

Contents

Preface	xv
Acknowledgments	xix
1 What are Theory, Computation, and Modeling?	1
1.1 Definition of Terms	1
1.2 Quantum Mechanics	4
1.3 Computable Quantities	5
1.3.1 Structure	5
1.3.2 Potential Energy Surfaces	6
1.3.3 Chemical Properties	10
1.4 Cost and Efficiency	11
1.4.1 Intrinsic Value	11
1.4.2 Hardware and Software	12
1.4.3 Algorithms	14
1.5 Note on Units	15
Bibliography and Suggested Additional Reading	15
References	16
2 Molecular Mechanics	17
2.1 History and Fundamental Assumptions	17
2.2 Potential Energy Functional Forms	19
2.2.1 Bond Stretching	19
2.2.2 Valence Angle Bending	21
2.2.3 Torsions	22
2.2.4 van der Waals Interactions	27
2.2.5 Electrostatic Interactions	30
2.2.6 Cross Terms	34
2.2.7 Parameterization Strategies	35
2.3 Force-field Energies and Thermodynamics	39
2.4 Geometry Optimization	40
2.4.1 Optimization Algorithms	40
2.4.2 Optimization Aspects Specific to Force Fields	46
2.5 Menagerie of Modern Force Fields	49
2.5.1 Available Force Fields	49
2.5.2 Validation	55
2.6 Case Study: (2 <i>R</i> *,4 <i>S</i> *)-1-Hydroxy-2,4-dimethylhex-5-ene	58

Bibliography and Suggested Additional Reading	60
References	61
3 Simulations of Molecular Ensembles	63
3.1 Relationship Between MM Optima and Real Systems	63
3.2 Phase Space and Trajectories	64
3.2.1 Properties as Ensemble Averages	64
3.2.2 Properties as Time Averages of Trajectories	65
3.3 Molecular Dynamics	66
3.3.1 Harmonic Oscillator Trajectories	66
3.3.2 Non-analytical Systems	68
3.3.3 Practical Issues in Propagation	71
3.3.4 Stochastic Dynamics	73
3.4 Monte Carlo	74
3.4.1 Manipulation of Phase-space Integrals	74
3.4.2 Metropolis Sampling	75
3.5 Ensemble and Dynamical Property Examples	76
3.6 Key Details in Formalism	82
3.6.1 Cutoffs and Boundary Conditions	82
3.6.2 Polarization	84
3.6.3 Control of System Variables	85
3.6.4 Simulation Convergence	87
3.6.5 The Multiple Minima Problem	89
3.7 Case Study: Silica Sodalite	90
Bibliography and Suggested Additional Reading	92
References	93
4 Foundations of Molecular Orbital Theory	95
4.1 Quantum Mechanics and the Wave Function	95
4.2 The Hamiltonian Operator	96
4.2.1 General Features	96
4.2.2 The Variational Principle	98
4.2.3 The Born–Oppenheimer Approximation	100
4.3 Construction of Trial Wave Functions	101
4.3.1 The LCAO Basis Set Approach	101
4.3.2 The Secular Equation	103
4.4 Hückel Theory	105
4.4.1 Fundamental Principles	105
4.4.2 Application to the Allyl System	106
4.5 Many-electron Wave Functions	109
4.5.1 Hartree-product Wave Functions	109
4.5.2 The Hartree Hamiltonian	111
4.5.3 Electron Spin and Antisymmetry	112
4.5.4 Slater Determinants	114
4.5.5 The Hartree-Fock Self-consistent Field Method	116
Bibliography and Suggested Additional Reading	119
References	120
5 Semiempirical Implementations of Molecular Orbital Theory	121
5.1 Semiempirical Philosophy	121
5.1.1 Chemically Virtuous Approximations	121
5.1.2 Analytic Derivatives	123
5.2 Extended Hückel Theory	124

5.3	CNDO Formalism	126
5.4	INDO Formalism	129
5.4.1	INDO and INDO/S	129
5.4.2	MINDO/3 and SINDO1	131
5.5	Basic NDDO Formalism	133
5.5.1	MNDO	133
5.5.2	AM1	135
5.5.3	PM3	136
5.6	General Performance Overview of Basic NDDO Models	137
5.6.1	Energetics	137
5.6.2	Geometries	139
5.6.3	Charge Distributions	141
5.7	Ongoing Developments in Semiempirical MO Theory	141
5.7.1	Use of Semiempirical Properties in SAR	141
5.7.2	d Orbitals in NDDO Models	142
5.7.3	SRP Models	144
5.7.4	Linear Scaling	144
5.8	Case Study: Asymmetric Alkylation of Benzaldehyde	146
	Bibliography and Suggested Additional Reading	149
	References	149
6	<i>Ab Initio</i> Implementations of Hartree–Fock Molecular Orbital Theory	153
6.1	<i>Ab Initio</i> Philosophy	153
6.2	Basis Sets	154
6.2.1	Functional Forms	155
6.2.2	Contracted Gaussian Functions	156
6.2.3	Single- ζ , Multiple- ζ , and Split-Valence	158
6.2.4	Polarization Functions	161
6.2.5	Diffuse Functions	163
6.2.6	The HF Limit	164
6.2.7	Effective Core Potentials	166
6.2.8	Sources	167
6.3	Key Technical and Practical Points of Hartree–Fock Theory	168
6.3.1	SCF Convergence	168
6.3.2	Symmetry	170
6.3.3	Open-shell Systems	175
6.3.4	Efficiency of Implementation and Use	178
6.4	General Performance Overview of <i>Ab Initio</i> HF Theory	179
6.4.1	Energetics	179
6.4.2	Geometries	183
6.4.3	Charge Distributions	185
6.5	Case Study: Polymerization of 4-Substituted Aromatic Enynes	186
	Bibliography and Suggested Additional Reading	188
	References	188
7	Including Electron Correlation in Molecular Orbital Theory	191
7.1	Dynamical vs. Non-dynamical Electron Correlation	191
7.2	Multiconfiguration Self-Consistent Field Theory	193
7.2.1	Conceptual Basis	193
7.2.2	Active Space Specification	195
7.2.3	Full Configuration Interaction	199
7.3	Configuration Interaction	199

