

Simulation and dynamics of entropy driven, molecular self-assembly processes

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ABSTRACT

Molecular self-assembly is frequently found to generate higher order, functional structures in biochemical systems. One such example is the self-assembly of lipids in aqueous solution forming membranes, micelles and vesicles, another is the dynamic formation and rearrangement of the cytoskeleton. These processes are often driven by local, short range forces and, therefore, the dynamics is solely based on local interactions.

In this paper, we introduce a cellular automata based simulation, the Lattice Molecular Automaton, in which data structures, representing different molecular entities like water, hydrophilic and hydrophobic monomers, share locally propagated force information on a hexagonal, 2D lattice.

The purpose of this level of description is the simulation of entropic and enthalpic flows in a microcanonical, molecular ensemble to gain insight about entropy-driven processes in molecular many-particle systems. Three applications are shown, i.e. modeling structural features of a polar solvent, cluster-formation of hydrophobic monomers in a polar environment, and the self-assembly of polymers. Processes leading to phase-separation on a molecular level are discussed.

A thorough discussion of the computational details, advantages, and limitations of the Lattice Molecular Automaton approach can be found in reference [1].

Keywords:

Molecular Self-Assembly, Water Structure, Molecular Dynamics, Cellular Automata, Lattice Gas, Thermodynamics, Constructive Dynamics, Higher Order Emergence

1 Introduction

1.1 Biological motivation

Many processes in biomolecular systems lack global, interfering control. The system dynamics is solely based on local interactions, providing, based on immediate reactions on environmental changes, the necessary flexibility and mean stability of the whole system. Considering the prokaryotic cell as a hierarchically structured, dynamical system, it is possible to characterize specific, functionally linked, mesoscopic complexes. One of these compounds is the semipermeable membrane separating space into an inside and an outside [2]. These membranes consist of a certain type of amphiphilic polymers (hydrophilic head, hydrophobic tail) acting in the highly polar environment of water.

A basic component as a membrane is, from the theoretical viewpoint, characterizable as a higher order, emergent structure [3, 4], dynamically formed by interactions between lipids due to an entropy gradient arising from the structured polar (water) environment. Phase-separation of e.g. lipids in water and a concomitant ordering to vesicles and micelles is a spontaneous process lasting from seconds to minutes [5, 6, 7, 8].

The resulting higher order structures have themselves rich dynamics, e.g. turn-over (flip-flop-mechanism) of single lipids within membrane-like structures. This flexibility is of major importance to maintain functionality in a cell membrane, which hosts systems at higher hierarchical levels as e.g. the complex for photosynthesis [9].

The Hydrophobic Effect (HE), describing mainly an entropic effect, seems to be of fundamental importance in the self-organization of such biological systems [10]. Various circumstances lead to the formulation of a hydrophobic *effect* rather than a hydrophobic *force*: The most reliable indication that it is indeed a hydrophobic effect comes from thermodynamics, considering free energy, enthalpy and entropy of solvation processes:

$$\Delta G = \Delta H - T\Delta S \quad (1)$$

ΔG ... change of free energy

ΔH ... change of enthalpy

T ... temperature

ΔS ... change of entropy

It is experimentally known that the free energy change of dissolution of hydrophobic molecules in a polar solvent is positive, although the change in enthalpy (at room temperature) is often zero or even negative [11]. Considering that liquid water has to some extent quasicrystalline features with highly ordered regions [12, 13], the HE is believed to be based on a change of the water structure in the vicinity of hydrophobic surfaces and a concomitant decrease of entropy. Following this model, the solvent is forced to form a “cave around” the hydrophobic surface. This reaction, often referred as hydrophobic solvation, is accomplished by a different dynamics of the solvent in the vicinity of hydrophobic surfaces compared to the bulk solvent phase: The accessibility of microstates decreases and thus the entropy decreases. Due to the high surface tension of such a molecular cave, the solvent tends to “minimize” its contact surface to hydrophobic molecules which leads eventually to the phase-separation between water and hydrophobic molecules.

Entropy gradients and resulting phase separation are, therefore, based on effects *generated* by the system dynamics. They are not observable as explicit interaction forces, but are the result of basic molecular interactions between hydrophobic particles and the polar solvent. They are *emergent* properties.

1.2 Simulation of molecular systems

1.2.1 Molecular Dynamics and Monte Carlo methods

Recently various new methods are applied to simulate structural and dynamic properties of macromolecular systems. One such example is genetic algorithms [14], implementing formal criteria of Darwinian evolution through a fitness function (which is in analogy to an energy function). With such a method it is for instance possible to determine secondary structure motifs of polymers as proteins. However, the classical tools to simulate large molecular systems are deterministic routines like molecular dynamics, solving Newton’s equations of motion [15], or stochastic algorithms like the Dynamic Monte Carlo method [16]. These tools are based on force field calculations considering the following terms: