Synthetic Biology: Opening a New Era of "Convergent" Research in the Life Sciences (Postprint)

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Abstract

The differences and connections in the spatiotemporal scales of research objects across various natural science disciplines determine both the distinctions between disciplines and their interdisciplinary cross-fertilization. After evolving into the "life sciences" stage characterized by mechanism-oriented research, biology—benefiting from interdisciplinary integration and technological innovation, and building upon the 20th-century revolutions in "molecular biology" and "genomics" —has given rise to "synthetic biology" through the introduction of engineering principles, thereby rapidly initiating the third revolution of "convergent research" . Based on an exposition of the essence of synthetic biology and a review of its disciplinary development trajectory and achievements, this article specifically addresses issues concerning the scientific and technological underpinning and social governance of synthetic biology, with the expectation of drawing attention from the scientific community, the general public, and governmental administrative levels.

Full Text

Synthetic Biology: Unsealing the Convergence Era of Life Science Research

Natural sciences investigate natural phenomena and the various material forms in nature. Their distinct spatial and temporal scales for studying natural phenomena and substances define both the differences and interconnections among disciplines. Like other sciences, biology began with observation and description. Due to the inherent complexity of life phenomena, by the late 19th century—despite revolutionary breakthroughs in understanding cell morphology, abstracting genetic laws, and comprehending biological evolution based on previous observations of biological processes (growth, reproduction, fermentation, etc.)—biology had not yet achieved a leap toward becoming "life science" that studies universal constitutive essence and laws of motion. During the first half of

the 20th century, the formation and development of biochemistry, cell biology, and developmental biology at the micro level, along with ecology and evolutionary biology at the macro level, propelled biology' s transformation from a traditional science characterized by classification and description to a modern science centered on mechanism research. Building on this foundation, life science research has successively experienced three revolutions since the mid-20th century: "molecular biology," "genomics," and "convergence" research.

The rise of synthetic biology, emerging from the integration of engineering strategies with modern biology, systems science, and synthetic science in the early 21st century, has broken through traditional biology' s "investigating nature to acquire knowledge" paradigm dominated by discovery, description, and qualitative analysis. It provides life science with a novel research philosophy of "building to understand," ushering in a new era of quantitative, computational, predictable, and engineering-enabled convergence research. Synthetic biology not only elevates human capacity to understand and transform life to an entirely new level but also offers important pathways for addressing global challenges relevant to human society.

The Connotations of Synthetic Biology

The core distinction between synthetic biology and other life sciences lies in its "engineering essence,"manifested in two primary aspects. First is its "bottom-up" forward engineering strategy. Therefore, component standardization → module construction → chassis adaptation, including understanding the composition and regulation of life processes, pathways, and networks, as well as the design and construction of "orthogonal life,"constitute its most central research content. The construction of artificial circuits (including next-generation "metabolic engineering") represents its most important engineering platform. Second is the goal-oriented construction (reconstruction) of "artificial life." Thus, "top-down" construction of "minimal genomes"or "bottom-up"synthesis of "artificial genomes" represents another core research focus, with large-scale genomic manipulation and transformation, as well as high-throughput, high-precision, low-cost DNA synthesis, serving as its two most critical enabling technologies. Genome construction (including "cell engineering" such as prototype cell synthesis) forms its most important engineering platform.

These two directions essentially capture the convergent origins of synthetic biology' s engineering research, encompassing "quantitative biology," "molecular biology," and "systems biology," which is fundamentally comprehensive and accurate. We can also elaborate its connotations more specifically across three dimensions [Figure 1: see original paper].

Engineering Connotation: The core of synthetic biology is its "convergent nature." Synthetic biology converges the "discovery capability" from scientific research, the "construction capability" from engineering principles, and the "invention capability"from disruptive technologies, thereby comprehensively enhancing

society' s "innovation capacity." The engineering essence of synthetic biology lies in adopting forward engineering "bottom-up" principles under artificial design guidance to standardize the characterization of biological components, establish universal modules, and construct artificial biological systems on simplified "cell" or "system" chassis through learning, abstraction, and design, achieving quantitative control of their operation.

