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On noise modeling in a nerve fibre

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ABSTRACT

We present a novel mathematical approach to model noise in dynamical systems. We do so by considering the dynamics of a chain of diffusively coupled Nagumo cells affected by noise. We show that the noise in a variable representing the transmembrane current can be effectively modeled as fluctuations in the model parameters corresponding to electric resistance and capacitance of the membrane. These fluctuations may account for the interactions between the membrane and the surrounding (physiological) solution as well as for the thermal effects. The proposed approach to model noise in a nerve fibre is an alternative to the standard technique based on the consideration of additive stochastic current perturbation (the Langevin type equations) and differs from it in important mathematical aspects, particularly, it points out to the non-Markov dynamics of transmembrane potential. Our scheme relates to a time scale which is shorter than the relaxation times of involved physiological processes.

1. Introduction

A typical nerve fibre is coated in myelin (the myelin sheath consists of a single Schwann cell which is wrapped about 100 times around the nerve fibre) with spatially periodic gaps, the nodes of Ranvier. The myelin sheath increases the membrane resistance roughly 100 times and decreases the membrane capacitance by about the same factor. Typically, the width of the Ranvier node is about 1 μm while the distance between nodes (the length of myelin sheath) is about 1.5 mm (which is roughly 100 times the nerve fibre diameter). The transmembrane ion flow occurs only at the nodes of Ranvier while the nodes are diffusively coupled by the axial currents in the fibre. These currents allow a propagation of changes in the transmembrane potential (action potential) from node to node. Thus, myelinated nerve fibres have a spatially discrete structure and there is a strong biological reason for this: the propagation of action potential along a myelinated fibre is considerably faster compare to that in nonmyelinated fibre. Because of the saltatory propagation of the action potential between the nodes its speed in a myelinated fibre is about 100 m/s while the speed in a nonmyelinated fibre is $1 \div 5$ m/s. For further details of the model, physical parameters and an equivalent electric circuit we refer to [1].

Before the middle of the 20th century it was commonly accepted that the noise is destructive to neural encoding [2,3]. The idea that the noise can play a positive role and enhance the neural functionality is relatively new. Today it is well established that the noise plays a constructive role in the performance of the nerve system [4–8]. This new paradigm was initiated by the research on stochastic resonance phenomena. It was shown that the stochastic resonance improves the transfer of information [9,10].

In this Letter, we accomplish two goals. First, we propose and study the deterministic scheme for modeling the noise in a nerve fibre. This scheme is based on the consideration of dynamical fluctuations in membrane affecting its electric

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characteristics through the negative feedback mechanism. Then, we ensure the ergodicity of the system by adjusting the feedback control to the intensity of stochastic perturbations. In contrast to the random noise model (see Section 3) our scheme operates with the only white noise process. Furthermore, our scheme is different from the standard one, based on the additive stochastic current perturbation and represented by the Langevin type equation, and has advantages for solving certain problems, including those that require consideration of time scales shorter compared to the time scales of physiological processes such as the duration of the action potential. Electrical properties of the membrane such as conductance and capacity represent its mean characteristics in interaction with the surrounding physiological solution which is also described by the mean concentration of ions. This is an approximation. The description of noise in terms of the random fluctuations in electric current across the membrane is a similar approximation. This approximation is a fruitful approach but it has drawbacks. For example, temperature effects, protein motions, and thus fluctuations in electric properties of the membrane are ignored. Interactions between the ions, water and proteins are ignored as well [1]. In short, the traditional approach relates to a relatively large time scale where the average electrical properties of the membrane and the surrounding physiological media are relevant. With our scheme, we intend to consider the noise and corresponding dynamics on a shorter time scale, and thus to take into account interactions between the membrane and surrounding solution. Since a detailed description of these interactions is not possible within a simple model, we represent them as a feedback control which takes place under certain conditions. To do so we introduce new dynamical variables that effectively relate the complex effect of interactions between the membrane, ion channels, salt solutions, and thermal factor to fluctuations in the membrane electric characteristics.

