Introduction to Easy and Fast Simulations with QwikMD

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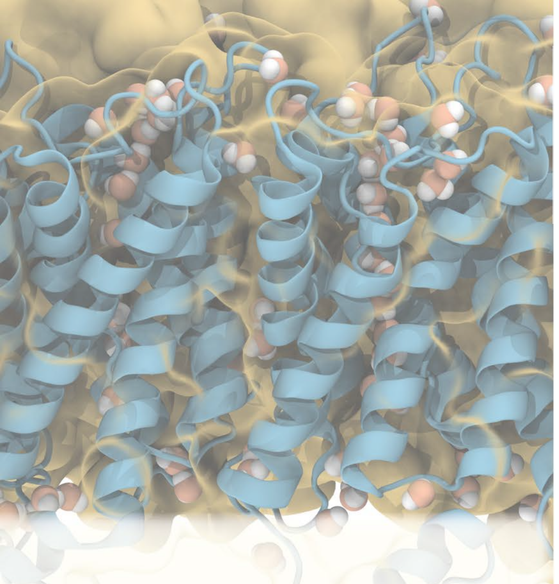
Pittsburgh Supercomputing Center
Pittsburgh, PA

Outline

- Accessible MD Simulations
- Integrative MD Toolkit for Novices and Experts
- QwikMD Workflow
  - Initial Structure
  - Structure Manipulation
  - Simulation Environment
  - Simulation Protocols
  - QwikMD and Reproducibility
  - Load Simulation Trajectories and Analysis
  - New QM/MM Simulation and Orbitals Visualization
- QwikMD Paper - Dissemination, Documentation and User Support
- QwikMD on the Amazon Cloud
- Training others...



Integrative MD Toolkit for Novices and Experts

QwikMD is a VMD plugin to assist the user in preparing, executing and analyzing MD simulations.

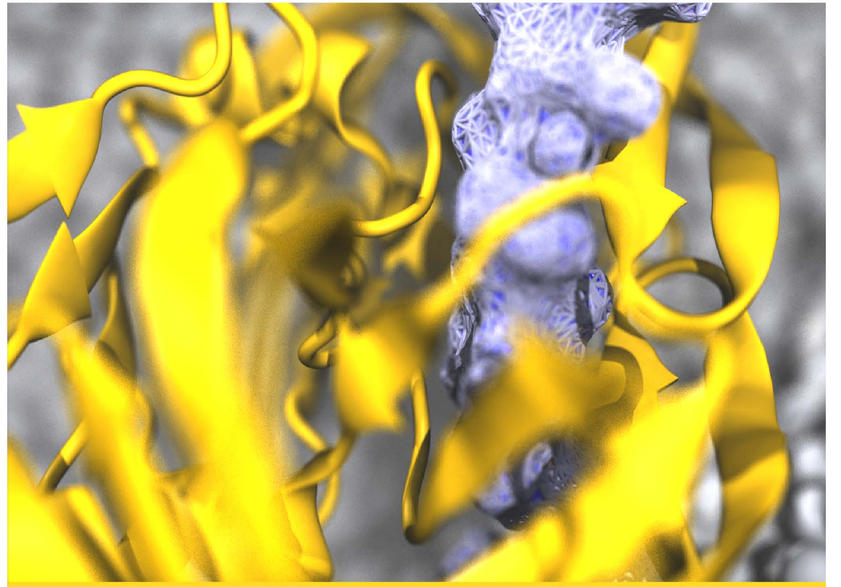
VMD
Visual Molecular Dynamics

NAMD
Scalable Molecular Dynamics

QwikMD
Gateway for Easy Simulation

QwikMD Features

- Easy Setup of MD Simulations
- Structure Manipulation
- Basic and Advanced Protocols
- Live View Simulations
- Integrated Analysis
- Info Buttons
- Reproducibility
- Available on Amazon Cloud



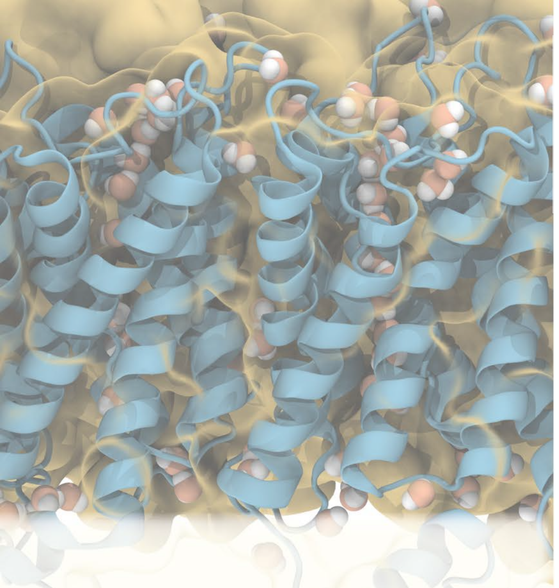
QwikMD

Gateway to Easy Simulation

www.ks.uiuc.edu/Research/qwikmd

QwikMD is freely available in VMD 1.9.3 and later

ILLINOIS
UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN



QwikMD Features

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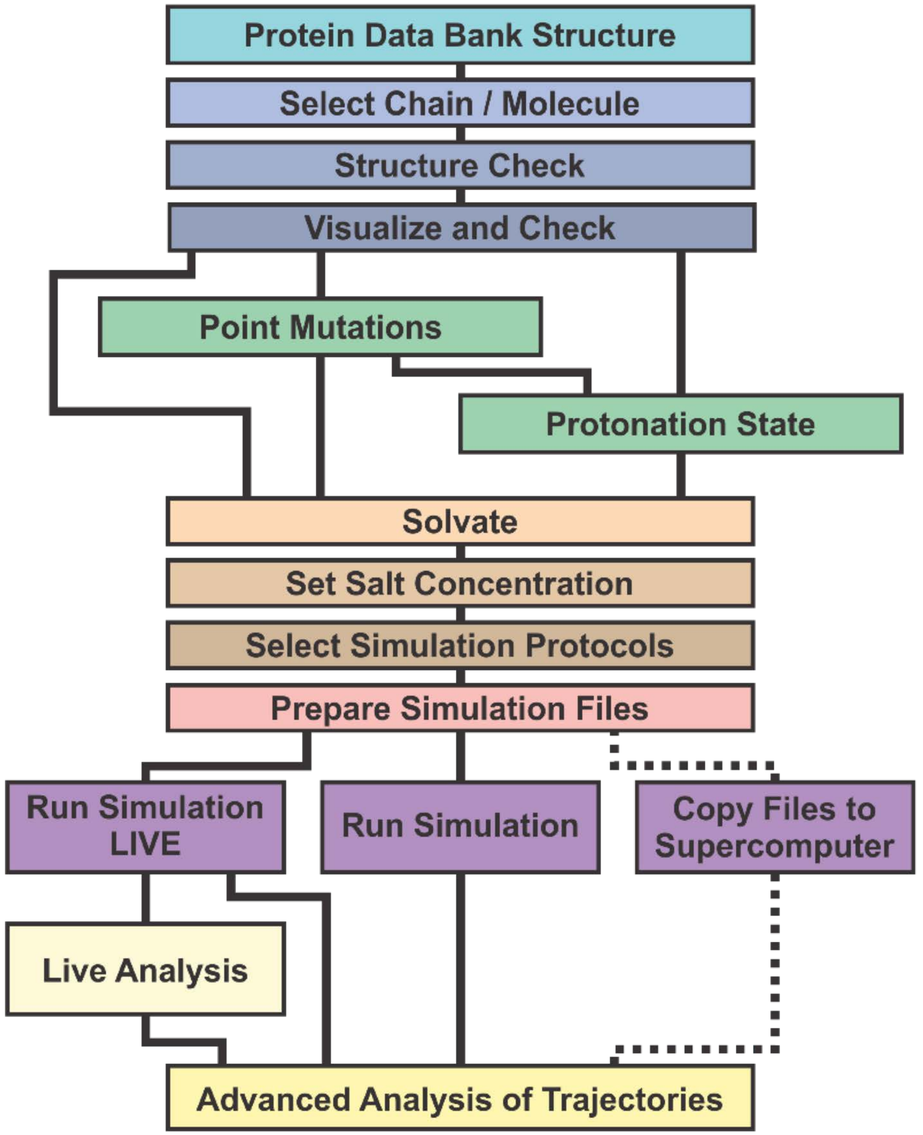
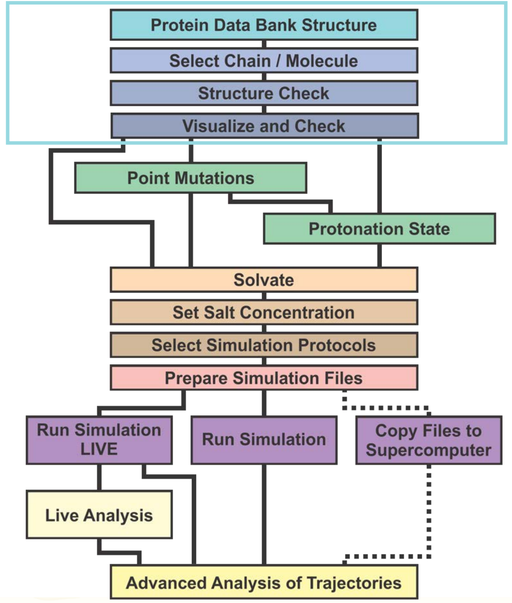
QwikMD Workflow



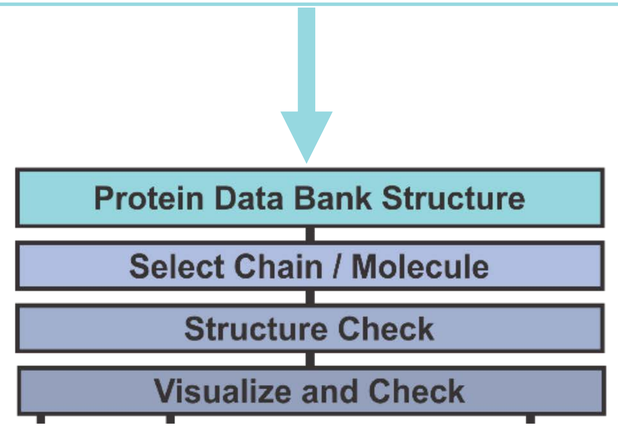


Initial Structure

VMD Visual Molecular Dynamics

NAMD Scalable Molecular Dynamics

RCSB PDB PROTEIN DATA BANK

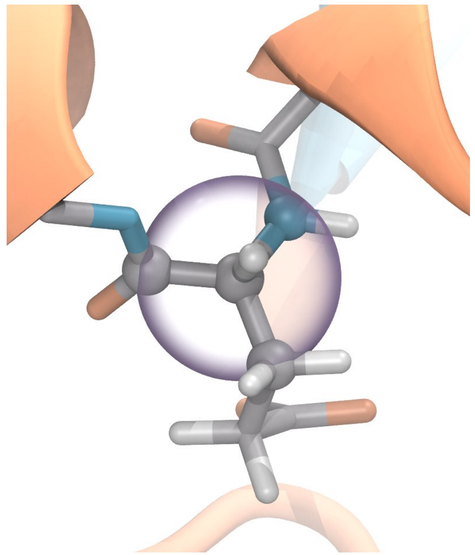


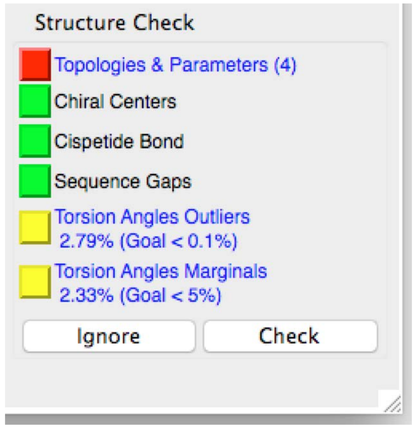
Structure Check

- Missing topologies
- Sequence Gaps
- Residues Alternative Insertions
- Chiral Centers
- Cis-peptide Bonds
- Backbone Torsion Angles
  - Marginals
  - Outliers

