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Dynamics of two-component membranes surrounded by viscoelastic media

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Abstract

We discuss the dynamics of two-component fluid membranes which are surrounded by viscoelastic media. We assume that membrane-embedded proteins can diffuse laterally and induce a local membrane curvature. The mean squared displacement of a tagged membrane segment is obtained as a generalized Einstein relation. When the elasticity of the surrounding media obeys a power-law behavior in frequency, an anomalous diffusion of the membrane segment is predicted. We also consider the situation where the proteins generate active non-equilibrium forces. The generalized Einstein relation is further modified by an effective temperature that depends on the force dipole energy. The obtained generalized Einstein relations are useful for membrane microrheology experiments.

Keywords: membrane, microrheology, diffusion

(Some figures may appear in colour only in the online journal)

I. Introduction

Biomembranes are thin two-dimensional fluids which separate inner and outer environments of organelles in cells. The fluidity of biomembranes is guaranteed mainly due to the lipid molecules which are in the liquid crystalline state at physiological temperatures. Proteins and other molecules embedded in biomembranes undergo lateral diffusion which plays important roles for biological functions [1]. It should be noted, however, that biomembranes are not isolated 2D systems, but are coupled to the surrounding polar solvent such as water.

Moreover, the solvent surrounding biomembranes is viscoelastic rather than purely viscous. This is a common situation in all eukaryotic cells whose cytoplasm is a soup of proteins and organelles, including a thick sub-membrane layer of actin-meshwork forming a part of the cell cytoskeleton [1]. The extra-cellular fluid can also be viscoelastic because it is filled with extracellular matrix or hyaluronic acid gel. Recently, Granek discussed the dynamics of an undulating bilayer membrane surrounded by viscoelastic media [2]. He calculated the frequency-dependent out-of-plane (transverse) mean squared displacement (MSD) of a membrane segment and the linear response to external forces.

In this work, we discuss the dynamics and responses of two-component membranes containing proteins such as ion channels, ion pumps, or photo-active proteins like bacteriorhodopsin. These proteins can diffuse laterally within the membranes. We use a model that incorporates curvature-concentration coupling as well as hydrodynamics interactions. We calculate the MSD of a tagged membrane segment by taking into account the viscoelasticity of the surrounding media as well as the diffusivity of the proteins. Our aim is to derive a generalized Einstein relation for the membrane-protein system, which is useful for membrane microrheology experiments.

Furthermore, the state of the membrane proteins can be either passive or active [3]. In the latter case, the proteins consume the chemical energy and drive the membrane out of equilibrium. It was experimentally shown that active forces due to ion pumps enhance membrane fluctuations [4–7].

There exist two important theoretical models for active membranes; (i) Prost–Bruinsma (PB) model which takes into account the stochastic nature of the pumps [8, 9], and (ii) Ramaswamy–Toner–Prost (RTP) model which considers the coupling between the protein density and membrane curvature [10]. In this paper, we use the simplified RTP model proposed by Sankararaman *et al* [11], and investigate the effects of the surrounding viscoelastic media on the membrane dynamics. As discussed in [11], one of our important assumptions is that the membrane is impermeable to the solvent both for the active and passive states.

In the next section, we describe the free energy of the membrane-protein system. In section III, we present dynamic equations which take into account the viscoelasticity of the surrounding media. On the basis of the model, we calculate the membrane MSD and obtain a generalized Einstein relation in section IV. The case of active membranes will be discussed in section V. Finally, the obtained MSD is related to the response function in the last section.

II. Free energy

A two-component fluid membrane is regarded as an infinitesimally thin two-dimensional (2D) surface embedded in three-dimensional (3D) space. In order to describe the membrane deformation, we use the Monge gauge which is valid for nearly flat surfaces. Here the membrane surface is specified by its height above the flat xy-plane, $h(\boldsymbol{\rho}, t)$, where $\boldsymbol{\rho} = (x, y)$ and t is time. In this representation, the mean curvature of the surface is given by $H = (\nabla^2 h)/2$ to the lowest order.

Next we denote the number density of the embedded membrane proteins by $\psi(\boldsymbol{\rho}, t)$. As shown in figure 1, these intercalated protein molecules are assumed to induce a local curvature of the membrane surface [12, 13]. To leading order in gradients of h, the free energy functional of the membrane-protein system is given by [5, 10, 11]

$$F[h, \psi] = \frac{1}{2} \int \mathrm{d}^2\rho \, [\kappa(\nabla^2 h)^2 - 2\kappa \bar{H} \psi (\nabla^2 h) + \chi_0^{-1} \psi^2], \quad (1)$$

where κ is the bending rigidity, $\bar{H}\psi$ the protein density dependent spontaneous curvature, χ_0^{-1} the susceptibility which is assumed to be positive here. The above model is limited to a liner level, and we do not address nonlinear effects [9]. For the clarity of our presentation, we only discuss tensionless membranes and do not include the surface tension energy proportional to $(\nabla h)^2$. Effects of surface tension have been discussed in detail in the literature [14].

