Biased Brownian Motion

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Abstract

The numerical experiment described in this report investigates how DNA oligomers of sizes $r = 12$ and 36nm behave and can be separated under biased Brownian motion. The maximum average velocity possible is determined to be $\langle v\rangle = 5{,}422 \pm 0{,}992$s and $\langle v\rangle = 1{,}873 \pm 0{,}642$s for the smallest and largest particle respectively. A separation resolution of above 10 is easily acquired, which is well above the needed resolution to separate DNA oligomers.

1. Introduction

Biased Brownian motion is a technique to induce net transport of particles and can be used to separate particles of different sizes. The method is based on diffusion in combination with deterministic motion induced by an externally applied time-dependent potential. The potential have been proven experimentally to work for different generating phenomena such as dielectrophoresis, optical teweezers and electrocapillary forces.

This report describes biased Brownian motion and the theory behind net transport movement in addition to present numerical results for different sized DNA oligomers. The results are compared to theory and later validated by a physical experiment. The experiment used charge-charge interaction to generate the potential, mostly due to the need of a strong potential as the particles under consideration are heavy.

2. Model

We treat the system as a one dimensional problem and look at a ratchet potential which is periodic and asymmetric. The potential is on the form $U(x,t) = U_r(x)f(t)$ where $f(t)$ takes the shape of a square wave signal with $t_{on}/t_{off} = 1/3$. The parameters t_{on} and t_{off} represents the time the potential is turned on and off during a cycle. A whole cycle of f is completed after the period τ. This turning on and off the potential will be called flashing the potential. The spatial part has periodicity L and takes the form

$$U_r(x) = \begin{cases} \frac{x}{\alpha L}\Delta U & 0 \le x < \alpha L, \\ \frac{L-x}{L(1-\alpha)}\Delta U & \alpha L \le x < L, \end{cases} \tag{1}$$

where ΔU is the strength of the potential and $\alpha \in [0,1]$ is the asymmetric factor.

If the potential is turned off, and we only consider Brownian motion, will the density $n(x,t)$ in an ensemble of particles N take the form

$$n(x,t) = \frac{N}{\sqrt{4\pi D t}} e^{-\frac{x^2}{4Dt}}. \tag{2}$$

This is the solution to the standard diffusion equation where all the particles are initially at origin. Here, $D = \frac{k_b T}{\gamma}$, is the diffusion constant. Considering a single particle this equation can be regarded as the probability $P(x,t)$ of finding the particle at position x at time t with $N = 1$. Considering hopping to only nearest-neighbouring potential-wells, the probability for a particle to move towards increasing x is $\beta = P_+ - P_-$, where P_i is the integrated probability over the neighbouring well, i.e $P_+ = \int_{L\alpha}^{L(1+\alpha)} P(x, t_{off})$. Here is is assumed that the particle starts at $x = 0$, and we inserted the time t_{off} which is the time the particle has to diffuse. Once the potential turns on again, the particle is assumed to end up at the bottom of its current well during time t_{on}. The averaged velocity after a number of cycles will then take form[1]

$$\langle v\rangle = \frac{\beta L}{\tau}. \tag{3}$$

The system may be solved with the Langevin equation, as suggested by [1]. Neglecting the inertial term, called the overdamped approximation, in the equation of motion it can be written on the form

$$\gamma_i \frac{dx}{dt} = -\frac{\partial U(x_i,t)}{\partial x} + \xi(t). \tag{4}$$

The i-index is here to denote the i$^{\text{th}}$ particle, which has mass m_i and radius r_i, considering each particle as a sphere. The left-hand side represents a drag force, with $\gamma_i = 6\pi\eta r_i$ where η is the viscosity, and the $\xi(t)$ variable is the stochastic part representing Brownian motion. Continuing as done in [3] we find an explicit Euler scheme of the form

$$x_{n+1} = x_n - \frac{1}{\gamma_i}\frac{\partial U(x_n,t_n)}{\partial x}\delta t + \sqrt{\frac{2k_bT\delta t}{\gamma_i}}\hat{\xi_n}. \tag{5}$$

[1]This derivation is gathered from [1].

