# A personal story on a renaissance in valence bond theory: A theory coming of age!

Sason Shaik

*The Hebrew University of Jerusalem, Institute of Chemistry and the Lise Meitner-Minerva Center for Computational Quantum Chemistry, Edmond J. Safra Campus, Givat Ram, Jerusalem 91904, Israel*

## ARTICLE INFO

## ABSTRACT

This is a personal story on the author's way of 'discovering' valence bond theory and using it to formulate unified models of chemical reactivity and bonding. Since scientific life is just a part of life, the story blends sub-stories of life events with stories on scientific events, colleagues, papers, meetings, and friendships. This is also a story of a wonderful and insightful theory, which is coming of age with applications and computational capabilities that start to match the most advanced post Hartree-Fock calculations.

## 1. Introduction

Valence Bond (VB) theory has been born thrice. The first time in 1916 [1] when Lewis postulated that the quantum unit of chemical bonding is an electron pair that glues the atoms of most known matter. In so doing he was able to derive electronic structure cartoons that are used to this day and age. Lewis further distinguished between shared (covalent) and ionic bonds, and laid the foundations for resonance theory and was even discussing geometry in terms looking like VSEPR's [2]. The second birth of VB transpired in 1927 when the young Heitler and London (HL) went to Zurich to work with Schrödinger [3]. In the summer of the same year, they came up with a quantum mechanical description of the bond in $H_2$, in terms of the resonance mixing of two forms, $1s_a(1)1s_b(2)$ and $1s_b(1)1s_a(2)$, which exchange electrons. In the winter of 1928, London generalized the properties of this shared bond. Pauling and

Slater masterminded the third birth in 1931, by extending the HL treatment to polyatomic molecules [4]. Though they both contributed the seminal ideas, Pauling's papers and his book [5], published first in 1939 have been more influential as they spoke to chemists in their language in terms of resonance structures and hybrids that seemed to describe many molecules quite well. MO theory was developed around the same time by Hund and Mulliken, and later extended by Lennard-Jones and mostly by Hückel [4]. The two theories became rivals within a short time [6], and for a while the tide was in favor of VB theory, but this was temporary...

The struggle between the Pauling camp and Mulliken's growing troops started to shift in favor of MO theory by mid-1950s. Many reasons combined to make this happen: the fast development of molecular orbital (MO)-based software, the synthesis of aromatic and antiaromatic molecules (a dichotomy that seemed to have evaded VB theory), and the formulation of attractive qualitative concepts, like Walsh diagrams, Fukui's frontier molecular orbital

*E-mail address:* sason.shaik@gmail.com

theory and the Woodward-Hoffmann rules of conservation of orbital symmetry, and the synthesis of molecules like ferrocene and the elegant interpretation of its unusual bonding by MO theory [4]. All these factors together contributed to the demise of VB theory, which has died slowly and painfully in mainstream chemistry, starting from the mid-1950s onwards to the 1970s. Except for the molecular dynamics community, where VB theory continued to be used, by and large the theory ceased to guide chemists to new experiments, and it was cast aside and branded with mythical failures (see chapter 5 in Ref. [4]). It seemed to have been condemned to oblivion.

While VB theory appeared to be safely residing in oblivion, it was nevertheless maintained as a Lingua Franca in chemistry through Lewis structures, resonance structures, hybridization, and so on. There were also a few groups who kept the fire alive by developing VB software, some of which, like generalized VB (GVB) [7] was even competitive with MO-based methods. There were ways to map MO-based wave functions to VB structures, and ways to relate the two wave functions by building up separately the electronic structures of the two spin sets [8–10]. New VB-based concepts slowly started to sprout in the late 1970s–early 1980s. Some VB renaissance seemed to have started its course, and while not quite the blossom as in Botticelli's Primavera, still this was VB infused with new life, and new ideas... [4,11,12].

As I was fortunate to participate in this new budding of VB theory, I was asked by the guest editors and the editor-in-chief to tell the story of this revival of VB theory and its future prospects. Since there are already ample reviews of VB methods [7,11–16], and VB concepts [11,13,17], I have made a decision to tell my own experiences and excursions into VB theory, and to do so in a style of an essay, rather than engaging in an additional exhaustive reviewing of VB theory and its applications.

## 2. Some initiating experiences during my short career as an experimentalist

As a BSc student in chemistry in the late 1960s, I was fascinated by the emerging chemical theory that was marked by highly imaginative and elegant concepts, like the Hund's rules, crystal-field theory, Hückel rules, hybridization and resonance theory, orbital-symmetry rules for chemical reactivity, Fukui's frontier molecular orbital theory, Hudson-Klopman's orbital vs. charge controlled reactivity, Salem's diagrams for photochemical reactions, and so on. During these schooling days, I started hearing statements about failures of a theory called valence bond (VB). This statement was accompanied by "proofs" like the "wrong" predictions of the ground state of $O_2$, the failure to predict the Hückel rules, and so on (see chapter 5 in Ref. [4]). Needless to say, I listened attentively to my teachers and believed the textbooks, even without knowing what was this VB theory that was just condemned before my eyes. Curiously, at the same time, all my teachers as well as I were using resonance theory and hybridization, but not being an expert on theory, I did not really associate these daily used concepts with the "failing theory" called VB. The fact that I did not know what was this VB theory that "failed so badly", and at the same time I was willing to believe this verdict, would become one of my lessons in science. Little did I know that a decade later I would become an avid proponent of this "failing" theory...

In those days, in the late 1960s and on, the reigning theory in chemistry was molecular orbital (MO) theory. The objects of the theory, the MOs, looked to me as pretty pictures that easily enabled me to predict chemical behavior. I loved MO theory. In the early 1970s I started my MSc studies under the guidance of Michael Albeck, and became an experimentalist. My project was to carry out reactions of $TeCl_4$ with unsaturated molecules in order to form π-complexes.

Nothing I did went too well. All my shiny spatulas were turning black; my flasks were full of black goo, and I was desperate. My only consolation was a course I was taking on MO theory (taught by Milon Sprecher). I immersed myself in deriving perturbation theory, and deducing from it the perturbation MO (PMO) theory of Dewar, the Hudson-Klopman arguments, and the MO mixing diagrams that Hoffmann and Epiotis were publishing on a variety of molecules. This was a lot of fun! And it would prove handy for my MSc thesis.

In October 1973, I left my MSc research in shambles, and joined many Israelis who went on reserve duties during the Yom Kippur War. At some point, my unit was flown to Egypt to man one of the captured airports. As the Egyptians were firing missiles at us, we have used the airplane shelters as living quarters that were pretty much protected from the missiles. During long hours we had nothing to do other than sitting and waiting for the shooting to stop...

At these meditative moments, my mind resurfaced the research difficulties, and I found myself constructing in my thoughts an MO-interaction diagram for $TeCl_4$. It dawned on me that the highest MO must have some antibonding character along the Cl—Te—Cl axis, and because of this instability, one of the Te—Cl bond should elongate, making the species looking like $TeCl_3^+Cl^-$. All of a sudden I realized that this reagent was a powerful oxidant that was undergoing nucleophilic attacks on the Cl substituent of the positive $TeCl_3^+$ moiety, thus producing $TeCl_2$ that in turn disproportionated to $Te + TeCl_4$. Everything became suddenly clear even the black goo; it was elemental tellurium, and it was masking the chlorinated compounds of the various unsaturated systems, which I used in the reactions with $TeCl_4$.

On my first vacation from the army service, I went back to the lab and subjected my black goo to sublimation, and lo and behold I got sparking yellow chlorinated compounds, which I identified and isolated. I have done mechanistic work, and had a nice MO model that explained the chemistry, and a few other goodies [18]. My M.Sc. thesis was over thanks to a little MO diagram that served me as a "thinking aid" to look through the black goo. Later (October 6, 1975), when I became a PhD student in the University of Washington, Roald Hoffmann wrote me a letter [19]. He had spotted the paper with the MO description of $TeCl_4$, and was sorry not to have seen it earlier to include it in the discussion in a paper he wrote on analogous sulfur compounds [20]. I answered him with an enthusiasm of a youngster being noticed by the highest authority...

## 3. PhD: life in MO land

MO theory registered in my mind as a winner. I decided to continue my PhD in theory. I wrote to Hoffmann who was (still is) the high priest of MO theory, and requested him to admit me as a PhD student. On March 4th, 1974, he responded in a detailed letter about the admission to graduate school, and the fact that I may have already missed the registration deadline. He advised me "*not to put my eggs in a single basket*" [21], which I took seriously and continued searching for a PhD adviser. I was attracted very much to the structural theory papers of Epiotis who used MO theory to predict nonbonded attractions [22], and other effects, which I found to be novel and imaginative. I was admitted to the University of Washington (UW), and was offered the duty of a teaching assistant. A few months after the war ended I left to the US to study with (the late) Nicolas D. Epiotis (Nick) in UW.

As a PhD student, I participated in the writing of a book, which attempted to demonstrate how MO theory could account for a

variety of problems in structural chemistry [23]. This was a tremendous experience, because I was forced to read copiously and find problems that could be included in the book. From Epiotis I learned to question everything I read, and to appreciate how simple mathematical models could lead to powerful predictions (e.g., the fact that $a^2 + b^2 > 2ab$ when $a \neq b$, could be applied to head-to-head vs. head-to-tail dimerizations of olefins using MO perturbation theory). I also took a few courses in theory. One on MO theory which was taught by Wes Borden, in which I learned about diradicals and disjoint orbitals, and another on quantum mechanics which was taught by Martin Gouterman (coincidentally, one of Hoffmann's PhD advisers), and in which I learned about the spin-orbit coupling (SOC) operator (which I will later use to derive selection rules for triplet organic reactions). I made a habit to apply MO ideas to every new thing that I learned in chemistry. I kept delving into the theory, developing my own simple models, and deriving all kinds of equations, which would later be helpful to me. MO theory was a dreamland.

This feeling was further strengthened when Roald Hoffmann visited UW during January 10–20th 1976, and gave a series of lectures (the Hyp Dauben Lectures), in which he showed how fruitful was MO theory in transition metal chemistry. He was cutting molecules into fragments, and from the fragments he made other molecules, and all these with the aid of small MO cartoons. This was magic! I could see that cutting and reassembling leads to new understanding.

In his usual way, Roald invited any wishing student to join him in the evening for a beer. I went. At some point, where the beer sufficiently relaxed me, I dared asking him a "journalist's" question: what did he think would be the future of theoretical quantum chemistry? He answered me in his usual thoughtful way that he thought that VB theory would make a comeback! Considering the consensus then on VB theory, what Hoffmann was saying sounded to me at best strange, and I thought to myself "*does he not know that VB theory is passe' and is anyway a wrong theory*?" Not long later, I myself would stumble over VB theory and would fall in love completely.

### 3.1. Stumbling into VB theory

At some stage during my PhD, I started thinking seriously about chemical reactivity. I was facing a conceptual puzzle, which preoccupied me as an MO-fan. MO theory could not reveal explicitly the origins of the barrier except for cases of forbidden reactions [24], where the orbital crossing gave a pictorial origin for the barrier. So, I kept asking myself, what were the origins of the barriers for other chemical reactions, like $S_N2$, a Diels Alder reaction, or H-abstraction? There was no clear answer to this question from delocalized MO theory. This quest led me to stumble over VB theory.

I started this quest by trying to understand the theory that my adviser, Nick Epiotis, published in *Angewandte Chemie* [25], in which he used fragment orbital (FO) configurations, to interpret chemistry. I realized that Mulliken used these configurations in his charge-transfer theory, and others in the descriptions of excimers and exciplexes in photochemistry and photophysics. At this stage I was not making any connection between this and VB theory (I now wonder if Mulliken was aware that he was doing VB theory, while fighting with Pauling). I simply wanted to find out systematically what was the relationship of the canonical MO description of molecules and transition states, to the description by means of FO configurations.

I spent many weeks in trying to decompose Slater determinants where the canonical MOs were replaced by linear combinations of fragment orbitals (FOs) or just hybrid atomic orbitals (HAOs). At some point I started getting some interesting trends, which seemed to resurface in the many examples I tested. Some of the

wave functions I was getting out of the MO-based Slater determinant looked like simple VB functions of a singlet-coupled electron-pair, like the one used by Heitler and London [3] to describe the bond in $H_2$. With some concern (since my mind was still echoing the admonition that VB theory was considered to be wrong, and hence unpopular), I started looking for quantum chemistry books that included VB theory. I found some, I read, I took notes....

Unfortunately, none of the books made a bridge between MO and VB, and in most of them the matrix elements between VB structures were cast in a pictorial manner. But, whereas a picture was supposed to elucidate the complex mathematics, these ones looked to me cryptically complex. I thought that either my derivations were wrong, or that I indeed found *an MO-VB bridge and maybe a new way to describe transition states for chemical reactions*, and to answer my questions about the origins of barriers in chemical reactions (that were not forbidden ones, for which MO correlation diagrams ascribed the barrier to orbital crossing [24]). I also realized that I knew much too little on VB theory, and that I needed first to educate myself. But the time came to complete my PhD, and I had to stop playing with MOs, FOs and VB.

## 4. Postdoc at Cornell: the art of crossing through mirrors

On November 28, 1977, Hoffmann offered me a postdoctoral fellowship, and I was excited. In the summer of 1978, I collected my notes, travelled to Cornell, and forgot all about VB theory for a while. Roald was away, and I took the time to educate myself on what his group was doing on transition metal (TM) chemistry with the kind assistance of Birgitte Schilling (then a PhD student in the group). I read a lot, but one paper by Elian and Hoffmann [26] attracted my attention because it reminded me the magic Roald was performing on the blackboard during his Hyp Dauben Lectures. In retrospect, this was the paper that led to what became to be known as the "the isolobal analogy" [27]. Also in retrospect, the isolobal analogy must have endowed me with confidence that my attempts to expand MO determinants into once containing VB structures were not a futile exercise. It was a labor of bridge building.

Elian and Hoffmann (E&H) were using MO description of metal hexa-carbonyl complexes, in order to understand the binding capabilities of $TM(CO)_n$ fragments with n < 6 [26]. They started with a $d^2sp^3$ hybridized shell for the TM, and made six TM—CO bonds. Then, by plucking off CO ligands, they showed that at each such vacant site, there grew a hybrid orbital. Thus, as shown in Scheme 1a, $TML_5$ (L = CO) had one such hybrid orbital, $TML_4$ two, $TML_3$ three. The binding capability of these hybrids depended on the d-electron count on the TM. For example, for $Mn(CO)_5$ where Mn possessed a $d^7$ configuration (and a filled $t_{2g}^6$ sub-shell), this hybrid was occupied by a single electron, and E&H could show that this was the driving force for these radicals to dimerize and for a Mn—Mn $\sigma$ bond, or to form a Mn—H bond, etc. The fragment Fe$(CO)_4$ had two singly occupied hybrids, while Co$(CO)_3$ had three such hybrids. All these MO transformations would later develop to the isolobal analogy, which likened the transition metal fragments to organic fragments and vice versa. Thus, as shown in Scheme 1a, $Mn(CO)_5$ was isolobal to $CH_3$, while Fe$(CO)_4$ to $CH_2$, and Co$(CO)_3$ to CH. The isolobal analogy meant that one could build *similarity bridges* between $Mn_2(CO)_{10}$ and $C_2H_6$, or $(OC)_5Mn$—H and $CH_3$—H, Fe$_2(CO)_8$ and $H_2C=CH_2$, so on. Later in 1981 Hoffmann in fact entitled his Nobel lecture as "*Building Bridges Between Inorganic and Organic Chemistry*" [27].

At some point in the E&H paper the authors went back to an MO description and formed from the hybrids' symmetry adapted orbitals, as shown in Scheme 1b for Fe$(CO)_4$ and Co$(CO)_3$. By taking advantage of orbital symmetry match, they were able to construct
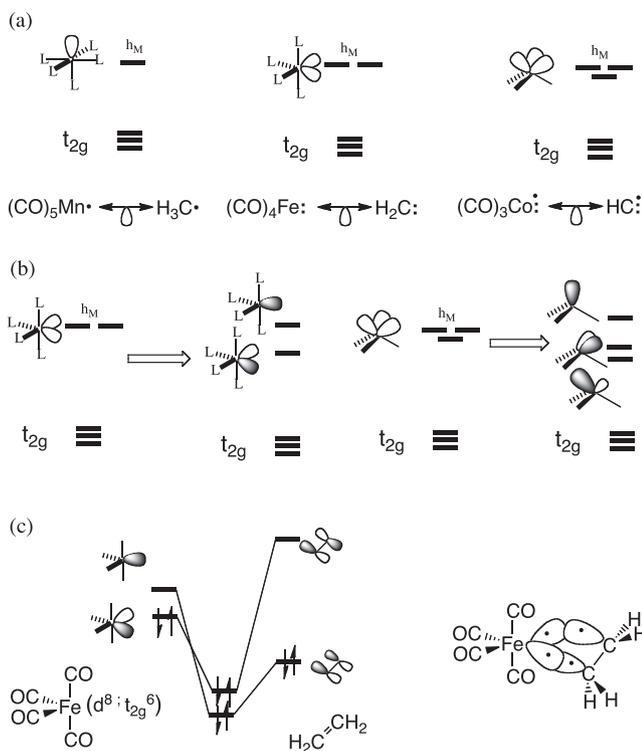
**Scheme 1.** (a) Cutting ligands L (L = CO) from TML$_6$ and getting hybrids at the vacant sites. TML$_n$ (n = 5–3) fragments with d$^7$, d$^8$, and d$^9$ configurations are isolobal (symbolized by the drop on the double headed arrow) to CH$_3$, CH$_2$, and CH fragments, respectively. (b) Symmetry adaptation of the hybrids. (c) Creating a new complex from (CO)$_4$Fe and ethylene, using either the symmetry-adapted hybrids (left) or electron-pairing cartoon (right).

new molecules with a variety of ligands. Scheme 1c shows an example using the combination of Fe(CO)$_4$ with an olefin. It is seen that the symmetry adaptation of the hybrids facilitated the understanding, showing that the two symmetry-adapted hybrids find match with the π and π* orbitals of the olefin and form thereby two bonds. On the right side, one can see the electron-pairing cartoon, which shows that the so formed complex has also a character of a metallacycle. The two cartoons showed complementary insight into the structure of the complex (the orientation of the olefin) and its rotational barrier.

In mid September 1978, Roald returned to Cornell from his sabbatical in Cambridge. We started having weekly group seminars (at times, twice a week), in which either we talked about what we were doing, or Roald would present extracts from his literature reading. He would usually take the new structures he collected and would analyze their orbital makeup. He would often apply the isolobal analogy in order to teach us. Fig. 1 shows Roald lecturing on the isolobal analogy at Ben-Gurion University (BGU) to where I moved after my postdoc.

### 4.1. Chemical reactions: laying initial bridges between MO and VB theories

By that time I had already wised a bit to know that the hybridization model was part of VB theory, and that it was developed by Pauling and Slater in the 1930s [5,28]. It became clear to me that Hoffmann was shifting back and forth between MO and VB-like representations, and using the advantages of both depending on the need. My take-home lesson was that the art of bridges and analogies was evidently much more powerful than the orthodoxy of staying in a single world of either MO or VB. I also realized



**Fig. 1.** Roald Hoffmann teaching organometallic chemistry at Ben-Gurion University, in 1981, shortly after his Nobel Prize. Courtesy of Roald Hoffmann.

that what I started doing while in UW was creating bridges between MO and VB theories for chemical reactions. So along with my postdoc research and my development of the role of spin inversion in photochemistry [29], I returned to carry out projection of the VB content of MO and MO-CI wave functions.

After a while, I finally found a systematic method to get the coefficients of these VB structures from the MO-based wave functions, and started looking how was the VB content of the wave function changing *along the reaction coordinate* [30]. I considered model reactions of H-atom transfer, nucleophilic displacement, and nucleophilic additions to double bonds. I used Hückel and extended Hückel orbitals, as well as Hartree-Fock calculations using a minimal basis set, and including CI. To my excitement, there emerged a unified description of transition state (TS) formation and clear origins of barriers in chemical reactions and means to predict barriers heights and variations. I proudly presented the model to my fellow postdocs and PhD students of the group, whenever they were willing to listen to me (what remained is one photo of me standing by a VB diagram drawn on the blackboard in the office I shared with Al Pinhas, Fig. 2). I still remember that Eluvatingal D. Jemmis, a postdoc in the group, and Al Pinhas, a PhD student with Barry Carpenter and Roald, were very interested and supportive. Al Pinhas even helped with some *ab initio* calculations. Roald himself was very supportive, and tolerated my spending time on these MO-VB games and the spin inversion projects.
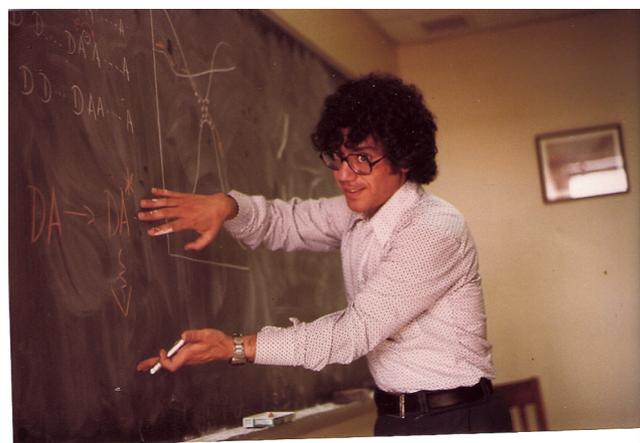


**Fig. 2.** The author posing by the blackboard and presenting a VB diagram in 1979 in Cornell.

In the midst of 1979 I received an offer from Ben-Gurion University to join its ranks. This left me very little time to enjoy the fun, inspiration and friendship I had experienced in Hoffmann's group. I started packing all my unfinished projects, among them were the MO-VB data I produced and organized, a paper on spin inversion in Diels Alder reactions [29b], and some outputs of calculations on electrostatic effects on molecules for which I was going to derive selection rules (which I ended doing much, much later with my postdocs Rajeev Ramanan and Debasish Mandal [31]).

## 5. Ben-Gurion University: piecing up energy profiles from VB building blocks

Upon my arrival to Ben-Gurion University (BGU), I had to overcome the expected cultural shock after having been away from Israel for five years. Since I did not have yet an office, I was given Addy Pross' office. As soon as I felt sufficiently settled (this includes meeting my future wife Sara), I returned to my preoccupation with MO-VB transformations, and with attempt to understand of the origins of the barrier of chemical reactions. I reexamined the results I produced, while at Cornell, by computing simple reactions and then projecting the wave functions unto more localized ones based on FOs, and subsequently all the way to classical VB wave function based on atomic orbitals (AOs) or hybrid AO (HAOs).

As FOs I chose the orbitals of the reactant state. For example, when projecting the MO wave function for $H:^- + H_2$ as a model of $S_N2$ reaction, the chosen FOs were those of the fragments $H:^-(1s)$ and $H_2$ ($\sigma$ and $\sigma^*$), and these assignments were kept unchanged throughout the pathway. In so doing, in any reaction I examined I observed that the initial reactant wave function was gradually diminishing along the reaction coordinate and being replaced by a collection of FO-based configurations. In the transition state (TS) one of these FO configurations became dominant and remained so *en route* to the product state.

Thus, for example, in the case of the $H:^- + H_2$ reaction the dominant FO-configuration was the charge transfer one, involving the following electronic structure, $1s^1\sigma^2\sigma^{*1}$ [30]. Augmentation of the MO wave function by CI enhanced the weight of the charge-transfer configuration and further clarified the picture. Using a double zeta basis set did not change the chemical nature of the FO-VB configurations; the basis set rather caused orbital 'rehybridization' in the original configurations. Use of Hückel orbitals led to the same dominance of the charge transfer configuration, thus demonstrating that the phenomenon was topologically independent of the quality of the orbitals or the wave function. Shifting to "larger" systems, e.g., nucleophilic attack on a double bond of ethylene or formaldehyde, I again retrieved the same description, and the very same picture reappeared in a model electrophilic attack. The inevitable conclusion was that in all electrophile-nucleophile combinations, the barrier arises due to the avoided crossing of the charge transfer and the reactant FO-VB configurations, as shown schematically in Fig. 3a.

The reason for this uniform avoided crossing picture became clear when the FO-VB charge-transfer configuration was further projected unto the HAO-VB structures. The projection revealed that the charge transfer configuration contained the covalent HAO-VB structure of the product, as exemplified for nucleophilic attacks on a C=O bond in Scheme 2. Thus, the charge transfer FO-VB configuration contained a *bond-pair* between the reactants in the $\phi_{Nu}$ and $\pi^*_{C=O}$ orbitals (Scheme 2a) that were rehybridized [30], compared with the original reactant orbitals, so as to maximize the bond-pair interaction. This bond pair could be written either in terms of the FO-VB configuration, $\Psi_{CT}$, of as the covalent Heitler-

London (HL) structure represented by the HAO-VB cartoon, $^+Nu\!-\!^\cdot C\!-\!O^-$, in Scheme 2b.

