Ligand fitting puzzles 2

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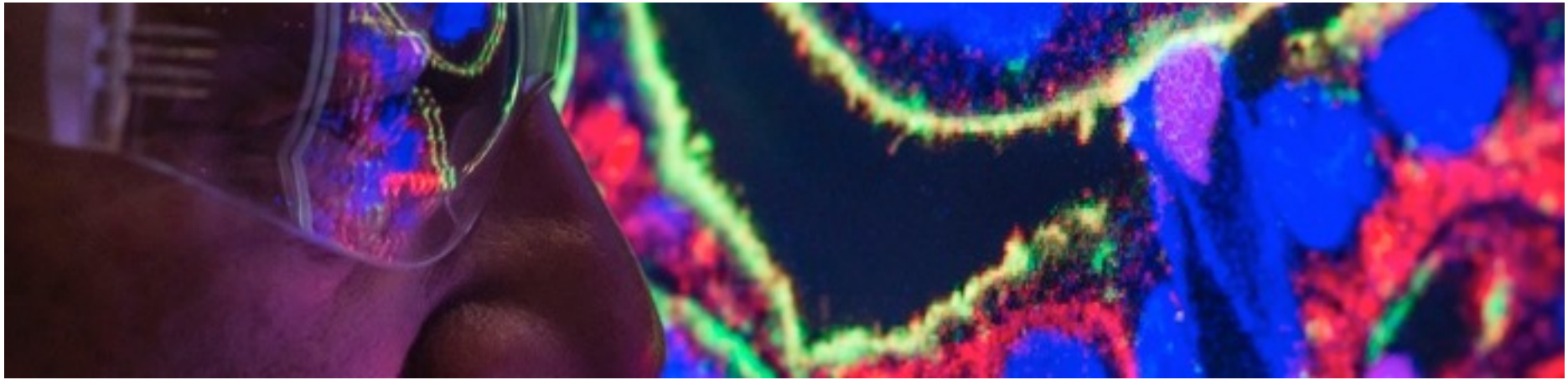
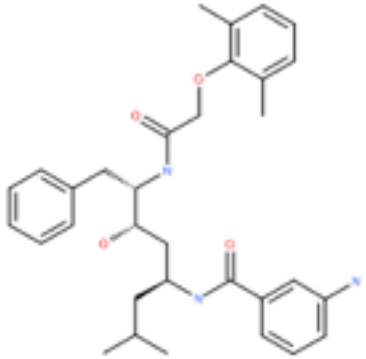
Ligands meeting

07 12 2016



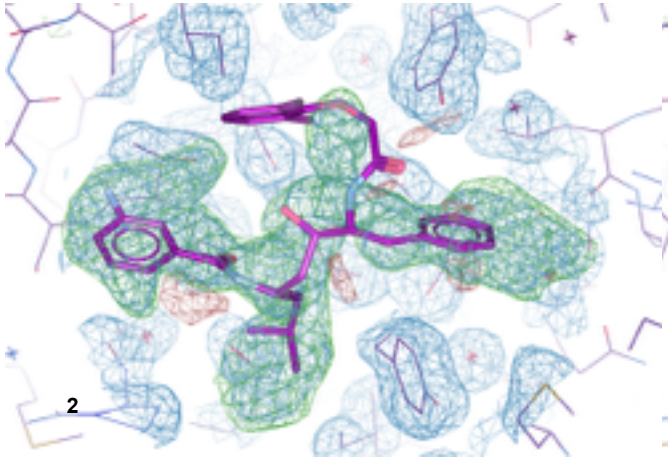
Problem 1.

