Agenda

Start	Title	Presenter
9:00 AM	PHENIX Overview	Paul Adams
9:15 AM	Cryo-EM Automated map improvement & model building	Paul Adams
10.15 AM	*Break and set-up of PHENIX on computers*	
10:45 AM	Cryo-EM structure refinement in PHENIX	Pavel Afonine
11:45 PM	Model Validation	Jane Richardson
12.30 PM	*Lunch*	
1:30 PM	Tutorial – Cryo-EM map improvement and model building	Paul Adams
2:30 PM	*Break*	
3:00 PM	Tutorial – Cryo-EM Refinement	Pavel Afonine
4:00 PM	Tutorial – Cryo-EM Validation	Jane Richardson/ Pavel Afonine
4:45 PM	*Workshop Survey and wrap-up*	

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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

Duke University

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

Cambridge University

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

An NIH/NIGMS funded Program Project

Adams PD et al., PHENIX: a comprehensive Python-based system for macromolecular structure solution. *Acta Cryst.* 2010, **D66**:213-221.

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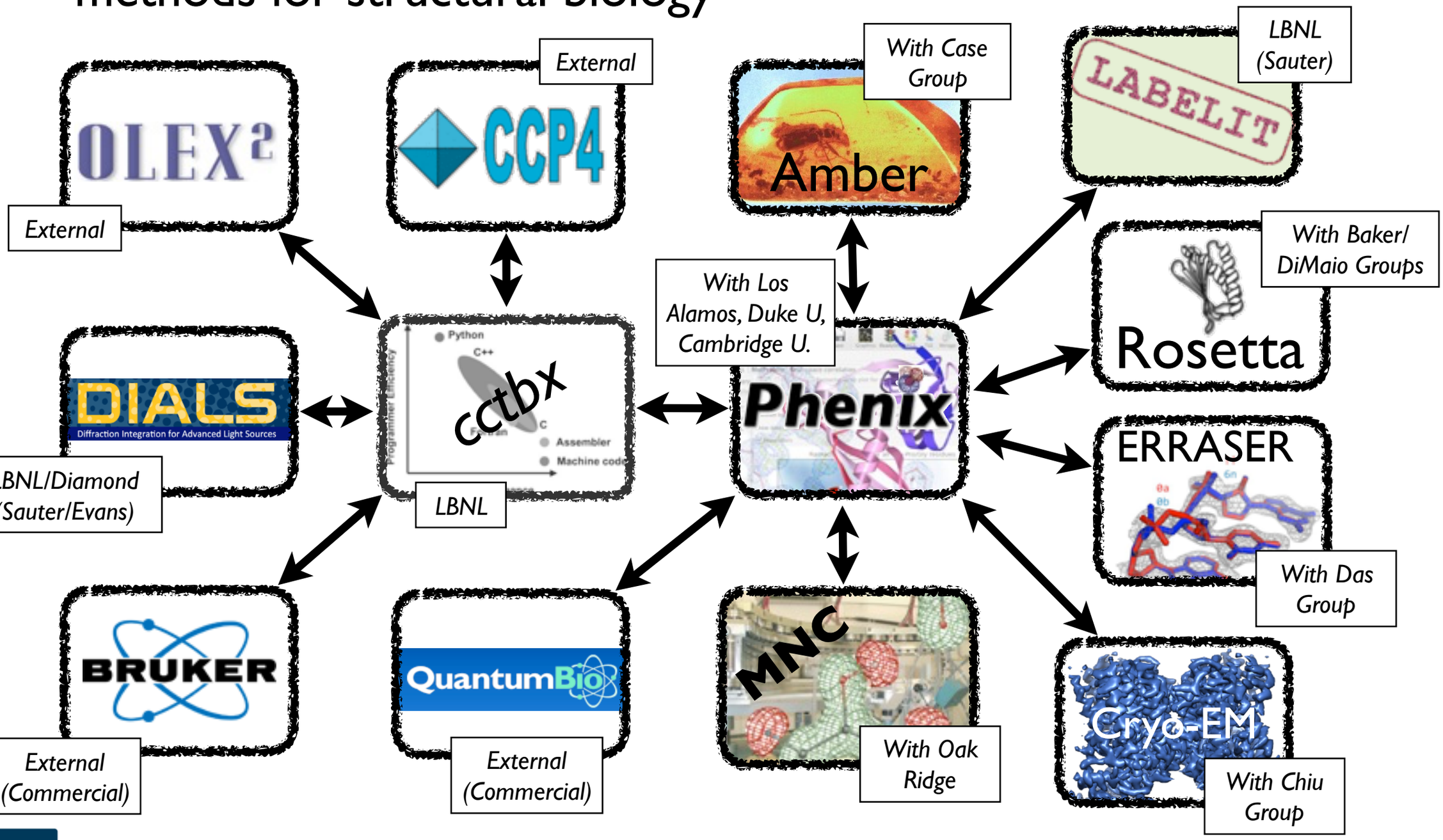
Phenix - a Structural Biology Hub