In the following, we introduce the 2D spatial Fourier transform of $h(\boldsymbol{\rho}, t)$ defined as

$$h(\boldsymbol{q}, t) = \int \mathrm{d}^2\rho \, h(\boldsymbol{\rho}, t) \mathrm{e}^{-\mathrm{i}\boldsymbol{q}\cdot\boldsymbol{\rho}}, \quad (2)$$

and similarly for $\psi(\boldsymbol{q}, t)$. Using the free energy equation (1), one can easily show that the static (equal-time) correlation functions are given by

Figure 1. Asymmetric proteins (triangles) embedded in a fluid bilayer membrane. Accumulation of the proteins induces a local curvature of the membrane. The membrane is surrounded by a viscoelastic medium with a frequency-dependent modulus $G(s)$.

$$\langle h(\boldsymbol{q}, t) h(-\boldsymbol{q}, t) \rangle = \frac{k_\mathrm{B} T}{\kappa_\mathrm{eff} q^4}, \quad (3)$$

$$\langle h(\boldsymbol{q}, t) \psi(-\boldsymbol{q}, t) \rangle = -\frac{k_\mathrm{B} T \kappa \bar{H}}{\kappa_\mathrm{eff} \chi_0^{-1} q^2}, \quad (4)$$

$$\langle \psi(\boldsymbol{q}, t) \psi(-\boldsymbol{q}, t) \rangle = \frac{k_\mathrm{B} T \kappa}{\kappa_\mathrm{eff} \chi_0^{-1}}, \quad (5)$$

where k_B is the Boltzmann constant, T the temperature, and κ_eff the effective bending rigidity given by $\kappa_\mathrm{eff} = \kappa(1 - \kappa \bar{H}^2/\chi_0^{-1})$. Notice that $\kappa_\mathrm{eff} < \kappa$ irrespective of the sign of $\bar{H}$ because $\chi_0^{-1} > 0$. The stability of the free energy requires that the coupling parameter $\bar{H}$ needs to be small enough to satisfy the condition $\kappa \bar{H}^2/\chi_0^{-1} < 1$.

III. Dynamics

Next we discuss the dynamics of two-component membranes. We follow the argument in [11] and assume that the membrane is impermeable to the surrounding solvent. This is valid over the length scales of concern in the experiments [5]. When the membrane is surrounded by viscoelastic media, as considered by Granek [2], a generalized Langevin equation for the motion of the displacement field $h(\boldsymbol{\rho}, t)$ is given by

$$\frac{\partial h(\boldsymbol{\rho}, t)}{\partial t} = -\int_0^t \mathrm{d}t' \int \mathrm{d}^2\rho' \, \Lambda(\boldsymbol{\rho} - \boldsymbol{\rho}', t - t') \frac{\delta F}{\delta h(\boldsymbol{\rho}', t')} + \xi(\boldsymbol{\rho}, t), \quad (6)$$

where $\Lambda(\boldsymbol{\rho}, t)$ is the retarded Oseen mobility. Its Laplace transform is given by

$$\Lambda(\boldsymbol{\rho}, s) = \int_0^\infty \mathrm{d}t \, \Lambda(\boldsymbol{\rho}, t) \mathrm{e}^{-st} = \frac{1}{8\pi\eta(s)\rho}, \quad (7)$$

where $\rho = |\boldsymbol{\rho}|$ and $\eta(s)$ is the frequency-dependent viscosity of the surrounding viscoelastic media (s being the frequency in the Laplace domain). The 2D Fourier transform of equation (7) is

$$\Lambda(\boldsymbol{q}, s) = \frac{1}{4\eta(s) q}, \quad (8)$$

with $q = |\boldsymbol{q}|$. The average of the thermal noise in equation (6) is $\langle \xi(\boldsymbol{\rho}, t)\rangle = 0$, whereas its correlation obeys the following fluctuation-dissipation theorem (FDT) [15, 16]

$$\langle \xi(\boldsymbol{\rho}, t)\xi(\boldsymbol{\rho}', t')\rangle = 2k_{\mathrm{B}}T\Lambda(\boldsymbol{\rho} - \boldsymbol{\rho}', t - t'). \tag{9}$$

Since the proteins diffuse freely on the membrane surface, the conserved quantity $\psi(\boldsymbol{\rho}, t)$ should obey the continuity equation of the form

$$\frac{\partial \psi(\boldsymbol{\rho}, t)}{\partial t} = L\nabla^2 \frac{\delta F}{\delta \psi(\boldsymbol{\rho}, t)} + \nabla \cdot \boldsymbol{\zeta}(\boldsymbol{\rho}, t), \tag{10}$$

where L is the transport coefficient which is assumed to be constant. In this diffusion, however, the hydrodynamic interaction is neglected [17]. The last term is a conserving Gaussian noise with $\langle \boldsymbol{\zeta}(\boldsymbol{\rho}, t)\rangle = 0$ and its correlations are given by

$$\langle \zeta_i(\boldsymbol{\rho}, t)\zeta_j(\boldsymbol{\rho}', t')\rangle = 2k_{\mathrm{B}}TL\delta_{ij}\delta(\boldsymbol{\rho} - \boldsymbol{\rho}')\delta(t - t'). \tag{11}$$

Equations (6) and (11) are the set of equations to be investigated.

