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A variational principle for molecular motors

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Dedicated to PIERO VILLAGGIO

1. Introduction

Intracellular transport in eukarya is attributed to motor proteins that transduce chemical energy into directed mechanical motion. Muscle myosin has been known since the mid nineteenth century and its role in muscle contraction demonstrated by A. F. Huxley and H. E. Huxley in the 1950's. Kinesins and their role in intracellular transport were discovered only in 1985, [20]. These nanoscale sized motors carry organelles and other cargo on microtubules. They function in a highly viscous setting with overdamped dynamics. Taken as a system, they are in configurations far from conventional notions of equilibrium even though they are in an isothermal environment. Because of the presence of significant diffusion in the environment they are sometimes referred to as Brownian motors. Since a specific type tends to move in a single direction, for example, either anterograde or retrograde to the cell periphery, these proteins are sometimes referred to as molecular rachets.

In this note we establish a dissipation principle that describes transport in a typical motor system like conventional kinesin. This begins a chain of events. It suggests, in a natural way, a variational principle and an implicit scheme in the sense of Otto [14], [15] and Jordan, Kinderlehrer and Otto [10]. This determines, in turn, a system of differential equations, by design that suggested by Adjari and Prost, cf. [16], or by Doering, Ermentrout, and Peskin [4] and Peskin, Ermentrout, and Oster [17]. We have a clear notion of equilibrium or minimum energy for a macroscopic process. However, to quote J. L. Ericksen, a great friend of Prof. Villaggio, most of the systems we meet are only metastable. It is, indeed, very common to model systems in a way that this metastability disappears. Moreover even when we permit this type of behavior, when we think of evolution, especially when we have in hand a smooth solution, we often neglect to recognize that in saying states are close to each other we are imposing an environment for

the motion. The novelty of our principle is that it sets this dynamical environment for the process in a weak topology as described by a Kantorovich-Wasserstein metric. This owes in part to a result of Benamou and Brenier [2]. Our derivation illustrates the feasibility of mesoscale modeling for these systems.

In [11] we discussed a different type of model, the flashing rachet, cf. Astumian [1]. Here we were successful in approximating the system by a Markov chain on Dirac masses and were able to show how this led to transport in the system.

The version of these descriptions that we consider is a two state model consisting of a system of Fokker-Planck Equations coupled by first order chemistry. For this, we take $\Omega = (0,1)$ and

$\sigma > 0$ constant

$\psi_i \geq 0$ and $\nu_i \geq 0$, $i = 1,2$, smooth and periodic of period $X = 1/M$

with supp ν_1 = supp ν_2 and $\nu_1 + \nu_2 \leq 1$.

M is an integer. We often abbreviate writing $b_i = \psi_i'$.

We ask for $\rho = (\rho_1, \rho_2)$ satisfying

$$
\left|
\begin{aligned}
&\frac{\partial \rho_1}{\partial t} = \frac{\partial}{\partial x}(\sigma \frac{\partial \rho_1}{\partial x} + b_1\rho_1) - \nu_1 \rho_1 + \nu_2 \rho_2 \\
&\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad \text{in } \Omega,\ t > 0 \\
&\frac{\partial \rho_2}{\partial t} = \frac{\partial}{\partial x}(\sigma \frac{\partial \rho_2}{\partial x} + b_2\rho_2) + \nu_1 \rho_1 - \nu_2 \rho_2 \\
&\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad (1.1) \\
&\sigma \frac{\partial \rho_1}{\partial x} + b_1\rho_1 = 0 \\
&\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad \text{on } \partial\Omega,\ t > 0 \\
&\sigma \frac{\partial \rho_2}{\partial x} + b_2\rho_2 = 0 \\
&\rho_1 = \rho_1^{(0)} \text{ and } \rho_2 = \rho_2^{(0)} \text{ in } \Omega, t = 0.
\end{aligned}
\right.
$$

We assume that

$$\rho_1^{(0)} \geq 0,\ \rho_2^{(0)} \geq 0, \text{ and } \int_\Omega (\rho_1^{(0)} + \rho_2^{(0)})\, dx = 1. \tag{1.2}$$

Explanations of these equations may be found in [4], [16], [17], cf. also [19]. We give our derivation in §4. It is a classical fact that under (1.2) solutions of the system (1.1) are nonnegative [18] and, thanks to the boundary condition,

$$\int_\Omega (\rho_1 + \rho_2)\, dx = 1 \quad \text{for all t.}$$

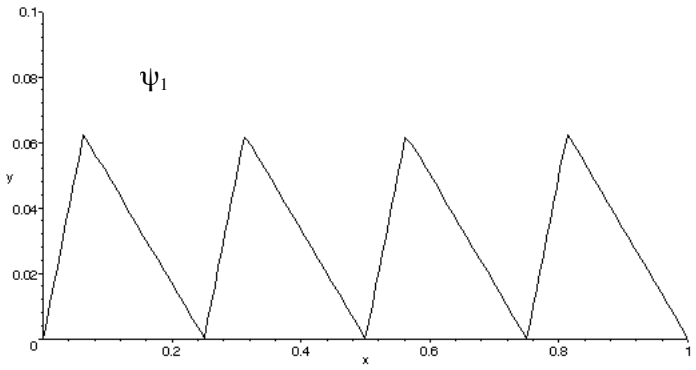

Fig. 1 A typical ψ_1.