Biotechnology Connotation: Synthetic biology represents the redesign and reconstruction of life systems at the molecular level, with circuit engineering, genome engineering, and cell metabolic engineering as its core technological and engineering manifestations. In a sense, synthetic biology can be considered an extension of biotechnology in the genomics and systems biology era, though this extension represents a qualitative leap. On one hand, synthetic biology elevates traditional biotechnology to a level of systematization and standardization, potentially advancing biotechnology to a platform-based engineering biology tier. On the other hand, engineering biotechnology that creates new life systems based on whole-genome and systems biology foundations can not only accomplish tasks difficult for traditional biotechnology but also foster technological innovation leaps through interdisciplinary integration.

Scientific Connotation: From its inception through current practice and future development, synthetic biology carries another important connotation: complementing "top-down" systems biology, it breaks through the traditional "reductionist" strategy of studying life science from whole to parts, opening new pathways to understand life essence through a "from creation to understanding" approach and establishing a new paradigm for life science research.

Development and Achievements of Synthetic Biology

From the early 20th century, when synthetic science enabled the concept, to the "vision" formed by molecular biology knowledge and DNA recombination technology breakthroughs [2], and finally to its "naming" through modern genomics blueprint-based engineering principles [3], synthetic biology has become a hallmark of convergence research, roughly experiencing three stages [4].

Stage 1: Founding Period (2000–2003): This period generated many research methods and theories with domain characteristics, particularly the establishment of genetic circuit engineering and its successful application in metabolic engineering.

Stage 2: Expansion and Development Period (2004–2007): Characterized by domain expansion but relatively slow engineering and technological progress.

Stage 3: Rapid Innovation and Application Translation Period (2008–2013): This stage saw the emergence of new technologies and engineering methods that greatly expanded synthetic biology research and application fields, particularly the ability to synthesize artificial genomes reaching near-Mb

(chromosome-length) scale and unprecedented breakthroughs in genome editing technology [Figure 2: see original paper].

Based on this, in 2014, the U.S. National Academy of Sciences proposed that convergence research represents the third revolution in life science [5]. The combination of engineering platform construction for enabling technologies and open-source application of biomedical big data is driving "Engineering Biology" toward a new stage of democratized development in biotechnology, bioindustry, and biomedicine—essentially taking a solid step toward the grand goal of human "capability enhancement."

Biological Components

Following engineering principles, synthetic biology designates the simplest, most basic functional units in living systems as "biological parts." Given their biomacromolecular nature, amino acid sequences (primary protein structure) or nucleotide sequences (primary nucleic acid structure) and related modifications constitute the most basic elements. The concept of "synthetic biology" was proposed based on innovative work constructing artificial logic "circuits" from biological "components," leading to the definition of "biological parts" in synthetic biology as "the simplest, most basic biological building blocks (BioBrick) in genetic systems—amino acid or nucleotide sequences with specific functions that can be combined with other components in larger-scale designs to form biological devices with specific functions" [2,6]. As synthetic biology research expands, the connotation of biological parts can no longer be limited to the original "genetic systems," nor solely serve "model systems" for circuit engineering. The non-nucleic acid portion of "biological parts" (particularly proteins and peptides) in typical biological systems, especially cellular systems, is essentially encoded by "genes" —DNA sequences. Therefore, a large portion of nucleic acid sequences in "biological parts" are genes encoding proteins (including regulatory proteins, structural proteins, and numerous enzymes).

Currently, biological parts primarily originate from nature, with screening and identification based on whole-genome or transcriptome sequencing and information mining as the mainstream approach. Analyzing functional proteins and characteristic transcriptional and translational sequences in genomes yields abundant resources of promoters, ribosome binding sites, protein-coding sequences, and terminators. Software such as FPROM, TSSG, and SCOPE exist for "regulatory element" prediction, while databases like Pfam are used for protein family and domain alignment. However, a massive gap remains between DNA sequence interpretation and functional utilization of encoded components, as functional identification of biosynthetic elements is often extremely difficult and inefficient. Using Taxol biosynthesis steps and related "biological element" mining in yew trees as an example: since revealing the first reaction in Taxol biosynthesis in 1997 [7], researchers have now analyzed eight cytochrome P450 monooxygenases, five acyl/aromatic transferases, and one aminomutase involved in subsequent steps, yet five gene functions remain to be studied [8].

