

Chapter 1

Introduction

1.1 Synopsis for non-crystallographers

Chemical crystallography and quantum chemistry encompass our knowledge about the detailed structure of molecules, their properties and reactions, and the distribution of electronic charge in their atoms and chemical bonds. On this insight are based all modern theories of chemical reactivity, and the design principles for new materials and drugs. Great advances in the last two decades have led to the present theoretical and experimental methods for determining molecular structure at the electronic level; we can in principle (and increasingly in practice) obtain not just the positions of atoms in molecules but all other topological properties of the associated electron distribution (ED).

A beam of X-rays is diffracted by the electrons in a crystalline material, just as visible light is diffracted by larger objects. Recombination of diffracted light by means of lenses can give a magnified image of the object; X-rays, having a wavelength about four orders of magnitude shorter than that of visible light, produce an image of the electron or charge density distribution characteristic of the diffracting crystal. There exist no lenses as such for X-rays, but recombination of diffracted rays into an image can be brought about by suitable detection followed by computational Fourier transformation. The experiment is effectively an X-ray microscope for the disposition of electronic charge.

In practice we can bypass the Fourier transformation, because quantum mechanics enables us to construct a mathematical model of the charge density in a crystal. The parameters of such a model can be adjusted to reproduce the experimentally-measured pattern of diffracted X-rays, given prior knowledge of the arrangement of atomic nuclei in the crystal lattice. For chemical (as distinct from biological) molecules this can usually be found routinely using the methods of conventional crystal structure analysis programmed in widely available computer packages. This leads to a "ball and stick" model of the atoms and bonds representing the topology of the charge density at the level of its most salient features, found at the positions of the atomic nuclei. It is obtained by Fourier transformation of the diffracted X-ray pattern at relatively low resolution. Next we can proceed with a far more elaborate, so-called "multipole" model of the crystalline density, fitting it to a diffraction experiment carried out at high resolution, such that two points as close together as 0.4×10^{-10} m can be distinguished. As mentioned earlier, we need no Fourier transformation at this stage because the charge density in fine detail can be computed directly from the fitted multipole model. One major component of the XD package is the program for least squares (lsq) fitting of a multipole model to the experimental data.

Once a charge distribution has been obtained experimentally, various chemical and physical properties that depend on the distribution can be derived. The chemical structure of molecules can be extracted from an analysis of the topology of the charge distribution, the features of which are summarized by the curvatures of the charge density at its critical points. Each feature, maximum, minimum or saddle has associated with it a point in space called a *critical point*, where the density is flat. One type of critical point has all three curvatures in 3-D space negative; it is found at the sites of atomic nuclei. Other types, with both positive and negative curvatures, are associated with bonding interactions between atoms. Because the strength and nature of the interactions are characterized by topology, the chemistry of the molecule can be recovered as a property of its charge distribution. A program for deriving molecular properties from the multipole model of the charge distribution is thus another major component of XD. Many of these properties can be

displayed pictorially, using the 2-D and 3-D graphics programs which plot contour, relief and iso-surface maps of selected properties such as the deformation density, the Laplacian of the total density, the electrostatic potential *etc.*

1.2 Experimental electron densities

X-ray diffraction was first applied with the purpose only of determining the positions of atoms in crystals and hence the geometrical structure of crystals and molecules. With the development of single-crystal diffractometers and computing facilities from the middle 1960s onwards came studies aimed at obtaining an experimental description of the chemical bonding to compare with the picture given by quantum chemistry theoretical calculations [1-4]. Accurate experimental measurement of the charge density in a crystal has been feasible since that time, following the development of sufficiently compact parameterized descriptions of molecular densities [5,6]. One of the most exciting applications of such an analysis is the evaluation of one-electron properties in molecular crystals. In a pioneering paper [7] Coppens *et al.* demonstrated the feasibility of this technique for a number of centrosymmetric crystals. However, applications to non-centrosymmetric materials, such as organic materials with non-linear optical applications, have been relatively few. In part, this is certainly due to the increased difficulty of obtaining accurate model structure factors when the phase is a continuous variable. Nevertheless, recent applications have demonstrated the usefulness and potential accuracy of the technique in the non-centrosymmetric case [8,9].

ED determinations [10] are based on intensity measurements of X-ray photons elastically scattered by crystals. In the next section a brief summary is given on some theoretical aspects of the procedure to extract the ED from X-ray diffraction data. For more detailed descriptions the reader is referred to references [11,12].

