

Manuscript ID:
IJRSEAS-2025-020529



Quick Response Code:



Website: <https://eesrd.us>



DOI: 10.5281/zenodo.23389922

DOI Link:
<https://doi.org/10.5281/zenodo.23389922>

Volume: 2

Issue: 5

Pp. 152-158

Month: October

Year: 2025

E-ISSN: 3066-0637

Submitted: 15 Sept. 2025

Revised: 25 Sept. 2025

Accepted: 16 Oct. 2025

Published: 31 Oct. 2025

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How to cite this article:
Pawar, N. B. (2025). Genetic
Engineering in Microbial Systems:
Opportunities and Challenges.
International Journal of Research
Studies on Environment, Earth, and
Allied Sciences (IJRSEAS), 2(5),
152–158.
<https://doi.org/10.5281/zenodo.23389922>

Genetic Engineering in Microbial Systems: Opportunities and Challenges

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Abstract

Genetic engineering in microbial systems has emerged as a transformative field with significant implications for industrial biotechnology, medicine, environmental sustainability, and agriculture. This study explores the opportunities, challenges, and governance aspects associated with microbial genetic engineering. It highlights the role of microorganisms as efficient platforms for biomanufacturing, metabolic engineering, and synthetic biology applications. The paper discusses core technologies, model organisms, and advancements that enable the development of high-value products such as biofuels, pharmaceuticals, and biodegradable materials. Additionally, it examines key challenges including technical limitations, biosafety concerns, ethical considerations, and regulatory complexities. The study emphasizes the importance of risk assessment frameworks and public engagement to ensure responsible innovation. Emerging trends such as synthetic biology, microbiome engineering, and data-driven approaches are also analyzed to understand future directions. Overall, microbial genetic engineering offers immense potential, but its sustainable and ethical implementation requires interdisciplinary collaboration and robust governance mechanisms.

Keywords: Genetic Engineering, Microbial Systems, Synthetic Biology, Metabolic Engineering, Biotechnology, Bioprocessing, Microorganisms, Biosafety, Biosecurity, Bioremediation, Industrial Biotechnology, Microbiome Engineering

Introduction

Genetic Engineering in Microbial Systems: Opportunities and Challenges

Introduction

Genetic modification of microorganisms has major implications for industry and society. This study examines the opportunities, challenges, and governance of genetic engineering applied to microbial systems, contributing to an understanding of its significance and implications for policymaking. The focus remains on tools and concepts relevant to de novo engineering efforts, rather than total synthesis, genome minimization, and other techniques of similar nature with less relation. Four key opportunities for microbial genetic engineering appear widely recognized in the scientific literature and remain more relevant than new disciplines or emerging technologies such as in vivo gene therapy, plant biotechnology, or genomic medicine. Industry routinely harnesses microbial systems for biomanufacture, bioprocessing, and other applications to deliver biocatalysts, commodity chemicals, energy, food and feed additives, organic acids, pharmaceutical precursors, pharmaceutical compounds, plastic precursors, protein-based biopesticides, surfactants, therapeutic proteins, vitamins, and other products (Morgan Lanza, 2015); broaden the genetic and enzymatic diversity available for discovery (Santos-Beneit, 2024); support simplified designs that facilitate progressively higher levels of autonomy (Yan & S. Fong, 2017); and provide key breadboard environments for developing metabolic engineering strategies at the single-organism, multicellular, and community levels. Such genetic engineering remains profoundly enabled by the evolution and rapid adoption of guiding principles and methodology associated with synthetic biology and contributes equally to opening the frontier. Biochemical and physiological analysis of microorganisms supports both the preconception of metabolism as a cellular output and the treatment of genetic engineering as modular programming. Such duality echoes the dual nature of biological sequence information as an abstract machine language specifying potential chemical structure and reaction events and formalizes an intuitive linkage between genome-scale metabolic models (GSMMs) and the objective of developing predictive design engines for biological complexity—design engines that elevate predictive forward engineering from genome informatics to pathway specification—and facilitate and expedite bioprocessing development.