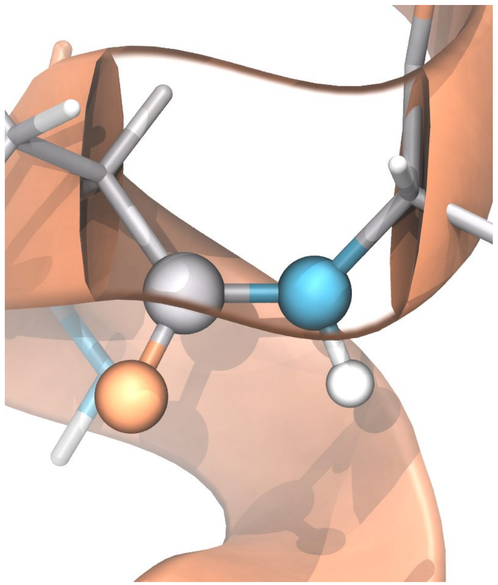
Chiral Centers

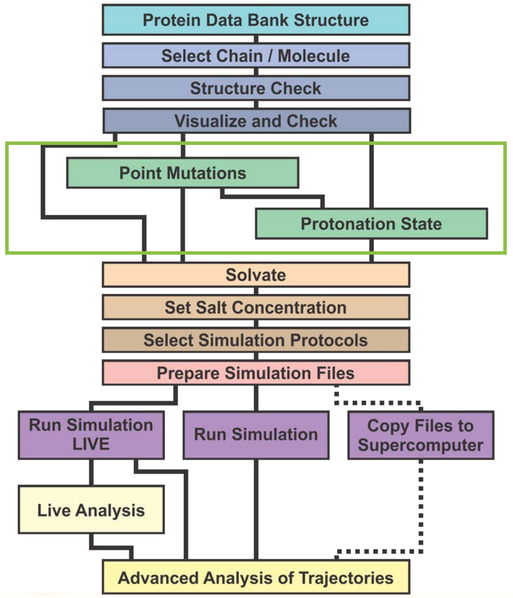
D-amino acids





Cis-peptide

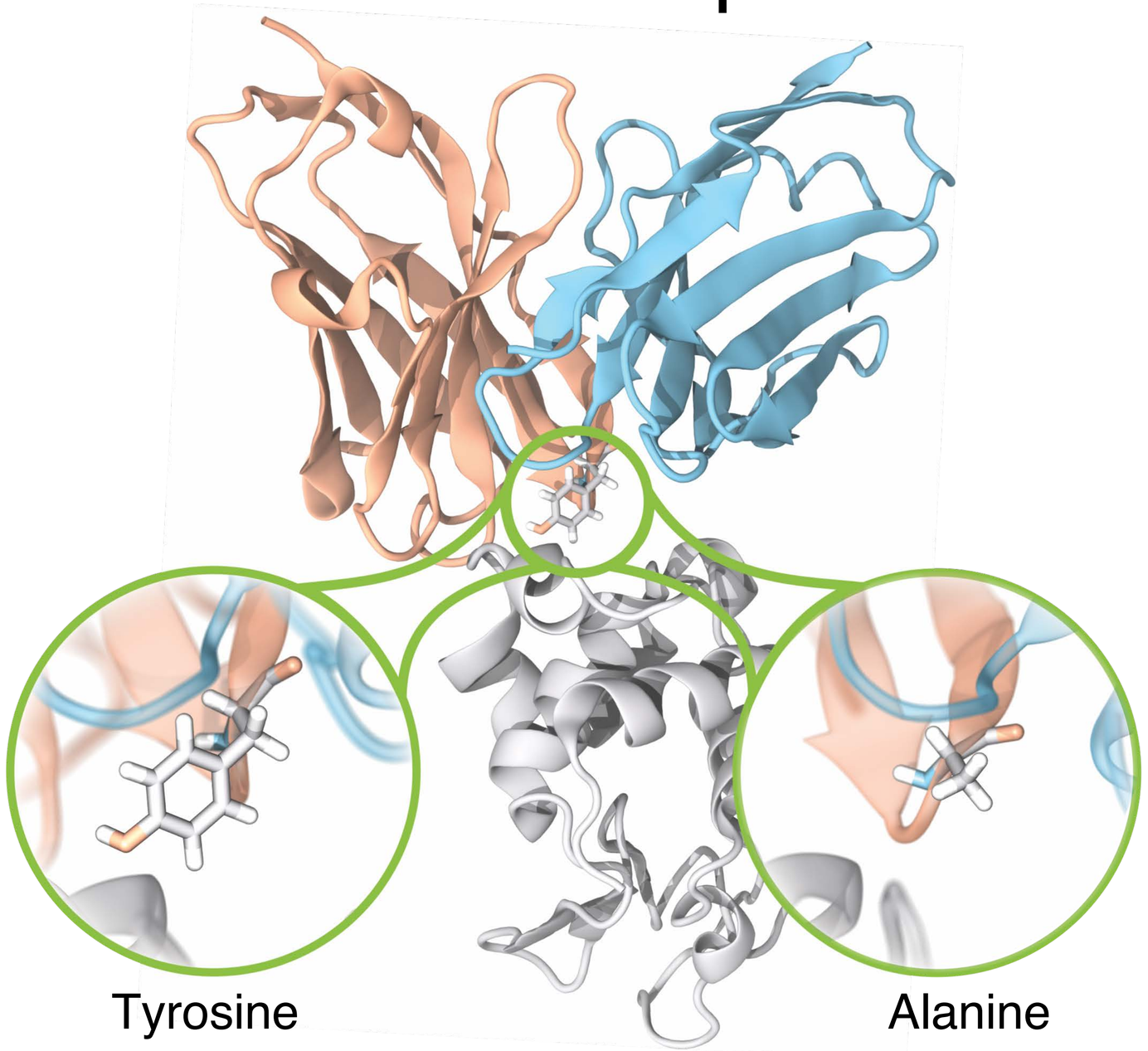


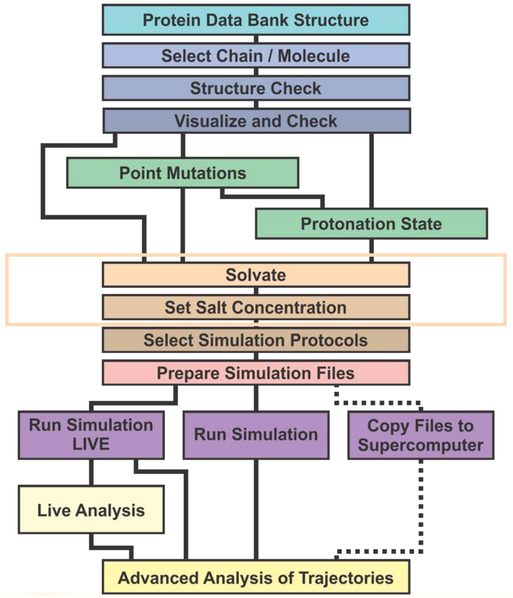


Structure Manipulation

- **<u>Point Mutations</u>**
- Protonation State Selection
- Partial Sequence Deletions
- Molecule's Type
- Assign Topologies
- Atom Editing
  - Name
  - Indexes

Structure Manipulation



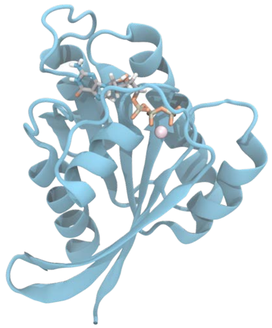


Simulation Environment

Simulation Environment

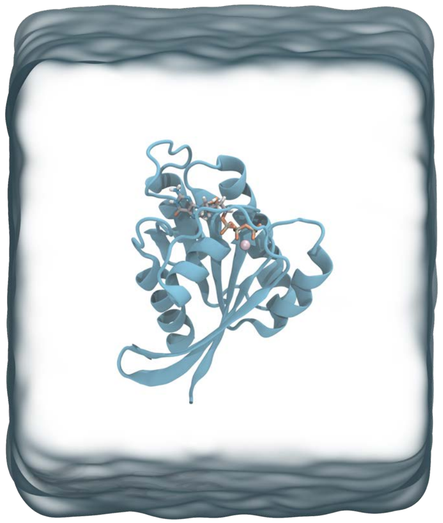
- Solvent Model
- Salt Concentration
- Water Box Size
  - Reduced Volume Available
- Membrane Protein Insertion

Vacuum

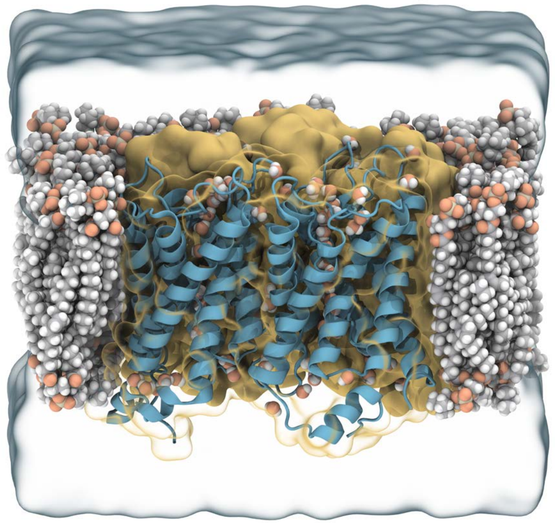


Implicit Solvent

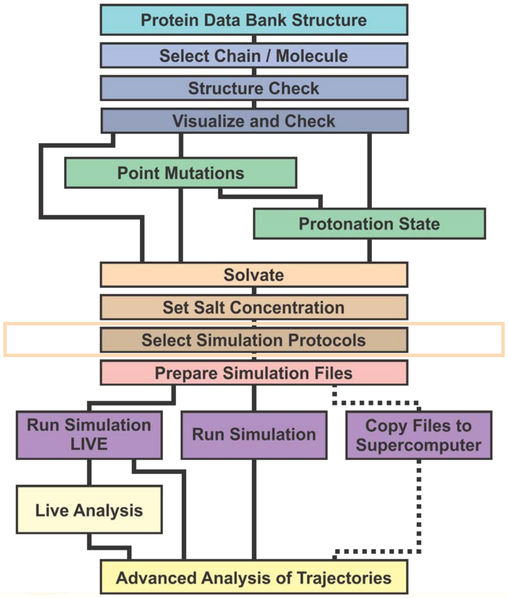
Explicit Solvent



Explicit Solvent + Membrane



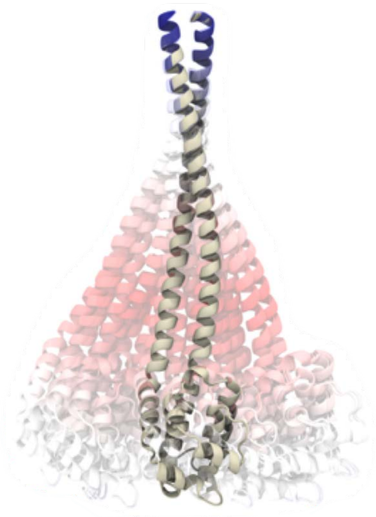
Simulation Protocols



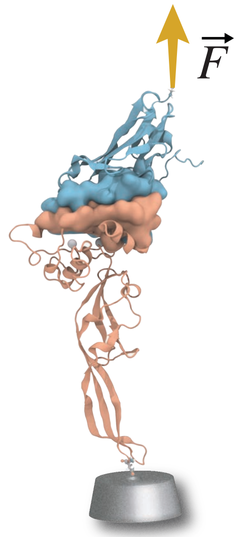
Simulation Protocol

- Molecular Dynamics
- Steered Molecular Dynamics
  - AFM
- Molecular Dynamics Flexible Fitting (MDFF)
  - cryo-EM Densities
- Quantum Mechanics / Molecular Mechanics (QM/MM) Simulations
  - MOPAC and ORCA