The model developed here differs from the Langevin type model in the following mathematically important aspect. The noise in our model affects the dynamics of transmembrane potential indirectly through the associated fluctuations in model parameters (describing the membrane) which appear after the integration. This can be understood as providing a memory effect, that is, the perturbed dynamics in transmembrane potential is non-Markov. The follow up question is under what limiting conditions our model transforms into the Langevin type model. Even if we do not deal with this problem here, we have to point out a possibility to provide the proper investigation by following [11,12].

2. Initial setup

We consider a lattice of diffusively coupled Nagumo cells described, in the absence of a noise, by the equations, $\dot{u}_i = l\triangle u_i + f(u_i)$, $i \in \mathbb{Z}$ is a spacial index, where $f(u)\colon \mathbb{R} \to \mathbb{R}$ has a bistable character, for example $f(u) = -ku(u-\alpha)(u-1)$, $0 < \alpha < 1$, $k > 0$; $\Delta u_i \equiv u_{i+1} - 2u_i + u_{i-1}$ is the standard three-point discretization of the Laplacian (discrete Laplacian), and $l > 0$ is a coefficient of the diffusive coupling. Furthermore, the "potential" $V(u)$ is defined by the differential equation, $V'(u) = -f(u)$, $V(0) = 0$. In these equations, the variable u corresponds to the transmembrane electric potential, k-to the membrane conductance and α-to the threshold potential. If $i \in I \subset \mathbb{Z}$ and I is bounded, we introduce boundary conditions, for example of the Neumann type. The introduced lattice system is a well-known model for the study of propagation of the action potential along a nerve fibre, although it has also been used for a study of other phenomena [13–15].

For what follows, it is convenient to represent the Nagumo equations in variational form. To do so we define the "energy" functional, $\mathcal{V}[u] = \sum_{\{i\}}[\frac{1}{2}l(\nabla u_i)^2 + V(u_i)]$, where $\nabla u_i = u_i - u_{i-1}$ is the discrete gradient. Hereafter we adopt the following notations for partial derivatives: $\frac{\partial}{\partial u_i} \equiv \partial_i$, $\frac{\partial^2}{\partial u_i^2} \equiv \partial_i^2$, $\frac{\partial}{\partial t} \equiv \partial_t$, and so on. Using these notations we rewrite the lattice of diffusively coupled Nagumo equations in the gradient form,

$$\dot{u}_i = -\partial_i \mathcal{V}[u], \quad i \in \mathbb{Z}. \tag{1}$$

Furthermore we can show that $\mathcal{V}[u]$ is the Lyapunov functional: $\dot{\mathcal{V}}[u] = -\sum_{\{i\}} (\partial_i \mathcal{V}[u])^2 \leq 0$.

Steady states of Eqs. (1) are the extrema of functional $\mathcal{V}[u]$. The minima and maxima of $\mathcal{V}[u]$ correspond respectively to stable and unstable solutions of Eq. (1). Let the time averaging for a continuous function $A(u)$ define as $\overline{A(u)} = \lim_{T\to\infty} \frac{1}{T}\int_0^T A(u(t))dt$. Assuming that $\mathcal{V}[u] > -\infty$ and applying the time averaging to $\dot{\mathcal{V}}[u] = -\sum_{\{i\}} (\partial_i \mathcal{V}[u])^2$ ($\mathcal{V}[u] > -\infty$) we get:

$$\begin{aligned}\overline{\sum_{\{i\}} (\partial_i \mathcal{V}[u])^2} &= \lim_{T\to\infty} \frac{1}{T}\int_0^T \sum_{\{i\}} (\partial_i \mathcal{V}[u])^2 \, dt = \lim_{T\to\infty} \frac{1}{T}\int_0^T \dot{\mathcal{V}}[u]dt \\ &= \lim_{T\to\infty} \frac{1}{T}\left(\mathcal{V}[u(T)] - \mathcal{V}[u(0)]\right) = 0.\end{aligned} \tag{2}$$

Thus the system spends almost all time at the extreme states of $\mathcal{V}[u]$. These extrema are solutions of the discrete lattice equation, $l\triangle u_i - \partial_i \mathcal{V}[u] = 0$, $i \in \mathbb{Z}$. This equation is supposed to be equipped with boundary conditions. Here we assume that $\nabla u_i \to 0$ as $i \to \pm\infty$.

