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Challenges in Advancing Biomanufacturing Toward Bioeconomy and Framework for Key Considerations in Policy Discussions

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*The original Japanese paper can be accessed below.
https://ifi.u-tokyo.ac.jp/wp/wp-content/uploads/2024/09/WP032.pdf

1. Background on Bioeconomy and Biomanufacturing

(1) Background: Biomanufacturing and the demand for the solution of societal issues through green innovation

In October 2020, Japan made a commitment to achieving Carbon Neutral by 2050, setting a goal of bringing net greenhouse gas emissions to zero by that year. To support this, vigorous efforts have been made to promote Green Transformation (GX)[1] initiatives, including a two-trillion-yen Green Innovation (GI) Fund that was established in the third supplementary budget for fiscal year 2020, and the Act on Promoting a Smooth Transition to a Decarbonized Growth-Oriented Economic Structure which was enacted in May 2023. There is also growing expectation, both domestic and international, for the realization of a bioeconomy, which seeks to offer solutions for societal issues such as global warming and other environmental issues while promoting economic growth by shifting the basis of the social and industrial structures from fossil resources and chemical processes to biomass resources and bioprocesses, as well as for "biomanufacturing"[2] driven by synthetic biology and engineering biology, which plays a central role in a bioeconomy.

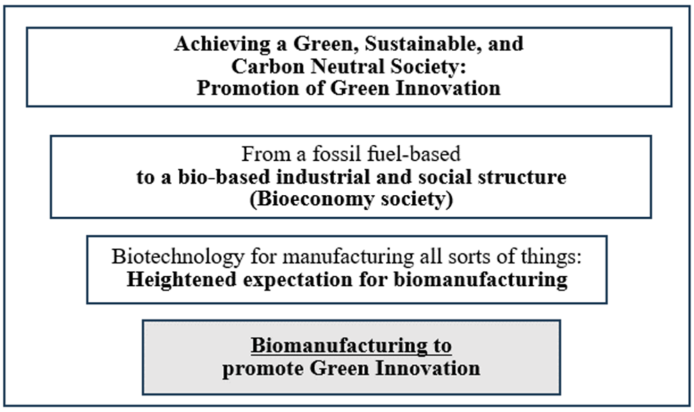

Figure 1. [Policies concerning societal challenges and the scope of this research project]

[1] The Act on the Promotion of Smooth Transition to a Decarbonized, Growth-Oriented Economic Structure (Act No. 32 of May 19, 2023) defines "decarbonized growth-oriented economic structure" (also known as Green Transformation (GX)) as follows: an economic structure that enables economic growth by strengthening industrial competitiveness without, in principle, allowing carbon dioxide derived from the energy and raw materials used in industrial activities to be emitted into the atmosphere.

[2] Biomanufacturing is defined as "a technology that produces useful materials through the metabolic functions of microorganisms, animals, plants or other organisms, or that creates foundations for producing useful materials using animal cells or the like, by increasing these cells or growing them to high density. In doing so, it is possible to produce valuable target materials or to increase productivity by modifying the genes or editing the genomes of the cells, etc". Source: Cabinet Office (2024). Bioeconomy Strategy. Integrated Innovation Strategy Promotion Council decision (June 3, 2024). https://www8.cao.go.jp/cstp/bio/bio_economy_en.pdf (English translation), p.10. https://www8.cao.go.jp/cstp/bio/bio_economy.pdf (Japanese)

(2) Growing expectations for biomanufacturing in leading countries

Leading countries have consistently promoted the bioeconomy[3] and advanced their science and technology policies with biotechnology, including synthetic biology and engineering biology, as one of key elements. In recent years, there has been a noticeable trend where countries make a renewed effort to introduce new measures and discussions to integrate these technologies and biomanufacturing into society.

In the United States, the President issued an Executive Order[4] to advance the National Biotechnology and Biomanufacturing Initiative (NBBI) in September 2022. The Fact Sheet[5] for the Executive Order refers to industry analysis that suggests possibilities of bioengineering accounting for more than a third of global output of manufacturing industries, or $30 trillion in value, before the end of the coming decade; based on this analysis, the Fact Sheet states that the initiative would focus on growing domestic biomanufacturing capacity, expanding market for bio-based products, accelerating research and development to solve societal challenges, improving data access and quality, developing human resources, increasing regulatory transparency and efficiency, securing biosafety and biosecurity, protecting the biotechnology ecosystem, and promoting partnerships with allied nations. With the NBBI as the basis, the Office of Science and Technology Policy (OSTP) published Bold Goals for U.S. Biotechnology and Biomanufacturing[6] in March of the following year (2023), the Department of Defense released its Biomanufacturing Strategy[7] and the Department of Commerce's Bureau of Economic Analysis published a report[8] on economic indicators related to the bioeconomy in the same month. In June of the same year, a report[9] on building a bioeconomy workforce, or "bioworkforce," was released. Additionally, the U.S. Congress established the National Security Commission on Emerging Biotechnology (NSCEB)[10] as a legislative branch advisory entity to examine emerging biotechnologies from a national security perspective.

