Brownian dynamics simulations to explore experimental microsphere diffusion with optical tweezers.

Manuel Pancorbo\textsuperscript{1}, Miguel A. Rubio\textsuperscript{2}, and P. Domínguez-García\textsuperscript{1}

\textsuperscript{1} Dep. Física Interdisciplinar, Universidad Nacional de Educación a Distancia (UNED), Senda del Rey 9, Madrid 28040, Spain.
\textsuperscript{2} Dep. Física Fundamental, Universidad Nacional de Educación a Distancia (UNED), Senda del Rey 9, Madrid 28040, Spain.

Abstract

We develop two-dimensional Brownian dynamics simulations to examine the motion of disks under thermal fluctuations and Hookean forces. Our simulations are designed to be experimental-like, since the experimental conditions define the available time-scales which characterize the solution of Langevin equations. To define the fluid model and methodology, we explain the basics of the theory of Brownian motion applicable to quasi-twodimensional diffusion of optically-trapped microspheres. Using the data produced by the simulations, we propose an alternative methodology to calculate diffusion coefficients. We obtain that, using typical input parameters in video-microscopy experiments, the averaged values of the diffusion coefficient differ from the theoretical one less than a 1%.

Keywords: Brownian dynamics simulations, colloids, Brownian motion, harmonic potentials, optical tweezers

1 Introduction

Brownian motion, i.e., the random movement of objects immersed in a fluid, was theoretically described by Einstein more than a century ago \cite{32} from a microscopic perspective, demonstrating the molecular structure of the fluid \cite{11}. The Einstein’s classical approach neglected hydrodynamics memory and inertia effects, since they appear at very short-time scales, something experimentally available only very recently \cite{24}. This assumption theoretically implies that the particle velocity cannot be defined and the trajectories of Brownian particles are fractal \cite{27}. Therefore, the study of Brownian motion is determined by the available experimental set-up, which defines the detected time-resolution of the stochastic jumps.

The standard experimental methodology to study Brownian motion is to mix a small concentration of micro-nanospheres with a certain fluid. The suspension sample is deposited into a glass cell which is inserted in an optical instrument, such as a video-microscopy or an interferometry set-up, where the trajectories of the beads can be recorded for ulterior analysis. A
common practice to facilitate the study of particles’ motion is using optical tweezers [1]. This technique exerts a restoring force under the object, allowing the experimentalist to move the particle inside the fluid in a quasi-two-dimensional plane. Many optical tweezers set-ups allow to trap several objects, but single-particle tracking is usually employed to improve spatial and temporal resolution.

During the last decades, optical traps have permitted to develop a wide variety of experiments in colloidal motion. To cite some examples: about the effects caused by confinement [21], the hydrodynamic interaction between particles [19], discovering resonances from hydrodynamic memory at short-time scales [15], regarding micro-rheology [31], or even to produce Brownian Carnot engines [26], along with many other applications [16].

In spite of the evident benefits of optical tweezers in the research of colloidal physics, this experimental methodology generates an external force under the bead which can modify the dynamics of the particle [25]. This force can be also itself modified by the thermo-physical properties of the surrounding complex fluid [7]. Therefore, a good dynamical characterization of the external harmonic potential detected by stochastic particle motion is needed to correctly measure the values of the diffusion coefficient.

Here, we study by experimental-like computer simulations the diffusion of a single sphere observed in a two-dimensional plane under optical tweezers, i.e., we investigate the Brownian motion of a disk under harmonic potentials. In this work, we show how the solution of the Fokker-Planck equation [29] allows us to propose an iterative approach as an alternative methodology to calculate the diffusion coefficient of the disk. Our objective in this work is to emulate the dynamics of a trapped single-bead in a video-microscopy experiment by means of Brownian dynamics simulations. These simulations are designed to be experimental-like using typical input parameters but without the limitations which appear in an experimental set-up, like image analysis miscalculations or confinement effects in the bead’s diffusion.

2 Brownian dynamics simulations

We develop Brownian dynamics simulations, which are a simplification of Stokesian dynamics, but neglecting hydrodynamic interactions (HI) between particles [18]. Our model of colloidal fluid is designed to be compared with video-microscopy (VM) experiments, where we can observe real-time motion of the colloids in two dimensions and where we can store the particles’ position for defined temporal steps, according to the frame-rate of the camera. The software simulates a suspension of micro-spheres in a Newtonian fluid in a 2D or pseudo-2D configuration of sedimented micro-particles [8]. In analogy with an image-based VM lab, we are able to change external parameters, expressed in physical units, such as the concentration of particles in the suspension, the viscosity of the fluid, the focal distance, the size of the spheres or the temperature of the bath.

