

Control of Chemical Equilibrium by Noise[†]

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We formulate a theory of reactive transport in the presence of environmental fluctuations that restart a transfer attempt, such as, for instance, during charge transfer through an intermediate state on a fluctuating bridge. It is shown that the rate and statistics of the fluctuations affect the steady-state populations of the reactants and products and the rate at which the steady state is approached. We give explicit examples in which the reactant/product populations can be *inverted* by varying the rate of environmental fluctuations. We thus propose a *design principle* of a controllable molecular scale device. We speculate that when noise-controlled charge transfer takes place in nature, as during electron transport in bacterial photosynthetic reaction centers, such a design can be used to maintain functionality over a wide temperature range and would be favored by evolution.

I. Introduction

The recent, exciting progress in manufacturing molecular-scale machines, analytical chemistry techniques, and single molecule experiments has necessitated the development of appropriate theoretical descriptions. The traditional tools of statistical physics have employed, with great success, coarse-grained approaches implying time- and length-scale separation. Such approaches, however, are inadequate in describing detailed processes in a highly textured system that exhibits a nearly continuous range of time and length scales.

We have recently formulated a kinetics based “interrupted escape” model, which addresses the kinematics of an irreversible process that is not necessarily time-scale-separated from environmental fluctuations.¹ There, we explicitly saw how non-adiabatic interaction with the medium led to the emergence of exponential relaxation characteristic of an ergodic system. In the model, the “interruptions” are assumed to restart an escape attempt by erasing the memory of the particle’s residence in its current metastable state, as though the particle was just placed, or “prepared”, in that state. Each interruption (assumed to occur instantaneously), thus, gives the particle another chance to sample the distribution of its uninterrupted escape times $\psi(t)$. If $\psi(t)$ is exponential, then interruption simply amounts to dephasing the particle’s motions (or randomizing its velocity, in the classical limit). Nonexponential $\psi(t)$, on the other hand, applies to a wider variety of physical situations.¹ If $\psi(t)$ is slower than exponential, this effectively means a distribution of transfer rates. In this case, interruptions will lead to more efficient sampling of the high-rate wing of the distribution, thus rendering individual transport events the more Poissonian, the faster the bath is, and also speeding up the transport overall. In contrast, faster-than-exponential processes are nearly deterministic and will be *slowed* by interruptions, because the medium forces an escape attempt that would otherwise be very likely successful to start over. This situation corresponds to the well-known phenomenon of motional narrowing.

Here, we extend the methodology of interrupted escape (IE) to incoherent transport within an arbitrary set of states. If

considered on a “small” number of states located nearby in space, such a process is, generically, a chemical reaction. If the states are situated on an extended lattice, this is diffusive (and possibly dispersive) transport. In the model, we assume that a chosen part of the total system—the “subsystem”—forms a set of distinct states that can be visited by a particle. A transition from site i to j within the “subsystem” will occur in a time t distributed according to a distribution function $\psi_{ji}(t)$, unless the environment restarts the transition attempt. Note that if formulated on a periodic lattice with uniform $\psi_{ji}(t) = \psi(t)$ and Poissonian interruption, the present model coincides with the dynamic disorder hopping (DDH) model of Druger et al.² In addition, posed in a translationally invariant continuous space, our model is quite analogous to the random walk with “regeneration” (see ref 3, p51). Now, the one-state IE model suggests interruptions will influence the effective rate of individual hops and may thus affect the overall chemical equilibrium. Consistent with these expectations, the present analysis shows the relative populations of $N > 1$ connected states can be manipulated, unless the original *uninterrupted* transport obeyed a master equation (ME) of rank N or less, with time-independent coefficients. A subtle but technologically important ramification of this notion is that even if each individual transition is Poissonian, such as commonly is the case, the overall kinetics are still affected by the interruption if $N > 2$ and we have nonuniform $\psi_{ij}(t)$. We will, in fact, demonstrate a population inversion in a three-state system with exponential kinetics as the rate of noise is varied. Such a population inversion in a two-state arrangement with double-exponential forward and exponential backward kinetics is also straightforwardly achieved. Many other, more complicated situations can be analyzed within the present formalism.

In the extreme limit of infinitely rapid interruptions, the resulting equilibration dynamics is shown to obey a master equation of rank N with time-independent coefficients, thus justifying, in a constructive way, the time-scale separation assumption used to derive such equations.

The utility of this theory for molecular-scale engineering will critically depend on one’s ability to vary the rate of “environmental fluctuations” within the reactive complex. We will suggest several ways to tune the rate of interruption in a specific

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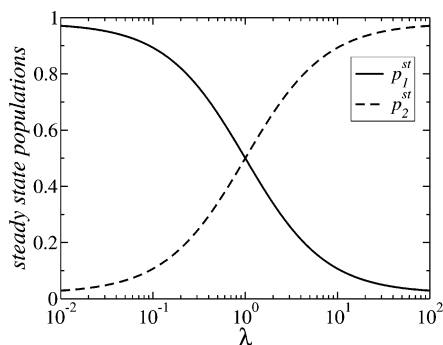


Figure 1. The steady-state populations in a noise-controlled two-state system as functions of the rate of noise λ (see text). The following values of parameters were used: $a = b = 0.5$, $\Gamma_{2a} = 100$, $\Gamma_{2b} = 0.01$, $\Gamma_{12} = 1$.

context. We will point out the possibility that noise-controlled reactions may actually have been observed in charge transfer in proteins. If uninterrupted kinetics exhibit a distribution of rates, interruption may be used to weaken the T dependence of the rates of biological processes and, thus, extend the functionality of a biological unit to a relatively wide temperature range.

This paper is organized in the following manner: In Section II, we motivate the analysis with a simple two-state system; in Section III, we consider the general N state system with interruptions and end by focusing on the important case of Poissonian interruptions. Finally, in Section IV, we apply this to three- and two-state systems and speculate on the applicability to problems in molecular electronics and biophysics.

