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Citation: Journal of Mathematical Physics **37**, 803 (1996); doi: 10.1063/1.531415
View online: http://dx.doi.org/10.1063/1.531415
View Table of Contents: http://scitation.aip.org/content/aip/journal/jmp/37/2?ver=pdfcov
Published by the AIP Publishing

Nonequilibrium fluctuation–dissipation relations for independent random rate processes with dynamical disorder

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(Received 3 May 1995; accepted for publication 16 August 1995)

A class of rate processes with dynamical disorder is investigated based on the two following assumptions: (a) the system is composed of a random number of particles (or quasiparticles) which decay according to a first-order kinetic law; (b) the rate coefficient of the process is a random function of time with known stochastic properties. The formalism of characteristic functionals is used for the direct computation of the dynamical averages. The suggested approach is more general than the other approaches used in the literature: it is not limited to a particular type of stochastic process and can be applied to any type of random evolution of the rate coefficient. We derive an infinity of exact fluctuation–dissipation relations which establish connections among the moments of the survival function and the moments of the number of surviving particles. The analysis of these fluctuation–dissipation relations leads to the unexpected result that in the thermodynamic limit the fluctuations of the number of particles have an intermittent behavior. The moments are explicitly evaluated in two particular cases: (a) the random behavior of the rate coefficient is given by a non-Markovian process which can be embedded in a Markovian process by increasing the number of state variables and (b) the stochastic behavior of the rate coefficient is described by a stationary Gaussian random process which is generally non-Markovian. The method of curtailed characteristic functionals is used to recover the conventional description of dynamical disorder in terms of the Kubo–Zwanzig stochastic Liouville equations as a particular case of our general approach. The fluctuation–dissipation relations can be used for the study of fluctuations without making use of the whole mathematical formalism. To illustrate the efficiency of our method for the analysis of fluctuations we discuss three different physicochemical and biochemical problems. A first application is the kinetic study of the decay of positrons or positronium atoms thermalized in dense fluids: in this case the time dependence of the rate coefficient is described by a stationary Gaussian random function with an exponentially decaying correlation coefficient. A second application is an extension of Zwanzig's model of ligand–protein interactions described in terms of the passage through a fluctuating bottle

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0022-2488/96/37(2)/803/33/$10.00
J. Math. Phys. **37** (2), February 1996

neck; we complete the Zwanzig's analysis by studying the concentration fluctuations. The last example deals with jump rate processes described in terms of two independent random frequencies; this model is of interest in the study of dielectric or conformational relaxation in condensed matter and on the other hand gives an alternative approach to the problem of protein–ligand interactions. We evaluate the average survival function in several particular cases for which the jump dynamics is described by two activated processes with random energy barriers. Depending on the distributions of the energy barriers the average survival function is a simple exponential, a stretched exponential, or a statistical fractal of the inverse power law type. The possible applications of the method in the field of biological population dynamics are also investigated. © *1996 American Institute of Physics.* [S0022-2488(96)02212-8]

I. INTRODUCTION

Rate processes with static or dynamic disorder are commonly encountered in nature.[1] A common approach to a first-order rate process with static disorder is based on the assumption that the observed survival (relaxation) function at time t, $\langle l(t)\rangle_{\text{static}}$ is an average of an exponential decay law $\exp(-Wt)$ with respect to the possible values of the rate coefficient W

$$\langle l(t)\rangle_{\text{static}}=\int_0^\infty \exp(-Wt)f(W)dW, \tag{1.1}$$

where $f(W)dW$ is the probability density of the rate coefficient. We note that the average survival function is simply the Laplace transform of the probability density $f(W)dW$ of the rate coefficient W. Such an approach has been used in the study of protein–ligand interactions in biochemistry;[2,3] in this case different conformational states of the protein have different activation barriers to rebinding, resulting in a statistical distribution of the rate coefficients. Similar approaches have been used for describing the combination processes of active intermediates in radiochemistry,[4] the extinction of fluorescence due to the direct energy transfer from excited donors to acceptors,[5–8] the description of dielectric relaxation,[8,9] for the random walk description of transport processes with static or temporal disorder,[10] and for the study of one-channel compound nuclear reactions,[11] or of linear viscoelasticity.[12]

The description of rate processes with dynamical disorder is more complicated. In this case the relaxation rate is a random function of time and the average (1.1) is replaced by

$$\langle l(t)\rangle_{\text{dynamic}}=\left\langle \exp\left(-\int_0^t W(t')dt'\right)\right\rangle_{\text{dynamic}}, \tag{1.2}$$

where the average can be reduced to the evaluation of a path integral over all possible trajectories $W=W(t')$, $t\geqslant t'\geqslant 0$

$$\langle l(t)\rangle_{\text{dynamic}}=\overline{\int\int} \exp\left(-\int_0^t W(t')dt'\right)\mathscr{P}[W(t')]D[W(t')], \tag{1.3}$$

where $\overline{\int\int}$ stands for the operation of path integration, $D[W(t')]$ is a suitable integration measure over the space of random rates $W(t')$, and

$$\mathscr{P}[W(t')]D[W(t')], \quad \text{with} \quad \overline{\int\int \mathscr{P}[W(t')]D[W(t')]} = 1 \tag{1.4}$$

is the probability density functional of the random rate coefficient $W(t')$. Equation (3) is a functional analog of the Laplace transform corresponding to the static disorder [Eq. (1)]. The evaluation of dynamical averages is much more difficult than the evaluation of static averages, mainly because the functional integral (3) can be computed only in a few particular cases; the major difficulty is due to the fact that for non-Gaussian processes we do not even have an appropriate definition for the integration measure $D[W(t')]$.

The first system with dynamical disorder studied in the literature is a simplified model for the line shape in magnetic resonance spectroscopy[13,14] suggested by Anderson and Kubo. This initial approach has been extended to other spectroscopical problems.[14–21] Similar rate processes with dynamical disorder have been used in connection with the study of earthquakes,[22] non-Gaussian diffusion,[23] the Taylor problem from hydrodynamics,[24] the description of transport processes in networks with dynamic percolation,[25] the Browniam motion description of very fast chemical processes without activation barriers,[26] the study of fluorescence depolarization[27] and of protein dynamics,[28] and in connection with the analysis of collective orientational relaxation in dense liquids.[29] In these studies most authors avoid the direct evaluation of the dynamical average (3) and use instead indirect methods such as the solving of certain stochastic Liouville equations.[1,30,31]

The approaches presented in the literature can be applied only to certain particular cases of stochastic processes, for instance, in the case of a Markovian or Gaussian behavior. A general treatment for the analysis of dynamical disorder for an arbitrary type of stochastic dependence is missing. The purpose of this article is to fill this gap in the literature and to derive an efficient method for evaluating the dynamical average for a rate process characterized by an arbitrary stochastic behavior. The initial motivation of our approach is the investigation of fluctuations for a model of ligand–protein interactions suggested by Zwanzig[32] and further studied by Wang and Wolynes.[33] The main sources of inspiration for our method are the initial Kubo approach[14] to the problem of line shape and the characteristic functional approaches used by the authors for the description of space and time-dependent colored noise,[34] of stochastic gravitational fluctuations,[35] and of fractal random processes.[36] The main advantage of our approach is its versatility and generality. It leads to an infinite number of fluctuation–dissipation relations which allow to study the fluctuations without using the whole mathematical apparatus of the theory.

The structure of the article is as follows. In Sec. II we give a general formulation of the problem. In Secs. III and IV a general approach for computing the dynamical averages is developed and the fluctuation–dissipation relations are derived. In Sec. V the moments of the survival function and of the number of surviving particles are explicitly derived for Markovian and stationary Gaussian processes. Sections VI, VII, and VIII deal with the application of the theory to three different problems from condensed matter physics and biochemistry. In Sec. IX the main results of the article are summarized and the possibilities of application to the theory in exobiology and biological population dynamics are pointed out. To make the body of the article easier the details of the computations are not presented in the text; they are given in Appendices A to D.

II. FORMULATION OF THE PROBLEM

We consider a system made up of a random number of independent particles or quasiparticles and assume that the rate of decomposition of a particle at a time between t and $t+dt$, $W(t)dt$, is a random function whose stochastic properties are characterized by the probability density functional (1.4) or by the corresponding characteristic functional

$$G[K(t')]=\left\langle \exp\left(i\int_0^t K(t')W(t')dt' \right) \right\rangle_{\text{dynamic}}$$
$$=\overline{\int\int} \exp\left(i\int_0^t K(t')W(t')dt' \right)\mathscr{P}[W(t')]D[W(t')], \tag{2.1}$$

where $K(t')$ is a suitable test function. The initial number N of particles is a random variable characterized by a probability

$$P(N,t=0), \quad \sum_N P(N,0)=1 \tag{2.2}$$

or by the corresponding generating function

$$g(z,t=0)=\sum_N z^N P(N,0), \quad |z|\leqslant 1, \tag{2.3}$$

where z is a complex variable with the absolute value at most equal to the unity.

The stochastic properties of the numbers $N(t_1),\ldots,N(t_m)$ of particles surviving at times $0\leqslant t_1\leqslant\cdots\leqslant t_m\leqslant t$ are characterized by an m-gate probability

$$P_m(N(t_m),t_m;\ldots;N(t_1),t_1), \tag{2.4}$$

with the normalization condition

$$\sum_{N_m}\cdots\sum_{N_1} P_m(N_m,t_m;\ldots;N_1,t_1)=1 \tag{2.5}$$

and

$$t_u=u\Delta t, \quad \Delta t=(t-t_0)/(m+1), \quad u=1,\ldots,m. \tag{2.6}$$

In the limit $m\to\infty$ ($\Delta t\to 0$), P_m becomes a probability functional which describes the stochastic properties of a random trajectory $N(t')$, $0\leqslant t'\leqslant t$

$$B[N(t');\quad 0\leqslant t'\leqslant t]=\lim_{\substack{m\to\infty\\(\Delta t\to 0)}} P_m(N_m,t_m;\ldots;N_1,t_1), \tag{2.7}$$

which obeys the normalization condition

$$\overline{\sum\sum} B[N(t');\quad 0\leqslant t'\leqslant t]=1, \tag{2.8}$$

where $\overline{\sum\sum}$ stands for a path sum which is a discrete analog of a path integral

$$\overline{\sum\sum}\cdots=\lim_{\substack{m\to\infty\\(\Delta t\to 0)}}\sum_{N(t_1)}\cdots\sum_{N(t_m)}\cdots. \tag{2.9}$$

In terms of the probability functional $B[N(t')]$ we can define the characteristic functional

$$\Xi[\mathscr{K}(t')]=\left\langle \exp\left(i\int_0^t \mathscr{K}(t')N(t')dt' \right) \right\rangle_{\text{dynamic}} = \overline{\sum\sum} \exp\left(i\int_0^t \mathscr{K}(t')N(t')dt' \right) B[N(t')]. \tag{2.10}$$

The central moments $\langle N(t_1)\cdots N(t_m)\rangle$ and the cumulants $\langle\langle N(t_1)\cdots N(t_m)\rangle\rangle$ of the number of surviving particles may be defined by the moment and cumulant expansions of $\Xi[\mathscr{K}(t')]$

$$\begin{aligned}\Xi[\mathscr{K}(t')] &= 1+\sum_{m=1}^{\infty} \frac{i^m}{m!} \int_0^t \cdots \int_0^t \langle N(t_1')\cdots N(t_m')\rangle \mathscr{K}(t_1')\cdots\mathscr{K}(t_m')dt_1'\cdots dt_m' \\ &= \exp\left\{ \sum_{m=1}^{\infty} \frac{i^m}{m!} \int_0^t \cdots \int_0^t \langle\langle N(t_1')\cdots N(t_m')\rangle\rangle \mathscr{K}(t_1')\cdots\mathscr{K}(t_m')dt_1'\cdots dt_m' \right\},\end{aligned} \tag{2.11}$$

that is, the central moments and the cumulants can be computed by evaluating the functional derivatives

$$\langle N(t_1)\cdots N(t_m)\rangle = (-i)^m \left. \frac{\delta^m \Xi[\mathscr{K}(t')]}{\delta\mathscr{K}(t_1)\cdots\delta\mathscr{K}(t_m)} \right|_{\mathscr{K}(t')=0}, \tag{2.12}$$

and

$$\langle\langle N(t_1)\cdots N(t_m)\rangle\rangle = (-i)^m \left. \frac{\delta^m \ln \Xi[\mathscr{K}(t')]}{\delta\mathscr{K}(t_1)\cdots\delta\mathscr{K}(t_m)} \right|_{\mathscr{K}(t')=0}. \tag{2.13}$$

On the other hand the rate process can be characterized by the moments of a realization of the survival function

$$l(t)=\exp\left(-\int_0^t W(t')dt' \right), \tag{2.14}$$

i.e., by the averages

$$\langle l(t_1)\cdots l(t_m)\rangle_{\text{dynamic}} = \overline{\int\int} l(t_1)\cdots l(t_m)\mathscr{P}[W(t')]D[W(t')]. \tag{2.15}$$

The aim of this article is to answer the following questions:

(1) Given the stochastic properties of the random rate coefficient and of the initial number of particles, which are the stochastic properties of the number of particles at any time?
(2) Which are the moments of the survival function $l(t)$?
(3) Is there any relationship between the moments of the survival function and the moments of the number of surviving particles?
(4) For which systems can the moments of the number of surviving particles and of the survival function be computed explicitly and which is the relationship between these functions and the experimentally accessible quantities?
(5) In order to answer these questions we should express the characteristic functional $\Xi[\mathscr{K}(t')]$ of the number of surviving particles in terms of the characteristic functional $G[K(t')]$ of the random rate coefficient. The main idea of our approach is to evaluate the dynamical average in Eq. (2.10) in two steps: first we consider a given realization of the random rate coefficient $W(t')$, $0\leqslant t'\leqslant t$ and average over all possible numbers of surviving particles which are

compatible with this realization; finally we average over all possible realizations of the random rate coefficient $W(t')$.

