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Fluctuating Poissonian Clocks, Fractal Random Processes and Dynamical Porter-Thomas Distributions: Applications to Evolutionary Molecular Biology, Enhanced Diffusion and Dynamical Relaxation

Marcel Ovidiu Vlad*

Centre for Nonlinear Dynamics in Physiology and Medicine, McGill University, 3655 Drummond Street, Montreal PQ Canada H3G 1Y6

Birgitt Schönfisch

Lehrstuhl für Biomathematik, Eberhard-Karls Universität Tübingen, Auf der Morgenstelle 10, D 72076 Tübingen, Germany

and

Michael C. Mackey

Departments of Physiology, Physics and Mathematics, McGill University, 3655 Drummond Street, Montreal PQ Canada H3G 1Y6

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Abstract

The influence of the memory effects on the Poissonian clocks with fluctuating counting rates is investigated by using the technique of characteristic functionals. A general approach for computing all cumulants of the number of counts is suggested based on an analogy with the theory of rate processes with dynamical disorder. The large time behavior of the cumulants is investigated for stationary random processes with short and long memory, respectively. For short memory in the long run all cumulants increase linearly in time and the averaged stochastic process describing the statistics of the number of counts, although generally non-Poissonian, is non-intermittent and can be used as a clock. For finite long memory described by a stationary fractal random process, even though the cumulants of the number of events increase faster than linearly in time, the fluctuations are still non-intermittent and the averaged random process is also a clock. For infinite memory, however, the fluctuations of the number of counts are intermittent and the averaged random process is not a clock any more. An alternative stochastic approach is developed based on the use of a dynamical analogue of the Porter-Thomas formula; the results are consistent with the first version of the theory. Three applications of the general theory are presented. The first application is related to the connection between the Kimura's neutral theory of molecular evolution and the Gillespie's episodic clock for the rate of amino acid substitutions through the evolutionary process. If the fluctuations of the rate of substitution have short memory or long finite memory then Gillespie's episodic clock is consistent with Kimura's theory. Only the infinite memory is not consistent with the neutral hypothesis. The second application is the study of a hopping mechanism for enhanced diffusion. A biased random walk is investigated by assuming that the distribution of the number of jumps is given by a Poissonian process with a fluctuating counting rate. If the fluctuations of the counting rate have short memory then the resulting biased diffusion is normal and obeys Einstein's linear equation for the mean square displacement of the moving particle. For long memory the mean square displacement of the moving particle increases faster than linearly in time and the diffusion is enhanced. An alternative approach for a random walk in the velocity space is developed. In this case the diffusion process is even more efficient than for a random walk in the real space. The third application is the study of Porter-Thomas relaxation for systems with dynamical disorder. It is shown that for small and moderately long times the relaxation function obeys a scaling law of the negative power law type followed by a fast decaying exponential tail which is determined by the fluctuation dynamics. This type of relaxation behavior is of interest both for nuclear and molecular physics and corresponds to a non-ideal statistical fractal.

* Permanent address: Romanian Academy of Sciences, Centre for Mathematical Statistics, Casa Academiei Romane, Calea 13 Septemberie No 13, Bucuresti 5 Zip Code 76100, România; current address after January 1, 1996: Department of Chemistry, Stanford University, Stanford CA 94305-5080 USA.

1. Introduction

The use of a stochastic process of the Poisson type as a clock has been suggested in connection with the use of the radioactive decay for the evaluation of time intervals (Olsson [1]). If initially there are N_0 nuclei characterized by the decay rate k the probability $P(N; t)$ that in a time interval of length t, N disintegration events have occurred is given by the Poissonian law

$$P(N; t) = \frac{(\lambda t)^N}{N!} \exp(-\lambda t), \quad N_0 \gg N, \tag{1}$$

where

$$\lambda = kN_0, \tag{2}$$

is the activity of the chemical element considered. For the Poissonian distribution (1) all cumulants of the number N of disintegration events, $\langle\langle N^m(t)\rangle\rangle$, $m = 1, 2, \ldots$ are equal to each other and to the product of the activity λ with the length t of the time interval considered

$$\langle\langle N^m(t)\rangle\rangle = \lambda t, \quad m = 1, 2, \ldots \tag{3}$$

The linear increase of the cumulants of the number of disintegration events with the length t of the time interval leads to a non-intermittent behavior of the fluctuations which is the theoretical basis for the use of the process of the decay as a clock for time measurements.

The idea of a random Poissonian clock has been borrowed from nuclear physics to molecular biology. Zuckerlandl and Pauling [2] showed that the observed rates of protein evolution measured by the number N of amino acid substitutions can be approximately represented by a Poissonian law of the type (1) where now λ is the rate of amino acid substitutions. The approximate Poissonian distribution of the number of amino acid substitutions is an argument in favor of Kimura's neutral theory of molecular evolution (Ohta and Kimura [3]; Kimura [4]) according to which the fixation of a gene in a population is entirely due to random fluctuations of the gene frequencies.

Recently the Poissonian nature of the clocks has been questioned both for the radioactive decay and for the molecular substitution of amino acids in evolutionary biology. In nuclear physics experimental evidence has been accumulated which shows that for certain nuclei the Poissonian distribution is not valid and that the data can be better represented by an $1/f$ noise stochastic process (see for instance Azhar and Gopala [5]). In this case the violation of the Poissonian law (1) seems to be due to the nuclear process itself. Note however that early studies of the radioactive clocks have reported random variations of the activity due to the transport of the nuclei in the system; of course such variations have nothing to do with the disintegration process itself which is assumed to be Poissonian (Olsson [1] and references therein).

Similar violations of the Poissonian law for other random processes of the counting type have been reported for the particle detection (Kobayashi [6]) and for the statistics of the jump events for dispersive transport (Haus and Kehr [7], Bouchaud and Georges [8]; Weiss [9]).

In molecular biology the possible occurrence of an episodic clock has been suggested for which the substitution rate λ is a stationary random function of time (Gillespie [10, 11]). This episodic clock is equivalent to the socalled doubly stochastic Poisson point process introduced independently by mathematicians (Cox and Isham [12]). In connection with the episodic clock a controversy has occurred in the literature. Gillespie [10, 11] has claimed that it is incompatible with Kimura's theory of neutral molecular evolution. On the other hand Takahata [13–15] has shown that the episodic clock is not incompatible with Kimura's theory.

Our interest in the study of Poissonian clocks with fluctuating counting rates has been stimulated by some unexpected analogies among a number of apparently unrelated problems, the theory of rate processes with dynamical disorder, (Zwanzig [16]; Wang and Wolynes [17, 18]; Vlad, Mackey and Ross [19]; Vlad and Mackey [20, 21]; Vlad, Ross and Mackey [22]), the study of ergodic behavior of stochastic cellular automata with long memory and of Mandelbrot's fractional Brownian motion (Schönfisch [23]; Schönfisch and Vlad [24]; Vlad, Schönfisch and Mackey [25]) and the study of enhanced diffusion in disordered systems (Araujo *et al.* [26]; Shlesinger *et al.* [27]; Vlad [28]). These analogies have suggested that the doubly stochastic Poisson process (Cox and Isham [12]) is in fact a special type of rate process with dynamical disorder which can be studied by applying the characteristic functional techniques developed in the physical literature for the study of these processes (Vlad, Mackey and Ross [19], Vlad and Mackey [20, 21]; Vlad, Ross and Mackey [22]). By combining this approach with a cumulant expansion technique developed for the study of ergodic behavior (Schönfisch [23]; Schönfisch and Vlad [24], Vlad, Schönfisch and Mackey [25]) it is possible to investigate the effect of long-range correlations of the fluctuations of the counting rate on the statistics of the number N of events occurring in a given time interval; until now this problem has not been investigated in the physical, biological and statistical literature.

The outline of the paper is as follows. In Section 2 we relate the stochastic properties of the number of events to the stochastic properties of the fluctuating counting rate. Sections 3 and 4 deal with the asymptotic behavior of the cumulants of the number of events for random processes with short and long memory, respectively. In Section 5 an alternative approach is developed based on the use of a dynamical analogue of the Porter-Thomas probability distribution. Section 6 deals with the implications of the formalism for the study of the connection between the Gillespie's episodic molecular clock and Kimura's theory of neutral molecular evolution. In Section 7 a fluctuating clock with long range memory is used for describing the biased enhanced diffusion in random systems with dynamical temporal disorder. Section 8 deals with the study of dynamical Porter-Thomas relaxation with applications to nuclear and molecular physics. Finally in Section 9 some limitations as well as possibilities of generalization of our approach are mentioned.

2. Fluctuating Poissonian clocks with dynamical disorder

For a given realization $\lambda(t')$ of the random counting rate the probablity $P(N; t)$ of the occurrence of N events in a time interval of length t is given by the following generalization of eq. (1):

$$P(N; t) = (N!)^{-1}\left(\int_0^t \lambda(t')\, t'\right)^N \exp\left(-\int_0^t \lambda(t')\, dt'\right). \tag{4}$$

Since $\lambda(t')$, $t \geqslant t' \geqslant 0$ is a random function the probability $P(N; t)$ is itself random. The corresponding average probability is given by

$$\bar{P}(N; t) = \left\langle (N!)^{-1}\left(\int_0^t \lambda(t')\, dt'\right)^N \exp\left(-\int_0^t \lambda(t')\, dt'\right)\right\rangle, \tag{5}$$

where the average $\langle \cdots \rangle$ is given by a path integral which takes into account the contributions of all possible random functions $\lambda(t')$, $0 \leqslant t' \leqslant t$.

