GRADUATE STUDIES 199

Applied Stochastic Analysis

Weinan E Tiejun Li Eric Vanden-Eijnden





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 $10 \ 9 \ 8 \ 7 \ 6 \ 5 \ 4 \ 3 \ 2 \ 1 \qquad 24 \ 23 \ 22 \ 21 \ 20 \ 19$ 

To our families

Hongjun, Jane, and Ilene Xueqing, Baitian, and Baile Jasna, Colette, Pauline, and Anais et Lilia

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## Introduction to the Series

It is fairly well accepted that to learn pure mathematics, a student has to take analysis, algebra, geometry, and topology. Until now there has not been an equally well-accepted curriculum for applied mathematics. There are many reasons one can think of. For one thing, applied mathematics is truly very diverse. Traditional subjects such as numerical analysis, statistics, operational research, etc., can all be regarded as part of applied mathematics. Beyond that, a huge amount of applied mathematics is practiced in other scientific and engineering disciplines. For example, a large part of fluid dynamics research has become computational. The same can be said about theoretical chemistry, biology, material science, etc. The algorithmic issues that arise in these disciplines are at the core of applied mathematics. Machine learning, a subject that deals with mathematical models and algorithms for complex data, is, at its heart, a very mathematical discipline, although at the moment it is much more commonly practiced in computer science departments.

In 2002, David Cai, Shi Jin, Eric Vanden-Eijnden, Pingwen Zhang, and I started the applied mathematics summer school in Beijing, with the objective of creating a systematic and unified curriculum for students in applied mathematics. Since then, this summer school has been repeated every year at Peking University. The main theme of the summer school has also evolved. But in the early years, the main topics were applied stochastic analysis, differential equations, numerical algorithms, and a mathematical introduction to physics. In recent years, a mathematical introduction to machine learning has also been added to the list. In addition to the summer school, these courses have also been taught from time to time during regular terms at New York University, Peking University, and Princeton University. The lecture notes from these courses are the main origin of this textbook series. The early participants, including some of the younger people who were students or teaching assistants early on, have also become contributors to this book series.

After many years, this series of courses has finally taken shape. Obviously, this has not come easy and is the joint effort of many people. I would like to express my sincere gratitude to Tiejun Li, Pingbing Ming, Shi Jin, Eric Vanden-Eijnden, Pingwen Zhang, and other collaborators involved for their commitment and dedication to this effort. I am also very grateful to Mrs. Yanyun Liu, Baomei Li, Tian Tian, Yuan Tian for their tireless efforts to help run the summer school. Above all, I would like to pay tribute to someone who dedicated his life to this cause, David Cai. David had a passion for applied mathematics and its applications to science. He believed strongly that one has to find ways to inspire talented young people to go into applied mathematics and to teach them applied mathematics in the right way. For many years, he taught a course on introducing physics to applied mathematicians in the summer school. To create a platform for practicing the philosophy embodied in this project, he cofounded the Institute of Natural Sciences at Shanghai Jiaotong University, which has become one of the most active centers for applied mathematics in China. His passing away last vear was an immense loss, not just for all of us involved in this project, but also for the applied mathematics community as a whole.

This book is the first in this series, covering probability theory and stochastic processes in a style that we believe is most suited for applied mathematicians. Other subjects covered in this series will include numerical algorithms, the calculus of variations and differential equations, a mathematical introduction to machine learning, and a mathematical introduction to physics and physical modeling. The stochastic analysis and differential equations courses summarize the most relevant aspects of pure mathematics, the algorithms course presents the most important technical tool of applied mathematics, and the learning and physical modeling courses provide a bridge to the real world and to other scientific disciplines. The selection of topics represents a possibly biased view about the true fundamentals of applied mathematics. In particular, we emphasize three themes throughout this textbook series: learning, modeling, and algorithms. Learning is about data and intelligent decision making. Modeling is concerned with physics-based models. The study of algorithms provides the practical tool for building and interrogating the models, whether machine learning-based or physics-based. We believe that these three themes should be the major pillars of applied mathematics, the applied math analog of algebra, analysis, and geometry.

While physical modeling and numerical algorithms have been the dominating driving force in applied mathematics for years, machine learning is a relatively new comer. However, there are very good reasons to believe that machine learning will not only change AI but also the way we do physical modeling. With this last missing component in place, applied mathematics will become the natural platform for integrating machine learning and physical modeling. This represents a new style for doing scientific research, a style in which the data-driven Keplerian paradigm and the first principle-driven Newtonian paradigm are integrated to give rise to unprecedented technical power. It is our hope that this series of textbooks will be of some help for making that a reality!

Weinan E, Princeton, 2018

### Preface

This book is written for students and researchers in applied mathematics with an interest in science and engineering. Our main purpose is to provide a mathematically solid introduction to the basic ideas and tools in probability theory and stochastic analysis. Starting from the basics of random variables and probability theory, we go on to discuss limit theorems, Markov chains, diffusion processes, and random fields. Since the kind of readers we have in mind typically have some background in differential equations, we put more weight on the differential equation approach. In comparison, we have neglected entirely martingale theory even though it is a very important part of stochastic analysis. The diffusion process occupies a central role in this book. We have presented three different ways of looking at the diffusion process: the approach of using stochastic differential equations, the Fokker-Planck equation approach, and the path integral approach. The first allows us to introduce stochastic calculus. The second approach provides a link between differential equations and stochastic analysis. The path integral approach is very much preferred by physicists and is also suited for performing asymptotic analysis. In addition, it can be extended to random fields.

In choosing the style of the presentation, we have tried to strike a balance between rigor and the heuristic approach. We have tried to give the reader an idea about the kind of mathematical construction or mathematical argument that goes into the subject matter, but at the same time, we often stop short of proving all the theorems we state or we prove the theorems under stronger assumptions. Whenever possible, we have tried to give the intuitive picture behind the mathematical constructions. Another emphasis is on numerical algorithms, including Monte Carlo methods, numerical schemes for solving stochastic differential equations, and the stochastic simulation algorithm. The book ends with a discussion on two application areas, statistical mechanics and chemical kinetics, and a discussion on rare events, which is perhaps the most important manifestation of the effect of noise.

The material contained in this book has been taught in various forms at Peking University, Princeton University, and New York University since 2001. It is now a required course for the special applied mathematics program at Peking University.

> Weinan E Tiejun Li Eric Vanden-Eijnden

December 2018

### Notation

- (1) Geometry notation:
  - (a)  $\mathbb{N}$ : Natural numbers,  $\mathbb{N} = \{0, 1, \ldots\}$ .
  - (b)  $\mathbb{Z}$ : Integers.
  - (c)  $\mathbb{Q}$ : Rational numbers.
  - (d)  $\mathbb{R}$ : Real numbers.
  - (e)  $\mathbb{R}$ : Extended real numbers,  $\mathbb{R} = [-\infty, \infty]$ .
  - (f)  $\mathbb{R}_+$ : Nonnegative real numbers.
  - (g)  $\overline{\mathbb{R}}_+$ : Extended nonnegative real numbers,  $\overline{\mathbb{R}}_+ = [0, \infty]$ .
  - (h)  $\mathbb{S}^{n-1}$ : (n-1)-dimensional unit sphere in  $\mathbb{R}^n$ .
  - (i)  $\mathbb{R}^{\mathbf{T}}$ : Collection of all real functions on time domain  $\mathbf{T}$ .
- (2) Probability notation:
  - (a)  $\mathbb{P}$ : Probability measure.
  - (b) E: Mathematical expectation.
  - (c)  $\mathbb{P}^i$ ,  $\mathbb{P}^x$ , or  $\mathbb{P}^{\mu}$ : Probability distribution conditioned on  $X_0 = i$ ,  $X_0 = x$ , or  $X_0 \sim \mu$ .
  - (d)  $\mathbb{E}^i$ ,  $\mathbb{E}^x$ ,  $\mathbb{E}^{\mu}$ : Mathematical expectation with respect to  $\mathbb{P}^i$ ,  $\mathbb{P}^x$ , or  $\mathbb{P}^{\mu}$ .
  - (e)  $\mathbb{E}^{x,t}$ : Mathematical expectation conditioned on  $X_t = x$ .
  - (f)  $\Omega$ : Sample space.
  - (g)  $\mathcal{F}$ :  $\sigma$ -algebra in probability space.
  - (h)  $\mathcal{R}, \mathcal{R}^d$ : The Borel  $\sigma$ -algebra on  $\mathbb{R}$  or  $\mathbb{R}^d$ .
  - (i)  $\sigma(\mathcal{B})$ : The smallest  $\sigma$ -algebra generated by sets in  $\mathcal{B}$ .
  - (j)  $\mathcal{R}^{\mathbf{T}}$ : The product Borel  $\sigma$ -algebra on  $\mathbb{R}^{\mathbf{T}}$ .
  - (k)  $\mathcal{U}(A)$ : Uniform distribution on set A.

