

NONLINEAR RANDOM REACTION-DIFFUSION SYSTEMS

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ABSTRACT. The various fields of mathematical biology in which reaction-diffusion systems occur are briefly reviewed. Progress made with linear stochastic partial differential equations is indicated. Two methods of analysis of nonlinear systems are outlined. The first consists of studying the multidimensional Markov process associated with the kinetic equations. Secondly, a perturbative approach is outlined and examples given.

1. INTRODUCTION

Our purpose in this article is to determine some properties of the solutions of stochastic nonlinear reaction-diffusion systems. We will first examine areas of mathematical biology in which such systems of equations either have occurred or are likely to occur. We will see that there is overlap with theoretical physics. We begin therefore with a brief summary of several deterministic reaction-diffusion systems. We restrict our attention to one space-variable; generalization to several presents no difficulty.

Genetics

Fisher (1937) and Kolmogorov et al (1937) considered the scalar equation

$$u_t = Du_{xx} + su(1 - u)$$

in connection with the frequency u of a gene which diffuses in space and has selection coefficient s . (We use subscripts t and x to denote partial derivatives with respect to these variables). The original problem to be studied here involved random quantities, so Fisher's equation is one in which averages have been taken. Note, however, that if one adds a zero mean noise term to Fisher's equation, the mean will not in general be the same as the solution of the deterministic equation. See Aronson and Weinberger (1978) for

analysis of related equations.

Neurobiology

(a) Action Potentials

Perhaps the first reaction-diffusion system which had a firm empirical foundation was that used to describe nerve membrane potential transients including action potentials. This is the Hodgkin-Huxley (1952) system

$$\begin{aligned} V_t &= DV_{xx} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + g_l (V - V_l) + I \\ n_t &= \alpha_n (1 - n) - \beta_n n, \\ m_t &= \alpha_m (1 - m) - \beta_m m, \\ h_t &= \alpha_h (1 - h) - \beta_h h, \end{aligned}$$

where V is electric potential, $D > 0$ contains physical constants, V_K , V_{Na} and V_l are equilibrium potentials, \bar{g}_K , \bar{g}_{Na} and g_l are constants and n , m and h are respectively the potassium activation, sodium activation and sodium inactivation. The applied current density is $I = I(x, t)$ and this quantity along with any of the conductances may be random.

Nagumo et al (1962) introduced simpler equations whose solutions also have propagating pulse-like solutions. The system is two-dimensional containing a voltage variable V and a recovery variable W :

$$\begin{aligned} V_t &= DV_{xx} + V(1 - V)(V - a) - W + I \\ W_t &= b(V - \gamma W), \end{aligned} \tag{1}$$

where $0 < a < 1$ and b, γ are constants. A random input current term $I(x, t)$ converts this to a nonlinear system of stochastic partial differential equations.

(b) Spreading Depression

Slowly moving (\sim mm/minute) waves of potential called spreading depression may be elicited in many brain structures. There are concomitant changes in concentrations of K^+ , Na^+ , Cl^- , Ca^{++} as well as increased metabolic rate and transient changes in neural firing rates. The phenomenon was first noticed by Leao (1944) and many fascinating properties are reviewed in Bures et al (1974). It has recently been implicated in transient global amnesia (Olesen and Jorgensen, 1986) and is used as an anatomical tool (see e.g., Guiffrida et al, 1986). It is an obvious candidate for occurrence during concussion since one method of instigating it is mechanical

pressure. Coupled with the possibility of reverberation around cortical pathways (Shibata and Bures, 1972) it is also an obvious candidate for arising during, or causing, certain comas.

