TFY4235/FY8904 : Computational Physics (spring 2020)

Assignment 2: Biased Brownian Motion: An Application to Particle Separation

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Soft deadline: Mar 14, 2020

Relevant fields: Classical Transport Theory (TFY4275/FY8907), Chemistry, Biophysics.

Mathematical and numerical methods: stochastic differential equations, random numbers, statistics.

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1 Introduction

When analyzing the composition of a solution, it may be of interest to be able to separate different constituents depending on their properties. For instance, one could wish to sort cells, or molecules from a biological sample by size in order to study one type of cell specifically or to estimate the different quantities of each constituent. One possible technique to achieve a separation can be centrifugation for example.

In this assignment, we investigate a potential method for separating particles of different sizes by the use of a so-called ratchet potential. By applying a flashing periodic asymmetric potential to a system of particles in solution, their Brownian motion can be biased and the particles consequently drift in a preferred direction. The drift velocity being dependent on the size of the particles, this method could in principle be used to sort particles with respect to their size.

Read the following article [1] for a good introduction on the subject:
`www.sciencemag.org/cgi/content/abstract/276/5314/917`

We propose to make a computer experiment of the concept sketched in Fig. 2 in [1] in a biological context, namely the separation of DNA molecules of different sizes. We will use relevant parameters taken from [2][1], where the real experiment has been done. To treat this problem we will use the so-called Langevin approach.

[1] `http://www.ncbi.nlm.nih.gov/pmc/articles/PMC23918/`

2 The Langevin approach

2.1 Position of the problem

The method presented below follows closely [3].

The system of interest is composed of objects of two different sizes undergoing Brownian motion in a solvent. This could be for instance some kind of micron sized particles, or macro-molecules in water, like DNA in our case. We assume the DNA molecules to be folded in a globular shape. In the following we will use the term 'particle' to denote such a globular molecule. The particles are thus assumed to be spherical with respective radius r_1 and r_2, and mass m_1, m_2. In addition to collisions with the solvent molecules, the particles are subjected to friction and to a flashing ratchet potential. For simplicity, we treat a 1D problem, higher dimensions can be treated in a similar fashion. The motion of such a particle, assuming that each can be treated independently, can be described by Newton's second law:

$$m_i \frac{\mathrm{d}^2 x_i}{\mathrm{d}t^2} = -\frac{\partial U}{\partial x}(x_i, t) - \gamma_i \frac{\mathrm{d}x_i}{\mathrm{d}t} + \xi(t) \,. \tag{2.1}$$

Here the subscript $i \in \{1, 2\}$ denotes the kind of particle under consideration, $\gamma_i = 6\pi\eta r_i$ is the friction constant, U is a potential energy (which we will refer as 'potential' in the following when there is no ambiguity), and ξ is a stochastic variable modeling the random collisions with the solvent molecules. This equation is known as the Langevin equation. We assume that the stochastic variable is an uncorrelated white noise with the properties

$$\langle \xi(t) \rangle = 0, \qquad \langle \xi(t)\, \xi(t') \rangle = 2\gamma_i\, k_\mathrm{B} T\, \delta(t - t') \,, \tag{2.2}$$

where k_B is the Boltzmann constant and T is the temperature of the solvent. The factor $2\gamma_i k_\mathrm{B} T$ is a consequence of the fluctuation-dissipation theorem. In our case, one can neglect the inertial term $m_i \frac{\mathrm{d}^2 x_i}{\mathrm{d}t^2}$ in Eq. (2.1). The equation of interest thus becomes

$$\gamma_i \frac{\mathrm{d}x_i}{\mathrm{d}t} = -\frac{\partial U}{\partial x}(x_i, t) + \xi(t) \,. \tag{2.3}$$

This looks like a first order ordinary differential equation in x_i, with the particularity that the right hand side contains a stochastic term. This type of equations are known as *stochastic differential equations*.

