Directed percolation in a two-dimensional stochastic fire-diffuse-fire model

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We establish, from extensive numerical experiments, that the two dimensional stochastic fire-diffuse-fire model belongs to the directed percolation universality class. This model is an idealized model of intracellular calcium release that retains both the discrete nature of calcium stores and the stochastic nature of release. It is formed from an array of noisy threshold elements that are coupled only by a diffusing signal. The model supports spontaneous release events that can merge to form spreading circular and spiral waves of activity. The critical level of noise required for the system to exhibit a nonequilibrium phase transition between propagating and nonpropagating waves is obtained by an examination of the *local slope* $\delta(t)$ of the survival probability $\Pi(t) \propto \exp[-\delta(t)]$ for a wave to propagate for a time t.

Ca^{2+} waves provide a highly versatile mechanism for intracellular and intercellular signaling [1]. Cellular calcium signals generally do not occur uniformly throughout a cell but are initiated at specific sites and spread in the form of saltatory waves [2]. The fluorescent imaging of localized Ca^{2+} release events has now made it clear that Ca^{2+} release dynamics is a stochastic process that occurs at spatially discrete sites that are clusters of IP_3 receptors in the endoplasmic reticulum or ryanodine receptors in the sarcoplasmic reticulum [3,4]. In this paper we describe the two-dimensional stochastic fire-diffuse-fire (FDF) model of Ca^{2+} release and use extensive numerical simulations to highlight the interesting statistical properties for the waves generated by the model. One of the main advantages of this model is that it is both biophysically realistic and computationally inexpensive. A threshold process is used to mimic the nonlinear properties of Ca^{2+} release channels. Moreover, release events have a simple on-off temporal structure and release sites are embedded at a discrete set of points within the cell model. The stochastic nature of release events is incorporated via the introduction of a simple probabilistic rule for the release of calcium from internal stores. Using numerical simulations we are able to identify a critical level of noise defining a nonequilibrium phase transition and show that the model belongs to the directed-percolation (DP) universality class (in two dimensions).

A recent review of the main features of the stochastic FDF model can be found in [5], where its historical development is traced from the original FDF model of Keizer *et al.* [6–8]. This Brief Report not only builds upon this body of work, but is complementary to that of Falcke *et al.* [9,10], which focuses on more biophysically detailed models of the stochastic release of calcium from internal stores.

In the two-dimensional stochastic FDF model (see also [5,11]), it is assumed that release times occur at multiples of the duration, τ, of a release event (which is small relative to other time scales in the model). Let $u(\mathbf{r},t)$ denote the concentration of Ca^{2+} at a point $\mathbf{r} \in \mathbb{R}^2$ at time $t \in \mathbb{R}^+$. Then the dynamics for $p\tau < t < (p+1)\tau$, $p \in \mathbb{Z}$, is determined in terms of the *release function* $a_n(p)$ and initial data $u_p(\mathbf{r}) = u(\mathbf{r}, p\tau)$ as

$$u(\mathbf{r},t) = \frac{\sigma}{\tau} \sum_{n \in \Gamma} a_n(p) G(\mathbf{r} - \mathbf{r}_n, t - p\tau) + (G \otimes u_p)(\mathbf{r},t), \quad (1)$$

where

$$G(\mathbf{r},t) = \frac{1}{4\pi D t} \exp\left(-\frac{t}{\tau_d}\right) \exp\left(-\frac{r^2}{4Dt}\right) \quad (2)$$

and $r = |\mathbf{r}|$. The decay time τ_d in Eq. (2) is associated with the action of linear SERCA pumps that resequester the Ca^{2+} back into the stores. The transport of Ca^{2+} in the model is assumed to be the result of isotropic Ca^{2+} diffusion between Ca^{2+} release sites with a diffusion coefficient D. Although, in real cells, calcium is heavily buffered, recent work by Strier *et al.* [12] suggests that working with an effective diffusion constant is reasonable (even for slow buffers) if the spacing between release sites is not too large. The vectors $\mathbf{r}_n$ in Eq. (1) determine the locations of the (point) Ca^{2+} release sites and Γ is a discrete set that indexes these release sites. The pth release event at the nth site is a binary process, where the $a_n(p) \in \{0,1\}$ act as coefficients in the expansion of the solution over a set of functions $G(\mathbf{r} - \mathbf{r}_n, t - p\tau)$. The strength of the release event is given by σ. The second term on the right-hand side in Eq. (1) represents a spatial convolution of the propagator $G(\mathbf{r}, t - p\tau)$ with initial data $u_p(\mathbf{r})$:

$$(G \otimes u_p)(\mathbf{r},t) = \int_{\mathbb{R}^2} G(\mathbf{r} - \mathbf{r}', t - p\tau) u_p(\mathbf{r}') d\mathbf{r}'. \quad (3)$$

