

## Surfactant-like peptides: Supramolecular assembly and peptide-membrane interaction to engineer novel drug delivery systems

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In the last few years, significant advances have been made in the use of peptides as building blocks to produce biological materials for a wide range of applications [1]. Thus, synthesis and characterization of short peptides that can adopt a stable three-dimensional structure in solution are crucial for the construction of bio-active and bio-inspired *de-novo* polypeptides.

Selected peptides and hybrid peptides (combinations of peptide sequences with organic moieties in a single molecule) self-assemble in a variety of motifs to form pores, channels and tubules. Various physiological functions, such as ion transport through cell membranes, and physical functions such as solubilizing difficult-to-dissolve molecules, are facilitated by the tubes that are formed by molecular assemblies [2]. Peptide nanotubes are constructed by highly convergent non-covalent processes by which cyclic peptides rapidly self-assemble into well-ordered three-dimensional structures when triggered appropriately by a chemical or by the medium. It is well known that the secondary structures are part of a larger system and that their conformational stability depends on non-covalent interactions, both intra- and inter-chain interactions, such as van der Waals', electrostatic and hydrophobic forces as well as hydrogen bonds [3].

Peptide-lipid membrane interactions play a critical role in the regulation of several biological phenomena, including the insertion and folding of membrane proteins, the translocation of polypeptides through membranes and the cytolytic action of antimicrobial peptides. However, a systematic study of the interaction of different peptide assemblies with membranes is still missing [4].

The aim of the present study is the systematic design and synthesis of cationic surfactant-like peptides, the structural characterization of spontaneously formed supramolecular entities, and the evaluation of their interactions with supported bilayers serving as a model for cell membranes. The development of such biologically inspired delivery vehicles should fulfill several criteria that

are important for the envisaged application such as biodegradability, cell-membrane transit promotion and lack of cytotoxicity.

To assess the approximate size of the peptide assemblies, dynamic light scattering measurement as well as transmission electron microscopy (TEM) will be used to study the supramolecular assembly of the samples in solution as a function of concentration and pH, complemented by morphological studies of peptide assemblies at surfaces based on atomic force microscopy.

Molecular mechanics calculations are performed to simulate the assembly of selected peptide sequences in aqueous media, and the comparison of such results with those experimentally obtained is also discussed.

### References

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