

The following is a SHORT review of the pertinent equations and high-level topics that constitute the main component of Molecular Dynamics (MD). This review is meant to supplement the information that was presented in class during the lecture. Keep in mind that the goal of molecular modeling is to perform computer simulations, or to do chemical experiments, with a computer rather than a laboratory bench. Familiarity with basic Calculus concepts is assumed.

1 Physics Refresher - Newton's Laws of Motion

Newton's equations of motions are used to derive the position and velocities of individual atoms of a biomolecular environment. First, recall that the instantaneous change in the position of a particle is the velocity of the particle:

$$\frac{d\mathbf{r}_i(t)}{dt} = \mathbf{v}_i(t) \quad (1)$$

and that the instantaneous change in the velocity of a particle is the acceleration of the particle:

$$\frac{d\mathbf{v}_i(t)}{dt} = \frac{\mathbf{F}_i(t)}{m_i} \quad (2)$$

where we have used the acceleration component of Newton's second law, Force equals mass times acceleration, $\mathbf{F} = m\mathbf{a}$. Thus, using equations 1 and 2, the atomic coordinates, \mathbf{r} , and the velocity, \mathbf{v} , of atom i , with mass, m_i , is a function of time.

2 Chemistry Refresher - Inter-atomic Interactions

The interaction between two atoms or molecules is caused by the "push and pull" forces that exist between the two atoms or molecules. A measure of the strength of the attraction (or repulsion) is called the potential energy. Information about the physical parameters of the two interacting atoms or molecules, along with their separation distance, can be used to determine the potential energy of the dual-atoms or dual-molecules. A potential energy function is the algorithmic procedure that takes as input the physical parameters of the atoms or molecules and their separation distance, and computes their potential energy.

Accurate potential energy functions take into account many of the physical and quantum-mechanical aspects of atom interactions. For example, the Lennard-Jones potential (also referred to as the L-J potential, 6-12 potential or, less commonly, 12-6 potential) is a simple mathematical model that has been shown to accurately approximate the non-bonded interactions that exist between atoms or molecules that are separated by a short distance. The non-bonded interactions include an attractive force at long ranges (van der Waals force), and a repulsive force at short ranges (the result

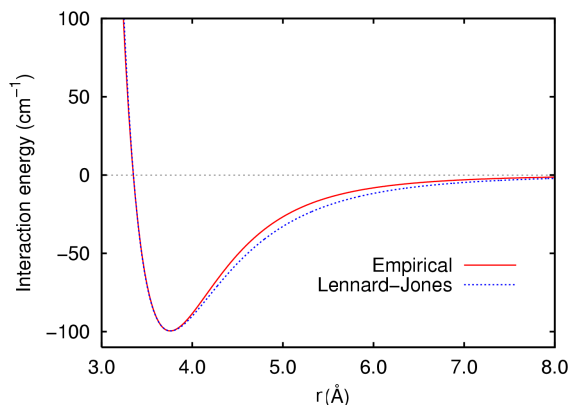


Figure 1: The Lennard-Jones potential is the mathematics representation of the two distinct forces that exist between two particles: the attractive van der Waals force, and the Pauli repulsion force. ϵ is the depth of the energy “well”, σ is the (finite) distance at which the inter-particle potential is zero (generally set to 2\AA), and r is the distance between the two particles.

of overlapping electron orbitals, referred to as Pauli repulsion force). The Lennard-Jones Potential is the following:

$$V(r) = 4\epsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right] \quad (3)$$

where $V(r)$ designates the potential energy of two atoms or molecules that are separated by a distance r , ϵ is the depth of the energy “well”, and σ is the (finite) distance at which the inter-particle or inter-molecule potential is zero. The values of ϵ and σ are dependent on the two atoms or molecules that are being simulated. So, the σ and ϵ values for two argon atoms will be different from the σ and ϵ values for two water molecules. Figure 1 is a graphical representation of the empirically derived potential energy between two argon atoms and the corresponding plot from the Lennard-Jones equation of the same phenomenon. Thus,

the main goal for using the Lennard-Jones potential is that we can determine the potential energy that exist between two atoms or molecules by just using a formula (and a rather simple one), instead of having to carry out lengthy quantum mechanics calculations.

