Introductory to multipolar modeling

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Radiation used in crystallography

- X-rays
- Electrons
- Neutrons

Table 4.1.3.1. *Average diffraction properties of X-rays, electrons, and neutrons*

	X-rays	Electrons	Neutrons
(1) Charge	0	-1 e	0
(2) Rest mass	0	9.11×10^{-31} kg	1.67×10^{-27} kg
(3) Energy	10 keV	100 keV	0.03 eV
(4) Wavelength	1.5 Å	0.04 Å	1.2 Å
(5) Bragg angles	Large	1°	Large
(6) Extinction length	10 μm	0.03 μm	100 μm
(7) Absorption length	100 μm	1 μm	5 cm
(8) Width of rocking curve	5"	0.6°	0.5"
(9) Refractive index	$n < 1$	$n > 1$	$n \lesseqgtr 1$
$n = 1 + \delta$	$\delta \approx -1 \times 10^{-5}$	$\delta \approx +1 \times 10^{-4}$	$\delta \approx \mp 1 \times 10^{-6}$
(10) Atomic scattering amplitudes f	10^{-3} Å	10 Å	10^{-4} Å
(11) Dependence of f on the atomic number Z	$\sim Z$	$\sim Z^{2/3}$	Nonmonotonic
(12) Anomalous dispersion	Common	–	Rare
(13) Spectral breadth	1 eV $\Delta\lambda/\lambda \approx 10^{-4}$	3 eV $\Delta\lambda/\lambda \approx 10^{-5}$	500 eV $\Delta\lambda/\lambda \approx 2$

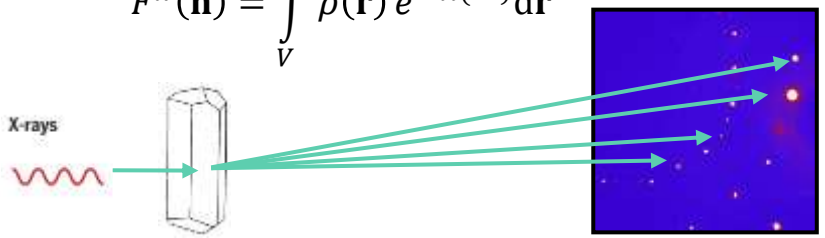
P.M.Dominiak, CNBCh UW

International Tables for Crystallography (2006). Vol. C, Chapter 4.1, pp. 186–190.

Each type of the beam (X-rays, electrons, etc.) is sensitive to the **specific property** of the crystal sample

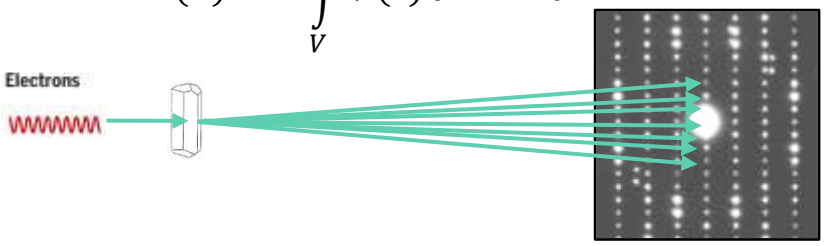
X-rays interact with the **electron density**

$$F^x(\mathbf{h}) = \int_V \rho(\mathbf{r})\, e^{2\pi i(\mathbf{hr})} \mathrm{d}\mathbf{r}$$



Electrons are scattered by the **electrostatic potential** generated by **electron density** and **nuclei**

$$F^e(\mathbf{h}) = K \int_V V(\mathbf{r})\, e^{2\pi i(\mathbf{hr})} \mathrm{d}\mathbf{r}$$

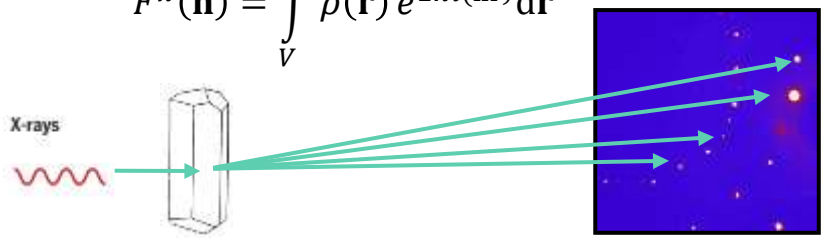


$$V(\mathbf{r}) = \sum_{i=1}^{N} \frac{Z_i}{|\mathbf{R}_i - \mathbf{r}|} - \int \frac{\rho(\mathbf{r}')}{|\mathbf{r}' - \mathbf{r}|} \mathrm{d}^3\mathbf{r}'$$

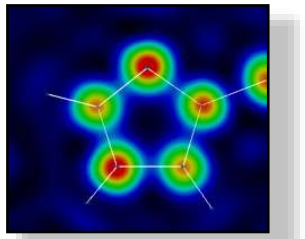
Information about that property can be **retrieved** directly from the diffraction/scattering data

Fourier image of **electron density**

$$F^x(\mathbf{h}) = \int_V \rho(\mathbf{r})\, e^{2\pi i(\mathbf{hr})}\mathrm{d}\mathbf{r}$$

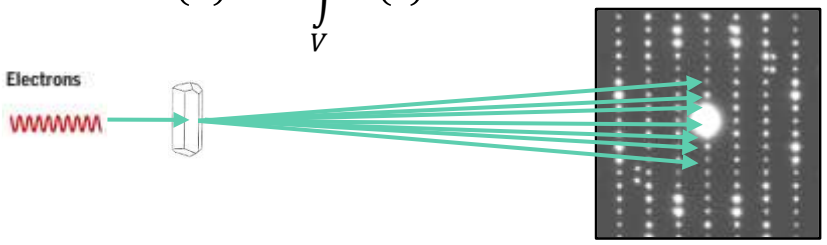


$$\rho(\mathbf{r}) = \frac{1}{V}\sum_{\mathbf{h}} F^x(\mathbf{h})\, e^{-2\pi i(\mathbf{hr})}$$

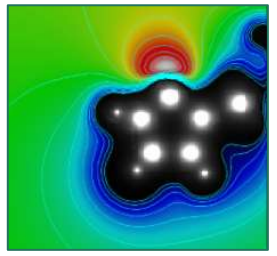


Fourier image of **electrostatic potential**

$$F^e(\mathbf{h}) = K\int_V V(\mathbf{r})\, e^{2\pi i(\mathbf{hr})}\mathrm{d}\mathbf{r}$$



$$V(\mathbf{r}) = k\sum_{\mathbf{h}} F^e(\mathbf{h})\, e^{-2\pi i(\mathbf{hr})}$$



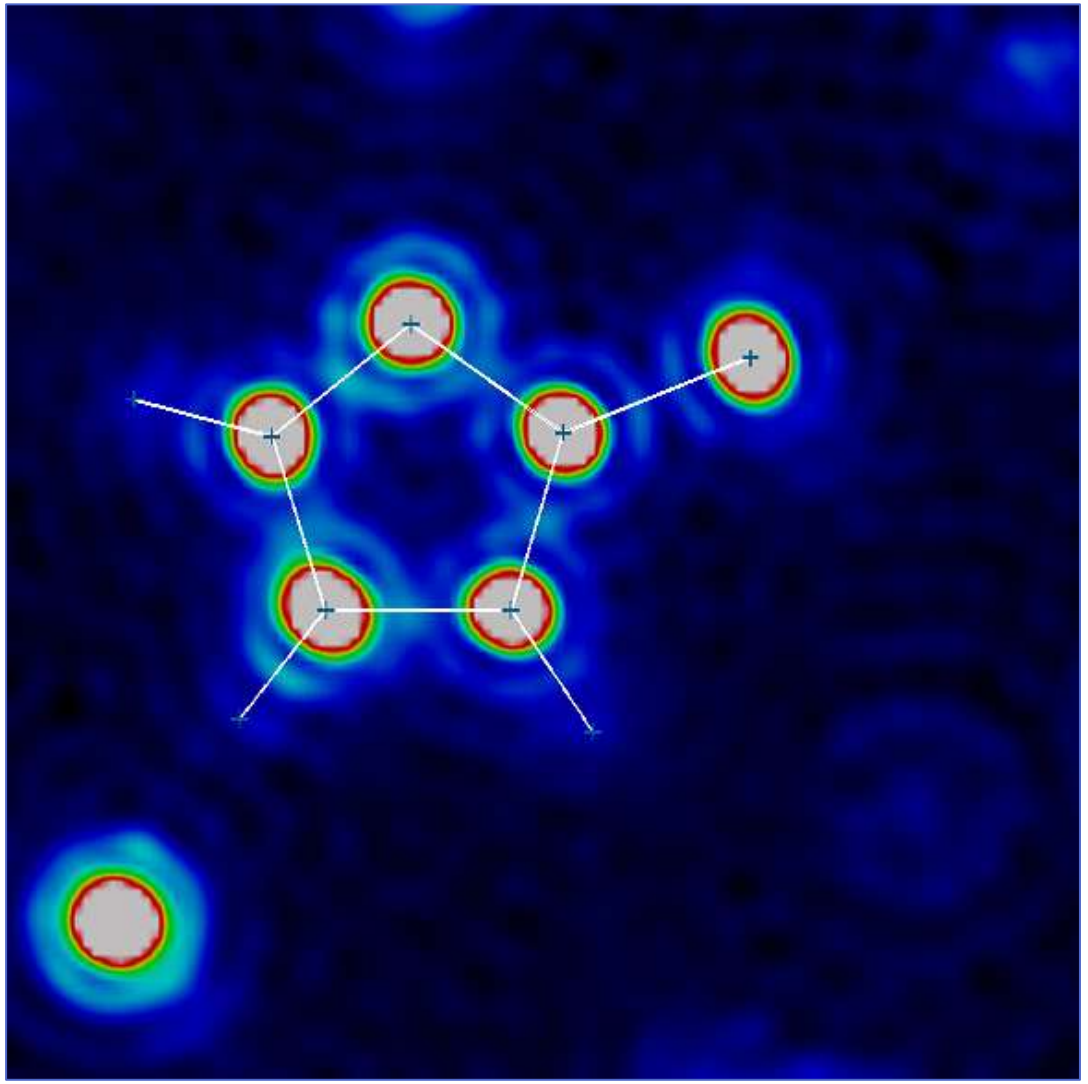
$$V(\mathbf{r}) = \sum_{i=1}^{N}\frac{Z_i}{|\mathbf{R}_i - \mathbf{r}|} - \int\frac{\rho(\mathbf{r}')}{|\mathbf{r}' - \mathbf{r}|}\mathrm{d}^3\mathbf{r}'$$

Fourier maps are hard to be analyzed directly

$$\langle \rho(\mathbf{r}) \rangle = \frac{1}{V} \sum_{\mathbf{h}}^{\infty} F^{x}(\mathbf{h})\, e^{-2\pi i(\mathbf{hr})}$$

$$\langle V(\mathbf{r}) \rangle = k \sum_{\mathbf{h}}^{\infty} F^{e}(\mathbf{h})\, e^{-2\pi i(\mathbf{hr})}$$

- lack of **phases**
- finite **resolution**
- experimental **errors**
- **thermal** motions, etc.



Predetermined model is needed

- **Only selected parameters** of a given model **are refined** against the experimental data

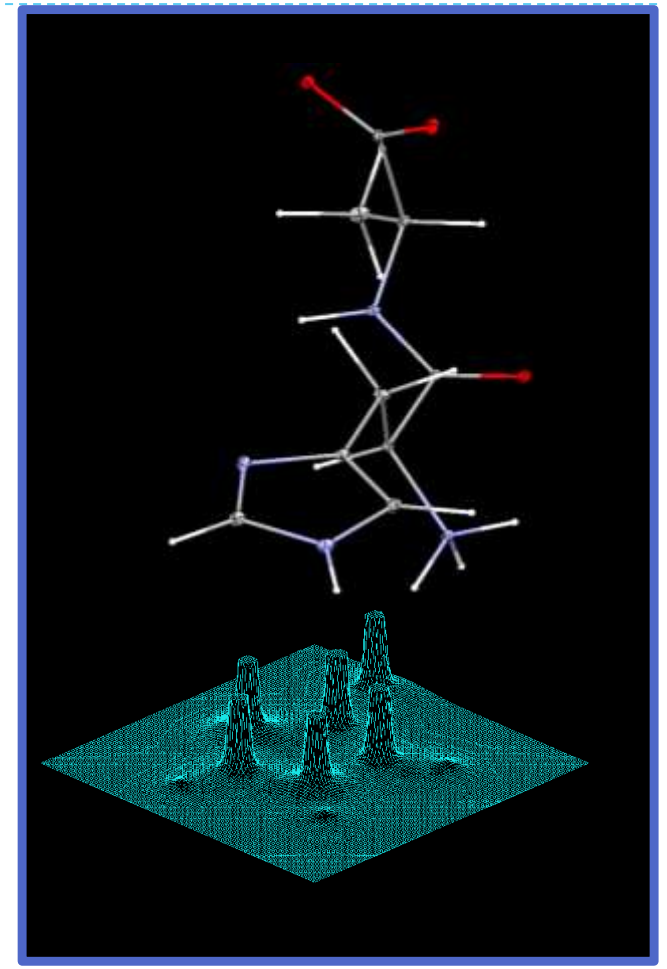
In **X-ray** crystallography crystal **electron density** is usually modelled as

a sum of atomic contributions

$$F(\mathbf{h}) = \sum_{i}^{N} f_i(\mathbf{h}) T_i(\mathbf{h}) e^{2\pi i(\boldsymbol{hR_i})}$$

Atomic scattering factor of atom *i*

Temperature factor of atom *i*



In **electron** crystallography analogous approach is used

Atomic scattering factors
X-ray radiation

In general, they are calculated based on knowledge of the **electron density** distribution of atoms, $\rho_{at}(\mathbf{r})$:

$$f^{x}(\mathbf{S}) = \int_{atom} \rho_{at}(\mathbf{r})\, e^{2\pi i(\mathbf{S}\,\mathbf{r})} \mathrm{d}\mathbf{r}$$

Atomic scattering factors
electron radiation

In general, they are calculated based on knowledge of the **electrostatic potential** distribution of atoms, $\varphi_{at}(\mathbf{r})$:

$$f^{e}(\mathbf{S}) = \int_{atom} \varphi_{at}(\mathbf{r})\, e^{2\pi i(\mathbf{S}\,\mathbf{r})} \mathrm{d}\mathbf{r}$$

The electrostatic potential is generated by both the charge of the **electron density** and the charge of the atomic **nuclei**

Atomic scattering factors
electron radiation

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$$f^e(\mathbf{S}) = \int_{atom} \varphi_{at}(\mathbf{r})\, e^{2\pi i(\mathbf{S}\,\mathbf{r})} \mathrm{d}\mathbf{r}$$

The electrostatic potential is generated by both the charge of the **electron density** and the charge of the atomic **nuclei**

In practice, they are calculated from the atomic X-ray scattering factors:

$$f^e(\mathbf{h}) = \frac{me^2}{8\pi^3\hbar^2\varepsilon_0}\frac{Z - f^x(\mathbf{h})}{\mathbf{h}^2}$$ **Mott–Bethe formula**

