SEMIEMPIRICAL METHODS: CURRENT STATUS AND PERSPECTIVES*

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Abstract: Semiempirical methods for calculating potential surfaces are reviewed, with particular emphasis on MNDO and related methods. Topics include the rigorous derivation of semiempirical methods from first principles, the analysis of correlation effects, a comparison between semiempirical and ab initio transition states, and a survey of applications. Possible improvements for MNDO-type methods are discussed, and specific refinements are suggested.

1. INTRODUCTION

Over the past two decades the semiempirical methods of quantum chemistry have been described in several books[1-5]. Therefore the present paper does not attempt a comprehensive review but focuses on current semiempirical methods for computing potential surfaces, particularly those originating from the Dewar group, i.e. MINDO/3[6], MNDO[7], and AM1[8]. These methods are widely used in computational studies of organic molecules. This i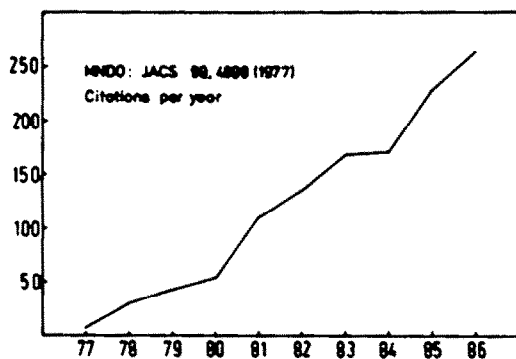s illustrated in Figure 1 which indicates that the number of citations of the original MNDO paper[7] now approaches 300 per year. There are probably two reasons for this popularity: First, the accuracy of the results is sufficient for many applications involving larger molecules as can be seen from Table 1 which lists average absolute MNDO errors[9] for a representative set of 138 molecules consisting of the elements H, C, N and O. Second, the methods are computationally efficient. This is demonstrated in Table 2 by timings for tetracene $C_{18}H_{12}$, buckminsterfullerene C_{60}, and an unbranched alkene $C_{50}H_{100}$. The geometry of the largest of these molecules with 297 geometrical variables can be optimized in less than 2 minutes on current supercomputers using a vectorized version of our program[10].

Figure 1. Citations per year for ref.7 from Science Citation Index.

In view of the widespread application of MNDO-type methods it seems desirable to reinvestigate their theoretical foundations based on important new developments in ab initio quantum chemistry over the past ten years. This will be done in the first part of the present paper which also includes a more detailed assessment of the performance of semiempirical methods in certain areas. The results from this dicussion will be used in the second part to explore some ideas for possible improvements of existing MNDO-type methods.

*Based on a lecture at the Dewar Symposium (Austin, February 26, 1988).

Table 1. MNDO: Mean absolute errors Δ for N comparisons[9].

	N	Δ
Heats of formation	138	6.3 kcal/mol
Bond lengths	228	0.014 Å
Bond angles	91	2.8°
Ionization potentials	51	0.48 eV
Dipole moments	57	0.30 D

Table 2. MNDO: Computation times (sec)[a]

Molecule	N_{AO}[b]	N_V[c]	T_{SCF}[d]	T_{GRD}[e]	T_{OPT}[f]
$C_{18}H_{12}$, D_{2h}	84	15	0.8	0.1	5.1
C_{60} , I_h	240	2	9.2	1.1	28.2
$C_{50}H_{100}$, C_s	300	297	14.6	5.1	104.3

a) For CRAY X-MP with a 8.5 ns cycle. In the scalar mode the times for
large molecules are higher by a factor of 10. b) Number of AOs.
c) Number of geometrical variables. d) Time for SCF calculation with
convergence criteria of 10^{-6} eV for the energy and 10^{-6} for the diagonal
density matrix elements. e) Time for gradient calculation.
f) Time for geometry optimization.

2. CURRENT STATUS OF SEMIEMPIRICAL METHODS

2.1 Derivation from first principles

The most rigorous theoretical justification for semiempirical methods rests on the theory of
effective valence shell Hamiltonians [11-13]. The basic concept of this approach is summarized as
follows [12]. Consider an infinite basis set consisting of core orbitals, valence orbitals, and
excited orbitals, and distinguish between two types of N-electron determinants: Those in the
primary space P with core orbitals filled, excited orbitals empty, and valence electrons
distributed among the valence orbitals in any conceivable manner, and those in the secondary space
Q with excitations from the core orbitals and/or into the excited orbitals. Now the objective is to
derive an effective valence shell Hamiltonian H^V such that a full configuration interaction (CI)
treatment in the primary valence space P yields the exact experimental energies E for the valence
states of a given system. This can be achieved by writing the exact Schrödinger equation in block
matrix form and solving formally for H^V. In standard matrix notation [12]:

$$\begin{pmatrix} H_{PP} & H_{PQ} \\ H_{QP} & H_{QQ} \end{pmatrix} \begin{pmatrix} C_P \\ C_Q \end{pmatrix} = E \begin{pmatrix} C_P \\ C_Q \end{pmatrix} \tag{1}$$

$$H^V = H_{PP} + H_{PQ}(E1_Q - H_{QQ})^{-1}H_{QP} \tag{2}$$

$$H^V C_P = E C_P \tag{3}$$

Hence an effective Hamiltonian exists which acts only on the valence space and nevertheless
produces the exact energies for all valence states. It is this effective Hamiltonian which
semiempirical methods try to approximate more or less successfully.

