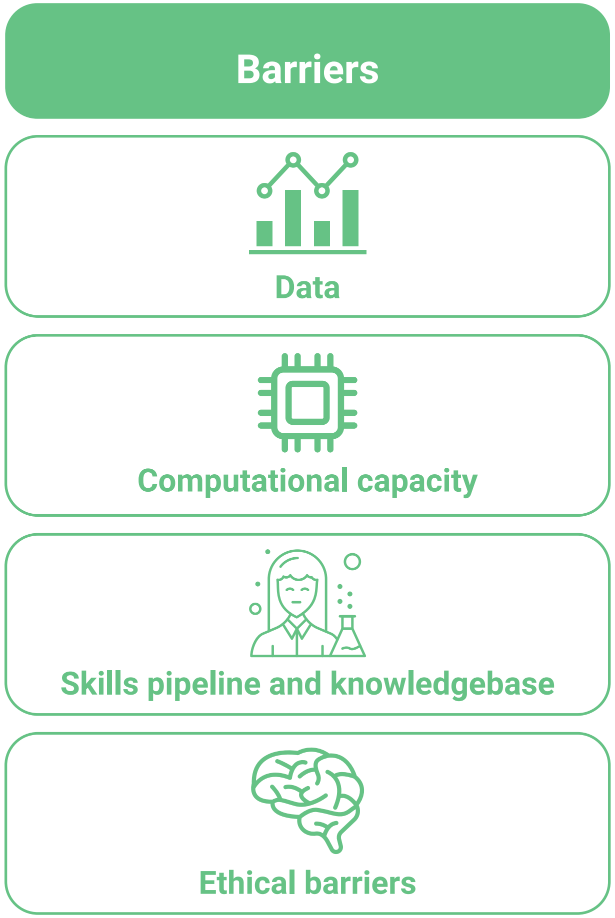
6.3. Key barriers to advancements

Despite the promise of practical advancements stemming from the use of ML and GE, there are several barriers to advancement. Some of these barriers exist within the specific technology sector, whereas others are amplified due to the two technologies coming together. Figure 11, opposite, illustrates the main thematic barriers encountered at the interface of these two fields.

Data

Data is a key barrier to future advancement – particularly the availability, quality and comprehensiveness of datasets. Information is currently fragmented, siloed and incomplete across many sectors, including medical records, genome data, omics datasets, environmental data and so on. Cell biology information is plagued by differences in sample collection, storage and processing, and metadata thus hindering comparisons across datasets and in training ML models. The black box (i.e., how and why ML models are creating inferences and predictions) also remains a challenge, particularly given value judgements and ethical considerations where human health and wellbeing decisions

Figure 11. Barriers to advancing ML and GE technologies



Source: RAND analysis 2023

216 INT_06, _07
217 Subject matter expert interviews

are to be made. Our experts also stated that success hinges on access to 'good' data.[218] Linked to these barriers, it is challenging to create accurate models with high fidelity, given the problems associated with datasets and scaling experimentation. There is a high potential for misinterpretation and false-positive or false-negative in the computational outputs generated. Note that the fundamental underpinnings of ML in quality data point to a potential focus for policy and regulation; monitoring and/or regulating the underlying data could prove effective in tracking ML and GE more broadly.

Computational capacity

As discussed previously, there are also computational barriers that arise with the rate of advancement in AI and ML and its outpacing of Moore's Law. As algorithms and the datasets that require analysis become more complex and volume heavy, computational power has become a barrier to continued advancement in this field. Despite access to supercomputers, many complex models can take a significant amount of time and processing power to create actionable outputs. Limitations in resources such as access to GPUs will no doubt hinder progress in the field, especially if select commercial enterprises responsible for developing GPUs and semiconductors become a policy lever for countries to exert competitive advantage.

218 INT_07, _09, _10, _11

Skills pipeline and knowledgebase

The lack of skilled personnel and the lack of any centralised plan for creating and nurturing a skills pipeline in this field was also identified as one of the barriers to future advancement. Some experts noted that a trend is emerging whereby AI tools such as TensorFlow and PyTorch are enabling production of low-quality publications and inadvertently reducing the skills threshold required to work in this sector.[219] If the models are flexible, deep expertise and prior knowledge about biology is not as crucial as it once was. Consequently, GE capabilities and even broader biotechnology-related capabilities become available to users who may not have the appropriate knowledge and background for safe and effective use. Furthermore, an underlying concern is that the models are not trained using appropriate data.

Ethical barriers

There are many ethical barriers to the advancement of this area, most of which revolve around underlying data used to develop and train models. These barriers include the lack inclusivity of underpinning training data, lack of standards and risk assessments at a globally aligned scale, and controls for access to data that can identify individuals or reveal commercially sensitive information.[220] [221] While the ethics of this space are vast and complex, the scope of our study does not extend to covering it.

6.4. Current developments in addressing barriers

The barriers to technological advancement are significant, but there are many current developments and commercial and political motivations to overcome these barriers in the coming decades. According to the experts interviewed in this study, numerous factors are driving advancements in technology at the intersection of ML and GE, such as the **democratisation of ML**, which is providing broad access to data and tools. Moreover, the promise of biology is itself driving advancements as companies, scientists, governments and even individuals explore the possibilities of applying ML to biology.[222]

Economic interest are also a critical factor, with extensive funding driving large language model development and the integration of ML with GE. Financial benefit can foster fierce competition from companies active in this ML, such as OpenAI, Microsoft Corporation and Google for large language models.

The promise of dramatically **improving global health** by developing vaccines and diagnostics for future pandemics and current ailments is also motivating people around the world to integrate these technologies.[223]

Other drivers include pursuit of **sustainable technologies** to generate materials like plastics and robust supply chains. On the international

219 INT_07
220 Naik et al. (2022).
221 Brokowski & Adli (2019).
222 INT_01, _03, _04, _05, _06, _07, _08, _10, _11, _12
223 INT_03, _06, _10

level, **competition with China** is driving research with ML applied to biotechnology.[224]

> 'Knowledge from diverse communities is needed to assess how these technologies are being perceived and to inform and engage the general public on both the promises and pitfalls of the technology. Public involvement could galvanize or unlock policy options that might be challenging or unorthodox.'

While it is not necessarily an incentive, a key factor that will determine how these technologies are applied and taken forward is the **interaction with the general public**. The general public will be affected by these technologies in numerous ways, particularly with regards to health, food supply and biomanufacturing.[225] Many of our experts suggested that engaging the public and considering public perception in any policymaking are crucial elements to creating and implementing relevant policies. The public can indirectly affect legislation and acceptance of technology through – for example – significant reluctance to accept GM foods, despite the genetic modification of food being proven as an efficient way of breeding crops that are safe to consume. This has led to the European Union and the United Kingdom making it extremely challenging to introduce GMOs in the market as per the GMO directive. In addition, stem cell research is still polarising among the general public, and this polarisation is compounded when GE is involved, and people take issue with scientists 'playing God'.[226]

6.5. Regulation across technology boundaries

Despite the risks and opportunities stemming from integrating ML and GE, there is minimal literature concerning relevant policies at the interface of these technologies. A more extensive and systematic study may be needed to uncover any current or emerging developments in this fast-moving area. However, to paint a picture of the complexity in policies governing intersecting technologies, we use the selective case study of AI as a medical device, where more deliberation and dialogue has advanced than in other areas of technology convergence concerning biotechnologies.

224 INT_01, _03
225 INT_03, _06, _07
226 INT_07

Technology convergence and policy challenges use case: AI as a medical device

Use of AI and ML to develop autonomous systems in healthcare has made substantive progress especially to advance digital health. This has led to not only use cases of using AI/software as a medical device but also ethical and safety considerations of such systems and how best to regulate them.[227]

Liability and accountability in AI-based decision-making tools

Legal and ethical issues around liability and accountability are a particularly urgent matter in medical decision-making tools. According to a review of ethical and legal considerations of AI in medical decision support tools[228] and a review of medico-legal risks in digital health,[229] current regulations across much of the world are ambiguous over where exactly responsibility and liability can lie, especially when patients are harmed. A common legal regime in the United States and the European Union when dealing with liability is fault-based, or negligence liability, where the plaintiff is given compensation if breach of duty, or violation of patient rights are proven.[230] Responsible entities must be identified, which in the case of AI-based decision-making tools in health is very challenging, since it is difficult to attribute blame onto an individual.[231] Some literature suggests that issues like this could be addressed by recording inputs and outputs (like in commercial flights), or by developing a unique legal status for AI such as robots to make **them** liable for their errors, but there has been limited policy development in this space.[232]

Transparency vs. the black box of ML-based software as a medical device

Many of the discussed challenges in establishing accountability or legal responsibility in the context of AI-based tools come from how opaque their algorithms are.[233] Regulators that deal with AI in medical devices, such as the FDA and sister organisations in China and the European Union, have thus far only tended to approve AI-based medical devices that use locked algorithms that cannot change.[234] However AI-based medical devices that use adaptive algorithms and respond to the changing environment, for example for different levels and amount of insulin being pumped in a diabetic based on their geolocation data, have very different policy implications.[235] Adaptive AI can often obscures decision-making processes (even to clinicians themselves) and hamper validation efforts. This lack of transparency can compound the liability determination challenge.

227 National Engineering Policy Centre (2023).
228 Čartolovni et al. (2022).
229 Oliva et al. (2022).
230 Čartolovni et al. (2022).
231 Oliva et al. (2022).
232 Oliva et al. (2022).
233 Čartolovni et al. (2022).
234 Reddy et al. (2020).
235 Reddy et al. (2020).

Part 2. Futures assessment: **exploring risks, opportunities and policy actions**

1.

Chapter 7.
Future of technology and policy: maximising the gains and minimising the risks of technology convergence out to 2045

Key findings

The group representing the United States argued that regulation should focus on end products rather than the process. They asserted that since the likelihood of preventing all harmful future applications is low, the country needs to have the capabilities to defend against biothreats on demand.

The group representing China sought to embed the convergence of AI and GE technologies in the country's growth-focused economic model and set the goal of achieving a strategic advantage in AI and biotechnology over the United States and Europe.

The group representing Europe called for limiting human GE to disease prevention and therapies. The group also emphasised the norm setting role of international standards and advocated for equity and benefit sharing in the peaceful uses of these technologies.

The game also tested reactive dynamics by providing the groups with each other's initial policy actions. In response, the teams proposed new policy actions, which were a mix of cooperative (e.g., cooperating against non-state threats, establishing an intergovernmental knowledge bank on biosecurity, increasing cooperation on IP protection measures) and competitive measures (e.g., the United States limiting one-way data flows to China, and China setting the goal of dominating AI and biotechnology supply chains). Commonly identified challenges were noted on whether existing international legal frameworks and guidelines were fit for purpose.

Existential risks were not a primary concern in the discussions.

As previously established, the convergence of ML and GE technologies is taking place in a complex system, driven by a range of political, economic, technological and other factors. While it is not possible to predict the future, futures methodologies can help imagine **possible** – and preferably, **plausible** – future scenarios, helping focus on what **could** happen, instead of attempting to guess what **will** happen. The landscape assessment which charted the historic progress and trends in technology development and the styles of policies that accompanied them provided the foundations for the future scenarios we have used in this study and, particularly, prompted ideas on where the current policy approach could benefit from changes.

We developed three distinct future scenarios, set in 2045, about the convergence of ML and GE technologies and designed a table-top game instructing participants to develop policy interventions that maximise gains and minimise harm across the range of scenarios. The participants assumed the roles of the United States, China and the European Union and presented their policies to the other groups to stimulate a second round of policy deliberations. This game ran virtually due to geographical constraints, but nevertheless served as an immersive experience for 13 expert participants and provided analytical outputs on risks, opportunities and possible policy actions rooted in the future scenarios.