The above equations can be conveniently solved by using the Laplace transform of $h(\boldsymbol{q}, t)$ and $\psi(\boldsymbol{q}, t)$ (see equation (7)). Then equations (6) and (11) can be written in the matrix form as

$$\begin{pmatrix} \Lambda(\boldsymbol{q}, s)\kappa q^4 + s & \Lambda(\boldsymbol{q}, s)\kappa \bar{H} q^2 \\ L\kappa \bar{H} q^4 & Dq^2 + s \end{pmatrix} \begin{pmatrix} h(\boldsymbol{q}, s) \\ \psi(\boldsymbol{q}, s) \end{pmatrix} = \begin{pmatrix} \xi(\boldsymbol{q}, s) + h_0 \\ \mathrm{i}\boldsymbol{q} \cdot \boldsymbol{\zeta}(\boldsymbol{q}, s) + \psi_0 \end{pmatrix}, \tag{12}$$

where $D = L\chi_0^{-1}$, $h_0 = h(\boldsymbol{q}, t = 0)$ and $\psi_0 = \psi(\boldsymbol{q}, t = 0)$. After some calculations, we obtain the solution as

$$\begin{aligned} h(\boldsymbol{q}, s) = {} & [(Dq^2 + s)h_0 - \Lambda(\boldsymbol{q}, s)\kappa \bar{H} q^2 \psi_0 \\ & + (Dq^2 + s)\xi(\boldsymbol{q}, s) - \mathrm{i}\Lambda(\boldsymbol{q}, s)\kappa \bar{H} q^2 \boldsymbol{q} \cdot \boldsymbol{\zeta}(\boldsymbol{q}, s)] \\ & \times [(\Lambda(\boldsymbol{q}, s)\kappa q^4 + s)(Dq^2 + s) \\ & - \Lambda(\boldsymbol{q}, s)L\kappa^2 \bar{H}^2 q^6]^{-1} \end{aligned} \tag{13}$$

$$\begin{aligned} \psi(\boldsymbol{q}, s) = {} & -[L\kappa \bar{H} q^4 h_0 + (\Lambda(\boldsymbol{q}, s)\kappa q^4 + s)\psi_0 \\ & - L\kappa \bar{H} q^4 \xi(\boldsymbol{q}, s) + \mathrm{i}(\Lambda(\boldsymbol{q}, s)\kappa q^4 + s)\boldsymbol{q} \cdot \boldsymbol{\zeta}(\boldsymbol{q}, s)] \\ & \times [(\Lambda(\boldsymbol{q}, s)\kappa q^4 + s)(Dq^2 + s) \\ & - \Lambda(\boldsymbol{q}, s)L\kappa^2 \bar{H}^2 q^6]^{-1} \end{aligned} \tag{14}$$

We use equation (13) to calculate the membrane MSD in the next section.

IV. Membrane mean squared displacement

The important quantity from the experimental point of view is the MSD of a tagged membrane segment defined as

$$\begin{aligned} \phi(t) &= \langle [h(\boldsymbol{\rho}, t) - h(\boldsymbol{\rho}, 0)]^2 \rangle \\ &= 2\int \frac{\mathrm{d}^2 q}{(2\pi)^2} [\langle h(\boldsymbol{q}, t)h(-\boldsymbol{q}, t)\rangle - \langle h(\boldsymbol{q}, t)h(-\boldsymbol{q}, 0)\rangle]. \end{aligned} \tag{15}$$

The first term in the above integrand is the equal-time correlation function given by equation (3). The Laplace transform of the time correlation function $\langle h(\boldsymbol{q}, t)h(-\boldsymbol{q}, 0)\rangle$ can be obtained from equation (13) as

$$\begin{aligned} \langle h(\boldsymbol{q}, s)h(-\boldsymbol{q}, t = 0)\rangle = {} & \frac{k_{\mathrm{B}}T}{\kappa_{\mathrm{eff}} q^4} \\ & \times \frac{(Dq^2 + s) + \Lambda(\boldsymbol{q}, s)\kappa^2 \bar{H}^2 q^4 / \chi_0^{-1}}{(\Lambda(\boldsymbol{q}, s)\kappa q^4 + s)(Dq^2 + s) - \Lambda(\boldsymbol{q}, s)L\kappa^2 \bar{H}^2 q^6}. \end{aligned} \tag{16}$$