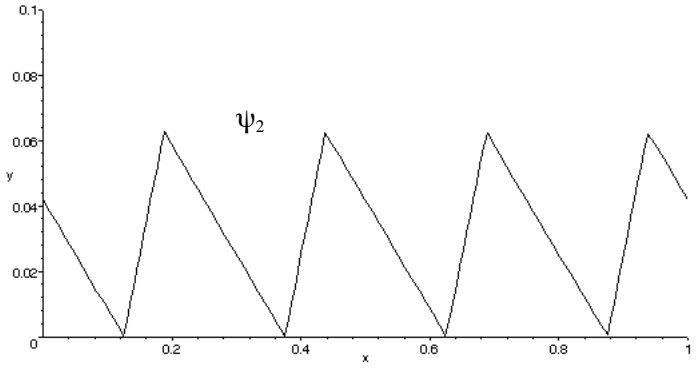

Fig. 2 A typical ψ_2. Note that the minima of ψ_2 interpolate the minima of ψ_1.

The key elements to achieve transport are

(a) asymmetry of the potentials ψ_i in a given period interval and

(b) the relationship of the conformation change factors ν_i to the ψ_i.

Here we provide results of simulations to illustrate this, leaving to a future work the analysis. Prior to proceeding, we would like to remark on a few aspects of (1.1).

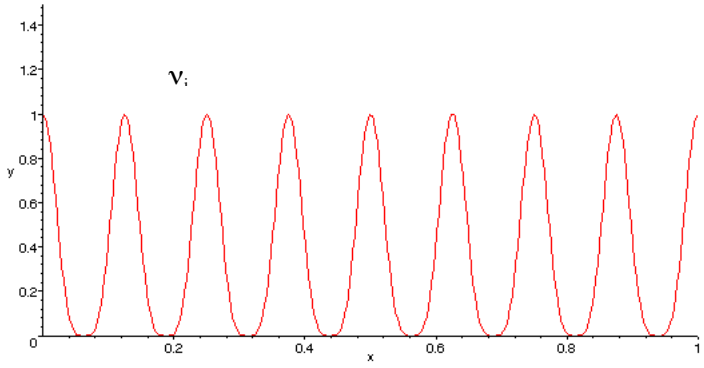

Fig. 3 Typical conformational change coefficient $\nu_1 = \nu_2$. Note that the maxima of ν_i are located at the minima of the potentials.

(i) ν_i constant. Suppose that the $\nu_i \geq 0$ with $\nu_1 + \nu_2 = 1$ are constants. For the moment denote by

$$\mu_i(t) = \int_\Omega \rho_i(x,t)\, dx \tag{1.3}$$

so $\mu_1 + \mu_2 = 1$. Then, using the boundary condition, we have a system of ordinary differential equations

$$\frac{d\mu_1}{dt} = -\nu_1 \mu_1 + \nu_2 \mu_2 \quad \text{and} \quad \frac{d\mu_2}{dt} = \nu_1 \mu_1 - \nu_2 \mu_2 \tag{1.4}$$

and thus

$$\mu(t) = (\nu_2,\nu_1) + c\, e^{-t}(1,-1) \rightarrow (\nu_2,\nu_1) \tag{1.5}$$

exponentially fast. Hence although the averages are not a good indicator of distance to equilibrium for the system, they do converge rapidly. For these averages we also have that their entropy is decreasing, namely,

$$\frac{d}{dt}(\mu_1 \log \mu_1 + \mu_2 \log \mu_2) < 0. \tag{1.6}$$

(ii) comparison with ordinary Fokker-Planck Equation. Consider briefly the problem

$$\left|\begin{array}{ll} \frac{\partial \rho}{\partial t} = \frac{\partial}{\partial x}(\sigma \frac{\partial \rho}{\partial x} + b\rho) & \text{in } \Omega,\ t > 0 \\ \sigma \frac{\partial \rho}{\partial x} + b\rho = 0 & \text{on } \partial\Omega,\ t > 0 \\ \rho = \rho_0 & \text{in } \Omega, t = 0. \end{array}\right. \tag{1.7}$$

where $\rho_0 \geq 0$ and $\int_\Omega \rho_0\, dx = 1$. Above $b = \psi'$, where $\psi \geq 0$ is a smooth potential. Let

