REVIEW

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A wavefunction model to chemical bonding

Gábor Náray-Szabó[1] | **Paul G. Mezey[2]**

[1]MTA-ELTE Protein Modelling Research Group, Laboratory of Structural Chemistry and Biology, Institute of Chemistry, Eötvös L. University, Budapest, Hungary

[2]Yukawa Institute for Theoretical Physics, Kyoto University, Kyoto, Japan

Correspondence
Gábor Náray-Szabó, MTA-ELTE Protein Modelling Research Group, Laboratory of Structural Chemistry and Biology, Institute of Chemistry, Eötvös L. University, 1117 Budapest, Hungary.
Email: narayszabo@yahoo.com

Paul G. Mezey, Yukawa Institute for Theoretical Physics, Kyoto University, Kyoto, Japan.
Email: paul.mezey@gmail.com

Abstract

In this paper we give a brief survey on some specific aspects of a wavefunction model for chemical bonding which are connected to or have been motivated in part by the work of the late István Mayer and colleagues. After a brief description of the early wavefunction models as reflected in Mayer's works, naturally leading to electron densities, we discuss localized molecular orbitals, and summarize some of the early initiatives and applications. The concept of the Chemical Hamiltonian, as introduced by Mayer, its extensions and some classical and some more advanced connections will be discussed. The twofold motivating role of Mayer in the development of the earliest, ab initio level macromolecular linear scaling methods, giving proven "ab initio quality" protein energy results by the adjustable density matrix assembler method, and in some other molecular fragment advances will be also pointed out.

KEYWORDS
chemical bond, chemical Hamiltonian, embedding, linear scaling, localized orbitals, transferability

1 | INTRODUCTION

The traditional bond concept has served chemistry well [1], although wavefunction-based representations of electron-density distributions have required some less-traditional approaches. To a good accuracy, many molecular properties can be obtained from wavefunction methodologies, far better than with early attempts trying to rely on idealized "atomic" or "atom-pair" properties. As it turns out, quantum chemistry methodologies had major effects on the modern concepts used for the interpretation and further application of the rather accurately computable molecular properties, all depending on the electron density distributions, leaving some older concepts, like valence bond theory at the sidelines [2].

The early focus of Prof Mayer's work has been on the problems and interpretations of localized orbitals and delocalization corrections, even used in the study of molecular conformation analysis problems [3–6].

He has been intrigued by the range of different opinions and alternative definitions, affecting some of the fundamental interpretations of valence and bonding [7]. Although his preference for precise mathematics has been evident, as also manifested by his book on rigorous proofs of some Quantum Chemistry theorems [8], still, he had a strong interest in the everyday concepts used by chemists.

Consequently, the interpretative questions of the quantum chemistry basis of common chemistry concepts have continued to play important roles in his publications [9, 10], and he has been also making connections between his wavefunction-dominant approaches and density functional theory (DFT) [11], a connection that can be also noticed in his Chemical Hamiltonian [12] approach (see more details below).

Mayer's efforts for interpretative connections between wavefunction methods and more classical chemical concepts has made natural connections with the atoms in molecules works of Bader [13], as well as with alternative approaches, such as the conceptual DFT of Geerlings, DeProft, Ayers and Toro-Labbe and other colleagues [14, 15].

We shall not attempt to give even a short survey of all the above fields where Prof Mayer has been involved, but we shall focus primarily on localization problems, and as a natural consequence, on the local–global aspects in molecules. As a connected "local" problem, Prof Mayer's

mathematically precise approaches [8] have given added motivation for an alternative to traditional molecular fragments: density matrix based fuzzy molecular fragments, some of which can serve as somewhat distant alternatives to localized orbitals.

Although as a concept fundamentally classical in nature, localized molecular orbitals received significant amount of interest [16–18]. While canonical molecular orbitals, obtained directly from the solution of the Hartree–Fock equations, typically extend over large parts of the entire molecule, however, the freedom in the wavefunction allows for localized molecular orbitals which are formally concentrated in limited spatial regions of a molecule, more reminiscent to the concepts of traditional chemical bonds. Traditional chemical bonds can be defined only qualitatively, as any attempt to a quantitative definition lacks either additivity or transferability, since, as acknowledged or not, all is based on molecular wavefunctions.