Moreover it is clear from the derivation that electron correlation is included partly in the
definition of the effective Hamiltonian (eq.(2)) and partly in the valence shell CI treatment

(eq.(3)). To be more specific any nondynamical correlation associated with near-degeneracies is recovered in the CI treatment whereas much of the dynamical correlation is incorporated into the Hamiltonian.

An ab initio evaluation of H^v is certainly desirable for an analysis of semiempirical methods. The computational implementation of eq.(2) requires a number of approximations[14]: Use of a large but finite basis set, a Rayleigh-Schrödinger perturbation expansion of the inverse matrix in eq.(2) around zero-order energies, and a quasidegenerate perturbation treatment through second or third order. This leads to an energy-independent Hamiltonian which includes nonclassical effective many-electron operators, i.e. three-electron terms in second order and four-electron terms in third order. Using these approximations ab initio calculations have been carried out for first- and second-row atoms[15-19], for transition metal atoms[20], for diatomic hydrides such as CH[21-23], for homonuclear diatomic molecules such as Li_2[24-25], O_2[26-27], and S_2[28], and for the simplest conjugated π-system (trans-butadiene)[29]. These calculations have established the effective Hamiltonian approach as a viable ab initio technique because the results are of similar accuracy as in more conventional ab initio studies employing basis sets of comparable quality.

In the present context the most important conclusions from these calculations are those [16,23,25,28,29] which relate the ab initio matrix elements of the effective Hamiltonian to existing semiempirical methods in order to check their validity and suggest possible improvements. The main results from this point of view are summarized in the following.

(a) In the case of atoms[15,16] the H^v approach leads to good agreement with the semiempirical one- and two-electron integrals[30] only after including a suitable average[16] of the nonclassical three-electron matrix elements of H^v. The semiempirical one-center integrals which have originally been derived from experimental energy levels can thus be reproduced by an ab initio procedure, within the accuracy of the latter.

(b) The H^v calculations for atoms[16,21] and for trans-butadiene[29] support the concept of reduced effective two-electron Coulomb interactions in current semiempirical methods[6-8]. The semiempirical Coulomb integrals are considerably lower than the corresponding ab initio values at the SCF level (from H_{pp} in eq.(2)). The lowering of the effective Coulomb repulsion is mainly due to σ-correlation in the case of trans-butadiene[29] (from the second term in eq.(2)) and to the nonclassical three-electron terms in the case of the atoms[16,21].

(c) The ZDO approximation for the two-center two-electron matrix elements of H^v holds reasonably well in a Löwdin orthogonalized basis[25]. The two-center two-electron Coulomb interaction from the H^v approach can be fitted[25] better with a Klopman-Ohno formula[31,32] than with a Mataga-Nishimoto formula[33].

(d) The one-center two-electron matrix elements of H^v show a correlation-induced bond length dependence[23,25,28] which is not included in current semiempirical schemes. Likewise, novel bond length dependences are suggested for several interactions on the basis of the H^v calculations [23,25,28].

(e) The generally assumed proportionality between resonance and overlap integrals turns out to be a reasonable approximation which can be improved by adding a second term proportional to the square of the overlap[23,25,28].

(f) The role of the nonclassical three-electron matrix elements of H^v which have no counterpart in traditional semiempirical methods requires further study. These terms are fairly large in atoms [15-18] and diatomic hydrides[21,23], but relatively small in S_2[28] and trans-butadiene[29]. It is not clear whether they can generally be absorbed with sufficient accuracy by averaging them into the one- and two-electron matrix elements[16].

After describing a number of interesting results from ab initio calculations based on the effective Hamiltonian approach[11,12] some practical limitations should also be pointed out (see

ref.13 for a critical theoretical discussion). First, at present the number of published H^v calculations seems too small to allow for safe generalizations, particularly with regard to the transferability of the results to larger molecules. Second, even in the favorable case of atoms [16,21], the quantitative accuracy of the H^v calculations is still limited as can be seen from a comparison between experimental and theoretical second- or third-order results (see e.g. Table 4 of ref. 21). Therefore, the H^v calculations have not yet reached the point where they could reliably predict an optimum semiempirical Hamiltonian and thus guide semiempirical developments into well-defined directions. Nevertheless, the effective Hamiltonian approach has already now been very valuable in clarifying the theoretical foundations of semiempirical methods, in providing new qualitative insights, and in suggesting certain improvements.

2.2 Analysis of correlation effects

As shown in the preceding section, a full CI treatment in a valence basis with a suitable effective Hamiltonian can, in principle, give exact energies for the valence states. This is the conceptual basis of the MNDOC method[34], a correlated version of MNDO. MNDOC employs a semiempirical Hamiltonian which is completely analogous to MNDO and which, in particular, contains reduced effective two-electron interactions accounting for a large part of the dynamical correlation (see eq. (2)). The correlation in the valence shell is treated explicitly in MNDOC (see eq. (3)).

