PLATON/SQUEEZE in the context of Twinning and SHELXL2013

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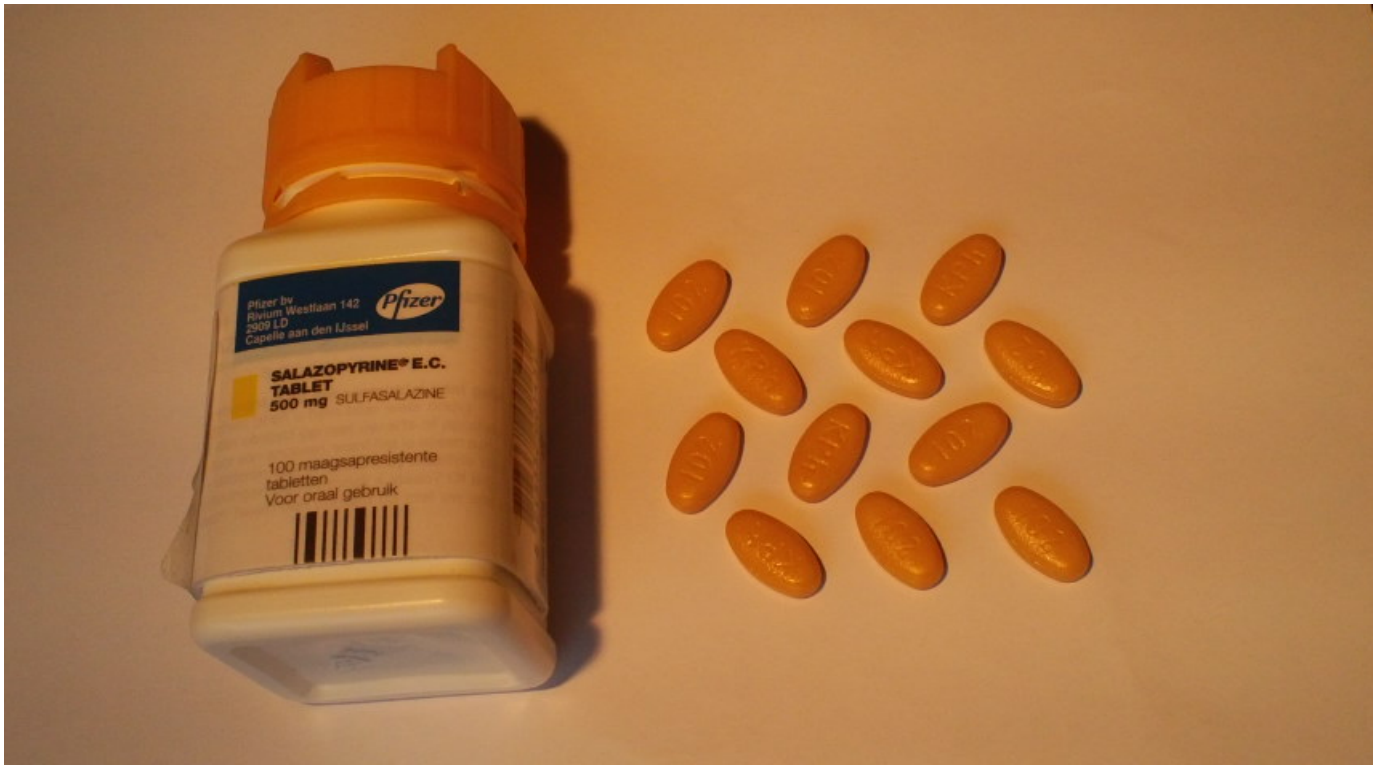
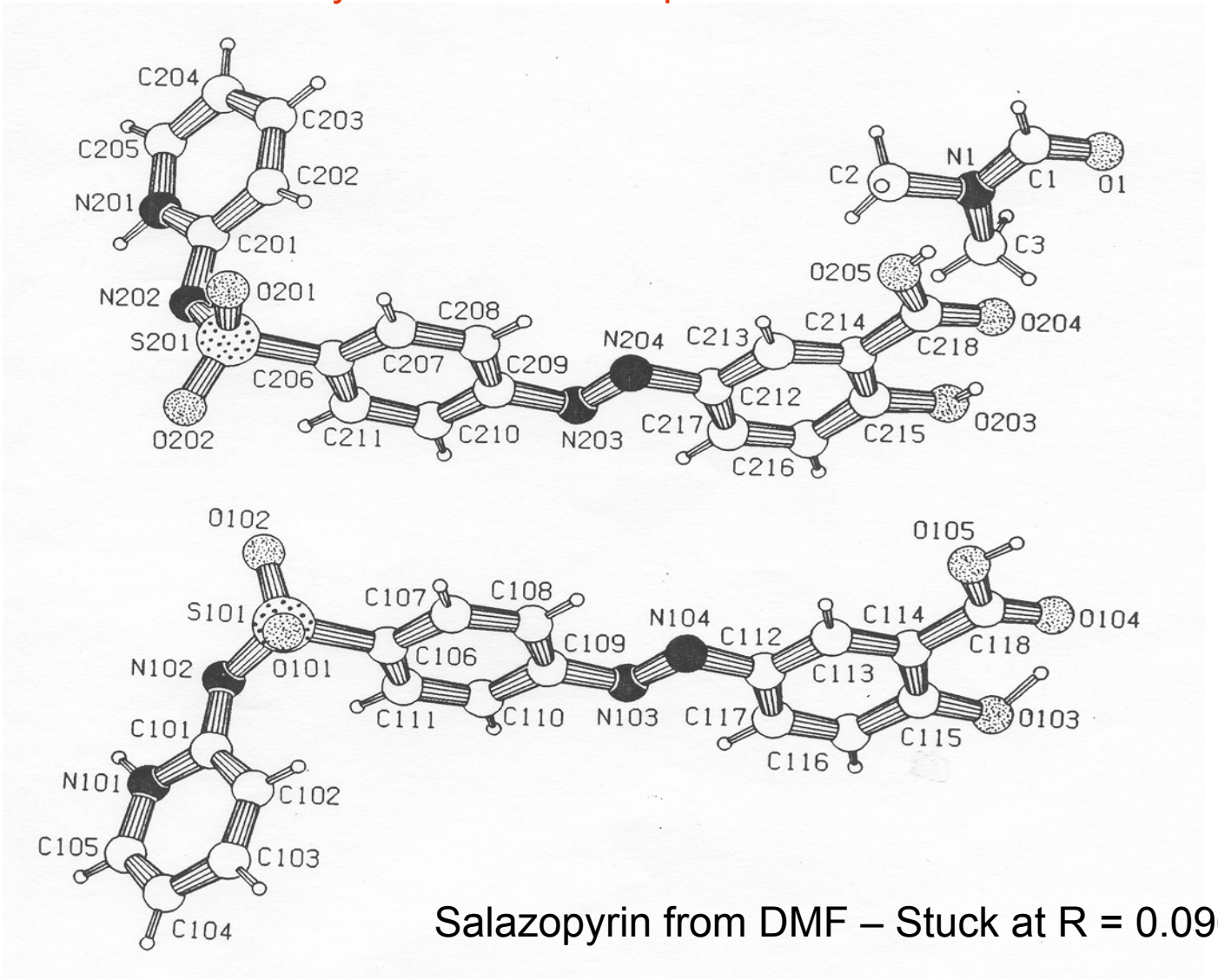
- The SQUEEZE Tool is already around for 25 years
- It is a method to take the scattering of a disordered solvent into account in L.S. as an alternative for a discrete disorder model.
- There are believers and dis-believers in the method, some rightly and some ill-informed.
- Its use is reported in the CSD at least 10000 x
- A ‘work-around’ was needed to run SQUEEZE along with a SHELX76/L97 based refinement.
- This issue is now addressed with SHELXL2013
- Handling solvent disorder + twinning possible

Development History



SQUEEZE has its origin in my interest in the determination of the crystal structure of the pharmaceutical in the pills above.

Crystals were eventually obtained from the pills by Paul van der Sluis after many unsuccessful crystallization attempts from different solvents

