Rates of Proton Transfer in Water from Semi-Empirical QM/MM Simulations

Henning Henschel[a,b] and Miika T. Nieminen[a,b,c]

[a]*Research Unit of Medical Imaging, Physics and Technology, University of Oulu, P. O. Box 8000, 90014 Oulu, Finland,* [b]*Medical Research Center, Oulu University Hospital and University of Oulu, Oulu, Finland,* [c]*Department of Diagnostic Radiology, Oulu University Hospital, Oulu, Finland.*
henning.henschel@oulu.fi

The long-term goal of our research is the development of novel magnetic resonance imaging (MRI) methodologies for the characterization of musculoskeletal tissues (in particular articular cartilage). Currently, we are focussing on strategies based on the longitudinal relaxation time in the rotating frame ($T_{1\rho}$). One of the mechanisms most likely contributing to the dispersion of $T_{1\rho}$ in many tissue types is the chemical exchange of protons between biomacromolecules and water. Due to the system size required to model representative fragments of the biomacromolecules with a significant water shell over a time frame long enough to characterise the proton transfer processes in question, we expect only quantum chemical methods with the very low resource requirements to be applicable to the problem. Therefore, we present here an overview over the performance of a series of semi-empirical methods with regards to the description of proton transfer processes in water.

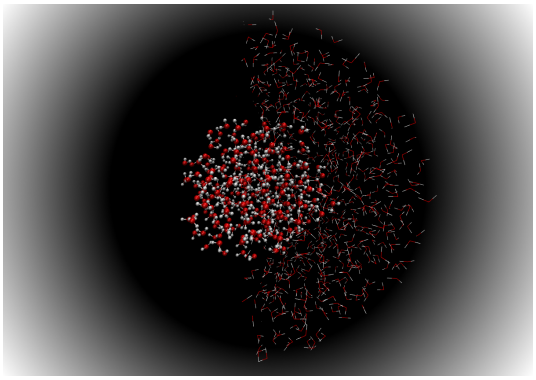

Figure 1: Schematic QM/MM system setup for excess hydrated proton simulations.

The system setup we have used for our simulations is illustrated in Figure 1: an $r = 12$ Å sphere of water molecules containing one excess proton is surrounded by a shell of classically simulated water molecules with a thickness of 10 Å. For each of the semi-empirical model chemistries 10 trajectories with a total length of 0.5 ns were run. Most of the methods tested were able to give proton transfer rate within an order of magnitude of the experimental value. Results from these calculation, combined with stationary calculations of the proton affinities of chondroitin sulfate, suggest escpecially PM7 and DFTB3-D3 as promising candidates for ensuing simulations including biomolecular fragments.