Technically speaking a full CI treatment in the valence space becomes too expensive for larger molecules so that suitable approximations must be used. Our reference method for ground states is a configuration interaction between the SCF determinant and all singly or doubly excited configurations, optionally with corrections for higher excitations[35-37]. In the framework of the MNDOC approach the results from such CI calculations are reproduced quite efficiently and accurately by second-order perturbation theory, particularly the Brillouin-Wigner variant with Epstein-Nesbet denominators (BWEN), where the deviations from the CI correlation energies are usually less than 2 kcal/mol. Therefore, this perturbation approach is the method of choice in MNDOC calculations of ground states. In excited states[38], or generally in cases with complicated bonding situations, it is necessary to use the more accurate PERTCI treatment[39], i.e. CI for the most important configurations according to the usual selection criteria followed by a BWEN perturbation treatment for the remaining configurations.

After these technical preliminaries we turn to a comparison between MNDOC and MNDO in order to analyze correlation effects at the semiempirical level. As indicated before MNDOC is parametrized after including valence shell correlation explicitly while MNDO is parametrized at the SCF level. These parametrizations attempt to correct for the shortcomings of semiempirical models, in an average sense. Hence, MNDOC and MNDO differ in that the MNDO parameters must also account for the effects of valence shell correlation which are treated explicitly in MNDOC.

Table 3 compares the MNDO and MNDOC results for a set of 64 organic ground-state molecules. It is obvious that the results are of similar quality, MNDOC being slightly superior for heats of formation and bond angles, but not for bond lengths. This similar overall performance indicates immediately that correlation effects in organic ground-state molecules are so uniform that they can effectively be absorbed, in an average sense, by a semiempirical parametrization at the SCF level. This view is confirmed by a more detailed analysis of the correlation effects in MNDOC. First, the correlation energies are approximately additive, i.e. one can define bond correlation energies[34] (e.g. for C-H, C-C, C=C, C≡C) and then estimate the correlation energies for larger molecules by adding these bond contributions. The deviations between these estimated and calculated correlation energies are small, typically 2 kcal/mol or less. Second, the correlation-induced changes in optimized bond lengths are also rather small and quite similar for a given bond in different molecules, e.g. for C=C in different alkenes[34].

Table 3. Mean absolute errors for ground states (N comparisons)[34].

	N	MNDO	MNDOC
Heats of formation (kcal/mol)	64	6.2	5.3
Bond lengths (Å)	148	0.014	0.017
Bond angles (deg)	71	2.9	2.6

These regularities are found not only at the MNDOC level, but also in ab initio calculations. In analogy to the MNDOC case ab initio bond correlation energies have been derived[40] at the second-order Moller-Plesset level for 3 standard basis sets and 21 types of bonds involving the elements H,C,N,O and F. Estimates of the correlation energies of 26 other molecules based on additivity of these bond contributions show mean absolute errors of only 2-3 kcal/mol. Similar results have been obtained [41] at the fourth-order Moller-Plesset level for a smaller set of molecules, with a mean absolute deviation from additivity of less than 2 kcal/mol.

Indirect support for the hypothesis of fairly uniform correlation energies in the ground states of organic molecules comes from recent attempts to derive heats of formation ΔH_f from ab initio SCF total energies E_{SCF} by substracting appropriate multiples of empirical atomic constants A_j.

$$H_f = E_{SCF} - \sum_j n_j A_j \qquad (4)$$

The resulting deviations from experiment depend on the basis sets[42] used and on the number (M_j) of empirical constants A_j per atom. Table 4 summarizes the results for neutral ground-state molecules 43-45.

If one employs one empirical constant per atom the 3-21G heats of formation show average absolute errors similar to AM1 or MNDO while those for 6-31G* are lower. If one introduces several such constants per atom depending on its molecular environment the 6-31G* results become impressively accurate. This success at the SCF level[43-46] is, of course, only possible if the ab initio correlation corrections to the total energy can be absorbed in the empirical constants of eq.(4) which implies an approximate additivity of these corrections.

Table 4. Mean absolute errors Δ(kcal/mol) for heats of formation
obtained from ab initio SCF total energies (N comparisons).

M_j								
H	C	N	O	F	Basis	N	Δ	Ref.
1	1	1	1	1	3-21G	78	6.6	43
1	1	1	1	1	6-31G*	88	4.3	43
3	1	1	1	-	6-31G*	52	1.9	44
5	6	7	5	2	6-31G*	75	1.2	45

In summary there is strong evidence both from semiempirical and ab initio calculations that the correlation effects on energies[34,40-46] and geometries[34,42] are bondspecific, transferable, and rather uniform in ground states of organic molecules. Therefore these effects can be taken into account by a parametrization at the SCF level, and fast semiempirical SCF methods such as MNDO or AM1 are well suited for studying these systems.

