

Technologies to Watch in 2020

2020/01

Mitsui & Co. Global Strategic Studies Institute Technology Trends Basic Research Center, Technology & Innovation Studies Div.

Introduction

In January of each year, MGSSI's Technology Trends Basic Research

Center identifies and selects technologies that deserve particular attention during the year, and provides an overview of those technologies and insights into the future. This year, the center focuses on: (1) human augmentation, (2) implantable devices, and (3) photon technology. The concept of (1) involves the augmentation of human capabilities through further integration with ever-advancing digital technologies, such as AI, IoT, robotics, etc. Implantables, (2), refer to devices embedded in the human body. While the adoption of this technology was limited to providing solutions for serious diseases, such as in the form of cardiac pacemakers, applications are now expanding due to the downsizing of batteries and semiconductors, along with the evolution of wireless communication technology and nanotechnology. Photon technology, (3), is a basic technology involving light — that is, electromagnetic waves classified into ultraviolet light, visible light, and infrared light — whose various applications are being explored by making use of both the wave properties and particle properties inherent in light.

Human Augmentation — Potential for Anticipated Industrial Applications	2
• Implantable Devices — Prospects for Expansion into Preventive Medicine Field	9
• Photon Technology — Next-generation Technologies Derived from Analog Element of Light	14
• Summary of Technologies Highlighted in 2019 — (BMI/Protein Engineering/Haptics)	20

Human Augmentation — Potential for Anticipated Industrial Applications —

Akira Yoshimoto

Consumer Innovation Dept., Technology & Innovation Studies Div.

What is Human Augmentation?

Human augmentation is a general term for technologies used to enhance or expand the physical and cognitive abilities of human beings. The technologies can be broadly divided into two categories: (1) prosthetic engineering to compensate or restore the original function of limbs or appendages lost due to accidents and other causes, and (2) technologies to further augment the inherent human abilities. (Figure 1)



Figure 1: What is human augmentation?

Source: Websites of the Japanese Academy of Prosthetists and Orthotists (JAPO), https://www.japo.jp/top/gisisoug.html, and inami-Hiyama Lab, Research Center for Advanced Science and Technology (RCAST), University of Tokyo, https://star.rcast.u-tokyo.ac.jp/

These technologies have quite a long history. Other than examples, such as eyeglasses, artificial limbs, and dentures, industrial tools for performing more precise work than fingertips can accomplish, and even clothing for keeping body heat, can also be thought of as human augmentation. Recently, however, the evolution and permeation of digital technologies, such as AI, 5G, and IoT, is laying the groundwork for advanced human augmentation, or man-machine fusions, which is clearly a major leap from traditional augmentation technologies to date. This is one of the reasons why human augmentation is currently attracting a great deal of attention. In particular, advancements of sensing (perception) and actuation (action) have contributed significantly to the evolution of human augmentation. Autonomous control of robots, cars, and other objects is becoming possible owing to rapid advances of sensing and actuation technologies, as well as AI, during the 2010s. In the context of human augmentation, these technologies are instead applied to expand human capabilities. From this perspective, autonomous control and human augmentation have common underlying technologies. In Japan, at the Visionary Council on the Moonshot R&D Program, which is a government-initiated program with a budget of JPY 100 billion, human augmentation was recognized as a technology that will lead to the realization of a society where "everyone can pursue their dreams" and "live to the age of 100 without any anxieties about

their health" and the council has established a designated subcommittee. This movement is attracting a great deal of interest.

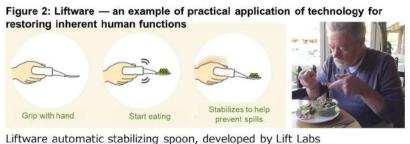
Digital technology-assisted human augmentation is about to help the realization of artificial limbs that are more comfortable than ever, and devices that complement the decline of physical functions due to illness or aging. These developments will greatly contribute to the restoration of human dignity. In addition, when human augmentation makes it possible to manipulate and control the kind of complex techniques that are currently difficult to master, as well as functions and abilities that cannot be achieved by the human body, the possibilities for experiences and self-realization are to widen exponentially. As these developments will contribute to fulfilling human desire, such as for social approval or for self-transcendence and also greatly enhance motivation, they have the underlying potential to create new value perspectives and transform consumer behavior. Examples include growth in demand related to sports, travel, and other such activities among the elderly, improvement in productivity at manufacturing sites, and a range expansion of hobbies with augmented reality (AR) and virtual reality (VR) technologies.

Useful Fields of Application

The following section of this report describes examples of technologies that are already at the stage of practical use.

Human augmentation in prosthetic engineering (development of prosthetic limbs)

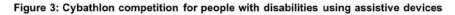
Prosthetic engineering is a technology for restoring the original function of extremities and other body parts that have been lost due to congenital defects, and in many cases, the outcome contributes to restoring human dignity. For example, Lift Labs (US), a subsidiary of Google, has developed the Liftware spoon that automatically stabilizes vibrations and reduces hand tremors for patients with Parkinson's disease and other conditions, enabling patients to regain the ability to eat on their own (Figure 2).



Liftware automatic stabilizing spoon, developed by Lift Labs Source: Website of France Bed Co., Ltd (distributor of Liftware in Japan), https://medical.francebed.co.jp/brand_site/liftware/

There is also an initiative that aims to promote the development of such prosthetic engineering technologies through physical competitions, which incorporates an entertainment factor. Cybathlon, organized by the Swiss Federal Institute of Technology Zurich (ETH Zurich), is a competition in which people with various disabilities (pilots) team up with engineers and use prosthetic engineering to perform physical tasks relevant to their daily lives. (Figure 3) For example, contestants in the powered wheelchair race compete to perform such tasks as ascending and descending stairs, as well as opening a door and passing through it. In the powered leg prosthesis race, tasks include sitting down on and sitting up

from a sofa, and passing through a door near a ramp. The winner is determined according to the number of tasks completed safely and correctly. The difference between this competition and the Paralympic Games is that the Cybathlon focuses on tasks and movements of everyday life rather than sports, and aims to realize a truly barrier-free environment that does not require infrastructure development. Engineering teams, including those from the major prosthetic manufacturers Össur (Iceland) and Ottobock (Germany), as well as the startup Xiborg (Japan), also participate in the tournament, and contribute directly to technical improvements on a practical level.





