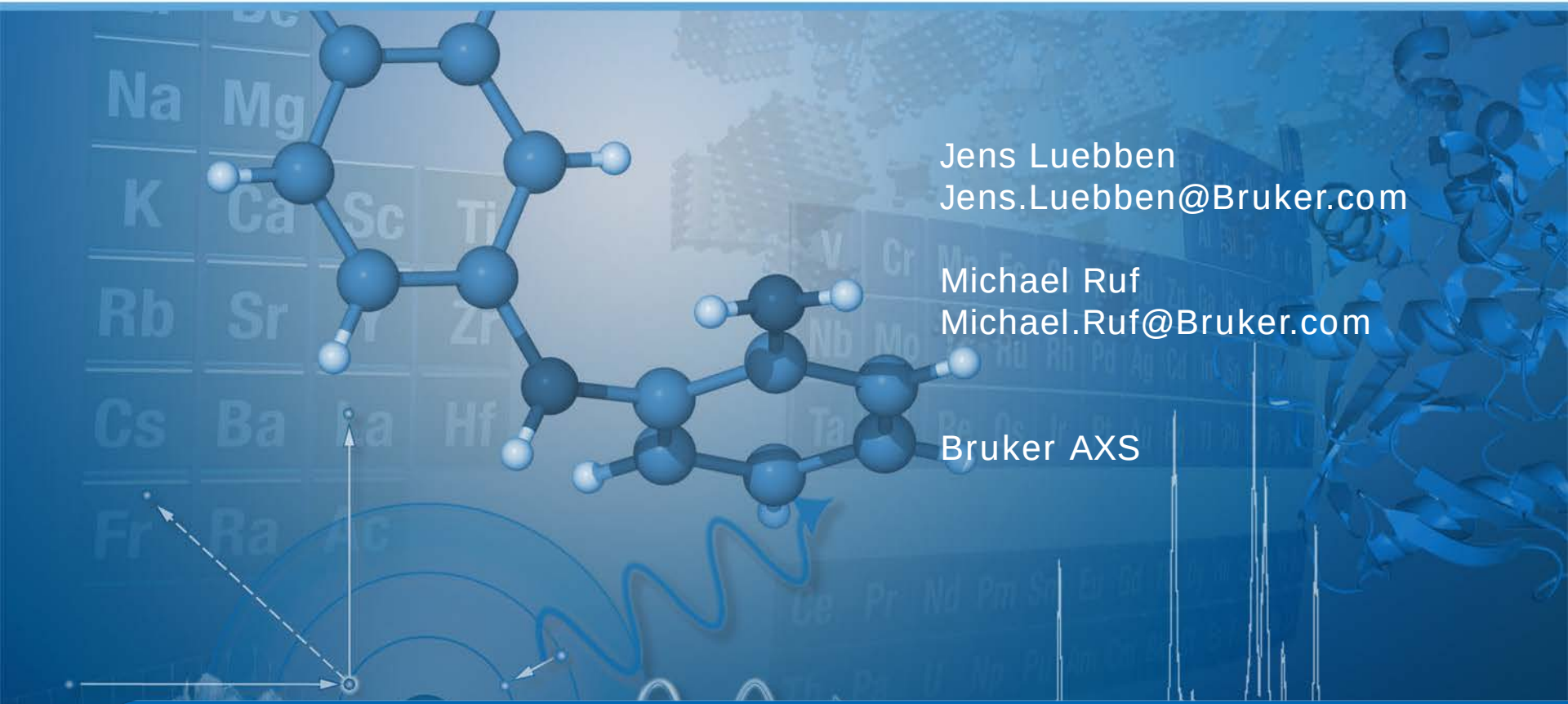
IDEAL - Have the Cake and Eat It Too!



Jens Luebben
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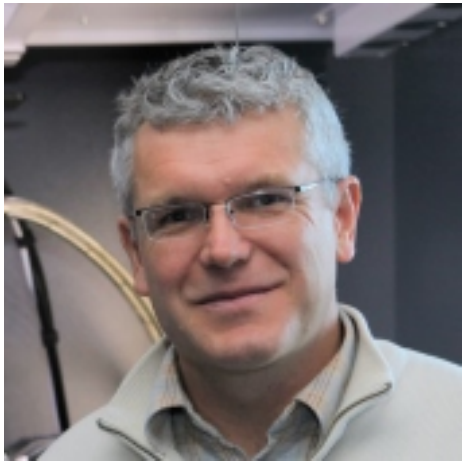
Bruker AXS

IDEAL
(Invariom Derived Electron AnaLysis)

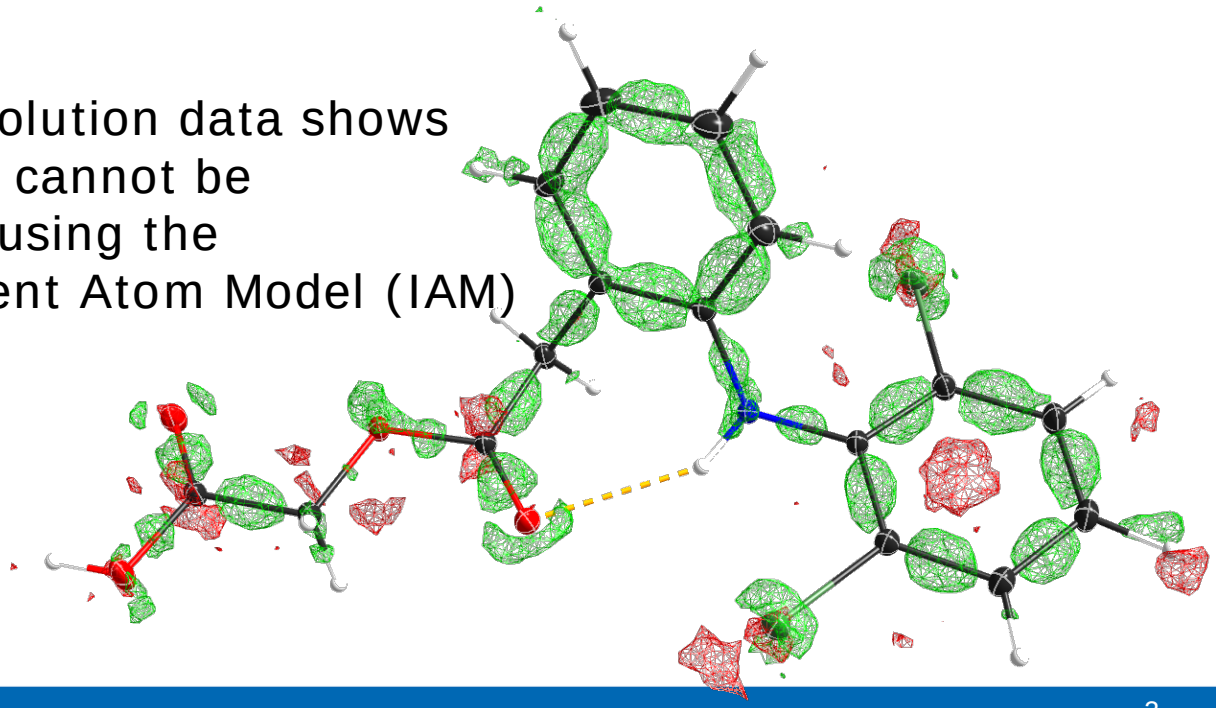
Dr. Jens Lübben
Software Developer
Bruker AXS
Karlsruhe, Germany



Dr. Michael Ruf
SC-XRD Product Manager
Bruker AXS
Madison, WI

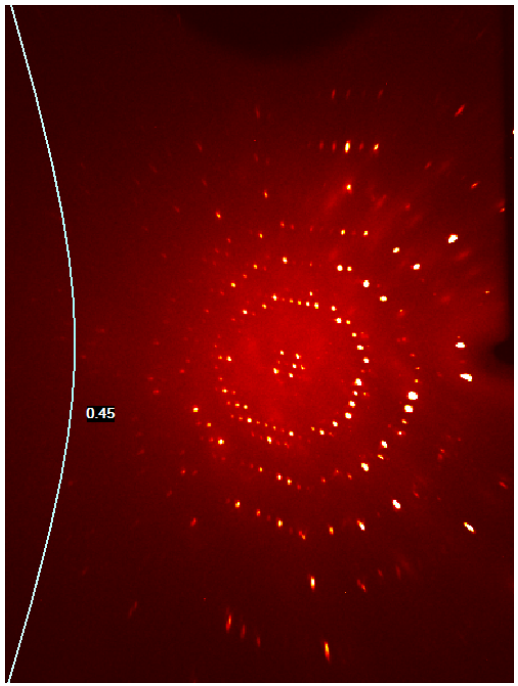
IDEAL - The Premise

- Over the years, data quality has constantly improved with better detectors and better X-ray sources
- Large detectors like the PHOTON II provide high quality high resolution data with one detector setting and short experiment times
- High quality high resolution data shows density features that cannot be sufficiently modeled using the traditional Independent Atom Model (IAM)



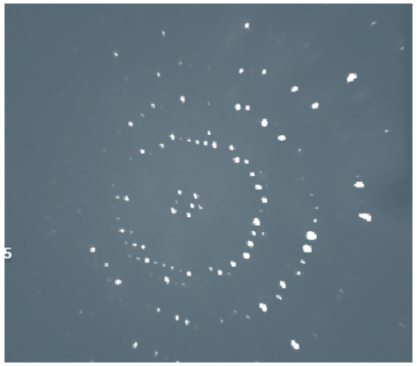
IDEAL - The Premise

- PHOTON II vs HPAD/HPC diffraction pattern
- Collect better quality data to higher resolution in one detector setting with the PHOTON II