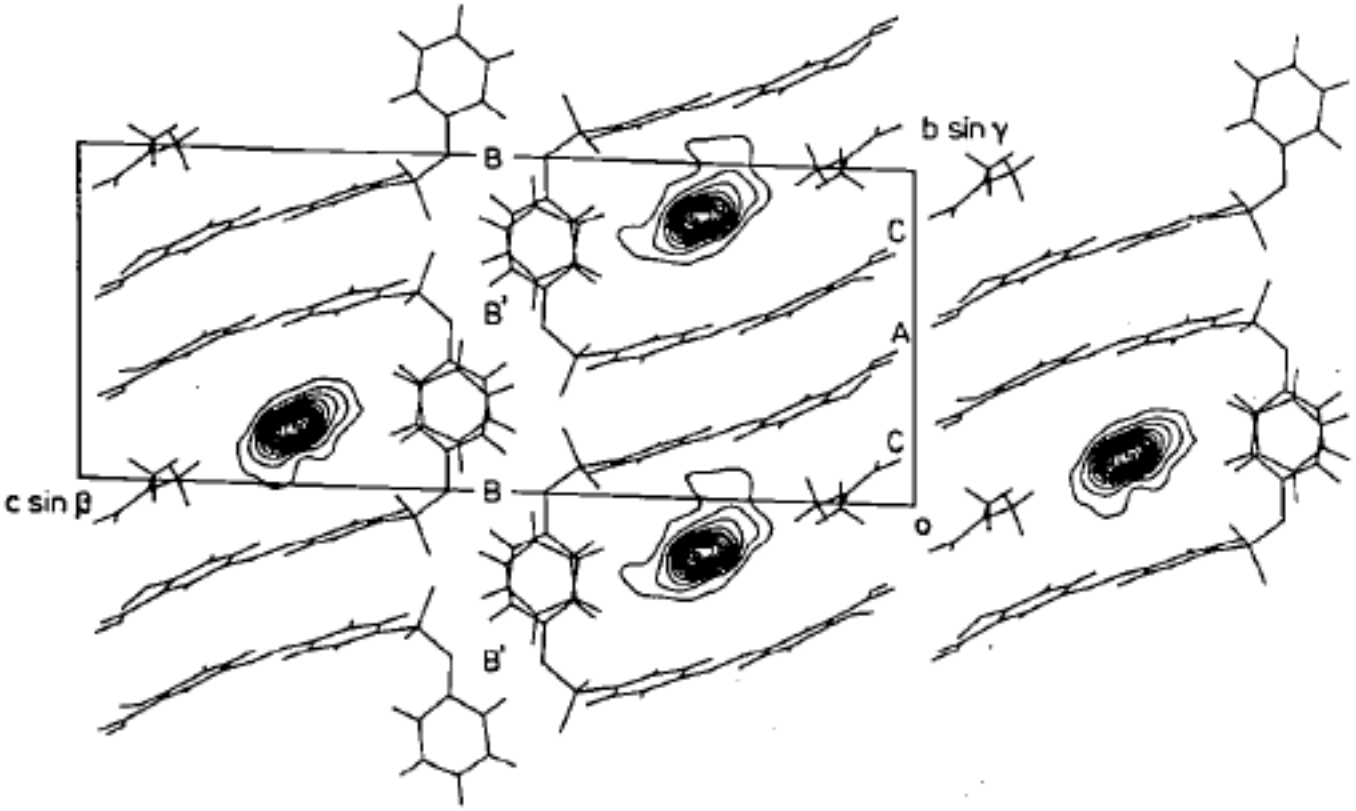


P-1

Salazopyrin from DMF – Stuck at R = 0.096

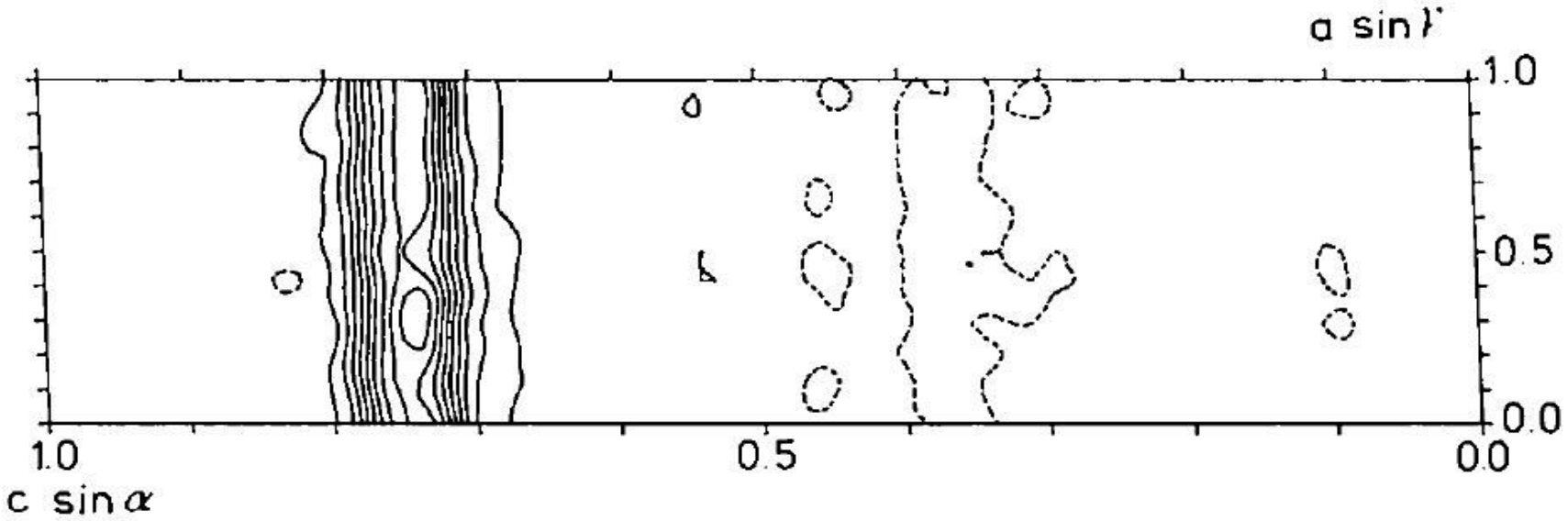
Status around 1988: Poor R-value / SHELXL76, WHY?, What to Do?

Always Inspect a Difference Density Map, Even when there are no Significant Peaks



Rotate by 90 degrees about x-axis => next slide

Structure Modelling and Refinement Problem for the Salazopyrin Structure



- The Contoured Difference Density Fourier map showed infinite channels with continuous density rather than discrete maxima.
- Peak search algorithms (such as implemented in SHELXL) will not always tell about this residual density since they attempt to model an atom like 3D ellipsoidal density distribution
- How to handle and model this density in the structure refinement ?

Our solution: The development of the BYPASS/SQUEEZE procedure.

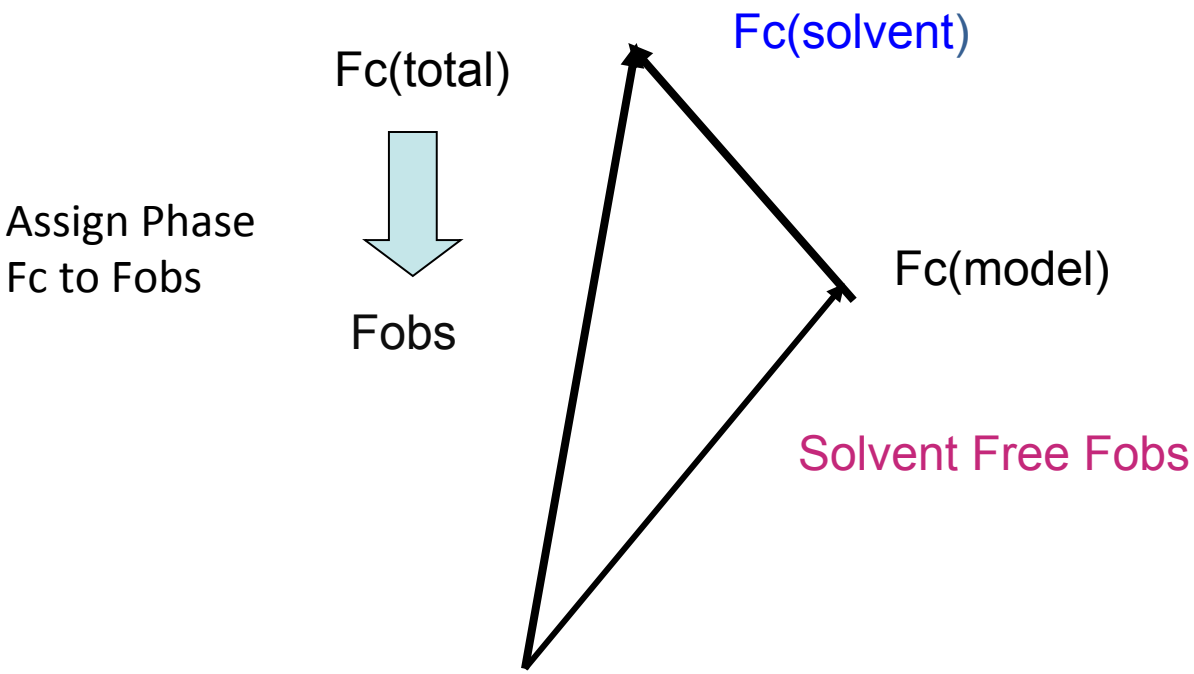
Origin of the SQUEEZE idea

The preliminary idea on how to handle our disordered solvent problem in the L.S. refinement came from a footnote in an Organometallics paper: Wehman et al. (1988) 7, 1477-1485 (Cu-complex + disordered toluene)

(41) The contribution of the solvent density to the scattering is calculated as $F_{hkl}^{solv} = \sum_i \sum_j \sum_k \rho(i, j, k) \Delta V \cos 2\pi(hx_i + ky_j + lz_k)$. The summation is over all grid points i, j, and k within the area of solvent electron density. (i, j, k) is the electron density $(e/Å)^3$ at the grid point i, j, k. x_i, y_j, and z_k are the fractional grid point coordinates. ΔV is the grid volume.

- It was immediately realized that this procedure of density recovery from a difference density map should be iterated.
- The authors used the XRAY76 system that accepted external contributions to the structure factor calculations as part of the L.S. refinement. Such a feature was not available with our refinement tool at that time: SHELX76.
- A 'work-around' was needed to use the idea along with SHELX76 refinement

BYPASS/SQUEEZE
In the Complex Plane
Trick needed to refine with SHELX



Black: Split Fc(total) into a discrete atom and solvent contribution
Red: For SHELX refinement, temporarily substract the recovered solvent contribution from Fobs. (To be reinstated after convergence)

The Prototype Refinement Solution based on SHELX-76

- Identify the disordered solvent volume
- Calculate by difference map iteration the contribution of the electron density found in the voids to the calculated structure factors.
- Subtract the solvent contribution from the observed data and continue SHELX refinement.
- The R-value improved from 9.6 to 4.5 %
- *P. van der Sluis & A.L.Spek (1990). Acta Cryst. C46, 883-886 and A46, 194-201* (BYPASS)

