Phenix Introduction

ECM32 Vienna
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The Phenix Project

Lawrence Berkeley Laboratory

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Baylor College of Medicine

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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

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

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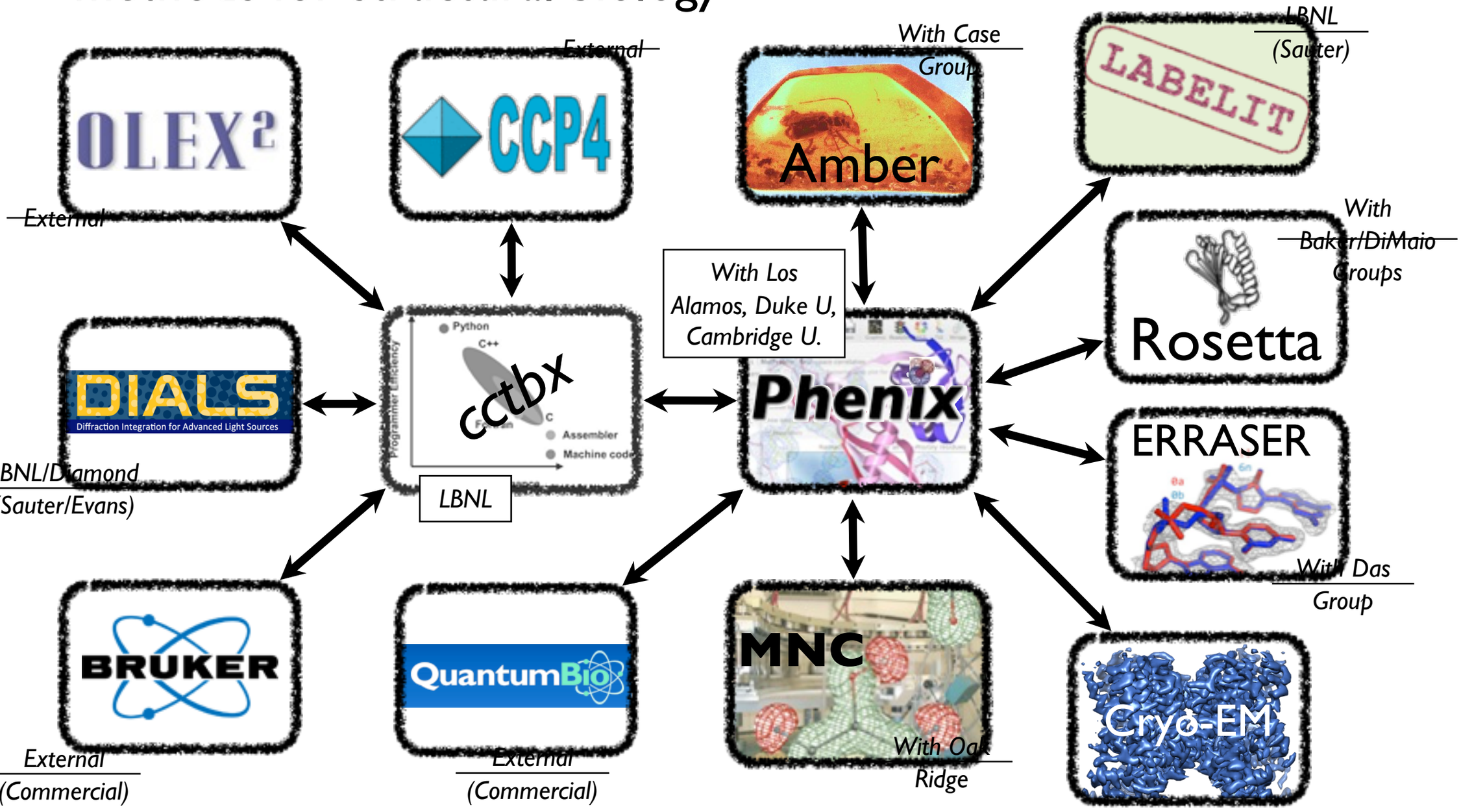
Phenix - a Structural Biology Hub