II. Motivation

Consider a two-state system characterized by a distribution of waiting times $\psi_{21}(t) \equiv \psi_{2 \leftarrow 1}(t)$ of transfer from state 1 to state 2, and $\psi_{12}(t)$ for the reverse transition. Choose further a double-exponential $\psi_{21}(t) = a\Gamma_{2a}e^{-\Gamma_{2a}t} + b\Gamma_{2b}e^{-\Gamma_{2b}t}$, ($a + b = 1$), and a single exponential $\psi_{12}(t) = \Gamma_{12}e^{-\Gamma_{12}t}$. Now expose the system to noise that restarts each transfer attempt. The effective rate of $1 \leftarrow 2$ processes is unaffected by noise, because a Poisson process collects no memory of past events. On the other hand, the effective rate of escape from state 1 will depend on the rate of noise. It was shown explicitly in ref 1 but is expected on general grounds that in the fast-bath limit, the effective rate of escape from state 1 should equal the average escape rate: $\Gamma_{\text{eff}} = a\Gamma_{2a} + b\Gamma_{2b}$. In the slow-bath limit, with no interruption, the *lifetimes* must be averaged, which yields an effective rate according to $1/\Gamma_{\text{eff}} = a/\Gamma_{2a} + b/\Gamma_{2b}$. Now suppose, with no loss of generality, $\Gamma_{2a} \gg \Gamma_{2b}$, and $a \sim b$. Clearly, varying the rate of noise will let one pick out either the faster rate Γ_{2a} or the slower rate Γ_{2b} as the effective rate of transfer from state 1 to state 2. Suppose further that the rate of the backward process $1 \leftarrow 2$ is intermediate between the two forward rates: $\Gamma_{2a} > \Gamma_{12} > \Gamma_{2b}$. This means that by tuning the rate of noise, one can shift the (steady state) equilibrium between states 1 and 2. This will be demonstrated explicitly later for a Poissonian bath fluctuating with rate λ , with the result shown in Figure 1. We now proceed with a general solution.

III. General Model

Our main tool will be the theory of semi-Markov processes,⁴ the most general description of stochastic phenomena. While powerful, it tends to be abstract at times, so let us begin with a simple illustration to set the stage. Consider a system of N linear first-order equations with time-independent coefficients,

frequently used to describe kinetics of (first-order) conversion between N reactive species near equilibrium: $\dot{\mathbf{p}} = -\mathbf{K}\mathbf{p}$. Here, \mathbf{K} is the usual rate constant matrix, and $\mathbf{p}(t) \equiv \{p_i(t)\}$ is the vector containing the concentrations of species, labeled with index $i = 1, \dots, N$. Solving the following equation,

$$\dot{\mathbf{P}} = -\mathbf{K}\mathbf{P} \quad (1)$$

where \mathbf{P} is now a *matrix* subject to the initial condition $\mathbf{P}(t=0) = \mathbf{1}$, solves the kinetic problem for *any* initial condition, so that $\mathbf{p}(t) = \mathbf{P}(t) \mathbf{p}(t=0)$. Here, $\mathbf{1}$ is a unit matrix: $\mathbf{1} \equiv \{\delta_{ij}\}$, where $\{\delta_{ij}\}$ is the Kronecker delta function. Note, \mathbf{P} is thus a Green's function. Formulated as a matrix equation, such as eq 1, the simple kinetic problem above also describes a particular, simple random walk on a lattice containing N sites (cf. ref 5; see also ref 3 for a general overview). Indeed, consider a set of N sites, and define a residence time τ_i on site i (this may be also associated with a "trapping" time: $\tau_i = \tau_{\text{micro}}e^{-\beta|E_i|}$, where E_i is the depth of the trap at site i). We postulate that once landed on site i , the particle will be released in time t , distributed according to a waiting time distribution $\psi_i(t) = (1/\tau_i)e^{-t/\tau_i}$, implying a simple Poisson process. Upon release, the particle will jump to site j with a probability π_{ji} ; π_{ii} gives the probability of remaining at the same site. For obvious reasons, $\sum_j \pi_{ji} \leq 1$, where the equality holds for probability-conserving processes. Only the latter are considered throughout the paper, hence $\pi_{ii} = 1 - \sum_{j \neq i} \pi_{ji}$. A unique feature of a recurring Poisson process with characteristic time τ is that it recurs, on average, once every time interval of length τ , regardless (!) of the sampling window size. One therefore may define a *flux* $\pi_{ij}\tau_j^{-1}p_j$ from site j to site i . Collecting all the fluxes in and out of site i , one gets by particle number conservation, $\dot{p}_i = \sum_j (\pi_{ji} - \delta_{ij})\tau_j^{-1}p_j$. It follows that the probability of being at site j at time t , given the particle started at site i at time zero is given by the matrix \mathbf{P} that solves eq 1, with the same initial condition, after one identifies $-K_{ij} = (\pi_{ji} - \delta_{ij})\tau_j^{-1}$.

