Vol. 49 (2018) *ACTA PHYSICA POLONICA B* No 8

ANALYTICAL DESCRIPTION OF TWO-STEP DECAY KINETICS AVERAGED EXACTLY OVER DICHOTOMOUS FLUCTUATIONS IN FORWARD RATE

Victor I. Teslenko[†], Oleksiy L. Kapitanchuk[‡]

Bogolyubov Institute for Theoretical Physics
National Academy of Sciences of Ukraine
Department for Theory of Quantum Processes in Nanosystems
14b, Metrolohichna Str., Kyiv 03680, Ukraine

(Received February 5, 2018; accepted March 29, 2018)

The problem of averaging the kinetics of two-stage decaying system subject to dichotomous fluctuations in the forward rate is solved exactly. It is shown that the temporal behavior of system's populations is four-exponential, given finite frequency and amplitude of fluctuations. For frequent fluctuations, this behavior is bimodal typical of deterministic decay, but oppositely, it reduces to three-exponential and bimodal forms, specific of low and resonance amplitude fluctuations. There is an immobilization of initial state at a stochastic resonance point, where forward rate coincides with fluctuation amplitude, whereas backward, decay and fluctuation rates are all negligible.

DOI:10.5506/APhysPolB.49.1581

1. Introduction

The two-step decay kinetic models are ubiquitous in theory and applications for trivial analytical solvability and transparent interpretability in most simple cases [1]. These models provide the temporal behavior of a system of interest with the double exponential kinetics whose exponents represent two time-independent rate constants as the relevant mode parameters. However, in the more complex general cases, the acquired information on these parameters is ambiguous since using only the bimodal exponential representation for kinetics of temporal data patterns becomes insufficient and requires tri-, tetra- or more modal exponential representations [2–4]. In these cases, due

---

[†] `vtes@bitp.kiev.ua`

[‡] `alkapt@bitp.kiev.ua`

to a far richer set of kinetic characteristics, it is hard to expect that involving a double modality in the complex multimodal kinetics provides a complete knowledge of the system. To overcome this hardness, one needs to introduce novel degrees of freedom in the two-step system, either in the form of new states hidden for direct observation but interconverting between each other with the additional rate coefficients, or by allowing new capabilities for the rate constants existed in the two-step system to be randomly fluctuated around their means with some average amplitudes and frequencies. Following the former way is frequent and common, particularly when considering spontaneous and induced kinetic processes in condensed phase systems at the different levels of complexity, see *e.g.* [5–10] and references therein. Rather, following the latter way is more rare and uncommon, even in abstract modeling, because obtaining strict analytical results for it is almost lacking hitherto. However, we should note here the paper of Weiss and Masoliver [11] devoted to describing the kinetic behavior of the two-state–single-stage reacting system with a one fluctuating rate constant according to a random telegraph signal and noticing, for the first time, that this system may be similar to some four-state–four-stage system with non-fluctuating rate constants, though only in the case, where those systems are not fully equivalent or equal between each other but isomorphic in their average characteristic distributions [12, 13]. Unfortunately, the more general problem of the behavior of a two-stage kinetic system subject to random fluctuations in, at least, its one rate constant remains unconsidered. Moreover, even for a single-stage reacting system with one fluctuating rate, the question on extent of its similarity to the other multi-stage kinetic systems lacking fluctuating rates is unanswered. The present paper aims at filling both these caveats by using the physically consistent and mathematically strict means of describing fluctuation processes, very appropriate for the case of adding dichotomous fluctuations to the forward rate of two-state decaying reacting system. We begin with giving a microscopic formulation of the multi-state problem, reduce it to the case of two-state decaying system with fluctuating forward rate and derive an exact analytical solution to the latter problem with establishing that the four-exponentiality in the time domain is its general property. Then, we analyze the limiting cases of solution and compare them with the other cases. Finally, the obtained results are discussed and concluded.

2. General description of two-step decay kinetics with fluctuating forward rate

Any use of a few-level representation as a compromise for simpler consideration of the complex multi-level systems, particularly in describing physicochemical or biological irreversible kinetic processes in terms of two-step decay models, should be based on rigorous theoretical treatments. One of the strictest methods for doing this correctly is to approach the problem with the density matrix theory for the non-equilibrium multi-state system coupled with its fluctuating equilibrium environment [14]. In the framework of this theory, it is possible to provide, in a weak coupling limit, an accurate derivation of the master equation for evolution of the system in the case where it is subjected to the time-dependent (random or regular) environmental influences and external fields (see *e.g.* [15–18] and references therein).

The density matrix theory is based on the Liouville–Von Neumann quantum evolution equation

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

for the density matrix $\rho(t)$ of the whole system, which at a weak system-environment coupling is factorized $\rho(t) = \rho_0(t)\rho_{\mathrm{bath}}$ by the non-equilibrium density matrix of the system $\rho_0(t)$ and the equilibrium density matrix of the environment $\rho_{\mathrm{bath}} = \exp(-H_{\mathrm{bath}}/k_{\mathrm{B}}T)/\mathrm{tr}_B \exp(-H_{\mathrm{bath}}/k_{\mathrm{B}}T)$ (k_{B} and T are the Boltzmann constant and temperature, respectively; trace is over the all states of the environment playing the role of a heat bath), with $L(t) = (1/\hbar)[H(t), \ldots]$ being the Liouville superoperator ($\hbar$ is the Planck constant) related to the whole system's Hamiltonian

$$H(t) = H_0(t) + H_{\mathrm{bath}} + V\,. \tag{2}$$

Therefore, to arrive at the desired level of rigor in representing irreversible kinetic processes by the two-step decay models, it is necessary to make the following steps, namely: *(i)* to define in (2) the time-dependent Hamiltonian $H_0(t)$ of the non-equilibrium system, the Hamiltonian H_{bath} of the equilibrium environment and the Hamiltonian V of their weak interaction accounted for to the second-order smallness; *(ii)* to solve Eq. (1) by averaging it over the thermal excitations of the environment (phonons) and the fast random fluctuations of a system's energy levels leading to their broadening; *(iii)* to find the probabilities of relaxation transitions between the broadened energy levels; and, finally, *(iv)* to determine the sufficient conditions for reduction of a complex multi-stage transition problem to a simpler two-stage decaying problem.

2.1. Microscopic Hamiltonian and master equation

Consider a quantum dynamical system, consisted of the $N+1$ microscopic states $|i = 0, 1, \ldots, N\rangle$, with the energies E_i and interactions between states V_{ij} ($i \neq j$) found in the adiabatic approximation. Let there be a weak coupling of the system with its condense phase environment, represented as the harmonic oscillator bath of normal modes ω_λ distributed according to the Bose function $n_\lambda = [\exp(\omega_\lambda/k_{\mathrm{B}}T) - 1]^{-1}$ (we set $\hbar \equiv 1$). Such a coupling non-adiabatically couples the process of creation and annihilation of environmental phonons, described by operators β_λ^+ and β_λ, to relaxation transitions between the states $|i\rangle$ and $|j \neq i\rangle$ of the system, respectively, so that to induce the singular perturbations of the generator of its unitary (adiabatic) dynamics, with the time-dependent force parameters $\kappa_{i\lambda}(t) = \kappa_{i\lambda}^{(0)} + \kappa_\lambda(t)$ being decomposed into the regular $\kappa_{i\lambda}^{(0)}$ and random $\kappa_\lambda(t)$ parts. This makes possible for the system to absorb or emit environmental phonons instantaneously, but at random times t, so that emitted phonons are carried away by their time-invariant environment dynamics and never come back again. This also allows for the system to transit from one state to another by balancing its transition energies $\Delta E_{ij} = E_i - E_j$ with the process of creation or annihilation in the environment of the corresponding phonons $\omega_\lambda = |\Delta E_{ij}|$. Then the microscopic Hamiltonian of the whole system

$$H(t) = H_S + H_{\mathrm{bath}} + H_{\mathrm{int}}(t) \tag{3}$$

can be written as a sum of three Hamiltonians, that is, the Hamiltonian of the non-equilibrium system

$$H_S = \sum_i E_i |i\rangle\langle i| + \sum_{i,j} V_{ij}(1 - \delta_{ij})|i\rangle\langle j|\,, \tag{4}$$

the Hamiltonian of the equilibrium environment

$$H_{\mathrm{bath}} = \sum_\lambda \omega_\lambda \left(\beta_\lambda^+ \beta_\lambda + 1/2\right)\,, \tag{5}$$

and the Hamiltonian of the system-environment interaction

$$H_{\mathrm{int}}(t) = \sum_i \sum_\lambda \kappa_{i\lambda}(t) \left(\beta_\lambda^+ + \beta_\lambda\right) |i\rangle\langle i|\,. \tag{6}$$

First two Hamiltonians relate to the regular dynamics, while the third one is indeterministic by involving in the time-dependent force $\kappa_{i\lambda}(t)$, a random term $\kappa_\lambda(t)$ being independent of $|i\rangle$.

