"**MoPro**" : a free software for electron density analysis.

of small compounds and biological macromolecules.

Laboratoire de **C**ristallographie & Résonance Magnétique & Modélisations (CRM2)

Christian Jelsch

CNRS Nancy Université France

* Charge density refinement with MoPro

* VMoPro visualisation tool of properties

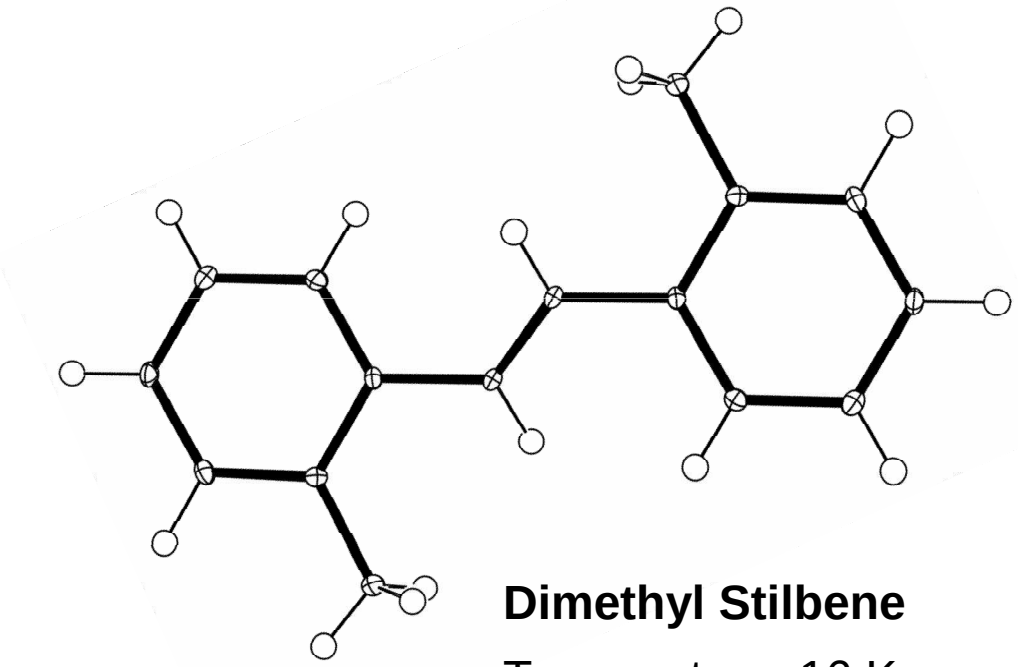
* Database Transfer

* Application to proteins

* Electrostatic Interaction Energy

Spherical Atom Model : approximation

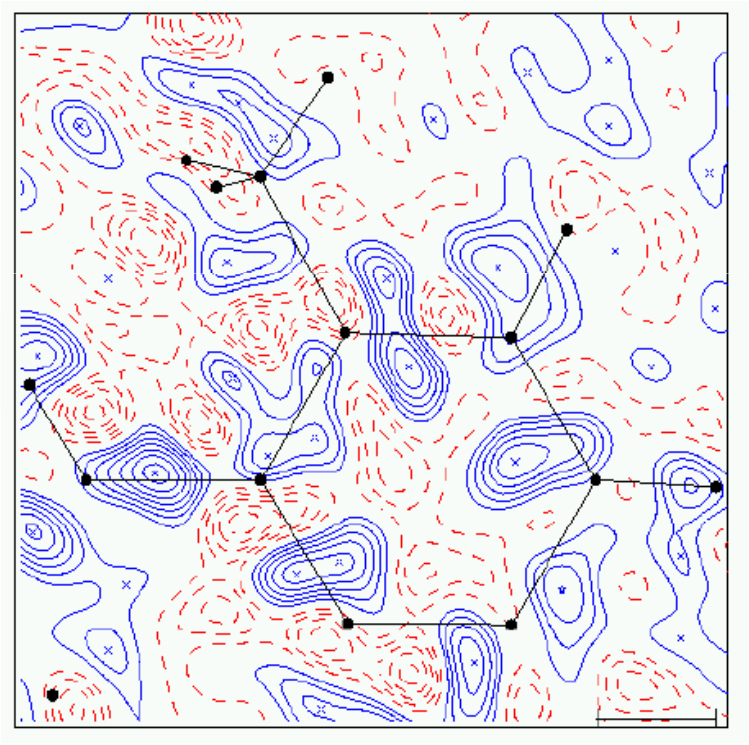
Fourier Residual Map $F_{obs} - F_{cal}$



Dimethyl Stilbene

Temperature 16 K

Resolution 0.65 Å



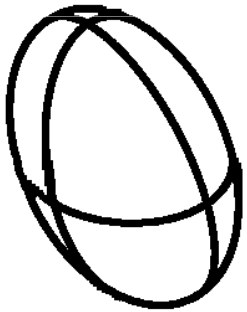
RESOLUTION & X-Ray CRISTALLOGRAPHY

Proteins *X Y Z* Molecular Structure

d **≈ 2 Å** **Thermal *B* factor isotropic**

ATOMIC **Thermal *B* anisotropic**

d **≈ 1 Å** **Hydrogen**



SUB-ATOMIC **Deformation Electron Density**

d **≈ 0.5 Å** **Atomic Charges**

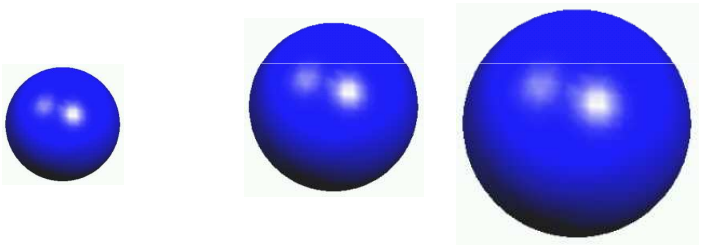
Multipolar Atom Model

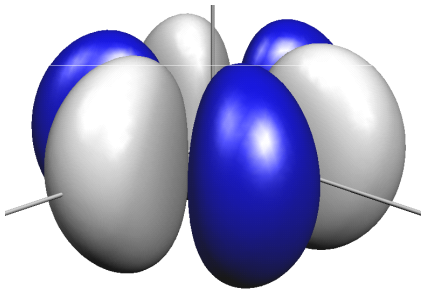
$$\rho(\mathbf{r}) = \rho_c(r) + P_{val}\,\kappa^3\,\rho(\kappa) + \Sigma\,\kappa'^3\,R(\kappa' r)\,\Sigma\,P_{lm}\,y_{lm}$$

Atom core

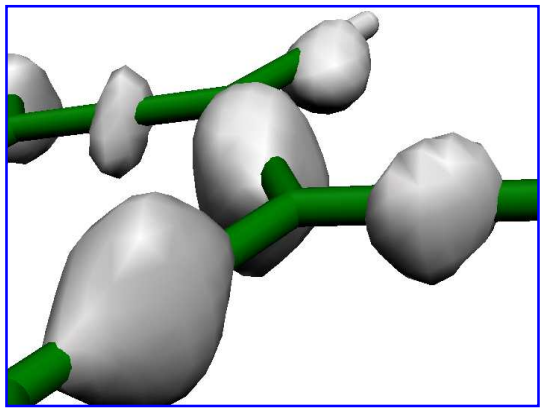
Valence Population

Multipole Populations

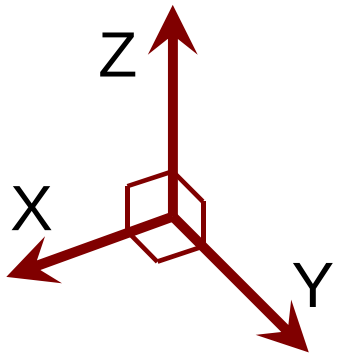




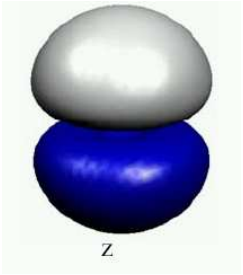
κ κ' expansion / contraction



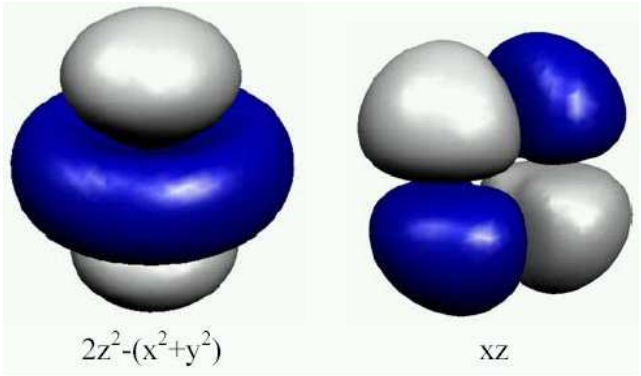
Hansen & Coppens
(1978) *Acta Cryst*. A34, 909



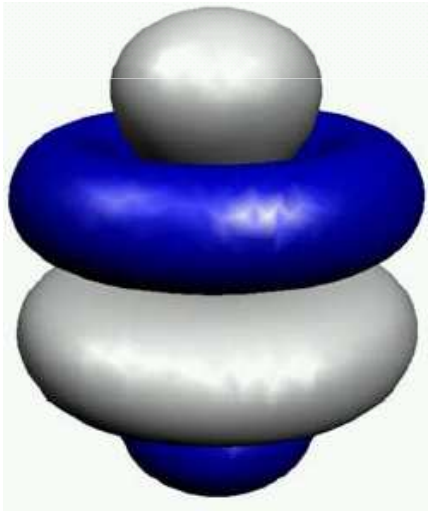
3 dipoles

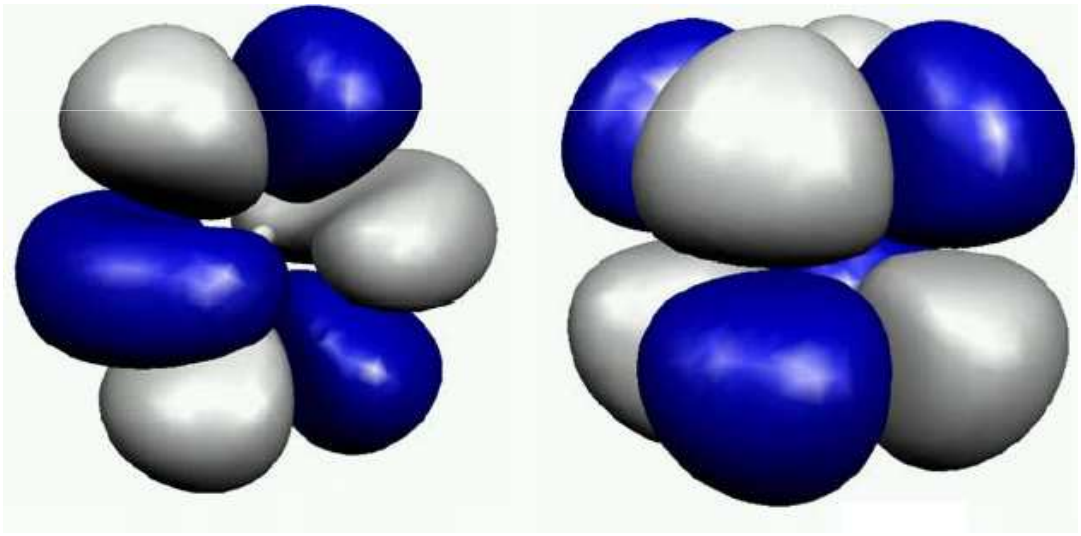


5 quadripoles



7 octupoles





$2z^3 - 3z(x^2+y^2)$

$x[4z^2-(x^2+y^2)]$

$y[4z^2-(x^2+y^2)]$

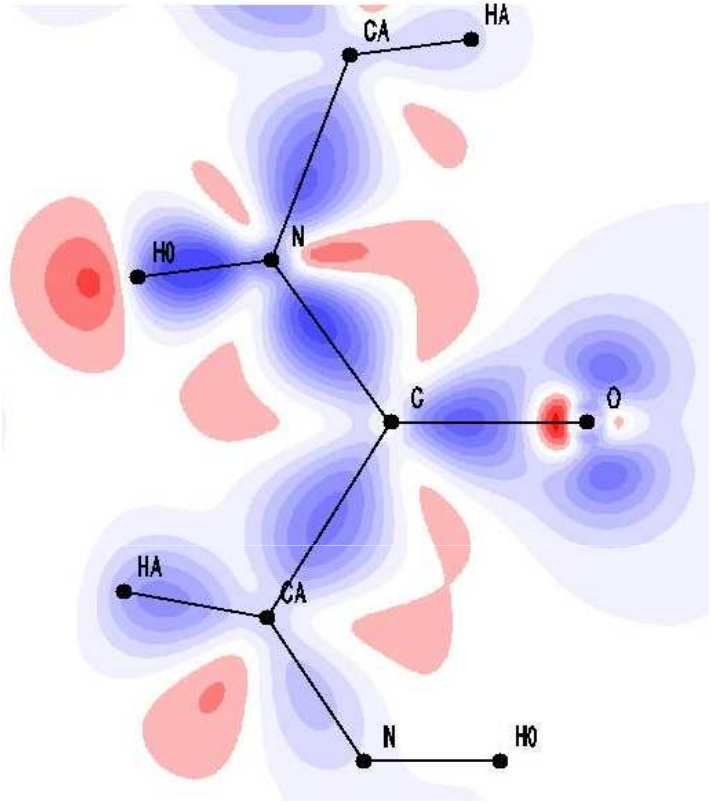
$x(x^2-3y^2)$

$y(y^2-3x^2)$

xyz

$(x^2-y^2)z$

Deformation of Electron Density
+/- 0.05 e/A^3



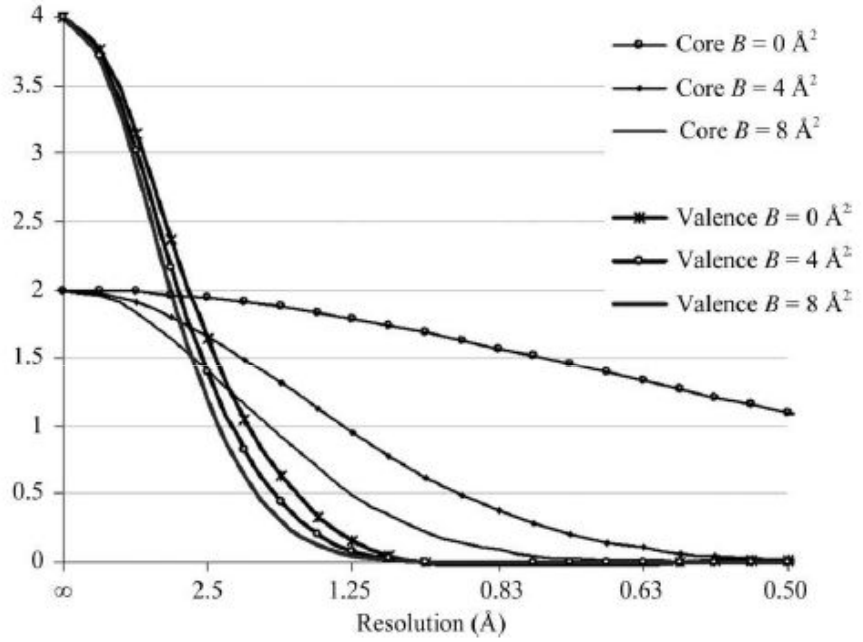
Multipolar Atom Model

$$\Delta\rho(\mathbf{r}) = \rho_{\text{molecule}} - \sum \rho_{\text{atoms\_spherical\_neutral}}$$

$$= (N_{val} - P_{val}) \kappa^3 \rho(\kappa) + \sum \kappa'^3 R(\kappa' r) \sum P_{lm} y_{lm}$$

High Order Refinement

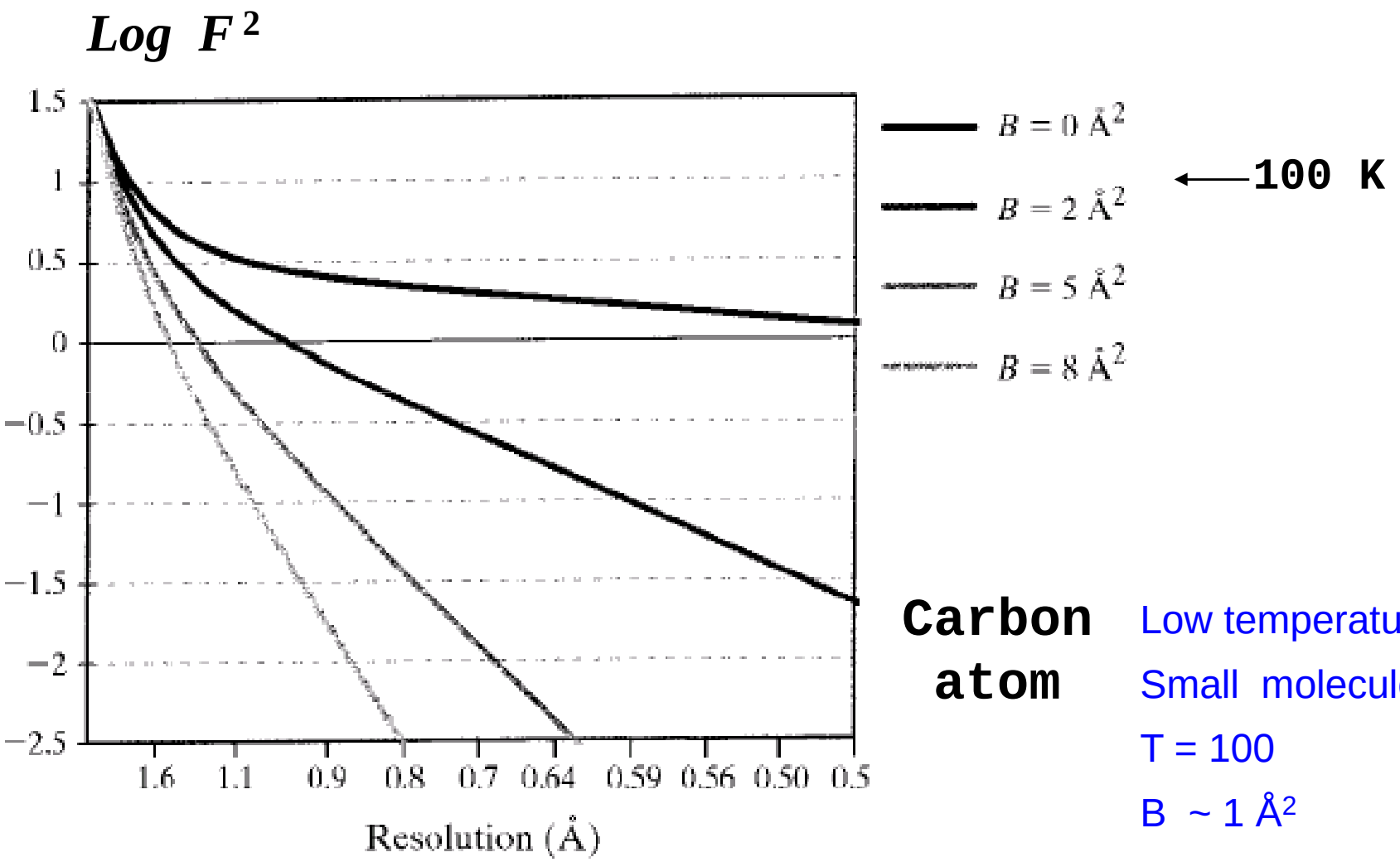
Scattering factor of a carbon atom



Refine vs. Reflections at **High resolution**

Deconvolution of thermal motion & deformation density

Diffraction Power & Temperature Factor



Carbon atom

Low temperature

Small molecules

T = 100

B ~ 1 Å^2

MOPRO Crystallographic Refinement Software

Subatomic Resolution Structure *&* Electron Density
~0.5Å

Atomic Resolution Structure with Hydrogen Atoms
0.7 – 1.5 Å Transfer Databank Electron Density

Small Compounds & Macromolecules

Guillot *et al*., J. Appl. Cryst. (2001) 34, 214-223
Jelsch *et al*., J. Appl. Cryst. (2005) . 38, 38-54

MoProSuite : the main programs

* **MoProGUI.jar**

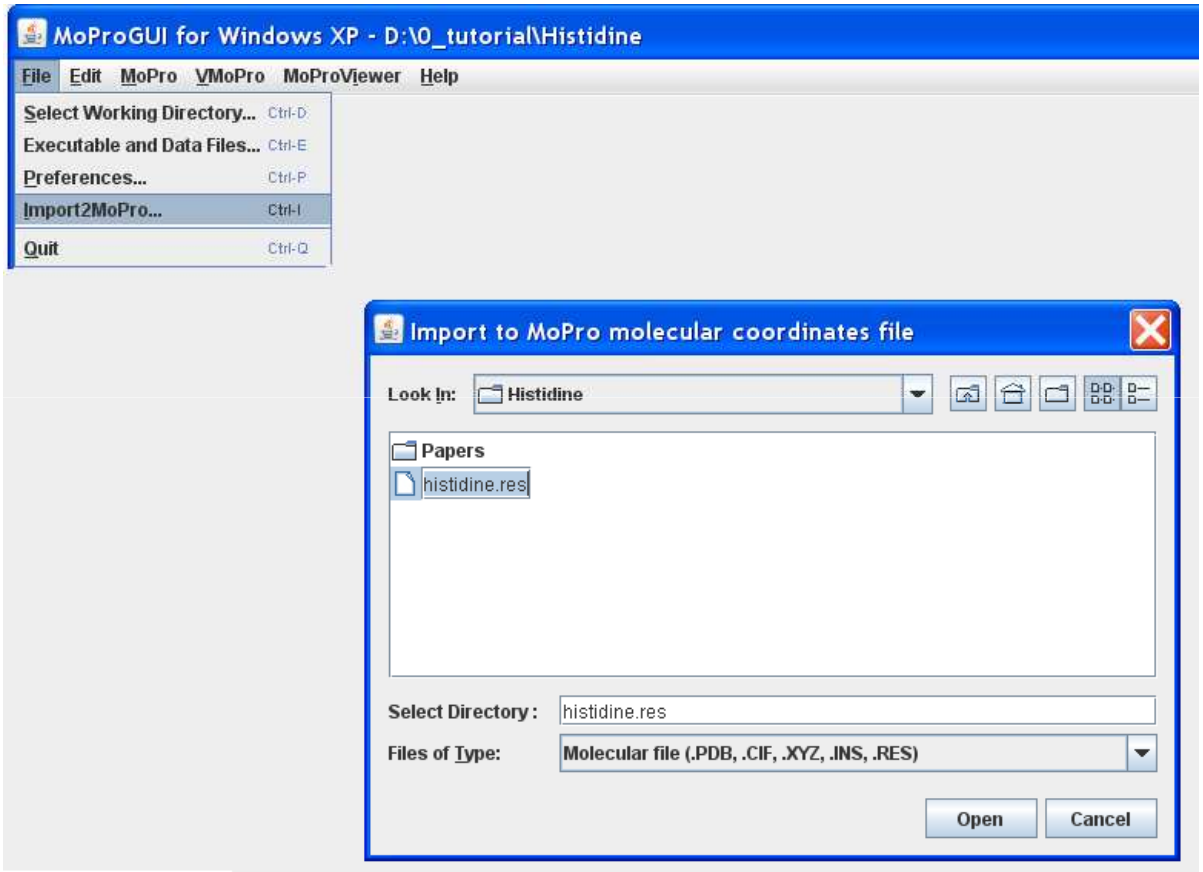
* **Import2MoPro**

* **MoPro** : crystallographic refinement
  & structure analysis

* **VMoPro :**
  visualisation maps, molecular properties

* **MoProViewer**
  molecule viewer & GUI

Import2MoPro.exe



Formats :