3. Random noise

To model the influence of noise on deterministic system (1), it is widely accepted in the literature that the noise is implemented in (1) by the additive stochastic currents, $\xi_i(t)$, $i \in \mathbb{Z}$, where $\{\xi_i(t)\}_{i\in\mathbb{Z}}$ is the set of independent standard generalized Gaussian δ-correlated processes completely characterized by the first two cumulants, $\langle \xi_i(t)\rangle = 0$

and $\langle \xi_i(t)\xi_j(t')\rangle = \delta_{ij}\delta(t-t')$; $\langle\cdots\rangle$ means averaging over all realizations of the random perturbations. The set of stochastic differential equations corresponding to (1) takes the form, $\dot{u}_i = l\triangle u_i + f(u_i) + \sqrt{2D}\xi_i(t) = -\partial_i\mathcal{V}[u] + \sqrt{2D}\xi_i(t)$, $i\in\mathbb{Z}$, where D is the noise intensity (we suppose that noise does not depend on node). It is convenient for what follows to represent this set as

$$\dot{u}_i = -\lambda\partial_i\mathcal{V}[u] + \sqrt{2\lambda D}\xi_i(t), \quad i\in\mathbb{Z}, \tag{3}$$

where the reference time scale λ is explicitly introduced. By rescaling the time in (3), $t\to\lambda^{-1}t$, and taking into account the scaling property of white noise, we return to the case $\lambda = 1$.

In system (3) the dissipative processes and random perturbations equilibrate each other. For the "energy", $\mathcal{V}[u]$, we obtain the stochastic differential equation (we specify this equation in the sense of Stratonovich (*e.g.* [16])),

$$\dot{\mathcal{V}}[u] = -\lambda\sum_{\{i\}}(\partial_i\mathcal{V}[u])^2 + \sqrt{2D\lambda}\sum_{\{i\}}\partial_i\mathcal{V}[u]\xi_i(t). \tag{4}$$

Eq. (4) defines how the noise affects the "energy" and gives the rate of its (stochastic) fluctuations. Assume that $\mathcal{V}[u] > -\infty$. Then after averaging over all realizations of the random perturbations we obtain the relation, $-\left\langle\sum_{\{i\}}(\partial_i\mathcal{V}[u])^2\right\rangle + D\left\langle\sum_{\{i\}}\partial_i^2\mathcal{V}[u]\right\rangle = 0$, that does not depend on λ; we assume $\langle V[u]\rangle = const$. This relation can be derived either by elementary calculations or by applying Novikov's formula [17]. This is an important relation that connects the noise intensity to the configurational ensemble averages and thus can be considered as the definition of noise intensity. In what follows we conjecture that the similar formula involving the time averaging instead of the ensemble averaging, $-\overline{\sum_{\{i\}}(\partial_i\mathcal{V}[u])^2} + D\overline{\sum_{\{i\}}\partial_i^2\mathcal{V}[u]} = 0$, is valid and thus defines the noise intensity in the framework of deterministic dynamics. In order to deepen the conjecture and to describe the dynamics of deterministic fluctuations, we have to further presume that the rate of dynamic fluctuations (r.d.f.) can be represented in the form:

$$\text{r.d.f.} \sim -\sum_{\{i\}}(\partial_i\mathcal{V}[u])^2 + D\sum_{\{i\}}\partial_i^2\mathcal{V}[u], \tag{5}$$

that is, instead of the random perturbations (that are not present in deterministic dynamics) we have to consider dynamic fluctuations of an appropriate variable. Indeed, in the absence of random perturbations we have to adopt another way to properly perturb the system. Fluctuations in the electric characteristics of membrane are conjugate to the fluctuations in electric current across the membrane. Thus it is reasonable to consider a certain electric characteristic of the membrane, supposedly RC (where R is resistance and C is capacitance), that defines the time scale and allows this characteristic to dynamically fluctuate.

