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REGULARIZATION OF ENVIRONMENT-INDUCED TRANSITIONS IN NANOSCOPIC SYSTEMS

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A novel method for regularization of environment-induced relaxation transitions in nanoscopic systems is proposed. The method, being compatible with the chaotic, stochastic, and transient time scales, is physically consistent and mathematically strict. It allows one to correctly reduce the evolution of a system to a master equation for the balance of populations of its states with the probabilities of transitions between states well satisfying both the temperature-independent activationless limit and the Arrhenius exponentially temperature-dependent activation-like limit. The results obtained are applied to the description of the kinetics of temperature-independent desensitization and degradation observed in receptor and circadian protein macromolecules.

Keywords: nanoscopic system, environment-induced transitions, Liouville–von Neumann equation, nonadiabatic interaction, relaxation processes, temperature-independent kinetics.

1. Introduction

In approaching the fine-grained kinetics of a finite-level open system nonadiabatically coupled to the noisy environment and exchanging with it by energy and particles, one commonly sets a direct correspondence between irreversible relaxation transitions from the one energy level to another one and the time evolution of the ensemble-average nonequilibrium population of levels toward the equilibrium. At that, the relaxation rates for the transitions are usually read off from the rule of summing over a set of final system's states weighted with probability amplitudes for transitions from initial states. This is similar to the Fermi golden rule for the rate of quantum-mechanically reversible transitions derived in the first order in weak resonant-like (adiabatic) intrasystem interactions [1–3]. However, contrary to the latter, the irreversible transitions are generated by the second-order terms in a perturbation expansion of the unitary evolu-

tion in a weak relaxation-like (nonadiabatic) interaction between the system and the environment. Therefore, in general, these transitions are united under the conventional name of “environment-induced transitions” [4, 5].

The environment-induced (also environment-driven and environment-assisted) transitions belong to the very fundamental processes in science and technology [5–7]. However, in many cases, there is the problem in exploring these transitions accurately. For example, if one deals with the isolated finite-level system, then it is straightforward to correctly calculate its partition function, as well as its two-point and higher correlation functions, as corresponding well-defined convergent sums or integrals over finitely many configurations in multiple dimensions. Rather, if to go from the finite to infinite systems, e.g., by embedding the finite-level closed (quantum) system in an open contact with the infinite-level (macroscopic) environment, then the partition functions and correlation integrals become ill-defined functionals involv-

ing divergent quantities [8]. This compels one to apply the special regularization techniques to the accurate calculation of physical processes of interest in the given order of perturbation theory, while trying to reproduce the available experimental data sufficiently well [9].

On the other hand, the environment-induced transitions, being so important and pervasive in the energy transformation processes, could essentially contribute to a consistent operation of the system on the different time and length scales, and to the time scale compatibility of system's relaxation kinetics with existing phenomenological laws as well. At the same time, when resorting to a coarse-grained kinetics instead of modeling a solely fine-grained one, for the most of the physical, chemical, biological, and information systems, it would be natural to simply regard them as functional nanosystems. However, as compared to the microscopic systems, the nanoscopic systems should be endowed with the fewer many relevant degrees of freedom allowing one to condense the different coarsely averaged properties of a system in only a few number of effective parameters that could be realized just on the nanometer length scale [7].

In last years, the research of functional nanosystems has been spurred strongly by having attracted high interest after the discovery of their ability to operate consistently and reproducibly not only in isolation but also in noisy and changeable environments. Instances of such an extraordinary performance are well exemplified in a lot of natural nanoscopic systems. The striking supporting examples are most nanomolecular structures of living organisms ranging from photo-synthesizing reaction centers [10] to ligand-operated molecular receptors [11] to voltage-gated ion channels [12] to promoter-driven genetic circuits [13,14] to ATP-dependent molecular motors and pumps [14,15], etc. The other significant examples are functional implementations of nanosystems in technologically relevant nonequilibrium relaxation processes such as the optical excitation energy transfer [16], donor-acceptor electron and proton transitions [6], nanomolecular conformational transformations [14, 17], energy-matter conversion [18], assembly of polyoxometalates [19], integration of semiconductor nanowires [20], as well as the application of nanoparticles and drug carriers in medicine [21], to name a few.

According to the formal definition taken from surface chemistry [22], a nanoscale system represents

the specific superatomic or supramolecular nanoobject organized so that to be able to assembly its distinct functional components and/or units, of size from one to tens nanometers, together in three dimensions [23,24]. But the size alone is not a key determinant for the revealed nanoscopic functionality. What is more important is that, because of generally strong surface effects [25], the nanosystems possess in themselves very specific energy spectra that are intermediate between the discrete energy-level spectrum of a separate atom or molecule and the broad band energy continuum of bulk matter [26]. Moreover, a nanoscale system is not static in space and time, as it could be expected for an thermodynamically isolated object [6]. Rather, being open to the fluctuating environment and providing the exchange of energy and particles with it through the environment-induced transitions in the sub- to supra-gigahertz frequency range, a nanosystem does constantly develop in space and time, according to the Liouville–von Neumann quantum evolution equation for the density matrix of the whole system, on transiently shorter to longer length and time scales [27–30]. On the other hand, the permanent occurrence of environment-induced transitions in nanoscopic systems is, as a rule, accompanied by the creation or annihilation of environmental vibration quanta (phonons). In this case, among relaxation transitions between the microscopically steady energy levels brought about by a weak bilinear coupling of the system to the environment, one must consider also the multitude of stochastic additions to the average position of energy levels owing to their thermodynamic fluctuations arisen because of nonlinear correlation effects in the system–environment interaction [31–35].

Nowadays, the existing phenomenological approach to modeling the elementary acts of stochastic transitions between energy levels on the macroscopic scale is well recognized [36–38]. At the same time, the more satisfactory kinetic formalism for describing the environment-induced relaxation and fluctuation processes occurring in nanosystems on the atomic to molecular-level scales remains elusive. In this paper, the nanoscopic approach to the evolution of a finite-level open system weakly coupled to a noisy environment is proposed for making a stochastic regularization of the environment-induced transitions between system's energy levels experiencing nanoscale fluctuations. We begin with describing the methods

of general use and then formulate the basic theoretical approach that will allow us to provide the rigorous derivation of a stochastically averaged master equation with microscopically balanced transition rate constants accounting for stochastic, kinetic, and macroscopic (thermodynamic) system's parameters. Further, we present particular applications of the master equation to two nanoscopic effects with concern to a description of one- and two-exponential decay kinetics of specific circadian and receptor proteins. Finally, we discuss the results obtained and end with conclusions.

2. Methods

One of the most fundamental methodological concepts in nanoscience is the concept of the whole system. It comprises as basic factors inherent in the dynamics and kinetics of a nanoobject itself, as well as the relevant effects of its surroundings, including the apparatus impacts and influences of external controls. But practically using this concept for realistic nanoscale systems excels by the strong diversity and dependence on the context of a problem, it appeals to solve. Nevertheless, in order to appreciating the concept in more formal terms, it is sufficient to use a simple convention, by referring the whole system to as of a compositionally closed one (C), and further to provide a partition of such a system into its finite-level (quantum) and infinite-level (macroscopic) parts like as $C = A + B$. With concern to the modeling, the nanosystem can be regarded then as the corresponding quantum part (A) being the nonequilibrium open system of interest, while the environment is considered as the respective macroscopic equilibrium part (B) representing the heat bath modeled by an infinite set of non-interacting harmonic oscillators at the temperature T . Additionally, there occur thermodynamic fluctuations of the particular (charged) functional groups which randomly perturb the positions of system's energy levels, already found for the part A . This sets complementary conditions to provide an averaging of the evolution over stochastic processes meaningfully occurring in the sub- to supra-terahertz frequency range with a necessary regularization procedure [27, 28].

At the same time, when called upon to operate well under changeful noisy conditions, a nanoscopic system should be functionally stable. This implies that, to be accurate in modeling the state energy spectrum

of the part A , one is forced to maintain the randomly fluctuating energy levels, in average, stationary and keep the relaxation transitions between them, in detail, balanced, both with respect to the oscillation frequencies characteristic of the part B . Essentially, to form the time-dependent positions of quantum levels and to transit from the one level to another one, the two processes well separated in time are: from tens of femtoseconds to picoseconds, for the first, and from milliseconds to seconds (or even hours), for the second [29]. Consequently, in order to regularize the kinetics of environment-induced transition processes by means of introducing the random energy fluctuations on the nanoscopic time scale, it is necessary to provide the temporal behavior of the nanosystem with the farther hierarchy of time scales so as to follow the evolution not only at very short times, at which level positions can be considered fixed, but also at intermediate times, during which the stochastization of the positions of energy levels is completed, as well as at far longer times, subsequent to which the relaxation transitions between fluctuating energy levels can only occur [6, 32, 34, 39].

The concept of the whole system is thus very general and embodies, in fact, the use of many approximate methods in contemporary science. Some of these methods are briefly outlined in this section.

2.1. Method of projection operator

Within the concept of the whole system, a most rigorous methodology in the description of the time evolution of a finite-level open system contacting with the fluctuating equilibrium environment is based on the nonequilibrium density matrix theory [37–41]. The adaptation of the theory to systems revealing the energy level randomization exploits the use of a multitude of methods for research, e.g., [34, 35, 42–47] and references therein. But the strictest of them is the projection-operator method of Nakajima [48] and Zwanzig [49, 50] applied to the whole closed system C . It allows one to derive the generalized master equation (GME) for the density matrix $\rho_0(t)$ of the open part A of the whole closed system C , which is subjected not only to a uniform but also to a time-dependent (random or regular) external field [51]. The idea of the method is that the interaction V between a small open part A and a large nearly closed part B , with the respective Hamiltonians $H_0(t)$ and

H_B , is assumed weak enough to hardly ever or even never affect the distribution of non-interacting states in the B . Thus, independently of the distribution of random energy levels in the A , the B always remains in the state of thermal equilibrium with the density matrix $\rho_B = \exp(-H_B/k_B T)/\text{tr}_B \exp(-H_B/k_B T)$ (k_B is the Boltzmann constant; trace is over the bath states). Moreover, the density matrix $\rho(t)$ of the whole system C is factorized into the nonequilibrium density matrix $\rho_0(t)$ of the A and the equilibrium density matrix ρ_B of the B like as $\rho(t) = \rho_0(t)\rho_B$. By introducing the projection operators $\hat{P} = I - \rho_B \text{tr}_B$ and $I - \hat{P} = \rho_B \text{tr}_B$ and applying them to the Liouville–von Neumann quantum evolution equation

$$\dot{\rho}(t) = -iL(t)\rho(t), \quad (1)$$

with $L(t) = (1/\hbar)[H(t), \dots]$ standing for the Liouville superoperator (\hbar is the Planck constant) that is related just to the Hamiltonian of the whole system C

$$H(t) = H_0(t) + H_B + V, \quad (2)$$

one gets an *exactly* strict description for $\rho_0(t)$ within the GME [50]

$$\begin{aligned} \dot{\rho}_0(t) = & -i\{L_0(t) + \text{tr}_B(L_V \rho_B)\}\rho_0(t) - \\ & - \int_0^t d\tau \text{tr}_B\{L_V \hat{\Theta}(\tau) \hat{\Theta}^+(\tau) L_V \rho_B\}\rho_0(\tau) + F_A(t). \end{aligned} \quad (3)$$

Here, the quantity

$$\hat{\Theta}(t) = \hat{D} \exp \left\{ -i \int_0^t d\tau (L_0(\tau) + \hat{P}L_V + L_B) \right\} \quad (4)$$

is the time-evolution superoperator with \hat{D} and $L_0(t) = (1/\hbar)[H_0(t), \dots]$, $L_B = (1/\hbar)[H_B, \dots]$, $L_V = (1/\hbar)[V, \dots]$ being the Dyson time-ordering operator and the Liouville superoperators related to the respective Hamiltonians of the open system, heat bath, and their interaction.