pdb

Cif

res / ins

Xyz

Molly

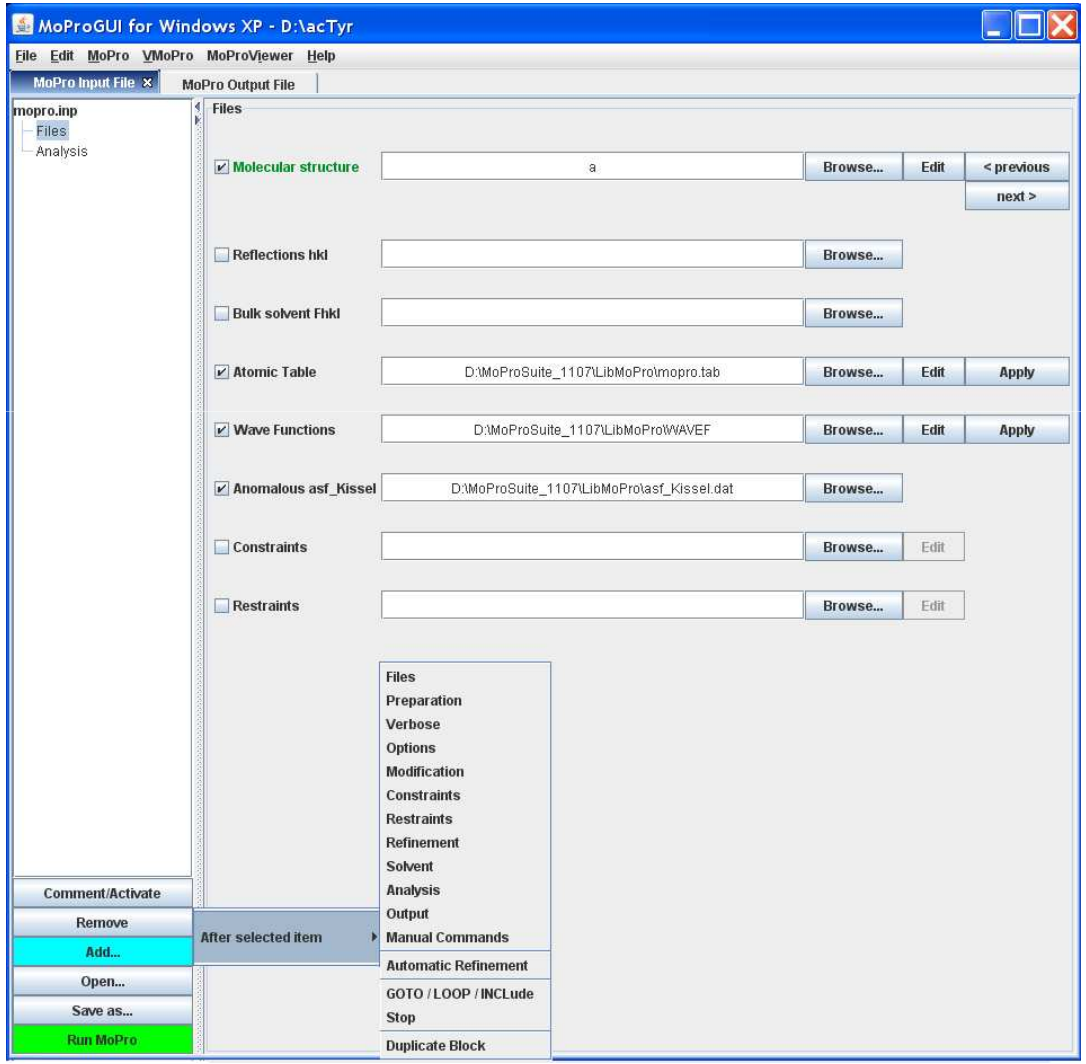
Mopro

XD

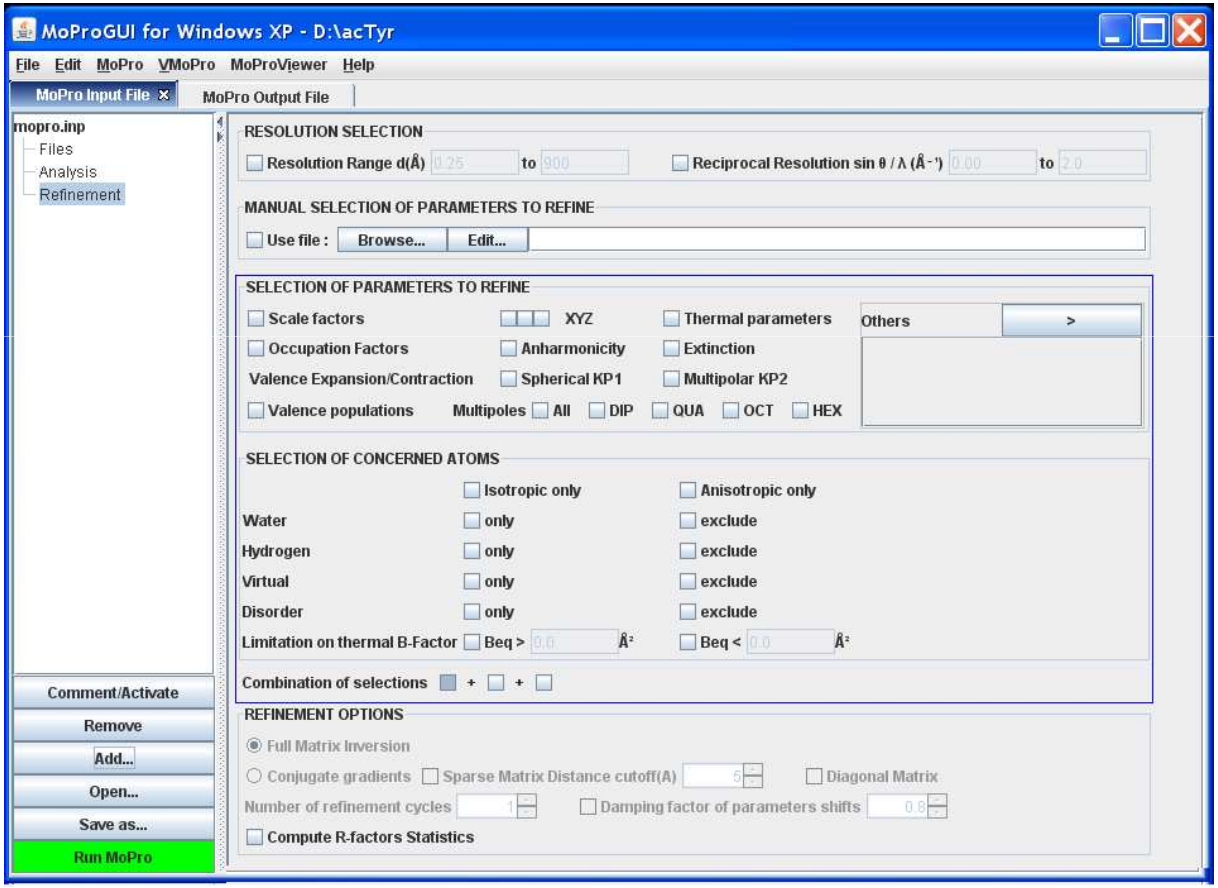
MoProGUI - MoPro : Main Menus.

File declarations

Graphical User Interface



Refinement of Variables



MoPro input commands file ”mopro.inp”

Example of script

```
RESO   0.4   0.7
SELE   XYZ   UIJ  NOH
REFI   LS  1

RESO   0.4    99.
SELE    KP1   +  KP2  NOH
REFI    LS  1     DAMP  0.5


CONS  DIST
WRIT   DIST
```

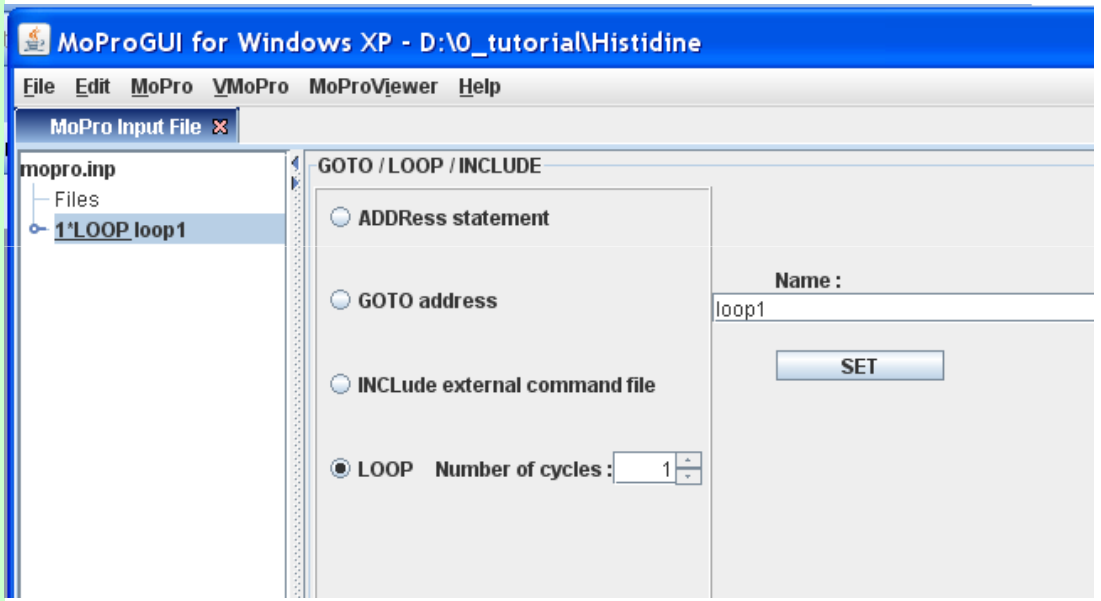
Can be generated by MoProGUI

(hydrogen H-X)

Print distances

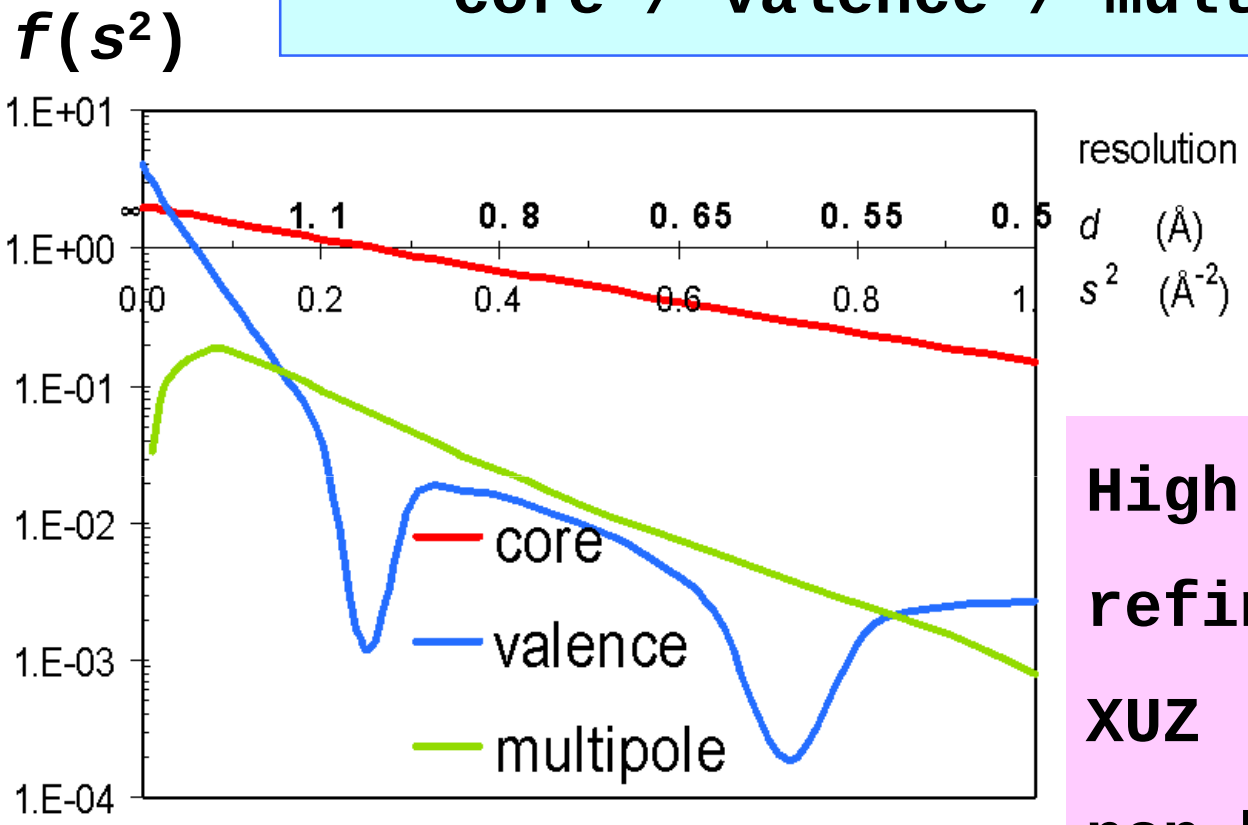
Example of loop in « mopro.inp »

```
LOOP   lp1   5

 RESO   0.4   0.7
 SELE   XYZ   UIJ  NOH
 REFI   LS  1

 RESO  0.4  99.
 SELE  SCA   PLM   VAL
 REFI  LS 1

ADDR   lp1
```



Scattering Factor

core / valence / multipolar



Carbon atom *P*val = 4 e

***B*iso = 4 Å²**

multipolar part averaged

High order refinement:

XUZ UIJ

non hydrogen atoms

⇒ Deconvolution

Uij & Δρ

Charge Density Refinement Strategy

HIGH ORDER : RESOLUTION d < 0.7 Å
XYZ UIJ non-hydrogen

WHOLE RESOLUTION
SUCCESSIVE INTRODUCTION OF VARIABLES

* SCALE FACTOR
* XYZ Uiso Hydrogen
* Valence populations
* Multipoles
* Kappa (spherical)
* Kappa’ (multipoles)

* MoPro
automatic charge density refinement
small molecules

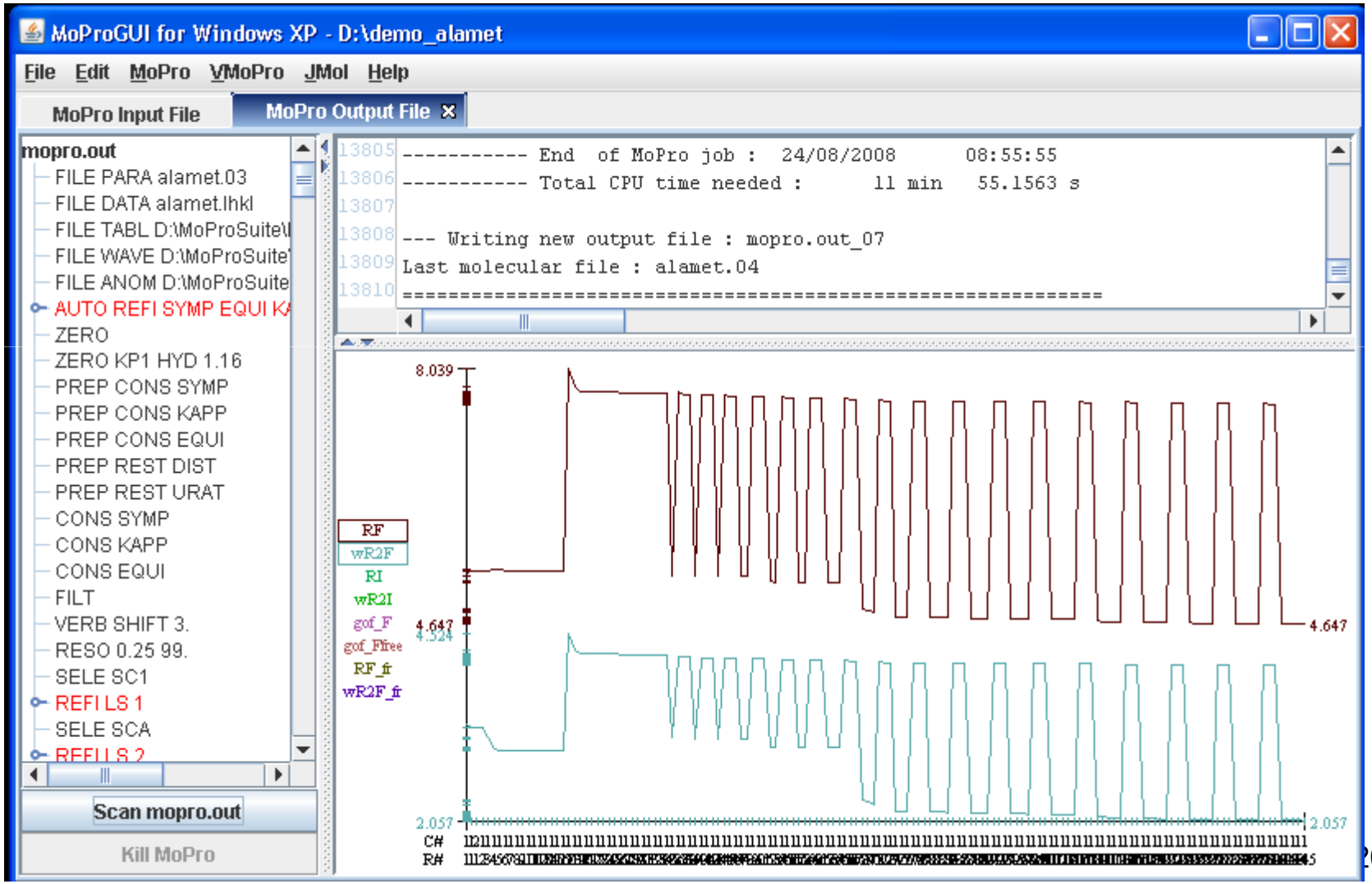
- Preparation of restraints & constraints

- High order refinement XYZ UIJ NOH

- Iterative & progressive refinement
  of VAL PLM KP1 KP2

- Progressive release of constraints

* MoPro automatic refinement



CRYSTALLOGRAPHIC REFINEMENT

LEAST SQUARES **MINIMIZATION**

$$\Sigma_{\mathbf{H}} \; (I_{\mathbf{H\,calc}} - I_{\mathbf{H\,obs}})^2 \; / \; \sigma_I^2$$

$$+ \quad \Sigma_r \; (\boldsymbol{R}_{\mathbf{calc}} - \boldsymbol{R}_{\mathbf{target}})^2 \; / \sigma_{\mathbf{r}}^2$$

H reflections (h,k,l) I_H Intensity

R restraints (stereochemistry: distances, angles,

thermal motion, charge density similarity, targets for κ & κ' …)

Least Squares Minimisation

1 refinement cycle : `solve`

A dP = V `normal equations`

$$V_p = \Sigma_{\mathbf{H}}\ w_{\mathbf{H}}\ (I_H^{obs} - I_H^{calc})\ \frac{\partial I_{\mathbf{H}}^{calc}}{\partial p}$$ `gradient`

Normal Matrix

$$A_{pq} = \Sigma_{\mathbf{H}}\ w_{\mathbf{H}}\ \frac{\partial I_{\mathbf{H}}^{calc}}{\partial p}\ \frac{\partial I_{\mathbf{H}}^{calc}}{\partial q}$$

Solve normal equations

$$A \; dP = b$$

matrix inversion $dP = A^{-1} b$

conjugate gradients iterative method

$dP_0 \rightarrow dP_1 \rightarrow \ldots \rightarrow dP_n$

► Useful for Large systems (sparse matrix)

Normal Matrix INVERSION

$$dP = A^{-1} V$$

B = A^{-1} matrix of (variance , covariance)

$$B_{pp} \cdot Z = \mathrm{VAR}(p) = \sigma^2(p)$$

$$B_{pq}\, Z = \mathrm{COV}(p,q) = \sigma(p)\ \sigma(p)\ \rho(p,q)$$

$$Z = \Sigma_H\ W_H(I_{obs}-I_{calc})^2/(N_{obs}-N_{var})]^{1/2}$$

goodness of fit

Binary correlation coefficient parameters *p* & *q*

$$\rho_{p,q} = \frac{B_{pq}}{(B_{pp}B_{qq})^{1/2}}$$

RESTRAINTS

distance, angles, planarity

Thermal motion URATIO ISOTRO
UIJRES UIJRAT

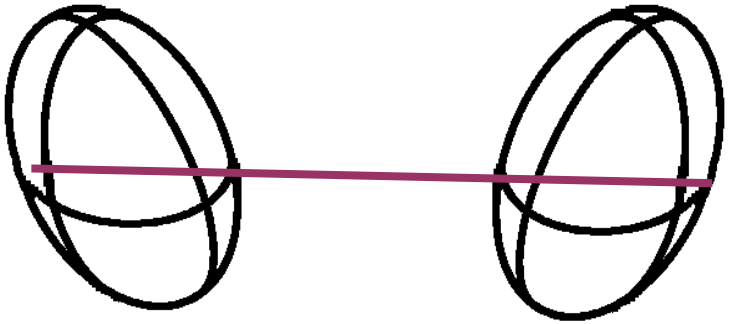
SIMDIS SIMANG
SIMVAL SIMPLM SIMKAP …

RSYPLM multipoles symmetry
KAPVAL KP1 & Pval correlated

RESTRAINTS

Thermal Displacement Parameters

Rigid Bond $U^{ij}_{proj} \sim U^{ij}_{proj}{}'$



Limited Anisotropy

Uiso proportional ***U*iso ~ *k* . *U*eq**

Uij proportional ***U*ij ~ *k* . *U*ij'**

Stereochemical CONSTRAINTS

Distances ***d*** **(Atom,Hydrogen)**

Angles **AXYZH** **AXYHH** **AXHHH**

AXYH **AXHH**

AXH **AHH**

Exemple for C-CH_3

CONANG AXHHH C1 C2 H11 H12 H13

Automatic preparation of constraints

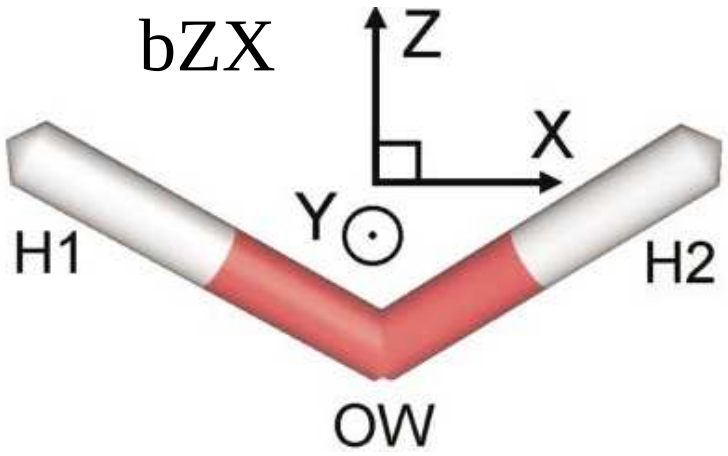
Restraints / Constraints on the charge density

in software MoPro

SYMPLM – symmetry of multipoles

CONPVM – valence and multipole populations
CONPLM – multipole populations
CONVAL – valence populations
CONKAP –kappas expansion/contraction

} Equivalence of atoms



OW has two mirrors

H1 & H2 equivalent

Symmetry CONSTRAINTS / RESTRAINTS on the Charge Density

Symmetry on Multipoles

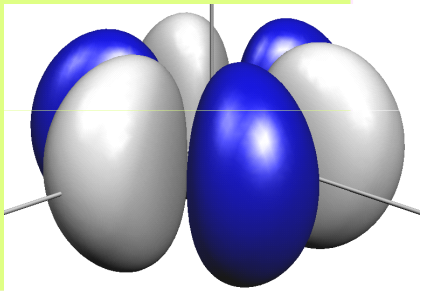
mx 1 mirror plane ⊥ x

mymz 2 mirrors aromatic C

3m 3m axis CH_3, NH_3+

i inversion centre

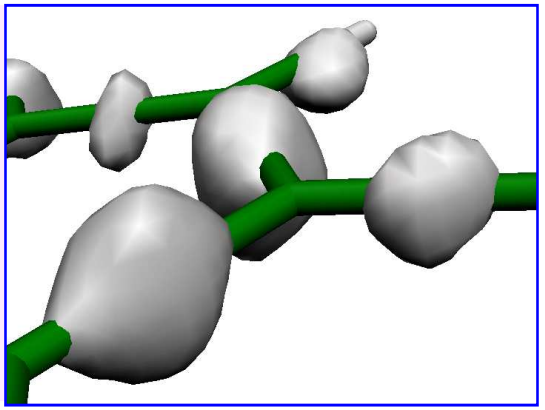
....