Powered wheelchair race course for the 2019 Cybathlon

First place team (pilot + engineers) being congratulated at Cybathlon 2019 awards ceremony

Source: Websites of the Graduate School of Science and Technology, Faculty of Science and Technology, Keio University, https://www.st.keio.ac.jp/news/cor/20190507_01.html, and Cybathlon Wheelchair Series Japan 2019, https://www.cybathlonseriesjp.com/

Human augmentation for more efficiently "learning the ropes" (know-how related to manufacturing processes, sports classes, etc.)

The combination of VR technology with motion capture technology, which is a method for recording human movements by tracking joint angle with sensing and AI technologies and converting them into digital data, makes it possible to incorporate human behavior into a virtual space represented by VR. Using these technologies, it becomes possible, for example, to improve exercise skills by practicing without being subjected to physical constraints, such as gravity, time, and space. In general, it is theorized that humans improve motor skills by progressing through three stages: (1) recognition of rules and methods, (2) coordination between sensation and movement, and (3) movements automation allowing for the unconscious performance of the movements. To reach the stage of automated movements, however, individuals need persistent, repetitive practice because they are too preoccupied with the performing movements to give attention to how good their results are. Training in a virtual space, where users can practice in slow motion, makes it possible to calmly perform exercises from the coordination stage, and practice with more focus on the "knack," i.e., the optimal way of training to produce good results and contribute to enhancing the efficiency of improving motor skills. This could also be described as a more tangible form of the mental process known as motor imagery, which is said to have the same effect. This technology is expected to enable the efficient transfer of professional know-how at manufacturing sites, support coaching for sports and hobbies (Figure 4), save space in practice areas, and provide an

advanced sports training environment for athletes by their joining virtualized professional sports teams. Furthermore, applications in other areas are expected to be, such as in the entertainment field, and for training operators of large machines and dangerous devices.



Figure 4: Example of improving athletic skills using VR (Kendama! VR app)



Screen view of Kendama! VR app

Even beginners can acquire the skills of a level-4 Kendama player in a short time

Source: Website of Kendama! VR, http://vrjug.tech/

Human augmentation as assistive technology (heavy loads transport, superhuman sports)

Wearable devices that augment the muscle strength of human beings will make it possible to transport heavy objects that are generally difficult to handle, and may lead to the introduction of new sports, among other possibilities.

Well-known examples for the former usage include the robot suit HAL developed by Cyberdyne (Japan) and the XOS-2 exoskeleton designed by Raytheon (US) (Figure 5). Also, Innophys (Japan) released a model named Muscle Suit Every which uses compressed air to realize low-cost and battery-less operation at the price of JPY 100,000 level in 2019. The suit's applications are not only the heavy goods transport, such as in the transportation industry but also the tasks that cannot be completely automated and require significant manpower, such as nursing care, snow removal, agricultural work, and disaster response. As such, the device is expected to increase the number of workers engaged in these tasks as well. Eventually, the motion assistance device is also expected to be applied in supporting the elderly in social engagements and in leisure activities that require physical strength.



Cyberdyne's HAL robot suit



Raytheon's XOS-2 exoskeleton

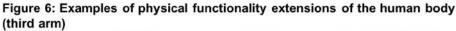
Source: Websites of Cyberdyne, https://www.cyberdyne.jp/products/LowerLimb_medical_jp.html, and Raytheon, http://raytheon.mediaroom.com/index.php?s=43&item=1652

As for proposals for new sports, leading the initiative in this area is the Superhuman Sports Society, which is co-chaired by Professor Masahiko Inami of the University of Tokyo's Research Center for Advanced Science and Technology (RCAST). Professor Inami is a leading expert in human augmentation technologies in Japan, and is a recipient of the "Coolest Invention of the Year" award given by TIME magazine in the US. The Superhuman Sports Society is pursuing activities to enhance people's quality of life, such as through developing new sports with digital technologies, and making it easy for people to participate in sports by compensating for differences in players' abilities.

The next section introduces examples of developments currently in the experimental stage, which are expected to see practical use in 5 to 10 years.

Human augmentation for realizing physical functionality extensions of the human body

The aforementioned Professor Inami of RCAST at the University of Tokyo, Professor Harry Asada of the Massachusetts Institute of Technology (MIT), and Professor Hiroyasu Iwata of Waseda University are respectively conducting research on an additional mechanical arm that a wearer can move freely just like a real arm, among other functionality. This technology has the potential to help address the working population decline, because in some cases, one person will be able to cover the work that previously required multiple people. For example, Professor Iwata is exploring how the wearing of a "third arm" could change people's everyday lifestyles, and is sharing his ideas with Panasonic to pursue practical application (Figure 6). This concept requires not only the technology to physically move mechanical arms, fingers, legs, or other appendages smoothly, but also the technology to transmit the intention of the wearer through myoelectric signals and brainwaves to the device to control it, as well to provide tactile and joint angle feedback to the wearer. Advancements in the development of the latter two technologies are considered to hold the key to future development.





Examples of how a "third arm" could change people's lifestyles, based on research by Iwata Lab, Waseda University

Hiroyasu lwata Lab collaborates with Panasonic to control mechanical arm movements with voice and vision sensory input to improve operational efficiency

Source: Materials from Hiroyasu Iwata's Human Assistive Robot Laboratory (Iwata Lab), Waseda University, and website, https://www.waseda.jp/top/news/65113

Human augmentation for releasing human consciousness from physical constraints (telexistence)

The human body performs sensory transmission using weak electrical signals, and now possibilities are emerging for the digitization of human consciousness by observing myoelectric signals and brainwaves and converting them into digital data. As mentioned above, research is being conducted into using this technology to allow a person to move a machine's arms or other parts at will. Similarly, it will also become possible to move a human arm by applying an external electric signal, and to transmit information to the human brain.

H2L (Japan) develops and supplies products based on its proprietary BodySharing technology that uses muscle displacement sensors, electrode pads, and other mechanisms (Figure 7). The company was co-founded by Emi Tamaki (currently an associate professor at Waseda University, and a researcher in the PRESTO program of the Japan Science and Technology Agency), and one of the company's earlier products was selected for TIME magazine's "The 50 Best Inventions" list in 2011. BodySharing is a technology that allows the bodies of humans and robots, for example, to mutually share various sensations (such as the sense of position, weight, and resistance). The unique aspect of the technology is that it is not limited to operations in one direction, but has to do with bidirectional information sharing. PossessedHand, a device already released by the company, enables a person's fingers and wrists to move independently of the person's intentions by applying electric stimulation from a belt with electrode pads attached wrapped around the arm. The device has achieved a level of precision that can support the playing of the koto, a Japanese stringed instrument. In the future, the use of these technologies is expected to open up the possibility of experiencing telexistence through sharing the sensations felt by others in remote locations and communicating that information.