III. CHARACTERISTIC FUNCTIONAL APPROACH TO DYNAMICAL DISORDER

In this section we consider a realization $W(t')$, $0 \leqslant t' \leqslant t$ of the rate coefficient and try to evaluate the corresponding generating functional of the number of surviving particles. First we notice that for a given realization of the rate coefficient the dynamical disorder does not exist; we deal with an ordered random system with a time-dependent rate coefficient. The study of such systems is not necessarily related to the problem of dynamical disorder; such a study is also of interest on its own, for instance, in connection with the statistical description of the death process in mathematical demography[37] or for the study of radiochemical reactions.[4,38] We introduce the ordered characteristic functional

$$\Xi_{\text{ordered}}[.\mathscr{K}(t')|W(t')] = \left\langle \exp\left(i \int_0^t .\mathscr{K}(t') N(t') dt' \right) \right\rangle_{\text{ordered}}, \tag{3.1}$$

where the average $\langle \cdots \rangle_{\text{ordered}}$ is computed with respect to the number of surviving particles compatible with the realization $W(t')$ $0 \leqslant t' \leqslant t$. The characteristic functional $\Xi[.\mathscr{K}(t')]$ of the disordered process is simply given by

$$\Xi[.\mathscr{K}(t')] = \langle \Xi_{\text{ordered}}[.\mathscr{K}(t')|W(t')] \rangle_{\text{disorder}} = \overline{\int \int} \Xi_{\text{ordered}}[.\mathscr{K}(t')|W(t')] \mathscr{P}[W(t')] D[W(t')], \tag{3.2}$$

where the average $\langle \cdots \rangle_{\text{disorder}}$ is computed with respect to all possible values of the random function $W(t')$, $0 \leqslant t' \leqslant t$.

In Appendix A we show that the generating functional $\Xi_{\text{ordered}}[.\mathscr{K}(t')|W(t')]$ can be expressed in terms of the realization $l(t)$ of the survival function as

$$\Xi_{\text{ordered}}[.\mathscr{K}(t')|W(t')] = g\left\{ z = 1 + \int_0^t l(t') i.\mathscr{K}(t') \exp\left[i \int_0^{t'} .\mathscr{K}(6) d6 \right] dt', \quad t = 0 \right\}. \tag{3.3}$$

In order to compute the characteristic functional $\Xi[.\mathscr{K}(t')]$ for systems with dynamical disorder we express the generating function $g(z,0)$ corresponding to the probability $P(N,0)$ in terms of the initial factorial moments of the number of particles

$$F_m(t=0) = \langle N(N-1)\cdots(N-m+1) \rangle_{\text{dynamic}}(t=0) = \sum_N N(N-1)\cdots(N-m+1) P(N,0); \tag{3.4}$$

we have

$$F_m(0) = N_0(N_0-1)\cdots(N_0-m+1) \tag{3.5}$$

for an initial canonical ensemble and

$$F_m(0) = (\langle N_0 \rangle)^m, \tag{3.6}$$

for an initial grand canonical ensemble.

From the definition (2.3) of $g(z,0)$ it follows that

$$F_m(0)=d^m g(z,0)/dz^m|_{z=1} \tag{3.7}$$

and thus $g(z,0)$ can be expressed as a Taylor series

$$g(z,0)=1+\sum_{m=1}^{\infty}\frac{1}{m!}F_m(0)(z-1)^m. \tag{3.8}$$

By combining Eqs. (3.2), (3.3), and (3.8) the characteristic functional $\Xi[\mathscr{K}(t')]$ for systems with dynamical disorder can be expressed as

$$\Xi[\mathscr{K}(t')]=1+\sum_{m=1}^{\infty}\frac{(i)^m}{m!}F_m(0)\int_0^t\cdots\int_0^t \mathscr{K}(t_1')\cdots\mathscr{K}(t_m')\exp\left(i\sum_{u=1}^{m}\int_0^{t_u'}\mathscr{K}(\mathscr{6})d\mathscr{6}\right)$$
$$\times\langle l(t_1')\cdots l(t_m')\rangle dt_1'\cdots dt_m', \tag{3.9}$$

where $\langle l(t_1')\cdots l(t_m')\rangle$ are dynamical averages given by Eqs. (2.15). By combining Eqs. (3.9) and (3.10) and using the definition (2.1) of the characteristic functional $G[K(t')]$ of the rate coefficient we can express $\langle l(t_1')\cdots l(t_m')\rangle$ as

$$\langle l(t_1')\cdots l(t_m')\rangle=\overline{\int\int}\exp\left(-\sum_{u=1}^{m}\int_0^{t_u'}W(\mathscr{6})d\mathscr{6}\right)\mathscr{P}[W(t')]D[W(t')]$$
$$=G\left[K(t')=i\sum_{u=1}^{m}h(t_u'-t')\right], \tag{3.10}$$

where $h(x)$ is the usual Heaviside step function. By inserting Eqs. (3.10) into Eq. (3.9) we have

$$\Xi[\mathscr{K}(t')]=1+\sum_{m=1}^{\infty}\frac{i^m}{m!}F_m(0)\int_0^t\cdots\int_0^t\mathscr{K}(t_1')\cdots\mathscr{K}(t_m')$$
$$\times\exp\left(i\sum_{u=1}^{m}\int_0^{t_u'}\mathscr{K}(\mathscr{C})d\mathscr{C}\right)G\left[K(t')=i\sum_{u=1}^{m}h(t_u'-t')\right]dt_1'\cdots dt_m'. \tag{3.11}$$

Equation (3.11) is the main result of this article. It expresses the stochastic properties of the number of surviving particles in terms of the stochastic properties of the random rate coefficient $W(t')$, $0\leqslant t'\leqslant t$.

Combining Eqs. (2.12) and (2.13) and Eq. (3.11) we can compute the first two cumulants of the number of surviving particles. We assume that the initial distribution of the number of particles is given by equilibrium statistical mechanics. We get

$$\langle\langle N(t)\rangle\rangle=N_0\langle l(t)\rangle, \tag{3.12}$$

$$\langle\langle N(t_1)N(t_2)\rangle\rangle=N_0[\langle l(t_2^*)\rangle-\langle l(t_1)l(t_2)\rangle]+(N_0)^2\langle\langle l(t_1)l(t_2)\rangle\rangle \tag{3.13}$$

for an initial canonical ensemble and

$$\langle\langle N(t)\rangle\rangle=N_0\langle l(t)\rangle, \tag{3.14}$$

$$\langle\langle N(t_1)N(t_2)\rangle\rangle=\langle N_0\rangle\langle l(t_2^*)\rangle+\langle N_0\rangle^2\langle\langle l(t_1)l(t_2)\rangle\rangle \tag{3.15}$$

for an initial grand canonical ensemble. Here

$$\langle\langle l(t_1)l(t_2)\rangle\rangle = \langle l(t_1)l(t_2)\rangle - \langle l(t_1)\rangle\langle l(t_2)\rangle \tag{3.16}$$

is the second cumulant of the survival function for systems with dynamic disorder. We have

$$\langle\langle l(t_1)l(t_2)\rangle\rangle \geqslant 0, \quad t_1, t_2 \ \text{finite}, \tag{3.17}$$

where the equality holds for systems without dynamical disorder. In both cases in the thermodynamic limit the relative fluctuation has the same asymptotic behavior

$$\rho_{\text{dynamic}}(t_1,t_2) \sim \left(\frac{\langle\langle l(t_1)l(t_2)\rangle\rangle}{\langle l(t_1)\rangle\langle l(t_2)\rangle} \right)^{1/2} \text{const} \quad \text{as} \quad N_0, \quad \langle N_0\rangle \to \infty. \tag{3.18}$$

Unlike in the case of ordered systems discussed in Appendix A for dynamical disorder the relative fluctuation of the number of particles does not decrease to zero but rather tends towards a constant value; in other words the fluctuations have an intermittent behavior.

The other moments and cumulants can be computed in a similar way, the complexity of computations increasing with the order of the moments. The computations are much simpler if we are interested in the analysis of fluctuations at a single time; in this case an infinity of fluctuation dissipation relations for all moments exist which are independent of the type of statistical ensemble which describes the initial state of the system. The derivation of these fluctuation–dissipation relations is presented in the following section.

IV. FLUCTUATION–DISSIPATION RELATIONS

We introduce the probability $P(N,t)$ of the number N of surviving particles at time t and the corresponding generating function

$$g(z,t) = \sum z^N P(N,t), \quad |z| \leqslant 1; \tag{4.1}$$

$P(N,t)$ can be expressed as an average of a functional Kronecker symbol over all possible trajectories $N(t')$, $0 \leqslant t' \leqslant t$

$$P(N,t) = \overline{\sum\sum B[N(t')]\delta^{(\text{funct})}_{N(t')N(t)}}, \tag{4.2}$$

where

$$\begin{aligned} \delta^{(\text{funct})}_{N(t')N(t)} &= \delta_{N(t)N(t')}, \quad \text{for} \quad t = t', \\ &= 0, \quad \text{for} \quad t \neq t' \end{aligned} \tag{4.3}$$

and $\delta_{NN'}$ is the usual numerical Kronecker symbol. By combining Eqs. (2.10) and (4.1) for $\Xi[\mathscr{K}(t')]$ and $g(z,t)$ and using Eqs. (4.2) and (4.3) we note that we have the relationship

$$g(z,t) = \Xi[i\mathscr{K}(t') = \delta(t-t')\ln z]. \tag{4.4}$$

By combining Eqs. (3.2), (3.10), (3.11), and (4.4) we obtain

$$g(z,t) = \overline{\int\int g(1+(z-1)l(t),0)\mathscr{P}[W(t')]D[W(t')]} = 1 + \sum_{m=1}^{\infty} \frac{1}{m!} F_m(0)\langle l^m(t)\rangle (z-1)^m, \tag{4.5}$$

where

$$\langle l^m(t)\rangle = \overline{\int\int} l^m(t)\mathscr{P}[W(t')]D[W(t')] \tag{4.6}$$

is the mth central moment of the survival function at time t. From Eqs. (2.14) and (4.6) we note that at one time all moments $\langle l^m(t)\rangle$ can be expressed in terms of the average value $\langle l(t)\rangle$, by replacing the instantaneous value of the rate coefficient $W(t')$ by $mW(t')$, $m=2,3,\ldots$.

$$\langle l^m(t)\rangle = \overline{\int\int} \exp\left(-m\int_0^t W(t')dt'\right)\mathscr{P}[W(t')]D[W(t')] = \langle l(t;W(t')\rightarrow mW(t'))\rangle. \tag{4.7}$$

On the other hand, by using Eq. (3.10) we can express the one-time moments of the survival function in terms of the characteristic functional $G[K(t')]$ of the random rate coefficient

$$\langle l^m(t)\rangle = G[K(t')=im]. \tag{4.8}$$

Now we note that the factorial moments of the number of particles at time t

$$F_m(t) = \langle N(N-1)\cdots(N-m+1)\rangle_{\text{dynamic}}(t) = \sum N(N-1)\cdots(N-m+1)P(N,t) \tag{4.9}$$

can be computed by differentiating the generating function $g(z,t)$

$$F_m(t) = d^m g(z,t)/dz^m|_{z=1}. \tag{4.10}$$

By differentiating Eq. (4.5) m times and making $z=1$ we come to

$$F_m(t) = F_m(0)\langle l^m(t)\rangle = F_m(0)\langle l(t,W(t')\rightarrow mW(t'))\rangle, \quad m=1,2,\ldots \tag{4.11}$$

Equations (4.11) are an infinity of fluctuation–dissipation relations which establish a connection between the average dissipative behavior of the rate process, expressed by the average survival function $\langle l(t;W(t')\rightarrow mW(t'))\rangle$ and all the factorial moments of the number of surviving particles, which express the fluctuation dynamics.

