

MolecoolQt and InvariomTool

Aspherical-atom modeling of organic
molecules from normal-resolution data

B. Dittrich, C.B. Hübschle

Institute for Inorganic Chemistry,
Tammannstr. 4

37077 Göttingen, Germany





Outline

- Introduction to charge density research and invariom refinement
 - IAM and multipole-model structure factor
 - Invarioms – What are they?
 - Results we can expect

 - Programs *Invariom Tool* and *MolecoolQt*, practical example of ciprofloxacin 6 H₂O
-



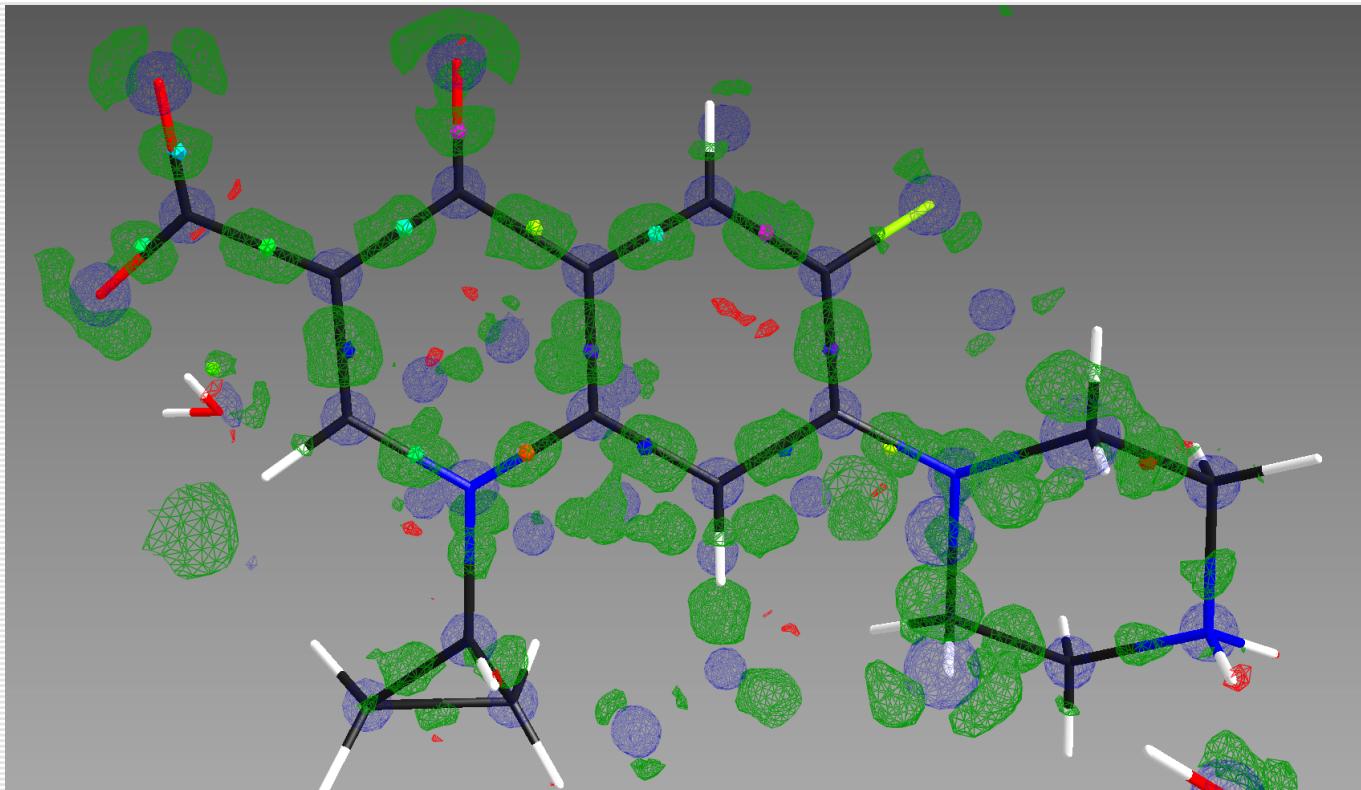
Conventional XRD

- X-ray structure determination from single-crystals:
 - Using Independent Atom Model (**IAM**)
 - Is considered routine in 75 % of cases
 - Still challenging with instable compounds, twins, incommensurates, extreme conditions, small specimen
 - Least-squares refinement gives **atomic positions**
 - 9 parameters per atom: positions xyz plus 6 U_{ij}

$$F_c(\mathbf{h}) = \sum_k^{atoms} f_k(\mathbf{r}) \exp^{2\pi i \mathbf{h} \cdot \mathbf{r}}$$

What do we miss in the IAM?