For a weak interaction between the system's states defined by matrix elements V_{ij} in (4), we can diagonalize the time-dependent Hamiltonian $H(t)$ (3) by using the unitary matrix [19]

$$U_t = \exp\left(\sum_i u_i(t)|i\rangle\langle i|\right)\,, \tag{7}$$

where $u_i(t) = \sum_\lambda g_{i\lambda}(t)\,(\beta_\lambda^+ - \beta_\lambda)$ is the i^{th} state displacement operator and $g_{i\lambda}(t) = \kappa_{i\lambda}(t)/\omega_\lambda$ is the dimensionless coupling. This allows us to perform the non-perturbation transformation of (3), implying a second quantization of the field of non-interacting environmental phonons (5) being under the influence of the system's deterministic dynamics (4). Multiplying (3) from the left by U_t and from the right by U_t^+ (7), we arrive *exactly* at the Hamiltonian (2). Now we see that, in contrast to (3) but as in (2), the transformed interaction Hamiltonian is time-independent

$$V = \sum_{i,j}(1-\delta_{ij})V_{ij}\exp\left(u_{ij}^{(0)}\right)|i\rangle\langle j| \tag{8}$$

with $u_{ij}^{(0)} = \sum_\lambda g_{ij\lambda}^{(0)}(\beta_\lambda^+ - \beta_\lambda)$ being the operator of phonon displacements depending on regular couplings $g_{ij\lambda}^{(0)} = [\kappa_{i\lambda}^{(0)} - \kappa_{j\lambda}^{(0)}]/\omega_\lambda$. Rather, the transformed Hamiltonian of the system

$$H_0(t) = \sum_i \tilde{E}_i(t)|i\rangle\langle i| \tag{9}$$

is time-dependent due to refining of its transformed energy levels $\tilde{E}_i(t)$ with a combination of randomly fluctuating terms $|\kappa_{i\lambda}(t)|^2/\omega_\lambda$ as follows:

$$\tilde{E}_i(t) = E_i - \sum_\lambda\left[\frac{|\kappa_{i\lambda}(t)|^2}{\omega_\lambda}\right]. \tag{10}$$

Nevertheless, Hamiltonian (9) is diagonal with respect to the specific phonon-dressed states with energies (10), such that the corresponding differences between them

$$\Delta\tilde{E}_{ij}(t) = \Delta\bar{E}_{ij} - 2\sum_\lambda g_{ij\lambda}^{(0)}\kappa_\lambda(t) \tag{11}$$

become the linear functions of random additions $\kappa_\lambda(t)$, with $\Delta\bar{E}_{ij} = \Delta E_{ij} - 2\sum_\lambda g_{ij\lambda}^{(0)}\bar{g}_{ij\lambda}^{(0)}\omega_\lambda$ and $\bar{g}_{ij\lambda}^{(0)} = [\kappa_{i\lambda}^{(0)} + \kappa_{j\lambda}^{(0)}]/2\omega_\lambda$ being the relative mean-field energy-level differences and the average dimensionless coupling shifts, both regular, respectively. Importantly, the term proportional to $|\kappa_{i\lambda}(t)|^2$ cancels out of Eq. (11) since it is approximately set independent of the state number $|i\rangle$. However, taking into account such dependence introduces serious complications and thus requires separate consideration.

The afore-formulated microscopic model for the description of the random fluctuations in energy levels of the system is advantageous in that it provides the reduced energy-level differences (11) with strictly linear random additions in the adiabatic approximation. When fluctuation processes underlying these additions occur faster than nonadiabatic transitions between the different energy levels that constitute a common Markovian approximation in condensed-phase systems [14–18, 20], then this allows us to describe the transition dynamics of the system by using the usual rate constant formalism in the framework of a coarse-grained master equation [21]. Furthermore, due to the presence of random fluctuations in positions of energy levels, a process of their relaxation becomes irreversible just because the memoryless exchange of vibrational excitations (phonons) between the system and the environment.

Following Ref. [20] (see also [22]), it is now possible to perform averaging (denoted as $\langle\langle\ldots\rangle\rangle$) over the random realizations of differences (11), given Hamiltonians (2), (9), (5) and (8) in (1). The result is the master equation

$$\dot{p}_j(t) = -p_j(t)\sum_{j'\neq j} W_{jj'} + \sum_{j'\neq j} p_{j'}(t) W_{j'j} \tag{12}$$

for the averaged population of the j^{th} energy level

$$p_j(t) = \left\langle\left\langle\left\{\langle j|\rho_0^{(d)}(t)|j\rangle\right\}\right\rangle\right\rangle \,, \tag{13}$$

where $\rho_0^{(d)}(t) = \hat{T}_d \rho_0(t)$ are the diagonal elements of $\rho_0(t)$ with $\hat{T}_d$ being the diagonalization operator. In (12), and in the sequel, the following quantities averaged over random fluctuations are introduced:

$$\begin{aligned} W_{jj'} &= 2\pi \sum_{\lambda} \left|\chi_{jj'\lambda}\right|^2 \left[n_\lambda \varLambda_{jj'\lambda} + (1+n_\lambda)\varLambda_{j'j\lambda}\right] \,, \\ \varLambda_{jj'\lambda} &= \gamma_{jj'} \left\{\pi \left[\gamma_{jj'}^2 + \left(\omega_\lambda + \Delta\bar{E}_{jj'}\right)^2\right]\right\}^{-1} \,, \\ \gamma_{jj'} &= -\lim_{\tau\to\infty} \left\{\frac{1}{\tau} \ln \left\langle\left\langle \exp\left[i\int_0^\tau \mathrm{d}t \sum_\lambda g_{jj'\lambda}^{(0)} \kappa_\lambda(t)\right]\right\rangle\right\rangle\right\} \,. \end{aligned} \tag{14}$$

Here, $W_{jj'}$, $\varLambda_{jj'\lambda}$ and $\gamma_{jj'} = \gamma_{j'j}$ stand for the probabilities of relaxation transitions in the system (transition rate constants from level j to level j'), the transition Lorentzians, and the parameters of adiabatic broadening responsible for fast random fluctuation processes, respectively, where $\chi_{jj'\lambda} = V_{jj'} g_{jj'\lambda}^{(0)}$ are the parameters of nonadiabatic coupling responsible for slow relaxation processes (for more details, see *e.g.* [20, 22]).

2.2. Transition rate constants and reduction to two-step decay process

The form of averaged transition rate constants (14) entering the coarse-grained master equation (12) for averaged populations (13) allows us to consider only the simplified versions of (14). For this, we note that in the case of fast fluctuations, the level broadening $\gamma_{jj'}$ does not depend on the levels' numbers and scales with the temperature simply as $\gamma_{jj'} = k_{\mathrm{B}}T$ [22]. Therefore, we easily calculate the quantum $|\Delta\bar{E}_{jj'}| \gg k_{\mathrm{B}}T$ and classical $|\Delta\bar{E}_{jj'}| \ll k_{\mathrm{B}}T$ limits of (14), respectively, as

$$W_{jj'} = J_{jj'} \begin{cases} \exp\left(\frac{-\Delta\bar{E}_{j'j}}{k_{\mathrm{B}}T}\right); & \Delta\bar{E}_{j'j} > 0\,, \\ 1\,; & \Delta\bar{E}_{j'j} \leq 0 \end{cases} \tag{15}$$

and

$$W_{jj'} = J_{jj'}\,, \tag{16}$$

where $J_{jj'} = \lim\limits_{\omega_\lambda \to |\Delta\bar{E}_{jj'}|} 2\pi \sum_\lambda (|\chi_{jj'\lambda}|^2/\omega_\lambda) = 2\pi \sum_\lambda |\chi_{jj'\lambda}|^2 \delta(|\Delta\bar{E}_{jj'}| - \omega_\lambda)$ is the rate speed limit for a symmetric one-phonon spectral function $J_{jj'} = J_{j'j} \equiv J_{jj'}(\omega_\lambda \approx |\Delta\bar{E}_{jj'}|)$ [23]. Furthermore, since in the system with $N+1$ states there can be $N(N+1)/2$ transition rate constants with only $2N-1$ of them linearly independent in the leading-order approximation [24], this system can be projected onto the equivalent N-stage absorbing Markov chain

$$|N\rangle \underset{W_{N-1N}}{\overset{W_{NN-1}}{\rightleftarrows}} |N-1\rangle \cdots |2\rangle \underset{W_{12}}{\overset{W_{21}}{\rightleftarrows}} |1\rangle \underset{W_{01}}{\overset{W_{10}}{\rightleftarrows}} |0\rangle\,. \tag{17}$$

