

IMPROVED POTENTIAL ENERGY FUNCTIONS FOR THE COMPUTATIONAL MODELLING OF CARBOHYDRATES

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For proteins and nucleic acids, classical force fields employing fixed charges have been the mainstay of biomolecular modelling. In the case of carbohydrates, however, describing the correct physical behaviour of these polar molecules, which incorporate stereoelectronic subtleties (anomeric, exo-anomeric and gauche effects), has been somewhat problematic at the molecular mechanical level; for example, this is evidenced by several reparametrizations of widely-used force fields such as AMBER and OPLS. Here, we describe our efforts to accurately model saccharides *via* a focused semi-empirical quantum mechanical approach within the framework of the PM3 model. We reparametrize the PM3 Hamiltonian based upon a representative training set of molecules. The modified PM3 Hamiltonian is denoted PM3CARB and exhibits improved performance in a number of respects. We also discuss the effect of training set size and composition on the quality of the model for carbohydrate conformation. Prospects of the strategy for accurate modeling of carbohydrates in a condensed phase environment will also be considered.