LIGANDS Meetings

- Previously:
 - Developer \rightarrow Users

- Now (also):
 - Users \rightarrow Developers
 - There are issue/problems with CCP4 software
 - Should the developers be held to account?
 - If so, by whom?

Accountability Tracking, Bugs, Issues, Feature Requests

| Program | Issue | Type | Date | Progress | Description | Dev Comment |
|---------|--|-------------|---------------|---------------|---|--|
| Acedrg | SMILES annotation string terminates execution | Severe | 26/09/2016 | In repo EXP | | |
| | COD vs CSD-based Acedrg for drug-like molecules | Severe | 26/09/2016 | | Does the CSD provide enrichment? | |
| | SMILES annotation string for residue name | Moderate | 26/09/2016 | In repo EXP | | |
| | It's slow | Moderate | 26/09/2016 | | | Fix will be in next CCP4 update |
| CCP4i2 | Refinement Duplicate/truncated H atom names | Severe | 26/09/2016 | | | |
| | Remove Acedrg interface RDKit Conformers | Moderate | 26/09/2016 | | | |
| | Raise awareness of pyrogen | Low | 26/09/2016 | | | |
| | File for SMILES input | Low | 26/09/2016 | | | |
| | Refmac R-factor graph with no points is ugly | Low | 26/09/2016 | | There's a graph. There are no points plot | ted |
| | Acedrg output Picture too small | Low | 26/09/2016 | | | |
| | still too slow on a remote NFS to be usable | ? | 26/09/2016 | | | |
| | Interface to Dimple? | Investigate | 26/09/2016 | | For more automated ligand fitting | |
| Coot | All ligands are INH, handle dictionaries for each | Severe | 26/09/2016 | in master | | Tricky |
| | Ligand Expert should be on by default | Moderate | 26/09/2016 | in master | Don't make me use configuration | In repo now, will be in next release |
| | Tidy up menu for Ligand tools | Moderate | 26/09/2016 | | | planned to be in 0.8.8 |
| | Enable SRS searching in Lidia | Moderate | 26/09/2016 | in master | | |
| | GUI availability of top-N solutions | Low | 26/09/2016 | in master | | |
| | Ligand Fit Post-Refine checkbutton | NiceToHave | 26/09/2016 | in master | | |
| | Better GUI on conformer generation | NiceToHave | 26/09/2016 | in master | | Involves timeouts or threads |
| | Can we fit these ligands without intervention? | Investigate | 26/09/2016 | | | Research project - may need to redo ligand f |
| Lidia | Chirality failure on Acedrg dict \rightarrow 2D | Severe | 26/09/2016 | in master | | |
| | SMILES \rightarrow 2D chirality failure | Severe | 26/09/2016 | | | |
| | What is happening when you press the apply button? | Moderate | 26/09/2016 | | Tell me what's running and how it's going | Waiting for a fix in Acedrg output |
| | Lidia → Acedrg molecule should bevia mmCIF | Moderate | 26/09/2016 | | | Currently is MOL file, move to mmCIF may h |
| | | | Important, no | ot done | | |
| | | | Moderate imp | portance, not | done | |
| | | | Done, availab | ble now/soon | | |
| | | | Reseach Pro | ject | | |
| | | | No Feedback | c | | |

Minutes: Items to add to Tracker

- Atom name matching in AceDRG
- Ability to stop hydrogen shuffling in AceDRG

Minutes: Items to deleted from Tracker

• CCP4i2 Dimple interface

Coot Updates

Dec 2016

Coot Updates

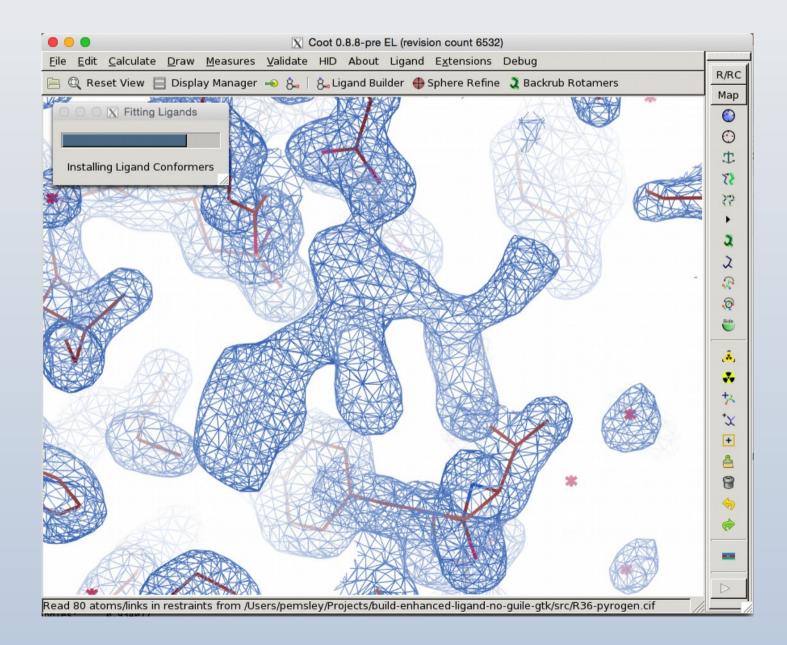
- Coot 0.8.7 released
 - Lidia Canvas scaling
 - Lidia CH3 Superatoms
 - Corrected bonds for WO4
 - File \rightarrow SMILES removed
 - GUI/widget updates
 - as suggested by the previous meeting

Ligand Fitting Interface

| | Find Ligands |
|---|----------------------------|
| | |
| | - |
| 4 | |
| Select Map: | |
| I Job 8: Weighted m | ap from refinement |
| 🔿 2 Job 8: Weighted di | fference map from refineme |
| | _ |
| | |
| | |
| Select Protein: (Mas | |
| | d by Prosmart_Refmac |
| O 3 R36_from_dict | |
| | _ |
| 4 | • |
| Mask Waters? | |
| Treat waters like pro | tein (mask) atoms |
| O Ignore waters for ma | ask |
| Where to Search? | |
| Everywhere | |
| Right here | |
| Sites Options | |
| Search Number of Top | o Sites: 10 |
| r.m.s.d level | 1 |
| 1.2 | rmsd |
| Conformer Options | to Grande Inc |
| Number of Conformers | |
| Solution Display Opt Multi-Solutions | |
| Fraction for Scoring | 0.82 |
| Fraction for Correlation | |
| Post-Fit Options | |
| Real Space Refine S | Solutions? |
| 4 | |
| | 🖑 Find Ligands 🛛 🐰 Cancel |
| _ | |