Here, the leading order rate constants $\{W_{jj'}\} \equiv \{W_{NN-1}, W_{N-1N}, \ldots, W_{21}, W_{12}, W_{10}\}$ are considered as a complete set of $2N-1$ independent variables calculable in the wide limits (15), (16), while the rate constant W_{01} of a system's transition from absorbing state $|0\rangle$ to nearest neighboring state $|1\rangle$ is regarded negligible

$$W_{01} \ll W_{NN-1}, W_{N-1N}, \ldots, W_{21}, W_{12}, W_{10}\,. \tag{18}$$

To get a representation (17) worthy of two-step decay model, we should additionally suppose

$$\begin{aligned} &W_{NN-1} = W_{N-1N} = \ldots = W_{32} = W_{23} \equiv W\,, \\ &W \gg W_{21}, W_{12}, W_{10}\,; \qquad W_{01} = 0\,. \end{aligned} \tag{19}$$

In these relations, all transient states of (17), but state $|1\rangle$, are assumed nearly equipopulated and quasidegenerate in energy at every time instant. This allows us to match the corresponding state's characteristics to the same levels $p_2(t) = p_{j=3,\ldots,N}(t)$ and $E_2 = E_{j=3,\ldots,N}$, respectively, so regarding the states ergodically mixed. Moreover, by considering such a joint sequence of states, we can introduce their aggregated population

$$p_{\{2\}}(t) = p_2(t)[N(t) - 1] \tag{20}$$

and then combine all of them in one effective state $|\{2\}\rangle$ as

$$|N(t)\rangle \underset{W}{\overset{W}{\rightleftarrows}} |N(t)-1\rangle \cdots |3\rangle \underset{W}{\overset{W}{\rightleftarrows}} |2\rangle \Leftrightarrow |\{2\}\rangle\,. \tag{21}$$

Here, the number $N(t) - 1$ of transient states in $|\{2\}\rangle$ is generally assumed to be not fixed, but a stationary fluctuating quantity with its own dynamics, due to some random structural transitions in the environment or conformational transformations of the environmental macromolecules. For example, if number $N(t)$ corresponds to the number of contacts of a ligand species with solvent molecules in a micro- or nano-volume of the well-stirred bulk solution, then this number will be a function of time that follows the changes in a local configuration of solvent molecules with the solute. Since the folding–unfolding kinetics of protein macromolecules can typically be fitted as the all-or-none two-state stationary random process [25], there is a possibility to allow for the number $N(t)$ to perform statistically independent stochastic displacements in time between the maximum $N_{\max}$ and minimum $N_{\min}$ values such as a discrete (dichotomous) process. The latter occurs because of sudden changes in the instantaneous local configurations of solvent molecules happen by virtue of the conformational transformations of some protein molecule present in the bulk [26]. This molecule does not directly influence the two-step decay as such but, causing random changes in the number of solvent molecules readily accessible for the forward reaction, indirectly impacts on its transition rate [27, 28].

Approximately solving the master equation (12) for the transient states (21) with using (19), we arrive at the reduced two-step decay problem

$$|\{2\}\rangle \underset{b}{\overset{a+\alpha(t)}{\rightleftarrows}} |1\rangle \xrightarrow{k} \tag{22}$$

edowed with an addition of a symmetric dichotomous stochastic process $\alpha(t)$ to the forward rate constant. For brevity, we use the notations

$$a + \alpha(t) \equiv W_{21}[N(t) - 1]^{-1}\,; \qquad b \equiv W_{12}\,; \qquad k \equiv W_{12} \tag{23}$$

and let for the process $\alpha(t)$ be exponentially correlated $\overline{\alpha(0)\alpha(t)} = \sigma^2 \exp(-2\nu t)$ with a zero mean $\overline{\alpha(t)} = 0$ (an overbar designates the averaging over all possible stochastic realizations), such that to perform random jumps between its two discrete values $\pm\sigma$ at mean frequency ν, by obeying the equalities [29, 30]

$$[\alpha(t)]^2 = \sigma^2\,; \qquad \dot{\alpha}(t) = -2\nu\alpha(t)\,. \tag{24}$$

Given these equalities as well as natural inequalities for the stochastic amplitude and fluctuating number of states such as $\sigma \leq a$ and $N_{\min} \leq N(t) \leq N_{\max}$, respectively, we get

$$\sigma = \frac{W_{21}}{2}\left(\frac{1}{N_{\min}} - \frac{1}{N_{\max}}\right) \leq a = \frac{W_{21}}{2}\left(\frac{1}{N_{\min}} + \frac{1}{N_{\max}}\right)\,. \tag{25}$$

Note that stochastic process $\alpha(t)$ involved in (22) to represent discrete dichotomous fluctuations in the forward rate constant comprises a type of macroscopic fluctuation processes. This type of fluctuations describes the stochastic behavior of an aggregate of ergodic states (21), exhibiting immediate jumps between two values of their number in the two local equilibriums at random times. The flight time of the jump is very fast close to the macroscopic diffusion/encounter time, that is, the time of the establishment of macroscopic equilibrium with the highest physical speed [23, 28]. At that, each such equilibrium remains thermodynamically unchanged during the every elapsed time between two successive jumps. Therefore, that aggregate of states represents in fact a single ergodic compartment which avoids any memory effects. In this regard, the macroscopic fluctuations can differ from the microscopic ones since the latter are nonlocal in time and operate not with the fluctuating numbers of locally equilibrium ergodic states in aggregates but energy differences between the different non-equilibrium states. However, in the limit of fast fluctuations of energy levels, the effect of nonlocality disappears and system (9) becomes memoryless or Markovian such as (12), but with the phonon-dressed (11) and randomly broadened (14) energy levels (for a discussion of non-Markovian effects in fluctuating kinetic systems, see *e.g.* [12, 13, 15–18, 20–24, 31]). On the other hand, this demands that in the case of macroscopic fluctuations, we should solve the resulting master equation involving a stochastic addition to the deterministic forward rate constant a exactly, without using any approximations throughout the derivation of a closed equation for the kinetics of stochastically averaged populations, though letting the other rate constants in (22), that is, backward b and decay k rate constants, be deterministically fixed.

