Biophysics of Cells and Single Molecules: Assignment 3

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Exercises week 1

Consider a particle (in 2-dimensions) in a potential given by equation 1.

$$V(x,y) = xy + xy^2 + x^2y \tag{1}$$

a) **Find the force (due to the potential) acting on the particle as a function of the particle position).**

The force is given by $\vec{F} = -\nabla V$, so we have to calculate the partial derivatives of V:

$$\frac{\partial}{\partial x}V = \frac{\partial}{\partial x}\left(xy + xy^2 + x^2y\right) = y + y^2 + 2xy.$$
$$\frac{\partial}{\partial y}V = \frac{\partial}{\partial y}\left(xy + xy^2 + x^2y\right) = x + 2xy + x^2.$$

Therefore, the force is:

$$\vec{F}(x,y) = -\nabla V = (-y - y^2 - 2xy, -x - 2xy - x^2).$$

b) **Let us assume that the particle is located at $\vec{r}(t_1) = (0,0)$ at time t_1. The goal is to find the particle's position at $t_2 = t_1 + \Delta t$, for a small Δt. Since Δt is small, we can assume that the force acting on the particle is constant in the Δt time interval. This operation is called "one MD step". There are several algorithms available for performing this operation. Among the most popular one is the leap-frog integrator**

$$\vec{v}\left(t + \frac{1}{2}\Delta t\right) = \vec{v}\left(t - \frac{1}{2}\Delta t\right) + \frac{\Delta t}{m}\vec{F}(t) \tag{2}$$

$$\vec{r}(t + \Delta t) = \vec{r}(t) + \Delta t\vec{v}\left(t + \frac{1}{2}\Delta t\right) \tag{3}$$

Use the leap-frog integrator and obtain the particle position at time t_2 by assuming that $\vec{v}(t_1 - \Delta t/2) = (1, 1)$ and $\Delta t = 0.1$.

We can start with equation (2) to calculate the speed $\vec{v}\left(t + \frac{1}{2}\Delta t\right)$ given the information we have. I will assume that $m = 1$.

$$\begin{aligned}\vec{v}\left(t_1 + \frac{1}{2}\Delta t\right) &= \vec{v}\left(t_1 - \frac{1}{2}\Delta t\right) + \frac{\Delta t}{m}\vec{F}(t_1) \\ &= (1, 1) + \frac{0.1}{1}\vec{F}(t_1)\end{aligned}$$

We just need to calculate the force at time t_1. For that, we can use that the position at said time is $\vec{r}(t_1) = (0, 0)$ and according to our result in the previous part of the exercise, $\vec{F}(x, y) = (-y - y^2 - 2xy, -x - 2xy - x^2)$, so that $\vec{F}(t = 0) = \vec{F}(0, 0) = (0, 0)$. Therefore, the equation for the for the final speed becomes:

$$\begin{aligned}\vec{v}\left(t_1 + \frac{1}{2}\Delta t\right) &= (1, 1) + \frac{0.1}{1}(0, 0) \\ &= (1, 1).\end{aligned}$$

Now we can use equation (3) to get the position at time $t_2 = t_1 + \Delta t$:

$$\begin{aligned}\vec{r}(t_1 + \Delta t) &= \vec{r}(t_1) + \Delta t\vec{v}\left(t_1 + \frac{1}{2}\Delta t\right) \\ &= (0, 0) + 0.1 \cdot (1, 1) \\ &= \boxed{(0.1, 0.1)}\end{aligned}$$

c) **Now assume that $\Delta t = 0.05$. Obtain $\vec{r}(t_1 + \Delta t)$ and then use the results (iterate) to obtain $\vec{r}(t_1 + 2\Delta t)$. Is the result different from the one obtained in b? Which one is more reliable (and why)?**

