

IDEAL - Have the Cake and Eat It Too!

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IDEAL (Invariom Derived Electron AnaLysis)



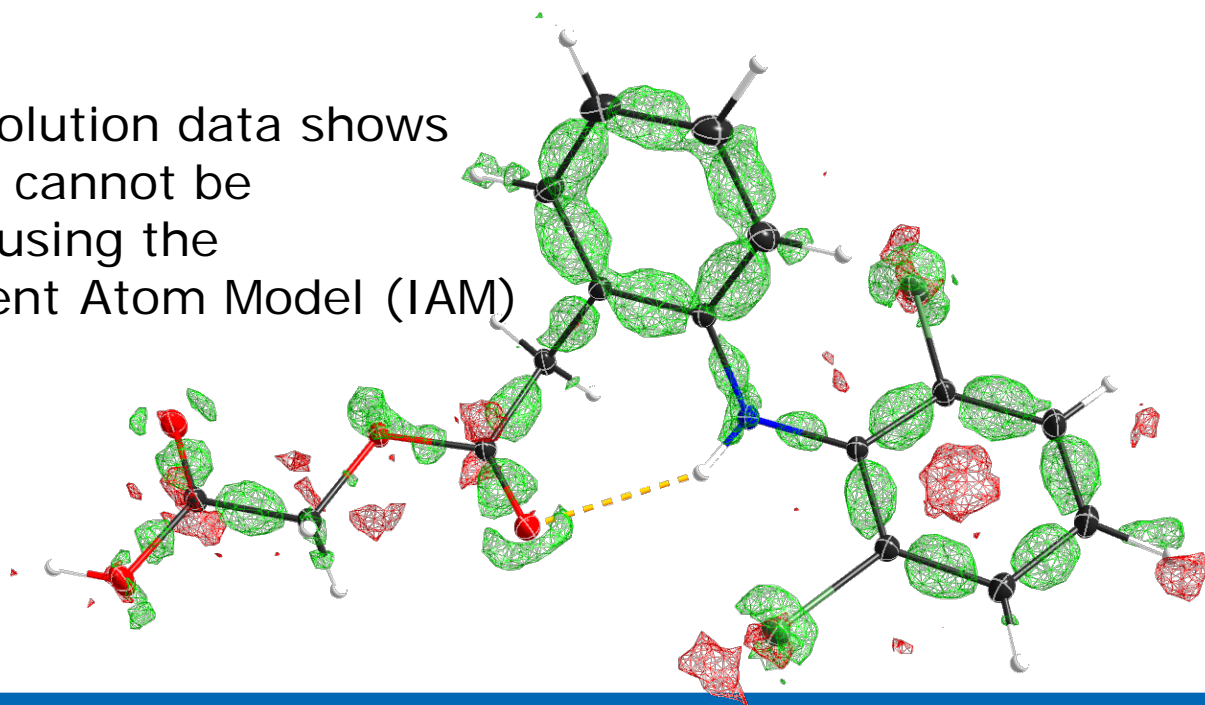
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Karlsruhe, Germany



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SC-XRD Product Manager
Bruker AXS
Madison, WI

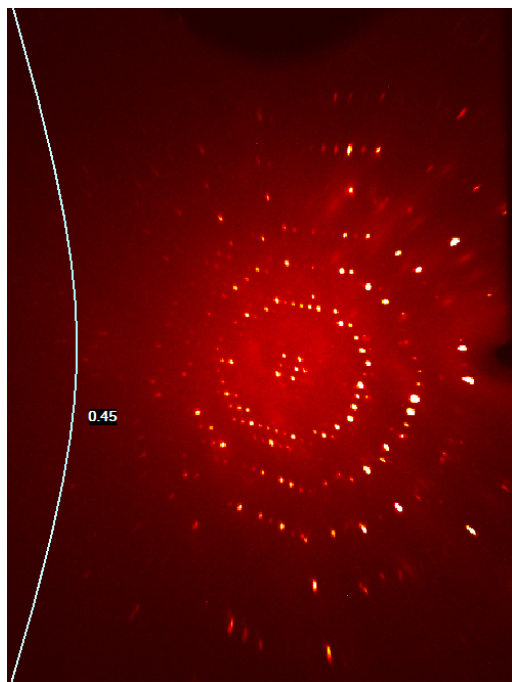
IDEAL - The Premise

- 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)



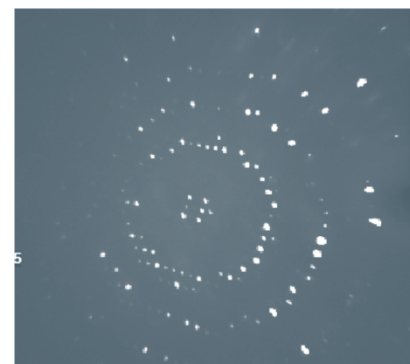
IDEAL - The Premise

- 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

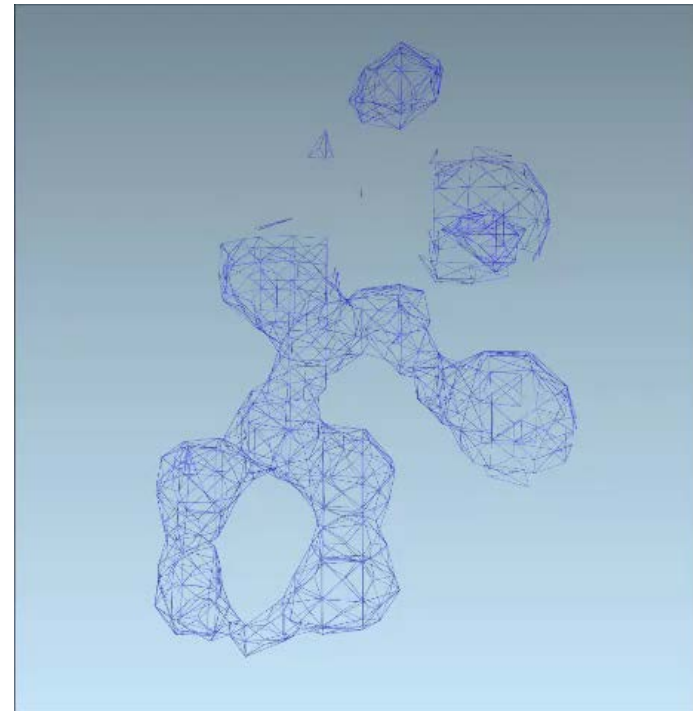
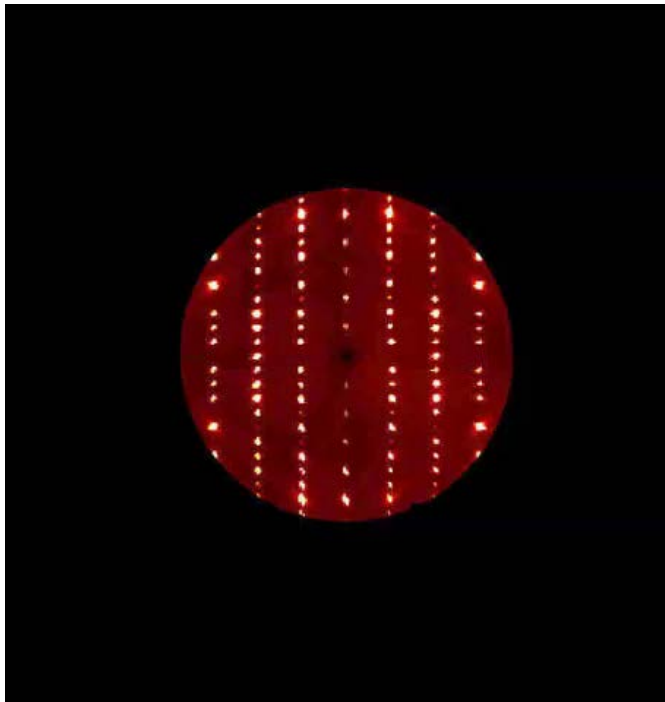


HPAD/HPC

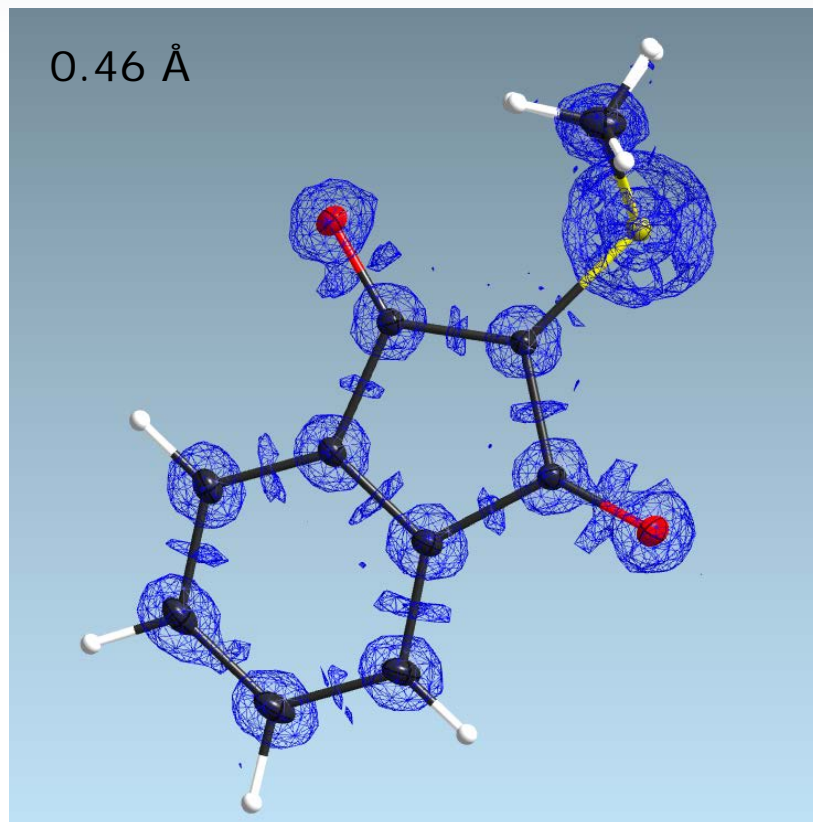
IDEAL - Resolution: Reciprocal space vs. real space



