Microrheology of filament networks from Brownian dynamics simulations

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Abstract. Microrheology is a technique that has been largely used to investigate viscoelasticity in biological systems. For example, it revealed that filament networks, which are the main component of the citoskeleton of eukaryote cells, show an interesting semisolid viscoelastic response that is characterized by a hardening behaviour at high frequencies. Here, we adopt a computational approach based on microrheology to study the relationship between the Brownian motion of probe particles immersed in a filament network and its viscoelastic response. In particular, we consider a simple model for the filament networks and perform Brownian dynamics simulations to obtain the mean-squared displacement of probe particles, which is used to evaluate the shear moduli $G'$ and $G''$ of the networks. Our numerical results indicate that the proposed numerical approach can reproduce several features observed in experiments, including the sol-gel transition observed when varying the density of filaments, and the aforementioned hardening behaviour at high frequencies.

1. Introduction

Filament networks, like those formed by the aggregation of biomolecules are part of a special class of biomaterials that display viscoelasticity. Important examples include actin networks which have an important role in cellular processes [1], and amyloid peptide networks, which form hydrogels that are known to be related to several human diseases [2]. Also, some networks formed by biomolecules can be surprisingly strong, as in the case of collagen and silk. The prediction of the mechanical properties of bio-inspired materials should help in the rational design of semisolids for tailored applications, e.g., in tissue engineering [3].

Importantly, the viscoelastic response of those materials are usually characterized by the complex modulus $G^*(\omega)$, which can be, in principle, obtained by oscillatory sweeping experiments that are performed with rheometers [4, 5]. The problem is that rheometry requires a relatively large amount of sample and most of rheometers cannot access very weak (or soft) mechanical responses, thus alternative approaches like those based on microrheology must be considered [6, 7]. Although there are several techniques that can be used to obtain the microrheology of biomolecular systems [8], the most well-known approach is the one that was developed by Mason and Weitz [9]. By assuming a linear viscoelastic (LVE) regime, they considered a generalized Stokes-Einstein relationship (GSER) to establish a link between the mean-squared displacement (MSD) of Brownian particles immersed in the medium and its viscoelastic response [10]. In the LVE regime one can obtain the compliance $J(t)$ of a material directly from the MSD of the probe particles [10, 11], and evaluate the complex modulus $G^*(\omega)$,
which is, in principle, the same mechanical property obtained by the experiments performed with rheometers, from the Fourier transform of the compliance \[12, 13\].

One of the most interesting and yet not fully understood phenomenon related to filament networks is that how their viscoelastic response changes as the system pass through the sol-gel transition. There are several experimental studies using microrheology in the characterization of the viscoelasticity of fibrillar networks during the sol-gel transition \[14, 15, 16, 17\], but there are only a few numerical and theoretical studies exploring it in the literature (see Refs. \[18, 19\] and references therein). A related experimental result which also needs further clarification is the semisolid viscoelastic response of those networks in the gel phase, i.e., the storage modulus \(G'(\omega)\) displays an approximately constant value \(G_0\) at low frequencies but shows a power-law hardening behaviour at high frequencies above a threshold value \[19\].

In general, numerical approaches have been used only in the characterization of filament networks (see, e.g., \[20, 21, 22\]), while aspects of their formation remain elusive \[18\]. The modelling of the filament networks can be very challenging \[23\], since one should take into account several length (from nm up to mm) and time (from ms to hours) scales to describe the structures and processes involved in the formation of network (e.g., colloidal particles, polymeric chains, filament formation, cross-linking, solvent effects, etc). Also, forces are typically weak, around piconewtons (pN), and molecular energies are close to the thermal energy \((k_B T)\), so that the stochastic nature of the processes involved must be considered as well.

Here we introduce a simple model for the filament networks and determine their viscoelastic properties by considering a microrheology analysis approach based on the motion of the probe particles that interacts with the filaments. The remainder of this manuscript is organized as follows. In Sec. 2 we make a brief review of the methodology involved in Brownian dynamics simulations presenting a simple example of a probe particle in a harmonic potential that is used to validate our microrheology analysis. We also describe in this Section the main features of our model, including the interaction between the probe particle and the filaments. The numerical results obtained for different density of filaments and different filament-particle interactions are presented in Sec. 3, while our main conclusions are presented in the last Section.