1.3 Theoretical aspects of electron density determination

According to the kinematical theory of scattering [13] the total diffraction intensity is

$$I_{tot} = \langle I \rangle_T \propto \langle |F(\mathbf{h}, \mathbf{q})|^2 \rangle_T \quad (\text{Eq. 1-1})$$

where $F(\mathbf{h}, \mathbf{q})$ is the Fourier transform of $\rho(\mathbf{r}, \mathbf{q})$, the static ED at a given nuclear configuration \mathbf{q} , \mathbf{h} is the Bragg vector with integral components h_1, h_2, h_3 relative to the

$$F(\mathbf{h}, \mathbf{q}) = \int_V \rho(\mathbf{r}, \mathbf{q}) \exp(2\pi i \mathbf{h} \cdot \mathbf{r}) d\mathbf{r} \quad (\text{Eq. 1-2})$$

reciprocal axes $\mathbf{a}^*, \mathbf{b}^*, \mathbf{c}^*$, V is the unit-cell volume and $\langle \rangle_T$ means thermal averaging over all vibrational states. By disregarding the diffuse scattering altogether

$$I_{tot} = I_{Bragg} = |\langle F(\mathbf{h}, \mathbf{q}) \rangle_T|^2 \quad (\text{Eq. 1-3})$$

it is assumed that the averaged scattering from a dynamic system can be well approximated by its main component, the scattering from the average structure [14,15]. This expression relates the intensity to the ED and its derivation implicitly includes assumptions not directly deducible from the experiment; assumptions on the coupling between nuclear and electronic motion and on the partitioning of the molecular ED into atomic components (convolution). Based on this equation the ED in the crystal can be given by a Fourier summation

$$\rho(\mathbf{r}) = V^{-1} \sum_{\mathbf{h}} F_{\mathbf{h}} \exp(-2\pi i \mathbf{h} \cdot \mathbf{r}) \quad (\text{Eq. 1-4})$$

This direct evaluation of ρ to a desired level of resolution, is subject to severe limitations: (i) the observed structure factors are affected by experimental errors, (ii) the phases are not measured, (iii) only a finite number of reflections can be collected. Due to these limitations

the interpretation of the X-ray data necessarily involves modelling the ED and optimizing its parameters by adjusting the calculated structure factors to those measured.

1.4 Electron density - Structure factor models

Within the convolution approximations the dynamic ED is

$$\langle \rho(\mathbf{r}) \rangle_T = \sum_k \rho_k(\mathbf{r} - \mathbf{q}_{ko} - \mathbf{u}_k) P(\mathbf{u}_k) d\mathbf{u}_k \quad (\text{Eq. 1-5})$$

where the summation runs over the density units ρ_k centered at \mathbf{q}_{ko} and $P(\mathbf{u}_k)$ is the probability distribution function (pdf) describing the displacement \mathbf{u}_k of the k -th center with respect to its equilibrium position. The structure factor is then the Fourier transform of $\langle \rho(\mathbf{r}) \rangle_T$

$$F(\mathbf{h}) = \sum_k f_k(\mathbf{h}) t_k(\mathbf{h}) \exp(2\pi i \mathbf{h} \cdot \mathbf{q}_{ko}) \quad (\text{Eq. 1-6})$$

where f_k is the static scattering power of the k -th density unit and t_k is the associated temperature factor. The commonly used scattering models differ in the description of f_k and t_k , both of which are, in general, complex functions of static and dynamic parameters, respectively.

1.5 Conventional formalism

This generalized form (1.6) is reduced to the conventional model if ρ_k is taken as the spherical atomic density and the nuclear motion is described within the harmonic approximation. This formalism disregards static deformations due to the chemical bonding and the least squares estimates of the corresponding parameters are likely to be biased. Such errors ("asphericity" shifts) usually manifest themselves in significantly shorter bond distances and smaller bond angles (at atoms with lone-pair electrons) relative to the values obtained by neutron diffraction. The accuracy of the thermal parameters is even more doubtful as the anisotropic displacements can absorb charge deformation. To overcome the inadequacy of the isolated atom model several methods can be applied.

1.6 High order refinement

In the atomic regions where the electron density is less affected by the bonding the isolated atom model is expected to be a fair approximation. The sharp core density has appreciable contribution to reflections at high Bragg angle where the scattering by the more diffuse valence or bond density is negligible. For this reason a refinement emphasizing the high-order data is expected to yield atomic parameters less biased by the inadequacy of the spherical-atom model [16].