Similar movements have been seen in Europe, as a Communication[11] outlining goals for promoting biotechnology and biomanufacturing was issued in March of this year (2024). This Communication acknowledges that

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[3] While there are different definitions of "bioeconomy," Japan's Bioeconomy Strategy defines it as follows: "A concept that expands a sustainable and renewable circular economy by using biotechnology, renewable biological resources, etc." Cabinet Office (2024) Bioeconomy Strategy. Integrated Innovation Strategy Promotion Council decision (June 3, 2024) *op. cit.*

[4] Executive Order on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy. https://www.whitehouse.gov/briefing-room/presidential-actions/2022/09/12/executive-order-on-advancing-biotechnology-and-biomanufacturing-innovation-for-a-sustainable-safe-and-secure-american-bioeconomy/

[5] White House website. FACT SHEET: President Biden to Launch a National Biotechnology and Biomanufacturing Initiative. https://www.whitehouse.gov/briefing-room/statements-releases/2022/09/12/fact-sheet-president-biden-to-launch-a-national-biotechnology-and-biomanufacturing-initiative/

[6] White house (2023). Bold Goals for U.S. Biotechnology and Biomanufacturing - Harnessing Research and Development to Further Societal Goals. https://www.whitehouse.gov/wp-content/uploads/2023/03/Bold-Goals-for-U.S.-Biotechnology-and-Biomanufacturing-Harnessing-Research-and-Development-To-Further-Societal-Goals-FINAL.pdf

[7] DoD (2023) Biomanufacturing Strategy. https://www.cto.mil/wp-content/uploads/2023/03/2023-Biomanufacturing-Strategy.pdf

[8] DoC (2023) Bureau of Economic Analysis, Developing a National Measure of the Economic Contributions of the Bioeconomy. https://www.bea.gov/system/files/papers/bea-bioeconomy-report.pdf

[9] White house (2024) Building the Bioworkforce of the Future. https://www.whitehouse.gov/wp-content/uploads/2023/06/Building-the-Bioworkforce-of-the-Future.pdf

[10] The National Security Commission on Emerging Biotechnology (NSCEB). The commission is expected to submit a comprehensive report to Congress in 2024. https://www.biotech.senate.gov/

[11] EU (2024) Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions, Building the future with nature: Boosting Biotechnology and Biomanufacturing in the EU. https://research-and-innovation.ec.europa.eu/document/download/47554adc-dffc-411b-8cd6-b52417514cb3_en

biomanufacturing is a key for the competitiveness and enhances the EU's strategic autonomy, and that it is a critical technology from the economic security perspective. It also discusses various applications and the current challenges, followed by a plan consisting of the eight actions: simplified regulatory framework; better support for scale-up and ease of navigating regulations; use of AI; encouragement of private and public investments; promotion of fair comparison with fossil-based products; bigger market; and review of the EU Bioeconomy Strategy.

In the U.K., a wide range of efforts have been made in synthetic biology. In December of last year (2023), the Department for Science, Innovation and Technology (DSIT) published the National Vision for Engineering Biology, committing to a two-billion-pound investment over the next decade.[12] This policy paper outlines a plan to set up an advisory body consisting of industry leaders called the Engineering Biology Steering Group to consolidate the sources of advice into a single body, and presented six objectives to work on including world-leading research and development, investment in infrastructure, development of talent and skills, regulatory issues and standardization, adoption in the wider economy, and responsible and trustworthy innovation.

At the international level, the OECD's Global Forum on Technology (GFTech) identified synthetic biology as one of key technologies and established a focus group on synthetic biology in November 2023 to have experts discuss governance in the field of synthetic biology, including biomanufacturing[13]. The focus group collects and organizes information on relevant technical, social and policy issues for the purpose of informing policymakers on these matters.

Discussions on international standardization are also underway. For instance, Engineering Biology Research Consortium (EBRC), a U.S.-based non-profit public-private partnership, hosted workshops on standardization last year in three regions, namely the Americas, Asia/Australia, and Europe/Africa, and created a report.[14]

In Japan, meanwhile, its bio-strategy established in 2019 contained elements that would lead to what is known today as biomanufacturing. When the strategy was updated in June 2024 and renamed as the Bioeconomy Strategy,[15] it streamlined and consolidated these elements into the concept of biomanufacturing. The market opportunities created by the implementation of biomanufacturing in the society are considered as one of the five key markets from a strategical perspective and are expected to be the primary driver of bioeconomy market's growth.

(3) Challenges recognized and objectives and methodology of this working paper

Recognizing challenges

Biomanufacturing has gained significant attention through a slew of policies developed rapidly in recent years. To make bioeconomy a reality, however, it is now argued that policymakers must fundamentally change their approach

[12] DSIT (2023) Policy paper, National Vision for Engineering Biology. https://www.gov.uk/government/publications/national-vision-for-engineering-biology/national-vision-for-engineering-biology
[13] OECD website. Synthetic Biology Briefing Document, 3 April 2024, Global Forum on Technology (GFTech). https://www.oecd.org/content/dam/oecd/en/networks/global-forum-on-technology/global-forum-on-technology-synthetic-biology-brief-2024.pdf
[14] EBRC website. Engineering Biology Metrics and Technical Standards for the Global Bioeconomy. https://ebrc.org/publications-metrics-and-standards/
[15] Cabinet Office (2024). *op. cit.*

with an emphasis on resilience and sustainability for the environment and society – rather than industrializing biology, the goal should be "biologizing industry,"[16] namely transforming current industrial practices to align with biomass resource- and bioprocess-based social and industrial structures (this concept is discussed in detail in Section 2).