In the example above, the "choice" of direction π_{ji} did not depend on how much time had elapsed since the particle landed on site i . In general, one may define probabilities $\Psi_{ji}(t)$ of jumping to site j during the time interval $[t, t + dt]$, where the time is counted from the moment of arrival at site i . By probability conservation, $\sum_j \int_0^\infty \Psi_{ji}(t) dt = 1$. Define now the long time probability of making a $j \leftarrow i$ transition: $\pi_{ji} \equiv \int_0^\infty \Psi_{ji}(t) dt$. One can subsequently define *normalized* probability density functions $\psi_{ji}(t) \equiv \Psi_{ji}(t)/\pi_{ji}$ of waiting times t of transitions from site i to site j . The transition probability matrix $\{\pi_{ij}\}$ defines an imbedded Markov process; and together with the waiting times distributions (WTD) $\{\psi_{ij}(t)\}$, it defines a semi-Markov process.⁴ If $\psi_{ji}(t) = \psi_i(t) (\forall j)$, one can also interpret $\psi_i(t)$ in the spirit of diffusion as a distribution of trapping (or residence) times at site i , upon which the particle will jump to site j with probability π_{ji} , as in the example above. In contrast, the case of distinct ψ_{ij} can (but does not have to) be interpreted or implemented by having the particle choose first the *direction* j upon arrival at site i , and then wait for a time sampled from a WTD ψ_{ji} . We see that flux is not a universally convenient concept, and a more general treatment may be necessary. Throughout the paper, we will consider processes that conserve particle density, $\sum_j \pi_{ji} = 1$; however, the results are easily extended to cases with population depletion by introducing a set of explicit "trap" states with very long escape times $\langle t_{i, \text{trap}} \rangle \rightarrow \infty, (\forall i, \text{"trap"})$. For mathematical simplicity and with no loss of generality, we may set $\pi_{ii} = 0$.

The basic object of the theory is a survival probability matrix $P_{ji}(t)$ giving the probability of being in state j at time t given

the particle was in state i at time zero (cf. the example above). At any time, $\sum_j P_{ji}(t) = 1$. At time zero, $P_{ij}(0) = \delta_{ij}$. The matrix $\mathbf{P}(t) \equiv \{P_{ij}(t)\}$ is a Green's function in that the population pattern in the system at time t is given by $\mathbf{p}(t) = \mathbf{P}(t)\mathbf{p}(0)$, where $\mathbf{p}(t) \equiv [p_1(t) p_2(t) \dots p_N(t)]^T$ is a column of height N whose entries are populations $p_i(t)$ of state i at time t . (Note, $\mathbf{P}(t)$ is generally not a semigroup.) The Laplace transform of the survival probability in the absence of interruption, $\mathbf{P}_u(s)$, is expressed as a function of π_{ij} and $\psi_{ij}(t)$ through a well-known formula,⁴

$$\tilde{\mathbf{P}}_u(s)^{-1}|_{ij} = [\delta_{ij} - \pi_{ij}\tilde{\psi}_{ij}(s)] \frac{s}{1 - \sum_k \pi_{kj}\tilde{\psi}_{kj}(s)} \quad (2)$$

where $\tilde{\psi}_{ij}(s) = \int_0^\infty dt e^{-st} \psi_{ij}(t)$. (From now on, all survival probabilities of an uninterrupted process will have a subscript “u”, as above.) The case of uniform $\psi_{ij}(t) = \psi(t)$ corresponds to the familiar case of a continuous time random walk.³

We now consider interruptions, or renewals, with the waiting time distribution of interruptions equal to $\psi_r(t)$ and the corresponding survival probability $p_r(t) = 1 - \int_0^t dt_1 \psi_r(t_1)$, where r signifies “renewal”. The physical scenario addressed here corresponds to all situations where particle does not affect the environment, whereas the environment, upon renewal (interruption or fluctuation), will have the effect of “shifting the clock” of the particle on its current site to zero, as if the particle just landed on that site from elsewhere. This is an adequate modeling assumption whenever the environment acts sufficiently nonadiabatically on the particle. Suppose at the time of a renewal (call it time zero), the particle was in state i . What is the probability of being in state j at time t in the presence of interruptions? We compute this probability by conditioning on how many interruptions have occurred between time zero and time t . Suppose there have been exactly n renewals at times $t_1 < t_2 < \dots < t_n$. Then the probability of being in state j equals $\sum_{k_1, \dots, k_n} \mathbf{P}_u(t - t_n)|_{jk_n} \mathbf{P}_u(t_n - t_{n-1})|_{k_n k_{n-1}} \dots \mathbf{P}_u(t_1)|_{k_1 i}$, where we have summed over all intermediate states k_1, k_2, \dots, k_n possibly visited during the random walk. The probability of having those n renewals in time intervals: $[t_1, t_1 + dt_1]$, $[t_2, t_2 + dt_2]$, ..., $[t_n, t_n + dt_n]$, respectively, is equal to $p_r(t - t_n) \prod_{k=1}^n dt_k \psi_r(t_k - t_{k-1})$, where $t_0 \equiv 0$. The total (interrupted) probability $P_{ji}(t)$ is found by summing over all possible numbers of renewals and integrating over the times t_i of each renewal, subject to $t_i \leq t_{i+1}$, of course. Each term in this sum is a convolution. The Laplace transform of the sum yields a geometric series in terms of the Laplace transform of the uninterrupted matrix $\mathbf{P}_u(t)$ times $\psi_r(t)$. Summing the series results in the following expression for the Laplace transform of the interrupted survival probability matrix

$$\tilde{\mathbf{P}}(s) = \int_0^\infty dt e^{-st} \mathbf{P}_u(t) p_r(t) [1 - \int_0^\infty dt e^{-st} \mathbf{P}_u(t) \psi_r(t)]^{-1} \quad (3)$$

Note that this result is identical to the survival probability of interrupted irreversible escape from a single state,¹ but now the particle can return. In addition, \mathbf{P} and \mathbf{P}_u are now matrices, not scalars, and the multiplication order might matter. Equation 3 is consistent with the conclusions of the regenerated random walk.³ If it turns out that interruption is site-specific, that is, the rate of environment fluctuations depends on where the particle is, this corresponds to a particle's hopping also producing an interruption. To compute the corresponding interrupted survival probability matrix, one simply uses the uninterrupted $\tilde{\mathbf{P}}_u(s)$ from eq 2, but substitutes for the $\tilde{\psi}_{ij}(s)$ its

interrupted values found in ref 1 for an *individual* interrupted process

$$\tilde{\psi}_{ij}(s) \rightarrow \tilde{\psi}_{ij}(s) = 1 - s\tilde{p}_{ij}(s)$$

where

$$p_{ij}(s) = \int_0^\infty dt e^{-st} \mathbf{p}_u(t)|_{ij} \mathbf{p}_r(t)|_{ij} / [1 - \int_0^\infty dt e^{-st} \mathbf{p}_u(t)|_{ij} \psi_r(t)|_{ij}]$$

and $\mathbf{p}_u(t)|_{ij}$ is the survival probability of each transition in the absence of interruption.

$$\mathbf{p}_u(t)|_{ij} = 1 - \int_0^t dt \psi_u(t)|_{ij}$$

Physically, $\psi_r(t)|_{ij} = \psi_r(t)|_j$, ($\forall i$), lest one introduces some peculiar correlations into the model. As already mentioned, in this work we assume the particle does not affect the environment.