7.1. Game context and future scenarios

The futures methodology of the study consisted of two main elements: the scenario development process and the design and facilitation of the seminar game. The methodological approach taken by the team is described in detail in Annex C.

The purpose of the scenario development process was to produce three future scenarios that would serve as the basis for the discussions in the seminar game. Specifically, the scenarios were intended to portray distinct and vastly different future landscapes that help uncover a wide range of future opportunities and risks rooted in them. By providing expert participants with three very different perspectives on what the future of GE could look like in 2045, enabled by advances in ML, the study team ultimately sought to stimulate a discussion on what the decision makers of today should consider considering the implications of possible futures. The scenario development process is outlined in Annex C, and consisted of identifying key drivers using the PESTLE-M as a structured framework (identifying political, economic, social, technological, legal, environmental and military drivers) based on the landscape assessment. The drivers were prioritised and the combination of their trends ultimately led to the development of the future scenarios which are outlined in Table 4, overleaf. The full scenarios can be found in Annex C.

Caveats and limitations

The findings of the game identified and discussed in the sections below are subject to a few caveats and limitations.

- The scenario methodology was adapted from the work of Gausemeier et al.,[236] to suit the study parameters. The driver prioritisation was achieved through an internal workshop with RAND staff and an internal scoring exercise based on the informed views of the study team, the landscape review and expert interviews. The driver identification and selection process may yield different results if repeated with a different group of experts.

236 Gausemeier et al. (1998).

Table 4. Overview of the three scenarios

Scenario A **Unrestrained innovation**	**Scenario B** **Innovation lags behind demand**	**Scenario C** **Innovation goes underground**
• The year is 2045. The competition for influence and resources is tense, driven by governments and profit-oriented tech giants. • Regulatory regimes are lax domestically, while cross-border regulation is strict to protect IP. • Lack of international technology frameworks due to interstate arms racing dynamics. • Scalable biological weapons, physiological and cognitive enhancements for soldiers. • Booming market for genetic enhancements: medical treatment of congenital diseases as well as aesthetic procedures. • Use of synthetic embryos made from stem cells abated fertility. • GE is also omnipresent in agriculture.	• The year is 2045. In the past two decades, countries have negotiated limitations on the militarisation of biotechnology, but little cooperation on technology otherwise. • Economic competition has hindered concerted climate action. • High demand for GE solutions (e.g., GM crops) due to environmental degradation and resource scarcity. • But innovation is lagging, with slow progress. • Most affected regions (Africa, the Middle East and South Asia) are unable to deliver technology solutions at scale for their populations. • Limited applications in medical sciences, only in case of life-threatening conditions. Robotic prosthetic limbs and brain-computer interfaces available in closely regulated private clinics.	• The year is 2045. Global powers recognised the risks of unconstrained technological competition and negotiated a robust framework of technology governance. • Regulated access to computing power, embargo on genetic sequence sharing, mandated assessment of any proposed human genetic modifications and ban on their commercial use. • East Asian epidemic in 2028, caused by North Korean lab leak instilled mistrust towards GE applications in the wider public. • However, technological progress could not be stifled, innovation just went underground, enabling a booming black market. • Pharmaceutical enhancements as intoxicants, assassinations with personalised biological weapons, synthetic embryo farms to harvest organs, 'dark tourism' for illegal GE services.

Source: RAND Europe (2023)

- The scenario development process was conducted between April and May 2023, and the findings and recommendations reflect the available information within this period.
- The entire study was conducted at the unclassified level using only open-source literature.
- Due to the high number of scenarios the possible combinations of drivers and their projections could produce the scenarios and any underlying assumptions are not meant to be interpreted as predictions or forecasts.
- The game was conducted as a table-top exercise with findings are based on the informed views of 13 experts with limited geographical coverage, aligned to the areas of interest for this study.
- The time constraints of the seminar game limited the quantity and granularity of the data produced by the participants. Consequently, the policy actions identified and discussed within this report serve as a primer for a full-scale study that could be commissioned by engaged policymakers.

7.2. Game outputs: policies to maximise gains and minimise harm

This section presents the key themes that emerged from the discussions during the table-top exercise. The themes below are based on the first set of discussions focused on the initial policy actions taken by the country groups against the objective of minimising harm and maximising gains across all three future scenarios in 2045.

United States

The US group produced five policy actions in the first instance (listed in Annex C). These were focused heavily on national security centric regulation while also on fostering R&D, more specifically augmenting the population to an equal baseline of health and wellness as a starting point, indicating the start of the posthumanism era. The underlying narrative of the discussions in the US group pertained to needing to regulate the applications – the end-product of these technologies rather than the development processes per se. While AI/ML may need to be regulated upstream of application, its application to biotechnology requires outcomes focused regulation; the focus should be biology and not the algorithm. The US group collectively held the view that it is unlikely to be able to prevent all harmful applications down the line. The focus, therefore, needs to be on defending against and mitigating such risks, and on the ability to respond at pace. The group also argued the need to stop relying on export controls, as that would incentivise countries and trading blocs to produce their own markets to prevent themselves from being left behind.

> ‘If you’re worried about some arbitrary threat coming out of an angry 16-year-old’s lab, then really the only way to counter that is to be able to create a medical countermeasure to an arbitrary threat on demand at will and at scale’ (RAND Europe Seminar game, 5 July 2023).

China

The China group produced three policy actions in the first instance (outlined in Annex C). There was a heavy focus on economic growth entwinned with technological progress and on gaining competitive advantage via dataset acquisition and focusing on IP laws. The theme of strategic advantage was predominant, looking to ensure 5 per cent annual growth, with a focus on ensuring that China's products must pass the 'international sniff test' (e.g., learn from the mistakes of Sinovac). Similarly, China's ability to centralise and aggregate vast amounts of its population's data is seen as advantageous when compared with regulations such as the EU's General Data Protection Regulation or the Health Insurance Portability and Accountability Act (HIPAA) of the United States; given access commercial enterprises would flock to China for product development and testing.

While the focus of the China group was primarily on protective strategic advantage, there was limited consideration given to biodefence in contrast to the United States and the European Union. Perhaps the only related measure amounted to the ban proposed on use of any weaponisation or military operations underpinned by genetic traits given the homogeneity of the Chinese population and the increased risk perceived.

Conversations also touched on the theme of ethics where it was felt that certain measures taken to fortify security or economic growth, which may seem authoritarian, such as state access to all academic and private data, may not be considered unethical in the same way as it is through a western lens.

> 'It was discussed that what may be considered "ethical" in China could be different to what is considered ethical elsewhere and policymaking will need to consider this distinction' (RAND Europe Seminar game, 5 July 2023).

Europe

The Europe group produced four policy actions firmly embedded in the precautionary approach with a heavy focus on security and equity. The group was largely cautious in its stance on GE, with a focus on defensive measures rather than driving innovation. The group agreed that human GE should remain restricted to disease prevention and therapies, but not in the human germline in its current state. They did not however proclaim that this temporary restriction would be their long-term policy and suggested they could be open to changes once the underlying science proves to be safe to use.

> 'The reason for starting with disease prevention is that there can be no guarantee of safety until these technologies are actually used. There will be a period of years of clinical research which would ultimately decide whether something is safe or not. It's not about saying no forever to anything' (RAND Europe Seminar game, 5 July 2023).

A high-level recommendation made by the group suggested adopting a three-stage approval process on GE: democratic engagement on whether society should allow it; clinical trials to determine whether it is safe and clinically desirable; and ethical reviews to examine matters of access and equity. Discussions around equity also had a distinct global lens to ensure countries are not shut out from the technological developments and agricultural innovations that they would need to facilitate their adaptation to the adverse effects of climate change.

The group expressed doubts about the suitability of the current international legal regime on biological weapons given their general-purpose criteria making it difficult to implement in a meaningful way. Instead, they focused on the importance of **international technical standards** (for commercial products and services) and the room for **normative frameworks** to be developed internationally alongside **soft law**.

7.3. Game outputs: reactive dynamics

In the second part of the game, participants were asked to examine the policy actions produced by the other groups and develop course corrections and capture reactions to other country policies.

United States

The US group concluded that the actions proposed by the other two groups (e.g., China's competitive R&D campaign or the European group's ban on non-treatment genetic engineering) would not cause them to course correct significantly but introduced one new policy and made some amends to existing policy. The US group felt that as the China group was stepping up its efforts in the genetic data acquisition field, the US group would need to **limit one-way data flows to China and find ways to restrict Beijing's access to US and Allied entities**. Nevertheless, participants noted that while some limitations should be put in place, the United States should not and could not mimic the autocratic regime of China.

A new US policy action proposed a cooperative measure, intended to bolster collective biosecurity globally. The US group pointed out the need to make a clear distinction between states and non-state actors when addressing the non- and counterproliferation of biological weapons. Participants suggested that the misuse of biotechnology by individuals or groups, be they terrorists or cults, is not in the interest of any government, and hence there could be grounds for intergovernmental cooperation in this area to reduce threats from non-state actors collaboratively. One of the ideas for what that could look like was the establishment of a knowledge bank about biosecurity, standards and exercises. Countries could contribute to and access this institution to prevent individuals from using AI and biotech knowledge and innovation to harm others as well as to tap into collective best practices on bolstering biodefence.

> 'China, North Korea, and Iran also do not want to die of bioweapons. They are willing to come to the table on these sorts of issues. There are places where we have mutual interests'
> (RAND Europe seminar game, 5 July 2023).

China

The response of the China group to the other two entities consisted of a mix of small tweaks to the initial policy actions as well as two additional policy proposals. First, the policy of aggressive R&D investments was expanded to include strategic investments in the biotechnology supply chain and manufacturing capabilities, to create explicit dependencies on China among the rest of the world. The second change concerned **ensuring the permissiveness of the Chinese regulatory ecosystem** in the service of Chinese ambitions for a strategic advantage in biotechnology.

The first of the two new policy actions adopted by this group focused on agriculture. The participants discussed that climate degradation and the systemic effects of climate change present a significant challenge for China, concerning food supply, public health and economic growth, which are ultimately linked to regime stability. Consequently, the China group identified the **use of GE applications in agriculture** as a new priority in the seminar game.

The goal of the second new policy action was even more ambitious than some of its previous policy goals and set the ambition of ensuring China's dominance in AI and biotechnology supply chains. The group noted that a current weakness of China lies in its lack of indigenous capability to **develop microprocessors to train large language models**. Therefore, the development of this indigenous capability was seen as a necessary part of the effort to secure supply chain dominance.

Europe

On receiving the initial policy actions from the other two groups, the European group perceived that there was **not enough focus on the existential risk of biothreats and argued that there should be more focus on building up the capabilities to defend against such threats**, both engineered and natural, including pandemic-level threats. They also noted that while the proposed cooperative measures held promise, the feasibility of working together internationally is questionable. Specifically, the group argued that applying internationally developed regulation or guidelines down to the national level could be challenging, as evidenced by the example of the Biological Weapons Convention and the challenges the European Union faces over member state adoption and adherence. The group also voiced their disillusionment because of how access to technologies and considerations of ethics and equity were not central to the conversation beforehand.

The European group did not amend their initial list of policy actions. However, they proposed two additional actions; to **proactively increase cooperation on IP protection measures to counter aggressive, predatory behaviours** and prevent biotechnologies from becoming siloed, and to ensure that **the risks and benefits of AI and biotech are considered not only at the national level, but also at the individual level**. They argued that if an innovation were to not involve humans, its implications in legal liability should be considered in policy development.