Informal Theory of the SQUEEZE Procedure

$$F_H = \int_V \rho(\vec{r})\, e^{2\pi i \vec{H}\cdot\vec{r}}\, dV$$

$$= \int_V \left(\rho^M(\vec{r}) + \rho^S(\vec{r})\right) e^{2\pi i \vec{H}\cdot\vec{r}}\, dV$$

$$\rho^M(\vec{r}) = \sum_{j=1}^{N} \rho(\vec{r} - \vec{r}_j)$$

$$F_H^M = \sum_{j=1}^{N} f_j\, e^{2\pi i \vec{H}\cdot\vec{r}_j}$$

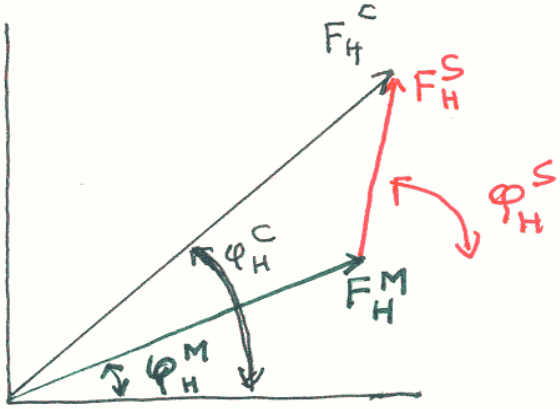
$$\rho^S(\vec{r}) \approx \Delta\rho(\vec{r}_k) \text{ on grid}$$

$$F_H^S = V_q \sum_S \Delta\rho(\vec{r}_k)\, e^{2\pi i \vec{H}\cdot\vec{r}_k}$$

$$F_H^C = F_H^M + F_H^S \Longrightarrow$$

M = Ordered

S = Solvent



Iterate (Initially $\rho_H^S = \rho_H^M$)

$$\Delta\rho(\vec{r}) = \frac{1}{V} \sum_H \left(s|F_H^o| e^{i\varphi_H^C} - |F_H^M| e^{i\varphi_H^M}\right) e^{-2\pi i \vec{H}\cdot\vec{r}} + \frac{F_o^S}{V}$$

Solvent Free ElectronCount

$$F_H^o : F_H^{o'} = |F_H^o| e^{i\varphi^C} - |F_H^S| e^{i\varphi^S}$$

$$: V_q \sum_S \Delta\rho(\vec{r}_k)$$

PLATON/SQUEEZE with SHELXL97

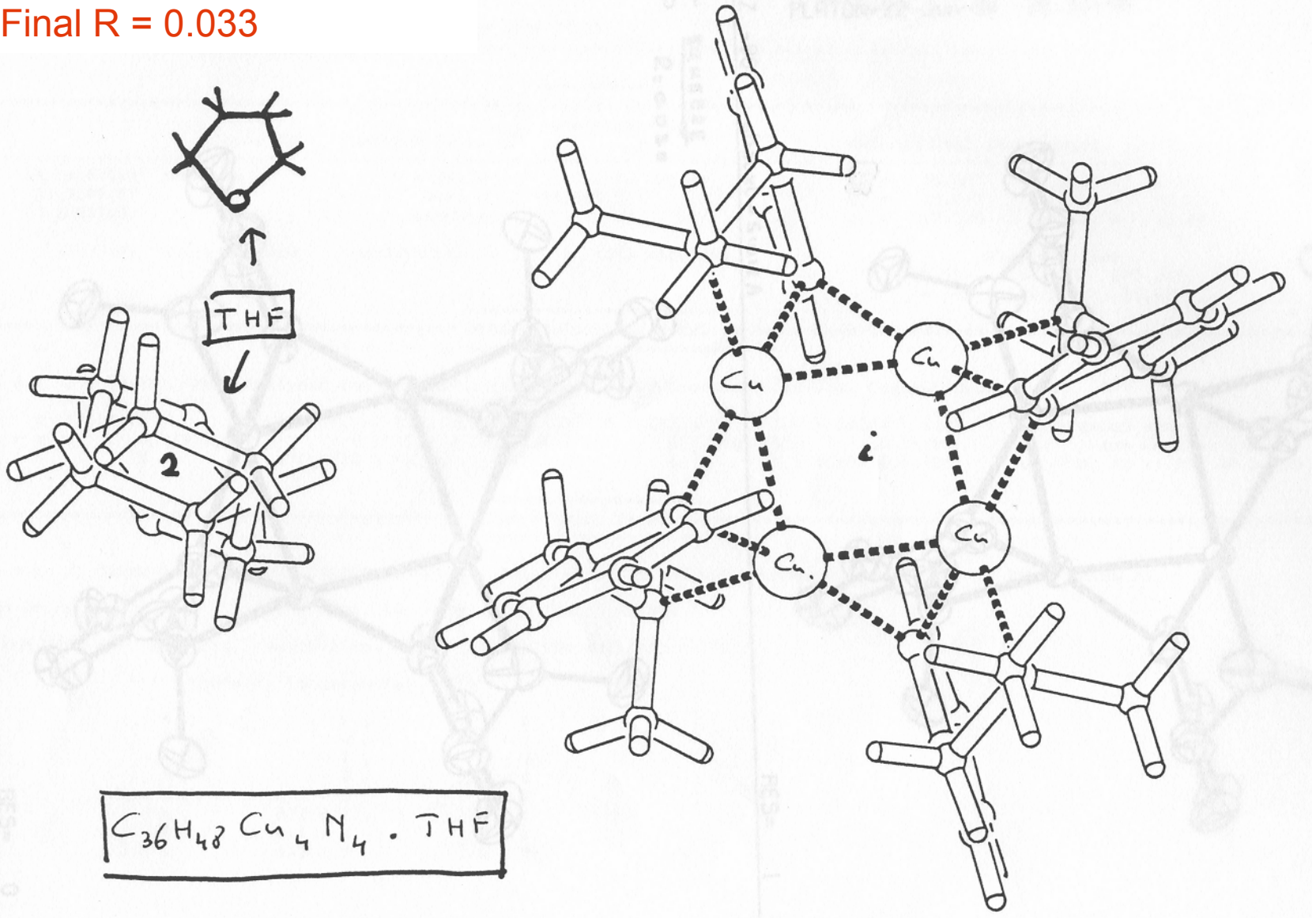
- A new and distributable version (now called SQUEEZE) was made part of the PLATON program and to work with SHELXL97 (LINUX/MAC-OSX/MS-WINDOWS versions)
- Input to SQUEEZE: 'shelxl.res' + 'shelxl.hkl'
- Output: a new solvent removed 'shelxl.hkl' suitable to continue with the final L.S. refinement with SHELXL97.
- A proper FCF file with original Fo^2 is created afterwards based on the information hidden beyond column 80.
- An often stated Point of Critic: The SHELXL97 refinement against modified observed data. In practice: no real difference with CRYSTALS refinement + observed data.

Early Test Calculations with SHELXL97

- Example: Organometallic compound + THF with two test refinements:
- A first calculation was based on a disorder model for the disordered solvent (THF)
- The second calculation invoked SQUEEZE with the shelxl.res and shelxl.hkl without the THF parameters in the shelxl.res model.
- The results of both calculations are very similar as shown with their ORTEP's

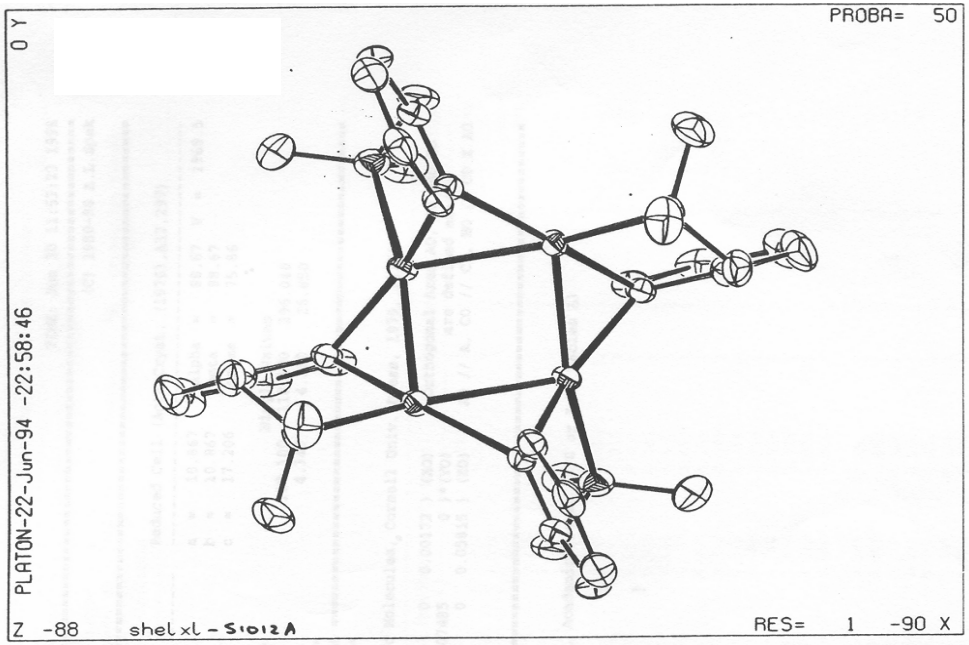
Disorder Model Refinement
Final R = 0.033

