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# Biocatalysis in Organic Synthesis: A Review of Enzyme-Catalyzed Reactions and Their Applications

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## Abstract

Biocatalysis has emerged as a transformative platform in modern organic synthesis, enabling highly selective, efficient, and sustainable routes to complex molecules that are challenging or inefficient by conventional methods. This review synthesizes current knowledge on enzyme-catalyzed reactions spanning hydrolases, oxidoreductases, transferases, lyases, isomerases, and ligases and examines how these catalyst classes enable hydrolysis/esterification, asymmetric redox chemistry, group transfer (including transamination and glycosylation), stereoselective C–C bond construction, rearrangements, and ATP-dependent ligations. Emphasis is placed on the mechanistic bases for the exceptional chemo-, regio- and enantioselectivity of enzymes and on practical considerations that govern their use in non-native synthetic contexts (stability, solvent compatibility, cofactor requirements, and kinetics). The review details contemporary strategies that have expanded enzymatic utility directed evolution and rational protein engineering, AI-guided design, cofactor engineering and recycling, immobilization, solvent engineering, and continuous-flow/process intensification and connects these advances to tangible industrial impact in pharmaceuticals, fine chemicals, flavors, and bio-based materials. Life-cycle and process-metric perspectives illustrate the sustainability advantages of biocatalytic routes, particularly in atom economy, waste reduction, and energy efficiency, while acknowledging persistent challenges such as enzyme cost, substrate scope limitations, and scale-up constraints. Finally, we identify emergent directions likely to shape the field: integrated chemo-enzymatic cascades, cell-free multi-enzyme systems, AI-driven discovery pipelines, and synthetic-biology-enabled production platforms. Collectively, these developments position biocatalysis as a central pillar of future sustainable chemical manufacturing and a fertile area for interdisciplinary research and industrial deployment.

**Keywords:** Biocatalysis, Enzyme catalysis, Organic synthesis, Green chemistry, Enantioselectivity and Sustainable catalysis

## Introduction

Catalysis lies at the heart of modern organic synthesis, enabling reactions that would otherwise be energetically unfavorable or inefficient. Through the lowering of activation

barriers, catalysts enhance rates and selectivity, making complex molecule construction both feasible and sustainable (Sheldon and Woodley, 2018). Over the past two decades, biocatalysis—the use of natural or engineered enzymes as catalysts has evolved from a niche research field into a

mainstream methodology that rivals traditional metal or organocatalysts. Enzymes offer exceptional chemo-, regio-, and stereoselectivity, often under mild, aqueous, and environmentally benign conditions, making them indispensable tools for chiral molecule synthesis and late-stage functionalization in pharmaceuticals and fine chemicals (Reetz, 2013). This growing role of enzymes in synthesis reflects a global trend toward sustainable chemistry and green manufacturing.

The evolution of biocatalysis mirrors advances in enzymology, molecular biology, and protein engineering. Originally limited to naturally occurring hydrolases and oxidoreductases, modern biocatalysis now employs an extensive repertoire of engineered enzymes designed for stability, activity, and substrate flexibility (Bornscheuer, Hauer, Jaeger and Schwaneberg, 2019). The development of directed evolution, as pioneered by Frances Arnold and co-workers, revolutionized this field by enabling laboratory-based natural selection for improved catalytic properties (Arnold, 2018). Complemented by computational modeling, high-throughput screening, and machine learning tools, these strategies have created catalysts that transcend native reactivity, allowing enzymes to perform abiological transformations such as C–Si and C–B bond formations (Yang, Wu and Arnold, 2019). This transformation has expanded the reach of enzymes from academic curiosities to reliable industrial workhorses.

The chemo-, regio-, and stereoselectivity inherent to enzyme catalysis stems from the precise molecular architecture of the active site, which governs substrate binding and transition-state stabilization (Sheldon and Woodley, 2018). This high degree of control is exemplified by the industrial synthesis of the antidiabetic drug sitagliptin, in which an engineered  $\omega$ -transaminase replaced a rhodium-catalyzed asymmetric hydrogenation step. The enzymatic process not only improved stereoselectivity but also reduced waste and eliminated precious metal use (Savile et al., 2010). Such examples demonstrate how biocatalysis can outperform conventional catalysis by combining high selectivity with sustainability and cost efficiency. Enzymes have similarly proven valuable in cascade reactions and dynamic kinetic resolutions, where they allow for integrated, multi-step synthesis in a single reactor without isolation of intermediates (Britton, Majumdar and Weiss, 2018).

Beyond selectivity, environmental and economic benefits have made enzyme-based processes central to green chemistry. Biocatalytic reactions typically display high atom economy, low E-factors, and operate under ambient temperature and pressure, minimizing both energy consumption and hazardous waste (Sheldon and Woodley, 2018). When combined with immobilization and cofactor regeneration systems, enzymes can be reused efficiently, extending their operational lifetime and reducing costs (Wu et al., 2021). Comparative life-cycle assessments consistently reveal that biocatalytic routes yield lower environmental burdens than metal-catalyzed analogues,

especially in pharmaceutical manufacturing (Reetz, 2013). Nonetheless, successful implementation requires addressing challenges such as limited solvent tolerance, enzyme instability, and substrate scope; issues that are progressively being overcome through protein engineering and process intensification.

The purpose of this review is to present a comprehensive and critical evaluation of biocatalysis in modern organic synthesis, emphasizing the breadth of enzymatic reactions, their mechanisms, and their growing industrial and environmental relevance. The review aims to bridge fundamental enzymology with practical synthetic applications, showcasing how natural and engineered enzymes contribute to sustainable chemical manufacturing. Central to this work is the systematic exploration of enzyme classes: oxidoreductases, hydrolases, transferases, lyases, isomerases, and ligases and their diverse roles in key transformations such as asymmetric reductions, esterifications, transaminations, and C–C bond formations. It also highlights the mechanistic principles that underlie enzymatic chemo-, regio-, and enantioselectivity, connecting molecular-level understanding to macroscopic process efficiency. Beyond mechanistic insight, the review evaluates emerging strategies for enhancing enzyme performance, including directed evolution, computational enzyme design, and artificial intelligence-guided screening. Industrial case studies from the pharmaceutical, fine chemical, and bio-based polymer sectors are discussed to demonstrate real-world applications and economic advantages. Finally, the review highlights future directions, particularly the integration of artificial intelligence, synthetic biology, and hybrid chemo-enzymatic systems, as key enablers of the next generation of sustainable chemical manufacturing.

## 2. Fundamentals of Biocatalysis

Biocatalysis lies at the intersection of biology and chemistry, leveraging the catalytic capabilities of enzymes to drive chemical transformations with exceptional selectivity and efficiency. The fundamental concept of biocatalysis revolves around the utilization of enzymes—nature’s molecular machines, to catalyze reactions that would otherwise require harsh conditions or yield low selectivity in conventional chemical synthesis (Fersht, 2017). These biological catalysts exhibit remarkable specificity, accelerating reaction rates by lowering activation energy barriers through transition-state stabilization. Their ability to operate under mild reaction conditions such as ambient temperature and neutral pH, while achieving high chemo-, regio-, and stereoselectivity, has positioned enzymes as sustainable alternatives to traditional chemical catalysts in modern synthesis (Warshel and Bora, 2016).

The principles of enzyme catalysis are grounded in the molecular recognition between enzyme and substrate. Classical models such as the “lock-and-key” and “induced-fit” theories have long described the specificity of enzyme–substrate interactions; however, recent structural and

computational studies have shown that enzymes are not static scaffolds but dynamic entities whose conformational flexibility is essential to their catalytic function (Warshel and Bora, 2016). Through precisely arranged active sites, enzymes bring reactants into optimal proximity and orientation, stabilizing the transition state and thereby reducing the activation energy required for bond rearrangements (Fersht, 2017). The efficiency of enzymatic catalysis is quantitatively expressed by kinetic parameters such as the Michaelis–Menten constant ( $K_m$ ) and the turnover number ( $k_{cat}$ ), which provide insights into catalytic efficiency and substrate affinity (Bisswanger, 2017). These kinetic principles form the foundation for understanding and optimizing enzymatic processes in both laboratory and industrial applications.