- (1)  $\mathcal{P}(\lambda)$ : Poisson distribution with mean  $\lambda$ .
- (m)  $\mathcal{E}(\lambda)$ : Exponential distribution with mean  $\lambda^{-1}$ .
- (n)  $[X, X]_t$ : Quadratic variation process of X.
- (o)  $X \sim \mathcal{P}(\lambda)$ : Distribution of X. The right-hand side can be distributions like  $\mathcal{P}(\lambda)$  or  $N(\mu, \sigma^2)$ , etc.
- (3) Function spaces:
  - (a)  $C_c^{\infty}(\mathbb{R}^d)$  or  $C_c^k(\mathbb{R}^d)$ : Smooth or  $C^k$ -functions with compact support in  $\mathbb{R}^d$ .
  - (b)  $C_0(\mathbb{R}^d)$ : Continuous functions in  $\mathbb{R}^d$  that vanish at infinity.
  - (c)  $C_b(\mathbb{R}^d)$ : Bounded continuous functions in  $\mathbb{R}^d$ .
  - (d)  $L_t^p$  or  $L^p([0,T])$ :  $L^p$ -functions as a function of t.
  - (e)  $L^p_{\omega}$  or  $L^p(\Omega)$ :  $L^p$ -functions as a function of  $\omega$ .
  - (f)  $\mathscr{B}, \mathscr{H}$ : Banach or Hilbert spaces.
  - (g)  $\mathscr{B}^*$ : Dual space of  $\mathscr{B}$ .
- (4) Operators:  $\mathcal{I}, \mathcal{P}, \mathcal{Q}, \mathcal{K}$ , etc.
- (5) Functions:
  - (a)  $\lceil \cdot \rceil$ : The ceil function.  $\lceil x \rceil = m+1$  if  $x \in [m, m+1)$  for  $m \in \mathbb{Z}$ .
  - (b)  $\lfloor \cdot \rfloor$ : The floor function.  $\lfloor x \rfloor = m$  if  $x \in [m, m+1)$  for  $m \in \mathbb{Z}$ .
  - (c)  $|\boldsymbol{x}|$ :  $\ell^2$ -modulus of a vector  $\boldsymbol{x} \in \mathbb{R}^d$ :  $|\boldsymbol{x}| = (\sum_{i=1}^d x_i^2)^{\frac{1}{2}}$ .
  - (d) ||f||: Norm of function f in some function space.
  - (e)  $a \lor b$ : Maximum of a and b:  $a \lor b = \max(a, b)$ .
  - (f)  $a \wedge b$ : Minimum of a and b:  $a \wedge b = \min(a, b)$ .
  - (g)  $\langle f \rangle$ : The average of f with respect to a measure  $\mu$ :  $\langle f \rangle = \int f(x)\mu(dx)$ .
  - (h)  $(\boldsymbol{x}, \boldsymbol{y})$ : Inner product for  $\boldsymbol{x}, \boldsymbol{y} \in \mathbb{R}^d$ :  $(\boldsymbol{x}, \boldsymbol{y}) = \boldsymbol{x}^T \boldsymbol{y}$ .
  - (i) (f,g): Inner product for  $L^2$ -functions  $f,g:(f,g) = \int f(x)g(x)dx$ .
  - (j)  $\langle f, g \rangle$ : Dual product for  $f \in \mathscr{B}^*$  and  $g \in \mathscr{B}$ .
  - (k) A : B: Twice contraction for second-order tensors, i.e.,  $A : B = \sum_{ij} a_{ij} b_{ji}$ .
  - (1) |S|: The cardinality of set S.
  - (m)  $|\Delta|$ : The subdivision size when  $\Delta$  is a subdivision of a domain.
  - (n)  $\chi_A(x)$ : Indicator function, i.e.,  $\chi_A(x) = 1$  if  $x \in A$  and 0 otherwise.
  - (o)  $\delta(x-a)$ : Dirac's delta-function at x = a.
  - (p) Range( $\mathcal{P}$ ), Null( $\mathcal{P}$ ): The range and null space of operator  $\mathcal{P}$ , i.e., Range( $\mathcal{P}$ ) = { $y|y = \mathcal{P}x$ }, Null( $\mathcal{P}$ ) = { $x|\mathcal{P}x = 0$ }.
  - (q)  $^{\perp}\mathscr{C}$ : Perpendicular subspace, i.e.,  $^{\perp}\mathscr{C} = \{x | x \in \mathscr{B}^*, \langle x, y \rangle = 0, \forall y \in \mathscr{C}\}$  where  $\mathscr{C} \subset \mathscr{B}$ .

### (6) Symbols:

- (a)  $c_{\varepsilon} \asymp d_{\varepsilon}$ : Logrithmic equivalence, i.e.,  $\lim_{\varepsilon \to 0} \log c_{\varepsilon} / \log d_{\varepsilon} = 1$ .
- (b)  $c_{\varepsilon} \sim d_{\varepsilon}$  or  $c_n \sim d_n$ : Equivalence, i.e.,  $\lim_{\varepsilon \to 0} c_{\varepsilon}/d_{\varepsilon} = 1$  or  $\lim_{n \to \infty} c_n/d_n = 1$ .
- (c)  $\mathcal{D}x$ : Formal infinitesimal element in path space,  $\mathcal{D}x = \prod_{0 \le t \le T} dx_t$ .

## Appendix

### A. Laplace Asymptotics and Varadhan's Lemma

Consider the Laplace integral

$$F(t) = \int_{\mathbb{R}} e^{th(x)} dx, \quad t \gg 1,$$

where  $h(x) \in C^2(\mathbb{R})$ , h(0) is the only global maximum, and  $h''(0) \neq 0$ . We further assume that for any c > 0, there exists b > 0 such that

$$h(x) - h(0) \le -b \quad \text{if } |x| \ge c.$$

Assume also that  $h(x) \to -\infty$  fast enough as  $x \to \infty$  to ensure the convergence of F for t = 1.

Lemma A.1 (Laplace method). We have the asymptotics

(A.1) 
$$F(t) \sim \sqrt{2\pi} (-th''(0))^{-\frac{1}{2}} \exp(th(0))$$
 as  $t \to \infty$ ,

where the equivalence  $f(t) \sim g(t)$  means that  $\lim_{t\to\infty} f(t)/g(t) = 1$ .

The above asymptotic results can be stated as

$$\lim_{t \to \infty} \frac{1}{t} \log F(t) = \sup_{x \in \mathbb{R}} h(x).$$

This formulation is what we will use in the large deviation theory. Its abstract form in the infinite-dimensional setting is embodied in the so-called Varadhan's lemma to be discussed later [**DZ98**, **DS84**, **Var84**].

**Proof.** Without loss of generality, we can assume h(0) = 0 by shifting h(x) correspondingly. With this condition, if  $h(x) = h''(0)x^2/2$ , h''(0) < 0, we

have

$$\int_{\mathbb{R}} e^{th(x)} dx = \sqrt{2\pi} (-th''(0))^{-\frac{1}{2}}.$$

In general, for any  $\epsilon > 0$ , there exists  $\delta > 0$  such that if  $|x| \leq \delta$ ,

$$\left|h(x) - \frac{h''(0)}{2}x^2\right| \le \epsilon x^2.$$

It follows that

$$\begin{split} \int_{[-\delta,\delta]} \exp\left(\frac{tx^2}{2}(h''(0)-2\epsilon)\right) dx &\leq \int_{[-\delta,\delta]} \exp\left(th(x)\right) dx \\ &\leq \int_{[-\delta,\delta]} \exp\left(\frac{tx^2}{2}(h''(0)+2\epsilon)\right) dx. \end{split}$$

By assumption, for this  $\delta > 0$ , there exists  $\eta > 0$  such that  $h(x) \leq -\eta$  if  $|x| \geq \delta$ . Thus

$$\int_{|x|\ge\delta} \exp\left(th(x)\right) dx \le e^{-(t-1)\eta} \int_{\mathbb{R}} e^{h(x)} dx \sim \mathcal{O}(e^{-\alpha t}), \ \alpha > 0, \quad \text{for} \quad t > 1.$$

We first prove the upper bound:

$$\begin{split} \int_{\mathbb{R}} \exp\left(th(x)\right) dx &\leq \int_{\mathbb{R}} \exp\left(\frac{tx^2}{2}(h''(0)+2\epsilon)\right) dx \\ &- \int_{|x|\geq \delta} \exp\left(\frac{tx^2}{2}(h''(0)+2\epsilon)\right) dx + \mathcal{O}(e^{-\alpha t}) \\ &= \sqrt{2\pi} \Big[t(-h''(0)-2\epsilon)\Big]^{-\frac{1}{2}} + \mathcal{O}(e^{-\beta t}) \end{split}$$

where  $\beta > 0$ . In fact, we ask for  $\epsilon < -h''(0)/2$  here.

The proof of the lower bound is similar. By the arbitrary smallness of  $\epsilon,$  we have

$$\lim_{t \to \infty} F(t) / \sqrt{2\pi} (-th''(0))^{-\frac{1}{2}} = 1.$$

which completes the proof.

**Definition A.2** (Large deviation principle). Let  $\mathscr{X}$  be a complete separable metric space and let  $\{\mathbb{P}^{\varepsilon}\}_{\varepsilon \geq 0}$  be a family of probability measures on the Borel subsets of  $\mathscr{X}$ . We say that  $\mathbb{P}^{\varepsilon}$  satisfies the large deviation principle if there exists a rate functional  $I: \mathscr{X} \to [0, \infty]$  such that:

(i) For any  $\ell < \infty$ ,

 $\{x: I(x) \leq \ell\}$  is compact.

(ii) Upper bound. For each closed set  $F \subset \mathscr{X}$ ,

$$\overline{\lim_{\varepsilon \to 0}} \varepsilon \ln \mathbb{P}^{\varepsilon}(F) \leq -\inf_{x \in F} I(x).$$

(iii) Lower bound. For each open set  $G \subset \mathscr{X}$ ,

$$\underline{\lim_{\varepsilon \to 0}} \varepsilon \ln \mathbb{P}^{\varepsilon}(G) \ge -\inf_{x \in G} I(x)$$

**Theorem A.3** (Varadhan's lemma). Suppose that  $\mathbb{P}^{\varepsilon}$  satisfies the large deviation principle with rate functional  $I(\cdot)$  and  $F \in C_b(\mathscr{X})$ . Then

(A.2) 
$$\lim_{\varepsilon \to 0} \varepsilon \ln \int_{\mathscr{X}} \exp\left(\frac{1}{\varepsilon}F(x)\right) \mathbb{P}^{\varepsilon}(dx) = \sup_{x \in \mathscr{X}} (F(x) - I(x))$$

The proof of Varadhan's lemma can be found in [DZ98, Var84].

### **B.** Gronwall's Inequality

**Theorem B.1** (Gronwall's inequality). Assume that the function  $f : [0, \infty) \to \mathbb{R}^+$  satisfies the inequality

$$f(t) \le a(t) + \int_0^t b(s)f(s)ds,$$

where  $a(t), b(t) \ge 0$ . Then we have

(B.1) 
$$f(t) \le a(t) + \int_0^t a(s)b(s) \exp\left(\int_s^t b(u)du\right) ds.$$

**Proof.** Let  $g(t) = \int_0^t b(s) f(s) ds$ . We have

$$g'(t) \le a(t)b(t) + b(t)g(t).$$

Define  $h(t) = g(t) \exp(-\int_0^t b(s) ds)$ . We obtain

$$h'(t) \le a(t)b(t) \exp\left(-\int_0^t b(s)ds\right).$$

Integrating both sides from 0 to t, we get

$$g(t) \le \int_0^t a(s)b(s) \exp\left(\int_s^t b(u)du\right) ds,$$

which yields the desired estimate.