We can do the same procedure as before to calculate $\vec{r}(t_1 + \Delta t)$ with the only difference that now $\Delta t = 0.05$:

$$\begin{aligned}\vec{v}\left(t_1 + \frac{1}{2}\Delta t\right) &= \vec{v}\left(t_1 - \frac{1}{2}\Delta t\right) + \frac{\Delta t}{m}\vec{F}(t_1) \\ &= (1, 1) + \frac{0.05}{1}\vec{F}(t_1)\end{aligned}$$

Just as before, $\vec{F}(t_1) = 0$, so that:

$$\vec{v}\left(t_1 + \frac{1}{2}\Delta t\right) = (1, 1).$$

With that result, we can now calculate $\vec{r}(t_1 + \Delta t)$:

$$\begin{aligned}\vec{r}(t_1 + \Delta t) &= \vec{r}(t_1) + \Delta t \vec{v}\left(t_1 + \frac{1}{2}\Delta t\right) \\ &= (0,0) + 0.05 \cdot (1,1) \\ &= (0.05, 0.05)\end{aligned}$$

Now we will iterate from this point to obtain $\vec{r}(t_1 + 2\Delta t) = \vec{r}(t_2 + \Delta t)$. Using again equation (2) with $t = t_2 = t_1 + \Delta t$, we can calculate $\vec{v}\left(t_2 + \frac{1}{2}\Delta t\right)$ as follows:

$$\vec{v}\left(t_2 + \frac{1}{2}\Delta t\right) = \vec{v}\left(t_2 - \frac{1}{2}\Delta t\right) + \frac{\Delta t}{m}\vec{F}(t_2)$$

According to our last result, the velocity at time $t_2 - \frac{1}{2}\Delta t = t_1 + \frac{1}{2}\Delta t$ is $(1,1)$. Moreover, the position at time $t_2 = t_1 + \Delta t$ turned out to be $(0.05, 0.05)$, so that the force at that time is $\vec{F}(t_2) = \vec{F}(0.05, 0.05) = (-0.05 - 0.05^2 - 2 \cdot 0.05^2, -0.05 - 2 * 0.05^2 - 0.05^2) = (-0.0575, -0.0575)$. Therefore:

$$\begin{aligned}\vec{v}\left(t_2 + \frac{1}{2}\Delta t\right) &= (1,1) + \frac{0.05}{1}(-0.0575, -0.0575) \\ &= (0.9971, 0.9971)\end{aligned}$$

With this, we can now use equation (3) to calculate the position at time $t_2 + \Delta t = t_1 + 2\Delta t$:

$$\begin{aligned}\vec{r}(t_2 + \Delta t) &= \vec{r}(t_2) + \Delta t \vec{v}\left(t + \frac{1}{2}\Delta t\right) \\ &= (0.05, 0.05) + 0.05 \cdot (0.9971, 0.9971) \\ &= \boxed{(0.0998, 0.0998)}\end{aligned}$$

The result is slightly different to that found in b). This result is more reliable, since the method works better for small Δt. The method is basically approximating that for a time Δt, the force is constant, which isn't true but is a better approximation the smaller the value of Δt.

d) **Write a Python code to obtain the trajectory of the particle for** 1000 **steps for different** Δt **values** ($\Delta t = 0.1, 0.05, 0.01$)**.**

The code is in shown and documented in the following figures.

Leap frog code to simulate the motion of a particle under a certain 2D potential.