At the molecular level, enzymes achieve catalysis through several distinct mechanisms, including acid–base catalysis, covalent catalysis, and metal ion catalysis. Each mechanism utilizes specific amino acid residues or cofactors within the enzyme's active site to stabilize reaction intermediates or transition states (Garcia-Viloca et al., 2017). For instance, serine residues often function as nucleophiles in hydrolases, while metal ions such as  $Zn^{2+}$  or  $Fe^{2+}$  can act as Lewis acids to polarize substrates. Advances in quantum mechanics/molecular mechanics (QM/MM) simulations have revealed that enzyme-catalyzed reactions are not merely the result of favorable binding energies but arise from a finely tuned interplay of structural dynamics and electronic rearrangements (Senn and Thiel, 2021). This understanding has spurred the rational engineering of enzymes, where targeted mutations or domain modifications can dramatically enhance substrate specificity, stability, or catalytic turnover. Enzyme activity is strongly influenced by physicochemical factors such as temperature, pH, solvent environment, and the presence of cofactors. Optimal catalytic performance is typically observed within a narrow range of these conditions, beyond which enzyme denaturation or reduced activity occurs (Stepankova et al., 2013). Temperature affects both the rate of catalysis and structural stability, while pH modulates the ionization states of catalytic residues. Similarly, ionic strength and solvent polarity can alter enzyme conformation and substrate accessibility (Xu et al., 2017). The use of non-traditional media such as ionic liquids, biphasic systems, and deep eutectic solvents has gained attention for expanding the applicability of enzymes to non-aqueous environments, improving solubility for hydrophobic substrates and enabling greener reaction conditions (Xu et al., 2017). Moreover, cofactors such as NADH/NAD<sup>+</sup> and FAD/FADH<sub>2</sub> are vital in redox transformations, and efficient regeneration systems for these cofactors are critical for sustainable biocatalytic processes.

Enzymes are systematically classified by the Enzyme Commission (EC) into six major categories: oxidoreductases, transferases, hydrolases, lyases, isomerases, and ligases

(Webb, 2022). Each class performs distinct catalytic functions that collectively encompass a vast range of biochemical transformations. In biocatalysis, hydrolases and oxidoreductases are particularly important due to their robustness, substrate versatility, and relevance in industrial applications. Hydrolases such as lipases and proteases are widely employed in kinetic resolutions and esterifications, while oxidoreductases catalyze oxidation–reduction reactions essential in pharmaceutical and fine chemical synthesis (Yi et al., 2021). Recent advances in metagenomics have expanded the known enzyme repertoire, revealing novel biocatalysts from extremophiles and uncultured microbial sources with unique catalytic properties suitable for harsh industrial environments (Yi et al., 2021). These discoveries, coupled with protein engineering, have led to the design of tailor-made enzymes optimized for specific synthetic routes.

A key consideration in biocatalysis is enzyme stability and reusability, particularly for industrial-scale operations. Free (soluble) enzymes often exhibit limited operational stability and are difficult to recover from reaction mixtures, which restricts their economic feasibility (Sheldon and Brady, 2018). To overcome these limitations, enzyme immobilization techniques such as adsorption, covalent attachment, entrapment, or encapsulation have been developed to enhance enzyme lifetime and facilitate catalyst recovery. Immobilized enzymes offer increased thermal and solvent stability, improved process control, and compatibility with continuous-flow systems. However, immobilization may also introduce mass transfer limitations or reduce catalytic turnover if enzyme orientation on the support is unfavorable (Stepankova et al., 2013). Hybrid strategies using nanomaterials, magnetic particles, or metal–organic frameworks (MOFs) are increasingly being explored to minimize these drawbacks while retaining high activity (Yi et al., 2021). In parallel, directed evolution and rational protein engineering have emerged as powerful tools for creating enzymes with enhanced thermostability, broader substrate scope, and improved tolerance to non-natural reaction media (Arnold, 2018; Bornscheuer et al., 2019). Machine learning-assisted enzyme engineering now enables the rapid prediction of beneficial mutations and accelerates the optimization of catalytic properties (Yang, Wu and Arnold, 2019).

Overall, understanding the fundamentals of biocatalysis provides the foundation for its expanding role in modern organic synthesis. The integration of enzyme engineering, immobilization technologies, and computational modeling is transforming biocatalysis from a niche scientific field into a cornerstone of sustainable chemistry. These advancements not only enhance catalytic performance but also support the transition toward greener and more efficient manufacturing processes in pharmaceuticals, fine chemicals, and materials science.

**Table 1.** Major enzyme classes and typical synthetic applications

EC Class	Representative enzymes	Typical synthetic transformations	Representative application / example
Oxidoreductases (EC 1)	ADHs, KREDs, P450s, peroxygenases	Asymmetric reductions, hydroxylations, oxidations	Chiral alcohols; selective C–H hydroxylation. (Hollmann et al., 2020; Hobisch et al., 2021)
Transferases (EC 2)	Transaminases, glycosyltransferases, methyltransferases	Amination, glycosylation, methylation	Chiral amines (transaminase routes). (Savile et al., 2010; Kelly et al., 2020)
Hydrolases (EC 3)	Lipases, esterases, proteases	Hydrolysis, esterification, transesterification	Ester/flavor synthesis; kinetic resolution. (Sheldon and Woodley, 2018)
Lyases (EC 4)	Aldolases, decarboxylases	Stereoselective C–C bond formation, eliminations	Asymmetric aldol couplings. (Schriftwieser et al., 2018)
Ligases (EC 6)	ATP-dependent ligases, peptide ligases	C–X bond formation (ligations)	Site-selective peptide/protein ligation. (Frazier et al., 2020)

### 3. Enzyme-Catalyzed Reactions in Organic Synthesis

Enzyme-catalyzed reactions constitute the practical core of biocatalysis, providing a rich repertoire of transformations for modern synthetic chemistry. Leveraging precise substrate recognition, transition-state stabilization, and conformational dynamics, enzymes perform hydrolyses, redox processes, group transfers, C–C bond formations, isomerizations, and ligations with high chemo-, regio- and stereoselectivity under mild conditions. This section discusses the major classes of enzyme-catalyzed reactions used in organic synthesis, highlighting their mechanisms, substrate specificities, and representative examples from industrial and academic research. Particular emphasis is placed on how these biocatalytic transformations contribute to sustainable and scalable synthetic chemistry.

