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Review

Advancements in biocatalysis: From computational to metabolic engineering

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ABSTRACT

Through several waves of technological research and un-matched innovation strategies, bio-catalysis has been widely used at the industrial level. Because of the value of enzymes, methods for producing value-added compounds and industrially-relevant fine chemicals through biological methods have been developed. A broad spectrum of numerous biochemical pathways is catalyzed by enzymes, including enzymes that have not been identified. However, low catalytic efficacy, low stability, inhibition by non-cognate substrates, and intolerance to the harsh reaction conditions required for some chemical processes are considered as major limitations in applied bio-catalysis. Thus, the development of green catalysts with multi-catalytic features along with higher efficacy and induced stability are important for bio-catalysis. Implementation of computational science with metabolic engineering, synthetic biology, and machine learning routes offers novel alternatives for engineering novel catalysts. Here, we describe the role of synthetic biology and metabolic engineering in catalysis. Machine learning algorithms for catalysis and the choice of an algorithm for predicting protein-ligand interactions are discussed. The importance of molecular docking in predicting binding and catalytic functions is reviewed. Finally, we describe future challenges and perspectives.

1. Introduction

Enzyme production with high-value and applied perspectives in different industrial and medicinal sectors is a pursuit central to modern industry. Among enzyme sources, microbial enzymes are preferred because of their advantageous characteristics such as economic feasibility, rapid microbial growth, overall cost-effective ratio, induce productivity, high yield, high catalytic efficacy, overall stability, and ease of product modification via immobilization, among others [1–3]. Biotechnologists and microbiologists have long considered enzymatic catalysis to have enormous potential in diverse fields for manufacturing specialty chemicals and pharmaceuticals, biofuel production, and food processing. High catalytic potentiality, stability, and repeatability of enzymes are characteristic features required for industrial bio catalytic processes [4]. Because of their efficient catalytic activity, biological catalysts or, simply, bio-catalysts are considered attractive for enhancing overall reaction feasibility [5]. Structural, chemical, and stress-based characteristics make enzymes more suitable bio-catalysts compared to their synthetic counterparts [6,7]. Enzymes not only increase reaction rates, but also help to block

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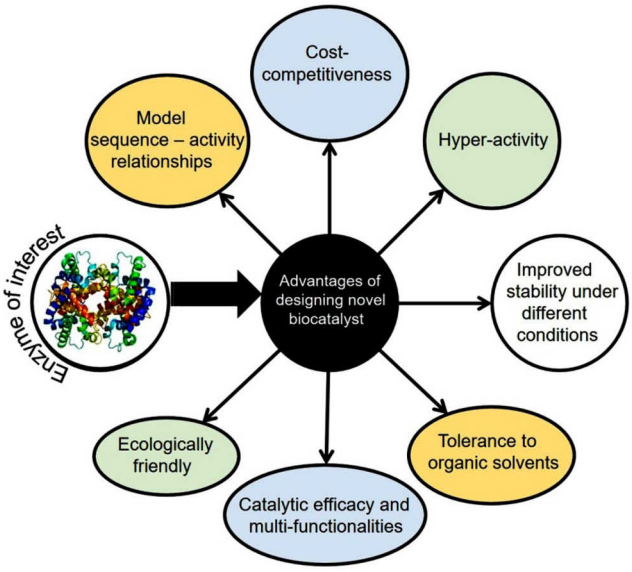

Fig. 1. Advantages of designing novel biocatalysts of interest.

reactions limiting flux towards a target [8]. Fig. 1 illustrates some advantages of designing novel biocatalysts of interest. Despite these advantages, the low stability of enzymes is a significant technical challenge in numerous applications. To overcome such limitations, biocatalytic evaluation and improvement strategies have been developed as shown in Fig. 2 [4].

Many enzymes with efficient catalytic activity in the production of important molecules and reactions within cells have not been discovered [6,9]. However, various protein engineering approaches have been reported to improve the catalytic activity of enzyme-based catalysts. Several in-practice classical strategies for designing catalyst are laborious and time-consuming [10–12]. Therefore, computational tools are required to design catalyst in a short time with the requisite catalytic characteristics [13].