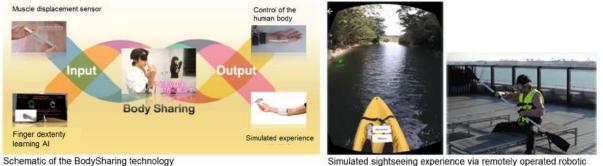


Figure 7: Examples of H2L's BodySharing technology allowing for physical control and simulated experiences

Simulated sightseeing experience via remotely operated robotic kayak, developed jointly by H2L and NTT DoCoMo

Source: Materials from H2L and company website, http://h2l.jp/2019/01/09/pressrelease20190109_h2l_docomo/

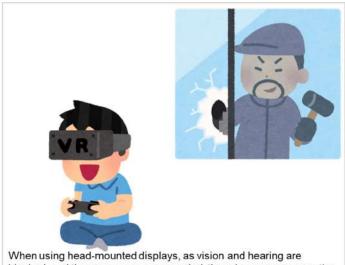
Future Prospects — Ethics and the Importance of Regulations

Although human augmentation is expected to be very useful and has the capability to meet the higher-order needs of human beings, the sheer power of its impact underscores the importance of clearly defining how such technology should be used. In recent years, in particular, innovations in technology have been evolving extremely quickly, which is giving rise to criticism that creating regulations after a technology has been established is too slow. As an example, it has been found that when a child uses a head-mounted display (HMD), there is a risk that the development of stereoscopic cells,

which continue to develop in humans until about the age of six, may be hindered or that strabismus (crossed eyes) could be caused. For this reason, in 2018, the Japanese institute, called Location-Based VR Association, published guidelines on the use of HMD for children under the age of 13, though it was only after more than 10 million HMDs had already been shipped in 2016 before the guidelines came into existence.

In addition, when experiencing telexistence, which is to share various sensations that occur in a remote place different from the user's actual location, the ability of the user to detect environmental changes at their real location is significantly reduced. This has raised the concern of a potential increase in accidents and crimes owing to the user's lack of awareness of serious situations, such as fire or theft. As such, critics are strongly emphasizing the need to discuss the establishment of regulations in parallel with technology development without waiting for development to reach completion.

Furthermore, unlike Europe and Japan, where human augmentation technologies have evolved on the back of prosthetic engineering advancements, the US started development of related technologies for military applications, and concerns about the diversion for military use are heightening. For example, the US military is working with MIT to develop a power-assistive suit that could also be used, in the event of an injury, as a cast for limbs or bones to immobilize the affected area. In fact, studies for military applications have already begun. In addition, if a human being can remotely control a drone or robot packed with explosives from a distant location, and control the device freely and easily as though the human were there on site, an explosive weapon with extremely advanced targeting precision could be developed. Considering the implications, it will become crucial for the international community as a whole to monitor the situation to ensure that these technologies are not applied for such destruction.



blocked, and the senses are preoccupied, there is a concern over the decreased ability to detect surrounding abnormalities and dangers.

Implantable Devices — Prospects for Expansion into Preventive Medicine Field —

Consumer Innovation Dept., Technology & Innovation Studies Div.

Mika Kinoshita

What are Implantable Devices?

With its downsizing and wireless communications technology advancement, ICT equipment has evolved from stationary personal computers to portable smartphones, and further to wearable devices that can be attached to a person's body. An extension of the evolution is the emergence of the "implantable device," which, in the narrow sense, refers to a chip or device that can be embedded in the body, and, in a broader sense, also includes the type that can be ingested.

Conventionally, in the medical field, implantable devices were adapted by deeply embedded into the body and only for the treatment of conditions for which no other alternative therapies existed, such as to prevent sudden cardiac arrest in patients with heart disease or to suppress the trembling of patients with Parkinson's disease who no longer respond to medications. In recent years, however, the use of implantable devices in everyday situations have come to be seen.

In August 2017, the Wisconsin-based US vending machine maker Three Square Market (32M) became the first US company to offer, in collaboration with the Swedish biometric sensor specialist Biohax International, its employees (those who are interested) subcutaneous microchip implants containing the registered personal information.

Biohax International was established in 2013 by Jowan Österlund, and since launching its implantable microchip for humans, the company has "chipped" more than 4,000 individuals (as of October 2018). The microchip uses recognition technology based on radio-frequency identification (RFID), which utilizes short-range wireless communications, and thus does not require charging. The chip enables users to carry out certain tasks, such as locking and unlocking their homes and cars, operating doors and printers in offices, and boarding trains (for the Swedish national railway system, the embedded microchip can be used in the same way as a passenger ticket) without their carrying IC cards or other things.

In addition, an ingestible form of digital medicine has been developed. Digital medicine is a tablet with a sensor component whose purpose is to improve patient care with medication management. To maximize the potential of drugs for mental illness, Otsuka Pharmaceutical partnered with the US venture company Proteus Digital Health and developed the digital medicine called Abilify MyCite. The digital medicine was approved by the US Food and Drug Administration (FDA) in 2017, and the company is to begin full-fledged sales in the US in 2020.

The antipsychotic medication Abilify has shown high therapeutic efficacy, which is naturally based on the assumption that patients take the medication as instructed by a physician. Mental illness recurs if the appropriate medication is not taken, and the symptoms worsen with each relapse. However, patients with mental illness finds it difficult to remember and manage their medications due to the symptoms of the disease. This digital medicine is expected to provide a solution to this problem.

Abilify MyCite is a package consisting of a medicinal tablet embedded with a square chip measuring approximately 1

mm (about the size of a grain of sand), a patch with a sensor, and a smartphone app. When the chip embedded in the tablet reacts with gastric fluids, it emits a weak signal. The patch with a sensor, which is affixed to the patient's abdomen, catches this signal and transmits the information to a smartphone app, enabling the user to keep track of the medications taken.

Practical Fields of Application — Preventive Medicine

Among the promising areas for implantable device applications is the preventive medicine field. As mentioned above, implantables in the medical field were mainly adapted for serious diseases in the past, but in 2019, its application saw expansion to preventive medicine, with the adoption of an implantable device for preventing heart failure when the heart's ability to pump blood to the rest of the body is insufficient. The background of this new application seems in the fact that despite increasingly effective medical therapy for heart failure and the fully established guidelines, the hospitalization rate is high and the prognosis for patients is poor. Also, the forecasted increase of patients with heart disease owing to the growing aging population, seems to have served as another factor.

