Dendritic cable with active spines: a modelling study in the spike-diffuse-spike framework

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Abstract

The spike-diffuse-spike (SDS) model describes a passive dendritic tree with active dendritic spines. Spine-head dynamics is modelled with a simple integrate-and-fire process, whilst communication between spines is mediated by the cable equation. Here we develop a computational framework that allows the study of multiple spiking events in a network of such spines embedded in a simple one-dimensional cable. This system is shown to support saltatory waves as a result of the discrete distribution of spines. Moreover, we demonstrate one of the ways to incorporate noise into the spine-head whilst retaining computational tractability of the model. The SDS model sustains a variety of propagating patterns.

Key words: spike-diffuse-spike, dendritic spines, saltatory waves, noise

Introduction

Experimental evidence indicates that the dendrites of many neurons are equipped with excitable channels located in dendritic spines that can support an all-or-nothing action potential response to an excitatory synaptic input. The biophysical properties of spines have been linked, for example, with mechanisms for Hebbian learning in the nervous system [9], the implementation of logical computations [7] and the amplification of distal synaptic input [5]. The spread of current from one spine along the dendrites may bring adjacent spines to threshold for impulse generation, resulting in a saltatory propagating wave in the distal dendritic branches [6]. The saltatory nature of the wave may be directly attributed to the fact that active spines are physically separated. Here we describe the spike-diffuse-spike (SDS) framework based on the original work of Baer and Rinzel [1] and later developed by Coombes and Bressloff [2] for studying spatio-temporal properties of a dendritic cable with active spines. The spines are coupled to the dendrites via a spine-stem resistance at discrete points. There is no direct coupling between neighbouring spines and they interact only by voltage spread along the cable. Spine-head dynamics is modelled with an integrate-and-fire process, whilst the dendrite is modelled with a passive cable equation. Here we describe a quasi-analytic approach for studying travelling waves. Moreover, we show the robustness of such solutions to both disorder in the spine distribution and noise in the generation of firing events. Throughout this paper we validate our work against direct numerical simulations.

The SDS model and travelling wave solutions

We consider a uniform dendritic cable with a given distribution of spines along its length (see schematic diagram in Fig. 1). The evolution of membrane

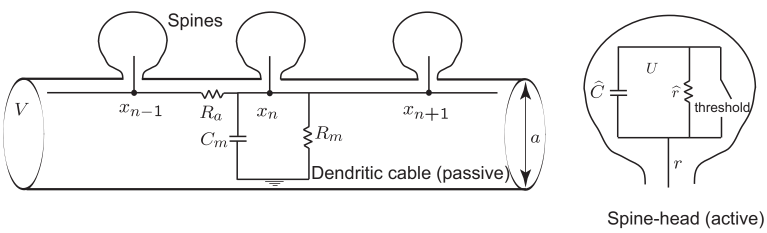

Fig. 1. A schematic representation of the SDS model.

voltage in the cable $V = V(x, t)$ is given in terms of the membrane time constant τ and the electronic space constant λ as

$$\tau \frac{\partial V}{\partial t} = \lambda^2 \frac{\partial^2 V}{\partial x^2} - V + \lambda^2 r_a \rho(x) I_{\text{sp}}, \tag{1}$$

where $\tau = C_m R_m$, $\lambda = \sqrt{aR_m/4R_a}$ and $r_a = 4R_a/\pi a^2$ denotes the intracellular resistance per unit length of cable . Here a is the diameter of the cable, R_a is the specific cytoplasmic resistivity, C_m and R_m are respectively a capacitance and a resistance of a unit area of passive membrane. Spines are connected to the cable at the discrete points x_n with the distribution function $\rho(x) = \sum_{n\in\Gamma} \delta(x - x_n)$, where Γ is a discrete set that indexes the spines. Each spine generates a sequence of action potentials in its spine-head (it "fires") and, thus, passes the spine current $I_{\text{sp}} = (\widehat{V} - V)/r$ into the cable. The spine-stem resistance of an individual spine is given by r. The mth firing time at the nth spine is denoted T_n^m. The function $\widehat{V}(x, t)$ represents voltage in the spine-head, and is considered to be a train of action potentials given by $\widehat{V}(x_n, t) = \sum_m \eta(t - T_n^m)$. The shape of an action potential is chosen to be a rectangular pulse $\eta(t) = \eta_0 \Theta(t)\Theta(\tau_S - t)$, where η_0 and τ_S are its strength and duration and $\Theta(t)$ is the Heaviside step function.