Other reactions, e.g., $H\cdot + H_2$, led to an avoided crossing scenario, but here the excited FO-VB configuration involved a triplet excited $H_2$, coupled with the attacking $H\cdot$ radical to a total of a doublet spin. The Diels-Alder and ethylene dimerization reactions required an FO-VB configuration where both reactants were excited to their triplet states and were coupled to a singlet state across the inter-molecular linkages. The reason for this crossing/avoided crossing became apparent upon further projection of these key excited configurations into the HAO-VB wave functions. The leading excited FO-VB configuration invariably contained the covalent HL structure of the product. *The excited FO-VB configuration itself contained the same number of bond-pairs as the number of bonds in the respective product state.*

This recognition led in turn to a general mechanism for barrier formation, shown in Fig. 3b which is a VB state correlation diagram (VBSCD). Thus, the reactants have specific bond pairing, and the only way to change this is to replace the reactants state by another one in which the reactants are "prepared for bonding" by having spin-paired odd electrons on the reaction centers that are bonded in the product state (**P**). Since at the geometry of the reactants, the "prepared state" (**R**\*) is an excited state of the reactants, this "preparation for bonding" occurs via the crossing/avoided crossing of the two configurations. The same applies to the reverse reaction where now the products' state **P** is being crossed by the corresponding prepared state **P**\*, along the reverse reaction coordinate.

At the crossing point the two configurations mix, avoid the crossing, and generate a transition state (TS) for the chemical reaction $\Psi^\ddagger$, and above it a twin-excited state $\Psi^*$. Thus, while the energy of $\Psi^\ddagger$ determines the barrier for the ground state ($\Delta E^\ddagger$) reaction, the twin state, $\Psi^*$, serves as the generator of the conical intersection that will funnel excited state species to the ground state products [17,32].

Importantly, **R**\* and **P**\* in the VBSCD *are electronic images (or templates)* of the ground states with which they correlate, and due to their relations to the ground states **R** and **P**, these excited states are referred to as the "promoted states" of reactants and products. Thus, given a pair of **R** and **P** states in a reaction, we know also the natures of **R**\* and **P**\*, and one can immediately trace the two principal curves that involve the VB correlations of **R** → **P**\* and **P** → **R**\*. The promoted states **R**\* and **P**\* for a given reaction type can be expressed using either FO-VB configurations or hybrid-atomic orbitals HAO-VB. Detailed guidelines how to do so can be found in a recent review [32] and in chapter 6 of Ref. [4]. The basic idea is rather straightforward, and is summarized in **Rule 1**.

**Rule 1.** Whenever the oxidation numbers of the reacting fragments change during the reaction, the promoted states of the VBSCD will be charge transfer states. By contrast, if there is no change of oxidation numbers, then the promoted states involve a triplet decoupling of each of the bonds that breaks during the reaction, while pairing up the electrons across the bonds to be formed.

Scheme 3 provides two archetypal examples; an $S_N2$ reaction and a radical addition to a double bond. In the first case, the oxidation numbers of the nucleophile and the leaving group change during the reaction (X:$^-$ loses an electron while Y gains one) and hence, the promoted state **R**\* is a charge transfer state, which can be expressed as such in terms of HAO-VB or FO-VB cartoons (similar arguments apply to the reverse reaction). In both representations there is a single bond pair between the electron left on the nucleophile X·, and the electron that was added to the substrate to create a radical-anion, $(AY)^{\cdot-}$.
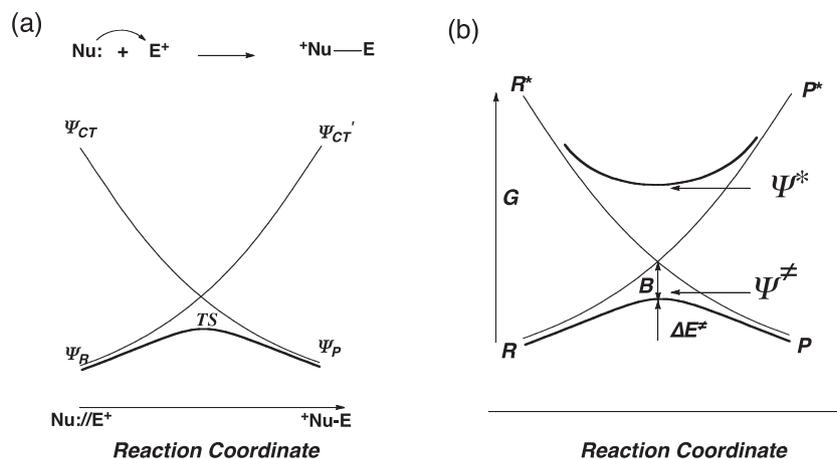
**Fig. 3.** (a) A common VB avoided crossing for a reaction between a nucleophile (Nu:) and an electrophile (E⁺). (b) A generic state correlation diagram (VBSCD) with two states curves anchored in ground (**R** and **P**) and prepared/promoted states (**R**ˣ and **P**ˣ). The avoided crossing leads to a TS (Ψ‡) and a twin-excited state (Ψ*). B is the resonance energy of Ψ‡ due to avoided crossing, ΔE‡ is the reaction barrier, and G is the promotion energy gap at the reactant side ($G_R$).
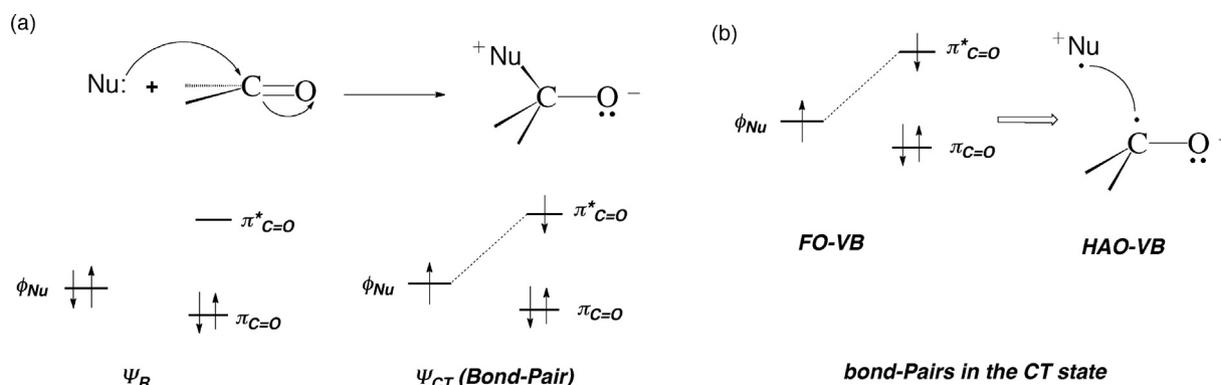


**Scheme 2.** (a) The primary states that participate in avoided crossing during nucleophilic attacks on a C=O bond. (b) The representation of the charge transfer (CT) state, using FO-VB and HAO-VB.
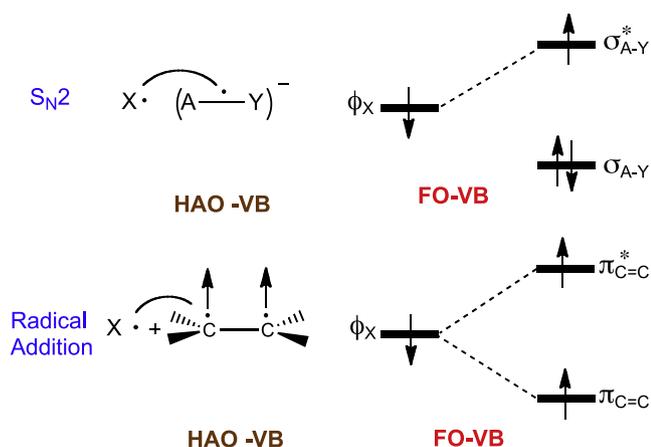


**Scheme 3.** HAO-VB and FO-VB representations of the promoted states $R^*$ for $S_N2$ and radical additions. Bond pairing in FO-VB is shown by dashed lines.

In the second example, in Scheme 3, the oxidation numbers of all reacting atoms remain unchanged. As such, the promoted state **R**ˣ involves triplet decoupling of the $\pi_{CC}$ bond-pair while spin pairing the triplet to the radical X· (such that the total spin sate is doublet). In the FO-VB representation the two dashed lines indicate that the radical is paired to an orbital, which is a combination of π and π* [17].

I keep using the two approaches because they give complementary information. Thus, the HAO-VB approach allows a systematic and elegant generation of the entire VB diagram from a basis set of VB structures as done in chapter 6 of Ref. [4]. On the other hand, the FO-VB enables to derive selection rules and reaction stereoselectivity or regioselectivity, by utilizing the symmetry/nodal properties of the FOs (chapter 6 of Ref. [4]) [33,34]. Together, the two representations are more powerful than each one separately.

In the end of the process, I concluded that what I have found was a generalized mechanism of barrier formation and TS description, and that the resulting VB diagram (Fig. 3b) forms a bridge from MO theory all the way to VB theory. This was not an ad hoc curve-crossing model. The diagram showed that energy profiles of chemical reactions could be pieced up systematically from VB building blocks, like in a game of LEGO (chapter 6 of Ref. [4]). *Thus, the projection of the MO-based wave functions generated the building blocks of energy profiles, transition states and reaction intermediates*, and enabled a systematic reconstruction and conceptualization of these "chemical reactivity objects". I decided therefore to finally write the paper, and since I was excited by the outcome of my labor I gave the paper the title, "*What happens to Molecules as They React?* . . ." [30].

In mid 1980 I submitted the paper to JACS along with another paper that deals with the role of geometric distortions along the reactions coordinate, and asked the editor to consider the two for publication. This latter paper was instantly rejected and never published (though its contents were included in subsequent papers).

I was convinced that the first paper would be accepted in flying colors. However, my little experience did not prepare me for the refereeing process. I got three referee reports. One rejected the paper because "*it did not have sufficient new results... and the 'chemical insight' gained by the author's circuitous path' is seriously flawed*". According to the referee, the charge transfer configuration was "*an artifact of the localized fragment configurations*", because "*electrons shift in pairs*". I would hear this objection to a description of nucleophilic/electrophilic reactions as *single electron-shift processes* again and again. The second report was not too bad, but it involved many comments. The third report was not too bad either, but the tone was somewhat harsh. The editor himself/herself was favorable to the ideas but also had many comments, acting as a 4th referee.

It takes years to get used to the refereeing system, but at that time, this constituted an unpleasant reception for the young faculty member that I was. In the end, the paper was accepted to JACS and appeared in 1981 [30]. Its title was attractive and its drew a lot of reprint requests...

### 5.1. A simple barrier equation based on the VBSCD

Already in the first paper [30], it was clear that the reaction barrier could be expressed using the promotion energy gaps in the diagram and its avoided crossing term. Thus, as can be seen from Fig. 3b, the energy difference between the $R/R^*$ states at the onset of the forward reaction is the promotion energy, $G$, at the reactant side; to specify this promotion energy let us label it as $G_R$. Furthermore, the mixing energy of the two sate-curves at the crossing point was the resonance energy or the delocalization energy of the TS, $B$.

Based on the VBSCD, the barrier can be expressed as a fraction ($f$) of the promotion gap, $G_R$, minus the resonance energy, as in Eq. (1):

$$\Delta E^{\ddagger} = fG_R - B; \quad f < 1 \tag{1}$$

This simple-looking expression is also rigorous. Thus, the term $fG_R$ is the height of the lowest-energy crossing point between the two state-curves; it constitutes the total reactants' distortion energies and Pauli repulsions that are required to destabilize the reactant state and bring it to resonance with the product state. In turn, the term $B$ is the resonance-stabilization energy of the TS due to delocalization of the electrons in the bonds undergoing breakage and remaking.

The easily accessible term in Eq. (1) is the promotion gap $G_R$, which is the excitation energy from the reactant state $R$ to a spectroscopic excited state $R^*$. Thus, $G_R$ can be obtained from experimental quantities or evaluated from MO-based or DFT computations. For example, for an $S_N2$ reaction we need the vertical ionization of the nucleophile $X:^-$ and the electron affinity of the molecule A-Y. Already in 1980, I derived some thermochemical expressions, and did simple semi-empirical VB calculations, which allowed me to estimate these quantities. This became handy, since in 1980, Pellerite and Brauman [35] published their seminal paper on gas phase identity reactions, in which they managed to quantify the barriers for a variety of $X:^-/CH_3—X$ systems. They found rather small barriers for the halides, and much higher barriers when the nucleophiles and leaving groups were $OH^-$ or $CH_3O^-$.

The experimental study posed an opportunity for testing the VBSCD model and making specific predictions. I realized that the $f$ factor in Eq. (1) is controlled by how steeply does the charge transfer state, $X^./(CH_3X)^{.-}$, correlate to the respective ground state along the reaction coordinate. This depends, among other factors, on the electronic structure of $(CH_3X)^{.-}$. Thus, whenever the unpaired electron is localized mostly on the $CH_3$ group, this will

lead to a strong $X^.---.CH_3$ coupling with the $X^.$, and will lead to a small $f$ value, and vice versa when the unpaired electron in $(CH_3-X)^{.-}$ is delocalized on both moieties. Scheme 4a vs. b shows the effect of the electron delocalization in the promoted states on $f$. Mathematical expressions for the state curves provide estimates for the range of possible $f$ values. For example, if the state curves can be approximated by parabolas the value of $f$ will be 0.25, while straight lines give $f = 0.5$, etc.

Using simple semi-empirical VB calculations, I showed that for $X$ = halogen the $(CH_3X)^{.-}$ radical anion was localized on the $CH_3$ moiety, but for OH or MeO the corresponding radical anion was quite delocalized over the two centers, and hence, $f_{Halide} < f_{OH (OMe)}$. The promotion energy gaps were also estimated using semiempirical VB calculations. Having estimates for gaps and $f$ factors, it was possible to demonstrate that the larger $f$ factor was responsible for the higher barriers for $X$ = OH or OMe compared with $X$ = halogen.

I wrote quickly a communication in which I treated a variety of identity $S_N2$ reactions. I submitted the work to JACS. Of the two referee reports, one was very positive. The second very negative and asserted: "*This papers is not publishable*", because "*the author has taken a model that gives nearly trivial results and has attached an unnecessarily complicated interpretation to them*". I was quite unhappy. I felt that while I was trying to do something new, general, and useful, my effort was being ridiculed and put down. In retrospect, this experience is not unique and it takes getting used to.

Nevertheless, since during 1980–1981 the number of JACS rejections was increasing, I was at loss as to how to handle the situation. I needed advice. In the summer of 1981, I went back to Cornell to visit Roald's group. I told Roald about my "publishing" experience. He asked me to sit down, went to his archives and pulled out a pack of referee reports and put them on the desk in front of me. I read many of the reports, and I saw that "even" Hoffmann is not treated with silk gloves by referees. My share was not unique...

Roald then made two practical suggestions, one was to send the communication on identity $S_N2$ reactions to *Nouveau Journal de Chimie* (NJC) – "*they are more open minded*" he said. His second advice was to directly appeal to the Editor in Chief, which helped me bypass the JACS editors who were rejecting my papers. Following these suggestions, the communication was published in NJC in 1982 [36] and the full paper on $S_N2$ was accepted in JACS [37]. Since then many papers were accepted by JACS and other journals, and it felt good to know that these papers caused a mini renaissance in VB theory [38].

Before shifting to describe my collaborations in BGU, let me demonstrate that the delocalization effect and its impact on $f$, which is used above for $S_N2$ reactions, is physically meaningful. Consider Fig. 4, which shows a plot of experimental free energies
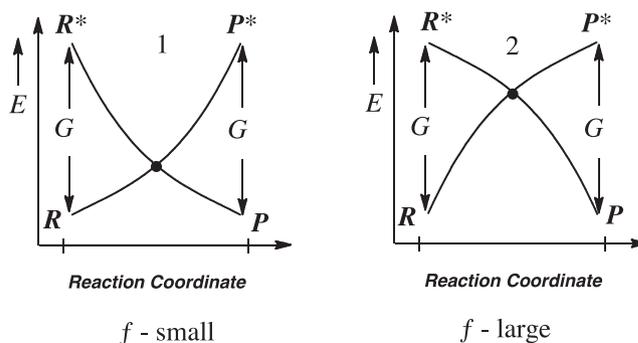


**Scheme 4.** Dependence of $f$ (Eq. (1)) on the delocalization properties of $X^.$ and $(CH_3X)^{.-}$ in the charge transfer states $R^*/P^*$ in the VBSCD for identity $S_N2$ reactions. Case 1 corresponds to localized states, while case 2 for delocalized ones.
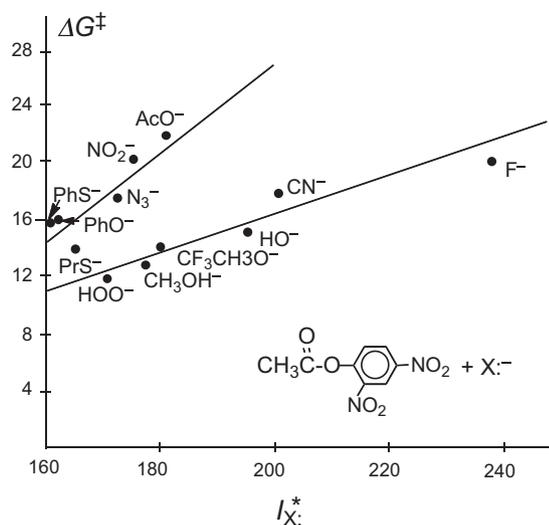
**Fig. 4.** Experimental free energies of activations ($\Delta G^{\ddagger}$) plotted against the vertical ionization potentials ($I^*_{X:}$) for a series of nucleophiles X:$^-$ activating the C=O in the ester depicted in the figure. Adapted with ACS permission from Ref. [39].

of activation for nucleophilic cleavage of an ester by a series of nucleophiles, X:$^-$, taken from a collaborative work with the groups of Erwin Buncel and the late Saul Wolfe [39].

According to experiment, the rate-determining step here is the nucleophilic attack on the carbonyl group of the ester. This step can be analyzed by use of the VBSCD in Fig. 3b and on Rule 1. Thus, the promoted state for reactions of nucleophiles with electrophiles is the charge transfer state, and for the reaction in question, $G_R = I^*_{X:} - A^*_{Ester}$, where $I^*_{X:}$ and $A^*_{Ester}$ are the vertical ionization potential and electron affinity of the nucleophile and ester, respectively, in the solvent used in the reaction. As such, the corresponding barrier is given by:

$$\Delta G^{\ddagger} = f[I^*_{X:} - A^*_{Ester}] - B \qquad (2)$$

Since the ester is common to the entire series, the respective electron affinity is a constant. If we assume that $B$ is a constant or a quasi-constant of the series, then Eq. (2) becomes simply Eq. (3):

$$\Delta G^{\ddagger} = fI^*_{X:} - C; \quad C - \text{constant} \qquad (3)$$

Eq. (3) predicts that a plot of $\Delta G^{\ddagger}$ vs. $I^*_{X:}$ will be a straight line with a slope equal to $f$. It is seen that the data set leads to two lines with different slopes. The lower line involves those nucleophiles, which possess localized radicals (such as F· and HO·) in the charge-transfer state, and hence the respective $f$ factor should be small and so is the slope of the line in Fig. 4. On the other hand, the upper line in Fig. 4 involves nucleophiles that lead to highly delocalized radicals (such as AcO·), and hence having a larger $f$ factor and a larger slope for the line. Clearly, therefore that the delocalization of the electrons of the bond-pairs in the promoted states is a factor which reduces the reactivity and must be reckoned with. This delocalization effect is common to many other reactions [40].

### 5.2. VB partners in BGU

As I wrote, my first office in BGU was Addy Pross' who was on a sabbatical leave in Australia. Addy returned in the summer of 1980 and naturally came to his office where I was sitting. I was on the way out to move to another office. We started talking and he asked me about my science. I described to him my work on spin inversion, and then the VB model I just developed in the paper "*What happens to Molecules as They React?*...". He asked me "*what can you do with it*"? Finally, I had a captive audience, so I told Addy at some length what I thought were the many potential uses of the diagram for discussing relative reactivity, stereochemistry, and reaction mechanisms. His eyes lit. He was interested...

Being a renowned physical organic chemist, Addy saw instantly how the model was specifically addressing the agenda of his field. I gave him the submitted draft of the first paper [30]. A few days later he came back to me and asked if I could translate all the FO-VB configurations to HAO-VB ones to facilitate the juggling between the two representations. I did so. After some time, he suggested that we collaborate on the S$_N$2 reactivity of benzyl derivatives. I immediately agreed and this turned out to be an intense and fortunate collaboration. Addy was (is) a fast writer, and being a prominent physical-organic chemist he was also very familiar with the mechanistic issues in the field. This paper passed quite easily through the JACS referees, and ended up being published in 1981 back-to-back [41] with the theoretical paper on "*What happens to Molecules as They React?*...".

This collaborative paper and the intellectual affinity between Addy and I forged an intense collaboration during 1980–1983. During this time we extended the art of piecing up energy profiles from VB building blocks to all the major mechanisms in physical organic chemistry. Dealing with reaction mechanisms and with the physical organic chemical culture of substituent effects expanded the scope of the VB-diagram model. This required also expansion of the diagram and fitting it to mechanistic considerations.

#### 5.2.1. VB diagrams for stepwise mechanisms

Let me refer to Fig. 5 to see how was this achieved. Fig. 5a shows again the VBSCD with two state curves that are anchored in the ground states (**R** and **P** and promoted states (**R*** and **P***) of reactants and products, and which by mixing avoid the crossing and lead to a TS and a barrier for an elementary chemical step. Besides the two promoted states of the principal state curves there exist many other excited states, which can affect chemical reactivity. The corresponding diagrams that contain more state curves than just the two principal curves, are called by the name VB configuration mixing diagrams (VBCMD) [17,32,42–44]. In the usual situation, which is shown in Fig. 5b, the intermediate-state curves will lie above the crossing point, and if sufficiently low in energy, they will mix into the TS of the two principal curves and lower the energy of the TS, while endowing it with their characters.

Fig. 5c is an extreme VBCMD case where an intermediate state gets stabilized (by substitution, solvent, etc.) [17,32,44,45] and drops well below the crossing point of the principal state curves. Here, one intermediate-state curve crosses the two principal curves, and the three-state mixing *leads to a stepwise mechanism with an intermediate between **R** and **P***.

The intermediate state curve can be the triple ionic structure X$^-$ R$^+$ Y$^-$ in nucleophilic substitution of alkyl halides, thus defining the S$_N$1 or S$_N$2-intermediate mechanisms. It can be a carbocationic or carbanionic intermediate in elimination reactions of substituted ethane derivatives, thus defining the mechanistic changes from the single step E2 mechanism to the stepwise ones, E1 (via R$^+$ intermediate) and E1$_{CB}$ (via R$^-$) [45], or any low-lying excited state (e.g., σ charge transfer states during nucleophilic cleavage of σ-bonds) [46]. As such, with just two diagrams, the VBSCD (Fig. 5a) and VBCMD (Fig. 5c), it became possible to describe a wide scope of chemical reactivity and mechanisms.

In 1983, the late Joe Bunnett who was the editor of Accounts of Chemical Research, visited BGU and invited Addy and me to write an account of the work on VB modeling of chemical reactivity, which we did [42]. After this paper, our interests diverted and the collaboration moderated. Eventually, Addy would dedicate
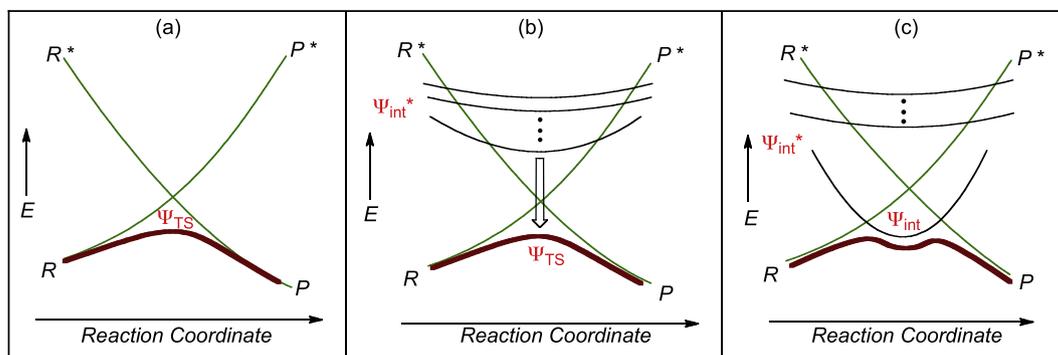
**Fig. 5.** (a) Generic VBSCD with just the two principal curves of reactants and products. (b) VBCMD showing in addition to the principal curves a manifold of intermediate state curves ($\Psi_{int}^*$), which do not correlate to **R** or **P**, but may mix into the TS. (c) VBCMD wherein one of the intermediate states drops well below the two principal curves and defines an intermediate ($\Psi_{int}$) in a stepwise mechanism. Adapted with permission of the RSC from Fig. 1 in Ref. [32].

his time to the origins of life problem, in which he published a wonderful book [47]. Fig. 6 is a photo of the two of us, taken by Leo Radom, in 1996 during the WATOC meeting in Jerusalem.

### 5.3. VB activities in BGU during 1980–1984

Along with reactivity, I started applying VB ideas to a variety of other problems. In 1981 I began addressing the relationship between organic conductors made from separate stacks of donor and acceptor molecules, and their isomeric charge transfer complexes made from alternating stacks of donors and acceptor [48]. I noted to myself then, that VB theory provided a lot of insight into this problem. VB was a great theory to use for understanding conductivity. Regrettably, though, I applied these VB ideas to conductivity in only one more paper [49], since my attention was swept away by other topics.