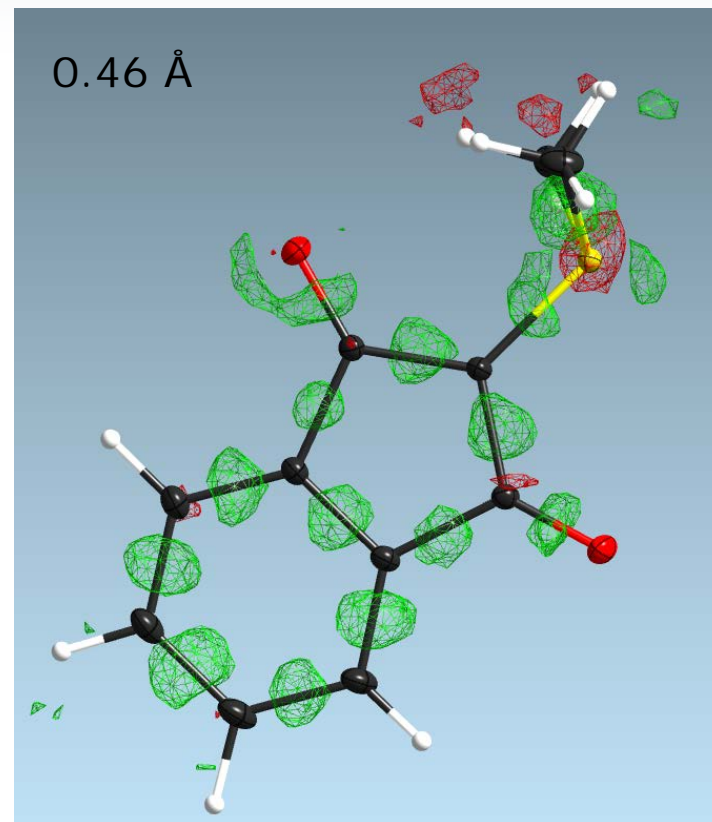
- Left: Data (reciprocal space) resolution increase in 0.1 Å steps (diffraction angle increases)
- Right: Structure (real space) resolution increases (more detail in density map)



IDEAL - High Resolution Data



"Observed" electron density



Residual electron density



The Independent Atom Model (IAM) vs The Multipole Model

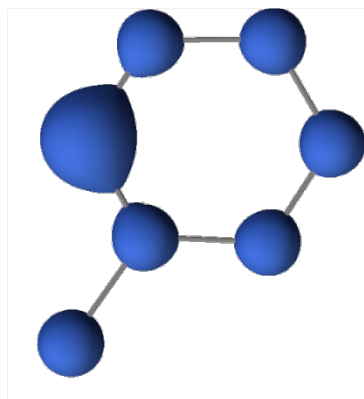


- Independent Atom Model
 - The atoms are regarded to be independent
 - The determined atom position and the displacement parameters can solely count for the right atom type at the correct lattice position with the right site occupation factor
 - It does not account for the interatomic region
 - IAM 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

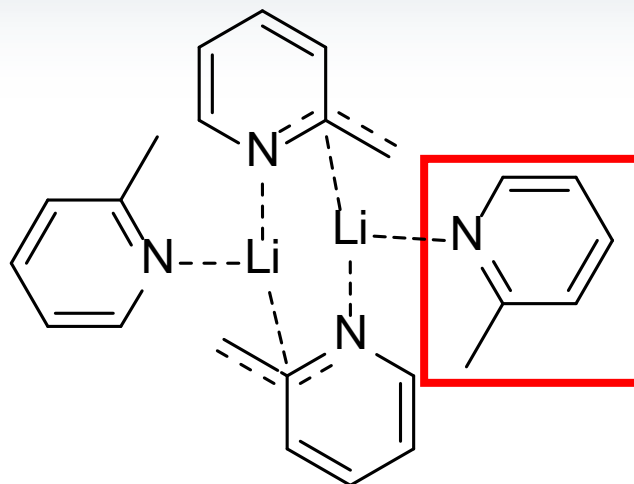
IAM vs. MM



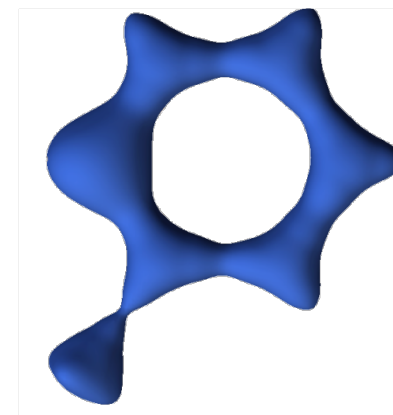
IAM



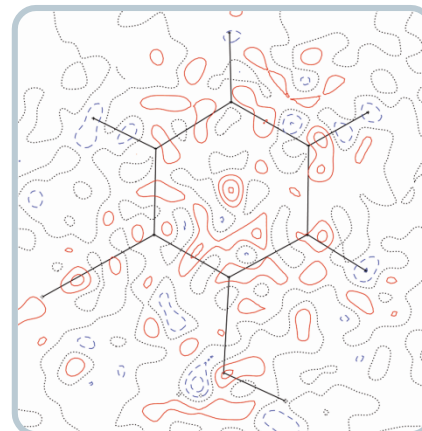
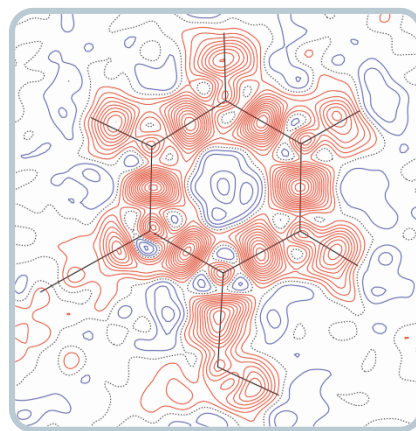
Electron
Density



Improved
Model

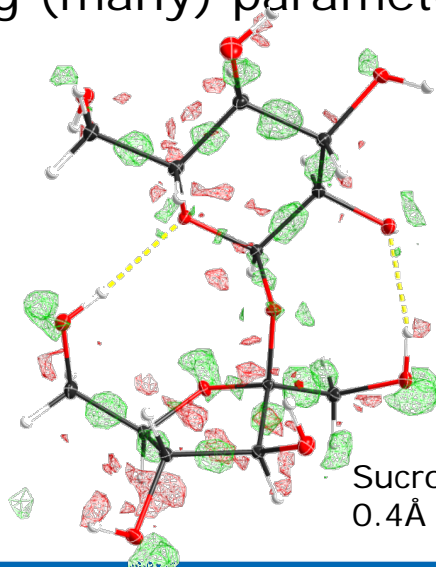


Electron
Density



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

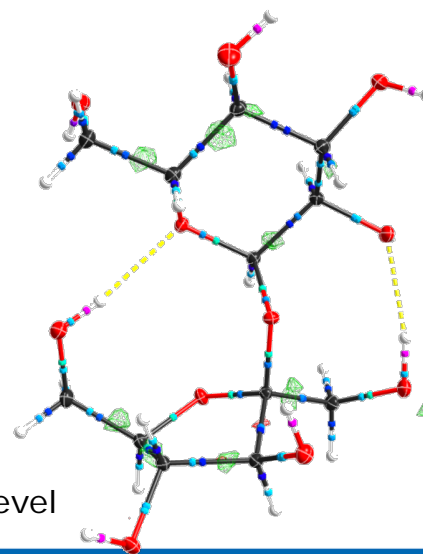


R1 = 1.84%



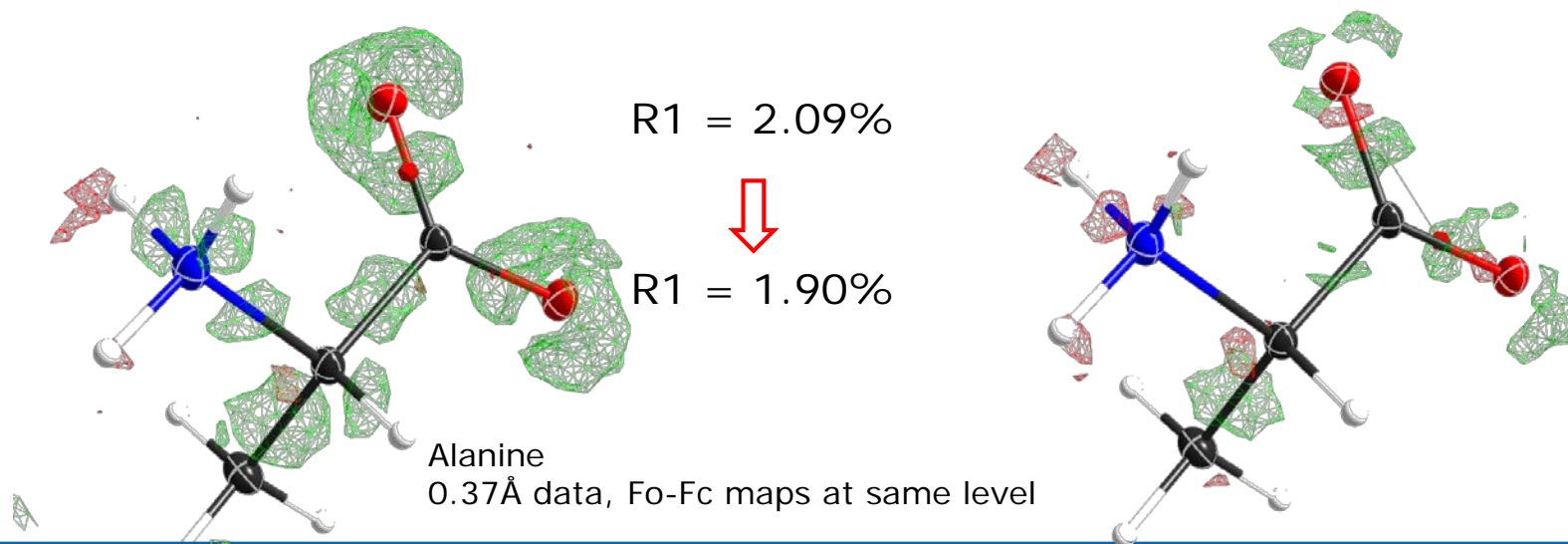
R1 = 1.43%

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



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:

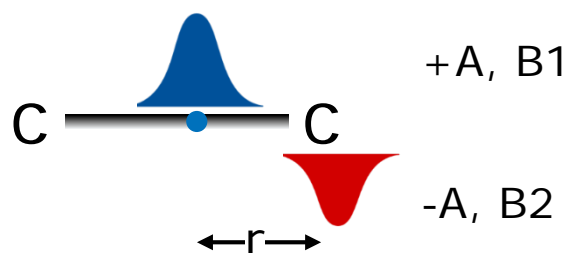
BEDE atom1 atom2 r A B1 B2

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

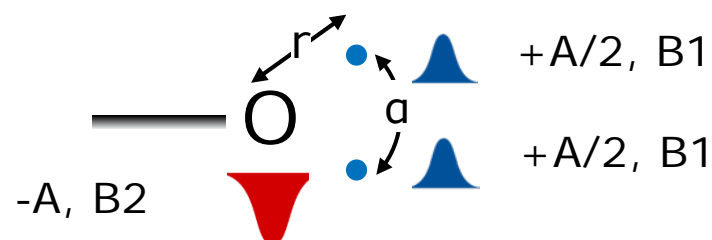
For $f(x) = \pm A e^{(-B_{1,2}(\sin(\frac{\theta}{\lambda}))^2)}$
B1 for +A, B2 for -A

