Phenix Introduction

Macromolecular Crystallography School

Madrid, May 2017

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The Phenix Project

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Randy Read, Airlie McCoy, Tristan Croll, Rob Oeffner

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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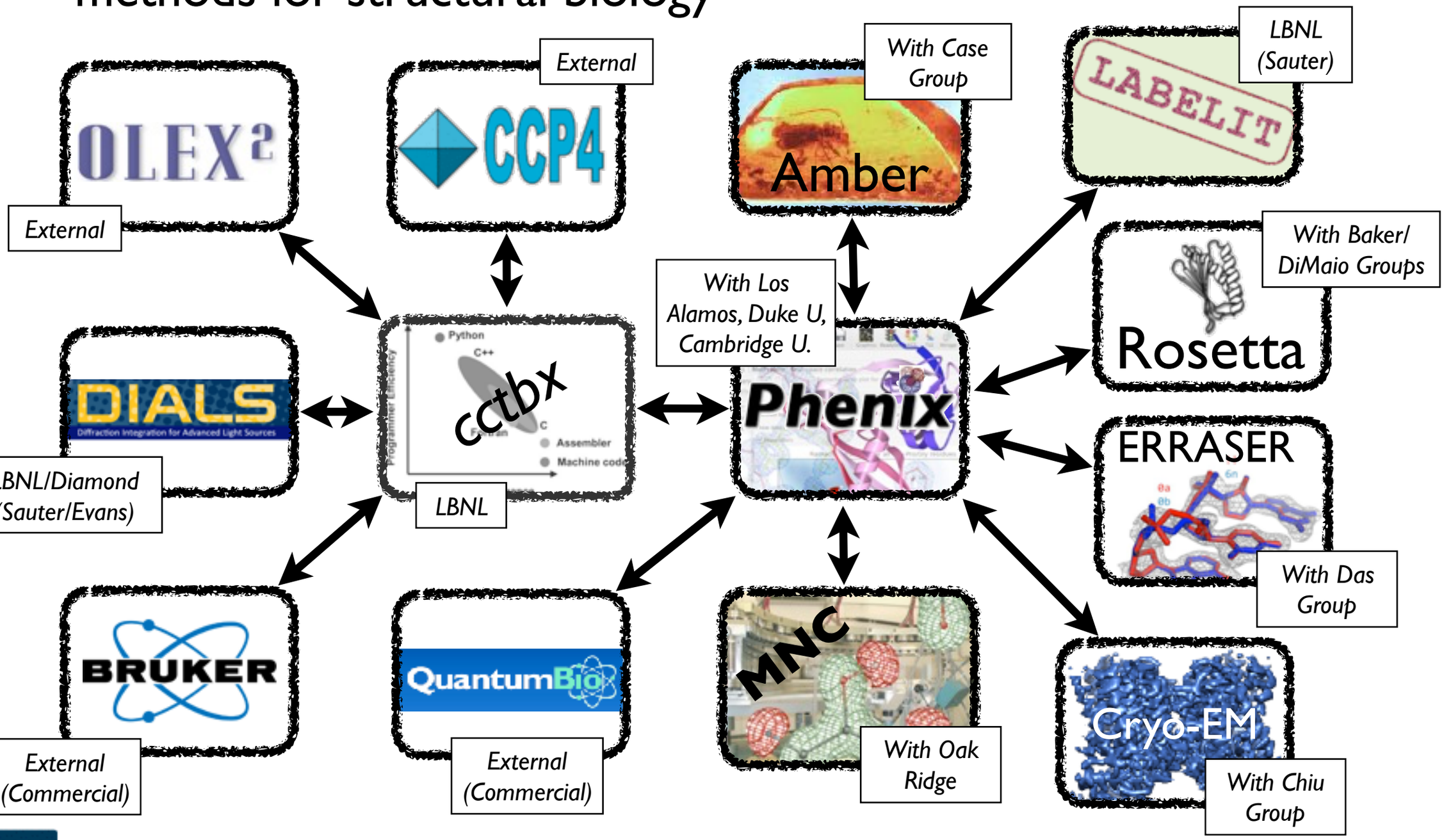
Phenix - a Structural Biology Hub