EXAMPLE with SHELXL97

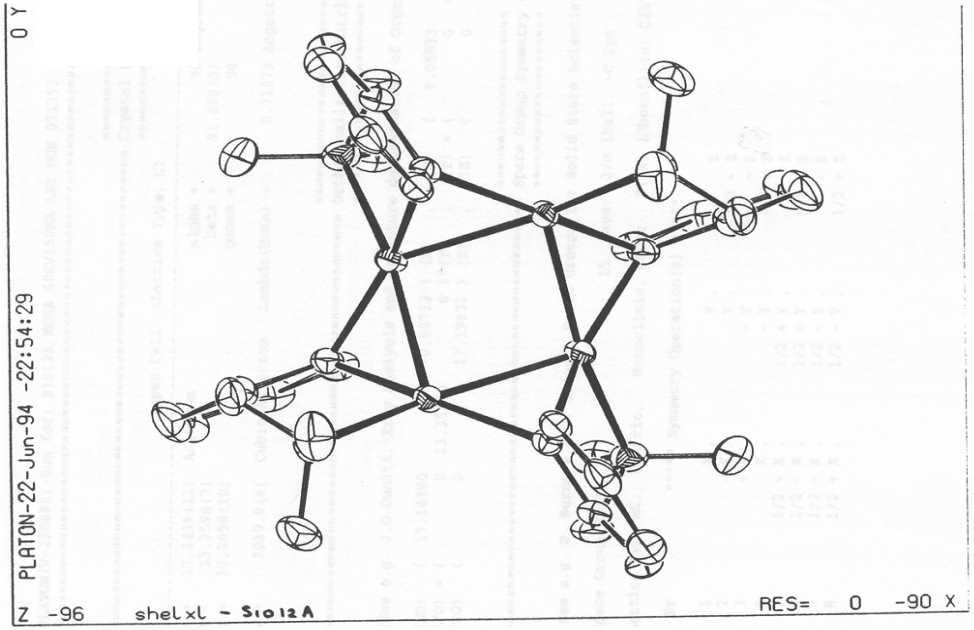


$C_{36}H_{48}Cu_4N_4 \cdot THF$

Comparison of the Results of the two Modeling Procedures



Disorder Model
R = 0.033

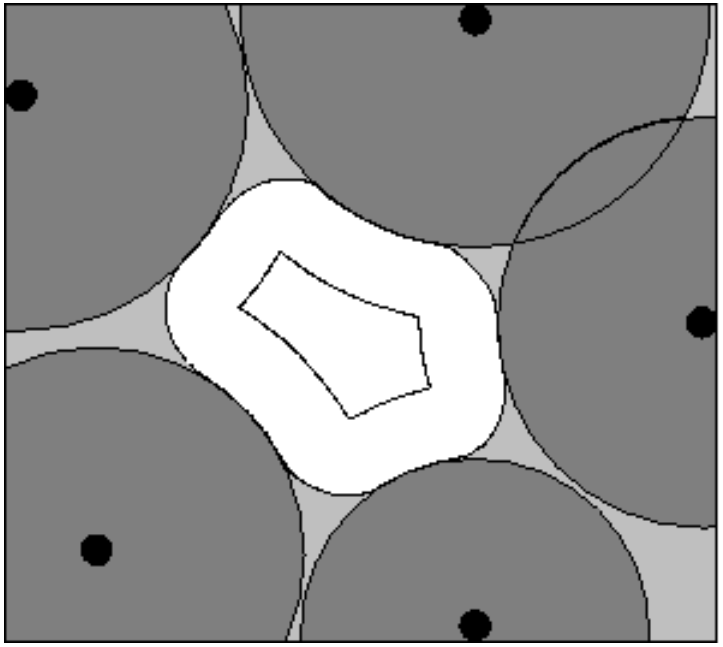


SQUEEZE Model
R = 0.030

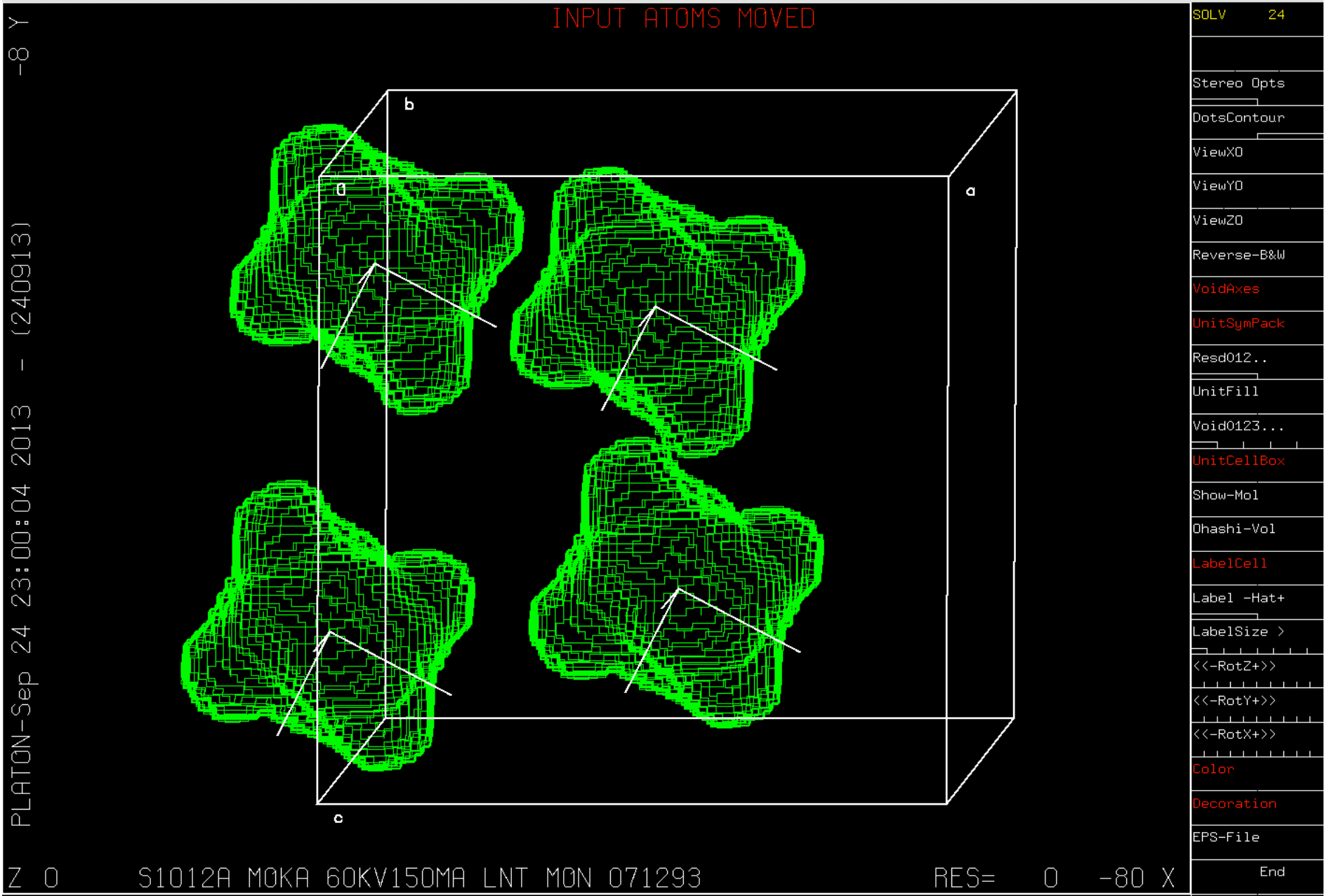
Automated Detection of Solvent Accessible Voids

- A typical crystal structure has only in the order of 65% of the available space filled.
- The remainder volume is in voids (cusps) in-between atoms (too small to accommodate an H-atom)
- Solvent accessible voids can be defined as regions in the structure that can accommodate at least a sphere with radius 1.2 Angstrom without intersecting with any of the van der Waals spheres assigned to each atom in the structure.
- Next Slide: Void Algorithm: Cartoon Style ➔

FIRST STEP OF THE SQUEEZE PROCEDURE: LOCATE SOLVENT ACCESSIBLE VOID



Black areas indicate discrete model atom with van der Waals radii assigned. The white area is the solvent accessible volume


P.L.A.T.O.N
INPUT ATOMS MOVED
-8 Y
PLATON-Sep 24 23:00:04 2013 - (240913)
b
a
c
Z 0 S1012A MOKA 60KV150MA LNT MON 071293 RES= 0 -80 X
SOLV 24
Stereo Opts
DotsContour
ViewXO
ViewYO
ViewZO
Reverse-B&W
VoidAxes
UnitSymPack
Resd012..
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UnitCellBox
Show-Mol
Ohashi-Vol
LabelCell
Label -Hat+
LabelSize >
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End
INSTRUCTION INPUT via KEYBOARD or LEFT-MOUSE-CLICKS (HELP with RIGHT CLICKS)
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The SQUEEZE Algorithm

1. Calculate the VOID-map
2. Calculate a difference density Fourier map (FFT)
3. Use the VOID-map as a mask on the FFT-map to set all density outside the VOID's to zero.
4. FFT^{-1} this masked Difference map -> contribution of the disordered solvent to the structure factors (A(cal) & B(cal)
5. Calculate an improved difference map with F(obs) phases based on the vectorial sum of F(calc) + F(solv) and F(calc) without the solvent contribution.
6. Recycle to 2 until convergence.

LISTING OF FINAL SQUEEZE CYCLE RESULTS

```
:: Cycle =  4, R(F) = 0.04, Nref(Hemi) =  8811, R(F > 4SIGF) = 0.03 Nref =  7380

Unique Density Maxima in Enhanced  Difference Map (CutOff level =  0.50 eA-3)
=============================================================================
      x     y     z  (e/A^3)     Shortest Contacts within 3.2 Angstrom (Excl. H)
=============================================================================
  1 0.490 0.220 0.281  4.57 void
  2 0.552 0.266 0.301  4.41 void
  3 0.475 0.379 0.212  3.54 void
  4 0.441 0.356 0.252  3.39 void
  5 0.499 0.297 0.252  0.89 void
  6 0.953 0.184 0.125  0.55      C16  0.68; C11  0.75; C15  1.90; C12  1.90; Cu2
  7 0.408 0.253 0.501  0.51      C13  0.61; C12  0.90; C14  1.85; C17  1.97; C11
  8 0.358 0.170 0.717  0.50      Cu1  1.11; C21  1.53; C22  2.11; C27  2.37; Cu2
  9 0.283 0.085 0.613  0.50      C18  0.77; N1   1.75; C19  2.46; Cu1  2.82; C17

VOID   Volume Ang^3 Electron-Count (e-) Volume per electron Vol/Atom
=============================================================================
    A          155              43          3.6                    29
    B          155              43          3.6                    29
    C          155              43          3.6                    29
    D          155              43          3.6                    29

Total (Positive) Electron Count in Voids/Cell =   172

Total (Fo-Fc)map Electron Count in  Unit Cell =   171

VOID-Fo-Fc-Map:     Rho(min) =   -0.28, Rho(max) =    4.57, RhoCutOff =    0.00
PeaksCloseToAtoms: Rho(min) =   -0.63, Rho(max) =    0.55, RhoCutOff =    0.50

:: Fo-scale =0.210538E+01 - SinT/L-Min = 0.20 for Fo/Fc-Scaling


:: Cycle =  5, R(F) = 0.04, Nref(Hemi) =  8811, R(F > 4SIGF) = 0.03 Nref =  7380
```