Key reflections from participants

The participants assumed the roles of the country groups and provided varied perspectives that underpinned their policy proposals, as outlined in Table 5, below. Some commonly identified challenges across the groups were noted where a prevalent view was that international outfits and conventions (e.g. the Biological Weapons Convention) are not fit for purpose to influence and implement national level change and that for these organisations to be impactful they need more direct influence and incentives. This view is in line with the landscape assessment presented in this study, whereby although international organisations filled a vacuum in providing ethical and scientific guidelines, they were not able to influence national policy explicitly. The group also agreed on the value of public dialogue with regards to technologies and seeking common ground for collaboration when addressing bioterrorism and national security. These reflections from the game crucially underpin the key recommendations in Chapter 8.

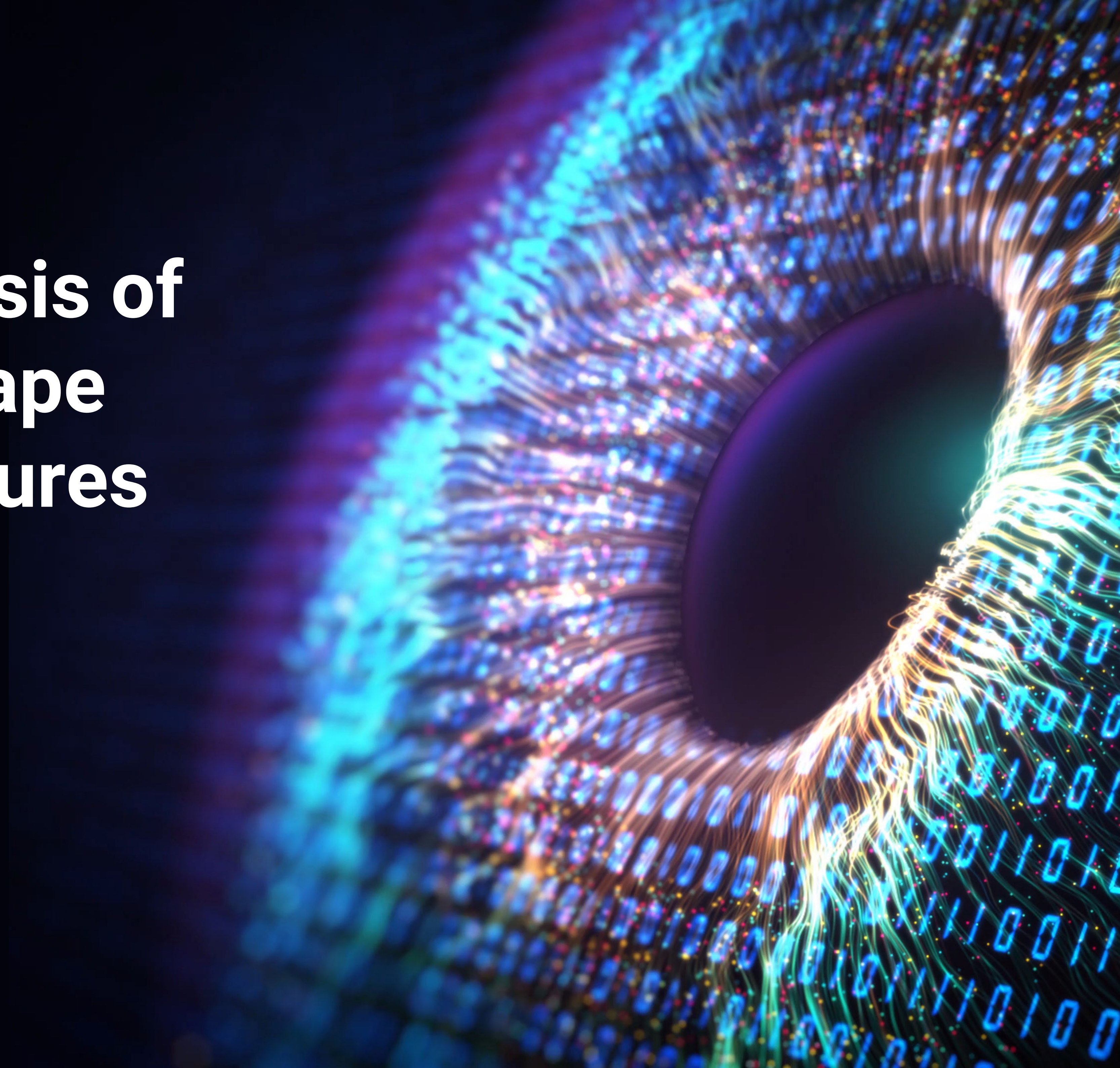
Table 5. Key perspectives and regimes that underscored the policy actions and discussions in the country groups

Country	Setting	Ethical perspective	Policy approach	What should policy look like?
United States	Democratic system requiring public input but with the challenge of having to control the cons of negative uses of biotech/ML applications (e.g., bioweapons)	Focus not just on potential harms to human health but the democratic inclusion of the public voice and opinion	Focus on optimisation biotechnologies can foster for the human body to aid in quality of life; mitigate the risk of individuals using technology or knowledge in a dangerous way (e.g., bioweaponry); tailor R&D efforts to counter rivals like China and use countermeasures to gain competitive advantage	Proactive policies to boost defences, to be one step ahead of malicious actors; avoid black market by controlling specific use cases of AI/biotech that are rare and malicious; make a distinction between what state actors and non-state actors should/should not do
Europe	EU-member state power dynamics at play with internal tensions as well as complex EU–UK dynamics	Ethics-centred perspective that makes it the only group that brings up issues of human rights and inequality, perspective of access and equity	Risk averse because of perceived potential harm of biotechnologies on environment and crops and people; very pre-emptive in policymaking, with a very cautious, safety-oriented approach	Since technologies evolve too fast, future proofing framework is as important as content itself; focus on mutual interest; more investment in 'extra-legal' mechanisms through which best practices, standards and guidelines can be developed; consider the way people oppose technology and their agendas (e.g., safety, big business, justice and equity)
China	An authoritarian regime with legitimacy based in economic growth	A perspective that can be seen as unethical from a western lens when assessing state control of data but could be seen as ethical by Chinese nationalists looking to secure advantage and progress for society	Less risk averse in innovation with suggested use of competitive advantage investments and acquisitions, IP protection and state control of assets	Sovereignty-based policy with which independence on food security and sustainability issues are of utmost importance, and biotechnology is a means to these ends

Source: RAND Europe (2023)

Part 3.
Synthesis of landscape and futures

2.



Chapter 8. Conclusion: risks, opportunities and policy considerations

8.1. Summary

The underlying technologies and applications for ML driven GE are advancing substantially across the globe. This presents a broad range of opportunities and risks, and effective policy is needed to leverage such opportunities and mitigate such risks. However, developing appropriate policy actions requires that one considers not only the intersection of these technologies but also their access, and dual-use applications. As emerging technologies mature more quickly, and as information is disseminated more rapidly – often making technologies more accessible to the non-technical users – critical analysis is needed to address the complexities of integrated technologies that are compounded by international relationships.

This pilot study has laid the groundwork for analysing the intersection of GE and ML, and in doing so has exposed a series of important themes, findings and recommendations. It involved developing a systematic and generalisable approach for exploring the interaction of emerging technologies with their key prevalent policies while considering multiple state and geographic regions, initially including the United States, the United Kingdom, China and the European Union. This approach essentially considered policy and technical developments in unison and parsed its practical applications and implications, not just the underlying technologies. Furthermore, it involves a new policy classification framework that can be extended to additional technologies and geographic regions. The approach of learning from historic trends and assessing policy styles can inform future policymaking agendas in many sectors. Through the detailed analysis of timelines for both technical developments and policy, in various countries, we demonstrate that as emerging technologies accelerate, activities across the globe are intimately related. Siloed development and policy generation are no longer viable options.

Pervasive themes arose during the analysis of technological and policy developments. These themes include the inherent interplay between technological and policy developments, the value of international brokers, sets of risks and benefits, and contextual aspects for policy development, all of which are referred to in the sections, followed by recommendations.

8.2. Discussion: learning from the interconnectedness of technology and policy

As the landscape analysis has shown, the milestones in ML and GE technology development and the relevant developments in policy relate to each other with a synergy that goes beyond the geographies of the United States, the United Kingdom, China and the European Union to the global stage. Most importantly, the regulation-focused developments in ML are visible in more recent times compared with the flurry of activity seen in the GE policy timeline, which has illustrated a precautionary and regulation heavy approach. The AI and ML policy timeline tells a story that is linked more to the earlier waxing and waning of government investment and funding in AI and to the consequent 'winter' or R&D droughts, depending on these top-down interests. The dominant policies observed were pro-innovation and focused on economic growth, whereas the more recent activity starting in as late as 2021 is focused on regulation and risk. The AI timeline also shows the significant role played by China's proactive approach to AI and economic growth, and how other geographies have reacted to those approaches.

The GE timeline was led primarily by the United States and United Kingdom and in the earlier years of the 1940–1970s, with instances of progress in one country spurring progress in the other, and the European Union making its own mark in developmental GE studies. These timelines highlight how technological development and the relevant developments in policy relate to each other in a dynamism that goes above the national levels of the United States, the United Kingdom, China and the European Union. A development in either technology or policy in one geography can encourage or catalyse a development in another geography.

This interdependence can make management and regulation challenging, but intermediary brokers may help. Coordinated global policy development lags behind technological advancement, and responsive policies have primarily been driven by intermediary brokers like the UN, OECD and WHO, that have stepped in to fill a vacuum on guidance experienced by developers of technologies. The proactive approach is the main purview of international brokers. The proactive styles of policymaking in GE and ML point to the significant broker function of international or supranational organisations. The convening power of the OECD, UNIDIR and the WHO around implications of GE and ML for society and setting guidelines that go beyond national-level plans are noteworthy. While there is a large body of research on normative functions served by many international actors, we limit our study to the role of select supranational organisations that have been prominent in the ML and GE sector; it is by no means exhaustive.

Alarmingly, there is no evidence of any policy development and deliberations being pursued at the intersection of technologies like ML and GE, and this exacerbates the absence of proactive assessments. Many national biosecurity strategies are now starting to cite AI advancements, and mention the interactivity between human, animal and plant advancement. Further development in policy regarding the intersection of AI and GE would benefit from considering the lessons learned in both GE and AI policymaking thus far. The proactive and pre-emptive efforts in GE have been successful, whereas the reactive and legacy-based approaches in AI have been less successful, pointing to the need for balance, so that there is room for:

- Long-term proactiveness that ensures constant dialogue about potential futures with the common good in mind

- Pre-emptive enough caution to help prevent harms to humans, animals and the environment without stifling innovation
- Short-term reactiveness to allow for real time, measured but appropriate policy responses to issues as they emerge
- A firm understanding of where legacy policies and regulation can (or not) be applied to novel technologies so as to take advantage of already-existing frameworks and thus potentially saving the time and effort of reproducing policies.

8.3. Discussion: risks and benefits to society and future considerations

Benefits

The integration of ML and GE has enabled significant and novel capabilities that have the potential to revolutionise society as we know it. Some of these capabilities are:

- Prediction of functional links between genes; prediction of effects of genetic manipulation
- Real time understanding of how cells, genes, proteins and molecular machinery functions and interacts with one another
- Amplification of scale and rapidity where scale of genetic manipulation and synthesis can be done at scale with more rapid canvassing of large datasets and generation of functional outputs
- Improved data utility by use of ML to plug data gaps and generate clusters, connectivity in data
- Improved targeting of genetic components for either drug design or delivery, or design of other functional compounds like biofuels.