$$\rho^{\#}(x) = \frac{1}{Z} e^{-\frac{\psi(x)}{\sigma}}, \quad Z = \int_\Omega e^{-\frac{\psi(x)}{\sigma}}\, dx, \tag{1.8}$$

denote the stationary solution of (1.7). It is a standard computation that

$$\begin{aligned} \frac{d}{dt}\, \sigma \int_\Omega \rho \log \frac{\rho}{\rho^{\#}}\, dx &= \frac{d}{dt} \int_\Omega (\psi \rho + \sigma \rho \log \rho)\, dx \\ &= -\int_\Omega \frac{1}{\rho} (\sigma \frac{\partial \rho}{\partial x} + b\rho)^2\, dx < 0, \end{aligned}$$

from which it follows that

$$\int_\Omega \rho \log \frac{\rho}{\rho^{\#}}\, dx \to 0 \text{ as } t \to \infty.$$

Since, by the Cesar - Kullback Inequality, just based on the fact that $t \log t$ is convex, [13] p. 15,

$$\left(\int_\Omega | \rho(x,t) - \rho^{\#}(x)| \, dx \right)^2 \leq 2 \int_\Omega \rho \log \frac{\rho}{\rho^{\#}} \, dx,$$

the decrease of the entropy implies that the solution

$$\rho(x,t) \rightarrow \rho^{\#}(x) \text{ in } L^1(\Omega) \text{ as } t \rightarrow \infty.$$

Consequently both in cases (i) and (ii) above, an entropy inequality is a key to the trend to equilibrium. We shall show this again, in a different context, for (1.7), but we are unable to determine such behavior in such a straightforward manner for our system (1.1). In fact, it is not even obvious that there is a stationary solution to (1.1); however a proof may be based on the Schauder Fixed Point Theorem.

2. Resumé of transport

In this section we give a brief description of the Kantorovich-Wasserstein metric and its relationship to transport, eg. [6]. Given densities $f, f^* \in L^1(\Omega)$ with

$$\int_\Omega f \, dx = \int_\Omega f^* \, dx = c > 0,$$

suppose that there is a strictly increasing continuous mapping

$$\phi : \Omega \rightarrow \Omega, \quad \phi(0) = 0, \quad \phi(1) = 1,$$

such that

$$\int_\Omega \zeta \, f \, dx = \int_\Omega \zeta(\phi(x)) f^*(x) \, dx \quad \text{for} \quad \zeta \in C(\Omega). \tag{2.1}$$

We then say that f is the push forward of f^* and ϕ is the associated transfer function. In particular, if $\zeta = \chi_A$, the characteristic function of $A \subset \Omega$, then

$$\int_A f(x)\,dx = \int_{\phi^{-1}(A)} f^*(x)\,dx,$$

or with $E = \phi^{-1}(A)$,

$$\int_{\phi(E)} f(x)\,dx = \int_E f^*(x)\,dx.$$

In particular for $E = [0, x]$,

$$\int_{[0,\phi(x)]} f(x')\,dx' = \int_{[0.x]} f^*(x')\,dx',$$

or

$$F(\phi(x)) = F^*(x),$$

where F and F^* are the distribution functions of f and f^*. Thus, in one dimension, the transfer function is uniquely determined as

$$\phi(x) = F^{-1}(F^*(x)), \quad x \in \Omega, \tag{2.2}$$

which was known to Frechet, [5].

Now ϕ is the unique solution of the Kantorovich formulation of the Monge-Kantorovich mass transfer problem: among all joint distributions $q(x,y)$ with marginals f and f^*.

$$d(f, f^*)^2 = \min \int_{\Omega\times\Omega} |x - y|^2\,dq(x,y) = \int_\Omega |x - \phi(x)|^2\, f^*(x)\,dx. \tag{2.3}$$

$|x - y|^2$ may be replaced by any suitable cost function in this one-dimensional situation. It turns out that d is a metric on the measures $f\,dx$ with mass c which induces the weak* topology on them (as the dual space of $C(\Omega)$).

Now suppose that $f(x,t),\ 0 \le t \le \tau$, and $f^*(x)$ are given with

$$\int_\Omega f(x,t)\,dx \;=\; \int_\Omega f^*\,dx \;=\; c \;>\; 0 \text{ with transfer functions } \phi(x,t).$$

Thus,

$$\int_\Omega \zeta(x)\, f(x,t)\,dx \;=\; \int_\Omega \zeta(\phi(x,t)) f^*(x)\;dx \quad \text{for} \quad \zeta \in C(\Omega),\ 0 \le t \le \tau, \qquad (2.4)$$

and in particular,

$$\int_{[0,\phi(x,t)]} f(x')\,dx' \;=\; \int_{[0.x]} f^*(x')\,dx'.$$

Assuming requisite smoothness, differentiate this expression with respect to x and t. Then

$$f(\phi(x,t),t)\,\frac{\partial \phi}{\partial x} \;=\; f^*(x) \quad \text{and}$$

$$f_\xi(\phi(x,t),t)\,\frac{\partial \phi}{\partial t}\,\frac{\partial \phi}{\partial x} \;+\; f_t(\phi(x,t),t)\,\frac{\partial \phi}{\partial x} \;+\; f(\phi(x,t),t)\frac{\partial^2 \phi}{\partial x \partial t} \;=\; 0.$$

