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Joseph E. Earley

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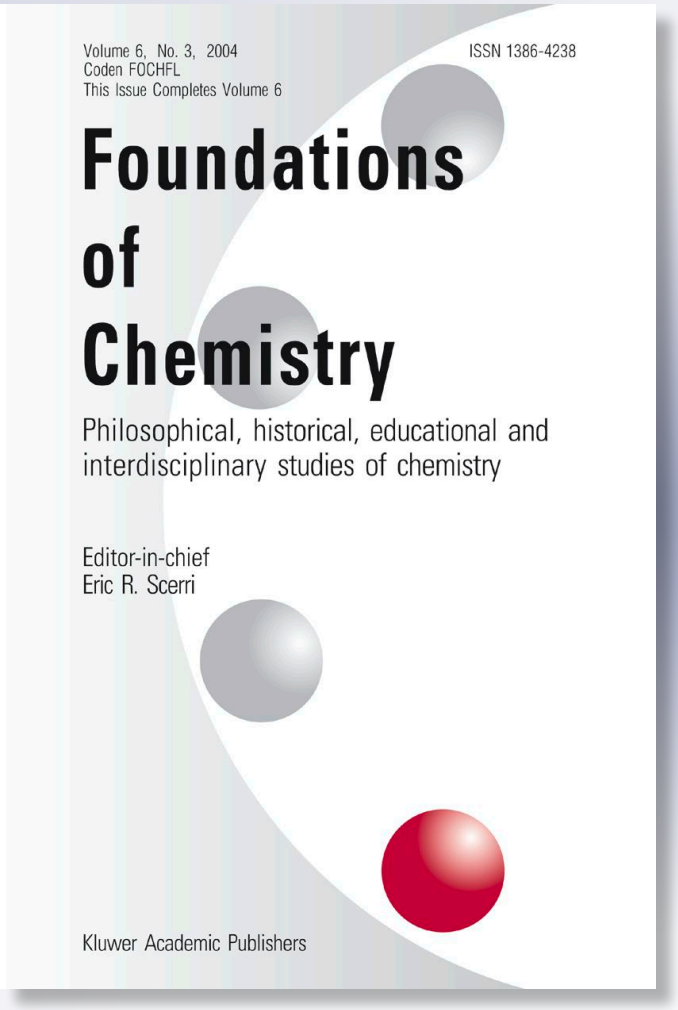

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A neglected aspect of the puzzle of chemical structure: how history helps

Joseph E. Earley Sr.

Abstract Intra-molecular connectivity (that is, chemical structure) does not emerge from computations based on fundamental quantum-mechanical principles. In order to compute molecular electronic energies (of C_3H_4 hydrocarbons, for instance) quantum chemists must insert intra-molecular connectivity "by hand." Some take this as an indication that chemistry cannot be reduced to physics: others consider it as evidence that quantum chemistry needs new logical foundations. Such discussions are generally *synchronic* rather than *diachronic*—that is, they neglect 'historical' aspects. However, systems of interest to chemists generally are *metastable*. In many cases chemical systems of a given elemental composition may exist in any one of several different metastable states depending on the history of the system. Molecular structure generally depends on contingent historical circumstances of synthesis and separation, rather than solely or mainly on relative energies of alternative stable states, those energies in turn determined by relationships among components. Chemical structure is usually 'kinetically-determined' rather than 'thermodynamically-determined.' For instance, cyclical hydrocarbon ring-systems (as in cyclopropene) are produced only in special circumstances. Adequate theoretical treatments must take account of the persistent effects of such contingent historical events whenever they are relevant—as they generally are in chemistry.

Keywords Synchronic · Diachronic · Isomers · Chemical structure · W*-algebra · Allene · Propyne · Propadiene · Philosophy of chemistry · Metastable · Potential energy surfaces · Equilibrium states · Transition states · Quantum chemistry · Historicity · Contextual emergence

Some problems can be dealt with on a *synchronic* basis, ignoring all considerations of time—others must be dealt with *diachronically*, with attention to the details of time-dependent processes. The greater simplicity of synchronic approaches historically has been

J. E. Earley Sr. (✉)
Department of Chemistry, Georgetown University, 502 W Broad St., Suite 501, Falls Church, VA 22046-3247, USA
e-mail: Earleyj@georgetown.edu

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(and now is) attractive to philosophers—some (e.g., Kim 2005) even discuss human mental functioning on a synchronic basis, eschewing any consideration of the *evolutionary* origins either of specifically human features or of the characteristics of human individuals. Paul Humphreys (2008) pointed out that conclusions that are based on approaches that ignore temporal processes are often quite different from corresponding decisions that are obtained by explicitly considering time-dependent influences—and therefore the synchronic results are frequently *quite incorrect*. This paper suggests that the extent to which quantum mechanics deals with chemical structure (as currently actively discussed in the philosophy of chemistry) would be clarified—and apparent puzzles resolved—by using an explicitly diachronic (history-related) approach.