If you are interested in having more details on Brownian motion, the Langevin equation, and the fluctuation-dissipation theorem, we recommend chapter 3 in [4][2].

Following [1, 2] we consider a potential energy of the form

$$U(x, t) = U_\mathrm{r}(x)\, f(t) \,, \tag{2.4}$$

with U_r being an asymmetric saw-tooth potential of period L, or so-called ratchet potential, and f is an asymmetric square signal whose effect is to turn on and off the ratchet potential at a period τ. From here on, we will refer to the function f as the flashing function. The restriction to one period of U_r and f thus read:

$$U_\mathrm{r}(x) = \begin{cases} \frac{x}{\alpha L}\, \Delta U & \text{if } 0 \le x < \alpha L \\ \frac{L - x}{L(1-\alpha)}\, \Delta U & \text{if } \alpha L \le x < L \end{cases} , \qquad f(t) = \begin{cases} 0 & \text{if } 0 \le t < \frac{3\tau}{4} \\ 1 & \text{if } \frac{3\tau}{4} \le t < \tau \end{cases} . \tag{2.5}$$

[2] Accessible online on Ingve Simonsen's webpage: `http://web.phys.ntnu.no/~ingves/Teaching/TFY4275/LectureNote`

$\alpha \in]0,1[$ is the asymmetry factor. Notice that our choice of flashing signal is consistent with that of [2], since the ratio of on and off times is 1/3.

Euler scheme

Since it can be a bit complicated to properly find a numerical scheme for a stochastic differential equation, we provide this to you. We will use the following forward Euler scheme

$$x_{n+1} = x_n - \frac{1}{\gamma_i}\frac{\partial U}{\partial x}(x_n, t_n)\,\delta t + \sqrt{\frac{2k_B T \delta t}{\gamma_i}}\,\hat{\xi}_n\,. \tag{2.6}$$

Here we dropped the subscript i on the position to avoid confusion. δt is the time step, $t_n = n\delta t$, x_n are respectively the time and position of the particle at the n^{th} step, and $\hat{\xi}_n$ is a random number drawn from a centered Gaussian distribution of unit standard deviation.

Important note: Which time step should you choose? Notice that if the time step is too large, a single step could make the particle jump through several variation of the potential. This situation would give wrong results. Thus one should make sure before any simulation that the increment in position will occur with a large probability in a region of constant force (since the potential is piece-wise linear). Since with a probability higher than 99.99% $\hat{\xi}_n$ will be drawn such that $|\hat{\xi}_n| < 4$ and that the shortest length of a constant force region is αL, one should satisfy

$$|x_{n+1} - x_n| \ll \alpha L \tag{2.7}$$

most of the time, which by a straight forward upper-bound of the left hand side yields the following heuristic criterion: δt must be chosen such that

$$\frac{1}{\gamma_i}\,\max\left|\frac{\partial U}{\partial x}\right|\delta t + 4\sqrt{\frac{2k_B T\delta t}{\gamma_i}} \ll \alpha L\,. \tag{2.8}$$

2.2 Numerical implementation and tasks

Pre-implementation tasks

Task 1 - reduced units: Show that the Euler scheme Eq. (2.6) can be expressed in reduced units as follow:

$$\hat{x}_{n+1} = \hat{x}_n - \frac{\partial \hat{U}}{\partial \hat{x}}(\hat{x}_n, \hat{t}_n)\,\delta\hat{t} + \sqrt{2\hat{D}\delta\hat{t}}\,\hat{\xi}_n\,, \tag{2.9}$$

where

$$\hat{x} = \frac{x}{L}, \qquad \hat{t} = \omega\, t, \qquad \omega = \frac{\Delta U}{\gamma_i L^2}, \qquad \hat{U}(\hat{x},\hat{t}) = \frac{U(x,t)}{\Delta U}, \qquad \hat{D} = \frac{k_B T}{\Delta U}\,. \tag{2.10}$$

Write down Eq. (2.5) and the criterion Eq. (2.8) in reduced units.

