Protein Simulation in LAMMPS Using the Martini Model

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Objectives

Part one: Model the Proteins as a set of simple large particles (A) surrounded by the solvent (B)

Part Two: Model the Proteins as a cluster or polymer (A) surrounded by the solvent (B)

Part three: Use a Martini model (a coarse-grained force field) to model the Protein (A) in the solvent (B)

Concept

Pre-transition effects mediate forces of assembly between transmembrane proteins

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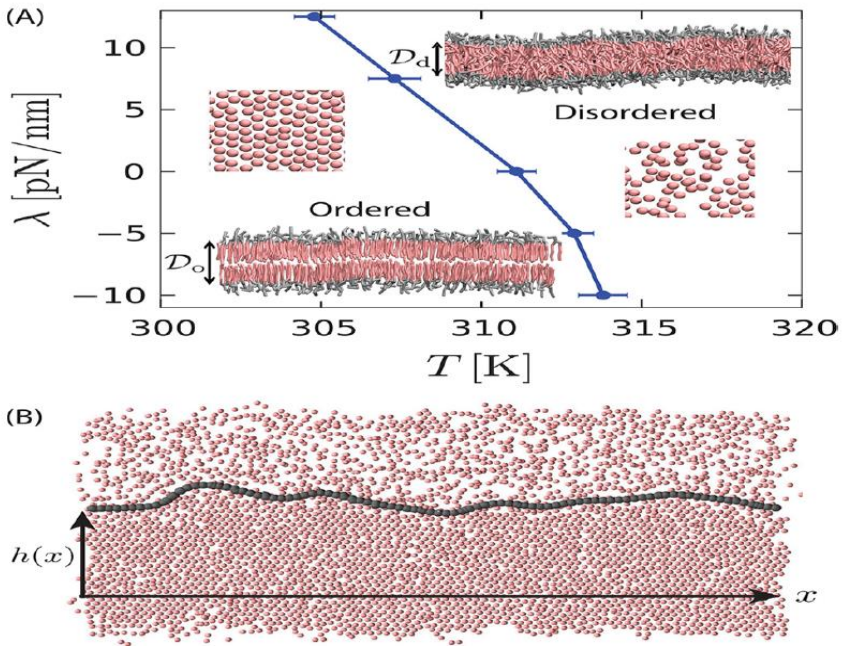
Abstract We present a mechanism for a generic, powerful force of assembly and mobility for transmembrane proteins in lipid bilayers. This force is a pre-transition (or pre-melting) effect for the first-order transition between ordered and disordered phases in the membrane. Using large-scale molecular simulation, we show that a protein with hydrophobic thickness equal to that of the disordered phase embedded in an ordered bilayer stabilizes a microscopic order–disorder interface. The stiffness of that interface is finite. When two such proteins approach each other, they assemble because assembly reduces the net interfacial energy. Analogous to the hydrophobic effect, we refer to this phenomenon as the 'orderphobic effect'. The effect is mediated by proximity to the order–disorder phase transition and the size and hydrophobic mismatch of the protein. The strength and range of forces arising from this effect are significantly larger than those that could arise from membrane elasticity for the membranes considered.

Katira *et al*. eLife 2016;5:e13150.



GROMACS molecular dynamics package

Suggested method (use Lammps):

1. Build big clusters, polymers and create a particle of bigger size surrounded by atoms with LJ interactions in liquid
2. Use a repulsive potential around the "colloid" to create lower density around it

The Martini Model

- **Martini** is a coarse-grained (CG) force field developed by Marrink and coworkers at the University of Groningen, initially developed in 2004 for molecular dynamics simulation of lipids, later (2007) extended to various other molecules.
- The force field applies a mapping of four heavy atoms to one CG interaction site and is parametrized with the aim of reproducing thermodynamic properties.
- For the Martini force field 4 bead categories have been defined: Q (charged), P (polar), N (nonpolar), and C (apolar). These bead types are in turn split in 4 or 5 different levels, giving a total of 20 beadtypes.
- Bonded interactions (bonds, angles, dihedrals, and impropers) are derived from atomistic simulations of crystal structures.

