

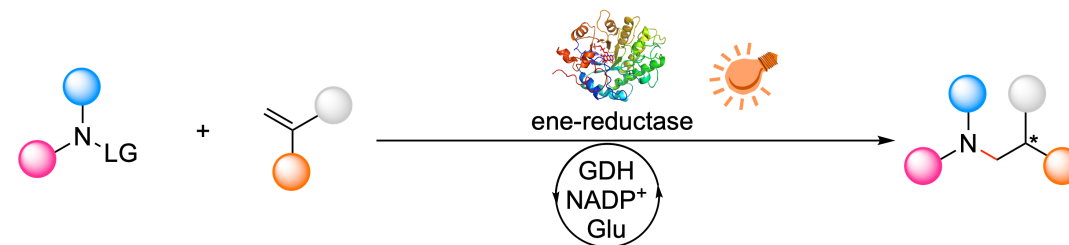
# Photoenzymatic Enantioselective Intermolecular Radical Hydroamination

## Background/Objective

Chiral amines are chemical building blocks that have wide applications in the synthesis of agrochemicals and other products. Currently, hydroamination reactions to produce chiral amines can be carried out by metal- or photo-catalysts but are a challenge due to side reactions, the short lifetime of nitrogen-centered radicals, and the lack of understanding of the fundamental catalytic steps. Here we report a photoenzymatic system that can control the unstable nitrogen-centered radicals in a reaction known as “enantioselective intermolecular radical hydroamination” by successfully repurposing an ene-reductase through directed evolution.

## Approach

- Designed a photoenzymatic system for the enantioselective intermolecular radical hydroamination reaction using ene-reductases.
- Optimized the catalytic behavior of the enzyme through directed evolution.
- Combined computational, experimental, and spectroscopic methods to investigate the reaction’s mechanism.



**Scheme of the hydroamination reaction.**

## Results

- Catalyzed the target reaction using enzymes under visible light with excellent efficiency and selectivity, without using an external catalyst.
- Determined the selectivity of the reaction is dependent on the radical addition step, while the reactivity is dependent on the radical initiation step.

## Significance/Impacts

We designed a novel, efficient reaction for chiral amine synthesis using a photoenzymatic system, which has the potential for biomass-derived fatty acids to be used as substrates for chemical manufacturing.

Zhang, Z., Feng, J., Yang, C., Cui, H., Harrison, W., Zhong, D., Wang, B., Zhao, H. July 31, 2023. “Photoenzymatic Enantioselective Intermolecular Radical Hydroamination.” *Nature Catalysis*. DOI: 10.1038/s41929-023-00994-5.