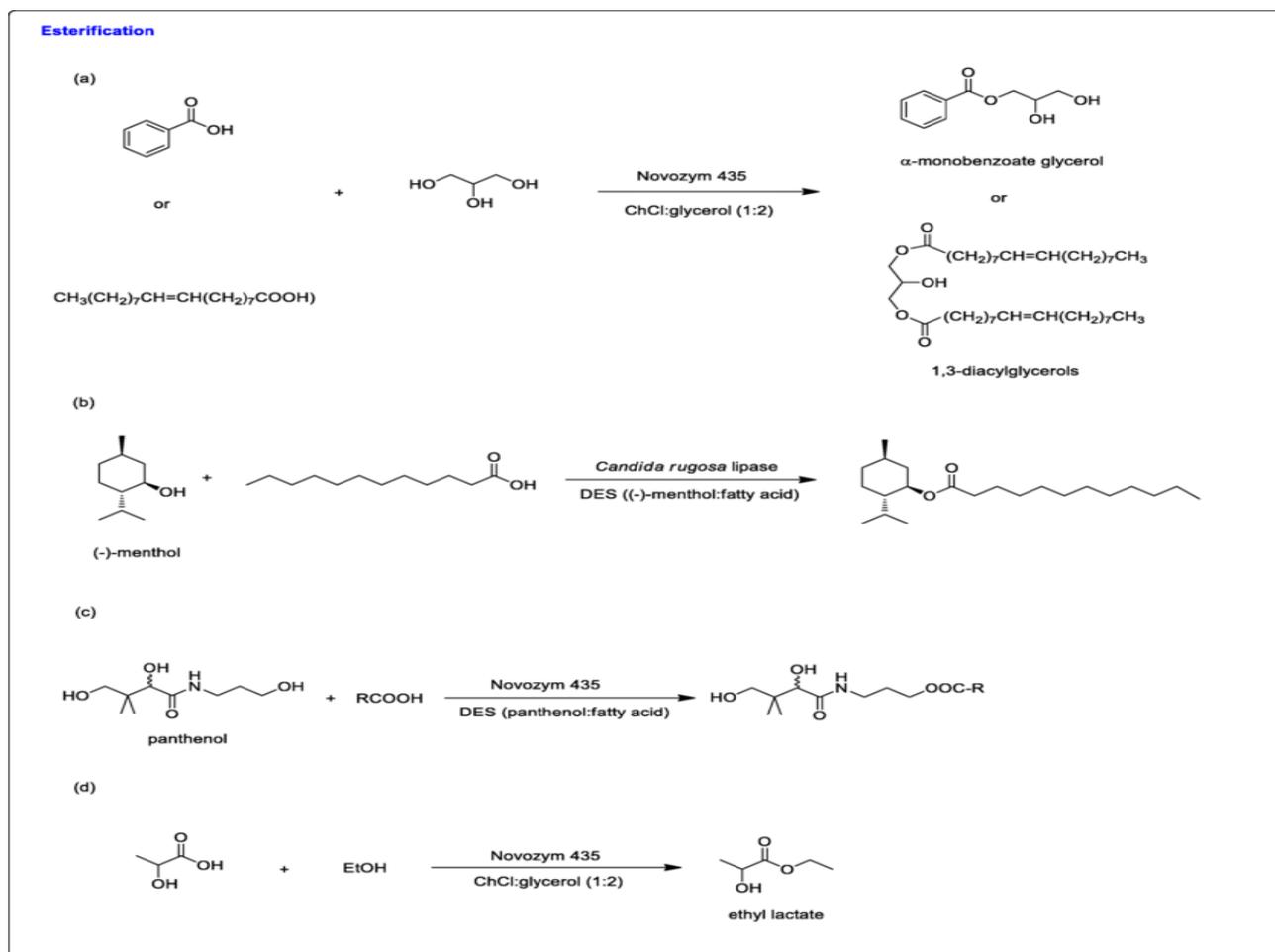
#### 3.1 Hydrolase-Catalyzed Reactions

Hydrolases (EC 3) are among the most widely applied biocatalysts in preparative chemistry due to their robustness, ease of use and the fact that many operate without redox cofactors. Lipases and esterases catalyze ester hydrolysis in aqueous media and, under low-water or organic conditions, mediate the reverse reactions—esterification and transesterification—enabling efficient formation of esters and estolides used in flavors, fragrances, and polymer precursors (dos Santos et al., 2023). Lipase-mediated kinetic resolutions and dynamic kinetic resolutions are well established routes to enantiopure alcohols and acids, often yielding high enantiomeric excess with minimal protecting-group manipulations (Eskandari et al., 2024). Proteases and engineered peptide-forming hydrolases (e.g., subtiligase

variants, peptide ligases) have been used for peptide bond formation and selective peptide modifications under mild conditions (Frazier et al., 2020). Industrial implementations favor immobilized hydrolases (e.g., CAL-B on supports) to allow enzyme reuse and process intensification in batch or continuous flow (dos Santos et al., 2023). Key limitations include substrate inhibition with bulky hydrophobic substrates and decreased activity in strongly non-aqueous media, but protein engineering and reaction engineering (e.g., solvent selection, biphasic systems) have mitigated many of these constraints (Stepankova et al., 2013).

#### 3.2 Oxidoreductase-Catalyzed Reactions

Oxidoreductases (EC 1) enable asymmetric reductions, oxygen insertions, and dehydrogenations critical to pharmaceutical and fine-chemical synthesis. Alcohol dehydrogenases (ADHs)/ketoreductases (KREDs) are heavily used for stereoselective reduction of prochiral ketones to chiral alcohols, typically coupled to NAD(P)H regeneration systems (e.g., glucose dehydrogenase or formate dehydrogenase) to be cost-effective at scale (Eskandari et al., 2024). Monooxygenases (including BVMOs and P450s) catalyze selective Baeyer–Villiger oxidations and C–H hydroxylations, offering site-selective oxygenations that are often challenging chemically (Gilio et al., 2021). Unspecific peroxygenases (UPOs) have recently attracted attention because they use H<sub>2</sub>O<sub>2</sub> directly (avoiding expensive nicotinamide cofactors) and perform regioselective oxyfunctionalizations under relatively mild conditions (Hobisch and Hollmann, 2021). Practical challenges for oxidoreductases remain cofactor dependency and oxidative damage (for peroxygenases and P450s); hybrid solutions (efficient cofactor recycling, in situ H<sub>2</sub>O<sub>2</sub> generation, electroenzymatic regeneration) are active areas of process development (Hobisch et al., 2021).



**Figure 1.** Examples of lipase-mediated esterification, hydrolysis, and transesterification reactions. This diagram illustrates typical lipase-catalyzed reactions, including esterification, hydrolysis, and transesterification. Lipases catalyze the formation and cleavage of ester bonds between fatty acids and alcohols, functioning efficiently in both aqueous and non-aqueous environments to produce esters, fatty acids, and alcohol derivatives

Source: Tan and Dou (2020)

### 3.3 Transferase-Catalyzed Reactions

Transferases (EC 2) effect the transfer of functional groups, enabling vital C–N and C–O bond constructions. Aminotransferases (transaminases) have become workhorses for producing chiral amines from ketones, allowing access to enantiopure amines without stoichiometric chiral auxiliaries or stoichiometric reducing agents; industrially notable examples include transaminase-mediated routes to pharmaceutical intermediates (Kelly et al., 2020). Glycosyltransferases and engineered glycosidases enable selective glycosylation and glycodiversification of natural products, improving solubility and bioactivity profiles (Desmet and Soetaert, 2011). Methyltransferases and other group-transfer enzymes are increasingly exploited for late-stage functionalization, leveraging SAM or engineered SAM mimics for regioselective methylation (Bornscheuer et al., 2019). Limitations include cofactor supply (e.g., PLP for transaminases, UDP-sugars for

glycosyltransferases) and narrow natural substrate scopes; these are being addressed via cascade designs that regenerate cofactors in situ and by enzyme engineering to broaden acceptor tolerance (Kelly et al., 2020).

### 3.4 Lyase- and Isomerase-Catalyzed Reactions

Lyases (EC 4) and isomerases (EC 5) mediate C–C bond formation, eliminations and rearrangements with exquisite stereocontrol. Aldolases catalyze stereoselective aldol couplings, producing polysubstituted stereocenters difficult to assemble chemically; modern engineered aldolases have improved substrate scope and stability making them attractive for statin side-chain and carbohydrate analog synthesis. Decarboxylases can provide enolate equivalents for C–C bond formation in umpolung strategies, while racemases/epimerases facilitate stereochemical interconversions used in dynamic kinetic resolution schemes. Compared with hydrolases and oxidoreductases, these classes have been less exploited industrially but are increasingly used in cascade sequences to

assemble complex architectures in fewer steps (Quin et al., 2017).