IDEAL – The Implementation

BEDE



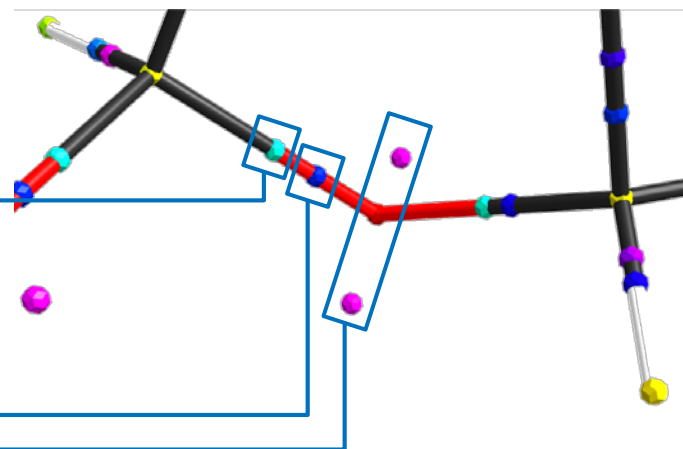
LONE



- 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

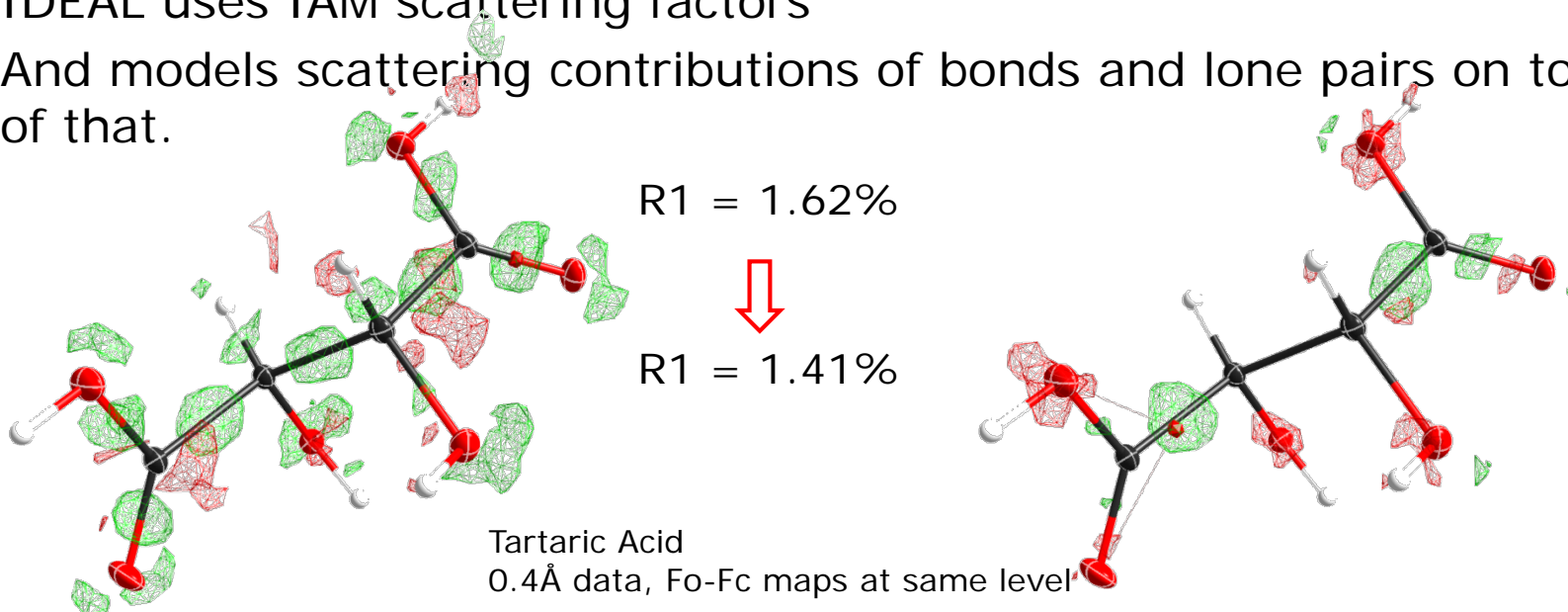
- **Invarioms** are aspherical atomic scattering factors that enable structure refinement of more accurate and more precise geometries than refinements with the conventional independent atom model (IAM).
- The use of single-crystal X-ray diffraction data of a resolution better than $\sin \theta/\lambda = 0.6 \text{ \AA}^{-1}$ (or $d = 0.83 \text{ \AA}$) 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

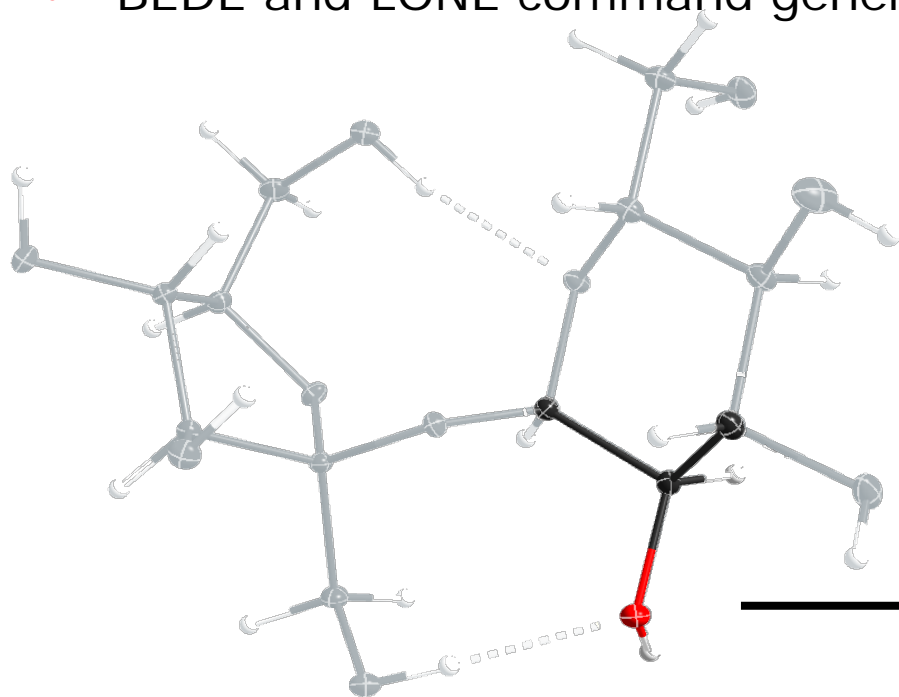
IDEAL –What's different

- 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.



IDEAL –The GUI

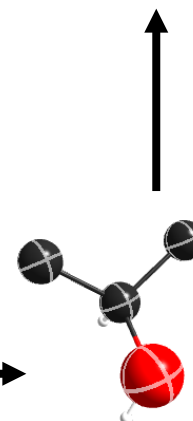
- Invariom partitioning
- Parameter transfer
- BEDE and LONE command generation



```

+ [x] [x] O1
+ [x] [x] O2
+ [x] [x] O1c1h_0
+ [x] [x] BEDE O2 C2 0.595 {}0.364 {}0.271 {}0.569
+ [x] [x] LONE O2 2 {}1.316 {}0.325 {}0.569 0.389 141.59
+ [x] [x] H2A
+ [x] [x] O3

```



IDEAL –The GUI



APEX3 v2018.5-RC4 - User: (dba) - Sample: sucrose - Temporary license (182 days remaining)

Sample Instrument Edit Settings View Pack ShelX Extra Tools Windows Help

Set Up
Evaluate
Collect
Reduce Data
Examine Data
Find Structure

AUTOSTRUCTURE
Solve Structure
Refine Structure
View Structure

Invariom partitioning
Parameter transfer
BEDE and LONE command generation

It is fast! 30s for sucrose to set up all parameters

Configuration
Ring Detection Threshold
Few Rings Many Rings Apply
Free Variable Setup
Use FVARs 2 3 4
Match Automatically Clear All Confirm

45 out of 45 atoms successfully matched

- ☒ H8A
- ☒ O9
- ☒ H9A
- ☒ O10
- ☒ O11
- ☒ H11
- ☒ C1

Assign Manually

C1o1o1c1h_0

BEDE	C1	H1	0.347	0.878	0.423	0.540
BEDE	C1	O1	1.013	0.484	0.552	0.540
BEDE	C1	O5	1.005	0.484	0.552	0.540
BEDE	C1	C2	1.075	0.505	0.340	0.540

Local Environment
Matched Environment

Environment View

Reset rotation center ☐ grow Q-peaks ☐ search for duplicates ☒ Calculate Maps ☐ fcf6 by hkl

Report

IDEAL –The GUI



APEX3 v2018.5-RC4 - User: (dba) - Sample: succrose - Temporary license (182 days remaining)

Sample Instrument Edit Settings View Pack ShelX Extra Tools Windows Help

Set Up
Evaluate
Collect
Reduce Data
Examine Data
Find Structure

AUTOSTRUCTURE
Solve Structure
Refine Structure
View Structure

Quick configuration for challenging structures

Visual representation of local environments and corresponding database fragments

Configuration
Ring Detection Threshold
Few Rings Many Rings Apply
Free Variable Setup
Use FVARs 2 3 4
Match Automatically Clear All Confirm

45 out of 45 atoms successfully matched

- ☒ H8A
- ☒ O9
- ☒ H9A
- ☒ O10
- ☒ O11
- ☒ H11
- ☒ C1

C1o1o1c1h_0

BEDE	C1	H1	0.347	0.878	0.423	0.540
BEDE	C1	O1	1.013	0.484	0.552	0.540
BEDE	C1	O5	1.005	0.484	0.552	0.540
BEDE	C1	C2	1.075	0.505	0.340	0.540

Local Environment

Matched Environment

Environment View

Reset rotation center ☐ grow Q-peaks ☐ search for duplicates ☒ Calculate Maps ☒ fcf6 by hkl ☐

Report

IDEAL–The GUI



APEX3 v2018.5-RC4 - User: (dba) - Sample: sucrose - Temporary license (182 days remaining)