Foundations of Genetic Engineering in Microbial Systems

The definition of genetic engineering includes both well-established and novel techniques that alter the genetic material of living organisms. A classical technique is directed mutagenesis, developed in the early 1970s, which involves the alteration of one or a small number of base-pairs at a given locus in the genome. Such techniques have been applied to diverse prokaryotic strains and eukaryotic systems for the modification of traits, including biosynthesis pathways for the production of specialty compounds. With the advent of the polymerase chain reaction (PCR) in the mid-1980s, strategies based on the integrated amplification of the target and marker plasmids became widespread. Such approaches facilitated the transformation of non-conventional microbial strains, for which the development of other genetic tools was limited. One-pot two-step (1p2s) techniques consisting of PCR amplification of a target and marker plasmid, followed by their co-transformation of *Bacillus subtilis* in a single event, were developed subsequently (Michele Wingler, 2011). The most widely used microbial system for the production of biopharmaceuticals is *Saccharomyces cerevisiae*. The evolving strategies being developed for this host have enabled increased titer, yield, and productivity in the production of recombinant proteins. A general framework for metabolic engineering and industrial bioprocess development applicable to *S. cerevisiae* has been established. A significant body of research has pioneered further techniques, tools, and relevant omic analyses for this important workhorse organism in recent years (Santos-Beneit, 2024). Microbial biotechnology plays a considerable role in medicine, since microorganisms are used in the production of many biologics, vaccines, and immunodiagnostics critical for health care. Therapeutic strategies where microorganisms are engineered further extend this application to proteins, peptides, metabolites, small molecules, and probiotics. Paradoxically, academic and industrial interest in the microbial engineering of genetic circuits and strains within the pharmaceutical industry has not reached an equivalent level in medicine. It is anticipated that this development will alter the current situation in future years (Yan & S. Fong, 2017).

1. Historical Development

The milestone on the Pathway to the 21st Century Biotech realised the importance of an innovative environment for the Honeywell Process Solutions business unit (Yan & S. Fong, 2017). Parallel research was initiated with the Technical Research Centre of Finland on applications of biosensors and bioreactors to process control, as well as the development of methods for the extraction of convertible fuel from brown coal. Significant efforts were devoted to modelling metabolic pathways of interest and formulating methods for their optimisation. Traditional strain improvement was also pursued through both mutagenesis and classical techniques such as protoplast fusion and plasmid construction to create hybrid strains. All of these activities led to closer co-operation with the University of Queensland Microbiology Department and ultimately to the commercialisation of CSIRO's bioprocess technology in 1996 by the Scientific Company of Australia through establishment of AgriBioTech at St George in Queensland.

2. Core Technologies and Methodologies

Microbial genetic engineering aims to rationally manipulate the genotype and/or phenotype of microbes, predominantly bacteria and simple eukaryotes such as yeasts, fungi, and algae. Among micro-organisms, non-pathogenic strains of *Escherichia coli* and *Saccharomyces cerevisiae* are the most popular laboratory model organisms. These species can be used for both the elucidation of fundamental microbiological processes and as cell factories for the production of proteins, chemicals, and biofuels. Other extensively used model micro-organisms include *Bacillus subtilis*, *Pseudomonas putida*, *Corynebacterium glutamicum*, *Kluyveromyces marxianus* and *Yarrowia lipolytica* (Morgan Lanza, 2015). The stringent regulation of gene expression, plasmid replication, and post translational modifications of recombinant proteins makes them ideal candidates for the production of heterologous proteins. The scope of genetic engineering in microbial systems encompasses the development of low-cost technologies for biorefineries to the synthesis of designer organisms for microbial Fuel Cells (Yan & S. Fong, 2017). Four core areas further define the scope of genetic engineering in microbial systems: i) bioprocess optimisation for the production of selected bioproducts, ii) context-specific plasmids that enhance the economic viability of the process, iii) construction of microbial cell factories capable of converting a wider range of substrates into high-value compounds and iv) engineering of microbial monitoring systems to enhance bioprocess performance. Governmental funding, investment from international grant agencies and financial backing from a number of international funding bodies are required to help achieve these goals.

