Interacting motor proteins in a flashing ratchet potential

Johanne B. Tjernshaugen

Praktisk informasjon

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Vurderingsansvarlig: Johanne B. Tjernshaugen, mail: `johanne.b.tjernshaugen@ntnu.no`
Innleveringsformat: Jupyter Notebook (lever kun én fil).

Notebooken skal være kjørt ved innlevering. For å sjekke om den er kjørt kan dere laste ned den endelige notebooken. Dere skal referere til oppgavenummer (for eksempel **2b**) i besvarelsen. Oppgavene skal besvares i riktig rekkefølge. Det er ikke nødvendig å skrive introduksjon, metode osv. som man vanligvis skriver i en labrapport. Svar kun på det oppgavene spør om.

Alle plott skal forklares/diskuteres, og alle akser skal ha navn ("labels"). Koden deres skal være enkel å lese og forståelig med informative variabelnavn. Bruk gjerne kommentarer. Godt dokumentert og strukturert kode vil trekke besvarelsen i positiv retning. Kjøretiden på koden deres vil variere avhengig av hvordan dere løser oppgavene, men vil ikke påvirke endelig karakter utover at rask/lur/godt strukturert kode vil telle i positiv retning. Det er fint mulig å få full uttelling med tregere kode. Dere oppfordres til å bruke lavere numerisk nøyaktighet (f.eks. færre partikler, tidssteg osv.) når dere tester koden for å slippe å vente på at den produserer feil resultater.

Karakteren blir satt ut fra hvor riktige resultatene er, diskusjonen av resultatene og presentasjonen av resultatene. Generelt vil de siste oppgavene telle mer på karakteren enn de første oppgavene. Resultater som åpenbart er ufysiske vil ikke gi maksimal poengsum, men diskusjonen av resultatene vil kunne trekke besvarelsen i positiv retning. Hvis dere forstår at svarene deres er ufysiske vil dere få en høyere poengsum hvis dere forklarer hva som er feil og hvorfor det er feil, ettersom dette viser fysisk intuisjon og forståelse. Presentasjonen av resultatene skal være oversiktlig med tydelige overskrifter, og det skal være enkelt å forstå hvilke figurer dere refererer til når dere diskuterer resultatene. Bruk markdown og hashtag for a markere starten på oppgaver og deloppgaver (## Exercise 1, ###1a).

Det er tillatt å bruke kunstig intelligens (KI), men direkte kopiering fra KI-verktøy anses som juks. Ved mistanke om direkte kopiering fra KI eller andre kilder kan man bli bedt om muntlig redegjørelse for det man har skrevet. Dersom dere bruker KI må dere inkludere et avsnitt i besvarelsen der dere deklarerer hvordan KI er brukt.

Denne øvingen er basert på Haakon Krogstads biofysikkprosjekt "Modelling motor proteins as particles diffusing in parallel potentials" fra 2020.