- We have nucleated the development of new computational methods for structural biology



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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

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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

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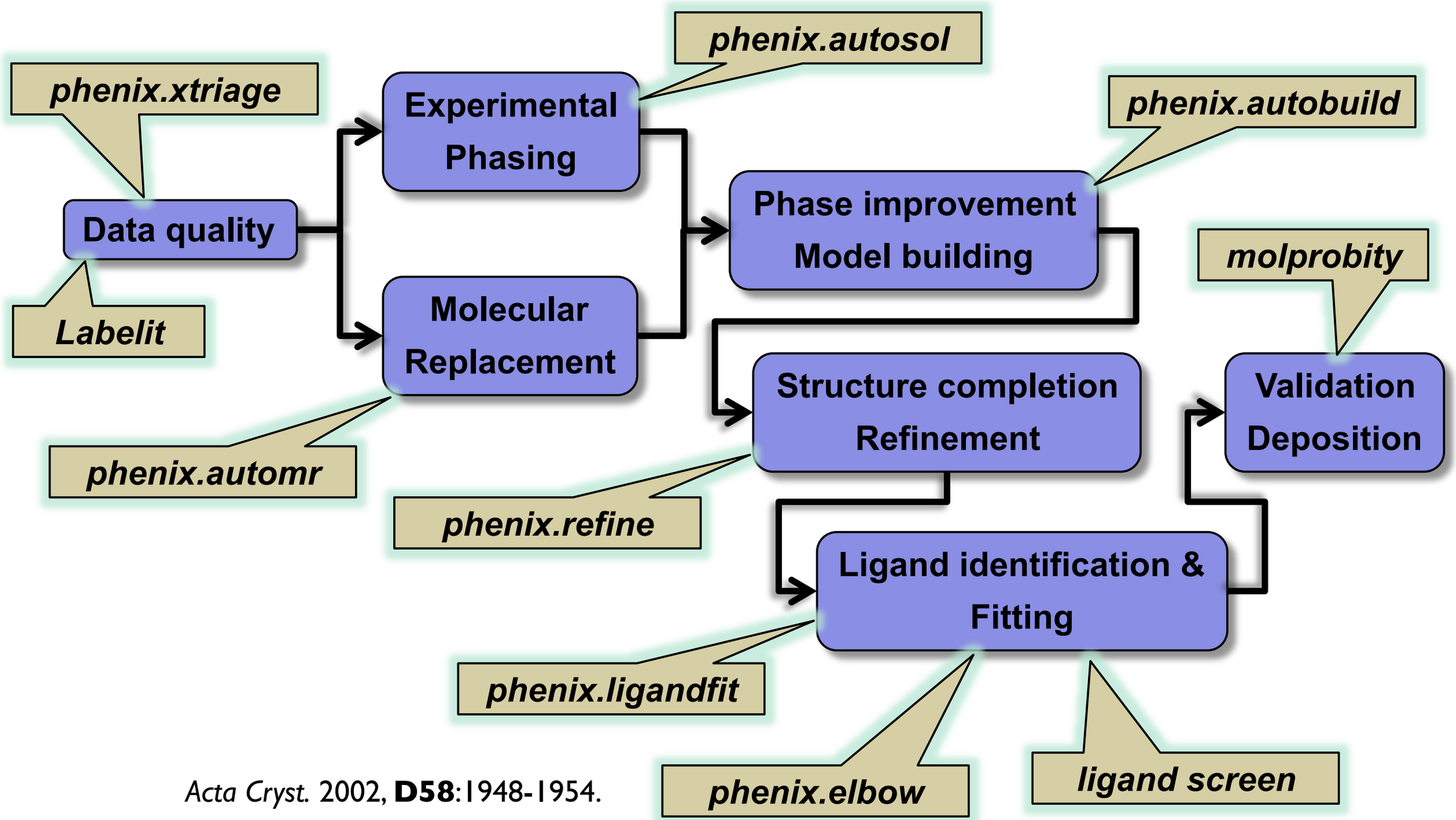
Automation of Structure Solution



Acta Cryst. 2002, **D58**:1948-1954.