We describe the stochastic properties of the random counting rate $\lambda(t')$ by means of a characteristic functional

$$\Xi[K(t'); t] = \left\langle \exp\left(i \int_0^t K(t')\lambda(t')\, dt'\right)\right\rangle, \tag{6}$$

where $K(t')$ is a suitable test function conjugate to the random rate $\lambda(t')$. If the cumulants $\langle\langle \lambda(t'_1) \ldots \lambda(t'_m)\rangle\rangle$, $m = 1, 2, \ldots$ of the counting rate exist and are finite then the characteristic functional $\Xi[K(t')]$ can be expressed by means of the cumulant expansion

$$\Xi[K(t'); t] = \exp\left\{\sum_{m=1}^{\infty} \frac{i^m}{m!} \int_0^t \ldots \int_0^t \langle\langle \lambda(t'_1) \ldots \lambda(t'_m)\rangle\rangle \times K(t'_1) \ldots K(t'_m)\, dt'_1 \ldots dt'_m\right\}. \tag{7}$$

For evaluating the stochastic properties of the number N of events we introduce the characteristic function $G(b; t)$ of the average probability $\bar{P}(N; t)$ as a discrete Fourier transform

$$G(B; t) = \sum_{N=0}^{\infty} \exp(ibN)\bar{P}(N; t), \tag{8}$$

where b is the Fourier variable conjugate to the number N of events. By assuming that the average over all functions $\lambda(t')$, $t \geqslant t' \geqslant 0$ and the sum over the number of events N commute we come to

$$\begin{aligned} G(b; t) &= \sum_{N=0}^{\infty} \langle P(N; t)\rangle \exp(ibN) \\ &= \left\langle \sum_{N=0}^{\infty} P(N; t) \exp(ibN) \right\rangle \\ &= \left\langle \exp\left(\left(\int_0^t \lambda(t')\, dt'[\exp(ib) - 1]\right)\right)\right\rangle \\ &= \Xi[K(t') = -i[\exp(ib) - 1]h(t - t')] \end{aligned} \tag{9}$$

where $h(x)$ is the usual Heaviside function. Equation (9) is the main result of this paper. It expresses the stochastic properties of the number N of events in terms of the stochastic properties of the random counting rate $\lambda(t')$, $t \geqslant t' \geqslant 0$; it is similar, though not identical, to the expressions for the average relaxation functions derived for rate processes with dynamical disorder (Vlad, Mackey and Ross [19]; Vlad and Mackey [20, 21]; Vlad, Ross and Mackey [22]).

If the cumulants $\langle\langle N^m(t)\rangle\rangle$ of the number of events exist and are finite then we can express the characteristic function $G(b)$ by means of a cumulant expansion similar to eq. (7):

$$G(b) = \exp\left\{\sum_{m=1}^{\infty} \frac{i^m}{m!} \langle\langle N^m(t)\rangle\rangle b^m\right\}. \tag{10}$$

By expressing in eq. (9) $\Xi[K(t'); t]$ and $G(b; t)$ by their cumulant expansions (7) and (10), expanding the different terms $[\exp(ib) - 1]^m$ in Taylor series in b, ordering the different powers of b and comparing the two sides of the resulting equation we can express the cumulants $\langle\langle N^m(t)\rangle\rangle$ of the number of events in terms of the cumulants $\langle\langle \lambda(t_1) \ldots \lambda(t_m)\rangle\rangle$ of the fluctuating counting rate. After lengthy computations we come to

$$\langle\langle N^m(t)\rangle\rangle = \sum_{n=1}^{m} \mathcal{S}_m^{(n)} \int_0^t \ldots \int_0^t \langle\langle \lambda(t_1) \ldots \lambda(t_n)\rangle\rangle\, dt_1 \ldots dt_n, \tag{11}$$

where

$$\mathcal{S}_m^{(n)} = \sum_{k=0}^{n} \frac{(-1)^{n-k} k^m}{k!(n-k)!}, \tag{12}$$

are the Stirling numbers of the second kind.

Similarly the average state probability $\bar{P}(N; t)$ can be expressed in terms of the characteristic functional $\Xi[K(t')]$ in the form:

$$\begin{aligned} \bar{P}(N; t) &= (N!)^{-1}\, d^N G(b = 0; t)/d[\exp(ib)]^N \\ &= (N!)^{-1}\, d^N \Xi \\ &\quad \times [-i[\exp(ib) - 1]h(t - t')]/d[\exp(ib)]^N|_{b=0}. \end{aligned} \tag{13}$$

For example if the fluctuations of the counting rate $\lambda(t')$ are described by a Gaussian random process all cumulants $\langle\langle \lambda(t_1) \ldots \lambda(t_m)\rangle\rangle$ of order bigger than two are equal to zero

$$\langle\langle \lambda(t_1) \ldots \lambda(t_m)\rangle\rangle = 0, \quad m \geqslant 3, \tag{14}$$

the characteristic functional $\Xi[K(t'); t]$ is given by

$$\begin{aligned} \Xi[K(t')] = \exp\Bigg[& i \int_0^t K(t')\langle\langle \lambda(t')\rangle\rangle\, dt' \\ & - \frac{1}{2} \int_0^t \int_0^t K(t_1')K(t_2')\langle\langle \lambda(t_1')\lambda(t_2')\rangle\rangle\, dt_1'\, dt_2' \Bigg], \end{aligned} \tag{15}$$

and the average probability $\bar{P}(N; t)$ of the number N of events can be easily evaluated from eqs (13) and (15):

$$\begin{aligned} \bar{P}(N; t) = & \exp[-\chi(t) + \tfrac{1}{2}\mu(t)] \\ & \times \sum_{k=0}^{[N/2]} \frac{[\chi(t) - \mu(t)]^{N-2k}[\mu(t)]^k}{2^k (N - 2k)!\, k!}, \end{aligned} \tag{16}$$

where the square brackets $[N/2]$ denote the integer part of $N/2$ and [19]

$$\chi(t) = \int_0^t \langle\langle \lambda(t')\rangle\rangle\, dt' = \langle\langle N(t)\rangle\rangle, \tag{17}$$

$$\mu(t) = \int_0^t \int_0^t \langle\langle \lambda(t_1')\lambda(t_2')\rangle\rangle\, dt_1'\, dt_2' = \langle\langle N^2(t)\rangle\rangle - \langle\langle N(t)\rangle\rangle. \tag{18}$$

Note that the stochastic process corresponding to the probability $\bar{P}(N; t)$ given by eq. (16) is similar to the Gauss–Poisson process of Milne and Wescott [29]. Such a stochastic process has been used for describing the response of neurons and of neuron networks (Hesselmans *et al.* [30]).

An important consequence of the calculations presented before is that, although being a dynamical superposition of Poissonian distributions, the average state probability $\bar{P}(N; t)$ is generally non-Poissonian.

3. Asymptotic behavior for short memory

For investigating the clock properties of the stochastic process described by the average probability $\bar{P}(N; t)$, we start out with the pure Poissonian process corresponding to eq. (1). We introduce the relative dispersion indices of different orders

$$I_m(t) = \langle\langle N^m(t)\rangle\rangle / \langle\langle N(t)\rangle\rangle, \quad m = 2, 3, \ldots \tag{19}$$

For a pure Poisson process characterized by a non-random counting rate λ which is constant the cumulants of the number N of events are given by eq. (3) and then all dispersion indices $I_m(t)$ are equal to unity

$$I_m(t) = 1, \quad m = 2, 3, \ldots \tag{20}$$

The randomness of the counting rate $\lambda(t')$ leads to the violation of the expressions (19) for the dispersion indices which can become either larger or smaller than the unity. In literature a random process with a dispersion index I_2 smaller or larger than unity is called sub-Poissonian or super-Poissonian, respectively (Van Kampen [31]).

For computing the cumulants $\langle\langle N^m(t)\rangle\rangle$ and the relative dispersion indices $I_m(t)$ for a fluctuating random rate $\lambda(t')$ we should take into accocunt the condition of stationarity of the random process. For a stationary random process the cumulants, $\langle\langle \lambda(t_1) \ldots \lambda(t_m)\rangle\rangle$, obey the condition of temporal invariance

$$\langle\langle \lambda(t_1) \dots \lambda(t_m) \rangle\rangle = \langle\langle \lambda(t_1 - \Delta t) \dots \lambda(t_m - \Delta t) \rangle\rangle, \tag{21}$$

where Δt is an arbitrary time difference. In particular by choosing the time difference Δt as the smallest of the times $t_1, \dots, t_m$

$$\Delta t = t_m^* = \min (t_1, \dots, t_m), \tag{22}$$

we can express the cumulant of the mth order of the fluctuating counting rate $\lambda(t')$ as a function of $m - 1$ time differences

$$\langle\langle \lambda(t_1) \dots \lambda(t_m) \rangle\rangle = C_m(t_1 - t_m^*, \dots, t_m - t_m^*). \tag{23}$$

In particular, as expected for a stationary process, the cumulant of the first order, which is equal to the average counting rate $\langle \lambda \rangle$, is independent of time

$$\langle\langle \lambda \rangle\rangle = \langle \lambda \rangle = \text{independent of } t. \tag{24}$$