Our simulation model has been implemented using an open-source Java-based software named “Easy Java/JavaScript Simulations” (EjsS) [13], allowing to create visual simulations of physical systems based on ordinary differential equations. The equations described in this section have been resolved numerically by EjsS using a Euler-Richardson algorithm—alternative algorithms are available but they provided the same results. This simulation methodology has been successfully developed and tested in more complex systems composed of many Brownian particles under different internal and external forces [7, 8].

Theoretically, the movement of particles under thermal fluctuations is studied by means of the Langevin equation [22], which is the Newton’s second law equation including a stochastic
Brownian dynamics simulations to explore microsphere diffusion... Pancorbo, Rubio and Domínguez-García

force $\mathbf{F}_B$:

$$ m\dot{\mathbf{v}} = \mathbf{F}_H + \mathbf{F}_B + \mathbf{F}_E + \mathbf{F}_D $$

(1)

for a sphere of radius $a$ and mass $m$ immersed in a medium of viscosity $\eta$ and density $\rho$. In eq. (1), $\mathbf{v}$ is the velocity vector, $\dot{\mathbf{v}} \equiv d\mathbf{v}/dt$, $\mathbf{F}_H$ are the hydrodynamic forces, $\mathbf{F}_E$ are external forces over the particles in the fluid, and $\mathbf{F}_D$ are hard-disk forces that avoid the particles from overlapping.

We neglect full hydrodynamic interactions, $\dot{\mathbf{v}} \sim 0$, and, therefore, the hydrodynamic contribution is reduced to $\mathbf{F}_H = -\gamma \mathbf{v}$, i.e., the Stokes drag of an isolated particle, where $\gamma = 6\pi \eta a$ is the friction coefficient. This inertial term can be neglected by evaluating the Reynolds number, $\text{Re}$, which compares inertial and viscous forces. For a bead of radius $a$ immersed in a fluid of viscosity $\eta$ and density $\rho$, we have $\text{Re} = \rho va/\eta$. For micro-particles in water-like fluids, $\text{Re}$ is low enough, allowing us to exclude hydrodynamic interactions when the experimental time-scale is not very low—in the order of the microsecond. When using HI, the lubrication forces prevent the particles to overlap. If not, hard-disk forces have to be included. In this work, we use single-particle configuration, and the hard-disk forces are not necessary.

The Brownian or stochastic force is characterized by $\langle \mathbf{F}_B \rangle = 0$ and by $\langle \mathbf{F}_B(0)\mathbf{F}_B(t)\rangle = 2k_B T\gamma \delta(t)$ where $k_B$ is the Boltzmann’s constant and $\delta(t)$ is the unit tensor. To implement this force, we use a random vector $\mathbf{n}$ with values in the interval $[-1, 1]$ generated by the Box-Muller transformation. Then, we have:

$$\mathbf{F}_B = \sqrt{2dk_B T\gamma/dt} \mathbf{n}$$

(2)

where here $d$ is the dimension, and $dt$ will be the time step in the simulations.

Regarding the external forces, we use a restoring Hooke-like one: $\mathbf{F}_E = -\kappa \mathbf{r}$, where $\kappa$ is the trap stiffness and assuming that the trapped disk is centered in its initial position. We do not include any difference between $x$ and $y$ coordinates, and we can define the harmonic potential in one-dimension $x$ as $U_{\kappa} = (1/2)\kappa x^2$. This potential is the harmonic approximation for a trapping potential generated by the focused laser beam of the optical tweezers, which is valid for the central region of the potential well.

Under this conditions, we have the following overdamped Langevin equation for the trapped disk:

$$\dot{\mathbf{r}} = \gamma^{-1} (-\kappa \mathbf{r} + \mathbf{F}_B)$$

(3)

where the stochastic term is given by eq. (2).

