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Converging quality by design, artificial intelligence, and biofoundry automation: A new paradigm for scalable circular biomanufacturing

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ABSTRACT

Synthetic biology applies engineering principles to the rational design of biological systems with the aim of producing predictable and tunable behaviour. Although the field's conceptual foundations and core technologies are well established, the recent simultaneous maturation of Quality by Design (QbD), artificial intelligence (AI)-assisted biological design, and automated biofoundry workflows is beginning to outline a more replicable pathway from laboratory innovation to industrial-scale circular biomanufacturing. This review argues that the convergence of these three elements, rather than any one alone, characterises the current phase of the field. We examine how the Design-Build-Test-Learn (DBTL) cycle is being transformed from a research heuristic into a systematic industrial development framework; show how shared toolsets now transfer across microbial, plant, and animal systems to enable a holistic bioeconomy; benchmark synthetic biology-derived products against conventional alternatives where techno-economic and life-cycle data permit; and examine scale-up, regulatory, and societal bottlenecks through recent market-scale case studies in which these bottlenecks have been navigated in practice. We also contrast EU and US regulatory frameworks to show how policy divergence shapes technology adoption. We conclude by identifying what the coming decade of convergent synthetic biology must deliver to support a circular bioeconomy at the scale the 2030 Agenda demands.

1. Introduction

The 2030 Agenda for Sustainable Development, adopted by the United Nations in 2015, set out 17 interconnected Sustainable Development Goals (SDGs) that collectively call for the eradication of poverty, the protection of the planet, and the assurance of prosperity for all (United Nations, 2015). A decade on, escalating environmental pressures have put the timely achievement of these goals at serious risk. Traditional manufacturing, reliant on finite resources, continues to drive environmental degradation and aggravate climate change. The need for sustainable production systems that can simultaneously mitigate climate impacts and reverse the loss of natural capital is now widely acknowledged.

Biological systems, shaped by millions of years of evolution, carry rich repertoires of metabolic and regulatory solutions well suited to the chemistries humans now need to reproduce sustainably (Brans et al., 2017; Reid et al., 2016; Yoshida et al., 2016). Synthetic biology seeks to capture these solutions through the rational design and construction of biological systems with predictable and tunable behaviour (Elowitz and Leibier, 2000; Endy, 2005; Khalil and Collins, 2010). Coupled with biorefinery concepts that convert renewable feedstocks into valuable products (Dahiya et al., 2018; Leong et al., 2021), synthetic biology offers a credible route to a bio-based, circular economy.

Several excellent reviews have already surveyed the conceptual foundations of synthetic biology, the molecular technologies that enable it, and its individual application domains. Against that background, a reasonable question is why another review is needed now. Our answer is that the field has entered a distinct phase defined not by any single breakthrough but by the convergence of three developments that, until recently, matured in parallel and largely in isolation:

- Quality by Design (QbD): originating in automotive manufacturing and then finding widespread adoption in the pharmaceutical industry (Benyahia et al., 2020), QbD emphasises identifying the

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product's critical quality attributes (CQAs) and critical process parameters (CPPs) early in the process design (Mu'azzam et al., 2024).
- AI-driven biological design: advances including next-generation structure prediction (AlphaFold 2 and 3), generative protein design (RFdiffusion, ESM3), and large-language-model agents for synthetic biology (CRISPR-GPT) are moving AI from a supporting analytical role into active, proposal-generating participation in the DBTL cycle (Abramson et al., 2024; Hayes et al., 2025; Jumper et al., 2021; Qu et al., 2025; Watson et al., 2023).
- Automated biofoundries: coordinated, high-throughput DBTL infrastructure is now operational in a distributed network of public and private biofoundries, making systematic strain and process development the norm rather than the exception (Chao et al., 2017; Lee et al., 2023; Stephenson et al., 2023).

Taken together, these three elements support an emerging industrial development framework for synthetic biology (Fig. 1). They help to de-risk the transition from bench to market, allow the same underlying toolkit to be deployed across microbial, plant, and animal systems, and align synthetic biology outputs with the regulatory and sustainability evidence frameworks on which market adoption depends. This review is organised around that convergence. Section 2 revisits the conceptual and methodological foundations with a sharper emphasis on DBTL and QbD as the industrial backbone. Section 3 summarises the cornerstone technologies focused on developments most directly relevant to industrial translation. Section 4 traces how shared tools transfer across microbial, plant, and animal systems. Section 5 benchmarks sustainable applications quantitatively against conventional alternatives where possible. Section 6 treats scale-up as an increasingly tractable engineering problem, illustrated through market-scale case studies. Section 7 examines regulatory divergence and societal acceptance, and Section 8 concludes with an outlook on the coming decade.

2. Foundations: Engineering Concepts, DBTL, and Quality by Design

Synthetic biology's engineering foundations are now well established, and we summarise them briefly before turning to what has changed. Four concepts imported from engineering underpin the rational design of biological systems (Fig. 2).

Standardisation reduces complex systems to minimum parts with defined functions, enabling characterised and interchangeable components (Canton et al., 2008; Galdzicki et al., 2014). Modularity decouples these parts into units that can be independently developed and integrated (Butti et al., 2025; Purnick and Weiss, 2009). Abstraction organises biological function across hierarchical levels of complexity so that engineering at one level does not require tracking every detail at another (Blount et al., 2012). Orthogonality ensures that engineered components function predictably without cross-talk with the host's endogenous systems (Costello and Badran, 2021; Edelstein et al., 2025; Wang et al., 2011). Combined, these principles enable the construction of biological logic gates and genetic circuits that behave predictably (Brophy and Voigt, 2014; Gander et al., 2017; Wang et al., 2025) and have been codified through community initiatives such as iGEM and repositories including the Registry of Standard Biological Parts, Addgene, and SynBioHub.

2.1. The DBTL cycle as an industrial backbone

The Design-Build-Test-Learn (DBTL) cycle is the central methodology through which these engineering principles are operationalised (Fig. 3). In the Design phase, the desired behaviour of a biological system is defined and the required genetic modifications are devised *in silico*, guided by bioinformatics tools and predictive models. In the Build phase, standardised parts are assembled into the designed construct and introduced into the host. In the Test phase, the engineered system is experimentally characterised: titres, yields, and productivities are measured, and metabolic fluxes and gene expression are quantified. In