The intensity D of random noise is commonly considered as an independent parameter. Indeed, the Fokker–Planck operator corresponding to (3) has the form, $\mathcal{F}^*\rho \equiv -\sum_{(i)}\partial_i(\partial_i\mathcal{V}[u]\rho) + D\sum_{(i)}\partial_i^2\rho$. The Fokker–Planck equation associated with $\mathcal{F}^*$, $\partial_t\rho = \mathcal{F}^*\rho$, allows the invariant solution, $\rho_\infty[u] \sim \exp\left\{-D^{-1}\mathcal{V}[u]\right\}$. We prove the identity, $\mathcal{F}^*\rho_\infty[u] \equiv 0$, by straightforward calculation. It is known that this distribution and the corresponding probabilistic measure, $d\mu \sim \exp\left\{-D^{-1}\mathcal{V}[u]\right\}\prod_{(i)}du_i$, are typically unique for dynamics (3). In short, the stochastic dynamics (3) is typically ergodic. This means that for every continuous function A, $\int A(u)d\mu = \lim_{T\to\infty}\frac{1}{T}\int_0^T A(u(t))dt$, almost for sure for all initial values $u(0)$. The invariant measure relates to the infinite time interval. Thus, the variable that scales the time does not affect the measure. The invariant (equilibrium) distribution ρ_∞ demonstrates the explicit dependence on the noise intensity, D. The only constraint on D arises when we presume a nondestructive role of the noise. Namely, in the case of a cubic nonlinearity of $f(u)$, the general form of $V(u)$ is the double-well. The noise can induce transitions from one well to another. The rate of these transitions depends on D and it is expected to be a slow enough process.

Now we can pose a problem: given a probability measure $d\mu$ (or an augmented measure on an extended phase space); it is required to find the dynamics such that $\lim_{T\to\infty}\frac{1}{T}\int_0^T A(u(t))dt = \int A(u)d\mu$ for every continuous function A. We consider this problem as a dynamic modeling of noise with $d\mu \sim \exp\left\{-D^{-1}\mathcal{V}[u]\right\}\prod_{(i)}du_i$ representing the invariant (ergodic) measure for the dynamics.

4. Deterministic modeling of noise

Now we will put together the above observations, namely, that the rate of feedback control of dynamic fluctuations and the invariant measure depend on the noise intensity, —with the aim to derive a model of deterministic noise of intensity D in a nerve fibre. The requirements are:

- Dynamics of the variable u depends on external dynamic variables (*e.g.*, λ is endowed with its own equation of motion);
- Rate of deterministic dynamic fluctuations is directly related to (5) (*e.g.*, the rate of fluctuations is a measure of the influence of environment on electrical characteristics of the membrane);
- Measure $d\mu \sim \exp\left\{-D^{-1}\mathcal{V}[u]\right\}\prod_{(i)}du_i$ is invariant for the dynamics;
- Dynamics is ergodic.

In other words, we will sample the invariant measure, $d\mu \sim \exp\left\{-D^{-1}\mathcal{V}[u]\right\}\prod_{(i)} du_i$, by the method proposed in [18,19] and thus to incorporate the noise intensity into the dynamics in accordance with (5). This procedure is quite reasonable since it involves dynamical fluctuations of the membrane electrical characteristics. To correctly sample the invariant measure, the dynamics must be ergodic.

