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# The Electrostatical Molecular Potential – A Tool for the Prediction of Electrostatic Molecular Interaction Properties

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Starting from the molecular potential we get, by using elementary electrostatics, information about energetically favoured regions for interaction with ions and dipoles around $H_2O$ and $H_2CO$. The molecule–dipole interaction is represented by the electric field patterns.

**Key words:** Electrostatic potential – Molecular interaction properties.

## 1. Introduction and Method

The molecular electrostatic potential (MEP) of the electronic distribution and the nuclear charges of molecules is an informative tool for the prediction of protonation sites or reactions of molecules with electrophilic agents. Despite time-consuming computations the MEP is widely used on the *ab initio* [1–6] and the semi empirical level [7–10]. Quantum chemists have felt largely intuitively how much information can be extracted from the MEP. For example several empirical formulae combine the interaction energy of hydrogen bonded systems with local values of the potential [11, 12]. The aim of the present paper is to show how the MEP may be used in a general way to represent interaction properties. This model is a heuristic method for the interpretation of intermolecular interactions. We studied the representation of interactions with point charges and point dipoles in a consistent manner.

The MEP $V(\boldsymbol{r})$ arising from a molecule is defined by the superimposed electronic and nuclear charge distribution $\rho(\boldsymbol{r})$ and is a solution of the Poisson equation [13]

$$\Delta V(\boldsymbol{r}) = -\frac{\rho(\boldsymbol{r})}{\varepsilon_0}. \tag{1}$$

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Within the LCAO-MO framework the general solution

$$V(\boldsymbol{r})=\frac{1}{4\pi\varepsilon_0}\int\frac{\rho(\boldsymbol{r}')}{|\boldsymbol{r}-\boldsymbol{r}'|}\,d^3r' \tag{2}$$

is given in terms of an atomic basis set $\{\chi_\mu\}$ by [1]

$$V(\boldsymbol{r})=\frac{1}{4\pi\varepsilon_0}\left[\sum_\alpha\frac{z_\alpha}{|\boldsymbol{r}-\boldsymbol{R}_\alpha|}-\sum_{\mu,\nu}P_{\mu\nu}\int\frac{\chi_\mu^*(\boldsymbol{r}')\chi_\nu(\boldsymbol{r}')}{|\boldsymbol{r}-\boldsymbol{r}'|}\,d^3r\right]. \tag{3}$$

To discuss the usefulness of the MEP for the interpretation of interaction properties we start from the general expression of the electrostatic interaction energy $E^{ei}$ of two charge distributions $\rho_\mathrm{A}$ and $\rho_\mathrm{B}$, located at separate centres of the molecules A and B, resp.

$$E^{ei}=\iint\frac{\rho_\mathrm{A}(\boldsymbol{r}_\mathrm{A})\rho_\mathrm{B}(\boldsymbol{r}_\mathrm{B})}{|\boldsymbol{r}_\mathrm{A}-\boldsymbol{r}_\mathrm{B}|}\,d^3r_\mathrm{A}\,d^3r_\mathrm{B}. \tag{4}$$

Eq. (4) can be rewritten as

$$E^{ei}=\int\rho_\mathrm{A}(\boldsymbol{r}_\mathrm{A})\cdot V_\mathrm{B}(\boldsymbol{r}_\mathrm{A})\,d^3r_\mathrm{A}. \tag{5}$$

If we expand $E^{ei}$ into a Taylor series at $\boldsymbol{r}_\mathrm{A}=0$ we obtain

$$E^{ei}=\int\rho_\mathrm{A}(\boldsymbol{r}_\mathrm{A})\cdot V_\mathrm{B}(0)\,d^3r_\mathrm{A}+\int\rho_\mathrm{A}(\boldsymbol{r}_\mathrm{A})\cdot\boldsymbol{r}_\mathrm{A}(\boldsymbol{\nabla}V_\mathrm{B}(0))\,d^3r_\mathrm{A}+\cdots. \tag{6}$$

The first term is the potential energy of a point charge in the field of molecule B, and the second term is the appropriate potential energy of a dipole in the electric field [13]

$$\boldsymbol{E}(\boldsymbol{r})=-\boldsymbol{\nabla}V(\boldsymbol{r}). \tag{7}$$

Thus the interaction of two molecules can be described such that one molecule (here A) is represented by a multipole series and for the other molecule the MEP and their derivatives are employed. The expansion (6) may be extended to higher terms than molecular dipole moments. For clarity we neglected terms higher than dipoles.

