Introduction to probability theory and stochastic processes

Cameron Ray Smith¹

¹Department of Systems and Computational Biology ²Dominick P. Purpura Department of Neuroscience ³Department of Pathology Albert Einstein College of Medicine ⁴Santa Fe Institute





Outline

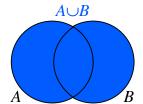
Theoretical background Conceptual introduction Measure theory

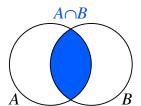
Stochastic processes

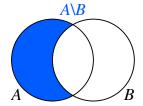
Biological applications

References

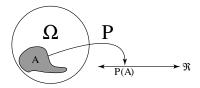
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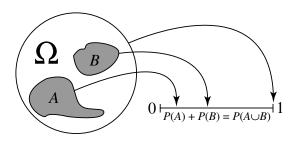




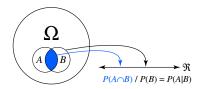
probability measure



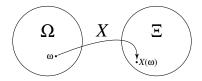
probability axioms



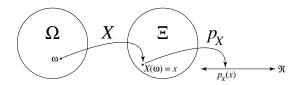
conditional probability



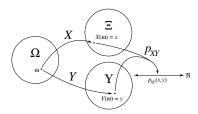
random variables



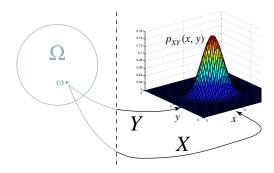
probability densities



joint probability densities



the reality



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• For the general theory of measure spaces, we first need a measurable space (Ω, Σ) , that is a set equipped with a collection Σ of measurable sets complete under certain operations. Then this becomes a measure space (Ω, Σ, μ) by throwing in a function μ from Σ to a space of values (such as the real line) that gets along with the set-theoretic operations that Σ has. If E is a measurable set, then $\mu(E)$ is called the measure of E with respect to μ . [1, 2]

- 1. Given a set Ω ,
- 2. a σ -algebra is a collection of subsets of Ω that is closed under complementation, countable unions, and countable intersections.
- 3. A **measurable space**, by the usual modern definition, is a set Ω equipped with a σ -algebra Σ .
- 4. The elements of Σ are called the **measurable sets** of Ω (or more properly, the measurable subsets of (Ω, Σ)).

A measure space is a measurable space equipped with a measure. There are many different types of measures parametrized by the type of their codomains. Let (Ω, Σ) be a measurable space. A **probability measure** on Ω (due to Kolmogorov) is a function μ from the collection Σ of measurable sets to the unit interval [0,1] such that:

- 1. The measure of the empty set is zero: $\mu(\emptyset) = 0$;
- 2. The measure of the entire space is one: $\mu(\Omega)=1$;
- 3. Countable additivity: $\mu(\bigcup_{i=1}^{\infty} S_i) = \sum_{i=1}^{\infty} \mu(S_i)$ whenever the S_i are mutually disjoint sets—disjoint. (Part of the latter condition is the requirement that the sum on the right-hand side must converge.)

It is sometimes stated (but in fact follows from the previous) that:

- Finitary additivity: $\mu(S \cup T) = \mu(S) + \mu(T)$ whenever S and T are disjoint.
- μ is increasing: $\mu(A) \leq \mu(B)$ if $A \subseteq B$.

Measures can be thought of in terms of integrals and densities are defined in terms of measures. Let A be, for example, one of the measurable sets from the collection of measurable sets, Σ , of our sample space Ω .

- $\mu(A) = \int_A dx$ or $\mu(A) = \int_A p(x) dx$
- $\mu(A)$ represents the mass of A which can be interpreted geometrically as an abstract volume or probabilistically as the probability mass of the event "random variable X takes a value within A"
- A density can then be defined intuitively as a function that transforms some measure μ_1 into a measure μ_2 by pointwise reweighting on the sample space Ω . Thus, densities are always relative measures.
- $d\mu_2(x) = f(x)d\mu_1(x)$ or $\frac{d\mu_2}{d\mu_2}(x) = f(x)$

Does a density always exist?

- A density function f is thus a function that is integrated to obtain information in terms of measure μ_2 from information in terms of measure μ_1 .
- $\mu_2(A) = \int_A d\mu_2(x) = \int_A f(x) d\mu_1(x)$ is not defined if $u_1(A) = 0$ and $u_2(A) \neq 0$.
- If this is never the case for all $A \in \Sigma$, then μ_2 is referred to as absolutely continuous with respect to μ_1 and this relationship is written $\mu_2 \ll \mu_1$.
- This conclusion is formalized in the Radon-Nikodym **theorem** which states that μ_2 has a density with respect to μ_1 if and only if $\mu_2 \ll \mu_1$.