The thermal energy k_bT enters as a result of the fluctuation-dissipation theorem, where the assumption of thermal equilibrium has been used. $\hat{\xi_n}$ is now a random number drawn from a standard normal distribution. The discretization is of the form $x_n = x(t_n)$ where $t_n = t_0 + n\delta t$. In order for the numerical scheme to work does the criterion $|x_{n+1} - x_n| << \alpha L$ has to be satisfied. The criterion can be manipulated to take the form

$$Q(\delta t, \Delta U, r_i) = \frac{\delta t}{\alpha L \gamma_i}\left(\max\left|\frac{\partial U}{\partial x}\right| + \sqrt{\frac{32 k_b T \gamma_i}{\delta t}}\right) << 1, \tag{6}$$

and thus puts a limitation on the step-size δt. It can be noted that the Euler scheme is appropriate since the potential term is a constant while the stochastic part is random in nature so a more advanced scheme will not acquire better accuracy.

The probability for a particle to occupy a state is given by the Boltzmann distribution $p = e^{-E/k_bT}/Z$. Neglecting the kinetic energy and normalizing the probability from zero to ΔU we find

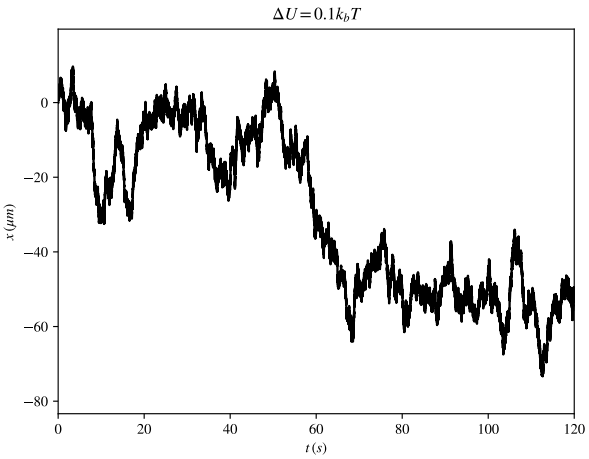
$$p(U) = \frac{e^{-\frac{U}{k_bT}}}{k_bT(1 - e^{-\frac{\Delta U}{k_bT}})}. \tag{7}$$

3. Results

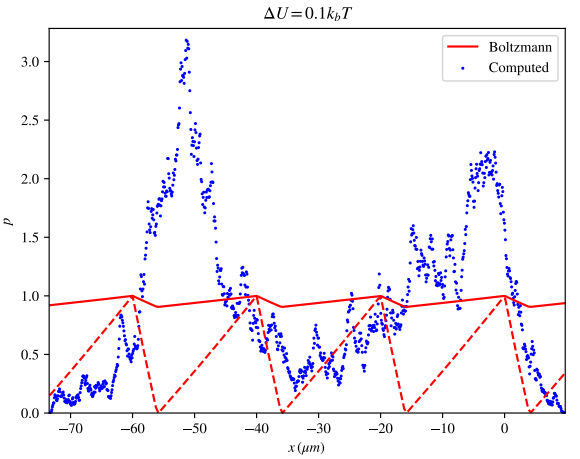
The datatype used for this numerical experiment is binary64 using the technical standard for floating point arithmetic IEE 754. The machine precision is thus $\epsilon = 2{,}2 \cdot 10^{-16}$ which is considered to be good enough for this experiment. The function *np.random.normal()*, found in Python's library *NumPy*, is used to generate random numbers. It makes use of the pseudo random number generator (PRNG) PCG-64 with a period of 2^{128}. No seed is entered so a new sequence of random numbers appears for each new run.

The following parameters are set to these values, $\alpha = 0{,}2$, $L = 20\mu$m, $\eta = 1$mPa s and the thermal energy is $k_bT = 26$meV. To test the implementation do we consider two cases, $\Delta U = 0.1k_bT$ and $\Delta U = 10k_bT$. In these cases are the flashing of the potential turned off and the single particle under consideration has radius $r = 12$nm. The trajectories, position as a function of time, along with the distribution of position and potential energy are shown in figure 1 and 2 after running the simulation till $T_{end} = 120$s. The step-size is $\delta t = 3 \cdot 10^{-5}$s and with the given ΔU and r is the time criterion (6) satisfied with the value $Q = 0{,}03$.

