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► **To cite this version:**

Igor Goychuk. Chemically driven electron tunnelling pumps. *Molecular Simulation*, 2006, 32 (09), pp.717-725. 10.1080/08927020600857297. hal-00514991

**HAL Id: hal-00514991**

**<https://hal.science/hal-00514991>**

Submitted on 4 Sep 2010

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Journal:	<i>Molecular Simulation</i> / <i>Journal of Experimental Nanoscience</i>
Manuscript ID:	GMOS-2006-0059.R1
Journal:	Molecular Simulation
Date Submitted by the Author:	07-Jun-2006
Complete List of Authors:	Goychuk, Igor; Institute of Physics, University of Augsburg
Keywords:	electron transfer, tunnelling, dissipation, nonequilibrium fluctuations, molecular electron pumps

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## Chemically driven electron tunnelling pumps

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(20 April 2006)

The simplest mechanism for molecular electron pumps is discussed which is based on nonadiabatic electron tunnelling and nonequilibrium conformational fluctuations. Such fluctuations can be induced, e.g. by random binding of negatively charged ATP molecules to the electron-transferring molecular complex, their subsequent hydrolysis and the products dissociation. The pumping rate can be controlled by the ATP concentration in solution. Depending on the model parameters there may exist a critical ATP concentration for the pump to function. Alternatively, nonequilibrium fluctuations can be induced by externally applied stochastic electric fields. For realistically chosen parameters, the mechanism is shown to be robust and highly efficient.

*Keywords:* Electron transfer, tunnelling, dissipation, nonequilibrium fluctuations, molecular electron pumps

### 1 Introduction

Electron transfer lies at heart of all bioenergetic processes. The energy of photoexcited electronic states, or one released in the oxidative breakdown of food molecules is used in a chain of electron-transfer reactions to create the transmembrane proton gradient storing ultimately the free energy ready to use in such "energetic" organelles of biological cells as mitochondria and chloroplasts (1; 2; 3; 4; 5). This electrochemical proton gradient is used there by the ATP-synthase molecular complexes to synthesise the molecules of adenosintriphosphate (ATP) – a free-energy "currency" utilised in the most biochemical cellular processes which occur far away from the thermodynamic equilibrium under the living cell conditions. It is well known that the ATP-synthase can work also in reverse using the energy of ATP hydrolysis to restore the proton gradient (3). The existence of the reverse electron transfer, where the energy of ATP hydrolysis, or the free energy derived from electrochemical transmembrane gradient of a sort of ions is used to energise the electrons, is coming gradually in the focus of attention (6; 7; 8; 9; 10). The proton pumping molecular complexes driven normally by the energy released in the downhill electron transfer can work in reverse, pumping the electrons uphill on the time scale of seconds and minutes (7; 10). It might even be the case that such reverse electron transfer evolutionary emerged earlier in archaebacteria existing at extremal environmental conditions (i.e., during the most earliest steps of the biological evolution). Moreover, the nitrogen fixation, which is realized by the nitrogenase protein complexes, utilises apparently the energy released in ATP hydrolysis (11; 12; 13; 14). These natural molecular nanomachines produce ammonia routinely, at normal conditions, while the standard industrial technological process requires large pressures of about 150 atmospheres and temperatures in the range of 650-720 K.

The electron transfer in nitrogenase provides one of the key steps in the overall reaction of ammonia synthesis. It is realized through a long-distance (about 14 Å) nonadiabatic electron tunnelling between two different metalloclusters situated in two different protein subunits. This process is gated by nonequilibrium conformational transitions of the whole protein complex due to ATP binding and hydrolysis, with two ATP molecules hydrolysed per one electron transferred. How nitrogenase works remains still a mystery, but a proper physical understanding gradually emerges (14). Such understanding is crucial not only for uncovering the working principles of biological nanomachinery in general, but also for the molecular design of such and similar molecular machines for a future nanobiotechnological use. It would allow for an intelligent parameter optimisation, performing ultimately better than nature. Below I consider a very

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simplified, minimal theoretical model for such chemically driven electron tunnelling pumps which is based on the previous treatments in (14; 15; 16; 17; 18).

## 2 Theoretical model

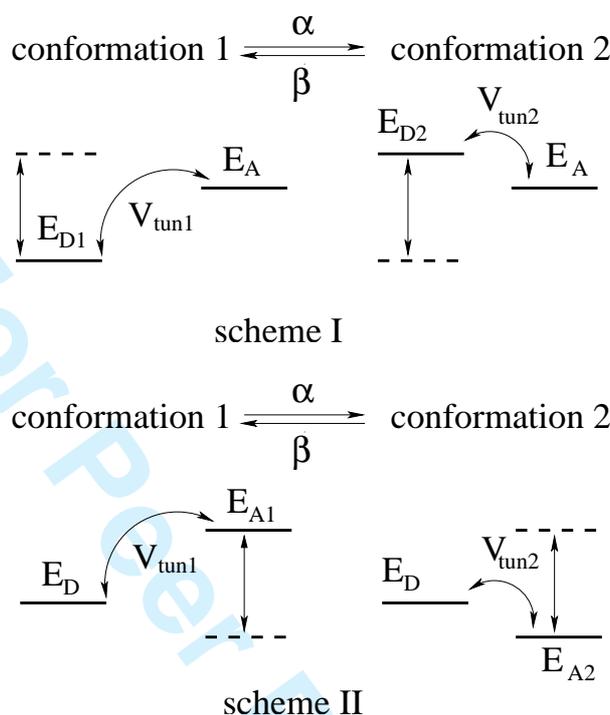


Figure 1. Electron pumping scenarios based on dissipative electron tunnelling and nonequilibrium conformational fluctuations. In the scheme I, the energy level of the donor state fluctuates in time. This is contrasted with the scheme II, where the acceptor level fluctuates in time. For dissipative tunnelling to occur from the donor site to the acceptor site of electron localisation, either the donor state should gain temporally in energy, or the acceptor site should temporally lose in energy (conformation 2). A combination of two scenarios is also possible. The condition  $V_{\text{tun1}} \ll V_{\text{tun2}}$  is required for the pumping mechanism to work robustly. It is necessary to block the reverse acceptor-to-donor electron transfer in the conformation 1. Temporal lifting of the electron energy is possible, e.g. due to binding a negatively charged ATP molecule nearby the corresponding site of localisation. The tunnelling coupling can be exponentially reduced, e.g. due to increase of the tunnelling distance, or due to disruption of the tunnelling pathway. The latter one can be induced also by reorientation of a bridging molecular group.