In this paper, focusing on the work of the late Prof Mayer and his colleagues, we shall give a brief survey on the contrast between local and more delocalized electron density concepts in quantum chemical methods, and on some of the various tools of interpretations.

First, we treat the quantum chemical basis of describing electron densities, then discuss orbital localization. We will show how localized orbitals can be applied for the calculation of some first-order physical properties. Then, the Chemical Hamiltonian concept of Mayer will be discussed. We finish this survey with descriptions of larger-scale, locally treated non-local problems, illustrated by "ab initio quality," linear scaling macromolecular quantum chemistry techniques and by the interesting roles of fuzzy molecular fragments containing possibly several nuclei.

2 | THE NATURE OF LOCAL AND GLOBAL ELECTRON DENSITIES IN MOLECULES

According to direct experimental evidence the electron density has local maxima near nuclei and, to a lesser extent, in bonding regions between two atoms. This has been the basis of early attempt to simplify molecular electron distributions even further, at the expense of many fine details. However, the delocalized nature of the wave function, which determines molecular properties, does not allow to find an exact counterpart of the chemical bond in quantum mechanics.

Most local electron densities in molecules in the range of neighboring atoms show severe deviations from the original, ideal, round shapes of individual, isolated atoms [19], a fact that has led to precise measures of both local and global molecular shapes both near and far from some local "bonding" regions [19].

As a consequence of the holographic electron density theorem, stating that in the electronic ground state, any small positive volume part of the molecular electron density cloud contains the complete molecular information, no molecular parts between two different molecules are ever fully transferable [20].

3 | LOCALIZED MOLECULAR ORBITALS

In the absence of symmetry constraints wave functions, obtained from the solution of the classical Hartree–Fock equations extend to all atoms of a molecule. It is therefore, in general, not straightforward to find simple relations between local ranges within molecules one may associate with some chemical bond. However, it is possible to perform a similarity transformation on the delocalized wave function, which provides orthogonal localized molecular orbitals with dominant parts on a few neighbor atoms. They can be used to interpret the results of molecular orbital calculations in more traditional bonding concepts.

The localization transformation involves the minimization or maximization of the expectation value of a specific operator, **L**. The Boys method [16] minimizes the spatial extent of the orbitals, thus $L = |r_1 - r_2|^2$, while the Edmiston–Ruedenberg procedure [17] maximizes the electronic self-repulsion energy, $L = |r_1 - r_2|^{-1}$. The Pipek–Mezey localization scheme [18] takes a slightly different approach, maximizing the sum of orbital-dependent partial charges on the nuclei, $L = \Sigma_{A,i} |q_{A,i}|^2$. It turned out that despite of the wide variation in the possible estimation of partial charges, the Pipek–Mezey orbitals are rather reproducible, not excessively sensitive to the scheme used in the localization process [21]. Accordingly, due to the ill-defined mathematical nature atomic charges, this is a better alternative and is shown to be superior in the case of well-localized systems [22].

Whereas actual shapes of electron density clouds [19] and the quantum-chemically unavoidable holographic constraints [20] are making simplistic interpretations somewhat misleading, nevertheless, in a more traditional setting bonds may be represented by strictly localized bond orbitals [23, 24]. For a σ bond this is a combination of normalized hybrid orbitals, pointing to the other atom of the bond; for a lone pair a single hybrid orbital in the right orientation, and for a π bond it is obtained as a linear combination of p_z orbitals located at the π-centers

$$\varphi(\sigma) = c_A h_A + c_B h_B$$
$$\varphi(\text{lp}) = h_A$$

$$\varphi(\pi) = \Sigma c_i u_i^{2p\perp}$$

These non-orthogonal orbitals form a simple basis for the expansion of the wavefunction of classical molecules, composed of σ and π bonds, as well as lone pairs. Lack of orthogonality may complicate the algebra, still, it allows the straightforward chemical fragmentation of the wave function, allowing its decomposition in a central, active region and environment [25, 26].

Natural bond orbitals offer an option for transforming the wavefunction representation of a molecule into the familiar language of chemical bonding [27]. They represent chemical bonds, refer to maximum electron density values in the bond region, providing an attractive natural Lewis structure model for the representation of the wavefunction.

