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Richardson diffusion in neurons

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The dynamics of an initial wave packet affected by random noise is considered in the framework of a comb model. The model is relevant to a diffusion problem in neurons where the transport of ions can be accelerated by an external random field due to synapse fluctuations. In the present specific case, it acts as boundary conditions, which lead to a reaction transport equation with multiplicative noise. The temporal behavior of the mean squared displacement is estimated analytically, and it is shown that the spreading of the initial wave packet corresponds to Richardson diffusion.

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Introduction. Recent experimental investigations show that transport of an initial wave packet can be accelerated inside space-time disordered media [1,2]. In particular, hyperdiffusion (as a quantum realization of Richardson diffusion [3]) has been observed, experimentally and numerically, and explained theoretically [4,5]. It is reasonable to believe that this phenomenon has a generic nature and takes place not only in the wave dynamics, and results from spatiotemporal characteristics of random fields. Here, we show that behind Richardson diffusion in the comb models, there is the same mechanism based on a phenomenological statistical approach, discussed in quantum mechanical observation of Richardson diffusion [5]. Dating back to work by Kolmogorov and Obukhov [6,7], it suggests this turbulent acceleration by means of a Gaussian delta correlated noise [8], added to the dynamical system $\ddot{x} + V(t) = 0$. In this case, due to the noise term $V(t)$, Richardson diffusion [3] takes place with the mean squared displacement (MSD) $\langle x^2(t)\rangle \sim t^3$, which is due to the diffusive spread of the velocity profile $\langle \dot{x}^2(t)\rangle \sim t$. We consider a diffusion problem in neurons in the framework of a comb model and show that the transport can be accelerated by an external random field, which, in the present specific case, acts as a boundary condition.

It has been shown in experimental and numerical studies that the transport of inert particles along the dendrite structure of neurons corresponds to anomalous diffusion (namely, subdiffusion), when the temporal behavior of the MSD is of the power law t^γ, where the transport exponent $0 < \gamma < 1$ depends on the geometry and density of the dendritic spines [9–11]. Dendritic spines are the basic functional units in pre- and postsynaptic activity of neurons [12], and further studies have shown that the comb model can be used to describe the movement and binding dynamics of particles, including reaction transport of Ca^{2+} ions inside the spines [13–15]. A comb model has been suggested as a simplified toy model, which reflects this property of anomalous diffusion, resulted from the geometry, which mimics the geometry of spiny dendrites, such that the backbone is the dendrite and the fingers are the spines (see Fig. 1).

A special property of such geometry is reflected in transport (diffusion) coefficients, such that transport along the x coordinate is possible along the backbone at $y = 0$ only, while diffusion along the y coordinate is homogeneous. Therefore, the probability to find a particle at the position (x, y) at time t is determined by the probability distribution function (PDF) $P = P(x, y, t)$, which is controlled by the Fokker-Planck equation [16]. The corresponding equation in the dimensionless variables reads

$$\partial_t P = \delta(y)\partial_x^2 P + \partial_y^2 P. \tag{1}$$

For infinite combs, there is subdiffusion along the backbone with the MSD of the order of $t^{1/2}$ [17]. This fractional diffusion in the comb reflects a neuronal property of the power law adaptation, which results in neuronal fractional differentiation, observed experimentally [18], as well. For a finite comb with finite length h of fingers, this subdiffusion takes place at times $t < h$, and then it switches to normal diffusion at $t > h$ [19,20].

It should be admitted that this multiscale dynamics in the finite combs depends also on boundary conditions at finite fingers spines. These boundary conditions are determined by unstable synapses [21], undergoing random fluctuations,[1] and can be considered as a random nose at boundaries. Eventually, we arrived at a simple model, the comb model, whose geometry mimics the neuron spiny dendrite and the boundary conditions mimic the synapse random fluctuations. These boundary conditions are defined as follows:

$$\partial_y P(x, y, t)|_{y=h} - \partial_y P(x, y, t)|_{y=-h} = W(x, t). \tag{2}$$

It is worth noting that the boundary conditions at $y = \pm h$ correspond to the same spine (or synapse). Therefore, $W(x, t)$ consists of two identical fluxes with the opposite directions.