J. Appl. Cryst. 2002, **35**:126-136.

Acta Cryst. 2010, **D66**: 213-221

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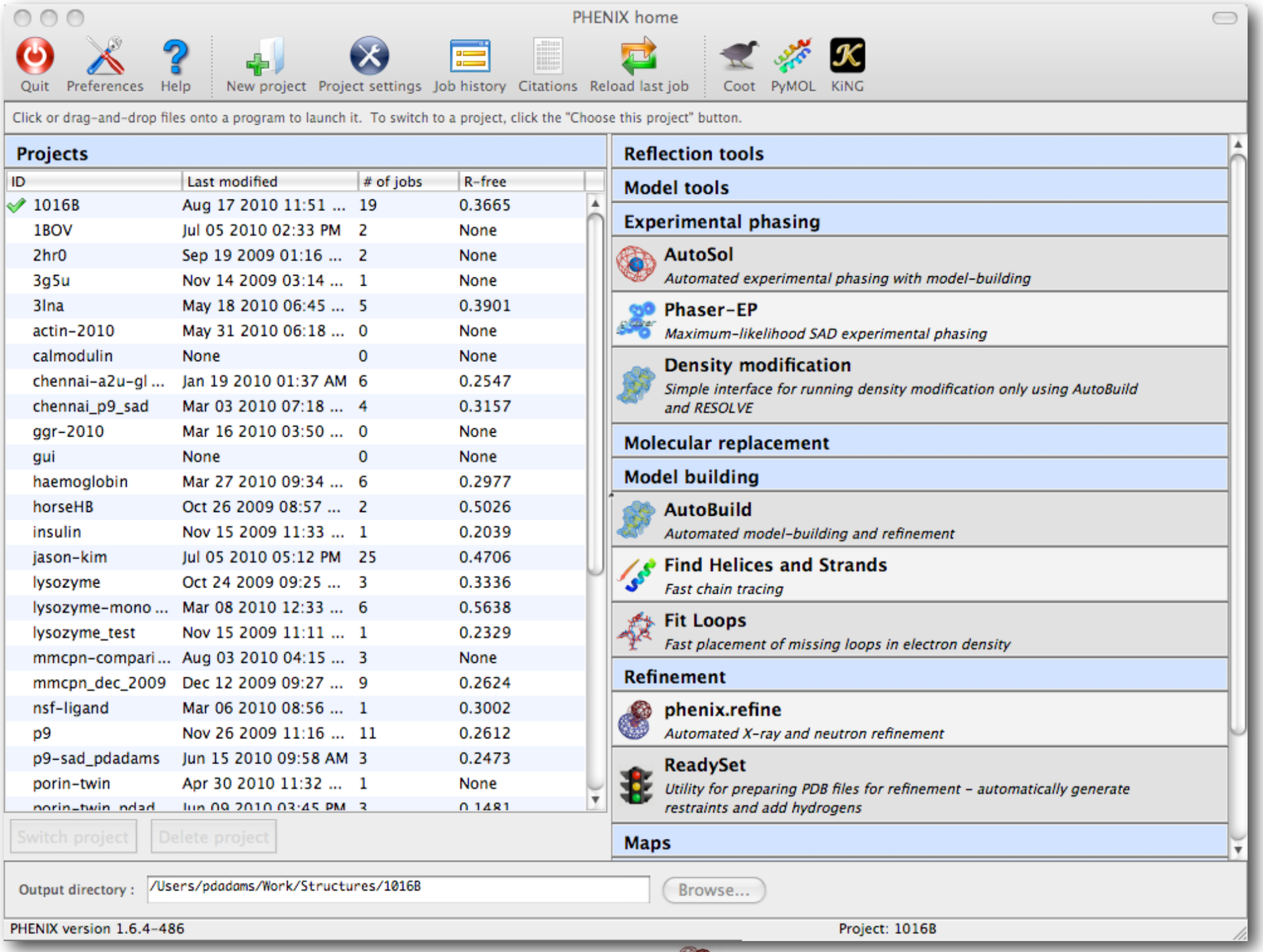
Command Line Tools

