Thermal stabilization of enzymes in lipidic mesophases governed by phase structure and transitions

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Lipidic mesophases (LMPs) provide nanoconfined environments with tunable structure and dynamics, offering a promising platform for controlling biomolecular stability. [1-3] While their structural versatility is well established, the relationship between mesophase architecture and enzyme stability at elevated temperatures remains insufficiently understood.
Here, we employ Dimodan-based LMP as a model system and investigate its structural stability and impact on enzyme denaturation. Small-angle X-ray scattering (SAXS) confirms that these mesophases maintain well-defined internal structures over a broad temperature range. Upon incorporation of enzymes into the LMP, we observe a significant increase in denaturation temperature compared to bulk buffer conditions.
Further analysis reveals that enzyme stability is strongly coupled to the mesophase structure and its phase transitions. In particular, the highly viscous bicontinuous cubic phase (Ia3d) enhances enzyme thermal stability, whereas transition to the more fluid hexagonal phase leads to rapid unfolding. Differential scanning calorimetry (DSC) demonstrates that enzyme denaturation coincides with these structural transitions. In addition, aggregation processes commonly observed in bulk aqueous systems are effectively suppressed within the LMP environment.
These findings suggest that LMPs stabilize enzymes through mechanical confinement. Our results highlight the critical role of mesophase symmetry and viscosity in regulating enzyme stability and provide a general strategy for designing soft nanoconfined systems for high temperature biocatalysis.

References:

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