Currently, the policy cycle is not structured to allow such a principle to be incorporated into a policy at its design stage. Research and development in this field have for the most part followed the patterns the biotechnology policy processes have taken as part of science and technology policies which assume a linear path from basic research to applied research. In addition, when they are applied to policymaking, policies are often developed separately as sector-specific policies (e.g. for food and agriculture, industrial, or healthcare) or purpose-specific policies (e.g. for research and development, industrial promotion, or environmental impact and safety management), rather than forming comprehensive holistic policies. These challenges are recognized not only in Japan, and it has been pointed out that achieving a bioeconomy requires "systems thinking"[17] that overcomes silos between different stakeholders and government agencies, combined with a policy coordination and a "whole-of-government" approach[18].

Among various different production processes that utilize biomass resources in order to achieve a bioeconomy, this working paper focuses on the promotion of biomanufacturing and provides a clear picture of frameworks and points at issue to encourage deeper policy discussions. In particular, as it is necessary to gain a holistic view of the biomanufacturing innovation portfolio in the fragmented policy processes discussed above, this paper presents a "schematic overview of R&D and policies in the biomanufacturing system" with a special attention to the characteristics unique to the bio-field.

Methodology

The framework was developed through a review of existing literature on the bioeconomy and biomanufacturing with a focus on policy documents from leading countries and reports from leading think tanks, interviews with domestic and international stakeholders, discussions held on the occasions of seminars and other events,[19] and analysis made jointly by the research team members who are academics and government officials. This research project is considered as an attempt to practice anticipatory governance through collaborative efforts between academia and currently serving government officials who actually make bioeconomy and biomanufacturing policies.

2. Challenges in Achieving a Bioeconomy: The Need for Systems Thinking in Biomanufacturing

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[16] Shapira, Philip, et al. "Building a bottom-up bioeconomy." *Issues in Science and Technology* 38.3 (2022): 78-83. https://issues.org/building-bioeconomy-engineering-biology-shapira/

[17] Marvik, Ole Jørgen, and Jim Philp. "The systemic challenge of the bioeconomy: A policy framework for transitioning towards a sustainable carbon cycle economy." *EMBO reports* 21.10 (2020): e51478, p.2. https://doi.org/10.15252/embr.202051478

[18] OECD (2023) OECD Science, Technology and Innovation Outlook Times of Crisis and Opportunity, Winickoff, Chap7 Accelerating innovation to meet global challenges: The role of engineering biology. https://www.oecd.org/innovation/oecd-science-technology-and-innovation-outlook-25186167.htm

[19] Seminars on bioeconomy are hosted as part of the University of Tokyo STIG's SciREX Coevolution Implementation Program "Promotion of Biomanufacturing that Enables Bioeconomy: Visualization of Policy Challenges and Institutional Design." During these seminars, participants engage in discussions on relevant topics, including for example, discussions on biomanufacturing within the context of the Bio Strategy, and a discussion with policymakers and researchers with the U.K. Department for Science, Innovation and Technology (DSIT) on the topic of biomanufacturing and other engineering biology matters. For more details, see the following website: https://stig.pp.u-tokyo.ac.jp/?cat=15

Policies

A biomanufacturing policy may be more accurately described as a policy aimed at transitioning the social and industrial structures from reliance on fossil resources and chemical processes to a framework rooted in biomass resources, particularly one based on biomass resources and bio-processes[20] as much as possible. With the current societal and industrial structures that rely on fossil resources and chemical processes, our social infrastructures are heavily dependent on the industries that procure, process, and utilize vast amounts of inexpensive fossil resources from abroad. Shifting this to a biomass- and bio-process-based structure involves, for instance, replacing the raw materials of chemicals, such as plastics, that are derived from fossil resources with renewable biomass, or shifting their production processes from energy-intensive chemical processes dependent on high temperatures and pressures to energy-efficient bio-processes that work at ambient temperatures and pressures. It also calls for actively replacing fossil fuel energy sources used in raw material procurement and production processes with renewable energy sources, including those derived from biomass. By transitioning to biomanufacturing and forming an industrial structure based on renewable biomass resources, the society as a whole can gain significant benefits, in the forms of a circular, self-sustaining socioeconomic system that does not rely on external fossil resource procurement, and reduced environmental impact through the expansion of low-energy consumption processes, among others.

However, biomass resources exist in relatively small quantities across widespread areas and are diverse in nature, in contrast to fossil resources which are often concentrated in specific regions and are relatively easy to extract and refine. This means that the industrial structures based on biomass resources are fundamentally different from those based on fossil resources and chemical processes,[21] in terms of production facilities and distribution systems. Simply grafting parts of a biomass-based industrial structure onto a one based on fossil resources and chemical processes would not allow biomass resources to realize their potential to the full extent. Moreover, it would also entail significant additional costs for modifying production facilities and distribution systems, as well as the depreciation costs for existing infrastructure. For these reasons, biomanufacturing is likely to remain relatively high-cost as long as fossil resources remain accessible, and such structural transformation will not progress on its own if left to the market forces alone.