On the other hand, as the cumulant of the mth order should be a symmetric function of $t_1, \dots, t_m$ (Kubo [32]), the function $C_m(t_1 - t_m^*, \dots, t_m - t_m^*)$ is also symmetric with respect to all permutations of $t_1 - t_m^*, \dots, t_m - t_m^*$. Under these circumstances Vlad, Schönfisch and Mackey [25] have shown that the time integrals in eq. (11) can be expressed as:

$$\int_0^t \dots \int_0^t \langle\langle \lambda(t_1') \dots \lambda(t_m') \rangle\rangle \, dt_1' \dots dt_m' = m \int_0^t d\theta \int_0^{t-\theta} d\tau_1 \dots \int_0^{t-\theta} d\tau_{m-1} C_m(\tau_1, \dots, \tau_{m-1}). \tag{25}$$

If moreover the mth cumulant can be factorized as a product of $m - 1$ time differences

$$C_m(t_1 - t_m^*, \dots, t_m - t_m^*) = A_m \prod_u \varphi(t_u - t_m^*),$$
$$C_1 = A_1 = \text{constant}, \tag{26}$$

then

$$\int_0^t \dots \int_0^t \langle\langle \lambda(t_1') \dots \lambda(t_m') \rangle\rangle \, dt_1' \dots dt_m' = mA_m \int_0^t d\theta \left(\int_0^{t-\theta} \varphi(\tau) \, d\tau \right)^{m-1}. \tag{27}$$

For a system with short memory the cumulants C_m are exponentially decreasing functions (Vlad, Schönfisch and Mackey [25]):

$$C_m(t_1 - t_m^*, \dots, t_m - t_m^*) = A_m \prod_u \{ \nu \exp [-\nu(t_u - t_m^*)] \}, \tag{28}$$

where the frequency ν is generally dependent on the order m of the cumulant. A stochastic process with short memory characterized by cumulants of the type (28) can be generated by a physical mechanism of the shot noise type (Van Kampen[31, 33]; Vlad, Mackey and Ross [19]). We assume that the counting rate $\lambda(t')$ is generated by a Poissonian distribution of events occurring with a constant frequency Ω in a large time interval of length, T, each event having an exponentially decreasing effect given by the contribution

$$c\varphi(t - t') = c\nu \exp [-\nu(t - t')] \quad \text{for } t \geqslant t', \qquad = 0 \quad \text{for } t < t', \tag{29}$$

where t' is the time of occurrence of an event, t is the current time, ν is the frequency of the decay of the effect and c is a dimensionless random amplitude factor selected from a known probability density with finite moments:

$$p(c) \, dc \quad \text{with} \quad \int_0^\infty p(c) \, dc = 1. \tag{30}$$

A realization of the counting rate is given by

$$\lambda(t) = \sum_{u=1}^{M} c_u \varphi(t - t_u'), \tag{31}$$

where M is the total number of shot events, $t_1', \dots, t_M'$ are their times of occurrence and $c_1, \dots, c_M$ are the corresponding realizations of the amplitude factors. By inserting eq. (31) into eq. (6) for the characteristic functional $\Xi[K(t'); t]$ and computing the average $\langle \cdots \rangle$ in terms of all possible values of the number of shot events M, their time of occurrence $t_1', \dots, t_M'$ and their amplitude factors $c_1, \dots, c_M$ and passing to the limit $T \to \infty$, we come to

$$\Xi[K(t'); t] = \exp \left\{ -\Omega \int_0^\infty dt' \int_0^\infty p(c) \times \left[1 - \exp \left(ic\nu \int_{t'}^t \exp [-\nu(t - t')] K(t) \, dt \right) \right] \right\}. \tag{32}$$

To save space the detailed derivation of eq. (32) is not given here. For similar computations see Van Kampen [31, 33]; Vlad, Mackey and Ross [19]. By expanding the exponential in eq. (32) in a functional Taylor series in $K(t')$ and comparing the result with the expansion (7) we can compute all cumulants of the counting rate. After lengthy computations we come to a general expression for the cumulants of the type (28), where the frequency ν is independent of the cumulant index m and the factor A_m is given by:

$$A = m^{-1} \Omega \langle c^m \rangle, \tag{33}$$

where

$$\langle c^m \rangle = \int_0^m c^m p(c) \, dc, \tag{34}$$

are the moments of the amplitude factor.

Equations (11) and (27)–(28) lead to the following expressions for the cumulants $\langle\langle N^m(t) \rangle\rangle$ of the number of counting events

$$\langle\langle N^m(t) \rangle\rangle = \sum_{n=1}^{m} A_n \mathcal{S}_m^{(n)} \left\{ nt + \sum_{k=1}^{n-1} \frac{n!(-1)^k}{k!(n-1-k)!} \times [1 - \exp(-\nu kt)] \nu^{-1} k^{-1} \right\}. \tag{35}$$

From eq. (35) we note that in the long run $t \to \infty$ the cumulants of the number of counting events increase linearly in time

$$\langle\langle N^m(t) \rangle\rangle \sim t \sum_{n=1}^{m} n \mathcal{S}_m^{(n)} A_n \quad \text{as } t \to \infty, \tag{36}$$

and thus in this limit all dispersion indices $I_m(t)$ are time-independent

$$I_m(t) \to I_m(\infty) \quad \text{as } t \to \infty, \tag{37}$$

where

$$I_m(\infty) = 1 + \sum_{n=2}^{m} \mathcal{S}_m^{(n)} n A_n / A_1. \tag{38}$$

By considering the shot-noise model developed before the amplitude factor c is non-negative, $c \geqslant 0$, $\langle c^m \rangle \geqslant 0$ and therefore

$$A_m = m^{-1}\Omega\langle c^m \rangle \geqslant 0, \tag{39}$$

and since $\mathcal{S}_m^{(n)} \geqslant 0$ it follows that in this case

$$I_m(\infty) \geqslant 1, \tag{40}$$

that is, the fluctuations of the number N of counting events are generally super-Poissonian.

Concerning the clock properties of the averaged random process, we note that, even though in the limit of large times the dispersion indices are generally bigger than in the pure Poissonian case, in this limit all cumulants of the number of the counting events are linear functions of time and thus the average random-process is still a clock. The clock property is ensured by the fact in the limit $t \to \infty$ all relative fluctuations

$$f_m(t) = \langle\langle N^m(t) \rangle\rangle / \langle\langle N(t) \rangle\rangle^m, \quad m \geqslant 2, \tag{41}$$

decrease to zero as

$$f_m(t) \sim [I_m(\infty)/(A_1)^{m-1}]t^{-(m-1)}, \quad m \geqslant 2 \text{ as } t \to \infty. \tag{42}$$

4. Asymptotic behavior for long memory

For long memory the cumulants $C_m(t_1 - t_m^*, \ldots, t_m - t_m^*)$ of the counting rate $\lambda(t')$ have long tails of the negative power law type (Vlad, Schönfisch and Mackey [25])

$$C_m(t_1 - t_m^*, \ldots, t_m - t_m^*) = B_m\left[\prod_u (t_u - t_m^*)\right]^{-H_m},$$

$$C_1 = B_1 = \text{constant}, \tag{43}$$

where H_m, $m = 1, 2, \ldots$ are non-negative fractal exponents smaller than unity

$$1 > H_m \geqslant 0, \quad m = 2, 3, \ldots \tag{44}$$

A mechanism generating long tails of this type is based on a probabilistic version (Vlad [34–39]) of the Shlesinger–Hughes [40] stochastic renormalization. We start out with a stationary random process with short memory characterized by a set of cumulants $C_m(t_1 - t_m^*, \ldots, t_m - t_m^*)$ of the counting rate with short tails. As $\tau_u = t_u - t_m^*$, $u = 1, 2, \ldots, m$ tend to infinity the tails of the cumulants C_m decrease exponentially or even faster towards zero. Following Shlesinger and Hughes [40] we apply to these cumulants a series of scale transformations of the renormalization group (RG) type, each time difference $\tau_u = t_u - t_m^*$, $u = 1, \ldots, m$ being treated independently

$$\tilde{C}_m(\tau_1, \ldots, \tau_{m-1}) = \sum_{q_1=1}^{\infty} \sum_{q_{m-1}=1}^{\infty} \prod_{u=1}^{m-1} [(1 - \lambda_u)(\lambda_u)^{q_u}] C_m(\tau_1(b_1)^{-q_1}, \ldots, \tau_{m-1}(b_{m-1})^{-q_{m-1}}), \quad b_u \geqslant 1, \quad 1 \geqslant \lambda_u \geqslant 0, \quad u = 1, \ldots, m-1, \tag{45}$$

where $\tilde{C}_m(\tau_1, \ldots, \tau_{m-1})$ are the renormalized cumulants, $b_1, \ldots, b_{m-1} \geqslant 1$ are characteristic multiplicative scaling factors attached to the different time differences $\tau_1, \ldots, \tau_{m-1}$ and $1 \geqslant \lambda_u \geqslant 0$, $u = 1 \ldots, m-1$ are the probabilities that a scaling step takes place for each of the time differences $\tau_1, \ldots, \tau_{m-1}$, respectively. Equation (45) has a structure typical for an RG equation, which generates negative power law tails in $\tau_1, \ldots, \tau_{m-1}$ for the renormalized cumulants $\tilde{C}_m(\tau_1, \ldots, \tau_{m-1})$, characterized by the fractal exponents

$$H_u = \ln(1/\lambda_u)/\ln b_u, \quad u = 1, \ldots, m-1, \tag{46}$$

modulated by logarithmic oscillations in $\ln \tau_1, \ldots, \ln \tau_{m-1}$ with the periods $\ln b_1 \ldots, \ln b_{m-1}$, respectively. In order to get rid of the logarithmic oscillations in $\ln \tau_1, \ldots, \ln \tau_{m-1}$ we introduce the limit

$$b_u \searrow 1, \quad \lambda_u \nearrow 1 \quad \text{with } H_u = \text{constant}, u = 1, \ldots, m-1. \tag{47}$$