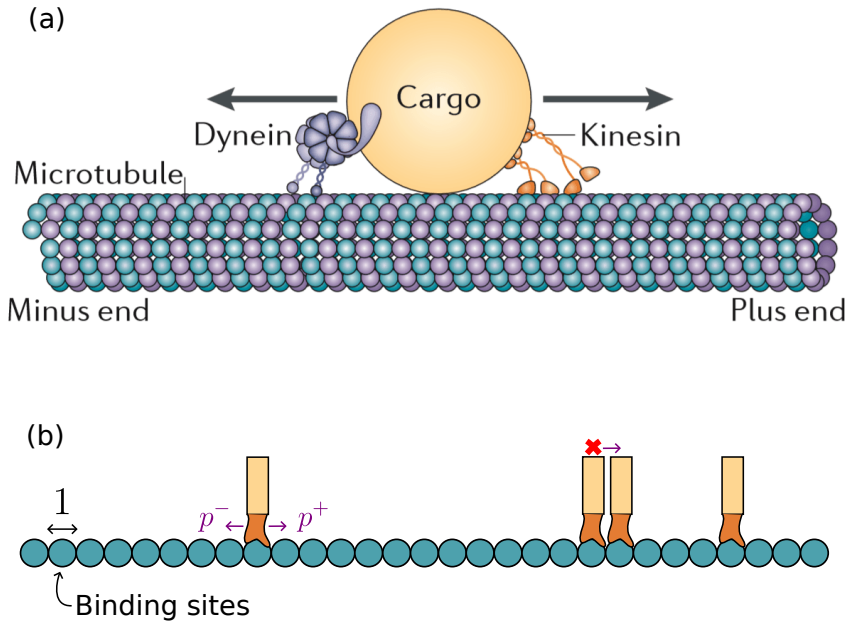

Figure 1: (a) Illustration of kinesin and dynesin moving cargo along a microtubule. The figure is retrieved from Hancock (2014) at https://doi.org/10.1038/nrm3853. (b) The motor proteins are modeled as hard rods. A particle can attempt to move one site to the left or right with probabilities p^- and p^+, respectively. If the particle attempts to move to a site that is already occupied, the move is aborted.

Introduction

Molecular motors are responsible for movement in living organisms. One class of such molecular motors is the cytoskeletal motors, which are motor proteins that move along the cytoskeleton of the cell by turning chemical energy in ATP into mechanical energy. Typical examples include myosin, kinesin and dynein. Myosin drags a thin filament parallel to the myofilament it is attached to, and the collective action of many such myosin proteins is what we know as muscle contractions. Kinesin and dynein move cargo inside cells, such as proteins, chromosomes, and organelles [see Fig. 1(a)].

The collective motion and interaction of a large number of molecular motors is a highly complex process. Typically, the cytoskeleton is crowded, and the motor proteins compete for a limited number of binding sites. A common way to model such processes theoretically is to model the motor protein as particles moving in several, parallel and periodic potentials. Transitions between the potentials (or energy levels) are triggered by catching an ATP molecule or releasing ADP + P. The particles interact via hard core exclusion, which means that they cannot overlap. If a particle tries to move to a site already occupied by another particle, the move is aborted. This is illustrated in Fig. 1(b).

In this exercise, we will model the motor protein transport as a current of particles moving in a 1-dimensional, two-level potential landscape, using random walk simulations.

1 The diffusion equation

Diffusion is a process where particles move down a concentration gradient. That is, particles move from regions with high concentration to regions with low concentration. The physical driving force of diffusion is simply the random movement of each particle. Diffusion of a substance, of which distribution is given by $\phi(x,t)$, is described by the diffusion equation. In one dimension (1D), the diffusion equation takes the form

$$\frac{\partial \phi(x,t)}{\partial t} = \frac{\partial}{\partial x}\left(D(x)\frac{\partial \phi(x,t)}{\partial x}\right), \tag{1}$$

where $D(x)$ is the (position-dependent) diffusion coefficient.

We will now show the correspondence between random walk in 1D and the diffusion equation. Random walk is defined as follows: let $X(t)$ be a stochastic process in time giving the position of a particle after a time t. At time $t = 0$, $X(0) = 0$. The particle makes a step in every time interval Δt. The particle can move left and right along an axis, or stay put, with the following probabilities

$$X(t+\Delta t) = \begin{cases} X(t)+h & \text{with probability } \frac{d}{2}, \\ X(t) & \text{with probability } 1-d, \\ X(t)-h & \text{with probability } \frac{d}{2}. \end{cases} \tag{2}$$

We now define the function $\phi(x,t) = P\{X(t) = x\}$. By conditional probabilities, we may straightforwardly write

$$\phi(x,t+\Delta t) = \frac{d}{2}\phi(x+h,t) + (1-d)\phi(x,t) + \frac{d}{2}\phi(x-h,t). \tag{3}$$

Slightly rewrite this to

$$\frac{\phi(x,t+\Delta t)-\phi(x,t)}{\Delta t} = \frac{dh^2}{2\Delta t}\frac{\phi(x+h,t)-2\phi(x,t)+\phi(x-h,t)}{h^2}. \tag{4}$$

Now suppose that $D = \frac{dh^2}{2\Delta t}$ is a constant. If we then let Δt and h^2 go simultaneously to zero, we find

$$\frac{\partial \phi(x,t)}{\partial t} = D\frac{\partial^2 \phi(x,t)}{\partial x^2}. \tag{5}$$

This is the diffusion equation with constant diffusion coefficient. We have therefore shown that random walk in the limit of infinitesimal steps in time and space corresponds to diffusion.

Exercise 1a)

Show that

$$\phi(x,t) = \frac{1}{\sqrt{4\pi D t}}\int_{-\infty}^{\infty} \mathrm{d}y\; h(y) e^{-\frac{(x-y)^2}{4Dt}} \tag{6}$$

is a solution of the diffusion equation.