Sample Instrument Edit Settings View Pack ShellX Extra Tools Windows Help

Set Up Evaluate Collect Reduce Data Examine Data Find Structure

AUTOSTRUCTURE Solve Structure Refine Structure View Structure

External file with BEDE and LONE commands that is called for refinement

Visual representation of positions for Bond Oriented Deformation Density

Refine Structure

zucker4_0m in P2(1)@ suc-bs.res

Select Part <Select residues> Line: 11 | Col: 13

```

1 TITL suker4_0m in P2(1)
2 suc-bs.res created by SHELXL-2016/2 at 18:34:44 on 16-Aug-2016
3 CELL 0.71073 0.71010 0.65910 10.80540 90.0000 102.9794 90.0000
4 ZERR 2.00 0.00020 0.00030 0.00030 0.0000 0.0011 0.0000
5 LATN -1
6 SYMM -x, y+1/2, -z
7 SFAC C H O
8 UNIT 24 44 22
9
10
11 Hsuc-bs bodi
12
13 LIST 6 ! automatically inserted. Change 6 to 4 for CHECKCIF!!
14 TEMP -173.160
15 SIZE 0.203 0.331 0.453
16 SHEL 99 0.4
17 OMIT 1 0 0
18 OMIT 1 1 2
19 OMIT -1 1 2
20 L.S. 20
21
22 FMAP 2
23 PLAN 10
24 BOND
25
26
27
28 WGT 0.0211 0.0149
29 EXTI 0.030585
30 FVAR 1.16999 0.07612 0.14355 0.09837 0.28652 0.16670 -0.06657
31 FVAR 0.19062 0.18564
32 O1 3 0.892036 0.088393 0.670938 11.00000 0.00736 0.00543 =
33 3 0.00580 0.00042 0.00094 -0.00024
34 O2 3 1.251067 0.000655 0.725781 11.00000 0.00740 0.01047 =
35 3 0.00977 0.00099 0.00339 -0.00099
36 H2A 2 1.926028 0.050771 0.763950 11.00000 -1.50000
37 O3 3 1.205724 -0.314075 0.808633 11.00000 0.01739 0.00937 =
38 3 0.01188 0.00309 0.00748 0.00610
39 H3A 2 1.234206 -0.329873 0.748409 11.00000 -1.80000
40 O4 3 0.855691 -0.300109 0.849540 11.00000 0.01654 0.00653 =
41 3 0.02077 -0.00237 0.00846 -0.00298
42 H4A 2 0.918392 -0.438092 0.843962 11.00000 -1.50000
43 O5 3 0.869137 0.037501 0.878366 11.00000 0.00876 0.00632 =
44 3 0.00718 0.00000 0.00360 -0.00019
    
```

LIST FILE: sucbs.res

Information Window

186624 grid points.
 nation: 0.1 s.
 Δ^2 ($\sigma = 0.037$)
 change:
 change
 s. 43530 Triangles drawn.

Reset rotation center ☐ grow Q-peaks ☐ search for duplicates ☒ Calculate Maps ☐ fcf6 by Hkl

Flack x parameter: 0.041(103)
 Parsons parameter: -0.003(29)

Information Window Refinement History

IDEAL—The GUI

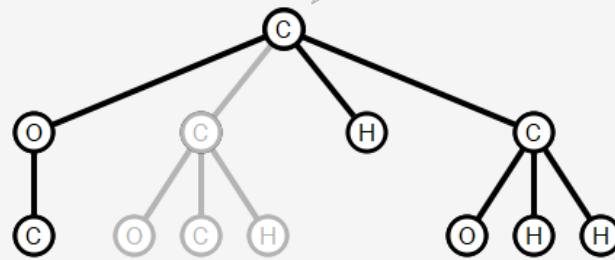
EnvironmentSelector

Local Environment

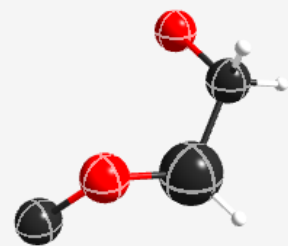
Bond Length Threshold: Few — Many

Ring Planarity: Few — Many

Edit Environment

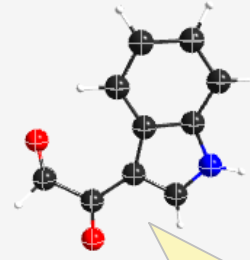


View Environment



Select Match

Select database match: C2o1c1h



BEDE C10 O10 0.732 {0.880 {0.359 {0.559
BEDE C10 H10 0.383 {0.565 {0.467 {0.559
BEDE C10 C11 0.872 {0.600 {0.311 {0.559

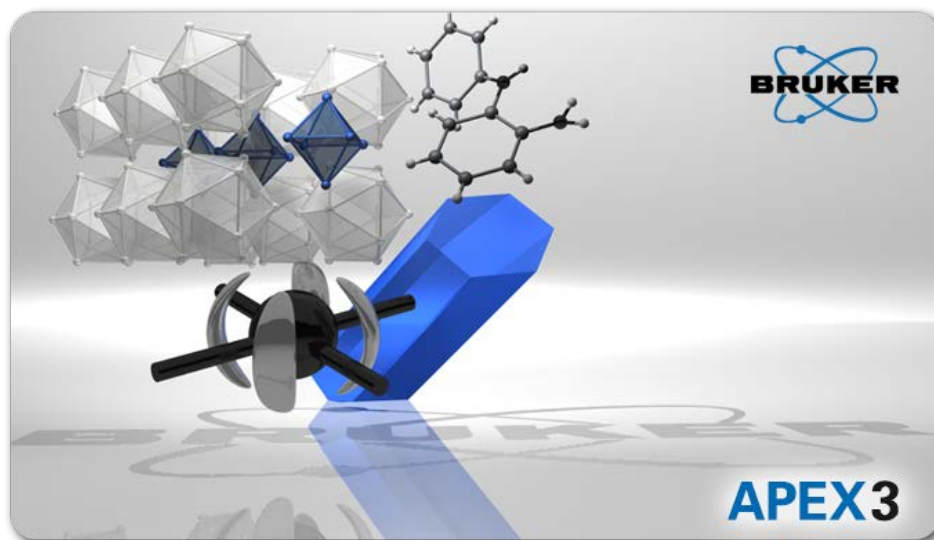
Manually select most suitable match from a sorted list of candidates

☒ Append To Current Parameters ☐ Replace Current Parameters

Accept

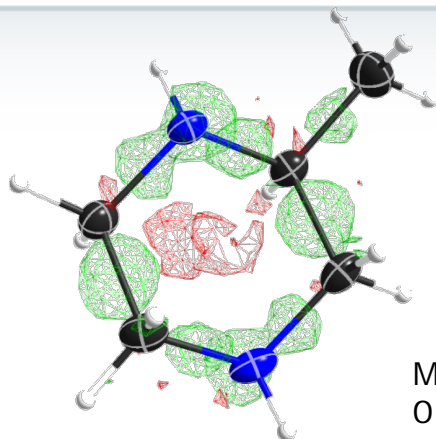
Fine tune database search by modifying input parameters with intuitive interface

APEX3 – Live Demo



- Live Demo of IDEAL in APEX3
- Bispyrazolone

IDEAL - More Examples 1

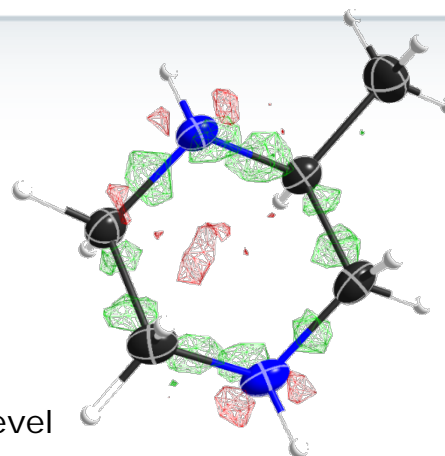


R1 = 2.72%



R1 = 2.35%

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

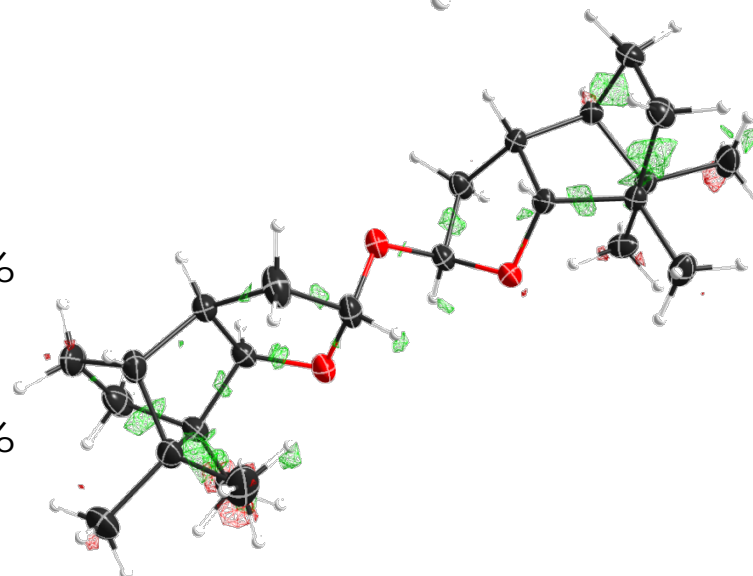
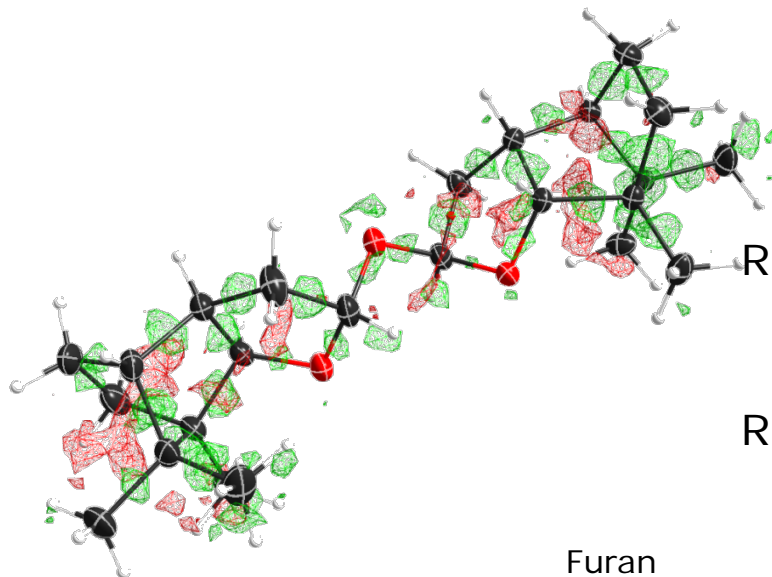