Upon integration by parts in eq 3

$$1 - \int_0^\infty dt e^{-st} \mathbf{P}_u(t) \psi_r(t) = \int_0^\infty dt e^{-st} [s\mathbf{P}_u(t)p_r(t) - \dot{\mathbf{P}}_u(t)p_r(t)]$$

one makes the following immediate conclusion from eq 3: Only processes that obey a master equation of rank N with time-independent coefficients are not affected by the interruption, regardless of its specific pattern. Indeed, substituting $\dot{\mathbf{P}}_u(t) = -\mathbf{K}\mathbf{P}_u(t)$, where \mathbf{K} is a matrix of rate coefficients, yields $\tilde{\mathbf{P}}(s) = [s\mathbf{1} + \mathbf{K}]^{-1} = \tilde{\mathbf{P}}_u(s)$. This may, in fact, be considered as a constructive way to see that equilibration within a set of N states that are in full thermal equilibrium with the environment must obey a set of N linear first-order differential equations with time-independent coefficients: we will call this a first-order process (a first-order $\mathbf{P}(t)$ is a semigroup: $\mathbf{P}(t_1 + t_2) = \mathbf{P}(t_2)\mathbf{P}(t_1)$). Such equations are frequently written empirically to describe (macroscopic) relaxation phenomena.^{6,7}

In this paper, we focus on the most important case of Poissonian interruptions. Define $p_r(t) = e^{-\lambda t}$. This leads to a greatly simplified expression for the interrupted survival probability,

$$[\tilde{\mathbf{P}}(s)]^{-1} = [\tilde{\mathbf{P}}_u(s + \lambda)]^{-1} - \lambda \mathbf{1} \quad (4)$$

with $\tilde{\mathbf{P}}_u$ from eq 2. This result is consistent with that of the DDH model.² We point out that unlike the general solution from eq 3, the exponential interruption case from eq 4 (as well as the original uninterrupted eq 2) can be shown to be equivalent to a generalized master equation (cf. ref 8). Furthermore, in the limit of infinitely fast bath fluctuations, this equation becomes a regular master equation. Suppose that $\lim_{t \rightarrow 0} \psi_{ij}(t) < \infty$. This means that the initial rate of decay $\gamma_{ij} = -\dot{p}_{ij}(0) = \psi_{ij}(0)$ of the corresponding survival probability $p_{ij}(t) = 1 - \int_0^t dt_1 \psi_{ij}(t_1)$ is finite. (Whenever $p_{ij}(t)$ can be presented as a superposition of exponential decays, $p_{ij}(t) = 1/n \sum_{k=1}^n e^{-(t/\tau_k)}$, $-\gamma_{ij}$ obviously equals the average rate $\langle 1/\tau \rangle = 1/n \sum_{k=1}^n (1/\tau_k)$.) Equations 2 and 4 give straightforwardly

$$\lim_{\lambda \rightarrow \infty} \tilde{\mathbf{P}}(s)^{-1}|_{ij} = \delta_{ij} [s + \sum_k \pi_{kj} \gamma_{kj}] - \pi_{ij} \gamma_{ij} \quad (5)$$

i.e., in the limit of true time-scale separation $\lambda/\gamma_{ij} \gg 1$, the transport within a set of N states must obey a set of N linear first-order differential equations with time-independent coefficients. (In the language of the example of eq 1, we have effective residence times $\tau_j = (\sum_k \pi_{kj} \gamma_{kj})^{-1}$, and effective

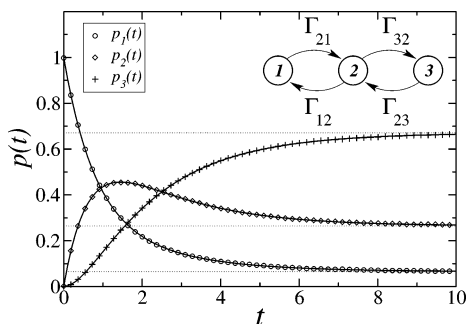


Figure 2. An example of the time evolution of populations $p_i(t)$, ($i = 1, 2, 3$) of the three states. Here, $p_1(0) = 1$. The symbols are a result of averaging over 10^5 trajectories (the event times were placed in 5000 uniformly sized bins). The solid curves are the exact expressions computed using the residues and poles from eq 6. The following values of parameters were used: $b = 0.4$, $\Gamma_{21} = 1$, $\Gamma_{12} = 0.2$, $\Gamma_{32} = 0.5$, $\Gamma_{23} = 1$, $\lambda = 0.6$. The straight lines are the steady-state populations computed using eq 7.

transition probabilities $\pi'_{ij} = \pi_{ij}\gamma_{ij}/\sum_k \pi_{kj}\gamma_{kj}$. Master equations akin to eq 5 are ordinarily written in an empirical way when describing small deviations from equilibrium on a macroscopic scale, although additional symmetry due to “microscopic reversibility” often applies.⁶ Finally, we mention several classic works in which master equations with time-dependent or heterogeneous coefficients have been used to study diffusion in dynamically disordered medium^{9,10} and reactions in fluctuating environments.^{11,12}

