Designing Life: Safety Risks and Ethical Challenges of Synthetic Biology Postprint

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Date: 2023-03-19T00:00:00+00:00

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Full Text

Policy and Social Issues

Design Life: Safety Risks and Ethical Challenges in Synthetic Biology

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Abstract

The rapid development of synthetic biology has attracted widespread attention in the academic community. The engineering characteristics of synthetic biology endow it with the practical connotations of "design" and "reconstruction," enabling artificially designed life to be introduced into the traditional DNA-based process of life evolution, thereby triggering a series of safety risks and ethical issues. This article explores the ethical controversies sparked by landmark events in the development of synthetic biology, analyzes the safety

risks, ethical dilemmas, and their underlying causes, and proposes approaches for ethical regulation of synthetic biology in China based on lessons drawn from regulatory mechanisms in Europe and the United States.

Keywords: synthetic biology, ethics, biosafety, biosecurity, regulation

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Synthetic biology refers to the artificial synthesis-based redesign and modification of naturally existing biological systems to create "artificial life" not found in nature[1]. In 1979, Nobel Chemistry laureate Har Gobind Khorana synthesized a 207-base-pair DNA sequence, marking the genesis of synthetic biology[2]. After 2000, biological research entered the genomic era, with the scale and complexity of DNA synthesis increasing rapidly, making it possible to artificially design and synthesize novel functional genes. Synthetic biology thus entered a stage of rapid development. However, since its inception, every frontier advance in synthetic biology has been accompanied by heightened public concern regarding its safety risks and ethical implications.

On August 1, 2018, *Nature* published online a groundbreaking achievement by the Qin Zhongjun team from the Chinese Academy of Sciences and their collaborators. Using an engineered precision design approach and CRISPR-Cas9 gene editing technology, the team performed large-scale trimming and rearrangement of the entire genome of *Saccharomyces cerevisiae*'s 16 chromosomes, "creating" a yeast cell that fused nearly all genetic information into a single ultra-long linear chromosome and establishing the first eukaryotic organism with a single linear chromosome (SY14 yeast)[3]. This major breakthrough brought humanity one step closer to the goal of creating synthetic life, stimulating public imagination and anticipation about scientists artificially creating non-natural life and once again triggering widespread concern about the safety and ethics of synthetic biology.

Historical Perspective on Ethical Debates

Historically, synthetic biology, as a disruptive technology, has seen each of its exciting advances accompanied by ethical controversies and concerns. In 1974, Jaenisch and Mintz implanted foreign genes into mouse blastocysts, creating the first transgenic mammal. The dangers of this experiment raised concerns within the scientific community. In the late 1990s, American biologist J. Craig Venter commissioned bioethicist Arthur Caplan at the University of Pennsylvania to conduct an ethical assessment of synthetic genomes and synthetic life[4]. Based on this research, Cho et al.[5] published an article in *Science* warning that "if the identification and synthesis of minimal genomes are presented by scientists, described by the media, and understood by the public as evidence that life can be reduced to or equated with DNA, this is extremely dangerous," and that "if life is explained solely through the technical discoveries of natural scientists, it will threaten the view that life is special."

The early 21st century witnessed a series of substantive achievements in synthetic biology. In 2002, Eckard Wimmer and colleagues successfully synthesized the human poliovirus. At a time still under the shadow of the 9/11 attacks and the anthrax incidents, Wimmer deliberately titled his publication "Generation of infectious virus in the absence of natural template"[6] to serve as a warning to the scientific community and to attract public attention[4]. In 2010, J. Craig Venter's team synthesized the first *Mycoplasma* cell, naming it "Synthia." Unlike viruses, mycoplasma represents the smallest life form capable of independent survival. This achievement overturned humanity's long-standing views on the nature of life and forced a reexamination of human existence and our position in the universe[7]. The profound impact of this event prompted then-President Barack Obama to request the Presidential Commission for the Study of Bioethical Issues, in conjunction with other groups, to submit a report on the potential medical, environmental, security, and other benefits and risks of synthetic biology[8]. In reality, Synthia's creator, J. Craig Venter, had consulted numerous ethics experts before the experiment, commissioned ethical assessment studies, and briefed the White House on the matter. Nevertheless, the research drew criticism from many. Opponents argued that artificial life would "open Pandora's box," and that synthetic organisms released into nature could cause genetic changes leading to environmental disasters or be used to develop biological weapons, inflicting endless suffering and catastrophe upon humanity[9]. Although Synthia was not truly synthetic life in the full sense, the public clearly expressed panic about designing and constructing artificial life. In 2012, Friends of the Earth, the Center for Technology Assessment (CTA), and the ETC Group, together with 111 organizations worldwide, issued a joint report calling for a moratorium on the release and commercial use of synthetic organisms and their products until government regulatory measures could be revised and implemented to prevent direct or indirect harm to humans and the environment[10]. The ethical controversy surrounding Synthia brought synthetic biology beyond the confines of academia into the purview of government and public discourse.