$|\mathbf{h}| = 2s = 2\sin\theta/\lambda$

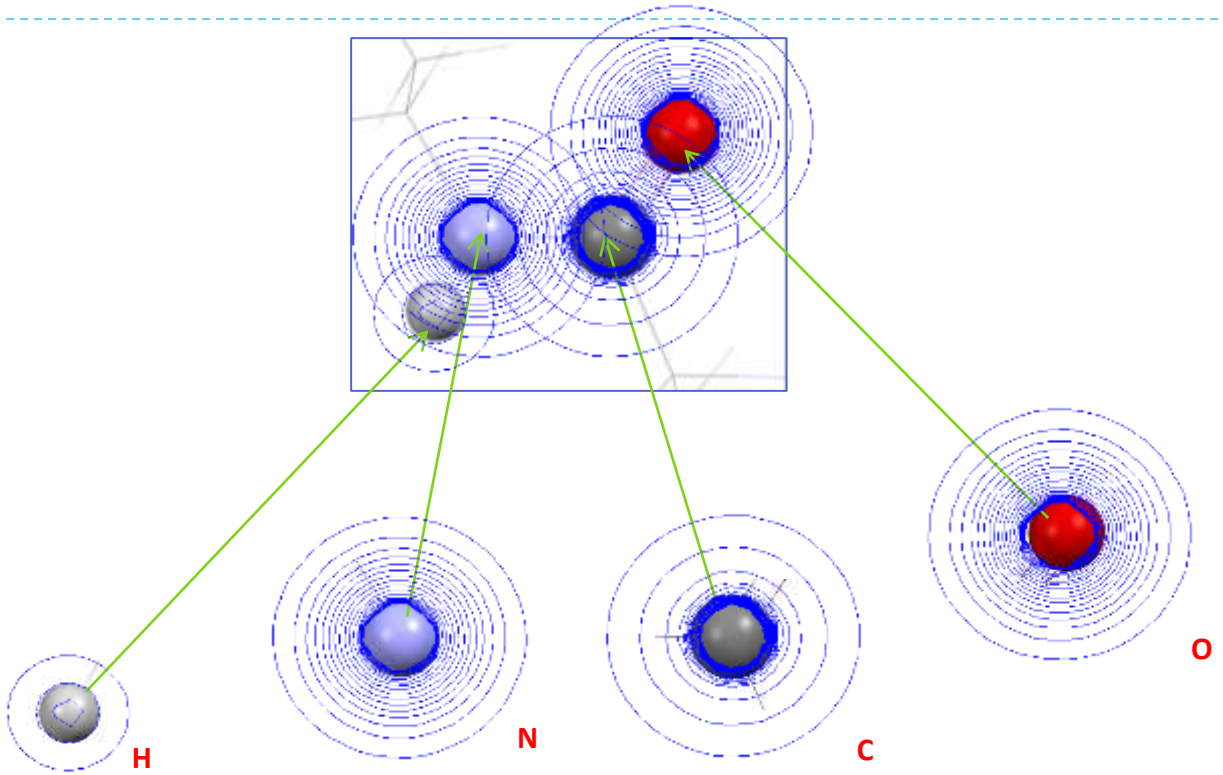
$\hbar = \mathrm{h}/2\pi$ where h is the Planck constans

Various models are used to model static electron density and compute atomic scattering factors

$$F(\mathbf{h}) = \sum_{i}^{N} f_i(\mathbf{h}) T_i(\mathbf{h}) e^{2\pi i(\boldsymbol{hR_i})}$$

Independent Atom Model (IAM)

a 100-years-old and still the most common model



Atomic electron denstities (electrostatic potentials) are precomputed by quantum mechanics methods
for isolated atoms of each chemical element

Compton, Nature, 1915, *94*, 343; **Hartree**, Philos. Mag. Ser. 6. 1925, *50*, 289

Independent Atom Model (IAM)

comes from **quantum chemical** calculations

$$\rho_{at}(r) = N_c\rho_{core}(r) + N_v\rho_{valence}(r)$$

$$f^x(\mathbf{h}) = \int_V \rho_{at}(\mathbf{r})\, e^{2\pi i(\mathbf{hr})}\mathrm{d}\mathbf{r}$$

X-ray

- **atomic wavefunctions** of **neutral** atoms
  (or ions with **integer charge**)
- for **isolated** atoms
- in the **ground** state
- **spherically** averaged

6.1.1.3. *Atomic scattering factor*

Atomic scattering factors for neutral atoms are listed in Table 6.1.1.1 for the range $0 < (\sin\theta)/\lambda < 6.0$ Å^{-1}. The values for hydrogen are calculated from the analytical solution to the Schrödinger equation and are effectively zero for $(\sin\theta)/\lambda > 1.5$ Å^{-1}. Those for heavier atoms are for relativistic wavefunctions, based on the calculations of Doyle & Turner (1968) using the wavefunctions of Coulthard (1967) (designated RHF in Table 6.1.1.1), or on those of Cromer & Waber (1968) using the wavefunctions of Mann (1968*a*) (designated *RHF).

Independent Atom Model (IAM)

comes from **quantum chemical** calculations

$$\rho_{at}(r) = N_c\rho_{core}(r) + N_v\rho_{valence}(r)$$

$$f^x(\mathbf{h}) = \int_V \rho_{at}(\mathbf{r})\, e^{2\pi i(\mathbf{hr})}\mathrm{d}\mathbf{r}$$

X-ray

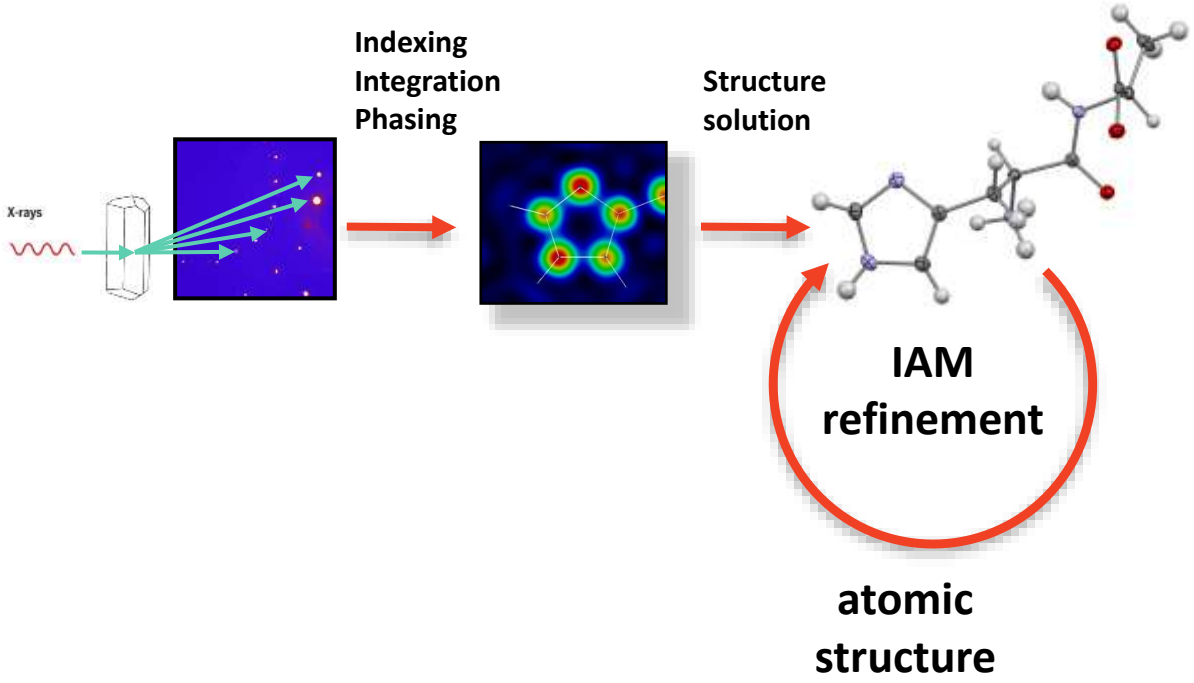
$$f^e(\mathbf{h}) = \frac{me^2}{8\pi^3\hbar^2\varepsilon_0}\frac{Z - f^x(\mathbf{h})}{\mathbf{h}^2}$$

electron

4.3.1.6. *Tables of atomic scattering amplitudes for electrons*

Tables 4.3.1.1 and 4.3.1.2 list values of $f^B(s)$ in Å for all neutral atoms and most chemically significant ions, respectively. The values have been given by Doyle & Turner (1968) for several cases, denoted by RHF using the relativistic Hartree–Fock atomic potentials of Coulthard (1967). For all other atoms and ions, $f^B(s)$ has been found using the Mott–Bethe formula [equation (4.3.1.15)] for $s \neq 0$, and the X-ray scattering factors of Table 2.2A of *IT* IV (1974). Thus all other neutral atoms except hydrogen are based on the relativistic Hartree–Fock wavefunctions of Mann (1968). These are designated by *RHF. For H and for ions below Rb, denoted by HF, $f^B(s)$ is ultimately based on the nonrelativistic Hartree–Fock wavefunctions of Mann (1968). For ions above Rb, denoted by *DS, modified relativistic Dirac–Slater wavefunctions calculated by Cromer & Waber (1974) are used.

Independent Atom Model (**IAM**) refinement



classic type of refinement

More realistic models of scattering

Atoms in molecules have partial charges

κappa model of electron density

$$\rho_{at}(\boldsymbol{r}) = N_c\rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r)$$

Takes into account:

- **charge transfer** between atoms (partial charges - Pv)
- **radial deformation** of the electron density of the atom (Pv, κ)

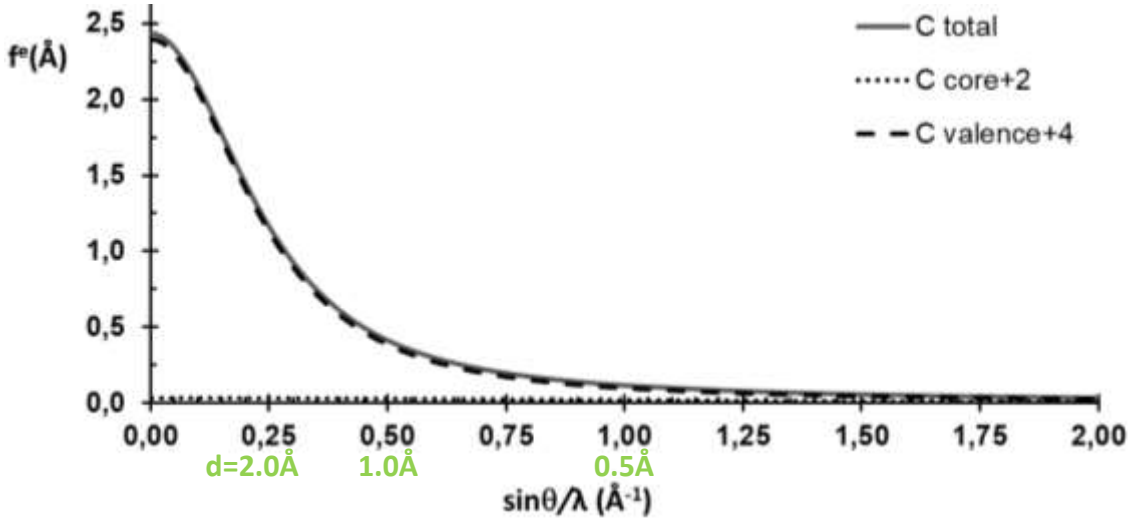
Coppens et al, Acta Cryst. A, 1979, *35*, 63

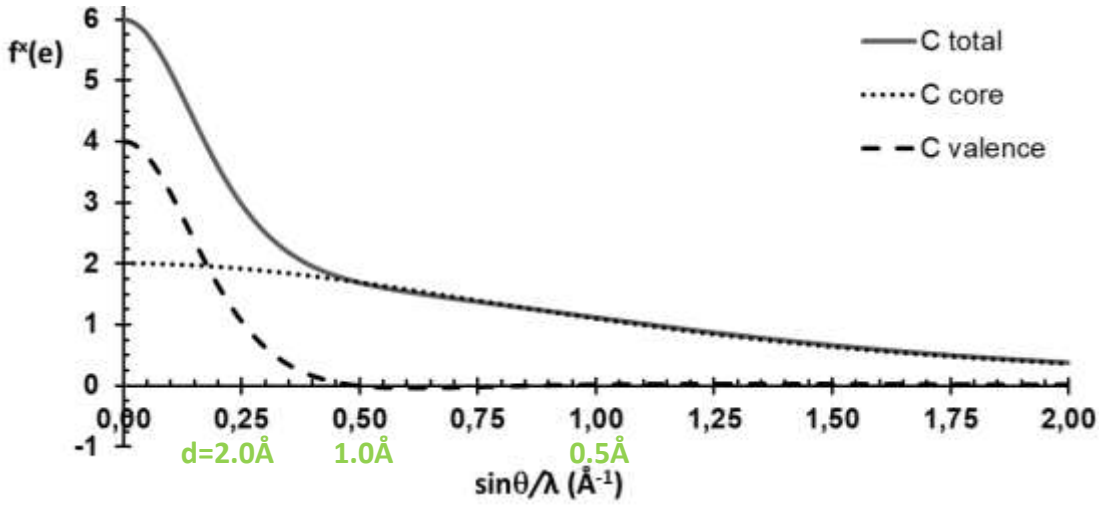
Valence electrons constribute more to **scattering** at low resolutions

$$\rho_{at}(\boldsymbol{r}) = N_c\rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r)$$

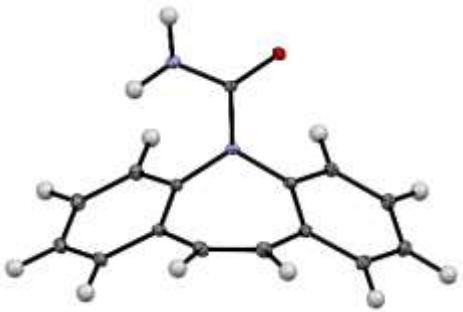
electron **X-ray**

electron shielding
effective nuclear charge





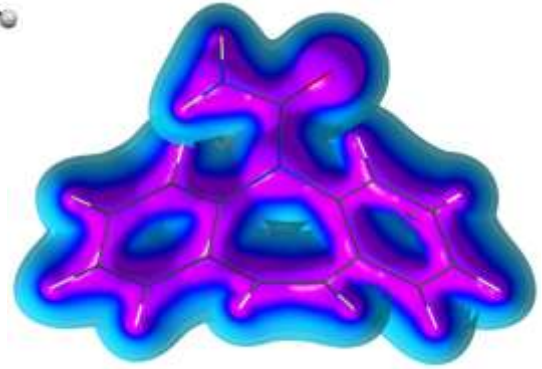
Electron densities of atoms in molecules are not spherical



