An approach for developing simple physics-type force field models for molecular simulation

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Coarse grained models, wherein groups of atoms are represented by a single interaction site, are often employed for large systems and/or when there is need to access longer time-scales. This representation means fewer particles in the system and hence enables larger systems to be simulated for longer times. There are two other additional gains: on coarse graining the interaction potential becomes softer, enabling the timestep to be increased from 0.002 ps to about 0.040 ps – a 20-fold advantage in the time-stepping process; the free energy surface also becomes softened which enables the system to equilibrate rapidly. Such coarse graining can be rigorous in that the loss in chemical specificity of the model is kept to a minimum. A similar but philosophically different approach is to use simpler models for the molecular system, which is a physics-type approach where the model represents a generic molecule, say a general phospholipid, rather than a specific lipid. Simulations using simplified models can be very powerful in that the insights are generic representing the behavior of a whole class of molecules, rather than a particular chemically-specified molecule.

A number of approaches to developing coarse grained models have been proposed. Of these perhaps the most widely employed is the semi-quantitative force field Martini [1]. Martini employs a 3-to-1 or 4-to-1 mapping to represent a chemical moiety comprising 3 or 4 atoms by a single coarse-grained particle. The coarse grained particles are generally uncharged and described by a Lennard Jones (LJ) interaction potential. Whilst the choice of the LJ σ parameter is dictated by the chemical moiety being represented, the parameter ε, which characterizes the affinity between the particles, is selected empirically from a set of 10 discrete levels depending on how polar the particle is perceived to be. This decision is informed by the characterization of certain building blocks based on free energies of vapourization, hydration and partitioning. The building blocks are limited focusing on phospholipids but have recently been extended to amino acids.

I shall present a new approach for developing simple, physics-type molecular models based on phase coexistence data. As with the Martini force field, the coarse grained particles are represent by a LJ interaction potential and utilize the well characterized LJ phase diagram to identify the appropriate LJ parameters for any given chemical moiety. The approach, which we term *PhaseD*, is simple, rapid and potentially universal, not being limited to a restricted set of building blocks. Furthermore, the approach augments the Martini force field in that it enables a more informed selection of the LJ ε parameter for a given chemical moiety being represented by a coarse grained particle.