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# Industrial Biocatalysis: Targets, Barriers, and Needs

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The most important challenge in lots of labs in industry and academia today is how to search novel biosynthetic pathways and how to design new biomolecules efficiently. Industrial biocatalysts including whole cell or enzyme have become an important component of numerous processes and products. Four areas of interest identified by Chemical and pharmaceutical industries are (1) new catalysts use, (2) major yield and selectivity improvements, (3) cleaner technology implantation, and (4) innovative novel biosynthetic pathways. These industries focus on extremophiles, directed evolution (or molecular breeding), high-level enzyme expression, and new economic and commercially available bioprocess models. Implantation of functional genomics, proteomics, metabolic pathway analysis, and *de novo* protein evolution tools are complementary to biocatalyst engineering. Application of Genomics creates a new opportunity for the healthcare industry and chemical industries, given the early stage of genomic evolution. One of the main reasons to do Metabolic or biosynthetic pathway engineering is the efficiency and speed in developing synthetic routes to complex molecules. It may provide a simpler and speedier ways for chemically unattainable multi-step processes, which need frequent side chain blocking and separations. By mimicking key process of Darwinian evolution, which creates mutant genes and selects those with desired characteristics, enzyme or protein functions required in the industry can be explored. These Mutants of various industrial enzymes that efficiently catalyze substrates in an unnatural environment have been successfully generated with enhanced stability and altered specificity. Furthermore, simple and multiple screening methods based on the different high-throughput screening (HTS) formats selecting fluorescence and visible colors allow us to isolate mutants of altered properties.

In order to extend the mutant library searching rates, recently, we are developing computer-based random gene mutagenesis and screening models for enantioselectively hydrolyzing biocatalysts. Virtual screening (VS) is an alternative where the selection of enzymes with predicted properties is being attempted in the computer-based property-discriminating descriptors. In contrast to HTS, VS provides a key solution for experimental deficiencies, e.g., limited biological assay or other effects that can puzzle scientists (false-positives or non-specific reactions). VS can be applied to screen either existing enzyme libraries or computer-generated virtual gene libraries (the same actions could be demonstrated as error-prone PCR or DNA shuffling does). Accordingly $10^{60\text{-}300}$ mutant numbers can be generated and screened and the impressive numbers provides scientists quite optimistic and enthusiastic perspectives. Therefore, the development of reliable, transferable methods that compute the energy of interaction between proteins and ligands is a major challenge for future screening.

These powerful molecular breeding tools can be used to generate a variety of practical biocatalysts for essential chemical transformation and to screen genetic libraries isolated from the environment. In addition, biocatalysis opens up the possibility for the design of smaller catalytic units with the same or better economics. Industrial applications of this technology to a broad range of examples will be discussed.

## References

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