DYNAMICS OF TRANSIENT PROCESSES IN IRREVERSIBLE KINETIC MODELS

V.I. TESLENKO, O.L. KAPITANCHUK

Bogolyubov Institute for Theoretical Physics, Nat. Acad. of Sci. of Ukraine
(14b, Metrolohichna Str., Kyiv 03680, Ukraine; e-mail: `vtes@bitp.kiev.ua`*)*

PACS 72.10.-d, 73.40.Gk,
73.40.Ei, 85.65.+h

A microscopic model of an open system interacting with an external medium and exhibiting quasiclassical fluctuations of its energy has been developed. The model is used to describe the irreversible process of binding between ligand and receptor molecules in a solution. Analytical expressions for the probabilities of transitions between non-stationary states of the system averaged over both equilibrium vibrations in the medium and stationary states in the system were derived. The explicit dependences of the transition rate constants on the ligand concentration, solution viscosity, and temperature were found for the irreversible model with three kinetic stages.

1. Introduction

While studying non-equilibrium processes in various physical, chemical, and biological systems (e.g., the exciton transport in low-dimensional ordered structures, the electron transfer in donor-acceptor molecular complexes, the dynamics of ligand-induced conformational transformations in receptor biomacromolecules, *etc.*) it is of importance to know the specific dependences of observables on internal (microscopic) and external (macroscopic) parameters. Recently, this problem got an additional motivation, in particular, in connection with the application of spectroscopy and atomic-force microscopy methods to the study of single molecules in homogeneous and heterogeneous environments [1–8]. As a result, there appeared a unique possibility to observe, in the real-time mode, the non-stationary (transient) evolution of separate electron-vibrational states of individual molecules caused by external perturbations applied to the system. From the physical viewpoint, such a process is similar to the instant filling of a certain initial state of the system, which is depopulated afterward owing to a redistribution among other states. The latter become, in their turn, gradually filled and, having achieved the maximal filling degree, start to depopulate through a certain additional channel of irreversible decay. In this case, for the statement of the problem to be consistent in the framework of an irreversible kinetic model, the microscopic description of relaxation transitions between the fluctuating states in an open dynamic system, which interacts with the environment, has to be carried out.

The microscopic approach to the kinetic description of relaxation processes in quantum-mechanical systems in the presence of energy-parameter fluctuations was developed in many works [9–21]. The main attention was given to the analysis of the random low-intensity modulations of energy differences between transient states [9, 10, 13, 14, 18, 19] and the influence of an external stochastic field on the slowest transition rates, which confine the establishment of an ultimate thermodynamic equilibrium throughout the system [11–17, 20, 21]. At the same time, it is well known that the state populations, which are experimentally monitored during long-time intervals, have substantially non-stationary values in open molecular systems [22–25] in general, and, in particular, in the majority of biological systems [26, 27]. Having achieved the corresponding maximum values, those state populations exponentially vanish, not obeying the equilibrium Boltzmann relations in the general case. Therefore, the quantitative description of transient states in open quantum-mechanical systems, which interact with a fluctuating molecular environment, demands that a more general approach should be applied. First, such an approach must be kinetically consistent at different time scales, simultaneously covering both a very quick filling of transient states and their rather slow depopulation. Second, in the framework of this approach, it is necessary to take into account simultaneously both the microscopic relaxation interaction, which invokes transitions between energy levels, and thermodynamic fluctuations, which stochastically change the positions of those levels following a certain statistics [26, 27]. In this work, we develop a microscopic model of non-stationary states in an open system, which is in contact with its molecular environment in the equilibrium state and undergoes quasiclassical fluctuations of its energy. Then, we obtain a master equation for the populations of those states, which is averaged over the fluctuations in the system and the vibrations in the environment. Then we derive an analytical expression for the averaged rate of transitions between the states. At last, we demonstrate that, in the generalized irreversible kinetic model of transitions between three states, the corresponding magnitudes of transition rates contain information needed for the description of the transition state dynamics depending on the temperature, solution viscosity, and reactant concentration.

2. Microscopic Model of the System and the Master Equation

Consider a one-to-one-particle model of an open system (OS), which evolves in time, depending on the initial condition, at a given temperature T by exchanging vibrational quanta (phonons) with the environment. The OS states $|m\rangle$ will be distinguished according to the contact positions of a selected individual molecule (it will be referred to as a ligand) with respect to molecules in the solution volume and a selected binding center in a certain macromolecule (the latter will be referred to as a receptor). For the receptor model, we confine the consideration to considering only one contact with the ligand characterized by the binding energy E_1. The corresponding bound state between the ligand and the receptor is designated as $|1\rangle$. Bearing in mind the generalization of the one-center model onto the irreversible case, let us suppose that, besides this state, there exists a state $|0\rangle$ with the energy E_0, in which the integrity of the ligand as a separate molecule can be broken. In particular, in this state, the ligand can decay into components owing to a catalytic process or enter into a structurally transformed state of the desensitized receptor as a subunit. In this case, the energy difference between the states of the ligand bound with the center and the degraded one will always be much higher than the thermal energy $E_1 - E_0 \gg k_{\mathrm{B}}T$, where k_{B} is the Boltzmann constant.

In contrast to the receptor case where, as a simplification, only one contact of the receptor with the ligand can be taken into consideration (it is the "one-to-one-particle" receptor model), the number of contacts of a ligand with molecules in the solution volume is macroscopically large. In this case, we must distinguish between the number $\aleph_V$ of such contacts with an arbitrary molecule in the homogeneous (in essence, bulk) phase, when the specific position of the ligand with respect to the receptor is uncertain, and the number $\aleph_S$ of contacts with a selected molecule in the heterogeneous (at the interface) phase, when the ligand is located in an immediate proximity of the binding center. As a result, the total number of possible states $|m\rangle$ in the OS is characterized by the quantity $M + 1 = 2 + \aleph_S + \aleph_V N$ ($m = 0, 1, 2, \ldots, M$), where $N = 1/C$ is the number of solvent molecules per one ligand with relative concentration C.

The following analysis of the OS dynamics aims at a quantitative description of the amplitude and kinetic characteristics of the transitions that take place between miscellaneous states in the OS. Such a dynamics depends on the transition probabilities under the given initial conditions, the fluctuation parameters of OS, and the parameters of the relaxation interaction between the OS and the environment. As the initial state, we select the OS state, which corresponds to an arbitrary contact between the ligand and an arbitrary molecule in the bulk phase, provided that the ligand is characterized by the equiprobable distribution over those states and the ergodic approximation for transitions according to the principle "everyone-with-everyone."