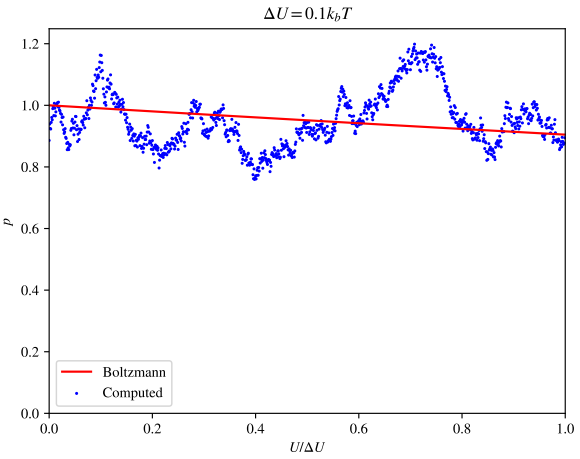
The trajectories are as imagined since in the high potential case is the particle trapped in a well, while in the low potential case does it have more thermal energy relative to ΔU to move around. Both the distribution of positions and potential seems to be in accordance with the Boltzmann probability, equation (7), in the high potential case. In the other case are both the positions and the potential almost uniformly distributed which causes a higher deviation. Since the relative thermal energy is



(a) Trajectory of a single particle.



(b) Distribution of positions.



(c) Distribution of potential energy.

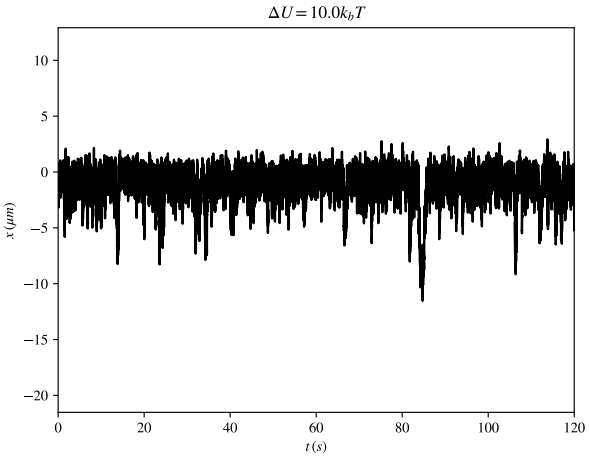
Figure 1: Flashing turned off in the $\Delta U = 0.1k_bT$ case. Figure 1b and 1c show the Boltzmann probability, the red line, in comparison. The dashed line in 1b is a stretched picture of the solid line.

much higher is there a higher degree of randomness in the system and we thus need more data and longer time to converge towards the analytic Boltzmann probability. Figure 1b could in fact be compared to equation (2) since ΔU is so small. A higher time $T_{end} \to \infty$ would be necessary to flatten the distribution and make it uniform. This could be done, however, we already see a good correlation between the computed and the analytic distribution in figure 1c for the high potential case, which is what we shall investigate in the upcoming. The results suggest that the Langevin approach works well, even when the overdamped approximation is utilized.