IV. Specific Examples

Equations 3 and 4, thus, demonstrate that a general semi-Markov process is affected by interruption unless it is described by the likes of eq 1 in the absence of interruption. On the other hand, most incoherent microscopic events are exponential, that is, $\psi_{ij}(t) = \Gamma_{ij}e^{-\Gamma_{ij}t}$. What are the conditions under which one can expect nontrivial effects in a collection of such exponential processes on a set of N states exposed to nonadiabatic perturbations? These conditions are straightforwardly outlined by using a simple counting argument: The kinetics of a simple first-order process from eq 1 are actually described by $(N - 1)$ independent time scales owing to the constraint $\sum_i K_{ij} = 0 \Rightarrow \sum_i p_i(t) = 1$, even though one defines N distinct residence times τ_i . On the other hand, specifying distinct waiting times τ_{ij} brings up the count of independent kinetic time scales to $(N^2 - N - 1)$ (recall that $\pi_{ii} = 0$, and again, $\sum_i p_i(t) = 1$). Upon comparing the two counts, one obtains that a set of elementary exponential processes within N states will not, in general, obey a master equation of rank N with time-independent coefficients when $N \geq 3$. This motivates us to consider a three-state system subject to interruptive interactions with the environment.

A. Three States, Poisson Kinetics. Here, we analyze the smallest system that demonstrates a noise-controlled approach to steady state, namely with $N = 3$ and with four nonzero coefficients π_{ij} : $\pi_{21} = 1$, $\pi_{12} = b$, $\pi_{32} = 1 - b$, and $\pi_{23} = 1$, where b is some number such that $0 < b < 1$. This arrangement can be thought of, for example, as a simple model of charge transfer between two substrates (states “1” and “3”) through a fluctuating bridge (state “2”) (see the inset of Figure 2). It is assumed that the “bridge” undergoes complicated, strongly anharmonic motions. We reiterate, bridge fluctuations must effectively erase the phase memory of the particle for this model to apply. Clearly, the exact amount of the coherence loss will depend on the degree of nonadiabaticity of the interruptions

and would have to be found from a detailed argument. Still, the present considerations should apply qualitatively, even if the bridge motions are not completely disruptive. Perhaps even quantitative conclusions could be made by reparametrizing the fluctuation rate. For instance, even though a particle in a dilute gas does not lose all of its memory on the time scale of a single collision, the velocity correlation will surely decay after 10 collisions, or likely even less. We will discuss, in some detail, possible ways of varying the fluctuation rate in the bridge setup in due time. For now, we note that the speed of bridge fluctuations can be tuned, for instance, by changing the mass of the bridge or by varying the viscosity of the solvent, if applicable. If the relevant fluctuations are caused by an activated process, then varying the barrier is a possibility. In the case of tunneling, the isotope effect may do the trick. Since only relative values of Γ_{ij} 's and λ matter for the steady-state populations, $p_i^{\text{st}} \equiv \lim_{t \rightarrow \infty} p_{ij}(t)$, changing the temperature is a way to modulate those relative values, because in general, each individual ($j \rightarrow i$) process has a different barrier, or its rate may even exhibit an algebraic T dependence if the dynamics is activationless. Finally, interruption by laser pulses (random or not) is a potential method. With regard to this, we point out that interaction with a *disruptive* laser pulse is distinct from stochastic resonance,¹³ in which the energy barrier is modulated “adiabatically”, in a periodic fashion, by an AC field.

When all $\psi_{ij}(t)$ are exponential, each element of $\tilde{\mathbf{P}}(s)$ is a meromorphic function that has N_π poles located at points s_p , including the pole at $s = 0$. Here, N_π is the number of nonzero entries of the matrix π_{ij} (degenerate poles present only a minor complication). Finding the poles requires solving a polynomial of order $N_\pi - 1$, since one of the roots is zero. Using the standard expansion of a meromorphic function through its values at the poles, $\tilde{\mathbf{P}}(s)$ is easily shown to equal

$$\tilde{\mathbf{P}}(s)|_{ij} = \sum_p \frac{(-1)^{i+j} M_{ji}(s_p)}{\lim_{s \rightarrow s_p} [\text{Det}(s)/(s - s_p)](s - s_p)} \frac{1}{(s - s_p)} \quad (6)$$

where $M_{ji}(s)$ is the minor $\{ji\}$ of the matrix $\tilde{\mathbf{P}}(s)^{-1}$, computed using eq 4, and $\text{Det}(s)$ is its determinant. The latter is equal to $\prod_p (s - s_p)$ times some nonzero function. Formula 6 applies generally, of course, as long as $\tilde{\mathbf{P}}(s)$ has no essential singularities, and allows one to present $P_{ij}(t)$ as a superposition of exponential decays. For our three-state example, the time evolution for particular values of Γ_{ij} and $p_1(0) = 1$ is shown in Figure 2.

Even though every item in eq 6 can be computed explicitly for the three-state, $N_\pi = 4$ example, the full result is too cumbersome to give here. Nevertheless, the coefficients at the $s = 0$ pole, which is the steady-state population itself, is quite compact

$$\begin{aligned} p_1^{\text{st}} &= b\Gamma_{12}\Gamma_{23}(\lambda + \Gamma_{32})/A \\ p_2^{\text{st}} &= \Gamma_{21}\Gamma_{23}[\lambda + (1 - b)\Gamma_{12} + b\Gamma_{32}]/A \\ p_3^{\text{st}} &= (1 - b)\Gamma_{32}\Gamma_{21}(\lambda + \Gamma_{12})/A \end{aligned} \quad (7)$$

where A is a normalization factor found from $p_1^{\text{st}} + p_2^{\text{st}} + p_3^{\text{st}} = 1$. Clearly, if the original rates Γ_{12} and Γ_{32} of exiting state 2 differ significantly in value, varying λ can be used to modify the relative value of the effective rates of population exchange of state 2 with each of the “terminal” states 1 and 3. The population of those states can, thus, be manipulated by tuning the rate of noise or even inverted for particular combinations