7.3.1	Single-determinant Reference	199
7.3.2	Multireference	203
7.4	Perturbation Theory	204
7.4.1	General Principles	204
7.4.2	Single-reference	207
7.4.3	Multireference	210
7.5	Coupled-cluster Theory	211
7.6	Practical Issues in Application	213
7.6.1	Basis Set Convergence	213
7.6.2	Sensitivity to Reference Wave Function	215
7.6.3	Price/Performance Summary	220
7.7	Parameterized Methods	222
7.7.1	Scaling Correlation Energies	222
7.7.2	Extrapolation	224
7.7.3	Multilevel Methods	224
7.8	Case Study: Ethylenedione Radical Anion	228
	Bibliography and Suggested Additional Reading	230
	References	231
8	Density Functional Theory	233
8.1	Theoretical Motivation	233
8.1.1	Philosophy	233
8.1.2	Early Approximations	234
8.2	Rigorous Foundation	236
8.2.1	The Hohenberg–Kohn Existence Theorem	236
8.2.2	The Hohenberg–Kohn Variational Theorem	238
8.3	Kohn–Sham Self-consistent Field Methodology	239
8.4	Exchange-correlation Functionals	241
8.4.1	Local Density Approximation	242
8.4.2	Density Gradient Corrections	247
8.4.3	Adiabatic Connection Methods	248
8.5	Advantages and Disadvantages of DFT Compared to MO Theory	252
8.5.1	Densities vs. Wave Functions	252
8.5.2	Computational Efficiency	253
8.5.3	Limitations of the KS Formalism	255
8.5.4	Systematic Improvability	258
8.5.5	Worst-case Scenarios	259
8.6	General Performance Overview of DFT	260
8.6.1	Energetics	260
8.6.2	Geometries	265
8.6.3	Charge Distributions	268
8.7	Case Study: Transition-Metal Catalyzed Carbonylation of Methanol	269
	Bibliography and Suggested Additional Reading	271
	References	271
9	Charge Distribution and Spectroscopic Properties	275
9.1	Properties Related to Charge Distribution	275
9.1.1	Electric Multipole Moments	275
9.1.2	Molecular Electrostatic Potential	278
9.1.3	Partial Atomic Charges	278
9.1.4	Total Spin	289
9.1.5	Polarizability and Hyperpolarizability	291
9.1.6	ESR Hyperfine Coupling Constants	293

9.2	Ionization Potentials and Electron Affinities	296
9.3	Spectroscopy of Nuclear Motion	297
9.3.1	Rotational	297
9.3.2	Vibrational	299
9.4	NMR Spectral Properties	309
9.4.1	Technical Issues	309
9.4.2	Chemical Shifts	310
9.4.3	Spin–spin Couplings	311
9.5	Case Study: Matrix Isolation of Perfluorinated <i>p</i> -Benzyne	314
	Bibliography and Suggested Additional Reading	315
	References	316
10	Thermodynamic Properties	319
10.1	Microscopic–macroscopic Connection	319
10.2	Zero-point Vibrational Energy	320
10.3	Ensemble Properties and Basic Statistical Mechanics	321
10.3.1	Ideal Gas Assumption	322
10.3.2	Separability of Energy Components	323
10.3.3	Molecular Electronic Partition Function	324
10.3.4	Molecular Translational Partition Function	325
10.3.5	Molecular Rotational Partition Function	326
10.3.6	Molecular Vibrational Partition Function	328
10.4	Standard-state Heats and Free Energies of Formation and Reaction	330
10.4.1	Direct Computation	331
10.4.2	Parametric Improvement	334
10.4.3	Isodesmic Equations	335
10.5	Technical Caveats	338
10.5.1	Semiempirical Heats of Formation	338
10.5.2	Low-frequency Motions	339
10.5.3	Equilibrium Populations over Multiple Minima	340
10.5.4	Standard-state Conversions	341
10.6	Case Study: Halocarbene Heats of Formation	342
	Bibliography and Suggested Additional Reading	344
	References	345
11	Implicit Models for Condensed Phases	347
11.1	Condensed-phase Effects on Structure and Reactivity	347
11.1.1	Free Energy of Transfer and Its Physical Components	348
11.1.2	Solvation as It Affects Potential Energy Surfaces	351
11.2	Electrostatic Interactions with a Continuum	355
11.2.1	The Poisson Equation	356
11.2.2	Generalized Born	363
11.2.3	Conductor-like Screening Model	366
11.3	Continuum Models for Non-electrostatic Interactions	367
11.3.1	Specific Component Models	367
11.3.2	Atomic Surface Tensions	368
11.4	Strengths and Weaknesses of Continuum Solvation Models	371
11.4.1	General Performance for Solvation Free Energies	371
11.4.2	Partitioning	374
11.4.3	Non-isotropic Media	375
11.4.4	Potentials of Mean Force and Solvent Structure	377
11.4.5	Equilibrium vs. Non-equilibrium Solvation	378

