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V.I. TESLENKO

Bogolyubov Institute for Theoretical Physics, Nat. Acad. of Sci. of Ukraine
(14b, Metrolohichna Str., Kyiv 03680, Ukraine; e-mail: vtes@bitp.kiev.ua)**FOURTH-ORDER DIFFERENTIAL
EQUATION FOR A TWO-STAGE ABSORBING
MARKOV CHAIN WITH A STOCHASTIC
FORWARD TRANSITION PROBABILITY**PACS 02.50.Wp, 05.40.Ca,
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The problem of averaging the kinetics of a two-stage absorbing Markov chain over random fluctuations in its forward transition probability approximated by the symmetric dichotomous stochastic process is solved exactly. It is shown that the temporal behavior of the population of chain's transient state obeys a fourth-order differential equation with the tetra-exponential form of a solution given the finite frequency and mean amplitude of fluctuations. In the limit of frequent fluctuations, this tetra-exponential solution reduces to a simple bi-exponential form typical of the deterministic two-stage decay process lacking fluctuations in its transition probability. Rather, in the limit of rare fluctuations, the tetra-exponential solution, while simplifying to the tri- and bi-exponential solutions, becomes specific both for the low amplitude and the resonance amplitude fluctuations, respectively. Furthermore, there is a stochastic resonance point, where the forward transition probability is in resonance with the mean fluctuation amplitude, whereas the backward transition probability, decay transition probability, and fluctuation frequency are negligibly small. In result, the stochastic immobilization of the two-stage absorbing Markov chain in its initial state occurs at this point.

Keywords: nonequilibrium systems, nonstationary kinetics, fluctuation phenomena, stochastic processes, absorbing Markov chain, ordinary differential equations.

1. Introduction

In physics, information on the dynamic and kinetic characteristics of a system of interest, such as its energy spectrum and probabilities of transitions between the different energy levels, is usually obtained from different measurement techniques. One common type of such techniques is the measurement of the decay (or, generally, rise and decay) kinetics of population of system's states in response to sudden changes in the external conditions controlled during experiments. In many cases, however, the desired information acquired from these measurements is incomplete, inadequate, and therefore impractical in perfectly identifying not only the energy spectrum of the system, but also the number of its energy levels, nor even to mention a kinetic model specifying a plausible chain of transformations of the levels with certain transition probabilities. For example, it is known that the kinetics of a two-stage model corresponds well to the bi-exponential representation [1], though there

are a lot of instances for kinetic data patterns requiring the tri-, tetra-, and more exponential representations [2–4]. In these cases, because a larger number of parameters must be introduced to simulate multi-exponential processes, one hardly expects that using the double exponential representation with a few independent parameters provides a complete knowledge of the system. To overcome a choice of opportunities in a consideration of the multiexponential kinetics, one can choose between two alternative ways of description.

The first way is to begin with a simple two-state model of the system in question and then endow it with novel degrees of freedom in the form of adding the new states hidden for a direct observation but interconverting between each other with the additional transition probabilities according to a more complex, but more realistic multistate desired model. This allows one to depict the model as a kind of kinetic diagram or flow chart, being the underlying Markov chain of the evolution process [5]. However, striving for a better description of the system leads to increas-

ing the number of its states, which makes the problem of finding a solution for all multiple states hard. In spite of this, using the first way of description is typical of considering the different spontaneous and induced kinetic phenomena in condensed phase systems (see, e.g. [6–10] and references therein).

On the contrary, the second way of description starts from the microscopic formulation of the problem, by associating each system's state with a single energy level, being distinct from those of other states. The time evolution of these states is governed by a set of kinetic balance equations for populations, whose every steady-state pair, when multiplied by corresponding interstate transition probabilities, obeys the condition of detailed balance. Of course, for a large number of kinetic equations, finding their solution comprises the hard-to-solve problem too, also known as the number-of-states problem [11, 12]. However, there are often the cases where one can use the two-compartment system's representations such as those of two-level atoms and the one-electron spin-1/2 systems [13] or in the frame of pharmacokinetics/pharmacodynamics modeling [14]. In these cases, the condition of local equilibrium for the populations of states is supposed to be established fast within each compartment, while the probabilities of transitions between two compartments, as well as those of their decay, are regarded low. In result, one can arrive at a two-level system with degenerate energy levels [15], whose degeneracy corresponding thus to compartment's dimensionality is let to be a stochastic variable with a capability to randomly fluctuate around its mean with average amplitude and frequency. Nonetheless, it is noteworthy to say that using this way of description is untypical and does not provide any strict analytical results hitherto even for a simplest two-level decay model (but see Ref. [16], where a single-stage reversible reaction with a one fluctuating rate constant was considered).

The present paper aims at combining the both aforementioned ways of description of the multiexponential processes in one microscopic approach. The approach is based on the density matrix formalism of the Liouville–von Neumann equation for the evolution of a finite state nonequilibrium system coupled weakly to the infinite state equilibrium environment. This formalism is shown to be well appropriate to describe microscopic fluctuations in the position of energy levels of the system caused by

stochastic forces acting from the environment [17–20]. However, mapping the Liouville–von Neumann equation to a master equation for kinetically balanced state populations and representing this equation as a linear absorbing Markov chain with the variable number of states in the leading order approximation [21] provide a description of macroscopic fluctuations too. As distinct from their microscopic counterparts, macroscopic fluctuations are associated not with fluctuations in the energy levels of the system but with stochastization of its level number, corresponding likely to fluctuations in its entropy, provided that local equilibrium conditions for the ergodic sets of Markov chain states are applied properly. Exactly how to perform the account of microscopic and macroscopic fluctuations most accurately constitutes the subject, to which Sections 2 and 3 of this paper are devoted. In Section 4, the reduced two-stage absorbing Markov chain with the stochastic forward transition probability is considered in detail. It is shown, to the best of our knowledge for the first time, that the temporal behavior of a transient-state population of the so-defined Markov chain obeys a fourth-order differential equation with constant positive coefficients. The limiting behavior of the tetraexponential solution to this fourth-order problem in different important cases of stochastic fluctuations including the frequent and rare fluctuations, as well as a stochastic resonance point, is described in Section 5. Finally, in Section 6, the results obtained are discussed and concluded.