Task 2: Argue why it is enough to use an Euler scheme for this problem.

Implementation

Note: the implementation should be done directly in reduced units. Although you can (and probably should) have inputs/outputs in physical units in order to make sure you are using physically relevant parameters and to be able to compare directly your results with experimental data.

Task 3: Implement a function which returns the potential as a function of time and position and a function returning the force. Notice that the force can be expressed explicitly and you do not really need the potential. However we will use the potential later for some consistency verification.

Task 4: Implement a function which returns Gaussian distributed random numbers. Check that the numbers you obtain are Gaussian distributed with mean 0 and unit standard deviation. (Hint: You may use a random number generator from a library or implement your own. For instance, implement the Box-Müller algorithm and use a standard random generator for a uniform distribution between $[0, 1]$ which is often built in with some compiler.)

Task 5: Implement the Euler scheme Eq. (2.9).

Task 6: Complete your program adding the criterion for the time step and the relevant parameters and input/output routines that seem relevant. In particular, time, position of the particle, and potential are a good start.

Simulations for a single particle

We now realize the computer experiment of that done in [2]. The physical parameters for the experiment are:

$$r_1 = 12 \text{ nm}, \quad L = 20 \ \mu\text{m}, \quad \alpha = 0.2, \quad \eta = 1 \text{ mPa.s}, \quad k_B T = 26 \text{ meV}, \quad \Delta U = 80 \text{ eV} .$$

The radius r_1 has been deduced from the the diffusion constant, simply to fix the ideas, although it was not really needed. We leave the flashing period τ as a tunable parameter. In order to get a physical feeling of the problem, we first run some tests with $r = r_1$, flashing off and different values of ΔU.

Task 7: Turn the flashing off (such that the ratchet potential is time independent) and run your program for values of ΔU being, say, 10 $k_B T$ and 0.1 $k_B T$. Discuss the physics in the different cases. Check that the distribution of position is consistent with Boltzmann distribution as one should get according to Statistical Mechanics. To illustrate your discussion, plots of trajectories x vs t, and the distribution of occupied potential energy compared to Boltzmann distribution are welcome. We recall that in thermal equilibrium, the distribution of occupied potential energy is given by the Boltzmann distribution:

$$p(U) = \frac{e^{-\frac{U}{k_B T}}}{k_B T \left(1 - e^{-\frac{\Delta U}{k_B T}}\right)} . \tag{2.11}$$

You will also check if this probability density is well normalized.

Task 8: Deduce and argue from your discussion on task 7, how one should choose ΔU to make the particle drift to the right (i.e. increasing x) when the flashing will be turned on and predict 3 regimes of drift efficiency with respect to the flashing τ. (If you find this question difficult get some inspiration from [1, 2] or do the next task first.)

From now on, we set $\Delta U = 80$ eV and keep $r = r_1$ unless specified otherwise.

Task 9: Turn the flashing on, and run the program for different values of τ. Plot some trajectories and comment. Then, compute the average drift velocity[3] $\langle v \rangle$ as a function of the flashing

[3] i.e. averaged along the trajectory and for several realizations. A good enough estimate can be to take the ending point divided by the ending time and consider the average of this quantity over many realizations. Don't forget error bars that you can give as $\pm$ one standard deviation for instance.

time τ and estimate the optimum flashing time, $\tau_{\rm op}$, that maximizes the drift velocity (the trend should look like Fig. 2.b in [1]).

Task 10: Check, by using the experimental data in Fig. 3 in [2], that the average drift velocity you computed is consistent with the one you can estimate from this figure.

Task 11: Now we wish to estimate how a bigger DNA molecule would drift in the same conditions. We thus consider a particle of radius $r_2 = 3\, r_1$. Show that in reduced units, this is equivalent to a change of time scale. Deduce then from your previous plot the average drift velocity as a function of τ for a particle of radius r_2, i.e. without recomputing specifically for this radius. What is the average drift velocity for the particle of radius r_2 when $\tau = \tau_{\rm op}$ (i.e. optimized for r_1)? Now run your code to compute the average drift velocity of a particle of radius r_2 and check that you get the result you predicted.