- 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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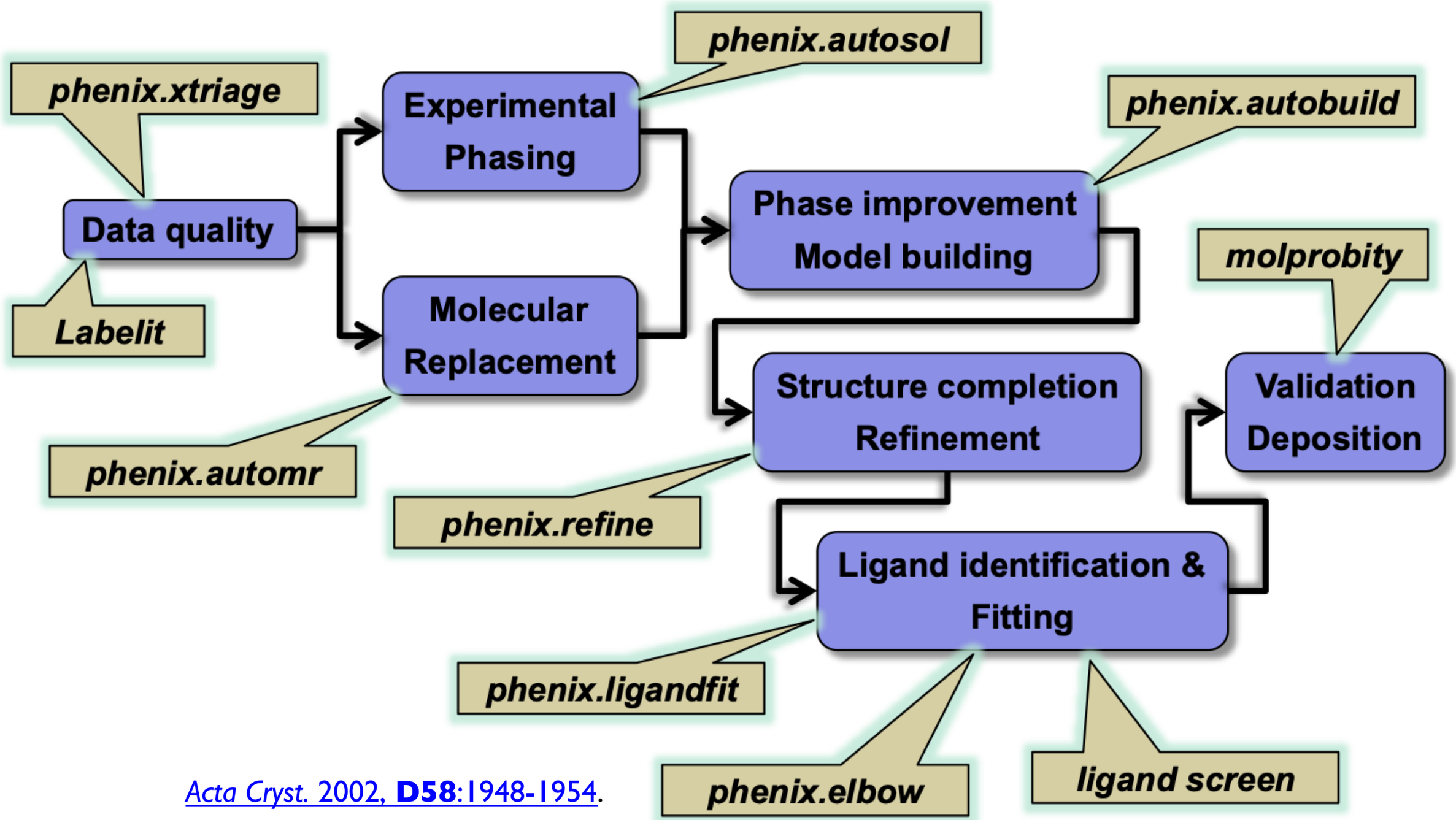
Automation of Structure Solution



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"`

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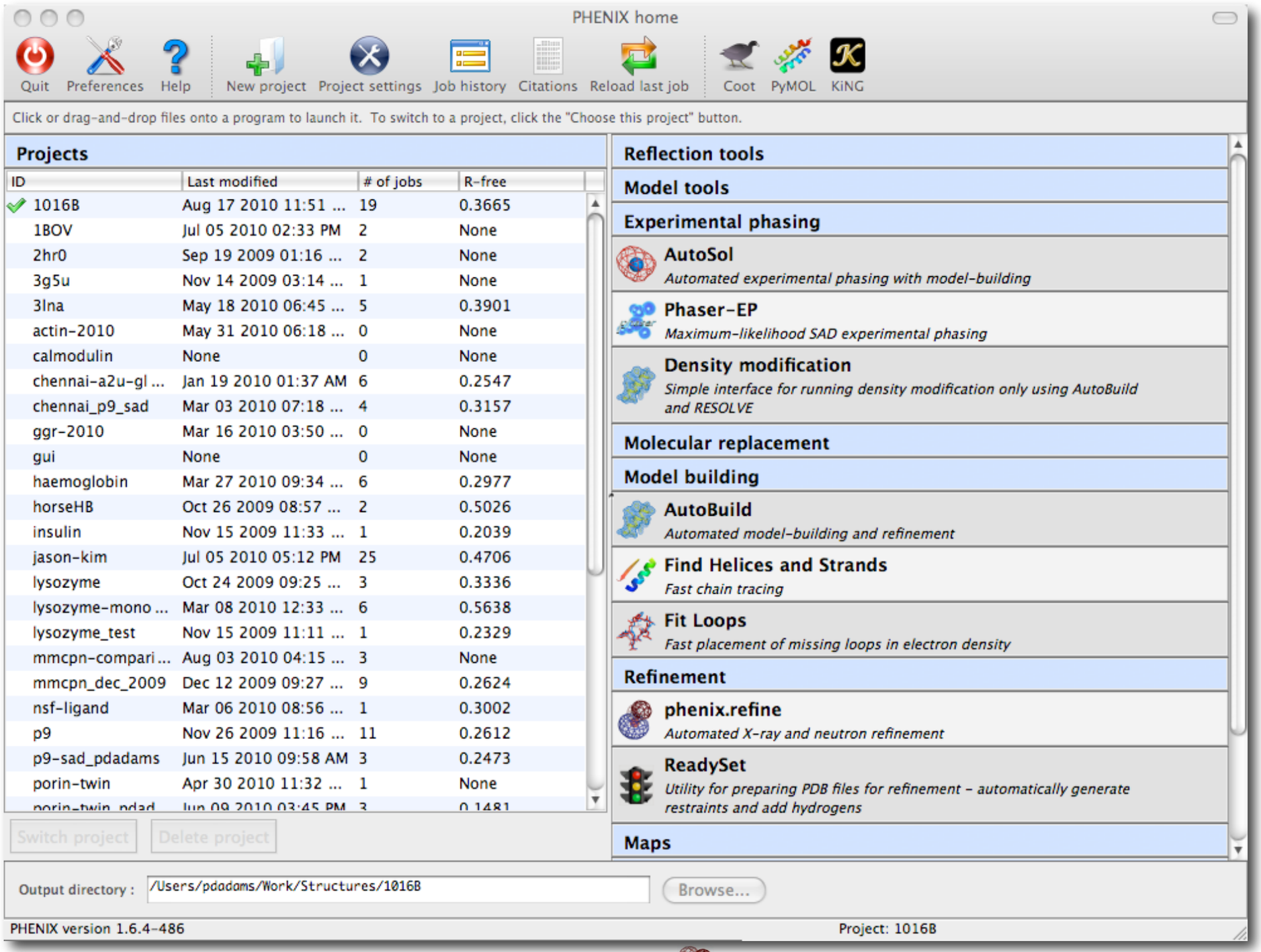
Phenix GUI

