Moonshot R&D MILLENNIA* Program

*Multifaceted investigation challenge for new normal initiatives program

“Survey on the Construction of a "DIGITAL BIOSPHERE" for Human Expansion into Space” Initiative Report

July 2021

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[I]. Concept

[1]-1. Proposed MS Goal

[1]-1-1. Proposed MS Goal title

By 2050, build a world in which all living things are digitized and achieve a manufacturing revolution for solving social issues.

[1]-1-2. Vision for 2050 society

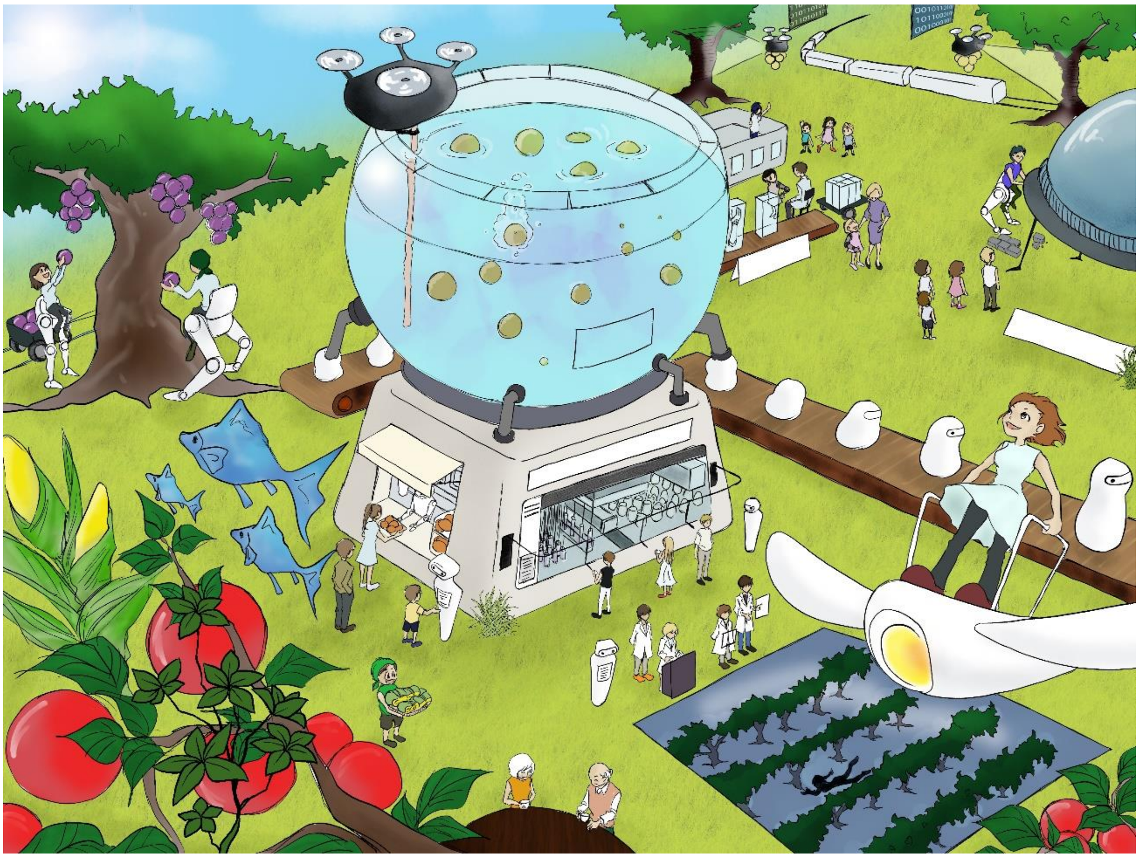

Fig. 1 Conceptual diagram of the proposed vision

The Japanese government has recently launched an initiative for solving scientific and technological issues over a relatively long time period of 5–10 years, with the idea that a single issue could be sufficiently solved with such a timeframe. We conducted a research study to determine what can be done in a longer timeframe of 30 years.

As a result, we propose a “forum” where new scientific /technological and industrial innovations can be formed. We expect that such a forum would have a future societal impact similar in magnitude to the present-day impact of the internet. Specifically, over the last 30 years, the internet has served as a forum for the exchange and synthesis of ideas from people from around the world, leading to countless innovations. Our vision is in the next 30 years, a forum where data on biological phenomena are collected, stored, analyzed, and exchanged around the world will drive innovation and lead to heretofore unheard-of gains for humanity.

To build such a forum, we envision a "DIGITAL BIOSPHERE," which is a world where all organisms are digitalized and expressed as data based on accumulated data on living organisms aggregated from around the world. We expect that the digital biosphere will be utilized to solve various issues faced by humankind, such as pandemics, climate change, food security, and natural disaster response. We also expect that the digital biosphere will enable a manufacturing revolution for solving social issues. Our goal for the digital biosphere is to drive innovation from academic, industrial, cultural, and social perspectives, and to serve as a catalyst for a bioindustry pioneering a "truly new physics." Furthermore, we hope that the innovation enabled by the digital biosphere will produce breakthrough technologies necessary for human beings to advance to the ultimate extreme environment of space.

[1]-2. Targets

MS Goal achievement

(1) By 2050, achieve a world without pandemics caused by new infectious diseases.

(2) By 2050, achieve net zero carbon, reducing net emissions of greenhouse gases such as carbon dioxide to zero while reducing atmospheric greenhouse gas content to safe levels.

(3) By 2050, digitally evolve organisms *in silico*, and freely design organisms that can adapt to environmental changes such as climate change.

(4) By 2050, utilize biodata to revolutionize robotics, and develop robots that can genetically evolve similarly to organisms.

Feasibility

(1) Predicting the genetic information of highly virulent viruses from past virus data accumulated in the digital biosphere enables the production and stockpiling of vaccines at an early stage, thereby preventing pandemics. Even if a pandemic occurs, early responses and solutions become possible.

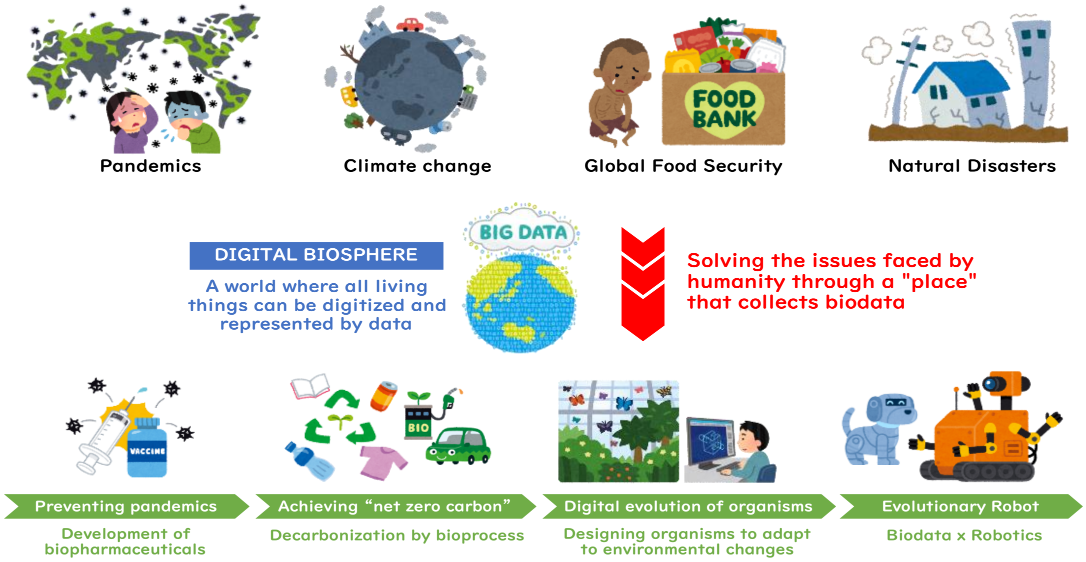

Fig. 2 Moonshot Goal targets

(2) Clarifying synthetic pathways for producing useful substances from CO_2 using genome analysis technology and introducing genome editing technology that freely modifies key genes should dramatically increase the CO_2 absorption capacity of microorganisms.