Hence, the dynamics is naturally separated into a part that keeps track of release from internal stores and another that

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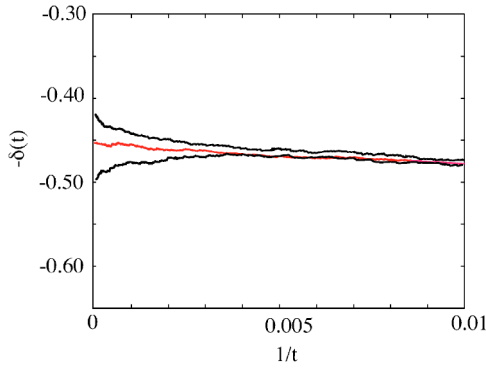[†]Electronic address: stephen.coombes@nottingham.ac.uk

FIG. 1. (Color online) A plot of $-\delta(t)$ as a function of t^{-1} for three different level of threshold noise, $\beta=0.23$ (upper curve), $\beta=0.2$ (middle curve), and $\beta=0.18$ (lower curve). System parameters: $D=30\ \mu m^2\ s^{-1}$, release site spacing $d=2\ \mu m$, $\tau=10$ ms, $\tau_d=200$ ms, $R=50$, $\sigma=1$, and $u_c=0.1$.
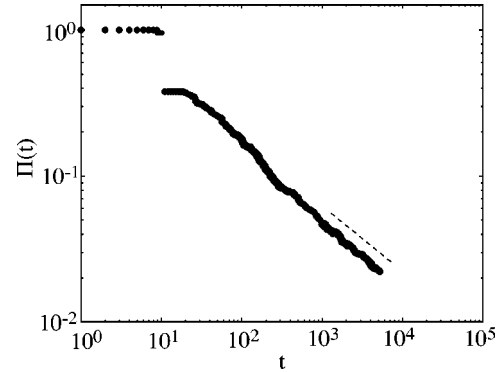

FIG. 2. The distribution of survival times for the stochastic FDF model at the critical noise defining the transition between propagating and abortive waves. For large t, $\Pi(t)$ scales as $t^{-0.45}$, indicating that this model belongs to the two-dimensional DP universality class.

describes the spread of Ca^{2+} by diffusion. Note that Eq. (1) only has to be sampled in discrete time to fully specify cell behavior since the $a_n(p)$ remain unchanged over the duration of release.

The stochastic nature of localized Ca^{2+} release is incorporated within the model via the introduction of a simple probabilistic rule. It is assumed that the probability of a release event (i.e., the probability that $a_n(p)=1$) is given in terms of the probability that $u(\mathbf{r}_n, p\tau)$ is bigger than some threshold u_c—i.e.,

$$P(a_n(p)=1)=f(u_n(p)-u_c)\prod_{m=1}^{\min(R,p)}[1-f(u_n(p-m)-u_c)],$$

(4)

for some function $f(u)$. Here $u_n(p)\equiv u(\mathbf{r}_n, p\tau)$ and $R\in\mathbb{Z}$. The first term on the right in Eq. (4) is the probability that $u_n(p)>u_c$ while the second term ensures that release events are unlikely to be closer than $R\tau$, which we take to be the refractory time scale. A natural choice for $f(u)$ is

$$f(u)=\left\{\frac{1}{1+e^{-\beta u}}-\frac{1}{1+e^{\beta u_c}}\right\}(1+e^{-\beta u_c}),$$

(5)

where $\beta>0$, so that the probability of release is zero when $u=0$ and tends to one as $u\to\infty$. Importantly, the level of noise can be linked to the number N of calcium release channels per cluster. In [5] it is shown that a sigmoidal form for the probability of release emerges from the mathematical analysis of a more detailed stochastic receptor cluster model, with steepness of the sigmoid controlled by N. Hence, in this heuristic model we use the parameter β to mimic finite-size effects, such that with decreasing β the system becomes more noisy (as expected with decreasing N). Thus, the stochastic FDF model is defined by Eq. (1) with the $a_n(p)$ treated as random variables such that $P(a=1)$ is given by (4).