In Japan, efforts are now being made to encourage collaborative research and development with regular opportunities for exchanging information in the promotion of biomanufacturing policies. Central to this are government-led projects such as the Ministry of Economy, Trade, and Industry (METI)'s GI Fund Projects (e.g., Promotion of Carbon Recycling Using CO_2 from Biomanufacturing Technology as a Direct Raw Material[22]), the Research and

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[20] This includes technologies used to produce chemicals and other products from biomass resources through chemical processes, such as biorefinery technology. They not only contribute to carbon neutrality but also have the advantage of allowing us to repurpose currently available equipment and methodologies used in chemical processes. However, they generally require higher temperatures than biomanufacturing processes do, which translates to higher steady-state energy consumption.

[21] Typical examples include large-scale petrochemical complexes built in coastal areas.

[22] NEDO website. Promotion of Carbon Recycling Using CO_2 from Biomanufacturing Technology as a Direct Raw Material. https://green-innovation.nedo.go.jp/project/bio-manufacturing-technology/
https://green-innovation.nedo.go.jp/en/project/bio-manufacturing-technology/ (English website)

Development of Technologies to Promote Biomanufacturing,[23] and the Development of Production Technology for Bio-based Products to Accelerate the Realization of Carbon Recycling,[24] and the Ministry of Education, Culture, Sports, Science and Technology (MEXT)'s Green Technologies of Excellence (in Biomanufacturing Area[25]). The Bioeconomy Strategy, meanwhile, outlines a medium- to long-term strategy for biomanufacturing products, which emphasizes the necessity of accepting higher initial costs as being inevitable, and focuses on high-value-added chemicals among those that can be produced to prioritize developing the early market, then leveraging economies of scale and gradually expanding into the broader market for generic products. The strategy also outlines the need to make efforts to visualize value through life cycle assessment (LCA) and create markets through public procurement in order to avoid simple price competition with fossil-based products.

Despite these ongoing efforts in research and development as well as various initiatives to establish biomanufacturing market, the underlying mindset remains rooted in a bottom-up approach, where a technology is developed, then implemented in the society. This is far from satisfactory from the perspective of transforming the social and industrial structures. For instance, where the cyclical use of biomass resources is concerned, the utilization of unexploited biomass materials such as agricultural residues and sludge is crucial; however, efforts in procuring these raw materials lag behind compared to research and development on the use of such materials. Securing large quantities of low-cost biomass resources is vital for the expansion of biomanufacturing, particularly in light of the fact, as has been pointed out, that the absolute quantity of biomass resources is vastly insufficient when taking the use of bioenergy into consideration. Another key challenge is to keep the transportation of raw materials to a minimum, given how biomass inherently contains a significant amount of moisture, which tends to make transportation costs relatively high. Considering these factors, having biomanufacturing production sites adjacent to large agricultural areas would be the most cost-effective option from the industrial standpoint. At a societal level, if a self-sustaining, circular unit-based societal structure with biomanufacturing as its core becomes a reality, it can help the society shift from the mass-production, mass-consumption structure reliant on inexpensive fossil resources and highly developed mobility to a more decentralized social structure.[26] Ensuing such forward-looking governance capabilities based on systems thinking is not only essential for leading discussions on establishing international rules, but it is also crucial for implementing the fruits of research and development in society and for carrying out necessary research and development in an appropriate manner.

Since it is not realistic to turn the social and industrial structure into a biomass resource- and bio-based one overnight, it is important to have stakeholders engage in discussions on how to move toward a bioeconomy society and on what timeline while maintaining alignment and coexistence with the traditional social and industrial structures and bringing

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[23] NEDO website. Research and Development of Technologies to Promote Biomanufacturing. https://www.nedo.go.jp/activities/ZZJP_100246.html
https://www.nedo.go.jp/english/activities/activities_ZZJP_100246.html (English website)
[24] NEDO website. Development of Production Technology for Bio-based Products to Accelerate the Realization of Carbon Recycling
https://www.nedo.go.jp/activities/ZZJP_100170.html
https://www.nedo.go.jp/english/activities/activities_ZZJP_100170.html (English website)
[25] JST website. Green Technologies of Excellence. https://www.jst.go.jp/gtex/field/bio.html
https://www.jst.go.jp/gtex/en/field/bio.html (English website)
[26] Examples include the 'Circular and Ecological Economy' (such as local SDGs) proposed in the 5th Basic Environmental Plan (Cabinet decision, 2018).

about a shift in vision and values.

3. Steps for Considering Policy Response and Schematic Overview of R&D and Policies in the Biomanufacturing System

3.1 Points for consideration in the policy cycle

Analysis of challenges and policies or discussion on policy response requires information derived from activities related to so-called “strategic intelligence.”[27]

As illustrated in Figure 2, this involves **i) Understanding the current landscape and identifying future trends** (Understanding environmental conditions; Determining the innovation portfolio; and Identifying relevant key actors and stakeholders); **ii) Conducting analysis of challenges and policies**; and **iii) Discussing policy responses and possible options** (Figure 2: Points for consideration in the policy cycle). It is also important to use the results from, and feedback on, the set of cycles[28] to improve subsequent cycles.