Visualization of the density of particles

Task 12: Modify your program so that it runs several realizations of the same system. Run it for the two kind of particles under consideration. Visualize the motion of the ensemble of particles and how the particle density behaves in time. Consider first the following check when the potential is turned off. In this case, one can show that the density of particles $n(x,t)$ should exhibit diffusion whose solution is

$$n(x,t) = \frac{N}{\sqrt{4\pi D t}}\, \exp\left(-\frac{x^2}{4Dt}\right)\,, \tag{2.12}$$

where N is the total number of particles and $D = \frac{k_B T}{\gamma_i}$ is the diffusion constant [4]. Check that the density of particles indeed follow the above expression up to some statistical noise that should improve by increasing the number of particles.

Task 13: Once the previous task is under control. Turn the potential on, and run for the two kind of particles with the optimum flashing time $\tau_{\rm op}$ you have found previously. Visualize and describe the particles density behaviour. What kind of partial differential equation, would you guess, describes the evolution of the particle density?

3 Report

Write a report of your work (maximum 6 pages). The report is expected to take the form of a scientific article, containing an abstract, a short introduction, the modeling of the problem, a few words on its numerical resolution, your results and discussion, a conclusion and references. The tasks are here to guide you, and you should not write your answers task by task in the report, but rather select the important pieces of information showing in a concise way how you dealt with the problem, and critically discuss your results. Your codes are not expected in the report, but must be attached to it if it is delivered during the exam. Codes must be clear, and commented.

References

[1] R. Dean Astumian. Thermodynamics and Kinetics of Brownian Motor. *Science 9*, Vol. 256 no. 5314:917–922, 1997.

[2] J. S. Bader, R. W. Hammond, S. A Henck, M. W. Deem, G. A. McDermott, J. M. Bustillo, J. W. Simpson, G. T. Mulhern, and J. M. Rothberg. DNA transport by a micromachined

Brownian ratchet device. *Proceedings of the National Academy of Sciences of the United States of America*, 96(23):13165–13169, Nov. 9, 1999.

[3] A. Belonoshko. Transport properties of a Brownian motor. *Lab in Computational Physics (SI2530) at KTH, Stockholm.*

[4] I. Simonsen. Lecture Notes in Classical Transport Theory. *http://web.phys.ntnu.no/ inges/Teaching/TFY4275/LectureNotes/.*

4 Complements

4.1 Overdamped approximation

Here we justify the use of the overdamped approximation. In other words, that on the time scale of interest, the inertial term in the Langevin equation can be neglected. For simplicity, let us assume that the Brownian particle is subjected to friction and a constant force. The equation of motion thus reads

$$m\frac{\mathrm{d}^2x}{\mathrm{d}t^2} = -\gamma\,\frac{\mathrm{d}x}{\mathrm{d}t} + F\,. \tag{4.1}$$

Our goal is to show that for observation time much larger than a certain characteristic damping time τ, that we will define, the equation of motion can be well approximated by

$$\gamma\,\frac{\mathrm{d}x}{\mathrm{d}t} = F\,. \tag{4.2}$$

We then start by writing Eq. (4.1) for the velocity instead

$$\frac{\mathrm{d}v}{\mathrm{d}t} + \frac{\gamma}{m}\,v = \frac{F}{m}\,. \tag{4.3}$$