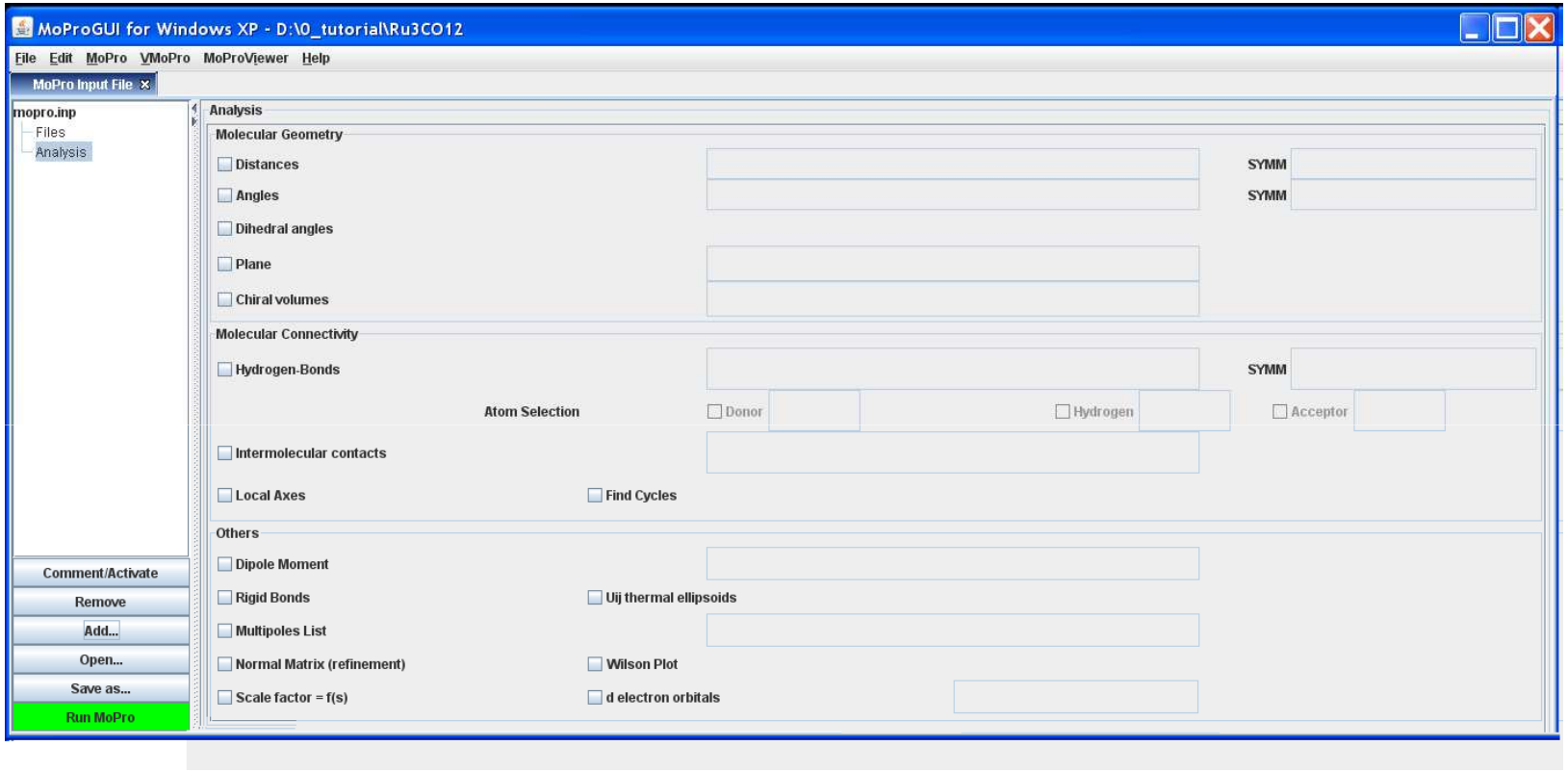
Exemple

SYMPLM 3m ALA CB

SYMPLM mymz PHE CD1

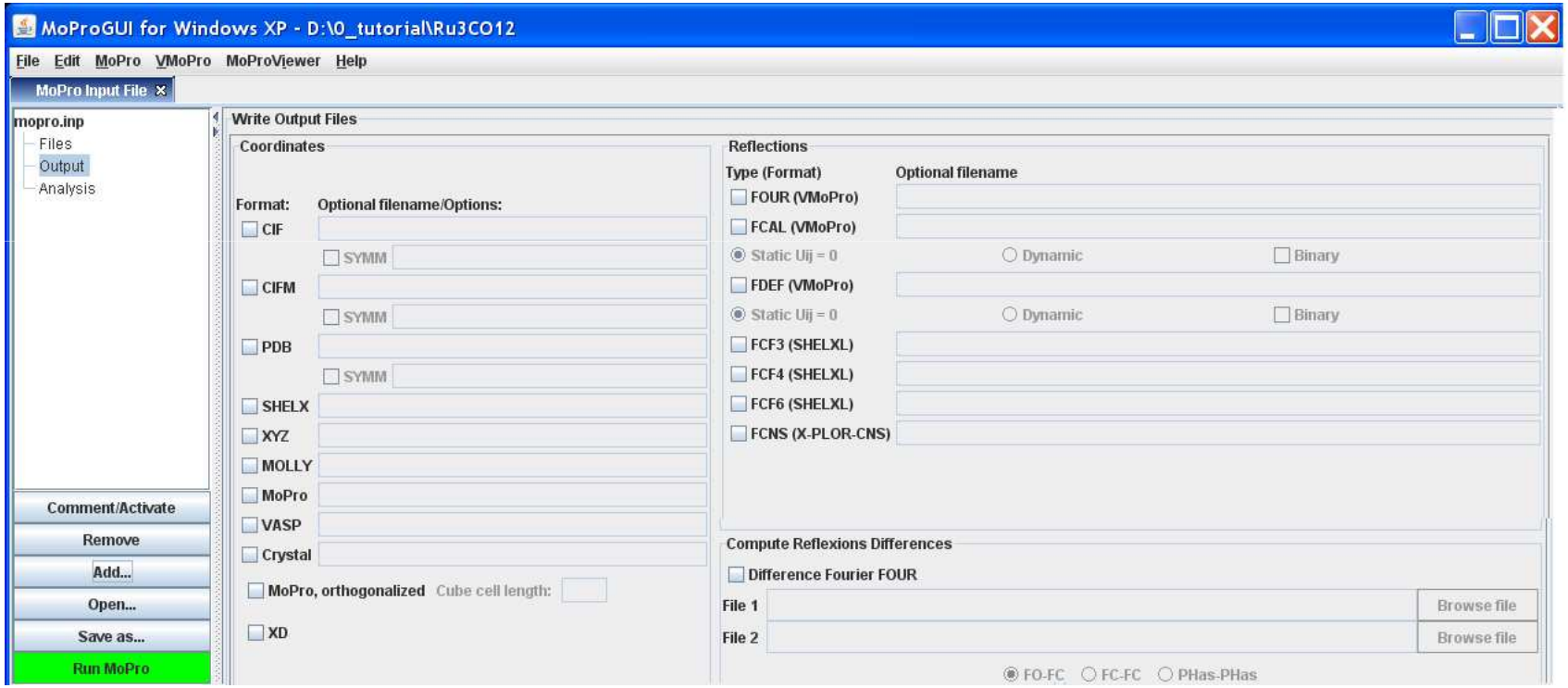


MoProGUI stereochemical analysis by MoPro



MoProGUI write ouput files

molecular structure & hkl reflections



* Charge density refinement with MoPro

*** VMoPro visualisation tool of properties**

* Database Transfer

* Application to proteins

* Electrostatic Interaction Energy

VMoPro

Properties computation & visualization

STAT : STATic (deformation) electron density

ELEC : ELECtrostatic potential map

FOUR : FOURier m*Fo-n*Fc electron density

LAPL : LAPLacian of total electron density

GRAD : GRADient NORM of electron density or electrostatic potential

CRIT : CRITical points search of density, laplacian or electrostatic potential

ENER : ENERgy computations

INTE : INTEgration : topology

SELE : define atoms SELEction for property calculation

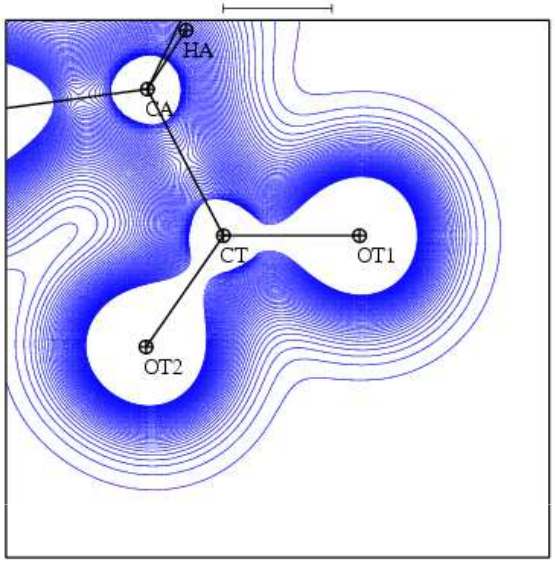
PARA : read new MoPro molecular parameters file

PLOT : create & PLOT postscript image from 2D grid

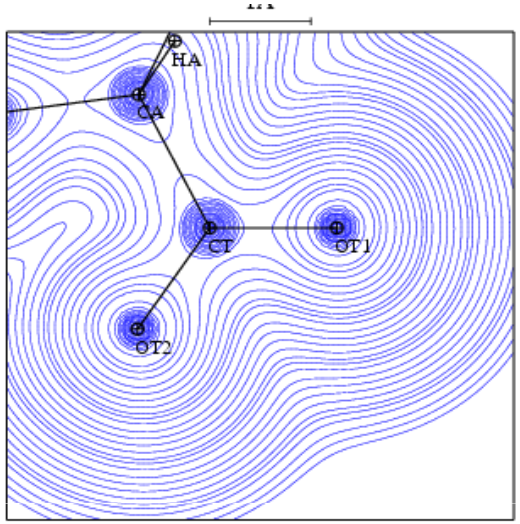
GRID : GRIDs handling (+ - x mask statistics)

CONT : set Gradient / Basin / CONTour lines options

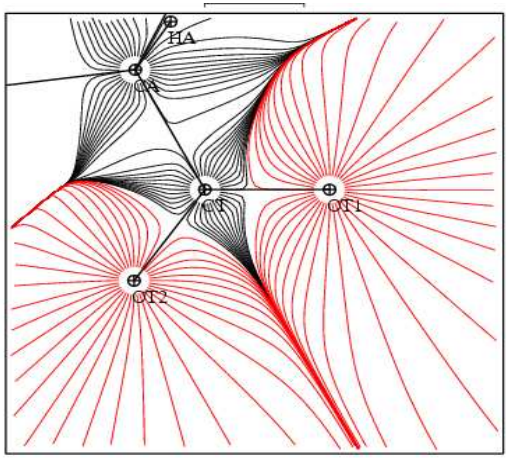
Static total electron density



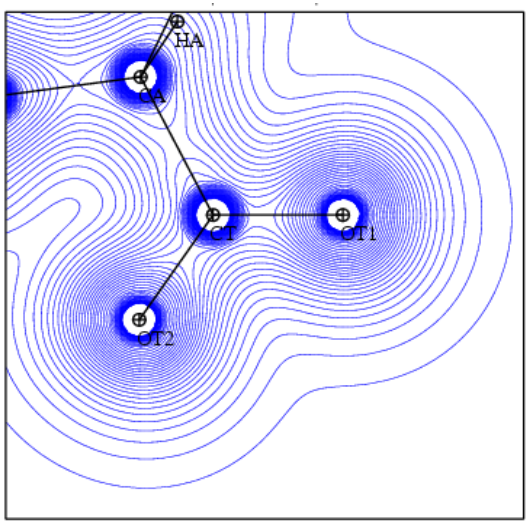
Regular contours



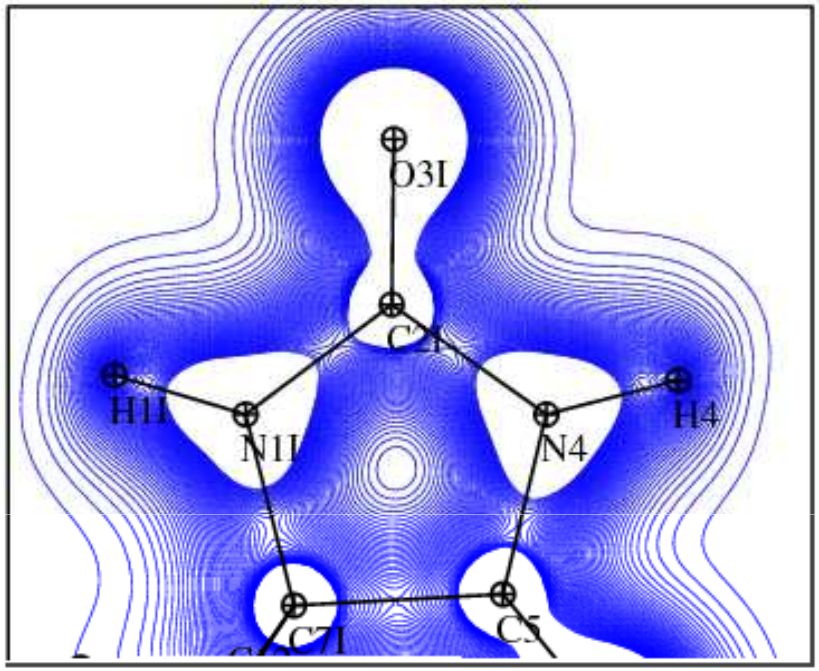
Log scale



Gradient lines

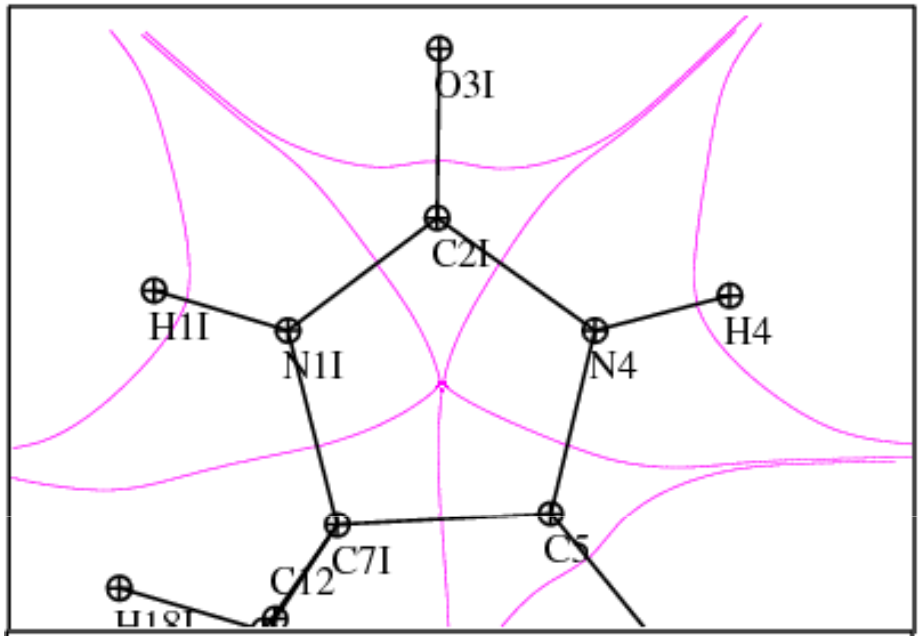


Square Root scale



Total Electron Density

Fidarestat



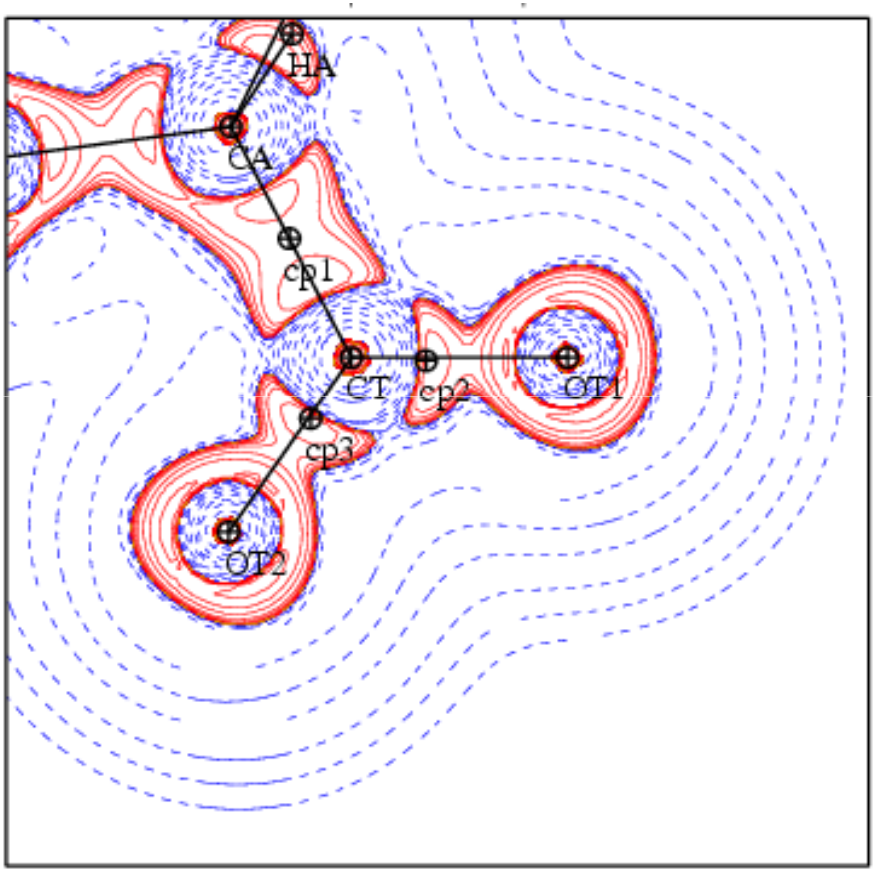
Basin Lines in 2D

Bader Theory : Atoms In Molecules

Grad(ρ) = **0**.

VMoPro Laplacian

$$\nabla^2\rho = \partial^2\rho/\partial x^2 + \partial^2\rho/\partial y^2 + \partial^2\rho/\partial z^2$$



ρ = total electron density

red $\nabla^2\rho < 0$

electron accumulation

cp critical points:

grad ρ = 0

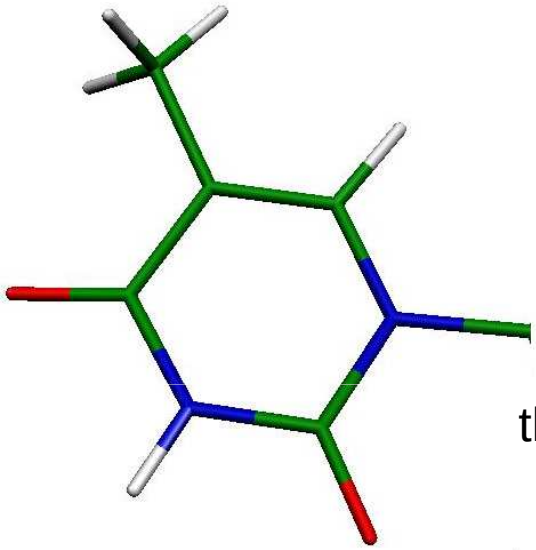
Analysis of CP

Covalent bonds

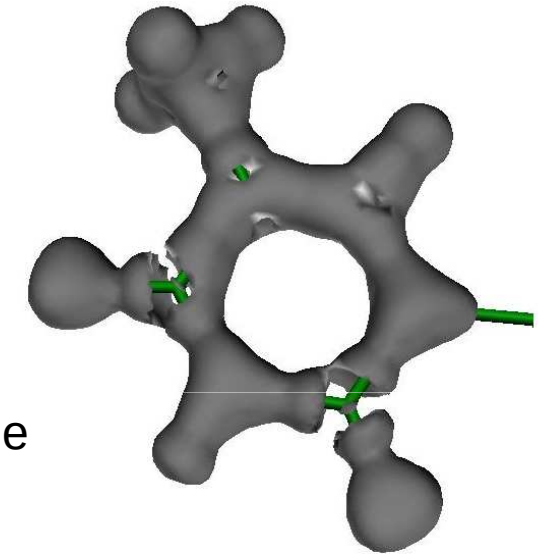
Hydrogen bonds

Ionic interactions

Surface of Zero Laplacien $\nabla^2\rho = 0$



thymidine



VMoPro Visualisation

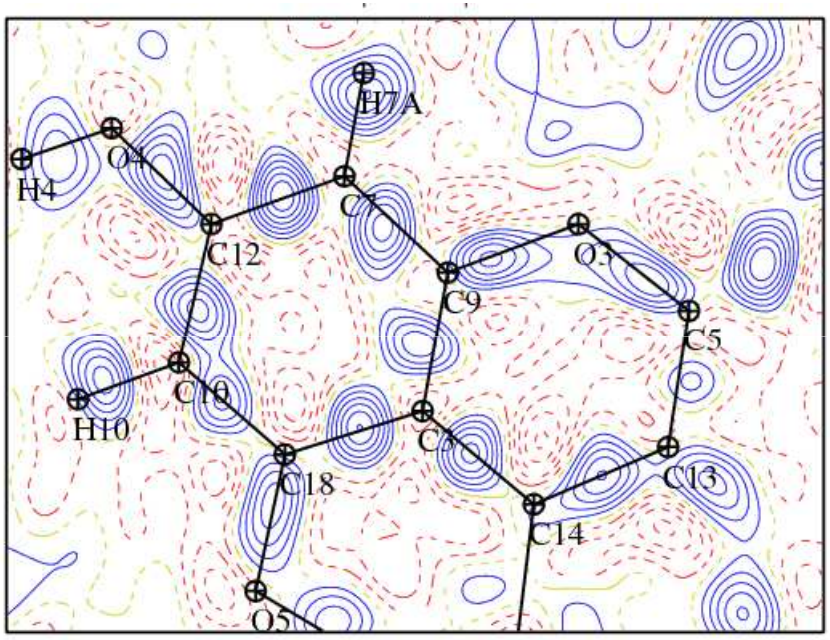
Reactivity Surface

Open surface:

sites for nucleophiles

VMoPro FOUR *m* * *Fo* – *n* * *Fc*

Fourier Residual map $m = n = 1$



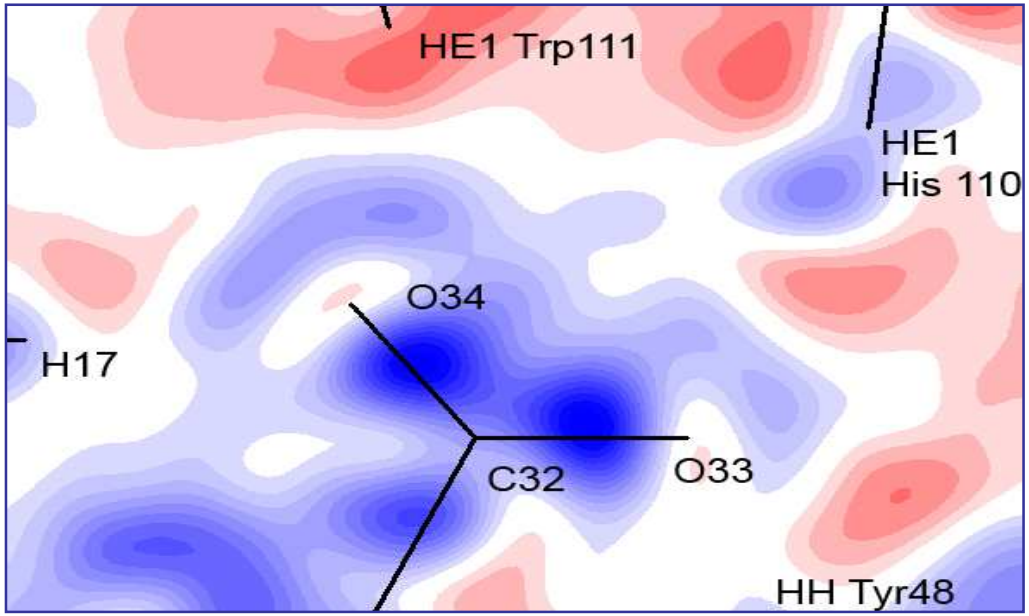
Fhkl ➜ grid rho(x,y,z)

FFT Fast Fourier Transform

Available for 3D maps of unit cell

Dynamic deformation electron density

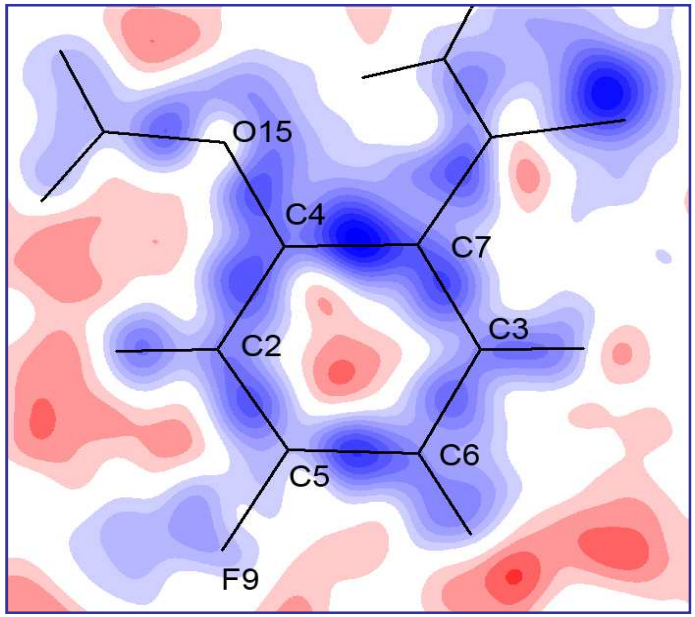
Aldose reductase & Idd594 inhibitor.



