Minutes

Meeting title	CCP4 Working Group 2 meeting (chaired by Jon Agirre, University of York)		
Date	Tuesday 16th of May 2023	**Time**	10.00 – 12.00
Location	Virtual only	**Zoom**	**yes**
Circulation	ccp4wg2@stfc.ac.uk		
Attending online	Arnaud Basle, Robbie Joosten, Marcin Wojdyr, Paul Emsley, Maria Fando, Daren Fearon, Mark Roe, Petr Kolenko, Ronan Keegan, Gabor Bunkoczi, Garib Murshudov, Gustavo Lima, Oliver Smart, Lucrezia Catapano, Jon Agirre, Michail Isupov, Sameer Velankar, Peter Moody, Luiso Fuentes-Montero, Ivo Tews, Antony Oliver, Rob Nicholls, Airlie McCoy, Ed Lowe, Keitaro Yamashita, Ibrahim Roshan, Paul Bond, Dan Rigden, Andy Purkiss, Deborah Harrus, David Waterman, Alan Roseman, Clemens Vornhein, Ivan Campeotto, Dave Briggs, Martyn Winn, Roberto Steiner, Marcin Wodjdyr, Paul Rowland, Briony Yorke, Ben Bax, Hannah Kwon, Pietro Roversi, Filo Sanchez Rodriguez, Charles Ballard, Stuart McNicholas, Ville Uski, Jonathan Grimes, Martin Mâly.		
Apologies from	Nick Pearce, Dave Brown		

10.00 **Welcome**

10.05 **Chair's update**

- Minutes from previous meeting were approved
- CCP4 general citation article
  The paper is now ready to go out, DOI is 10.1107/S2059798323003595
- CCP4 SW 2023 (special issue)
  JA and DW report. DW expect 19 papers (JA: this is pretty good)
- CCP4 SW 2024: *Choosing tools, predictions and pipelines - automated and manual macromolecular crystallography*.
  Organisers: Clemens Vonrhein, Helen Ginn, Nicholas Pearce.
  JA reporting.
- CCP4/BCA Summer School (York).
  JA reporting. School moved earlier in late August because teaching in York takes place earlier in September. Clashes with ECM, IUCr and everything else, but now it cannot be avoided if organising it at a uni that does semesters.
- Sponsored meetings (South-western, Northern).
  JA Nottingham this year. In November. Organised by Ivan Campeotto.
  Ivo reports on Southwestern. No longer be able to be free from students. 25k cost with 8.5k contribution from CCP4. Possibility to have a computer room on the 11th of July (anyone would like to demo something? Get in touch with Ivo directly). Meeting is on the 10th of July.

10.15 **Servalcat, Monomer Library updates** (Keitaro Yamashita, MRC-LMB Cambridge)
JA introduction.

KY - Paper published from SW2022. Started as a Refmac5 pipeline for cryoEM. Now it has its own refinement engine. Overcome refmac5 limitations using GEMMI and in the future replace refmac5 with Servalcat. GEMMI-fied refmac5 = Refmacat: MAKECIF replaced with GEMMI - use refmacat instead of refmac5 and same keywords.

New mechanism for updating and releasing the monomer library: this is now available on Github (https://github.com/MonomerLibrary/monomers); as the master branch is protected from pushes (just like most projects), pull requests should be used – the team will then review updates requested and integrate changes as required.

New feature in monomer library: introduced Alias mechanism to use standard atoms names.

Refmacat is faster, gzipped files used, extended PDB used, monomer alias, complicated alternative locations supported. Progress on refinement program reported. Summary and Acknowledgements.

Questions:

JA comparison in terms of speed between Servalcal and refmac5?
KY: you can try but the refinement is the same. Preparation part is fast.

BB: Can sodium ions be restrained and changed?
KY: they are restrained using ener_lib.cif data if LINK header is there or "make link y" is given. From the next version it will use metals.json data. To change the ideal value, a link dictionary needs to be given.

10.35 **Grade 2 and the Grade web server** (Oliver Smart, Global Phasing Ltd.)