Consider the dynamics in the extended phase space $(\{u_i\}, \lambda, \{\eta_i\})$,

$$\dot{u}_i = -\lambda\partial_i\mathcal{V}[u] + \eta_i, \qquad \dot{\lambda} = g(u), \qquad \dot{\eta}_i = h_i(u), \quad i \in \mathbb{Z}; \tag{6}$$

where the functions $g(u)$ and $h_i(u)$ are to be determined. The extra dynamical variables λ and η_i model the environment and thus they represent the noise effect on the Nagumo dynamics.

Remark. The term η_i in the dynamical equations (6) is important. Indeed, assume that $\eta_i \equiv 0$. Then, at the equilibrium $\partial_i\mathcal{V}[u] = 0$, the evolution comes to halt and no longer fluctuates, irrespective of the time dependence of λ. For initial conditions with $\partial_i\mathcal{V}[u] \neq 0$ after a time variable rescaling, it is a gradient flow as defined in [20], and all phase space trajectories move along paths with equilibrium points at either end. This dynamics is not ergodic. For a further discussion we refer to [18,19].

To determine the functions $g(u)$ and $h_i(u)$, we calculate, in the analogy with (4),

$$\dot{\mathcal{V}}[u] = -\lambda\sum_{\{i\}}(\partial_i\mathcal{V}[u])^2 + \sum_{(i)}\eta_i\partial_i\mathcal{V}[u]. \tag{7}$$

With respect to the second term on r.h.s. of (7) we put the following requirement to the time average, $\overline{\sum_{(i)}\eta_i\partial_i\mathcal{V}[u]} = 0$. A series of η-dynamics satisfies this condition. Two principal limit cases are: the fluctuations of current in different nodes are independent or synchronous. Correspondingly we endow variables $\{\eta_i\}$ with the following dynamical equations,

$$\dot{\eta}_i \sim \partial_i\mathcal{V}[u], \quad i \in \mathbb{Z}, \quad \text{and} \quad \dot{\eta}_i \sim \sum_{(j)}\partial_j\mathcal{V}[u], \quad \forall i \in \mathbb{Z}. \tag{8}$$

However, with regard to the first term in r.h.s. of (7), we cannot repeat the trick and set $\dot{\lambda} \sim \sum_{\{i\}}(\partial_i\mathcal{V}[u])^2$, since this results in no noise effect. To overcome this difficulty, we implement the conjecture (5) into λ-dynamics and (7), and explicitly set

$$\dot{\lambda} \sim \sum_{\{i\}}(\partial_i\mathcal{V}[u])^2 - D\sum_{\{i\}}\partial_i^2\mathcal{V}[u]. \tag{9}$$

Lemma 1. *Assume λ to be a bounded variable, its dynamics is given by (9) and $\overline{\sum_{(i)}\eta_i\partial_i\mathcal{V}[u]} = 0$ (e.g. one of dynamical equations (8)). Then $\overline{\lambda\sum_{\{i\}}\partial_i^2\mathcal{V}[u]} = 0$.*

Proof. First we multiply (9) by λ and take into account Eq. (7). Then we apply the time averaging to the resulted equation. Thus we easily accomplish the lemma. Indeed,

$$0 = \overline{-\lambda\left[\sum_{\{i\}}(\partial_i\mathcal{V}[u])^2 - D\sum_{\{i\}}\partial_i^2\mathcal{V}[u]\right]} = \overline{-\dot{\mathcal{V}}[u] + \sum_{(i)}\eta_i\partial_i\mathcal{V}[u] - D\lambda\sum_{\{i\}}\partial_i^2\mathcal{V}[u]} = D\overline{\lambda\sum_{\{i\}}\partial_i^2\mathcal{V}[u]}. \quad \square$$

This lemma, together with the Eqs. (7)–(9), allows us to determine functions the $g(u)$ and $h_i(u)$ explicitly,

$$g = \frac{1}{Q_\lambda}\sum_{(i)}\left[(\partial_i\mathcal{V}[u])^2 - D\partial_i^2\mathcal{V}[u]\right], \qquad h_i = -\frac{1}{Q_\eta}\partial_i\mathcal{V}[u] \quad \text{or} \quad h_i = -\frac{1}{Q_\eta}\sum_{(j)}\partial_j\mathcal{V}[u], \quad i \in \mathbb{Z}, \tag{10}$$

where Q_λ and Q_η are parameters. Variables η_i and corresponding functions h_i are not unique and dynamical equations can be simplified.