The US company Endotronix has developed Cordella, an implantable device for monitoring the pressure at which the heart pumps blood. The product is intended as a preventive medical device for home use by healthy individuals who are at high risk of experiencing heart failure. It is known that in the stage before a person experiences heart failure, the pressure at which the heart pumps blood increases due to constriction of the pulmonary arteries, thickening of the inner walls of the blood vessels, thrombus formation, etc. Monitoring intracardiac blood pressure with Cordella makes it possible to provide treatment to prevent heart failure. Data gathered at the developmental stage shows that the comprehensive disease management using Cordella reduces the possibility of hospitalization by 48%,¹ and treatment with an intracardiac blood pressure monitor reduces hospitalization by 37% ² and mortality by 57%.³ Upon receiving FDA approval, on August 1, 2019, Endotronix announced that it would start clinical trials for Cordella. Then in November of the same year, the results of a 90-day trial were presented at an academic conference of the American Heart Association held in Philadelphia, confirming the product's high degree of safety and its accuracy in blood pressure measurement. Additionally, the data for remote monitoring of intracardiac blood pressure showed that 98% of patients self-administered the medication as instructed.

Future Prospects — Technologies That Prompt Expanding Adoption and Associated Challenges

Technologies driving wider adoption

Among the technologies helping increase the adoption of implantable devices are those related to all-solid-state batteries,

¹ Anderson WL et al. Minnesota Managed Care Longitudinal Data Analysis. U.S. Dept of Health and Human Services Contract #HHSP23320100021WI. March 31, 2016.

² Abraham WT et al. Wireless pulmonary artery heamodynamic monitoring in chronic heart failure: a randomized controlled trial. Lancet. 2011 Feb 19;377(9766):658-66.

³ Abraham, WT et al. Pulmonary artery pressure management in heart failure patients with reduced ejection fraction significantly reduces heart failure hospitalizations and mortality above and beyond background guideline-directed medical therapy. Abstract 902-04, ACC 2015.

which realize longer battery lifespans; bioelectric energy without the need for an external power source; and molecular robots, which respond to the biological substance adenosine triphosphate (ATP) and other substances.

(1) All-solid-state batteries

All-solid-state batteries use a solid electrolyte, instead of the conventional liquid electrolyte, for driving the movement of lithium ions between the electrodes of a lithium-ion battery. The properties of the battery make it possible to reduce the structure thickness, increase the capacity by stacking layers, improve durability, and perform high-speed charging/discharging. Endotronix's Cordella, mentioned above, uses an all-solid-state wirelessly rechargeable battery supplied by the nanotechnology venture company Ilika Technologies (UK). Until now, implanted medical devices have been replaced every few years through surgery. However, in order to alleviate the burden on patients, technologies related to battery lifespans and wireless charging have advanced and improved, resulting in the reduced frequency of replacements. Ilika's all-solid-state battery has achieved a lifespan of up to 10 years when charged/discharged once a day.

(2) Bioelectric energy

Bioelectric energy, which does not need an external power source, is a technology whose energy comes from heart pulsations, lung movements (respiration), and other biological functions, on the basis of battery technology for suppressing the natural discharge of energy. The abovementioned UK company Ilika has already developed an all-solid-state battery that suppresses the natural discharge of energy, and plans to develop this battery into one capable of generating bioelectricity.

Although still in the research stages, the New Mexico State University in the US is developing a low-frequency piezoelectric energy harvester for securing energy from heartbeat vibrations; while MIT is developing a new technology called in-vivo networking (IVN) for wireless power supply to and data communication with an ultra-small battery-free device that is implanted deep inside the human body. Animal experiments using pigs have confirmed the IVN system's capability to supply power from a distance of 1 m to devices implanted at a depth of 10 cm from the body's surface. If human clinical trials for this device prove its effectiveness, commercialization is expected by 2024 for a variety of applications in the medical field, including targeted cell drug delivery, monitoring, and therapy.

As for the social implementations of bioelectric energy technologies, the US market research firm Frost & Sullivan predicts a range expansion of bioelectricity applications in 2020, and widespread adoption of the technologies in low-powered electronic devices, including medical implantables, from 2021 onward.⁴

(3) Molecular robotics

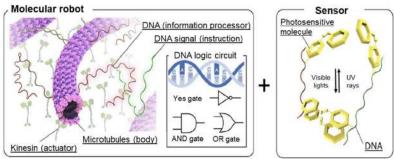
Molecular robots are ultra-tiny robots of micrometer to nanometer size made of biomolecules, such as DNA and proteins, and artificial macromolecules. It consists of a "drive system," which serves as the energy source, an "intelligence and control system" for giving commands, and a "sensor" for switching executions on and off. As it can operate autonomously like a cell in response to biomolecules, it does not require a power supply.

⁴ TechVision Group of Frost & Sullivan, TechVision Analysis / D7FA / 00, Technology Impact Assessment of Micro Energy Harvesting. 2018-05-31

In addition, molecular robots are designed using the properties of the constituent molecules themselves, and are built by the self-assembly of molecules, similar to the growth of snow crystals, the pulsation of the heart, and the formation of patterns on the surface of living organisms. If molecular-level accuracy equivalent to that in nature can be achieved, potential applications will include in-vivo calculations, diagnosis, treatment, and artificial cell membrane construction. In recent years, there have been reports⁵ on the development of tiny folded DNA nanorobots that deliver drugs only to targeted cancer cells, which are also helping fuel interest in molecular robots.

Associate Professor Akira Kakugo of the Faculty of Science, Hokkaido University, has succeeded in creating the world's smallest molecular robot with the aim of performing in-vivo tasks. ^{6,7} The drive system of this molecular robot is composed of kinesin, a motor protein that has the function of transporting substances in the body, and microtubules, which are proteins that serve as a scaffold for the kinesin. The intelligence and control system uses DNA, and the sensor part uses DNA incorporated with molecules whose structures change when exposed to light (Figure 1).