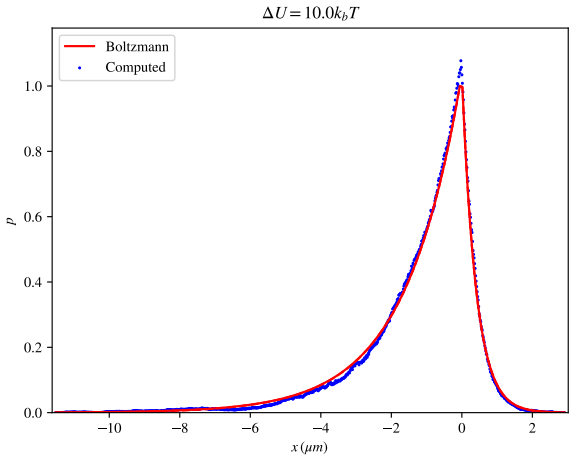
Turning the flashing on we investigate how a particle of the same size moves in a potential of strength $\Delta U = 80$eV with different periods τ. The potential is here much larger than the thermal energy, a ratio of approximately 3000, so it is safe to assume that the particle moves without diffusion when the potential is turned on. The time criterion is now satisfied with the value $Q = 0{,}097$ using a step-size of $\delta t = 2 \cdot 10^{-5}$s. To achieve directional motion do we need to adjust τ such that the particle has a certain probability P_+ to diffuse to the next potential-well during the time t_{off}, while minimizing the probability to end up in the previous well P_-, as discussed in 2. This can be done since the ratchet potential is asymmetric. In particular, we want the particle to diffuse the distance αL during time t_{off}. Using the characteristic length scale for diffusion, $x = \sqrt{2Dt}$, we want $t_{off} \sim \frac{(\alpha L)^2}{2D} << \frac{(L-\alpha L)^2}{2D}$. The last inequality ensures only nearest-neighbouring hopping. Inserting the values of the physical parameters, and using $t_{off} = \frac{3\tau}{4}$, we find an estimate for the period $\tau \sim 0{,}58\text{s} << 9{,}28\text{s}$. An assumption made in 2 is that the particle always starts at the bottom of the well, which is achieved if the time t_{on} is large enough. Using the criterion for t_{on} as given in [2] we find that the period should satisfy $\tau > 0{,}02$s. It can also be mentioned that if the time t_{off} is too short then the particle will always remain in the zeroth well.

Figure 3 shows the trajectories of a single particle with cycle-frequency $f = 25{,}0$, 1,0, and 0,04Hz. In the high frequency case, $f = 25{,}0$Hz, can we clearly see that the particle remains in its zeroth well, which puts a lower boundary on τ. In the low frequency case does the particle behave a bit randomly since the particle moves both forward and backward. In this case is $\tau = 25$s which is well above our limit for only nearest-neighbouring hopping. Even though it moves backwards sometimes, it has an averaged positive velocity. This can be explained by the fact that the potential is asymmetric and thus more 'area' tilts towards positive drift. Put in other words, the uphill of the potential is shorter than the downhill so a particle located at a random position will, in average, move forward. The plot suggests that an intermediate state $f \sim 1$Hz seems appropriate and confirms our earlier discussion.

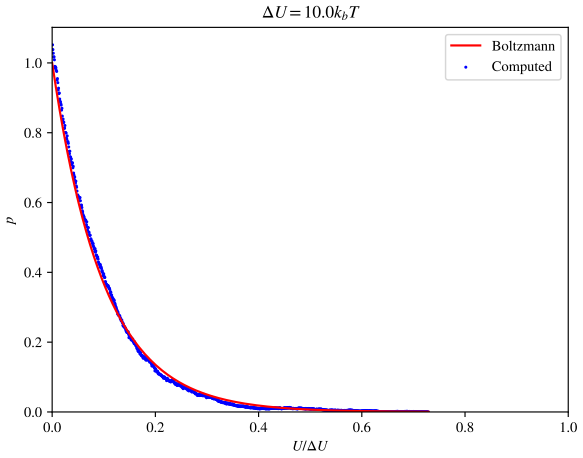
Figure 4 shows the averaged velocity as a function of τ for particles of size $r_1 = 12$nm, as considered earlier, and $r_2 = 36$nm. The values of τ range from $[0{,}05, 2{,}0]$s as



(a) Trajectory of a single particle.



(b) Distribution of positions.



(c) Distribution of potential energy.

Figure 2: Flashing turned off in the $\Delta U = 10 k_b T$ case. Figure 2b and 2c show the Boltzmann probability, the red line, in comparison.

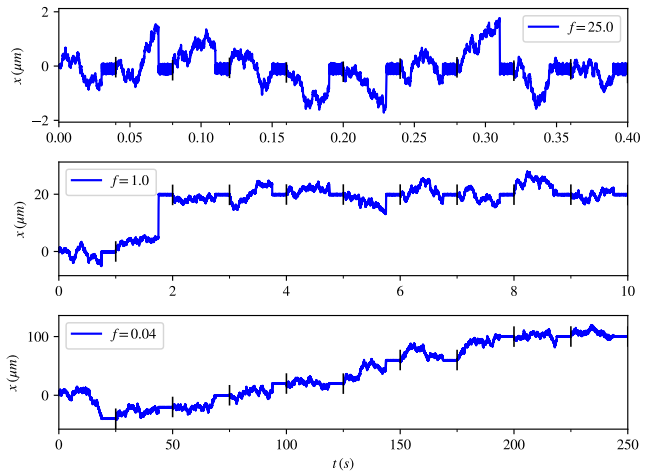


Figure 3: The figure shows trajectories of a single particle with flashing frequencies f = 25,0, 1,0, and 0,04Hz. The trajectories are run for 10 cycles and the black vertical lines indicate the end of each cycle.