### 2.1 Nonadiabatic electron transfer

Let us start from nonadiabatic electron tunnelling coupled to molecular vibrational modes considered within a standard two-state, donor acceptor model (cf. one “frozen” conformation in Fig.1). This tunnelling can be described, e.g., within a spin-boson like model captured by the following Hamiltonian (19; 20; 21; 22; 23; 24; 25)

$$\hat{H} = E_D |D\rangle\langle D| + E_A |A\rangle\langle A| + V_{\text{tun}}(|D\rangle\langle A| + |A\rangle\langle D|) + \frac{1}{2}(|D\rangle\langle D| - |A\rangle\langle A|) \sum_j \kappa_j (\hat{b}_j^\dagger + \hat{b}_j) + \sum_j \hbar\omega_j (\hat{b}_j^\dagger \hat{b}_j + 1/2). \quad (1)$$

Wherein,  $|D\rangle$  and  $|A\rangle$ , are the localised electronic states with the energies  $E_D$  and  $E_A$ , correspondingly;  $V_{\text{tun}}$  denotes the effective electron tunnelling matrix element which incorporates the intervening medium

influence (a superexchange tunnelling mechanism is assumed (26; 27; 28; 29; 30)). The coupling of electron tunnelling to the molecular vibrational modes  $\omega_j$  is characterised by the coupling constants  $\kappa_j$  and the corresponding spectral density  $J(\omega) = (2\pi/\hbar^2) \sum_j \kappa_j^2 \delta(\omega - \omega_j)$ . This coupling modulates the energy difference between the donor and acceptor states. The corresponding fluctuations are described by (quantum) random force  $\hat{\xi}(t) = \sum_j \kappa_j (b_j^\dagger e^{i\omega_j t} + b_j e^{-i\omega_j t})$  with thermally equilibrium autocorrelation function  $\langle \hat{\xi}(t)\hat{\xi}(0) \rangle_T = \frac{\hbar^2}{2\pi} \int_0^\infty J(\omega) [\coth(\hbar\omega/2k_B T) \cos(\omega t) - i \sin \omega t] d\omega$ . The medium's reorganisation energy  $\lambda = \hbar \int_0^\infty d\omega J(\omega)/(2\pi\omega)$  serves as an integral characteristic of this coupling. Another important medium's characteristic is the upper frequency  $\omega_c$  of low-frequency molecular vibrations, or solvent modes coupled to the electron transfer (ET), i.e.  $J(\omega) = 0$  for  $\omega \gg \omega_c$ . For  $V_{\text{tun}} \ll \lambda, \sqrt{k_B T \hbar \omega_c}$ , the transfer kinetics occurs in the nonadiabatic tunnelling regime described by the quantum master equations of the Pauli type for the populations of donor and acceptor states (19; 20; 21; 22; 23; 24; 25),

$$\begin{aligned} \dot{p}_D(t) &= -k_f p_D + k_b p_A, \\ \dot{p}_A(t) &= -k_b p_A + k_f p_D, \end{aligned} \quad (2)$$

with the forward, donor-to-acceptor rate given by the quantum Golden Rule expression

$$k_f = \frac{2V_{\text{tun}}^2}{\hbar^2} \int_0^\infty d\tau \exp[-Q'(\tau)] \cos [Q''(\tau) - \epsilon\tau/\hbar], \quad (3)$$

where  $\epsilon = E_D - E_A$  is the difference of free energies (or the thermodynamic driving force  $-\Delta G$  in chemical notations,  $\epsilon = -\Delta G$ ). Furthermore, the functions  $Q'(t)$  and  $Q''(t)$  in (3) denote the real and imaginary parts of the doubly-integrated bath autocorrelation function with the reorganisation energy contribution added,

$$Q(t) = \frac{1}{\hbar^2} \int_0^t dt_1 \int_0^{t_1} \langle \hat{\xi}(t_2)\hat{\xi}(0) \rangle_T dt_2 + i\lambda t/\hbar. \quad (4)$$

The backward rate  $k_b$  satisfies the Boltzmann relation

$$k_b = k_f \exp(-\epsilon/k_B T) \quad (5)$$

for any  $J(\omega)$  (22). This yields equilibrium Boltzmann-Gibbs distribution  $p_D(\infty)/p_A(\infty) = \exp(-\epsilon/k_B T)$  at temperature  $T$ , consistently with the condition of detailed balance,  $p_D(\infty)k_f = p_A(\infty)k_b$ . It must be stressed, however, that the existence of the Boltzmann relations for rates like one in Eq. (5) at constant  $\epsilon$  and  $V_{\text{tun}}$  does not guarantee, generally, the detailed balance and the Boltzmann-Gibbs equilibrium distribution when these parameters explicitly fluctuate in time (25), or when a stationary flux is present (given open, or cyclic boundary conditions even at constant rates). This is true even if the rates follow adiabatically to the instant values of the energy levels and the tunnelling coupling so that the condition (5) is valid at any instant of time.