OS: Grade paper to come but maybe late. Grade was 2010 from GPL. Issues: misidentification of planes. Bond orders for ligands sometimes messed up. Occasional chiral error from SMILES. Grade2 uses the ideas from Grade but none of the code. RDKit and CDS python API. First released in 2021. Much faster. Included with Buster. Documentation available online. Different plane sigmas are implemented to account for different situations. Grade web server public in 2012. Major update in 2022.
OS gives a demo.
Grade2 gives logging warnings. Match the InChiKey: it is a very useful identifier. Acknowledgements.
Questions:

PE about neutron distances.
OS yes same standard used.

PE: What takes the time?

OS: Mogul does.

PE: Does the user choose plane models?
OS: Yes they do.

RN: Lack of chirality in smiles?
OS: yes set as a warning.

10.55 **Updated pipeline for small molecule data processing at PDBe** (Ibrahim Roshan, PDBe team, Cambridge)
IR: Introduction to PDB. Pipelines: pdb-chem, pdbe-interactions, pdbe-relic. Process CCD information. Enrich CCD data with pdbeccutils. Updates: GEMMI used for mmCIF parsing. RDKit, bm_reader: bound molecule identification and InChiKey generation. Examples given.

Pdbe-interactions pipeline presented (GEMMI, Openbabel 3.0, remove alternative conformers, pip installable). Next planned to do PDB-wide interaction analysis and aggregate views of ligands. Acknowledgment.

11.15 **Discussion: the future of refinement in CCP4** (Keitaro Yamashita, MRC-LMB Cambridge)
JA: monomer library had a few changes, as outlined by Keitaro.
KY leads discussion. Metal-ligand distance restraints clarified.
AB: occupancies. It is there but the interface to the user needs to be improved. JA will take it to an i2 meeting.

11.30 **DUI2 demo** (Luis Fuentes-Montero, Diamond Light Source)
https://github.com/ccp4/DUI2
LFM: Server running in Mexico. Client running on laptop, which Luiso says is a Chromebook type lightweight machine.
Live demo given.
AB: What runs what? All run on server besides reciprocal lattice viewer. Should work under windows as well.

Import_serial (Martin Maly, University of Southampton)
MM: introduction to serial MX. Presentation of the I2 task. Technical aspects for developers: cs be installed no dependencies. Not distributed yet with CCP4.

11.55 **Any other business**

Zoom Chat (reads comic book style):

Ivo Tews 19:36
IT: You got to be careful to have submissions in before the summer break, otherwise there is not enough time for the review process

Airlie McCoy 22:35
AM: August dates overlap with IUCr

Ivo Tews 23:54
IT: SWSBC: massive problems on finance, things seemingly become more expensive; we will need to ask students for a registration fee which is not ideal and against the ethos of such meetings. Despite a raised contribution from CCP4 this year. We have opportunity for demos on Tuesday 11th with computer rooms booked if there is interest.

Airlie McCoy 27:37
AM: My closed caption said "survival cats" !!

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Ivan Campeotto 29:46
IC: We are facing the same issue with the increase of prices for the Northern meeting. I think we will need to scrap the idea of offering travel Fellowships to keep registration free for students and we may just break even thanks to VAT exemption and to external sponsors (TBC)

David Briggs 33:38
DB: I'm organising an afternoon seminar at the Crick with some folks from Diamond, and for a seminar room for an afternoon here, for ~80 people, the Crick ents people are charging us £600.

Ivan Campeotto 39:01
IC: I am negotiating for a seminar room for ~ 100 people and an additional smaller one for the option of a lunch demo. They asked 3,300 GBP per day (incl VAT) with 3 coffee breaks included. This is without catering.

2 Replies 😗 1

David Briggs 40:57
DB: Yes, my £600 is an internal rate, before catering as well.

Andy Purkiss 49:43
AP: Having checked e-mails, it was about double that at the Crick for the BCA meeting last December plus £250 for the hydrid Zoom setup.

Rob Nicholls - MRC-LMB 48:17
RN: I think Ben is requesting that it be transparent exactly what restraints are used (in general) after a Refmacat execution, e.g. in the log file, or some structured output file

Clemens Vonrhein (Glo... 48:39
CV: Are these really distance restraints similar to a bond (for metals) or rather what is called "ideal distances", i.e. anti-bumping restraints?