GME (3) contains the inhomogeneous term $F_A(t) = i \text{tr}_B(L_V \hat{\Theta}(t) \hat{P} \rho(0))$ associated with the density matrix at $t = 0$. However, in the cases very typical of nanoscale systems, the interaction V appears to vary much slower than energy level fluctuations. Thus, it can safely be assumed adiabatically switched at a distant past, not impacting the factorization condition $\rho(t) = \rho_0(t)\rho_B$. Therefore, one sets $\rho(0) = \rho_0(0)\rho_B$, which yields $\hat{P}\rho(0) = 0$,

so that $F_A(t) = 0$. An additional simplification occurs if $\text{tr}_B(V\rho_B) = 0$. In this case, the first term on the right-hand side of (3) is reduced to the $-iL_0(t)\rho_0(t)$. But using the renormalized interaction $\tilde{V} = V - \text{tr}_B(V\rho_B)$ instead V and then substituting $H_0(t)$ for $\tilde{H}_0(t) = H_0(t) + \text{tr}_B(V\rho_B)$, the aforementioned regularization is achieved without any loss of generality.

For evident analytical reasons, the calculus of the nonequilibrium density matrix from the complicated integral differential Liouville–von Neumann evolution equation (1)–(3), describing the temporal behavior of a few-level open system, whose Hamiltonian can occasionally depend on the time via some time-dependent energy coupling (due, e.g., to environmental random fluctuations or some time-dependent external force), is generally intractable [52]. Furthermore, typically to most chaotic systems, the form of the time-dependent Hamiltonian not straightforwardly to be defined is almost unpredictable. Only some statistical properties of stochastic trajectories of the temporal behavior of quantum energy levels can be measured and described sufficiently accurately [53].

Thus, even using both the nonequilibrium density matrix method and the Nakajima–Zwanzig projection-operator method does not offer a clear answer how to strictly describe the kinetic behavior, as well as the dynamics of a nanoscopic system contacting with the changeful noisy environment. The reason for this is that these approaches do not provide a unique solution and generally require employing the additional approximations for the practical implementation. Such approximations should be based upon the other specific methods, particularly those consistently providing a coarse-graining of the system with the kinetics framework would be compatible with reduced system’s description on the relevant time scales in a mathematically simple, but physically correct form. Hence, to proceed further in finding a solution of the GME (3) should be a method that assumes the hierarchy of time scales for making consistent averages of the overall dynamics of the nonequilibrium density matrix [54].

2.2. Method of hierarchy of time scales

In quantum mechanics, the eigenstate vectors are not accessible for the straightforward observation. The same is so for the density matrices in the unitary (reversible) quantum dynamics of a closed system. Ho-

wever, in both cases, one can conveniently deal with the mathematical expectations by making the corresponding averages of the physical quantities of interest over the respective state vectors and matrices. On the other hand, in the open system, this very simple realization, often being much complicated, becomes indefinite or even unpredictable in many cases. Therefore, to overcome this difficulty, one needs to have recourse for establishing the rule of primarily ordering and successively decomposing the averaging procedures involved in employing the calculations of one- and many-point functionals.

Let us consider the example. It is well known that the *exact* relation of the nonequilibrium density matrix $\rho_0(t)$ to the observable ensemble-averaged probability of finding the open system A in its m th quantum state (or a population of the m th proper energy level of the A) is given by

$$P_m(t) = \langle \langle m | \rho_0(t) | m \rangle \rangle. \quad (5)$$

Here, the symbol $\langle \langle \dots \rangle \rangle$ denotes the stochastic averaging of stochastically non-averaged populations $p_m(t) = \langle m | \rho_0^{(d)}(t) | m \rangle$ due to the exact relation $\langle m | \rho_0^{(d)}(t) | m \rangle = \langle m | \rho_0(t) | m \rangle$, while $\langle m | \dots | m \rangle$ is the statistical ensemble averaging over the nonequilibrium eigenstate vectors applied to the diagonal elements of the density matrix $\rho_0^{(d)}(t) = \hat{T}_d \rho_0(t)$. The latter is obtained according to the action of the diagonal projection operator \hat{T}_d that, together with its off-diagonal counterpart $\hat{T}_{nd} = I - \hat{T}_d$, can expand any operator into its diagonal (respectively, off-diagonal) component, whose matrix elements are just the state populations (respectively, the coherences of states). In (5), one assumes, in fact, a perfect order of averaging: at first, to perform the statistical ensemble averaging with diagonalizing the density matrix and then defining, by its diagonal elements, the eigenenergy levels found at each time instant, and only then to provide the stochastic averaging over the random realizations of the positions of these levels. Therefore, this example means that there will be a particular relation between the characteristic times, at which these operations are done. In other words, the time required for making the statistical average has necessarily to be much less than that for the stochastic average.

Another example is a decoupling relation for the stochastic averaging procedure. In many situations,

there may be the need to factorize the averaging of products of the two-time stochastic functionals. To circumvent this problem, we need to use the steady-state approximation and then make the average of separate factors. For the some stochastically variable stationary functional $f_m(t, t')$ revealing fast random alternations and the non-averaged population $p_m(t)$ varying more slowly, this approximation yields

$$\langle \langle f_{mm'}(t, t') p_m(t') \rangle \rangle \equiv \langle \langle f_{mm'}(t, t - \Delta t) p_m(t - \Delta t) \rangle \rangle \approx F_{mm'}(\Delta t) P_m(t). \quad (6)$$

Here,

$$F_{mm'}(\Delta t) = \langle \langle f_{mm'}(t, t - \Delta t) \rangle \rangle \quad (7)$$

is the stochastically averaged correlation function changing on fast stochastic intervals $\Delta t = t - t'$, while $P_m(t) = \langle \langle p_m(t) \rangle \rangle$ is the much slower stochastically averaged population appeared as a result of the formal expansion $P_m(t - \Delta t) = \exp[-\Delta t(d/dt)] P_m(t) \approx \exp(-\kappa_{\text{rel}} \Delta t) P_m(t) \approx P_m(t)$. As one sees, this example establishes the other type of relation between nanosystem's characteristic times. Namely, on the short-time scale, Δt of steadying fast changes in the energy level stochastic variation completing the change in level populations with far slower relaxation rate $\kappa_{\text{rel}} \ll (\Delta t)^{-1}$ can safely be neglected. The latter conclusion is supported by the well-known observation that, in the Born approximation for an expansion of the evolution dynamics over the relaxation interaction V to the second order, the steady-state fast intermittent process $f_m(t, t')$ does not introduce any noticeable change in a slow relaxation kinetics of the population $P_m(t)$, if observed at the short times (5)–(7) [40]. Hence, the main objective is to consistently describe the kinetics of $P_m(t)$, by using the GME (3) endowed with approximations (5)–(7) that can follow from the supposed hierarchy of time scales.

For being referred to as consistent, such a hierarchy of the time scales in nanosystems can be reduced to three most relevant ones – chaotic, stochastic, and transient – attributed with the corresponding characteristic times τ_{ch} , τ_{st} and τ_{tr} , respectively, to be related by

$$\tau_{\text{ch}} \ll \tau_{\text{st}} \ll \tau_{\text{tr}}. \quad (8)$$

On the first time scale, the microscopic structure of the Hamiltonians of the whole closed system C , conditioned with factorization of its density matrix, is

formed. On the second time scale, the stationary distribution for random fluctuations of energy level positions in the open part A of the C is complete. On the third time scale, the averaged probabilities of transitions between the levels of the part A embodied in the evolution of level populations are balanced. The price to pay for using the time scales (8) is that one does not regard the evolution of A traced exactly at every instant any more. Instead, one follows up the evolution only subsequent to the chaotic time $t > \tau_{\text{ch}}$ and only with a stationary distribution of random fluctuations of energy levels, which must be completed at the times $t \geq \tau_{\text{st}}$ independently of initial conditions. Moreover, for the nanosystem to be ergodic, one should suppose this stationary distribution unique [55], particularly so as to be a Cauchy-type distribution or a Lorenz-line-shape distribution [56]. Note that, solely subsequent to those periods, i.e., at intermediate times $t \gg \tau_{\text{st}} \gg \tau_{\text{ch}}$, one could be rigorous in saying something about the transient kinetics of steady-state populations of the A at the times $t \geq \tau_{\text{tr}}$, given initial conditions that are compatible with chaotic and stochastic boundary conditions. Therefore, in order to understand the behavior of A in stricter terms, making a dynamic average over the chaotic and stochastic processes at intermediate times needs to be associated with the physical processes, to which these chaotic and stochastic times would be characterized.

As such, the chaotic attribute must indicate that, to proceed further from the very short times $t \ll \tau_{\text{ch}}$, at which the A energy levels are intrinsically highly correlated to the chaotic times $t \approx \tau_{\text{ch}}$, one will reduce the groups of strongly interacted levels to the effectively uncoupled ones and then chaotize them in accordance with some pre-existed distribution (e.g., the Gaussian one). Thus, the chaotic time is expected to be close to the interaction/encounter/scattering time or to the time of establishment of a local equilibrium within A with a highest physical rate. On the other hand, for the highly coherent dynamics of A , the initial chaotization implies that the individual positions of energy levels become not time-independent, but rather statistically distributed. There is, no doubt, a situation of modeling such level positions microscopically unchanged during the elapsed times between two successive encounters. Therefore, if microscopically treating the problem, one can additionally stochastize the eigenenergy levels of the Hamiltonian

of A on such a stochastic coupling time scale (inverse encounter rate scale), which has so to be largely extended from both the corresponding relaxation transition time and the pre-supposed random chaotic time such as $\tau_{\text{st}} \ll \tau_{\text{tr}}$ in (6) and $\tau_{\text{st}} \gg \tau_{\text{ch}}$ in (5), respectively, or as in (8), jointly.