Can quantum mechanics deal with molecular structure?

Showing that, in saturated hydrocarbons, the four bonds pertaining to each carbon-center are directed as if toward the vertices of a tetrahedron was a major intellectual triumph of nineteenth-century chemistry (Chalmers 2009). Alfred Werner's proof (by an extensive program of carefully-planned chemical syntheses) that metallic centers in transition-metal compounds are often surrounded by *six* non-metallic centers that are distributed as if at the vertices of an octahedron (Basolo and Pearson 1967) was a related (and independently highly significant) achievement. Such structural insights—combined with quantum-mechanical interpretations of data produced by several varieties of spectroscopy—made possible detailed understanding of chemical structure and reactivity and thereby led to much scientific and technological progress. In view of the central importance of both structural and quantum-theoretic reasoning in chemistry, it may be surprising to read R. G. Woolley's (1998, 3) statement that: "… from the point of view of the quantum theory … the existence of isomers, and the very idea of molecular structure that rationalizes it, remains a central problem for chemical physics."

Three distinct hydrocarbons—allene (also called propadiene), cyclopropene, and propyne (also called methylacetylene)—correspond to the overall composition C_3H_4. Each of these three isomers is characterized by a different 'connectivity' of their common constituents—three carbon centers and four hydrogens are joined differently in each isomer (Table 1).

Woolley uses the C_3H_4 system as his example, and recognizes that quantum chemists are able to compute total electronic energy for C_3H_4—but only if the nuclei are first "placed in [specific] arrangements." (Repeating such calculations while systematically varying the arrangement of nuclei would generate a potential energy surface (PES) for the C_3H_4 system. In a slightly simpler system (Czakó and Bowman 2011), "the Cl + CH_4 PES is a permutationally invariant fit to roughly 16,000 high-level ab initio electronic energies.") But Woolley continues (1998, p.11):

Table 1 Stable Isomers of C_3H_4

 Cyclopropene	$H_3CC\equiv CH$ Propyne (methylacetylene)	$H_2C{=}C{=}CH_2$ Allene (propadiene)

> Suppose we apply quantum mechanics to *all* the particles [For C_3H_4: 3 carbon nuclei, 4 protons and 22 electrons.] in one go, what do we get? It is easier to say what we have never found so far—no suggestion of three distinct isomers for the molecules of allene, cyclopropene and methylacetylene. This negative result does not mean that either quantum mechanics or chemistry must be 'wrong'—it does mean that we do not know how to formulate the quantum mechanics (i.e., write down explicit equations) so that the theory predicts, in this case, three isomers. Lacking that, we have had no choice but to put the molecular structure in by hand. This is not a problem of not having a big enough computer; rather it is the problem of not knowing what to compute. That means we need a new idea.

Robert Bishop (2005) also considers the inability of quantum theory to deal with chemical structure and connects this feature with reduction/emergence discussions, pointing out that proper attention to the *context* relevant to a particular inquiry can resolve otherwise intractable problems (see also Bishop and Atmanspacher 2006). Robin Hendry (2010) interpreted the inability of quantum mechanics to derive the structures of chemical substances from first principles as demonstrating that (contrary to widespread opinion) chemistry has not been reduced to physics. Also, he seems to endorse a remarkable concept: "The emergentist posits that non-resultant or 'configurational' Hamiltonians govern the behaviour of at least some complex systems" (Hendry 2010, 185). In an editorial in this journal, Eric Scerri (2011) discussed a *Stanford Encyclopedia of Philosophy* article in which the coauthors (including Hendry) also discuss the problematic relationship between chemical structure and quantum mechanics. Scerri reports that decoherence (wave-function collapse) is now recognized *not* being instantaneous (as was formerly supposed) but rather to take some time—and this changed understanding removes some difficulties with respect to quantum understanding of chemical structure. In a rapid response to Scerri's editorial, Sutcliffe and Wooley (2011) pointed out: "We don't see [putting ideas (structure) in by hand] as a problem or a difficulty: it is a generic feature of many-body physics … and results in remarkably powerful and fruitful theoretic formalisms." Possibly, many-body physics (like chemistry) is in fact not reducible to fundamental quantum mechanics—or perhaps (as the present paper suggests) the whole complex discussion of the relationship of quantum mechanics and chemical structure has neglected certain 'historical' features that are essential to properly posing the interesting questions.