(3) Effective data analysis can be achieved by developing next-generation large-capacity memory technology as well as elemental technologies (e.g., quantum computing) to store and analyze vast amounts of data from living organisms in different ecosystems around the world.

(4) Effective data collection can be achieved by designing robots that collect environmental information and adapt their responses to their environment using structural and functional knowledge from successfully evolved organisms.

Interim goals for 2030

(1) By 2030, achieve bio-manufacturing to develop biological products utilizing the genome, and construct a rapid production system for vaccines and bio-pharmaceuticals.

(2) By 2030, transition to bio-production from petroleum-dependent chemical synthesis, and promote decarbonization.

(3) By 2030, establish a large-capacity memory technology for storing vast data of organisms.

(4) By 2030, develop robots that autonomously collect biodata from the environment and transfer it to a base station.

[1]-3. Background

[1]-3-1. Why now?

- Cutting-edge technology for maximizing biological function is now emerging that could address various social issues faced by humankind, such as early/rapid testing for infectious and other diseases, development of novel vaccine and therapeutic modalities, and improvement of crops and livestock that can withstand environmental changes to enhance food security.
- To harness these trends, solve global problems facing humankind, and achieve a “bioeconomy” that enables sustainable development, a backcasting approach based on a future vision is essential. In particular, various biological and environmental data need to be collected, big data need to be stored and analyzed, and an accessible forum where everyone can work on solving social problems must be built.
- We therefore propose the MS Goal of constructing a digital biosphere, which is a world where all organisms are digitized and expressed as data, and achieving a manufacturing revolution that solves social issues. This can be considered a project to build a 21st-century digital version of the Library of Alexandria in ancient Egypt, which is said to have accumulated knowledge from all over the world and driven innovation by the ancients in multiple disciplines, and will be a source of industrial competitiveness for Japan.

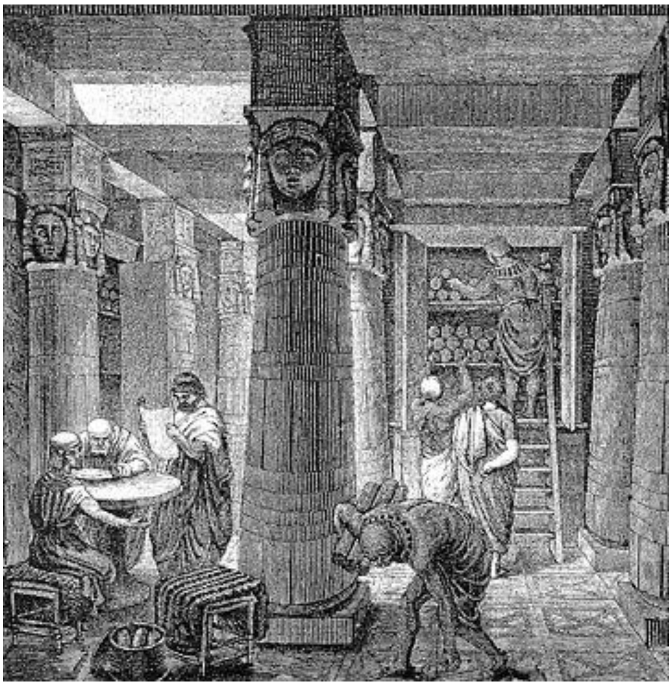

Fig. 3 The Library of Alexandria, which was said to be the “accumulation of human wisdom” in ancient Egypt (Source：Wikipedia)

[1]-3-2. Social significance

The construction of the digital biosphere would allow anybody free access to necessary information, and we would provide a “laboratory” that produces solutions for social issues and the creation of new business by using vast biodata and analytics to realize the ideas of the users. We believe that this would have an impact on industry and society much like that of the internet, which allowed for the birth of revolutionary services and changed our lives through information becoming accessible to people worldwide and enabling them to explore ways to use such information freely with their own ingenuity.

(1) Pandemic measures

SARS-CoV2 is an RNA virus that is prone to mutations, and highly infectious variants have already been appearing in succession. RNA viruses generally mutate at a rate approximately 1 million times that of the human genome, as is the case with the viruses for AIDS, influenza, and SARS [1]. We expect that construction of the digital biosphere will enable the development of technologies for instantaneously analyzing genetic information, in turn enabling rapid virus detection, mutation prediction by data analysis, and acceleration of vaccine development.

(2) Achieving net zero carbon

Climate change is expected to disrupt the stable supply of food, for example through failure of crops, and there is increasing momentum for decarbonization and net zero carbon worldwide. The power of microorganisms and plants that produce useful substances from CO_2 can be developed to transition into a highly efficient bioprocess that produces substances such as biofuels and biomaterials, thus achieving net zero carbon while creating great value. The digital biosphere would accumulate biodata on a global scale, allowing researchers to identify the key biosynthetic genes and genetic pathways involved and to freely modify these genes and pathways using genome editing technologies.

(3) Digital evolution of organisms

An approach that designs organisms that can rapidly adapt to changing environments is becoming necessary in light of both climate change and the future potential of space travel. Such genetic design requires the collection of the genomes of organisms and understanding of changes in gene expression (transcriptome), epigenetic modifications (epigenome), and metabolite levels (metabolome) in response to environmental factors, but this requires massive amounts of data. Storage of such vast data using large-capacity memory technology and analysis of such vast data using advanced computing resources, both developed in the course of this project, would enable effective, comprehensive *in silico* simulation of biological phenomena evolution, and enable the design organisms that can adapt to environmental change.

(4) Evolutionary robots

Biodata can be used not only for organismal programming but also for non-living robots. We can reference organisms that have adapted and evolved to the global environment over long periods of time ever since the birth of life, and by modeling their structure/function and response to environmental information, we can develop robots that learn and act on their own. Development of robots that collect/analyze organismal samples from the environment using these concepts would automate and increase the efficiency of biodata collection needed to construct the digital biosphere. Using the vast data obtained in this manner, we could design new robots that operate effectively even in dangerous environments where humans cannot go.

[1]-3-3. Action outline

Interdisciplinary fusion in the scientific and technological fields is important to achieve the MS Goal. Constructing the digital biosphere requires various elemental bio-digital technologies and their combination to achieve the digitization and "programming" of organisms.

With regards to efforts to preserve and unify the DNA data of organisms, international nucleotide sequence databases are being linked in Japan, the United States, and Europe [2,3,4]. Furthermore, international workshops (BioHackathon) have been established to promote the sharing, organization, and integration of biodata; participants in these workshops have standardized biodata and conducted technological development for database integration [5]. The wisdom of humankind must be brought together from such a framework of international cooperation.

To accelerate efforts for directly connecting newly created technological seeds to industry, it is important to establish a perspective of global business development, such as creating startups spun off from these projects and bridging to players who are responsible for social implementation in each industrial sector, as well as establishing a path for earning profits and becoming independent.