ML is a powerful tool that can help speed up and scale up screening processes that are necessary in biotechnology. This makes it possible to create effective vaccines faster, speed up drug creation, and predict the evolution of pathogens. It enables the capability to sort through a large database with genetic parts and extract what's useful. ML also allows for more in silica work before moving to the riskier physical side of laboratory work. Creating enzymes to eat plastic and pollutants (e.g., forever chemicals), artificial meats and biofuels could dramatically alter the world we live in in the near and distant future. These technologies are possible solutions to problems of global health, climate change, health equity and other pressing issues.[237]

Most of the implications and thus applications of these advancements fall under the medical sector with some uses in agriculture, energy and climate, but there is potential for their use in other sectors like the military, national security or human performance. Further acceleration of these technologies and consequent increased benefits requires barriers to be overcome, such as developing better compute power with access to powerful GPUs, access to good and integrated datasets for model training, development of a progressive and sustainable workforce, ethical considerations of access to technologies, and transitioning proof-of-concept experiments at scale in a real-world setting.

Risks

One the risks of technology convergence is the dual-use nature of ML when applied to GE. While these technologies can lead to breakthroughs that may vastly improve lives, they may also be used for nefarious

237 Subject matter expert interviews

purposes. The creation of bioweapons,[238] dangerous chemical compounds and malware are some of the dangers of unfettered access to these technologies. Those working on the ML side of the intersection of ML and GE are not necessarily aware of the downsides of the technology to the same extent that those who work on the biotechnology side are.[239]

Although the democratisation of ML provides access to powerful tools that may benefit people and developing countries around the world, this aspect of ML can also provide powerful capabilities for misuse. Easy access to ML tools can empower users; however, lack of sufficient knowledge to resolve complex problems can lead to poor analysis and inaccurate scientific studies.[240] Many scientists are concerned that too heavy a reliance on AI in science may lead to a cessation of human thinking and irresponsible use.[241] Moreover, more *in silica* work could have workforce issues and lead to fewer laboratory scientists being employed, since the demand for bench scientists may be significantly reduced. Talent pipelines might be limited, making it difficult to find skilled workers, since the skill sets are so new and continuously changing.

Some additional risks are competition with other countries, such as China, which prioritises their own bioeconomy and has established itself as having superior access to data. China has declared genetic data to be a national resource and is not hampered by HIPAA[242] or privacy and human subject protections, like the United States and the United Kingdom are.[243]

Overall, developments are moving faster than the ability to govern, so technology presents both risks and benefits. Regulating the use of ML when applied to GE, and preventing harmful uses while preserving innovation, is risky due to the many unknowns with large language models. Predicting when and how models will perform a specific capability or task is not known until the models have completed the task in question.[244]

Future considerations to minimise risks and maximise benefits

This section proposes considerations for moving the dial on policy development for governing this intersection of technologies based on the evidence that arose from the landscape assessment and the table-top game.

When developing policy, context matters, and there are key considerations that should feed policy development in this regard. First, there is a significant difference in culture between GE and ML communities, and the policies that follow must recognise this to build consensus and propose measures that are relevant and relatable to these communities. For instance, the GE community has primarily been cautious given the impact on human health whereas the ML community tends to be more proactive in pushing forward developments and making

238 Currently, the models are not yet advanced enough for anyone other than an expert in biology to develop biological weapons but access to ML has lowered the barrier to developing these weapons and more bad actors could have access in the future (INT_11).

239 INT_03, _07

240 INT_03, _07, _10

241 INT_07, _10

242 HIPAA refers to the Health Insurance Portability and Accountability Act of 1996, which governs how health care providers and insurers can see and share health information. More information can be found at https://www.hhs.gov/ (as of 16 October 2023).

243 INT_01, _04

244 INT_06, _07

them accessible to the masses. Policies that focus on education and awareness could be beneficial in bridging the gap between the two sectors. More awareness raising of the applications of the technology is needed so that the narrative is not lost in debating the technical aspects of the technologies. Lack of awareness of technology and its potential also makes it challenging for regulators to develop sound policies, as many do not understand the technologies.

Second, related to improved education and awareness is the requirement to consider public perception, and elicit public dialogue and acceptance for both technology use and development of the relevant policy tools to govern it appropriately. Awareness of public perception can be especially important for addressing ethical issues.

Third, technology is clearly moving faster than we can govern, and many experts suggest that controlling data access can slow it down. Access to data opens both political and ethical concerns with regards to who has access, why and how to ensure there is informed consent. There are wildly different views in this regard, and of course democratised access brings with it vulnerabilities concerning dual-use technologies and potentially poor science.

Fourth, policies must also withstand changes in government administrations and consider the international dimension and competitiveness.

Lastly, there is a large amount of unpredictability at the intersection of technologies. Although there has been a move to govern at the application stage of technology rather than regulating technical platforms, the unpredictability of uses and applications can create a very reactive policy environment, which must be balanced with a proactive and pre-emptive approach in tandem.

Policy mechanisms and styles to consider

A multitude of policymaking styles of AI and GE regulation has been used over the last few decades. There are pros and cons that come with each style and remit of policymaking.

The benefit of adopting **pre-emptive** approaches is that by being risk averse to new developments in GE, policymakers have largely avoided harmful and unforeseen consequences in human health and the environment. The pre-emptive approach is important to consider, especially when technology is new and there are limited studies, for instance, in the case of gene drives.[245] The risk in this policy style is the potential of missed opportunities and benefits, where for instance the lack of pre-emptive regulation in AI has culminated in immense opportunities for societal progression.

The most obvious benefits of the **proactive** approach are the longer view and expert-led perspectives that are incorporated in developing policy. As was discussed in the previous section about the international organisations as brokers, without the proactive approach often adopted by supranational organisations like the WHO, the humanitarian, ethical angle, and many of the in-depth considerations of GE development, may not always be considered at the national level. The proactive approach brings with it a thoroughness of depth and scope in policymaking as well as the involvement of multiple relevant stakeholders, thus culminating in sound policy, especially when based on otherwise ambiguous and complicated ethical grounds. A risk in adopting the proactive approach, however, is that it is too long term in thinking and so inclusive of stakeholders that it may not be pragmatic enough for national-level policymakers to adopt (national policymakers have term limits, must be accountable to specific constituencies, etc.) hence this may be one of

245 European Parliament (2020b).

the reasons why our analysis showed limited examples of national-level policymaking that was proactive.

Where the proactive regime is thoughtful and considered, the **reactionary** regime is situational and direct. This has the benefit of allowing innovations to flourish since there is light touch regulation, which is especially beneficial for innovations in GE and AI because many aspects of both are constantly evolving quicker than regulation can be debated, formulated and implemented. However, an immediate risk of adopting solely a reactionary approach without policy in place *a priori* is that negative consequences could arise from innovations in a way that has immediate ethical ramifications. The bans in China that resulted from the He Jiankui controversy, for instance, also resulted in a halt on innovations in the field of GE.

A benefit of **legacy** regimes is that they rely on pre-existing regulations or guidelines, at times from other sectors, making it convenient and pragmatic enough for national-level policymakers to consider fast-paced development in the fields of GE and AI. As previously discussed, the United States has done this successfully through its coordinated framework. Too much reliance on legacy policy however is that such (older) guidance may not apply to certain aspects (data protection, etc.) and implications of new GE technologies that may not have existed in the domains that such policy was originally developed for. New and flexible policies are needed to regulate the intersection of ML with GE and wider biotechnology. Yet, many challenges exist when enacting any new policies. Nonetheless, the need to be proactive and balanced is crucial to regulating this space successfully. As one expert said**, 'You don't win the space race by playing defence all the time.'**[246]

The tension between the need for regulation to avoid catastrophes through the misuse of technologies and the need to encourage innovation is a major challenge.[247] Regulation of this area has not been a specific agency's or country's problem to fix, and no incident has yet occurred that has exploited that issue.[248]

8.4. Key recommendations

Drawing on the analysis throughout this study and the discussion of critical themes provided above, the following are primary high-level recommendations for policymakers and research-funding institutes to consider in order to bring due attention to the convergence of these technologies and to balance risk mitigation with opportunity realisation. The recommendations can also be applied to other technology sectors at the cusp of convergence.

1. **Concurrently analyse the trajectory of both policy and technology development in multiple countries at scale for the emerging intersections of diverse technologies.** This can foster better understanding and planning of international cooperation and/or competition. Considering the interaction between multiple emerging technologies and their consequences across geographies, it is critical to study technology and policy in tandem and through a multilateral and international lens for developing appropriate and effective policies. This could also spur international competition in technologies and applications, which need not always be viewed as negative. Especially with AI and GE, technology developments and national actions plans in one region can spur broad advancements

246 INT_01
247 INT_01, _02, _03, _04, _05, _06, _07, _08, _09, _10, _11, _12
248 INT_12

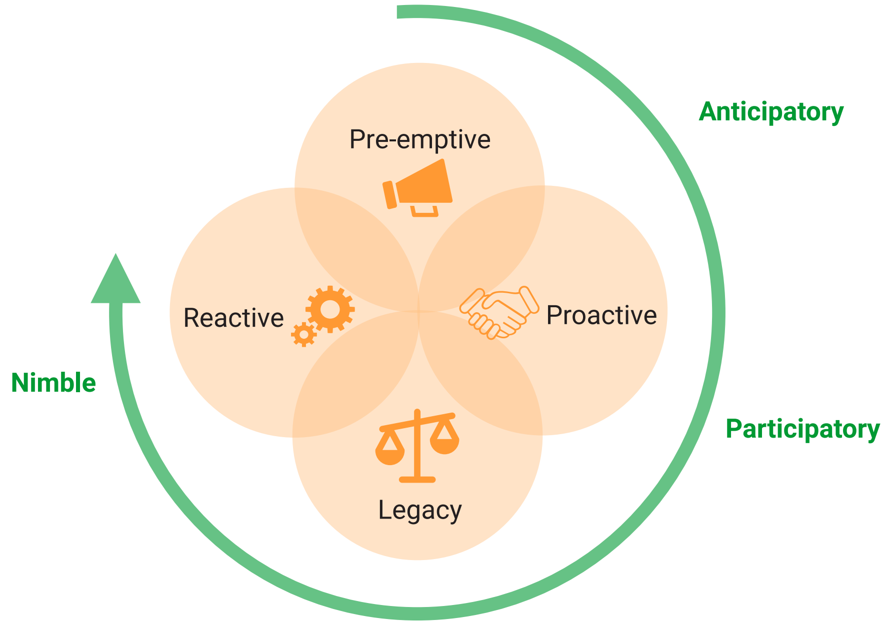
elsewhere. A practical next step could be a large-scale study built on the outputs of this study to encompass wider geographies and policymakers alongside technical specialists.

2. **Incentivise international coordination and direct national level influencing from supranational bodies and forums.** Transparency and collaboration (where appropriate) across regions are critical in policymaking. This requires incentivising international collaboration and coordination, which may be achieved or enhanced with the following actions:
   - Identify and clearly publicise potential national and international stakeholders in a sector or application of interest, thus fostering more active communication.
   - Increasingly leverage and coordinate existing international brokers, and develop a stronger influencing mandate that trickles down to a national level, especially given evidence that these bodies can often lack any ability to influence national plans.
   - Encourage the technical community to communicate more frequently to non-technical audiences.
3. **Governments and international brokers should develop and incentivise the use of international standards that can foster international agreements (for commercial products and services).** Indeed, common standards are often discussed with respect to AI, but there is room for normative frameworks to be developed internationally.
4. **National-level policymakers should create frameworks and opportunities to support more public education and deliberative dialogue to support sociotechnical progress across society.** Evidence has illustrated that public perception can have a huge influence on technology adoption and adaptation as seen in the case of the EU GMO directive. Including the broader social voice in this importance space may allow access to untapped opportunities for considering different types of policies.
5. **Governments should develop a centralised workforce development plan that targets all levels of education and targets both ML and GE and their interface.** Capacity and capability building are critical at the convergence of technologies both for those who are developing untested technologies and for those who are making policies. Education programmes focused on workforce development and skills-generation in a holistic way can provide a policy lever to enable more cross-disciplinary training across atypical sectors (e.g., geology and genetics).
6. **Governments and national policymakers should adopt both upstream and downstream regulation, pertaining to underlying data and technologies, and applications and outcomes respectively.** Indeed, our evidence shows that both types of regulatory stances are required, given the complexity of the convergence of ML and GE. While ML could be regulated upstream at the hardware stage, and GE can be regulated upstream to some extent via data access controls, downstream regulation with the ability to be reactive and agile is critical, given the unknown applications that will arise from the intersections of these technologies.
7. **To track and regulate AI and GE, policymakers should regulate the accessibility and distribution of the underlying data** as an upstream regulatory stance. While hardware, software and computational speed will change faster than any regulatory body can adapt, different classes of data likely will not, and they can be archived. For both GE and AI, data is fundamental and critical, and the data requires global accountability and transparency for effective collaboration and regulation.

