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# Dynamics of active membranes with internal noise

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**Abstract.** – We study the time-dependent height fluctuations of an active membrane containing energy-dissipating pumps that drive the membrane out of equilibrium. Unlike previous investigations based on models that neglect either curvature couplings or random fluctuations in pump activities, our formulation explores two new models that take both of these effects into account. In the first model, the magnitude of the nonequilibrium forces generated by the pumps is allowed to fluctuate temporally. In the second model, the pumps are allowed to switch between "on" and "off" states. We compute the mean-squared displacement of a membrane point for both models, and show that they exhibit distinct dynamical behaviors from previous models, and in particular, a superdiffusive regime specifically arising from the shot noise.

*Introduction.* – While the physics of biomembranes in equilibrium is fairly developed [1], recent studies focus on active membranes that contain proteins, such as ion channels, ion pumps, and photo-active proteins like bacteriorhodopsin. These proteins consume the chemical energy of ATP, dissipate it into the medium, and thus drive the membrane out of equilibrium [2, 3]. The importance of active processes has been demonstrated in an experiment showing that the fluctuations in the shape of red blood cells depend on the viscosity of the environment and on ATP concentrations [4]. In *in vitro* experiments, nonequilibrium forces arising from ion pumps embedded in a membrane are shown to enhance its fluctuations [5–7]. There are currently two theoretical models for active membranes [3]. The Prost-Bruinsma (PB) model takes nonequilibrium forces in the form of active noises that include diffusion and the stochastic nature (shot noise) of the pumps, but ignores the coupling between the pumps and membrane curvature [8–10]. The other model proposed by Ramaswamy, Toner and Prost (RTP) incorporates this coupling but ignores the random nature of the protein activity [11,12]. For *steady state* measurements of active membranes, the RTP model agrees quite well with experiments [6, 7]. In this letter, we further explore the dynamical properties of the RTP model, argue that it is important to include the shot noise for *dynamical* measurements, and present two new models that include both curvature effects and pump stochasticity. In the first model, which may be an appropriate description for light-activated pumps such as bacteriorhodopsin, the magnitude of the nonequilibrium force fluctuates on a time scale that is fast compared to that of membrane fluctuations. The second model, the two-state model, which may be realized in typical ion channels [2], describes pumps that are able to switch from "on" to "off" state on a time scale that is long compared to membrane fluctuation time. These models represent natural generalizations of the RTP model, and they show distinct dynamical behaviors. In particular, the two-state model predicts that the mean-squared displacement (MSD) of a membrane point exhibits superdiffusion in the experimentally relevant regime, whereas the RTP model would predict subdiffusion. Our predictions should be accessible to microrheological experiments as carried out in ref. [13] for similar systems.

*Membrane dynamics in the RTP model.* – Consider a 2D tensionless, asymptotically flat, fluid membrane embedded a 3D space, lying on the $x$-$y$ plane. Confined to move in the membrane are two types of mobile active pumps. They can either be oriented up or down (for the orientation of the force dipole see [12]) with respect to the normal of the membrane, whose shape is described by a height field $h(\boldsymbol{r},t)$ [14]. Their local coarse-grained densities are, respectively, $\rho^{\uparrow}(\boldsymbol{r},t)$ and $\rho^{\downarrow}(\boldsymbol{r},t)$, where $\boldsymbol{r}$ denotes the 2D position vector. The RTP model describes the dynamics of $h(\boldsymbol{r},t)$ and the imbalance field, $\psi(\boldsymbol{r},t)\equiv\rho^{\uparrow}(\boldsymbol{r},t)-\rho^{\downarrow}(\boldsymbol{r},t)$, taking into account the curvature coupling and nonequilibrium forces arising from the pump activities. Here, we first summarize the RTP model and further discuss its dynamical properties.

