

Contents

Foreword VII

Preface XIX

List of Abbreviations Appearing in this Volume XXVII

List of Contributors XXXIII

1 An Introduction to the Quantum Theory of Atoms in Molecules 1

Chérif F. Matta and Russell J. Boyd

- 1.1 Introduction 1
- 1.2 The Topology of the Electron Density 1
- 1.3 The Topology of the Electron Density Dictates the Form of Atoms in Molecules 5
- 1.4 The Bond and Virial Paths, and the Molecular and Virial Graphs 8
- 1.5 The Atomic Partitioning of Molecular Properties 9
- 1.6 The Nodal Surface in the Laplacian as the Reactive Surface of a Molecule 10
- 1.7 Bond Properties 10
 - 1.7.1 The Electron Density at the BCP (ρ_b) 11
 - 1.7.2 The Bonded Radius of an Atom (r_b), and the Bond Path Length 11
 - 1.7.3 The Laplacian of the Electron Density at the BCP ($\nabla^2 \rho_b$) 11
 - 1.7.4 The Bond Ellipticity (ε) 12
 - 1.7.5 Energy Densities at the BCP 12
 - 1.7.6 Electron Delocalization between Bonded Atoms: A Direct Measure of Bond Order 13
- 1.8 Atomic Properties 15
 - 1.8.1 Atomic Electron Population [$N(\Omega)$] and Charge [$q(\Omega)$] 16
 - 1.8.2 Atomic Volume [$\text{Vol.}(\Omega)$] 16
 - 1.8.3 Kinetic Energy [$T(\Omega)$] 17
 - 1.8.4 Laplacian [$L(\Omega)$] 17
 - 1.8.5 Total Atomic Energy [$E_e(\Omega)$] 18

1.8.6	Atomic Dipolar Polarization [$\mu(\Omega)$]	20
1.8.7	Atomic Quadrupolar Polarization [$Q(\Omega)$]	24
1.9	“Practical” Uses and Utility of QTAIM Bond and Atomic Properties	25
1.9.1	The Use of QTAIM Bond Critical Point Properties	25
1.9.2	The Use of QTAIM Atomic Properties	26
1.10	Steps of a Typical QTAIM Calculation	27
	<i>References</i>	30

Part I Advances in Theory 35

2 The Lagrangian Approach to Chemistry 37

Richard F. W. Bader

2.1	Introduction	37
2.1.1	From Observation, to Physics, to QTAIM	37
2.2	The Lagrangian Approach	38
2.2.1	What is The Lagrangian Approach and What Does it Do?	38
2.2.2	The Lagrangian and the Action Principle – A Return to the Beginnings	39
2.2.3	Minimization of the Action	40
2.2.4	Steps in Minimizing the Action	41
2.3	The Action Principle in Quantum Mechanics	42
2.3.1	Schrödinger’s Appeal to the Action	42
2.3.2	Schrödinger’s Minimization	42
2.3.2.1	Two Ways of Expressing the Kinetic Energy	43
2.3.3	Obtaining an Atom from Schrödinger’s Variation	44
2.3.3.1	The Role of Laplacian in the Definition of an Atom	45
2.3.4	Getting Chemistry from $\delta G(\psi, \nabla\psi; \Omega)$	46
2.4	From Schrödinger to Schwinger	48
2.4.1	From Dirac to Feynman and Schwinger	48
2.4.2	From Schwinger to an Atom in a Molecule	49
2.5	Molecular Structure and Structural Stability	52
2.5.1	Definition of Molecular Structure	52
2.5.2	Prediction of Structural Stability	53
2.6	Reflections and the Future	53
2.6.1	Reflections	53
2.6.2	The Future	55
	<i>References</i>	57

3 Atomic Response Properties 61

Todd A. Keith

3.1	Introduction	61
3.2	Apparent Origin-dependence of Some Atomic Response Properties	62
3.3	Bond Contributions to “Null” Molecular Properties	64