This limit has been introduced for one-variable systems by Vlad [38]; it leads to the vanishing of the logarithmic oscillations even though the long tails of the negative power law type are left unchanged. In the limit (47) the sums over $q_1, \ldots, q_{m-1}$ become integrals and after a suitable change of variables we come to

$$\tilde{C}_m(\tau_1, \ldots, \tau_{m-1}) = \left(\prod_u \tau_u\right)^{-H_m} \times (H_m)^{m-1} \int_0^{\tau_1} \cdots \int_0^{\tau_{m-1}} \left(\prod_u a_u\right)^{H_m - 1} \times C_m(a_1, \ldots, a_{m-1})\, da_1 \ldots da_{m-1}. \tag{48}$$

In eqs (48) we have taken into account that, due to the symmetry of the non-renormalized and renormalized cumulants with respect to any permutation of the time differences $\tau_1, \ldots, \tau_{m-1}$, the fractal exponents H_u should be independent of the label u of the time differences; however for cumulants of different orders the corresponding exponents may have different values $H_2, H_3, \ldots, H_m$. Note that the tails of the renormalized cumulants $\tilde{C}_m(\tau_1, \ldots, \tau_{m-1})$ given by eqs (48) have the same form as eqs (43) postulated by Vlad, Schönfisch and Mackey [25], where the constants B_m are given by

$$B_1 = C_1, \quad B_m = (H_m)^{m-1} \int_0^{\infty} \cdots \int_0^{\infty} \left(\prod_u a_u\right)^{H_m - 1} \times C_m(a_1, \ldots, a_{m-1})\, da_1 \ldots da_{m-1}, \quad m = 2, 3, \ldots \tag{49}$$

The convergence of the integrals in eqs (49) is ensured by the fact that as $a_1, \ldots, a_{m-1} \to \infty$ the tails of the non-renormalized cumulants decrease exponentially or faster to zero.

From eqs (11), (27) and (43) we get the following expressions for the cumulants of the number N of counting events

$$\langle\langle N^m(t) \rangle\rangle = \sum_{n=1}^{m} \mathcal{S}_m^{(n)} \frac{B_n n t^{n(1-H_n)+H_n}}{[n(1 - H_n) + H_n](1 - H_n)^{n-1}}. \tag{50}$$

From eq. (50) we get the following expressions for the asymptotic behavior of the cumulants $\langle\langle N^m(t) \rangle\rangle$ as $t \to \infty$:

$$\langle\langle N^m(t) \rangle\rangle \sim \mathcal{S}_m^{[l(m)]} B_{l(m)}\, l(m) (\sigma_m^*)^{-1} (1 - H_{l(m)})^{1 - l(m)} t^{\sigma_m^*} \quad \text{as } t \to \infty, \tag{51}$$

where the exponents σ_m are given by

$$\sigma_m = m(1 - H_m) + H_m, \tag{52}$$

σ_m^* is the maximum exponent from the set $\sigma_1, \ldots, \sigma_m$:

$$\sigma_m^* = \max(\sigma_1, \ldots, \sigma_m), \tag{53}$$

and $l(m)$ is the label corresponding to σ_m^*:

$$\sigma_m^* = \sigma_{l(m)}, \tag{54}$$

As $1 > H_m \geqslant 0$ (see eq. (44)) we have

$$m \geqslant \sigma_m > 1, \quad m \geqslant 2; \quad \sigma_1 = 1. \tag{55}$$

Note that in this case in the limit $t \to \infty$ the dispersion indices $I_m(t)$ are time-dependent

$$I_m(t) = 1 + \mathscr{E}_m t^{\sigma_m^* - 1}, \quad m = 2, \ldots \tag{56}$$

where

$$\mathscr{E}_m = \mathbb{S}_m^{[l(m)]} B_{l(m)} l(m) / [\sigma_m^* (1 - H_{l(m)})^{l(m)-1} B_1], \quad m = 2, \ldots \tag{57}$$

As $\sigma_m > 1$ it follows that the dispersion indices $I_m(t)$ diverge slowly to infinity as $t \to \infty$. Despite this divergent behavior of $I_m(t)$ as $t \to \infty$ the fluctuations of the number of the counting events N are non-intermittent. Indeed the relative fluctuations $f_m(t)$ of the number of events decrease to zero as $t \to \infty$ provided that the fractal exponents H_m are positive:

$$f_m(t) \sim [\mathscr{E}_m / (B_1)^{m-1}] t^{-H_{l(m)}[l(m)-1]}, \quad H_{l(m)} \neq 0, \tag{58}$$

Thus the long and finite memory does not lead to intermittency; its only effect is that it leads to a decrease of the time exponents in the expressions of the relative fluctuations.

Equation (51) for the asymptotic behavior of the cumulants $\langle\langle N^m(t) \rangle\rangle$ can be rewritten as

$$\langle\langle N(t) \rangle\rangle \sim B_1 t, \quad \langle\langle N^m(t) \rangle\rangle = B_1 \mathscr{E}_m t^{\sigma_m^*}; \quad m \geqslant 2, \quad t \to \infty. \tag{59}$$

Note that the first cumulant increases linearly in time, which is a typical clock property. As $\sigma_m > 1$, $m \geqslant 2$, the cumulants of second and higher order increase faster than linearly in time. However, since the fluctuations are non-intermittent this nonlinearity does not affect the clock properties of the averaged stochastic process.

A special situation occurs when the fractal exponents H_m attached to the cumulants of different orders are equal to zero

$$H_m = 0. \tag{60}$$

In this case the stochastic process describing the time evolution of the fluctuating counting rate $\lambda(t')$ has infinite memory and the fluctuations of the number of events are intermittent. Indeed, as $t \to \infty$, the relative fluctuations $f_m(t)$ tend towards constant values different from zero

$$f_m(t) \sim \mathscr{E}_m (B_1)^{-m+1} \neq 0 \quad \text{as } t \to \infty, \mathscr{E}_m \neq 0, B_1 \text{ is finite}. \tag{61}$$

Due to the intermittency of the fluctuations of the number N of counting events the averaged stochastic process corresponding to the probability $\bar{P}(N; t)$ is not a clock anymore.

5. Dynamical analogue of the Porter-Thomas distribution

For clarifying under what circumstances the fluctuations of the counting rate $\lambda(t')$ can be described by a given type of stochastic dependence in this section we develop an alternative model, different from the shot-noise model used in Sections 3 and 4. We assume that the counting rate $\lambda(t')$ is made up of the sum of n squares of n amplitude factors $A_1, \ldots, A_n$:

$$\lambda(t') = \sum_{u=1}^{n} A_u^2(t'), \tag{62}$$

where each amplitude $A_u(t')$ is a real random variable with average value zero

$$\langle A_u(t') \rangle = 0, \quad u = 1, \ldots, n. \tag{63}$$

obeying stationary Gaussian statistics. Each amplitude is characterized by the same correlation function

$$g(t, t') = g(|t - t'|) = \langle\langle A_u(t) A_u(t') \rangle\rangle. \tag{64}$$

Due to the stationarity of the Gaussian process considered the correlation function $g(t, t')$ depends only on the absolute value of the time difference $t - t'$ and is independent of the individual times t and t'. Such a model has a justification in quantum mechanics where for a reactive system with n reaction channels the total rate of transformation is the sum of the squares of the individual amplitudes attached to the different channels rather than the sum of the amplitudes themselves. Such an approach was initially suggested in nuclear physics (Porter and Thomas [41], Mehta [42], Brody *et al.* [43]) where usually the possible time dependence of the correlation function $g(t, t')$ is ignored. The method has been recently extended to molecular dynamics (Levine [44]).

From the above considerations it follows that the amplitudes $A_u(t)$ are independent random functions selected from the same Gaussian probability density functional

$$p[A(t')]D[A(t')] = \exp\left\{-\frac{1}{2}\iint \mathscr{M}(t, t') A(t) A(t') \, dt \, dt'\right\} D[A(t')]. \tag{65}$$

with the normalization condition

$$\overline{\iint} p[A(t')]D[A(t')] = 1, \tag{66}$$

where $\mathscr{M}(t, t')$ is a continuous commutative matrix which is the inverse of the correlation matrix $g(t, t')$:

$$\int \mathscr{M}(t, t'') g(t'', t') \, dt'' = \int g(t, t'') \mathscr{M}(t'', t') \, dt'' = \delta(t - t'), \tag{67}$$

$D[A(t')]$ is the usual Gaussian integration measure (Kleinert [45], Zinn-Justin [46]) and the symbol $\overline{\iint}$ stands for the path integration over the space of functions $A(t')$.

