Contents

Preface v

1. Introduction 1

1.1 Computational statistical physics: some landmarks 1
1.1.1 Some orders of magnitude 2
1.1.2 Aims of molecular simulation 3
1.2 Microscopic description of physical systems 6
1.2.1 Interactions 6
1.2.2 Dynamics of isolated systems 13
1.2.3 Thermodynamic ensembles 20
1.3 Free energy and its numerical computation 33
1.3.1 Absolute free energy 34
1.3.2 Relative free energies 37
1.3.3 Free energy and metastability 44
1.3.4 Computational techniques 51
1.4 Summary of the mathematical tools and structure of the book 59

2. Sampling methods 61

2.1 Markov chain methods 63
2.1.1 Some background material on the theory of Markov chains 64
2.1.2 The Metropolis-Hastings algorithm 67
2.1.3 Hybrid Monte-Carlo 72
2.1.4 Generalized Metropolis-Hastings variants 74
2.2 Continuous stochastic dynamics 77

2.2.1 Mathematical background on Markovian continuous processes . . . 78
2.2.2 Overdamped Langevin process . . . 86
2.2.3 Langevin process . . . 88
2.2.4 Overdamped limit of the Langevin dynamics . . . 97
2.3 Convergence of sampling methods . . . 105
2.3.1 Sampling errors . . . 105
2.3.2 Rate of convergence for stochastic processes . . . 113
2.4 Methods for alchemical free energy differences . . . 118
2.4.1 Free energy perturbation . . . 119
2.4.2 Bridge sampling . . . 132
2.5 Histogram methods . . . 138
2.5.1 Principle of histogram methods . . . 138
2.5.2 Extended bridge sampling . . . 142

3. Thermodynamic integration and sampling with constraints 149
3.1 Introduction: The alchemical setting . . . 150
3.1.1 General strategy . . . 150
3.1.2 Numerical application . . . 152
3.2 The reaction coordinate case: configurational space sampling . . . 154
3.2.1 Reaction coordinate and free energy . . . 154
3.2.2 The mean force . . . 163
3.2.3 Sampling measures on submanifolds of $\mathbb{R}^n$ . . . 168
3.2.4 Sampling measures on submanifolds of $\mathbb{R}^n$: discretization . . . 180
3.2.5 Computing the mean force . . . 188
3.2.6 On the efficiency of constrained sampling . . . 200
3.3 The reaction coordinate case: Phase space sampling . . . 203
3.3.1 Constrained mechanical systems . . . 204
3.3.2 Phase space measures for constrained systems . . . 209
3.3.3 Hamilton and Poisson formalisms with constraints . . . 219
3.3.4 Constrained Langevin processes . . . 227
3.3.5 Numerical implementation . . . 232
3.3.6 Thermodynamic integration with constrained Langevin processes . . . 242

4. Nonequilibrium methods 259

4.1 The Jarzynski equality in the alchemical case 260
4.1.1 Markovian nonequilibrium simulations 260
4.1.2 Importance weights of nonequilibrium simulations 262
4.1.3 Practical implementation 266
4.1.4 Degeneracy of weights 269
4.1.5 Error analysis 275
4.2 Generalized Jarzynski-Crooks fluctuation identity 284
4.2.1 Derivation of the identity 285
4.2.2 Relationship with standard equalities in the physics and chemistry literature 291
4.2.3 Numerical strategies 293
4.3 Nonequilibrium stochastic methods in the reaction coordinate case 296
4.3.1 Overdamped nonequilibrium dynamics 296
4.3.2 Hamiltonian and Langevin nonequilibrium dynamics 305
4.3.3 Numerical results 323
4.4 Path sampling strategies 324
4.4.1 The path ensemble 324
4.4.2 Sampling switching paths 327

5. Adaptive methods 339
5.1 Adaptive algorithms: A general framework 340
5.1.1 Updating formulas 343
5.1.2 Extended dynamics 350
5.1.3 Discretization methods 353
5.1.4 Classical examples of adaptive methods 365
5.1.5 Numerical illustration 369
5.2 Convergence of the adaptive biasing force method 372
5.2.1 Presentation of the studied ABF dynamics 372
5.2.2 Precise statements of the convergence results . . . 377
5.2.3 Proofs 390

6. Selection 405
6.1 Replica selection framework 407
6.1.1 Weighted replica ensembles 407
6.1.2 Resampling strategies 413

6.1.3 Discrete-time version 419
6.1.4 Numerical application 422
6.2 Selection in adaptive methods 424
6.2.1 Motivation for the selection term 424
6.2.2 Numerical application 428

Appendix A Most important notation used throughout this book 431

A.1 General notation 431
A.2 Physical spaces and energies 433
A.3 Spaces with constraints, projection operators 434
A.4 Measures 436
A.5 Free energy 438

Bibliography 441

Index 455