Here we have used equations (3) and (4) for the equal-time correlation functions. Another important assumption to derive the above correlation function is that the stochastic thermal noise ξ and $\boldsymbol{\zeta}$ are uncorrelated with the initial condition of the height $h(\boldsymbol{q}, t = 0) = h_0$, which is somewhat non-trivial [15]. Using equations (3) and (16) in equation (15), the Laplace transformed MSD of a membrane segment can be conveniently written as [2]

$$\begin{aligned} \phi(s) = {} & 2\int \frac{\mathrm{d}^2 q}{(2\pi)^2} \frac{k_{\mathrm{B}}T}{\kappa_{\mathrm{eff}} q^4} \\ & \times \left(\frac{1}{s} - \frac{(Dq^2 + s) + \Lambda(\boldsymbol{q}, s)\kappa^2 \bar{H}^2 q^4 / \chi_0^{-1}}{(\Lambda(\boldsymbol{q}, s)\kappa q^4 + s)(Dq^2 + s) - \Lambda(\boldsymbol{q}, s)L\kappa^2 \bar{H}^2 q^6} \right). \end{aligned} \tag{17}$$

Hereafter we use the general viscoelasticity relation for the frequency dependent modulus $G(s) = s\eta(s)$. Using equation (8) for $\Lambda(\boldsymbol{q}, s)$, one can rearrange the integrand in equation (17) as

$$\begin{aligned} \phi(s) = {} & \frac{1}{\pi} \frac{k_{\mathrm{B}}T}{4sG(s)} \\ & \times \int_0^\infty \mathrm{d}q \left(\frac{\kappa q^3}{4G(s)} + 1 - \frac{D\kappa^2 \bar{H}^2}{4\chi_0^{-1} G(s)} \frac{q^5}{Dq^2 + s} \right)^{-1}. \end{aligned} \tag{18}$$

Although it is impossible to perform the above integral analytically, equation (18) can be regarded as a generalized Einstein relation for a segment of two-component membranes.

We recall here that the coupling parameter $\bar{H}$ should be small enough to satisfy the stability condition of the free energy equation (1). When $\kappa \bar{H}^2 / \chi_0^{-1} \ll 1$, equation (18) can be expanded in powers of $\bar{H}$, and the approximated form can be obtained as

$$\begin{aligned} \phi(s) \approx {} & \frac{1}{\pi} \frac{k_{\mathrm{B}}T}{4sG(s)} \left[\int_0^\infty \mathrm{d}q \left(\frac{\kappa q^3}{4G(s)} + 1 \right)^{-1} \right. \\ & \left. + \frac{D\kappa^2 \bar{H}^2}{4\chi_0^{-1} G(s)} \int_0^\infty \mathrm{d}q \left(\frac{\kappa q^3}{4G(s)} + 1 \right)^{-2} \frac{q^5}{Dq^2 + s} \right]. \end{aligned} \tag{19}$$

Here both of the integrals can be performed analytically. Especially, by defining dimensionless quantities $\hat{q}^3 = \kappa q^3 / 4G(s)$ and $\hat{s} = (s/D)(\kappa / 4G(s))^{2/3}$, the second integral can be written in the form

$$\int_0^\infty \mathrm{d}q \left(\frac{\kappa q^3}{4G(s)} + 1 \right)^{-2} \frac{q^5}{Dq^2 + s} = \left(\frac{\kappa}{4G(s)} \right)^{-4/3} \frac{I(\hat{s})}{D}, \tag{20}$$

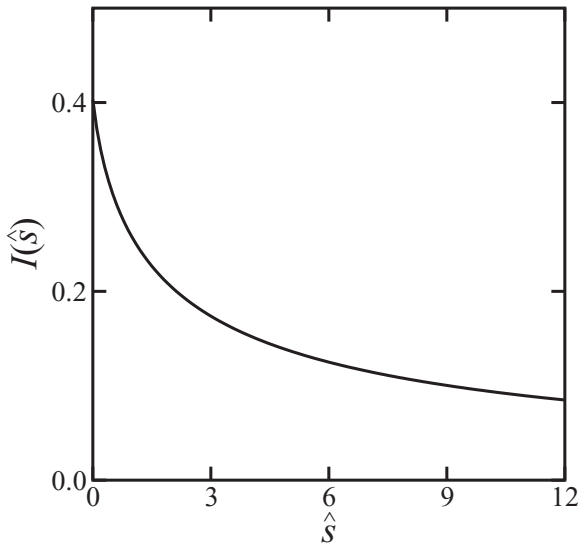

Figure 2. The plot of the integral $I(\hat{s})$ defined in equation (21). Here the variable is $\hat{s} = (s/D)(\kappa/4G(s))^{2/3}$.

