TRANSITION DENSITIES FOR SOME CLASSES OF BIOLOGICAL RANDOM PROCESSES

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ABSTRACT.

Stochastic differential equations containing a Gaussian random process are considered. Transition probability density functions are obtained in closed form for processes satisfying certain types of equation which include several applications to random processes in neurobiology, population genetics and population growth. A generalization of a result due to Stratonovich concerning the Fokker-Planck equation of a random process satisfying a certain kind of fluctuation equation.

1. INTRODUCTION

We are interested in finding transition probability density functions(p.d.f.'s), ϕ_X ,for random processes, $X(t)$,which obey stochastic differential equations of the type

$$\frac{dX}{dt} = f(X) + g(X)\lambda(t), \tag{1}$$

where $\lambda(t)$ is a random process. Stochastic equations of this kind have arisen frequently in models for random processes in neurobiology, population genetics and population growth. A brief review of such models is now presented in order to indicate our motivation in attempting to determine ϕ_X from (1).

Neurobiology. $X(t)$ represents a neuron's membrane potential. If the time constant of the membrane is τ ,then, under the influence of a stochastic input process $\mathcal{A}(t)$ which is attributed to randomly arriving inhibitory and excitatory post-synaptic potentials, we may write for a simplified neural model

$$\frac{dX}{dt} = -\frac{X}{\tau} + \mathcal{A}(t). \tag{2}$$

This differs from the usual approach where the incoming signals are assumed Poisson distributed(Johannesma(1968);Roy and Smith (1969); Capocelli and Ricciardi(1971); Cowan(1972)) and the Fokker-Planck equation for ϕ_X heuristically derived. This approach is equivalent to assuming that $\mathcal{A}(t)$ is a Gaussian, delta-correlated stationary random process.

Population Genetics. $X(t)$ represents an allele frequency and is restricted to the unit interval. The differential equation for $X(t)$ is often of the form

$$\frac{dX}{dt} = s(t)X^m(1-X)^n, \tag{3}$$

where $s(t)$ represents the random selection coefficient. When $m = n = 1$ we have the case of no dominance, whereas if $m = 1$ and $n = 2$ or $m = 2$ and $n = 1$ we have complete dominance with the dominant or recessive allele, respectively, favored. This problem has been considered by Kimura(1964,1970) but see Crow and Kimura (1970) for the derivation of the equations and an extensive bibliography. More recently the non-dominant case has been considered by Gillespie(1972) and all three cases treated by Tuckwell(1974b) when $s(t)$ is a white noise process.

One also encounters the problem of random fluctuations in migration rate $m(t)$, in which case , after Crow and Kimura(1956), one has

$$\frac{dX}{dt} = -m(t)(X - \xi), \tag{4}$$

where ξ is the fraction of the allele, whose frequency is $X(t)$, in the immigrants.

<u>Population Growth.</u> Here $X(t)$ is the continuous approximation to the population size. The processes divide into the categories of restricted(or density dependent) growth where $0 \leq X(t) \leq K < \infty$, and unrestricted(density independent) growth where $0 \leq X(t) < \infty$. In the latter category we find Malthusian growth, studied by Levins(1969), Lewontin and Cohen(1969), Goel,Maitra and Montroll (1971) and Capocelli and Ricciardi(1973a).The fluctuation equation is simply

$$\frac{dX}{dt} = r(t)\,X \tag{5}$$

where $r(t)$ is a random process. The only other unrestricted growth process so far considered is one due to Levins(1969) which combines Malthusian growth with random sampling in the deaths. $X(t)$ is assumed to satisfy an equation of the form

$$\frac{dX}{dt} = rX + \sqrt{X}\,\mathcal{E}(t) \tag{6}$$

where r is constant and $\mathcal{E}(t)$ is a random process. This problem has been recently treated by Kiester and Barakat(1973) and an alternative model has been developed by Tuckwell and Lande(1973).

For density dependent growth one may write

$$\frac{dX}{dt} = r(t)X^{m}\left[1-\left(\frac{X}{K}\right)^{n}\right]^{p} \tag{7}$$

where m, n, and p are usually taken to be positive integers, and K is a constant which represents the theoretical upper limit of the population size and is often referred to as the 'carrying capacity'. The case $m = n = p = 1$ results in the so called Pearl-Verhulst logistic growth process and this has been considered by Levins(1969) and Goel,Maitra and Montroll(1971). Another model of interest is that of Malthusian growth with a logarithmic regulation function which was introduced by Capocelli and Ricciardi(1973b). In this case one has

$$\frac{dX}{dt} = X\left(r(t) - \beta \log X\right) \tag{8}$$

where β is a constant. When $r(t) = r$, a constant, this equation represents a restricted process with $0 \leqslant X < e^{r/\beta}$, but when $r(t)$ is a random process on $(-\infty, \infty)$ the upper bound on the population size is removed. It has been noted by Smith and Tuckwell (1973) that the process described by (8) is directly related to the so-called Gompertz growth model which has been treated as a stochastic process by Goel,Maitra and Montroll(1971).