1.7 The aspherical-atom formalism

The accuracy of the parameters can be significantly increased by implementing aspherical density models into the fit of all measured data. To account for the density deformations due to chemical bonding, several methods have been developed and applied [17,18]. One of the most successful refinement techniques is based on the nucleus-centered finite multipole expansion of the ED [6]. This formalism, refined by Hansen & Coppens [19] is implemented in XD. The aspherical atomic ED is divided into three components:

$$\rho(\mathbf{r}) = \rho_c(r) + P_v \rho_v(\kappa \mathbf{r}) + \rho_d(\kappa' \mathbf{r}) \quad (\text{Eq. 1-7})$$

where ρ_c and ρ_v are the core and spherical valence densities (sphv), respectively and

$$\rho_d(\kappa' \mathbf{r}) = \sum_l R_l(\kappa' r) \sum_{m=-l}^l P_{lm} y_{lm} \left(\frac{\mathbf{r}}{r} \right) \quad (\text{Eq. 1-8})$$

is the term accounting for valence deformations. The y_{lm} are density normalized, real spherical harmonics, such that:

$$\int_{\phi=0}^{2\pi} \int_{\theta=0}^{\pi} |y_{lm}| d\Omega = 2, l > 0 \quad (\text{Eq. 1-9})$$

$$= 1, l = 0 \quad (\text{Eq. 1-10})$$

while R_l are properly chosen radial functions, and an element of solid angle $d\Omega = \sin \theta d\theta d\phi$.

The isolated-atom valence density and the radial functions R_l are modified by the screening constants (κ and κ' , respectively) to account for the radial expansion or contraction of the valence shell. The corresponding scattering factor is

$$f(\mathbf{h}) = f_c(H) + P_v f_v \left(\frac{h}{\kappa} \right) + \sum_l \left\langle J \left(\frac{h}{\kappa'} \right) \right\rangle_l \sum_{m=-l}^l P_{lm} y_{lm} \left(\frac{\mathbf{h}}{h} \right) \quad (\text{Eq. 1-11})$$

where $\langle J_l \rangle$ is the l -th order Fourier-Bessel transform of R_l :

$$\langle J_l \rangle = 4\pi^l \int j_l(2\pi H r) R_l(r) r^2 dr \quad (\text{Eq. 1-12})$$

with j_l being the l -th order spherical Bessel function. Closed-form expressions for evaluating $\langle J_l \rangle$ using different types of radial functions have been given in reference [18].

1.8 Orbital vs. Multipole formalism

For a single-Slater determinant atomic wavefunction composed of orthogonal spin-orbitals the electron density is given by

$$\rho = \sum_i n_i |\phi_i|^2 \quad (\text{Eq. 1-13})$$

where n_i is the orbital occupation number (1 or 2) of the i th atomic orbital,

$$\phi_i = \phi_{nlm} = R_{nl} y_{lm} \quad (\text{Eq. 1-14})$$

If the radial part R_{nl} is expanded in terms of basis functions

$$R_{nl} = \sum_j C_{nli} O_{lj} \quad (\text{Eq. 1-15})$$

the density unit ρ_{nlm} corresponding to ϕ_{nlm} is given by the following linear combination:

$$\rho_{nlm} = \left[\sum_{jk} D_{nj} O_{lj} O_{lk} \right] y_{lm} y_{lm} = R_{nl}^2 y_{lm} y_{lm} \quad (\text{Eq. 1-16})$$

The spherical harmonics form a complete basis set, thus their product can be expanded over spherical harmonics:

$$y_{lm} y_{l'm'} = \sum_{LM} C_{LL'Mmm'YLM} \quad (\text{Eq. 1-17})$$

Clebsch-Gordon coefficients ($C_{Ll'l'mm'l'}$) are given for both complex and real spherical harmonics (up to $l, l' = 2$) in the literature [12]. It follows that the orbital product representation of the atomic density is completely equivalent to the multipolar description. This equivalence does not hold for molecules because of the two-center orbital products occurring in expression (1.13).

1.9 Radial functions and scattering factors

The core and spherical valence density are calculated from Hartree-Fock atomic wavefunctions [20] expanded in terms of Slater-type basis functions:

$$O_l = [2n(l)!]^{-1/2} (2\zeta_l)^{(n(l)+1)/2} r^{n(l)} \exp(-\zeta_l r) \quad (\text{Eq. 1-18})$$

where ζ_l are energy optimized orbital exponents.

