

## Biocatalysis in Asia and the Pacific



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Biocatalysis has entered its Golden Age<sup>1</sup> with increasing adoption in organic chemistry,<sup>2</sup> pharmaceutical research and development,<sup>3</sup> and exciting new applications in biopharmaceuticals.<sup>4</sup> Interest is particularly growing in the Asia-Pacific area with its expanding population, urbanization, and rising disposable incomes which in turn drives the need for innovative green and sustainable chemical technologies that biocatalysis can provide [<https://www.unescap.org/projects/gd>]. This strong interest in new green technologies has caused a dramatic increase in fundamental research in biocatalysis, with large numbers of research groups from different disciplines entering the field. The breadth of research in biocatalysis in the Asia-Pacific area is showcased in this Virtual Special Issue, titled *Biocatalysis in Asia and Pacific*, which includes a snapshot of a collection of articles published in *JACS Au* in 2023/2024.

Despite many successes in the general application of biocatalysis in industry, there remain many fundamental scientific challenges, some of which are addressed in this selection of papers. One particular challenge concerns the need for expensive cofactors such as nicotinamides which are for example needed for reduction and oxidation reactions. A perspective describes the very elegant solution of “biocatalytic hydrogen borrowing”, which uses multistep sequences including dehydrogenation and hydrogenation in one pot by hydride shuffling between NAD(P)<sup>+</sup> and NAD(P)H [DOI: [10.1021/jacsau.4c00026](https://doi.org/10.1021/jacsau.4c00026)]. Another common challenge is active protein expression, and in a novel approach, unspecific peroxigenases have been successfully expressed using a superfolder-green-fluorescent protein in bacteria [DOI: [10.1021/jacsau.4c00129](https://doi.org/10.1021/jacsau.4c00129)]. For multistep biocatalytic processes, cellular engineering guided by proteomic analysis can dramatically increase product titers, as shown for the production of  $\alpha$ -bisabolene in yeast [DOI: [10.1021/jacsau.4c00106](https://doi.org/10.1021/jacsau.4c00106)].

An area of great interest is the design of reactions and reaction sequences beyond those found in nature. Some successful approaches shown here explore substrate promiscuity for challenging CO<sub>2</sub> fixation reactions [DOI: [10.1021/jacsau.4c00290](https://doi.org/10.1021/jacsau.4c00290)] or atroposelective synthesis of aldehydes [DOI: [10.1021/jacsau.3c00814](https://doi.org/10.1021/jacsau.3c00814)]. Alternatively, biocatalysis can be combined with chemical reactions in chemo-enzymatic strategies, including for example Au catalysis [DOIs: [10.1021/jacsau.4c00222](https://doi.org/10.1021/jacsau.4c00222), [10.1021/jacsau.3c00688](https://doi.org/10.1021/jacsau.3c00688)]. Such biocatalytic processes are not only applicable to the synthesis of target molecules but also in bioremediation strategies as demonstrated by removal of the toxic metabolite deoxynivalenol in plants [DOI: [10.1021/jacsau.3c00696](https://doi.org/10.1021/jacsau.3c00696)] and engineering of a

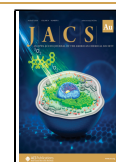
metal reductase for the bioremediation of anthropogenic electronic wastes [DOI: [10.1021/jacsau.4c00297](https://doi.org/10.1021/jacsau.4c00297)].

In addition to small molecule substrates, biocatalysis is also very attractive for larger biomolecules, such as complex glycoproteins that make up a significant number of the leading biopharmaceutical products. Glycoengineering using biocatalysis provides a tool for improving the therapeutic profile of antibodies, and using a structure-based design approach, an endoglycosidase was engineered to provide a novel toolbox for conjugating glycans to specific glycoprotein sites [DOI: [10.1021/jacsau.4c00004](https://doi.org/10.1021/jacsau.4c00004)]. Glycoengineering often requires sugar nucleotide cofactor regeneration systems, and one such example for UDP-Xylose has been designed as bifunctional chimeras to minimize the need for additional proteins and improved activity [DOI: [10.1021/jacsau.4c00288](https://doi.org/10.1021/jacsau.4c00288)].

Computational tools are making a great impact in biocatalysis, in particular in protein engineering, and it is interesting that several papers in this *Virtual Special Issue* make use of machine learning and modeling tools to find new and better activities: directed evolution and machine learning are used in combination to enhance the diastereoselectivity of a ketoreductase [DOI: [10.1021/jacsau.4c00284](https://doi.org/10.1021/jacsau.4c00284)]. Molecular dynamics simulations and quantum mechanical calculations have been used to redesign a P450 monooxygenase [DOI: [10.1021/jacsau.4c00075](https://doi.org/10.1021/jacsau.4c00075)]. Computational enzyme redesign has been used to find mutants of a lyase with enhanced tolerance to denaturants for peptide C-terminal amidation [DOI: [10.1021/jacsau.3c00792](https://doi.org/10.1021/jacsau.3c00792)]. Finally, density functional theory calculations and molecular dynamic simulations were used to identify and reduce energy barriers of key transition states to enhance C–N cleavage efficiency of an amino acid oxidase [DOI: [10.1021/jacsau.3c00672](https://doi.org/10.1021/jacsau.3c00672)].

It is striking how even a small collection of papers in biocatalysis from Asia and the Pacific showcases the engagement of a very diverse group of scientists in areas ranging from computational to synthetic chemistry, chemical biology, biochemistry, and synthetic biology to applications in engineering, cell biology, and medicine. Similarly diverse are the challenges addressed beyond the synthesis of bioactive compounds, driven by demands to solve societal problems in medicine with a more green and sustainable production of

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pharmaceutical and biopharmaceutical entities. There are also contributions from biocatalysis in directly solving environmental issues such as detoxification, removal of waste from the environment, and CO<sub>2</sub> fixation. This [Virtual Special Issue](#) clearly shows that the topic of biocatalysis is very actively pursued at the highest international level using leading experimental and computational tools. Biocatalysis is very important to Asia and the Pacific, and the community is well placed to solve many of the challenges that lie ahead.

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## Notes

Views expressed in this editorial are those of the authors and not necessarily the views of the ACS.

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