In the regime where inertial effects are negligible, the dynamics of an active membrane is governed by Darcy's law, which states that the relative flow of the solvent with respect to the membrane is proportional to the normal force per unit area, $F_m(\boldsymbol{r},t)$, exerted on it: $\partial_t h(\boldsymbol{r},t)-v_{sz}(\boldsymbol{r},t)=\lambda_p F_m(\boldsymbol{r},t)$, where $v_{sz}(\boldsymbol{r},t)$ is the $z$-component of the fluid velocity field at the surface of the membrane, $\lambda_p$ is the membrane permeability, and $F_m(\boldsymbol{r},t)$ is the sum of two contributions: a passive part, $F_p(\boldsymbol{r},t)=-\delta\mathcal{H}/\delta h(\boldsymbol{r},t)$, arising from membrane elasticity and an active part from pump activities [6,11], $F_A(\boldsymbol{r},t)=F_1(\boldsymbol{r},t)\,\psi(\boldsymbol{r}\,t)+F_2(\boldsymbol{r},t)\,\rho(\boldsymbol{r},t)\,\nabla^2 h(\boldsymbol{r},t)$, where $\rho(\boldsymbol{r},t)\equiv\rho^{\uparrow}(\boldsymbol{r},t)+\rho^{\downarrow}(\boldsymbol{r},t)$. Note that the expression for $F_A(\boldsymbol{r},t)$ is the only possible form that is linear in the density fields obeying the symmetry: $(h,\psi,\rho,F_A)\to(-h,-\psi,\rho,-F_A)$. In the RTP model, $\rho(\boldsymbol{r},t)=\rho_0$ is assumed to be uniform, and more importantly, $F_1(\boldsymbol{r},t)=F_1$ and $F_2(\boldsymbol{r},t)=F_2$ are assumed to be constant in space and time, capturing only an average force produced by each pump. (For simplicity, we set $F_2=0$ throughout this paper, *i.e.* ignoring higher-order contributions from the $F_2$ term.) The membrane free energy is given by [15]

$$\mathcal{H}=\frac{1}{2}\int \mathrm{d}^2\boldsymbol{r}\,\left[\kappa(\nabla^2 h)^2+\chi\psi^2-2\,\Xi\,\psi\nabla^2 h\right], \tag{1}$$

where $\kappa$ is the bare bending modulus, $\chi$ is the osmotic modulus of the pumps, and $\Xi$ is the curvature coupling parameter which arises from head-tail asymmetry of the pumps. In equilibrium, $\kappa$ is renormalized to $\kappa_e\equiv\kappa-\Xi^2/\chi$, which must be positive to ensure stability. The fluid velocity $\boldsymbol{v}(\boldsymbol{x},t)$ surrounding the membrane obeys Stokes' law: $\eta\nabla^2\boldsymbol{v}(\boldsymbol{x},t)=\nabla p(\boldsymbol{x},t)-\boldsymbol{F}_m(\boldsymbol{x},t)$, where $\eta$ is the solvent viscosity, $p(\boldsymbol{x},t)$ is the pressure field which ensures the incompressibility condition: $\nabla\cdot\boldsymbol{v}=0$, and $\boldsymbol{F}_m(\boldsymbol{x},t)$ is the total force exerted on the fluid by the membrane. It contains two parts: a passive part, $\boldsymbol{F}_p(\boldsymbol{x},t)=-[\delta\mathcal{H}/\delta h(\boldsymbol{r},t)]\delta(z)\,\hat{\boldsymbol{z}}$, arising from membrane elasticity, and an active part arising from the force exerted by the pumps on the fluid, modelled as a dipolar force density with force centers located at $z=w$ and $z=-w'$ [6,12]: $\boldsymbol{F}_A(\boldsymbol{x},t)=F_A(\boldsymbol{r},t)[\delta(z-w)-\delta(z+w')]\,\hat{\boldsymbol{z}}$. Assuming $\psi(\boldsymbol{r},t)$ obeys the conserved dynamics: $\partial_t\psi=\Lambda\nabla^2\delta\mathcal{H}/\delta\psi+\nu$ and eliminating the fluid velocity from Darcy's law, we obtain in Fourier space two coupled Langevin equations [6]:

$$\begin{aligned}\partial_t h(\boldsymbol{q},t)+\omega_h h(\boldsymbol{q},t) &= \beta\,\psi(\boldsymbol{q},t)+\mu(\boldsymbol{q},t),\\ \partial_t\psi(\boldsymbol{q},t)+\omega_\psi\psi(\boldsymbol{q},t) &= \gamma\,h(\boldsymbol{q},t)+\nu(\boldsymbol{q},t),\end{aligned} \tag{2}$$