- Ciprofloxacin, residual bonding density after converged SHELXL-refinement ($0.4 \text{ e}/\text{\AA}^3$):





Charge-density research

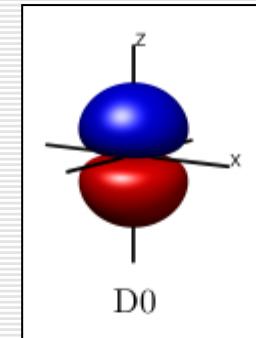
- Most often employing Hansen/Coppens multipole model (R.F. Stewart)
 - 25+2 additional atomic parameters
 - Requires good, high-resolution data
 - Gives us an **experimental** $\rho(\mathbf{r})$ from LSQ
 - “Coming of age” has been proclaimed for organics, still far from routine for inorganics

- Alternative approach ‘Hirshfeld atom refinement’ is available



Hansen/Coppens' multipole model

- Combines radial functions j_l with spherical harmonic functions d_{lm} (density-normalized y_{lm})
- Analytical representation of $\rho(\mathbf{r})$
- Fixed core density
- Scattering factor f is different to IAM



$$F_c(\mathbf{h}) = \sum_k^{atoms} [P_{k,core} f_{k,core} + P_{k,val.} f_{k,val.} \left(\frac{h}{\kappa} \right)^2 + 4\pi \sum_{l=0}^{l_{max}} i^l \langle j_l \left(\frac{h}{\kappa} \right) \rangle \sum_{m=-l}^l P_{k,lm} d_{k,lm}] \cdot \exp^{2\pi i \mathbf{h} \cdot \mathbf{r}}$$



Charge density research

- Established for elements of 1st, 2nd period
- Additional information on chemical bonding (Baders AIM Theory, Source funct., ELI/ELF)
- Still challenging in inorganic chemistry
- Can give similar information than quantum chemistry, both are directly comparable
- Analysis typically gives:
 - Topological analysis
 - Dipole moments
 - The molecular electrostatic potential
 - Covalent and H-bond properties, localization
 - Approximate electrostatic interaction energies



Invariom refinement

- In invariom ref. the multipole parameters are obtained from theory (DFT/B3LYP), no experimental $\rho(\mathbf{r})$
- Improves geometry, ADPs, and figures of merit
- Can also give us **more detailed information on chemical bonding** in comparison to IAM
- Like in IAM only xyz and U_{ij} are refined while multipole parameters are fixed, no extra parameters
- **High resolution is not needed, normal data**
- While fatal for charge density, disorder is no big problem in invariom refinement



Practical steps in invariom refinement

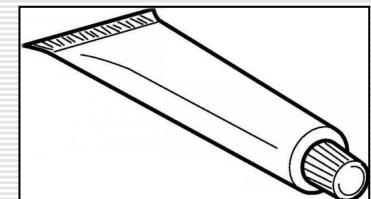
- ⇒ We partition a molecule into atomic fragments



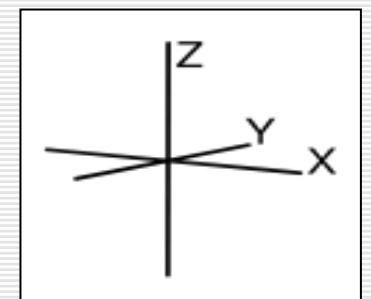
- ⇒ We calculate a suitable model compound