Let $\phi(x,t)$ represent a distribution of particles along the x-axis at time $t \geq 0$. Give a physical interpretation of $h(y)$ (*Hint:* let $t \to 0$ in Eq. (6)).

Exercise 1b)

Assume that the probability of finding a particle at position x in a potential landscape $V(x)$ is given by[1]

$$P(x) = \frac{e^{-\beta V(x)}}{Z}, \tag{7}$$

where $V(x)$ is the particle's potential energy at position x, $\beta = (k_{\mathrm{B}}T)^{-1}$ where k_{B} is the Boltzmann's constant and T is the temperature, and Z is the canonical partition function of the system.

We now want to perform a random walk using these probabilities to determine the movement of the particles. At each step in the random walk, we allow the particle only to move one step to the right, one step to the left, or stay put. We define the probability of moving one step to the right as p^+, the probability of moving one step to the left as p^-, and the probability of staying put as p^0. Let the probability of a particle moving to position x from a position $x_0 \in \{x-1,\, x,\, x+1\}$ during one time step be proportional to $P(x)$, and assume that the proportionality constant is equal for all step options.

Show that, if the position of the particle before a random walk step is x_0, the probabilities $\{p^+,\, p^0,\, p^-\}$ are

$$\begin{aligned}
p^+ &= \frac{1}{1 + e^{-\beta[V(x_0-1)-V(x_0+1)]} + e^{-\beta[V(x_0)-V(x_0+1)]}}, \\
p^0 &= \frac{1}{1 + e^{-\beta[V(x_0-1)-V(x_0)]} + e^{-\beta[V(x_0+1)-V(x_0)]}}, \\
p^- &= \frac{1}{1 + e^{-\beta[V(x_0+1)-V(x_0-1)]} + e^{-\beta[V(x_0)-V(x_0-1)]}}.
\end{aligned} \tag{8}$$

Exercise 1c)

What happens to the probabilities $\{p^+,\, p^0,\, p^-\}$ given by Eq. (8) when the temperature T satisfies the following conditions:

- $k_{\mathrm{B}}T \gg |V(x+1) - V(x)|$ for any x?
- $k_{\mathrm{B}}T \ll |V(x+1) - V(x)|$ for any x?

An important tool for physicists is identifying the energy scales relevant to what we want to compute. In certain situations, we may ignore some interactions in a problem because the corresponding energy scale can be neglected compared to some other interaction. For example, when you compute the driving time from Trondheim to Oslo, you can, with great precision, ignore quantum effects and relativistic effects such as time dilation, as these effects are small on the relevant energy scale.

How can we simplify the random walk problem using an energy scale argument in the two limits given above?

[1] This is not a totally random probability distribution, but a well-known (although slightly simplified) result from statistical physics.

2 Random walk

We will now work through some examples of random walk in one dimension. In all examples, start with 101 particles placed next to each other on different binding sites. Let the particles be subject to a random walk for 200 time steps, where the step length is $h = 1$, and the time step is $\Delta t = 1$ (we use dimensionless time and space axes).

Exercise 2a)

In the absence of interactions between the particles, simulate the random walk by picking a random number between 0 and 1 for each particle. Walk to the left if this number is equal to or less than p^-, walk to the right if it is greater than $(1 - p^+)$, and stay put otherwise. In each example a potential is defined, and you should use Eq. (8) to determine $\{p^+, p^0, p^-\}$ for each particle at each time step.

For each of the potentials below, perform the random walk simulation 100 times, resetting the particles' position to their initial positions each time. Plot the average particle distribution along the x-axis. Let $\beta k = 1$.

i) $V(x) = k$

ii) $V(x) = -kx$

Exercise 2b)

The diffusion equation describes the motion of a single particle in the absence of other particles. The interaction between two particles can be approximated with hard core repulsion, which means that particles are not allowed to overlap. Simulate random walk with hard core repulsion as follows. At each time step, all the particles will try to move once. Choose a random order of the particles at each time step, and let each of them try to move by choosing a random number between 0 and 1, as before. The particle attempts to walk to the left if this number is equal to or less than p^-, and to the right if it is greater than $(1 - p^+)$. If there already is a particle at the site that the particle attempts to move to, the move is aborted, and the particle stays put.