To verify the requirement on the invariant measure, we prove the following theorem.

Theorem 2. *Assume the extended dynamics in form (6) where functions g and h_i are given by (10), $Q_\lambda > 0$ and $Q_\eta > 0$. Then the augmented measure,*

$$d\mu \sim \exp\{-D^{-1}\mathcal{V}[u]\}\exp\left[\left\{-D^{-1}\left(\frac{1}{2}Q_\lambda\lambda^2 + \frac{1}{2}Q_\eta\sum_{(i)}\eta_i^2\right)\right\}\right]\prod_{(i)}du_i d\lambda d\eta_i = \rho_\infty\prod_{(i)}du_i d\lambda d\eta_i, \tag{11}$$

is invariant for the extended dynamics.

Remark. It should be noted that the η-dynamics is not unique and allows a variety of η-factors of the augmented measure, although they all are Gaussian. *E.g.*, with the synchronous dynamical fluctuations, $\dot{\eta} = -\frac{1}{Q_\eta}\sum_{(j)}\partial_j\mathcal{V}[u]$, we arrive at $\exp[\{-D^{-1}\frac{1}{2}Q_\eta\eta^2\}]d\eta$.

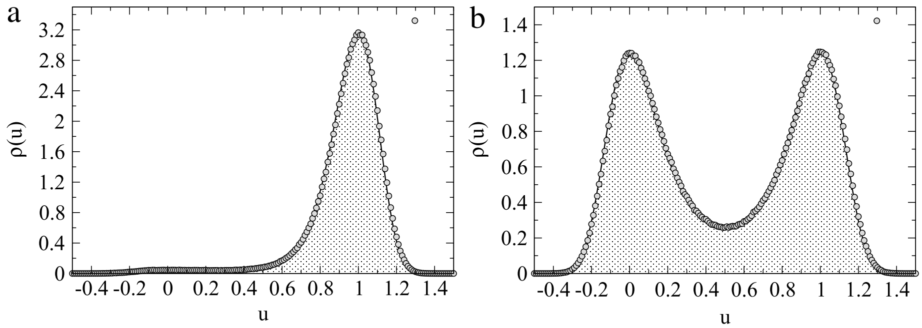

Fig. 1. Probability distributions of variable u in Eqs. (12): exact analytical distribution is given by the solid line and shown as dashed background. Densities are calculated as normalized sojourn distributions. Probability distributions are shown: (a) for $\alpha = 0.25$ and (b) for $\alpha = 0.5$.

Proof. The Liouville operator corresponding to the dynamics in the extended phase space (6) has the form, $\mathcal{L}^*\rho = -\sum_{(i)} \partial_i [(-\lambda \partial_i \mathcal{V}[u] + \eta_i)\rho] - \partial_\lambda [g(u)\rho] - \sum_{(i)} \partial_{\eta_i}[h_i(u)\rho]$, and the Liouville equation reads $\partial_t \rho = \mathcal{L}^*\rho$. Therefore, to prove the theorem we have to prove the identity, $\mathcal{L}^*\rho_\infty \equiv 0$, that means the dynamics (6) preserves the augmented measure (11). A straightforward calculation of all partial derivatives that are involved in $\mathcal{L}^*\rho_\infty$ with further simplification brings to the required identity, $\mathcal{L}^*\rho_\infty \equiv 0$. The theorem is proved. □

From the perspective of numerical simulations and further mathematical analysis, *e.g.* the Hamiltonian representation of the proposed dynamics, it is important to find a first integral of motion. We accomplish this task with the following lemma.