I continued to develop the VBSCD model with an aim of demonstrating its applicability to a variety of problems. In 1983 I addressed solvation, and showed how solvent effect could be predicted semi-quantitatively, using the VBSCD with non-equilibrium solvation in the promoted states. This development enabled me to estimate $S_N2$ barriers successfully in many solvents. The paper was published in 1984 in JACS [50]. Together with the previous full papers on gas phase $S_N2$ reactivity [37] and on α- and β-carbon substituent effects [51], I finally had in my hands a model that was making qualitative as well as semi-quantitative predictions. Quite a few years later, my collaborators and I would use this



**Fig. 6.** The author with Addy Pross in a photo taken on July 7th, 1996 during the reception in the WATOC conference in Jerusalem. Courtesy of L. Radom.

VBSCD/(solvent) model in *ab initio* VB computations that addressed the Menshutkin reaction [52].

Still in 1983, my friend and former classmate, Ronny Bar, from the BSc days in Bar Ilan University, called and asked if she could do again (after stopping in 1980) some research with me. Ronny is a superb scholar, and I was fortunate that she wanted to do research. Already in 1982, I had an idea, which seemed a bit crazy, considering all the education I went through. The idea was that all the π-electronic components of delocalized systems like benzene and allylic species, were in fact transition states trapped by their σ-frames.

This idea surfaced in one of the Fridays in my favorite Cafe in downtown Beer-Sheva. While sitting with my friend, the painter Oded Israeli, watching the people go by, an idea captivated me, namely, that an application of the VBSCD model only to the π-electrons, would predict that the delocalized π-electronic system was a transition with a sizable barrier. As such, in the real molecules the π-electronic components must be prevented to distort by the σ-frame. Ronny Bar did the calculations using Extended Hückel, and showed that the *π-electronic components of allylic species were transition states with a propensity to distort to a localized state, and at the same time these π-component exhibited rotational barriers.*

Ronny and I further considered the isoelectronic series of each π-electronic component (e.g., XHX· or $X_3$ e.g., X = H, $CH_3$, F, Cl, Br, I, Li, Cu, etc., for π-allyl radical, and $X_6$ species for X = H, Li, π-benzene, etc.). We showed that using the promotion energy gap $G$ in the corresponding VBSCD made it possible to predict whether the delocalized species will be a stable cluster or a transition state for an exchange reaction. Thus for example, $G$ for $H_6$ was 8 times as large as the same promotion gap for $Li_6$, and therefore $H_6$ is a very high-energy transition state for an exchange reaction, while $Li_6$ is a stable cluster. The same considerations apply to $H_6$ vs. $Li_6$. Generally, since the $G$ quantity increased in proportion to the binding energy of the diatomic molecules, and since the π-bond is rather strong, the π-electronic components of the allylic species and of benzene were deemed to be among the unstable species. Similar predictions were made for π-allyl anion and its $X_3^-$ isoelectronic species, as well as to the $X_4$ isoelectronic species and π-cyclobtadiene. The paper was published in NJC in 1984, after having gone through 7 referees [53]. Not that any of the reports was bad, but there was a significant degree of disbelief in this idea, which will later force my collaborators and I to struggle for any additional publication.

The two years 1983 and 1984 were quite eventful for the family. I decided to take a sabbatical leave in the French laboratory established in Paris Sud (Orsay) by Lionel Salem. In the meantime, our daughter, Yifat Sela, was born and she had a heart-related problem,

from which she seemed initially to recover. I completed a huge review on the VB model of reactivity, which I entitled "*The Collage of $S_N2$ reactivity Patterns*" (eventually published in Progress in Physical Organic Chemistry in 1985 [44]). While the focus was $S_N2$, the review gave a general scope of how to apply the VBSCD and VBCMD models to pattern data and to make new predictions.

Subsequently, the late Saul Wolfe visited Ben-Gurion University. He was doing *ab initio* calculations of $S_N2$ reactions and wanted to meet "*this guy who calculated all the trends with a paper and pencil*" (in Saul's own words). Saul was an eminent chemist and I was glad he was interested in what I was doing. In our meeting he suggested we write a book on $S_N2$ reactivity using the VB model and all the computational data his group in Kingston assembled. The enthusiasm of Saul was contagious and I found myself saying sort of a feeble "yes".

## 6. 1984–1991: VB in Orsay and in Kingston, and back to BGU

As we prepared to go to France, I flew to Paris, and the plan was that my family would join me after full recovery of our daughter Yifat from here surgery, and after she and Sara get their French VISAs. We were perhaps lucky that the French administration was not too fast to issue the VISAs, and Yifat had more than one month to recover. We were lucky also since by the time Sara and Yifat were allowed to join me, I could already manage somehow with my newly acquired French to know how to select the delicious foods Paris could offer. Until that time, the only word I knew was a *rillettes* sandwich – which means an animal-fat sandwich that I have been eating for the whole month whenever I would eat by myself. In the meantime, I found an apartment and prepared it; it was in *Rue Massenet* adjacent to the place where the role of the French in the Suez war was planned. Finally, my family joined me in February 1984. This was a wonderful year in every respect!

### 6.1. Science in Orsay

In Orsay I already had two friends from the Cornell days, Odile Eisenstein and Christian Minot, but I did not know all the other members of this large and world-renowned laboratory. In my first visit to the lab, Philippe Hiberty approached me and said he wanted to collaborate with me on the problem of $\pi$-electrons. It turned out he was one of the 7 referees who reviewed the *NJC* paper [53], and he was at the same time both intrigued by the whole idea as well as disbelieving it. I knew Hiberty's work on projection of MO-CI wave functions to VB structures [9], and I was very happy to team with another lover of VB theory.

Philippe invented all kinds of ways to probe the $\pi$-distortivity of conjugated molecules, which was predicted by applying the VBSCD to the $\pi$-electrons. There was a lot of resistance in the way to publishing these papers, but we somehow managed, initially in NJC, then in JOC and slowly also in JACS [54–56].

Believing that science is a polylogue, we welcomed any logical criticism and made a habit to respond it. Every response used a new way to interrogate the $\pi$-electronic component [57,58]. Eventually, vibrational spectroscopy of the ground state and the $^1B_{2u}$ excited state would provide a simple experimental evidence for the distortivity of the $\pi$-electrons of benzene [59,60]. The work on the root cause of $\pi$-delocalization started an intense collaboration between Hiberty and I (Fig. 7), along with friendship. It continues to these days.

During the same year in Orsay, I fervently continued to develop the VBSCD and VBCMD models and to apply them to more complex reactions, which were stepwise and involved mechanistic changes, such as nucleophilic-vinylic substitution [61]. Philippe, other members of the Orsay lab and I applied the VBCMD model to



**Fig. 7.** Philippe Hiberty and the author in the Jean Paul Malrieu Fest in Lagrasse in 2004. Courtesy of P. C. Hiberty.

understand the stability of hypervalent radicals [62], and the stability of $SiH_5^-$ vs. the extremely high energy of $CH_5^-$ [63,64]. Together with Saul Wolfe, Dave Mitchell and Berny Schlegel, we showed that in accord with the VBSCD model, the gas phase $S_N2$ barriers correlated with the deformation energy of the $CH_3X$ molecule [65].

The review on $S_N2$ was published in 1985 [44], and Jean-Jacques Perrier who already knew me, saw it and invited me to Toulouse to give a mini-course on chemical reactivity for one month. I went to Toulouse in January 1985 in the bitter winter when even Toulouse was snowed down. The warm friendship of the Toulouse group and my excitement to give this course on VB approach to reactivity compensated for the low temperatures outside. I also gave talks in the group of Jean-Paul Malrieu and found myself in the midst of an intense (but friendly) debate with him. The French chemists were excited about ideas and I felt very welcome. The model was acquiring gradually some popularity among chemists.

### 6.2. Starting quantitative VB calculations in Orsay

Early on during the sabbatical, Hiberty and I decided to collaborate on the VBSCD model, but to try to calculate these diagrams for real reactions. This collaboration extended well beyond the sabbatical year in 1984–1985. I became a frequent traveller to France.

#### 6.2.1. VBSCD calculations

Luckily, Philippe found an old VB program that was written in the Orsay group by Jean-Michel Lefour and Jean-Pierre Flament. We used the program to construct the VBSCD model for $S_N2$ reactions, initially for $H^- + CH_3{-}H \rightarrow H{-}CH_3 + H^-$ [66]. Good few years later, we looked at another $S_N2$ reaction, $F^- + CH_3{-}F \rightarrow F{-}CH_3 + F^-$ [67]. These applications verified the qualitative considerations regarding the connection between the $f$ factor and the delocalization of the radical anion in the charge transfer sate. Thus, for the hydride $S_N2$ exchange the VB calculation led to $f = 0.42$ while for the fluoride exchange $f = 0.15$ (Scheme 3). We also computed the VB diagram for the radical exchange reactions $X^· + X{-}X \rightarrow X{-}X + ·X$ (X = H, Li), for which we verified the nature of the promoted state as nascent from the triplet decoupling of the bond undergoing cleavage [68]. Even more importantly, we verified the VBSCD prediction that for both X = H and X = Li the same type of avoided crossing transpires. However, since in the case of X = H, the G value is 8 times as large as that for X = Li, the avoided crossing led to a delocalized $H_3$ transition state, whereas for X = Li the avoided

crossing led to stable delocalized $Li_3$ intermediate, as shown in Scheme 5.

Scheme 5 is not restricted to the two cases presented; it is rather a generic portrayal of many cases. It highlights a natural division of the periodic table to weak binders (many of the metals) which form stable delocalized species, and the strong binders for which the delocalized species are TSs of chemical reactions. The VBSCD projects this natural division in an easy and clear manner by mere inspection of the relative $G$ values for the corresponding diatomic molecules.

Generally, the heights of the barriers or the depths of the energy wells followed the previous semi-empirical/qualitative estimates based on considerations of the VBSCD [53]. Nevertheless, the quantitative VB calculations taught us quite a bit on effects that affect the $f$ and $B$ factors (Eq. (1)), and increased our confidence in the qualitative reasoning. Thus, we found that for the radical exchange reaction with X = Li, the $f$ factor was rather small (0.13), while for X = H the $f$ was significant (0.37) [68], and as already noted, for $H^-$/$CH_4$ the $f$ was large (0.44). We also found that the TS resonance energies ($B$) for radical exchange reactions were proportional to the strength of the bonds undergoing activation, whereas in electrophile/nucleophile reactions the $B$ values changed in a narrow range. Understanding the root causes of all these trends enriched the qualitative theory and refined all future applications [17,32,40,43].

### 6.2.2. Discovery of charge-shift bonding – recharting the mental map of bonding

Doing VB calculations faced us also with good surprises. One of these led to the discovery of a new bonding motif. Gergji Sini, Philippe's PhD Student, was engaged in generating the VB diagram for the $S_N2$ process, of $F^-$ + $CH_3F$. One day I asked Gergji to show me the results of his calculations. To my great surprise I found that the resonance energy of the covalent and ionic structures of the C—F bond was huge, almost as big as the experimental bond dissociation energy. I was stunned; until that moment I believed the Pauling paradigm according to which there were covalent/polar covalent bonds and ionic bonds, and that in both classes the corresponding covalent-ionic resonance energies were relatively small compared with the stabilization energies endowed by the dominant VB structures (the covalent or ionic) themselves. Suddenly, the structures in $CH_3$—F aren't important! What was holding the bond was the resonance energy between the structures. Such a bond is neither covalent nor ionic...

My hunch told me this is a significant result. Philippe and I discussed the matter and decided to ask Sini and Philippe Maître, a new student in the group, to run VB calculations of a few bonds [69]. Soon enough it became clear that some bonds, which included electronegative atoms, had huge covalent-ionic resonance energies, even when the bonds were homopolar, such as F—F and O—O. We found quite a bit of experimental support for a new class of bonding, which we summarized in due time.
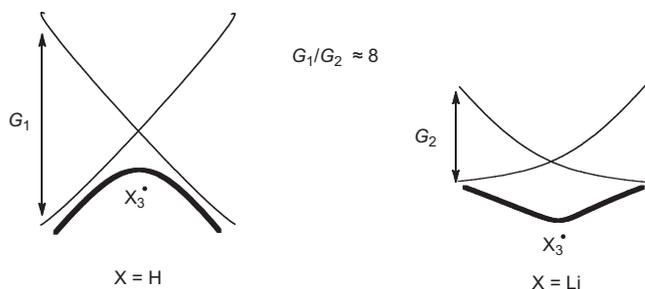
Our first paper was published in 1991 [69], but it was clear that these calculations and VB conceptualization of bonding might have just scratched the surface of a much bigger problem. Indeed, in the years to come, starting 1992, this idea has developed into the concept of "*charge-shift bonds*". Thus, in the beginning of 1992, Philippe would visit me for the last time in Beer-Sheva, and we would write together the 1992 *JACS* paper [70] in which we analyzed the origins of charge-shift bonding (CSB) in chemistry and related it to the virial theorem. We predicted the expected occurrence of CSB in the periodic table and some of its experimental manifestations.

In 1992, Philippe developed the breathing orbital VB (BOVB) method [71], which enabled us to calculate bond dissociation energies with good accuracies, while keeping the wave function extremely compact. With BOVB at hand we could systematically investigate chemical bonding. This research, which is still ongoing, has changed the mental map of bonding. Thus, usage of VB theory initiated the recharting of the mental map of bonding; suddenly a whole new family of bonds was added to the traditional covalent (polar-covalent) and ionic families. This is the CSB family, as shown in Scheme 6.

The logic behind the three bonding families derives from the description of the bond by three elements; covalent and ionic type VB structures, and the covalent-ionic resonance energies. Each one of these elements generates its bonding family. Molecules like [1.1.1] propellane were found to possess CSB [72,73]. Much later, we would form a bridge; now stretching from VB to MO, in which we show that the CSB family is also native to MO theory [74].

### 6.3. 1985: VB activity in Kingston

Close to the end of 1984, when I was still in Orsay, Saul Wolfe called and suggested to visit Queen's University, and discuss the book with him and Berny Schlegel. During these discussions it became clear that I would have to take a leave of absence from BGU and spend about six months in Queens. After completing the sabbatical year in Paris my family and I went back to Israel for one month. Yifat, our daughter, was already chattering in French. Soon enough we flew to Canada and arrived at Queens University in April 1985. Yifat had to learn English and for a long while she would not speak to us. We were very concerned so we asked the teacher at Yifat's day care, if there was something wrong. She told us that Yifat speaks ceaselessly, and because she thinks we do not know English she does not speak to us.

Saul was a great host and he made a supreme effort to let us have the best conditions. Saul, Berny and I used to have periodic discussions on what kind of a book we should aim. Berny and I were coming from different schools in theoretical chemistry, and these discussions were extremely important to bridge the chasms, and establish a mutual understanding and respect for each other's way in science.

The book was initially planned to treat only $S_N2$ reactivity, using the computational data of Dave Mitchell, Saul and Berny, and the review I wrote for *Progress in Physical Organic Chemistry*, as a basis. The idea of a small book was reasonable and attractive. However, in that stage in my life I was in the midst of developing the VB



**Scheme 5.** Schematic comparison of the VBSCDs for $H_3$ vs. $Li_3$.
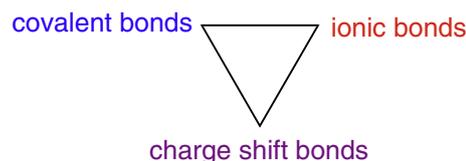


**Scheme 6.** The triangle of the covalent, CBS and ionic bond families.

model and expanding its coverage, so that deep down, my creative urge was pushing me towards a more general treatment of reactivity.

Writing a book with an inner conflict can be a nightmare... It took me time to curb down my ambitious plan and focus on $S_N2$ reactivity in the gas phase and in solution. In late August 1985, Sara and Yifat flew back to Israel. I stayed one more month to complete my share in the book. It was decided that I would leave all the chapters in Saul's hands and he will finalize the book. Fig. 8 shows the late Saul Wolfe and I talking in a relaxed atmosphere at his home where the Wolfe's celebrated my birthday.

A few days later, Saul and I flew to Chicago to participate in the Physical Organic Chemistry Symposium of the ACS Meeting, and subsequently I flew back to Israel. The Israeli airport in those years was small and all the family members would wait outside for their passenger to come out. The first thing I saw when I came out was the face of my two years old daughter who was held up by Sara. Yifat saw me, and then like a flash she recognized me, and she started gasping with excitement (she did not yet speak Hebrew, and for her we did not know English). She clung on to me for the next few days, as if not to let me off her sight so she will not lose me again. A week later I flew to France, and when I came back she ignored me for a few days – I was not reliable. This was a realization that my scientific work was tearing me away from my family. I had to learn the secrets of balance...

During the next six years, Saul coordinated the work on the book. He, Berny and I communicated by mail back and forth over the drafts of the book; this was not easy. But finally, Saul managed to condense the various chapters and to unify them into a coherent book. The book was published in 1992. When it came out the three authors were proud and evoked a sigh of relief [75].

### 6.4. 1986–1991: Back to BGU

In the period after my return to BGU in 1985 and till 1991, I resumed my activity in all fronts; teaching general chemistry and applied quantum chemistry, and working on: organic conductors, and further development of the VB ideas and applications to new reactions, bonding, and the behavior of π-electrons.

In 1987 the department started the process of my promotion to a Full Professor, but the pace was sluggish. This changed when Lowry and Richardson's textbook of (*Mechanism and Theory in Organic Chemistry, 3rd Ed.*) [76] came out, and contained extensive coverage of the VB work that Addy Pross and I did during

1981–1983. This made a deep impression on the Provost and the President of BGU and I was immediately promoted. Addy and I were very satisfied to see our efforts going into a textbook. Later, another textbook by Carroll included an even more extensive coverage of the VB diagrams [77].

In 1986 I received a second invitation to give a mini course on VB theory: this time from Sam McManus and Milton Harris from the University of Alabama, Huntsville. The time in Huntsville was very productive. Milton and I even started a collaboration, which however, would never be consummated... It is in Huntsville, in the restaurant near campus, that I was introduced to Korean food by being a frequent eater in the restaurant.

In 1987 I got the third invitation to come and give a series of lectures on the VB diagram model for chemical reactivity, this time in Lund and Gothenburg in Sweden. The late Per Ahlberg, Jan Sandström, and the late Lennart Eberson organized jointly this invitation. I gave these lectures only in 1989, just before the IUPAC meeting in Stockholm. This was a mini-course, which I titled: "*The LEGO Way: Curve Crossing Diagrams as General Conceptual Models for Chemical Reactivity and Structure*". My family and I spent a few weeks in Lund and a period of two months in Gothenburg, living near the fountain with the beautiful Carl Miles sculpture of Poseidon. The VB model was gaining some followers...

The benzene story was getting its share of attention too. In 1988 I flew to Switzerland upon the invitation of the late Edgar Heilbronner and Jack Duntiz to give The Kahlbaum Lecture in Basel and two talks in the ETH. Edgar was interested in the π-electronic ideas we published, and already while I still was in Orsay, he wrote me on August 5, 1985, a letter, and in his special sense of humor he let me know that he took our paper along with a few detective books to his vacation on the Swiss mountains. The ideas on the distortivity of the π-electrons of benzene were well accepted, even though they were still considered controversial. Edgar told me about his dialog with Binsch in the aromaticity symposium in Jerusalem (1971); Edgar asked what is an aromatic molecule, and Binsch replied, "*Benzene is a perfect example*", to which Edgar responded: "*Name a second one!*"...

In 1991, Edgar would publish a lovely paper in *The Journal of Chemical Education* [78], which was entitled "*Why is my molecule not symmetric*?" and this was the first positive reception of the idea. Edgar and I would publish together later on π-systems, but more importantly he impressed me by his engaging intellect and became in some ways one of my four important teachers. I learnt a lot from him and from his wonderful stories and quick wits.

### 6.5. 1988–1991: Self-education beyond resonance theory

While still in Orsay I reached the conclusion that whereas I knew quite a bit about VB structures, I had no good clues about the matrix element that were responsible for the VB mixing. VB theory without knowledge of matrix elements was merely resonance theory, and resonance theory ultimately failed because *it lacked selectivity* (any new resonance structure one could invoke was considered to stabilize the molecule). I recalled that Evans [79], treated the dimerization of ethylene and the Diels Alder reactions, already in 1930s, using the empirical VB calculations Polanyi and he developed. He found that the mixing of the VB curves in the TS for the Diels-Alder reaction was larger than the same quantity in the dimerization of ethylene. This led him to conclude/predict that the matrix element will increase in proportion to the number of π-electrons, which undergo delocalization in the TS. As such, Evans missed the opportunity to formulate those reactivity rules, which were later derived by Woodward and Hoffmann through orbital symmetry [80]. A related problem was that VB calculations of benzene and cyclobutadiene, which Pauling and Wheland were doing using only the covalent structures. These calculations led to the



**Fig. 8.** The late Saul Wolfe and the Author, September 1st 1985, Kingston.

conclusion that the resonance energy of cyclobutadiene is larger than that of benzene; something which has been marked as a serious failure of VB theory [4]. It turned out later that what made the 4n + 2/4n difference were the ionic structures, which mixed efficiently with the covalent ones in benzene but less so in cyclobutadiene [81].

I was determined to understand the mixing patterns in VB theory. However, unlike MO-based theory, where just two Slater Rules controlled the configuration mixing, in VB theory, due to retention of overlap between the HAOs all the VB structures maintained among them matrix elements. Thus, while FO-VB had the benefit of orbital-symmetry insight into the mixing, the HAO-VB approach did not, and it is here where ionic structures are numerous and their impact on the energy was huge. I therefore decided to struggle with VB matrix elements, and thought to derive a Hückel type VB theory.

A few events have pushed me to actually achieve these goals. One was an invitation from the late Imre Csizmadia to participate as a speaker-teacher-tutor in the NATO school in Saint Feliu in 1988. I was supposed to teach a few hours and then to have a few tutoring sessions. Looking at the list of other teachers-speakers, I saw Don Truhlar, Bill Miller, Paul Schleyer, Berny Schlegel, Paul Mezey, Mike Robb, etc. It was clear to me that if I wanted to rise to the occasion; I had to develop something new.

I resumed my attempt to derive analytically all the energy expressions and the mixing patterns of VB structures. Since the matrix elements scaled by the overlap to the power of the number of differently occupied HAOs (AOs), it became possible to restrict the VB matrix elements to only two rules; (a) one for VB structures which differed in one HAO (AO) occupancy, and (b) the second for VB structures which differed in two HAOs (AOs) occupancies.

I ended up developing a Hückel/Extended-Hückel type VB theory, and since VB theory deals with states, the scheme included effectively also the electron-electron repulsion terms. This was a lot of fun; once I figured out the rules for taking the matrix elements of VB structures and trimming them, I found that the VB-structures-set for a given problem interacted either in Hückel or Möbius patterns, and I could therefore use a simple Hückel MO program to solve the state problems. I derived the VB rules of aromaticity and antiaromaticity, including for odd electron systems, and had an immediate handle on excited states. This work was written as a Chapter in the *NATO ASI* series, which was published in 1989 [33]. It would become one of the foundations for the book [4] written by Philippe and I, 19 years later (see Chapter 3 in Ref. [4]).

Other motivators to focus on VB matrix elements further were the deliberations on the relationships between electron transfer (ET) and polar reactions, which in the late 1980s became a hot area in physical organic chemistry. Both Addy Pross and I addressed these relationships. The late Lennart Eberson, a prominent physical-organic chemist, has written a monograph in 1987 in which he outlined the ET/Polar relationship using the VB diagram model [82]. In 1989 the IUPAC chemistry congress was held in Stockholm and one of the major topics was the ET/Polar dichotomy in organic reactions, and I was invited to talk about the dichotomy. This has diverted some of my attention to electron transfer theories and especially to the Marcus-Hush theory.

Something that struck me was the outer-sphere model that was developed for distant electron transfer events in enzymes, was nevertheless being used to derive the reorganization energies of many organic ET reactions, where the reactants may have significant overlap because they can come close together. As such, from a VB point of view there should be a strong mixing between the two intersecting state curves, and I was confident that usage of VB matrix elements would lead me to orbital selection rules for the ET/Polar dichotomy. I did so, using FO-VB, and found that ET and Polar reactions are controlled by different orbitals, and would have therefore distinct TS structures [17].

During the meeting in Stockholm, Lennart and I decided to write a paper on this issue and to revise his older reorganization energies that were derived using the outer-sphere assumption. The paper, published in JACS in 1990 [83], derived orbital selection rules, and showed that the known experimental data matched an ET scenario wherein $B$ was significant, reaching >10 kcal/mol for dissociative ET of radical anions reacting with alkyl halides. In the same year, my postdoc Cho and I published a communication which showed that both the ET and the substitution TSs for the reaction of a nucleophile with ethane cation-radical, were bonded [84]. The ET-TS was far from the outer-sphere model usually assumed to take place. For a few subsequent years, I would write and give talks in which I asked my physical organic colleagues: "*Why should any transition state give up bonding and be outer-sphere?*"

Later during the years 1994–1998 (when I already moved to Jerusalem), my postdoc G. Narahary Sastry would investigate the reactions of ketyl radical anions with alkyl halides, and show that the ET and Polar processes follow different orbital selection rules that lead to different stereoselectivities and chemoselectivities and which could be predicted from the VB model of the ET/Polar dichotomy. Sastry would further demonstrate that the ET TS is strongly bonded, and that these transition states create entangled ET-Polar reactivity [17,85,86]. In this scenario the two processes share initially the same trajectory leading to a strongly bonded TS. From there onward the trajectory will bifurcate leading to ET and substitution products, *such that a single TS serves two mechanisms*. Importantly, Sastry and I also characterized *the recoil mechanism* that led the electron-transferred fragments dissociate away from each other past the tight TS. The entangled ET-Polar reactivity would later be verified by molecular dynamics simulation studies with Berny Schlegel and his coworkers [87]. Entangled mechanisms are expected in any mechanistic group, such as $S_N1$-$S_N2$, or E1-E1$_{CB}$-E2, which shares the same set of VB structures. I am sorry for never dedicating the time to deal with this generalization.

