Diphenylalanine nanotubes

The short diphenylalanine (FF) peptide self-assembles into nanotubes with many interesting properties and applications. They have high mechanical strength, and are stable in both a variety of solvents and at high temperatures. In addition, they are inexpensive, biocompatible, and environmentally friendly. Their applications range from templating other nanomaterials to enhancing interfacial surface areas of biosensors and super-capacitors. However, little is known about their self-assembly mechanism or the intermolecular interactions underlying their stability. Our study uses atomic-resolution simulations of FF peptides and its analogues to gain insight into the early stages of oligomerization and the driving forces for assembly in both solution and vacuum environments.

All-atom simulation methodology

All simulations were performed using the Amber simulation package developed at UCSF.

Diphenylalanine in zwitterionic form

1) 12 peptide system at a concentration of 55 mg/mL in water at 300 K for 35 ns
2) 12 peptide system at a concentration of 136 mg/mL in water at 300 K for 35 ns

Diphenylalanine with capped (uncharged) termini

3) 12 peptide system at a concentration of 61 mg/mL in water at 300 K for 35 ns

Cyclic diphenylalanine

4) 36 peptide system at 64 mg/mL in vacuum at 343 K, 388 K, 433 K, 478 K, and 523 K for 35 ns

Self-assembly of diphenylalanine in water

While electrostatic interactions exist in the nanotube crystal structure, hydrophobic interactions between the rings on the side chains are stronger and contribute more to stability. In particular, interactions between the second ring in each FF are prominent.

The structural motifs seen in the crystal structure are also observed in oligomers formed in the 12 FF peptide system (simulation 2). Hydrophobic interactions between the rings and electrostatic interactions between charged termini stabilize these structures.

Contact maps evaluate the frequency that non-hydrogen atoms on different peptides come within 6 Å of each other. A large number of contacts indicates interactions. In the 12 FF peptide systems (simulations 1 and 2), we observe that second ring interactions increase at higher concentrations, in agreement with the behavior seen in the crystal structure contact map. The capped FF peptide system (simulation 3) also aggregates, showing the same favoritism for second ring interactions, demonstrating that self-assembly is driven by hydrophobic interactions.

The distribution of the angle between the two rings shows that they tend to prefer a cis-conformation, particularly in the crystal structure.

Self-assembly of diphenylalanine in vacuum

When vapor deposited, diphenylalanine has been shown to cyclize and form both nanotubes and fibers.

This contact map shows that interactions in cyclic FF are principally driven by hydrogen bonding. When visualizing the simulation, we see the emergence of fiber-like aggregates stabilized by hydrogen bonds (right) that represent potential precursors the final structure.

Peptides are simulated in a periodic box with explicit water molecules.

Simulations can be visualized without water to identify oligomers formed between peptides.

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