- 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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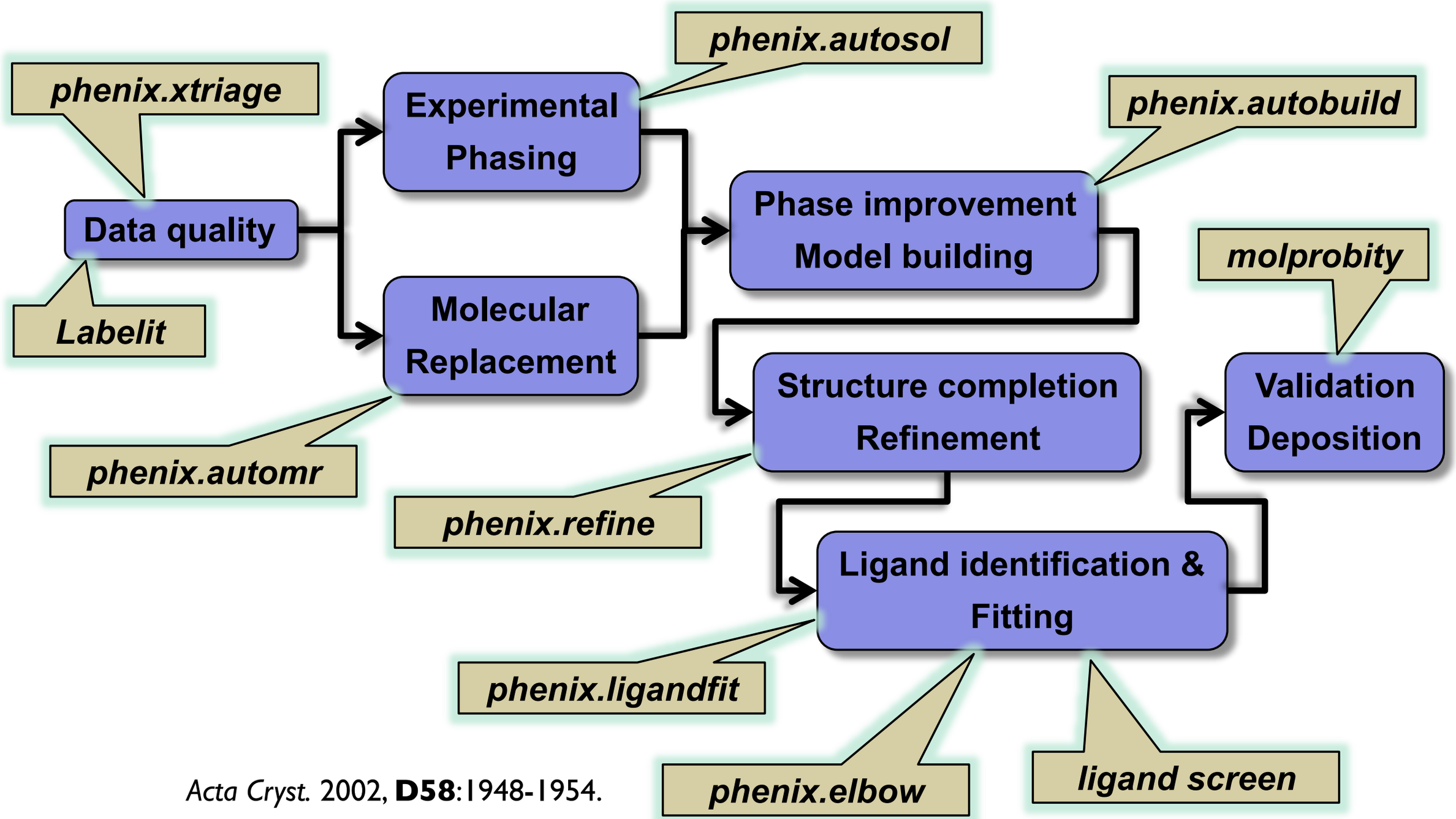
Automation of Structure Solution