This absence of key biological components has directly prevented the realization of Taxol' s synthetic biology manufacturing.

To achieve predictive design, construction, and optimization of target biological devices or systems, it is necessary to modify existing biological components' structures and functions. Protein directed evolution technology established by U.S. scientists (awarded the 2018 Nobel Prize in Chemistry) remains the primary strategy for biological component modification. Constructing promoter libraries of various strengths is also a powerful tool for precise gene regulation. A typical example involves modifying the TEF1 promoter in engineered lycopene-producing yeast strains to establish a mutant promoter library, yielding a series of promoters with different strengths [9]. Further study of 11 such promoters revealed activities ranging from 8% to 120% of the wild type [10]. Additionally, engineering ribosomes in E. coli enables in-depth study of ribosomal mechanisms and antibiotic interactions; expanding cellular genetic coding methods could enable these engineered ribosomes to synthesize new polymers and potentially transform cells into multipurpose "cell factories" [11].

More attractively and challengingly, designing and synthesizing components nonexistent in nature represents a frontier. For instance, Cambridge University researchers used artificial genetic material to create the world' s first artificial enzyme [12]. With advances in high-performance computing, quantum mechanics, and molecular dynamics theory and methodology, computational protein design has played a significant role in core component enzyme catalysis design [13], ushering in a new stage of enzyme engineering. Using computational iteration methods starting from the inactive protein scaffold HG-1, eight designed enzymes all exhibited significant catalytic activity, substantially improving the success rate of computational enzyme design [14]. Recently, Chinese researchers used codon expansion methods to modify a 28 kD fluorescent protein, successfully mimicking light energy absorption in natural photosynthetic systems and reducing carbon dioxide to carbon monoxide—a key step toward establishing artificial photosynthesis pathways for energy acquisition [15].

Synthetic biology' s "bottom-up" forward engineering nature necessitates establishing component libraries. In practice, enhanced capabilities in quantitative prediction, precise design, standardized synthesis, and accurate regulation depend on engineering platforms and standard component libraries to scale up solutions for bioengineering problems and respond to societal needs. The BioBricks™ component library established in 2012 was the first to legally permit individuals, companies, and research institutions to produce standardized biological components for free sharing under relevant protocol frameworks, though much work remains in this direction.

Circuit Engineering

The landmark work in synthetic biology' s formation is the design and synthesis of artificial gene circuits. Using well-characterized gene components and

following electronic engineering principles, researchers construct simple, regulatable gene circuit modules that can be described by corresponding mathematical models and regulated by environmental signals. These models enable evaluation and redesign for optimization. In 2000, Gardner et al. constructed a genetic toggle switch—a pioneering work in engineering gene circuits with designed functions [16]. Elowitz and Leibler designed an oscillator using three gene modules with mutual inhibition and de-inhibition to achieve regular oscillation of output signals [17]. Weiss and Basu established methods for engineering transcriptional logic gates, making important contributions to circuit language design [18]. After the first Synthetic Biology 1.0 conference, the goal of constructing combinatorial gene circuits to enhance bioengineering levels was proposed [19]. Some E. coli signal circuit and component design studies have expanded synthetic circuit design from transcriptional regulation to post-transcriptional and translational regulation [20]. By designing quorum-sensing circuits, researchers began constructing multicellular patterns [21].