The consideration routine for such processes is standard. In the adiabatic approximation, they are represented as a motion along multidimensional potential-energy surfaces, which are usually associated with the ground state in the OS. In simple OSs, in which the trajectory of motion is definite, this motion can approximately be considered as one-dimensional, and its trajectory can be associated with a reaction coordinate. Such an approximation turns out justified, e.g., for the relative length of a chemical bond in two-atom molecules. However, in the cases where the selected frequency of transitions between the ground and excited states in the OS is of the order of or lower than the characteristic phonon frequency in the environment, the adiabatic approximation fails [28]. In such cases, the transitions do not take place as a result of the strong adiabatic interactions, which form the potential surfaces of continuous motion in the space of energies of the ground and excited states in the OS, but are invoked exclusively by weaker non-adiabatic interactions, which couple together discrete (quantum) displacements of nuclei in the OS and environment molecules. In the bilinear approximation for those displacements, the non-adiabatic transitions are, mainly, of one-phonon character [27]. This circumstance substantially facilitates their analysis. However, in order that the consideration of such transitions in the second order of perturbation theory with respect to the magnitude of non-adiabatic interaction be correct, certain adiabatic corrections to the state energies must be calculated exactly (without use of perturbation theory). Such corrections, which are often taken into consideration in the form of stochastic terms [9, 10, 12, 13, 18–21, 26], can be substantial, as it happens in the classical limit for quasiisoenergic transitions [27], the frequencies of which are low in comparison with the thermal one. In the quantum-mechanical limit for endoergic transitions, the frequencies of which are much higher than the thermal one, those corrections can result in an increase of transition probabilities [18].

Bearing in mind the above consideration, let the energy $E_m(t)$ of the OS state $|m\rangle$ be given in the general form, $E_m(t) = E_m + \Delta E_m(t)$, where $\Delta E_m(t)$ is a stochastic increment of the stationary value E_m. The transitions between OS states take place now against a background of random shifts $\Delta E_m(t)$ of the energies from their corresponding average values E_m. Therefore, for the description of observable physical quantities to be correct, an averaging over stochastic realizations of this process has to be made (below, this operation is designated as $\langle\langle\ldots\rangle\rangle$). In particular, it is necessary to find the averaged populations of states $P_m(t) = \langle\langle p_m(t)\rangle\rangle$, where $p_m(t) = \langle m|\rho_0(t)|m\rangle$ are the non-averaged populations and $\rho_0(t)$ the density matrix for the OS, as well as the averaged probabilities of transitions between states, $W_{mm'}$. The latter are considered in the next section.

Let us define the Hamiltonian of the whole system (WS),

$$H(t) = H_0(t) + V + H_T \tag{1}$$

as a sum of the Hamiltonian for the OS,

$$H_0(t) = \sum_m E_m(t)|m\rangle\langle m|, \tag{2}$$

the Hamiltonian of the environment,

$$H_T = \sum_\lambda \hbar\omega_\lambda(b_\lambda^\dagger b_\lambda + 1/2) \tag{3}$$

($\hbar$ is Planck's constant), and the operator of a bilinear interaction between the OS and the environment,

$$V = \sum_{mm'}(1-\delta_{mm'})\sum_\lambda \chi_{mm'}^\lambda(b_\lambda^\dagger + b_\lambda)|m\rangle\langle m'|, \tag{4}$$

where $b_\lambda^\dagger$ and b_λ are the operators of creation and annihilation, respectively, of a normal vibration with frequency ω_λ in the environment. Owing to such a non-adiabatic coupling between the OS and the environment, which is characterized by the parameters $\chi_{mm'}^\lambda$ in Eq. (4), the processes of phonon creation and annihilation in the environment accompany the transitions between the OS states, with the energy conservation law for the WS being preserved.

Let us write down the stochastic Liouville equation for the density matrix $\rho(t)$ of the WS in the form

$$\dot\rho(t) = -\frac{i}{\hbar}[H(t), \rho(t)]. \tag{5}$$

The trace of the operator $\rho(t)$ over the environment states, $\rho_0(t) = \mathrm{Tr}_T\rho(t)$, composes a non-equilibrium density matrix for the OS, the evolution of which is assumed to be the slowest in the WS and is characterized by the times of relaxation transitions $\tau_{\rm tr}$. Therefore, since the establishment times of a vibrational equilibrium in the environment are much shorter, $\tau_{\rm vib} \ll \tau_{\rm tr}$, the density matrix for the WS can be factorized: $\rho(t) = \rho_0(t)\rho_T$, where $\rho_T = e^{-H_T/k_{\rm B}T}/\mathrm{Tr}_T e^{-H_T/k_{\rm B}T}$ is the equilibrium density matrix for the environment. In addition, the coarsened equation for $\rho_0(t) = \rho_d(t) + \rho_{nd}(t)$, obtained owing to the action of the diagonal, T_d, and non-diagonal, T_{nd}, projective operators, becomes closely related to the diagonal part of the OS density matrix $\rho_d(t) = \sum_m \langle m|\rho_0(t)|m\rangle|m\rangle\langle m| = T_d\rho_0(t)$, $(\rho_{nd}(t) = T_{nd}\rho_0(t))$. Applying the Nakajima–Zwanzig method [29, 30] to the stochastic equation (5) [27], we obtain the coarsened master equation for $\rho_d(t)$,

$$\dot\rho_d(t) = -\frac{1}{\hbar^2}\int\limits_0^t d\tau T_d[V, U(\tau)[V, \rho_d(t-\tau)]U^\dagger(\tau)], \tag{6}$$

where $U(\tau) = \hat D\exp\{-\frac{i}{\hbar}\int_0^\tau dt'[H_0(t') + H_T]\}$ is the stochastic operator of evolution, and $\hat D$ is the Dyson operator of chronological ordering. Equation (6) demonstrates that, in the second order of perturbation theory in the magnitude of interaction between the OS and the environment (4), the non-Markovian evolution of OS, coarsened over discretization times $\Delta t > \tau_{\rm vib}$, is governed by the evolution of only the diagonal part of the OS density matrix and the diagonal stochastic fluctuations in the non-perturbed OS (2), which take place against the background of equilibrium vibrational processes in the environment (3).

3. Kinetic Equations and Averaged Transition Probabilities

Knowing the specific form of a Hamiltonian for the WS (see Eqs. (1)–(4)) allows one to use Eq. (6) to obtain a closed system of non-Markovian kinetic equations for non-averaged state populations in the OS,

$$\dot p_m(t) = -\frac{2}{\hbar^2}\mathrm{Re}\sum_{m'}\int\limits_0^t d\tau[Q_{mm'}(\tau)p_m(t-\tau) -$$

