MD Simulations with NAMD and VMD

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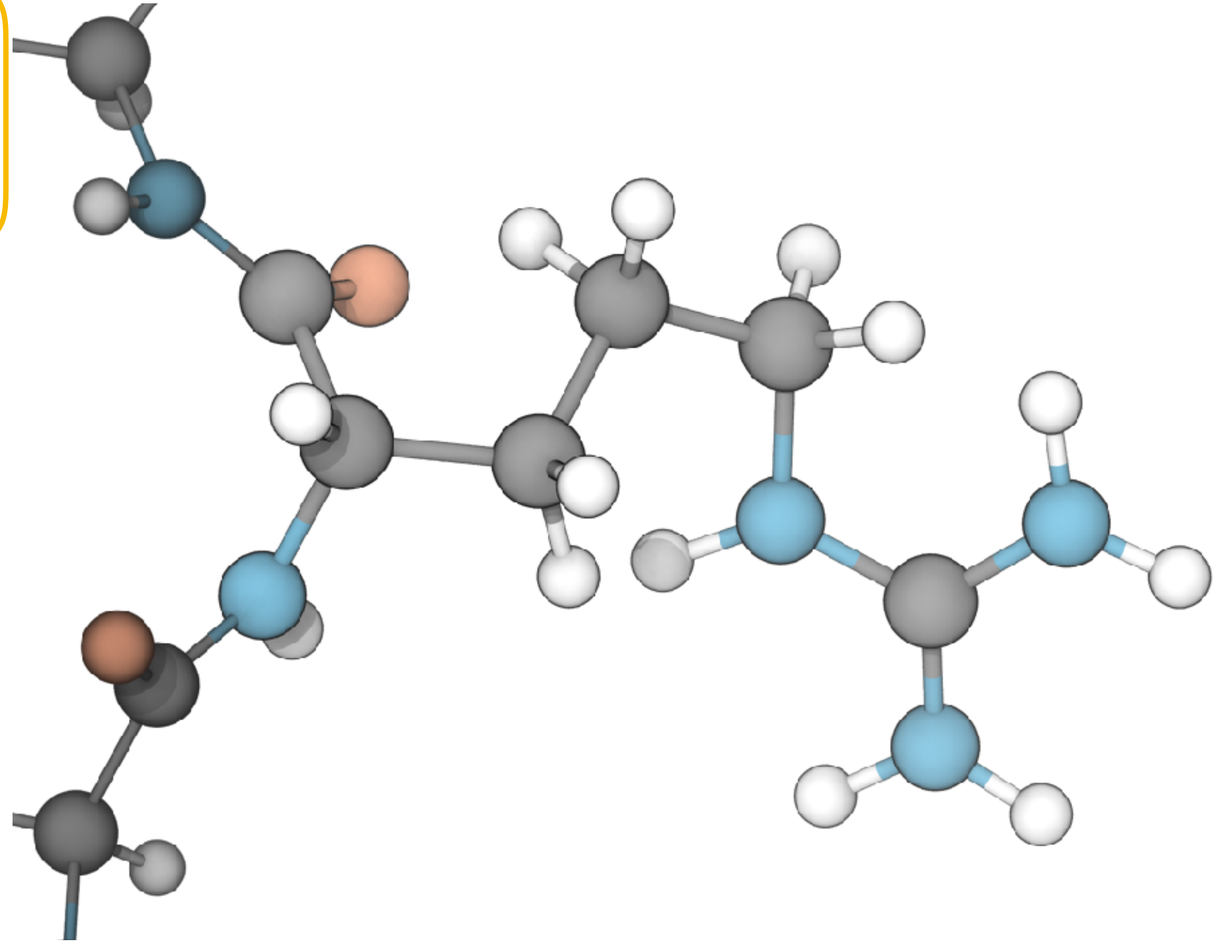
Pittsburgh, PA

Overview

- Simulation Preparation
- The PDB and PSF files
- Solvate the System
- Simulation Environment
- Configure and Execute NAMD
- Load and Analyze Simulations in VMD
- Integrative Molecular Modeling with VMD and NAMD

What do we need to run a Simulation?

- Coordinates
  - X-Ray or NMR, Homology Modeling (Rosetta or Modeller), Cryo-EM,…
- Structure Topology
  - Atoms Types
  - Bonds, Angles, Dihedrals and Improper Angles
- Description the Atoms' Interaction
  - Bonds, Angles, Dihedrals and Improper Angles Force Constants
  - Non-Bonded Terms



Initial Structure

https://www.rcsb.org/

1ubq.pdb

- Experimental Information
- Sequence Annotations
- Rich Source of Information + Paper

```
HEADER    CHROMOSOMAL PROTEIN                     02-JAN-87   1UBQ
TITLE     STRUCTURE OF UBIQUITIN REFINED AT 1.8 ANGSTROMS RESOLUTION
COMPND    MOL_ID: 1;
COMPND   2 MOLECULE: UBIQUITIN;
COMPND   3 CHAIN: A;
COMPND   4 ENGINEERED: YES
SOURCE    MOL_ID: 1;
SOURCE   2 ORGANISM_SCIENTIFIC: HOMO SAPIENS;
SOURCE   3 ORGANISM_COMMON: HUMAN;
SOURCE   4 ORGANISM_TAXID: 9606
KEYWDS    CHROMOSOMAL PROTEIN
EXPDTA    X-RAY DIFFRACTION
AUTHOR    S.VIJAY-KUMAR,C.E.BUGG,W.J.COOK
REVDAT   5   09-MAR-11 1UBQ    1       REMARK
REVDAT   4   24-FEB-09 1UBQ    1       VERSN
REVDAT   3   01-APR-03 1UBQ    1       JRNL
REVDAT   2   16-JUL-87 1UBQ    1       JRNL   REMARK
REVDAT   1   16-APR-87 1UBQ    0
JRNL        AUTH   S.VIJAY-KUMAR,C.E.BUGG,W.J.COOK
JRNL        TITL   STRUCTURE OF UBIQUITIN REFINED AT 1.8 A RESOLUTION.
JRNL        REF    J.MOL.BIOL.                   V. 194   531 1987
JRNL        REFN                      ISSN 0022-2836
JRNL        PMID   3041007
JRNL        DOI    10.1016/0022-2836(87)90679-6
REMARK   1
REMARK   1 REFERENCE 1
REMARK   1  AUTH   S.VIJAY-KUMAR,C.E.BUGG,K.D.WILKINSON,R.D.VIERSTRA,
REMARK   1  AUTH 2 P.M.HATFIELD,W.J.COOK
REMARK   1  TITL   COMPARISON OF THE THREE-DIMENSIONAL STRUCTURES OF HUMAN,
REMARK   1  TITL 2 YEAST, AND OAT UBIQUITIN
REMARK   1  REF    J.BIOL.CHEM.                  V. 262  6396 1987
REMARK   1  REFN                      ISSN 0021-9258
REMARK   1 REFERENCE 2
REMARK   1  AUTH   S.VIJAY-KUMAR,C.E.BUGG,K.D.WILKINSON,W.J.COOK
REMARK   1  TITL   THREE-DIMENSIONAL STRUCTURE OF UBIQUITIN AT 2.8 ANGSTROMS
```

Initial Structure - 1ubq.pdb

- No Hydrogen Atoms
- Crystallographic Water Molecules and Ions
- Other Molecules
- Missing residues (Possible Sequence Gaps) - Homology Modeling
- Poorly Defined Atom's Position - MDFF or Fix Chiral Centers

```
ATOM    562  CD1 LEU A  71      35.003  35.084  20.920  1.00 17.51           C
ATOM    563  CD2 LEU A  71      36.533  37.087  20.917  1.00 19.57           C
ATOM    564  N   ARG A  72      34.930  34.384  25.451  1.00 21.47           N
ATOM    565  CA  ARG A  72      35.161  34.174  26.896  1.00 25.83           C
ATOM    566  C   ARG A  72      36.671  34.296  27.089  1.00 27.74           C
ATOM    567  O   ARG A  72      37.305  33.233  26.795  1.00 30.65           O
ATOM    568  CB  ARG A  72      34.717  32.760  27.286  1.00 28.49           C
ATOM    569  CG  ARG A  72      35.752  32.054  28.160  1.00 31.79           C
ATOM    570  CD  ARG A  72      35.612  30.577  28.044  1.00 34.05           C
ATOM    571  NE  ARG A  72      35.040  30.252  26.730  1.00 35.08           N
ATOM    572  CZ  ARG A  72      34.338  29.103  26.650  1.00 34.67           C
ATOM    573  NH1 ARG A  72      34.110  28.437  27.768  1.00 35.02           N
ATOM    574  NH2 ARG A  72      34.014  28.657  25.457  1.00 34.97           N
ATOM    575  N   LEU A  73      37.197  35.397  27.513  0.45 28.93           N
ATOM    576  CA  LEU A  73      38.668  35.502  27.680  0.45 30.76           C

TER     603      GLY A  76
HETATM  604  O   HOH A  77      45.747  30.081  19.708  1.00 12.43           O
HETATM  605  O   HOH A  78      19.168  31.868  17.050  1.00 12.65           O
HETATM  606  O   HOH A  79      32.010  38.387  19.636  1.00 12.83           O
HETATM  607  O   HOH A  80      42.084  27.361  21.953  1.00 22.27           O
HETATM  608  O   HOH A  81      21.314  20.644   8.719  1.00 18.33           O
HETATM  609  O   HOH A  82      31.965  38.637   3.699  1.00 31.69           O
HETATM  610  O   HOH A  83      27.707  15.908   4.653  1.00 20.30           O
HETATM  611  O   HOH A  84      19.969  32.720  14.769  1.00 10.14           O
HETATM  612  O   HOH A  85      29.847  13.577  10.864  1.00 29.65           O
HETATM  613  O   HOH A  86      23.893  27.864   1.501  1.00 23.48           O
HETATM  614  O   HOH A  87      19.638  23.312   4.775  1.00 18.40           O
HETATM  615  O   HOH A  88      34.628  29.369   4.779  1.00 26.17           O
HETATM  616  O   HOH A  89      42.240  24.744  25.707  1.00 31.34           O
HETATM  617  O   HOH A  90      30.290  42.500   8.820  1.00 16.49           O
HETATM  618  O   HOH A  91      24.512  39.162  10.841  1.00 13.14           O
HETATM  619  O   HOH A  92      26.557  43.450  19.940  1.00 19.38           O
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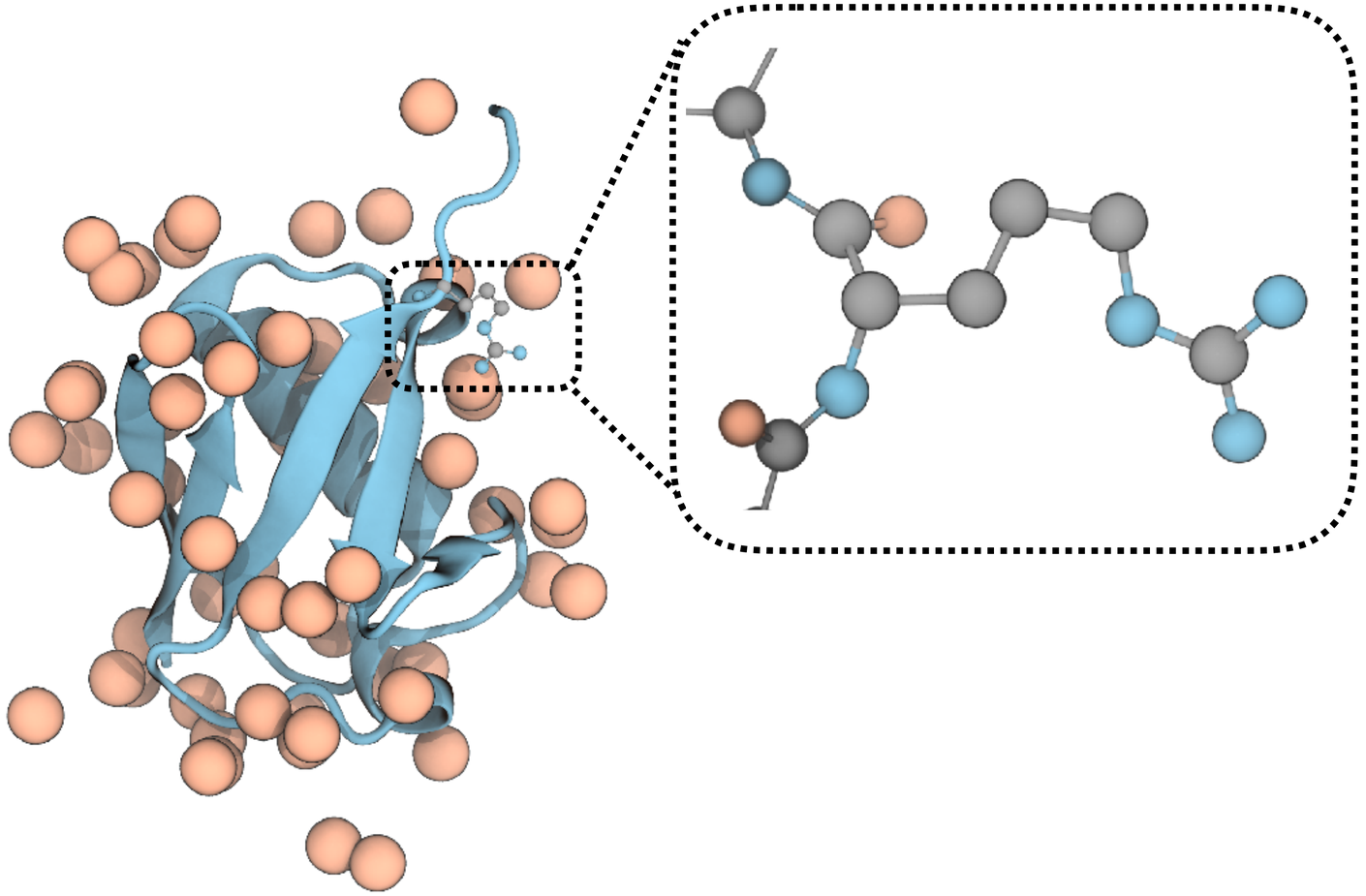
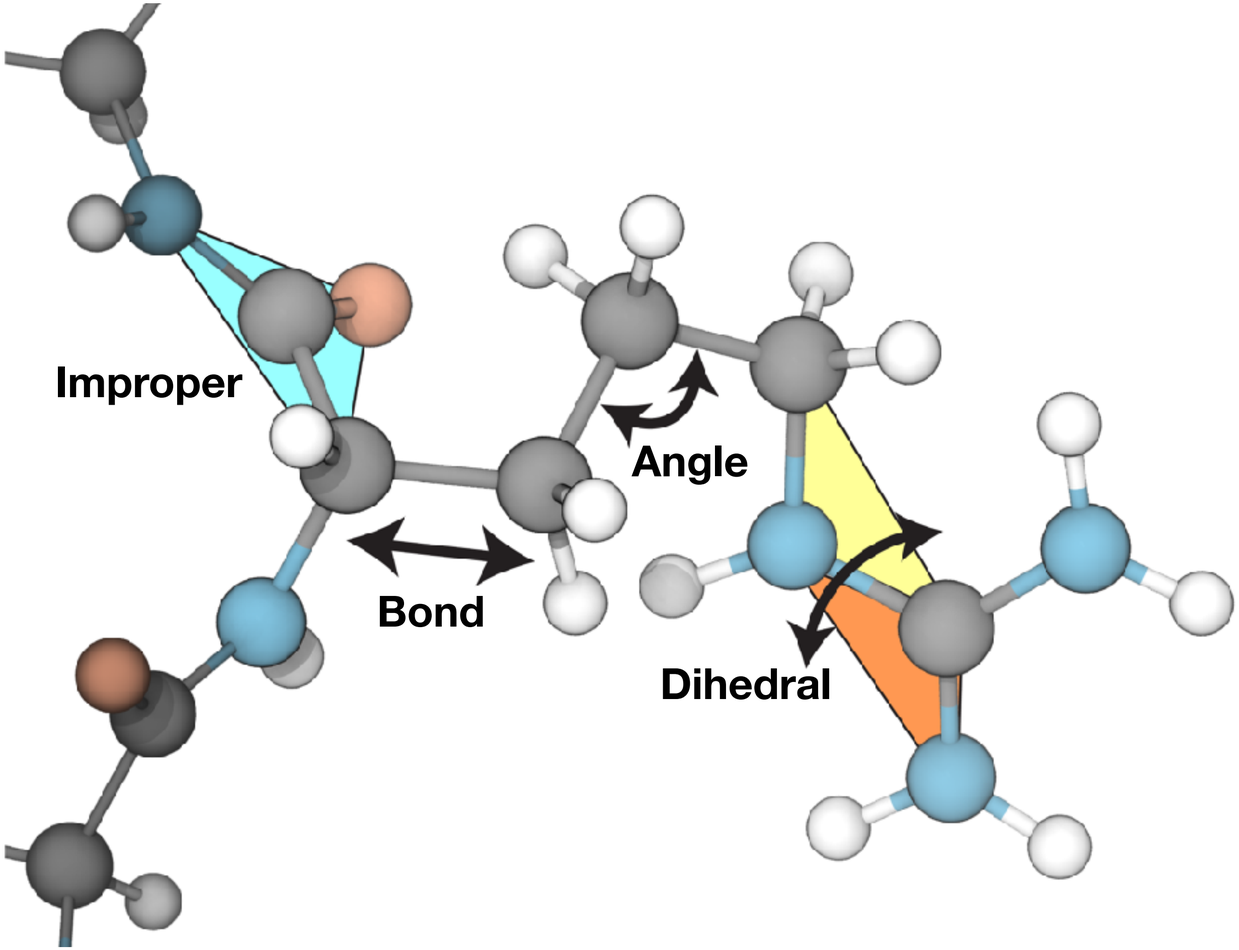


PDB tools list: https://www.rcsb.org/pdb/static.do?p=software/software_links/analysis_and_verification.html
MolProbity: http://molprobity.biochem.duke.edu/
Structure Check Tutorial: https://www.ks.uiuc.edu/Training/Tutorials/#structcheck
ModelMaker VMD plugin: https://www.ks.uiuc.edu/Research/ModelMaker/

What do we need to run a Simulation?

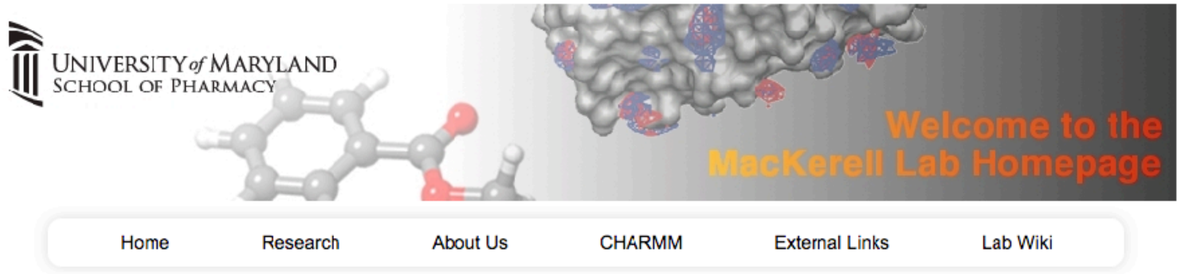
- Coordinates
  - X-Ray or NMR, Homology Modeling (Rosetta or Modeller), Cryo-EM,…
- Structure Topology
  - Atoms Types
  - Bonds, Angles, Dihedrals and Improper Angles
- Mathematical Description the Atoms' Interaction
  - Bonds, Angles, Dihedrals and Improper Angles Force Constants
  - Non-Bonded Terms



CHARMM Force Field

In Short: Mathematical description of the interactions between atoms (bonded and not bonded)

$$V = \sum_{\text{bonds}} k_b \left(b - b_0\right)^2 + \sum_{\text{angles}} k_\theta \left(\theta - \theta_0\right)^2 + \sum_{\text{dihedrals}} k_\phi \left[1 + \cos\left(n\phi - \delta\right)\right]$$
$$+ \sum_{\text{impropers}} k_\omega \left(\omega - \omega_0\right)^2 + \sum_{\text{Urey-Bradley}} k_u \left(u - u_0\right)^2$$
$$+ \sum_{\text{nonbonded}} \epsilon \left[\left(\frac{R_{\min_{ij}}}{r_{ij}}\right)^{12} - \left(\frac{R_{\min_{ij}}}{r_{ij}}\right)^{6}\right] + \frac{q_i q_j}{\epsilon r_{ij}}$$



CHARMM Force Field Files

Quick Links:
CHARMM Additive Force Field Files
CHARMM Drude Force Field Files
CHARMM36 Files for GROMACS
CHARMM36 Files for Anton
References

Force Field File Types:

Residue Topology File (**RTF**)

- Atoms
  - Mass
  - Charges
- Residues
- Patches (Modifications)

Parameter (**PAR**)

- Mathematical Constants

Stream (**STR**)

- Topology
- Parameters

CHARMM Force Field Files:http://mackerell.umaryland.edu/charmm_ff.shtml
Force Field Tutorial:https://www.ks.uiuc.edu/Training/Tutorials/science/forcefield-tutorial/forcefield-html/node5.html

Topology File - CHARMM Force Field

top_all36_prot.rtf - Protein