The Lennard-Jones potential only describes the non-bonded interactions that occur between atoms or molecules, but there are bonded interactions, also, for which there are mathematical equations. Bonded interactions include bond stretching, bond bending, bond stretching and bending, as well as torsion effects. The TOTAL potential energy between two atoms or molecules is thus a sum of the potential energies that are caused by the bonded and non-bonded interactions.

3 Molecular Dynamics - Potential Energy and Atom Position

Assuming that we can calculate the potential energy between all atoms in a simulation, how can we use that information to determine the motion of the atoms? First, recall Newton’s Laws Of

Motion, specifically Equation 2. If you know the Force that is imparted on an atom, then you can calculate the velocity of the atom, and if you can calculate the velocity of an atom, then you can determine the location of the atom at each time step of the motion. That is the main idea of Molecular Dynamics. But first, one more piece of information is required:

The force \mathbf{F}_i exerted on atom i by the other atoms in the system is given by the negative gradient of the potential energy function V which in turn depends on the coordinates of all N atoms in the system:

$$\mathbf{F}_i(t) = \frac{-\partial \mathbf{V}(\mathbf{r}_1(t), \mathbf{r}_2(t), \dots, \mathbf{r}_N(t))}{\partial \mathbf{r}_i(t)} \quad (4)$$

where \mathbf{r} is a vector that designates the location of a particle, and thus $\mathbf{r}_1(t)$ is the location of particle (or atom, in this case) 1 at time t . $\mathbf{V}(\mathbf{r}_1(t), \mathbf{r}_2(t), \dots, \mathbf{r}_N(t))$ is the potential energy for the entire system at time t , and is based on the position of all of the atoms, as described in the previous section. Taking the partial derivative of the potential energy of the system with respect to a single atom in the system, atom i , allows us to the force that is imparted on the atom i .

Thus, assuming that we can calculate the potential energy of all of the atom interactions in a system, we can use Equation 4 to determine the Force that each atom feels, and we then can use the following simplified equations of Newton's Laws of Motion (Equations 1 and 2):

$$\mathbf{v}_i(t + \delta t/2) = \mathbf{v}_i(t - \delta t/2) + \frac{\mathbf{F}_i(t)}{m_i} \delta t \quad (5)$$

$$\mathbf{r}_i(t + \delta t) = \mathbf{r}_i(t) + \mathbf{v}_i(t + \delta t/2) \delta t \quad (6)$$

to determine the location and velocity of each atom of a simulation at some moment δt in the future. In the case of atom motion, we want to be sure that we perform calculations often enough to account for any displacement of any atom that might have occurred. Because individual atoms move very quickly, they can change their position every few femto seconds, and so δt in this example must be on the order of femtoseconds. In fact, most MD simulations set δt to 1 or 2 femtoseconds.

The idea of Molecular Dynamics is thus quite elegant: (1) compute the potential energy between all interacting atoms in a system using the Lennard-Jones and other potentials, (2) from the potential energy, Calculate the force that each atom feels, (3) using the force and a small δt , use Newton's equations of motion to determine the position and velocity of each atom in the system, (4) repeat.

Molecular Dynamics thus performs the above calculations for many time steps (most often billions of time steps, each of which is a few femto-seconds in length), during each of which the position and velocity of each atom are calculated. Successive positions of each atom in a simulation can be sequentially concatenated to produce the motion of each atom, and if all of the motions of all of the atoms are calculated, then the motion of the entire bimolecular structure can thus be determined.

Molecular Dynamics IS the use of the above equations to determine the location and velocity of the atoms in a biological system.