$$\rho(\mathbf{r}) = \Psi \cdot \Psi^*$$

- ⇒ We reconstruct molecular densities from so-derived fragments

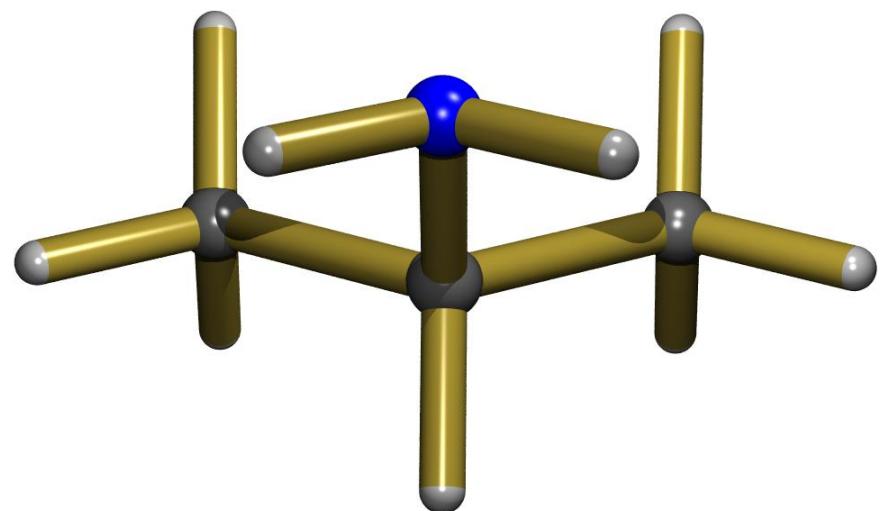


- ⇒ Invariom (**invariant pseudoatom**) needs to be oriented, process is automated



Invariom notation

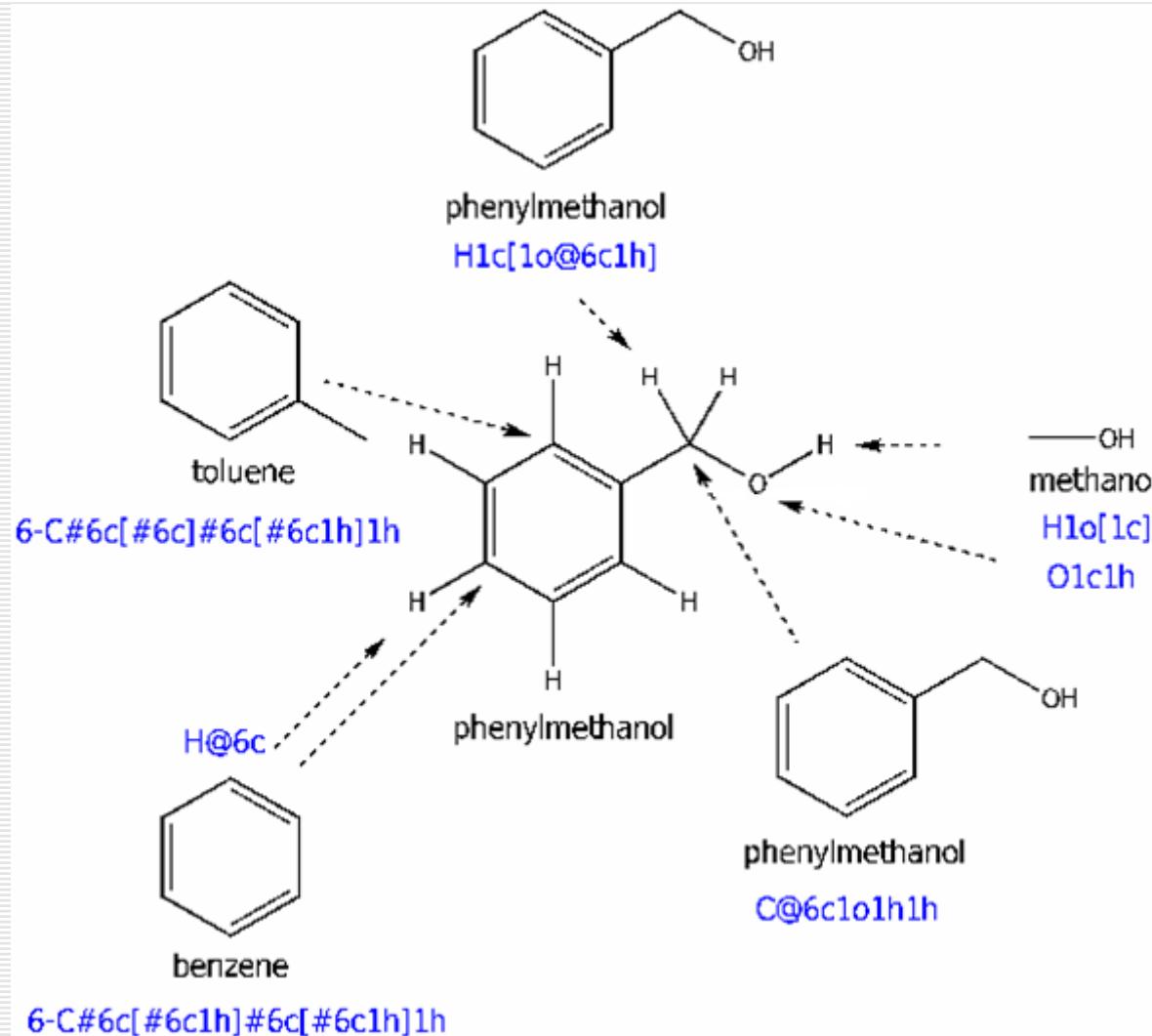
To organize scattering factors in the database
they get a name based on their local
chemical environment.