2. Methods

2.1. Brownian dynamics simulations

We assume that the probe particles with radius \(a\) are immersed in a solvent with viscosity \(\eta\), so that their equation of motion can be described by Langevin equation in the overdamped regime as

\[
\alpha \frac{d\vec{r}}{dt} = \vec{F}_{\text{ext}} + \vec{F}_{a}(t) ,
\]

where \(\alpha = 6\pi a \eta\) is the solvent’s friction coefficient, \(\vec{F}_{a}(t)\) is a random force due to collisions with the solvent molecules, and \(\vec{F}_{\text{ext}}\) is a force that is acting in the probe particles (e.g., an optical tweezer or the filaments of the network).

In the case of a probe particle moving in a one-dimensional \((d = 1)\) space, Eq. 1 becomes

\[
\frac{dx}{dt} = \tilde{F}_{\text{ext},x} + \tilde{F}_{a}(t) ,
\]

where \(\tilde{F}_{\text{ext},x} = F_{\text{ext},x}/\alpha\) and \(\tilde{F}_{a}(t) = F_{a}(t)/\alpha\). In practice, we consider a finite time interval \(\Delta t = t_{i+1} - t_i\), so that Eq. 2 can be discretized and rewritten as

\[
x_{i+1} = x_i + \Delta t \tilde{F}_{\text{ext},x} + \Delta t \tilde{F}_{a} ,
\]

and the random force \(F_{a}(t)\) is evaluated as \[24\]

\[
F_{a}(t) = \sqrt{\frac{2\alpha k_B T}{\Delta t}} N(0,1) ,
\]
where $N(0,1)$ denotes a gaussian variable with zero mean and variance equals to one. Thus, by defining the free diffusion coefficient as $D_0 = k_BT/\alpha$, where $k_B$ is the Boltzmann’s constant and $T$ is the absolute temperature, Eq. 3 is finally written as

$$x_{i+1} = x_i + \Delta t \bar{F}_{\text{ext},x} + \sqrt{2D_0\Delta t} \, N(0,1).$$

(5)

For simulations in more than one spatial dimension $(d > 1)$, as in the case of the filaments networks that we study in the following, one can use similar equations (with independent gaussian random variables) to evaluate the motion of the probe particle in the other directions.

As an example, and to illustrate the implementation of Brownian dynamics simulations and validate our microrheology analysis method, we now consider the particular case of a particle in a harmonic potential, $U(x) = kx^2/2$, where $k$ is an effective spring constant which mimics the elastic response of the structures in the medium (note that it excludes the molecules of the solvent). By replacing the external force $F_{\text{ext},x} = -dU(x)/dx = -kx$ in Eq. 5 one gets

$$x_{i+1} = (1 - \bar{\gamma}\Delta t) x_i + \sqrt{2D_0\Delta t} \, N(0,1),$$

(6)

where $\bar{\gamma} = k/\alpha$. Figure 1 shows the results we have obtained by performing Brownian dynamics simulations using Eq. 6 for three distinct values of the effective elastic constant $k$. For each simulation, we evaluate the mean-squared displacement $\langle (\Delta x^2(t)) \rangle$ from $N_t = 10^5$ independent trajectories considering $D_0 = 1\,\mu m^2/s$ and $T = 310\,K$, which are typical values observed in experiments (see, e.g., Ref. [17]). Also, we set $x_0 = 0\,\mu m$ as an initial position for all simulations and the time interval considered was $\Delta t = 0.01\,s$ for $k = 0.427.10^{-2}\,pN/\mu m$ and $k = 0.0427.10^{-2}\,pN/\mu m$, but $\Delta t = 0.001\,s$ for the highest $k$.