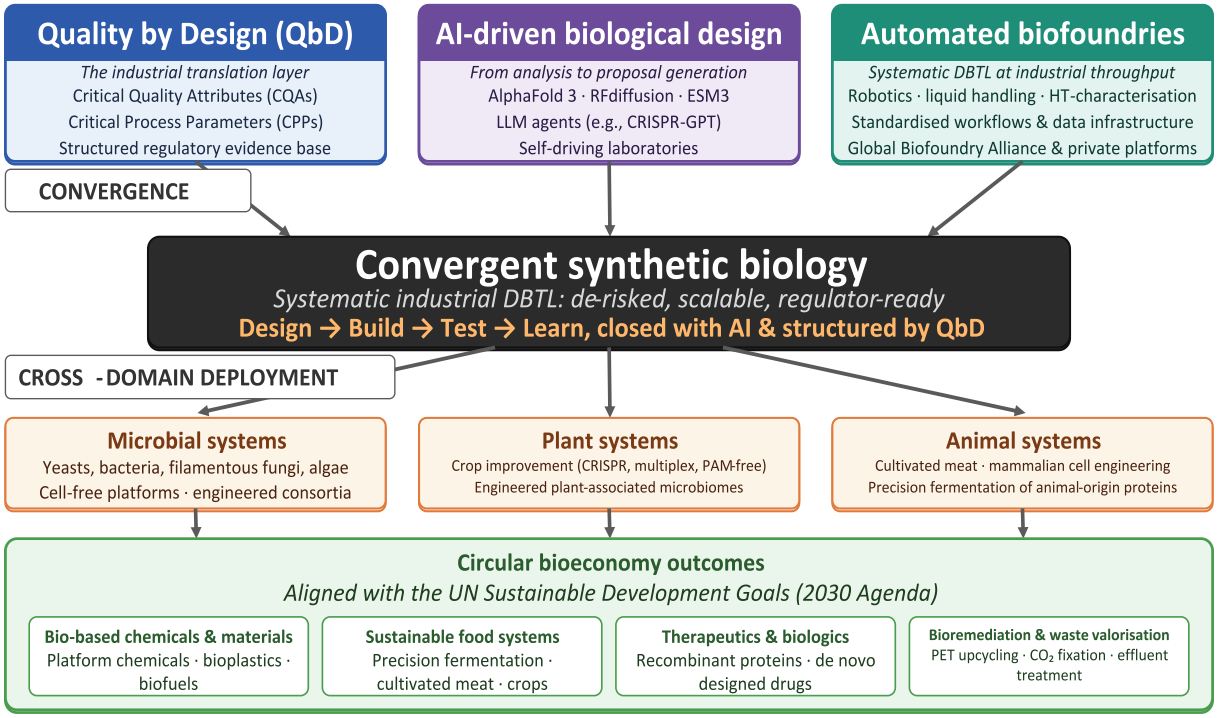

Fig. 1. The convergence paradigm underpinning scalable circular biomanufacturing. Three developments that matured in parallel, Quality by Design (QbD) as the industrial translation layer, artificial intelligence (AI)-driven biological design as an active participant in the Design-Build-Test-Learn (DBTL) cycle, and automated biofoundries as the high-throughput DBTL infrastructure, are now converging into an integrated industrial synthetic biology framework.

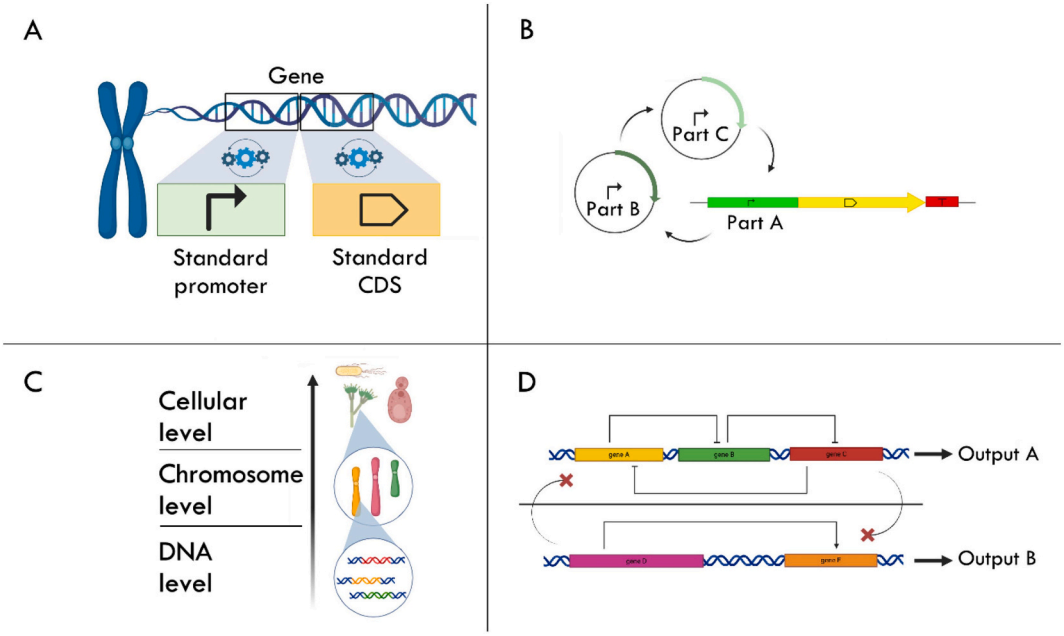

Fig. 2. Concepts imported from engineering fields and adapted to biology. a) Standardisation happens at the genetic level when gene parts such as promoters or coding sequences (CDS) are identified, extracted and adapted for combinatorial design, so that their output is defined. b) Modularity allows the substitution of standard parts for others that fulfil the same function, allowing interchangeability. c) Abstraction enables focusing on a particular level of complexity without considering challenges spilling from other levels of complexity. d) Orthogonality prevents cross-interactions between designed systems so that output is always the expected. Created with BioRender.

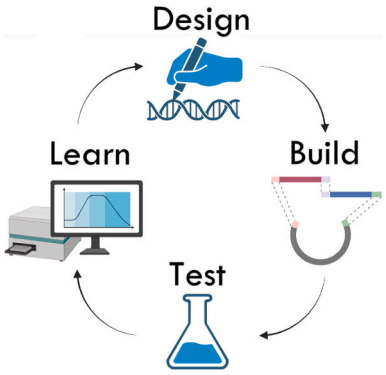

Fig. 3. Schematic representation of the DBTL cycle in synthetic biology. The iterative framework integrates rational design of biological systems, building of such synthetic systems, experimental testing of their performance and learning from their outcome to refine subsequent design rounds, thereby accelerating strain development and biotechnological innovation. Created with BioRender.

the Learn phase, experimental data are used to identify improvements and to inform the next design iteration (Carbonell et al., 2018; Chao et al., 2017; Nielsen and Keasling, 2016). What has changed most recently is not the concept of the cycle but the speed and scale at which it can now be executed: automated biofoundries routinely run hundreds of designs per cycle, AI tools propose non-obvious design alternatives, and computational modelling anticipates scale-up behaviour before fermenter-level testing (see Sections 3 and 6).

2.2. *Quality by Design as the industrial translation layer*

For DBTL to produce industrially viable outcomes, the target attributes of the engineered system must be defined with the precision that downstream bioprocessing and regulatory agencies require. Quality by Design (QbD) was originally a regulatory agency-led structured approach to process development that emphasises product and process understanding to reduce quality and regulatory risks (Mu'azzam et al., 2024). In the context of synthetic biology, QbD makes two practical contributions. First, it stresses early identification of the process parameters that will affect the product quality, such as oxygen transfer, concentration gradients, and genetic stability, among other variables, and so steers the Design phase away from choices that may fail in the bioreactor (Olsson et al., 2022). Second, it generates a structured evidence base that regulators in the pharmaceutical and food sectors expect, shortening the gap between a successful laboratory result and a market-ready product.

3. Cornerstone Technologies Enabling the New Paradigm

The technologies that support synthetic biology are well covered elsewhere. Here we focus on the most recent developments and those with the greatest bearing on industrial translation.