In the case when  $a(t) \equiv a$  and  $b(t) \equiv b$ , we have

$$f(t) \le a \exp(bt).$$

**Theorem B.2** (Discrete Gronwall's inequality). Assume that  $F_n$  satisfies

(B.2) 
$$F_{n+1} \le (1+b_n\delta t)F_n + a_n, \quad F_0 \ge 0$$

where  $\delta t, a_n, b_n \geq 0$ . Then we have

(B.3) 
$$F_n \le \exp\left(\left(\sum_{k=0}^{n-1} b_k\right) \delta t\right) F_0 + \sum_{k=0}^{n-1} \left(a_k \exp\left(\left(\sum_{l=k+1}^{n-1} b_l\right) \delta t\right)\right).$$

**Proof.** From (B.2), we have

$$F_n \le \prod_{k=0}^{n-1} (1+b_k \delta t) F_0 + \sum_{k=0}^{n-1} \left( a_k \sum_{l=k+1}^{n-1} (1+b_l \delta t) \right).$$

The estimate (B.2) follows by a straightforward application of the inequality  $1 + x \le e^x$ .

When  $F_0 \leq C\delta t^p$ ,  $b_n \equiv b$ ,  $a_n = K\delta t^{p+1}$ , and  $n\delta t \leq T$ , we have

$$F_n \le C e^{bT} \delta t^p + K e^{bT} \frac{\delta t^{p+1}}{1 - e^{-b\delta t}}$$

This is the commonly used *p*th-order error estimate in numerical analysis.

### C. Measure and Integration

Let  $(\Omega, \mathcal{F})$  be a measurable space.

**Definition C.1** (Measure). The measure  $\mu : \mathcal{F} \to \mathbb{R}_+ = [0, \infty]$  is a set function defined on  $\mathcal{F}$  that satisfies

- (a)  $\mu(\emptyset) = 0;$
- (b) the countable additivity; i.e., for pairwise disjoint sets  $A_n \in \mathcal{F}$ , we have

$$\mu\left(\bigcup_{n=1}^{\infty} A_n\right) = \sum_{n=1}^{\infty} \mu(A_n),$$

where we assume the arithmetic rules (2.7) on the extended reals  $\mathbb{R}_+$ .

When the set function  $\mu$  takes values in  $\mathbb{R} = [-\infty, \infty]$  and only the countable additivity condition is assumed,  $\mu$  is called a *signed measure*.

**Definition C.2** (Algebra). An algebra (or field)  $\mathcal{F}_0$  is a collection of subsets of  $\Omega$  that satisfies the following conditions:

- (i)  $\Omega \in \mathcal{F}_0$ ;
- (ii) if  $A \in \mathcal{F}_0$ , then  $A^c \in \mathcal{F}_0$ ;
- (iii) if  $A, B \in \mathcal{F}_0$ , then  $A \cup B \in \mathcal{F}_0$ .

**Theorem C.3** (Measure extension). A finite measure  $\mu$  on an algebra  $\mathcal{F}_0 \subset \mathcal{F}$ , *i.e.*,  $\mu(\Omega) < \infty$ , can be uniquely extended to a measure on  $\sigma(\mathcal{F}_0)$ .

**Definition C.4** (Measurable function). A function  $f : \Omega \to \mathbb{R}$  is called *measurable* or  $\mathcal{F}$ -measurable if  $f^{-1}(A) \in \mathcal{F}$  for any  $A \in \mathcal{R}$ .

**Definition C.5** (Simple function). A function  $f : \Omega \to \mathbb{R}$  is called a simple function if it has the representation

$$f(\omega) = \sum_{i=1}^{n} a_i \chi_{A_i}(\omega),$$

where  $a_i \in \mathbb{R}$  and  $A_i \in \mathcal{F}$  for  $i = 1, \ldots, n$ .

**Theorem C.6.** Any nonnegative measurable function f on space  $(\Omega, \mathcal{F})$ can be approximated by a sequence of monotonically increasing nonnegative functions  $\{f_n\}$ ; that is,  $0 \leq f_n(\omega) \leq f_{n+1}(\omega)$  for any n and

$$\lim_{n \to \infty} f_n(\omega) = f(\omega).$$

We will denote such a monotone approximation as  $f_n \uparrow f$  for short.

**Definition C.7** (Integration of a simple function). The integral of the simple function  $f(\omega) = \sum_{i=1}^{n} a_i \chi_{A_i}(\omega)$  is defined as

$$\mu(f) = \int_{\Omega} f\mu(d\omega) = \sum_{i=1}^{n} a_i \mu(A_i).$$

**Theorem C.8** (Properties of the integral of simple functions). Suppose that  $f_n$ ,  $g_n$ , f, and g are nonnegative simple functions. Then we have:

- (a)  $\mu(\alpha f + \beta g) = \alpha \mu(f) + \beta \mu(g)$  for any  $\alpha, \beta \in \mathbb{R}_+$ .
- (b) If  $f \leq g$ , then  $\mu(f) \leq \mu(g)$ .
- (c) If  $f_n \uparrow f$ , then  $\lim_{n \to \infty} \mu(f_n) = \mu(f)$ .
- (d) If  $f_n$  and  $g_n$  are monotonically increasing and  $\lim_{n\to\infty} f_n \leq \lim_{n\to\infty} g_n$ , then  $\lim_{n\to\infty} \mu(f_n) \leq \lim_{n\to\infty} \mu(g_n)$ .

**Definition C.9.** Let f be a nonnegative measurable function. The integral of f is defined as

$$\mu(f) = \int_{\Omega} f(\omega)\mu(d\omega) = \lim_{n \to \infty} \mu(f_n),$$

where  $f_n \uparrow f$  are nonnegative functions.

It is easy to see that the integral is well-defined, say using Theorem C.8(d).

**Definition C.10.** Let f be a measurable function. The integral of f is defined as

$$\mu(f) = \int_{\Omega} f(\omega)\mu(d\omega) = \mu(f^+) - \mu(f^-),$$

where  $f^+ = f \vee 0$  and  $f^- = (-f) \vee 0$  are both nonnegative measurable functions. If both  $\mu(f^+)$  and  $\mu(f^-)$  are finite, f is called an integrable function.

**Theorem C.11** (Monotone convergence theorem). Suppose that  $\{f_n\}$  are nonnegative integrable functions and  $f_n \uparrow f$  almost everywhere. Then

$$\lim_{n \to \infty} \mu(f_n) = \mu(f).$$

**Theorem C.12** (Fatou lemma). Let  $\{f_n\}$  be nonnegative integrable functions. We have

$$\mu(\liminf_{n \to \infty} f_n) \le \liminf_{n \to \infty} \mu(f_n).$$

**Theorem C.13** (Dominated convergence theorem). Suppose that  $\{f_n\}$  are integrable functions and  $f_n \to f$  almost everywhere. If  $|f_n| \leq g$  for any n and  $\mu(g) < \infty$ , then

$$\lim_{n \to \infty} \mu(f_n) = \mu(f).$$

**Definition C.14** ( $\sigma$ -finite measure). A measure  $\mu$  on  $(\Omega, \mathcal{F})$  is  $\sigma$ -finite if there exists a countable partition of  $\Omega$ ; i.e.,  $\Omega = \bigcup_{n=1}^{\infty} A_n$  where  $\{A_n\}$  are pairwise disjoint, such that  $\mu(A_n) < \infty$  for any n.

**Definition C.15** (Absolute continuity). Let  $\mu$ ,  $\eta$  be a  $\sigma$ -finite measure and a signed measure, respectively. Here  $\eta$  is called absolutely continuous with respect to  $\mu$  if  $\mu(A) = 0$  implies  $\eta(A) = 0$  for any  $A \in \mathcal{F}$ . It is also denoted as  $\eta \ll \mu$  for short.

**Theorem C.16** (Radon-Nikodym theorem). Let  $\mu$  be a  $\sigma$ -finite measure on  $(\Omega, \mathcal{F})$  and let  $\eta$  be a signed measure which is absolutely continuous with respect to  $\mu$ . Then there exists a measurable function f such that

$$\eta(A) = \int_A f(\omega) \mu(d\omega)$$

for any  $A \in \mathcal{F}$ . Here f is unique in the  $\mu$ -equivalent sense; i.e.,  $f \stackrel{\mu}{\sim} g$  if  $\mu(f = g) = 1$ . It is also called the Radon-Nikodym derivative of  $\eta$  with respect to  $\mu$ , abbreviated as  $f = d\eta/d\mu$ .

The readers may refer to [Bil79, Cin11, Hal50] for more details.

### **D.** Martingales

Consider the probability space  $(\Omega, \mathcal{F}, \mathbb{P})$  and a filtration  $\{\mathcal{F}_n\}_{n \in \mathbb{N}}$  or  $\{\mathcal{F}_t\}_{t \geq 0}$ .

**Definition D.1** (Martingale). A continuous time stochastic process  $X_t$  is called an  $\mathcal{F}_t$ -martingale if  $X_t \in L^1_{\omega}$  for any  $t, X_t$  is  $\mathcal{F}_t$ -adapted, and

(D.1) 
$$\mathbb{E}(X_t | \mathcal{F}_s) = X_s$$
 for all  $s \le t$ .

 $X_t$  is called a submartingale or supermartigale if the above equality is replaced by  $\geq$  or  $\leq$ . These concepts can be defined for discrete time stochastic processes if we replace (D.1) by  $\mathbb{E}(X_n | \mathcal{F}_m) = X_m$  for any  $m \leq n$ . The discrete submartingale or supermartingale can be defined similarly.

The following theorem is a straightforward application of the conditional Jensen inequality

**Theorem D.2.** Assume  $\phi$  is a convex function such that  $\phi(X_t) \in L^1_{\omega}$  for any t. Then  $\phi(X_t)$  is a submartingale.

The simplest choices of  $\phi$  include  $\phi(x) = |x|, x^+ := x \vee 0$ , or  $x^2$  if  $X_t$  is a square-integrable martingale.

**Theorem D.3** (Martingale inequalities). Let  $X_t$  be a submartingale with continuous paths. Then for any  $[s,t] \subset [0,\infty)$  and  $\lambda > 0$ , we have:

(i) *Doob's inequality:* 

$$\mathbb{P}\left(\sup_{u\in[s,t]}X_u\geq\lambda\right)\leq\frac{\mathbb{E}X_t^+}{\lambda}.$$

(ii) Doob's  $L^p$ -maximal inequality:

$$\mathbb{E}\left(\sup_{u\in[s,t]}X_u\right)^p \le \left(\frac{p}{p-1}\right)^p \mathbb{E}X_t^p, \qquad p>1.$$

Useful results follow immediately if we take  $X_t = |Y_t|$  where  $Y_t$  is a martingale. Similar inequalities also hold for discrete time martingales. See **[Chu01, Dur10, KS91]** for more details.