- Central GUI to view job control and launch new jobs



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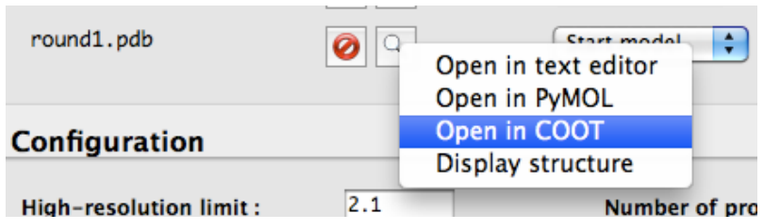
GUI: Nat Echols (LBL)

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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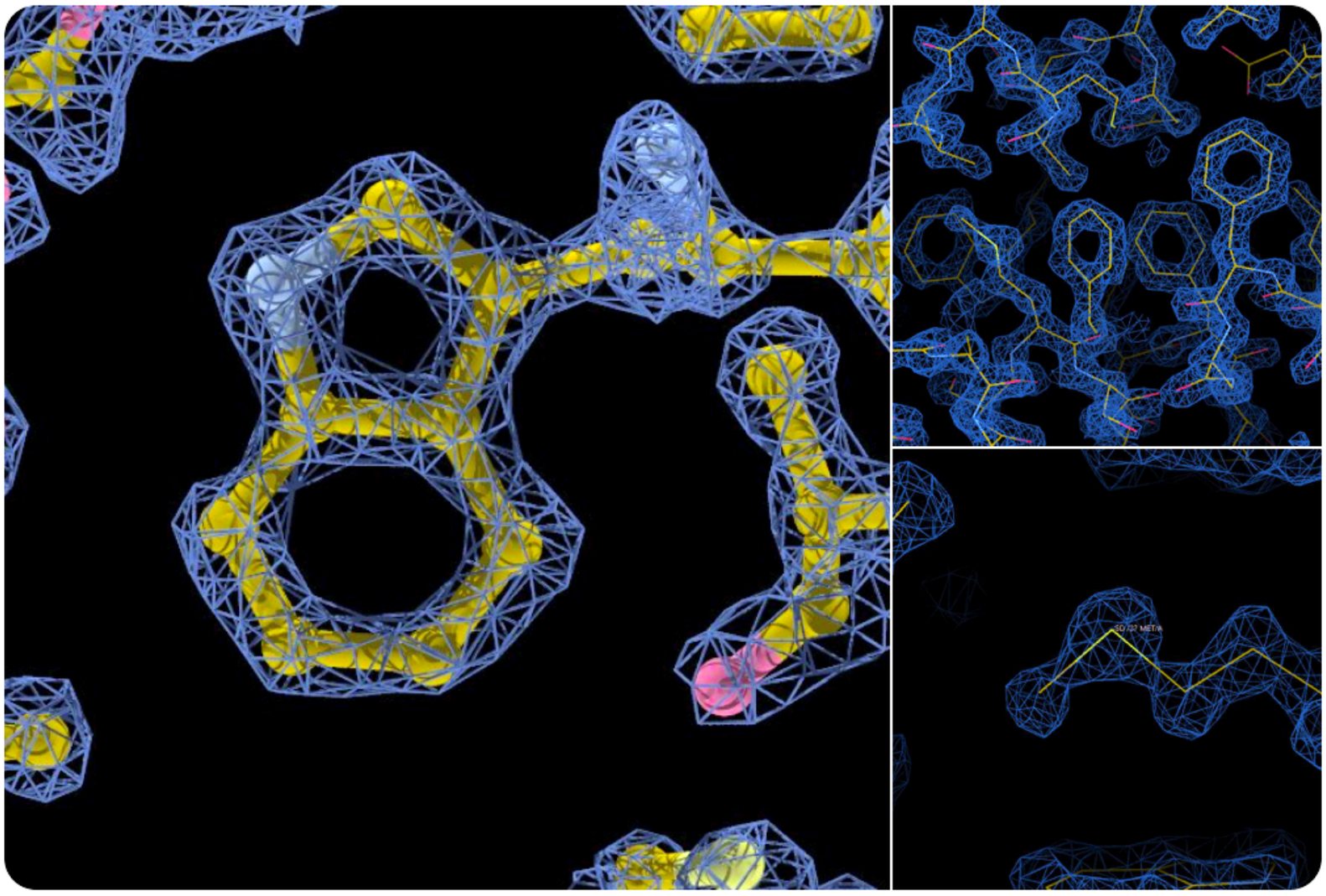
Impressive Cryo-EM Achievements