In our calculations we used semi empirical CNDO/2 wavefunctions and approximation III of Ref. [7]: all nuclear attraction integrals which contain basis functions $\chi_\mu$ and $\chi_\nu$ located at the same atom are computed exactly by the STO-3G expansion method [15]. The other terms are neglected. To calculate the electric field strength we approximated Eq. (7) by

$$\boldsymbol{E}(\boldsymbol{r})=-\sum_{i=1}^{3}d^{-1}\,\delta V_i(\boldsymbol{r})\boldsymbol{e}_i, \tag{8}$$

where $d$ means the point distance along the coordinate axis $i$ $(=x, y, z)$ and

$$\delta V_i(\boldsymbol{r})=V(\boldsymbol{r}+d\boldsymbol{e}_i)-V(\boldsymbol{r}) \tag{9}$$

is the change of the potential along axis *i*. For a sufficiently small increment *d* Eq. (8) is a good approximation to Eq. (7). In principle the electric field strength can be given in analytical form by the derivation of Eq. (3), but a new type of integrals must be calculated and the computational expanse increases rapidly.

## 2. Results and Discussion

### *2.1. The MEP as an Ion Interaction Indicator*

A typical example of electrostatic interactions is the ion–molecule interaction. Molecular complexes with metal and alkali earth cations have been studied extensively [16–18]. Energy partitioning techniques [19, 20] have often been used to study the nature of the ion binding. In all cases the electrostatic contribution dominates and near the equilibrium ion–molecule distance it can be used to represent the total interaction energy [21]. Because of this well-known situation we present the results for the representation of ion interactions by the MEP only in a summarized form. In Fig. 1 the potential curves for water and formaldehyde along the $C_2$ axis on the oxygen side are plotted. The results of ab initio supermolecule calculations including several cations (for $H^+$ only the minimum site is indicated) are also given. The arrays in Fig. 1 represent the range in interaction energies and equilibrium distances dependent on molecular geometry, basis set etc. In all cases the interaction energies with respect to "exact" distances follow the electrostatic curve. The casual numerical agreement cannot be overrated, but the tendency justifies the use of the MEP to discuss the possibility and the strength of ion–molecule interactions. The MEP opens up the possibility to predict ion interactions and to explain the specific selectivity of molecules toward ions.

### *2.2. Electric Field Strength*

The electric field strength $\boldsymbol{E}$ represents the electrostatic force field of the charge distribution $\rho(\boldsymbol{r})$ outside the molecular skeleton without any consideration of polarization effects on the partner sites. Such an $\boldsymbol{E}(\boldsymbol{r})$ is only an idealization of the real intermolecular forces. On the other hand the field patterns give a clear picture of the strength and orientation of electrostatic forces. Thus the field orientation indicates the preferred way to form ion–molecule complexes, and the preferred direction of an associated dipole. To our knowledge only Ranghino and Clementi have so far presented electric fields based on a point charge approximation for the molecule [22]. In a more general way we calculated the field strength $\boldsymbol{E}(\boldsymbol{r})$ using approximation (8) outside the van der Waals volume of the molecules. The field strength of water and formaldehyde in two perpendicular planes is given point by point in Fig. 2. The maximum field strength near the van der Waals distance are of the order of $10^7$ V/m. This is the effective field strength for interactions with small ions, such as $Li^+$. The field strength in the oxygen region of formaldehyde is smaller than around the water oxygen, because of the small electronic charge on the former.