we suspect the maximum velocity to occur somewhere in between. The averaged velocity is found by running the simulation to T_{end} = 100s, calculating the velocity, and taking the average using a dataset of d =120 particles. The values of T_{end} and d were determined by minimizing the standard deviation while keeping the computation time manageable.

Given the values of $\langle v_1 \rangle$ for r_1 one can estimate $\langle v_2 \rangle$ for r_2. Equation (5) can be expressed in dimensionless variables with $\hat{t_i} = \omega_i t$ and $\hat{x} = x/L$, with $\omega_i = \frac{\Delta U}{\gamma_i L^2}$. Now, since $r_2 = 3r_1$ and thus, $\omega_2 = \omega_1/3$, one finds $\hat{t_2} = \hat{t_1}/3$. To relate the results of particle 1 to 2, we must change the time scale accordingly $t_2 \to 3t_2$, and a consequence of this is that $v_2 = v_1/3$. In summary, $v_2(\tau) = v_1(3\tau)/3$. This estimation is shown in figure 4, the red squares, and seems to be a good estimate.

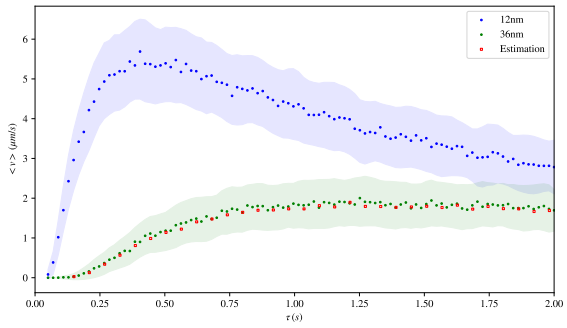


Figure 4: The figure shows data acquired of $\langle v \rangle$ as a function of τ for particles of size r_1 = 12nm and r_2 = 36nm. The red square is the estimated values of $\langle v_2 \rangle$ for r_2 using $\langle v_1 \rangle$. The colored fields represents deviation with size $\pm\sigma$.

We find the maximum velocity and optimized period τ_{op} using curve-fitting in combination with an optimized numerical method that estimates the maximum of a function. In particular, we use the functions *scipy.optimize.curve_fit* and *scipy.optimize.fmin* from Pythons's library *Scipy*. The trial function needed for curve-fitting is the analytic function for $\langle v \rangle$, equation (3), with adjustable parameters $L \to a$ and $D \to bD$. Figure 5 shows the acquired data for $\langle v \rangle$, as shown in figure 4, together with the analytic and curve-fitted function for both r_1 and r_2. The figure indicates a large deviation between our results and the analytic function. The deviation can be explained by the fact that the assumption that all particles start at exactly $x = iL,\ i \in \mathbb{Z}$ at the beginning of each cycle, as assumed in the derivation of equation (3), does not hold. In reality will each particle be located at a position according to a probability distribution that looks like figure 2b, only with narrower width due to a stronger potential. Doing some numerical tests we find that the mean position is shifted by $x \approx -0{,}1$µm and some particles end up as far as $x = -0{,}3$µm. This decreases the probability β to hop to next well, and thus, also the velocity.

The analytic expression was obtained by only considering nearest-neighbour hopping. This approximation holds for low τ. In the worst case, when τ = 2s, will an inclusion of two more wells increase the probability by 1.004. The approximation is therefore good and will not come with severe consequences.

Looking at the obtained values for the adjustable parameters, which are a = 11,2µm and b = 0,95 for r_1 and a = 11,3µm and b = 0,98 for r_2, we see that the effective length that the particles move is much lower. However, the value of the diffusion constant seems to be in accordance with our experiment. This confirms our reasoning for why the deviation to the analytic function is so large, namely that it originates from the asymmetric distribution of positions when the potential is turned on, which shifts the mean leftover.