Fourier transform of

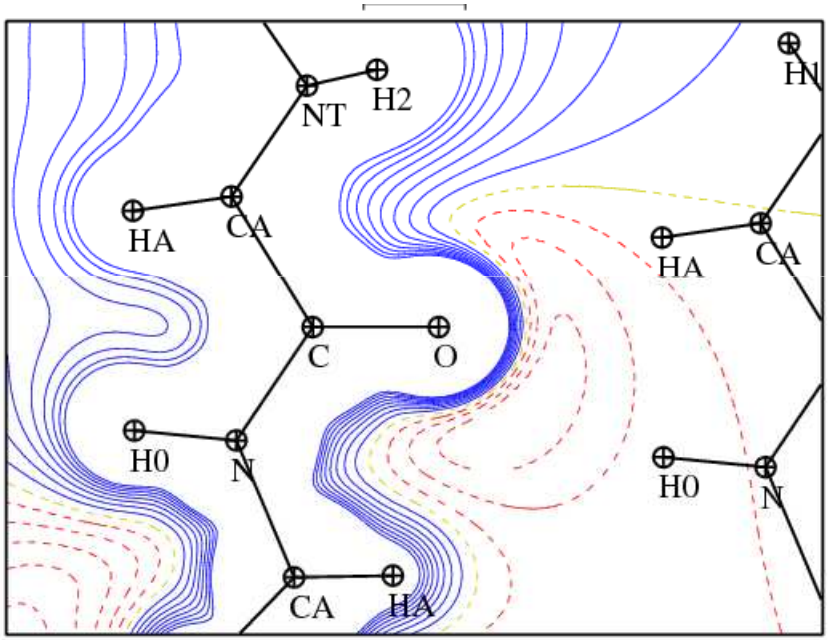
$|F_{obs}|exp(i\Phi_{mult}) - |F_{calc,sph}|exp(i\Phi_{sph})$

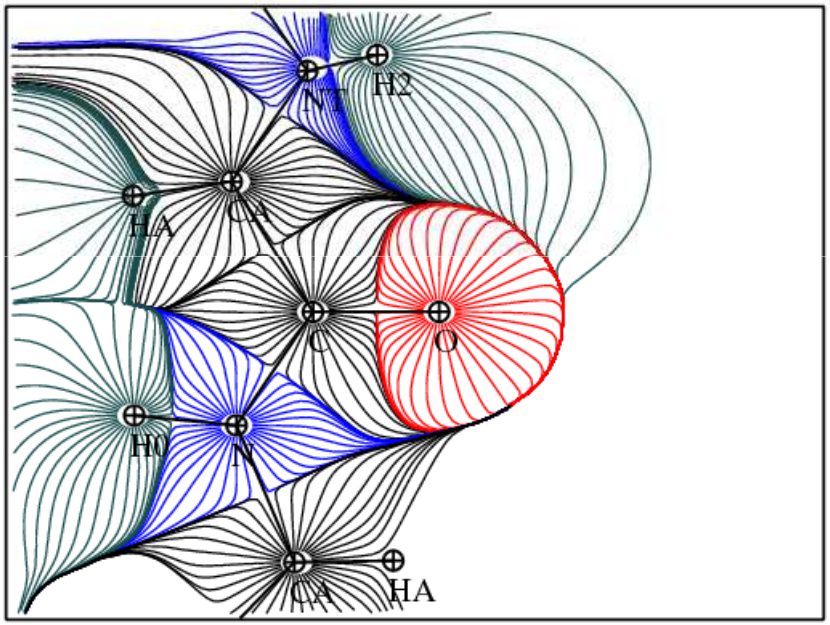
Difference of 2 Fourier files



VMoPro ELEC

Electrostatic potential and gradient lines





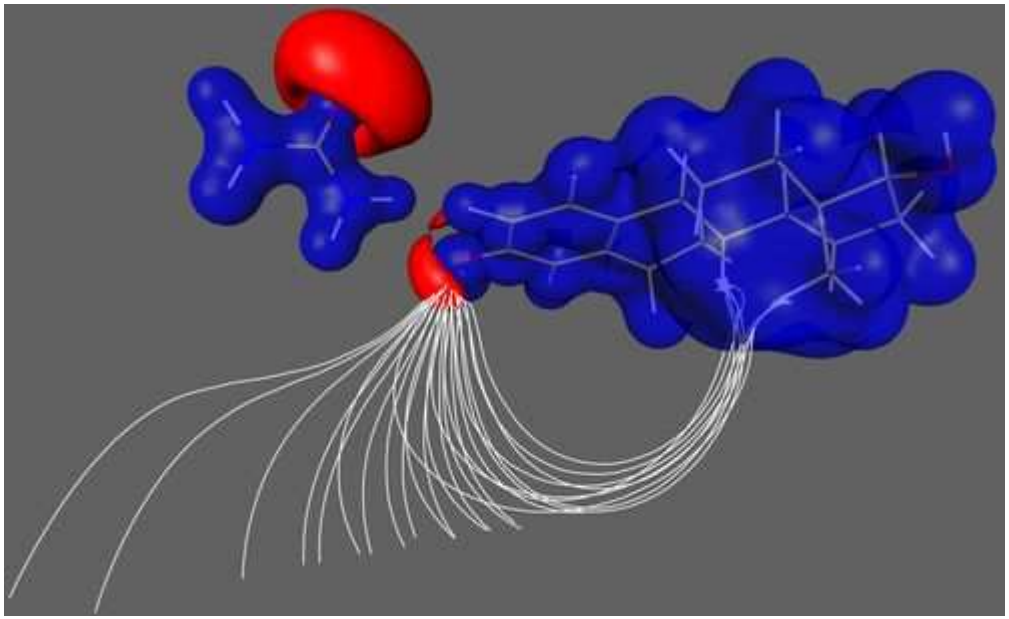
Contour +/- 0.05 e/A

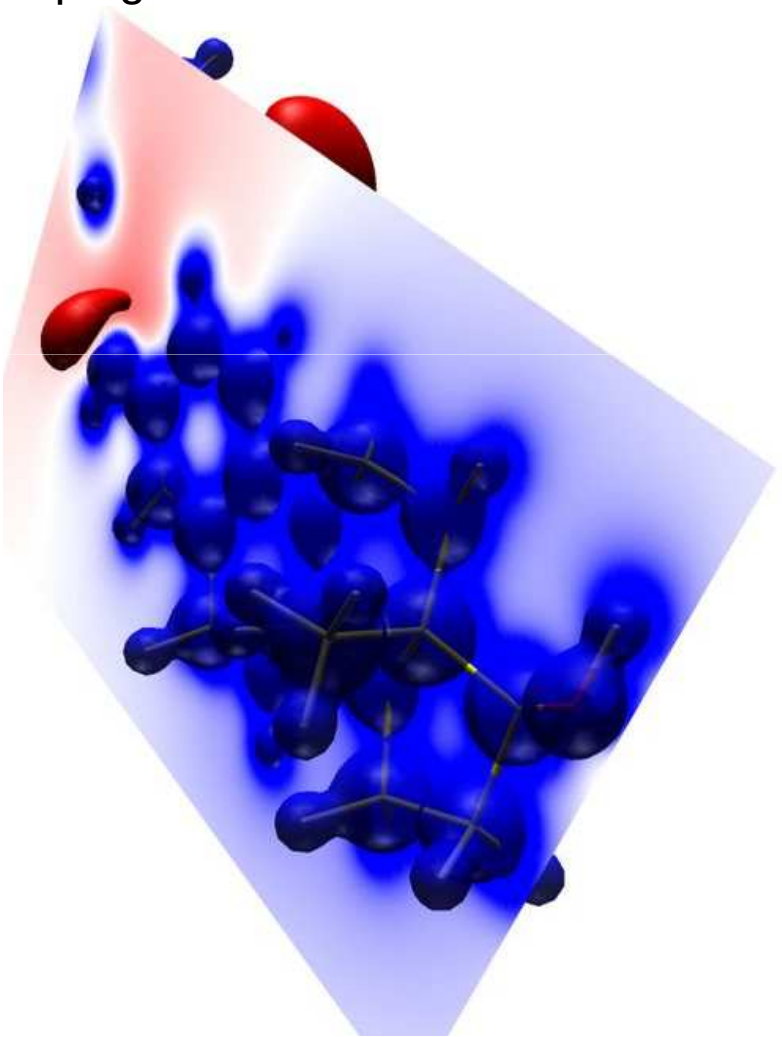
Gradient lines

MoProViewer : a graphical layer for MoPro

(Benoît Guillot)

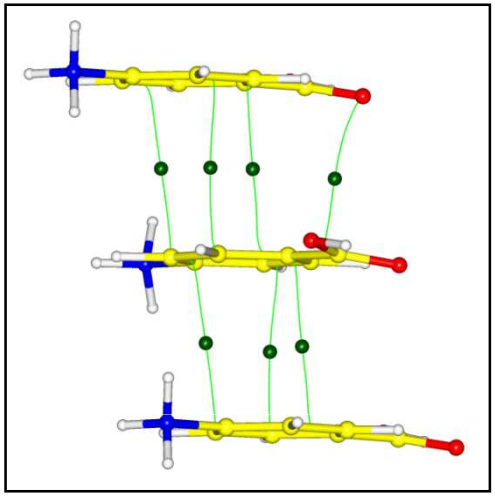
- Reads MoPro (and other) file formats
- Easy and graphically aided 2D / 3D VMoPro maps generation
- Classical functionalities of molecular viewer :
    - lines, sticks, ball & sticks representations
    - stereochemistry computation
- Maps representations :
    - iso-surfaces
    - gradient lines
    - 2D slices

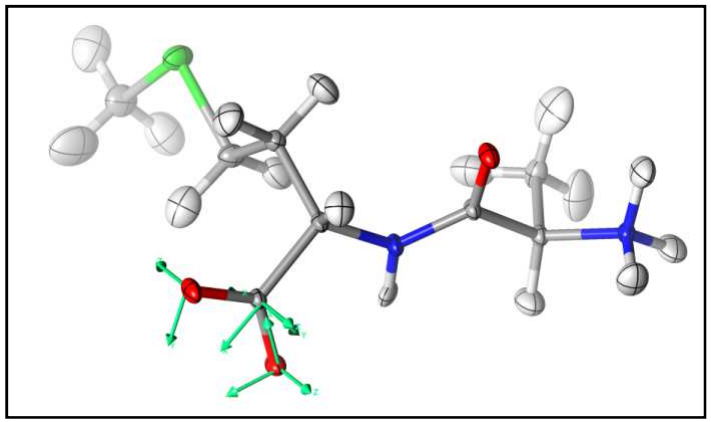




Some other examples of MoProViewer capabilities :

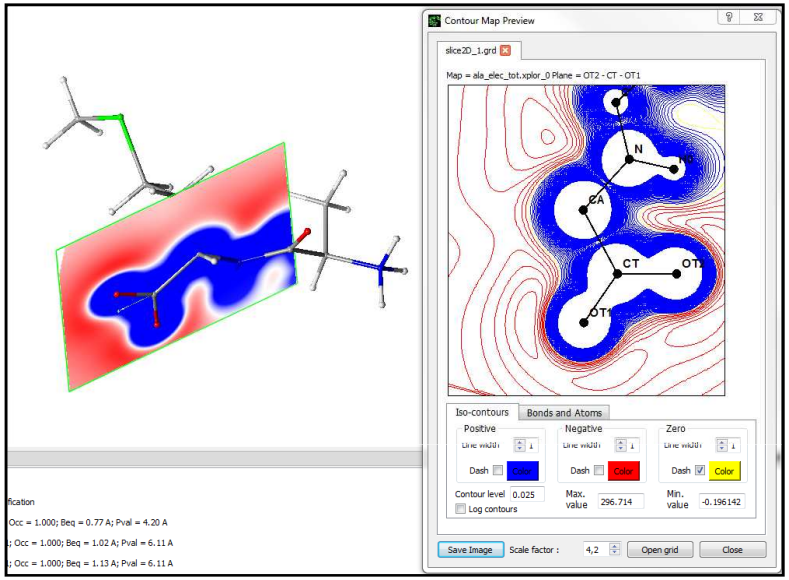
Carboxyphenylammonium stacking with C-C interactions bond paths and their (3,-1) critical points shown as green spheres

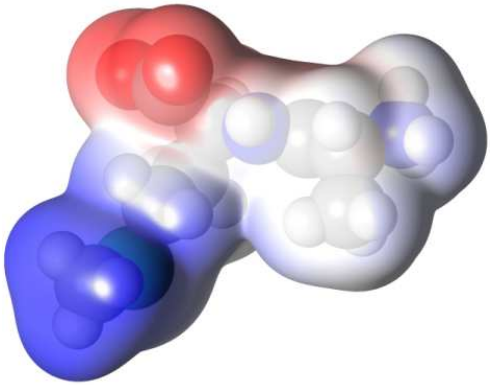




AlaMet molecule with 50% probability thermal ellipsoids, and orthogonal atomic axis systems represented for the COO atoms

AlaMet molecule with a plane showing a slice of the electrostatic potential in the COO plane (left), and its corresponding 2D contour map (right).





AlaMet electron density isosurface of 0.01 e/Å^3 colored according to the molecular electrostatic potential values

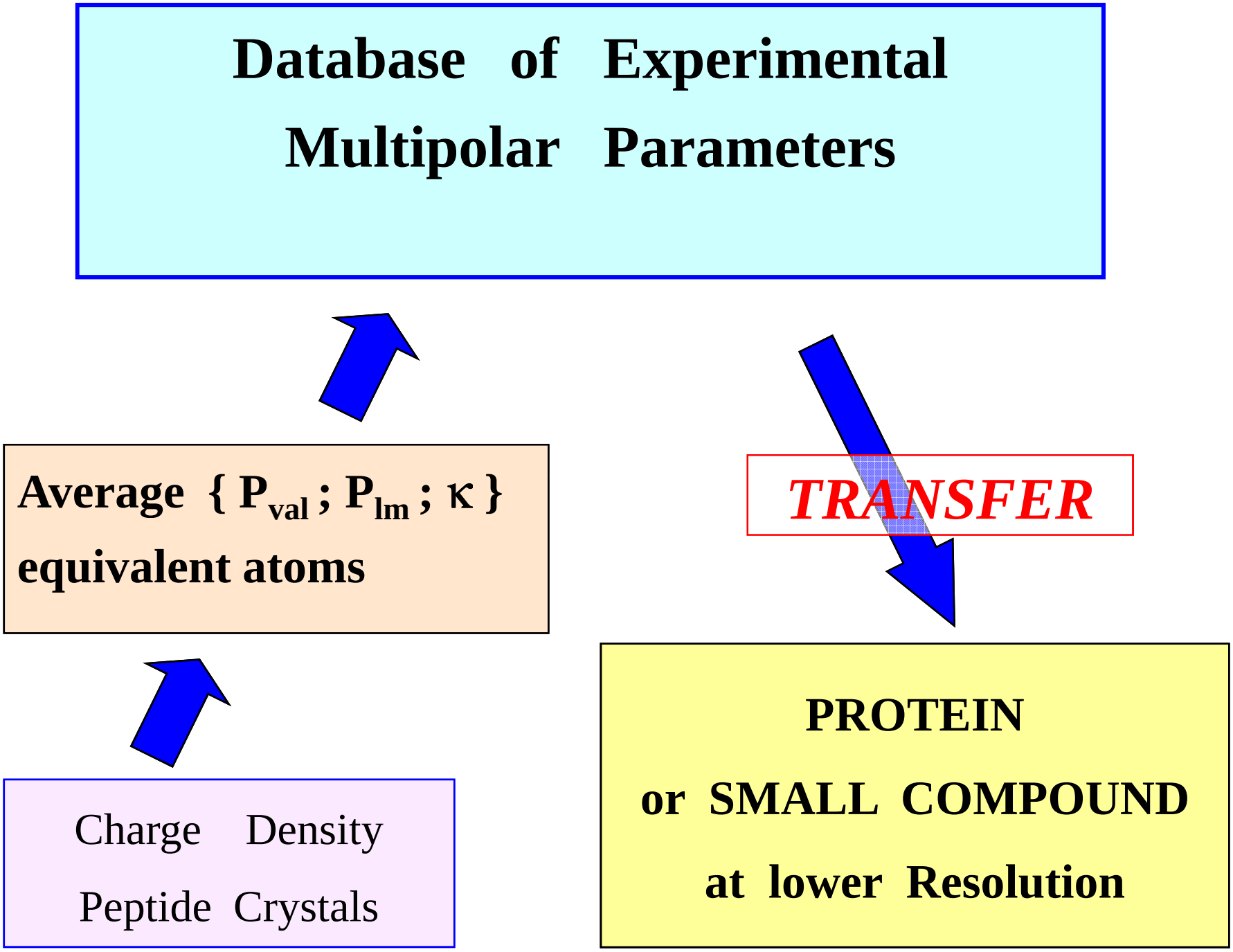
* Charge density refinement with MoPro

* VMoPro visualisation tool of properties

* **Database Transfer**

* Application to proteins

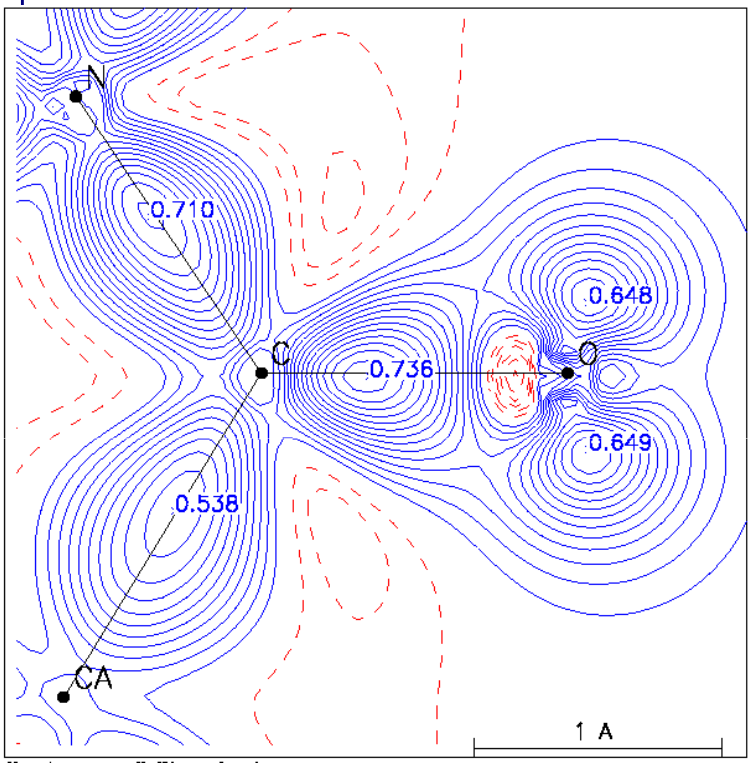
* Electrostatic Interaction Energy


Database of Experimental Multipolar Parameters
Average { P_{val} ; P_{lm} ; κ } equivalent atoms
TRANSFER
Charge Density Peptide Crystals
PROTEIN or SMALL COMPOUND at lower Resolution

Experimental Library Multipolar Atom Model

TRANSFER

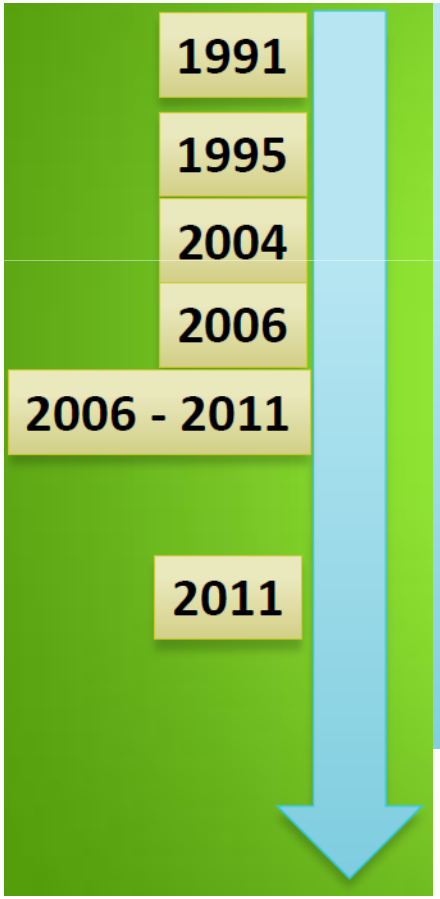
Protein or Small Compound at Lower Resolution



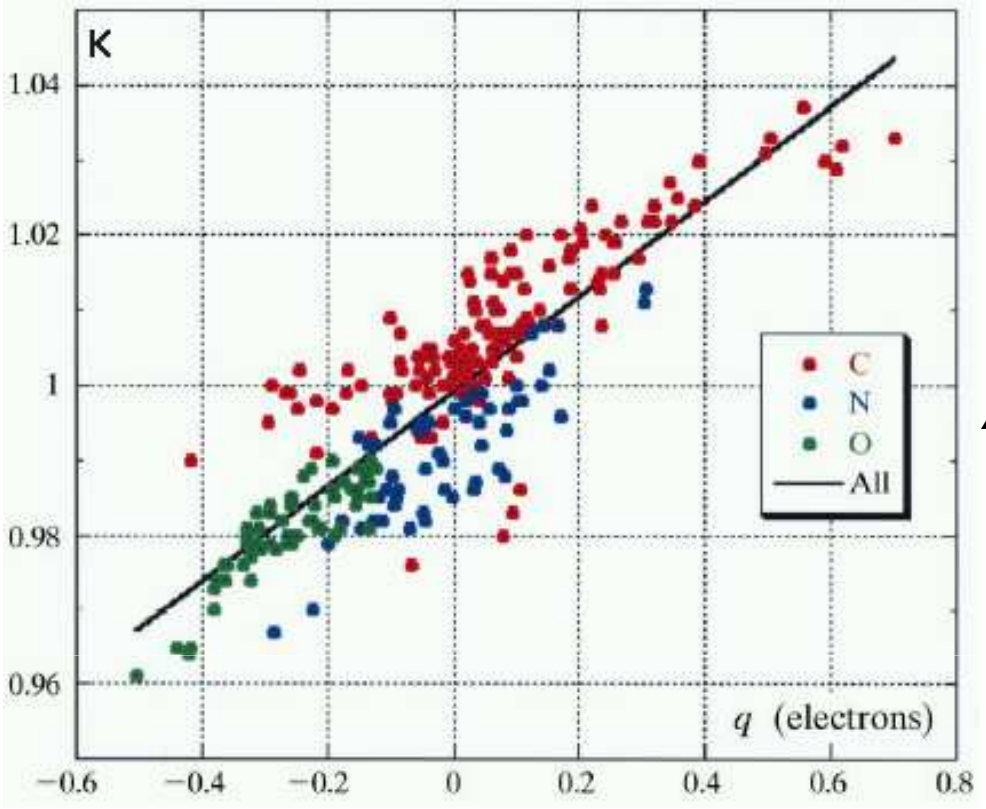
Crystal Structure More Precise
- **Thermal Motion,**
- **Hydrogen Positions**
- **lower *RF & RF*-free factors**

Electron Density Databases

History



- Idea - Brock *et al.*
- ELMAM - Pichon-Pesme *et al.*
- UBDB – theoretical databank
- Invariom – Dittrich *et al.*
- Improvement and development of the databases
- ELMAM2 – extension and Improvement of ELMAM



Volkov, Abramov & Coppens

Acta Cryst (2001). A57, 272

relation between

expansion/contraction of valence shell (κ)

& net atomic charge (q)

for carbon, nitrogen & oxygen atoms

(multipole refinements of crystal B3LYP/ 6-31G** structure factors)

Experimental Library

Multipolar Atom Model

ELMAM proteins

Zarychta, B., Pichon-Pesme, V., Guillot, B., Lecomte, C. & Jelsch, C. (2007). Acta Cryst. A63, 108-125

ELMAM2 common chemical groups
optimal local axes for multipoles symmetry

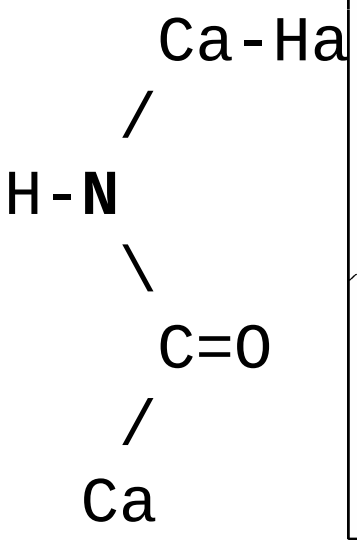
Domagala S, Munshi P, Ahmed M, Guillot B & Jelsch C. Acta Cryst. (2011). B67. 1-16.