2.3. Exact averaging of stochastic differential equations for two-step decay model

Finding a solution to problem (22) requires solving a set of two linear stochastic differential equations, which read as follows:

$$\begin{cases} \dot{p}_1(t) = -(b+k)p_1(t) + [a+\alpha(t)]p_{\{2\}}(t)\,; \\ \dot{p}_{\{2\}}(t) = bp_1(t) - [a+\alpha(t)]p_{\{2\}}(t)\,. \end{cases} \tag{26}$$

To integrate these equations means to provide an averaging of them over a stochastic process and then solve resulting equations with respect to the unknown averages. Introducing the average populations of states $|1,\{2\}\rangle$ as $P_{1,2}(t) = \overline{p_{1,\{2\}}(t)}$ and accounting for the commutativity between operations of averaging and differentiating, we find

$$\begin{cases} \dot{P}_1(t) = -(b+k)P_1(t) + aP_2(t) + \overline{\alpha(t)p_{\{2\}}(t)}\,; \\ \dot{P}_2(t) = bP_1(t) - aP_2(t) - \overline{\alpha(t)p_{\{2\}}(t)}\,. \end{cases} \tag{27}$$

The averaged equations (27) contain the unknown stochastic correlation functional $\overline{\alpha(t)p_{\{2\}}(t)}$. Therefore, they are not closed with respect to average populations $P_{1,2}(t)$ and cannot be solved without specifying the differential equation for $\overline{\alpha(t)p_{\{2\}}(t)}$. For the latter, however, there is the Shapiro–Loginov formula [29] for differentiation of exponentially correlated stochastic functions

$$\overset{\bullet}{\overline{\alpha\, p_{1,\{2\}}}} = \overline{\alpha\, \dot{p}_{1,\{2\}}} + \overline{\dot{\alpha}\, p_{1,\{2\}}} = \overline{\alpha\, \dot{p}_{1,\{2\}}} - 2\nu\overline{\alpha\, p_{1,\{2\}}}\,, \tag{28}$$

where the notation of time dependence (t) is dropped for brevity. However, the use of (28) for $\overset{\bullet}{\overline{\alpha\, p_{\{2\}}}}$ after differentiating of (27) leads to the unknown $\overline{\alpha\, \dot{p}_{\{2\}}}$. Multiplying the second equation of (26) by α and averaging it with the use of (24) and (27), we obtain

$$\begin{cases} \dot{P}_2 = -\dot{P}_1 - kP_1\,; \\ \overline{\alpha\, \dot{p}_2} = b\overline{\alpha\, p_1} - a\dot{P}_1 - a(b+k)P_1 + \left(a^2 - \sigma^2\right) P_2\,. \end{cases} \tag{29}$$

Then, applying a second differentiation to the first equation of (27) with using (28), (29) yields

$$\ddot{P}_1 + (2a+b+k+2\nu)\dot{P}_1 + [a(b+2k) + 2\nu(b+k)]P_1 = b\overline{\alpha\, p_1} + \left[a\,(a+2\nu) - \sigma^2\right] P_2\,. \tag{30}$$

In Eq. (30), there are the unknown P_2 and $\overline{\alpha\, p_1}$. Differentiating (30) leads to the equation

$$\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{d}t}\ddot{P}_1 + (2a+b+k+2\nu)\ddot{P}_1 + \left[(a+b)(a+2\nu) + 2k(a+\nu) - \sigma^2\right]\dot{P}_1 \\
&+k\left[a(a+2\nu) - \sigma^2\right] P_1 = b\,\overset{\bullet}{\overline{\alpha\, p_1}} \qquad (31)
\end{aligned}$$

that due to (28) contains the unknown $\overline{\alpha\, \dot{p}_1}$. This, however, can be considered as a nuisance. By using the first equation of (26) multiplied by α and then averaged, and the second equation of (29), we can get the auxiliary differential equation

$$\overset{\bullet}{\overline{\alpha\, p_1}} = -(b+k)\overline{\alpha\, p_1} + a\dot{P}_1 + a(b+k)P_1 + \left(\sigma^2 - a^2\right) P_2\,. \qquad (32)$$

Differentiating (32) with accounting for the first equation of (29) yields

$$\overset{\bullet\bullet}{\overline{\alpha\, p_1}} + (b+k+2\nu)\,\overset{\bullet}{\overline{\alpha\, p_1}} = a\ddot{P}_1 + \left[a(a+b+k) - \sigma^2\right]\dot{P}_1 + k\left(a^2 - \sigma^2\right) P_1\,. \qquad (33)$$

Multiplying Eq. (33) by b and taking into account in its left-hand side the left-hand part of (31), we derive the resulting differential equation with respect to P_1. Finally, the sought solution to problem (22) can be expressed via the closed differential equation as follows:

$$\begin{aligned}
&k\Big\{2\frac{\mathrm{d}}{\mathrm{d}t}\ddot{P}_1(t) + [2(a+b+2\nu)+k]\ddot{P}_1(t) \\
&+2\left[(a+b)(a+2\nu) + (k+2\nu)(a+\nu) - \sigma^2\right]\dot{P}_1(t)\Big\} \\
&+k\left\{k\left[a(a+2\nu) - \sigma^2\right] + 2\nu\left[a(a+b+2\nu) - \sigma^2\right]\right\} P_1(t) \\
&+\frac{\mathrm{d}}{\mathrm{d}t}\left[\left(\frac{\mathrm{d}}{\mathrm{d}t} + 2\nu\right) D^{(2)}\right] P_1(t) = 0\,, \qquad (34)
\end{aligned}$$

where

$$D^{(2)} = \frac{\mathrm{d}^2}{\mathrm{d}t^2} + 2(a+b+\nu)\frac{\mathrm{d}}{\mathrm{d}t} + \left[(a+b)(a+b+2\nu) - \sigma^2\right] \qquad (35)$$

is an ancillary second-order differential operator, acting on population $P_1(t)$ independently of k.

Equation (34) is the linear homogeneous ordinary fourth order differential equation with constant positive coefficients. Its exact analytical solution is found by standard methods and has the four-exponential form

$$P_1(t) = \sum_{j=1}^{4} c_j \exp(\lambda_j t)\,, \qquad (36)$$

where λ_j are the eigenvalues that correspond to the different modes and c_j are the coefficients determined by the initial conditions. Since the exponents λ_j are non-positive due to the Hurwitz theorem [32] in the case of (34), solution (36) is Lyapunov-stable. Moreover, if all modes λ_j are different, this solution is over-critically damped and is damped critically only with coincident λ_j. However, a concrete expression of (36) is complicated by the presence of a large number of kinetic parameters in (34) and (35), which makes it inappropriate for a comprehensive analytical analysis (but see a less complicated expression presented in Ref. [20] for the deterministic three-stage decay kinetic model). Though, in the case of simple initial conditions, such for instance as $\frac{\mathrm{d}}{\mathrm{d}t}\ddot{P}_1(0) = -1$ (initial jerk), $\ddot{P}_1(0) = 1$ (initial acceleration), $\dot{P}_1(0) = 0$ (initial velocity), $P_1(0) = 0$ (initial displacement), and the trivial boundary equilibrium condition $P_1(t \to \infty) = 0$, it can be analyzed numerically. As an example, Fig. 1 depicts linear (A) and log (B) 3D plots of a four-exponential pattern (36) in its dependence on the value of dichotomous stochastic frequency ν, given fixed other values of rate constants in (22) (inserted in Fig. 1 in inverse time units). Its anterior cross section comprises the biexponential transient of bimodal rise-decay form (see Figs. 1 (A) and 1 (B) at large ν), which is very typical of the usual kinetics of deterministic two-step reactions [33, 34]. However, this form is sighted as a result of progressive transformation of the initial four-exponential form (seen in the posterior cross section of Fig. 1 (B) at $\nu = 0$) via the intermediate three-exponential form (seen in Fig. 1 (B) at moderate ν) to the resulting bimodal form as ν further increases. That trend towards transformation

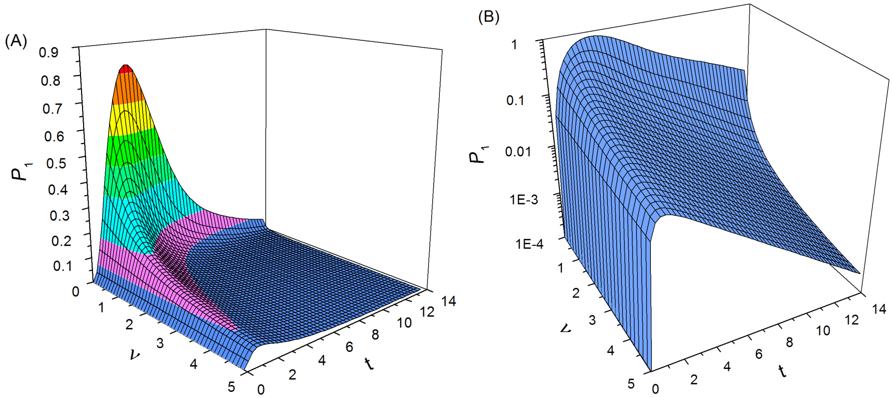

Fig. 1. Linear (A) and logarithmic (B) 3D plots of a four-exponential solution (36) of Eq. (34) for the transient-state population $P_1(t)$ of a two-step decay model (22) in the dependence on time t (in arbitrary units) and stochastic fluctuation frequency ν (in inverse time units); the values of other parameters and initial conditions are as follows: $a = 2, b = 0.2, k = 0.5, \sigma = 0.6, P_1(0) = 0, \dot{P}_1(0) = 0, \ddot{P}_1(0) = 1, \frac{\mathrm{d}}{\mathrm{d}t}\ddot{P}_1(0) = -1$.