Figure 1: Molecular robots developed by research groups of Hokkaido University and Kansai University



Source: Press release by Hokkaido University and Kansai University, https://www.hokudai.ac.jp/news/180201_pr.pdf

For an energy source, this motor protein uses ATP, which is abundant in the body, meaning there is no need for a power supply. DNA is composed of four types of bases — adenine, guanine, cytosine, and thymine — and each base can bond only with a specific base partner. Therefore, when the original double helix structure is unraveled, single-stranded DNA can recognize molecules (bases) that are paired with itself, and using that recognition ability, it has become possible to control the motor protein. According to the Delphi analysis-based foresight surveys on science and technology trends conducted by the National Institute of Science and Technology Policy, which is a research institution under the Ministry of Culture, Sports, Science and Technology of Japan, technological development and societal implementation of the photon technologies for unrestricted control and measurements of the arrangement and movement of micro/nano-machines and biomolecules, are estimated to be realized between 2030 and 2033.

MITSUI & CO. GLOBAL STRATEGIC STUDIES INSTITUTE

⁵ Li S et al. A DNA nanorobot functions as a cancer therapeutic in response to a molecular trigger in vivo. Nature Biotechnology 36, 258-264(2018)

⁶ Keya JJ et al. DNA-assisted swarm control in a biomolecular motor system. Nat Commun. 31;9(1):453(2018)

⁷ Japan Science and Technology Agency, Science Portal website:

https://scienceportal.jst.go.jp/clip/20191007_01.html

Challenges Ahead — Protection of Personal Information/Cybersecurity and Safety for Human Body

Implantable devices can make it possible to carry out smooth transactions in various everyday situations, such as for authenticating personal identifications and making payments, and have also spawned new medical treatments. At the same time, however, a number of issues need careful deliberation. They include privacy and personal information security, cybersecurity vulnerabilities, long-term physical safety, the need for surgical procedure in the event of equipment updates, and device failures.

The US FDA has been reviewing cybersecurity vulnerabilities related to implantable devices since 2017. Meanwhile in the EU, the enactment of legislation related to medical devices is expected in 2020. If relevant oversight and regulations are tightened, product manufacturers will face the need to develop cybersecurity measures for their devices, such as updated software and firmware to prevent unauthorized access. How this factor will impact the spread of implantable devices is worth watching. Regarding safety, the FDA officially announced in 2005 that RFID chips, which are the mainstream of embedded microchips, are safe to be placed under the skin. Zoltan Istvan⁸, a noted transhumanists who was among the first adopters of the technology, says that a tube can be implanted under the skin to make microchip replacement easy.

Despite various challenges, if safe implantable devices are developed with the evolution of nanotechnology and biotechnology, social implementation is expected to progress further and the use of implantable devices in everyday situations will then likely expand. For example, an implantable device can collect highly specific and accurate vital data for disease prediction unobtainable from smartwatches and other wearables, and is thus expected to contribute to predictive medicine.

In addition, as the development of molecular robots progresses, methods of test for disease diagnosis and treatment may

change dramatically. A possibility in the future is to have molecular robots live and patrol in the body, and, once an abnormality is detected, rush to the affected area with drugs to perform treatment. In this way, molecular robots could complete treatment before the condition becomes aggravated (Figure 2).

How people's values will change in the future warrants attention — that is, the change in the balance between people's hesitation toward the idea of embedding microchips into their bodies vs. the convenience and necessity of such devices.

Source: Compiled by MGSSI

Figure 2: Schematic view of molecular robots treating disease in vivo

⁸ A proponent of transhumanism. Transhumanism is described as the ideology and movement to transcend biological limits through the active use of science and technology, and its philosophy (Transhumanist Association).

Photon Technology —Next-generation Technologies Derived from Analog Element of Light —

Yutaka Abe, Technology Trends Basic Research Center

What is Photon Technology?

Photon technology is a basic technology of light— that is, electromagnetic waves classified into ultraviolet light, visible light, and infrared light — for various applications by making use of both the wave and particle properties inherent in light. In the course of evolution, human beings acquired the light of fire and took a step forward toward civilization, and since the early modern era, scientists have long been seeking the answer to the question, "What is light?" As research on light progressed, opinions became divided contradictorily between those claiming that light is a "wave" that travels through space, and those saying that light is a minute "particle." In 1905, Albert Einstein published his "light quantum hypothesis," ⁹ suggesting that the smallest unit of light was the photon, and this gave credence to the particle theory for some time. However, based on subsequent studies and experiments, light was determined to have both wave and particle properties (light duality), and this view has been upheld to this day. ¹⁰

Photon technology	Description	Promising applications/devices
(1) Photon technology to manipulate: Optical tweezers	Method to manipulate proteins and fine particles using a highly focused laser beam.	Plasmon optical tweezers, synthetic cell production Addition of sugar chains and proteins to cell surfaces
(2) Photon technology to treat: Photoimmunotherapy	A medical treatment combining photodynamic (near-infrared radiation) therapy and immunotherapy.	Cancer treatment (superficial cancers, such as head and neck cancers) In the future, treatment of deeper cancers
(3) Photon technology to measure: Optical lattice clock	A next-generation clock with a level of accuracy approximately 1,000 times that of the currently most precise atomic clock.	Next-generation high precision clock Quazi-Zenith Satellite System equipped with optical lattice clock
Metamaterial	A material engineered to reflect, refract, and absorb light in ways not usually seen with natural materials.	Optical camouflage, asymmetric transmission shield
Laser cooling	A laser is used to irradiate atoms to stop their movement, sharply dropping the temperature of the object.	Superfluidity (Bose-Einstein condensation) Optical lattice quantum computing
Optical additive manufacturing Femtosecond laser processing	A 3D printer that uses a laser to melt and stack metals, such as titanium and iron. Processing by laser irradiation using ultrashort pulses of one quadrillionth of a second.	Metal 3D printer, multitasking processing machine, Femto laser machining
Quantum entanglement optical imaging	Ultra-precision measurement using peculiar properties of quantum (quantum entanglement).	Quantum inertial sensor, quantum biological sensor
Quantum radar	Application of quantum entanglement to radar technology to detect stealth aircraft.	Military-use quantum radar, early warning radar
Terahertzradiation	Submillimeter radiation featuring properties of both light and radio waves, and also excellent transparency. Considered a frontier sciences technology.	6G communication technology Non-destructive testing, pathology testing, etc.
Optogenetics	Technology for controlling nerve cells by illuminating light-activated proteins.	Cranial nerve research, brain disease treatment

Figure 1: Overview of main photon technologies and expected applications

Note: (1), (2), and (3) are technologies discussed in this report. Source: Compiled by MGSSI

⁹ Einstein's "light quantum hypothesis" theorizes that when light behaves as particles, the smallest unit is a photon. The hypothesis was an extensive application of Max Planck's quantum hypothesis to light. Einstein received the Nobel Prize in Physics for his quantum of light hypothesis (discovery of the photoelectric effect).