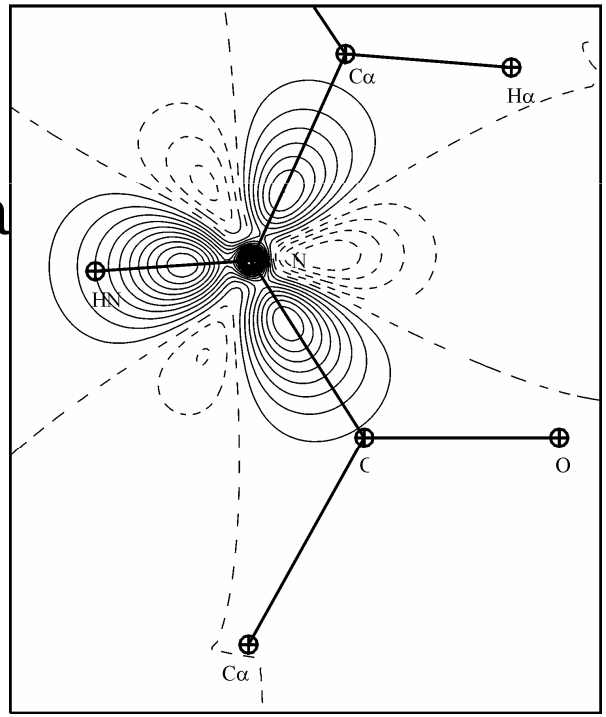
Experimental Multipolar Database for Proteins

	Pv	Dx	Dy	Dz	Qz2	Qxz	Qyz	Qx2-y2	Qxy
actr	5.445	0.029	-0.104	-0.019	-0.154	0.021	0.002	-0.056	-0.001
actr	5.445	0.029	-0.104	-0.019	-0.154	0.021	0.002	-0.056	-0.001
acdelt	5.216	0.033	-0.071	-0.010	-0.036	0.013	0.003	-0.004	-0.042
acdelt	5.027	-0.002	-0.169	-0.028	-0.034	0.025	-0.045	-0.039	-0.063
enkad	5.371	-0.024	-0.104	0	-0.074	0	0	0.036	0.111
enkad	5.371	-0.024	-0.104	0	-0.074	0	0	0.036	0.111
enkad	5.371	-0.024	-0.104	0	-0.074	0	0	0.036	0.111
enkad	5.371	-0.024	-0.104	0	-0.074	0	0	0.036	0.111
trigqa	5.330	0.041	-0.048	-0.016	-0.062	-0.021	-0.016	0.042	0.031
trigqa	5.440	-0.031	-0.114	0.017	-0.042	0.012	-0.027	-0.008	0.013
trigqa	5.381	0.006	-0.015	0.014	-0.016	-0.003	0.059	-0.013	0.018
trigqa	5.444	0.001	-0.069	-0.016	0.010	0.020	0.018	0.012	0.007
YGG	5.306	-0.059	-0.070	0	-0.024	0	0	-0.014	0.07
YGG	5.311	-0.083	-0.068	0	-0.061	0	0	-0.029	0.016
GD	5.426	-0.019	-0.052	0	0.06	0	0	-0.008	0.118
actyr	5.154	-0.025	-0.042	-0.028	-0.028	-0.002	0.003	-0.055	0.009
GT	5.313	-0.025	-0.010	0	0.027	0	0	0.053	-0.034
prohis	5.255	0.004	-0.014	0.008	-0.067	0.053	0.004	0.011	0.048
prohis	5.255	0.004	-0.014	0.008	-0.067	0.053	0.004	0.011	0.048
acgln	5.108	-0.017	-0.121	-0.031	-0.069	-0.032	0.049	0.031	0.013
alamet	5.206	0.018	-0.021	-0.014	-0.044	0.008	-0.001	-0.019	0.020
<p>	**5.312**	-0.009	**-0.072**	-0.006	**-0.050**	0.008	0.003	0.000	0.034
SEM	0.026	0.007	0.01	0.003	0.011	0.004	0.005	0.008	0.012

+octapoles

K κ′



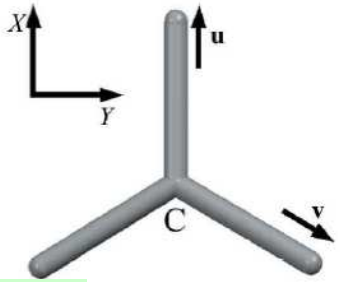


Atom Type N

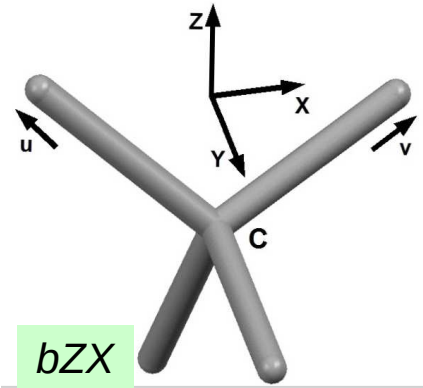
Extension of multipolar database

ELMAM	ELMAM2
• average values from 14 peptides , amino acids	• average values from 54 high resolution structures
• limited to proteins	• extension common chemical groups
• XY local axes, no symmetry constraints	• optimal local axes & symmetry constraints to improve refinements & average statistics
• manual selection of atom types (chemical intuition)	• automatic assignement based on connectivity & chemical environment of atoms

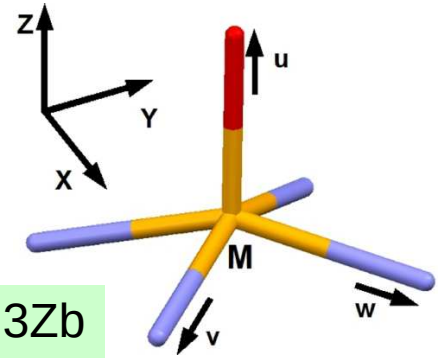
ELMAM2 Database : Optimal local axes systems for multipoles



XY

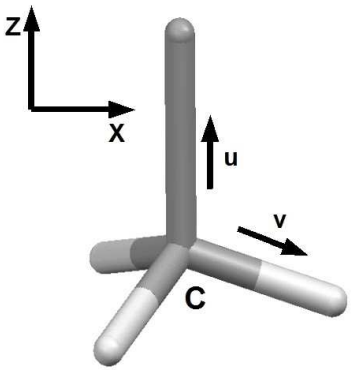


bZX

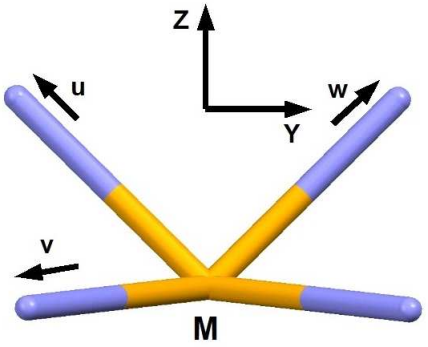


3Zb

3ZX

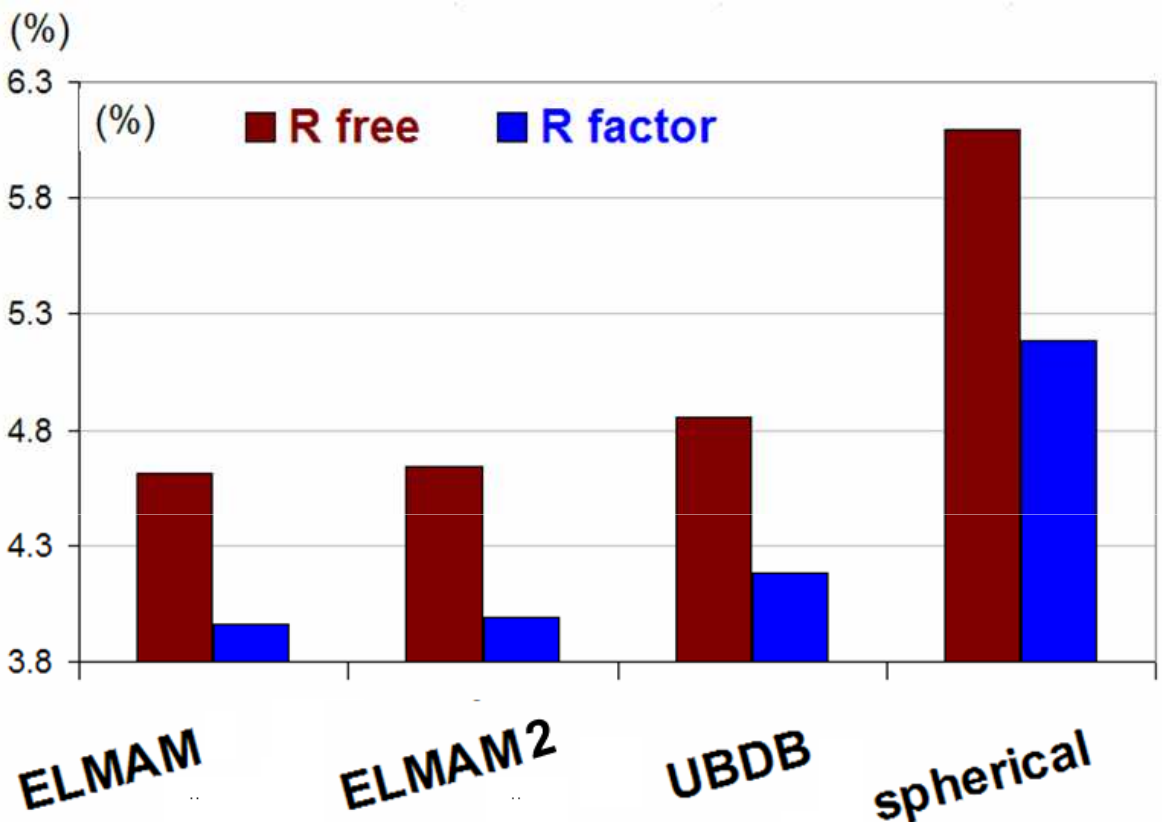


3bZ

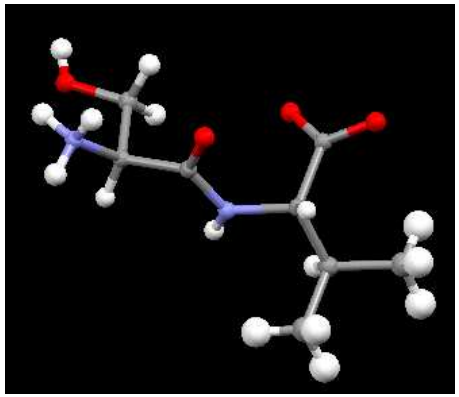


Domagala & Jelsch (2008) J. Applied Cryst. 41, 1140–1149

Effect of Database Transfer



Univ. Buffalo



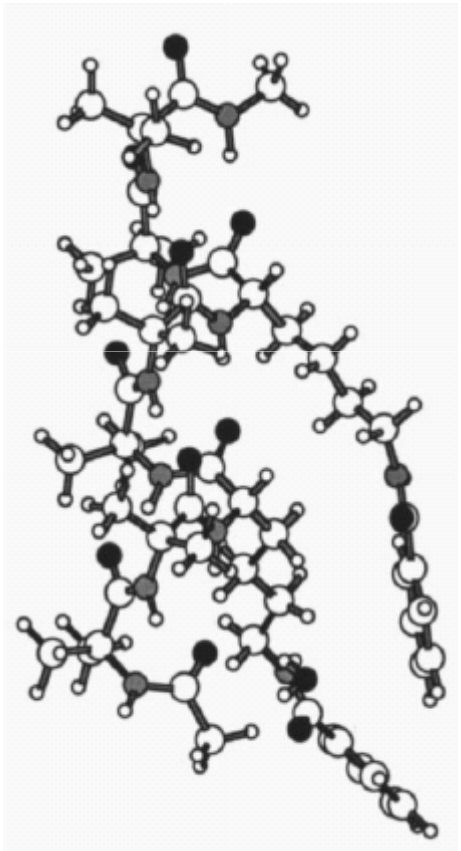
L-Seryl
-L-valine

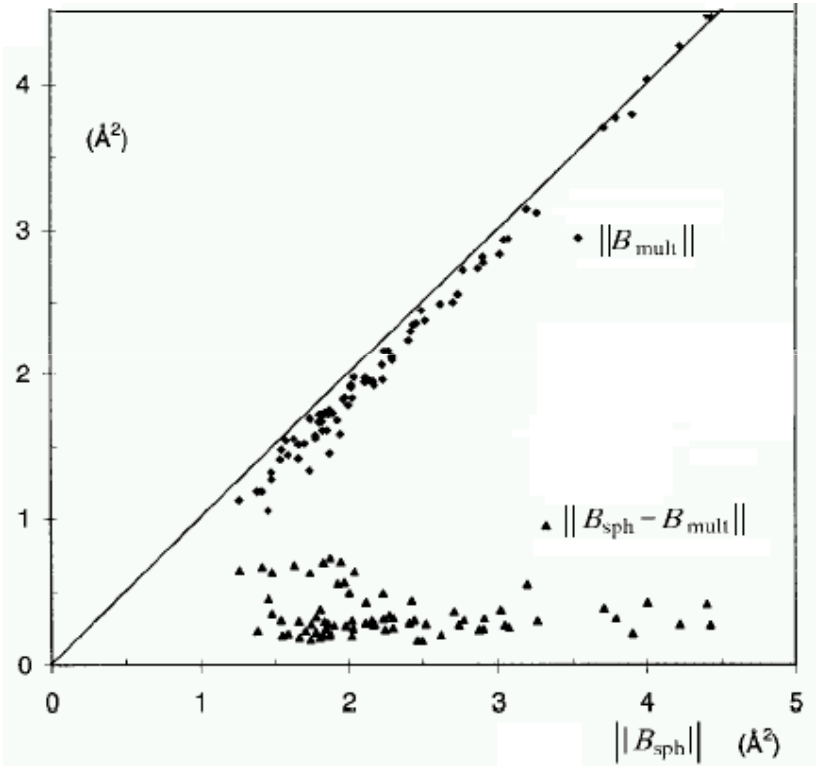
Moen *et al.*, 2004, Acta Cryst. C60, o564–o565

0.73 Å resolution

Same number of variables & restraints

EFFECT of TRANSFER on *B*-FACTORS



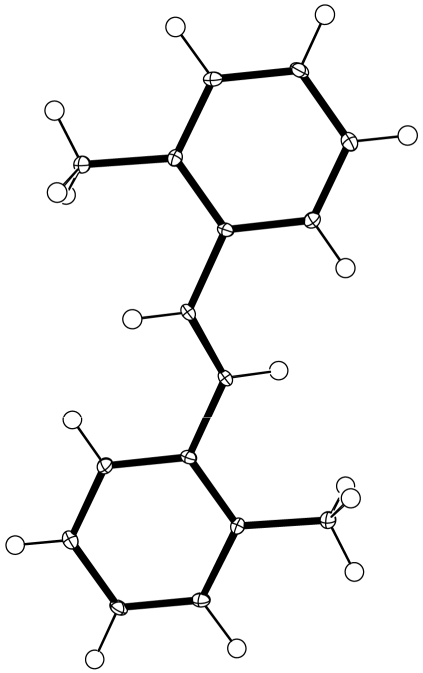


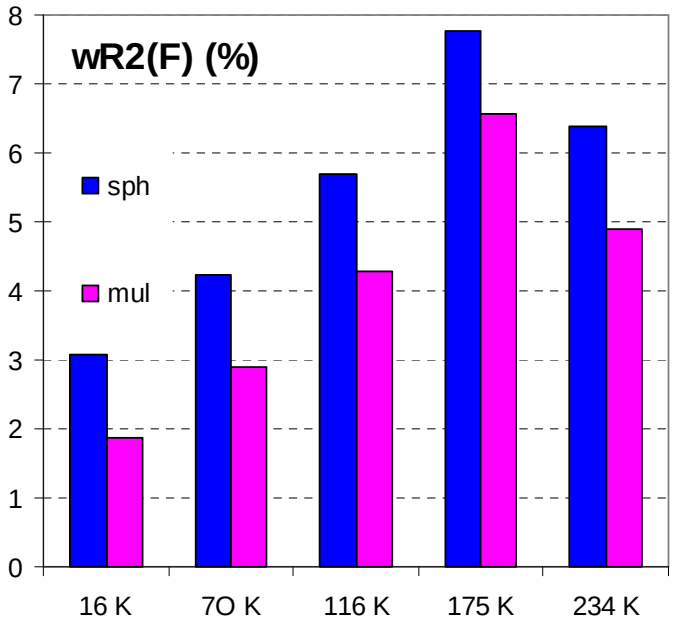
Helical octapeptde

***Acta Cryst* (1998) D54 1306**

Small Compound & Spherical or Multipolar Atom

(E)-2,2'-dimethylstilbene (Ogawa *et al*. 1992)





Transfer Library Multipoles & Refinement

Maximal Constraints: atom equivalencies & local symmetries

=> Improved Thermal Displacement Parameters

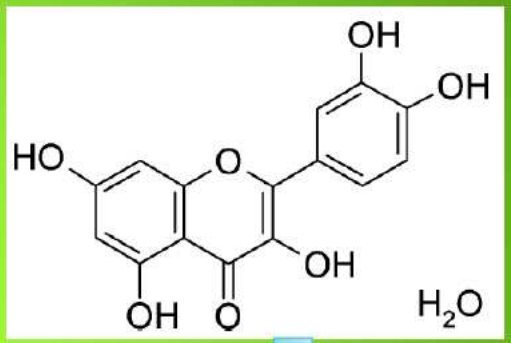
Dynamical Analysis (Pr Bürgi Bern)

Multipole modelling of quercetin

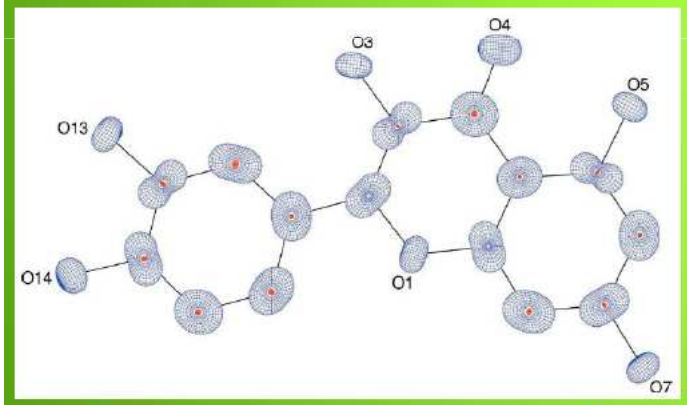
ELMAM2

12 atom-types

Transfer

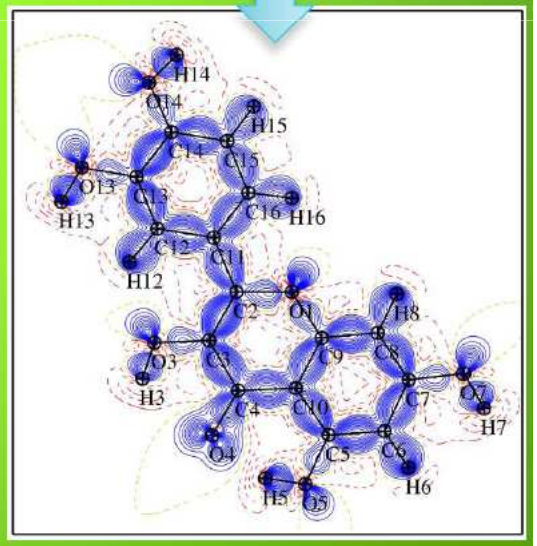


Peanut representation



Improvement of ADPs
IAM – ELMAM2

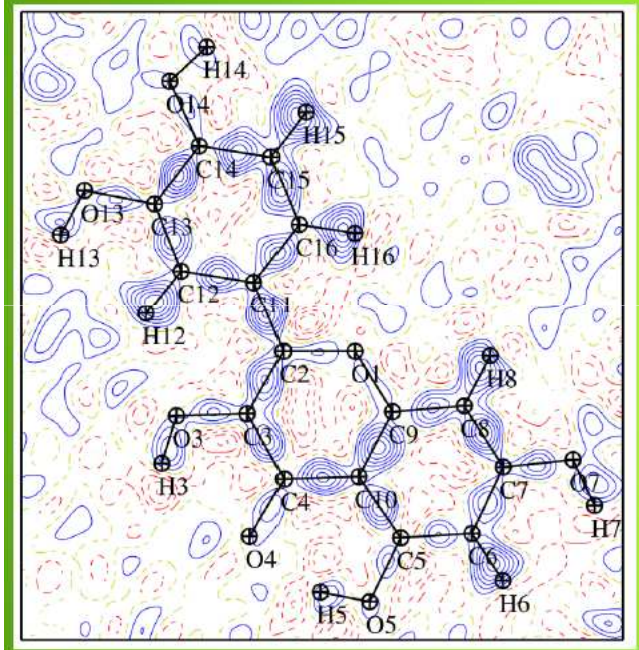
Static deformation density
Contour: ± 0.05 eÅ^{-3}



