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The AGBNP implicit solvent model: recent advances and applications to biological macromolecules

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The Analytical Generalized Born plus Non-Polar (AGBNP) model is an analytical implicit water model suitable for molecular dynamics simulations of small molecules and macromolecules. It is based on an analytical pairwise descreening implementation of the continuum dielectric Generalized Born (GB) model and a non-polar hydration free energy model. AGBNP computes the descreening scaling factors that account for atomic overlaps from the geometry of the solute rather than treating them as geometry-independent parameters fit to numerical or experimental data. The non-polar hydration free energy model is decomposed into a cavity component based on the solute surface area and a solute-solvent van der Waals dispersion energy estimator. The aim of the model is to achieve atomic-resolution accuracy for modelling the many biological systems in which global conformational features are regulated by small and localized control elements. Since its introduction AGBNP has been employed to study a variety of biological problems ranging from peptide conformational propensity and folding, protein allostery, conformational equilibria of protein-ligand complexes, binding affinity prediction, and, more recently, to intrinsically disordered proteins, protein aggregation, the design of virus vaccine carriers, and macromolecular X-ray structure refinement. Recent development work has focused on computational performance enhancements and on improving the accuracy of the model with respect to explicit solvent simulation results. By comparing the details of the solvent potentials of mean force of several peptides calculated with explicit and implicit solvation, we have identified some aspects of the AGBNP model in need of improvement. We are exploring several strategies to address them including the adoption of a molecular surface description of the solute volume, the modelling of high-occupancy hydration sites, and the optimization of the non-polar free energy model.