Conformer Enumeration Expert Mode Multi-Solution Post-Refinement

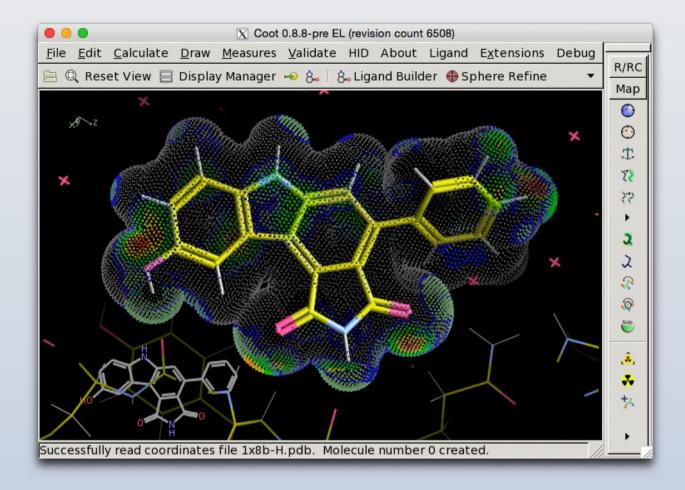
Ligand-Fitting Interface



Molecule-specific Dictionaries

| | | Size Modified |
|---------------|----------------------|----------------------------|
| laces | Name | Size Modified |
| Search | 🛅 quo-vadis | 24/05/2016 |
| Recently Used | 📄 mery | 18/05/2016 |
| src | 🛅 all-comp-ids | 29/04/2016 |
| 📄 pemsley | acedrg | 28/04/2016 |
| 🗋 Desktop | 🛅 clemens | 08/04/2016 |
| 🛿 File System | 🛅 coot_refmac | 16/03/2016 |
| 📄 checkout | 🛅 abid | 11/03/2016 |
| 🗎 GlyHb | 📄 greg-tests | 09/02/2016 |
| 🗎 bucca-test | 📄 R36-pyrogen.cif | 19.2 kB 19:27 |
| 🗎 quo-vadis | C7M.cif | 23.2 kB 01:05 |
| | C6A.cif | 45.0 kB 00:47 |
| | C70.cif | 27.8 kB Yesterday at 22:13 |
| | C.cif | 13.1 kB Yesterday at 11:47 |
| | 🗋 XIN-acedrg.cif | 42.7 kB 15/11/2016 |
| | 🗋 1lee-no-ligand.cif | 296.9 kB 06/11/2016 |
| | 🗋 1lee.cif | 368.4 kB 06/11/2016 |
| | | |

New: Coot Ligand Interactions

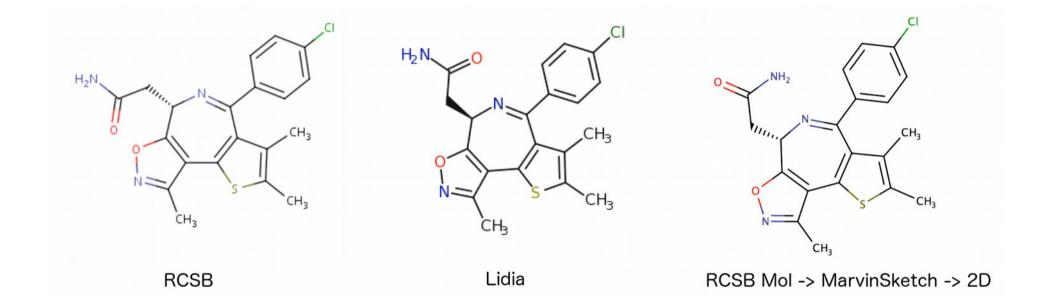


"Reduce" & "Probe":

Protein (including HIS), RNA, DNA, Ligands

But not OH optimisation by clique analysis

1XB: an Example of the Chirality Problem

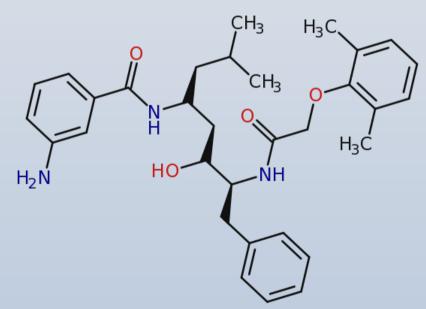


C14 has "S" pdbx stereo config

Ligand Fitting Trials 2

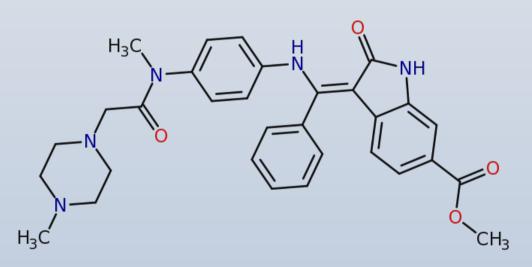
Ligand Fitting Trials 2: Dec 2016

- Problem 1:
 - Target: Plasmodium falciparum enzyme (an aspartic acid protease), important in malaria pathology
 - Resolution 1.9 Å
 - R-factor 23.6%



Ligand Fitting Trials 2: Dec 2016

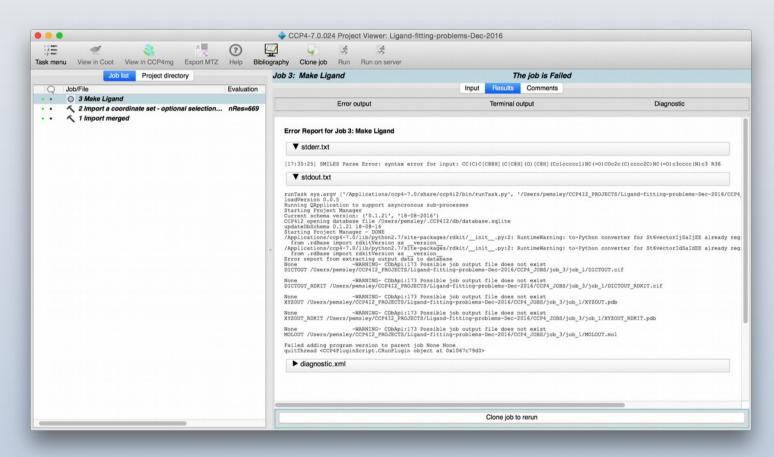
- Problem 2:
 - Adaptor Protein 2 Associated Kinase (AAK1)
 - Structural Genomic Consortium
 - Resolution 1.9 Å
 - R-factor 18.1%



"User" Hat

Problem 1: Acedrg Still Fails

Cut and paste annotated SMILES string



CCP4 version 7.0.024 CCP4i2 version: 0.05 Acedrg version: ???

Problem 1: Acedrg Still Fails

• Vast space, uneditable SMILES string

| | | | | | CCP4-7.0.024 Project Viewer: Ligand-fitting-problems-Dec-2016 |
|---|--|-----------------------------|--------------|--------|---|
| - 10 Equits - 2 Equits - 2 - Equits | a de la companya de l | 3 | R | ? | |
| Task menu | View in Coot | View in CCP4mg | Export MTZ | Help | Bibliography Clone job Run Run on server |
| | Job list | Project directory | | | Job 3: Make Ligand The job is Failed |
| Q | Job/File | | | Evalua | Input Results Comments |
| • • | 3 Make Ligand | | | - | Input data Advanced |
| | 2 Import a coo 1 Import merg | ordinate set - option ed | al selection | nHes | Job title Make Ligand |
| | | | | | |
| | | | | | Start point |
| | | | | | Start with molecular structure from a SMILES string |
| | | | | | SMILES string |
| | | | | | Three letter code for output monomer R36 |
| | | | | | |

Problem 1: Acedrg Interface Fail

• (Still) no mechanism to provide a dictionary, a list of dictionaries, a list of three letter codes for reference atom name matching

- EJD: We need a program that will take a molecule description (e.g. SMILES, mol) and provide a list of molecules in the CCD that are similar
 - And CCP4i2 interface to this