To ensure that ELSI needs are met, it will also be important to communicate purpose and progress of the project the from the initial stage of research and development. A path toward social implementation can be drawn by achieving comprehensive knowledge through the fusion of the humanities and social sciences. To do so, we will appropriately disclose information, promote science communication, and promote efforts to foster a sense of ethics in society.

[1]-4. Benefits for industry and society

The bioindustry is projected to grow to approximately 200 trillion yen by 2030, and the driving force behind this growth will be the fusion between biological and digital [6]. Reductions in genome analysis costs and time will allow accessible, inexpensive digitization of organismal information. IT/AI/ML-based analyses will advance the elucidation of genome sequences and organismal functions. We thus expect future organismal functions can be discovered through multiomics analyses and targeted by genome editing will be possible.

Genomic data has a size of several dozens of GB. When considering the number of species (estimated to be approximately 8.7 million on earth) and their individuals, a revolutionary memory technology that is capable of vast data will be needed [7,8].

The construction of the digital biosphere will enable the creation of an environment where the accumulated biodata can be used by anybody worldwide, democratizing people to freely perform new analyses driven by their own ideas. This is expected to lead to a major shift toward a social/industrial structure where anyone can create innovation, and innovative services will be created one after another.

For example, when a new pandemic such as COVID-19 occurs, access to the digital biosphere by global innovators would enable the construction of a rapid inspection system and the development of biopharmaceuticals with high specificity and efficacy. In the face of climate change, access to the digital biosphere by global innovators could enable the production of new varieties that can adapt to environmental changes.

Constructing the digital biosphere ahead of the rest of the world would allow us to update Japan's traditional strength in manufacturing, revitalize Japan's scientific and technological capabilities, compete with the world (including the United States and China), and achieve a strengthening of industrial competitiveness.

As we move toward this expected change in social/industrial structure, it is essential that Japan exhibits strong leadership today to gather the wisdom of humankind and start these initiatives.

[II]. Analysis

[II]-1. Essential scientific/social components

To address our MS Goal, we backcasted from the Goal and conducted research on the types of research and development projects required to achieve the vision.

In particular, achieving the social vision presented here requires overcoming scientific and technological hurdles regarding next-generation communication, data storage, AI/ML, and quantum computing, focusing on the concepts of genome editing and digital technology.

Simultaneously, we need to bring together human wisdom to tackle ethical, legal, and social issues, such as how to handle "digitized" genetic resources and the extent to which organisms should be "programmed".

Fig. 4 shows a schematic representation of building the digital biosphere by creating new innovation through the fusion of different fields.

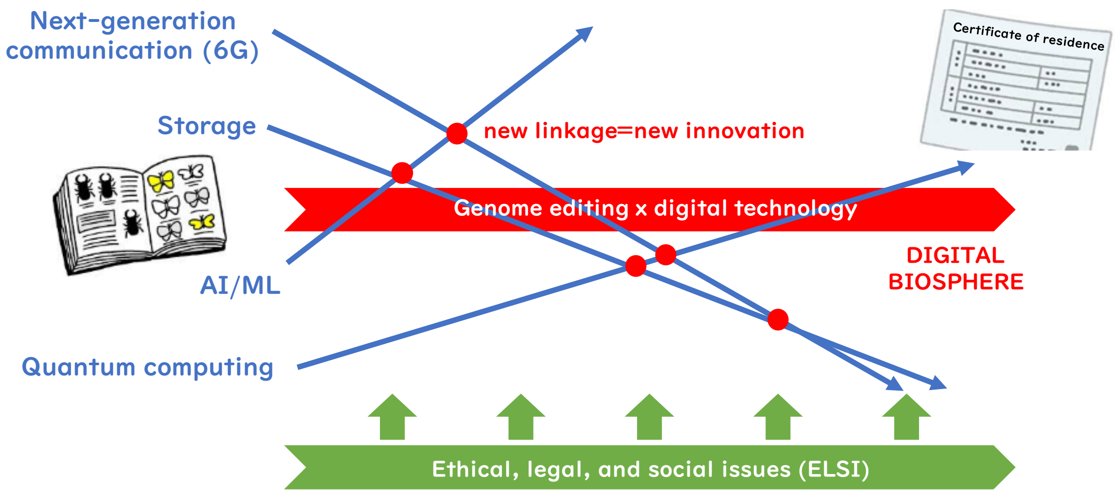

Fig. 4　Issues for achieving the MS Goal: broad overview

The digital biosphere is generated by collecting vast data, including on species and the environment. Such data can include changes in gene expression due to environmental conditions (environmental response) and interactions between organisms in addition to biodata, such as at the genomic, epigenomic, transcriptomic, proteomic, and metabolomic levels.

Biotechnology, computing, and robotics to achieve the digitization and programming of organisms are important for constructing the digital biosphere.

[II]-2. Science and technology map

The issues that need to be overcome using science and technology are in the fields of biotechnology, computing, and robotics, and the structure of relevant fields and technologies is summarized in Fig. 5.

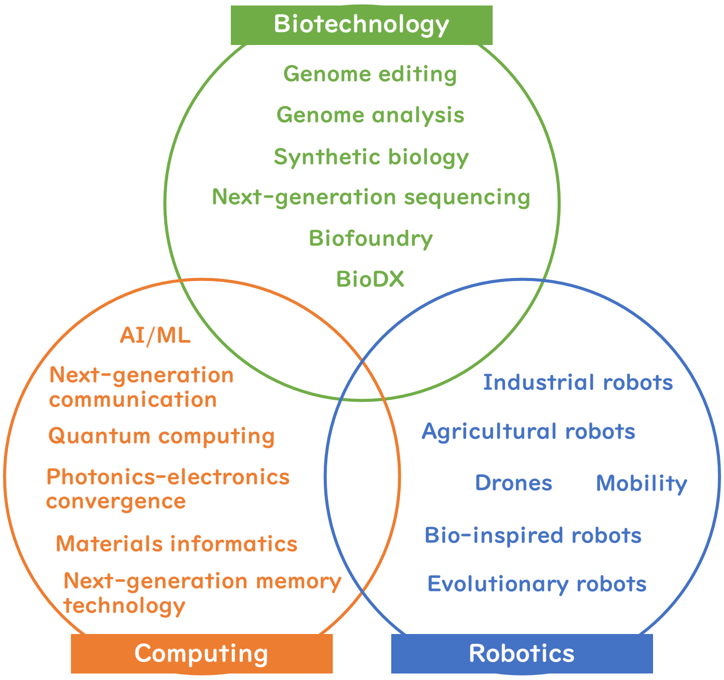

Fig. 5 Structure of relevant research fields and technologies

For biotechnology, the data accumulated in public databases in Japan and overseas and the bio-digital transformation (Bio DX) used in our own research will used to generate new knowledge.

For computing, next-generation memory technology that can store the entire vast data of the digital biosphere will be a breakthrough. The team leader Sadafumi Nishihara was the first in the world to develop a monomolecular dielectric, which exhibits ferroelectric behavior using a single molecule, and this discovery has attracted a great deal of attention from both academia and industry [10,11].

For robotics, breakthroughs in automating and robotizing the process of biodata collection from the environment will also be necessary. We expect to take on new challenges in this area by relying on the strength of Japan's manufacturing industry.

[II]-3. Japan's position in overseas trends

(a) Biotechnology

The technological elements in which Japan has strengths in biotechnology are summarized in Fig. 6 based on the data of JST-CRDS "Overview Report of Research and Development" in the field of life science and clinical medicine (2021) [12].