Continuous optimization of engineering design and construction methods accelerates circuit engineering development. The construction of a fast, robust, and tunable genetic oscillator in E. coli represented a major breakthrough in oscillatory circuit design and theoretical research [22]. Synthesis of a mammalian cell oscillator first achieved periodic regulation of gene expression in mammalian cells [23]. Synthetic gene circuits with counting functions, using recombinase-mediated DNA rearrangement to form permanent memory, represent a long-standing goal in circuit engineering [24]. During this period, RNA-based circuit engineering also developed continuously, with biosensing providing methods for RNA computing and enabling construction of RNA devices for logic regulation of gene expression [25].

In recent years, module and circuit design capabilities have continuously improved. Optimizing gene logic circuits at the single gene cluster level enables transplantation of prokaryotic gene circuits into eukaryotic cells [26]; utilizing intercellular signal transduction mechanisms to regulate gene expression in multiple cell types has achieved coupled positive and negative feedback loops for dual signals [27]. Synthetic circuits endow cells with more powerful functions, strongly promoting protein circuit applications in biotechnology [28]. Andrews et al. [29] used quantitative methods to design combinable sequential logic with feedback loops in cells, representing a key step toward executing advanced computations within cells.

Metabolic Engineering

The primary goal of metabolic engineering is to design, modify, and construct metabolic pathways or networks in chassis (in vitro—molecular machines; in vivo —cell factories) to produce desired products with gradually improving efficiency. Due to the complexity of cellular metabolic networks, identifying appropriate modification targets among thousands of metabolic genes and regulatory circuits is challenging. However, computational analysis of large-scale metabolic

networks to design optimal synthetic pathways for specific bioproducts can help identify suitable metabolic engineering strategies and obtain optimal strains more quickly. Representative work includes the engineered optimization of the artemisinin precursor pathway (including component adaptation) [30,31], ultimately forming an optimized yeast artemisinic acid synthesis pathway licensed to Sanofi for production—a milestone in synthetic biology application [32]. In 2015, researchers achieved complete biosynthesis of opioid drugs in yeast, representing the longest plant natural compound metabolic pathway constructed in microbes to date [33].

Metabolic engineering has reached a level enabling construction of predictive synthetic pathway models, utilizing host cell metabolic system information combined with all known and predicted enzyme function information to identify pathways of interest. Forward engineering of model pathways using exogenous enzyme function information obtained through genome mining fills gaps in host cell metabolic systems. Multiple teams have successfully modified amino acid biosynthesis pathways in E. coli chassis to produce isobutanol [34,35], fatty acid-based biodiesel [36], gasoline [37], and bioplastic 1,4-butanediol [38]. Researchers have also integrated synthetic regulatory pathways into production strains to achieve dynamic regulation of metabolic pathways in response to metabolic intermediates or environmental conditions [39]. However, dynamic regulation of metabolic flow in interaction with cellular systems remains a challenge [40].

With China's growing demands for energy materials, environmental ecology, and public health, there is urgent need to improve metabolic engineering efficiency using synthetic biology. On one hand, building on China' s bioengineering foundation, the Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences, has rapidly developed a batch of industrially transformable metabolic engineering achievements. On the other hand, combining Traditional Chinese Medicine heritage with chemical biology foundations in natural drug development, Chinese scientists have made important progress in cell factory synthesis of plant natural compounds. Breakthroughs have been achieved in device mining, integration, heterologous synthesis, and regulation of numerous medicinal and edible natural compounds (such as terpenoids, steroids, flavonoids, antibiotics), establishing a pipeline from rare plant genome sequencing and gene mining to recombinant synthesis, obtaining recombinant cells with different performance characteristics. Yeast cell factories have achieved de novo synthesis of rare ginsenosides CK, Rh2, Rg3, F1, and Rh1 from glucose, with breakthrough improvements in yield, some entering pharmaceutical development [41-43]. Additionally, a novel biosynthetic pathway for polyphenol amino acid-derived drugs was created, enabling efficient biosynthesis of danshensu (7.1 g/L) [44]; biosynthesis of steroid hormone precursors from simple sugars achieved efficient production of multiple sterol drug precursors including 7-dehydrocholesterol (49.9 mg/L) and campesterol (355 mg/L). This work features both "new herbal" innovation from microbial to plant natural compounds and "biomedicine" translation combining biology with medicinal chemistry and

pathophysiology, representing an important direction for China' s metabolic engineering development.