11.5	Case Study: Aqueous Reductive Dechlorination of Hexachloroethane	379
	Bibliography and Suggested Additional Reading	381
	References	382
12	Explicit Models for Condensed Phases	385
12.1	Motivation	385
12.2	Computing Free-energy Differences	385
12.2.1	Raw Differences	386
12.2.2	Free-energy Perturbation	388
12.2.3	Slow Growth and Thermodynamic Integration	391
12.2.4	Free-energy Cycles	393
12.2.5	Potentials of Mean Force	394
12.2.6	Technical Issues and Error Analysis	397
12.3	Other Thermodynamic Properties	399
12.4	Solvent Models	400
12.4.1	Classical Models	400
12.4.2	Quantal Models	402
12.5	Relative Merits of Explicit and Implicit Solvent Models	403
12.5.1	Analysis of Solvation Shell Structure and Energetics	403
12.5.2	Speed/Efficiency	405
12.5.3	Non-equilibrium Solvation	405
12.5.4	Mixed Explicit/Implicit Models	406
12.6	Case Study: Binding of Biotin Analogs to Avidin	406
	Bibliography and Suggested Additional Reading	409
	References	409
13	Hybrid Quantal/Classical Models	411
13.1	Motivation	411
13.2	Boundaries Through Space	412
13.2.1	Unpolarized Interactions	413
13.2.2	Polarized QM/Unpolarized MM	414
13.2.3	Fully Polarized Interactions	419
13.3	Boundaries Through Bonds	420
13.3.1	Linear Combinations of Model Compounds	421
13.3.2	Link Atoms	426
13.3.3	Frozen Orbitals	428
13.4	Empirical Valence Bond Methods	430
13.4.1	Potential Energy Surfaces	431
13.4.2	Following Reaction Paths	434
13.4.3	Generalization to QM/MM	435
13.5	Case Study: Catalytic Mechanism of Yeast Enolase	435
	Bibliography and Suggested Additional Reading	437
	References	438
14	Excited Electronic States	441
14.1	Determinantal/Configurational Representation of Excited States	441
14.2	Singly Excited States	446
14.2.1	SCF Applicability	447
14.2.2	CI Singles	450
14.2.3	Rydberg States	452
14.3	General Excited State Methods	452
14.3.1	Higher Roots in MCSCF and CI Calculations	453
14.3.2	Propagator Methods and Time-dependent DFT	455

14.4	Sum and Projection Methods	456
14.5	Transition Probabilities	460
14.6	Solvatochromism	463
14.7	Case Study: Organic Light Emitting Diode Alq3	466
	Bibliography and Suggested Additional Reading	468
	References	468
15	Adiabatic Reaction Dynamics	471
15.1	Reaction Kinetics and Rate Constants	471
15.1.1	Unimolecular Reactions	472
15.1.2	Bimolecular Reactions	473
15.2	Reaction Paths and Transition States	474
15.3	Transition-state Theory	476
15.3.1	Canonical Equation	476
15.3.2	Variational Transition-state Theory	483
15.3.3	Quantum Effects on the Rate Constant	485
15.4	Condensed-phase Dynamics	489
15.5	Non-adiabatic Dynamics	490
15.5.1	General Surface Crossings	490
15.5.2	Marcus Theory	492
15.6	Case Study: Isomerization of Propylene Oxide	495
	Bibliography and Suggested Additional Reading	497
	References	497
Appendix A	Acronym Glossary	499
Appendix B	Symmetry and Group Theory	505
B.1	Symmetry Elements	505
B.2	Molecular Point Groups and Irreducible Representations	507
B.3	Assigning Electronic State Symmetries	508
B.4	Symmetry in the Evaluation of Integrals and Partition Functions	510
Appendix C	Spin Algebra	513
C.1	Spin Operators	513
C.2	Pure- and Mixed-spin Wave Functions	514
C.3	UHF Wave Functions	519
C.4	Spin Projection/Annihilation	519
	Reference	522
Appendix D	Orbital Localization	523
D.1	Orbitals as Empirical Constructs	523
D.2	Natural Bond Orbital Analysis	526
	References	527
Index		529