- 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 seq_file=correct.seq`
- Automated ligand fitting
  - `phenix.ligandfit data=nsf-d2.mtz model=noligand.pdb ligand=atp.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



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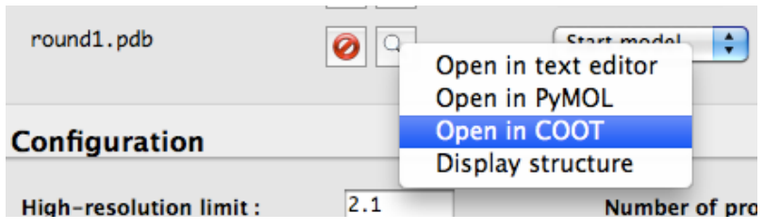
GUI: Nat Echols (LBL)

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]*

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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

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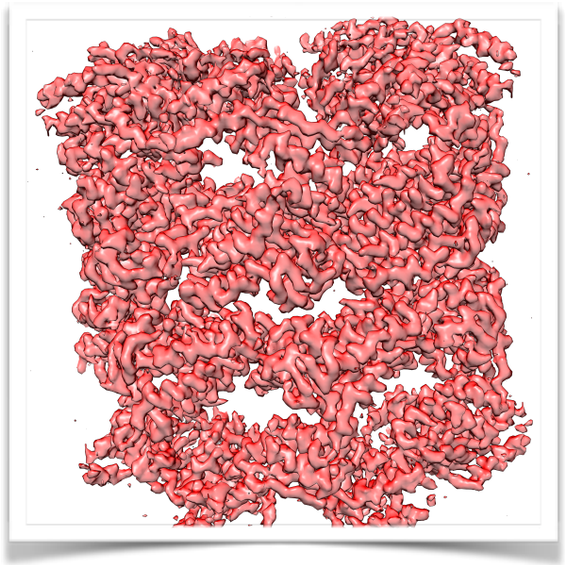
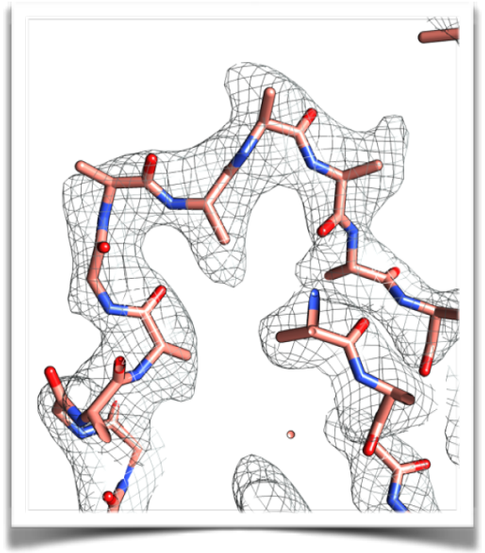
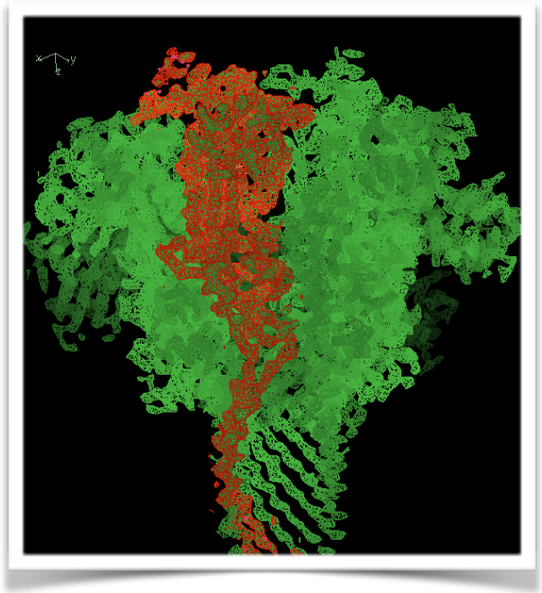
New Tools for Cryo-EM in Phenix