Domagała et al., *Acta Cryst.* **2011**, B67, 63-78

Quality of the multipolar transfer

IAM model refinement



ρ_{max} = +0.39 eÅ^{-3}

ρ_{min} = −0.24 eÅ^{-3}

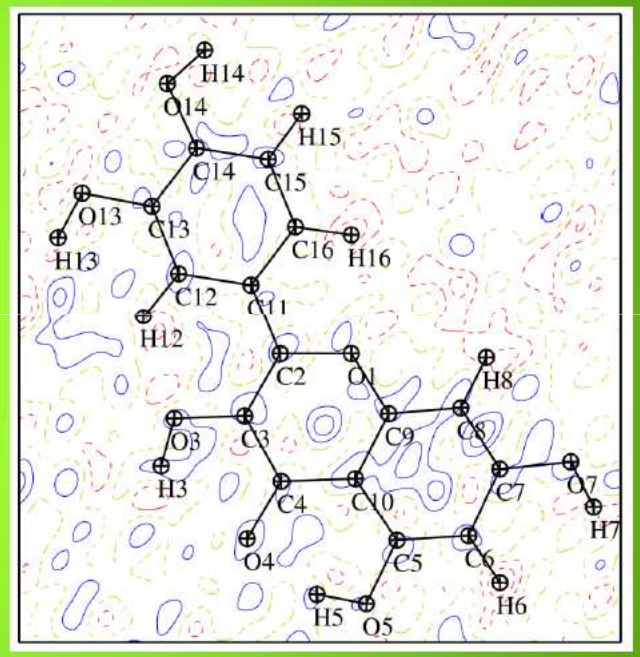
R(F) = 4.00 %

Residual Density

Contour ± 0.05 eÅ^{-3}

quercetin

ELMAM2 + xyz & U_{ij} refinement



ρ_{max} = +0.14 eÅ^{-3}

ρ_{min} = −0.16 eÅ^{-3}

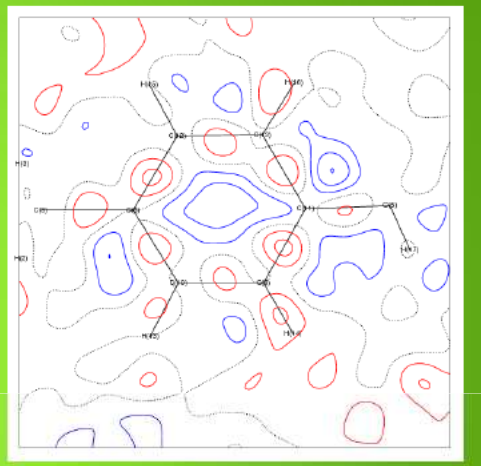
R(F) = 2.20%

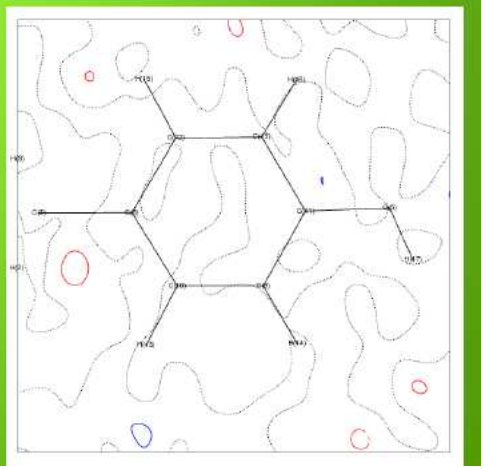
Refinements of experimental X-ray data

Application of the databanks to low-resolution data (transferred aspherical atom model refinement, TAAM):

- significantly **lowers** the conventional **R-factor** (1% or more)
- **improves** the determination of **bonds** and **angles** to within 0.002-0.003 Å and 0.09-0.17° of values obtained from a complete multipolar refinement of high-resolution datasets
- **improves** the determination of **phase** angles by 2-6° compared to the standard independent atom refinement (IAM)
- **removes** majority of the bonding features from the **residual** Fourier difference maps
- **improves** atomic **displacement parameters** (ADPs) and results of the Hirshfeld rigid-bond test

Volkov et al Acta Cryst D, 2007, D63, 160





Main applications of the databases published so far

- Electron Density Transfer & Refinement of small molecules

- increasing precision of the refined Flack parameter (Dittrich, Strumpel *et al.*, 2006)

- used as a starting point in refinement of the constrained multipolar parameters of Proteins (Jelsch *et al.,* 2000; Guillot *et al*., 2008)

- calculation of the electrostatic interaction energy (Li *et al.*, 2006; Dominiak *et al.*, 2007; Dominiak *et al.*, 2009; Fournier *et al.*, 2009)

- modelling of ED of disordered groups & detecting disorder (Dittrich *et al.*, 2007; Bąk *et al.*, 2009; Dittrich, Warren *et al.*, 2009)

- calculation of electrostatic potential of macromolecules (Muzet *et al.*, 2003; Liebschner *et al.*, 2009; Dittrich, Weber *et al*., 2009; Dittrich *et al.*, 2010

* Charge density refinement with MoPro

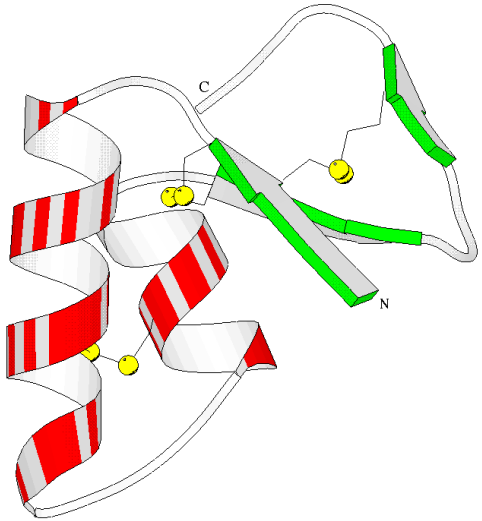
* VMoPro visualisation tool of properties

* Database Transfer

*** Database Application to Proteins**

* Electrostatic Interaction Energy

Protein Crambin



0.54 Å resolution

Database Transfer & Refinement

Peptide

ab initio calculation

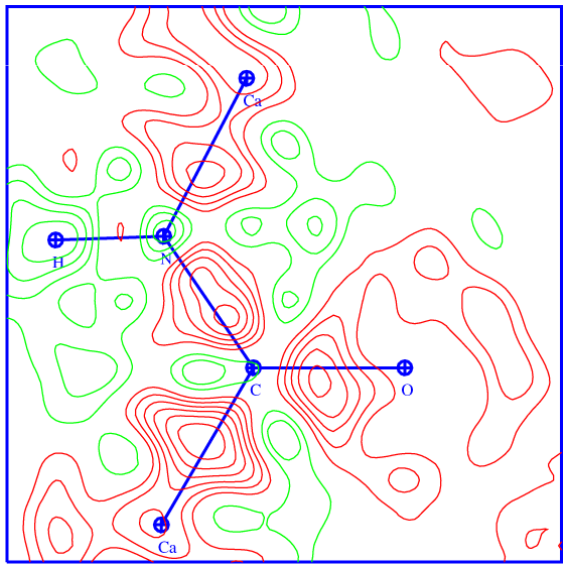
Hartree-Fock

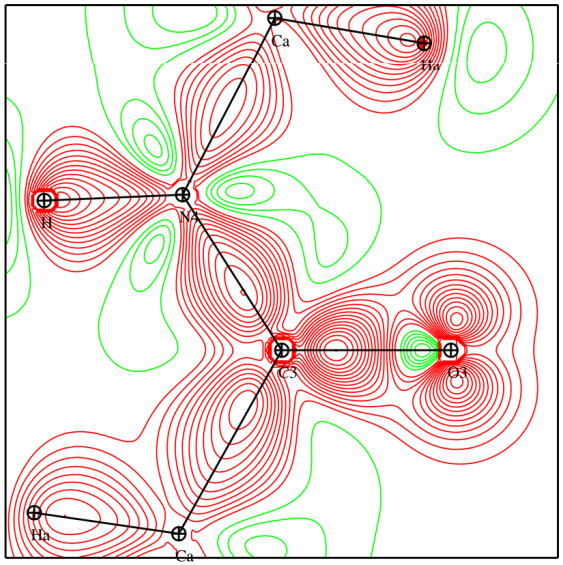
self-consistent field
triplezeta-plus-
(C,N,O-*d* and H-*p*)-
polarization-function
Gaussian basis set.

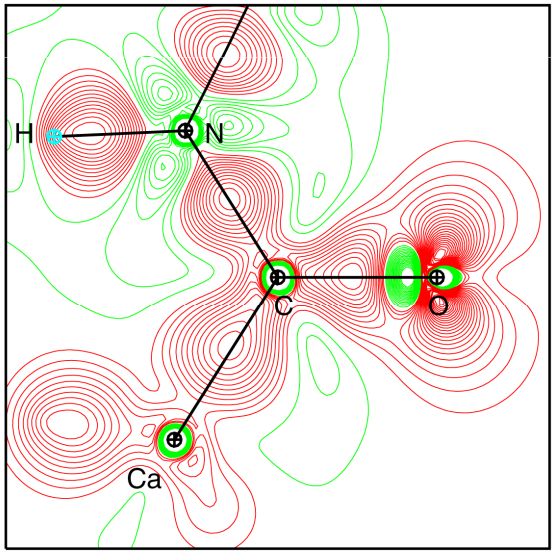
average polypeptide

Electron Density

Spherical Residual & Static Deformation





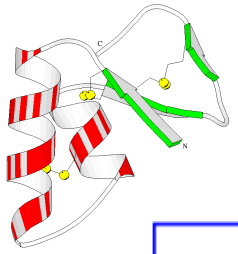


Jelsch *et al.*, P.N.A.S. 2000, 97.

+/- 0.05 $e^-/Å^3$

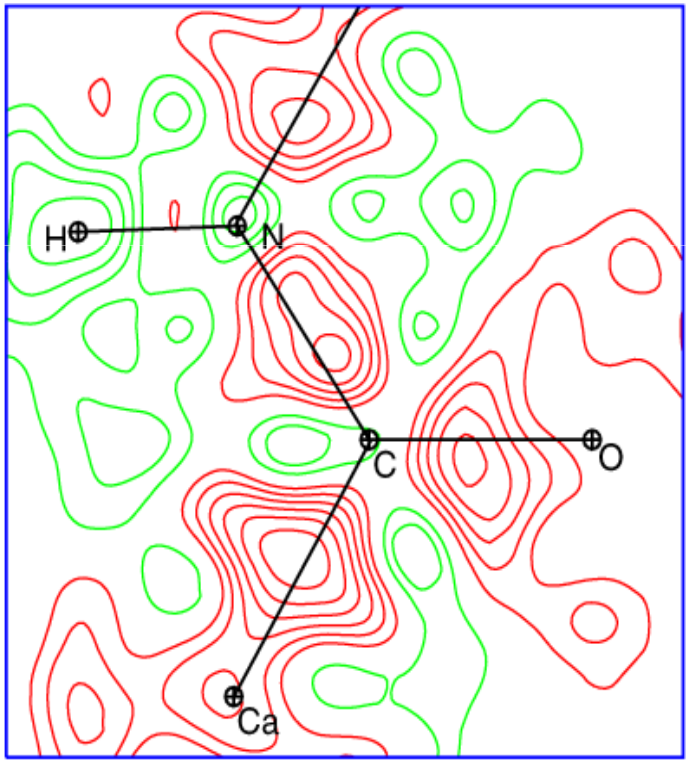
Corr = 88% $|\Delta\rho|$ = 0.18 & 0.20 e/A^3

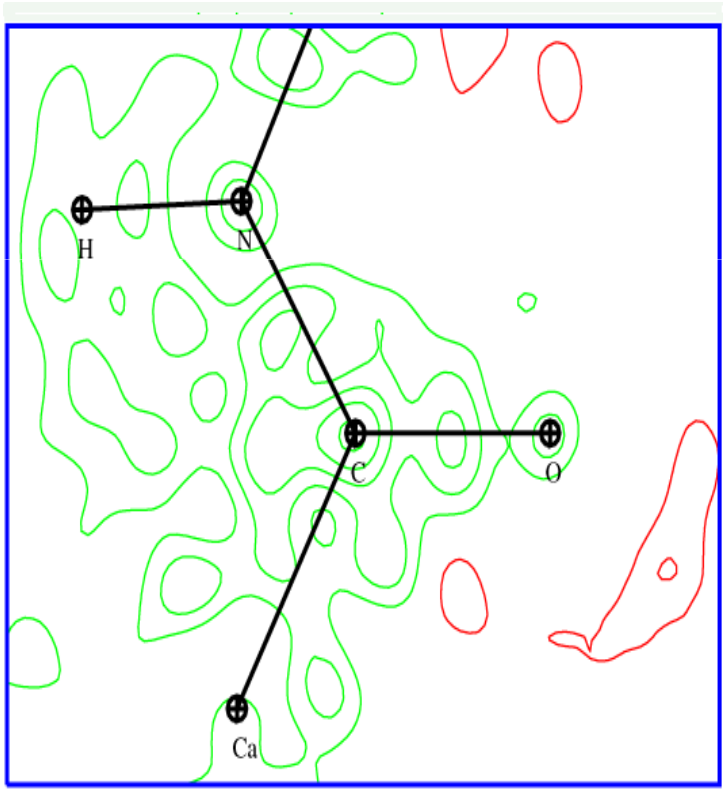
Crambin Residual Electron Density



Spherical Atom Model Multipolar

Database Transfer & Refinement





+/- 0.02 $e^-/Å^3$ Average 34 peptides

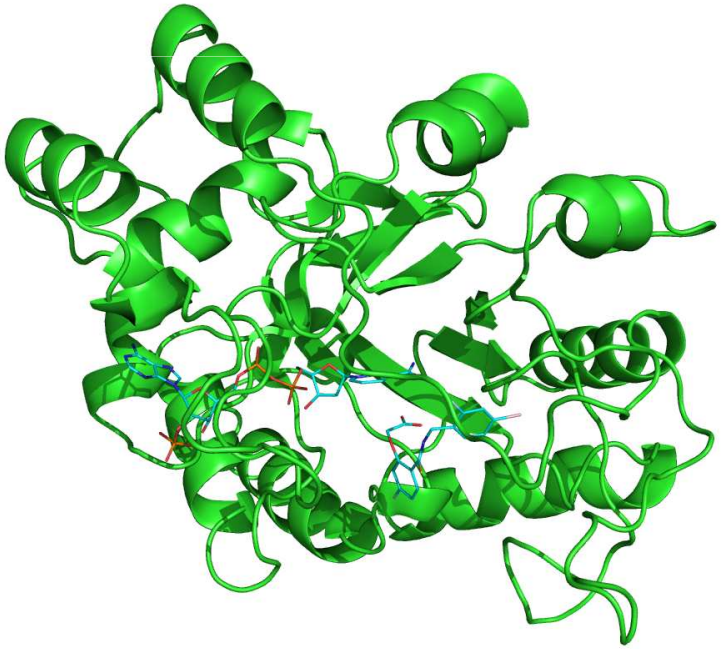
Human Aldose Reductase

Résolution 0.65 Å

Collab. Podjarny *et al*.

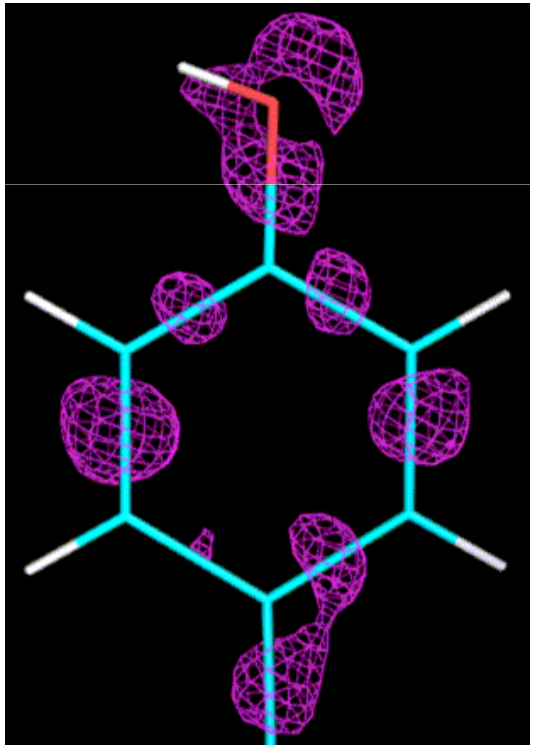
IGBMC Strasbourg

Complications Diabetis



Spherical Atom Model

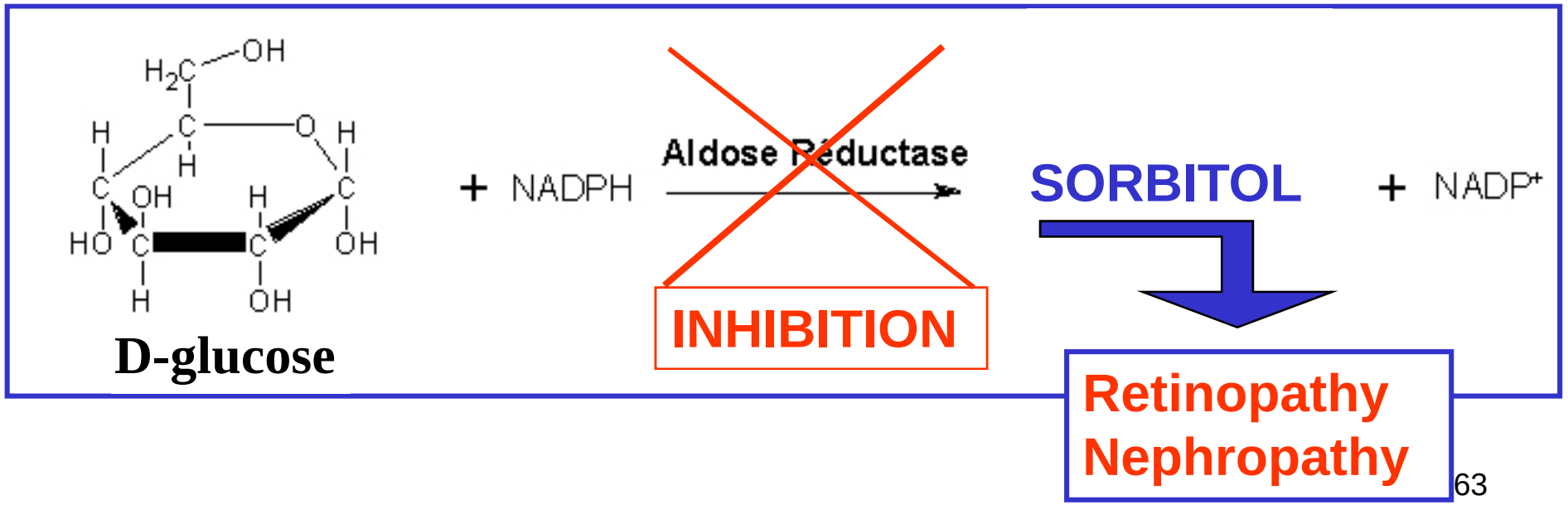
Residual electron density



The Human Aldose Reductase

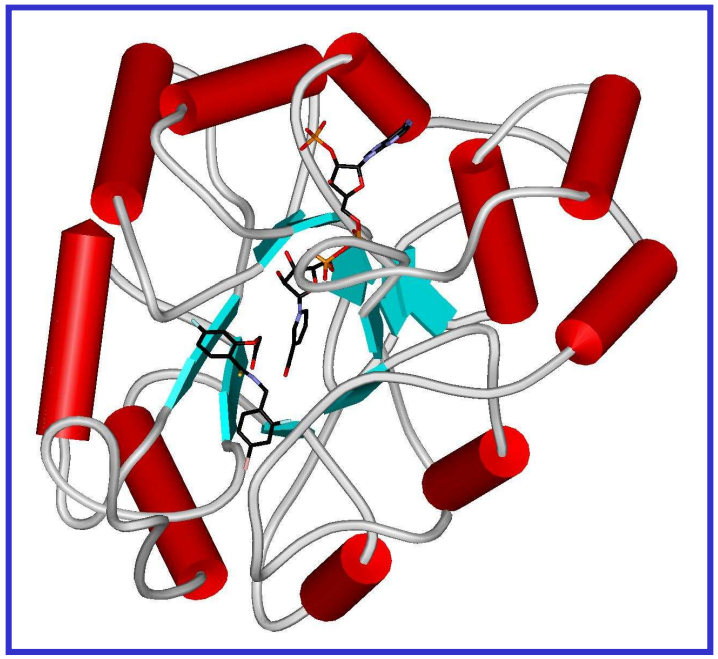
Involved in Diabetes complications

- Normal conditions : glycolysis (hexokinase adds phosphate)
- Hyperglycemic conditions : the polyol pathway