The solution of this first order ordinary differential equation is given by the sum of a solution of the homogeneous equation (i.e. for $F = 0$), which reads $v^\circ(t) = C\,e^{-\frac{t}{\tau}}$, with $\tau = \frac{m}{\gamma}$, and a particular solution. A trivial particular solution is a constant velocity equals to $\frac{F}{\gamma}$. Thus the solution reads

$$v(t) = C\,e^{-\frac{t}{\tau}} + \frac{F}{\gamma}\,. \tag{4.4}$$

If the initial velocity is known to be v_0, we can express C and the final form of the solution reads

$$v(t) = v_0\,e^{-\frac{t}{\tau}} + \left(1 - e^{-\frac{t}{\tau}}\right)\,\frac{F}{\gamma}\,. \tag{4.5}$$

We see that $\tau = \frac{m}{\gamma}$ is a characteristic damping time, i.e. that after a time $t \gg \tau$ the velocity reduces to

$$v(t) = \frac{F}{\gamma}\,. \tag{4.6}$$

which is simply the equation of motion where the inertial term has been neglected. The above derivation is of course very much simplified by the assumption of F being constant, and a rigorous justification for a space and time dependent force, and even stochastic, will require more care, and tools from analysis and probability. However the key argument that the observation time is much larger than the damping time is already caught by our simple model, so we will not attempt very technical justifications.

In our case, the time step of the simulation will typically be of the order of 0.1 ms but let us say that we wish to take a time step of the order of 1 μs. Is the approximation valid? To answer this question we need to verify that $\delta t \gg \tau$. With the parameters at hand, $\gamma = 6\pi\,\eta\,r \sim 2 \times 10^{-10}$ kg.s^{-1} and we can safely say that $m \ll 10^{-20}$ kg (this would be a metallic particle of the same size of the DNA globular molecule). This yields $\tau \ll 10^{-10}$ s, which justifies the approximation.

4.2 Fluctuation-dissipation theorem

In this complement we explain the origin of the factor $2\gamma\, k_B T$ in the property of the stochastic term, Eq. (2.2). It is important to have this factor correct if we wish to model a physical system since, as we will see, it originates from a deep physical notion, namely that of thermal equilibrium of the Brownian particle with the solvent. Since the property of the random collisions between the water molecules and the Brownian particle do not depend on the ratchet potential, it is sufficient to study the case of pure diffusion (i.e. $U = 0$). The Langevin equation, written for the velocity of the Brownian particle thus reads

$$m\,\frac{\mathrm{d}v}{\mathrm{d}t} = -\,\gamma\, v + \xi\,. \tag{4.7}$$

If you recall your Mathematics course on first order ordinary differential equation, seeing ξ as a 'usual' function, the solution reads

$$v(t) = v_0\, e^{-\frac{\gamma}{m}\,t} + \frac{1}{m}\,\int_0^t \mathrm{d}t'\, e^{-\frac{\gamma}{m}(t-t')}\,\xi(t')\,. \tag{4.8}$$

Here v_0 is the initial velocity of the Brownian particle. Considering now the kinetic energy K of the Brownian particle, we have:

$$K = \frac{1}{2}\,m\,v^2(t) \tag{4.9}$$

$$= \frac{m\,v_0^2}{2}\,e^{-\frac{2\gamma}{m}\,t} + v_0\,e^{-\frac{\gamma}{m}\,t}\,\int_0^t \mathrm{d}t'\, e^{-\frac{\gamma}{m}(t-t')}\,\xi(t') + \frac{1}{2m}\,\left(\int_0^t \mathrm{d}t'\, e^{-\frac{\gamma}{m}(t-t')}\,\xi(t')\right)^2\,. \tag{4.10}$$

We now take the ensemble average of the previous equation and obtain

$$\langle K\rangle = \frac{m\,v_0^2}{2}\,e^{-\frac{2\gamma}{m}\,t} + v_0\,e^{-\frac{\gamma}{m}\,t}\,\int_0^t \mathrm{d}t'\, e^{-\frac{\gamma}{m}(t-t')}\,\langle\xi(t')\rangle + \frac{1}{2m}\,\left\langle\left(\int_0^t \mathrm{d}t'\, e^{-\frac{\gamma}{m}(t-t')}\,\xi(t')\right)^2\right\rangle\,. \tag{4.11}$$