The radial functions of the deformation density are also taken as simple Slater functions:

$$R_l(r) = \frac{a_l^{n(l)+3}}{(n(l)+2)!} r^{n(l)} \exp(-a_l r) \quad (\text{Eq. 1-19})$$

with $n(l) \geq l$ to obey Poisson's equation [21] and with values for a_l as deduced from the single- ζ wavefunctions. As shown above, the evaluation of the scattering factor of an orbital product requires the calculation of L th-order Fourier Bessel transforms of $O_l O_{l'}$ ($\langle j_L \rangle_{ll'}$). The simple scheme below shows how L is related to l and l' ($l=0,1,2$ for s,p and d, respectively):

$l \setminus l'$	s	p	d
s	0	1	2
p		0 2	1 3
d			0 2 4

Taking the carbon atom as an example, the following scattering factors can be generated from the wavefunction:

core: $\langle j_0 \rangle (1s1s)$

sphv: $\langle j_0 \rangle (2s2s) + \langle j_0 \rangle (2p2p)$

Dipolar ($l=1$) and quadrupolar ($l=2$) radial scattering functions included in the deformation term in (1.8) could be composed as the Fourier-Bessel transforms of sp and pp type orbital products:

defv: $\langle j_1 \rangle (2s2p), \langle j_2 \rangle (2p2p)$

1.10 The temperature factor

In harmonic approximation the vibrational pdf of the nuclear displacement vector \mathbf{u} , taken with respect to the equilibrium position ($\mathbf{u} = \mathbf{q} - \mathbf{q}_0$), is a normal distribution:

$$P_o(\mathbf{u}) = (2\pi)^{-3/2} (\det \mathbf{U})^{-1/2} \exp(-1/2 \mathbf{u}' \mathbf{U}^{-1} \mathbf{u}) \quad (\text{Eq. 1-20})$$

where \mathbf{U} is the mean-square displacement amplitude (MSDA) matrix.

The corresponding atomic anisotropic temperature factor is the Fourier transform of $P_o(\mathbf{u})$:

$$t_o(\mathbf{h}) = \exp(-2\pi^2 \mathbf{h}' \mathbf{U} \mathbf{h}) \quad (\text{Eq. 1-21})$$

Anharmonic models in practical use are based on statistical approaches. If the anharmonicity is small the corresponding pdf can be expanded about the normal distribution. In the Gram-Charlier expansion [22] implemented in XDLSM, the anharmonic pdf is approximated in terms of zero and higher derivatives of the normal distribution:

$$P(\mathbf{u}) = (1 + \frac{1}{3!} C_{jkl} H_{jkl} + \frac{1}{4!} C_{jklm} H_{jklm} + \dots) P_o \quad (\text{Eq. 1-22})$$

where $H_{jkl\dots}$ are three dimensional Hermite polynomials being functions of \mathbf{U} and \mathbf{u} , while the coefficients $C_{jkl\dots}$ are the quasi-moments being related to the moments of the pdf. The advantage of this form is that its Fourier transform is reduced to a simple power series expansion about the harmonic temperature factor:

$$T(H) = (1 - \frac{4}{3} \pi^3 i C_{jkl} h_j h_k h_l + \frac{2}{3} \pi^4 C_{jklm} h_j h_k h_l h_m + \dots) T_o(H) \quad (\text{Eq. 1-23})$$

1.11 Deformation electron density

The conventional model is based on the pro-molecular density which is the superposition of the spherical atomic densities $\rho_k(\mathbf{r})$ centered at the actual nuclear positions in the molecule. The promolecule can serve as a reference state relative to which charge migrations due to bond formations are expected to become visible [23].

$$\delta\rho(\mathbf{r}) = \rho_{mol}(\mathbf{r}) - \sum_k \rho_k(\mathbf{r} - \mathbf{r}_k) \quad (\text{Eq. 1-24})$$

To interpret the $\delta\rho(\mathbf{r})$ one always has to critically examine not only the method yielding the molecular electron density but the effect of the preconceptions applied in composing the promolecule. For atoms with a degenerate ground state, ρ_k is obtained by sharing the valence electrons among orbitals of different angular dependence regardless of their ability to form a bond in the actual arrangement of the atoms. As a result the obtained deformation electron density may not show the expected features of the covalent bond or lone-pair density [24].

In order to obtain a chemically meaningful deformation electron density, an alternative promolecule has been proposed for which the configuration and the orientation of the ground state of each constituent atom is correctly specified by a fitting procedure [25]. To elucidate important aspects of delocalization, effects of substitution or intermolecular interactions, one can consider fragments or molecules to choose as the basis for comparison [26,27]. Atoms prepared for bond formation can also serve as references [28].

If the deformation electron density is evaluated by a Fourier summation

$$\delta\rho(\mathbf{r}) = \sum_{\mathbf{h}} [F_o(\mathbf{h}) - F_c(\mathbf{h})] \exp(-2\pi i \mathbf{h} \mathbf{r}) \quad (\text{Eq. 1-25})$$

the series termination error is considerably decreased. The phases and the F_c are usually calculated from the promolecule with atomic and positional parameters obtained from (i) neutron diffraction data (X-N) [29], (ii) conventional refinement on high-order X-ray data (X- X_{ho}), (iii) full-data aspherical-atom refinement (X- X_{mul}).