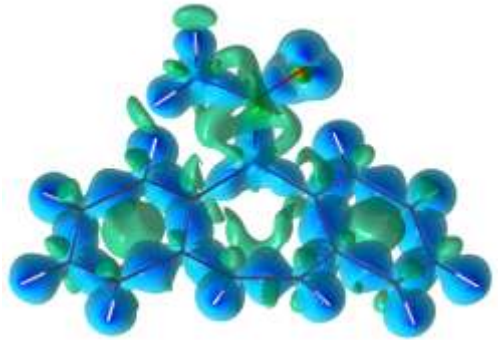
Shortcomings of the **IAM**

theoretical simulations

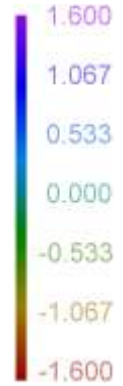
X-ray



electron density

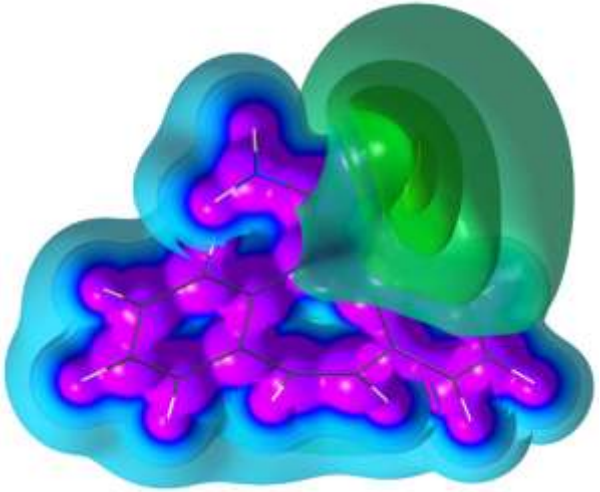


deformation electron density

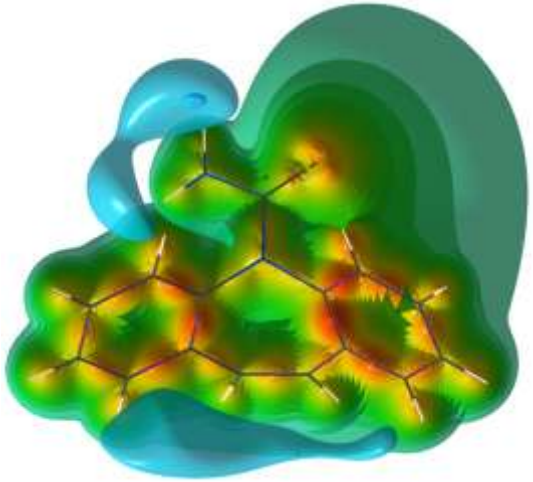


(eÅ^{-3})

electron



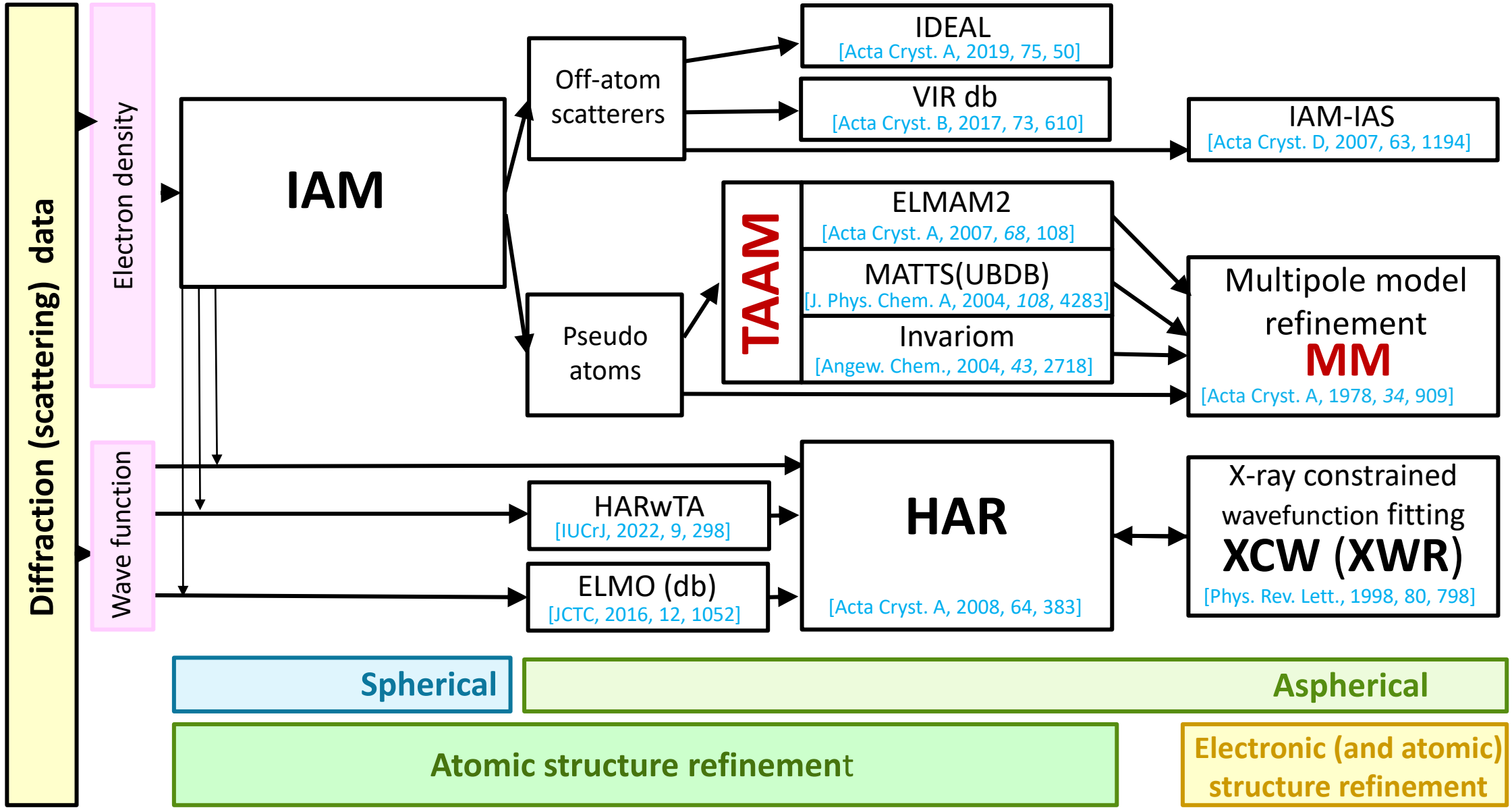
electrostatic potential



deformation electrostatic potential

(eÅ^{-1})

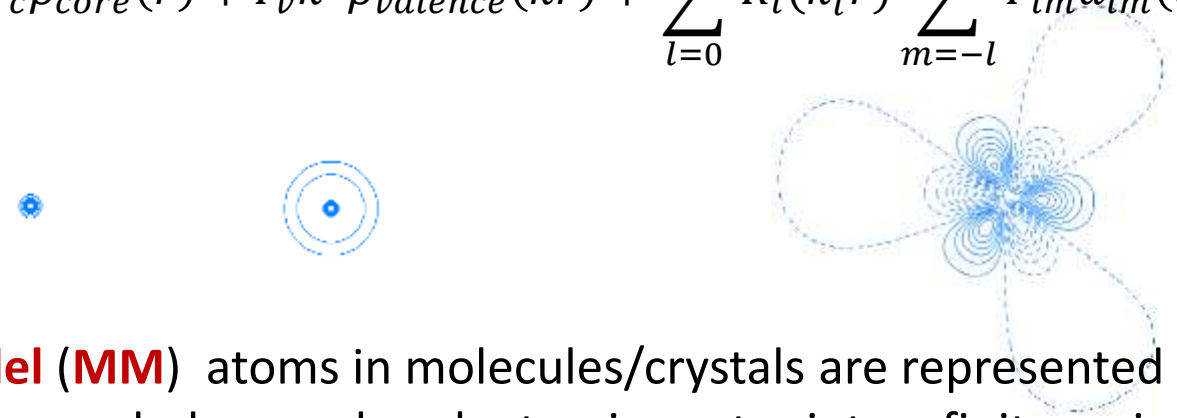
Scattering models currently the most popular in **Quantum Crystallography**



Electron density modelling

Multipole model

$$\rho_{at}(\boldsymbol{r}) = P_c\rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r) + \sum_{l=0}^{l_{\max}} R_l(\kappa_l' r) \sum_{m=-l}^{l} P_{lm} d_{lm}(\theta, \varphi)$$



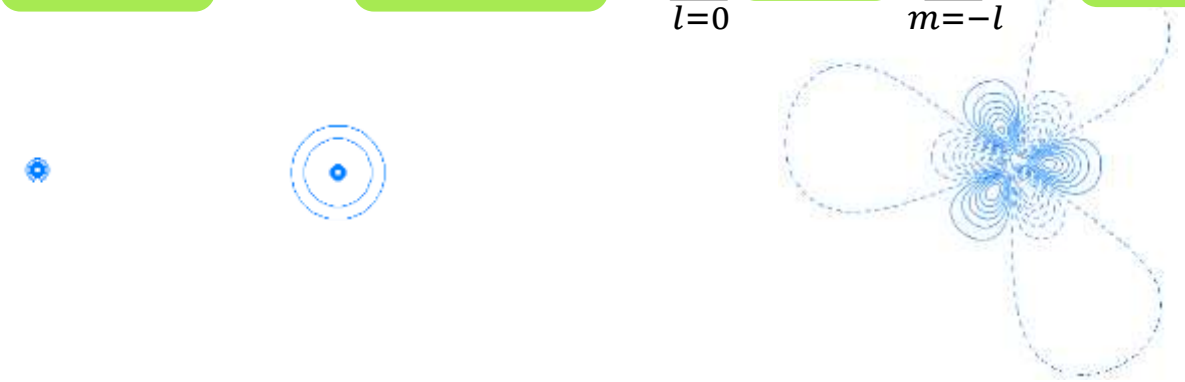
- In the **multipole model** (**MM**) atoms in molecules/crystals are represented by the electron density expanded around each atomic center into a finite series of spherical harmonics
- This expansion is called a **pseudoatom**
- MM takes into account the **charge transfer** between atoms and the **radial** and **angular** (aspherical) **deformation** of the electron density of atoms
- The Hansen-Coppens model (**HC-MM**), shown above, is the most common variant of MM

Hansen & **Coppens,** Acta Cryst. A, 1978, *34*, 909

Electron density modelling

Multipole model

$$\rho_{at}(\boldsymbol{r}) = P_c\rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r) + \sum_{l=0}^{l_{\max}} R_l(\kappa_l' r) \sum_{m=-l}^{l} P_{lm} d_{lm}(\theta,\varphi)$$



- Certain **functions** and **parameters** are precomputed from **atomic wavefunctions** using quantum mechanics and kept fixed

Hansen & Coppens, Acta Cryst. A, 1978, *34*, 909

Radial functions

$$\rho_{at}(\boldsymbol{r}) = P_c\rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r) + \sum_{l=0}^{l_{max}} R_l(\kappa_l' r) \sum_{m=-l}^{l} P_{lm} d_{lm}(\theta,\varphi)$$

The choice of the radial basis is in principle arbitrary, except that the analytical angular behaviour requires $R_{nlm}r^{-1}$ to be *finite at the origin*. In practice either Gaussian or **Slater** type functions have been used.

K. Kurki-Suonio *Isr. J. Chemistry* **1977**, *16*, 132

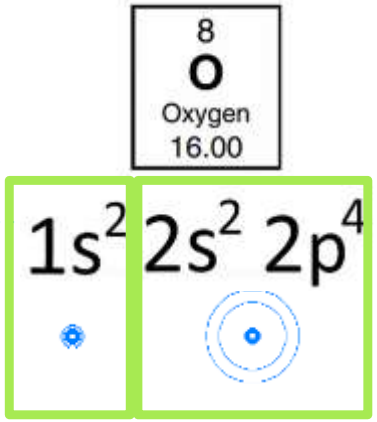
In the **HC-MM** Slater type fuctions are used

$$R(r) = Nr^{n-1}e^{-\zeta r}$$

$$N = (2\zeta)^n \sqrt{\frac{2\zeta}{(2n)!}}$$

Hansen & **Coppens,** Acta Cryst. A, 1978, *34*, 909

Radial functions for core and valence



$$\rho_{at}(\boldsymbol{r}) = P_c \rho_{core}(r) + P_v \kappa^3 \rho_{valence}(\kappa r) + \sum_{l=0}^{l_{\max}} R_l(\kappa_l' r) \sum_{m=-l}^{l} P_{lm} d_{lm}(\theta, \varphi)$$

Traditionally:

Clementi, E. & **Roetti**, C. (1974). *At. Data Nucl. Data Tables*, **14**, 177-478.

From the self-consistent-field **Roothan-Hartree-Fock** energy-optimization,

for the ground state isolated atoms, and more relevant ions, **from He up to Xe**,

expanded in Slater-type basis set:

atom *wfn*: $$\psi(r) = \left|\varphi_1 \varphi_2 \ldots \varphi_i\right\rangle = \left| \ldots \sum_{j=1}^{m} \left[(2n_j(l))!\right]^{-1/2} (2\zeta_j)^{n_j(l)+1/2} c_{ji} r^{n_j(l)-1} \exp(-\zeta_j r) \right\rangle$$

orbital: $$\varphi(r) = \sum_{j=1}^{m} \left[(2n_j(l))!\right]^{-1/2} (2\zeta_j)^{n_j(l)+1/2} c_j r_i^{n_j(l)-1} \exp(-\zeta_j r_i)$$

Relativistic *wfn* from **multi-configuration Dirac-Fock** calculation

Su, Z.; **Coppens**, P. *Acta Cryst* **1997,** *A53*, 749, Su, Z.; Coppens, P. *Acta Cryst* **1998,** *A54*, 646,

Macchi, P.; Coppens, P. *Acta Cryst.*, **2001**, *A57*, 656

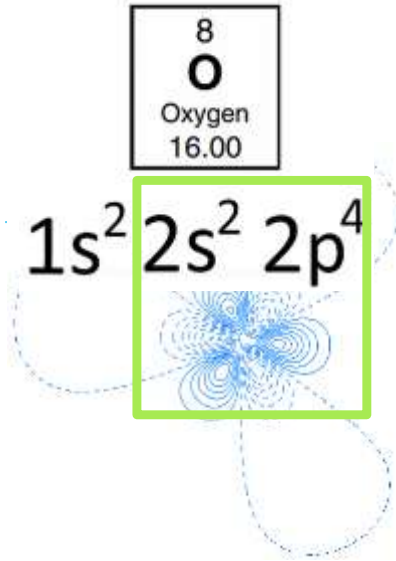
Radial functions for core and valence

atom *core* or *valence* electron density normalized to one electron:

$$\rho = \sum_{i} n_i \left|\psi_i\right|^2$$

density functions are products of atomic orbitals

Radial functions for valence deformation term



$$\rho_{at}(\boldsymbol{r}) = P_c\rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r) + \sum_{l=0}^{l_{\max}} R_l(\kappa_l' r) \sum_{m=-l}^{l} P_{lm} d_{lm}(\theta,\varphi)$$

$$R_l(\kappa_l' r) = (\kappa_l'\alpha_l)^3 \frac{(\kappa_l'\alpha_l r)^{n(l)}}{[n(l)+2]!} \exp(-\kappa_l'\alpha_l r)$$

$$\alpha_l = 2\zeta(l)$$

Single Slater-type function

with parameters of the radial functions ($n(l)$, $\zeta(l)$) obtained from the Hartree–Fock optimized single-ζ exponents of the valence-orbital wavefunctions calculated for free atoms

Clementi, E. & **Raimondi**, D. L. (1963). *J. Chem. Phys*. **38**, 2686-2689.