¹⁰ In 1905, Einstein published three papers, including the quantum of light hypothesis, won Brownian motion, and on the special theory of relativity. In 1927, Niels Bohr published a concept of quantum mechanics called the Copenhagen Interpretation. Einstein was skeptical of Bohr's concept and continued to debate with Bohr until his own death. Bohr's argument was eventually proven to be correct.

Speculation and experimentation to explore the essence of light have produced the quantum theory and the theory of relativity, which are the cornerstones of modern physics. It can be said that the very study of light has led revolutionary shift from the time of Isaac Newton's classical mechanics to modern physics. Then, in 1960, the invention of the laser provided a breakthrough in optical technologies, which have since driven the cutting-edge science advancements. Today, such as optical fibers, solar cells, LED lighting, DVDs, LCD televisions, photocatalysts, and surgical-use laser scalpels, are adapted into people's everyday lives as mature technologies.

These optical technologies, widely used in our daily lives, have been improved in precision and miniaturization on the back of semiconductor manufacturing technology, which makes full use of lithography and other fine processing technologies. However, as Moore's Law indicates, their technological development is reaching its limits. In order to break such limitations and to innovate optical technologies, scientists are developing laser technologies and devices, such as photodetectors, based on new photonic concepts. (Figure 1) This report first focuses on technologies to (1) manipulate, (2) treat (3) measure, and then review the most recent developments related to the quantum internet, which represents the pinnacle of photon technology.

Promising Fields of Application

(1) Photon Technologies to Manipulate: Optical Tweezers

The 2018 Nobel Prize in Physics was awarded to three physicists who developed a technique called optical tweezers, the establishment of which was recognized by the prize. The principle of optical tweezers uses the property of light in which an ultraslight pressure is exerted on a substance upon the irradiation of light. The pressure of light is between one billionth and 10 billionth of a newton,¹¹ and humans do not feel this pressure. However, proteins and other fine substances are affected by light pressure. Optical tweezers are a technique for manipulating fine substances by using this light pressure. As shown in Figure 2, laser light is concentrated by a lens and irradiated onto the substance to be moved. By utilizing

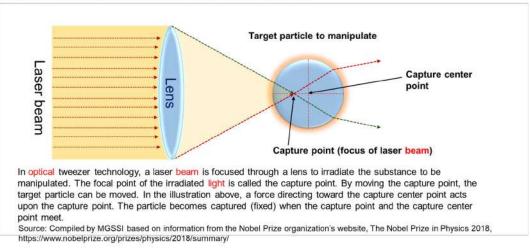


Figure 2: Schematic representation of optical tweezers

 11 The newton is a unit of power. A force that causes a mass of 1 kg to accelerate 1 m/s2 is defined as 1 newton.

the pressure of the focused light, the substance can be rotated, pushed, pulled, or set in a fixed position without directly touching it. Optical tweezers are now an indispensable technology for studying the biological materials of cells, such as DNA, RNA, proteins, and mitochondria.

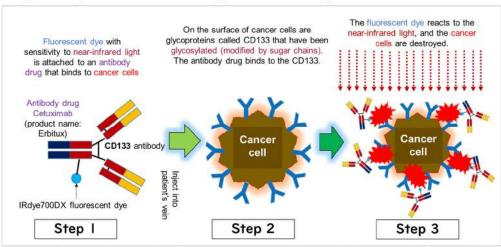
Behind the optical tweezer's receiving the Nobel Prize lies another important technology, a pulse technique for generating a laser for an ultrashort amount of time. Current pulse technology has reached the femtosecond level. One femtosecond is one quadrillionth of a second. For example, light travels at a speed of approximately 300,000 km per second (a distance equivalent to seven and a half times the Earth's circumference), and travels about 0.3 µm in one femtosecond. Researchers in the field of photon technology are now developing an even more astounding pulse technology, called attosecond pulse technology (an attosecond is one quintillionth of a second), which is shorter than a femtosecond. It is said that the attosecond level optical pulse can capture the movement of electrons. Electrons are the elementary particles involved in chemical reactions, such as redox, and electrical phenomena. The development of technology allowing for observation of the individual movements of these electrons is possibly expected to open up a whole new realm of scientific technologies because it will enable visualization of phenomena inside biological and electronic materials to clarify biological phenomena and the principles of various physical phenomena.

(2) Photon Technologies to Treat: Photoimmunotherapy (cancer therapy)

Figure 3: Diagram of cancer treatment by photoimmunotherapy

Conventional cancer treatment involves the surgical excision of cancer sites or irradiation of the affected area with radiation therapy, using X-ray or proton beams, which can affect normal cells as well. Photoimmunotherapy is different in that it can be used to kill only cancer cells by applying harmless "light" to the site. The light used in photoimmunotherapy is near-infrared light that penetrates into the body. This photoimmunotherapy technology was developed by the US National Cancer Institute.

Photoimmunotherapy is a three-step treatment. In the first step, a drug is prepared by combining a chemical substance that reacts when exposed to light, and an antibody that binds to a protein on the surface of cancer cells. This is then injected into the patient's vein. In the second step, the antibody traverses the body looking for the unique proteins on the surface of cancer cells and binds to those cells. The third step is the irradiation of near-infrared light to the drugs that



Source: Compiled by MGSSI with reference to publications of the US National Cancer Institute, H. Kobayashi et al., Cancer Cell-Selective In Vivo Near Infrared Photoimmunotherapy Targeting Specific Membrane Molecules (PMID:22057348) have swarmed to the cancer lesion. ¹² Then, the light triggers a chemical reaction with the chemical substance bound to the antibody, and the energy is used to destroy the cell membrane and the cancer cell dies. (Figure 3) The near-infrared rays used in photoimmunotherapy do not affect normal cells. However, the benefits of this treatment are currently limited to superficial cancers.

In April 2018, a clinical trial of photoimmunotherapy began at the National Cancer Center Hospital East (Kashiwa, Chiba Prefecture) for patients with head and neck cancer. In addition, on July 1, 2019, Rakuten Medical, which is working to commercialize photoimmunotherapy, announced the results of clinical trials in the US, reporting that out of the 30 trial subjects (head and neck cancer patients) who had failed to respond to conventional treatments, such as chemotherapy, the effect of photoimmunotherapy on their cancers resulted in the disappearance of lesions in four patients, and a reduction in the size of lesions in nine. Photoimmunotherapy has become a focus of attention because, as mentioned above, it greatly alleviates the physical burden on patients, unlike conventional treatments, and it has been reported that the National Cancer Center received many applications from patients who want to participate in its clinical trials.