Another physical-organic chemist, whom I met in the IUPAC meeting, was Joe Dinnocenzo from Rochester, who was investigating reaction mechanisms of organic cation radicals. Joe was a student of Mel Goldstein in Cornell, and recognized me from the talk I gave in the group while in Cornell. We became friendly during the meeting and spent our lunches and dinners together in a merry company, which included Christian Amatore and Ole Hammerich, having great laughs, drinking beer and paying exorbitant prices.

During the posters session, I decided to stop by Joe's poster, which was showing that nucleophilic cleavage reactions of cyclopropylic cation radicals proceeded in a stereospecific manner. He revealed in his poster that frontier orbital theory could not make a prediction, because in odd-electron reactions the two different orbital interactions of the HOMO of the nucleophile with the SOMO and the LUMO of the one-electron $(C \cdot C)^+$ bond seemed equally important. Since I was thinking then in terms of FO-VB as the means to derive orbital-selection rules for chemical reactions, I immediately presented him with a VB analysis showing that it is the LUMO of the cation radical would determine the stereochemistry, leading thereby to inversion of configuration at the carbon site of attack. Joe's eyes lit. We decided to collaborate and write a communication on the problem. I drafted a short paper, and Joe added all the experimental insights and even corrected some of my errors in theory. The paper was published in *the Journal of Organic Chemistry* in 1990 [34]. We used the FO-VB formalism and predicted the observed reaction stereochemistry. To date this is the first and only paper that derived the stereochemical rules for odd electron reactions such as nucleophilic attacks on cation-radicals and the isoelectronic radical cleavage of σ-bonds [17].

Joe and I would publish a few more papers and would maintain friendship and a continuous communication on the application of VB theory to chemical reactivity.

## 7. 1992: Moving to the Hebrew University

In 1991 we moved to our newly built house in Beer-Sheva, which shows that I had no talent for predicting my own future - the move to Jerusalem. The move was initiated when Mordecai Rabinovitz from the Hebrew University (HU), who was at the time the chairperson of the institute of chemistry, visited BGU for a colloquium. While we were talking, Mordecai asked me if I would consider moving to the Hebrew University. I said, "*Let me have some time to think about your initiative*".

In those days (1991), it was almost unheard of to move between universities. In fact, I was already having a flirt with the Weizmann Institute, but the President of the institute vetoed "*taking away good people from the young university*". Another obstacle was the way we live in Israel; there are not many apartments for rent and this meant that we had to sell our newly built house in Beer-Sheva and buy an apartment in Jerusalem. The price ratio was 1:2 and is now even higher. Despite these obstacles I was encouraged by Sara to consider the move.

What helped the most to make a positive decision were the tension in the department, which created around me a very negative atmosphere, and Saddam Hussein who started firing missiles on Israel on January 15, 1991. My postdoc at the time, J.K. Cho, fled the country immediately; my research was left in shambles. I could not do anything anyway, because most of the time was spent sitting in shelters. My brother and his family were living with us, since their city (Ramat Gan) was badly hit by Sadam's missiles.

After getting fed up with the situation, I called Rabinovitz and said, "*I do*". A week or so later, Rabinovitz called me, while I was sitting in the shelter and informed me that my case passed with flying colors and what I had to do now is send him a "*shopping list*". It was so quick that I had no time to think; I knew that if I hedged too long, this might be my last chance to move in Israel. I also thought to myself that a university that could recruit so quickly must be a terrific place to move to.

A few months later I realized that I was simply lucky; the new HU President, the late Yoram Ben-Porath, was a dynamic character and was intent on rejuvenating the university, and as such made many critical decisions by himself bypassing the lengthy procedures in committees. After Rabinovitz discussed my candidacy with him, Ben-Porath instantly called the proposed referees, and after these telephone conversations he gave the green light for my appointment. Ben Porath and his family died in a tragic car accident shortly afterwards.

By March 1991, I got a letter from HU, offering me a position as Full Professor at the Institute of Chemistry. This was followed by negotiations over the conditions of the move, with the new chairperson of the Institute, the late Eli Grushka, and the Dean Michael Ottolenghi. The Institute of chemistry treated me with generosity; I would be a member of the department of organic chemistry and of the Fritz Haber Center of theoretical chemistry, would receive start-up money to buy a good computing facility, I would be allowed to hire a computing specialist who would work with my group, as keeper of know-how, and so on. I was due to move on March 1st, 1992. The Chairman, Eli Grushka and the Dean, Ottolenghi, were exceptionally generous and allowed me to purchase the workstation (IBM/RISC 6000 model 550) early and use it while I was still in Ben Gurion University.

At about the same time, my colleague Yitzhak Apeloig from the Technion, recommended to me his postdoc, David Danovich, who was an immigrant from Russia and had a PhD in quantum chem-

istry. He thought David would make a wonderful computing specialist. I interviewed David in Ben-Gurion University and could immediately see two features: He was highly skilled with computers and with use of quantum chemistry, and he was a very nice person, easy to get along with. So, in January 1992, when the IBM workstation landed in Ben Gurion, it was immediately put to use by David Danovich and Alexander Ioffe, another Russian immigrant working with me at the time. I started my service at HU on March 1st, 1992, and on August 12, 1992, my family joined me, and we moved to a University apartment near the campus.

One of the surprises, which made the move looking eminently "meaningful", was the meeting with Meir Zadok, the General Manager of the Israeli Academy of Sciences. We quickly realized that we are relatives, and belonging to the same family, Sadiq – which in Hebrew means "the righteous". Meir gave me a genealogy map of the family that dates back to the 18th century. This map reached back all the way to a rabbi, who left Jerusalem in the 18th century, going to Iraq to raise money for his community. This was at the same time when Napoleon started his Mediterranean campaign. So this Jerusalemite forefather ended up being stranded in Iraq, where he got married and started a family. His first-born son was called Sadiq, and this name has become the family name (of my mother's side) thereafter. The rabbi was called Sason…

The move to a new place was also an opportunity for a change of research directions. Computational chemistry was then on a big rise, and one could do descent computational studies of chemical reactivity and structure. Having the IBM/RISC 6000 (model 550) enables these studies quite efficiently. On the other hand, VB calculations were carried out with TURTLE, and as the name hints, the calculations were slow, very slow (even though TURTLE was then the fastest VB program). It was very tempting to change course in my research, and abandon VB calculations in favor of computational chemistry (especially DFT), which opened the entire molecular world to computations. However, using the words of prophet Jeremiah (Jeremiah Ch. 20 verse 9) VB theory was "*in my heart as it were a burning fire shut up in my bones, and I weary myself to hold it in*", but I could not, and certainly, could not abandon it. My dopamine made me accustomed to thinking with VB and the resulting thrill of making successful predictions. In the next 26 years, I would struggle to find a way to do both and bring VB concepts into any area I ended up investigating.

### 7.1. VB and other activities during 1992–1995

Already during 1992, I had a small group at HU; Chandra Reddy a postdoc (former student of Jemmis), Alexander Ioffe who used to come once a week from Beer Sheva, and David Danovich. Later in 1993 came the second postdoc, G. Narahary Sastry (another former student of Jemmis), and subsequently, Avital Shurki joined the group as a PhD student (now a professor in pharmaceutical chemistry).

Danovich was the only one who could make the program TURTLE work; he was teaching the postdocs and students to do VB calculations. Avital started to investigate with TURTLE the $H_3E$-Cl (E = C, Si, Ge, Sn, Pb) bonds, in order to explore the domain of charge-shift bonds. She was also engaged in VB calculations of benzene with an interest of supporting or refuting the prediction that its $\pi$-electronic component was distortive. Reddy and Sastry were doing cation- and anion-radical chemistries using the VB ideas developed in past years (see above). In 1993, I resigned from BGU, we sold our house in Beer-Sheva and bought a new apartment in Jerusalem; it was on paper still…

Sometime in early 1993, the computational needs exceeded the capability of our new workstation. A new one came on the market, the RISC 590 model, which was defined as a "supercomputer". I started raising the money to upgrade my old 550 to the 590 model,

and was generously helped by Ilan Chet, the Vice President for research and development, and Avinoam Ben-Shaul, the vice Dean for research in the faculty of science. While I managed to do so, I realized that securing state-of-the-art computing facilities at any given time is going to be a major problem in the future.

After a while I learnt about the possibility to establish a new center with endowment from the Minerva Foundation in Germany. I also understood, from Charlotte Goldfarb, the Head of Germany Desk at the research and development authority, that Minerva would favorably regard a multi-institutional center. I naturally contacted Yitzhak Apeloig and we decided to team and submit a proposal. We needed however, support of the idea by a few prominent German scientists.

Our natural choice was Helmut Schwarz; he and Yitzhak were close friends, and Helmut and I knew each other quite well from the many conferences, and the many visits of Helmut to Israel and in particular to Jerusalem and the Technion. The second person was Lenz Cederbaum, whom I befriended and knew very well already from the Cornell days. Helmut suggested that I write to Sigrid Peyerimhoff, one of the most highly esteemed theoreticians in Germany, and the Vice President of the DFG. So I did. Apeloig suggested the late Paul Schleyer who was then at Erlangen and Athens. And finally, Helmut suggested that I write to or visit Joachim Sauer who was a theoretician in the east and was now appointed to form a theory group in the revitalized Humboldt University. I was familiar with Joachim's work, as well as with the work of his spouse, Angela Merkel, who did theoretical work on $S_N2$ reactivity and cited my own work extensively, while still being in the East.

In June 1993 I visited Helmut Schwarz. This would be one of the many visits to Berlin and the establishment of long and very friendly relationships, with Helmut and his group members, and would lead to the establishment of the *Lise Meitner Minerva Center for Computational Chemistry*, with me as its Director to this day. The Lise Meitner Center makes a fascinating story by itself [88], but I must skip it for the sake of telling the VB story.

The Schwarz group was conducting then research on bond activation of small transition metal cationic species and accumulated quite a few puzzles [89]. One of these puzzles was the reactivity of $FeO^+$ in hydrogen abstraction. I had a talk with the group members, and learnt from the late Andreas Fiedler, the student who was doing his PhD on the topic, that he was running calculations with Wolfram Koch, and they were getting that the ground state of $FeO^+$ is $^6\Sigma$. Andreas further added that all their attempts to understand the reactivity of this species with $H_2$ failed.

My subsequent visit to Berlin was in November 1993. I gave a mini-series of talks on the VB model of reactivity, and had a discussion with Helmut, and the group members involved in the $FeO^+$ research. November 20 and 21, 1993, were bitter cold days. I tried going out to see some more of Berlin, but the cold chased me back into my hotel room. So, I sat in there and drafted two documents: one of these was a draft of the paper on the reactivity $FeO^+$ with $H_2$ [90]. In the draft of the paper, I used VB theory to show that the electronic structure of $FeO^+$ was analogous to $O_2$, with a high-spin ground state and a low-spin excited state. I further suggested that much like in the case of $O_2$, where the more reactive state is the $^1\Delta_g$ state, in $FeO^+$ with the $^6\Sigma$ ground state, the reactive state is the lower spin quartet state analog of $^1\Delta_g$, which would cross the high spin state and mediate the oxidation of $H_2$ to water. Using VB ideas I could even predict the structure of the transition state.

On the eve of November 21 (Sunday), the draft of the paper was finished, and I mentioned it to Helmut during the break in the concert of Maurizzio Pollini. On Monday, I presented the ideas to Helmut and his involved coworkers. This paper was finally submitted to JACS, and was the study that ushered two-state reactivity (TSR)

as a mechanism of bond activation [90], which was further articulated in the 1995 study [91]. The TSR concept, another brainchild of VB thinking, has started another long and intense collaboration, and became one of the major mechanisms in bioinorganic chemistry, and in the chemistry of metalloenzymes like Cytochrome P450 and nonheme enzymes [89].

The research program of my group was getting increasingly diverse. Looking at metallo-enzymes and their synthetic analogs gave me the opportunity to get back to MO theory, understand the MO-electronic structure of these transition metal complexes, comprehend the ordering of the different spin states, and at the same time trying to understand the field in terms of VB ideas. These were new and exciting challenges...

### 7.2. Sabbatical in Rochester – a course in VB theory

In August 1995 my family and I left Israel on our way for a sabbatical year in Rochester University, mainly to work with Joe Dinnocenzo on cation radicals and teach a VB course in his department. I have only vague memories of the atmosphere during the course, and the only reminder is a set of hilarious cartoons designed by Joe. The first one showed me likened to Moses, and preaching VB theory at the exclusion of all other approaches ("*throw your 'idols' and believe in one theory*"). I used VB theory to show that the reactivity-selectivity principle is completely wrong [44], that the Bell-Evans-Polanyi Principle will often break down, that outer-sphere TSs will exist only in pre-constrained systems but not otherwise [17], that frontier orbital theory cannot make predictions as well as VB theory does for odd electron systems [17], and so on and so forth. I do not wish to show this cartoon since it is against the bridging spirit of this essay. I am showing herein the one Joe designed after Lecture # 4, in which I taught the audience the details of VB mixing.

The cartoon (Fig. 9) speaks for itself – I was teaching with enthusiasm, which Joe portrayed as zeal. Considering that most of the attendees were experimentalist physical organic chemists, I should have in retrospect given up the "art" of matrix elements. This course taught me to curb some of my desire to teach everything I know, and indeed the next invited VB courses (in Stockholm and then in Berlin) were delivered in a lighter format. The Rochester course and those that followed formed a basis for a book on VB theory, which Philippe and I would write and publish later in 2008 [4].

Other than the maddening weather in Rochester, this was a very productive year. During this time, Avital completed her VB study of benzene and the frequency of its $b_{2u}$ mode. She showed that the $\pi$-electronic component experiences avoided crossing along this mode, and thereby generates the twin states, the ground state $^1A_{1g}$ and the excited $^1B_{2u}$ state, which correspond to the positive and negative combinations of the Kekulé structures, $K_1 + K_2$ and $K_1 - K_2$, respectively. Consequently, the $\pi$-component of the ground state behaved as distortive TS being forced into a $D_{6h}$ structure by the $\sigma$-frame. Therefore the total force constant for the bond-alternating $b_{2u}$ mode, $k(\pi) + k(\sigma)$, was small due to the negative $k(\pi)$, and so was the corresponding vibrational frequency. On the other hand, the $\pi$-electronic component of the $^1B_{2u}$ excited state was attractive along the same mode, so that the corresponding total force constant was high due to the positive force constant $k(\pi)$ and a high vibrational frequency. This paper was published in JACS in 1996 [59]. It was followed by a short review for *Accounts of Chemical Research,* in which Shmuel Zilberg, the late Yehuda Hass, and I demonstrated that this behavior of the $b_{2u}$ mode and its frequency was general, and constituted a spectroscopic probe of the $\pi$-distortivity in the ground state, while being exalted in the excited state [60].

**Fig. 9.** A cartoon designed by J. P. Dinnocenzo (U. Rochester) after the lecture on matrix elements between VB structures. Courtesy of J. P. Dinnocenzo.

In July 7, 1996, I travelled back to Jerusalem to participate as a plenary speaker in the WATOC conference. It was a lot of excitement to see friends (see Fig. 6), my group members, and my apartment that was being all too slowly constructed. In my lecture I talked about the new outlook on benzene. According to the notes in my diary it was very well received. A year later Avital studied the tri-annelated benzene derivative made by Jay Siegel [92], and found to exhibit strong bond alternation in the ground state. She ably demonstrated that in the 1st excited state, which is analogous to the twin state $^1B_{2u}$ in pristine benzene, the bond alternation virtually vanishes. This paper was highlighted in *Chemistry and engineering News* (in Science and technology Concentrates in *C&E News*, November 3, 1997). The late Jeremy Burdett included in his 1997 book a whole chapter on the benzene story [93]. Support for the π-distortivity started accumulating [94], and in 2001, the late Paul Schleyer stated in his introduction to the special Chemical Reviews issue on aromaticity (Vol. 101), "*The basis for the conclusion that the $D_{6h}$ structure of benzene is due to the σ framework, now widely accepted…*". In 2011 Ulusoy and Nest [95] showed that scrambling the $^1A_{1g}$ and $^1B_{2u}$ states by laser pulse enables one to follow the dynamics of the single Kekulé structure conversion to the ground state on a nano-second time scale. *Thus, the Kekulé structure can be dressed with physical reality*, by probing the vibrational frequency of the bond alternation mode, as well as by scrambling the states that are made from the two Kekulé structures and following the decay of a Kekulé structure to the ground state.

During the sabbatical, the late Lennart Eberson and Björn Roos, Dinoccenzo and I teamed on a paper that tested the predicted orbital-selection rules based on the VB model on the regioselectivity of nucleophilic substitution of odd-nonalternant hydrocarbon radical cations [96]. Dinnocenzo and I formulated a VB model that can predict the structural patterns of σ-cation radicals (we never published the material). More stuff was coming out on CS bonding, and on bonded ET-transition states. I had intensive discussions with Dinnocenzo on the possibility of TSR in cytochrome P450, based on the work he had done in collaboration with Jeffrey Jones on KIE determination for alkane hydroxylation by cytochrome P450. Later, their results will form a basis to show that KIE serves as a probe of the reactive spin state in P450 [97].

### 7.3. Establishment of the Lise Meitner-Minerva center – a VB haven

In the summer of 1996 I was notified that the Minerva grant for establishing a center for computational quantum chemistry was awarded to Apeloig and me. My family and I left Rochester in August 1996 and returned to Israel. Our apartment was not yet ready, and we lived shortly in a rented university apartment. Finally, in early September we moved to our new apartment. But already in September 5, I had to fly to Berlin to start the Alexander von Humboldt award. I left unknowing even my precise home address, and coming back the taxi driver asked me where to take me, and my answer was that I was not sure what my address was, which caused him to give me a diagonal look that is reserved for strangeness.

I spent two months in Berlin and during that time, I managed to reconstruct the electronic structure of the active species (Compound I) of P450, and to recover the two-state nature of the reagent, but these were degenerate ferromagnetic and antiferromagnetic states of three unpaired electrons, one residing on the porphyrin, the other two on the FeO moiety. I prepared a rough draft of a paper, and after many rounds, it was completed in 1997 during the inauguration of the center in Jerusalem, in July 1997 [98].

The center was inaugurated in the course of an international conference, including the members of the center and many guests. It was named as *The Lise Meitner – Minerva Center for Computational Quantum Chemistry*. I was appointed the Director of the center and Yitzhak Apeloig as co-Director. Helmut Schwarz was appointed as the chairperson of the scientific board of the center (in German: *Beirat*). In addition to Helmut, the other *Beirat* members were Sigrid Peyerimhoff, Joachim Sauer, the late Eli Grushka, Nimrod Moiseyev, and Addy Pross (which within 6–9 years will be replaced by Peter Schreiner, Walter Thiel, Amiram Goldblum, and Zeev Gross, with Helmut remaining as chair). As Director, I had to organize almost every year- to a year-and-a-half a conference that would present the work of the members, and would bring in guest speakers from other countries.

The P450 paper (that was eventually published in *Chemistry A European Journal* [98]) and the establishment of the center would define a new phase in my scientific activity, which stretches from

1997 till this day. The paper [98] brought TSR into the lime lights in the P450 community, and induced my future commitment to understand the P450 chemistry. The center enabled us to purchase a computing facility that was yearly updated and kept at a state-of-the art form till 2003, thus enabling us to do more demanding calculations. We had money for guests, small grants to members, awards, conferences, etc. But above all, the sheer existence of the center has served as a seed to raise more money. I, for example, had from 1997 on several active grants, which gave me the means to increase my group and to do more extensive scientific work on metallo-enzymes.

Another goal that the center fulfilled was the establishment of a quantum chemistry school in Israel, a school that was sorely missing in view of the otherwise very strong theoretical chemistry in Israel. I also became extremely busy, having a sizeable group, a serious administrative duty and a secretary! I lost my freedom forever, but in retrospect I gained much in return. The VB work has greatly benefited from the Center. First, there was David Danovich, who became a wonderful VB expert and kept the know-how (now for 26 years). Second, I did not need anymore to ask for grants to do VB work (from experience, these anyway had little chance to be funded). The work was supported by the Lise Meitner center, which became a little VB haven for David, me, and all our future projects. Fig. 10 shows David and part of the group members in 2001.

### 7.4. A second phase of quantitative VB - this time, in Jerusalem

In 1997–1999 the group has expanded to include a few excellent young scientists. The first was Wei Wu, from Xiamen in Mainland China. He wrote to me when I was still in Rochester about his wish to join my group and do research on VB theory. Wei had done a postdoctoral research with Roy McWeeny (who was then in Pisa). When I asked Roy his opinion, he wrote an enthusiastic letter about Wei and I decided to offer Wei a fellowship. He joined us in 1997.

Wei was (is) a wonderful programmer, and a former PhD student of Qianer Zhang, a student of Lu Jiaxi, who was Pauling's student. Upon Lu's return to China, he became a major force in the development of the chemistry department there, and importantly, he preserved the VB culture (which at the time was slowly dying in the West). Wei Wu, a physicist by training, wrote a VB program as a PhD student with Zhang, and Zhang encouraged him to go for postdoctoral research in the West. Wei's presence in the group marked the second phase of quantitative VB theory.

In the same year, 1997, Johnny Galbraith a former student of Fritz Schaefer, joined my group with a specific intention to learn VB theory. With Wei, David, Avital and Johnny we had a critical mass to form a VB sub-group that investigated bonding and reactivity: Avital looked at CSBs and π-distortivity, Johnny was investigating transition metal hydrides, π bond energies in double bonded molecules, and Bergman cyclization, while David and Wei were looking at no-pair bonding of $^{n+1}M_n$ species, where M is a monovalent atom, like Li, Cu, etc. [99].

With Wei being around, we developed during these years a semi-empirical VB method, with DFT input, so called VBDFT(s) [100–102], with which we investigated large polyenes in the ground and hidden excited state $2^1A_g$ [102], and showed for the first time that (a) polyenes longer than $C_{12}H_{14}$ had a major diradicaloid/polyradicaloid nature, and (b) much like in benzene, in polyenes too, the force constant in the bond alternating vibrational mode was small in the ground state and larger in the $2^1A_g$ excited state. Wei and I also started marrying DFT and VB theories in a nonempirical VB-DFT method [103].

Subsequently, we launched a master plan for VB development for years to come. This plan focused on the development of VB methods along the philosophy of Post Hartree-Fock theories, thus creating VBCI [104], VBPT2 [105], VBPCM [106], and DFVB [107]. These methods along with BOVB, provided a considerable VB arsenal for looking at a variety of problems and testing the qualitative models, VBSCD and VBCMD with inclusion of solvation [52,108–111]. Wei and I (Fig. 11) are still collaborating in 2016 and maintaining our friendship.

Thus along with Wei's former students, my former students and postdocs, and Philippe and his former students, the VB community, while still small, has grown to a respectable size.

### 7.5. The metallo-enzyme research - back to VB modeling of reactivity

Another postdoc was Michael Filatov, who joined us after a postdoc period with Walter Thiel. Michael was (is) a DFT expert who did methodology and application. Soon enough, the group started doing DFT calculations, which were essential for entering the field of metallo-enzymes and bioinorganic chemistry. The first such calculation was carried out by Nathan Harris, formerly a postdoc of Koop Lammertsma. Nathan came with a Fulbright Fellowship and was a superb computational chemist with immense patience and perseverance. I admitted also to the group a few undergraduate students, among them Shimrit Cohen who would later become my PhD student (see Fig. 10).

With Michael Filatov, Nathan Harris and Shimrit Cohen we could start DFT calculations of P450 species. These calculations



**Fig. 10.** Standing in the author's office in 2001 are, David Danovich (far right), with Sam de Visser, Jose Kaneti, François Ogliaro, and Shimrit Cohen (far left).



**Fig. 11.** Wei Wu and the author in the 1999 visit to Xiamen. Courtesy W. Wu.

were painfully slow back then, but nevertheless, the results enabled to treat pieces of the reaction mechanism of alkane hydroxylation by P450; we published these papers in 1998 and 1999 in *Angewandte Chemie*, and thereby laid the foundations for TSR in P450 [112,113]. Michael Filatov developed also DFT methods for treating open-shell systems with more than one Kohn-Sham determinant, and akin to VB theory [114,115].

In 1999, I visited Berlin for the last portion of my Alexander von Humboldt Award. In that year and in the previous one, Yitzhak Apeloig and I coordinated our stays and had a lot of fun in Berlin and having in addition the company of Helmut whenever his feet would touch the soil of Berlin back from his many, many trips.

I also went for a seminar tour in Germany, France, London, and Switzerland. I brought with me my usual set of talks and added one on P450. Of all the set, the P450 story was the star, and was selected with priority everywhere I lectured (including Germany, France, London, and Switzerland – where I were twice as a Trosième-Cycle Lecturer). This popularity of the topic conspired with one's dopamine to create commitment – Indeed, I seem to be committed to P450 till this very day.