Country	Phase	Macromolecular drug discovery (antibody)	Microbial molecular production	Plant factories	Fisheries	Genome editing and epigenome editing	Synthetic biology
Japan	Basic	◎↗	○→	◎→	◎→	○↗	◎↘
	Applied	○↗	○↗	◎↗	◎→	△→	○→
US	Basic	◎→	◎↗	○↗	○↘	◎↗	◎→
	Applied	◎→	◎→	○↗	△→	◎↗	◎→
Europe	Basic	◎↗	◎→	△↗	○↗	○→	◎↗
	Applied	◎↗	◎↗	△↗	◎↗	○→	○↗
China	Basic	◎↗	○↗	○↗	○↗	○→	△→
	Applied	○→	○↗	○↗	△→	◎↗	○↗

Fig. 6　Research and development trends (biotechnology)

In polymer drug discovery (antibody), increasing emphasis is placed on new pathway analysis technologies using AI/ML and big clinical data as well as *in silico* molecular design, which makes full use of AI/ML and molecular dynamics. Projects are underway where investigators trained in mechanical engineering and information engineering are participating in drug development, such as with the use of robotics and AI/ML.

For microbial molecule production, bio-foundry initiatives, such as the fusion of biological (biochemistry) and digital (AI) approach as well as automation by robotics and batch synthesis of gene clusters, are mainly under way in the United States and Europe, and Japan must catch up to these efforts.

Japan has strengths in the fields of cultivation and breeding of industrial organisms, such as vertical farming and fisheries; its competitiveness in these areas can be further enhanced through the digital biosphere.

For genome/epigenome editing, basic research is being actively conducted on CRISPR-Cas9, which was awarded the Nobel Prize in Chemistry in 2020, but advancing its commercialization requires licensing from multiple international intellectual property holders. Furthermore, there have been intellectual property disputes, and rights relationships are unclear; this has been a hindrance to industrial use. Professor Takashi Yamamoto of the Genome Editing Innovation Center of Hiroshima University leads Japan's genome editing research as the president of the Japanese Society for Genome Editing, and in 2019, he was ranked second in the world among the top 15 most published in the field of genome editing by *Nature Biotechnology* [13]. The unique technology that Professor Yamamoto's group developed, "Platinum TALEN," is being adopted for use in industry as a genome editing tool that is optimized for industrial use.

This genome editing and the strengths of synthetic biology for constructing artificial cells will be combined for the technological development that enables the programming of organisms.

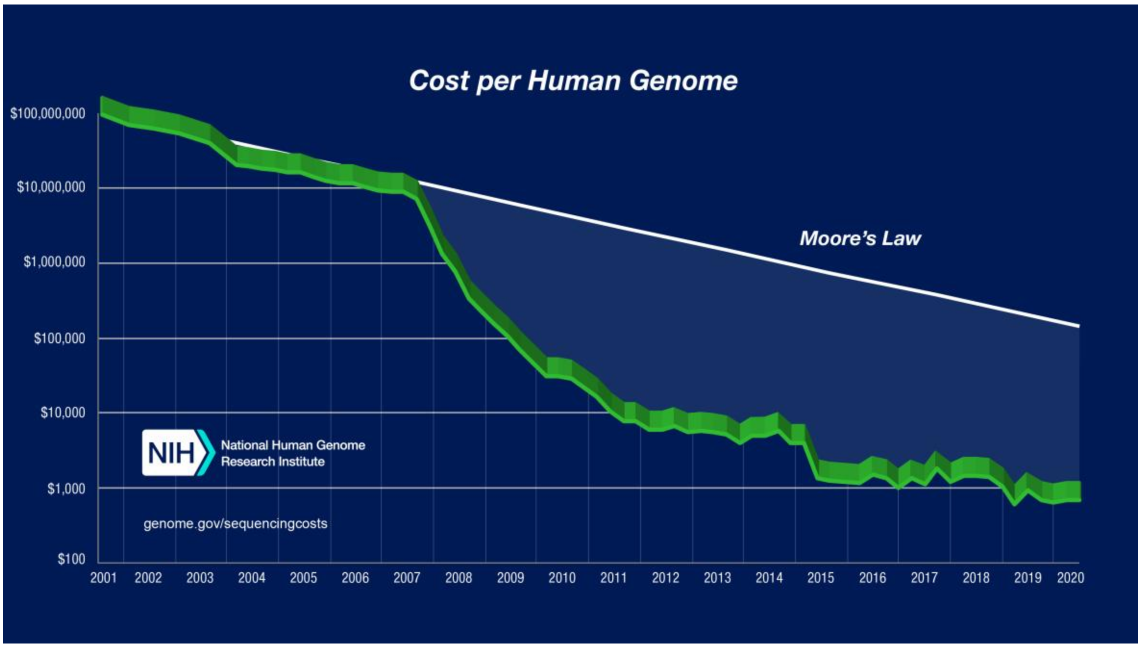

Fig. 7 Changes in the cost of human genome sequencing

The cost and time for sequencing genomes have been significantly reduced with the introduction of next-generation sequencing (NGS), enabling the production of enormous amounts of data. The cost of sequencing the human genome is now less than $1,000 per sample (Fig. 7) [14].

If a USB-type sequencer is used, then the analysis can even be completed in approximately 10 min. Nanopore sequencing (Oxford NANOPORE Technologies) is used for analyzing long-chain DNA sequences and can generate approximately 30 Gb of DNA sequence data or 7–12 million reads. It also enables long reads (several hundred kb). Long sequences can be read when this method is used, but because potential differences can arise in the DNA sequencing, low accuracy is an issue.

The number of species on Earth is estimated to be approximately 8.75 million [7]. For a biomass sample in a given land area, a method has been reported for estimating the number of individuals from the mass of all organisms [8].

The human genome has a size of approximately 3 Gb, but the genome size is different for each organism, and for species other than humans, there are only a few model organisms whose genome has been deciphered. For example, an estimated 1 million species of insects are thought to exist, but the genomes of only approximately 600 insect species (0.06%) have been fully sequenced.

Little research has been done to link genomic information to phenotypes, and understanding individual differences requires the simultaneous acquisition of genomic and phenotypic information.

Therefore, the data accumulated in public DBs in Japan and overseas and the bio-digital transformation (Bio DX) used for our own research will be a breakthrough. Hidemasa Bono, who is a specially appointed professor at the Graduate School of Integrated Life Sciences at Hiroshima University, discovered multiple novel hypoxia-responsive genes by applying Bio DX to public gene expression data and literature **i**. This is a precursor to a practical example of data-driven research (Fig. 8) [9]. This is a pioneering case of data-driven research utilizing Bio DX and provides a glimpse of how the vast data accumulated in the digital biosphere will be used.