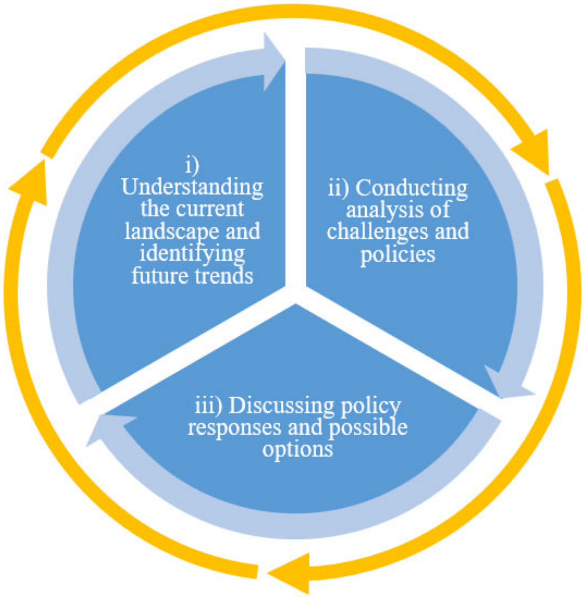

Figure 2: Points for consideration in the policy cycle

(1) Understanding the current landscape and identifying future trends

When analyzing challenges and policies or discussing policy response, it is essential first to establish a fact-based understanding of the current situation and identify future trends based on literature[29] reviews and interviews, by means of the following:

i) **Understanding environmental conditions:** Gathering information that helps gain a clear understanding of the policy environment is critical. This involves understanding social visions,[30] the immediate societal challenges, the international landscape (including geopolitical environment), anticipated market size, and future

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[27] OECD (2024), OECD Science, Technology and Industry Policy Papers Agenda for Transformative Science, Technology and Innovation Policies. https://www.oecd-ilibrary.org/docserver/ba2aaf7b-en.pdf?expires=1724078825&id=id&accname=guest&checksum=C34C4315410551657A36592EE35DF7A4

[28] Cooperation between players at each step is also crucial (for instance, to link the analysis by funding agencies and academic at stage i) with the policy review by government policymakers at stage iii))

[29] There is a large body of research conducted, including: McKinsey Global Institute (2020) The Bio Revolution: Innovations transforming economies, societies, and our lives.
https://www.mckinsey.com/industries/life-sciences/our-insights/the-bio-revolution-innovations-transforming-economies-societies-and-our-lives
Hodgson and Maxon (2022) The U.S. Bioeconomy: Charting a Course for a Resilient and Competitive Future. New York, New York: Schmidt Futures.
https://doi.org/10.55879/d2hrs7zwc

[30] Transition Strategies toward Nature Positive Economy, published jointly by the Ministry of the Environment, the Ministry of Agriculture, Forestry and Fisheries, the Ministry of Economy, Trade and Industry, and the Ministry of Land, Infrastructure, Transport and Tourism.
https://www.env.go.jp/press/press_03041.html
NEDO website. TSC Foresight “Nature Symbiotic Economy～Sustainable Economy coexistence with Nature～”.
https://www.nedo.go.jp/library/future_3.html

technological trends based on sources such as technology foresight and horizon scanning reports.[31] In addition to gauging the Technology Readiness Level (TRL) of a specific technology, we should also assess the level of readiness[32] of the society in which the technology is to be implemented, and gain a understanding of the availability of biomass resources in Japan.[33]

ii) **Determining the innovation portfolio[34]:** This entails identifying research and development, policies and activities that are currently in place, and visualizing the portfolio of policies that concern biomanufacturing. We need to organize business and policy initiatives into a system map according to the research and development and the cyclical supply chain processes for relevant technologies or products (This will be discussed in detail in Section 3.2).

iii) **Identifying relevant key actors and stakeholders:** Key actors and stakeholders should be identified at global, national, and regional levels as well as for different sectors (by focusing on who will be key actors in the industry, government, academia, and finance,[35] taking the biomanufacturing value chain into consideration). When doing so, attention should be paid not only to established/known actors but also to different industries or sectors and emerging actors (e.g., areas related to convergence of digital and AI technologies).

(2) Conducting analysis of challenges and policies

The following analysis should be conducted building on the information gathered in (1) above:

i) Cross-cutting issues and gaps should be identified with a view to the assessment of the societal impacts of the technology (i.e. technology assessment (TA) –this includes evaluating areas such as knowledge and information, regulations (safety and security), social values, R&D ecosystems, infrastructure, social systems, community development, education, and skills and human resource development. Analysis of domestic and international policy recommendations[36] and challenges should also be conducted.

ii) Taking the innovation portfolio into account, we need to identify the relationship between the overall policy vision or objectives and the policy measures, and challenges, as well as measures to take to address such challenges, in creating synergies within the policy mix. This should be based on case studies and field research, and focus on links between policies by different government agencies (e.g. R&D, industrial, and environmental policies), links between policies with different objectives (e.g. promotion, management, and oversight), or links between policies at different levels (e.g. from national policies to national programs, and then to projects within