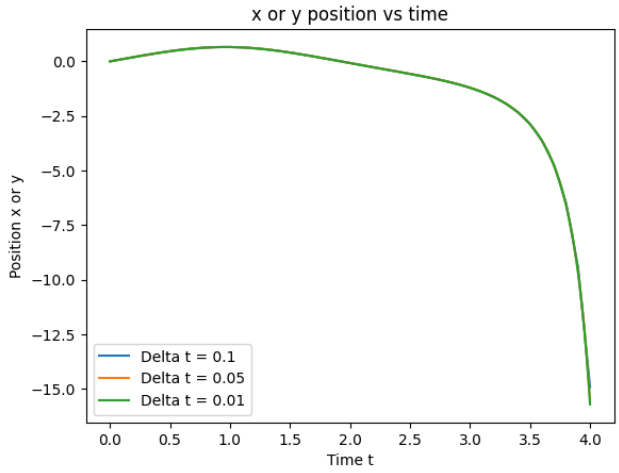
In [45]:

```python
#Import numpy as matplotlib
import numpy as np
import matplotlib.pyplot as plt


#Define the force function, which depends on the position and maybe on
# the velocity.
def F(r,v):
    '''Force function, returns the force at point r and velocity v.'''
    #Get the position and velocity coordinates
    x,y = r
    vx,vy = v

    #Return the force vector [fx, fy].
    return(np.array([-y-y**2-2*x*y
                     , -x-2*x*y-x**2 ]))


def step(ri,vi,Deltat,m):
    '''Takes one step of the leap frog algorithm.
    vi and ri are the previous velocity and speed, deltat the
    time step and m the mass'''

    #Update the speed using the last speed and the force
    vf = vi + Deltat/m * F(ri,vi)

    #Update the position using this new speed vf and the last position
    rf = ri + Deltat*vf

    #return the next position and speed
    return(rf,vf)


```

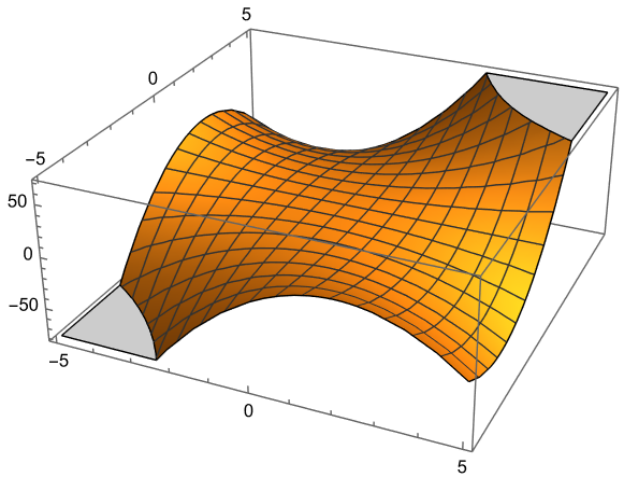
```python

def whole_process(r0,v0,Deltat,m,N):
    '''Function to take N leap frog steps starting from r0, v0
    and save the whole trayectory and velocities'''

    trayectory = [np.array(r0)]
    velocities = [np.array(v0)]

    r = r0
    v = v0
    for i in range(N):
        r,v = step(r,v, Deltat,m)
        trayectory.append(r)
        velocities.append(np.array(v))

    return(np.array(trayectory), np.array(velocities))


```

```
#Run it for the given start conditions and for 20 seconds with Deltat=0.0

r0 = [0,0]
v0 = [1,1]

tf = 20
deltat = 0.01
m = 1
N = int(tf/deltat)


ts = np.linspace(0,N*deltat,N+1)
ts
trayectory, velocities = whole_process(r0,v0,deltat,m,N)
```

However, when we plot the resulting x position as a function of time, we get that the particle goes to minus infinity (and the same happens for the y position, since the potential and the starting point are symmetric when exchanging x and y). Here is a plot of the x position as a function of time for 4 seconds.

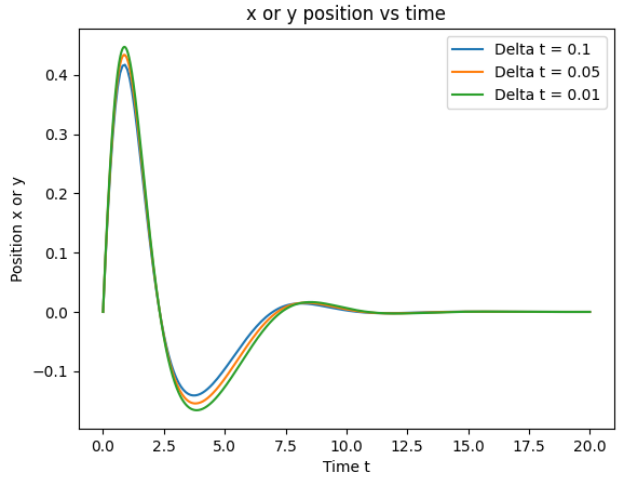


We can see that after getting a little bit higher, the position then becomes negative and gets more and more negative as time passes. This is actually to be expected, since the potential has the following form:



We can see that the potential gets arbitrary lower in the direction of $(-\infty, -\infty)$, and clearly a particle that starts in $(0, 0)$ with a velocity $(1, 1)$, will only go a little bit in that direction and then flow back towards $(-\infty, \infty)$.

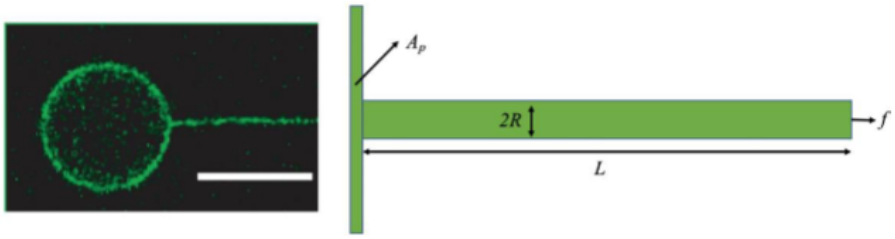
To have a more visible result, I added another term to the force function. I added $-v_x$ to the x component of the force and $-v_y$ to the y component. This effectively is like adding drag to the particle. With that change, the particle doesn't go to infinity and the resulting plot of x as function of time is:



The plot was made with the x data obtained by the code, but it is valid for both $x(t)$ and $y(t)$ given the symmetry of the potential and the starting conditions (they stay the same if we switch x and y).

1 Exercises Week 2

Pulling a nanotube from membranes:
Membrane nanotubes (shown in below Figure), ranging in radius from $10 - 100s$ nanometers, can be pulled from vesicles by an external force. This method was initially designed to measure the elastic properties of the membrane and vesicles, e.g., bending rigidity. Currently, the method is actively used to study a wide range of cellular processes such as protein interactions on curved membranes. In this exercise, we are attempting to determine the nanotube's radius as a function of the system parameters.



Consider a flat membrane with area A that is under mechanical tension τ. A constant force f is applied to a small segment of the membrane with area of a_0. For $a_0 << A$; and sufficiently large f, this leads to the formation of very long nanotube.

a) **Find the radius of the nanotube as a function of κ and τ.**

We start by writing out the total energy of this configuration. To do it, we first assume that the big part of the membrane does not change much its form, so that we can ignore its curvature energy. Then, we only need the curvature energy of the cylinder.

To do it, we identify three components of the energy, the one due to bending, a tension component and the work done by pulling the tube.

1) **Bending energy:** To calculate it, we first need the curvatures of the cylinder. In the long direction, the cylinder is like a straight line, so that $c_1 = 0$. On the other hand, if we go around the cylinder, the curve is a circle of area R, so that the curvature is $c_2 = 1/R$. These are the minimum and maximum curvatures.

Therefore, we have that $H = \dfrac{c_1 + c_2}{2} = \dfrac{1}{2R}$ and $K = c_1 c_2 = 0$. Then, using the

Helfrich Hamiltonaian, we have that the bending energy is:

$$\begin{aligned} E_b &= \oint \frac{\kappa}{2}(2H)^2 - \kappa_G K \, dA \\ &= \oint \frac{\kappa}{2}\frac{1}{R^2} dA \\ &= \frac{\kappa}{2R^2} A \\ &= \frac{\kappa}{2R^2}(2\pi RL) \\ &= \boxed{\kappa\pi\frac{L}{R}} \end{aligned}$$

We ignored the area of the cap of the nanotube, since it will depend on R^2, but R is much smaller than L, so that it doesn't contribute much to the energy.