Herein, we highlight the role of synthetic biology and metabolic engineering in catalysis. We first focus on machine learning algorithms for catalysis and the choice of an algorithm for predicting protein-ligand interactions. In the next part, the importance of molecular docking is reviewed, including the prediction of binding and catalytic functionalities. Several advantages and disadvantages of this system are described. Artificial metalloenzymes for creating catalytically novel proteins are presented in the third part. The fourth part emphasizes the role of synthetic biology and metabolic engineering in catalysis aiming to construct highly efficient microbial cell factories as novel platforms for the next-generation bio-economy. We conclude by describing future challenges and perspectives.

2. Machine learning algorithms for catalysis

Machine learning algorithms are helpful for building models of unknown proteins by comparative homology based on their sequence and structural characteristics [14,15]. Fig. 3 illustrates a general approach for machine learning of protein (ChR) structure-function relationships [15]. A key limitation to the development of novel biocatalysts is that many experiments

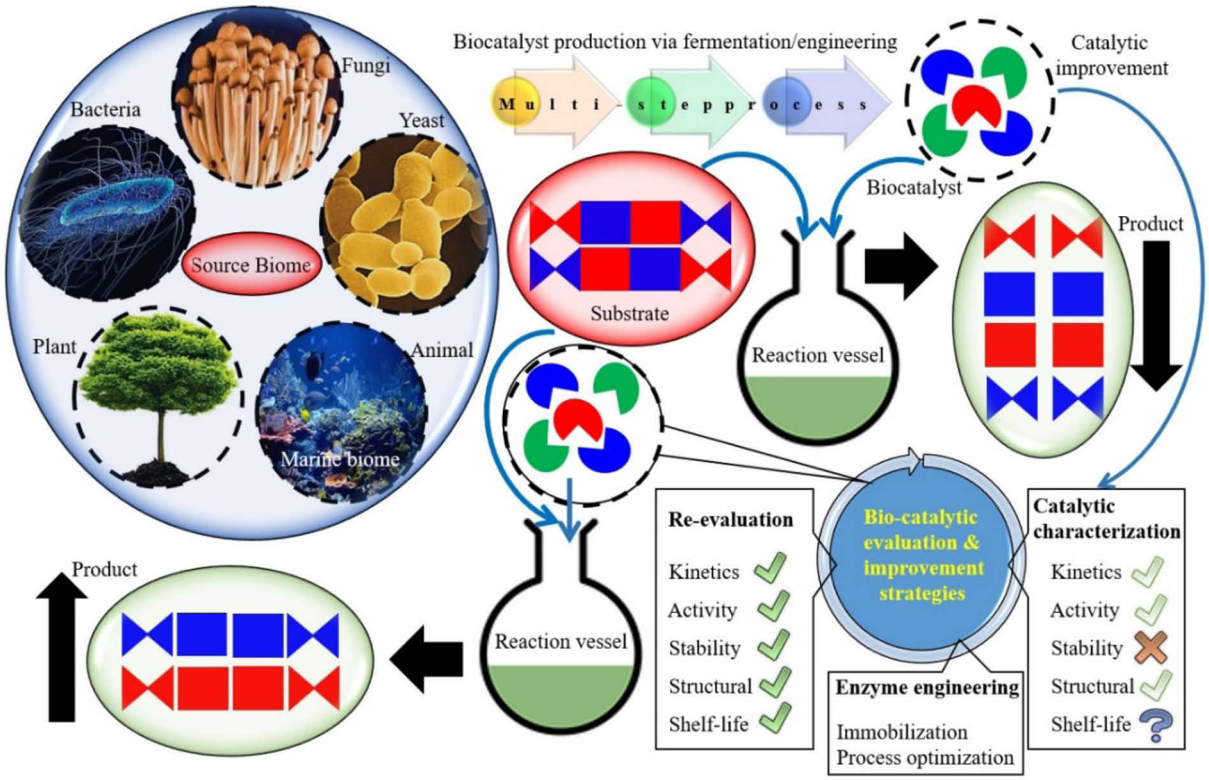

Fig. 2. Biocatalytic evaluation and improvement strategies. A complete overview from biocatalyst (enzyme) production via fermentation and/or engineering to catalytic pathway. The low substrate conversion can be significantly improved by enzyme engineering. Reproduced from Ref. [4], with permission from Elsevier.