1.12 Experimental requirements

The applicability of the above formalism depends on the compound to be studied and its crystalline form, the radiation used and the method of the data collection. The kinematic theory is valid only in a certain frequency range: $\mu_r > \mu > \mu_K$, where μ_K corresponds to the K absorption edge of any atom in the molecule and μ_r is the frequency limit, where relativistic effects occur. Accordingly, atoms with high atomic number ($Z > 18$) are not well suited for charge density studies when a standard X-ray source is used. Bonding effects are likely to be invisible for atoms with small valence to core electron ratio [30].

The most important requirement for an accurate measurement is to maintain kinematical conditions or to make the systematic errors, due to dynamic scattering, correctable. To reveal these effects equivalent reflections should be measured. To minimize the diffuse scattering the data should be collected at low temperature. Details of the data reduction can be found in references [31-34].

1.13 Determination of atomic and structural properties from charge distributions

1.13.1 Critical points of the charge density

Once a charge distribution has been obtained experimentally, various chemical and physical properties that depend on the distribution can be derived. Bader [35] shows how the chemical structure of molecules can be extracted from an analysis of the topology of $\rho(\mathbf{r})$, the features of which are summarized by the curvatures of $\rho(\mathbf{r})$ at its critical points. Each feature, maximum, minimum or saddle has associated with it a point in space called a *critical point*, where the first derivatives of $\rho(\mathbf{r})$ vanish. At such a point, denoted by position vector \mathbf{r}_c ,

$$\nabla\rho(\mathbf{r}_c) = \hat{\mathbf{i}}\frac{\partial\rho}{\partial x} + \hat{\mathbf{j}}\frac{\partial\rho}{\partial y} + \hat{\mathbf{k}}\frac{\partial\rho}{\partial z} = 0$$

where $\hat{\mathbf{i}}$, $\hat{\mathbf{j}}$, $\hat{\mathbf{k}}$ are unit vectors. Whether a function is a maximum or minimum is determined by the sign of its second derivative, or curvature, at the stationary point. In general, for an arbitrary choice of coordinate axes, there will be nine second derivatives of the form $\partial^2\rho/\partial x\partial y$ in the determination of the curvatures of ρ at a point in space. Their ordered 3x3 array, the *Hessian matrix* of the charge density, can be diagonalized to yield the principal axes of curvature, with respect to which the magnitudes of the three second derivatives of ρ are extremized. The principal axes and their corresponding curvatures at a critical point in ρ are obtained as the eigenvectors and corresponding eigenvalues (λ) of the Hessian matrix of $\rho(\mathbf{r})$. The *rank* ω of a critical point is the number of non-zero eigenvalues or curvatures of ρ at the critical point, while its *signature* σ is the algebraic sum of the signs of the curvatures at that point. The critical point is labelled by giving the pair of values (ω, σ). With few exceptions the critical points of charge distributions for stable molecules are of rank three, and there are four possible signature values and labels:

- (3,-3)** all curvatures are negative and ρ is a local maximum at \mathbf{r}_c .
- (3,-1)** two curvatures are negative and ρ is a maximum at \mathbf{r}_c in the plane defined by their corresponding axes. ρ is a minimum at \mathbf{r}_c along the third axis, perpendicular to this plane.
- (3,+1)** two curvatures are positive and ρ is a minimum at \mathbf{r}_c in the plane defined by their corresponding axes. ρ is a maximum at \mathbf{r}_c along the third axis, perpendicular to this plane.
- (3,+3)** all curvatures are positive and ρ is a local minimum at \mathbf{r}_c .

The traditional association of nuclear positions with local maxima in $\rho(\mathbf{r})$ can now be formalized as the statement that nuclear positions behave topologically as (3,-3) critical points in the charge distribution.

