

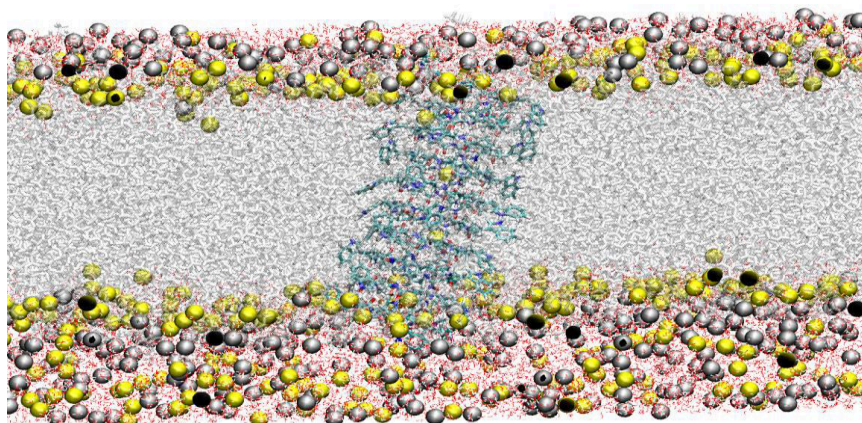
**Molecular Dynamics study of the transmembrane ion transport by derivatized self-assembling  $\alpha,\gamma$ -peptide nanotubes**

**Juan Outeiral**, Rebeca García-Fandiño, Saulo Vázquez and Juan R. Granja

Department of Organic Chemistry and Department of Physical Chemistry. Center for Research in Biological Chemistry and Molecular Materials, Campus Vida, Santiago de Compostela University, E-15782 Santiago de Compostela, (Spain)

[juanantonio.outeiral@rai.usc.es](mailto:juanantonio.outeiral@rai.usc.es)

Self-assembling cyclic peptide nanotubes (SCPNs) have attracted a great deal of attention from the scientific community in recent years due to their applications in biology, chemistry and material science.<sup>1</sup> The  $\alpha,\gamma$ -SCPNs are a special class of peptide nanotubes derived from cyclic peptides that alternate  $\alpha$ - with  $\gamma$ -amino acids. In particular, the  $\alpha,\gamma$ -SCPNs developed in our group include a 3-aminocycloalkanecarboxylic acid, which imparts additional properties on the nanotube; for example, while almost all of the cyclic peptide nanotubes that have been developed so far have hydrophilic inner surfaces, thus allowing the permeation of only polar molecules, in the  $\alpha,\gamma$ -SCP systems the methylene group of each cycloalkane moiety is projected into the lumen of the cylindrical structure to generate a partially hydrophobic cavity. Furthermore, the cavity properties can be modulated by simple chemical modification of the cycloalkane and this allows, in principle, finer control of the transport properties of a very wide range of molecules in the nanotube.<sup>3</sup>



Molecular Dynamics (MD) simulations, when acting as a virtual microscope with high spatial and temporal resolution, can provide powerful information about the fine details of the effect of the lumen functionalization of these systems on the ion transport when they are inserted into a lipid bilayer. In this work we study the influence of the presence of different position and number of hydroxylic groups in the lumen of these channels when they are inserted into a DOPC bilayer and how they affect to the structural and dynamical behaviour of the modified peptide nanotubes. The

transmembrane transport of different ions ( $\text{Li}^+$ ,  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cs}^+$  and  $\text{Ca}^{2+}$ ) was investigated using equilibrium and non-equilibrium MD simulations, and compared to the non-derivatized  $\alpha,\gamma$ -SCP<sub>N</sub>,<sup>4</sup> observing for first time to our knowledge, ion crossing in the scale of nanoseconds without the need of applying a transmembrane voltage or concentration gradient.

The results obtained allow the full characterization of the structural, energetic, dynamic, and transport properties of this interesting new class of  $\alpha,\gamma$ -SCP<sub>N</sub>, constituting the first theoretical study on SCP<sub>N</sub>s with chemically modified lumens presented to date.

## References

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