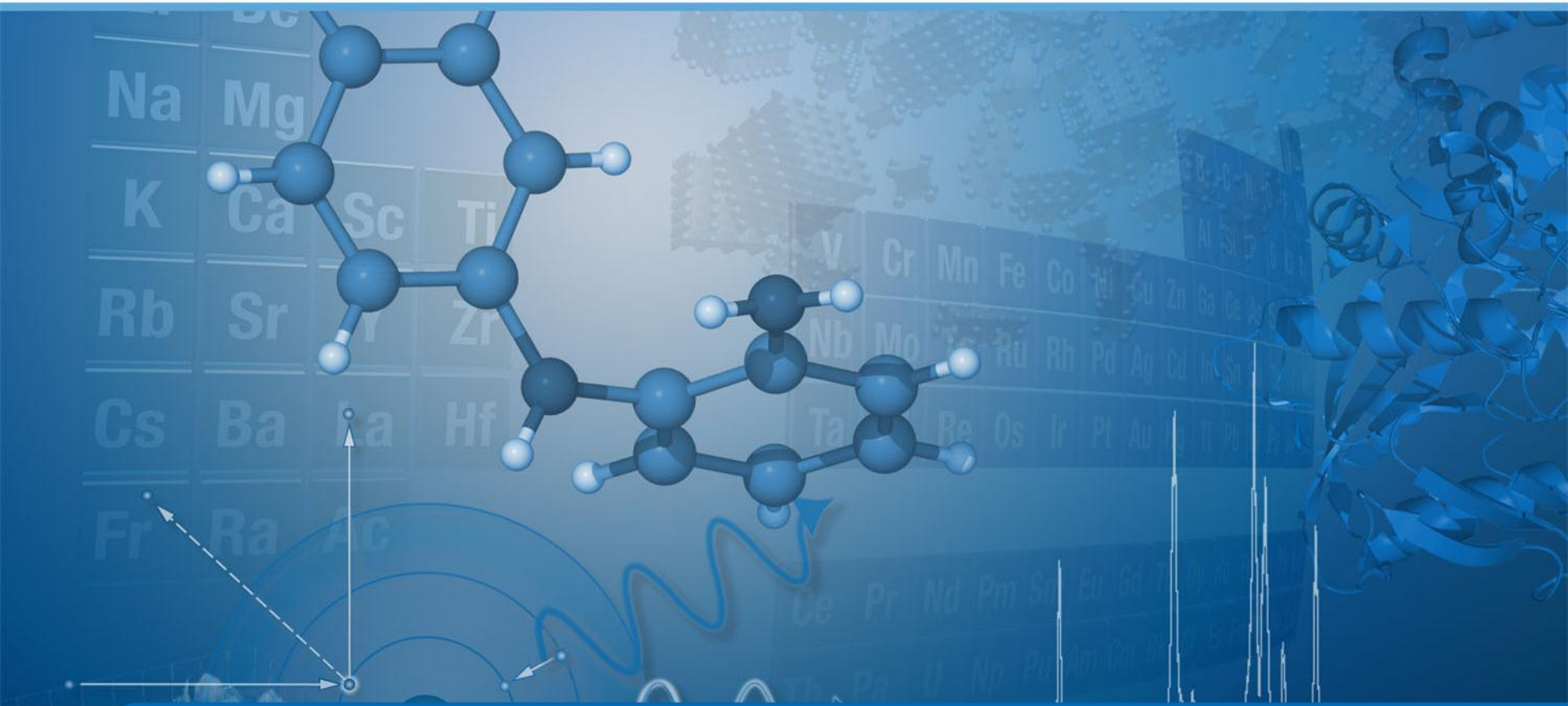
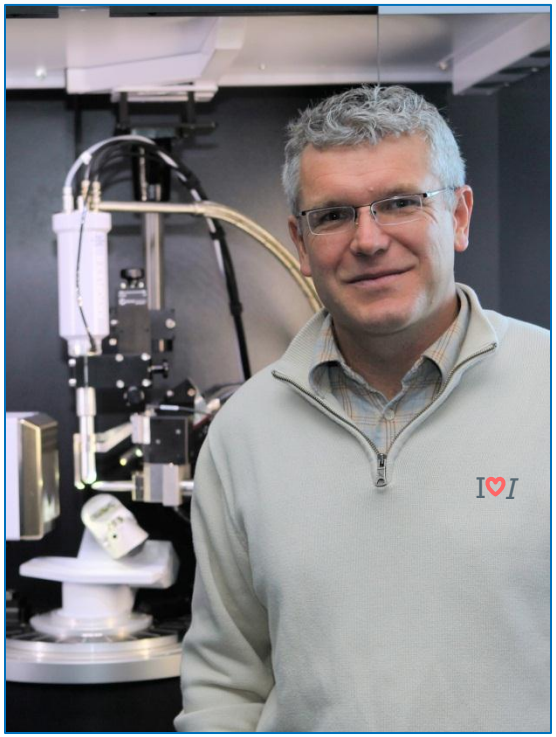
Fast, Intuitive Structure Determination IV: Space Group Determination and Structure Solution



November 25, 2013

Welcome



Dr. Michael Ruf
Product Manager – Crystallography
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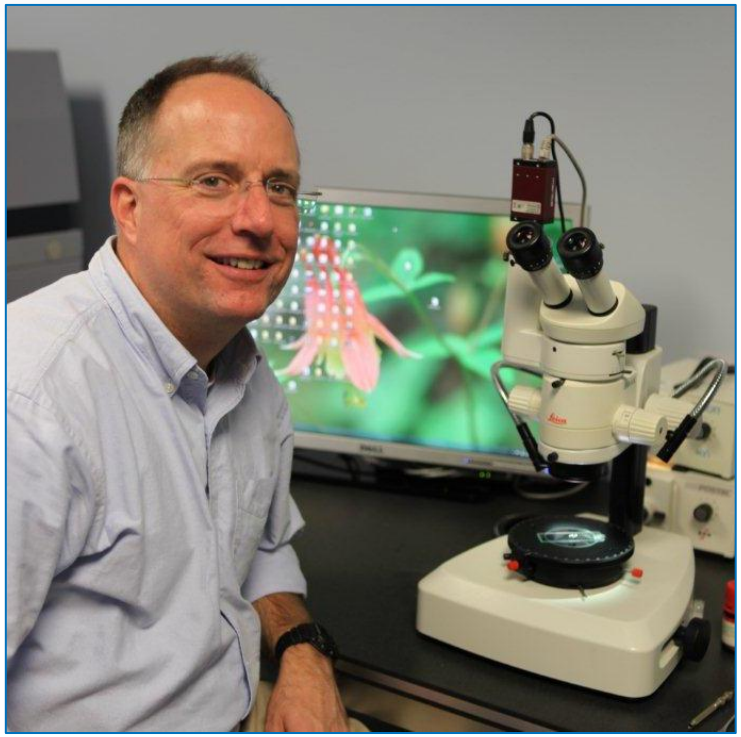

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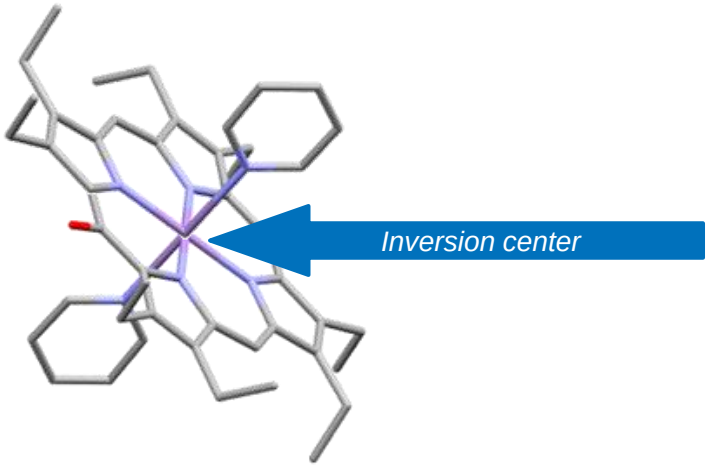
Space Group Determination

Overview

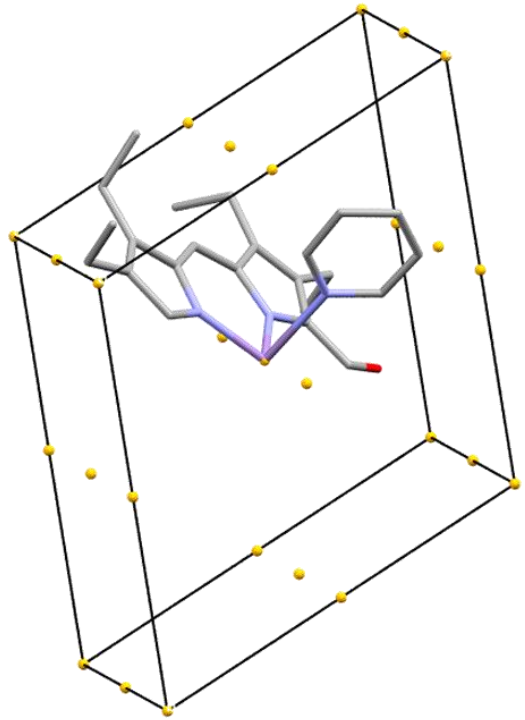
- The space group defines relationships between the asymmetric unit, the contents of the unit cell, and the entire crystal.
- Determining the proper three-dimensional symmetry facilitates the mathematics underlying the structure determination.
- Determination of the space group is made by examination of the Laue symmetry, $|E|$ statistics, and systematic absences.

Crystallographic symmetry



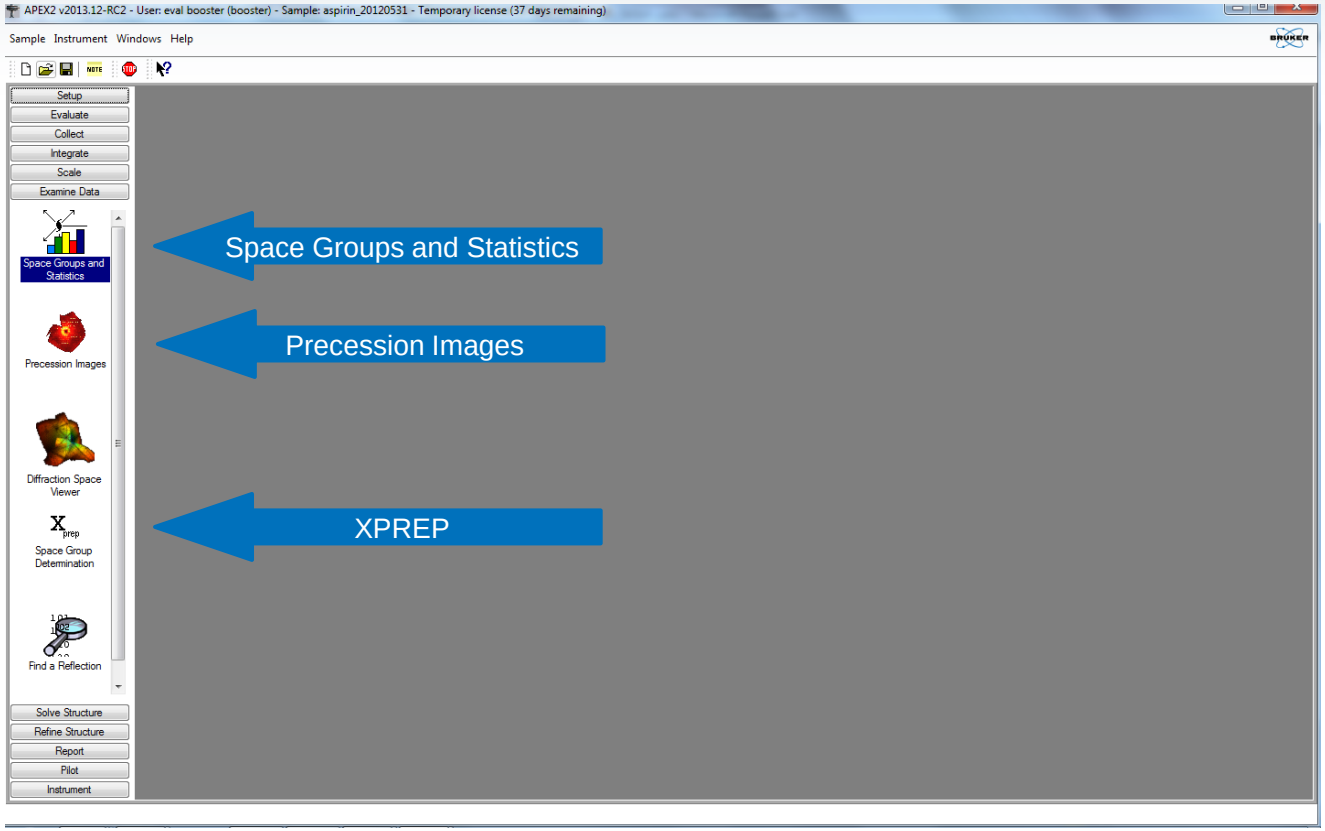
- Symmetry defines structure.
- Asymmetric unit: smallest set of atoms to generate crystal structure from symmetry elements of space group.
- Asymmetric unit possesses no crystallographic symmetry except the identity element.