3.1. *Reading and writing DNA*

Short-read (Illumina) and long-read (PacBio, Oxford Nanopore) sequencing together now provide high-throughput, cost-effective access to genomic information, with long reads resolving repetitive regions, structural variants, and full-length transcripts that short reads cannot (Amarasinghe et al., 2020; Balarezo-Cisneros et al., 2023; Bentley et al., 2008; Eid et al., 2009; Loman et al., 2015). Nanopore sequencing has also extended into single-molecule protein sequencing, exploiting ionic-current changes as peptides pass through engineered pores (Brinkerhoff et al., 2021; Wei et al., 2023; Yusko et al., 2017). Because it avoids bulk degradation and permits multiple reads of the same molecule, this approach offers a scalable alternative to mass spectrometry for proteoform analysis.

Reading DNA (sequencing) no longer poses a cost obstacle, but the cost of DNA synthesis creates a significant bottleneck (Fig. 4). Phosphoramidite chemistry (Beaucage and Caruthers, 1981) dominates for short oligonucleotides, with enzymatic concatenation extending current commercial reach to roughly 5 kbp. Fully enzymatic synthesis, currently

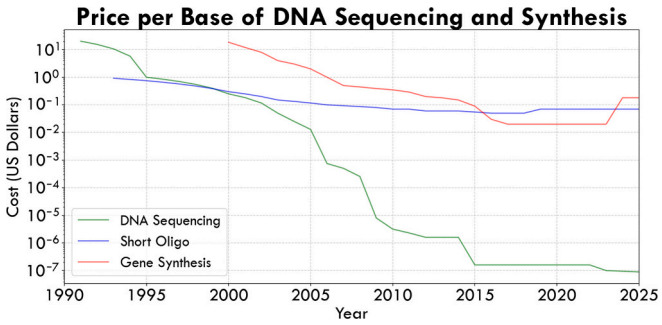

Fig. 4. Historical trends in the cost per base of DNA sequencing (green), short oligonucleotide synthesis (blue), and gene synthesis (red). Adapted from (Carlson, 2025).

entering the market, promises improved fidelity and much longer strands (up to 50 kbp) at competitive cost (Hoose et al., 2023; Palluk et al., 2018). The emerging capacity to synthesise large DNA molecules has enabled ambitious synthetic-genome projects, from the landmark Mycoplasma genitalium chemical synthesis (Gibson et al., 2010) to *Escherichia coli* syn61 (Fredens et al., 2019), the Sc2.0 effort to synthesise an entire yeast genome (Annaluru et al., 2014; Erpf et al., 2025), and the recent construction of human artificial chromosomes (Gambogi et al., 2024).

3.2. DNA assembly and genome editing

Golden Gate Assembly (Engler et al., 2008; Weber et al., 2011) and Gibson Assembly (Gibson et al., 2009) remain the workhorses for combining DNA parts into larger constructs, complemented by BioBricks, Gateway cloning, and Transformation-Associated Recombination for more specific contexts (Ellis et al., 2011). For *in vivo* editing, CRISPR-Cas9 and its derivatives now dominate (Jinek et al., 2012; Mali et al., 2013). Variants including CRISPRa/i for transcriptional control (Qi et al., 2013; Shaw et al., 2022), base editing (Komor et al., 2016), and prime editing (Anzalone et al., 2019; Yarnall et al., 2022) extend the toolkit from gene-scale disruption to single-nucleotide precision, often without the double-strand breaks those complicated earlier methods. RNA-guided recombinases acting via bridge RNAs now enable programmable insertion, excision, and inversion independent of host homologous-recombination machinery, directly addressing one of the main barriers to applying CRISPR in non-model hosts (Durrant et al., 2024; Hiraizumi et al., 2024; Yan and Fong, 2017). The practical consequence for industrial synthetic biology is a growing set of editing tools that work reliably across a wider range of production organisms, a point we return to in Section 4.

3.3. Engineered microbial consortia

Early synthetic biology focused on monocultures, but there is sustained interest in engineering microbial communities to perform complex tasks collectively (Brenner et al., 2008; McCarty and Ledesma-Amaro, 2019). Consortia distribute metabolic burden across strains, exploit natural ecological interactions, and can achieve greater resilience under dynamic conditions. Applications demonstrated to date include waste degradation, carbon capture, soil health improvement, and defined probiotic formulations (Chen et al., 2024; Mousa et al., 2024; Ruan et al., 2024; Wei et al., 2024). Advances in synthetic communication modules, orthogonal quorum-sensing systems, and metagenomic and single-cell tracking are improving characterisation and control of community dynamics (Henry and Bergelson, 2025; Jia et al., 2024; Kim et al., 2024; Wu et al., 2022).

At an industrial scale, however, consortia face distinct challenges. Maintaining defined strain ratios in stirred-tank fermenters, preventing cheater outgrowth, and monitoring division-of-labour dynamics in real time remain open problems. Deployment at present is concentrated in applications where the fermentation environment itself exerts strong selection (anaerobic digesters, soil-based agricultural inoculants) or where a single dominant strain carries most of the process burden, with supporting strains providing niche functions. Extending consortia to bulk biomanufacturing will require advances in process analytical technology, which intersects directly with the QbD framework set out in Section 2.2.

3.4. Cell-free systems

Cell-free systems operate outside living cells, using purified cellular machinery to express genetic circuits or biosynthetic pathways *in vitro* (Garenne et al., 2021; Hodgman and Jewett, 2012; Rice et al., 2025). They offer rapid prototyping, decoupling of circuit design from cellular metabolism, improved scalability for small-footprint applications, and simplified biosafety. Demonstrations now span biomolecule production, biosensing under conditions toxic to living cells, and point-of-care diagnostics; the freeze-dried, paper-based nucleic-acid sensors deployed during the COVID-19 pandemic are a well-documented example of real-world cell-free deployment (Grubbe et al., 2020; Kay and Jewett, 2020; Wang et al., 2024). Commercial translation is most advanced in high-value, low-volume applications, including conjugate vaccines, on-demand peptide and antibody fragment production, and mRNA synthesis, where titre and cost-per-reaction limitations are offset by product value and flexibility. Applying cell-free systems to bulk chemicals remains economically challenging without substantial further reductions in extract and cofactor costs.

3.5. Bioinformatics and artificial intelligence

Bioinformatics has long been indispensable for the analysis, interpretation, and visualisation of the biological data generated by the technologies above. Genome assembly software, sequence alignment tools, databases, custom pipelines, and online repositories enable routine management of complex datasets, and computational models of synthetic organisms provide frameworks for predicting and optimising how genetic modifications, metabolic fluxes, and environmental interactions affect host metabolism (García-Jiménez et al., 2021; Lopatkin and Collins, 2020; Mandakovic et al., 2020; Nielsen and Keasling, 2016; Wagner et al., 2021).