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[31] Examples of reports on synthetic biology include: Kemp, Luke, et al. "Bioengineering horizon scan 2020." *Elife* 9 (2020): e54489. https://elifesciences.org/articles/54489
As for the horizon scanning discussion by JST Green Technologies for Excellence (GteX)/Biomanufacturing Area "Development of DBTL Technologies for Bioengineering to Pioneer Diverse Microbial Functions" (Project Leader:Kohsuke Honda) member, see Matsuo (2024),Mini Horizon Scanning Round-Table Discussion by GteX Members: Report
https://www.gtex-microbe.jp/wp-content/uploads/2024/09/20240905_mini-HS.pdf

[32] In addition to Technology Readiness Level (TRL), there are other indicators such as Business Readiness Level (BRL), Governance Readiness Level (GRL), Social (Communal) Readiness Level (S(C)RL), and Human Resource Readiness Level (HRL).

[33] For instance, NEDO conducted a study on the availability of renewable raw materials. https://www.nedo.go.jp/library/ZZNA_100080.html

[34] OECD website. Innovation Portfolios, Building clarity of purpose for innovation.
https://oecd-opsi.org/work-areas/innovation-portfolios/

[35] In this report, we made a point of adding "finance" to the list of sectors (industry, government, and academia) to underscore the importance of the financial sector when considering actors in different sectors. This importance is also acknowledged in the Bioeconomy Strategy.

[36] Examples include "Recommendations for Revision of the Bio Strategy," issued jointly by the Japan Bioindustry Association (JBA), the Japan Association of Bioindustries Executives (JABEX), and Greater Tokyo Biocommunity (GTB) (April 2024)
https://www.jba.or.jp/web_file/202404_2_teigen.pdf; and "Key Measures for the Realization of Biotransformation (BX)" issued by the Japan Business Federation https://www.keidanren.or.jp/policy/2024/034_honbun.html

individual programs).

(3) Discussing policy responses and possible options

Policy responses to the challenges identified in (2) above should be discussed with timelines and priorities in mind. Possible transition management for the path for implementing the policy responses should also be planned, taking the following into consideration:

i) Mutual learning with international counterparts (e.g., leading countries, OECD) on initiatives in other countries that may have implications for Japan (by exchanging opinions with policymakers in leading countries) as well as comparisons should be pursued (in addition, we should identify Japan’s strengths, weaknesses, and challenges, determine what initiatives should be made at the international and/or national levels, and develop agenda for national, regional, and local discussions).

ii) Interests, and trade-offs among key actors and relevant players in the context of policy response should be analyzed. It is also necessary to organize useful tools for effective policy promotion and management.

3.2 Proposed schematic overview of R&D and policies in the biomanufacturing system

(1) Developing the Schematic Overview

In Section 3.1, we outlined the elements required in the policy cycle for biomanufacturing. Among these, we found that today’s biomanufacturing policy processes lacks in the determination and visualization of the innovation portfolio, which is a basic prerequisite in policy analysis. Based on this finding, we propose a schematic overview of R&D and policies in the biomanufacturing system (hereafter the “Schematic Overview”) in an attempt to help to make it possible to determine and visualize the innovation portfolio, as illustrated in Figure 3.

In developing the Schematic Overview, our aim was to organize the necessary policy actions in line with a series of processes and supply chains within biomanufacturing. To organize the actions for research and development purposes and for policy response purposes, we segmented the schematic diagram into two separate lanes: one for research and development programs and the other for policy responses related to business environment development and market introduction.[37]

The biomanufacturing process begins with the designing of biological cells, followed by the production of materials and product commercialization. Possible policy responses may include providing support for the development of platforms for cell design, developing infrastructure for the subsequent scale-up, and addressing challenges specific to different applications and industrial sectors.[38] In parallel to these responses, it is necessary to devise measures to expand investment, implement regulations, and establish rules for standardization. These steps in turn require measures to stimulate initial demand, visualization and enhancement of economic value, coordination with existing

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[37] It should be noted that the concentric circles in the diagram do not indicate that an inner circle is a subset of an outer circle. Rather, they are intended to represent the “lanes” for R&D and policies that should be carried out in line with the biomanufacturing processes.

[38] Chemicals and materials; textiles; pulp and paper; cosmetics and fragrances; food; energy (SAF); and pharmaceuticals.

industries, and support for the creation of industrial ecosystems through new cross-industry collaboration. It is crucial that these activities are seamlessly integrated in the policy implementation process.

There is a growing awareness of the importance of large-scale cultures and smooth steps to scaling up from the cell design stage to the product commercialization stage, as evidenced by the U.S., EU, and U.K. policy documents referenced in the first part of this report, all of which highlight the challenge of scale-up. While scaling up does present a challenge, it should also be noted that, in contrast to the upstream technological development in cell design which is often relatively versatile, commercialization of products according to different uses requires more complex and customized applications, and the importance of design strategies that can accommodate these complexities has been pointed out.[39] As discussed in Section 2. in relation to the recognition of challenges, it has also been suggested that the materials used in the social implementation and product commercialization should be taken into account in the initial stage of the systems thinking-based bioeconomy policy frameworks.[40] Marvik and Philp highlight that a four-step matrix (raw materials, technology, industrialization, and market) developed in Norway's national bioeconomy strategy allowed to grasp the overall picture and helped to promote cooperation between different government agencies. This underscores the importance of a systemic approach that sees the entire picture, starting from the raw materials and up to bringing the product into market.