In 2011, the Synthetic Yeast Genome Project (SC2.0) was launched. Since its implementation, synthetic biology has achieved breakthroughs in eukaryotic research, substantially increasing the scale of genome design and synthesis. On March 10, 2017, *Science* published seven papers on the successful synthesis of five yeast chromosomes. Although scientists viewed their work not as creating new life but rather as domestication—essentially accelerating yeast cell evolution[11]—this major advance once again sparked public debate about the meaning of life. Scientists argued that currently created life remains confined to laboratory environments with cautious safeguards and strict review systems, thus posing minimal risk to the natural environment. Yet concerns persist that genetically synthesized organisms released into nature could cause unforeseen harm, and that if terrorists exploited this technology to create biological weapons, society would face even greater dangers. Most synthetic biologists believe that synthesizing the human genome is ultimately probable, and that

from a technological development perspective, achieving such a leap remains necessary[11], though people still worry that artificial "humans" could become reality one day.

The 2018 breakthrough by Qin Zhongjun's team marked another milestone. For the first time internationally, they artificially created a eukaryotic cell with a single chromosome (SY14 yeast), achieving a technical breakthrough and leap from prokaryotic to eukaryotic organisms. This represents another landmark achievement in synthetic biology following the artificial synthesis of crystalline bovine insulin. The disruptive nature of this accomplishment lies in its demonstration that complex natural life structures can be simplified through artificial intervention, natural life boundaries can be broken, and entirely novel life forms can be artificially created. It once again challenges fundamental conceptions about the nature of life.

Frontier advances in synthetic biology have further intensified concerns about the safety risks of "garage biology." Garage biology refers to biological technology activities conducted by amateur biology enthusiasts, characterized by non-professionalism, privacy, and non-institutionalization[12]. Compared with institutionalized scientific research, its safety risks are more difficult to prevent and regulate, and it is more susceptible to exploitation by bioterrorism, making it highly controversial.

Safety Risks, Ethical Dilemmas, and Their Causes

As a frontier technology in life sciences, synthetic biology brings both benefits and aspirations to human society while harboring enormous safety risks. These risks can be categorized into biosafety and biosecurity, which have distinct focuses yet overlap. The principle and engineering practice of designing and creating "artificial life" in synthetic biology pose tremendous challenges to traditional ethical concepts. To better understand the social factors underlying these debates, it is necessary to deeply analyze the connotations and causes of synthetic biology's safety risks and ethical dilemmas.

Uncertainty of Synthetic Organisms and Biosafety Biosafety generally refers to "policies, practices, equipment, facilities, and medical measures to protect workers and the environment from accidental exposure to hazardous experimental reagents and materials"[8], with a focus on "protecting humans, plants, animals, and the environment from accidental contact with pathogens or toxins that may have potential adverse effects"[13]. Regarding safety issues in synthetic biology research, primary concerns include risks present in all stages from design, preparation, and storage to transportation, application, and environmental release. Currently, relatively comprehensive safety regulations, such as the NIH Guidelines for Research Involving Recombinant DNA[14], essentially ensure the safety of synthetic biology research within laboratories. However, uncontrolled environmental release of synthetic biological products still carries

the possibility of unforeseen consequences and uncontrollable diffusion, thereby threatening biodiversity.

The safety risks posed by synthetic organisms are primarily determined by their "uncertain" characteristics. Uncertainty refers mainly to the unpredictable functions and evolution of synthetic organisms. Functionally, synthetic biology research involves unknown quantities in living organisms and uses materials that may be uncontrollable; humans lack definitive knowledge of their complete functions. From an evolutionary perspective, synthetic organisms in laboratories operate in controlled environments; if released into nature, they could spread and interact with their surroundings in unpredictable ways. Moreover, the multidimensionality, complexity, and unpredictability of scientific research, combined with the randomness of environmental events, can produce variables that exceed existing experience and cognitive levels, leading to uncertain consequences.

The 2003 SARS virus laboratory leakage incidents in Singapore, mainland China, and Taiwan[15] remain fresh in memory, demonstrating that when conducting experiments using biotechnology, unintentional or negligent accidents can occur. Even well-intentioned creation and use, faced with technological complexity and uncertainty and constrained by human cognitive limitations regarding the known world, cannot be completely controlled regarding potential negative impacts. Therefore, addressing safety risks arising from technological uncertainty primarily involves ethical responsibility issues, including the distribution of responsibility among different stakeholders such as scientists, governments, and enterprises.