where $\omega_h=\kappa q^3/(4\eta)+\kappa\lambda_p q^4$, $\beta=\lambda_p F_1-(P_1 w+\Xi)q/(4\eta)-\Xi\,\lambda_p q^2$, $\omega_\psi=\Lambda\,\chi\,q^2\equiv Dq^2$, $D$ is the pump's diffusion constant, $\gamma=-\Lambda\,\Xi\,q^4$, and $P_1=F_1(w^2-w'^2)/(2w)$. The noises $\mu(\boldsymbol{q},t)$ and $\nu(\boldsymbol{q},t)$ are assumed to be thermal in origin: $\langle\mu(\boldsymbol{q},t)\rangle = \langle\nu(\boldsymbol{q},t)\rangle = 0$, and $\langle\mu(\boldsymbol{q},t)\,\mu(-\boldsymbol{q},t')\rangle = 2k_BT[\lambda_p + 1/(4\eta q)]\delta(t-t') \equiv \Gamma_1\delta(t-t')$ and $\langle\nu(\boldsymbol{q},t)\,\nu(-\boldsymbol{q},t')\rangle = 2k_BT\Lambda q^2\delta(t-t') \equiv \Gamma_2\delta(t-t')$, where $\Lambda$ is the pump mobility, $k_B$ is the Boltzmann constant and $T$ is the temperature.

It is straightforward to evaluate the two-point correlation function, $\langle h(\boldsymbol{q},t)h(-\boldsymbol{q},0)\rangle$:

$$\langle h(\boldsymbol{q},t)h(-\boldsymbol{q},0)\rangle = \frac{\Gamma_1\,[M_+\,e^{-\omega_+t} - M_-\,e^{-\omega_-t}]}{2AB\,(\omega_+-\omega_-)} + \frac{\Gamma_2\,\beta^2\,[\omega_+\,e^{-\omega_-t} - \omega_-\,e^{-\omega_+t}]}{2AB\,(\omega_+-\omega_-)}\,, \tag{3}$$

where $A \equiv \omega_h\omega_\psi - \beta\gamma$, $B \equiv \omega_h + \omega_\psi$, $\omega_\pm = [\omega_h + \omega_\psi \pm \sqrt{(\omega_h-\omega_\psi)^2 + 4\beta\gamma}]/2$, and $M_\pm \equiv A\,\omega_\pm - \omega_\psi^2\,\omega_\mp$. We assume that $\omega_\pm > 0$, so that the system is dynamically stable and reaches a steady state whose distribution is Gaussian, as expected. Its variance is given by (setting $t=0$ in eq. (3)), $\langle h(\boldsymbol{q},0)h(-\boldsymbol{q},0)\rangle = [\Gamma_1(A+\omega_\psi^2) + \Gamma_2\beta^2]/(2AB) \sim k_BT_{\rm eff}/(\kappa_e q^4)$, in the $\lambda_p \sim 0$ limit [16], where $T_{\rm eff} = \kappa_e T[1 + P_1 w(\Xi + P_1 w)/(\chi\kappa)]/(\kappa_e - P_1 w\,\Xi/\chi)$ [6,7]. This effective temperature $T_{\rm eff}$ is found to be largely consistent with the experimental observations.

Here, we now discuss the dynamical aspects of eq. (3). For simplicity, we assume that the curvature coupling is small, *i.e.* $\omega_h\omega_\psi \gg \beta\gamma$, which is indeed the case for the experiments in ref. [7]. However, this approximation may not be always true in general and some of the conclusions below may be modified in the strong-coupling limit. Within the small curvature coupling approximation, eq. (3) simplifies to

$$\langle h(\boldsymbol{q},t)h(-\boldsymbol{q},0)\rangle \simeq \frac{\Gamma_1}{2\,\omega_h}\,e^{-\omega_h t} + \frac{\Gamma_2\beta^2}{2\,(\omega_h^2-\omega_\psi^2)}\left[\frac{e^{-\omega_\psi t}}{\omega_\psi} - \frac{e^{-\omega_h t}}{\omega_h}\right]. \tag{4}$$