For applying the fluctuation–dissipation relations (4.11) we should be able to evaluate the average survival function $\langle l(t;W(t')\rightarrow mW(t'))\rangle$. If the cumulants of the random rate coefficient

$$\sigma_q(t_1,\ldots,t_q) = \langle\langle W(t_1)\cdots W(t_q)\rangle\rangle_{\text{dynamic}} \tag{4.12}$$

exist and are finite the characteristic functional $G[K(t')]$ can be expressed in the form of a cumulant expansion

$$G[K(t')] = \exp\left\{\sum_{q=1}^{\infty}\frac{i^q}{q!}\int_0^t\cdots\int_0^t \sigma_q(t_1,\ldots,t_q)K(t_1)\cdots K(t_q)dt_1\cdots dt_q\right\}. \tag{4.13}$$

By combining Eq. (4.13) with the expressions (4.8) for the one-time moments of the survival function and with the fluctuation–dissipation relations (4.11) we come to

$$F_m(t)/F_m(0) = \langle l^m(t)\rangle = \exp\left\{\sum_{q=1}^{\infty}\frac{(-m)^q}{q!}\int_0^t\cdots\int_0^t \sigma_q(t_1,\ldots,t_q)dt_1\ldots dt_q\right\}. \tag{4.14}$$

This is a general expression for the one-time moments of the number of surviving particles and of the survival function; for applying it we should evaluate the integrals and the series in the exponential.

In Appendix B we show how Eqs. (4.11)–(4.14) can be used for computing the central moments and the cumulants of the number of surviving particles.

V. EXACTLY SOLVABLE MODELS

In this section we consider two particular cases for which, at least in principle, the formal expressions (4.8) or (4.11) for the moments of the survival function can be explicitly evaluated.

In the first case we assume that the random rate coefficient $W(t')$ is a known function of a generally non-Markovian random vector $\mathbf{y}_1$ which can be embedded in a more complicated Markovian random process characterized by a higher dimensional random vector

$$\mathbf{x}=(\mathbf{y}_1,\mathbf{y}_2), \tag{5.1}$$

where $\mathbf{y}_2$ is the vector of the minimum number of additional random variables necessary for a Markovian description. The random rate coefficient $W(t')$ can be expressed as

$$W(t')=W(\mathbf{x}(t')=(\mathbf{y}_1(t'),\mathbf{y}_2(t'))=W(\mathbf{y}_1(t')). \tag{5.2}$$

The dynamical averages $\langle l^m(t)\rangle$ can be computed by evaluating the characteristic functional $G[K(t')]$ with the help of the method of curtailed characteristic functionals suggested by Lax[39] and Van Kampen.[40] The computations are presented in Appendix C. The moments of the survival function are equal to

$$\langle l^m(t)\rangle=\int \Lambda_m(\mathbf{x},t)d\mathbf{x}, \tag{5.3}$$

where m is a positive number, not necessarily an integer, and $\Lambda_m(\mathbf{x},t)$ is the solution of the evolution equation

$$\partial_t\Lambda_m(\mathbf{x},t)=\mathbb{L}\Lambda_m(\mathbf{x},t)-mW(\mathbf{x})\Lambda_m(\mathbf{x},t), \tag{5.4}$$

with the initial condition

$$\Lambda_m(\mathbf{x},0)=P(\mathbf{x},0) \quad \text{independent of} \quad m. \tag{5.5}$$

$P(\mathbf{x};0)$ is the probability density of the state vector at $t=0$ and $\mathbb{L}$ is a linear Markovian evolution operator. For a time-homogeneous Fokker–Planck process

$$\mathbb{L}\cdots=-\sum_q \partial_{x_q}[A_q(\mathbf{x})\cdots]+\sum_{q,q'}\partial^2_{x_qx_{q'}}[D_{qq'}(\mathbf{x})\cdots], \tag{5.6}$$

whereas for a pure jump Markovian process we have

$$\mathbb{L}P(\mathbf{x},t|\mathbf{x}_0,0)=\int[\mathscr{W}(\mathbf{x}'\rightarrow\mathbf{x})P(\mathbf{x}',t|\mathbf{x}_0,0)-\mathscr{W}(\mathbf{x}\rightarrow\mathbf{x}')P(\mathbf{x},t|\mathbf{x}_0,0)]d\mathbf{x}'. \tag{5.7}$$

Here $A_q(\mathbf{x})$ and $D_{qq'}(\mathbf{x})$ are probability drift and diffusion coefficients, respectively, and $\mathscr{W}(\mathbf{x}'\rightarrow\mathbf{x})d\mathbf{x}$ is the jump rate from a state $\mathbf{x}$ to a state with a random vector between $\mathbf{x}$ and $\mathbf{x}+d\mathbf{x}$.

To clarify the physical significance of the function $\Lambda_m(\mathbf{x},t)$ we introduce the logarithmic decrement of the survival function

$$\varepsilon(t)=-\ln\, l(t). \tag{5.8}$$

Borrowing a commonly used name from nuclear physics, we call the function $\varepsilon(t)$ the lethargy variable. We denote by

$$\phi(\varepsilon,\mathbf{x};t)d\varepsilon d\mathbf{x}, \quad \text{with} \quad \int\int \phi(\varepsilon,\mathbf{x};t)d\varepsilon\ d\mathbf{x}=1 \tag{5.9}$$

the probability that at time t the lethargy has a value between ε and $\varepsilon+d\varepsilon$ and that the state vector is between $\mathbf{x}$ and $\mathbf{x}+d\mathbf{x}$. In Appendix C we show that the function $\Lambda_m(\mathbf{x},t)$ can be expressed in terms of the Laplace transform of $\phi(\varepsilon,\mathbf{x};t)$ with respect to ε:

$$\tilde{\phi}(\beta,\mathbf{x};t)=\int_0^\infty \exp(-\beta\varepsilon)\phi(\varepsilon,\mathbf{x};t)d\varepsilon, \tag{5.10}$$

where β is the Laplace variable conjugated to ε. We have (see Appendix C)

$$\Lambda_m(\mathbf{x},t)=\tilde{\phi}(\beta=m,\mathbf{x};t), \tag{5.11}$$

that is, the function $\Lambda_m(\mathbf{x},t)$ is the Laplace transform of the lethargy-state vector joint probability density $\phi(\varepsilon,\mathbf{x};t)$ for $\beta=m$. From this physical interpretation of the function $\Lambda_m(\mathbf{x},t)$ it follows that the probability density

$$C(l,t)dl, \quad \text{with} \quad \int_0^1 C(l,t)dl=1 \tag{5.12}$$

of the survival function at time t can be expressed as

$$C(l,t)=\int\int \delta(l-\exp(-\varepsilon))\phi(\varepsilon,\mathbf{x};t)d\mathbf{x}\ d\varepsilon=l^{-1}\int \tilde{\phi}(-\ln l,\mathbf{x};t)d\mathbf{x}=l^{-1}\int \Lambda_{m=-\ln l}(\mathbf{x},t)d\mathbf{x}. \tag{5.13}$$

A second case for which the moments of the survival function can be explicitly evaluated corresponds to a time-homogeneous Gaussian behavior of the rate coefficient $W(t')$ for which the cumulants $\sigma_q(t_1,\ldots,t_q)$ are given by

$$\sigma_1=\langle W\rangle \quad \text{independent of} \quad t, \tag{5.14}$$

$$\sigma_2=\sigma(|t_1-t_2|)=\langle \Delta W(t_1)\Delta W(t_2)\rangle, \tag{5.15}$$

$$\sigma_q=0, \quad q>2. \tag{5.16}$$

Here $\langle W\rangle$ and $\langle \Delta W(t_1)\Delta W(t_2)\rangle$ are the average value and the absolute autocorrelation function of the rate coefficient, respectively. Due to the stationary character of the process the average rate $\langle W\rangle$ is independent of time and the autocorrelation function $\langle \Delta W(t_1)\Delta W(t_2)\rangle$ depends only on the absolute value of the difference of the two times, t_1 and t_2. In this case Eq. (4.14) becomes

$$F_m(t)/F_m(0)=\langle l^m(t)\rangle=\exp\{-m\langle W\rangle t+m^2\langle \Delta W^2(0)\rangle \mathscr{J}(t)\}, \tag{5.17}$$

where

$$\langle \Delta W^2(t)\rangle=\langle \Delta W^2(0)\rangle \tag{5.18}$$

is the stationary one-time dispersion of the rate coefficient

$$\mathscr{J}(t)=\int_0^t (t-\sigma)\mathscr{E}(|\sigma|)d\sigma \geqslant 0, \tag{5.19}$$

is a non-negative function of time and

$$\mathscr{E}(|t_1-t_2|)=\langle \Delta W(t_1)\Delta W(t_2)\rangle/\langle \Delta W^2(0)\rangle \tag{5.20}$$

is the relative correlation function of the rate coefficient.

The multitime moments and cumulants of the correlation function can be computed in a similar way. By applying Eq. (3.10) to the case of a stationary Gaussian process we obtain

$$\begin{aligned}\langle l(t_1)l(t_2)\rangle &= G[W(t')=(h(t_1-t')+h(t_2-t'))i] \\ &= \exp\Bigg\{-\langle W\rangle(t_1+t_2)+\tfrac{1}{2}\langle \Delta W^2(0)\rangle \int_0^t\int_0^t \mathscr{E}(|t_1'-t_2'|)[h(t_1-t_1') \\ &\quad +h(t_2-t_1')][h(t_1-t_2')+h(t_2-t_2')]dt_1'\,dt_2'\Bigg\}, \quad \text{with} \quad t_1,t_2\leqslant t. \end{aligned} \tag{5.21}$$

After lengthy algebraic manipulations the double integral in Eq. (5.21) can be expressed in terms of the function $j(t)$, resulting in

$$\langle l(t_1)l(t_2)\rangle=\exp\{-\langle W\rangle(t_1+t_2)+\langle \Delta W^2(0)\rangle[2\not{j}(t_1)+2\not{j}(t_2)-\not{j}(|t_1-t_2|)]\} \tag{5.22}$$

and

$$\begin{aligned}\langle\langle l(t_1)l(t_2)\rangle\rangle &= \exp\{-\langle W\rangle(t_1+t_2)+\langle \Delta W^2(0)\rangle[\not{j}(t_1)+\not{j}(t_2)]\} \\ &\quad \times\{\{\exp\{\langle \Delta W^2(0)\rangle[\not{j}(t_1)+\not{j}(t_2)-\not{j}(|t_1-t_2|)]\}-1\}. \end{aligned} \tag{5.23}$$

The first two cumulants of the number of surviving particles for initial canonical and grand canonical ensembles can be computed by combining the general equations (3.12)–(3.18) with Eqs. (5.17) and (5.22), (5.23). In the thermodynamic limit the relative fluctuation is given by

$$\rho_{\text{dynamic}}(t_1,t_2)=\{\exp\{\langle \Delta W^2(0)\rangle[\not{j}(t_1)+\not{j}(t_2)-\not{j}(|t_1-t_2|)]\}-1\}^{1/2}. \tag{5.24}$$

VI. POSITRON LIFETIME DISTRIBUTIONS IN DENSE FLUIDS

As a first application of the approach developed here, we consider the problem of the distribution of the lifetime of positrons or positronium atoms in dense fluids. A positron or a positronium atom thermalized in a dense fluid can become localized.[41] This type of localization is due to the interaction of the trapped particles with the environment, for instance, via the Fermi repulsion, and it is different from the usual Anderson localization typical for disordered systems.[42] Eventually the trapped particles decay due to the annihilation reaction with the neighboring electrons. With respect to this annihilation-self-trapping phenomenon it is not clear whether the positron actively creates a well in the fluid in which it localizes, or randomly visits favorable fluctuations. Density functional theory calculations[43] support the idea of a definite localized state for the trapped particle and under these circumstances one normally expects to have a well definite decay rate. This point of view is consistent with the ease with which experimentalists are able to assign specific annihilation rates to each decay mode. In contrast, quantum Monte Carlo calculations[44] show that substantial fluctuations occur in the neighborhood of a trapped particle resulting in a broad distribution of decay rates. These Monte Carlo simulations seem to contradict the experimental measurements which lead to single, definite decay rates.

To solve this contradiction Miller, Reese, and Worrell[45] (MRW) have recently suggested an approximate stochastic model with dynamical disorder. They have shown that the difference between the density functional and Monte Carlo calculations is due to a misinterpretation of the results of simulations in terms of a model with static disorder. Both the Monte Carlo and the density functional approaches are recovered as particular cases of the MRW dynamical stochastic

model.[45] In the MRW treatment the rate coefficient is a quantum mechanical operator $\hat{W}$ which depends on the electron density in the neighborhood of the trapped particle. The time-dependent instantaneous rate coefficient $W(t)$ is a quantum mechanical average

$$W(t)=\langle\psi(t)|\hat{W}|\psi(t)\rangle. \tag{6.1}$$

Due to the environmental fluctuations of the density the quantum mechanical average $W(t)$ is a fluctuating quantity that can be written in the form

$$W(t)=\langle W\rangle+\Delta W(t), \tag{6.2}$$

where $\langle W\rangle$ is a time-independent statistical average rate coefficient and $\Delta W(t)$ is the fluctuating part of $W(t)$.