Dual-Use Nature of Synthetic Biology and Biosecurity Synthetic biology technology possesses dual-use characteristics, meaning that well-intentioned research may be used for either benevolent or malicious purposes[16], creating a dual-use dilemma. The emphasis is that regardless of intent—good or evil, intentional or unintentional—once the knowledge, information, products, or technologies provided by synthetic biology are misused, they may cause potential or actual harm to human society. For instance, biological agents are fundamental resources for detection, identification, prevention, and treatment, but bacteria, viruses, fungi, and toxins can also be exploited by terrorists using biological induction, genetic modification, and synthesis technologies to manufacture biological weapons.

Biosecurity refers to "the protection, control, and accountability of biological agents and toxins, as well as critical biological materials and information, to prevent unauthorized possession and to prevent loss, theft, misuse, diversion, or intentional release that could cause serious consequences"[8]. Its focus is "preventing the misuse of biological agents and technologies by certain groups"[13] and curbing potential harm from dual-use applications. For example, the U.S. National Academies of Sciences, Engineering, and Medicine, in its recent report *Biodefense in the Age of Synthetic Biology*, states that synthetic biology expands the possibilities for creating new weapons. The report summarizes the

most common concerns, with the highest-level worries including "re-creating known pathogenic viruses," "producing biochemical compounds through in situ synthesis," and "using synthetic biology to increase the danger of existing bacteria"[17].

Overall, biosecurity addressing "dual-use" is often more difficult to achieve than biosafety, because no highly effective measures exist to prevent illegal synthesis. This poses challenges for how organisms are designed and how the processes of creation and use are monitored[2]. Consequently, malicious use of synthetic biology technology creates ethical risks for humanity, and preventing inappropriate applications and avoiding the misuse of research results constitute regulatory challenges for synthetic biology.

Benefits and Risks of Synthetic Biology As a frontier discipline in life sciences, synthetic biology has broad application prospects but may also bring enormous risks to human society. Benefits refer to advantages. Synthetic biology technology is widely applied in renewable energy, medicine, agriculture, and environmental protection, offering numerous benefits to humanity. For example, it holds important value in providing clean energy, affordable drugs, and novel materials, as well as in waste degradation and environmental remediation; it possesses disruptive potential in rapid drug synthesis, genetic improvement, and rapid human injury repair.

Risk is a major characteristic of modern society. Risks in modern society reflect a risk structure dominated by "manufactured risk"[18]. As a disruptive technology, synthetic biology embodies the irreversibility of creation, thereby exposing humanity and society to unpredictable risks. The uncertainty characteristic of synthetic biology technology means that laboratory research cannot fully verify the correctness of knowledge—that is, people cannot accurately predict potential hazards before new technologies enter society. Society becomes a "laboratory" for new technology, indicating that some attributes and risk characteristics of new technologies can only be identified and discovered through social application[19].

Therefore, if excessive pursuit of benefits from synthetic biology research and its technological applications leads to premature introduction of new technologies into society, it may expose the public to the risks of technological "trial and error"[19]. Risk is both real and socially "constructed," and the social construction of risk often leads to its infinite amplification. If risks are excessively amplified, it will inevitably hinder the development and application of synthetic biology. Thus, how to maximize benefits while keeping risks within socially acceptable limits is an ethical issue that humanity must seriously confront and resolve.

Ethical Dilemmas from "Designing" Life Through standardized, modular, and digital engineering methods, synthetic biology redesigns and modifies

naturally existing biological systems to create "artificial life" not found in nature[1]. As a technology of "design" and "reconstruction," synthetic biology inherently carries profound ethical and moral implications. It is precisely these internal ethical and moral dimensions that give synthetic biology far-reaching impacts on social fairness and justice, raising a series of urgent questions: Who holds the power to design and reconstruct? What are the bases for design and standards for reconstruction? Who should be responsible for the impacts or even harms caused by artificial organisms? These questions demand serious reflection. If an excessively human-centric approach leads to life design that transcends ethical boundaries, it will ultimately bring great risks to humanity. Therefore, "designing" responsibly is crucial.

At a deeper level, artificially designing life means embedding human will and culture into the evolutionary process of life. This breaks the traditional natural evolutionary process based on DNA as the genetic foundation and challenges conventional life ethics grounded in natural laws of biological evolution. Generally, culture possesses agency, representing an internal driving force for cultural change. The embedding of human will and culture, or even their dominance in life evolution, will subject the direction and future of human evolution to greater uncertainty. The development of synthetic biology compels humanity to confront reflections and inquiries about the meaning of life and dilemmas in understanding what it means to be "human."