8. **Governments should consider establishing a knowledge bank about biosecurity measures, technology standards and frameworks.** This would enable countries to contribute to and tap into collective best practices on bolstering biodefence. This could be emulated much in the way intelligence is shared across Interpol or large genetic knowledge libraries such as the Global Initiative on Sharing All Influenza Data, but with access controls built in to prevent misuse.

9. **To accommodate the fast pace of technology advancement and the uncertainty with international relationships, policy must be anticipatory, participatory and nimble.** With recent advancements and increased speed of knowledge dissemination, technology emergence is outpacing government policymaking, which for the United States, the United Kingdom and the European Union is relatively slow by design. This will make it increasingly difficult to manage technology-based risks and opportunities. Thus as technology develops and matures, it could be beneficial to follow a concurrent policymaking path using the varying style of policymaking across the technology life cycle. Just as there are technology maturity and readiness levels, one may consider a policy maturity scale, which should accelerate as the technology progresses, as illustrated in Figure 12. At the early stage of technology development, when the technology may be entirely untested, policies may adopt a pre-emptive stance to prevent harm and misuse. As technology matures to validation in a lab setting, proactive policies could help progress the technology in an ethical manner. This would necessarily entail engaging in participatory dialogue with scientists and with public and private enterprises. Once the technology has been trialled in a real-world setting and its use cases become apparent, legacy frameworks could be used and a nimbler stance of reactive policymaking could be adopted against new and emerging use cases. As technology takes a different direction or evolves significantly, the same cycle could be repeated. While this is a simplified view of technology and policy development, the principles are noteworthy and could be useful to test and operationalise using in a sandbox setting.

Figure 12. Policy development lifecycle in parallel with technology maturity



Source: RAND Europe (2023)

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Annex A. **Landscape methodology**

Desk research

For the desk research, we first identified the key search terms to use in search engines to look for in academic and grey literature. We focused on terms that were related to the geographies of interest (the United States, the United Kingdom, China and the European Union), policy and regulation, AI and ML, and biotechnology and GE (see Table 6, below). We pulled from team members' expertise in the field to identify an initial round of key terms, which were then used to input in the PubMed Medical Subject Headings (or MeSH) term vocabulary thesaurus to explore related terms. Through this process other terms were added, collapsed or taken away.

We then combined these terms in various combinations of strings into Google Scholar and PubMed to obtain relevant sources on the development and policy around AI and biotechnology in the United States, the United Kingdom, China and the European Union.

For each search string combination in PubMed or Google Scholar, we limited the year to 2018 onwards and limited our sources to those in English. We reviewed the first five pages for relevant articles. The citations of each source deemed relevant was inputted into an Excel list. This list was reviewed, and three to five academic and grey literature sources were selected from each search combination, with reviews, state-of-the-art coverage, and articles with a breadth of topics covered prioritised. We recorded references and links with each document to snowball as well.

Table 6. Search terms

Search terms	Geographies of interest: ('United States' OR America OR USA OR US OR American) ('United Kingdom' OR UK OR 'Great Britain' OR England OR Scotland OR Wales OR 'Northern Ireland') (Europe* OR EU OR 'European union') ('China') Policy and regulation: (policy OR legislat* OR jurisprudence OR litigat* OR governance OR law OR legal OR ethics) Artificial intelligence and machine learning: ('artificial intelligence' OR AI OR A.I. OR 'computational intelligence' OR 'machine intelligence' OR 'neural network*' OR 'machine learning' OR 'deep learning' OR 'hierarchical learning' OR 'predictive model*' OR 'computer-assisted' OR 'computer assisted' OR algorithm* OR 'natural language processing' OR nlp OR 'pattern recognition' OR 'reactive machines' OR 'theory of mind') Biotechnology and gene editing: (((gene* OR genomic OR embry* OR DNA OR 'directed molecular evolution') AND (edit* OR manipulat* OR modif* OR mutation OR predict* OR engineering OR techniques OR enhance* OR therap* or shuffling)) OR biotech* OR bio-tech* OR 'biomedical tech*' OR biomed* OR bio-med* OR 'gene drive technolog*' OR 'metabolic engineering' OR 'targeted gene repair' OR bioinformat* OR bio-informat* OR 'computational biolog*' OR diagnostic* OR therapeutic* OR 'drug develop*' OR 'medication development' OR 'pharmaceutical development' OR 'drug target prediction' OR 'precision medicine' OR 'personalized medicine' OR 'predictive medicine' OR 'individualized medicine' OR ((medical) AND (device OR equipment OR tech*)) OR crispr OR 'synthetic biolog*')

Source: RAND Europe (2023)

Once identified, we reviewed the sources and extracted data into an Excel sheet, recording when and where main developments and policies took place. We also extracted information about their implications.

Analysis involved synthesising the findings from the construction of the timelines of AI and biotechnology developments and related policies.

Horizon scanning

The study team used a news aggregator to gather articles relating to recent developments in AI and biotechnology. This was not intended to provide a comprehensive list of every article relevant to this study, but rather to give an indication of developments happening in – and at the intersection of – these technologies. The study team set up two feeds: one for academic literature and the other for grey literature and news sources.

The team began by conducting numerous online searches using the Google search engine to find relevant articles and the publication or platform they were published on. The team then used the Really Simple Syndication feed from these sites, which contain details about every piece of content the site has published. The feeds in Table 7 (below) were used for this study.

Table 7. Lists of academic feeds and grey and news feeds

Academic feeds	Grey literature and news feeds
• ACS Synthetic Biology: Latest Articles (ACS Publications) • Bioinformatics Advance Access • Bioinformatics Current Issue • BioMed Central Bioinformatics • bioRxiv Subject Collection: Bioinformatics • Computational biology and bioinformatics: nature.com subject feeds • CRISPR-Cas systems: nature.com subject feeds • Frontiers in Bioengineering and Biotechnology | New and Recent Articles • Gene Therapy • Genetics: nature.com subject feeds • Harvard Gazette • JMIR Medical Informatics • Journal of the American Medical Informatics Association Advance Access • Latest Results for Artificial Intelligence Review • MaryAnnLiebert: Human Gene Therapy: Table of Contents • MaryAnnLiebert: Journal of Computational Biology: Table of Contents • Max Planck Society – Research • MedTech Intelligence • MIT Technology Review	• Addgene • AI News • Artificial Intelligence • Biology News – Evolution, Cell theory, Gene theory, Microbiology, Biotechnology • BioPharma Dive • BioSpace – Biotech News • Biotechblog • Biotechnology News – Biology News • Cell Biology News – ScienceDaily • Computational Biology News – ScienceDaily • Computational Intelligence and Neuroscience • CRISPR • FierceBiotech • GEN – Genetic Engineering and Biotechnology News • Gene Therapy News – ScienceDaily • Genetic Algorithms: algorithms and programming tips • Genetic engineering • Genetics News – Genetics Science, Genetics Technology, Genetics

Academic feeds	Grey literature and news feeds
• National Institutes of Health (NIH) • Nature Biomedical Engineering • Nature Biotechnology • PLOS Computational Biology • ScienceDirect Publication: Artificial Intelligence in Medicine • ScienceDirect Publication: Journal of Biotechnology • ScienceDirect Publication: Metabolic Engineering • Synthetic biology: nature.com subject feeds • University of Cambridge – Research • Yale Scientific Magazine	• Genetics News – ScienceDaily • Johnson & Johnson News Releases • LaBiotech • Labiotech.eu • Natural Language Processing • Press releases for AstraZeneca • Section Page News – GenomeWeb • ThePharmaLetter

Source: RAND Europe (2023)

Two team members reviewed these sources and flagged articles relevant to this study. These articles, as well as selected additional relevant articles found by team members, were entered into an extraction template. Five researchers coded 124 articles found through the news content aggregator and additional research. The extraction template consisted of the following categories:

- Name of the technological development or innovation
- Source (URL)
- Year
- Country
- Field of technology
- Field of research
- What was the application?
- Advancement–capability
- Technological maturity (TRL)
- Impact or objectives
- Barriers.

The field of technology indicated whether an article was about developments in AI or biotechnology, or related to both. The field of research indicated more specifically areas such as synthetic biology, computational modelling and drug development. The application indicated how the development was used, such as drug candidate development or cancer diagnostics. The advancement–capability category indicated how this development was novel. Team members estimated the technological maturity (TRL) value to gauge the relative maturity of the development. The impact indicated the broader implications of the development, while barriers included areas such as where developments were still at a conceptual stage, or where more testing will be needed before more widespread adoption of a technology.

Expert interviews

We conducted 14 semi-structured virtual interviews (typically of 60 minutes each) with individuals from government, academia, non-governmental organisations and industry. All individuals interviewed were subject matter experts in GE, synthetic biology, ML and/or biotechnology. The research team developed an interview protocol through an iterative process to determine the questions to be posed. The questions asked were tailored according to the expertise of the interviewee; during the interviews, questions were often added to the core list to explore topics raised and probe further. One to three team members were present for each interview and all team members present took notes.