Namba Lab, Osaka

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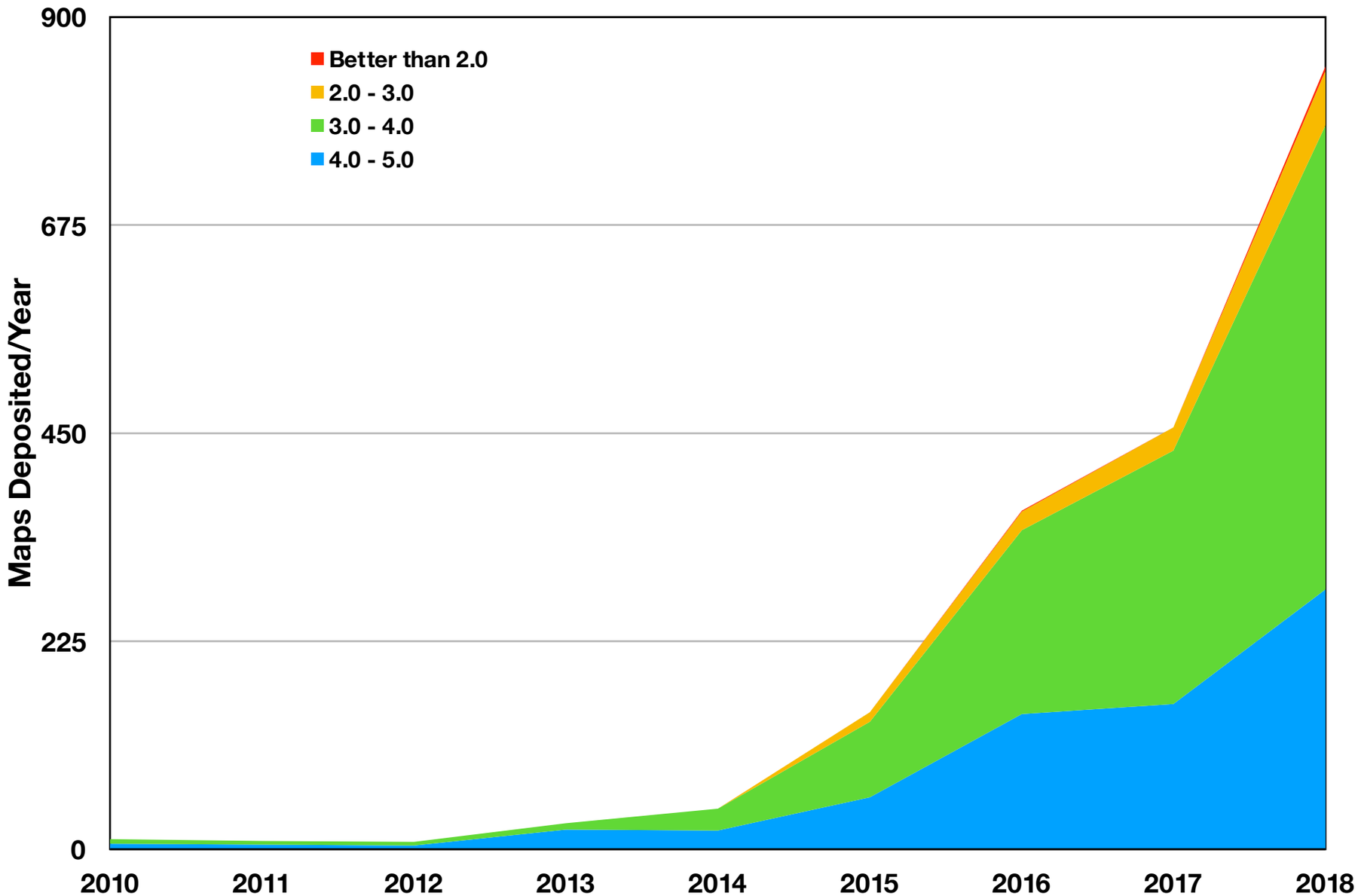
Map Resolution

- Biggest growth is in the 3-4Å range
- Substantial number of maps in 4-5Å range



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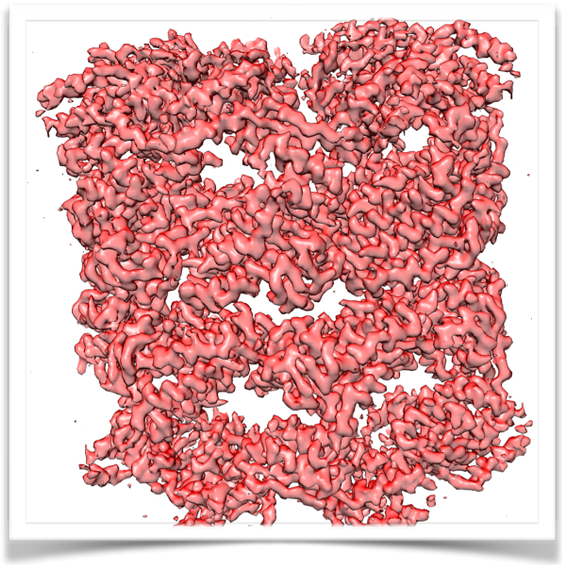
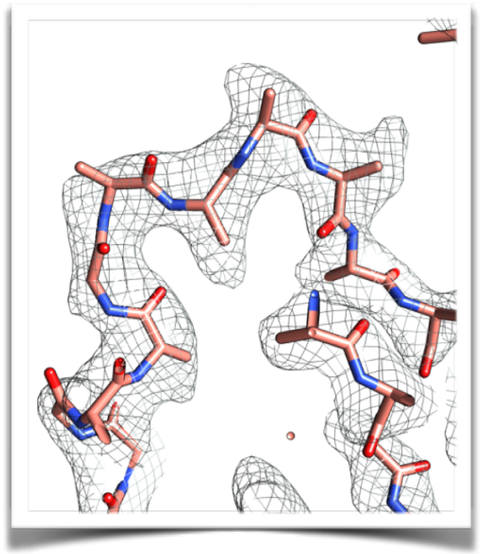
** Not all maps have an associated model*