1.13.2 Interatomic surfaces and chemical bonds

A useful function is obtained in the form of the *gradient vector field* of the charge density, represented through a display of the trajectories traced out by the vector $\nabla\rho$. The gradient vector points in the direction of the greatest increase in ρ , so these trajectories are perpendicular to the contour lines of ρ . They have the property of originating or terminating at critical points in ρ . The charge distribution is partitioned into disjoint regions by surfaces for which

$$\nabla\rho(\mathbf{r}) \cdot \mathbf{n}(\mathbf{r}) = 0$$

where \mathbf{n} is the vector normal to the surface. These so-called *zero flux surfaces* are the *interatomic surfaces* or quantum mechanical boundaries of the atoms, and contain (3,-1) critical points when the atoms are chemically bonded. The pairs of gradient paths which originate at each (3,-1) critical point and terminate at the nuclei define a line through the charge distribution linking the neighbouring nuclei, along which $\rho(\mathbf{r})$ is a maximum with respect to any neighbouring line. This line is called a *bond path* and the (3,-1) critical point is referred to as a *bond critical point*. This is the topological definition of a chemical bond, formalizing the theoretically predicted and experimentally observed accumulation of charge between bonded nuclei. Chemical structure can thus be recovered as a property of the charge distribution. The strength and nature of the chemical bond can be characterized by the value of various properties evaluated at the bond critical points, *e.g.* bond order, bond ellipticity, $\rho(\mathbf{r}_c)$, $\nabla^2\rho(\mathbf{r}_c)$ [35].

The value of ρ_c in a bond measures its strength [36]; the trace of the Hessian at \mathbf{r}_c measures the extent of depletion or concentration of charge; and the ratio of eigenvalues of this matrix (the bond 'ellipticity' ε) measures the degree of planarity or conjugation. More precisely, $\varepsilon = (\lambda_2/\lambda_1) - 1$, where the λ 's are the two eigenvalues of the Hessian corresponding to directions perpendicular to the bond.

Stationary points in ρ have been applied in characterizing benzenoid aromaticity [37], homoaromaticity and hyperconjugativity [38-40], and electrophilic substitution [41,42]. A number of applications of the topological properties of experimental charge distributions obtained from neutron and X-ray diffraction data for organic molecular crystals have been reported [43-46].

1.13.3 Lewis electron pairs - the Laplacian

The trace of the Hessian matrix, the quantity

$$\nabla^2\rho(\mathbf{r}) = \frac{\partial^2\rho}{\partial x^2} + \frac{\partial^2\rho}{\partial y^2} + \frac{\partial^2\rho}{\partial z^2}$$

is termed the *Laplacian* of ρ and has physical meaning as representing local concentrations, where $\nabla^2\rho(\mathbf{r}) < 0$, and depletions, where $\nabla^2\rho(\mathbf{r}) > 0$, of the charge density. Electronic charge is compressed above its average distribution in regions where the Laplacian is negative, and expanded relative to its average distribution where the Laplacian is positive. Maxima and minima in the function $\nabla^2\rho(\mathbf{r})$ are to be distinguished from local maxima and minima in the charge density itself. Although the topology of ρ yields a faithful mapping of the chemical concepts of atoms, bonds and structure, there is no indication of maxima in ρ corresponding to the localized electron pairs of the Lewis model of electronic structure, of great importance to our interpretation of chemical reactivity and molecular geometry. The physical basis of this model is one level of abstraction above the visible topology of the

charge density and appears instead in the topology of the Laplacian of ρ , the scalar derivative of the gradient vector field of the charge density.

The Laplacian distribution recovers the electronic shell model of an atom by exhibiting a corresponding number of pairs of shells of charge concentration and charge depletion. For a spherical free atom, the outer or valence shell of charge concentration (VSCC) contains a sphere of uniform concentration of electronic charge. Upon entering into chemical combination, this shell is distorted and maxima, minima and saddles appear. The maxima correspond in number, location and size to the localized pairs of electrons assumed in the Lewis and VSEPR models of electron pairs. A local charge concentration is a Lewis base or nucleophile, while a local charge depletion is a Lewis acid or electrophile, and a chemical reaction corresponds to the combination of complementary features of the VSCC of the base and acid. The Laplacian distribution can thus be used to locate possible sites of nucleophilic attack, and to predict characteristics (such as hydrogen bonding) of the chemical reactivity in general.

Stationary points in $\nabla^2\rho(\mathbf{r})$, points of maximum charge concentration or depletion, are being extensively applied in studies of basicity and acidity [47-52]; to more general reactivity [53-56]; in accounts of molecular geometries [57]; and to directionality of hydrogen bonding [58,59]. Such points may generally be associated with either bonded or non-bonded electron pairs. Experimental determinations of $\nabla^2\rho$ distributions are included in [60-63].

Finally we note that the use of the bipolar model for characterising chemical bonds solely on the basis of the magnitude of $\rho(\mathbf{r}_c)$ and the sign and magnitude of $\nabla^2\rho(\mathbf{r}_c)$ [35], is a useful model for light atom compounds (*i.e.* elements from the first three periodic rows). It ceases to be so useful for compounds of heavier elements such as the transition metals, where the bond critical points involving these elements invariably lie in a region of positive $\nabla^2\rho(\mathbf{r}_c)$. The reader is directed to recent reviews [64,65], which discuss extensions to the bipolar model in considerable detail.