ANALYSIS OF R-VALUE IMPROVEMENT VERSUS RESOLUTION WITH SQUEEZE

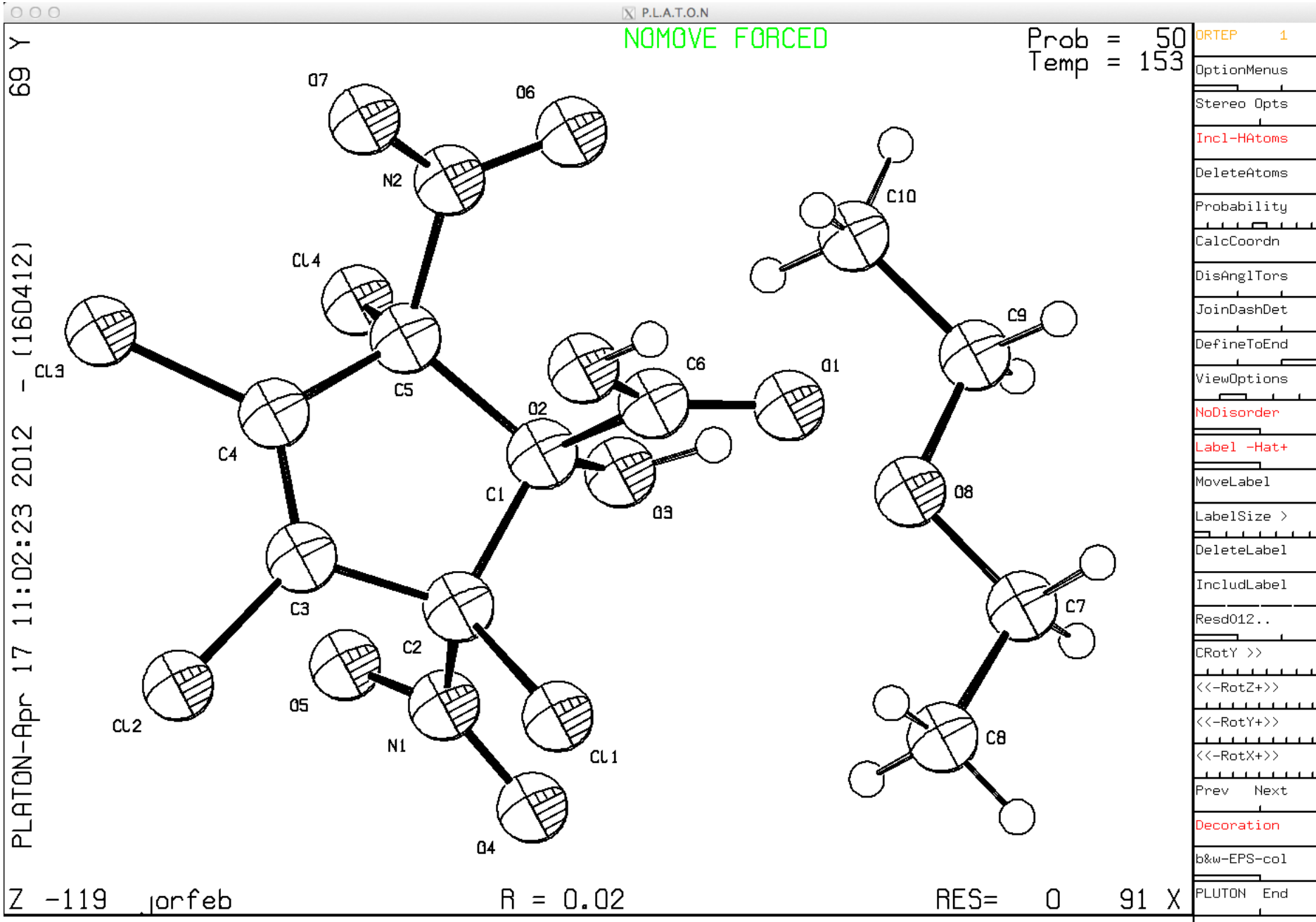
SQUEEZE Statistics on the Difference Map Phasing

FcMod = Average contribution to Fc from discrete model
FcSolv = Average contribution to Fc from solvent region
FcTot = Average Fc total (= model + solvent contrib.)
DelMS = Average Phase difference between model and solvent contrib.
DelMT = Average Phase difference between model and combined contrib.
N = Number of reflections in Sin(Theta)/Lambda range
R(Mod) = SIGMA(ABS(ABS(FcMod) - Fo)) / SIGMA(Fo)
R(Tot) = SIGMA(ABS(ABS(FcTot) - Fo)) / SIGMA(Fo)

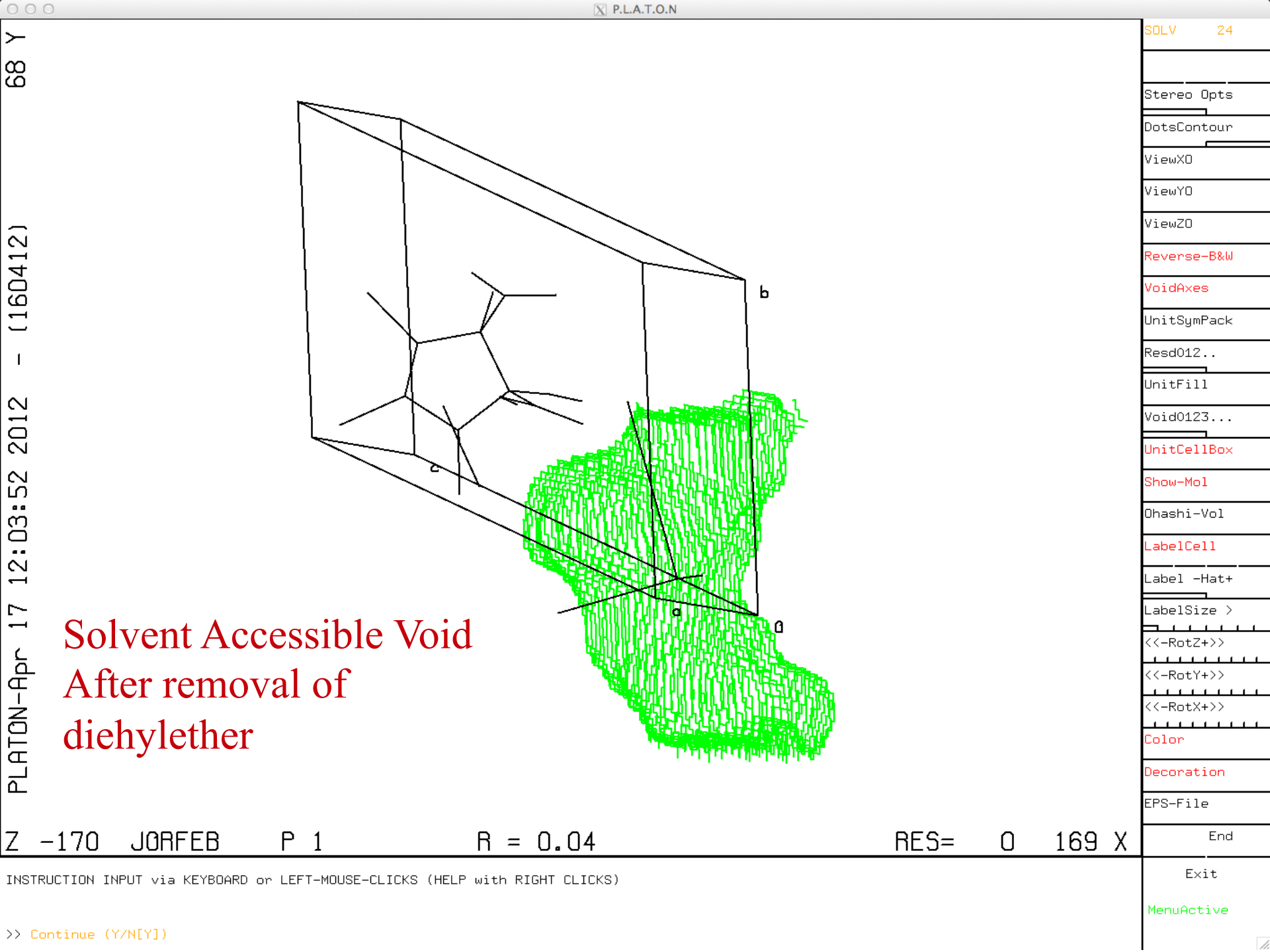
SinT/L	<FcMod>	<FcSolv>	<FcTot>	<Fo>	<DelMS>	<DelMT>	N	R(Mod)	R(Tot)
0.05	269.40	95.86	278.98	275.37	100.00	0.01	18.	0.336	0.033
0.10	143.62	47.76	157.32	160.98	77.17	12.87	56.	0.281	0.043
0.15	105.09	16.83	107.15	110.76	86.51	8.88	122.	0.155	0.048
0.20	114.13	8.59	115.03	116.75	87.75	3.38	210.	0.090	0.041
0.25	116.69	8.11	116.64	117.74	87.17	1.18	322.	0.080	0.038
0.30	88.12	6.28	88.18	88.41	91.33	2.29	480.	0.083	0.037
0.35	71.70	4.12	71.60	71.80	91.11	3.11	632.	0.070	0.039
0.40	60.71	3.18	60.94	60.76	87.13	1.15	842.	0.074	0.047
0.45	53.95	2.79	54.11	53.87	88.69	2.19	1036.	0.075	0.051
0.50	49.89	2.26	49.87	49.59	92.77	1.79	1262.	0.071	0.055
0.55	40.11	1.61	40.15	39.83	88.48	1.11	1138.	0.075	0.063
0.60	30.62	1.02	30.62	30.91	89.65	1.57	917.	0.089	0.078
0.65	28.65	0.86	28.69	28.90	87.74	0.51	481.	0.098	0.086

Test Example with Calculated Data

- ‘Observed Data’ were calculated from the published coordinates.
- The ether molecule was subsequently removed
- SQUEEZE was tested to see whether the method recovers the ether contribution to the structure factors.