### E. Strong Markov Property

Consider a finite Markov chain  $\{X_n\}_{n\in\mathbb{N}}$  on S with initial distribution  $\mu$  and transition probability matrix P.

**Theorem E.1** (Markov property). Conditional on  $X_m = i$   $(m \in \mathbb{N})$ ,  $\{X_{m+n}\}_{n \in \mathbb{N}}$  is Markovian with initial distribution  $\delta_i$  and transition probability matrix  $\mathbf{P}$ , and it is independent of  $(X_0, X_1, \ldots, X_m)$ .

**Theorem E.2** (Strong Markov property). Let N be a stopping time. Conditional on  $\{N < \infty\}$  and  $X_N = i$ ,  $\{X_{N+n}\}_{n \in \mathbb{N}}$  is Markovian with initial distribution  $\delta_i$  and transition probability matrix **P**.

The above results also hold for the Q-process  $\{X_t\}_{t>0}$  with generator Q.

**Theorem E.3** (Markov property). Conditional on  $X_t = i$   $(t \ge 0)$ ,  $\{X_{t+s}\}_{s\ge 0}$  is Markovian with initial distribution  $\delta_i$  and generator Q, and it is independent of  $\{X_r, r \le t\}$ .

**Theorem E.4** (Strong Markov property). Let T be a stopping time. Conditional on  $\{T < \infty\}$  and  $X_T = i$ ,  $\{X_{T+t}\}_{t\geq 0}$  is Markovian with initial distribution  $\delta_i$  and generator Q.

See [Dur10, Nor97] for more details.

### F. Semigroup of Operators

Let  $\mathscr{B}$  be a Banach space equipped with the norm  $\|\cdot\|$ .

**Definition F.1** (Operator semigroup). A family of bounded linear operators  $\{S(t)\}_{t\geq 0} : \mathscr{B} \to \mathscr{B}$  forms a strongly continuous semigroup if for any  $f \in \mathscr{B}$ :

(i) 
$$S(0)f = f$$
; i.e.,  $S(0) = I$ 

- (ii) S(t)S(s)f = S(s)S(t)f = S(t+s)f for any  $s, t \ge 0$ .
- (iii)  $||S(t)f f|| \to 0$  for any  $f \in \mathscr{B}$  as  $t \to 0+$ .

We will call  $\{S(\cdot)\}$  a contraction semigroup if  $||S(t)|| \leq 1$  for any t, where ||S(t)|| is the operator norm induced by the metric  $||\cdot||$ .

The simplest examples of semigroups include the solution operator for the system

$$\frac{d\boldsymbol{u}(t)}{dt} = \boldsymbol{A}\boldsymbol{u}(t),$$

where  $\boldsymbol{u} \in \mathbb{R}^n, \boldsymbol{A} \in \mathbb{R}^{n \times n}, \mathcal{B} = \mathbb{R}^n$ , and  $S(t)\boldsymbol{f} := \boldsymbol{u}(t)$  by solving the ODE with initial condition  $\boldsymbol{u}(t)|_{t=0} = \boldsymbol{f}$ . Similarly, consider the PDE

 $\partial_t u = \Delta u \quad \text{in } U, \qquad u = 0 \quad \text{on } \partial U,$ 

where U is a bounded open set with smooth boundary. We can take  $\mathscr{B} = L^2(U)$  and S(t)f := u(t), where u(t) is the solution of the above PDE with initial condition u(x, t = 0) = f.

**Definition F.2** (Infinitesimal generator). Denote

$$D(\mathcal{A}) = \left\{ f \in \mathscr{B} : \lim_{t \to 0+} \frac{S(t)f - f}{t} \text{ exits in } \mathscr{B} \right\}$$

and

$$\mathcal{A}f := \lim_{t \to 0+} \frac{1}{t} (S(t)f - f), \qquad f \in D(\mathcal{A})$$

The operator  $\mathcal{A}$  is called the infinitesimal generator of the semigroup S(t);  $D(\mathcal{A})$  is the domain of the operator  $\mathcal{A}$ .

It can be shown that the infinitesimal generators of the two examples above are  $\mathcal{A} = \mathcal{A}$  and  $\mathcal{A} = \Delta$  and their domains are  $\mathbb{R}^n$  and the Sobolev space  $H_0^1(U) \cup H^2(U)$ , respectively.

**Theorem F.3** (Basic properties). Let  $f \in D(\mathcal{A})$ . We have:

(i) 
$$S(t)f \in D(\mathcal{A})$$
 and  $S(t)\mathcal{A}f = \mathcal{A}S(t)f$  for any  $t \ge 0$ .  
(ii)  $f(t) := S(t)f$  is differentiable on  $(0,\infty)$  and  
 $\frac{df(t)}{dt} = \mathcal{A}f(t), \qquad t > 0.$ 

**Theorem F.4.** The generator  $\mathcal{A}$  is a closed operator and  $D(\mathcal{A})$  is dense in  $\mathscr{B}$ .

In general, the generator  $\mathcal{A}$  is unbounded, e.g.,  $\mathcal{A} = \Delta$  in the previous PDE example, so we only have  $D(\mathcal{A}) \subsetneq \mathscr{B}$ .

**Definition F.5** (Resolvent set and operator). Let  $\mathcal{A}$  be a closed linear operator with domain  $D(\mathcal{A})$ . The resolvent set of  $\mathcal{A}$  is defined by

 $\rho(\mathcal{A}) = \{\lambda : \lambda \in \mathbb{R} \text{ and } \lambda I - \mathcal{A} \text{ is bijective from } D(\mathcal{A}) \text{ to } \mathscr{B} \}.$ 

If  $\lambda \in \rho(\mathcal{A})$ , the resolvent operator  $R_{\lambda} : \mathscr{B} \to \mathscr{B}$  is defined by

$$R_{\lambda}f := (\lambda I - \mathcal{A})^{-1}f.$$

The closed graph theorem ensures that  $(\lambda I - \mathcal{A})^{-1}$  is a bounded linear operator if  $\lambda \in \rho(\mathcal{A})$ .

**Theorem F.6** (Hille-Yosida theorem). Let  $\mathcal{A}$  be a closed, densely defined linear operator on  $\mathcal{B}$ . Then  $\mathcal{A}$  generates a contraction semigroup  $\{S(t)\}_{t\geq 0}$ if and only if

$$\lambda \in \rho(\mathcal{A})$$
 and  $||R_{\lambda}|| \leq \frac{1}{\lambda}$  for all  $\lambda > 0$ .

Interested readers are referred to [Eva10, Paz83, Yos95] for more details on semigroup theory.

# Bibliography

| [AC08]   | A. Abdulle and S. Cirilli, S-ROCK: Chebyshev methods for stiff stochastic dif-<br>ferential equations, SIAM J. Sci. Comput. <b>30</b> (2008), no. 2, 997–1014, DOI<br>10.1137/070679375. MR2385896   |
|----------|--|
| [ACK10]  | D. F. Anderson, G. Craciun, and T. G. Kurtz, Product-form stationary distribu-<br>tions for deficiency zero chemical reaction networks, Bull. Math. Biol. <b>72</b> (2010),<br>no. 8, 1947–1970, DOI 10.1007/s11538-010-9517-4. MR2734052      |
| [AGK11]  | D. F. Anderson, A. Ganguly, and T. G. Kurtz, <i>Error analysis of tau-leap simulation methods</i> , Ann. Appl. Probab. <b>21</b> (2011), no. 6, 2226–2262, DOI 10.1214/10-AAP756. MR2895415  |
| [AH12]   | <ul> <li>D. F. Anderson and D. J. Higham, Multilevel Monte Carlo for continuous time Markov chains, with applications in biochemical kinetics, Multiscale Model. Simul. 10 (2012), no. 1, 146–179, DOI 10.1137/110840546. MR2902602</li> </ul> |
| [AL08]   | A. Abdulle and T. Li, S-ROCK methods for stiff Itô SDEs, Commun. Math. Sci. ${\bf 6}$ (2008), no. 4, 845–868. MR2511696  |
| [And86]  | H. L. Anderson, Metropolis, Monte Carlo and the MANIAC, Los Alamos Science ${\bf 14}$ (1986), 96–108.  |
| [App04]  | D. Applebaum, <i>Lévy processes and stochastic calculus</i> , Cambridge Studies in Advanced Mathematics, vol. 93, Cambridge University Press, Cambridge, 2004. MR2072890   |
| [ARLS11] | M. Assaf, E. Roberts, and Z. Luthey-Schulten, <i>Determining the stability of genetic switches: Explicitly accounting for mrna noise</i> , Phys. Rev. Lett. <b>106</b> (2011), 248102.   |
| [ARM98]  | A. Arkin, J. Ross, and H. H. McAdams, Stochastic kinetic analysis of developmen-<br>tal pathway bifurcation in phage lambda-infected Escherichia coli cells, Genetics<br><b>149</b> (1998), 1633–1648.   |
| [Arn89]  | V. I. Arnol'd, <i>Mathematical methods of classical mechanics</i> , 2nd ed., translated from the Russian by K. Vogtmann and A. Weinstein, Graduate Texts in Mathematics, vol. 60, Springer-Verlag, New York, 1989. MR997295                    |
| [BB01]   | P. Baldi and S. Brunak, <i>Bioinformatics</i> , 2nd ed., The machine learning approach;<br>A Bradford Book, Adaptive Computation and Machine Learning, MIT Press,<br>Cambridge, MA, 2001. MR1849633  |

