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WHITE PAPER

How to harness engineering biology for sustainable production of bulk chemicals

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Engineering biology has the power to significantly reduce resource requirements, CO2 emissions, and energy demands traditionally associated with producing commodity chemicals. Downstream industries, such as consumer goods, that use these chemicals are showing a high level of interest, and governmental organisations around the world are looking for ways to support production. So, what is engineering biology, how can it aid environmental sustainability in the chemicals industry - and by extension in consumer packaged goods- and what challenges need to be overcome? This white paper considers how chemical companies, consumer goods manufacturers, and agri-tech industries can embrace engineering biology techniques, outlining practical guidance for large-scale production.

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As a major contributor to industrial CO2 emissions, chemical manufacture faces a high level of scrutiny. The industry's heavy reliance on petrochemicals as feedstock exacerbates and further complicates the issue. Engineering biology is seen as a lead solution to these complex sustainability challenges (see Table 1). However, it's not a silver bullet and brings its own difficulties which demand close attention. So, how can chemical manufacturers unlock engineering biology's potential?

Governmental commitments to engineering biology and biomanufacturing

US government: $2bn pledged for a national initiative to expand domestic biomanufacturing[3].

UK government: £2bn (US$2.5bn) of investment announced to "seize the potential of engineering biology"[4].

Government of Japan: plans to advance its biotechnology sector and become "the world's most advanced bioeconomy society by 2030" with a value of 92 trillion yen (US$837 billion)[5].

Engineering biology for chemical manufacture

At present, commercial success stories for engineering biology in the chemicals sector mostly involve the production of low-volume, high-value ingredients such as fragrances. Delivering more meaningful sustainability gains requires greater emphasis on the fundamental chemicals that account for around three quarters of the industry's total energy and non-energy use of petrochemicals. This is where engineering biology currently falls short. Unit economics cannot yet rival traditional synthesis of commodity chemicals, putting commercial viability out of reach. What's more, a lack of production capacity is a significant barrier both regionally and globally.

The good news is that change is on the horizon. Technological advancements offer new ways to address the unit economics challenges. What's more, public bodies in the US, UK, and Japan have committed to investing in specialist infrastructure that will help increase capacity. Large chemicals companies, whose funding and operational know-how will be fundamental to the development of this sector, are also partnering with and investing in engineering-biology companies: e.g., **Sumitomo** investing in **Visolis** (who use biomass waste to produce mevalonic acid, a key chemical intermediate for several compounds and materials, including isoprene)[1], **LG** has invested in **Lygos**, a start-up making isobutyric acid.[2]

Together, these developments could significantly improve the viability of large-scale production, signalling that the time is right for chemical manufacturers to invest in engineering biology strategies and processes.

Sustainability benefits of engineering biology for chemical production

More sustainable manufacture	Engineering biology processes are less reliant on fossil fuels than conventional chemical synthesis. For instance, replacing 1 ton of a conventional surfactant with 1 ton of precision-fermentation-derived sophorolipid would eliminate 1.5 tons of CO_2 emissions. Producing chemicals via metabolic engineering also reduces the need to use petrochemicals as feedstock.
Supporting the circular economy	Industrial waste can be valorised as a feedstock for metabolic engineering processes for chemical production. The resultant materials can be designed to be more readily biodegradable too. For example, **Mango Materials** produces biodegradable, low-toxicity plastics from methane gas generated from waste streams[6].
Greener supply chains	With metabolic engineering, manufacture can happen in closer proximity to raw materials and/or primary products. This reduces the need for extensive shipping and storage. It can also eliminate the use of raw materials derived from rare or endangered plants and animals, as seen in the production of squalene (originally obtained from shark liver oil) via precision fermentation.

Table 1

Consumer Packaged Goods: from high-value to high-volume chemicals

Engineering biology is increasingly used to produce functional active ingredients, colourants, flavours, and fragrances used in cosmetics, food and beverage, and household cleaning products. To foster a more holistic sustainability stance, it's necessary to progress beyond the niche production of these low-volume, high-value chemicals. Producing high-volume ingredients such as carriers, surfactants, and excipients via metabolic engineering would improve the overall sustainability of many CPG products. Engineering biology could also be harnessed to produce alternative packaging materials, reducing the amount of petrochemical-derived plastic used.

Sustainable production of bulk chemicals

The sustainability vision for engineering biology in chemical manufacture hinges on the ability to make commodity chemicals cost-effectively. Producing high-volume, low-value products like olefins (ethylene, propylene, butadiene), ammonia, methanol, and carbon black will be key.