Unit Cell



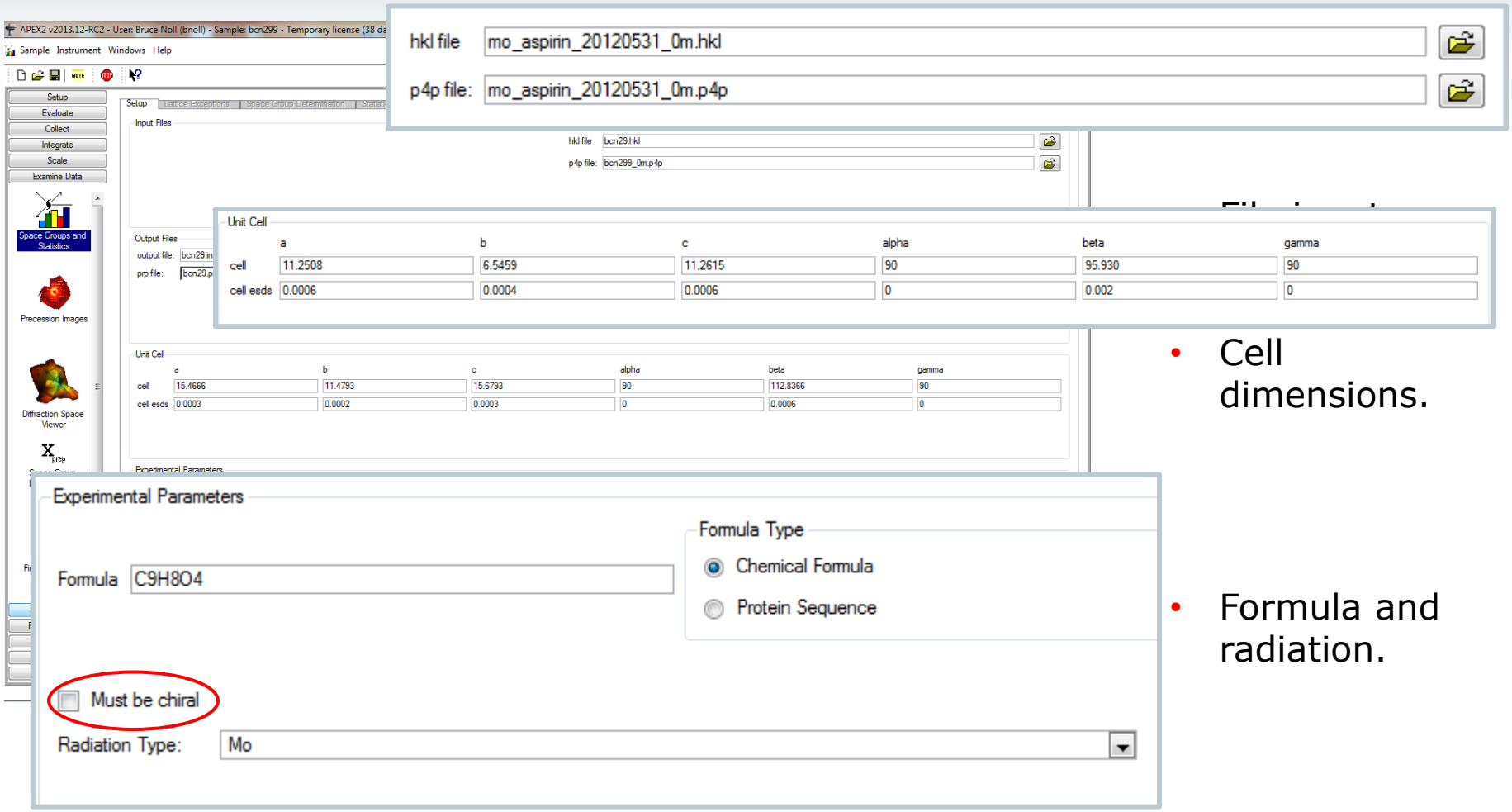
- The unit cell is the smallest repeating set.
- Neighboring sets can be generated by translation.

Determining the Space Group with APEX2



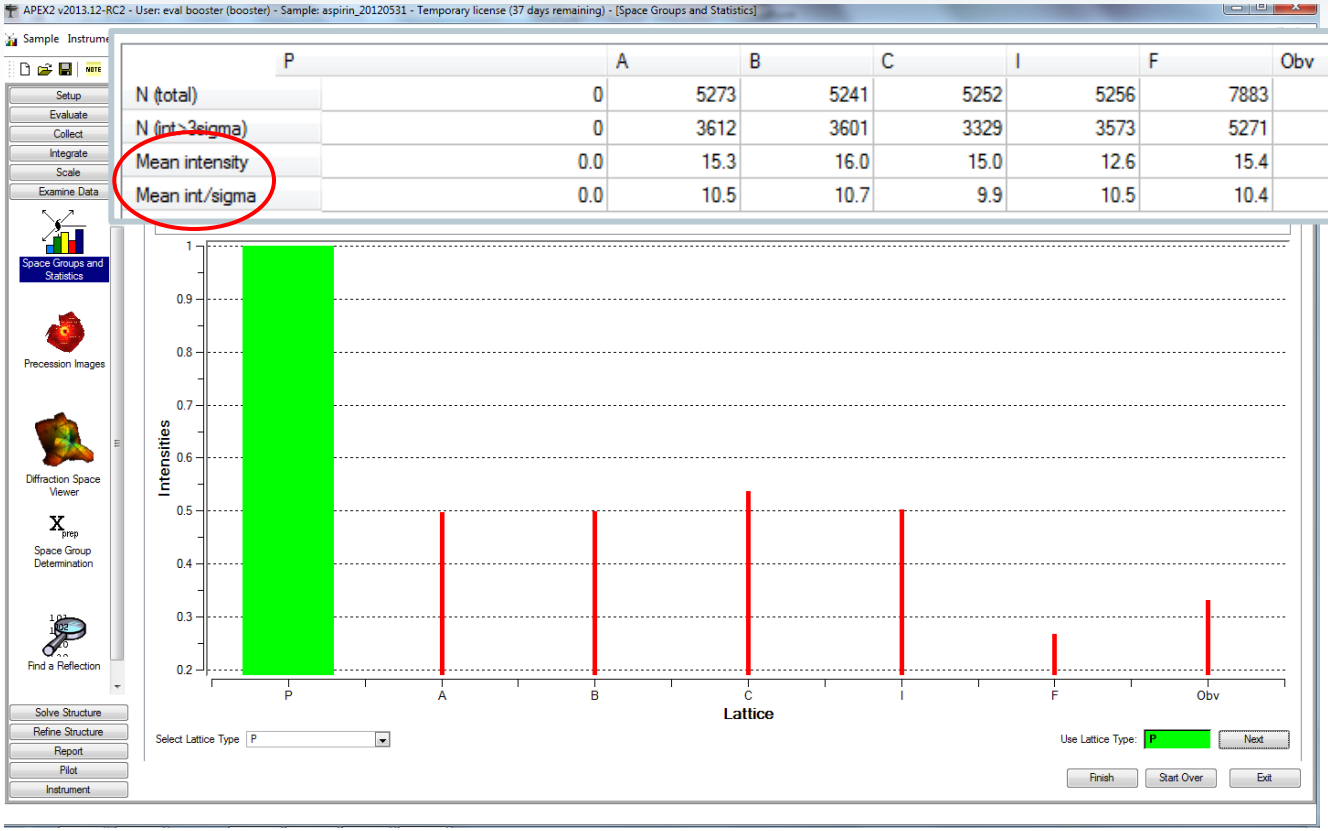
- The Examine Data set of tools.
- Space Groups and Statistics: GUI for XPREP.
- Precession Images: inspect reciprocal lattice layers.
- XPREP: Engine for data analysis.

Space Groups and Statistics



- Cell dimensions.
- Formula and radiation.