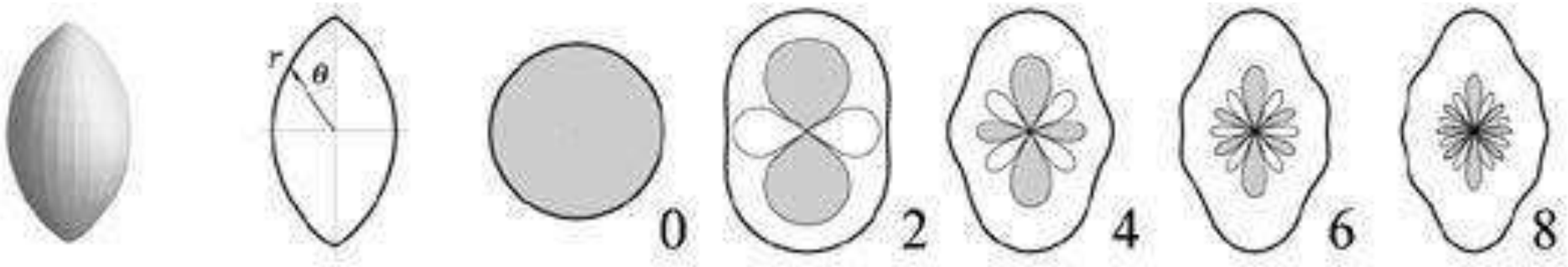
Z	1s	2s	2p
2.	1.6875		
3.	2.6906	0.6396	
4.	3.6848	0.9560	
5.	4.6795	1.2881	1.2107
6.	5.6727	1.6083	1.5679
7.	6.6651	1.9237	1.9170
8.	7.6579	2.2458	2.2266
9.	8.6501	2.5638	2.5500
10.	9.6421	2.8792	2.8792

Electron density modelling

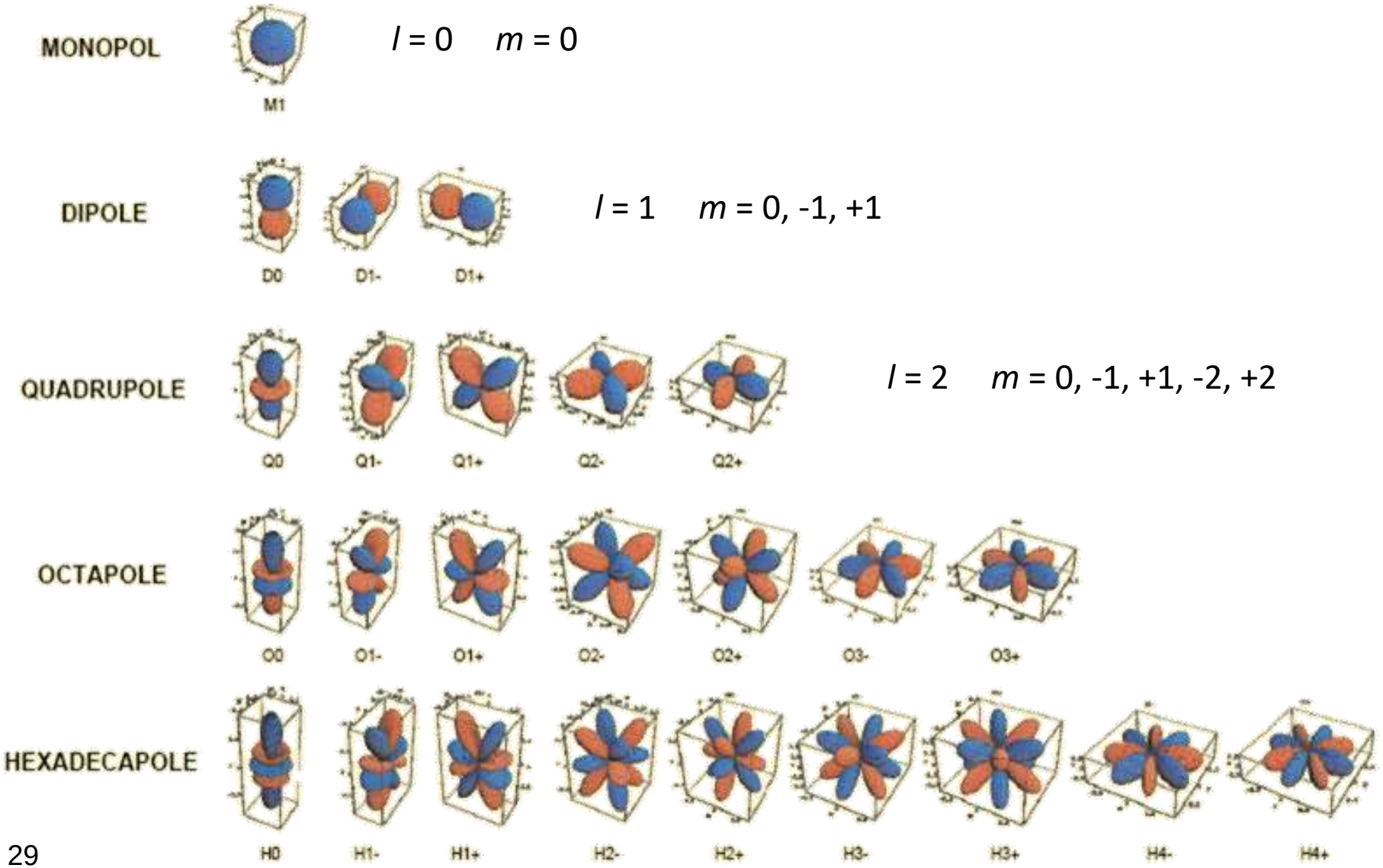
Multipole model

$$\rho_{at}(\boldsymbol{r}) = P_c\rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r) + \sum_{l=0}^{l_{\max}} R_l(\kappa_l' r) \sum_{m=-l}^{l} P_{lm} d_{lm}(\theta,\varphi)$$

The spherical harmonics are a complete set of orthogonal functions on the sphere



Real **spherical harmonics** for valence deformation term



Multipoles

P. Coppens, *X-ray Charge Densities and Chemical Bonding*, IUCr texts on Crystallography, Oxford Univ. Press, **1997**.

Real **spherical harmonics** – coordinate system

$$\rho_{at}(\boldsymbol{r}) = P_c\rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r) + \sum_{l=0}^{l_{\max}} R_l(\kappa_l' r) \sum_{m=-l}^{l} P_{lm} d_{lm}(\theta, \varphi)$$

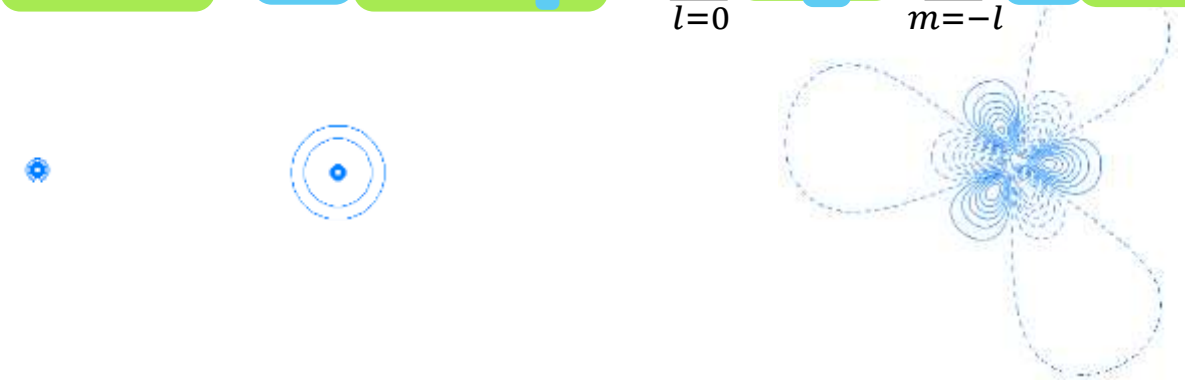
Real spherical harmonics are expressed in the local coordinate system centred on atom position

Any framework is valid, but it is wise to choose a convenient reference

- to be able to use symmetry constraints
- to minimize number of highly populated multipoles
- to compare atoms and be able to use chemical constraints

Electron density modelling
Multipole model

$$\rho_{at}(\boldsymbol{r}) = P_c\rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r) + \sum_{l=0}^{l_{\max}} R_l(\kappa_l' r) \sum_{m=-l}^{l} P_{lm} d_{lm}(\theta,\varphi)$$



- Certain **functions** and **parameters** are precomputed from atomic wavefunctions using quantum mechanics and kept fixed

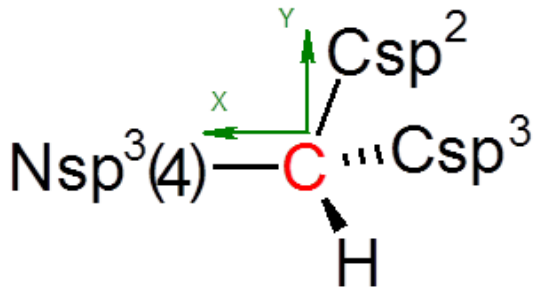
- Populations P_v and P_{lm}, and expansion-contraction parameters κ and κ' are adjusted

Hansen & **Coppens,** Acta Cryst. A, 1978, *34*, 909

Electron density parameters of multipole model are almost identical for atoms in similar chemical environments (topologies)

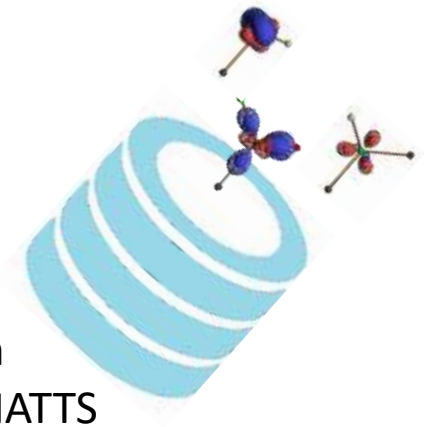
$$\rho_{at}(\boldsymbol{r}) = P_c\rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r) + \sum_{l=0}^{l_{\max}} R_l(\kappa_l' r) \sum_{m=-l}^{l} P_{lm} d_{lm}(\theta,\varphi)$$

Atom ID	...	P_{11+}	P_{20}	P_{22+}	P_{31+}	P_{31-}	...
1		-0.11	0.05	-0.16	-0.10	-0.18	
2		-0.11	0.06	-0.18	-0.11	-0.20	
3		-0.10	0.09	-0.13	-0.11	-0.20	
4		-0.12	0.08	-0.13	-0.12	-0.21	
5		-0.12	0.08	-0.15	-0.14	-0.20	
...		...	...	...	...	...	
Av.		**-0.11(1)**	**0.07(1)**	**-0.15(2)**	**-0.12(1)**	**-0.20(1)**	



Pichon-Pesme, et al.., 1995, J Phys Chem, 99, 6242

Electron density parameters of MM can be stored in a data bank



[Acta Cryst. A, 2007, *68* 108] ELMAM

[Angew. Chem., 2004, 43, 2718] Invariom

[J. Phys. Chem. A, 2004, 108, 4283] UBDB/MATTS

[JCIM, 2022, 62, 3752 & 3766] ....

and **transfered** on demand to build **TAAM** for a studied system

Pseudoatom data banks

- **ELMAM**, **MATTS/UBDB** and **Invariom** banks differ by:
  - source of geometries of model molecules (experimental or theoretical)
  - methods of obtaining electron density (experimental or theoretical)
  - protocols for refining the MM model
  - definitions of the types of atoms
  - averaging the parameters of pseudoatoms of a given type of atom within a family of model molecules
    or no averaging (one model molecule for one type of atom)

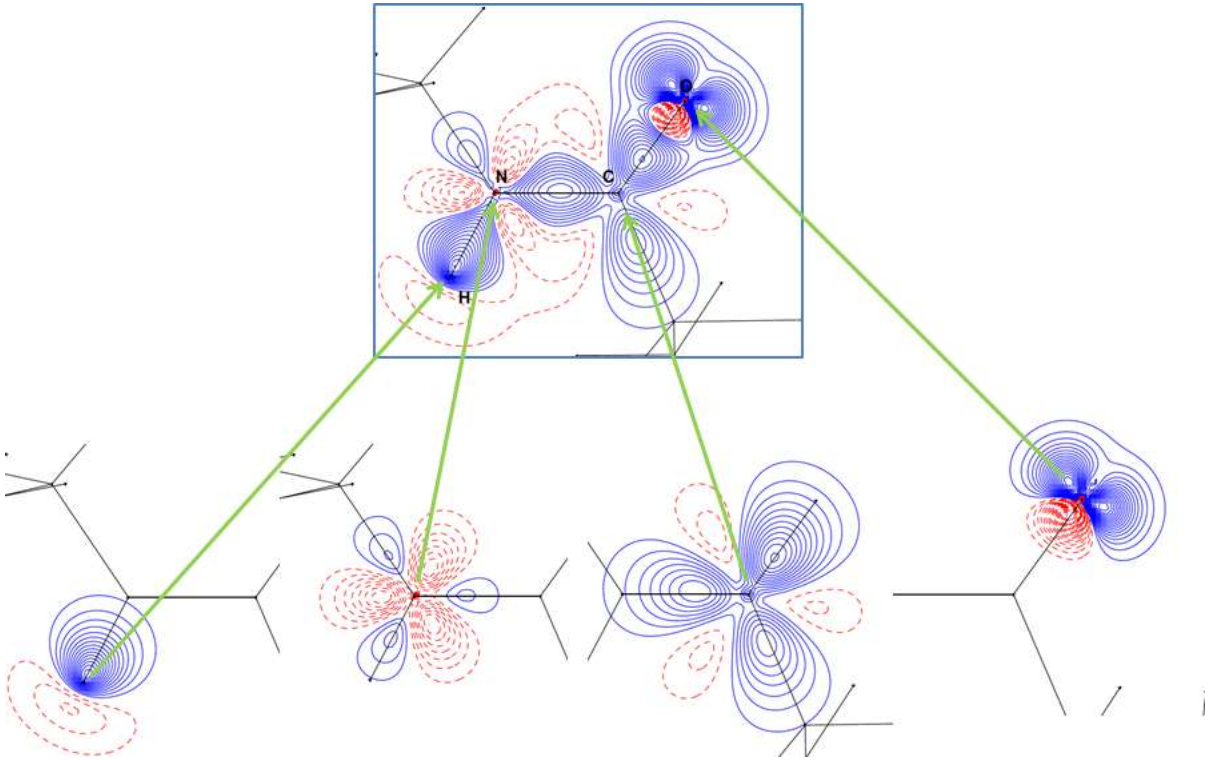
Acta Cryst. A*68*, 139; **Acta Cryst. A***68*, 337; **Acta Cryst. D***62*, 1325; **Acta Cryst**. A*67*, 141