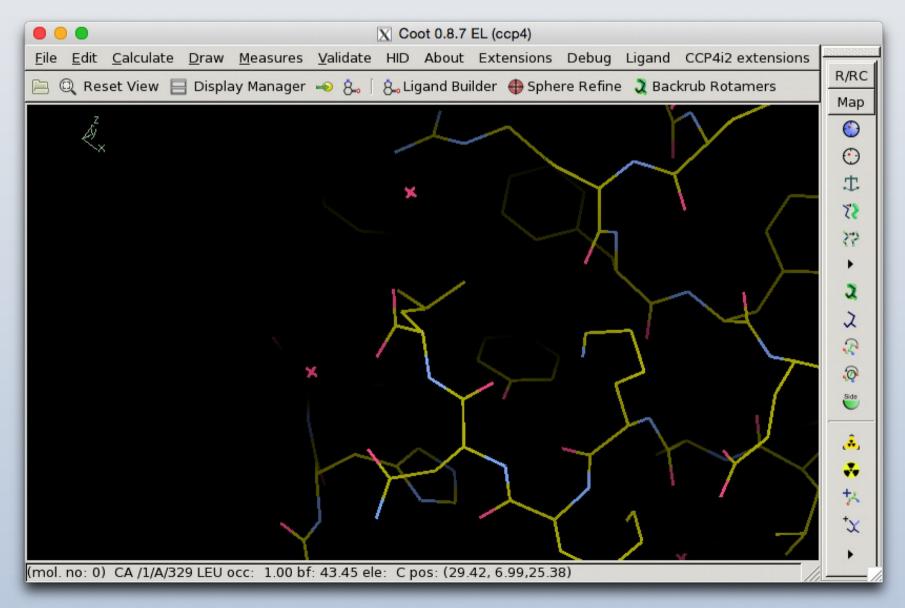
Problem 1: CCP4i2 Pictures Fail

• Still too small to be useful

| ask menu | View in Coot | View in CCP4mg | Export MTZ | (?) Help | CCP4-7.0.024 | 4 3 | چ Run on ser | | | | | | | |
|----------|---|----------------------------|---------------|-------------|---------------|----------|-----------------|----------|---------------|--------------|---------------|-----------------|--------|-----|
| | Job list | Project directory | | | Job 4: Make I | igand. | | | Th | e job is Fin | nished | | | |
| | lob/File | | | Evalua | | | | Input | Results | Comments | | | | |
| 2 | 4 Make Ligand 3 Make Ligand 2 Import a cod 1 Import merg | f ordinate set - optior | nal selection | nRes | 2D Structures | Pictures | Chirals | Torsions | Planes | Bonds | Angles | Energy vs. rank | Biblio | Run |
| | | | | | Picture | | | | | | | | | |
| | | | | • | • | | | er. | £ | | R36_RDKit.pdb | , | | |
| | | | | | | | View in | CCP4mg | View in | n Coot | | | | |
| | | | | _ | | | | Manu | al model buik | ding - COOT | | | | |

Problem 1: Ugly Coot

• CCP4 Build of *Coot* for Mac is not antialiased:



Problem 1: Refmac Fails to Run

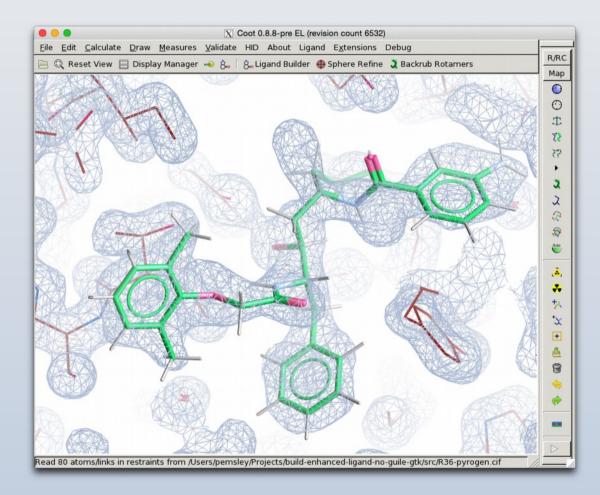
• OXT in residue LEU at C-terminus

PDB code:1LEE PDB name:plasmepsin, aspartic protease, plasmodium falciparum, HYDROLASE PDB date:XX-XXX-XX ERROR : atom :OXT LEU329 Ais absent in the libraryATTENTION: atom:OXT HOH1341 Ais missing in the structureWARNING : HOH1341 A: back_atom for OXT is absentNumber of chaipsImage: Addition of the structure : -Number of chains 1 669 Total number of monomers : 6185 Number of atoms Number of missing atoms : 1 Number of rebuilt atoms : 2539 Number of unknown atoms 1 Number of deleted atoms 0 IERR = 1 There is an error. See above ===> Error: Fatal error. Cannot continue

Problem 1: *Coot* Flexible failed using Acedrg Dictionary

- Exited immediately with error message
 ERROR: in install_simple_wiggly_ligands() Atom name(s) not found in residue. Unassigned atoms:
 " H1 "
- Non-conformer fit search Failed also
 - Acedrg conformer very unlike the density

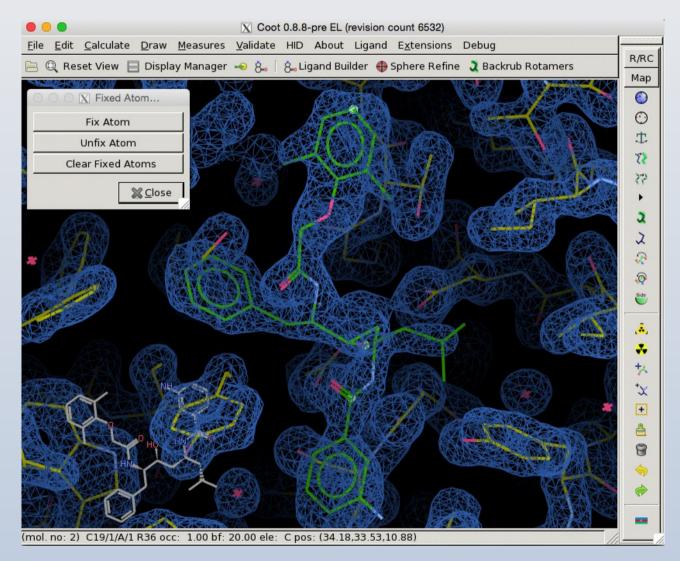
Problem 1: Ligand Fitting with Pyrogen Dictionary



Increased to 200 Conformers

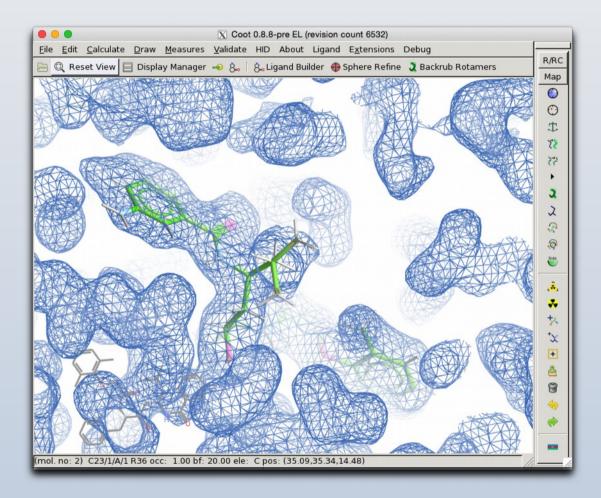
The amino group of the amino-benzamide is flipped out Why? Hint, hint!

Problem 1: (Back to Acedrg dictionary): Use Fixed Atoms



Fix Atoms (Green Spots) and drag them into place (very manual)