The average survival function is given by

$$\langle l(t)\rangle=\exp(-\langle W\rangle t)\left\langle \exp\left(-\int_0^t \Delta W(t')dt'\right)\right\rangle. \tag{6.3}$$

To evaluate the dynamical average in Eq. (6.3) Miller, Reese, and Worrell[45] do not use the characteristic functional method suggested in this article. Instead they use a nonsystematic approximation based on two series expansions. They expand the exponential under the average brackets in a Taylor series and keep the first three terms, resulting in

$$\langle l(t)\rangle\cong\exp(-\langle W\rangle t)\left\{1+\frac{1}{2}\int_0^t\int_0^t\langle\Delta W(t_1')\Delta W(t_2')\rangle dt_1'\,dt_2'\right\}. \tag{6.4}$$

The next step is to take the logarithm of the average survival function and to approximate the logarithm containing the double integral by the first term from its Taylor expansion

$$\ln\langle l(t)\rangle\cong-\langle W\rangle t+\frac{1}{2}\int_0^t\int_0^t\langle\Delta W(t_1')\Delta W(t_2')\rangle dt_1'\,dt_2'. \tag{6.5}$$

The simplest assumption for the time dependence of the correlation function $\langle\Delta W(t_1)\Delta W(t_2)\rangle$ is an exponential decay

$$\langle\Delta W(t_1)\Delta W(t_2)\rangle=\langle\Delta W^2(0)\rangle\exp(-|t_1-t_2|/\bar{\tau}_W), \tag{6.6}$$

where $\bar{\tau}_W$ is a characteristic relaxation time for the regression of fluctuations. Equations (6.5) and (6.6) lead to

$$\ln\langle l(t)\rangle=-\langle W\rangle t+\langle W\rangle^2\zeta^2\bar{t}_W\{1-(\bar{\tau}_W/t)[1-\exp(-t/\bar{\tau}_W)]\}, \tag{6.7}$$

where

$$\zeta=\langle W^2(0)\rangle^{1/2}/\langle W\rangle. \tag{6.8}$$

Miller, Reese, and Worrell[45] have estimated the parameters entering Eq. (6.7) for the orthopositronium atom (o-Ps) in xenon at 340 °K and for the bare positron (e^+) at 300 °C. The result of this estimation is that for o-Ps the macroscopic relaxation time scale

$$\bar{t}_{\text{macro}}=1/\langle W\rangle \tag{6.9}$$

is much larger than the regression time of fluctuations $\bar{\tau}_W$: $\bar{t}_{\text{macro}}\gg\bar{\tau}_W$; in this case the fluctuations are very fast and the average survival function is practically exponential

$$\ln\langle l(t)\rangle \cong -\langle W\rangle t, \tag{6.10}$$

which corresponds to a definite effective relaxation rate $\langle W\rangle$. This behavior is a particular case of a general feature of the systems with dynamic disorder and very fast fluctuations.[1] For the bare positronium, however, the macroscopic and fluctuation time scales are less well separated and the average survival function is given by Eq. (6.7).

Now we investigate the MRW model from the point of view of our approach. First note that within the framework of our theory the MRW approximative equations (6.5) and (6.7) *are exact for a Gaussian and Markovian process*. According to Doob's theorem the only possible expression for the correlation function of a stationary Gaussian and Markovian process is the exponential form given by Eq. (6.6). Inserting Eq. (6.6) into Eq. (5.20) and using Eqs. (5.19) and (5.17) for $m=1$ we recover the MRW equation (6.7). If the stochastic process describing the behavior of the random rate coefficient $W(t')$ is close to a Gaussian process then the superior cumulants lead to small corrections in the expression of the average survival function [see the general non-Gaussian relationships (4.14)].

Examining the MRW derivation of Eq. (6.7) it follows that this equation is valid only if

$$\frac{1}{2}\int_0^t\int_0^t \langle \Delta W(t_1')\Delta W(t_2')\rangle dt_1'\, dt_2' = \langle W\rangle^2 \xi^2 t\bar{\sigma}_W\{1-(\bar{\sigma}_W/t)[1-\exp(-t/\bar{\sigma}_W)]\} \ll 1. \tag{6.11}$$

Indeed, only if this restriction is fulfilled are the series expansions used in Eqs. (6.4) and (6.5) justified. Our approach, however, shows that the restriction (6.11) is not necessary. For a stationary Gaussian and Markovian process the MRW equation (6.7) is exact for any values of the integral term in Eq. (6.11). Miller, Reese, and Worrell did not notice this relationship between their approach and the stationary Gaussian and Markovian processes. We do not know whether the actual random properties of the rate coefficient are accurately described by a stationary Gaussian and Markovian process. Note, however, that the standard description of stationary fluctuations is based on the use of such a process.[46] The broad range of validity of Eq. (6.7) is surprising but it is due to the fact that in the MRW derivation the errors due to the two series expansions in Eqs. (6.4) and (6.5) compensate each other.

The exponential or nonexponential structure of the average survival function is governed by the relationship between the macroscopic and the microscopic (fluctuation) time scales. From the MRW approach it follows that in the case of very rapid fluctuations the system behaves as if the dynamical disorder were missing. Our approach, however, shows that this is not the case. Applying the expression (5.24) for the relative fluctuation of the number of particles in the thermodynamic limit we obtain

$$\rho_{\text{dynamic}}(t_1,t_2) \sim \exp\{(\bar{\sigma}_W)^2\langle \Delta W^2(0)\rangle[2\min(t_1,t_2)/\bar{\sigma}_W - 1 - \exp(-|t_1-t_2|/\bar{\sigma}_W) + \exp(-t_1/\bar{\sigma}_W) + \exp(-t_2/\bar{\sigma}_W)] - 1\}^{1/2}, \quad \text{as} \quad N_0, \langle N_0\rangle \to \infty. \tag{6.12}$$

For large t_1, t_2 Eq. (6.12) takes a simpler form

$$\rho_{\text{dynamic}}(t_1,t_2) \sim \exp\{(\bar{\sigma}_W)\langle \Delta W^2(0)\rangle \min(t_1,t_2)\}, \quad t_1,t_2 \to \infty, \tag{6.13}$$

that is, the relative fluctuation increases exponentially to infinity. From Eqs. (6.12) and (6.13) we notice that the intermittent behavior of the fluctuations exists even if the fluctuations are very rapid. This is a surprising result which cannot be obtained by applying the MRW approach. It might be possible that the intermittent character of fluctuations of the number of particles can be observed experimentally.

The existence of dynamical disorder decreases the efficiency of the annihilation process. This is reflected in the fact that the decrease of the survival function given by Eq. (6.11) is slower than in the case when the fluctuations of the rate coefficient are missing. By using the method devel-

oped here, we can show that this slowing down effect due to the dynamical disorder is also present in the case of Gaussian, non-Markovian fluctuations of the rate coefficient for which the correlation function $\langle \Delta W(t_1)\Delta W(t_2)\rangle$ is generally nonexponential. If the dynamical disorder is missing we have $\langle \Delta W(t_1)\Delta W(t_2)\rangle = 0$, $\not{\gamma}(t)=0$ and Eqs. (5.17) lead to

$$\langle l^m(t)\rangle_{\text{ordered}} = (F_m(t)/F_m(0))_{\text{ordered}} = \exp(-m\langle W\rangle t). \tag{6.14}$$

As $\not{\gamma}(t)$ is generally non-negative by comparing Eqs. (120) with Eqs. (6.14) we obtain

$$\langle l^m(t)\rangle_{\text{ordered}} = (F_m(t)/F_m(0))_{\text{ordered}} \geqslant \langle l^m(t)\rangle_{\text{dynamic}} = (F_m(t)/F_m(0))_{\text{dynamic}}, \quad m=1,2,\ldots \tag{6.15}$$

The slowing down generated by the dynamical disorder affects not only the moments of the survival function but also the factorial moments of the number of particles.

VII. PASSAGE THROUGH A FLUCTUATING GEOMETRICAL BOTTLENECK

The model for the binding of a ligand to a protein molecule suggested by Zwanzig[32] is based on the following assumptions:

(1) The rate determining process is the passage of a ligand molecule through a geometrical bottleneck formed by the protein chain. The rate coefficient W is proportional to the area of the bottleneck

$$W(r) = \alpha r^2, \tag{7.1}$$

where r is the radius of the bottleneck and α is a positive coefficient with dimension $[\text{time}]^{-1}[\text{length}]^{-2}$.

(2) Due to the conformational fluctuations of the protein molecule the radius r of the bottleneck is a random variable which obeys a Langevin equation

$$dr/dt = -\lambda r + F(t), \tag{7.2}$$

in which λ is the rate of regression of a fluctuation in r and $F(t)$ is thermal (Gaussian white) noise. The stochastic properties of $F(t)$ are completely characterized by the cumulants

$$\langle\langle F(t)\rangle\rangle = 0, \quad \langle\langle F(t)F(t')\rangle\rangle = 2\lambda\theta\delta(t-t') \tag{7.3}$$

and

$$\langle\langle F(t_1)\ldots F(t_q)\rangle\rangle = 0, \quad q>2, \tag{7.4}$$

where θ is the second moment of the radius r

$$\theta = \langle r^2\rangle. \tag{7.5}$$

Using these two assumptions Zwanzig has computed the expression of the average survival function $\langle l(t)\rangle$ of the ligand molecules. In this section we complete the Zwanzig's analysis by evaluating the fluctuations of the number of ligand molecules. This is more than a simple academic exercise; indeed, even though the fluctuations are not easily experimentally accessible the theoretical investigation of their behavior would lead to the clarification of the nature of the process in the thermodynamic limit. We shall see in the following that, like in the case of positron trapping in fluids, the Zwanzig's model leads to an intermittent behavior.

Equation (7.2) shows that the radius of a bottleneck is a Markovian random variable. It follows that we can apply the Markovian approach developed in Sec. V. In this case the state

vector $\mathbf{x}$ is made up of one component $\mathbf{x}=(r)$. Reducing the Langevin description (7.2)–(7.4) to a Fokker–Planck description it turns out that the evolution operator $\mathbb{L}$ is given by

$$\mathbb{L}\cdots=\lambda\partial_r(r\cdots)+\lambda\theta\partial_{r^2}^2(\cdots), \tag{7.6}$$

which is a particular case of Eq. (5.6). The factorial moments of the number of surviving particles and the moments of survival functions can be derived by applying the fluctuation–dissipation relation (4.11). The details of computations are presented in Appendix D. By combining our formalism with the data available in the literature[32,47] we obtain

$$F_m(t)/F_m(0)=\langle l^m(t)\rangle=\mathscr{S}_m(t), \tag{7.7}$$

where

$$\mathscr{S}_m(t)=\left\{\frac{\lambda+2\alpha m\theta}{(\lambda^2+4\alpha m\theta\lambda)^{1/2}}\sinh[(\lambda^2+4\alpha m\theta\lambda)^{1/2}t]+\cosh[(\lambda^2+4\alpha m\theta\lambda)^{1/2}t]\right\}^{-1/2}\exp(\lambda t/2). \tag{7.8}$$

For $m=1$ Eqs. (7.7) and (7.8) reduce to the Zwanzig's expression for the average survival function. The expressions (7.7) and (7.8) for $m>1$ for the fluctuations of the survival function and of the number of ligand molecules are new.

The average rate coefficient is equal to

$$\langle W\rangle=\langle\alpha r^2\rangle=\alpha\theta. \tag{7.9}$$

In terms of $\langle W\rangle$ and λ the macroscopic time scale $\bar{t}_{\text{macro}}$ and the fluctuation time scale $\bar{\mathscr{C}}_{\text{fluct}}$ can be expressed as

$$\bar{t}_{\text{macro}}=1/\langle W\rangle=(\alpha\theta)^{-1},\quad \bar{\mathscr{C}}_{\text{fluct}}=1/\lambda. \tag{7.10}$$

The limit behavior of Eqs. (7.7) and (7.8) can be analyzed in terms of the ratio y of the two time scales

$$y=\bar{\mathscr{C}}_{\text{fluct}}/\bar{t}_{\text{macro}}=\alpha\theta/\lambda. \tag{7.11}$$

For $y\to\infty$ the fluctuations are slow, the disorder is static, and Eqs. (7.7) and (7.8) become

$$F_m(t)/F_m(0)=\langle l^m(t)\rangle\sim(1+2m\alpha\theta t)^{1/2},\quad m=1,2,\ldots,\quad y\to\infty. \tag{7.12}$$

In the opposite case of rapid fluctuations $y\to 0$ and the moments decrease exponentially in time

$$F_m(t)/F_m(0)=\langle l^m(t)\rangle\sim\exp(-m\alpha\theta t),\quad m=1,2,\ldots,\quad y\to 0. \tag{7.13}$$

The one-time central moments and the cumulants of the number of ligand molecules can be computed by using the relationships presented in Appendix B. To save space we give here only the expression of the one-time relative fluctuation

$$\rho(t)=\langle\Delta N^2(t)\rangle^{1/2}/\langle N(t)\rangle=[(1+\rho^2(0))\mathscr{S}_2(t)/(\mathscr{S}_1(t))^2-1+(1-\mathscr{S}_2(t)/\mathscr{S}_1(t))/\langle N(0)\rangle]^{1/2}$$
$$\sim[(1+\rho^2(0))\mathscr{S}_2(t)/(\mathscr{S}_1(t))^2-1]^{1/2},\quad \langle N(0)\rangle\to\infty. \tag{7.14}$$

Note that in the thermodynamic limit $\langle N(0)\rangle \to \infty$ the fluctuations are intermittent. To estimate the intensity of the intermittent behavior we analyze the asymptotic expressions for the factorial moments $F_m(t)$ and for the one-time relative fluctuation $\rho(t)$. For large time both $F_m(t)$ and $\rho(t)$ are exponentials

$$F_m(t)/F_m(0)=\langle l^m(t)\rangle \sim \frac{2(1+4my)^{1/4}}{1+(1+4my)^{1/2}} \exp\{-\tfrac{1}{2}\lambda t[(1+4my)^{1/2}-1]\},$$

$$t \gg 0, \tag{7.15}$$

$$\rho(t) \sim (1+\rho^2(0))^{1/2} R(y) \exp[\tfrac{1}{4}\lambda t Q(y)], \quad t \gg 0, \tag{7.16}$$

where

$$R(y)=\frac{(1+8y)^{1/8}[1+(1+4y)^{1/2}]}{(1+4y)^{1/4}[1+(1+8y)^{1/2}]^{1/2}\sqrt{2}}, \tag{7.17}$$

$$Q(y)=2(1+4y)^{1/2}-(1+8y)^{1/2}-1>0, \quad \text{for} \quad y>0. \tag{7.18}$$

As time increases the factorial moments $F_m(t)$ of the number of ligand molecules decrease exponentially to zero and the relative fluctuation $\rho(t)$ increases exponentially to infinity.