– **Tension energy:** We also need to add the term for the tension energy, which is $-\tau A_p$, with A_p the projected area. To get the projected area, we may consider that the total area $\mathcal{A}$ must remain constant. Therefore, considering the figure, we can see that creating the nanotube reduces the projected area, since before pulling it, all the area that is now in the nanotube was part of the cell and contributed to the projected area. However, now the projected area of the nanotube is just the inner area of the tube a_0. Therefore, we lost an amount $2\pi RL$ (the area of the cylinder) from the projected area. Then, the projected area is $A_p = \mathcal{A} - 2\pi RL$ and therefore the energy is:

$$E_\tau = -\tau A_p = -\tau\mathcal{A} + 2\pi\tau RL.$$

3. **Work force:** The work done on the membrane by pulling the nanotube is $W = -\int f dl$ and considering that f is constant, we get:

$$W = -fL$$

Therefore, the total energy is:

$$\begin{aligned} E_{tot} &= E_b + E_\tau + W \\ &= \kappa\pi\frac{L}{R} - \tau\mathcal{A} + 2\pi\tau RL - fL \end{aligned}$$

We can actually ignore the term $-\tau\mathcal{A}$ since it is constant and adding a constant to the energy does nothing physically. Therefore:

$$\boxed{E_{tot} = \left(\kappa\pi\frac{1}{R} + 2\pi\tau R - f\right) L}$$

Then, the system will be in equilibrium when energy is minimized with respect to R. To minimize it, we calculate the derivative and set it equal to 0:

$$\begin{aligned}
&\frac{\partial E_{tot}}{\partial R} = 0 \\
&\Rightarrow \left(-\kappa\pi\frac{1}{R^2} + 2\pi\tau\right) L = 0 \\
&\Rightarrow \kappa\pi\frac{1}{R^2} = 2\pi\tau \\
&\Rightarrow \boxed{R = \sqrt{\frac{\kappa}{2\tau}}}
\end{aligned}$$

Notice that it is a minimum, since the second derivative is positive: $\frac{\partial^2 E_{tot}}{\partial R^2} = 2\kappa\pi L\frac{1}{R^3}$.

b) **How large must f be in order to pull a nanotube?**

First, let us write the total energy as before, but substituting the value of R we found:

$$\begin{aligned}
E_{tot} &= \left(\kappa\pi\sqrt{\frac{2\tau}{\kappa}} + 2\pi\tau\sqrt{\frac{\kappa}{2\tau}} - f\right) L \\
&= \left(\pi\sqrt{2\tau\kappa} + \pi\sqrt{2\tau\kappa} - f\right) L \\
&= (2\pi\sqrt{2\tau\kappa} - f)L
\end{aligned}$$

Notice that the energy is of the form $E_{tot} = \alpha L$, with $\alpha = (2\pi\sqrt{2\tau\kappa} - f)$.
Therefore, if α is positive, the energy increases with increasing value of L, so that the nanotube won't extend and the equilibrium value of L is the smallest possible, $L = 0$. On the other hand, if α is negative, energy decreases with increasing L, so that we are actually able to extend the nanotube and increase L.

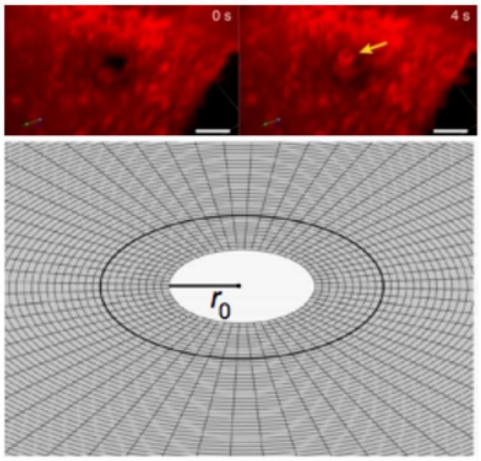
Therefore, the force must be at least enough for α to be equal to 0 or negative:

$$\begin{aligned}
&\alpha \leq 0 \\
&\Rightarrow (2\pi\sqrt{2\tau\kappa} - f) \leq 0 \\
&\Rightarrow \boxed{f \geq 2\pi\sqrt{2\tau\kappa}}
\end{aligned}$$

c) **What is the equilibrium length of the nanotube?**

As we found in the previous question, $E = \alpha L$, with α a negative number (otherwise we won't be able to pull the tubule). Therefore, E keeps decreasing as we increase L, so there is no equilibrium length and the tube keeps increasing in size as long as the force is enough to make $\alpha < 0$.