PHOTON II

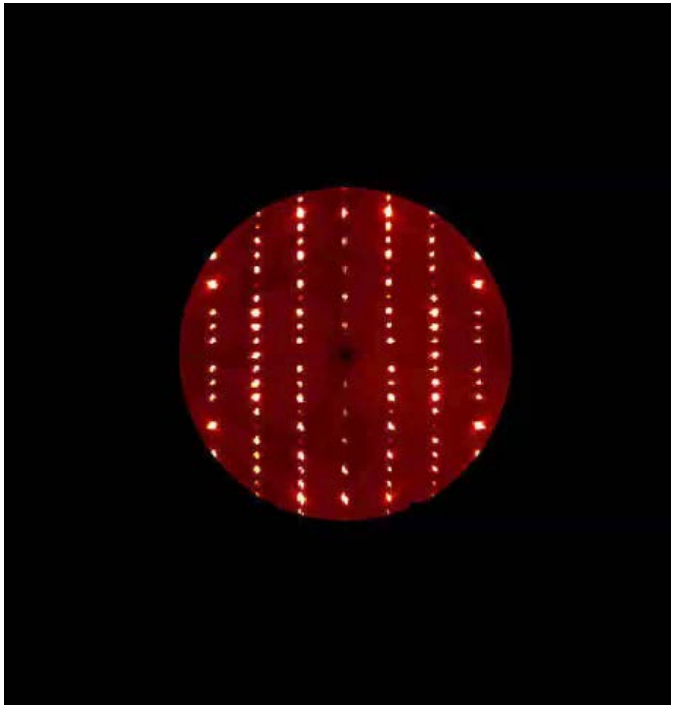
2.4 : 1 size ratio

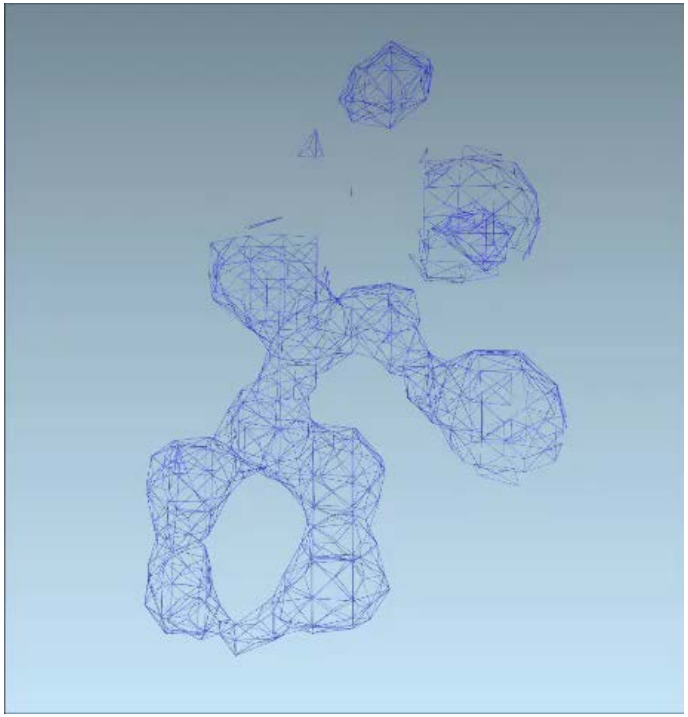


HPAD/HPC

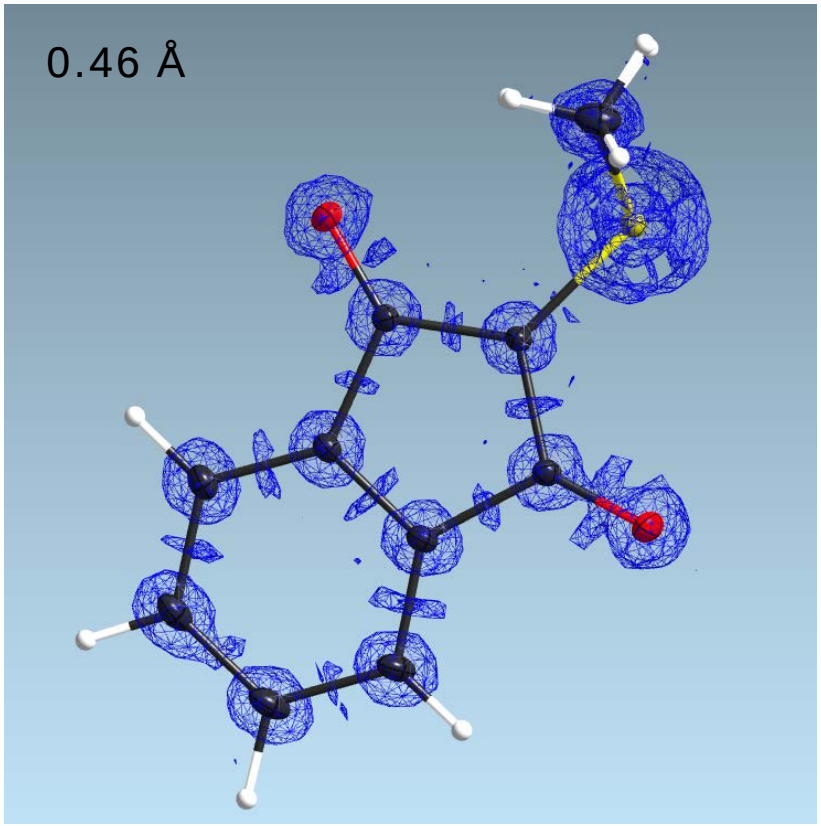
IDEAL - Resolution:
Reciprocal space vs. real space

- Left: Data (reciprocal space) resolution increase in 0.1 Å steps (diffraction angle increases)
- Right: Structure (real space) resolution increases (more detail in density map)

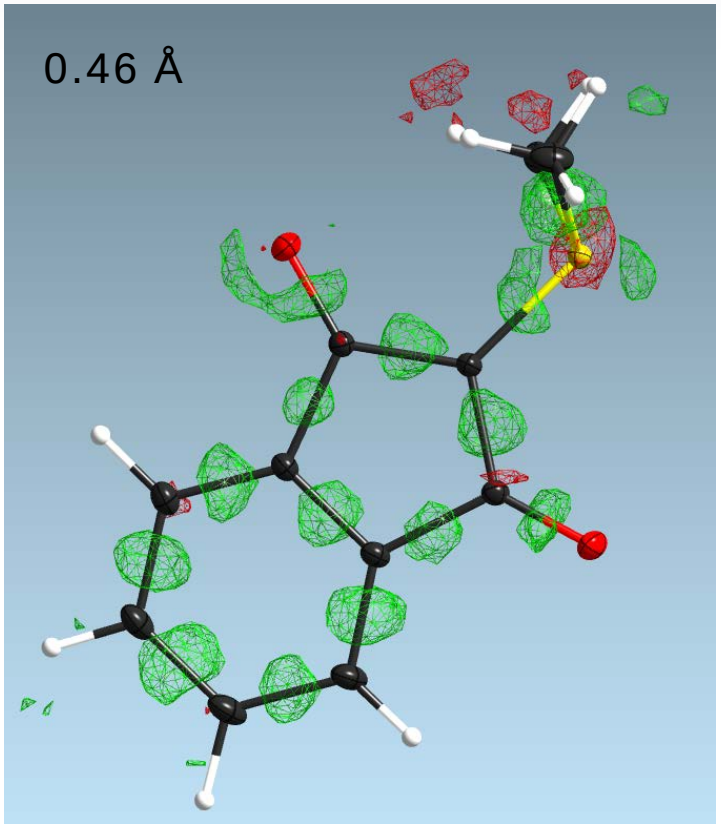




IDEAL - High Resolution Data



“Observed” electron density



Residual electron density

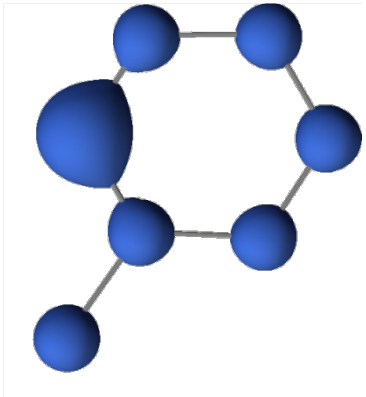
The Independent Atom Model (IAM) vs The Multipole Model

- Independent Atom Model
  - The atoms are regarded to be independent
  - The determined atom position and the displacement parameters can solely count for the right atom type at the correct lattice position with the right site occupation factor
  - It does not account for the interatomic region
  - IAM does NOT describe bonds, lone pairs, charges, charge transfer effects, …

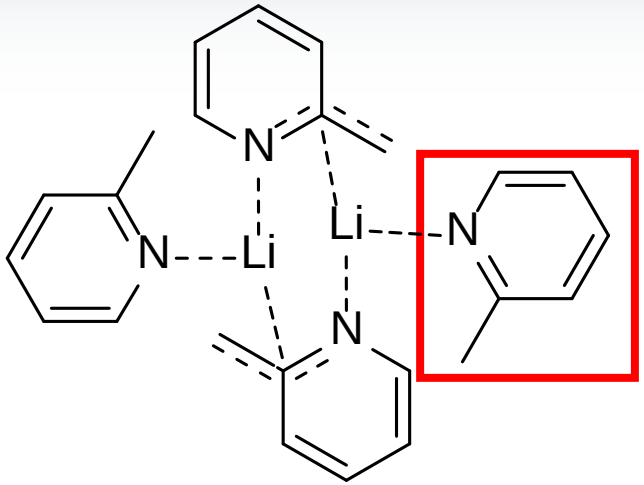
- Multipole Model
  - It models the interatomic area, the most important feature, the chemical bond
  - It assigns the gross charge density to spherical harmonics, the so-called multipoles
  - For example a dipole along the interatomic vector can account for the bond charge density

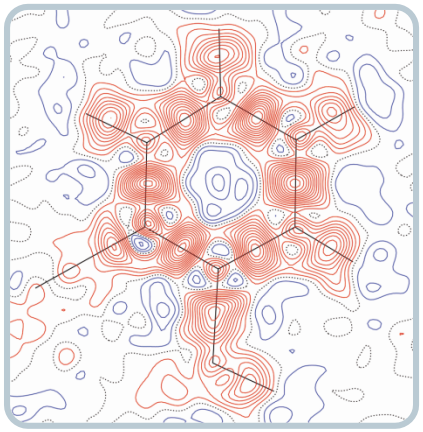
IAM vs. MM

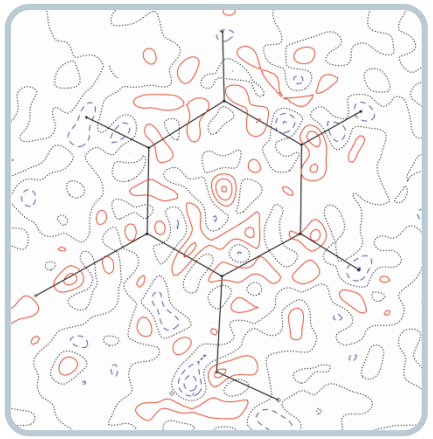
IAM



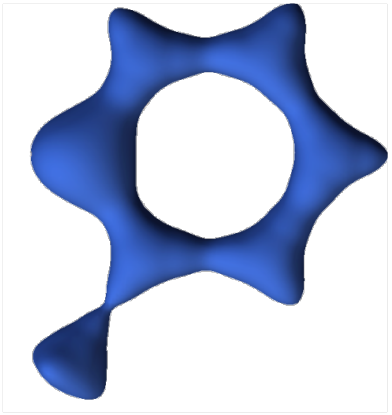
Electron Density







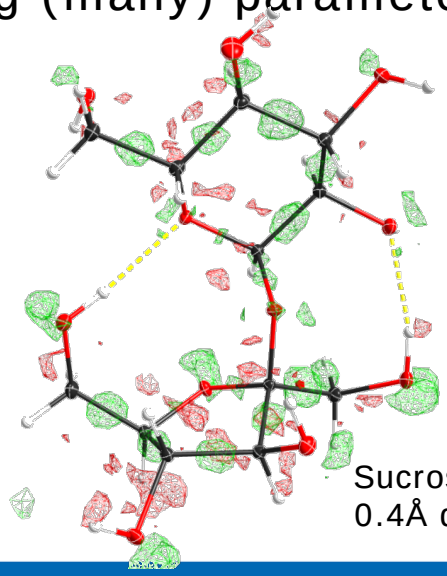
Improved Model



Electron Density

IDEAL – The Solution

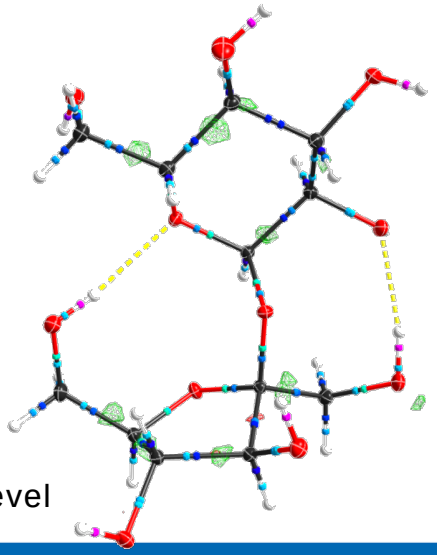
- Add bond-oriented deformation density to the Independent Atom Model (IAM) to more accurately model density
- Create a version of XL that can refine Bond Electron Density as well as Lone Pair Electron Density
- Deliver not only better data, but also better structures without adding (many) parameters



R1 = 1.84%

⇩

R1 = 1.43%



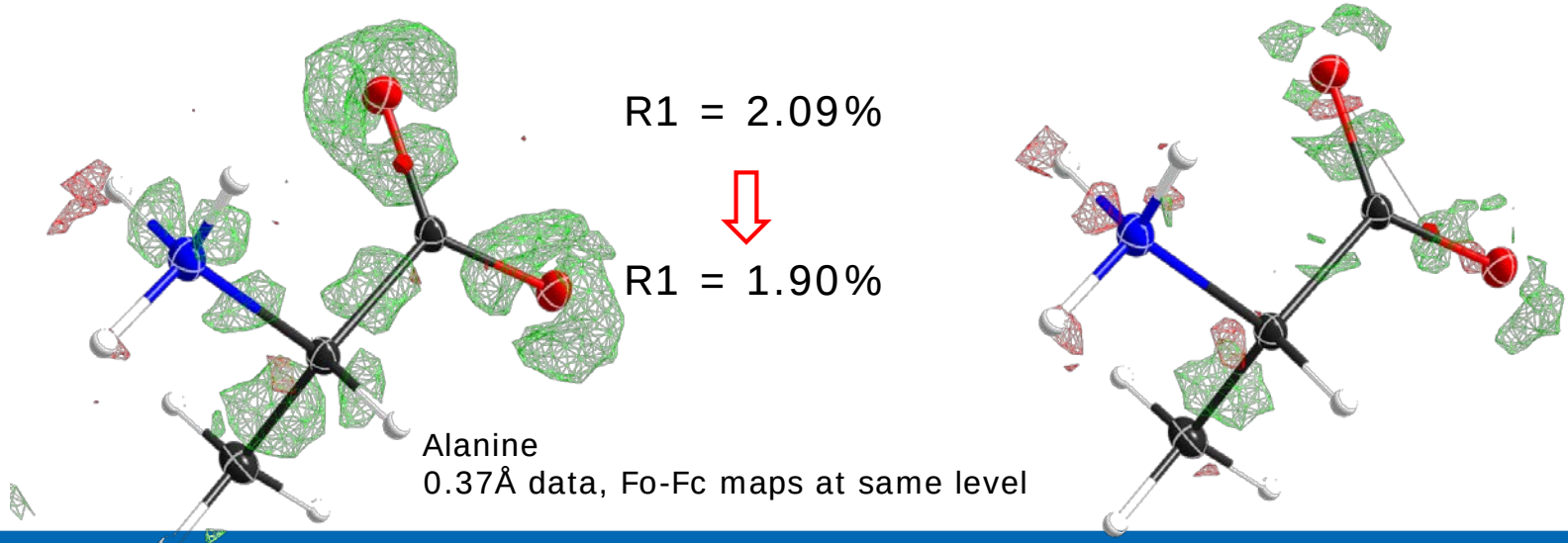
Sucrose
0.4Å data, Fo-Fc maps at same level

IDEAL – The Implementation

- BEDE and LONE instructions were added to XL. BEDE adds bond electron density and LONE adds Lone pair electron density – George Sheldrick