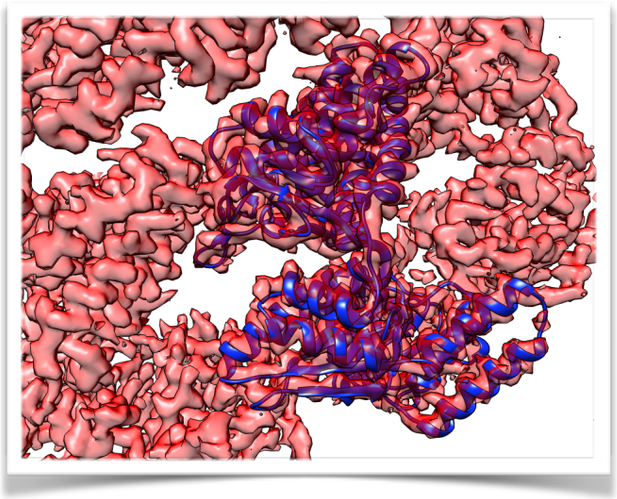
Symmetry from a map



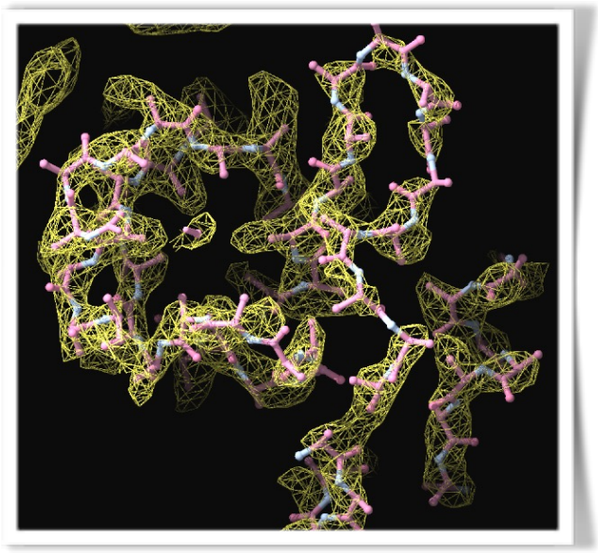
Automated map sharpening



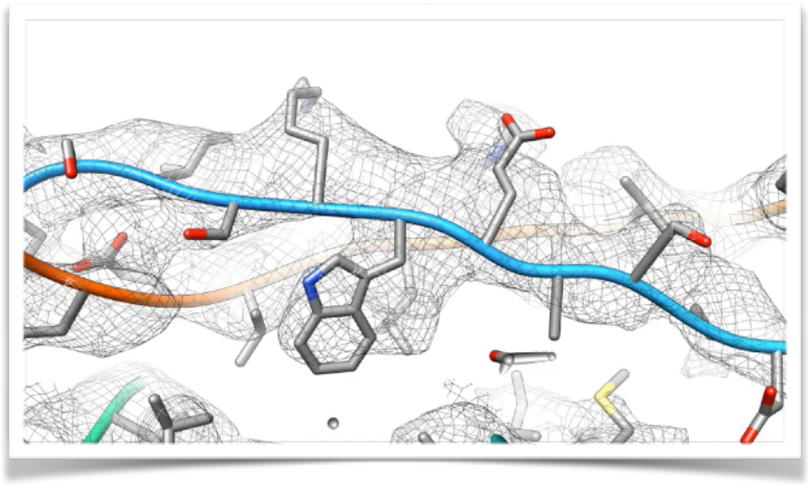
Map segmentation



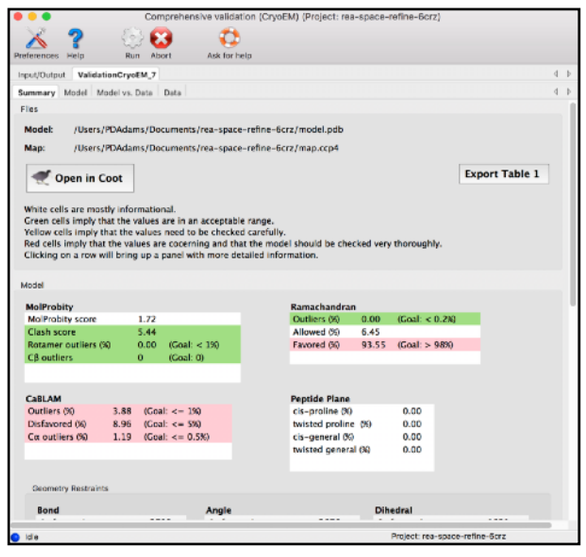
Rigid model docking



Automated model building



Real space refinement



Model and map validation

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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