2.3 Transition states

Qualitative arguments and experience from ab initio studies suggest that specific correlation effects may occur in electronically excited states, in reactive intermediates with unusual bonding situations, and in transition states of chemical reactions where bonds are being broken or formed. In these cases an explicit treatment of correlation is expected to be necessary even at the semiempirical level so that the MNDOC approach should be appropriate. This section will focus on

one of these areas, namely transition states, because there is an additional reason for this choice.

As often stated a major motivation in the development of semiempirical methods is the desire to study the detailed course of chemical reactions where theory may provide information which is hard to obtain experimentally, e.g. transition structures. MNDO-type methods may face an objection in this regard because they have been parametrized for ground-state minima on potential surfaces so that their predictions for transition states may be viewed merely as uncertain extrapolations on potential surfaces. It is therefore important to establish the reliability of semiempirical calculations in this area and to clarify the role of correlation effects in this connection. Due to the lack of sufficient experimental data this can only be done by comparing the semiempirical results with those from high-level ab initio calculations which are now available for transition states of small organic systems[42,47].

For these comparisons[48,49] we have selected a set of 24 thermal reactions on the potential surfaces of ethylene, formaldehyde, methanol, ketene, propene, formic acid, and glyoxal. This set includes six [1,2]- and two [1,3]- sigmatropic hydrogen shifts, five other intramolecular rearrangements, four 1,1 - and three 1,2- eliminations of H_2, and four other dissociation reactions. We find that the qualitative features of the potential surfaces are generally predicted by MNDO and MNDOC SCF calculations in complete analogy to the ab initio SCF calculations[48]. The same types of minima and transition states are obtained, with only one exception on the methanol surface[48]. When compared with the best correlated ab initio treatments, MNDO, MNDOC and ab initio SCF share one particular qualitative deficiency in that they predict significant barriers to [1,2]-hydrogen shifts in certain carbenoid species[48] which disappear at higher theoretical levels. Therefore, MNDO and MNDOC appear suitable for scanning potential surfaces to assess their qualitative features although it might happen that some feature may change at higher theoretical levels.

More detailed results are presented in Figure 2 and Table 5. It is obvious from Figure 2 that the optimized MNDOC and ab initio SCF geometries are quite similar for all planar transition states studied; the same applies for the nonplanar structures[48]. The statistical evaluation in Table 5 indicates that MNDOC reproduces the ab initio SCF transition structures slightly better than MNDO, the mean absolute deviation being 0.07 (0.03) Å for the bond lengths of "active" ("passive") bonds, 6° for bond angles, and 8° for dihedral angles. Furthermore, in the majority of cases, the MNDOC SCF transition structures are similar to the ab initio SCF one in the sence that every single
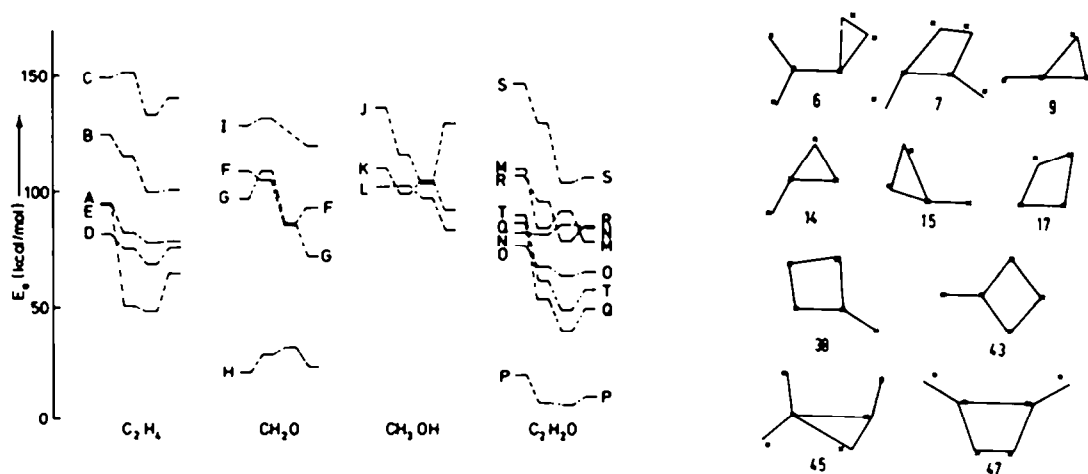

Figure 2   (a) Correlations between calculated barriers. From left to right for each system: MNDO SCF, ab initio SCF, ab initio BEST, MNDOC BWEN. See ref. 48 for details.(b) Planar structures drawn to scale. Solid lines - ab initio SCF, crosses - atomic positions in MNDOC.

Table 5. Mean absolute deviations[a] of transition state predictions[48].

	N[b]	MNDO	MNDOC	ab initio reference
Bond length (Å)	112	0.057	0.056	SCF
-active[c]	70	0.078	0.073	SCF
-passive[c]	42	0.018	0.025	SCF
Bond angle (deg)	58	7.9	6.2	SCF
Dihedral angle (deg)	20	11.6	7.9	SCF
Barrier (kcal/mol)	24	13.6	11.2	SCF
	22	21.9	8.7	BEST

a) Semiempirical vs. ab initio. b) Number of comparisons. c) "Active"
bonds are broken or formed, "passive" bonds remain formally unchanged.

deviation in the bond lengths and angles is below 0.1 Å and 10°, respectively. Based on these
similarities one may usually expect semiempirical SCF transition structures to be realistic
although there will certainly be exceptions. Therefore the following two checks are always
recommended.