2.3. Method of shortening of description

In physics, quantitatively treating nanoscale systems, one recognizes that the hardness of the problem depends on the complexity of the description. For example, in the small A characterized by $M + 1$ levels $m = 0, 1, \dots, M$ with energies E_m , the description of the equilibrium population P_m^∞ of levels corresponding to the Boltzmann–Gibbs distribution requires M state variables, say, the energy differences $\Delta E_{mm'} = E_m - E_{m'}$ counted from the lower level bound usually let equal zero: $E_{m'=0} = 0$. These form the oscillation time scale $\tau_{\text{os}} = \{|\Omega_{mm'}^{-1}|\}$ with $\Omega_{mm'} = \Delta E_{mm'}/\hbar$ being the natural oscillation frequencies associated with the energies of A . Rather, describing the time-dependent behavior of the nonequilibrium level population $P_m(t)$ expands this set of state variables to a far greater, possibly exponentially great, number of independent parameters, say, the probabilities $W_{mm'}$ of transitions from level m to level $m' \neq m$ constrained by the condition of detailed balance (the principle of microscopic reversibility) [57, 58]. These are brought about by the perturbations of A induced by its weak interaction V with B occurring on the transition time scale $\tau_{\text{tr}} = \{W_{mm'}^{-1}\}$. Here, the main problem is to define a complete set of time constants that will be characteristic of all relaxation transitions between and irreversible decays of the different energy levels of A . However, finding these constants requires solving a set of $M + 1$ ordinary differential equations for generally non-conserved level populations $P_m(t)$ with the exponentially large number of free parameters and the given initial conditions, which comprises the hard “number-of-states” problem [59]. Although the locally Lyapunov-stable solution to this problem always exists [60, 61], to perform an exact calculus of the A kinetics is often unnecessary and expensive computationally. Instead, one intends to understand how the potentially significant number $M + 1$ of levels is correlated so that the descriptions of both microscopically reversible and macroscopically irreversible kinetics are shortened to these for only a few, possi-

bly two-three most relevant effective levels; and how to control the correlations between levels in order to be consistent in associating the calculated amplitudes of level populations with the thermodynamic quasi-averages like the level dimensionality and particles' concentration. Note that this is in a direct correspondence to Bogolyubov's procedure of shortening of the description of nonequilibrium systems originally formulated as the principle of weakening of correlations in solving the initial value problem for the infinite-state integral differential equations, which is equivalent to a procedure of contracting of the number of independent variables in the boundary condition problem for these equations in a distant past, by basing on the idea of a hierarchy of relaxation times in the system [62–65].

2.4. Method of stochastic averaging

This is the case for many functionally significant nanoscale systems that to provide their specific description on the different time and length scales with a necessary accuracy requires giving the specific sense to the otherwise generally random fluctuation processes inevitably observable at the level of experimental data precision. To surmount such insufficiency, one necessitates the correct representations of stochastic phenomena within the limited number of effective parameters that adequately characterize the distributions of random amplitudes and frequencies, as well as biasing for signals. However, when one is interested in obtaining the *exact* analytical results of stochastic averaging, two general scenarios for providing the quantitative analysis can be pointed out. The one scenario deals with modeling a stochastic process by solely discrete random jumps like as in the Kubo–Anderson or kangaroo process [66, 67], while another scenario does with representing it by a continuous time process like the Ornstein–Uhlenbeck process or a Gaussian colored noise [67, 68]. Several important calculations on both scenarios have been done in last decades (see, e.g., [32, 34, 42–44, 47, 54] and references therein). To signify the progress achieved in the field thus far, let us accomplish the method of stochastic averaging on specific examples in more details.

Consider, for instance, a time variation of the stochastic value $\alpha(t)$ that manifests the dichotomous or trichotomous discrete random Markov process of the kangaroo type (cf. Fig. 1). Let each deviation σ_j of

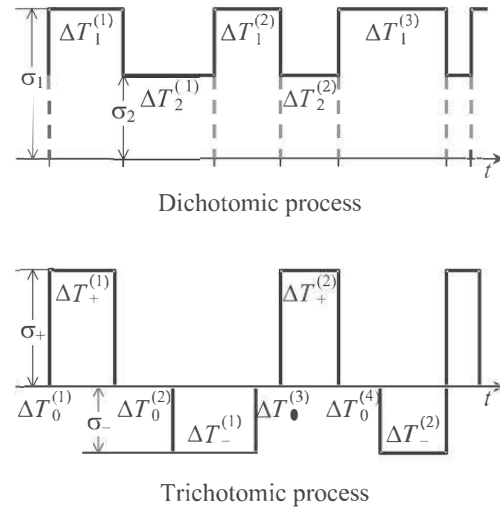


Fig. 1. Examples of two random processes performing discrete jumps between the fixed levels σ_j with the stochastic intervals $T_j^{(i)}$

the random quantity $\alpha(t)$ be equipped with the probability $w_j = T_j / \sum_{j=1}^N T_j$, where $T_j = \nu_j^{-1}$ is the mean stochastic life-time for the j th discrete state of $\alpha(t)$; $j = 1, \dots, N$; so that ν_j is the respective escape frequency. In the theory of discrete stochastic processes [69], the main problem is that, given distributions for σ_j and ν_j , to provide the *exact* stochastic averaging of the products of some stochastic quantities by representing the solution in the general form

$$\langle\langle \alpha(t) f(t) \rangle\rangle = -i \dot{F}(t), \quad (9)$$

without using the decomposition approximation like (6). Here, $f(t) \equiv f[\alpha(t); t]$ stands for the stochastic functional being a dynamic variable obeying the Kubo oscillator equation [70]

$$\dot{f}(t) = i \alpha(t) f(t), \quad (10)$$

while

$$F(t) \equiv \langle\langle f(t) \rangle\rangle = \langle\langle \exp[i \int_0^t \alpha(t') dt'] \rangle\rangle, \quad (11)$$

is the stochastically averaged formal solution of Eq. (10). Since this equation is inherent in many of the stochastic problems of physics [66, 68], the averaged quantity $F(t)$ (11), representing the stochastically averaged characteristic functional of the random variable $\alpha(t)$, is considered as the sought closed solution.

Following to the Brissaud–Frish approach [71], the Laplace-transform $\phi(s) = \int_0^\infty e^{-st} F(t) dt$ of $F(t)$ can be found from the equation

$$\phi(s) = \phi_0(s) + \phi_1(s) \frac{1}{\langle\langle\nu\rangle\rangle - \phi_2(s)} \phi_1(s), \quad (12)$$

where $\langle\langle\nu\rangle\rangle = \sum_j w_j \nu_j$ is the mean escape frequency of the random quantity and

$$\phi_n(s) = \sum_j w_j \frac{\nu_j^n}{(s + \nu_j) + i\sigma_j} \quad (13)$$

is the partial contribution. With Eq. (13), Eq. (12) reduces to the form $\phi(s) = \Phi(s)/\Psi(s)$ with $\Phi(s)$ and $\Psi(s)$ being the polynomials in s . Thus, the general form for the averaged function $F(t)$ reads

$$F(t) = \sum_j \exp(s_j t) \sum_{l=1}^{n(j)} \frac{t^{l-1}}{(l-1)!} \times \\ \times \lim_{s \rightarrow s(j)} \frac{d^{l-1}}{ds^{l-1}} \left[\phi(s) (s - s_j)^{n(j)} \right], \quad (14)$$

where s_1, s_2, \dots, s_N are the roots of the polynomial $\Psi(s)$, and $n(j)$ is the multiplicity of the j th root $s(j) \equiv s_j$.

For applying (12)–(14) to the cases of dichotomous and trichotomous processes, one has to identify both the random $\alpha(t)$ and the averaged $F(t)$ quantities with the corresponding random frequency shift $\omega_{mm'}(t) = [\varepsilon(t)_m - \varepsilon_{m'}(t)]/\hbar$ between two levels m and $m' \neq m$ having the time-dependent energy $E_m(t) = E_m + \varepsilon_m(t)$ with the stochastic addition $\varepsilon_m(t)$, and the averaged correlation function $F_{mm'}(t)$ (6) of stochastically variable positions of these levels, respectively.

a. Dichotomous case. An example of the random behavior of $\omega_{mm'}(t) \equiv \alpha(t)$ having two possible realizations σ_1 and σ_2 is depicted in the upper part of Fig. 1. The corresponding probabilities of these realizations are $w_1 = \nu_2/(\nu_1 + \nu_2)$ and $w_2 = \nu_1/(\nu_1 + \nu_2)$, with each escape frequency $\nu_j = T_j^{-1}$ expressed via the mean escape time $T_j = \lim_{t \rightarrow \infty} (1/t) \sum_k \Delta T_j^{(k)}$ and the random time-interval $\Delta T_j^{(k)}$, respectively. Using (12) and (13) gives

$$\phi(s) = \{s + \nu_c + i[\langle\langle\omega\rangle\rangle + \Delta\sigma(w_2 - w_1)]\} / \\ / \{(s + i\langle\langle\omega\rangle\rangle)^2 + (s + i\langle\langle\omega\rangle\rangle)[\nu_c + i\Delta\sigma(w_2 - w_1)] + \\ + \Delta\sigma^2 w_1 w_2\}, \quad (15)$$

where $\langle\langle\omega\rangle\rangle = \sum_{j=1,2} w_j \sigma_j$, $\nu_c = (\nu_1 + \nu_2)/2$, and $\Delta\sigma = \sigma_1 - \sigma_2$ correspond to the mean stochastic realization of $\omega_{mm'}(t) \equiv \alpha(t)$, the arithmetic mean frequency, and the difference between stochastic realizations, respectively. Determining the roots $s_{1,2} = -i\langle\langle\omega\rangle\rangle - \kappa_{1,2}$ of the polynomial in the denominator of (15) finally yields

$$F(t) = -\exp(-i\langle\langle\omega\rangle\rangle t) [\kappa_2 \exp(-\kappa_1 t) - \\ - \kappa_1 \exp(-\kappa_2 t)] (\kappa_1 - \kappa_2)^{-1}, \quad (16)$$

where

$$\kappa_{1,2} = (1/2) \{(\nu_c \pm q_+) + i[\Delta\sigma(w_1 - w_2) \pm q_-]\}, \quad (17)$$

and

$$q_\pm = \frac{1}{\sqrt{2}} \sqrt{q^2 \pm (\nu_c^2 - \Delta\sigma^2)}; \quad (18) \\ q^2 = \sqrt{(\nu_c^2 - \Delta\sigma^2)^2 + 4\nu_c^2 \Delta\sigma^2 (w_2 - w_1)}.$$

In the case of a symmetric dichotomous process, when $\nu_{1,2} \equiv \nu$; $\sigma_{1,2} \equiv \pm\sigma$; $w_{1,2} \equiv 1/2$ and $\langle\langle\omega\rangle\rangle = 0$, the faster and slower rate constants (17) in (16) fully coincide with the corresponding roots in (15), reducing them to the well-known form $\kappa_{1,2} = s_{1,2} = -(1/2)(\nu \pm \sqrt{\nu^2 - 4\sigma^2})$, see [32, 34]. Therefore, if the energy levels exhibit the high-frequency, but low-amplitude dichotomous jumps $\nu \gg 2\sigma$, then the respective rates simply become $\kappa_1 = -\nu$; $\kappa_2 = -\sigma^2/\nu$. Hence, the main time evolution mostly occurs in this case in the moderately extended characteristic time interval $\nu^{-1} \ll \Delta t \ll \sigma^{-1}$ with

$$F(t) \approx \exp[-(\sigma^2/\nu) t] \quad (19)$$

describing the very high frequency (quantum) limit for the stochastically averaged coarse-grained dynamics in (10), (11).