Independently of other details of electron-vibrational coupling, the quantum Golden Rule rate acquires in the high-temperature limit  $k_B T \gg \hbar\omega_c$  and the quasi-static approximation of electron energy fluctuations,  $\langle \hat{\xi}(t)\hat{\xi}(0) \rangle_T \approx \langle \hat{\xi}^2(0) \rangle_T \approx 2\lambda k_B T$ , the semiclassical Marcus-Levich-Dogonadze form (31; 32)

$$k_f = \frac{2\pi}{\hbar} \frac{V_{\text{tun}}^2}{\sqrt{4\pi\lambda k_B T}} \exp[-(\epsilon - \lambda)^2/(4\lambda k_B T)]. \quad (6)$$

Such a universality explains the widespread use of Eq. (6) in interpretation of experimental data. It involves (apart from temperature) three parameters only: the free energy difference  $\epsilon$ , the electron tunnelling coupling  $V_{\text{tun}}$  and the reorganisation energy  $\lambda$ . When a coupling to high-frequency, essentially quantum modes is present, the expression (6) can be readily generalised accordingly (33; 34). This presents one of

the basic theories of electron transfer in molecular systems (34; 23; 24). Of course, it is not truly universal, but it does provide a milestone and the simplest theoretical framework of practical relevance.

## 2.2 Nonequilibrium conformational fluctuations

Furthermore, let us assume that the electron-transferring protein complex (or its corresponding molecular subunit) can be in either of two conformations depending on binding a ligand, say ATP molecule (cf. Fig. 1). This assumption is quite in spirit of the Monod-Wyman-Changeux model of allosteric enzymes (35; 36; 37). These two conformations possess very different  $V_{\text{tun}}$  (distance between the donor and acceptor sites is changed, or some bridging molecular group changes its orientation interrupting, or vice versa, establishing thereby the electron-tunnelling pathway). These conformations can correspond also to very different energy differences between the localised electron levels, e.g. the energy of the donor or acceptor state is changed (ATP and the hydrolysis products, ADP and the phosphate group  $P_i$ , are all charged and the electrostatic effects are of utmost importance here (14)). The attachment/detachment of ligand is a random process and both  $\epsilon(t) = E_D(t) - E_A(t)$  and  $V_{\text{tun}}(t)$  in Eq. (1) become stochastic functions of time. Alternatively, a strong two-state stochastic electric field can be externally applied to drive the electron transfer process. This is the starting point of the stochastically driven spin-boson model of Refs. (15; 16; 17; 18; 25). It must be noted that modelling of the equilibrium conformational fluctuations in such a way should be considered with a great care (25) (see also below), but the approach suits well to model non-equilibrium fluctuations like those considered (25). Within the approximations leading to Eqs. (2)-(4), the quantum rates entering equations (2) become stochastic *functionals* of  $V_{\text{tun}}(t)$  and  $\epsilon(t)$ . Namely, the term  $\epsilon\tau$  in Eq. (3) is replaced by  $\int_{t-\tau}^t \epsilon(t')dt'$  and instead of  $V_{\text{tun}}^2$  in the front of integral there appears  $V_{\text{tun}}(t)V_{\text{tun}}(t-\tau)$  in the integrand (15; 16). However, if  $\epsilon(t)$  and  $V_{\text{tun}}(t)$  fluctuate sufficiently slow on the time scale of  $Q(t)$ , one can use an *adiabatic driving* approximation resulting in fluctuating rates following to the instantaneous values of  $\epsilon(t)$  and  $V_{\text{tun}}(t)$ . This approximation is reasonable as a simple starting point for modelling and it can be justified in many cases. For these reasons, it is used below. The discussed adiabatic assumption means that after every conformational jump the *vibrational* relaxation to the new equilibrium of the vibrational degrees of freedom occurs very fast as compare with the mean duration of time spent in the corresponding conformation. Otherwise, the adiabatic driving approximation cannot be justified and the theory becomes essentially more intricate (15; 16; 17; 18).

Furthermore, let us assume that the conformational fluctuations are Markovian and occur with the rates  $\alpha$  and  $\beta$  which do not depend on where the electron is localised, but are controlled by thermodynamically nonequilibrium concentrations of ATP, ADP,  $P_i$  in the solution (i.e. ATP is continuously supplied<sup>1</sup>). To be more concrete, let us assume that the conformational transition “1→2” is caused by the ATP binding to the electron-transferring molecular complex (scheme I). Then, the transition rate  $\alpha$  should obviously be proportional to the ATP concentration,  $[\text{ATP}]$ , in the solution, i.e.  $\alpha \propto [\text{ATP}]$ , since the binding frequency is proportional to  $[\text{ATP}]$ . On the contrary, the rate  $\beta$  of the conformational transition “2→1” caused by the ATP hydrolysis and the products dissociation should not depend on  $[\text{ATP}]$ , but be rather determined by the activation barrier between two conformations and the energy released by breaking the phosphate bond. Such nonequilibrium fluctuations fuelled by this, or another source of chemical energy can drive electron transfer (ET) uphill. Alternatively, they can be induced by an externally applied stochastic electric field, **similar to the case of ionic pumps** (38; 43). It can either be directly coupled to the electron transfer (16; 17; 18) **via the Stark effect** (39; 40), or modulate the electron levels indirectly, via the electroconformational coupling (38). **In the case of ionic pumps, this latter possibility has been realized experimentally (41; 42). It seems feasible, although still not investigated experimentally, for electron-transferring proteins as well.** Then, within the discussed approximations, the ET transfer kinetics is described by the kinetic equations (2) with time-dependent rates undergoing two-state Markovian fluctuations. Formally, this is a typical problem of dynamical disorder (44; 45; 46; 47). It can

<sup>1</sup>In the living cells ATP is perpetually synthesised from ADP and  $P_i$  by the ATP-synthase membrane complexes fuelled by the electrochemical proton gradient (3; 5)

equivalently be described by the four-state Markovian kinetic scheme depicted in Fig. 2<sup>2</sup>. Similar schemes are standard by considering the problem of free energy transduction in biology (51; 52; 53).