- Database of bond-oriented deformation density parameters from the Invariom database of *ab initio* calculations of model compounds

- GUI implementation



Alanine
0.37Å data, Fo-Fc maps at same level

IDEAL – The Implementation

- Adding Gaussian shaped densities on bonds and subtracting this density by a different Gaussian of the same height from the bonded atoms

- Adding a Gaussian shaped density at lone pair positions and subtracting the density from the atom they belong to

- Instructions with fixed values parameterized for model compounds from the Invariom database

Syntax:

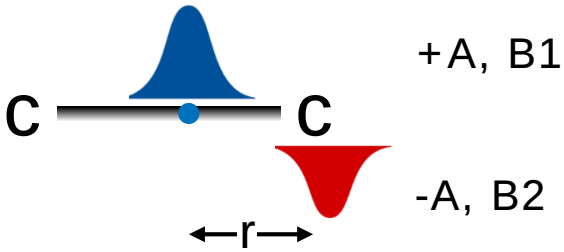
BEDE atom1 atom2 r A B1 B2

LONE m atom1 r A B1 B2
m is analogous to AFIX m

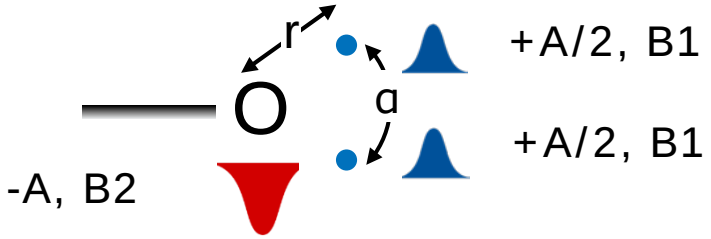
For f(x) = ± A $e^{(-B1,2(\sin(\frac{\Theta}{\lambda})^2)}$
B1 for +A, B2 for -A

IDEAL – The Implementation

BEDE



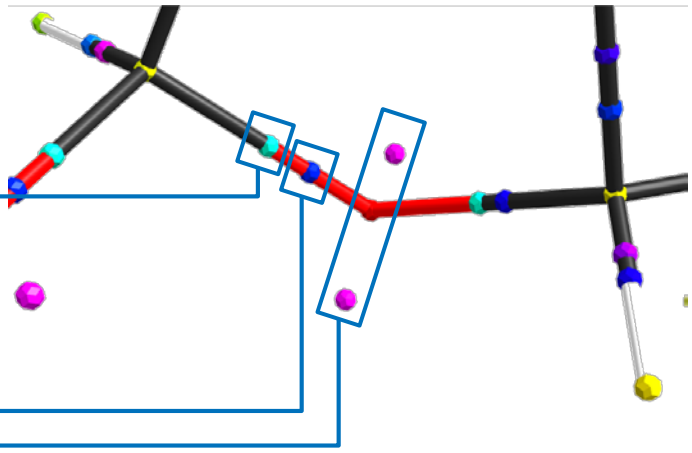
LONE



- Example

```
!ATOM C13!
!INVARIOMNAME C1o1o1c1h_0!
BEDE C13 H13 0.370 20.878 30.423 40.540
BEDE C13 O1 1.016 20.484 30.552 40.540
BEDE C13 O3 1.008 20.484 30.552 40.540
BEDE C13 C14 1.070 20.505 30.340 40.540

!ATOM O3!
!INVARIOMNAME 3-O#3c[#3c1c1h]#3c[#3c1c1h]_0!
BEDE O3 C13 0.672 20.108 30.442 40.558
BEDE O3 C16 0.683 20.108 30.442 40.558
LONE O3 2 21.070 30.321 40.558 0.482 137.60
```



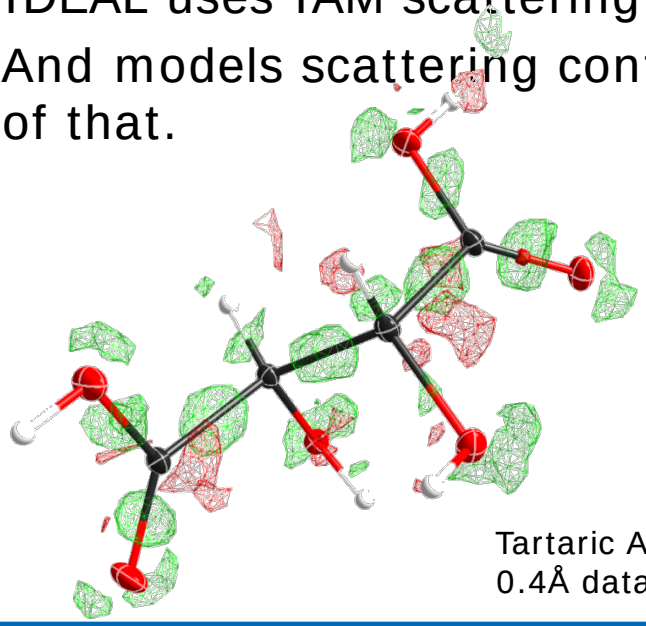
IDEAL –The Theory

- **Invarioms** are aspherical atomic scattering factors that enable structure refinement of more accurate and more precise geometries than refinements with the conventional independent atom model (IAM).
- The use of single-crystal X-ray diffraction data of a resolution better than $\sin\theta/\lambda = 0.6\ \text{Å}^{-1}$ (or $d = 0.83$ Å) is recommended.
- The invariom scattering-factor database contains transferable pseudoatom parameters of the Hansen–Coppens multipole model and associated local atomic coordinate systems.
- Parameters were derived from geometry optimizations of suitable model compounds, whose IUPAC names are also contained in the database.
- With over 2750 entries it now covers a wide sample of general organic chemistry

The generalized invariom database (GID)
B. Dittrich,[a*] C. B. Hübschle,[a] K. Pröpper,[a] F. Dietrich,[a] T. Stolper[a] and J. J. Holstein[a]

IDEAL –What's different

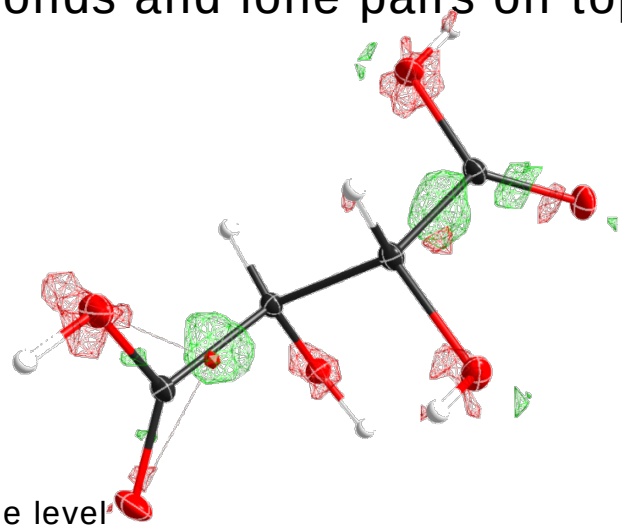
- Invarioms assemble a molecule's scattering characteristics atom by atom
- Invarioms replace IAM scattering factors and describe bonds by superimposing atomic scattering factors
- IDEAL uses IAM scattering factors
- And models scattering contributions of bonds and lone pairs on top of that.



R1 = 1.62%

⇩

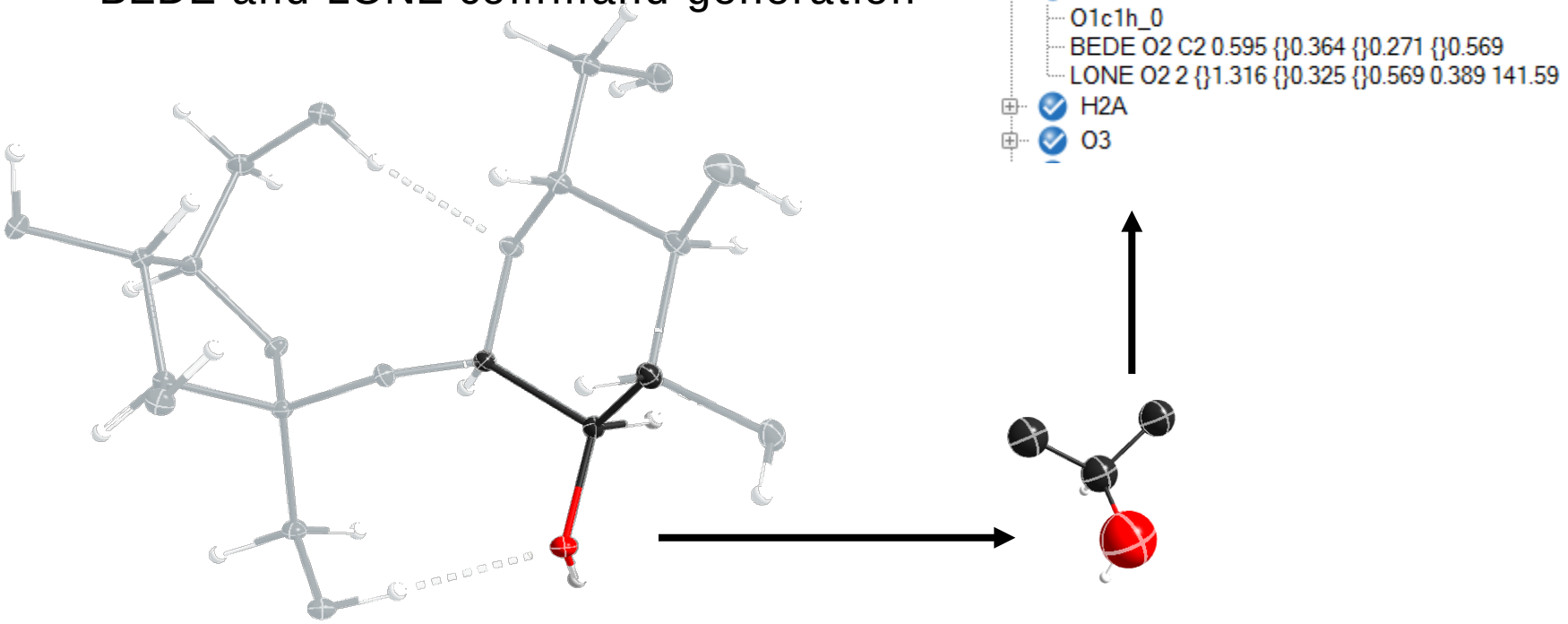
R1 = 1.41%



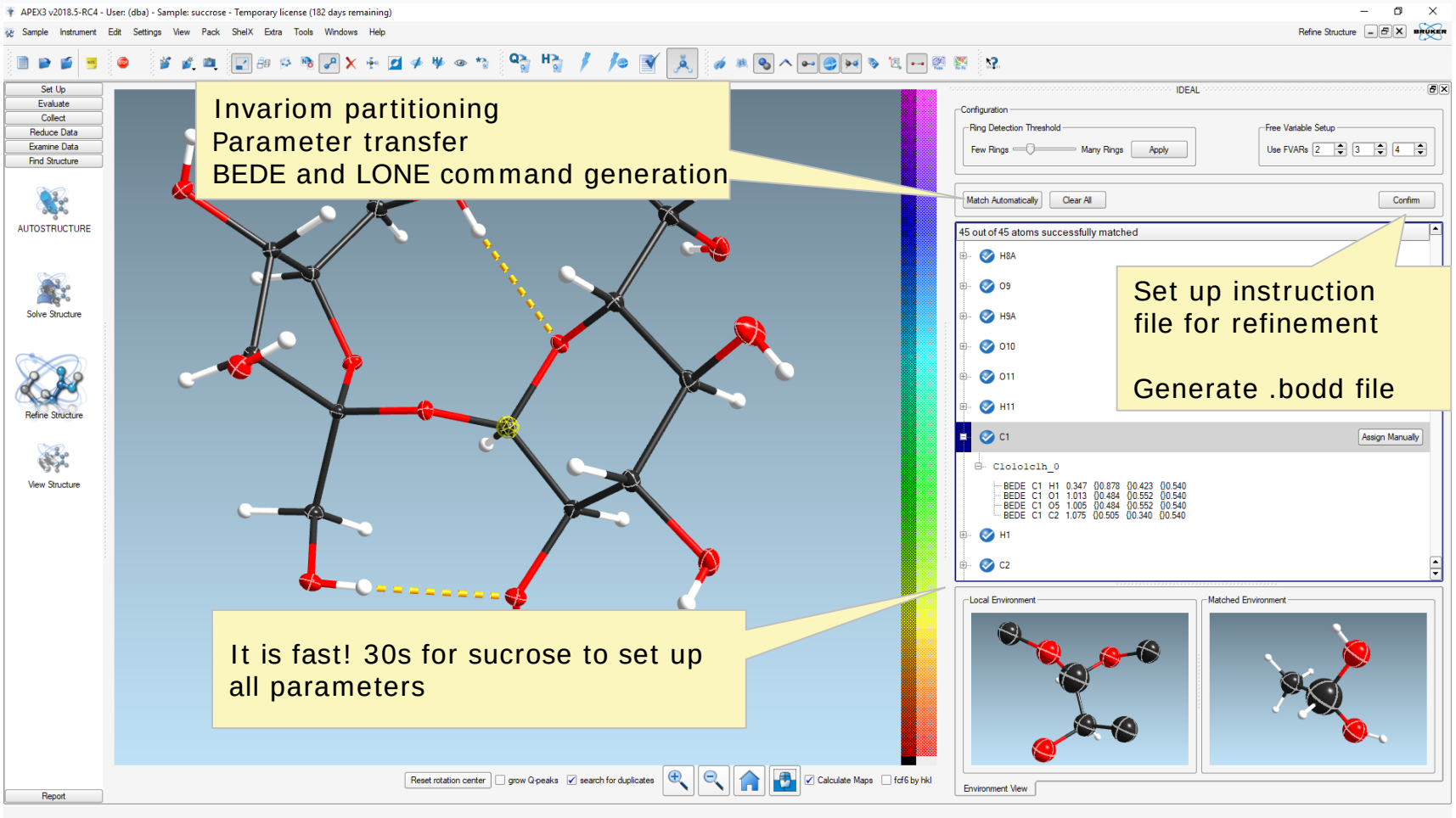
Tartaric Acid
0.4Å data, Fo-Fc maps at same level