Genome and Cell Engineering

The synthesis of "artificial life" represents a milestone in synthetic biology history and has laid the most fundamental enabling technical foundation for large-scale synthetic biology development. Early examples trace back to China' s total chemical synthesis of physiologically active bovine insulin in the 1960s, while classic cases include the vision of "synthetic biology" proposed by renowned Polish geneticist Waclaw Szybalski in 1974–1978 following DNA recombination technology breakthroughs. Since the 1990s, breakthroughs in genome sequencing and annotation technology have enabled "reading" genomes in principle, naturally deriving "design" possibilities; various directed DNA mutation, amplification, and cloning technologies (and recent editing technologies) have enabled "editing" or reprogramming genomes; while large-scale DNA synthesis and assembly capabilities have enabled "writing" or synthesizing genomes. Consequently, genome engineering targeting synthetic genomes and genome editing, along with associated cell engineering, has become one of synthetic biology' s most urgent and challenging tasks over the past two decades.

As early as 2002, researchers chemically synthesized cDNA complementary to the poliovirus genome RNA, transcribing it into viral RNA using in vitro RNA polymerase to ultimately reassemble infectious virus particles [45]; subsequently, through oligonucleotide synthesis and stepwise assembly, a fully chemically synthesized ϕX174 phage genome was obtained, achieving breakthroughs in Mycoplasma genomic DNA transfer and artificial synthesis [46]. In 2010, Gibson et al. designed, synthesized, and assembled a 1.08 Mb Mycoplasma mycoides genome and transplanted it into Mycoplasma capricolum recipient cells, creating the world' s first self-replicating "new cell—Synthia" controlled solely by a chemically synthesized chromosome [47]. In the same year, Gibson et al. chemically synthesized the mouse mitochondrial genome for the first time by combining it with enzyme and chemical reagent mixtures [48]. Researchers subsequently used genome synthesis methods to chemically synthesize two chromosome arms of Saccharomyces cerevisiae—the world' s first successful synthesis of partial eukaryotic genomes [49]. Beginning in 2011, researchers from multiple countries launched the first eukaryotic genome synthesis project—Synthetic Yeast Genome Project (Sc2.0)—successfully synthesizing yeast chromosome synIII in 2014 [50]. Although this was the smallest of yeast' s 16 chromosomes, it represented a critical step toward building a complete eukaryotic cellular genome, particularly establishing computer-aided chromosome sequence design technology. In March 2017, scientists participating in Sc2.0 completed synthesis and assembly of chromosomes 2, 5, 6, 10, and 12, achieving major breakthroughs in eukaryotic genome design and chemical synthesis [51]. In 2018, Chinese researchers fully leveraged CRISPR-Cas gene editing enabling technologies and synthetic biology' s "design-synthesis-test" engineering philosophy to successfully create

single-chromosome brewer' s yeast cells—a milestone breakthrough in synthetic biology genome and cell engineering. This not only opens new directions for studying life' s essence (the scientific question of whether eukaryotic genomes can be encoded by a single chromosome) but also provides an excellent model for studying human telomere function and cellular aging [52].

From Enabling Technology Innovation to Engineering Platform Construction

Disruptive enabling technologies are crucial for supporting synthetic biology development, with DNA synthesis and efficient genome editing as core enabling technologies. The mainstream gene synthesis method uses oligonucleotide synthesizers to produce oligonucleotides, then employs PCR and other means for gene synthesis. Engineering of this technology has dramatically increased synthesis throughput, spawning numerous biotech companies and substantially reducing synthesis costs. However, to further reduce costs for ultra-long sequences (such as genomes), many teams are developing chip-based methods for synthesizing high-precision oligonucleotide pools combined with different assembly methods. Beyond chemical oligonucleotide synthesis, scientists are exploring using terminal deoxynucleotidyl transferase (TdT) for direct rapid DNA synthesis, potentially enabling direct synthesis of DNA chains ten times longer than current methods [53] without toxic chemicals. As DNA synthesis costs decrease, DNA-based information storage also represents a promising future direction.