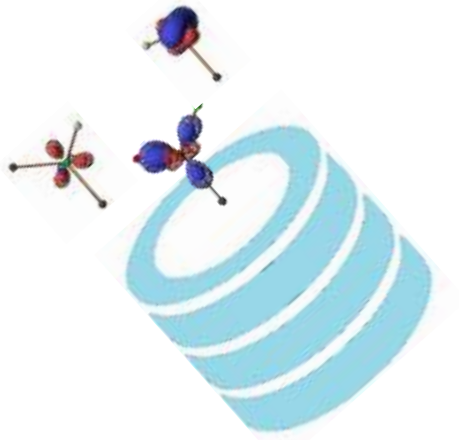
Pseudoatom data banks

- ELMAM - averaging experimental electron densities, crystal geometries
- Invariom – electron density from one model molecule with geometry optimized in vacuo
- MATTS/UBDB - averaging theoretical electron densities, crystal geometries
  - There is no practical difference between these banks when it comes to using them as the source of aspherical scattering factors in the TAAM refinement
  - All three banks lead to a similar quality of structure data and all have a comparative advantage over the IAM model
  - Properties calculated from the reconstructed densities can vary

Bąk, **Dominiak**, et al., Acta Cryst. A, 2011, 67, 141

Transferable Aspherical Atom Model **(TAAM)**
used to compute aspherical scattering factors

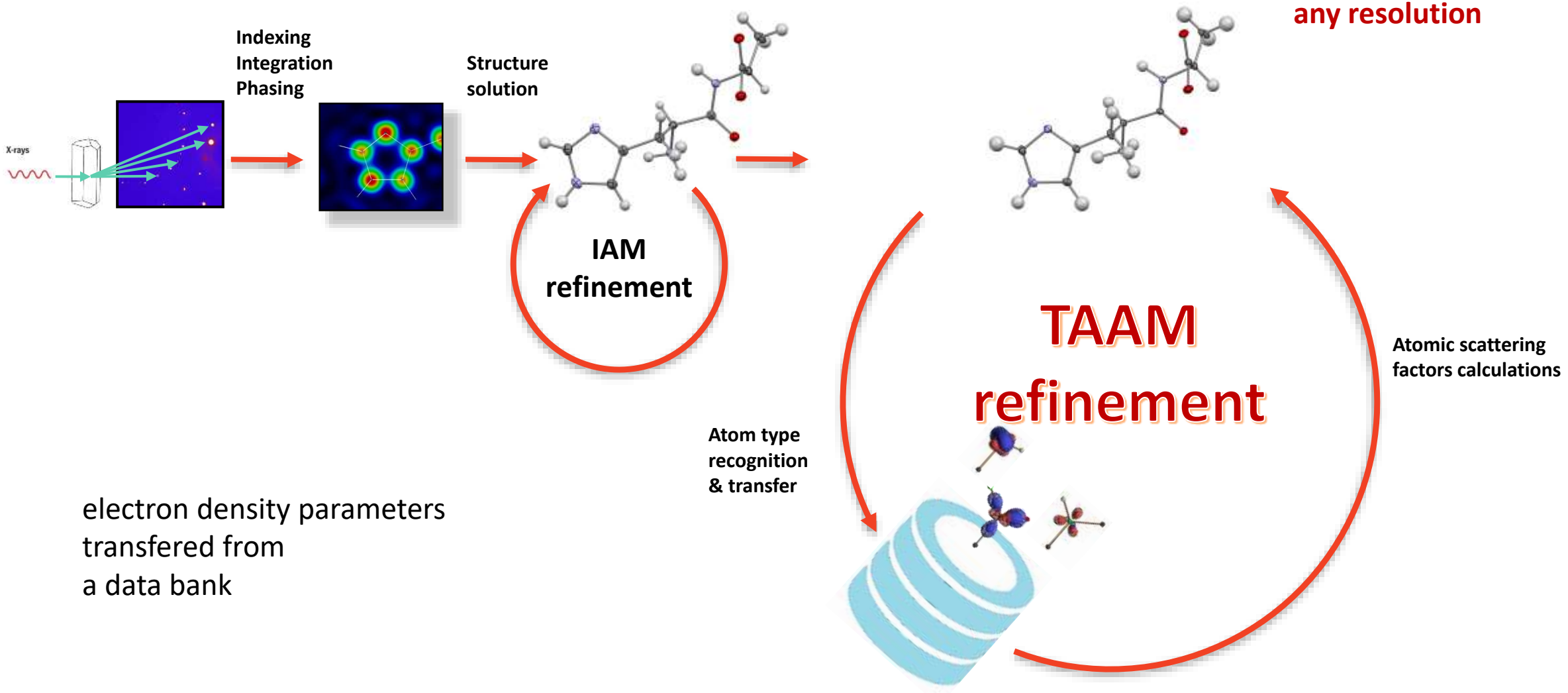




Against the experimental data **refined are**:

- the average **positions of atoms** in the unit cell (**x, y, z**)
- the parameters describing the **displacement of atoms** from their average position (**ADPs**)

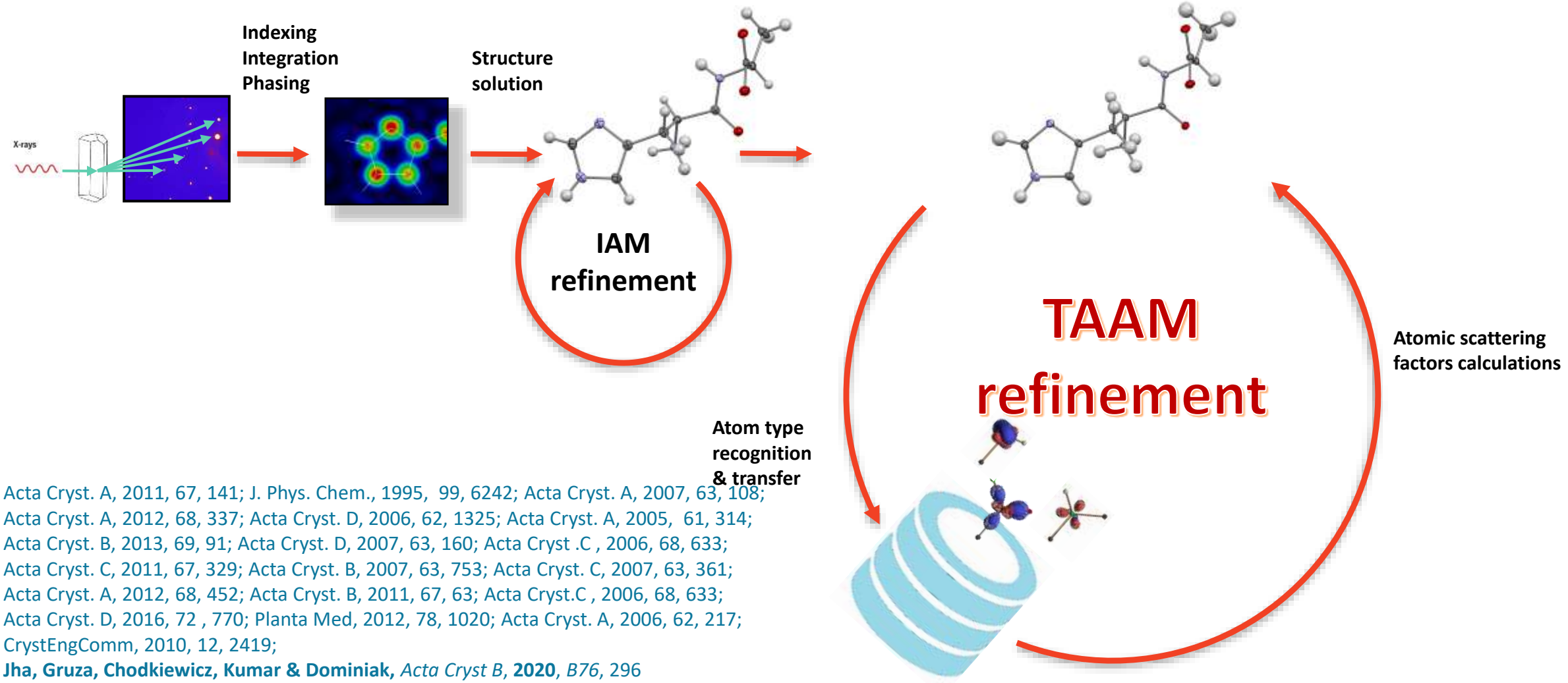
Transferable Aspherical Atom Model (**TAAM**) refinement



electron density parameters
transfered from
a data bank

Only x, y, z coordinates and ADPs
are refined against experimental data

Transferable Aspherical Atom Model (**TAAM**) refinement

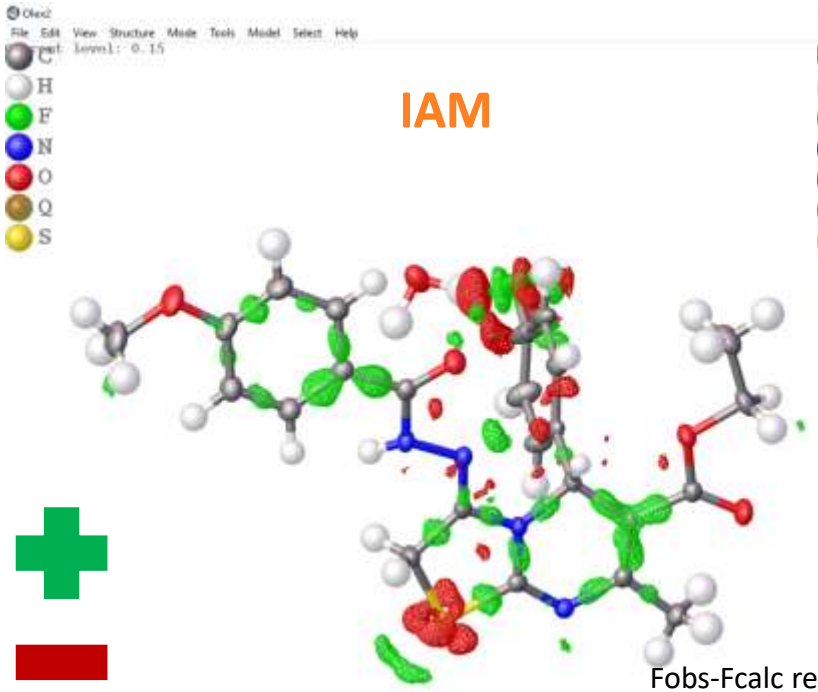


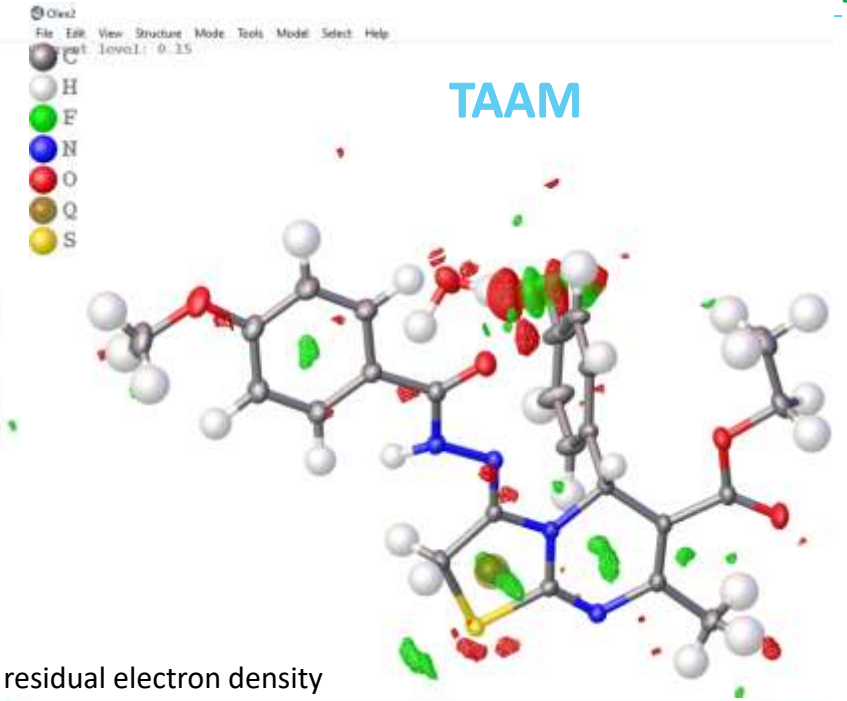
Acta Cryst. A, 2011, 67, 141; J. Phys. Chem., 1995, 99, 6242; Acta Cryst. A, 2007, 63, 108;
Acta Cryst. A, 2012, 68, 337; Acta Cryst. D, 2006, 62, 1325; Acta Cryst. A, 2005, 61, 314;
Acta Cryst. B, 2013, 69, 91; Acta Cryst. D, 2007, 63, 160; Acta Cryst .C , 2006, 68, 633;
Acta Cryst. C, 2011, 67, 329; Acta Cryst. B, 2007, 63, 753; Acta Cryst. C, 2007, 63, 361;
Acta Cryst. A, 2012, 68, 452; Acta Cryst. B, 2011, 67, 63; Acta Cryst.C , 2006, 68, 633;
Acta Cryst. D, 2016, 72 , 770; Planta Med, 2012, 78, 1020; Acta Cryst. A, 2006, 62, 217;
CrystEngComm, 2010, 12, 2419;
Jha, Gruza, Chodkiewicz, Kumar & Dominiak, *Acta Cryst B*, **2020**, *B76*, 296
Jha, Kleemiss, Chodkiewicz & Dominiak, *J. Appl. Cryst*, **2023**, *56*, 116

...