| [BE67]  | <ul> <li>L. E. Baum and J. A. Eagon, An inequality with applications to statistical estimation for probabilistic functions of Markov processes and to a model for ecology, Bull. Amer. Math. Soc. <b>73</b> (1967), 360–363, DOI 10.1090/S0002-9904-1967-11751-8. MR0210217</li> </ul>      |
|---------|---|
| [Bil79] | P. Billingsley, <i>Probability and measure</i> , Wiley Series in Probability and Mathematical Statistics, John Wiley & Sons, New York-Chichester-Brisbane, 1979. MR534323   |
| [BKL75] | A. B. Bortz, M. H. Kalos, and J. L. Lebowitz, New algorithm for Monte Carlo simulations of Ising spin systems, J. Comp. Phys. 17 (1975), 10–18.   |
| [Bou95] | C. A. Bouman, Markov random fields and stochastic image models, available from http://dynamo.ecn.purdue.edu/ $\sim$ bouman, 1995.   |
| [BP98]  | S. Brin and L. Page, <i>The anatomy of a large-scale hypertextual web search engine</i> ,<br>Computer Networks and ISDN Systems <b>30</b> (1998), 107–117.  |
| [BP06]  | Z. P. Bažant and S. Pang, Mechanics-based statistics of failure risk of quasibrittle structures and size effect of safety factors, Proc. Nat. Acad. Sci. USA <b>103</b> (2006), 9434–9439.  |
| [BPN14] | G. R. Bowman, V. S. Pande, and F. Noé (eds.), An introduction to Markov state models and their application to long timescale molecular simulation, Advances in Experimental Medicine and Biology, vol. 797, Springer, Dordrecht, 2014. MR3222039  |
| [Bre92] | L. Breiman, <i>Probability</i> , corrected reprint of the 1968 original, Classics in Applied Mathematics, vol. 7, Society for Industrial and Applied Mathematics (SIAM), Philadelphia, PA, 1992. MR1163370  |
| [Cam12] | M. K. Cameron, Finding the quasipotential for nongradient SDEs, Phys. D <b>241</b> (2012), no. 18, 1532–1550, DOI 10.1016/j.physd.2012.06.005. MR2957825  |
| [CGP05] | <ul> <li>Y. Cao, D. Gillespie, and L. Petzold, Multiscale stochastic simulation algorithm<br/>with stochastic partial equilibrium assumption for chemically reacting systems,</li> <li>J. Comput. Phys. 206 (2005), no. 2, 395–411, DOI 10.1016/j.jcp.2004.12.014.<br/>MR2143324</li> </ul> |
| [CGP06] | Y. Cao, D. Gillespie, and L. Petzold, <i>Efficient stepsize selection for the tau-leaping method</i> , J. Chem. Phys. <b>124</b> (2006), 044109.  |
| [CH13]  | A. J. Chorin and O. H. Hald, <i>Stochastic tools in mathematics and science</i> , 3rd ed.,<br>Texts in Applied Mathematics, vol. 58, Springer, New York, 2013. MR3076304  |
| [Cha78] | D. Chandler, Statistical mechanics of isomerization dynamics in liquids and the transition state approximation, J. Chem. Phys. <b>68</b> (1978), 2959–2970.   |
| [Cha87] | D. Chandler, Introduction to modern statistical mechanics, The Clarendon Press, Oxford University Press, New York, 1987. MR913936   |
| [CHK02] | <ul> <li>A. J. Chorin, O. H. Hald, and R. Kupferman, Optimal prediction with memory, Phys. D 166 (2002), no. 3-4, 239–257, DOI 10.1016/S0167-2789(02)00446-3.</li> <li>MR1915310</li> </ul>   |
| [Cho03] | A. J. Chorin, Conditional expectations and renormalization, Multiscale Model.<br>Simul. 1 (2003), no. 1, 105–118, DOI 10.1137/S1540345902405556. MR1960842  |
| [Chu97] | F. R. K. Chung, <i>Spectral graph theory</i> , CBMS Regional Conference Series in Mathematics, vol. 92, Published for the Conference Board of the Mathematical Sciences, Washington, DC; by the American Mathematical Society, Providence, RI, 1997. MR1421568                              |
| [Chu01] | K. L. Chung, $A\ course\ in\ probability\ theory,$ 3rd ed., Academic Press, Inc., San Diego, CA, 2001. MR1796326  |
| [Cin11] | E. Çınlar, <i>Probability and stochastics</i> , Graduate Texts in Mathematics, vol. 261, Springer, New York, 2011. MR2767184  |

| [CKVE11] | M. Cameron, R. V. Kohn, and E. Vanden-Eijnden, <i>The string method as a dynamical system</i> , J. Nonlinear Sci. <b>21</b> (2011), no. 2, 193–230, DOI 10.1007/s00332-010-9081-y. MR2788855  |
|----------|---|
| [CLP04]  | Y. Cao, H. Li, and L. Petzold, <i>Efficient formulation of the stochastic simulation algorithm for chemically reacting systems</i> , J. Chem. Phys. <b>121</b> (2004), 4059–4067.   |
| [CM47]   | R. H. Cameron and W. T. Martin, The orthogonal development of non-linear functionals in series of Fourier-Hermite functionals, Ann. of Math. (2) 48 (1947), 385–392, DOI 10.2307/1969178. MR0020230   |
| [CT06]   | T. M. Cover and J. A. Thomas, <i>Elements of information theory</i> , 2nd ed., Wiley-Interscience [John Wiley & Sons], Hoboken, NJ, 2006. MR2239987   |
| [CVK05]  | A. Chatterjee, D. G. Vlachos, and M. A. Katsoulakis, <i>Binomial distribution based tau-leap accelerated stochastic simulation</i> , J. Chem. Phys. <b>122</b> (2005), 024112.  |
| [CW05]   | K. L. Chung and J. B. Walsh, <i>Markov processes, Brownian motion, and time symmetry</i> , 2nd ed., Grundlehren der Mathematischen Wissenschaften [Fundamental Principles of Mathematical Sciences], vol. 249, Springer, New York, 2005. MR2152573  |
| [DE86]   | M. Doi and S. F. Edwards, <i>The theory of polymer dynamics</i> , Oxford University Press, New York, 1986.  |
| [DLR77]  | A. P. Dempster, N. M. Laird, and D. B. Rubin, <i>Maximum likelihood from incomplete data via the EM algorithm</i> , J. Roy. Statist. Soc. Ser. B <b>39</b> (1977), no. 1, 1–38. With discussion. MR0501537  |
| [DMRH94] | M. I. Dykman, E. Mori, J. Ross, and P. M. Hunt, Large fluctuations and optimal paths in chemical kinetics, J. Chem. Phys. <b>100</b> (1994), 5735–5750.   |
| [Doo42]  | J. L. Doob, The Brownian movement and stochastic equations, Ann. of Math. (2) ${\bf 43}$ (1942), 351–369, DOI 10.2307/1968873. MR0006634  |
| [Doo84]  | J. L. Doob, <i>Classical potential theory and its probabilistic counterpart</i> ,<br>Grundlehren der Mathematischen Wissenschaften [Fundamental Principles of<br>Mathematical Sciences], vol. 262, Springer-Verlag, New York, 1984. MR731258        |
| [DPZ92]  | G. Da Prato and J. Zabczyk, <i>Stochastic equations in infinite dimensions</i> , Encyclopedia of Mathematics and its Applications, vol. 44, Cambridge University Press, Cambridge, 1992. MR1207136  |
| [DS84]   | JD. Deuschel and D. W. Stroock, <i>Large deviations</i> , Pure and Applied Mathematics, vol. 137, Academic Press, Inc., Boston, MA, 1989. MR997938  |
| [DSK09]  | E. Darve, J. Solomon, and A. Kia, <i>Computing generalized Langevin equations and generalized Fokker-Planck equations</i> , Proc. Nat. Acad. Sci. USA <b>106</b> (2009), 10884–10889.   |
| [Dur10]  | R. Durrett, <i>Probability: theory and examples</i> , 4th ed., Cambridge Series in Statistical and Probabilistic Mathematics, vol. 31, Cambridge University Press, Cambridge, 2010. MR2722836   |
| [DZ98]   | A. Dembo and O. Zeitouni, <i>Large deviations techniques and applications</i> , 2nd ed., Applications of Mathematics (New York), vol. 38, Springer-Verlag, New York, 1998. MR1619036  |
| [E11]    | W. E, <i>Principles of multiscale modeling</i> , Cambridge University Press, Cambridge, 2011. MR2830582   |
| [EAM95]  | R. J. Elliott, L. Aggoun, and J. B. Moore, <i>Hidden Markov models: Estimation and control</i> , Applications of Mathematics (New York), vol. 29, Springer-Verlag, New York, 1995. MR1323178  |
| [Eck87]  | R. Eckhardt, Stan Ulam, John von Neumann, and the Monte Carlo method, with contributions by Tony Warnock, Gary D. Doolen, and John Hendricks; Stanislaw Ulam, 1909–1984, Los Alamos Sci. <b>15</b> , <b>Special Issue</b> (1987), 131–137. MR935772 |