The characteristic functional $\Xi[K(t'); t]$ can be expressed as a multiple Gaussian path integral over the different realizations $A_1(t'), \ldots, A_n(t')$ of the amplitudes corresponding to the different terms in the sum (62)

$$\Xi_n[K(t'); t] = \overline{\iint} \cdots \overline{\iint} \prod_{u=1}^{n} \{p[A_u(t')]D[A_u(t')]\} \times \exp\left(i \sum_{u=1}^{n} \int K(t') A_u^2(t') \, dt'\right) = [\Xi_1[K(t'); t]]^n, \tag{68}$$

where

$$\Xi_1[K(t'); t] = \overline{\iint} p[A(t')]D[A(t')] \exp\left(i \int K(t') A^2(t')\right), \tag{69}$$

is the characteristic functional corresponding to a single degree of freedom ($n = 1$). In Appendix I we show how the path integrals in eqs (68)–(69) can be computed analytically by making use of the trace technique from quantum field theory (Zinn-Justin [46]). The final expression for the characteristic functional of the random counting rate $\Xi_n[K(t'); t]$ is:

$$\Xi_n[K(t'); t] = \exp\left\{\frac{1}{2} n \sum_{m=1}^{\infty} \frac{(2i)^m}{m} \int \dots \int g(t'_1, t'_2) \times g(t'_2, t'_3) \dots g(t'_{m-1}, t'_m) \times g(t'_m, t'_1) K(t'_1) \dots K(t'_m)\, dt'_1 \dots dt'_m\right\}. \quad (70)$$

Equation (70) has a structure similar with the cumulant expansion (7) with the difference that the integrands in the different terms are not symmetrical with respect to the permutations of the integration variables. By expressing the integrands in eq. (70) in a symmetrical way and comparing the result with eq. (7) we get the following expressions for the cumulants of the counting rate:

$$\langle\langle \lambda(t_1) \dots \lambda(t_m) \rangle\rangle = nm^{-1}2^{m-1} \sum'_{j_1, \dots, j_m} g(t_{j_1}, t_{j_2}) \times g(t_{j_2}, t_{j_3}) \dots g(t_{j_{m-1}}, t_{j_m}) g(t_{j_m}, t_{j_1}), \quad (71)$$

where the prime sign shows that the summation labels $j_1, \dots, j_m$ should be distinct.

The cumulants $\langle\langle N^m(t) \rangle\rangle$ of the number of counting events can be easily evaluated from eqs (11) and (71). To save space the detailed computations are left to the reader and we present only the results. The cumulants $\langle\langle N^m(t) \rangle\rangle$ are made up of the additive contributions of many terms of the form (11) where $\langle\langle \lambda(t_1) \dots \lambda(t_m) \rangle\rangle$ is replaced by a multiple product $g(t_{j_1}, t_{j_2}) \dots g(t_{j_v}, t_{j_1})$:

$$\langle\langle N^m(t) \rangle\rangle = \sum_{v=1}^{m} \mathcal{S}_m^{(v)} \int_0^t \dots \int_0^t nv^{-1}2^{v-1} \sum'_{j_1, \dots, j_v} g(t_{j_1}, t_{j_2}) \times g(t_{j_2}, t_{j_3}) \dots g(t_{j_{v-1}}, t_{j_v}) g(t_{j_v}, t_{j_1})\, dt_1 \dots dt_v. \quad (72)$$

From eq. (72) it follows that the asymptotic behavior of $\langle\langle N^m(t) \rangle\rangle$ as $t \to \infty$ is essentially the same as in the case of the shot-noise model used for illustration in Sections 3 and 4. For short memory

$$g(\Delta t) \sim g(0) \exp(-v |\Delta t|), \quad (73)$$

all cumulants of the number of counting events N increase linearly asymptotically in time as $t \to \infty$

$$\langle\langle N^m(t) \rangle\rangle \sim \text{const. } t \quad \text{as } t \to \infty, \quad (74)$$

whereas in the case of a stochastic process with long memory characterized by a fractal exponent H

$$g(\Delta t) \sim \text{const. } (|\Delta t|)^{-H}, \quad (75)$$

we have a scaling law similar to eq. (51)

$$\langle\langle N^m(t) \rangle\rangle \sim \text{const. } t^{\sigma'_m}, \quad \text{as } t \to \infty. \quad (76)$$

The most interesting situation corresponds to the case when the fractal exponent H is equal to zero and the correlation function is constant

$$g(t, t') = g \text{ independent of } t, t'. \quad (77)$$

In this case the memory is infinite, all cumulants of the fluctuating counting rate $\lambda(t')$ are time-independent and given by

$$\langle\langle \lambda(t_1) \dots \lambda(t_m) \rangle\rangle = n(m-1)!\,2^{m-1} g^m, \quad (78)$$

and the cumulants $\langle\langle N^m(t) \rangle\rangle$ of the number N of counting events are polynomial functions of time

$$\langle\langle N^m(t) \rangle\rangle = \sum_{v=1}^{m} \mathcal{S}_m^{(v)} (v-1)!\, ng^v 2^{v-1} t^v \sim \mathcal{S}_m^{(m)} (m-1)!\, ng^m 2^{m-1} t^m \quad \text{as } t \to \infty \quad (86)$$

Just like in the case of the shot-noise model with the fractal exponents H_m equal to zero, $H_m = 0$, in this case the relative fluctuations $f_m(t)$ tend towards values different from zero in the limit $t \to \infty$:

$$f_m(t) \sim 2^{m-1} n^{-(m-1)} \mathcal{S}_m^{(m)} (m-1)! \neq 0 \quad \text{as } t \to \infty, \quad (79)$$

that is, the fluctuations are intermittent and the averaged stochastic process cannot be used as a clock anymore.

For the model considered in this section the infinite memory corresponds to a system with static disorder which is essentially the same as the Porter-Thomas model used in nuclear physics (Porter and Thomas [41], Mehta [42], Brody *et al.* [43]) and in molecular physics (Levine [44]). In this case the sum in the expression (70) for the characteristic functional $\Xi_n[K(t'); t]$ can be computed exactly, resulting in

$$\Xi[K(t'); t] = \left[1 - 2ig \int K(t')\, dt'\right]^{-n/2}. \quad (80)$$

From the definition (6) of the characteristic functional $\Xi[K(t'); t]$ it follows that for

$$K(t') = k\delta(t - t'),$$

$\Xi[K(t'); t]$ reduces to the Fourier transform of the one-time probability density $P(\lambda; t)\, d\lambda$ of the counting rate. We have

$$\Xi[K(t') = k\delta(t - t')] = (1 - 2igk)^{-n/2} = \int \exp(ik\lambda) P(\lambda; t)\, d\lambda, \quad (81)$$

from which, by means of an inverse Fourier transformation, we get

$$P(\lambda; t) = (2\pi)^{-1} \int (1 - 2igk)^{-n/2} \exp(-ik\lambda)\, dk = [\Gamma(n/2)]^{-1} [n/(2\langle\lambda\rangle)]^{n/2} \lambda^{(1/2)n-1} \times \exp[-n\lambda/(2\langle\lambda\rangle)], \quad (82)$$

where $\Gamma(x) = \int_0^\infty t^{x-1} \exp(-t)\, dt$, $x > 0$, is the complete gamma function and

$$\langle\lambda\rangle = \int \lambda P(\lambda; t)\, d\lambda = ng, \quad (83)$$

is the average value of the fluctuating counting rate.

We note that the state probability $P(\lambda; t)$ is given by a chi square distribution which has the same form as the Porter-Thomas law in nuclear physics. For the systems described by eqs (80) and (82) the fluctuations of the counting rate are completely frozen; a fluctuation, once it occurs, it is never destroyed and lasts forever and the dynamical average in eq. (5) is replaced by a static average. The characteristic function $G(b)$ can be computed from eqs (9) and (80), resulting in

$$G(b) = \{n/[n + 2\langle\lambda\rangle t(1 - \exp(ib))]\}^{n/2}, \quad (84)$$

from which, by applying eq. (13) we get a probability distribution $\bar{P}(N; t)$ of the number of count events of the negative binomial type

$$\bar{P}(N; t) = \frac{\Gamma(N + \frac{1}{2}n)}{N!\,\Gamma(\frac{1}{2}n)} \left(\frac{2\langle\lambda\rangle t}{n + 2\langle\lambda\rangle t}\right)^N \left(\frac{n}{n + 2\langle\lambda\rangle t}\right)^{(1/2)n}. \quad (85)$$

It is easy to check that the same negative binomial distribution can be obtained by direct averaging of the Poissonian (4), applied for $\lambda =$ independent of time, over all possible values of the average counting rate λ selected from the Porter-Thomas ditribution (82):

$$\bar{P}(N; t) = \int_0^\infty \frac{(\lambda t)^N}{N!} \exp(-\lambda t) \frac{1}{\Gamma(\frac{1}{2}n)} \times \left(\frac{n}{2\langle\lambda\rangle}\right)^{n/2} \lambda^{(1/2)n - 1} \exp\left(-\frac{n\lambda}{2\langle\lambda\rangle}\right) d\lambda. \quad (86)$$

By computing the integral over λ, eq. (86) leads to eq. (85).

6. Overdispersed molecular clocks

From the point of view of molecular biology our results concerning the fluctuating Poissonian clocks are generalizations of the results of Gillespie [10, 11] and Takahata [13–15] concerning the so-called episodic molecular clock. As mentioned in the introduction, Gillespie has claimed that the consistency with the experimental data on amino acid substitutions with a Poissonian distribution with a fluctuating rate $\lambda(t')$ contradicts Kimura's theory of neutral molecular evolution because it leads to overdispersion, corresponding to a non-Poissonian averaged random process. By studying the overdispersed molecular clocks with short memory Takahata [13–15] has outlined that however the overdisposition does not contradict the neutral theory because the dispersion indices have finite values for large times and thus this type of overdispersion does not lead to intermittency.