b. Trichotomous case. A random behavior of $\omega_{mm'}(t) \equiv \alpha(t)$ is represented in the lower case of Fig. 1, with realizations of $\alpha(t)$ given by the quantities $\sigma_0 (= 0)$; σ_+ and σ_- . The probability of the j th realization $w_j = T_j/(T_0 + T_+ + T_-)$ is determined by the mean escape times T_0 ; T_+ , and T_- or, equally, escape frequencies $\nu_j = T_j^{-1}$ with $j = (0, +, -)$. For the sake of simplicity, it is enough to consider the case where the positive and negative deviations, σ_+ and σ_- , are equal to each other $\sigma_\pm = \pm\sigma_T$, equally probable $w_\pm = w_T$, and realized with equal frequencies $\nu_\pm = \nu_T$. So, noting that $\sigma_0 = 0$, we get

$$\phi(s) = [s^2 + s\nu_T(1 + \xi) + w_0\sigma_T^2 + \xi\nu_T^2] / [s^3 +$$

$$+ s^2 \nu_T (1 + \xi) + s(\sigma_T^2 + \xi \nu_T^2) + 2\xi w_T \nu_T \sigma_T^2], \quad (20)$$

where $\xi = \nu_0 / (w_0 \nu_0 + 2w_T \nu_T)$ is the relative escape frequency. Since the denominator of (20) has three roots s_j , there are three characteristic times $\tau_j = |s_j|^{-1}$ associated with the time evolution with the slowest time τ_{slow} corresponding to the asymptotic behavior of $F(t)$ in (11). It follows from (16) that, on the slowest time scale $\Delta t \sim \tau_{\text{slow}}$, one achieves the result more general than in (19):

$$F_{mm'}(t) = \exp(-\gamma_{mm'} t) \quad (21)$$

with

$$\gamma_{mm'} \cong \tau_{\text{slow}}^{-1} = |s_{\text{slow}}| = \frac{2\xi w_T \nu_T \sigma_T^2}{\xi \nu_T^2 + \sigma_T^2} \quad (22)$$

defining the effective half-width of (or a decay rate for) the m, m' -pair of energy levels arisen owing to their stochastic fluctuations. The same quantity is associated with the friction coefficient for the movement within the system that, in accordance with the Stokes law, is proportional to the viscosity of the environment. In the case of the Anderson–Kubo trichotomous process where $\nu_0 = \nu_T \equiv \nu$ and so $w_0 = w_T = 1/3$, the effective half-width (decay) parameter (22) reduces to the expression

$$\gamma_{mm'} \approx \tilde{\sigma}^2 / \tilde{\nu} \quad (23)$$

with $\tilde{\sigma} = \sigma_T / \sqrt{3}$ and $\tilde{\nu} = \nu + (1/4\nu)\sigma_T^2$ being the effective amplitude and frequency parameters of the trichotomous process, which differ from those, σ and ν , respectively, for the dichotomous process (19). This gives a correct calculus of $F_{mm'}(t)$ (21) not only in the quantum limit $\nu \gg \sigma$ of fast stochastic fluctuations as in (19), but also in the classical limit $\sigma \gg \nu$ of moderate stochastic fluctuations realized in nanosystems on a much longer time scale $\Delta t \gg \nu^{-1} \gg \sigma^{-1} \gg \nu/\sigma^2$. Thus, in the latter case, the half-width (decay rate) of (21) turns out to be insensitive to σ

$$\gamma_{mm'} = 4\nu / \sqrt{3}, \quad (24)$$

whereas in the former case, the same quantity to within the redefinition of a natural stochastic amplitude $\tilde{\sigma} = \sigma$ is equal to the half-width of (19),

$$\gamma_{mm'} = \sigma^2 / \nu. \quad (25)$$

c. Sum of infinitely many dichotomous processes. The afore-described trichotomous process, being richer as compared with the dichotomous one in quantitatively characterizing the stochastic behavior of a nanosystem on the different time scales corresponds, in effect, to the case of the sum of two identical and statistically independent dichotomous processes with stochastic amplitude $\tilde{\sigma}$ and frequency ν . However, in the case of an infinite sum of dichotomous processes $\alpha_j(t)$ with identical frequencies ν , where the respective random value $\alpha(t) = \sum_{j=1}^{\infty} \alpha_j(t)$ is regarded bounded in a sense of having the finite summary dispersion $\sigma^2 = \langle\langle [\alpha(t)]^2 \rangle\rangle = \lim_{N \rightarrow \infty} \sum_{j=1}^N \langle\langle [\alpha_j(t)]^2 \rangle\rangle$, using Eq. (14) for the calculus of the stochastically averaged characteristic functional $F(t)$ (11) that has the infinite number of denominator's roots becomes impracticable. But, according to the central limit theorem, this case comprises the Ornstein–Uhlenbeck noise (which is a Gaussian process) [67], for which the corresponding functional exactly reads [68]

$$F(t) = \exp \left[-\frac{\sigma^2}{\nu^2} (\nu t + e^{-\nu t} - 1) \right]. \quad (26)$$

In a full accordance with cases of both the dichotomous (16) and trichotomous (21) processes constrained to considering the slowest time scale $\Delta t \gg \nu^{-1}$, the Ornstein–Uhlenbeck process (26) provides $F(t)$ to have a half-width (decay rate) being dependent on both σ and ν at such extended times $t \gg \nu^{-1}$ like (25). However, contrary to (19) and (23), expression (26) allows one to correctly cover the extremely short times $t \ll \nu^{-1}$ as well. Indeed, in this case,

$$F(t) = \exp(-\sigma^2 t^2 / 2). \quad (27)$$

This form directly corresponds to the familiar Gaussian (or normal) distribution for the characteristic correlation functional (11) [68] with the dispersion σ^2 and the apparent half-width

$$\gamma = \sigma \sqrt{2 \ln 2} \quad (28)$$

that now is independent of ν .

2.5. Method of regularization of transitions

Making a stochastic average of random quantities is the generic situation in physics. Particularly, there is a crucial necessity in stochastic averaging methods above, when the regularization procedures are used

to introduce a definiteness into divergent terms of the perturbation expansion of a physical quantity of interest in some small parameters [8, 9]. For example, the hyperbolic-function terms responsible for the appearance of environment-induced transitions in a power series of the expansion of an evolution operator in the weak system-environment interaction up to a second order are generally ill-defined. Hence, one needs to provide these terms with a new stochastically averaged parameter able to transform them into the well-regularized functionals of the Lorentzian or Gaussian type with the single effective width parameter. This comprises the core of applying any stochastic averaging methods, consisting, for instance, in the introduction of exponential cut-offs in the corresponding divergent integrals (see, e.g., [32, 42–44, 47]). To go further in this direction, one can make more sense for stochastic quantities, by using a thermodynamic model for random fluctuations of the energy of a harmonic oscillator of characteristic frequency ω_c that relates the dispersion and the frequency of such fluctuations with the corresponding values (see, e.g. [34, 35, 54]) $\sigma^2 = \omega_c^2 n(\omega_c)[n(\omega_c) + 1]$ and $\nu = \omega_c[n(\omega_c) + 1/2]$, respectively. Thus, given a (m, m') -pair of energy levels, the effective half-width (23) reads

$$\gamma_{mm'} = \frac{2\omega_c n(\omega_c)[n(\omega_c) + 1]}{2n(\omega_c) + 1}. \quad (29)$$

It is a very remarkable property of this model that, in the case of classical modes $\omega_c \ll k_B T/\hbar$, which are associated with the adiabatic coupling of a nanosystem to an auxiliary molecule oscillating in the gigahertz frequency range at room temperature, the both aforementioned values are reduced to $\sigma^2 = (k_B T/\hbar)^2$, $\nu = k_B T/\hbar$ and so

$$\gamma_{mm'} \approx k_B T/\hbar \approx 4 \times 10^{13} \text{ s}^{-1}. \quad (30)$$

Consequently, for such classical modes, the effective half-widths in (23)–(25), (28) are of the same order and enter with a factor close to 1 into Eq. (21) equivalently for all (m, m') as

$$F_{mm'}(t) = \exp[(-k_B T/\hbar)t]. \quad (31)$$

Due to its generality, this equation comprises the valuable means for providing the truncation regularization of divergent integrals, when describing

the environment-induced transitions that occur with slowest relaxation rates $\kappa_{\text{rel}} \sim \tau_{\text{tr}}^{-1}$, to be much slower than the energy fluctuation rates $\kappa_{\text{fluc}} \sim \tau_{\text{st}}^{-1} \gg \tau_{\text{tr}}^{-1}$ at room temperature, according to a hierarchy of time scales introduced by (8).

There are other important circumstances for properly attaining the regularization objective in nanoscopic systems. First, representing a nanosystem as the small open part of the much bigger closed system assumes that the energy levels one involves for the former (cf. (1)–(4)) do not be inferred deterministically but rather chaotically by supposing an averaged position of levels fixed on the very short chaotic time scale $\Delta t \approx \tau_{\text{ch}}$ of femtoseconds, while letting an immediate position of levels randomly fluctuating on the longer stochastic time scale $\Delta t \approx \tau_{\text{st}} \gg \tau_{\text{ch}}$ of picoseconds. Second, accounting for random fluctuations is made unperturbatively so that using it to provide the regularization of environment-induced transitions treated within the second-order perturbation theory in the interaction V between the nanosystem and its environment is adequate. Third, since the dimensionality of the nanosystem (or the number of most relevant degrees of freedom necessary to describe the kinetic behavior) grows exponentially with the number of its states, considering the evolution of not only level populations, but also states coherences (respective on- and off-diagonal elements of the nonequilibrium density matrix) is almost undecidable and rejected. Finally, last and most, the nanoscopic systems could generally be considered as the very flexible and intrinsically disordered nanoobjects [72–74]. They can make as very fast diffusive jumps over their multidimensional energy surfaces by turning, coiling, bending, twisting, and looping, as well the relaxation transitions between these surfaces of forming the covalent and non-covalent bonds. This leads, in fact, to reducing nanoscale systems to those having that band energy spectrum, which is composed of a large variety of isolated (local) energy levels of stable and/or meta-stable bound states, as well as the very narrow bands of quasiisoenergetic energy levels. Moreover, the latter are becoming only occasionally degenerated, not because of overlapping the respective nearest-neighboring states between each other, but owing to the great number of near-degenerate weakly interacting configurations present around nanosystem’s functional groups within the inherently unstructured disordered regions and in bulk [73, 74].