Now define a velocity by

$$\frac{\partial \phi}{\partial t} \;=\; v(\phi,\, t) \quad \text{so} \quad \frac{\partial^2 \phi}{\partial x \partial t} \;=\; v_\xi(\phi,\, t)\,\frac{\partial \phi}{\partial x}.$$

Substituting gives

$$f_t \;+\; (v f)_x \;=\; 0 \quad \text{in } \Omega,\ 0 \;<\; t \;<\; \tau. \qquad (2.5)$$

So f is the solution to a continuity equation. The converse is easy to check. Brenier and Benamou [2] show that

$$d(f^{**},f^{*})^2 \;=\; \tau \min_{v} \int_0^\tau \int_\Omega v^2 f \, dx \, dt, \tag{2.6}$$

where

$$\begin{aligned} &f_t + (vf)_x \;=\; 0 \quad \text{in } \Omega, \;\; 0 < t < \tau, \\ &f(x,0) = f^{*}(x), \; f(x,\tau) = f^{**}(x). \end{aligned} \tag{2.7}$$

We review their verification of this. Let $\hat{\phi}$ denote the transfer function for f^{**}, f^{*}. Given $f(x,t)$ satisfying (2.7), by (2.4),

$$\int_\Omega v(\xi,t)^2 f(\xi,t)\, d\xi \;=\; \int_\Omega v(\phi(x,t),t)^2 f^{*}(x)\, dx \quad \text{and}$$

$$\begin{aligned} \tau \int_0^\tau \int_\Omega v(\xi,t)^2 f(\xi,t)\, d\xi\, dt \;&=\; \tau \int_0^\tau \int_\Omega v(\phi(x,t),t)^2 f^{*}(x)\, dx\, dt \\ &=\; \tau \int_0^\tau \int_\Omega \phi_t(x,t)^2 f^{*}(x)\, dx\, dt. \end{aligned}$$

On the other hand, recalling that $\phi(x,0) = x$, by Schwarz's Inequality,

$$\begin{aligned} |\, x - \phi(x,\tau)| \;&=\; |\, \phi(x,0) - \phi(x,\tau)| \;\le\; \int_0^\tau |\, \phi_t(x,t)\,| \, dt \\ &\le\; \sqrt{\tau}\, \Big(\int_0^\tau \phi_t(x,t)^2 \, dt \Big)^{1/2}. \end{aligned}$$

Multiplying by f^{*} and integrating gives

$$d(f^{**},f^{*})^2 \;=\; \int_\Omega |\, x - \phi(x,\tau)|^2 f^{*}(x)\, dx \;\le\; \tau \int_0^\tau \int_\Omega \phi_t(x,t)^2 f^{*}(x)\, dx\, dt \tag{2.8}$$

$$= \tau \int_0^\tau \int_\Omega v(\xi,t)^2 \, f(\xi,t) \, d\xi \, dt.$$

Thus

$$d(f^{**},f^*)^2 \le \inf \tau \int_0^\tau \int_\Omega v(\xi,t)^2 \, f(\xi,t) \, d\xi \, dt.$$

Now choose the special $\phi(x,t) = x + \frac{t}{\tau}(\hat{\phi}(x) - x)$. For this choice,

$$\phi_t(x,t) = \frac{1}{\tau}(\hat{\phi}(x) - x),$$

and equality holds in (2.8). This shows (2.6).

3. Dissipation and the Kantorovich-Wasserstein metric

In this section, we discuss a dissipation inequality and use it to suggest a variational principle for a general Fokker-Planck Equation. To begin, we establish an expression for the dissipation in an ensemble of mass-spring-dashpot systems. For a single elementary mass-spring-dashpot system, we commonly write an ordinary differential equation

$$\begin{aligned} m\frac{d^2\xi}{dt^2} + \gamma\frac{d\xi}{dt} + \kappa\xi &= F, \quad 0 < t < \tau \\ \xi(0) &= x \\ \frac{d\xi}{dt}(0) &= 0 \end{aligned} \tag{3.1}$$