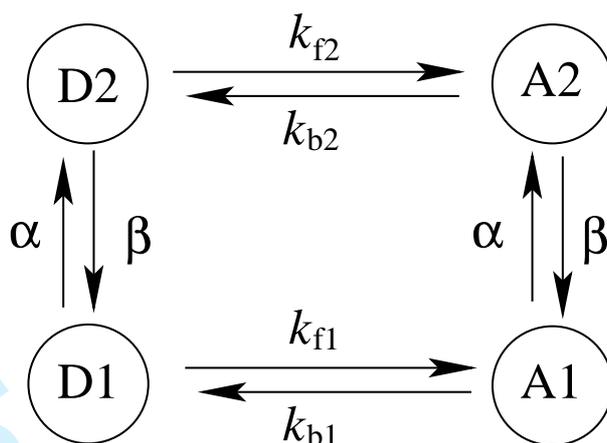


Figure 2. Equivalent kinetic scheme corresponding to electron transfer with quantum tunnelling rates undergoing two-state Markovian fluctuations. Such ET process can be embedded as four-state composite process with unfluctuating rates. For example, the composite state D1 corresponds to electron in the donor state D and to ET complex in the conformation 1. Transitions from this to other composite states A1 and D2 occur either due to the electron transfer (with rate  $k_{f1}$ ), or due to the conformational transition (with rate  $\alpha$ ), correspondingly. Similar description holds for other composite states yielding Eq. (7).

Let us denote the population of the donor and acceptor states in the conformation  $i = 1, 2$  as  $p_{Di}$  and  $p_{Ai}$ , correspondingly. They obviously satisfy the master equations,

$$\begin{aligned}
 \dot{p}_{D1} &= -(k_{f1} + \alpha)p_{D1} + \beta p_{D2} + k_{b1}p_{A1} , \\
 \dot{p}_{D2} &= \alpha p_{D1} - (\beta + k_{f2})p_{D2} + k_{b2}p_{A2} , \\
 \dot{p}_{A1} &= k_{f1}p_{D1} - (\alpha + k_{b1})p_{A1} + \beta p_{A2} , \\
 \dot{p}_{A2} &= k_{f2}p_{D2} + \alpha p_{A1} - (\beta + k_{b2})p_{A2} .
 \end{aligned}
 \tag{7}$$

These equations describe the process at thermodynamical equilibrium if the overall stationary flux is absent, i.e. clockwise and counterclockwise fluxes are mutually compensated. This requires that the product of forward rates along the cycle is equal to the product of backward rates, see e.g. in (52; 54; 55; 56). Otherwise, a nonequilibrium steady state (NESS) emerges with a persistent flux present. In such a case, one either requires a free energy supply to produce the corresponding stochastic cyclic motion (uphill motion on an effective free energy landscape), or this energy will be released (in the downhill motion). Let us consider the situation where the averaged free energy bias  $\bar{\epsilon} = \epsilon_1 p_1^{st} + \epsilon_2 p_2^{st}$  is negative,  $\bar{\epsilon} < 0$  ( $p_1^{st}$  and  $p_2^{st}$  are the stationary probabilities of the corresponding conformations). Then the cycling in the clockwise direction in Fig. 2 is required to pump the electrons against the averaged free energy bias  $\bar{\epsilon} < 0$  – the case of our interest here. If NESS corresponds to the counterclockwise total probability flux in Fig. 2, the roles of donor and acceptor states are interchanged and the conformational fluctuations can be driven by the energy released in the downhill electron transfer. These conformational fluctuations can in turn be coupled to an ion flux to produce the uphill ion flow against the corresponding electrochemical gradient. This is the operating principle of the electron-driven proton pumps (3; 54). The details are, of course, much more involved (a more complex, extended kinetic scheme is required to describe these processes in a consistent manner) and still not completely understood. The operating principle is, however, rather clear due to (nonlinear) nonequilibrium thermodynamics considerations. In the present context, we combine them with a quantum treatment of the electron transfer kinetics.

<sup>2</sup>Non-Markovian generalisation of this scheme accounting for complex dynamics with memory within a conformation can be done, e.g., in the framework of a stochastic trajectories description, cf. Refs. (48; 49; 50; 25)

The free energy  $\Delta G_{\text{drive}}$ , which is required to drive one cycle on average in the clockwise direction in Fig. 2 is determined by the well-known condition (52)

$$\begin{aligned} \Delta G_{\text{drive}} &= k_B T \ln \left( \frac{k_{f2} \beta k_{b1} \alpha}{k_{b2} \beta k_{f1} \alpha} \right) \\ &= k_B T \ln \left( \frac{k_{f2} k_{b1}}{k_{b2} k_{f1}} \right) = \epsilon_2 - \epsilon_1 = E_{D2} - E_{D1}. \end{aligned} \quad (8)$$

For the scheme II,  $\Delta G_{\text{drive}} = E_{A1} - E_{A2}$ . In the second line, we took Eq. (5) into account. As discussed above, this energy can be delivered, e.g., due to the ATP hydrolysis (breaking the energy rich phosphate bond), or derived from any other free energy source (the proton gradient, for example, via protonation/deprotonation of the molecular pump). Obviously, if only the tunnelling matrix element is modulated by the conformational transitions, then no pumping is possible and the described scheme agrees with the thermodynamic equilibrium, since no overall flux is present. We return back to the well-known problem of dynamical disorder in equilibrium systems and no more. To pump, one has to modulate the difference of electron energy levels  $\epsilon$  in time. With  $V_{\text{tun}} = \text{const}$  a pumping scenario conditioned on the existence of inverted Marcus regime of electron transfer, where the transfer rate decreases with the increase of the energy bias, is possible. It was described in Ref. (18). In this respect, it is worth to notice that the very existence of the inverted ET regime presents a profoundly quantum-mechanical feature of nonadiabatic ET. Therefore, such an electron pump would be essentially quantum-mechanical. However, such a pumping scenario based on the sole modulation of  $\epsilon(t)$  would be rather inefficient and too demanding for the system parameters in practice. Therefore, it is not likely to be used by nature. On the contrary, a properly concerted modulation of  $\epsilon(t)$  and  $V_{\text{tun}}(t)$  can allow to pump highly efficiently. In essence, for this one has to ensure  $V_{\text{tun}1} \ll V_{\text{tun}2}$  in Fig. 1 and a proper timing when ET kinetics is gated and locked to conformational fluctuations. Two possible pumping scenarios are depicted in Fig. 1. In the scheme I, the donor energy level is lifted upon binding negatively charged ATP molecule(s). Alternatively, one can modulate the acceptor energy level in time, scheme II in Fig. 1. In the reality, a combination of both possibilities can take place. For example, in the case of nitrogenase the donor level is lifted by 300 meV and the acceptor level increases simultaneously by 100 meV, with the total increase of the driving energy bias by 200 meV (14). This compares well with the energy release from the hydrolysis of one ATP molecule which is about 0.3 – 0.5 eV under the living cell conditions. This basic pumping mechanism will be detailed and quantified below.