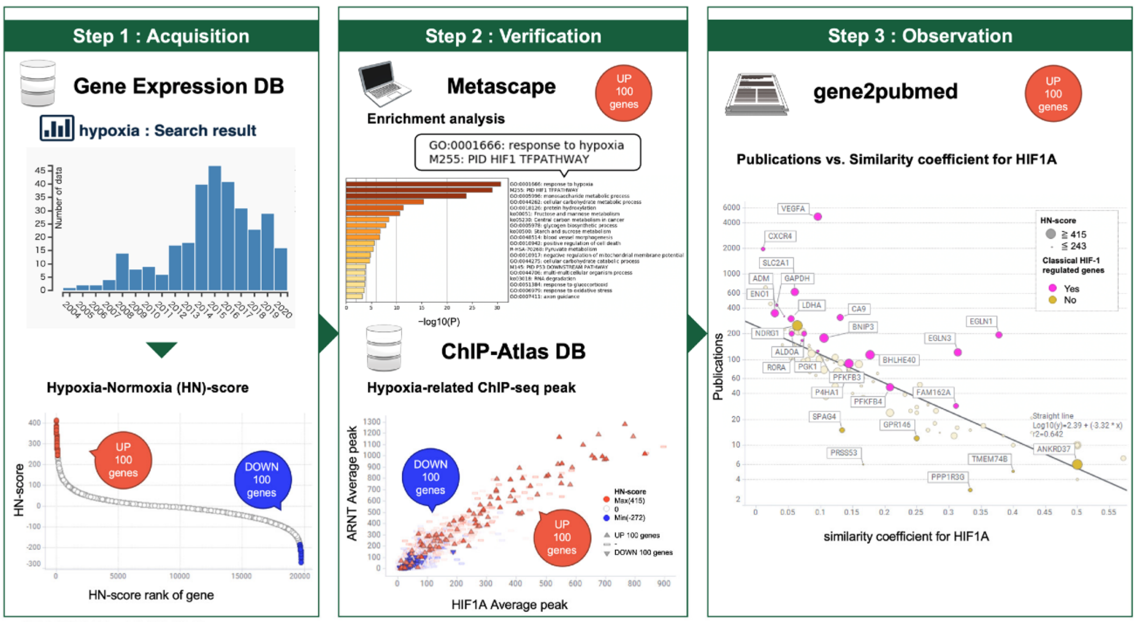

Fig. 8 Multi-omics analysis for discovering new hypoxia-responsive genes

(b) Computing

The technological fields where Japan has strengths in computing are summarized in Fig. 9, mainly based on the data of JST-CRDS "Overview Report of Research and Development" in the field of nanotechnology and materials (2021) [16].

Country	Phase	AI software engineering	Data-driven problem solving	New functional nanoelectronic devices	Quantum information and communication	Molecular technology	Materials informatics
Japan	Basic	○↗	○↗	○→	○→	◎↗	○↗
	Applied	○↗	○↗	○→	○→	◎→	○↗
US	Basic	○↗	◎↗	◎→	◎↗	◎↘	◎↗
	Applied	○↗	◎↗	◎→	◎→	◎↗	○↗
Europe	Basic	○↗	○↗	◎→	◎↗	◎→	○↗
	Applied	○↗	○→	○→	◎↗	○→	○↗
China	Basic	△→	○→	○↗	○↗	○↗	○↗
	Applied	△→	◎↗	○→	○↗	○↗	○↗

Fig. 9 Research and development trends (computing)

In the field of AI/ML, massive IT companies mainly based in the United States, such as Google, Microsoft, and Facebook, continue to gather talented engineers from all over the world and are actively engaged in basic and applied research and development.

For AI software engineering, "reliable AI" was set as a strategic goal of the Ministry of Education, Culture, Sports, Science and Technology in Japan in 2020, and AI reliability-related research issues have been promoted in JST programs (e.g., ERATO, MIRAI, CREST, and PRESTO).

For data-based problem-solving, efforts to expand the potential of scientific discoveries by utilizing AI/ML are called data/AI-driven science, and the promotion of data-driven research has been listed in the 6th Science and Technology/Innovation Basic Plan.

For nano-electronic devices with new functionalities, various groups are attempting to increase the capacity of non-volatile NAND-type flash memory by forming a highly laminated structure. Japanese industry has extensive technology and human resources in the field of semiconductor electronics, but these resources are rapidly dissipating and being lost. Therefore, there a mechanism is needed to avoid such dissipation and to effectively utilize human resources and equipment.

For quantum information/communication, the Cabinet Office formulated a quantum technology innovation strategy in Japan in 2020 and a domestic industry-academia collaboration system, which is centered on RIKEN, is being established. In terms of industry, startup companies in the United States, Canada, and Europe have become active and have increased their presence among the large American companies, such as Google, IBM, Intel, and Microsoft. In Japan, companies such as NEC and Fujitsu, which are strong in the field of high-performance computing, have begun to enter the field.

Molecular technology refers to a series of technologies for creating the desired physical, chemical, and biological functions at a molecular level and implementing such functions by purposefully designing, synthesizing, operating, controlling, and accumulating molecules. This is a research and development area that originates in Japan, and Japan has an advantage in advanced materials.

Materials informatics enables the dramatic acceleration of the design, exploration, and discovery of new materials based on physical property prediction using computational science and data science, high-throughput material synthesis/evaluation, and feature extraction by data mining. As this is an important tool for material development, the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Economy, Trade and Industry announced "Toward a Government Strategy for Strengthening Material Innovation Power" in 2020, where they have launched the material DX platform concept, as the basis for Japan to strategically create and utilize data.

In this international context, full use of molecular technology, which is one of Japan's strengths, must be implemented to regain dominance in the semiconductor industry, which in turn supports the DX society.

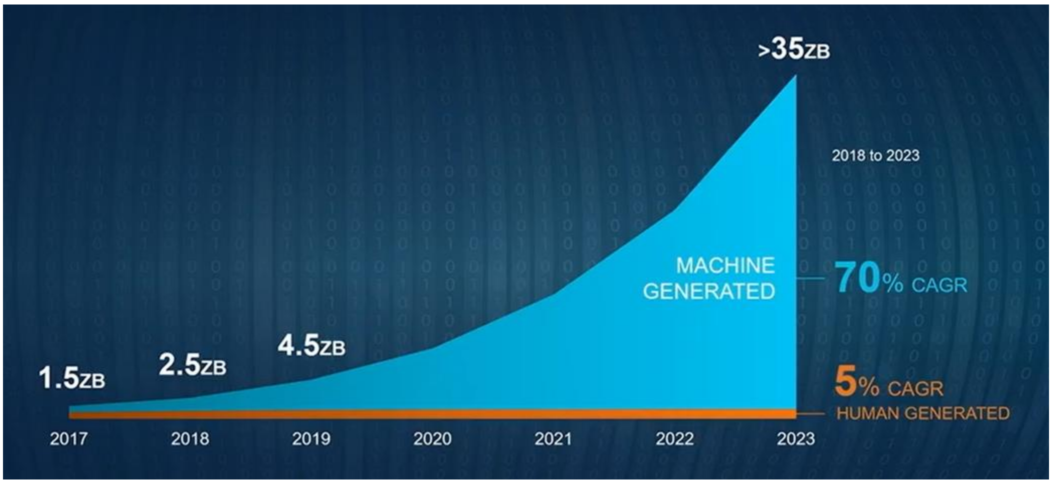

Fig. 10 Changes in the amount of data

Gary Dickerson Keynote – AI Design Forum™ 2019

As shown in Fig. 10, the amount of data worldwide is increasing exponentially, and there is a demand for innovative memory technology that is truly disruptive rather than just being an extension of conventional memory technology [17].

Currently, in the JST Program for Creating Start-ups from Advanced Research and Technology (START), a high-speed/high-density/low power consumption non-volatile memory device has been developed using cage-shaped molecules that can record information in a single 1 nm-sized molecule, and efforts are being made at commercialization through establishment of a venture that contributes to the realization of innovative computing to support the age of AI/ML and big data [10,11].

This next-generation memory technology will be a breakthrough that will enable storage of the entire vast data in the digital biosphere.