R1 = 3.00%

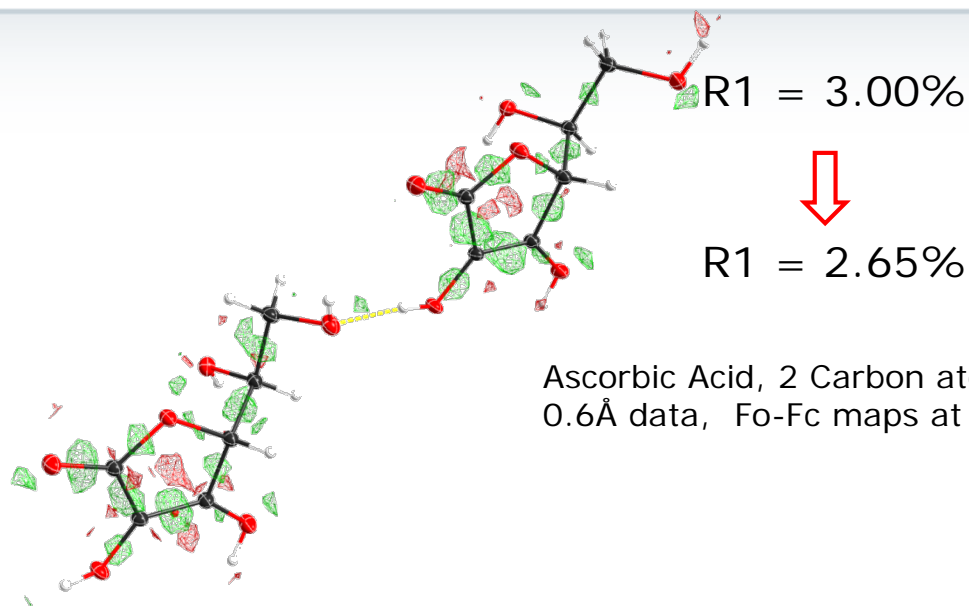


R1 = 2.51%

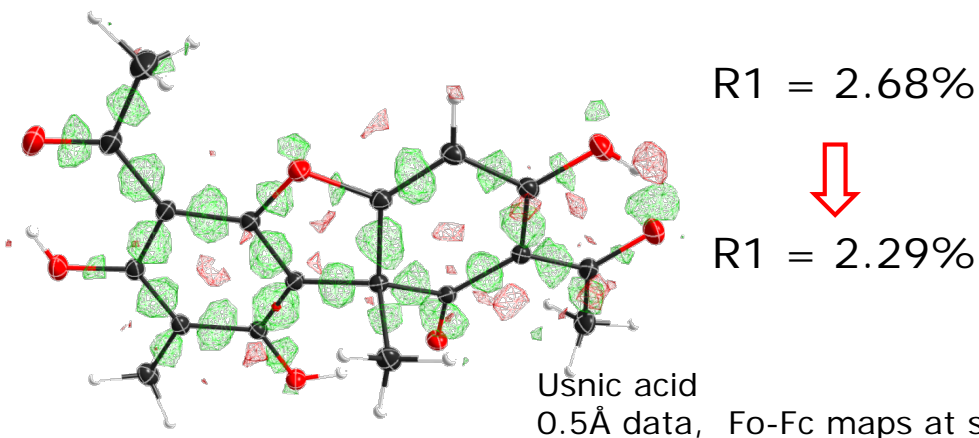
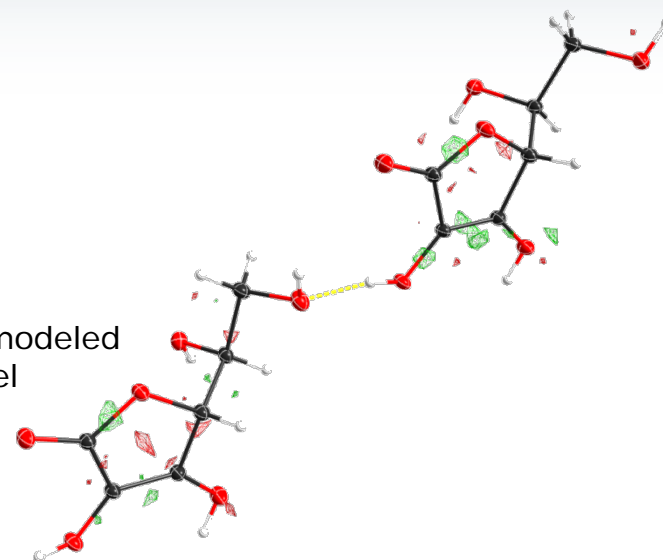
Furan
0.55Å data, Fo-Fc maps at same level



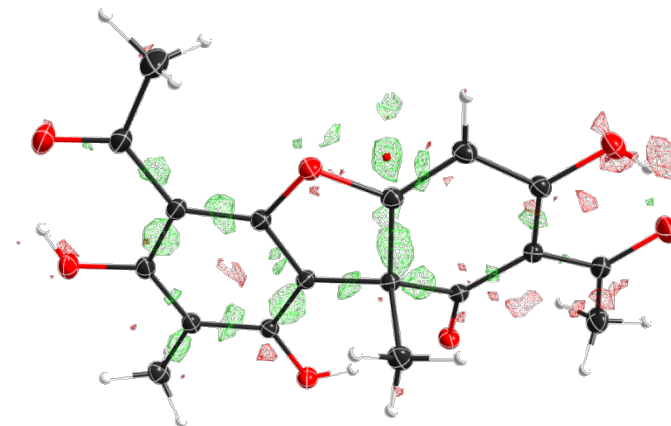
IDEAL - More Examples 2



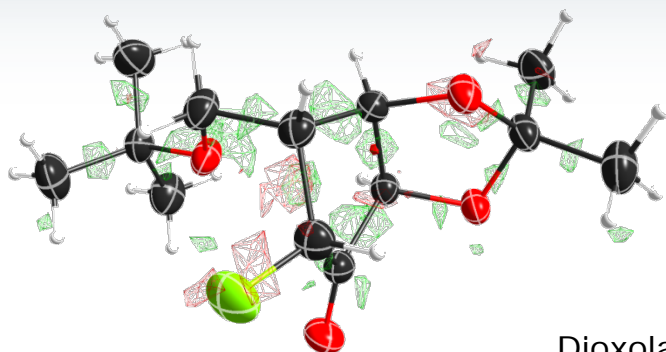
Ascorbic Acid, 2 Carbon atoms not modeled
0.6Å data, Fo-Fc maps at same level



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



IDEAL - More Examples 3

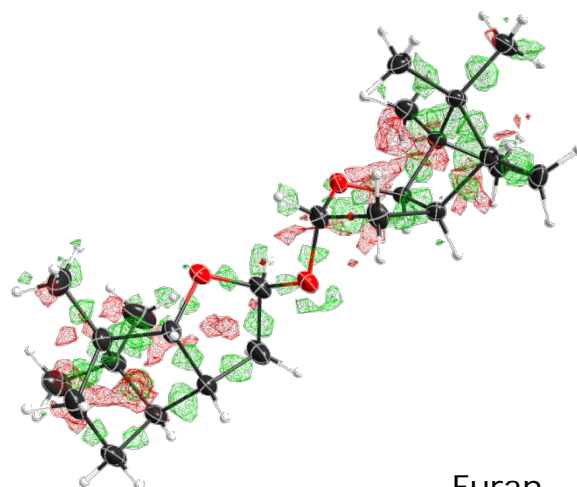
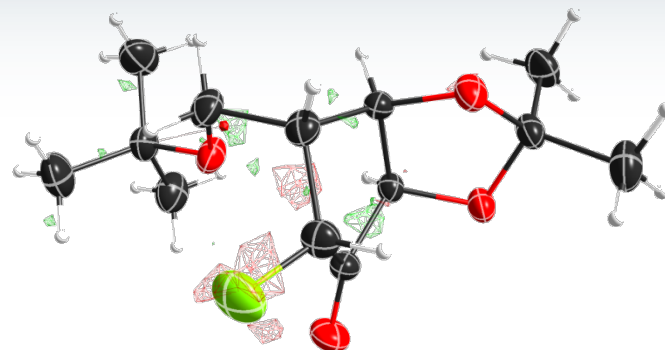


R1 = 2.95%



R1 = 2.50%

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

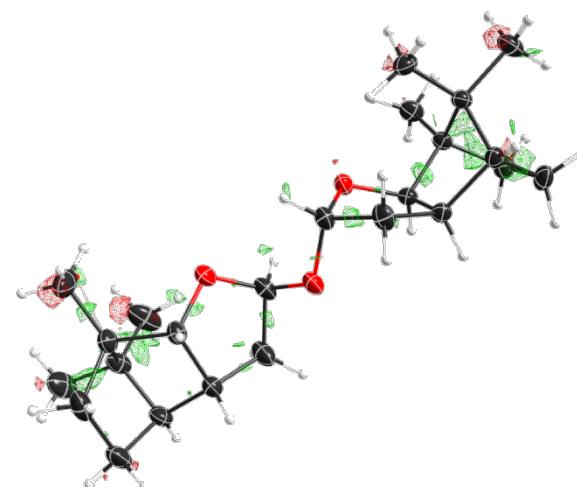


R1 = 2.99%

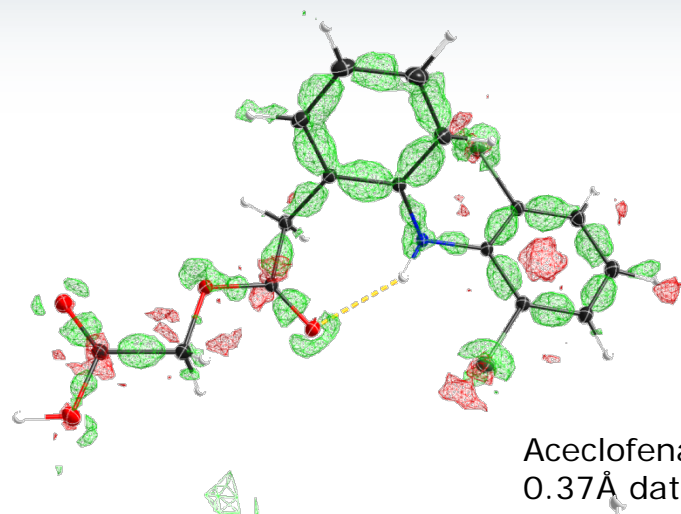


R1 = 2.51%

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



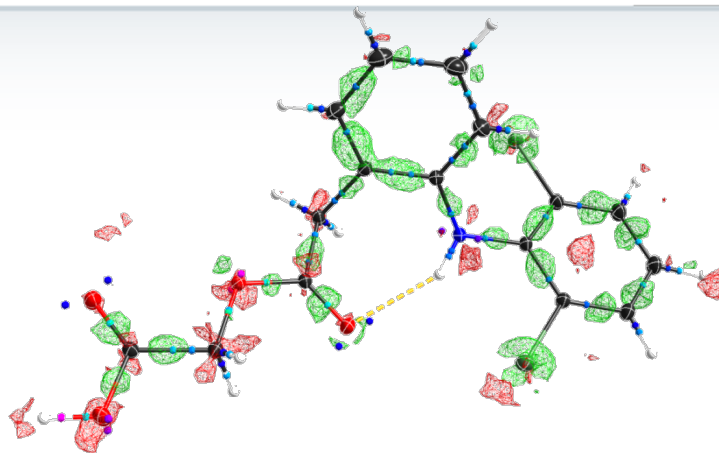
IDEAL - More (Problematic) Examples



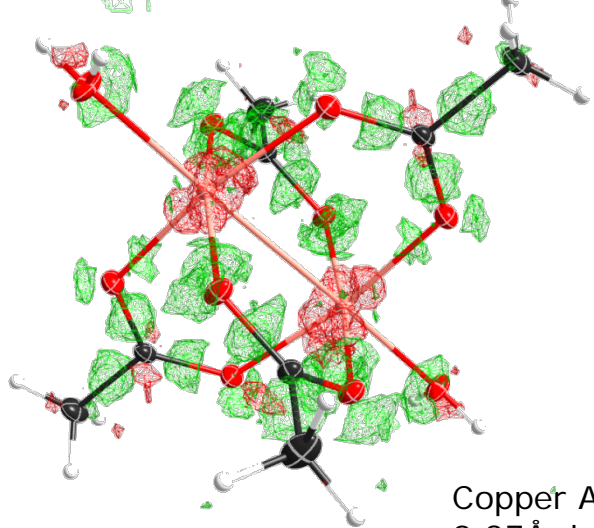
R1 = 2.33%



R1 = 2.13%



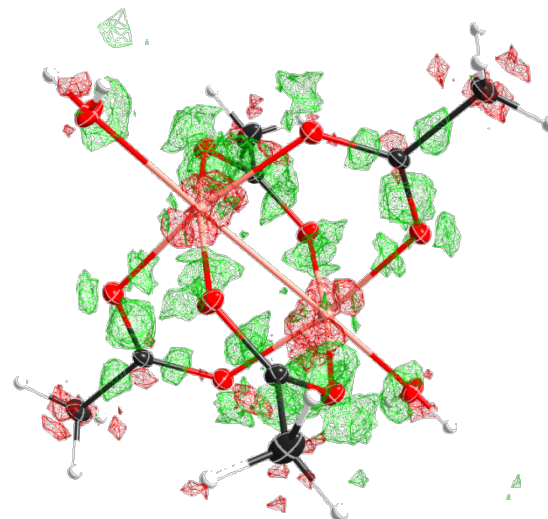
Aceclofenac, Chloride bonds not modeled
0.37Å data, Fo-Fc maps at same level