Mathematical models for spreading depression are complex because of the large number of interacting variables and the different time and space scales involved. The first simplified model was proposed by Grafstein (and Hodgkin) (1963) which was actually the first of Nagumo's equations given above in which V is now the potassium ion concentration in the extra-cellular space. A more elaborate model consists of a multi-component reaction-diffusion system (Tuckwell and Hermansen, 1981). Many of the fundamental properties of the phenomenon are nevertheless embraced in simplified model (Tuckwell, 1981) consisting of the two equations,

$$\begin{aligned}u_t &= D_1 u_{xx} + \alpha(u - c_1 v^2 - c_2) \\v_t &= D_2 v_{xx} + \beta(v + c_3 u^2),\end{aligned}$$

in which u and v represent the concentrations of potassium and calcium ions in the extracellular space. There are many sources of random fluctuations in these systems; one example is K^+ extruded during spontaneous neural discharges.

Population Growth

Both animal and plant populations diffuse and grow and decline due to various forces including those due to interactions between species. An example is provided by an equation proposed to describe budworm populations in North American forests:

$$u_t = u_{xx} + u(1 - u) - \frac{c_1 u^2}{(c_2 + u^2)},$$

where c_1 , c_2 are constants. This is a re-scaled version of an equation of Ludwig et al (1978).

Epidemics

Diseases may be transmitted and spread throughout a population. Such phenomena have been modeled with reaction-diffusion equations. Mollison (1977) discusses a number of such models and describes methods for quantifying the velocity of spread.

Development Biology

Reaction-diffusion equations have been employed as models for pattern formation and the growth of organs in development. This was first done by Turing (1952) and subsequently by Gierer and Meinhardt (1972) (See Segel, 1984, for an interesting introduction).

It is interesting to note that in the last several years, random nonlinear reaction-diffusion equations have arisen also in

quantum field theory (see for example Parisi and Wu, 1981; Floratos and Iliopoulos, 1983). Stochastic partial differential equations viewed as evolution equations in abstract (e.g. Hilbert) spaces are considered in Curtain and Falb (1971) and Curtain (1977).

2. PHENOMENA OF INTEREST

We will be concerned with systems of reaction-diffusion equations whose general form in the absence of noise is

$$\underline{u}_t = \underline{D} \underline{u}_{xx} + \underline{f}(\underline{u}),$$

where $\underline{u} = \underline{u}(x,t)$ has n -components and \underline{D} is an $n \times n$ matrix of diffusion coefficients.

In connection with such systems matters of interest include:

- (i) exact or numerically computed solutions given certain boundary and initial data;
- (ii) on finite spatial domains, the stability properties of stationary solutions;
- (iii) properties of solutions as parameters vary as for example in bifurcation to periodic behavior;
- (iv) the existence and properties of travelling wave solutions. These may be of the saturating type (heteroclinic) as occur in, for example, Fisher's equation, or of the solitary wave type (homoclinic) as occur in nerve action potentials or spreading depression;
- (v) threshold effects such as whether a certain stimulus strength is required to elicit a wave or will any stimulus do this? What changes in parameters will prevent/promote the occurrence of travelling waves?

Effects of Randomness

There are many ways in which randomness enters the reaction-diffusion systems given in the above examples. Then if Ω is a suitable probability space, the quantity \underline{u} above becomes $\underline{u}(x,t,\omega)$ where $\omega \in \Omega$ and the collection of \underline{u} 's is called a random field. The variable ω is suppressed which is the usual practice so that from now on \underline{u} is a random quantity.

One of the simplest classes of random reaction-diffusion systems consists of those with additive noise:

$$\underline{u}_t = \underline{D} \underline{u}_{xx} + \underline{f}(\underline{u}) + \underline{g}$$

where $\underline{g} = \underline{g}(x,t)$ is itself a random quantity. This system of stochastic partial differential equations is interpreted mathematically through stochastic integrals in the same way as one-dimensional equations.

The kinds of properties sought for \underline{u} will depend on the nature of \underline{g} . In particular whether \underline{g} is sustained or transient. To illustrate, consider a stimulus applied to a system capable of supporting solitary waves. If the random stimulus elicits a wave, which it may do with a certain probability, the wave may propagate

undiminished when the stimulus is off. However, if the stimulus remains on, a travelling wave may approximately form but then almost collapse. This may be called wave crash. Of course a wave may re-emerge later depending on the nature of equations. Naturally the stability properties of solutions in the deterministic case are replaced by the corresponding stochastic stability properties.