First, for a given reaction, the energy difference between reactants and products should be
calculated reasonably well because otherwise general considerations such as the Bell-Evans-Polanyi
principle[50] and the Hammond postulate [51] would suggest that the transition state might be too early
or too late on the reaction coordinate. Second, a correlated calculation should be carried out at
the SCF transition structure to make sure that the SCF configuration is dominant and represents the
zero-order wavefunction well. This is true for most of the thermal reactions studied[49] but there
are several cases where the SCF configuration contributes less than 90% to the correlated
wavefunction. In these cases the transition structure should be reoptimized at the correlated level
which may lead to changes of more than 0.1 Å and 10° in distances and angles, respectively[49].

Correlated calculations at the SCF transition structures also show that activation energies
may be influenced significantly by correlation effects even when geometries are not affected much.
For the reactions studied inclusion of valence shell correlation in MNDOC tends to decrease the SCF
barriers by varying amounts, in the range between 0 and 20 kcal/mol. This is due to the fact that
the correlation energy is usually larger in the transition state than in the reactants which is
intuitively reasonable since bonds are being broken and formed in the transition state. This
"extra" correlation energy is typically of the order of 10 kcal/mol in the MNDOC framework. It is
not taken into account in MNDO SCF calculations which consequently tend to overestimate the
barriers.

Figure 2 illustrates how the calculated activation energies are lowered by the correlation
corrections which are often actually of similar magnitude at the MNDOC and ab initio levels[49]. If
we accept the best available correlated ab initio barriers as reliable reference data, the
correlated MNDOC barriers are more accurate than the MNDO SCF ones, with a mean absolute deviation
of about 9 kcal/mol (or 11%) for MNDOC (see Table 5). Hence explicit inclusion of electron
correlation does help to improve the semiempirical activation energies.

In conclusion it is often sufficient in semiempirical studies of thermal reactions to locate
the transition structures at the SCF level whereas barriers should preferably be determined with
correlation corrections. This procedure is computationally feasible because the calculations become
costly only if geometry optimizations have to be carried out at the correlated level[34,49]. More
detailed guidelines are available[49] concerning the treatment of correlation in more complicated
cases. Generally speaking the comparisons between the semiempirical and high-level ab initio
results have clarified the accuracy which can be expected in semiempirical calculations of
transition states, not only for geometries and energies (as discussed here), but also for
zero-point vibrational corrections to barriers and for activation entropies[48].

2.4 Survey of applications

For an assessment of the current status of MNDO-type methods it would certainly be desirable to present comparisons with experiment and to discuss applications as comprehensively as possible. The literature up to 1982 has been reviewed[52] for MINDO/3 and MNDO based on the entries in Chemical Abstracts, with some additional references from 1983 and 1984. In view of the growing number of publications in this area (see Figure 1) a complete survey of applications is not feasible. Therefore this section will concentrate mainly on MNDO applications since 1983 and list references to selected papers which either give comprehensive evaluations for certain properties or report studies of chemical reactions.

Comparisons with experimental heats of formation, geometries, ionization potentials, and dipole moments are usually included in the papers which provide the parameters for a given element. MNDO parameters are available for hydrogen[7,9], lithium[53], beryllium[54], boron[55], carbon[7,9], nitrogen[7,9], oxygen[7,9], fluorine[56], aluminum[57], silicon[58,59], phosphorus[58], sulfur[60,61], chlorine[62], zinc[63], germanium[64], bromine[65], tin[66], and iodine[67]. Systematic MNDO evaluations have been reported for cations[68] (119 closed-shell and open-shell systems; H,C,N,O), for radicals[69] (62 systems; H,C,N,O,F,Cl), and for anions[70] (65 systems; H,C,N,O,F). First and higher MNDO ionization potentials[71,72] (289 ionizations between 6 and 20 eV; H,C,N,O,S) show a mean absolute error of 0.55 eV at the SCF level (Koopmans' theorem) which drops to 0.29 eV after including correlation corrections[72]. Electron affinities[70] are calculated with a mean absolute error of 0.43 eV in molecules with a delocalized HOMO (26 systems; H,C,N,O,F). MNDO vibrational frequencies[73] (686 vibrations of 51 molecules; H,C,N,O,F,S,Cl) show fairly regular deviations from experiment, e.g. stretching frequencies being too high by 10-20%. Systematic MNDO evaluations are also available for proton affinities[74,75] (see ref.76 for AM1 results), isotope effects[77,78], and excited states[38,79].

