Differences in Aggregation Profiles Between Coarse-Grained and All-Atom Simulations: a Case Study of the IMGIIA Hexapeptide

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Supramolecular peptide nanostructures derive their function out of the combination of self-assembly morphology and sequence chemistry of their peptide building blocks. Depending on sequence design, their applications range from peptide glass, biosensors, drug delivery hydrogels, and cell culture scaffolds [1]. Modeling self-assembling peptides is commonly approached through molecular dynamics (MD): all-atom (AA) simulations resolve precise binding mechanisms, while coarse-grained (CG) methods enable screening of larger systems and longer timescales [2]. While CG has this advantage, AA is more accurate because they capture hydrogen bonding directly. In CG, backbone properties are predefined based on assumed hydrogen bonding and are less reliable for sidechain interactions.

Here we aim to test multiple backbone setups and concentrations to determine which CG simulations are the closest to AA results based on simulation setups from a previous paper [3].

For this purpose, we simulated the IMGIIA hexapeptide [4] in CG simulations using 200 peptides in an 8000 nm^3 box and in AA simulations using 30 peptides in a 125 nm^3 box. Inter-chain contact events were used to quantify aggregation kinetics, aggregate size and distribution, residue contact frequency, interaction types, and pairwise peptide alignments present during the simulations. A contact event was defined using distance cutoffs of 5.1 Å (AA) and 7.05 Å (CG) and this was measured and processed using a Python code built on MDAnalysis.

The results showed that CG simulations with nonpolar backbones are the closest in cluster size and peptide pair populations to AA.

This work offers an alternative aggregation propensity measurement through aggregate population analysis and shows how AA and CG can simulate complete aggregation through different mechanisms by observing pairwise peptide binding.

References:

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