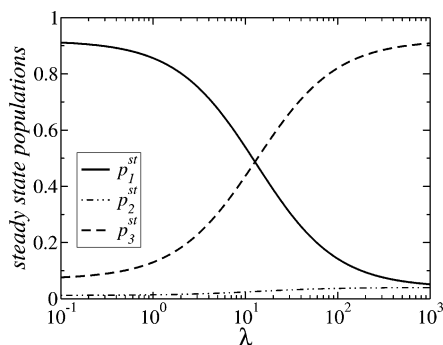


Figure 3. The steady-state populations of a noise-controlled 3-state system as functions of λ . The following values of parameters were used: $b = 0.01$, $\Gamma_{21} = 0.01$, $\Gamma_{12} = 1$, $\Gamma_{32} = 300$, $\Gamma_{23} = 13$.

of Γ_{ij} and λ , as demonstrated in Figure 3. Such inversion could be used to one's advantage in data storage or in small electric junctions where control of the transmission coefficients is desired. It is essential that the molecular unit accommodating the site 2 perform motions between at least two metastable configurations. Assume this is the case, for the sake of the argument, and call those configurations "2a" and "2b". The speed of converting between substates 2a and 2b and, hence, λ can be controlled by, for instance, varying the local electrical field if the bridge has a nonzero electric moment. (An analogy with the gate voltage in a field transistor is useful.) Suppose the bridge fluctuation is an activated process with a barrier small enough that it can be modified by the "gate" field of realistic magnitude. Since the prefactors are commonly in the range of femto- to picoseconds, the "clock frequency" of the three-state device will be probably at most of the order GHz. Nevertheless, the design allows for using well-localized electronic states on each site; the dimensions of the junction, therefore, can be made as small as a few angstroms, implying a large number of operations per unit volume of the whole "microchip", in a unit time. We note that to modify the barrier height without significantly changing the energies of the alternative configurations of state 2—2a and 2b, the "transition state" between those substates must couple more strongly to the field than the substates 2a and 2b themselves. According to Figure 3, one would like to vary λ within at least 4 orders of magnitude, which translates into ~ 10 $k_B T$ in barrier height, or 0.2 – 0.3 eV at room temperature. Corresponding fields may be difficult to create by local means within a microscopic device. We therefore suggest a different approach: use the field to move another molecular unit (call it "pin") in and out of the way of the bridge. By varying the amount of steric hindrance to those movements, one can change the energy of the transition state to a desired extent, if the pin's own potential is engineered to be shallow, and by using only weak fields. Finally, if one decides to apply field directly to the bridge, it may be necessary to use a theory with an inhomogeneous λ , because the response of the bridge to the "gate" field and its fluctuation rate may depend on the bridge's charge. This means the interruption is site-specific, and one should proceed according to the discussion following eq 3.

Why Use Interruption-Based Design, As Opposed to Static Control? Note that a purely static design, in which the energy of state 2 is controlled, is not nearly as efficient in controlling the mutual steady-state populations of the terminal states 1 and 3. This is easy to see by considering Boltzmann weights: $e^{-\beta E_1/Z}$, $e^{-\beta E_2/Z}$, and $e^{-\beta E_3/Z}$ ($Z = \sum_i e^{-\beta E_i}$), and scanning through possible values of E_2 . Nevertheless, this brings up the notion that in a real device, the rates Γ_{ij} may depend on the

configuration of the system, so that interruptions not only restart transfer but also modify rates. If all those alternative states are well-connected, then one arrives at nonexponential effective $\psi_{ij}(t)$ (see shortly). If, in contrast, the connectivity pattern is sparse, then we have a multistate random walk.³ Generalizing our results to such multistate walks is straightforward.

Detailed Balance. Clearly, the usual detailed balance⁷ does not apply to the three-state example, consistent with the steady-state populations p_i^{st} being dependent on λ . First, note that $\Gamma_{12} \neq \Gamma_{32}$, so that one cannot define a "residence" time at state 2 and a corresponding "chemical potential". One can still emulate the resulting dynamics in a long-time, coarse-grained sense by a first-order process (cf. ref 5); however, the usual zero flux condition $\sum_j K_{ij} p_j^{\text{st}} = \sum_j K_{ji} p_i^{\text{st}}$, will contain an *effective* rate constant matrix \mathbf{K} , that will also reflect the λ value, in addition to the bare quantities π and Γ . (The corresponding time scales correspond to the two smallest (nonzero) poles of the Green's function $\tilde{\mathbf{P}}(s)$.) In contrast, the *intermediate* time kinetics of the 3-state model is not first-order and, thus, will be affected by interruption, as anticipated by Section III. Detailed balance is actually a significantly stricter constraint saying the total flux must be zero within each *pair* of states:⁷ $K_{ij} p_j^{\text{st}} = K_{ji} p_i^{\text{st}}$. This is only possible when the \mathbf{K} matrix possesses additional symmetry analogous to the Onsager's reciprocal relations and stemming from "microscopic reversibility",⁶ in clear distinction from the setup above. From a somewhat different perspective, a classical Hamiltonian with specified energies has no intrinsic dynamics; therefore, the equilibrium populations (of N states) must be specified by an (entirely static) transition probability matrix π_{ij} alone. The choice of dynamical rules is then arbitrary. Let us choose Poisson kinetics with a defined residence time on each site so that $\psi_{ij} = \psi_j(t) \equiv \Gamma_j e^{-\Gamma_j t}$ ($\forall i$). By eq 2, this yields a master equation with t -independent coefficients of rank N . In the three-state arrangement above, the characteristic polynomial is *fourth*-, not *third*-order in s (except when $\Gamma_{12} = \Gamma_{32}$). The "extra" time scale in the problem may be further associated with a fourth, "hidden" state; alternatively, the three original states can be thought of not as simple, but *compound*, and then detailed balance does not apply in the usual way. (The corresponding four-state model is Markovian; however, the coefficients at the distinct exponential components are related to those of the three-state model in an untrivial, nonlinear way.) In a real device, the number of "hidden" states would probably be larger. Let us adopt here, for the sake of argument, the (somewhat restrictive) interpretation of the distinct ψ_{ij} 's as "choose direction first", then wait for the corresponding time. To realize a situation in which a direction is chosen first (probability b to go left, $1 - b$ to go right) and *then* the "particle" waits for a time that depends on that chosen direction, one must prevent the particle from going back after the direction is selected. Chemically, this can be achieved by having two intermediates, $\tilde{1}$ and $\tilde{3}$, that are created with probabilities b and $1 - b$, respectively, from state 2. Those intermediates decay into states 1 and 3 with rates Γ_{12} and Γ_{32} , respectively, but are relatively unlikely to reverse back to state 2. Thus, each individual trajectory does not retrace itself at the molecular level, but is circular on average, consistent with the lack of "microscopic reversibility". One can thus map the three states onto a problem of two interacting molecular rotors. Viewed this way, the action of interruption is rather trivial: by using the steric hindrance mentioned earlier, one simply releases one of the rotors, but blocks the other and vice versa. Indeed, with the parameters from Figure 3, little interruption means the system spends relatively little time in the {23} subset, ac-