3.4	Bond Contributions to Atomic Charges in Neutral Molecules	70
3.5	Atomic Contributions to Electric Dipole Moments of Neutral Molecules	71
3.6	Atomic Contributions to Electric Polarizabilities	73
3.7	Atomic Contributions to Vibrational Infrared Absorption Intensities	78
3.8	Atomic Nuclear Virial Energies	82
3.9	Atomic Contributions to Induced Electronic Magnetic Dipole Moments	88
3.10	Atomic Contributions to Magnetizabilities of Closed-Shell Molecules	90
	<i>References</i>	94
4	QTAIM Analysis of Raman Scattering Intensities: Insights into the Relationship Between Molecular Structure and Electronic Charge Flow	95
	<i>Kathleen M. Gough, Richard Dawes, Jason R. Dwyer, and Tammy L. Welshman</i>	
4.1	Introduction	95
4.2	Background to the Problem	96
4.2.1	Conceptual Approach to a Solution	97
4.2.1.1	Experimental Measurement of Raman Scattering Intensities	97
4.2.1.2	Theoretical Modeling of Raman Scattering Intensities: What We Did and Why	99
4.3	Methodology	100
4.3.1	Modeling α and $\partial\alpha/\partial r$	101
4.3.2	Recouping α From the Wavefunction, With QTAIM	102
4.3.3	Recovering $\partial\alpha/\partial r$ From QTAIM	103
4.4	Specific Examples of the Use of AIM2000 Software to Analyze Raman Intensities	103
4.4.1	Modeling α in H_2	104
4.4.1.1	Modeling $\Delta\bar{\alpha}/\Delta r$ in H_2	106
4.4.2	Modeling α and $\Delta\bar{\alpha}/\Delta r$ in CH_4	106
4.4.3	Additional Exercises for the Interested Reader	108
4.5	Patterns in α That Are Discovered Through QTAIM	109
4.6	Patterns in $\partial\alpha/\partial r_{CH}$ That Apply Across Different Structures, Conformations, Molecular Types: What is Transferable?	111
4.6.1	Patterns in $\Delta\bar{\alpha}/\Delta r_{CH}$ Revealed by QTAIM	111
4.6.1.1	QTAIM Analysis of $\Delta\bar{\alpha}/\Delta r_{CH}$ in Small Alkanes	111
4.6.1.2	What Did We Learn From QTAIM That Can be Transferred to the Other Molecules?	113
4.7	What Can We Deduce From Simple Inspection of $\partial\bar{\alpha}/\partial r_{CH}$ and $\partial\bar{\alpha}/\partial r_{CC}$ From Gaussian?	114
4.7.1	Variations in $\partial\bar{\alpha}/\partial r_{CH}$ Among the Alkanes	114
4.7.2	$\Delta\bar{\alpha}/\Delta r_{CH}$ in Cycloalkanes, Bicycloalkanes, and Hedranes	116
4.7.3	Patterns That Emerge in $\Delta\bar{\alpha}/\Delta r_{CC}$ of Alkanes	116

4.7.4	Unsaturated Hydrocarbons and the Silanes: C–H, C=C, and Si–Si Derivatives	117
4.8	Conclusion	118
	References	119
5	Topological Atom–Atom Partitioning of Molecular Exchange Energy and its Multipolar Convergence	121
	<i>Michel Rafat and Paul L. A. Popelier</i>	
5.1	Introduction	121
5.2	Theoretical Background	123
5.3	Details of Calculations	128
5.4	Results and Discussion	130
5.4.1	Convergence of the Exchange Energy	130
5.4.2	Convergence of the Exchange Force	136
5.4.3	Diagonalization of a Matrix of Exchange Moments	136
5.5	Conclusion	139
	References	139
6	The ELF Topological Analysis Contribution to Conceptual Chemistry and Phenomenological Models	141
	<i>Bernard Silvi and Ronald J. Gillespie</i>	
6.1	Introduction	141
6.2	Why ELF and What is ELF?	142
6.3	Concepts from the ELF Topology	144
6.3.1	The Synaptic Order	145
6.3.2	The Localization Domains	145
6.3.3	ELF Population Analysis	147
6.4	VSEPR Electron Domains and the Volume of ELF Basins	149
6.5	Examples of the Correspondence Between ELF Basins and the Domains of the VSEPR Model	153
6.5.1	Octet Molecules	153
6.5.1.1	Hydrides (CH ₄ , NH ₃ , H ₂ O)	153
6.5.1.2	AX ₄ (CH ₄ , CF ₄ , SiCl ₄)	154
6.5.1.3	AX ₃ E and AX ₂ E ₂ (NCl ₃ , OCl ₂)	154
6.5.2	Hypervalent Molecules	155
6.5.2.1	PCl ₅ and SF ₆	155
6.5.2.2	SF ₄ and ClF ₃	155
6.5.2.3	AX ₇ and AX ₆ E Molecules	155
6.5.3	Multiple Bonds	156
6.5.3.1	C ₂ H ₄ and C ₂ H ₂	156
6.5.3.2	Si ₂ Me ₄ and Si ₂ Me ₂	157
6.6	Conclusions	158
	References	159