The cruve-fitted parameters for D show a smaller effective diffusion constant. This could be because we have utilized the overdamped approximation, as was used to establish the numeric scheme. However, it could also be due to the Langevin approach being an inaccurate description or maybe it is only due to statistical noise. Investigating more we see that the overdamped approximation holds when the characteristic damping time $\tau_d = m/\gamma$ is much smaller than the time in focus. For our case must $\tau_d << \delta t$. Inserting the numbers yield $\tau_d << 1 \cdot 10^{-10}$s, which is much smaller than the used δt [4]. The deviation in D is small and is not considered the explanation for why the large deviation in velocity occurs.

Table 1 shows the obtained results for the optimum period τ_{op} that maximizes $\langle v \rangle$ for particles of sizes r_1 and r_2. The standard deviation to τ_{op} is the grid spacing of the τ-values we chose to use. The standard deviation of $\langle v \rangle$ is the standard deviation of the velocities of all d = 120 particles. The estimated value of v_2 and τ_{op_2}, using the data of r_1 is, v_2 = 1,807µm/s and τ_{op_2} = 1,284s. This is less than 4% deviation from the obtained values in the

table. This suggests that the method described above for determining the velocity of one particle, given the velocity of another particle, works.

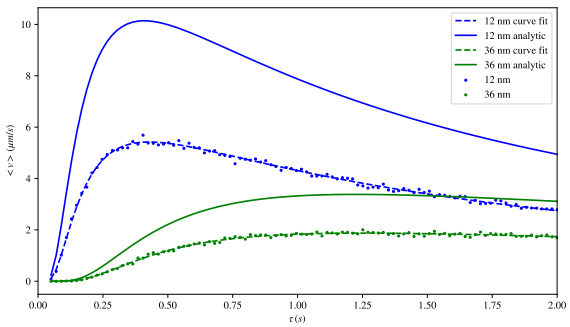


Figure 5: The figure shows data acquired of $\langle v \rangle$ as a function of τ for particles of size $r_1 = 12$nm and $r_2 = 36$nm. The solid lines are the analytic function (equation (3)) for each r_i, and the dashed lines are the analytic function curve-fitted to data points.

Table 1: Estimated τ_{op} and $\langle v \rangle_{max}$.

r_i (nm)	τ_{op} (s)	$\langle v \rangle$ (µm s^{-1})
12	0,428 ± 0,020	5,422 ± 0,992
36	1,253 ± 0,020	1,873 ± 0,642

A physical experiment, [2], that determined the velocity of rhodamine-labeled DNA 50-mer was done using electrodes of sizes 2µm and a flashing ratchet potential of strength $\Delta U = 80$eV. The parameters used in this numerical experiment is assumed to fit with the ones used there, with $r = 12$nm, as indicated in [4]. Looking at figure 3 in [2] we compare with figure 6 and observe a good agreement. Estimating their velocity by eye-balling it, their obtained value of $v = 2{,}8$µm/s is close to the one obtained here $v = 3{,}5$µm/s. We note that in both cases is the frequency $f = 0{,}7$Hz. The numerical experiment achieves a larger velocity mainly due to the fact that we treat the problem one-dimensional. In reality will the particles also diffuse along an axis orthogonal to the axis in focus, and hence reduce the average velocity. The electrodes used as potential generators are certainly not infinitely thin wires as we have assumed. This is another factor that reduces the physically measured velocity. Another issue regards the validity of the used parameters, for instance would a smaller viscosity η alter the result. The overdamped approximation does neither here seem to be a large contributor to the deviation.