From Eqs. (7.15) we see that the effective exponential rate constant $W_{\text{eff}}(m)$ for the decay of fluctuations is a parabolic function of the moment index m. Equations (7.15) may be rewritten in the form

$$F_m(t) \sim \exp[-W_{\text{eff}}(m)t], \quad t \to \infty, \tag{7.19}$$

with

$$W_{\text{eff}}(m)=\tfrac{1}{2}\lambda[(1+4my)^{1/2}-1] \sim (m\alpha\lambda\theta)^{1/2}, \quad y \gg 1; \tag{7.20}$$

for $m=1$ Eq. (7.20) reduces to a relation derived by Zwanzig[32]

$$W_{\text{eff}}(1) \sim (\alpha\lambda\theta)^{1/2}, \quad y \gg 1. \tag{7.21}$$

As the relaxation rate λ of the radius fluctuations is inversely proportional to the viscosity η of the solvent[32,48] Eq. (7.21) leads to

$$W_{\text{eff}}(1) \sim \eta^{-1/2} \tag{7.22}$$

a relationship which is approximately consistent with the experimental data which can be fitted by the law[49]

$$W_{\text{eff}}(1) \sim \eta^{-K}, \quad \text{with} \quad 0.8>K>0.4. \tag{7.23}$$

A possible explanation of the existence of an exponent different from $\frac{1}{2}$ would be the fact that the fluctuations of the radius r of the bottleneck are actually non-Gaussian. The Gaussian behavior of a geometrical parameter of a polymeric chain is generally related to the description of the conformational fluctuations by a noncorrelated random walk.[50] For real polymers, however, the excluded volume effect necessarily leads to non-Gaussian behavior.[50] A generalization of the Zwanzig's model which provides a theoretical derivation of the experimental law (7.23) is based on the assumption that the non-Gaussian fluctuations can be described by using the fractional diffusion equation.[51] Details concerning this model will be given elsewhere. We mention that Wang and Wolynes[33] suggest a different explanation for the experimental law (7.23). They assume

that the fluctuations of the radius r are Gaussian but that the corresponding correlation function $\langle \Delta r(t_1)\Delta r(t_2)\rangle$ is a nonexponential function of the time interval t_1-t_2.

VIII. JUMP RATE PROCESSES AND RELAXATION

The third application of our approach is an exactly solvable model with dynamical disorder which can be used both in biochemistry and condensed matter physics. We assume that the random time evolution of the rate coefficient $W(t')$ can be described in terms of a jump process. For each jump a new value of W is randomly selected from a given probability density $f(W)dW$. The jump frequency is also a random function $\Omega(t')$ which obeys a similar dynamics. For each jump a new frequency Ω is picked up from another probability density $\xi(\Omega)d\Omega$. For this kind of model the random function $W(t')$ is generally non-Markovian. However the set (Ω,W) has a Markovian behavior characterized by the jump rate

$$\mathscr{W}(\Omega',W' \rightarrow \Omega,W)d\Omega\ dW\ \Delta t=\Omega'\xi(\Omega)f(W)d\Omega\ dW\ \Delta t, \tag{8.1}$$

where $\Delta t \rightarrow 0$ is the length of the time interval in which a jump occurs. This type of model is a particular case of the Markovian processes studied in Sec. V. The state vector $\mathbf{x}$ is given by

$$\mathbf{x}=(\Omega,W) \tag{8.2}$$

and the evolution operator $\mathbb{L}$ can be computed by inserting Eq. (8.1) into Eq. (5.7). Using the expression for $\mathbb{L}$ the evolution equations (5.4), (5.5), and (5.10) for $\Lambda_m(\Omega,W,t)=\tilde{\phi}(\beta=m,\Omega,W;t)$ become

$$\partial_t\tilde{\phi}(\beta,\Omega,W;t)=\xi(\Omega)f(W)\int\int \Omega'\tilde{\phi}(\beta,\Omega',W')d\Omega'\ dW'-(\Omega+\beta W)\tilde{\phi}(\beta,\Omega,W;t), \tag{8.3}$$

with the initial condition

$$\tilde{\phi}(\beta,\Omega,W;t=0)=P(\Omega,W,t=0)=\xi(\Omega)f(W). \tag{8.4}$$

Equation (182) can be solved by introducing the auxiliary function

$$b(\beta,t)=\int\int \Omega\tilde{\phi}(\beta,\Omega,W;t)d\Omega\ dW. \tag{8.5}$$

We express the integral in Eq. (8.3) in terms of $b(\beta,t)$ and integrate the resulting equation by assuming the function $b(\beta,t)$ is known. This gives

$$\tilde{\phi}(\beta,\Omega,W;t)=\xi(\Omega)f(W)\left[\exp(-(\Omega+\beta W)t)+\int_0^t b(\beta,t-t')\exp(-(\Omega+\beta W)t')dt'\right]. \tag{8.6}$$

Inserting Eq. (8.6) into Eq. (8.5) we obtain a linear integral equation for $b(\beta,t)$

$$b(\beta,t)=\langle l^{\beta}(t)\rangle_{\text{static}}\psi(t)+\int_0^t \langle l^{\beta}(t')\rangle_{\text{static}}\psi(t')b(\beta,t-t')dt', \tag{8.7}$$

where

$$\langle l^{\beta}(t)\rangle_{\text{static}}=\int_0^{\infty} l^{\beta}f(W)dW=\int_0^{\infty}\exp(-\beta Wt)f(W)dW \tag{8.8}$$

is the one-time fractional static moment of order β of the survival function $l(t)$ and

$$\psi(t)=\int_0^\infty \Omega\ \exp(-\Omega t)\xi(\Omega)d\Omega \tag{8.9}$$

is the static average of the probability density of the waiting time between two jumps. Combining Eqs. (5.3), (4.11), and (8.6) we can express the dynamic moments of the survival function and of the number of surviving particles in terms of the function $b(\beta,t)$

$$F_m(t)/F_m(0)=\langle l^m(t)\rangle=\langle l^m(t)\rangle_{\text{static}}\,\mathscr{S}(t)+\int_0^t b(m,t-t')\mathscr{S}(t')\langle l^m(t')\rangle_{\text{static}}\,dt', \tag{8.10}$$

where

$$\mathscr{S}(t)=\int_t^\infty \psi(t')dt'=\int_0^\infty \exp(-\Omega t)\xi(\Omega)d\Omega \tag{8.11}$$

is the probability that in a time interval of length t no jump processes occur. Equation (8.7) is a linear convolution equation in $b(\beta,t)$ which can be solved by using the Laplace transformation. We denote the Laplace transform of the real time variable t by an overbar

$$\bar{b}(\beta,s)=\int_0^\infty \exp(-st)b(\beta,t)dt,\quad \text{etc.}, \tag{8.12}$$

where s is the Laplace variable conjugated to the time t. We apply the Laplace transform to Eqs. (5.13) and (8.6)–(8.8), eliminate the function $b(\beta,s)$ from the resulting equations, and come back to the real time variable t. After lengthy calculations we get the following expressions for the probability density $C(l,t)$ of the survival function l at time t and for the dynamic averages $\langle l^m(t)\rangle$ and $F_m(t)$

$$C(l,t)=(2\pi i l)^{-1}\int d\beta\ \exp(\beta\ \ln l)\mathscr{L}^{-1}\times\left\{\left[\int\int \frac{\xi(\Omega)f(W)d\Omega\ dW}{\Omega+\beta W+s}\right]\Big/\left[\int\int \frac{(s+\beta W)\xi(\Omega)f(W)d\Omega\ dW}{\Omega+\beta W+s}\right]\right\}, \tag{8.13}$$

$$F_m(t)/F_m(0)=\langle l^m(t)\rangle=\mathscr{L}^{-1}\left\{\left[\int\int \frac{\xi(\Omega)f(W)d\Omega\ dW}{\Omega+mW+s}\right]\Big/\left[\int\int \frac{(s+mW)\xi(\Omega)f(W)d\Omega\ dW}{\Omega+mW+s}\right]\right\}, \tag{8.14}$$

where the complex integral over β is computed along a vertical line from the left hand side of the complex plane from $-i\infty$ to $+i\infty$ and $\mathscr{L}^{-1}$ denotes the inverse Laplace transformation with respect to the s variable conjugated to the real time.

The probability density $P(x,t)=P(\Omega,W,t)$ of the rates Ω and W at time t can be evaluated in a similar way. We have

$$P(\Omega,W,t)=\int \phi(\mathscr{E},\Omega,W;t)d\mathscr{E}=\tilde{\phi}(\beta=0,\Omega,W;t). \tag{8.15}$$

Combining Eq. (8.15) with the Laplace transform of Eq. (8.6) we obtain

$$P(\Omega,W,t)=\xi(\Omega)f(W)\mathscr{L}^{-1}[(s+\Omega)^{-1}(1-\bar{\psi}(s))^{-1}], \tag{8.16}$$

where

$$\bar{\psi}(s)=\int_0^\infty \exp(-st)\psi(t)dt=\int_0^\infty \frac{\Omega}{s+\Omega}\,\xi(\Omega)d\Omega \tag{8.17}$$

is the Laplace transform of the average probability density of the waiting time between two jumps.

The above equations allow us to express the dynamic averages $\langle l^m(t)\rangle$ and $F_m(t)$ in terms of static averages over the rates Ω and W. Equations (8.14) may be rewritten as

$$F_m(t)/F_m(0)=\langle l^m(t)\rangle=\langle l^m(t)\rangle_{\text{static}}\otimes\psi(t)\otimes\chi(t), \tag{8.18}$$

where $\langle l^m(t)\rangle_{\text{static}}$ is given by Eq. (8.18), $\otimes$ denotes the temporal convolution product, and the function $\chi(t)$ is given by

$$\chi(t)=\mathscr{L}^{-1}[(1-\varphi_m(s))^{-1}], \tag{8.19}$$

with

$$\varphi_m(s)=\int_0^\infty \exp(-st)\psi(t)\langle l^m(t)\rangle_{\text{static}}\,dt. \tag{8.20}$$

According to Eq. (8.18) the intermediate time behavior of the dynamical averages $\langle l^m(t)\rangle$ and $F_m(t)$ can be quite complicated; the large time behavior, however, is dominated by the most rapidly decreasing functions on the right hand side of Eq. (8.18). The asymptotic behavior of the static averages $\langle l^m(t)\rangle_{\text{static}}$ and $\psi(t)$ can be investigated by using the methods developed in the literature dealing with systems with static disorder.[10] On the other hand the behavior of $\chi(t)$ can be investigated by making an analogy with Lotka's theory of stable populations.[37,52] Equation (8.19) shows that the function $\chi(t)$ depends on the roots of the transcendental equation

$$\varphi_m(s)=\int_0^\infty \exp(-st)\psi(t)\langle l^m(t)\rangle_{\text{static}}\,dt=1. \tag{8.21}$$

Equation (8.21) has exactly the same form as the well-known Lotka equation for the intrinsic rate of growth from population dynamics.[37,52] By using this analogy it follows that Eq. (8.21) has a single real root $s=s_0$ which is nonpositive. We have[37,52]

$$s_0<0 \quad \text{if} \quad \varphi_m(0)<1 \quad \text{and} \quad s_0=0 \quad \text{if} \quad \varphi_m(0)=1. \tag{8.22}$$

Equation (30) can also have at most a countable number of complex roots $s_{\pm q}=u_q\pm iv_q$, $q=1,2,...$ with real parts u_q smaller or at most equal to the real root s_0 (Refs. 37 and 52)

$$u_q\leqslant s_0, \quad q=1,2,\ldots \tag{8.23}$$

If the complex roots are simple then $\chi(t)$ can be expressed as

$$\chi(t)=(I_0)^{-1}\exp(-|s_0|t)+2\sum_{q=1}^{\infty}\exp(-|u_q|t)\{[I_q^+\cos(v_qt)-I_q^-\sin(v_qt)]/[(I_q^+)^2+(I_q^-)^2]\}, \tag{8.24}$$

where

$$I_0=\int\int \frac{\Omega\xi(\Omega)f(W)}{(\Omega+mW)^2}\,d\Omega\;dW \tag{8.25}$$

and

$$I_q^{\pm}=\int\int \frac{\Omega\xi(\Omega)f(W)}{[(\Omega+mW-u_q)^2+v_q^2]^2}\begin{Bmatrix}(\Omega+mW-u_l)^2-v_l^2\\ 2(\Omega+mW-u_l)v_l\end{Bmatrix}d\Omega\;dW. \tag{8.26}$$

The expansion (8.24) is physically consistent only if the integrals (8.25) and (8.26) exist and are finite.