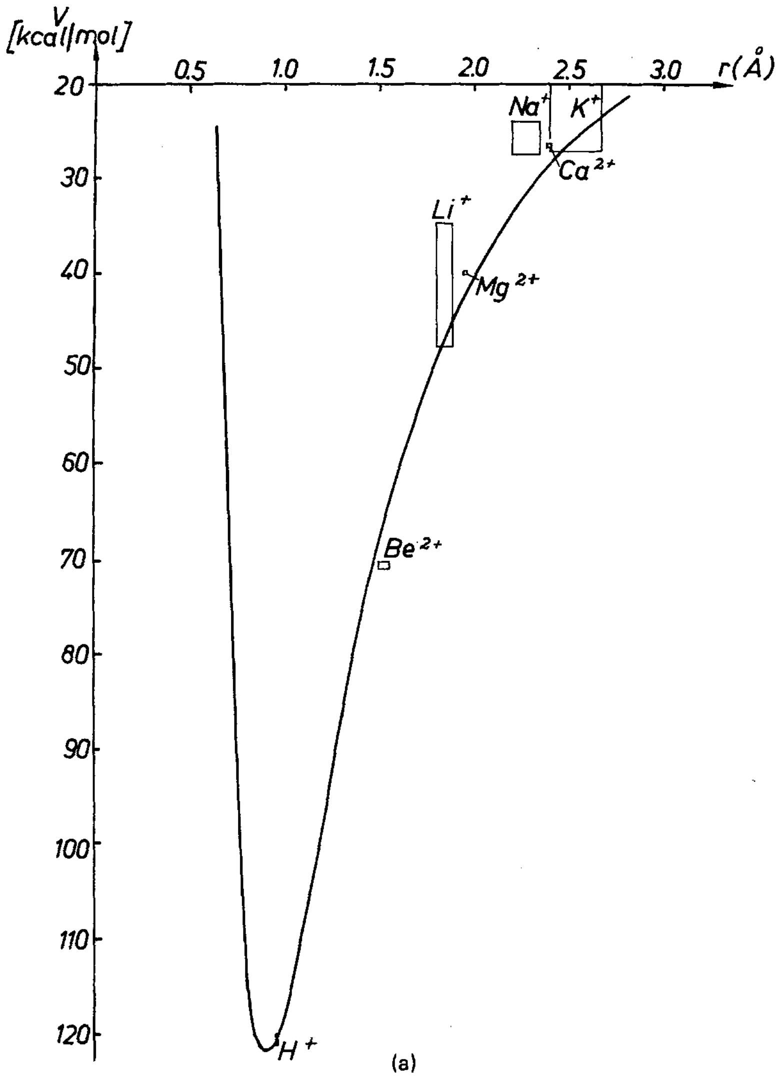

**Fig. 1.** Electrostatic potential curve along the $C_2$ axis on the oxygen side for *a* water, and *b* formaldehyde. The indicated results for *ab initio* calculations were taken from Ref. [17]

### 2.3. Dipole Interaction

According to Eq. (6) we calculated the potential energy of a polarizable dipole in the field $\boldsymbol{E}(\boldsymbol{r})$. Such a consideration may be used as a model for a hydrogen bonded system. It is well known that the electrostatic contribution to hydrogen bonding at equilibrium geometry approximates the total interaction energy fairly well. The other repulsive and attractive contributions nearly compensate each other [23]. We used this fact to represent the interaction properties of polar molecules by simple electrostatics. We tested this approximation in order to investigate preferred binding sites of water and formaldehyde with a water dipole $\mu = 1.85$ D