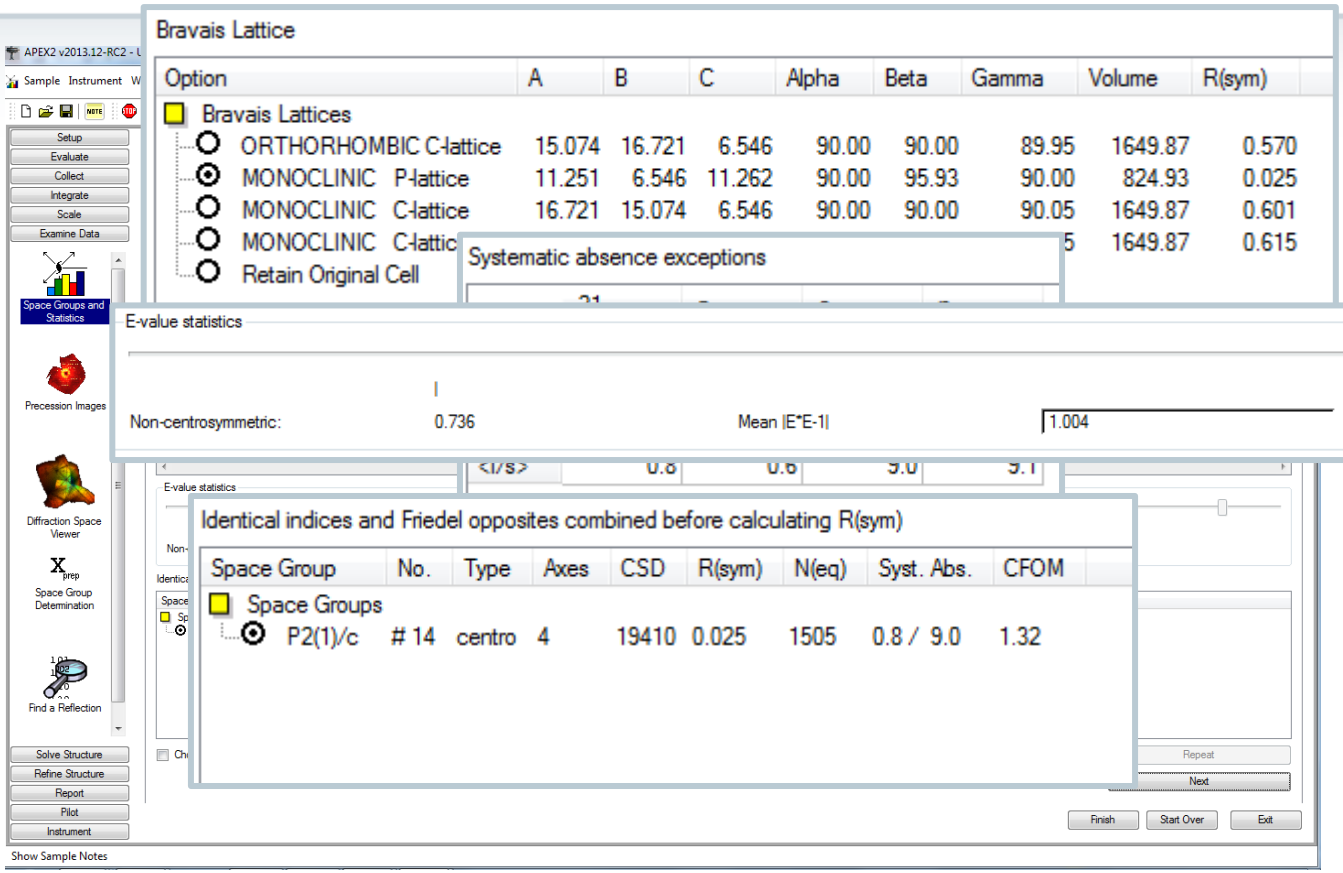
Lattice Exceptions



...on for

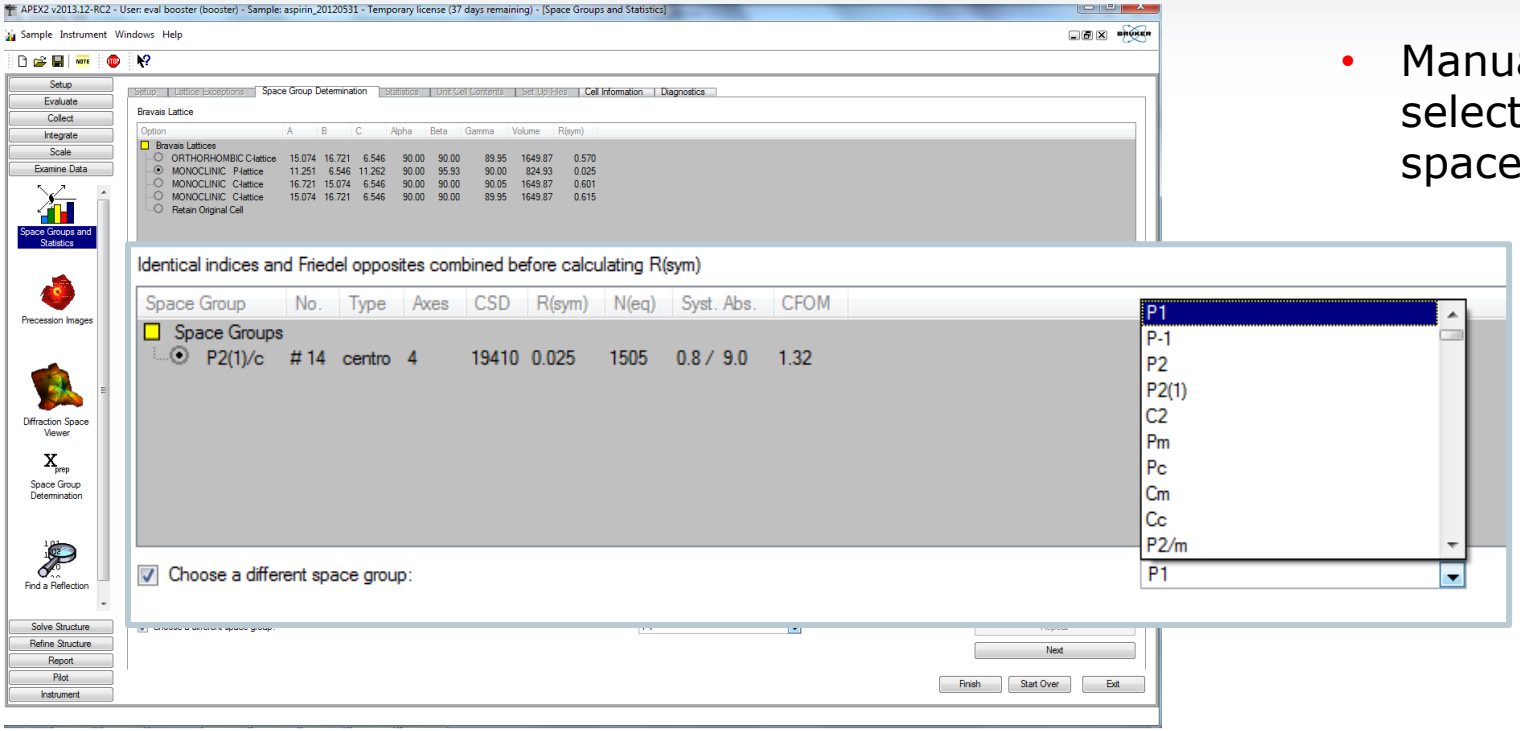
- For condition to be met, <I> and <I/σ> approach zero.

Space Group Determination



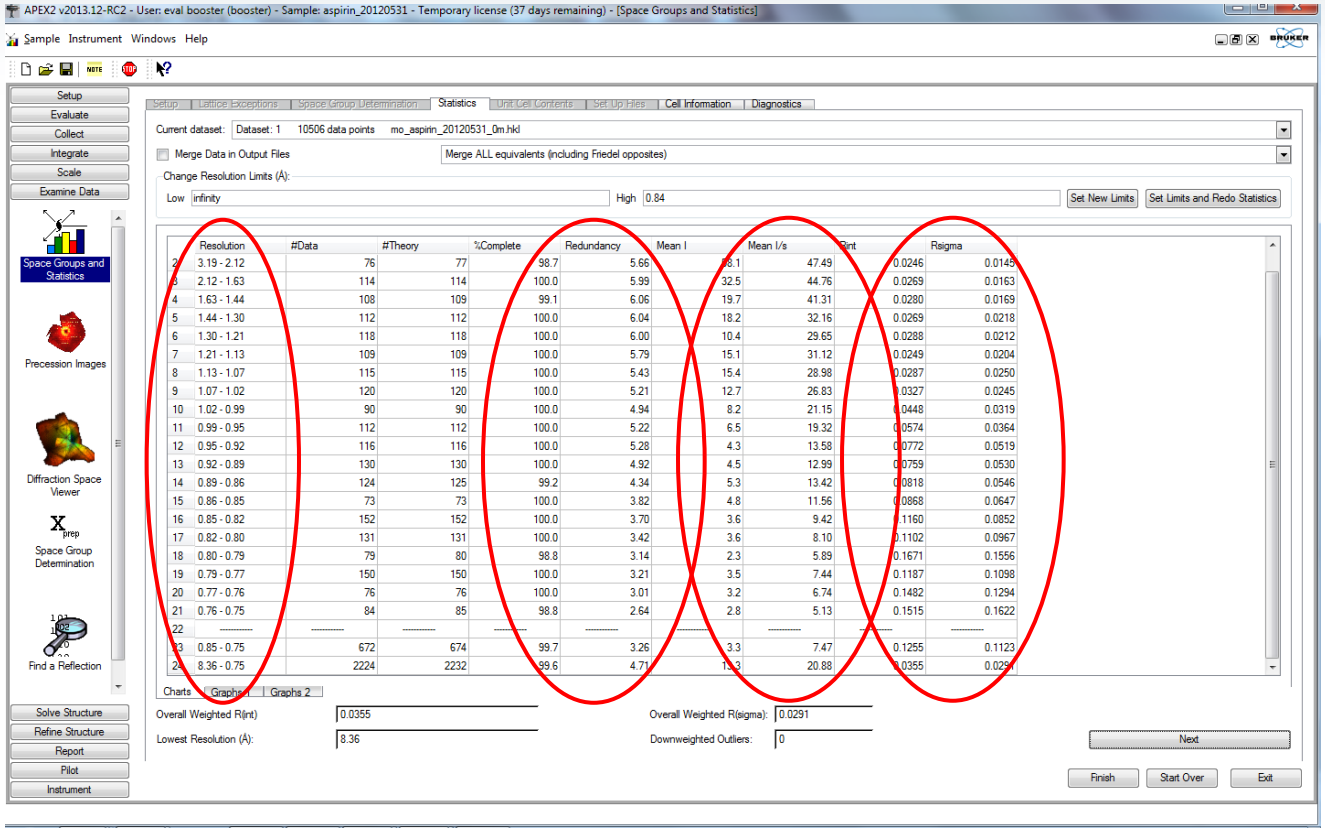
- Bravais lattice determination.
- Systematic
- Calculation of $|E^2-1|$.
- Possible space groups.

Space group selection



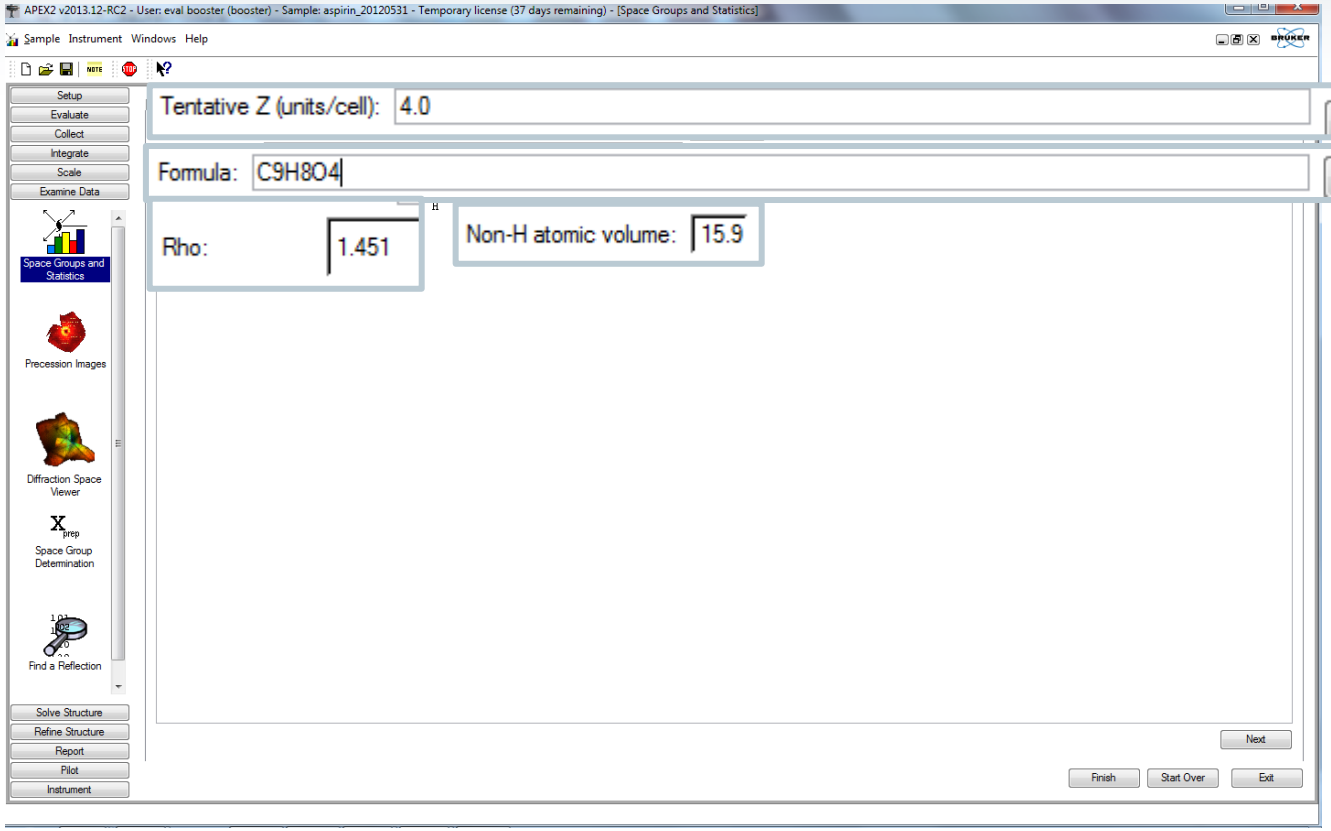
- Manual selection of space group.

Summary Statistics



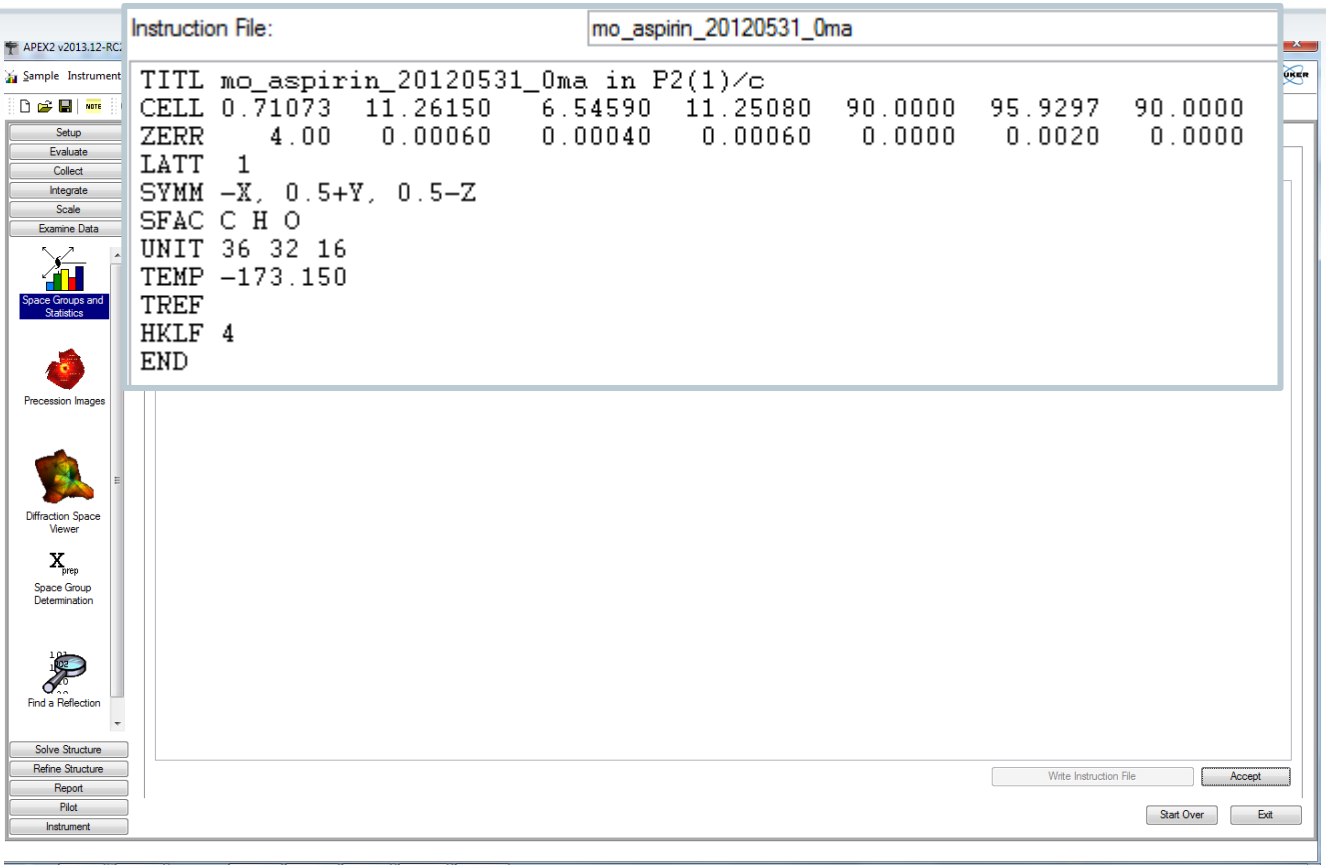
- Ranked by resolution shells
- Completeness and redundancy
- Intensity and I/σ
- R(int) and R(sigma)