R1 = 1.38%



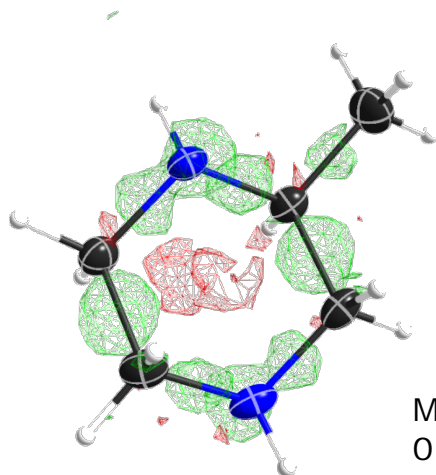
R1 = 1.36%



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?

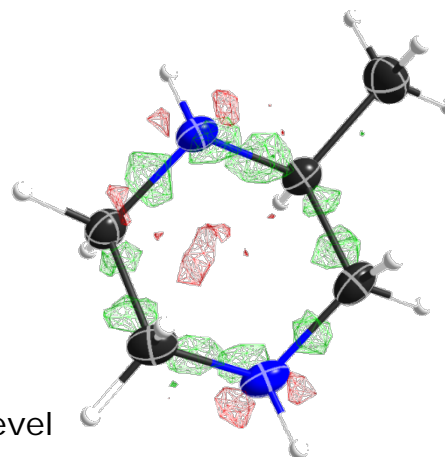


$R1 = 2.72\%$



$R1 = 2.35\%$

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

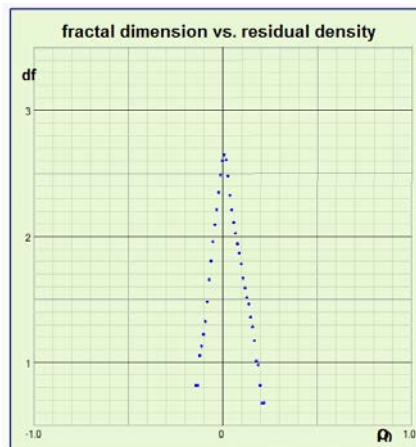
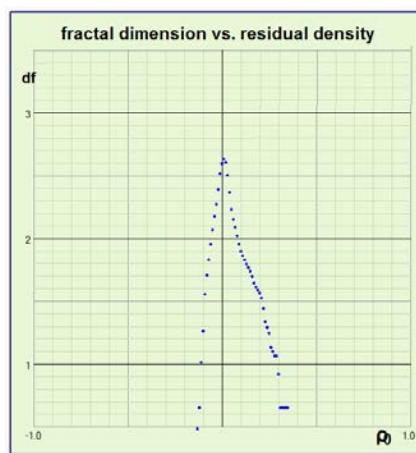
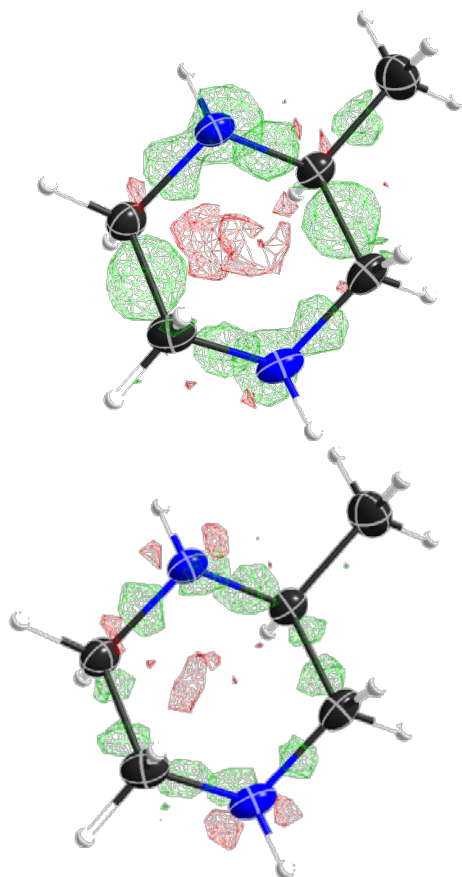


IDEAL - Fractal dimension analysis



- 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
pmin (d=2)	-0.067 eÅ ⁻³
pmax (d=2)	0.070 eÅ ⁻³
pmin	-0.141 eÅ ⁻³
pmax	0.343 eÅ ⁻³
e gross	3.59 e ⁻
Δ ρ	0.484 e ⁻ Å ⁻³

Residual density descriptors

df0	2.66
pmin (d=2)	-0.051 eÅ ⁻³
pmax (d=2)	0.064 eÅ ⁻³
pmin	-0.154 eÅ ⁻³
pmax	0.218 eÅ ⁻³
e gross	3.00 e ⁻
Δ ρ	0.372 e ⁻ Å ⁻³

Residual density descriptors

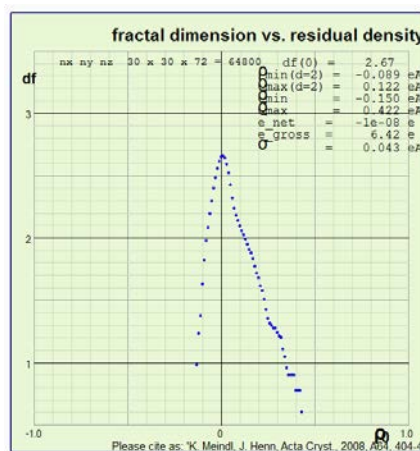
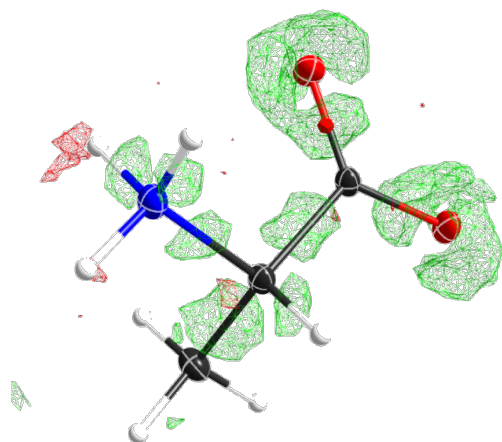
- **e gross** - The gross residual electrons describe the total inadequacies that arise from the following error:
 - Noise
 - Inadequate data processing
 - Density model errors
 - Can artificially lowered by truncating the experimental resolution
- **df0** - measure for the featurelessness of the residual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

IDEAL - Fractal dimension analysis



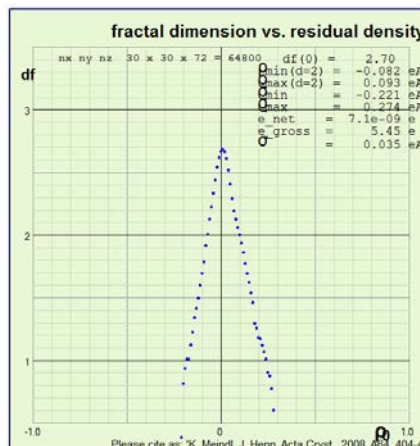
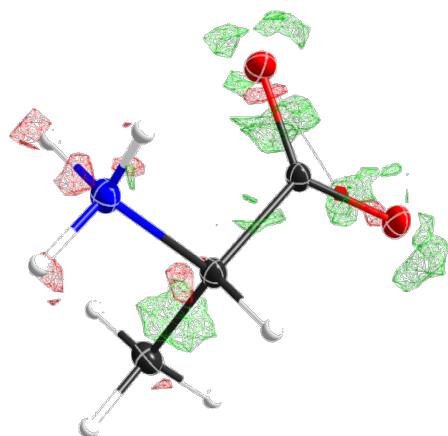
- Fractal dimension analysis

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



Residual density descriptors

df0	2.67
pmin (d=2)	-0.089 eÅ ⁻³
pmax (d=2)	0.122 eÅ ⁻³
pmin	-0.150 eÅ ⁻³
pmax	0.422 eÅ ⁻³
e gross	6.42 e ⁻
Δ ρ	0.572 e ⁻ Å ⁻³



Residual density descriptors

df0	2.70
pmin (d=2)	-0.082 eÅ ⁻³
pmax (d=2)	0.093 eÅ ⁻³
pmin	-0.221 eÅ ⁻³
pmax	0.274 eÅ ⁻³
e gross	5.45 e ⁻
Δ ρ	0.495 e ⁻ Å ⁻³

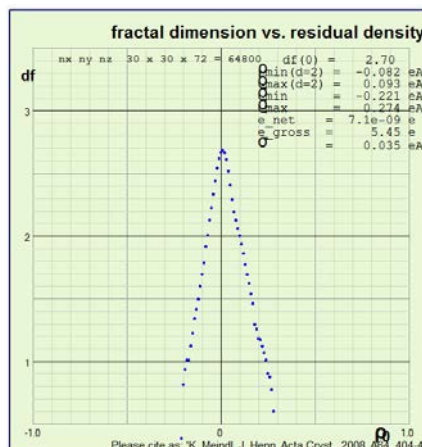
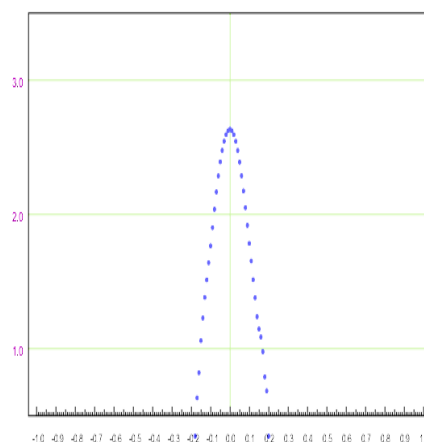
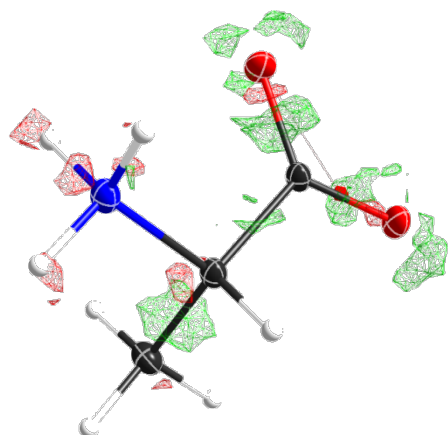
IDEAL - Fractal dimension analysis

how does it compare



- Fractal dimension analysis

MoPro Multipole
refinement



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Residual density descriptors