As one can see in Fig. 1(a), our numerical results present a nice agreement to what is expected from the theory (see Appendix A). In particular, MSD curves agreed well with the theoretical expression derived in Appendix A, Eq. A.5, which is

$$\langle (\Delta x)^2 \rangle = \frac{k_BT}{k} \left[ 1 - \exp \left( -\frac{2}{\tau} \right) \right],$$

(7)

Figure 1. (a) mean-squared displacement $\langle (\Delta x)^2 \rangle$, and (b) stationary position distributions $H(x)$, for probe particles in a harmonic potential with different effective elastic constants $k$. Filled symbols correspond to data obtained from Brownian simulations with $D_0 = 1\,\mu m^2/s$ and $T = 310\,K$, and the dashed lines are the results expected from theory, i.e., Eq. 7 for the MSD, and Eq. 8 for $H(x)$. 

k = 0.0427.10^{-2} \, pN/\mu m

k = 0.427.10^{-2} \, pN/\mu m

k = 4.27.10^{-2} \, pN/\mu m

Eq. 7

Eq. 8
with $\tau = \alpha/k$ (note that the value of $\alpha$ can be obtained from the values of $D_0$ and $k_B T$). Also, the normalized distributions in Fig. 1(b) are well described by the steady-state solution of the Fokker-Planck equation, which for the case of a harmonic potential is [25]

$$H(x) = \sqrt{\frac{k}{2\pi\alpha D_0}} \exp\left(-\frac{kx^2}{2\alpha D_0}\right). \quad (8)$$

Essentially, the results in Fig. 1 indicate that the motion of the probe particles are more localized for a material with the highest effective spring constant.

### 2.2. Microrheology

In the following we describe how one can use microrheology to obtain the viscoelastic properties of a system by considering the motion of probe particles immersed on it [8, 10, 6, 7]. We illustrate our approach by evaluating the shear moduli $G'(\omega)$ and $G''(\omega)$ from the MSD obtained by the Brownian dynamics simulations for the case of the probe particle in a harmonic potential.

As mentioned in the Introduction, the compliance $J(t)$ of a material can be directly obtained from the MSD of the probe particles through a simple relation, which is given by [10, 11]

$$J(t) = \frac{3\pi a}{d k_B T} \langle \Delta r^2(t) \rangle, \quad (9)$$

where $a$ is the radius of the probe particle, $d$ is the number of Euclidean dimensions of the random walk. Equation 9 is only valid in the LVE regime and can be applied under some conditions [10]. One important condition for the microrheology analysis based on Eq. 9 to reproduce results from bulk rheology is that the radius of the probe particles is larger than the largest structures in the system (e.g., mesh size of the network or porous size of the gel) [8, 7]. Just to illustrate our methodology, we present in Fig. 2 the compliance $J(t)$ evaluated from the MSD curves obtained from our Brownian simulations that were previously showed in Fig. 1(a) (here we consider that the radius of the probe particles is $a = 0.2 \, \mu m$).

Once one have the Fourier transform of the compliance $\hat{J}(\omega)$, the complex modulus $G^*(\omega) = G'(\omega) + iG''(\omega)$ can be evaluated by the following expression [8, 12],

$$G^*(\omega) = \frac{1}{i\omega \hat{J}(\omega)}. \quad (10)$$

**Figure 2.** Compliance $J(t)$ of an elastic material with effective spring constant $k$ obtained from the MSD data displayed in Fig. 1(a) through Eq. 9. Dashed lines corresponds to Eq. A.6 while the straight line indicates the short time liquid-like behaviour, i.e., $J(t) \propto t$. 

$k = 0.0427 \cdot 10^{-2} \, \text{pN} \cdot \text{µm}$  
$k = 0.427 \cdot 10^{-2} \, \text{pN} \cdot \text{µm}$  
$k = 4.27 \cdot 10^{-2} \, \text{pN} \cdot \text{µm}$  

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\[Eq. A.6\]
Importantly, one can compute the Fourier transform \( \hat{J}(\omega) \) numerically by using the method presented in Refs. [12, 13], which reads

\[
-\omega^2 \hat{J}(\omega) = i\omega J(0) + (1 - e^{-i\omega t_1}) \frac{(J_1 - J(0))}{t_1} + \hat{J}_\infty e^{-i\omega t_N} + \sum_{k=2}^{N} \frac{J_k - J_{k-1}}{t_k - t_{k-1}} (e^{-i\omega t_{k-1}} - e^{-i\omega t_k}),
\]

(11)

where \( J(0) = \lim_{t \to 0} J(t) \) and \( \hat{J}_\infty = \lim_{t \to \infty} dJ(t)/dt \).