Unit Cell Contents



- Chemical formula
- Value of Z
- Density
- Non-hydrogen atomic volume

Set Up Files



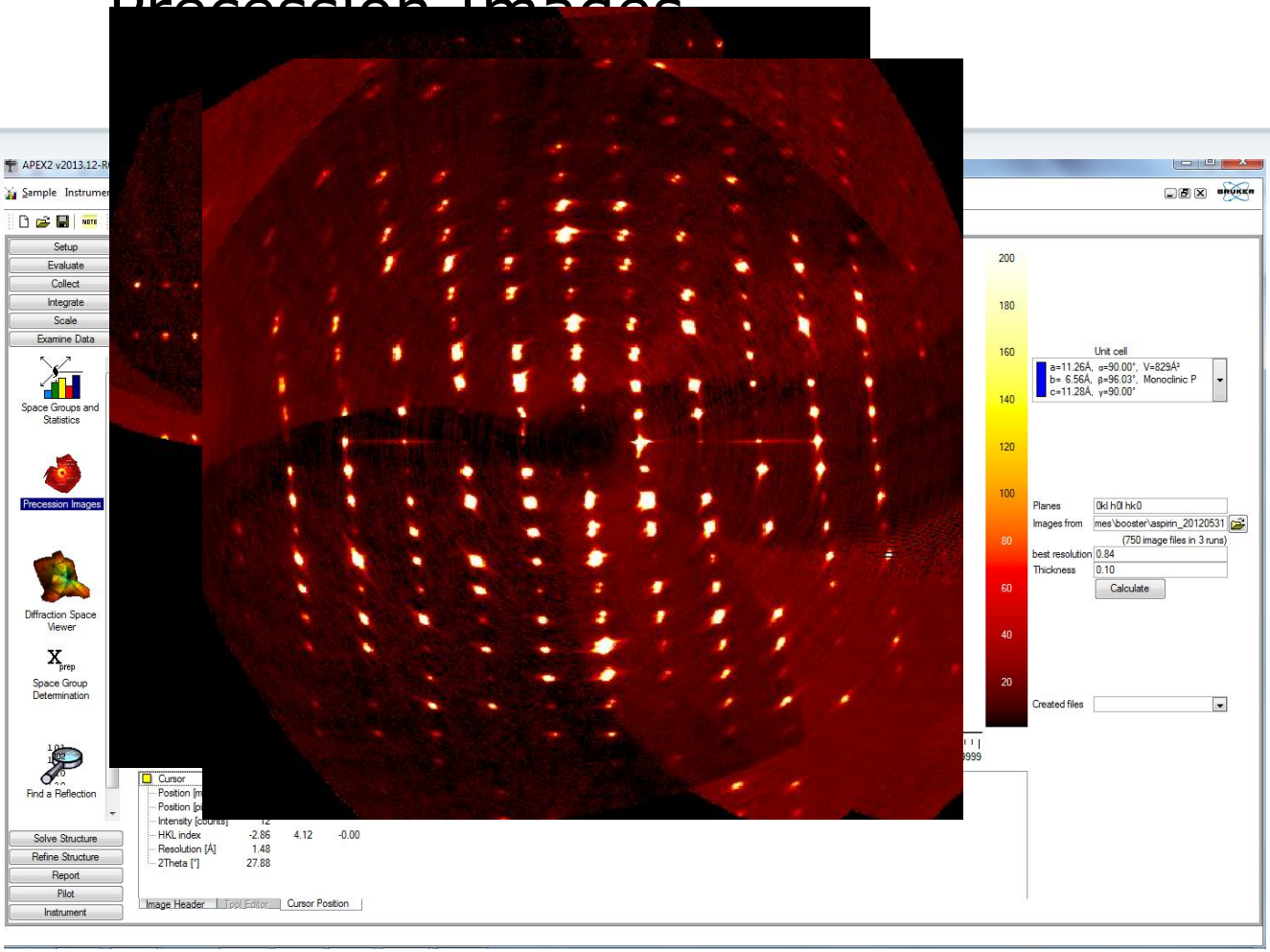
- Instructions for SHELX solution programs
- HKL file with current orientation and limits.

XPREP

```
++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++
+  XPREP - Reciprocal space exploration  - Version 2013/3 for Windows  +
+  COPYRIGHT(c) 2013 Bruker-AXS                  All Rights Reserved  +
++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++

Screen size: 1440 x  900
Window size:  640 x  799
Font size:      8 x   16  (  125 x  206 )
Number of colors:    256

When xprep is started without a filename on the command line, the filename
is prompted for and then the type of data (SHELX, SCALEPACK, XDS or XENGEN)
requested.  To generate ideal data, a SHELX .ins or .res file, if necessary
made from a PDB file using SHELXPRO or XPRO, should be given.

'xprep name' reads a SHELX HKLF 4 format file name.hkl, then tries to find
name.spin or name.p4p to extract the cell dimensions and their esds.
'xprep name1 name2' reads name1.hkl and name2.p4p (or name2.spin).

-Ln on the command line allocates space for 1000000n data (default n=4).

** Data multiplied by   0.1000  to bring onto reasonable scale **

  10506 Reflections read from file mo_aspirin_20120531_0m.hkl
  Mean (I/sigma) =   10.43


Lattice exceptions: P      A      B      C      I      F     Obv    Rev    All

N (total) =           0   5273   5241   5252   5256   7883   7002   7021  10506
N (int>3sigma) =      0   3612   3601   3329   3573   5271   4815   4816   7192
Mean intensity =    0.0   15.3   16.0   15.0   12.6   15.4   15.4   15.8   15.3
Mean int/sigma =    0.0   10.5   10.7    9.9   10.5   10.4   10.3   10.5   10.5

Lattice type [P, A, B, C, I, F, O(obv.), R(rev. rhomb. on hex. axes)]

Select option [P]:
```

- XPREP drives the Space Groups and Statistics plug-in.
- Full functionality of XPREP is retained in separate plug-in.

Precession Images



- Precession images created from collected frames.
- On hk0 image, 0k0 = 2n → 2_1 element.
- On h0l image, h= 2n → a-glide element.

Space Group Determination

- APEX2 has outstanding capabilities for data analysis and space group determination through George Sheldrick's XPREP.
- Precession images are useful for diagnosing difficult questions of symmetry.
- The tools of APEX2 facilitate space group assignment, leading to success with structure solution and refinement.

Structure solution with APEX2 software

Structure solution with APEX2 software

- APEX2 software provides a powerful interface for interactive structure solution

- The “Structure Solution” plugin is a wrapper around George Sheldrick’s programs for structure solution and includes
  - XS for Direct Methods
  - XS for Patterson Methods
  - XM for “dual space methods”
  - XT for “Intrinsic phasing”

- Data statistics
- Intelligent default parameters
- Manual input
- Molecule viewer

The Phase Problem

- A diffraction pattern produced by shooting monochromatic X-rays at a crystal can be understood as the Fourier transform of the complete electron density of the crystal structure. In principle the electron density can be simply reconstructed by Fourier synthesis.

- In reality, the problem is that only the intensities of the waves of the diffraction pattern can be recorded. The information about the phase of the wave, the relative timing when each wave hits, is lost in the experiment

- The problem of elucidating the phases when only the magnitudes are known is referred to as the “Phase Problem”

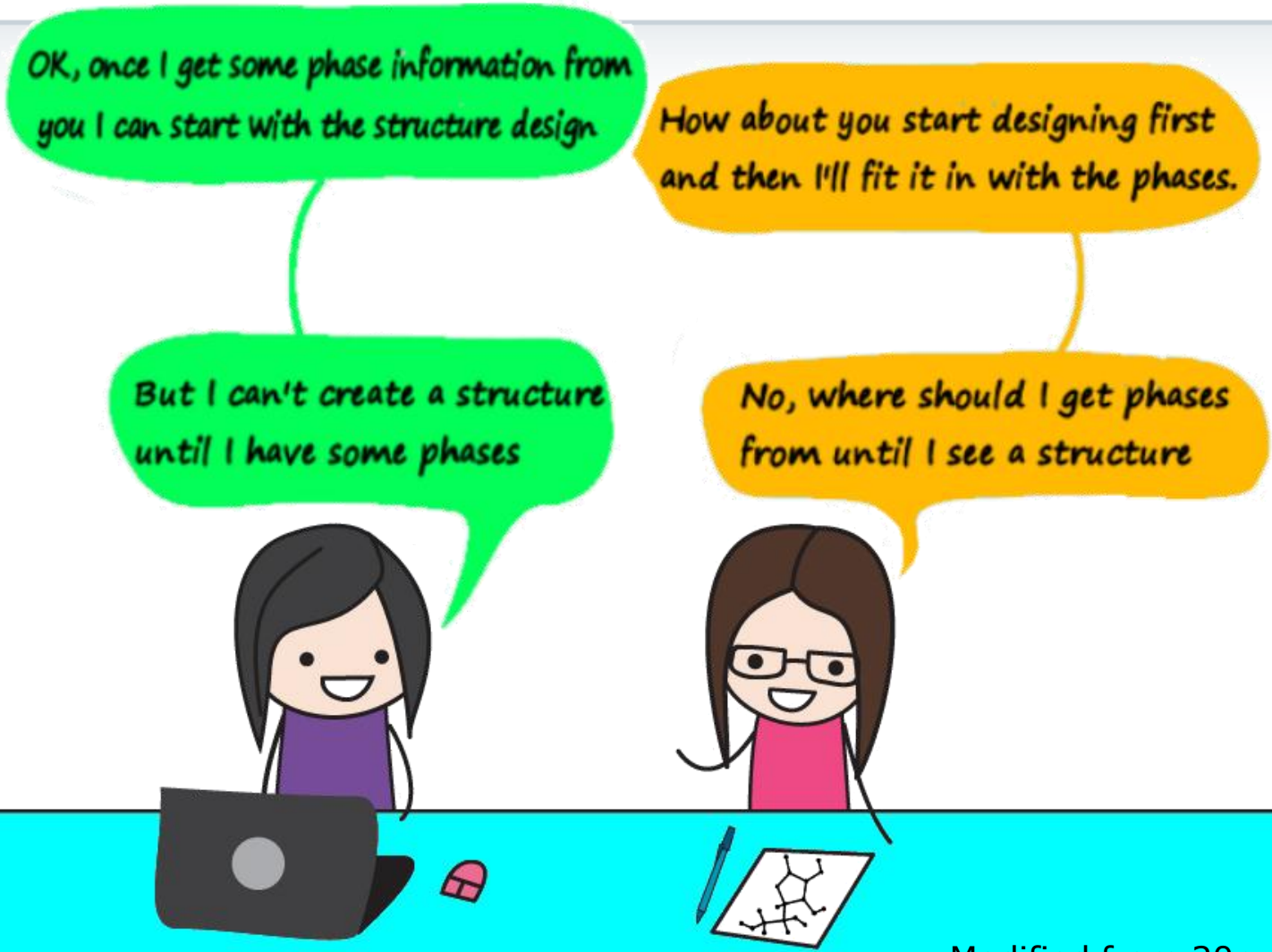
Structure solution

- Crystallographers consider a crystal structure to be solved when the phases of enough reflections are well enough determined so that most if not all of the atoms in the unique part of the unit cell are revealed.

- The problem of elucidating the phases when only the magnitudes are known is referred to as the “phase problem”.

- There are several ways to solve the crystal structure of a small molecule compound.