Finally, we make the Stokes-Einstein relation for self-diffusion coefficient explicit:

$$D = k_B T\gamma^{-1}$$

(4)

This diffusion coefficient, $D$, is the quantity we want to obtain by analyzing the data of the simulations. The most simple version of micro-rheology consists in estimating the value of the fluid’s viscosity, $\eta$, by calculating $D$ from the analysis of particle motion in the fluid.

### 3 Harmonic potentials in stochastic motion

The solution of the complete set of Langevin equations for a spherical particle in harmonic potentials with no-slip boundaries in a Newtonian fluid and with hydrodynamic effects only depends on several timescales: $\tau_f = \rho_f a^2/\eta$, $\tau_p^* = m^*/\gamma$, and $\tau_{\kappa} = \gamma/\kappa$, where $\rho_f$ is the density of the fluid, $m_p$ and the mass of the particle and $m^* = m_p + m_f/2$ is a modified mass influenced by hydrodynamics, where $m_f$ is the mass of the displaced fluid. The two first time
scales are related to fluid vortex propagation and inertial time-scales, whereas $\tau_\kappa$ measures the ratio between the Stokes friction coefficient and the optical trap constant, $\kappa$.

The most applied statistic magnitude in the analysis of Brownian motion is the mean-square displacement (MSD), defined by:

$$\text{MSD}(t) \equiv \langle \Delta r^2(t) \rangle \equiv \langle (r(t) - r(0))^2 \rangle$$  \hspace{1cm} (5)

The MSD for a micro-sized particle immersed in a Newtonian fluid, in time scales lower than $\tau_\kappa$, behaves as $\text{MSD}(t) = 2dDt$, where $d$ is the dimension on the MSD. This expression defines the diffusive behavior and allows to calculate the diffusion coefficient $D$. At even lower timescales, the ballistic regime is predominant initiating a temporal power-law behavior, where $\text{MSD}(t) \sim t^2$. At higher times, when $t \sim \tau_\kappa$, the optical trap is dominant, and the MSD shows a plateau equal to $\text{MSD}(t > \tau_\kappa) = 2k_BT/\kappa$. The one-dimensional MSD of a harmonically trapped bead in a Newtonian fluid, without inertia effects, is [6]:

$$\langle \Delta x^2(t) \rangle = \frac{2k_BT}{\kappa} \left(1 - e^{-\kappa t/\gamma}\right)$$  \hspace{1cm} (6)

A standard method to obtain the self-diffusion coefficient is to fit eq. (6) to the MSD data calculated from the disk’s positions.

An important statistical quantity is the probability distribution of the particles’ jumps, $\Delta r$, also called Gaussian propagator or van Hove autocorrelation function [19]:

$$\rho_D(\Delta r, \tau) = \frac{1}{(4\pi DT)^{d/2}} \exp \left(-\frac{\Delta r^2}{4DT}\right)$$  \hspace{1cm} (7)

for a fixed and constant time-lapse $\tau$ between particles’ jumps in $d$ dimensions. If we assume there is no difference in the diffusion process by using $\tau$ (lapse time) or $t$ (absolute time), the moments of the distribution can be obtained from the propagator by $\delta r^n(t) \equiv \langle |\Delta r(t)|^n \rangle = \int |\Delta r|^n \rho_D(\Delta r, t) d^d(\Delta r)$. And then, the MSD is calculated using $n = 2$, obtaining $\delta r^2(t) \equiv \text{MSD}(t) = 2dT$.

The diffusion coefficient can be extracted from the one-dimensional variance of the Gaussian distribution [7] since $\sigma_x^2 = 2DT$. A similar approach can be applied to the trap stiffness through Boltzmann statistics [14] on the particles’ positions. The average motion of a trapped particle can be described by means of the probability density distribution $\rho(x, t)$ which obeys the Fokker-Planck equation [29, 17]. This can be written [5] in a simple one-dimensional form as $d\rho(x)/dx = (k_BT)^{-1} F(x) \rho(x)$. If we use an optical trap modeled as a restoring force with spring constant $\kappa$, the solution is a Gaussian function on the coordinate $x$:

$$\rho_\kappa(x) = \left(\frac{\kappa}{2\pi k_BT}\right)^{1/2} \exp \left(-\frac{\kappa x^2}{2k_BT}\right)$$  \hspace{1cm} (8)

The variance of the distribution allows to obtain the stiffness of the trap by $\sigma_\kappa^2 = k_BT/\kappa$. An example of these one-dimensional distributions can be seen in Fig. [1].