Release events are easily calculated since Ca^{2+} concentration at the release sites are defined as a sum of two terms that are both amenable to fast numerical evaluation. In particular $u_p(\mathbf{r})$ may be written in terms of the *basis* functions $G(\mathbf{r}$

$-\mathbf{r}_n, p\tau)$. Since these are fixed for all time, they need only be computed once. The convolution in Eq. (1) may be performed efficiently using fast Fourier transform (FFT) techniques. Once again the FFT of $G(\mathbf{r},\tau)$ need only be computed once, so that it is only necessary to successively construct the FFT of $u_p(\mathbf{r})$ for $p=0,1,2,\ldots$ .. The statistical properties of dynamical behavior in the one-dimensional stochastic FDF model have previously been studied in [11]. Note that the first evidence for directed percolation in a one-dimensional model of stochastic calcium release is due to Bär *et al.* [13]. In what follows we will focus on the statistical properties of spreading waves that arise naturally in *two* dimensions, more realistic of real cells.

Sufficiently large threshold noise in the stochastic FDF model is able to terminate a wave prematurely, suggesting the interesting possibility of a critical noise that defines a border between waves which *survive* or eventually go *extinct*. In the latter case the system becomes trapped in a completely inactive or absorbing state. This is typical of models which exhibit a nonequilibrium phase transition belonging to the DP universality class. Precisely at the critical point the survival probability $\Pi(t)$ that a wave initiated from a single site has not aborted after t time steps is expected to scale asymptotically as $t^{-\delta}$, where δ is a universal scaling parameter. The current estimate for the critical exponent of DP in two dimensions is $\delta=0.451$ [14]. The analysis of the DP universality class is highly nontrivial and it has not been possible to obtain critical exponents for models in this class analytically.

We shall treat the effective noise parameter β as the one controlling the DP phase transition and denote the critical value of β at the phase transition between propagating and abortive waves by β_c. To obtain a good estimate of the critical exponent δ we construct the effective exponent:

$$\delta(t)=\frac{\ln[\Pi(rt)/\Pi(t)]}{\ln r},$$

(6)

where $\ln r$ is the distance used for estimating the slope of $\Pi(t)$. For $\beta\neq\beta_c$, $\delta(t)$ will deviate from a straight line (in the

large t limit) so that plots of $\delta(t)$ for various choices of β may be used to predict β_c. An estimate of δ is obtained by extrapolating the behavior of $\delta(t)$ to $t^{-1}=0$. In Fig. 1 we plot $\delta(t)$ for various β, showing that for our choice of systems parameters $\beta_c \sim 0.2$, with the release sites placed on a square lattice of period d. In Fig. 2 we plot the corresponding distribution of survival times for the activation process started from a single active site placed in the middle of the left edge of a square lattice. Percolation has been checked over sites from one (the left) edge to the opposite (right) edge of the square lattice. Using our value of β_c we find $\delta \sim 0.45$, suggesting that the stochastic FDF model in two dimensions does indeed belong to the DP universality class.

To date, the critical behavior of DP, especially the values of the critical exponents, has not yet been confirmed experimentally. It has been estimated in various dimensions only thanks to extensive numerical simulations, transfer matrix techniques, series expansions, and field-theoretic calculations [15]. The analysis of the computationally inexpensive two-dimensional model of calcium release that we have presented here lends further support to the idea that the experimental realization of DP may be found in cell biology and, specifi-

cally, intracellular calcium waves [15]. Moreover, simulations of heterogeneous versions of the model, some of which are presented in [5,16], show that the qualitative behavior of the stochastic FDF model is robust to perturbations in both the spatial distribution of release sites (away from a regular lattice) and the spatial distribution of the threshold (away from the choice of a fixed threshold at every release site). Since moderate changes in, say, external $[Ca^{2+}]$ can switch a cell from a saltatory wave-propagating regime to a wave-blocking one [2] further analysis of the stochastic FDF cell model will be useful in determining the critical levels of extracellular $[Ca^{2+}]$ and values of other controllable variables, necessary for an experiment to exhibit the types of abortive waves that would signal the onset of a DP phase transition. Since directed percolation is the testing ground for many ideas about nonequilibrium phase transitions, this is a potentially explosive subject area and may encourage a further cross fertilization of ideas between the fields of computational cell biology and nonequilibrium statistical physics.

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