Thus, to bear the responsibility in providing a proper functionality of nanosystems, there are two principal factors. One is to model the energy level structure for a system of interest, and another is to introduce the interaction of such a system with its environment. However, to provide a capacity for being constructive, that interaction should be involved consistently at the different time scales. Indeed, the highly local interatomic interactions are associated with the formation of nanosystem's energy levels at fast chaotic times. Forcing these levels to adiabatically fluctuate round average positions at moderate stochastic times is rather associated with more extended van der Waals interactions, whereas inducing nonadiabatic transitions between the levels at far longer transient times are almost due to the very weak, highly delocalized interactions of nanosystem's states responsible for the slow relaxation processes. In these cases, to form the time-dependent energy levels, to maintain the levels stationary, and to transit a steady-state level to another one with the particular rate are in a direct correspondence to the environment-driven, environment-controlled, and environment-induced processes, respectively. Therefore, to rigorously describe different environment-dependent processes at the molecular level necessitates introducing, for nanoscopic systems, a consistent kinetics framework compatible with the temporal behavior of the most significant microscopic, mesoscopic, and macroscopic physical phenomena on the chaotic, stochastic, and transient time scales (8).

3. Theory

In nanoscopic systems, any dynamic or transient process contains contributions from the different types of environmental vibrations. Some of them define the common potential energy surfaces involved in transitions, while the others can be referred to as of a heat bath. Just due to a coupling with the equilibrated vibrations of a heat bath, transitions between the different energy levels of a nanosystem appear in the form of time-irreversible kinetic processes. The latter comprise the evolution of nanosystem's levels toward the thermal equilibrium, where their populations obey the Boltzmann relations. However, the stochastic fields created by the interior motion of nanosystem's charged groups significantly influence

the time evolution of state populations. One natural way to account for these fields is to directly introduce them into the unperturbed nanosystem Hamiltonian. This simplifies the quantitative description of kinetic processes and allows one to use only a limited number of stochastic field parameters like the averaged intensity (or amplitude) σ and the mean frequency ν (23), (25).

3.1. Stochastic Hamiltonian

When the exact positions of all atoms in the nanoscopic system is unknown or even indefinite (could be the case for many functional macromolecules), the modeling of environment-induced transition processes should be based on general physical principles embracing the multiple time scales within the consistent kinetics framework. To practically construct a model, three different types of motion in functional nanoscopic systems and their exterior might be considered. First, to form the eigenenergy levels for the nanoscopic system states and the bath states with regard for the chaotization of the positions of these levels due to the action of the strongest interactions within the system. This type of motion is attributed by the shortest time τ_{ch} termed as chaotic. Second, to force the eigenenergy levels, defined at chaotic times, to adiabatically fluctuate due to the action of not very strong random fields. This type of motion, induced by high frequency fluctuations of charged molecular groups, is attributed by the shorter time τ_{st} so-called stochastic. Third, to transit some eigenenergy level of the nanosystem to another one due to a normal vibration (phonon) exchange with the heat bath, in result of a weak nonadiabatic interaction accounted for in second-order perturbation theory. This type of motion, appearing as the irreversible relaxation process, when the phonon energy exactly covers the energy level difference, is attributed with well longer time τ_{tr} named transient. The three times above are combined into a hierarchy of time scales (8).

Consider now the microscopic model, where nanosystem's eigenenergy levels exhibit the stochastic shifts caused by the interaction with the surrounding structural groups, while the relaxation transitions between these levels are associated with harmonic vibrations (phonons) of the heat bath. Let the respective Hamiltonian of the whole system (nanosystem +

+ bath + interaction) have the form

$$H(t) = \sum_m \left\{ E_m(t) + \sum_\lambda \left[\kappa_m^{(\lambda)} (\beta_\lambda^+ + \beta_\lambda) + \hbar\omega_\lambda (\beta_\lambda^+ \beta_\lambda + 1/2) \right] \right\} |m\rangle \langle m| + \sum_{mm'} V_{mm'} (1 - \delta_{mm'}) |m\rangle \langle m'|. \quad (32)$$

Here, $E_m(t) = E_m + \varepsilon_m(t)$ is the energy of the m th nanosystem state (E_m is the adiabatic steady-state energy held in the absence of a random time-dependent classical field in nanosystem's interior, $\varepsilon_m(t)$ is the addition due to this field), $\kappa_m^{(\lambda)}$ is the parameter that describes the deviation of nuclei along the λ th normal coordinate from the nuclear equilibrium position, and ω_λ is the λ th vibration mode (phonon) belonging to the bath Hamiltonian H_B , supposed time-independent, with β_λ^+ and β_λ being, respectively, the operators of creation and annihilation of the corresponding phonon in the heat bath.

In this consideration, the whole system consists of two basic parts. The first part is the nanoscale system (A) with the set of distinct states $\{|m\rangle\}$ and respective time-dependent energies $\{E_m(t)\}$. The second part is the heat bath (B) with a set of non-interacting vibrational modes $\{\omega_\lambda\}$. Both sets are referred to as of forming at every time instant, but with advance of the chaotic times $\Delta t \geq \tau_{\text{ch}}$, while the random alternations of energy levels $\{\varepsilon_m(t)\}$, being regarded less frequent, are completed stationary in advance of the stochastic times $\Delta t \sim \tau_{\text{st}} \gg \tau_{\text{ch}}$. The transitions between already steady-state levels are determined by the last term in (32) containing the matrix elements $V_{mm'}$. These are modeled separately depending on the character and the intensity of the interaction between the nanosystem and the environment. However, for most functional nanoscale systems, this interaction can be considered weak enough, so that it can be attributed with a sufficiently large characteristic time of its occurring, namely the transient time $\tau_{\text{tr}} \gg \tau_{\text{st}} \gg \tau_{\text{ch}}$, in a full accordance with relation (8). In these cases, it is possible to expand the interaction in the nuclear displacements $(\beta_\lambda^+ - \beta_\lambda)$ of the heat bath and then, neglecting the zero-order term, which is trivial for the eigenstate basis $\{|m\rangle\}$, to consider the corresponding linear (one-phonon) and nonlinear (multi-phonon) terms of this expansion as respective perturbations. To accumulate these in a

single term at all orders is the Holstein (polaron-like) transformation [75, 76] using a unitary matrix $U = \exp(\sum_m u_m |m\rangle \langle m|)$, with $u_m = \sum_\lambda g_m^{(\lambda)} (\beta_\lambda^+ - \beta_\lambda)$ being the operator of nuclear displacements in the m th state, and $g_m^{(\lambda)} = \kappa_m^{(\lambda)} / \hbar\omega_\lambda$ is the dimensionless coupling. Multiplying Eq. (32) from the left by U and from the right by U^+ arrives *exactly* at Eq. (2), where

$$H_0(t) = \sum_m (E_m + \varepsilon_m(t) - \sum_\lambda |\kappa_m^{(\lambda)}|^2 / \hbar\omega_\lambda) |m\rangle \langle m| \quad (33)$$

is the angstrom-scale Hamiltonian, whose eigenenergy levels include not only the immediate stochastic (second term in brackets) but also the polaron-like (third term in brackets) shifts,

$$H_B = \sum_\lambda \hbar\omega_\lambda (\beta_\lambda^+ \beta_\lambda + 1/2), \quad (34)$$

is the heat bath Hamiltonian, and

$$V = \sum_{mm'} (1 - \delta_{mm'}) V_{mm'} \exp(u_{mm'}) |m\rangle \langle m'| \quad (35)$$

is the operator of interaction characterizing the relaxation transitions between “phonon-dressed” nanosystem's states with the operators of nuclear displacements $u_{mm'} = \sum_\lambda g_{mm'}^{(\lambda)} (\beta_\lambda^+ - \beta_\lambda)$ and relative dimensionless couplings $g_{mm'}^{(\lambda)} = [\kappa_m^{(\lambda)} - \kappa_{m'}^{(\lambda)}] / \hbar\omega_\lambda$.

Thus, the processes of energy level chaotization within both the nanosystem and the heat bath are assumed to be almost due to the strongest physical interactions immediate in duration and intermittent in occurrence frequency. On the other hand, the interactions underlying the random fluctuations of energy levels are supposed less strong in magnitude and not so rapid in switching time. Yet, these interactions moderate in frequency are adiabatically slaved with respect to far weaker interactions embodied in much slower relaxation transitions between the different energy levels. Moreover, the former reveal themselves in regard to the latter not as a stochastic process of discrete energy shifts, but rather as a stationary Cauchy (Lorentz-like) distribution of the energy levels [56] ultimately appearing as a statistically ensemble-averaged regulator of the environment-induced relaxation transition processes.

3.2. Stochastic equation for a diagonal part of the nonequilibrium density matrix

To perform a kinetic analysis of the temporal behavior of a nanoscale system, the master equation for the evolution of the observable level populations $P_m(t)$ (5), being as statistically, as well stochastically averaged, is required. However, practically achieving this objective is usually done in two steps [32, 34, 35]: to derive a statistically averaged equation for the stochastically non-averaged diagonal part of the nonequilibrium density matrix and to provide the averaging of such a stochastic equation to obtain the master equation for state populations. On the first step, one usually starts from the stochastic Liouville–von Neumann equation in its common form (1) and acts on it by the projection operators \hat{T}_d and $\hat{T}_{nd} = I - \hat{T}_d$. This generates the following coupled system of differential equations for the corresponding diagonal and off-diagonal parts of the density matrix, $\dot{\rho}^{(d)}(t) = \hat{T}_d \dot{\rho}(t)$ and $\dot{\rho}^{(nd)}(t) = \hat{T}_{nd} \dot{\rho}(t)$, respectively:

$$\begin{cases} \dot{\rho}^{(d)}(t) = -i\hat{T}_d L_V \rho^{(nd)}(t), \\ \dot{\rho}^{(nd)}(t) = -i\hat{T}_{nd} [L_0(t) + L_V] \rho^{(nd)}(t) - \\ -iL_V \rho^{(d)}(t). \end{cases} \quad (36)$$

Substituting the second equation into the first one leads to the integral differential equation for the diagonal part of the density matrix

$$\dot{\rho}^{(d)}(t) = - \int_0^t dt' \left[\hat{T}_d L_V S(t, t') L_V \rho^{(d)}(t') \right], \quad (37)$$

where

$$S(t, t') = \exp \left[-i \int_{t'}^t d\tau \hat{T}_{nd} (L_0(\tau) + L_V) \right] \quad (38)$$

is the stochastic evolution operator. In view of the definition of the nonequilibrium density matrix of a nanoscopic system Eq. (37) reads

$$\dot{\rho}_0^{(d)}(t) = tr_B \dot{\rho}^{(d)}(t'). \quad (39)$$

However, owing to both the factorization condition $\rho(t) = \rho_0(t)\rho_B$ for the density matrix of the whole system and Boltzmann's equilibrium condition for the density matrix of the heat bath

$\rho_B = \exp(-H_B/k_B T)/tr_B \exp(-H_B/k_B T)$ well-established in advance of chaotic times $\Delta t \geq \tau_{ch}$ within a hierarchy (8), one can safely execute the coarse-graining of the generally complicated stochastic equation (39):

$$\dot{\rho}_0^{(d)}(t) = - \int_0^t dt' \hat{M}(t, t') \rho_0^{(d)}(t'), \quad (40)$$

where

$$\hat{M}(t, t') = tr_B \left(\hat{T}_d L_V S(t, t') L_V \rho_B \right) \quad (41)$$

is the stochastic transition kernel superoperator.