I want that structure…

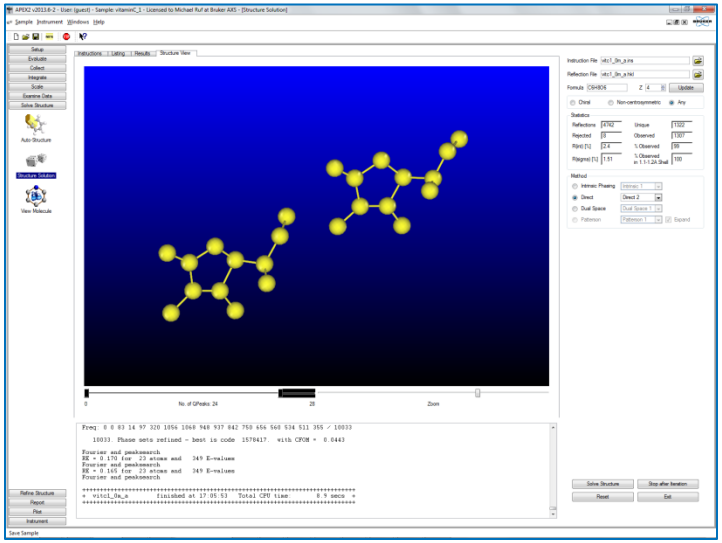


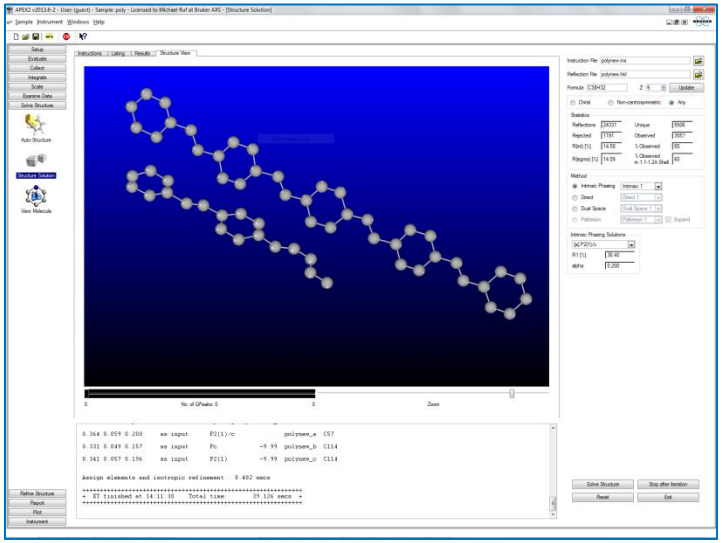
Modified from 20px.com

Structure solution with APEX2

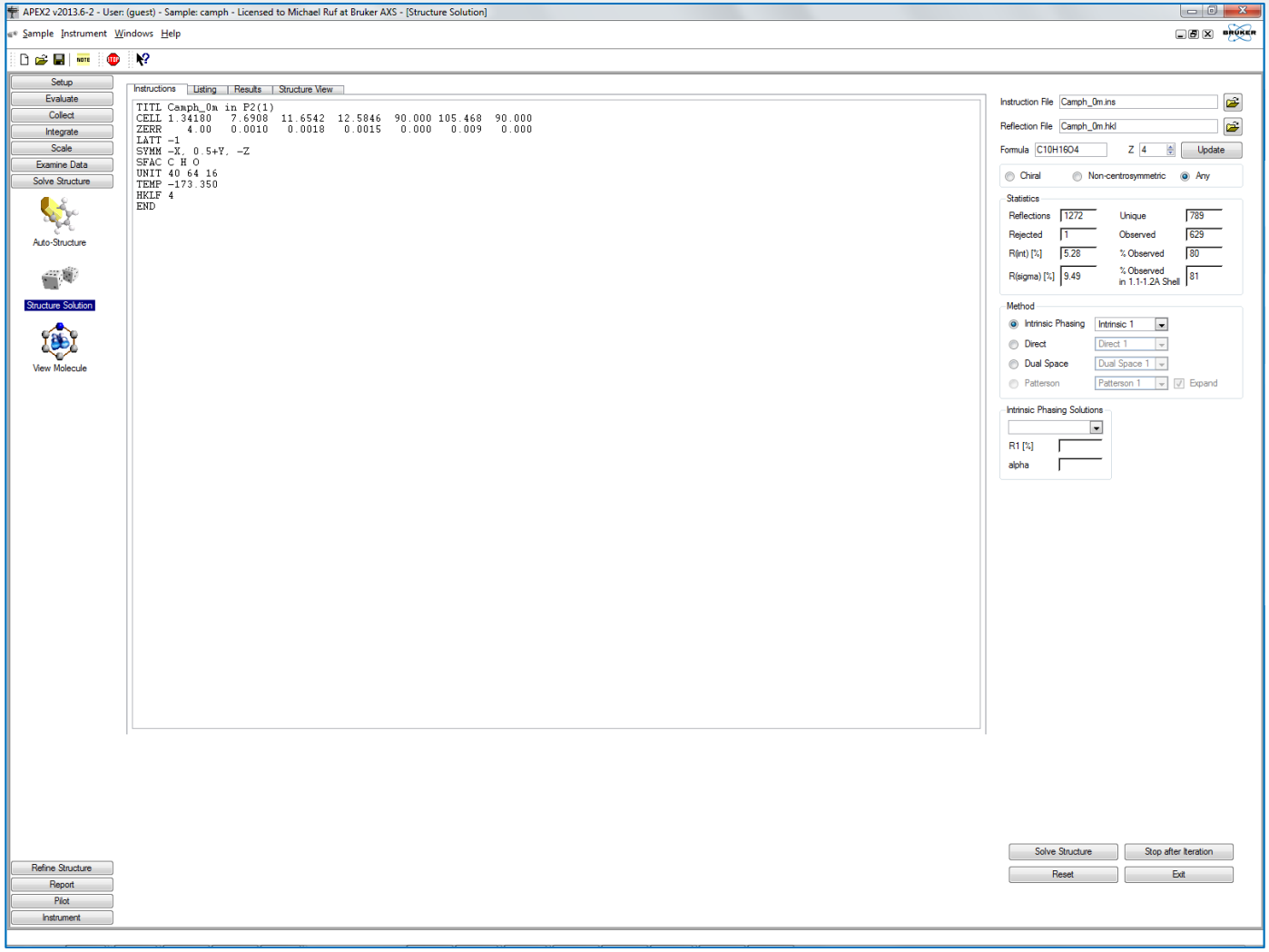
- Traditional direct methods, Patterson methods and dual space methods have been an integral part of the APEX2 structure solution plugin from day one and have provided fast and effective structure solution for years.

- The latest addition and the current default method of the solution plugin are Intrinsic Phasing implemented with SHELXT.



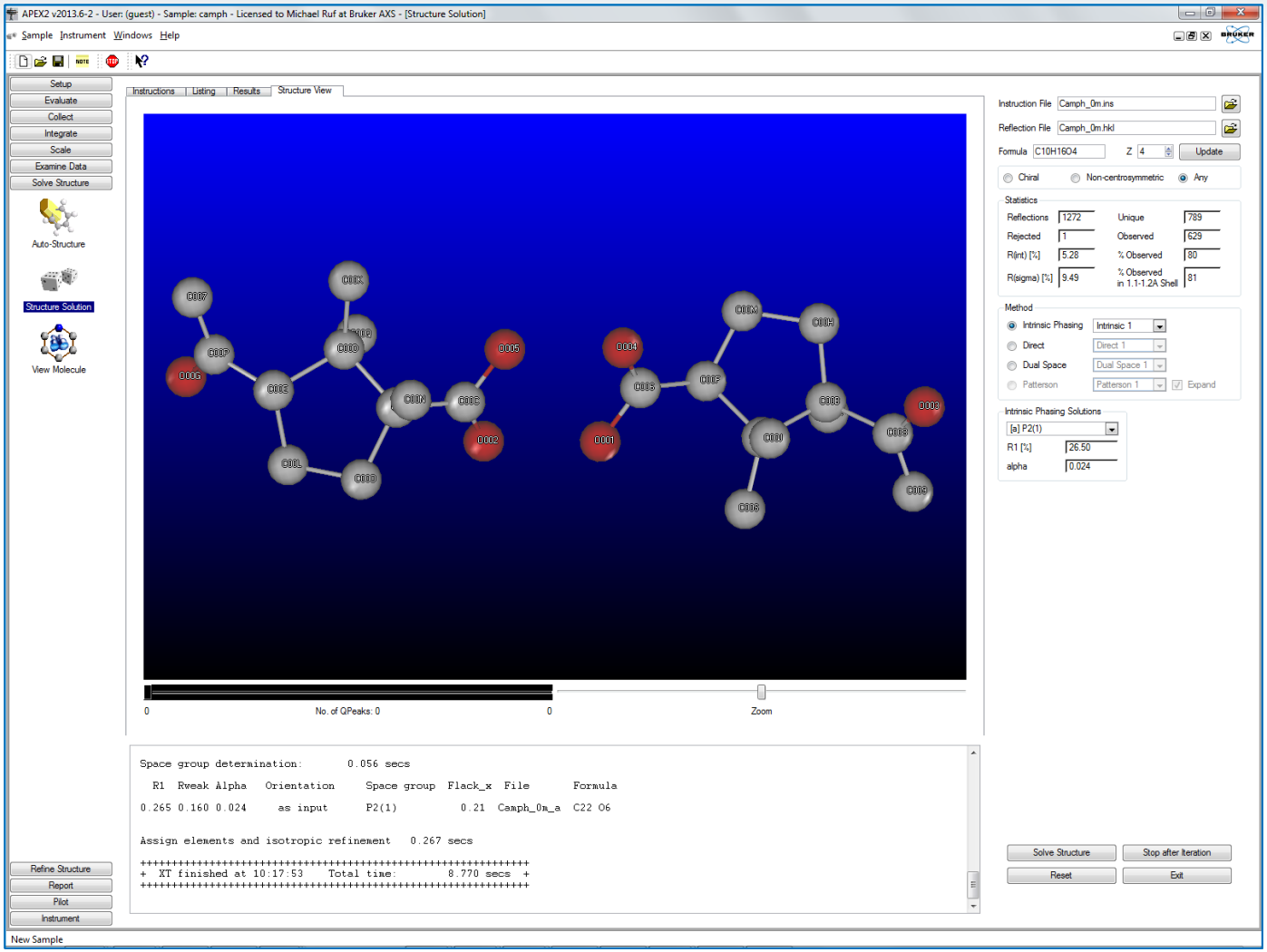


The Structure Solution plugin



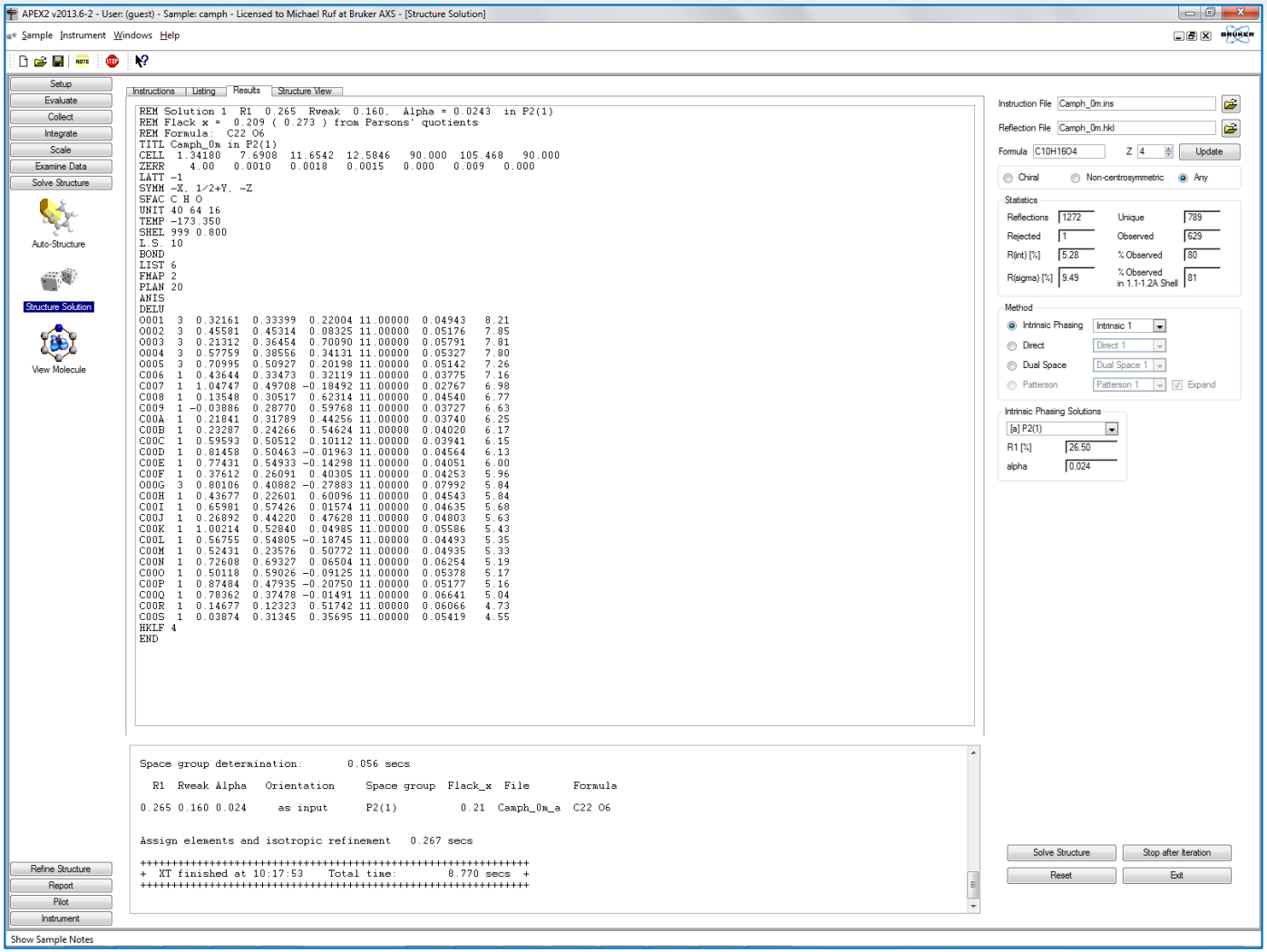
- Easy and intuitive to use
- Intelligent defaults
- Easy setup