Scientists have continuously explored precise genome editing (particularly for higher eukaryotic genomes), developing zinc-finger nucleases (ZFN) and transcription activator-like effector nucleases (TALEN). Due to CRISPR systems' advantages in efficiency, convenience, and cost-effectiveness, these methods have gradually been phased out since the development of CRISPR. Since 2012, scientists have leveraged the programmable and precise cleavage features of the CRISPR-Cas system to develop a series of genome editing tools [54], with host coverage currently spanning from bacteria to higher organisms and continuing to expand.

The basic principle of CRISPR-Cas-mediated genome editing involves using guide RNA to direct Cas proteins to induce dsDNA breaks at specific target sequences, then employing homologous recombination for precise DNA sequence replacement or non-homologous end joining for target gene disruption. Based on this, numerous derivative methods have been developed, such as using Cas9 nickase mutants that cleave only one strand to reduce off-target effects [55]. Recently, single-base editors developed from CRISPR enable precise genome editing by deaminating specific bases without causing target DNA breaks, showing good development prospects [56]. Additionally, deactivated Cas proteins can be used for target gene transcriptional regulation, epigenetic modification studies, and genome imaging [57]. Notably, beyond genome editing, Cas13, Cas12, and Cas14 proteins trigger collateral cleavage activity upon binding target DNA, enabling next-generation molecular diagnostics—an area where Chinese scientists

have made original contributions [58-62].

Due to life' s high complexity, artificially designed gene circuits rarely work exactly as intended and often require prolonged iterative tuning. The most effective solution is establishing engineering research platforms that massively test combinations of various components, circuits, and chassis to obtain vast experimental data for guiding further engineering optimization and rational design. The core of such platforms is automated synthetic biology research facilities, also known as biofoundries, which organize workflows following the "design-build-test-learn"closed-loop strategy for engineering-scale trial-and-error to rapidly obtain synthetic life forms with target functions. Examples include the Agile BioFoundry at Lawrence Berkeley National Laboratory, iBioFAB at the University of Illinois, MIT-Broad Foundry at MIT, London DNA Foundry at Imperial College London, and industrial entities like Amyris, Zymergen, and Ginkgo. In this context, China plans to construct the world' s largest major scientific infrastructure for synthetic biology research, undertaken by the Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences. Notably, from original discovery to industrial application, automation facilities alone are insufficient. For example, the artificial yeast cell production of artemisinin—synthetic biology' s most successful industrialization case to date—was led by Professor Jay Keasling, who established a complete R&D system around the engineering platform: Lawrence Berkeley National Laboratory handles upstream original discovery, the Joint BioEnergy Institute (JBEI) manages midstream technology development, and Amyris company oversees downstream industrial application. These institutional and mechanism innovations surrounding engineering platforms warrant in-depth study to provide important references for fully leveraging China' s major scientific infrastructure to drive synthetic biology research, innovation, and industry.

Translation and Application Research

Synthetic biology technology may solve long-standing technical challenges in gene therapy and biological therapy, developing more effective drugs and treatments for complex diseases like cancer and diabetes. It may also break through technical bottlenecks in biofuel development, design simpler and more efficient biological processes, produce more complex natural products, and synthesize more organic chemical products.

In medicine, beyond widely discussed cell therapies like CAR-T [63,64], designing circuits to promote bacterial invasion of tumor cells represents a pioneering example of cell engineering under synthetic biology guidance and an early case of cell therapy [65]. Subsequently, engineered phage therapy and cell therapy have matured, such as constructing probiotic E. coli that can recognize and eliminate Pseudomonas aeruginosa [66] or blocking Vibrio cholerae toxicity by expressing heterologous quorum-sensing signals [67].