In a more general case of stochastic motion confined by harmonic potentials, the solution of the Fokker-Plank equation leads to a more complicated distribution [29]. In that situation, the probability of transition of a trapped colloidal particle from the position $x_0$ to $x$ in lapse-time $\tau$ is:

$$\rho_{FP}(x_0, x, \tau) = \frac{1}{\sqrt{2\pi \alpha(\tau)}} \exp \left[-\frac{(x - x_0 e^{-\lambda \tau})^2}{2\alpha(\tau)}\right]$$  \hspace{1cm} (9)
Brownian dynamics simulations to explore microsphere diffusion... Pancorbo, Rubio and Domínguez-García

Figure 1: Example of probability density distribution in the $x$ coordinate from the motion of a disk under harmonic potentials in Brownian dynamics simulations (diameter $d = 1.9$ $\mu$m, $T = 295.5$ K, time-lapse $\tau = 2.5$ ms, see Results section). We show the distribution for two input optical stiffnesses: $\kappa_o = 0.5$ $\mu$N/m (blue points) and 1.6 $\mu$N/m (red points). The red lines are non-linear fits to Gaussian functions. The value of $\kappa$ can be recovered through the variance of the distributions.

where:

$$\lambda \equiv \kappa / \gamma$$  \hspace{1cm} (10a)

$$\alpha(\tau) \equiv \frac{k_BT}{\kappa} \left(1 - e^{-2\lambda \tau}\right)$$  \hspace{1cm} (10b)

Note that $\lambda$ can be written in terms of the diffusion coefficient as $\lambda = \kappa D / k_BT$ by using eq. 41 and 10a. For short values of the time-step, $\tau \ll 1/\lambda$, this distribution is identical to the standard Gaussian propagator, 7. On the other hand, for long values of the temporal step, it approximates to distribution of particle positions, 5. For intermediate times, the distribution depends on a memory factor which appears in the initial position for every jump of the particle. To obtain that memory factor, $e^{-\lambda \tau}$, first we need to know the diffusion coefficient, $D$, which is the quantity we want to estimate from the disk’s movement. It is important to observe that, when $\tau \ll 1/\lambda$, we obtain $\alpha(t) = 2Dt$. Eq. 10b only differs from the standard MSD, eq. 4, by a factor 2 in the spring constant ($\kappa \rightarrow \kappa/2$). This will allow us to define a relaxed MSD through the temporal jumps with memory effect, which we will identify with eq. 11b.

4 Results

We use the model previously explained, where the disk’s positions are obtained following the overdamped Langevin equation, eq. 5, to analyze the diffusion of a trapped simulated disk, always under standard experimental conditions, when we increase the stiffness of applied the restoring force. The input data are those of a typical experiment using commercial optical tweezers: trapped particle of diameter $d = 1.9$ $\mu$m, at temperature $T = 295.5$ K, time-lapse $\tau = 2.5$ ms (400 images per second in the video-microscopy set-up), during a total time of 50 s. The internal time step in the simulations, $dt$, is fixed to $dt = 10^{-4}$ s. The typical stiffnesses of the traps are $\kappa \sim 0.02 - 2$ $\mu$N/m. The surrounding fluid is water ($\eta = 0.95$ mPa.s) and the bead is located far enough from the influence of nearby walls 3. Using these experimental
input values, we are in the intermediate situation of the Fokker-Planck solution described in the former section. Indeed, $1/\lambda \sim 9 - 840 \text{ ms}$ is obtained in the interval of typical $\kappa$, not far from the input time-step, $\tau = 2.5 \text{ ms}$. Here lies the importance of using experimental-like simulations, since Brownian motion theoretical explanations depend on the time scale of observation. Under this conditions, the theoretical diffusion coefficient is $D = 0.239 \mu \text{m}^2 / \text{s}$ according to eq. (4).