Reflections on Synthetic Biology Regulatory Mechanisms

With the development of synthetic biology, international concern about its safety risks and ethical issues is growing. Consequently, how to address these challenges has become a common governance challenge for the international community. Currently, two different regulatory models exist: (1) a proactionary principle-based model, and (2) a precautionary principle-based model. The former reflects a view of technological progress, believing that ethical issues can always be resolved with scientific and technological development, making it unnecessary to restrict scientific and technological advancement, or advocating a "act first, consider later" approach. The latter is founded on risk society theory. As Ulrich Beck pointed out, risks in modern society are undergoing structural transformation, evolving from a risk structure dominated by "natural risks" to one dominated "manufactured risks." Consequently, modern society faces operational failures caused by contradictions between risk-taking institutions and safety-oriented institutions—namely, "institutional" risks[18]. The precautionary principle-based model asserts that "if an action or policy has the potential to cause harm to the public or the environment, even without scientific consensus that the action or policy is harmful, the burden of proof that it is not harmful falls on those taking the action or making the policy"[20].

Faced with rapid technological development and its profound impact on human health and lifestyles, the precautionary principle is increasingly becoming the foundation or framework for constructing synthetic biology regulatory mecha-

nisms. Countries and regions such as Germany, the United States, and the European Union have established national ethics committees or biosafety oversight bodies[8,21,22] and corresponding regulatory mechanisms[13,23,24].

The U.S. regulatory mechanism embodies a multi-agency model where various departments regulate based on their respective responsibilities. The regulatory scope extends from laboratories and workplaces to the environment and market, with specific safety conditions set for institutions and projects receiving federal funding[8]. However, this multi-agency model can lead to unclear agency missions and, when regulatory disputes arise, adversarial legalism can complicate regulatory issues[25]. The EU adopts a unified legal framework with decentralized national regulation, primarily relying on Directives 2001/18/EC and 2009/41/EU, as well as Regulation (EU) 428/2009. The EU implements these directives and regulations into national legislation through cooperation with each member state[25]. Both the U.S. and EU models highlight cooperation and sharing among government, industry, and non-governmental organizations, and adopt "adaptive governance" approaches that track frontier developments in synthetic biology to continuously improve risk assessment and regulation. These measures place European and American countries in an active position in addressing synthetic biology ethics and risk regulation.

Rapidly developing technologies require equally rapid decision-making, and regulation of synthetic biology cannot remain based on understandings of biotechnology from the 1990s[26]. To date, China's ethics regulation remains in a proactionary "act first, consider later" mode, with relatively deficient ethical norms and a voiceless position in international ethics regulation. This often subjects China's biotechnology research and applications to ethical questioning from the international academic community, and the resulting decision-making lag has to some extent hindered research development. The accompanying safety risks and ethical issues have made existing regulatory models inadequate for the future development of synthetic biology in China.

Based on foreign experiences and China's realities, China's regulatory model for synthetic biology should shift from a "proactionary principle" to a "precautionary principle" model, and reconstruct its ethical regulatory mechanism for synthetic biology through five approaches: (1) Establish a professional national ethics review and oversight body, with regulation of dual-use technology research breaking through disciplinary and academic boundaries to fully leverage ethics management's supervisory and safeguarding functions in scientific research. (2) Create appropriate interdisciplinary research platforms that broadly attract scientific groups potentially engaged in synthetic biology research to participate in dialogue. (3) Combine self-management with government regulation, maintaining communication and exchange with frontier synthetic biology research teams to continuously discuss emerging safety and ethical issues during technological development. (4) Strengthen ethics education for all participants in synthetic biology research and applications to enhance researchers' ethical awareness. (5) Innovate science communication efforts, adhere to preventive

and forward-looking principles, cultivate scientific and rational ground, and actively seek public understanding and support.

Conclusion

Synthetic biology has propelled humanity's transformation from understanding life to designing life, a revolution that is both conceptual and practical. Synthetic biology development holds broad application prospects while simultaneously presenting inherent requirements for ethical assessment, risk prevention, and regulation.

Reflecting on the safety risks and ethical issues triggered by synthetic biology and exploring strategies to prevent risks and resolve conflicts, we argue that to ensure the healthy development of synthetic biology: On one hand, we should closely track frontier developments in synthetic biology, conduct real-time assessments of potential safety and ethical risks, establish corresponding ethical regulatory mechanisms and risk prevention and control systems, maximize the avoidance of possible harms, and keep risks within socially acceptable limits. On the other hand, we should attach great importance to science communication and popularization of frontier technologies including synthetic biology, innovate communication methods, ensure the integrity of communication content, thereby avoid infinite amplification of risks, and promote public understanding and support for synthetic biology.

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Note: Figure translations are in progress. See original paper for figures.