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 Bond and Virial Paths, and the Molecular and Virial Graphs  8
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 \( \rho_b \)  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 \( e \)  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

References 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
2.3.2.1 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
References 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

References 94

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 $\alpha$ and $\partial \alpha / \partial r$ 101
4.3.2 Recouping $\alpha$ 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 $\alpha$ in H$_2$ 104
4.4.1.1 Modeling $\Delta \alpha / \Delta r$ in H$_2$ 106
4.4.2 Modeling $\alpha$ and $\Delta \alpha / \Delta r$ in CH$_4$ 106
4.4.3 Additional Exercises for the Interested Reader 108
4.5 Patterns in $\alpha$ That Are Discovered Through QTAIM 109
4.6 Patterns in $\partial \alpha / \partial r$ and $\partial \alpha / \partial r$ That Apply Across Different Structures, Conformations, Molecular Types: What is Transferable? 111
4.6.1 Patterns in $\Delta \alpha / \Delta r$ Revealed by QTAIM 111
4.6.1.1 QTAIM Analysis of $\Delta \alpha / \Delta r$ 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 $\partial \alpha / \partial r$ and $\partial \alpha / \partial r$ From Gaussian? 114
4.7.1 Variations in $\partial \alpha / \partial r$ Among the Alkanes 114
4.7.2 $\Delta \alpha / \Delta r$ in Cycloalkanes, Bicycloalkanes, and Hedranes 116
4.7.3 Patterns That Emerge in $\Delta \alpha / \Delta r$ 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
Michel Rafat and Paul L. A. Popelier

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
Bernard Silvi and Ronald J. Gillespie

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 (CH4, NH3, H2O) 153
6.5.1.2 AX4 (CH4, CF4, SiCl4) 154
6.5.1.3 AX3E and AX2E2 (NCl3, OCl2) 154
6.5.2 Hypervalent Molecules 155
6.5.2.1 PCl5 and SF6 155
6.5.2.2 SF4 and ClF3 155
6.5.2.3 AX7 and AX6E Molecules 155
6.5.3 Multiple Bonds 156
6.5.3.1 C2H4 and C2H2 156
6.5.3.2 Si2Me4 and Si2Me2 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 x 1) Clean and Hydrogen-covered Surfaces 180
7.4.2 Si(111)(2 x 1) Reconstructed Surface 184
7.5 QTAIM Applied to Host–Guest Systems 186
7.5.1 Type I Inorganic Clathrates A8Ga16Ge30 (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 Luañá, 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

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.3.1</td>
<td>Catalyst Models</td>
<td>237</td>
</tr>
<tr>
<td>9.3.2</td>
<td>The Full ( \rho(r) ) Topology of the MoS₂ Bulk</td>
<td>241</td>
</tr>
<tr>
<td>9.3.3</td>
<td>The ( \rho(r) ) Topology of the MoS₂ Edges</td>
<td>245</td>
</tr>
</tbody>
</table>

### References

254

### Part III Experimental Electron Densities and Biological Molecules

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Interpretation of Experimental Electron Densities by Combination of the QTAMC and DFT</td>
<td>259</td>
</tr>
<tr>
<td>11</td>
<td>Topological Analysis of Proteins as Derived from Medium and High-resolution Electron Density: Applications to Electrostatic Properties</td>
<td>285</td>
</tr>
</tbody>
</table>

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

**Vladimir G. Tsirelson**

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.1</td>
<td>Introduction</td>
<td>259</td>
</tr>
<tr>
<td>10.2</td>
<td>Specificity of the Experimental Electron Density</td>
<td>261</td>
</tr>
<tr>
<td>10.3</td>
<td>Approximate Electronic Energy Densities</td>
<td>262</td>
</tr>
<tr>
<td>10.3.1</td>
<td>Kinetic and Potential Energy Densities</td>
<td>262</td>
</tr>
<tr>
<td>10.3.2</td>
<td>Exchange and Correlation Energy Densities</td>
<td>271</td>
</tr>
<tr>
<td>10.4</td>
<td>The Integrated Energy Quantities</td>
<td>275</td>
</tr>
<tr>
<td>10.5</td>
<td>Concluding Remarks</td>
<td>276</td>
</tr>
</tbody>
</table>

### References

278

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

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

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.1</td>
<td>Introduction</td>
<td>285</td>
</tr>
<tr>
<td>11.2</td>
<td>Methodology and Technical Details</td>
<td>287</td>
</tr>
<tr>
<td>11.2.1</td>
<td>Ultra-high X-ray Resolution Approach</td>
<td>287</td>
</tr>
<tr>
<td>11.2.2</td>
<td>Medium-resolution Approach</td>
<td>289</td>
</tr>
<tr>
<td>11.2.2.1</td>
<td>Promolecular Electron Density Distribution Calculated from Structure Factors</td>
<td>289</td>
</tr>
<tr>
<td>11.2.2.2</td>
<td>Promolecular Electron Density Distribution Calculated from Atoms</td>
<td>290</td>
</tr>
<tr>
<td>11.2.3</td>
<td>A Test System – Human Aldose Reductase</td>
<td>291</td>
</tr>
<tr>
<td>11.3</td>
<td>Topological Properties of Multipolar Electron Density Database</td>
<td>294</td>
</tr>
<tr>
<td>11.4</td>
<td>Analysis of Local Maxima in Experimental and Promolecular Medium-resolution Electron Density Distributions</td>
<td>298</td>
</tr>
<tr>
<td>11.4.1</td>
<td>Experimental and Promolecular Electron Density Distributions Calculated from Structure Factors</td>
<td>299</td>
</tr>
<tr>
<td>11.4.2</td>
<td>Promolecular Electron Density Distributions Calculated from Atoms (PASA Model)</td>
<td>301</td>
</tr>
<tr>
<td>11.5</td>
<td>Calculation of Electrostatic Properties from Atomic and Fragment Representations of Human Aldose Reductase</td>
<td>305</td>
</tr>
<tr>
<td>11.5.1</td>
<td>Medium- and High-resolution Approaches of Electrostatic Potential Computations</td>
<td>307</td>
</tr>
</tbody>
</table>
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
References 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 \( J_{HH} \) 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
References 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 para-Delocalization Index (PDI) 404
15.4.2 The Aromatic Fluctuation Index (FLU) 406
15.4.3 The \( \pi \)-Fluctuation Aromatic Index (FLU\( _\pi \)) 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 \( \pi \)-Sextet Rule 416
15.5.4 Aromaticity Along the Diels–Alder Reaction. The Failure of Some Aromaticity Indexes 418
15.6 Conclusions 419
References 421
16 Topological Properties of the Electron Distribution in Hydrogen-bonded Systems 425
Ignasi Mata, Ibon Alkorta, Enrique Espinosa, Elies Molins, and José Elguero

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
References 450

17 Relationships between QTAIM and the Decomposition of the Interaction Energy – Comparison of Different Kinds of Hydrogen Bond 453
Sławomir J. Grabowski

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 \( \mathbf{H}^-\cdots\pi \) Interactions 464
17.5.2 Hydride Bonds 466
17.6 Summary 467
References 468

Part V Application to Biological Sciences and Drug Design 471

18 QTAIM in Drug Discovery and Protein Modeling 473
Nagamani Sukumar and Curt M. Breneman

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

References 494

19 Flesshing-out Pharmacophores with Volume Rendering of the Laplacian of the Charge Density and Hyperwall Visualization Technology 499
Preston J. MacDougall and Christopher E. Henze

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

References 514

Index 515