Bibliography

1. P. Coppens, *J. Chem. Ed.* **61**, 761-765 (1984).
2. K. Angermund, K.H. Claus, R. Goddard and C. Krüger, *Angew. Chem. Int. Ed.* **24**, 237-247 (1985).
3. P. Coppens, *J. Phys. Chem.* **93**, 7979-7984 (1989).
4. P. Coppens, *Ann. Rev. Phys. Chem.* **43**, 663-692 (1992).
5. (a) R.J. Weiss, *X-ray Determination of Electron Distributions*, North Holland Publishing Co.: Amstersdam, 1966. (b) B. Dawson, *Proc. Royal Soc.* **A298**, 255 (1967).
6. R.F. Stewart, *J. Chem. Phys.* **58**, 1668 (1973).
7. P. Coppens, T.N. Guru Row, P. Leung, E.D. Stevens, P.J. Becker & Y.W. Yang, *Acta Cryst.* **A35**, 63-72 (1979).
8. M. Souhassou, C. Lecomte, R. H. Blessing, A. Aubry, M. M. Rohmer, R. Wiest, M. Benard and M. Marraud, *Acta Cryst.* **B47**, 145 (1991).
9. S.T. Howard, M.B. Hursthouse, C.W. Lehmann, P.R. Mallinson and C.S. Frampton, *J. Chem. Phys.* **97**, 5616-5630 (1992).
10. P. Coppens and M.B. Hall, Eds. *'Electron Distributions and the Chemical Bond'*, Plenum Press 1982.
11. F. L. Hirshfeld, *Cryst. Rev.* **2**, 169-204 (1981).
12. P. Coppens and P.J. Becker, *International Tables for Crystallography*, Vol. C, 627-644, Kluwer Academic Publishers, 1992.
13. M. Born, *Zeitschr. für Physik* **38**, 803-811 (1926).
14. R.F. Stewart, *Isr.J. of Chem.* **16**, 137-143 (1977).
15. P.J. Becker, *Electron and Magnetization Densities in Molecules and Solids*, 173-211, Becker, P.J. Ed., Plenum Press: New York and London, 1980.
16. G.A. Jeffrey and D.W.J. Cruickshank, *Quart. Rev. Chem. Soc.* **7**, 335-376 (1953).
17. R.F. Stewart, *J. Chem. Phys.* **51**, 4569-4577 (1969).
18. R. Restori, *Acta Cryst.* **A46**, 150-151 (1990).
19. N.K. Hansen and P. Coppens, *Acta Cryst.* **A34**, 909-921 (1978).
20. E. Clementi and C. Roetti, *Atomic Data and Nuclear Data Tables* **14**, 177-478 (1974).
21. R.F. Stewart, *Israel J. Chem.* **16**, 124-131 (1977).
22. C.K. Johnson and H.A. Levy, *International Tables for X-ray Crystallography*, Vol. IV, 311-336, Birmingham: Kynoch Press, 1974.
23. M. Roux, S. Besnainou and R. Daudel, *J. Chim. Phys.* **53**, 218-223, 1956.
24. J.D. Dunitz, W.B. Schweizer and P. Seiler, *Helv. Chim. Acta* **66**, 123-133 (1983).