H1c[1c1h1h]
C1c1h1h1h
C1n1c1c1h
H1c[1n1c1c]
N1c1h1h
H1n[1c1h]



Example of benzylalcohol



Single bonds: use nearest neighbors

Hydrogens: use next-nearest neighbors

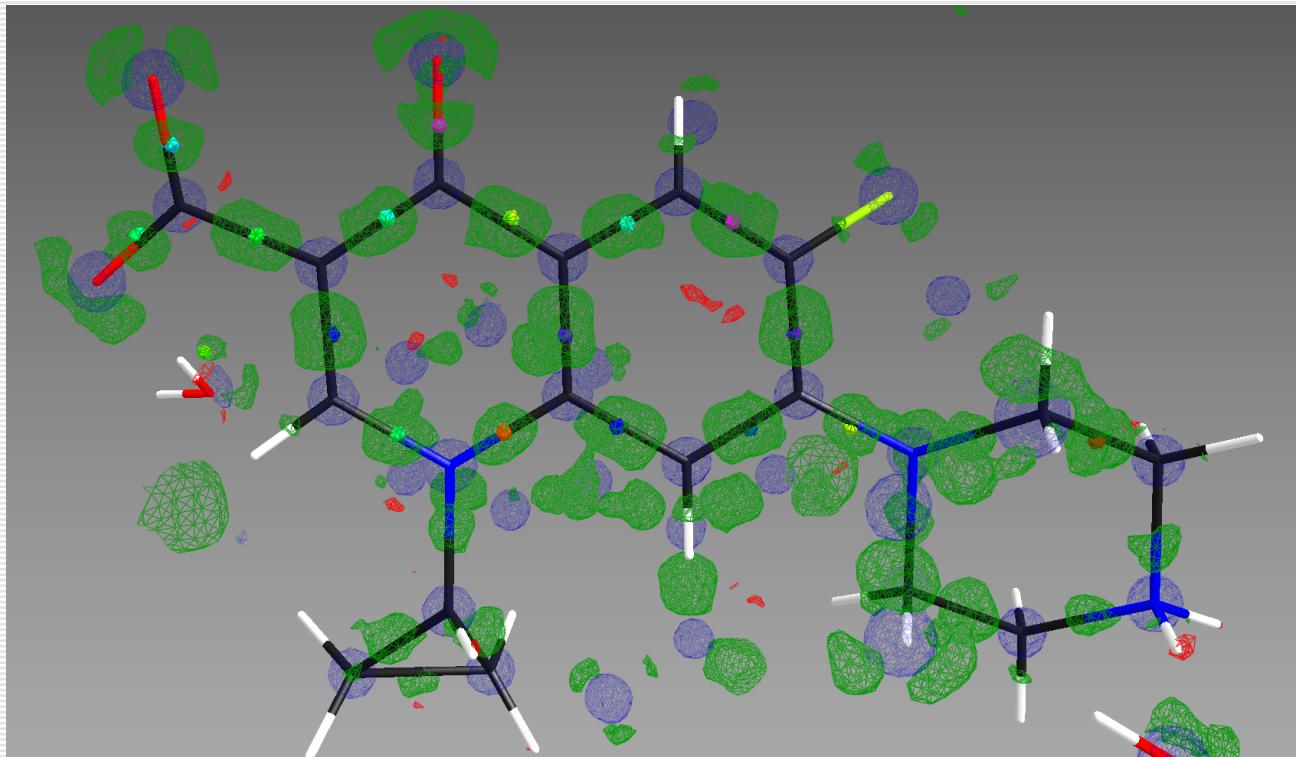
Delocalisation:
Use the best suited mesomeric system