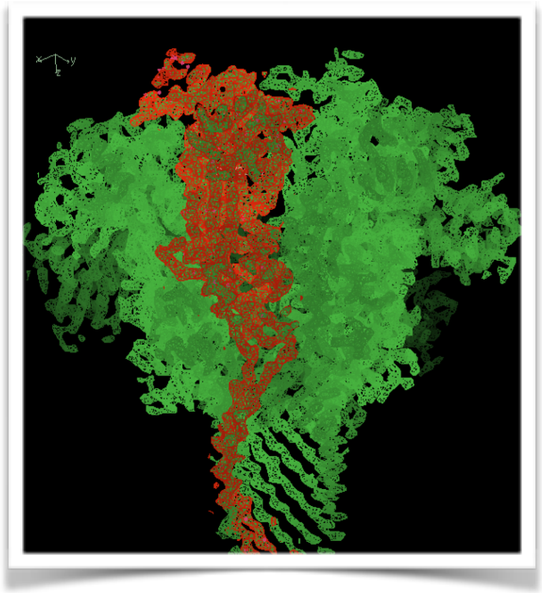
New Tools for Cryo-EM in Phenix



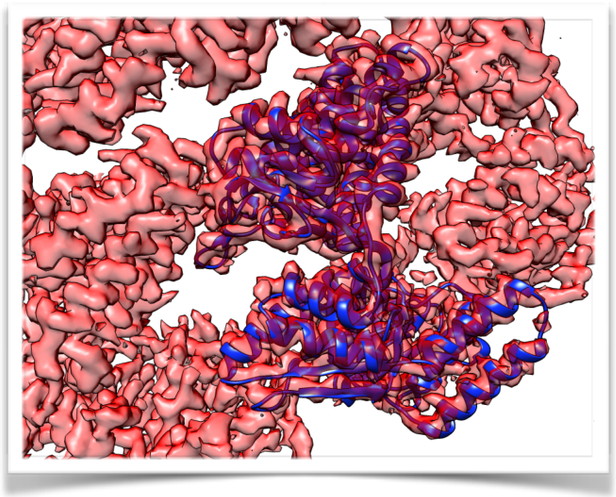
Symmetry from a map



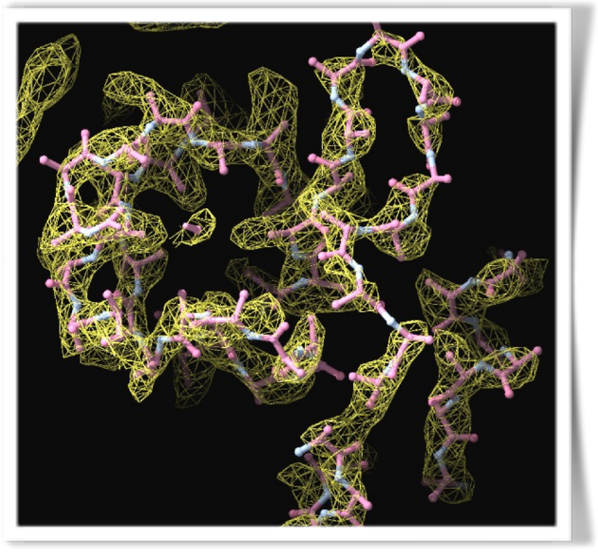
Automated map sharpening



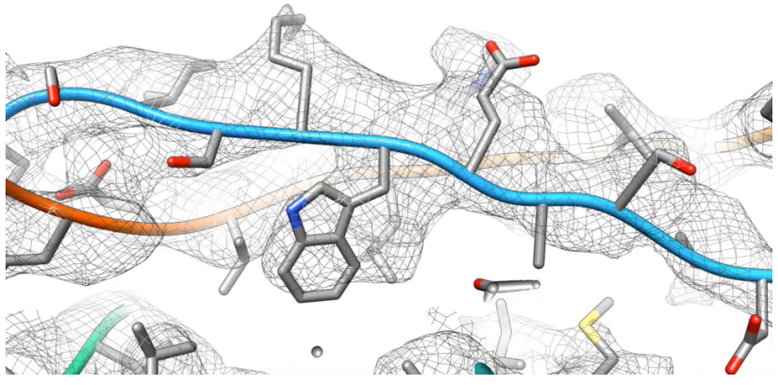
Map segmentation



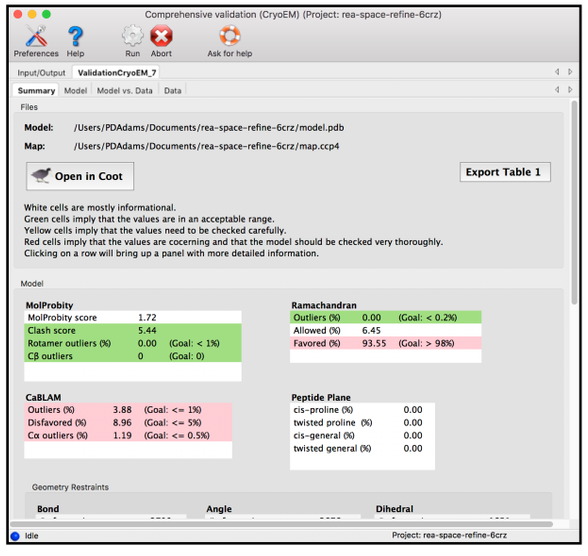
Rigid model docking



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 crystallographic process
- Automated understanding of chemistry