Theoretical studies of chemical reactions are among the most important applications of MNDO and related methods. The following list contains a number of typical examples for such applications.

a) Rearrangement of azulene to naphthalene[80].

b) Rearrangement of tetra-tert-butyltetrahedrane to tetra-tert-butylcyclobutadiene[81] and analogous reaction in the tetramethyl cation[82].

c) Allowed and forbidden dimerisations of benzene[83,84].

d) Stereoselectivity of the addition of alkylidenecarbenes to olefines[85].

e) Stereospecific [2+2] cycloaddition of cyclopentyne with olefines[86].

f) Regiospecific alkylation of amides[87].

g) Regioselectivity in [3+2] cycloadditions and dipolar 1,4 cycloadditions[88,89].

h) Regioselective second metalation of Li-substituted aromatic systems[90,91].

i) Mechanism of the Canizzaro reaction[92].

j) Mechanism of the Claisen rearrangement[93].

k) Mechanism of the benzilic acid and related rearrangements[94].

l) Cheletropic reactions of polycyclic compounds[95].

m) Decarbonylation of neutral and cationic tropones and benzotropones[96].

n) Unimolecular reactions of methyl acetate and its sulphur analogues[97].

o) Reactions of bent alkynes with ethylene, water, and hydroxide anions[98].

p) Hydroboration of alkenes, alkynes and carbonyls[99,100].

q) Photochemical [1,3] OH-shift in $CH_2=CH-CH_2-OH$[101].

r) Photochemical rearrangement of naphthvalene to naphthalene[102].

s) Photochemical α-cleavage in singlet and triplet states of formaldehyde[103].

t) Alkylation of nucleophiles by diazonium ions as a model for DNA reactions[104].

u) Reaction of atomic oxygen (^{3}P) with organic molecules as a model for enzymatic reactions (cytochrome P450)[105-108].

Although the above list is certainly far from being complete it should indicate what types of MNDO applications are feasible in the field of chemical reactivity. Concluding this section it is

hoped that the literature given[6-9,34,38,48,49,52-108] will enable the reader to assess the strengths and weaknesses of current semiempirical methods and to form an own opinion on their capabilities.

3. PERSPECTIVES

3.1 General considerations

In spite of the usefulness of the existing MNDO-type methods there is always the need for improvements. From an application-oriented point of view the following features would seem desirable in the development of an improved method.

a) The results should become more accurate (cf. Table 1).

b) Calculations should be possible for still more elements including e.g. transition metals and heavy main-group elements.

c) Reliable results should be obtained for more properties. As an example, photochemical applications would benefit if the ground-state surface and the lower excited-state surfaces could be calculated with the same accuracy.

d) Any new semiempirical method should be designed such that analytical first and second derivatives are available for the efficient exploration of potential surfaces.

e) The computational speed of the current methods should be retained as much as possible (cf.Table 2).

From a more technical point of view it would also be advantageous to formulate a new semiempirical method in terms of a Gaussian basis to make use of available ab initio codes for integral evaluation, e.g. in the context of analytical derivatives.

In principle there are two ways for improving existing semiempirical methods, either with regard to the underlying theoretical model or with regard to the parametrization. When faced with this choice it seems more promising to aim for improvements in the model. This follows from a comparison of existing methods: The superiority of MNDO over MINDO/3, for example, can be traced back to a more refined treatment of the two-center Coulomb interactions since it can be shown[109] that the inclusion of higher multipole interactions in MNDO produces specific effects in the calculation of molecular properties which account for most of the qualitative differences between MNDO and MINDO/3. Likewise, in those cases where MNDOC is superior to MNDO, one can usually find specific correlation effects which are responsible for these differences. Also relevant in this connection is the comparison between AM1 and MNDO. AM1 is based on the same theoretical model as MNDO but uses a more flexible and highly parametrized core repulsion function. For certain important areas of application AM1 is more suited than MNDO but the mean absolute errors for the two methods remain of comparable magnitude and are generally only slightly lower in AM1. Given the considerable effort that has gone into the AM1 parametrization it seems unlikely that further significant overall improvements of an MNDO-type method can be found by a mere reparametrization.

Looking for improvements in the underlying theoretical model it should be clear from our previous discussion that correlation effects are presently not the limiting factor for the accuracy of MNDO-type treatments, at least in the case of ground-state organic molecules. Therefore the next sections will focus on improvements at the SCF level which is certainly appealing from a computational point of view.

3.2 Effective core potentials

The core electrons are treated in MNDO-type methods as point charges located at the respective nucleus, i.e. each core electron is assumed to reduce the effective nuclear charge by 1. Many ab initio studies over the past decade have shown, however, that in addition to this zero-order effect the core electrons produce an effective repulsive potential acting on the valence electrons which is mainly due to exchange repulsion and orthogonality constraints (see ref.110 for a review). If one includes these effective core potentials properly, ab initio valence-electron calculations lead to similar results for relative energies, geometries, and force fields[111] as ab initio all-electron

calculations with similar basis sets. There seems to be a general consensus that the effective core potentials are best represented in semilocal form[110]. Simple Gaussian expansions for these potentials have been published for most atoms in the Periodic Table along with compact Gaussian basis sets[112-114]. Computer codes are available for the relevant integrals up to analytical second derivatives[115] which can easily be incorporated into semiempirical programs provided that one is prepared to work with Gaussian basis sets which is desirable anyway (see above).