### 3.5 Ligase-Catalyzed Reactions

Ligases (EC 6) catalyze bond formation coupled to nucleotide triphosphate hydrolysis and are central to peptide and complex natural-product assembly. Recent development of peptide ligases (e.g., asparaginyl ligases, sortases, butelase) and engineered enzyme variants has opened efficient, site-selective peptide ligation and protein conjugation strategies that avoid protecting groups and harsh coupling chemistries (Frazier et al., 2020). These ligases are increasingly used in late-stage peptide modification and in semi-synthetic protein engineering workflows; their cofactor independence (for some ligases) and high chemoselectivity make them powerful for

biopharmaceutical manufacture. The main barriers remain substrate specificity and the requirement, in some systems, for molecular recognition sequences that must be engineered into substrates (Narayanan et al., 2022).

### 4. Strategies for Enhancing Biocatalytic Performance

Enzyme performance is often constrained by stability, substrate scope, solvent tolerance, cofactor dependency, and operational conditions. To unlock the full potential of biocatalysis in organic synthesis, recent years have seen intensive development of engineering, computational, immobilization, and process strategies. The following subsections describe leading advances with verified literature.

**Table 2. Representative biocatalytic reactions, typical conditions and benefits**

Reaction Class	Representative enzyme(s)	Typical conditions (solvent/temp/cofactors)	Key synthetic/sustainability benefit	References
Asymmetric reduction	KRED / ADH	Aqueous/MeOH, 20–30 °C, NAD(P)H (recycled)	High ee; mild conditions, low waste	Hollmann et al., 2011
Transamination	$\omega$ -Transaminase	Aqueous/buffer 25–40 °C, PLP cofactor, amine donor	Direct chiral amine access; avoids chiral auxiliaries	Savile et al., 2010; Kelly et al., 2020
Esterification / transesterification	Lipase (e.g., CAL-B)	Low water activity, organic solvent or solvent-free, 25–60 °C	High regio/enantioselectivity; mild processing	Sheldon and Woodley, 2018
Selective C–H oxyfunctionalization	Peroxygenase / P450	Buffer or biphasic, 20–30 °C, H <sub>2</sub> O <sub>2</sub> or O <sub>2</sub>	Site-selective oxidations using benign oxidants	Hobisch et al., 2021

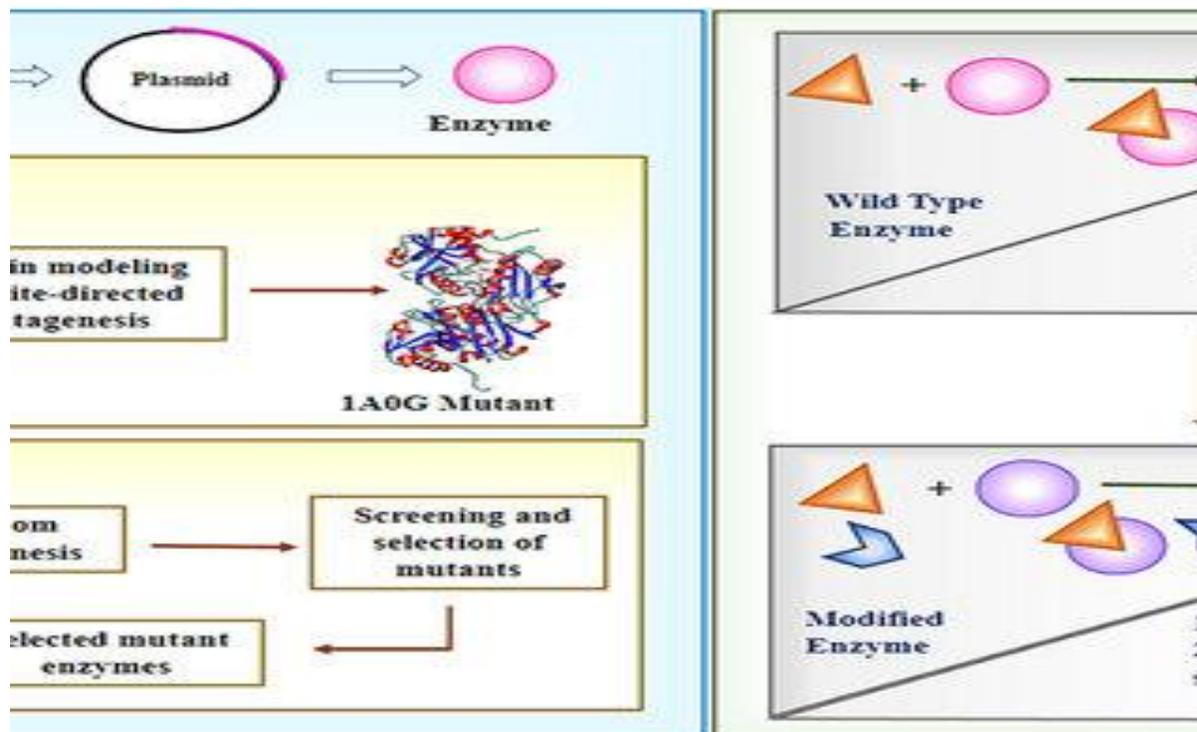
#### 4.1 Protein engineering and directed evolution

Protein engineering, both rational design and directed evolution, remains central to improving enzyme thermostability, substrate specificity, activity under non-native conditions, and enantioselectivity. For example, Zhou and Huang (2024) reviewed structure-based design and machine

learning models to efficiently explore enzyme sequence-function landscapes and optimize catalysis. These approaches have improved enzyme activity under elevated temperature and altered substrate scope. Directed evolution continues to be used in laboratories and industry to generate enzyme variants with enhanced performance under process conditions (Li and Cirino, 2014).

#### 4.2 Computational Biocatalysis and AI-driven Enzyme Design

Recent reviews emphasize the growing role of artificial intelligence (AI) and molecular simulation tools in de novo enzyme design, catalytic stability optimization, and high-throughput variant prediction. The Oxford review “A review of enzyme design in catalytic stability by artificial intelligence” (2023) details methods using models such as AlphaFold2, FireProt, ProteinMPNN, etc., to predict stability metrics ( $\Delta T_m$ ,  $\Delta \Delta G$ , etc.), helping target mutations for enhanced robustness (Ming et al., 2023). Similarly, generative AI models are emerging for enzyme design validated experimentally, with attention to folding, catalytic site geometry, and functional outputs.



**Figure 2.** Protein Engineering tools employed for Biocatalysis. This diagram highlights key protein engineering tools used in biocatalysis. These techniques enable the modification of enzyme structure and function to improve stability, specificity, and catalytic efficiency for various industrial and synthetic applications.

Source: Vikhrankar *et al.* (2024)

### 4.3 Cofactor Engineering and Recycling

Many enzyme-catalyzed reactions, especially oxidoreductases and dehydrogenases, depend on cofactors such as NAD(P)H, FAD, etc. Engineering strategies aim to reduce cofactor cost and dependency via efficient recycling or cofactor retention. The mini-review “Cofactor and Process Engineering for Nicotinamide Recycling and Retention in Intensified Biocatalysis” (Rocha *et al.*, 2022) describes methods to retain,

recycle or chemically modify nicotinamide cofactors for intensified continuous or flow biocatalysis. Additionally, broader landmark discoveries in cofactor regeneration are discussed in Biocatalysis: landmark discoveries and applications in chemical synthesis (RSC 2024), which highlights cofactor recycling as a key requirement for industrial scale-up (Connell *et al.*, 2024).