25. W.H.E. Schwarz, L. Mensching, P. Valtazanos and W. von Niessen, *Int. J. Quantum Chem.* **30**, 439-444 (1986).
26. K. Hermansson and S. Lunell, *Acta Cryst.* **B38**, 2563-2569 (1982).
27. J. Buschmann, T. Koritsanszky, R. Kuschel, P. Luger and K. Seppelt, *J. Am. Chem. Soc.* **113**, 233-238 (1991).
28. H. Takazawa, S. Ohba and Y. Saito, *Acta Cryst.* **B45**, 432-437 (1989).
29. P. Coppens, *Science* **158**, 1577-1579 (1967).
30. P. Coppens, *Isr. J. Chem.* **16**, 159-162 (1977).
31. R.H. Blessing, *Cryst. Rev.* **1**, 3-58 (1987).
32. P. Seiler, *Measurement of Accurate Bragg Intensities, in Accurate Molecular Structures*, Chapter 7, Domenicano, A., Hargittai, I., Eds., Oxford University Press, 1991.
33. P. Coppens, *J. Phys. Chem.* **93**, 7979 (1989).
34. P. Coppens, *Ann. Rev. Phys. Chem.* **43**, 663 (1992).
35. R.F.W. Bader, *Atoms in Molecules: A Quantum Theory*, Oxford University Press, 1990.
36. R.F.W. Bader, T.S. Slee, D. Cremer and E. Kraka, *J. Am. Chem. Soc.* **105** 5061 (1983).
37. S.T. Howard and T.M. Krygowski, *Can. J. Chem.* **75**, 1174-1181 (1995).
38. D. Cremer, E. Kraka, T.S. Slee, R.F.W. Bader, C.D.H. Lau, T.T. Nguyen-Dang and P.J. MacDougall, *J. Am. Chem. Soc.* **105**, 5069 (1983).
39. D. Cremer and E. Kraka, *J. Am. Chem. Soc.* **107**, 3800 (1985).
40. D. Cremer and E. Kraka, *J. Am. Chem. Soc.* **107**, 3811 (1985).
41. R.F.W. Bader and C. Chang, *J. Phys. Chem.* **93**, 2946 (1989).
42. R.F.W. Bader and C. Chang, *J. Phys. Chem.* **93**, 5095 (1989).
43. (a) S. Swaminathan, B.M. Craven and R.K. McMullan, *Acta Cryst.* **B40**, 300 (1984). (b) S. Swaminathan, B.M. Craven, M.A. Spackman and R.F. Stewart, *Acta Cryst.* **B40**, 398 (1984).
44. (a) J. Epstein, J.R. Ruble and B.M. Craven, *Acta Cryst.* **B38**, 140 (1982). (b) R.K. McMullan, J. Epstein, J.R. Ruble and B.M. Craven, *Acta Cryst.* **B35**, 688 (1979).
45. (a) R.K. McMullan, P. Benci and B.M. Craven, *Acta Cryst.* **B36**, 1424 (1980). (b) B.M. Craven and P. Benci, *Acta Cryst.* **B37**, 1584 (1981).
46. G.A. Jeffrey, J.R. Ruble, R.K. McMullan and J.A. Pople, *Proc. Roy. Soc.* **A414**, 47 (1987).
47. T. Slee, R.F.W. Bader, *J. Mol. Struct. THEOCHEM* **87**, 173 (1992).
48. P. Speers, K.E. Laidig, *J. Chem. Soc., Perkin Trans.* **2**, 799 (1994).
49. J.A. Platts, S.T. Howard and K. Woniak, *J. Org. Chem.* **59**, 4647 (1994).
50. S.T. Howard, J.A. Platts and R.W. Alder, *J. Org. Chem.* **60**, 6085-6090 (1995).
51. J.A. Platts and K.E. Laidig, *J. Phys. Chem.* **99**, 6487-6492 (1995).
52. S.T. Howard and J.A. Platts, *J. Phys. Chem.* **99**, 9027-9033, (1995).
53. Z. Shi and R.J. Boyd, *J. Phys. Chem.* **95**, 4698 (1991).
54. Y. Aray, J. Rodríguez, J. Murgich and F. Ruette, *J. Phys. Chem.* **97**, 8393 (1993).
55. Z. Shi and R. J. Boyd, *J. Phys. Chem.* **95**, 9614 (1993).
56. M. Alcamí, O. Mó, M. Yáñez and J.-L.M. Abboud, *J. Phys. Org. Chem.* **4**, 177 (1991).
57. R.J. Gillespie, and I. Hargittai, *The VSEPR model of Molecular Geometry*, Chapter 10, Allyn and Bacon: Boston, 1991.
58. M.T. Carroll and R.F.W. Bader, *Mol. Phys.* **65**, 695 (1988).
59. J.A. Platts, S.T. Howard and B.R.F. Bracke, *J. Am. Chem. Soc.* **118**, 2726-2733 (1996).
60. R.F. Stewart, in *The Application Of Charge Density Research to Chemistry and Drug Design*, Eds. G.A. Jeffrey and J.F. Piniella, NATO ASI Series B, Physics **250**, Plenum Press, 1991.
61. S.T. Howard, M.B. Hursthouse, C.W. Lehmann, P.R. Mallinson and C.S. Frampton, *J. Chem. Phys.* **97**, 5616 (1992).
62. S.T. Howard, J.P. Huke, P.R. Mallinson and C.S. Frampton, *Phys. Rev. B* **49**, 7124 (1994).
63. T. S. Koritsanszky and P. Coppens *Chem. Rev* **101** 1583-1627 (2001).
64. P. Macchi and A. Sironi *Coord Chem. Rev* **238-239**, 383-412 (2003).
65. C. Gatti *Z. Kristallogr* **220**, 399-457 (2005).