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# Channel Transport and Molecular Motors without Brownian Ratchets

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Brownian rotors are a large and important class of molecular motors in biological systems. Usually the function of these molecular machines is described as being a Brownian ratchet. However, Brownian ratchets need non-equilibrium fluctuations of an asymmetric potential for its function. We demonstrate that the Brownian ratchet paradigm does not apply to Brownian rotors. Rather, recent analytical results on facilitated transport through biological channels (W. R. Bauer & W. Nadler, PNAS 103, (2006) 11446) can be employed to understand also these purely concentration gradient-driven systems.

## 1 Introduction

Rotary molecular motors play a central role in biological cells where they transduce electrochemical or chemical energy into mechanical force. An archetype is the F<sub>0</sub> portion of the F-ATP synthase which converts the electrochemical energy difference of protons or sodium cations across the inner membrane of mitochondria into a mechanical torque<sup>1</sup>. It consists of a rotary ring, which works as a proton or sodium carrier across the membrane<sup>2</sup>.

Surprisingly, such rotary molecular motors are usually described as Brownian ratchets<sup>1,3</sup>. However, Brownian ratchets need non-equilibrium fluctuations of a force field to function<sup>4,5</sup>. But the only non-equilibrium aspect of biological molecular rotary motors is a concentration gradient across the membrane.

This situation is reminiscent of the problem of facilitated and asymmetric transport in biological channels<sup>6,7</sup>. There also non-equilibrium fluctuations of a force field were discussed to describe that phenomenon<sup>8</sup>. However we were able to show that a thorough analysis of the diffusive transport is sufficient<sup>9</sup>. We will sketch that theory and discuss how it can be applied to the situation of Brownian rotors. To compare the basic biological situations, see also Fig. 1.

## 2 Theory

The dynamics of the density of the molecules inside a channel,  $\rho(x, t)$ , is determined by the Smoluchowski equation<sup>10</sup>,

$$\partial_t \rho(x, t) = D \partial_x [\partial_x - F(x)] \rho(x, t), \quad (1)$$

where  $x$  is the channel coordinate and  $D$  is the diffusion coefficient.  $F(x)$  is the force that describes the molecule-channel interaction that can always be derived from a potential function in one dimension,  $F(x) = -\Phi'(x)$ . At the ends of the channel we assume that

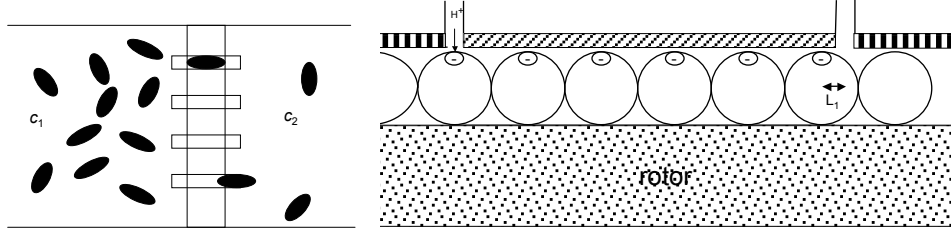


Figure 1. Basic biological situations: (*left*) A membrane separates two baths with molecular concentrations  $c_1$  and  $c_2$ . The baths are connected by channels (hatched rectangles) allowing only access of a single molecule. (*right*) Brownian rotor driven by a  $H^+$  gradient. The relevant component of the motor is a ring carrying identical hairpin-like protomers in which the amino acid Asparagine works as proton carrier. In order to emphasize the analogy to the channel situation, the rotor is drawn linearly, and periodic boundary conditions are assumed.

baths hold the molecular densities constant at  $\rho(0, t) \equiv c_1$  and  $\rho(L, t) \equiv c_2$ , respectively, as seen e.g. in Fig. 1a.

Extending an old approach by Hardt<sup>11</sup> we have shown recently<sup>12</sup> that in very general situations described by a Smoluchowski equation (1) the flow  $J$  of non-interacting particles across some region is given by a macroscopic version of Fick's law<sup>13</sup>

$$J = \frac{n}{\tau} (c_1 - c_2) \quad (2)$$

where  $\tau$  is the mean first passage time<sup>10</sup> to cross the region and  $n$  is a measure of the steady state particle number in that region.

In reality transported molecules are interacting, in particular they cannot pass each other. In order to allow for that fact the above approach has to be extended. We now interpret  $\rho(x, t)$  as the probability density that a channel contains a particle at  $x$ . The empty channel has to be added as an additional state, the probability of which we will denote as  $\rho_0$ . This additional empty channel state leads to a cyclic state model, see Fig. 2, since a molecule can enter the empty channel from either side. The corresponding transition rates between the empty channel state and the states in which a molecule is attached to either end  $\rho_1 = \rho(0, t)$ ,  $\rho_2 = \rho(L, t)$  are proportional to the concentration of molecules of the adjacent baths which we denote again as  $c_1$  and  $c_2$ . In the steady state the equation system

$$J_{0 \rightarrow 1} = c_1 k_+^{(1)} \rho_0 - k_-^{(1)} \rho_1, \quad (3)$$

$$J_{1 \rightarrow 2} = \frac{n}{\tau} (\rho_1 - \rho_2), \quad (4)$$

$$J_{2 \rightarrow 0} = k_-^{(2)} \rho_2 - c_2 k_+^{(2)} \rho_0, \quad (5)$$

holds, where Eq. (4) derives from Eq. (2).  $k_{\pm}^{(i)}$ ,  $i = 1, 2$ , are the reaction rate constants describing attachment of molecules to and dissociation from either end of the channel. In the steady state all flows of Eqs. (3-5) are identical. In addition, we have to consider that the total probability is conserved. Including such a normalization condition<sup>9</sup> we obtain an expression for the flow similar to Eq. (2) where  $n$  is replaced by a nonlinear function of  $n$