(3) Photon Technologies to Measure: Optical Lattice Clock

Since the dawn of history, time has been determined with reference to astronomical cycles, such as the Earth's revolution and rotation. At present, the world standard for time is based on the cesium atomic clock. At the 1967 General Conference on Weights and Measures (CGPM), the second was redefined on the basis of the radiation frequency at which cesium atoms emits, and this definition stands to this day. Cesium atomic clocks have exceptionally high accuracy, losing only 1 second every 30 million years. However, the development of clocks with accuracy surpassing that of cesium atomic clocks is currently underway in Europe, the US, and Japan.

Based on Einstein's theory of relativity, the passage of time changes depending on physical conditions. For example, moving to a position 1 cm higher from the original position will make time pass faster, albeit by an exceedingly minute degree. ¹³ This is because gravity weakens proportionally to the 1 cm change in altitude. The optical lattice clock can measure such extremely delicate changes in time. The cesium atomic clock, which boasts the highest precision at present, measures the frequency of one cesium atom and calculates the measurement 1 million times to minimize error, thereby achieving high precision. ¹⁴

The optical lattice clock has a different approach. It uses laser light to confine 1 million atoms at a time into a specific area, referred to as the optical lattice (Figure 4), and measures the radiation frequency of the atoms in the field. It is a mechanism for obtaining a measurement with an unparalleled level of precision.¹⁵

The accuracy of optical lattice clocks is reportedly 100-1,000 times higher than that of cesium atomic clocks, at an

¹² The area around the cancer cells is pierced with several hypodermic needles containing optical fibers and then irradiated for several minutes.

¹³ According to the theory of relativity, moving to a position 1 cm higher than the current position will make time pass faster by 0.00000000000000000 seconds.

 $^{^{14}}$ One second is defined as the duration of 9,192,631,770 oscillations of cesium atoms.

¹⁵ With a cesium atomic clock, 1 million measurements and calculations are required, which takes about 10 days. Optical lattice clocks have the advantage of requiring much less time because they measure and calculate 1 million atoms at once.

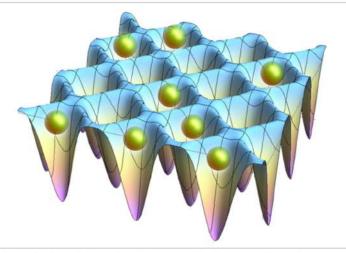


Figure 4: Schematic representation of an optical lattice

Source: Professor Hidetoshi Katori, Department of Applied Physics, School of Engineering, The University of Tokyo

inaccuracy of 1 second in 30 billion years. If the cosmology that puts the age of the universe at approximately 14 billion years is correct, it could be said that the optical lattice clock effectively makes no error. Even current precision clocks, including atomic clocks represent not conspicuous but essential technology, serving as a foundation for various operations in our society, such as high-frequency financial transactions, timestamps in electronic commerce, car navigation using the global positioning system (GPS), and the control of data transmission/reception synchronization of cellular base stations. If optical lattice clocks are adopted in society instead of atomic clocks, it is said that they could be used for sensing changes in the Earth crust and for exploring underground mineral resources, among other applications.¹⁶

Future Prospects

Going forward, photon technology is expected to lead to innovative developments, such as optical devices, optical measurement/analysis devices, and optical information processing systems, and is viewed as one of the breakthrough technologies to provide solutions for social and industrial problems. Of particular interest is the quantum internet. The quantum internet is an advanced type of "photonic network" consisting of photonic computers for performing high-speed calculations using light, and photonic devices for recording and transmitting information. The existing Internet is supported by such as communication lines made of optical fiber or metal wire, relay devices enabling long-distance communication, and communication control servers. The photonic network concept in which all of these communication devices are comprised only of photon devices is currently under study. On a global basis, ICT systems consume more than 10% of the power generated worldwide, and the figure is projected to reach 20% by 2030.¹⁷ The kinds of

¹⁶ According to the theory of relativity, the presence of a large mass distorts the space around it, and this distortion slows down the progress of light, making it possible to identify the presence or change of a substance with a large mass. Specifically, tens to hundreds of optical lattice clocks would be integrated into a "photonic network," and the variation in the arrival time of the photons of each optical lattice clock would be calculated to determine the presence or absence of a large underground mass.
¹⁷ Nature (September 13, 2018) Vol. 561, The Information Factories.

communication technologies needed in the future are those with low power consumption and large processing capacity without latency. The most promising technology to meet those requirements is the photonic network. By replacing the fiber optic repeater in an optical network with a quantum repeater¹⁸ capable of quantum communication, the "quantum internet" can be realized.

Until recently, the realization of a quantum relay was expected to take a long time because of many associated technical challenges. However, on January 25, 2019, a team consisting of Nippon Telegraph and Telephone (NTT), Osaka University, and the University of Toyama succeeded in verifying the principle of a quantum relay using optical devices. The breakthrough represents a big step forward toward realizing the quantum internet. As the quantum repeater had been considered the toughest technical hurdle, Japan has now moved one step ahead of the rest of the world.

NTT, which took a leading role in the experiment, has proposed the IOWN¹⁹ initiative, and it is working to drastically change its technological strategy, upholding its vision to move "from the era of electronics into photonics." Furthermore, in November, NTT announced it would collaborate with the US National Aeronautics and Space Administration (NASA), Stanford University, and others to develop a quantum computing system using photonic technologies. As these developments suggest, the trend of future technology advancements will be the one aiming to achieve social implementation of an information network integrating quantum computing with a quantum internet, making the most of the properties of the analog element of light. This new information network is expected to be a safe, secure, ultra-high-speed, energy-saving network in place of the current Internet, and will likely provide a social infrastructure that will lead to the resolution of various issues facing human society and the realization of a truly "smart" society. Attention is thus warranted for photon technology development trends in 2020 and beyond.

¹⁸ In the case of quantum communication, an extremely subtle physical state of quantum mechanics called quantum entanglement is used. It is very difficult to maintain "entanglement" over long distances. A device that can maintain this delicate entanglement over long distances is a "quantum repeater."

¹⁹ IOWN (pronounced ai-on) is an abbreviation for NTT's technology vision, called Innovative Optical and Wireless Network.