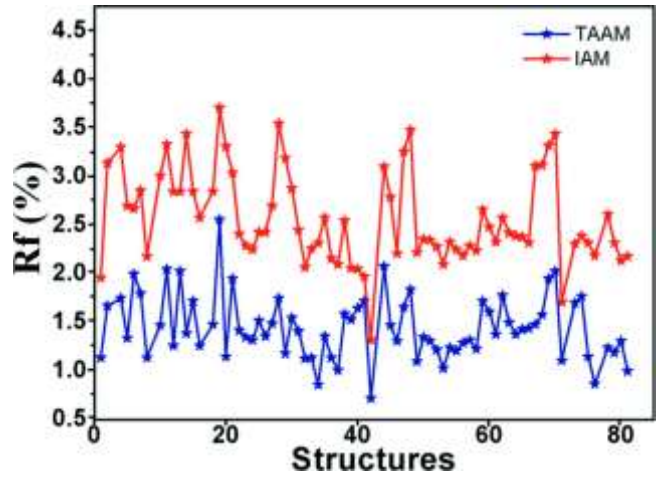
Improvements after **TAAM** refinement in **routine** small-molecule **X-ray** crystallography

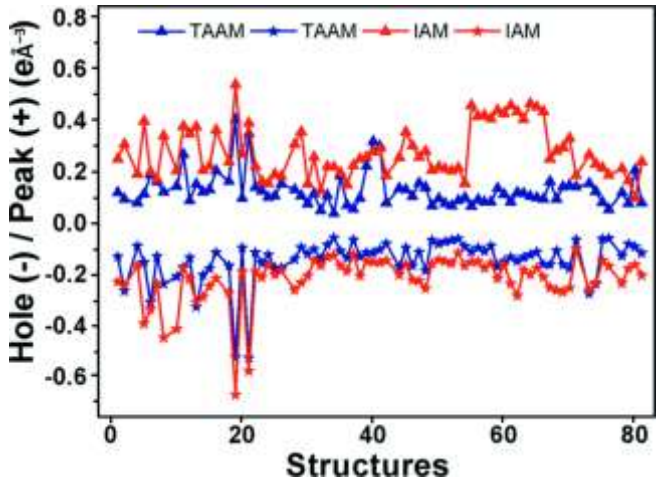
UBDB/MATTS





Fobs-Fcalc residual electron density





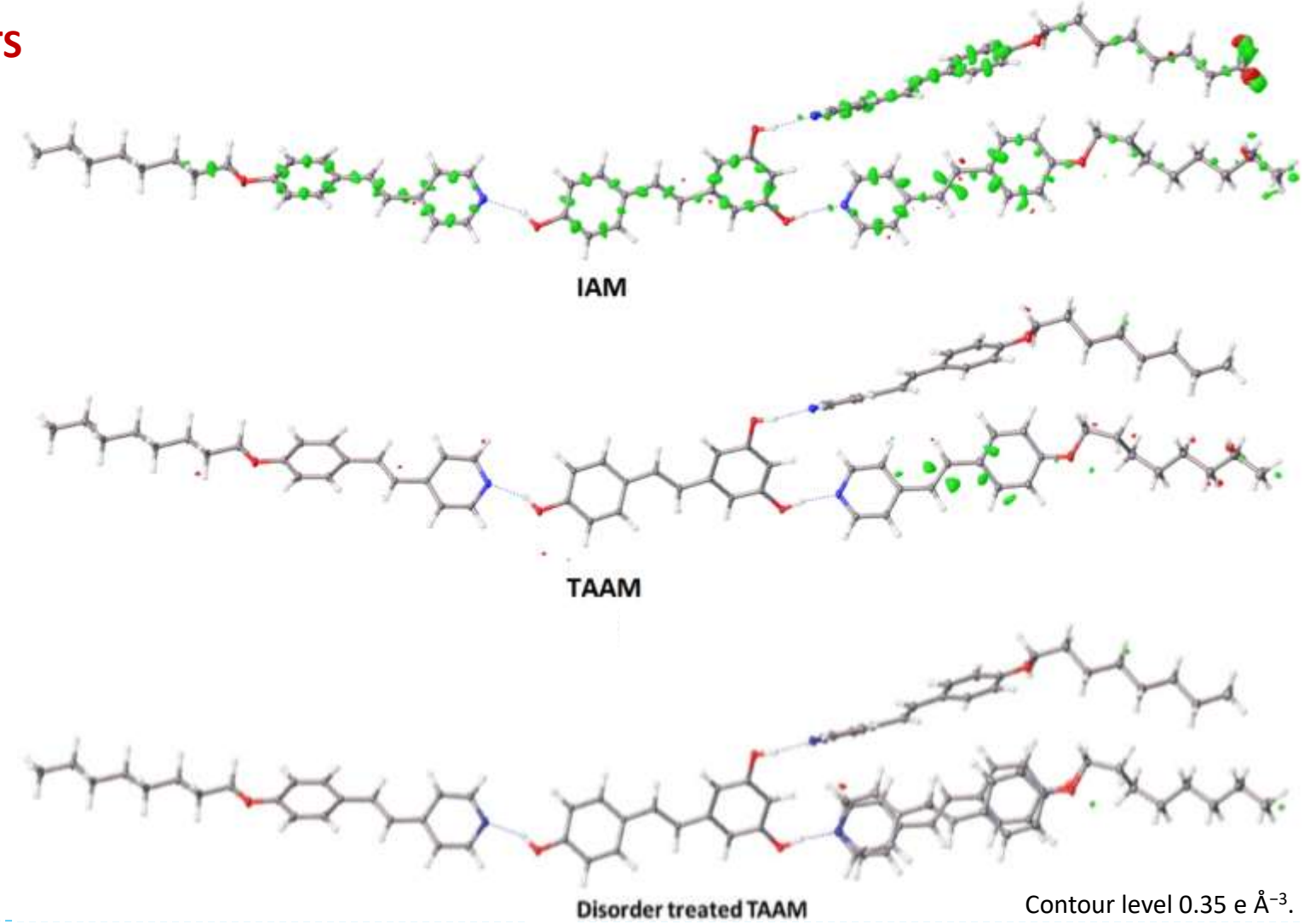
CRYSTALLOGRAPHIC COMMUNICATIONS *Acta Cryst.* (2022). E78

Jha, et al.., *Acta Cryst B*, **2020**, *B76*, 296 P.M.Dominiak, CNBCh UW

Woińska et al. *Sci. Adv*. **2016**, *2*, e1600192

TAAM refinement with **X-ray diffraction** data of **atomic resolution** allows to see & model more details

MATTS



	IAM
$R1_{all}$ (%)	8.50
$R1_{gt}$ (%)	5.17
Hole/ Peak (e Å^{-3})	0.69/ -0.37

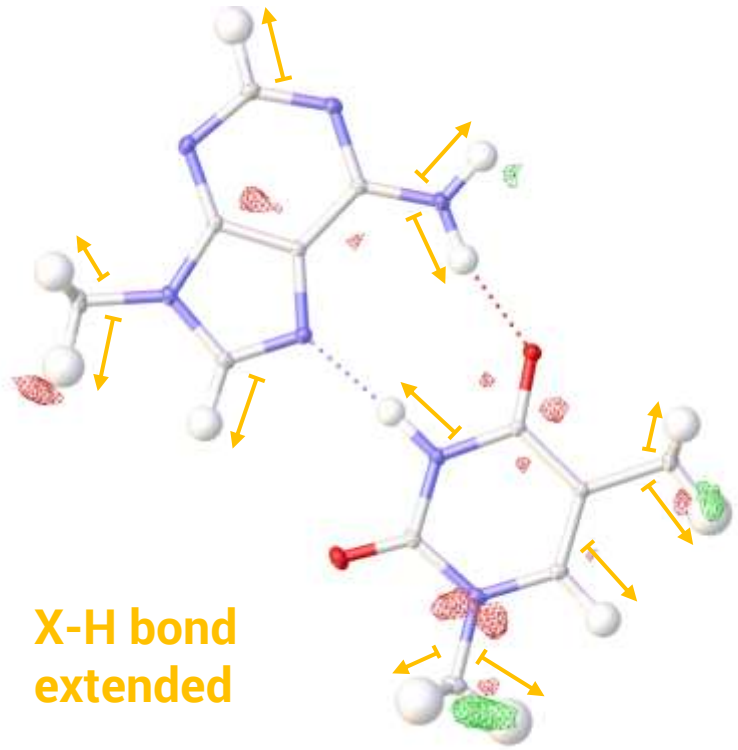
	TAAM
$R1_{all}$ (%)	7.06
$R1_{gt}$ (%)	3.71
Hole/ Peak (e Å^{-3})	0.72/ -0.46

	5% disorder TAAM
$R1_{all}$ (%)	6.65
$R1_{gt}$ (%)	3.31
Hole/ Peak (e Å^{-3})	0.36/ -0.35

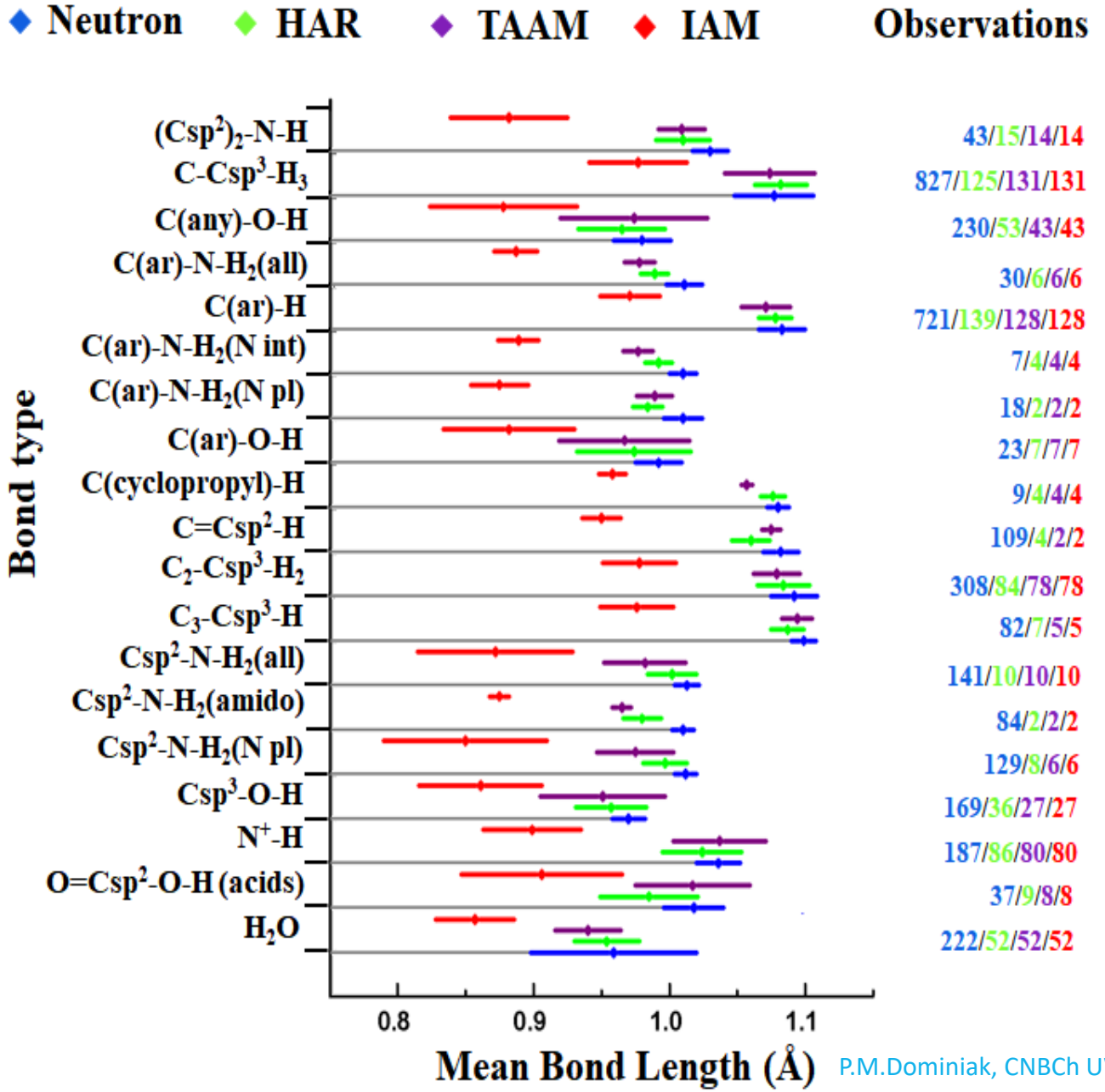
Contour level 0.35 e Å^{-3}.

Jha, Kleemiss, Chodkiewicz & Dominiak, *J. Appl. Cryst*, **2023**, *56*, 116

TAAM & HAR refinement with X-ray diffraction data of atomic resolution improves location of hydrogen atoms



X-H bond extended



P.M.Dominiak, CNBCh UW

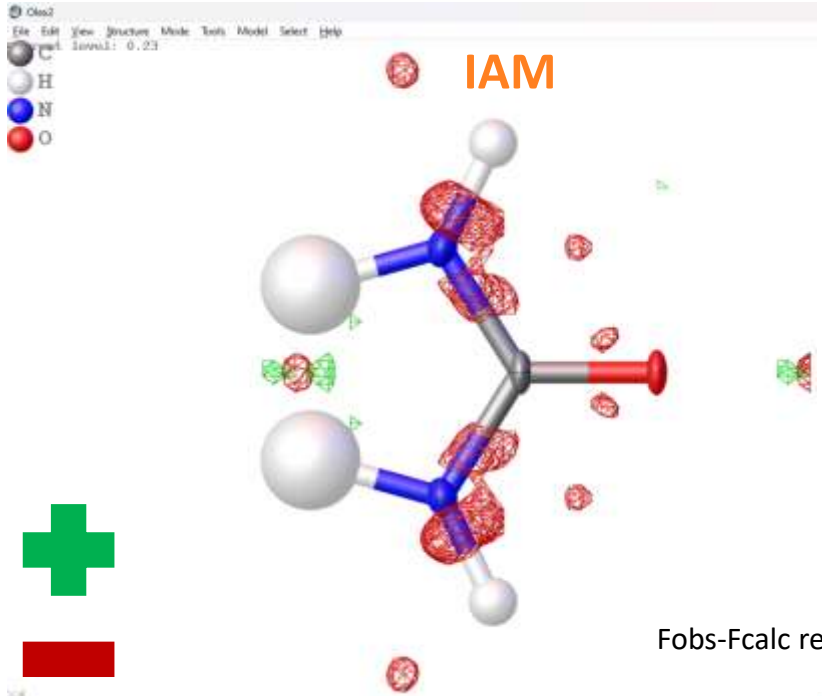
UBDB/MATTS

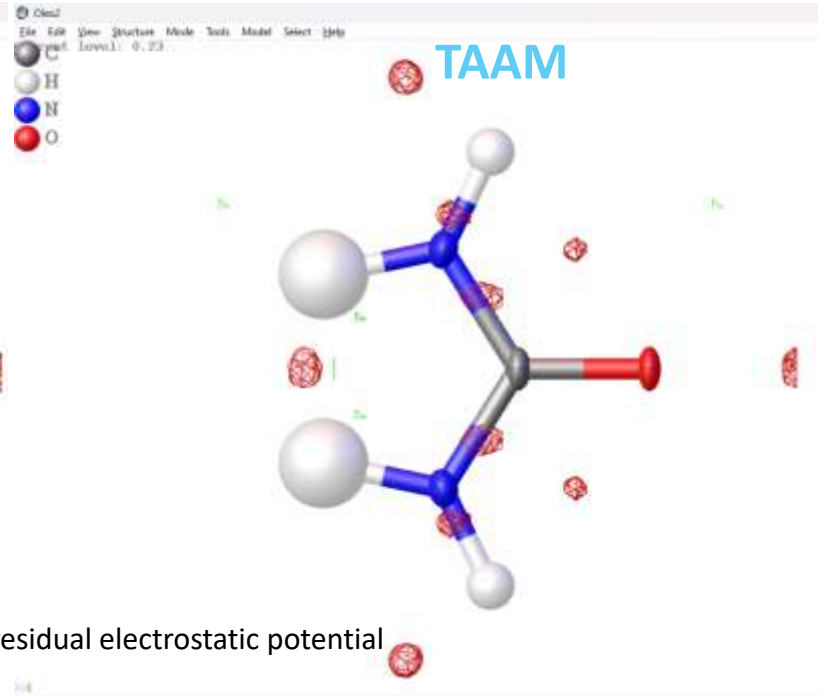
Jha, Gruza, Chodkiewicz, Kumar & Dominiak, *Acta Cryst B*, **2020**, *B76*, 29