The central quantity of experimental interest is the MSD of a membrane point defined by $\langle\Delta h^2(t)\rangle \equiv \langle[h(\boldsymbol{r},t) - h(\boldsymbol{r},0)]^2\rangle = \int_{\pi/L}^{\pi/a} q\,({\rm d}q/2\pi)\,[\langle h(\boldsymbol{q},0)h(-\boldsymbol{q},0)\rangle - \langle h(\boldsymbol{q},t)h(-\boldsymbol{q},0)\rangle]$, where $a$ and $L$ are, respectively, the microscopic and the system size. They introduce two time scales, $t_a \sim \eta\,a^3/\kappa$ and $t_L \sim \eta L^3/\kappa$, that are assumed to be, respectively, the shortest and longest time scales in the problem. Note also that $\langle\Delta h^2(t)\rangle$ roughly corresponds to transverse fluctuations of a particle embedded in a membrane in microrheological experiments [17]. From eq. (4), we see that there are two contributions: $\langle\Delta h^2(t)\rangle = \langle\Delta h_{th}^2(t)\rangle + \langle\Delta h_a^2(t)\rangle$. The first term comes from thermal fluctuations with the well-known scaling law $\langle\Delta h_{th}^2(t)\rangle = 0.17(k_BT/\kappa^{1/3}\eta^{2/3})t^{2/3}$ [18]. The second term arises from the diffusion of the pumps. There are two cases to consider: i) In the permeation-dominated regime, in which $\beta \simeq \lambda_p F_1$, we find

$$\left\langle\Delta h_a^2(t)\right\rangle \simeq \begin{cases} 1.62\,\frac{k_BT\Lambda\lambda_p^2F_1^2\eta^{4/3}}{\kappa^{4/3}}t^{5/3}, & \text{for } t \ll t_{c1}\,,\\ \frac{k_BT\lambda_p^2F_1^2}{6\pi D\chi}t\ln(t/t_{c1})\,, & \text{for } t \gg t_{c1}\,, \end{cases} \tag{5}$$

where $t_{c1} \equiv \kappa^2/(16\eta^2D^3)$. Thus, there is a superdiffusion at short time which crosses over to an almost normal diffusion at long time. This is similar to the findings in ref. [10], where the dynamics of the PB model was analyzed. However, eq. (4) does not contain a term that arises from the switching of the pumps that is explicitly included in the PB model. Note also that the superdiffusion in eq. (5) is a purely nonequilibrium phenomenon in the sense that membranes with passive inclusion only show subdiffusion [19]. ii) In the experimental relevant regime in which $\lambda_p = 0$, *i.e.* permeation is negligible [16], and $\beta = -(P_1w+\Xi)/(4\eta)\,q \equiv -\beta_1 q$, we now find

$$\left\langle\Delta h_a^2(t)\right\rangle \simeq \begin{cases} -0.85\,\frac{k_BT\beta_1^2\eta^2\Lambda}{\kappa^2}t\ln(t/t_{c1})\,, & \text{for } t \ll t_{c1}\,,\\ 1.08\,\frac{k_BT\beta_1^2\eta^{2/3}}{D\chi\kappa^{2/3}}t^{1/3}, & \text{for } t \gg t_{c1}\,. \end{cases} \tag{6}$$