$$-Q_{m'm}(\tau)p_{m'}(t-\tau)]. \tag{7}$$

Here, $Q_{mm'}(\tau) = \sum_\lambda |\chi^\lambda_{mm'}|^2 f_{mm'}(\tau) R_\lambda(\tau) e^{i\Omega_{mm'}\tau} = Q^*_{m'm}(\tau)$ are the time-dependent transition coefficients, $f_{mm'}(\tau) = f_{m'm}(-\tau) = f^*_{mm'}(-\tau) = e^{i\int_0^\tau \Delta\Omega_{mm'}(t')dt'}$ are the stochastic functionals of relative random frequency shifts $\Delta\Omega_{mm'}(t) = [\Delta E_m(t) - \Delta E_{m'}(t)]/\hbar$ for the transition frequencies $\Omega_{mm'} \equiv (E_m - E_{m'})/\hbar$, $R_\lambda(\tau) = R^*_\lambda(-\tau) = n(\omega_\lambda)e^{i\omega_\lambda\tau} + [1 + n(\omega_\lambda)]e^{-i\omega_\lambda\tau}$ is the one-phonon correlation function, and $n(\omega_\lambda) = [e^{\hbar\omega_\lambda/k_\mathrm{B}T} - 1]^{-1}$ is the Bose distribution function for vibrations. The main complexity for the solution of Eqs. (7) consists in the non-Markovian behavior of their integrand expressions and the necessity to average the stochastic functionals in the explicit form. However, if the positions of energy levels depend on thermodynamic fluctuations, which correspond, at room temperature, to intermolecular collisions with the frequency $\nu \equiv \omega_T/2\pi = k_\mathrm{B}T/2\pi\hbar \cong 6 \times 10^{12}$ s^{-1}, the average time intervals between consecutive collision events, $\tau_\nu = \nu^{-1}$, are much shorter than the transition times, $\tau_\nu \ll \tau_\mathrm{tr}$. As a consequence, the stochastic averaging of functionals on the right-hand side of expression (7) can be factorized, provided that the discretization time $\Delta t > \tau_\nu$: $\langle\langle f_{mm'}(\tau)p_m(t-\tau)\rangle\rangle = F(\tau)P_m(t)$. Here, we supposed that the relative frequency fluctuations $\Delta\Omega_{mm'}(t) = \Delta\Omega(t)$ do not depend on the numbers of states in the OS,

$$F(\tau) = \langle\langle e^{i\int_0^\tau \Delta\Omega(t')dt'}\rangle\rangle = F_{mm'}(\tau) = \langle\langle f_{mm'}(\tau)\rangle\rangle. \tag{8}$$

We also took into account that the non-Markovian behavior does not reveal itself in the second order of perturbation theory [27]. Therefore, $P_m(t-\tau) \approx P_m(t)$.

The dependence of the correlation function $F(t)$ on stochastic frequency shifts (8) is dictated by a specific model for the stochastic processes under consideration. However, in the case of the most widespread processes such as a damped dichotomic process, the Gaussian Markov process, or the white noise, a simple exponential Kubo representation $F(t) = e^{-\gamma t}$, where the meaning of γ-parameter is the fluctuation half-width of the level, is more adequate. The latter is usually directly associated with the friction coefficient, which is linearly proportional, in accordance with the Stokes law, to the viscosity [12, 13]. It can be shown [26, 27] that the parameter γ is expressed in terms of the standard energy deviation ε and the average frequency fluctuation ν as follows: $\gamma = \varepsilon^2/(4\pi^2\hbar^2\nu)$. Therefore, the time $\tau_\gamma = \gamma^{-1} = (4\pi^2\hbar^2\nu)/\varepsilon^2$ needed for the correlation function $F(t) = e^{-t/\tau_\gamma}$ to change is short enough relative to the characteristic variation time τ_tr for $P_m(t)$, $\tau_\gamma \ll \tau_\mathrm{tr}$. This circumstance allows the upper limit of the integral on the right-hand side of Eq. (7) to be safely extended to infinity, which is equivalent to the neglect of the t-dependence in the integral kinetic coefficients for the discretization times $\Delta t > \tau_\gamma$.

Hence, for the stochastic averaging of Eqs. (7) to be correct, we must (i) factorize the products of stochastic functionals, (ii) neglect the non-Markovian behavior of the populations and the kinetic coefficients, and (iii) write down the correlation function (8) in the form $F(t) = e^{-\gamma t}$, in which the effective coefficient of viscosity contains information about stochastic fluctuations. In the framework of this algorithm, the non-Markovian stochastic equations (8) become simpler, being reduced to the kinetic equations for the observable populations $P_m(t)$,

$$\dot{P}_m(t) = -P_m(t)\sum_{m'} W_{mm'} + \sum_{m'} P_{m'}(t)W_{m'm}. \tag{9}$$

It is important that, in contrast to standard kinetic equations of the balance type [17], the corresponding transition probabilities in Eqs. (9),

$$W_{mm'} = \frac{2\gamma}{\hbar^2}\sum_\lambda |\chi^\lambda_{mm'}|^2 \times$$

$$\times \left[\frac{n(\omega_\lambda)}{\gamma^2 + (\Omega_{mm'} + \omega_\lambda)^2} + \frac{n(\omega_\lambda) + 1}{\gamma^2 + (\Omega_{mm'} - \omega_\lambda)^2}\right] \tag{10}$$

are averaged over equilibrium vibrations in the environment and thermodynamic fluctuations in the OS. Despite that the characteristic durations of those processes are less than the times of discretization of the observations in the system, $\tau_\mathrm{vib} \sim \tau_\nu \sim \tau_\gamma < \Delta t \ll \tau_\mathrm{tr}$, they are not rejected (not filtered out), but are consistently taken into consideration in the form of their averaged characteristics, namely, the occupation numbers $n(\omega_\lambda)$ for vibrations in the environment and the viscosity coefficient γ for fluctuations in the OS. As a result, the coarsened description (Eqs. (9) and (10)) reduces the fast processes to equilibrium (for vibrations) and stationary (for fluctuations) ones, as well as traces, on the average, the kinetics of slower non-equilibrium (irreversible non-stationary) processes.

4. Kinetics of the Generalized Three-Phase Irreversible Process

There are no general relations describing the dependences of dynamic characteristics of some process on its kinetic parameters. The application of the approximate balance kinetic equations (9) with the transition rate constants presented in form (10) gives a coarsened description of transient processes against the background of the completed equilibrium and stationary stages. In the framework of such a statement of the problem, the open systems, whose states are depopulated following the exponential law with given rate constants, are of special interest. An essential aspect of this problem is the development of simple analytical models, which would reveal key factors, owing to which the variation of rate constants at definite kinetic stages could affect certain dynamic characteristics of the process.

As an example of such a model, let us consider a system with three states ($i = 1, 2, 3$) and the initial conditions $P_3(0) = 1$ and $P_2(0) = P_1(0) = 0$. If an irreversible kinetic stage is available, the system states are depopulated in the course of time, with their total population falling down exponentially from 1 to 0. This irreversible stage, which starts, for definiteness, from the state $i = 1$, will be characterized by the rate constant k. Our aim is to compare this system with the general system (Eq. (9)) in the framework of the kinetic problem considered in Section 2. For this purpose, the state $i = 1$ must simulate a state of point contact between the bound ligand and the receptor, the state $i = 2$ must combine $\aleph_S$ contact states of the ligand in the heterogeneous phase, and the state $i = 3$ must cover the set of $\aleph_V N$ ligand states in the homogeneous (bulk) phase, and the numbers of local contacts of the ligand can be different in different phases. Therefore, we may assume that $W_{21} = W_{31} = \ldots = W_{\aleph+11} \equiv A$, $W_{12} = W_{13} = \ldots = W_{1\aleph+1} \equiv B$, $W_{2\aleph+2} = W_{3\aleph+2} = \ldots = W_{\aleph+1\aleph+2} = W_{2\aleph+3} = \ldots = W_{\aleph+1\aleph(N+1)+1} \equiv \overline{W}$, and $W_{\aleph+22} = \ldots = W_{\aleph+2\aleph+1} = W_{\aleph+32} = \ldots = W_{\aleph(N+1)+1\aleph+1} \equiv W$ in Eq. (9). It is equivalent to the assumption that, when the states of every phase are combined into the corresponding cumulative state, the transition probabilities of all stages are ergodically equivalent. Again, according to the principle of microscopic reversibility of the processes, we should consider a certain state $i = 0$ such that the probability of the transition from it into the state $i = 1$ is much lower than those of other transitions, $W_{01} \ll W, \overline{W}, A, B, W_{10}$. If the energy of this state is decreased infinitely, $E_0 \to -\infty$, it is equivalent to that the irreversible kinetic stage with the transition probability $k \equiv W_{10}$ is included into the dynamics of the system. In what follows, the system with three states is considered as a basic one. This system represents a simplified case, $\aleph_V = \aleph_S = N = 1$, of the general case with $M + 1$ states (9), for which $\aleph_{V,S} \geq 1$ and $N \geq 1$. To distinguish among those cases, let the small letters a, b, w, and $\overline{w}$ designate the probabilities of transitions in the basic system. Having obtained an exact solution for the three-state case, we compare each of those probabilities with the probabilities in the general case A, B, W, and $\overline{W}$. Note at once that $B = b$, because those probabilities do not depend on the numbers of contact states in different phases.