```
*>>>>>>>>>CHARMM36 All-Hydrogen Topology File for Proteins <<<<<<
*>>>>> Includes phi, psi cross term map (CMAP) correction <<<<<<<
*>>>>>>>>>>>>>>>>>>>>>>>>>>>> May 2011 <<<<<<<<<<<<<<<<<<<<<<<<<<<<
* All comments to the CHARMM web site: www.charmm.org
*             parameter set discussion forum
*
36  1

!references
!
!Robert B. Best, R.B., Xiao Zhu, X., Shim, J., Lopes, P.
!Mittal, J., Feig, M. and MacKerell, A.D., Jr. "Optimization of the
!additive CHARMM all-atom protein force field targeting improved
!sampling of the backbone phi, psi and sidechain chi1 and chi2
!dihedral angles," JCTC, 8: 3257-3273, 2013, PMC3549273

!MacKerell, A.D., Jr., Feig, M. and Brooks, III, C.L. "Improved
!treatment of the protein backbone in empirical force fields," Journal
!of the American Chemical Society, 126: 698-699, 2004
!
!MacKerell, Jr., A. D.; Bashford, D.; Bellott, M.; Dunbrack Jr., R.L.;
!Evanseck, J.D.; Field, M.J.; Fischer, S.; Gao, J.; Guo, H.; Ha, S.;
!Joseph-McCarthy, D.; Kuchnir, L.; Kuczera, K.; Lau, F.T.K.; Mattos,
!C.; Michnick, S.; Ngo, T.; Nguyen, D.T.; Prodhom, B.; Reiher, III,
!W.E.; Roux, B.; Schlenkrich, M.; Smith, J.C.; Stote, R.; Straub, J.;
!Watanabe, M.; Wiorkiewicz-Kuczera, J.; Yin, D.; Karplus, M.  All-atom
!empirical potential for molecular modeling and dynamics Studies of
!proteins.  Journal of Physical Chemistry B, 1998, 102, 3586-3616.
!

MASS  -1  H          1.00800 ! polar H
MASS  -1  HC         1.00800 ! N-ter H
MASS  -1  HA         1.00800 ! nonpolar H
MASS  -1  HP         1.00800 ! aromatic H
MASS  -1  HB1        1.00800 ! backbone H
MASS  -1  HB2        1.00800 ! aliphatic backbone H, to CT2
MASS  -1  HR1        1.00800 ! his he1, (+) his HG,HD2
MASS  -1  HR2        1.00800 ! (+) his HE1
MASS  -1  HR3        1.00800 ! neutral his HG, HD2
MASS  -1  HS         1.00800 ! thiol hydrogen
MASS  -1  HE1        1.00800 ! for alkene; RHC=CR
MASS  -1  HE2        1.00800 ! for alkene; H2C=CR
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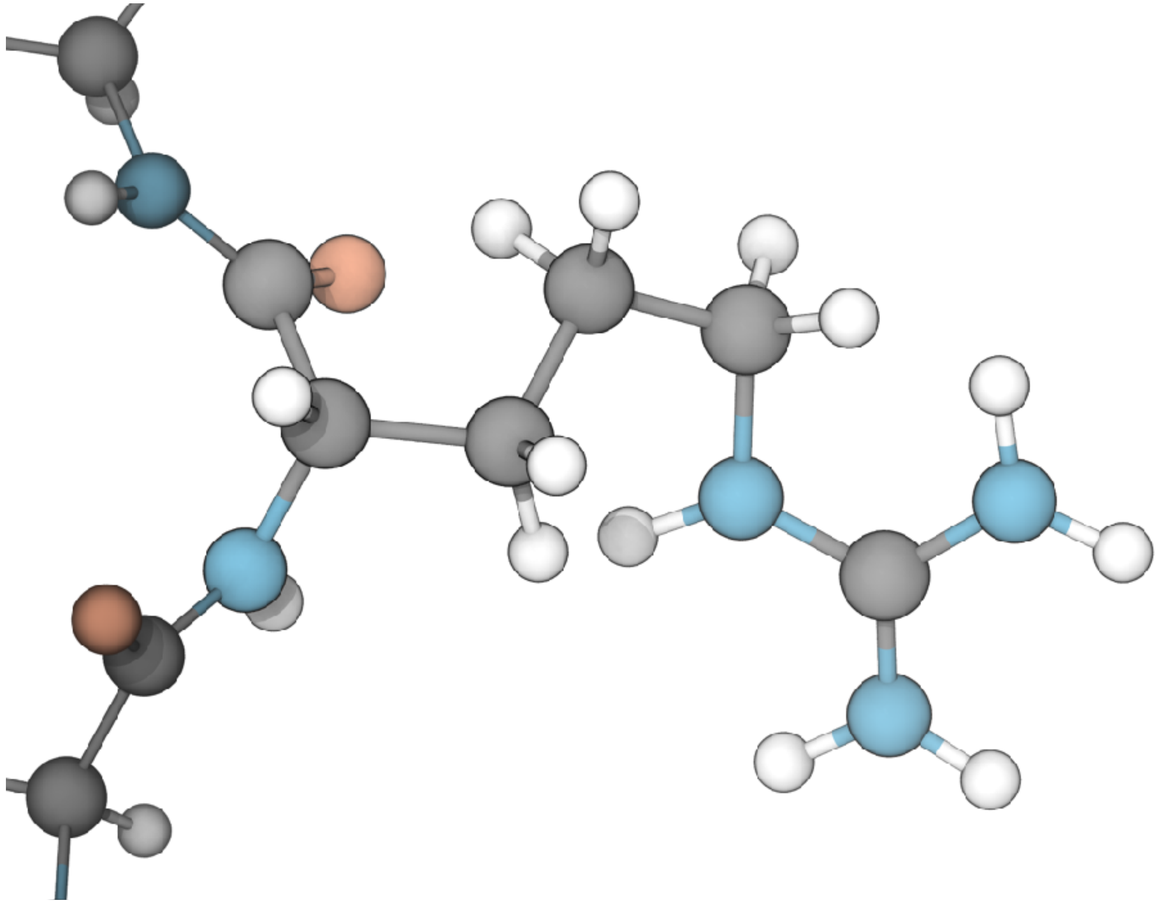


Force Field Tutorial:https://www.ks.uiuc.edu/Training/Tutorials/science/forcefield-tutorial/forcefield-html/node6.html

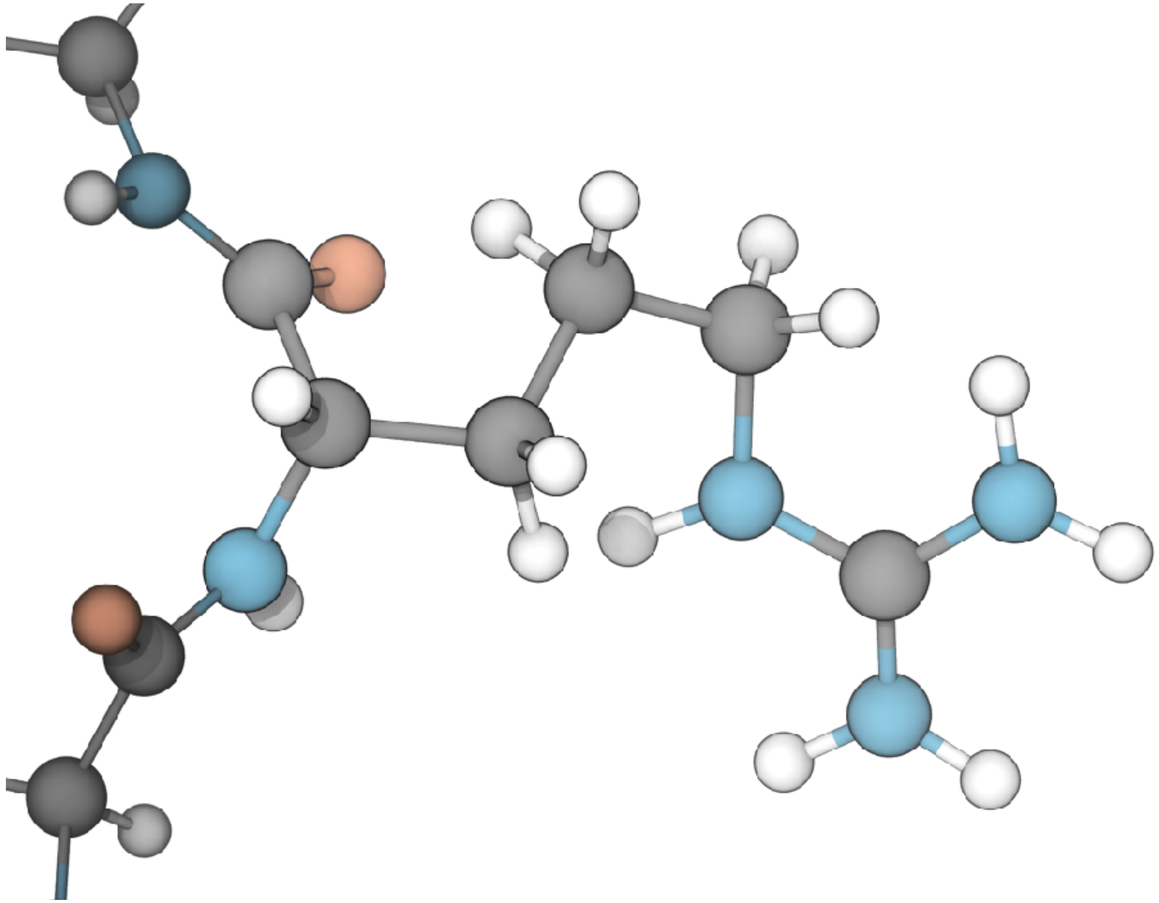
Topology File - CHARMM Force Field

Residue's Name | **Total Charge**

```
RESI ARG          1.00
GROUP
ATOM N    NH1    -0.47  !      |                        HH11
ATOM HN   H       0.31  !  HN-N                          |
ATOM CA   CT1     0.07  !     |    HB1 HG1 HD1 HE      NH1-HH12
ATOM HA   HB1     0.09  !     |    |   |   |   |     //(+)
GROUP                   !  HA-CA--CB--CG--CD--NE--CZ
ATOM CB   CT2    -0.18  !     |    |   |   |          \
ATOM HB1  HA2     0.09  !     |    HB2 HG2 HD2        NH2-HH22
ATOM HB2  HA2     0.09  !   O=C                        |
GROUP                   !     |                       HH21
ATOM CG   CT2    -0.18
ATOM HG1  HA2     0.09
ATOM HG2  HA2     0.09
GROUP
ATOM CD   CT2     0.20
ATOM HD1  HA2     0.09
ATOM HD2  HA2     0.09
ATOM NE   NC2    -0.70
ATOM HE   HC      0.44
ATOM CZ   C       0.64
ATOM NH1  NC2    -0.80
ATOM HH11 HC      0.46
ATOM HH12 HC      0.46
ATOM NH2  NC2    -0.80
ATOM HH21 HC      0.46
ATOM HH22 HC      0.46
GROUP
ATOM C    C       0.51
ATOM O    O      -0.51
```