Bonded to heavier nucleus: use next-nearest Neighbor

Heavier nucleus: nearest neighbor

Reminder: we miss valence def. in IAM

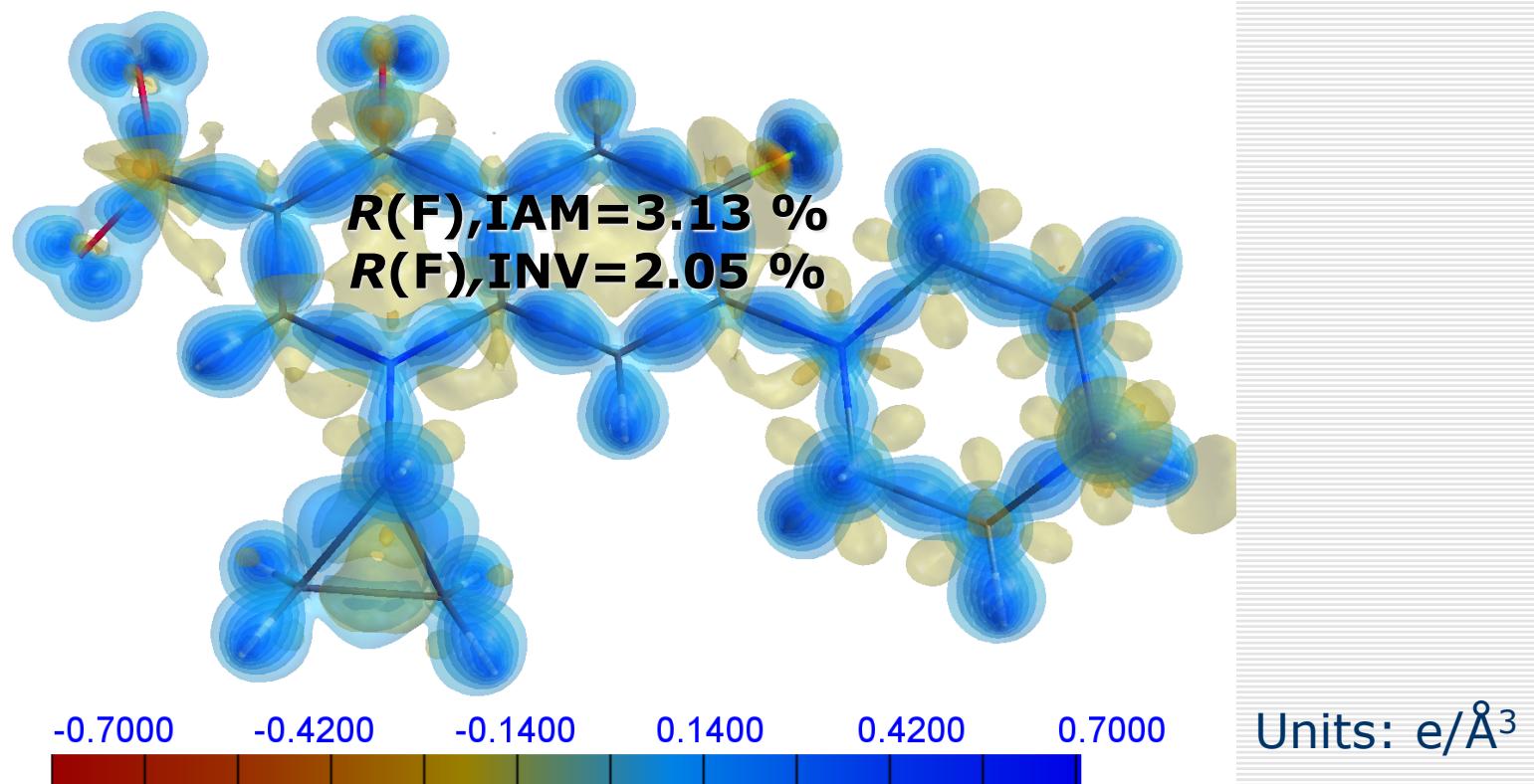
- Ciprofloxacin hexahydrate, residual bonding density after converged SHELXL-refinement:



- Isosurfaces with +10 (blue) and ± 0.25 (red/green) $e/\text{\AA}^3$

What do we model with invarioms

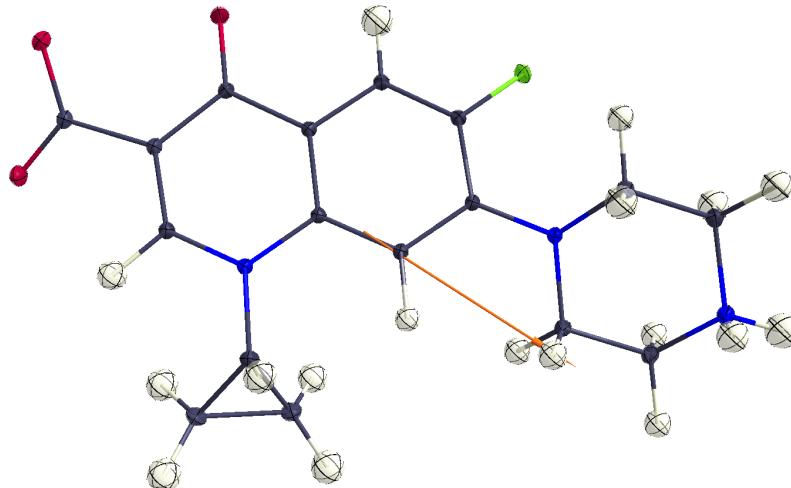
- Ciprofloxacin hexahydrate, imposed density from invariom database:



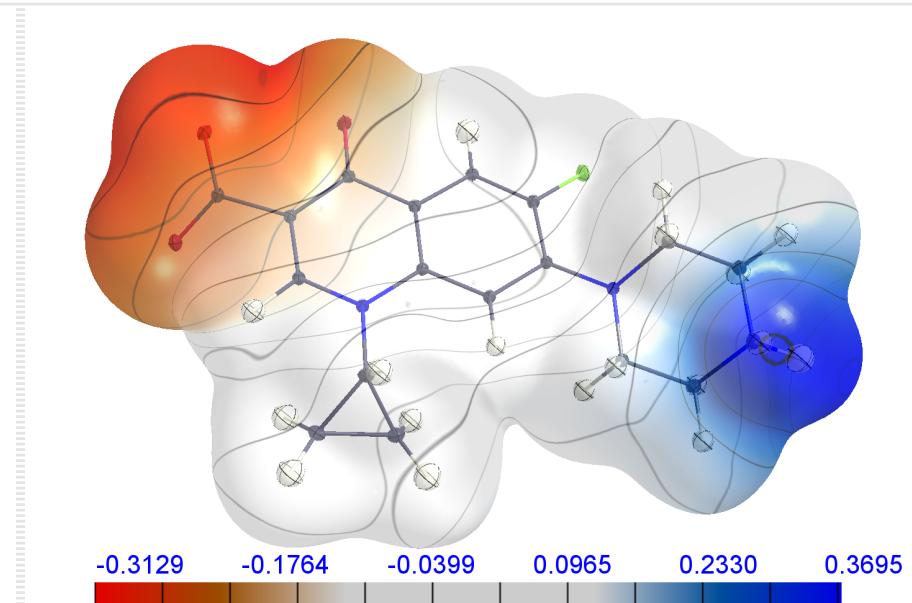


What do we get out using invariants?

- Improvement in the *R*-Factor and FOMs
- More accuracy and better precision (esd)
- Dipole moments and electrostatic potential



Strongly dipolar molecule, 38.9 D



Units: $e/\text{\AA}$ on $0.0067 \text{ e}/\text{\AA}^3$ isosurf.



Summary

- We can construct an accurate non-spherical electron density from invariom database fragments, covering a wide area of organic chemistry
 - More insight in bonding also for inorganics
 - Better structures (accuracy and precision, Figures of Merit, ADPs)
 - Open source program development for easier use
-



Acknowledgement

DI 921/3-1,2 associated to SPP1178

'Australian Synchrotron
Research Program'



DFG



C.B. Hübschle, G.M. Sheldrick, F.P.A. Fabbiani,
J.J. Holstein, K. Pröpper, R. Ghadwal, H.W. Roesky

M.A. Spackman, D. Jayatilaka, B. Corry,

P. Luger, M. Strumpel,
D. Zobel, M. Weber

J. Bak, P. Dominiak, K. Wozniak

Luc Bourhis, Horst Puschmann



FUNDACJA WSPÓŁPRACY
POLSKO-NIEMIECKIEJ
STIFTUNG
FÜR DEUTSCH-POLNISCHE
ZUSAMMENARBEIT