The generator of action potentials in the nth spine-head evolves according to

$$\widehat{C}\frac{\partial U_n}{\partial t} = -\frac{U_n}{\widehat{r}} + \frac{V_n - U_n}{r} - \underbrace{\widehat{C}h\sum_m \delta(t - T_n^m)}_{\text{reset}}, \tag{2}$$

where $V_n = V(x_n, t)$. Here the parameters $\widehat{C}$ and $\widehat{r}$ describe the electrical properties of the spine-head membrane, its capacitance and resistance respectively. The spine's firing times are defined in terms of an integrate-and-fire process according to

$$T_n^m = \inf\{t \mid U_n(t) \geq h,\ t > T_n^{m-1} + \tau_R\}, \tag{3}$$

i.e. a spine fires whenever U_n, driven by current from the shaft, crosses some threshold potential h. Just after a firing event the variable U_n resets to zero. This reset is modelled by the last term in equation (2). Multiple spiking events from an individual spine are controlled by a refractory time scale $\tau_R = R\tau_S$, with $R \geq 1$ so as to ensure that the firing times of an individual spine are separated by at least τ_S.

Under the approximation that $\lambda^2 r_a/(\tau r) \ll 1$, the spine current reduces to $I_{\text{sp}} = \widehat{V}/r$ and the solution of equation (1) may be found explicitly [3] as

$$V(x,t) = \frac{Dr_a}{r}\sum_{k,\ m} H(x - x_k, t - T_k^m), \qquad \max_{k,\ m}\{T_k^m\} \leq t < T_j^\ell\ , \tag{4}$$

where k is the index of spines that have fired and $m = m(k)$ counts firing events at each spine. Expression (4) holds for times t between $\max_{k,m}\{T_k^m\}$ (*i.e.* the last firing event across all spines), and T_j^ℓ defined to be the new firing event(s) that occur as the ℓth firing at spine(s) j. $D = \lambda^2/\tau$ is the diffusion coefficient for the cable. The function $H(x,t)$ is expressed in terms of the Green's function of the uniform cable equation as $H(x,t) = \int_0^t G(x, t-s)\eta(s)\mathrm{d}s$, where $G(x,t) = \mathrm{e}^{-\varepsilon t - x^2/(4Dt)}\Theta(t)/\sqrt{4\pi Dt}$ and $\varepsilon = 1/\tau$. For the chosen form of $\eta(t)$ the function $H(x,t)$ can be found in closed form as $H(x,t) = A_\varepsilon(x, t - \min(t, \tau_S)) - A_\varepsilon(x,t)$ with a standard integral $A_\varepsilon(x,t)$ given explicitly in [3].

The firing times for the construction of solution (4) may be found from the set of threshold conditions $U_n(t) = h,\ n \in \Gamma$, with $U_n(t)$ obtained by integrating equation (2). In particular, to find a new firing time $T_j^\ell > \max_{k,m}\{T_k^m\}$ corresponding to the spine at location x_j we have to solve the set of threshold conditions for the functions

$$U_n(t) = \frac{Dr_a}{\widehat{C}r^2}\sum_{k,\ m}\widehat{H}(x_n - x_k, t - T_k^m) - h\sum_m \mathrm{e}^{-\varepsilon_0(t - T_n^m)}, \tag{5}$$

where

$$\widehat{H}(x,t) = \int_0^t \mathrm{e}^{\varepsilon_0(s-t)}H(x,s)\mathrm{d}s, \tag{6}$$