### 2.3 Solution of the model

How to proceed further is standard and well-known (45). The solution of the master equations (7) with the initial conditions  $p_{j'}(0) = 1$ , where  $j' = D1, D2, A1, A2$  yields the corresponding conditional probabilities of the state  $j$ ,  $P_{jj'}(t)$ . We are interested in several quantities, such as (i) the asymptotic population of the donor state  $\langle p_D(\infty) \rangle$ ; (ii) the time course of the donor state relaxation  $\langle p_D(t) \rangle$ , provided that the electron was initially prepared in the donor state; (iii) the distribution of the first arrival times,  $\psi_D(\tau)$ , at the acceptor state and the corresponding mean forward transfer time  $\langle \tau_f \rangle := \int_0^\infty \tau \psi_D(\tau) d\tau = \int_0^\infty \Phi_D(\tau) d\tau$ , where  $\Phi_D(\tau) = \int_\tau^\infty \psi_D(\tau) d\tau$  is the corresponding survival probability. Given the conditional probabilities  $P_{jj'}(t)$ , the contracted probability of states  $D1$  and  $D2$  with the electron being localised initially on the donor site is

$$\langle p_{D1}(t) \rangle = P_{D1D1}(t) p_1^{st} + P_{D1D2}(t) p_2^{st} \quad (9)$$

and

$$\langle p_{D2}(t) \rangle = P_{D2D1}(t) p_1^{st} + P_{D2D2}(t) p_2^{st}, \quad (10)$$

correspondingly. In the above equations, it is tacitly assumed that the donor site has the same affinity to the transferring excess electron in the both protein conformations and these conformations are met with

the stationary probabilities  $p_1^{st} = \beta/(\alpha + \beta)$  and  $p_2^{st} = \alpha/(\alpha + \beta)$ . The former assumption is trivially valid for the scheme II. However, for the scheme I it might be the case that the electron affinity to D2 state is much smaller than to D1, i.e. the protein binds the transferring electron with a much higher probability in the first conformation (when no negatively charged ATP is bound nearby the donor state). In such a situation (which is not considered here for the sake of simplicity and analytical tractability of the results), one should put  $p_1^{st} \rightarrow 1$  and  $p_2^{st} \rightarrow 0$  in Eqs. (9) and (10). In any case, the averaged population of the donor state is  $\langle p_D(t) \rangle = \langle p_{D1}(t) \rangle + \langle p_{D2}(t) \rangle$ .

The formal solution can be found most conveniently using the Laplace-transform method. After some lengthy algebra we obtain (assuming equal electron binding affinities of the D1 and D2 states):

$$\langle \tilde{p}_D(s) \rangle = \frac{1}{s} \frac{\tilde{A}(s)}{\tilde{B}(s)}, \quad (11)$$

where

$$\tilde{A}(s) = s^2 + [\nu + p_2^{st}(k_1 + k_{b2}) + p_1^{st}(k_2 + k_{b1})]s + p_2^{st}k_{b2}(k_1 + \nu) + p_1^{st}k_{b1}(k_2 + \nu), \quad (12)$$

$$\tilde{B}(s) = s^2 + (\nu + k_1 + k_2)s + k_1k_2 + (p_1^{st}k_1 + p_2^{st}k_2)\nu, \quad (13)$$

and  $\nu = \alpha + \beta$ ,  $k_1 = k_{f1} + k_{b1}$ ,  $k_2 = k_{f2} + k_{b2}$ . In Eq. (11),  $\langle \tilde{p}_D(s) \rangle$  denotes the Laplace transform,  $\langle \tilde{p}_D(s) \rangle = \int_0^\infty \exp(-st) \langle p_D(t) \rangle dt$ . The averaged asymptotic population of the donor level follows as  $\langle p_D(\infty) \rangle = \tilde{A}(0)/\tilde{B}(0)$ ,

$$\langle p_D(\infty) \rangle = \frac{p_2^{st}k_{b2}(k_1 + \nu) + p_1^{st}k_{b1}(k_2 + \nu)}{k_1k_2 + (p_1^{st}k_1 + p_2^{st}k_2)\nu}. \quad (14)$$

The averaged relaxation of the donor state population is obtained by the inversion of Eq. (11) to the time domain. It is bi-exponential and reads

$$\langle p_D(t) \rangle = \langle p_D(\infty) \rangle + [1 - \langle p_D(\infty) \rangle]R(t), \quad (15)$$

where  $R(t) = \sum_{i=1,2} c_i \exp(-\Gamma_i t)$  is the relaxation function with the rate constants

$$\Gamma_{1,2} = \frac{1}{2} \left[ k_1 + k_2 + \nu \pm \sqrt{(k_1 + \alpha - k_2 - \beta)^2 + 4\alpha\beta} \right] \quad (16)$$

and the weighting coefficients

$$c_{1,2} = \frac{1}{2} \left[ 1 \pm \frac{k_1 + k_2 + \alpha + \beta - 2c_0/a_0}{\sqrt{(k_1 + \alpha - k_2 - \beta)^2 + 4\alpha\beta}} \right]. \quad (17)$$