The Structure Solution plugin



- Scrollable log file display
- Structure display

The Structure Solution plugin

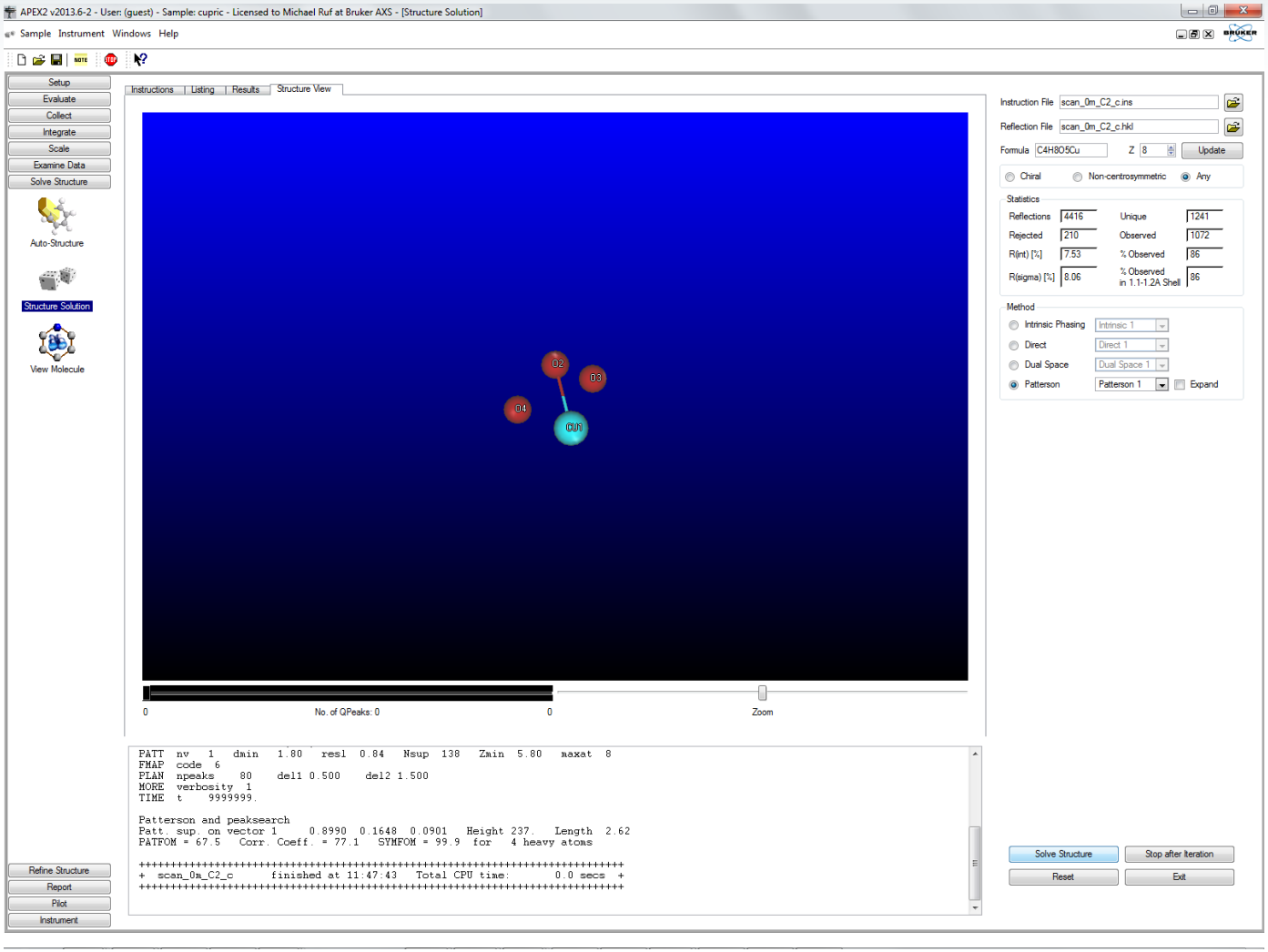


- Listing display tab
- Numerical results display tab

Patterson methods

- Patterson methods employ Fourier maps with the squared amplitudes of the structure factor as coefficients and phase angles all assumed to be 0° .
- These maps give peaks corresponding to all vectors between any given pair of points. The peak heights are proportional to the atomic numbers of atoms in the structure and the peaks can be used to derive the positions of atoms .
- Traditionally Patterson methods were the first choice for the solution of structures containing a few heavy atoms.
- Patterson, A. L. (1935).

Patterson methods



- Two default settings
- Option for partial structure expansion

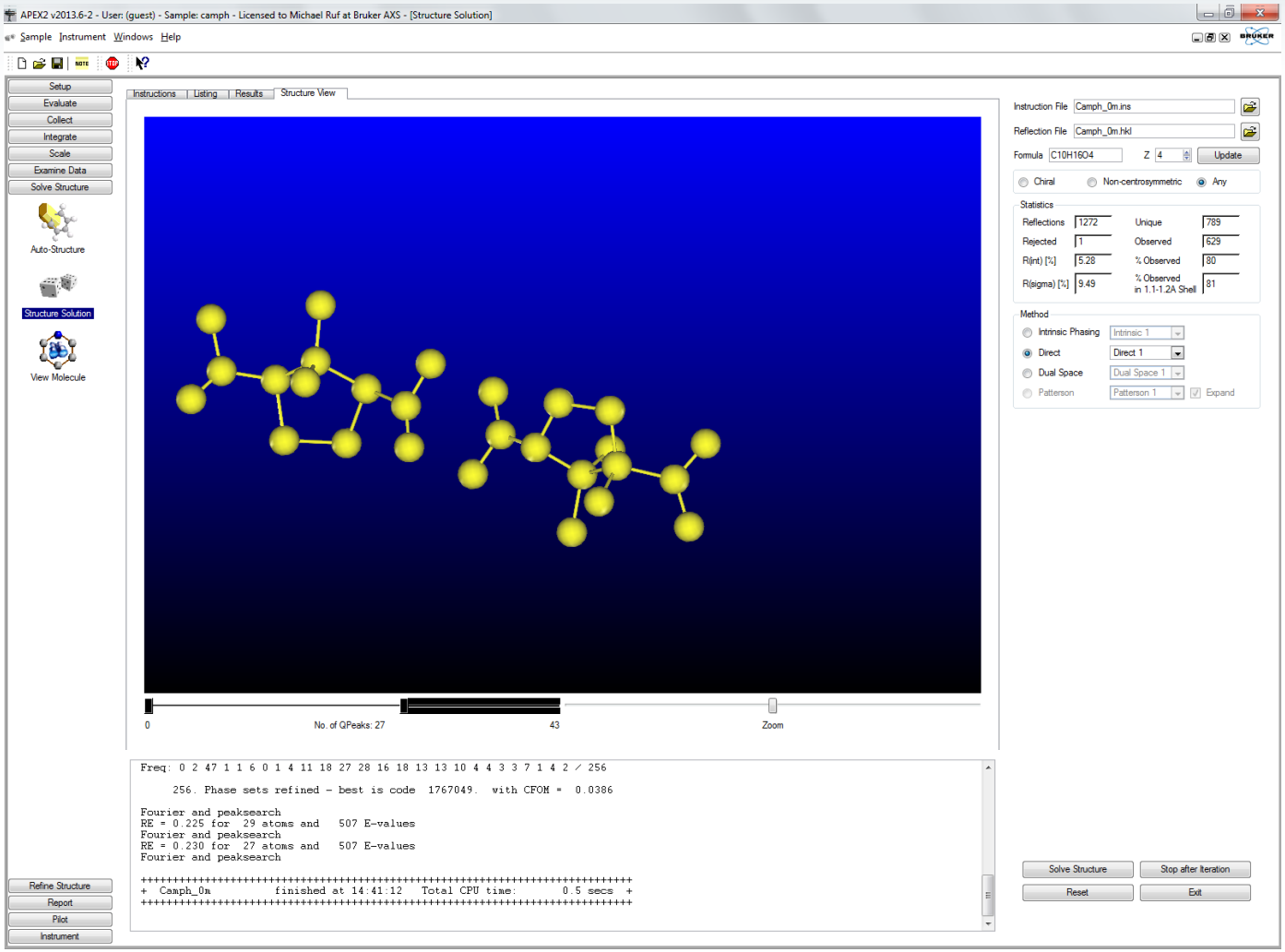
Direct methods

- The term “direct methods” refers to a mathematical-statistical approach that tries to solve the phase problem by limiting the possible relationships between phase and intensity to a range of probabilities.

- The key point behind the direct method derives from invoking prior structural knowledge, usually that the crystal is composed of discrete atoms, with atoms being small and distinct points relative to the spaces between them.

- MULTAN (Main *et al*., 1980),
  SHELXS, XS (Sheldrick, 1990),
  SAYTAN (Debaerdemaeker *et al.*, 1985)
  and SIR (Burla *et al.*, 1989)

Direct Methods



- Three default settings
- Increasing exhaustiveness of search

Dual space methods

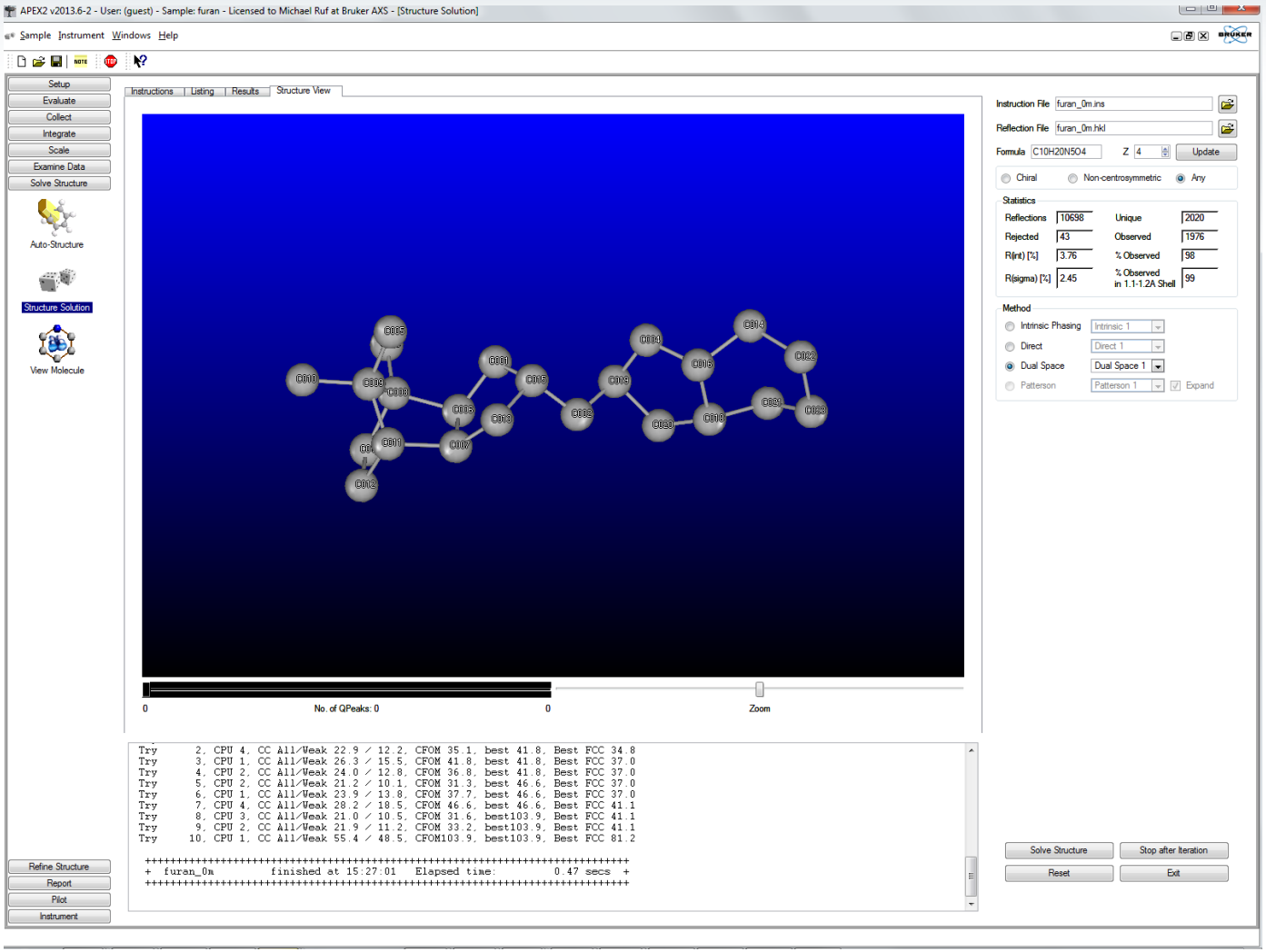
- Shake-and-bake differs from conventional direct methods by employing a minimal function which is optimized through alternate cycles of reciprocal space phase and real space filtering.