2. Model of Microscopic Fluctuations

To construct a model of fluctuations in the positions of microscopic energy levels, let us consider a finite quantum dynamical system composed of the $N+1$ different states with the energies E_i ($i = 0, 1, \dots, N$) and interactions between states V_{ij} ($i \neq j$) found in the adiabatic approximation. Let this system be weakly coupled to its environment represented as an infinite sum of non-interacting harmonic oscillators (normal modes ω_λ) equilibrated with the ambient temperature T according to the Bose distribution for the vibration numbers $n_\lambda = [\exp(\omega_\lambda/k_B T) - 1]^{-1}$, where k_B is the Boltzmann constant (we set $\hbar \equiv 1$). Let this coupling be a nonadiabatic coupling of the environmental phonons to relaxation transitions between the states of the system [22], such that the singular perturba-

tions of a generator of its unitary (adiabatic) dynamics are induced with the stochastic force parameters $\kappa_{i\lambda}(t) = \kappa_{i\lambda}^{(0)} + \kappa_{i\lambda}(t)$ involving regular $\kappa_{i\lambda}^{(0)}$ and random $\kappa_{i\lambda}(t)$ parts. This creates the possibility for the system being in its different states $|i\rangle$ to absorb or emit environmental phonons of various energies ω_λ instantaneously, but at random times t , so that emitted phonons are carried away by their time-invariant environment dynamics and never come back again. Furthermore, this allows for the system to transit from one state to the other, but with holding the condition of energy balance for each transition difference $\Delta E_{ij} = E_i - E_j$, by accompanying it with the simultaneous process of creation or annihilation in the environment of the corresponding phonon of the energy $\omega_\lambda = |\Delta E_{ij}|$. Then the stochastic Hamiltonian of the whole system “nonequilibrium system + equilibrium environment + their interaction” is decomposed into three parts

$$H(t) = H_S + H_B + H_{\text{int}}(t). \quad (1)$$

The first part represents the Hamiltonian of a nonequilibrium system

$$H_S = \sum_i E_i |i\rangle\langle i| + \sum_{i,j} V_{ij} (1 - \delta_{ij}) |i\rangle\langle j|. \quad (2)$$

The second part is the Hamiltonian of a heat bath representing the equilibrium environment

$$H_B = \sum_\lambda \omega_\lambda (\beta_\lambda^+ \beta_\lambda + 1/2). \quad (3)$$

Both parts relate to the deterministic dynamical behaviors. Thus, the matrix elements V_{ij} in (2) define the dynamics of system’s states, whose improper energies E_i are found in isolation with the environment, while β_λ^+ and β_λ in (3) stand for the operators of creation and annihilation of phonons being the vibrational eigenstates of harmonic excitations of the environment itself. In the Fock space representation, the latter corresponds to the second quantization of a field of non-interacting bosons obeying the canonical commutation relations $[\beta_\lambda^+, \beta_\mu] = -\delta_{\lambda\mu}$ for an infinite sum of discrete normal modes constrained by a non-degeneracy condition for their energies $\omega_\lambda \neq \omega_\mu$ ($\lambda \neq \mu$) [22, 23]. Rather, the third part of (1) is the time-dependent interaction Hamiltonian

$$H_{\text{int}}(t) = \sum_i \sum_\lambda \kappa_{i\lambda}(t) (\beta_\lambda^+ + \beta_\lambda) |i\rangle\langle i|. \quad (4)$$

It relates to the indeterministic effects in the dynamics, involving the time-dependent force $\kappa_{i\lambda}(t) = \kappa_{i\lambda}^{(0)} + \kappa_{i\lambda}(t)$ with the stochastic addition $\kappa_{i\lambda}(t)$. The latter can be intrinsic in the system, e.g., by the chaoticization of its trajectories, or imposed extrinsically due to some random, but zero in mean, environmental fluctuations, whose average characteristics are independent of state $|i\rangle$.

If the overlapping between system’s states defined by matrix elements V_{ij} is weak, it is possible to diagonalize the time-dependent Hamiltonian $H(t)$ (1). This can be done, e.g., by expanding the first term on the right-hand side of (2) (the non-eigenenergy term) in the displacements of the phonon operators $(\beta_\lambda^+ - \beta_\lambda)$ so that the linear (one-phonon) or nonlinear (multiphonon) terms are considered as perturbations induced by the environment in the system. The non-perturbative transformation [24] uses the time-dependent unitary matrix $U_t = \exp(\sum_i u_i(t) |i\rangle\langle i|)$, where $u_i(t) = \sum_\lambda g_{i\lambda}(t) (\beta_\lambda^+ - \beta_\lambda)$ is the displacement operator of the i -th state, and $g_{i\lambda}(t) = \kappa_{i\lambda}(t)/\omega_\lambda$ is a dimensionless coupling. This allows us to perform the second quantization of the phonon field (3) being under the influence of system’s deterministic dynamics (2). Thus, multiplying (1) from the left by U_t and from the right by U_t^+ , we get *exactly*

$$H(t) = H_0(t) + H_B + V. \quad (5)$$

Here, in contrast to (4), the transformed interaction Hamiltonian is time-independent

$$V = \sum_{i,j} (1 - \delta_{ij}) V_{ij} \exp(u_{ij}^{(0)}) |i\rangle\langle j| \quad (6)$$

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

$$H_0(t) = \sum_i \tilde{E}_i(t) |i\rangle\langle i| \quad (7)$$

is stochastic due to the refining of the transformed energy levels by fluctuating time-dependent terms proportional to the reduced random forces $|\kappa_{i\lambda}(t)|^2/\omega_\lambda$ as follows:

$$\tilde{E}_i(t) = E_i - \sum_\lambda [|\kappa_{i\lambda}(t)|^2/\omega_\lambda]. \quad (8)$$

At the same time, Hamiltonian (7) becomes diagonal, though with respect to “phonon-dressed” system’s states. So, from this point on, the notations for “phonon-dressed” states in (7) and “bare” states in (2), (4) as well as for “shifted” and “unshifted” phonon operators in (3), (5) are regarded the same for brevity so that states $|i\rangle$ and the Hamiltonian H_B are not modified in the following. Furthermore, the quadratic fluctuations in the microscopic energy levels (8) reduce to a linear dependence of the energy-level differences

$$\Delta\tilde{E}_{ij}(t) = \Delta\bar{E}_{ij} - 2 \sum_{\lambda} g_{ij\lambda}^{(0)} \kappa_{\lambda}(t) \quad (9)$$

on the stochastic force $\kappa_{\lambda}(t)$, 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 shifts and the average dimensionless couplings, both deterministic, respectively. This result justifies an analogous linear addition of stochastic terms to the eigenenergies of quantum states due to the presence of random fields that has been done previously as an *ad hoc* assumption in a number of papers (see, e.g., [17–21, 25–28]).