Many of the above models were considered previously by Tuckwell(1974), in the case where the random processes $\lambda(t)$ were delta-correlated. A stochastic differential equation of the form of (1) where

$$f(X) = -\beta g(X) \int^{X} g(X')^{-1} dX', \quad \beta \geqslant 0, \tag{9}$$

was transformed to that of either a Wiener process or an Ornstein-Uhlenbeck process so that if $g(X)$ satisfied certain conditions then the transition p.d.f. could be obtained. In this paper we wish to consider cases where $\lambda(t)$ has a more general covariance kernel. We will find that this generalization can be made and closed form expressions for $\emptyset_X$ still obtained but in some cases at the expense of certain domains of the random process $X(t)$. In part our motivation has been due to the works of Gillespie(1972) and Kiester and Barakat(1973) who considered certain problems(mentioned above) where the fluctuations in $X(t)$ arise from a more general type than a delta-correlated $\lambda(t)$.

2. Transition p.d.f. of X(t) when f(X)=0.

We now consider equation (1) when $f(X)$ is identically zero so that $X(t)$ satisfies

$$\frac{dX}{dt} = g(X)\lambda(t), \quad x_1 < X < x_2. \tag{10}$$

It is assumed that $\lambda(t)$ is a Gaussian process whose mean value function is

$$E[\lambda(t)] = m_\lambda(t), \tag{11}$$

and whose covariance kernel is

$$E[\lambda(t_1)\lambda(t_2)] - E[\lambda(t_1)]E[\lambda(t_2)] = K_\lambda(t_1, t_2). \tag{12}$$

Let the function defined by

$$Y(X) = \int^{X} g(X')^{-1} dX' \tag{13}$$

be strictly monotonic and with non-zero derivative on $(x_1 \ ,x_2\ )$, so that if ϕ_Y is the transition p.d.f. of Y(t), then, after Ash(1972), we have,

$$\phi_Y(y,t|y_0,t_0) = |g(x)|^{-1} \phi_X(x,t|x_0,t_0) \tag{14}$$

Furthermore Y(t) satisfies

$$\frac{dY}{dt} = \lambda(t) \tag{15}$$

and if $m_\lambda(t)$ and $K_\lambda(t_1,t_2)$ are continuous functions of their arguments then we may write

$$E[Y(t)] = Y(t_0) + \int_{t_0}^{t} m_\lambda(t')dt' , \tag{16}$$

$$Var[Y(t)] = 2\int_{t_0}^{t}\left(\int_{t_0}^{t''} K_\lambda(t',t'')dt'\right)dt'' \ . \tag{17}$$

The transition p.d.f. of Y(t) thus satisfies the forward Kolmogorov equation

$$\frac{\partial\phi_Y}{\partial t} = -m_\lambda(t)\frac{\partial\phi_Y}{\partial y} + \frac{\dot{\sigma}_\lambda(t)}{2}\frac{\partial^2\phi_Y}{\partial y^2} \tag{18}$$

where $\dot{\sigma}_\lambda(t)$ is the rate of change of the variance of Y(t) and is given by

$$\dot{\sigma}_\lambda(t) = 2\int_{t_0}^{t} K_\lambda(t',t)dt' . \tag{19}$$

If the range of the function in (13) is $(-\infty\ ,\infty\ )$ the transition p.d.f. of X(t) is immediately found to be

$$\phi_X(x,t|x_0,t_0) =$$

$$\frac{|g(x)|^{-1}}{\sqrt{4\pi\iint K_\lambda(t',t'')dt'dt''}} \exp\left[-\frac{\left(\int_{x_0}^{x} g(x')^{-1}dx' - \int_{t_0}^{t} m_\lambda(t')dt'\right)^2}{4\iint K_\lambda(t',t'')dt'dt''}\right] , \tag{20}$$

where $x_0 = X(t_0)$ and the omitted ranges of integration have been given above.