**Table 3. Cofactor regeneration strategies: methods, pros/cons, examples**

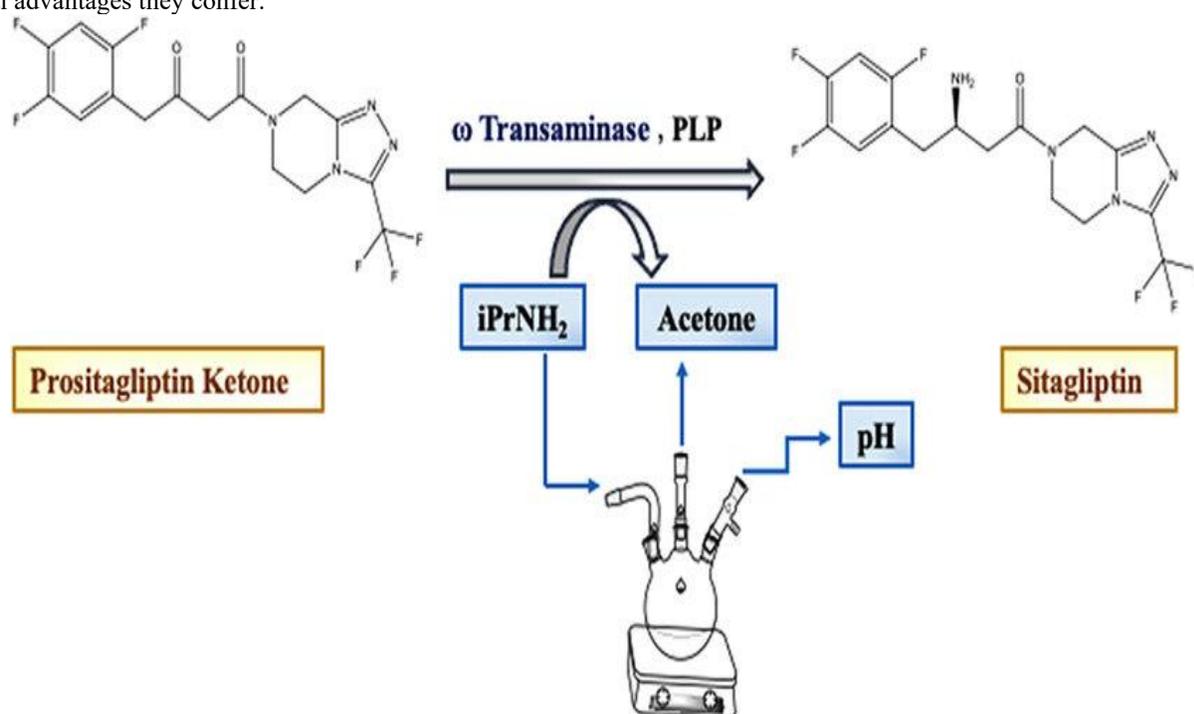
Regeneration strategy	Example System	Primary advantages	Key Limitation	References
Enzymatic recycling (auxiliary dehydrogenase)	Formate dehydrogenase (FDH) for NADH; glucose dehydrogenase (GDH) for NADPH	High specificity; simple operation	By-product management (CO <sub>2</sub> , gluconate); cost of sacrificial substrate	Hollmann <i>et al.</i> , 2020; Tufvesson <i>et al.</i> , 2010
Substrate-coupled (stoichiometric donor)	2-propanol with ADH	Cheap donor; drives equilibrium	Requires removal of co-product (acetone)	Hollmann <i>et al.</i> , 2020
Electrochemical regeneration	Cathodic NAD(P) <sup>+</sup> reduction at electrode	No enzyme required; controllable	Electrode fouling, integration complexity	Hollmann <i>et al.</i> , 2020
Photochemical / photocatalytic	Photoenzymatic systems (sensitizer + reductant)	Uses light; potential sustainability	Complexity, photostability issues	Hollmann <i>et al.</i> , 2020

#### 4.4 Immobilization, Solvent Systems, and Flow Biocatalysis

Immobilization of enzymes on solid supports or within materials has regained momentum due to its benefits: enhanced enzyme stability, easier separation and reuse, tolerance to harsh solvents and elevated temperature, and compatibility with flow reactors. Federsel, Moody, & Taylor (2021) surveyed recent trends in enzyme immobilization, including concepts of novel carriers and support systems. Organic–inorganic frameworks, graphene-based supports, MOFs and nanomaterials are being used to improve mass transfer, loading capacity, and cost efficiency. Flow biocatalysis is being paired with such immobilization methods to allow continuous processes with enhanced productivity and lower environmental impact (Tadesse and Liu, 2025).

#### 5. Applications of Biocatalysis in Organic Synthesis

Biocatalysis has transitioned from academic demonstration to industrial practice across multiple sectors. The intrinsic selectivity and mild-operating profiles of enzymes reduce synthetic complexity, lower environmental burden, and enable access to molecular architectures that can be difficult or inefficient to obtain by classical chemistry. Below we discuss four major application domains — pharmaceuticals, fine chemicals and flavors, bio-based polymers and renewable chemicals, and natural product/alkaloid synthesis highlighting how enzymatic methods have been implemented and the practical advantages they confer.



**Figure 3:**  $\omega$ -Transaminase catalyzed reaction for the sitagliptin synthesis. This diagram depicts the  $\omega$ -transaminase-catalyzed synthesis of sitagliptin, where the enzyme facilitates the stereoselective amination of a ketone precursor to produce the chiral amine intermediate. **Source:** Vikhrankar *et al.* (2024)

#### 5.1 Pharmaceutical Industry

The pharmaceutical sector has been a major driver for the adoption of biocatalysis because of the sector's premium on stereochemical purity, regulatory pressure to reduce toxic impurities, and strong incentives to streamline synthetic routes. A landmark industrial example is the transaminase-based synthesis of a key intermediate in the manufacture of the antidiabetic drug sitagliptin: Merck and Codexis developed an engineered  $\omega$ -transaminase that replaced a rhodium-catalyzed asymmetric hydrogenation, delivering the desired enantiomer with high enantiomeric excess and substantially improved process sustainability (Savile *et al.*, 2010). More generally, reviews of industrial biocatalysis document numerous examples in which ketoreductases, transaminases, lipases, and monooxygenases have been integrated into GMP-compatible routes to active pharmaceutical ingredients (APIs) and intermediates, reducing step count, waste, and reliance on precious metals (Sheldon and Woodley, 2018; Wu *et al.*, 2021). These transformations are often accompanied by cofactor-recycling schemes and process intensification (immobilization, flow reactors) to meet regulatory and throughput requirements.

## 5.2 Fine Chemicals and Flavors

Enzymatic methods are widely used in the synthesis of fine chemicals and flavor/fragrance compounds, where product purity and stereoisomer composition are critical for sensory properties. Hydrolases (lipases, esterases) are commonly employed for esterification and transesterification to produce flavor esters and aroma compounds under mild, solvent-minimized conditions (Wu et al., 2021). The operational simplicity of many hydrolase processes (e.g., low temperature, benign media) reduces byproduct formation and downstream purification efforts, which is especially valuable for high-value small-volume products.

## 5.3 Bio-based Polymers and Renewable Chemicals

Biocatalysis contributes to the growing bioeconomy by enabling synthesis of monomers and polymer precursors from renewable feedstocks. Enzymatic polymerizations and enzyme-catalyzed functionalization of biomass-derived intermediates offer routes to polyesters, polyamides, and other materials with reduced fossil-carbon content. Reviews and perspectives note the role of lipases and cutinases in polyester synthesis and of engineered enzymes for converting platform molecules (e.g., 5-HMF) into polymer building blocks, facilitating more sustainable materials production (Sheldon

and Woodley, 2018; Wu et al., 2021). Integration with biorefinery concepts allows coupling of enzymatic steps to biomass valorization streams, improving overall resource efficiency.

## 5.4 Natural Product and Alkaloid Synthesis

Enzymes have been incorporated into total syntheses and semi-synthetic routes to complex natural products and alkaloids, particularly for late-stage functionalizations that require site- and stereoselectivity. Biocatalytic oxidations, glycosylations, and C–C bond formations can obviate protecting-group strategies and simplify synthetic sequences. Reviews of synthetic methods report multiple examples where single enzymatic steps such as a selective hydroxylation or an enzymatic glycosylation dramatically shorten routes and improve stereochemical outcomes (Paddon and Keasling, 2014; Wu et al., 2021). Such chemoenzymatic strategies combine the breadth of chemical methods with the precision of biology to access complex scaffolds more efficiently.