Traditionally, commercialization and social implementation tended to be viewed as the endpoints of policy. Considering the characteristics of biotechnology, however, it is necessary to adopt the perspective associated with cyclical use of biomass resources and apply it to the overall process, where post-consumption waste is viewed as unused resources to be reprocessed into raw materials, which can then be reused in subsequent cell designs. This approach informed our creation of the Schematic Overview, which takes the form of a circular diagram where the process extends beyond product commercialization to include post-commercialization steps, including consumption, waste management, and reprocessing into raw materials/feedstocks.

When discussing the utilization of unused resources at the waste management stage, it is necessary to explore various questions,[41] including: how much biomass resources, including potential resources, are in existence (in other words, identifying the availability of biomass resources)?; how are they consumed and in what environment?; how are they recovered and reprocessed into raw materials?; do raw materials/feedstocks exist in sufficient quantities in our country or region, and if not, how would they be procured from abroad? This circular approach allows us to design products and discuss ideal consumption patterns that account for reprocessing of the waste into raw materials/feedstocks.

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[39] For an analysis of different complex applications that are required for different uses, see: WEF (2022) Accelerating the Biomanufacturing Revolution, White paper, p.11, Figure 3. https://www3.weforum.org/docs/WEF_Accelerating_the_Biomanufacturing_Revolution_2022.pdf
[40] Marvik and Philp (2020), *op. cit.* Figure 1. A bioeconomy innovation policy matrix on page 3 presents the four-step matrix. https://doi.org/10.15252/embr.202051478
[41] This notion that the bioeconomy should be viewed within the context of cyclical structure that includes the disposal stage is increasingly more emphasized; for example, see: WEF (2024) Accelerating the tech-driven bioeconomy, p.22, Figure 11. https://www.weforum.org/publications/accelerating-the-tech-driven-bioeconomy/

Other matters that need to be addressed and objectives that need to be met throughout the entire process include education, human resource development, and safety and security.