| [Ein05]   | A. Einstein, On the movement of small particles suspended in a stationary liquid demanded by the molecular kinetic theory of heat, Ann. Phys. (in German) <b>322</b> (1905), 549–560.  |
|-----------|--|
| [EK86]    | S. N. Ethier and T. G. Kurtz, <i>Markov processes: Characterization and conver-<br/>gence</i> , Wiley Series in Probability and Mathematical Statistics: Probability and<br>Mathematical Statistics, John Wiley & Sons, Inc., New York, 1986. MR838085 |
| [Ell85]   | R. S. Ellis, Entropy, large deviations, and statistical mechanics, Grundlehren der<br>Mathematischen Wissenschaften [Fundamental Principles of Mathematical Sci-<br>ences], vol. 271, Springer-Verlag, New York, 1985. MR793553                        |
| [ELSS02]  | M. B. Elowitz, A. J. Levine, E. D. Siggia, and P. S. Swain, <i>Stochastic gene expression in a single cell</i> , Science <b>297</b> (2002), 1183–1186.   |
| [ELVE05a] | <ul> <li>W. E, D. Liu, and E. Vanden-Eijnden, Analysis of multiscale methods for stochas-<br/>tic differential equations, Comm. Pure Appl. Math. 58 (2005), no. 11, 1544–1585,<br/>DOI 10.1002/cpa.20088. MR2165382</li> </ul>                         |
| [ELVE05b] | W. E, D. Liu, and E. Vanden-Eijnden, Nested stochastic simulation algorithm for chemical kinetic systems with disparate rates, J. Chem. Phys. <b>123</b> (2005), 194107.   |
| [ELVE07]  | <ul> <li>W. E, D. Liu, and E. Vanden-Eijnden, Nested stochastic simulation algorithms for<br/>chemical kinetic systems with multiple time scales, J. Comput. Phys. 221 (2007),<br/>no. 1, 158–180, DOI 10.1016/j.jcp.2006.06.019. MR2290567</li> </ul> |
| [ELVE08]  | W. E, T. Li, and E. Vanden-Eijnden, Optimal partition and effective dynamics<br>of complex networks, Proc. Natl. Acad. Sci. USA 105 (2008), no. 23, 7907–7912,<br>DOI 10.1073/pnas.0707563105. MR2415575   |
| [ERVE02]  | W. E, W. Ren, and E. Vanden-Eijnden, <i>String method for the study of rare events</i> , Phys. Rev. B <b>66</b> (2002), 052301.  |
| [ERVE03]  | W. E, W. Ren, and E. Vanden-Eijnden, <i>Energy landscape and thermally activated switching of submicron-sized ferromagnetic elements</i> , J. Appl. Phys. <b>93</b> (2003), 2275–2282.   |
| [ERVE07]  | <ul> <li>W. E, W. Ren, and E. Vanden-Eijnden, Simplified and improved string method for<br/>computing the minimum energy paths in barrier-crossing events, J. Chem. Phys.<br/>126 (2007), 164103.</li> </ul>   |
| [Eva10]   | L. C. Evans, <i>Partial differential equations</i> , 2nd ed., Graduate Studies in<br>Mathematics, vol. 19, American Mathematical Society, Providence, RI, 2010.<br>MR2597943   |
| [EVE10]   | W. E and E. Vanden-Eijnden, <i>Transition-path theory and path-finding algorithms</i> for the study of rare events, Ann. Rev. Phys. Chem. <b>61</b> (2010), 391–420.   |
| [Fel68]   | W. Feller, An introduction to probability theory and its applications, Third edition, John Wiley & Sons, Inc., New York-London-Sydney, 1968. MR0228020   |
| [Fre85]   | M. Freidlin, Functional integration and partial differential equations, Annals of<br>Mathematics Studies, vol. 109, Princeton University Press, Princeton, NJ, 1985.<br>MR833742   |
| [Fri75a]  | A. Friedman, Stochastic differential equations and applications. Vol. 1, Probability<br>and Mathematical Statistics, Vol. 28, Academic Press [Harcourt Brace Jovanovich,<br>Publishers], New York-London, 1975. MR0494490                              |
| [Fri75b]  | A. Friedman, Stochastic differential equations and applications. Vol. 2, Probability<br>and Mathematical Statistics, Vol. 28, Academic Press [Harcourt Brace Jovanovich,<br>Publishers], New York-London, 1976. MR0494491                              |
| [FS02]    | D. Frenkel and B. Smit, Understanding molecular simulations: From algorithms to applications, 2nd ed., Academic Press, San Diego, 2002.  |
| [FW98]    | M. I. Freidlin and A. D. Wentzell, <i>Random perturbations of dynamical systems</i> , 2nd ed., translated from the 1979 Russian original by Joseph Szücs, Grundlehren  |

der Mathematischen Wissenschaften [Fundamental Principles of Mathematical Sciences], vol. 260, Springer-Verlag, New York, 1998. MR1652127

- [Gal99] G. Gallavotti, Statistical mechanics: A short treatise, Texts and Monographs in Physics, Springer-Verlag, Berlin, 1999. MR1707309
- [Gar09] C. Gardiner, Stochastic methods: A handbook for the natural and social sciences, 4th ed., Springer Series in Synergetics, Springer-Verlag, Berlin, 2009. MR2676235
- [GB00] M. A. Gibson and J. Bruck, Efficient exact stochastic simulation of chemical systems with many species and channels, J. Phys. Chem. A 104 (2000), 1876– 1889.
- [Gey91] C. Geyer, Markov chain Monte Carlo maximum likelihood, Computing Science and Statistics: Proceedings of the 23rd Symposium on the interface (New York) (E. Keramigas, ed.), American Statistical Association, 1991, pp. 156–163.
- [GHO17] R. Ghanem, D. Higdon, and H. Owhadi (eds.), Handbook of uncertainty quantification, Springer International Publishing, Switzerland, 2017.
- [GHP13] D. Gillespie, A. Hellander, and L. Petzold, Perspective: Stochastic algorithms for chemical kinetics, J. Chem. Phys. 138 (2013), 170901.
- [Gil76] D. T. Gillespie, A general method for numerically simulating the stochastic time evolution of coupled chemical reactions, J. Computational Phys. 22 (1976), no. 4, 403–434, DOI 10.1016/0021-9991(76)90041-3. MR0503370
- [Gil92] D. T. Gillespie, Markov processes: An introduction for physical scientists, Academic Press, Inc., Boston, MA, 1992. MR1133392
- [Gil00] D. Gillespie, The chemical Langevin equation, J. Chem. Phys. 113 (2000), 297.
- [Gil01] D. Gillespie, Approximate accelerated stochastic simulation of chemically reacting systems, J. Chem. Phys. 115 (2001), 1716–1733.
- [Gil08] M. B. Giles, Multilevel Monte Carlo path simulation, Oper. Res. 56 (2008), no. 3, 607–617, DOI 10.1287/opre.1070.0496. MR2436856
- [Gil14] M. B. Giles, Multilevel Monte Carlo methods, Monte Carlo and quasi-Monte Carlo methods 2012, Springer Proc. Math. Stat., vol. 65, Springer, Heidelberg, 2013, pp. 83–103, DOI 10.1007/978-3-642-41095-6\_4. MR3145560
- [GJ87] J. Glimm and A. Jaffe, Quantum physics: A functional integral point of view, 2nd ed., Springer-Verlag, New York, 1987. MR887102
- [Gla04] P. Glasserman, Monte Carlo methods in financial engineering: Stochastic modelling and applied probability, Applications of Mathematics (New York), vol. 53, Springer-Verlag, New York, 2004. MR1999614
- [Gol80] H. Goldstein, Classical mechanics, 2nd ed., Addison-Wesley Publishing Co., Reading, Mass., 1980. Addison-Wesley Series in Physics. MR575343
- [Gol92] N. Goldenfeld, *Lectures on phase transitions and the renormalization group*, Perseus Books Publishing, Massachusetts, 1992.
- [GS66] I. M. Gelfand and G. E. Shilov, *Generalized functions*, vols. 1-5, Academic Press, New York and London, 1964–1966.
- [GS12] R. Ghanem and P. Spanos, Stochastic finite elements: A spectral approach, revised ed., Dover Publications Inc., Mineola, 2012.
- [GT95] C. Geyer and E. Thompson, Annealing Markov chain Monte Carlo with applications to ancestral inference, J. Amer. Stat. Assoc. 90 (1995), 909–920.
- [Hal50] P. R. Halmos, Measure Theory, D. Van Nostrand Company, Inc., New York, N. Y., 1950. MR0033869
- [HEnVEDB10] C. Hijón, P. Español, E. Vanden-Eijnden, and R. Delgado-Buscalioni, Mori-Zwanzig formalism as a practical computational tool, Faraday Disc. 144 (2010), 301–322.

| [HJ85]  | R. A. Horn and C. R. Johnson, <i>Matrix analysis</i> , Cambridge University Press, Cambridge, 1985. MR832183  |
|---------|---|
| [HJ99]  | G. Henkelman and H. Jónsson, A dimer method for finding saddle points on high dimensional potential surfaces using only first derivatives, J. Chem. Phys. <b>111</b> (1999), 7010–7022.   |
| [HJ00]  | <ul> <li>G. Henkelman and H. Jónsson, Improved tangent estimate in the nudged elastic<br/>band method for finding minimum energy paths and saddle points, J. Chem. Phys.<br/>113 (2000), 9978–9985.</li> </ul>                    |
| [HNW08] | E. Hairer, S. P. Norsett, and G. Wanner, <i>Solving ordinary differential equations</i><br><i>I: Nonstiff problems</i> , 2nd ed., Springer-Verlag, Berlin and Heidelberg, 2008.   |
| [HPM90] | P. Hanggi, P. Talkner, and M. Borkovec, <i>Reaction-rate theory: fifty years after Kramers</i> , Rev. Modern Phys. <b>62</b> (1990), no. 2, 251–341, DOI 10.1103/RevMod-Phys.62.251. MR1056234                                    |
| [HR02]  | E. L. Haseltine and J. B. Rawlings, Approximate simulation of coupled fast and slow reactions for stochastic kinetics, J. Chem. Phys. <b>117</b> (2002), 6959–6969.   |
| [HS08]  | T. Hida and S. Si, <i>Lectures on white noise functionals</i> , World Scientific Publishing Co. Pte. Ltd., Hackensack, NJ, 2008. MR2444857  |
| [HVE08] | M. Heymann and E. Vanden-Eijnden, The geometric minimum action method: a least action principle on the space of curves, Comm. Pure Appl. Math. <b>61</b> (2008), no. 8, 1052–1117, DOI 10.1002/cpa.20238. MR2417888               |
| [IW81]  | N. Ikeda and S. Watanabe, Stochastic differential equations and diffusion pro-<br>cesses, North-Holland Mathematical Library, vol. 24, North-Holland Publishing<br>Co., Amsterdam-New York; Kodansha, Ltd., Tokyo, 1981. MR637061 |
| [Jel97] | F. Jelinek, Statistical methods for speech recognition, MIT Press, Cambridge, 1997.   |
| [JM09]  | D. Jurafsky and J. H. Martin, Speech and language processing: An introduction<br>to natural language processing, computational linguistics, and speech recognition,<br>2nd ed., Pearson Prentice Hall, Upper Saddle River, 2009.  |
| [JQQ04] | DQ. Jiang, M. Qian, and MP. Qian, Mathematical theory of nonequilibrium steady states: On the frontier of probability and dynamical systems, Lecture Notes in Mathematics, vol. 1833, Springer-Verlag, Berlin, 2004. MR2034774    |
| [Kal97] | O. Kallenberg, <i>Foundations of modern probability</i> , Probability and its Applications (New York), Springer-Verlag, New York, 1997. MR1464694   |
| [Kes80] | H. Kesten, The critical probability of bond percolation on the square lattice equals $\frac{1}{2}$ , Comm. Math. Phys. <b>74</b> (1980), no. 1, 41–59. MR575895   |
| [KK80]  | C. Kittel and H. Kroemer, <i>Thermal physics</i> , 2nd ed., W. H. Freeman and Company, New York, 1980.  |
| [Kle06] | H. Kleinert, Path integrals in quantum mechanics, statistics, polymer physics, and financial markets, 4th ed., World Scientific Publishing Co. Pte. Ltd., Hackensack, NJ, 2006. MR2255818   |
| [Knu98] | D. E. Knuth, <i>The art of computer programming. Vol. 2</i> , Addison-Wesley, Reading, MA, 1998. Seminumerical algorithms, third edition [of MR0286318]. MR3077153  |
| [Kol56] | A. N. Kolmogorov, <i>Foundations of the theory of probability</i> , translation edited by Nathan Morrison, with an added bibliography by A. T. Bharucha-Reid, Chelsea Publishing Co., New York, 1956. MR0079843                   |
| [KP92]  | P. E. Kloeden and E. Platen, Numerical solution of stochastic differential equa-<br>tions, Applications of Mathematics (New York), vol. 23, Springer-Verlag, Berlin,<br>1992. MR1214374   |
| [Kra40] | H. A. Kramers, Brownian motion in a field of force and the diffusion model of chemical reactions, Physica 7 (1940), 284–304. MR0002962  |