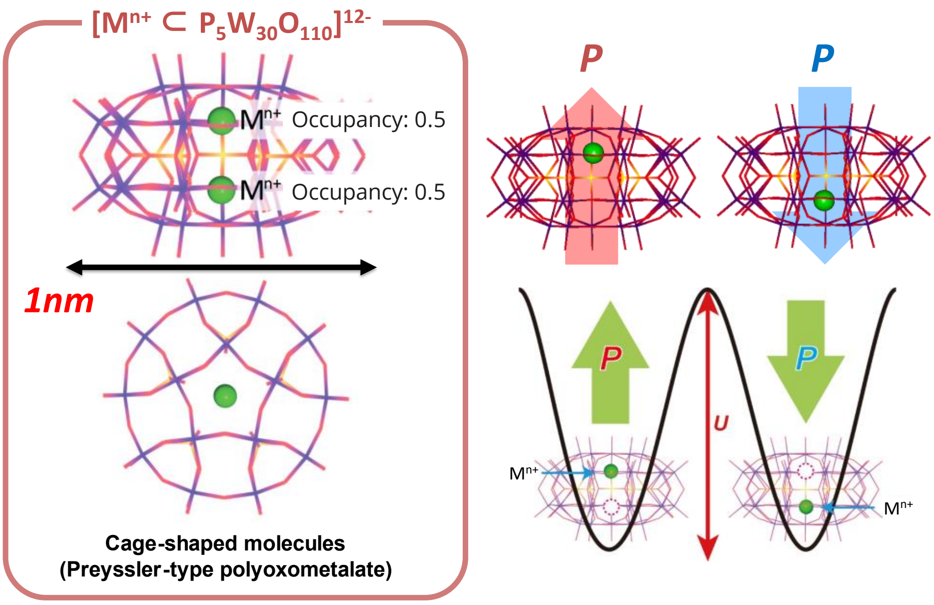

Fig. 11　Cage-shaped single molecule memory, which records information using a single molecule

(c) Robotics

The technological elements of robotics where Japan has strengths are summarized in Fig. 12 based on the data of JST-CRDS "Overview Report of Research and Development" in the field of system/information science and technology (2021) [18].

Country	Phase	Bio-inspired robotics	System Technology	Mobility robots	Life support care robots	Service robots	Agriculture, forestry and fisheries robots
Japan	Basic	○↗	○→	○↘	◎↗	◎↗	○→
	Applied	○→	◎↘	○→	◎↗	◎↗	◎↗
US	Basic	◎↗	◎→	◎→	◎→	◎↗	◎→
	Applied	◎↗	◎→	○↗	○→	◎↗	◎↗
Europe	Basic	○↗	○→	◎→	◎→	○→	○→
	Applied	○→	○↗	○→	◎↗	×↘	◎↗
China	Basic	○→	○↗	◎→	△↗	○↗	◎↗
	Applied	◎↗	◎↗	◎→	○↗	◎↗	△→

Fig. 12 Research and development trends (robotics)

Bio-inspired robotics is a research and development area that actively incorporates the superior functions, abilities, and structures inherent in naturally evolved organisms into the design process of robots to improve the performance of robots. Market sales of bipod robots (Agility Robotics) and quadruped robots (Boston Dynamics, recently acquired by Hyundai) have started in the United States, and full-scale expansion of application in the real world is expected, mainly in the field of logistics.

System technology is used to design and control robot systems by integrating multiple elemental technologies. Japan has the highest levels of applied research and development in this field, as demonstrated during the decommissioning of the Fukushima nuclear power plant. However, the commercialization and social implementation of system technology approaches have not progressed well, and Japan's competitiveness in this field is decreasing. We expect to see a recovery through projects stemming from Moonshot Goal 3: "By 2050, develop robots that learn and act by themselves and co-exist with people."

For mobility robots, China is dominant, with 42.4% of the world's patent applications. The number of drones made in China accounts for 70% of the world's total. Active research is being promoted in Japan, such as research on AI applications for improving drone flight safety at NEDO

(2019–2023), and ISO international standardization activities are also under way. However, there is a large difference when comparing Japan with China and the West in terms of the number of patent applications (6.2% of the number of applications).

Japan has extensive resources for basic research on biological support/nursing care robots, including elemental technologies for robots, such as mobile robots and manipulators. In particular, Japan is home to academic activities centered on the Robotics Society of Japan, Japan Society of Mechanical Engineers, Japanese Society for Wellbeing Science and Assistive Technology, and the Society of Life Support Engineering, as well as funding at every stage, from basic research to social implementation (NEDO, JST). In terms of applied research and development, Cyberdyne Inc. developed HAL, a work support robot that is being used to reduce the burden on workers who handle heavy objects at logistics sites. HAL is also being used clinically for rehabilitation from neurological injuries and disease. Major companies such as Softbank and Sony are engaged in abundant applied research and development for communication robots. There has also been an increasing number of startup companies related to robots in recent years, such as Meltin MMI, and it is expected these companies will collaborate with AI/ML companies, focusing on their technology and advanced properties.

Service robots refer to cleaning robots at home, security robots in public facilities, customer service robots, and catering robots in stores, among others. The market is expected to grow with the use of such robots for replacing cumbersome housework, dangerous outdoor work, and late-night work at convenience stores and family restaurants as the working population decreases due to declining birth rates and an aging population. Japan's research and development as well as commercialization of entertainment service robots are ahead of those of other regions. Various robots that co-exist with humans, such as Sony's Aibo, NEC's PaPeRo, the soothing robot Paro, and Softbank Robotics' Pepper are commercially available, and standard platform robots, such as those by Toyota Motor Corporation (HSR), are under active development; thus, Japan is in a superior position for this field.

Agriculture/forestry/fisheries robots include the world's first unmanned robotic agricultural machine, which was socially implemented in Japan in 2018, and unmanned tractors and unmanned rice transplanters are commercially available. Multiple collaborative work systems and fully autonomous driving with remote monitoring are currently in the demonstration phase for robotic agricultural machinery, which would be the first demonstration of such technologies in the world, and this is becoming a highly competitive field.

The introduction of the Boston Dynamics quadruped walking robot "Spot" into the New York Police Department (NYPD) as a police dog recently made news in the United States (Fig. 13) [19], as did Boston Dynamics' acquisition by Hyundai. A future application example included the robot entering crime scenes and collecting DNA samples. However, the NYPD stopped using Spot within months due to public backlash over the perception of overly aggressive policing when using a robot. Such concerns over the potential for robots to hurt humans and also over the extent of surveillance will have to be addressed as part of ELSI, as other countries may be less accepting of robots, particularly autonomous robots, than Japan.

Fig. 13 "Robot police dog" by Boston Dynamics

New breakthroughs that make full use of evolutionary robotics, such evolutionary development of behaviors enabling robots to autonomously collect environmental information and DNA samples of organisms, will be important for constructing the digital biosphere through research projects that integrate robotics, biology, and mathematical science.

[III]. Plan for Realization

[III]-1. Areas and fields for challenging R&D, research subject for realization of the Goals

[III]-1-1. Areas and fields for promoting challenging R&D

To construct the digital biosphere, we set the following three fields / areas for promoting challenging research and development (Fig. 14).