Atoms' Charge

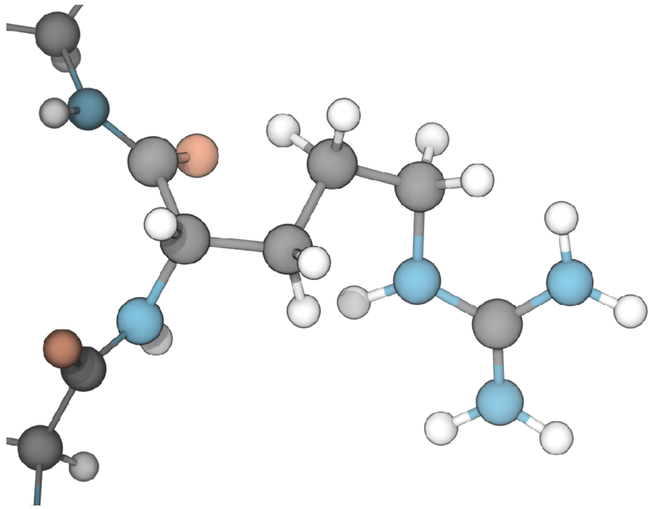
Atoms' Name | **Atoms' Type**



Force Field Tutorial:https://www.ks.uiuc.edu/Training/Tutorials/science/forcefield-tutorial/forcefield-html/node6.html

Topology File - CHARMM Force Field

```
RESI ARG          1.00
GROUP
ATOM N     NH1    -0.47  !      |                          HH11
ATOM HN    H       0.31  !  HN-N                           |
ATOM CA    CT1     0.07  !      |    HB1 HG1 HD1 HE      NH1-HH12
ATOM HA    HB1     0.09  !      |    |   |   |   |     //(+)
GROUP                    !  HA-CA--CB--CG--CD--NE--CZ
ATOM CB    CT2    -0.18  !      |    |   |   |          \
ATOM HB1   HA2     0.09  !      |    HB2 HG2 HD2         NH2-HH22
ATOM HB2   HA2     0.09  !    O=C                          |
GROUP                    !      |                        HH21
ATOM CG    CT2    -0.18
ATOM HG1   HA2     0.09
ATOM HG2   HA2     0.09
GROUP
ATOM CD    CT2     0.20
ATOM HD1   HA2     0.09
ATOM HD2   HA2     0.09
ATOM NE    NC2    -0.70
ATOM HE    HC      0.44
ATOM CZ    C       0.64
ATOM NH1   NC2    -0.80
ATOM HH11  HC      0.46
ATOM HH12  HC      0.46
ATOM NH2   NC2    -0.80
ATOM HH21  HC      0.46
ATOM HH22  HC      0.46
GROUP
ATOM C     C       0.51
ATOM O     O      -0.51
```



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ATOM     562  CD1  LEU A   71
ATOM     563  CD2  LEU A   71
ATOM     564  N    ARG A   72
ATOM     565  CA   ARG A   72
ATOM     566  C    ARG A   72
ATOM     567  O    ARG A   72
ATOM     568  CB   ARG A   72
ATOM     569  CG   ARG A   72
ATOM     570  CD   ARG A   72
ATOM     571  NE   ARG A   72
ATOM     572  CZ   ARG A   72
ATOM     573  NH1  ARG A   72
ATOM     574  NH2  ARG A   72
ATOM     575  N    LEU A   73
ATOM     576  CA   LEU A   73
```

Topology File - CHARMM Force Field

Automatically Assignment of Angles and Dihedrals

```
BOND CB  CA  CG  CB  CD CG  NE CD  CZ NE
BOND NH2 CZ  N  HN  N  CA
BOND C   CA  C  +N  CA HA  CB HB1
BOND CB  HB2 CG  HG1 CG HG2 CD HD1 CD HD2
BOND NE  HE  NH1 HH11  NH1 HH12  NH2 HH21  NH2 HH22
DOUBLE O  C    CZ  NH1
IMPR N  -C  CA  HN   C CA +N O
IMPR CZ  NH1  NH2  NE
IMPR NH1 HH11 HH12 CZ
IMPR NH2 HH21 HH22 CZ
CMAP -C  N  CA  C   N  CA  C  +N
DONOR HN N
DONOR HE NE
DONOR HH11 NH1
DONOR HH12 NH1
DONOR HH21 NH2
DONOR HH22 NH2
ACCEPTOR O C
IC -C   CA   *N   HN    1.3496 122.4500  180.0000 116.6700  0.9973
IC -C   N    CA   C     1.3496 122.4500  180.0000 109.8600  1.5227
IC N    CA   C    +N    1.4544 109.8600  180.0000 117.1200  1.3511
IC +N   CA   *C   O     1.3511 117.1200  180.0000 121.4000  1.2271
IC CA   C    +N   +CA   1.5227 117.1200  180.0000 124.6700  1.4565
IC N    C    *CA  CB    1.4544 109.8600  123.6400 112.2600  1.5552
IC N    C    *CA  HA    1.4544 109.8600 -117.9300 106.6100  1.0836
IC N    CA   CB   CG    1.4544 110.7000  180.0000 115.9500  1.5475
IC CG   CA   *CB  HB1   1.5475 115.9500  120.0500 106.4000  1.1163
IC CG   CA   *CB  HB2   1.5475 115.9500 -125.8100 109.5500  1.1124
IC CA   CB   CG   CD    1.5552 115.9500  180.0000 114.0100  1.5384
IC CD   CB   *CG  HG1   1.5384 114.0100  125.2000 108.5500  1.1121
IC CD   CB   *CG  HG2   1.5384 114.0100 -120.3000 108.9600  1.1143
IC CB   CG   CD   NE    1.5475 114.0100  180.0000 107.0900  1.5034
IC NE   CG   *CD  HD1   1.5034 107.0900  120.6900 109.4100  1.1143
IC NE   CG   *CD  HD2   1.5034 107.0900 -119.0400 111.5200  1.1150
IC CG   CD   NE   CZ    1.5384 107.0900  180.0000 123.0500  1.3401
IC CZ   CD   *NE  HE    1.3401 123.0500  180.0000 113.1400  1.0065
IC CD   NE   CZ   NH1   1.5034 123.0500  180.0000 118.0600  1.3311
IC NE   CZ   NH1  HH11  1.3401 118.0600 -178.2800 120.6100  0.9903
IC HH11 CZ   *NH1 HH12  0.9903 120.6100  171.1900 116.2900  1.0023
IC NH1  NE   *CZ  NH2   1.3311 118.0600  178.6400 122.1400  1.3292
IC NE   CZ   NH2  HH21  1.3401 122.1400 -174.1400 119.9100  0.9899
IC HH21 CZ   *NH2 HH22  0.9899 119.9100  166.1600 116.8800  0.9914
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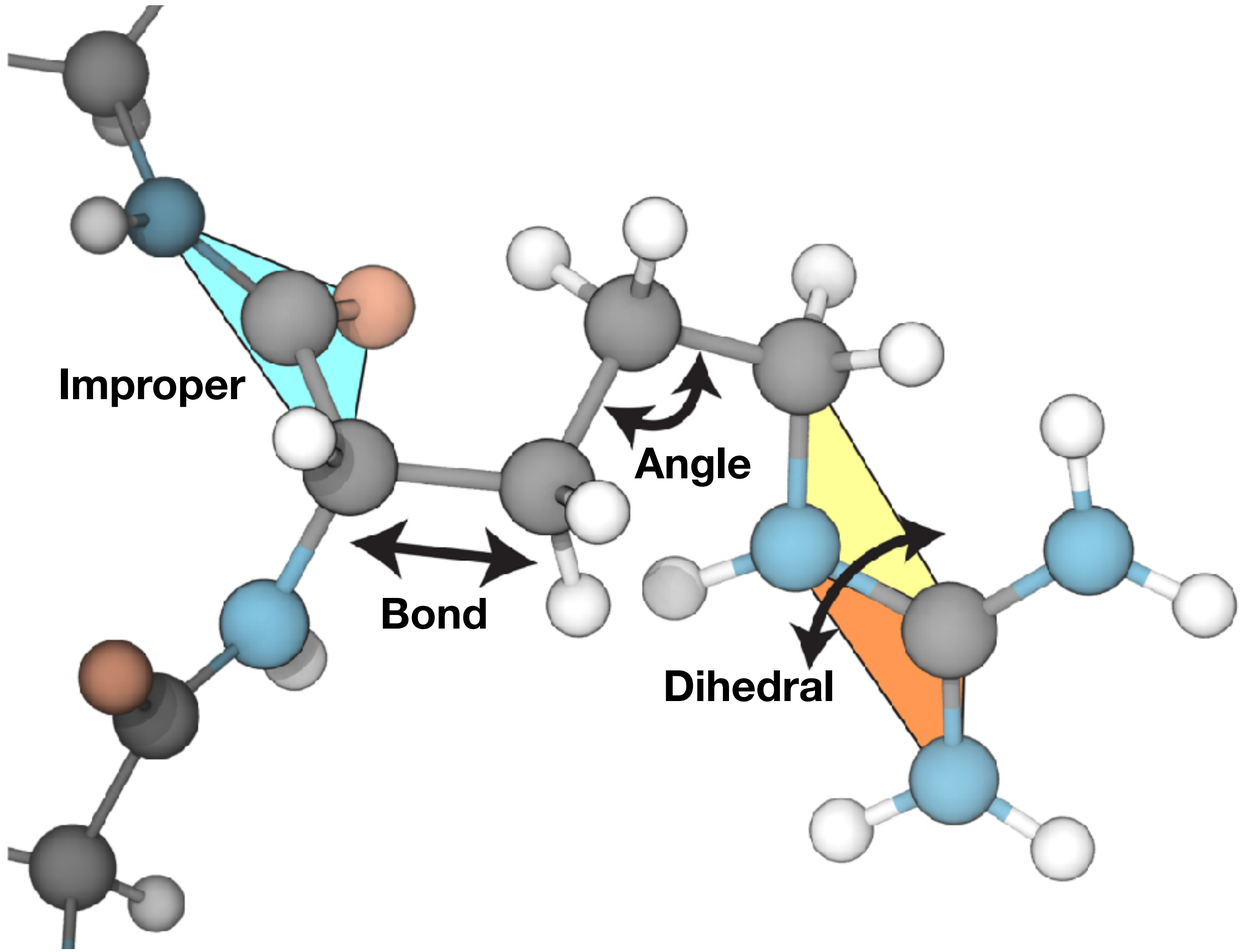
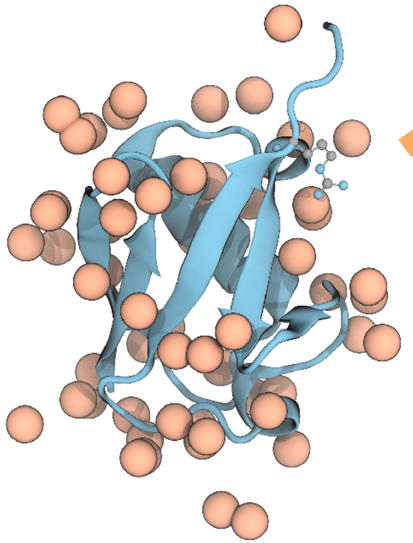


Force Field Tutorial:https://www.ks.uiuc.edu/Training/Tutorials/science/forcefield-tutorial/forcefield-html/node6.html

Building Initial System

Structure Coordinates



RCSB PDB
PROTEIN DATA BANK

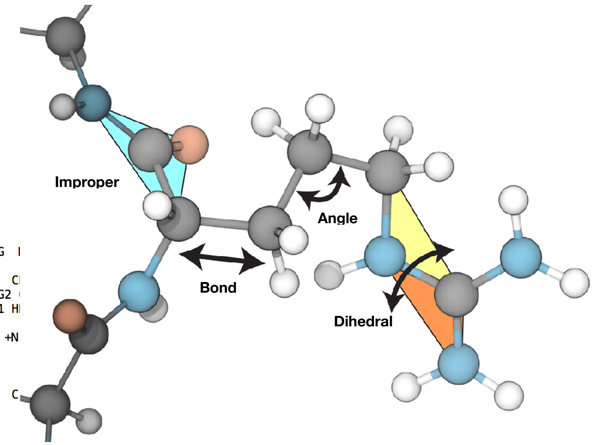
PSFGEN

Complete Initial System

- Usually in form of PSF and PDB files
- Ready to Simulate
- No Solvent
- No Ions

Structure Topology

```
RESI ARG          1.00
GROUP
ATOM N    NH1    -0.47  !    |                    HH11
ATOM HN   H       0.31  !  HN-N                    |
ATOM CA   CT1     0.07  !     |   HB1 HG1 HD1 HE     NH1-HH12
ATOM HA   HB1     0.09  !     |   |   |   |   |    //(+)
GROUP                   !  HA-CA--CB--CG--CD--NE--CZ
ATOM CB   CT2    -0.18  !     |   |   |   |        \
ATOM HB1  HA2     0.09  !     |   HB2 HG2 HD2        NH2-HH22
ATOM HB2  HA2     0.09  !   O=C                        |
GROUP                   !     |                    HH21
ATOM CG   CT2    -0.18
ATOM HG1  HA2     0.09
ATOM HG2  HA2     0.09
GROUP
ATOM CD   CT2     0.20
ATOM HD1  HA2     0.09
ATOM HD2  HA2     0.09
ATOM NE   NC2    -0.70
ATOM HE   HC      0.44
ATOM CZ   C       0.64
ATOM NH1  NC2    -0.80
ATOM HH11 HC      0.46
ATOM HH12 HC      0.46
ATOM NH2  NC2    -0.80
ATOM HH21 HC      0.46
ATOM HH22 HC      0.46
GROUP
ATOM C    C       0.51
ATOM O    O      -0.51
BOND CB  CA  CG  CB  CD CG  I
BOND NH2 CZ  N  HN  N  CA
BOND C   CA  C  +N  CA HA  C
BOND CB  HB2 CG  HG1 CG HG2
BOND NE  HE  NH1 HH11  NH1 H
DOUBLE O  C    CZ  NH1
IMPR N  -C  CA  HN   C CA +N
IMPR CZ  NH1  NH2  NE
IMPR NH1 HH11 HH12 CZ
IMPR NH2 HH21 HH22 CZ
CMAP -C  N  CA  C   N  CA  C
DONOR HN N
DONOR HE NE
DONOR HH11 NH1
DONOR HH12 NH1
DONOR HH21 NH2
DONOR HH22 NH2
ACCEPTOR O C
```



