

Introduction to probability theory and stochastic processes

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August 17, 2012

Outline

Theoretical background

Conceptual introduction

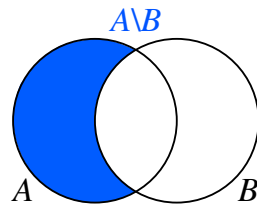
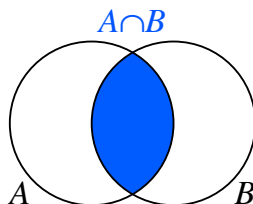
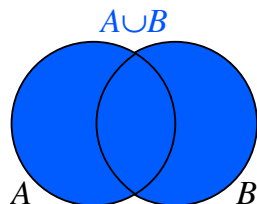
Measure theory

Stochastic processes

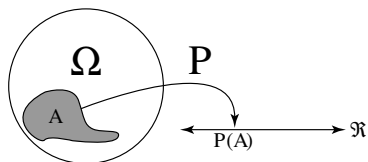
Biological applications

References

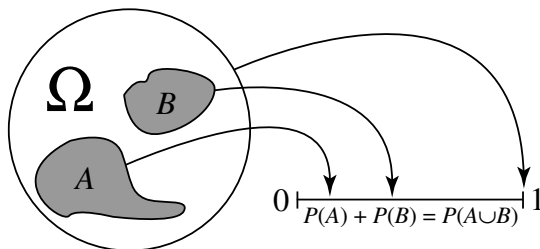
sets



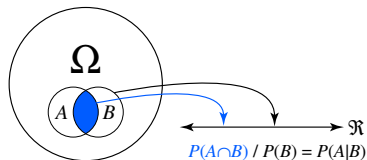
probability measure



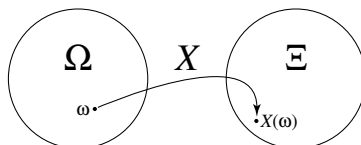
probability axioms



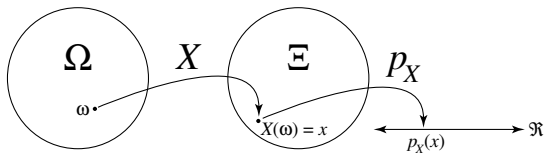
conditional probability



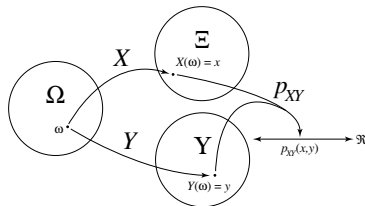
random variables



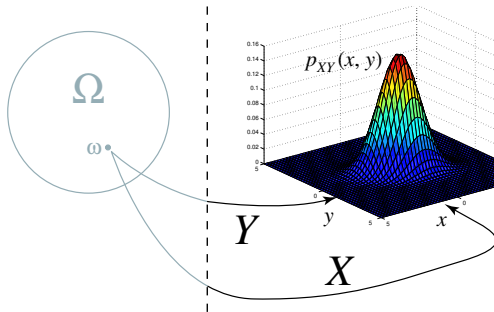
probability densities



joint probability densities



the reality



- 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 $\frac{d\mu_2}{d\mu_1}(x) = f(x)$

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 $\mu_1(A) = 0$ and $\mu_2(A) \neq 0$.
- 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

Outline

Theoretical background

Stochastic processes

Definition

Examples

Biological applications

References

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

- In most applications, stochastic processes model systems that evolve randomly in time, which is likely the origin of the word *process* in the name, but stochastic processes are not restricted to the temporal metaphor. Think about *order* as a generalization of time.
- The order of this evolution can be described through the use of an index and an index set respectively $t \in T$.

Definition

Consider a random experiment with sample space Ω , a σ -algebra Σ , a base probability measure $\mu : \Sigma \rightarrow [0, 1]$, 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 $\{X_n, n = 0, 1, 2, \dots\}$.

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 $\{t_1, \dots, t_n\}$ such that $t_1 < \dots < t_n$ and associated $\{x_1, \dots, x_n\}$ we must determine $P(X_{t_1} \leq x_1, \dots, X_{t_n} \leq x_n)$

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 $P(X_{t_1} \leq x_1, \dots, X_{t_n} \leq x_n)$ [3]

The necessary conditions are

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

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 $X_t : T \times \Omega \rightarrow \mathbb{R}^n$ with the families X_{t_1}, \dots, X_{t_n} as finite-dimensional marginal distributions.

Markov processes

The Chapman-Kolmogorov equation

The Master equation

The Fokker-Planck Equation

Stochastic differential equations

Outline

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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]

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References

- [1] David Insua, Fabrizio Ruggeri, and Mike Wiper.
Bayesian Analysis of Stochastic Process Models.
Wiley, 2012.
- [2] NLab.
Measure space.
<http://ncatlab.org/nlab/show/measure+space>.
- [3] Bernt Øksendal.
Stochastic Differential Equations: An Introduction with Applications.
Springer, 2010.
- [4] Peter S Swain, Michael B Elowitz, and Eric D Siggia.
Intrinsic and extrinsic contributions to stochasticity in gene expression.
PNAS, 99(20):12795–800, October 2002.

- [5] Johan Paulsson.
Summing up the noise in gene networks.
Nature, 427(6973):415–8, January 2004.
- [6] Andreas Hilfinger and Johan Paulsson.
Separating intrinsic from extrinsic fluctuations in dynamic biological systems.
PNAS, 2011(9), July 2011.
- [7] Ioannis Lestas, Glenn Vinnicombe, and Johan Paulsson.
Fundamental limits on the suppression of molecular fluctuations.
Nature, 467(7312):174–178, September 2010.
- [8] Mukund Thattai and Alexander van Oudenaarden.
Stochastic gene expression in fluctuating environments.
Genetics, 167(1):523–30, May 2004.

- [9] B. Munsky, G. Neuert, and A. van Oudenaarden.
Using Gene Expression Noise to Understand Gene Regulation.
Science, 336(6078):183–187, April 2012.