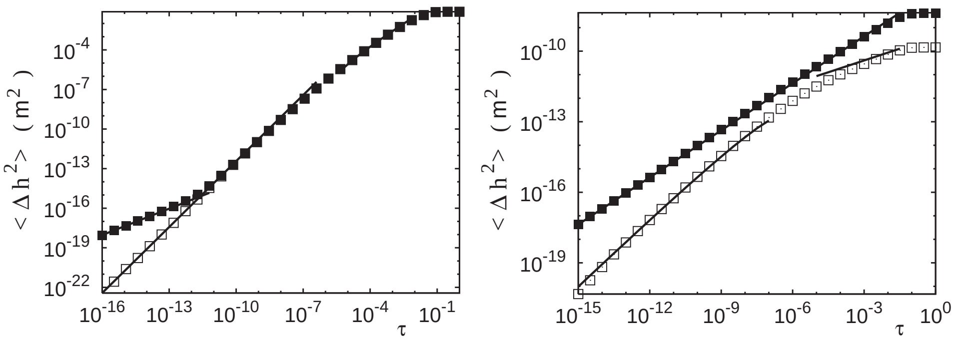


Fig. 1 – The active part of the MSD $\langle \Delta h_a^2(t) \rangle$ (empty symbols) and the overall MSD (full symbols) as a function of $\tau \equiv t/t_L$ for the RTP model in the permeation-dominated regime ($\lambda_p \neq 0$, left) and the regime with negligible permeation ($\lambda_p = 0$, right). The solid lines are scaling laws of eqs. (5) and (6) which compare well with points obtained from numerically integrating eq. (3). The parameters used are drawn from experimental values in refs. [6, 7]: $\kappa = 10\, k_B T$, $\eta = 10^{-3}\,\mathrm{kg\,m^{-1}\,s^{-1}}$, $w = 5\,\mathrm{nm}$, $w' = 4\,\mathrm{nm}$, $\Xi = w k_B T$, $P_1 = 10\, k_B T$, $D \sim 10^{-12}\,\mathrm{m^2/s}$, $L = 1\,\mathrm{mm}$, $\rho_0 = 3 \cdot 10^{15}\,\mathrm{m^{-2}}$, and when $\lambda_p \neq 0$ we choose $\beta = 5 \cdot 10^{-18}\,\mathrm{m^3/s}$. In both cases, the crossover time is $t_{c1}/t_L \sim 10^{-6}$, where $t_L \equiv \eta L^3/\kappa \sim 10^8\,\mathrm{s}$.

In contrast to case i), the MSD shows an almost normal diffusion at short time and a sub-diffuse regime at long times. We have verified these scaling laws (eqs. (5) and (6)) by numerically computing the MSD as shown in fig. 1. For case i), the thermal MSD dominates at short time, while the active MSD dominates at long time. In constrast, for case ii), the thermal MSD is the dominant contribution. Note also that eq. (6) suggests that membranes containing active pumps and those containing passive pumps obey the same scaling law. Therefore, the RTP model leads to the conclusion that dynamical measurements cannot distinguish active membranes from passive ones in the experimentally relevant regime. However, as noted above, the RTP model ignores the stochastic nature of the pumps, which may be a serious approximation made in so far as dynamics is concerned. The natural question to ask is: how does the shot noise contribute to the membrane dynamics? We address this question below.

*Active membranes with temporal force fluctuations.* – Recall that the active force density $F_A(\boldsymbol{r}, t)$ contains $F_1(\boldsymbol{r}, t)$ and $F_2(\boldsymbol{r}, t)$ that are assumed to be constant in the RTP model. Thus, the most direct way to incorporate pump stochasticity is to allow them to fluctuate in time. Here, we focus on the direct force fluctuations: $F_1(\boldsymbol{r}, t) = F_1 + \delta F(t)$ in the $\lambda_p \sim 0$ regime. Assuming separation of time scales, $\delta F(t)$ is described by a Gaussian white noise with zero mean: $\langle \delta F(t) \rangle = 0$ and $\langle \delta F(t) \delta F(t') \rangle = 2W\delta(t-t')$, where $W$ characterizes the strength of the fluctuations. This generalization of the RTP model may capture the effects of fast temporal fluctuations of the nonequilibrium forces exerted on the fluids by pumps. Incorporating $\delta F(t)$ into the RTP equations, eq. (2), we see that it contributes an additional term $\delta\beta(t)\,\psi(\boldsymbol{q}, t)$ to the $h$-equation with $\langle \delta\beta(t)\delta\beta(t') \rangle = \Gamma_s \delta(t - t')$, where $\Gamma_s \equiv 2W[\Omega(q)/(4\eta q)]^2$ and $\Omega(q) = (1 + qw)\, e^{-qw} - (1 + qw')\, e^{-qw'}$ is the "structure factor" for the force dipole [6, 12].

The Langevin equations of this model involve multiplicative and additive noises in a spatially extended system [20, 21], which in general could pose a mathematically challenging problem; however, in this case they can be solved exactly. It is straightforward to derive the corresponding Fokker-Planck equation [22], which describes the time evolution of the probability distribution $\mathcal{P}[\{h(\boldsymbol{q})\}, \{\psi(\boldsymbol{q})\}; t]$. Since different $\boldsymbol{q}$'s are decoupled, we can write

$\mathcal{P}[\{h(\boldsymbol{q})\}, \{\psi(\boldsymbol{q})\}; t] = \prod_{\boldsymbol{q}} P[h(\boldsymbol{q}), \psi(\boldsymbol{q}); t]$, where $P[h(\boldsymbol{q}), \psi(\boldsymbol{q}); t]$ satisfies

$$\partial_t P = \partial_h \left[ (\omega_h h - \beta\psi)\, P \right] + \partial_\psi \left[ (\omega_\psi \psi - \gamma h)\, P \right] + (\Gamma_1/2)\, \partial_h^2 P + (\Gamma_2/2)\, \partial_\psi^2 P + (\Gamma_s\, \psi^2/2)\, \partial_h^2 P. \quad (7)$$