The remaining quantities  $a_0$  and  $c_0$  in Eq. (17) are

$$a_0 = \alpha k_{f2}(k_1 + \alpha) + \beta k_{f1}(k_2 + \beta) + \alpha\beta(k_{f1} + k_{f2}),$$

$$c_0 = \nu^2(\alpha k_{f2} + \beta k_{f1}) + \alpha k_1 k_{f2}(2\alpha + k_1) + \beta k_2 k_{f1}(2\beta + k_2) + \alpha\beta(k_1 + k_2)(k_{f1} + k_{f2}). \quad (18)$$

The distribution of the first arrival times at the acceptor state  $\psi_D(\tau)$  can be immediately obtained from the survival probability  $\Phi_D(\tau)$  which in turn follows from the above relaxation function  $R(\tau)$  by setting

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$k_{b1}, k_{b2} \rightarrow 0$ , i.e. by assuming that the acceptor state is absorbing. This yields immediately

$$\Phi_D(\tau) = \sum_{i=1,2} c_i \exp(-\Gamma_i \tau), \quad (19)$$

where the rate constants  $\Gamma_i$  and the coefficients  $c_i$  reduce to

$$\Gamma_{1,2} = \frac{1}{2} \left[ k_{f1} + k_{f2} + \nu \pm \sqrt{(k_{f1} + \alpha - k_{f2} - \beta)^2 + 4\alpha\beta} \right], \quad (20)$$

and

$$c_{1,2} = \frac{1}{2} \left[ 1 \mp \frac{\alpha + \beta + (k_{f2} - k_{f1})(\beta - \alpha)/(\alpha + \beta)}{\sqrt{(k_{f1} + \alpha - k_{f2} - \beta)^2 + 4\alpha\beta}} \right], \quad (21)$$

respectively. These are the same expressions as, e.g., Eqs. (7)-(10) in Ref. (50) obtained there using a different method. The corresponding mean forward transfer time is

$$\langle \tau_f \rangle = \frac{(\alpha + \beta)^2 + \alpha k_{f1} + \beta k_{f2}}{(\alpha + \beta)[\alpha k_{f2} + \beta k_{f1} + k_{f1} k_{f2}]}. \quad (22)$$

All the quantities, we are interested in, are thus formally determined.

#### 2.4 Conditions for pumping

Let us suppose that the ET is characterised by Eq. (6) with the negative bias  $\epsilon_1 < 0$  and the tunnelling matrix element  $V_{\text{tun1}}$  in conformation 1 and the positive bias  $\epsilon_2 > 0$  and the tunnelling matrix element  $V_{\text{tun2}}$  in conformation 2. In addition, one assumes that the reorganisation energy  $\lambda$  is the same in both conformations. Then for the ratio of the averaged donor and acceptor populations we obtain from Eq. (14):

$$\frac{\langle p_D(\infty) \rangle}{\langle p_A(\infty) \rangle} = \exp\left(-\frac{\epsilon_2}{k_B T}\right) \frac{1 + \zeta \xi}{1 + \zeta/\xi}, \quad (23)$$

where

$$\zeta = \frac{p_1^{st}}{p_2^{st}} \frac{(\nu + k_2)F \cosh(\epsilon_2/2k_B T)}{\nu \cosh(\epsilon_2/2k_B T) + k_2 F \cosh(\epsilon_1/2k_B T)}, \quad (24)$$

$$F = \left(\frac{V_{\text{tun1}}}{V_{\text{tun2}}}\right)^2 \exp[-(\epsilon_1^2 - \epsilon_2^2)/(4\lambda k_B T)] \quad (25)$$

and  $\xi = \exp[-(\epsilon_1 - \epsilon_2)/(2k_B T)]$ . The pumping is most efficient when  $\langle p_D(\infty) \rangle / \langle p_A(\infty) \rangle \ll 1$ . This requires  $\epsilon_2 \gg k_B T$  and  $\zeta \xi \ll 1$ . Moreover, to have the averaged energy gained by the transferring electrons maximal, i.e.  $\bar{\epsilon} = p_1^{st} \epsilon_1 + p_2^{st} \epsilon_2 \approx \epsilon_1$ , one has to ensure that  $p_2^{st} \ll p_1^{st}$  which contradicts, however, at the first look to the condition  $\zeta \ll 1$  in Eq. (24). To resolve this contradiction, one requires sufficiently small values of  $F \ll 1$  and this in turn demands  $V_{\text{tun1}} \ll V_{\text{tun2}}$ . How small is small depends on the system parameters. For example, for nitrogenase  $\Delta\epsilon = \epsilon_2 - \epsilon_1 \approx 200$  meV (14). Therefore, at the room temperatures,  $k_B T \approx 25$  meV,  $\xi \approx 54.6$  is pretty large. Furthermore, let us assume for simplicity that  $|\epsilon_1| = \epsilon_2$ , so that  $\zeta = (\beta/\alpha)(\nu + k_2)F/(\nu + k_2 F)$  and  $F = (V_{\text{tun1}}/V_{\text{tun2}})^2$ . Moreover, we assume for a moment that  $\alpha = 0.1\beta$ , so that the conformation 1 is about ten times more probable than the conformation 2. Then, to satisfy  $\zeta \xi \ll 1$  and to have an efficient pumping,  $V_{\text{tun1}}$  should be smaller than  $V_{\text{tun2}}$  by, at least, two orders of magnitude. In such a case,  $k_2 \gg k_1$ , and for  $k_1 \ll \nu \ll k_2$ , one can expect that the

Table 1. Tunnelling coupling energies (in eV) and the corresponding Marcus rates (in  $\text{sec}^{-1}$ )

Tunnelling coupling energies	$k_{f1}$	$k_{b1}$	$k_{f2}$	$k_{b2}$
$V_{\text{tun1}} = 5 \cdot 10^{-6}$ , $V_{\text{tun2}} = 10^{-4}$	0.54	29.5	$1.18 \cdot 10^4$	216
$V_{\text{tun1}} = 10^{-6}$ , $V_{\text{tun2}} = 10^{-4}$	0.02	1.18	$1.18 \cdot 10^4$	216
$V_{\text{tun1}} = 5 \cdot 10^{-6}$ , $V_{\text{tun2}} = 5 \cdot 10^{-5}$	0.54	29.5	$2.95 \cdot 10^3$	53.9
$V_{\text{tun1}} = 5 \cdot 10^{-6}$ , $V_{\text{tun2}} = 2 \cdot 10^{-5}$	0.54	29.5	471	8.63

overall transfer will become gated by the conformational fluctuations. Namely, it follows from Eq. (22) that for  $k_{f1} \ll \alpha \ll \beta \ll k_{f2}$ ,  $\langle \tau_f \rangle \approx 1/\alpha$  (50), i.e. the pumping of electrons is locked to the conformational transitions caused by the binding of ATP molecules somewhere nearby the electron donor site (scheme I)<sup>1</sup>, or vice versa by their hydrolysis and dissociation nearby the acceptor site (in the scheme II).