As we see, the model for the description of microscopic fluctuations in the system devised above is very advantageous in that it provides the reduced energy-level differences (9) with strictly linear stochastic components in the adiabatic approximation. If the stochastic process underlying these components occurs much faster than nonadiabatic transitions between the different energy levels that comprises the common Markovian approximation for condensed-phase systems [22, 25], then this allows us to describe the transition dynamics of the system, by using the usual rate constant formalism of the coarse-grained master equation [23]. Moreover, due to microscopic fluctuations in the energy levels, the process of their relaxation becomes irreversible because of the memoryless exchange of phonons between the system and the environment. In result, in the weak system-environment coupling limit, the density matrix $\rho(t) = \rho_0(t)\rho_B$ of the whole system is factorized by the density matrix $\rho_B = \exp(-H_B/k_B T)/\text{tr}_B \exp(-H_B/k_B T)$ of the equilibrium environment and the density matrix $\rho_0(t) = \text{tr}_B \rho(t)$ of the nonequilibrium system (trace is taken over all environmental phonons). In turn, this reduces the stochastic Liouville–von Neumann quantum evolution equation

$$\dot{\rho}(t) = -iL(t)\rho(t) \quad (10)$$

with $L(t) = [H(t), \dots]$ being the corresponding stochastic Liouville superoperator related to the stochastic Hamiltonian (5) to the master kinetic equation

$$\dot{p}_j(t) = -p_j(t) \sum_{j' \neq j} W_{jj'} + \sum_{j' \neq j} p_{j'}(t) W_{j'j} \quad (11)$$

for the stochastically averaged (denoted as $\langle\langle \dots \rangle\rangle$) population of the j th microscopic state of the system

$$p_j(t) = \langle\langle \{ |j\rangle \rho_0^{(d)}(t) |j\rangle \} \rangle, \quad (12)$$

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. Here,

$$W_{jj'} = 2\pi \sum_{\lambda} |\chi_{jj'\lambda}|^2 [n_{\lambda} \Lambda_{jj'\lambda} + (1 + n_{\lambda}) \Lambda_{j'\lambda j}] \quad (13)$$

determines the probability of the stochastic transition in the system from level j to level j' with the corresponding Lorentzian $\Lambda_{jj'\lambda} = \gamma_{jj'} \{ \pi [\gamma_{jj'}^2 + (\omega_{\lambda} + \Delta\bar{E}_{jj'})^2] \}^{-1}$, where $\chi_{jj'\lambda} = V_{jj'} g_{jj'\lambda}^{(0)}$ and $\gamma_{jj'} = \gamma_{j'j} = -\lim_{\tau \rightarrow \infty} \{ \frac{1}{\tau} \ln \langle\langle \exp[i \int_0^{\tau} dt \sum_{\lambda} g_{jj'\lambda}^{(0)} \kappa_{\lambda}(t)] \rangle\rangle \}$ are the nonadiabatic relaxation coupling and adiabatic stochastic broadening parameters, respectively (see, e.g., [17, 21, 25] for more details).

3. Model of Macroscopic Fluctuations

The master equation (11) in the form of the balance of populations of microscopically fluctuating energy levels derived in the previous section is essentially a kinetic equation local in time. It consistently follows from the microscopic formulation of the problem conditioned by three assumptions: (i) The system couples to the environment by exchanging the energy of vibration excitations (phonons); (ii) The system-environment coupling is weak so that the most relevant physical variables can be represented by the local-in-time populations of system’s states, while the nonlocal correlations and coherences of states are regarded non-relevant variables effectively condensed in the local-in-time probabilities of transitions between the states; (iii) There exists a hierarchy of characteristic times such that it takes much more time to transit the system from its one state to another than to retain the memory in the environment on the energy differences and relative phases involved in any state-to-state transition. As such, in the system with $N + 1$ states, there can be $N(N + 1)/2$ probabilities of transitions between states with only $2N - 1$

of them be linearly independent [29]. Therefore, this system can formally be projected onto the equivalent N -stage absorbing Markov chain as follows:

$$|N\rangle \begin{array}{c} \xrightarrow{W_{NN-1}} \\ \xleftarrow{W_{N-1N}} \end{array} |N-1\rangle \dots |2\rangle \begin{array}{c} \xrightarrow{W_{21}} \\ \xleftarrow{W_{12}} \end{array} |1\rangle \begin{array}{c} \xrightarrow{W_{10}} \\ \xleftarrow{W_{01}} \end{array} |0\rangle. \quad (14)$$

Here, $2N - 1$ leading order transition probabilities $\{W_{jj'}\} \equiv \{W_{NN-1}, W_{N-1N}, \dots, W_{21}, W_{12}, W_{10}\}$ are considered as independent variables, while the remaining transition probability W_{01} of not well resolved system's recovery from the absorbing state $|0\rangle$ to its nearest neighboring state $|1\rangle$ is regarded negligible

$$W_{01} \ll W_{NN-1}, W_{N-1N}, \dots, W_{21}, W_{12}, W_{10}. \quad (15)$$

In this context, the master equation (11), if taken in its generalized matrix form

$$\dot{\Gamma}(t) = K \cdot \Gamma(t), \quad (16)$$

where $\Gamma(t) = \text{col}(p_0(t), \dots, p_N(t))$ are system's state vectors, and K is a transition probability matrix with the components $K_{jj'} = W_{jj'} - \delta_{jj'} \sum_{i=0}^N W_{ij}$, directly corresponds to the Liouville–von Neumann equation (10) written in the vector-state representation for the diagonal elements of the density matrix and employing the imaginary transformation of the time $t \rightarrow it$. This is almost analogous to mapping the reversible quantum evolution equation onto the stochastic diffusion equation used in the Monte Carlo methods for irreversibly guiding the system toward its ground state over time [30]. More formally, the master equation is seen as a series of the four projections provided in the Liouville–von Neumann equation for the imaginary time in the following order: (i) onto the space of diagonal elements of the density matrix; (ii) onto the ensemble-averaged population space of energy levels; (iii) onto the population space stochastically averaged over the microscopic energy-level fluctuations; and (iv) onto the transition probability space generating a complete set of system's independent parameters.