Part II Solid State and Surfaces 163**7 Solid State Applications of QTAIM and the Source Function – Molecular Crystals, Surfaces, Host–Guest Systems and Molecular Complexes 165***Carlo Gatti*

- 7.1 Introduction 165
- 7.2 QTAIM Applied to Solids – the TOPOND Package 166
- 7.2.1 QTAIM Applied to Experimental Densities: TOPXD and XD Packages 168
- 7.3 QTAIM Applied to Molecular Crystals 170
- 7.3.1 Urea 171
- 7.3.1.1 Urea: Packing Effects 172
- 7.4 QTAIM Applied to Surfaces 179
- 7.4.1 Si(111)(1 × 1) Clean and Hydrogen-covered Surfaces 180
- 7.4.2 Si(111)(2 × 1) Reconstructed Surface 184
- 7.5 QTAIM Applied to Host–Guest Systems 186
- 7.5.1 Type I Inorganic Clathrates $A_8Ga_{16}Ge_{30}$ (A = Sr, Ba) 186
- 7.5.2 Sodium Electrosodalite 190
- 7.6 The Source Function: Theory 192
- 7.6.1 The Source Function and Chemical Transferability 194
- 7.6.2 Chemical Information from the Source Function: Long and Short-range Bonding Effects in Molecular Complexes 196
- 7.6.3 The Source Function: Latest Developments 201
- References 202*

8 Topology and Properties of the Electron Density in Solids 207*Víctor Luaña, Miguel A. Blanco, Aurora Costales, Paula Mori-Sánchez, and Angel Martín Pendás*

- 8.1 Introduction 207
- 8.2 The Electron Density Topology and the Atomic Basin Shape 209
- 8.3 Crystalline Isostructural Families and Topological Polymorphism 213
- 8.4 Topological Classification of Crystals 215
- 8.5 Bond Properties – Continuity from the Molecular to the Crystalline Regime 217
- 8.6 Basin Partition of the Thermodynamic Properties 219
- 8.7 Obtaining the Electron Density of Crystals 222
- References 227*

9 Atoms in Molecules Theory for Exploring the Nature of the Active Sites on Surfaces 231*Yosslen Aray, Jesus Rodríguez, and David Vega*

- 9.1 Introduction 231
- 9.2 Implementing the Determination of the Topological Properties of $\rho(r)$ from a Three-dimensional Grid 231

- 9.3 An Application to Nanocatalysts – Exploring the Structure of the Hydrodesulfurization MoS₂ Catalysts 236
- 9.3.1 Catalyst Models 237
- 9.3.2 The Full $\rho(r)$ Topology of the MoS₂ Bulk 241
- 9.3.3 The $\rho(r)$ Topology of the MoS₂ Edges 245
- References* 254

Part III Experimental Electron Densities and Biological Molecules 257

10 Interpretation of Experimental Electron Densities by Combination of the QTAMC and DFT 259

Vladimir G. Tsirelson

- 10.1 Introduction 259
- 10.2 Specificity of the Experimental Electron Density 261
- 10.3 Approximate Electronic Energy Densities 262
- 10.3.1 Kinetic and Potential Energy Densities 262
- 10.3.2 Exchange and Correlation Energy Densities 271
- 10.4 The Integrated Energy Quantities 275
- 10.5 Concluding Remarks 276
- References* 278

11 Topological Analysis of Proteins as Derived from Medium and High-resolution Electron Density: Applications to Electrostatic Properties 285

Laurence Leherste, Benoît Guillot, Daniel P. Vercauteren, Virginie Pichon-Pesme, Christian Jelsch, Angélique Lagoutte, and Claude Lecomte