IDEAL –The GUI

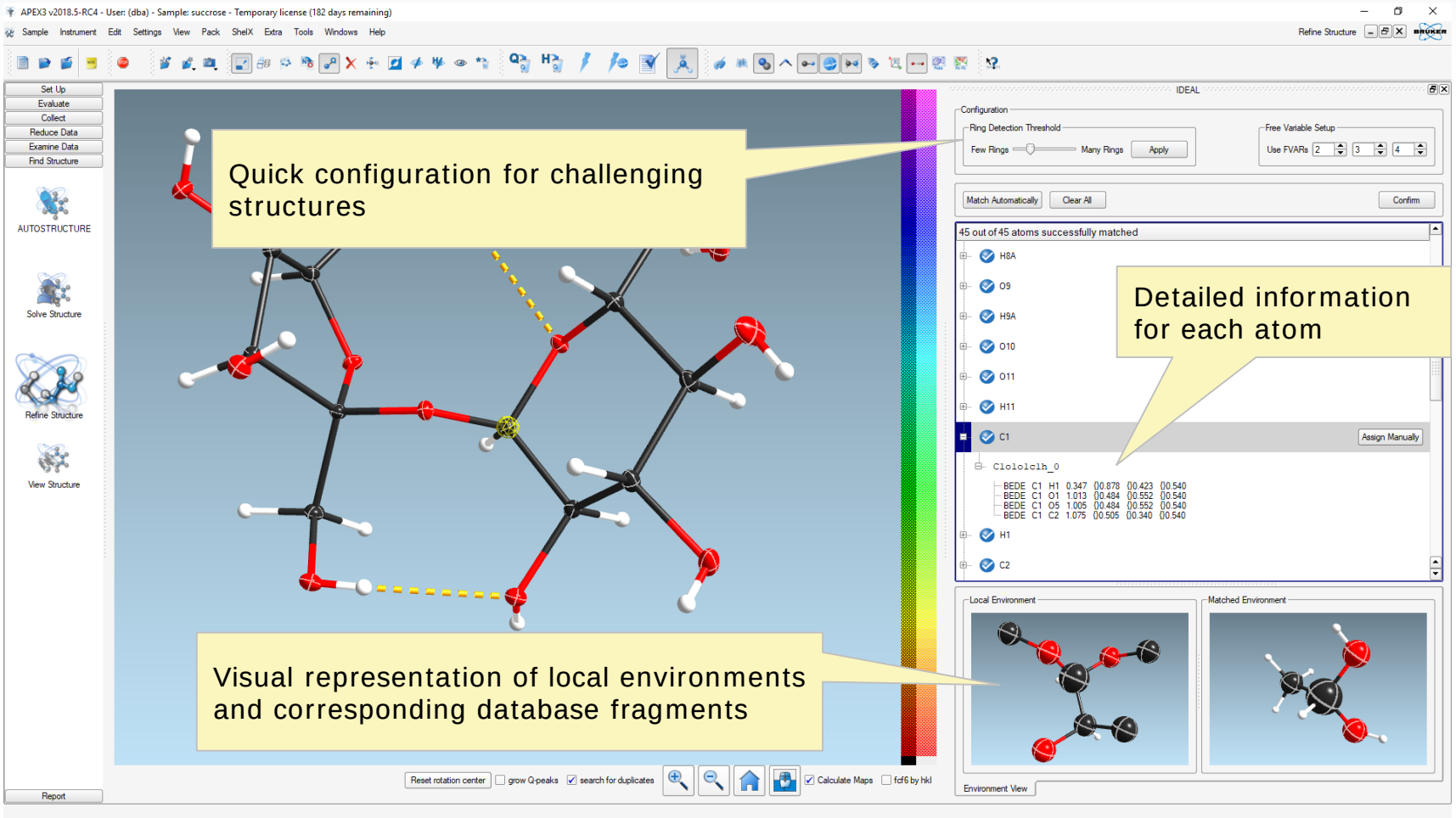
- Invariom partitioning
- Parameter transfer
- BEDE and LONE command generation