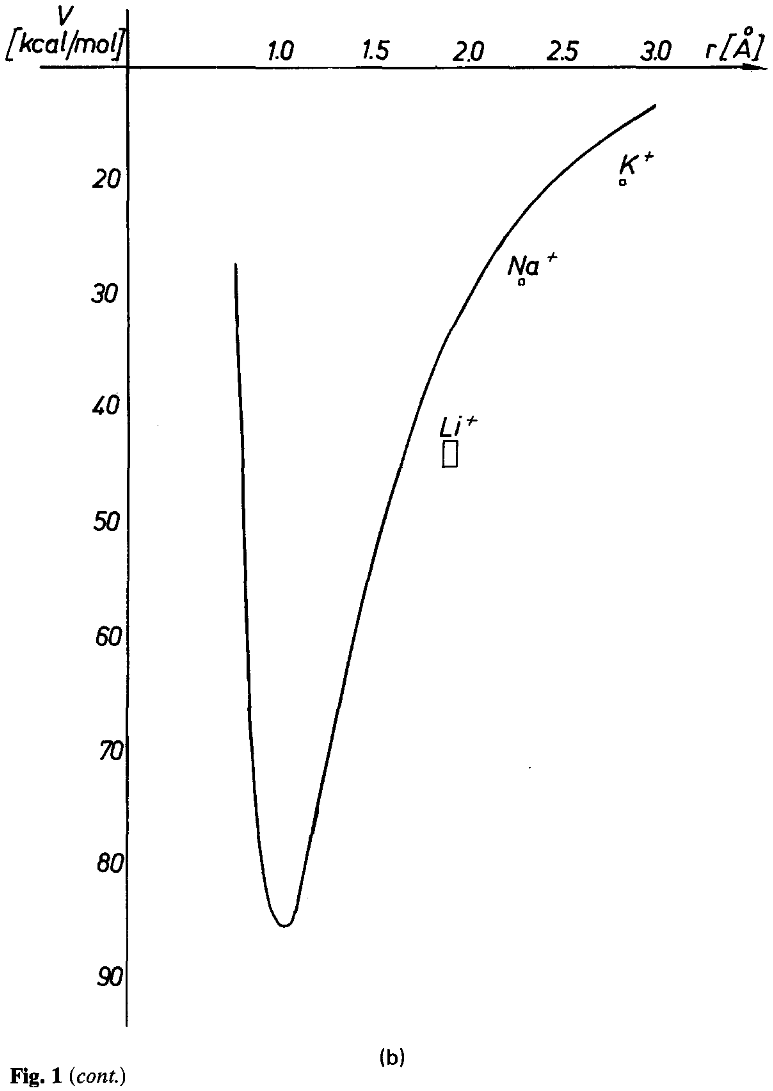

Fig. 1 (*cont.*)

having a polarizability $\alpha = 1.48$ Å$^3$. The preferred interaction sites calculated for our two molecules with distances from oxygen and carbon greater than 2 Å are depicted in Fig. 3. For these points the field orientation is also shown by arrows. The field orientation coincides with the preferred orientation of the associated dipole. Thus the possible structures of molecular aggregates can be predicted and the interaction energy can be estimated. In all cases the contribution of the electrostatic interaction energy according to Eq. (6) does not appreciably exceed the value of 10 kcal/mole. This is a good approximation to the real H-bond energy in these systems of about 5 kcal/mole. The results for the association of a water dipole around the water molecule as given in Fig. 3a are in good agreement with