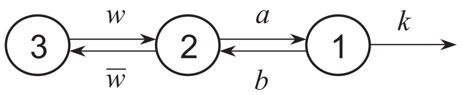

Fig. 1. Block diagram for the irreversible kinetic model of transitions between three states

The diagram of the basic model for transitions between three states with an irreversible stage is depicted in Fig. 1. The rigorous solution of the kinetic problem for the state populations in this model is determined from a system of three differential equations, which is reduced to a system of nine algebraic equations with nine unknown variables. The exact solution of this problem looks like

$$P_3(t) = w\overline{w}\sum_{i=1}^{3}(\lambda_i - b - k)e^{-\lambda_i t}\times$$

$$\times\left[(\lambda_i - w)\prod_{j=1;j\neq i}^{3}(\lambda_i - \lambda_j)\right]^{-1};$$

$$P_2(t) = w\sum_{i=1}^{3}(b + k - \lambda_i)e^{-\lambda_i t}\left[\prod_{j=1;j\neq i}^{3}(\lambda_i - \lambda_j)\right]^{-1};$$

$$P_1(t) = wa\sum_{i=1}^{3}e^{-\lambda_i t}\left[\prod_{j=1;j\neq i}^{3}(\lambda_i - \lambda_j)\right]^{-1}, \qquad (11)$$

where λ_1, λ_2, and λ_3 are the real-valued positive roots (for definiteness, let they be arranged in the growing order) of the characteristic equation

$$\lambda^3 - \lambda^2(w + \overline{w} + a + b + k)+$$

$$+\lambda[(w + \overline{w})(b + k) + a(w + k)] - wak = 0. \qquad (12)$$

Solution (11), (12) is mathematically rigorous, because it excludes, in fact, the exact coincidence of two or three roots (this event is considered to be infinitely rare or almost negligible). The kinetic description of populations $P_i(t)$ (11) is made within the whole admissible scale of relaxation times $\lambda_3^{-1} < \lambda_2^{-1} < \lambda_1^{-1}$, provided that the paired differences between the roots, which are in the denominators of exponential components, never vanish. In this case, it is necessary to know the explicit dependences of the root values on the parameters of the characteristic equation (12). The exact Cardano formula provides no visualization for the real-valued roots of the cubic equation. More ostensive is the Vieta algorithm, in which separate scales for times are introduced explicitly. In the framework of this algorithm, Eq. (12) can be identically transformed to the form

$$\lambda^3 - \lambda^2 \tau_{\text{eq}}^{-1} + \lambda(\tau_{\text{eq}}\tau_{\text{st}})^{-1} - (\tau_{\text{eq}}\tau_{\text{st}}\tau_{\text{eff}})^{-1} = 0, \tag{13}$$

where the kinetic processes are grouped according to the time values, which are most typical of them. Here, the fastest processes are defined by the time of the establishment of a local equilibrium in the system,

$$\tau_{\text{eq}} = (\lambda_1 + \lambda_2 + \lambda_3)^{-1} = (w + \overline{w} + a + b + k)^{-1}. \tag{14}$$

The processes that correspond to an intermediate equilibrium between states of the system are characterized by the stationary time

$$\tau_{st} = (\lambda_1 + \lambda_2 + \lambda_3)(\lambda_1\lambda_2 + \lambda_1\lambda_3 + \lambda_2\lambda_3)^{-1} =$$

$$= (w + \overline{w} + a + b + k)\times$$

$$\times[(w + \overline{w})(b + k) + a(w + k)]^{-1}, \tag{15}$$

whereas the slowest processes that confine the ultimate depopulation of states of the system correspond to the effective time

$$\tau_{\text{eff}} = 1/\lambda_1 + 1/\lambda_2 + 1/\lambda_3 = \frac{\tilde{a}(1 + k/w) + b + k}{k\tilde{a}}, \tag{16}$$

where

$$\tilde{a} \equiv \frac{a}{1 + \overline{w}/w} \tag{17}$$

is a predicted rate constant for filling the final state. Hence, instead of engaging the times $\lambda_3^{-1} < \lambda_2^{-1} < \lambda_1^{-1}$, which must be determined from Eq. (12) numerically, provided that that the relations between them are arbitrary, the kinetic description of system (11) can be carried out analytically (Eqs. (13)–(16)) in the resolved-time scale $\tau_{\text{eq}} \ll \tau_{\text{st}} \ll \tau_{\text{eff}}$. This circumstance can make the results obtained more understandable from the physical viewpoint, in particular, while analyzing the dynamic characteristics of the system.

Equations (11)–(13), taking Eqs. (14)–(17) into account, allow exact expressions to be obtained for the magnitudes of separate integral yields, $\theta_i = \int_0^\infty dt P_i(t)$, and for the total integral yield, $\theta_{\text{eff}} = \int_0^\infty dt P(t)$, of states of the system, which are, by definition, the integrals of the separate populations $P_i(t)$ and the total population $P(t) = \sum_{i=1}^3 P_i(t)$, respectively, over the whole time interval. The magnitudes of those yields, which have the meaning of a dynamic duration for the depopulation of corresponding states, are given by the expressions

$$\theta_1 = \frac{1}{k}; \quad \theta_2 = \frac{K}{k}; \quad \theta_3 = \frac{1 + \theta_2\overline{w}}{w}; \quad \theta_{\text{eff}} = \tau_{\text{eff}}, \tag{18}$$

where $K = (b + k)/a$ is the equilibrium constant for the final state. Equations (18) demonstrate that the dynamic duration θ_1 of the depopulation of the final state is determined only by the time $1/k$, which is given for the kinetic channel of irreversible decay in the system. The quantity θ_1 and the duration θ_2 of the intermediate state depopulation satisfy the general equality

$$\frac{\theta_1 K}{\theta_2} = 1, \tag{19}$$

which does not depend on the input stage. On the other hand, the dynamic duration θ_{eff} of the ultimate (effective) depopulation of states coincides with the effective (slowest) time τ_{eff} (Eqs. (13) and (16)) of the kinetic evolution of the system. In contrast to the quantities θ_1 and θ_2, the quantity $\tau_{\text{eff}} = \theta_{\text{eff}}$ substantially depends on the rate constants at the input stage (Eqs. (14) and (15)). This dependence manifests itself both directly, by means of the initial state depopulation time $1/w < \theta_3$ (18), and indirectly, by means of the equilibrium constant $\overline{w}/w$ for the bulk stage with respect to the transient state. The latter influences the population rate a of the final state by reducing it to a certain predicted value $\tilde{a}$ (17).

