Book Review

Mass Spectrometry in Biophysics: Conformation and Dynamics of Biomolecules By Igor A. Kaltashov and Stephen J. Eyles (University of Massachusetts at Amherst). From the Wiley-Interscience Series in Mass Spectrometry. Edited by Dominic M. Desiderio and Nico M. M. Nibbering. John Wiley & Sons, Inc.: Hoboken, NJ. 2005. xvi + 458 pp. $89.95. ISBN 0-471-45602-0.

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BOOK REVIEWS

Quantal Density Functional Theory. By Viraht Sahni (City University of New York, Brooklyn). Springer-Verlag: Berlin, Heidelberg, New York. 2004. xiv + 256 pp. $129.00. ISBN 3-540-40884-3.

If Albert Einstein had to learn density functional theory (DFT), he might well choose this book. In this volume we find a complete exposition of DFT in terms of the fields and sources familiar from classical physics. The exposition is clean, exceptionally systematic, and very rigorous, and the approach is quite novel within the field. For these reasons, those interested in new insights into density functional theory might well find inspiration within this volume. On the other hand, Sahni's style makes evident his passion for the subject, which lends invigorating support for any reader of this very technical work.

On the whole, the many proofs are very clean and supported by clear physical reasoning. The "derivative discontinuity" proof is one of my favorites. It is very unique, very rigorous, and very convincing. The topic of derivative discontinuities is closely related to the physical concept of the (electro)chemical potential. Sahni is able to identify correlation contributions to the kinetic energy as being responsible for derivative discontinuities, while also showing that other energy contributions do not have derivative discontinuities.

In addition to insights into issues surrounding the chemical potential, Sahni's approach gives a unique insight into why the local density approximation (LDA) works as well as it does. Somehow the usual sequence of assumptions and approximations leads to results that generally work better than one has any right to expect based on those assumptions and approximations. This observation has been a topic of much inconclusive discussion. The answer within the field-source perspective turns out be that, to a certain level of approximation, the LDA consists of three source terms, not two as one might surmise from uniform electron gas theory. One source corresponds to the Hartree potential, and a second is responsible for the exchange energy, but not the exchange potential. It is the third source that produces the exchange potential, and yet does not contribute to the energy. This third source depends on the gradient of the local Fermi energy, thereby introducing an element of correlation.

Chemists will need to pay close attention to the definitions of otherwise familiar terms. In particular, care is needed in keeping Sahni's definition of correlation energy clearly in mind. The term here means an energy defined in reference to a system of noninteracting electrons, all with the same effective potential. Thus, the Hartree−Fock energy has contributions from correlation energies. Another term, chemical potential, means electrochemical potential in this book.

Care must also be taken in reading the later chapters of the book, in part, oddly enough, because Sahni's presentation is so smooth. Some of the issues discussed in Chapters 7 and 8 might sound as though they are completely resolved. Some are not. In particular, the introduction to Chapter 8 connects the chemical potential to both addition and removal of electrons from atoms or molecules and charge transfer involved in strong chemical bonds. The topic as addressed by Sahni is rigorous for the addition and removal of electrons, but the issue of charge transfer within chemical bonding and its relationship to chemical potential is still an area of active investigation.

With these few minor caveats in mind, any serious student of DFT, even if it's Einstein, can seriously consider *Quantal Density Functional Theory* when searching for a fresh source of ideas.

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Mass Spectrometry in Biophysics: Conformation and Dynamics of Biomolecules. By Igor A. Kaltashov and Stephen J. Eyles (University of Massachusetts at Amherst). From the Wiley-Interscience Series in Mass Spectrometry. Edited by Dominic M. Desiderio and Nico M. M. Nibbering. John Wiley & Sons, Inc.: Hoboken, NJ. 2005. xvi + 458 pp. $89.95. ISBN 0-471-45602-0.

This is an impressive book that addresses in detail the basic underlying principles behind the use of mass spectrometry for delving into the structure of biopolymers. Kaltashov is a growing figure in the mass spectrometry community, and Eyles, the more senior author, is well-known. Both authors have active research and teaching programs in mass spectrometry and have produced a compact volume that contains a wealth of information for those who seek to understand the principles and state-of-the-art in this broad field. The bulk of the text is devoted to the analysis of proteins, although one of the eleven chapters is devoted to the analysis of DNA, RNA, and oligosaccharides. The treatment of each subject is impressive in scope, up-to-date in references, and comprehensive.

The first three chapters are devoted to a general outline of the principles of mass spectrometry as it is used for biopolymer, principally protein, structural analysis. Those who are new to or have a limited background in mass spectrometry will find that these chapters provide a solid introduction to the field. The scope of the presentation should satisfy all but the most sophisticated afficionados. These chapters also provide a good overview of the theoretical basis of some other traditional techniques that are used to study biomolecular structures and dynamics, including X-ray crystallography, solution light scattering techniques, cryo-electron microscopy, NMR spectroscopy, etc. Chapter 3 is a detailed account of the techniques and instruments used today in biopolymer mass spectrometry.

Chapters 4−7 cover in detail protein structural analysis by mass spectrometry. The treatment of this large subject is impressive in detail and scope, and the references are extensive and up-to-date. A variety of experimental approaches are discussed with emphasis on cross-linking and particularly hydrogen/deuterium exchange experiments, perhaps reflecting

the authors' own research interests. Experiments in hydrogen/deuterium exchange are featured in several of these chapters, and fair treatment is given to the comparison of what can be learned from these experiments using mass spectrometry or NMR spectroscopy. Chapter 5 includes a nice discussion of the issue of gas-phase scrambling of hydrogen/deuterium atoms on small peptides and how or when MS/MS experiments can be used in conjunction with H/D exchange to elucidate the structure of these molecules. In Chapter 6, the authors describe the methods available for studying the kinetics of protein folding and enzyme reaction rates, and in Chapter 7, they discuss protein/protein and protein/ligand interactions and how they can be studied using mass spectrometry. The authors also discuss the limitations of this latter approach, something that is never or rarely mentioned in research publications and is refreshing to see here. Those who are contemplating using mass spectrometry to study these types of interactions are well advised to read the comments presented here. As the authors point out, caution should be exercised when extrapolating from solution behavior of solvated molecules and complexes to gas-phase behavior of naked molecules and complexes.

The topics of Chapters 8−11 branch into another set of issues that are of interest to those in the field, such as how mass spectrometry can and should be used in conjunction with other biophysical techniques to unravel complex structural problems, applications of mass spectrometry to other biopolymers (Chapter 9), and the influence of a solvent-free environment on protein structure (Chapter 10). In the final chapter, the authors present their views on the future of this broad field. The volume concludes with an account of the physics of the electrospray phenomenon, which includes an historical description of its discovery.

In summary, this is a scholarly volume worthy of a place in the library of all those, not only mass spectroscopists, who study biopolymer and, particularly, protein structure. The authors' treatments of the topics will remain current for a long time, and the principles described are timeless. The presentation is excellent, the hard-bound book is durable, and the text is replete with many fine figures and diagrams (always appropriately acknowledged), some of which are in color.

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