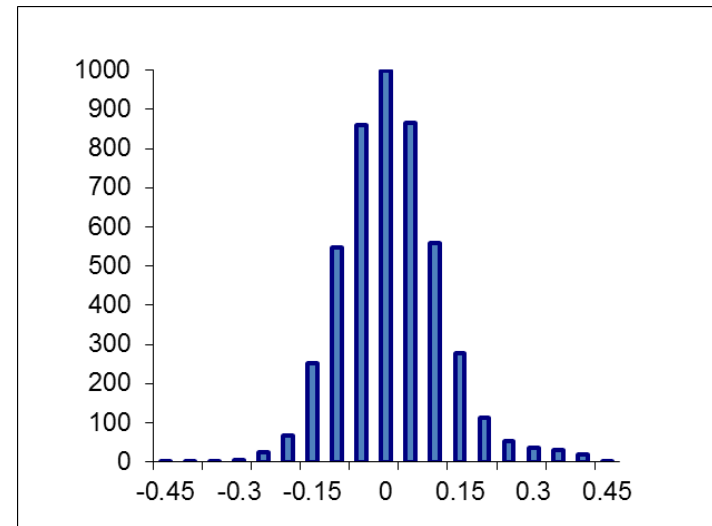
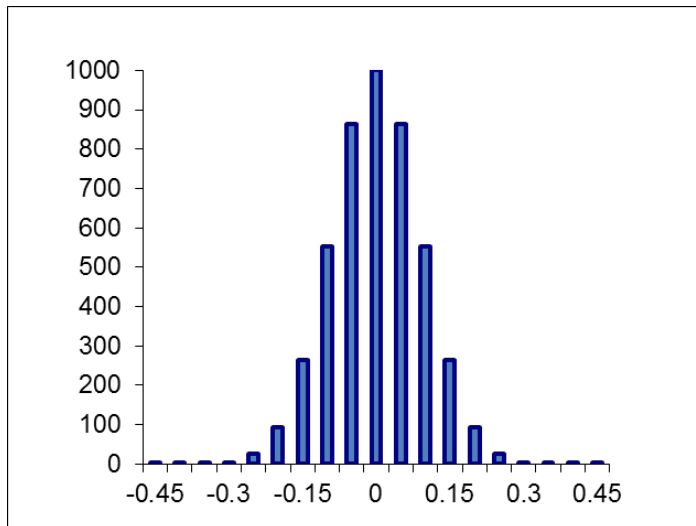
df0	2.6345
pmin (d=2)	-0.083 eÅ ⁻³
pmax (d=2)	0.084 eÅ ⁻³
pmin	-0.18 eÅ ⁻³
pmax	0.21 eÅ ⁻³
e gross	5.43 e ⁻
Δ ρ	0.39 e ⁻ Å ⁻³

Residual density descriptors

df0	2.70
pmin (d=2)	-0.082 eÅ ⁻³
pmax (d=2)	0.093 eÅ ⁻³
pmin	-0.221 eÅ ⁻³
pmax	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

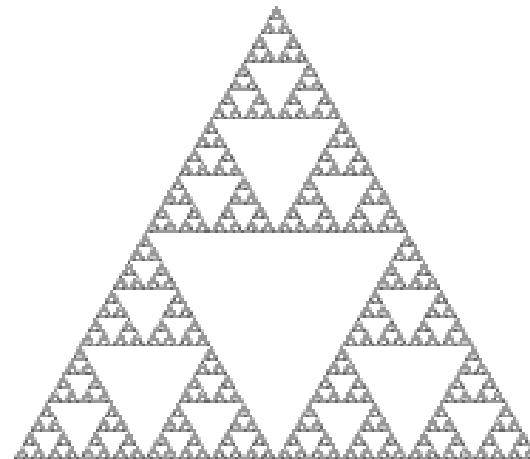


Fractal dimension analysis

- 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

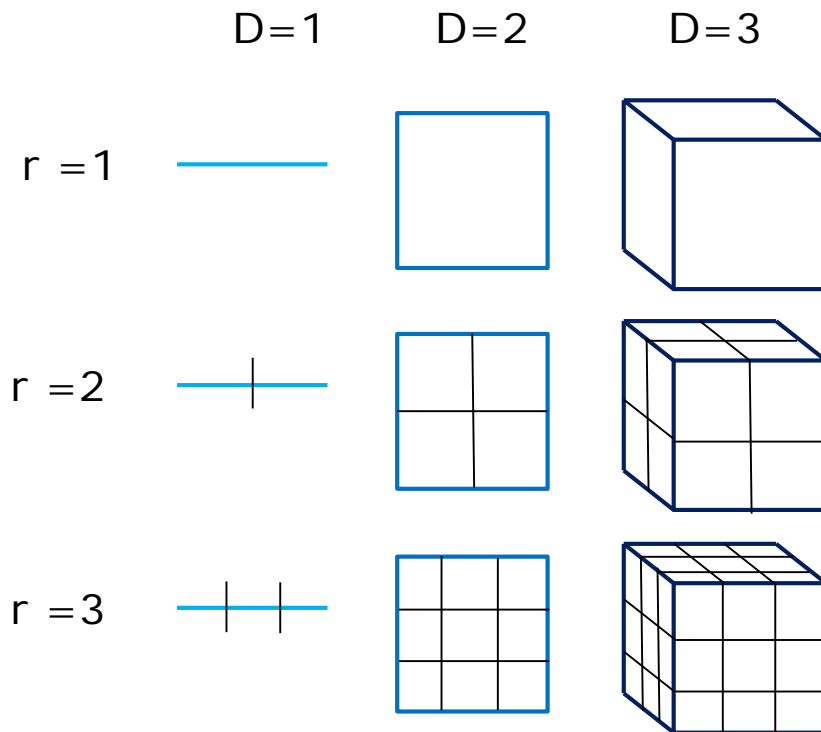
What is a fractal dimension?

- **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 $N=r^D$
- $\log(N) = D \log(r)$.

- **$D = \log(N)/\log(r)$**

- **$D = \frac{\log(\text{number of self-similar pieces})}{\log(\text{magnification factor})}$**

- 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

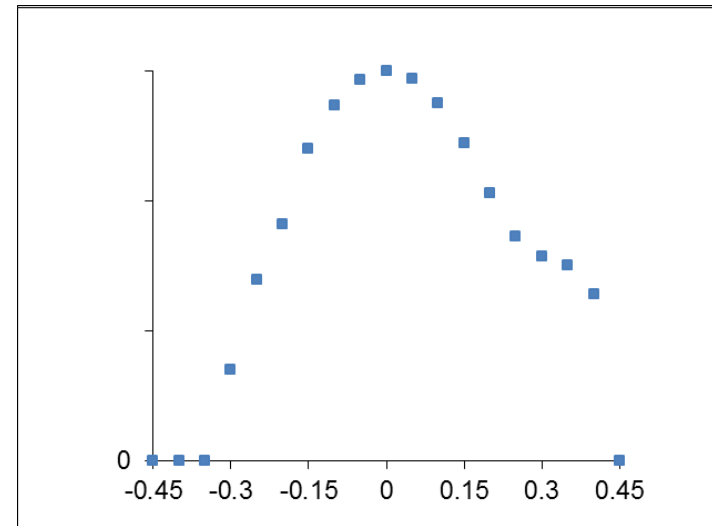
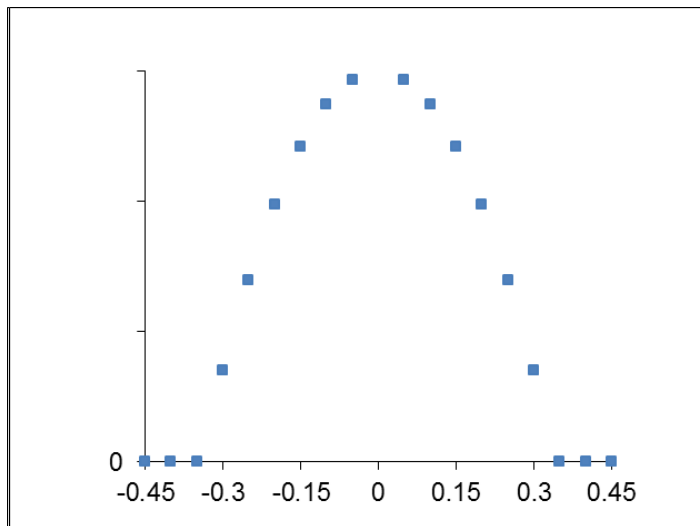


- The fractal dimension of a residual-density iso-surface of constant value x can be evaluated by a box counting algorithm using a finite grid
- If one is interested in the zero residual-density iso-surface, one just counts the number of boxes containing at least one point of zero residual density
- 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