Lemma 3. *Let the dynamical system* (6) *and* (10) *be augmented with the redundant dynamical variable* ζ, $\dot{\zeta} = -\lambda \sum_{\{i\}} \partial_i^2 \mathcal{V}[u]$. *Then* $I = \mathcal{V}[u] + \frac{1}{2} Q_\lambda \lambda^2 + \frac{1}{2} Q_\eta \sum_{(i)} \eta_i^2 - D\zeta$ *is the first integral of the augmented dynamical system.*

Proof. We derive $\dot{I} = 0$ by direct calculation. □

Remark. Since the origin of coordinates of the redundant variable ζ is arbitrary, it is always possible for an arbitrary fixed trajectory to set $I = 0$. I is an apparent control parameter in numerical simulations. Besides, I is related to ρ_∞ and thus it can be considered from the perspective of Hamiltonian reformulation of dynamics on the level set $I = 0$ [18]. However we do not consider this problem here.

We can now ask whether the dynamics (6) and (10) is ergodic. There is no a definite answer to this question. Following [18] we can apply the Frobenius theorem of differential geometry [21] but this provides with a partial answer only. Here, in order to provide ergodicity, we adopt the method proposed in [18] and rigorously investigated in [22]. Namely, we add a Gaussian random noise to the λ-dynamics. In contrast to the model outlined in Section 3, where stochastic currents are added at each node, this approach relies on single and indirect stochastic perturbation that affects the dynamics in transmembrane potential through electric characteristics of the membrane after integration providing a memory effect, that is, the perturbed dynamics in u is non-Markov. Experiments [22] reveal that, in context of the molecular dynamics, it results in a relatively weak perturbance effect on deterministic dynamics. Thus, we reformulate λ-dynamics (6) in the form,

$$\dot{u}_i = -\lambda \partial_i \mathcal{V}[u] + \eta_i, \qquad \dot{\lambda} = g(u) - \gamma\lambda + \sqrt{2\gamma D Q_\lambda^{-1}}\,\xi(t), \qquad \dot{\eta}_i = h_i(u), \quad i \in \mathbb{Z}, \tag{12}$$

where $\gamma > 0$ is a parameter.

Theorem 4. *Assume stochastically perturbed extended dynamics in the form* (12) *where the functions g and h are given by* (10), $Q_\lambda > 0$, $Q_\eta > 0$. *Then the augmented measure* (11) *is invariant for this dynamics.*

Proof. The Fokker–Planck operator corresponding to (12) has the form, $\mathcal{F}^*\rho = \mathcal{L}^*\rho + \gamma \partial_\lambda \left[\left(\lambda + D Q_\lambda^{-1} \partial_\lambda\right)\rho\right]$, and the Fokker–Planck equation reads $\partial_t \rho = \mathcal{F}^*\rho$. After a series of routine calculations we arrive at $\mathcal{F}^*\rho_\infty \equiv 0$. Thus the stochastically perturbed dynamics (12) preserves the augmented measure (11). □

Dynamics (12) can be shown to be ergodic [22].

Test simulations. Single cell dynamics.

Low dimensional systems often reveal the ergodicity problem in a dynamical sampling of probability distribution. For this reason, it is important to test the capability of the presented noise modeling method to generate the right statistics for a single Nagumo cell. For this test we choose the function $f(u) = -4u(u-\alpha)(u-1)$ and parameters $D = 0.04$, $\gamma = 1$, $Q_\lambda = 1$, and $Q_\eta = 2$ for $t = 10^6$. Fig. 1 shows the probability distribution of variable u simulated numerically using the dynamical Eqs. (12) and compared with the exact analytical solution. Their solid agreement brings a severe test of our approach.