Test structure in P1. Delete diethylether molecule


P.L.A.T.O.N
68 Y
PLATON-Apr 17 12:03:52 2012 - (160412)
b
c
a
Solvent Accessible Void
After removal of
diehylether
SOLV 24
Stereo Opts
DotsContour
ViewXO
ViewYO
ViewZO
Reverse-B&W
VoidAxes
UnitSymPack
Resd012..
UnitFill
Void0123...
UnitCellBox
Show-Mol
Ohashi-Vol
LabelCell
Label -Hat+
LabelSize >
<<-RotZ+>>
<<-RotY+>>
<<-RotX+>>
Color
Decoration
EPS-File
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Z -170 JORFEB P 1 R = 0.04 RES= 0 169 X
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MenuActive

P.L.A.T.O.N

Search for and Analysis of Solvent Accessible Voids in the Structure

Area	#GridPoint	VolPerc.	Vol(A^3)	X(av)	Y(av)	Z(av)	Eigenvector(frac)			Sig(Ang)
1	21018[3311]	34	144[22.6]	0.178	0.014	0.182	1	0.122	1.000	0.231	2.33
							2	1.000	-0.844	0.918	1.37
							3	1.000	0.311	-0.658	1.27

A solvent accessible volume of 144 Ang**3 is found

This volume will be used as a mask on the difference density Fourier map following the SQUEEZE recycling procedure.

PLATON 10

OptionMenus

NoMove

Join-Expand

Organic

Round

Parentheses

Label-Alias

R/S-Determ

Norm-H-bond

NoSymm

NoDisorder

LstARU RCel

LstCellSymm

ListAtoms

ListBonds

LstFlagRadi

Exclude H

MinQPeakHgt

MinQPeakDis

Q-Peak-Incl

KeyInstruct

Prev Next

SAVE-InstrS

ENTRY-LIST

Reset End

Exit

MenuActive

INSTRUCTION INPUT via KEYBOARD or LEFT-MOUSE-CLICKS (HELP with RIGHT CLICKS)

>> WW

P.L.A.T.O.N

PLATON/SQUEEZE

Cycle	R(F)	Nref(Heml)	R(F .gt. 4Slg Nref		El/Cell
1	0.187	1942	0.165	1932	0
2	0.092	1942	0.081	1932	28
3	0.052	1942	0.045	1932	43
4	0.044	1942	0.038	1932	44
5	0.040	1942	0.035	1932	45
6	0.038	1942	0.034	1932	45

SQUEEZE converges at 45 electrons recovered from the masked Difference map, slightly more than the 42 of diethyl ether.

PLATON 10
OptionMenus
NoMove
Join-Expand
Organic
Round
Parentheses
Label-Alias
R/S-Determ
Norm-H-bond
NoSymm
NoDisorder
LstARU RCel
LstCellSymm
ListAtoms
ListBonds
LstFlagRadi
Exclude H
MinQPeakHgt
MinQPeakDis
Q-Peak-Incl
KeyInstruct
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SAVE-InstrS
ENTRY-LIST
Reset End
Exit
MenuActive

INSTRUCTION INPUT via KEYBOARD or LEFT-MOUSE-CLICKS (HELP with RIGHT CLICKS)

>> Hit RETURN to Continue

Summary for SHELXL97/SQUEEZE

- The SQUEEZE procedure is NOT refinement: it just determines the disordered solvent contribution to the structure factors. The discrete model parameters remain fixed.
- The final SHELXL97 refinement only optimizes the discrete parameter model
- Residual Issues: #1:The estetically not nice but technically needed subtraction of the solvent contribution from I(obs) and #2: the handling of cases with additional Twinning.

PLATON/SQUEEZE with SHELXL2013

- SHELXL2013 elegantly solved issue #1 by now accepting a fixed solvent contribution to F(calc) in the refinement against $F(obs)^2$.
- The input to SQUEEZE is now a .cif and .fcf and the output a (.lis), .ins, .hkl & .fab for the final SHELXL2013 refinement (SQUEEZE info in .fab)
- New: Handling of issue #2: SQUEEZE + Twinning: Based on the detwinning option in SHELXL2013 via a LIST 8 style FCF (as opposed to a LIST 4 FCF)

Input Files for SQUEEZE

- The current SQUEEZE tool can either be run *old-style* with name.res and name.hkl as input files (Mode 1) or with the pair name.cif and name.fcf (Mode 2). Mode 2 is preferred in combination with SHELXL2013
- Output files are either named 'name_sq.ext' or 'name_sqd.ext' (sq for sum and sqd for difference)
- The use of the 'sq' files (i.e. $F(obs)^2$ unmodified) is to be preferred in combination with SHELXL2013
- In case of twinning, the name.fcf should be of the SHELXL2013 'LIST 8' type

How to run SQUEEZE

- SQUEEZE can be run either from the PLATON menu (going through the various stages) or the terminal window command line as 'PLATON –q name.cif'. The latter without any further interaction (i.e. a filter)
- There are options to visualize the voids

PLATON

A Multipurpose Crystallographic Tool

GRAPHICS	GEOM-CALC	VOIDS FLIP	SYMMETRY	ABSORPTION	REPORT	MISC-TOOLS
PlutonAuto	Calc All	Calc Solv	ADDSYM	MULscanABS	Validation	SYSTEM-S
Ortep-Plot	Calc Intra	Calc K.P.I	ADDSYM-EQL	ABSPsiScan	ASYM-VIEW	fcf2hkl
NewmanPlot	Calc Inter	Squeeze	EXT	ABSTompa	FCF-Valid	Expand2P1
Ring-Plots	Calc Coord	Bypass	ADDSYM-PLT	ABSGauss	DifFourier	FCF-Gener
Plane-Plot	Calc Metal	CalcFCF-SQ	ADDSYM-SHX	ABSXtal	ANALofVAR	HKL-Gener
Polyhedra	Calc Geom	Contour-SQ	NEWSYM	ABSSphere	BijvoetPair	HKL-Transf
ContourDif	Calc Hbond	Solv F3D	NONSYM	SHXABS	ASYM-EXPCT	EXOR-RES
Contour-Fo	Calc TMA	Solv Plot	LePage	AnomDisVal	ASYM-Valid	ANIS-RES
AutoMolFit	L.S.-PLANE	CavityPlot	DelRed	AnomDisPlt	SupplMater	Rename-RES
HKL2Powder	DihedAngle		MOLSYM	MuPlot	EXPECT-HKL	Auto-Renum
SimPowderP	AngleLines	FLIP MENU	SPGRfromEX		CSD-CELL	Create-spf
RadDistFun	AngLsplLin	Flip Show	ASYM		CSD-QUEST	Create-res
Patterson	CremerPopl	Flip Patt	ASYMaverFR		StructTidy	Create-cif
ShelxtPlot	BondValenc	FLIPPER 25	LePageTwin	XtlPlanAgl	StrainAnal	Create-pdb
PlutONatlv	HFIX - RES	STRUCTURE?	TwinRotMat	Xtal Habit	LocCIF-acc	cif2shelxl

Xtal Data (RES) squeeze.res- Set 1(1): S1012A M0

Refl Data (HKL) squeeze.hkl [DIR-COS] (0):

http://www.platonsoft.nl/PLATON-MANUAL.pdf

Browser - HELP

INSTRUCTION INPUT via KEYBOARD or LEFT-MOUSE-CLICKS (HELP with RIGHT CLICKS)

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PLA-SP2 12
OptionMenus
Print-Level
EPS-Listing
PDF-Listing
PageHeader
KeepMon-I-n
NoExpand
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PLATON

A Multipurpose Crystallographic Tool

GRAPHICS	GEOM-CALC	VOIDS FLIP	SYMMETRY	ABSORPTION	REPORT	MISC-TOOLS
PlutonAuto	Calc All	Calc Solv	ADDSYM	MULscanABS	Validation	SYSTEM-S
Ortep-Plot	Calc Intra	Calc K.P.I	ADDSYM-EQL	ABSPslScan	ASYM-VIEW	fcf2hkl
NewmanPlot	Calc Inter	Squeeze	ADDSYM-EXT	ABSTompa	FCF-Valid	Expand2P1
Ring-Plots	Calc Coord	Bypass	ADDSYM-PLT	ABSGauss	DifFourier	FCF-Gener
Plane-Plot	Calc Metal	CalcFCF-SQ	ADDSYM-SHX	ABSXtal	ANALofVAR	HKL-Gener
Polyhedra	Calc Geom	Contour-SQ	NEWSYM	ABSSphere	ByvoetPair	HKL-Transf
ContourDif	Calc Hbond	Solv F3D	NONSYM	SHXABS	ASYM-EXPCT	EXOR-RES
Contour-Fo	Calc TMA	Solv Plot	LePage	AnomDisVal	ASYM-Valid	ANIS-RES
AutoMolFit	L.S.-PLANE	CavityPlot	[illegible]	AnomDisPlt	SupplMater	Rename-RES
HKL2Powder	DihedAngle		MOLSYM	MuPlot	EXPECT-HKL	Auto-Renum
SimPowderP	AngleLines	FLIP MENU	SPGRfromEX		CSD-CELL	Create-spf
RadDistFun	AngLsplLin	Flip Show	ASYM		CSD-QUEST	Create-res
Patterson	CremerPopl	Flip Patt	ASYMaverFR		StructTidy	Create-clf
ShelxtPlot	BondValenc	FLIPPER 25	LePageTwin	XtlPlanAgl	StrainAnal	Create-pdb
PlutONatlv	HFIX - RES	STRUCTURE?	TwinRotMat	Xtal Habit	LocCIF-acc	clf2shelxl

Xtal Data (RES) squeeze.res- Set 1(1): S1012A M0

Refl Data (HKL) squeeze.hkl [DIR-COS] (0):