In the same year (1999), the WATOC conference was held in London. I gave a talk there on P450, which was very well received by the audience; theorists like it when theory can be used to make order in such a complex system. After my talk, Walter Thiel, who was then still in Zürich, suggested we collaborate on this topic using the QM/MM method he was developing then. Walter and I had known each other for quite a few years, and we seemed to get along extremely well; we still do. I of course agreed, but it took two years to consummate the collaboration.

The full P450 treatment had to wait till 1999, when François Ogliaro (see Fig. 10), a former PhD of Saillard and a postdoc of David Cooper, joined us as a Marie Curie Fellow, and reinforced the P450 team. Initially with guidance from Nathan and then independently, François undertook, even if somewhat reluctantly at the beginning, the study of the full mechanism of alkane hydroxylation by P450. We started with methane as a model alkane, but nevertheless what François found then is a still viable model for the TSR paradigm in P450 reactions in general. We found that the quartet (ferromagnetic) and doublet (antiferromagnetic) states of the active iron-oxo species, so called Compound I (Cpd I) performed hydrogen abstraction, at almost equal energy barriers, leading to the formation of weakly coordinated alkyl radicals/iron-hydroxo species. Subsequently the two surfaces bifurcated: the quartet state process encountered an additional barrier for the formation of the ferric-alcohol complex, while the doublet state process was barrier free. This excellent work of François, which clarified many of the major puzzles and controversies in the field, was published in the year 2000 in JACS [116], and introduced TSR as a new mechanistic paradigm in the P450 field.

In the year 2000, Sam de Visser (see Fig. 10), a former postdoc of Mike Robb, joined my group. His start was sluggish, but very soon he blossomed and became a highly productive postdoc. Furthermore, Sam was a very patient teacher and he took charge of educating many of the undergraduate students who were in the group. He and François got along well and started collaborating and producing together first-rate work and lots of it. Then Pankaz Sharma, a former PhD student of Jemmis, joined the group, followed by Jose Kaneti, a senior researcher from Bulgaria (see Fig. 10), and Shimrit Cohen who has started her graduate research with me. The P450 team grew significantly. We had many new ideas on P450, and the group was constantly excited and generating wonderful results.

Initially François looked at the effect of bulk polarity and amidic-type hydrogen bonding to the thiolate ligand of Cpd I, and found that the electronic structure including the Fe—S bond distance were undergoing large variations compared with the gas

phase; it was then that we started calling Cpd I "*a chameleon species*" that adopts itself to the environment that accommodates it [117]. We presented a VB model, which helped conceptualizing the variable nature of Cpd I. Then with a team effort lead by François, we looked at a larger model system and showed that Cpd I was behaving like a chameleon also for this larger model system. Subsequently, Sam, François and Pankaz, showed that this "chameleon" feature of Cpd I carries over to its reactivity-selectivity in C—H hydroxylation vs. double bond epoxidation of propene [118].

Later in 2002 when Devesh Kumar would join, he and Sam would forge a highly efficient mini-group that studied many problems in P450. Devesh, a physicist and a former student of Roychoudhury, had initially difficulties with the chemistry issues, but very soon he developed a wonderful chemical intuition. He explored extensively the KIE patterns of TSR in alkane hydroxylation, and established what was noted in the preliminary study by François [119], that KIE measurements probe the reactive spin state during TSR. This is now part of the normal science in bioinorganic chemistry [97,120,121].

In the year 2001, David Danovich, François Ogliaro and Shimrit Cohen travelled to Mülheim to learn QM/MM, by interaction with Walter Thiel's student Jan Schöneboom and his postdoc Natalie Reuter. It was decided to look at Cpd I of the enzyme P450$_{cam}$, which is a bacterial enzyme that hydroxylates camphor. To our satisfaction, the QM/MM results produced by Jan Schöneboom supported completely the conclusion of the model system that Cpd I behaved like a chameleon species and accommodated its electronic structure to the protein environment of the enzyme. The paper, which was published in JACS in 2002, was as far as we know the first QM/MM treatment of a complex metallo-enzymatic species [122]. In 2006, an experimental paper by Brian Hoffmann, John Dawson and coworkers would verify the results of these calculations, using the analogous enzyme chloroperoxidase (CPO).

Subsequently, the QM/MM investigations of Jan Schöneboom and Shimrit Cohen, recovered fully the TSR mechanism of camphor hydroxylation by P450$_{cam}$ [123]. This compatibility of a carefully chosen model system with a complete treatment of the species in its native protein environment was encouraging. So, in the next years we continued to use a blend of model calculations and QM/MM treatments. The collaboration between Walter's and my groups would continue with intensity till 2010. During this period we published two major Chemical Review Articles [124,125], and each one of these would include a section on applications of VB; to the electronic structure of Cpd I and the VBCMD for alkane hydroxylation.

### 7.5.1. VB modeling of P450 reactivity

Ever since my group mastered the electronic structure of the active species of cytochrome P450 and its TSR in alkane hydroxylation, olefin epoxidations, aromatic hydroxylation, sulfoxidation, etc., I had a dream to be able one day to apply the VB diagram model to the reactivity patterns of P450, and to use VB theory to understand bonding in these enzymes. This goal was like a fire "*shut in my bones*", and as I was weary to continue holding it in ... I determined to achieve this modeling.

A major obstacle was the preservation of the formalism of oxidation states (oxidation numbers), which is so useful in transition metal chemistry, and which predicts the number of electrons in the d-orbital block. However, because many of the bonds to transition metals are in fact covalent, whereas this electron counting formalism is based on the tacit assumption that the bonds are all ionic, the "oxidation number" is not a native concept in VB theory. I was seeking for ways to narrow this chasm, Eventually I managed to embed the oxidation number formalism into the VB diagram

and this opened the road for VB modeling of P450 reactivity [124–129].

Fig. 12 illustrates these diagrams for alkane (A—H) hydroxylation. These are VBCMDs, which involve two principal curves, anchored at the ground states (**R**, **P**) and their two promoted states (**R***, **P***), for the direct O-transfer to the alkane, A—H. This process is, however, catalyzed by an intermediate-state curve (**I**) that cuts through the higher-energy ridge for direct oxo-transfer, and splits the process into H-abstraction followed by radical rebound to form the ferric-alcohol product. At the intermediate state, the two spin-states diverge in their energies. The doublet (2S + 1 = 2) state has generally a barrier free rebound. In contrast, the quartet state (2S + 1 = 4) which involves an additional promotion energy $(\pi^*(d_{xz}) \rightarrow \sigma^*(d_{z^2}))$, has a finite barrier for rebound via $^4TS_{reb}$. With small changes this diagram describes also C=C epoxidation and arene activation. However, in [O] atom transfer (OAT) e.g., to sulfur or phosphor, there is no intermediate state curve, and the reaction is fully concerted, described by a VBSCD [128].

I discussed this modeling in the early 2000s in-group meetings, but it took time to test if the model indeed worked well for a set of reactions. The first VB modeling alkane hydroxylation was published in 2008 with my postdocs Sam and Devesh [126]. Later, as the group was joined by a few more excellent coworkers, the initial VB applications was followed by treatments of sulfoxidation (with Chen, Yong, Wenzhen, Song, and Meir) [127], aromatic C—H activation (with Milko, Dandamudi, Chen, and Wenzhen) [129], and later by reviews which included also epoxidation (with Li, Chen, Danovich, Whenzen, Dandamudi) [32,40,128]. In the end by 2014, about 11 postdocs and students participated in the VB application to cytochrome P450.

In 2007, Fahmi Himo from the Royal Institute of technology in Sweden invited me to give a mini-course of 12 h on VB theory of bonding and reactivity. By that time, the VB modeling of P450 reactivity has already been conceived, so I could include some of the story in the mini-course. The research on P450, other heme enzymes, and nonheme ones, continues to be a major research track in my group, and unfortunately I have to cut it short in order to continue with more events in the VB journey.

### 7.5.2. VB modeling of electric field effects on chemical reactivity

Let me first leap backwards in time to my PhD days. In 1974, when I arrived to UW, I attended a course by Y. Pocker. He taught us about catalysis of heterolytic reactions ($S_N1$ and proton transfer) in ether solutions containing up to 7 M LiClO$_4$ [130]. Pocker observed rate enhancements of $10^6$ fold, which he ascribed to "*electrostatic catalysis*". This impressed me a lot, and once in a while I would try to understand it in some effective manner. While at Cornell, I tried to derive selection rules for electrostatic interactions using MO theory. However, along with the development of the VB model, it became clear that electrostatic catalysis is associated with stabilization of ionic structures. While at BGU, I even tried to organize a few colleagues to look at electric field effects on cellular processes, but not much if anything was achieved other than corridor conversations.

I resumed my interest in electrostatic catalysis later in 1998 during the preparation of the review article on the VB diagram model in *Angewandte Chemie* [17], in which Avital and I addressed the catalytic effect of metal ions on solvolysis. It was evident that using VB theory elucidates the effect of electric fields on reactivity.

However, as in the mean time I got preoccupied with P450 chemistry and with chemical bonding, I left the idea on cold ice. In the early 2000s, when my group started QM/MM research of P450 enzymes, we played a bit with the intrinsic electric fields of the P450 proteins, and found that these fields had a specific orientation vis-à-vis the substrate that would undergo oxidation by the active species. I suggested to Sam and Devesh to pursue the idea and see if it were possible to induce regioselectivity by oriented-external-electric fields (OEEFs), in P450 oxidation of propene. The results were spectacular. We found that orienting the field along the reaction axis, S—Fe—O—propene, catalyzed C—H hydroxylation in one direction, and when the field was simply flipped, it catalyzed C=C epoxidation [131].

After the publication of this paper (2004), a few new postdocs and students joined the group. Among them, Hajime Hirao, a former student of Hiroshi Fujimoto, Kyung Bin Cho, a former student of Per Siegbahn, Maria-Angels Carvajal, a former student of Santiago Alvarez and Juan Novoa, Hui Chen, a former student of Shuhua Li, Yong Wang, a former student of Keli Han, and Wenzhen Lai
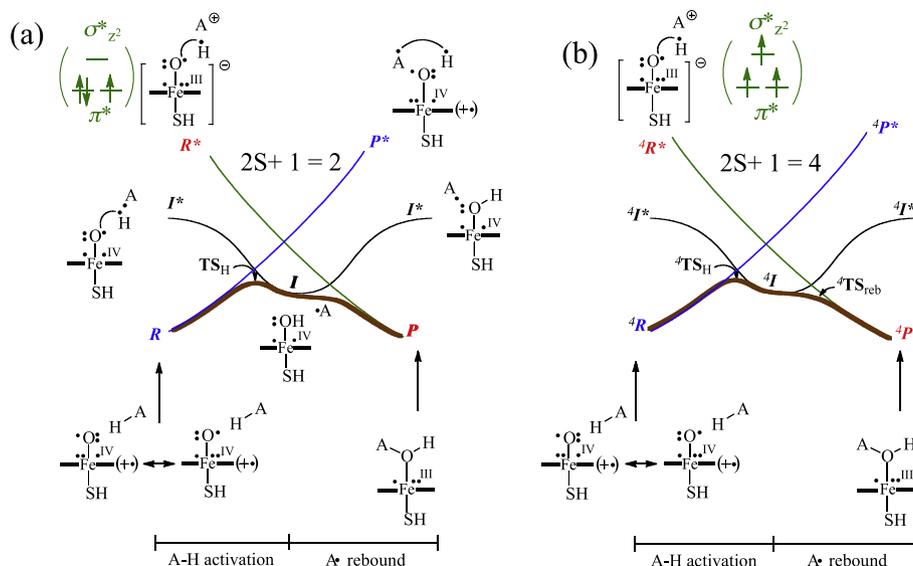


**Fig. 12.** VBCMDs for alkane (A—H) hydroxylation by Cpd I of P450: (a) in the doublet state (2S + 1 = 2). (b) In the quartet state (2S + 1 = 4). The difference between the spin states is shown in the small green orbital diagram near **R***, which illustrates the different occupations in the d-orbitals. Adapted with ACS permission from Ref. [128]. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

(Chen's spouse), a former student of Diaqian Xie. I was surrounded by a growing number of smart young coworkers... Together with Hirao, Maria, Wang, and Chen we applied the idea to C—H hydroxylation by nonheme Fe(IV)-oxo complex, and found a spectacular effect on the barrier and on spin-state selectivity [132]. The OEEF preferred the reactivity of the quintet state, and it changed the mechanism from stepwise (via a radical intermediate) to concerted formation of the alcohol product [132].

In the mean time, Kyung-Bin Cho wrote a script to apply OEEFs to enzymes while doing QM/MM calculations. I convinced Wenzhen to apply the OEEF to the entire catalytic cycle. Wenzhen teamed with Kyung-Bin and Chen, and she carried out this colossal study. We found that the OEEF affected all the steps in the cycle and could either catalyze or inhibit the cycle, depending on the orientation of the field vis-à-vis the S—Fe—O axis. The results of these thought experiments were thrilling, and we are still pursuing this idea. We had great difficulties to publish the paper since referees argued that the enzyme would undergo denaturation (now we know that this is not true, and many P450 preserve their structures during long time scale molecular dynamics). The rejected paper was published eventually in the *Journal of Physical Chemistry Letters*, which just came out in 2010 [133]. In all the cases we studied there was a distinguished axis along which the OEEF effect was the largest. This direction is the "*reaction axis*" along which the electrons reorganize by uncoupling the old bonds and creating the new ones.

Subsequently, I managed to convince Rinat Meir who joined the group for her MSc degree, to look at OEEF effects on Diels-Alder reactions, with supervision by Chen and Wenzhen. This time, I decided to use the VB diagram model with an aim of understanding the mechanisms whereby the OEEF affect this reaction, which involves making two C—C bonds in a single step, and if possible to make also some new predictions.

Fig. 13a shows a VBCMD for a generic Diels-Alder reaction. The barrier arises from avoided crossing and mixing of the two principal curves, which describe the bonds of reactants and products. However, there is also a charge-transfer-state curve ($\Phi_{CT}$), which involves an electron transfer from the diene to the dienophile, and which can mix into the TS and thereby lower its barrier. It is clear that an OEEF oriented along the negative direction of the reaction axis (Z) will lower the charge-transfer state and will

thereby increase its mixing into the TS, which will be lowered, thus resulting in catalysis of the Diels-Alder process. On the other hand, if we flip the field to +Z, this will inhibit the reaction. Furthermore, as shown in Fig. 13b, one can predict that at a sufficiently strong −Z field, this will be stabilize the charge-transfer-state well below the crossing point of the principal curves. In this case, the mixing of the three states will give rise to a zwitterionic intermediate ($\mathbf{I}_{zwitterion}$), and will change thereby the mechanism.

The calculations supported all the predictions of the VB diagram [134]. It became clear that the catalytic power of OEEF involved the stabilization of ionic structures, which enhanced the electron reorganization along the reaction axis. To our surprise, we had serious difficulties to publish this paper too. I tried different journals, and in the end, Greta Heydenrych, the editor of *ChemPhysChem* decided to accept the paper based on the old report and our response to them [134].

The paper was published in 2010 and it was largely ignored, and so was the entire field. But life is full of twists and turns. At the end of February 2016, I was contacted by two renowned science writers who asked me if I would care to write a comment on a recent experiment that verified the predictions we made on the Diels-Alder reaction [135,136]. I was of course ready... But more so, I had a first chance to look at the paper, which was just accepted in Nature [137], and included a collaboration of Australian and Spanish groups. Their single-molecule experiment was breathtakingly elegant, *and it demonstrated that a reaction that involves two C—C bond making could be catalyzed by oriented electric fields, in a rational and predesigned manner*. In a recent perspective [31] we outlined the future prospects of the field, and demonstrated the huge impact of the ionic structures. *The electric field converts excited states to ground states and changes reactivity and selectivity dramatically...*

## 8. VB applications and events during 2012–2016

The past five years have been productive on several fronts. The new front was the initial organization of a VB community that has its own meetings; three already took place in 2012, 2015, and 2016, and two are planed for 2017 and 2018. The other front is the application of VB theory to new problems. Let me recount first the second story.
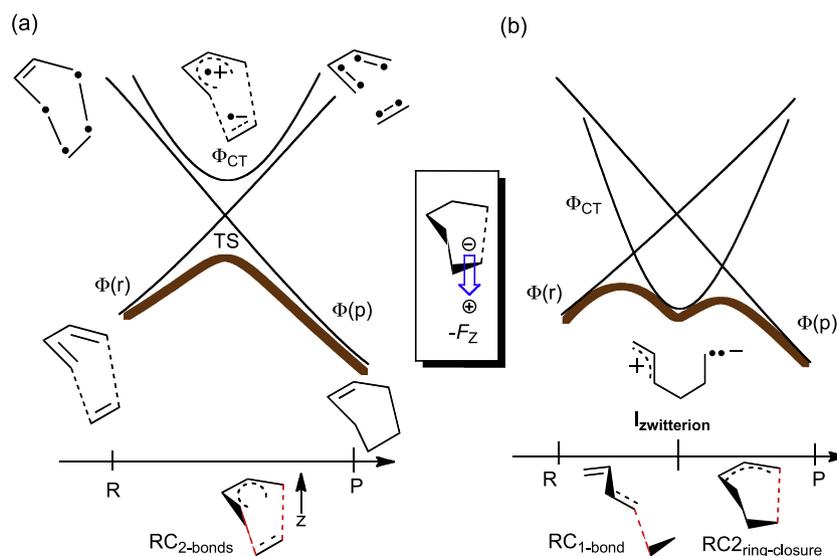


**Fig. 13.** (a) VBCMD showing the barrier formation in a generic Diels-Alder reaction. Shown are the principal curves ($\Phi(r)$ and $\Phi(p)$) and the charge-transfer state's curve ($\Phi_{CT}$). In the inset on the middle we show the direction of the external electric field that will lower the barrier. (b) The same three curves in a strong field, now generating a zwitterionic intermediate in a stepwise mechanism. Adapted with permission of Wiley VCH from Ref. [134].

## 8.1. A generalized treatment of H-abstraction

During the past five years the VB activity increased in my group, spreading over a mélange of new problems in reactivity and bonding. Let me start with reactivity. Sometime in 2011, Helmut Schwarz rekindled my interest in H-abstraction, and told me about disagreements he was having with Jim Mayer over the question of what are the important factors in H-abstraction reactivity. We discussed the issues and as a result of this discussion we both ended writing reviews that were published later in *Angewandte Chemie* [40,138]. One of the points of contention was whether or not the H-abstractor was required to be a radical. Thus, Mayer argued that even closed-shell molecules, e.g., $CrO_2Cl_2$ or $MnO_4^-$, participated in H-abstraction as well, but Schwarz had solid evidence that in the gas phase H-abstraction did not transpire unless the abstractor had a localized oxyl radical (most of the abstractors had oxygen centers, and hence the referral to oxyl). There were many other issues, like the relationship of H-abstraction by Cpd I of cytochrome P450 (and analogs thereof), and simple H-abstractions, as e.g., in $H \cdot + H_2$.

I realized that it would be necessary to treat the H-abstraction in broader manner than was done in 2004 [111]. As a first step, the unification of H-abstraction reactions required abandoning the simple barrier equation (Eq. (1)), and using a more explicit one that considers explicitly the promotion gaps, and $f$ factors for both reactant and product sides of the VB diagram, as well as the thermodynamic driving force in the VBSCD in Fig. 14a.

Such an explicit expression that treats the forward and reverse barriers on equal footing is given in Eq. (4):

$$\Delta E^{\ddagger} = f_0 G_0 + 1/2 \Delta E_{RP} + 1/2 \Delta E_{RP}^2 / G_0 - B \tag{4a}$$

$$G_0 = 1/2[G_R + G_P] \tag{4b}$$

$$f_0 = 1/2[f_R + f_P] \tag{4c}$$

Here $G_0$ and $f_0$ are average factors for the two sides of the diagram, while $\Delta E_{RP}$ is the thermodynamic driving force.

Fig. 14b shows the corresponding promoted states and promotion gaps for H-abstraction. Thus, the promotion gaps involve singlet-triplet decoupling of the H—Y and X—H bonds, which can be approximate well by the corresponding vertical bond energies ($D$), which are given by the sum of the corresponding bond dissociation energies ($BDE$s) and reorganization energies of radicals ($\Delta E_{ST} \sim 2(BDE_{H-X} + RE_{X \cdot})$) [40]. The term B is ¼ of the sum of the

two *BDE*s, while $\Delta E_{RP}$ is given as the difference of the corresponding BDEs. The $f$ terms are equal to ∼0.3 according to semi-empirical VB. As such, one could simply use empirical data (or calculated BDEs) to estimate barriers.

Let me just flash quickly two plots in Fig. 15 that reflect the performance of the VBSCD. Fig. 15a plots the VB predicted barriers against computed ones for 45 reactions, $Y \cdot + H—X \rightarrow Y—H + X \cdot$, which include identity (X = Y) and nonidentity (X ≠ Y) reactions of radicals ($X \cdot$, $Y \cdot$ = H, $CH_3$, $SiH_3$, Cl, F, CN, $NCCH_2$, HCC, $PhCH_2$, etc.), studied at the CCSD(T)/CBS-limit, as well as all the DFT reaction of H-abstraction by Cpd I of cytochrome P450. The correlation of the predicted barriers with the computed ones is not too bad considering the wide variety of reactions and the mixed quality of the calculations (the correlation coefficient is much better for the CCSD(T)/CBS data alone). The model equation (Eq. (4)) of the VBSCD seems to capture the essence of the bond activation during a variety of H-abstraction reactions [40].

A major contribution to the barrier is the reorganization energy of the radical, $X \cdot$ ($RE_{X \cdot}$), from its relaxed geometry to the geometry it possesses in the H—X molecule. For identity reactions ($X \cdot + H—X \rightarrow X—H + \cdot X$), the radical reorganization energy is the key to understanding the barriers. Thus, using Eq. (4a) and the expressions of the various quantities in terms of $BDE$s and $RE_{X \cdot}$, we find the following expression for the identity barrier [40]:

$$\Delta E^{\ddagger} = 0.6(RE_{X \cdot}) + 0.1(BDE_{H-X}) \tag{5}$$

It shows that what the size of the identity barrier is dominated the reorganization energy term for the radical $X \cdot$. For example, for X = HCC$\cdot$ vs. $NCCH_2$, the identity barrier is larger for the latter even though the bond dissociation energy of HCC—H is huge compared with $NCH_2$—H (132.9 s, 95.7 kcal/mol). The reason is the much higher reorganization energy of the $NCCH_2$ radical (10.7 vs. 0.1 kcal/mol), which is delocalized and planar in the relaxed form while being localized and pyramidal in the $NCH_2$—H molecule [32,40,139].

Fig. 15b shows predicted VB barriers based on Eq. (4) plotted against experimental free energies of activation, for a variety of reactions including closed-shell H-abstractors like $CrO_2Cl_2$, $MnO_4^-$, and α-methylstyrene. As seen, the VB model predicts well the experimental trends, and shows that all the closed shell abstractors have high barriers (compared e.g., with localized oxyls). These high barriers originate in the reorganization energies that the closed-shell abstractor must invest in order to localize the radical on the site that forms the new Y—H bond [32,40,139]. As such, both Schwarz and Mayer were correct regarding their parts of the data.
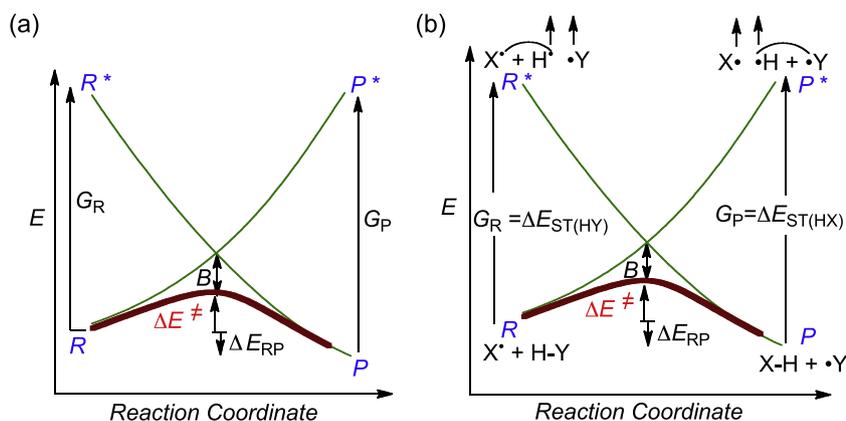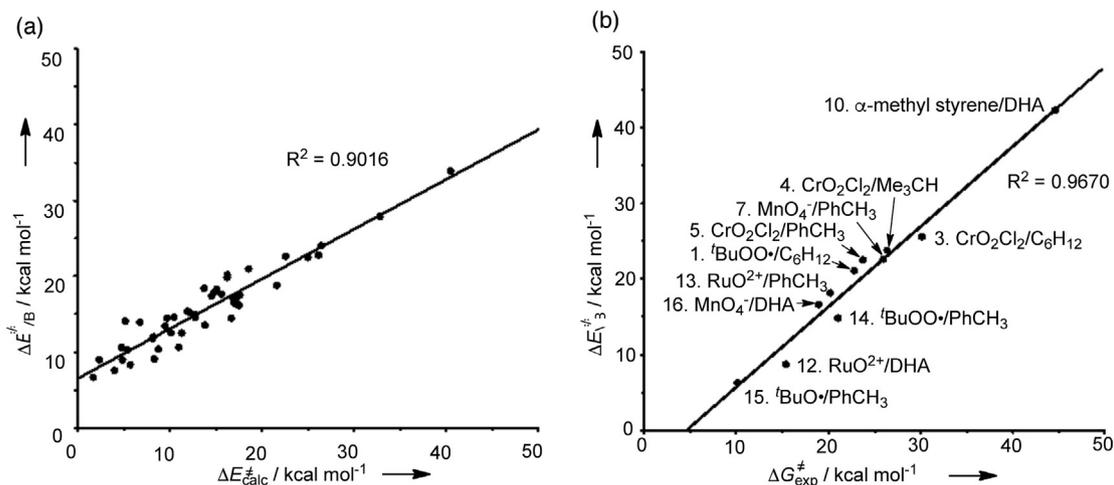


**Fig. 14.** (a) A Generic VBSCD with the different quantities affecting the barrier. (b) A VBSCD for H-abstraction along with the specific quantities for this reaction type. Adapted with RSC permission from Ref. [32].