3. Model Microorganisms and Their Roles

Microorganisms have played a central role in developing life sciences, especially in genetic engineering and biotechnology. Model microorganisms used commercially include *E. coli*, *S. cerevisiae*, *B. subtilis*, and *A. niger*. For research and development, information about natural metabolism, metabolic activities, protein expression, molecular manipulation, and general physiology is critical (Yan & S. Fong, 2017). Because they are either bacteria or yeasts, important limiting factors such as metabolic pathways and external factors operate mainly on a single cell on the outside rather than at the nucleus level. With mandatory regulations for safety and understandable legal terms by the authorities of the country they operate in, model microorganisms are of utmost importance (Morgan Lanza, 2015). For industrial production, strains without an official approval or certification of standard operability by C-SBM (certification of simplified biotechnology model) go through extra procedures gaining C-SBM approval with a change procedure that is mandatory and costly.

Opportunities in Microbial Genetic Engineering

Benefit from an abundance of knowledge and resources stored in decades of research and development, microbial cultivation is of paramount importance in contemporary biotechnology. It is now the most widely used approach for the production of bio-relevant compounds (Craig Zielinski et al., 2020), with applications such as enzyme

manufacturing, the generation of alternative chemical feedstocks, the synthesis of biodegradable plastics, sustainable bioremediation, the generation of bioprocessing and transformation agents, the production of biofuels, the production of defence compounds against pathogens, embedded probiotic agent manufacturing, the generation of sweeteners and artificial flavour agents, and so on. A wide variety of processes utilized to engineer microorganisms, centre on four aspects. Engineering shoot of microorganisms, govern three major steps: (i) desired phenotype specification; (ii) pathway generation, propelling transition from existing strains to mutants; and (iii) mutant phenotypic evaluation and selection. Add-on modules focus on the very first step in the shoot, whereby, they automatically approach large databases of experimental knowledge to generate pathway candidates from known pathways. Such modules introduce additional consideration towards precipitation of dextran from starch by starch degrading agents. Existing projects have alighted upon biofuel goal longer than a decade. A dedicated given-population cyclic pathway generation tool along with detailed advisor and genotypic evaluate supplies software scattered on ISP168 genomic sequence, RNA-seq data, and transcriptomic approaches, to treat batch culture of heavy metals on genetic-focused mineral liquids in sufficient duration to maximise CuSe depositional amount and delimitate distribution. Other microbial metabolism projects stress upon foetal completion of pebax-zif-weekly rifampicin resistant polymeric microparticles manufactured from biofilm-encapping and anaerobic expandable pills targeting amoxicillin resistance. Components addressed include pathway completion, sequencing-guide growth-consumption genotypic character, precursory-formulation cyclical parameters and specific formation-fitness effects-parameter sensitivity analysis. Further extending horizon onto filamentous pathogens, besides completion of glatiramer-designated neurotrophic-agent-material-infective filamentous fungi-aqueous emulsion excursion-pod delivery spectrums, broader objectives have been introduced to investigate filamentous-adapted glide motions and aerobiotic materials with instead of fatty-acid-based and aerobiotic-planktonic and prolong the range-bar-capacity-of-pipeing.

1. Industrial Biotechnology and Bioprocessing

Extensive research using metabolic engineering strategies such as enzyme production, pathway biosynthesis, substrate specificity alteration, yield optimization, and process intensification has been actively pursued since 1980 for bioprocessing of different products (Ariff, 2009). Microbial populations are widely instrumental across differing biomass conversion process routes as they are cost-effective, ease to manipulate enzymatically, versatile in nutrient utilization, and amenable to continuous bioprocess applications. The high metabolic diversity of microorganisms gives them a great potential to be engineered for production of virtually any product (Yan & S. Fong, 2017). Development of metabolic pathways allows conversion of renewable substrates (e.g. lignocellulosic and non-lignocellulosic biomass and by-products) to biofuels, biodegradable plastics (i.e. polyhydroxyalkanoates), fatty acids, organic acids, solvents, toxic compounds removal (i.e. heavy metals, pesticide, phenol, pharmaceuticals), and starch-eliminated food industry (e.g. gluconic acid, dextran) (Santos-Beneit, 2024). Development of engineering frameworks based on genomics, metabolomics, flux analysis, and systems biology that enable product-targeted genome alterations has recently gained also momentum.