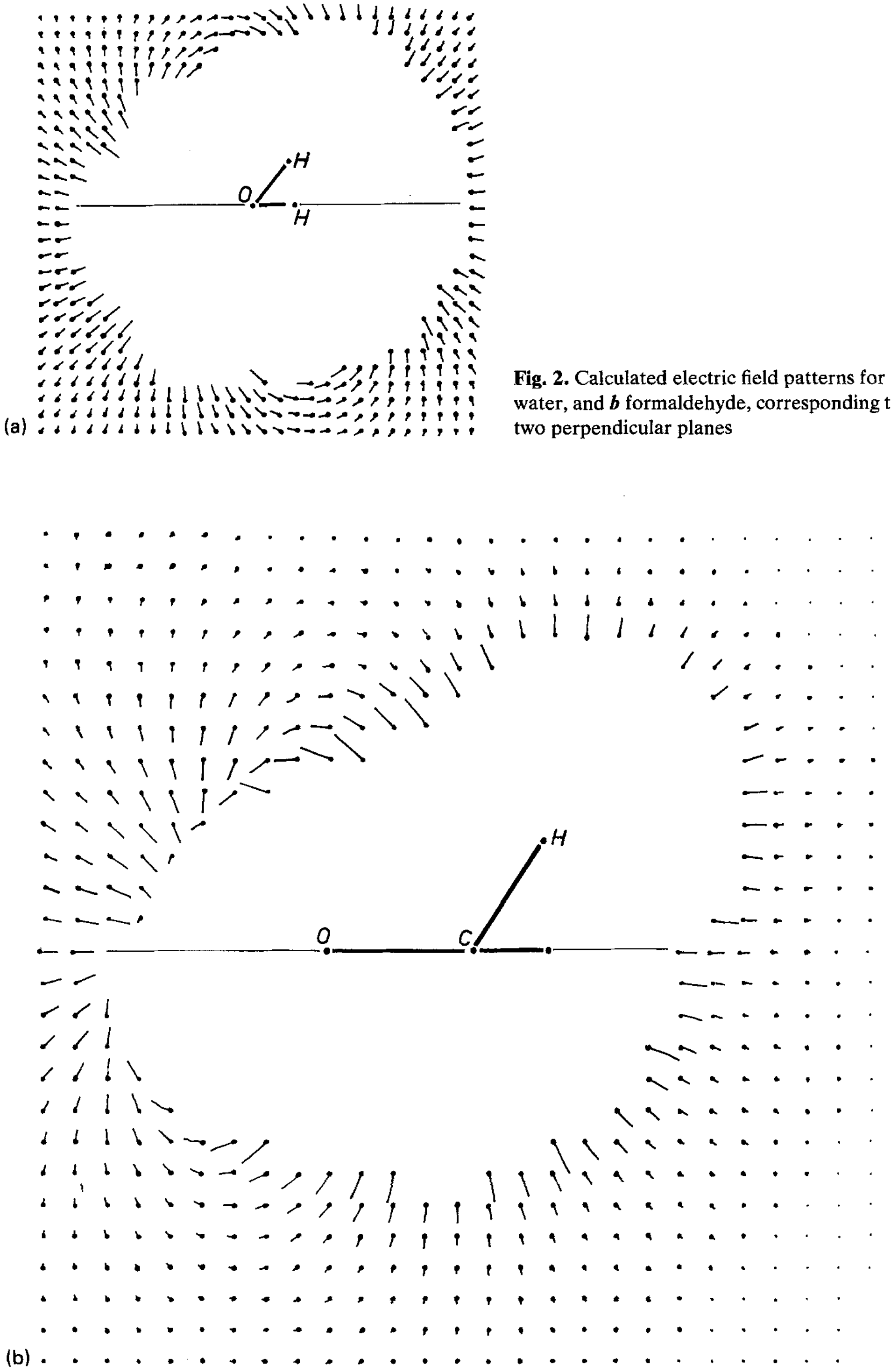

**Fig. 2.** Calculated electric field patterns for ***a*** water, and ***b*** formaldehyde, corresponding to two perpendicular planes

