pH and thermo-sensitive self-assembling properties in aqueous solution of the lipopetide lauril-Gly-Gly-D-Ser-D-Lys-NH_2

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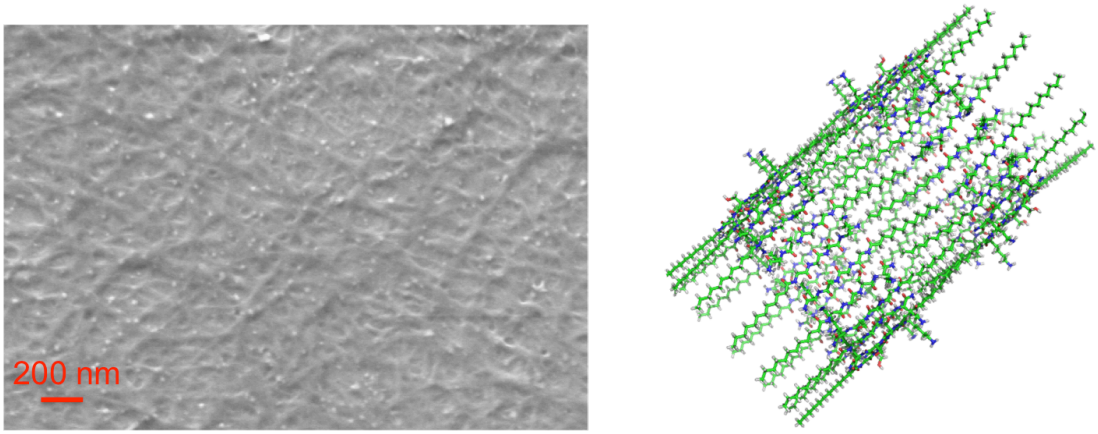
Lipopeptides are hybrid bio-inspired materials obtained by conjugating fatty acids and hydrophilic peptides that are able to self-assemble in nanostructures useful for drug delivery, imaging, and applications in gene therapies. Lipopeptide self-assembly depends on the hydrophile/lipophile balance of the molecules and on the peptide portion that are able to adopt predesigned secondary structure and respond to external stimuli such as pH and temperature. Herein, the self-assembling properties of the lipopeptide lauril-Gly-Gly-D-Ser-D-Lys-NH_2 are investigated. The amphiphilic lipopeptide was prepared through a highly efficient solid-phase synthesis and characterized. The self-assembling behaviour of the lipopeptide was assessed by NMR, circular dichroism (CD), fluorescence spectroscopies, dynamic light scattering (DLS), SEM and TEM microscopies. The sensitivity of the lipopeptide self-assembly was investigated at various temperatures and pHs exploiting the presence of the amino group in the side chain of the lysine residue. Preliminary results obtained by CD spectroscopy and DLS showed that at acidic pH the lipopeptide probably self-assemble to form micelles while by increasing the pH the secondary structure of the peptide undergoes a reversible transition from random coil to β-sheet forming a gel in about 12 hours. SEM micrographs, achieved from deposition of the gel, showed that the lipopeptide is organized in nanofibres (Figure 1A). Based on molecular mechanical calculations carried out in vacuum on the lipopeptide aggregate adopting AMBER-99 as a force field, a structural model of assembled lipopeptides is proposed, where the peptide segment is in anti-parallel β-sheet conformation (Figure 1B).



A B

Figure 1 A) SEM micrograph of lauril-Gly-Gly-D-Ser-D-Lys-NH_2 gel; B) a structural model of assembled lipopeptides.

[1] I. W. Hamley, *Chem. Commun.*, 2015, **51**, 8574.