of the temporal pattern (36) with ν is summarized in Fig. 2, presenting the differential cross-section plots taken from Fig. 1 (B) at different ν. The form of these plots is informative since the number of bends on them seems most likely to be equal to the number of modes of the temporal pattern less one. According to this representation, the differential of log of a unimodal pattern has no bends (not shown), whereas the differential of log of a bimodal pattern has one bend (shown in Fig. 2 as plot (1)), the differential of log of a three-exponential pattern has two bends (shown in Fig. 2 as plot (2)), and the differential of log of a four-exponential pattern has three bends (shown in Fig. 2 as plot (3)). Thus, we see that an increase of no more than one order of value of ν (from 0.31 to 3.0 in Fig. 2) is necessary to complete the transformation of a four-exponential pattern to its reduced bimodal form. Therefore, the variability of fluctuation frequency ν is thought of as means to play a pivotal role in both the emergence and the reduction of the four-exponentiality of differential equation (34) from and towards its simpler bimodal form, respectively, as the common property of two-step decay kinetics with dichotomously fluctuating forward rate (22). In order to make this effect analytically transparent, let us consider some limiting cases.

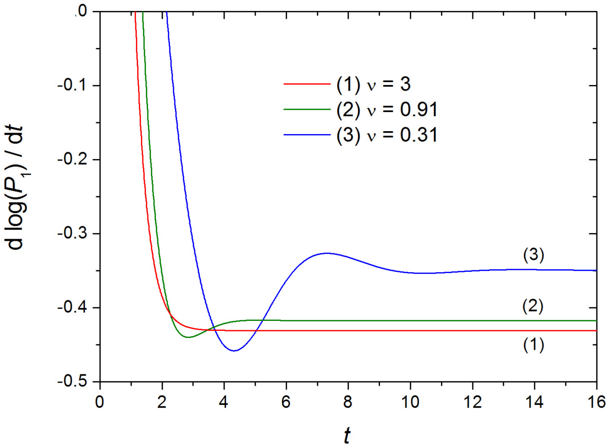

Fig. 2. Differential cross section of 3D plots in Fig. 1 (B) at three stochastic fluctuation frequencies ν (shown in inset in inverse time units).

3. Limiting cases for two-step decay kinetics with fluctuating forward rate

There are several exact cases which allow us to perform a simplified description of the two-step decay problem (22) in analytical terms. The first case is very natural and corresponds to the limit of infinitely large frequency of stochastic fluctuations $\nu \to \infty$. In this limit, Eq. (34) reduces to the well-known equation for the decay of dimensionless amplitude $P_1(t)$ of a harmonic oscillator

$$\ddot{P}_1(t) + (a + b + k)\dot{P}_1(t) + akP_1(t) = 0 \tag{37}$$

whose biexponential solution

$$P_1(t) = \frac{a}{\lambda_1 - \lambda_2}\left[\exp(\lambda_1 t) - \exp(\lambda_2 t)\right] \tag{38}$$

has two eigenmodes $\lambda_{1,2} = (1/2)[-(a + b + k) \pm \sqrt{(a + b + k)^2 - 4ak}]$ that depend on parameters of deterministic rate constants a, b and k only, but are independent of stochastic frequency ν and amplitude σ parameters. However, in the limit of negligibly small stochastic amplitude $\sigma \to 0$, Eq. (34) does not reduce to any bimodal equation and retains its four-exponential form with the explicit dependence on ν being finite. Therefore, from a physics point of view, neglecting a stochastic process $\alpha(t)$ in the initial stochastic equations (26) cannot be achieved by avoiding a stochastic amplitude $\sigma = 0$ as a single means, given that a stochastic frequency ν is bounded, but exclusively by making a stochastic frequency infinite $\nu \to \infty$, even if a stochastic amplitude is arbitrary. There are also other limiting cases, which are worth examining analytically.

3.1. Stochastic reversible one-stage reaction

The stochastic reversible reaction between two states $|i = \{2\}, 1\rangle$, populations $p_i(t)$ of which are normalized $p_1(t) + p_{\{2\}}(t) = 1$, corresponds to the case $k = 0$ in (22). This implies the bi-directed one-stage kinetic model

$$|\{2\}\rangle \ \underset{b}{\overset{a+\alpha(t)}{\rightleftarrows}} \ |1\rangle \tag{39}$$

leading to the stochastic master equation (26) for $p_1(t)$ as follows:

$$\dot{p}_1(t) = -[a + b + \alpha(t)]p_1(t) + a + \alpha(t)\,. \tag{40}$$

Averaging Eq. (40) and substituting the result for $\overline{\alpha(t)p_1(t)}$ in (30) with $P_2(t) = 1 - P_1(t)$ yield the second-order equation

$$D^{(2)}P_1(t) = F_1\,. \tag{41}$$

Here, $F_1 = a(a+b+2\nu) - \sigma^2$ is the initial force that acts on a stochastically averaged population $P_1(t)$ to establish for it its stationary mean value attained at equilibrium

$$P_1^{\infty} = \frac{a(a+b+2\nu) - \sigma^2}{(a+b)(a+b+2\nu) - \sigma^2} \,. \tag{42}$$

An analogous force $F_2 = b(a+b+2\nu)$ acting on the population $P_2(t)$ gives a stationary value $P_2^{\infty} = b(a+b+2\nu)/[(a+b)(a+b+2\nu) - \sigma^2]$. The same result follows from the fourth-order equations (34), (35) at $k = 0$ too, given the normalization condition. This means that, in general, the four-exponentiality of (34) is divided into two parts — the fully reversible part (35), (39) governing the establishment of a local equilibrium between the states provided values of their equilibrium populations are shifted, and the irreversible part, given in the figure brackets of (34), responsible for the decay of these populations to zero with the rate constant proportional to k.

For the initial conditions $P_1(0) = \dot{P}_1(0) = 0$; $\ddot{P}_1(0) = F_1$ and the stationary condition (42), solving (41) is elementary

$$P_1(t) = \frac{a(a+b+2\nu) - \sigma^2}{(a+b)(a+b+2\nu) - \sigma^2} \left[1 - \frac{\lambda_1 \exp(\lambda_2 t) - \lambda_2 \exp(\lambda_1 t)}{\lambda_1 - \lambda_2}\right] , \tag{43}$$

where $\lambda_{1,2} = -(a+b+\nu) \mp \sqrt{\nu^2 + \sigma^2}$. However, despite its elementarity, solution (43) does not correspond to that of any one found in the frame of some equivalent deterministic four-state system, which is constructed so that to be compatible with a stochastic two-state kinetic system (39), as has been noted in Ref. [11]. Moreover, such an equivalence can be achieved only in the limiting case $b \to 0$, where the deterministic four-state system takes the form of

$$\left|1^{(-)}\right\rangle \underset{a-\sigma}{\longleftarrow} \left|2^{(-)}\right\rangle \underset{\nu}{\overset{\nu}{\rightleftarrows}} \left|2^{(+)}\right\rangle \overset{a+\sigma}{\longrightarrow} \left|1^{(+)}\right\rangle . \tag{44}$$

For this system, starting from a master equation for populations $p_{1,2}^{(\pm)}$ of individual states $|1^{(\pm)}\rangle$ and $|2^{(\pm)}\rangle$, introducing for them the corresponding aggregated populations $\Gamma_{1,2} = p_{1,2}^{(+)} + p_{1,2}^{(-)}$ and solving the equations obtained for these populations, respectively, we indeed simply find that $\Gamma_1(t) = 1 - [\lambda_1 \exp(\lambda_2 t) - \lambda_2 \exp(\lambda_1 t)]/(\lambda_1 - \lambda_2)$, which coincides with (43) at $b = 0$. But if $b \neq 0$, for this case to be consistent with (39), we must equip (44) with the additional transitions not only from states $|1^{(\pm)}\rangle$ to states $|2^{(\pm)}\rangle$ with rates b but also between the states $|1^{(-)}\rangle$ and $|1^{(+)}\rangle$ with rates ν. In result, the equivalence between the stochastic two-state system and the deterministic four-state system loses its sense, due to incompatibility both with the normalization condition for populations and the detailed balance condition for the every closed cycle of rate constants, which emerge in the deterministic system. This signifies the novelty of solution (43) with respect to that obtained in [11], due to its ability of combining together the consideration of deterministic and stochastic processes into a unified approach in the framework of kinetic master equation (12) accounting for both the microscopic and macroscopic fluctuations in the system.