The representation above is advantageous in that it allows us to describe the population kinetics of microscopically fluctuating energy levels of the system without clarifying what its mean-field energy-level differences $\Delta \bar{E}_{jj'}$, adiabatic stochastic broadening $\gamma_{jj'}$, as well as nonadiabatic $\chi_{jj'\lambda}$ and adiabatic $\kappa_{j\lambda}^{(0)}$ system–environment couplings, all enter-

ing the stochastically averaged microscopic transition probabilities $W_{jj'}$ (13), exactly are, given the vibrational modes ω_λ and temperature of the environment. Instead, we are interested in which transition probability taken from the reduced space $\{W_{jj'}\}$ (15) influences the time evolution of the populations of energy levels so strongly that we can consider the act of populating these levels as well controllable. Thus, having a linear $(N + 1)$ -state absorbing Markov chain (14) with the transition probabilities (15), which form a set of $2N - 1$ independent parameters chosen arbitrary, and one recovery transition probability put among these parameters nearly zero in the absorbing limit, we can employ such a kind of representation as an *ad hoc* simulation approach to very different kinetic processes (see, e.g. [21, 30]).

Another advantage of representation (14) is that it can also provide a description of macroscopic fluctuations in the system. In doing so, it is sufficient to assume that, in general, the number N of transient states in the absorbing Markov chain is not fixed in advance but rather well adjusted as the time-dependent parameter having its own dynamics determined by the phase transitions in the environment or conformational transformations of the environmental macromolecules. For example, if number N corresponds to the number of contacts of a single ligand and species with the different solvent molecules in micro- or nanovolumes of the well-stirred bulk solution, then this number can be a function of the time $N(t)$ that must follow all the changes in a local configuration of solvent molecules with the solute. Thus, since the folding–unfolding kinetics of most simple protein macromolecules is well fitted typically as an all-or-none two-state process [31], there is a valid possibility of allowing for the number $N(t)$ to perform statistically independent stochastic displacements in time between its maximum N_{\max} and minimum N_{\min} values presenting a discrete (dichotomous) random process. The latter occurs because of sudden changes in the instantaneous local configurations of solvent molecules happened by virtue of the conformational transformations of some protein molecule present in the bulk [32]. This protein does not directly influence the two-stage absorbing Markov chain as such but, causing random changes in the number of solvent molecules readily accessible for the forward chain reaction, indirectly affects its transition probability. Adapting that situation to the absorbing Markov

chain (14) infers a simplification of relations (15) as follows:

$$W_{NN-1} = W_{N-1N} = \dots = W_{32} = W_{23} \equiv W; \quad (17)$$

$$W \gg W_{21}, W_{12}, W_{10}; \quad W_{01} = 0.$$

In these relations, all transient states in (14) but state $|1\rangle$ are supposed nearly equipopulated at every time instant and quasidegenerate in their energy with matching them to the same levels of $p_2(t) = p_{j=3,\dots,N}(t)$ and $E_2 = E_{j=3,\dots,N}$, respectively. Therefore, for such a joint sequence of those states, being in fact the ergodically mixed ones, we can introduce their aggregated population

$$p_{\{2\}}(t) = p_2(t)[N(t) - 1] \quad (18)$$

and then combine all of these states in a single effective state $|\{2\}\rangle$ represented by

$$|N\rangle \begin{matrix} \xrightarrow{W} \\ \xleftarrow{W} \end{matrix} |N-1\rangle \dots |3\rangle \begin{matrix} \xrightarrow{W} \\ \xleftarrow{W} \end{matrix} |2\rangle \Leftrightarrow |\{2\}\rangle. \quad (19)$$

Consequently, taking (18) and (19) into account in the master equation (11) in approximation (17) transforms a complex linear absorbing Markov chain problem (14) to a much simpler problem of the two-stage decay

$$|\{2\}\rangle \begin{matrix} \xrightarrow{a+\alpha(t)} \\ \xleftarrow{b} \end{matrix} |1\rangle \xrightarrow{k}, \quad (20)$$

which is equipped, however, with the addition of a stochastic process to its forward transition probability. Henceforth, to shorten the description, the following notations are used:

$$a+\alpha(t) \equiv W_{21}[N(t)-1]^{-1}; \quad b \equiv W_{12}; \quad k \equiv W_{12}. \quad (21)$$

Here, $\alpha(t)$ is a symmetric dichotomous stochastic process that has a zero mean $\overline{\alpha(t)} = 0$ and is exponentially correlated as $\overline{\alpha(0)\alpha(t)} = \exp(-2\nu t)$ (an overbar designates a stochastic averaging over the macroscopic fluctuations). It performs random jumps between the discrete values $\pm\sigma$ at the mean frequency ν to obey the exact equalities [33, 34]

$$[\alpha(t)]^2 = \sigma^2; \quad \dot{\alpha}(t) = -2\nu\alpha(t). \quad (22)$$

Given these equalities, as well as inequalities for the mean stochastic amplitude $\sigma \leq a$ and the fluctuating

number of states $N_{\min} \leq N(t) \leq N_{\max}$, it is appropriate to arrive at the inequality

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

$$= \frac{W_{21}}{2} \left(\frac{1}{N_{\min}} + \frac{1}{N_{\max}} \right). \quad (23)$$