As one can see in Fig. 2 for the case of the probe particle in a harmonic potential, we can assume that both \( J(0) \) and \( \hat{J}_\infty \) are zero. Thus, by using Eqs. 10 and 11, we obtain the real, \( G'(\omega) \), and the imaginary, \( G''(\omega) \), parts of the complex modulus \( G^*(\omega) \), which are displayed in

![Figure 3](image3.png)

**Figure 3.** (a) storage modulus \( G'(\omega) \), and (b) loss modulus \( G''(\omega) \), both obtained from the compliance curves \( J(t) \) presented in Fig. 2 through Eqs. 10 and 11. Filled symbols denote numerical results obtained from the Brownian simulations while dashed lines indicate the theoretically predicted curves (see Eq. A.9 in Appendix A).

![Figure 4](image4.png)

**Figure 4.** Linear relationship between the low frequency value of the storage modulus \( G_0 \) and the effective spring constant \( k \) of the harmonic potential. Filled squares are data from Brownian dynamics simulations while the straight line corresponds to the theoretically expected relationship indicated by Eq. A.9 in Appendix A, i.e., \( G_0 = k/(3\pi a) \).
Fig. 3(a) and 3(b), respectively. The numerical results presented in Fig. 3(a) show that the storage modulus $G'(\omega)$ is independent of the frequency, while the results in Fig. 3(b) indicate that the loss modulus $G''$ displays a linear behaviour as a function of the frequency. Those results agreed very well with the theoretically expected values obtained in Appendix A. For instance, from Eq. A.9, one should expect that the storage modulus should display a plateau with a value that is linearly proportional to the elastic constant, i.e., $G_0 = \lim_{\omega \to 0} G'(\omega) = k/(3\pi a)$, which is the behaviour observed in Fig. 3(a) and illustrated by the data presented in Fig. 4. In other words, for larger values of the effective spring constant $k$, the storage modulus $G_0$ is higher and the elastic response of the system is greater. Also, Eq. A.9 indicates that the loss modulus should be related to the viscosity of the solvent, i.e., $\eta = \lim_{\omega \to 0} G''(\omega)/\omega$, which is essentially what one see in the curves displayed in Fig. 3(b).

2.3. Filament networks
In this Section we describe the methodology used to take into account the filament network in the Brownian dynamics simulations.

We consider a simple model based on Ref. [20], where the network corresponds to $N$ filaments (i.e., straight lines) that are randomly deposited and oriented in a square system ($d = 2$) with linear size $L$, as shown in Fig. 5(a). Here we characterize the network by the density of filaments in the system, which is given by $\phi = N/L^2$.

For simplicity, we assume that the interaction between the probe particle, which is spherical and have radius $R$, and the filament, which is cylindrical and have radius $r$, is given by the force

$$\vec{F}_j(d_j) = F_0 \exp \left(-\frac{d_j^2}{2\sigma^2}\right) \hat{n}_j,$$

where $F_0$ is a constant that determines the interaction strength, $d_j$ is the smallest distance between the centre of the probe particle and the centre of the $j$-th filament, $\sigma$ is a constant that sets a characteristic length that is based on both radius and is given by $\sigma = (r + R)/3$ (see Fig. 5(b) for details), and $\hat{n}_j$ is an unitary vector which is perpendicular to the filament’s direction and which goes from the centre of the probe particle to the $j$-th filament so that the force $\vec{F}_j$ will be repulsive if $F_0 < 0$ but attractive if $F_0 > 0$.

