EXPLORING THE POTENTIAL OF COARSE-GRAINED SIMULATIONS: NOVEL MODELS AND BROADER APPLICATIONS FOR SACCHARIDES

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The molecular simulation of saccharides presents a significant challenge due to their structural complexity and conformational heterogeneity. Coarse-grained (CG) models offer a promising solution by enabling the simulation of longer polysaccharide chains at a reduced computational cost. In this work, we present advancements in CG modeling for saccharides, focusing on three main aspects: the development of a CG model based on the Martini 3 force field, efforts to extend it for glycosaminoglycans, and the development of an alternative Monte Carlo-based coarse-grained model for polysaccharides.

Regarding the development, refinement, and validation of the Martini 3 force field for saccharides, we designed a model for glucopyranose-based saccharides and hyaluronic acid. The model, parameterized based on atomistic MD simulations and experimental data, successfully captures the structural and conformational features of saccharides of interest, as well as their interactions with other biomolecules. Most notably, the developed model accurately predicts the location of binding sites for saccharides on the surface of carbohydrate-binding proteins, highlighting its potential for large-scale simulations of carbohydrate-protein-containing biomolecular systems.

As an alternative to molecular dynamics-based simulations, we developed a Monte Carlo-based coarse-grained model (referred to as CG MC) that focuses on the conformational properties of polysaccharides. The CG MC model is designed for rapid conformational sampling of long carbohydrate chains of realistic length (hundreds of monomers). This model uses data from atomistic simulations of short saccharide chains to extrapolate their behavior to longer polysaccharides, incorporating the effects of glycosidic linkage conformations and local structural features. We demonstrate the ability of the CG MC model to predict the persistence length and other polymer properties, showing that even small discrepancies in force fields or local conformational properties can lead to significant differences in the predicted conformations of longer polysaccharide chains. The model's flexibility allows for the simulation of polysaccharides of arbitrary length, making it a valuable tool for large-scale simulations and comparative analysis of different force fields.

Together, these two types of models provide new insights into the behavior of saccharides and enable large-scale simulations of complex carbohydrate systems.

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References:

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