In the first instance one will be interested in obtaining statistical properties of solutions such as moments and spectral densities. In some cases these may be compared with the experimentally obtained quantities. Before giving some methods for doing this we will briefly examine properties of linear stochastic partial differential equations, especially in relation to neural modeling.

3. LINEAR STOCHASTIC PARTIAL DIFFERENTIAL EQUATIONS AND NEURONAL MODELING

A hierarchy of neural models has been proposed and analyzed (see Tuckwell, 1988a, b, for reviews). The simplest consist of just Poisson processes or Wiener processes with drift. For these, first passage time densities, which correspond to the densities of the interspike time in a renewal process approach, are well known. Next in complexity is Stein's model in which Poisson excitation and inhibition drive a cell and exponential decay tends to restore the rest state. The threshold is fixed or time varying and the determination of first passage times is difficult. Not quite so-difficult, because a transition is made from functional to differential equations, are the problems connected with a diffusion approximation to Stein's model which is the Ornstein-Uhlenbeck process (OUP).

Real neurons, however, have spatial extent which is ignored in the above models. Properly treated, the response of a neuron involves, minimally, the use of cable theory for each dendritic segment. However because this leads usually to an intractable problem, the use of mapping procedures from dendritic trees to single nerve cylinders has proven very fruitful.

Thus one is led to consider as a reasonable approximation for subthreshold behavior of a neuron, a linear cable equation. If there are random inputs at a point x_0 which may be approximated by white noise then we have

$$V_t = V_{xx} - V + \delta(x - x_0)(\alpha + \beta W_t),$$

where $0 < x < L$, say, $t > 0$, $0 < x_0 < L$, α and β are constants and $\{W(t), t \geq 0\}$ is a standard Wiener process.

Results for this stochastic cable equation are relatively easy to obtain with the standard boundary conditions. At fixed x , V can be expanded as an infinite series of OUP's:

$$V(x,t) = \sum_n V_n(t) \phi_n(x),$$

where each $\{V_n(t), t \geq 0\}$ is an OUP,

$$dV_n = (-\mu_n^2 V_n + \alpha \phi_n(x_0))dt + \beta \phi_n(x_0)dW .$$

Here the μ_n 's are eigenvalues and ϕ_n 's are eigenfunctions of the deterministic cable equation. The mean depolarization in the absence of a threshold is given by

$$E(V(x,t)) = \alpha \sum_n \frac{(1 - \exp\{-\mu_n^2 t\})}{\mu_n^2} \phi_n(x) \phi_n(x_0) ,$$

and other statistical properties are easily obtained (see Wan and Tuckwell, 1979 and Tuckwell and Wan, 1980). For this kind of model first passage times may be calculated in two ways. The first consists of truncating the infinite series at a finite number of terms and then using standard first exit time theory for multidimensional diffusions. The second is to use computer simulation for a finite number of terms. Both of these methods were employed in Tuckwell et al (1984). The shape of the firing time density was found to be quite strongly dependent on input position:- an effect which of course could not be discerned with one-dimensional models. In conclusion one sees that linear stochastic cable theory is in principle essentially worked out save for computations and a few mathematical technicalities which are inconsequential for neural modeling.

4. NONLINEAR KINETIC EQUATIONS

If one assumes uniform behavior in space then reaction-diffusion systems become systems of ordinary differential equations sometimes referred to as kinetic equations. Perturbation theory for such systems with additive noise has been given by Freidlin and Wentzell (1984). For example, they treat

$$d\bar{X}(t;\varepsilon) = \bar{g}(\bar{X}(t;\varepsilon))dt + \varepsilon d\bar{W}$$

where ε is a small parameter and \bar{W} is a multi-component standard Wiener process. However, an exact treatment is possible as the following illustrates.