On the other hand, the steady-state population P_1^∞ (42) can be expressed in also a new form

$$P_1^\infty = \frac{\tilde{a}}{(\tilde{a}+b)}\,, \tag{45}$$

where $\tilde{a} = a - \sigma^2/(a+b+2\nu)$ is the renormalized forward rate constant. If now to apply this expression to a macroscopic deterministic two-state system initiated from state $|2\rangle$ with rate $\tilde{a}$

$$|\{2\}\rangle \underset{b}{\overset{\tilde{a}}{\rightleftarrows}} |1\rangle \tag{46}$$

and allow for it the stochastic resonance condition $a = \sigma$ at the critical point $b = \nu = 0$ where $\tilde{a} = 0$, then we can observe the effect of stochastic immobilization of this system in that state: $P_1^\infty = P_1(t) = 0; P_2^\infty = P_2(t) = 1$. In this process, the system is pulled stochastically into its initial state every time once it is about transfer to the other state. Indications for the stochastic pulling effects are found in telecommunication fibres and electron devices [35, 36]. Other examples of stochastic resonance processes in macroscopic two-state systems such as displayed by a particle in a two-well potential are diffusion in crystals, conformational transitions in macromolecules, activated chemical reactions, *etc.*, see *e.g.* [37] and references therein. However, when trying to interpret these processes by doing the same trick with a stochastic resonance for the kinetics of population $P_1(t)$ in (43) as for its stationary value P_1^∞ in (45), one inevitably is faced with an incompatibility: Namely, the statements are that a stochastic one-step reaction (39) follows the second-order differential equation (41) and is hence bimodal (43), while a deterministic one-step reaction (46) follows the first-order differential equation such as $\dot{P}_1(t) = -(a+b)P_1(t) + a$ and is, therefore, unimodal $P_1(t) = [a/(a+b)]\{1 - \exp[-(a+b)t]\}$, which is contradictory. Furthermore, this incompatibility cannot be relaxed fully for any instance of the two-, three- or more state system, for example, by increase both in the number of states and in the number of rates for transitions between states.

However, there is a single exception for the case $b = 0$ of stochastic unidirected one-step reaction (39) entirely equivalent in its bimodal kinetics to the deterministic behavior of a three-stage system (44).

3.2. Stochastic irreversible two-step decay

The stochastic decay from initial state $|2\rangle$ through intermediate state $|1\rangle$ via the two irreversible steps in (22) corresponds to the unidirected two-stage reaction

$$|2\rangle \xrightarrow{a+\alpha(t)} |1\rangle \xrightarrow{k} \; . \tag{47}$$

Setting $b = 0$ in Eq. (30) and differentiating it with the use of the first equation of (29) yield

$$\begin{aligned} &\frac{\mathrm{d}}{\mathrm{d}t}\ddot{P}_1(t) + [2(a+\nu)+k]\ddot{P}_1(t) + \left[a(a+2k+2\nu) + 2k\nu - \sigma^2\right]\dot{P}_1(t) \\ &+k\left[a(a+2\nu) - \sigma^2\right]P_1(t) = 0\,. \end{aligned} \tag{48}$$

According to (36) for the initial conditions

$$P_1(0) = \dot{P}_1(0) = 0\,; \qquad \ddot{P}_1(0) = -\frac{\mathrm{d}}{\mathrm{d}t}\ddot{P}_1(0)[2(a+\nu)+k]^{-1} = f_1\,, \tag{49}$$

where $f_1 = a(a+2\nu) - \sigma^2$ is the spontaneous initial force virtually acting on an evolving in time population $P_1(t)$ due to fluctuations in the forward rate, an exact three-exponential solution of (48) reads

$$\begin{aligned} P_1(t) = {} & \left[a(a+2\nu) - \sigma^2\right] \\ & \times\left[\frac{\exp(\lambda_1 t)}{(\lambda_1-\lambda_2)(\lambda_1-\lambda_3)} + \frac{\exp(\lambda_2 t)}{(\lambda_2-\lambda_1)(\lambda_2-\lambda_3)} + \frac{\exp(\lambda_3 t)}{(\lambda_3-\lambda_1)(\lambda_3-\lambda_2)}\right]. \end{aligned} \tag{50}$$

This solution is over-critically damped with three non-positive modes $\lambda_{1,2,3}$ obeying the equation

$$\lambda^3 + [2(a+\nu)+k]\lambda^2 + \left[a(a+2k+2\nu) + 2k\nu - \sigma^2\right]\lambda + \left[a(a+2\nu) - \sigma^2\right]k = 0\,. \tag{51}$$

It is hence instructive to consider the reduced cases of (50) by relating to different deterministic, a and k, and stochastic, ν and σ, parameters.

The first case corresponds to the limit of very frequent stochastic fluctuations

$$2\nu \gg a, k\,. \tag{52}$$

In this limit, expression (50) reduces to a bimodal solution

$$P_1(t) = \frac{a}{a-k}\left[\exp(-kt) - \exp(-at)\right] \tag{53}$$

that directly coincides with solution (38) at $b = 0$. Moreover, solution (53) represents a well-known equation typical of describing the different two-step transient irreversible processes from ligand-controlled reactions [38] to radioactive decay [39].

The second case is the limit of negligibly small stochastic amplitude $\sigma \to 0$. In this case, solving (51) gives $\lambda_1 = -k; \lambda_2 = -a; \lambda_3 = -(a+2\nu)$. For (50), this leads to a three-exponential solution

$$\begin{aligned} P_1(t) = {} & \frac{a(a+2\nu)}{2\nu(a+2\nu-k)} \\ & \times \left\{\exp[-(a{+}2\nu)t] + \frac{2\nu}{a-k}\left[\exp(-kt) - \frac{a+2\nu-k}{2\nu}\exp(-at)\right]\right\} . \end{aligned} \tag{54}$$

Solution (54) differs from its reversible analog (43) at $\sigma = 0$, because the latter reduces to a unimodal form $P_1(t) = [a/(a+b)]\{1 - \exp[-(a+b)t]\}$ that is independent of ν, while the former remains three-exponential being dependent on ν.

The third case is the limit of very rare fluctuations

$$2\nu \ll a, k \tag{55}$$

that is opposite to (52). If to combine this limit with the second case $\sigma \to 0$, a three-exponential solution (54) ceases to depend on ν, approaching the unusual quasi-bimodal form

$$P_1(t) = \left[\frac{a}{(a-k)}\right]^2 \left\{\exp(-kt) - [1 + (a-k)t]\exp(-at)\right\} . \tag{56}$$

Finally, the fourth case is when the stochastic amplitude reaches its maximum such as $\sigma \cong a$. In this case, the limit taken for the stochastic frequency ν, either (52) or (55), can influence on the bimodal parameters. Thus, as expected from (38), solution (50) reduces to its usual form (53) in limit (52), whereas in limit (55), the diverse bimodal solution follows:

$$P_1(t) = \left[\frac{2a}{(2a-k)}\right]\left[\exp(-kt) - \exp(-2at)\right] . \tag{57}$$

This solution is different as with regard to that (43) of reversible reaction (39) as well as to both those (53) and (56) of irreversible reaction (47) with, respectively, the frequent (52) and the rare (55) low-amplitude fluctuations in the forward rate.

Figure 3 compares the temporal behavior of bimodal solutions for the first, third and fourth cases noted above in the corresponding limits of stochastic fluctuation parameters ν and σ, given the deterministic rate constant parameters a and k. As seen, three solutions (53), (56), (57) for irreversible reaction (47), while all being bimodal or, at least, quasi-bimodal in their form and look very similarly, are in fact not close to one another in the full time interval. Consequently, in the conditions of fluctuating forward rate constant, a single information that some transient intermediate of decay reaction in question, say a non-stationary state population, evolves in time according to a bimodal distribution is insufficient and does not determine by itself both the order of reaction — one-step or two-step and the type of reaction — deterministic or stochastic, as well as does not define the most appropriate values of its rate and fluctuation parameters. The same is true, even to a greater extent, for tri-, tetra- and more modal distributions of populations too. However, in these cases, the substantial additional information about the character of concrete multi-modal temporal patterns is required.