PSFGEN

Structure Preparation Tool

Available at:

- NAMD
- VMD
- Stand Alone Tool

Additional Points to Be Aware During Structure Preparation:

- Protonation State (pKa)
- Histidine Residues Prot. State
- Special “Modifications”
  - e.g. Group Heme
  - Terminal Patches

TCL Interface Example:

```
package require psfgen
topology top_all36_prot_.rtf
pdbalias residue HIS HSE
pdbalias residue HOH TIP3
pdbalias atom ILE CD1 CD
pdbalias atom TIP3 O OH2

segment U {
   pdb ubqp.pdb
   first NTER
   last  CTER
}

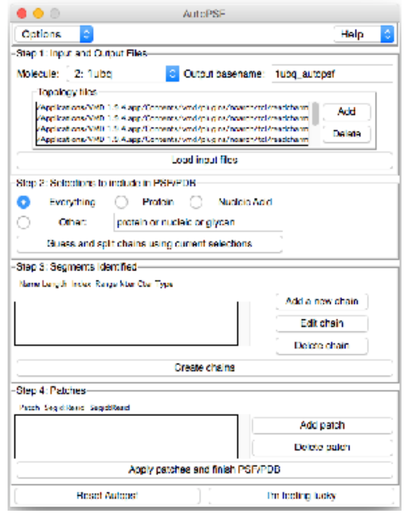
#patch DISU BPTI:5 BPTI:55

coordpdb ubqp.pdb U
guesscoord
writepdb ubq.pdb
writepsf ubq.psf
```

‘#’ Denotes Commented Line in TCL

Autopsf

- VMD Plugin
- Automates the PSF and PDB files Generation using PSFGEN
- Graphical User Interface and Command Line
- Extensions -> Modeling -> Automatic PSF Builder



PSFGEN: https://www.ks.uiuc.edu/Research/vmd/plugins/psfgen/ug.pdf
PSFGEN Tutorial: https://www.ks.uiuc.edu/Training/Tutorials/namd/namd-tutorial-html/node5.html
Autopsf: https://www.ks.uiuc.edu/Research/vmd/plugins/autopsf/
PropKa: http://nbcr-222.ucsd.edu/pdb2pqr_2.0.0/

PSF Format
(Generated by PSFGEN)

Atom Index	Seg. Name	Res ID	Res Name	Atoms' Name	Atoms' Charge	Atoms' Mass	
1140	AP1	71	LEU	O	O	-0.510000	15.9990	0
1141	AP1	72	ARG	N	NH1	-0.470000	14.0070	0
1142	AP1	72	ARG	HN	H	0.310000	1.0080	0
1143	AP1	72	ARG	CA	CT1	0.070000	12.0110	0
1144	AP1	72	ARG	HA	HB1	0.090000	1.0080	0
1145	AP1	72	ARG	CB	CT2	-0.180000	12.0110	0
1146	AP1	72	ARG	HB1	HA2	0.090000	1.0080	0
1147	AP1	72	ARG	HB2	HA2	0.090000	1.0080	0
1148	AP1	72	ARG	CG	CT2	-0.180000	12.0110	0
1149	AP1	72	ARG	HG1	HA2	0.090000	1.0080	0
1150	AP1	72	ARG	HG2	HA2	0.090000	1.0080	0
1151	AP1	72	ARG	CD	CT2	0.200000	12.0110	0
1152	AP1	72	ARG	HD1	HA2	0.090000	1.0080	0
1153	AP1	72	ARG	HD2	HA2	0.090000	1.0080	0
1154	AP1	72	ARG	NE	NC2	-0.700000	14.0070	0
1155	AP1	72	ARG	HE	HC	0.440000	1.0080	0
1156	AP1	72	ARG	CZ	C	0.640000	12.0110	0
1157	AP1	72	ARG	NH1	NC2	-0.800000	14.0070	0
1158	AP1	72	ARG	HH11	HC	0.460000	1.0080	0
1159	AP1	72	ARG	HH12	HC	0.460000	1.0080	0
1160	AP1	72	ARG	NH2	NC2	-0.800000	14.0070	0
1161	AP1	72	ARG	HH21	HC	0.460000	1.0080	0
1162	AP1	72	ARG	HH22	HC	0.460000	1.0080	0
1163	AP1	72	ARG	C	C	0.510000	12.0110	0
1164	AP1	72	ARG	O	O	-0.510000	15.9990	0
1165	AP1	73	LEU	N	NH1	-0.470000	14.0070	0
1166	AP1	73	LEU	HN	H	0.310000	1.0080	0

Atoms' Type

```
PSF CMAP

       6 !NTITLE
 REMARKS original generated structure x-plor psf file
 REMARKS 2 patches were applied to the molecule.
 REMARKS topology test_qwikmd_mutation_formatted_autopsf-temp.top
 REMARKS segment AP1 { first NTER; last CTER; auto angles dihedrals }
 REMARKS patch CTER AP1:76
 REMARKS patch NTER AP1:1

    1222 !NATOM


 1228 !NBOND: bonds
     1       5       2       1       3       1       4       1
     5       6       7       5       7       8       7       9
    10       7      10      11      10      12      13      10
    14      13      14      15      14      16      14      17


 2242 !NTHETA: angles
     1       5       6       1       5      18       2       1       5
     2       1       4       2       1       3       3       1       5
     3       1       4       4       1       5       5      18      19
     5      18      20       5       7       9       5       7       8


 3272 !NPHI: dihedrals
     1       5       7      10       1       5       7       8
     1       5       7       9       1       5      18      20
     1       5      18      19       2       1       5       7
     2       1       5      18       2       1       5       6

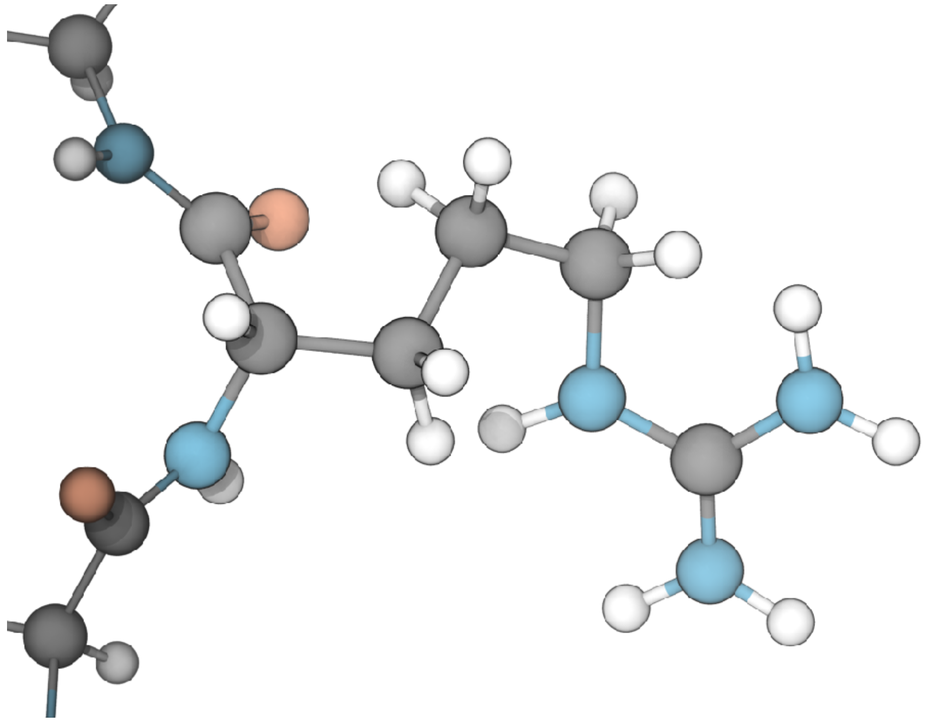

    210 !NIMPHI: impropers
    18       5      20      19      20      18      22      21
    30      32      27      31      30      27      32      31
    32      30      33      34      32      30      34      33
    35      22      37      36      37      35      39      38


    74 !NCRTERM: cross-terms
    18      20      22      35      20      22      35      37
    35      37      39      54      37      39      54      56
    54      56      58      74      56      58      74      76
    74      76      78      90      76      78      90      92
```

PSF Files: https://www.ks.uiuc.edu/Training/Tutorials/namd/namd-tutorial-unix-html/node23.html

PDB Format

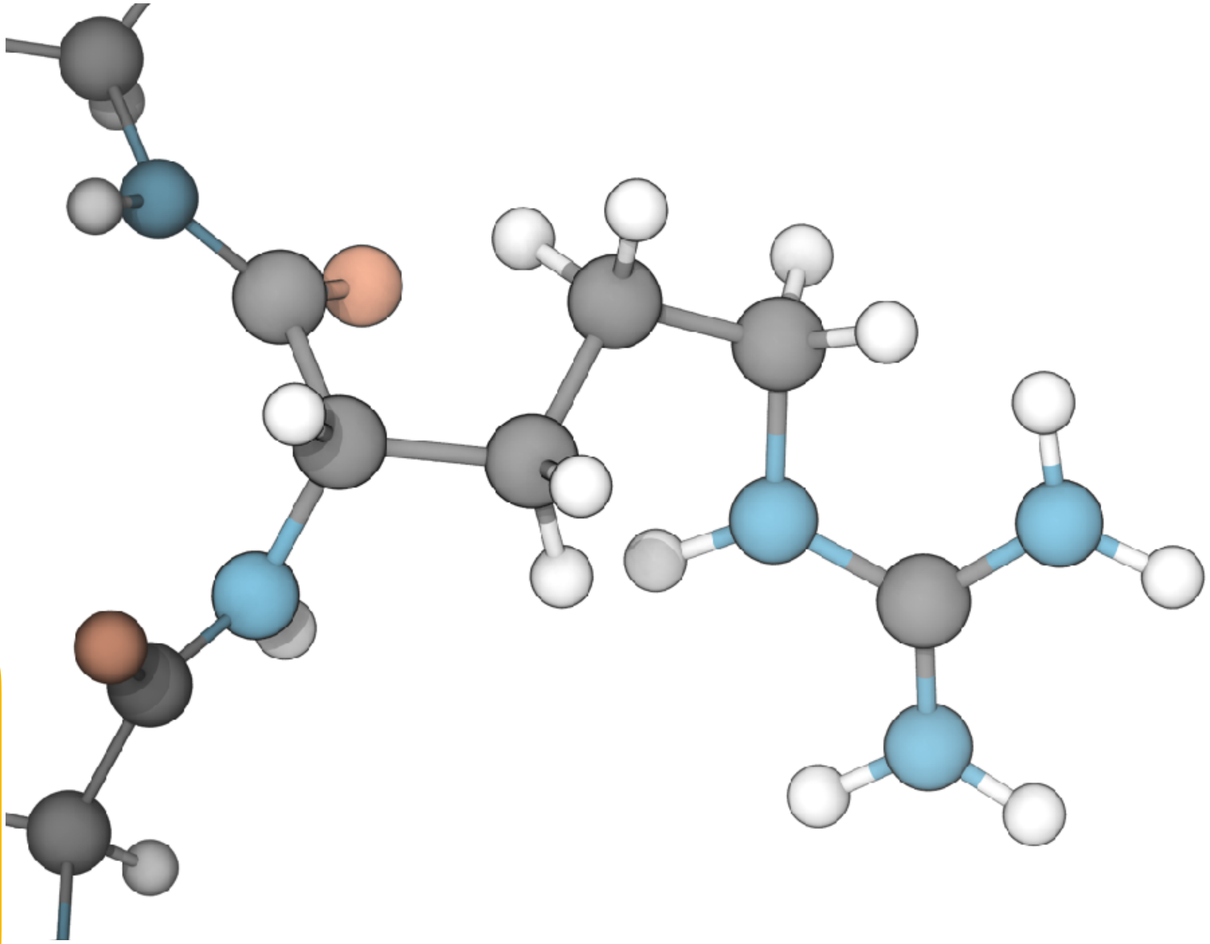
Atom Card	Atom Index	Atom Name	Residue Name	Chain ID	Residue ID	X	Y	Z	Occupancy	Beta	Seg. Name	Element
ATOM	1140	O	LEU	A	71	3.435	7.080	10.380	1.00	0.00	AP1	O
ATOM	1141	N	ARG	A	72	4.658	5.267	10.103	1.00	0.00	AP1	N
ATOM	1142	HN	ARG	A	72	5.073	4.605	9.483	0.00	0.00	AP1	
ATOM	1143	CA	ARG	A	72	4.889	5.057	11.548	1.00	0.00	AP1	C
ATOM	1144	HA	ARG	A	72	4.437	5.851	12.131	0.00	0.00	AP1	
ATOM	1145	CB	ARG	A	72	4.445	3.643	11.938	1.00	0.00	AP1	C
ATOM	1146	HB1	ARG	A	72	3.488	3.757	12.502	0.00	0.00	AP1	
ATOM	1147	HB2	ARG	A	72	4.193	3.066	11.021	0.00	0.00	AP1	
ATOM	1148	CG	ARG	A	72	5.480	2.937	12.812	1.00	0.00	AP1	C
ATOM	1149	HG1	ARG	A	72	6.490	3.312	12.537	0.00	0.00	AP1	
ATOM	1150	HG2	ARG	A	72	5.327	3.242	13.873	0.00	0.00	AP1	
ATOM	1151	CD	ARG	A	72	5.340	1.460	12.696	1.00	0.00	AP1	C
ATOM	1152	HD1	ARG	A	72	6.341	0.983	12.811	0.00	0.00	AP1	
ATOM	1153	HD2	ARG	A	72	4.658	1.051	13.477	0.00	0.00	AP1	
ATOM	1154	NE	ARG	A	72	4.768	1.135	11.382	1.00	0.00	AP1	N
ATOM	1155	HE	ARG	A	72	4.973	1.826	10.679	0.00	0.00	AP1	
ATOM	1156	CZ	ARG	A	72	4.066	-0.014	11.302	1.00	0.00	AP1	C
ATOM	1157	NH1	ARG	A	72	3.838	-0.680	12.420	1.00	0.00	AP1	N
ATOM	1158	HH11	ARG	A	72	3.349	-1.541	12.403	0.00	0.00	AP1	
ATOM	1159	HH12	ARG	A	72	4.299	-0.339	13.242	0.00	0.00	AP1	
ATOM	1160	NH2	ARG	A	72	3.742	-0.460	10.109	1.00	0.00	AP1	N
ATOM	1161	HH21	ARG	A	72	3.154	-1.252	10.021	0.00	0.00	AP1	
ATOM	1162	HH22	ARG	A	72	3.928	0.139	9.341	0.00	0.00	AP1	
ATOM	1163	C	ARG	A	72	6.399	5.179	11.741	1.00	0.00	AP1	C
ATOM	1164	O	ARG	A	72	7.033	4.116	11.447	1.00	0.00	AP1	O
ATOM	1165	N	LEU	A	73	6.925	6.280	12.165	1.00	0.00	AP1	N
ATOM	1166	HN	LEU	A	73	6.425	7.110	12.405	0.00	0.00	AP1	
ATOM	1167	CA	LEU	A	73	8.396	6.385	12.332	1.00	0.00	AP1	C



PDB Files: https://www.ks.uiuc.edu/Training/Tutorials/namd/namd-tutorial-unix-html/node22.
PDB Format: http://www.wwpdb.org/documentation/file-format

What do we need to run a Simulation?