## 5.5 Biocatalysis in Green and Sustainable Chemistry

Biocatalysis has become an indispensable pillar of modern green chemistry, offering environmentally benign alternatives to traditional chemical catalysis. Enzymes, as biocatalysts, facilitate reactions under mild conditions of temperature and pressure, in aqueous or non-toxic solvents, and with exceptional chemo-, regio-, and stereoselectivity (Sheldon and Woodley, 2018). This high selectivity reduces the need for protecting groups, auxiliary reagents, and extensive

purification, which are typically associated with waste generation in conventional chemical processes. Consequently, biocatalysis embodies several of the Twelve Principles of Green Chemistry, including energy efficiency, waste minimization, and the use of renewable feedstocks (Sheldon, 2021).

In the context of sustainable industrial manufacturing, enzymatic processes are increasingly integrated into the synthesis of pharmaceuticals, fine chemicals, agrochemicals, and bio-based materials. Advances in protein engineering and directed evolution have enabled the tailoring of enzymes to perform reactions beyond their natural scope, significantly broadening their industrial applicability. For instance, transaminases, ketoreductases, and lipases have been engineered to catalyze stereoselective transformations in complex organic synthesis with high yields and reduced environmental burdens (Woodley, 2019). The incorporation of biocatalysis into process design has led to enhanced process efficiency and reduced ecological footprints compared to purely chemical routes.

A key measure of sustainability is the life cycle assessment (LCA), which evaluates the overall environmental impact of a process from raw material acquisition to product disposal. LCA studies consistently show that biocatalytic routes exhibit lower E-factors (mass of waste generated per mass of product) and carbon footprints compared with conventional chemical syntheses (Sheldon, 2021). For example, an enzymatic oxidation route for pharmaceutical intermediates has been demonstrated to reduce greenhouse gas emissions and energy consumption by over 40% relative to chemical oxidation processes (Woodley, 2019). This evidence reinforces the role of biocatalysis as not only a technological innovation but also a sustainable intervention in the pursuit of greener industrial chemistry.

Biocatalysis also enhances atom economy and minimizes waste by enabling direct conversions without stoichiometric reagents or hazardous by-products (Tufvesson et al., 2013). Process intensification strategies such as flow biocatalysis and enzyme immobilization have further improved catalytic performance, scalability, and reusability (Federsel et al., 2021). Immobilized enzymes can be reused for multiple reaction cycles, thereby reducing material waste and production costs. These developments align closely with the circular economy model, in which resources are reused and recycled to minimize environmental degradation.

Another emerging aspect of sustainable biocatalysis is the integration of enzymes with green solvent systems and renewable feedstocks. Conventional organic solvents are being replaced by greener alternatives such as water, ionic liquids, and deep eutectic solvents (DESSs), which not only improve enzyme stability but also enhance substrate solubility and recyclability (Toledo Hijo et al. 2022). Furthermore, coupling biocatalytic processes with renewable raw materials, such as lignocellulosic biomass or glycerol from biodiesel production,

provides a sustainable pathway for the generation of high-value chemicals (Hobisch et al., 2021). The convergence of enzymatic catalysis with renewable feedstocks and environmentally benign solvents has thus established biocatalysis as a central strategy in achieving carbon-neutral and resource-efficient chemical production.

In alignment with global sustainability objectives, biocatalysis contributes significantly to the United Nations Sustainable Development Goals (SDGs), particularly those targeting responsible consumption and production (SDG 12), industry and innovation (SDG 9), and climate action (SDG 13). By enabling low-emission and low-waste processes, biocatalysis fosters industrial innovation while conserving natural resources (Bornscheuer et al., 2012). As the chemical industry continues to evolve toward decarbonization and circularity,

enzyme-driven processes will play an essential role in achieving sustainable and resilient production systems.

In summary, biocatalysis represents a powerful convergence of biological precision and environmental stewardship. It not only provides efficient routes to complex molecules but also offers scalable, safe, and economically viable alternatives to traditional catalysis. With ongoing advancements in enzyme engineering, computational design, and bioprocess intensification, the scope and sustainability of biocatalysis will continue to expand, reinforcing its role as a cornerstone of green

**Table 5. Sustainability metrics: enzymatic vs. conventional chemical routes (representative case studies)**

Case (example)	Conventional chemical route	Biocatalytic route	Relative sustainability metric (qualitative)	References
Chiral amine synthesis (sitagliptin intermediate)	Rh-catalyzed hydrogenation, high metal use	$\omega$ -Transaminase (engineered)	Lower metal usage, lower waste, improved E-factor (biocatalysis better)	Savile et al., 2010; Sheldon and Woodley, 2018
Ester synthesis (flavor esters)	Acid or base catalysis at elevated T	Lipase catalysis at mild T	Reduced by-products and energy demand	Sheldon and Woodley, 2018
Selective hydroxylation	Stoichiometric oxidant / harsh conditions	Peroxygenase using $H_2O_2/O_2$	Lower overoxidation, improved atom economy	Hobisch et al., 2021

## 6. Challenges and Limitations

Despite the significant advancements in biocatalysis, several challenges continue to limit its widespread adoption in industrial organic synthesis. One of the primary barriers is the cost and availability of enzymes at scale. Although recombinant expression systems have reduced production costs, large-scale enzyme manufacturing still requires extensive downstream purification and stabilization processes, which remain expensive (Sheldon and Woodley, 2018). Furthermore, the short operational lifespan of enzymes under non-native or harsh reaction conditions such as extreme temperatures, high substrate concentrations, or organic solvents significantly reduces their industrial feasibility (Wu et al., 2021).

Another limitation lies in the restricted substrate scope and solvent tolerance of many enzymes. Native enzymes often exhibit narrow substrate specificity, restricting their application to a limited range of compounds (Bornscheuer et al., 2019). While protein engineering and directed evolution have expanded enzyme diversity, the process is still resource-intensive and unpredictable (Arnold, 2018). Similarly, enzyme deactivation in organic or biphasic solvent systems remains a persistent issue, particularly for hydrophobic substrates and non-aqueous catalysis (Stepankova et al., 2013).

Cofactor dependency is another major limitation for oxidoreductases and transferases, as enzymatic redox reactions often require stoichiometric cofactors such as NADH or NADPH. Continuous regeneration of these cofactors adds additional complexity and cost to large-scale operations (Hollmann et al., 2011). Synthetic cofactor analogues and electrochemical regeneration systems are promising, but their industrial implementation remains limited due to compatibility issues and scalability challenges (Zhang et al., 2018).

Process scale-up also poses substantial difficulties. Translating biocatalytic reactions from the laboratory to pilot or production scale is nontrivial due to differences in mixing, oxygen transfer, and heat management (Woodley, 2019). Furthermore, integrating multi-enzyme cascades for complex molecule synthesis requires precise control of enzyme ratios and reaction kinetics, which can be challenging to maintain under industrial conditions (Bornscheuer et al., 2012).

Lastly, regulatory and operational challenges including enzyme stability during storage, batch-to-batch reproducibility, and process validation—continue to slow down industrial adaptation. While biocatalysis aligns well with the principles of green chemistry, overcoming these technological and economic barriers is critical to its full realization as a sustainable platform for organic synthesis (Clouthier and Pelletier, 2019).

## 7. Future Perspectives

The future of biocatalysis in organic synthesis is poised for remarkable expansion, driven by advances in enzyme engineering, computational biology, and systems integration. The convergence of synthetic biology and biocatalysis is enabling the construction of tailor-made enzymatic cascades capable of performing complex multi-step reactions with exceptional precision (Wu et al., 2021). The integration of cell-free systems and artificial enzyme assemblies provides a flexible and controllable alternative to whole-cell biotransformations, reducing undesired side reactions and improving yields (Sheldon and Brady, 2019).