| [KS76]   | J. G. Kemeny and J. L. Snell, <i>Finite Markov chains</i> , reprinting of the 1960 original, Undergraduate Texts in Mathematics, Springer-Verlag, New York-Heidelberg, 1976. MR0410929   |
|----------|--|
| [KS91]   | I. Karatzas and S. E. Shreve, <i>Brownian motion and stochastic calculus</i> , 2nd ed., Graduate Texts in Mathematics, vol. 113, Springer-Verlag, New York, 1991. MR1121940  |
| [KS07]   | L. B. Koralov and Y. G. Sinai, <i>Theory of probability and random processes</i> , 2nd ed., Universitext, Springer, Berlin, 2007. MR2343262  |
| [KS09]   | J. Keener and J. Sneyd, <i>Mathematical physiology</i> , 2nd ed., Springer-Verlag, New York, 2009.   |
| [KTH95]  | R. Kubo, M. Toda, and N. Hashitsume, <i>Statistical physics</i> , vol. 2, Springer-Verlag, Berlin, Heidelberg and New York, 1995.  |
| [Kub66]  | R. Kubo, The fluctuation-dissipation theorem, Rep. Prog. Phys. 29 (1966), 255.   |
| [Kur72]  | T. G. Kurtz, The relation between stochastic and deterministic models for chem-<br>ical reactions, J. Chem. Phys. 57 (1972), 2976–2978.  |
| [KW08]   | M. H. Kalos and P. A. Whitlock, <i>Monte Carlo methods</i> , 2nd ed., Wiley-Blackwell, Weinheim, 2008. MR2503174   |
| [KZW06]  | S. C. Kou, Q. Zhou, and W. H. Wong, <i>Equi-energy sampler with applica-</i><br><i>tions in statistical inference and statistical mechanics</i> , with discussions and<br>a rejoinder by the authors, Ann. Statist. <b>34</b> (2006), no. 4, 1581–1652, DOI<br>10.1214/009053606000000515. MR2283711 |
| [Lam77]  | J. Lamperti, Stochastic processes: A survey of the mathematical theory, Applied Mathematical Sciences, Vol. 23, Springer-Verlag, New York-Heidelberg, 1977. MR0461600  |
| [Lax02]  | P. D. Lax, <i>Functional analysis</i> , Pure and Applied Mathematics (New York), Wiley-Interscience [John Wiley & Sons], New York, 2002. MR1892228   |
| [LB05]   | D. P. Landau and K. Binder, A guide to Monte Carlo simulations in statistical physics, 2nd ed., Cambridge University Press, Cambridge, 2005.   |
| [LBL16]  | H. Lei, N. A. Baker, and X. Li, <i>Data-driven parameterization of the generalized Langevin equation</i> , Proc. Natl. Acad. Sci. USA <b>113</b> (2016), no. 50, 14183–14188, DOI 10.1073/pnas.1609587113. MR3600515   |
| [Li07]   | T. Li, Analysis of explicit tau-leaping schemes for simulating chemically re-<br>acting systems, Multiscale Model. Simul. 6 (2007), no. 2, 417–436, DOI<br>10.1137/06066792X. MR2338489  |
| [Liu04]  | J. S. Liu, Monte Carlo strategies in scientific computing, Springer-Verlag, New York, 2004.  |
| [LL17]   | T. Li and F. Lin, Large deviations for two-scale chemical kinetic processes, Com-<br>mun. Math. Sci. 15 (2017), no. 1, 123–163, DOI 10.4310/CMS.2017.v15.n1.a6.<br>MR3605551   |
| [LLLL14] | C. Lv, X. Li, F. Li, and T. Li, Constructing the energy landscape for genetic switching system driven by intrinsic noise, PLoS One 9 (2014), e88167.   |
| [LLL15]  | C. Lv, X. Li, F. Li, and T. Li, Energy landscape reveals that the budding yeast cell cycle is a robust and adaptive multi-stage process, PLoS Comp. Biol. <b>11</b> (2015), e1004156.  |
| [LM15]   | B. Leimkuhler and C. Matthews, <i>Molecular dynamics: With deterministic and stochastic numerical methods</i> , Interdisciplinary Applied Mathematics, vol. 39, Springer, Cham, 2015. MR3362507  |
| [Loè77]  | M. Loève, <i>Probability theory. I</i> , 4th ed., Graduate Texts in Mathematics, Vol. 45, Springer-Verlag, New York-Heidelberg, 1977. MR0651017  |

| [Lov96]  | L. Lovász, Random walks on graphs: a survey, Combinatorics, Paul Erdős is eighty,<br>Vol. 2 (Keszthely, 1993), Bolyai Soc. Math. Stud., vol. 2, János Bolyai Math. Soc.,<br>Budapest, 1996, pp. 353–397. MR1395866  |
|----------|---|
| [LX11]   | G. Li and X. S. Xie, Central dogma at the single-molecule level in living cells,<br>Nature <b>475</b> (2011), 308–315.  |
| [Mar68]  | G. Marsaglia, Random numbers fall mainly in the planes, Proc. Nat. Acad. Sci.<br>U.S.A. 61 (1968), 25–28, DOI 10.1073/pnas.61.1.25. MR0235695   |
| [MD10]   | D. Mumford and A. Desolneux, <i>Pattern theory: The stochastic analysis of real-</i><br>world signals, Applying Mathematics, A K Peters, Ltd., Natick, MA, 2010.<br>MR2723182   |
| [Mey66]  | PA. Meyer, <i>Probability and potentials</i> , Blaisdell Publishing Co. Ginn and Co., Waltham, MassToronto, OntLondon, 1966. MR0205288  |
| [MN98]   | M. Matsumoto and T. Nishimura, Mersenne twister: A 623-dimensionally equidis-<br>tributed uniform pseudo-random number generator, ACM Trans. Mod. Comp.<br>Simul. 8 (1998), 3–30.   |
| [MP92]   | E. Marinari and G. Parisi, Simulated tempering: A new Monte Carlo scheme,<br>Europhys. Lett. 19 (1992), 451–458.  |
| [MP10]   | P. Mörters and Y. Peres, <i>Brownian motion</i> , with an appendix by Oded Schramm<br>and Wendelin Werner, Cambridge Series in Statistical and Probabilistic Mathe-<br>matics, vol. 30, Cambridge University Press, Cambridge, 2010. MR2604525  |
| [MPRV08] | U. M. B. Marconi, A. Puglisi, L. Rondoni, and A. Vulpiani, <i>Fluctuation-dissipation: Response theory in statistical physics</i> , Phys. Rep. <b>461</b> (2008), 111–195.  |
| [MS99]   | C. D. Manning and H. Schütze, <i>Foundations of statistical natural language processing</i> , MIT Press, Cambridge, MA, 1999. MR1722790   |
| [MS01]   | M. Meila and J. Shi, A random walks view of spectral segmentation, Proceedings of the Eighth International Workshop on Artificial Intelligence and Statistics (San Francisco), 2001, pp. 92–97.   |
| [MT93]   | S. P. Meyn and R. L. Tweedie, <i>Markov chains and stochastic stability</i> , Commu-<br>nications and Control Engineering Series, Springer-Verlag London, Ltd., London,<br>1993. MR1287609  |
| [MT04]   | G. N. Milstein and M. V. Tretyakov, <i>Stochastic numerics for mathematical physics</i> , Scientific Computation, Springer-Verlag, Berlin, 2004. MR2069903  |
| [MTV16]  | A. Moraes, R. Tempone, and P. Vilanova, Multilevel hybrid Chernoff tau-leap,<br>BIT 56 (2016), no. 1, 189–239, DOI 10.1007/s10543-015-0556-y. MR3486459   |
| [Mul56]  | M. E. Muller, Some continuous Monte Carlo methods for the Dirichlet prob-<br>lem, Ann. Math. Statist. 27 (1956), 569–589, DOI 10.1214/aoms/1177728169.<br>MR0088786   |
| [MY71]   | A. S. Monin and A. M. Yaglom, <i>Statistical fluid mechanics: Mechanics of turbulence</i> , vol. 1, MIT Press, Cambridge, 1971.   |
| [Nor97]  | J. R. Norris, Markov chains, Cambridge University Press, Cambridge, 1997.   |
| [Oks98]  | <ul> <li>B. Øksendal, Stochastic differential equations: An introduction with applications,</li> <li>5th ed., Universitext, Springer-Verlag, Berlin, 1998. MR1619188</li> </ul>   |
| [Pap77]  | <ul> <li>G. C. Papanicolaou, Introduction to the asymptotic analysis of stochastic equa-<br/>tions, Modern modeling of continuum phenomena (Ninth Summer Sem. Appl.<br/>Math., Rensselaer Polytech. Inst., Troy, N.Y., 1975), Lectures in Appl. Math.,<br/>Vol. 16, Amer. Math. Soc., Providence, R.I., 1977, pp. 109–147. MR0458590</li> </ul> |
| [Pav14]  | G. A. Pavliotis, Stochastic processes and applications: Diffusion processes, the<br>Fokker-Planck and Langevin equations, Texts in Applied Mathematics, vol. 60,<br>Springer, New York, 2014. MR3288096   |