![Figure 5](image-url)

**Figure 5.** (a) Network configuration obtained with $N = 100$ randomly oriented straight lines in a two-dimensional system with linear size equal to $L = 100$. The density of filaments is given by $\phi = N/L^2 = 10^{-2}$. (b) Schematic representation of the (spherical) probe particle with radius $R$ and the (cylindrical) filament with radius $r$ that sets the interaction range $\sigma$ of the force, Eq. 12.
In practice, the Brownian simulations used to obtain the motion of the probe particles immersed in the filament networks are implemented using a scheme based on Eq. 5, that is

$$x_{i+1} = x_i + \Delta t \tilde{F}_{\text{ext},x} + \sqrt{2D_0\Delta t} N(0,1),$$

$$y_{i+1} = y_i + \Delta t \tilde{F}_{\text{ext},y} + \sqrt{2D_0\Delta t} N(0,1),$$

where $\tilde{F}_{\text{ext},x} = \sum_j F_{j,x}(d_j)/\alpha$ and $\tilde{F}_{\text{ext},y} = \sum_j F_{j,y}(d_j)/\alpha$ are the components of the total force applied to the probe particle due to all filaments of the network ($j = 1, \ldots, N$). It is worth mentioning that, as we use periodic boundary conditions, we had also to implement the minimum image method [26] in order to avoid discontinuities on the forces that the filaments exert on the particle.

3. Results

In this Section we present the results from our Brownian simulations for the system defined by the filament networks. Below we consider both the influence of the density of filaments and the effect of the interaction between them and the probe particle.

For all simulations, we set the values for the radius of the filament and the radius of the probe particles, respectively, as $r = 0.02 \mu m$ and $R = 2 \mu m$ (those radii were taken from typical values observed in experiments; see, e.g., Ref. [27]). We assume that $k_B T = 4.12 \text{pN.nm}$ ($\sim 25^\circ\text{C}$) and $\eta = 0.89 \text{mPa.s}$ (water at $25^\circ\text{C}$), which gives $\alpha = 6\pi\eta R = 0.03355 \text{pN.s/}\mu \text{m}$ and $D_0 = k_B T/\alpha = 0.1228 \mu \text{m}^2/\text{s}$. Also, we take $L = 100 \mu m$, $\Delta t = 0.001 \text{s}$, and the final MSD results correspond to values averaged over $N_t = 10^5$ trajectories, each one with a different static random filament network. Importantly, it can be difficult to extract the Fourier transform of $J(t)$ from the raw data due to statistical fluctuations, thus we consider Eq. 5 of Ref. [19], which provides a good fit to the MSD data for $t \geq 10^{-1} \text{s}$, to evaluate the shear moduli $G'(\omega)$ and $G''(\omega)$ with Eqs. 10 and 11.

First, we consider the effect of the density of filaments $\phi$ on the motion of the probe particles. Figure 6 shows that the mean-squared displacement $\langle \Delta r^2(t) \rangle$ decreases as the number

Figure 6. Mean-squared displacement $\langle \Delta r^2(t) \rangle$ of probe particles immersed in networks with different densities of filaments $\phi$ that interacts through a repulsive force with strength $F_0 = -3.355 \text{pN}$ ($\tilde{F}_0 = -100 \mu \text{m}/\text{s}$). Filled symbols correspond to data obtained from Brownian simulations.
Figure 7. (a) Storage modulus $G'(\omega)$, and (b) loss modulus $G''(\omega)$, for different densities of filaments $\phi$. The shear moduli are evaluated from the MSD data of Fig. 6 through Eqs. 10 and 11. Results were obtained by Brownian simulations considering a repulsive force between the probe particles and the filaments with interaction strength equal to $F_0 = -3.355 \text{ pN (} \tilde{\text{F}}_0 = -100 \text{ } \mu\text{m/s).}$

of filaments increases. For a low density of filaments, the MSD curves are almost linear functions of time, indicating that the probe particles motion display a normal diffusion behaviour which is typical of particles immersed in simple liquids. When $\phi$ is increased, the motion of the particles becomes more restrict and the MSD changes to a qualitative behaviour that is similar to what we observe in Fig. 1(a) for the probe particles in a harmonic potential.