Stochastic Fokker-Planck equation. Therefore, the influence of the boundary fluctuations on the particle transport (including reactions) in neurons is studied in the framework of the comb model (1) with random boundary conditions for the fingers described in Eq. (2). Here we consider a multiplicative noise $w(x, t)$ in the form $W(x, t) = w(x, t)\rho(x, t)$, where $\rho(x, t)$ is a marginal PDF, which determines transport along

[1] See this discussion in Ref. [21], and references therein.

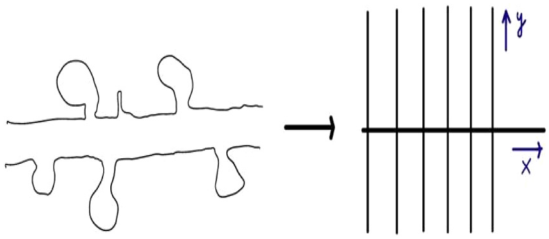

FIG. 1. Mapping of a spine dendrite on a comb, where fingers correspond to spines. There is an infinite number of y channels continuously distributed along the x coordinates. In this case at each x, the probability to enter to a finger is 1/2 (in either direction) and the probability to move along the backbone is 1/2 as well. This relation between the real three-dimensional Laplace operator and the Laplace operator of the comb model (1) was established in Ref. [20].

the backbone. The distribution of $w(x,t)$ and its spatiotemporal characteristics will be defined in the text in such a way that it will be suitable for the MSD calculations.

The backbone transport is described by either marginal PDF

$$\rho(x,t) = \int_{-h}^{h} P(x,y,t)dy, \tag{3}$$

or by the backbone PDF $P(x, y=0, t)$. Here we consider a diffusion process on the times $t > h$. In this case, there is a simple relation between these PDFs $P(x, y=0, t) \sim h\rho(x,t)$, which reduces to the equality at the asymptotically large time scale, $t \gg h$. As follows from Ref. [15], this relation should be also true for random finger's length with the finite mean length of the order of h.

Performing integration with respect to y, one arrives at the stochastic Fokker-Planck equation (SFPE)

$$\partial_t \rho(x,t) = h\partial_x^2 \rho(x,t) + w(x,t)\rho(x,t) \tag{4}$$

with the initial condition $\rho_0(x) = \rho(x, t=0) = \delta(x)$. In the case of additive noise, this equation is also known as an Edwards-Wilkinson equation [22].

An important caution here is that to avoid an avalanche [exponential increasing of the number of transporting particles due to the random reaction term $w(x,t)\rho(x,t)$], we impose the restriction condition, which controls the total number of particles. In particular, we can consider a conservation rule of the total number of particles at every realization of the random noise $w(x,t)$. It reads[2]

$$\int_x \rho(x,t)dx = 1. \tag{5}$$

The solution of the SFPE (4) can be presented in the form of the time-ordered exponentials as follows:

$$\rho(x,t) = \hat{T}\,\exp\left\{\int_0^t \left[h\partial_x^2 + w(x,\tau)\right]d\tau\right\}\rho_0(x), \tag{6}$$

where $\hat{T}$ is the time-ordering operator, and under this sign all values are commuted. Applying the Hubbard-Stratonovich transformation for the second derivative, we present it as a shift operator

$$e^{ht\partial_x^2} = \int \prod_\tau \frac{d\lambda(\tau)}{\sqrt{4\pi/hd\tau}} e^{-h/4\int_0^t \lambda^2(\tau)d\tau} e^{h\partial_x \int_0^t \lambda(\tau)d\tau}. \tag{7}$$

This yields solution (6) in the form of the Feynman-Kac path integral

$$\rho(x,t) = \int \prod_\tau \frac{d\lambda(\tau)}{\sqrt{4\pi/hd\tau}} \times e^{-h/4\int_0^t \lambda^2(\tau)d\tau} e^{\int_0^t w(x_\tau(t),\tau)d\tau}\delta(x(t)), \tag{8}$$

where

$$x_\tau(t) = x + h\int_\tau^t \lambda(\tau)d\tau, \quad x(t) = x + h\int_0^t \lambda(\tau)d\tau. \tag{9}$$