Precision fermentation, a widely used engineering biology technique, can produce certain types of commodity chemicals without requiring petrochemicals as feedstock. One example is using engineered microbes to produce organic chemicals such as 1,3-propanediol and isobutanol with renewable feedstocks like corn or sugar cane. Surfactants, widely used, among other things, in consumer products such as detergents, cosmetics, and toiletries, are another class of chemical where metabolic engineering can deliver sustainability gains. See the below section for more information.

While these examples hold promise, they don't go far enough to achieve the sustainability vision. One area of concern centres on the cost, availability, and sustainability credentials of biological feedstocks. Most commercial-scale bio-manufacture is dependent on sugar-based feedstock, yet sugar cane cultivation is resource-intensive and often associated with deforestation. The reliance on fossil fuels for energy to power the production of sugar-based feedstock is another sticking point. Then there's the high cost of processing, especially for the purification stage of chemical production.

Chemical manufacturers looking to begin or extend the use of engineering biology might resolve some of these issues with alternative sourcing and novel techniques (see Table 2). However, there is another major limiting factor: the technical challenges that hinder the effective scale-up of metabolic engineering processes. Overcoming these challenges demands focused attention and specialist expertise from disciplines including physics, engineering, and data science.

Opportunities for sustainable surfactants

Surfactants' extensive use across diverse applications, from personal care and household cleaning to crop protection and industrial processes, makes them a prime target for engineering biology. Conventional surfactants are generally petroleum-based or derived from palm oil, bringing sustainability concerns linked to intensive agriculture and loss of habitats and biodiversity. So, the development of biosurfactants produced via the fermentation of yeast or bacteria is attracting a great deal of attention.

There are several commercial examples of fermentation-based production of rhamnolipid biosurfactants. **Stepan** acquired a plant with a 20,000-ton annual capacity,[7] and **Evonik** opened a facility with a 10,000-ton annual capacity in January 2024[8]. **Holiferm** is scaling its capacity to 15,000 tons per year and has also addressed cost-related challenges linked to downstream processes[9].

The biosurfactants market is predicted to grow rapidly from $1.2 billion in 2022 to $2.3 billion by 2028[10]. Yet, it only represents around 10 percent of the overall surfactants market. A significant barrier to widespread use is cost, which is estimated to be 20 to 30 percent higher for biosurfactants than conventional surfactants[11]. There are two key reasons for this: the high cost of substrates used as feedstocks and the necessary purification steps, which can account for 50 to 60 percent of overall production costs.

Overcoming barriers to facilitate sustainable and cost-efficient production of bio-based chemicals

Barriers	Potential solutions
Feedstock costs and sustainability	Source more sustainable, lower-cost substrate materials (e.g. agro-industrial waste, which is rich in carbohydrates and lipids).
Expensive downstream processes	Explore novel technical solutions with lower costs attached, such as using gravity separation for purification. Improve the efficiency of column chromatography. Adopt continuous and automated processing.
Use of fossil fuels in production or processing	Introduce production methods that are more compatible with renewable energy sources.

Table 2

Addressing the technical challenges of engineering biology at scale

It's widely acknowledged that most engineering biology technologies fail because they cannot be scaled. While metabolic engineering processes can be very effective in the laboratory, adapting them for mass production is not straightforward.

Challenges often centre on production costs and yield because the productivity of metabolic pathways generally decreases as scale increases. Maintaining the stability and performance of chemicals produced from genetically engineered organisms can also be difficult. This can have a detrimental impact on chemicals' functionality and efficacy downstream.

Nevertheless, it is possible to address these matters and enhance the viability and feasibility of large-scale production. It's useful to consider the challenges from the perspective of precision fermentation and cell culture, two widely used engineering biology techniques. At present, cells are typically grown in bioreactors and then used to produce high-value, low-volume ingredients. Scaling these methods to facilitate large-scale production of commodity chemicals is the logical next step. However, the natural variability of biological systems and the sensitivity of bioprocesses to environmental conditions mean that simply increasing bioreactor volume is not the answer. It risks compromising the transport efficiency of oxygen, nutrients, and waste products as the bioreactor tank is stirred, impacting quality, yield, and titre.

These scale-up challenges are significant, but not insurmountable. They can be mitigated using novel bioengineering methods, process optimisation, and genetic engineering along with advancements in AI and machine learning. To this end, we have devised a three-step process that supports the leap from the bench to the bioreactor for cost-effective large-scale production of commodity chemicals.

A three-step process for scale-up of commodity chemicals

Step 1: Bench-scale prototyping

Characterise the process and demonstrate feasibility via metabolic modelling.