Problem 1: JED-Flip the "Valine" sidechain

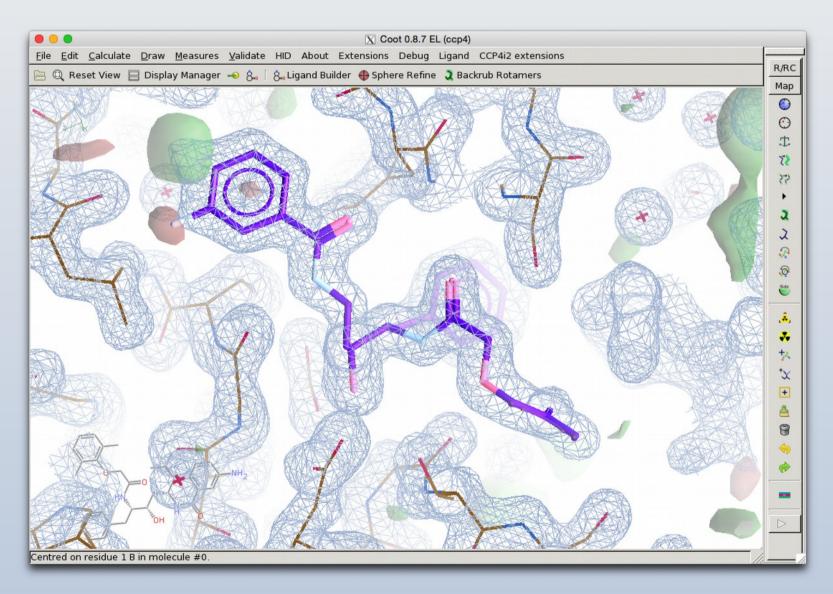


Refmac in CCP4i2

• Works OK

| Task menu | View in Coot | View in CCP4mg Export N | 0 | CCP4-7.0.024 Proje | ් S b Run Run on | ŝ | | | | |
|-----------|---|-------------------------------------|----------|--------------------------|---------------------|----------------|------------------------|---------------------|-----------------|-------------------|
| | Job list | Project directory | | Job 11: Refinement | - REFMAC5 | | The job i | is Finished | | |
| | Job/File | | Eval | | | Input | Results Comm | nents | | |
| | | del building - COOT | | Default weight | Per cycle | Picture | Outliers | Other | Biblio | Run |
| | 11 Refinement | nt - REFMAC5 del building - COOT | R=0 | | | | | | | |
| •• | < 8 Refinement | | R=0 | Refinement - REFMAC5 | | | | | | 19:17 04-Dec-2016 |
| •• | 6 Refinement 5 Analyse ge | ometry | | ▼ Refinement | | | | | | |
| | 4 Make Ligan | | | Statistic | Value | | Runni | ng refmac R-factors | ٢ | |
| | 3 Make Ligan 2 Import a co | ordinate set - optional selec | tion nRe | Resolution | 69.85-1.80 | | 0.250 | | | - 0.022 |
| | < 1 Import mer | | | No. reflections all/free | 23618 / 1181 | | 9 00 | | R_Factor | - 0.021 |
| | | | | R-factor/R-free | 0.156 / 0.224 | 2 | 0.225 | 1000 | R_Free | 0.020 |
| | | | | RMS Deviations | | R-factor | | | rmsBond | - 0.019 |
| | | | | Bonds | 0.0165 | 10 | 0.200 | | | - 0.018 |
| | | | | Angles | 1.903 | - | 0.175 | | | - 0.017 |
| | | | | Chain mean B | | | 0.175 | | | -0 0.016 |
| | | | | (No. atoms) | | | 0.150 | | <u> </u> | 0.015 |
| | | | | AA | 25.2(5034) | | 2 | 4 6 | 8 | 10 |
| | | | | Download | | | | Cycle | | |
| | | | | | | | | | | |
| | | | | Current weight | applied to X | -ray term is (| 0.3839853 | | | |
| | | | | Per cycle stat | istics | | | | | |
| | | | | ► Picture | | | | | | |
| | | | | Outliers identif | ied by Refmac | | | | | |
| | | | | Other plots from | m log file | | | | | |
| | | | | | | | | | | |
| | | | | Refinemer | t - REFMAC5 | T Man | ual model building - C | 00T | Autobuild - BUC | CANEED |

Problem 1: Is it the right ligand?



No, it isn't

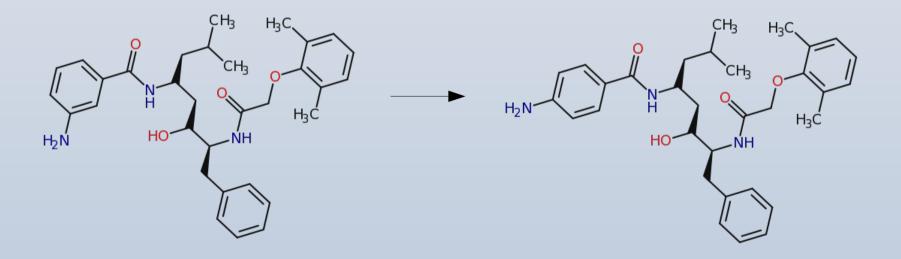
Edit the Molecule: How?

| ••• | | | CCP4-7.0.024 Project Viewer: Ligand-fitting-problems-Dec-2016 | | | | | | | | | | |
|-----------|---|------|--|--|------------------|------------|------------|----------|------------------|--------------|-----------------|------------|---------------|
| E | | 3 | | | | | | | | | | | |
| Task menu | View in Coot View in CCP4mg Export MTZ H Job list Project directory | | Bibliography Clone job Run Run on server Job 12: Make Ligand The job is Running | | | | | | | | | | |
| Q | | Eval | Input Results Comments | | | | ~ | | | | | | |
| | 🤧 12 Make Ligand | Lva | Input data Advanced | | | | | | | | | | |
| . : : | 12 Manual model building - COOT 11 Refinement - REFMAC5 | R=0 | Job title Make Ligand | | | | | | | | | | |
| | S 9 Manual model building - COOT | 11=0 | Job title make Ligand | | | | | | | | | | |
| Þ • • | 8 Refinement - REFMAC5 7 Manual model building - COOT | R=0 | | | | | | | | | | | |
| | © 6 Refinement - REFMAC5 | | Reducted | | | | | | | | | | |
| ••• | 5 Analyse geometry 4 Make Ligand | | Start point Start with molecular structure from a | ketch | | | | | | | | | |
| | © 3 Make Ligand | | Will launch Lidia to sketch molecule. Click Apply and Close in Lidia when sketch is ready. | | | | | | | | | | |
| » · · | 2 Import a coordinate set - optional selection 1 Import merged | nRe | Optionally can provide a starting monomer for the Lidia sketch: | | | | | | | | | | |
| | - I import merged | | Mol file 4 MOL file from RDKIT | | | | | | | | | | |
| | | | | | P. | | | X Lic | lia: Coot's Liga | nd Builder | | | |
| | | | Output monomer | | splay <u>H</u> e | lp | | | | | | | |
| | | | | | 4 | | _ | = | | \otimes | 9 | | |
| | | | | Clear | Undo | Single | | | ereo Charge | Cut Del | ete Hydrogens S | | |
| | | | | ······································ | ondo | Single | Double | mpie se | | Cut Dei | | MEES Huy | 00 |
| | | | | \triangle | | 0 | \bigcirc | 0 | 00 | + | 2 | | |
| | | | | 3-C | 4-C | 5-C | 6-C (| 6-Arom | 7-C 8-C | Env. Residue | es Key | | |
| | | | | C | | | | | | | | | 1 |
| | | | | N | | | | | | | | | |
| | | | | 0 | | | | | | | | | |
| | | | | s | | | | | | | | | |
| | | | | Р | | | | | | | | | |
| | | | | н | | | | | | | | | |
| - | | _ | | F | | | | | | | | | |
| | | | And the second | СІ | | | | | | | | | |
| | | | | | | | | | | | | | 100 |
| | | | | • - | | | | | | 1 | | | |
| | | | | | | | | | | | | Scale 1.00 | |
| | | | | SMILES: | | | | | | | | | 121 |
| | | | | QED: | | | | | | | | Sho | w Alerts |
| | CCP4i2 vs l | i | dia: Edit | Mol. V | Veight | | | cLogP | | #HBA | #Don | ors | |
| | | | | | PSA | | #Ro | tBonds | | #Arom | #Ale | | |
| | Durautions AA | | | | | | | | | | | | |
| | Previous M | 0 | iecule fall | Flip Arou | und X I | Flip Arour | nd Y Rot | ate Z 10 | degrees < | Apply | | | |
| | | | | | | | | | Search Data | abase | | 1 | 1 |
| | | | | | | | | | 0 | .1 | 1 .1 | | Close |
| | | | | | | | | | Searc | h Similarity | : 0.95 🔻 | Apply 💥 | <u>C</u> lose |
| | | | | | | | | | | _ | | | / |