We substitute this solution in the restriction condition (5) and take into account the delta function for the integration with respect to x. The path integral is estimated by the extremum principal Hamiltonian function, or action S_e, which yields Eq. (5) as follows:

$$F(t)e^{-S_e(T)} = 1. \tag{10}$$

Here, the prefactor $F(T)$ stands for the normalization condition and compensates the exponential proliferation of particles.[3] The extremum action is determined from the condition $\delta S(T) = 0$, where

$$S(T) = \int_0^T L(\dot{X}, X, t)dt = \int_0^T \left[\frac{1}{4h}\dot{X}^2 - w(-X,t)\right]dt.$$

Here the velocity and the coordinate are $\dot{X} = h\lambda(t)$ and $X = x + h\int_0^t \lambda(\tau)d\tau$, correspondingly. The extremum action $S_e(T)$ is determined by the Euler-Lagrange equation, which corresponds to the velocity functional

$$\lambda(t) = 2h\int_0^t \frac{\partial w(-X,\tau)}{\partial X}d\tau. \tag{11}$$

Richardson diffusion. Now the MSD $\langle\langle x^2(t)\rangle\rangle_w$, averaged over all possible realizations of the random force $f(x,t) = \frac{\partial w(-X,\tau)}{\partial(-X)}$ can be estimated. Taking into account Eq. (10), we have

$$\langle\langle x^2(t)\rangle\rangle_w = \left\langle \int_x x^2 \rho(x,t)dx \right\rangle_w = 4h^2 \int_0^T dt \int_0^t d\tau \int_0^T dt' \int_0^{t'} d\tau' \langle f(x,\tau)f(x,\tau')\rangle_w. \tag{12}$$

[2]Later, we shall suggest a more realistic Fisher-Kolmogorov-Petrovskii-Piskunov mechanism of the reaction control. At this point we do not specify a mechanism of such restriction. However, if for every realization of $w(x,t)$ and for any random walk of a particle, the probability to find it inside the boundaries is 1, then condition (5) is fulfilled. It is worth noting that the implementation of this condition supposes also free boundary conditions at the dendrite-axon connection $x = x_{\text{d-a}} \equiv X$, which leads to a free nonzero current $j(X,t)$ from the dendrite to the axon. Therefore, integration of the equation with respect to x yields $\int_x w(x,t)\rho(x,t)dx = j(X,t)$. In this case, there are no restrictions of the random noise $w(x,t)$.

[3]In fact, it is an unknown, complicated random function. However, due to this restriction condition, the explicit form for this prefactor is not important.

Now we can suppose the correlation properties of the random noise, in such a way that both $w(x,t)$ and $f(x,t)$ are Gaussian, translational invariant in time and space, and delta correlated in time, and their correlation functions $C_R(x,t;x't') = \langle R(x,t)R(x',t')\rangle_w$ with $R = \binom{w}{f}$ are determined by a spectral density $S(k)$ as follows:

$$C_w(x,t;x',t') = C_w(x-x')\delta(t-t') = \int S(k)\cos[k(x-x')]dk\delta(t-t'), \quad (13a)$$

$$C_f(x,t;x',t') = C_f(x-x')\delta(t-t') = \int k^2 S(k)\cos[k(x-x')]dk\delta(t-t'). \quad (13b)$$

Taking into account correlation (13b) in Eq. (12), we arrive at Richardson diffusion [8] with the MSD

$$\langle\langle x^2(t)\rangle\rangle_w = 2h^2Dt^3, \quad (14)$$

where $D = \int k^2 S(k)dk$ is a transport coefficient

Reaction front propagation. An important part of the analysis is the restriction, or control of the number particles. It is a common statement for any mechanism of the control of the number of diffusive particles, which prevents the uncontrolled exponential increasing of the particle's number due to the random reaction term $w(x,t)\rho(x,t)$ in SFPE (4). However, the number conservation condition (5) is too strong, as admitted above, and in a general case, the number of particles cannot be conserved due to reactions. In this case, a more reasonable and realistic mechanism of the reaction control is due to a FKPP (Fisher-Kolmogorov-Petrovskii-Piskunov) term, which should be inserted in SFPE (4). The latter now reads

$$\partial_t\rho = h\partial_x^2\rho + w(1-\rho)\rho. \quad (15)$$

This stochastic reaction-transport equation can be important for the understanding of translocation waves of Ca^{2+} ions in spiny dendrites, studied in the framework of the FKPP scheme [14,23]. The stochastic FKKP term in Eq. (15) is a random generalization of a standard FKPP reaction term $\rho(1-\rho)$, which is widely used in reaction transport equations [24].