As far as we know the study of long memory effects has been completely ignored in the biological literature. Our analysis of long but finite memory confirms Takahata's idea concerning the consistency between Kimura's neutral theory and overdispersion. Although for long and finite memory the dispersion indices of different orders diverge to infinity for large times, this divergence is not strong enough to generate the intermittency of the fluctuations of the number of substitutions. For infinite memory however an intermittent behavior eventually emerges for large times, the fluctuations of the number of amino acid substitution events are very large and intermittent and as a result the substitution process cannot be used as a clock anymore. At the present stage of research it is not clear whether such infinite memory can actually exist in biological systems; for answering this question further analysis of the genetic data is necessary. Anyway an infinite memory seems to be inconsistent with the present form of Kimura's theory for which the fluctuations are of the sampling nature and non-intermittent.

7. Application to enhanced diffusion in disordered systems

In this section we apply the theory of fluctuating Poissonian clocks developed in this article to the study of enhanced diffusion in disordered systems with dynamical temporal disorder.

We assume a hopping mechanism for the diffusion process. For each step, due to the temporal dynamical disorder, the frequency $\lambda(t')$ of occurrence of a jump is a stationary random function of time which plays the same role as the counting rate in the theory of fluctuating clocks. The number N of jumps occurring in a time interval of length t is a random variable characterized by the averaged probability $\bar{P}(N; t)$ or by its characteristic function $G(b; t)$. For each step of the moving particle the length of the jump is characterized by a displacement vector $\Delta\boldsymbol{r}$ randomly selected from a given probability density

$$p(\Delta\boldsymbol{r})\, d\Delta\boldsymbol{r} \quad \text{with} \quad \int p(\Delta\boldsymbol{r})\, d\Delta\boldsymbol{r} = 1. \quad (87)$$

We assume that the movement is biased in a given direction and that the cumulants of first and second order of the components of the displacement vector $\Delta\boldsymbol{r}$ are finite and different from zero

$$\langle\langle \Delta r_{u_1} \rangle\rangle = \int \Delta r_{u_1} p(\Delta\boldsymbol{r})\, d\Delta\boldsymbol{r} = \text{finite} \neq 0, \quad (88)$$

$$\langle\langle \Delta r_{u_1}\, \Delta r_{u_2} \rangle\rangle = \int (\Delta r_{u_1} - \langle\langle \Delta r_{u_1} \rangle\rangle(\langle\langle \Delta r_{u_2} \rangle\rangle\langle\langle \Delta r_{u_2} \rangle\rangle)) \times p(\Delta\boldsymbol{r})\, d\Delta\boldsymbol{r} = \text{finite} \neq 0. \quad (89)$$

After N steps the particle has a position equal to the sum of the different displacement vectors attached to the steps 1, 2, ..., N, respectively

$$\boldsymbol{r} = \Delta\boldsymbol{r}_1 + \cdots + \Delta\boldsymbol{r}_N, \quad (90)$$

where we have assumed, without loss of generality, that the particle was initially placed at $\boldsymbol{r} = 0$. In Appendix II we show how the cumulants of the total displacement vector $\boldsymbol{r}$ can be computed as functions of time. In particular the cumulants of order one and two are given by the following expressions:

$$\langle\langle r_u \rangle\rangle(t) = \langle\langle N(t) \rangle\rangle \langle\langle \Delta r_u \rangle\rangle, \quad (91)$$

$$\langle\langle r_{u_1} r_{u_2} \rangle\rangle(t) = \langle\langle N(t) \rangle\rangle \langle\langle \Delta r_{u_1}\, \Delta r_{u_2} \rangle\rangle + \langle\langle \Delta r_{u_1} \rangle\rangle \langle\langle \Delta r_{u_2} \rangle\rangle \langle\langle N^2(t) \rangle\rangle. \quad (92)$$

Since for short memory all cumulants $\langle\langle N^m(t) \rangle\rangle$ of the number of jumps are proportional to the time t as $t \to \infty$ (eq. (36)) it follows that in this case the correlation matrix $[\langle\langle r_{u_1} r_{u_2} \rangle\rangle(t)]$ of the position vector at time t is proportional to the length t of the time interval considered

$$\langle\langle r_{u_1} r_{u_2} \rangle\rangle(t) \sim 2D_{u_1u_2} t \quad \text{as } t \to \infty, \quad (93)$$

where the diffusion tensor $D_{u_1u_2}$ is given by

$$D_{u_1u_2} = \tfrac{1}{2} A_1(\langle\langle \Delta r_{u_1} \Delta r_{u_2} \rangle\rangle + \langle\langle \Delta r_{u_1} \rangle\rangle \langle\langle \Delta r_{u_2} \rangle\rangle + A_2 \langle\langle \Delta r_{u_1} \rangle\rangle \langle\langle \Delta r_{u_2} \rangle\rangle. \quad (94)$$

It follows that for short memory, after a transient regime, for large time a classical (Fick-type) diffusion process eventually emerges for which the components $\langle\langle r_{u_1} r_{u_2} \rangle\rangle(t)$ of the correlation matrix obey the Einstein's relation (93).

For long memory, however, the large time behavior of the components of the correlation matrix of the position vector is different. In this case we get:

$$\langle\langle r_{u_1} r_{u_2} \rangle\rangle(t) \sim 2\mathscr{D}_{u_1 u_2} t^{\sigma_2^*} \quad \text{for } \langle\langle \Delta r_u \rangle\rangle \neq 0,\ t \to \infty, \tag{95}$$

$$\langle\langle r_{u_1} r_{u_2} \rangle\rangle(t) \sim 2D_{u_1 u_2} t \quad \text{for } \langle\langle \Delta r_u \rangle\rangle = 0,\ t \to \infty, \tag{96}$$

where

$$\mathscr{D}_{u_1 u_2} = \tfrac{1}{2}\langle\langle \Delta r_{u_1} \rangle\rangle \langle\langle \Delta r_{u_2} \rangle\rangle B_1 \mathscr{E}_2, \tag{97}$$

$$D_{u_1 u_2} = \tfrac{1}{2} B_1 \langle\langle \Delta r_{u_1} \Delta r_{u_2} \rangle\rangle, \tag{98}$$

are anomalous and normal diffusion tensors, respectively.

We notice that if the motion of the particle has an asymmetric (biased) component $\langle\langle \Delta r_u \rangle\rangle \neq 0$ then the diffusion is enhanced because the exponent σ_2^* is generally larger than unity (see eqs (53–(55)). The most efficient diffusion corresponds to an infinite memory ($H_2 = 0$) for which the anomalous diffusion exponent σ_2^* has the maximum value 2. If the motion of the particle is unbiased, then the memory effects, if any, do not show up in the expression of the correlation matrix of the position vector and the diffusion is normal, i.e. Fickian, and obeys an equation of the Einstein's type corresponding to $\sigma_2^* = 1$.

Our model for enhanced diffusion can be easily extended to the case of a super-efficient diffusive behavior described by an equation of the type (95) where the anomalous diffusion exponent σ_2^* is larger than 2. The main idea is to consider that the random additive quantity which is the sum of the contributions of the different steps is the velocity of the particle rather than the position vector:

$$\boldsymbol{v} = \Delta \boldsymbol{v}_1 + \cdots + \Delta \boldsymbol{v}_N. \tag{99}$$

Here $\boldsymbol{v}$ is the velocity of the particle after n steps and $\Delta \boldsymbol{v}_1, \ldots, \Delta \boldsymbol{v}_N$ are speed increments or decrements corresponding to the different steps. The detailed analysis of this model, which is of interest both for physics and population biology, will be presented elsewhere. Here we give only the main results of the computations. By expressing the position vector $\boldsymbol{r}(t)$ as

$$\boldsymbol{r}(t) = \int_0^t \boldsymbol{v}(t')\, \mathrm{d}t', \tag{100}$$

neglecting the transient inertial effects, and making use of the expressions of the cumulants $\langle\langle N^m(t) \rangle\rangle$ of the number of steps derived in Sections 3 and 4, we get the following expressions for the correlation matrix of the position vector:

$$\langle\langle r_{u_1} r_{u_2} \rangle\rangle(t) \sim \text{const. } t^3 \quad \text{as } t \to \infty, \tag{101}$$

for short memory and

$$\langle\langle r_{u_1} r_{u_2} \rangle\rangle(t) \sim \text{const. } t^{\varepsilon} \qquad \text{for } \langle\langle \Delta v_u \rangle\rangle \neq 0 \text{ as } t \to \infty, \tag{102}$$

$$\langle\langle r_{u_1} r_{u_2} \rangle\rangle(t) \sim \text{const. } t^3 \qquad \text{for } \langle\langle \Delta v_u \rangle\rangle = 0 \text{ as } t \to \infty, \tag{103}$$

for long memory, where the exponent ε is between three and four:

$$4 \geqslant \varepsilon > 3. \tag{104}$$

For short memory and for long memory with no preferred direction of the random velocity field ($\langle\langle \Delta \boldsymbol{v} \rangle\rangle = 0$) we get the t^3 Richardson law which is of interest both in physics (relative turbulent diffusion, Richardson [47]; Batchelor [48]; Masoliver [49, 50]; Masoliver and Porrà [51]; Porrà, Masoliver and Lindenberg [52]; Seki, Kitahara and Nicolis [53]) and in population biology (anticrowding diffusion, Okubo [54]). For long memory with an average velocity increment $\langle\langle \Delta \boldsymbol{v} \rangle\rangle = 0$ the process is more efficient than the Richardson diffusion, and the anomalous diffusion exponent is between three and four, the maximum value four corresponding to an infinite memory.