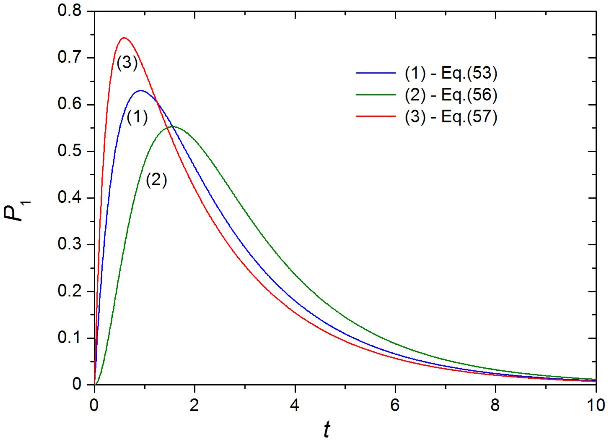

Fig. 3. Bimodal and quasi-bimodal population plots in three limiting cases of parameters $a = 2, b = 0.2, k = 0.5$ given in inverse time units.

3.3. Stochastic resonance point

Limiting cases described above are typical in a sense that they implement within themselves the bimodal projections (38), (53), (56), (57) of the four-exponential case (34) most clearly and correctly. There is hence high confidence in their ability for describing in (34) also a stochastic resonance point. A resonance point of the stochastically perturbed system represents a specific critical point in its multi-modal dynamics where eigenvalues of two or more modes coincide with one another so that direction of the preferential relaxation process — forward or backward — is indeterminate and the resulting overall relaxation rate is zero, given appropriate initial conditions. Formally, a stochastic resonance point corresponds to a consistent zero point implicit in the zeroth- and first-order time derivative terms of differential equation. With respect to the bimodal equation (41) of reversible one-stage model (39) and the three-exponential equation (48) of irreversible two-stage model (47), both with the nonzero forward rate constant $a > 0$, jointly taking the corresponding terms to zero leads to two respective identities

$$a(a+2\nu)+2b(a+\nu)-\sigma^2=0\,; \qquad a(a+2k)+2\nu(a+k)-\sigma^2=0\,. \tag{58}$$

A union of these identities is compatible with a single quadruple point of a stochastic resonance

$$\sigma=a\,; \qquad \nu=0\,; \qquad b=0\,; \qquad k=0 \tag{59}$$

consistent with a zero point of the four-exponential equation (34) for a two-step decay model (22) too.

The afore-defined point (59) is a four-dimensional coordinate (x_1, x_2, x_3, x_4) that denotes a single position $(1,0,0,0)$ in the reduced rate constant space $(x_1=\sigma/a, x_2=\nu/a, x_3=b/a, x_4=k/a)$ scaled with a nonzero a to form a natural scale for the rate constants in (22). Due to criterion of matching the forward rate and stochastic amplitude $(a=\sigma)$, this point comprises the necessary stochastic resonance condition. On the other hand, point (59) is a critical point in the vicinity of which three sufficient conditions are in addition realized to allow for the over-critically damped four-exponentiality (34) to be damped critically in a bimodal fashion (53), (56), (57). While coinciding the forward rate a with stochastic amplitude σ resonantly, three other system's rates, that is, the backward rate b, the decay rate k, and the fluctuation rate ν turn out to be almost insignificant with respect to a at this point. Physically, this directly corresponds to the effect of stochastic immobilization noticed above in (45), (46). The same effect follows from solution (50) for also the irreversible two-stage model (47), but only if to apply the resonance condition (59) in perfect order: first $k=0$ and then $\nu\to 0$. In this case, we approximately derive from (50) a bimodal solution

$$P_1(t)=\left[1-\frac{\lambda_1\exp(\lambda_2 t)-\lambda_2\exp(\lambda_1 t)}{\lambda_1-\lambda_2}\right] \tag{60}$$

with two modes $\lambda_{1,2} = -(a+\nu) \mp \sqrt{\nu^2 + a^2}$, and further arrive at a mode free solution

$$P_1(t)|_{(\nu/a)\to 0} \cong \left[1 - \exp(-\nu\, t) + \left(\frac{\nu}{2a}\right)\exp(-2at)\right]\Big|_{(\nu/a)\to 0} \to 0\,. \qquad (61)$$

The latter really signifies for the two-state system (47), conditioned by $k = 0$, its immobilization in the initial state $|2\rangle$, occurring due to the presence of zero in frequency ($\nu = 0$) yet resonant in amplitude ($\sigma = a$) fluctuations in the forward rate.

However, applying a resonance condition (59) to (50) in the opposite order, first $\nu = 0$ and then $k/a \to 0$, reduces the corresponding mode free solution, which arises now from (57), to

$$P_1(t) = [1 - \exp(-2at)] \underset{t\to\infty}{\longrightarrow} 1\,. \qquad (62)$$

This does not cause immobilization of system (47) in its initial state $|2\rangle$ but instead leads to a strange attraction of the system to its final state $|1\rangle$. Such an attraction is furthermore strange since it does not occur in the reversible one-stage model (39) at all. Immobilization in this model always occurs in the initial state $|2\rangle$ independently of the order in which the critical values of rate parameters ν and b are actually taken to zero, that is, either first $b = 0$ and then $\nu \to 0$ or first $\nu = 0$ and then $b \to 0$. Indeed, for both orders, we get the limit $P_1(t) \underset{t\to\infty}{\longrightarrow} 0$, which is opposite to (62) but almost corresponds to (61). Therefore, not only in the case of low amplitude fluctuations $\sigma \to 0$ (56), but also in the case of fluctuations with resonant amplitude $\sigma = a$ (57), the limit of very rare fluctuations (55) is untypical for the irreversible two-stage model (47). The temporal behavior of the latter does not reproduce kinetics (43) of the reversible one-stage model (39) in this limit, as well as does not correspond to kinetics (38) that must be common for the limiting models of irreversible two-step decay (47), with $b = 0$ and $k \neq 0$, and reversible one-step decay (39), with $b \neq 0$ and $k = 0$, at large fluctuation frequency $\nu \to \infty$ (52).

The above is true even with a bigger count of the general two-step decay model (22) too. With respect to the four-exponentiality in its transient-state population kinetics accounting for the infrequent and resonant discrete stochastic fluctuations in the forward rate, such a more complex two-step decay model has a far greater complexity than both an irreversible two-step decay model and a reversible one-step model. However, the desired detailed analysis of this item, particularly with concern to the distinction between ordering of alternatively removing either the deterministic decay rate or the stochastic fluctuation rate in slowly decaying and rarely fluctuating two-step–two-state systems, requires separate consideration.

4. Discussion and conclusions

In the present paper, the problem of the two-step decay in a microscopically reduced two-state system subject to discrete macroscopic fluctuations in the forward rate (22) approximated by a symmetric dichotomous stochastic process is solved exactly. Using the Liouville–Von Neumann microscopic approach (1)–(9) for description of the time evolution (12) of population (13) of the ergodically degenerated and randomly broadened system's energy levels (14), the equation for kinetics of transient population in the two-state system averaged over the stochastic process is derived in a closed analytical form (34). It is shown that the solution of this equation, which is in general four-exponential (36), reduces to the three-exponential (50), (54) and bimodal (38), (43), (53), (56), (57) forms, respectively, in the corresponding limiting cases (47) and (39). That reduction appears as adequate for a full range of the rate constant space in (22), but a stochastic resonance point (59). At this point, forward rate a is resonantly coincident with stochastic amplitude σ, while decay rate k, backward rate b, and fluctuation rate ν are negligible with respect to a. However, in the vicinity of stochastic resonance point, the order of vanishing k and ν is important. Thus, if one would like to take to zero first k and then ν, then irreversible two-stage system (47) correctly reproduces the effect of stochastic immobilization (61) in the system's initial state typical of the unidirected reversible one-stage system (39), (46). On the contrary, if one would like to do so in the opposite order, first $\nu = 0$ and then $k \to 0$, the effect of vanishing of k cannot be neglected, leading instead to an attraction of the system to its final state (62).

