

Controlling Self-Assembled Structures via Different Hydrophobic Amino Acids in Short Peptide Amphiphiles

[Martina Baumann](#)¹, [Erik Reimhult](#)¹, [Marcus Textor](#)¹

¹ *Department of Materials, Laboratory for Surface Science and Technology (LSST), ETH Zurich, Switzerland*

INTRODUCTION: Designing and functionalizing structures on the nanoscale is a goal of research fields ranging from materials science to nanomedicine¹. Self-assembly of molecular building blocks presents a promising route towards controlled engineering of functional macromolecular parts. The ability to self-assemble into ordered structures as well as the straight forward production of peptides make them excellent building blocks to design and build biocompatible structures on the nanoscale, with relevant applications in e.g. drug delivery vehicles, tissue engineering scaffolds and nano-templating^{2,3}. To gain control over the formed structures, insight into the physicochemical processes underlying the self-assembly is crucial.

METHODS: We investigate the influence of systematical changes in the amino acid sequence of short amphiphilic peptides on the self-assembled macromolecular structures. Cationic surfactant-like peptides with systematically varied tail and head regions serve in this study as model peptides, resembling phospholipids from biological membranes in dimension and architecture². Two positively charged amino acids comprise the polar head, and the hydrophobic tail is formed by a repetitive sequence of one apolar amino acid. Such peptides are especially of interest for investigating interactions with negatively charged cell membranes, e.g. for drug delivery applications. The self-assembled structures of Ac-Ile6Lys2-NH₂ (I6K2), Ac-Leu6Lys2-NH₂ (L6K2) and Ac-Val6Lys2-NH₂ (V6K2) were characterized as function of concentration and temperature. The hydrophobic amino acids were chosen to systematically vary the propensity to form an α -helical secondary structure while conserving the overall hydrophobicity of the sequence⁴. Characterizations of the assembled supramolecular structures were made using transmission electron microscopy (TEM) and atomic force microscopy.

RESULTS: For all three peptides distinct macromolecular structures were found with TEM.

I6K2 assembles into flat ribbon-like structures whereas L6K2 and V6K2 assemble into micellar fibres depending on peptide concentration. CD spectroscopy was used to determine the secondary structure. CD data reveals a β -sheet structure for I6K2 peptides in the assemblies and a random coil structure with an α -helical content for L6K2 and V6K2.

DISCUSSION & CONCLUSIONS: The results show, that for short amphiphilic peptides prediction of the secondary structure from helix-propensity can be used to understand the assembled macromolecular structures. Furthermore, the effect of different kinetic pathways, on intermediate states, secondary structure and assembled superstructure are investigated. In particular annealing at higher temperature has shown to yield a pronounced increase in secondary order and stability.

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