- 11.1 Introduction 285
- 11.2 Methodology and Technical Details 287
- 11.2.1 Ultra-high X-ray Resolution Approach 287
- 11.2.2 Medium-resolution Approach 289
- 11.2.2.1 Promolecular Electron Density Distribution Calculated from Structure Factors 289
- 11.2.2.2 Promolecular Electron Density Distribution Calculated from Atoms 290
- 11.2.3 A Test System – Human Aldose Reductase 291
- 11.3 Topological Properties of Multipolar Electron Density Database 294
- 11.4 Analysis of Local Maxima in Experimental and Promolecular Medium-resolution Electron Density Distributions 298
- 11.4.1 Experimental and Promolecular Electron Density Distributions Calculated from Structure Factors 299
- 11.4.2 Promolecular Electron Density Distributions Calculated from Atoms (PASA Model) 301
- 11.5 Calculation of Electrostatic Properties from Atomic and Fragment Representations of Human Aldose Reductase 305
- 11.5.1 Medium- and High-resolution Approaches of Electrostatic Potential Computations 307

11.5.2	Electrostatic Potential Comparisons	309
11.5.3	Electrostatic Interaction Energies	312
11.6	Conclusions and Perspectives	312
	<i>References</i>	314
12	Fragment Transferability Studied Theoretically and Experimentally with QTAIM – Implications for Electron Density and Invariom Modeling	317
	<i>Peter Luger and Birger Dittrich</i>	
12.1	Introduction	317
12.2	Experimental Electron-density Studies	318
12.2.1	Experimental Requirements	318
12.2.2	Recent Experimental Advances	319
12.2.2.1	Synchrotron Radiation Compared with Laboratory Sources	319
12.2.2.2	Data Collection at Ultra-low Temperatures (10–20 K)	321
12.3	Studying Transferability with QTAIM – Atomic and Bond Topological Properties of Amino Acids and Oligopeptides	323
12.4	Invariom Modeling	328
12.4.1	Invariom Notation, Choice of Model Compounds, and Practical Considerations	330
12.4.2	Support for Pseudoatom Fragments from QTAIM	331
12.5	Applications of Aspherical Invariom Scattering Factors	334
12.5.1	Molecular Geometry and Anisotropic Displacement Properties	334
12.5.2	Using the Enhanced Multipole Model Anomalous Dispersion Signal	335
12.5.3	Modeling the Electron Density of Oligopeptide and Protein Molecules	336
12.6	Conclusion	338
	<i>References</i>	339
Part IV	Chemical Bonding and Reactivity	343
13	Interactions Involving Metals – From “Chemical Categories” to QTAIM, and Backwards	345
	<i>Piero Macchi and Angelo Sironi</i>	
13.1	Introduction	345
13.2	The Electron Density in Isolated Metal Atoms – Hints of Anomalies	345
13.3	Two-center Bonding	349
13.3.1	The Dative Bond	350
13.3.1.1	Metal Carbonyls	351
13.3.1.2	Donor–Acceptor Interactions of Heavy Elements	352
13.3.2	Direct Metal–Metal Bonding	352
13.4	Three-center Bonding	356
13.4.1	π -Complexes	357
13.4.2	σ -Complexes	363

13.4.2.1	Dihydrogen and Dihydride Coordination	364
13.4.2.2	Agostic Interactions	364
13.4.2.3	Hydride Bridges	367
13.4.3	Carbonyl-supported Metal–Metal Interactions	370
13.5	Concluding Remarks	371
	<i>References</i>	372

14 Applications of the Quantum Theory of Atoms in Molecules in Organic Chemistry – Charge Distribution, Conformational Analysis and Molecular Interactions 375

Jesús Hernández-Trujillo, Fernando Cortés-Guzmán, and Gabriel Cuevas

14.1	Introduction	375
14.2	Electron Delocalization	375
14.2.1	The Pair-density	375
14.2.2	$^3J_{\text{HH}}$ Coupling Constants and Electron Delocalization	378
14.3	Conformational Equilibria	380
14.3.1	Rotational barriers	380
14.3.1.1	Rotational Barrier of Ethane	380
14.3.1.2	Rotational Barrier of 1,2-Disubstituted Ethanes	382
14.3.2	Anomeric Effect on Heterocyclohexanes	386
14.4	Aromatic Molecules	391
14.4.1	Electronic Structure of Polybenzenoid Hydrocarbons	391
14.5	Conclusions	395
	<i>References</i>	396