Does history influence chemistry?

In passing, Woolley mentioned the desirability of dealing with *kinetic* problems such as those connected with chemical syntheses, but observed (1998, 9): "Faced with such an horrendous problem, we retreat and focus instead on equilibrium mixtures." That is, he explicitly adopts a *synchronic* (time-independent) rather than a *diachronic* approach—and concentrates on thermodynamic stability, rather than on *metastabilty* due to activation barriers. (Which is sometimes rather inelegantly called 'kinetic stability.') Some chemical systems are '*labile*'—they respond rapidly to changing circumstances by rapidly shifting configuration as circumstances change. But many other chemical systems are '*non-labile*', '*inert*,' or '*robust*'—they respond to environmental changes but only do so more or less slowly—sometimes so slowly that they may appear not to change. Many chemical systems are 'bistable' (or 'multistable')—they have access to *two* (or more) stable equilibrium

states. In such cases, the actual (present) configuration of the system depends on the specific *history* of the situation—the precise structure of (some, many, or all) previous (past) states of the system.

David Slutsky (2012) challenged a widely-held presupposition: that "history makes a special difference to the subjects of biology and psychology, and that history does not make this special difference to other parts of the world." He argues that "although history is special, it is special in the same way to all parts of the world." The properties of present-day biological and cultural systems result from large numbers of contingent events which happened in the past (including natural selection of biological species and the corresponding culling (only sometimes involving biology) of cultural entities. But physical and chemical systems also have histories—and present properties of specific physical and chemical systems also depend on details of the contingent events that comprise the histories of those same systems, including events that occurred in the distant, even very distant, past.

The differences that exist among particular samples of C_3H_4 (such as whether a specific sample is allene, cyclopropene, or methylacetylene) directly result from the diversity of processes that were involved (whether intentionally or not) in the generation of those samples, and also in their purification and storage. Prior history is relevant, diachronic approaches are needed: in such cases, synchronic treatments rarely (if ever) work.

Cyclopropene was first synthesized in Russia in 1922. Later, Maurice Schlatter (1941) devised a ten-step procedure by which he converted a starting material (1,3,propanediol) to a mixture of γ-bromo- and γ-chloro-butryonitrile, which mixture he then converted to cyclopropylcyanide by treating it with sodamide in liquid ammonia, thereby closing the three-carbon ring-structure. By applying standard methods to cyclopropylcyanide he prepared cyclopropylamine and then, from that, trimethylcyclopropylammonium hydroxide. Thermal decomposition ($\sim$320°C) of that quaternary base (using a platinum catalyst supported on asbestos), followed by fractional distillation, gave cyclopropene (boiling point −36°C at 744 mm) in 45% yield. The two other stable isomers of C_3H_4—methylacetylene (MA) and propadiene (PD)—appear together (in an equilibrium mixture called MAPD) as troublesome side-products in the catalytic cracking of propane ($CH_3CH_2CH_3$) to produce propene ($CH_3CH{=}CH_2$). (Propene is the feedstock used to make polypropylene, a thermoplastic polymer widely used for packaging, textiles, and other purposes. During 2007 worldwide production of polypropylene was 45 million tons—about $65 billion in market value.) The connectivity of atomic centers in methylacetylene differs from that in propadiene in the position of a single hydrogen and also in the distances between carbon centers: neither methylacetylene or propadiene has the three-carbon ring- structure that is characteristic of cyclopropene.

The C_3H_4 potential energy surface (PES)

Quantum chemists have been working on developing C_3H_4 PES for several decades (Lebedev et al. 1979; Su 2008). Several computational approaches, including well-tested ab initio methods using both smaller and larger 'basis sets,' are now widely available (e.g., Mebel et al. 1998). Maeda and Ohno (2005) have developed the *Scaled Hypersphere Search* (SHS) method to examine a PES for energy minima (corresponding to stable equilibrium states, designated EQ) and also to locate 'saddle points' corresponding to transition states (designated TS) for inter-conversion of isomers, for their decomposition (for instance, by loss of H_2), or for internal rotation ('twisting' of the molecule). The SHS

was first applied to C_3H_4 data generated by Hartee-Foch (HF/6-31G) theory to locate candidate minima or saddle points on the propyne PES. Then the seven EQ and 32 TS identified for propyne were further refined by successive use of two higher-level ab initio theories (CCSD(T)/cc-pVTZ and B3LYP/6-311++G(d, p)). Structures and energies for the three 'stable' isomers of C_3H_4, and for four additional less-stable isomers, are shown in Fig. 1. Figure 2 shows structures (and energies) corresponding to thirty-two saddle-points on the propyne PES. Each saddle-point corresponds to the transition state for change of one of the (more or less stable) isomers into another isomer, or to a decomposition or internal rotation reaction of a single isomer.