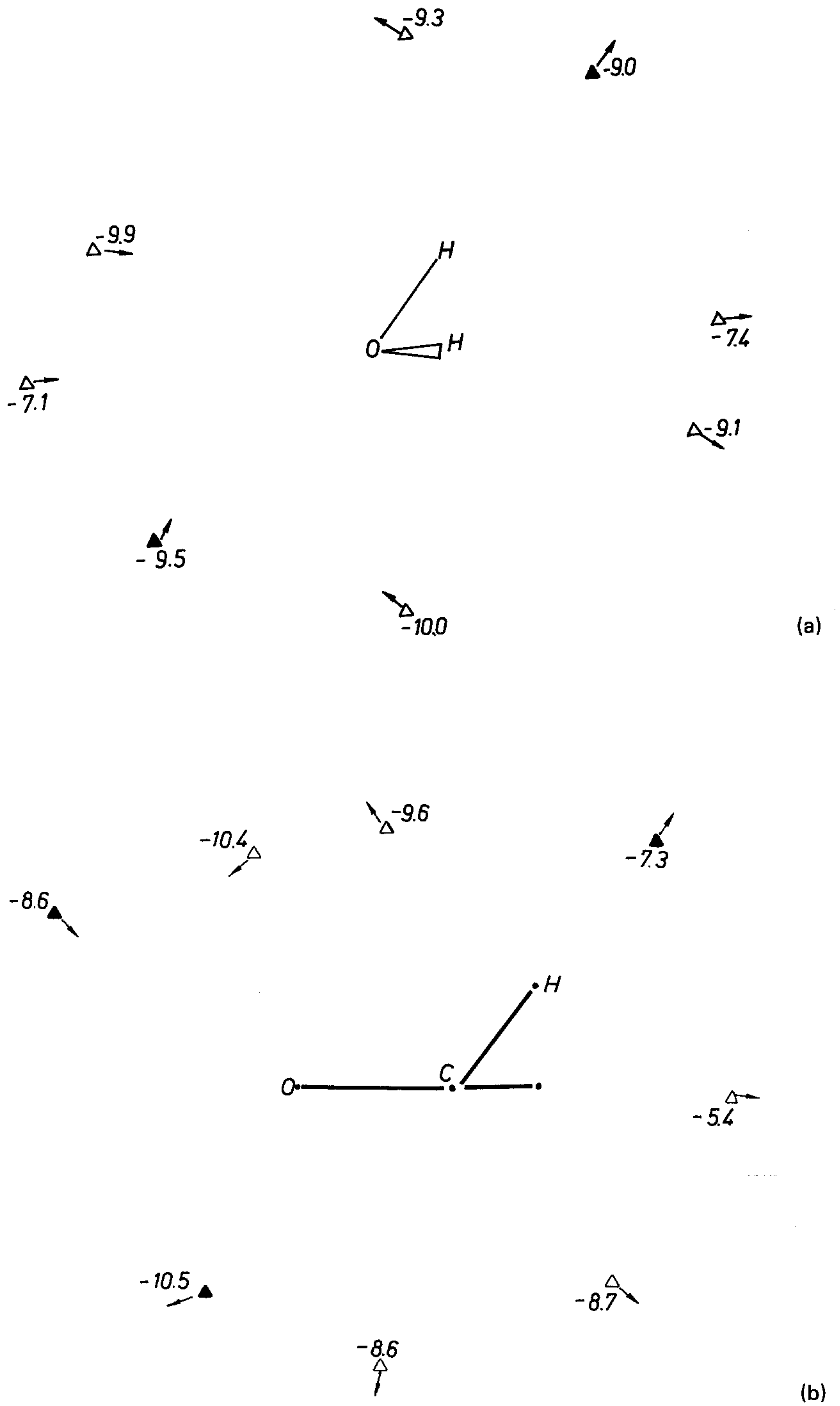

**Fig. 3.** Preferred interaction sites for a water dipole around ***a*** water, and ***b*** formaldehyde. Energies in kcal/mol

results of extensive calculations of Kistenmacher et al. [24]. This is a typical example for the discussion of hydrogen bonds. We found several types of association of the water dipoles: closed forms representing the long-range behaviour of antiparallel dipole orientations, and open forms representative of linear H-bonds in O–H bond direction (proton donor site) and following the $sp^3$ oxygen lone pair direction (proton acceptor site). These open structures clearly follow the general hybridization model [25] which describes an idealized hydrogen bond as arising when a directed lone pair on the proton acceptor atom takes part in the formation of a linear X–H . . . Y bond. The same situation could be found for the formaldehyde molecule. Preferred sites are the C–H bond direction, and the $sp^2$ hybridized oxygen lone pairs. Because semi empirical wavefunctions poorly describe the MEP around double bonds [26], the formation of $\pi$-electron hydrogen bonds in the numerical approximation used cannot be discussed here. The electrostatic energy in the surroundings of formaldehyde in the proton donor as well as in the proton acceptor direction region is smaller than in the surroundings of water. This fact underlines the well known situation that formaldehyde forms weak hydrogen bonds as compared with water [20, 27]. A simplified model of hydrogen bonding proposed by Allen [11] is very similar to our electrostatic procedure. His empirical formula for the interaction energy (in Allen's nomenclature)

$$E^{ei} = k \cdot \mu_{\mathrm{AH}} \cdot \Delta I_{\mathrm{B}} \cdot \mathrm{R}_{\mathrm{AB}}^{-1} \tag{10}$$

is only a rough approximation of Eq. (6). In his expression $\mu_{\mathrm{AH}}$ represents the local bond dipole moment of the donor A–H bond, $\Delta \mathrm{I}_{\mathrm{B}}$ is the difference in ionization potentials between the acceptor atom B and the next higher rare gas atom, and $\mathrm{R}_{\mathrm{AB}}$ is the distance between atoms A and B, $k$ is an empirical calibration constant. In Eq. (10) $\mu_{\mathrm{AH}}$ takes the place of the whole dipole moment $\mu$ in Eq. (6), and $\Delta I_{\mathrm{B}} \cdot R_{\mathrm{AB}}^{-1}$ plays the role of an electric field strength $\boldsymbol{E}$. While the use of Eq. (10) is limited to linear hydrogen bonds our formalism permits the study of general interactions of polar molecules.