accompanied by slow, but steady $1 \leftrightarrow 2$ exchange (this corresponds to releasing the rotor on the left). At large λ , the system spends more time in the $2 \leftrightarrow 3$ exchange mode as the interruption cuts off the (relatively sluggish) attempts go left (recall $\Gamma_{12} \ll \Gamma_{32}$), thus activating the right-hand side rotor.

B. Two States, Non-Poisson Kinetics. In order for a two-state system to be sensitive to noise, at least one of the $\psi_{ij}(t)$'s must be nonexponential. The two-state incarnation of the model is simplistic; nevertheless, it allows one to see the mechanism of steady-state control a bit more explicitly than the previous, three-state example.

$\mathbf{P}(s)$ for $N = 2$ is easy to compute explicitly. Here, we only give the steady-state populations of each state,

$$\begin{aligned} p_1^{\text{st}} &= \tilde{\psi}_{12}(\lambda)[1 - \tilde{\psi}_{21}(\lambda)]/A \\ p_2^{\text{st}} &= \tilde{\psi}_{21}(\lambda)[1 - \tilde{\psi}_{12}(\lambda)]/A \end{aligned} \quad (8)$$

where A is a normalization factor found from $p_1^{\text{st}} + p_2^{\text{st}} = 1$ (note, $\pi_{12} = \pi_{21} = 1$). Suppose all $\langle t_{ij} \rangle \equiv \int t \psi_{ij}(t) dt$ and γ_{ij} exist. Trivially, $\lim_{\lambda \rightarrow 0}(p_1^{\text{st}}/p_2^{\text{st}}) = \langle t_{21} \rangle / \langle t_{12} \rangle$ is the ratio of the lifetimes of irreversible decays from states 1 and 2, respectively. In contrast, $\lim_{\lambda \rightarrow \infty}(p_1^{\text{st}}/p_2^{\text{st}}) = (1/\gamma_{21})/(1/\gamma_{12})$ is the ratio of inverse initial decay rates from states 1 and 2 (or average rates, if applicable). Therefore, if a particular uninterrupted decay profile exhibits qualitatively different behaviors at long and short times, varying the degree of interruption gives one a choice of the apparent long-time asymptotics of the interrupted profile; this was discussed in great detail in ref 1. (It can be checked directly from eq 8 that the steady state is λ -independent, if both $\psi(t)$'s are exponential.)

To demonstrate this noise-selected long-time behavior, we consider the two-level arrangement mentioned earlier: $\psi_{21}(t) = a\Gamma_{2a}e^{-\Gamma_{2a}t} + b\Gamma_{2b}e^{-\Gamma_{2b}t}$, ($a + b = 1$), and $\psi_{12}(t) = \Gamma_{12}e^{-\Gamma_{12}t}$. This yields $p_1^{\text{st}}/p_2^{\text{st}} = \Gamma_{12}[\lambda + (b\Gamma_{2a} + a\Gamma_{2b})]/[\lambda(a\Gamma_{2a} + b\Gamma_{2b}) + \Gamma_{2a}\Gamma_{2b}]$. Hence, $\lim_{\lambda \rightarrow 0}(p_1^{\text{st}}/p_2^{\text{st}}) = (a/\Gamma_{2a} + b/\Gamma_{2b})/(1/\Gamma_{12})$ when no noise is present. In the opposite limit of an infinitely fast bath, $\lim_{\lambda \rightarrow \infty}(p_1^{\text{st}}/p_2^{\text{st}}) = \Gamma_{12}/(a\Gamma_{2a} + b\Gamma_{2b})$. Optimal conditions for noise-controlled population inversion are achieved when there is significant mismatch between the "forward" rates Γ_{2a} and Γ_{2b} , and the "backward" rate Γ_{12} having an intermediate value. Such conditions are realized when, for instance, $\Gamma_{2a}/\Gamma_{12} \gg a$, $1/a$ and at the same time, $\Gamma_{2b}/\Gamma_{12} \ll b$, $1/b$ (see Figure 1).

This 2-state scheme implies state 1 is compound and may be realized as consisting of two disconnected substates a and b that are equivalent in terms of some quality of interest (charge configuration, for instance) but have distinct rates of transfer to state 2. The reverse process can be thought of as conversion from state 2 to some short-living intermediate that decays (with equal probability) into those substates a and b . The particle transfer between the substate a (or b) and state 2 does not retrace itself, but occurs in a circular fashion, as in a molecular rotor. Detailed balance clearly does not apply to the two-state example.