Stochastic Space-Clamped Nagumo Equations

If we set the space derivatives in (1) equal to zero and let I be a one-parameter white noise, we obtain a two-component diffusion with stochastic differential equation

$$dX = (f(X) - Y + \mu)dt + \sigma dW$$

$$dY = b(X - \gamma Y)dt ,$$

where $f(X) = X(1 - X)(X - a)$ and μ and σ are constants. Now define a transition probability function

$$P(x, y, t; \bar{x}, \bar{y}, \bar{t}) = \Pr\{X(t) \leq x, Y(t) \leq y | X(\bar{t}) = \bar{x}, Y(\bar{t}) = \bar{y}\}, \bar{t} \leq t ,$$

with density p . Then from standard Markov process theory, p satisfies a pair of Kolmogorov equations, the forward one being

$$p_t = \frac{\sigma^2}{2} p_{xx} - (p\{f(x) - y + \mu\})_x - (p\{b[x - \gamma y]\})_y.$$

This is a linear partial differential equation which can be easily solved numerically. Solutions, when obtained, will be most interesting as one expects them to portray such things as pulse-like behavior and repetitive firing. These matters will be reported in the near future. Similarly one may obtain equations associated with the space-clamped Hodgkin-Huxley equations. See Tuckwell (1986) for details.

5. SCALAR NONLINEAR RANDOM REACTION-DIFFUSION

Consider a scalar nonlinear stochastic p.d.e. of the form

$$u_t = u_{xx} + f(u) + g, \quad x_1 < x < x_2, \quad t > 0, \quad (2)$$

where g is a random source term. If one takes expectations one obtains a deterministic p.d.e.

$$\bar{u}_t = \bar{u}_{xx} + E(f(u)) + \bar{g},$$

where overbars denote averages. This equation, however is difficult to handle in general. As a first attack we try the following.

Perturbative Approach

Considerable progress is possible with statistical properties of solutions when the additive noise involves a small parameter ϵ . This method of analysis however works just as well when the forcing term is deterministic. Let us put therefore for solutions of (2) with

$$g = \epsilon h$$

$$u = u_0 + \sum_{k=1}^{\infty} \epsilon^k u_k,$$

where u_0 is an equilibrium point for the corresponding kinetic equations and $u_k = u_k(x, t)$. Then on substituting in (2) and matching coefficients of powers of ϵ we obtain a sequence of recursively coupled linear partial differential equations:

$$u_{1,t} = u_{1,xx} + f'(u_0)u_1 + h$$

$$u_{2,t} = u_{2,xx} + f'(u_0)u_2 + f''(u_0)u_1^2/2!$$

$$u_{3,t} = u_{3,xx} + f'(u_0)u_3 + f''(u_0)u_1u_2 + f'''(u_0)u_1^3/3!$$

and so forth.

The first of these equations contains the original driving term

and its solution is easily obtained if a Green's function is available. Assuming that the initial value is $u(x,0) = u_0$, then we have, with $x_1 = a$, $x_2 = b$,

$$u_1(x,t) = u_0 \int_a^b G(x,y;t)dy + \int_a^b \int_0^t G(x,y;t-s)h(y,s)dsdy .$$

Subsequent equations may be similarly integrated to obtain the solution to as many terms as required. In Tuckwell (1987a) the case of a reduced Fitzhugh-Nagumo equation driven by two-parameter white noise $\alpha + \beta W_{xt}$ was considered, where $\{W(x,t)\}$ is a 2-parameter Wiener process. The expansion was about the asymptotically stable point $u_0 = 0$ and the leading term in the expansions is just

$$u_1(x,t) = \alpha \int_a^b \int_0^t G(x,y;t-s)dsdy + \beta \int_a^b \int_0^t G(x,y;t-s)dW(y,s)$$

where the second term is a stochastic integral. Properties of u_1 in this case were given by Tuckwell and Walsh (1983).

The mean of $u(x,t)$ and the covariance of $u(x,s)$ and $u(y,t)$ have been found to order ϵ^3 . This enabled the asymptotic spectral density to be found. Such calculations are very lengthy, involving multiple stochastic integrals, and will not be reproduced in detail here. Some preliminary results are contained in Tuckwell (1987a) and a further report is in preparation.