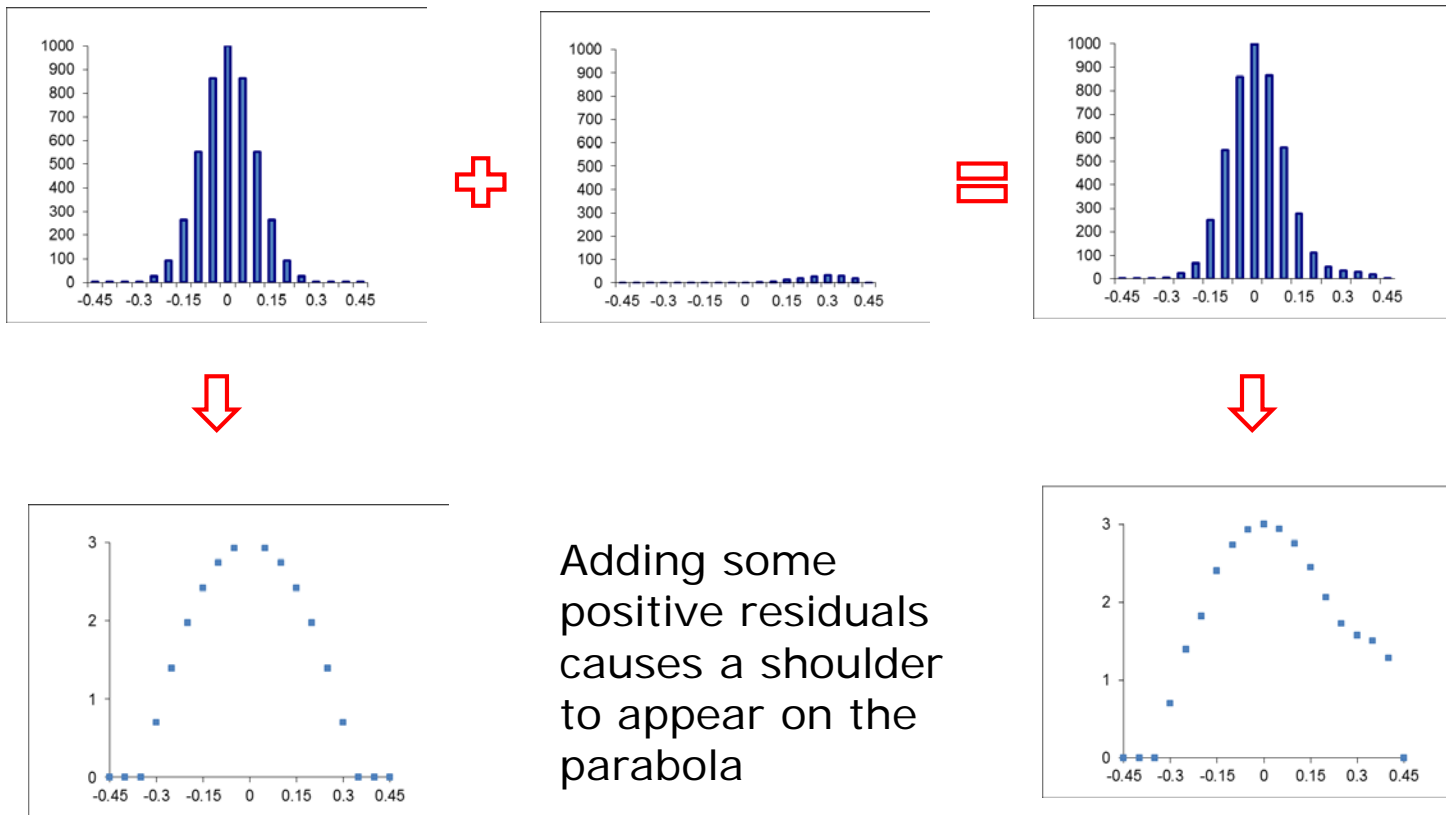


- In the special case of a distribution containing Gaussian noise with a mean of zero and no model errors the corresponding fractal dimension distribution is of parabolic shape
- The max value of df_0 is 3



Fractal dimension in residual density analysis

- So where does the shoulder come from?



IDEAL - Fractal dimension analysis



- Fractal dimension analysis

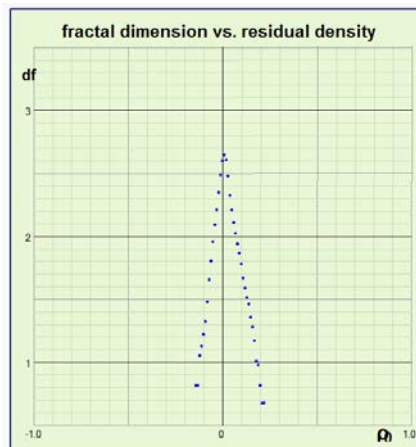
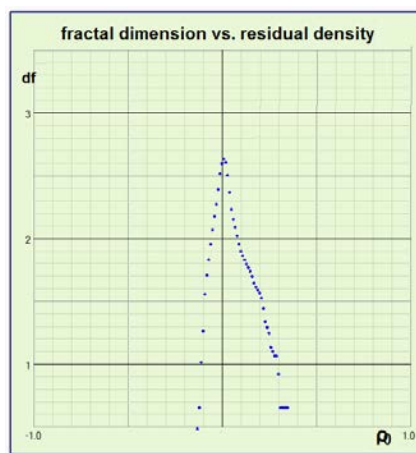
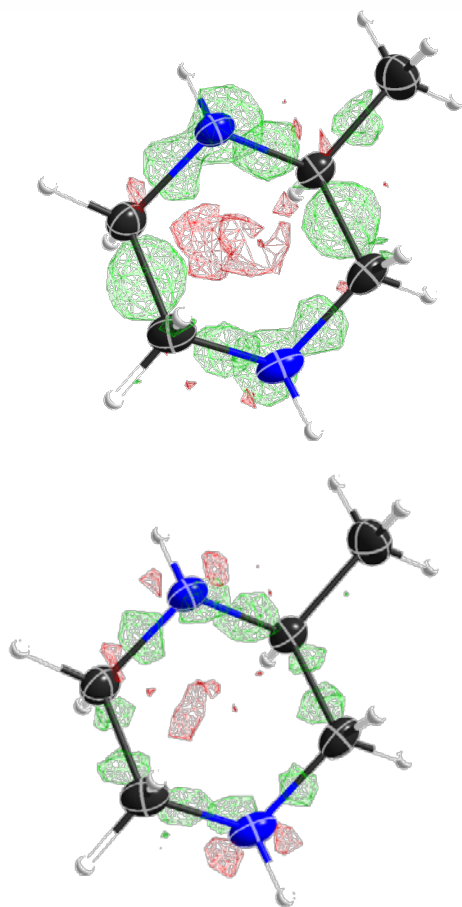
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Residual density descriptors

df0	2.65
pmin	-0.141 eÅ ⁻³
pmax	0.343 eÅ ⁻³
e gross	3.59 e ⁻
Δ ρ	0.484 e ⁻ Å ⁻³

Residual density descriptors

df0	2.66
pmin	-0.154 eÅ ⁻³
pmax	0.218 eÅ ⁻³
e gross	3.00 e ⁻
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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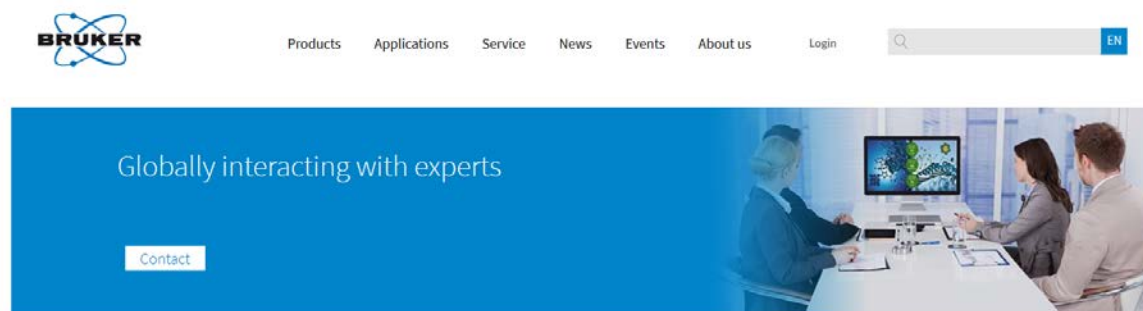
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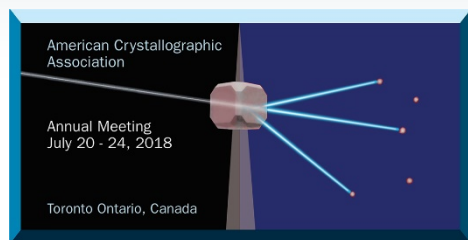
Webinar	Content
Jul 10, 2018	In this 45-minute webinar Jens Lubben and Michael Ruf will talk about a new addition to Bruker's APEX3 software for structure analysis: IDEAL - Invariom Derived Electron Analysis. Jens will introduce you to the theory of IDEAL, while Michael will focus on its practical application and implementation in APEX3.
IDEAL - Invariom Derived Electron Analysis: Have the Cake and Eat It Too!	Register now!

単結晶X線構造解析の測定において一つ一つの反射強度をできるだけ正確にS/Nよく測定することは、言うまでもなく最重要課題です。装置は年々進化し、そのパフォーマンスはどんどんよくなっています。同じ測定条件下で測定し、アモルファス試料の測定結果を比較すると、その差は顕著です。これは、装置の進化によるものです。この webinar では、最新の APEX3 ソフトウェアの IDEAL (Invariom Derived Electron Analysis) という新しい機能について、その理論と実践的な応用について詳しく説明します。また、この機能が APEX3 に実装されている点についても触れます。

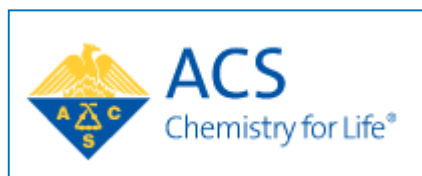
Webinar	Content
Dec 12, 2016	In this 45-minute webinar, Przemyslaw Dera and Michael Ruf will talk about high-pressure crystallography performed on a Bruker home-lab instrument. Przemek's will start with a brief introduction to high-pressure crystallography.
High-pressure X-ray Crystallography for the Home Lab	View recording or download slides

Oct 25, 2016	In this 40-minute webinar, Matt Benning will discuss the current trends in Native SAD phasing. This webinar will focus on the basic theory and experimental practices involved in SAD phasing as well as sub-structure determination and phasing using the SHELX suite.
Protein X-ray Crystallography: Native SAD	

Meet us at these upcoming events



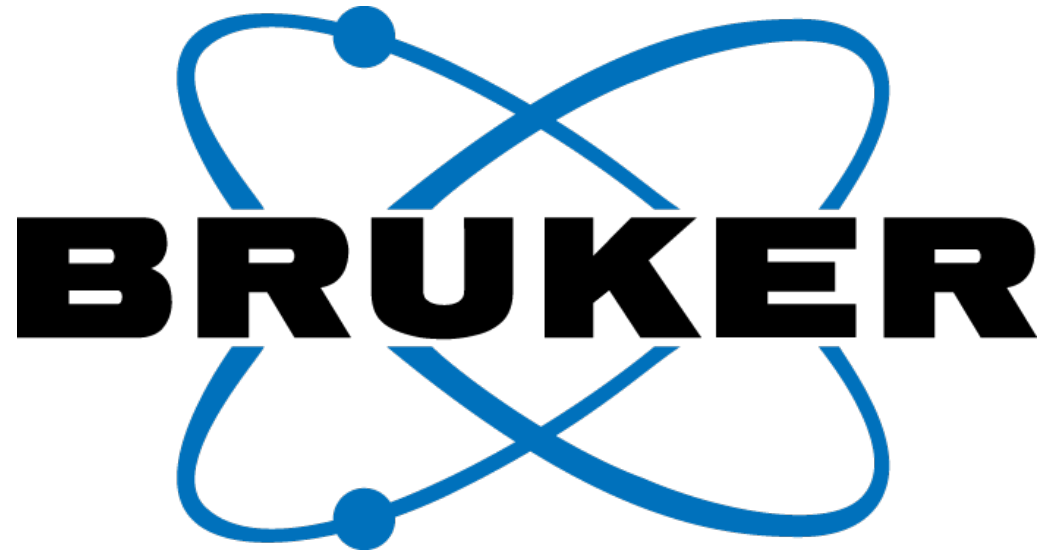
ACA Annual Meeting
July 20 to 24, 2018
Toronto, Canada



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