Using that ξ as the property $\langle\xi\rangle = 0$, the second term vanishes and we are left with

$$\langle K\rangle = \frac{m\,v_0^2}{2}\,e^{-\frac{2\gamma}{m}\,t} + \frac{1}{2m}\,\left\langle\left(\int_0^t \mathrm{d}t'\, e^{-\frac{\gamma}{m}(t-t')}\,\xi(t')\right)^2\right\rangle\,. \tag{4.12}$$

Now let us work with the last term

$$\left\langle\left(\int_0^t \mathrm{d}t'\, e^{-\frac{\gamma}{m}(t-t')}\,\xi(t')\right)^2\right\rangle = \left\langle\int_0^t\int_0^t \mathrm{d}t\mathrm{d}t''\, e^{-\frac{\gamma}{m}(2t-t'-t'')}\,\xi(t')\,\xi(t'')\right\rangle \tag{4.13}$$

$$= \int_0^t\int_0^t \mathrm{d}t\mathrm{d}t''\, e^{-\frac{\gamma}{m}(2t-t'-t'')}\,\langle\xi(t')\,\xi(t'')\rangle\,. \tag{4.14}$$

The second property of the stochastic variable $\langle\xi(t')\,\xi(t'')\rangle = C\,\delta(t'-t'')$ yields

$$\left\langle\left(\int_0^t \mathrm{d}t'\, e^{-\frac{\gamma}{m}(t-t')}\,\xi(t')\right)^2\right\rangle = C\,\int_0^t\int_0^t \mathrm{d}t\mathrm{d}t''\, e^{-\frac{\gamma}{m}(2t-t'-t'')}\,\delta(t'-t'') \tag{4.15}$$

$$= C\,\int_0^t \mathrm{d}t'\, e^{-\frac{2\gamma}{m}(t-t')} \tag{4.16}$$

$$= \frac{Cm}{2\gamma}\,\left(1 - e^{-\frac{2\gamma}{m}t}\right)\,. \tag{4.17}$$

By plugging the last term back in Eq. (4.12), we get

$$\langle K \rangle = \frac{m\, v_0^2}{2}\, e^{-\frac{2\gamma}{m}\, t} + \frac{C}{4\gamma}\, \left(1 - e^{-\frac{2\gamma}{m} t}\right) . \tag{4.18}$$

In thermal equilibrium, or $t \to \infty$, the exponential terms will vanish, and we are left with

$$\langle K \rangle_{\text{th}} = \frac{C}{4\gamma} . \tag{4.19}$$

It is time to use a result of statistical physics, namely the equipartition theorem which yields in that case that $\langle K \rangle_{\text{th}} = \frac{1}{2} k_B T$, with T being the temperature of the solvent. Thus we can express the unknown constant C as a function of the temperature of the solvent T and the friction coefficient γ.

$$C = 2\, \gamma\, k_B T . \tag{4.20}$$

This then shows where the coefficient $2\, \gamma\, k_B T$ in Eq. (2.2) comes from.

4.3 Integration of stochastic differential equations

We have seen that the Langevin equation is a differential equation containing a stochastic term. These kind of equations are known as stochastic differential equations (SDE). A rigorous study of SDEs requires quite advanced mathematics and is a subject of active research. However the numerical resolution of such equations has some similitude with that of an ordinary differential equation. One may construct numerical schemes as the Euler scheme or Runge-Kutta types of scheme for a SDE, although some care must be taken. Here we will motivate the Euler scheme which was given to you in the assignment without going into the trouble of the theory of integration of stochastic functions, in particular we will avoid the discussion around Ito's calculus. Thus the following derivation must be taken as being very formal.