In recent years, Chinese scientists have used synthetic biology to modify several

high-yield drug-producing strains for industrial application, achieving fermentation levels at internationally or domestically leading standards, with nearly 1 billion RMB in new sales. Using gene expression gradient regulation technology to optimize compatibility between natamycin synthetases achieved maximum natamycin fermentation levels of 15.0 g/L [68]; analyzing and reconstructing the cascade regulatory mechanism and key genes in daptomycin biosynthesis in Streptomyces roseosporus achieved daptomycin fermentation titers above 2.5 g/L [69]; reconstructing tacrolimus synthesis modules in Streptomyces tsukubaensis achieved maximum fermentation titers of 1,405 g/mL [70].

In biofuels, researchers used synthetic toggle switches and quorum-sensing systems to coordinate biomass expansion and ethanol production [71]; designed and constructed biodiesel-producing E. coli with integrated multifunctional modules, introducing exogenous enzymes to enable simultaneous synthesis of fatty esters, fatty alcohols, and waxes while utilizing simple five-carbon sugars as substrates [72], opening new avenues for microbial engineering-based energy refining.

In chemical biosynthesis, computational design and synthetic characterization of functional components for hundreds of important chemicals were performed based on chemical reaction characteristics and intracellular regulatory sites, laying the material foundation for chemical synthesis pathways and efficient artificial synthetic cells. Using DNA assembly and precise expression regulation technology [73], pathways from glucose to succinic acid, pentamethylenediamine, adipic acid, and 5-aminolevulinic acid were created and optimized. Among these, 5-aminolevulinic acid production reached 50 g/L, five times higher than international levels; succinic acid production reached 125 g/L with a conversion rate of 105% from glucose (capable of partially fixing CO2) [74], placing technical indicators at internationally leading levels and beginning industrial translation. Based on systematic study and understanding of photosynthetic cyanobacterial chassis cell physiological regulation mechanisms, a series of photosynthetic cyanobacterial chassis cells with improved stress resistance were constructed [75]. Through reconstruction and optimization of photosynthetic modules, CO2 fixation, and biosynthesis modules, biosynthesis of typical compounds such as ketones, alcohols, and acids from CO2 was achieved, providing possibilities for developing and utilizing new carbon resources. Among these, acetone, D-lactic acid, and 3-hydroxybutyric acid were all first reported internationally [76,77].

Scientific and Technological Support and Social Governance for Synthetic Biology

The multidisciplinary "fusion"in synthetic biology is no longer merely traditional "interdisciplinarity" but represents "convergence" of science, technology, engineering, and even natural sciences with social sciences and management science. This convergence not only poses tremendous challenges to traditional discipline-based research models but also signifies major reforms in organizational management and cultural construction. Therefore, synthetic biology development requires building an ecosystem adapted to convergent research capabilities, in-

volving research, education, management, collaboration, and funding [78], requiring multi-level, comprehensive collaborative networks formed through policy guidance, infrastructure construction, mechanism support, innovative talent cultivation, and engineering team aggregation. Simultaneously, as an emerging disruptive field, synthetic biology requires long-term research on institutions, regulations, and public opinion guidance to gradually form a systematic risk management and control system ensuring healthy and rapid development.

Research and Development System Policy Guidance and Capacity Building for Innovation: Synthetic biology development requires not only national funding and policy guidance but also mobilizing enthusiasm from industry, academia, research, and finance to form an innovation value chain with scientific creativity, industrial transformation capacity, and socioeconomic benefits. According to different goals at various value chain stages, diversified funding support should be sought to achieve multi-level, phased rapid and stable development from basic research to technological innovation, from engineering platform construction to product development and industrial translation. Government investment should particularly emphasize supporting synthetic biology-characteristic component libraries, databases, and engineering platform construction for translational research. National-level infrastructure or national laboratory construction can not only solve interdisciplinary convergence issues but also more effectively leverage the roles of R&D institutions, funding agencies, and regulatory bodies. Additionally, policy incentives should encourage enterprises to increase R&D investment to support talent team building and enhance R&D capabilities, while supporting pioneer companies in establishing and promoting standards during technology and product (including technical service products) development to guide industrial transformation.