... so the answer is ... no, which is the reason for going through all this abstract stuff

Theoretical background

Stochastic processes
Definition
Gaussian noise
Markov processes
Master equation

Biological applications

References

Intuitively, **stochastic processes** are ∞ -dimensional probability distributions.

 The order of this evolution can be described through the use of an index and an index set respectively t ∈ T.

Definition

Consider a random experiment with sample space Ω , a σ -algebra Σ , a base probability measure $\mu: \Sigma \to [0,1]$, and a collection of random variables X_t indexed by a set T. A **stochastic process** is then defined by the set $\{X_t, t \in T\}$.

• This definition can be specialized to the case of discrete or continuous stochastic processes by taking the index set to be $T \in \mathbb{N}$ or $T \in \mathbb{R}_+$ respectively.

In the discrete case imagine indexing by natural numbers, \mathbb{N} , such that the process could be represented as a sequence $\{X_n, n=0,1,2,\ldots\}$.

How should we understand the continuous case?

- For each $\omega \in \Omega$, consider $X_t(\omega) = g_\omega(t)$. $g_\omega(t)$ can then be thought of as a function of t that realizes or samples from the stochastic process.
- For any given t, X_t is a random variable, thus to completely describe the stochastic process we need a description of the joint family of random variables $\{X_t, t \in T\}$ as opposed to just the individual random variables as if they were independent.
- For any discrete subset of times $\{t_1, \ldots, t_n\}$ such that $t_1 < \cdots < t_n$ and associated $\{x_1, \ldots, x_n\}$ we must determine $P(X_{t_1} \le x_1, \ldots, X_{t_n} \le x_n)$

How should we understand the continuous case?

• The **Kolmogorov extension theorem** ensures that the potentially infinite distribution $\{X_t, t \in T\}$ where, for example $T \in \mathbb{R}_+$, i.e. $T = [0, \infty)$, can be generated from the finite-dimensional families defined by $P(X_{t_1} < x_1, \ldots, X_{t_n} < x_n)$ [3]

- Exchangeability: for all permutations π of $1, \ldots, n$ and x_1, \ldots, x_n , $P(X_{t_1} \leq x_1, \ldots, X_{t_n} \leq x_n) = P(X_{t_{\pi(1)}} \leq x_{\pi(1)}, \ldots, X_{t_{\pi(n)}} \leq x_{\pi(n)})$
- Extendability: for all $x_1, ..., x_n$ and $t_{n+1}, ..., t_{n+m}$, $P(X_{t_1} \le x_1, ..., X_{t_n} \le x_n) = P(X_{t_1} \le x_1, ..., X_{t_n} \le x_n, X_{t_{n+1}} < \infty, ..., X_{t_{n+m}} < \infty)$

How should we understand the continuous case?

• Given that the conditions are satisfied then there exists a probability space $(\Omega, \Sigma, \mathbb{P})$ with an associated stochastic process $X_t: T \times \Omega \to \mathbb{R}^n$ with the families X_{t_1}, \ldots, X_{t_n} as finite-dimensional marginal distributions.

If random variables at different points in time are mutually independent then the joint distribution is simply the product of all its marginals

$$p_2(x_1, t_1; x_2, t_2) = p_1(x_1, t_1)p_1(x_2, t_2)$$

The covariance of this distribution is

$$<(X_{t_1} - \mu_1)(X_{t_2} - \mu_2) >$$

= $\int dx_1 dx_2 (x_1 - \mu_1)(x_2 - \mu_2) p_2(x_1, t_1; x_2, t_2) = 0$ (1)

where the mean value at time t_i is

$$\mu_i = < X_i > = \int dx \times p_1(x, t_i)$$

If $p_1(x,t)$ is independent of time such that $p_1(x,t) \equiv p_1(x)$ then the associated sequence of random variables is said to be identically and independently distributed (IID) with mean μ and variance σ^2

$$X(t) \sim IID(\mu, \sigma^2)$$

If $p_1(x)$ is the density of a normal distribution then this stochastic process is referred to as Gaussian noise or white noise. The X(t) are then independently and normally distributed at each point in time, which we denote as

$$X(t) \sim N(0, \sigma^2)$$

If we denote Gaussian noise as $\eta(t)$ then $<\eta(t)>=0$. The covariance function between two timepoints in the discrete and continuous cases respectively are

$$<\eta(t)\eta(t')> = \sigma^2\delta_{tt'},$$
 (2)

$$<\eta(t)\eta(t')> = \sigma^2\delta(t-t').$$
 (3)

The Fourier transform of the stationary two-time covariance function for a continuous-time process is

$$F(\omega) = \int d\tau < \eta(t)\eta(t+\tau) > e^{i\omega\tau} = \sigma^2.$$

first order Markov processes are characterized by the so-called Markov condition

$$p_n(x_n, t_n | x_{n-1}, t_{n-1}; \dots; x_1, t_1) = p_2(x_n, t_n | x_{n-1}, t_{n-1}).$$

The Markov condition means that the probability for a transition from x_{n-1} to x_n during the time interval from t_{n-1} to t_n is independent of the x_i associated to timepoints prior to t_{n-1} . All the information that is useful for attempting to make predictions is embodied in the present.