If the range of X(t) is such that the range of Y(t) is semi-infinite, $[Y(a), \infty)$, say, then we lose considerable generality if we still seek closed form expressions for ϕ_X. We can only successfully use Andre's(1887) reflection principle in the cases where $m_\lambda(t) = k\dot{\sigma}_\lambda(t)$, k being a constant which may be zero. In that event and $x = a$ is regarded as an absorbing barrier we find that

$$\phi_X(x,t|x_0,t_0) = \frac{|g(x)|^{-1}}{\sqrt{4\pi\iint K_\lambda(t',t'')dt'dt''}} \times$$

$$\times \left\{ \exp\left[- \frac{\left(\int_{x_0}^{x} g(x')^{-1}dx' - \int_{t_0}^{t} m_\lambda(t')dt'\right)^2}{4\iint K_\lambda(t',t'')dt'dt''}\right] - \exp\left[2k\int_{x_0}^{a} g(x')^{-1}dx'\right] \times \right. \tag{21}$$

$$\left. \times \exp\left[- \frac{\left(\int_{a}^{x} g(x')^{-1}dx' + \int_{a}^{x_0} g(x')^{-1}dx' - \int_{t_0}^{t} m_\lambda(t')dt'\right)^2}{4\iint K_\lambda(t',t'')dt'dt''}\right]\right\}$$

We note that other kinds of boundary conditions may be imposed (reflecting or mixed) but that absorbing barriers are usually encountered in biological problems. We also point out that Lax (1966) has indicated the method of solution of random processes satisfying equation (10) in certain cases.

3. Transition p.d.f. of X(t) when f(X) has a particular form.

Ideally we would like to find the transition p.d.f. of X(t) satisfying (1) when f(X) is arbitrary. This has not been achieved but we note that many random processes in biology satisfy (1) when f(X) has the form given in equation (9). X(t) then sattisfies

$$\frac{dX}{dt} = g(x)\left[\lambda(t) - \beta\int^{X} g(x')^{-1}dx'\right]. \tag{22}$$

Using the same change of variable as in equation (13) we obtain

$$\frac{dY}{dt} = -\beta Y + \lambda(t), \tag{23}$$

which is in the same form as the fluctuation(Langevin)equation of the Ornstein-Uhlenbeck model for the motion of a Brownian particle which has been formulated by Uhlenbeck and Ornstein(1930) and Wang and Uhlenbeck(1945). The further transformation,

$$Z = e^{\beta t} Y, \tag{24}$$

enables us to write the the simple stochastic differential equation

$$\frac{dZ}{dt} = e^{\beta t}\lambda(t), \tag{25}$$

where by our assumptions above the right hand member is a Gaussian random process. Furthermore, if ϕ_Z is the transition p.d.f. of Z(t) then we must have

$$\phi_Z(z, t|z_0, t_0) = e^{-\beta t}\phi_y(y, t|y_0, t_0). \tag{26}$$

The mean value function of Z(t) is readily found to be

$$E[Z(t)] = z_0 + \int_{t_0}^{t} e^{\beta t'} m_\lambda(t')dt' \tag{27}$$

where $z_0 = Z(t_0)$, and its variance is given by

$$Var[Z(t)] = 2\int_{t_0}^{t}\left(\int_{t_0}^{t''} e^{\beta(t'+t'')} K_\lambda(t', t'')dt'\right)dt'' \tag{28}$$

If we now assume that the range of Y(X) and hence of Z(t) is $(-\infty, \infty)$ then the transition p.d.f. of the original process, X(t), is given by

$$\phi_X(x,t|x_0,t_0) = \frac{|g(x)|^{-1} e^{\beta t}}{\sqrt{4\pi \iint e^{\beta(t'+t'')} K_\lambda(t',t'')\,dt'dt''}} \times$$

$$\times \exp\left[- \frac{\left(e^{\beta t}\int^{x} g^{-1}dx' - e^{\beta t_0}\int^{x_0} g^{-1}dx' - \int_{t_0}^{t} e^{\beta t'} m_\lambda(t')dt' \right)^2}{4\iint e^{\beta(t'+t'')} K_\lambda(t',t'')\,dt'dt''} \right], \tag{29}$$

where $\int g^{-1}dx'$ has been used as an abbreviation for $\int g(x')^{-1}dx'$.

If we now consider the cases where Y(X) has a semi-infinite range we find that we can only write down a closed form expression for ϕ_X when $Y(X) \in [0,\infty)$ or $(-\infty, 0]$ and when the mean value function of $\lambda(t)$ is a constant multiple of the rate of change of the variance of the unrestricted process Z(t) so that

$$m_\lambda(t) = k\,\frac{d}{dt}\left[\mathrm{Var}\,Z(t)\right]. \tag{30}$$

Regarding $x = a = Y^{-1}(0)$ (where Y^{-1} denotes the inverse function) as an absorbing barrier we then find upon utilizing the reflection principle that the transition p.d.f. of X(t) is given by

$$\phi_X(x,t|x_0,t_0) = \frac{|g(x)|^{-1} e^{\beta t}}{\sqrt{4\pi \iint e^{\beta(t'+t'')} K_\lambda(t',t'')\,dt'dt''}} \times$$

$$\times \left\{ \exp\left[- \frac{\left(e^{\beta t}\int^{x} g^{-1}dx' - e^{\beta t_0}\int^{x_0} g^{-1}dx' - \int_{t_0}^{t} e^{\beta t'} m_\lambda(t')dt' \right)^2}{4\iint e^{\beta(t'+t'')} K_\lambda(t',t'')dt'dt''} \right] \right. \tag{31}$$

$$- \exp\left[-2k e^{\beta t_0}\int^{x_0} g^{-1}dx' \right] \times$$

$$\left. \times \exp\left[- \frac{\left(e^{\beta t}\int^{x} g^{-1}dx' + e^{\beta t_0}\int^{x_0} g^{-1}dx' - \int_{t_0}^{t} e^{\beta t'} m_\lambda(t')dt' \right)^2}{4\iint e^{\beta(t'+t'')} K_\lambda(t',t'')dt'dt''} \right] \right\} .$$