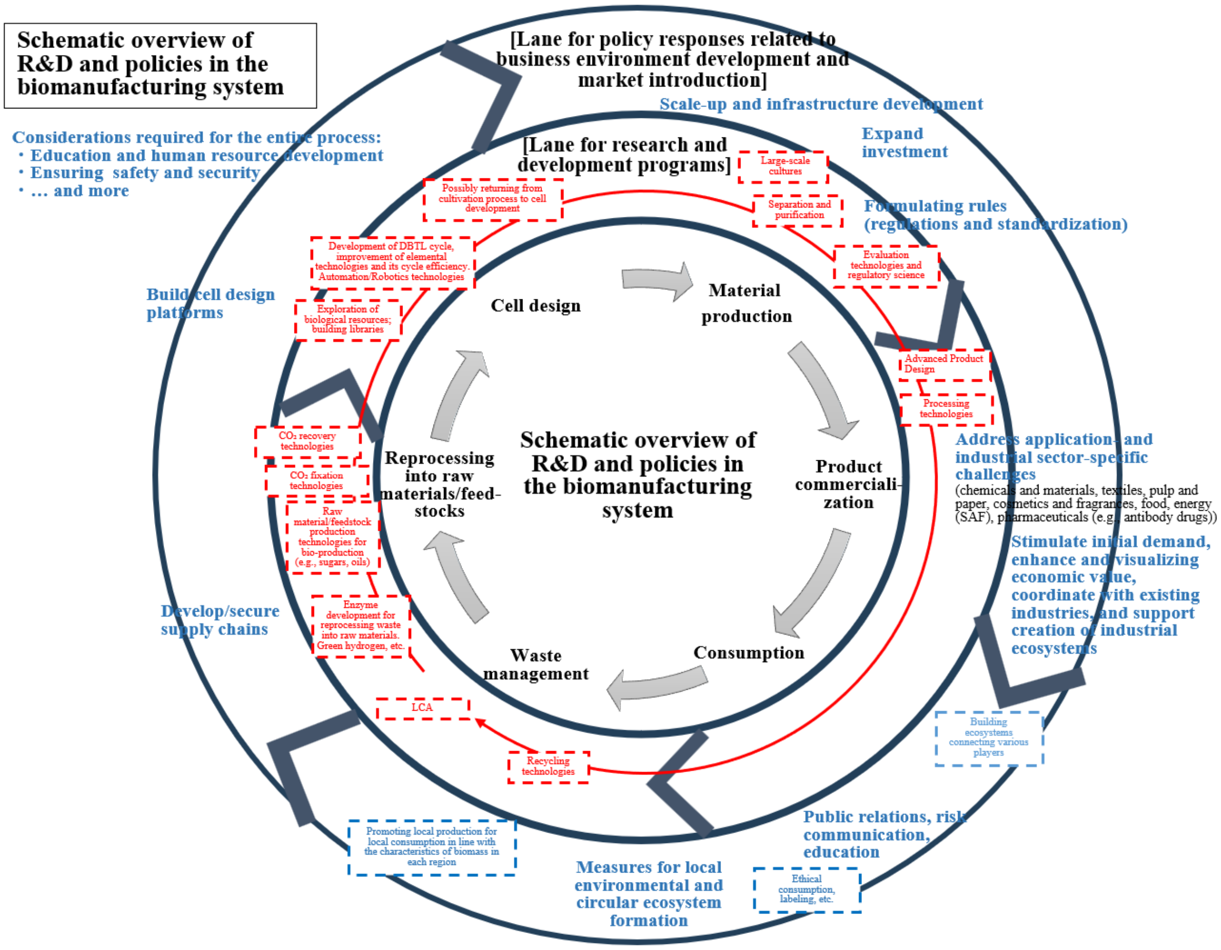

Figure 3. schematic overview of R&D and policies in the biomanufacturing system

(2) Usefulness of the Schematic Overview

The usefulness of the Schematic Overview lies in that it presents the entire biomanufacturing process as a cyclical cycle, and maps outs what is needed in technological development and what policy response should be taken over this cycle. This allows for a clear understanding of how different policies are interconnected, what is required before and after a process, and where one's activities are positioned in the overall picture. The importance of "by design" is often emphasized, and capturing the entire picture and visualizing it enables us to purposefully design both technological development and policy response. One implication of this Schematic Overview is that, when we have a holistic view of the entire supply chain, we can move away from treating biomass resources and raw materials as given in research and development and come to become more conscious of their characteristics and availability, which in turn may influence the way how we approach technological development, product commercialization, and consumption.

As discussed in Section 2, the realization of a bioeconomy society based on biomass resources and bio-processes can ultimately lead to industrial policies to build decentralized production systems that utilize bio-resources specific to the relevant region,[42] as well as regional policies that promote the development of resource-circulating, decentralized community. While the implications of decentralization in the bioeconomy are not widely discussed in Japan, it is perceived as a natural consequence of bioeconomy and has sparked lively discussion elsewhere in the world.[43]

4. Next Steps

This working paper is grounded in the understanding that, in order for biomanufacturing policies to truly contribute to solving societal challenges, we must go beyond the individual policies developed by various different government agencies and implement government-wide response based on systems thinking and coordinated policy development, and the working paper outlines the activities necessary to make this possible. The authors identified that the current biomanufacturing policy process lacks the determination and visualization of the innovation portfolio, which is a basic prerequisite in policy analysis. Recognizing that this is an issue requiring urgent attention, we present the 'schematic overview of R&D and policies in the biomanufacturing system' as a tool to help rectify the shortfalls.

The importance of having a holistic and comprehensive view of the entire social system and contemplating how it should be by adopting a systems-thinking approach with a focus on mission-driven innovation aimed at changing society has been highlighted by experts[44] during discussions on updating the Bioeconomy Strategy. This vision, however, has yet to be fully realized. This research project may be in a position to suggest ways to address these policy challenges that still remain. Addressing these challenges may also help to build a framework to practice anticipatory governance effectively, taking into account long-term societal changes and advancements in technological development.

Moving forward, it will be necessary to refine this Schematic Overview by integrating actual R&D programs and policy responses related to biomanufacturing in it. Our hope is that policymakers and stakeholders will use such a refined version of the Schematic Overview as a tool for continuous discussions between themselves as part of policy analysis and as a way of promoting better biomanufacturing policies.

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Coevolution Implementation Program "Promotion of Biomanufacturing That Enables Bioeconomy: Visualization of Policy Challenges and Institutional Design" (Principal Investigator: Makiko Matsuo, Project Associate Professor, The University of Tokyo Graduate School of Public Policy) (October 2023–March 2026);[45] the following ministerial divisions and their members are jointly responsible for this program: Life Science

[42] For instance, the makeup of unexploited resources is region-specific. Both food waste and sludge of a given area reflect the local consumption, and the amount recoverable also varies by region.

[43] For instance, see: WEF (2024) *op. cit.* and Hodgson and Maxon (2022) *op. cit.* p.18.

[44] An excerpt of the proceedings from the 9th meeting of the Expert Committee for the Promotion of Strengthening Innovation Policies "Bio Strategy," May 20, 2024.

[45] https://scirex.grips.ac.jp/project/coevolution3-2.html

Division, Research Promotion Bureau, Ministry of Education, Culture, Sports, Science and Technology (MEXT) (Ayano Yoshida, Nobuaki Tanuma, and Kazuki Yoshida); Secretariat of Science, Technology and Innovation Policy, Cabinet Office (Takuro Matsumoto); Bio-Industry Division, Commerce and Service Industry Policy Group, Ministry of Economy, Trade and Industry (METI) (Daisuke Ishizuka).

* Coevolution Program: A MEXT SciREX program that bring together government policymakers and researchers to work on research themes they select through conversations based on specific national policy challenges. Neither a project driven solely by researcher's academic interests nor a contracted research project run by government officials, this approach represents a new practice of evidence-based policy making (EBPM) where people on the both sides work together from the early stages of a research project where they set their research theme.