What has changed in the past few years is the emergence of AI as an active participant in biological design rather than simply an analytical layer. AlphaFold demonstrated that protein structure could be predicted from sequence with transformative accuracy (Jumper et al., 2021; Senior et al., 2020). Its successor AlphaFold 3 extends this to biomolecular complexes, including protein-ligand, protein-nucleic acid, and protein-protein interactions (Abramson et al., 2024). Generative models now routinely design proteins with novel folds and binding specificities: RFdiffusion enables *de novo* protein design conditioned on functional requirements (Watson et al., 2023), and ESM3 is a multimodal foundation model that reasons jointly over sequence, structure, and function (Hayes et al., 2025). Recent applications include *de novo* designed proteins that neutralise snake-venom toxins (Vázquez Torres et al., 2025), demonstrating that generative design is beginning to tackle problems of direct therapeutic relevance. In parallel, large-language-model agents such as CRISPR-GPT guide researchers through complex experimental design tasks including Cas variant selection, guide RNA design, delivery choice, protocol drafting, and result interpretation (Qu et al., 2025); SignalP 6.0 predicts all five types of signal peptides using protein language models (Teufel et al., 2022); and machine-learning methods for strain and pathway engineering are producing non-obvious designs that routinely outperform human intuition (Huang et al., 2021; Nielsen et al., 2016; Yang et al., 2019; Zou et al., 2024).

These advances should be read alongside their limitations, which are

increasingly relevant as the field moves from demonstration to deployment. The training data underpinning most biological foundation models are heavily skewed toward a narrow slice of biology, such as well-studied model organisms (*E. coli*, *S. cerevisiae*, CHO cells, among a few others), soluble single-domain proteins, and a small number of experimentally characterised functions from which annotations propagate. Non-conventional yeasts, membrane proteins, intrinsically disordered regions, and the metabolisms of microbial consortia and plant systems are correspondingly underrepresented, so model confidence in these regimes is often overstated (Lopatkin and Collins, 2020; Lu et al., 2024; Poppeliers et al., 2025). The predictions themselves are also largely opaque: a high-confidence AlphaFold structure does not guarantee *in vivo* folding, solubility, or activity, and generative-design pipelines still depend on extensive wet-lab screening because the mechanistic basis of a model's recommendation is rarely recoverable. This limited interpretability constrains hypothesis generation when designs fail and slows root-cause analysis. Finally, even successful *in silico* predictions can be brittle when transferred to industrial phenotypes: growth models trained on purified-protein or defined-medium data do not capture the shear, oxygen gradients, substrate heterogeneity, metabolic burden, and long fermentation times of a production-scale bioreactor, and pathways optimised for steady-state flux frequently underperform under fed-batch dynamics or in more complex, multi-substrate, industrial media. The closed-loop systems described below are in part a response to this gap: by routing experimental data back into the model, biofoundries can correct the biases and edge-case failures that purely *in silico* optimisation cannot.

Integrating these AI advances with robotic liquid-handling platforms and automated data collection produces what is often called a self-driving laboratory: a closed-loop system in which AI proposes designs, biofoundries build and test them, and the results update the model for the next cycle (Carbonell et al., 2019; Gong et al., 2026; Stephenson et al., 2023). This closed loop is the operational expression of the convergence this review describes, and we return to its industrial implications in Section 6.

4. Cross-Domain Transferability of Synthetic Biology Tools

A frequent limitation of reviews in this field is the focus on a single platform organism or host. In practice, the toolkit that defines modern synthetic biology, multiplex CRISPR and prime editing, bridge-RNA recombinases, Golden Gate and Gibson assembly, AI-guided design, and automated biofoundry workflows, is now deployed across microbial, plant, and animal systems. Recognising this cross-domain transferability is important because a circular bioeconomy at the scale required by the SDGs will depend on all three domains working in concert rather than in isolation. This section traces how the same tools translate across systems, and what domain-specific adaptations are required.

4.1. Microbial systems as the proving ground

Most modern tools are developed and stress-tested in microbial chassis, particularly *Escherichia coli* and *Saccharomyces cerevisiae*, but increasingly in a range of additional species. Microbial systems combine fast generation times, well-characterised genetics, and amenability to automated handling, making them the natural proving ground for new editing chemistries and high-throughput DBTL workflows (Poppeliers et al., 2025; Xu et al., 2025). Biofoundries typically begin with microbial pipelines before extending to other domains, and non-traditional yeasts and bacteria are increasingly adopted where feedstock flexibility, tolerance to extreme conditions, or post-translational machinery demand it (Al-Hammadi et al., 2025; Balarezo-Cisneros et al., 2023; Larroude et al., 2018).

Microbial chassis are also increasingly deployed to produce molecules that have traditionally been sourced from animals, including caseins, whey proteins, ovalbumin, collagen and heme. This activity, now generally referred to as precision fermentation, is recognised as one of the principal modalities within the broader field of *cellular agriculture* (Ancelin et al., 2025; Bae et al., 2025; Biermann et al., 2025; Hettinga and Bijl, 2022; Mirsalami and Mirsalami, 2025; Teng et al., 2021). Although the target molecules are of animal origin, the host, the genetic toolkit, and the bioprocess engineering are all microbial; precision fermentation therefore sits firmly within microbial synthetic biology, while contributing to the same food-system outcomes as the animal-cell-based work discussed in Section 4.3.

4.2. Plant synthetic biology

Translating microbial-origin tools to plants has required adaptations in delivery and regeneration, but the conceptual toolkit is now genuinely shared. Multiplex CRISPR-Cas9 has been used to address drought and salt tolerance in wheat and soybean, to stack disease resistance in rice and sweet orange, and to modify seed oil profiles (Abdallah et al., 2022; Huang et al., 2022; Liu et al., 2022; Liu et al., 2018). CRISPR-mediated chromosome engineering is enabling large-scale structural rearrangements for crop improvement (Rönspies et al., 2021). Beyond direct plant modification, synthetic biology is increasingly deployed at the plant-microbiome interface: engineered root-associated bacteria release plant-available phosphate from phytate (Shulse et al., 2019), engineered microbial inoculants confer nitrogen fixation on cereals in fertilised fields (Wen et al., 2021), and defined synthetic microbiomes are being designed to enhance soil health under climate stress (Jansson et al., 2023; Ke et al., 2021; Mousa et al., 2024). Because microbial inoculants are regulated differently from genetically modified crops in many jurisdictions, this microbiome route also offers a pragmatic path around parts of the GMO regulatory framework (see Section 7).

4.3. Animal synthetic biology

Animal synthetic biology, as we use the term here, encompasses activities in which animal cells themselves are engineered or cultivated. Two principal activities currently dominate: production of biopharmaceuticals in engineered mammalian cell lines, and cellular agriculture, which uses animal cell culture to produce food (Ancelin et al., 2025). Microbial production of animal-origin molecules, although it serves overlapping food-system goals, is a microbial activity and is discussed in Section 4.1 under precision fermentation.

The biopharmaceutical strand is the more mature of the two. Chinese hamster ovary (CHO) cells and related mammalian lines have been engineered for decades to produce monoclonal antibodies, recombinant clotting factors, and other complex therapeutics that require mammalian post-translational machinery (Bachhav et al., 2023; Listov et al., 2024; Zhao et al., 2024). The synthetic biology contribution to this field is increasingly visible: drag-and-drop CRISPR-directed integrases now enable insertion of large payloads at defined sites without double-strand breaks (Yarnall et al., 2022), and multiplex CRISPR/Cas9 has been applied even to genome editing in human embryos for correction of pathogenic mutations (Ma et al., 2017). Folding, glycosylation, and secretion remain the principal technical bottlenecks and the focus of ongoing engineering work.

