BMB/Bi/Ch 173 – Winter 2018
Homework Set 9.1 – Assigned 3-6-18, due 3-14-18 by 10:30 a.m
TA – Taylor Stevens tstevens@caltech.edu
Office hours – Friday Mar 9 1:00pm - 3:00pm (in SFL 229) and Monday Mar 12 3:30pm - 5:00pm (in SFL 229), or by appointment

1. Methods of Integration (50 points)
Several methods exist to numerically integrate Newton's equations of motion and solve molecular dynamics problems. Two of the most commonly used are Euler integration and Velocity Verlet integration.

Please refer to the following resources to understand and compare these methods:
https://en.wikipedia.org/wiki/Verlet_integration
https://en.wikipedia.org/wiki/Euler_method
http://gafferongames.com/game-physics/integration-basics/

Note: There are three common flavors of Verlet integration schemes: the Basic Verlet algorithm, the Verlet Leapfrog algorithm, and the Velocity Verlet algorithm. This problem set asks about the Velocity Verlet algorithm.

a. (16 points) The Euler and Velocity Verlet integration methods follow different algorithms to numerically integrate. The Velocity Verlet algorithm has 4 steps, listed below. Referring to the above sources, fill in the missing components (denoted by light gray boxes) for the Velocity Verlet integration algorithm:

1. Calculate: $\vec{v}\left(t+\frac{1}{2}\Delta t\right) = \vec{v}(t) +$ [ ]
2. Calculate: [ ] $= \vec{x}(t) + \vec{v}\left(t+\frac{1}{2}\Delta t\right)\Delta t$
3. Derive $\vec{a}(t+\Delta t)$ from the interaction potential using $\vec{x}(t+\Delta t)$ where $\vec{a} = \frac{\vec{F}(x)}{m}$
4. Calculate: $\vec{v}(t+\Delta t) = \vec{v}(t) +$ [ ]

b. (5 points) Which of these two integration methods is simpler?

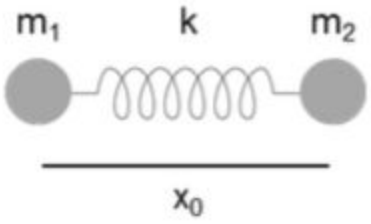
c. (10 points) Under what condition will Euler integration yield a correct result?

d. (10 points) How can one adjust Euler Integration to get a more accurate result? What is the tradeoff in doing this?

e. (9 points) As you can see, MD simulation is constrained by the choice of the numerical integration algorithm used. What are three other limits of MD simulation?

2. Harmonic Potential (50 points)

Next, we will use molecular dynamics to solve a classic two-body problem: simulation of the positions of two masses connected by a spring. Consider m_1 and m_2, shown below, on a spring with a force constant k describing the stiffness of the spring. The initial distance between the two masses is x_0.

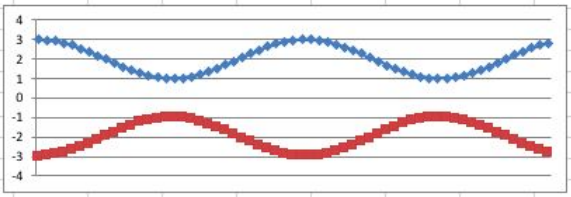


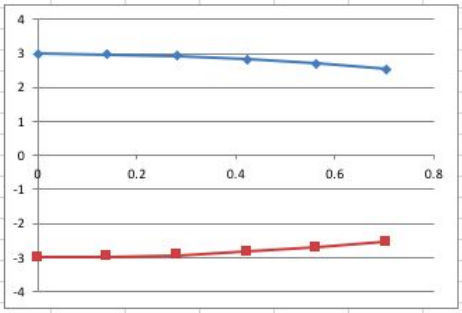
The potential energy can be modeled as the following harmonic potential:

$$U(x) = \left(\frac{k}{2}\right)(x - x_0)^2$$

In the spreadsheet associated with this homework, the Velocity Verlet algorithm can be used to simulate the positions of the two masses. An example of the filled in spreadsheet is below. The orange box denotes the input parameters.