8. Rate processes with dynamical disorder

In this section we apply the generalized Porter-Thomas formalism developed in Section 5 to the study of rate processes with dynamical disorder. We investigate a rate process for which the rate coefficient $\lambda(t')$ is a stationary random function obeying the dynamical analogue of the Porter-Thomas formula. Such an approach is of interest both in connection with the study of compound reactions in nuclear physics (Dittes, Harney and Müller [55]) and with the study of fast chemical reactions in molecular physics (Levine [44]).

The dynamics of the relaxation process is described by the average relaxation (survival) function

$$\phi(t) = \langle l(t) \rangle_{\text{dynamical}}, \tag{105}$$

where the dynamical average $\langle \cdots \rangle_{\text{dynamical}}$ is given by a path integral which takes into account all possible random relaxation rates $\lambda(t')$ and the instantaneous (fluctuating) relaxation function $l(t)$ obeys the differential equation

$$\mathrm{d}l(t)/\mathrm{d}t = -\lambda(t) l(t), \quad l(0) = 1, \tag{106}$$

and therefore

$$l(t) = \exp\left(-\int_0^t \lambda(t')\, \mathrm{d}t'\right), \tag{107}$$

$$\phi(t) = \left\langle \exp\left(-\int_0^t \lambda(t')\, \mathrm{d}t'\right)\right\rangle. \tag{108}$$

From eqs (6) and (108) it is easy to see that the relaxation function $\phi(t)$ can be expressed in terms of the characteristic functional $\Xi[K(t'); t]$:

$$\phi(t) = \Xi[K(t') = \mathrm{i}h(t - t'); t]. \tag{109}$$

By combining eq. (109) with eq. (70) for the characteristic functional $\Xi[K(t'); t]$ of the dynamic analogue of the Porter-Thomas statistics we come to:

$$\phi(t) = \exp\left\{-\frac{1}{2} n \sum_{m=1}^{\infty} \frac{(-1)^{m-1}}{m} \times \int_0^t \cdots \int_0^t g(t_1', t_2') \ldots g(t_{m-1}', t_m') g(t_m', t_1') \times \mathrm{d}t_1' \ldots \mathrm{d}t_m'\right\}. \tag{110}$$

Further development of the theory requires knowledge of the concrete form of the correlation function $g(t, t')$ of the amplitude factors $A_u(t')$. We start out with the case of static disorder for which

$$g(t, t') = g = \text{constant}. \tag{111}$$

In this case the evaluation of the integrals and of the sum in eq. (110) is straightforward. After some calculations we get a relaxation function $\phi(t)$ with a long tail of the statistical fractal type

$$\phi(t) = (1 + 2n^{-1}\langle \lambda \rangle t)^{-(1/2)n} \sim t^{-n/2} \quad \text{as } t \to \infty, \tag{112}$$

where the average decay rate $\langle\lambda\rangle$ is given by eq. (83). Equation (112) has already been derived in the literature by taking the average of the instantaneous survival function $l(t)$ given by eq. (110) applied for $\lambda(t) = \text{constant}$, where the average is computed in terms of the static Porter-Thomas distribution (82) [55]:

$$\phi(t) = \int_0^\infty \exp(-\lambda t) \frac{1}{\Gamma(\frac{1}{2}n)} \left(\frac{n}{2\langle\lambda\rangle}\right)^{(1/2)n} \times \lambda^{(n/2)-1} \exp\left(-\frac{n\lambda}{2\langle\lambda\rangle}\right) d\lambda = (1 + 2n^{-1}\langle\lambda\rangle t)^{-(1/2)n}. \quad (113)$$

The problem of dynamical disorder cannot be solved in the general case. In this paper we limit ourselves to the particular case of a very slow exponential decay of the correlation function of the amplitude factor $A_u(t')$

$$g(t, t') = g \exp(-\omega|t - t'|), \quad g = \text{constant}, \quad (114)$$

where the frequency ω of decay of the amplitude fluctuations is close to zero

$$\omega \sim 0. \quad (115)$$

In this case the exponential in eq. (110) can be approximately evaluated by symmetrizing the terms of the sum with respect to $t'_1, \ldots, t'_m$ and evaluating the integrals over $t'_1, \ldots, t'_m$ and the resulting series. After lengthy but standard manipulations we obtain

$$\phi(t) \sim \exp\left\{-\frac{n}{2}\left[\left(1 + 2\omega t + \frac{n\omega}{\langle\lambda\rangle}\right) \times \mathscr{J}(t) + \exp(-2\omega t) - 1\right]\right\} \quad \text{as } \omega \sim 0, \quad (116)$$

where the function $\mathscr{J}(t)$ is given by

$$\mathscr{J}(t) = 2n^{-1}\langle\lambda\rangle \int_0^t (1 + 2n^{-1}\langle\lambda\rangle\tau)^{-1} \exp(-2\omega\tau)\, d\tau = \exp(n\omega/\langle\lambda\rangle)[E_1(n\omega\langle\lambda\rangle^{-1}) - E_1(n\omega\langle\lambda\rangle^{-1} + 2\omega t)], \quad (117)$$

and

$$E_1(z) = \int_z^\infty t^{-1} \exp(-t)\, dt \quad (118)$$

is the exponential integral.

For small to moderate times the relaxation function $\phi(t)$ is practically identical with the statistical fractal law (112) characteristic for static disorder

$$\phi(t) \sim (1 + 2n^{-1}\langle\lambda\rangle t)^{-(1/2)n} \quad \text{as } t \ll 1/\omega, \quad (119)$$

whereas for very large times the relaxation function is practically exponential

$$\phi(t) \sim f \exp(-\lambda_{\text{eff}}\, t) \quad t \gg 1/\omega, \quad (120)$$

where the preexponential factor is given by

$$f = \exp\left\{-\frac{n}{2}\left[\left(\frac{n\omega}{\langle\lambda\rangle} + 1\right) \exp\left(\frac{n\omega}{\langle\lambda\rangle}\right) E_1\left(\frac{n\omega}{\langle\lambda\rangle}\right) - 1\right]\right\}, \quad (121)$$

and the effective relaxation rate λ_{eff} is determined by the frequency ω of the attenuation of amplitude fluctuations

$$\lambda_{\text{eff}} = n\omega \exp\left(\frac{n\omega}{\langle\lambda\rangle}\right) E_1\left(\frac{n\omega}{\langle\lambda\rangle}\right). \quad (122)$$

The physical interpretation of these results is simple. The amplitude fluctuations correspond to the intranuclear redistribution of the energy among the intrinsic degrees of freedom in nuclear physics and to the intramolecular redistribution of energy in molecular physics. For static disorder $t \ll 1/\omega$, the regression of fluctuations is practically inexistent and the relaxation process is determined by the average rate $\langle\lambda\rangle = ng$ and described by the statistical fractal relaxation law (119). For very large times, $t \gg 1/\omega$, however, the regression of energy fluctuations is the rate-determining process and is taking over the dynamics of the relaxation, resulting in the exponential decay (120) of the survival function. The passage from an initial negative power law decay to an exponential tail corresponds to a non-ideal statistical fractal behavior characteristic for many systems with dynamical disorder. Such a crossover from a negative power law to an exponential decay has been also identified for the passage over a random energy barrier with dynamical disorder (Vlad and Mackey [21]) and for the statistical description of the onset of an epidemic (Vlad, Mackey and Schönfisch [56]).

9. Conclusions

In this paper the clock properties of the doubly stochastic Poisson processes with fluctuating counting rates have been studied by using a characteristic functional approach borrowed from the statistical physics of disordered systems. The results of this physical approach have been compared with the other less general treatments presented in the mathematical, physical and biological literature. Special attention has been paid to the implications of long memory on the clock properties, an aspect of the problem completely ignored in the literature. It has been shown that the clock properties are related to the non-intermittency of the fluctuations of the number of counting events. Our investigation has led to the conclusion that for long, but however finite, memory, even though the dispersion indices diverge to infinity as $t \to \infty$, this divergence is not strong enough for generating the intermittency of fluctuations and thus under these circumstances the double stochastic Poisson process is a clock. The clock property is violated only for infinite memory, in which case the fluctuations of the number of counting events are intermittent.

The general approach developed in the article has been applied to the study of three different biological and physical problems. The first application is related to the study of overdispersed molecular clocks in evolutionary biology and its connections with Kimura's neutral theory of molecular evolution. We have extended Takahata's [13–15] analysis of the Gillespie's episodic clock. We have shown that the episodic clocks with long but finite memory are compatible with the neutral theory. For infinite memory, however, the process of amino acid substitution through evolution is not a clock anymore and moreover it seems that this possibility is incompatible with the neutral theory of molecular evolution.

The second application is the study of a hopping mechanism for the process of enhanced diffusion in disordered systems. We have shown that the long memory of the fluctuations of the jump frequency leads to enhanced diffusion provided that there is a peferred direction of the motion. For a hopping mechanism of the displacement vector the theory predicts an anomalous scaling exponent between one and two where the maximum value two corresponds to an infinite memory and the minimum value one to an exponentially decaying short memory. For a hopping mechanism in the velocity space the diffusion exponent is between three and four where the maximum value four corresponds to an infinite memory and the minimum value three (the Richardson exponent) corresponds to an exponentially decaying short memory. These results are consistent with a complementary model for enhanced diffusion recently studied in the literature [26, 27]. Despite the apparent similarity of the predictions of the two models the corresponding physical mechanisms assumed by the two approaches are however different. In refs, [26, 27] the statistics of the jump events is not given by a doubly stochastic Poisson process with a fluctuating jump rate but by a non-Markovian renewal process.