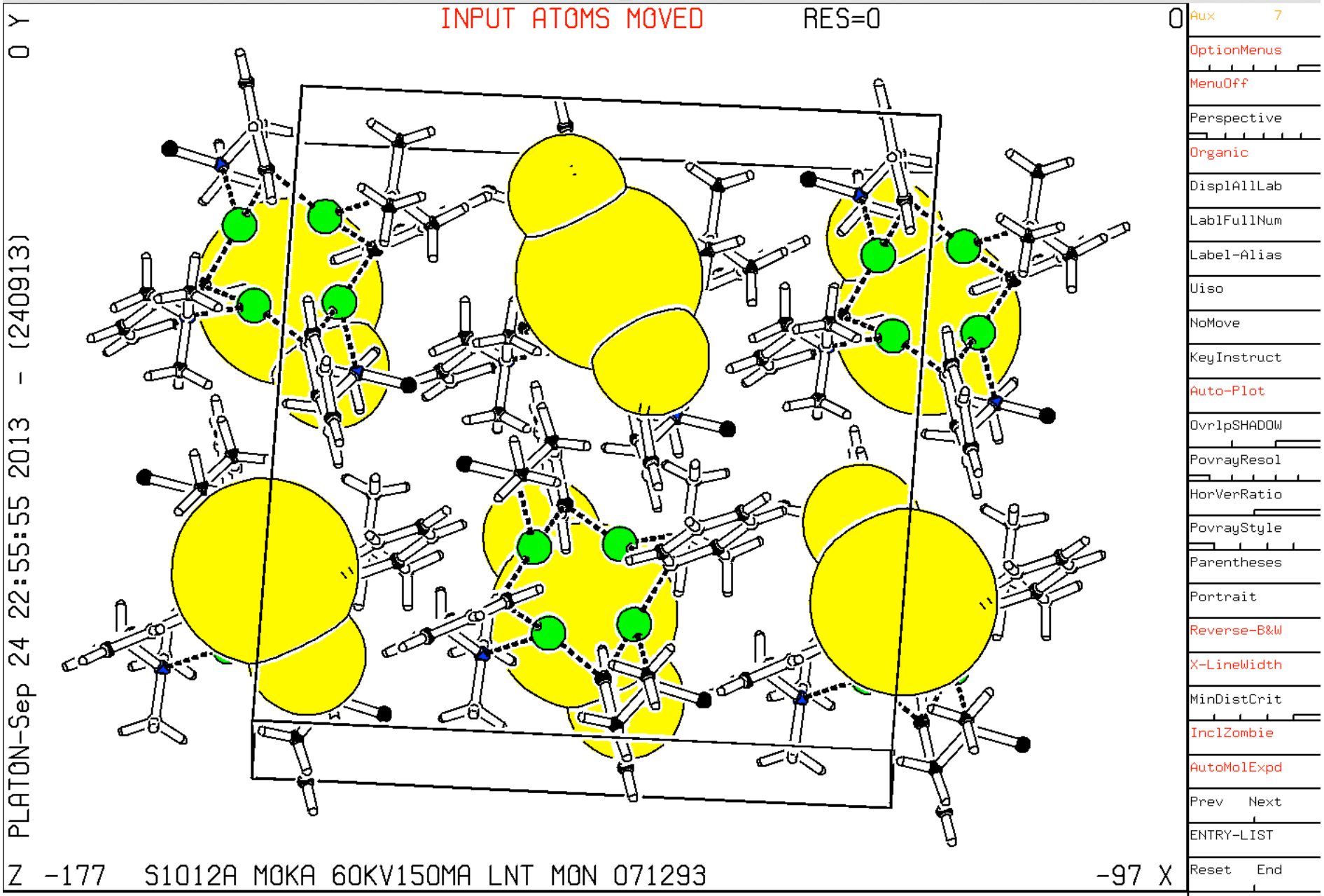
http://www.platonsoft.nl/PLATON-MANUAL.pdf

Browser - HELP

INSTRUCTION INPUT via KEYBOARD or LEFT-MOUSE-CLICKS (HELP with RIGHT CLICKS)

>>

PLA-SP2 12
OptionMenus
Print-Level
EPS-Listing
PDF-Listing
PageHeader
KeepMon-I-n
NoExpand
FCF-Calc
PNG
ReflListing
DebugOutput
SetWindSize
Portrait
GenerRandom
EPS HPGL
Auto-Plot
X-LineWidth
Reverse-B&W
Browser
Reset End
Exit
MenuActive


P.L.U.T.O.N
INPUT ATOMS MOVED
RES=0
0
Aux 7
OptionMenus
MenuOff
Perspective
Organic
DisplAllLab
LablFullNum
Label-Alias
Uiso
NoMove
KeyInstruct
Auto-Plot
OvrlpSHADOW
PovrayResol
HorVerRatio
PovrayStyle
Parentheses
Portrait
Reverse-B&W
X-LineWidth
MinDistCrit
InclZombie
AutoMolExpd
Prev Next
ENTRY-LIST
Reset End
Exit
MenuActive
0 Y
PLATON-Sep 24 22:55:55 2013 - (240913)
Z -177 S1012A MOKA 60KV150MA LNT MON 071293
-97 X
INSTRUCTION INPUT via KEYBOARD or LEFT-MOUSE-CLICKS (HELP with RIGHT CLICKS)
Alternative Void Display
>>

Disordered Solvent + Twinning Refinement protocol with SHELXL2013 and SQUEEZE

- Step 1: SHELXL refinement based a twin.ins (that should include 'LIST 8', 'ACTA', 'BASF' and 'HKLF5' records) and a twin.hkl file [merohedral: BASF/TWIN]
- Step 2: Run PLATON with the twin.cif and twin.fcf files produced in Step 1
- Step 3: Continue SHELXL refinement with the files twin_sq.ins, twin_sq.hkl and twin_sq.fab produced by PLATON in step 2.
- Note: The twin5_sq.fab file contains the solvent contribution to the SF and the details of SQUEEZE

SQUEEZE2013 Example: Coordination Compound

((M. Lutz et al.)

Space Group P21

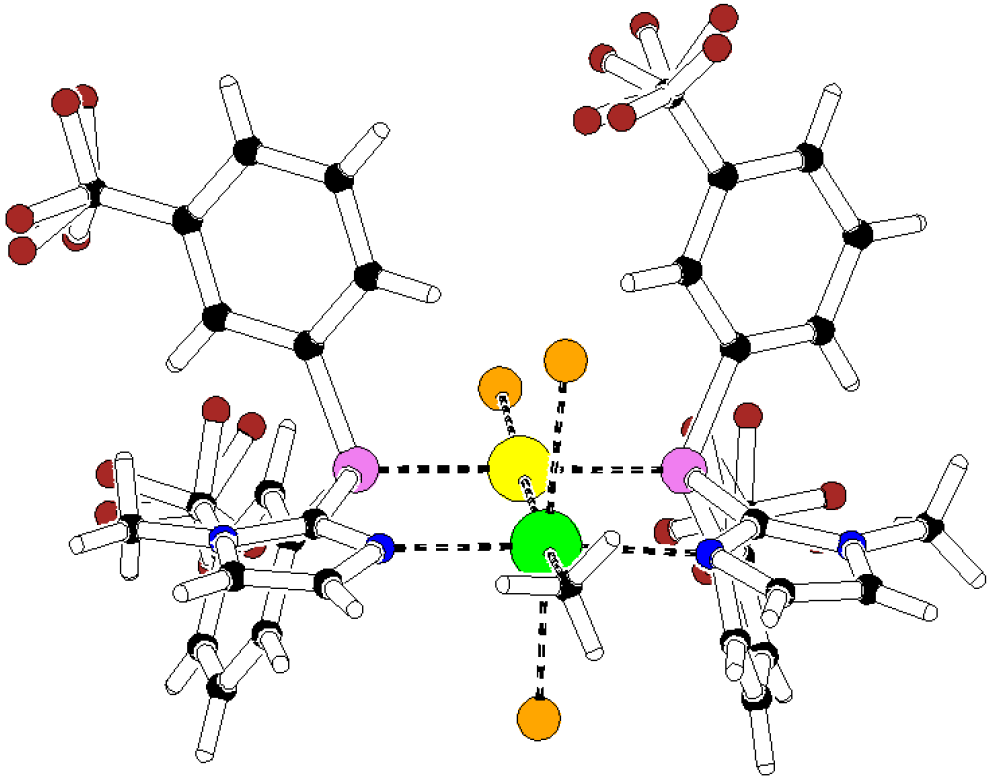
Z = 4, Z' = 2

60:40 Twin

Twin axis: (0 0 1)

150 K

Twinabs data



Step 1 (SHELXL2013) ➔ R1 = 0.047, wR2 = 0.1445

Step 2 (SQUEEZE) ➔ 188 electrons found in unit cell

Step 3 (SHELXL2013) ➔ R1 = 0.0275, wR2 = 0.0679, S = 1.064

Search for and Analysis of Solvent Accessible Voids in the Structure

Area	#GridPoint	VolPerc.	Vol(A^3)	X(av)	Y(av)	Z(av)	Eigenvector(frac)			Sig(Ang)
1	12055[1364]	2	100[11.3]	-0.063	0.498	-0.053	1	0.135	-0.083	1.000	1.75
							2	1.000	-0.262	-0.032	1.30
							3	0.467	1.000	0.135	1.03
2	12060[1364]	2	100[11.3]	0.063	0.998	0.053	1	0.135	0.083	1.000	1.74
							2	1.000	0.256	-0.031	1.30
							3	-0.456	1.000	-0.134	1.02
3	21531[2623]	4	178[21.7]	0.448	0.169	0.563	1	1.000	0.008	0.370	3.56
							2	-0.269	-0.287	1.000	1.33
							3	0.122	-1.000	-0.394	0.97
4	21530[2623]	4	178[21.7]	0.552	0.669	0.437	1	1.000	-0.008	0.369	3.56
							2	-0.268	0.288	1.000	1.33
							3	-0.122	-1.000	0.396	0.98
5	11604[1374]	2	96[11.3]	0.303	0.356	1.070	1	0.376	-0.212	1.000	1.80
							2	1.000	-0.399	-0.374	1.28
							3	0.737	1.000	0.181	0.97
6	11604[1374]	2	96[11.3]	0.697	0.856	0.930	1	0.379	0.214	1.000	1.79
							2	1.000	0.395	-0.376	1.27
							3	-0.731	1.000	-0.183	0.96