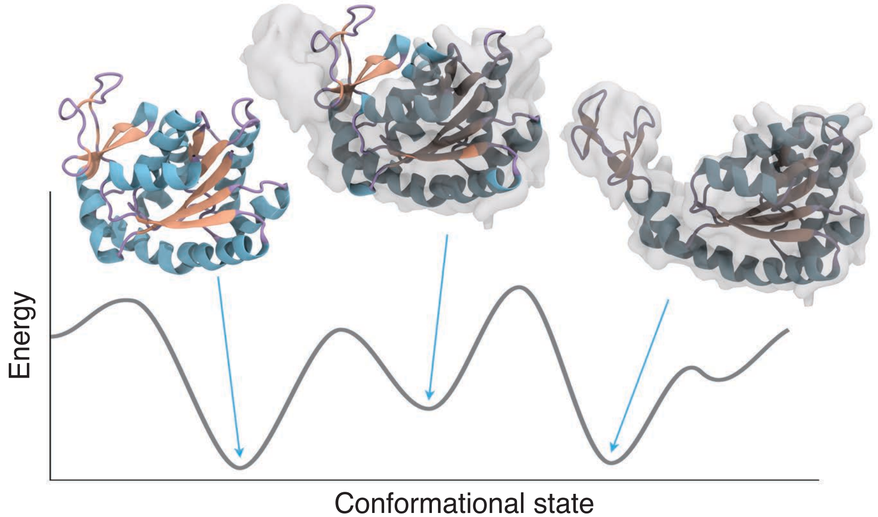
Molecular Dynamics



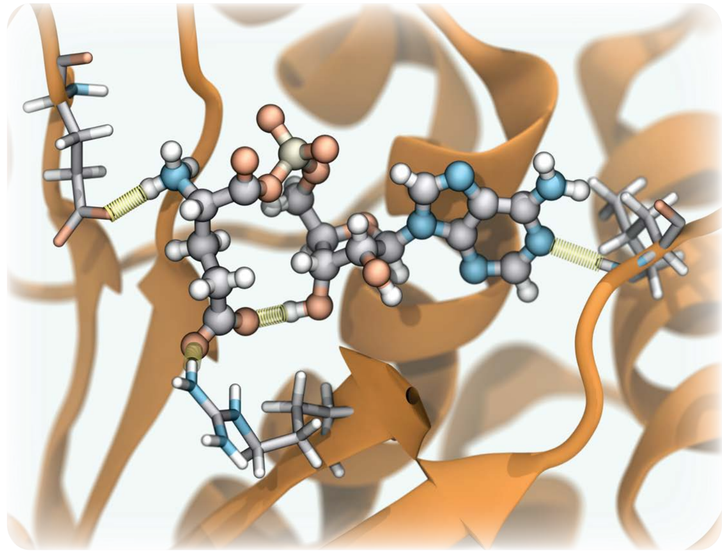
Steered MD



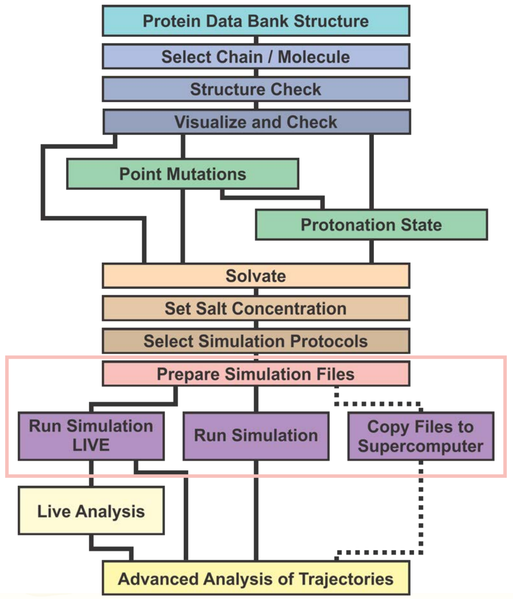
MDFF



QM/MM *(New)*



QwikMD and Reproducibility



Reproducibility

- All Steps Logged
- Loading Script and Text Log Files
- Reproduce and/or Share the Process to the End Result

"InputFileName.qwikmd" File

"InputFileName" Folder

"InputFileName.infoMD" File

Text File:
- Struct Man. Info
- File Locations
- MD Protocols details:
  - Temperatures
  - Steps
  - Method section (with references)

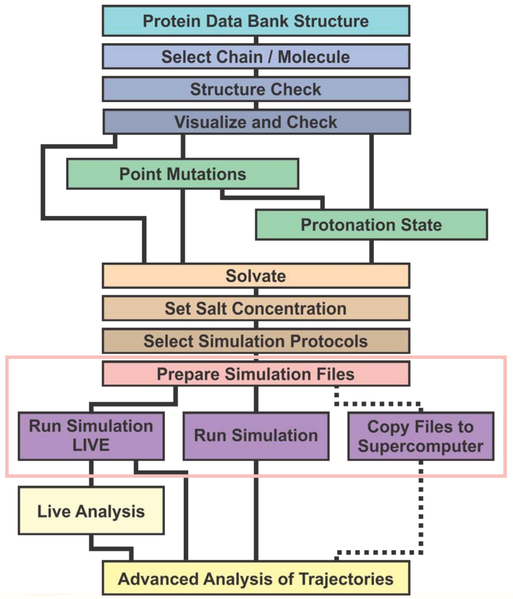
Setup Folder

- Auxiliary Files
- Intermediary PDBs
- Intermediary PSFs
- Renumber Residues Table
- Topology+Parameter Files

Run Folder

- MD Configuration Files
- PDB Files
- PSF Files
- Parameter Files
- Simulation Log Files
- Simulation Trajectories

QwikMD and Reproducibility



Reproducibility

- All Steps Logged
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QwikMD Inputfile

"InputFileName.qwikmd" File

```
nucleicmcr {(not name QWIKMDDELETE and nucleic)}
::proteinmcr {(not name QWIKMDDELETE and protein)}
:heteromcr {(not name QWIKMDDELETE and hetero and not
protein and not qwikmd_lipid and not qwikmd_nucleic and not
glycan and not water)}
set QWIKMD::glycanmcr {(not name QWIKMDDELETE and glycan)}
set QWIKMD::lipidmcr {(not name QWIKMDDELETE and lipid)}
atomselect macro qwikmd_protein $QWIKMD::proteinmcr
atomselect macro qwikmd_nucleic $QWIKMD::nucleicmcr
atomselect macro qwikmd_glycan $QWIKMD::glycanmcr
atomselect macro qwikmd_lipid $QWIKMD::lipidmcr
atomselect macro qwikmd_hetero $QWIKMD::heteromcr
$QWIKMD::topGui.nbinput select 0
set QWIKMD::prepared 1
QWIKMD::changeMainTab
$QWIKMD::topGui.nbinput.f1.nb select 0
QWIKMD::ChangeMdSmd 1
set aux "[file rootname $QWIKMD::basicGui(workdir,0)]"
set QWIKMD::outPath ${aux}
cd ${QWIKMD::outPath}/run/
set QWIKMD::inputstrct {Ubiquitin_QwikMD.psf Ubiquitin_QwikMD.pdb}
QWIKMD::LoadButt {Ubiquitin_QwikMD.psf Ubiquitin_QwikMD.pdb}
array set QWIKMD::basicGui {live 0 currenttime {Completed 0.000 of 0.000
ns} plength 10.0 desktop white temperature,0 27 temperature,1 27
saltconc,0 0.15 scheme {VMD Classic} mdPrec,0 0 pspeed 2.5 saltions,0 NaC
mdtime,0 5.0 mdtime,1 4.0 currenttime,0 {} currenttime,1 {} solvent,0
Explicit }
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5.0 mdtime,1 4.0 currenttime,0 {} currenttime,1 {} solvent,0 Explicit
addmol 10 protocoltb,SMD,1,restrIndex {} protocoltb,MD,0 Minimization
membrane,efect translate protocoltb,MD,1 Annealing analyze,basic,selcombo
backbone protocoltb,SMD,2,lock 0 protocoltb,MD,2 Equilibration
protocoltb,MD,3 MD scheme {VMD Classic} membrane,multi 1
protocoltb,SMD,2,restrsel {} protocoltb,MD,0,smd 0
protocoltb,MD,0,restrsel {} protocoltb,MD,2,smd 0 mdff,min 200
```