The constant $\varphi_m(0)$ can be expressed as

$$\varphi_m(0)=\int\int \frac{\Omega}{\Omega+mW}\,\xi(\Omega)f(W)d\Omega\;dW=\left\langle\frac{\Omega}{\Omega+mW}\right\rangle_{\text{static}}. \tag{8.27}$$

In most cases the average $\langle\Omega/(\Omega+mW)\rangle_{\text{static}}$ is smaller than unity and thus $s_0<0$ and

$$\chi(t)\sim(I_0)^{-1}\,\exp(-|s_0|t)\quad\text{as}\quad t\to\infty. \tag{8.28}$$

In this case the dynamical averages $\langle l^m(t)\rangle$ and $F_m(t)$ decrease to zero exponentially or faster. In some exceptional cases it may happen that $\langle\Omega/(\Omega+mW)\rangle_{\text{static}}=1$. In this situation there are two possibilities: if $1-\varphi_m(s)$ is analytic near $s=0$

$$1-\varphi_m(s)\sim s\quad\text{as}\quad s\to 0\quad\text{and}\quad\chi(t)\sim\text{const}\quad\text{as}\quad t\to\infty. \tag{8.29}$$

If Eq. (8.29) holds then the dynamical averages $\langle l^m(t)\rangle$ and $F_m(t)$ are completely determined by the static averages $\langle l^m(t)\rangle_{\text{static}}$. The second possibility is that $1-\varphi_m(s)$ is nonanalytic near $s=0$ so

$$1-\varphi_m(s)\sim s^a,\quad 1>a>0\quad\text{as}\quad s\to 0. \tag{8.30}$$

In this case the integrals (8.25) and (8.26) are infinite, the expansion (8.24) breaks down and the asymptotic behavior of $\chi(t)$ as $t\to\infty$ is given by

$$\chi(t)\sim t^{a-1}/\Gamma(a)\quad\text{as}\quad t\to\infty. \tag{8.31}$$

The asymptotic fractal time behavior of $\chi(t)$ may lead to an exotic (i.e., nonexponential) large time behavior for $\langle l^m(t)\rangle$ and $F_m(t)$.

As expected for very rare jumps the dynamical moments $\langle l^m(t)\rangle$ and $F_m(t)/F_m(0)$ are the same as the static averages

$$\langle l^m(t)\rangle=\langle l^m(t)\rangle_{\text{static}}. \tag{8.32}$$

In this case we have $\xi(\Omega)=\delta(\Omega)$ and Eq. (8.14) reduces to Eq. (8.8). In the other extreme of very frequent jumps we have $\xi(\Omega)=\delta(\Omega-\Omega')$, $\Omega'\to\infty$ and Eq. (8.14) becomes

$$F_m(t)/F_m(0)=\exp\left(-t\int Wf(W)dW\right)=\exp(-\langle W\rangle t)\quad\text{as}\quad t\to\infty. \tag{8.33}$$

Equation (8.33) is similar with Eqs. (6.9) and (7.13) derived in Secs. VI and VII.

It is easy to check that for the jump process considered here the fluctuations of the number of surviving particles are also intermittent. A straightforward calculation shows that the expression (7.14) for the one-time relative fluctuation remains valid provided that the functions $\mathscr{S}_{1,2}(t)$ are replaced by the functions $\langle l^m(t)\rangle$, $m=1,2$ given by Eq. (8.14).

A more detailed analysis requires knowledge of the probability densities $\xi(\Omega)$ and $f(W)$. We consider here only a few particular situations which may generate exotic relaxation. We assume the validity of the random activation energy model (RAEM[53,54]), i.e., that both the jump and the rate processes are activated phenomena corresponding to a random distribution of energy barriers. We have

$$\Omega(E)=\mu\ \exp(-E/kT), \quad W(E)=\nu\ \exp(-E/kT), \tag{8.34}$$

where the activation energy E may take any value between zero and infinity, the pre-exponential factors μ and ν are the maximum values of the rates Ω and W, respectively, k is the Boltzmann's constant, and T is the absolute temperature of the system. The activation energies corresponding to Ω and W are random variables selected from two different probability densities

$$\eta_{\Omega,W}(E)dE, \quad \text{with} \quad \int \eta_{\Omega,W}(E)dE=1. \tag{8.35}$$

Combining Eqs. (8.34) and (8.35) it follows that the probability densities $\xi(\Omega)$ and $f(w)$ of the rates Ω and W can be expressed as

$$\xi(\Omega)=\int \eta_{\Omega}(E)\,\delta[\Omega-\mu\ \exp(-E/kT)]dE, \tag{8.36}$$

$$f(W)=\int \eta_{W}(E)\,\delta[W-\nu\ \exp(-E/kT)]dE. \tag{8.37}$$

Depending on the choice of the probability densities $\eta_{\Omega,W}(E)dE$ we distinguish the following cases:

(1) We assume that the jump dynamics is Markovian, i.e., that the height of the energy barrier corresponding to the jump process is constant

$$\eta_{\Omega}(E)=\delta(E-E_{\Omega}) \tag{8.38}$$

and that the height of the energy barrier corresponding to the rate process is exponentially distributed

$$\eta_{W}(E)=(kT_{W})^{-1}\ \exp(-E/kT_{W}), \quad T_{W}\geqslant T. \tag{8.39}$$

The probability law (8.39) corresponds to a canonical distribution of energies ''frozen'' at the temperature T_0. This type of distribution was introduced almost sixty years ago in surface chemistry;[55] it has also been used in the study of transport processes in disordered systems.[10,53,54] In this case the dynamical moments $\langle l^{m}(t)\rangle$ and $F_{m}(t)$ and the relative fluctuation $\rho(t)$ are given by

$$F_{m}(t)/F_{m}(0)=\langle l^{m}(t)\rangle\ \frac{\Gamma(1+H)(m\nu t)^{-H}\ \exp(-\Omega_{0}t)}{1-H(\Omega_{0}/m\nu)^{H}B[H,1-H,m\nu/(\Omega_{0}+m\nu)]}, \quad t\to\infty, \tag{8.40}$$

$$\rho(t)\sim(1+\rho^{2}(0))^{1/2}\ \frac{1-H(\Omega_{0}/\nu)^{H}B[H,1-H,\nu/(\Omega_{0}+\nu)]}{\{\Gamma(1-H)[1-H(\Omega_{0}/2\nu)^{H}B[H,1-H,2\nu/(\Omega_{0}+2\nu)]]\}^{1/2}}\ (\nu t/2)^{H/2}$$
$$\times\exp(\tfrac{1}{2}\Omega_{0}t), \quad \text{as} \quad t\to\infty, \tag{8.41}$$

where

$$\Gamma(p)=\int_0^\infty t^{p-1}\,\exp(-t)dt,\quad B(p,q,x)=\int_0^x t^{p-1}(1-t)^{q-1}\,dt \tag{8.42}$$

are the complete gamma and the incomplete beta Eulerian integrals, respectively,

$$H=T/T_W\leqslant 1, \tag{8.43}$$

and

$$\Omega_0=\mu\,\exp(-E_\Omega/kT). \tag{8.44}$$

(2) The distribution of the height of jump barriers is given by a positive Gompertz law[10] with a characteristic energy E_0

$$\eta_\Omega(E)=(E_0)^{-1}\,\exp[E/E_0-\exp(E/E_0)-1] \tag{8.45}$$

and the probability density of the rate coefficient W is given by the exponential law (8.39). In this case the large time behavior of the dynamical moments $\langle l^m(t)\rangle$ and $F_m(t)$ is given by a stretched exponential

$$F_m(t)/F_m(0)=\langle l^m(t)\rangle\sim\Gamma(1+H)(m\nu)^{-H}\mu t^{1-H}\,\exp[-\sigma(\mu t)^\alpha], \tag{8.46}$$

where

$$\sigma=[1+kT/E_0]/(kT/E_0)^\alpha \tag{8.47}$$

and

$$\alpha=kT/(E_0+kT)\leqslant 1. \tag{8.48}$$

The one-time relative fluctuation diverges to infinity as $t\to\infty$ according to a positive stretched exponential

$$\rho(t)=\left(\frac{1+\rho^2(0)}{\mu\Gamma(1+H)}\right)^{1/2}(\nu/2)^{H/2}t^{-(1-H)/2}\,\exp[\tfrac{1}{2}\sigma(\mu t)^\alpha],\quad \text{as}\quad t\to\infty \tag{8.49}$$

(3) Both activation barriers are exponentially distributed; $\eta_W(E)$ is given by Eq. (218) and $\eta_\Omega(E)$ is given by a similar canonical distribution "frozen" at temperature T_Ω

$$\eta_\Omega(E)=(kT_\Omega)^{-1}\,\exp(-E/kT_\Omega),\quad T\leqslant T_\Omega\,. \tag{8.50}$$

We have

$$F_m(t)/F_m(0)=\langle l^m(t)\rangle\sim\Gamma(\mathscr{K}+1)\Gamma(H+1)(\mu/m\nu)^H(\mu t)^{-(H+\mathscr{K})},$$

$$\nu\gg\mu,\quad t\gg\mu^{-1}, \tag{8.51}$$

$$\rho(t)=\left(\frac{1+\rho^2(0)}{\Gamma(1+\mathscr{K})\Gamma(1+H)}\right)^{1/2}(\nu/2\mu)^{H/2}(\mu t)^{(H+\mathscr{K})/2},$$

$$\nu\gg\mu,\quad t\gg\mu^{-1}, \tag{8.52}$$

where

$$\mathscr{K}=T/T_\Omega\leqslant 1. \tag{8.53}$$

Thus the large time decrease of the dynamical moments $F_m(t)$ and $\langle l^m(t)\rangle$ is given by a statistical fractal law with an exponent $\mathscr{H}+H$ and the relative fluctuation increases to infinity according to a statistical fractal law with an exponent $\frac{1}{2}(\mathscr{H}+H)$.

The probability density $P(\Omega,W,t)$ of the rates Ω and W can be evaluated from Eq. (8.16). If the average time between two jumps

$$\langle t\rangle=\int_0^\infty t\psi(t)dt=\int_0^\infty \Omega^{-1}\xi(\Omega)d\Omega=\langle\Omega^{-1}\rangle_{\text{static}}, \tag{8.54}$$

exists and is finite, then

$$P(\Omega,W,t)\sim\xi(\Omega)f(W)/[\Omega\langle\Omega^{-1}\rangle_{\text{static}}] \quad \text{as} \quad t\to\infty. \tag{8.55}$$

If $\langle t\rangle$ is infinite then the state $\Omega=0$ acts as a trap and in the limit $t\to\infty$ the random jumps cease. We have

$$P(\Omega,W,t)\to\delta(\Omega)f(W) \quad \text{as} \quad t\to\infty. \tag{8.56}$$

For example, if the distribution of jump activation energies is given by the exponential law (8.50) then $\langle t\rangle=\infty$ and for $\Omega\neq 0$ the probability density $P(\Omega,W,t)$ decreases to zero according to an inverse power law

$$P(\Omega,W,t)\sim\frac{f(W)}{\Omega^{2-\mathscr{H}}}\frac{\sin(\pi\mathscr{H})}{\pi\Gamma(\mathscr{H})}t^{-(1-\mathscr{H})}, \quad \Omega\neq 0, \quad t\to\infty. \tag{8.57}$$

We have checked the validity of the asymptotic laws (8.46) and (8.51) by assuming that $\nu/\mu\sim 10$–10^2 and $H,\mathscr{H}\sim 0.5$–0.9. For this range of parameters the stretched exponential (8.46) and the inverse power law (8.51) describe the behavior of the tail of the average survival function for $0.15\geqslant -\!-0.10\geqslant\langle l(t)\rangle\geqslant 0$ and 0.12–$0.08\geqslant P(l(t)\rangle\geqslant 0$, respectively.

Although the above analysis provides a mathematical description of dynamical disorder in terms of pure jump processes it does not clarify its physical significance. By rephrasing the pure jump model in a physical language, we distinguish three different features:

(1) There are two different types of dynamical processes: a first process, described in terms of the jump frequency Ω, is responsible for the occurrence of dynamical disorder, whereas the second is the rate process itself characterized by the random rate coefficient W.

(2) Although no direct relations concerning the relative values of the frequencies Ω and W are assumed, their statistical behavior is correlated due to their mechanism of change. For each new step two new values of the frequencies Ω and W are randomly selected from two different probability laws. For this assumption to be fulfilled it is necessary that the interaction process corresponding to a step is very strong, resulting in a loss of memory concerning the previous states of the system. Such an assumption, known in the literature as the ''strong collision hypothesis,'' has been commonly used in spectroscopy,[14–17] chemical kinetics,[56] and condensed matter physics.[10,21,23,57]

(3) The third assumption is the one concerning the random distribution of the rates Ω and W which describe activated phenomena with a random distribution of energy barriers. This assumption has been used in biochemistry,[2,3] chemical kinetics,[4] the structural or dielectric relaxation in glassy materials,[53] transport phenomena in disordered systems,[54] etc. For this assumption to be satisfied it is necessary that a state of local equilibrium exists, i.e., that besides the jump and rate processes taken explicitly into account there is another type of process which ensures the thermalization of the system. Besides, it is necessary that the particles involved in the rate process can exist in a large variety of different states, to which correspond different activation barriers.