Multiplying by $\frac{d\xi}{dt}$ and integrating over $(0,\tau)$ gives the familiar relation

$$\tfrac{1}{2} m \frac{d\xi}{dt}(\tau)^2 + \gamma \int_0^\tau \left(\frac{d\xi}{dt}\right)^2 dt + \frac{\kappa}{2}\xi(\tau)^2 = \frac{\kappa}{2}x^2 + F(\xi(\tau) - x), \tag{3.2}$$

relating the kinetic energy, the potential energy, the work done on the system, and the energy loss due to frictional dissipation. In particular,

$$\gamma \int_0^{\tau} \left(\frac{d\xi}{dt} \right)^2 dt$$

is the term which represents the dissipation. We may regard τ as a relaxation time. Our interest is in the left hand side of (3.2). Suppose an ensemble is distributed with a number density $f^*(x)$. Set $\xi = \phi(x,t)$. Then at time τ we have for this ensemble

$$\tfrac{1}{2} m \int_\Omega \phi_t(x,\tau)^2 f^*(x)\, dx + \gamma \int_0^{\tau} \int_\Omega \phi_t(x,t)^2 f^*(x)\, dx\, dt + \frac{\kappa}{2} \int_\Omega \phi(x,\tau)^2 f^*(x)\, dx$$

which identifies

$$\delta = \gamma \int_0^{\tau} \int_\Omega \phi_t(x,t)^2 f^*(x)\, dx\, dt \tag{3.3}$$

as the energy dissipated in the system. Define the transported density $f(\xi,t)$ by

$$\int_\Omega \zeta(\xi) f(\xi,t)\, dx = \int_\Omega \zeta(\phi(x,t)) f^*(x)\, dx, \quad 0 \le t \le \tau \tag{3.4}$$

so we have that

$$\delta = \gamma \int_0^{\tau} \int_\Omega v(\xi,t)^2 f(\xi,t)\, dx\, dt \quad \text{with} \tag{3.5}$$

$$f_t + (vf)_\xi = 0 \quad \text{in} \quad \Omega, \quad 0 < t < \tau,$$

analogous to the discussion of the last section. For a fixed initial distribution f^* and terminal distribution $f(x) = f(x,\tau)$,

$$\min \int_0^\tau \int_\Omega v(\xi,t)^2 f(\xi,t)\, dx\, dt \;=\; \frac{1}{\tau}\, d(f, f^*)^2, \tag{3.6}$$

where d is the Kantorovich-Wasserstein distance.

The above permits us to write the dissipation inequality for successive states of the system as an implicit scheme. First recall that our system is overdamped and kinetic energy may be ignored, as discussed in the introduction. Suppose that we are given a potential $\psi \geq 0$ and a diffusion coefficient σ. Take $\gamma = \frac{1}{2}$ for simplicity. Assume that the system starts from a distribution f^* and relaxes to a distribution f during a relaxation time τ. Then we require that

$$\tfrac{1}{2}\int_0^\tau \int_\Omega v(\xi,t)^2 f(\xi,t)\, dx\, dt \;+\; \int_\Omega \{\, \psi(\xi) f(\xi) \;+\; \sigma\, f(\xi) \log f(\xi) \,\}\, d\xi \;\leq$$
$$\int_\Omega \{\, \psi(\xi) f^*(\xi) \;+\; \sigma\, f^*(\xi) \log f^*(\xi) \,\}\, d\xi \tag{3.7}$$

whenever

$$f_t \;+\; (v f)_\xi \;=\; 0 \quad \text{in} \quad \Omega,\;\; 0 < t < \tau,$$
$$f(x,0) \;=\; f^*(x),\;\; f(x,\tau) \;=\; f(x). \tag{3.8}$$

So,

$$\frac{1}{2\tau}\, d(f, f^*)^2 \;+\; \int_\Omega \{\, \psi(\xi) f(\xi) \;+\; \sigma\, f(\xi) \log f(\xi) \,\}\, d\xi \;\leq$$
$$\int_\Omega \{\, \psi(\xi) f^*(\xi) \;+\; \sigma\, f^*(\xi) \log f^*(\xi) \,\}\, d\xi \tag{3.9}$$

Our dissipation principle is: given a probability density $f^* \geq 0$, find a probability density f such that

$$\frac{1}{2\tau}\, d(f, f^*)^2 \;+\; \int_\Omega \{\, \psi\, f \,+\, \sigma\, f \log f \,\}\, dx \;=\; \min. \tag{3.10}$$

Since f^* is among the admissible competitors in (3.10) and $d(f^*, f^*) = 0$, (3.9) is automatically satisfied when f satisfies (3.10).