In total 6 solvent accessible voids are detected (of three types)

Difference map iteration

PLATON/SQUEEZE

Cycle	R(F)	Nref(Heml)	R(F .gt. 4Slg	Nref	El/Cell
1	0.047	21986	0.043	20938	0
2	0.036	21986	0.032	20938	141
3	0.029	21986	0.026	20938	194
4	0.028	21986	0.026	20938	189
5	0.028	21986	0.025	20938	188
6	0.028	21986	0.025	20938	188

S U M M A R Y

Total (Positive) Electron Count in Voids/Cell = 188
Number of Missing Reflections below sin(th)/L = 0.3 = 2
Electron Count Uncertain

==========

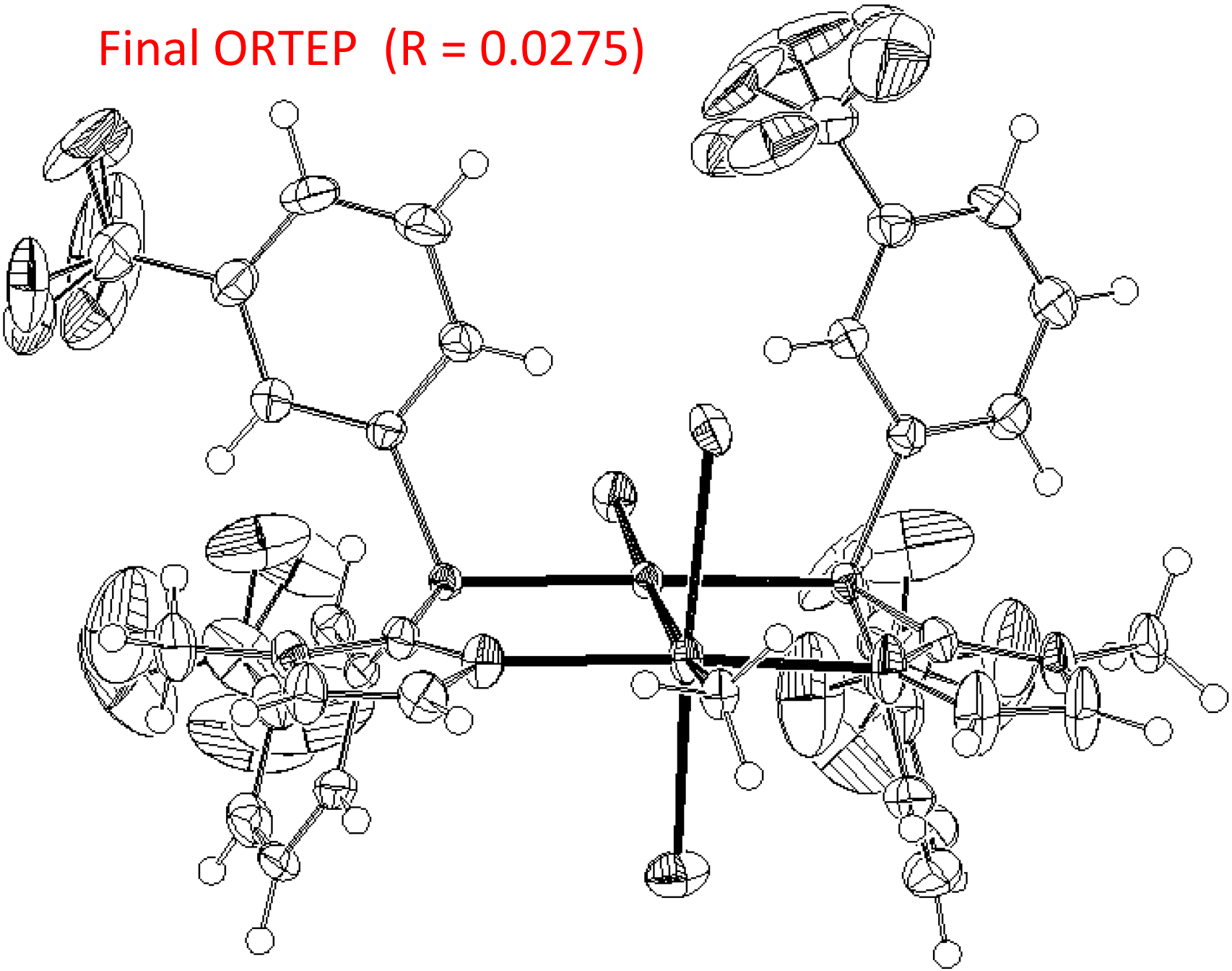
HOW TO PROCEED with L.S. refinement after running SQUEEZE:

==========

SHELXL2Oxy: Continue refinement in the presence of the three files name_sq_s.ins, name_sq_s.hkl & name_sq_s.fab

==========

Final ORTEP (R = 0.0275)



CheckCIF Validation Aspects

- The '.res', '.hkl' ,'.fab' and checksum information that is embedded in the SHELXL2013 CIF should be left untouched.
- The embedded '.fab' contains info about the use of SQUEEZE and will suppress certain irrelevant ALERTS related to the SQUEEZE use.
- It is probably best not to include the SQUEEZED solvent info in the formula and related items such as MolWeight and density .
- Report the details in the experimental section.

Embedded SQUEEZE info at the end of the .fab file

```
 -1    8   20      0.33      0.05
  0    0    0      0.00      0.00
# SQUEEZE RESULTS (APPEND TO CIF)
# Note: Data are Listed for all Voids in the P1 Unit Cell
# i.e. Centre of Gravity, Solvent Accessible Volume,
# Recovered number of Electrons in the Void and
# Details about the Squeezed Material
loop_
  _platon_squeeze_void_nr
  _platon_squeeze_void_average_x
  _platon_squeeze_void_average_y
  _platon_squeeze_void_average_z
  _platon_squeeze_void_volume
  _platon_squeeze_void_count_electrons
  _platon_squeeze_void_content
   1 -0.063  0.498 -0.053       98        25 ' '
   2  0.063  0.998  0.053       99        25 ' '
   3  0.448  0.169  0.563      176        45 ' '
   4  0.552  0.669  0.437      176        45 ' '
   5  0.303  0.356  1.070       96        24 ' '
   6  0.697  0.856  0.930       95        24 ' '
_platon_squeeze_details
TITL twin5     P 21         R = 0.05
CELL   15.2996   19.9385   15.8554     90.00     97.66     90.00
SPGR P21
# Note: Atoms in Void as Cxxx and Qxxx all others
C101 0.284 0.340 0.153 !       5.30 eA-3
C102 0.296 0.355 0.087 !       4.82 eA-3
C103 0.066 1.000 0.081 !       4.67 eA-3
C104 0.061 0.985 0.987 !       4.52 eA-3
```

Requirements

- There should be no residual unresolved density in the discrete model region of the structure because of its impact in the solvent region.
- The data set should be reasonably complete and with sufficient resolution [i.e. sin(theta)/lambda >0.6]. Low temperature data help a lot.
- There should be no unresolved charge balance issues that might effect the chemistry involved (e.g. The valency of a metal in the ordered part of the structure)

Limitations

- The SQUEEZE technique can not handle cases where the solvent region is not constant but varies due to (coupled) disorder in the discrete part of the model.
- The solvent region is assumed not to contain significant anomalous scatterers (Friedels averaged)
- Designed for ‘small molecule structures’

The ‘NEXTRA’ Issue

- One of the issues that needs to be addressed is the number of additional parameters to be added in the calculation associated with SQUEEZE on the L.S. Command. The default value is set to: (E x n) / (Z x m) where
- E = the number of recovered electrons in the unit cell
- Z = the number of asymmetric units
- m = the number of electrons in a CH2 fragment (=8)
- n = the number of parameters usually refined for a CH2 fragment (=9)

- This formula has the nice property that it vanishes when there is no residual density in the void

The MAIN Cycle

- The original BYPASS paper described a procedure involving an inner and an outer loop. In general only the inner loop (SQUEEZE) is done.
- Under certain conditions (large disorder contribution to the SF or twinning) the full BYPASS procedure including the outer loop (i.e. L.S./ SQUEEZE/L.S./SQUEEZE/. ..) can be attempted. [INVOKED as BYPASS with name.cif and name.fcf]. This routine assumes SHELXL2013.

BYPASS LOOP EXAMPLE

Instruction: Platon –q3 name.cif

SQUEEZE-SHELXL LOOP RESULTS

CYC	R1	wR2	S	RhoMax	RhoMin	Electrons	Volume
1	0.0669	0.2037	2.6450	3.97	-0.49	177.3	624.4
2	0.0304	0.0747	0.9560	0.47	-0.35	177.6	623.3
3	0.0303	0.0746	0.9550	0.47	-0.35	177.7	623.3

Concluding Remarks

- The use of SQUEEZE is recommended in cases of severe solvent disorder (being often of unknown composition or a mixture). Otherwise a disorder model should (at least) be attempted.
- The peaklist file ‘name.sqz’ that is produced from the optimized difference map as part of the SQUEEZE calculation may suggest a solvent model afterall.
- The use of the SQUEEZE procedure should always be detailed in the experimental section of a paper that is based on its use.
- Further development of BYPASS/SQUEEZE is ongoing.

PLATON runs from a terminal window under LINUX, MAC-OSX and MS-Windows (+ Louis Farrugia's MS-Windows GUI)

(http://www.cryst.chem.uu.nl/spek)
(http://www.platonsoft.nl/xraysoft)
(including a copy of this presentation)

Suggestions & Comments (with data) are Welcome: send to a.l.spek@uu.nl

Thanks

to

George Sheldrick for the new SHELXL2013

and

Martin Lutz for the Twin/Disorder example

and

Multiple User Comments (with data !)