As shown in Fig. 7(a), the decrease in the MSD observed in Fig. 6 is accompanied by an increase in the storage modulus $G'(\omega)$, indicating that the filament network becomes more rigid, and, as the number of filaments increases, it becomes more difficult to shear it. Also, it is worth

Figure 8. $G'(\omega)$ and $G''(\omega)$ at a fixed frequency $\omega = 0.01 \text{ rad/s}$ as a function of the density of filaments $\phi$ for two different values of the interaction strength $F_0$. The intersection between the storage $G'(\omega)$ and the loss $G''(\omega)$ moduli determines the density of filaments $\phi_g \approx 4.10^{-3} \text{ } \mu\text{m}^{-2}$ and can be related to the gelation transition, which is the transition separating the phase where the filament network behaves like a complex liquid from the phase where it displays a solid-like viscoelastic response.
noting that \(G'(\omega)\) display a power-law behaviour at high frequencies. Such viscoelastic response is typical of semi-solid materials [4], and have been observed in simulations of semiflexible elastic networks [22], and experiments on gels formed by fibrillar networks [19].

In Fig. 8 we show the shear moduli \(G'\) and \(G''\) measured at a constant frequency \(\omega = 0.01\) rad/s as a function of the density of filaments for two different values of the interaction strength, \(\tilde{F}_0 = -10\) \(\mu\)m/s (or \(F_0 = -0.3355\) pN) and \(\tilde{F}_0 = -100\) \(\mu\)m/s (or \(F_0 = -3.355\) pN). One can observe that both moduli increase as \(\phi\) increases, which is a behaviour commonly observed in experiments. Also, we observe that, at low densities, there is virtually no difference between the values of the moduli for the two different interaction strengths. The difference between the shear moduli becomes more apparent as one increases the density of filaments \(\phi\). Interestingly, we see that there is a specific value \(\phi_g\) for the density which is close to \(4.10^{-3}\) \(\mu\)m\(^{-2}\) where there is an intersection between \(G'\) and \(G''\). Such value can be defined as a kind of “gelation point” in analogy to the sol-gel transition [4, 5]. For densities below this characteristic density (\(\phi < \phi_g\)), the loss modulus \(G''\) is greater than the storage modulus \(G'\) and the viscoelastic response of the filament network is similar to that of a complex fluid. As expected, the effect of the interaction strength \(F_0\) is very small in this range of densities since the probe particles barely interacts with the filaments. As the density \(\phi\) increases, the interaction between the filaments and the probe particles becomes stronger, and the effect of the interaction strength becomes more prominent for \(\phi > \phi_g\), e.g., the difference between the storage moduli is almost one order of magnitude for \(\phi = 0.0192\) \(\mu\)m\(^{-2}\). Importantly, when \(\phi > \phi_g\), one can observe that the storage modulus \(G'\) is greater than the loss modulus \(G''\), thus the system display a viscoelastic response which is more like a complex solid.

4. Concluding remarks

In this work we show how to extract the viscoelastic response of a filament network from the motion of probe particles obtained by Brownian dynamics simulations by using an analysis method based on micro rheology. Interesting, despite of simplicity of our model for the filament network, our numerical approach was able to reproduce several features that are observed in experiments [15]. In particular, our simulations were used to access the effect of density of filaments on the viscoelastic response of the filament network, and the results revealed a transition similar to a gelation transition where the system display a complex fluid-like mechanical behaviour at low densities but behaves like a semisolid for densities greater than \(\phi_g\). Our simple approach also revealed the hardening behaviour observed in experiments [19], where the storage modulus shows a power-law increasing behaviour at high frequencies.

Obviously, here we have presented just a proof-of-concept study, but such promising results should pave the way to further developments of our numerical simulations where we may consider a more detailed description of the filament network. Finally, it is worth mentioning that several other studies can follow from our numerical approach, including fundamental tests of the micro rheology theory and studies more focused on applications of bio-inspired materials in nanotechnology.