Therefore it seems feasible to improve semiempirical models by explicitly including effective core potentials which have proven to be realistic in ab initio studies[110-114]. This will lead to an additional steep short-range repulsion between atoms with core electrons. An improved description of the core electrons is expected to be especially important for atoms with a large core, e.g. for second-row atoms and other heavy atoms where MNDO faces more problems than in the first row. For atoms on the left side of the Periodic Table, e.g. the alkali metals, the additional introduction of a core-polarization potential may be necessary to account for the relatively high polarizability of the corresponding core electrons as shown in recent ab initio work[116].

3.3 Orthogonalization and penetration effects

Turning to the valence electrons it is well-known that the semiempirical integral approximations are best justified when using a Löwdin orthogonalized basis set[117,118]. In this case the NDDO approximation for the two-electron integrals is valid through second order in overlap [119-121], and numerical calculations have confirmed that the third-order corrections to these two-electron integrals are small[122]. However, the situation is less favorable for the one-electron integrals[120,121,123-127]. This can be seen most clearly if the transformation

$$^{\lambda}H = S^{-1/2} H S^{-1/2} \tag{5}$$

of the one-electron core Hamiltonian matrix from the usual nonorthogonal basis to the Löwdin orthogonalized basis ($H \rightarrow {}^{\lambda}H$) is written for the special case of a homonuclear molecule with two orbitals (ϕ_{μ} at atom A, ϕ_{ν} at atom B, overlap $S_{\mu\nu}$):

$$^{\lambda}H_{\mu\mu} = H_{\mu\mu} - S_{\mu\nu}M_{\mu\nu}/(1-S_{\mu\nu}{}^2) \tag{6}$$
$$^{\lambda}H_{\mu} = M_{\mu\nu}/(1-S_{\mu\nu}{}^2) \tag{7}$$
$$M_{\mu\nu} = H_{\mu\nu} - S_{\mu\nu}(H_{\mu\mu}+H_{\nu\nu})/2 \tag{8}$$

Eqs.(6)-(8) are exact. The approximate expressions from a second-order expansion of the $S^{-1/2}$ matrix[117-121] have the same structure but neglect the denominators $(1-S_{\mu\nu}{}^2)$ in eqs.(6)-(7) which approach 1 for small overlap.

In MNDO-type treatments the two-center matrix elements of the core Hamiltonian, i.e. the resonance integrals, are assumed to be proportional to the corresponding overlap integrals. According to eq.(7) this seems reasonable since there is agreement in the literature that the quantity[128] $M_{\mu\nu}$ (see eq.(8)) should be roughly proportional to the overlap. As for the one-center matrix elements, MNDO-type treatments formally only include the first term of eq.(6), but not the second one which arises from the orthogonalization. This second term is repulsive since $S_{\mu\nu}$ and $M_{\mu\nu}$ usually have opposite signs, and it depends on the bond length approximately like the square of the overlap (see above). In the two-orbital case this repulsive term is easily seen to be responsible for the fact that antibonding orbitals are destabilized more than bonding orbitals are stabilized, relative to the atomic orbitals. Moreover, looking at the He_2 case, it is obvious that this term also causes most of the Pauli exchange repulsion between closed shells. Considering its physical significance it seems advisable to include this repulsive term explicitly in improved MNDO-type models. A reasonable approximation for the general case of a polyatomic molecule may be provided by parametric expressions based on a second-order expansion of the $S^{-1/2}$ matrix.

With regard to the two-center Coulomb interactions current semiempirical methods usually neglect the penetration integrals[1-5], i.e. they assume that the interaction of an electron at atom A with a point charge at the nucleus of atom B is of the same magnitude as the interaction with a valence s electron at atom B which is certainly not true in reality. An analytical evaluation of the penetration integrals (i.e. of the differences between these two interactions) shows that they are attractive and asymptotically approach zero like the square of an overlap. The same asymptotic behavior is also found for the repulsive orthogonalization terms (see above) so that it would seem consistent[127] to include the penetration integrals along with the orthogonalization terms and thereby improve the description of the two-center Coulomb interactions. The actual representation of the penetration integrals in an MNDO-type framework must, of course, be compatible with that of the other Coulomb interactions[6-8].

3.4 Preliminary test of proposed improvements

The discussion in the preceding sections suggests that MNDO-type models may be improved by explicitly including effective core potentials, orthogonalization corrections, and penetration integrals into the one-center part of the core Hamiltonian. It should be stressed that these ideas are by no means new[119-131] and that some of these refinements are at least partly incorporated in other semiempirical methods[130,131]. In the existing MNDO-type treatments[6-8] the three terms above must "somehow" be contained in the core repulsion function. The simple exponential function used in MNDO is certainly overburdened when trying to represent these three physically distinct interactions. In AM1 the core repulsion function is more flexible and can therefore mimic these interactions more closely, but even so the resulting net repulsion in AM1 does not depend on the charge distribution in the molecule wheras the interactions above are, of course, population-dependent.The following improvements may be expected from the suggested extension of MNDO-type models.