We take a moment to interpret (3.10) as an implicit scheme, [10]. With $f^{(0)}$ given, and $f^{(1)}, \ldots, f^{(k-1)}$ known, determine $f^{(k)}$ by solving (3.10) with $f^* = f^{(k-1)}$ and lable the solution $f^{(k)}$. Define

$$f^{(\tau)}(x,t) \;=\; f^{(k)}(x) \qquad \text{for} \quad k\tau \,\le\, t \,<\, (k+1)\tau. \tag{3.11}$$

In [10], it is shown that $f^{(\tau)} \to f$ as $\tau \to 0$ and f is a solution of the Fokker-Planck Equation

$$\left|\begin{array}{ll} \dfrac{\partial f}{\partial t} \;=\; \sigma\, \dfrac{\partial^2 f}{\partial x^2} \;+\; \dfrac{\partial}{\partial x}(\psi' f) & \text{in } \Omega,\ t > 0 \\ \sigma\, \dfrac{\partial f}{\partial x} \;+\; \psi' f \;=\; 0 & \text{on } \partial\Omega,\ t > 0 \\ f \;=\; f^{(0)} & \text{in } \Omega,\ t = 0 \end{array}\right. \tag{3.12}$$

4. A variational principle for a molecular motor

Let us discuss the hand-over-hand (rotating cross-bridge) model for conventional kinesin, [8]. Conventional kinesin has two identical head domains (heavy chains) which walk in a hand over hand fashion along a rigid microtubule. A head may be thought of as having two states: an a state when it undergoes conformational change owing to release of ADP and binding of ATP and a b state executing a powerstroke when it steps along the microtubule, releasing Pi. The a state for head 1 induces the b state for head 2. We regard the a state conformational change to be governed by a first order chemistry description and the b state by interaction with potentials, diffusion, and dissipation.

Divide the heads of the ensemble of motors into two sets, set 1 and set 2; for example the set 1 motors attach to the odd-labeled sites on microtubules and the set 2 motors attach to even labled sites. This permits distance along the microtubule to be used as a process variable. Let ρ_1 and ρ_2 denote the relative densities of set 1 and set 2 motors in state *b*, the powerstroke state. Introduce, the the standard way, the potentials and coefficients for conformational change

$$\begin{aligned} &\sigma > 0 \text{ constant} \\ &\psi_i \geq 0 \text{ and } \nu_i \geq 0,\ i = 1,2, \text{ smooth and periodic of period } X = 1/M \\ &\qquad \text{with supp } \nu_1 = \text{supp } \nu_2 \text{ and } \nu_1 + \nu_2 \leq 1. \end{aligned} \tag{4.1}$$

Let

$$\nu = \begin{pmatrix} -\nu_1 & \nu_1 \\ \nu_2 & -\nu_2 \end{pmatrix} \quad \text{and} \quad P = \mathbf{1} + \tau\,\nu, \tag{4.2}$$

where τ is a relaxation time. In view of the discussion above, set 1 heads enter the *a* state at the rate that set 2 heads enter the *b* state and vice versa. We may thus envision a cycle, starting with a density $\rho^* = (\rho_1^*, \rho_2^*)$

$$\rho^* \quad \rightarrow \quad \rho^* P \quad \rightarrow \quad \rho \tag{4.3}$$

subject to the dissipation principle: given ρ^*, such that

$$\int_\Omega (\rho_1^* + \rho_2^*)\, dx = 1 \quad \text{and} \quad \rho_i^* \geq 0 \ \text{ in } \Omega,$$

determine ρ by

$$\sum_{i=1,2} \frac{1}{2\tau}\, d(\rho_i, (\rho^* P)_i)^2 + \sum_{i=1,2} \int_\Omega \{\psi_i\, \rho_i + \sigma\, \rho_i \log \rho_i\}\, dx = \min. \tag{4.4}$$

among all ρ satisfying

$$\int_\Omega \rho_i \, dx \;=\; \int_\Omega (\rho * P)_i \, dx, \quad \text{and} \quad \rho_i \;\geq\; 0 \;\text{ in }\; \Omega, \; i = 1,2.$$

This variational principle leads to (1.1). In reprise, looking at the cycle (4.3) and the dissipation inequality (4.4), we realize that there are many systems that can be described in a very similar fashion. Moreover, (4.4) is not unique in leading to (1.1).

Note that for τ small and ν constant, P is a probability matrix and $\rho * \;\rightarrow\; \rho * P$ is one step in a Markov chain.

5. From the variational principle to the equations

The variational principle of the previous section and its implicit scheme give rise to the system of equations (1.1) of the introduction. In this section we sketch how. There are two major ingredients to this demonstration. The first is to determine the Euler Equation of the variational principle, (5.3) below. The second is that there is sufficient control in the limit process as the relaxation time τ tends to 0 to obtain the system (1.1).

Choose $\tau > 0$ small enough that $P(x)$ is a 2×2 ergodic probability matrix for $x \in \Omega$. Let

$$\mathbf{P} \;=\; \Big\{ \eta \;=\; (\eta_1, \eta_2) \;\in\; L^1(\Omega): \;\; \int_\Omega (\eta_1 \;+ \eta_2) \, dx \;=\; 1, \;\; \eta_i \;\geq\; 0 \;\text{ in }\; \Omega, \, i = 1,2 \Big\} \quad (5.1)$$

denote partial probability distributions and

$$F(\eta) \;=\; \sum\nolimits_{i \,=\, 1,2} \int_\Omega \{ \psi_i \, \eta_i \;+\; \sigma \, \eta_i \log \eta_i \} \, dx, \quad \eta \in \mathbf{P}, \qquad (5.2)$$

denote the free energy of η. Introduce, as in the last section, the variational principle:

> Given $\rho * \in \mathbf{P}$, find $\rho \in \mathbf{P}$ such that

$$\sum_{i=1,2} \frac{1}{2\tau}\, d(\rho_i, (\rho^* P)_i)^2 \;+ F(\rho) \;=\; \min_{\mathbf{P}} \qquad (5.3_1)$$

subject to

$$\int_\Omega \rho\, dx \;=\; \int_\Omega \rho^* P\, dx\,. \qquad (5.3_2)$$

(5.3_2) is a vector equation. Our implicit scheme, suggested in §3, is defined by choosing $\rho^{(0)} \in \mathbf{P}$ and determining $\rho^{(k)}$ as the solution of (5.3) with $\rho^* = \rho^{(k-1)}$. We then set

$$\rho^{(\tau)}(x,t) \;= \rho^{(k)}(x) \quad \text{for} \quad k\tau \le t \le (k+1)\tau \qquad (5.4)$$

Our objective is to show that $\rho^{(\tau)}$ converges to the solution of (1.1).

Suppose for a moment that $\nu_i \ge 0$ are constant, $\nu_1 + \nu_2 = 1$. Then the averages

$$\alpha^{(k)} \;=\; \int_\Omega \rho^{(k)}\, dx$$

satisfy

$$\alpha^{(k)} \;=\; \alpha^{(k-1)} P \qquad (5.5)$$

and are iterates of a Markov Chain. As mentioned above, this is analogous to (1.4) for the system (1.1). Hence the single statistic of the process

$$\alpha^{(k)} \;\to\; \alpha^{(k)} P$$

satsifies

$$\alpha^{(k)} \;\to\; \alpha^{\#} \;=\; (\nu_2, \nu_1)$$

its equilibrium value, exponentially fast. The system itself may be very far from equilibrium.

It is straightforward to check that (5.3) admists a solution since the functional F is convex, superlinear, and bounded below. The novel feature of this variational principle is

that we cannot control $F(\rho)$ in terms of $F(\rho*)$, and, indeed, the sequence $F(\rho^{(k)})$ need not be decreasing. The control we have is given by the elementary fact about Markov chains that a step in the chain reduces relative entropy. More precisely, abusing our notation for a moment:

> Let $P = (p_{ij})$, $p_{ij} > 0$, be a probability matrix with stationary distribution $\mu^{\#}$. Then
>
> $$\sum (\mu P)_j \log \frac{(\mu P)_j}{\mu_j^{\#}} \leq \sum \mu_j \log \frac{\mu_j}{\mu_j^{\#}} \tag{5.6}$$
>
> for $\mu_j \geq 0$ (μ does not have to be a probability vector)

Now observe that $\eta = \rho^* P$ is admissible in (5.3) and, of course, $d((\rho^*P)_i, (\rho^*P)_i) = 0$. Hence,

$$\sum_{i=1,2} \frac{1}{2\tau} d(\rho_i, (\rho^*P)_i)^2 + F(\rho) \leq F(\rho^*P) \tag{5.7}$$

Let $\mu\#(x)$ denote the stationary distribution of $P(x)$, whence by (5.6),

$$\sum_{i=1,2} \int_\Omega (\rho^*P)_i \log \frac{(\rho^* P)_i}{\mu_i^{\#}} \, dx \leq \sum_{i=1,2} \int_\Omega \rho_i^* \log \frac{\rho_i^*}{\mu_i^{\#}} \, dx \tag{5.8}$$

So

$$F(\rho^*P) = \sum_{i=1,2} \int_\Omega \left\{ (\psi_i + \sigma \log \mu_i^{\#})(\rho^*P)_i + \sigma (\rho^*P)_i \log \frac{(\rho^* P)_i}{\mu_i^{\#}} \right\} dx$$

$$\leq \sum_{i=1,2} \int_\Omega \left\{ (\psi_i + \sigma \log \mu_i^{\#})(\rho^*P)_i + \sigma \rho_i^* \log \frac{\rho_i^*}{\mu_i^{\#}} \right\} dx$$

$$= F(\rho^*) + \tau \sum_{i=1,2} \int_\Omega (\psi_i + \sigma \log \mu_i^{\#})(\rho^*\nu)_i \, dx.$$

Thus we arrive at our main control estimate

$$\sum_{i=1,2} \frac{1}{2\tau}\, d(\rho_i, (\rho^* P)_i)^2 \;+ F(\rho) \;\le F(\rho^*) \;+\; \tau \sum_{i=1,2} \int_\Omega (\psi_i \;+\; \sigma \log\, \mu_i^{\#})(\rho^* \nu)_i \; dx. \tag{5.9}$$

Note that the second term is bounded by $C\tau$ since all of $\psi_i, \mu_i^{\#}$, and ν are bounded and ρ^* is bounded in L^1.