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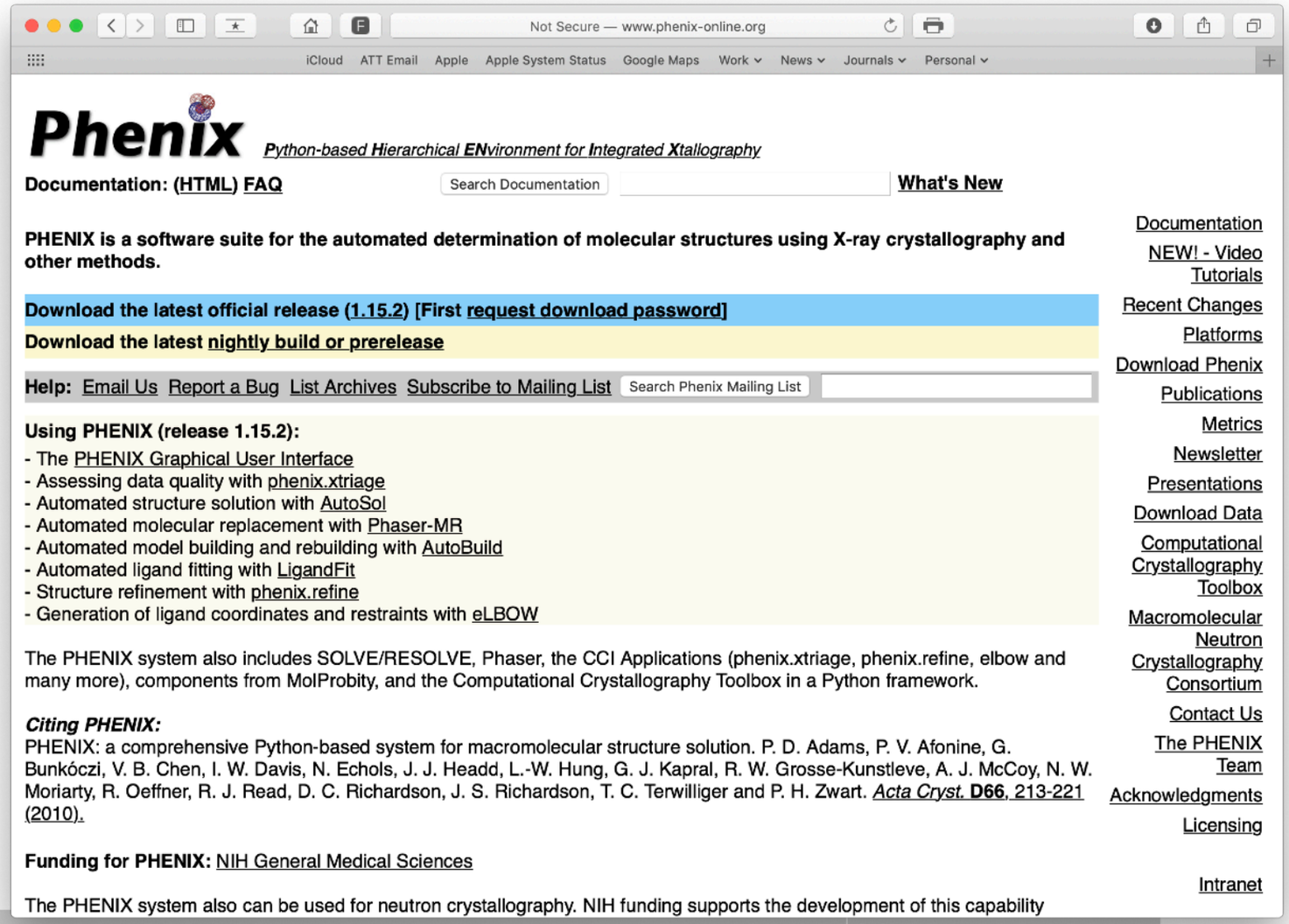
PHENIX Availability

- `phenix-online.org`

- Supported on:
  - Linux (RedHat, Fedora)
  - Mac OSX
  - Windows

- Extensive documentation

- Nightly builds:



Version	Date	Status	Logs	Info
dev-3512	2019-05-21	successful	ci, intel-windows-x86_64, intel-linux-2.6-x86_64-centos6, mac-intel-osx-x86_64	docs; changelog
dev-3500	2019-05-09	successful	ci, intel-linux-2.6-x86_64-centos6, mac-intel-osx-x86_64, intel-windows-x86_64	docs; changelog
dev-3494	2019-05-03	successful	intel-linux-2.6-x86_64-centos6, ci, mac-intel-osx-x86_64, intel-windows-x86_64	docs; changelog
1.15.2-3472	2019-04-11	successful	ci, intel-windows-x86_64, intel-linux-2.6-x86_64-centos6, mac-intel-osx-x86_64	Official 1.15.2 release; docs; changelog