- Coordinates
  - X-Ray or NMR, Homology Modeling (Rosetta or Modeller), Cryo-EM,…
- Structure Topology
  - Atoms Types
  - Bonds, Angles, Dihedrals and Improper Angles
- Description the Atoms' Interaction
  - Bonds, Angles, Dihedrals and Improper Angles Force Constants
  - Non-Bonded Terms



Parameter File - CHARMM Force Field

```
ATOMS
MASS     31 H      1.00800 ! polar H
MASS     32 HC     1.00800 ! N-ter H
MASS     33 HA     1.00800 ! nonpolar H
MASS     34 HP     1.00800 ! aromatic H
MASS     35 HB1    1.00800 ! backbone H
MASS     36 HB2    1.00800 ! aliphatic backbone H, to CT2
MASS     37 HR1    1.00800 ! his he1, (+) his HG,HD2
MASS     38 HR2    1.00800 ! (+) his HE1
MASS     39 HR3    1.00800 ! neutral his HG, HD2
```

```
DIHEDRALS
!
!V(dihedral) = Kchi(1 + cos(n(chi) - delta))
!
!Kchi: kcal/mole
!n: multiplicity
!delta: degrees
!
!atom types             Kchi    n   delta
!
!Neutral N terminus
NH2  CT1  C    O        0.0000  1     0.00
NH2  CT1  C    NH1      0.0000  1     0.00
H    NH2  CT1  CT1      0.0000  1     0.00
```

```
BONDS
!
!V(bond) = Kb(b - b0)**2
!
!Kb: kcal/mole/A**2
!b0: A
!
!atom type Kb          b0
!
NH2  CT1   240.000     1.4550 ! From LSN NH2-CT2
!
!Indole/Tryptophan
CA   CAI   305.000     1.3750 ! from CA CA
CAI  CAI   305.000     1.3750 ! atm, methylindole, fit CCDSS
CPT  CA    300.000     1.3600 ! atm, methylindole, fit CCDSS
CPT  CAI   300.000     1.3600 ! atm, methylindole, fit CCDSS
```

```
ANGLES
!
!V(angle) = Ktheta(Theta - Theta0)**2
!
!V(Urey-Bradley) = Kub(S - S0)**2
!
!Ktheta: kcal/mole/rad**2
!Theta0: degrees
!Kub: kcal/mole/A**2 (Urey-Bradley)
!S0: A
!
!atom types      Ktheta    Theta0   Kub     S0
!
H    NH2  CT1    50.000    111.00
NH2  CT1  CT1    67.700    110.00
NH2  CT1  CT2    67.700    110.00
```

```
IMPROPER
!
!V(improper) = Kpsi(psi - psi0)**2
!
!Kpsi: kcal/mole/rad**2
!psi0: degrees
!note that the second column of numbers (0) is ignored
!
!atom types           Kpsi                   psi0
!
HE2  HE2  CE2  CE2     3.0             0      0.00   !
          ! for ethene, yin/adm jr., 12/95
HR1  NR1  NR2  CPH2    0.5000          0      0.0000 !
                ! his, adm jr., 7/05/90
HR1  NR2  NR1  CPH2    0.5000          0      0.0000 !
```

```
NONBONDED nbxmod  5 atom cdiel fshift vatom vdistance vfswitch -
cutnb 14.0 ctofnb 12.0 ctonnb 10.0 eps 1.0 e14fac 1.0 wmin 1.5
              !adm jr., 2013 correction
!
!V(Lennard-Jones) = Eps,i,j[(Rmin,i,j/ri,j)**12 - 2(Rmin,i,j/ri,j)**6]
!
!epsilon: kcal/mole, Eps,i,j = sqrt(eps,i * eps,j)
!Rmin/2: A, Rmin,i,j = Rmin/2,i + Rmin/2,j
!
!atom  ignored    epsilon      Rmin/2   ignored   eps,1-4       Rmin/2,1-4
!
!carbons
C       0.000000  -0.110000     2.000000 ! ALLOW   PEP POL ARO
              ! NMA pure solvent, adm jr., 3/3/93
CA      0.000000  -0.070000     1.992400 ! ALLOW   ARO
              ! benzene (JES)
CC      0.000000  -0.070000     2.000000 ! ALLOW   PEP POL ARO
```

Parameter Files: https://www.ks.uiuc.edu/Training/Tutorials/namd/namd-tutorial-unix-html/node25.html

Solvate the Initial System

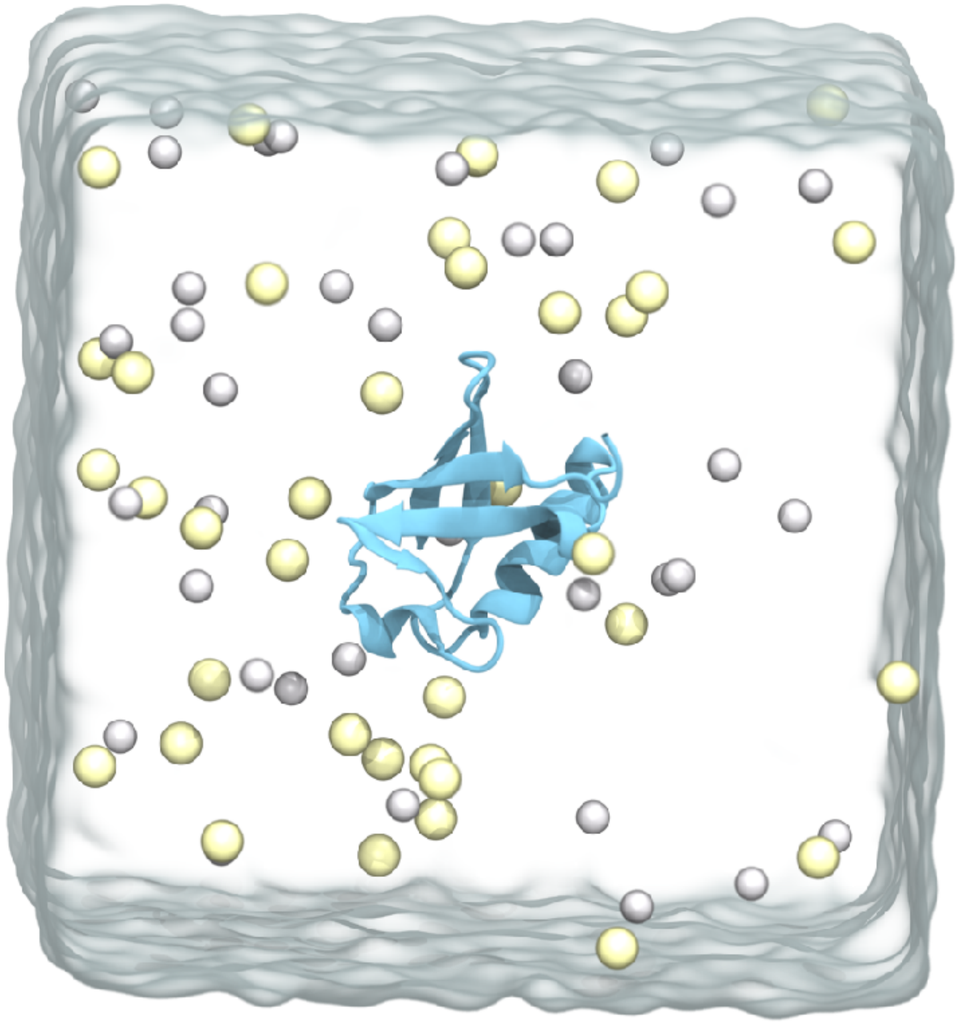
Water plays a crucial role in many biological system, even explicitly participating in enzymatic mechanisms.

Reason to Solvate a System

- Where Many Biological Processes Occur
- “Crowd Effect” and Electrostatic Contributions:
  - Molecular Conformation,
  - Electronic properties,
  - Binding energies

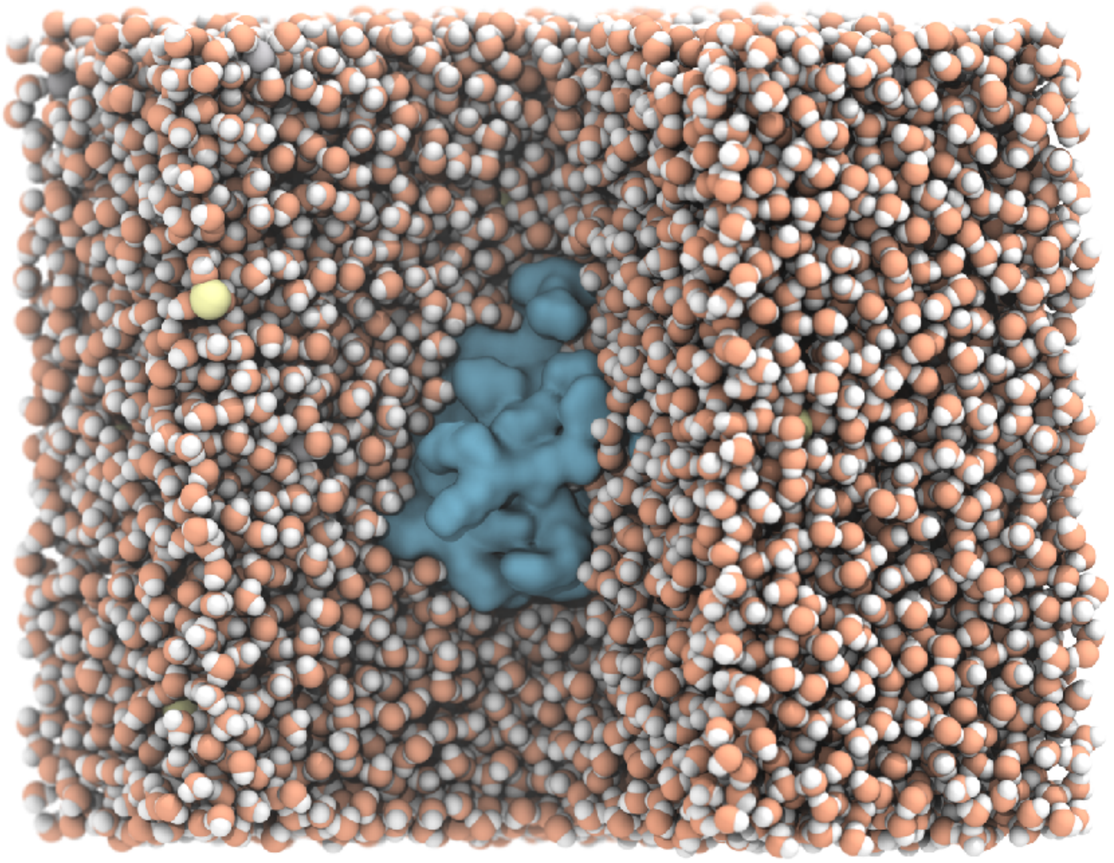
Solvent Models:

- Explicit Water Models:
  - Tip3p, Tip4p and Tip5p
- Implicit Solvent (Generalized Born Implicit Solvent in NAMD)



Solvate the Initial System

Water plays a crucial role in many biological system, even explicitly participating in enzymatic mechanisms.



Reason to Solvate a System

- Where Many Biological Processes Occur
- “Crowd Effect” and Electrostatic Contributions:
  - Molecular Conformation,
  - Electronic properties,
  - Binding energies

Solvent Models:

- Explicit Water Models:
  - Tip3p, Tip4p and Tip5p
- Implicit Solvent (Generalized Born Implicit Solvent in NAMD)

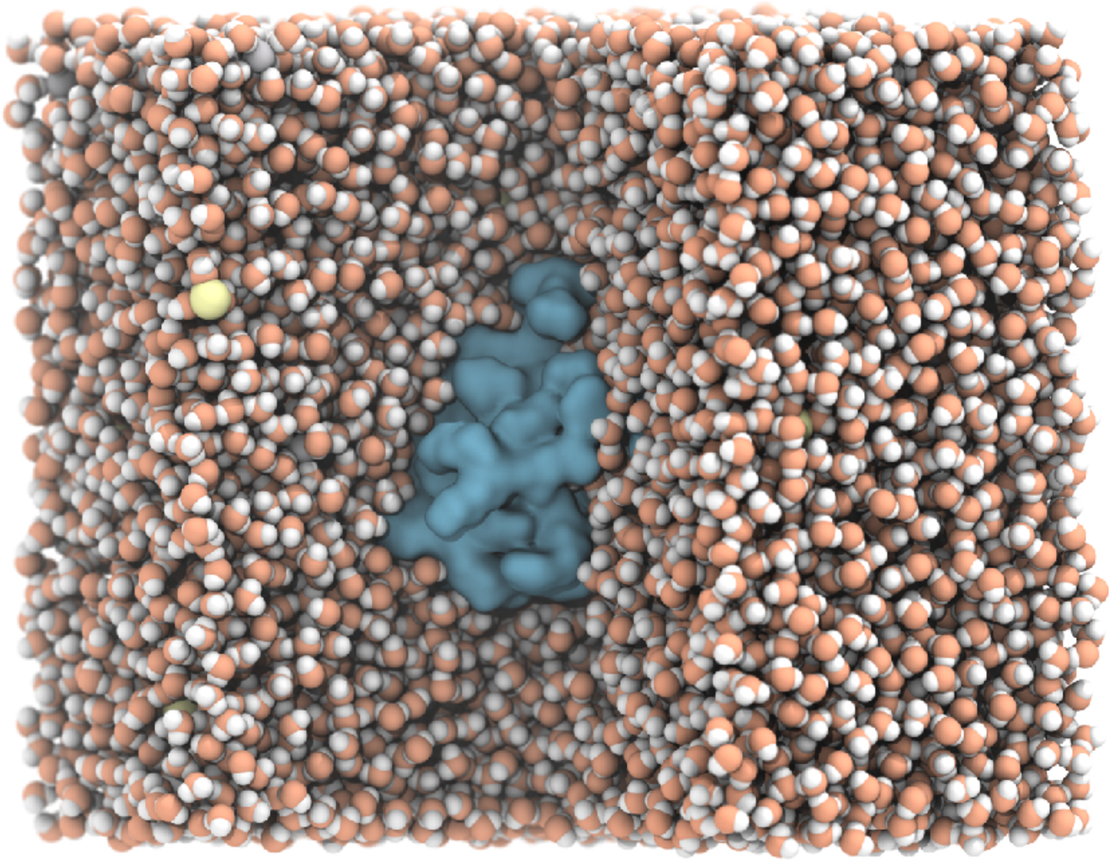
Build Simulation Environment

Why add ions?

- Protein might be sensitive to ionic strength of the surrounding solvent.
- The particle-mesh Ewald (PME - long-range electrostatic) calculation requires the system to be electrically neutral.
- Mimic experimental salt concentration

Why add membrane?

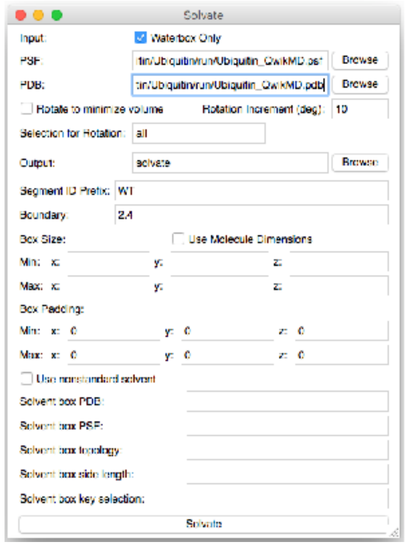
- Many proteins are membrane proteins, and their function critically depends on the physical and electrostatic influence of the membrane.