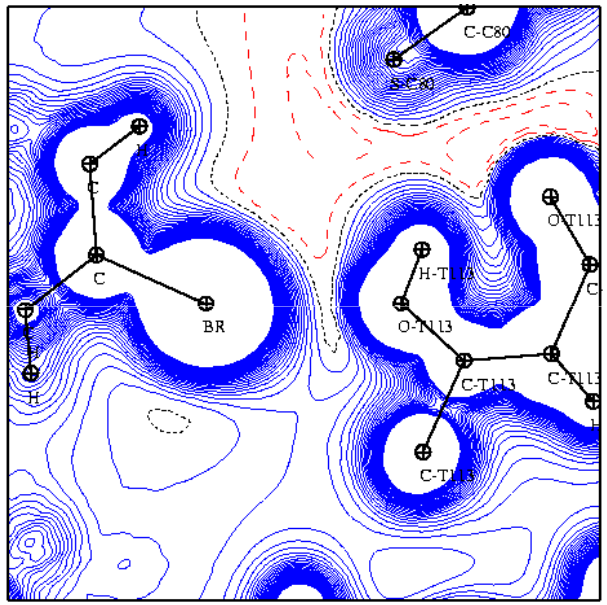


Aldose Réductase Humaine

Enzyme & $NADP^+$ & Inhibiteur



Ligand IDD - Protéine



Complementarity

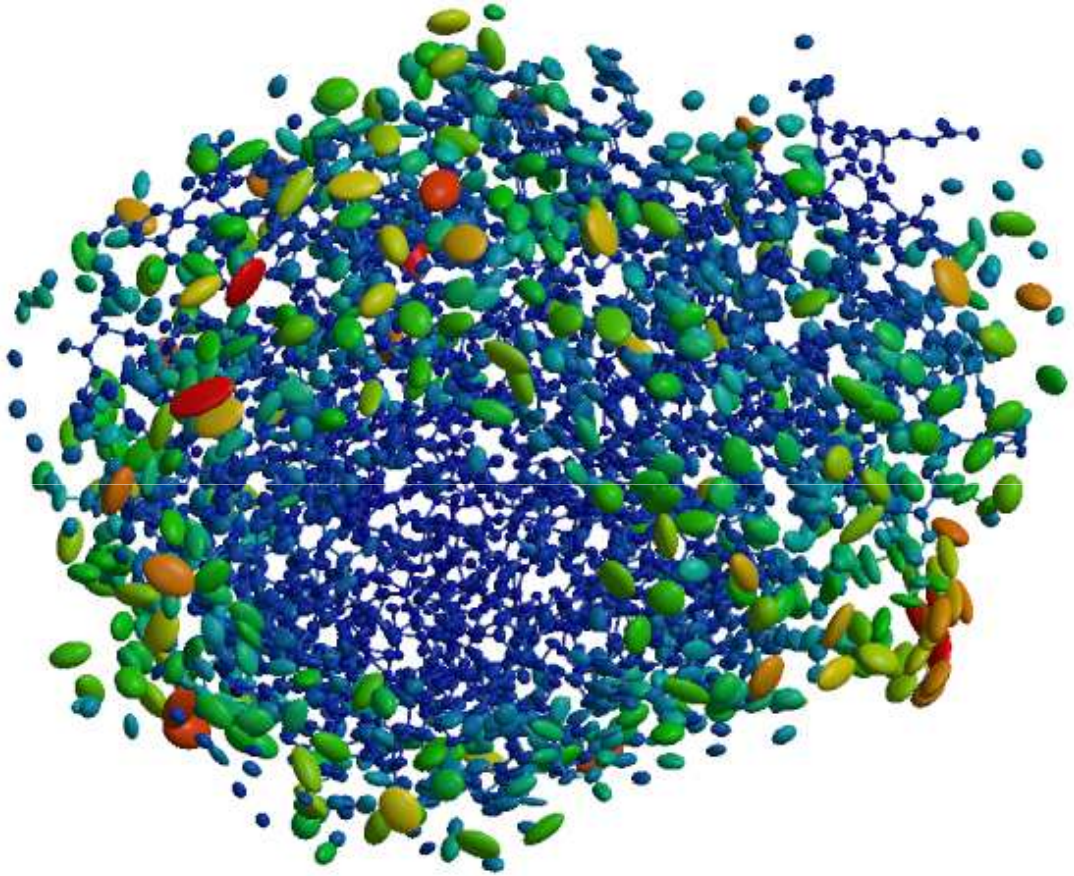
Electrostatic Potential

& Deformation Density

Muzet et al. **P.N.A.S. 2003**

Thermal ellipsoids

h. Aldose Reductase



(Blue) **2.41 <** B_{eq} **< 51 Å^2 (*Red)***

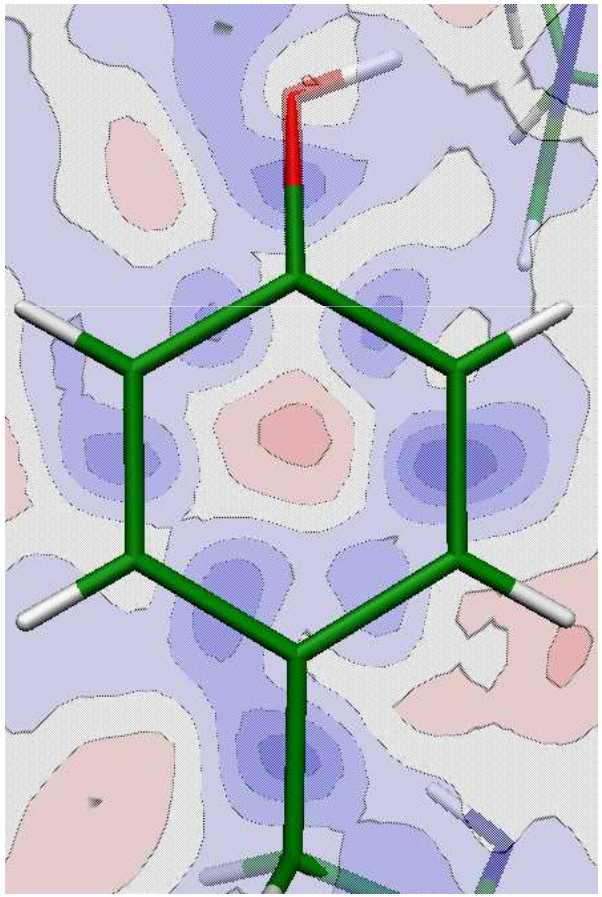
50% probability level

Residual electron density Aldose Reductase

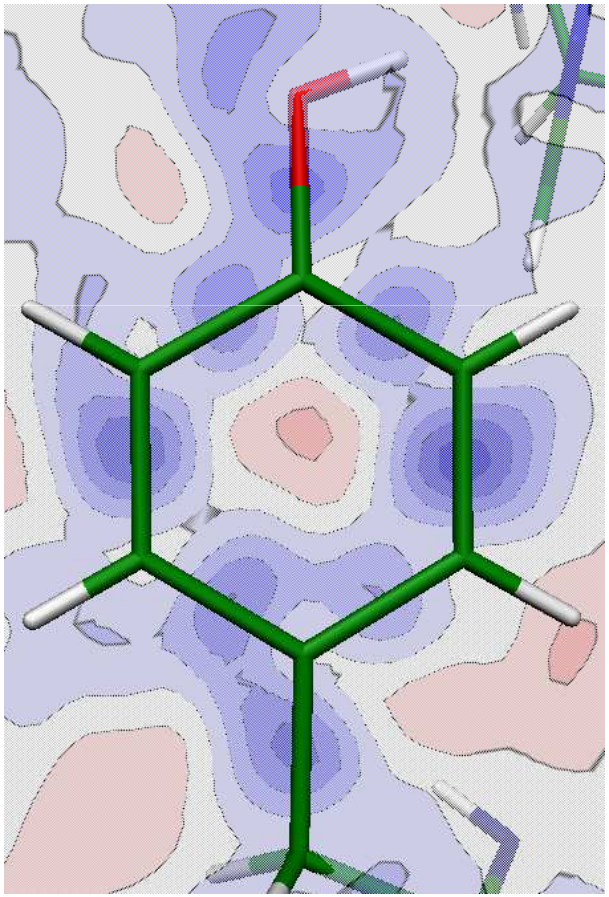
spherical atom

standard refinement

high order refinement.



tyr48



-0.5 e/Å^3

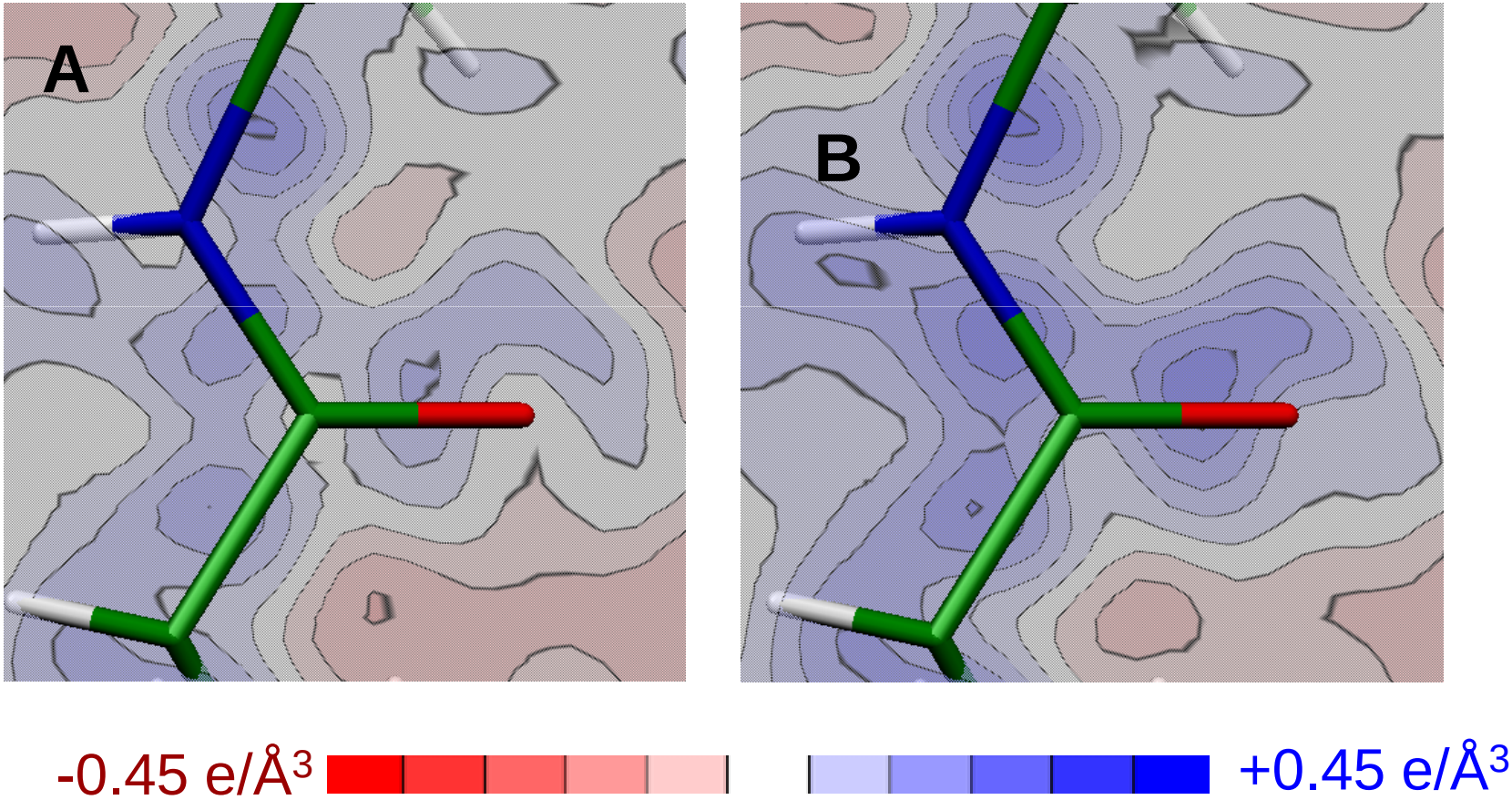
+0.5 e/Å^3

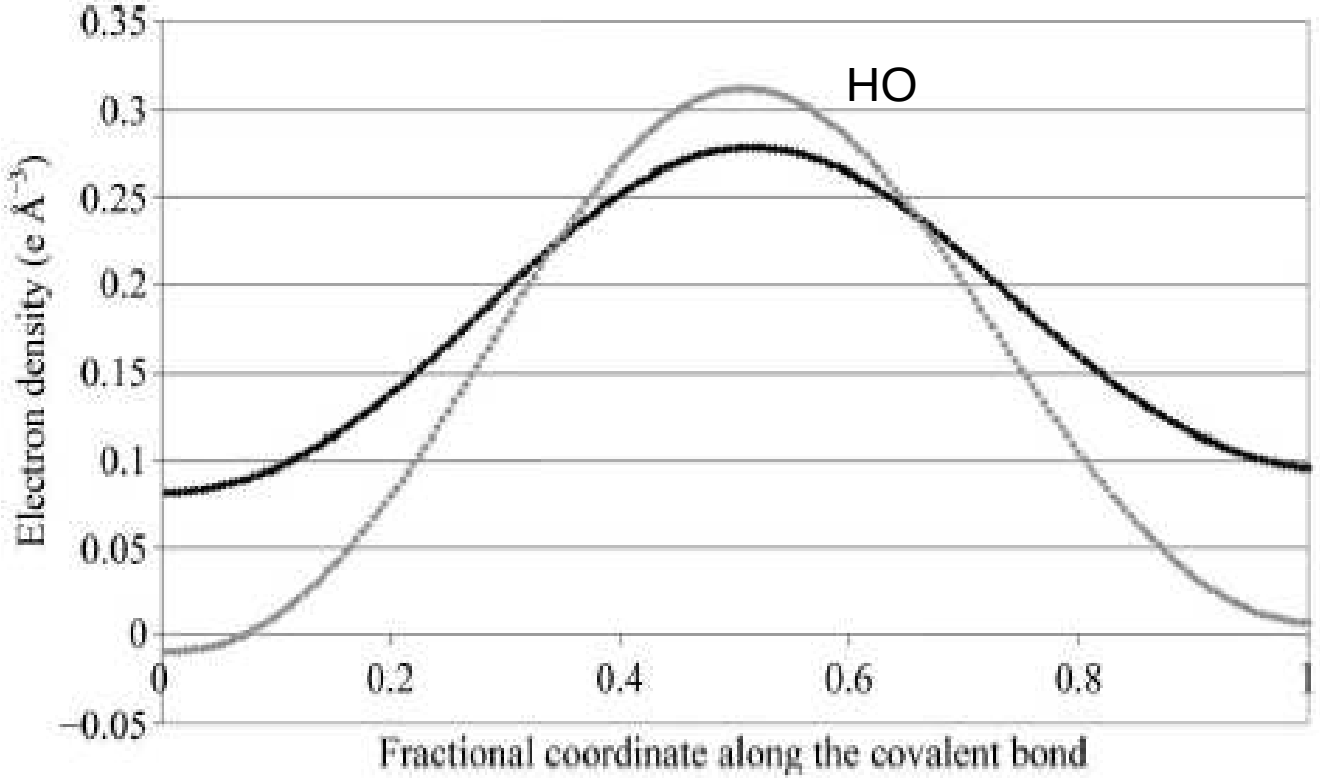
Residual electron density following transfer

A: standard spherical refinement.

B: high order refinement.

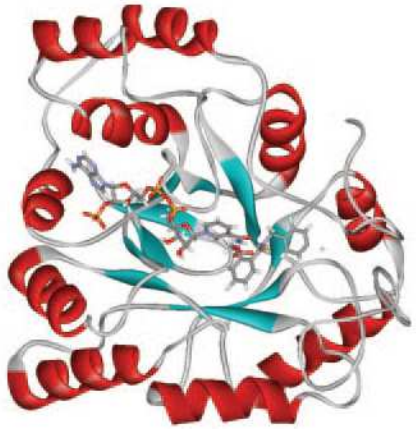
Lys262





Average residual electron-density profile along covalent bonds between non-H atoms of the subsystem refined against high-resolution data: black curve, after IAM refinement; grey curve, after IAM HO refinement.

Main Chain Constrained Multipolar Refinement



Protein Human Aldose Reductase

0.66 Å resolution

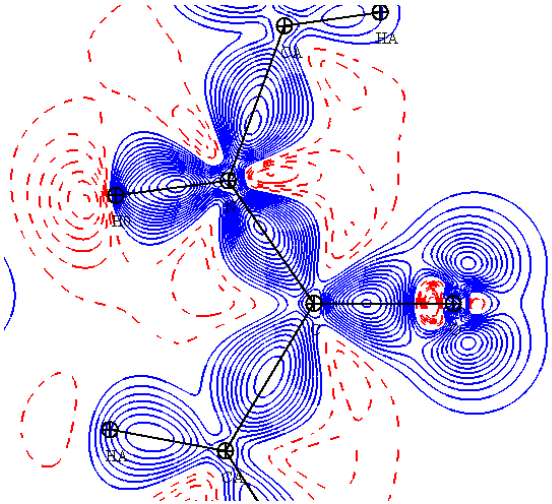
$\Delta\rho$ **contour**

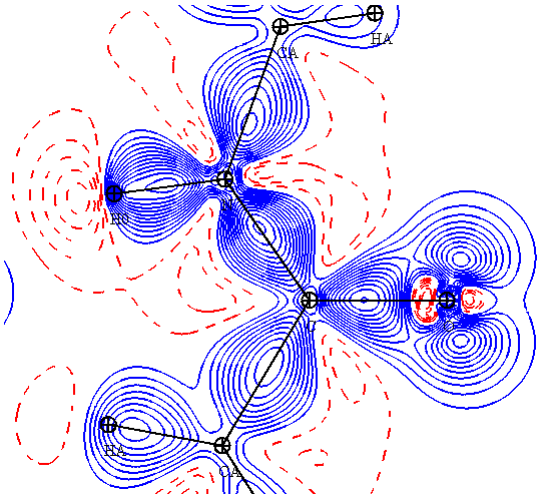
+/- 0.05 e/Å^3

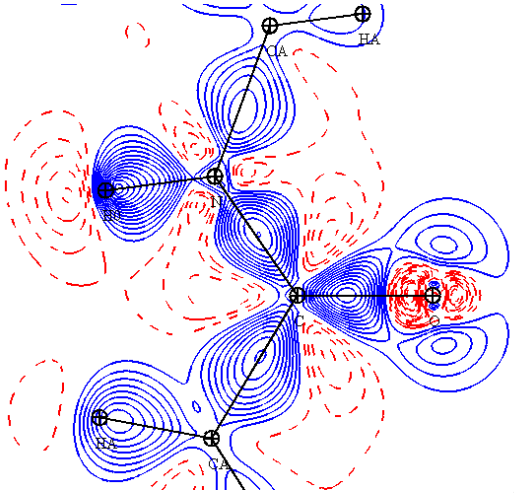
DATABANK TRANSFER

DATABANK TRANSFER + REFINEMENT

REFINEMENT from $\Delta\rho = 0$







Aldose Reductase Statistical Improvement

Transfer, all ordered protein atom, except IDD594

	Spherical	Transfer	Transfer & Refine Constrained Multipoles	Refine
$R(F)$ (%)	9.28	**8.79**	**8.71**	**8.86**
$R_{free}(F)$	9.45	**9.16**	**9.12**	**9.30**

Multipolar refinement

Aldose Reductase

Main Chain Valence Electron populations

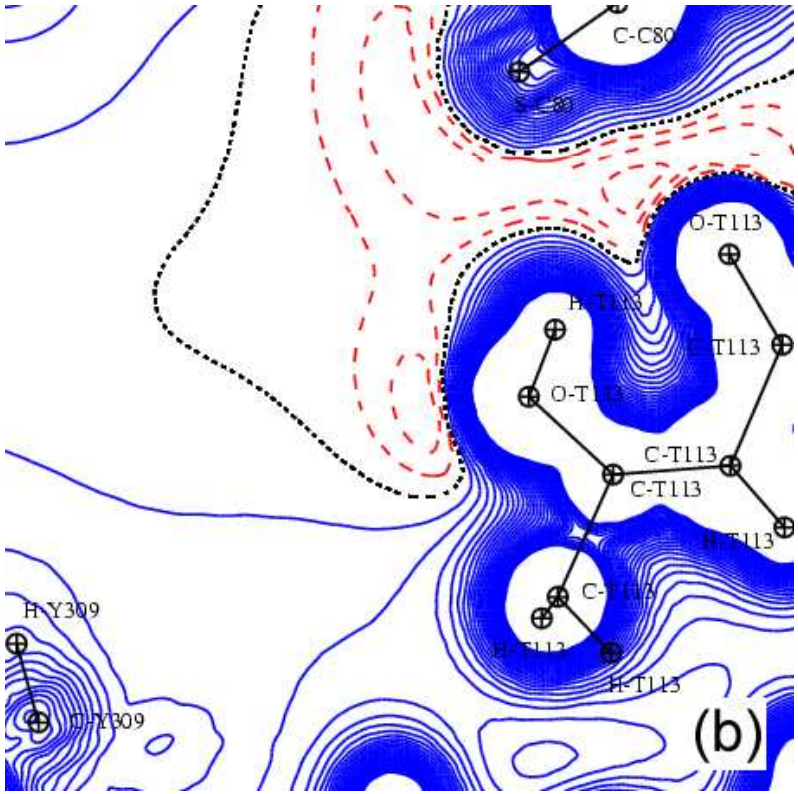
	Transfer	Trf + Ref	Ref
Cα	4.12	4.06(2)	4.02(2)
C	3.89	3.92(2)	3.97(2)
O	6.31	6.30(2)	6.15(2)
N	5.32	5.24(2)	5.09(2)
Hα	0.81	0.89(3)	0.92(3)
H0	0.69	0.76(3)	0.85(3)

Electrostatic potentials : Inhibitor binding

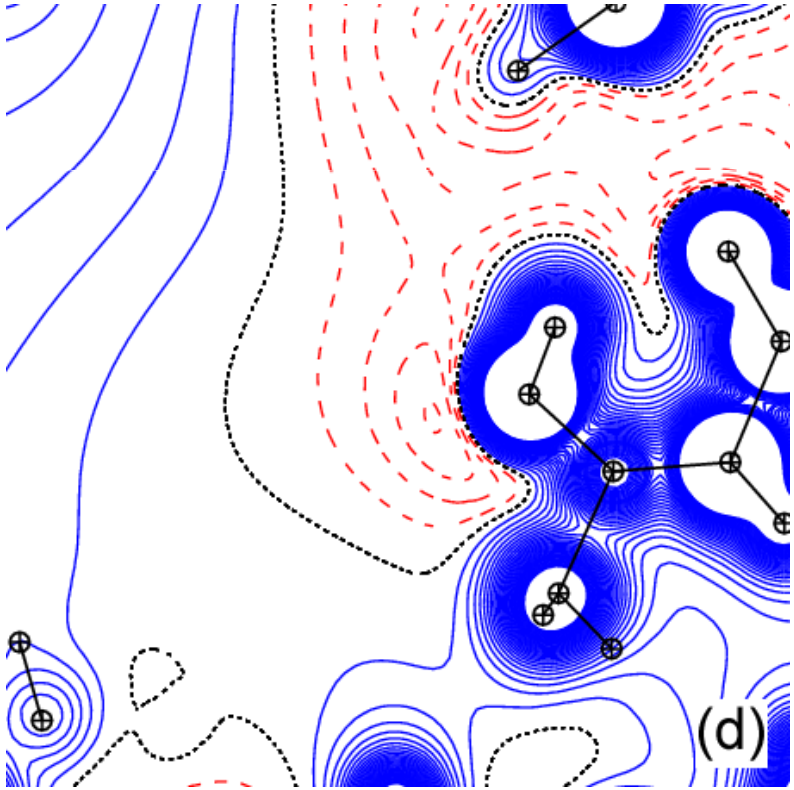
Aldose reductase

Active site Bromine anchor point

DFT



Experimental

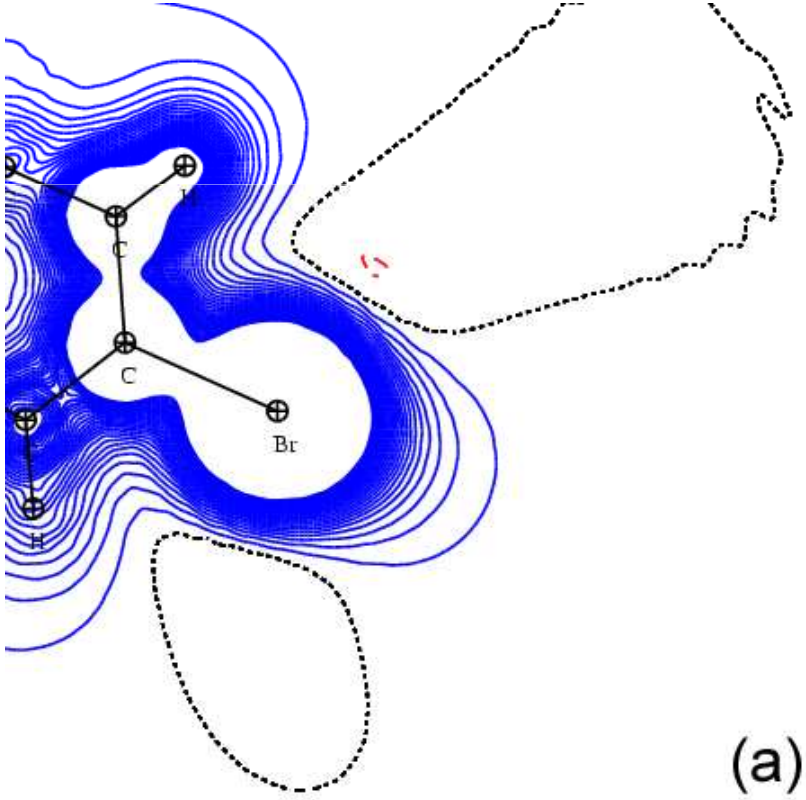


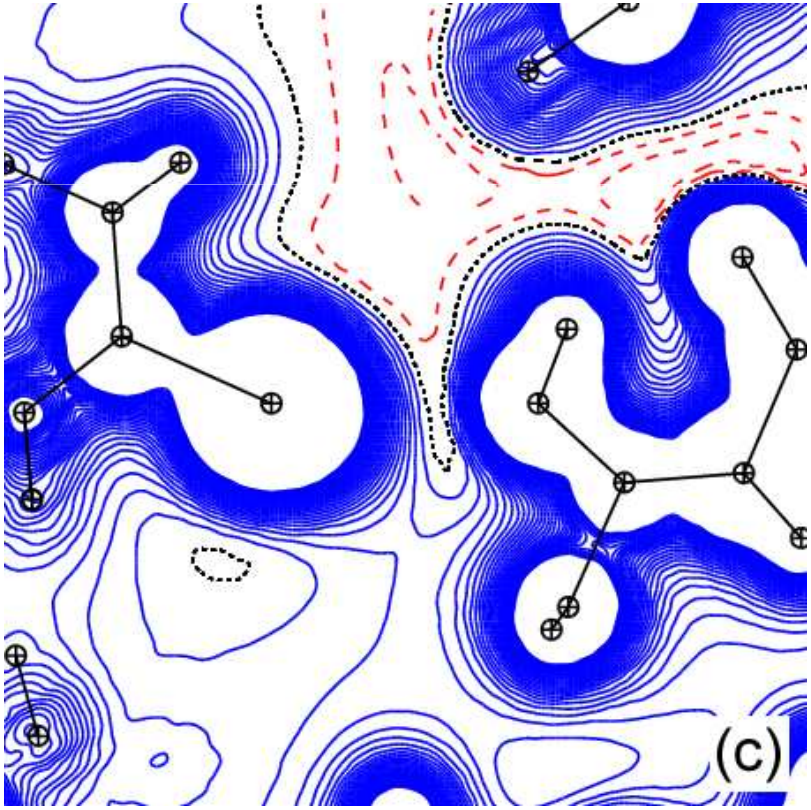
0.05 e.Å^{-1}

Electrostatic potentials : Inhibitor binding

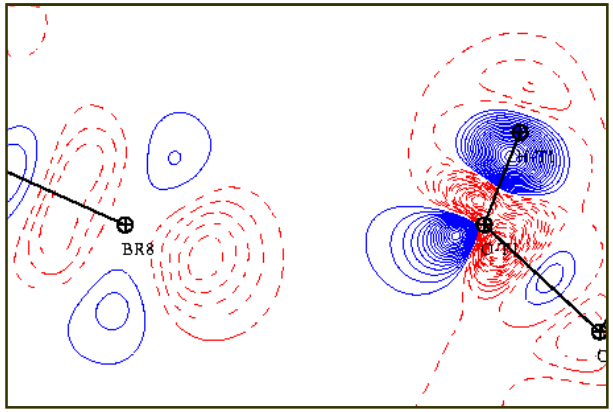
Complex Active site DFT calculation

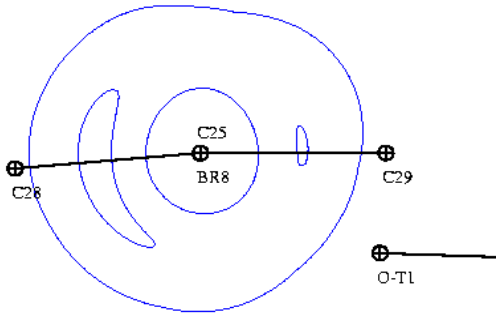
inhibitor : Bromine BR …. Og(THR)