"Methods Section" format

"InputFileName.infoMD" File

```
========== MD Protocols ==========

ionized.psf was prepared using VMD[2] and the plugin QwikMD[3].
ations in the present study were performed employing the NAMD molecular dynamics
]. The CHARMM36 force field[5,6] was used in all MD simulations.


The Minimization and Constrained equilibration MD Simulation  was performed with explicit
solvent using the TIP3 water model[1] in the NpT ensemble.
A temperature ramp was performed consisted of 0.24 ns of simulation where the temperature was
raised from 60 K to 300.00 K The pressure was maintained at 1 atm using Nosé-Hoover Langevin
piston[7,8]. A distance cut-off of 12.0 Å was applied to short-range, non-bonded interactions,
and 10.0 Å for the smothering functions.  Long-range electrostatic interactions were treated
using the particle-mesh Ewald (PME)[9] method. The equations of motion were integrated using
the r-RESPA multiple time step scheme[4] to update the short-range interactions every 1 steps
and long-range electrostatics interactions every 2 steps. The time step of integration was
chosen to be 2 fs for all simulations. Before the MD simulations all the systems were submitted
to an energy minimization protocol for 1000 steps. In this step consisted of 1.00 ns of
simulation, the atoms defined by the selection "protein and backbone" were restrained.


The MD Simulation without constrains  was performed with explicit solvent using the TIP3 water
model[1] in the NpT ensemble.
The temperature was maintained at 300.00 K using  Langevin dynamics. The pressure was
maintained at 1 atm using Nosé-Hoover Langevin piston[7,8]. A distance cut-off of 12.0 Å was
applied to short-range, non-bonded interactions, and 10.0 Å for the smothering functions.
Long-range electrostatic interactions were treated using the particle-mesh Ewald (PME)[9]
method. The equations of motion were integrated using the r-RESPA multiple time step scheme[4]
to update the short-range interactions every 1 steps and long-range electrostatics interactions
every 2 steps. The time step of integration was chosen to be 2 fs for all simulations.In this
step consisted of 5.0 ns of simulation, no atoms were constrained.



Bibliography:
{1} Jorgensen, W. L., Chandrasekhar, J., Madura, J. D., Impey, R. W. and Klein, M. L.,
"Comparison of simple potential functions for simulating liquid water", J. Chem. Phys., 1983,
vol 79, 6127-6129.

{2} Humphrey, W., Dalke, A. and Schulten, K., "VMD - Visual Molecular Dynamics", J. Molec.
Graphics, 1996, vol. 14, pp. 33-38.

{3} Ribeiro, J. V., Bernardi, R. C., Rudack, T., Stone, J. E., Phillips J. C., Freddolino P. L.
and Schulten, K.,"QwikMD-integrative molecular dynamics toolkit for novices and experts", Sci.
Rep., 2016