The cellular agriculture strand uses cultivation of animal cells, increasingly including fish and other aquatic species, to produce food products that resemble those derived from conventional animal rearing or fisheries. The term, coined in 2015, now covers a range of products variously described as “cultured meat”, “cultivated meat”, or “cell-based meat” (Ancelin et al., 2025; Post, 2012; Reiss et al., 2021). Production typically combines cell-line engineering for sustained proliferation with serum-free media development, scaffold design, and, in some cases, combination with components produced by precision fermentation (for example, haem or specific lipids). Recent progress includes the generation of spontaneously immortalised muscle stem cell lines for cultured

fish meat (Xue et al., 2024); on the regulatory front, the first UK regulatory approval of a cultivated meat product (Meatly, approved for use as pet food in July 2024) illustrates that market entry pathways are beginning to open in the European regulatory space, complementing earlier approvals in Singapore, the United States, and Israel.

Both strands share their upstream synthetic biology toolkit with microbial and plant systems, including CRISPR-based editing, AI-driven design, and biofoundry-style automation, but face additional, domain-specific challenges in folding, glycosylation, and tissue-level organisation that are absent or attenuated in unicellular hosts.

4.4. Implications of cross-domain transferability

The practical implication of this cross-domain picture is that investments in core synthetic biology infrastructure, biofoundries, AI design tools, shared part repositories, standardised characterisation pipelines, yield returns across multiple application domains simultaneously. A biofoundry capable of designing and testing microbial strains can, with well-understood adaptations, also support plant protoplast workflows and mammalian cell engineering, and AI models trained on large microbial datasets are transferring meaningfully to plant and animal systems. From a circular-bioeconomy perspective, this transferability is essential: microbial systems produce feedstocks and platform chemicals, plants deliver biomass and carbon capture at scale, and animal systems provide proteins and tissues that may displace the most resource-intensive conventional agricultural products. Treating these as separate technical communities obscures the shared infrastructure that increasingly underpins all three.

5. Sustainable Applications in the Circular Bioeconomy

Synthetic biology contributes to circular bioeconomy objectives through biomimicry and the rational repurposing of natural metabolic capability (Himel et al., 2023; Liu et al., 2022; Waeterschoot et al., 2024). In this section we focus on five application areas where synthetic biology-derived products can be benchmarked against conventional alternatives. Where published life-cycle assessments (LCA) or techno-economic analyses (TEA) are available, we report indicative

Table 1
Benchmarking selected synthetic biology-derived products against conventional alternatives. Where published life-cycle assessment (LCA) or techno-economic analysis (TEA) data are available, the direction and approximate magnitude of reported differences are summarised; exact figures should be consulted in the cited primary references. "Net-negative" indicates a reported greenhouse gas (GHG) intensity below zero when waste-gas feedstocks are used. References marked with superscripts refer to the manuscript reference list.

Product	Conventional benchmark	Synthetic biology route / host	Environmental performance	Economic performance	Scale & market status	Key reference(s)
Precision-fermented ovalbumin	Chicken egg-white ovalbumin	*Trichoderma reesei* heterologous expression	Substantial reduction in global warming potential when combined with low-carbon electricity; reductions in land use reported across scenarios.	Pre-commercial cost; projected approach to parity with egg-derived protein isolates at scale.	Early commercial in the US market through food-industry partners; active scale-up and regulatory approval pathways in additional jurisdictions.	Järviö et al., *2021*
Cultivated meat (beef proxy)	Conventional beef (feedlot or pasture)	Immortalised bovine muscle stem cell culture in serum-free media	Land-use reductions achievable; overall GHG profile dominated by energy mix and media production; benefit not universally established.	Substantial gap to conventional beef retail price; media and growth factor costs dominant cost driver.	Pilot / demonstration; limited regulatory approvals (US, Singapore, Israel); scale-up economics debated.	Humbird, *2021*; Post, *2012*; Reiss et al., *2021*; Xue et al., *2024*
Gas-fermented acetone and isopropanol	Petrochemical acetone / isopropanol (cumene or propylene hydration routes)	Engineered *Clostridium autoethanogenum* fermentation of CO / CO_2 waste gas streams	Reported net-negative GHG intensity at industrial pilot scale when using waste-gas feedstocks.	Economics depend on feedstock gas stream and colocation with emitter; commercial pilot plants operational.	Gas fermentation to ethanol at full commercial scale (six LanzaTech sites worldwide since 2018, >350,000 t/y combined output); acetone and isopropanol at industrial pilot scale.	Liew et al., *2022*
Semi-synthetic artemisinin	Extraction from Artemisia annua (plant-based)	Engineered *Saccharomyces cerevisiae* producing artemisinic acid; chemical conversion to artemisinin	Reduces dependence on cultivated plant feedstock subject to climatic and agricultural variability; stabilises global supply.	Cost-comparable to plant extraction at scale; commercially deployed to supplement plant supply.	Commercial; WHO prequalified and integrated into public-health supply chains.	Paddon et al., *2013*; Ro et al., *2006*
Heterologous cannabinoids	Extraction from Cannabis sativa	Complete biosynthesis in engineered *S. cerevisiae*; also *Nicotiana benthamiana*	Eliminates cultivation footprint for compound-specific targets; enables access to minor cannabinoids difficult to source from plants.	Early-stage commercial margins compound-dependent; high-value minor cannabinoids first target.	R&D to early commercial; several companies active.	Gülck et al., *2020*; Luo et al., *2019*
Bio-based itaconate	Conventional sugar-based fermentation (Aspergillus terreus); potential petrochemical routes	*Ustilago maydis* fermentation scaled on crude substrates	Valorises side streams; lower footprint when crude or waste substrates are used versus refined sugars.	Competitive at industrial pilot scale; depends on substrate cost and downstream separation.	Industrial pilot scale demonstrated.	Helm et al., *2024*
PET degradation and upcycling	Virgin PET production from petrochemicals; PET end-of-life via incineration or landfill	Engineered microbial consortia and heterologous PET hydrolases in bacterial hosts	Avoids virgin PET production where upcycled monomers are reused; closes plastic loop.	Demonstration-stage economics; competitiveness depends on access to sorted waste streams.	Laboratory to pilot demonstrations; no commercial-scale deployment yet.	Bao et al., *2023*; Brandenberg et al., *2022*; Soon et al., *2025*; Yoshida et al., *2016*

Notes. Environmental and economic figures are scenario- and assumption-dependent; where LCA or TEA studies report ranges, the direction of the difference vs. the conventional benchmark is summarised here and readers are directed to the cited primary references for quantitative detail.

figures; Table 1 consolidates the principal comparisons.

5.1. Bioproduction of chemicals, fuels, and active pharmaceutical ingredients

Microbial hosts have been repurposed for sustainable bioproduction of platform chemicals, biofuels, and high-value compounds by integrating heterologous pathways (Antonovsky et al., 2016; Fu et al., 2017; Gutiérrez et al., 2024; Helm et al., 2024; Keasling et al., 2021; Larroude et al., 2018; Liew et al., 2022; Peng et al., 2023; Walker et al., 2024). Particularly illustrative is the semi-synthetic production of the antimalarial artemisinin in yeast, which reached WHO prequalification and has been integrated into public-health supply chains (Paddon et al., 2013; Ro et al., 2006). Complete yeast biosynthesis of opioids (Galanie et al., 2015) and of cannabinoids and their unnatural analogues (Luo et al., 2019) illustrates how complex natural-product pathways can now be reconstructed in tractable hosts (Gülck et al., 2020; Kobayashi et al., 2021). On the commodity side, gas fermentation of carbon monoxide and carbon dioxide streams by *Clostridium autoethanogenum* is now operating at full commercial scale: LanzaTech operates six production sites worldwide producing waste-gas-derived ethanol since 2018, with combined annual output exceeding 350,000 tonnes (LanzaTech, 2025). Extension of the platform to higher-value products including acetone and isopropanol has been demonstrated at industrial pilot scale, converting waste gas emissions into platform chemicals with substantially lower GHG intensity than petrochemical routes (Liew et al., 2022). Itaconate production from crude substrates has been scaled by Ustilago maydis to industrially relevant titres (Helm et al., 2024), and recent work on formate-based bioproduction using metal-dependent formate dehydrogenase in *E. coli* points toward one-carbon feedstocks as a substrate for future circular bioproduction (Cowan et al., 2025).

5.2. Agricultural biotechnology

Synthetic biology approaches in agriculture span direct genetic modification of crops and engineering of the associated microbiome. Bt-crops remain the canonical case (Vaeck et al., 1987), with successive generations of CRISPR-engineered lines now delivering disease resistance, stress tolerance, and enhanced nutritional content (Huang et al., 2022; Li M. et al., 2021; Mateos Fernández et al., 2022; Rönspies et al., 2021; Sundararajan et al., 2025; Yang and Reyna-Llorens, 2023; Zhang et al., 2021; Zhu et al., 2024). Microbiome-oriented approaches, altering the root- or phyllosphere-associated microbial community rather than the plant itself, aim to improve productivity while sidestepping GMO classification in jurisdictions that focus regulation on the engineered organism (Jansson et al., 2023; Ke et al., 2021; Shulse et al., 2019; Wen et al., 2021). The regulatory consequences of this distinction are taken up in Section 7.

5.3. Precision Fermentation and Cellular Agriculture

Food system applications may prove among the most consequential of synthetic biology's sustainable applications. The two principal modalities are precision fermentation and cellular agriculture (Ancelin et al., 2025). Precision fermentation refers to the use of engineered microbial hosts to produce specific target molecules for the food industry, notably animal-origin proteins such as caseins, whey, ovalbumin, collagen and heme (Bae et al., 2025; Biermann et al., 2025; Hettinga and Bijl, 2022; Järviö et al., 2021; Mirsalami and Mirsalami, 2025; Teng et al., 2021). Cellular agriculture refers to the use of cells themselves to produce lab-grown foods, food components, it applies mostly prominently to cultivated meat, in which animal cells are grown in bioreactors to produce meat- or fish-like food products (Lambert et al., 2024; Lei et al., 2023; Post, 2012; Reiss et al., 2021; Xue et al., 2024). Published LCA for precision-fermented ovalbumin using *Trichoderma reesei* culture combined with low-carbon energy reports notable reductions in land use and GHG emissions compared with chicken-egg-derived ovalbumin (Järviö et al., 2021). For cultivated meat, the best available techno-economic analyses to date point to substantial cost reductions over time but persistent gap to cost parity with conventional meat, with the media and growth factor costs identified as the dominant challenge (Humbird, 2021). Commercial pipelines are established for animal-free dairy proteins, eggs, palm oil substitutes, and seafood alternatives (Xue et al., 2024); their trajectory will depend heavily on the scale-up questions addressed in Section 6 and the regulatory questions in Section 7.

5.4. Therapeutic proteins and de novo biologics

Heterologous protein production for therapeutic use began with insulin in *E. coli* (Goeddel et al., 1979) and now spans a wide range of hosts and products, including antibodies, growth hormones, and clotting factors (Balasubramanian et al., 2021; Cutolo et al., 2022; Ghag et al., 2021; Liu et al., 2023; Walsh and Walsh, 2022). Post-translational modifications, folding, and secretion remain the principal technical challenges (Bachhav et al., 2023; Listov et al., 2024; Zhao et al., 2024), and recent work addresses these through glycosylation engineering (Liu C.P. et al., 2018), secretion pathway optimisation (de Ruijter et al., 2016; Xu et al., 2025), and, increasingly, de novo protein design. Generative models such as RFdiffusion and ESM3 are being used to produce proteins with desired functions from scratch (Abramson et al., 2024; Hayes et al., 2025; Kortemme, 2024; Watson et al., 2023), and de novo designed proteins have recently been shown to neutralise lethal snake-venom toxins (Vázquez Torres et al., 2025). This illustrates how AI-driven design is entering clinical territory rather than remaining a theoretical capability.

5.5. Bioremediation and pollution management

Synthetic biology offers new routes for bioremediation, pollution management, and waste valorisation by engineering biological systems to detect, degrade, or sequester contaminants, including heavy metals, hydrocarbons, pesticides, carbon dioxide, and plastics (Brandenberg et al., 2022; Cowan et al., 2025; Prather et al., 2018; Ren et al., 2025; Soon et al., 2025), or to convert them into higher-value products (Johnson et al., 2025). Engineered biosensors can detect trace contaminants with high specificity (Dong et al., 2017; Garabello et al., 2024; Kumar et al., 2017), and microbial consortia can be optimised for cooperative degradation of complex waste streams (Bao et al., 2023). These capabilities align closely with circular-bioeconomy logic, converting waste streams into feedstocks for further bioproduction.

6. From Laboratory to Market: Scale-up, Biofoundries, and Case Studies

Replicating laboratory performance at an industrial scale is the central bottleneck for commercial synthetic biology (Kampers et al., 2021). In this section, we treat scale-up not as a list of challenges but as a tractable engineering problem that the convergence of QbD, AI, and biofoundry automation is now beginning to solve, and we illustrate with four case studies in which market-scale products have successfully navigated the laboratory-to-industry path.

6.1. Scale-up effects and their mechanisms

The so-called "scale-up effect" arises from a combination of process phenomena that emerge or intensify at an industrial scale. Substrate, oxygen, temperature, and pH gradients form along large fermenters and generate heterogeneous microenvironments that select for subpopulations with altered behaviour (Becker et al., 2023; Bylund et al., 1998; Delvigne and Goffin, 2014; Shabestary et al., 2024; Spadiut et al., 2013). Industrial conditions, crude feedstocks, variable oxygen

transfer, extended fermentation times, are rarely reproduced during strain construction (Becker et al., 2023; Olsson et al., 2022). Genetic parts tuned in minimal laboratory media often perform poorly under industrial conditions, leading to suboptimal promoter, terminator, or regulatory-element choices surfacing only after scale-up (Garrigós-Martínez et al., 2021; Georgiadis et al., 2023; Kittler et al., 2025; Pan et al., 2023). Together, these factors compromise critical performance metrics in ways that are predictable in principle but difficult to anticipate without structured analysis.