In what follows, we must definitely determine how the quantities a, w, and $\overline{w}$ can depend on the number of ligand contact positions in the bulk and heterogeneous phases. Since the corresponding numbers are directly related to the bulk concentration of a ligand and the entropy factors, we can use this way to find the specific relations between the parameters of the three-state model (Fig. 1) and the corresponding quantities A, W, and $\overline{W}$ for the general system (Eq. (9)). For this purpose, however, we must consider a model, which describes the dynamics of a ligand in the bulk and heterogeneous phases.

Let the parameter $\overline{W} = D/\Delta l^2$ determine the probability for the ligand to make a diffusion jump over the distance Δl, which corresponds to the distance between its neighbor contact positions, in a solution with the diffusion coefficient D. The same probability is inherent to the jump of the ligand from an arbitrary state in the heterogeneous phase into an arbitrary state in the homogeneous phase. If the initial state of a ligand in the solution is random, we may put its contact positions into the correspondence with the centers in some regular or disordered lattice. Then, according to the graph theory theorem [31], the most probable number of jumps needed for the ligand to cross the distance between arbitrary centers equals $M^{1/d}$, where M is the number of lattice centers per one ligand, and d is the lattice dimension. If the lattice centers are equivalent and connected with one another in such a way that the probabilities of transitions between them are identical, the topology of such a lattice is ergodic, its dimension coincides with that of a surface ($d = 2$), and the ligand states in the lattice become degenerate. In the equilibrium case, we may change from the identical states of the ligand in the solution bulk to a single summary $\aleph_V N$-fold degenerate state $i = 3$ [32, 33], as well as from the ligand states in the heterogeneous phase to an $\aleph_S$-fold degenerate state $i = 2$. This causes a reduction of the probability for the effective jump from the summary state $i = 3$ into the summary state $i = 2$ with respect to the probability of a backward jump by a factor of $\Re N$, with the corresponding heterogeneity factor $\Re \equiv \aleph_V/\aleph_S$:

$$w = \frac{W}{\aleph_S} = \frac{\overline{W}}{\aleph_V N} = \frac{\overline{w}C}{\Re}. \tag{20}$$

In the non-equilibrium case, along with $\aleph_V N$ bulk ligand states, it is also necessary to consider the average distance $\bar{l}$ crossed by the ligand, when wandering over the bulk phase until it contacts with the heterogeneous phase. Under the ergodic initial conditions, this distance is equal to $\bar{l} = \Delta l\sqrt{\aleph_V N}$. Therefore, we obtain the probability $w = D/\bar{l}^2 = \overline{w}/\Re N$ for the effective jump over this distance, which coincides with expression (20). Analogously, for the predicted constant $\tilde{a}$ (see Eq. (17)), we have

$$\tilde{a} = \frac{A}{\aleph_V N + \aleph_S} = \frac{aC}{C + \Re}, \tag{21}$$

where $a = Ae^{-\sigma}$, and $\sigma \equiv \ln \aleph_S$ is the entropy factor (in natural units), which reveals the advantage of a joint ligand position over a local one in the heterogeneous phase.

In general, the kinetic scheme for transitions in the three-state system with an irreversible stage, which was considered in this section, appended by the regularities found using formulas (20) and (21) for the rate constants at its input stages, is a basic model for the generalized three-phase irreversible process. This process is completely adequate to the problem, which was formulated in Section 2 for the description of the non-stationary dynamics of relaxation transitions in open quantum-mechanical systems. In this case, we must adopt that, in the framework of the kinetic scheme depicted in Fig. 1, the rate constants contain averaged internal and external parameters, the variation of which affects the dynamic characteristics of the system.

5. Simplified Kinetics of Irreversible Processes

While analyzing the experimental data, besides the expressions for populations (11) in the form of a sum of three exponential components, it is also necessary to have the simplified expressions, which would contain sums of two such components or even be represented as a single component. However, for this purpose, it has to be indicated in Eqs. (13)–(16) which of the three kinetic stages – the bulk, heterogeneous, or decay one – plays the dominating role in the establishment of a local equilibrium in the system. From the general physical reasons, we may consider that the heterogeneous processes with the relaxation times $(a+b)^{-1}$ run much more slowly than the bulk ones, which are characterized by the times $(w + \overline{w})^{-1}$,

$$a + b \ll w + \overline{w}. \tag{22}$$

Moreover, in order that the population magnitudes for the transient states be not very low, we may suppose that the characteristic depopulation rate of the final state at the stage of irreversible decay is much slower than the corresponding population rate w of the transient state at the input stage,

$$k \ll w. \tag{23}$$

Therefore, below, we may adopt that a local equilibrium in the system is reached owing to superfast processes running just in the bulk phase.

Conditions (22) and (23) determine the quasistationary approximation $a+b+k \ll w+\overline{w}$ for the transient and final stages with respect to the equilibrium input stage. It is equivalent to the requirement that the semistrong inequalities $\tau_{\text{eq}} \ll \tau_{\text{st}} < \tau_{\text{eff}}$ and $\lambda_3 \gg \lambda_2 > \lambda_1$ in Eqs. (13) and (12) be satisfied, respectively. Therefore, the exact three-exponential expressions (11) are transformed into the simplified forms with two exponents each,

$$P_2(t) = (\lambda_2 - \lambda_1)^{-1}[(\lambda_2 - \tilde{a})e^{-\lambda_1 t} + (\tilde{a} - \lambda_1)e^{-\lambda_2 t}];$$

$$P_1(t) = \tilde{a}(\lambda_2 - \lambda_1)^{-1}[e^{-\lambda_1 t} - e^{-\lambda_2 t}]\,, \qquad (24)$$

where

$$\lambda_{1,2} = \frac{1}{2}[(\tilde{a} + b + k) \mp \sqrt{(\tilde{a} + b + k)^2 - 4\tilde{a}k}]. \qquad (25)$$

In this case, the kinetic description of the system is carried out on the scale of equilibrium discretization times, $\Delta t > \tau_{\mathrm{eq}}$ (14). Those times, by their essence, are completely similar to the discretization times for the vibrational, τ_{vib}, and fluctuational, $\tau_\nu \sim \tau_\gamma$, equilibria introduced in Sections 2 and 3, although the former considerably exceed the latter by magnitude: $\Delta t > \tau_{\mathrm{eq}} \gg \tau_{\mathrm{vib}} \sim \tau_\nu \sim \tau_\gamma$.