where

$$I(\hat{s}) = \int_0^\infty \mathrm{d}\hat{q}\, \frac{\hat{q}^5}{(\hat{q}^3+1)^2(\hat{q}^2+\hat{s})} = \frac{1}{(1+\hat{s}^3)^2}\left[\frac{2\pi}{3^{5/2}} - \frac{2\pi\hat{s}}{3^{5/2}} - \left(\frac{1}{3}+\frac{\ln\hat{s}}{2}\right)\hat{s}^2 + \frac{14\pi\hat{s}^3}{3^{5/2}} - \pi\hat{s}^{7/2} + \frac{10\pi\hat{s}^4}{3^{5/2}} - \left(\frac{1}{3}-\frac{\ln\hat{s}}{2}\right)\hat{s}^5\right]. \tag{21}$$

The behavior of $I(\hat{s})$ is illustrated in figure 2. Performing the first integral in equation (19) and using equation (20), we obtain the Laplace transformed MSD as

$$\phi(s) \approx \frac{2}{3^{3/2}}\frac{k_\mathrm{B}T}{D\kappa}\left(\frac{\kappa}{4G(s)}\right)^{4/3}\frac{1}{\hat{s}}\left[1+\frac{3^{3/2}}{2\pi}\frac{\kappa\bar{H}^2 I(\hat{s})}{\chi_0^{-1}}\right], \tag{22}$$

which is the (approximated) generalized Einstein relation for membrane-protein systems in the weak coupling limit.

We denote the first and the second terms in equation (22) as $\phi_\mathrm{mem}(s)$ and $\phi_\mathrm{diff}(s)$, respectively, so that the total MSD is expressed as $\phi(s) = \phi_\mathrm{mem}(s) + \phi_\mathrm{diff}(s)$. The first term $\phi_\mathrm{mem}(s)$ due to the membrane itself can be rewritten as

$$\phi_\mathrm{mem}(s) = \frac{1}{3^{3/2}2^{1/3}}\frac{k_\mathrm{B}T}{\kappa^{1/3}sG(s)^{2/3}}, \tag{23}$$

which coincides with the result by Granek [2], as it should. The second term $\phi_\mathrm{diff}(s)$ is our new contribution due to the diffusion of proteins in the membrane;

$$\phi_\mathrm{diff}(s) = \frac{1}{\pi}\frac{k_\mathrm{B}T\bar{H}^2}{D\chi_0^{-1}}\left(\frac{\kappa}{4G(s)}\right)^{4/3}\frac{I(\hat{s})}{\hat{s}}, \tag{24}$$

where $\hat{s} = (s/D)(\kappa/4G(s))^{2/3}$ as before. We note here that ϕ_diff vanishes in the limit of $\bar{H}\to 0$.

As a working example, we consider the situation where both sides of the membrane are occupied by the same viscoelastic media with a frequency-dependent modulus that obeys a power-law behavior [2, 18, 19];

$$G(s) = G_0 s^\alpha, \tag{25}$$

where $0 \leqslant \alpha \leqslant 1$. This behavior is commonly observed for various polymeric solutions at high frequencies. Examples are $\alpha = 1/2$ and $\alpha = 2/3$ for Rouse and Zimm dynamics, respectively [20], $\alpha = 3/4$ for semi-dilute solutions of semi-flexible polymers such as actin filaments [21]. The limits of $\alpha = 0$ and 1 correspond to the purely elastic and purely viscous cases, respectively.

For such power-law viscoelastic media, the membrane part of the time-dependent MSD can be readily obtained by performing the inverse Laplace transform [2]

$$\phi_\mathrm{mem}(t) = \frac{1}{3^{3/2}2^{1/3}\Gamma(1+2\alpha/3)}\frac{k_\mathrm{B}T}{\kappa^{1/3}G_0^{2/3}}t^{2\alpha/3}, \tag{26}$$

where $\Gamma(z)$ is the gamma function. In the purely elastic case of $\alpha = 0$, we have

$$\phi_\mathrm{mem}(t) = \frac{1}{3^{3/2}2^{1/3}}\frac{k_\mathrm{B}T}{\kappa^{1/3}G_0^{2/3}}, \tag{27}$$

which is independent of time. On the other hand, in the purely viscous case of $\alpha = 1$, equation (26) reduces to

$$\phi_\mathrm{mem}(t) = \frac{1}{3^{3/2}2^{1/3}\Gamma(5/3)}\frac{k_\mathrm{B}T}{\kappa^{1/3}G_0^{2/3}}t^{2/3} = 0.169\frac{k_\mathrm{B}T}{\kappa^{1/3}\eta_0^{2/3}}t^{2/3}, \tag{28}$$

where we have replaced G_0 with η_0 in the last expression. This result was previously obtained by Zilman and Granek for single component membranes [22, 23].