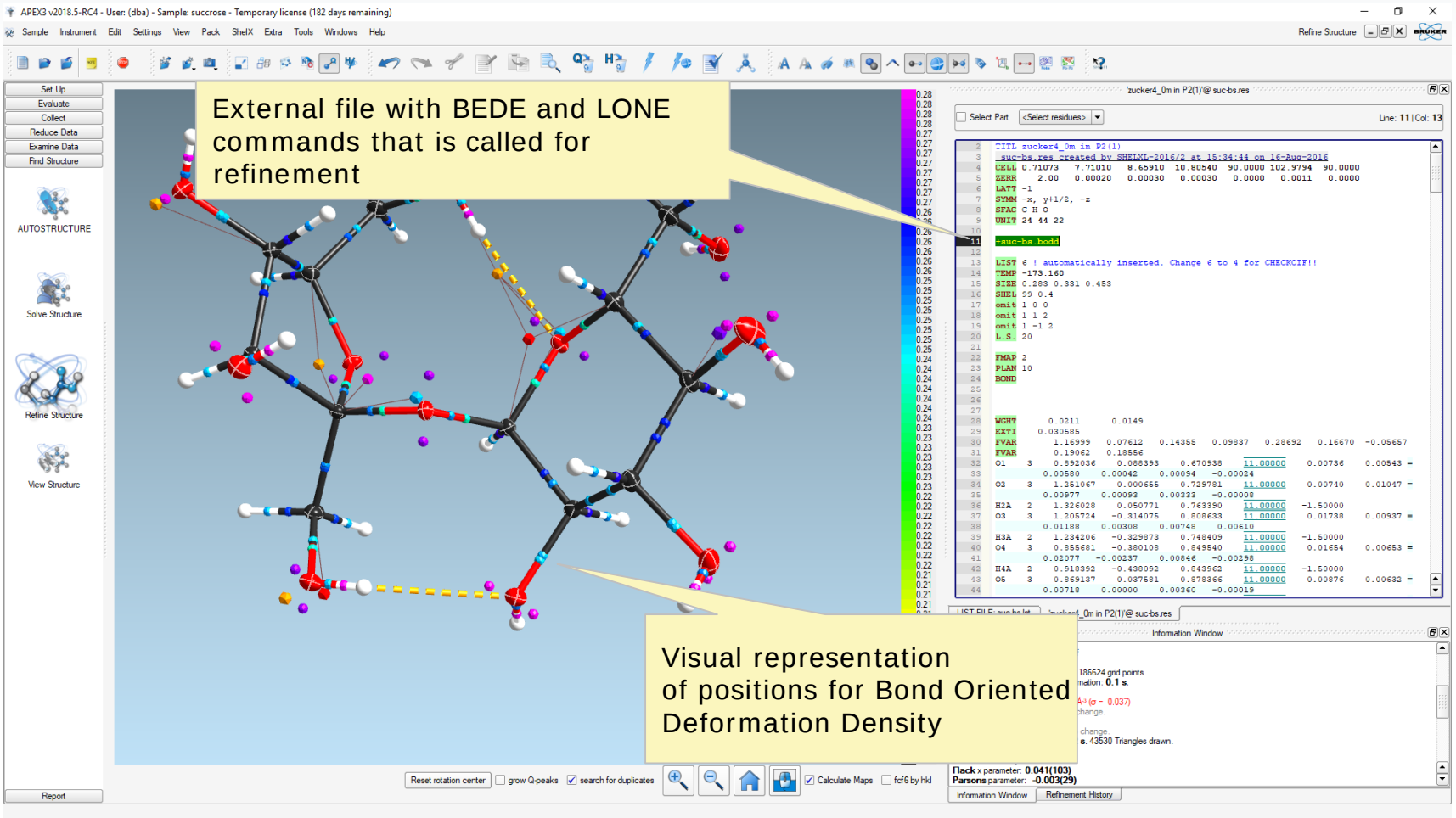
IDEAL –The GUI



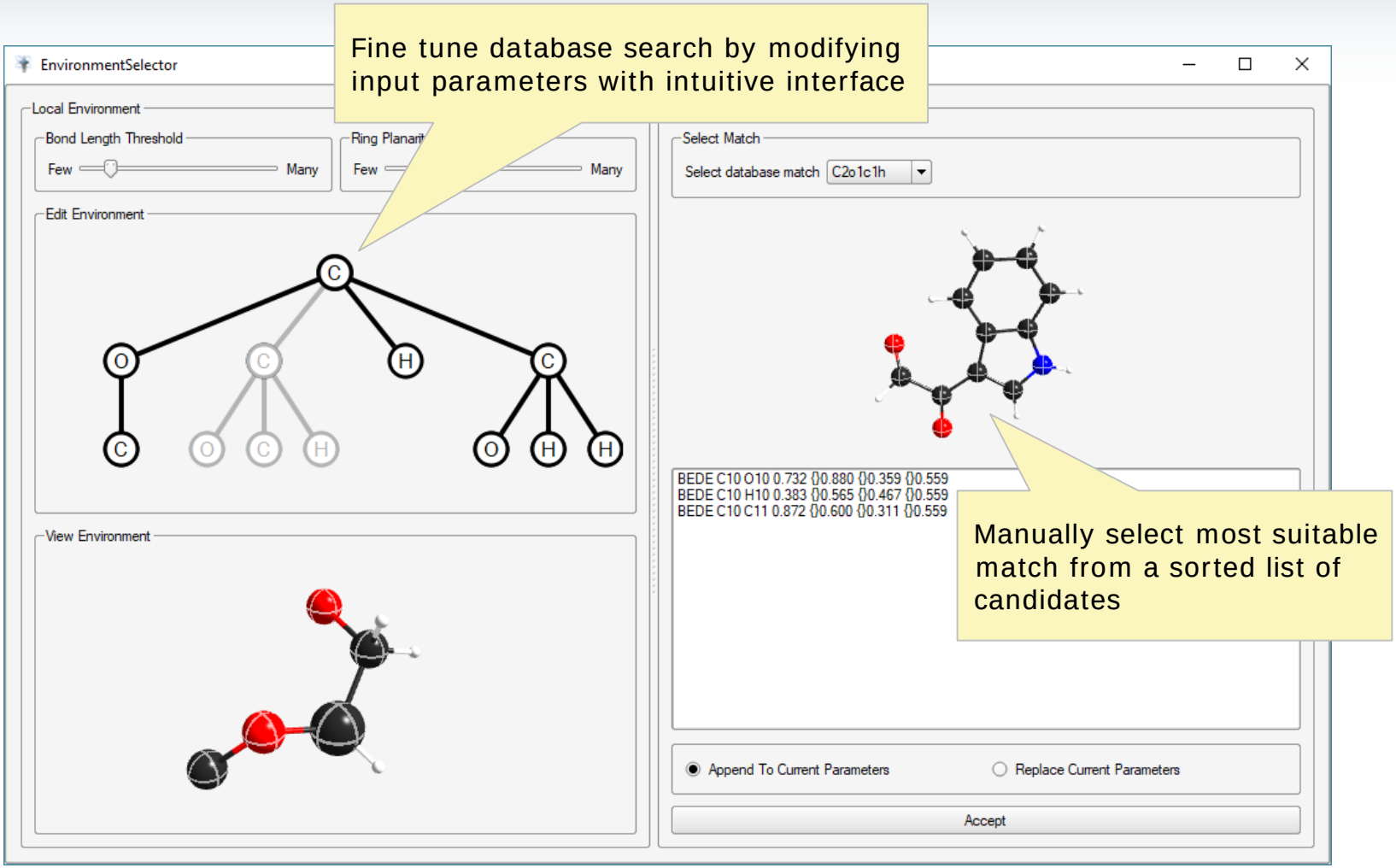
IDEAL –The GUI



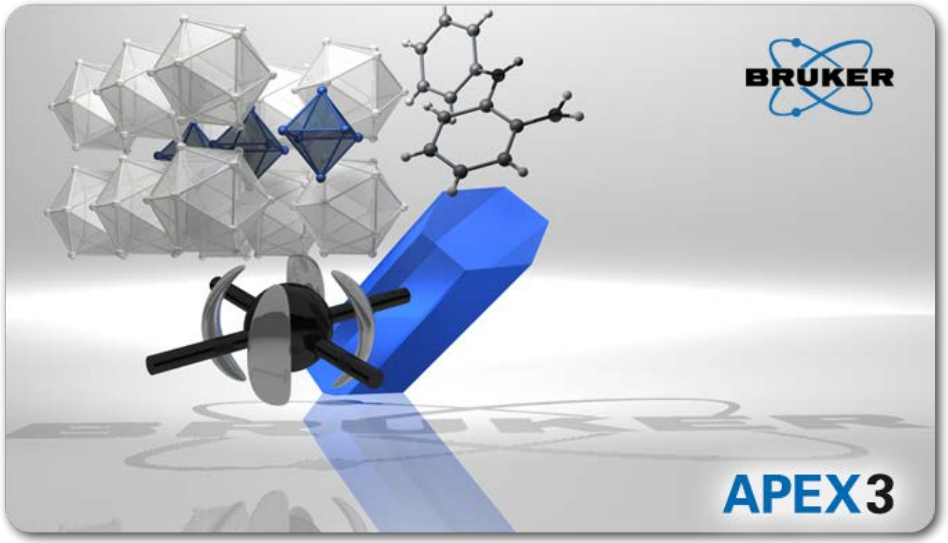
IDEAL–The GUI



IDEAL–The GUI

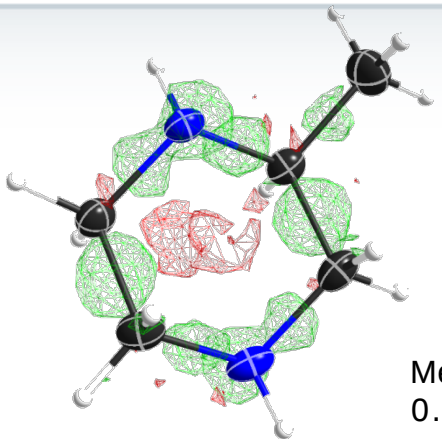


APEX3 – Live Demo



- Live Demo of IDEAL in APEX3
- Bispyrazolone

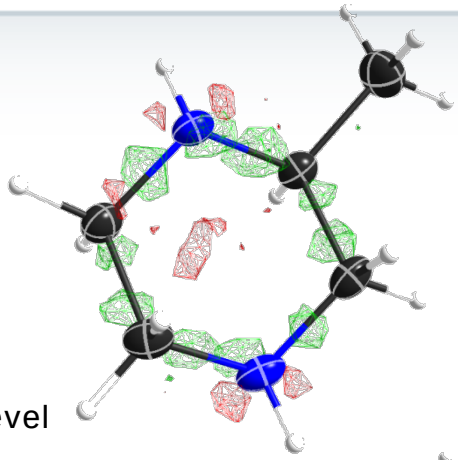
IDEAL - More Examples 1



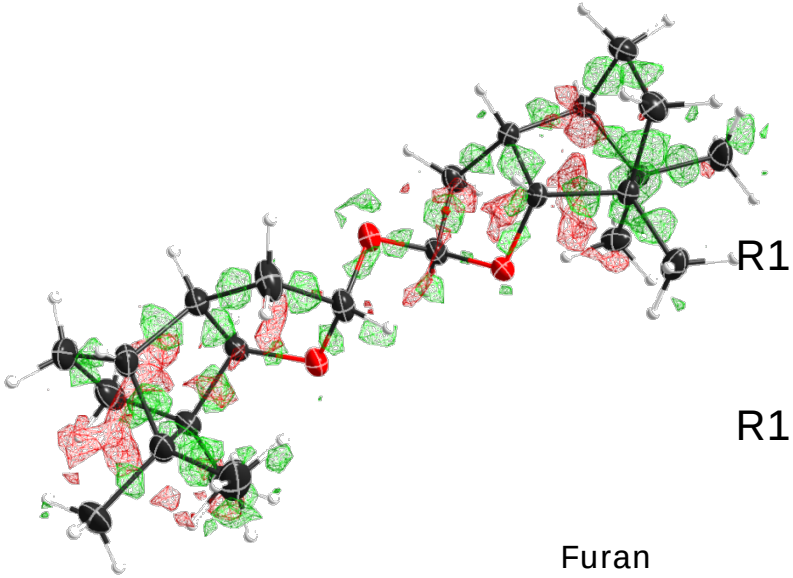
R1 = 2.72%

⇩

R1 = 2.35%



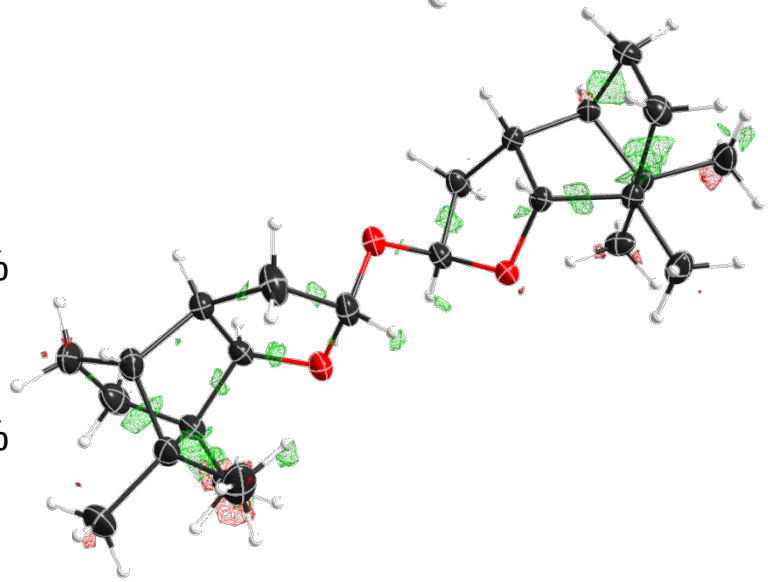
Methyl-Piperazine
0.5Å data, Fo-Fc maps at same level



R1 = 3.00%

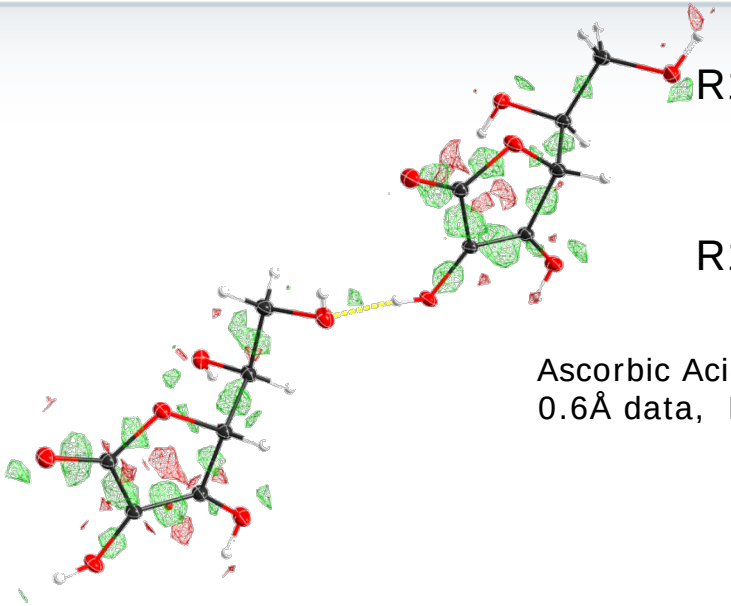
⇩

R1 = 2.51%



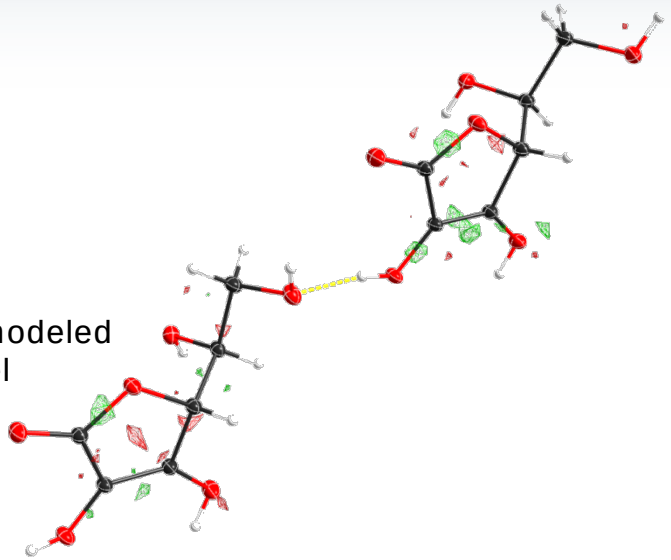
Furan
0.55Å data, Fo-Fc maps at same level

IDEAL - More Examples 2

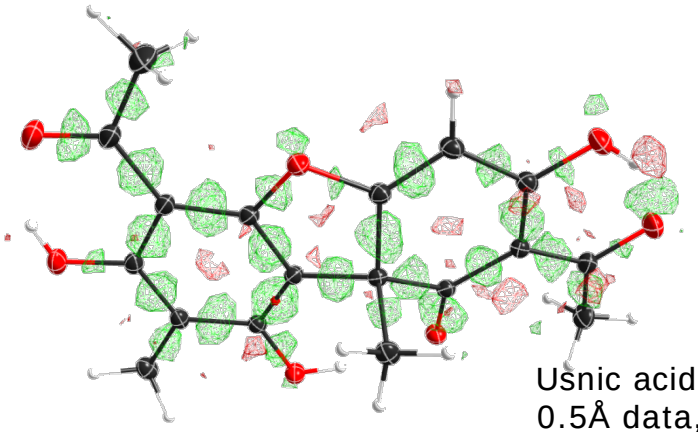


R1 = 3.00%

R1 = 2.65%

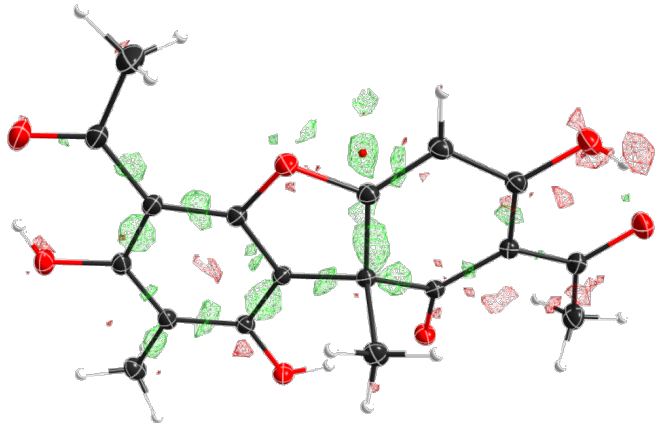


Ascorbic Acid, 2 Carbon atoms not modeled
0.6Å data, Fo-Fc maps at same level



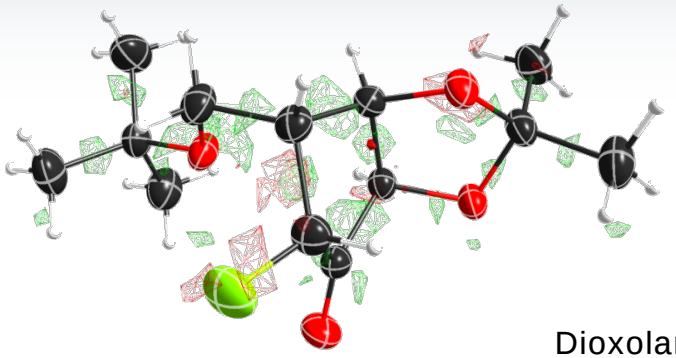
R1 = 2.68%

R1 = 2.29%



Usnic acid
0.5Å data, Fo-Fc maps at same level

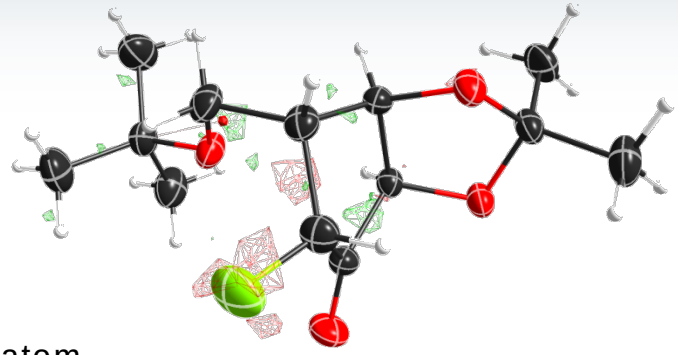
IDEAL - More Examples 3



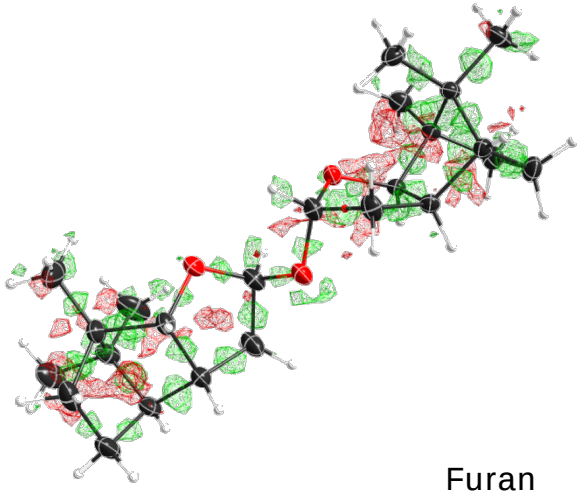
R1 = 2.95%

⇩

R1 = 2.50%



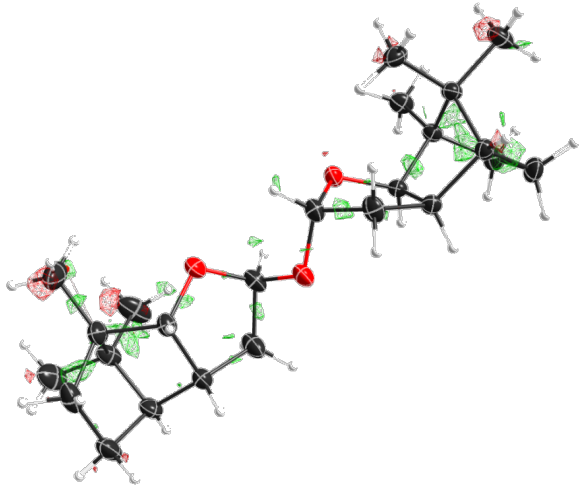
Dioxolane compound with Fluorine atom,
0.8Å Cu data, Fo-Fc maps at same level