Note that a stochastic process $\alpha(t)$ involved in the two-stage Markov chain (20) to represent random discrete dichotomous fluctuations in its forward transition probability belongs to macroscopic fluctuation processes. These fluctuations characterize the stochastic behavior of the sequence of ergodically mixed states (19) that are strictly in a local thermodynamic equilibrium. With respect to fluctuations, such a sequence exhibits immediate jumps between two different realizations of the number of ergodic states intrinsic in its two locally equilibrium configurations at random times. A flight time of the jump itself is extremely fast, being close to the macroscopic diffusion/encounter/scattering time, that is, the time of the establishment of a local macroscopic equilibrium with the highest physical speed [27, 28, 35, 36]. On the other hand, each such equilibrium remains thermodynamically unchanged during every elapsed time between two successive jumps. Formally, for a sequence, this represents a single ergodic compartment, which avoids any memory effects. In this regard, the macroscopic fluctuations differ significantly from the microscopic ones, since the latter are nonlocal in nature and operate not with the fluctuating numbers of states in the locally equilibrium ergodic sequences, but rather with the energy differences between different states in nonequilibrium sequences. This leads, in turn, to the non-Markovianity of microscopically fluctuating kinetic systems (for a discussion of non-Markovian effects in the condensed phase systems, see, e.g. [20, 21, 27, 37–39]). At the same time, this demands that, in the case of macroscopic fluctuations, we must solve the master equation involving the stochastic additions to deterministic kinetic coefficients strictly exactly, without using any approximations throughout the derivation of a closed-form equation for the kinetics of stochastically averaged populations. In the next section, we present a straightforward way of how to solve this problem analytically, which is the main goal of the paper.

4. Stochastically Averaged Differential Equation

Consider the temporal behavior of the two-stage absorbing Markov chain (20). According to the results of Sections 2 and 3, it should obey the stochastic master equation (11) conditioned by relations (17), (18), (21)–(23). So, the problem reduces to finding a solution to a system of two linear stochastic differential equations of the first order, which read as follows:

$$\begin{cases} \dot{p}_1(t) = -(b+k)p_1(t) + [a + \alpha(t)]p_{\{2\}}(t); \\ \dot{p}_{\{2\}}(t) = bp_1(t) - [a + \alpha(t)]p_{\{2\}}(t). \end{cases} \quad (24)$$

To integrate these equations in a physically relevant way implies to provide their averaging over a stochastic process and then to solve the resulting equations with respect to all unknown averages. Denoting, by $P_{1,2}(t) = \overline{p_{1,\{2\}}(t)}$, the average population of states $|1, \{2\}\rangle$ and considering the commutativity between the averaging and differentiating operations, we get the following averaged stochastic equations:

$$\begin{cases} \dot{P}_1(t) = -(b+k)P_1(t) + aP_2(t) + \overline{\alpha(t)p_{\{2\}}(t)}; \\ \dot{P}_2(t) = bP_1(t) - aP_2(t) - \overline{\alpha(t)p_{\{2\}}(t)}. \end{cases} \quad (25)$$

Since these equations contain the unknown stochastic correlation functional $\overline{\alpha(t)p_{\{2\}}(t)}$, 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, we can use the Shapiro–Loginov formula [33] for the differentiation of exponentially correlated stochastic functionals as follows:

$$\overline{\dot{\alpha} p_{\{2\}}(t)} = \overline{\alpha \dot{p}_{\{2\}}(t)} + \overline{\dot{\alpha} p_{\{2\}}(t)} = \overline{\alpha \dot{p}_{1,\{2\}}(t)} - 2\nu \overline{\alpha p_{1,\{2\}}(t)}, \quad (26)$$

where the notation of time dependence (t) is dropped for brevity. But using (26) for $\overline{\alpha \dot{p}_{\{2\}}(t)}$ after the differentiation of (25) leads to the unknown $\overline{\alpha \dot{p}_{\{2\}}(t)}$. Multiplying the second equation in (24) by α and averaging it with the use of (22) and (25), we get

$$\begin{cases} \dot{P}_2 = -\dot{P}_1 - kP_1; \\ \overline{\alpha \dot{p}_{\{2\}}(t)} = b\overline{\alpha p_1} - a\dot{P}_1 - a(b+k)P_1 + (a^2 - \sigma^2)P_2. \end{cases} \quad (27)$$

Then, applying the second differentiation to the first equation in (25) with the use of (26) and (27) yields

$$\ddot{P}_1 + (2a + b + k + 2\nu)\dot{P}_1 + [a(b + 2k) +$$

$$+ 2\nu(b + k)]P_1 = b\overline{\alpha p_1} + [a(a + 2\nu) - \sigma^2]P_2. \quad (28)$$

As we see, in the two-stage absorbing Markov chain (20), there emerge the unknown P_2 and one more unknown stochastic correlation functional $\overline{\alpha p_1}$. After the differentiation of (28), this leads to the following third-order equation:

$$\ddot{\ddot{P}}_1 + (2a + b + k + 2\nu)\ddot{P}_1 + [(a + b)(a + 2\nu) + 2k(a + \nu) - \sigma^2]\dot{P}_1 + k[a(a + 2\nu) - \sigma^2]P_1 = b\overline{\alpha \dot{p}_1}. \quad (29)$$

According to (26), this equation is equivalent to the emergence of another unknown functional $\overline{\alpha \dot{p}_1}$. However, the latter may be considered as a nuisance. Indeed, if to use the first equation in (24) multiplied by α and then averaged, and the second equation in (25), we arrive at the auxiliary equation

$$\overline{\alpha \dot{p}_1} = -(b+k)\overline{\alpha p_1} + a\dot{P}_1 + a(b+k)P_1 + (\sigma^2 - a^2)P_2. \quad (30)$$

Differentiating (30) with regard for the first equation in (27) gives the equation

$$\overline{\alpha \dot{\dot{p}}_1} + (b + k + 2\nu)\overline{\alpha \dot{p}_1} = a\ddot{P}_1 + [a(a + b + k) - \sigma^2]\dot{P}_1 + k(a^2 - \sigma^2)P_1. \quad (31)$$

