<table>
<thead>
<tr>
<th>Start</th>
<th>Title</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>9:00 AM</td>
<td>PHENIX Overview</td>
<td>Paul Adams</td>
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<tr>
<td>9:15 AM</td>
<td>Cryo-EM Automated map improvement &amp; model building</td>
<td>Paul Adams</td>
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<tr>
<td>10:15 AM</td>
<td><em>Break and set-up of PHENIX on computers</em></td>
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<tr>
<td>10:45 AM</td>
<td>Cryo-EM structure refinement in PHENIX</td>
<td>Pavel Afonine</td>
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<tr>
<td>11:45 PM</td>
<td>Model Validation</td>
<td>Jane Richardson</td>
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<td>12:30 PM</td>
<td><em>Lunch</em></td>
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<td>1:30 PM</td>
<td>Tutorial – Cryo-EM map improvement and model building</td>
<td>Paul Adams</td>
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<td>2:30 PM</td>
<td><em>Break</em></td>
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<td>3:00 PM</td>
<td>Tutorial – Cryo-EM Refinement</td>
<td>Pavel Afonine</td>
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<tr>
<td>4:00 PM</td>
<td>Tutorial – Cryo-EM Validation</td>
<td>Jane Richardson/Pavel Afonine</td>
</tr>
<tr>
<td>4:45 PM</td>
<td><em>Workshop Survey and wrap-up</em></td>
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Phenix Introduction

ACA Meeting Cryo-EM Workshop
July 2019

Paul Adams
Lawrence Berkeley Laboratory and
Department of Bioengineering UC Berkeley
The Phenix Project

Lawrence Berkeley Laboratory
Paul Adams, Pavel Afonine, Dorothee Liebschner, Nigel Moriarty, Billy Poon, Oleg Sobolev

Los Alamos National Laboratory
New Mexico Consortium
Baylor College of Medicine
Tom Terwilliger, Li-Wei Hung, Matt Baker

Lawrence Berkeley National Laboratory
Los Alamos National Laboratory
New Mexico Consortium
Baylor College of Medicine

Cambridge University
Randy Read, Airlie McCoy, Tristan Croll, Rob Oeffner, Kaushik Hatti, Massimo Sammito, Duncan Stockwell

Duke University
Jane & David Richardson, Chris Williams, Vincent Chen, Bradley Hintze

An NIH/NIGMS funded Program Project

Phenix - a Structural Biology Hub

- We have nucleated the development of new computational methods for structural biology
What is PHENIX?

• Package for automated structure solution
• Modern programming concepts and new algorithm development
• Designed to be used by both novices and experienced users
• Long-term development and support
• Why is it called PHENIX?
  • Python Hierarchical ENvironment for Integrated Xtallography
Key Features

• Python
  • Easy scripting of repetitive tasks
  • Enables rapid prototyping and development
• Advanced algorithms
  • Experimental phasing
  • Molecular replacement
  • Automated model building and rebuilding
  • Structure refinement and validation
  • Ligand coordinate and restraint generation
• Rapid development and bug fixing
Automation of Structure Solution

1. Data quality
   - Labelit
   - phenix.xtriage

2. Experimental Phasing
   - phenix.autosol

3. Molecular Replacement
   - phenix.automr
   - phenix.refine

4. Phase improvement
   - phenix.autobuild

5. Model building
   - molprobity

6. Structure completion
   - Validation Deposition

7. Refinement
   - phenix.elbow
   - ligand screen

8. Ligand identification & Fitting

References:


Acta Cryst. 2010, **D66**: 213-221
Command Line Tools

• Data validation
  • phenix.xtriage porin_fp.mtz

• Automated structure solution
  • phenix.autosol data=peak.sca seq_file=nsf-d2.seq

• Automated model building
  • phenix.autobuild data=scale.mtz model=mr.pdb
  • phenix.autobuild data=scale.mtz model=mr.pdb
  • phenix.autobuild data=scale.mtz model=mr.pdb
  • phenix.autobuild data=scale.mtz model=mr.pdb

• Automated ligand fitting
  • phenix.ligandfit data=nsf-d2.mtz model=noligand.pdb
  • phenix.ligandfit data=nsf-d2.mtz model=noligand.pdb
  • phenix.ligandfit data=nsf-d2.mtz model=noligand.pdb
  • phenix.ligandfit data=nsf-d2.mtz model=noligand.pdb

• Structure refinement
  • phenix.refine nsf-d2.mtz nsf.pdb

• Building ligand coordinates and restraints
  • phenix.elbow --smiles="C12CC3CC(C2)CC(C1)C3"
Phenix GUI

- Central GUI to view job control and launch new jobs
Coot/PyMOL integration

- Most results can be opened directly in graphics apps.

- Any PDB file listed in GUI can also be opened.

- AutoSol, AutoBuild, and phenix.refine will update Coot continuously while running.

- Coot must have Python support (default on Mac).

- Specific paths to executables usually required on Linux.

- Preferences->Graphics->Full path to Coot [...PyMOL]
Recent Developments

- Automated structure solution with weak anomalous data
- Translational NCS corrections in SAD phasing
- MR_Rosetta and morphing for rescuing poor MR solutions
- Translational NCS corrections in MR
- New Rosetta methods for RNA rebuilding (ERRASER)
- Automated ion placement in refinement
- Automated ligand pipeline
- DIALS included in Phenix distribution
- Support for mmCIF format (for structure deposition)
- Video Tutorials

- Low resolution refinement algorithms:
  - Rosetta refinement
  - Reference model
  - Torsion NCS
  - Structure restraints
- New model validation metrics
- New hydrogen validation tools
- New riding hydrogen model
- Feature Enhanced Maps to improve interpretability
- Polder maps for better ligand density
- Ensemble refinement to understand dynamics and structural variability

Phenix
New Tools for Cryo-EM in Phenix

- Symmetry from a map
- Automated map sharpening
- Map segmentation
- Rigid model docking
- Automated model building
- Real space refinement
- Model and map validation
Challenges

- Low resolution structure solution and refinement
- Structure completion
  - Automated identification, fitting and refinement of ligands, metals, ions, and water
  - Identification, fitting and refinement of discrete disorder (multiple conformations)
  - Representing other forms of disorder
- Automated parameterization of models in refinement
  - ADPs, TLS groups, NCS, hydrogens
- Handling different kinds of twinning and integrating it into the whole structure solution process
- Automated understanding of chemistry
PHENIX Availability

- phenix-online.org
- Supported on:
  - Linux (RedHat, Fedora)
  - Mac OSX
  - Windows
- Extensive documentation
- Nightly builds:

<table>
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<th>Version</th>
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<th>Status</th>
<th>Logs</th>
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<td>2019-05-21</td>
<td>successful</td>
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Video Tutorials

Dorothee Liebschner, Nigel Moriarty, Miffy Mifsud, Tom Terwilliger
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Matt Baker

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PHENIX Testers & Users

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