2. Injured membranes: Cell membrane is selectively permeable layer allowing specific molecules or ions to pass via active or passive transport. Long-lived disruptions in the membrane compromise its selective permeability, allowing intracellular components to escape and permit toxic levels of extracellular milieu to enter. Therefore, survival requires that lesions to be repaired quickly. Eukaryotic cells are equipped with efficient repair mechanisms to cope with membrane disruptions. Malfunction in the repair mechanism is associated with several diseases such as muscular dystrophies, heart failure, neurodegeneration, and cancer. How does cellular repair machinery works is still an active area of research? In this exercise, we want to understand how large an injury should be to demand the repair machinery (or what is the criteria for spontaneous resealing). Consider a flat membrane of area $\mathcal{A}$ with hole of radius R that is under mechanical tension τ. The rim of the hole is described by line tension energy with the line tension λ.



1. **Is there any stable hole?**
   First we will write the total energy of the membrane, which has a membrane tension term and line tension term, which we now calculate:

   - **Line tension:** This is the tension around the line of the hole in the membrane, which is given by $E_\lambda = \lambda L$ with L the length of the hole, which is $L = 2\pi R$, so that:

   $$E_\lambda = 2\pi\lambda R.$$

   - **Membrane tension:** We know that membrane tension is proportional to the projected area as $E_\tau = -\tau A_p$. When we make a hole in the membrane, since the total area of the membrane does not change, the lipids that were in the part where we made the hole move towards the outside of the membrane and therefore the projected area increases by πR^2 (the area of the hole), so that the final projected area is $\mathcal{A} + \pi R^2$. Therefore, the energy is:

   $$E_\tau = -\tau\mathcal{A} - \tau\pi R^2.$$

Therefore, the total energy (ignoring the term $-\tau\mathcal{A}$, since it is just a constant) is:

$$\boxed{E_{tot} = 2\pi\lambda R - \tau\pi R^2}$$

The hole will be in equilibrium when E_{tot} reaches an extremum, which we can find by setting the derivative equal to zero:

$$\begin{aligned} \frac{\partial E_{tot}}{\partial R} &= 0 \\ \Rightarrow\ 2\pi\lambda - 2\pi\tau R &= 0 \\ \Rightarrow\ \boxed{R = \frac{\lambda}{\tau}} & \end{aligned}$$

However, this is a maximum point, since the second derivative is negative: $\frac{\partial^2 E_{tot}}{\partial R^2} = \frac{\partial}{\partial R}(2\pi\lambda - 2\pi\tau R) = -2\pi\tau$.
Therefore, this equilibrium point is not stable, since we are in a maximum of energy and any change in R would decrease the total energy.

2. **What are the conditions for spontaneous closing of the hole?**

As we saw in the previous question, the energy as a function of R is a parabola with a maximum at $R = \lambda/\tau$. Therefore, for $\boxed{R < \lambda/\tau}$, energy decreases as R decreases so that R will decrease in order to keep decreasing the total energy. That is, the hole will close when $R < \lambda/\tau$.

3. **What happens to the membrane if the conditions in 2 is not fullfilled?**

Just as in the previous question, we know that the energy as a function of R is a parabola with maximum at $R = \lambda/\tau$ and therefore, E decreases as R gets bigger than λ/τ. This implies that if we make R even just slightly bigger than the equilibrium value, the hole will keep on increasing in size in order to decrease the total energy, so the cell will break.