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

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

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

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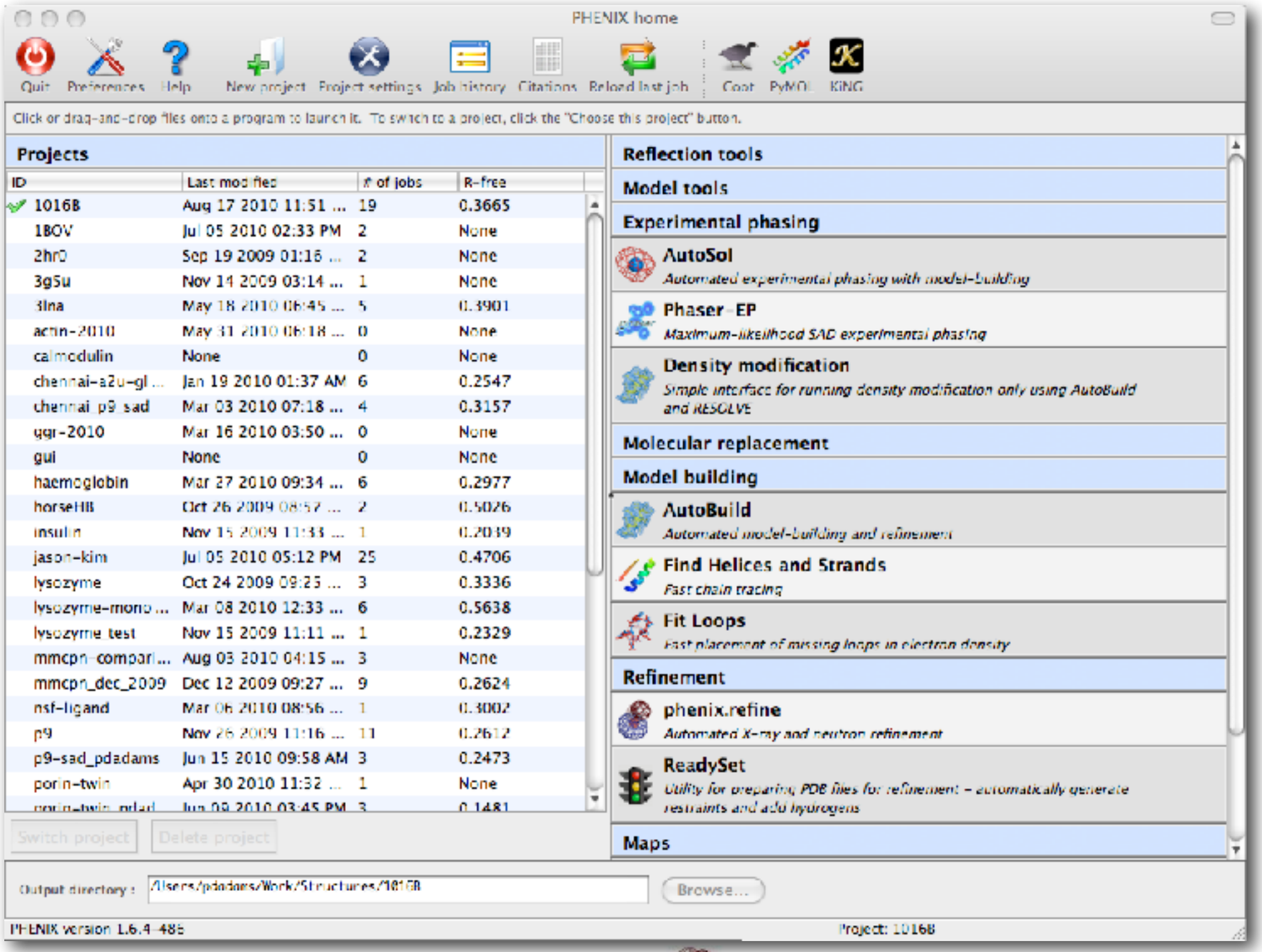
Command Line Tools

- 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"`

Phenix GUI

- Central GUI to view job control and launch new jobs

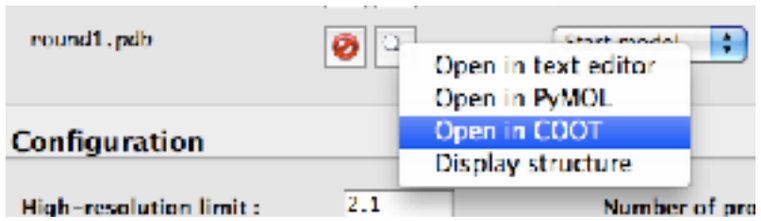


GUI: Nat Echols (LBL)