The PES for C_3H_4 qualifies as a 'rugged' landscape. (Energies given below are all in kcal/mol.) Although two of the isomers, propyne (EQ1) and propadiene (EQ2), have quite similar energies (0.0 and 0.8), the transition state for their inter-conversion is at high energy (TS 1/2a = 77.7) corresponding to a slow reaction. Four of the seven equilibrium structures (EQ5, EQ6 and EQ7) have energies above 60 kcal/mole and are not protected by high activation barriers: therefore they are not considered as 'stable isomers.' EQ4 has lower energy (46.3) but there is no significant barrier to its reversion to EQ1 (TS 1/4a = 45.9) so EQ4 does not exist in significant amounts and hence is also not considered 'stable.' The cyclopropene (EQ3)

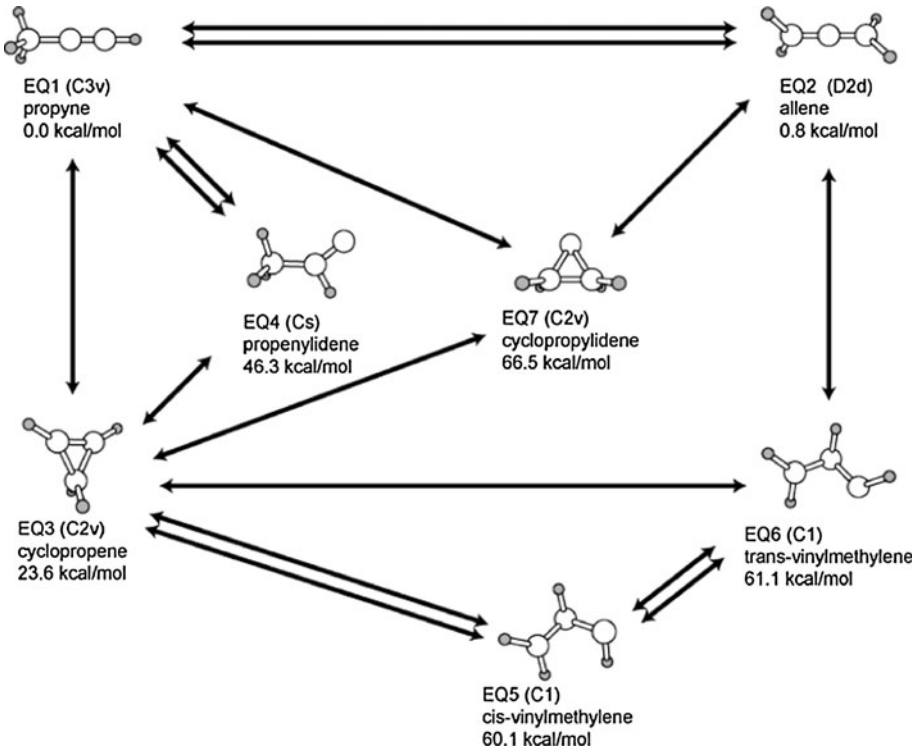

Fig. 1 Connections between equilibrium structures (EQ) corresponding to energy minima identified by the scaled hypersphere search method (SHS) on the propyne potential energy surface (PES). *Arrows* indicate independent intrinsic reaction coordinate (IRC) connections between a pair of EQs. Relative energy (including zero-point energy corrections) values (in kcal/mol) with respect to the propyne molecule (EQ1) are also shown (*Symbols* in *parentheses* indicate the symmetry point-group that corresponds to each structure). Figure reprinted (and caption adapted) with permission, from Figure 6 of Maeda and Ohno (2005). Copyright (2005) American Chemical Society