6. SYSTEMS OF NONLINEAR RANDOM REACTION-DIFFUSION EQUATIONS

In order to study multidimensional equations we introduce Green's function matrices (Tuckwell, 1987c). Thus suppose we are given the system of equations

$$u_t = \underline{D}u_{xx} + \underline{A}u + \underline{f} , \quad (3)$$

where \underline{A} is a constant matrix of coefficients, \underline{D} is a diagonal matrix of diffusion coefficients. Let suitable linear boundary conditions be given and suppose the initial data are

$$u(x,0) = \underline{v}(x) .$$

Let $\underline{G}(x,y;t)$ be the solution of

$$\underline{G}_t = \underline{D}\underline{G}_{xx} + \underline{A}\underline{G} + \delta(t) \delta(x - y)\underline{I}$$

where \underline{I} is an identity matrix and $\underline{G} \equiv 0$ for $t < 0$. Then the solution of (3) is

$$\begin{aligned} u(x,t) &= \int \underline{G}(x,y;t)\underline{v}(y)dy \\ &+ \int \int \underline{G}(x,y;t - s)\underline{f}(y,s)dsdy \end{aligned}$$

Now consider the system

$$\underline{u}_t = \underline{D}u_{xx} + \underline{f}(u) + \varepsilon \underline{g} \quad (4)$$

where $\underline{g} = \underline{g}(x,t)$ is a random (or deterministic) forcing term. Write the solution as

$$\underline{u} = \underline{u}_0 + \sum_{k=1}^{\infty} \varepsilon^k \underline{u}_k$$

where \underline{u}_0 is an asymptotically stable equilibrium point. Then substitution in (4) gives a recursive system of linear systems of stochastic partial differential equations. Each of these equations can be solved immediately using the Green's function matrix.

To illustrate, consider the Nagumo system with diffusion in both components and added Gaussian white noise:

$$u_t = u_{xx} + u(1-u)(u-a) - v + \varepsilon(\alpha + \beta W_{xt})$$

$$v_t = v_{xx} + b(u - \gamma v).$$

Choosing $\underline{u}_0 = 0$, we put

$$\underline{u}_k = \begin{pmatrix} u_k \\ v_k \end{pmatrix}, \quad \underline{A} = \begin{pmatrix} -a & -1 \\ b & -b\gamma \end{pmatrix}$$

and obtain a recursive system whose first three members are

$$\begin{aligned} \underline{u}_{1,t} &= \underline{u}_{1,xx} + \underline{A}\underline{u}_1 + \begin{pmatrix} \alpha + \beta W_{xt} \\ 0 \end{pmatrix} \\ \underline{u}_{2,t} &= \underline{u}_{2,xx} + \underline{A}\underline{u}_2 + \begin{pmatrix} (1+\alpha)u_1^2 \\ 0 \end{pmatrix} \\ \underline{u}_{3,t} &= \underline{u}_{3,xx} + \underline{A}\underline{u}_3 + \begin{pmatrix} 2(1+\alpha)u_1u_2 \\ 0 \end{pmatrix}. \end{aligned}$$

Letting $\underline{G}(x,y;t)$ be the Green's function matrix for

$$\underline{u}_t = \underline{u}_{xx} + \underline{A}\underline{u},$$

and assuming that $\underline{u}(x,0) = 0$, then the first term is

$$\underline{u}_1(x,t) = \int \int_0^t \underline{G}(x,y;t-s) \underline{f}_1(y,s) ds dy$$

where $\underline{f}_1 = (\alpha + \beta W_{xt}, 0)^T$. In this case

$$\underline{G}(x,y;t) = \exp(\underline{A}t)\underline{G}(x,y;t)$$

where \underline{G} is the Green's function for the scalar heat equation

$$u_t = u_{xx}.$$

Thus the required integrals may be easily found and hence the statistical properties of u to any desired order of ε . Some further details are given in Tuckwell (1987b) and a further report is in preparation.

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