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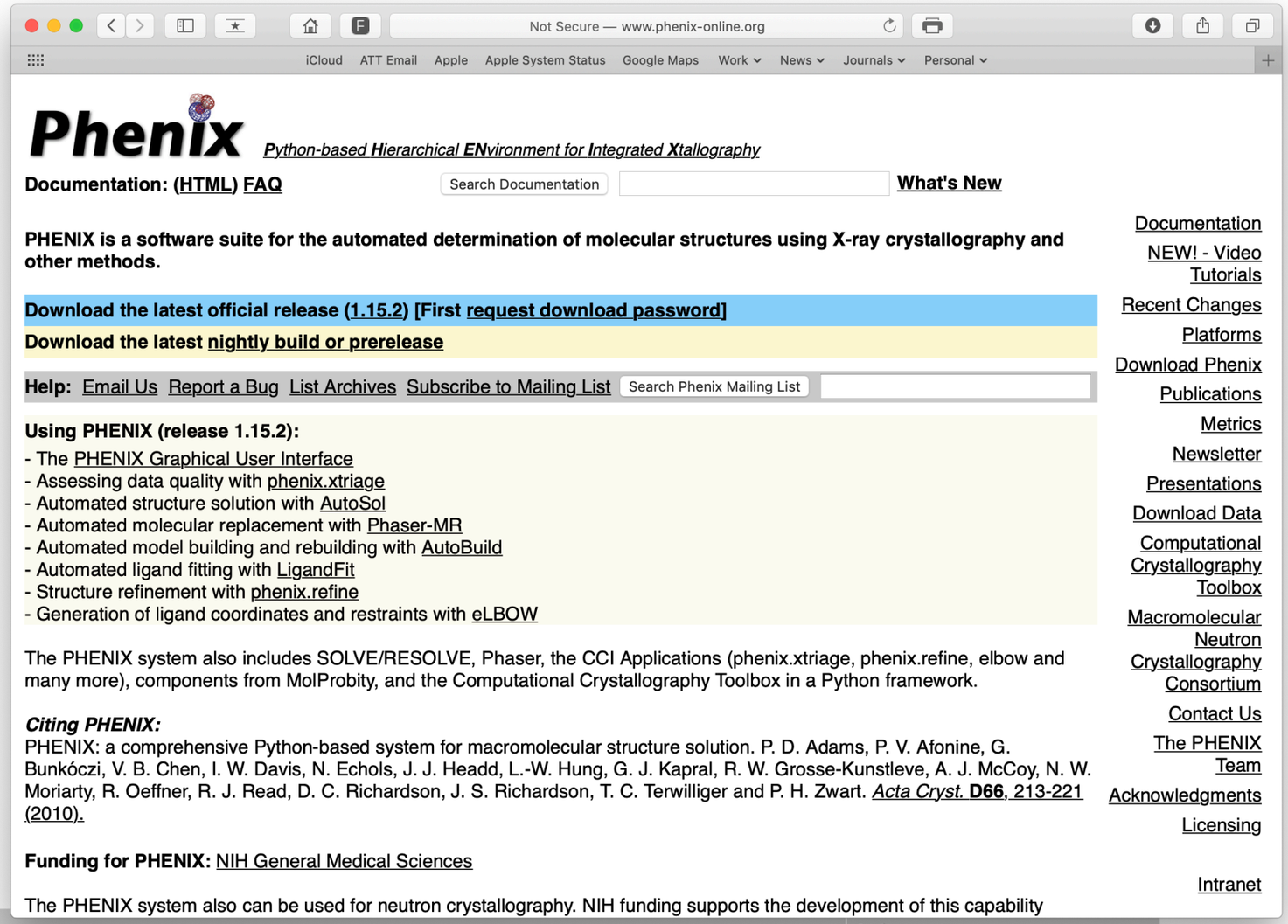
PHENIX Availability