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

- Automated model building for cryo-EM maps

- New Rosetta methods for RNA rebuilding (ERRASER)

- Automated ion placement in refinement
- Automated ligand pipeline

- DIALS included in Phenix distribution

- Real space refinement (for X-ray and cryo-EM)

- Low resolution refinement algorithms:
  - Rosetta refinement
  - Reference model
  - Torsion NCS
  - Structure restraints

- Feature Enhanced Maps to improve interpretability
- Polder maps for better ligand density
- Ensemble refinement to understand dynamics and structural variability

- New validation methods for cryo-EM models

- Support for mmCIF format (for structure deposition)
- Video Tutorials

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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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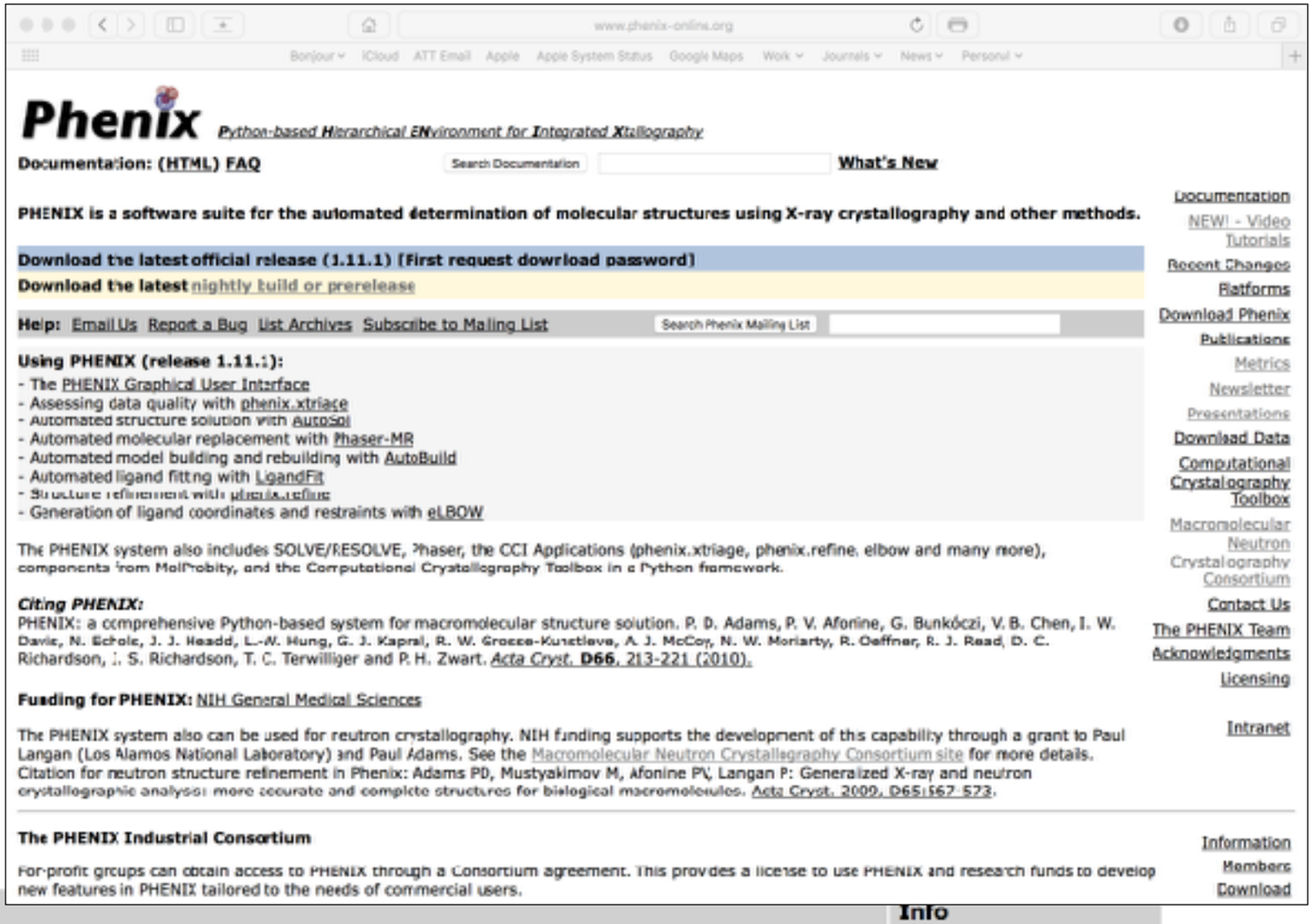
PHENIX Availability