Summary of Technologies Highlighted in 2019 (BMI/Protein Engineering/Haptics)

Following is a brief summary of the subsequent developments of BMI (Brain Machine Interface), protein engineering, and haptics, which were introduced in our report entitled *Technologies to Watch in 2019* published in January 2019.

BMI (Brain Machine Interface)

BMI is a generic term for technologies that directly or indirectly connect the brain and a machine to look inside the brain, enhance functions of the brain, or treat diseases of the brain. The January 2019 report predicted that BMI technologies, development of which has taken place mainly in the military field, would likely spread to the civilian sector and give rise to new products and services.

As expected, 2019 was a notable year for both non-invasive and invasive BMI.

In April, the Israeli company Brainsway was listed on the NASDAQ stock exchange. Brainsway is a medical device manufacturer engaged in the development and sales of non-invasive BMI devices utilizing Deep Transcranial Magnetic Stimulation (Deep TMS) technology. The company's Deep TMS system received marketing approval from the US Food & Drug Administration (FDA) for the treatment of depression (2013) and obsessive-compulsive disorder (2018), and it has built up a track record with these conditions. Brainsway has announced plans for clinical trials of Deep TMS for other areas, including smoking cessation, post-traumatic stress disorder (PTSD), opioid addiction, and post-stroke rehabilitation, and the use of BMI in the treatment of brain and neurological disorders is likely to progress in the future. In terms of invasive BMI, Elon Musk, CEO of the US company Neurolink, attracted a great deal of attention in July 2019 when he announced that clinical trials will commence in 2020 on the 'N1 implant' device being developed by the company. The N1 implant is a device that utilizes multiple thread-like electrodes that are implanted into the cerebral cortex, and consists of four chips that process signal information from the brain, as well as a wearable computer. Neurolink is also developing a neurosurgical robot to insert the N1 implant into the cortex, and the system has been highly evaluated by experts in the field.

As described above, the BMI development has already produced concrete results, and from 2020, its application is expected to expand from the medical field to other fields, including entertainment, education, and marketing. (Yutaka Abe, Technology Trends Basic Research Center)

Protein Engineering

Protein engineering is a technology for modifying proteins, such as natural antibodies and enzymes, to enhance their functions or equip them with new functions. This technology has ushered in a new era where, in addition to modifying proteins, it has become possible to design and produce completely new proteins from scratch. Last year's report described protein engineering developments which are recently being applied in the agricultural, food, and materials fields, other than in the medical field so far.

In 2019, protein engineering progressed from the research and development stage to the widespread utilization and expansion stage.

The US protein design company, Arzeda, has commenced collaboration with Mitsubishi Rayon (currently Mitsubishi Chemical) and Germany's Evonik Industries, two large corporations with strengths in large-scale commercial production. In April 2019, Codexis, another US company that designs and develops proteins, concluded a multi-year agreement with the UK's Tate & Lyle to supply a particular type of enzyme with a view to expanding production of the TASTEVA M sweetener developed by Tate & Lyle in 2018. The US company Modern Meadow has strengthened its relationship with Evonik, as seen in the investment from Evonik Venture Capital in September 2019. While last year's report highlighted the development of plant-based egg, it was plant-based meat that attracted more attention. The US company Beyond Meat raised USD 240 million in its initial public offering in May, and its plant-based meats have been adopted by Kentucky Fried Chicken and McDonald's in the US. Impossible Foods, another US plant-based meat manufacturer, is also gaining popularity and expanding sales, including the adoption of its products by the US Burger King chain, and commencement of sales in retail stores. In Japan, too, the development of plant-based meat by companies, including Otsuka Foods, Marukome, Fuji Oil, and Morinaga, attracted media coverage. In addition, Japan's Spiber and Goldwin teamed up to produce clothing made from protein fiber produced by microbial fermentation, launching a T-shirt in August followed by an outdoor jacket in December. In March, Spiber also concluded a joint research agreement with Sumitomo Mitsui Construction with the aim of developing new protein-based materials and technologies for the construction sector.

Having entered the stage of widespread utilization and expansion, protein engineering is now extending its reach into new fields. Protein engineering holds new possibilities that will impact the industrial world going forward, and it is a technology that warrants continued attention. (Consumer Innovation Dept.)

Haptics

Haptics is a technology that transmits tactile sensations through vibration or force. Last year's report noted that haptics will prove to be an important technology that will further enhance the user experience in applications such as gesture recognition feedback to enable hands-free control of devices in situations where a high level of hygiene management is required, and teleoperation and VR in medical and manufacturing scenarios.

In October 2019, Sony Interactive Entertainment (SIE) announced that haptics technology will be incorporated into the controller of the PlayStation 5 to be released at the end of 2020. According to SIE, this will give gamers an even more immersive experience. More specifically, in the words of an SIE spokesperson: "Crashing into a wall in a racing car feels very different to tackling on the football field," "You can even enjoy the feeling of running through fields of grass or wading through mud," and "The intense sensation of drawing a bow, and the at once acceleration sensation of an off-road vehicle on a rugged, rocky terrain can be reproduced more vividly."

In addition, in July 2019, Toyoda Gosei announced the development of e-Rubber, a rubber that expands and contracts with the application of voltage. To reproduce various nuance of softness, such as elastic and springy kinds, it is necessary to generate complex waveform vibrations in the low-frequency range (200Hz or less). e-Rubber has realized this, and it is said that it can be used for such as the realistic reproduction of a pulse in telemedicine.

In other examples, Teijin and Keio University announced the development of a suit that gives the wearer a simulated tactile experience, while the demonstration of a teleoperated robot incorporating haptics technology at SoftBank World 2019 offered the prospect of future applications in telemedicine and agriculture. 2019 proved to be a year of growing expectations for the practical application of haptic technology in the years ahead. (Akira Yoshimoto, Consumer Innovation Dept.)

Any use, reproduction, copying or redistribution of this report, in whole or in part, is prohibited without the prior consent of Mitsui & Co. Global Strategic Studies Institute (MGSSI). This report was created based on information and data obtained from sources believed to be reliable; however, MGSSI does not guarantee the accuracy, reliability, or completeness of such information or data. Opinions contained in this report represent those of the author and cannot in any way be considered as representing the unified opinion of MGSSI and the Mitsui & Co. group. MGSSI and the Mitsui & Co. group will not be liable for any damages or losses, whether direct or indirect, that may result from the use of this report. The information in this report is subject to change without prior notice.

🔅 MITSUI & CO. GLOBAL STRATEGIC STUDIES INSTITUTE