and $\varepsilon_0 = (1/\widehat{r}+1/r)/\widehat{C}$. Numerical evaluation of the integral in (6) can be readily performed for the explicitly given function $H(x,t)$. Moreover, for $\varepsilon > \varepsilon_0$ this integral can be found in closed form as $\widehat{H}(x,t) = (A_\varepsilon(x,0)(\mathrm{e}^{-\varepsilon_0(t-\min(t,\tau_S))} - \mathrm{e}^{-\varepsilon_0 t}) + \widehat{A}(x, t-\min(t,\tau_S)) - \widehat{A}(x,t))/\varepsilon_0$ with

$$\widehat{A}(x,t) = \mathrm{e}^{-\varepsilon_0 t}\left[A_{\varepsilon-\varepsilon_0}(x,0) - A_\varepsilon(x,0) - A_{\varepsilon-\varepsilon_0}(x,t)\right] + A_\varepsilon(x,t). \qquad (7)$$

By solving the set of threshold conditions with $U_n(t)$ defined by (5) we obtain a vector of times showing when each spine in Γ is able to reach the threshold potential h. The smallest time from this vector, T_j^ℓ, that satisfies the refractory restriction $T_j^\ell - T_j^{\ell-1} > \tau_R$ defines a new spiking event at location x_j. As a result the functions $U_n(t)$ are updated by adding extra terms into both sums in (5) associated with the newly fired spine. The same routine can be performed again using the updated functions $U_n(t)$ for finding the next firing event for $t > T_j^\ell$. We now show some examples of waves that are generated by the SDS model. The waves are saltatory as a result of the discrete spine distribution that breaks the translation symmetry in the system. Fig. 2A shows an example of a solitary travelling wave propagating along the cable with regularly distributed spines at locations $x_n = nd$ with spacing d. The wave is initiated from an activated single spine at one end of the cable and free boundary conditions are assumed. The SDS model given as a system of differential equations (1) and (2) with the spine current $I_{\mathrm{sp}} = \widehat{V}/r$ was implemented in NEURON [4] to compare with the explicit solution given by (5), with firing times determined from a MATLAB root-finding routine. The obvious major advantage of the second approach is that the analytical integration of the equations of motion obviates the need for the numerical solution of a partial differential equation. In Fig. 2B we plot the membrane voltage of the periodic travelling wave solution at the location of the 10th spine along the cable. The results of numerical simulations (crosses) show excellent agreement with the quasi-analytic solution of the SDS model (solid line). From now on we only consider

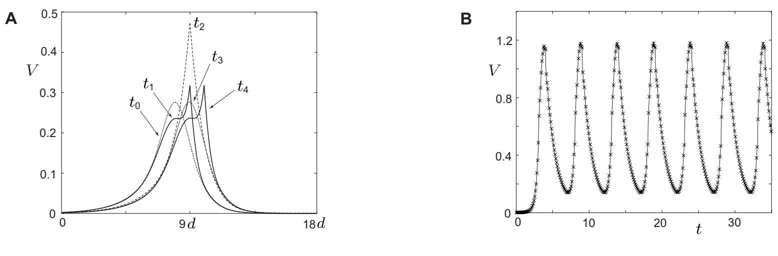

Fig. 2. A: An example of saltatory travelling wave for the following system parameters: $D = 1$, $\varepsilon = 1$, $\tau_S = 1$, $\varepsilon_0 = 0.8$, $\eta_0 = 1$, $r = 1$, $\widehat{C} = 2.5$, $\widetilde{h} \equiv h/r_a = 0.05$, $d = 0.85$, $\tau_R = 6$. Snapshots are shown for times $t_0 = 9\Delta$, $t_1 = t_0 + 0.08\tau_S$, $t_2 = t_0 + \tau_S$, $t_3 = 10\Delta$ and $t_4 = t_3 + 0.08\tau_S$, where $\Delta = 1.1306$. B: Voltage profile of the periodic travelling wave at the location $x = 9d$ along the cable with $d = 0.4$ and $\tau_R = 5$. Other parameters as in A. Quasi-analytical (numerical) solution: solid line (crosses).

the solution of the model given explicitly by (4) and (5). Fig. 3 shows the space-time density plots of voltage in the cable and illustrates the difference between the propagating waves in the system with regular (A) and irregular (B) distribution of spines. The positions of spines in the right-hand plot were defined as in the left one perturbed by a small random vector of size ϵd. If the degree of spatial disorder is sufficiently large we observe propagation failure.