(a) Biotechnology field: bio DX

(b) Computing field: next-generation memory technology

(c) Robotics field: evolutionary robotics

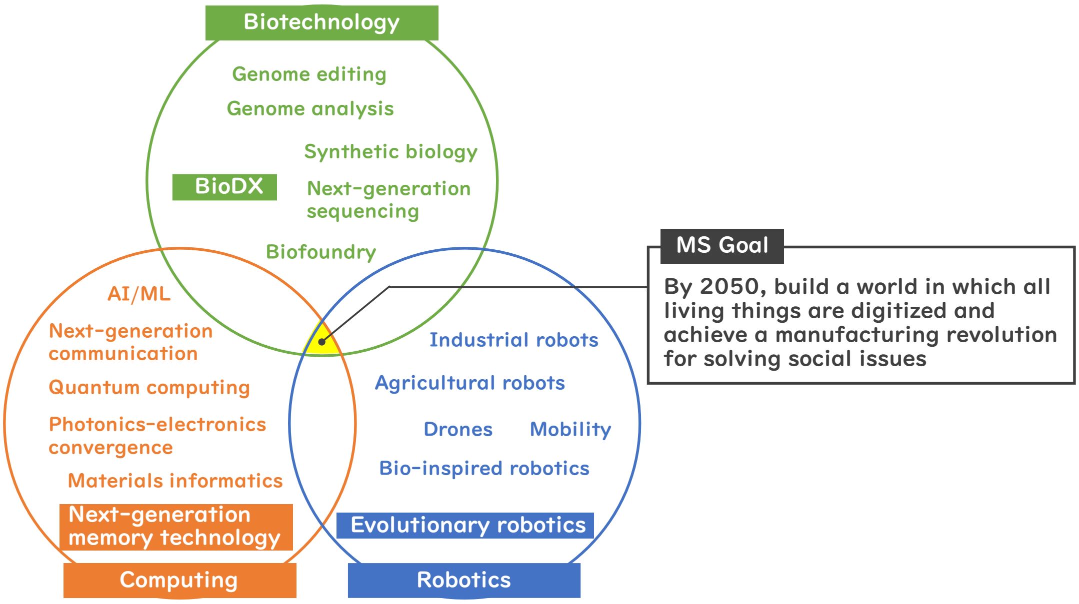

Fig. 14 Fields / areas where challenging research and development should be promoted: broad overview

[III]-1-2. Research subject for realization of MS Goal

The following three research issues should be addressed to achieve the MS Goal:

(a) Biotechnology field: bio DX

"Data-driven bio-DX research that makes full use of multi-omics analysis"

(b) Computing field: next-generation memory technology

"Next-generation memory technology that is capable of entirely storing super-big data"

(c) Robotics field: evolutionary robotics

"Development of evolutionary robots that can autonomously collect environmental data and biodata"

[III]-2. Direction of R&D for realizing the Goal

Milestones to be achieved, research and development for achieving milestones, and ripple effects in 2030, 2040, and 2050）

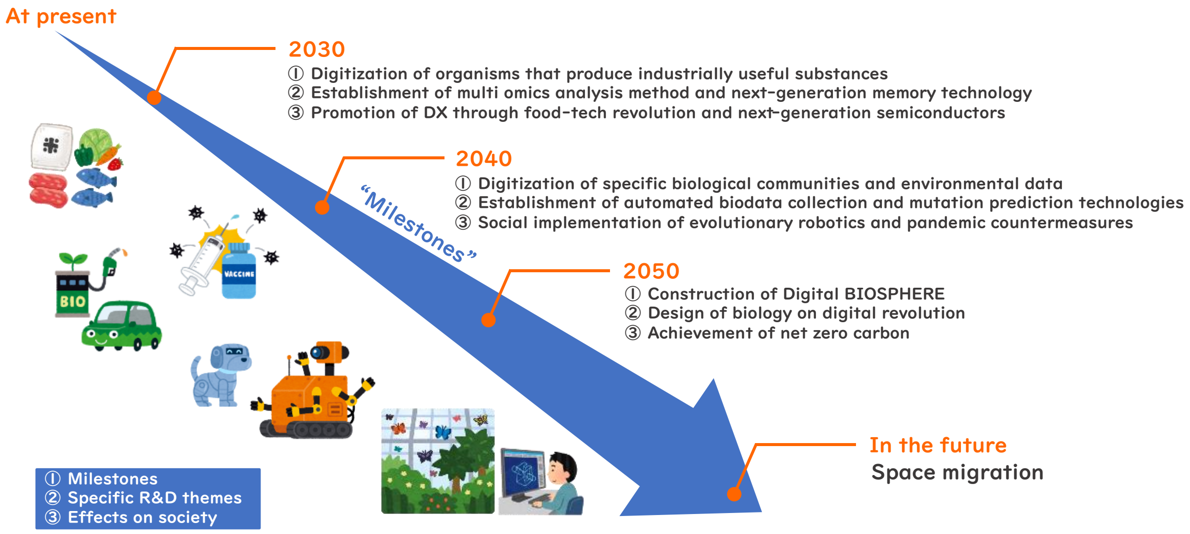

Fig. 15 Scenario for achieving the proposed social vision

① Specific milestones that should be and are expected to be achieved in 2030, 2040, and 2050

2030：Digitization of organisms that produce industrially useful substances

2040：Digitization of specific biotic communities alongside environmental data

2050：Construction of the digital biosphere

② Specific research and development themes to be addressed for achieving the milestones

2030：Establishment of multi-omics analysis methods and next-generation memory technology

2040：Establishment of automatic biodata collection technology and mutation prediction technology

2050：Organismal design by digital evolution

③ Effects of achieving milestones on society

2030：Food tech revolution, DX promotion by next-generation semiconductors

2040：Social implementation of evolutionary robots, pandemic measures

2050：Achievement of net zero carbon

[III]-3. International cooperation

For the DNA data of organisms, the DNA Data Bank of Japan (DDBJ) Center operated by the National Institute of Genetics, along with the European Bioinformatics Institute (EMBL-EBI) of Europe and the National Center for Biotechnology Information (NCBI) of the United States, have been participating in the International Nucleotide Sequence Database Collaboration (INSDC) and providing a supercomputer system for analysis [2,3,4].

Additionally, the JST Bioscience Database Center (NBDC), which is responsible for sharing, organizing, and integrating biodata and facilitating the extraction of knowledge from data, co-sponsors international workshops (BioHackathon) with the Database Center for Life Science (DBCLS)[5]. These events gather the brightest minds in bioinformatics in the United States, Europe, and Japan (over 100 participants) for technological development, including biodata standardization and database integration in camp-style workshops over the course of a week. Utilizing such a framework of international cooperation and expanding its use are essential for constructing a platform to achieve the digital biosphere.

[III]-4. Interdisciplinary cooperation

The technological seeds that are newly created in this project should be connected to industry to achieve the MS Goal. Thus, it is important to establish a perspective of global business development, such as creating startups spun off from these projects, bridging players who are responsible for the social implementation in each sector, and establishing a path for earning profits and becoming independent.

The biotechnology industry is considered to be the target with the largest impact for our MS Goal. As shown in Fig. 16, large domestic / international markets are expected to open up in various fields such as food and agricultural technology, drug discovery / medical care, and energy [20-28].

The size of the non-volatile memory market that supports the semiconductor industry is projected to grow from US$ 54.3 billion in 2020 to US$ 83.6 billion in 2025, with a CAGR of 9.0%, indicating an increasing demand for high-speed / low power consumption / highly expandable memory devices [29]. The demand for semiconductors is expected to continue to grow for the foreseeable future as semiconductors play a central role in digital transformation, particularly in the context of the growing demand for staying at home / nesting in response to COVID-19.

The major U.S. semiconductor company Micron Technology has been engaged in development and mass production at domestic sites such as Hiroshima to strengthen cooperation with Japan in the development of advanced memory; investments in Japan have reached US$7 billion (approximately 770 billion yen) for the past three years.