Garib Murshudov 50:53
GM: @Clemens These are similar to bonds. if users do not want bonds then antidumping restraints are used. (Ionic distances if interacting atoms are ions, vdw if one of the interacting atoms is not ion)

Ivo Tews 53:19
IT: Restraining metal distances may not be ultimately correct as this is a moving target in any data collection (due to radiation damage); agree with Rob that it must be reported and modifiable by the user; that's all possible but not really transparent.

Pietro Roversi 59:10
PR: See Dale Tronrud's twopenny worth in his pet hate 2: "The best solution, when your data set is of sufficiently high quality to resolve the geometry around the metal atom and the density is strong enough to keep the ion in place on its own, is to leave the metal–ligand geometry unrestrained but ensure convergence by including at least the diagonal of the second-derivatives matrix"

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Ivo Tews 59:17
IT: What is the reason for the use going up this year, do we know?

Garib Murshudov 59:18
GM: In case of multiple values all values are used and particular value is selected during refinement. Users (or controller programs) should be able to select one or change any of them. Mechanism is there.

Garib Murshudov 01:02:23
GM: @pietro
If you have good quality data then yes. However, when you are dealing with low resolution then you have to. Moreover coordinations may need to be predicted (at lower resoltions)

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Clemens Vonrhein (Glo... 01:07:30
CV: In Grade2 restraint CIF files:
_chem_comp_bond.value_dist_nucleus
_chem_comp_bond.value_dist_nucleus_esd
_chem_comp_bond.value_dist
_chem_comp_bond.value_dist_esd

👍 2

Clemens Vonrhein (Glo... 01:09:32
CV: https://www.globalphasing.com/buster/manual/grade2/manual/planes.html

https://gphl.gitlab.io/grade2_docs/planes.html

Rob Nicholls - MRC-LMB 01:10:26
RN: I see users get frustrated when their conformer is "wrong" (i.e. not what they expect) due to lack of chirality info in their input SMILES string. Do you think lack of chirality info in a SMILES string should be considered a warning? Or otherwise some other way of communicating this with users?

Collapse All

Jon Agirre 01:11:03
JA: Great question!

Pietro Roversi 01:17:42
PR: I do not hear anything anymore - I assume this a break in the meeting - correct?

David Waterman - STF... 01:17:55
DW: yes, that's right

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Rob Nicholls - MRC-LMB 01:27:47
RN: To what degree is the covalent linkage info identified using bm_reader in sync with the authors' deposited model (and associated publications)?

8 Replies

Pietro Roversi 01:43:07
PR: I will be trivial and ask if you looked at the 10 things Dale and I hate about refinement ("https://journals.iucr.org/d/issues/2021/12/00/qt5008/"). A few of the issues discussed in that paper may be good directions of travel for real-space refinement too.

Ben Bax 01:45:09
BB: Re: Metals. Would it be possible to show users alternatives?

2 Replies

Oliver Smart 01:45:44
OS: Paul asked a question about plane handling in Grade2 and flavin ring. There is a chapter on this https://gphl.gitlab.io/grade2_docs/planes.html

Charles Ballard - STFC ... 01:46:44
CB: Note: refmacat (servalcat) are in current release series for testing wrapping of refmac

4 Replies

Garib Murshudov 01:47:33
GM: We would like pipelines using refmac to use servalcat. It will be longer term sustainable.

" Re: Metals. Would it be possible to show users alternatives?
Do you mean users to select one of the alternatives? Or to show what values are used?

Clemens Vonrhein (Glo... 01:48:39
CV: We (BUSTER world) found that the tricky bit with occupancy refinement starts with coordinated paterns of altConfs and partial occupancies (multiple ligand poses, alternate waters, side-chains etc). We try to do rhe best automatically for the more obvious combos/situations ... but a complete solution doing the right thing when it comes to occ-refinement definitions is tricky.

👍 2

Oliver Smart 01:49:36
OS: Someone asked about whether there is a Grade2 warning about handling SMILES ambiguous (unset) chiral centres. Testing with "OC1C(O)C(OC(O)C1O)CO" glucopyranose without chirals you get: a warning
WARNING: Ambiguous chiral center(s) so restraint(s) set to "both".

https://grade.globalphasing.org/cgi-bin/grade2_server.cgi?runid=42800-EXFfoEEsNsQ

20 Replies 😃 1

Oliver Smart 01:51:38

Sorry the fully warning is
WARNING: Ambiguous chiral center(s) so restraint(s) set to "both".
WARNING: ---- The 3D coordinates and other records will be for one stereo
WARNING: ---- configuration. So take care in fitting and consider replacing
WARNING: ---- the restraint dictionary once configuration is known.