- Reciprocal space refinement employs density modification and real-space filtering impose the phase constraints that are implicit in real space.

- The shake-and-bake technique has been successfully used to determine the structures of several small proteins.

- *SnB* (Miller *et al.*, 1994; Weeks & Miller, 1999),
- SHELXD, XM (Sheldrick,1997, 1998)

Dual Space Methods



- Two default settings
- Increasing exhaustiveness of search
- Default 2 determines the number of atoms to be searched for from the volume and the symmetry

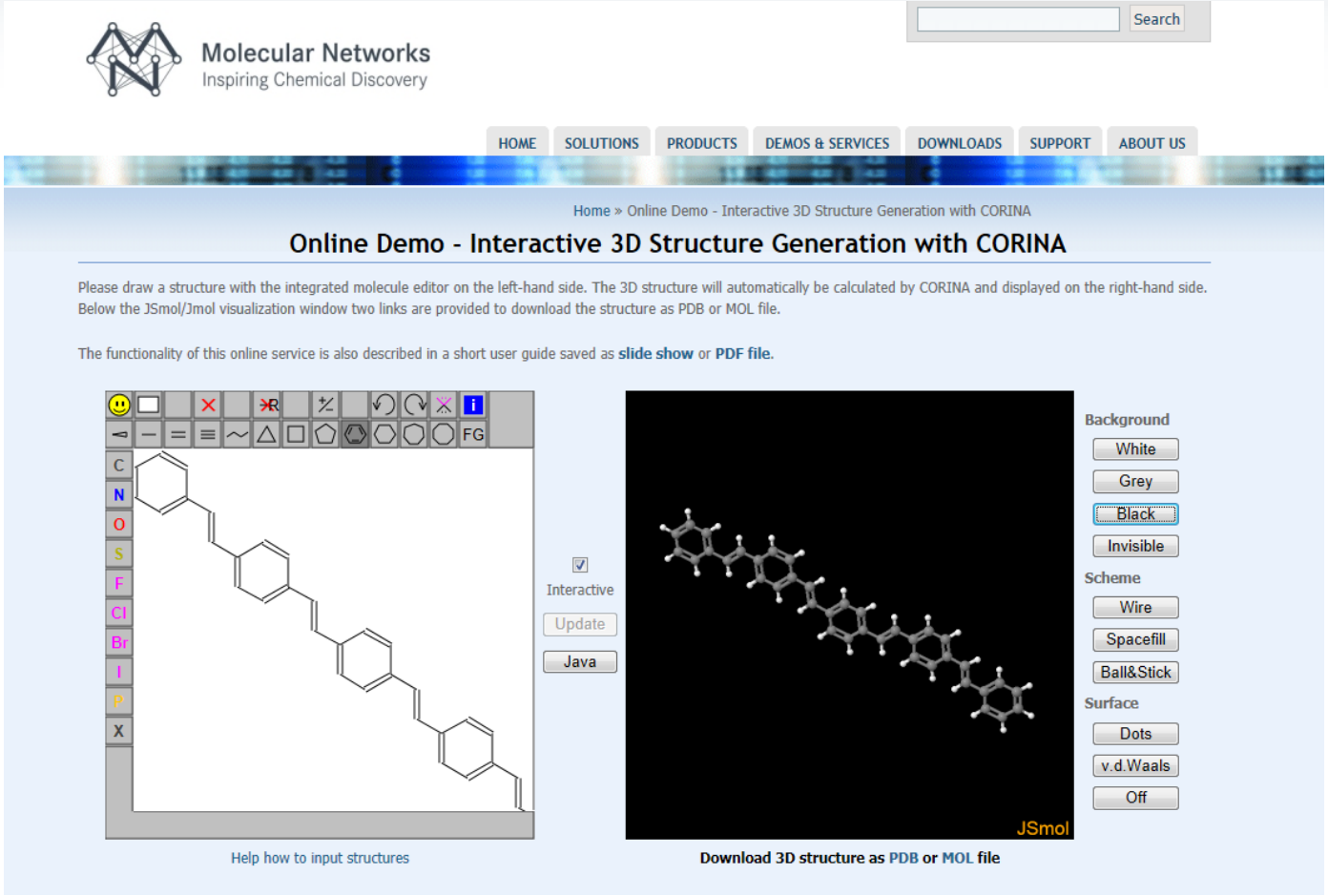
Charge flipping

- Charge flipping is also an iterative algorithm for reconstructing electron densities from diffraction amplitudes.
- It works on high resolution diffraction data using Fourier recycling. Modification in real space changes the sign of charge density below a threshold, while in reciprocal space the Fourier map is modified without any weighting.
- Compared to traditional direct methods it requires much less prior information.
- Charge flipping needs neither symmetry nor an assumption of atoms. This makes it particularly suitable for structure solution of modulated structures and quasicrystals.
- (Oszlanyi and Suto, 2004; 2005).
- SUPERFLIP Palatinus (2004).

Fragment Search

- The algorithm locates a fragment of known geometry by integrated Patterson, packing, and direct methods
- A rotation search can find the orientation of a search model of any size and allows one torsional degree of freedom.
- A translation search may locate up to two independent fragments of any size and can take known atoms at fixed positions into account .
- PATSEE (Egert, 1985)

Fragment Search – model calculation



- http://www.molecular-networks.com/online_demos/corina_demo_interactive

Intrinsic Phasing

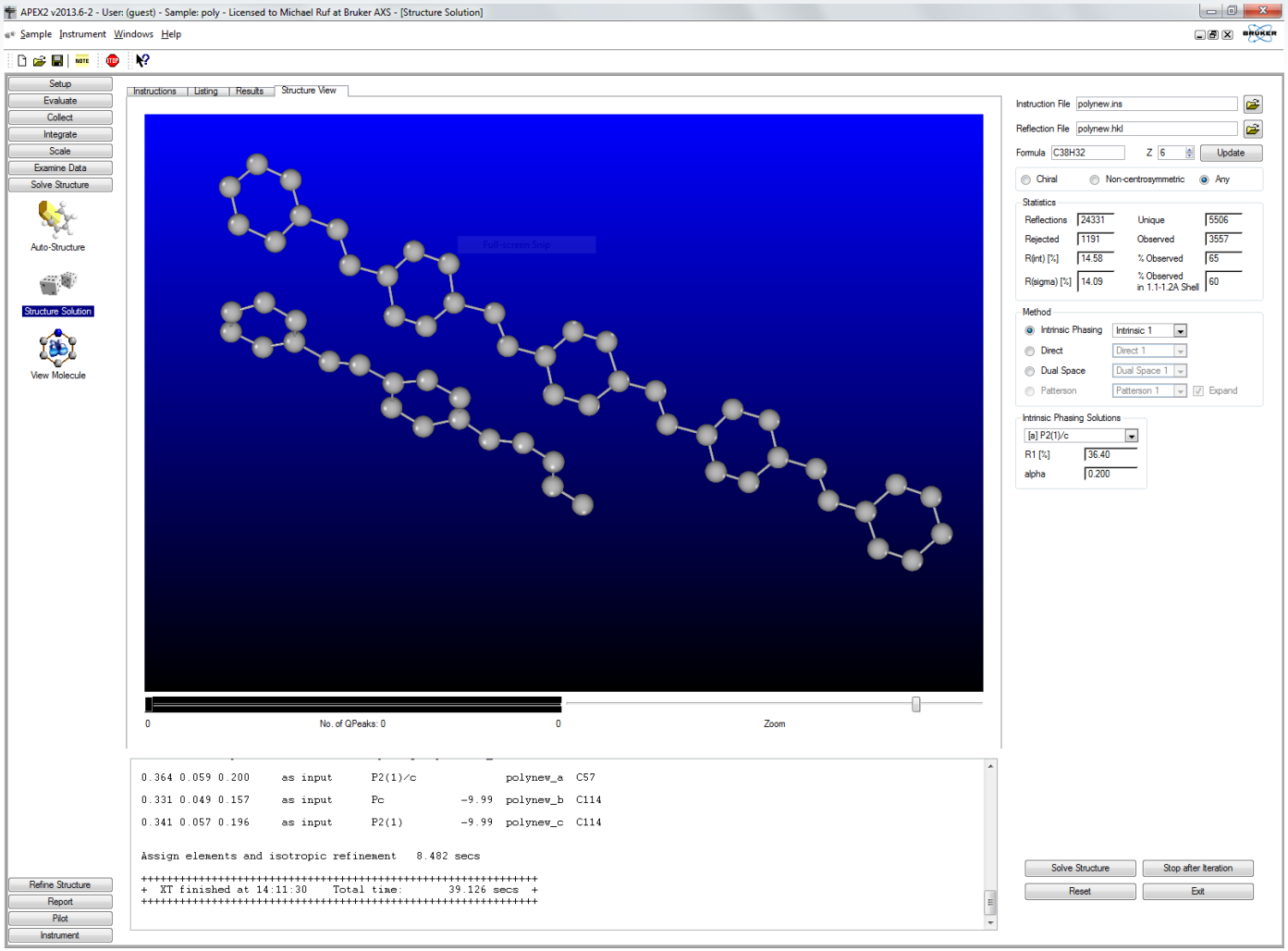
- Intrinsic Phasing plays to the strengths of direct methods solving structures best in space group P1. With the Laue group known, equivalent intensities are averaged and the data is then expanded to P1.
- A departure from classical direct methods is to start the structure solution process not from random phases but from a Patterson superposition minimum function.
- The initial phases provided by the structure solution are then used to determine the appropriate space group which provides the symmetry information for averaging phases for calculating improved electron densities.
- Further dual-space recycling is performed to improve the quality of the electron density. Dual-space recycling employs random omit maps where a certain percentage of the peaks are randomly omitted and only the remaining atoms are used to calculate phases.

Intrinsic Phasing

- The free lunch algorithm has been implemented to use density modification to calculate phases for reflections that have not been measured completing the data to a given resolution.
- Atoms are then assigned to the density's maxima.
- This method proves to work amazingly well and is less demanding on completeness and data quality compared to other direct methods.