As we see, if conditions (22) and (23) are satisfied, the fast kinetic component $P_3(t) \sim e^{-\lambda_3 t}$ in Eq. (11), which characterizes the bulk stage, disappears from expressions (24). However, the averaged information about it remains to be included into the predicted rate $\tilde{a}$ (17). Now, if we suppose that the stronger inequalities, $\tau_{\mathrm{eq}} \ll \tau_{\mathrm{st}} \ll \tau_{\mathrm{eff}}$ and $\lambda_3 \gg \lambda_2 \gg \lambda_1$, are satisfied in Eqs. (13) and (12), respectively, the heterogeneous component $P_2(t) \sim e^{-\lambda_2 t}$ also disappears from the consideration. In this case, the description of the system becomes coarsened to a single component

$$P_1(t) = \mathrm{P}_1^{\mathrm{st}} e^{-t/\tau_{\mathrm{eff}}}, \qquad (26)$$

where $\mathrm{P}_1^{\mathrm{st}} = \tilde{a}/(\tilde{a} + b + k)$ is the magnitude of the final state population $P_1(t)$, which is established in the stationary regime. However, such a coarsened description is no more complete. Really, unlike the total population $P_1(t)+P_2(t)$ in Eq. (24), the population $P_1(t)$ in Eq. (26) falls down to zero not from unity at $t = 0$, but from a lower value $\mathrm{P}_1^{\mathrm{st}} < 1$. According to Eqs. (18), (21), and (25), this quantity depends on the bulk concentration C of a ligand, following the modified Langmuir isotherm

$$\mathrm{P}_1^{\mathrm{st}} = C[C(1 + K) + \Re K]^{-1}. \qquad (27)$$

This enables the magnitude of $\mathrm{P}_1^{\mathrm{st}}$ to be varied within a wide interval ranging from zero at $C = 0$ to $(1+K)^{-1} < 1$ at $C \to \infty$. The same quantity, in effect, governs the corresponding times of stationary population and effective depopulation of states (Eqs. (23)–(26), (15), and (16)),

$$\tau_{\mathrm{st}} = \mathrm{P}_1^{\mathrm{st}}(\tilde{a})^{-1} \qquad \text{i} \qquad \tau_{\mathrm{eff}} = (\mathrm{P}_1^{\mathrm{st}} k)^{-1}. \qquad (28)$$

Hence, formula (26) is not practically valid at $t = 0$, being true only at the stationary discretization times $\Delta t > \tau_{\mathrm{st}} \gg \tau_{\mathrm{eq}}$ (Eqs. (14) and(15)). Only after those times have passed, the one-exponential description (26) for the behavior of the system, which is characterized by the effective time $\tau_{\mathrm{eff}} \gg \tau_{\mathrm{st}}$ (see Eqs. (16) and (28)), becomes possible.

Note that, at $\tau_{\mathrm{st}} \ll \tau_{\mathrm{eff}}$ or, equivalently, $\tilde{a}k < \tilde{a}(b + k) \ll (\tilde{a} + b + k)^2$ (see Eqs. (16) and (28)), the following inequality is satisfied:

$$\mathfrak{D}_1 = \mathrm{P}_1^{\mathrm{st}}(1 - \mathrm{P}_1^{\mathrm{st}}) \ll 1. \qquad (29)$$

Here, $\mathfrak{D}_1$ means the distribution dispersion for the random amplitude of a stationary binary process with the probability $\mathrm{P}_1^{\mathrm{st}}$, and it is associated with the uncertainty in the determination of some values of magnitudes. Therefore, inequality (29) actually means that, for the magnitudes of transient state populations to obtain maximal definiteness (or minimal uncertainty), the process should run as close to the stationary one as possible. According to Eq. (27), this requirement constrains the applicability of the Briggs–Haldane solution for the Michaelis–Menten problem in the stationary mode [34], by reducing it only to the case of a very high concentration, $C \gg K$, and/or a considerable affinity of the ligand to the receptor, $K^{-1} \gg 1$. In the cases of moderate C and K where inequalities (23) and (29) are not satisfied, more exact equations (11)–(18) or their simplified analogues (24) and (25) are to be used.

6. Influence of Parameters of the System on the Dynamics of Transient States

Knowing the analytical dependences of state populations on the rates of kinetic stages (see Eqs. (11)–(13)), as well as the dependences of the latter on various structural (relaxation, fluctuation, entropy) factors (see Eqs. (10), (20), and (21)), it is possible to analyze the influence of macroscopic parameters (concentration, viscosity, and temperature) on the dynamics of states of the system. Since this influence is different for different phases, we have to consider those parameters separately. Note that, under ergodic conditions for the diagram in Fig. 1, the ligand concentration C, which affects only the input population rate w for the transient state (20), can influence other parameters of the system only by means of this quantity (see Eqs. (14)–(28)). Therefore, by fixing the rate $\overline{w}$, which is reciprocal to the rate w, at a certain value satisfying the condition $w/\overline{w} = C/\Re \ll 1$, we can study the concentration dependence in Eqs. (11) in terms of the relative change of the final state population magnitude $\overline{\mathrm{P}}_1 = \max\{\mathrm{P}_1(0 \le t < \infty)\}$, i.e. the ratio $\overline{\mathrm{P}}_1/(1-\overline{\mathrm{P}}_1)$, as a function of the quantity $\tilde{a} = aC/\mathfrak{R}$ (see Eqs. (20) and (21)). On the log-log scale, the slope of the plot of this function coincides with the Hill coefficient n_{H} describing the cooperativity of the system [35], provided that the system can freely carry out a controllable variation of the magnitudes of its dynamic characteristics, when the concentration changes. If $n_{\mathrm{H}} = 1$, the system is considered to be non-cooperative; the value $n_{\mathrm{H}} > 1$ means a positive cooperativity; and $n_{\mathrm{H}} < 1$ testifies to a "negative" cooperativity. In Fig. 2, an example of the cooperative effect owing to a certain variation of the kinetic parameters in Eq. (11) is shown. In the stationary limit (Eq. (29)), the concentration dependence of the final state population magnitude $\overline{\mathrm{P}}_1(C)$ must coincide with that for the stationary quantity $\mathrm{P}_1^{\mathrm{st}}(C)$ and, consequently, must be described by a non-cooperative (Langmuir) concentration dependence (27). As Fig. 2 demonstrates, this case can be realized only in a very narrow range of parameters, when the rate constant for the irreversible decay of the final state is negligibly small. Practically for all other values of the parameters, the system reveals a negative cooperativity, with the lowest value among $n_{\mathrm{H}} < 1$ being achieved in the limiting case of non-stationary mode, in which two of three roots of the characteristic equation (12) become degenerate, $\lambda_1 = \lambda_2 \ll \lambda_3$.