meta \rightarrow para

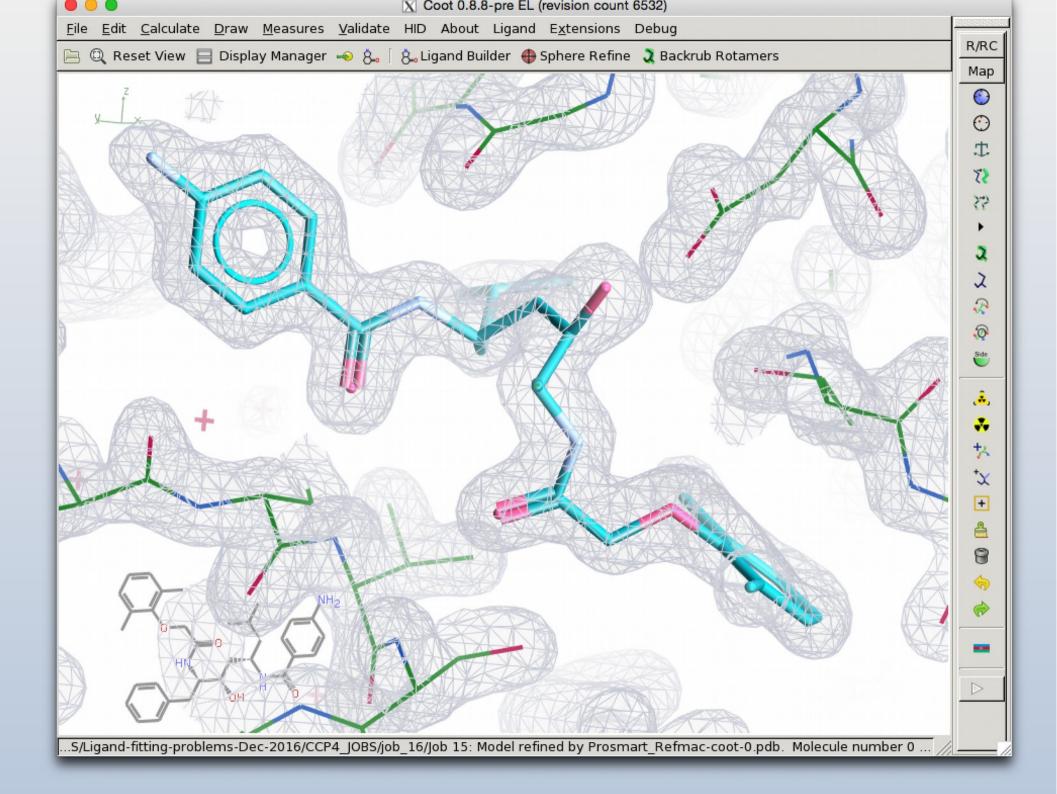
So, back to Lidia...

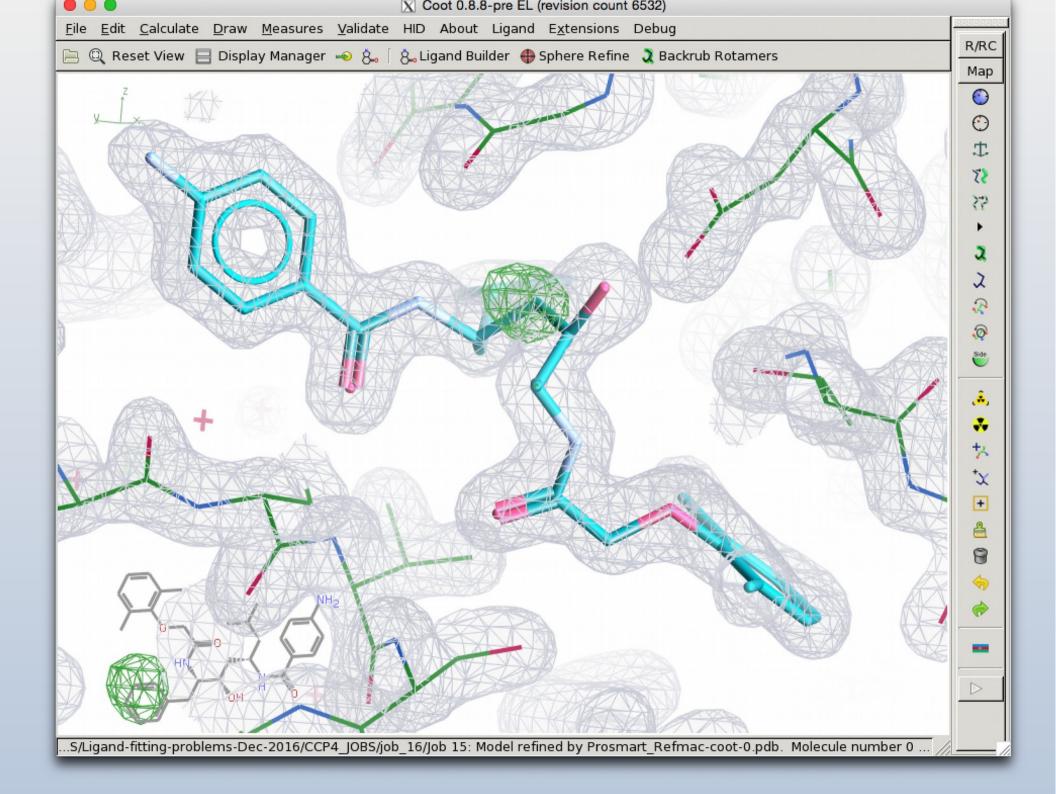
Read in SMILES string Edit molecule Apply