**Fig. 15.** (a) A plot of VB calculated barriers for 45 H-abstraction reaction vs. CCSD(T)/CBS and DFT calculated ones. (b) A plot of VB calculated barriers for a few H-abstraction reactions (indicated on the line) vs. corresponding experimental free energies of activation. Adapted with permission of Wiley VCH from Ref. [40].

### 8.2. The HAT/PCET dichotomy

The generalized treatment of hydrogen-abstraction provided an opportunity to address also the fact that abstracting H from electronegative centers, like O and H encounters generally much lower barriers compared with H atom transfer (HAT) e.g., between carbon centers. In HAT, the H is transferred as an atom from one X to the other, along the X---H---X axis, such that the unpaired electron undergoes delocalization within the σ orbitals of the XHX moiety. However, in H-transfer between electronegative atoms, these events often occur in different manners. Thus, Borden and Mayer showed that in the reaction of e.g., phenol radical with phenol, the odd electron of the radical is transferred via the π-system, while H is transferred as a proton along the O---H---O axis [140]. These reactions are referred to as proton-coupled electron transfer (PCET).

The dichotomy between HAT and PCET was treated in Jerusalem during 2012–2014 and involved Usha Dandamudi, David Danovich, Chunsen Li, Wehnzhen Lai, and Hui Chen [32,40,139]. We showed that for all H-abstraction reactions, in addition to the normal HAT states (see above Fig. 14b), which delocalize the radical in the σ MOs along the axis of (X---H---Y)˙, there are proton transfer/electron transfer (PT/ET) state curves which describe a proton transfer along the σ-axis as a proton, along with a radical transfer from X to Y via the π-system. The latter states are the generators of the PCET mechanism. When X and Y are alkyls or hydrocarbon radicals, the PCET states lie well above the HAT states, and the reaction proceeds via a normal HAT mechanism. However, when X and Y are heteroatoms, the HAT and PCET states are close to one another. As such, the two state types can mix (e.g., by bending of the moiety (X---H---Y)˙), giving rise to a TS with a mixed character. Finally, if the PCET state is much lower in energy, then the H-abstraction will transpire via the PCET mechanism, as shown in Fig. 16.

Skipping the details of the VB analysis we show in Fig. 17, a diagnostic plot of PCET vs. HAT mechanisms, which is taken from the recent study by my former postdoc Usha Dandamudi, Andy Borovik, David Lacy and me [141]. This is a plot of the total deformation energy ($\Delta E_{def}$) in the TS vs. the corresponding barrier ($\Delta E^{\ddagger}$), for C—H, N—H, and O—H bond activations by nonheme iron-oxo complexes. The straight line has a slope of unity, and is the location of the TSs where $\Delta E_{def} = \Delta E^{\ddagger}$. It is seen that the reactions marked in black spheres and red squares cluster near the line. These are the HAT cases involving C—H activation, in which the barrier derives from the deformation energy of the reactants. However, well above

the line we see reactions marked in blue squares. These reactions involve N—H and O—H bond activations, and correspond to the PCET type. Thus, the PCET mechanism is characterized by TSs, which involve large deformation energies but small barriers, due to large stabilization energy of the corresponding TSs by the VB mixing of all the states (Fig. 16c) [141]. Spectacular examples of this diagnostic plot were found recently in gas phase studies by Helmut Schwarz and his Berlin group, in collaboration with me [142,143].

### 8.3. Bonding issues treated by VB theory

#### 8.3.1. Bound triplet pairs

During the years 2012–2016, David Danovich and I consolidated the case for bonding in clusters of monovalent atoms where the bonding does not involve even a single electron pair, but rather identical spins that interact along the lines connecting the atoms [99]. Some of these beautiful no-pair clusters are shown in Fig. 18, where one can see a tetrahedral $^5Cu_4$ clusters, a prismatic $^9Au_8$ cluster, an icosahedral $^{11}Li_{10}$ clusters, and even a chiral tetrahedral cluster, $^5CuAuAgLi$.

The numbers underneath the clusters correspond to the bond dissociation energies for a dimer within the cluster. It is seen that for the Cu cluster already in $^5Cu_4$ the bonding reaches 27.5 kcal/-mol for a dimer unit, and this value converges to 36–39 kcal/mol for at $^{11}Cu_{10}$. Thus, without any electron pairing, the bonding of triplet pairs reaches almost the bonding energy of the singlet ground state dimers. VB theory predicts this bonding patterns and reproduces quantitatively the bond energies as a function of the cluster size. The mechanism *that binds the triplet pairs* involves the mixing of triplet-excited covalent and charge transfer states into the repulsive $ns^1ns^1$ fundamental VB structure [144,145].

Importantly, triplet-bound clusters are known experimentally and can be synthesized using the helium droplet isolation technique [146]. Something new in bonding is awaiting exploration…

#### 8.3.2. The nature of the V state of ethylene

In 2014, Wei, Huaiyu Zhang (Wei's Ph.D. student), Benoit, Philippe and I decided to address the longstanding dilemma of the "V state" of ethylene [147]. This is the first singlet-excited state ($^1B_{1u}$) of ethylene, and its computation has generated a long and tortuous Odyssey. Early Hartree-Fock calculations of the V state led to a very diffuse wave function (with $\langle x^2 \rangle > 40\ a_0^2$) that looked more like a Rydberg than a valence state. Expansion of the
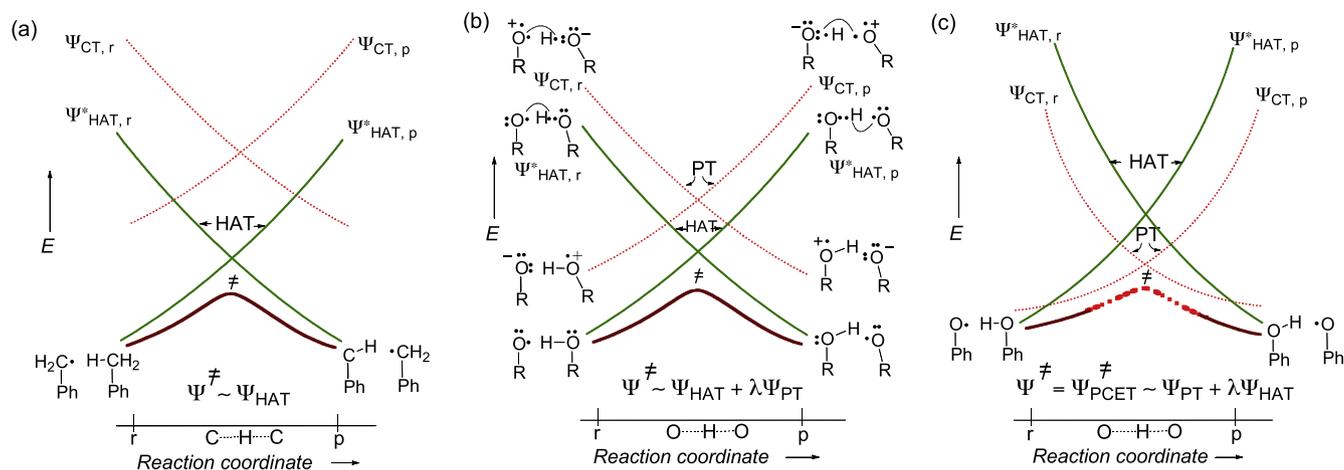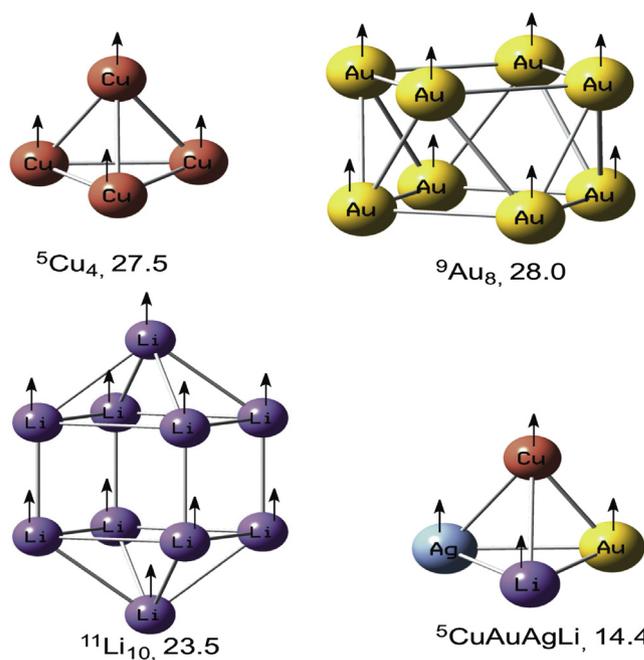
**Fig. 16.** VBCMDs for H-abstraction reactions, showing both HAT and PECT states. The latter involve proton transfer (PT) and are anchored in charge-transfer (CT) states: (a) H-abstraction involving benzyl radical/toluene pair. Here the PT-CT states lie well above the HAT state, and the process is predominantly HAT. (b) H-abstraction by an alkoxy radical from an alcohol. Here the PT-CT states are lower lying and mix significantly into the TS of the HAT process, thus lowering the barrier. (c) H-abstraction by phenoxyl radical from phenol. Here the PT-CT states lie well below the HAT states and the corresponding TS has a predominant PCET character. Adapted with RSC permission from Ref. [32].
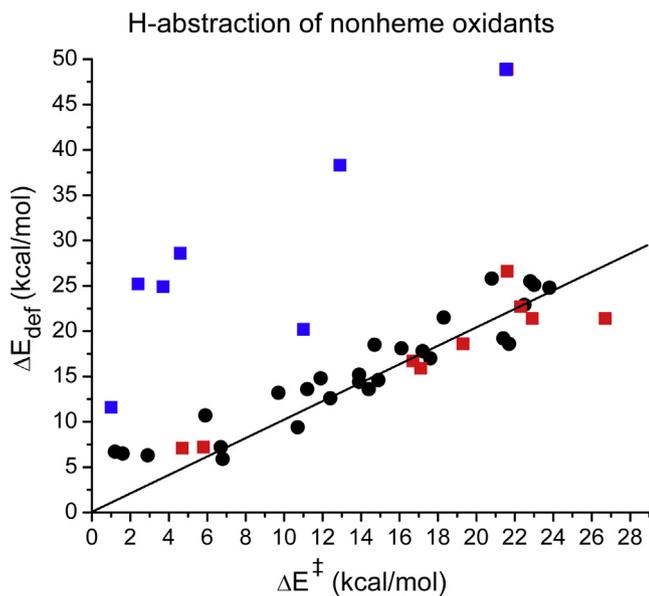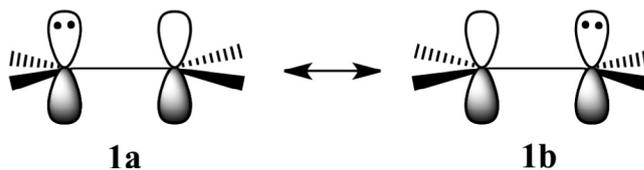


**Fig. 17.** A plot of the deformation energies ($\Delta E_{def}$) of the reactants in the TS against the corresponding barriers ($\Delta E^{\ddagger}$) for X—H bond activation reactions (X = C, N, O) by a variety of nonheme iron-oxo complexes. The line in the figure has a slope of unity, where $\Delta E_{def} = \Delta E^{\ddagger}$. All the reactions marked by black spheres and red squares correspond to C—H activations, for which $\Delta E_{def}$ and $\Delta E^{\ddagger}$ are rather close; these are HAT processes. The reactions marked in blue squares correspond to N—H and O—H activations for which $\Delta E_{def} \gg \Delta E^{\ddagger}$; the difference between the quantities is the stabilization energy due to interaction between the TS fragments. These are the PCET processes. There are also borderline cases. Adapted with ACS permission from Ref. [141]. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)



**Fig. 18.** Some no-pair clusters and their bonding dissociation energy (in kcal/mol) per a dimer unit. Adapted with ACS permission from Fig. 1 in Ref. [144].



**Scheme 7.** The zwitterionic structures of the V state of ethylene.

Hartree-Fock-wave function for the V state reveals the root cause for the apparent diffuseness of the state. Thus, the expansion leads to the two zwitterionic VB structures shown in Scheme 7, and which understandably required very diffuse orbitals to describe the state.

Inclusion of CI reduced the diffuseness of the state, but did not resolve all the issues. In fact, very extensive MRCI calculations (with up to $8 \times 10^7$ configurations) were needed to rid of this artificial mixing of the V state with the adjacent Rydberg state, and to produce a reasonably compact state (with $\langle x^2 \rangle$ = 19–20 $a_0^2$).

Using BOVB calculations (in which the doubly occupied AOs were split into inner and outer lobes) we were able to show however, that a very compact wave function of the four structures in Scheme 8 produces a valence like V state, and an excitation-energy close to the experimental value.
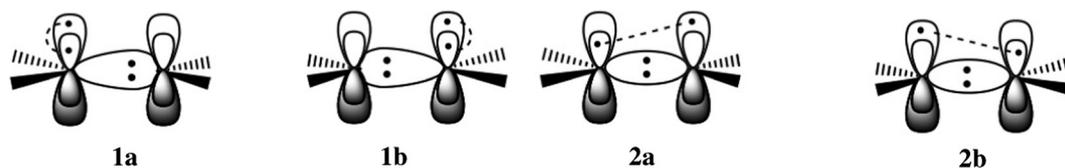
**Scheme 8.** The VB wave function for the V state of ethylene ($\Psi_V = [\mathbf{1a} - \mathbf{1b}] \Leftrightarrow [\mathbf{2a} - \mathbf{2b}]$).

Thus, in addition to the two ionic structures, $\Phi_{ion}(\mathbf{1a})$ and $\Phi_{ion}(\mathbf{1b})$, the right answer required adding just two covalent π-bonded structures, $(\Phi_{cov}(\mathbf{2a}) - \Phi_{cov}(\mathbf{2b}))$, which are present already in the CASSCF(2,2) wave function, and which possess $B_{1u}$ symmetry. These covalent structures are non-symmetric and involve pairing of one electron in the outer lob on one atom with one in the inner lobe of the other atom. Nevertheless, the importance of these covalent structures does not imply that carbon has suddenly acquired five valence orbitals in the V state. The effect of $\Phi_{cov}(\mathbf{2a})$ and $\Phi_{cov}(\mathbf{2b})$ is essentially perturbational; they lower the electron-electron repulsion due to the doubly occupied 2p orbitals in the zwitterionic structures, and add some resonance energy stabilization to the wave function.

Let me just add that this is the right answer for the right reason, since as we explain in the paper, these structures exist already within the CAS(2,2) wave function [147]. This compact description of a wave function, which has been a hard nut to crack, underscores the beauty and elegance of VB theory.

### 8.3.3. Bonding in hypercoordinated molecules

In 2013 Benoit Braïda and Philippe used VB calculations and treated hypervalent bonding in $XeF_2$ [148]. They showed that none of the VB structures, which contribute to the wave function, has any bonding by itself. All the bonding in the molecule originates from the charge-shift resonance energy between the ionic and the covalent spin paired structure. They also explained the reason why hypercoordination requires elements of the third raw and beyond and electronegative ligands. As such, and as predicted qualitatively [72,73] this study extended CSB to hypercoordination, and consolidated the case for this new family of bonds. Another extension was made by Johnny Galbraith to the bond holding amino-boranes [149]. Many more members of the CSB family are still lurking at the dark...

### 8.3.4. Weak intermolecular interactions

Treatments of weak interactions have been traditionally restricted to high-level *ab initio* calculations employing very large basis sets. Generally speaking, MO-based CI techniques always require extensive calculations to converge binding energies. By contrast, VB calculations, which are by nature multi-referenced, require less effort and can be carried out with much more compact wave function. This contrast was just demonstrated above in the case of the V state of ethylene. As such, in VB, the weak interaction is brought about by improvement of the VB structures and their mutual mixing, and often one does not need many structures or overly extended basis sets to account for these interactions. With this introduction, let me tell about the two adventures my coworkers and I had in the area of weak interactions.

In July 20–24 2008, during the ICCC-38 meeting in Jerusalem, Santiago Alvarez interested me in looking at CH···HC interactions. Admittedly, out of sheer ignorance, I may have never tried to consider these flimsy interactions by my own initiative. Nevertheless, Santiago made a persuasive case, and argued why should we try to do so using VB calculations. He sent his PhD student Jorge Echeverria to Jerusalem, and together with David Danovich they worked on VB calculations of CH···HC interactions in alkanes.

This was the time to construct a VB-based energy decomposition analysis (VB-EDA) to handle these weak interactions. I suggested to David and Jorge how to proceed, and after some struggle, we overcame the difficulties. Jorge went back to Barcelona, and David continued to implement the VB-EDA approach in actual calculations. In 2011, we published a preliminary MP2 exploration of these interactions, and showed their impact on the melting points of the various molecules [150]. Sometime later, the VB-EDA approach worked out successfully, and David could apply it to the hydrocarbons we already studied with MP2.

When we applied the method to two interacting methane molecules, we found something quite beautiful: the entire weak $H_3CH\cdots HCH_3$ interaction arose due to internal changes in the Lewis-bond wave function of the two interacting molecules, as shown in Fig. 19. Thus, for two C—H bonds there are four ionic structures made from the $C^+H^-$ and $C^-H^+$ combinations for each bond. The dashed line in Fig. 19 shows that at a long CH···HC distance (no interaction), the weights of the $C^+H^-$ and $C^-H^+$ structures for each C—H bond were equal, and hence the ratio of these weights, $W[C^+H^-\cdots^+H\ C^-]/[C^-H^+\cdots^-H^+C]$, is unity. However, in the optimum distance, two of the ionic structures grew in importance, and the other two were quenched as shown by the rectangles in Fig. 19. The ionic structures that grew in weight were those having charge alternation $(\Phi_8 + \Phi_9)$, $C^+H^-\cdots^+HC^-$ and $C^-H^+\cdots^-H^+C$. These are precisely the oscillating dipoles in the original London model of dispersion. This oscillating-dipole interaction overrode the Pauli repulsion between the two C—H bonds, and led to a small energy stabilization of the methane dimer.

As the alkyl group grew in size, this interaction remained as one of the stabilizing factors of the dimer. However, now the larger Pauli repulsion required other effects, e.g., two-ways charge transfer and spin recoupling, which came into play and stabilized the
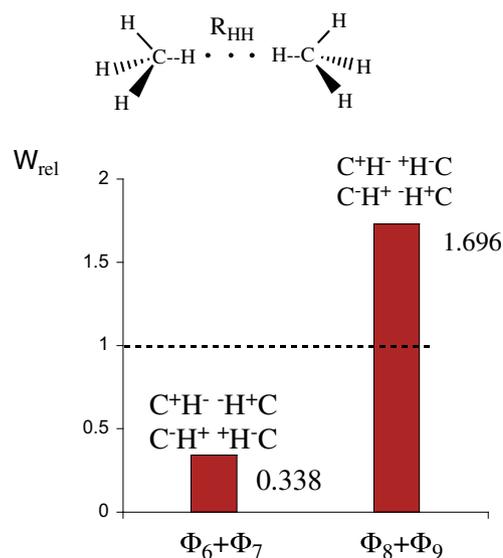


**Fig. 19.** Relative weights (W) of the indicated ionic structures. Adapted with ACS permission from Fig. 6 in Ref. [151].

dimer. The total interaction energies obtained by VB-EDA gave identical trends to the total interaction energies obtained by CCSD(T), MP2, and CEPA/1 calculations [151].

This experience with CH···HC interactions encouraged me to explore other types of weak interactions. In 2013, when Changwei Wang (a common PhD student of Wei Wu and Yirong Mo) joined my group as a postdoc, I decided that we should try to understand the very popular halogen-bonding interaction using VB theory and the block-localized wave function (BLW) approach [152], which was devised by Yirong Mo. Yirong joined us, and our team included also David Danovich who did all the VB-EDA calculations. We selected more than 50 cases of halogen bonds, and we found that halogen bonding is dominated by charge-transfer interactions, which is the model suggested by Mulliken many decades ago. Fig. 20, shows some of the results.

Thus, once again VB theory demonstrates that the weak interaction is brought about by improvement of the VB structures and their mixing, and often one does not need many structures or overly extended basis sets to account for these interactions. Similar treatments of hydrogen bonding were conducted by Yirong, Wei, Philippe, Benoit and Changwei [153], who reached similar conclusions that VB-based EDA does not require heavy duty methods and basis sets.

## 9. The VB workshops (2012–2018)

With the advent of a good software for running VB calculations (XMVB [154]) and with the growing of the mini-VB-communities, in Xiamen, France and Jerusalem, there was a feeling that the time has come to have an international meeting on VB theory and its applications. Benoit Braïda (a former PhD student of Philippe) and Etienne Derat (my former postdoc and a former PhD student of Stephane Humbel, who was a former student of Philippe and is now a Professor in the Institute des Sciences Moléculaire de Marseille) took the initiative and organized the first VB workshop in Paris during 17–23 of July 2012. The workshop was funded by the Paris-area node of Centre Européen de Calcul Atomique et Moléculaire (CECAM), and it received a coverage in a paper in *ChemPhysChem* [155]. It was a great success with more than 80 participants, exciting lectures and hands-on experience with VB calculations (with tutors coming from Jerusalem, Marseille, Paris

and Xiamen: D. Danovich, A. Shurki, S. Humbel, M. Linares, P. Su, X. Chen, J. Song and F. Ying). The main message that emerged from this workshop was that VB- and MO-based approaches to chemistry constitute a reunified-thought-culture of chemistry, and their chasm of the past is narrowing.

Encouraged by this success, Wei Wu and his group organized the second VB workshop in Xiamen, during June 14–18, 2015, as a satellite of the ICQC Meeting in Beijing. The conference entitled "*The Chemical Bond in the 21st Century*", involved more than 30 speakers and approximately 150 participants. As in the first workshop, here too, we had a series of know-how sessions in running VB calculations and solving problems.

The 2013 Nobel Prize (to Karplus, Levitt and Warshel) in a way recognized also the importance of the EVB (empirical VB) method in modeling reactions. This has prompted a third VB gathering, which was organized by Lynn Kamerlin (former postdoc of Warshel) and Fernanda Duarte (her former postdoc) during June 23–25, 2016 in Uppsala. The meeting brought together the EVB and the VB communities, who discovered that they have much in common.

This successful meeting may end up serving as a catalyst to the formation of a VB organization (suggested acronym is VALBO). The next workshops will take place in Aachen in September 2017, as a satellite of the WATOC-17 meeting, and in Marseille in June/July 2018, as a satellite of the ICQC Meeting in Menton. These two workshops will include both the VB and EVB communities, as well as any other groups/individuals seeking insight in chemistry.

The increasing number of XMVB users (based on the number of requests for the software currently there are more than 100) and of young participants in the workshops attests to the importance of the know-how sessions. In one case I am aware of, there are already productive results: Renana Gershoni-Poranne (a former PhD student of A. Stanger from the Technion) participated in the VB workshop in Paris and managed to do well all the calculations and problem sets. One of the calculations was the comparison of a covalent bond ($H_2$) to a CSB ($F_2$). Recently, she moved to the ETH (postdoc with P. Chen) and in one of her projects she demonstrated that some of the chemical bonds, they were investigating by experimental means, are CSBs. This work is in press in Chemistry – A European Journal.
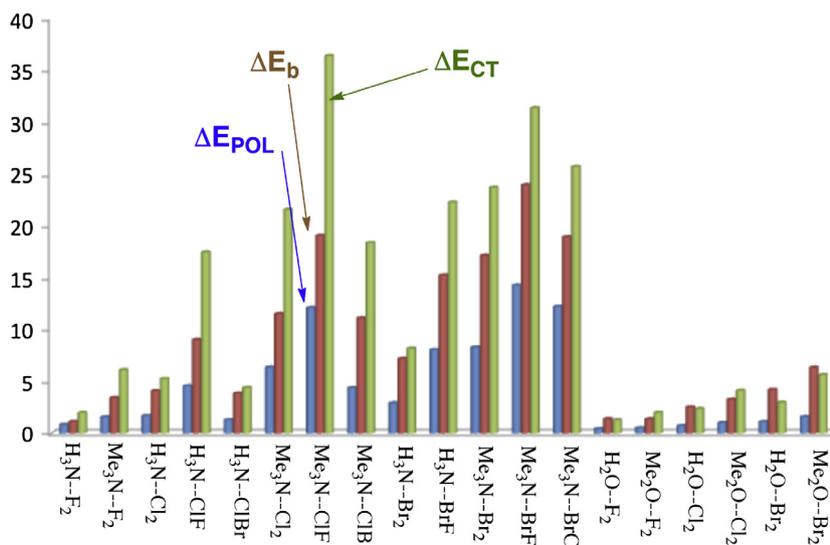


**Fig. 20.** Total binding energies ($\Delta E_b$) for the halogen bonds, indicated on the abscissa, and the contributions due to polarization ($\Delta E_{POL}$), and charge-transfer ($\Delta E_{CT}$). Note that the charge transfer bonding is dominant (all calculations correspond to BOVB/6-31G$^*$). Courtesy of David Danovich.