For each of the potentials below, perform the random walk simulation 100 times, resetting the particles' positions to their initial positions each time. Plot the average particle distribution along the x-axis, and compare the particle distributions to the non-interacting particle distributions obtained in 2a). Let $\beta k = 1$.

i) $V(x) = k$

ii) $V(x) = -kx$

Exercise 2c)

What happens with the particle distributions in 2a) and 2b) if the temperature decreases such that $\beta k = 1000$?

3 Random walk in a ratchet potential without interactions

We will now create a toy model for motor protein motion by modelling them as particles moving in two parallel and periodic potentials. Although the model is simplified, this is in fact one of the main theoretical principles used to model motor protein motion. In this exercise, we consider non-interacting particles to gain an understanding of how a single particle would move in a flashing ratchet potential.

Define two potentials, $V_1(x)$ and $V_2(x)$. The particles can move inside the potential landscapes defined by $V_1(x)$ and $V_2(x)$, and they can be excited (de-excited) between these energy levels. $V_2(x)$ is a constant function of x, and its magnitude is not important. $V_1(x)$ is a periodic potential. Let the x-axis be discretized with step length $h = 1$, and let the spatial period of $V_1(x)$ be N_x steps. We then have $V_1(x + nN_x) = V_1(x)$ for $n \in \mathbb{Z}$. $V_1(x)$ is defined on the interval $x \in \langle -(1-\alpha)N_x,\, \alpha N_x]$ as

$$V_1(x) = \begin{cases} k\frac{x}{\alpha N_x} & 0 < x \leq \alpha N_x, \\ -k\frac{x}{(1-\alpha)N_x} & -(1-\alpha)N_x < x \leq 0, \end{cases} \tag{9}$$

where $0 \leq \alpha \leq 1$. The shape of this potential is a so-called sawtooth wave. α defines the x-positions of the teeth's peaks. In particular, $\alpha = 0.5$ results in a symmetric potential about $x = 0$, while $\alpha = 0$ and $\alpha = 1$ corresponds to V_1 falling discontinuously to zero. k determines the strength of the potential.

The particles living in this system are excited and de-excited between the energy levels 1 and 2 with respective potential landscapes $V_1(x)$ and $V_2(x)$ at even intervals T_p. That is, if the particles start in energy level 2 at $t = 0$, the particles are de-excited to energy level 1 at $t = T_p$. They live in the potential landscape defined by $V_1(x)$ in the time interval $T_p \leq t < 2T_p$, before the particles are excited to live in the potential landscape defined by $V_2(x)$ in the time interval $2T_p \leq t < 3T_p$, etc. In the (de-)excitation process, the x-coordinate is conserved, so that a particle situated at x_j before an excitation moves from $V_1(x_j) \to V_2(x_j)$.

Define the normalized particle current $J(t_i)$ as

$$J(t_i) = \frac{n^+(t_i) - n^-(t_i)}{N_p}, \tag{10}$$

where $n^+(t_i)$ is the number of particles moving to the right on the time interval $(t_i - t_{i-1})$, $n^-(t_i)$ is the number of particles moving to the left, and N_p is the total number of particles in the system.

Exercise 3a)

Let $\alpha = 0.8$ and $T_p = 500$. Use step length $h = 1$, $N_x = 100$ steps per potential period, time step $\Delta t = 1$ and $\beta k = 1000$. Define an x-axis that fits two full sawtooth peaks (in total $2N_x = 200$ discrete points), and use periodic boundary conditions. That is, if a particle moves to the left from the leftmost point x_0, it arrives at x_{199} (if we use zero-based numbering). Let the number of particles in the system be $N_p = 12N_x$. Let the particles start in $V_2(x)$ and be evenly distributed along the x-axis at $t = 0$, so that there are six particles per discrete x-point to start with. Run the random walk simulation for $20T_p = 10000$ time steps, that is 10 cycles. Calculate the cycle-averaged current for each of the 10 cycles, $J_{\text{avg}}(n) = \frac{1}{2T_p}\sum_{i=1+2T_p n}^{2T_p(n+1)} J(t_i)$, where n labels the cycles. You should obtain negative average currents.

- Write down the 10 cycle-averaged currents you obtain.
- Why do we get non-zero currents? Give a physical interpretation of this.
- Compare $J_{\text{avg}}(0)$ with $J_{\text{avg}}(n)$ for $n > 0$. Give a physical interpretation of this difference.