Woińska et al. *Sci. Adv*. **2016**, *2*, e1600192

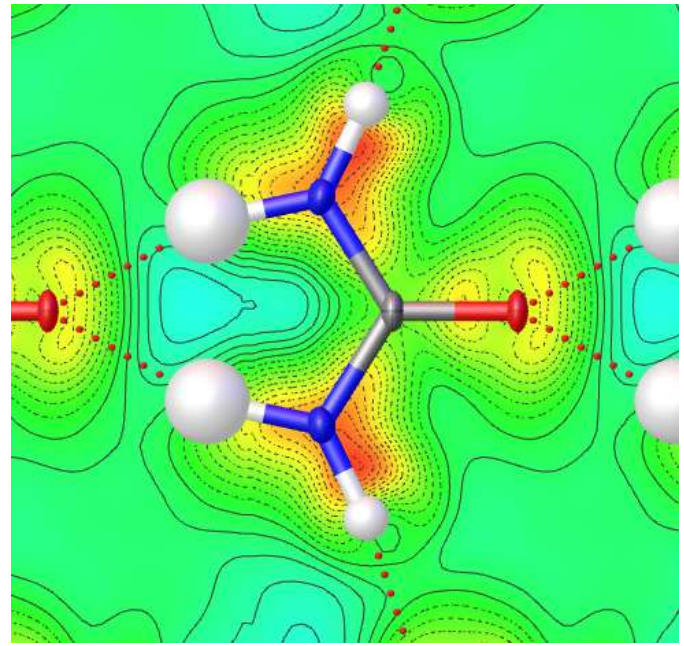
TAAM refinement with electron diffraction

Kinematical refinement

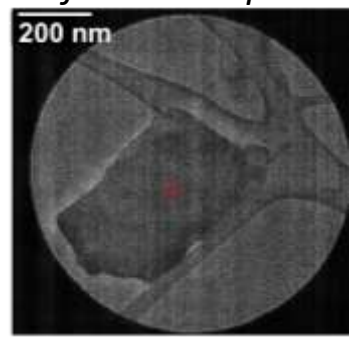




Fobs-Fcalc residual electrostatic potential



Simulated deformation potential maps

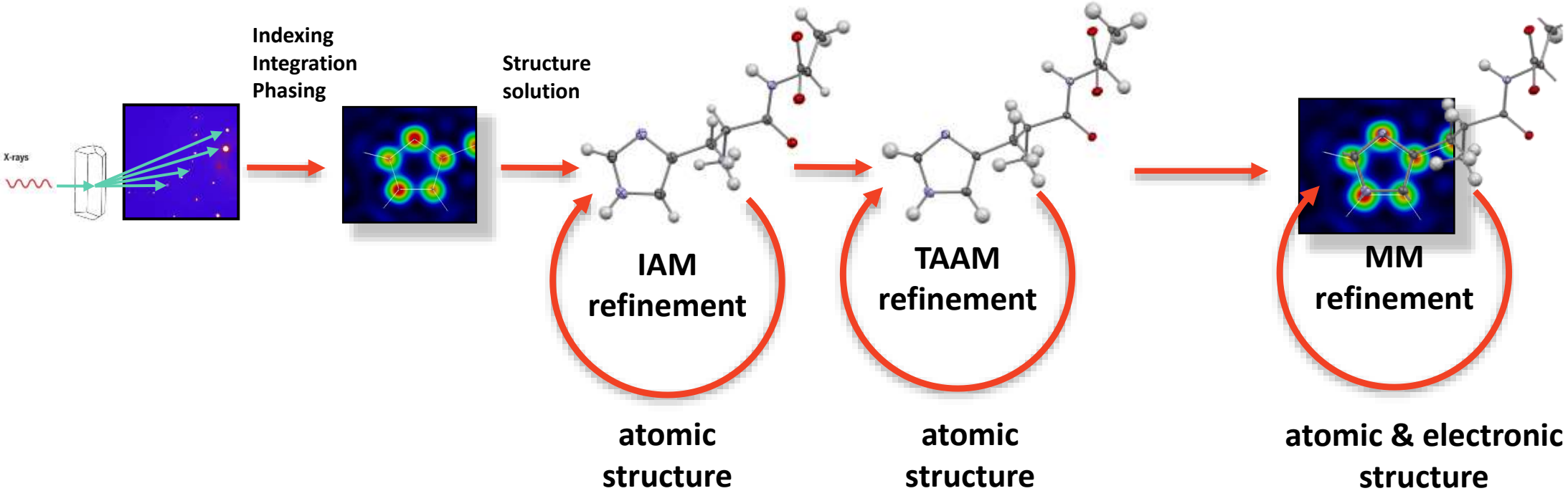


UNIWERSYTET WARSZAWSKI

CeNT

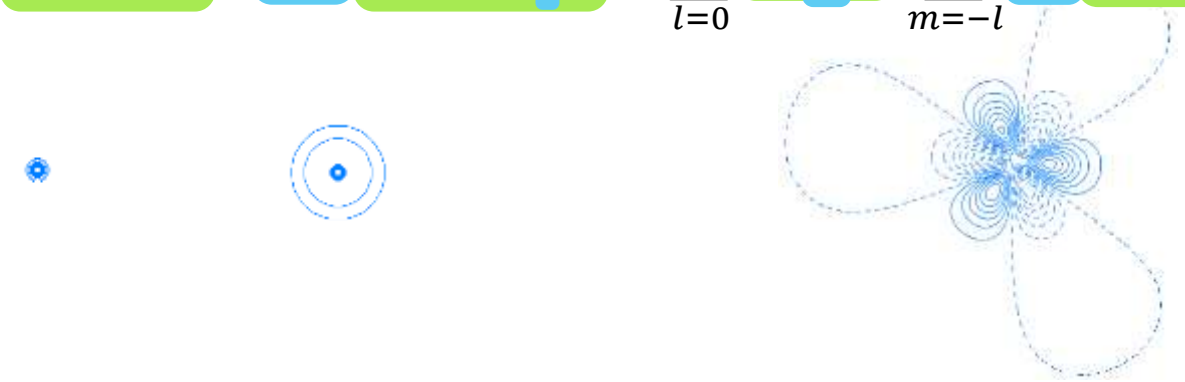
Kumar et al., 2024, Acta Cryst C, 80, 264

Multipole Model (MM) refinement on **subatomic resolution** data



Selected **electron density parameters** are refined on experimental data

$$\rho_{at}(\boldsymbol{r}) = P_c\rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r) + \sum_{l=0}^{l_{max}} R_l(\kappa_l' r) \sum_{m=-l}^{l} P_{lm} d_{lm}(\theta,\varphi)$$



- Certain **functions** and **parameters** are precomputed from atomic wavefunctions using quantum mechanics and kept fixed
- Populations P_v and P_{lm}, and expansion-contraction parameters κ and κ' are refined
- The numer of parameters per atom increase –> large numer of reflections is needed –> subatomic resolution

 Hansen & **Coppens,** Acta Cryst. A, 1978, *34*, 909

Practical problems in charge density refinement using multipole model

- Hydrogen atoms positions
  - collect neutron diffraction data for the crystal and build constrains/restrains for the X-H bond lengths from them
  - use mean values of the X-H bond lengths from neutron data
  - use HAR or TAAM refinement (?)

- Hydrogen atoms thermal motions
  - collect neutron diffraction data for the crystal and transfer the ADPs, check if scalling is needed
  - use estimates from neutron data – SHADE
  - do NoMore refinement (?)
  - use HAR or TAAM refinement (?)

- Influence of the starting point & convergance problems
  - do high-order refinement for non-H to deconvolute better thermal motion from static electron density
  - do HAR or TAAM refinement
  - use a pseudoatom data bank values as a starting point
  - do step-by-step refinement, slowly increasing numer of parameters (level by level, symmetry – no symmetry, etc.)
  - do iterative block refinement

- Kappa parameters
  - take them from a pseudoatom data bank
  - take them from multipole refinement againts theoretical structure factors computed with periodic DFT

Verification of refinement and model

FIT:

- Residual statistical indicies
- Fourier diffrence map

MODEL:

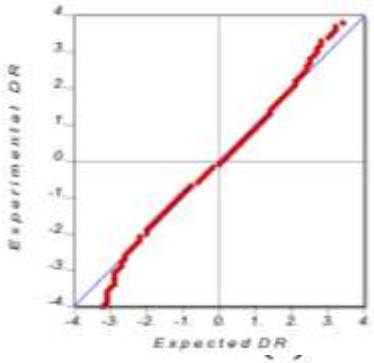
- ADPs – Hirshfeld rigid bond test
- Deformation maps, Laplacian maps, etc.

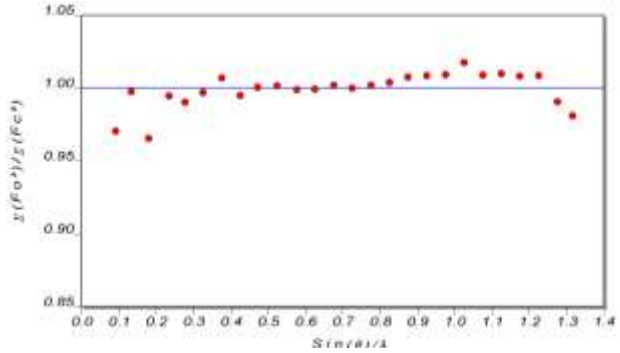
Verification of refinement and model

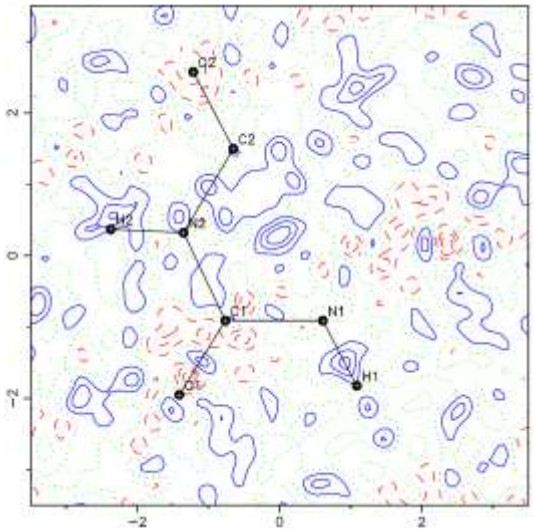
Fourier maps computed for all data.

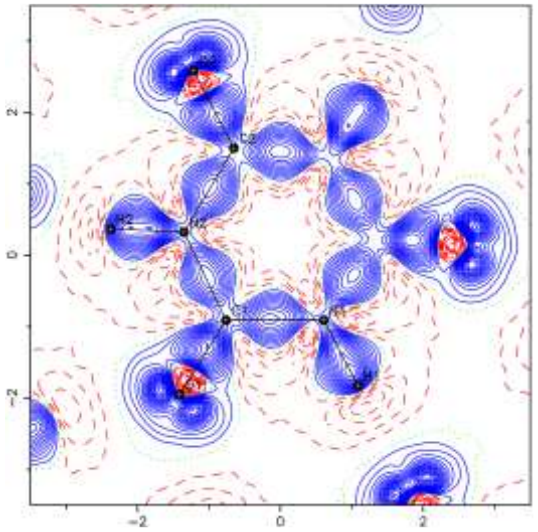
Contouring at 0.05 e·Å^{-3}; blue solid lines – positive values, red dashed lines – negative values.

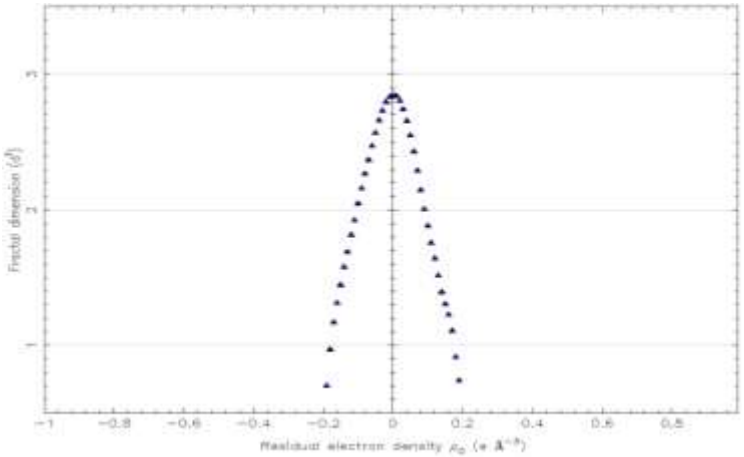
FIT:











Refinement parameters[#]

No. of reflections / parameters / restraints	6322 / 198 / 0
$R[F]$ $(I \geq 3\sigma(I))$ / (all data)	1.15% / 1.72%
$wR2[F^2]$ $(I \geq 3\sigma(I))$ / (all data)	3.18% / 3.41%
$R[F^2]$ $(I \geq 3\sigma(I))$ / (all data)	1.59% / 1.62%
$S[F^2]$ $(I \geq 3\sigma(I))$ / (all data)	0.989 / 0.979
$\Delta\rho_{min}$ / $\Delta\rho_{max}$ / e·Å^{-3} $(I \geq 3\sigma(I))$	−0.14 / +0.15
$\Delta\rho_{min}$ / $\Delta\rho_{max}$ / e·Å^{-3} (all data)	−0.15 / +0.14

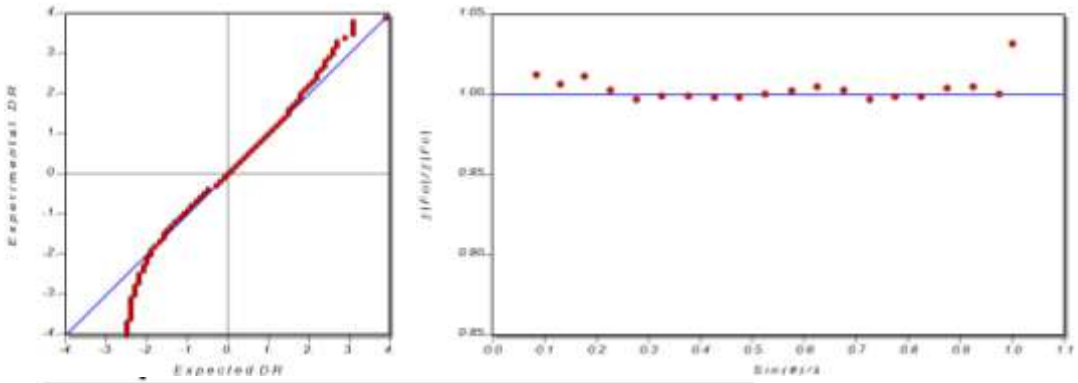
Meindl & Henn, Acta Cryst. A, 2008, *64*, 404

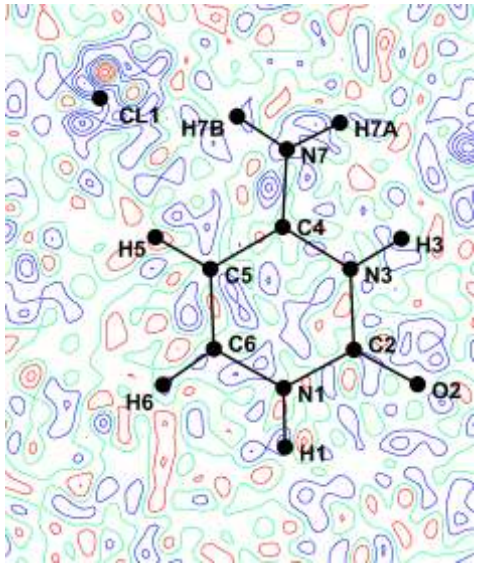
Verification of refinement and model

Fourier maps computed for all data.