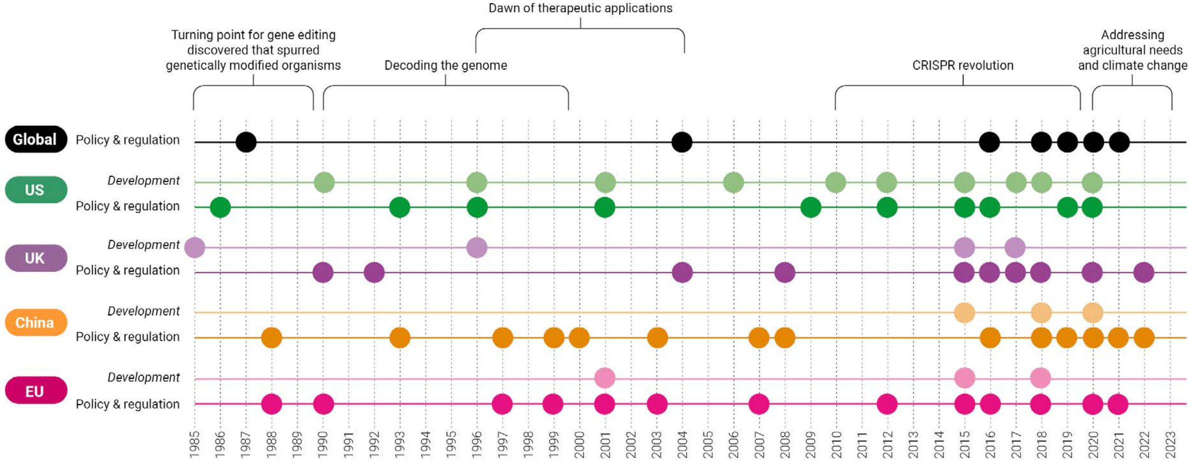
Interview protocol for subject matter experts

1. *What is the state of the art for synthetic biology?*
    a. *What are the primary drivers for advancement?*
2. *What is the state of the art of machine learning (ML)?*
    a. *What are the primary drivers for advancement?*
3. *How is ML currently being applied to biotechnology, specifically in in genome editing?*
    a. *How might this evolve over the next ten years?*
    b. *What are the big developments to watch out for?*
4. *What kinds of problems could ML applied to genome editing solve that could not be solved in other ways?*
5. *What do you think are the biggest challenges to applying ML to problems in synthetic biology/genome editing?*
6. *What are the biggest risks/concerns?*
7. *What are the most pressing issues for policies governing the use of ML and synthetic biology/genome editing?*
8. *Could you describe any obstacles with developing and implementing policies?*
9. *What would advancements and coming together of these technologies mean from a practical viewpoint?*
    a. *How will it change the way we live and operate?*
    b. *What are the implications for the population at large?*
10. *How important is public perception/acceptance in accepting these technologies and in implementing policies?*
11. *Is there anything else that you would like to tell us (anything we did not ask about, but you feel is important)?*

Members of the study team analysed interview transcripts and recordings by coding by category according to the interview protocol (questions). They recorded how respondents answered a particular question on a spreadsheet and analysed all responses. For example, any comments and responses about the state of the art of synthetic biology were categorised as a group, so that comments from all interviewees about that subject could be analysed together. Not all interviewees were knowledgeable about the subject matter of every question and sometimes not every question was asked owing to time limitations and interviewee expertise, so not every category had responses from every interviewee. Responses by category were then analysed for themes.

Annex B. **Figures of timelines for GE and AI/ML**

Figure 13. GE policy timeline in relation to technological advancement



Global

1987	CRISPR technology discovered (Japan)
2004	UN supports biotech, endorses crops that can address global hunger
2016	ISSCR publishes guidelines, becomes default standard bearer
2018	OECD identifies disparate biotech regulation based on the process or final product characteristics or both as biggest challenge to biotech development
2019	Call for a global framework to police germline editing
2020	WHO advisers call for consideration of how IP will affect pricing of GE therapies
2020	A committee of ten countries concludes technology is not ready for use in human embryos destined for implantation
2021	WHO outlines governance framework overseeing research in human genome
2021	ISSCR guidelines updated

United States

1986	Coordinated Framework outlines the responsibilities of United States Department of Agriculture (USDA), FDA and EPA in reviewing biotechnology
1990	*Human Genome Project begins*
1993	Gene therapies to be regulated as a drug, device or biologic by FDA depending on intended use and final product
1996	Dickey-Wicker Amendment prevents research funding that involves embryos
1996	*First genetically modified crop, corn, adopted in the US*
2001	Federal ban on funding for embryonic stem cell research
2001	*First gene targeted therapy is developed (for Chronic myelogenous leukaemia)*
2006	*HPV vaccine Gardasil is developed using gene editing breakthrough*
2009	Executive order removes barriers to stem cell research
2010	*Creation of first synthetic life form*
2010	*The gene-editing function of TAL nucleases first discovered*
2012	FDA streamlines development of breakthrough drugs, with breakthrough therapy designation
2012	*Cas9 engineered to find and cut DNA target specified by guide RNA (2020 Nobel Prize winner)*
2015	*Gene drives for malaria resistant mosquitos is developed*
2015	Executive order for EPA, FDA and USDA to develop long-term strategy for biotechnology
2015	FDA approves GM virus to treat melanoma
2016	GMO Labelling Act passes
2016	National Institutes of Health allows implant of human stem cells in animal embryos
2017	*First time a US-based group edited human embryos*
2018	*CRISPR gene drives tested in mammals for first time*
2019	California bans do-it-yourself genetic engineering kits
2020	USDA updates SECURE biotechnology regulation
2020	FDA releases guidance on gene therapy product development
2020	*Stem cell therapy for diabetes*

United Kingdom

1985	*Zinc finger nucleases is discovered for targeted genetic engineering*
1990	Human Fertilisation and Embryology Act regulates human germline editing
1990	First directive on GMOs established, focusing on process to create seed rather than final product
1992	Committee on the Ethics of Gene Therapy states that gene therapy should be limited to life threatening diseases
1996	*Dolly the sheep is successfully cloned*
2004	Medicines for Human Regulations provides guidance for gene therapy clinical trials
2008	Human Fertilisation and Embryology Act enables researchers to obtain HFEA research licence to edit human embryos
2015	Human Fertilisation and Embryology Regulations enables mitochondrial therapy
2015	*Gene therapy clinical trials completed for various types of cancer, e.g., head and neck, liver, ovarian, prostate, breast, colorectal, cervical, melanoma and non-Hodgkin's lymphoma*
2015	*CAR T-cell therapy clinical trials (using patients' own immune cells to treat their cancer) completed for various types of cancer including leukaemia, head and neck cancer and melanoma*
2016	HFEA approves CRISPR gene editing
2017	HFEA provides first licence for mitochondrial replacement therapy
2017	*Mitochondrial replacement therapy becomes possible*
2018	Nuffield Council on Bioethics argues that changing embryo's DNA could be permissible
2019	MHRA provides guidance on clinical trial regulations in face of No Deal Brexit
2020	UK leaves EU
2022	Genetic Technology (Precision Breeding) Bill simplifies regulations around precision bred plants and animals, introduced to Parliament (ongoing)

China

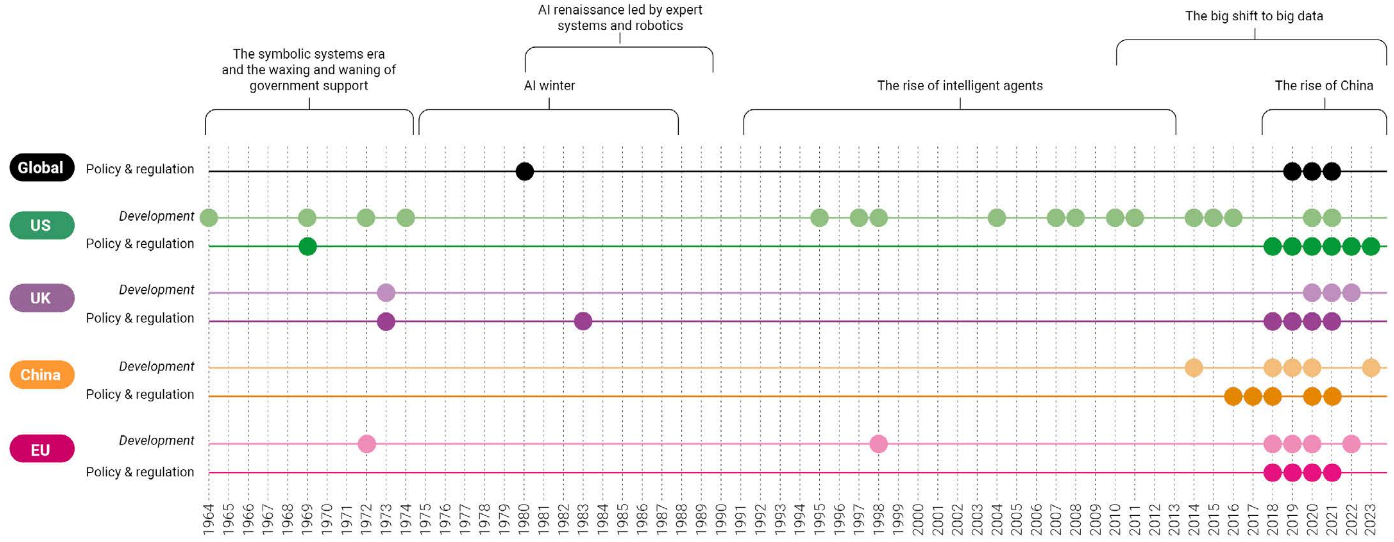
1988	Chinese Medical Association founds the Society of Medical Ethics
1993	Ministry of Public Health releases 'An Outline of Quality Controls for Clinical Studies of Human Somatic and Gene Therapy'
1997	Medical research institutes establish research ethics committees
1999	Guidelines for human gene therapy clinical trials published
2000	Guidelines and measures for assisted human reproduction released by Ministry of Health
2003	Ethical principles of research of human embryonic stem cells developed
2007	Ethical review of biomedical research involving humans (for trial implementation) released
2008	Ministry of Health creates Medical Ethics Expert Committee
2015	*At least 11 clinical trials testing CRISPR gene therapies for cancer treatment (e.g., oesophageal); Anhui Kedgene Biotechnology start-up involved in most trials*
2015	*CRISPR on germline editing in human embryos*
2016	Five-year plan encourages GE research in agriculture
2018	*Global outcry when scientist carries genetically modified human embryos to term*
2018	Temporary ban on human GE research as response to Dr He Jiankui controversy
2019	Studies involving human embryos cannot harm people's health, according to new civil code
2020	*Herbicide-resistant soy is developed*
2020	China commits to various reforms in agricultural biotechnology policies under the US–China Economic and Trade Agreement
2020	Biosafety certificates issued for import of two new events along with six renewals
2021	Biosecurity Law
2022	Guidelines for approving gene edited plants

European Union

1988	European Medical Research Council argues against germline gene therapy
1990	The first directive on GMOs focuses on regulating the process used to create the seed
1997	Council of Europe convenes the Oviedo Convention, the only multilateral institution that polices GE (UK and Germany not signatories)
1999	Council of Europe (distinct from EU) Convention on Human Rights and Biomedicine bans 'modification in the genome of any descendants'
2001	European GMO Directive strictly regulates the process of developing organisms altered through genetic modification
2001	*CRISPR coined to describe clustered regularly interspaced short palindromic repeats*
2003	Regulation No 1829/2003 strictly regulates genetically modified food and feed
2007	Commission outlines guidance for approving gene therapies
2012	A gene therapy is approved for first time
2015	Directive 2015 allows member states to restrict cultivation of GMOs without new evidence
2015	*Gene drives to lessen spread of malaria via mosquitos is developed*
2015	*First stem cell therapy developed in Europe to treat eye burns*
2016	France asks the Court of Justice of the European Union (ECJ) to interpret GMO Directive in light of new gene editing techniques (e.g., New Breeding Techniques)
2018	ECJ deems GE organisms GMOs, EU scientific advisors warn this will block development of beneficial plants
2018	*GM pigs used as human models*
2020	Push for international prohibition on using gene drive technologies in wild
2020	France lists techniques exempt from GMO restrictions
2021	European green deal sets legal framework for plant modification

Source: RAND Europe (2023)

Figure 14. AI policy timeline in relation to technological development



Global

1980s	Japan's increased investment in their Fifth Generation Computers Systems Project spurs international cooperation
2019	OECD AI principles
2019	Beijing Consensus
2020	US–UK declaration of AI R&D cooperation
2021	US–EU Trade and Technology Council set up