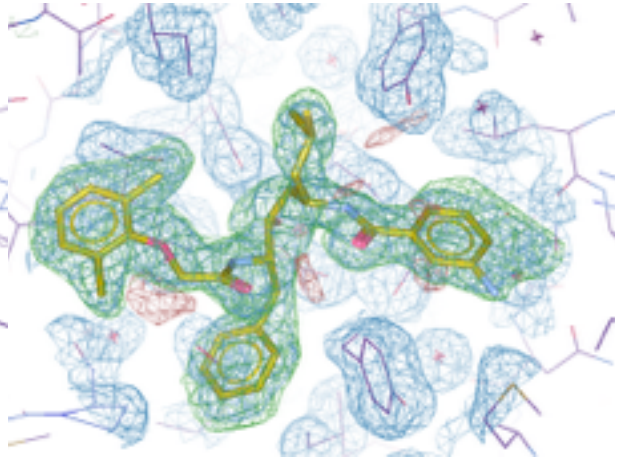


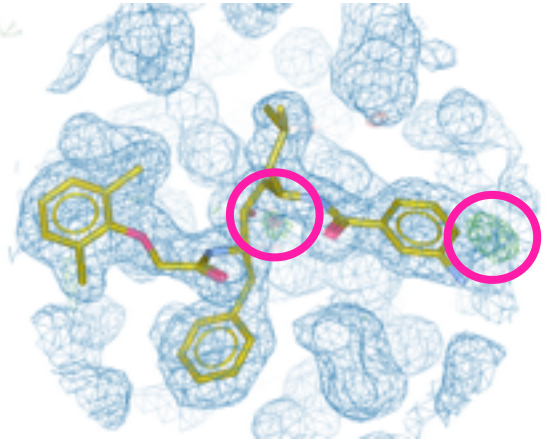
- mixed ligand population issue

workflow

- smi → pdb, cif with grade, acedrg and pyrogen
  - acedrg fell over on the smi file if it contained description does the newer version fix this?)
- basic ligand fitting in coot
  - coot misplaced the ligand – not enough conformers tested?
  - ligand expert is now default – good!
  - manual intervention: fix chirality – not sure where it went wrong!
- extra density which can't be water due to close proximity – probably missing atom..





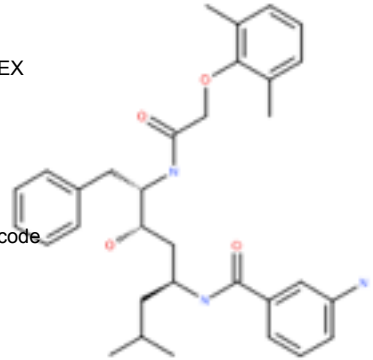


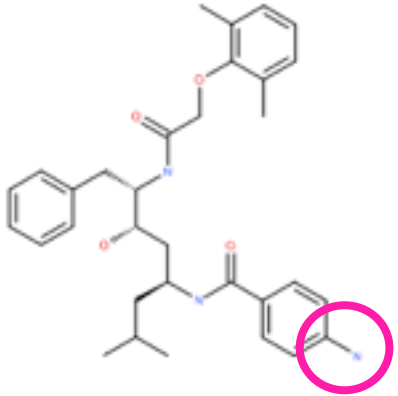
Problem 1.

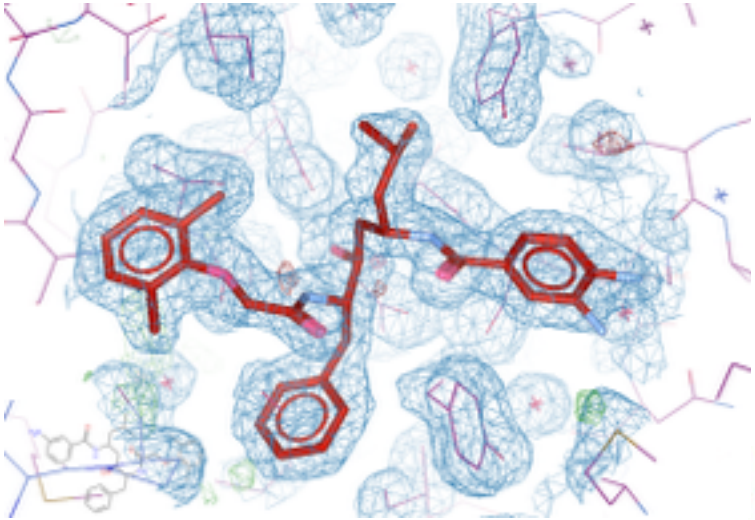
- extra density which can't be water due to close proximity – probably missing atom…

PDB 1LEE and 1LF2: CRYSTAL STRUCTURE OF PLASMEPSIN FROM P. FALCIPARUM IN COMPLEX WITH INHIBITOR RS367

- useful to know what's in the tube
- 2 similar ligands R36 and R37 – probably have a mixture of both in 1LEE.
- model this as two different ligands at occ=0.5
- generate cif dictionary for second form
  (did this by modifying the smi file and re-running pyrogen/acedrg), different (non-default) three letter code
- need to merge two cif files for refmac to run
  (buster accepts two cif files separately which is easier for the user)
- Lidia falls over!