### 3 Results and discussion

The outlined mechanism should be very robust. We illustrate it in Figs. 3, 4 for the following realistic test parameters which partially correspond to nitrogenase (14) and partially are chosen just to demonstrate the essential effects:  $\lambda = 1.2$  eV,  $\epsilon_1 = -0.1$  eV,  $\epsilon_2 = 0.1$  eV; the tunnelling coupling energies are given in the Table 1 together with the corresponding Marcus rates. Furthermore, the value  $\beta = 1000 \text{ sec}^{-1}$  is used in calculations and the rate  $\alpha$  is varying as a control parameter assuming its proportionality to the ATP concentration [ATP].

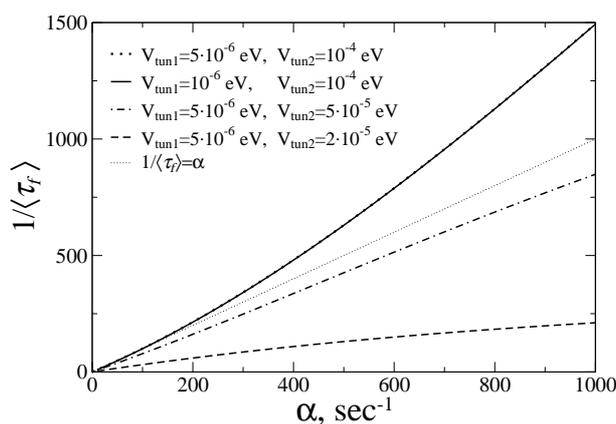


Figure 3. Dependence of the inverse of mean forward transfer time on the rate of conformational transitions  $\alpha \propto [\text{ATP}]$  (scheme I is assumed).

As it is clearly seen in Figs. 3, 4 the pumping effect is indeed present for  $V_{\text{tun2}}/V_{\text{tun1}} = 100$  (**cf. continuous lines which approximately correspond to ET in nitrogenase**). Moreover, the mean forward time is locked to the rate  $\alpha$  for  $\alpha < 200 \text{ sec}^{-1}$ , being practically its inverse. Furthermore, the calculation of the survival probability  $\Phi_D(t)$  shows, e.g. for  $\alpha = 100 \text{ sec}^{-1}$ ,  $\Phi_D(t) \approx 0.08 \exp(-12790t) + 0.92 \exp(-92t)$ ;  $\alpha = 200 \text{ sec}^{-1}$ ,  $\Phi_D(t) \approx 0.14 \exp(-12798t) + 0.86 \exp(-184t)$ , etc., that the transfer is almost single exponential and  $\langle \tau_f \rangle^{-1} \approx \alpha$  can be regarded as the pumping rate. With the further increase of  $\alpha$ , the transfer kinetics becomes, however, ever more nonexponential with the effective rate  $\langle \tau_f \rangle^{-1}$  being larger

<sup>1</sup>In the case of nitrogenase, where the ATP binding site is located at the distance of about  $15 \text{ \AA}$  from the electron donor site, the actual electrostatic mechanism is more intricate (14). Namely, binding of ATP molecules causes a structural rearrangement of the protein complex with the donor metallocluster relocating from the protein surface, where it is exposed to water (with a large dielectric constant of about  $\epsilon_w \approx 80$ ), into the protein interior (with much smaller dielectric constant,  $\epsilon_p \sim 3-10$ ). Roughly speaking, the increase of the electron donor energy in the conformation 2 can be related to the extra change of Born solvation energy of the donor metallocluster due to the excess, transferring electron (i.e. change of the charging energy due to the desolvation of metallocluster).

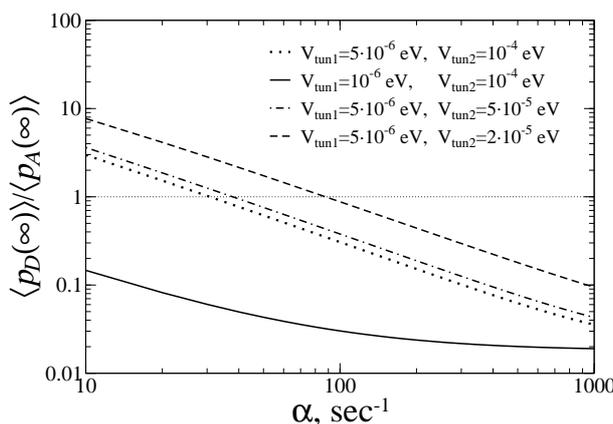


Figure 4. Dependence of the ratio of donor and acceptor populations on the rate of conformational transitions  $\alpha \propto [\text{ATP}]$ .

than  $\alpha$ , cf. Fig. 3. Here, the conformational transitions cease gradually to be the rate-limiting step and the tunnelling time  $1/k_{f2}$  becomes ever more important for the overall kinetics. However, this regime presents lesser interest in the present context since  $\bar{\tau} = 0$  for  $\alpha = \beta$  and the pumping effect then vanishes.