The third application is the generalization of the Porter-Thomas relaxation for systems with dynamical disorder. A dynamical analogue of the Porter-Thomas distribution has been suggested by assuming that the correlation function of the amplitude factors is time-dependent. The characteristic functional as well as all cumulants of the process have been computed exactly by using the trace technique from quantum field theory for evaluating path integrals. The relaxation function of the dynamical process has been approximately evaluated for a slow exponential decay of the correlation function of the amplitude factors. The relaxation function derived for this particular case corresponds to a non-ideal statistical fractal behavior: for short to moderate times it displays self-similarity followed by a fast decreasing exponential tail for large times.

Further research concerning the approach introduced in this paper should focus in many different directions. A more detailed study of the stochastic process itself should be carried out. Such a study should include the evaluation of the grand canonical Janossy and product densities, of the multievent correlation functions and of the corresponding characteristic functionals. The knowledge of these functions is essential for any further applications, especially for a more detailed investigation of enhanced diffusion. Concerning the problem of overdispersed molecular clocks in molecular biology it is necessary to investigate whether an infinite memory for the process of amino acid substitution can actually exist and under what circumstances. Finally concerning the dynamical analogue of the Porter-Thomas relaxation further studies should consider the connection between the non-ideal statistical fractal behavior of the relaxation function and the dynamics of the process as well as the evaluation of the relaxation function for moderate or large regression frequencies.

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Appendix I

For computing the path integrals in eqs (68)–(69) we pass to a discrete description

$$A(t) \to A_j; \quad g(t, t') \to g_{jj'}, \quad \mathscr{M}(t, t') \to \mathscr{M}_{jj'},$$
$$K(t')\,dt' \to K_{j'}, \tag{I.1}$$

where we take $\mathscr{N}$ different points. In this discrete description the path integral (69) becomes a discrete $\mathscr{N}$-dimensional Gaussian integral

$$\Xi_1[K(t'); t]_{\text{discrete}} = \int_{-\infty}^{\infty} \cdots \int_{-\infty}^{\infty} (2\pi)^{-\mathscr{N}/2} (\det \mathbf{g})^{-1/2}$$
$$\times \exp\{-\tfrac{1}{2}\mathbf{A}^{+}\mathbf{g}^{-1}\mathbf{A} + i\mathbf{A}^{+}\mathbf{K}\mathbf{A}\}\,d\mathbf{A}, \tag{I.2}$$

where

$$\mathbf{A} = [A_j], \quad \mathbf{K} = [\delta_{jj'}\,K_{j'}]. \tag{I.3}$$

The $\mathscr{N}$-dimensional Gaussian integral (A.2) can be easily evaluated resulting in

$$\Xi_1[K(t'); t]_{\text{discrete}}$$
$$= (2\pi)^{-\mathscr{N}/2}(\det \mathbf{g})^{1/2}(2\pi)^{\mathscr{N}/2}[\det(\mathbf{g}^{-1} - 2i\mathbf{K})]^{-1/2}$$
$$= [\det(\mathbf{I} - 2i\mathbf{g}\mathbf{K})]^{-1/2}. \tag{I.4}$$

Now we use the standard identity

$$\ln \det \mathbf{M} = \operatorname{Tr}(\ln \mathbf{M}), \tag{I.5}$$

from quantum field theory (Zinn-Justin [46]). We consider that

$$\mathbf{M} = \mathbf{I} - 2i\mathbf{g}\mathbf{K}, \tag{I.6}$$

expand the logarithm of the matrix in a Taylor series and take the trace of the result. After some elementary algebraic manipulations we get

$$\Xi_n[K(t'); t]_{\text{discrete}}$$
$$= [\Xi[K(t'); t]_{\text{discrete}}]^n$$
$$= \exp\{-\tfrac{1}{2}n \operatorname{Tr}[\ln(\mathbf{I} - 2i\mathbf{g}\mathbf{K})]\}$$
$$= \exp\left\{\tfrac{1}{2}n \sum_{m=1}^{\infty} \frac{(2i)^m}{m} \sum_{j_1,\ldots,j_m} g_{j_1 j_2}\right.$$
$$\left.\times\, g_{j_2 j_3} \cdots g_{j_{m-1} j_m} g_{j_m j_1} K_{j_1} \cdots K_{j_m}\right\}. \tag{I.7}$$

By passing to the continuous limit in eq. (A.7) we come to eq. (70) for the characteristic functional $\Xi_n[K(t'); t]$ of the random counting rate $\lambda(t')$.

Appendix II

The finiteness of the cumulants of first and second order of the displacement vector $\Delta\mathbf{r}$ can be expressed as:

$$\langle\langle \Delta r_{u_1} \rangle\rangle = (-i)\partial \ln \bar{p}(\mathbf{k} = 0)/\partial k_{u_1}$$
$$= \text{finite} \neq 0, \quad u_1 = 1, \ldots, d_s, \tag{II.1}$$

$$\langle\langle \Delta r_{u_1} \Delta r_{u_2} \rangle\rangle = (-i)^2 \partial^2 \ln \bar{p}(\mathbf{k} = 0)/\partial k_{u_1} \partial k_{u_2}$$
$$= \text{finite} \neq 0, \quad u_1, u_2 = 1, \ldots, d_s \qquad \text{(II.2)}$$

where

$$\bar{p}(\mathbf{k}) = \int \exp(i\mathbf{k} \cdot \Delta \mathbf{r}) p(\Delta \mathbf{r}) \, d\Delta \mathbf{r}, \qquad \text{(II.3)}$$

is the characteristic function of the probablity density $p(\Delta\mathbf{r})$ written as a Fourier transform, $\mathbf{k}$ is the wave vector conjugate to the displacement vector $\Delta\mathbf{r}$, and d_s is the space dimension. In the literature of condensed matter physics the characteristic function $\bar{p}(\mathbf{k})$ also bears the name of structure function (Haus and Kehr [7]).

By taking into account eq. (90) it follows that the probability density of the position $\mathbf{r}$ of the particle after N steps is the N-fold convolution of the jump probability density $p(\Delta\mathbf{r})$:

$$[p(\mathbf{r}) \otimes]^{(N)} \qquad \text{(II.4)}$$

where the symbol $\otimes$ denotes the space convolution product. The probability density

$$P(\mathbf{r}; t) \, d\mathbf{r}, \quad \text{with} \int P(\mathbf{r}; t) \, d\mathbf{r} = 1, \qquad \text{(II.5)}$$

of the position vector at time t can be expressed as an average of eq. (II.4) over all possible values of the number N of steps:

$$P(\mathbf{r}; t) = \sum_{N=0}^{\infty} \bar{P}(N; t)[p(\mathbf{r}) \otimes]^{(N)}, \qquad \text{(II.6)}$$

from which, by introducing the characteristic function

$$\bar{P}(\mathbf{k}; t) = \int \exp(i\mathbf{k} \cdot \mathbf{r}) P(\mathbf{r}; t) \, d\mathbf{r}, \qquad \text{(II.7)}$$

we obtain

$$\bar{P}(\mathbf{k}; t) = \sum_{N=0}^{\infty} \bar{P}(N; t) \bar{p}^N(\mathbf{k}) = G(b = -i \ln \bar{p}(\mathbf{k}); t). \qquad \text{(II.8)}$$

By expressing in eq. (II.8) the characteristic function $G(b; t)$ in terms of the cumulant expansion (10) we come to

$$\bar{P}(\mathbf{k}; t) = \exp\left\{ \sum_{m=1}^{\infty} \frac{1}{m!} \langle\langle N^m(t) \rangle\rangle [\ln \bar{p}(\mathbf{k})]^m \right\}. \qquad \text{(II.9)}$$

Now we expand the logarithm of the structure function $\bar{p}(\mathbf{k})$ in terms of the cumulants of the components of the displacement vector $\Delta\mathbf{r}$

$$\ln \bar{p}(\mathbf{k}) = \sum_{m=1}^{\infty} \frac{1}{m!} \sum_{u_1} \cdots \sum_{u_m} \langle\langle \Delta r_{u_1} \ldots \Delta r_{u_m} \rangle\rangle k_{u_1} \ldots k_{u_m}, \qquad \text{(II.10)}$$

insert eq. (II.10) into eq. (II.9), expand the terms $[\ln \bar{p}(\mathbf{k})]^m$ in power series in $k_1, \ldots, k_{d_s}$ and order the different powers of $\mathbf{k}$. By comparing the result of these operations with the standard cumulant expansion of the characteristic function $\bar{P}(\mathbf{k}; t)$,

$$\bar{P}(\mathbf{k}; t) = \exp\left\{ \sum_{m=1}^{\infty} \frac{1}{m!} \sum_{u_1} \cdots \sum_{u_m} \langle\langle r_{u_1} \ldots r_{u_m} \rangle\rangle(t) k_{u_1} \ldots k_{u_m} \right\}, \qquad \text{(II.11)}$$

we can compute, at least in principle, all cumulants $\langle\langle r_{u_1} \ldots r_{u_m} \rangle\rangle(t)$, $m = 1, \ldots, m, \ldots$ of the components of the position vector of the moving particle at time t. The computations are tedious, their complexity increasing with the order m of the cumulants. In particular, for $m = 1, 2$, eqs (II.9)–(II.11) lead to eqs (91)–(92).

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