The last term in eq. (7), arising from force fluctuations, is a nonlinear term which may render eq. (7) difficult to solve. However, we find, quite remarkably, a closed set of equations for the moments of the form $\Psi_{m,k}(t) \equiv \langle h^m(t)\, \psi^k(t) \rangle$, which directly follows from eq. (7):

$$\begin{aligned} \partial_t \Psi_{m,k}(t) &= -m \left( \omega_h \Psi_{m,k} - \beta \Psi_{m-1,k+1} \right) - k \left( \omega_\psi \Psi_{m,k} - \gamma \Psi_{m+1,k-1} \right) + \\ &\quad + m(m-1) \left( \Gamma_1\, \Psi_{m-2,k} + \Gamma_s\, \Psi_{m-2,k+2} \right)/2 + \Gamma_2\, k(k-1) \Psi_{m,k-2}/2, \end{aligned} \quad (8)$$

where $m = n - k$, $0 \le k \le n$, and $n$ is a positive integer. From eq. (8), we can compute all the moments of the steady-state distribution which, in contrast to the RTP model, is clearly non-Gaussian. Furthermore, we can obtain the exact *two-point* correlation function:

$$\langle h(\boldsymbol{q}, t) h(-\boldsymbol{q}, 0) \rangle = \frac{2\,\Gamma_1 \left[ M_+\, e^{-\omega_+ t} - M_-\, e^{-\omega_- t} \right]}{(4AB - \Gamma_s \gamma^2)\,(\omega_+ - \omega_-)} + \frac{2\,\Gamma_2 \left[ N_+\, e^{-\omega_- t} - N_-\, e^{-\omega_+ t} \right]}{(4AB - \Gamma_s \gamma^2)\,(\omega_+ - \omega_-)}\,, \quad (9)$$

where $N_\pm = \beta^2 \omega_\pm + \Gamma_s [B(\omega_\pm - \omega_h) + \gamma\beta]/2$. Note that eq. (9) reduces to eq. (3) if we set $\Gamma_s = 0$, as it should be. It is interesting to observe that the denominator in eq. (9) contains the factor $4AB - \Gamma_s \gamma^2$, which could become zero at finite $q$ for sufficiently large $W$, signaling a dynamical instability. An analysis of this instability will be presented in a separate publication, along with the mathematical details leading to eq. (9). For small $W$, we find that $\langle h(\boldsymbol{q}, 0) h(-\boldsymbol{q}, 0) \rangle \simeq k_B T_{\text{eff}}(q)/(\kappa_e q^4)$, with a scale-dependent effective temperature: $T_{\text{eff}}(q) = \kappa_e T[1 + W\Omega(q)^2/(4\eta q \chi) + P_1 w(\Xi + P_1 w)/(\chi\kappa)]/(\kappa_e - P_1 w\, \Xi/\chi)$, which is plotted in the inset of fig. 2. It shows that force fluctuations greatly enhance membrane fluctuations mostly in the region $q \sim 1/w$. Note also that $T_{\text{eff}}(q)$ depends on the viscosity of the solvent, whereas $T_{\text{eff}}$ in the RTP model does not. Furthermore, temporal force fluctuations contribute significantly to the active MSD, *i.e.* the second term in eq. (9), as can be seen in fig. 2. Note that the active MSD in our model is drastically increased at short time, though it does not predict superdiffusion. Thus, in contrast to the RTP model, the short-time behavior of the overall MSD is now dominated by the active contributions.

*Modelling shot-noise with a two-state model.* – A two-state model has recently been introduced to address the dynamical instability of an active membrane containing inclusions with two internal conformational states [23]. Such a two-state model of pumps switching between "on" and "off" states may also capture the stochastic nature of the pumps. It may be a natural model for typical ion channels since they undergo random transitions between open and closed states [2,24]. We model the transition between "on" and "off" as a chemical reaction with rate constants $k_p$ and $k_a$: on $\xrightarrow{k_p}$ off $\xrightarrow{k_a}$ on, and introduce imbalance fields for the "on" pumps, $\psi_a(\boldsymbol{r}, t) = \rho_{\text{on}}^{\uparrow}(\boldsymbol{r}, t) - \rho_{\text{on}}^{\downarrow}(\boldsymbol{r}, t)$, and "off" pumps, $\psi_p(\boldsymbol{r}, t) = \rho_{\text{off}}^{\uparrow}(\boldsymbol{r}, t) - \rho_{\text{off}}^{\downarrow}(\boldsymbol{r}, t)$. The active contribution to the force exerted on the fluid is assumed to come only from the "on" pumps: $\boldsymbol{F}_A(\boldsymbol{x}, t) = F_1\, \psi_a(\boldsymbol{r}, t) \left[ \delta(z - w) - \delta(z + w') \right] \hat{\boldsymbol{z}}$. In analogy to eq. (2), the general equations of motion for the two-state model in the regime with negligible permeation ($\lambda_p = 0$) are