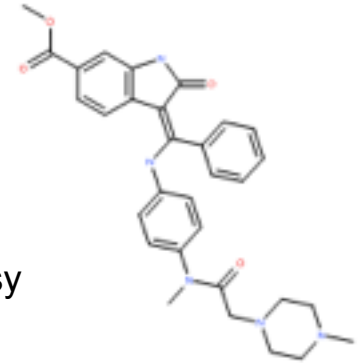


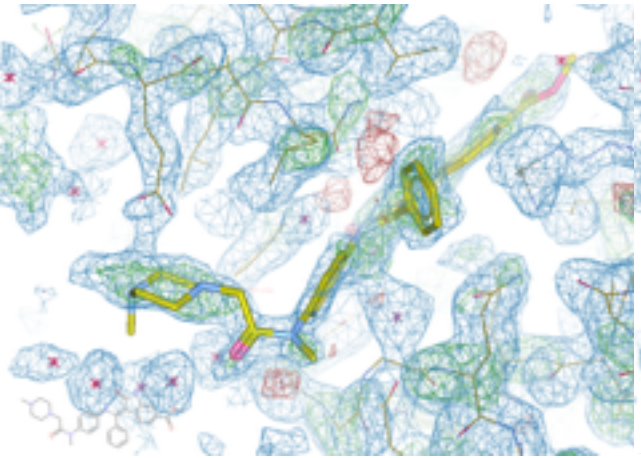


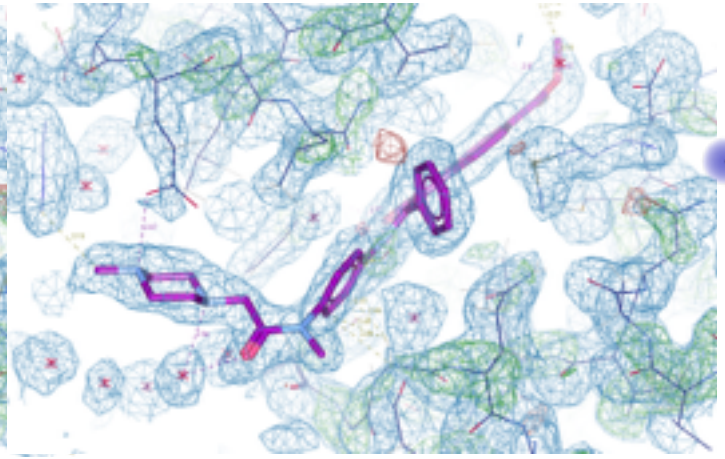


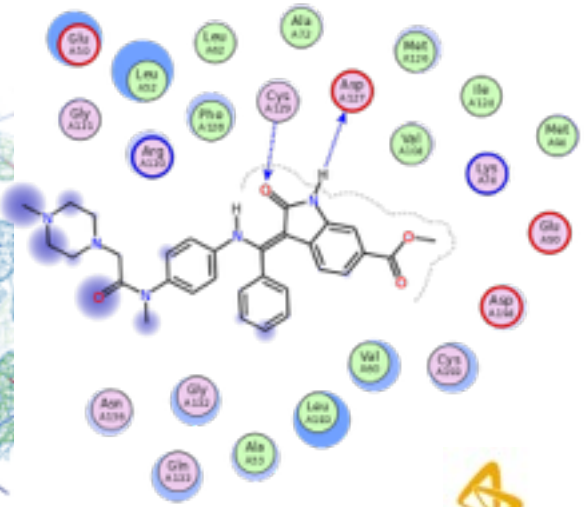
Problem 2.

- high resolution, straight-forward ligand fitting
- smi → pdb, cif with grade, acedrg and pyrogen
- ligand fitting in coot – worked well except Me-piperazine – wrong conformation here, needed manual intervention.
- piperazine is also probably protonated – close proximity to acid side chain, but this is missed in Lidia even though we do have a 2.9Å contact. It is also quite easy to fit this group the wrong way round.









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