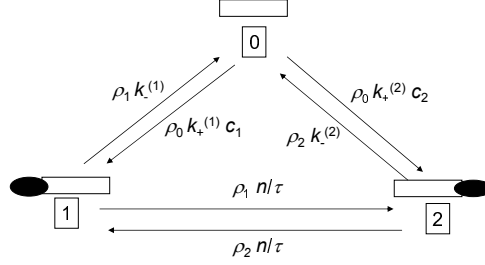


Figure 2. Cyclic state model of molecular transport through the channel that allows for interacting particles. Three states of the channel are depicted: 0 refers to the empty channel, 1 and 2 are channel states with a single molecule attached either of at one or the other end. The respective unidirectional flows between the states are shown above the corresponding arrows.

(and other parameters),

$$J = \frac{f(n)}{\tau} (c_1 - c_2) . \quad (6)$$

This function shows a nonlinear dependence on the concentrations  $c_1$  and  $c_2$  that exhibits analogies to a Michaelis-Menten-type<sup>14</sup> behavior:

$$f(n) = \frac{n}{1 + n(c_1 + c_2) + \Delta n(c_1 - c_2) + \frac{n}{\tau} \left[ \frac{1}{k_-^{(1)}} + \frac{1}{k_-^{(2)}} + 2n \left( \frac{c_2}{k_-^{(1)}} + \frac{c_1}{k_-^{(2)}} \right) \right]} . \quad (7)$$

Consequences from this expression on transport facilitation, optimality of parameters, and asymmetric transport are analyzed in detail in Ref. 9.

### 3 Discussion

In Brownian rotors the transport of  $H^+$  bound to the protomers, see Fig. 1b, is coupled directly to the movement of the rotor. Therefore, applying the above theory for determining the  $H^+$ -current also gives expressions for the rotation. Note, however, that in the above considerations no potential difference between the baths was assumed. But Brownian rotors under workload are best described by an additional macroscopic potential gradient<sup>3</sup>. Our model can be readily adapted to such a situation when  $\Phi(0) = \Phi_1 \neq \Phi(L) = \Phi_2$ . In particular, flow vanishes if the chemical potentials of the baths  $\mu_i = \Phi_i + \ln(c_i)$  are equal. Using potential corrected specific particle numbers  $\tilde{n}$  and first passage times  $\tilde{\tau}$ <sup>9</sup>, Fick's diffusion law in Eq. (2) can be generalized to

$$J = \frac{\tilde{n}}{\tilde{\tau}} (e^{\mu_1} - e^{\mu_2}) . \quad (8)$$

Also all other results Ref. 9, e.g. Eq. (7), can be generalized to this situation by replacing concentrations  $c_i$  by the activities  $e^{\mu_i}$  and introducing the corresponding potential corrected parameters. In this way a straightforward analysis of Brownian rotors is readily possible<sup>15</sup>.

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## References

1. W. Junge (2004) *Photosynth. Res.* **80** 197.
2. See <http://www.biologie.uni-osnabrueck.de/biophysik/junge/> for an illustrative animation.
3. H. Wang (2005) *J. Phys.: Condens. Matter* **17**, S3997.
4. Frey, E. & Kroy, K. (2005) *Ann. Phys. (Leipzig)* **14**, 20.
5. P. Hänggi, F. Marchesoni, & F. Nori (2005) *Ann. Phys. (Leipzig)* **14**, 51.
6. Schwarz, G., Danelon, C., & Winterhalter, M. (2003) *Biophys. J.* **84**, 2990.
7. Alcaraz, A., Nestorovich, E.M., Aguilera-Arzo, M., Aguilera V. M., & Bezrukov, S.M. (2004) *Biophys. J.* **87**, 943.
8. Kostin, I. & Schulten, K. (2004) *Phys. Rev. Lett.* **93**, 238102.
9. Bauer, W.R. & Nadler W. (2006) *Proc. Natl. Acad. Sci. USA* **103**, 11446.
10. Gardiner, C.W. (1985) *Handbook of Stochastic Methods*, 3rd ed. (Springer, Berlin).
11. Hardt, S. (1981) *Bull. Math. Biol.* **43**, 89.
12. Bauer, W.R. & Nadler W. (2005) *J. Chem. Phys.* **122**, 244904.
13. D A. Fick (1855) *Ann. Phys.* **94**, 59.
14. L. Michaelis & M. L. Menten (1913) *Biochem. Z.* **49**, 333.
15. Bauer, W.R. & Nadler W. (2007) manuscript in preparation.