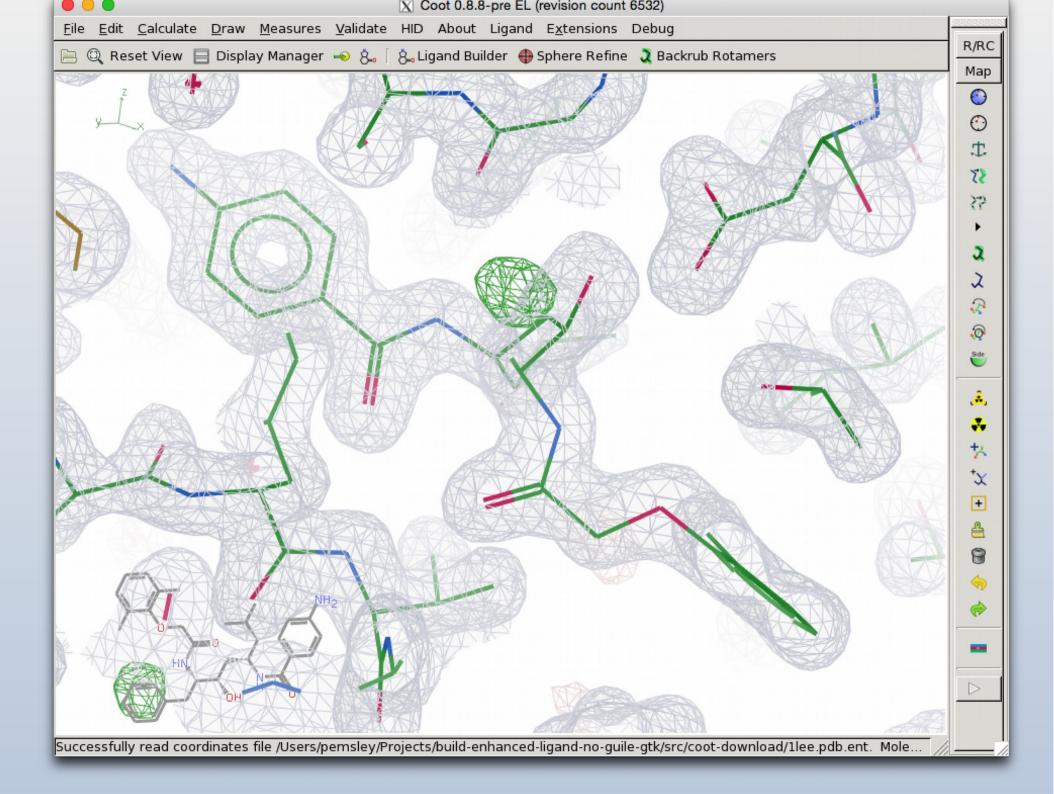


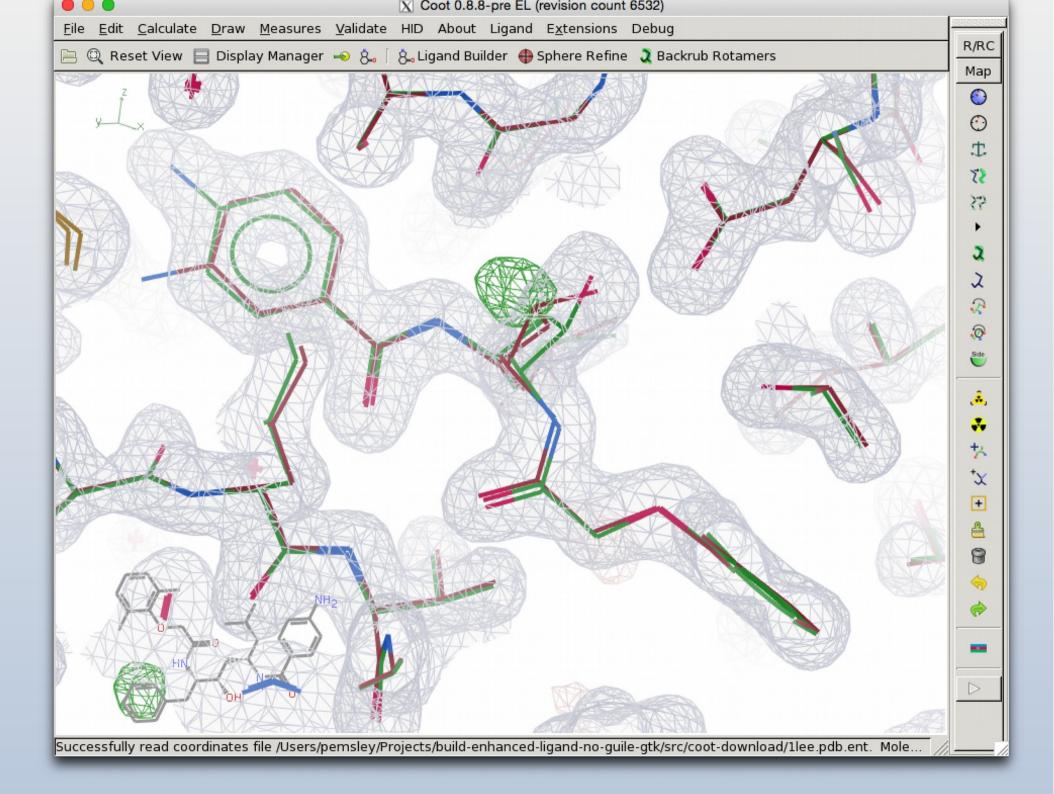
Re-refine

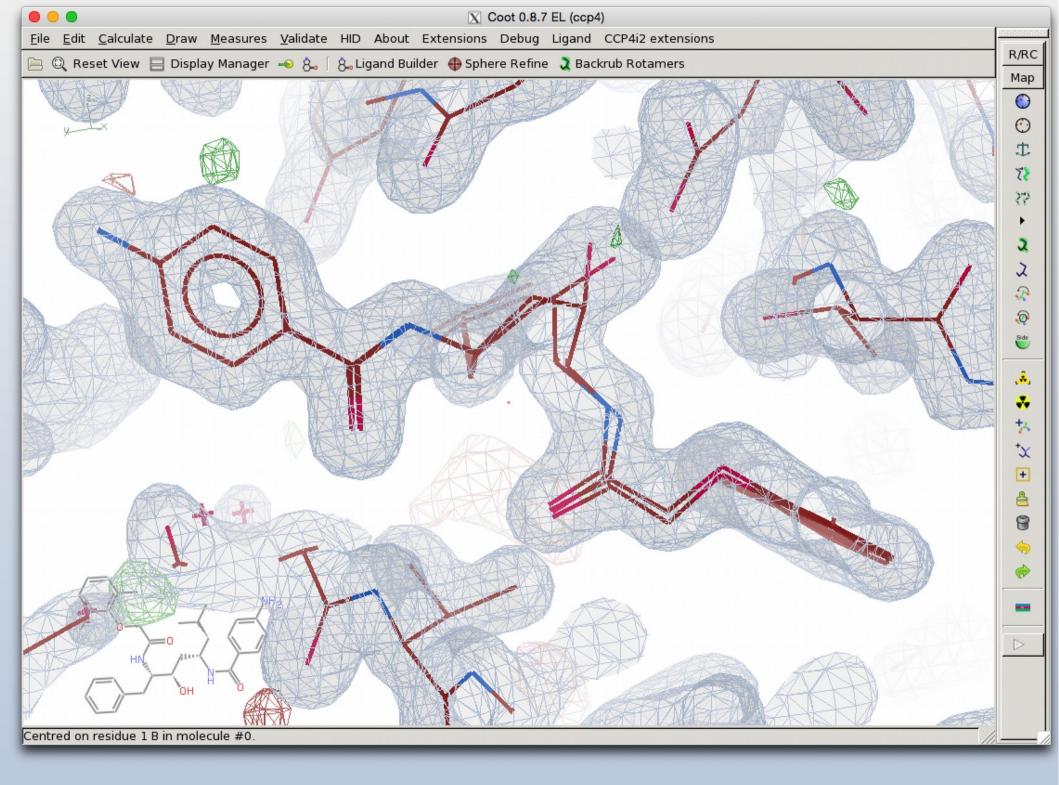
- In the updated, Acedrg dictionary, the atom names are the same, one bond is different
 - Read old model and use new dictionary
 - RSR Refine
 - Not needed of course, once the above is recognised
 - Refmac
 - Works fine now, inconsistent chirality of C19
 - R and R-free 15.6% 22.4%