{4} Phillips J. C., Braun, R. , Wang, W., Gumbart, J. , Tajkhorshid, E., Villa, E. , Chipot,
C. , Skeel, R. D., Kale, L., and Schulten, K., "Scalable molecular dynamics with NAMD", J.
Comp. Chem, 2005, vol 26, pp. 1781-1802
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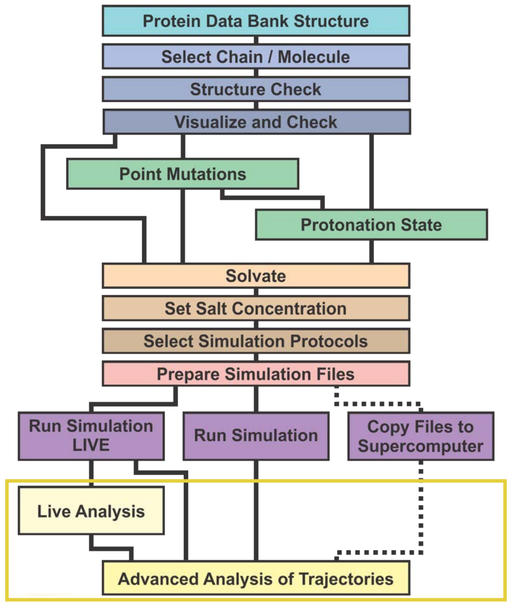
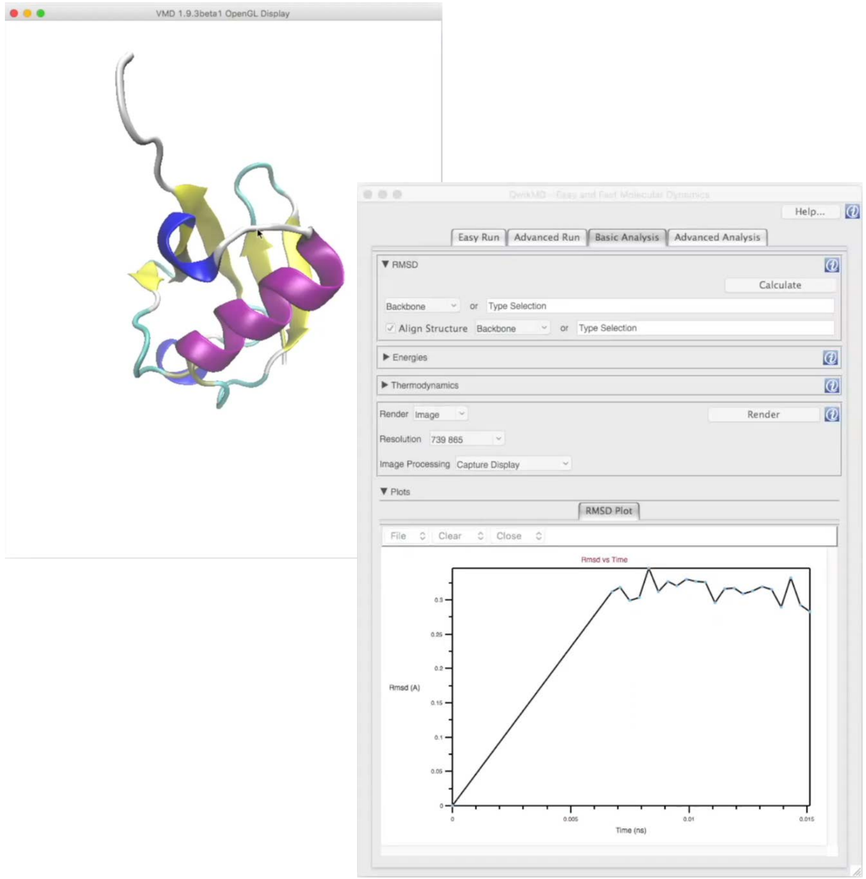
Load Simulation Trajectories and Analysis



Live Simulation and After Load Analysis



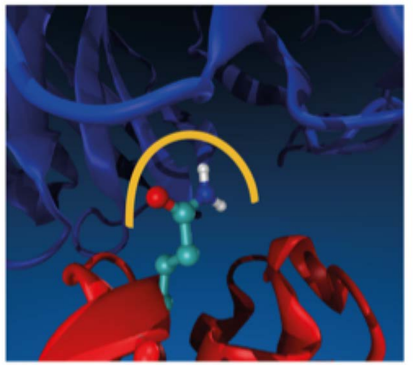
Analyses Available:

- Energies
- Temperature, Pressure and Volume
- RMSD
- Hydrogen Bonds
- SASA
- **Contact Area**
- QM Energies

Contact Area

First Implemented in CompASM as Hot Spots Filter

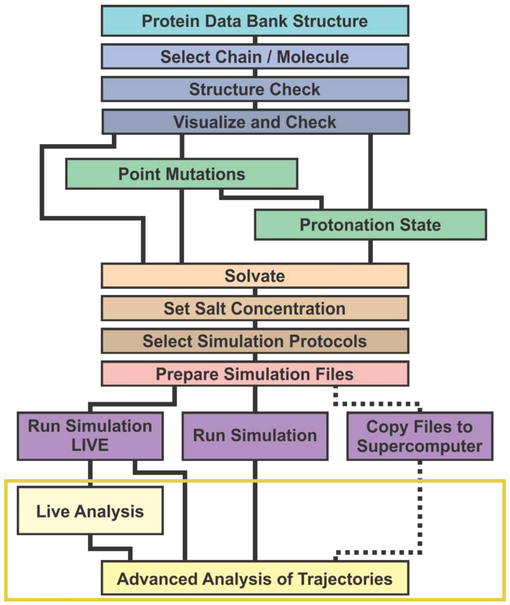
Ligand SASA *subtracted* Ligand SASA in the presence of the Receptor



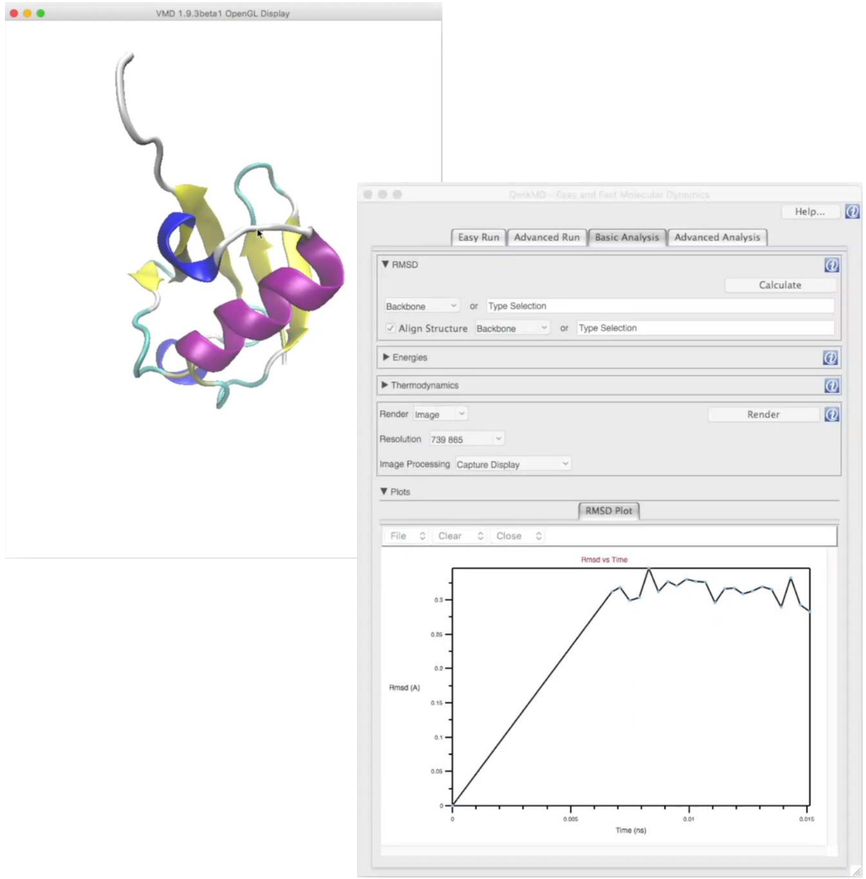
Ligand Exposed/Contact Surface Area

Load Simulation Trajectories and Analysis

Dr. Rafael Bernardi



Live Simulation and After Load Analysis



Contact Area

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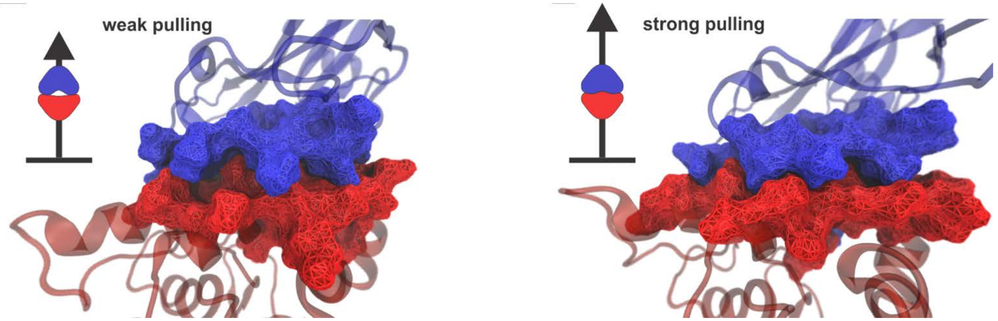

Schoeler C., *et al.*,Ultrastable cellulosome-adhesion complex tightens under load*, Nat. Commun.,* **2014**, 6, 5635.

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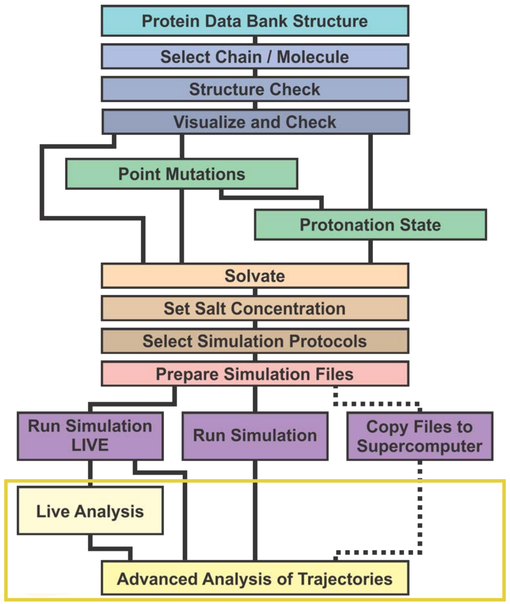
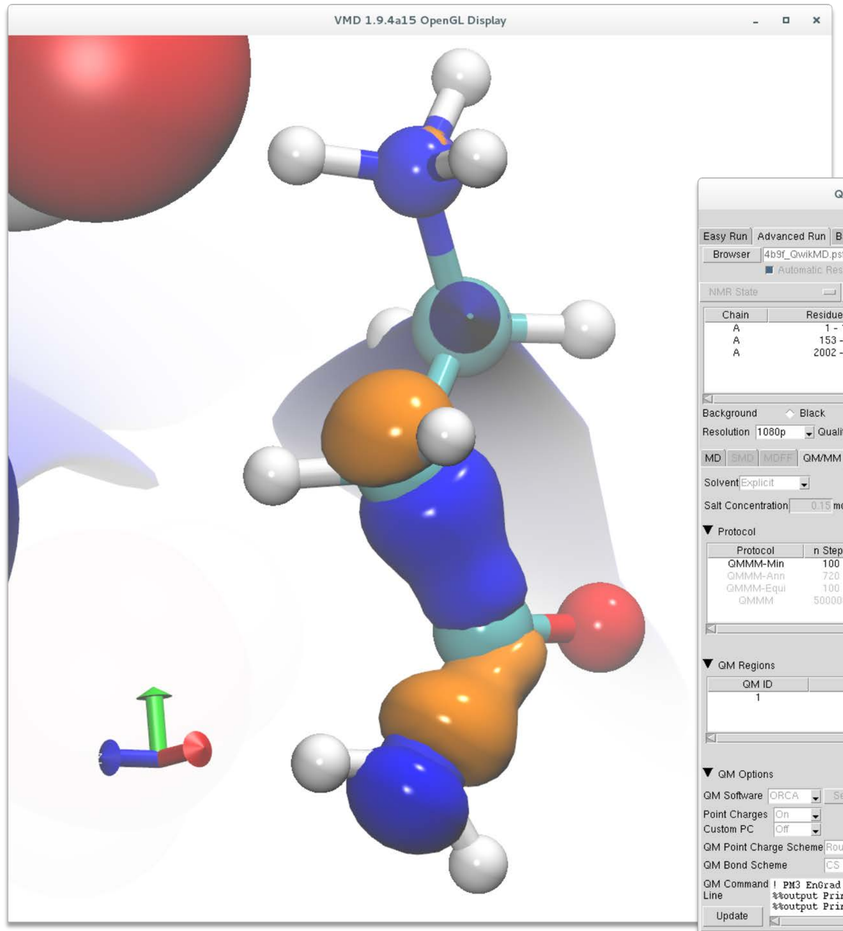
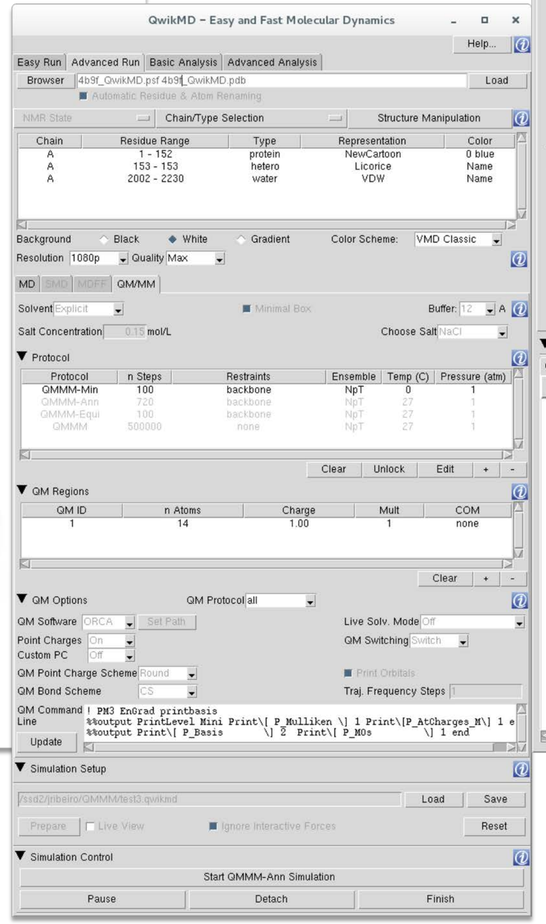


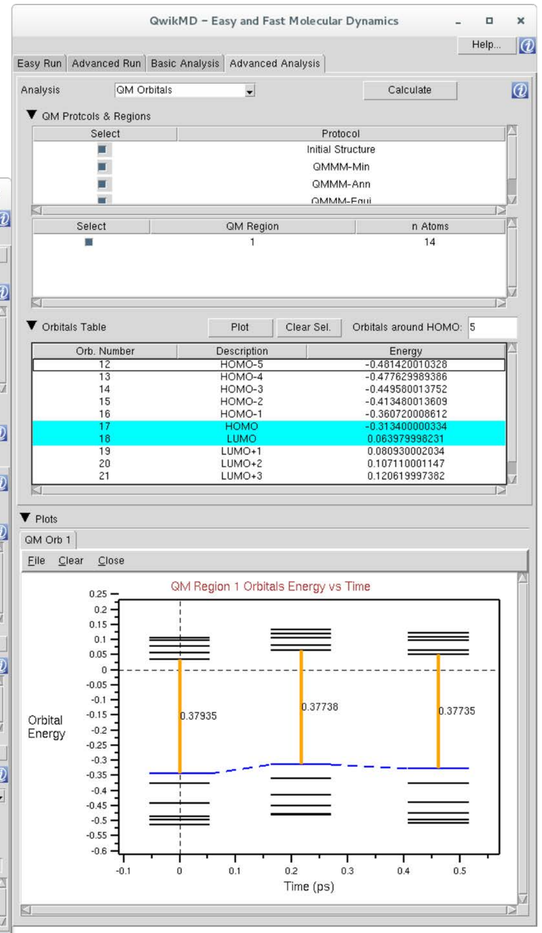
New QM/MM Simulation and Orbitals Visualization

Analyses Available:

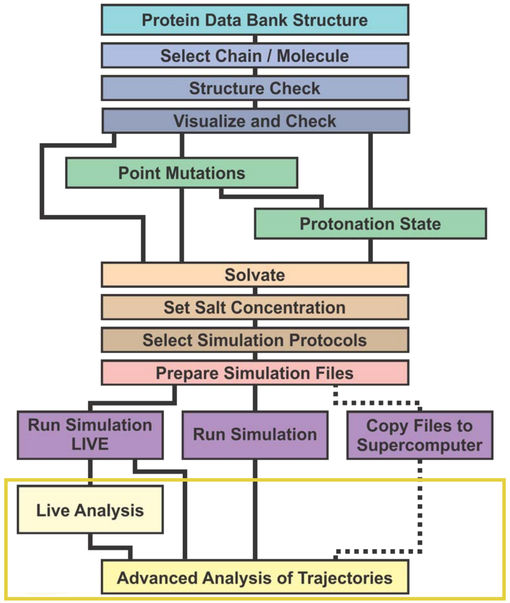
- Energies
- Temperature, Pressure and Volume
- RMSD
- Hydrogen Bonds
- SASA
- Contact Area
- QM Energies
- **QM Orbitals Visualization**
- **Nature Methods 2018**







New QM/MM Simulation and Orbitals Visualization



Analyses Available:

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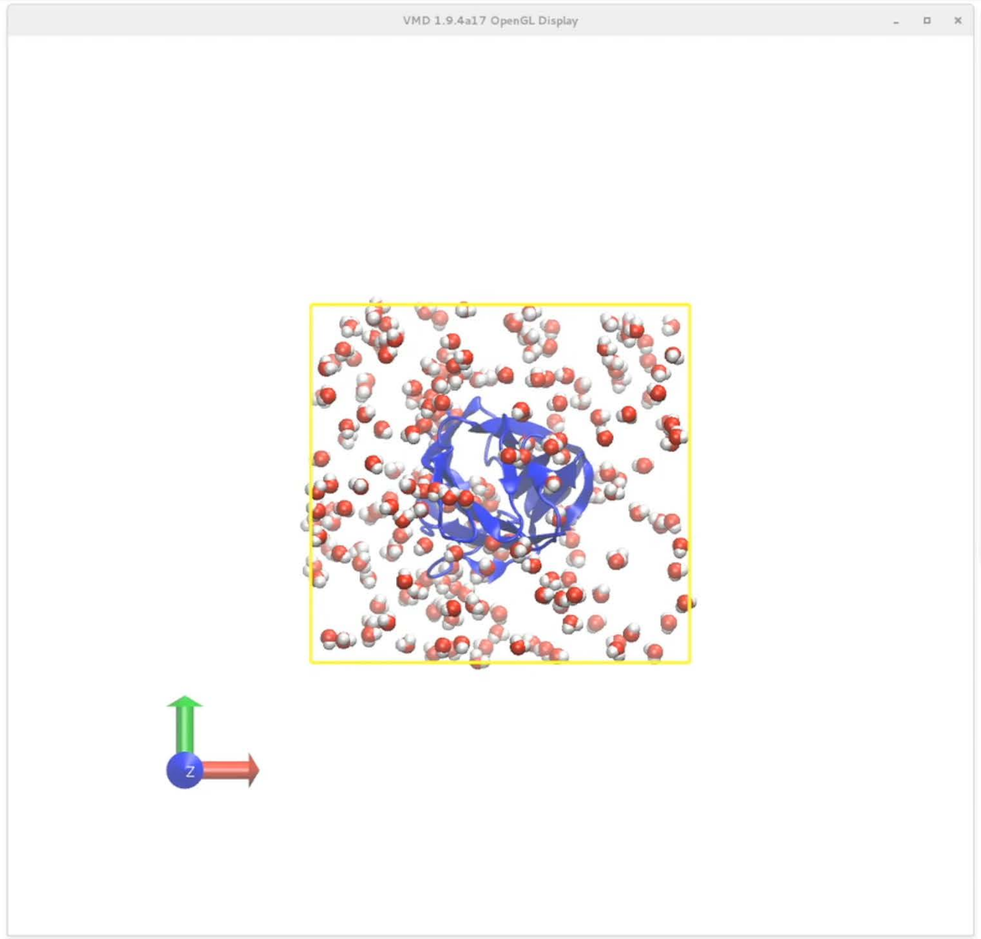
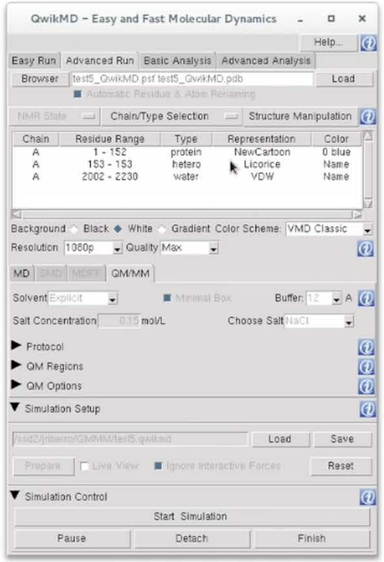
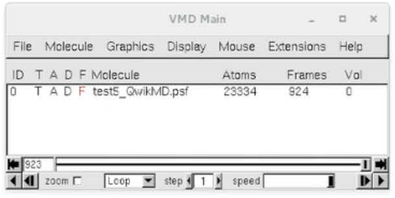
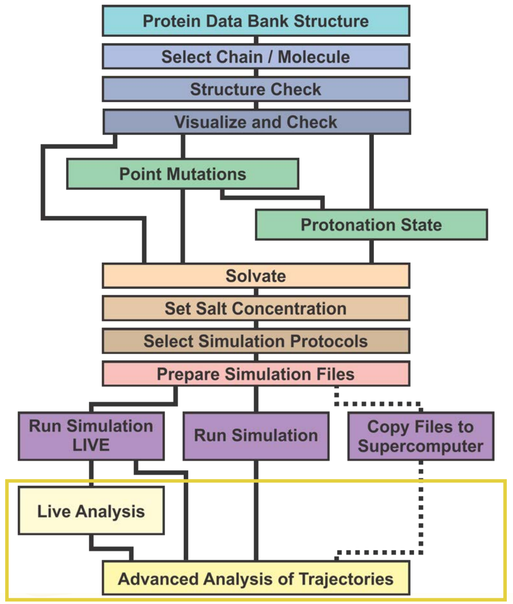
- Contact Area
- QM Energies
- **QM Orbitals Visualization**
- **Nature Methods 2018**



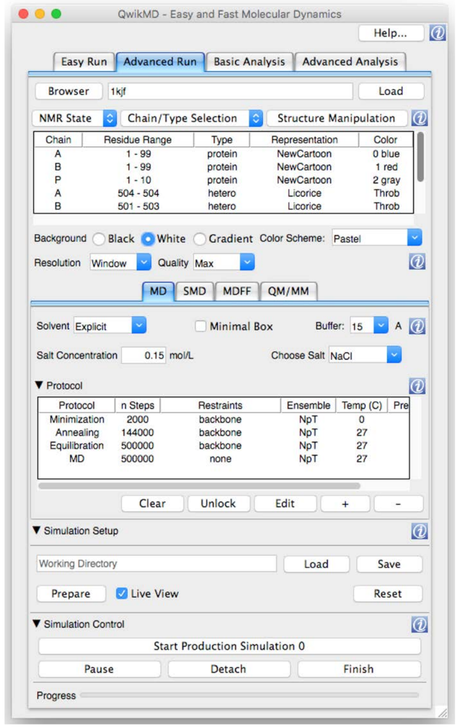




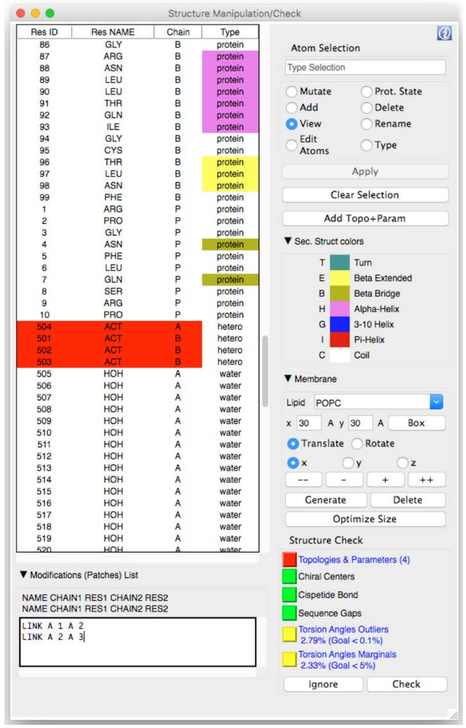


QwikMD Graphical User Interface

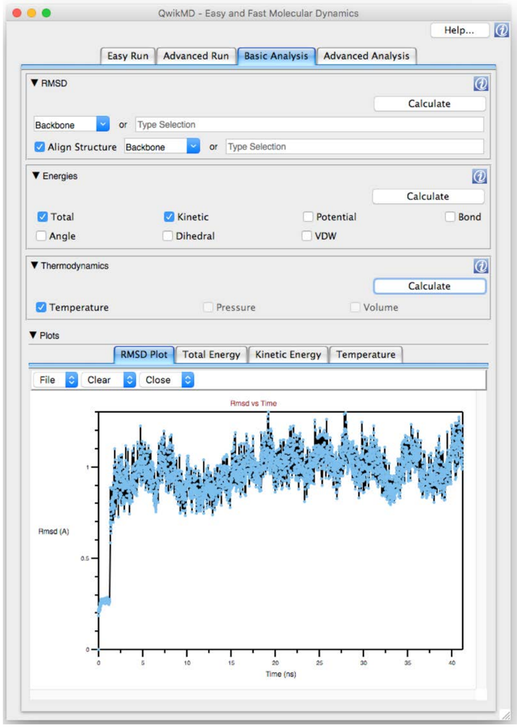
Simulation Preparation



Struct. Manipulation



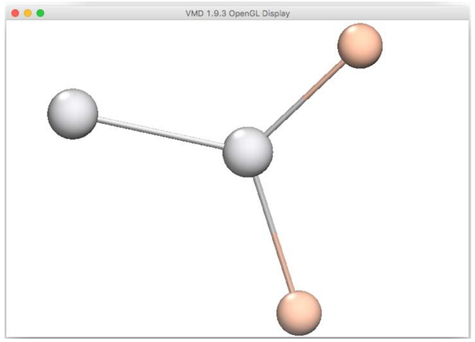
Simulation Analysis

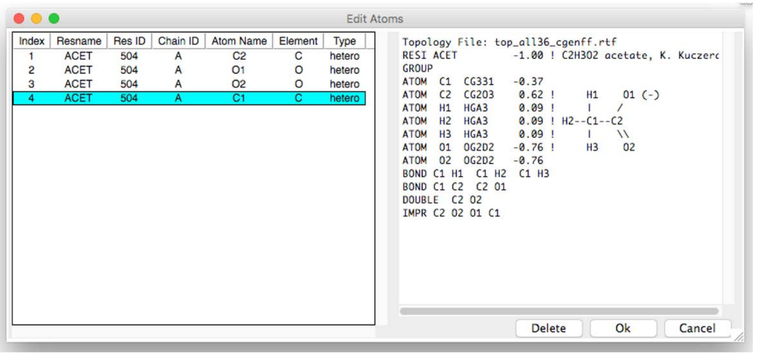


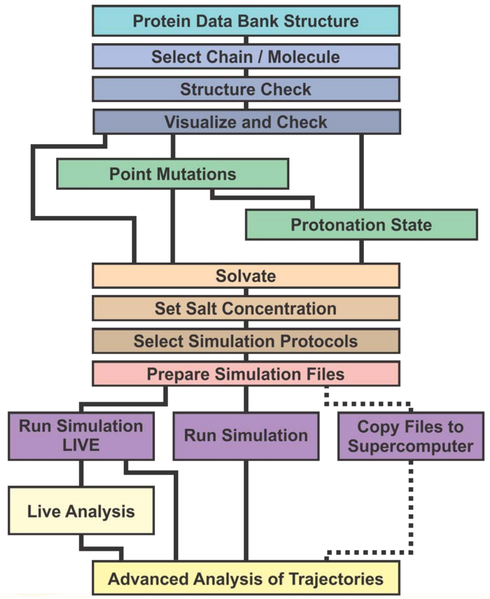
Other Features:

- Info Buttons
- Simulation Controls

Atom Editing







QwikMD Papers

QwikMD:

- Scientific Reports
- BPS 2016
- BPS 2017
- **BPS 2018 (February)**

[Ribeiro, J. V, et al., QwikMD — Integrative Molecular Dynamics Toolkit for Novices and Experts. Scientific Reports, 2016, 6, 26536.]

www.nature.com/scientificreports

SCIENTIFIC REPORTS

OPEN

QwikMD—Integrative
Dynamics Toolkit for N