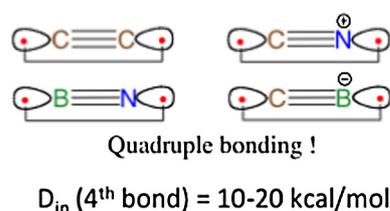## 10. The $C_2$ story: a need for a bridge over troubled water

In 2003, Roald, Philippe and I participated in a trialogue on the MO and VB wars [156]. Our conclusion was that "MO and VB constitute . . . a tool kit, simple gifts from the mind to the hands of chemists. Insisting on a journey . . . equipped with one set of tools and not the others puts one at a disadvantage. Discarding anyone of the two theories undermines the intellectual heritage of chemistry".

The story of the bonding in $C_2$ took quite a different course. In 2011, we (the Jerusalem-, Orsay- and Xiamen-groups) investigated by means of VB calculations the bonding in $C_2$. We found that the molecule had a strong triple bond and a 4th pair between the dangling exo-hybrids along the C—C axis. At some point, my co-authors and I started discussing the strength of this exo-bond coupling. About the same time, Henry Rzepa wrote to me and asked my opinion on the bonding in $CN^+$, which he was investigating. He laid the story in his Blog and used bond orders from NBO calculations to argue about a quadruple bond in this species. This was a lucky coincidence and "a marriage of true minds", and we all joined forces to probe the bonding in $C_2$ and its isoelectronic species.

After many studies and an arduous reviewing process, in 2012, David Danovich, Wei Wu, Peifeng Su, Henry Rzepa, Philippe Hiberty, and I published a paper in *Nature Chemistry* [157]. The paper showed that *$C_2$ and its first-row isoelectronic species possess quadruple bonds*. The corresponding bonding-cartoons are depicted in Scheme 9, which illustrates that all the species possess three normal internal bonds (two π and one σ), and an exo-σ-bond between the outer sp-lobes. We demonstrated [157] that this bonding pattern arises from both VB and full-CI wave functions. Estimation of the bond-interaction energies (called $D_{in}$ where "in" stands for in-situ), led to the conclusion that the internal triple bond is strong, while the exo-σ-bond was weak, of the order of 10–20 kcal/mol [158]. The beauty of this VB description is the clarity of a novel bonding picture: *there are four bonding electron pairs, and each contributes to the bonding energy of the molecule*. There is no ambiguity.

This characterization of the bonding in $C_2$ did not go unnoticed. Early on, Roald Hoffmann has written to me about his reservations, and after some email correspondence we agreed to try and thrash out the differences in a dialogue or a trialogue. Henry agreed to join us, so we engaged for a while in an exciting trialogue, and decided to publish it. It was published in 2013 in *Angewandte Chemie* [159], and with a catchy title; *One Molecule, Two Atoms, Three Views, Four Bonds?* We disagreed, we argued, we closed gaps of disagreements, but above all we searched for understanding. This was an enriching experience, in which we created some bridges and learned a great deal from each other.

Subsequently, Gernot Frenking and Markus Hermann wrote a comment on the trialogue [160]. They criticized the quadruple bond idea using effective bond order (EBO) of $C_2$, which comes out to be slightly over 2, and by invoking the Badger Rule. EBO emerges ingenuously from the simple bond order (BO) formula of MO theory, in which one sums the electrons in bonding orbitals and subtracts the number residing in anti bonding orbitals, and
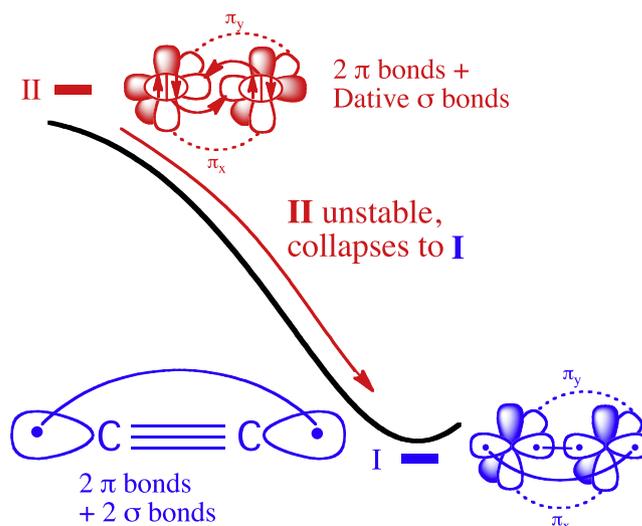
divides by two to get a BO. In a multi-configurational wave function (e.g., CASSCF), getting the EBO requires a bit more algebra but the idea is essentially the same as BO, with the exception that now the population of antibonding orbitals is induced by the multi-configurational nature of the wave function. The resulting EBO of 2.2–2.3 places $C_2$ in between C=C and C≡C [160], indicating essentially two π bonds with some residual σ interaction.

In fact, Roald already raised these points in the trialogue, using MO argument. During that trialogue, the three of us agreed that using BO analysis for $C_2$ is problematic since the $2\sigma_u$ orbital, which is counted as antibonding is essentially a nonbonding MO. Such reasoning led Roald to suggest that $C_2$ has an internal triple bond and a 4th pair weakly coupled, ·C≡C·. This is similar to the cartoon in Scheme 9; wherein VB theory adds that the weakly coupled 4th bond is 15–20 kcal/mol strong, which is estimated from both VB calculations and experimental data [159]. In our response to the comment of Frenking and Hermann, we raised again all these issues, and more [161].

Subsequently, we wrote an essay in *Chemistry – European Journal* [158], in which we tried to respond to these and other concerns, which have been raised in the interim time. This work was followed by three papers, which were submitted to *Chemistry – A European Journal* [162], by Frenking and Hermann, Zou and Cremer and Piris and Ugalde. The three papers criticized the notion of a quadruple bond in $C_2$. Two of these papers were based by and large on CASSCF, while the third on a related method. To articulate bonding, CASSCF needs exo-theoretical tools like EBO, which lead to a bond count smaller than 3. But without any bridging to VB theory, which has a clear definition of what is a bond, who is right and who is wrong becomes a matter of belief, and creates a Rashomonic effect. . .

To undo this confusion, David, Benoit, Philippe and I responded in a paper, which was published back-to-back with the group of three papers of the quadruple bond opponents. We demonstrated that the VB wave function with the quadruple bond reproduces the bond length, the force constant, and the bond dissociation energy of $C_2$ [163]. We also showed that the EBO underestimates the bond order of $C_2$ since it regards the $2\sigma_u$ orbital as an antibonding orbital, while in fact, its overlap population of this orbital is close to zero. We further demonstrated that *all the wave functions of lesser bonding than 4 collapsed unto the quadruply bonded VB wave function during the variational procedure* (see Scheme 10).

**Quadruple bonding !**

$D_{in}$ (4th bond) = 10-20 kcal/mol

Scheme 9. The quadruple bond cartoons for $C_2$ and a few of its isoelectronic species, along with the range of the in-situ bonding interaction of the 4th bond.

2 π bonds + Dative σ bonds

**II** unstable, collapses to **I**

2 π bonds + 2 σ bonds

Scheme 10. The collapse of all wave functions with lesser bond order than 4 to the quadruply bonded structure during the variational VB procedure. Adapted with permission of Wiley VCH from the TOC of Ref. [163].

We thought that this would be a decisive result, which should put the controversy to rest. But, this was not the case. Frenking and Hermann sent an additional comment to *Chemistry – A European Journal*, which we again responded to. This comment and its response will be published soon [164,165]. A bridge between MO-based theory and VB theory never formed over these troubled waters.

Struggles and even warring camps are part of science. However, early on I learned to appreciate the bridges, not because I am a conciliatory character. On the contrary, during my career, I participated in quite a few struggles over my way and my ideas. Winning is fun, but ending the struggle with bridges is much more productive. *The research controversy of the bonding of $C_2$ requires such a bridge.* We showed one, by transforming the Full CI wave function to a VB-type with a quadruple bond [157]. Later, Min Zhang et al. [166], created an additional bridge by showing that transforming the CASSCF orbitals produces a wave function that has an internal triple bond and a 4th exo-bond, precisely as in Scheme 9. A more recent paper by Liu, Frankcombe and Schmidt uses a tiling method of the electron density at the CASSCF level and reaches the very same conclusions [167]. Even more recently, Ritter reviewed the International Conference on Chemical Bonding (ICCB) in Hawaii and reported that Klaus Ruedenberg modeled $C_2$ and found precisely what is depicted in Scheme 9. Furthermore, it was communicated to me that usage of maximum probability domains [168], which have little if anything to do with VB theory, leads to a picture akin to the quadruply bonded model of $C_2$. The emerging bonding involves three internal and equivalent banana bonds and an exo pair of singly occupied domains that is coupled to a singlet spin [169]. So the bridges do exist over these troubled waters, and once these bridges are used all theories show that $C_2$ is definitely quadruply bonded...

## 11. Summary: valence bond – what an insightful theory it is!

This is a good point to summarize this essay, in which I tried to show on the fly my own excursion through VB theory. Sometimes this was done from a bird's eye view, while other times in some details. My goal was to create a panoramic view of VB applications to chemistry. As such, I feel that the breadth of the work demonstrates what an insightful and wonderful theory VB is! It has come a long way from its state in the late 1950s.

My second goal was to preach in favor of one culture, not two, or as put succinctly in the trialogue with Roald Hoffmann and Philippe Hiberty: "*MO and VB constitute . . . a tool kit, simple gifts from the mind to the hands of chemists. Insisting on a journey . . . Discarding anyone of the two theories undermines the intellectual heritage of chemistry*" [156]. I think this preaching is quite evident throughout.

The story told herein focuses on the work done with the partners I was lucky to have during this long VB-March. However, the VB community is much larger, and it includes many other proponents who developed methods, and applied them to a variety of problems. To name but a few, and in a somewhat random order, these are the schools of Goddard, Carter, Dunning, Cooper-Raimondi-Garrett, Gallup, Harcourt, Karplus and Balint-Kurti, Malrieu, McWeeny, Nascimento, Amovelli, Harcourt, Hirao, Havenith, Klein, Gao, Jiang and Li, van Lenthe, and others. Their work is described in reviews [13,16] and monographs (see chapter 9 in Ref. [4]) [12,170]. A summary of VB software can also be found in several sources (see chapter 9 in Ref. [4]) [13,16]. VB development is an active front, and the VB capabilities keep increasing. For example, the most recent XMVB capability of the Xiamen Group reaches 20 electrons in 20 VB orbitals [171]. Similarly, Olsen [172] published recently his bi-orthonormal expansion algorithm,

implemented in LUCIA, that enhances the efficiency of VB calculations using Coulson-Fisher orbitals.

Indeed, VB theory never really died. Now it flourishes qualitatively, it is sprouting quantitatively, and will soon stand shoulder-to-shoulder with the most sophisticated MO-based methods.

## References

[1] G.N. Lewis, The atom and the molecule, J. Am. Chem. Soc. 38 (1916) 762–785.
[2] S. Shaik, The Lewis legacy: the chemical bond – a territory and heartland of chemistry, J. Comput. Chem. 28 (2007) 51–61.
[3] W. Heitler, F. London, Z. Phys. 44 (1927) 455–472.
[4] S. Shaik, P.C. Hiberty, A Chemist's Guide to Valence Bond Theory, Wiley, Hoboken, NJ, 2008 (Chapter 1).
[5] L. Pauling, The Nature of the Chemical Bond, third ed., 1960., Cornell University Press, Ithaca, New York, 1939.
[6] (a) S.G. Brush, Dynamics of theory change in chemistry: Part 1. The Benzene problem 1865–1945, Stud. Hist. Phil. Sci. 30 (1999) 21–79;
(b) S.G. Brush, Dynamics of theory change in chemistry: Part 2. Benzene and molecular orbitals, 1945–1980, Stud. Hist. Phil. Sci. 30 (1999) 263–302.
[7] (a) W.A. Goddard III, T.H. Dunning Jr., W.J. Hunt, P.J. Hay, Generalized valence bond description of bonding in low-lying states of molecules, Acc. Chem. Res. 6 (1973) 368–376;
(b) M.M. Goodgame, W.A. Goddard III, Modified generalized valence-bond method: a simple correction for the electron correlation missing in generalized valence-bond wave functions; prediction of double-well states for $Cr_2$ and $Mo_2$, Phys. Rev. Lett. 54 (1985) 661–664.
[8] (a) W. Moffitt, J. Scanlan, Some calculations on the ethylene molecule, Proc. Roy. Soc. Lond. A 218 (1953) 464–486;
(b) P. Karafiloglou, G. Ohanessian, Understanding molecular orbital wave functions in terms of resonance structures, J. Chem. Educ. 1991 (68) (1991) 583–586.
[9] P.C. Hiberty, C. Leforestier, Expansion of molecular orbital wave functions into valence bond wave functions. A simplified procedure, J. Am. Chem. Soc. 100 (1978) 2012–2017.
[10] J.W. Linnett, The Electronic Structure of Molecules: A New Approach, John Wiley & Sons, London, 1964.
[11] S. Shaik, P.C. Hiberty, Valence bond theory, its history, fundamentals, and applications – a primer, Rev. Comput. Chem. 20 (2004) 1–100.
[12] D.L. Cooper (Ed.), Valence Bond Theory, vol. 10, Elsevier, Amsterdam, 2002.
[13] W. Wu, P. Su, S. Shaik, P.C. Hiberty, Classical valence bond approach by modern methods, Chem. Rev. 111 (2011) 7557–7593.
[14] D.L. Cooper, J. Gerratt, M. Raimondi, Applications of spin-coupled valence bond theory, Chem. Rev. 91 (1991) 929–964.
[15] J.P. Malrieu, in: D.J. Klein, N. Trinajstic (Eds.), Valence Bond Theory and Chemical Structure, Elsevier, Amsterdam, 1990, p. 135.
[16] P.C. Hiberty, S. Shaik, A survey of developments in ab initio valence bond theory, J. Comput. Chem. 28 (2007) 137–151.
[17] S. Shaik, A. Shurki, Valence bond diagrams and chemical reactivity, Angew. Chem. Int. Ed. 38 (1999) 586–625.
[18] M. Albeck, S. Shaik, Reactions of tellurium(IV) halides with anthracene and other organic compounds, J. Chem. Soc. Perkin I (1975) 1223–1229.
[19] Correspondence between Roald Hoffmann and Sason Shaik (October 6 and 13, 1975). Courtesy of R. Hoffmann.
[20] M.M.L. Chen, R. Hoffmann, Sulfuranes. Theoretical aspects of bonding, substituent site preferences, and geometrical distortions, J. Am. Chem. Soc. 98 (1976) 1647–1653.
[21] Correspondence between Roald Hoffmann and Sason Shaik (March 4th, 1974). Courtesy of R. Hoffmann.
[22] (a) N.D. Epiotis, S. Sarkanen, D. Bjorkquist, L. Bjorkquist, R. Yates, Open shell interactions, nonbonded attraction, and aromaticity. Implications for regiochemistry, J. Am. Chem. Soc. 96 (1974) 4075–4084;
(b) N.D. Epiotis, D. Bjorkquist, L. Bjorkquist, S. Sarkanen, Attractive nonbonded interactions in 1-substituted propenes. Consequences for geometric and conformational isomerism, J. Am. Chem. Soc. 95 (1973) 7558–7562;
(c) N.D. Epiotis, Attractive nonbonded interactions in organic molecules, J. Am. Chem. Soc. 95 (1973) 3087–3096.

[23] N.D. Epiotis, W. Cherry, S. Shaik, R.L. Yates, F. Bernardi, Structural theory of organic chemistry, Top. Curr. Chem. 70 (1977) 1–250.

[24] R.B. Woodward, R. Hoffmann, The Conservation of Orbital Symmetry, Verlag Chemie, Academic Press, GmbH, Weinheim, Germany, 1971.

[25] N.D. Epiotis, The theory of pericyclic reactions, Angew. Chem. Int. Ed. 13 (1974) 751–780.

[26] M. Elian, R. Hoffmann, Bonding capabilities of transition metal carbonyl fragments, Inorg. Chem. 14 (1975) 1058–1076.

[27] R. Hoffmann, Building bridges between inorganic and organic chemistry, Angew. Chem. Int. Ed. 21 (1982) 711–724.

[28] J.C. Slater, Directed valence in polyatomic molecules, Phys. Rev. 37 (1931) 481–489.

[29] (a) S.S. Shaik, Triplet (2 + 2) cycloadditions. Spin inversion control of stereoselectivity, J. Am. Chem. Soc. 101 (1979) 3184–3196;
(b) S.S. Shaik, N.D. Epiotis, Spin inversion in triplet Diels-Alder reactions, J. Am. Chem. Soc. 102 (1980) 122–131.

[30] S.S. Shaik, What happens to molecules as they react? A valencebond approach to reactivity, J. Am. Chem. Soc. 103 (1981) 3692–3701.

[31] S. Shaik, D. Mandal, R. Ramanan, Oriented electric fields as future smart reagents in chemistry, Nat. Chem. 8 (2016) 1091–1098.

[32] U. Dandamudi, W.Z. Lai, C. Li, H. Chen, D. Danovich, S. Shaik, A tutorial for understanding chemical reactivity through the valence bond approach, Chem. Soc. Rev. 43 (2014) 4968–4988.

[33] S.S. Shaik, A qualitative valence bond approach to organic reactions, in: J. Bertran, G.I. Csizmadia (Eds.), New Theoretical Concepts for Understanding Organic Reactions, NATO ASI Series C267, Kluwer Publ., Dordrecht, Holland, 1989.

[34] S.S. Shaik, J.P. Dinnocenzo, Nucleophilic cleavage of one-electron $\sigma$ bonds are predicted to proceed with stereoinversion, J. Org. Chem. 55 (1990) 3434–3436.

[35] M.J. Pellerite, J.I. Brauman, Intrinsic barriers in nucleophilic displacements, J. Am. Chem. Soc. 102 (1980) 5993–5999.

[36] S.S. Shaik, On the origins of the barrier in the $S_N2$ identity exchange, Nouv. J. Chim. 6 (1982) 159–161.

[37] S.S. Shaik, A. Pross, $S_N2$ reactivity of $CH_3X$ derivatives. A valence bond approach, J. Am. Chem. Soc. 104 (1982) 2708–2719.

[38] R. Hoffmann, Chemistry in Britain, Valence Bond Theory (March 1991). Courtesy of R. Hoffmann.

[39] J.E. Buncel, S.S. Shaik, I.-H. Um, S. Wolfe, A. Theoretical, Treatment of nucleophilic reactivity in additions to carbonyl compounds. The role of the vertical ionization energy, J. Am. Chem. Soc. 110 (1988) 1275–1279.

[40] W.Z. Lai, C. Li, H. Chen, S. Shaik, Hydrogen-abstraction reactivity patterns from A to Y: the valence bond way, Angew. Chem. Int. Ed. 51 (2012) 5556–5578.

[41] A. Pross, S.S. Shaik, Reactivity-selectivity relationships. A quantum mechanical approach to transition state structure. Application to the $S_N2$ reaction of benzyl derivatives, J. Am. Chem. Soc. 103 (1981) 3702–3709.

[42] A. Pross, S.S. Shaik, A qualitative valence-bond approach to organic reactivity, Acc. Chem. Res. 16 (1983) 363–370.

[43] S. Shaik, Valence bond all the way: from the degenerate H-exchange to cytochrome P450, Phys. Chem. Chem. Phys. 12 (2010) 8706–8720.

[44] S.S. Shaik, The collage of $S_N2$ reactivity patterns: a state correlation diagram model, Prog. Phys. Org. Chem. 15 (1985) 197–337.

[45] A. Pross, S.S. Shaik, A. Qualitative, Valence-bond approach to organic reactivity. Application to elimination reactions, J. Am. Chem. Soc. 104 (1982) 187–195.

[46] S. Shaik, P.C. Hiberty, Valence bond mixing and curve crossing diagrams in chemical reactivity and bonding, Adv. Quant. Chem. 26 (1995) 99–163.

[47] A. Pross, What is Life?, Oxford University Press, Oxford, UK, 2012

[48] S.S. Shaik, On the stability and properties of organic metals and their isomeric charge-transfer complexes, J. Am. Chem. Soc. 104 (1982) 5328–5334.

[49] S.S. Shaik, M.-H. Whangbo, Electronic and intramolecular structural localizations in conducting organic salts, Inorg. Chem. 25 (1986) 1201–1209.

[50] S.S. Shaik, Solvent effect on reaction barriers. the $S_N2$ reaction. 1. Application to the identity exchange, J. Am. Chem. Soc. 106 (1984) 1227–1232.

[51] S.S. Shaik, $\alpha$- and $\beta$-carbon substituent effect on $S_N2$ reactivity. a valence-bond approach, J. Am. Chem. Soc. 105 (1983) 4359–4367.

[52] P. Su, F. Ying, W. Wu, P.C. Hiberty, S. Shaik, The Menshutkin reaction in the gas phase and in aqueous solution: a valence bond study, ChemPhysChem 8 (2007) 2603–2614.

[53] S.S. Shaik, R. Bar, How important is resonance in organic species?, Nouv J. Chim. 8 (1984) 411–420.

[54] S.S. Shaik, P.C. Hiberty, When does electronic delocalization become driving force of molecular shape and stability? The aromatic sextet, J. Am. Chem. Soc. 107 (1985) 3089–3095.

[55] S.S. Shaik, P.C. Hiberty, G. Ohanessian, J.M. Lefour, Allylic resonance is forced upon the $\pi$-system by the $\sigma$-framework, Nouv. J. Chim. 9 (1985) 385–388.

[56] P.C. Hiberty, S.S. Shaik, J.M. Lefour, G. Ohanessian, Is the delocalized $\pi$-system of benzene a stable electronic system?, J Org. Chem. 50 (1985) 4657–4659.

[57] P.C. Hiberty, S.S. Shaik, G. Ohanessian, J.M. Lefour, The $\pi$-distortive propensities in benzene and the allyl radical. A reply to a criticism, J. Org. Chem. 51 (1986) 3908–3909.

[58] S.S. Shaik, P.C. Hiberty, G. Ohanessian, J.-M. Lefour, When does electronic delocalization become a driving force of chemical bonding?, J Phys. Chem. A 92 (1988) 5086–5094.

[59] S. Shaik, A. Shurki, D. Danovich, P.C. Hiberty, Origins of the exalted $b_{2u}$ frequency in the first excited state of benzene, J. Am. Chem. Soc. 118 (1996) 666–671.

[60] S. Shaik, S. Zilberg, Y. Haas, A Kekulé-crossing model for the anomalous behavior of the $b_{2u}$ modes of polyaromatic hydrocarbons in the lowest excited $^1B_{2u}$ state, Acc. Chem. Res. 29 (1996) 211–218.

[61] D. Cohen, R. Bar, S.S. Shaik, Nucleophilic vinylic substitution. A theoretical study, J. Am. Chem. Soc. 108 (1986) 231–240.

[62] A. Demolliens, O. Eisenstein, P.C. Hiberty, J.M. Lefour, G. Ohanessian, S.S. Shaik, F. Volatron, Hypercoordinated $XH_{n+1}$ radicals for first- and second-row atoms. A valence bond analysis, J. Am. Chem. Soc. 111 (1989) 5623–5631.

[63] G. Sini, P.C. Hiberty, S.S. Shaik, The origins of the different bonding features in $SiH_5^-$ and $CH_5^-$. A valence bond curve crossing model, J. Chem. Soc. Chem. Commun. (1989) 772–774.

[64] G. Sini, G. Ohanessian, P.C. Hiberty, S.S. Shaik, Why is $SiH_5^-$ a stable intermediate while $CH_5^-$ is a transition state? A quantitative curve crossing valence bond study, J. Am. Chem. Soc. 112 (1990) 1407–1413.

[65] D.J. Mitchell, H.B. Schlegel, S.S. Shaik, S. Wolfe, Relationships between geometries and energies of identity $S_N2$ transition states: the dominant role of the distortion energy and its origins, Can. J. Chem. 63 (1985) 1642–1649.

[66] G. Sini, S.S. Shaik, J.M. Lefour, G. Ohanessian, P.C. Hiberty, Quantitative valence bond computation of a curve crossing diagram for a model $S_N2$ reaction $H^- + CH_3H' \rightarrow HCH_3 + H'^-$, J. Phys. Chem. 93 (1989) 5661–5665.

[67] G. Sini, S. Shaik, P.C. Hiberty, Quantitative valence-bond computations of curve crossing diagrams for a gas-phase $S_N2$ reactions, $F^- + CH_3F \rightarrow FCH_3 + F^-$, J. Chem. Soc. Perkin Trans. 2 (1992) 1019–1025.

