

advancing structural science

What's Up Customer Update Webinar

20th May 2021





Today's presenters







Research and Applications Scientist

Sofia da Fonseca

Channel Manager

Chris Tromans Agile Coach



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Overview

In this webinar we will discuss:

- Latest updates and news
- CSD Ligand Overlay
- Agile Development at CCDC
- Q&A: the floor is yours





Latest updates

 CSD-Theory released > search, display and analyse crystal structure prediction (CSP) data through a web-based platform and the API.



• Database Evolution: to provide a better foundation for our future. Phase 1 launched



Latest news from CCDC

CCDC are pleased to announce Cloud Scientific as our distributor for China





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Find out more at www.ccdc.cam.ac.uk/news

Upcoming events from CCDC



- Librarians Teatime 25th May
 - For Chemistry Librarians in the Americas
- Science Day 26th May
 - Hear from the CCDC sponsored PhD students on their research
- JAICI and CCDC webinar: Optimising Material Properties 2nd June
 - For scientists in Japan.
- Discovery Science Meeting 9th and 10th June
 - Theme: High Performance data meets High Performance Computing.

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• For anyone interested in Drug Discovery!

CCDC will be attending:

• 6th European Crystallographic School – 4th to 10th July



The CCDC team is growing...

- Currently hiring for roles including:
 - Software engineers
 - Research and Applications Scientist
 - Postdoctoral Research Associate Modified Crystal Growth Models
 - Summer Placement assistant to Data and Community team



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CSD Software

Agile Development at CCDC



Chris Tromans Agile Coach





First - Why Do We Use Agile?

- Higher quality product
- Increased customer satisfaction
- More opportunities to learn about our products
- Easily adapt to change
- Minimize risk
- Better stakeholder engagement
- Continuous improvement
- Increased collaboration







So... On To Those 4 Values...

Individuals and Interactions over Process and Tools

Working Software over Comprehensive Documentation

Customer Collaboration over Contract Negotiation

Responding to Change over Following a Plan



High Level Product Management at CCDC



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Emergent Hierarchical Backlog

- Ideas and feedback coming into a backlog and are developed in an iterative + incremental way
- We always know/define more about the items we're doing now or soon
- The darker the blue = the more detail we know



Agile Prioritisation



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Let's Look at What's Important In a Team

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- Google's Project Aristotle
- 2 years spent studying 180 teams
- Aristotle "The whole is greater than the sum of it's parts"

Psychological Safety

Team members feel safe to take risks and be vulnerable in front of each other.

Dependability

Team members get things done on time and meet Google's high bar for excellence.

Structure & Clarity

Team members have clear roles, plans, and goals.

Meaning

Work is personally important to team members.

Impact

Team members think their work matters and creates change. re:Work

So How Do We Start Projects?



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Extreme Programming

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- Test Driven Development
- Pair Programming
- Refactoring
- Continuous Integration
- Sit Together
- Informative Workspace

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- Roles
 - Product Owner orders the work
 - Scrum Master helps create the right environment
 - Scrum Team creates the increment of work

Remote Agile!

- What's changed for CCDC in the last year
 - Video calls for all Scrum events using Microsoft Teams
 - Virtual whiteboarding using Miro
 - Virtual estimation using PlanItPoker
- What's even more important at this remote time?
 - Pairing interaction with each other
 - Seeing each other on video body language
 - Focus on psychological safety and wellbeing
 - Virtual information radiation we can't see the big screens in the office



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CSD Discovery

CSD Ligand Overlay



Dr Vera Prytkova Research and

Applications Scientist





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Ligand-based pharmacophore hypothesis

In absence of three-dimensional structures of potential drug targets:

- Ligand-based drug design is an alternative approach for drug discovery and lead optimisation
- Alignments are not trivial, especially if the molecules are very flexible
- Multiple overlays can be generated that present legitimate hypotheses for binding

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Ligand-Based Virtual Screening Framework





(C(C))C

- Aligning molecules is an under-determined problem
- The program returns multiple overlay solutions, all plausible hypotheses for binding

Taylor R., et al. J. Comput. Aided. Mol. Des. (2012) 26, 451-472.
 Giangreco I., et al. J. Chem. Inf. Model. (2014) 54, 3091-3098.
 Giangreco I., et al. J. Chem. Inf. Model. (2013) 53, 852-866.

Representing ligands

- Each conformer is represented by "fitting points" placed on hydrophobe centroids, H-bond donors and H-bond acceptors
- Donors and acceptors are defined by SMARTS
- Other feature types are possible





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Generating overlays

- Find all fitting-point triplets in all conformations of all ligands
- Assign each triplet to a "triplet type" defined by three feature types and three distance binds



- Order triplet types by frequency of occurence
- Loop over the n most common triplet types and, for each, generate overlays from an "alignment fingerprint"

Scoring overlays

- Union volume
- H-bond matching
 - Number of ligands
 - Position
 - Direction
 - Strength
 - Accessibility
- Hydrophobe matching
 - Number of ligands
 - Position
 - Direction
- Energy
 - Torsional and VdW terms of Tripos force field



Filtering overlays

- Score overlays (obtained from fingerprint searching) with several objective functions; Pareto rank; compute and order of Borda tallies
- Reject solutions with Pareto rank > 5
- Accept solution with best Borda tally and reject all similar solutions
- Typically limit to max 20 overlays
- Optional overlay refinement to bring overlaid groups into tighter alignment



Q&A

• Type your questions in the box as shown

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Next What's Up Webinar

- Next webinar: July 22nd
 - GOLD Docking with the API
 - Finding crystal structures with WebCSD and Access Structures
- Follow us on social media
- Send us your ideas and news
 - hello@ccdc.cam.ac.uk





Thank you

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