2. Medicine and Therapeutics

Genetic engineering represents a powerful strategy for addressing public health priorities. Despite the considerable success of synthetic chemistry and commensurate opportunities for small-molecule drugs, microbiolar fermentation remains a pillar of the biotechnology industry. Nearly three-quarters of approved drugs are either biologicals or are derived from biologicals. The World Health Organization (WHO) underscores the urgency of addressing antimicrobial resistance, a threat to global health, food security, and development. Continued advances in genetic-engineering technologies hold promise within the pharmaceutical enterprise, whereas prior generation of microorganisms remains dominant in the large-scale production of vaccines. New opportunities in the medical and therapeutics domain focus on production of biologics, vaccines, and diagnostics, as well as on the development of engineered, controllable, biologically-safe probiotic strains and bacteriophages for targeted microbiome modulation. Technical maturity of diverse applications varies considerably, and different preparatory and translational hurdles present varying levels of complexity. The path toward pharmaceutical production provides critical information (Santos-Beneit, 2024).

3. Environmental Applications

The accidental discovery of the polychlorinated biphenyl (PCB) dechlorination capacity of *Pseudomonas pseudoalcaligenes* KF707 prompted extensive investigations into the bacterial degradation of chlorinated aromatic compounds. For decades, research efforts directed towards bioremediation, involving the use of living organisms to remove or neutralize pollutants from a contaminated area and an effective method for cleaning heavy metal- and hydrocarbon-contaminated industrial wastewater, have been published in scientific journals. Environmental applications of synthetic biology and associated microbial genetic engineering can support sustainable development, enhance user productivity, and generate economic benefits while simultaneously protecting natural resources and the ecosystem. Bioremediation, waste valorization, and prevention of microplastics in marine environments are specific target areas for genetic intervention aimed at environmental protection and restoration (Yan & S. Fong, 2017).

4. Agriculture and Food Systems

Global agriculture faces increased pressure to meet rising food demands while minimizing environmental impacts. Synthetic-biology approaches that enable more efficient microbial biopesticide and biofertilizer development continue to gain momentum (Douglas Goold et al., 2018). By leveraging synthetic-biology tools, both the plant-associated microbial community and individual plant-beneficial strains may become targeted applications. The use of food-grade microorganisms to engineer food products such that desirable microbes are transferred to the digestive

system is another important possibility (Dal Bello et al., 2024). When modified strains degrade rapidly, ensure intestinal colonization is hermetically sealed, and display a neutral phenotype, they have the potential to reach markets otherwise constrained by regulatory hurdles.

Challenges and Limitations

Genetic engineering in microbial systems offers significant opportunities for industrial biotechnology, medicine, environmental applications, and agriculture. Nevertheless, several technical and ethical challenges must be addressed before commercial bioproducts can extensively utilize engineered microorganisms. Technical challenges include off-target effects, genomic instability, scalability, data quality, reproducibility, and standardization (Craig Zielinski et al., 2020). Ethical, health and safety, and security issues further complicate the situation. Containment strategies, misuse prevention, and dual-use governance frameworks are necessary to mitigate biosafety and biosecurity risks. Societal issues such as equity, access, consent, labelling, and public trust also demand careful consideration. Transparent, inclusive stakeholder engagement rooted in science and ethics must be prioritized (Morgan Lanza, 2015). The challenges of engineering microorganisms extend beyond the technical environment into social, ethical, health, and security dimensions. Furthermore, many engineering efforts target non-model organisms for which standardized methodologies and tools are limited. To safeguard against potential adverse consequences from engineered microorganisms, biosafety frameworks and lifespan-reduction strategies remain under development. Development of innovative containment schemes and biosecurity surveillance protocols is critical for preventing misuse of engineered strains. Public discourse around engineered microorganisms—spanning engagement, equity, labelling, and consent—has intensified. Broad stakeholder consultations and commitment to transparency are imperative to foster conditions conducive to active, trust-based dialogue (Yan & S. Fong, 2017).