One reason for this discrepancy is that at a very low, but finite k, the two-state decaying system (22) becomes non-ergodic, because the first equation for a state's populations in (29) breaks down the normalization condition of these populations typical of the two-state reversible system (39). Moreover, there can appear different types of stochastic motion in the two-state system (22). In general, one indicates relaxation motion which reversibly takes the system toward its stationary state with the forward a and backward b rates, decaying motion which irreversibly degrades it away from this state with the rate k, and fluctuation motion which randomly interrupts its forward rate by means of symmetric dichotomous stochastic process with the mean amplitude $\sigma \leq a$ and frequency ν. In the two-state system (22), these motions can be in the distinction between using them for description of the temporal behavior of populations. Especially, such a distinction is apparent in the case of resonant and rare fluctuations, *i.e.* in the vicinity of a stochastic resonance point. The latter is typical of the many non-stationary non-equilibrium systems, such as analogue electrical circuits [40], bistable optical devices [41], or bistable macromolecular reactions [42]. Therefore, in terms of its temporal behavior, the two-state system (22) can be considered as a first approximation to those more complex systems, which exhibit a lack of both the detailed balance condition for relaxation rates and the normalization condition for populations in their kinetics, and demonstrate the breaking of symmetry between relaxation and fluctuation phenomena under the stochastic resonance condition as well [40]. In this context, it would be likely to suppose that relations (50), (53), (54), (56), (57) obtained here in the various limits (52), (55) may reveal some new kinetic properties at the level of simple two-state decaying systems subject to resonant and rare fluctuations in their rate constants, and can be observed in the future experiments as two-, three- and four-exponential temporal patterns (38), (50), (34)–(36) of a transient state's populations probed in the different conditions.

Thus, basing on the results obtained, the main conclusions are as follows:

1. Allowing for the forward rate in the two-state decaying system, whose deterministic time evolution is known to be simply bimodal, to dichotomously fluctuate with finite mean frequency and finite amplitude makes the stochastically averaged kinetics of a system's transient-state population essentially four-exponential.

2. This four-exponentiality reduces to the simpler three-exponential and bimodal temporal behaviors in the corresponding limits of very rare and very frequent stochastic fluctuations, respectively.

3. There is a stochastic resonance point, where the forward rate is in perfect resonance with stochastic amplitude, while the backward rate, decay rate and stochastic frequency are all negligible.

4. At a stochastic resonance point, the effect of stochastic immobilization of the two-state system in its initial state emerges.

5. There occurs a critical behavior in the vicinity of a stochastic resonance point exhibiting itself as the dependence of stochastic immobilization in one or another system's state on the order in which vanishing either the decay rate or the stochastic frequency is provided first before both arriving at zero exactly.

The present work was partially supported by the Program of Fundamental Research of the Department of Physics and Astronomy of the National Academy of Sciences of Ukraine (project No. 0117U000240).

REFERENCES

[1] R.A. Alberty, W.G. Miller, *J. Chem. Phys.* **26**, 1231 (1957).

[2] R.K. Bohn, K.N. Casleton, Y.V.C. Rao, G.W. Flynn, *J. Chem. Phys.* **86**, 736 (1982).

[3] A.N. Macpherson *et al.*, *Biophys. J.* **80**, 923 (2001).

[4] N. Kanamaru, J. Tanaka, *Bull. Chem. Soc. Jpn.* **59**, 569 (1976).

[5] B. Novakovic, I. Knezevic, Quantum Master Equations in Electronic Transport, in: *Nano-Electronic Devices: Semiclassical and Quantum Transport Modeling*, ed. D. Vasileska, S.M. Goodnic, Springer, New York 2011, Chapter 4, pp. 249–287.

[6] A.I. Burshtein, in: *Advances in Chemical Physics*, ed. S.A. Rice, vol. 129, Wiley, Hoboken, New Jersey 2004, pp. 105–418.

[7] L. Valkunas, D. Abramavicius, T. Mancal, *Molecular Excitation Dynamics and Relaxation. Quantum Theory and Spectroscopy*, Wiley-VCH, Weinheim 2013.

[8] E.J. Crampin, S. Schnell, P.E. McSharry, *Prog. Biophys. Mol. Biol.* **86**, 77 (2004).

[9] K. Banerjee, K. Bhattacharyya, *J. Chem. Phys.* **143**, 235102 (2015).

[10] M.J. Lawson, L. Petzold, A. Hellander, *J. R. Soc. Interface* **12**, 20150054 (2015).

[11] G.H. Weiss, J. Masoliver, *Physica A* **296**, 75 (2001).

[12] A.M. Berezhkowsky, G.H. Weiss, *Physica A* **303**, 1 (2002).

[13] A.M. Berezhkowsky, A. Szabo, G.H. Weiss, *J. Chem. Phys.* **110**, 9145 (1999).

[14] K. Blum, *Density Matrix Theory and Application*, Plenum Press, New York 1996.

[15] I.A. Goychuk, E.G. Petrov, V.I. Teslenko, *Phys. Lett. A* **185**, 343 (1994).

[16] A. Fuliński, *Acta Phys. Pol. B* **29**, 1523 (1998).

[17] I.A. Goychuk, P. Hanggi, *Adv. Phys.* **54**, 525 (2005).

[18] E.G. Petrov, *Eur. Phys. J. Special Topics* **216**, 205 (2013).

[19] T. Holstein, *Ann. Phys. (N.Y.)* **8**, 343 (1959).

[20] O.L. Kapitanchuk, O.M. Marchenko, V.I. Teslenko, *Chem. Phys.* **472**, 249 (2016).

[21] C.W. Gardiner, P. Zoller, *Quantum Noise: A Hadbook of Markovian and Non-Markovian Quantum Stochastic Methods with Applications to Quantum Optics*, Springer-Verlag, New York 2004.

[22] E.G. Petrov, V.I. Teslenko, *Chem. Phys.* **375**, 243 (2010).

[23] V.I. Teslenko, O.L. Kapitanchuk, Y. Zhao, *Chin. Phys. B* **24**, 028702 (2015).

[24] N.G. van Kampen, *Stochastic Processes in Physics and Chemistry*, North Holland, Amsterdam 1981.

[25] S.E. Jackson, *Fold. Des.* **3**, R81 (1998).
[26] M. Bixon, *Annu. Rev. Phys. Chem.* **27**, 65 (1976).
[27] H. Frauenfelder, P.G. Wolynes, *Science* **229**, 337 (1985).
[28] A. Nitzan, J. Ross, *J. Stat. Phys.* **10**, 379 (1974).
[29] V.E. Shapiro, V.M. Loginov, *Physica A* **91**, 563 (1978).
[30] V.M. Loginov, *Acta Phys. Pol. B* **27**, 693 (1996).
[31] V.I. Teslenko, O.L. Kapitanchuk, *Int. J. Mod. Phys. B* **27**, 1350169 (2013).
[32] A. Hurwitz, *Math. Ann.* **46**, 273 (1895).
[33] D. Jacewicz, A. Łapińska, A. Dąbrowska, L. Chmurzyński, *Transition Metal Chem.* **31**, 111 (2006).
[34] D. Jacewicz *et al.*, *Sensors* **8**, 4487 (2008).
[35] S. Sergeyev, *Opt. Express* **19**, 24268 (2011).
[36] M.F. Bukhori, S. Roy, A. Asenov, *IEEE Trans. Electron Devices* **57**, 795 (2010).
[37] T. Wellens, V. Shatochin, A. Buchleitner, *Rep. Prog. Phys.* **67**, 45 (2004).
[38] I.C. Kleppe, H.P.C. Robinson, *Biophys. J.* **77**, 1418 (1999).
[39] E.A. Moelwyn-Hughes, *Physical Chemistry*, University Press, Cambridge 1940, Appendix 9, pp. 633–641.
[40] D.G. Luchinsky, P.V.E. McClintock, *Nature* **389**, 463 (1997).
[41] M.I. Dykman *et al.*, *Appl. Phys. Lett.* **67**, 308 (1995).
[42] M.I. Dykman *et al.*, *J. Chem. Phys.* **100**, 5737 (1994).