In this nonlinear case, the exact analytical treatment is not possible anymore, and we apply an analytical approximation to estimate the overall velocity of the reaction front propagation without resolving the exact shape of the front. The method is based on a hyperbolic scaling of space-time variables (x,t) by a small parameter ε. Following Ref. [25], we introduce this parameter ε at the derivatives. To this end, we rescale $x \to x/\varepsilon$ and $t \to t/\varepsilon$, and for the marginal PDF we have $\rho(x,t) \to \rho^\varepsilon(x,t) = \rho(\frac{x}{\varepsilon},\frac{t}{\varepsilon})$. We look for the asymptotic solution in the form of the Green's approximation

$$\rho^\varepsilon(x,t) = \exp[-S^\varepsilon(x,t)/\varepsilon]. \quad (16)$$

The main strategy of the implication of this construction is the limit $\varepsilon \to 0$ that yields the asymptotic solution at finite values of x and t, such that $\rho^\varepsilon(x,t)$ is not vanishing only when $S^\varepsilon(x,t) = 0$. Therefore, expression (16) is an extremum solution, which determines the position of the reaction spreading front. Substituting solution (16) in Eq. (15), scaled by ε, and taking limit $\varepsilon \to 0$, we obtain that $S^\varepsilon(x,t)$ is an extremum solution: $\lim_{\varepsilon\to 0} S^\varepsilon(x,t) = S_e(x,t)$, which is the extremum action, or the Hamilton's principal function. It is determined by the Hamilton-Jacobi equation

$$-\partial_t S_e = h(\partial_x S_e)^2 + w(x,t). \quad (17)$$

Taking into account that $-\partial_t S_e = H$ is Hamiltonian and $\partial_x S_e = p$ is the momentum, we arrive at the particle dynamics in a random noise potential with the Hamiltonian $H = hp^2 + w(x,t)$.

Further analysis differs from the standard approach of Ref. [25], where a particle is free, but here it is in a random potential. Eventually, we arrived at the same mechanism of turbulent diffusion, considered above in Eq. (11). Therefore, in the framework of the Hamiltonian approach, the overall velocity of the reaction front reads

$$V = \dot{x} = 2hp = 2h\int_0^t f(x,\tau)d\tau. \quad (18)$$

The correlation properties of the random force are described by Eq. (13b), and we obtain the mean squared velocity $\langle V^2(t)\rangle_w = 4h^2Dt$, which corresponds to Richardson diffusion with the MSD $\langle x^2(t)\rangle_w = 2h^2Dt^3$. It coincides exactly with the MSD in Eq. (14). Note that in both cases, h is accounted as the particle inverse mass.

Discussion. We obtained that the SFPE (4) with the restriction condition (5), or the FKPP mechanism controlling the number of transporting particles, describes a reaction-transport process in the presence of random boundary conditions. The latter plays a role of accelerator mechanism of reaction transport and leads to Richardson diffusion. An important condition of the applicability of the SFPE (4) for the transport inside the comb model considered as a toy model of spiny dendrites, is the long-time asymptotics. In this case the transport corresponds to normal diffusion. Eventually, it corresponds to a kind of Edwards-Wilkinson equation, where the random term is a multiplicative noise. However, this equation does not describe the initial time dynamics, which is important as well for the timescale $t < h$. In this case the underlying kinetics inside the backbone dendrite is subdiffusion, due to the relation in the Laplace space $\tilde{P}(x, y = 0, s) = \sqrt{s}\tilde{\rho}(x,s)$. This case leads to essential difficulties of the analysis and can be an important issue for future studies.

In conclusion, it should be admitted that an important motivation of the research is possible experimental studies of transport inside neurons, including artificial neurons [26]. Another interesting possibility relates to experimental investigations of reaction transport in a microfluidic device of the comb geometry [20,27] with the boundary control of fingers.

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