As follows from Eq. (10), the rates of relaxation transitions must depend explicitly on the fluctuation halfwidth γ of the levels. However, this dependence manifests itself mainly for one-phonon quasiisoenergic transitions, when the frequencies of transitions in the system coincide with the frequencies of vibrations in the environment, being at the same time lower in comparison with the thermal frequency, $|\Omega_{mm'}| = \omega_\lambda \ll \omega_T$. This criterion is satisfied by transitions occurring in the homogeneous phase, where the parameter γ corresponds to the friction coefficient, which is proportional to the viscosity. Within the single-mode representation for the spectral function, $J = (2\pi/\hbar^2)\sum_\lambda \sum_{mm'} \omega_\lambda^{-1} |\chi^\lambda_{mm'}|^2 \delta(|\Omega_{mm'}| - \omega_\lambda)$, Eqs. (10) and (21) yield

$$w = \frac{\overline{w}}{\mathfrak{R}N} = \frac{D}{\Delta l^2 M} = 2J\frac{k_{\mathrm{B}}T}{\hbar\gamma}. \tag{30}$$

Here, the dependence on the viscosity γ reveals itself by means of the diffusion coefficient D, which obeys the Einstein relation $D = 2k_{\mathrm{B}}T/\gamma$. Besides Eq. (30), we have $J = \hbar/\Delta l^2 M$. In other words, the spectral function J corresponds to the quantum of least action $\hbar$, which is related to the dispersion Δl^2 of elementary shifts stimulated by this action, and to the degree of state degeneracy M of the system. This means that the quantity J depends only on the structure factors of the relaxation interaction and characteristic vibrations in the system [27], whereas the coefficient D contains information about macroscopic parameters of the system, such as the viscosity and the temperature.

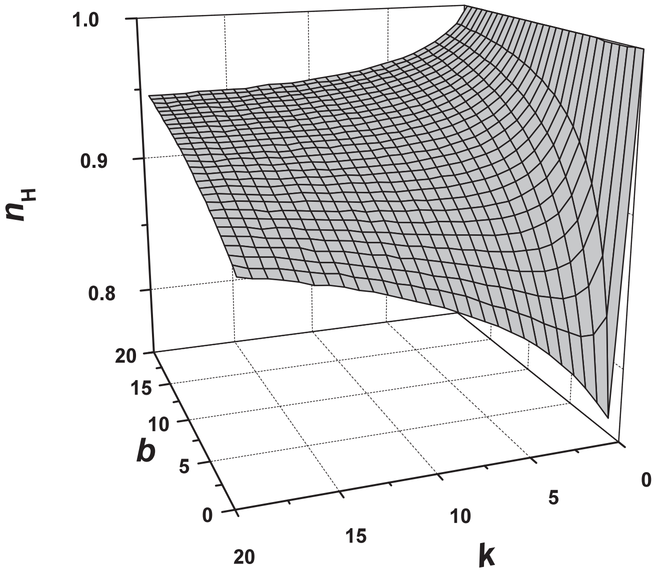

Fig. 2. Dependence of the Hill coefficient n_{H} on the rate constants b and k (see the diagram in Fig. 1), provided that $w/\overline{w} = \tilde{a}/a = C/\mathfrak{R} \ll 1$

From the exact expressions (11)–(16), we see that the viscosity effects (30) may, most probably, manifest themselves in strongly degenerate systems with $M \gg 1$ (low C's), owing to the term $\sim k/w$, which is included into the time τ_{eff} (16) of effective state depopulation in the three-phase model (Fig. 1). However, the increase of γ gives rise to only a weak growth of τ_{eff} against an insignificant decrease of the magnitude $\overline{\mathrm{P}}_1$ of the final state (11), accompanied by an increase of the integral yields of the summary, θ_{eff}, and initial, θ_3, states (18). In addition, at low C's, the magnitudes of the dynamic characteristics of the system are very insignificant, the corresponding values being of the same order as their errors. Therefore, the viscosity effects, most likely, do not authentically manifest themselves at the stages of ultimate depopulation of states of the system.

At last, let us dwell on the temperature dependences, which can be observed during transient processes. It is a general problem, because almost all transition rates must be more or less dependent on the temperature in that or another way. In some cases, the temperature dependences can be completely analyzed at the quantitative level and, therefore, systematized [26, 27, 36–39]. However, such dependences remain undetermined for the overwhelming majority of transient processes. First of all, this concerns the kinetic and dynamic parameters, which enter into the sums of exponents in the expressions for the populations of transient states (11). If the external conditions (in particular, the temperature) are varied, the evaluation of those parameters is an inverse problem, which is ill-posed from the mathematical viewpoint [40–42] and can be inexact in principle. To a less extent, this concerns the integral yields of states (18). Those quantities are directly related to the dynamic characteristics for separate kinetic stages of the system. Therefore, they allow the regressive analysis to be carried out in terms of a well-formulated direct problem. For instance, the integral yield θ_1 of the final state unambiguously characterizes the duration of its depopulation, $1/k$, which sometimes turns out absolutely independent of the temperature [26,39]. On the contrary, the integral yield θ_2 of the transient state depends on the equilibrium constant b/a for the heterogeneous stage. This quantity substantially depends on the temperature, the dominating contribution being played by the rate b of endothermic dissociation of the ligand from the receptor. This process is characterized by the activation energy, which is the highest for the system and which is estimated, in accordance with Eq. (10), as $E^a = \hbar\Omega_{21} \gg k_{\rm B}T$. We note that it is just the energy that is measured directly in experiments [39]. Therefore, knowing the quantity E^a, putting $b = B = A\exp(-E^a/k_{\rm B}T)$ in accordance with Eq. (9) and Fig. 1, and taking the established dependence (21) into account, we find the following upper limit for the entropy factor:

$$\sigma \le \ln\frac{b}{a} + \frac{E^a}{k_{\rm B}T}. \tag{31}$$

In work [39], it was shown that, for $P2X_3$ receptors, which are activated by adenosine triphosphate ligands, the typical values of equilibrium constant and activation energy are, respectively, $b/a = 10^{-11}$ and $E^a = 1.7$ eV $\approx 70k_{\rm B}T$. Taking into account that $\ln 10 \approx 7/3$ and using Eq. (31), we directly obtain the estimate $\sigma \le 44$, which can be applied to the entropy factors for organic molecules in nanovolumes.

A temperature behavior similar to that of θ_2 is also demonstrated by the equilibrium constant $K = \theta_2 k$ (18); in particular, it enters into expression (27) for the amplitude $\mathrm{P}_1^{\rm st}$. However, since the temperature dependence of K manifests itself only at insignificant concentrations $C \ll K$, i.e., when $\mathrm{P}_1^{\rm st}$ is small, this analysis is little informative. To make a more reliable estimation for K, both the temperature and concentration variations are to be applied. In so doing, it is possible to experimentally verify the validity of the predicted theoretical equality (19), which is insensitive to such a variation.