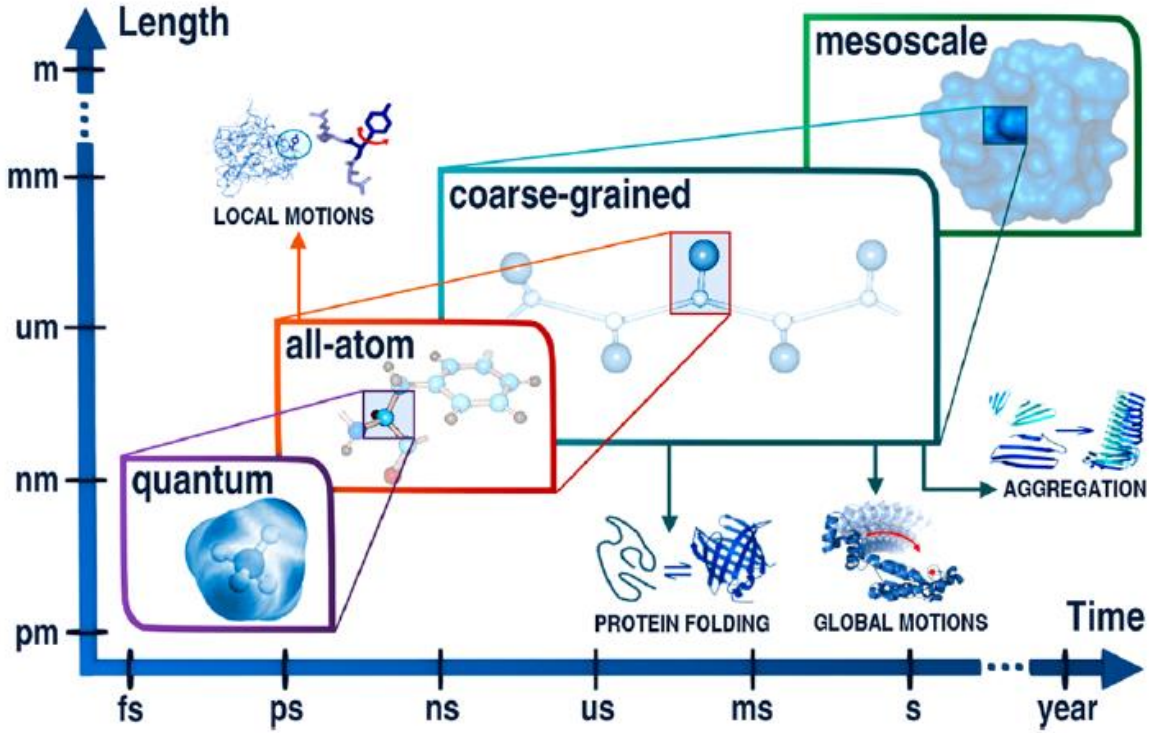
J. Phys. Chem. B 2007, 111, 7812-7824

Applications of CG Modeling

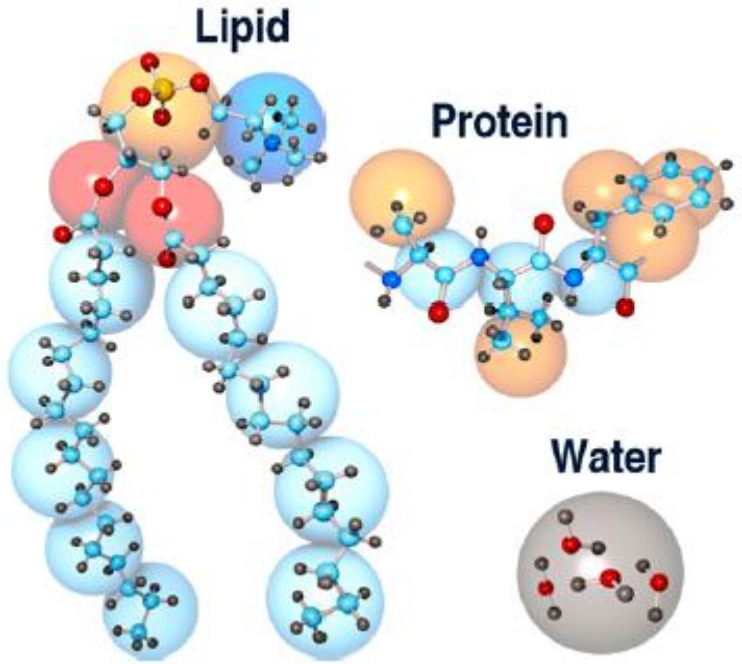
- The traditional computational modeling of protein structure, dynamics, and interactions remains difficult for many protein systems.
- It is mostly due to the size of protein conformational spaces and required simulation time scales that are still too large to be studied in atomistic detail.
- Lowering the level of protein representation from all-atom to coarse-grained opens up new possibilities for studying protein systems.

Chem. Rev. 2016, 116, 7898-7936

Application ranges



Application ranges for molecular modeling at different resolutions: quantum, all-atom, coarse-grained, and mesoscale. The plot shows approximate ranges of time scales and system sizes (lenghts).