6.2. Computational modelling and digital twins

Advanced computational modelling is increasingly being used to anticipate and mitigate scale-up effects before fermenter commissioning. Genome-scale metabolic models predict how genetic modifications redistribute flux under substrate limitation; dynamic kinetic models capture transient responses to environmental change; and hybrid mechanistic/data-driven digital twins of bioprocesses integrate strain behaviour with reactor hydrodynamics and process analytical technology outputs (García-Jiménez et al., 2021; Lopatkin and Collins, 2020; Lu et al., 2024; Mandakovic et al., 2020; Wagner et al., 2021). Guided by the QbD framework discussed in Section 2.2, these models translate laboratory observations into CQA-CPP relationships that can be queried and optimised at scale. AI and hybrid models, in particular, are expanding the design space considered during the Design phase so that candidates likely to fail at scale are filtered out before Build and Test (Mu'azzam et al., 2024).

6.3. Biofoundries as systematic scale-up enablers

Automated biofoundries integrate robotics, liquid-handling platforms, high-throughput characterisation, and standardised data infrastructure to execute DBTL cycles at scales not feasible manually (Carbonell et al., 2019; Chao et al., 2017; Gong et al., 2026; Lee et al., 2023; Stephenson et al., 2023). The Global Biofoundry Alliance now coordinates public biofoundries across multiple countries and dedicated private biofoundry operators run commercial DBTL pipelines at industrial throughput. Two capabilities matter most for scale-up. First, biofoundries routinely characterise hundreds to thousands of variants per cycle, so strain performance is benchmarked across a much larger design space than traditional approaches allow, reducing the probability that the chosen lead is a local optimum that will collapse at scale. Second, standardised workflows produce structured, machine-readable datasets that feed directly into AI models, closing the loop described in Section 3.5. Together, these capabilities can substantially shorten the time from initial design to a robust, industrially viable process

6.4. Case studies of successful laboratory-to-market translation

6.4.1. LanzaTech: gas fermentation from pilot to commercial scale

LanzaTech's commercialisation of gas fermentation is one of the most fully-developed contemporary demonstrations of scaled synthetic biology. The underlying system is an acetogenic *Clostridium* engineered to ferment carbon-rich industrial waste gases (CO, CO_2, H_2) into liquid products. Commercial deployment began in 2018 with ethanol production at the Shougang facility in China, and the platform now operates at six production sites worldwide, with combined annual ethanol output exceeding 350,000 tonnes from waste-gas feedstocks (LanzaTech, 2025). More recently, the platform has been extended to higher-value products: carbon-negative acetone and isopropanol have been demonstrated at industrial pilot scale by redirecting flux from native solventogenesis toward target products (Liew et al., 2022).

The translation to commercial operation required coordinated work on three fronts that map directly onto the convergent framework advocated in this review: strain engineering to redirect carbon flux; bioreactor and gas-transfer physics, where CO solubility and mass transfer constrain achievable productivity; and continuous-process engineering for steady-state operation on variable industrial gas streams. QbD-style identification of CQAs (product titre, gas conversion efficiency, strain stability) and CPPs (gas composition, pH, dissolved CO, recycle ratios) provided the structured evidence base needed for both process optimisation and regulatory and customer qualification. As a case study, LanzaTech illustrates how multi-scale integration, not biology alone, and not engineering alone, enables synthetic biology to operate at commercial scale.

6.4.2. Amyris and Sanofi semi-synthetic artemisinin

The semi-synthetic artemisinin programme remains the canonical case of a yeast-based synthetic biology platform reaching pharmaceutical-grade scale and full regulatory qualification (Paddon et al., 2013; Ro et al., 2006). The translation path required more than a decade of iterative strain engineering to lift artemisinic acid titres in *Saccharomyces cerevisiae* to a level compatible with downstream chemical conversion to artemisinin, together with WHO prequalification of the final active pharmaceutical ingredient and integration into the public-health antimalarial supply chain via Sanofi.

Industrial production of semi-synthetic artemisinin was discontinued in 2015. The reasons were not technical: by that point yields had increased sharply for plant-derived artemisinin from *Artemisia annua* cultivation, market prices had fallen below the fermentation cost base, and the economic justification for the semi-synthetic route was lost. The programme remains instructive precisely because of this outcome. It demonstrates that synthetic biology can deliver a complex natural product to pharmaceutical standards and into public-health supply chains; equally, it shows that long-term commercial viability depends on co-evolution with the conventional supply chain whose displacement is being attempted. Several of the development lessons, the cost of late-stage strain rework, the value of process-integrated strain engineering, and the importance of structured CQA-CPP definition early in development, directly inform the convergent framework advocated here.

6.4.3. Precision fermentation: multiple start-up companies

Precision fermentation of animal-origin proteins (whey, casein, heme, ovalbumin, and collagen) illustrates synthetic biology navigating both scale-up and novel-food regulatory pathways simultaneously. Companies operating in this space have had to co-develop strain performance, fermentation scale-up, and regulatory evidence packages (US GRAS filings, EU novel food applications) from early in the development cycle. Recently published work on heme-containing globin production by precision fermentation in recombinant yeast (Bae et al., 2025) and recombinant bovine α_{S1}-casein in genome-reduced *Bacillus subtilis* (Biermann et al., 2025) indicates the technical maturity of the platform; published LCA work for ovalbumin (Järviö et al., 2021) supports the environmental case.

6.4.4. Ginkgo Bioworks: a horizontal biofoundry platform

Ginkgo Bioworks exemplifies the horizontal biofoundry model, providing strain engineering services to commercial partners across food, pharma, and agriculture (Ginkgo Bioworks, 2025). Its scale rests on the same convergence highlighted throughout this review: standardised strain design at scale, AI-driven design space exploration, and systematic strain characterisation. That convergence enables autonomous laboratories, which will be a major feature of future biotechnology. The horizontal model is evidence that synthetic biology infrastructure itself, not just individual products, can now be commercialised, broadening access for smaller developers that lack internal biofoundry capability.

6.4.5. Limitations and partial failures in the wider commercial landscape

A balanced view requires acknowledging that the case studies in Sections 6.4.1 to 6.4.4 sit alongside others in which technically successful platforms have nonetheless faced significant commercial

difficulties. Several recent episodes illustrate the gap that can open between technical demonstration and durable commercial success, and merit brief consideration here.

Amyris itself, beyond the artemisinin programme discussed in Section 6.4.2, commercialised farnesene-derived ingredients including the cosmetic emollient squalane and several fragrance compounds, yet filed for Chapter 11 bankruptcy in August 2023 citing debt and capital constraints rather than technology failure. The case illustrates that the timelines and capital intensity of industrial synthetic biology can outlast investor patience and balance-sheet flexibility, even where the underlying biology and products are technically sound.

The earlier generation of synthetic biology-based biofuel ventures provides a parallel lesson. Companies including Solazyme (engineered microalgae), LS9 (engineered *Escherichia coli*), and Joule Unlimited (engineered cyanobacteria for direct CO2-to-fuel conversion) developed technically remarkable platforms but were unable to achieve cost parity with petroleum at the oil prices prevailing through 2014 to 2020; most either pivoted to higher-value products or ceased operations. The transferable insight is that platforms whose commercial viability depends on displacing low-margin commodity products are particularly vulnerable to external market dynamics, and that platform companies often require higher-value markets to sustain capital intensity during scale-up.

More recently, Bolt Threads ceased production of its Mylo mycelium-based leather alternative in 2023, despite high-profile partnerships with major fashion brands, citing inability to raise the capital required for next-stage scale-up. The episode demonstrates that brand-side commercial demand does not automatically translate into the project finance needed for facility-scale production, and that biofoundry-stage success must be matched by a very different funding logic at industrial demonstration scale.

Regulatory approval is also not equivalent to commercial scale. Cultivated meat has now received clearances in Singapore (2020), the United States (USDA and FDA, 2023), and the United Kingdom (Meatly, pet food, 2024; see Section 4.3), but global production volumes remain very small and the cost gap to conventional meat documented by Humbird (2021) has narrowed only slowly.

Together, these episodes do not negate the cases in Sections 6.4.1 to 6.4.4, but they sharpen their interpretation. The convergent framework advocated in this review, QbD-structured development, AI-guided design, and biofoundry automation, addresses technical sources of late-stage failure such as strain rework, scale-up surprises, and regulatory documentation gaps. It does not by itself resolve external pressures: feedstock and commodity prices, capital availability, customer adoption rates, and the time horizons of public-market financing all remain decisive in determining which technically successful platforms become durably commercial. A realistic view treats these factors as additional risks to be designed for from the outset, alongside the engineering and biological challenges on which most of the synthetic biology literature focuses.

7. Regulatory and Societal Landscape

7.1. Regional regulatory divergence: EU and US frameworks

Regulatory frameworks for synthetic biology products vary substantially across jurisdictions, creating both opportunities and frictions for global developers (Turnbull et al., 2021; Wesseler et al., 2023; Wong and Chan, 2016). The most consequential divergence for biomanufacturing sits between the European Union and the United States.

The EU operates a predominantly process-based framework. Genetically modified organisms are regulated under Directive 2001/18/EC and Regulation (EC) No 1829/2003, with the European Food Safety Authority (EFSA) conducting pre-market risk assessment (Frankel and Chapman, 2000; Hayashi et al., 2024; More et al., 2022; Mullins et al., 2024; Son et al., 2021). A long-standing question has been how to treat organisms produced by New Genomic Techniques (NGTs), CRISPR-edited plants in particular, which a 2018 Court of Justice ruling placed within the GMO Directive. An ongoing EU legislative process that aims to introduce a lighter regulatory path for "plants produced by certain new genomic techniques" (essentially cisgenic plants or those with fewer than 20 introduced edits) is a positive step (https://www.europarl.europa.eu/legislative-train/schedule). It is also anticipated that changes, especially regulatory simplification, that will be introduced in the European Biotech Act II (due late 2026/early 2027) will also lead to a more streamlined and predictable regulatory process and timeframe in Europe. In this regard, it is important that regulators consider the full breadth of industrial biotechnology, encompassing plants, animals, and microbes.

The US operates a predominantly product-based framework under the Coordinated Framework for the Regulation of Biotechnology, with oversight split between the FDA (food and drugs), USDA-APHIS (plants and animal products), and EPA (pesticides and some microbial products). For engineered plants, the USDA-APHIS "SECURE" rule (2020) exempts from regulation plant modifications that could have been achieved by conventional breeding, materially accelerating market entry for many gene-edited crops. For microbial and precision-fermentation products, the FDA's GRAS (Generally Recognised as Safe) notification pathway has been the principal route for food ingredients, while new animal-cell-derived products (cultivated meat) are regulated through a joint FDA-USDA framework.

The downstream consequences of this divergence are visible in market trajectories. Several gene-edited crops and precision-fermented ingredients have reached the US market substantially earlier than in the EU, and companies designing products for both jurisdictions generally have to maintain parallel evidence packages. For global synthetic biology developers, this regulatory complexity intersects directly with QbD: structured CQA-CPP documentation and process understanding generated early in development can serve as the evidence base for both frameworks, reducing the marginal cost of dual-market access (Mu'azzam et al., 2024).

7.2. Biosafety, biocontainment, and evidence-based regulation

Advances in synthetic biology also offer technical responses to the biosafety concerns that drive regulation. These include streamlined or recoded genomes that limit horizontal gene transfer potential (Leprince et al., 2012; Robertson et al., 2021), kill switches and engineered auxotrophies that constrain persistence outside controlled environments (Asin-Garcia et al., 2022; Hayashi et al., 2024; Mandell et al., 2015; Rottinghaus et al., 2022), and tightly controlled gene circuits that limit the conditions under which engineered functions are expressed (Asensio-Calavia et al., 2024). Together, these tools can provide the evidence base for risk-proportionate, adaptive regulatory frameworks, and are a natural complement to QbD-based process development.

7.3. Societal acceptance

Regulation sets the floor for what is permissible; public acceptance determines what reaches scale. Consumer perception of synthetic biology is shaped by concerns about safety, naturalness, and cultural familiarity, with food, health, and environmental-release applications attracting scrutiny (Bearth et al., 2022; The Good Food Institute, 2025; Hocquette et al., 2025; Lanz et al., 2024). Industrial biocatalysis and closed-loop bioremediation, by contrast, generally face lower public opposition (Olynk Widmar et al., 2017). Transparent communication, robust safety data, and genuine engagement with ethical, cultural, and environmental concerns are essential for building trust (Beghin and Gustafson, 2021; Koralesky et al., 2023; Paudel et al., 2023). Semantic clarity also matters: proposals to harmonise biotechnology terminology across research, regulation, and public communication (Ancelin et al., 2025) will help reduce the definitional confusion that currently

undermines informed public debate.

8. Conclusions

Synthetic biology has matured substantially over the past two decades by integrating engineering principles into biological design. This review has argued that what distinguishes the current moment is not the continuing refinement of any single enabling technology, but the convergence of three previously parallel developments: Quality by Design as the industrial translation layer, AI-driven design as an active participant in the DBTL cycle, and automated biofoundries as the infrastructure that operationalises both at scale. Together these elements are beginning to outline a credible and increasingly repeatable pathway from laboratory innovation to industrial circular biomanufacturing.

This convergence has three consequences for how the field should now be viewed. First, the core synthetic biology toolkit is increasingly domain-transferable, supporting coherent engineering across microbial, plant, and animal systems that together underpin a broader bioeconomy. Second, scale-up is increasingly being addressed prospectively through first-principles and AI-informed modelling, and biofoundry throughput, rather than treated as an intractable source of late-stage failure; market-scale case studies in gas fermentation, antimalarial production, precision fermentation, and horizontal biofoundry services indicate that this shift is producing measurable results in specific application areas. Third, the regulatory and societal frameworks that govern real-world adoption are themselves evolving, and the structured evidence bases that convergent synthetic biology generates appear increasingly well aligned with the emerging requirements of both EU and US pathways.

Significant challenges remain. The complexity of living cells continues to exceed our full understanding (Adamala et al., 2024; Bervoets and Charlier, 2019; Lu et al., 2024; O'Malley et al., 2008), cost-competitive production of low-margin commodities remains difficult (Danchin, 2012; Humbird, 2021; Rasul et al., 2022), and public acceptance is conditional and hard-won. However, much of the infrastructure needed to address these challenges systematically is now emerging, even if its capabilities remain uneven across application areas. The contribution of synthetic biology to the circular bioeconomy over the coming decade will depend on continued investment in the convergent framework described here, on interdisciplinary collaboration across engineering, biology, computation, and regulation, and on responsible implementation that engages society as a partner rather than a spectator.

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