R1 = 2.99%

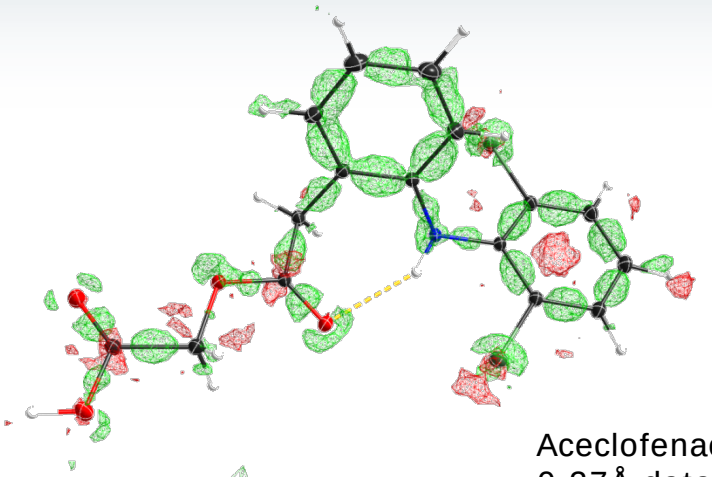
⇩

R1 = 2.51%



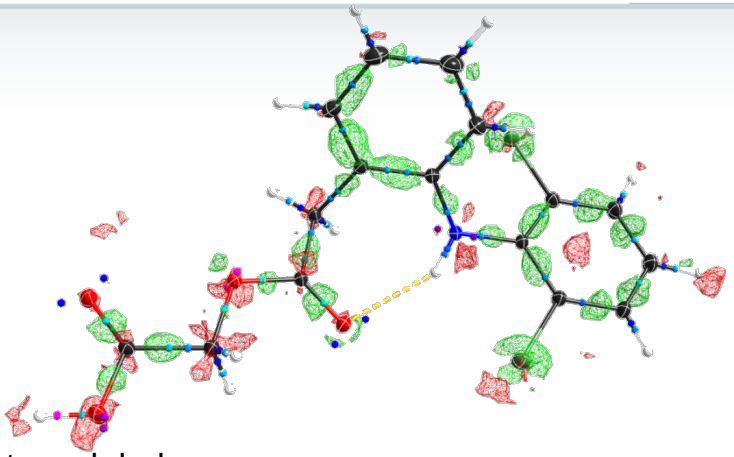
Furan
0.80Å Cu data, Fo-Fc maps at same level

IDEAL - More (Problematic) Examples

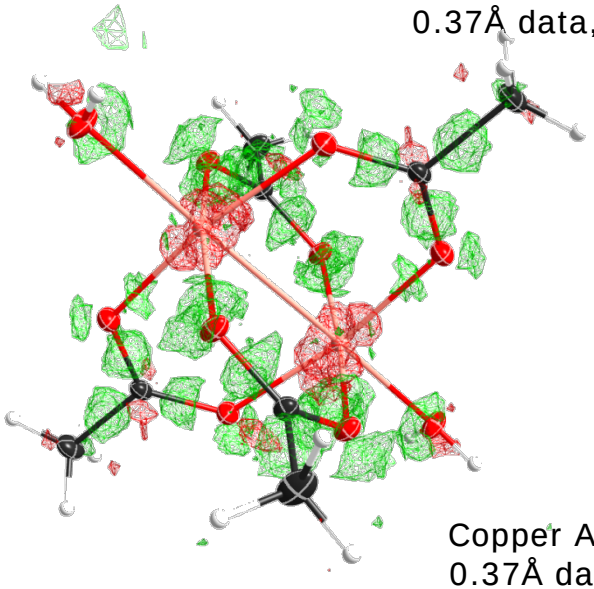


R1 = 2.33%

R1 = 2.13%

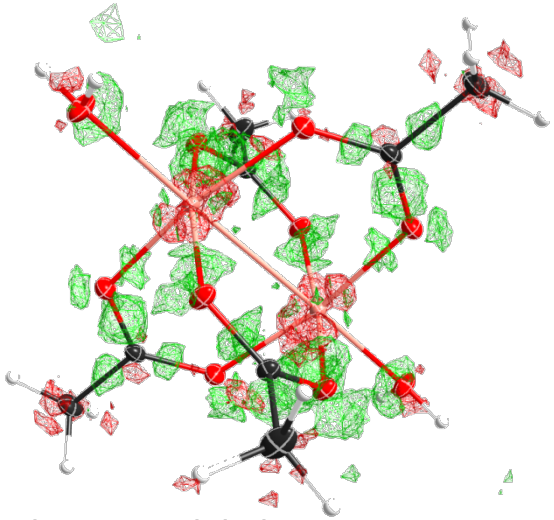


Aceclofenac, Cloride bonds not modeled
0.37Å data, Fo-Fc maps at same level



R1 = 1.38%

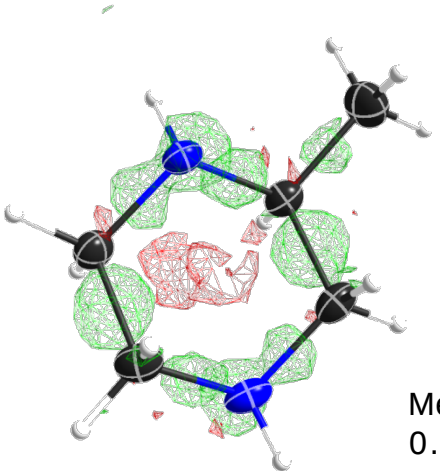
R1 = 1.36%



Copper Acetate, Cu and most Oxygen bonds not modeled
0.37Å data, Fo-Fc maps at same level

IDEAL - Reliability Criteria

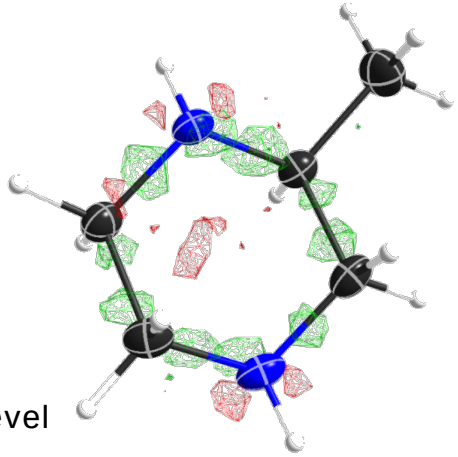
- Reduced R1
- Visual inspection of residual densities
- Can we do better?



R1 = 2.72%

⇩

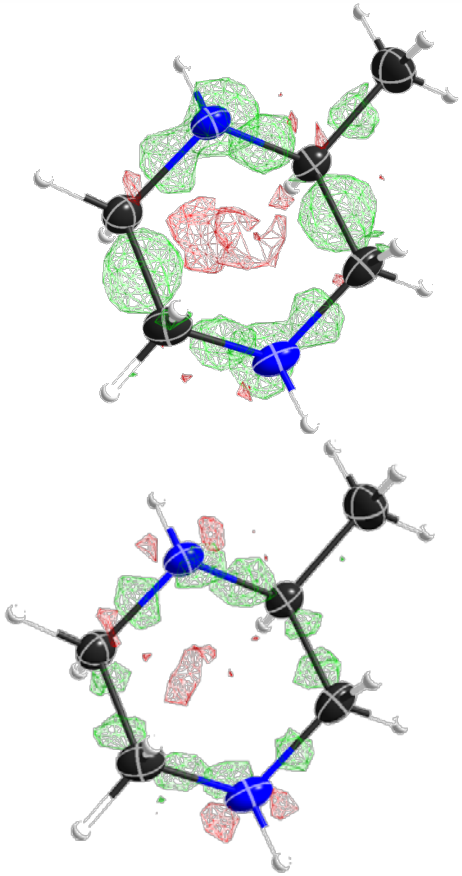
R1 = 2.35%

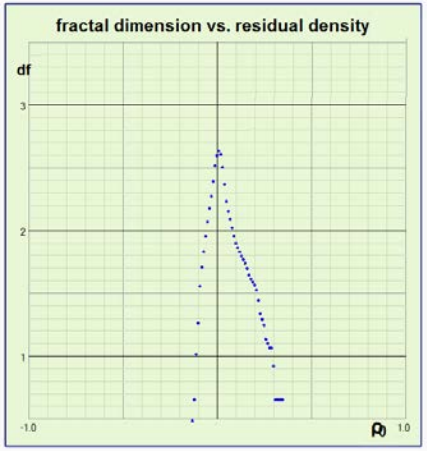


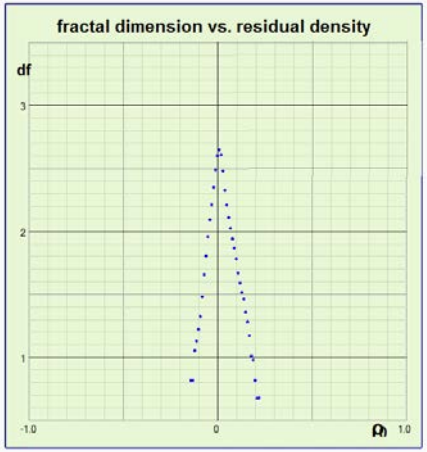
Methyl-Piperazine
0.5Å data, Fo-Fc maps at same level

IDEAL - Fractal dimension analysis

- Fractal dimension analysis







Foundations of residual-density analysis
Kathrin Meindl and Julian Henn
Acta Cryst. (2008). A64, 404–418

Residual density descriptors	
df0	2.65
ρmin (d=2)	-0.067 eÅ^{-3}
ρmax (d=2)	0.070 eÅ^{-3}
ρmin	-0.141 eÅ^{-3}
ρmax	0.343 eÅ^{-3}
e gross	3.59 e^{-}
Δ ρ	0.484 e^{-}Å^{-3}

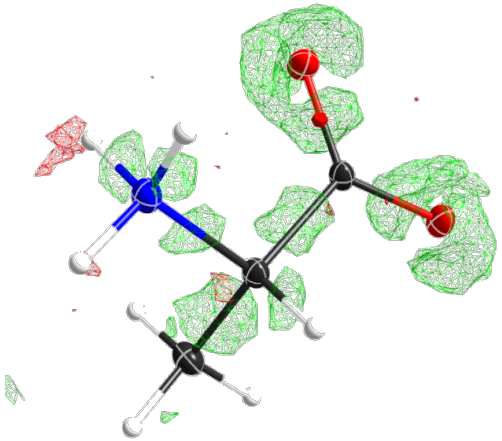
Residual density descriptors	
df0	2.66
ρmin (d=2)	-0.051 eÅ^{-3}
ρmax (d=2)	0.064 eÅ^{-3}
ρmin	-0.154 eÅ^{-3}
ρmax	0.218 eÅ^{-3}
e gross	3.00 e^{-}
Δ ρ	0.372 e^{-}Å^{-3}