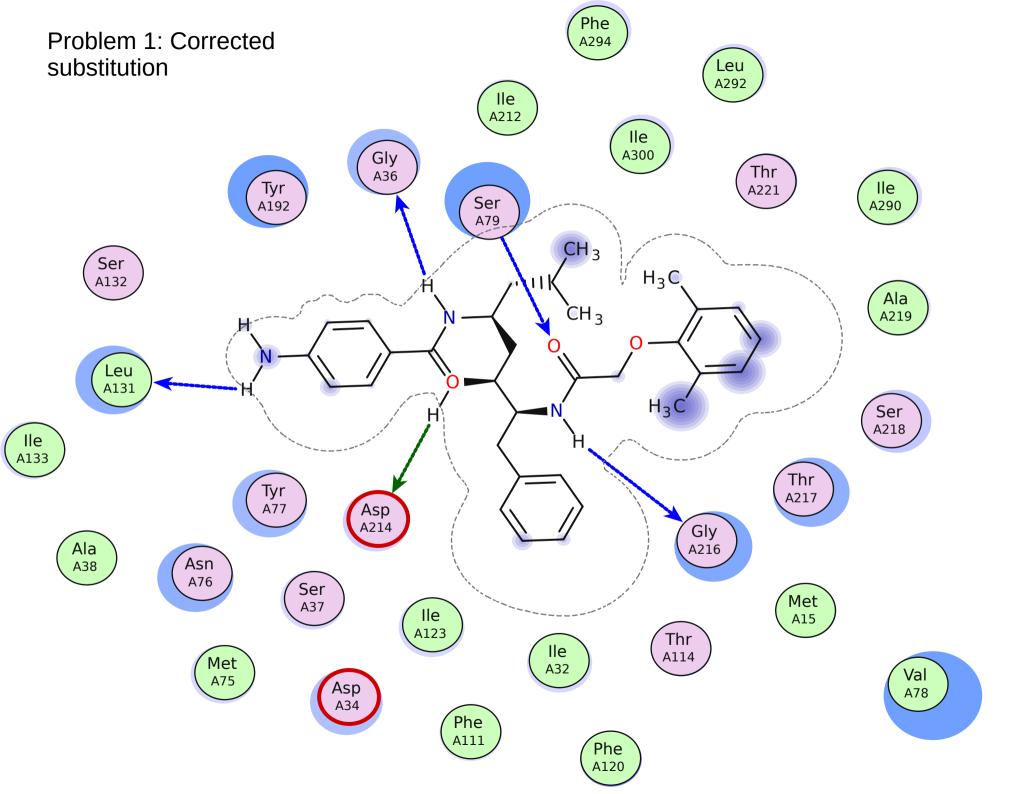








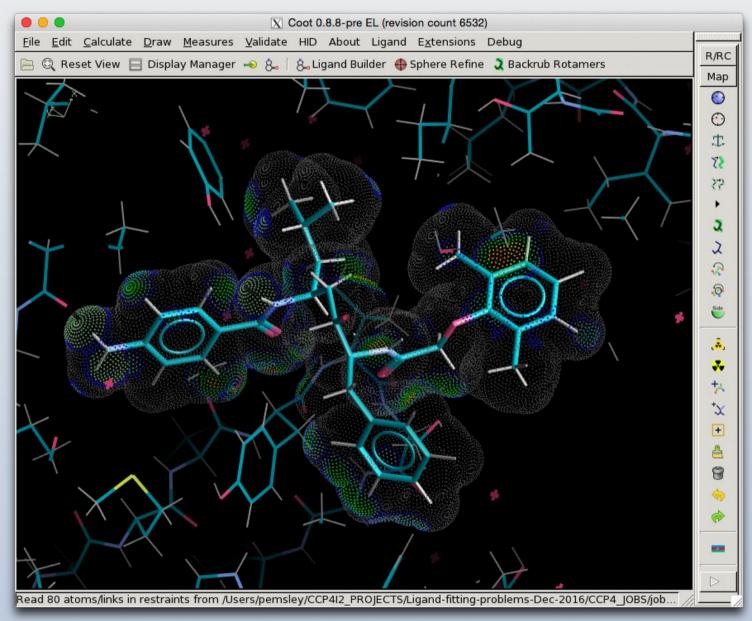




Coot Flatland Ligand Environment View

- congestion problems
- SVG, pdf output looks fine
- png output is boxed/truncated

Coot's Probe & Reduce



Pre-release (not release)

Problem 2: Importing

| 14 Manual model building - COOT 13 Make Ligand 12 Make Ligand 12 Manual model building - COOT 11 Refinement - REFMAC5 9 Manual model building - COOT | | | Q | Job/File | Evaluation |
|---|---|---|---|--|-------------------|
| 16 Manual model building - COOT 15 Refinement - REFMAC5 14 Manual model building - COOT 13 Make Ligand 12 Manual model building - COOT 12 Manual model building - COOT 11 Refinement - REFMAC5 9 Manual model building - COOT 8 Refinement - REFMAC5 8 Refinement - REFMAC5 7 Manual model building - COOT 6 Refinement - REFMAC5 7 Manual model building - COOT 6 Refinement - REFMAC5 7 Manual model building - COOT 6 Refinement - REFMAC5 7 Manual model building - COOT 2 Import a coordinate set - optional selection nRes=669 | | • | | 17 Import a coordinate set - optional selectio | |
| 15 Refinement - REFMAC5 14 Manual model building - COOT 13 Make Ligand 12 Make Ligand 12 Manual model building - COOT 11 Refinement - REFMAC5 9 Manual model building - COOT 9 Manual model building - COOT 8 Refinement - REFMAC5 7 Manual model building - COOT 6 Refinement - REFMAC5 5 Analyse geometry 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | Þ | ٠ | • | 16 Import merged for problem 2 | |
| 14 Manual model building - COOT 13 Make Ligand 12 Make Ligand 12 Manual model building - COOT 11 Refinement - REFMAC5 9 Manual model building - COOT 8 Refinement - REFMAC5 8 Refinement - REFMAC5 8 Refinement - REFMAC5 7 Manual model building - COOT 6 Refinement - REFMAC5 6 Refinement - REFMAC5 6 Refinement - REFMAC5 6 Refinement - REFMAC5 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | | ٠ | • | 🤧 16 Manual model building - COOT | |
| 13 Make Ligand 12 Make Ligand 12 Manual model building - COOT 11 Refinement - REFMAC5 9 Manual model building - COOT 9 Manual model building - COOT 8 Refinement - REFMAC5 8 Refinement - REFMAC5 7 Manual model building - COOT 6 Refinement - REFMAC5 6 Refinement - REFMAC5 5 Analyse geometry 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | • | • | • | 15 Refinement - REFMAC5 | R=0.15 RFree=0.22 |
| 12 Make Ligand 12 Manual model building - COOT 11 Refinement - REFMAC5 9 Manual model building - COOT 8 Refinement - REFMAC5 8 Refinement - REFMAC5 7 Manual model building - COOT 6 Refinement - REFMAC5 6 Refinement - REFMAC5 6 Refinement - REFMAC5 5 Analyse geometry 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | • | ٠ | • | 🔨 14 Manual model building - COOT | |
| 12 Manual model building - COOT 11 Refinement - REFMAC5 9 Manual model building - COOT 8 Refinement - REFMAC5 8 Refinement - REFMAC5 7 Manual model building - COOT 6 Refinement - REFMAC5 6 Refinement - REFMAC5 6 Refinement - REFMAC5 5 Analyse geometry 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | • | ٠ | • | 🔨 13 Make Ligand | |
| 11 Refinement - REFMAC5 9 Manual model building - COOT 8 Refinement - REFMAC5 8 Refinement - REFMAC5 7 Manual model building - COOT 6 Refinement - REFMAC5 6 Refinement - REFMAC5 5 Analyse geometry 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | • | ٠ | • | 🔨 12 Make Ligand | |
| 9 Manual model building - COOT 8 Refinement - REFMAC5 7 Manual model building - COOT 6 Refinement - REFMAC5 6 Refinement - REFMAC5 5 Analyse geometry 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | | ٠ | • | 12 Manual model building - COOT | |
| 8 Refinement - REFMAC5 R=0.19 RFree=0.2 7 Manual model building - COOT 6 Refinement - REFMAC5 5 Analyse geometry 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | • | • | • | 11 Refinement - REFMAC5 | R=0.16 RFree=0.22 |
| 7 Manual model building - COOT 6 Refinement - REFMAC5 5 Analyse geometry 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | • | ٠ | • | 🔨 9 Manual model building - COOT | |
| 6 Refinement - REFMAC5 5 Analyse geometry 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | • | • | • | 🔨 8 Refinement - REFMAC5 | R=0.19 RFree=0.25 |
| 5 Analyse geometry 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | • | • | • | 🔨 7 Manual model building - COOT | |
| 4 Make Ligand 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | • | ٠ | • | 6 Refinement - REFMAC5 | |
| • • • • • 2 Import a coordinate set - optional selection nRes=669 | | ٠ | • | 🔨 5 Analyse geometry | |
| | • | ٠ | • | 🔨 4 Make Ligand | |
| • • 🔨 1 Import merged | • | • | • | 1 Import a coordinate set - optional selection | nRes=669 |
| | • | ٠ | • | 🔨 1 Import merged | |
| | | | | | |
| | | | | | |

- Two Job 12s, two job 16s. Surely that a mistake?
- All text is **bold italic** ugly