United States

1964	*Joseph Weizenbaum invents first chatbot, Eliza*
1969	*Marvin Minsky releases Perceptrons, a publication about artificial neural networks*
1969	Mansfield Amendment puts a stop on much DARPA funding, spurring AI winter that lasts till early 1980s
1972	*Stanford Research Institute's Artificial Intelligence Center develops Shakey, a mobile intelligent robot*
1974	*Paul Werbos lays foundation for backpropagation, designed to aid in teaching neural networks how to recognise patterns*
1995	*Richard Wallace presents ALICE, a chatbot inspired by Eliza but with enhanced NLP*
1997	*IBM's Deep Blue chess-playing computer beats human world champion chess player Garry Kasparov*
1998	*MIT designs Kismet, the first robot able to express emotions*
2004	*DARPA initiates Grand Challenge to develop autonomous vehicles*
2007	*Nvidia releases Compute Unified Device Architecture*
2008	*Google app on iPhone allows for voice recognition*
2010	*Initial release of ImageNet*
2011	*Apple releases Siri as voice activated virtual assistant*
2011	*Google Brain founded to focus on AI*
2014	*Amazon releases Alexa, a voice activated virtual assistant*
2014	*Meta's DeepFace outperforms humans in performing the 'Faces in the Wild' test, ushering in an era of deepfake and facial recognition applications*
2015	*Initial release of TensorFlow as an open-source tool triggered the current renaissance*
2016	*AlphaGo beats Lee Seidol*
2018	DoD outlines AI strategy
2018	DARPA funds Next-Generation Nonsurgical Neurotechnology (N3) programme
2019	US National AI strategy: executive order on maintaining American leadership in AI
2020	National AI Initiative Act
2020	*OpenAI release Generative Pre-trained Transformer 3 (GPT-3), a natural language model using deep learning to produce human-like responses*
2021	FDA issues AI/ML-Based Software as a Medical Device Action Plan
2021	*Initial release of Dall-E by OpenAI*
2021	*Midjourney*
2021	The National Artificial Intelligence Initiative Office set up to enforce and regulate the National AI initiative act
2022	US bans sale of high-end GPUs to China, and pushes Denmark to stop selling high-end lithography hardware to China
2023	The newly introduced Transparent Automated Governance Act would require federal agencies to disclose when they use AI systems to make critical decisions and inform people when they interact with an AI employed by the government

United Kingdom

1973	Professor James Lighthill's negative AI report to Parliament ushers in defunding of research in area
1973	*University of Edinburgh builds Freddy robot, which is able to use visual perception to build models*
1983–1988	Alvey project spurs investment in AI
2018	Automated and Electric Vehicles Act passes
2019	Office for AI publishes guidelines on using AI in public sector
2019	Senior AI Council is established as an expert committee to serve as advisory board on adoption of AI
2020	The Centre for Connected and Autonomous Vehicles asks the Law Commission of England and Wales and the Scottish Law Commission to review legal framework for automated vehicles
2020	*DeepMind's AlphaStar is Grandmaster level in the game StarCraft II*
2021	Government releases National AI Strategy
2021	*Stable Diffusion (Stability AI)*
2022	*DeepMind releases Gato, first generalist AI*

China

2014	*Government announced seven-year plan to have a social credit scoring system using AI*
2014	*SenseTime, one of the world's most highly valued AI start ups, is founded*
2016	Ministry of Industry and Information Technology sets three-year guidance for Internet Plus AI Plan
2017	Government sets ambitious AI 2030 strategy
2018	Ministry of Education's action plan to integrate AI education in higher education curricula
2018	*China implements facial recognition in its mass surveillance system*
2018	*Beijing Institute of Technology opens first ever course in military AI geared toward children*
2019	*China is top publisher of AI-related papers*
2020	Ministry of Industry and Information Technology releases standards for autonomous driving
2020	*China has biggest capital market for AI start ups*
2021	National Governance Committee for the New Generation AI releases ethical norms its use
2021	The State Council's 14th five-year plan includes priorities for investing and developing China's AI capabilities.
2023	*China's investment (via Byte Dance) in buying hardware from NVIDIA*

European Union

1972	*Prolog language developed by Alain Colmerauer with Philippe Roussel*
1998	*First Environment and AI Workshop in Europe held*
2018	*European Lab for Learning and Intelligent Systems is established to compete with China and US AI investment and efforts*
2018	Commission's Coordinated Plan on AI
2018	GDPR goes into effect
2018	Commission establishes the AI Alliance initiative to encourage experts to collaborate and promote dialogue across academia and industry
2019	Commission establishes AI Watch to monitor and facilitate the Coordinated Plan on AI
2019	Commission publishes guidelines for ethical and trustworthy AI
2019	*Allianz Insurance first to use AI to completely automate injury claims*
2020	Commission identifies robustness and explainability as vital aspects of AI that must be considered in regulation
2020	*BMW integrates AI applications throughout its production process, maximising efficiency and productivity*
2021	AI, data and robotics partnership in Horizon Europe funding
2021	Commission publishes AI legislative package, which updates coordinated AI plan with member states
2022	*French AI firm Prophesee designs near-human level vision for robotics*

Source: RAND Europe (2023)

Annex C. **Futures methodology**

The futures methodology used in this study consisted of two main components: the development of three future scenarios and the design and delivery of a virtual seminar game. The purpose of this annex is to describe the methodological approach taken by the study team.

Given the inherent uncertainty of the future and the dynamic evolution of the technologies in the scope of this work, the research objective of the study team for this element of the research was to the explore various future trends regarding the convergence of GE and ML and discuss the implications of possible future developments for contemporary policymaking. This effort was intended to complement the landscape assessment presented in this report. To achieve that, the study team designed a bespoke futures methodology approach, developing three future scenarios and designing and delivering a three-hour virtual seminar game, at which the future scenarios served as the vehicles for discussion. The methodological approach to the scenarios and the seminar game is described in this annex, while our findings are presented and analysed in Chapter 8.

Scenario development

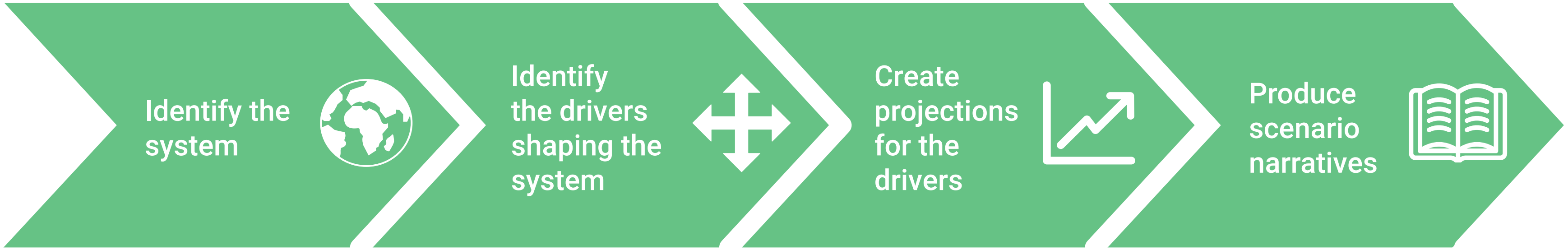
Scenarios are a useful analytical tool to address future uncertainty by depicting what *could* happen and facilitating discussions around the implications.[249] The scenario development process was largely based on the scenario management methodology described in Gausemeier et al.,[250] which was adapted because of the budgetary and time constraints of this study.

The purpose of the scenario development process was to produce three future scenarios that would serve as vehicles for discussion in the seminar game. Specifically, the scenarios were intended to portray distinct and considerably different future landscapes regarding the convergence of ML and GE technologies out to 2045, to help uncover a range of potential opportunities and risks rooted in them. By providing expert participants with three very different perspectives on what the future of GE could look like in 2045, enabled by advances in ML, the study team ultimately sought to stimulate a discussion on what the decision makers of today should consider in light of the implications of possible futures. As noted in the caveats and limitations here, the scenarios were not intended to be and should not be interpreted as forecasts or predictions about the future. The scenario development process consisted of four steps as depicted in Figure 15, below.

249 Pillkahn (2008).

250 Gausemeier et al. (1998).

Figure 15. Scenario development process



Source: RAND Europe Centre for Futures and Foresight Studies (n.d.).

As the first step, the study team identified the convergence of ML and GE technologies as the system of interest. Following this scoping decision, the second step was to identify so-called drivers of change, which are key characteristics and factors that shape and influence the identified system. These drivers are outcome-agnostic, which means that the direction of the change caused by the driver is not yet considered or determined at this point. For example, a driver of change may be 'the pace of technological innovation' instead of 'accelerating/slowing technological innovation'. The study team generated a longlist of 58 drivers of change based on the thematic outputs of the landscape assessment and the expert interviews, which was subsequently narrowed down to seven key drivers through an internal prioritisation and scoring exercise.

The third step was to generate qualitative projections for each of the drivers. The projections are different trajectories a driver can take (e.g., 'increases/improves – stays the same or status quo – decreases/ worsens'), and they are not intended to be mutually exclusive and collectively exhaustive. The fourth and last step of the scenario development process was to produce the three scenario narratives based on the combination of the different driver projections. Here the main consideration was to cover a wide range of the possible future landscapes through using as many projections as possible, while also ensuring that multiple drivers do not contradict one another within a given scenario. Table 8, below, depicts the combination of driver projections on which the three scenario narratives were built.

The combination of drivers and their different projections formed three different future worlds for the three scenarios. Table 8 contains the overview of each scenario, while the full scenario narratives are described below.

The seminar game, which was the second element of the futures methodology, served two research objectives. The first objective was to engage participants in the three future scenarios and develop policy action from the perspectives of the United States, China and the European Union with the aim of maximising gains and minimising risks across all three scenarios (Table 8). Consequently, participants were allocated into three country or region groups and asked to assume the role of decision makers of one of the three entities to fulfil this objective.

Table 8. The drivers of change and their projections, which underpin the scenarios

Drivers of change	Scenario A Unrestrained innovation	Scenario B Innovation behind demand	Scenario C Innovation goes underground
State of geopolitics between states with high technology investments	Increased tensions and lack of frameworks for international technology governance	Mix of competition and cooperation with limited cooperation on tech governance	Cooperative shift, including technology governance across a range of international fora
Market demand and business incentives for the convergence of ML and GE	The convergence of ML and GE is a booming market with high market demand and high business incentives to invest in this area		Loss of commercial interest
Societal demand for applications that combine ML and GE technologies	High societal demand		Only niche societal demand
The pace of technological innovation	High pace, transformational technological breakthroughs	Mediocre pace, gradual technological advances only	
Public attitudes towards the convergence of ML and GE technologies	High public accessibility and strong trust	Public acceptability varies widely between communities and different demographics	Strong opposition to and distrust in solutions that combine ML and GE
The extent of data sharing and the democratisation of access to technologies	High: widespread access to 'good' data and technologies that combine ML and GE	Medium: data sharing and access to the technologies are selectively restricted	Low: strict restrictions on data and narrow access to solutions that combine ML and GE
Military interest in the convergence of ML and GE technologies	High military interest, widespread military applications	No military interest or use	Limited military use

Source: RAND Europe (2023)

The second research objective for the seminar game was to explore the reactive dynamics of policymaking across these entities and whether the scenarios encourage cooperative or competitive behaviours. To aid this, the groups received the policy actions prepared by the other two groups halfway through the event. After that, the groups had to reflect on their initial work considering the proposed actions of the other two entities represented in the game. This prompted participants to react to each other as well as to consider amending initial and creating new policy actions, reflective of the competitive and collaborative dynamics at play.

Full scenarios

Scenario A: Unrestrained innovation

The year is 2045. The state of geopolitics is more tense than ever. The United States, China and the European Union are locked into intense competition for influence and resources. The race for technological supremacy is driven by both governments and profit-oriented tech giants. Over the past two decades, governments have kept regulatory regimes lax domestically, while maintaining strict cross-border regulation to protect IP. As a result of interstate arms racing dynamics, there are no international agreements on technology governance.

Countries like the United States, China, India and Iran have developed biological weapons that can be set to target selected genetic traits at scale. Moreover, more than two dozen countries have adopted physiological and cognitive human enhancement technologies for military purposes, creating elite ‘super soldiers’.