[68] P. Mâitre, P.C. Hiberty, G. Ohanessian, S.S. Shaik, Quantitative valence bond computation of a curve crossing diagram for model atom exchange reactions, J. Phys. Chem. 94 (1990) 4089–4093.

[69] G. Sini, P. Mâitre, P.C. Hiberty, S.S. Shaik, Covalent, ionic and resonating single bonds, J. Mol. Struct. (THEOCHEM) 229 (1991) 163–188.

[70] S. Shaik, P. Maitre, G. Sini, P.C. Hiberty, The charge-shift bonding concept. Electron-pair bonds with very large ionic-covalent resonance energies, J. Am. Chem. Soc. 114 (1992) 7861–7866.

[71] P.C. Hiberty, J.P. Flament, E. Noizet, Compact and accurate valence bond functions with different orbitals for different configurations: application to the two-configuration description of $F_2$, Chem. Phys. Lett. 189 (1992) 259–265.

[72] S. Shaik, D. Danovich, W. Wu, P.C. Hiberty, Charge-shift bonding and its manifestations in chemistry, Nat. Chem. 1 (2009) 443–449.

[73] S. Shaik, D. Danovich, B. Braida, W. Wu, P.C. Hiberty, New landscape of electron-pair bonding: covalent, ionic and charge-shift bonds, Struct. Bond. 170 (2016) 169–212 (The Chemical Bond II – 100 Years Old and Getting Stronger).

[74] H. Zhang, D. Danovich, W. Wu, B. Briada, P.C. Hiberty, S. Shaik, Charge-shift bonding emerges as a distinct electron-pair bonding family from both valence bond and molecular orbital theories, J. Chem. Theor. Comput. 10 (2014) 2410–2418.

[75] S.S. Shaik, H.B. Schlegel, S. Wolfe, Theoretical Aspects of Physical Organic Chemistry. Application to the $S_N2$ Transition State, Wiley Interscience, 1992.

[76] T.H. Lowry, K.S. Richardson, Mechanism and Theory in Organic Chemistry, third ed., Harper & Row. Publ., New York, NY, 1987, pp. 218–222, 220, 354, 354–360, 381–382, 412, 604, 685.

[77] F.A. Carroll, Perspectives on Structure and Mechanism in Organic Chemistry, second ed., John Wiley & Sons, Hoboken, New Jersey, 2010, pp. 19, 27, 205, 238, 240, 276, 309, 365, 479, 500, 503, 513, 417, 533, 724.

[78] E. Heilbronner, Why do some molecules have symmetry different from that expected?, J Chem. Educ. 66 (1989) 471–478.

[79] M.G. Evans, The activation energies of reactions involving conjugated systems, Trans. Faraday Soc. 35 (1939) 824–834.

[80] J.A. Berson, Chemical Creativity: Ideas from the Work of Woodward, Hückel, Meerwein, and Others, Wiley-VCH, New York, 1999.

[81] A. Shurki, P.C. Hiberty, F. Dijkstra, S. Shaik, Aromaticity and antiaromaticity: what role do ionic configurations play in delocalization and induction of magnetic properties?, J Phys. Org. Chem. 16 (2003) 731–745.

[82] L. Eberson, Electron Transfer Reactions in Organic Chemistry, Springer-Verlag, Heidelberg, Germany, 1987, pp. 8, 141–142, 192.

[83] L. Eberson, S.S. Shaik, Electron-transfer reactions of radical anions: do they follow outer- or inner-sphere mechanisms?, J Am. Chem. Soc. 112 (1990) 4484–4489.

[84] J.K. Cho, S. Shaik, Electron transfer vs polar mechanisms. Transition-state structures and properties for reactions of a cation radical and a nucleophile, J. Am. Chem. Soc. 113 (1991) 9890–9891.

[85] G.N. Sastry, D. Danovich, S. Shaik, Towards the definition of the maximum allowable tightness of an electron transfer transition state in the reactions of radical anions and alkyl halides, Angew. Chem. Int. Ed. 35 (1996) 1098–1100.

[86] G.N. Sastry, S. Shaik, Structured electron transfer transition state. Valence bond configuration mixing analysis and ab initio calculations of the reaction of formaldehyde radical anion with methyl chloride, J. Phys. Chem. 100 (1996) 12241–12252.

[87] V. Bakken, D. Danovich, S. Shaik, H.B. Schlegel, A single transition state serves two mechanisms: an ab initio classical trajectory study of the electron transfer and substitution mechanisms in reactions of ketyl radical anions with alkyl halides, J. Am. Chem. Soc. 123 (2001) 130–134.

[88] S. Shaik, M. Karni, D. Danovich, Y. Apeloig, The Lise Meitner-Minerva center for computational quantum chemistry: 18 years of Israeli-German collaboration, Isr. J. Chem. 55 (2015) 1167–1176.

[89] S. Shaik, An anatomy of the two-state reactivity concept: personal reminiscences in memoriam of Detlef Schröder, Int. J. Mass Spectrom. 354–355 (2013) 5–14.

[90] A. Fiedler, D. Schröder, S. Shaik, H. Schwarz, Electronic structures and gas-phase reactivities of cationic late transition-metal-oxides, J. Am. Chem. Soc. 116 (1994) 10734–10741.

[91] S. Shaik, D. Danovich, A. Fiedler, D. Schröder, H. Schwarz, Two-state reactivity in organometallic gas-phase ion chemistry, Helv. Chim. Acta 78 (1995) 1393–1407.

[92] A. Shurki, S. Shaik, The distortive tendency of benzene $\pi$-electrons: how is it related to structural observables?, Angew Chem. Int. Ed. 36 (1997) 2205–2208.

[93] J.K. Burdett, Chemical Bonds. A Dialog, John Wiley & Sons, Chichester, UK, 1997, pp. 113–120 (Chapter 12).

[94] S. Shaik, A. Shurki, D. Danovich, P.C. Hiberty, A different story of $\pi$-delocalization – the distortivity of $\pi$-electrons and its chemical manifestations, Chem. Rev. 101 (2001) 1501–1539.

[95] I.S. Ulusoy, M. Nest, Correlated electron dynamics: how aromaticity can be controlled, J. Am. Chem. Soc. 133 (2011) 20230–20236.

[96] L. Eberson, R. González-Luque, M. Merchán, F. Radner, B.O. Roos, S. Shaik, Radical cations of non-alternant systems as probes of the Shaik-Pross VB configuration mixing model, J. Chem. Soc. Perkin Trans. 2 (1997) 463–472.

[97] C. Li, W. Wu, D. Kumar, S. Shaik, Kinetic isotope effect is a sensitive probe of spin state reactivity in C-H hydroxylation of N, N-dimethylaniline by cytochrome P450, J. Am. Chem. Soc. 128 (2006) 394–395.

[98] S. Shaik, M. Filatov, D. Schröder, H. Schwarz, Electronic structure makes a difference: cytochrome P-450 mediated hydroxylation of hydrocarbons as a two-state reactivity paradigm, Chem. Eur. J. 4 (1998) 193–199.

[99] D. Danovich, W. Wu, S. Shaik, No-pair bonding in the high-spin $^3\sum_u^+$ state of $Li_2$. A valence bond study of its origins, J. Am. Chem. Soc. 121 (1999) 3165–3174.

[100] W. Wu, S.-J. Zhong, S. Shaik, VBDFT(s): a Hückel-type semi-empirical valence bond (VB) method scaled to density functional energies. Application to linear polyenes, Chem. Phys. Lett. 292 (1998) 7–14.

[101] W. Wu, Y. Luo, L. Song, S. Shaik, VBDFT(s) – a semiempirical valence bond method: application to linear polyenes containing oxygen and nitrogen heteroatoms, Phys. Chem. Chem. Phys. 3 (2001) 5459–5465.

[102] W. Wu, D. Danovich, A. Shurki, S. Shaik, Using valence bond theory to understand electronic excited states: application to the hidden excited state $(2\,^1A_g)$ of $C_{2n}H_{2n+2}$ (n = 2–14) polyenes, J. Phys. Chem. A 104 (2000) 8744–8758.

[103] W. Wu, S. Shaik, VB-DFT: a nonempirical hybrid method combining valence bond theory and density functional energies, Chem. Phys. Lett. 301 (1999) 37–42.

[104] W. Wu, L. Song, Z. Cao, Q. Zhang, S. Shaik, Valence bond configuration interaction: a practical ab initio valence bond method that incorporating dynamic correlation, J. Phys. Chem. A 106 (2002) 2721–2726.

[105] L. Song, W. Wu, Q. Zhang, S. Shaik, A practical valence bond method: a configuration interaction method approach with perturbation theoretic facility, J. Comput. Chem. 25 (2004) 472–478.

[106] L. Song, W. Wu, Q. Zhang, S. Shaik, VBPCM: a valence bond method that incorporates a polarizable continuum model, J. Phys. Chem. A 108 (2004) 6017–6024.

[107] F. Ying, P. Su, Z. Chen, S. Shaik, W. Wu, DFVB: a density-functional-based valence bond method, J. Chem. Theory Comput. 8 (2012) 1608–1615.

[108] L. Song, W. Wu, P.C. Hiberty, D. Danovich, S. Shaik, An accurate barrier for the hydrogen exchange reaction from valence bond theory: is this coming of age?, Chem Eur. J. 9 (2003) 4540–4547.

[109] S. Shaik, S.P. de Visser, W. Wu, L. Song, P.C. Hiberty, Reply to comment on: "Identity Hydrogen Abstraction Reactions, $X^{\bullet} + H-X' \rightarrow XH + X'^{\bullet}$ (X = X' = $CH_3$, $SiH_3$, $GeH_3$, $SnH_3$, $PbH_3$): A Valence Bond Modeling", J. Phys. Chem. A 106 (2002) 5043–5045.

[110] L. Song, W. Wu, P.C. Hiberty, S. Shaik, The identity $S_N2$ reactions $X^- + CH_3$-$X \rightarrow X$-$CH_3 + X^-$ (X = F, Cl, Br, and I) in the vacuum and in aqueous solution: a valence bond study, Chem. Eur. J. 12 (2006) 7458–7466.

[111] P. Su, L. Song, W. Wu, P.C. Hiberty, S. Shaik, Valence bond calculations of hydrogen transfer reactions: a general predictive pattern derived from theory, J. Am. Chem. Soc. 126 (2004) 13539–13549.

[112] M. Filatov, N. Harris, S. Shaik, On the 'Rebound' mechanism of alkane hydroxylation by cytochrome P450: electronic structure of the intermediate and the electron transfer character in the rebound step, Angew. Chem. Int. Ed. 38 (1999) 3510–3512.

[113] N. Harris, S. Cohen, M. Filatov, F. Ogliaro, S. Shaik, Two-state reactivity in the rebound step of alkane hydroxylation by cytochrome P-450. Origins of free radicals with finite lifetimes, Angew. Chem. Int. Ed. 39 (2000) 2003–2007.

[114] M. Filatov, S. Shaik, Diradicaloids: description by the spin-restricted, ensemble-referenced Kohn-Sham (REKS) density functional method, J. Phys. Chem. A 104 (2000) 6628–6636.

[115] M. Filatov, S. Shaik, Artificial symmetry breaking in radicals is avoided by the use of the ensemble-references Kohn-Sham (REKS) method, Chem. Phys. Lett. 332 (2000) 409–419.

[116] F. Ogliaro, N. Harris, S. Cohen, M. Filatov, S.P. de Visser, S. Shaik, A model 'Rebound' mechanism of methane hydroxylation by cytochrome P450: stepwise and effectively concerted pathways, and their reactivity patterns, J. Am. Chem. Soc. 122 (2000) 8977–8989.

[117] F. Ogliaro, S. Cohen, S.P. de Visser, S. Shaik, Medium polarization and hydrogen bonding effects on compound I of cytochrome P450: what kind of a radical is it really?, J. Am. Chem. Soc. 122 (2000) 12892–12893.

[118] S.P. de Visser, F. Ogliaro, P.K. Sharma, S. Shaik, Hydrogen bonding modulates the selectivity of enzymatic oxidation by P450: a chameleon oxidant behavior by compound I, Angew. Chem. Int. Ed. 41 (2002) 1947–1951.

[119] F. Ogliaro, M. Filatov, S. Shaik, Alkane hydroxylation by cytochrome P450: is kinetic isotope effect a reliable probe of transition state structure?, Eur J. Inorg. Chem. 2455–2458 (2000).

[120] D. Kumar, S.P. de Visser, P.K. Sharma, S. Cohen, S. Shaik, Radical clock substrates, their C-H hydroxylation mechanism by cytochrome P450, and other reactivity patterns: what does theory reveal about clocks' behavior?, J Am. Chem. Soc. 126 (2004) 1907–1920.

[121] S. Shaik, H. Hirao, D. Kumar, Reactivity of high-valent iron-oxo species in enzymes and synthetic reagents: a tale of many states, Acc. Chem. Res. 40 (2007) 532–542.

[122] J.C. Schöneboom, H. Lin, N. Reuter, W. Thiel, S. Cohen, F. Ogliaro, S. Shaik, The elusive oxidant of cytochrome P450 enzymes: characterization by combined quantum mechanical/molecular mechanical (QM/MM) calculations, J. Am. Chem. Soc. 124 (2002) 8142–8151.

[123] J.C. Schöneboom, S. Cohen, H. Lin, S. Shaik, W. Thiel, Quantum mechanical/molecular mechanical investigation of the mechanism of C-H hydroxylation of camphor by cytochrome $P450_{cam}$: theory supports a two-state rebound mechanism, J. Am. Chem. Soc. 126 (2004) 4017–4034.

[124] S. Shaik, D. Kumar, S.P. de Visser, A. Altun, W. Thiel, Theoretical perspective on the structure and mechanisms of cytochrome P450 enzymes, Chem. Rev. 105 (2005) 2279–2328.

[125] S. Shaik, Y. Cohen, H. Wang, D. Chen, W. Kumar, Thiel, P450 enzymes: their structure, reactivity and selectivity – modeled by QM/MM calculations, Chem. Rev. 110 (2010) 949–1017.

[126] S. Shaik, D. Kumar, S.P. de Visser, A valence bond modeling of trends in hydrogen abstraction barriers and transition states of hydroxylation reactions catalyzed by cytochrome P450 enzymes, J. Am. Chem. Soc. 130 (2008) 10128–10140 ((Correction) 130 (2008) 14016).

[127] S. Shaik, Y. Wang, H. Chen, J. Song, R. Meir, Valence bond modeling and density functional theory calculations of reactivity and mechanism of cytochrome P450 enzymes: thioether sulfoxidation, Faraday Discuss. 145 (2010) 49–70.

[128] S. Shaik, W.Z. Lai, H. Chen, Y. Wang, The valence bond way: reactivity patterns of cytochrome P450 enzymes and synthetic analogs, Acc. Chem. Res. 43 (2010) 1154–1165.

[129] S. Shaik, P. Milko, P. Schyman, D. Usharani, H. Chen, A valence bond modeling trends in aromatic oxidation catalyzed by cytochrome P450 enzymes, J. Chem. Theor. Comput. 7 (2011) 327–339.

[130] Y. Pocker, R.F. Buchholz, Electrostatic catalysis by ionic aggregates. II. The reversible elimination of HCl from t-butyl chloride and the rearrangement of 1-phenylallyl chloride in lithium perchlorate-diethyl ether solutions, J. Am. Chem. Soc. 92 (1970) 4033–4038.

[131] S. Shaik, S.P. de Visser, D. Kumar, An external electric field will control the selectivity of enzymatic-like bond activations, J. Am. Chem. Soc. 126 (2004) 11746–11749.

[132] H. Hirao, H. Chen, M.A. Carvajal, Y. Wang, S. Shaik, Effect of external electric fields on the C-H bond activation reactivity of nonheme iron-oxo reagents, J. Am. Chem. Soc. 130 (2008) 3319–3327.

[133] W. Lai, H. Chen, K.-B. Cho, S. Shaik, External electric field can control the catalytic cycle of cytochrome $P450_{cam}$: a QM/MM study, J. Phys. Chem. Lett. 1 (2010) 2082–2087.

[134] R. Meir, H. Chen, W. Lai, S. Shaik, Oriented electric fields accelerate the Diels-Alder reactions and control the endo/exo selectivity, ChemPhysChem 11 (2010) 301–310.

[135] B. Halford, Zapping Diels-Alder reactions, C&E News 7 (2016) 8 (March).

[136] A. Extance, Electrostatic field powers up reaction rate, Chem. World (2016) (March 2).

[137] A.C. Aragonès, N.L. Haworth, N. Darwish, S. Ciampi, N.J. Bloomfield, G.G. Wallace, I. Diez-Perez, M.L. Coote, Electrostatic catalysis of a Diels-Alder reaction, Nature 531 (2016) 88–91.

[138] N. Dietl, M. Schlangen, H. Schwarz, Thermal hydrogen-atom transfer from methane: the role of radicals and spin states in oxo-cluster chemistry, Angew. Chem. Int. Ed. 51 (2012) 5544–5555.

[139] C. Li, D. Danovich, S. Shaik, Blended hydrogen atom abstraction and proton-coupled electron transfer mechanisms of closed-shell molecules, Chem. Sci. 3 (2012) 1903–1918.

[140] M. Lingwood, J.R. Hammond, D.A. Hrovat, J.M. Mayer, W.T. Borden, MPW1K performs much better than B3LYP in DFT calculations on reactions that proceed by proton-coupled electron transfer (PCET), J. Chem. Theory Comput. 2 (2006) 740–745.

[141] D. Usharani, D.C. Lacy, A.S. Borovik, S. Shaik, Dichotomous hydrogen atom transfer vs. proton-coupled electron transfer during activation of X-H bonds (X = C, N, O) by nonheme iron-oxo complexes of variable basicity, J. Am. Chem. Soc. 135 (2013) 17090–17104.

[142] J. Li, S. Zhou, J. Zhang, M. Schlangen, D. Usharani, S. Shaik, H. Schwarz, Mechanistic variants in gas-phase metal-oxide mediated activation of methane at ambient conditions, J. Am. Chem. Soc. 138 (2016) 11368–11377.

[143] J. Li, S. Zhou, J. Zhang, M. Schlangen, T. Weiske, D. Usharani, S. Shaik, H. Schwarz, Electronic origins of the variable efficiency of room-temperature methane activation by homo- and heteronuclear cluster oxide cations $[XYO_2]^+$ (X, Y = Al, Si, Mg): competition between proton-coupled electron transfer and hydrogen-atom transfer, J. Am. Chem. Soc. 138 (2016) 7973–7981.

[144] D. Danovich, S. Shaik, Bonding with parallel spins: high-spin clusters of monovalent metal atoms, Acc. Chem. Res. 47 (2014) 417–426.

[145] D. Danovich, S. Shaik, On the nature of bonding in parallel spins in monovalent metal clusters, Annu. Rev. Phys. Chem. 67 (2016) 419–439.

[146] (a) J. Higgins, C. Callegari, J. Reho, F. Stienkemeier, W.E. Ernst, M. Gutowski, G. Scoles, Helium cluster isolation spectroscopy of alkali dimers in the triplet manifold, J. Phys. Chem. A 102 (1998) 4952–4965;
(b) A. Bertlet, J.D. Close, F. Federmann, N. Quaas, J.P. Toennies, Gold metal clusters: helium droplets as a nanoscale cryostat, Phys. Rev. Lett. 77 (1996) 3525–3528.

[147] W. Wu, H. Zhang, B. Braïda, S. Shaik, P.C. Hiberty, The V state of ethylene: valence bond theory takes up the challenge, Theor. Chem. Acc. 133 (2014) 1441.

[148] B. Braïda, P.C. Hiberty, The essential role of charge-shift bonding in hypervalent prototype $XeF_2$, Nat. Chem. 5 (2013) 417–422.

[149] A.A. Fiorillo, J.M. Galbraith, A valence bond description of coordinated covalent bonding, J. Phys. Chem. A 108 (2004) 5126–5130.

[150] J. Echeverria, G. Aullon, D. Danovich, S. Shaik, S. Alvarez, Dihydrogen contacts in alkanes are subtle but not faint, Nat. Chem. 3 (2011) 323–330.

[151] D. Danovich, S. Shaik, F. Neese, J. Echeverria, G. Aullon, S. Alvarez, Understanding the nature of the CH⋯HC interactions in alkanes, J. Chem. Theor. Comput. 9 (2013) 1977–1991.

[152] (a) Y. Mo, S.D. Peyerimhoff, Theoretical analysis of electronic delocalization, J. Chem. Phys. 109 (1998) 1687–1697;
(b) Y. Mo, L. Song, Y. Lin, Block-localized wavefunction (BLW) method at the density functional theory (DFT) level, J. Phys. Chem. A 111 (2007) 8291–8301.

[153] (a) X. Chang, Y. Zhang, X. Weng, P. Su, W. Wu, Y. Mo, Red-shifting versus blue-shifting hydrogen bonds: a perspective from ab initio valence bond theory, J. Phys. Chem. A 120 (2016) 2749–2756;
(b) Y. Mo, C. Wang, L. Guan, B. Braïda, P.C. Hiberty, W. Wu, On the nature of blueshifting hydrogen bonds, Chem. Eur. J. 20 (2014) 8444–8452.

[154] Z. Chen, F. Ying, X. Chen, J. Song, P. Su, L. Song, Y. Mo, Q. Zhang, W. Wu, XMVB 2.0: a new version of Xiamen valence bond program, Int. J. Quant. Chem. 115 (2015) 731–737.

[155] B. Braïda, E. Derat, S. Humble, P.C. Hiberty, S. Shaik, The valence bond workshop in Paris: the phoenix rises from the ashes or, has a love story with MO-based theories begun?, ChemPhysChem 13 (2012) 4029–4030

[156] R. Hoffmann, S. Shaik, P.C. Hiberty, A conversation on VB vs. MO theory: a never ending rivalry?, Acc. Chem. Res. 36 (2003) 750–756.

[157] S. Shaik, D. Danovich, W. Wu, P. Su, H.S. Rzepa, P.C. Hiberty, Quadruple bonding in $C_2$ and analogous eight-valence electron species, Nat. Chem. 4 (2012) 195–200.

[158] D. Danovich, P.C. Hiberty, W. Wu, H.S. Rzepa, S. Shaik, The nature of the fourth bond in the ground state of $C_2$: the quadruple bond conundrum, Chem. Eur. J. 20 (2014) 6220–6232.

[159] S. Shaik, H.S. Rzepa, R. Hoffmann, One molecule, two atoms, three views, four bonds?, Angew Chem. Int. Ed. 52 (2013) 3020–3033.

[160] G. Frenking, M. Hermann, Critical comments on "One Molecule, Two Atoms, Three Views, Four Bonds?", Angew. Chem. Int. Ed. 52 (2013) 5922–5925.

[161] D. Danovich, S. Shaik, H.S. Rzepa, R. Hoffmann, A response to the critical comments on 'One Molecule, Two Atoms, Three Views, Four Bonds?, Angew Chem. Int. Ed. 52 (2013) 5926–5928.

[162] (a) M. Hermann, G. Frenking, The chemical bond in $C_2$, Chem. Eur. J. 22 (2016) 4100–4108;
(b) W. Zou, D. Cremer, $C_2$ in a box: determining its intrinsic bond strength for the X $^1\sum_g^+$ ground state, Chem. Eur. J. 22 (2016) 4087–4099;
(c) M. Piris, X. Lopez, J.M. Ugalde, The bond order of $C_2$ from a strictly N-representable natural orbital energy functional perspective, Chem. Eur. J. 22 (2016) 4109–4115.

[163] S. Shaik, D. Danovich, B. Braïda, P.C. Hiberty, The quadruple bonding in $C_2$ reproduces the properties of the molecule, Chem. Eur. J. 22 (2016) 4116–4128.

[164] G. Frenking, M. Hermann, Comment on "The Quadruple Bonding in $C_2$ Reproduces the Properties of the Molecule", Chem. Eur. J. 22 (2016) 18975–18976.

[165] S. Shaik, D. Danovich, B. Braïda, P.C. Hiberty, A response to a comment by G. Frenking and M. Hermann on: "The Quadruple Bonding in C2 Reproduces the Properties of the Molecule", Chem. Eur. J. 22 (2016) 18977–18980.

[166] R. Zhong, M. Zhang, H. Xu, Z. Su, Latent harmony in dicarbon between VB and MO theories through orthogonal hybridization of $3\sigma_g$ and $2\sigma_u$, Chem. Sci. 7 (2016) 1028–1032.

[167] Y. Liu, T.J. Frankombe, T.W. Schmidt, Chemical bonding motifs from a tiling of the many-electron wavefunction, Phys. Chem. Chem. Phys. 18 (2016) 13385–13394.

[168] (a) A. Scemama, M. Caffarel, A. Savin, Maximum probability domains from quantum Monte Carlo calculations, J. Comput. Chem. 28 (2007) 442–454;
(b) M. Menéndez, A. Martín Pendás, B. Braïda, A. Savin, A view of covalent and ionic bonding from maximum probability domains, Comput. Theor. Chem. 1053 (2015) 142–149.

[169] B. Braïda, A. Savin, Private Communication.

[170] G.A. Gallup, Valence Bond Methods: Theory and Applications, Cambridge University Press, Cambridge, UK, 2002.

[171] W. Wu, Personal Communication.

[172] J. Olsen, Novel methods for configuration interaction and orbital optimization for wave functions containing non-orthogonal orbitals with applications to the chromium dimer and trimer, J. Chem. Phys. 143 (2015) 114102.