3.3. Stochastic kinetic equation for non-averaged state populations

Equations (40) and (41) can be treated as the basic coarse-grained stochastic equations for a mathematically strict and physically rigorous description of environment-induced relaxation transitions between nanosystem's levels on the transient time scale $\Delta t \sim \tau_{tr}$ within the hierarchy of time scales (8). The form of (40) is very convenient for providing the expansion procedures in the interaction V of the nanoscopic system with the environment. Particularly, in the Born approximation, one can simply provide $V = 0$ for the evolution superoperator (38), which yields

$$\dot{\rho}_0^{(d)}(t) = -(1/\hbar^2) \int_0^t dt' tr_B \left\{ \hat{T}_d [V, U(t, t')] \left[V, \rho_0^{(d)}(t') \times \right. \right. \\ \left. \left. \times \rho_B \right] U^+(t, t') \right\}, \quad (42)$$

where $U(t, t') = \hat{D} \exp \left[-(i/\hbar) \int_{t'}^t d\tau (H_0(\tau) + H_B) \right]$ is the respective zero-order two-time evolution superoperator.

Since we are mainly interested in the environment-induced relaxation processes occurring in a nanoscopic system on the transient time scale, let us, in what follows, consider only those transitions between the different energy levels, which are caused by their weak coupling to bath phonons. In this case, the “dressed” transition operators $V_{mm'} \exp(u_{mm'})$ with the off-diagonal relaxation interaction (35) are considered as perturbations [34, 35]. Employing perturbation theory to a second order on these operators, one derives

the stochastic kinetic equation for the non-averaged level populations

$$p_m(t) = - \sum_{m'} \int_0^t dt' \left[G_{mm'}(t, t') p_m(t') - G_{m'm}(t, t') p_{m'}(t') \right], \quad (43)$$

where the kernel

$$G_{mm'}(t, t') = (2/\hbar^2) |V_{m'm}|^2 \text{Re}\{Q_{mm'}(t-t') \times f_{mm'}(t, t') \exp[i\Omega_{mm'}(t-t')]\} \quad (44)$$

exhibits a random behavior through the frequency stochastic process $\omega_{mm'}(\tau) = [\varepsilon_m(\tau) - \varepsilon_{m'}(\tau)]/\hbar$ involved in the functional

$$f_{mm'}(t, t') = \exp \left\{ i \int_{t'}^t d\tau \omega_{mm'}(\tau) \right\}, \quad (45)$$

while $\Omega_{mm'} = (1/\hbar) (E_m - \sum_{\lambda} |\kappa_m^{(\lambda)}|^2/\hbar\omega_{\lambda} - E_{m'} + \sum_{\lambda} |\kappa_{m'}^{(\lambda)}|^2/\hbar\omega_{\lambda})$ is the “dressed” natural oscillation frequency and $Q_{mm'}(t-t') = \text{tr}_B\{\rho_B \times \exp[u_{mm'}(0)] \exp[u_{mm'}(t-t')]\}$ is the correlation function reflecting a coupling to the heat bath. If the bath is associated with non-interacting harmonic oscillators (phonon normal modes), then

$$u_{mm'}(\tau) = \sum_{\lambda} g_{mm'}^{(\lambda)} [b_{\lambda}^{\dagger} \exp(-i\omega_{\lambda}\tau) - b_{\lambda} \exp(i\omega_{\lambda}\tau)]. \quad (46)$$

So, we have

$$Q_{mm'}(\tau) = \exp[-\Phi_{mm'}(\tau)], \quad (47)$$

where

$$\Phi_{mm'}(\tau) = \frac{1}{2\pi} \int_0^{\infty} d\omega \frac{J_{mm'}(\omega)}{\omega^2} \left[\coth \frac{\hbar\omega}{k_B T} \times (1 - \cos \omega\tau) + i \sin \omega\tau \right] \quad (48)$$

is of basic importance for any calculations done within the spin-boson model [77–79]. In Eq. (48),

$$J_{mm'}(\omega) = 2\pi \sum_{\lambda} \left(g_{mm'}^{(\lambda)} \omega_{\lambda} \right)^2 \delta(\omega - \omega_{\lambda}) \quad (49)$$

is the spectral function that includes the information on both the normal-mode spectral properties of nanoscopic systems and characteristics of their coupling to the bath vibrational modes.

The representation of $Q_{mm'}(\tau)$ in (47) is not unique and can be presented in the equivalent form

$$Q_{mm'}(\tau) = \exp(-D_{mm'}) \Upsilon_{mm'}(\tau), \quad (50)$$

where $D_{mm'} = \sum_{\lambda} (g_{mm'}^{(\lambda)})^2 [2n(\omega_{\lambda}) + 1]$ specifies the temperature-dependent Debye–Waller factor, while the function

$$\Upsilon_{mm'}(t) = \int_{-\infty}^{\infty} d\omega \prod_{\lambda} \exp(i\omega t) \sum_{q(\lambda)=-\infty}^{\infty} I_{|q(\lambda)|}(z_{\lambda}) \times \left[\frac{n(\omega_{\lambda})}{n(\omega_{\lambda}) + 1} \right]^{q(\lambda)/2} \delta \left(\omega - \sum_{\lambda} q(\lambda) \omega_{\lambda} \right) \quad (51)$$

defines the time-dependence of the correlation function $Q_{mm'}(t-t')$ in (44), with $I_q(z)$ and $n(\omega) = [\exp(\hbar\omega/k_B T) - 1]^{-1}$ being the modified Bessel function and the Bose distribution function, both, respectively, being temperature-dependent. The coupling to the phonons is concentrated in the parameter $z_{\lambda} \equiv 2(g_{mm'}^{(\lambda)})^2 \sqrt{n(\omega_{\lambda})[n(\omega_{\lambda}) + 1]}$, while index $q(\lambda)$ indicates the number of phonons of the λ th mode that accompany the transition. The minimal number of phonons is equal to 1, so that $\sum_{\lambda} q(\lambda) \geq 1$. Form (50) is advantageous with respect to (47), particularly in the case of small nuclear displacements along the λ th normal coordinate, when $z_{\lambda} \ll 1$. This allows us to get the asymptote $I_{|q|}(z) \approx (z/2)^{|q|}/|q|!$, pointing to a single-phonon process as the main contribution to the transition. Therefore, setting both $I_0(z \ll 1) \approx 1$ and $I_1(z \ll 1) \approx (z/2)$ and regarding the other terms in (51) insignificant reduce it to

$$\Upsilon_{mm'}(t) = \sum_{\lambda} \left(g_{mm'}^{(\lambda)} \right)^2 R_{\lambda}(t), \quad (52)$$

where $R_{\lambda}(t) = n(\omega_{\lambda}) \exp(i\omega_{\lambda}t) + [n(\omega_{\lambda}) + 1] \times \exp(-i\omega_{\lambda}t)$ is the respective one-phonon correlation function. Moreover, since $\exp(-D_{mm'}) \approx 1$ in this case, one can further specify the stochastic kinetic equation (43), (44) by solely a single-phonon kernel simply setting

$$Q_{mm'}(t-t') = \sum_{\lambda} \left(g_{mm'}^{(\lambda)} \right)^2 \{ n(\omega_{\lambda}) \exp[i\omega_{\lambda}(t-t')] + [n(\omega_{\lambda}) + 1] \exp[-i\omega_{\lambda}(t-t')] \}. \quad (53)$$

3.4. Stochastically averaged master equation

Deriving the equation for observable populations $P_m(t)$ necessitates to provide an averaging of the stochastic equation (43) within a hierarchy of time scales (8). To this end, the second inequality in (8) implies that the duration of an observation of a target population, provided for a long transient time τ_{tr} , is assumed, in fact, to be much longer than a stochastic time τ_{st} , which so bounds, by itself, the very capability of such observation. This factorizes the averaging of products of the stochastic functionals involved in (43), by employing the possibility for making an average of their separate stationary parts like in (6) with determining both the corresponding observable population $P_m(t)$ (5) and the stochastic correlation functional $F_{mm'}(t)$ (7), respectively.

There are two additional problems in practically performing the calculation of the populations $P_m(t)$ basing on the otherwise strict equation (43). First, the order of taking on the calculus of (43) is of quite basic importance: at first to take a sum over the infinite number $\Lambda \rightarrow \infty$ of phonon modes $\lambda = 1, \dots, \Lambda$, which diverges in general, and only then to take the integral over time t' in the interval from 0 to t . To change the orders of summing and integrating in (43), we must make assumptions about the interrelation between $\gamma_{mm'}$ in $F_{mm'}(t)$ (7) and $\{|\Omega_{mm'}|\}$ in (44), as well as the dependence of the reduced environment-induced coupling parameters on λ :

$$|\chi_{mm'}^\lambda|^2 = |V_{mm'}|^2 [g_{mm'}^{(\lambda)}]^2. \quad (54)$$

Second, setting kernel (53) in Eqs. (43) and (44) assumes that to cover the difference between energy levels involved in the relaxation of the nanosystem is mainly the process of creation or annihilation in the bath of only a one phonon, while the role of multiphonon processes is minor. But this assumption is not critical for describing the transition processes caused by the weak coupling of nanosystem's levels to bath vibrations and can be relaxed in the Born approximation over the nonadiabatic interaction [80, 81].

The both aforementioned arguments allow one to safely turn the upper limit of the integral over t' in (43) to infinity on the transient time scale. As a result, by using (29) and (32) in order to make the average for different stochastic realizations of the non-Markovian integral differential equation (43), one can reduce it to the master equation in the stochastically

averaged form

$$\dot{P}_m(t) = -P_m(t) \sum_{m'} W_{mm'} + \sum_{m'} P_{m'}(t) W_{m'm}. \quad (55)$$

Here, the populations $P_m(t)$, averaged due to (5) and normalized as $\sum_m P_m(t) = 1$, are supposed Markovian on both the transition and the stochastic time scales, as well as regarded properly balanced with the rate constants (transition probabilities) given by

$$W_{mm'} = \frac{2Re}{\hbar^2} \int_0^\infty d\tau \exp[(i\Omega_{mm'} - \gamma_{mm'})\tau] \times \\ \times \sum_\lambda |\chi_{mm'}^\lambda|^2 \{n(\omega_\lambda) \exp(i\omega_\lambda\tau) + [1 + n(\omega_\lambda)] \exp(-i\omega_\lambda\tau)\}. \quad (56)$$

The master equation (55) is typical of the different approaches to the description of the nonadiabatic transition processes in nonequilibrium condensed phase systems [82]. Here, it appears as a result of the averaging over random fluctuations of the energy levels of a nanoscopic system on the stochastic time scale τ_{st} and is necessary for the calculation of the transition probabilities (56) in a wide range of involved characteristic times including the longest transient times τ_{tr} . Importantly, the hierarchy of those times (8) does not enter the master equation (55) explicitly, but is especially required for its derivation in the form of a balance of populations with the rate constants (56). Any information about the involved time scales is neither lost nor filtered out, but rather is correctly accounted for by the corresponding averages – equilibrium occupation phonon numbers $n(\omega_\lambda)$ formed in the bath at chaotic times τ_{ch} , intensities $\gamma_{mm'}$ of the stationary adiabatic fluctuations of the energy levels established in the nanoscopic systems at stochastic times τ_{st} , and parameters $|\chi_{mm'}^\lambda|^2$ of the phonon assisting (i.e. environment-induced) nonadiabatic interaction between the nanoscopic system and the bath, thus being responsible for the irreversible relaxation processes occurred at transition times τ_{tr} , respectively.