Next we discuss the time-dependence of the diffusive MSD $\phi_\mathrm{diff}(t)$ in the presence of power-law fluid media as given by equation (25). For this purpose, we first consider the asymptotic behaviors of $I(\hat{s})$ in equation (21). In the limit of $\hat{s}\to 0$, we have

$$I(\hat{s}) \approx \frac{2\pi}{3^{5/2}} - \frac{2\pi}{3^{5/2}}\hat{s}, \tag{29}$$

whereas in the opposite limit of $\hat{s}\to\infty$, we get

$$I(\hat{s}) \approx -\left(\frac{1}{3}-\frac{\ln\hat{s}}{2}\right)\frac{1}{\hat{s}}. \tag{30}$$

In order to calculate $\phi_\mathrm{diff}(t)$, it is convenient to introduce a characteristic time scale defined by

$$\tau = \left(\frac{\kappa}{4G_0D^{3/2}}\right)^{2/(3-2\alpha)}, \tag{31}$$

which is dependent on α. (Notice that the dimension of G_0 also depends on α.) In what follows, we shall use a dimensionless time defined by $\tilde{t} = t/\tau$. Using the above asymptotic expressions in equation (24) and performing the inverse Laplace transform, we obtain in the long time limit of $\tilde{t}\to\infty$ as

$$\phi_\mathrm{diff}(\tilde{t}) \approx \frac{1}{\pi}\frac{k_\mathrm{B}T\bar{H}^2}{D\chi_0^{-1}}\left(\frac{\kappa}{4G_0}\right)^{4/3}\tau^{4\alpha/3-1} \times \frac{2\pi}{3^{5/2}}\left[\frac{\tilde{t}^{2\alpha/3}}{\Gamma(1+2\alpha/3)} - \frac{\tilde{t}^{4\alpha/3-1}}{\Gamma[4\alpha/3]}\right]. \tag{32}$$

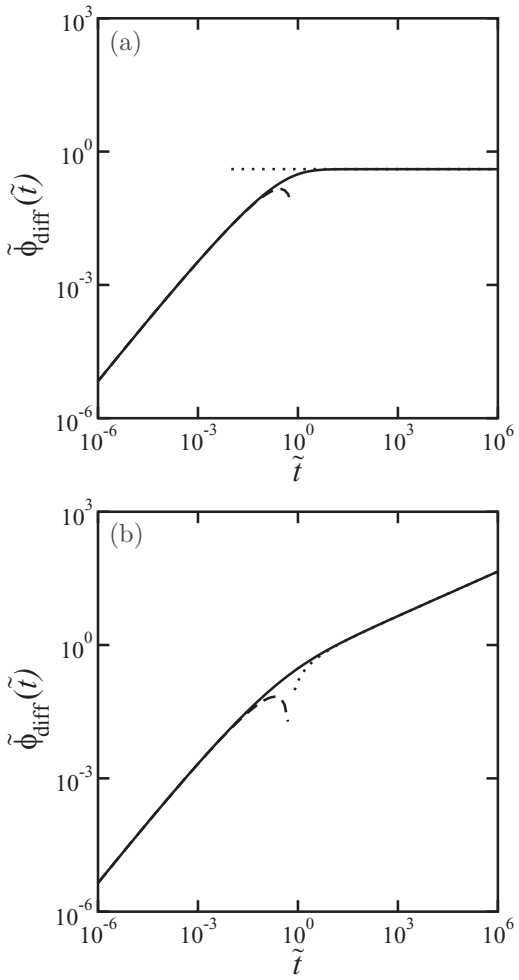

Figure 3. Dimensionless MSD due to the diffusion as a function of time when (a) $\alpha = 0$ and (b) $\alpha = 1/2$. Here $\tilde{\phi}_{\rm diff} = \phi_{\rm diff}/[(k_{\rm B}T\bar{H}^2/\pi D\chi_0^{-1})(\kappa/4G_0)^{4/3}\tau^{4\alpha/3-1}]$ and $\tilde{t} = t/\tau = t/(\kappa/4G_0D^{3/2})^{2/(3-2\alpha)}$. The dotted and the dashed lines are asymptotic expressions given by equations (32) and (33).

Here the first term is proportional to $t^{2\alpha/3}$ as in equation (26), and can be also expressed as $(\kappa\bar{H}^2/3\chi_0^{-1})\phi_{\rm mem}(t)$, where $\phi_{\rm mem}(t)$ is given by equation (26). The same result would have been obtained simply by replacing κ in equation (26) by $\kappa_{\rm eff}$. The second term, on the other hand, is proportional to $t^{4\alpha/3-1}$ showing a different exponent.

In the short time limit of $\tilde{t} \to 0$, we obtain

$$\phi_{\rm diff}(\tilde{t}) \approx \frac{1}{\pi}\frac{k_{\rm B}T\bar{H}^2}{D\chi_0^{-1}}\left(\frac{\kappa}{4G_0}\right)^{4/3}\tau^{4\alpha/3-1} \times \frac{\tilde{t}}{6}[(2\alpha-3)\ln\tilde{t} + (2\alpha-3)\gamma - 2\alpha + 1], \tag{33}$$

where $\gamma = 0.5772\cdots$ is Euler's constant. Since $\alpha \leqslant 1$, this MSD essentially grows like $t\ln(1/t)$. Such a logarithmic correction leads to a time-dependent diffusivity. Equations (32) and (33) are the important results of this paper.