For illustration we consider two possible applications of the theory. The first example is the problem of protein–ligand interactions which has already been mentioned earlier. In this context the jump model is a generalization of the model with static disorder suggested by Frauenfelder *et al.*[2,3] We assume that the passage from a conformation to another is not an instantaneous process but rather it is characterized by a distribution of time scales $\mathscr{C}_{\text{fluct}}=1/\Omega_u$ corresponding to different jump frequencies Ω_u, $u=1,2,...$. For this problem the strong collision assumption means that the interaction between the ligand and the protein is sufficiently strong that it leads to a conformational change of the protein which is relatively independent of the state of the protein molecule before the interaction. Although the constraints imposed by the model seem to be rather strong, they are less restrictive than the ones corresponding to the models with static disorder presented in the literature.[2,3]

A second possible application of the theory is the study of interactions between the collective orientational relaxation in dense fluids and the kinetics of chemical processes.[29] In this case the collective orientational relaxation is responsible for the occurrence of dynamical disorder and it plays a role which is similar to the role played by the process of conformational relaxation in protein dynamics. The chemical reaction plays the role of the rate process.

IX. COOPERATIVITY VERSUS STATISTICAL INDEPENDENCE FOR RANDOM RELAXATION RATES

A referee of this article has pointed out that our approach is based on the implicit assumption that all particles making up the system are controlled by the same realization of the random rate $W(t')$. In this section we investigate the general implications of this assumption and suggest an alternative approach of random relaxation processes for which the above-mentioned assumption does not hold anymore.

The assumption that the relaxation behavior of all particles is controlled by the same realization of the random rate $W(t')$ corresponds to a very strong cooperative behavior. As the above-mentioned referee has pointed out this cooperative behavior of all particles is the physical cause which generates the intermittent behavior of the process characterized by the general fluctuation–dissipation relations (4.11). We emphasize that this cooperative behavior is related only to the dynamical disorder and has nothing to do with the particles themselves which in the framework of our approach are otherwise supposed to be independent.

Although the cooperativity of a dynamical-disordered process is not an unreasonable assumption there is no guarantee that it is universally valid. In two of the three applications considered in this article, the positron lifetime distributions and the passage through a fluctuating geometrical bottleneck, one expects to have only a partial cooperative behavior, limited to the particles trapped in a given region of the fluid or to the number of particles passing through the same bottleneck. However, the theory developed in the preceding sections remains valid, provided that the number N_0 of particles is not the total number of particles from the system, but rather the number of the particles from a given cluster corresponding to a given region of the fluid or to a given bottleneck, respectively. Generally speaking, for such a system with partial cooperativity, in addition to the two averages considered in this article, over the sample fluctuations and over the dynamical disorder, we should consider an additional averaging, over the all possible numbers and sizes of the clusters. Concerning the jump process model investigated in Sec. VIII the cooperative or noncooperative behavior of dynamical disorder should be examined for each possible applications of the model.

We emphasize that the cooperative or noncooperative behavior of dynamical disorder does not influence the expressions for the average survival functions derived in this article; only the behavior of the fluctuations is influenced by the type of dynamical disorder considered. For illustration in this section we investigate the other extreme of complete statistical independence for which the fluctuations of the relaxation rates attached to the different particles are completely independent. In this case the average in definition (2.10) of the characteristic functional $\Xi[.\mathscr{K}(t')]$ of the

number of particles should be computed by taking into account all possible realizations of different random relaxation functions $W(t_1'),\ldots,W(t_N')$ which are assumed to be independent of each other. Equation (3.2) should be replaced by

$$\Xi[\mathscr{K}(t')]=\left\langle \exp\left(i\int_0^t \mathscr{K}(t')\langle N(t')\rangle_{\text{disorder}}\, dt'\right)\right\rangle, \tag{9.1}$$

where

$$\langle N(t')\rangle_{\text{disorder}}=N_0\left\langle \exp\left(-\int_0^{t'} W(t'')dt''\right)\right\rangle_{\text{disorder}} \tag{9.2}$$

is a dynamical average of the type (3.10). The characteristic functional $\Xi[\mathscr{K}(t')]$ can be expressed by an expansion of the type (3.9)

$$\begin{aligned}\Xi[\mathscr{K}(t')]&=g\left\{ z=1+\int_0^t \langle l(t')\rangle_{\text{dynamic}} i\mathscr{K}(t')\exp\left[i\int_0^{t'}\mathscr{K}(\mathscr{C})d\mathscr{C}\right]dt',\quad t=0\right\}\\ &=1+\sum_{m=1}^{\infty}\frac{(i)^m}{m!}F_m(0)\int_0^t\cdots\int_0^t \mathscr{K}(t_1')\cdots\mathscr{K}(t_m')\\ &\quad\times\exp\left(i\sum_{u=1}^{m}\int_0^{t_u'}\mathscr{K}(\mathscr{C})d\mathscr{C}\right)\langle l(t_1')\rangle\cdots\langle l(t_m')\rangle dt_1'\cdots dt_m'.\end{aligned} \tag{9.3}$$

By following the same steps as in Secs. II–IV from Eq. (9.3) we can show that for independent fluctuations of the random rates $W(t_1'),\ldots,W(t')$ the two-time cumulants of the second order of the number of particles and the factorial cumulants $F_m(t)$ are given by

$$\langle\langle N(t_1)N(t_2)\rangle\rangle=N_0[\langle l(t_2^*)\rangle-\langle l(t_1)\rangle\langle l(t_2)\rangle] \tag{9.4}$$

and

$$F_m(t)=F_m(0)\langle l(t)\rangle^m. \tag{9.5}$$

We notice that, in contrast with the case of cooperative dynamical disorder, for independent fluctuating rates the cumulants of the second order of the number of particles depend on the first power of the total number N_0 of particles and not on the second power N_0^2. As a result in the thermodynamic limit $N_0\to\infty$ the relative fluctuation of the number of particles decreases to zero as $(N_0)^{-1/2}$ as $N_0\to\infty$, a situation which corresponds to a nonintermittent behavior.

The choice between these two limit approaches corresponding to correlated and noncorrelated fluctuations of the relaxation rates, respectively, should be done depending on the characteristics of the particular system studied. It may happen that for certain systems none of the two approaches developed in in this article may be used and thus the development of an averaging procedure corresponding to a partially correlated behavior may be necessary.

X. DISCUSSION

Dynamical disorder occurs when there is a partial overlapping between the time scales of two correlated random processes. In this article we have addressed two problems concerning systems with dynamical disorder, to which little attention has been paid in the literature:

(1) The elaboration of an efficient method for the direct evaluation of the dynamical averages and

(2) The study of fluctuations of the number of surviving particles for independent rate processes with dynamical disorder.

Our method of direct averaging is based on the use of characteristic functionals; within its framework the direct evaluation of means is less unpleasant and less formidable than has been claimed in the literature.[1] We have derived a general class of fluctuation–dissipation relations which can be used to evaluate all moments of the number of surviving particles in terms of the average survival function. For applying these fluctuation–dissipation relations it is not necessary to use the whole mathematical apparatus of the theory. Our approach can be used to evaluate not only the fluctuations of the number of particles but also the moments of the survival functions as well as other properties of the systems. It is more general than the indirect methods of averaging used in the literature, in particular it is not confined to a certain class of stochastic processes. For Markovian processes the method of stochastic Liouville equations[1,30,31] is recovered as a particular case of our approach.

A surprising result of our treatment is that for systems with dynamical disorder the fluctuations of the number of particles have an intermittent behavior. In the thermodynamic limit the relative fluctuation does not decrease to zero, but rather tends to a constant value. In all particular cases investigated the relative fluctuation diverges to infinity for large time. This type of behavior is very different from the equilibrium behavior of systems made up of independent particles for which the relative fluctuation decreases to zero in the thermodynamic limit as the reciprocal value of the square root of the number of particles.[58] An important consequence of the intermittent behavior is that for systems with dynamical disorder the fluctuations should play an important role even in the macroscopic limit, and should lead to observable macroscopic effects. These effects would be the stochastic analog of the macroscopic quantum effects.

Although this article is long, it does not exhaust the possibilities of the application of our method. A first generalization would be the development of a field theory in which the spatial distribution of the particles is taken into account. The development of this type of theory is of importance in connection with the measurement of large fluctuations corresponding to the intermittent behavior by means of light scattering.[59] A second generalization would be to the study of the interaction between an annihilation process and a generation process of the particles (or quasiparticles). In this case nonequilibrium steady states may occur for which the generation and annihilation processes compensate each other. For these processes the fluctuation–dissipation relations may serve as a basis for the derivation of a generalized thermodynamic description of nonequilibrium steady states by using the method suggested by Ross, Hunt, and Hunt.[60]

Another possible application is related to the analysis of new experimental techniques for the study of radical kinetics by applying external variable magnetic fields, for instance, the study of geminate recombination of radical pairs by means of the stimulated polarization of nuclei (SPN[61]).

The possibilities of application of the theory are not limited to the study of physical or chemical phenomena. The method can also be used in population dynamics for the analysis of the influence of environmental fluctuations on the growth of a population[62] or in exobiology for the evaluation of the probability of the existence of extraterrestrial life.[63]

ACKNOWLEDGMENTS

The authors thank Drs. J. Wang and P. Wolynes for providing copies of their publications and to an anonymous referee for pointing out the connection between the intermittency of fluctuations and the cooperative behavior of dynamical disorder. This research has been supported in part by NATO, the Air Force Office of Scientific Research, and the Natural Sciences and Engineering Research Council of Canada, by the Alexander von Humboldt Foundation, and by the Department of Energy, Basic Energy Sciences Engineering Program.

APPENDIX A: TIME-DEPENDENT, ORDERED SYSTEMS

For computing the generating functional $\Xi_{\text{ordered}}[\mathscr{K}(t')|W(t')]$ we come back to the discrete representation (2.6) of the time variable and notice that for a given realization of the rate coefficient $W(t')$, $0\leqslant t'\leqslant t$ the m-gate probability $P_m(N_m,t_m;\ldots;N_1,t_1)$ is a superposition of binomial distributions

$$P_m(N_m,t_m;\ldots;N_1,t_1)=\sum_{N_0} P(N_0,0)\,\frac{N_0!}{(N_0-N_1)!N_1!}\,(1-p_1)^{N_1}(p_1)^{N_0-N_1}\cdots\,\frac{N_{m-1}!}{(N_{m-1}-N_m)!N_m!}$$
$$\times(1-p_m)^{N_m}(p_m)^{N_{m-1}-N_m},\quad m\gg 1, \tag{A1}$$

where

$$p_u=W(u\Delta t)\Delta t,\quad u=1,\ldots,m \tag{A2}$$

is the probability of disappearance of a particle in a small time interval limited by the times $u\Delta t$ and $(u+1)\Delta t$. Equation (A1) has been derived by taking into account that the disappearance of a particle is a statistical process independent of the evolution of other particles and by making a balance of the surviving particles from time interval to time interval. The generating function of the m-gate probability $P_m(N_m,t_m;\ldots;N_1,t_1)$

$$\Xi_m(z_m,t_m;\ldots;z_1,t_1)=\sum_{N_m}\cdots\sum_{N_1}\prod_{u=1}^{m}(z_u)^{N_u}P_m(N_m,t_m;\ldots;N_1,t_1),$$
$$\text{with}\quad |z_u|\leqslant 1,\quad u=1,\ldots,m \tag{A3}$$

can be computed by a repeated application of the binomial summation formula. By combining Eqs. (2.3), (A1), and (A3) after some elementary algebraic manipulations we come to

$$\Xi_m(z_m,t_m;\ldots;z_1,t_1)=g(\varphi_m(z_1,\ldots,z_m),0), \tag{A4}$$

where

$$\varphi_m(z_1,\ldots,z_m)=p_1+z_1(1-p_1)p_2+z_1z_2(1-p_1)(1-p_2)p_3+\cdots+z_1\cdots z_{m-1}$$
$$\times(1-p_1)\cdots(1-p_{m-1})p_m+z_1\cdots z_m(1-p_1)\cdots(1-p_m) \tag{A5}$$

and $g(z,0)$ is the generating function of the initial distribution of particles [Eq. (2.3)].