3.5. Transition rate constants

As suggested by its form, the probability of transitions between the different states of a nanoscopic system (56) appears as some kind of the Fermi golden

rule where, however, the main attention is paid not to summing over a proper dense set of energy levels of nanosystem's final state [1, 2, 39], but rather to providing a correct averaging on stochastic trajectories for transitions with their different exponentially weighted contributions, according to a Cauchy distribution [56]. This allows one to analyze the different regimes for transition processes dependently on the relation between the thermal broadenings (30) of energy levels controlled by the temperature of the heat bath and the natural frequencies $\{|\Omega_{mm'}|\}$ of quantum oscillations varying from zero to infinity subject to the energy spectrum of a nanosystem.

Taking on the integral over τ in (56) simply yields

$$W_{mm'} = \frac{2\pi}{\hbar^2} \sum_{\lambda} |\chi_{mm'}^{\lambda}|^2 \{n(\omega_{\lambda})\Lambda_{mm'}^{(+)}(\omega_{\lambda}) + [1 + n(\omega_{\lambda})]\Lambda_{mm'}^{(-)}(\omega_{\lambda})\}, \quad (57)$$

where $\Lambda_{mm'}^{(\pm)}(\omega_{\lambda}) = \gamma_{mm'} \{\pi[\gamma_{mm'}^2 + (\Omega_{mm'} \pm \omega_{\lambda})^2]\}^{-1}$ is the high-frequency limit for the stochastic field generated (SFG) Lorentzian [34, 35]. However, to further take on the sum over λ in (57) requires knowing the energy level spectrum of the nanosystem and the relevant values of environment-induced relaxation parameters responsible for its functioning. Therefore, if focusing on a simple, but correct description of relaxation processes in functional nanosystems on the molecular-level scale, one will be interested in only the calculable cases for transition probabilities (57). Moreover, in order to be associated with the specific reaction rates, these transition probabilities must easily be interpretable in the different situations.

Let us confine ourselves to considering the important situation for a nanoscopic system in two limiting cases: the nonadiabatic transitions with $|\Omega_{mm'}| \approx \omega_{\lambda} \gg \gamma_{mm'} \rightarrow +0$ and the adiabatic transitions with $\gamma_{mm'} \gg \omega_{\lambda} \geq |\Omega_{mm'}| \rightarrow +0$. Since relation (30) for $\gamma_{mm'} = k_{\text{B}}T/\hbar$ holds, these cases correspond to the quantum and classical limits, $\hbar|\Omega_{mm'}| \gg k_{\text{B}}T$ and $\hbar|\Omega_{mm'}| \ll k_{\text{B}}T$, respectively. Furthermore, irrespective of the temperature, one can introduce a single rate limit for the symmetric frequency-independent asymptotes $J_{mm'} = J_{m'm} \equiv J_{mm'}(\omega \approx |\Omega_{mm'}|)$ of the one-phonon spectral function (49):

$$J_{mm'} = \lim_{\omega_{\lambda} \rightarrow |\Omega_{mm'}|} (2\pi/\hbar^2) \sum_{\lambda} (|\chi_{mm'}^{\lambda}|^2/\omega_{\lambda}) =$$

$$= (2\pi/\hbar^2) \sum_{\lambda} |\chi_{mm'}^{\lambda}|^2 \delta(|\Omega_{mm'}| - \omega_{\lambda}). \quad (58)$$

Consequently, by introducing the distribution function

$$n(\Omega_{mm'}) = [\exp(\hbar\Omega_{mm'}/k_{\text{B}}T) - 1]^{-1}, \quad (59)$$

with regard for the property $n(\Omega_{mm'}) + n(\Omega_{m'm}) = -1$, and the generalized signum function

$$\text{sgn}(\Omega_{mm'}) = \begin{cases} 1, & \Omega_{mm'} > 0, \\ 0, & \Omega_{mm'} = 0, \\ -1, & \Omega_{mm'} < 0 \end{cases} \quad (60)$$

defined for all $\Omega_{mm'}$ including $\Omega_{mm'} = 0$ with a convention $n(0) \text{sgn}(0) = 1$, one can transform the rate constant (57) to the following generalized form:

$$W_{mm'} = J_{mm'} n(\Omega_{mm'}) \text{sgn}(\Omega_{mm'}). \quad (61)$$

This mathematically unified and physically rigorous relation satisfies the principle of microscopic reversibility (a condition of detailed balance)

$$W_{mm'} = W_{m'm} \exp(\hbar\Omega_{mm'}/k_{\text{B}}T) \quad (62)$$

regardless of the presence of even irreversible kinetic processes in a nanosystem by considering the reverse rates for them to be infinitely rare or almost insignificant. Moreover, expression (61) reproduces well the activationless limit

$$W_{m'm} = J_{mm'} \quad (63)$$

having the near zero or negligibly small activation energy $E^{\text{act}} \equiv |\hbar\Omega_{mm'}| \ll k_{\text{B}}T$, as well as the Arrhenius activation-like limit

$$W_{mm'} = J_{mm'} \exp(-E^{\text{act}}/k_{\text{B}}T) \quad (64)$$

characterized by the sufficiently larger activation energy $E^{\text{act}} \equiv |\hbar\Omega_{mm'}| \gg k_{\text{B}}T$. Therefore, on the stochastic time scale τ_{st} , one can provide the rates of transitions between fluctuating energy levels of a nanoscopic system with accurate regularization and then, on the transient time scale τ_{tr} , consistently endow them with classification by only one of two important types: the mechanistic type (63) of temperature-independent transitions and the Arrhenius type (64) of exponentially temperature dependent transitions.

4. Experimental Support

To illustrate how the rate of the aforementioned environment-induced relaxation transitions (61) calculated for nanosystems on the transient time scale τ_{tr} with the use of the regularization of these transitions performed on the stochastic time scale τ_{st} is implemented in the specific functional biomolecular structures, particularly for interpretation of the temperature-independent kinetics of receptor and circadian proteins in living cells, let us consider two applications, where the comparison of the theory and experiment is salient.

4.1. Temperature-independent desensitization of ATP P2X₃ receptors kinetics of protein macromolecules

The P2X₃ receptors belong to the family of ionotropic receptors widely evolved in the peripheral nervous system. These receptors are highly specific membrane proteins, which link the binding of ATP molecules and/or their analogs to the opening and the closing of the special gate of a selective transmembrane ion pore [83]. Therefore, analyzing the kinetics of the opening and closing processes in the P2X₃ receptors can be compared with the main consequences that follow from the theoretical expressions devised above (61)–(64).

Experimental data reproduced in the upper case of Fig. 2 with the corresponding symbols have been obtained for P2X₃ receptors at the various physiologically important temperatures of 25, 30, 35, and 40 °C, respectively [84]. It has been shown that the different ATP-induced transients measured as activated selective ionic currents at distinct thermostatically controlled temperatures manifest themselves as the same (almost identical) two-stage decrease. To our knowledge, this was the first quantitative observation of a temperature-independent kinetics in application to the gating process of a specific biomolecular structure functioning at the cell membrane level [84]. The evolution of the transient is well described by the theoretical curve shown as a solid line in the upper case of Fig. 2. This curve reflects the double-exponential kinetics for transitions between the open “op” and the closed “cl” (or desensitized) states according to the equation for the desensitization probability:

$$P_{cl}(t) = 1 - P_{op}(t) = 1 - A \exp(-t/\tau_1) - (1 - A) \exp(-t/\tau_2), \quad (65)$$

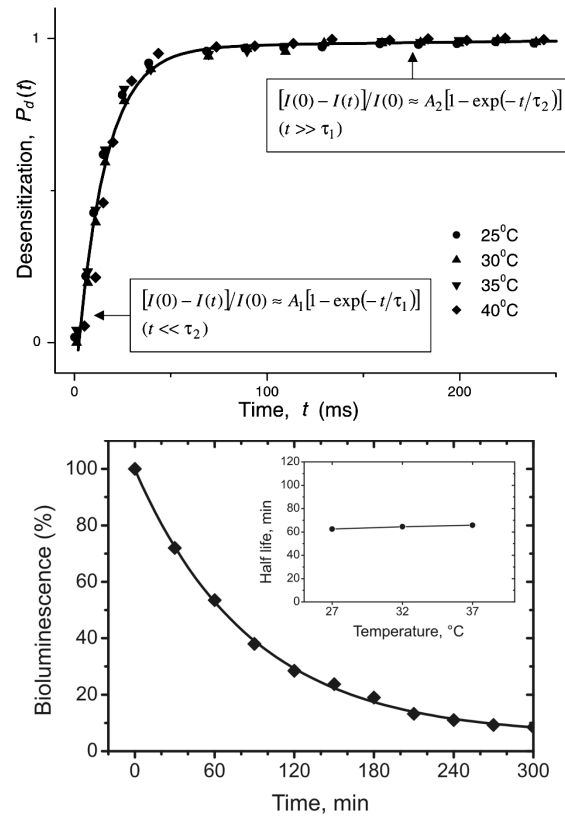


Fig. 2. Two-exponential (upper case) and one-exponential (lower case) temperature-independent kinetics corresponding to the onset of the desensitization of P2X₃ receptors (adapted from [84]) and the degradation of bioluminescence of PER2 protein (adapted from [85]), respectively, and their fit by the expression (65) in the text (solid line) with $I(t)/I(o) \equiv P_{op}(t) = 1 - P_{cl}(t)$ and $A_1 = 1 - A_2 \equiv A$ at different temperatures (shown)

with $A = 0.968$, $\tau_1 = 14.7$ ms and $\tau_2 = 231$ ms being the pre-exponential weight and the two temperature-independent characteristic time constants, respectively.

The physical explanation of the temperature independence of the desensitization process, specifically responsible for the pain sensitivity that to be physiologically relevant should be the same at different temperatures, is straightforward. Especially, it is directly reflected by expression (63) for the mechanistic type of activationless temperature-independent transitions. Nevertheless, the irreversible essentially transient character of the decay (65) can point to the case of highly exoergic quantum limit of (64), which is also temperature-independent. The alternative ex-

planations particularly based on the interpretation of the desensitization process as an order-disorder transition or that which occurs between the nearly degenerate energy levels generally present in the flexible biomolecular structures on the nanoscopic length scale can also be provided [34, 35].