Another transformative development is the application of machine learning (ML) and artificial intelligence (AI) for enzyme discovery, design, and optimization. By training models on massive biochemical and structural datasets, AI has begun predicting enzyme–substrate interactions, catalytic efficiencies, and thermostability profiles with unprecedented accuracy. This approach shortens the experimental design cycle and facilitates de novo enzyme generation, a key enabler for scaling biocatalysis in industrial applications (Bornscheuer et al., 2018). Similarly, quantum mechanical simulations and molecular dynamics now assist in understanding transition-state stabilization and catalytic mechanisms, bridging the gap between theoretical enzymology and practical process design (Rudroff et al., 2018).

Looking forward, hybrid catalytic systems—integrating chemo-, photo-, and biocatalysis offer exciting prospects for sustainable synthesis. Such systems combine the selectivity of enzymes with the versatility of chemical catalysts or light-driven activation processes, allowing sequential or concurrent reactions in single-pot processes (Hobisch et al., 2021). Meanwhile, the rise of flow biocatalysis and microreactor technologies is improving reaction efficiency, scalability, and product quality under continuous operation.

At the industrial scale, the adoption of AI-driven process analytics, enzyme immobilization on advanced nanomaterials, and modular reactor platforms will further enhance productivity and reproducibility. Moreover, coupling biocatalysis with renewable feedstocks and green solvents such as deep eutectic solvents and supercritical fluids will strengthen its role in achieving carbon-neutral manufacturing and advancing several UN Sustainable Development Goals (SDGs) (Sheldon, 2021).

In essence, the next decade of biocatalysis will be characterized by its full integration into digital and sustainable chemistry frameworks, transforming it from a specialized niche to a core enabling technology for precision synthesis and green manufacturing.

## Conclusion

Biocatalysis has emerged as a vital technology in sustainable organic synthesis, offering high selectivity, mild operating conditions, and reduced environmental impact. Advances in enzyme engineering, computational design, and process optimization have significantly broadened its industrial applications, especially in pharmaceuticals and fine chemicals. Despite these achievements, challenges such as enzyme instability, limited substrate scope, and high production costs still hinder wider industrial adoption. Addressing these issues will depend on integrating machine learning, directed evolution, and continuous flow technologies to enhance enzyme efficiency and scalability. In summary, biocatalysis continues to transform modern chemistry by aligning innovation with sustainability. With ongoing interdisciplinary collaboration, it is poised to remain a cornerstone of green and precision chemical manufacturing.

## Authors' Contributions

The authors of this research have significantly contributed to the study's conception, data collection, and manuscript development. All authors were involved in writing the manuscript or critically reviewing it for its intellectual value. They have reviewed and approved the final version for submission and publication and accept full responsibility for the content and integrity of the work.

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## Conflict of Interest

The authors declared that there are no conflicts of interest.

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## References

- Arnold F. H. (2018). Directed Evolution: Bringing New Chemistry to Life. *Angewandte Chemie*. 57(16); 4143–4148. <https://doi.org/10.1002/anie.201708408>
- Bisswanger, H. (2017). *Enzyme kinetics: Principles and methods* (3rd ed.). Wiley-VCH
- Bornscheuer U. T. (2018). The fourth wave of biocatalysis is approaching. *Philosophical transactions. Series A, Mathematical, physical, and engineering sciences*. 376(2110); 20170063. <https://doi.org/10.1098/rsta.2017.0063>
- Bornscheuer, U. T., Hauer, B., Jaeger, K. E. and Schwaneberg, U. (2019). Directed Evolution Empowered Redesign of Natural Proteins for the Sustainable Production of Chemicals and Pharmaceuticals. *Angewandte Chemie*. 58(1); 36–40. <https://doi.org/10.1002/anie.201812717>.
- Bornscheuer, U. T., Huisman, G. W., Kazlauskas, R. J., Lutz, S., Moore, J. C. and Robins, K. (2012). Engineering the third wave of