- `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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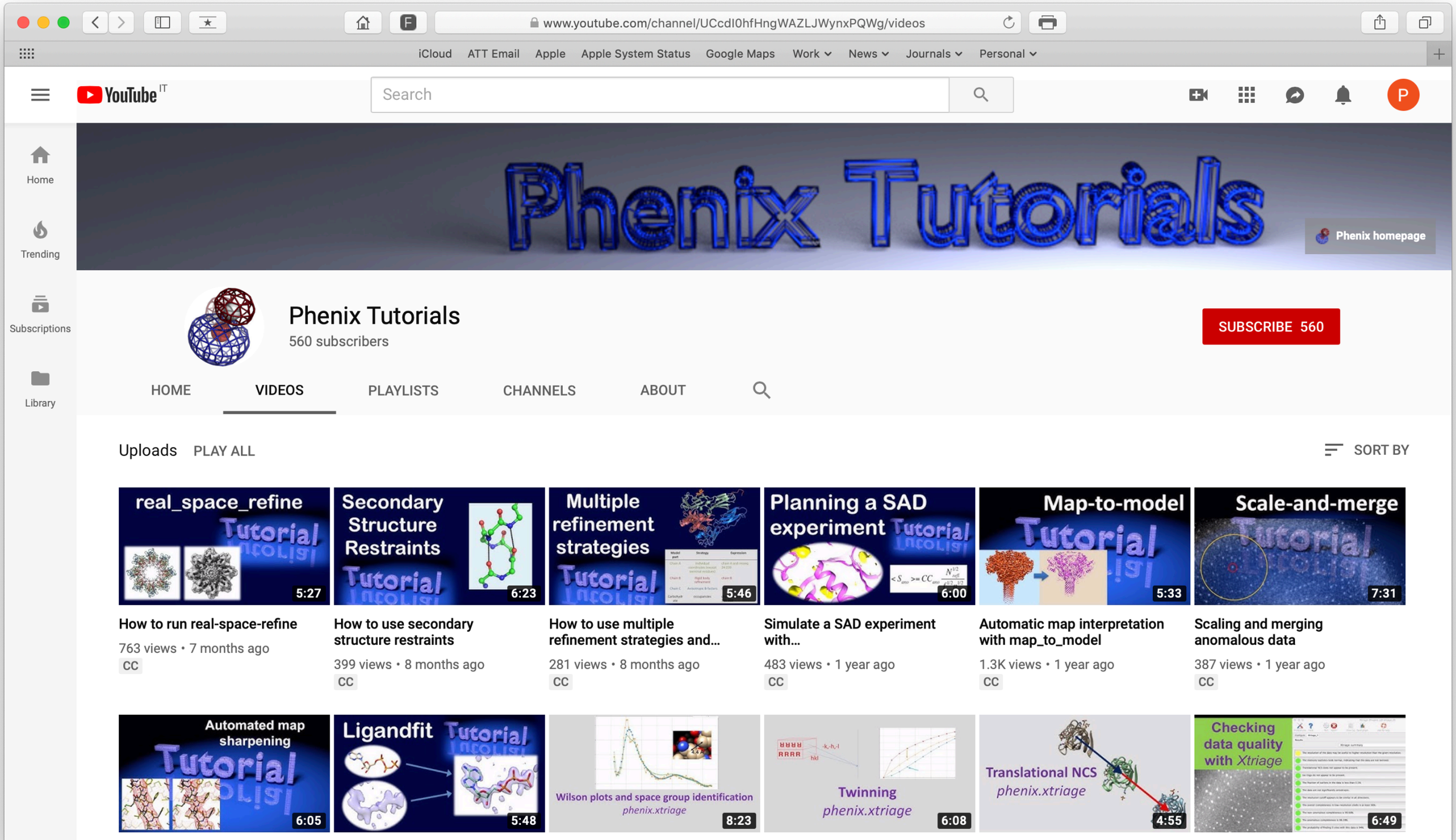
Video Tutorials



Dorothee Liebschner, Nigel Moriarty, Miffy Mifsud, Tom Terwilliger

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Acknowledgements

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Pawel Janowski, David Case
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Garib Murshudov & Alexi Vagin
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David Abrahams
PHENIX Testers & Users

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- NIH/NIGMS: P01GM063210, P50GM062412, P01GM064692, R01GM071939
- PHENIX Industrial Consortium
- Lawrence Berkeley Laboratory

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Tutorials

- Cryo-EM model placement and building
  - Symmetry determination
  - Rigid body model fitting
  - Map sharpening
  - Map segmentation
  - Automated model building
- Atomic model optimization and validation
  - Structure refinement (crystallography and cryo-EM)
  - Validation

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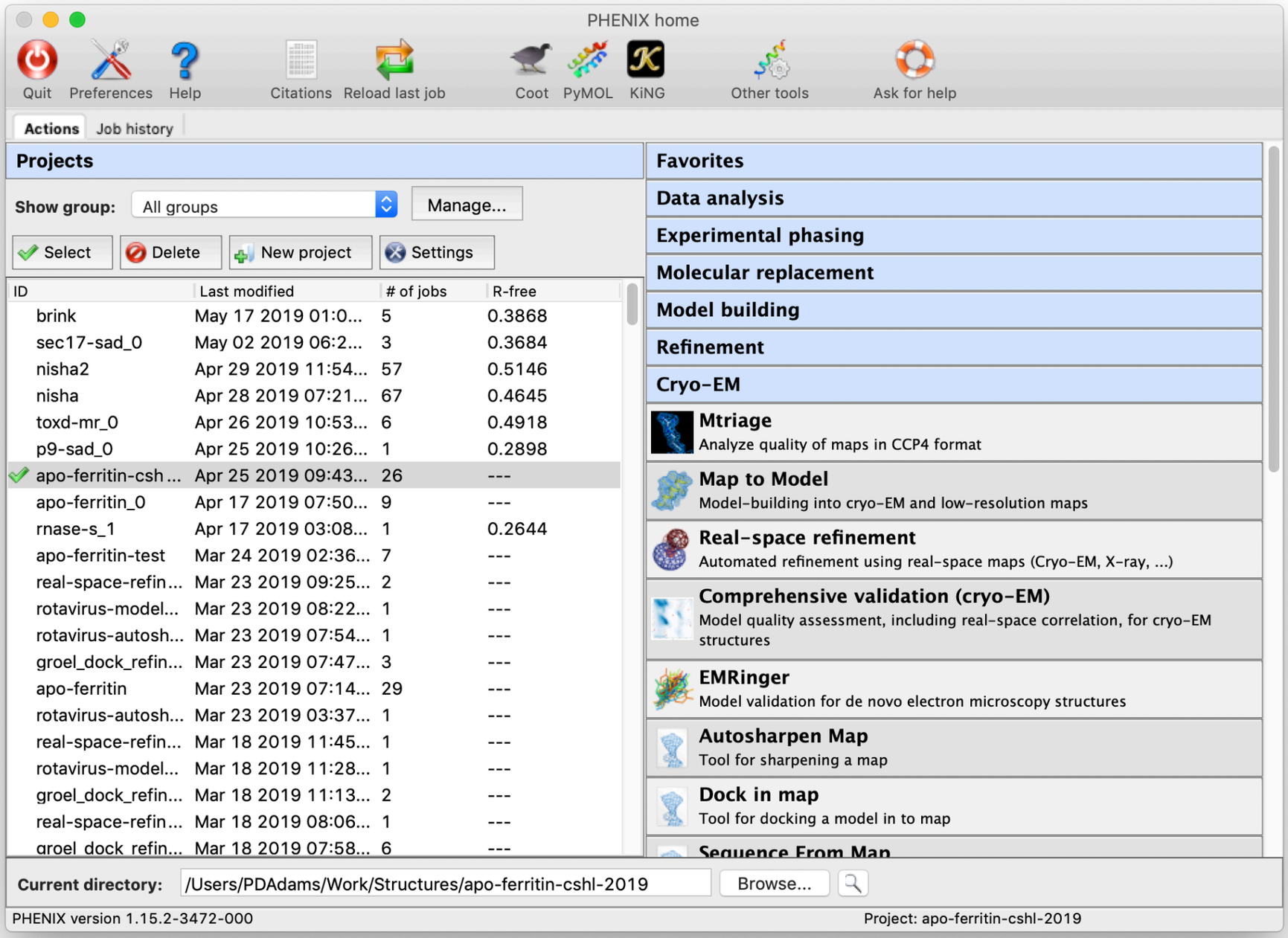
Tutorial Format

