Pharmaceutical BIOPROCESSING

Synthetic Biology with Metabolic Engineering

Emily George*

University of Waikato, New Zealand

*Author for correspondence:

georgeemily@rediff.com

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Abstract

The generation of microbial strains capable of manufacturing chemicals and materials effectively is made possible through metabolic engineering, but industrialising the strains takes a lot of time, money, and effort. Recently, high-performance strain generation has been aided by systems metabolic engineering, which combines classical metabolic engineering with systems biology, synthetic biology, and evolutionary engineering tools and tactics. This interdisciplinary approach has been continually enhanced over the last ten years in order to create overproducer strains that are competitive in the industrial market. This article reviews recent advancements in host strain selection, metabolic route reconstruction, tolerance augmentation, and metabolic flux optimization. It also reviews current trends in systems metabolic engineering, including tools and methodologies. Future difficulties and opportunities are also covered.

Keywords: Bio-refinery • Evolutionary engineering • Industrial biotechnology • Synthetic biology • Systems biology • Systems metabolic engineering

Introduction

The interactions that take place in the internal environment of microorganisms and the intricacy of the regulatory network serve as a reminder of the significance of creating systematic modelling methods for biological systems and tractable mechanistic models of cellular processes. In order to do this, the current approaches to process systems engineering can be used as a means of comprehending, integrating, and developing biological systems and processes. Here, we examine how a comprehensive strategy has been used to create mathematical models of biological systems, from the model's original conceptualization through its eventual use in model-based control and optimization. In an effort to improve the empirical expressions typically used to describe the kinetics of microorganism development, we also talk about the usage of mechanistic models that take gene regulation into account. We also highlight present and upcoming difficulties in mathematical biology. The modelling research methodology covered in this article may be useful for creating the best bioprocesses possible, applying practical and logical methods for producing chemicals and medications in an effective manner [1-4].

The process analytical technology initiative (PAT) and quality by design (QbD) approaches, which are intended to improve the knowledge of more interconnected processes, have a significant impact on the manufacturing of biopharmaceuticals and pharmaceuticals. The main goal of this project can be summed up as creating a mechanistic understanding of a variety of process phases, which includes creating technology for online measurements, real-time control, and optimization. Also, it is intended to reduce the number of empirical experiments and explore the process design space with model assistance. Even though there has been a lot of progress made so far, more work needs to be done in order to fully utilise the toolbox for process systems engineering. An overview of the most recent advances in process systems engineering for biopharmaceutical and pharmaceutical manufacturing processes is provided in this Special Issue of Processes. These include model-based process design, Digital Twins, computer-aided process understanding, process development and optimization, and monitoring and control of bioprocesses. The biopharmaceutical processes discussed concentrate on the synthesis of adeno-associated viruses, cell spheroids for cell treatments, and the production of biopharmaceuticals, primarily using Chinese hamster ovary (CHO) cells.

Growing desire for natural items that are more environmentally friendly and sustainable is the result of increased awareness of the health and environmental risks associated with consuming chemically produced goods. Despite their significance, however, the low yield and high expense of the bioprocesses have made it difficult to produce natural products on an industrial scale. Systems metabolic engineering has been used to effectively create natural products from renewable biomass to address this issue. Here, we cover contemporary systems metabolic engineering techniques used to increase the production of natural products with added value, along with relevant examples. Systems-level engineering and cell physiology engineering techniques are given special attention. Also, future perspectives are considered [5-8].

Discussion

Notwithstanding the value of natural products for their use as medicines, nutraceuticals, cosmetics, and food additives, the low yield and high cost of the bioprocesses have limited their industrial-scale manufacture. Nonetheless, due to lately increased knowledge of the environmental and health risks associated with consuming chemically manufactured items, the demand for natural products has been rising quickly. Furthermore, because of their complicated chemical structures or the presence of several chiral centres, natural compounds are frequently challenging to chemically synthesise. Due to recent developments in systems metabolic engineering, industrially significant microbes have been modified to manufacture natural products from renewable biomass in order to address these problems. Industrial model microorganisms like Escherichia coli or Saccharomyces cerevisiae are widely used because of their many benefits, including the availability of well-established engineering tools and genome-scale models, quick growth, and capacity for high-cell-density culture. For maximising the production of target chemicals, systems metabolic engineering, which combines synthetic biology, systems biology, and evolutionary engineering with traditional metabolic engineering, should be used in addition to traditional metabolic engineering, which entails knockout or overexpression of rationally chosen target genes. In particular, novel biosynthetic pathways and enzymes have recently been designed using systems metabolic engineering and computational approaches, including artificial intelligence. Random techniques can be used to quickly create microbial strains with the necessary performance when rational strain engineering is challenging. Even without needing to build the biosynthetic pathways, current attempts in engineering cell physiology based on the traits of the microbial hosts have shown significant increase in the production of target compounds. In this article, we present the most recent developments in cell physiology engineering and systems metabolic engineering methodologies for improved production of natural products. The main tactics covered in this paper are listed. We also talk about future prospects and factors that should be taken into account for scaling up [9-10].

In order to create a sustainable chemical industry, metabolic engineering has become more significant in the development of microbial cell factories for the manufacture of diverse chemicals and materials. Today, there are numerous methods and techniques for doing systems metabolic engineering that enable systems-level metabolic engineering in more complex and varied ways by embracing quickly developing systems biology, synthetic biology, and evolutionary engineering methodology and tools. As a result, it is now possible to create microbial cell factories that are more effective. In this article, we examine current developments in systems metabolic engineering tools and techniques along with relevant application examples. We also discuss the simultaneous and synergistic interactions of various tools and approaches to create unique microbial cell factories.

One of the biggest hazards facing the world now is climate change, which demands top emphasis. Our extensive use of fossil fuels, such as oil and gas, is one of the main causes of climate change. Hence, instead of relying on petrochemical methods, there has been a lot of interest in generating chemicals and minerals via microbial cell factories from renewable non-food biomass. Although microbes have the ability to create all of the metabolites found in their metabolic network, doing so would be extremely inefficient for the majority, if not all, of these compounds. Titer yield and productivity three crucial performance indices have all been enhanced through metabolic engineering in the bio-based synthesis of valuable chemicals and minerals. Early positive performance findings inspired us to work harder to advance metabolic engineering methodologies in order to create bio-refinery processes that can produce a variety of chemicals and materials in an affordable way.

Conclusion

A key technology for creating effective microbial cell factories is systems metabolic engineering. Recently, as stated throughout the paper, the potential of systems metabolic engineering has been further boosted by the creation of cutting-edge tools and techniques. More and more information is becoming available on how to successfully generate microbial strains through systems metabolic engineering for the increased production of desired compounds and minerals. There are, however, still additional spaces for new.

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