15 Aromaticity Analysis by Means of the Quantum Theory of Atoms in Molecules 399

Eduard Matito, Jordi Poater, and Miquel Solà

15.1	Introduction	399
15.2	The Fermi Hole and the Delocalization Index	401
15.3	Electron Delocalization in Aromatic Systems	403
15.4	Aromaticity Electronic Criteria Based on QTAIM	404
15.4.1	The <i>para</i> -Delocalization Index (PDI)	404
15.4.2	The Aromatic Fluctuation Index (FLU)	406
15.4.3	The π -Fluctuation Aromatic Index (FLU_{π})	407
15.5	Applications of QTAIM to Aromaticity Analysis	409
15.5.1	Aromaticity of Buckybowls and Fullerenes	409
15.5.2	Effect of Substituents on Aromaticity	412
15.5.3	Assessment of Clar's Aromatic π -Sextet Rule	416
15.5.4	Aromaticity Along the Diels–Alder Reaction. The Failure of Some Aromaticity Indexes	418
15.6	Conclusions	419
	<i>References</i>	421

16	Topological Properties of the Electron Distribution in Hydrogen-bonded Systems	425
	<i>Ignasi Mata, Ibon Alkorta, Enrique Espinosa, Elies Molins, and José Elguero</i>	
16.1	Introduction	425
16.2	Topological Properties of the Hydrogen Bond	426
16.2.1	Topological Properties at the Bond Critical Point (BCP)	426
16.2.2	Integrated Properties	429
16.3	Energy Properties at the Bond Critical Point (BCP)	431
16.4	Topological Properties and Interaction Energy	435
16.5	Electron Localization Function, $\eta(r)$	438
16.6	Complete Interaction Range	440
16.6.1	Dependence of Topological and Energy Properties on the Interaction Distance	440
16.6.2	Perturbed Systems	448
16.7	Concluding Remarks	450
	<i>References</i>	450
17	Relationships between QTAIM and the Decomposition of the Interaction Energy – Comparison of Different Kinds of Hydrogen Bond	453
	<i>Śławomir J. Grabowski</i>	
17.1	Introduction	453
17.2	Diversity of Hydrogen-bonding Interactions	456
17.3	The Decomposition of the Interaction Energy	459
17.4	Relationships between the Topological and Energy Properties of Hydrogen Bonds	460
17.5	Various Other Interactions Related to Hydrogen Bonds	464
17.5.1	$H^+ \cdots \pi$ Interactions	464
17.5.2	Hydride Bonds	466
17.6	Summary	467
	<i>References</i>	468
Part V	Application to Biological Sciences and Drug Design	471
18	QTAIM in Drug Discovery and Protein Modeling	473
	<i>Nagamani Sukumar and Curt M. Breneman</i>	
18.1	QSAR and Drug Discovery	473
18.2	Electron Density as the Basic Variable	474
18.3	Atom Typing Scheme and Generation of the Transferable Atom Equivalent (TAE) Library	476
18.4	TAE Reconstruction and Descriptor Generation	478
18.5	QTAIM-based Descriptors	480
18.5.1	TAE Descriptors	482
18.5.2	RECON Autocorrelation Descriptors	485
18.5.3	PEST Shape–Property Hybrid Descriptors	485

18.5.4	Electron Density-based Molecular Similarity Analysis	487
18.6	Sample Applications	489
18.6.1	QSAR/QSPR with TAE Descriptors	489
18.6.2	Protein Modeling with TAE Descriptors	491
18.7	Conclusions	492
	<i>References</i>	494
 19	Fleshing-out Pharmacophores with Volume Rendering of the Laplacian of the Charge Density and Hyperwall Visualization Technology	499
	<i>Preston J. MacDougall and Christopher E. Henze</i>	
19.1	Introduction	499
19.2	Computational and Visualization Methods	501
19.2.1	Computational Details	501
19.2.2	Volume Rendering of the Laplacian of the Charge Density	501
19.2.3	The Hyperwall	505
19.2.4	Hyper-interactive Molecular Visualization	505
19.3	Subatomic Pharmacophore Insights	507
19.3.1	Hydrogen-bonding Donor Sites	507
19.3.2	Inner-valence Shell Charge Concentration (i-VSCC) Features in Transition-metal Atoms	509
19.3.3	Misdirected Valence in the Ligand Sphere of Transition-metal Complexes	511
19.4	Conclusion	513
	<i>References</i>	514
	Index	515