Build Simulation Environment

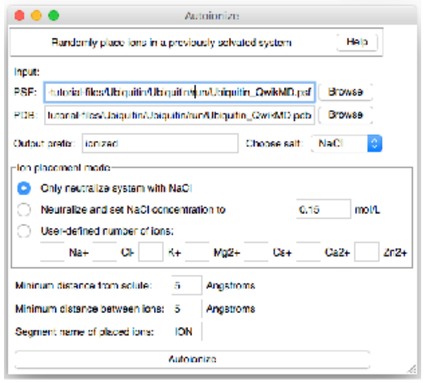
Solvent Plugin

- Box Dimensions
- Box Padding
- Rotate to Minimize Volume
- Non Standard Solvent
- Graphical User Interface and Command Line
- Extensions -> Modeling -> Add Salvation Box



Autoionize Plugin

- Neutralize
- Salt Concentration
- Mix of Ions
- Replace Water Molecules
- Graphical User Interface and Command Line
- Extensions -> Modeling -> Add Ions
- Cionize



VMD Membrane Plugin

- Pure POPC or POPE
- Command Line

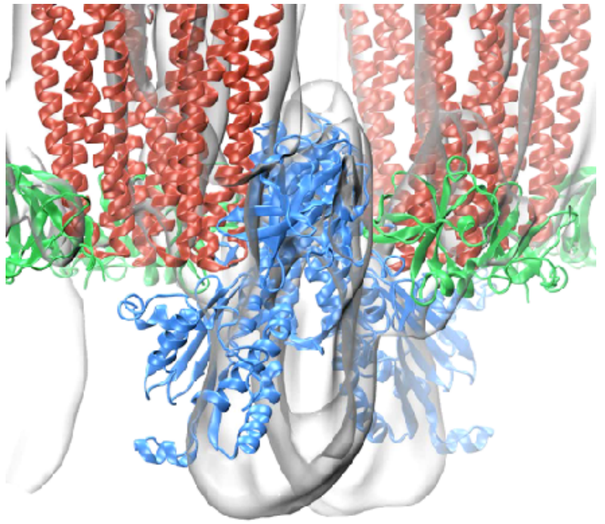
CHARMM-GUI

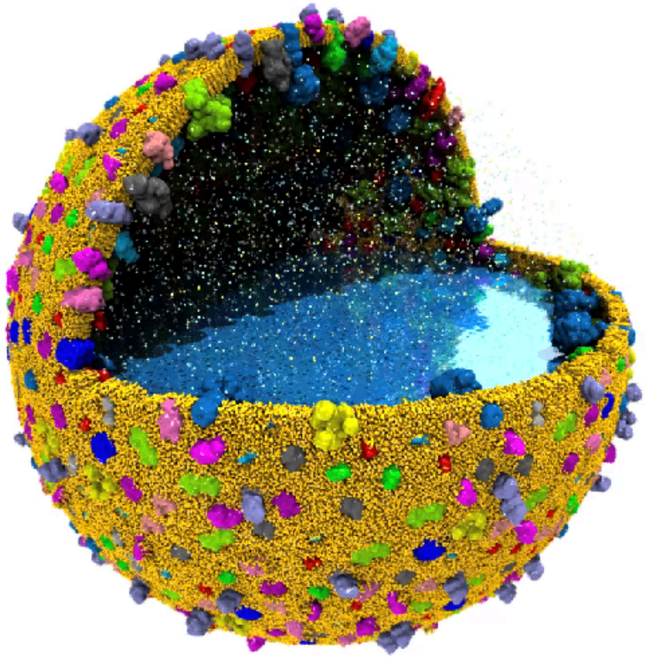
- Comprehensive Simulation Preparation Tool
- A large variety of membranes composition and distribution
- Highly Mobile Membrane-Mimetic (HMMM) Model

Solvate: https://www.ks.uiuc.edu/Research/vmd/plugins/solvate/
Solvate Tutorial: https://www.ks.uiuc.edu/Training/Tutorials/namd/namd-tutorial-unix-html/node7.html
Autoionize:https://www.ks.uiuc.edu/Research/vmd/plugins/autoionize/
Cionize: https://www.ks.uiuc.edu/Research/vmd/plugins/cionize/
Membrane Builder: https://www.ks.uiuc.edu/Research/vmd/plugins/membrane/
Membrane Tutorial: https://www.ks.uiuc.edu/Training/Tutorials/#memprot
CHARMM-GUI: http://www.charmm-gui.org/?doc=input/membrane.bilayer
CellPack: http://www.cellpack.org/

Running NAMD

- NAMD - “NAnosclae Molecular Dynamics”
- Parallel molecular dynamics simulations
  - Free of charge
  - Supports all major OS and platforms
  - Supports NSF supercomputers, AWS cloud
  - Supports NVIDIA GPUs, Intel Xeon Phi
- Sample of Features
  - Diverse MD simulation flavors
  - Enhanced sampling techniques
  - QM/MM calculations
  - Constant pH simulations
  - Efficient multiple replica simulations





Configuring NAMD

NAMD Configuration File is a TCL Script File

- Setting Simulation Variables
- TCL Commands:
  - For and while loops
  - Conditional states
  - Workflows and Algorithms
    - Temperature Ramp
    - Milestoning

NAMD Conf File: https://www.ks.uiuc.edu/Research/namd/2.13/ug/node9.h

```
# Initial pdb and pdf files

coordinates Ubiquitin_QwikMD.pdb
structure Ubiquitin_QwikMD.psf


# Simulation conditions
set temperature 300.00; # Conversion of 27 degrees Celsius + 273
temperature 0


# Harmonic constraints

constraints on
consref qwikmd_equilibration_0_constraints.pdb
conskfile qwikmd_equilibration_0_constraints.pdb
constraintScaling 2
consexp 2
conskcol B


# Output Parameters

binaryoutput no
outputname qwikmd_equilibration_0
outputenergies 400
outputtiming 400
outputpressure 400
binaryrestart yes
dcdfile qwikmd_equilibration_0.dcd
dcdfreq 10000
XSTFreq 10000
restartfreq 10000
restartname qwikmd_equilibration_0.restart


# Periodic Boundary Conditions
cellBasisVector1     75.59   0.0   0.0
cellBasisVector2     0.0   75.59   0.0
cellBasisVector3     0.0    0     75.59
cellOrigin           0.38  1.37  2.06


# PME Parameters

PME on
PMEGridspacing 1


# Thermostat Parameters

langevin on
langevintemp 60
langevinHydrogen    off
langevindamping 1


# Barostat Parameters

usegrouppressure yes
useflexiblecell no
useConstantArea no
langevinpiston on
langevinpistontarget 1.01325
langevinpistonperiod 200
langevinpistondecay 100
langevinpistontemp 60
```

```
wrapAll on
wrapWater on


# Integrator Parameters

timestep 2
fullElectFrequency 2
nonbondedfreq 1


# Force Field Parameters

paratypecharmm on
parameters par_all36_carb.prm
parameters par_all36_cgenff.prm
parameters par_all36_lipid.prm
parameters par_all36_na.prm
parameters par_all36_prot.prm
parameters toppar_all36_carb_glycopeptide.str
parameters toppar_water_ions_namd.str
exclude scaled1-4
1-4scaling 1.0
rigidbonds all
cutoff 12.0
pairlistdist 14.0
stepspercycle 10
switching on
switchdist 10.0


# Script

minimize 1000
reinitvels 60
for {set t 60} {$t <= $temperature} {incr t} {
     langevinpistontemp $t
     run 500
     langevintemp $t
}
run 500000
set file [open qwikmd_equilibration_0.check w+]
set done 1
if {[file exists qwikmd_equilibration_0.restart.coor] != 1 ||
[file exists qwikmd_equilibration_0.restart.vel] != 1 ||
[file exists qwikmd_equilibration_0.restart.xsc] != 1 } {
      set done 0
}
if {$done == 1} {
     puts $file "DONE"
    flush $file
  close $file
} else {
     puts $file "One or more files filed to be written"
   flush $file
  close $file
}
```

Configuring NAMD I

Define Initial Structure

Define Variable “temperature”

Define Initial Temperature
Temperature Distribution

Define Restraints (e.g. backbone)
- Uses an extra PDB file with beta column 1 to identify the atoms subject to the restraint

Output parameters
- Printing into files or to the console is very expensive in terms of computation, harming the performance of NAMD if done to often

```
# Initial pdb and pdf files

coordinates Ubiquitin_QwikMD.pdb
structure Ubiquitin_QwikMD.psf
```

```
# Simulation conditions
set temperature 300.00; # Conversion of 27 degrees Celsius + 273
temperature 0
```

```
# Harmonic constraints

constraints on
consref qwikmd_equilibration_0_constraints.pdb
conskfile qwikmd_equilibration_0_constraints.pdb
constraintScaling 2
consexp 2
conskcol B
```

```
# Output Parameters

binaryoutput no
outputname qwikmd_equilibration_0
outputenergies 400
outputtiming 400
outputpressure 400
binaryrestart yes
dcdfile qwikmd_equilibration_0.dcd
dcdfreq 10000
XSTFreq 10000
restartfreq 10000
restartname qwikmd_equilibration_0.restart
```

Input & Output Files: https://www.ks.uiuc.edu/Research/namd/2.13/ug/node12.html
Temperature: https://www.ks.uiuc.edu/Research/namd/2.13b2/ug/node36.html
Constraints and Restraints: https://www.ks.uiuc.edu/Research/namd/2.13/ug/node27.html

Configuring NAMD II

Definition of the Periodic Cell

```
# Periodic Boundary Conditions
cellBasisVector1     75.59   0.0    0.0
cellBasisVector2     0.0    75.59   0.0
cellBasisVector3     0.0     0      75.59
cellOrigin           0.38   1.37   2.06
```

Particle Mesh Ewald (PME) - long range electrostatic interactions

```
# PME Parameters

PME on
PMEGridspacing 1
```

NPT - Constant Number of Particle, Pressure and Temperature

Temperature Control Parameters - Thermostat

```
# Thermostat Parameters

langevin on
langevintemp 60
langevinHydrogen    off
langevindamping 1
```

Pressure Control Parameters - Barostat

```
# Barostat Parameters

usegrouppressure yes
useflexiblecell no
useConstantArea no
langevinpiston on
langevinpistontarget 1.01325
langevinpistonperiod 200
langevinpistondecay 100
langevinpistontemp 60
```

PBC: https://www.ks.uiuc.edu/Research/namd/2.13/ug/node33.html
Temperature Control: https://www.ks.uiuc.edu/Research/namd/2.13/ug/node36.html
Pressure Control: https://www.ks.uiuc.edu/Research/namd/2.13/ug/node37.html

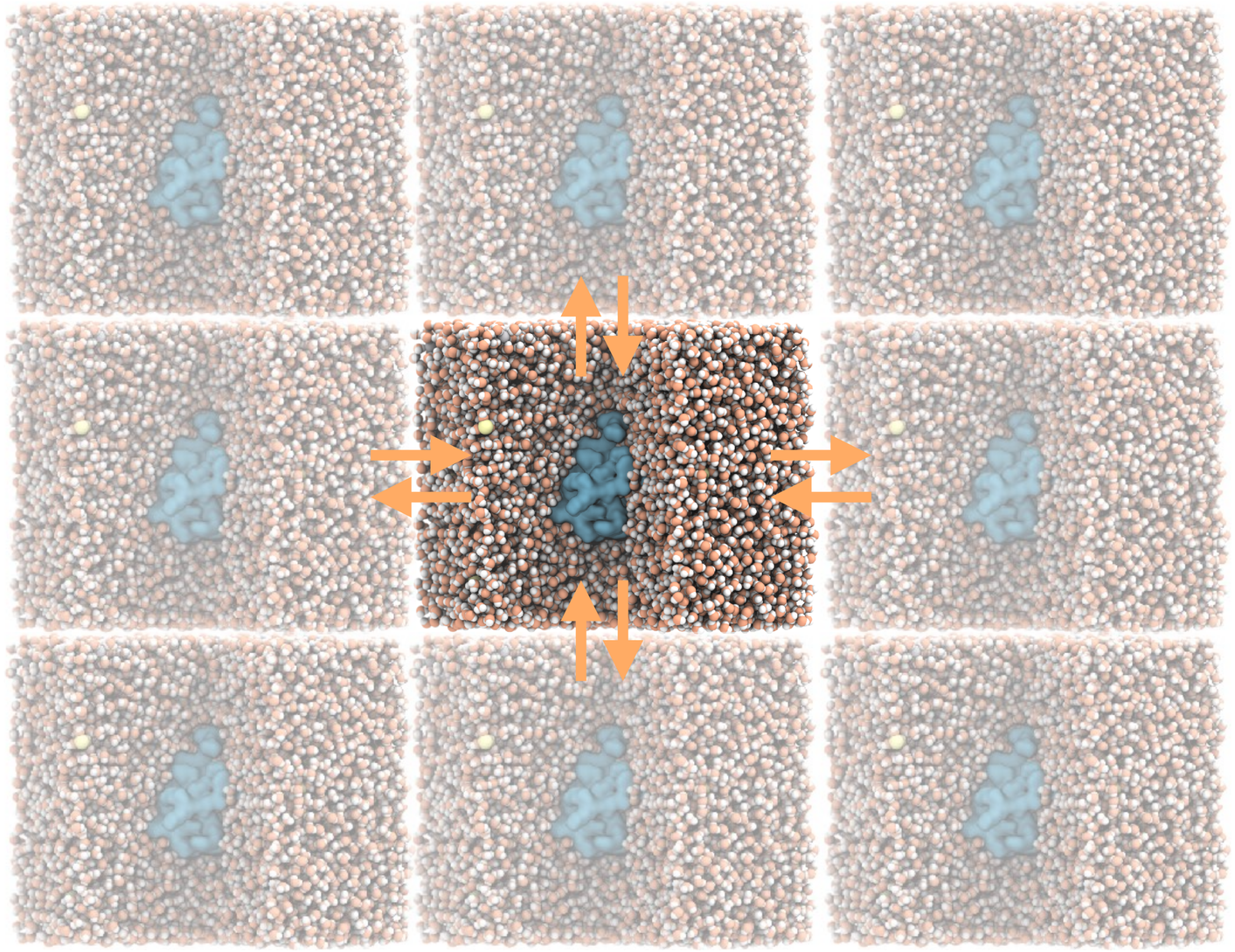
Periodic Boundary Conditions

The use of PBC

- avoids surface effects
- permits particle mesh Ewald (PME) electrostatics
- permits pressure control

Points to Be Aware

- Size of the box
- Tumbling of the system
- Self interaction
- System's volume tends to shrink during the initial steps of the simulation
  - Can be a source of errors if the box shrinks too fast



