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FROM DYNAMIC STRUCTURES TO FUNCTIONAL MATERIALS

Reaction-encoded structural plasticity in peptide nanofibrils for adaptive supramolecular catalysis

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Peptide-based supramolecular assemblies offer a versatile platform for mimicking enzyme-like catalysis, yet their structures are typically static and lack the adaptive behavior found in natural enzymes. Here, we introduce a native chemical ligation-inspired transthioesterification strategy that imparts structural plasticity to catalytic peptide assemblies. Naphthyl thioester donors transfer hydrophobic groups to cysteine-containing, Lys- or His-rich acceptor peptides, generating mono- and di-substituted products with distinct self-assembly behavior and nanostructures.

By varying the donor-to-acceptor ratio, the ligation reaction produces nanofiber ensembles with tunable retro-aldolase- and hydrolase-like activities. Cryogenic electron microscopy reveals that dynamic ligation governs fiber morphology and internal order while enabling access to structural states that cannot be achieved through direct assembly of pre-synthesized ligation products. Comparison of in situ ligation, direct assembly, and iterative addition protocols further demonstrates that gradual, reaction-driven formation of ligation products is essential for generating highly ordered assemblies with enhanced catalytic performance. These findings establish reaction-driven structural plasticity as a powerful strategy for programming the structure and function of supramolecular peptide catalysts, bringing synthetic catalytic assemblies closer to the adaptive behavior of natural enzymes.

This poster will be presented together with Maximilian Schuler.