4 | LIMITS TO TRANSFERABILITY

As it has been pointed out above, transferability is severely affected by both the highly intricate shapes of molecular electron densities [19], and those constraints represented by the holographic electron density theorem [20]. It is no surprise that the case of classical organic molecules, like saturated hydrocarbons, their simple, substituted derivatives, have been used as frequent examples, avoiding the intricacies of more involved molecules.

Nevertheless, various first-order properties, that is, partial atomic charges [28, 29], the dipole moment, electrostatic potential and polarizability have been used in approximate transferability schemes. Strictly localized bond orbitals are, to a certain extent, also transferable and this allows to use them, for example, in the calculation of molecular electrostatic potentials [23].

The development of group-theoretical systematization of molecular electron density shape analysis has turned out to provide not only critical tests for transferability, but also methods for applications in applied fields, like strict shape comparisons [30].

5 | THE CHEMICAL HAMILTONIAN APPROACH

Mayer introduced the concept of the chemical Hamiltonian [31], avoiding the explicit appearance of three- and four-center integrals in the expression of the molecular energy, without neglecting them. This allows a significant reduction of the computational work, still conserving its fully ab initio character. The Hamiltonian is decomposed into the following terms: (a) sum of effective atomic contributions; (b) electrostatic interactions in the point-charge approximation; (c) electrostatic effects due to the deformation of the point-like charge distribution; (d) two-center overlap effects and at last finite basis correction terms, which have practical significance. This approach allows to overcome the problem of basis set superposition errors and to provide, within the framework, a suitable definition of atomic charges, valences and bond orders [32].

He proposed a chemical energy component analysis for the ab initio wave functions, which is based on a variant of the technique used in his chemical Hamiltonian approach [33]. In quantum mechanical calculations molecules are represented by the wave function, extending over all atoms, while in the classical chemical description they are considered as systems of atoms and bonds. A deeper understanding of the molecular structure and proper interpretation of the calculated results require a clear distinction between these alternatives. A possibility is to calculate bond orders and valence indices from the wave function. Using a proper technique, the energy of a molecule is expressed, approximately, but to a reasonable accuracy as a sum of atomic and diatomic contributions, the computation of which requires the use of one- and two-center integrals only. This scheme is appropriate to perform an approximate analysis of the wave function obtained in an actual calculation, the energy components obtained permit us to identify the different chemically relevant interactions in a molecule and provide a useful tool for the interpretation of the calculated results.

6 | EMBEDDING

A special application of the local molecular ranges in quantum mechanical calculations is embedding. Large covalent systems, where a local change (e.g., bond breaking) takes place, can be treated as a combination of the central region and its environment, described with higher and lower sophistication, respectively. This is the philosophy of the combined quantum mechanical/molecular mechanical approach, introduced by Warshel and Levitt already 45 years ago [34]. A critical question is the separation of the subsystem from its environment, since the boundary crosses the molecule. Borderline atoms and bonds often need a special treatment in the calculations. Application of strictly localized bond orbitals can be used to separate subsystems as distinct groups of bonds.

The application of strictly localized bond orbitals with semiempirical wave-functions is well established but their use with ab initio wave-functions requires the proper treatment of the overlap between them and the molecular orbitals of the subsystem. A basic problem if using them is that their overlap is nonzero, therefore the conventional Hartree–Fock–Roothaan equations cannot be used directly. A potential solution is to use the Adams–Gilbert equation [35, 36]. An approximate form and the corresponding energy expression has been proposed to obtain the orbitals [37, 38]. This latter is based on the series expansion of the inverse overlap matrix and the neglect of higher order terms. This expression may replace the one based on orthogonal orbitals.

In many applications, the subsystems are covalently bound and taken with frozen localized orbitals at the boundary, and can be used to separate the former and to ensure an appropriate description of the electronic structure near to the boundary. A complication in these methods is that orthogonality between optimized and frozen orbitals has to be warranted and this is usually achieved by an explicit orthogonalization of the basis set to the frozen orbitals. An alternative to this approach is proposed by calculating the wave-function from the Huzinaga equation that guarantees orthogonality to the frozen orbitals without basis set orthogonalization [39].