Now we describe the approximate Euler Equation of (5.3), whose derivation is based on the classical method of variation of domain. Details of this will be presented elsewhere, but cf. [3],[9], [10],[12],[14],[15]. Let ρ denote the solution of the variational principle (5.3) for a given ρ^*. Then

$$\Big| \sum_{i=1,2} \int_\Omega \{ (\tfrac{1}{\tau}\,(\rho_i - \rho_i^*) - (\rho^* \nu)_i)\, \xi_i - \sigma\, \xi_i''\, \rho_i + \psi_i'\, \rho_i\, \xi_i' \}\, dx \Big|$$

$$\le \tfrac{1}{2} \max \sup |\xi_i''|\; \tfrac{1}{\tau} \sum_{i=1,2} d(\rho_i, (\rho^* P)_i)^2 \tag{5.10}$$

$$\le \tfrac{1}{2} \max \sup |\xi_i''|\; (F(\rho*) - F(\rho) + C\tau) \tag{5.11}$$

$$\text{for } \zeta = (\zeta_1, \zeta_2) \in C_0^\infty(\Omega)$$

where we have used the main estimate (5.9) in (5.11).

Suppose that $T = n\tau$ and that $\rho^{(k)}$ denote the solutions of the iterative scheme. Summing (5.16), we arrive at the estimate

$$\Big| \sum_{i=1,n} \sum_{i=1,2} \int_{\Omega} \{ \big(\tfrac{1}{\tau} \, (\rho_i^{(k)} - \rho_i^{(k-1)} \big) - (\rho^{(k-1)} \nu)_i \big) \, \xi_i - \sigma \, \xi_i'' \, \rho_i^{(k)} + \psi_i' \, \rho_i^{(k)} \, \xi_i' \} \, dx \, \tau \Big|$$

$$\leq C_0 \, \tau \, (F(\rho^{(n)}) - F(\rho^{(0)}) + C \, T) \qquad (5.12)$$

This leads to convergence of the sequence $\rho^{(\tau)}$ defined in (5.4)

6. Some results of simulations

In this section we present a brief summary of the results of some simulations. For these we chose the potentials depicted in Figure 1 and Figure 2 and a diffusion coefficient $\sigma = 2^{-7}$. Both simulations were run for a time $T = 2^5$. Figure 4 represents the result of choosing $\nu_1 = \nu_2$ with maxima near the well minima, where the densities are highly populated, pictured in Figure 3. This exhibits exceptional transport. The same figure, in fact, is produced by choosing $\nu_1 = \nu_2 = 1$. Figure 5 represents the result of choosing $\nu_1 = \nu_2$ but with maxima near the well maxima, where the densities are scarcely populated. This shows negligable transport. These simulations show that the present theory is consistent with the work of Hackney [7] who determined that the hydrolization step occurs when the kinesin heads are in their bound state.

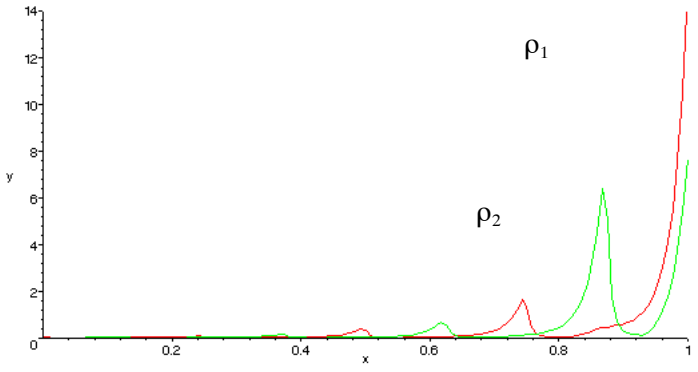

Fig. 4 Simulation with conformational coefficients localized to well minima, illustrating transport.

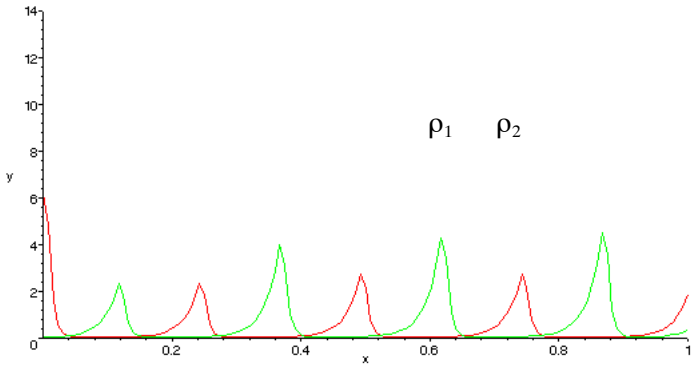

Fig. 5 Simulation with conformational coefficients localized to well maxima, illustrating failure of transport.

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