## 3. Concluding Remarks

Regardless of the numerical accuracy of the wavefunctions used and approximations to calculate the MEP, the presented results illustrate the large amount of information on interaction properties of molecules which can be obtained from simple electrostatics. Calculated electric field patterns illustrate the force field of the molecule acting on a dipole and give a rough estimate of the interaction energy by electrostatics. Such information is of interest for the discussion of the formation of molecular aggregates and solvation systems. The formalism presented may be extended without difficulty to cover solid systems and molecular crystals in the study of internal and surface electric fields.

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## References

1. Scrocco, E., Tomasi, J.: Top. Curr. Chem. **42**, 95 (1973) and references therein
2. Petrongolo, C., Preston, H. J. T., Kaufmann, J. J.: Int. J. Quant. Chem. **13**, 457 (1978)
3. Berthod, H., Pullman, A.: Chem. Phys. Letters **32**, 233 (1975)
4. Pullman, A.: Colloques internatiaux du C.N.R.S. No. 256, p. 103, Menton 1976
5. Pullman, B., Goldblum, A., Berthod, H.: Biochem. Biophys. Res. Comm. **77**, 1166 (1977)
6. Goldblum, A., Pullman, B.: Theoret. Chim. Acta (Berl.) **47**, 345 (1978)
7. Giessner-Prettre, C., Pullman, A.: Theoret. Chim. Acta (Berl.) **25**, 83 (1972)
8. Giessner-Prettre, C., Pullman, A.: Theoret. Chim. Acta (Berl.) **33**, 91 (1974)
9. Giessner-Prettre, C., Pullman, A.: Theoret. Chim. Acta (Berl.) **37**, 335 (1975)
10. Caballol, R., Gallifa, R., Martin, M., Carbo, R.: Chem. Phys. Letters **25**, 89 (1974)
11. Allen, L. C.: J. Am. Chem. Soc. **97**, 6921 (1975)
12. Kollman, P. A.: J. Am. Chem. Soc. **100**, 2974 (1978)
13. $\Delta = \text{div grad}$; $\nabla = \text{grad}$
14. Margenau, H., Kestner, N. R.: Theory of intermolecular forces. Oxford: Pergamon Press; 1969
15. Stuart, R. F.: J. Chem. Phys. **50**, 2485 (1969)
16. Schuster, P., Marius, W., Pullman, A., Berthod, H.: Theoret. Chim. Acta (Berl.) **40**, 323 (1975)
17. Schuster, P., Jakubetz, W., Marius, W.: Top. Curr. Chem. **60**, 1 (1975)
18. Pullman, A., in: Metal–ligand interactions in organic chemistry and biochemistry, part 1, p. 1, (B. Pullman, N. Goldblum, eds.) Dordrecht: D. Reidel 1977
19. Kollman, P. A., Allen, L. C.: Theoret. Chim. Acta (Berl.) **19**, 20 (1970)
20. Morokuma, K.: J. Chem. Phys. **55**, 1236 (1971)
21. Schuster, P., in: Intermolecular interactions: From diatomics to biopolymers, p. 363 (B. Pullman, ed.) New York: J. Wiley 1978
22. Ranghino, G., Clementi, E.: Gazz. Chim. Ital. **108**, 157 (1978)
23. Schuster, P., in The hydrogen bond, p. 25. (P. Schuster, G. Zundel, C. Sandorfy, eds.), Amsterdam: North Holland 1976
24. Kistenmacher, H., Lie, G. C., Popkie, H., Clementi, E. J. Chem. Phys. **61**, 546 (1974)
25. DelBene, J. E. J. Chem. Phys. **55**, 4633 (1971)
26. Petrongolo, C., Popkie, H. E., Preston, H. J. T., Kaufmann, J. J.: Int. J. Quant. Chem. (in press)
27. DelBene, J. E.: J. Chem. Phys. **58**, 3139 (1973)

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