7 | CORRELATION ENERGY PROBLEMS

Localized orbitals allow to reduce calculation of electron correlation energies. In the early local treatment, proposed by Pulay [40, 41], large savings can be achieved by neglecting correlation between distant pairs, or treating it at a lower level. Thus the dimension of the virtual space depends only on the basis set. This concept was followed by several authors, who improved the technique further and proposed linearly scaling methods for the calculation of electronic correlation energies [42–45].

Electron correlation methods have been developed that are "technically" scalable in the sense that the total time of a calculation becomes nearly independent of the molecular size when the number of processors grows linearly with the molecular size. The total correlation energy is evaluated as the sum of the individual contributions. The computation time of this approach scales linearly with the system size, while its memory and disk space requirements are independent thereof. The method can be routinely applied to molecules of up to 100 atoms with appropriate basis sets [44].

8 | LINEAR SCALING AND FUZZY FRAGMENT TECHNIQUES

Fortunately, density matrix formalism allows very efficient alternatives to the more conventional fragmentation problem of electron densities, leading not only to quantum-chemically correct interpretations, but also to efficient linearly scaling macromolecular quantum chemistry computation methods [46–55].

Consider a macromolecule, and imagine that its electron density cloud is thrown apart into many, say hundreds of small (say, 3–4 A diameter) fuzzy electron density clouds, but in such a way, that by pushing all these fuzzy clouds together again, the exact macromolecular electron density is perfectly restored.

For each such fuzzy density fragment consider now itself, and also, the whole set of other such fragments surrounding it within a 6 or 8 A radius inside the macromolecule.

This collection of fragments may not be chemically viable, however, by adding H atoms to appropriate locations on its periphery, a model of a viable, artificial molecule can be created. Note that this molecule, still much smaller than the original macromolecule, is still small enough for direct quantum chemistry calculation. This molecule is called the "parent molecule" of the original fragment, in the center of it.

After a direct calculation on this parent molecule, the density matrix contribution from the central fragment can be identified and stored, also including half for each of those interaction density matrix elements between the central fragments and other fragments within the parent molecule.

The same is repeated for all fragments, new parent molecules for each, ensuring that the "other halves" of interaction density matrix elements from all other fragments are eventually all included, following exactly the spirit of a Mulliken's population analysis, without integration for "charge," leaving it as electron density, that is, as a density matrix for the given basis set.

Carrying this through for all fragments of the macromolecule, the fragment density matrices can be combined into a macromolecular density matrix, that can generate both macromolecular electron densities as well as practically any other macromolecular properties.

Within the quantum chemistry method, be it Hartree–Fock, Moller–Plesset, or DFT, the accuracy depends only on the size of the parent molecules. Since the size of parent molecules is usually decided at the start of the computation, and each parent molecule takes about the same computer time, the adjustable density matrix assembler (ADMA) method scales linearly with the size of the macromolecule.

For very large parent molecules, the method provides virtually identical results to a full computation for the macromolecule. For parent molecules of 9A, a "part-per-billion" accuracy has been achieved relative to the full, Hartree–Fock result for a protein.

The above ADMA method was the very first method that has generated ab initio quality results for protein electron densities and protein energies, and other properties, using fuzzy electron density fragments, in direct contrast to some traditional molecular representations.

There has been large number of applications of the ADMA method [46–53], some of them in combination with fuzzy electron density molecular fragment approaches [54, 55], where these fragments may contain several nuclei, yet they "bond" with each other showing very similar electron density features to bonds between individual atoms, also providing a quantum chemical definition for the limited autonomy of typical functional groups within molecules [55].

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AUTHOR CONTRIBUTIONS

Gabor Naray-Szabo: Conceptualization; project administration; writing-original draft. **Paul Mezey:** Conceptualization; supervision; writing-review & editing.

DATA AVAILABILITY STATEMENT

This is a review of papers, which are openly available.