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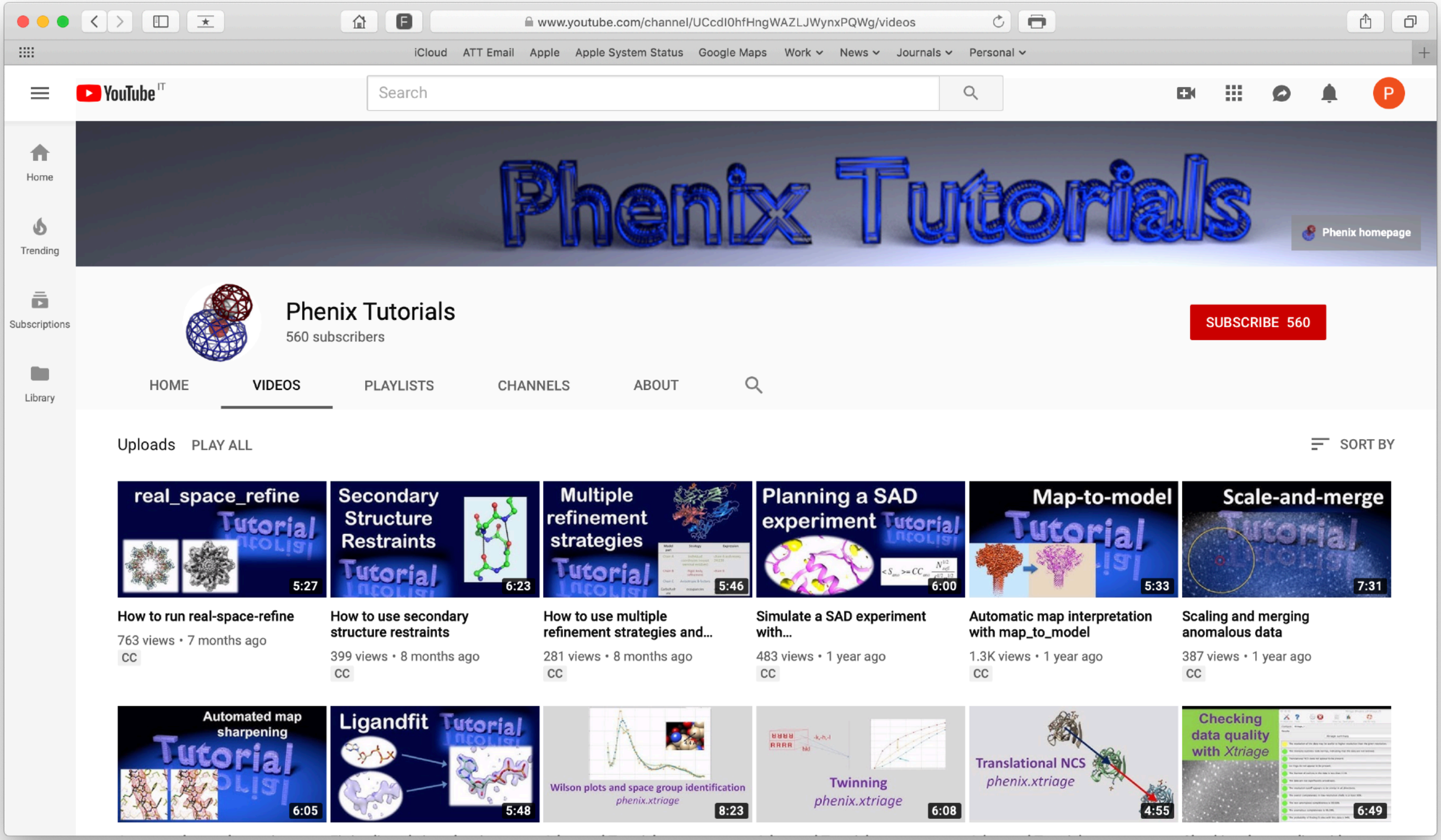
Video Tutorials



Dorothee Liebschner, Nigel Moriarty, Miffy Mifsud, Tom Terwilliger

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PHENIX Testers & Users

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