Jon Agirre 01:53:14

That's sensible

Rob Nicholls - MRC-LMB 01:53:15

That's great. Helping users to do this easily has been one of the outstanding issues. It's easy when you know how, but not if you're a novice user.

Jon Agirre 01:54:10

What do the PDB do when users supply CIFs with 'both' on chiral volumes?

Rob Nicholls - MRC-LMB 01:54:41

The PDB ignores user supplied CIFs - provenance of restraints is not maintained, unfortunately

Jon Agirre 01:55:01

Don't you have to supply a CIF file for new ligands?

(all my newer depositions have been handled by other people, so I'm not up to date with this)

Rob Nicholls - MRC-LMB 01:55:44

It uses minimal info about chemical connectivity, but not restraints, as far as I'm aware

Sameer Velankar - EMB... 01:55:55

We are going to take these into account. That work is planned for tjis year

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Jon Agirre 01:56:03

Ah, superb

Sameer: what you do you take at present, just a SMILES?

Sameer Velankar - EMB... 01:56:51

To begin with we will use connectivity and links to map correct ligands and the rest needs to be taken into account during validation which will take some time

We get smiles or images or uploaded fmol files but these are ignored - this is what we are trying to address :-)

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Rob Nicholls - MRC-LMB 01:58:11

@Jon Agirre I don't think SMILES is mandatory in CIF files - it's the atom & connection info that's always there (with coordinates, which may be nonsense!)

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Garib Murshudov 02:03:45

(Particular) canonical smiles and InChi codes are useful for searching exact matches in a database. Otherwise all information are in the list of bonds and element names. Sometimes bond orders are also useful (but not always, they are not unique)

Andy Purkiss 02:05:01

Just a small comment: Sometimes chirality of 'both' will be correct for the refinement and hence deposition steps. For example, some buffer molecules will be racemic mixtures and it may not be obvious which form is 'correct' at low resolution.

Oliver Smart 02:07:48

Would it not be easiest for most users for the PDB deposition to take chemical information from the restraint CIF the user used. If there is anything missing from Grade2, eLBOW, or AceDRG or OpenEye (I do not think there is) then I am sure the developers can add? We certainly would be happy to do this.

Rob Nicholls - MRC-LMB 02:09:41

@Andy this is a relevant point, in the context of restraints. Though it's typical to start with a single conformer... and the chirality of that conformer may disagree with what the user wants, and in the case of ambiguity the chirality of the starting conformer could bias the model. So we need to think about both restraints and conformers in this context.

Sameer Velankar - EMB... 02:13:41

@oliver that is the plan and work will be carried out this year

Andy Purkiss 02:15:33

@Rob it is also an issue with validation For example, in the dim and distance past, I had a structure with two differently automatically annotated DTT (covalently-linked to the same CYS in different chains).

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Garib Murshudov 01:49:44

@Clemens: complete solution requires identification of overlapping networks which is extremely hard problem

1 Reply

Luiso 02:02:16

Dui2 new features that the old Dui is incapable to do

To show / Test

1. Client server architectur
2. Multi - tasking capabilitie
3. Multi-crystal analysis and joint refinemen
4. New optional command node with any Dials command
5. More clever decision on what to do nex
6. Implementation of dials.ssx_index, dials.ssx_integrate and dials.merge command

7. E.D. initial suppor

8. Output of Dials command help message in console previous to executio

9. Versatile layou

10. Hide/show branches featur

11. Reset entire tree featur

12. Optional download html report or load in web browser featur

13. Adaptable to desktop bright mod

To install Dui2 follow the instructions on

https://github.com/ccp4/DUI

Next / Ongoing

1. Windows version needs testing / tuning

2. Test feature: For all local run, to bypass the

2. Test feature: For all local run, to bypass the request/response mechanism and replace it with a new all in one process approach

Airlie McCoy 02:15:38

AM

Thank you to all presenters

David Briggs 02:15:49

DB

Thank you everyone!

Roberto Steiner 02:15:51

RS

Thank you all

Oliver Smart 02:15:55

OS

Thank you all

EOT