Refining Polarizable Force Fields for Predictive Glycomaterial Modeling

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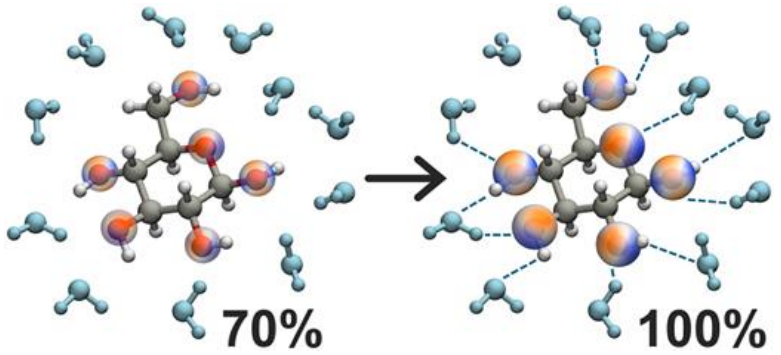
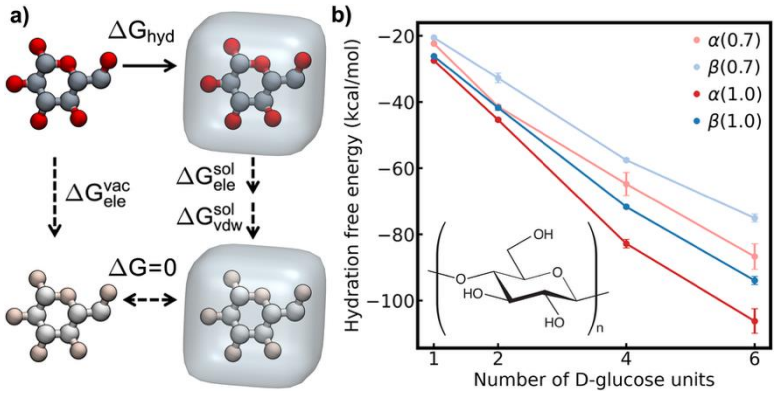
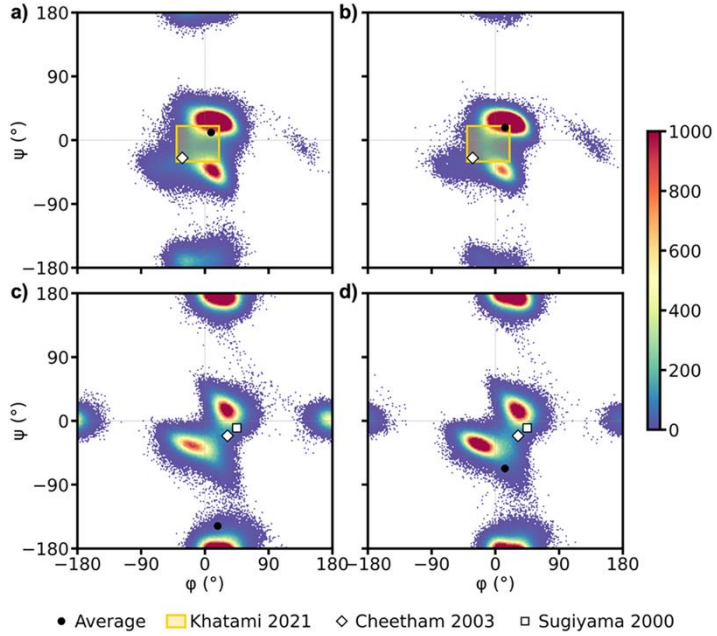
Predictive atomistic models are central to enabling the rational design of glycomaterials. Unlike conventional modeling force fields that use fixed charge distributions, polarizable force fields allow molecular electrostatics to respond dynamically to their environment, providing a more realistic description of hydration and intermolecular interactions. Polarization effects are prevalent in glycomaterial systems, yet polarizable modeling of carbohydrates remains relatively unexplored.

In a recent study, GlycoMIP researchers at Virginia Tech refined the AMOEBA polarizable force field by restoring full gas-phase oxygen quadrupole magnitudes in D-glucose parameters. Raising this scaling from the recommended 0.7 to 1.0 shifted the equilibrium-weighted hydration free energy to −26.6 kcal/mol, close to experimental consensus, while increasing glucose–water hydrogen bonding and donor hydrogen-bond lifetimes without altering hydration-shell structure. Extending the parameters to 1→4-linked oligomers strengthened intramolecular hydrogen bonding, restricted conformational sampling, and revealed distinct hydroxyl environments within glucan chains, with OH2 and OH3 dominated by intrachain interactions and OH6 remaining water-exposed, consistent with its high reactivity.

The results demonstrate that a polarizable model validated for monosaccharides can successfully transfer to linked glucans, advancing the ability to predict how carbohydrate molecular architecture influences hydration, conformation, and ultimately glycomaterial properties.







Figures. Left Top: Refinement of oxygen quadrupole scaling in the AMOEBA force field. **Left Bottom:** Hydration free energies of α- and β-D-glucose oligomers as a function of chain length for 0.7 and 1.0 oxygen quadrupole scaling. **Right:** Contributions of water and glucose to hydroxyl electric fields in monosaccharides and 10-unit oligomers.