- `phenix-online.org`

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

- Extensive documentation

- Nightly builds:



Phenix *Python-based Hierarchical ENvironment for Integrated Xtallography*

Documentation: (HTML) FAQ Search Documentation **What's New**

PHENIX is a software suite for the automated determination of molecular structures using X-ray crystallography and other methods.

Download the latest official release (1.11.1) (First request download password)

Download the latest nightly build or prerelease

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Using PHENIX (release 1.11.1):
- The PHENIX Graphical User Interface
- Assessing data quality with phenix.xtriage
- Automated structure solution with AutoSol
- Automated molecular replacement with Phaser-MR
- Automated model building and rebuilding with AutoBuild
- Automated ligand fitting with LigandFit
- Structure refinement with phenix.refine
- Generation of ligand coordinates and restraints with eLBOW

The PHENIX system also includes SOLVE/RESOLVE, Phaser, the CCI Applications (phenix.xtriage, phenix.refine, elbow and many more), components from MolProbity, and the Computational Crystallography Toolbox in a Python framework.

Citing PHENIX:
PHENIX: a comprehensive Python-based system for macromolecular structure solution. P. D. Adams, P. V. Afonine, G. Bunkóczi, V. B. Chen, I. W. Davis, N. Echols, J. J. Headd, L.-W. Hung, G. J. Kapral, R. W. Grosse-Kunstleve, A. J. McCoy, N. W. Moriarty, R. Oeffner, R. J. Read, D. C. Richardson, J. S. Richardson, T. C. Terwilliger and P. H. Zwart. *Acta Cryst.* **D66**, 213-221 (2010).

Funding for PHENIX: NIH General Medical Sciences

The PHENIX system also can be used for neutron crystallography. NIH funding supports the development of this capability through a grant to Paul Langan (Los Alamos National Laboratory) and Paul Adams. See the Macromolecular Neutron Crystallography Consortium site for more details.
Citation for neutron structure refinement in Phenix: Adams PD, Mustyakimov M, Afonine PV, Langan P: Generalized X-ray and neutron crystallographic analysis: more accurate and complete structures for biological macromolecules. Acta Cryst. 2009, D65:567-573.

The PHENIX Industrial Consortium

For-profit groups can obtain access to PHENIX through a Consortium agreement. This provides a license to use PHENIX and research funds to develop new features in PHENIX tailored to the needs of commercial users.

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Macromolecular Neutron Crystallography Consortium
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Version	Date	Status	Logs	Info
dev-2747	2017-04-17	successful	intel-windows-x86_64, intel-linux-2.6-x86_64-centos5, intel-linux-2.6-x86_64-centos5, mac-intel-osx-x86_64, intel-linux-2.6-centos5, ci, intel-windows	docs; changelog
dev-2744	2017-04-13	successful	ci, intel-linux-2.6-x86_64-centos6, intel-linux-2.6-x86_64-centos5, intel-linux-2.6-centos5, mac-intel-osx-x86_64, intel-windows, intel-windows-x86_64	docs; changelog
dev-2733	2017-04-02	successful	intel-linux-2.6-x86_64-centos6, ci, intel-windows, mac-intel-osx-x86_64, intel-windows-x86_64, intel-linux-2.6-x86_64-centos5, intel-linux-2.6-centos5	docs; changelog
dev-2722	2017-03-22	successful	ci, intel-linux-2.6-centos5, intel-windows-x86_64, mac-intel-osx-x86_64, intel-windows, intel-linux-2.6-x86_64-centos5, intel-linux-2.6-x86_64-centos5	docs; changelog
dev-2621	2016-12-11	successful	intel-windows, ci, mac-intel-osx-x86_64, intel-windows-x86_64, intel-linux-2.6-centos5, intel-linux-2.6-x86_64-centos6, intel-linux-2.6-x86_64-centos5	docs; changelog