Repeat this process, only this time with $\alpha = 0.1$. Give a physical interpretation of the cycle-averaged currents compared to what you obtained with $\alpha = 0.8$.

Exercise 3b)

Choose 50 values of T_p equally spaced between 1 and 1001, and run the random walk simulation for one cycle for each of these values. Let the number of particles in the system be $N_p = 40N_x$, and use $\alpha = 0.8$. Start each simulation with half of the particles at each of the two x-coordinates which coincide with the minima of $V_1(x)$ (however, let the particles start in energy level 2 defined by $V_2(x)$). Reset the system into this state for every new set of parameters T_p. Calculate one cycle-averaged current J_{avg} for all the values of T_p. Plot J_{avg} as function of T_p. What do you observe? Give a physical interpretation of the results.

Analytical solution

In the simple sawtooth-shaped potential which we encountered in the last section, there exists in fact an analytical solution to the current in certain parameter limits. Let us briefly go through the argument that leads to the solution:

When the particles find themselves in the sawtooth-shaped potential $V_1(x)$, they will relax towards the potential minima. Hence, as the particles are excited to the second energy level defined by $V_2(x)$, they start out localized at positions $x_n = nN_x$, $n \in \mathbb{Z}$. Since $V_2(x)$ is a constant potential, the particles will be subject to isotropic diffusion once excited to energy level 2. We learned in the theory section that random walk in a flat potential corresponds to diffusion with constant diffusion coefficient. If the particle distribution at $t = 0$ is $\phi(x, t = 0) \sim \delta(x)$, where $\delta(x)$ is the Dirac delta function, one can show that the normalized solution of the diffusion equation at $t > 0$ is

$$\phi(x,t) = \frac{1}{\sqrt{4\pi D t}} e^{-\frac{x^2}{4Dt}}, \tag{11}$$

where $D = \frac{dh^2}{2\Delta t}$ (all these quantities are defined in the theory section). Random walk in a flat potential corresponds to $d = 2/3$. We moreover have $h^2/\Delta t = 1$, so that $D = 1/3$. After diffusion with duration $t = T_p$, the particles are de-excited into $V_1(x)$, where the particles once again move down the potential gradient into one of the minima. The particles on the interval $-(1-\alpha) \leq x < \alpha$ will therefore move towards $x = 0$. The particles having diffused to the right of αN_x will be caught in a minimum to the right, and the particles to the left of $-(1-\alpha)N_x$ will be caught in a minimum to the left.

The number of particles having moved to the right after a cycle of length $2T_p$ can be found by using Eq. (11),

$$n^+ = N_p \sqrt{\frac{3}{4\pi T_p}} \int_{\alpha N_x}^{\infty} \mathrm{d}x \; e^{-\frac{3x^2}{4T_p}}, \tag{12}$$

and the number of particles having moved to the left after the cycle of length $2T_p$ follows as

$$n^- = N_p \sqrt{\frac{3}{4\pi T_p}} \int_{-\infty}^{-(1-\alpha)N_x} \mathrm{d}x \; e^{-\frac{3x^2}{4T_p}}. \tag{13}$$

The normalized, cycle-averaged particle current can therefore be expressed as

$$J_{\text{avg}} = \frac{N_x}{2T_p} \sqrt{\frac{3}{4\pi T_p}} \left(\int_{\alpha N_x}^{\infty} \mathrm{d}x \; e^{-\frac{3x^2}{4T_p}} - \int_{-\infty}^{-(1-\alpha)N_x} \mathrm{d}x \; e^{-\frac{3x^2}{4T_p}} \right). \tag{14}$$

Some algebra later, we arrive at

$$J_{\text{avg}} = \frac{N_x}{4T_p} \left[\operatorname{erfc}\left(\frac{\alpha N_x}{2} \sqrt{\frac{3}{T_p}} \right) - \operatorname{erfc}\left(\frac{(1-\alpha)N_x}{2} \sqrt{\frac{3}{T_p}} \right) \right], \tag{15}$$

where $\operatorname{erfc}(x) = \frac{2}{\sqrt{\pi}} \int_x^{\infty} \mathrm{d}z \; e^{-z^2}$ is the "complimentary error function".

Exercise 3c)

Let $T_p = 500$, choose 50 equally spaced values of α between 0 and 1, and run the random walk simulation for one cycle for each of these values of α. Let the number of particles in the system be $N_p = 12N_x$. Calculate the cycle-averaged current J_{avg} for all these values of α. Compare the results with the analytical current [Eq. (15)] as function of α. Plot both the numerical and analytical J_{avg} as functions of α in the same figure.