ORCID

Gábor Náray-Szabó https://orcid.org/0000-0002-7170-8474

REFERENCES

[1] L. Pauling, *The Nature of the Chemical Bond*, Cornell University Press, Ithaca, NY **1960**.
[2] W. A. Goddard, T. H. Dunning, W. J. Hunt, P. J. Hay, *Acc. Chem. Res.* **1973**, *6*, 368.
[3] P. R. Surján, I. Mayer, *Theor. Chim. Acta* **1981**, *59*, 603.
[4] P. R. Surján, G. Náray-Szabó, I. Mayer, *Int. J. Quantum Chem.* **1982**, *22*, 929.
[5] I. Mayer, *Chem. Phys. Lett.* **1983**, *97*, 270.
[6] I. Mayer, P. R. Surján, *J. Chem. Phys.* **1984**, *80*, 5649.
[7] I. Mayer, *Chem. Phys. Lett.* **1984**, *110*, 440.
[8] I. Mayer, Simple Theorems, Proofs, and Derivations in Quantum Chemistry. in *Mathematical and Computational Chemistry Book Series* (Ed: P. G. Mezey), Kluwer Academic/Plenum Publishers, New York **2003**.
[9] J. G. Ángyán, M. Loos, I. Mayer, *J. Phys. Chem.* **1994**, *98*, 5244.
[10] P. Salvador, M. Duran, I. Mayer, *J. Chem. Phys.* **2001**, *115*, 1153.
[11] M. Kieninger, S. Suhai, I. Mayer, *Chem. Phys. Lett.* **1994**, *230*, 485.
[12] I. Mayer, *Int. J. Quantum Chem.* **2002**, *90*, 89.
[13] R. F. W. Bader, *Atoms in Molecules: A Quantum Theory*, Oxford University Press, New York **1994**.
[14] F. DeProft, P. W. Ayers, P. Geerlings, The Conceptual Density Functional Theory Perspective of Bonding. in *The Chemical Bond: Fundamental Aspects of Chemical Bonding* (Eds: G. Frenking, S. Shaik), Wiley, New York **2014**, p. 233.
[15] P. Geerlings, P. W. Ayers, A. Toro-Labbé, P. K. Chattaraj, F. De Proft, *Acc. Chem. Res.* **2012**, *55*, 683.
[16] S. F. Boys, *Rev. Mod. Phys.* **1960**, *32*, 296.
[17] C. Edmiston, K. Ruedenberg, *Rev. Mod. Phys.* **1963**, *35*, 457.
[18] J. Pipek, P. G. Mezey, *J. Chem. Phys.* **1989**, *90*, 4916.
[19] P. G. Mezey, *Shape in Chemistry: An Introduction to Molecular Shape and Topology*, VCH Publishers, New York **1993**.
[20] P. G. Mezey, *Mol. Phys.* **1999**, *96*, 169.
[21] S. Lehtola, H. Jonsson, *J. Chem. Theor. Comput.* **2014**, *10*, 642.
[22] J. W. Boughton, P. Pulay, *J. Comput. Chem.* **1993**, *14*, 736.
[23] G. Náray-Szabó, *Int. J. Quantum Chem.* **1979**, *16*, 265.
[24] P. R. Surján, M. Révész, I. Mayer, *J.C.S. Faraday Trans. II* **1981**, *77*, 1129.
[25] G. Náray-Szabó, P. R. Surján, *Chem. Phys. Lett.* **1983**, *96*, 499.
[26] G. G. Ferenczy, J. L. Rivail, P. R. Surján, G. Náray-Szabó, *J. Comput. Chem.* **1992**, *13*, 830.
[27] F. Weinhold, *J. Comput. Chem.* **2012**, *33*, 2363.
[28] R. S. Mulliken, *J. Chem. Phys.* **1955**, *23*, 1833.
[29] B. H. Besler, K. M. Merz, P. A. Kollman, *J. Comput. Chem.* **1990**, *11*, 431.
[30] P. G. Mezey, *Int. J. Quantum Chem., Quant. Biol. Symp.* **1987**, *14*, 127.
[31] I. Mayer, *Int. J. Quantum Chem.* **1983**, *23*, 341.
[32] I. Mayer, *Int. J. Quantum Chem.* **1986**, *29*, 73.
[33] I. Mayer, *Chem. Phys. Lett.* **2000**, *332*, 381.
[34] A. Warshel, M. Levitt, *J. Mol. Biol.* **1976**, *103*, 227.
[35] W. H. Adams, *J. Chem. Phys.* **1961**, *34*, 89.
[36] T. L. Gilbert, Localized Orbitals in Polyatomic Systems. in *Molecular Orbitals in Chemistry, Physics and Biology* (Eds: P.-O. Löwdin, B. Pullman), Academic Press, New York **1964**, p. 409.
[37] G. G. Ferenczy, *Int. J. Quantum Chem.* **1995**, *53*, 485.
[38] G. G. Ferenczy, *Int. J. Quantum Chem.: Quant. Chem. Symp.* **1996**, *57*, 361.
[39] G. G. Ferenczy, *J. Comput. Chem.* **2013**, *34*, 862.
[40] P. Pulay, *Chem. Phys. Lett.* **1983**, *100*, 151.
[41] S. Saebo, P. Pulay, *Ann. Rev. Phys. Chem.* **1993**, *44*, 213.
[42] S. K. Burger, W. Yang, *J. Phys. Condens. Matter* **2008**, *20*, 294.
[43] C. Pisani, L. Maschio, S. Casassa, M. Halo, M. Schütz, D. Usvyat, *J. Comput. Chem.* **2008**, *29*, 2113.