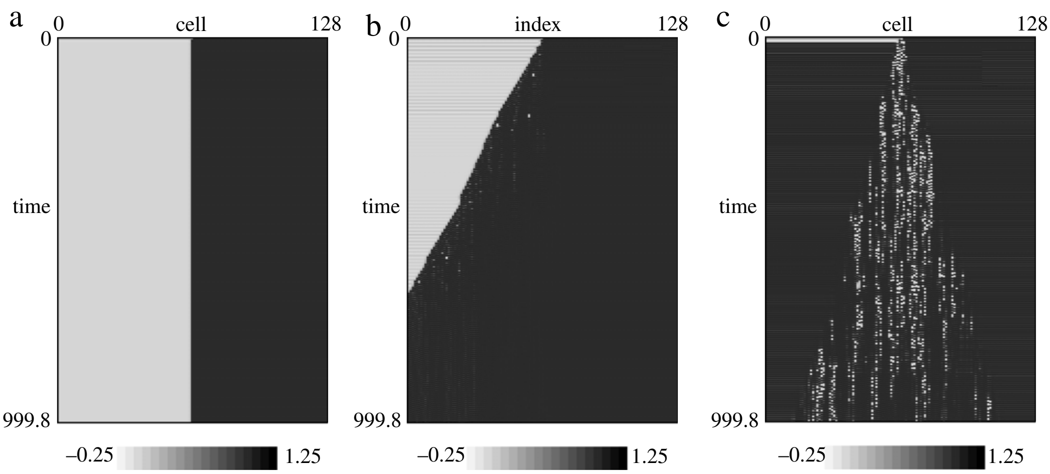

Fig. 2. Numerical simulations of the fibre dynamics (12). The fibre has 128 cells. The amplitude of the u-variable is shown by a shadow of gray ranging from white ($u < -0.25$) to black ($u > 1.25$). The horizontal axis corresponds to position along the fibre and the vertical axis corresponds to time. Simulations are performed at three noise intensities: (a) $D = 0$, (b) $D = 0.003$, and (c) $D = 0.03$.

Test simulations. Fibre dynamics.

Now we simulate dynamics of a fibre consisting of 128 cells. In dynamical Eqs. (12) we fix the following global parameters: $\alpha = 0.25$ $\gamma = 0.1$, $Q_\lambda = 1$, $Q_\eta = 2$, $l = 0.065$, and $f(u)$ is the same as in the single cell simulations; the specific initial conditions are $\{u_i\}_{i=1}^{64} = 0.24$, $\{u_i\}_{i=65}^{128} = 1.01$. Here we test the failure of excitation propagation along the fibre. Fig. 2 shows (a) a kink pinning in the absence of noise ($D = 0$); (b) a front propagation (depinning) in the presence of a small intensity noise ($D = 0.003$); (c) development of large amplitude spatiotemporal fluctuations from a germ kink in the presence of an intensive noise ($D = 0.03$).

5. Conclusion

We have presented a novel mathematical approach to model noise in dynamical systems. To develop this approach, we have considered dynamics of a chain of diffusively coupled Nagumo cells affected by noise. The effect of noise was considered at a time scale which is shorter than that in the Langevin type stochastic perturbation approach. Besides, the noise in our approach is associated with the dynamics of transmembrane potential as related to the interactions between the membrane and the surrounding salt solution as well as to the thermal effects. It is a feature of our approach that the noise does not directly affect the dynamics in transmembrane potential, but does so through the noise in electric characteristics of the membrane after integration. This can be understood as a memory effect indicating that the perturbed dynamics of the transmembrane potential is non-Markov. Our scheme provides a potential for investigation of effects arising due to mutual influence of the membrane together with its proteins and surrounding salt solution.

Additionally, let us note that the ability to dynamically generate the probability density $\exp\left\{-D^{-1}\mathcal{V}[u]\right\}$ also allows to sample an arbitrary probability density $r[u]$. The ansatz is to set $\mathcal{V}[u] = -D\ln\{r[u]\}$. This is potentially important for dynamical modeling of a given spatial pattern.

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