Multiplying this equation by b and accounting, on its left-hand side, for the left-hand part of (29), we derive the fully closed fourth-order differential equation for P_1 . In result, the sought solution to problem (20) finally reads

$$\begin{aligned} &k\{2\ddot{\ddot{P}}_1(t) + [2(a + b + 2\nu) + k]\ddot{P}_1(t) + \\ &+ 2[(a + b)(a + 2\nu) + (k + 2\nu)(a + \nu) - \sigma^2]\dot{P}_1(t)\} + \\ &+ k\{k[a(a + 2\nu) - \sigma^2] + 2\nu[a(a + b + 2\nu) - \sigma^2]\}P_1(t) + \\ &+ \frac{d}{dt} \left[\left(\frac{d}{dt} + 2\nu \right) D^{(2)} \right] P_1(t) = 0, \end{aligned} \quad (32)$$

where

$$\begin{aligned} D^{(2)} \equiv D^{(2)}(a, b, \nu, \sigma) &= \frac{d^2}{dt^2} + 2(a + b + \nu)\frac{d}{dt} + \\ &+ [(a + b)(a + b + 2\nu) - \sigma^2] \end{aligned} \quad (33)$$

is the second-order differential operator acting on the populations $P_{1,2}(t)$ of states $|1, \{2\}\rangle$ in (20) interchangeably with respect to the permutation $a \leftrightarrow b$ and independently of k .

Equation (32) is a linear homogeneous ordinary differential equation of the fourth order with constant

positive coefficients. Its exact solution is found by standard methods and has the form

$$P_1(t) = \sum_{j=1}^4 c_j \exp(\lambda_j t), \quad (34)$$

where λ_j are the eigenvalues corresponding to the different exponential modes of evolution of the two-stage absorbing Markov chain (20), and c_j are the coefficients determined by the initial conditions. Since, due to the Hurwitz theorem [40], the exponents λ_j are nonpositive in the case of (32), (33), solution (34) is Lyapunov-stable. Moreover, if all modes λ_j are different, it is overcritically damped and is damped critically only with coincident λ_j . In general, even for the simplest initial conditions

$$\begin{aligned} P_1(t=0) &\equiv P_1^\circ = 0; \dot{P}_1^\circ = 0; \\ \ddot{P}_1^\circ &= f_1 = \text{const}; \ddot{\ddot{P}}_1^\circ = \varphi_1 = \text{const} \end{aligned} \quad (35)$$

and a trivial steady-state boundary condition $P_1(t \rightarrow \infty) \equiv P_1^\infty = 0$, the specific form of solution (34) is very complicated and inappropriate for providing the comprehensive analysis. However, for the limiting cases considered in the following section, it can be analyzed analytically.

5. Limiting Cases for Reversible and Irreversible Processes

There are at least two cases of simplified stochastic evolution of the two-stage absorbing Markov chain (20) which are worth noting. The first important case is the reversible one-stage stochastic process



with the normalized state's populations $p_1(t) + p_{\{2\}}(t) = 1$. This process corresponds to the case $k = 0$ in (20), by leading to the stochastic master equation

$$\dot{p}_1(t) = -[a + b + \alpha(t)]p_1(t) + a + \alpha(t). \quad (37)$$

Averaging (37) and substituting the result for $\alpha(t)p_1(t)$ in (28) with $P_2(t) = 1 - P_1(t)$ yield the second-order equation

$$D^{(2)}P_1(t) = F_1. \quad (38)$$

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

$$P_1^\infty = [a(a + b + 2\nu) - \sigma^2] / [(a + b)(a + b + 2\nu) - \sigma^2]. \quad (39)$$

An analogous stationary value for $P_2(t)$ is $P_2^\infty = b(a + b + 2\nu) / [(a + b)(a + b + 2\nu) - \sigma^2]$. The same result follows from the fourth-order equation (32), (33) at $k = 0$ too, given the normalization condition. This implies that the tetra-exponential evolution of (32) is divided into two parts – the fully reversible part (33), (38) governing the establishment of the local equilibrium between the states provided the values of their equilibrium populations are shifted and the irreversible part, given in the braces in (32), responsible for the decay of these populations to zero with a decay transition probability proportional to k . For the initial conditions $P_1^\circ = \dot{P}_1^\circ = 0; \ddot{P}_1^\circ = F_1$ and the stationary condition (39), solving (38) is trivial and gives the bi-exponential solution

$$\begin{aligned} P_1(t) &= \frac{a(a + b + 2\nu) - \sigma^2}{(a + b)(a + b + 2\nu) - \sigma^2} \times \\ &\times \left[1 - \frac{\lambda_1 \exp(\lambda_2 t) - \lambda_2 \exp(\lambda_1 t)}{\lambda_1 - \lambda_2} \right], \end{aligned} \quad (40)$$

where $\lambda_{1,2} = -(a + b + \nu) \mp \sqrt{\nu^2 + \sigma^2}$ are the two nonpositive modes.

The second case corresponds to the entirely irreversible stochastic two-stage decay



Setting $b = 0$ in Eq. (28) and differentiating it with the use of the first equation in (27) yield

$$\begin{aligned} \ddot{P}_1(t) &+ [2(a + \nu) + k]\dot{P}_1(t) + \\ &+ [a(a + 2k + 2\nu) + 2k\nu - \sigma^2]P_1(t) + \\ &+ k[a(a + 2\nu) - \sigma^2]P_1(t) = 0. \end{aligned} \quad (42)$$

According to (34), for the initial conditions

$$P_1^\circ = \dot{P}_1^\circ = 0; \ddot{P}_1^\circ = -\ddot{\ddot{P}}_1^\circ [2(a + \nu) + k]^{-1} = f_1 = \text{const}, \quad (43)$$

where $f_1 = a(a + 2\nu) - \sigma^2$ is a spontaneous initial force virtually acting on the population evolving in time

$P_1(t)$ owing to fluctuations in the forward transition probability, the emerging tri-exponential solution to (42) reads

$$P_1(t) = [a(a + 2\nu) - \sigma^2] \left[\frac{\exp(\lambda_1 t)}{(\lambda_1 - \lambda_2)(\lambda_1 - \lambda_3)} + \frac{\exp(\lambda_2 t)}{(\lambda_2 - \lambda_1)(\lambda_2 - \lambda_3)} + \frac{\exp(\lambda_3 t)}{(\lambda_3 - \lambda_1)(\lambda_3 - \lambda_2)} \right]. \quad (44)$$