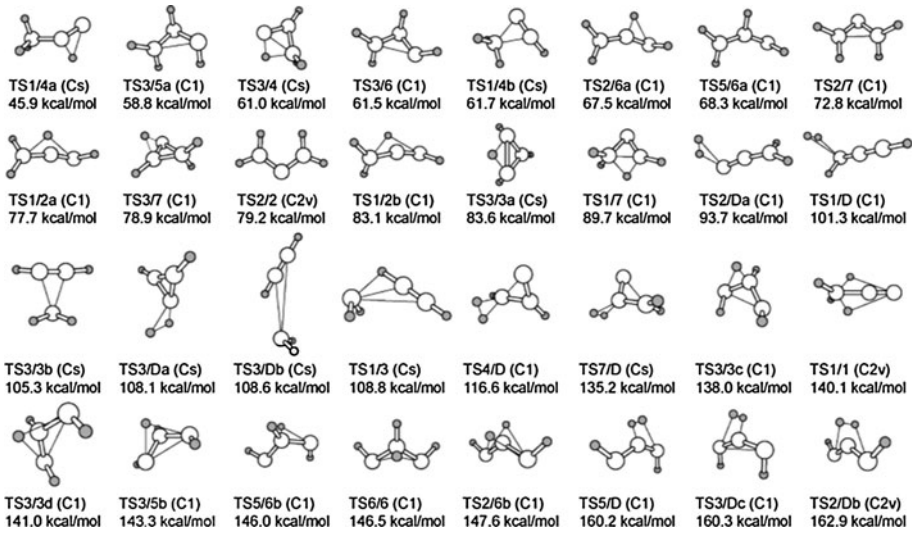

Fig. 2 Transition states (TS) between equilibrium structures (EQ) corresponding to first-order saddle points identified by the scaled hypersphere search method (SHS) on the propyne potential energy surface. TS between EQn and EQm are labeled as TSn/m, or TSn/ma, TSn/mb,…, if there are multiple connections between EQn and EQm. TS for dissociation channels from EQn are labeled as TSn/D, or TSn/Da, TSn/Db,…, if there are multiple connections. Relative energy (including zero-point energy corrections) values (kcal/mol) with respect to the propyne molecule (EQ1) are also shown, increasing in energy from *upper left* to *lower right*. For each structure, *double solid lines* denote chemical bonds, and *thin single lines* indicate a set of bonds rearranging at the TS. (*Symbols* in *parentheses* indicate the symmetry point-group that corresponds to each TS structure.) Figure reprinted (and caption adapted) with permission, from Figure 7 of Maeda and Ohno (2005). Copyright (2005) American Chemical Society

structure, with energy of 23.6, is thermodynamically unstable with respect to either EQ1 or EQ2, but major activation barriers (TS 1/3 = 108.8, TS 3/4 = 61.0, TS 3.5a = 58.8, TS 3/6 = 61.5, TS 3/7 = 78.9) reduce the likelihood of all of the possible ring-opening reactions. Although the three-membered ring (EQ3) has a significant strain-energy, that cyclical form will persist in the absence of sufficient energy to surmount the rather high activation-barriers that protect it (cf. Leigh 1993). This circumstance makes it necessary to consider the *specific history* of a C_3H_4 aggregate in order to compute its energy by any theory whatsoever. This is the reason why it is necessary to specify in advance ('put in by hand') whether the specific C_3H_4 aggregate of interest is linear or cyclical.

The neglected aspect of quantum treatment of chemical structure

It would *not* be reasonable to consider the C_3H_4 structural problem as one that involved 18 neutrons, 22 protons and 22 electrons—because events that occurred in stellar atmospheres long ago irreversibly joined certain sets of hadrons (now 6 protons and 6 neutrons) into specific carbon nuclei. It would be even less reasonable to attempt a C_3H_4 energy-computation starting from 120 quarks and 22 electrons, since what happened shortly after the initial cosmological singularity ('the big bang') irreversibly produced hadrons, including the predecessors of the protons and neutrons of the current universe. It would be just as unreasonable to ignore whether the specific sample C_3H_4 with which a computation is to be

concerned originated from cracking of propane (and so is linear) or was produced by gentle thermal decomposition of some cyclopropylammonium salt (and therefore contains a three-carbon ring-structure). The prior constraint of connectivity determined by prior contingent events (that is, 'chemical structure') must be explicitly recognized—a diachronic rather than a synchronic approach must be used. Such an approach would be consistent with the notion of 'contextual emergence' (Bishop 2005; Bishop and Atmanspacher 2006)—providing that the continuing importance of *prior* events is appropriately recognized as part of the relevant present context.