$$\begin{aligned} \partial_t h(\boldsymbol{q}, t) + \omega_h h(\boldsymbol{q}, t) &= \beta_a \psi_a(\boldsymbol{q}, t) + \beta_p \psi_p(\boldsymbol{q}, t) + \mu(\boldsymbol{q}, t), \\ \partial_t \psi_a(\boldsymbol{q}, t) + \omega_a \psi_a(\boldsymbol{q}, t) &= \gamma_a\, h(\boldsymbol{q}, t) + k_a \psi_p(\boldsymbol{q}, t) + \nu_a(\boldsymbol{q}, t) + \xi(\boldsymbol{q}, t), \\ \partial_t \psi_p(\boldsymbol{q}, t) + \omega_p \psi_p(\boldsymbol{q}, t) &= \gamma_p\, h(\boldsymbol{q}, t) + k_p \psi_a(\boldsymbol{q}, t) + \nu_p(\boldsymbol{q}, t) - \xi(\boldsymbol{q}, t), \end{aligned} \quad (10)$$

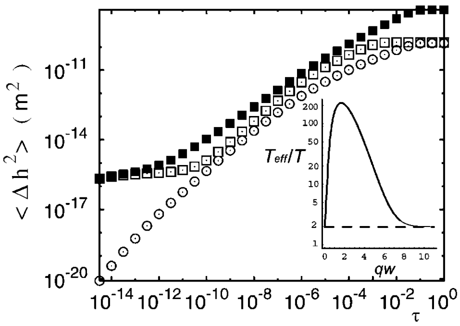


Fig. 2

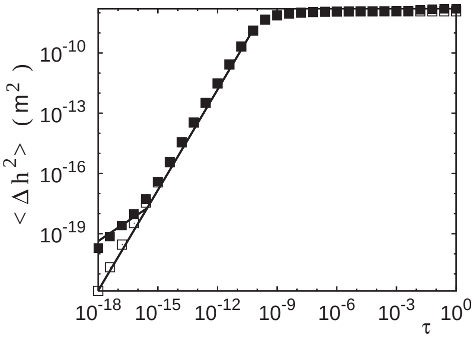


Fig. 3

Fig. 2 – The active part of the MSD $\langle \Delta h_a^2(t)\rangle$ (open squares) and the overall MSD (solid squares) in the presence of temporal force fluctuations as obtained from eq. (9). For short time, the behavior of the active MSD is drastically different from that of the RTP model (open circles). Inset: The scale-dependent effective temperature $T_{\rm eff}(q)$ induced by force fluctuations (solid curve). In the RTP model, $T_{\rm eff}/T \simeq 1.9$ (straight line) for parameters listed in fig. 1 and $W = 3.4\cdot 10^{-26}\,{\rm N}^2\,{\rm s}$.

Fig. 3 – Same as fig. 1 but for the two-state model as obtained from eq. (11). The parameters are same as fig. 1, and $k_a = 0.1\,{\rm s}^{-1}$, $\tau_R \sim 10^{-2}\,{\rm s}$, and $\Gamma_3 = 10^{24}\,{\rm s}^{-1}\,{\rm m}^{-2}$. In contrast to the RTP model in the $\lambda \sim 0$ limit, this MSD exhibits superdiffusion which scales as $\sim t^{5/3}$.