To summarize, the process of irreversible binding between the ligand and the receptor in the solution depends on the ligand concentration, as well as on the viscosity and the temperature of the solution. The concentration dependence, which arises owing to the degeneracy of states in the open system, extends over all kinetic stages of the process. This dependence, in its stationary-state limit, coincides with the Langmuir non-cooperative isotherm (27). However, in the non-stationary case, it becomes negatively cooperative in whole (Fig. 2). On the contrary, the viscosity dependence reflects bulk phase fluctuations in the system and has almost nothing in common with its heterogeneous and solid phases. Therefore, at the transient and final stages of the process, this dependence does not manifest itself, as a rule. At last, the temperature dependence is completely governed by the occupation numbers for vibrations that correspond to the characteristic frequencies of transitions (10) between states of the system. This dependence mainly reflects the activation processes, which occur at the phase interface. At low temperatures, the rate of endoergic heterogeneous transitions becomes exponentially small. It may probably result in the degeneration of the roots of the characteristic equation (12), which complicates the separation of the kinetic processes by their characteristic times (13)–(16). Therefore, at low temperatures, an irreversible system, which becomes non-stationary, starts to demonstrate a negative cooperativity, which brings about a reduction in the controllability degree of its amplitude characteristics (29).

1. Y. Jia, D.S. Talaga, W.L. Lau, H.S.M. Lu, W.F. DeGrado, and R.M. Hochstrasser, Chem. Phys. **247**, 69 (1999).
2. M. Dahan, A.A. Deniz, T. Ha, D.S. Chemla, P.G. Schultz, and S. Weiss, Chem. Phys. **247**, 85 (1999).
3. W.E. Moerner, J. Phys. Chem. B **106**, 910 (2002).
4. M. Orrit, Single Mol. **3**, 255 (2002).
5. H.P. Lu, L. Xun, and X.S. Xie, Science **282**, 1877 (1998).
6. P.B. English, W. Min, A.M. van Oijen, K.T. Lee, G. Luo, H. Sun, B.J. Cherail, S.C. Kou, and X.S. Xie, Nat. Chem. Biol. **2**, 87, (2006).
7. J.M. Fernandez and H. Li, Science **303**, 1674 (2004).
8. D.J. Muller and Y.F. Dufrene, Nat. Nanotech. **3**, 261 (2008).
9. P.W. Anderson, J. Phys. Soc. Jpn. **9**, 888 (1954).

10. R. Kubo, J. Phys. Soc. Jpn. **17**, 1100 (1962).
11. I. Oppenheim, K.E. Shuler, and G.H. Weiss, *Stochastic Processes in Chemical Physics: The Master Equation* (MIT Press, Cambridge, MA, 1977).
12. E.G. Petrov and V.I. Teslenko, Teor. Mat. Fiz. **84**, 446 (1990).
13. E.G. Petrov and V.I. Teslenko, Ukr. Fiz. Zh. **35**, 1106 (1990).
14. K. Lindenberg and B.J. West, *The Nonequilibrium Statistical Mechanics of Open and Closed Systems* (VCH, New York, 1990).
15. V.M. Kenkre and P. Reineker, *Exciton Dynamics in Molecular Crystals and Aggregates* (Springer, Berlin, 1982).
16. N.G. Van Kampen, *Stochastic Processes in Physics and Chemistry* (North-Holland, Amsterdam, 1984).
17. U. Weiss, *Quantum Dissipative Systems, Series in Modern Condensed Matter Physics, Vol.2* (World Scientific, Singapore, 1993).
18. E.G. Petrov, V.I. Teslenko, and I.A. Goychuk, Phys. Rev. E **49**, 3894 (1994).
19. E.G. Petrov, I.A. Goychuk, V.I. Teslenko, and V. May, Physics Lett. A **218**, 343 (1996).
20. E.G. Petrov, Phys. Rev. E **57**, 94 (1998).
21. I. Goychuk and P. Hanggi, Adv. Phys. **54**, 525 (2005).
22. Y. Jung, E. Barkai, and R.J. Silbey, Adv. Chem. Phys. **123**, 119 (2002).
23. Y.R. Chemla, J.R. Moffitt, and C. Bustamante, J. Phys. Chem. B **112**, 6025 (2008).
24. A.I. Burshtein, Adv. Phys. Chem. **2009**, 214219 (2009).
25. J. Cao and R.J. Silbey, J. Phys. Chem. A **113**, 13825 (2009).
26. E.G. Petrov and V.I. Teslenko, Chem. Phys. **375**, 243 (2010).
27. V.I. Teslenko, E.G. Petrov, A. Verkhratsky, and O.A. Krishtal, Phys. Rev. Lett. **104**, 178105 (2010).
28. V.A. Benderskii, E.V. Vetoshkin, and E.I. Kats, Zh. Èksp. Teor. Fiz. **124**, 259 (2003).
29. S. Nakajima, Progr. Theor. Phys. **20**, 948 (1958).
30. R. Zwanzig, Physica **30**, 1109 (1964).
31. S.N. Dorogovtsev, A.V. Goltsev, and J.F.F. Mendes, Rev. Mod. Phys. **80**, 1275 (2008).
32. V.I. Teslenko, Ukr. Fiz. Zh. **34**, 1748 (1989).
33. T.G. Lombardo, F.H. Stillinger, and P.G. Debenedetti, Proc. Nat. Acad. Sci. USA. **106**, 15131 (2009).
34. A. Fersht, *Structure and Mechanism in Protein Science: A Guide to Enzyme Catalysis and Protein Folding* (Freeman, New York, 1999).
35. N.M. Goodey and S.J. Benkovic, Nat. Rev. Chem. Biol. **4**, 474 (2008).
36. B.M. Rodriguez, D. Sigg, and F. Bezanilla, J. Gen. Physiol. **112**, 223 (1998).
37. M.E. Peterson, R.M. Daniel, M.J. Danson, and R. Eisenthal, Biochem. J. **402**, 331 (2007).
38. J.F. Gillooly, J.H. Brown, G.B. West, V.M. Savage, and E.L. Charnov, Science **293**, 2248 (2001).
39. V. Khmyz, O. Maximyuk, V. Teslenko, V. Verkhratsky, and O. Krishtal, Pflugers Arch. Eur. J. Physiol. **456**, 339 (2008).
40. A. A. Istratov and O. F. Vyvenko, Rev. Sci. Instrum. **70**, 1233 (1999).
41. J. Fisher and T. A. Henzinger, Nat. Biotech. **25**, 1239 (2007).
42. A. Raue, C. Kreutz, T. Maiwald, J. Bachmann, M. Schilling, U. Klingmuller, and J. Timmer, Bioinformatics **25**, 1923 (2009).

Received 23.06.11.
Translated from Ukrainian by O.I. Voitenko

ДИНАМІКА ПЕРЕХІДНИХ ПРОЦЕСІВ У НЕЗВОРОТНИХ КІНЕТИЧНИХ МОДЕЛЯХ

В.І. Тесленко, О.Л. Капітанчук

Резюме

Для опису процесу незворотного зв'язування молекул ліганду і рецептора у розчині побудовано мікроскопічну модель відкритої системи, що взаємодіє із зовнішнім середовищем та зазнає квазікласичних флуктуацій своєї енергії. Отримано аналітичні вирази для ймовірностей переходів між нестаціонарними станами системи, що усереднюються як за рівноважними коливаннями у середовищі, так і за стаціонарними станами у системі. Для незворотної моделі із трьома кінетичними стадіями знайдено явні залежності констант швидкостей переходів від концентрації ліганду, в'язкості розчину та температури.