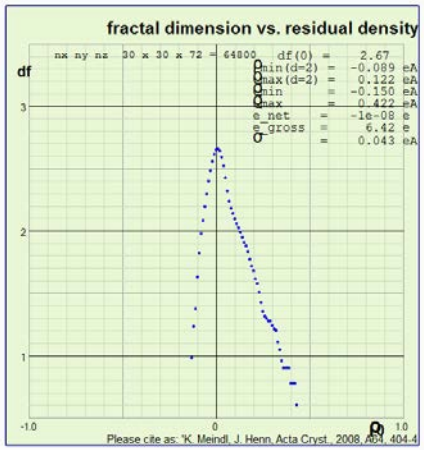
Residual density descriptors

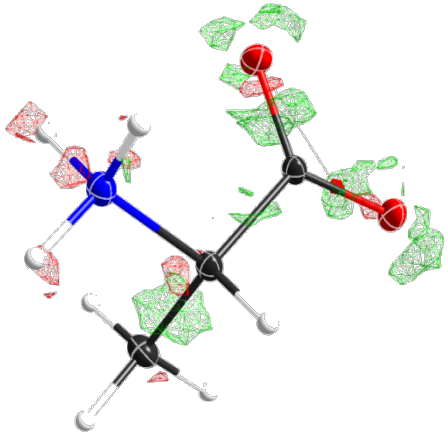
- **e gross** - The gross residual electrons describe the total inadequacies that arise from the following error:
  - Noise
  - Inadequate data processing
  - Density model errors
  - Can artificially lowered by truncating the experimental resolution
- **df0** - measure for the featurelessness of the residual density distribution
- The **shape** indicates the presence /absence of systematic errors
- **Δ ρ** - the width – indicates the flatness of the distribution

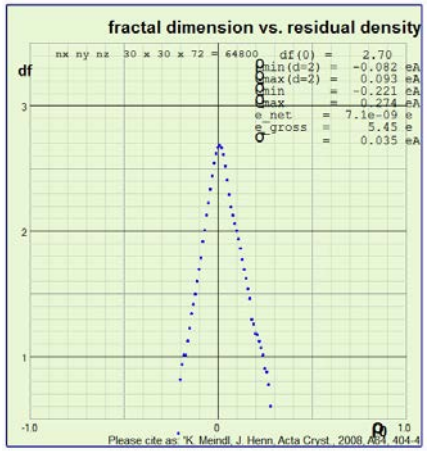
IDEAL - Fractal dimension analysis

- Fractal dimension analysis









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Residual density descriptors	
df0	2.67
ρmin (d=2)	-0.089 eÅ^{-3}
ρmax (d=2)	0.122 eÅ^{-3}
ρmin	-0.150 eÅ^{-3}
ρmax	0.422 eÅ^{-3}
e gross	6.42 e^{-}
Δ ρ	0.572 e^{-}Å^{-3}

Residual density descriptors	
df0	2.70
ρmin (d=2)	-0.082 eÅ^{-3}
ρmax (d=2)	0.093 eÅ^{-3}
ρmin	-0.221 eÅ^{-3}
ρmax	0.274 eÅ^{-3}
e gross	5.45 e^{-}
Δ ρ	0.495 e^{-}Å^{-3}

IDEAL - Fractal dimension analysis how does it compare

- Fractal dimension analysis

Foundations of residual-density analysis
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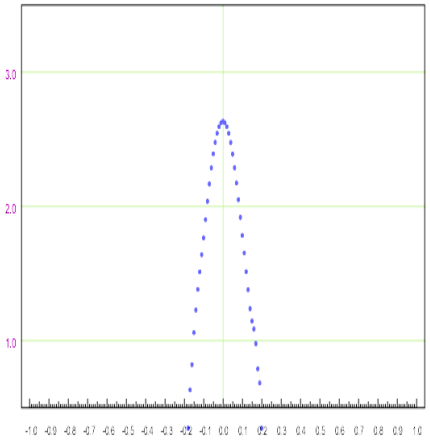
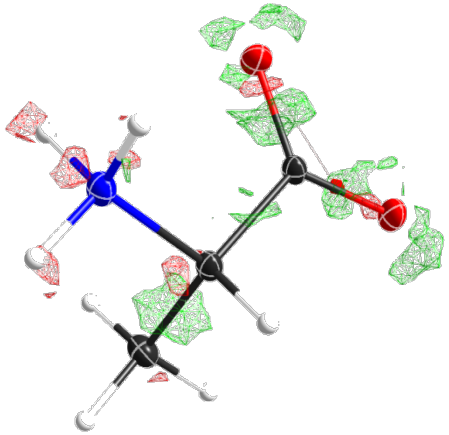
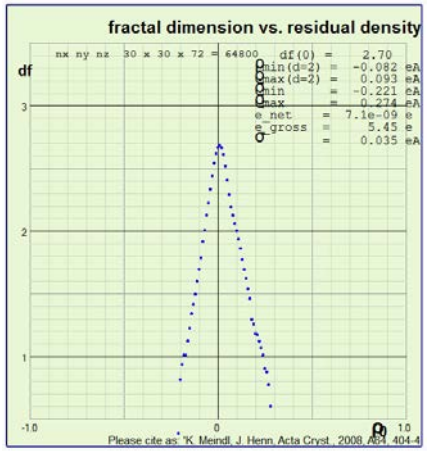
MoPro Multipole refinement





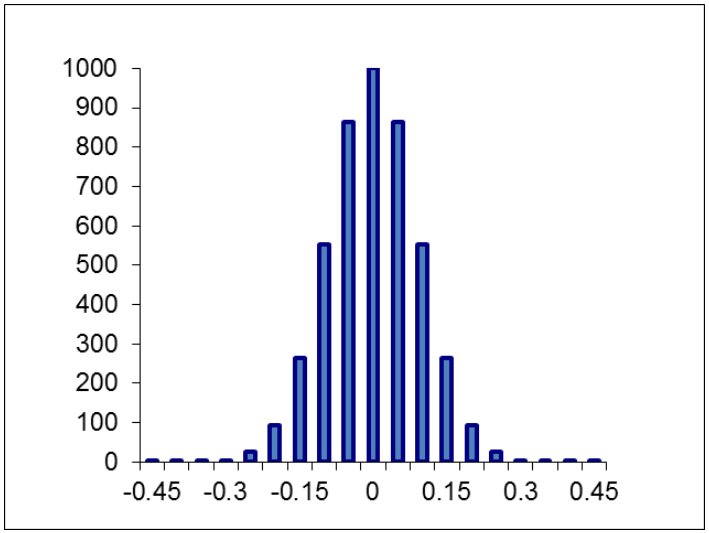


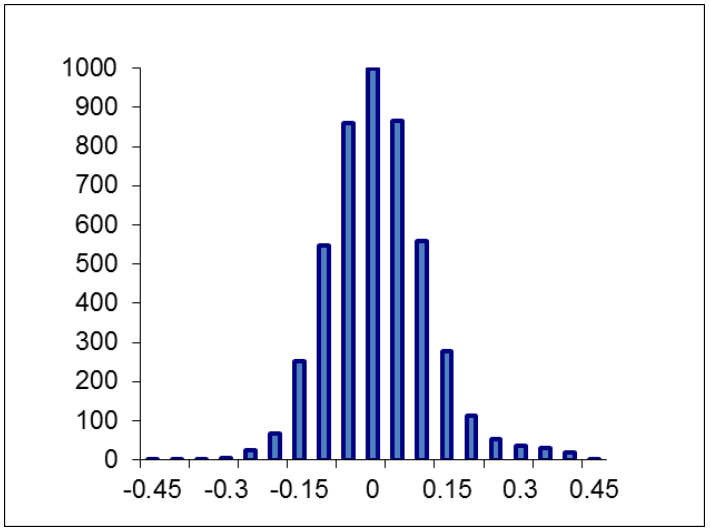
Residual density descriptors	
df0	2.6345
ρmin (d=2)	-0.083 eÅ^{-3}
ρmax (d=2)	0.084 eÅ^{-3}
ρmin	-0.18 eÅ^{-3}
ρmax	0.21 eÅ^{-3}
e gross	5.43 e^{-}
Δ ρ	0.39 e^{-}Å^{-3}

Residual density descriptors	
df0	2.70
ρmin (d=2)	-0.082 eÅ^{-3}
ρmax (d=2)	0.093 eÅ^{-3}
ρmin	-0.221 eÅ^{-3}
ρmax	0.274 eÅ^{-3}
e gross	5.45 e^{-}
Δ ρ	0.495 e^{-}Å^{-3}

Residual density analysis

- A simple approach is to calculate a histogram of the residual density and compare it to a Gaussian distribution
- Due to the high frequency of residuals values close to zero details in the periphery cannot be observed easily

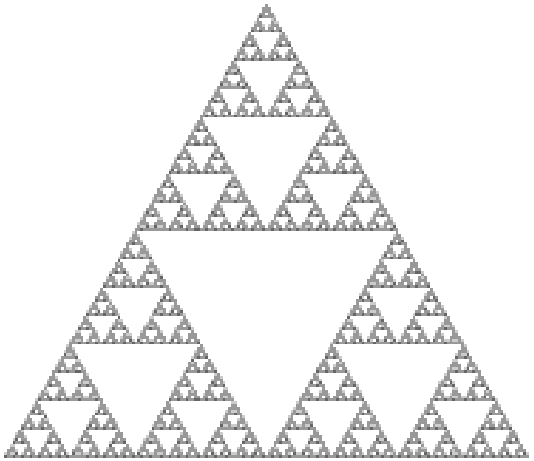




Fractal dimension analysis

- A fractal analysis on how statistically self-similar the distribution of residual density is for a given structure
- Why fractal?

Your hand if you look closely enough

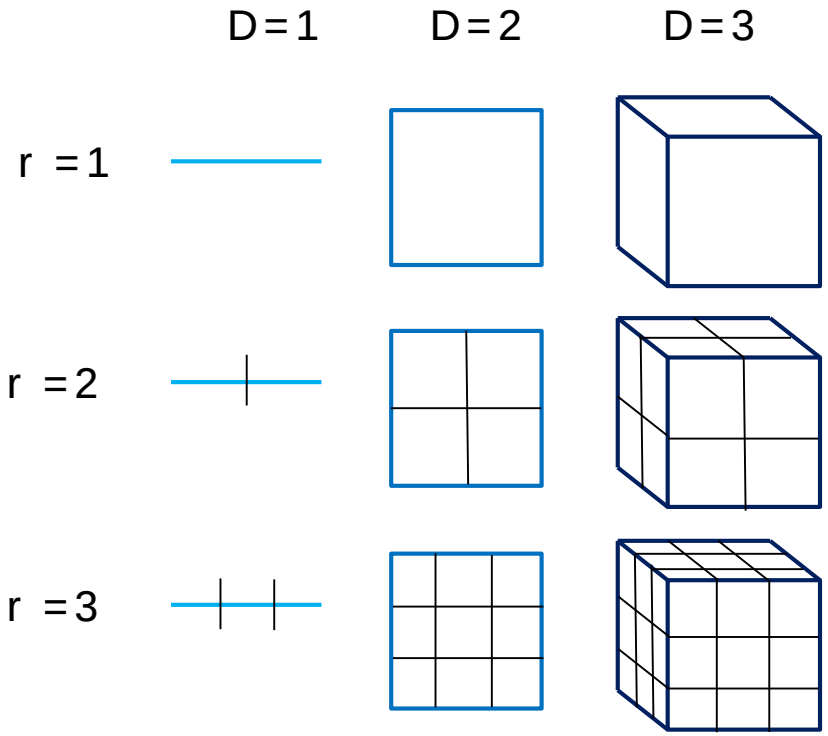


Sierpinski triangle

What is a fractal dimension?

- **The Concept of Dimension**
  - The three dimensions of Euclidean space (D=1,2,3)

- **The Hausdorff Dimension (or Fractal dimension)**
  - Fractals, which are irregular geometric objects, require another meaning, the fractal dimension as a measure of how self-similar the object is



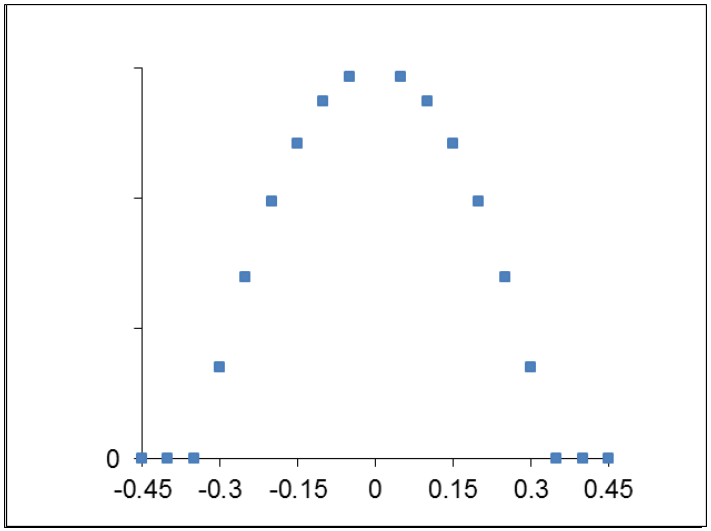
- Object residing in Euclidean dimension D
- Reduce its linear size by 1/r in each spatial direction (length, area, or volume)
- The number of objects increases to $N=r^D$ times the original
- take the log of both sides of $N=r^D$
- log(N) = D log(r).
- **D = log(N) / log(r)**
- **D = log(number of self-similar pieces) / log(magnification factor)**
- D need not be an integer, as it is in Euclidean geometry
- This generalized treatment of dimension is named after the German mathematician, Felix Hausdorff
- It has proved useful for describing natural objects and for evaluating trajectories of dynamic systems