Experts

Received: 10 March 2016
Accepted: 03 May 2016
Published: 24 May 2016

João V. Ribeiro[1,2,*], Rafael C. Bernardi[1,2,*], Till Rudack[1,*], Jo
Peter L. Freddolino[3] & Klaus Schulten[1,2,4]

The proper functioning of biomolecules in living cells requires th
and to undergo conformational changes. Both biomolecular stru
using a wide variety of techniques, but none offers the level of d
simulations. Integrating two widely used modeling programs, n
created a robust, user-friendly software, QwikMD, which enable
biomedically relevant questions, where often only molecular dy
answers. Performing both simple and advanced MD simulations
as many steps as necessary for preparing, carrying out, and anal
common errors and enabling reproducibility. QwikMD meets als
increasing the efficiency and quality of their work by carrying ou
enabling easy control of every step. Whether carrying out simula
a small laptop or performing complex and large simulations on s
QwikMD uses the same steps and user interface. QwikMD is free
personal computers. It is also available on the cloud at Amazon V

[Melo, M. C. R., *et al.*, NAMD goes quantum: an integrative suite for hybrid simulations. Nature Methods. 2018, 15:5]

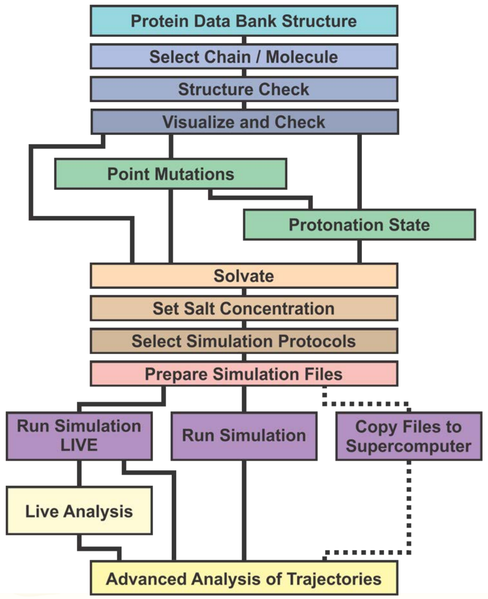
BRIEF COMMUNICATIONS

NAMD goes quantum: an integrative suite for hybrid simulations

Marcelo C R Melo[1,2,13], Rafael C Bernardi[1,13], Till Rudack[1,3], Maximilian Scheurer[4,5], Christoph Riplinger[6], James C Phillips[1], Julio D C Maia[7], Gerd B Rocha[8], João V Ribeiro[1], John E Stone[1], Frank Neese[9], Klaus Schulten[1,10,12] & Zaida Luthey-Schulten[1,2,10,11]

comprehensive, customizable, easy-to-use set of features to make such tools broadly attractive to chemists, structural biologists, and material engineers.

NAMD[9] is a widely used software package for molecular dynamics (MD) simulations, particularly for large biomolecular systems, using supercomputers. NAMD's scalability and large array of enhanced sampling and free energy methods[10], as well as its seamless integration with VMD[11], which provides extended setup, visualization, and analysis capabilities, make it an invaluable tool for exploring complex biological systems. Here we present a comprehensive QM–MM suite implemented in NAMD, to provide a broad range of QM–MM methods, and in VMD, for easy setup, visualization, and analysis through the graphical user interface QwikMD[12]. In NAMD, the QM–MM interface supports the simulation of many independent QM regions and smooth integration with a collection



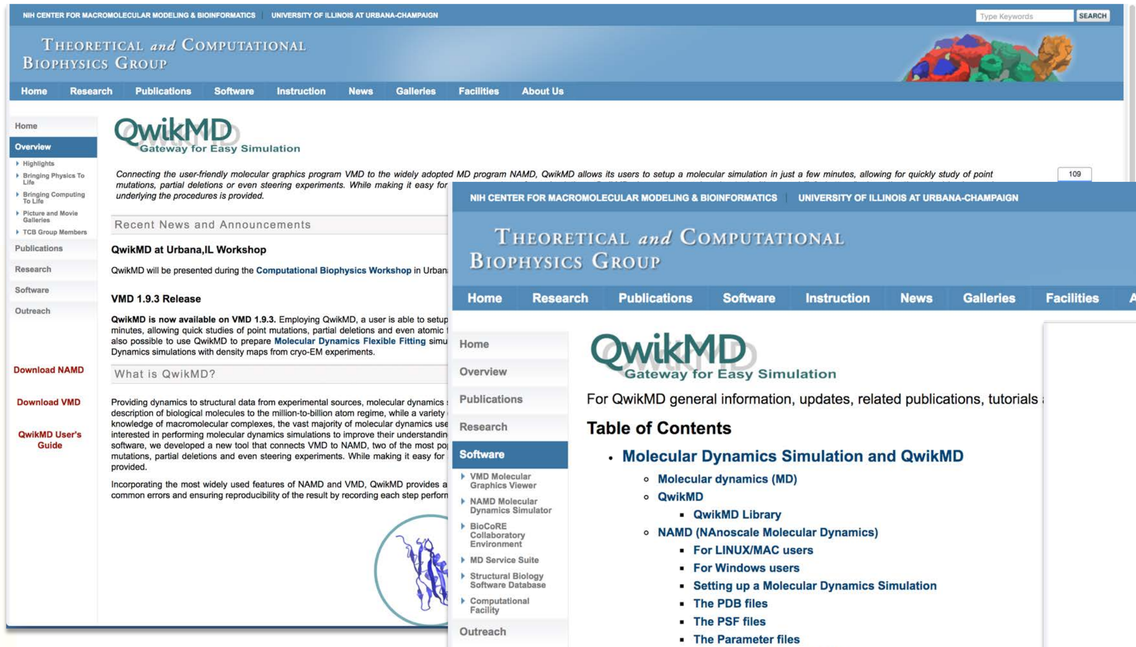
Dissemination, Documentation and User Support

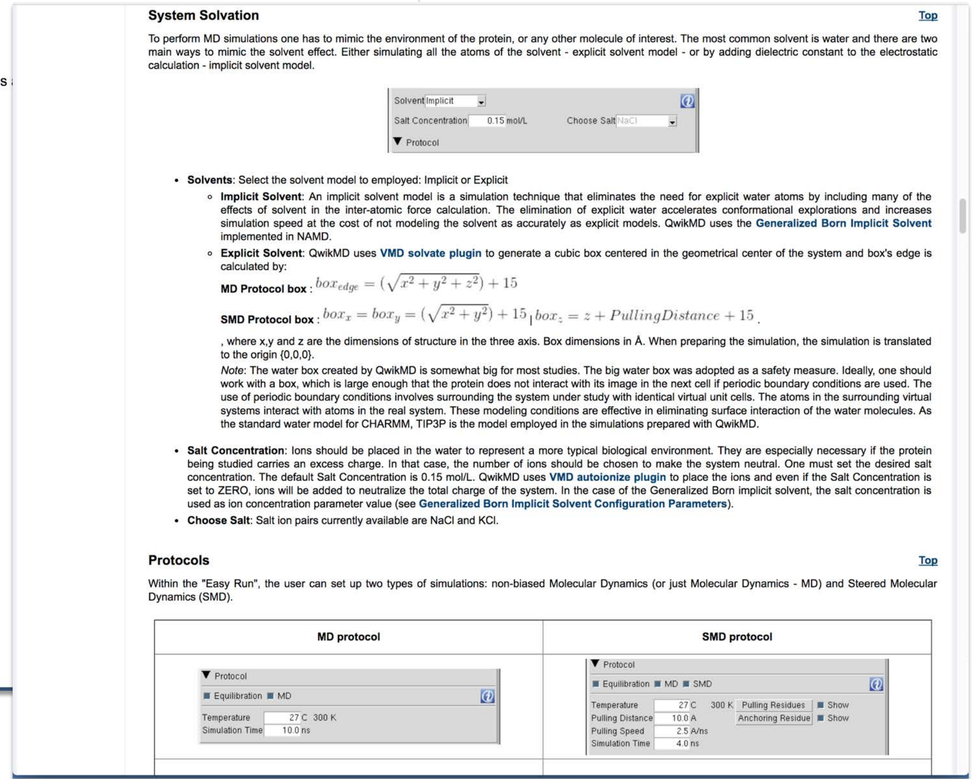
www.ks.uiuc.edu/Research/qwikmd

User's Guide

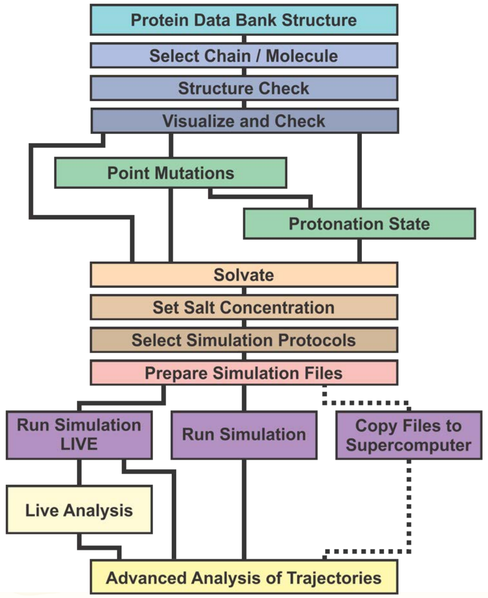
Webpages:

- Home page