It's common for bench-scale engineering biology to focus on demonstrating the feasibility of a given chemical's production. However, scale-up requirements should also be considered at this early stage. It's useful to characterise the process's dependence on various parameters in terms of underlying metabolic mechanisms as well as outputs.

Acquiring this insight necessitates the strategic design of experiments that explore different process parameters. These experiments may be intentionally sub-optimal in some respects to generate a range of data surrounding genomic, proteomic, metabolic, and environmental factors. The resultant data can be processed to produce a mathematical metabolic model that guides system development.

Various modelling frameworks can be used to describe fermentation processes, including Constraint-Based Modelling, Flux Balance Analysis, and Metabolic Flux Analysis. These mechanistic models provide a useful framework. However, they can be taken further with machine learning, which is increasingly used to determine parameters from experimental data, yielding a hybrid approach to metabolic modelling.[11]

The initial application of the metabolic model is to identify critical environmental parameter ranges (this is a key input for step two). It can also help identify critical measures for process monitoring and control.

Machine learning and artificial intelligence are being increasingly used to guide these early stages of development. London-based **Umkele**, for instance, a company working on producing chemicals including polyhydroxyalkanoates (a class of polyesters that can be used as a bioplastic) using cyanobacteria, states that its "modular microbial bioprocess utilizes synthetic biology, machine learning, and artificial intelligence to guide its development.[13] Another start-up, **Arsenale Bioyards**[14] uses advanced sensors and controls as well as AI for a 'learning loop' that is claimed to accelerate scale-up 'by enabling learning within and across scales'.

Step 2: Development of design rules

Think big from the outset. Consider large-scale process characteristics and automation.

Using engineering biology to achieve commercial-scale production that rivals traditional chemical synthesis in terms of cost-compatibility with end-products is a major difficulty. To help address this, all phases of scale-up should be considered at the outset, not on an incremental basis. This allows focused use of intermediate phases to establish and de-risk aspects of the full-scale process.

For example, the first phase could demonstrate the design principle for maintaining efficient transport of gases, nutrients and waste products, as well as demonstrating productivity. The next phase could involve additional monitoring and process control, demonstrating robustness. More sophisticated approaches can be introduced during the final phase. This might include automation for lifecycle processes such as loading, extraction, and sterilisation, thereby demonstrating the ability to run with a reduced workforce, which aids commercial viability.

Design rules, drawn from the bench-scale metabolic model combined with a fluidic model of the system, should be used to drive bioreactor design. Simply taking a large, stirred tank and modelling the fluidics in detail is unlikely to deliver performance improvements during scale-up. It will only mitigate the limitations intrinsic to that design.

Achieving the efficient transport of gases, nutrients and waste products often leads to novel reactor geometries. This is particularly true for cell culture processes which are based on a scaffold and may require mechanical stimulus. The requirements for the lifecycle processes and monitoring sensors also contribute design rules for the reactor geometry.

Once these design rules are identified, fluidic modelling develops in tandem with the design. Simple models are usually sufficient to assess high-level design options and select a preferred architecture. Then, computational fluid dynamics (CFD) of subsections aids component-level design. When the design is complete (i.e., a complete CAD model is available), CFD of the whole system enables final optimisation and prototype validation. Standard bioreactor designs (such as open geometry and impellers which provide indirect control of the flow field) can require complicated CFD. However, a system design driven by design rules is more likely to have a geometry where flows are controlled more directly, which in turn makes fluidic modelling more straightforward.

Step 3: System modelling and digital twins

Validate and verify processes. Make intelligent use of sensors to guide scaled-up plant operations.

Once a prototype is operational, a system model and digital twin can be used to monitor performance, support control, and diagnose issues. A key part of design validation and verification is to check that low-level measurands (such as species concentrations) are performing as expected, as well as ensuring high-level metrics (like productivity) are performing well. This is where sensor technology comes to the fore.

While bioreactors typically use simple sensors to assess pH, dissolved oxygen, and CO2, electrochemical sensors are emerging for glucose and lactate. This technology is well-established for monitoring a whole range of metabolic species in medical applications. However, the transition to bioreactor applications has been slow for commercial reasons. Similarly, there are well-established medical biosensor technologies that could be used, such as ELISA assays to monitor proteins and antibodies from bioreactor samples.

Fingerprinting technologies like Raman spectroscopy take these capabilities further, offering ways to sense more subtle properties such as cell viability. This would likely involve microfluidic sampling, which indicates how sensing requirements can influence bioreactor design. Sensing over a range of positions, rather than at a single point or port of the bioreactor, also has significant design implications.