| [Paz83]                  | A. Pazy, Semigroups of linear operators and applications to partial differential equations, Applied Mathematical Sciences, vol. 44, Springer-Verlag, New York, 1983. MR710486  |
|--------------------------|--|
| [PTVF95]                 | W. H. Press, S. A. Teukolsky, W. T. Vetterling, and B. P. Flannery, <i>Numerical recipes in C</i> , 2nd ed., Cambridge University Press, Cambridge, New York, Port Chester, Melbourne and Sydney, 1995.  |
| [RÖ3]                    | A. Rößler, Runge-Kutta methods for the numerical solution of stochastic differ-<br>ential equation, Shaker-Verlag, Aachen, 2003.   |
| [Rab89]                  | L. R. Rabiner, A tutorial on hidden Markov models and selected applications in speech recognition, Proceedings of the IEEE 77 (1989), 257–286.   |
| [Ram69]                  | J. F. Ramaley, Buffon's noodle problem, Amer. Math. Monthly ${\bf 76}$ (1969), 916–918, DOI 10.2307/2317945. MR0254893   |
| [RC04]                   | C. P. Robert and G. Casella, <i>Monte Carlo statistical methods</i> , 2nd ed., Springer Texts in Statistics, Springer-Verlag, New York, 2004. MR2080278  |
| [Rea10]                  | A. Rukhin et al., A statistical test suite for random and pseudorandom number generators for cryptographic applications, available from https://nvlpubs.nist.gov/nistpubs/legacy/sp/nistspecialpublication800-22r1a.pdf, April 2010.   |
| [Rei98]                  | L. E. Reichl, A modern course in statistical physics, 2nd ed., A Wiley-Interscience Publication, John Wiley & Sons, Inc., New York, 1998. MR1600476  |
| [Ris89]                  | H. Risken, The Fokker-Planck equation: Methods of solution and applications, 2nd ed., Springer Series in Synergetics, vol. 18, Springer-Verlag, Berlin, 1989. MR987631   |
| $[\operatorname{Roc}70]$ | R. T. Rockafellar, <i>Convex analysis</i> , Princeton Mathematical Series, No. 28, Princeton University Press, Princeton, N.J., 1970. MR0274683  |
| [Roz82]                  | Yu. A. Rozanov, <i>Markov random fields</i> , translated from the Russian by Constance M. Elson, Applications of Mathematics, Springer-Verlag, New York-Berlin, 1982. MR676644   |
| [RSN56]                  | F. Riesz and B. SzNagy, <i>Functional analysis</i> , Blackie & Son Limited, London and Glasgow, 1956.  |
| [RVE13]                  | W. Ren and E. Vanden-Eijnden, A climbing string method for saddle point search, J. Chem. Phys. <b>138</b> (2013), 134105.  |
| [RW94a]                  | L. C. G. Rogers and D. Williams, <i>Diffusions, Markov processes, and martingales:</i><br><i>Foundations, Vol. 1</i> , 2nd ed., Wiley Series in Probability and Mathematical Sta-<br>tistics: Probability and Mathematical Statistics, John Wiley & Sons, Ltd., Chich-<br>ester, 1994. MR1331599 |
| [RW94b]                  | L. C. G. Rogers and D. Williams, <i>Diffusions, Markov processes, and martingales: Itô calculus, Vol. 2</i> , Wiley Series in Probability and Mathematical Statistics: Probability and Mathematical Statistics, John Wiley & Sons, Inc., New York, 1987. MR921238                                |
| [RW09]                   | R. T. Rockafellar and R. J-B. Wets, <i>Variational analysis</i> , Springer-Verlag, Berlin and Heidelberg, 2009.  |
| [RY05]                   | D. Revuz and M. Yor, <i>Continuous martingales and Brownian motion</i> , 3rd ed., Springer-Verlag, Berlin and Heidelberg, 2005.  |
| [Sch80]                  | Z. Schuss, Singular perturbation methods in stochastic differential equations of mathematical physics, SIAM Rev. <b>22</b> (1980), no. 2, 119–155, DOI 10.1137/1022024. MR564560   |
| [Sei12]                  | U. Seifert, Stochastic thermodynamics, fluctuation theorems and molecular machines, Rep. Prog. Phys. <b>75</b> (2012), 126001.   |
| [Sek10]                  | K. Sekimoto, <i>Stochastic energetics</i> , Lecture Notes in Physics, vol. 799, Springer-Verlag, Heidelberg, 2010.   |

| [Shi92] | A. N. Shiryaev (ed.), <i>Selected works of A.N. Kolmogorov</i> , vol. II, Kluwer Academic Publishers, Dordrecht, 1992.  |
|---------|---|
| [Shi96] | A. N. Shiryaev, <i>Probability</i> , 2nd ed., translated from the first (1980) Russian edition by R. P. Boas, Graduate Texts in Mathematics, vol. 95, Springer-Verlag, New York, 1996. MR1368405  |
| [Sin89] | Y. Sinai (ed.), Dynamical systems II: Ergodic theory with applications to dynam-<br>ical systems and statistical mechanics, Encyclopaedia of Mathematical Sciences,<br>vol. 2, Springer-Verlag, Berlin and Heidelberg, 1989.  |
| [SM00]  | J. Shi and J. Malik, Normalized cuts and image segmentation, IEEE Trans. Pattern Anal. Mach. Intel. <b>22</b> (2000), 888–905.  |
| [Soa94] | P. M. Soardi, <i>Potential theory on infinite networks</i> , Lecture Notes in Mathematics, vol. 1590, Springer-Verlag, Berlin, 1994. MR1324344  |
| [Sus78] | H. J. Sussmann, On the gap between deterministic and stochastic ordinary differential equations, Ann. Probability ${\bf 6}$ (1978), no. 1, 19–41. MR0461664   |
| [SW95]  | A. Shwartz and A. Weiss, <i>Large deviations for performance analysis</i> , Queues, communications, and computing, with an appendix by Robert J. Vanderbei, Stochastic Modeling Series, Chapman & Hall, London, 1995. MR1335456   |
| [Szn98] | AS. Sznitman, Brownian motion, obstacles and random media, Springer Monographs in Mathematics, Springer-Verlag, Berlin, 1998. MR1717054   |
| [Tai04] | K. Taira, Semigroups, boundary value problems and Markov processes, Springer Monographs in Mathematics, Springer-Verlag, Berlin, 2004. MR2019537  |
| [Tan96] | M. A. Tanner, Tools for statistical inference: Methods for the exploration of pos-<br>terior distributions and likelihood functions, 3rd ed., Springer Series in Statistics,<br>Springer-Verlag, New York, 1996. MR1396311  |
| [TB04]  | T. Tian and K. Burrage, <i>Binomial leap methods for simulating stochastic chemical kinetics</i> , J. Chem. Phys. <b>121</b> (2004), 10356–10364.   |
| [TKS95] | M. Toda, R. Kubo, and N. Saitô, <i>Statistical physics</i> , vol. 1, Springer-Verlag, Berlin, Heidelberg and New York, 1995.  |
| [Tou09] | H. Touchette, <i>The large deviation approach to statistical mechanics</i> , Phys. Rep. <b>478</b> (2009), no. 1-3, 1–69, DOI 10.1016/j.physrep.2009.05.002. MR2560411  |
| [TT90]  | D. Talay and L. Tubaro, Expansion of the global error for numerical schemes solving stochastic differential equations, Stochastic Anal. Appl. 8 (1990), no. 4, 483–509 (1991), DOI 10.1080/07362999008809220. MR1091544   |
| [Van83] | E. Vanmarcke, $Random\ fields:\ Analysis\ and\ synthesis,\ MIT\ Press,\ Cambridge,\ MA,\ 1983.\ MR761904$   |
| [Var84] | S. R. S. Varadhan, <i>Large deviations and applications</i> , CBMS-NSF Regional Conference Series in Applied Mathematics, vol. 46, Society for Industrial and Applied Mathematics (SIAM), Philadelphia, PA, 1984. MR758258  |
| [VK04]  | N. G. Van Kampen, <i>Stochastic processes in physics and chemistry</i> , 2nd ed., Elsevier, Amsterdam, 2004.  |
| [Wal02] | D. F. Walnut, An introduction to wavelet analysis, Applied and Numerical Harmonic Analysis, Birkhäuser Boston, Inc., Boston, MA, 2002. MR1854350  |
| [Wel03] | L. R. Welch, Hidden Markov models and the Baum-Welch algorithm, IEEE Infor. Theory Soc. Newslett. ${\bf 53}~(2003),$ 10–13.   |
| [Wie23] | N. Wiener, Differential space, J. Math. and Phys. 2 (1923), 131–174.  |
| [Win03] | G. Winkler, Image analysis, random fields and Markov chain Monte Carlo meth-<br>ods, 2nd ed., A mathematical introduction, with 1 CD-ROM (Windows), Stochas-<br>tic Modelling and Applied Probability, Applications of Mathematics (New York),<br>vol. 27, Springer-Verlag, Berlin, 2003. MR1950762 |

| [WZ65]    | E. Wong and M. Zakai, On the convergence of ordinary integrals to stochastic integrals, Ann. Math. Statist. <b>36</b> (1965), 1560–1564, DOI 10.1214/aoms/1177699916. MR0195142  |
|-----------|--|
| [XK02]    | D. Xiu and G. E. Karniadakis, <i>The Wiener-Askey polynomial chaos for stochas-</i><br><i>tic differential equations</i> , SIAM J. Sci. Comput. <b>24</b> (2002), no. 2, 619–644, DOI 10.1137/S1064827501387826. MR1951058 |
| [YLAVE16] | T. Yu, J. Lu, C. F. Abrams, and E. Vanden-Eijnden, <i>Multiscale implementation of infinite-swap replica exhange molecular dynamics</i> , Proc. Nat. Acad. Sci. USA <b>113</b> (2016), 11744–11749.                        |
| [Yos95]   | K. Yosida, <i>Functional analysis</i> , reprint of the sixth (1980) edition, Classics in Mathematics, Springer-Verlag, Berlin, 1995. MR1336382   |
| [ZD12]    | J. Zhang and Q. Du, Shrinking dimer dynamics and its applications to sad-<br>dle point search, SIAM J. Numer. Anal. <b>50</b> (2012), no. 4, 1899–1921, DOI<br>10.1137/110843149. MR3022203                                |
| [ZJ07]    | J. Zinn-Justin, <i>Phase transitions and renormalization group</i> , Oxford Graduate Texts, Oxford University Press, Oxford, 2007. MR2345069   |
| [ZL16]    | P. Zhou and T. Li, Construction of the landscape for multi-stable systems: Poten-<br>tial landscape, quasi-potential, A-type integral and beyond, J. Chem. Phys. <b>144</b><br>(2016), 094109.                             |

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