This solution is overcritically damped with three non-positive modes obeying the characteristic equation

$$\lambda^3 + [2(a + \nu) + k]\lambda^2 + [a(a + 2k + 2\nu) + 2k\nu - \sigma^2]\lambda + [a(a + 2\nu) - \sigma^2]k = 0. \quad (45)$$

In the limit of frequent stochastic fluctuations

$$2\nu \gg a, k, \sigma, \quad (46)$$

solution (44) becomes independent of the both stochastic fluctuation parameters, σ and ν , and, hence, comprises essentially the deterministic expression of the bi-exponential form

$$P_1(t) = \frac{a}{a - k} [\exp(-kt) - \exp(-at)]. \quad (47)$$

Expression (47) represents the well-known two-exponential equation typical of the description of the various deterministic two-stage decay processes ranging from two-step kinetics [41, 42] to ligand-controlled reactions [43] and the radioactive decay [44]. Therefore, limit (46) can be considered as a sufficient condition for the transformation of the stochastic two-stage decay model (20) into its deterministic counterpart lacking a stochastic process in the forward transition probability. Nevertheless, the same does not come into effect in the case of making the stochastic amplitude small without setting the stochastic frequency large. Indeed, solving (45) with $\sigma \rightarrow 0$, we obtain $\lambda_1 = -k$; $\lambda_2 = -a$; $\lambda_3 = -(a + 2\nu)$. Accounting for these modes in (44) leads to the tri-exponential solution

$$P_1(t) = \frac{a(a + 2\nu)}{2\nu(a + 2\nu - k)} \left\{ \exp[-(a + 2\nu)t] + \frac{2\nu}{a - k} \left[\exp(-kt) - \frac{a + 2\nu - k}{2\nu} \exp(-at) \right] \right\} \quad (48)$$

that shows the anomalous dependence on the stochastic frequency ν . Really, solution (48) reduces to the

common deterministic two-exponential equation (47) in limit (46), as before. In the opposite limit of rare stochastic fluctuations,

$$2\nu \ll a, k, \sigma, \quad (49)$$

it is described by the uncommon two-exponential equation with a time-dependent coefficient

$$P_1(t) = [a/(a - k)]^2 \{ \exp(-kt) - [1 + (a - k)t] \exp(-at) \}. \quad (50)$$

Solution (48) differs in its irreversible behavior from that of the reversible solution (40): at $\sigma = b = 0$, solution (40) reduces to the one-exponential behavior $P_1(t) = 1 - \exp(-at)$, which does not depend on ν , whereas solution (48) does depend on ν and is tri-exponential.

The effect of low-frequency stochastic fluctuations (49) is even more apparent, when, instead of tending to zero $\sigma \rightarrow 0$, the stochastic fluctuation amplitude reaches its maximum such as $\sigma \cong a$. In this so-called ‘‘infrequent fluctuation resonance amplitude’’ limit, we have

$$2\nu \ll \sigma \cong a \quad (51)$$

provided the stochastic frequency ν to be independent of the decay transition probability k , the order, in which the turning of ν to zero with respect to k is made, appears to be of importance. Thus, for a finite nonzero k in limit (49) of (48), the non-typical bi-exponential solution is as follows:

$$P_1(t) = [2a/(2a - k)] [\exp(-kt) - \exp(-2at)]. \quad (52)$$

This solution is distinct from that of (40) for the reversible process (36), as well as from the solutions of (47) and (50) for the irreversible process (41) with frequent (46) and rare (49) low-amplitude fluctuations in its forward transition probability, respectively. However, passing to the limit $k/2a \rightarrow 0$ in (52) leads to the natural result $P_1(t) = [1 - \exp(-2at)] \xrightarrow{t \rightarrow \infty} 1$, by implying the eventual ultimate absorption of system (41) in state $|1\rangle$ at $a \neq 0$. On the contrary, taking firstly $k = 0$ and then $\nu = 0$ for (44) yields the solution $P_1(t) = 1 - [\lambda_1 \exp(\lambda_2 t) - \lambda_2 \exp(\lambda_1 t)]/(\lambda_1 - \lambda_2)$ with the modes $\lambda_{1,2} = -(a + \nu) \mp \sqrt{\nu^2 + a^2}$ leading to $P_1(t)|_{(\nu/a) \rightarrow 0} \cong [1 - \exp(-\nu t) + (\nu/2a) \exp(-2at)] \xrightarrow{t \rightarrow \infty} 0$ at

$\nu = 0$. This signifies the immobilization of the two-state system (41) conditioned by $k = 0$ in its initial state $|2\rangle$ due to the presence of zero-frequency fluctuations ($\nu = 0$), but resonant in amplitude ($\sigma = a$) in the forward transition probability. During the immobilization, the system is pulled stochastically into its initial state every time, as it is about the transfer to another state. Indications for the stochastic pulling effects are found in telecommunication fibers and electron devices [45, 46]. Other examples of similar stochastic resonance processes in macroscopic two-state systems such as those displayed by a particle in the two-well potential are the diffusion in crystals, conformational transformations in macromolecules, activated chemical reactions, *etc.* (see, e.g. [47] and references therein).