The conditional probability $p_2(x, t|x', t')$ is named the transition probability. A Markov process whose transition probability depends only on the time interval is called homogeneous. If, additionally, $p_1(x, t)$ is independent of t, then the process is called stationary. A Markov process is uniquely determined through $p_1(x, t)$ and $p_2(x_2, t_2|x_1, t_1)$. This is a result of the fact that the Markov property ensures that all joint distributions p_n for n > 2 can be expressed in terms of p_1 and p_2 as

$$p_{n}(x_{n}, t_{n}; x_{n-1}, t_{n-1}; \dots; x_{1}, t_{1})$$

$$= p_{2}(x_{n}, t_{n}|x_{n-1}, t_{n-1})p_{2}(x_{n-1}, t_{n-1}|x_{n-2}, t_{n-2}) \cdots p_{1}(x_{1}, t_{1}).$$
(4)

mth order Markov processes are characterized by a generalized form of the first-order Markov condition

$$p_{n}(x_{n}, t_{n}|x_{n-1}, t_{n-1}; \dots; x_{1}, t_{1})$$

$$= p_{m+1}(x_{n}, t_{n}|x_{n-1}, t_{n-1}, \dots, x_{n-m}, t_{n-m}). \quad (5)$$

The m^{th} order Markov condition means that the probability for a transition from x_{n-1} to x_n during the time interval from t_{n-1} to t_n is independent of the x_i associated to timepoints prior to t_{n-m} . All the information that is useful for attempting to make predictions is embodied in a history that is m timesteps long.

Stochastic processes

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The hidden Markov process is defined on a pair of random variables (I, X). I is taken to be a discrete random variable over some subset of natural numbers $\{1, 2, \dots, k\} \subset \mathbb{N}$. Realizations of X are in \mathbb{R}^m . Assuming one exists at all, there is a joint density function p(i, x; t) whose marginals are denoted

$$p(i;t) = \int d^m x \ p(i,x;t)$$
 (6)

$$p(x;t) = \sum_{i=1}^{k} p(i,x;t)$$
 (7)

and whose conditional densities are denoted

$$p(x;t|i;t) = \frac{p(i,x;t)}{p(i;t)}$$

$$p(i;t|x;t) = \frac{p(i,x;t)}{p(x;t)}$$
(8)

$$p(i;t|x;t) = \frac{p(i,x;t)}{p(x;t)}$$
 (9)

The dynamics of the hidden Markov process can be specified under the assumption of a Gaussian first-order Markov process. In this case we can express the transition probability, where p(x, t|i, i', x'; t') is a Gaussian distribution and t > t', as

$$p(i, x; t|i', x'; t') = p(x, t|i, i', x'; t')p(i; t|i', x'; t').$$

Stochastic processes

The Wiener process (also called Brownian motion or random walk) has transition probability

$$p_2(x,t|x',t') = \frac{1}{\sqrt{2\pi(t-t')}}e^{-(x-x')^2/2(t-t')},$$

and $p_1(x, t)$ can be taken to be

$$p_1(x,t) = \frac{1}{\sqrt{2\pi t}}e^{-x^2/2t}.$$

As $t \to 0$, $p_1(x,t)$ approaches a δ function and for $t \neq 0$, $p_1(x,t)$ is a Gaussian distribution with mean 0 and variance t. This function is also the solution of the deterministic partial differential heat conduction equation in one dimension.

Stochastic processes

The Poisson process (a special case of more general point processes) for the random variable N(t) denoting the number of events of some type that have occurred up to time t for the discrete variable $n \subset \mathbb{N}$, $\alpha > 0$, and for $t_2 > t_1$ has transition probability

$$p_2(n_2, t_2 | n_1, t_1) = \begin{cases} \frac{[\alpha(t_2 - t_1)]^{n_2 - n_1}}{(n_2 - n_1)!} e^{-\alpha(t_2 - t_1)}, & \text{for } n_2 \ge n_1, \\ 0 & \text{for } n_2 < n_1, \end{cases}$$

and probability that n events have taken place in the interval [0, t]

$$p_1(n,t) = \frac{(\alpha t)^n}{n!} e^{-\alpha t}$$

A trajectory of the Poisson process n(t) consists of unit jumps at random times.