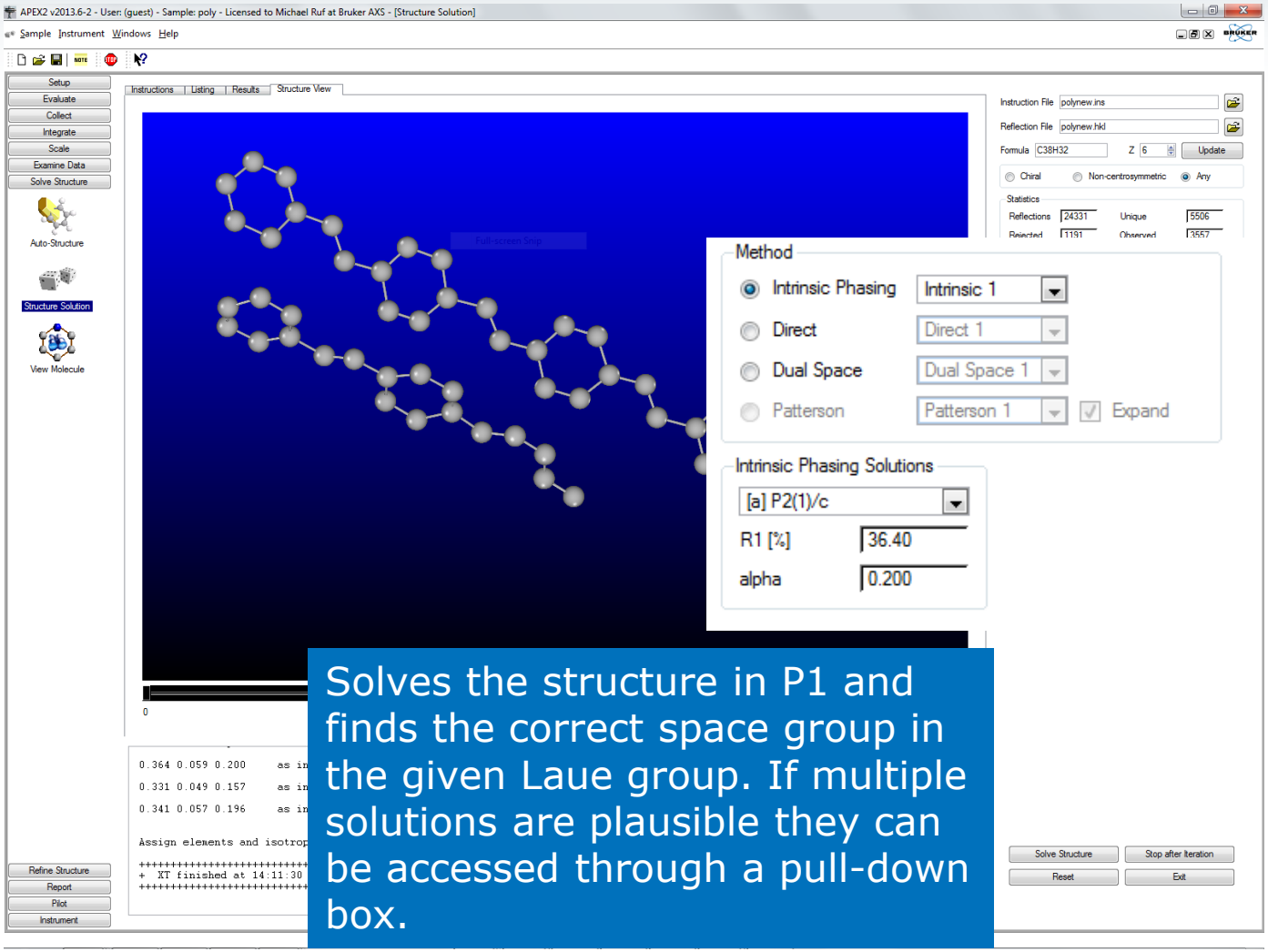
- SHELXT, XT (Sheldrick, 2013)

Intrinsic Phasing



- The most powerful method in Structure solution
- Gives the most complete models
- 15 years ago it took a week to solve this structure with molecular modeling and PATSEE

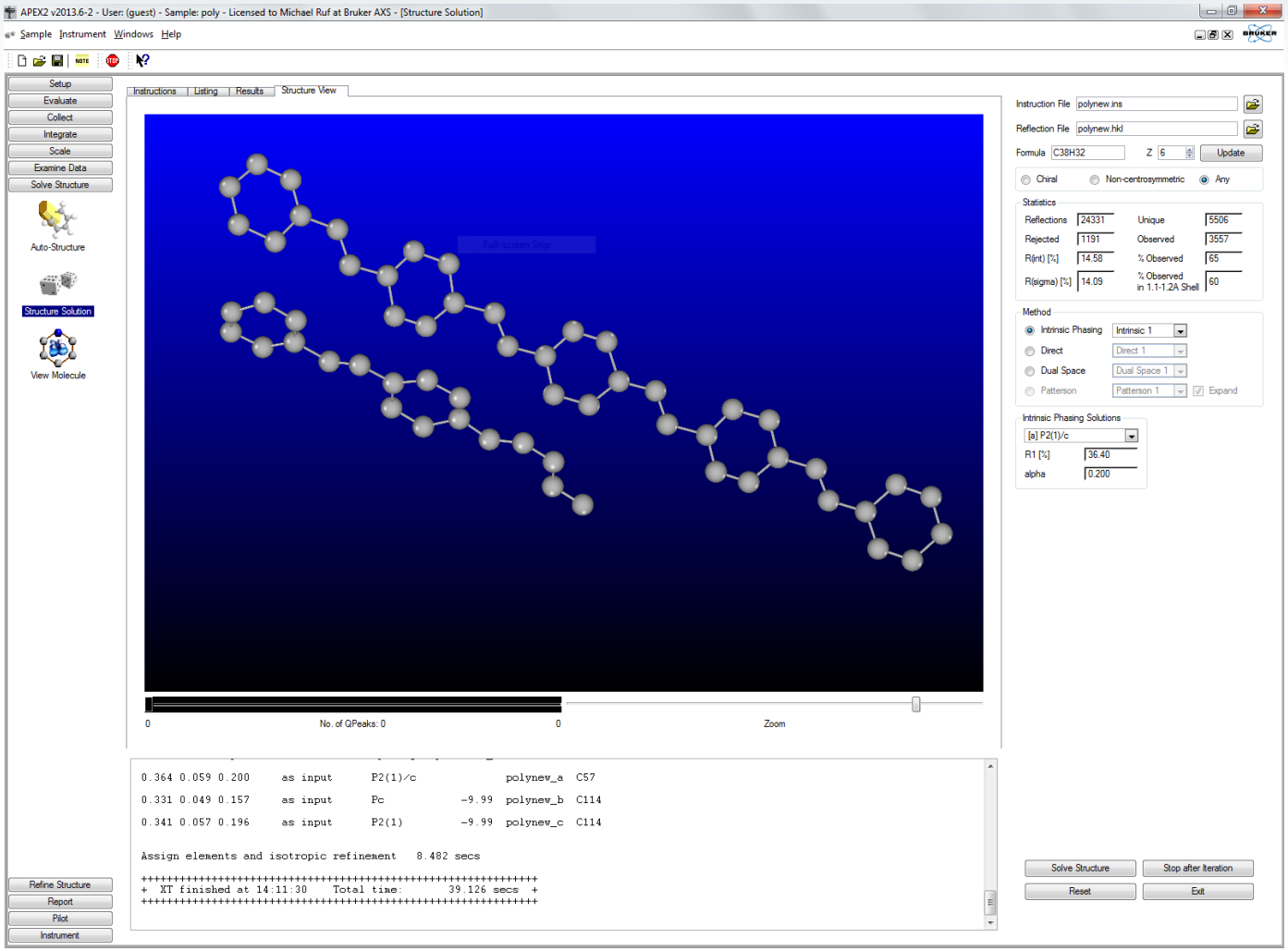
Intrinsic Phasing



Solves the structure in P1 and finds the correct space group in the given Laue group. If multiple solutions are plausible they can be accessed through a pull-down box.

- The most powerful method in Structure solution
- Gives the most complete models
- 15 years ago it took a week to solve this structure with molecular modeling and PATSEE

Intrinsic Phasing



- The most powerful method in Structure solution
- Gives the most complete models
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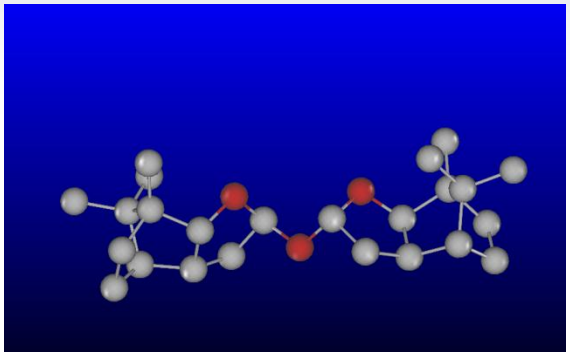
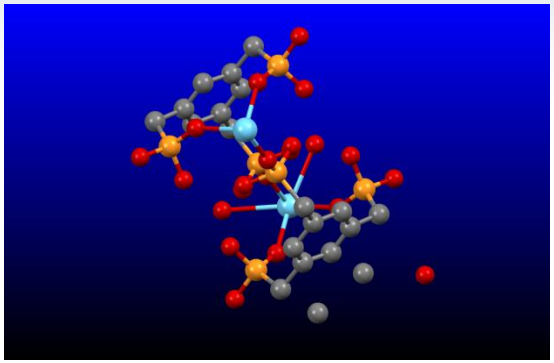
So how powerful is Intrinsic Phasing

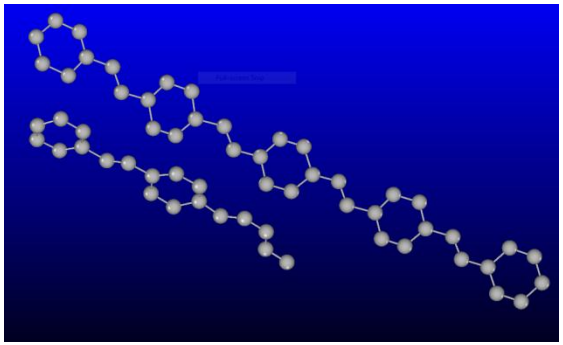
Furan
in 3s



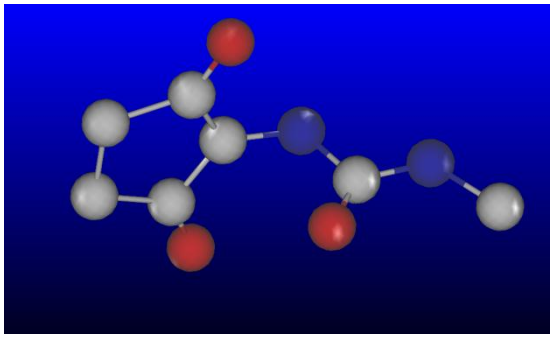
MOF
in 20s



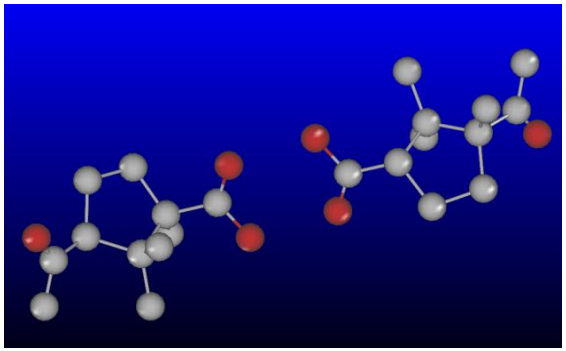
"Poly"
in 40s



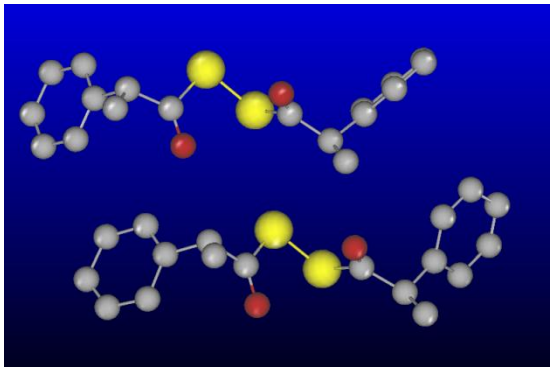
Carbamate
in 1s



Camphoric
acid in 11s



Disulfide
6s



18TH ANNUAL BRUKER/MIT SYMPOSIUM

MODERN APPROACHES IN CRYSTAL STRUCTURE SOLUTION

Friday, February 21st to Sunday, February 23rd 2014

http://web.mit.edu/x-ray/bmit14.html

Questions and Answers

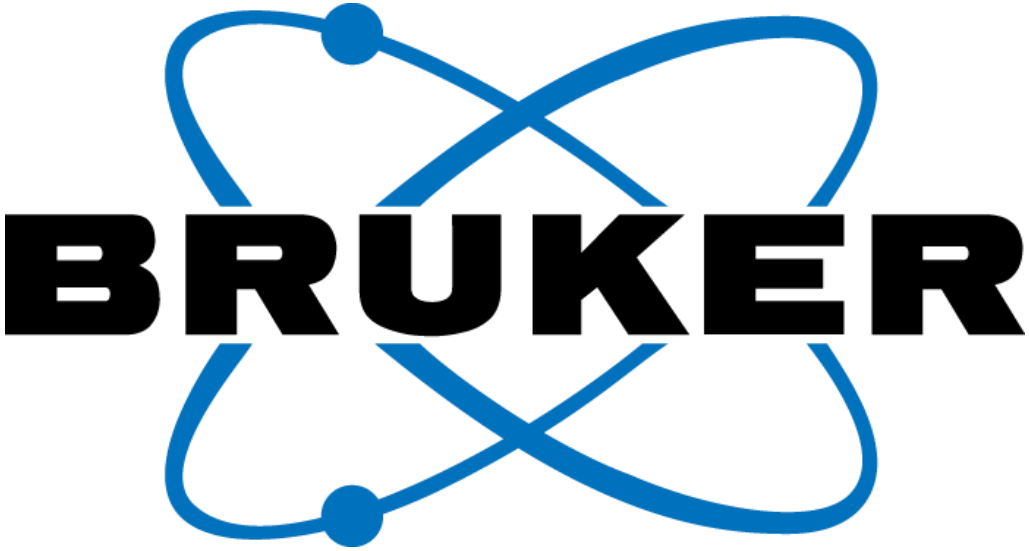
Any questions?

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

How did we do?

When you exit the webinar, please fill out our evaluation survey to let us know. We appreciate your feedback.

Thank you!



Innovation with Integrity