	A	B	C	D	E	F	G
1		m1	1				
2		m2	1		resonance	1.414214	
3		x0	4				
4		k	1		MAX t	8.46	
5		Dt	0.141				
6							
7	t	x_1	v_1	x_2	v_2	F_{12}	F_{21}
8	0	3	0	-3	0	-2	2
9	0.0705		-0.141		0.141		
10	0.141	2.980119	-0.2792	-2.98012	0.27919678	-1.96024	1.960238
11	0.2115		-0.41739		0.41739356		
12	0.282	2.921267	-0.54729	-2.92127	0.54729214	-1.84253	1.842533
13	0.3525		-0.67719		0.67719071		
14	0.423	2.825783	-0.79363	-2.82578	0.79362606	-1.65157	1.651565
15	0.4935		-0.91006		0.91006141		
16	0.564	2.697464	-1.0084	-2.69746	1.00840383	-1.39493	1.394928
17	0.6345		-1.10675		1.10674625		
18	0.705	2.541413	-1.18309	-2.54141	1.18308544	-1.08283	1.082825
19	0.7755		-1.25942		1.25942464		
20	0.846	2.363834	-1.31073	-2.36383	1.31072521	-0.72767	0.727668
21	0.9165		-1.36203		1.36202579		
22	0.987	2.171788	-1.38625	-2.17179	1.38624793	-0.34358	0.343576
23	1.0575		-1.41047		1.41047007		
24	1.128	1.972912	-1.40665	-1.97291	1.40665065	0.054176	-0.05418
25	1.1985		-1.40283		1.40283124		
26	1.269	1.775113	-1.37112	-1.77511	1.37112214	0.449775	-0.44977
27	1.3395		-1.33941		1.33941303		
28	1.41	1.586256	-1.28108	-1.58626	1.28107506	0.827489	-0.82749
29	1.4805		-1.22274		1.22273708		
30	1.551	1.41385	-1.14009	-1.41385	1.14008987	1.172301	-1.1723
31	1.6215		-1.05744		1.05744267		
32	1.692	1.26475	-0.95377	-1.26475	0.95377244	1.4705	-1.4705





a. (5 points) Note that in the table, all of the values in rows 8 and 10 are filled in, while values are missing in row 9. This is on purpose. Explain the reason for this choice in terms of Velocity Verlet integration algorithm. What is the computational benefit of this choice?

b. (25 points) Now, let's use Velocity Verlet integration to simulate this system.
i. (10 points) First, derive the force (F(x)) for this harmonic oscillator.

ii. (15 points) Next, write equations to update the velocity and position as well. Use these equations to fill in the missing rows of the spreadsheet. Take the time out to cell A128. You will know you have the correct solution when your values match those in the screenshot above.

c. (10 points) The equation for the resonance frequency, ω, is found in cell F2.

By the way, the resonance frequency is found by solving the equations of motion analytically:

$$F(x) = ma = m\frac{d^2x}{dt^2}$$

Substituting in what we know about our system, we can arrive at the following second order linear differential equation:

$$\frac{d^2x}{dt^2} = \omega^2 x$$

$$\text{where } \omega = \sqrt{\frac{k(m_1+m_2)}{m_1 m_2}} = \sqrt{\frac{k}{\mu}} \ .$$

The solution to this differential equation is of the form:

$$x(t) = A\cos\omega t + B\sin\omega t$$

Why is the resonance frequency important for this system? What constraint does it place on an important MD parameter?

d. (10 points) Now try modifying the time step in the spreadsheet and describe what happens as the time step approaches the resonant frequency, and then after the time step is greater than the resonant frequency. Based on your observations, what rules would you follow to pick an appropriate time step for a molecular dynamics simulation?

3. Coarse-grained molecular dynamics (25 points)
To gain a better understanding of how coarse-grained simulation can be used, let's read through the following publication (https://www.sciencedirect.com/science/article/pii/S0006349506721701) from Klaus Schulten's group. In this paper, the authors use a coarse-grained simulation to analyze the motions of a bacterial flagellum.

a. (6 points) What did the authors want to analyze with their simulations and why couldn't they do this with an all-atom MD simulation? What limitations could they bypass in a coarse grained simulation?

b. (6 points) How many beads are used to model a flagellin monomer? What is the total number of beads in the largest simulation? What do the authors need to do in order to determine the parameters for describing the physical interaction between each of the beads?

c. (7 points) All-atom MD simulations typically use time steps of 1-2 fs. For the simulations described in this publication, the authors use a much larger time step. Explain why it might be acceptable to use a larger time step for a coarse grained simulation than for an all atom simulation. (Hint: read over the equations from the last problem).

d. (6 points) List 2 drawbacks to the approach used in these simulations.