If we set the flashing period to be $\tau = \tau_{op_1}$ then particles of size r_1 will move with velocity $v_1 = 5{,}422$µm/s while particles of size r_2 have average velocity $v_2 = 1{,}055$µm/s. This suggests that it is in fact possible to separate the two types of particles in a flashing ratchet potential. Figure 7 illustrates this where we have used $N = 1000$ particles of each type and completed 150 cycles. This corresponds

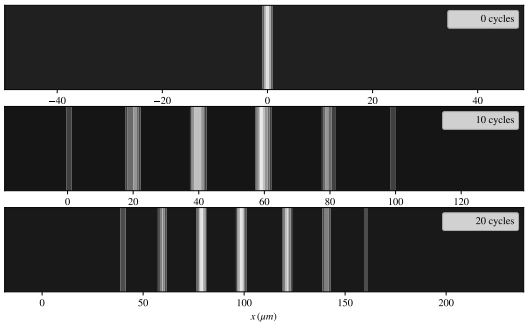


Figure 6: The figure illustrates the movement of an ensemble of particles with size $r = 12$nm after 0, 10 and 20 cycles. The flashing frequency is $f = 0{,}7$Hz.

to an end time of $T_{end} = 64{,}2$s. The separation distance, computed as the difference between the mean values, is 290,1µm. We can see that the density moves as a Gaussian distribution and has values only at each potential-well, at least when the potential is turned on. One might suspect that the width, the standard deviation, of this Gaussian distribution increases with time and that it is dependent on the probability β to hop to the next well. According to [2] is the standard deviation on the form $\sigma^2(c) = cL^2\kappa(1-\kappa)$, where c is the number of cycles and κ is the probability. In this derivation is κ the probability to move forwards, integrating from αL to infinity, and is therefore not equal to our probability measure β. The distribution plotted in figure 7 indicates that this is valid since the distribution of r_1 is much wider than the one for r_2.

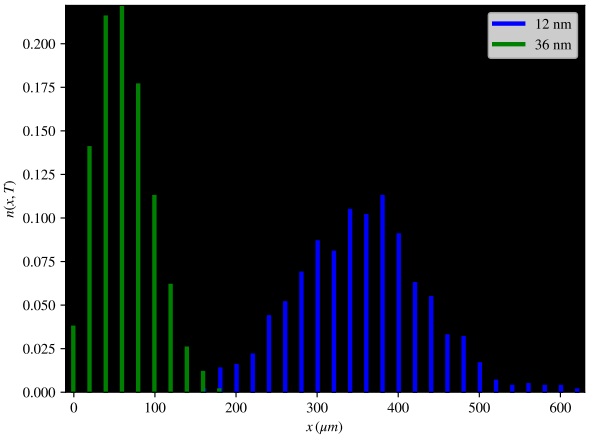


Figure 7: Density distribution of $N = 1000$ particles of sizes $r_1 = 12$nm and $r_2 = 36$nm. Shown after completed 150 cycles with periodicity $\tau_{op_1} = 0{,}428$s.

The resolution between the species is defined as

$$\text{Res} = \frac{|x_1(c) - x_2(c)|}{0.5|\sigma_1(c) - \sigma_2(c)|}, \tag{8}$$

and is estimated to be Res = 12,6, after a simple test

run with the given values above. According to [2] is a resolution of 1 a typical resolution needed for separating DNA molecules. A lower number of cycles could then have been used to satisfy this criterion.

Conclusion

The numerical results obtained for the average velocity of the two particles does not fit with the analytical ones. Performing the experiment with a stronger potential would localize the particles even more in the t_{on}-state and potentially better our results. However, it is doubtful that this solves the entire problem. Increasing the number of particles for each dataset in combination with increasing the end time will also reduce the deviation. Another explanation is that the chosen Langevin equation in combination with the overdamped approximation yields only an approximate picture of the dynamics and reduces the effective diffusion constant and hence the average velocity. It can also be mentioned that the probability for forward movement may be computed in a different manner, as in [2], and might suggest that the analytical expression used here is imprecise.

A comparison of our gathered data with the data from the physical experiment, [2], we can say there is a good agreement. The major contributions to the deviation are mainly due to all physical assumptions made to ease the calculations, i.e. reducing the problem to a one-dimensional problem with infinitely thin electrodes and regarding the DNA-molecules as spheres. These simplifications increase the average velocity.

We see clear indications that biased Brownian motion is a useful technique for separating the two DNA oligomers. There is a clear distinction between the velocity curves we obtain for each particle, and after a simple test do we observe that a separation distance of several hundred micrometers is achieved after a minute. This amounts to a high resolution feasible to separate the two species.

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