Mechanisms and Culture for Convergent Research: Since convergent research heavily depends on integrating expertise from multiple fields and partners, open and inclusive culture, organizational structures and management, common concepts and standards, and shared goals are essential for supporting such close collaboration. First, policies supporting interdisciplinary convergence should be formulated, establishing unified coordination mechanisms, setting up corresponding research units (institutions) with tailored management frameworks to promote cross-disciplinary research beyond traditional organizational structures. Additionally, effective organizational culture should be established to create opportunities for idea exchange and improve understanding of disciplinary differences, with fair and flexible budget and cost-sharing policies, matching resource investment and funding mechanisms, and reformed personnel recruitment, promotion, and evaluation systems to better support interdisciplinary convergence research.

Education and Talent Cultivation Disciplinary Education Strengthening Multidisciplinary Foundations: Synthetic biology's convergent development model requires innovative education and talent cultivation models. Syn-

thetic biology education should teach not only specific theories and experimental techniques but also convey its values and philosophy. These values include commitment to interdisciplinary innovation through collaboration beyond traditional biological disciplines and support for open-source resource development and utilization. Convergent education programs and training projects should be carefully designed and implemented. Notably, at the current stage, establishing a "synthetic biology" major is not necessarily required. Instead, educational resources should be synergized to strengthen multidisciplinary foundations, emphasizing convergence between relevant parts of "fused" disciplines, establishing teaching faculties adapted to synthetic biology development through mutual teaching and learning, and further improving innovative education systems for undergraduates and graduate students while emphasizing integration of discipline construction with talent cultivation and combining base construction with team building.

Cultivating Interdisciplinary Work Capacity and Quality: Synthetic biology talent cultivation should emphasize and advocate awareness and philosophy of innovation, openness, and cooperation [79] to nurture a new generation of synthetic biologists. The International Genetically Engineered Machine (iGEM) competition, originating from MIT' s synthetic biology course in 2003, attracts numerous university and even high school teams globally each year. Through student-initiated project selection and mentor-provided laboratory guidance, iGEM enables students to apply knowledge to actual research while comprehensively developing scientific thinking, autonomous learning, interpersonal skills, teamwork, and interdisciplinary communication [80]. This cultivation of convergent research capabilities maintains a unique culture of innovation and collaboration, fostering interdisciplinary research teams and talent to collectively solve key scientific and industrial translation problems in synthetic biology.

Social Impact Research and Governance The rapid development of synthetic biology technology challenges traditional ethical concepts, directly raising issues involving open-source sharing versus intellectual property/biosafety and security. Currently, research is lacking in ethics, law, sociology, and related technical and methodological studies supporting standard establishment.

Standards and Market Access: Promoting synthetic biology product development and industrial application requires establishing standards for related components and technical services. During upstream R&D stages, emphasis should be placed on intellectual property (including standardization) protection and management to promote open resource sharing. When market applications develop to certain levels, relevant technical/scientific standards, environmental/safety standards, and reproducible measurement standards should be formulated in a timely manner, with strengthened exchanges and cooperation with international standards organizations. Market access for synthetic biology products is a critical node for ensuring technology-driven industrial transformation

and social progress. For purified products (e.g., drugs) and non-food products, existing regulatory principles can generally be applied. For non-purified food products, this opportunity should be used to establish scientific, rational, safe, and efficient evaluation norms, clarify application and approval pathways for new products, unify market access standards and review systems, and accelerate new product market entry.

Healthy Development Supervision and Management: Ensuring biosafety of synthetic biology technologies and products and preventing technology misuse and ethical conflicts has become extremely important and urgent. Close tracking of new biosafety and ethical issues arising from synthetic biology development is needed, with vigorous risk research on new features and changes. Existing management policies should be reviewed for problems, loopholes, and gaps, with timely supplementation and revision. Researchers' safety awareness should be enhanced, public outreach and participation emphasized, and credit-based qualification review systems improved to promote self-regulation.

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