Now we compare the definitions of the ordered characteristic functional $\Xi_{\text{ordered}}[\mathscr{K}(t')|W(t')]$ and of the m-gate generating function $\Xi_m(z_m,t_m,\ldots,z_1,t_1)$; the comparison shows that in the limit $\Delta t\to 0$ we have

$$\Xi_{\text{ordered}}[\mathscr{K}(t')|W(t')]=\lim_{\substack{\Delta t\to 0\\(m\to\infty)}}\Xi_m(z_u=\exp(i\mathscr{K}(u\Delta t)\Delta t),\quad u=1,\ldots,\ldots,m). \tag{A6}$$

By combining Eqs. (A2) and (A4)–(A6) we obtain the following expression for the ordered characteristic functional:

$$\Xi_{\text{ordered}}[\mathscr{K}(t')|W(t')]=g\left\{z=\int_0^t\mathscr{F}(t')\exp\left(i\int_0^{t'}K(\mathscr{C})d\mathscr{C}\right)dt'+l(t)\exp\left(i\int_0^t K(\mathscr{C})d\mathscr{C}\right),0\right\}, \tag{A7}$$

where

$$\mathcal{F}(t)=-[\partial l(t)/\partial t]=W(t)\exp\left(-\int_0^t W(t')dt'\right). \tag{A8}$$

Performing a partial integration in Eq. (A7) we come to Eq. (3.3).

The central moments $\langle N(t_1)\cdots N(t_m)\rangle_{\text{ordered}}$ and the cumulants $\langle\langle N(t_1)\cdots N(t_m)\rangle\rangle_{\text{ordered}}$ of the number of surviving particles for a given realization of the random rate coefficient are given by

$$\langle N(t_1)\cdots N(t_m)\rangle_{\text{ordered}}=(-i)^m\left.\frac{\delta^m \Xi_{\text{ordered}}[\mathcal{K}(t')]}{\delta\mathcal{K}(t_1)\cdots\delta\mathcal{K}(t_m)}\right|_{\mathcal{K}(t')=0} \tag{A9}$$

and

$$\langle\langle N(t_1)\cdots N(t_m)\rangle\rangle_{\text{ordered}}=(-i)^m\left.\frac{\delta^m \ln\,\Xi_{\text{ordered}}[\mathcal{K}(t')]}{\delta\mathcal{K}(t_1)\cdots\delta\mathcal{K}(t_m)}\right|_{\mathcal{K}(t')=0}. \tag{A10}$$

For an initial canonical ensemble we get the following expressions for the first two moments of the number of particles:

$$\langle\langle N(t)\rangle\rangle_{\text{ordered}}=\langle N(t)\rangle_{\text{ordered}}=N_0 l(t) \tag{A11}$$

and

$$\langle\langle N(t_1)N(t_2)\rangle\rangle_{\text{ordered}}=\langle N(t_1)N(t_2)\rangle_{\text{ordered}}-\langle N(t_1)\rangle_{\text{ordered}}\langle N(t_2)\rangle_{\text{ordered}}=N_0[l(t_2^*)-l(t_1)l(t_2)], \tag{A11$'$}$$

where

$$t_m^*=\max(t_1,\ldots,t_m). \tag{A12}$$

The relative fluctuation of the number of particles is equal to

$$\rho_{\text{ordered}}(t_1,t_2)=\left(\frac{\langle\langle N(t_1)N(t_2)\rangle\rangle_{\text{ordered}}}{\langle\langle N(t_1)\rangle\rangle_{\text{ordered}}\langle\langle N(t_2)\rangle\rangle_{\text{ordered}}}\right)^{1/2}=(N_0)^{-1/2}\left(\frac{l(t_2^*)}{l(t_1)l(t_2)}-1\right)^{1/2}. \tag{A13}$$

In the thermodynamic limit $\langle N_0\rangle\to\infty$ the relative fluctuation of the number of particles decreases to zero as $(N_0)^{-1/2}$, that is, in the thermodynamic limit the fluctuations are insignificant, i.e., they have a nonintermittent behavior.[58]

For an initial grand canonical ensemble the generating function $g(z,0)$ depends exponentially on $z-1$, all terms in the functional Taylor expansion of $\ln\,\Xi_{\text{ordered}}[\mathcal{K}(t')|W(t')]$ can be computed exactly, which allows the evaluation of all cumulants. After some calculus we come to

$$\langle\langle N(t_1)\cdots N(t_m)\rangle\rangle_{\text{ordered}}=m2^{1-m}l(t_m^*)\langle N_0\rangle. \tag{A14}$$

The relative fluctuation of the number of particles is given by an equation similar to Eq. (A13)

$$\rho_{\text{ordered}}(t_1,t_2)=(\langle N_0\rangle)^{-1/2}\left(\frac{l(t_2^*)}{l(t_1)l(t_2)}\right)^{1/2}. \tag{A15}$$

For an initial grand canonical ensemble in the thermodynamic limit $\langle N_0\rangle\to\infty$ the fluctuations are also nonintermittent.

APPENDIX B: MOMENTS AND CUMULANTS

The central moments of the number of particles, $\langle N^m(t)\rangle$, can be expressed in terms of the factorial moments by using the Stirling numbers of the second and first kind $\$_m^{(q)}$ and $S_m^{(q)}$, respectively,[34]

$$\$_m^{(q)}=\sum_{k=0}^{q}\frac{(-1)^{q-k}k^m}{k!(q-k)!}, \tag{B1}$$

$$S_m^{(q)}=\sum_{k=0}^{m-q}(-1)^k\frac{(m-1+k)!}{(m-q+k)!(q-1)!}\cdot\frac{(2m-q)!}{(m-q-k)!(m+k)!}\$_{m-q+k}^{(k)}. \tag{B2}$$

We have

$$\langle N^m(t)\rangle=\sum_{q=0}^{m}\$_m^{(q)}F_q(0)\langle l^q(t)\rangle=\sum_{q=0}^{m}\sum_{v=0}^{q}\$_m^{(q)}S_q^{(v)}\langle N^v(0)\rangle\langle l^q(t)\rangle. \tag{B3}$$

The one-time cumulants $\langle\langle N^m(t)\rangle\rangle_{\text{dynamic}}=C_m(t)$ can be computed in terms of the factorial moments by comparing the logarithm of Eq. (4.5) with an expansion of $\ln g(z,t)$ similar to the expansion used in Eq. (2.11) for the characteristic functional $\Xi[\mathscr{K}(t')]$. We obtain

$$C_m(t)=\sum_{m_1,m_2,\ldots}m!(-1)^{\Sigma m_v}(\Sigma m_v-1)!\prod_v(\langle N^v(t)\rangle/[(v!)^{m_v}m_v!])^{m_v}, \tag{B4}$$

where $\Sigma v m_v=m$ is a partition of the integer m into smaller integers $m_1,m_2,\ldots$, and $\langle N^v(t)\rangle$ are given by Eq. (B3).

APPENDIX C: CURTAILED CHARACTERISTIC FUNCTIONALS

Following Lax[39] and Van Kampen[40] the characteristic functional $G[K(t')]$ of the rate coefficient $W(t')$ can be expressed as an integral of a curtailed generating functional $\mathscr{G}[K(t');\mathbf{x}]$ over all possible values of the random vector $\mathbf{x}$

$$G[K(t')]=\int\mathscr{G}[K(t'),\mathbf{x}]d\mathbf{x}, \tag{C1}$$

where $\mathscr{G}[K(t'),\mathbf{x}]$ is the solution of the evolution equation

$$\partial_t\mathscr{G}[K(t'),\mathbf{x}]=\mathbb{L}\mathscr{G}[K(t'),\mathbf{x}]+iK(t)W(\mathbf{x})\mathscr{G}[K(t'),\mathbf{x}], \tag{C2}$$

with the initial condition

$$\mathscr{G}(t=0)=P(\mathbf{x},0). \tag{C3}$$

To compute the one-time moments of the survival function, $\langle l^m(t)\rangle$, we need to evaluate $\mathscr{G}[K(t'),\mathbf{x}]$ for a constant test function $K(t')=im$ [see Eq. (4.8)]. Combining Eqs. (4.8) and (C1)–(C3) yields Eqs. (5.3)–(5.5).

From Eqs. (2.14) and (5.8) it follows that the lethargy variable $\varepsilon(t)$ obeys a differential equation with random parameters

$$d\varepsilon(t)/dt=W(\mathbf{x}(t)),\quad\text{with}\quad\varepsilon(0)=0, \tag{C4}$$

where the random evolution of $\mathbf{x}(t)$ is determined by the evolution operator $\mathbb{L}$. From Eq. (C3) it follows that the probability density $\phi(\varepsilon,\mathbf{x};t)$ obeys the stochastic Liouville equation

$$\partial_t \phi(\varepsilon,\mathbf{x};t) + W(\mathbf{x})\partial_\varepsilon \phi(\varepsilon,\mathbf{x};t) = \mathbb{L}\phi(\varepsilon,\mathbf{x};t), \tag{C5}$$

with the initial condition

$$\phi(\varepsilon,\mathbf{x};t=0) = \delta(\varepsilon)P(\mathbf{x},0). \tag{C6}$$

Through Laplace transformation Eqs. (C5)–(C6) become

$$\partial_t \tilde{\phi}(\beta,\mathbf{x};t) = \mathbb{L}\tilde{\phi}(\beta,\mathbf{x};t) - \beta W(\mathbf{x})\tilde{\phi}(\beta,\mathbf{x};t), \tag{C7}$$

$$\tilde{\phi}(\beta,\mathbf{x};t=0) = P(\mathbf{x},0). \tag{C8}$$

By comparing Eqs. (5.4) and (5.5) with Eqs. (C7) and (C8) we obtain Eq. (5.11).

APPENDIX D: FLUCTUATING GEOMETRICAL BOTTLENECKS

We introduce the joint probability density of the number N of ligand molecules and of the radius r of the bottleneck

$$\mathscr{B}(N,r;t)dr, \quad \text{with} \quad \sum \int \mathscr{B}(N,r;t)dr = 1. \tag{D1}$$

$\mathscr{B}(N,r;t)$ is the solution of a stochastic Liouville equation

$$\partial_t \mathscr{B}(N,r;t) = \alpha r^2[(N+1).\mathscr{B}(N+1;r;t) - N.\mathscr{B}(N,r;t)] + \lambda\,\partial_r[r.\mathscr{B}(N,r;t)] + \lambda\,\theta\partial_{r^2}^2[.\mathscr{B}(N,r;t)], \tag{D2}$$

with the initial and boundary conditions

$$\mathscr{B}(N,r;t=0) = P(N,0)(\pi\theta)^{-1/2}\exp(-r^2/4\theta), \tag{D3}$$

$$\partial_r \mathscr{B}(N,r=0;t) = 0. \tag{D4}$$

The boundary condition (D4) expresses the fact the radius r of the bottleneck cannot be negative, whereas the initial condition (D3) corresponds to an initial equilibrium truncated Gaussian distribution which obeys the condition $r \geqslant 0$.

Introducing the marginal generating function

$$g^*(z,r,t) = \sum z^N \mathscr{B}(N,r;t), \quad |z| \leqslant 1. \tag{D5}$$

Equations (D2)–(D4) become

$$\partial_t g^*(z,r,t) = \alpha r^2(1-z)\partial_z g^*(z,r,t) + \lambda\,\partial_r[r g^*(z,r,t)] + \lambda\,\theta\partial_{r^2}^2[g^*(z,r,t)], \tag{D6}$$

$$g^*(z,r,t=0) = g(z,0)(\pi\theta)^{-1/2}\exp(-r^2/4\theta), \tag{D7}$$

$$\partial_r g^*(z,r=0,t) = 0.$$

We express the factorial moments $F_m(t)$ in terms of the marginal generating function $g^*(z,r,t)$. We obtain

$$F_m(t) = \sum N(N-1)\cdots(N-m+1)\int \mathscr{B}(N,r;t)dr = \int F_m^*(r,t)dr, \tag{D8}$$

where the functions $F_m^*(r,t)$ are given by

$$F_m^*(r,t)=\partial^m g^*(z,r,t)/\partial z^m|_{z=1}. \tag{D9}$$

From Eqs. (D5)–(D7) and (D9) we get a set of partial differential equations in $F_m^*(r,t)$

$$\partial_t F_m^*(r,t)=-\alpha m r^2 F_m^*(r,t)+\lambda\partial_r[rF_m^*(r,t)]+\lambda\theta\partial_{r^2}^2[F_m^*(r,t)], \tag{D10}$$

with the initial and boundary conditions

$$F_m^*(r,0)=F_m(0)(\pi\theta)^{-1/2}\exp(-r^2/4\theta), \tag{D11}$$

$$\partial_r F_m^*(r=0,t)=0. \tag{D12}$$

Equation (D10) have the same formal structure as a differential equation used by Zwanzig[32] for the evaluation of the average survival function. An eigenfunction solution of the same type of equation has been given by Weiss[47] in a different physical context. Equation (D10) can be solved by searching for Gaussian solutions of the type

$$F_m^*(r,t)=A_m(t)\exp[-r^2 b_m(t)], \quad m=1,2,\ldots, \tag{D13}$$

which obviously are compatible with the initial and boundary conditions (D11) and (D12). Inserting Eqs. (D13) into Eqs. (D10)–(D12) we obtain a chain of ordinary differential equations in $A_m(t)$ and $b_m(t)$. Solving these differential equations and inserting the solutions into Eqs. (D13) we can compute the functions $F_m^*(r,t)$. The calculations are lengthy but standard. Substituting the expressions for $F_m^*(r,t)$ into Eqs. (D8) and using the fluctuation–dissipation relations (4.11) we come to Eqs. (7.7) and (7.8).

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