SOLVENT MODELS AND CHARGE SCALING: BENCHMARKING FOR MOLECULAR DYNAMICS SIMULATIONS OF GLYCOSAMINOGLYCANS

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Glycosaminoglycans (GAGs) are highly negatively charged polysaccharides found extensively on the surface of cells and in the extracellular matrix. They possess a vast range of biological functions involved in cell signaling, cardiovascular health, tissue regeneration, inflammation and neurodegeneration [1]. The intrinsic properties of GAGs makes them difficult to study effectively but, recent efforts to quantify the efficacy of various forcefields and water models within GAG simulations has highlighted promising routes to more accurate modelling of GAGs. Regarding forcefields, a novel approach of implicitly polarisable forcefields for GAGs has been demonstrated to overcome the limits of nonpolarisable forcefields and the computational demand of explicitly polarisable forcefields [2]. For the choice of water models, recent work has demonstrated the limits of the conventional TIP3P water model used and highlighted more appropriate alternatives [3]. By combining and comparing these approaches we have implemented the “charge-scaled” method for various implicit and explicit water models to identify the best compromise in terms of both computational efficiency and efficacy in simulating GAGs. In this work, both unbound heparin (HP) and heparin bound with basic fibroblast growth factor (FGF) were simulated with five implicit and six explicit water models to mirror previous work whilst also implementing charge scaling developed for the GLYCAM-ECC75 forcefield. From these simulations, we aim to identify the best approach for simulating GAGs within the context of both solvent model and forcefield choice.

References:

1. Perez, S., Makshakova, O., Angulo, J., Bedini, E., Bisio, A., de Paz, J. L., Fadda, E., Guerrini, M., Hricovini, M., Hricovini, M., Lisacek, F., Nieto, P. M., Pagel, K., Paiardi, G., Richter, R., Samsonov, S. A., Vivès, R. R., Nikitovic, D., & Ricard Blum, S. JACS Au, 2023, 3(3), 628–656.
2. Riopedre-Fernandez, M., Kostal, V., Martinek, T., Martinez-Seara, H., & Biriukov, D. Journal of Chemical Information and Modeling, 2024, 64(18), 7122–7134.
3. Marcisz, M., & Samsonov, S. A. Journal of Chemical Information and Modeling, 2023, 63(7), 2147–2157.