- User's Guide Page





Dissemination, Documentation and User Support



Webpages:

- Home page
- User's Guide Page
- QwikMD Bug Report
- VMD Mailing List
- NAMD Mailing List

[Bug Report Form](#)

vmd-l@ks.uiuc.edu

namd-l@ks.uiuc.edu

QwikMD Bugs Report

*Obrigatório

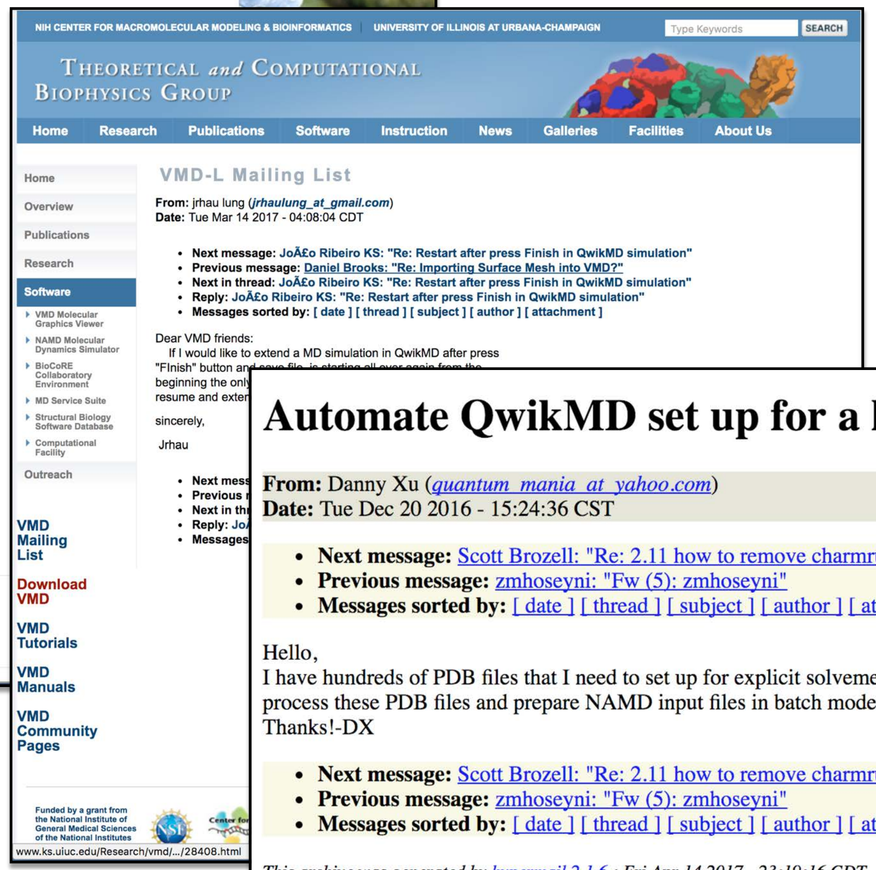
Author *
Your name
A sua resposta

Email
A sua resposta

Priority *
Urgent
Not Urgent
Suggestion

General description *
A sua resposta

Steps to reproduce Bug *
A sua resposta



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Type Keywords SEARCH

THEORETICAL and COMPUTATIONAL BIOPHYSICS GROUP

Home | Research | Publications | Software | Instruction | News | Galleries | Facilities | About Us

Home
Overview
Publications
Research
Software
- VMD Molecular Graphics Viewer
- NAMD Molecular Dynamics Simulator
- BioCoRE Collaboratory Environment
- MD Service Suite
- Structural Biology Software Database
- Computational Facility

Outreach

VMD Mailing List
Download VMD
VMD Tutorials
VMD Manuals
VMD Community Pages

VMD-L Mailing List

From: jrhau lung (*jrhaulung_at_gmail.com*)
Date: Tue Mar 14 2017 - 04:08:04 CDT

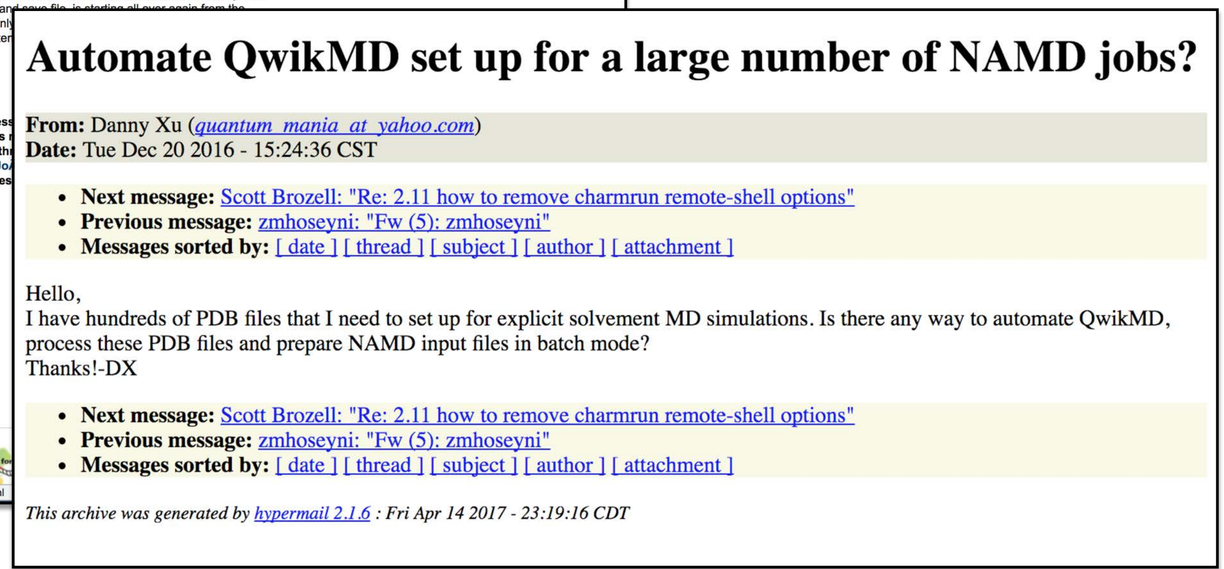
- **Next message:** JoÃ£o Ribeiro KS: "Re: Restart after press Finish in QwikMD simulation"
- **Previous message:** Daniel Brooks: "Re: Importing Surface Mesh into VMD?"
- **Next in thread:** JoÃ£o Ribeiro KS: "Re: Restart after press Finish in QwikMD simulation"
- **Reply:** JoÃ£o Ribeiro KS: "Re: Restart after press Finish in QwikMD simulation"
- **Messages sorted by:** [date] [thread] [subject] [author] [attachment]

Dear VMD friends:
If I would like to extend a MD simulation in QwikMD after press "FInish" button and save file, is starting all over again from the beginning the only
resume and exter
sincerely,
Jrhau

- Next mess
- Previous
- Next in th
- Reply: Jo
- Messages

Funded by a grant from the National Institute of General Medical Sciences of the National Institutes

www.ks.uiuc.edu/Research/vmd/.../28408.html



Automate QwikMD set up for a large number of NAMD jobs?

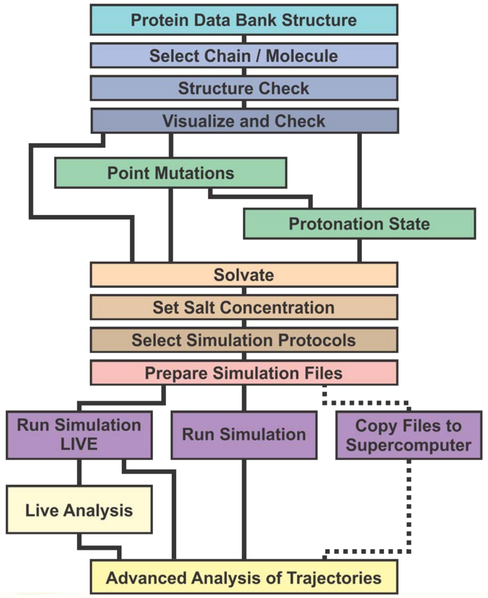
From: Danny Xu (*quantum_mania_at_yahoo.com*)
Date: Tue Dec 20 2016 - 15:24:36 CST

- **Next message:** Scott Brozell: "Re: 2.11 how to remove charmrun remote-shell options"
- **Previous message:** zmhoseyni: "Fw (5): zmhoseyni"
- **Messages sorted by:** [date] [thread] [subject] [author] [attachment]

Hello,
I have hundreds of PDB files that I need to set up for explicit solvement MD simulations. Is there any way to automate QwikMD, process these PDB files and prepare NAMD input files in batch mode?
Thanks!-DX

- **Next message:** Scott Brozell: "Re: 2.11 how to remove charmrun remote-shell options"
- **Previous message:** zmhoseyni: "Fw (5): zmhoseyni"