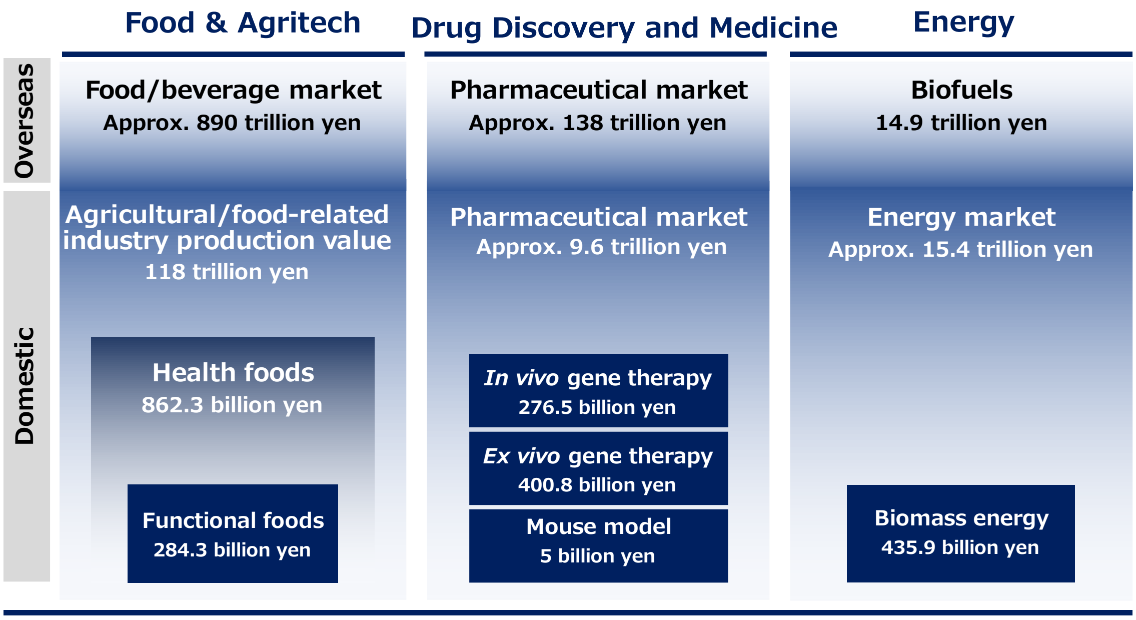

Fig. 16 Total addressable market in the biotechnology industry

There is increasing demand for robots in the manufacturing industry in the context of a global labor shortage, and automation is particularly progressing in the automotive and wireless communication fields. The 2025 global market for such robots is expected to reach approximately 2.3 trillion yen with the progress of smart factories aimed at improving productivity, increased corporate capital investment due to the increased demand for smartphones as 5G spreads, and the renewal of production lines due to the spread of self-driving cars [30].

Business / service robots are widely used in various fields such as medical / nursing care, homes, construction, infrastructure inspection, offices, and stores. Labor shortages have become a serious issue in Japan and other countries worldwide where the birthrate is declining and the population is aging. There is also an increasing number of tasks that only robots can do, such as working in dangerous areas and collecting large-scale data using cameras and sensors. The global market in 2025 for such robots is predicted to expand to approximately 4.7 trillion yen.

The technological seeds created by the construction of the digital biosphere are expected to have a large impact on the biotechnology industry, the semiconductor industry, and the robot industry.

Therefore, we expect that our efforts with government support for the first 10 years toward the

MS Goal will produce results that will attract private investment. Eventually the project will thus cross over to the private sector, with the following 20 years of activity resulting in independence of the digital biosphere as its own entity by 2050.

Achieving such an approach requires efforts from targets directly linked to industry, including actively involving players in industry from the initial stage of research and development, and collaborating across sectors while accurately grasping exit needs.

[III]-5. ELSI (Ethical, Legal, Social Issues)

Matters considered as ELSI when achieving the digital biosphere include the handling of "digitized" genetic resources and the regulation of "programmed" organisms, as well as policies related to the use of autonomous robots for data collection.

(1) Handling of "digitized" genetic resources

Access and benefit sharing (ABS) must currently be considered when collecting biological samples overseas [31]. Specifically, after genetic resources are acquired in accordance with the laws and regulations of the country providing the sample, the necessary procedures for ABS must then be performed, and profits must be appropriately distributed to the locale from which the sample was taken. The information obtained by DNA analysis from biological samples would also become the property of the originating country, and the handling of "digitized" genetic resources must be discussed.

(2) Regulation of "programmed" organisms

There are ELSI problems when using genome editing technologies that enable the genetic programming of organisms. As the genes of all organisms such as microorganisms, plants, insects, and animals can be freely edited, sufficient discussions must be held on how to generate and use such organisms.

For example, basic research on genome editing of fertilized human eggs is being performed mainly in China, the United Kingdom, and the United States, but clinical applications have been banned worldwide due to an incident in China. In Japan, the Ministry of Education, Culture, Sports, Science and Technology established the "Ethical Guidelines for Research Using Genetic Information Modification Technology for Fertilized Human Embryos" regarding research using genome editing technology for fertilized human embryos, which includes a policy for allowing research after examinations for basic research.

Although such care is needed, this technology can be a solution for various social problems faced by humankind, and thus a framework for discussions in society as a whole beyond just the scientific and technological community must be developed.

The 6th Science and Technology Basic Plan states the following: "From 2021, there will be increased funding for research and development related to issues that require the use of 'comprehensive knowledge' through the fusion of the humanities / social sciences and the natural sciences, such as citizen participation in ELSI support from the initial stage of research and development."

Promotion of research and development as well as communication with society is needed to achieve this MS Goal. We will appropriately disclose information, promote science communication, and foster ethics in society to openly discuss how to use these new technologies.

[IV]. Conclusion

This research study was conducted by a diverse team, including Sadafumi Nishihara, who seeks to revolutionize the semiconductor memory industry; Keisuke Okuhara, who is a startup CEO responsible for the social implementation of genome editing technology; Moe Nakazora, who specializes in cultural anthropology and investigates ELSI considerations; Yumiko Kusakabe, who is familiar with global business; Devang Thakor, who is a Silicon Valley-based scientific, strategic, and business advisor and patent agent specializing in biotechnology and serving startups, global 500 corporations, VCs, and universities; and Rumiko Shimabara, who supports the interdisciplinary research.

Initially, the MS Goal was set to achieve innovations for human beings to advance into space. We interviewed leading figures in various fields. Based on interviews with astronaut and general manager of the JAXA Space Exploration Innovation Hub, we felt that the digital biosphere would become an essential technology for space colonization. After receiving advice from VL and deepening our investigation on its feasibility, we decided to put space colonization beyond the MS Goal and instead focus on solving issues facing humankind on earth.

Based on the dramatic societal changes brought by the internet over the past 30 years, the digital biosphere was redefined as a forum for driving innovation in science / technology and industry, and we conducted further research in this regard. Specifically, we set four focus areas for the MS Goal: pandemic countermeasures, achievement of net-zero carbon, digital evolution of organisms, and evolutionary robots. We also advanced our research based on literature analysis and evidence from interviews in 18 areas within three fields (biotechnology, computing, robotics), obtaining new research issues from each of the three fields as a result.

As the digital biosphere that we propose is centered on the accumulation of biodata, we believe that synergy could be achieved by collaborating across disciplines and sectors, particularly for research issues involving biodata, among the Millenia Program Goal Review Team and ongoing Moonshot Research and Development Projects.

End

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