Problem 2: Issues

- Similar issue to Problem 1
 - Acedrg output files fail with multiple conformations in Coot
- Ligand search without conformation search works in this case
- The positions of the hydrogen atoms is important
 - stripping hydrogen atoms when producing the output is a reasonable default... but
 - how do I tell CCP4i2 to leave them on?
 - not obvious to me
- I edited the SMILES string to add H to the piperazine
- RDKit is still being used at the back-end of the Acedrg job

Problem 2: Issues

- I edited the SMILES string to add H to the piperazine
- Stop coot start again
 - XIN dictionary read at start-up
 - Get Monomer
 - No hydrogens!
 - Why...?
 - Because they are not in the dictionary

XIN dictionary from Acedrg

| XIN | C24 | С | CR1 | 6 0.000 | 0.844 | -0.96 | -0.644 |
|-----|-----|---|-----|---------|----------|-----------------|--------|
| XIN | C25 | С | CR1 | 6 0.000 | 0 -0.347 | - 0.356 | -0.719 |
| XIN | C26 | С | CR6 | 0.000 | -3.137 | -0.152 | 0.738 |
| XIN | C27 | С | CR1 | 6 0.000 |) -2.673 | 8 -0.057 | 1.997 |
| XIN | C28 | С | CR1 | 6 0.000 |) -2.688 | 3 -1.237 | 2.887 |
| XIN | C29 | С | CR1 | 6 0.000 | -3.156 | 5 -2.408 | 2.443 |
| XIN | C30 | С | CR1 | 6 0.000 | -3.645 | 5 -2.528 | 1.054 |
| XIN | C31 | С | CR1 | 6 0.000 |) -3.627 | ′ -1.465 | 0.241 |
| XIN | H1 | Н | Н | 0.000 | • | | |
| XIN | H2 | Н | Н | 0.000 . | | | |
| XIN | H3 | Н | Н | 0.000 . | | | |
| XIN | H4 | Н | Н | 0.000 . | | | |
| XIN | H5 | Н | Н | 0.000 . | • | • | |
| XIN | H6 | Н | Н | 0.000 . | | | |

• Acedrg need to output correct Hydrogen atom names with coordinates

CCP4i2 & Coot

- Running Refmac
 - Makes CCP4i2 sluggish, beachball and the computer turns on its fans to full power – processes refmac5, ccp4i2, kernel_tasks. Then unresponsive
- There was a lot of opening and closing coot
- I don't like that
 - I'd rather work in coot and submit refinement jobs, and import and export new models and ligands
 - i.e. CCP4i2 should be a browser and database interface
 - not the only "front-end" by which jobs can be executed
 - I want a database/job browser in Coot
 - Compared to the Phenix interface, it's primitive and static
- .dict is not a good extension for a restraints dictionary cif file
 - use.cif or .pdbxr
 - The file selector uses *.cif

| Job list Project directory | Job 31: Refinement - REFMAC5 | | The job is Running | | |
|--|-------------------------------------|------------|--------------------------|----------|---------|
| ob/File Evaluation | | Input R | Results Comments | | |
| 31 Refinement - REFMAC5 30 Import a coordinate set - optional selectio nRes=1 29 Make Ligand | | D | efault weight | | |
| 25 Refinement - REFMAC5 R=0.19 RFree=0.22 24 Manual model building - COOT | ▼ Refinement | | | | |
| 23 Make Ligand 22 Manual model building - COOT | Cycle R-factor R-free RMS Deviation | | Running refmac R-factors | \$ | |
| 21 Make Ligand 20 Refinement - REFMAC5 R=0.20 RFree=0.22 | 1 0.1531 0.2195 0.017 | 0.24 | | R_Factor | - 0.030 |
| 19 Import merged 17 Import a coordinate set - optional selectio nRes=619 | R-factor | | | rmsBonds | - 0.020 |
| 16 Import merged for problem 2 15 Refinement - REFMAC5 R=0.15 RFree=0.22 14 Manual model building - COOT | т. 2 | 0.18 | 0 | | - 0.015 |
| 14 Manual Model Building - COOT 13 Make Ligand 12 Make Ligand | | 0.16 | • | | - 0.010 |
| 11 Refinement - REFMAC5 R=0.16 RFree=0.22 9 Manual model building - COOT | • | 0.14 | 1 | | - 0.005 |
| 8 Refinement - REFMAC5 R=0.19 RFree=0.23 | | | Cycle | | |
| 6 Refinement - REFMAC5 5 Analyse geometry | Current weight applied to X-ray t | term is 0. | 4014201 | | |
| 4 Make Ligand 2 Import a coordinate set - optional selection nRes=669 | | | | | |
| 1 Import merged | | | | | |
| | | | | | |
| | | | | | |

Terminal output

opentask times total 0.0682530403137 opentask times drawing 1.00135803223e-05 ERROR loading params file /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 JOBS/job 31/input params.xml SYMINFO file set to /Applications/ccp4-7.0/lib/data/syminfo.lib extractMtzData spaceGroup I 2 2 2 SYMINFO file set to /Applications/ccp4-7.0/lib/data/syminfo.lib extractMtzData spaceGroup | 2 2 2 Can convert ? 4 no 2 CTextViewer.open /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 JOBS/job 31/log.txt application/refmac-external-restraints True opentask times total 0.342795133591 opentask times drawing 0.218330144882 Done resetting side bar Icon not found arcimboldo 2016-12-06 18:15:29.288 ccp4i2[66583:3330033] modalSession has been exited prematurely - check for a reentrant call to endModalSession: blockLocal prosmart refmac False Copying file /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 JOBS/job 13/R36 RDKIT.dict-C19-both.cif to /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 IMPORTED FILES/R36 RDKIT.dict-C19-both 1.cif CDbApi.createImportFile calculated checksum /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 JOBS/job 13/R36 RDKIT.dict-C19-both.cif f57f6d6396a53b78ccd705e175f8b51c Database recording file /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 IMPORTED FILES/R36 RDKIT.dict-C19-both 1.cif imported from /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 JOBS/job 13/R36 RDKIT.dict-C19-both.cif file id: fd5c9dd4bbdf11e681bd60f81dd2910c PROJECTSMANAGER.importFiles resetting path DICT /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 IMPORTED FILES/R36 RDKIT.dict-C19-both 1.cif Recording file in database matches existing XYZIN /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 JOBS/job 30/XYZOUT.pdb 8986a90abbd911e6ae7560f81dd2910c 498c75e6bbd911e6b5af60f81dd2910c Recording file in database XYZIN /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 JOBS/job 30/XYZOUT.pdb 8986a90abbd911e6ae7560f81dd2910c Recording file in database matches existing F SIGF /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 JOBS/job 1/OBSOUT.mtz 966383e6ba4711e6a4b260f81dd2910c 6d876ea8ba4711e68eec60f81dd2910c Recording file in database F_SIGF /Users/pemsley/CCP4I2_PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4_JOBS/job_1/OBSOUT.mtz 966383e6ba4711e6a4b260f81dd2910c Recording file in database matches existing FREERFLAG /Users/pemsley/CCP4I2_PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4_JOBS/job_1/FREEOUT.mtz 9663abcaba4711e6ae1460f81dd2910c 6d876ea8ba4711e68eec60f81dd2910c Recording file in database FREERFLAG /Users/pemsley/CCP4I2 PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4 JOBS/job 1/FREEOUT.mtz 9663abcaba4711e6ae1460f81dd2910c Recording file in database matches existing DICT /Users/pemsley/CCP4I2_PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4_IMPORTED_FILES/R36_RDKIT.dict-C19both 1.cif fd5c9dd4bbdf11e681bd60f81dd2910c 93fb4d6ebbd911e6b0df60f81dd2910c Recording file in database DICT /Users/pemsley/CCP4I2_PROJECTS/Ligand-fitting-problems-Dec-2016/CCP4_IMPORTED_FILES/R36_RDKIT.dict-C19-both_1.cif fd5c9dd4bbdf11e681bd60f81dd2910c