**Computational design of novel hydrolases**

The design of enzymes is incredibly challenging due to their complex architectures and the subtle movements they make along the reaction coordinates they catalyze. Previously, enzymes were designed by placing active sites into pre-existing protein scaffolds, limiting our ability to accurately capture the catalytic geometries required for catalysis. Recent advances in machine learning now allow us to build proteins around a desired active site and predict the structures of reaction intermediates. Leveraging this technology, we designed serine hydrolases with atomic accuracy, with efficiencies up to $10^5$ $M^{-1}$ $s^{-1}$, and in folds not utilized by native hydrolases. We have started applying this approach to valuable reactions of interest including peptide bond cleavage and plastic deconstruction.