Contouring at 0.05 e·Å^{-3}; blue solid lines – positive values, red dashed lines – negative values.

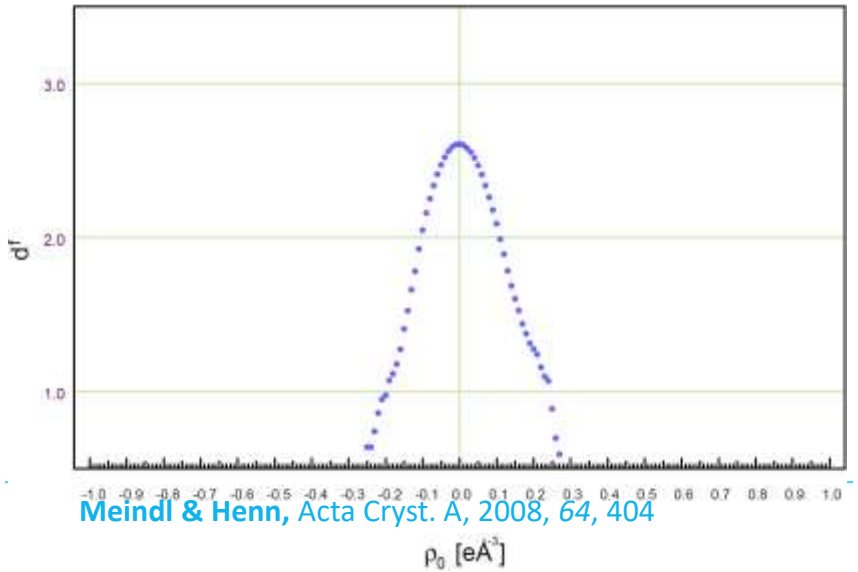
FIT:





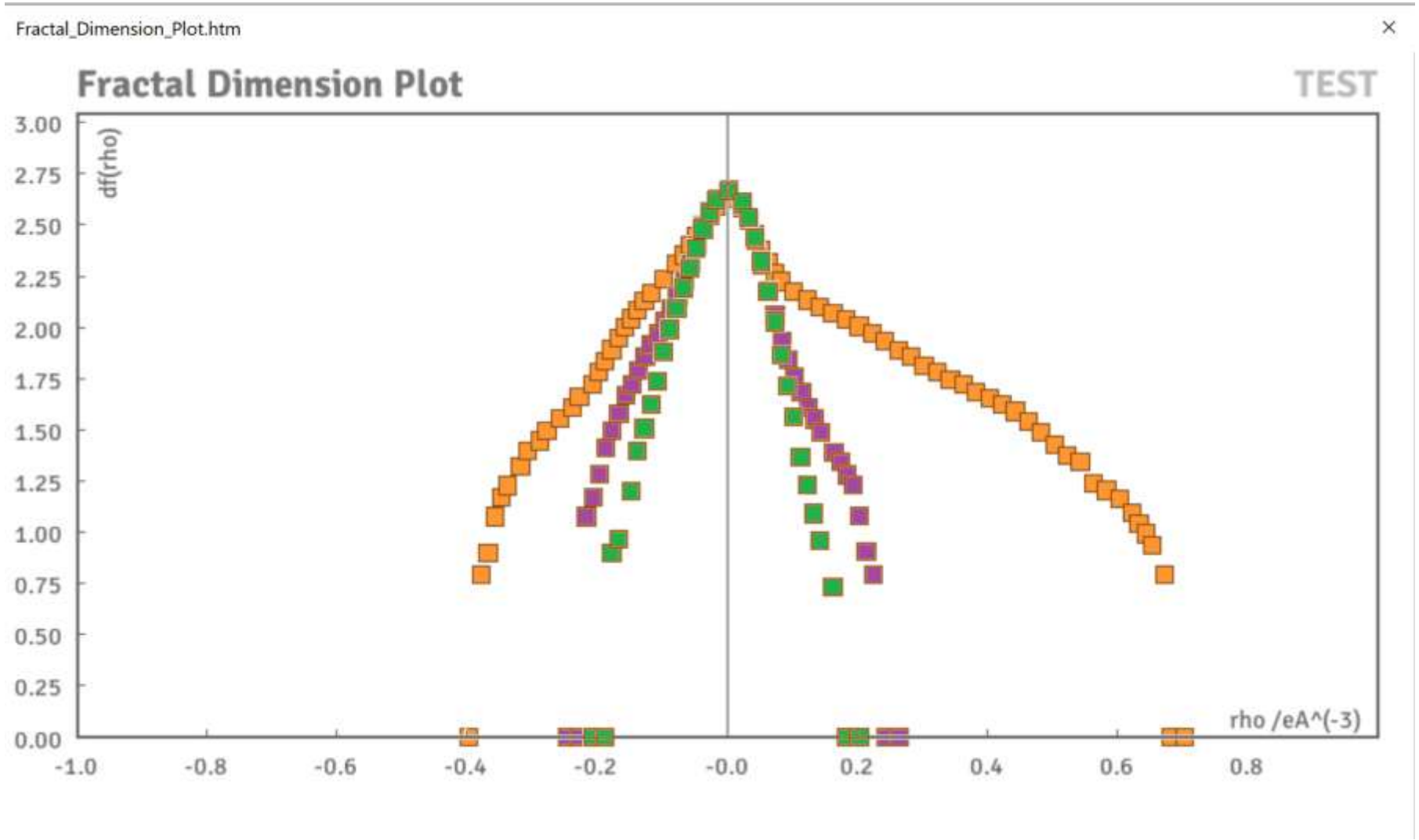
Multipole Refinement Statistics
for ionic Cl^{-1} scattering radial functions (top)
and neutral Cl^{0} one (bottom, *italic*)

I/sig(I) cutoff	2.0
N obs/N restr/N par	4590/6/276
R(F), wR2(F)(%)	1.59, 2.37 *1.58, 2.37*
R(I), wR2(I)(%)	1.85, 4.28 *1.74, 4.28*
wGOF on F^2	1.21 *1.22*
Largest diff. peak/hole eÅ^{-3}	0.27, -0.26 *0.26, -0.26*



Meindl & Henn, Acta Cryst. A, 2008, *64*, 404

IAM -> TAAM(MATTS) -> MM



dmin= 0.38 A

- R1 = 2.31 %
- R1 = 1.39 %
- R1 = 1.21 %

Pros and *Cons* of multipole model refinement

BENEFITS:

- Simple but efficient, formally correct
- Experimental errors are effectively filtered out
- It allows the deconvolution of thermal vibrations
- Easy to constrain: site & chemical symmetry, equivalence
- Transferability & locality
- The multipole model is an extrapolation to infinite resolution based on finite-resolution experimental data
- The resulting static density can be easily compared to direct quantum chemical calculations
- Allows derivation of properties

DISADVANTAGES:

- The results depend on the correct description of the thermal vibrations
- The tiny details of the density distribution depend on the choice of radial functions
- The multipole model is an extrapolation to infinite resolution based on finite-resolution experimental data
- Not all interesting properties are accessible

Pros and Cons of multipole model refinement

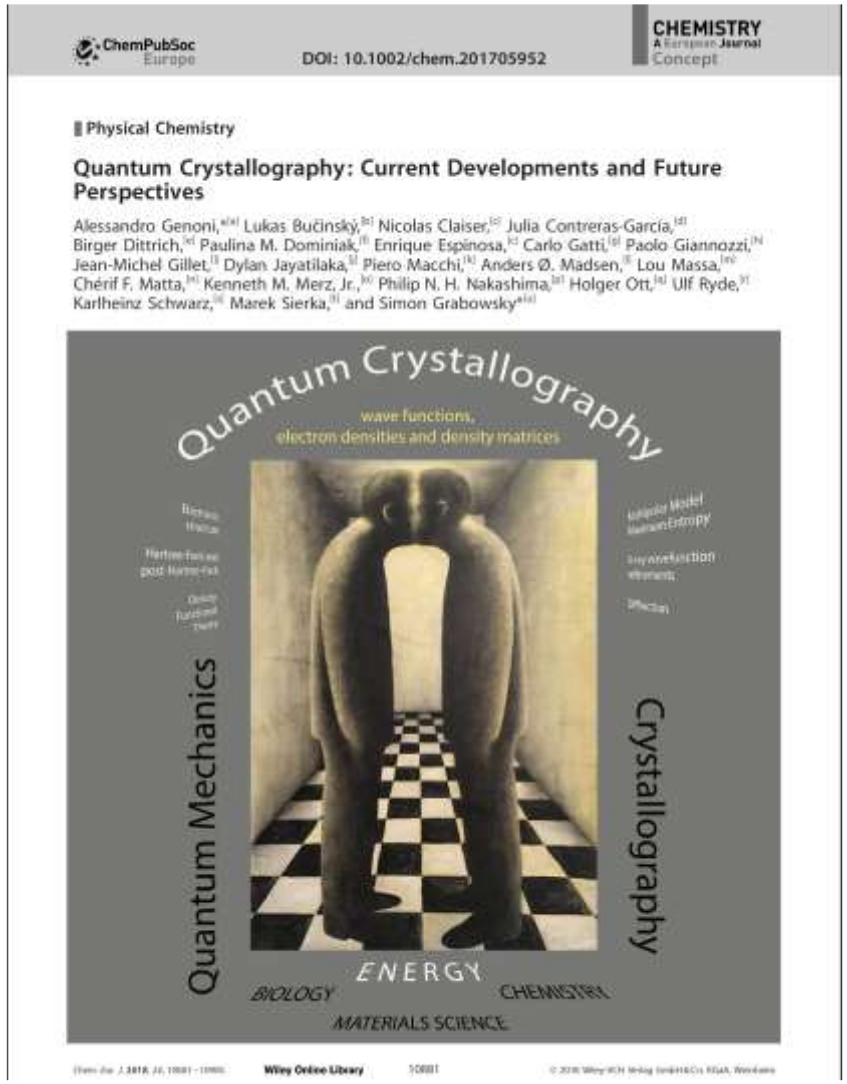
LIMITATIONS:

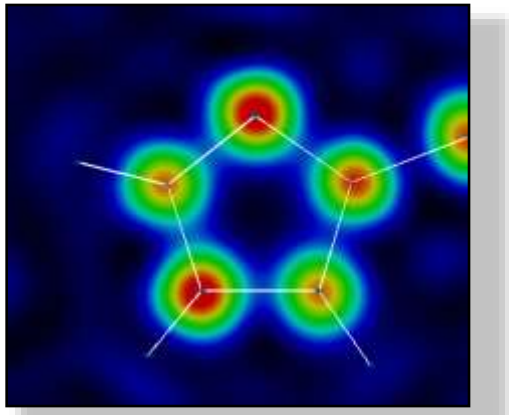
- Spatial behavior of the density
  - positivity
  - cusp condition
- Spherical components
  - frozen core approximation
  - uniform radial deformation of the valence sub-shells
- Deformation components
  - level of expansion
  - radial functions

ATTEMPTS TO IMPROVE:

- More flexible radial functions
- Extended Hansen-Coppens model (core polarization, kappa-core)
- Addition of higher multipoles

Quantum Crystallography
on subatomic X-ray diffraction data



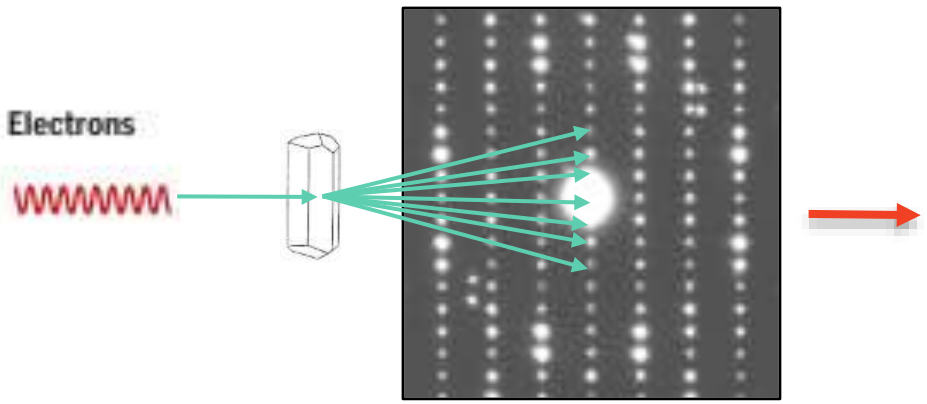


many success stories

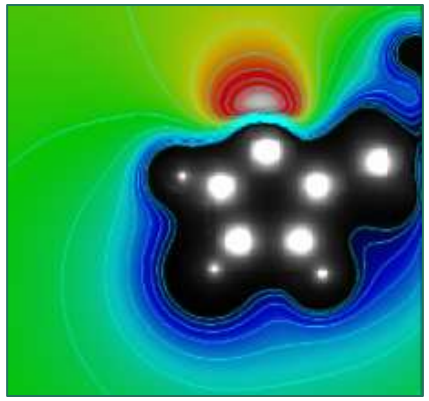
Genoni et al., Chem. Eur. J., 2018, *24*, 1088-10905
Tolborg & Iversen, Chem. Eur. J., 2019, *25*, 15010-15029
Macchi, et al., Cryst. Rev., 2020, *26*, 209-268
Grabowsky, et al., 2020, DOI: 10.1007/430_2020_62
Genoni & Macchi, Crystals, 2020, 10, 473
Gillet & Macchi, Acta Cryst., 2021. *B77*, 862–864
Macchi, Quantum Crystallography: Expectations vs Reality, 2022
Krawczuk & Genoni, Acta Cryst. 2024, B80, 249-274

Focus Issue on Quantum Crystallography:
https://journals.iucr.org/special_issues/2025/QCr/

Quantum Crystallography
on subatomic electron diffraction data



subatomic resolution
electron diffraction data



quantitative
electrostatic
potential,
electron density,
wave function

some pioneering works

Zuo et al., Nature 1999, 401 49-5
Tsirelson, J. Phys. Chem. B 2001, 105, 5068-5074
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Conclusions

While it still depends on a case-to-case basis, in general we can recommend:

- **never stop at the IAM refinement**
- **do TAAM refinement whenever possible**
  because it is fast and give about the same structural parameters as HAR, including hydrogen atoms
- **do hybrid HAR/TAAM or pure HAR if TAAM is not possible**
- **do HAR if time is not an issue**, or you **want to account for fine features** of electron density,
  like charge polarization by neighbouring molecules, relativistic effects, etc.
- **do aspherical refinement even with poor data or low resolution**,
  because most often some improvements of structural model are still achievable and often the source of problems in the data or modelling could be detected
- with **subatomic resolution** data (d<0.5Å) **consider** to do **multipolar refinement** or **wave function refinement**

Although for heavier elements it seems than already IAM is good enough to determine geometry, we still recommend to do aspherical refinement just to be sure than no hidden errors or unaccounted features are present in the data.