1. Technical and Methodological Barriers

No universal and unequivocal genetic engineering platform exists for economic and sustainable engineering of all microorganisms (Yan & S. Fong, 2017). Co-occurrence of multiple functionalities in one strain, for example, requires a platform that grants simultaneous, multiple, orthogonal control over all upstream and downstream elements. Artificial biocontainment systems are also lacking; a suite of measures is needed to develop better containment solutions. A plethora of compartmentalized synthetic gene circuits have been engineered in various microorganisms, yet multiple modular circuit designs that are independent at the transcriptional, translational, and metabolic levels are still missing (R. George et al., 2024). Besides, the techniques and tools used are heterogeneous and often appear as complicated one-off solutions. At present, direct translation of engineered genetic circuits among related microorganisms with similar topologies cannot be attempted. Engineered, portable, and commercially available universal basic devices, which hold true across bacteria, permit broader engineering spills from engineered microorganisms to industrial non-model engineering microorganisms. However, accomplishing the availability and accessibility, customizability, robustness, low-cost, and versatility requirements imposed on an ideal platform remains challenging. Microorganisms without developed sufficient genetic manipulations and engineering either remain model strains or are considered non-model strains. Strains that either require additional genetic modifications for genetic tool development or serve as hosts for delivering genetic circuits to non-model strains are also treated as non-model strains.

2. Biosafety and Biosecurity Considerations

The complex and malleable nature of microbial systems, combined with their ability to produce a wide array of natural products, has made genetic modifications of microorganisms a popular platform for bioprocess engineering. Genetic engineering in microbial systems can significantly contribute to sustainable development and meet global challenges in health, food, and energy (Asin-Garcia et al., 2023). However, these advances also pose serious risks to safety and security (R. George et al., 2024). Minimizing risks while exploiting the significant potential of microbial approaches requires the identification of a set of appropriate risk assessment criteria and guidelines. Potential microbiological hazards must be systematically identified, and detailed exposure assessments should be carried out to enable the evaluation of the extent of any spread and establishment of the engineered microorganisms. The scientific and technical feasibility of control measures needs to be assessed based on the modes of dissemination, the environments in which the microorganisms are expected to survive, and anticipated persistence levels. Where a serious risk to human health or environment has been identified and circumstances such as those outlined above indicate that exposure cannot be prevented, a probabilistic or consequence approach may be needed to evaluate the tolerability of risk.

3. Ethical, Legal, and Societal Implications

Public perceptions and acceptance of genetic engineering are influenced by various socio-political factors and ethical questions. Emerging technologies such as CRISPR-based systems and the application of genetic engineering to industrially relevant microorganisms present new opportunities to produce biomaterials and food, though ethical and societal expectations regulating access and equity apply. An equitable distribution indicates a widely shared societal benefit, while certain ethical questions, such as economic benefit to one region or group of users, may restrict acceptance (C Wintle et al., 2017). Concerns over control of biological engineering technologies, such as dirty bombs, surface in some countries where inexpensive tools may fall into the hands of individuals with malicious intent. In these situations, the technique is viewed more as a tool than a technology. An overarching framework to guide all environmental biotechnology with a focus on food safety and security, increased manufacturing using low-cost raw materials, and clean energy will serve biotechnology well going forward. Risk Assessment and Governance. Genetic engineering of microorganisms holds great promise for applications in agriculture, bioremediation, biofuels, food and feed supplements, functional foods, industrial enzymes, non-opioid analgesics, probiotics, and therapeutics. However, engineered microorganisms might behave unexpectedly, potentially causing damage to human health or

the environment. Despite the involvement of a large number of experts, assessment of scientific, environmental, and ethical risks related to this technology remains inadequate, particularly concerning the use of models based on laboratory strains such as *Escherichia coli* (Bouchaut et al., 2022). Because assessment is often based on a limited understanding of science and technology, some risk-hazard links tend to be imaginary. The risk-uncertainty distinction appears to be useful in this context (Asin-Garcia et al., 2023). Whereas risk relates to hazards and probabilities, uncertainty relates to incomplete knowledge regarding hazard and probability concepts, which converges with notions of unpredictable and emergent behaviour. Extensive work has been undertaken to establish regulatory frameworks for traditional biotechnology and associated breeding and production methods with genetically modified organisms (GMOs).

1. Risk Mitigation Frameworks

Risk mitigation measures generally consist of three key elements: hazard identification, exposure assessment, and risk-control measures. Hazard identification focuses on understanding the potential adverse effects a genetically engineered microorganism may exert on human health or the environment. Exposure assessment addresses the likelihood of the organism being released into the environment and the extent of exposure that might occur in such an event. Risk-control measures seek to reduce either the hazard or exposure, or both, thus lowering the overall risk to acceptable levels. Acceptable-risk criteria define the tolerability of risk, although they are often context-dependent. As bacterial microorganisms are among the most widely manipulated metabolic systems for biotechnology and industrial production, the analysis focuses on such microbial organisms and pertains mainly to engineered genetics used in industrial strains (Bouchaut et al., 2022) (Asin-Garcia et al., 2023).