Configuring NAMD III

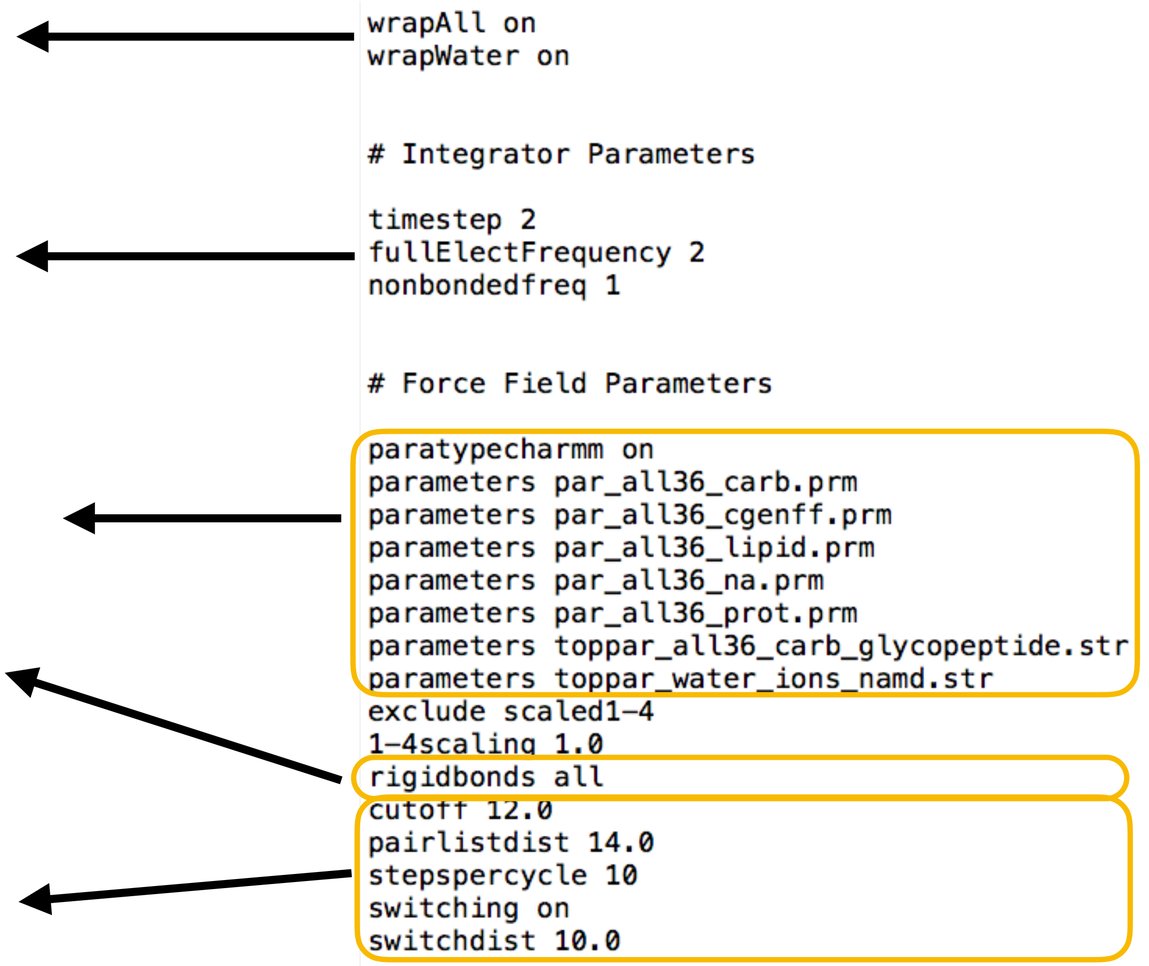
Keep Molecules Inside the Periodic Cell. No Physical Value Changes, Only Its Representation

Multi Time Stepping
Integration time 2fs
Short Non-Bonded Interaction (2fs)
Full Electrostatics (PME - 4 fs)

Input Parameters Files

What Allows the 2fs Integration Step
Water Oxygen-Hydrogen bonds (opt = water)
Heavy Atom-Hydrogen bonds (opt = all)

Non-Bonded Parameters
Cutoff - VDW interaction
Switching - Smoothly Tend to 0
Pairlistdist - Dist. To Pair of Atoms in VDW Interactions
Stepspercyle - Cycles between evaluating PairList



```
wrapAll on
wrapWater on


# Integrator Parameters

timestep 2
fullElectFrequency 2
nonbondedfreq 1


# Force Field Parameters

paratypecharmm on
parameters par_all36_carb.prm
parameters par_all36_cgenff.prm
parameters par_all36_lipid.prm
parameters par_all36_na.prm
parameters par_all36_prot.prm
parameters toppar_all36_carb_glycopeptide.str
parameters toppar_water_ions_namd.str
exclude scaled1-4
1-4scaling 1.0
rigidbonds all
cutoff 12.0
pairlistdist 14.0
stepspercycle 10
switching on
switchdist 10.0
```

PBC: https://www.ks.uiuc.edu/Research/namd/2.13/ug/node33.html
Temperature Control: https://www.ks.uiuc.edu/Research/namd/2.13/ug/node36.html
Pressure Control: https://www.ks.uiuc.edu/Research/namd/2.13/ug/node37.html
Non-Bonded Int. : https://www.ks.uiuc.edu/Research/namd/2.13/ug/node23.html
Pair List: https://www.ks.uiuc.edu/Research/namd/2.13/ug/node92.html

Configuring NAMD IV

Minimize Potential Energy

Re-Set Temperature

Temperature Ramp (example of scripting)

Run Simulation for 1 ns (2 * 500.000 fs)

Example of Checking for Normal Termination of the Simulation

```
# Script

minimize 1000
reinitvels 60
for {set t 60} {$t <= $temperature} {incr t} {
     langevinpistontemp $t
     run 500
     langevintemp $t
}
run 500000
set file [open qwikmd_equilibration_0.check w+]
set done 1
if {[file exists qwikmd_equilibration_0.restart.coor] != 1 ||
[file exists qwikmd_equilibration_0.restart.vel] != 1 ||
[file exists qwikmd_equilibration_0.restart.xsc] != 1 } {
      set done 0
}
if {$done == 1} {
     puts $file "DONE"
    flush $file
  close $file
} else {
     puts $file "One or more files filed to be written"
   flush $file
  close $file
}
```

Minimization: https://www.ks.uiuc.edu/Research/namd/2.13/ug/node34.html

Executing NAMD

Execute the command

- namd2 +p{number of processors} {Configuration File} > {Log File}
  - namd2 +p8 namd.conf > logfile.log
- NAMD versions
  - multicore -> multi CPU processors
  - multicore-CUDA -> multi CPU processors + Nvidia GPU
- NAMD lists the GPUs (devices)
  - +devices 0,1,2,3… defines the GPUs to be used

NAMD version

When NAMD was built

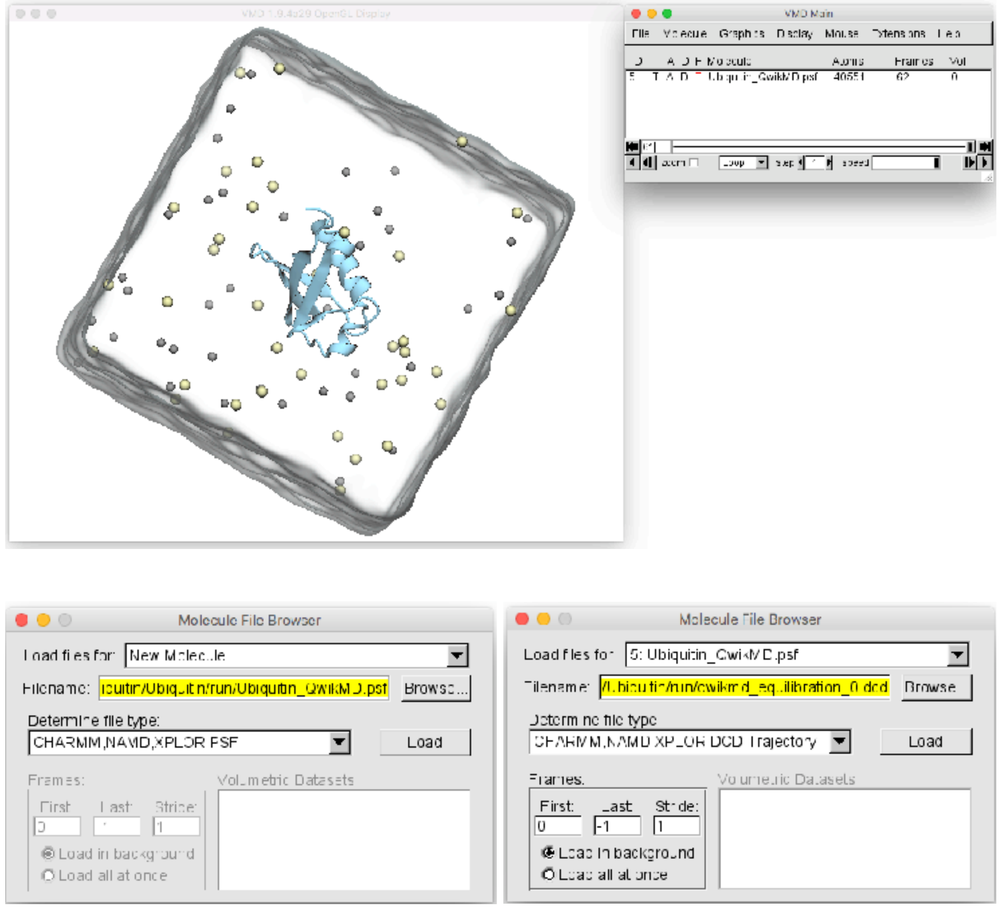
How many CPU processors

```
CharmLB> Load balancer assumes all CPUs are same.
Charm++> Running on 1 unique compute nodes (56-way SMP).
Charm++> cpu topology info is gathered in 0.017 seconds.
Info: Built with CUDA version 9010
Did not find +devices i,j,k,... argument, using all
Pe 4 physical rank 4 binding to CUDA device 4 on berlin.ks.uiuc.edu: 'TITAN V'  Mem: 12036MB  Rev: 7.0  PCI: 0:c:0
Pe 3 physical rank 3 binding to CUDA device 3 on berlin.ks.uiuc.edu: 'TITAN V'  Mem: 12036MB  Rev: 7.0  PCI: 0:8:0
Pe 5 physical rank 5 binding to CUDA device 5 on berlin.ks.uiuc.edu: 'TITAN V'  Mem: 12036MB  Rev: 7.0  PCI: 0:d:0
Pe 0 physical rank 0 binding to CUDA device 0 on berlin.ks.uiuc.edu: 'TITAN V'  Mem: 12036MB  Rev: 7.0  PCI: 0:4:0
Pe 6 physical rank 6 binding to CUDA device 6 on berlin.ks.uiuc.edu: 'TITAN V'  Mem: 12036MB  Rev: 7.0  PCI: 0:e:0
Pe 2 physical rank 2 binding to CUDA device 2 on berlin.ks.uiuc.edu: 'TITAN V'  Mem: 12036MB  Rev: 7.0  PCI: 0:7:0
Pe 1 physical rank 1 binding to CUDA device 1 on berlin.ks.uiuc.edu: 'TITAN V'  Mem: 12036MB  Rev: 7.0  PCI: 0:6:0
Pe 7 physical rank 7 binding to CUDA device 7 on berlin.ks.uiuc.edu: 'TITAN V'  Mem: 12036MB  Rev: 7.0  PCI: 0:f:0
Info: NAMD Git-2019-05-08 for Linux-x86_64-multicore-CUDA
Info:
Info: Please visit http://www.ks.uiuc.edu/Research/namd/
Info: for updates, documentation, and support information.
Info:
Info: Please cite Phillips et al., J. Comp. Chem. 26:1781-1802 (2005)
Info: in all publications reporting results obtained with NAMD.
Info:
Info: Based on Charm++/Converse 60800 for multicore-linux64-iccstatic
Info: Built Wed May 8 02:23:17 CDT 2019 by jim on belfast.ks.uiuc.edu
Info: 1 NAMD  Git-2019-05-08  Linux-x86_64-multicore-CUDA  8    berlin.ks.uiuc.edu  jribeiro
Info: Running on 8 processors, 1 nodes, 1 physical nodes.
Info: CPU topology information available.
Info: Charm++/Converse parallel runtime startup completed at 8.5059 s
```

Analyzing Trajectories

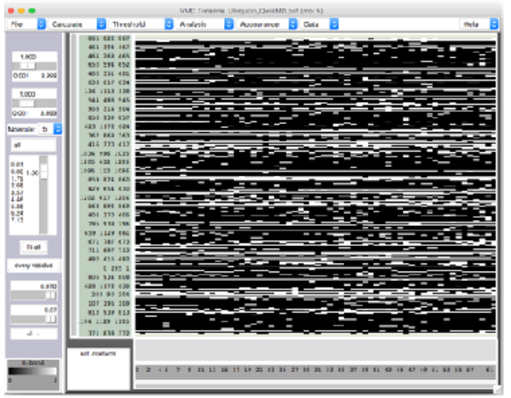
Load Trajectories (dcd) Files Into VMD:

- Using the Menu:
  - File-> “New Molecule” - Select PSF file first (recommended)
  - File-> “New Molecule” - Select the dcd file
- Command Line:
  - “mol new Ubiquitin_QwikMD.psf”
  - mol addfile traj.dcd waitfor all



VMD Load Traj: https://www.ks.uiuc.edu/Training/Tutorials/vmd/tutorial-html/node3.html

Analyzing Trajectories



- TimeLine Plugin
  - Temporally changing per-residue attributes of a molecular structure
- RMSD Trajectory Tool
  - Root Mean Square Deviation calculator and visualizer
- Normal Mode Wizard <-> ProDY
  - Analysis and visualization of normal mode data
- pyContacts:
  - Python plugin for VMD to non-covalent interactions
- MDAnalysis
  - Object-oriented Python library to analyze trajectories

VMD Analysis: https://www.ks.uiuc.edu/Training/Tutorials/vmd/tutorial-html/node7.html
Analysis Script: https://www.ks.uiuc.edu/Research/vmd/current/ug/node200.html
VMD Timeline: https://www.ks.uiuc.edu/Research/vmd/plugins/timeline/
VMD Plugins: https://www.ks.uiuc.edu/Research/vmd/plugins/
pyContacts: https://pycontact.github.io/
MDAnalysis: https://www.mdanalysis.org/

Integrative MD Toolkit for Novices and Experts

Features

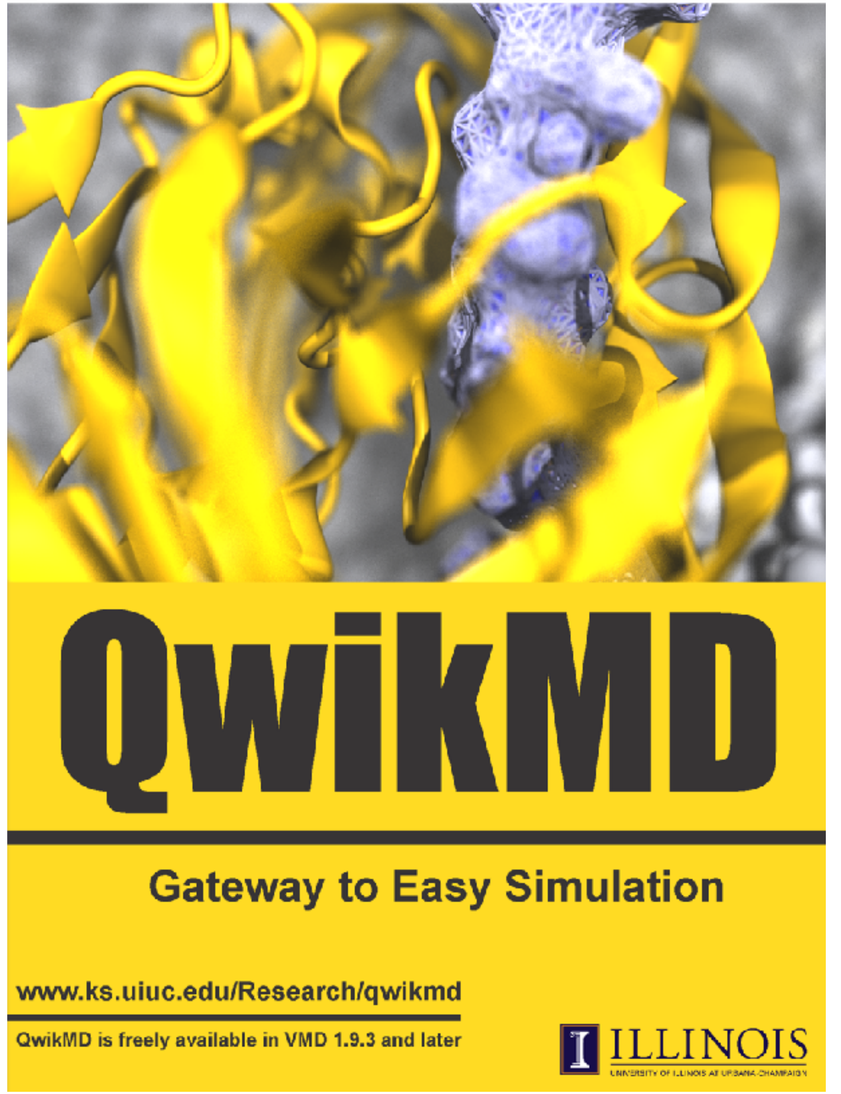
- Easy Setup of MD Simulations
- Structure Manipulation
- Basic and Advanced Protocols
- Live View Simulations
- Integrated Analysis
- Info Buttons
- Reproducibility
- Available on Amazon Cloud