To have into account this effect, we develop an alternative iterative method to obtain the diffusion coefficient. From a step $n$ to a total number of steps $N$, we define a relaxed mean-squared displacement, $\text{MSD}^*(t)$:

$$\text{MSD}^*(t) \equiv \langle \Delta x_{n,\lambda}^2 \rangle = \frac{1}{N-n} \sum_i (x_{n+i} - x_i e^{-\lambda n \tau})^2$$

where this MSD should verify eq. (10b). By using here that $\sigma_\kappa^2 \equiv k_B T / \kappa$, we can define a function $\xi(n\tau)$:

$$\xi(n\tau) \equiv -\log \left( 1 - \frac{\langle \Delta x_{n,\lambda}^2 \rangle}{\sigma_\kappa^2} \right) = 2\lambda n\tau$$

The function $\xi(n\tau)$ grows linearly with time with slope $2\lambda$, something which allows to obtain $\lambda$ from a linear regression. By calculating $\kappa$ independently from the distribution $\rho_\kappa(r)$ (as in Fig. 1) or by the plateau in the MSD, and applying an iterative method until obtaining a stable $\lambda$ value.

In Fig. 2 we show an example of one-dimensional standard MSD calculation, eq. (5) and the relaxed MSD$^*$ defined by eq. (11), for several values of the input trap stiffness $\kappa_o$. Both quantities have a similar behavior, displaying a plateau at higher times when reaching the time-scale $\tau_\kappa$. However, the MSD$^*$ shows a correction on this plateau, which increases when the restoring force is more intense. In the Inset of Fig. 2 the linear behavior of the defined function $\xi(t)$, eq. (12), can be seen, allowing to obtain $\lambda$ and, consequently, $D$.

In Table 1 we show a complete set of the values for self-diffusion coefficients in the range of the trap stiffnesses used in video-microscopy experiments. We summarize the values for
the self-diffusion coefficients calculated using the standard MSD and eq. (6), obtained from the iterative method. The table summarizes the results for $D_\kappa$ obtained from the simulated data of the position of the disk to be compared with the input allowing to calculate an average value for $D$.

| $\kappa_o$ (\(\mu\)N/m) | $\kappa$ (\(\mu\)N/m) | $\lambda$ (s\(^{-1}\)) | $D^*$(\(\mu\)m\(^2\)/s) | $D$ (\(\mu\)m\(^2\)/s) |
|----------------|----------------|----------------|----------------|----------------|
| 0.02 | 0.020 ± 0.002 | 1.2 ± 0.2 | 0.24 ± 0.02 | 0.247 ± 0.005 |
| 0.04 | 0.052 ± 0.006 | 3.1 ± 0.6 | 0.24 ± 0.02 | 0.242 ± 0.011 |
| 0.06 | 0.052 ± 0.003 | 2.97 ± 0.03 | 0.232 ± 0.012 | 0.239 ± 0.004 |
| 0.08 | 0.077 ± 0.005 | 4.6 ± 0.3 | 0.242 ± 0.002 | 0.236 ± 0.006 |
| 0.1 | 0.099 ± 0.002 | 5.9 ± 0.5 | 0.243 ± 0.014 | 0.239 ± 0.003 |
| 0.2 | 0.19 ± 0.02 | 10.4 ± 1.7 | 0.223 ± 0.010 | 0.227 ± 0.005 |
| 0.3 | 0.31 ± 0.03 | 19 ± 3 | 0.25 ± 0.02 | 0.226 ± 0.003 |
| 0.4 | 0.400 ± 0.002 | 23.9 ± 1.3 | 0.244 ± 0.012 | 0.245 ± 0.002 |
| 0.5 | 0.487 ± 0.0010 | 28.5 ± 0.3 | 0.238 ± 0.003 | 0.233 ± 0.004 |
| 0.6 | 0.613 ± 0.004 | 37.7 ± 1.3 | 0.251 ± 0.007 | 0.238 ± 0.002 |
| 0.8 | 0.801 ± 0.014 | 46 ± 2 | 0.233 ± 0.007 | 0.235 ± 0.004 |
| 1.0 | 0.988 ± 0.012 | 60 ± 4 | 0.249 ± 0.012 | 0.240 ± 0.0012 |
| 1.2 | 1.20 ± 0.04 | 68 ± 4 | 0.231 ± 0.007 | 0.238 ± 0.002 |
| 1.4 | 1.407 ± 0.004 | 83.5 ± 0.4 | 0.242 ± 0.002 | 0.243 ± 0.002 |
| 1.6 | 1.59 ± 0.04 | 96 ± 4 | 0.248 ± 0.004 | 0.242 ± 0.004 |
| 1.8 | 1.79 ± 0.03 | 107 ± 3 | 0.243 ± 0.011 | 0.240 ± 0.006 |
| 2.0 | 1.96 ± 0.09 | 117 ± 7 | 0.243 ± 0.003 | 0.241 ± 0.003 |