4.2. Temperature-independent kinetics of degradation of circadian proteins

The direct observation of a temperature-independent conformational transformation in proteins has recently been provided at the level of a living clock cell [85]. It is known that a circadian periodicity in different organisms from bacteria to mammals, which are functioning well under different ambient conditions, should remain very robust in the extended temperature range [86]. One explanation of such a basic property is that it occurs due to the temperature insensitivity of the degradation of the specific PER2 protein, which is the key period-determining protein in the mammalian circadian clock cascade. In this context, a circadian periodicity appears to be quite similar to the pain sensation and, hence, can be explained analogously. It has been shown that the phosphorylated PER2 degrades with a particular rate, which is extremely sensitive to a variety of chemical perturbations, but is remarkably unaffected by a physical perturbation such as temperature shifts [85]. *In vivo*, the degradation of the endogenous PER2 is regulated by the casein kinase I_e -dependent phosphorylation. During the phosphorylation, the ATP molecule is hydrolyzed, thus donating inorganic phosphate oxygen groups to the chemical structure of PER2. These groups, being negatively charged, can generate hydrogen bond fluctuations at thermal frequencies on the stochastic time scale $\tau_{st} \sim \hbar/k_B T$ (30) which will affect, in turn, the protein degradation related to far slower conformation motions on the transient time scale $\tau_{tr} \gg \tau_{st}$. Therefore, as for the previous example of P2X₃ receptors, where the characteristic decay times τ_1 and τ_2 are on the transient time scale, while the duration of a dynamical mixing between nearly isoenergetic levels is on the stochastic time scale, the method of regularization of the kinetics for the stochastic time scale regulation of the temperature-independent transition rate of degradation of the endogenous PER2 is quite applicable.

Experimentally, the PER2 degradation is monitored by the bioluminescence decay (the lower case

in Fig. 2). It appears as a single exponential drop of the reduced bioluminescence amplitude, which theoretically corresponds to expression (65) for $P_{op}(t)$ with $A = 1$ and $\tau_1 = 588$ s. As one can see (cf. the inset in the lower case of Fig. 2), the half-times of decays have negligible temperature dependence and may so be considered as temperature-insensitive. The physical mechanism of such temperature independence in the physiologically significant temperature region may be also associated with equilibrium thermodynamic fluctuations occurring on the stochastic time scale against the background of order-disorder transformations in the structure of the protein and its exteriors. This reduces the kinetics of quasiisoenergetic transitions to the irreversible one with the temperature-independent time constant τ_1 analogous to the activationless effect of (63).

5. Discussion and Conclusions

In this contribution, a novel method for the compatible regularization of the environment-induced relaxation transitions in functional nanoscopic systems on the chaotic, stochastic, and transient time scales is proposed. The method is limited to the case of treating the Liouville–von Neumann quantum evolution equation (1) for a density matrix of the whole closed system (C) (2) by the Nakajima–Zwanzig method (3) which considers C as a sum of its small open (A) part (functional nanosystem) and the environment (B) part (heat bath) plus their interaction (V) with projecting the overall evolution of C on state variables of A only. We use the Born–Markov approximation to reduce the dynamic integral differential master equation (40) for the density matrix of A to the kinetic equation (42) and then to the balance master equation (55) for state populations (5). To provide a gain-loss balance for those with relaxation rates by averaging them over both the random fluctuations in A and the equilibrium vibrations in B , we use the quantum approach originally formulated in [32]. In this approach, the Hamiltonian of A (33) is modeled as a diagonal operator involving stochastic additions to eigenenergies, the Hamiltonian of B (34) is considered secular represented by an infinite sum of harmonic oscillators, whereas the operator V of weak interaction between A and B (35) nonadiabatically couples the transitions in A and the processes of creation or annihilation of a one vibrational quantum (phonon) in B with holding the energy balance in C [32, 34, 35, 43].

To be regarded as compatible, the proposed methodology for the regularization of the environment-induced transitions in a nanoscopic system is based upon the method of a hierarchy of time scales. This method provides the nanosystem with a specific kinetics framework that would generally be inherent in it. Such kinetics framework could be thought of that which is able to consistently follow the evolution of populations of the energy levels (5), being statistically and stochastically (see (6) and (7)) averaged on the different time scales. One distinguishes between three most well-separated time scales – chaotic, stochastic, and transient – attributed with the corresponding characteristic times τ_{ch} , τ_{st} , and τ_{tr} , respectively (8). On the first time scale $\Delta t \approx \tau_{\text{ch}}$, the angstrom-level Hamiltonians of the weakly interacted A and B (2), (32)–(35) developed in time due to the Liouville–von Neumann quantum evolution equation (1) for the factorizable density matrix of C are formed. On the same time scale, the reduced equations for the time evolution of diagonal elements of the density matrix of A (37)–(43) governed by the respective transition kernels (44)–(53) are generated. On the second time scale $\Delta t \approx \tau_{\text{st}} \gg \tau_{\text{ch}}$, the stationary distribution (7) for fluctuations of random positions of the energy levels of A (6) is complete, and stochastically averaged master equations (55) balanced with the respectively averaged transition probabilities (56) are established. On the third time scale $\Delta t \approx \tau_{\text{tr}} \gg \tau_{\text{st}} \gg \tau_{\text{ch}}$, the nonstationary transient evolution of the observable populations (5) with the stochastically averaged reaction rates (57) is realized. The price to pay for quantitatively employing the time scales above is that one cannot consider the observable kinetics as a property would be equally controllable at all times. Instead, one should feature the kinetic characteristics as averaged, but changeable and then treat them as those depending on the external controls acting on the different time scales.

To make the method of regularization of the environment-induced transitions constructive, two other general methods are used. These are the method of shortening of description and the method of stochastic averaging. The first method is very useful in providing a nanoscopic system with the contracted number of the most relevant degrees of freedom, allowing one to accurately treat the degenerate energy levels within the efficient two-level schemes (65). Rather, the second method is at the heart of regulariza-

tion techniques developed for the quantitative kinetic analysis. Thus, just the stochastic averaging of the discrete dichotomous (16)–(19) and trichotomous (21), (22) random processes, as well as the continuous Gaussian process (26), (27), provides a method of regularization with the remarkable expression for the energy level half-width (29) due to the thermodynamic fluctuations in a nanosystem. This expression gives the reaction rate constants (57) by exponential cut-offs (31) leading to the convergence even at high temperatures (61)–(64).

In application, we consider the nanoscopic phenomenon, for which the regularization of environment-induced relaxation transitions is very essential. This is the temperature-independent kinetics of nonstationary nanosystems, with the main attention being focused on the nearly isoenergetic transitions. Here, the physical mechanism intended to explain the temperature-independent effect at room temperature largely differentiates from that referring to the quantum tunneling mechanism accompanied by the emission of high-frequency (optical) phonons. Instead, being mechanistic, it works in the classical region of ambient temperatures and at the weak coupling to the environment phonons. Under such conditions, the transition is accompanied by the creation or annihilation of a single low-frequency (acoustic) phonon. The lack of the temperature dependence in the rate constants (63) occurs due to the commonly attended thermodynamic stochastic alternation of participating energy levels with the thermal frequencies. Two experimental observations of the temperature-independent phenomena confirm the proposed approach. Essentially, both observations show the presence of specific band-like energy spectra containing the nearly degenerate bands and the separated energy levels as well in nanoscopic systems. This points to a hierarchy of time scales within the kinetics framework, embodying as short chaotic and stochastic times, as well far longer transient times, at which the environment-induced transitions could only be observed.

In conclusion, the functional nanosystems represent the superatomic structures efficiently operating in changeful noisy environments on the chaotic, stochastic, and transient time scales. Chaotic times have the order of femtoseconds. Before these times, one can hardly say something definite about a nanoscopic system, but, subsequent to them, both the

number and the position of system's energy levels can be determined. The energy levels of the nanosystem persistently fluctuate around their means according to some averaged distributions completed on the stochastic time. The order of the stochastic time scale is ranged from hundreds of femtoseconds to picoseconds, so forming the upper bound for random fluctuations of the thermodynamic environment. Therefore, to have a finite discrete state energy spectrum, the nanosystem first decoheres fast at chaotic times on the angstrom (atomic-level) scale and then classicalizes more slowly at stochastic times on the nanoscopic (single-molecule) scale, before anything of relevant significance happens on the far slower microscopic (macromolecular) and mesoscopic (supramolecular) scales. The functional nanosystems work due to the coupling to the environmental structures. Such a coupling is much weaker than the interaction, which stabilizes both the nanosystem itself and the environment. The bilinear coupling originates from the environment-induced transitions between nanosystem's energy levels. This coupling concerns with the occurrence of one-phonon (harmonic) processes, while higher-order interactions provide a nanoscopic system with the multiphonon (anharmonic) fluctuation processes in positions of the energy levels. The environment-induced transitions occur on the most slow transient time scale, ranging from microseconds to seconds (or even hours), whereas levels' fluctuations are guaranteed for the steady-state completion certainly subsequent to nanoseconds. The rate constants describing the environment-induced transitions are well characterized by only one of two types: the mechanistic-like activationless temperature-independent type of isoergic or highly exoergic transitions and the Arrhenius activation-like exponential temperature-dependent type of highly endoergic transitions. Other rate constants can be reduced to these two types by learning the number and position of the energy levels for a specific functional nanoscopic system under study.

Most generally, using the method for a compatible regularization of environment-induced relaxation transitions consistently describes the evolution of various functional nanoscopic systems on the chaotic, stochastic, and transient time scales. Doing this for nanosystems having isolated energy levels and narrow nearly degenerate energy-level bands, the respective description provides a physical understanding of not

only the phenomena exponentially depending on the temperature such as the enzyme catalysis, but also temperature-independent processes like as the pain desensitization onset or the circadian periodicity in living cells.

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РЕГУЛЯРИЗАЦІЯ ІНДУКОВАНИХ СЕРЕДОВИЩЕМ ПЕРЕХОДІВ У НАНОСКОПІЧНИХ СИСТЕМАХ

Резюме

Запропоновано новий метод регуляризації релаксаційних переходів, що індуються середовищем у наноскопічних системах. Являючи сумісність з хаотичною, стохастичною та перехідною шкалами часу, метод є фізично послідовним та математично строгим. Він дозволяє коректно редукувати еволюцію системи до керуючого рівняння балансу заселеностей її станів із ймовірностями переходів між станами, які добре задовольняють як температурно-незалежній безактиваційній границі, так й ареніусовській експоненційно температурно-залежній границі активаційного типу. Отримані результати прикладаються до опису кінетики температурно-незалежних процесів десенситизації та деградації, що спостерігаються в рецепторних і циркадних білкових макромолекулах.