We conclude this section by pointing out the appropriateness of the various transition p.d.f.'s for the random biological processes cited in the first section. The expression (20) is certainly the most useful and enables one to describe gene-frequency evolution under the influence of random fluctuations in selection intensity for the three types of dominance already mentioned. It is also appropriate for the exponential growth model and for many density dependent growth problems of the form of (7). The transition p.d.f. (21) is suitable for the problem of random migration rates and their effect on gene-frequency distributions but under limited conditions(given above) on m(t). Equation (29) provides a solution for the neural model of (4) as well as the growth process with logarithmic regulation described by (8). Furthermore the result (31) has only been found to apply to the growth model of equation (6), where, after Levins(1969), $\mathcal{E}(t)$ has a mean value of zero.

4. The generalization of a result due to Stratonovich.

Stratonovich(1963) has obtained the following useful result for random processes satisfying equation (1) when $\lambda(t)$ is a white noise process of mean μ and intensity σ^2. If the Fokker-Planck equation for ϕ_X is wriiten in the usual way

$$\frac{\partial \phi_X}{\partial t} = -\frac{\partial}{\partial x}\left[K_1(x,t)\phi_X\right] + \frac{1}{2}\frac{\partial^2}{\partial x^2}\left[K_2(x,t)\phi_X\right], \tag{32}$$

then the first and second infinitesimal moments to be inserted in this equation are given by the relations

$$K_1(x,t) = K_1(x) = f(x) + \mu g(x) + \frac{1}{4}\frac{dK_2(x)}{dx}, \tag{33}$$

$$K_2(x,t) = K_2(x) = \sigma^2 g(x)^2. \tag{34}$$

We wish to generalize this result when $\lambda(t)$ is Gaussian with mean value function and covariance kernel as defined above in the case where f(X)=0. We then have from equations (13) and (18) that the transition density of X(t) satisfies the Fokker-Planck equation

$$\frac{\partial \phi_X}{\partial t} = -m_\lambda(t)\frac{\partial}{\partial x}\left(g(x)\phi_X\right) + \frac{\dot{\sigma}_\lambda(t)}{2}\frac{\partial}{\partial x}\left[g(x)\frac{\partial}{\partial x}\left(g(x)\phi_X\right)\right]. \tag{35}$$

Utilizing the relation

$$\frac{\partial^2}{\partial x^2}\left[g(x)^2\phi_X\right] = \frac{\partial}{\partial x}\left[g(x)\frac{\partial}{\partial x}\left(g(x)\phi_X\right) + g(x)\phi_X\frac{\partial g(x)}{\partial x}\right], \tag{36}$$

we find that (35) can be written in the form of (32) with first moment given by

$$K_1(x,t) = m_\lambda(t)g(x) + \frac{1}{4}\frac{\partial K_2(x,t)}{\partial x}, \tag{37}$$

where the second moment is

$$K_2(x,t) = \dot{\sigma}_\lambda(t)\, g(x)^2. \tag{38}$$

Thus the result of Stratonovich may be quite simply extended to cases where $\lambda(t)$ is no longer a delta-correlated process.

We note that the solution of (35) under the condition that the range of Y(X) in (13) is $(-\infty, \infty)$ is given by the expression (20). It is worth pointing out the somewhat surprising fact that the transition probabilities obtained explicitly in this paper not only satisfy the Fokker-Planck equation (35) but also the Chapman-Kolmogorov integral equation

$$\phi(x,t|x_0,t_0) = \int dx_1\, \phi(x,t|x_1,t_1)\, \phi(x_1,t_1|x_0,t_0), \tag{39}$$

which is usually associated with a(continuous)Markov process. The processes considered are, of course, not Markov, unless the quantity $\lambda(t)\,dt$ is a Wiener process increment. Thus the time integrals of Gaussian random processes can be used to generate a large class of non-Markovian processes which nevertheless have transition densities satisfying the Chapman-Kolmogorov equation. In the discrete case an example of such a process has been constructed by Feller (1957,p423).

Acknowledgements

The author appreciates useful discussions with Professor L.M.Ricciardi and the financial support of an Alfred P. Sloan Fellowship.

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