One-Shot Industrial Enzyme Design

From target reaction to decision-ready *de novo* catalysts in one compact cycle. By combining catalytic-motif scaffolding with state-of-the-art diffusion design and atomistic refinement we can offer de novo enzymes that can reach evolved-like activity and stereoselectivity with minimal screening, while retaining high thermal stability.

BACKGROUND

Finding or evolving a natural enzyme for a new reaction is slow, screening-intensive, and uncertain. Catalytic-motif scaffolding with pocket enforcement and iterative backbone/sequence refinement changes the starting point: active, enantioselective, and heat-stable de novo enzymes have been obtained for mechanistically distinct reactions after testing only a few dozen sequences. We acknowledge ranking limitations and address them with complex-based metrics and MD/QM triage to keep wet-lab effort focused.

TECHNOLOGY

In collaboration with the Graz University of Technology and based on a recent Nature publication this offer introduces a practical "one-shot" route: catalytic-motif scaffolding with a hybrid diffusion/atomistic pipeline (Riff-Diff) that places functional groups with near-atomic precision and enforces realistic binding pockets, then refining sequences and geometries iteratively (LigandMPNN, FastRelax, ESM/AlphaFold) before ligand-state ranking. The result is design sets where most candidates are folded, soluble, and measurably active, reducing time to a usable starting catalyst

In the paper's retro-aldol case, 35 designs were made; 91% were active, and top variants achieved kcat ≈3.1–3.7×10^{-2} s^{-1} (≈5×10^{6} rate acceleration), approaching the efficiency of extensively evolved references. In the aldol direction, enantioselectivity reached 99% ee, and most designs remained folded above 90 °C. A second, non-natural reaction (Morita–Baylis–Hillman) yielded active enzymes that outperformed small-molecule nucleophiles and, in one case, exceeded a variant obtained after eight rounds of evolution.

OFFER

acib translates this capability into an industry program tailored to your chemistry. You define the target reaction and constraints; we derive or select a catalytic array, generate a compact set of de novo designs, express and screen prioritized candidates, and deliver a decision-ready package: sequences and models, activity and selectivity data with agreed analytics, stability profiles, and a practical route for scale-up testing. Optional modules include wet-lab testing and transfer into your chassis and process. Work proceeds under NDA; project-specific results, data, and materials can be fully assigned to you.

Provide any IP or regulatory constraints up front, and we'll align the design strategy and timeline accordingly.

EXPERTS

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DEVELOPMENT STATUS:

Status of the project proposal – Technology Readiness Level 4 (technology validated in lab)

KEYWORDS

- *de novo* Enzymes
- Generative Protein Design
- Riff-Diff
- RF-Diffusion
- Atomistic Refinement
- Catalytic Motif Scaffolding
- Active-Site Motif Transplant
- MD Validation
- QM/MM Prioritization
- Enantioselective Biocatalysis
- Thermal Stability
- Pocket Enforcement
- Fast Candidate Selection
- Low-Screening Workflow
- Scale-Up Readiness
- Tech-Transfer

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