Table 1: Results from experiment-like Brownian dynamics simulations by increasing the input trap stiffness $\kappa_o$. We show the obtained $\kappa$ values, $\lambda$ and, finally, the diffusion coefficients $D^*$ obtained from the iterative method. The table summarizes the results for $D$ calculated using the standard MSD and eq. (9). The averages provide $\langle D^* \rangle = 0.241 ± 0.008 \ \mu\text{m}^2/\text{s}$, and $\langle D \rangle = 0.238 ± 0.007 \ \mu\text{m}^2/\text{s}$, while the theoretical value is $D = 0.239 \ \mu\text{m}^2/\text{s}$.

the self-diffusion coefficients calculated using the standard MSD and eq. (6), $D$, and through the iterative method, $D^*$. The data shown is an average of the calculations for coordinates $x$ and $y$, which have been analyzed separately after simulations. We also show the $\kappa$ values obtained from the simulated data of the position of the disk to be compared with the input data. This comparison between $\kappa_o$ and $\kappa$ allows to understand the reach of the experimental-like simulations, which are statistically limited, as it should be when measuring with a standard video-microscopy set-up. The coefficient of diffusion values do not depend on the $\kappa$ value, allowing to calculate an average value for $D$ from the data of Table 1. The averages provide $\langle D^* \rangle = 0.241 ± 0.008 \ \mu\text{m}^2/\text{s}$ and $\langle D \rangle = 0.238 ± 0.007 \ \mu\text{m}^2/\text{s}$. Both values nicely agree with the theoretical value, with a relative error lower than 1%.

5 Conclusions

We have developed experiment-like Brownian dynamics simulations of two-dimensional disks under harmonic potentials to evaluate the reach of experiments of microsphere diffusion with optical tweezers, which are modeled as external Hookean forces. These type of computational studies, based on emulating experimental set-ups, are quite useful to design time- and cost-efficient experimental procedures. After summarize the basic theory of Brownian motion applied to the relevant time-scale, we observe that the solution of the Fokker-Planck equation to this stochastic system allows us to modify the standard definition of the mean-square displacement by including a memory term in the initial position of the disk’s jumps. Based on this relaxed MSD, we propose an alternative method to obtain the self-diffusion coefficient. The values
Brownian dynamics simulations to explore microsphere diffusion... Pancorbo, Rubio and Domínguez-García

calculated through that method are compared to the self-diffusion coefficients obtained using the standard mean-square displacement. Under the experimental conditions, the averaged values of the diffusion coefficients obtained from both methods return values which differ from the theoretical less than 1%.

6 Acknowledgments

We want to thanks F. Ortega for joined investigations with optical tweezer, J.A. Torre for his computational support and J.C. Gómez-Sáez for her proofreading of the English texts. This research has been supported by MINECO by project FIS2013-47350-C5-5-R.