So, for a randomly perturbed two-stage system in the limit (51), we can say about the emergence of a stochastic resonance point in it, where the eigenvalues of its two principal modes coincide with one another so that the direction of a preferential relaxation process – forward or backward – is indeterminate, and the resulting overall transition probability is zero, given the 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 the differential equation. With respect to the bi-exponential equation (40) of the reversible one-stage model (36) and the tri-exponential equation (44) of irreversible two-stage model (41), both with the nonzero forward deterministic transition probability $a > 0$, setting the corresponding terms to zero leads jointly to the identities

$$\begin{aligned} a(a + 2\nu) + 2b(a + \nu) - \sigma^2 &= 0; \\ a(a + 2k) + 2\nu(a + k) - \sigma^2 &= 0. \end{aligned} \quad (53)$$

The union of these identities is compatible with only a single stochastic resonance point

$$\sigma = a; \quad \nu = 0; \quad b = 0; \quad k = 0 \quad (54)$$

that is consistent with a zero point of the tetra-exponential equation (32) for the irreversible two-stage Markov chain (20) as well. Due to criterion of matching the forward transition probability a and fluctuation amplitude σ , this point comprises the necessary stochastic resonance condition. On the other hand, point (54) is a critical point. In its vicinity, three additional sufficient conditions are realized to allow for the overcritically damped tetra-exponential

equation (32) to be damped critically in the bimodal fashion (47), (50), (52). While a resonant coincidence between a and σ , three other parameters, namely, the backward transition probability b , the decay transition probability k , and the stochastic fluctuation frequency ν , turn out to be almost insignificant with respect to a at that point. In this context, requiring for the decay transition probability to be the first in the turning to zero is equivalent to reducing the two-stage absorbing Markov chain (20) to its reversible one-stage counterpart (36), whose equilibrium populations (39) obey the relations $P_1^\infty = 0$; $P_2^\infty = 1$ for $\sigma = a, b = 0$, and $\nu = 0$. From the physical point of view, this directly corresponds to creating the conditions of a stochastic immobilization for the irreversible two-state system (20) in its initial state $|2\rangle$, as is set forth above with applying firstly $k = 0$ and then $\nu \rightarrow 0$ for it.

6. Discussion and Conclusions

In the present paper, the nonequilibrium density matrix approach is used to explicitly describe the temporal behavior of populations of the two-stage absorbing Markov chain (20) subject to discrete macroscopic fluctuations in its forward transition probability represented as a symmetric dichotomous stochastic process, given the presence of microscopic fluctuations (7) in the energy levels of chain's states. The equation for the kinetics of a transient-state population averaged over the stochastic process is derived in a closed analytical form (32). It is shown that the solution of this equation, which is tetra-exponential (34) in the general case, reduces to its tri-exponential (44), (48) and bi-exponential (40), (47), (50), (52) forms for the corresponding irreversible two-stage (41) and reversible one-stage (36) kinetic models, respectively. Such reduction is accurate in the full transition probability space for (20), but a stochastic resonance point (54). At this point, the forward transition probability a is resonantly coincident with the stochastic amplitude σ , while the backward transition probability b , decay transition probability k , and fluctuation frequency ν are negligible with respect to a . However, in a vicinity of the stochastic resonance point, the order of vanishing k and ν becomes important. Thus, if we set firstly k and then ν to zero, the irreversible two-stage Markov chain (41) demonstrates the effect of stochastic immobilization (39) in its initial state typical of the reversible one-

stage Markov chain (36). Rather, if we do so in the opposite order, firstly $v = 0$ and only then $k \rightarrow 0$, the attraction of the absorbing Markov chain to its final state occurs.

One reason for this discrepancy is that the two-state decaying system (20) becomes nonergodic at a very low, but finite k , since the first equation for the populations of states in (27) breaks down the normalization condition of these populations typical of the two-state reversible system (36). Moreover, different types of stochastic motion in the two-state system (20) can appear. In general, one indicates the relaxation motion, which reversibly takes the system toward its stationary state with the forward a and backward b rates, whose decaying motion irreversibly degrades it away this state with the rate k , and the fluctuation motion. The role of the latter is two-fold. First, it stochastically changes the position of the microscopic energy levels of system (7)–(9). In the Markovian approximation, this leads to the energy level broadening with the width proportional to the intensity of those intrinsic microscopic fluctuations (13). Second, it randomly perturbs system's conventional rate constants by means of extrinsic macroscopic fluctuations, whose mean amplitudes and frequencies are comparable with the deterministic rates. In the two-state system (20), all types of motion can be in the distinction between using them for the description of a temporal behavior of populations. Especially, such a distinction is apparent in the case of resonant and rare fluctuations, i.e. in a vicinity of the stochastic resonance point. The latter is typical of many nonstationary nonequilibrium systems such as analog electrical circuits [48], bistable optical devices [49], and bistable macromolecular reactions [50]. Therefore, in terms of its temporal behavior, the simple two-state decaying system (20) can be considered as the first approximation to the kinetics of those more complex systems, which reveal the lack of both the detailed balance condition for their relaxation rates and the normalization condition for populations and demonstrate the breaking of symmetry between relaxation and fluctuation phenomena, which is particularly seen under the stochastic resonance conditions [48].

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В.І. Тесленко

ДИФЕРЕНЦІАЛЬНЕ РІВНЯННЯ ЧЕТВЕРТОГО ПОРЯДКУ ДЛЯ ДВОСТАДІЙНОГО АБСОРБУЮЧОГО ЛАНЦЮГА МАРКОВА ІЗ СТОХАСТИЧНОЮ ЙМОВІРНІСТЮ ПРЯМОГО ПЕРЕХОДУ

Резюме

Надано точного розв'язку проблемі усереднення кінетики двостадійного абсорбуючого ланцюга Маркова за випадковими флуктуаціями ймовірності прямого переходу, що апроксимується симетричним дихотомічним стохастичним процесом. Показано, що часова поведінка заселеності пере-

хідного стану ланцюга задовольняє диференціальне рівняння четвертого порядку, чий розв'язок має чотириекспоненційний вигляд за скінчених частоти та середньої амплітуди флуктуацій. У границі частих флуктуацій цей чотириекспоненційний розв'язок зводиться до простого двоекспоненційного вигляду, що є типовим для детерміністичного процесу двостадійного загасання, якому бракує флуктуацій у ймовірності переходу. Проте у границі рідких флуктуацій чотириекспоненційний розв'язок, хоча й набуває спрощеного вигляду три- чи двоекспоненційного розв'язку, стає переважно специфічним у відношенні як до низько амплітудних, так і до резонансно амплітудних флуктуацій. Більше того, існує точка стохастичного резонансу, де ймовірність прямого переходу збігається з середньою амплітудою флуктуацій, тоді як ймовірності загасання і зворотного переходу, а також частота флуктуацій є незначними. Як результат, в цій точці здійснюється стохастична імобілізація двостадійного абсорбуючого ланцюга Маркова у його початковому стані.