In figure 3, we plot the dimensionless MSD $\phi_{\rm diff}$ due to the diffusion as a function of $\tilde{t} = t/\tau$ by performing the numerical inverse Laplace transform of equation (24) with full $I(\hat{s})$ when (a) $\alpha = 0$ and (b) $\alpha = 1/2$. We also compare it with the asymptotic expressions equations (32) and (33) which are in good agreement with the numerical result. In both cases, we see a clear crossover from the almost liner behavior to the power-law behavior of $\tilde{t}^{2\alpha/3}$. In the case of purely elastic media of $\alpha = 0$, both the membrane and diffusive contributions to MSD become independent of time for large $\tilde{t}$ [2].

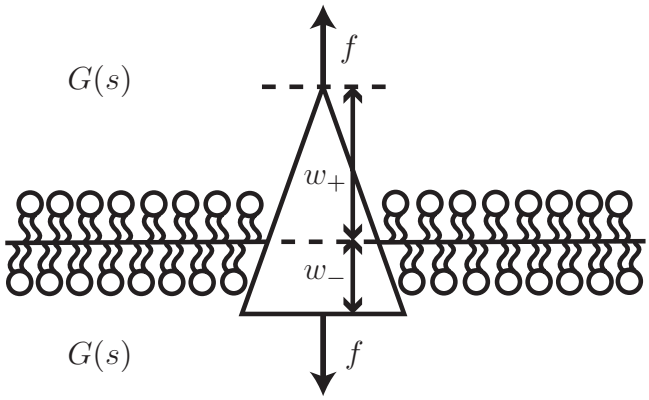

Figure 4. The asymmetric dipole model for a membrane protein. The force centers are located at distances w_+ and w_- from the bilayer midpoint. The magnitude of the active force is denoted by f. The membrane is surrounded by a viscoelastic medium with a frequency-dependent modulus $G(s)$.

V. Active membranes

We now discuss the dynamic properties of a two-component membrane with active pumps which exert non-equilibrium forces on the surrounding fluid. As considered by Manneville *et al* [5], each pump is represented as a force dipole, i.e. two force centers of opposite sign but equal magnitude separated by a distance w. This is justified because there should be no external force on the combined system of pump/membrane/solvent whose overall momentum is conserved. If the positive and negative force centers are located asymmetrically with respect to the midpoint of the membrane, the pumps exert nonzero active forces on the membrane and the surrounding media. When the force centers are located at $z = w_+$ and $z = -w_-$, as shown in figure 4, the active force is proportional to the protein density and can be written as[1]

$$\boldsymbol{F}_{\rm pump} = f\psi(\boldsymbol{\rho}, t)[\delta(z - w_+) - \delta(z + w_-)]\hat{\boldsymbol{z}}, \tag{34}$$

where f is the magnitude of the active force (taken to be constant) and $\hat{\boldsymbol{z}}$ is the unit vector along the z-direction.

Here we assume that pumps are always in the active state over the time scales of interest, and the membrane feels the active forces only via the surrounding fluid [11]. The presence of the active force due to the pumps modifies equation (6) and can be conveniently expressed in the Fourier-Laplace domain. Corresponding to equation (12), we then have

[1] In [5, 11], the difference between the densities of pumps transferring ions in the up and down direction is denoted by ψ.

$$\begin{pmatrix} \Lambda(\boldsymbol{q},s)\kappa q^4 + s & \Lambda(\boldsymbol{q},s)[\kappa\bar{H}q^2 - f\Omega(\boldsymbol{q})] \\ L\kappa\bar{H}q^4 & Dq^2 + s \end{pmatrix} \begin{pmatrix} h(\boldsymbol{q},s) \\ \psi(\boldsymbol{q},s) \end{pmatrix} = \begin{pmatrix} \xi(\boldsymbol{q},s) + h_0 \\ \mathrm{i}\boldsymbol{q}\cdot\boldsymbol{\zeta}(\boldsymbol{q},s) + \psi_0 \end{pmatrix}, \tag{35}$$

where

$$\begin{aligned} \Omega(\boldsymbol{q}) &= -(1+qw_-)\mathrm{e}^{-qw_-} + (1+qw_+)\mathrm{e}^{-qw_+} \\ &\approx \frac{q^2}{2}(w_-^2 - w_+^2) + \frac{q^2}{3}(w_-^3 - w_+^3) + \cdots \end{aligned} \tag{36}$$

is the 'structure factor' for the force dipole calculated in [5, 11]. Here we take into account only the first quadratic term in q and approximate as $f\Omega(\boldsymbol{q}) \approx -Pwq^2$, where $w = w_+ + w_-$ is the size of the pump and $P = f(w_+^2 - w_-^2)/2w$ represents the force dipole energy.