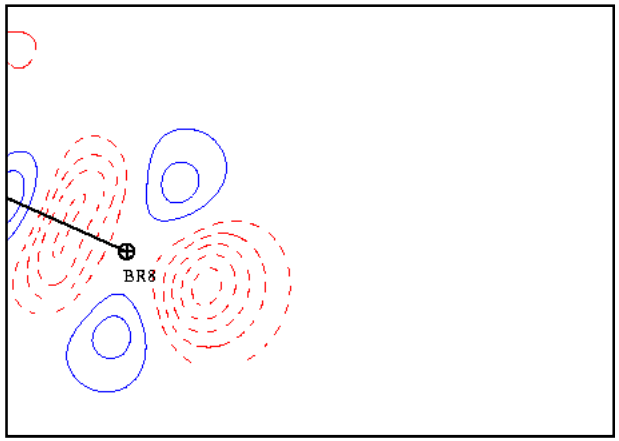


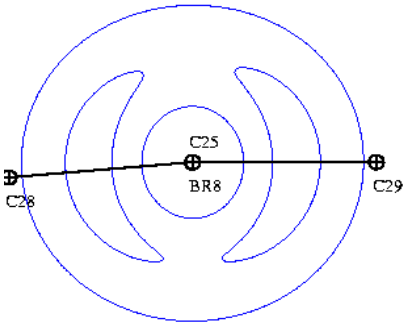
Theoretical Deformation Electron Density DFT



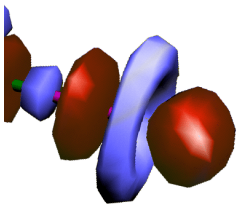


Br…OG1-Thr113
inhibitor aldose reductase NADP+





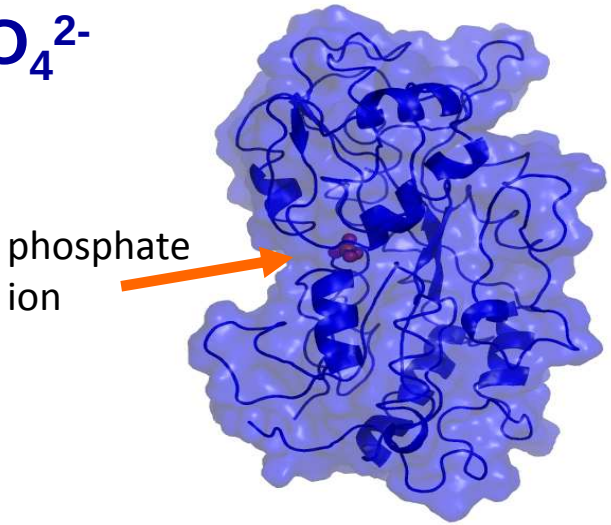
Inhibitor alone

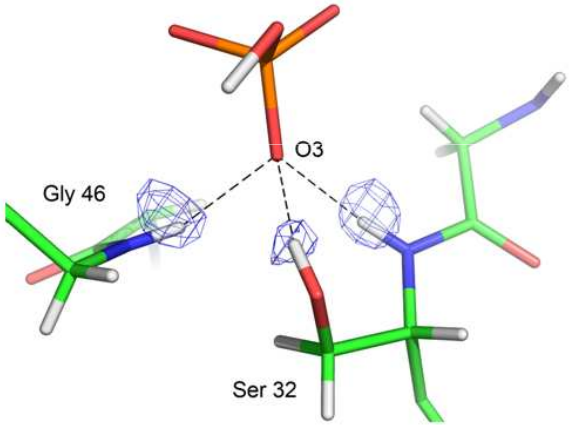


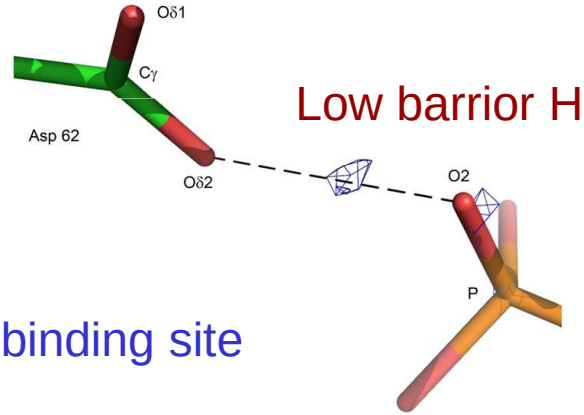
+/ - 0.05 $e^{-}/Å^{3}$

SIESTA software

ELUCIDATION OF PHOSPHATE HPO_4^{2-} BINDING to PfluDING PROTEIN







Low barrior H-bond

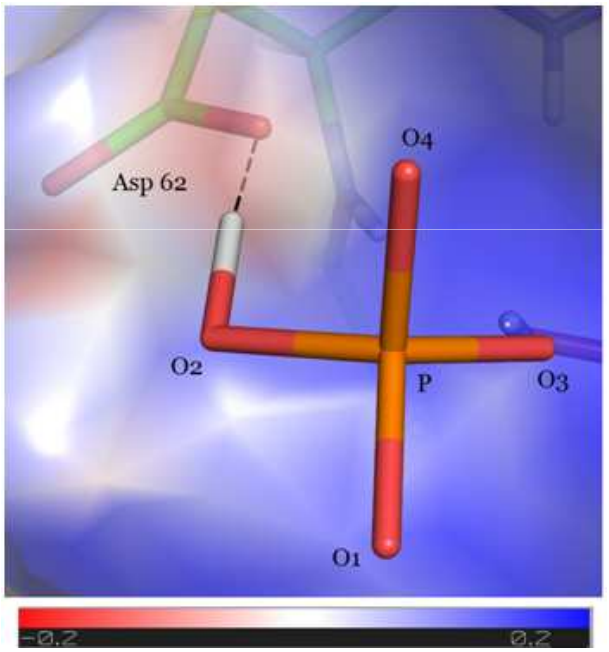
H atoms
Visible in binding site

PfluDING is a bacterial protein isolated from *Pseudomonas fluorescens.*
The three-dimensional structure was obtained at sub-Ångstrom resolution (0.88Å and 0.98Å) at two different pH (4.5 and 8.5).

ELUCIDATION of PHOSPHATE HPO_4^{2-} BINDING to PfluDING PROTEIN

Contrary to previous theories on phosphate binding proteins,
ELMAM multipolar database electrostatic potential calculations show that the binding cleft has a positive electrostatic potential

The PfluDING structures reveal that the protein is specific for the dibasic form of phosphate (notably HPO_4^{2-} vs. SO_4^{2-}).



Electrostatic potential

Liebschner *et al*., JACS, 2009

* Charge density refinement with MoPro

* VMoPro visualisation tool of properties

* Database Transfer

* Application to proteins

*** Electrostatic Interaction Energy**

Electrostatic Interaction Energy

Integration $E_{electrostatic} = \iiint_V \rho_1 \cdot \Phi_2 \cdot dv$

ρ electron density from :

* refinement vs. Xray diffraction data
* refinement vs. theoretical data
* experimental databank transfer
* theoretical databank transfer

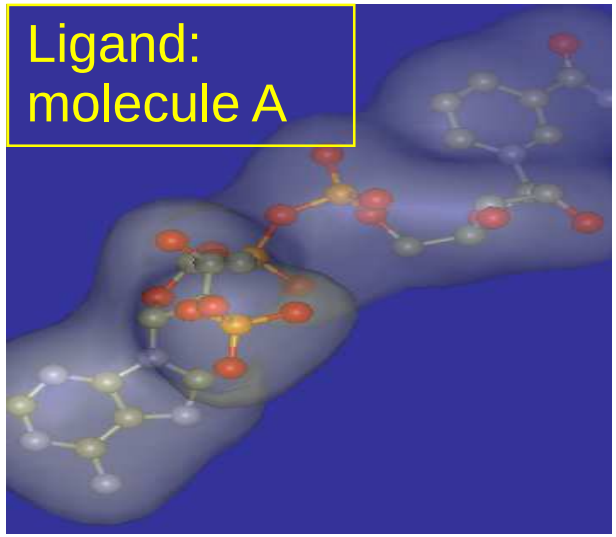
Electrostatic Interaction Energy

(1) $E_{total,\ electrostatic} = \sum_{grid} w_i \cdot \rho_A(\boldsymbol{r}_i) \cdot V_B(\boldsymbol{r}_i)$ **VMoPro**

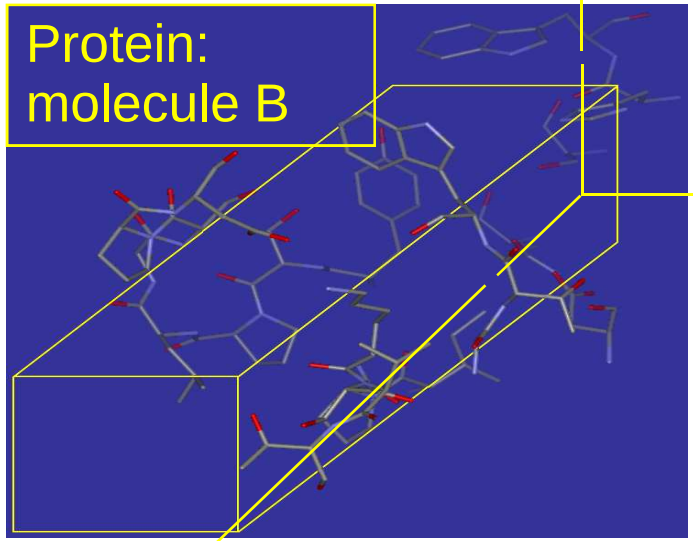
* High Order Numerical Grid Integration (Taylor formulas 5th order)
* Zooming on regions with large variations

(2) SP : spherical integration

(3) BU : spherical integration / Buckingham summation

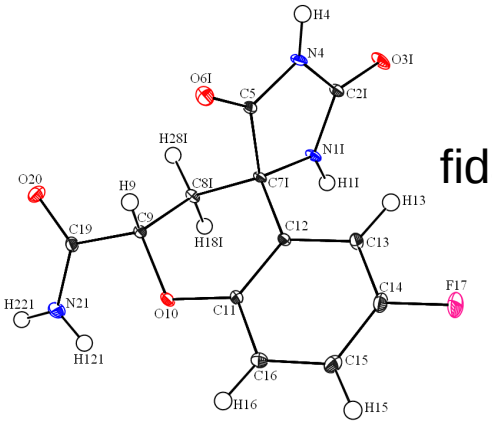


Charge density $\rho_A(\boldsymbol{r})$



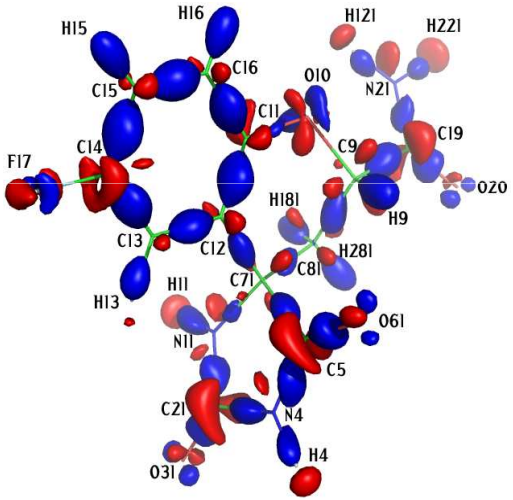
Electrostatic potential $\boldsymbol{V_B(r)}$

Protein / Ligand
Electrostatic interaction energy.

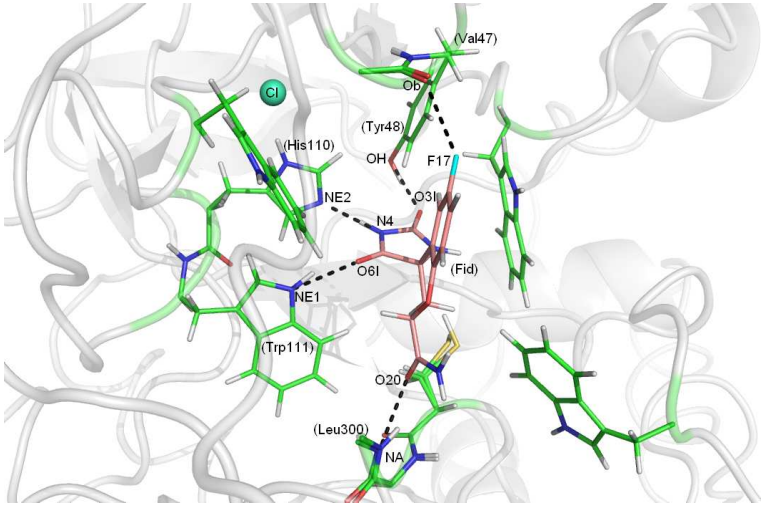


fidarestat

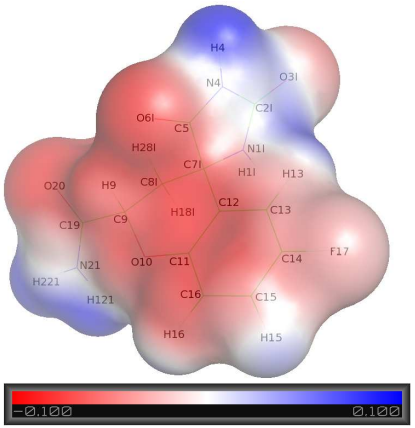
Experimental deformation
electron density
resolution = 0.50 Å



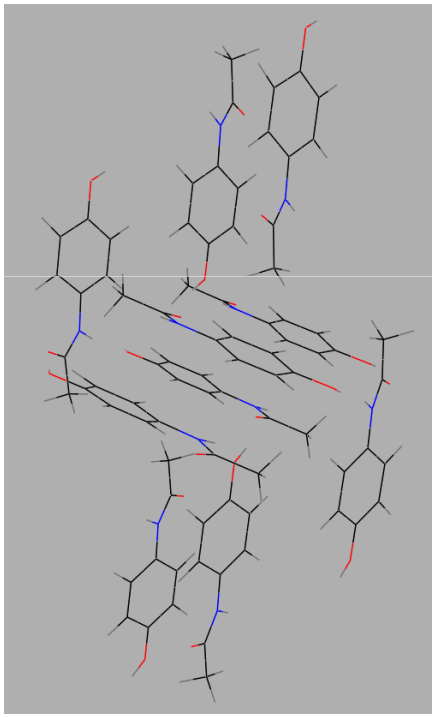
Fidarestat Inhibitor / Human Aldose Reductase



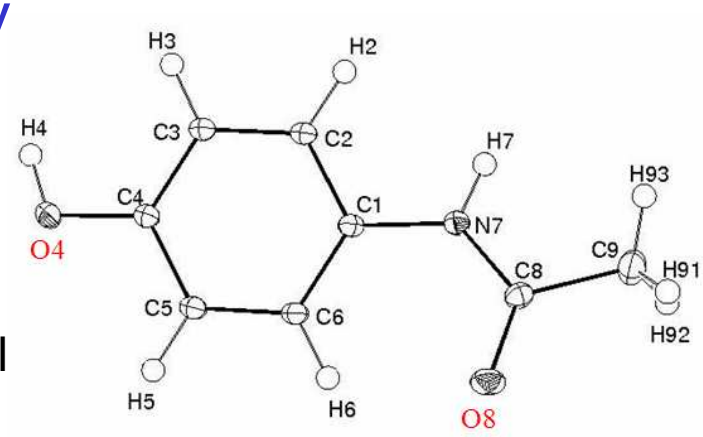
Electrostatic Potential on van der Waals surface



Electrostatic Interaction Energy between dimers in the crystal packing



Paracetamol



Dimer #	Atom 1	Atom 2	Distance (Å)	Symmetry	E_{def} kcal/mol
1	O4	H7	1.9275	X-½ ; -Y+½ ; Z-½	-15.23
	H7	O4	”	X+½ ; -Y+½ ; Z+½	”
2	O8	H4	1.6966	X-½ ; -Y+½ ; Z+½	-11.15
	H4	O8	”	X+½ ; -Y+½ ; Z-½	”
3	H92	O8	2.7062	-X+3/2 ; Y-½ ; -Z+3/2	-9.86
	O8	H92	”	-X+3/2 ; Y+½ ; -Z+3/2	”
4	H92	H4	2.6565	-X+2 ; -Y ; -Z+1 (inv)	-5.69
5	H93	H2	2.5015	-X+5/2 ; Y-½ ; -Z+3/2	-0.32
	H2	H93	”	-X+5/2 ; Y+½ ; -Z+3/2	”
6	H6	H6	2.2263	-X+1 ; -Y ; -Z+1 (inv)	-0.01
7	H5	H4	2.7269	-X+3/2 ; Y-½ ; -Z+½	1.71
	H4	H5	”	-X+3/2 ; Y+½ ; -Z+½	”

Bouhmaida *et al.*
Acta Cryst B 2009

Closest atoms

Tutorial MoPro

1) Database transfer & structure refinement

molecule with diffraction data at usual resolution

2) Charge density refinement

data at ultra high resolution (0.5 Å)

Acknowledgements to MoPro developpers

Angélique Lagoutte

Sophie Alexandre

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Dorothee Liebschner

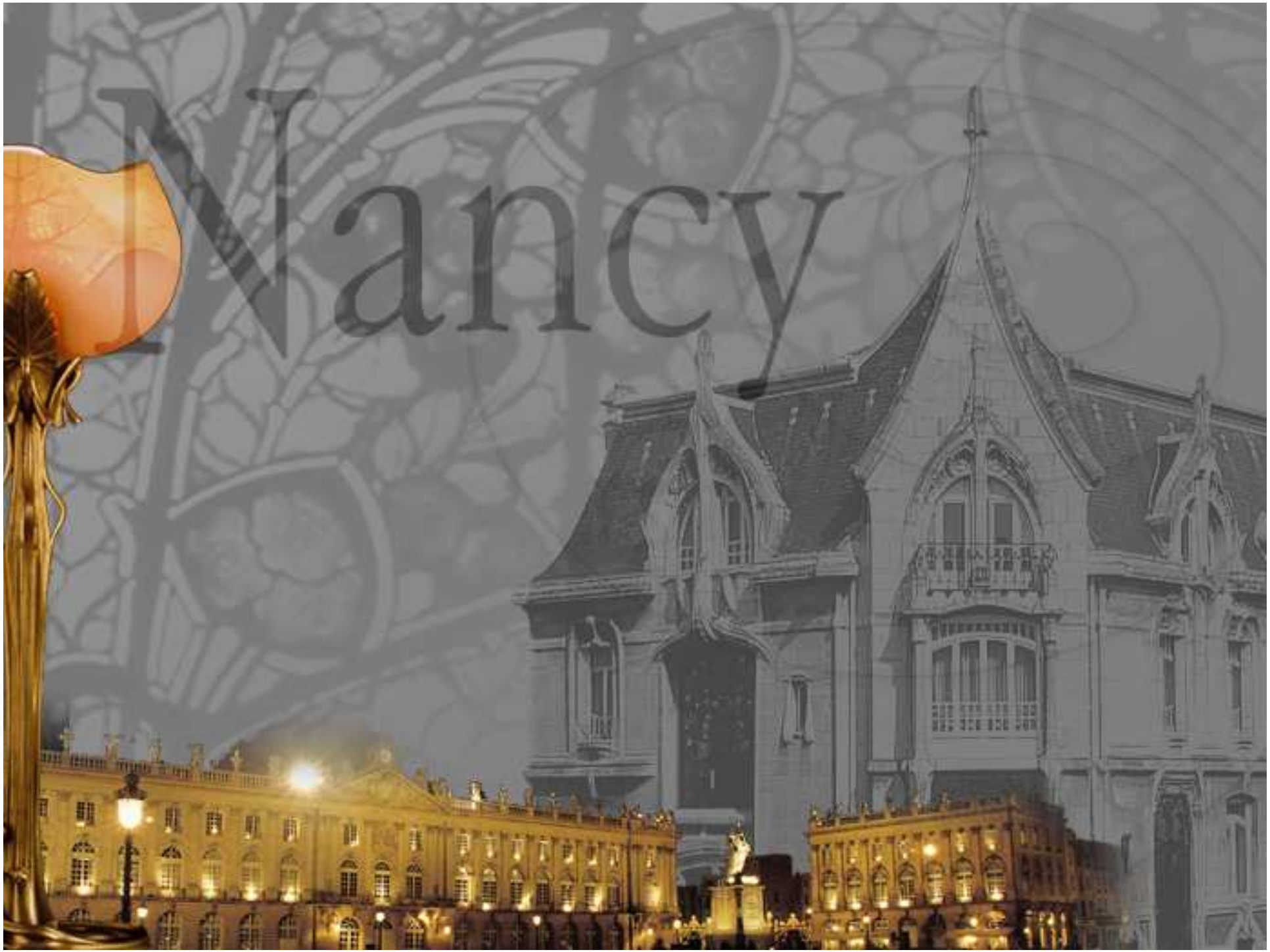
Slawomir Domagala

Ignasi Mata

Benoît Guillot

& students programming MoProGUI

Thanks to the organizers Claude Lecomte & Fernando J. Lahoz


Nancy