References

[1] A. Ashkin. Applications of laser radiation pressure. Science, 210(4474):1081–1088, 1980.
[2] G. E. P. Box and M. E. Muller. A note on the generation of random normal deviates. Ann. Math. Statist., 29(2):610–611, 1958.
[3] H. Brenner. The slow motion of a sphere through a viscous fluid towards a plane surface. Phys. Rev. E, 68:021401, 1961.
[4] Clercx, H.J.H. and Schram, P.P.J.M. Brownian particles in shear flow and harmonic potentials: a study of long-time tails. Phys. Rev. A, 46:1942–1950, 1992.
[5] T. J. Davis. Brownian diffusion of nano-particles in optical traps. Opt. Express, 15(5):2702–2712, 2007.
[6] M. Doi and S. F. Edwards. The Theory of Polymer Dynamics. Clarendon Press, Oxford, 1986.
[7] P. Domínguez-García, L. Forró, and S. Jeney. Interplay between optical, viscous, and elastic forces on an optically trapped brownian particle immersed in a viscoelastic fluid. Appl. Phys. Lett., 109(14):143702, 2016.
[8] P. Domínguez-García and M. A. Rubio. Single and multi-particle passive microrheology of low-density fluids using sedimented microspheres. Appl. Phys. Lett., 102:074101, 2013.
[9] P. Domínguez-García. Microrheological consequences of attractive colloid-colloid potentials in a two-dimensional brownian fluid. Europhys. J. E. Soft. Matter., 35:73, 2012.
[10] E. Dufresne, T. M. Squires, M. P. Brenner, and D. G. Grier. Hydrodynamic coupling of two brownian spheres to a planar surface. Phys. Rev. Lett., 85(15):3317–3320, 2000.
[11] A. Einstein. The motion of elements suspended in static liquids as claimed in the molecular kinetic theory of heat. Ann. Phys., 17(8):549–560, 1905.
[12] A. Einstein. On the theory of brownian motion. Ann. Phys., 19:371–381, 1906.
[13] F. Esquembre. Easy java simulations: a software tool to create scientific simulations in java. Comput. Phys. Commun., 156:199–204, 2004.
[14] E.-L. Florin, A. Pralle, E. H. K. Stelzer, and J. K. H. Hörber. Photonic force microscope calibration by thermal noise analysis. Appl. Phys. A, 66:875–878, 1998.
[15] T. Franosch, M. Grimm, M. Belushkin, F. M. Mor, G. Foffi, L. Forró, and S. Jeney. Resonances arising from hydrodynamic memory in brownian motion. Nature (London), 478:85–88, 2011.
[16] D.G. Grier. A revolution in optical manipulation. Nature, 424(6950):810–816, 2003.
[17] Y. Harada and T. Asakura. Radiation forces on a dielectric sphere in the rayleigh scattering regime. Opt. Commun., 124(5-6):529–541, 1996.
[18] H. Hess and R. Klein. Generalized hydrodynamics of systems of brownian particles. Appl. Phys., 32(2):173–283, 1983.
Brownian dynamics simulations to explore microsphere diffusion... Pancorbo, Rubio and Domínguez-García

[19] F. Hofling and T. Franosch. Anomalous transport in the crowded world of biological cells. *Rep. Prog. Phys.*, 76(4):046602, 2013.

[20] R. Huang, I. Chavez, K.M. Taute, B. Lukic, S. Jeney, M.G. Raizen, and E-L. Florin. Direct observation of the full transition from ballistic to diffusive brownian motion in a liquid. *Nature Physics*, 7(6):576, 2011.

[21] S. Jeney, B. Lukić, J. A. Kraus, T. Franosch, and L. Forró. Anisotropic memory effects in confined colloidal diffusion. *Phys. Rev. Lett.*, 100:240604, 2008.

[22] Langevin, P. Sur la theorie du mouvement brownien. *C.R. Acad. Sci. Paris*, 146:530–533, 1908.

[23] R. G. Larson. *The Structure and Rheology of Complex Fluids*. Oxford University Press, New York, 1999.

[24] T. Li and M.G. Raizen. Brownian motion at short time scales. *Ann. Phys.*, 525(4):281–295, 2013.

[25] B. Lukić, S. Jeney, Z. Sviben, A. J. Kulik, E.-L. Florin, and L. Forró. Motion of a colloidal particle in an optical trap. *Phys. Rev. E*, 76:011112, 2007.

[26] I. A. Martinez, E. Roldan, L. Dinis, D. Petroc, J.M.R. Parrondo, and R.A. Rica. Brownian carnot engine. *Nature Physics*, 12(1):67–70, 2016.

[27] P. N. Pusey. Brownian motion goes ballistic. *Science*, 332(6031):802–803, 2011.

[28] A.C. Richardson, S.N.S. Reihani, and L.B. Oddershede. Non-harmonic potential of a single beam optical trap. *Opt. Express*, 16(20):15709–15717, 2008.

[29] H. H. Risken. *The Fokker-Planck equation: methods of solution and applications*. Springer series in synergetics. Springer-Verlag, Berlin, New York, 1984.

[30] K. Svoboda and S.M. Block. Biological applications of optical forces. *Annu. Rev. Biophys. Biomol. Struct.*, 23:247–85, 1994.

[31] Tassieri, M., Evans, R.M.L., Warren, R.L., Bailey, N.J., and Cooper, J.M. Microrheology with optical tweezers: data analysis. *New Journal of Physics*, 14(115032), 2012.

[32] B. Xin, C. Kim, and G.E. Karniadakis. 111 years of brownian motion. *Soft Matter*, 12:6331–6346, 2016.