where $\omega_h = \kappa q^3/(4\eta)$, $\beta_a = -(P_1 w + \Xi_a)q/(4\eta) \equiv -\beta_1 q$, $\beta_p = -\Xi_p q/(4\eta)$, $\omega_{a,p} = D_{a,p}q^2 + k_{p,a}$, and $\gamma_{a,p} = -\Lambda_{a,p}\Xi_{a,p}q^4$. As in the RTP model, $\mu(\boldsymbol{q},t)$, $\nu_a(\boldsymbol{q},t)$, and $\nu_p(\boldsymbol{q},t)$ are thermal noises with zero mean and $\langle \mu(\boldsymbol{q},t)\,\mu(-\boldsymbol{q},t')\rangle = k_BT/(2\eta q)\delta(t-t')$ and $\langle \nu_i(\boldsymbol{q},t)\,\nu_j(-\boldsymbol{q},t')\rangle = 2k_BT\Lambda_i\, q^2\delta_{ij}\,\delta(t-t')$. In eq. (10), $\xi(\boldsymbol{r},t)$ denotes the "chemical noise" associated with the transitions between the two states; since the switching process may involve ATP, which is clearly not an equilibrium process, its variance is not constrained by the Fluctuation-Dissipation Theorem. We simply assume that $\xi(\boldsymbol{r},t)$ has zero mean and $\langle \xi(\boldsymbol{r},t)\xi(\boldsymbol{r}',t')\rangle = \Gamma_3\,\delta(\boldsymbol{r}-\boldsymbol{r}')\delta(t-t')$, with $\Gamma_3$ being constant in space and time.

Although an exact, but complicated, expression for the two-point correlation function can be obtained analytically, we find it convenient to introduce the following simplifying approximations in order to illustrate the essential features: $\Lambda_a = \Lambda_p = \Lambda$, $\chi_a = \chi_p = \chi$, $D_a = D_p = D$, $\beta_a^2 \gg \beta_p^2$, and $\omega_h\omega_a \gg \beta_a\gamma_a$. Under these approximations, we obtain

$$\begin{aligned}\langle h(\boldsymbol{q},t)h(-\boldsymbol{q},0)\rangle &= \frac{\Gamma_1}{2\,\omega_h}e^{-\omega_h t} + \frac{\Gamma_2\beta_a^2 k_a\omega_p}{(\omega_h^2-\omega_1^2)\,(\omega_2^2-\omega_1^2)}\left[\frac{e^{-\omega_1 t}}{\omega_1} - \frac{e^{-\omega_h t}}{\omega_h}\right] + \\ &\quad + \frac{\beta_a^2}{2\,(\omega_h^2-\omega_2^2)}\left[\Gamma_3 + \Gamma_2\left(1 - \frac{2k_a\omega_p}{\omega_2^2-\omega_1^2}\right)\right]\left[\frac{e^{-\omega_2 t}}{\omega_2} - \frac{e^{-\omega_h t}}{\omega_h}\right], \qquad (11)\end{aligned}$$

where $\Gamma_1 \equiv k_BT/(2\eta q)$, $\Gamma_2 \equiv 2k_BT\Lambda\, q^2$, $\omega_1 = Dq^2$, $\omega_2 = Dq^2 + 1/\tau_R$, and $\tau_R \equiv 1/(k_a+k_p)$. The first two terms in eq. (11) have the same physical origins as the corresponding terms in eq. (4). In particular, the second term gives rise to a MSD which has the same scaling laws as in eq. (6), except that its magnitude is reduced by a factor of $\sim (k_a\tau_R)^2$. The third term, which is absent in the RTP model, arises from the noise associated with the switching process between "on" and "off" states of the pumps and their diffusion. It is analogous to the shot-noise term in the PB model [10] but ours contains curvature couplings, which are absent in the PB model. Note also that the analysis of ref. [10] assumes that the system is in the permeation-dominated regime [16]. Assuming $\Gamma_3$ is sufficiently large, the MSD arising from the third term in eq. (11), $\langle \Delta h_s^2(t)\rangle$, obeys the following scaling laws:

$$\langle \Delta h_s^2(t)\rangle \simeq \begin{cases} 0.32\,\Gamma_3\beta_1^2(\eta/\kappa)^{4/3}t^{5/3}, & \text{for } t \ll \tau_R\,, \\ 0.16\,\Gamma_3\beta_1^2(\eta/\kappa)^{4/3}\tau_R^{5/3}, & \text{for } t \gg \tau_R\,. \end{cases} \tag{12}$$

Therefore, we find that the MSD exhibits superdiffusion $\sim t^{5/3}$ at short time. This is qualitatively different from the prediction of RTP model in eq. (6) as well as the force fluctuations model in eq. (9). Since the first two terms in eq. (11) exhibit only subdiffusion at short time, $\langle \Delta h_s^2(t)\rangle$ is the dominant contribution to the MSD, which is plotted in fig. 3. As an estimate, $\tau_R$ may be about 0.01 s for typical ion pumps [2, 25].

In summary, we have generalized the RTP model by incorporating the shot noise of the pumps and demonstrated its significance to the dynamics of an active membrane.

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