Meanwhile, there is a booming market for genetic enhancements in the commercial realm, too. These include the medical treatment of congenital diseases as well as aesthetic procedures such as changing one’s eye colours. The use of synthetic embryos created from stem cells has abated infertility and allowed parents, including same-sex couples, to determine their children’s gene pool.

GE is also omnipresent in agriculture to mitigate the impact of climate degradation through higher-yield and more resistant crops.

Scenario B: Innovation lags behind demand

The year is 2045. In the previous two decades, strategic competition has been selective. On certain issues, such as the militarisation of biotechnology, countries reached a mutual understanding and negotiated mutually limiting technology governance regimes to prevent destabilising arms racing.

However, economic competition continues, thwarting the prospect for slowing global warming. Environmental degradation and resource scarcity have created a high demand, and indeed a pressing humanitarian need for technological solutions such as GM crops.

But innovation is lagging. The convergence of ML and GE technologies has been evolutionary rather than revolutionary, so countries most affected in Africa, the Middle East and South Asia are unable to deliver solutions at scale to feed their populations.

Technological progress is also merely gradual in the medical sphere. GE treatments are only authorised in the case of life-threatening conditions. Robotic prosthetic limbs and brain–computer interfaces are available to treat disabilities but only in closely regulated private clinics.

Scenario C: Innovation goes underground

The year is 2045. After a decade of tensions in the 2020s, global powers recognised the risks of unconstrained technological competition and negotiated a robust framework of technology governance.

A range of international treaties regulated access to computing power, imposed embargos on genetic sequence sharing for business and academia, mandated case-by-case regulator assessment of any proposed human genetic modifications or synthetic development applications, while also banning their commercial use.

The willingness to negotiate was also driven by a regional East Asian epidemic in 2028, caused by an engineered virus that leaked from a North Korean lab. This disaster also instilled mistrust towards genetic engineering applications among the populations of most developed countries.

However, strict regulation and the lack of market demand could not stifle technological progress – innovation just went underground, enabling a booming black market. Pharmaceutical enhancements with temporary effects have become popular intoxicants. Contract killers use personalised biological weapons to carry out targeted assassinations without a trace. Organised crime groups are running synthetic embryo farms to harvest and sell organs. And an expanding 'dark tourism' sector provides illegal GE services at secret locations to billionaires who crave a longer, healthier life for themselves or their offspring.

Seminar game approach

Seminar game objectives

The overarching intent for the seminar game was to explore different trajectories for the convergence of ML and GE technologies and discuss policy actions relevant for today based on the futures-focused discussions. Specifically, the seminar game had two research objectives:

1. Develop policy actions for the United States, China and Europe in the context of three future scenarios.
2. Explore the reactive dynamics of policymaking in this technology area.

Given the analytical focus of the game as part of the broader research project, the activities in the game were designed to produce research data for the study team. The game had two main forms of outputs (see also below): a standardised data capture template for each of the three groups as well as the notes on the plenary and group discussions, which were captured by RAND staff.

Seminar game structure

To facilitate the participation of experts from different geographical locations, the event ran virtually. The time allocated to the event was three hours, which was seen as a suitable amount of time to have meaningful discussions on the topics related to the seminar game objectives, while also considering the limited availability of the participants, and that a considerably longer virtual session may take a toll on the level of participant engagement.

The format of activities was a mix of plenary discussions and group work in breakout sessions, both facilitated by members of the RAND study team. The agenda of the event is presented below in Table 9.

Table 9. Seminar game agenda

Time (EDT)	Activity	Format
11:00	Welcome and briefing on RAND study context	Plenary
11:15	Scenario briefing	Plenary
11:25	Planning for an uncertain future	Breakout
12:10	Backbrief and plenary discussion	Plenary
12:30	Break	
12:40	Revising policy interventions	Breakout
13:15	Backbrief and plenary discussion	Plenary
13:45	Discussion of main takeaways	Plenary
13:55	Wrap up	Plenary

Source: RAND Europe (2023)

At the beginning of the seminar game, the participants were briefed on the game approach, the three scenarios, the data capture templates and the guiding principles of the game. After this, participants were allocated into three breakout groups, representing decision makers of the United States, China and Europe (which represented a combined entity of the European Union and the United Kingdom for the purposes of this event). Participants were told that any of the three future scenarios may occur by 2045, which could present a multitude of distinct risks and benefits depending on the scenario. As the main activity for the first breakout session, the groups were asked to produce three to five policy actions that consider all three future scenarios and could be adopted today, in 2023. These proposed policy actions were supposed to address the scenarios collectively to maximise gains and minimise harm for their respective groups, hedging against an uncertain future in 2045. The first breakout session was followed by a plenary back brief, where each group summarised their policy actions, followed by an opportunity for participants and the RAND facilitators to ask clarifying questions and briefly comment on the presentations.

Following this plenary discussion, participants moved back to the group breakout sessions to explore the reactive dynamics of policymaking in this field. To facilitate that, the groups received the list of policy actions that the other two groups had compiled in the previous breakout session. They were then asked to:

- React to those policy actions (to note if there were any surprising and challenging elements in them)
- Reflect on their own initial policy actions and discuss whether some of those should be changed
- Consider adding a maximum of two new policy actions in addition to the previous ones, considering the proposed policy actions of the other two entities.

The second group session was also followed by a plenary back brief, after which participants discussed the reactive dynamics and reflected on issues concerning cooperation and competition (e.g., whether the groups took a more cooperative or more competitive approach considering the policy actions proposed by the other two entities, or what opportunities were identified and what incentives could facilitate more cooperation on technology governance).

The final session of the seminar game was a quick reflection exercise. Every participant was asked to share a takeaway from the event, thereby giving the attendees the opportunity to underscore their personal highlights, policy priorities or any other high-value thoughts they gained from the event.

Seminar game participants

The seminar game brought together 13 experts on ML and bioengineering from government, academia, industry and RAND. The participants were allocated into three groups during the seminar game, and the study team aimed to ensure that each group contains a cross-section of perspectives and affiliations. The relatively small size of the groups (four or five participants per group) allowed all participants to contribute actively to the discussions. Each group had a facilitator and a rapporteur from the RAND study team to steer the discussions in line with the data capture plan and ensure that the outputs were recorded and produced as required for subsequent analysis.

Data capture plan

The data capture plan for the seminar game consisted of two main forms of outputs: a standardised data capture template built around the research objectives for the seminar game as well as the notes on the plenary and group discussions, which were captured by note-takers. Each group completed a predesigned data capture template during the breakout sessions. The data capture template (see Figure 17, below) required groups to log their proposed policy actions in a structured manner, asking for details on the policy actions. This included information on the description of a policy action, its objective, its classification in the policymaking style typology presented in this report, and various other considerations about implementation (e.g., relevant policy tools and levers, stakeholders involved). In line with the research objectives, the data capture plan also required participants in the second breakout session to record their reaction to the work of the other two groups, and to conduct revisions and/or additions to the list of initial policy actions.

The data capture template was hosted on an online whiteboard software called Mural.[251] The participants were responsible for populating the data capture template, while the note-takers captured the content of the discussion in parallel to that. To ensure the comparability of the group activities, the RAND facilitators were using a set of facilitator prompts to structure the discussion around the research objectives and the data capture plan.

251 Mural (2023).

Figure 17. Data capture template

DRAFTING POLICY ACTIONS							REVISING THE POLICY ACTIONS	
Instructions: Any of the three scenarios may occur by 2045, bringing a multitude of potential risks and benefits. You are asked to produce 3-5 policy actions that consider ALL three future scenarios and could be adopted today, in 2023. **These proposed policy actions should address the scenarios collectively to maximise gains and minimise harm for your country group, shaping and hedging against an uncertain future.** ***You can add a sticky note by double-clicking on the screen or by clicking on the top icon of the black vertical panel on the left hand side.***							**Instructions:** 1) Please examine the policy actions of the other two groups (they are inserted below this table) and then respond to the two questions about surprise and challenges below. 2) Please reflect on how your list of policy actions could and should be changed in light of the policy actions of the other two groups. The elements of surprise and challenges identified may also inform your responses. If justified, produce 1 or 2 new policy actions under your original list (see the two extra rows of the table coloured in purple).	
	What is the outline of the policy action? (one-sentence summary)	**What is the objective of the policy action?**	**Which policy-making style does it belong to? (preemptive, proactive, reactionary, legacy or none of the above)**	**What policy tools (e.g. levers, incentives, investments, subsidies) could be employed to achieve the objective?**	**What stakeholders are involved in the implementation? (e.g. leading and supporting; domestic and international)**	**Is this policy action driven by cooperation or competition?**	**Is there anything that you would change about your initial policy actions in light of the plans of the other two groups?** Please add them in this column in the appropriate row.	**What surprised you from the policy actions of the other two groups?** ***Please list them on sticky notes below.***
1								
2								
3								
4								**What challenges do the policy actions of the other two groups create for your initial plans?** ***Please list them on sticky notes below.***
5								
New policy action #1 (if needed)								
New policy action #2 (if needed)								

Source: RAND Europe (2023)

Seminar game outputs

US policy interventions proposed

1. **Strengthen biological defence** and be capable of creating medical countermeasures on demand in response to an emerging biological threat. Additional policy tools mentioned in relation to this policy action included federal funding for research, IP policies to incentivise industry to create countermeasures and allowing insurance payments by the Centers for Medicare & Medicaid Services for sequencing routine cases or paying for capacity to do it.
2. **Regulate scientific research study design and dissemination** to help slow down the ability of malicious actors to use scientific knowledge in harmful ways.
3. **Limit opportunities for malicious actors** to design and develop biological weapons through universal, mandatory gene synthesis screening. The group noted that export controls could play a role in realising this policy action.
4. **Foster R&D in the area of engineering** to improve the quality of life and equalise good health across the population creating a new human 'baseline' of wellbeing indicating the new era of posthumanism. This would require establishing necessary domestic legal frameworks, putting R&D funding in place, and fostering cooperation between domestic R&D agencies, the private sector and academia.
5. **Invest in high volume datasets** to develop a deep understanding of genotype-to-phenotype relationships. This would serve the aim of generating the capability to engineer any function into biology to create new products and medical innovations. This policy action would involve US domestic R&D agencies, the private sector and academia. The group noted that investment in R&D, data and computing power as well as IP policies to protect value generation would also be needed.

China policy interventions proposed

1. **Prohibit the use of AI tools for the purposes of GE and the development of weapons** based on genetic traits unless used in a therapeutic setting.
2. **Embed the convergence of AI and GE technologies in the country's economic model.** Specifically, the group suggested that, externally, China should meet international product standards and guidelines in AI and biotech, while putting such top-down incentives in place internally that spur an aggressive R&D to ensure the competitiveness of Chinese technologies.
3. **Combine China's data aggregation advantage, IP laws and export controls** to carve out strategic advantage in the development of AI and biotechnology over the United States and Europe.

Europe policy interventions proposed

1. **Restrict the application of GE solutions to disease prevention** through statute-defined restrictions around use.
2. **Proactively set norms around GE** by establishing processes to elicit democratic access to technologies related to the convergence of AI and GE. Devise an 'extra-legal' mechanism through which standards, guidelines and a code of best practice can be developed.
3. **Strengthen biosecurity measures** spanning preventing accidental leaks to detecting and identifying intentional releases up to building capabilities for rapid therapeutics. Such defensive measures would likely come at a significant cost requiring investments in physical security, detection, screening, characterisation, personal protective equipment and facilities.
4. **Closely link the convergence of AI and GE technologies to equity and benefit-sharing in the peaceful uses of these technologies.** Efforts should be made to build trust and strengthen cooperation globally to prevent the misuse of technology, while ensuring that it is used appropriately in response to pressing global needs, such as food security challenges stemming from climate degradation.