Hydrophobicity gradients control function in short peptide self assembled nanostructures

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Supramolecular peptide assemblies (SPAs) are increasingly recognized as versatile building blocks for biomedical and nanotechnological applications due to their sequence-controlled self-assembly and tunable physicochemical properties [1]. However, establishing clear structure-property relationships that link peptide sequence to supramolecular organization remains challenging and requires an integrated experimental-computational approach. Here, we investigate a library of short peptides that self assemble into fibrillar supramolecular structures through sequence-encoded hydrophobicity gradients. Self-assembly onset is quantified through fluorescence spectroscopy by determining Critical Aggregation Concentrations, while Atomic Force Microscopy, Circular Dichroism, and Fourier-Transform Infrared spectroscopy are used to confirm fibrillar morphologies and reveal sequence-dependent variations in secondary structure. These results demonstrate that subtle sequence modifications strongly influence intermolecular ordering, aggregate size, and critical concentration, with several systems displaying coexisting supramolecular morphologies. To bridge experimental observables with molecular-level insight, we aim to identify experimentally accessible descriptors that correlate with coarse-grained molecular dynamics simulations [2]. Importantly, we seek to establish whether these descriptors can also predict the performance of SPAs as antibacterial materials. This will be directly tested though experiments examining the interaction of selected peptide assemblies with Pseudomonas aeruginosa bacterial strains, allowing us to evaluate how supramolecular organization influences biological response. Overall, this integrative strategy links macroscopic characterization, molecular modelling, and preliminary biological evaluation, providing a rational framework for the design of customizable SPAs with controlled architectures and tailored biological performance [3].

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