All-atom representation is shown in balls and sticks, while coarse-grained representation in large spheres.

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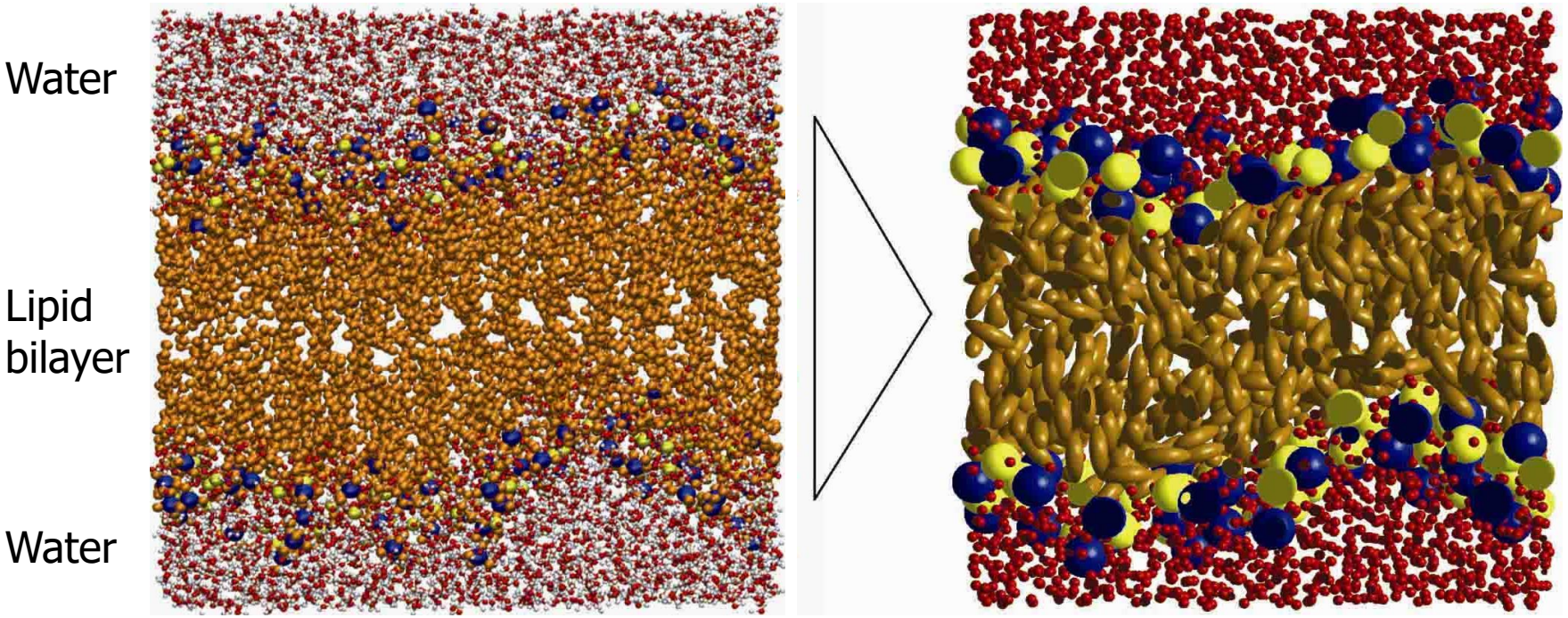
Membrane modeling