Harnessing CO2 for largescale ethylene production

In July 2023 Technip Energies and LanzaTech announced a Joint Collaboration Agreement[15] for the transformation of waste carbon into ethylene, an important commodity chemical. **LanzaTech** previously developed a production method involving the fermentation of gases containing CO, CO_2, and H_2, with ethylene selectively produced from the CO2 using a specially engineered biocatalyst. The resultant ethanol is used in various consumer products from fragrances to textiles. In March 2024, the companies were jointly invited to begin award negotiations for up to $200 million in Bipartisan Infrastructure Law and Inflation Reduction Act funding by the **US Department of Energy (DOE) Office of Clean Energy Demonstrations**[16]. If negotiations are successful, this award could accelerate the development of a replicable large-scale production plant.

The time is right to focus on large-scale use of engineering biology for commodity chemical production

Companies that harness engineering biology for large-scale commodity chemical production will earn pole position in a market that's forecast to hit over $100 billion by 2032.[17] They will also move the needle on sustainability, both for the chemicals industry and the downstream industries that rely on bulk chemicals.

To achieve this, manufacturers will have to implement technologies that help maintain efficient and effective chemical production as engineering biology processes are scaled. Strategic planning, with expert multidisciplinary input, will be essential. As governments follow through on their infrastructure commitments for engineering biology, it will become easier to derive a good return from investment in these production capabilities. Manufacturers that have already optimised the unit economics of core processes and overcome other scale-up challenges will be the first to benefit.

How Sagentia Innovation can help

Engineering biology promises to support many sectors in their sustainability journeys. At Sagentia Innovation, we help leading organisations navigate the challenges and opportunities of emerging technologies.

Talk to us if:

You need to understand the impact of engineering-biology-derived chemicals and raw materials on different aspects of sustainability

You are unsure how engineering biology will affect the competitive landscape and commercial opportunities in your markets of interest

You need to know how engineering biology, and biomanufacturing more broadly, will affect your supply chains in the short and long terms

You want to explore how biomanufactured ingredients affect your formulations, and you want to reformulate using them.

You need mathematical models to design effective bioreactors

You want clarity on how regulations will affect engineering biology

Key case studies from Sagentia Innovation working within engineering biology

Challenges and opportunities of cellular agriculture in CPG

The client wished to understand the opportunities that cellular agriculture could present for them in the mid- and long-term, both for their existing portfolio and for future developments.

The project team identified opportunities by analysing simultaneously the benefits and barriers of cellular agriculture and the client's ambitions and challenges.

Sagentia Innovation delivered a report that outlined the areas where cellular agriculture can help our client resolve current challenges and prepare for future ambitions, and we provided recommendations on areas where our client could invest to take advantage of cellular agriculture opportunities.

Next-generation raw materials: horizon scanning of alternative sources and identification of key opportunities

Our client, a consumer sector company, wanted to understand trends and attitudes over a three- to ten-year horizon regarding current and future sources of alternative raw materials for their products and how they should prepare for such changes.

Sagentia Innovation identified established and developmental sources for precursors and for alternative raw materials that could replace those in existing raw material supply chains. We conducted a scenario analysis to outline the opportunities and challenges in utilising the sources relevant to the target application. This is an assessment of criteria such as functional performance, commercial viability, consumer and regulatory attitudes, and sustainability profile.

We supplied recommendations for the viability of replacing current raw material sources, a time frame for the readiness of best-bet alternatives, and a 10-year roadmap for their potential use.

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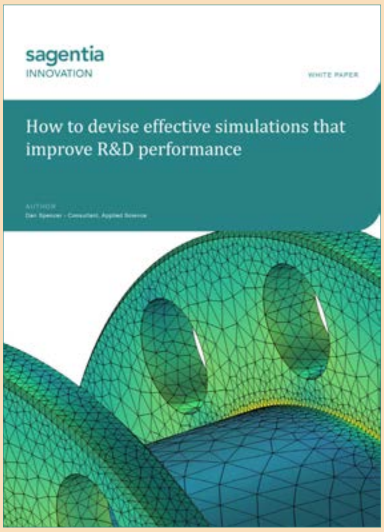

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About Sagentia Innovation

Sagentia Innovation provides independent advisory and leading-edge product development services focused on science and technology initiatives. Working across industrial, chemical, energy, food and beverage, and consumer markets, Sagentia Innovation works with start-up disruptors through to world leading brands to extract maximum value from R&D and innovation investments.

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