[44] Z. Rolik, M. Kállay, *J. Chem. Phys.* **2011**, *135*, 104111.

[45] H. J. Werner, G. Knizia, C. Krause, M. Schwilk, M. Dornbach, *J. Chem. Theory Comput.* **2015**, *11*, 484.

[46] P. G. Mezey, *Struct. Chem.* **1995**, *6*, 261.

[47] P. G. Mezey, *Int. J. Quantum Chem.* **1997**, *63*, 39.

[48] P. G. Mezey, *Int. Rev. Phys. Chem.* **1997**, *16*, 361.

[49] T. E. Exner, P. G. Mezey, *J. Phys. Chem. A* **2002**, *106*, 11791.

[50] T. E. Exner, P. G. Mezey, *J. Comput. Chem.* **2003**, *24*, 1980.

[51] T. E. Exner, P. G. Mezey, *J. Phys. Chem.* **2004**, *108*, 4301.

[52] T. E. Exner, P. G. Mezey, *Phys. Chem. Chem. Phys.* **2005**, *7*, 4061.

[53] Z. S. Szekeres, T. E. Exner, P. G. Mezey, *Int. J. Quantum Chem.* **2005**, *104*, 847.

[54] P. G. Mezey, *Phys. Chem. Chem. Phys.* **2012**, *14*, 8516.

[55] P. G. Mezey, *Acc. Chem. Res.* **2014**, *47*, 2821.

AUTHOR BIOGRAPHIES

Gabor Naray-Szabo, author of seven books and 300 papers on theoretical chemistry, computer-aided molecular design, structural biology and professional affairs in chemistry and engineering in general. Invited speaker in theoretical chemistry and structural biology at more than 100 national and international conferences, in professional affairs at more than 20 meetings. Former or current member of editirial boards of 8 international journals. Member of the Hungarian Academy of Sciences, Académie des Arts, des Sciences et des Lettres (Paris), and the European Academy of Sciences and Arts.

Paul G. Mezey, MSc, MSc, PhD, DSc, DSc, Editor of J. Math. Chem. (Springer), Distinguished Visiting Prof. at Yukawa Inst. Theor. Phys, Kyoto University (2017-cont.), Canada Research Chair Tier 1 as Prof. Chem. Memorial Univ., NL Canada (2003-2017). Author of 440 publications, of books: Potential Energy Hypersurfaces (Elsevier 1987), Shape in Chemistry: An Introduction to Molecular Shape and Topology (VCH-Wiley 1993). Main results: Reaction Topology, Molecular Identity in PES Catchment Regions, Detailed Molecular Shape Analysis Method, QShAR (Quantitative Shape Activity Relations), Similarity Measures, Generalized Symmetries: Syntopy and Symmorphy, Pipek-Mezey Localization, Holographic Electron Density Theorem, Fuzzy Molecular Fragments, ab initio quality "ADMA" Macromolecular Quantum Chemistry Method, Quantum Chemical Functional Groups, Combinatorial Quantum Chemistry, Universal Molecule. As mathematician, his Erdos number is 2.