We start from the overdamped Langevin equation

$$\frac{\mathrm{d}x}{\mathrm{d}t} = -\frac{1}{\gamma}\, \frac{\partial U}{\partial x} + \frac{1}{\gamma}\, \xi , \tag{4.21}$$

which we integrate between the times t_n and t_{n+1}:

$$\int_{t_n}^{t_{n+1}} \frac{\mathrm{d}x}{\mathrm{d}t}\, \mathrm{d}t = -\frac{1}{\gamma} \int_{t_n}^{t_{n+1}} \frac{\partial U}{\partial x}\, \mathrm{d}t + \frac{1}{\gamma} \int_{t_n}^{t_{n+1}} \xi\, \mathrm{d}t . \tag{4.22}$$

The left hand side is simply the difference of position at times t_n and $t_{n+1} = t_n + \delta t$ and we can approximate the first term in the right hand side as $\frac{\partial U}{\partial x}\, \delta t$, just as in a classic Euler scheme. The last term needs more care and we simply define

$$\mu_n = \int_{t_n}^{t_{n+1}} \xi(t)\, \mathrm{d}t . \tag{4.23}$$

The Euler scheme thus reads

$$x_{n+1} = x_n - \frac{1}{\gamma}\, \frac{\partial U}{\partial x}\, \delta t + \frac{1}{\gamma}\, \mu_n . \tag{4.24}$$

Now we need to know how the random numbers μ_n relates to the properties of the stochastic variable ξ. To do this we split the integral in Eq. (4.23) on a subdivision of $[t_n, t_{n+1}]$ of step ϵ,

$$\mu_n = \sum_{i=0}^{N-1} \int_{t_n + i\epsilon}^{t_n + (i+1)\epsilon} \xi(t)\, \mathrm{d}t = \sum_{i=0}^{N-1} w_i , \tag{4.25}$$

with $N\epsilon = \delta t$ and $w_i = \int_{t_n+i\epsilon}^{t_n+(i+1)\epsilon} \xi(t)\,\mathrm{d}t$. The w_i are random number produced by integration of ξ on disjoints intervals, it seems thus natural to claim that they form a sequence of independent identically distributed random variables with the properties:

$$\langle w_i \rangle = \int_0^\epsilon \langle \xi(t) \rangle \ \mathrm{d}t = 0 \tag{4.26}$$

$$\left\langle w_i^2 \right\rangle = \int_0^\epsilon \int_0^\epsilon \langle \xi(t)\xi(t') \rangle \ \mathrm{d}t\mathrm{d}t' \tag{4.27}$$

$$= \int_0^\epsilon \int_0^\epsilon 2\,\gamma\,k_B T\,\delta(t-t')\,\mathrm{d}t\mathrm{d}t' \tag{4.28}$$

$$= 2\,\gamma\,k_B T \int_0^\epsilon \mathrm{d}t \tag{4.29}$$

$$= 2\,\gamma\,k_B T\,\epsilon\,. \tag{4.30}$$

The μ_n are a sum of independent identically distributed random variables w_i with finite variance, thus the Central Limit Theorem ensures that when $N \to \infty$, (i.e. $\epsilon \to 0$) the μ_n converge in law to a normal distribution of average 0 and variance $2\,\gamma\,k_B T\,\delta t$ (following the properties of w_i). Consequently, the μ_n must be drawn from a normal law $\mathcal{N}(0, 2\,\gamma\,k_B T\,\delta t)$ or equivalently by a change of variable

$$\mu_n = \sqrt{2\,\gamma\,k_B T\,\delta t}\,\hat{\xi}_n\,, \tag{4.31}$$

where the $\hat{\xi}_n$ follow a centered normal law with unit standard deviation. Plugging this into the Euler scheme, Eq. (4.24) yields

$$x_{n+1} = x_n - \frac{1}{\gamma}\,\frac{\partial U}{\partial x}\,\delta t + \sqrt{\frac{2\,k_B T\,\delta t}{\gamma}}\,\hat{\xi}_n\,. \tag{4.32}$$

where the $\hat{\xi}_n$ follow the probability law $\mathcal{N}(0,1)$ as announced in the assignment.