Furthermore, let us to keep  $V_{\text{tun2}}$  the same, but to increase  $V_{\text{tun1}}$  such that the ratio  $V_{\text{tun2}}/V_{\text{tun1}}$  becomes much smaller,  $V_{\text{tun2}}/V_{\text{tun1}} = 20$  (fat dotted lines in Figs. 3, 4). This does not affect  $\langle \tau_f \rangle$  in Fig. 3, but changes dramatically the ratio of populations in Fig. 4. The pumping effect is present for sufficiently large rates  $\alpha$  (cf. negative values of  $\langle p_D(\infty) \rangle / \langle p_A(\infty) \rangle$  in Fig. 4). The pumping efficiency drops, however, essentially. Moreover, the critical values of the rate  $\alpha_c$  and the associated ATP concentration  $[\text{ATP}_c]$  emerge. The overall transfer occurs in the “donor  $\rightarrow$  acceptor” direction if only  $\alpha > \alpha_c$ . On the other hand, one must keep  $\alpha < \beta$ . Otherwise, the transferred electrons will start to lose in energy on average. Clearly, such a pump would not function perfectly. To realize a good electronic pump, the ratio  $V_{\text{tun2}}/V_{\text{tun1}}$  must be large.

The inversion of the transfer direction depending on the rate of “1  $\rightarrow$  2” conformational transition, cf. Fig. 4 at several combinations of the tunnelling couplings, is rather intriguing. Namely, for sufficiently small  $\alpha$  the roles of the donor and acceptor states are interchanged. Here, the effective rate of the backward “acceptor  $\rightarrow$  donor” ET, defined as the inverse of the corresponding mean first passage time  $\langle \tau_b \rangle$ , can be used to quantify the rate of transfer in this direction (assuming  $\langle p_D(\infty) \rangle / \langle p_A(\infty) \rangle \gg 1$ ).  $\langle \tau_b \rangle$  can be obtained from Eq. (22) by setting there  $k_{f1} \rightarrow k_{b1}, k_{f2} \rightarrow k_{b2}$ . This quantity is depicted in Fig. 5. It is

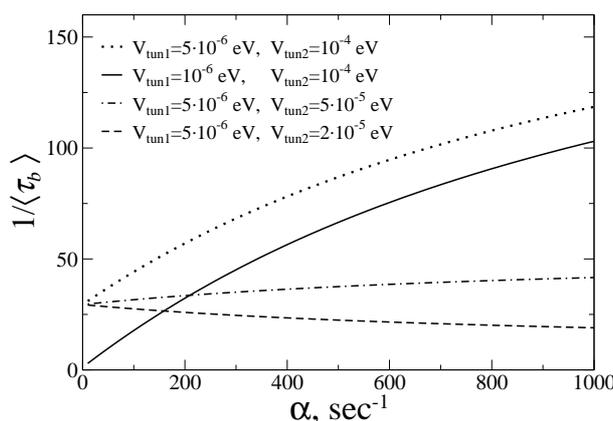


Figure 5. Dependence of the inverse of mean backward transfer time on the rate of conformational transitions  $\alpha$ .

clearly seen in Fig. 5 that the effective backward rate is not gated by the conformational fluctuations for

the used sets of parameters. Nevertheless, it can strongly depend on  $\alpha$ , being almost linearly proportional to  $\alpha$  at small  $\alpha$  (see the continuous line in Fig. 5). It might thus resemble a gating regime.

One more interesting feature is that with the decrease of  $V_{\text{tun}2}$  the effective transfer rate becomes smaller than  $\alpha$ , with the tunnelling providing the rate-limiting step when  $\alpha$  increases (see dashed line in Fig. 3).

### 3.1 Pumping efficiency

The maximal pumping efficiency can be defined as the averaged energy gained by the transferred electron relative to the energy required to drive one transfer cycle, i.e.  $\eta = |\bar{\epsilon}|/\Delta G_{\text{drive}}$ , or

$$\eta = \frac{p_1^{st}|\epsilon_1| - p_2^{st}\epsilon_2}{\epsilon_2 + |\epsilon_1|}. \quad (26)$$

For the above parameters (corresponding to the continuous lines in Figs. 3, 4 and  $\alpha \sim 100$ ), the maximal pumping efficiency is rather high approaching  $\eta = 0.5^1$ . It can be even higher approaching one, if the affinity of the donor state D1 to electrons is much larger than the affinity of the state D2 (scheme I), i.e. the protein complex takes preferably electrons from the bulk in the conformation I (the formal solution of the model has to be modified in this case, but the qualitative features remain).

## 4 Conclusions

The considered generic model might seem somewhat oversimplified. It is indeed aimed primarily to highlight the basic working principles and their practical relevance. This model should be extended and generalised further in several directions, e.g. a correlated two-electron transfer should probably be considered in nitrogenase as an elementary step rather than single-electron transfer and a proper treatment of the ATP binding, hydrolysis and dissociation of the hydrolysis products would require to introduce more conformations than two. Moreover, the external uptake and release of electrons from and to the donor and acceptor sites, e.g., from mobile electron carriers should be incorporated in the complete model. Nevertheless, the considered elementary model does allow to manifest the main operating principles which are not much different from those well established and clearly understood, both phenomenologically and in progressing details, for ionic pumps (3; 4; 36). Moreover, it allows one to clarify some important conditions for the efficient pumping such as a large ratio of the tunnelling couplings in the different conformations and a possible existence of the critical ATP concentrations. The profound physical difference between the ionic and electronic pumps is, however, that the electron is essentially a quantum particle and it tunnels over a large distance between metalloclusters in nitrogenase (also in other electron transfer complexes, like cytochrome  $bc_1$ ) using virtually protein bridging states. This is why the *details* here are definitely very different from ionic pumps. They do matter and are important to arrive in a future at the detailed (quantum)-mechanistic, molecular-dynamic understanding which still is lacking at present. Unlike to the many-years, extensive research on ionic pumps we undertake here really the first steps. The research domain of electron transfer driven by a chemical energy source through nonequilibrium conformational fluctuations is just emerging.

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<sup>1</sup>It compares well with the efficiency of various ionic pumps which can be as high as  $\eta = 0.75$  (5).

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