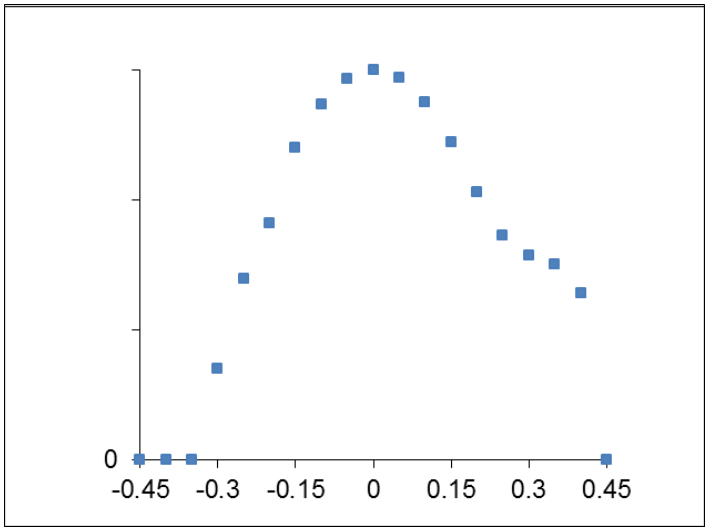
Fractal dimension distribution of the residual density

- The fractal dimension of a residual-density iso-surface of constant value x can be evaluated by a box counting algorithm using a finite grid
- If one is interested in the zero residual-density iso-surface, one just counts the number of boxes containing at least one point of zero residual density
- In the special case of a distribution containing Gaussian noise with a mean of zero and no model errors it follows that the corresponding fractal dimension distribution is of parabolic shape

Fractal dimension
in residual density analysis

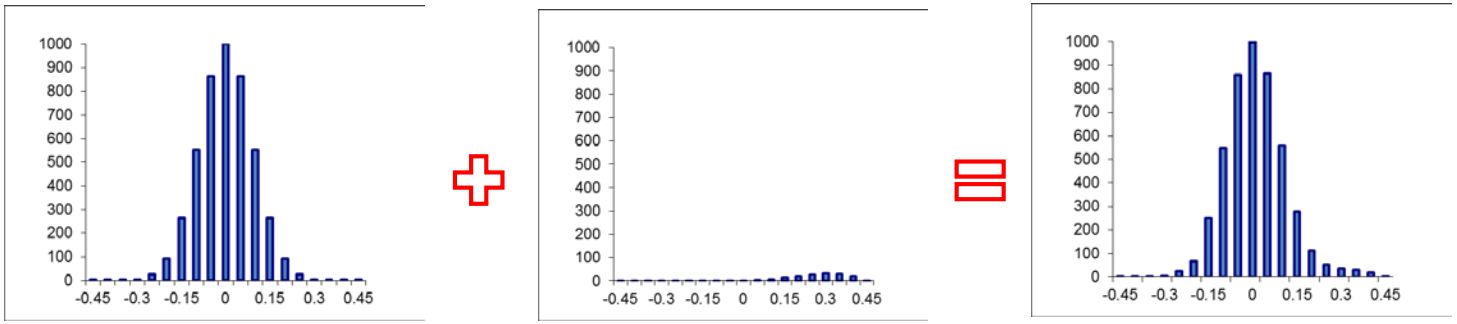
- In the special case of a of a distribution containing Gaussian noise with a mean of zero and no model errors the corresponding fractal dimension distribution is of parabolic shape
- The max value of df0 is 3

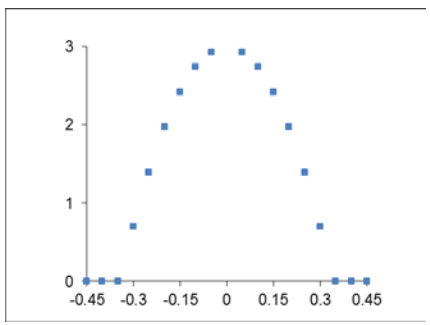




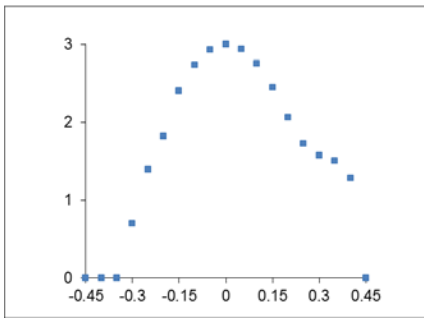
Fractal dimension in residual density analysis

- So where does the shoulder come from?



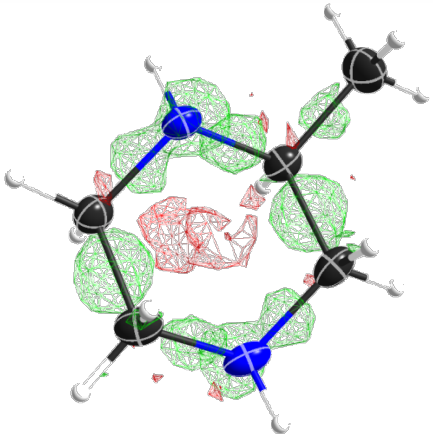


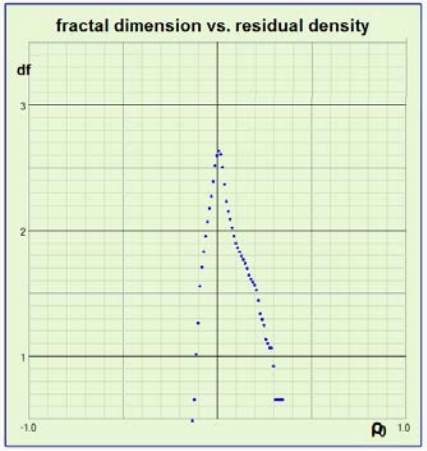
Adding some positive residuals causes a shoulder to appear on the parabola

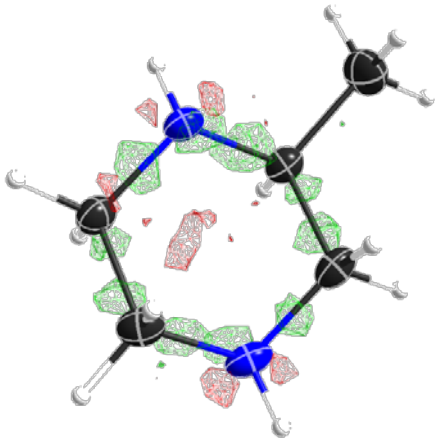


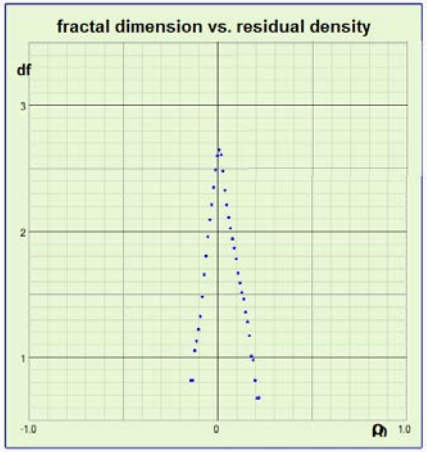
IDEAL - Fractal dimension analysis

- Fractal dimension analysis









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Δ ρ	0.372 e^{-}Å^{-3}

IDEAL–The Value Proposition

- Better structure description – better R values
- Increased model accuracy
- Access to more detailed model properties
- Easy to use
- Fully automated - Interactivity optional
- Seamless integration into APEX3
- Compatibility with checkcif

- IDEAL is proprietary to Bruker
- XL with BEDE and LONE functionality will be exclusive to Bruker for 5 years

Questions and Answers

Any questions?

Please type any questions you may have for our speakers in the Q&A panel and click Send.

Thank you!

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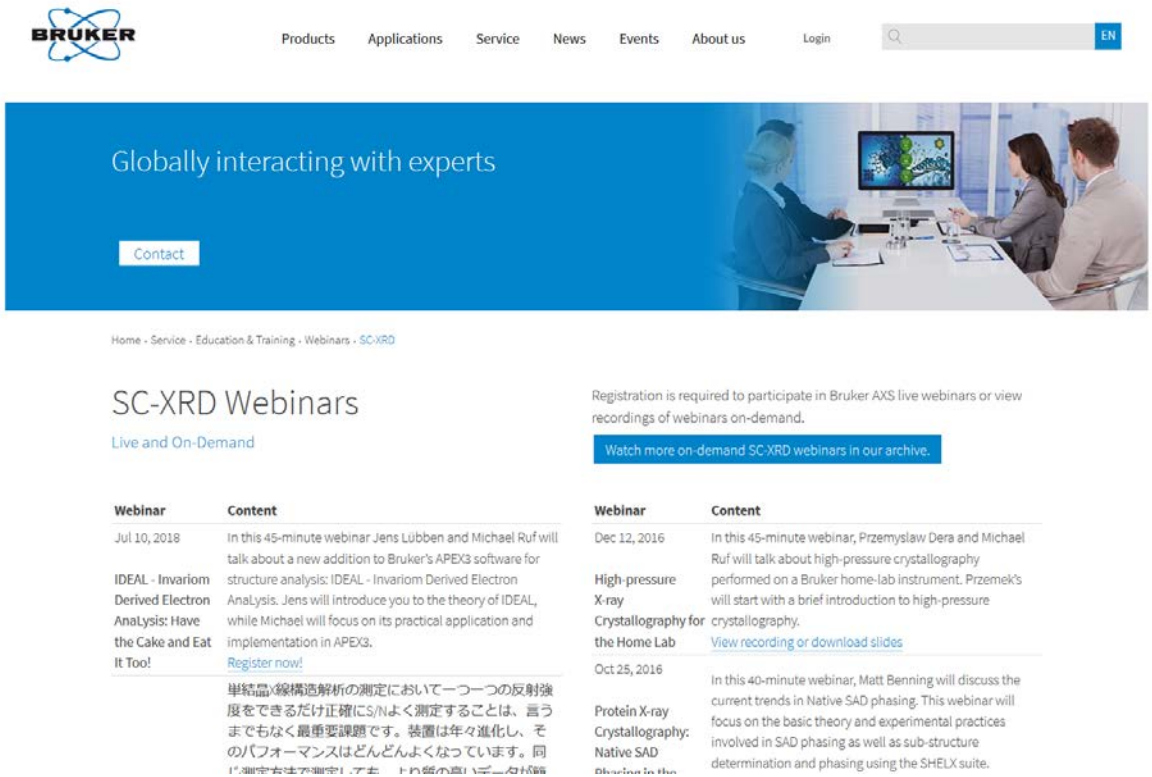
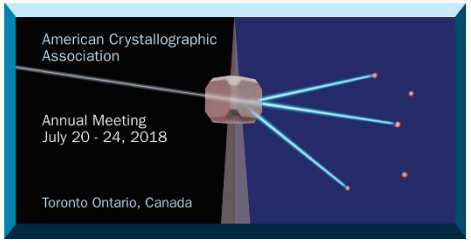


Meet us at these upcoming events



ACA Annual Meeting

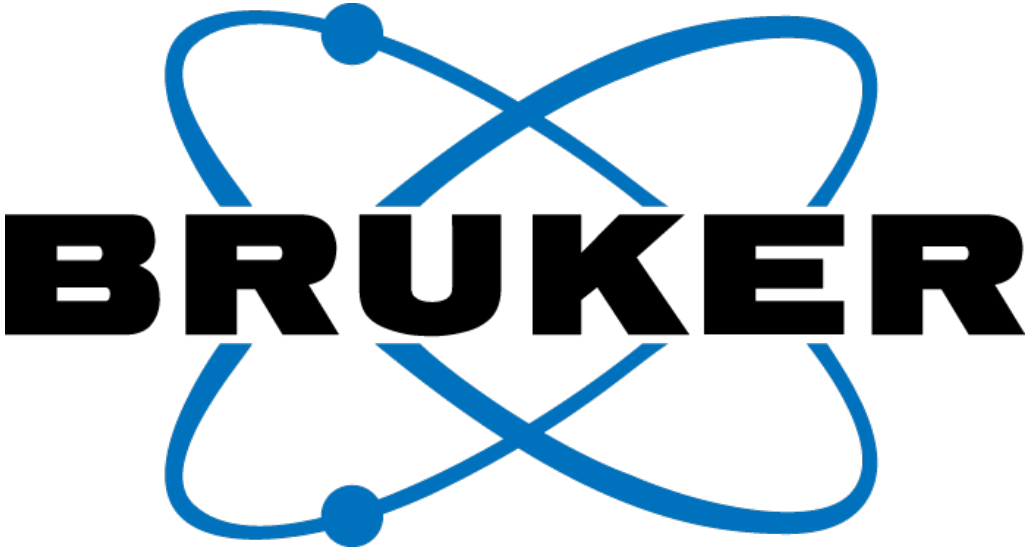
July 20 to 24, 2018
Toronto, Canada

ACS Fall Meeting

Aug 19 to 23, 2018
Boston, Massachusetts, USA

ECM31, European Crystallographic Meeting

Aug 20 to 27, 2018
Oviedo, Spain



Innovation with Integrity