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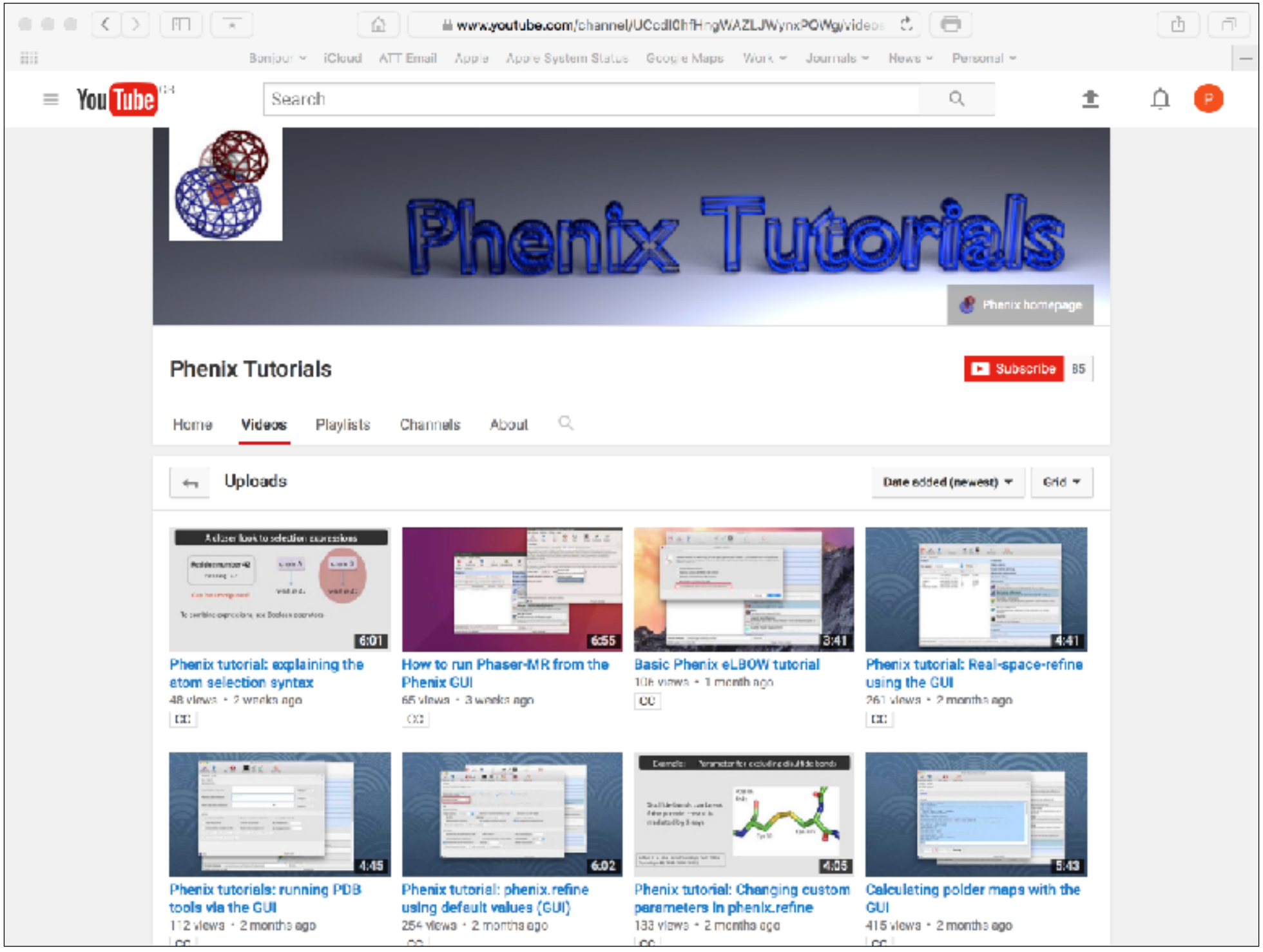
Video Tutorials



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Acknowledgments

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  - Tom Terwilliger, Li-Wei Hung
- **Cambridge University**
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  - Lawrence Berkeley Laboratory