What do you observe? Give a physical interpretation of the results.

Exercise 3d)

Repeat programming exercise 3c), but this time with $\beta k \in \{0.01, 1, 2, 3, 5, 10\}$. Compare the analytical and numerical results.

Exercise 3e)

Repeat Ex. 3b), but this time with 20 values of T_p equally spaced between 80 and 1500, and use $\alpha = 0.8$ and $N_x = 10$ (so that the system is discretized into 20 spatial steps). We use these parameters in order to avoid a very long computation time. Compare the numerical results with the analytical current [Eq. (15)]. Plot both the numerical and analytical J_{avg} as functions of T_p in the same figure. Compare and comment on the graphs.

Exercise 3f)

Your results in 3d) and 3e) should indicate that the "analytical argument" presented above has some limitations. That is, the argument is not waterproof. Identify which parts of the argument contain implicit assumptions, and under what circumstances these assumptions do not hold.

4 Random walk in a ratchet potential with interactions

In exercise 2b), we considered random walk in two different potentials, where the interacting particles were not allowed to sit at the same binding site. In this exercise, we consider random walk in the sawtooth potential encountered in exercise 3. We generalize the model to particles of size b, see Fig. 2. That is, a particle is not allowed to be within a distance b or smaller from another particle. This is an extension of exercise 2b), where the particles were smaller than the spacing between the binding sites (i.e. $b < 1$). Use periodic boundary conditions, and make sure that the hard core repulsion also holds across the boundary.

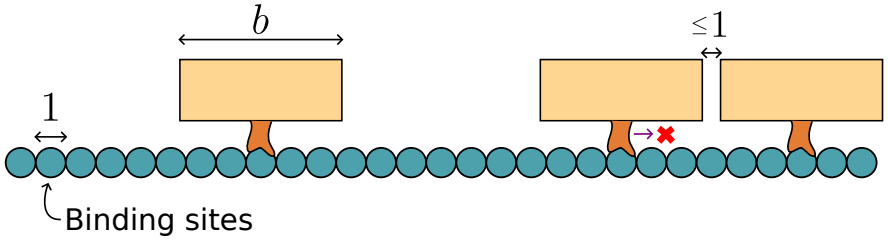

Figure 2: The particles are of size b, and they are not allowed to overlap. If a particles will touch another particle when attempting to move, the move is aborted.

Exercise 4a)

Let $\beta k = 1000$, $N_x = 20$, $\alpha = 0.2$, $T_p = 40$ and define an x-axis that fits four full sawtooth peaks. Choose a suitable number of particles, particle size, and initial positions of the particles. Let the particles interact via hard core repulsion, and run the random walk simulation in the flashing ratchet for five cycles. Plot the position of each particle at each time step and discuss how the particles move in the potential landscape.

Exercise 4b)

The particle density is given by $\rho = bN_p/(N_sN_x)$, where N_s is the number of full sawtooth peaks. Vary the particle density by changing N_p while keeping b, N_s and N_x fixed. Let $\beta k = 1000$, $N_x = 100$, $T_p = 300$, $N_s = 10$, $\alpha = 0.2$, and $b = 20$. Let the particles be evenly distributed along the x-axis, and run the simulation for $N_c = 100$ cycles for each density ρ. Calculate and plot the cycle-averaged current as a function of densities $0 \leq \rho \leq 1$, and comment on the result.

Exercise 4c)

What happens to the results in 4b) if T_p changes? Keep $T_pN_c = 30\ 000$ constant. Check for both smaller and higher time steps T_p, and provide a physical interpretation for the results.

Exercise 4d)

One of the most important steps in developing a simulation of a physical system is to confirm that the code gives the expected results in the regimes where answers are already known. A common strategy is to reproduce results from published research papers. Therefore, part of being good at doing scientific computations is to find and understand the results of relevant papers. Find a research paper that studies particles interacting via hard core repulsion in a flashing ratchet potential. Take one of their results (one figure) and explain briefly what they find, how it differs from non-interacting particles, and the model they use.

Notes: You are *not* supposed to read and understand the full paper. It is unlikely that the method and parameters used in the paper you find are exactly the same as those in the exercises you have done. Therefore, you should not expect your results to be identical to the results in the paper.