- Use graphical user interface



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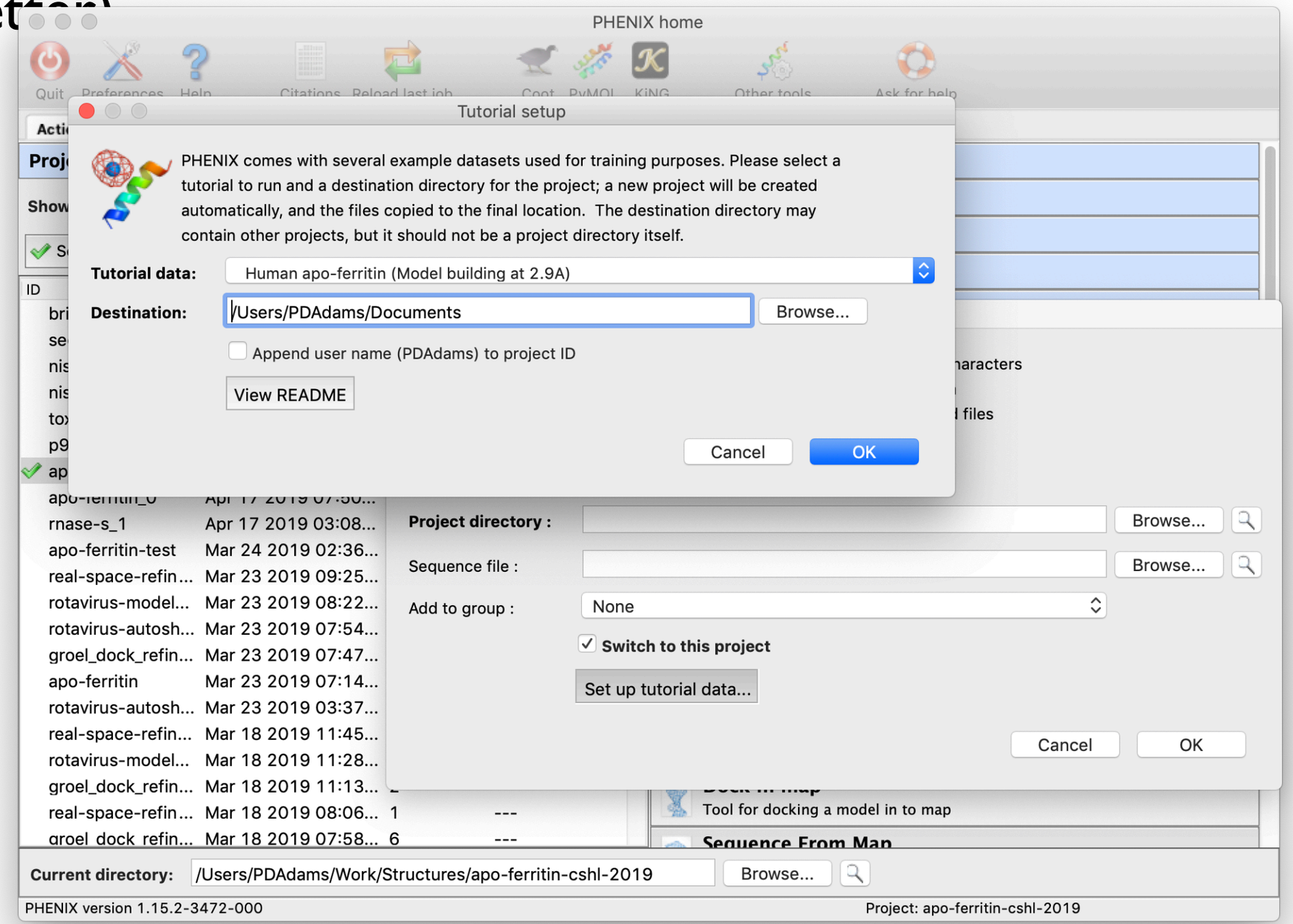
Tutorial Format

- Use tutorial datasets distributed with Phenix
- Should run on most laptops (2GB RAM, multiple CPUs better)



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