C. Electron Transfer in Photosynthetic Bacteria: an Example of Noise-Controlled Rates? When assessing the plausibility of employing interruption as a control on the transport properties of microscopic systems, one may inquire whether the signature of interruption has been seen in existing systems. Here, we argue this may be the case in biological electron transport systems. We focus on the specific example of bacterial photosynthetic reaction centers (RC) (see, e.g., refs 14 and 15 and references therein). These include the reduction of the oxidized chlorophyll dimer either directly by cytochrome

c oxidation or by a "back recombination", slower transfer from a quinone; these transfer events ready the inactive antenna for absorbing the next photon. Oxidation of photoexcited bacteriochlorophylls (BChl)₂ is also studied. Electron transfer (ET) in RC has received an enormous amount of attention in the past four decades, both experimentally and theoretically, and so an adequate account of the field is beyond the scope of this letter. Nonetheless, the few works we do quote here (in support of our qualitative statements) are an adequate starting point for our purposes.

Decades after the discovery of a large T -independent region of the rate dependencies of laser-induced cytochrome oxidation in *Chromatium* by DeVault and Chance¹⁶ and an apparent negative activation energy of the back transport by Hales,¹⁷ it is now clear that the Marcus picture of regular nonadiabatic electron transfer¹⁸ does not apply straightforwardly in these and other bacterial photosynthetic complexes. First, the relaxation is often nonexponential.^{19,20} Second, if such relaxation is fit by a multiexponential, each component's rate does not always obey the dependence on the free energy bias expected from the Marcus expression, as has been discovered either by applying electric field or by mutating the protein.^{19,21} The usual suspects include T -dependence of electronic coupling due to the protein's thermal expansion,^{14,17} vibration-assisted barrier crossing,²¹ temperature-dependent reorganization energy,^{19,22} difference in vibrational entropy between the terminal states,^{23,24} coupling to a glassy fluctuating medium,²⁵ and coupling to a diffusive degree of freedom.²⁶ Many of these draw on the idea that several distinct relaxations take place during the ET, as proposed in the seminal work of Bixon and Jortner.¹⁵

Prima facie evidence for conformational changes and nuclear relaxation during such transfer comes from monitoring several absorption bands during electron transfer from the excited singlet state P^* of the special pair (BChl)₂ to ubiquinone Q_A through an early electron acceptor I in *Rhodospseudomonas sphaeroides* RC: $P^+I^- \rightarrow P^+Q_A^-$.²⁴ The decay/recovery rates of fluorescence at (up to four) distinct wavelengths were comparable, although differing in value. Regardless of the degree of localization of the mode probed at each wavelength, the possibility of simple charge-transfer interacting with a harmonic bath can be ruled out. Most likely, jumps between conformational states of the local portions of the protein (and the solvent) take place so as to readjust to the shifting charge distribution.²⁴ One can separate the effects of conformational changes on the transfer into two distinct phenomena. One is static and arises from the sensitivity of the electron tunneling amplitude to the exact protein configuration in a photosynthetic RC, as demonstrated by Balabin and Onuchic.²⁷ We have seen in the earlier discussion of interruption that switching between the conformational states will also affect the overall transfer rate if the switching rate is comparable to individual electron jump rates in a specific conformation. Thus, the "dynamically controlled protein tunneling paths"²⁷ lead to a dynamically controlled transfer rate. We find an explicit illustration of this dynamical, or noise-induced control in the T dependence of the single-exponential components of the overall time dependence of P^+ reduction in *Rhodospseudomonas viridis*.²⁰ By mutating the L162 residue, situated between the cytochrome's tetraheme and the special pair (BChl)₂, Ortega et al.²⁰ have been able to single out up to four distinct exponential components in some of the organisms and follow the temperature dependence of their contribution to the total decay profile. In several cases, while the rates of two components change, their contributions also reverse as the temperature is varied, in a fashion similar to Figures 1 and 3.

We interpret this situation as a natural prototype of the interrupted two-state system discussed above. (Note that other ways to fit those decay curves that would lead to a power law at long times have been proposed.²⁶⁾

Of the multitude of distinct electron transfers in RC, one expects those that are faster and are critical for functionality, such as P^{*} oxidation, to be exponential and to have a low reorganization energy and little accompanying protein backbone rearrangement; the slow ones, on the other hand, such as the back transport, to be strongly influenced by conformational changes.²⁸ The latter has been seen directly by rapid quenching a suspension of *R. rubrum* chromatophores in a mixture of water and glycerol. By varying the speed of cooling, Chamarovsky et al.²⁹ have achieved different relative weights of distinct decay components in the dark P870⁺ recombination at $T \lesssim 250$ K. Clearly, by such quenching, one is able to prevent the system from reaching some of its configurational states. Single-molecule studies of this and similar processes would help determine directly the number of statistically significant configurations of the protein contributing to these slow transfer events. Such studies would be especially fruitful now that complete theoretical estimates of transfer rates in each individual conformation have become possible³⁰ (and may, in fact, conform to Marcus theory). We stress, however, that even in fast processes, signatures of (rapid interchange between) distinct conformational states can be seen.²⁴

To summarize, electron transfer processes in photosynthetic reaction centers exhibit a varying amount of nonexponentiality that increases as the temperature is lowered. The nonexponentiality arises because the transfer interacts with anharmonic degrees of freedom signifying transitions between conformational states of the RC. The transition rates corresponding to each conformation and the rates of switching between the conformations will change their relative value as temperature is changed. This constitutes, in our language, a noise-controlled reaction (although we recognize that these effects may well be subdominant to the effects of the T dependence of the Boltzmann weights of different conformations). We have proposed to use noise to tune transport properties of microscopic devices. In nature, we speculate, such design is employed to make effective transfer rates less sensitive to minor mutations by giving the RC choice of many alternative transfer channels. Even if some of those channels are inefficient, interruptions due to the anharmonic transitions will eventually put the system into a more efficient configuration. The resultant effective rate is determined mostly by the rate of interruptions, not the rates corresponding to the "slow" channels.¹

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