Acknowledgement

The authors thank Dr. Álvaro V. N. C. Teixeira for the useful discussions about the implementation of the Brownian dynamics simulations, the financial support by the Brazilian agencies CAPES and CNPq (Grant N° 306302/2018-7), and also the computational resources made available by GISC-UFV.
Appendix A. Particle in a harmonic potential

Appendix A.1. Overdamped Langevin dynamics

As discussed in Sec. 2, the one-dimensional Langevin’s equation for a particle in a harmonic potential in the overdamped regime can be written as

$$\frac{dx}{dt} + \gamma x = F_a(t), \quad (A.1)$$

where $\gamma = k/\alpha$ and $F_a(t) = F_a(t)/\alpha$. The solution of Eq. A.1 can be written as

$$x(t) = x_0 \exp(-\gamma t) + \exp(-\gamma t) \int_0^t \exp(\gamma t') F_a(t') dt', \quad (A.2)$$

where one can use the statistical properties of the random force $F_a(t)$, i.e., $\langle F_a(t) \rangle = 0$ and $\langle F_a(t) F_a(t') \rangle = C \delta(t - t')$, to evaluate the mean position, $\langle x(t) \rangle = x_0 \exp(-\gamma t)$, the deviation from the mean

$$\Delta x = x(t) - \langle x(t) \rangle = \exp(-\gamma t) \int_0^t \exp(\gamma t') F_a(t') dt', \quad (A.3)$$

and the mean-squared displacement,

$$\langle (\Delta x)^2 \rangle = \exp(-2\gamma t) \int_0^t \int_0^{t'} \exp(\gamma (t' + t'')) \langle F_a(t') F_a(t'') \rangle dt' dt'' = \frac{C}{2\gamma} (1 - \exp(-2\gamma t)) \quad (A.4)$$

Thus, by invoking the equipartition theorem, one finds that the pre-factor in Eq. A.4 should be $C = 2k_B T/\alpha$, so that the mean-squared displacement can be finally written as

$$\langle (\Delta x)^2 \rangle = \frac{k_B T}{k} \left[ 1 - \exp \left( -\frac{2t}{\tau} \right) \right], \quad (A.5)$$

where $\tau = \alpha/k$ defines a characteristic time that separates the normal diffusion regime, where $t \ll \tau$ and $\langle (\Delta x)^2 \rangle = (2k_B T/\alpha) t$, from the regime where $t \gg \tau$ and the MSD is constant, that is, $\langle (\Delta x)^2 \rangle = k_B T/k$.

Appendix A.2. Shear moduli

As discussed in Sec. 2, the complex modulus $G^*(\omega) = G'(\omega) + iG''(\omega)$ can be evaluated directly from the Fourier transform of the compliance $J(t)$, which, in turn, can be related to the MSD of the probe particles. In this Appendix we illustrate this procedure for the case of a particle in a harmonic potential.

First, by considering a $d$-dimensional MSD given by an expression similar to Eq. A.5, we use Eq. 9 that establishes the relationship between the compliance $J(t)$ and the MSD to get

$$J(t) = \frac{3\pi a}{k} \left[ 1 - \exp \left( -\frac{2t}{\tau} \right) \right], \quad (A.6)$$

with $\tau = \alpha/k$. Thus, by following the approach introduced by Mason and Weitz [9], we compute the Laplace transform of Eq. A.6, which yields

$$\mathcal{L}[J(t), s] = \frac{3\pi a}{k} \left( \frac{1}{s} - \frac{1}{s + 2/\tau} \right), \quad (A.7)$$

Then we take $s = i\omega$ to get the Fourier transform of $J(t)$, which is given by

$$J(\omega) = \frac{3\pi a}{k} \left( \frac{1}{i\omega} - \frac{1}{i\omega + 2/\tau} \right). \quad (A.8)$$
Finally, through Eq. 10 in Sec. 2, we obtain the complex modulus from the Fourier transform of the compliance $\hat{J}(\omega)$, that is,

$$G^*(\omega) = \frac{k}{3\pi a} + i\eta\omega,$$  \hspace{1cm} \text{(A.9)}

where $\eta = \alpha/6\pi a$ is the viscosity of the fluid. As noted in Ref. [13], this last expression is similar to the expression one would get when considering a Kelvin-Voigt material.

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