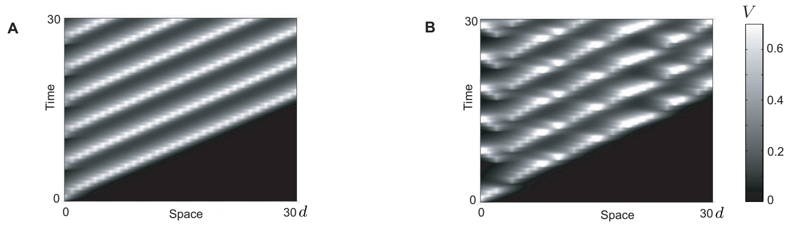

Fig. 3. Periodic travelling waves in the SDS model with regular (A) and irregular (B) distribution of spines. Parameters as in Fig. 2B except $d = 0.6$ and $\epsilon = 0.5$.

One of the ways to incorporate stochastic effects into the SDS framework is to introduce a source of noise at the threshold level. This can be modelled under the replacement $h \to h + \xi$ where ξ is an additive noise term with distribution $\rho(\xi)$. Then the probability of a firing event is

$$P(U_n > h) = \int \rho(\xi)\Theta(U_n - h - \xi)\mathrm{d}\xi = f(U_n - h), \tag{8}$$

where $\rho(\xi) = f'(\xi)$. For the natural choice of bell-shaped noise distribution for ρ, f is a sigmoidal function. Here we use $f(U) = (1 + \mathrm{e}^{-\beta h})/(1 + \mathrm{e}^{-\beta U}) - \mathrm{e}^{-\beta h}$, so that the probability of a firing event is zero and one respectively for $U = 0$ and $U \to \infty$. The parameter β controls the level of noise. Fig. 4 demonstrates examples of waves generated in the SDS model, with a regular distribution of spines, in the presence of a finite amount of noise. Low noise (Fig. 4A) leads to behaviour similar to that observed in the deterministic SDS model with an irregular distribution of spines (see Fig. 3B). An increase in noise level leads to more irregular wave patterns as shown in Fig. 4B (and it is even possible to see purely noise induced wave phenomenon). For high levels of noise propagation failure may also occur.

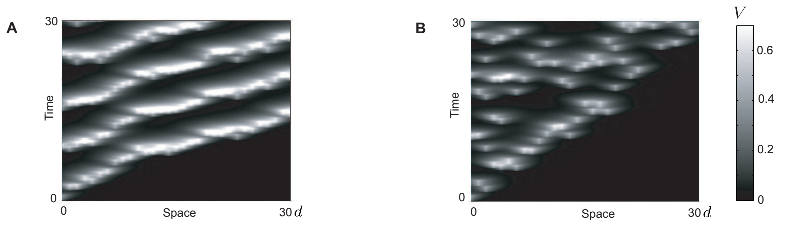

Fig. 4. Stochastic travelling waves in the SDS model with spine-head threshold noise for (A) $\beta = 10$ (low noise) and (B) $\beta = 1$ (high noise). Other parameters as in Fig. 3A except $\tau_R = 6$.

Conclusions

We have described the SDS framework for the analysis of saltatory wave propagation along a spiny dendritic cable and presented an efficient numerical scheme for studying spines at discrete points on the cable. The computational simplicity of the model makes it ideal for exploring the effects of spine distributions as well as stochastic spike generation on patterns of propagating activity. In a companion paper [8] we go beyond the approximation scheme used here and show that the qualitative wave features we have observed are also found in both a higher-order quasi-analytic treatment and numerical simulations of the full model. For further discussion of solitary and periodic travelling waves, irregular waves, propagation failure, and spatio-temporal filtering properties, we refer the reader to [8].

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