- **Messages sorted by:** [date] [thread] [subject] [author] [attachment]

This archive was generated by hypermail 2.1.6 : Fri Apr 14 2017 - 23:19:16 CDT



QwikMD beta Version – Latest Developments

www.ks.uiuc.edu/Research/qwikmd

QwikMD beta:

- Latest Implementations
- Bug Fixes
- Available Before VMD Release

Availability

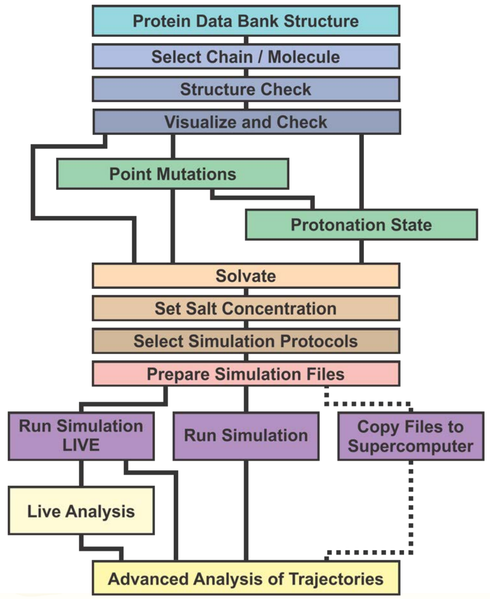
QwikMD is available free of charge on VMD 1.9.3 and newer.

Download VMD for free here

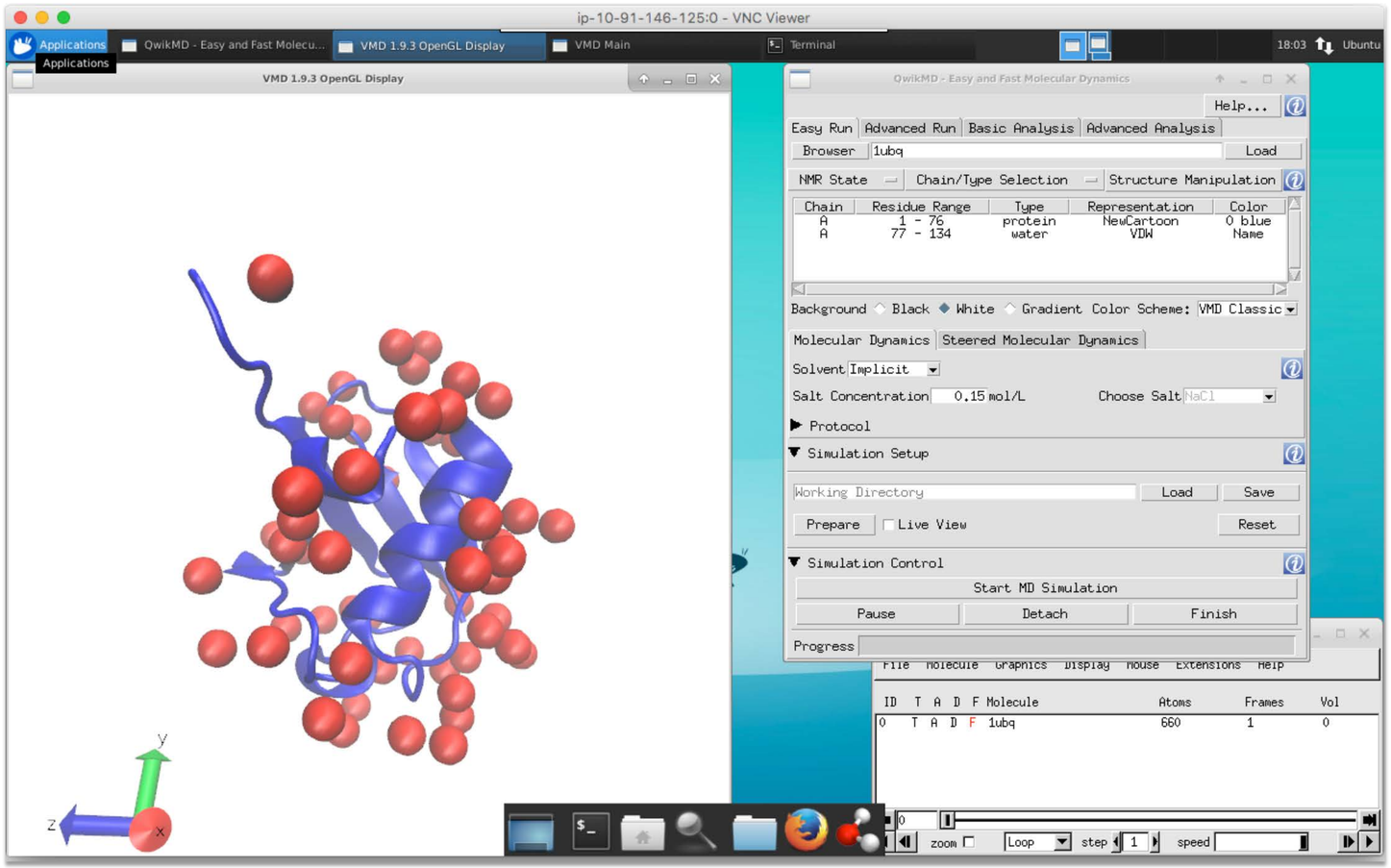
To perform Molecular Dynamics simulations you will also need the widely employed **NAMD** program, which is available free of charge **here**.

QwikMD beta. The latest version of the QwikMD including the most recent bug fixes can be downloaded **here** **(last update on April 20, 2018)**. Please follow the instructions in the **README** file included in the qwikmd folder on how to install the beta version.

Employing QwikMD on your research? Please don't forget to cite us: *J.V. Ribeiro, R.C. Bernardi, T. Rudack, J.E. Stone, J.C. Phillips, P.L. Freddolino, K. Schulten;* **QwikMD: Integrative Molecular Dynamics Toolkit for Novices and Experts;** Scientific Reports, 6, 26536 **(2016)**



QwikMD on the Amazon Cloud

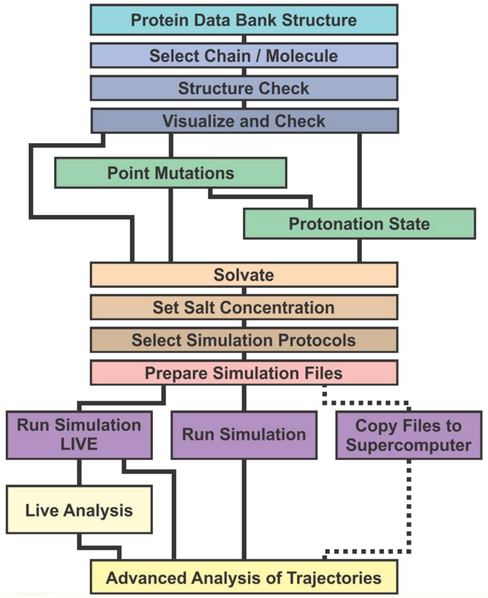


Amazon Web Services:

- Virtual Machine
- VMD & NAMD
- QwikMD and MDFF
- Used in the Center's Workshops

- http://www.ks.uiuc.edu/Training/Workshop/Urbana2017a/
- http://www.ks.uiuc.edu/Training/Workshop/Urbana2018
- http://www.ks.uiuc.edu/Research/cloud/

amazon web services™



Training others...

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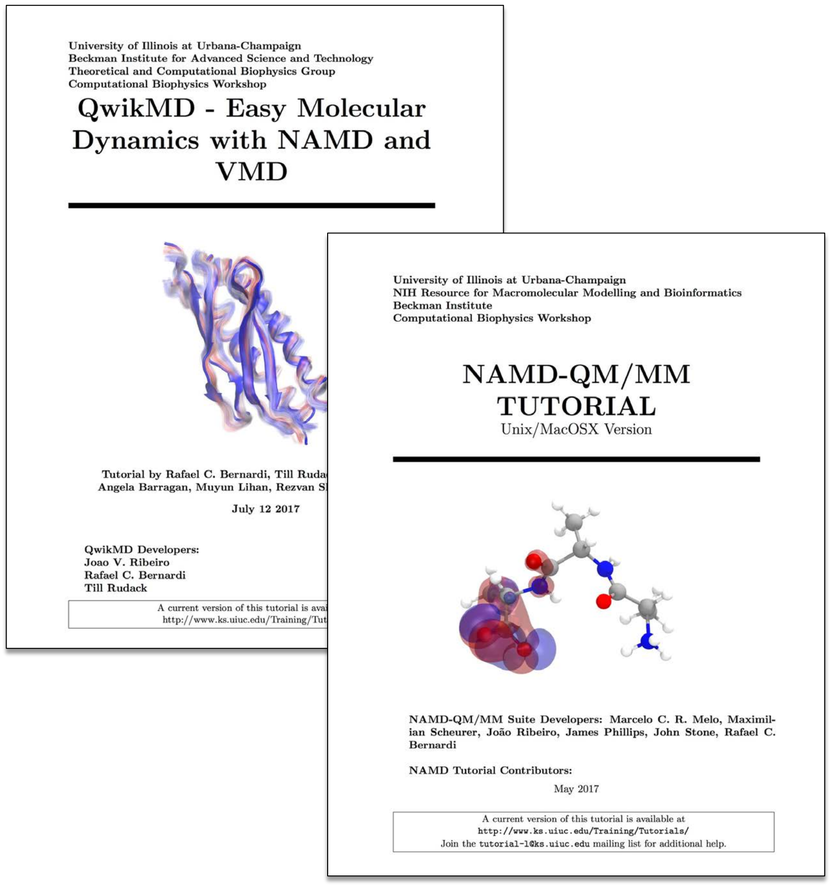
- NAMD Mailing List

QwikMD Tutorials



University of Illinois at Urbana-Champaign
Beckman Institute for Advanced Science and Technology
Theoretical and Computational Biophysics Group
Computational Biophysics Workshop

QwikMD - Easy Molecular Dynamics with NAMD and VMD

Tutorial by Rafael C. Bernardi, Till Ruda
Angela Barragan, Muyun Lihan, Rezvan S

July 12 2017

QwikMD Developers:
Joao V. Ribeiro
Rafael C. Bernardi
Till Rudack

A current version of this tutorial is ava
http://www.ks.uiuc.edu/Training/Tut

University of Illinois at Urbana-Champaign
NIH Resource for Macromolecular Modelling and Bioinformatics
Beckman Institute
Computational Biophysics Workshop

NAMD-QM/MM TUTORIAL
Unix/MacOSX Version

NAMD-QM/MM Suite Developers: Marcelo C. R. Melo, Maximilian Scheurer, João Ribeiro, James Phillips, John Stone, Rafael C. Bernardi

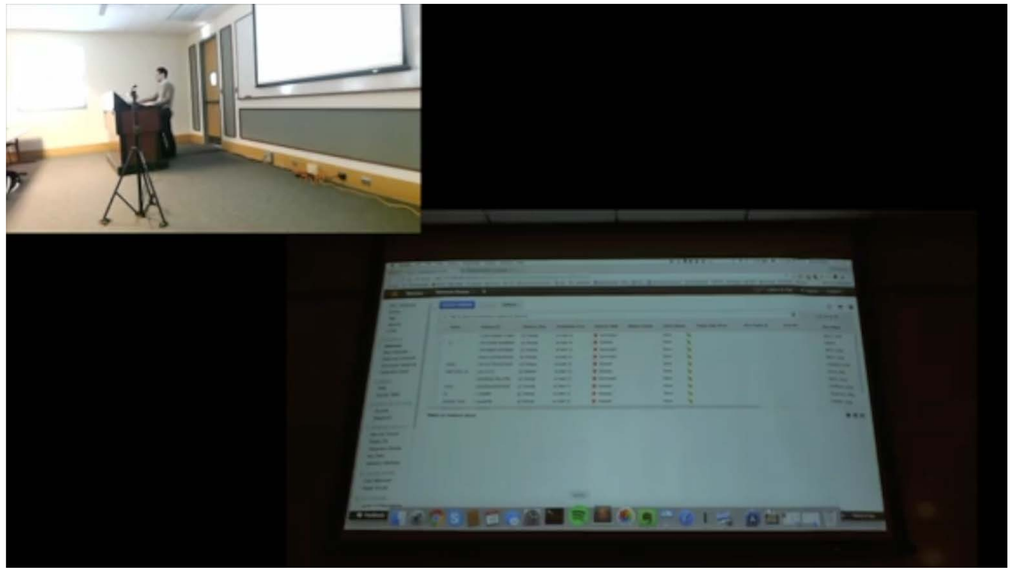
NAMD Tutorial Contributors:

May 2017

A current version of this tutorial is available at
http://www.ks.uiuc.edu/Training/Tutorials/
Join the tutorial-l@ks.uiuc.edu mailing list for additional help.

QwikMD on Amazon

Workshop Live-Streamed on Facebook



https://www.youtube.com/user/tcbguiuc