- biocatalysis. *Nature*. 485(7397); 185–194. <https://doi.org/10.1038/nature11117>
- Britton, J., Majumdar, S. and Weiss, G. A. (2018). Continuous flow biocatalysis. *Chemical Society Reviews*. 47(15); 5891–5918. <https://doi.org/10.1039/C7CS00906B>
- Clouthier, C. M. and Pelletier, J. N. (2019). Expanding the organic toolbox: A guide to integrating biocatalysis in synthesis. *Chemical Society Reviews*. 41; 1585–1605. <https://doi.org/10.1039/C2CS15286J>
- Connell, A. O., Barry, A., Burke, A. J., Hutton, A. E., Bell, E. L., Green, A. P. and Elaine O. R. (2024). Biocatalysis: landmark discoveries and applications in chemical synthesis. *Chem. Soc. Rev.* 53; 2828–2850.
- Desmet, T. and Soetaert, W. (2011). Enzymatic glycosyl transfer: Mechanisms and applications. *Biocatalysis and Biotransformation*. 29(1):1-18. DOI:10.3109/10242422.2010.548557
- Dos Santos, L. N., Perna, R. F., Vieira, A. C., de Almeida, A. F. and Ferreira, N. R. (2023). Trends in the Use of Lipases: A Systematic Review and Bibliometric Analysis. *Foods*. 12(16); 3058. <https://doi.org/10.3390/foods12163058>
- Eskandari, A., Leow, T. C., Rahman, M. B. A. and Oslan, S. N. (2024). Recent insight into the advances and prospects of microbial lipases and their potential applications in industry. *International microbiology : the official journal of the Spanish Society for Microbiology*. 27(6); 1597–1631. <https://doi.org/10.1007/s10123-024-00498-7>
- Federsel, H. J. and Moody, T. S. and Taylor, S. J. C. (2021). Recent Trends in Enzyme Immobilization—Concepts for Expanding the Biocatalysis Toolbox. *Molecules*. 26(9); 2822. <https://doi.org/10.3390/molecules26092822>
- Fersht, A. R. (2017). *Structure and mechanism in protein science: A guide to enzyme catalysis and protein folding* (2nd ed.). W. H. Freeman.
- Frazier, C. L. and Weeks, A. M. (2020). Engineered peptide ligases for cell signaling and bioconjugation. *Biochemical Society transactions*. 48(3); 1153–1165. <https://doi.org/10.1042/BST20200001>
- Garcia-Viloca, M., Gao, J., Karplus, M. and Truhlar, D. G. (2004). How enzymes work: analysis by modern rate theory and computer simulations. *Science (New York, N.Y.)*, 303(5655); 186–195. <https://doi.org/10.1126/science.1088172>
- Gilio, A. K., Thorpe, T., Turner, N.J. and Grogan, G. (2021). Reductive Aminations by Imine Reductases: From Milligrams to Tons. *Chemical Science*. 13(3). DOI:10.1039/D2SC00124A
- Hobisch, M., Holtmann, D., Gomez de Santos, P., Alcalde, M., Hollmann, F. and Kara, S. (2021). Recent developments in the use of peroxygenases - Exploring their high potential in selective oxyfunctionalisations. *Biotechnology advances*. 51; 107615. <https://doi.org/10.1016/j.biotechadv.2020.107615>
- Hollmann, F., Arends, I. W. C. E., Buehler, K., Schallmeyer, A., & Bühler, B. (2011). Enzyme-mediated oxidations for the chemist. *Green Chemistry*. 13(2); 226–265. <https://doi.org/10.1039/C0GC00595A>
- Kelly, S. A., Mix, S., Moody, T. S. and Gilmore, B. F. (2020). Transaminases for industrial biocatalysis: novel enzyme discovery. *Applied microbiology and biotechnology*. 104(11); 4781–4794. <https://doi.org/10.1007/s00253-020-10585-0>
- Li, Y. and Cirino, P. C. (2014). Recent advances in engineering proteins for biocatalysis. *Biotechnology and bioengineering*. 111(7); 1273–1287. <https://doi.org/10.1002/bit.25240>
- Ming, Y., Wang, W., Yin, R., Zeng, M., Tang, L., Tang, S. and Li, M. (2023). A review of enzyme design in catalytic stability by artificial intelligence. *Briefings in Bioinformatics*. 24(3). <https://doi.org/10.1093/bib/bbad065>
- Narayanan, K. B. and Han, S. S. (2022). Peptide ligases: A Novel and potential enzyme toolbox for catalytic cross-linking of protein/peptide-based biomaterial scaffolds for tissue engineering. *Enzyme and microbial technology*. 155; 109990. <https://doi.org/10.1016/j.enzmictec.2022.109990>
- Paddon, C. J. and Keasling, J. D. (2014). Semi-synthetic artemisinin: a model for the use of synthetic biology in pharmaceutical development. *Nature reviews. Microbiology*. 12(5); 355–367. <https://doi.org/10.1038/nrmicro3240>
- Quin, M. B., Wallin, K., Zhanga, G. and Schmidt-Dannert, C. (2017). Spatial organization of multi-enzyme biocatalytic cascades. *Organic & Biomolecular Chemistry*. 15; 4260–4271. <https://doi.org/10.1039/C7OB00391A>
- Reetz M. T. (2013). Biocatalysis in organic chemistry and biotechnology: past, present, and future. *Journal of the American Chemical Society*. 135(34); 12480–12496. <https://doi.org/10.1021/ja405051f>
- Rocha, R., North, A. J., Speight, R. E., Williams, C. C. and Scott, C. (2022). Cofactor and Process Engineering for Nicotinamide Recycling and Retention in Intensified Biocatalysis. *Catalysts*. 12(11). 10.3390/catal12111454
- Rudroff, F., Mihovilovic, M. D., Gröger, H., Snajdrova, R., Iding, H. and Bornscheuer, U. T. (2018). Opportunities and challenges for combining chemo- and biocatalysis. *Nature Catalysis*. 1(1); 12–22. <https://doi.org/10.1038/s41929-017-0010-4>
- Savile, C. K., Janey, J. M., Mundorff, E. C., Moore, J. C., Tam, S., Jarvis, W. R., Colbeck, J. C., Krebber, A., Fleitz, F. J., Brands, J., Devine, P. N., Huisman, G. W. and Hughes, G. J. (2010). Biocatalytic asymmetric synthesis of chiral amines from ketones applied to sitagliptin manufacture. *Science*. 329(5989); 305–309. <https://doi.org/10.1126/science.1188934>
- Schrittweiser, J. H., Velikogne, S., Hall, M. and Kroutil, W. (2018). Artificial Biocatalytic Linear Cascades for Preparation of Organic Molecules. *Chemical reviews*. 118(1); 270–348. <https://doi.org/10.1021/acs.chemrev.7b00033>
- Senn, H. M. and Thiel, W. (2009). QM/MM methods for biomolecular systems. *Angewandte Chemie*. 48(7); 1198–1229. <https://doi.org/10.1002/anie.200802019>
- Sheldon, R. A. (2021). Metrics of green chemistry and sustainability: Past, present, and future. *ACS Sustainable Chemistry & Engineering*. 6(1); 7602–7612. <https://doi.org/10.1021/acssuschemeng.1c01791>
- Sheldon, R. A. and Brady, D. (2019). Broadening the Scope of Biocatalysis in Sustainable Organic Synthesis. *ChemSusChem*. 12(13); 2859–2881. <https://doi.org/10.1002/cssc.201900351>
- Sheldon, R. A. and Woodley, J. M. (2018). Role of Biocatalysis in Sustainable Chemistry. *Chemical reviews*. 118(2); 801–838. <https://doi.org/10.1021/acs.chemrev.7b00203>
- Stepankova, V., Bidmanova, S., Koudelakova, T., Prokop, Z., Chaloupkova, R. and Damborsky, J. (2013). Strategies for stabilization of enzymes in organic solvents. *ACS Catalysis*. 3(12); 2823–2836. <https://doi.org/10.1021/cs400684x>
- Tadesse, M. and Liu, Y. (2025). Recent Advances in Enzyme Immobilization: The Role of Artificial Intelligence, Novel Nanomaterials, and Dynamic Carrier Systems. *Catalysts*. 15(6); 571. <https://doi.org/10.3390/catal15060571>
- Tan, J. N. and Dou, Y. (2020). Deep eutectic solvents for biocatalytic transformations: focused lipase-catalyzed organic reactions. *Applied Microbiology and Biotechnology*. 104(8). DOI: 10.1007/s00253-019-10342-y
- Toledo Hijo, A. A. C., Alves, C., Farias, F. O., Peixoto, V. S., Meirelles, A. J. A., Santos, G. H. F. and Maximo, G. J. (2022).

- Ionic liquids and deep eutectic solvents as sustainable alternatives for efficient extraction of phenolic compounds from mate leaves. *Food research international*. 157; 111194. <https://doi.org/10.1016/j.foodres.2022.111194>
- Tufvesson, P., Lima-Ramos, J., Nordblad, M. and Woodley, J. M. (2010). Guidelines and cost analysis for catalyst production in biocatalytic processes. *Organic Process Research & Development*. 15(1). DOI:10.1021/op1002165.
- Vikhrankar, S. S., Satbhai, S., Kulkarni, P. and Ranbhor, R. (2024). Enzymatic Routes for Chiral Amine Synthesis: Protein Engineering and Process Optimization. *Targets and Therapy*. 18:165-179. DOI:10.2147/BTT.S446712
- Warshel, A. and Bora, R. P. (2016). Perspective: Defining and quantifying the role of dynamics in enzyme catalysis. *The Journal of chemical physics*. 144(18); 180901. <https://doi.org/10.1063/1.4947037>
- Webb, E. C. (2022). *Enzyme nomenclature 2022: Recommendations of the International Union of Biochemistry and Molecular Biology*. Academic Press.
- Woodley J. M. (2019). Accelerating the implementation of biocatalysis in industry. *Applied microbiology and biotechnology*. 103(12); 4733–4739. <https://doi.org/10.1007/s00253-019-09796-x>
- Wu, S., Snajdrova, R., Moore, J. C., Baldenius, K. and Bornscheuer, U. T. (2021). Biocatalysis: Enzymatic Synthesis for Industrial Applications. *Angewandte Chemie*. 60(1); 88–119. <https://doi.org/10.1002/anie.202006648>
- Wu, S., Snajdrova, R., Moore, J. C., Baldenius, K. and Bornscheuer, U. T. (2021). Biocatalysis: Enzymatic Synthesis for Industrial Applications. *Angewandte Chemie*. 60(1); 88–119. <https://doi.org/10.1002/anie.202006648>
- Xu, P., Zheng, G.W., Zong, M. H., Li, N. and Lou, W.Y. (2017). Recent progress on deep eutectic solvents in biocatalysis. *ChemCatChem*. 9(22); 2940–2947. <https://doi.org/10.1002/cctc.201700546>
- Yang, Y., Wu, N. and Arnold, F. H. (2019). Machine-learning-guided directed evolution for protein engineering. *Nature Methods*. 16(8); 687–694. <https://doi.org/10.1038/s41592-019-0496-6>
- Yi, D., Bayer, T., Badenhorst, C. P. S., Wu, S., Doerr, M., Höhne, M. and Bornscheuer, U. T. (2021). Recent trends in biocatalysis. *Chemical Society Reviews*. 50(14); 8003–8049. <https://doi.org/10.1039/D0CS01575J>
- Zhang, W., Fernández-Fueyo, E., Ni, Y., van Schie, M., Gacs, J., Renirie, R., Wever, R. and Hollmann, F. (2018). Cofactor-free oxidations catalyzed by heme-dependent peroxidases. *Nature Catalysis*. 1(1); 55–62. <https://doi.org/10.1038/s41929-017-0008-3>
- Zhou, J. and Huang, M. (2024). Navigating the landscape of enzyme design: from molecular simulations to machine learning. *Chem. Soc. Rev.* 53; 8202-8239. DOI: 10.1039/D4CS00196F

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