The calculation of the membrane MSD closely follows that of the previous section. In the small coupling limit of $\kappa\bar{H}^2/\chi_0^{-1} \ll 1$, we obtain

$$\begin{aligned} \phi(s) \approx{}& \frac{2}{3^{3/2}}\frac{k_\mathrm{B}T_\mathrm{eff}}{D\kappa}\left(\frac{\kappa}{4G(s)}\right)^{4/3}\frac{1}{\hat{s}} \\ &\times\left[1 + \frac{3^{3/2}}{2\pi}\frac{\kappa\bar{H}^2 I(\hat{s})}{\chi_0^{-1}}\left(1 + \frac{Pw}{\kappa\bar{H}}\right)\right], \end{aligned} \tag{37}$$

where T_eff is the effective temperature defined by

$$T_\mathrm{eff} = T\left(1 - \frac{\kappa\bar{H}Pw}{\kappa_\mathrm{eff}\chi_0^{-1}}\right). \tag{38}$$

This effective temperature decreases when $\bar{H}P > 0$, while it increases when $\bar{H}P < 0$[2]. The other difference between equations (22) and (37) is that the second term in equation (37) has an additional correction due to the pumps. Notice that these non-equilibrium contributions vanish when $w_+ = w_-$, implying that an asymmetry in the positions of the force centers ($w_+ \neq w_-$) is necessary for finite active forces.

Nevertheless, since the s-dependence is the same between equations (22) and (37), the MSD of membranes containing passive pumps and those containing active pumps exhibit the same scaling behavior. A similar result was also obtained by Lacoste and Lau [24] who showed that these two cases lead to a sub-diffusive behavior when membrane permeation is negligible and the surrounding fluid is purely viscous. For highly permeable membranes, on the other hand, a super-diffusive behavior was predicted by Granek and Pierrat [25] for membranes described by the PB model, and later by Lacoste and Lau [24] for those represented by the RTP model. Hence the permeability is crucial for the membrane dynamics, whereas the stochastic nature of the pumps could also lead to short time super-diffusion, as discussed before [8, 24–26]. The latter effect in the presence of viscoelastic media will be discussed in a separate publication. We also note that the effective temperature in equation (38) is different from that obtained by Manneville *et al* in [5]. This is because we have calculated equation (38) from the lowest-oder diffusive terms as in [11], while they neglected these diffusive terms in favor of higher-order terms.

[2] Our effective temperature differs from that in [11] because the correction term has an opposite sign.

VI. Summary and discussion

In this paper, we have discuss the dynamics of two-component fluid membranes that are surrounded by viscoelastic media. We have assumed that membrane proteins diffuse laterally and induce a local curvature of the membrane. We obtained the MSD of a tagged membrane segment by taking into account the viscoelasticity of the surrounding media. When the elasticity of the surrounding media obeys a power-law behavior, $G \sim (\mathrm{i}\omega)^\alpha$, the MSD due to protein diffusion shows a crossover from $t\ln(1/t)$ to $t^{2\alpha/3}$ behaviors. We have also discussed the situation when the proteins generate active non-equilibrium forces. The generalized Einstein relation is further modified by an effective temperature that depends on the force dipole energy. The generalized Einstein relations that we obtained for two-component membranes (see equations (22) and (37)) are useful to measure the viscoelastic properties of cytoplasm and/or extracellular matrix.

The obtained membrane MSD (in the Laplace domain) can be used to express the response of a membrane to transverse forces when it is surrounded by viscoelastic fluids. Within the linear response theory, one can write

$$h_\omega = \alpha^*(\omega)F_\omega, \tag{39}$$

where h_ω is the Fourier transform of the mean membrane deformation profile under the action of an external point force $F(t)$ at the origin $\boldsymbol{\rho} = 0$, F_ω is the Fourier transform of $F(t)$, and $\alpha^*(\omega) = \alpha'(\omega) + \mathrm{i}\alpha''(\omega)$ is the complex response function. In terms of the response function, the FDT can be written as [15, 16]

$$(h^2)_\omega = \frac{2k_\mathrm{B}T}{\omega}\alpha''(\omega), \tag{40}$$

where $(h^2)_\omega$ is the power spectral density. Hence the membrane response function can be related to the membrane MSD by

$$\alpha^*(\omega) = \frac{\mathrm{i}\omega}{2k_\mathrm{B}T}\phi^*(\omega), \tag{41}$$

where $\phi^*(\omega)$ is obtained from $\phi(s)$ by substituting $s = \mathrm{i}\omega$, i.e. an analytic continuation. Since $\phi^*(\omega) = \phi^*_\mathrm{mem}(\omega) + \phi^*_\mathrm{diff}(\omega)$, the mechanical response of two-component membranes differs from that of single-component membranes.

In our future work, we shall consider an active membrane containing proteins with two internal conformational states [27, 28], and the effects of viscoelasticity of the surrounding media. This can be a natural model for ion channels because they undergo random transitions between 'on' and 'off' states. The case of two-component membranes in a quasispherical shape (vesicles) [29] is also worth considering in order to study the rheology of cells.

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