(a) The use of effective core potentials should improve the description of second-row and heavier atoms (see section 3.2).

(b) The inclusion of orthogonalization corrections should improve the results for excited states (see section 3.3).

(c) One may hope for a general gain in accuracy because additional physically important interactions are included in the model.

In order to check these expectations we have carried out some very preliminary tests of a crude implementation of this approach. Table 6 gives an indication of the results obtained for hydrocarbons[132], with the understanding that the formalism is certainly not yet final and that the parametrization has therefore not yet been pushed to its limit. It is obvious from Table 6 that the ground-state results from these preliminary tests are already of similar quality as in MNDO but that the energies of the excited states are much improved as expected (see above).

Table 6. Mean absolute errors for hydrocarbons (N comparisons)

	N	MNDO[9]	TEST[a]
ΔH_f(kcal/mol)	58	6.0	6.3
Bond lengths (Å)	104	0.011	0.012
Bond angles (deg)	38	1.9	1.7
Dipole moments (D)	11	0.25	0.12
IP_{vert} (eV)[b]	22	0.41	0.26
E_{vert}(eV)[c]	30	1.49	0.38

a)Approximations as in MNDO except: Effective core potentials according to ref. 129, orthogonalization corrections from parametric expressions based on second-order expansion of $S^{1/2}$, Klopman-Ohno scaling of penetration integrals, no extra core repulsion function. b) First vertical ionization potential (Koopmans' theorem). c) Vertical electronic excitation energies.

Given the preliminary nature of these tests it seems probable that the errors in the last column of Table 6 can be reduced in the future.

3.5. Larger basis sets

Another potential improvement of semiempirical SCF methods involves the use of a split-valence basis set, in analogy to ab initio methods where e.g. the 3-21G results are much superior to the STO-3G results without costing too much additional computational effort[42]. In a semiempirical context, however, one may be more sceptical about the prospects of a split-valence basis set. The use of such a basis would increase the computation times on a scalar computer by almost an order of magnitude and thus compromise the computational efficiency which is one of the trademarks of existing semiempirical methods. To justify this drawback the results from such an approach ought to be much more accurate than e.g. from MNDO. This goal has not been achieved in an exploratory study [133] using a split-valence basis set in the framework of MNDO-type approximations. Therefore the suggestions in the preceding sections would seem to be more promising than the introduction of a split-valence basis set.

MNDO-type methods in their present form do not include d-orbitals in their minimal valence basis. In the case of second-row and heavier elements this choice restricts applications to those compounds where these elements appear in their normal valency. However, systematic ab initio studies have shown[42] that even for such compounds the basis set should contain d-orbitals, e.g. for a reliable prediction of bond lengths. For hypervalent compounds d-orbitals are mandatory[42], of course. At the semiempirical level an INDO-based method (SINDO1[130]) has recently been extended to second-row elements[134], with acceptable results being obtained only after including d-orbitals in the basis. The combined evidence from ab initio and semiempirical calculations thus suggests that any improved MNDO-type model should make use of an spd-basis for second-row or heavier elements. This is probably at least as important as the introduction of effective core potentials for these atoms.

3.6. Reference data for energies

In the development of MNDO-type methods heats of formation at 298 K have been employed as reference data in the parametrization although the calculations yield only total energies and binding energies directly. The conversion to heats of formation at 298 K assumes implicitly that the zero-point vibrational energies and the thermal energies for going from 0K to 298 K are composed of additive increments which can be absorbed by the semiempirical parametrization. There is some independent evidence for the validity of this assumption [135,136] (see also section 2.2). A direct confirmation has recently been obtained[137] by a test in which the MNDO method has been reparametrized for hydrocarbons using binding energies instead of heats of formation as reference data and keeping everything else as in MNDO. The resulting parameters were very close to the MNDO ones, and the overall performance of the results was very similar to MNDO. Hence, the choice of heats of formation as reference data is not responsible for weaknesses in the existing methods[6-8]. Nevertheless, for the sake of theoretical consistency, it seems preferable to use binding energies for this purpose in future parametrizations.

4. CONCLUDING REMARKS

The present paper has attempted to review the current status of semiempirical MNDO-type methods and to discuss the perspectives for their further improvement which has led to some specific suggestions for refinements of MNDO-type models. Much of our discussion benefits from the progress in the ab initio field over the past decade which helps to clarify the theoretical foundations of semiempirical methods, to analyze their performance in certain areas, and to provide new ideas and guidance for further methodical developments.

Applications of MNDO-type methods have been treated only briefly in the present paper, mainly by a survey of the literature which indicates the widespread use of the semiempirical methods originating from the Dewar group. Looking at the literature there seems to be the tendency for a combined use of the available computational tools[52] (i.e. molecular mechanics, semiempirical, ab initio) to solve chemical problems which may involve the development of truly integrated approaches [138,139] where the electronically important part of a large system is treated as accurately as needed and the remainder by a reasonable model. It is anticipated that the combined use of computational methods will become more important in future studies of chemical behaviour and may even open new areas of application.

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