The Chapman-Kolmogorov equation is a statement of the transitivity induced by the Markov property that the transition probability of any Markov process must satisfy

Stochastic processes

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$$p_2(x_3, t_3; x_1, t_1) = \int dx_2 \ p_3(x_3, t_3; x_2, t_2; x_1, t_1)$$

$$= \int dx_2 \ p_2(x_3, t_3|x_2, t_2) p_2(x_2, t_2|x_1, t_1) p_1(x_1, t_1)$$

And the conditional probability is then

$$p_2(x_3, t_3|x_1, t_1) = \int dx_2 \ p_2(x_3, t_3|x_2, t_2) p_2(x_2, t_2|x_1, t_1)$$

Master equations

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$$\lim_{t\to\infty} p_1(x,t) \equiv p_{stat}(x) \neq 0$$

exists, then p_{stat} is named the stationary distribution, which is achieved as t approaches ∞. Now, because

$$p_1(x_3, t_3) = \int dx_2 \ p_2(x_3, t_3|x_2, t_2) p_1(x_2, t_2),$$

then for the stationary distribution

$$p_{stat}(x) = \int dx_2 \ p_2(x, t_3|x_2, t_2) p_{stat}(x_2),$$

for all t_2 and t_3 .

stochastic process.

Master equations

We may place some conditions on the infinitesimal-time behavior of the transition probabilities in order to use the Chapman-Kolmogorov equation to derive a differential equation specifying the dynamics of the density function characterizing the

Imagine a Markov process with transition probability $p_2(x, t + \tau | x'', t)$. For small (and secretly infinitesimal) values of τ the form of this transition probability will be taken to be

$$\begin{aligned} \rho_2(x, t + \tau | x'', t) \\ &= [1 - a(x, t)\tau]\delta(x - x'') + \tau w(x, x'', t) + O(\tau^2) \end{aligned}$$

Master equations

Given that the transition probability $p_2(x, t + \tau | x'', t)$ is assumed to be normalized, which means that the integral over its domain of definition is 1, then the equation

$$p_2(x, t + \tau | x'', t)$$
= $[1 - a(x, t)\tau]\delta(x - x'') + \tau w(x, x'', t) + O(\tau^2)$

implies that

$$a(x'',t) = \int dx \ w(x,x'',t)$$

From the Chapman-Kolmogorov equation we can derive

Stochastic processes

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$$p_{2}(x, t + \tau | x', t') = \int dx'' \ p_{2}(x, t + \tau | x'', t) p_{2}(x'', t | x', t')$$

$$= [1 - a(x, t)\tau] p_{2}(x, t | x', t')$$

$$+ \tau \int dx'' \ w(x, x'', t) p_{2}(x'', t | x', t')$$

$$+ O(\tau^{2})$$

And the master equation results from taking the limit $au
ightarrow \infty$

$$\frac{\partial}{\partial t} p_2(x, t|x', t') = \int dx'' \ w(x, x'', t) p_2(x'', t|x', t') - \int dx'' \ w(x'', x, t) p_2(x, t|x', t')$$

Master equations

A more intuitive form of the master equation given knowledge of the form of the initial distribution is obtained via multiplication by $p_1(x',t')$ and integration over x' to obtain

$$\frac{\partial}{\partial t} p_1(x,t) = \int dx' \ w(x,x',t) p_1(x',t) - \int dx' \ w(x',x,t) p_1(x,t)$$

If the variable x is taken to be discrete $n \in \mathbb{N}$, then $p_n(t) \equiv p_1(x,t)$ and $w_{nn'}(t) \equiv w(x,x',t)$ results in

$$\dot{p}_{n}(t) = \Sigma_{n'}[w_{nn'}(t)p_{n'}(t) - w_{n'n}(t)p_{n}(t)]$$

This discrete form is perhaps the most intuitive. It says that the change in probability of finding the label n at time t can be described in terms of two components. The first is the number of transitions into (or creations) $n' \rightarrow n$ and the second is the number of transitions from (or annihilations) $n \to n'$.

Master equations

$$\dot{p}_n(t) = \sum_{n'} [w_{nn'}(t)p_{n'}(t) - w_{n'n}(t)p_n(t)]$$

This discrete state form is perhaps the most intuitive so far. It says that the change in probability of finding the label n at time t can be described in terms of two components. The first is the number of transitions into (or creations) $n' \to n$ and the second is the number of transitions from (or annihilations) $n \to n'$.

Biological applications

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References

The Fokker-Planck Equation

Stochastic differential equations

Outline

Theoretical background

Stochastic processes

Biological applications Population genetics Gene expression

References

Population genetics

TODO: topics to cover

Determinism and stochasticity in gene expression

- Elowitz [4]
- Paulsson [5, 6, 7]
- Van Oudenaarden [8, 9]

Outline

Theoretical background

Stochastic processes

Biological applications

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