It is difficult to understand the precise meaning of Woolley's project of "apply[ing] quantum mechanics to *all* the particles [of C_3H_4] in one go." How would the seven nuclei be distributed in space for this proposed calculation? (Only something like Aristotle's "prime matter" could be *totally without structure*—and, strictly speaking, even prime matter did not have *substantial* existence: *hyle* was not itself *ousia*.) Any possible arrangement of nuclei would correspond to one or another point on the C_3H_4 PES. Any optimizing procedure would eventually lead such a point to 'move' to one of the seven local potential-energy minima (EQs)—just as evolutionary systems moving on 'fitness landscapes' generally wind up on local 'fitness peaks' (Kauffman 1993). Any computation with a starting configuration within the potential well associated with cyclopropene (EQ3) would, with high probability, remain in that well indefinitely: any starting configuration outside that well would, rapidly enough, move to either EQ1 or EQ2.

Oversights and confusions related to the ones that this paper concerns may be quite widespread. For instance, biochemical researchers dealing with complexes of several enzymes firmly bound together may sometimes erroneously assume that the characteristics of those complexes primarily depend (synchronically) on *properties of their components*. In such cases, the alternative (or supplementary) interpretation that the characteristics of these complexes are determined (in greater or lesser part) by their biochemical *function* may easily be overlooked. Judy Hirst (2011, p. e1) poses the question:

> The prokaryotic and eukaryotic homologues of [mitochondrial] complex **I** (proton-pumping NADH:quinone oxidoreductase) perform the same function in energy transduction, but the eukaryotic enzymes are twice as big as their prokaryotic cousins, and comprise three times as many subunits. Fourteen core subunits are conserved in all complexes **I**, and are sufficient for catalysis – so why are the eukaryotic enzymes embellished by so many supernumerary or accessory subunits?

After extensive consideration, Hirst (2011, p. e3) tentatively provided an answer to her query. "Thus it is possible to speculate that gradual improvements in energy conservation by complex **I** were accomplished by gradual decreases in stability of the core complex and compensated by the recruitment of supernumerary proteins to stabilize the assembly." Information concerning the components of these complexes is important to the answer that Hirst tentatively proposes for this question—but the *main determinants* of the response are the selection processes that have acted on the biological function (Roca et al. 2007) of complex **I** through long intervals of time. Hirst's approach is definitely diachronic rather than synchronic.

More puzzles of molecular quantum mechanics

Hans Primas (1983, 10–17) identified ten "puzzles of molecular quantum mechanics." These conundrums point out problems and paradoxes that interfere with using quantum

mechanics to gain understanding of phenomena of interest to chemists: they also prevent theoretical physics from generating explanations of fundamental principles of chemistry. Few quantum chemists are much concerned with riddles of this type, since several well-developed (semi-empirical and ab initio) methods reliably generate useful results—even though those methods may *not* have firm foundations in fundamental theory. Primas (1983, p. 8) observed:

> Despite the erudition, imagination and common sense used to create the semiempirical methods of quantum chemistry, the success of this craft remains a central enigma for the theoreticians. The models of semiempirical quantum chemistry are built on an inadequate conceptual basis, and their conceptual foundations are so wobbly that they are a source of frustration. Moreover they give us an image of matter that does not conform to what we are led to expect from the first principles of quantum mechanics. But experimentalists are not at all impressed by such scruples. *And properly so*. (Emphasis is in the original.)

Primas proposed that resolving the puzzles of molecular quantum mechanics that he identified (and thereby also dealing with the problem of molecular structure that Bishop, Hendry, Scerri, Sutcliff and Woolley discuss) would require a major *shift in logic*. Following suggestions made in 1936 by Birkhoff and von Neumann, Primas maintains that the logical systems employed by 'pioneer quantum mechanics' (and still used in quantum chemistry) need to be replaced by what he calls "*W*-logics*" (Primas 1983, Chapter 5). These are related to what are called W*-algebras or "von Neumann algebras" which are "non-Boolean temporal logics"—they deal with time explicitly (using concepts such as 'until' and 'next') but are not restricted to values of 0 or 1 (Primas 1983, p. 258). Primas claims that the puzzles he has identified do not arise if such logics are used. Perhaps this suggestion might well be the 'new idea' that Woolley concluded is needed to allow quantum mechanics to deal with chemical structure. Whether or not this should turn out to be the case, careful use of *diachronic* rather than *synchronic* approaches will still definitely be necessary to reduce or avoid difficulties with respect to quantum-theoretic treatments of chemical structure.

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