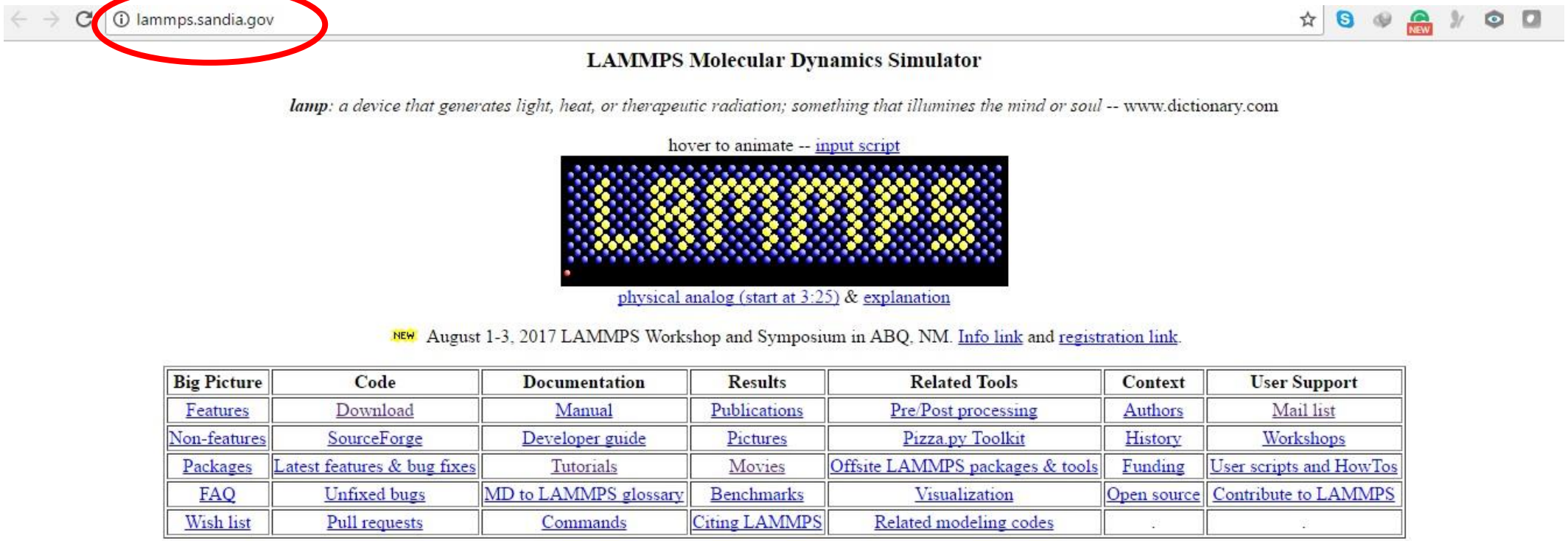


- Atomistic models:
  - Accurate but computationally demanding
- Coarse-Grain (CG) models:
  - Orders of magnitude faster to simulate

LAMMPS

- **Large-scale Atomic/Molecular Massively Parallel Simulator** (**LAMMPS**) is a molecular dynamics program from Sandia National Laboratories. LAMMPS makes use of Message Passing Interface (MPI) for parallel communication and is free and Open-source software.
- For computing efficiency, LAMMPS uses neighbor lists (Verlet Lists) to keep track of nearby particles. The lists are optimized for systems with particles that repel at short distances, so that the local density of particles never grows too large.

Large-scale Atomic/Molecular Massively Parallel Simulator (LAMMPS)



Lammps Manual
http://lammps.sandia.gov/doc/Manual.html

Lammps Tutorial
https://icme.hpc.msstate.edu/mediawiki/index.php/LAMMPS_tutorials

Steps/Procedures

- Define the large particles (A): mass/density/size
- Define the small particles (B): mass/density/size
- Define the interactions of the large particles with each other (AA): zero/yukawa
- Define the interactions of the small particles with each other (BB): Lj fluid interactions
- Define the interactions between large particles with small particles (AB): Repulsive hare/soft
- Set size of simulation grid
- Set percentage of area filled with particles/density of particles
- Number of particles
- Set temperature/energy level of system
- Set time step information: How long time step and Number of time steps
- Set image information
- Save an image every 10000 frames
- Run the simulation

Code run in CCBM cluster

```
#number of particles
variable npart  equal 8000

units       lj
dimension 2
atom_style  atomic
boundary        p p p
#particle interact with other particles within a max distance of 6
neighbor        6   bin
neigh_modify    every 1 delay 0 check yes

# define 2D box region
region box block -64 64 -64 64 -0.1 0.1

#create the simulation box with two types of particles
create_box 2 box

#put z=0 all the time
fix 2d  all enforce2d

#put particles with type 1 randomly into the box
#the strange number is a seed for the random generator
create_atoms 1 random ${npart} 324523 box

#create one particle of type 2 which is our brownian particle
#changing number of particles from 1 to 5
create_atoms 2 random 100 32524523 box

#all light particles has mass 1, the brownian particle mass 50
mass    1    1
mass    2    500

#define lennar-jones interactions between small particles (1) with 1
#define yukawa interactions between large particles (2) with 2
#define soft repulsive interactions between 1 and 2
#define the interaction sytle and cutoff (yukawa has screening length argument in-between), between atom _ and atom _
# then the next number is the energy level and the last number is the global cutoff

pair_style hybrid lj/cut 2.0 soft 7.0 yukawa 3.5 5.0
pair_coeff 1 1 lj/cut 1.0 1.0
pair_coeff 1 2 soft 10.0 5.0
pair_coeff 2 2 yukawa 10.0 5.0

#pair_style hybrid lj/cut 2.0 soft 7.0 lj/cut 2.0
#pair_coeff * * lj/cut 1.0 1.0
#pair_coeff 1 2 soft 10.0 5.0
#pair_coeff 2 2 lj/cut 1.0 1.0
```