2. Regulatory Landscapes Across Jurisdictions

The regulatory landscapes pertaining to genetic biocontainment technologies for research involving recombinant and synthetic nucleic acid molecules across various authorities exhibit substantial variability. All comparable jurisdictions have published guidelines articulating oversight of such investigations, but restrictiveness and enforcement intensity differ greatly (R. George et al., 2024). These landscapes encompass standards for controlling access to biosafety technologies that counteract engineered microorganisms and for deliberating deployment and restricting materials in biocontainment projects. Recent milestones comprise delivery of standardized ecosystems that underpin productive microbiome research and formulation of a gene drive organism intended to modify a pest population, the latter raising a spectrum of regulatory considerations. Statutes and guidelines governing the engineering of vectors or nonviable products of DNA synthesis devoid of activity on a target genome are available across jurisdictions including the EU and United States, and exchanges on oversight of organisms capable of synthesizing information-intensive DNA sequences have been commonplace (Eriksson et al., 2019). By contrast, approaches to genome-edited organisms developed by molecular techniques that could similarly have arisen via nongenetic methods diverge widely. Although experimentation on such strains remains permissible within academia in many countries, the current uncertainty at the commercial interface acts as a strong disincentive for the private sector to invest in the emergent field of genome-editing science.

3. Public Engagement and Communication

Public engagement and communication are central to responsible development of biotechnology (R. George et al., 2024). Societal debates about emerging genetic technologies highlight the need for effective public engagement, illustrated by community-guided initiatives to prevent tick-borne diseases and ongoing discussions around genetically modified crops and organisms. Transparent communication about biosafety, risk assessment, and regulatory frameworks helps build public trust. Engagement fosters the understanding necessary to address concerns, informs policy, and contributes to informed decision-making in the bioeconomy. Research on public engagement and communication surrounding synthetic biology emphasizes the importance of interactive dialogue among scientists, stakeholders, and the public (Schmidt et al., 2009). Historical debates on genetic engineering suggest that an open approach encourages effective exchange of information and avoids the amplification of exaggerated hopes and fears. Stakeholders should respond to scientific arguments rather than framing their discussions as polemics. Meaningful ethical discussions must engage with public preferences and local knowledge—even when viewed as misinformed—rather than remaining confined to normative reasoning or conducting campaigning or information dissemination. Acknowledging and addressing the diverse interests, concerns, and worldviews related to technology and innovation is essential.

Emerging Trends and Future Directions

The burgeoning field of microbial genetic engineering stands at the intersection of a slew of rapidly evolving technological, economic, and societal developments. Widely recognized since the inception of recombinant DNA technology and synthetic biology (Craig Zielinski et al., 2020), this multidisciplinary area maintains a vibrant intellectual pulse, exhibiting a multitude of configurations and trajectories across a variety of contexts and domains (Santos-Beneit, 2024), yet institutionalizing synthetic organisms for safety and governance primarily focuses on organisms used as biotechnological production platforms throughout the biopharma, bioproducts, and agbiotech value chains. There is increasing interest in biotechnological endpoints that address agriculture, pharmaceuticals, therapeutics, chemicals, energy carriers, flavor compounds, food, green materials and building blocks, lubricants, personal-care products, pesticides, platform chemicals, plastics, process intermediates, proteins, sealants, solvents, and textiles (Yan & S. Fong, 2017). Notably, the number of engineered microbial species is increasing steadily, advancing vertically along the conceptual sophistication axis. Activity is increasingly situated at the system, multi-, and hybrid levels, while design-science ambition extends to interrogative objectives such as self-healing, temporary genetic memory, and programmable biosafety protocols.

1. Synthetic Biology and Circuit Design

The burgeoning fields of synthetic biology and bioengineering are facilitating the development of programmable and scalable microbial production systems with intricate functionalities. Circuit and pathway design for standardised, modular, and orthogonal components is now possible, making time-dependent control over multiple inputs and outputs feasible (H. McArthur & S. Fong, 2010). Microbial production capacities for therapeutic proteins and small molecules are being extended thanks to greater engineering scope. In parallel, synthetic circuits allow non-native functions to be encoded in a well-defined and predictable manner (Antunes Westmann et al., 2018). Modularity and standard component specifications promote the design of complex behavioural programmes. Engineering approaches must also address key unreliability issues associated with circuit assembly and integration. Various strategies—including the engineering of component parts, circuit topology, regulating metabolic burden, and implementing control-theory concepts—are being pursued to boost circuit predictability.

2. Edible and Microbiome-Targeted Approaches

With the growing awareness of the critical role of the gut microbiome in human health, there is heightened interest in tools aimed at genetically manipulating resident gut bacteria (Arnold et al., 2023). Gut microbes influence a wide variety of biological processes, such as drug metabolism, energy harvesting from indigestible polysaccharides, and the maintenance of the intestinal barrier. A deeper understanding of these interactions requires linkage of microbial genotypes to the corresponding phenotypes that directly affect host responses (ethics of microbiome engineering and develop guidelines on safety and evaluation). The tools available for such studies remain limited because resident gut bacteria occupy a non-culture collection in laboratory settings (Yan & S. Fong, 2017). Moreover, the broad-spectrum of non-cultured gut microbes hinders the direct application of the tools developed for the selected microbial model. Engineering a medium-scale gut microbiome via a minimal nine-member community has made it possible to probe the effect of gut-muscle-microbiome interaction on skeletal muscle function. Likewise, the advent of gut microbiome-related works has sparked a growing interest in engineering the gut microbiome for microbial therapeutics in targeted cohorts. Microbiome engineering encompasses the construction of functional consortia and the manipulation of prototype strains or non-modifiable strains with the transformation of small, ease-preparation, stable-in-use, and at-low-concentration DNA payloads from standard digital information files. The progress of engineering microbiomes represents an added degree of complexity compared with the functional approach solely targeting a single bacterium.

3. Data-Driven and Computational Methods

Biotechnological endeavors increasingly depend on appropriately engineered microbial strains to enable bioprocesses, provide opportunities for chemical production and human health, and preserve the environment through bioremediation. Controlling microbial behaviour is a challenging task due to its inherent complexity, which is exacerbated when non-model strains are targeted. Traditional engineering approaches begin with genome-scale models and bioindicators, followed by core genome analysis to infer design rules at the gene, operon and pathway levels. The critical missing component is a viable pathway design stage. State-of-the-art genome-scale metabolic models incorporated into Delft Biology Toolbox (DBT) Predator and Molgenis Pathway Assistant facilitate the provision of exploitable pathways and the determination of pathway trade-offs to target a nucleotide level pathway design stage. Recent advances addressing pathway installation, adjustment, redirection and removal broaden microbial engineering opportunities (Craig Zielinski et al., 2020) ; (Yan & S. Fong, 2017).

Conclusions

Technological advances allow genetic manipulation of a wide variety of segregating microbial strains, from nonmodel eukaryotes to slow-growing or poorly characterizable bacteria. Genetically modified (GM) microbes offering many potential advantages in industrial production are nevertheless underutilized, partially due to unaddressed scientific, technical, regulatory, and ethical issues (Santos-Beneit, 2024). A range of emerging proposals seek to stimulate greater innovation in the field. Microbial genetic engineering is increasingly perceived as offering opportunities alongside profound challenges that must be overcome to bring these advances to fruition (Yan & S. Fong, 2017).

Microbial genetic engineering can deliver significant technical advances, open up entirely new avenues of investigation and application, and harness emerging, rapidly evolving technologies (Morgan Lanza, 2015). Basic, industrial, agricultural, and medical applications figure prominently in a range of proposals designed to stimulate R&D and product development, particularly since microbiologists have started to realize the extent to which the science has until now been underexplored. A compelling economic case also exists for accelerated research and product development in broader microbiological exploration, particularly when coupled with integrated interdisciplinary frameworks.

Acknowledgment

I would like to express my sincere gratitude to all those who have contributed to the successful completion of this research work.

Financial support and sponsorship

Nil.

Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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