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

VMD
Visual Molecular Dynamics

NAMD
Scalable Molecular Dynamics

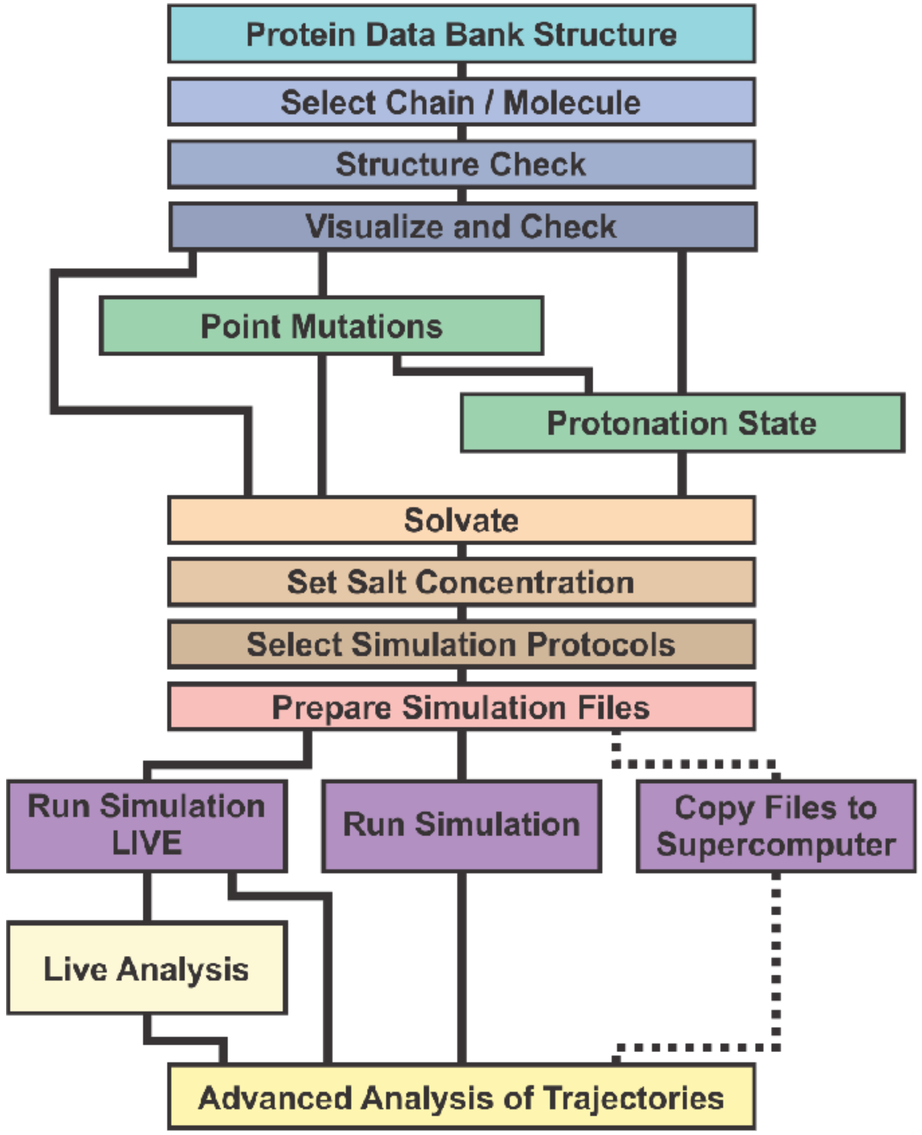
QwikMD
Gateway for Easy Simulation

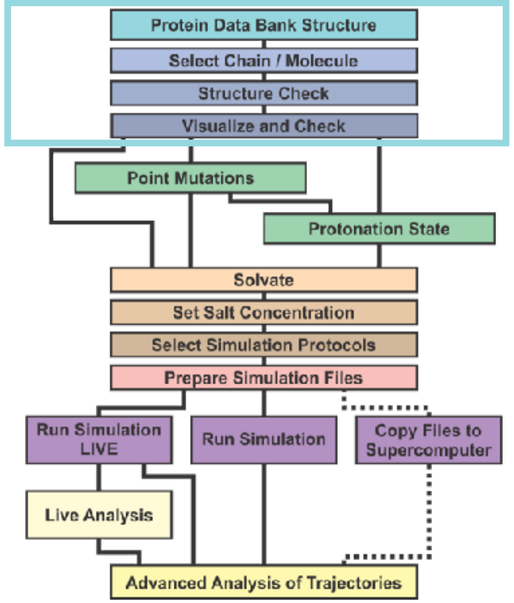


QwikMD Workflow

Features

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





Initial Structure

VMD Visual Molecular Dynamics

NAMD Scalable Molecular Dynamics

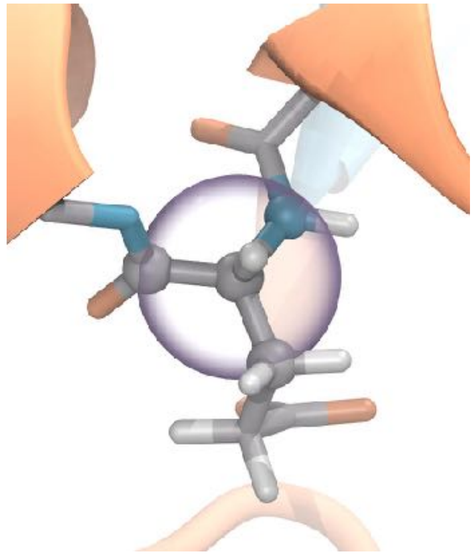
RCSB PDB PROTEIN DATA BANK

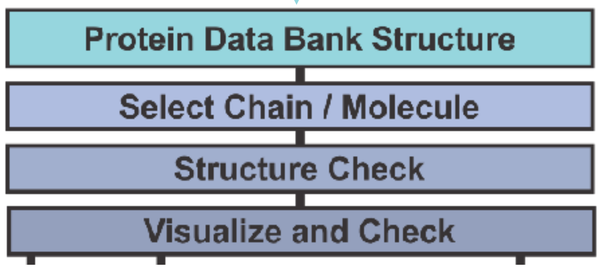
Structure Check

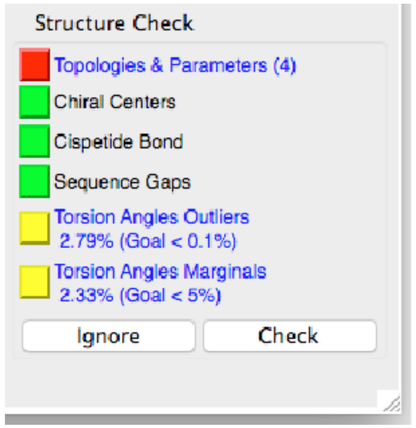
- Missing topologies
- Sequence Gaps
- Residues Alternative Insertions
- Chiral Centers
- Cis-peptide Bonds
- Backbone Torsion Angles
  - Marginals
  - Outliers

Chiral Centers

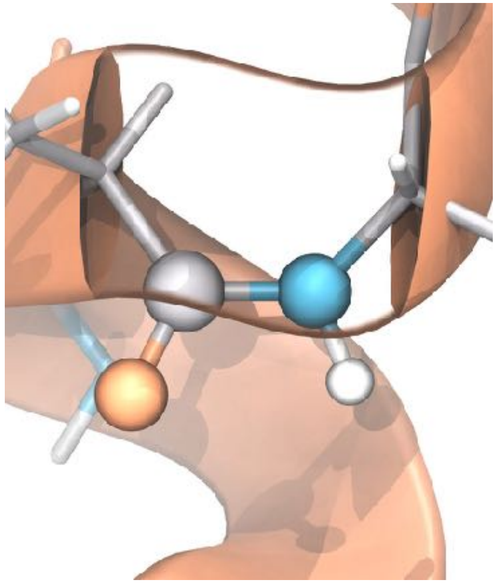
D-amino acids

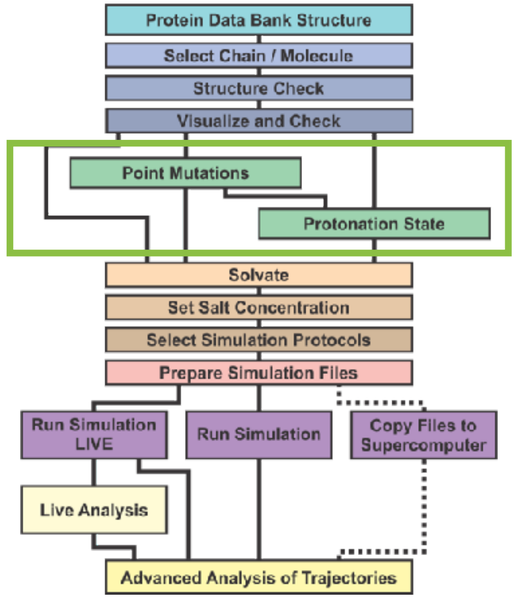






Cis-peptide

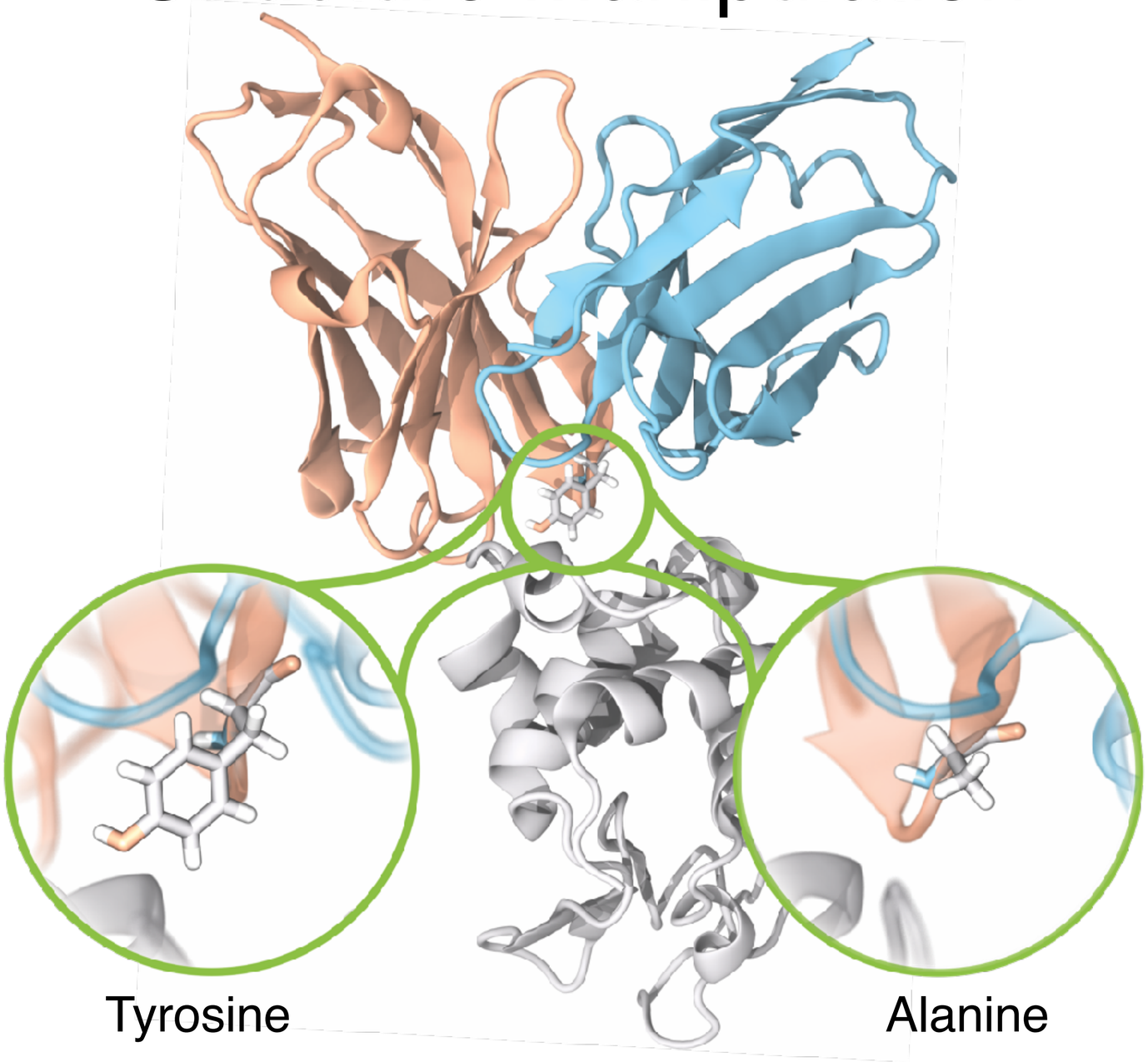


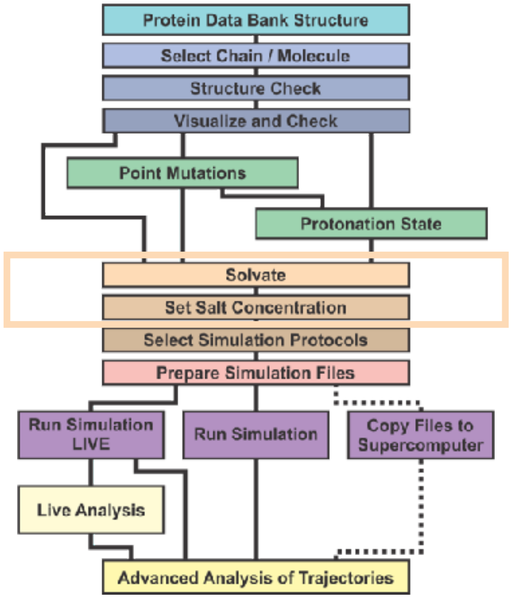


Structure Manipulation

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

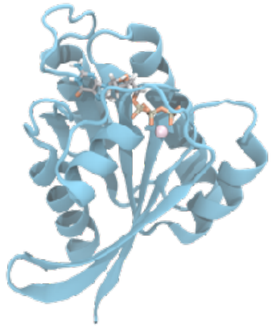
Structure Manipulation





Simulation Environment

Vacuum

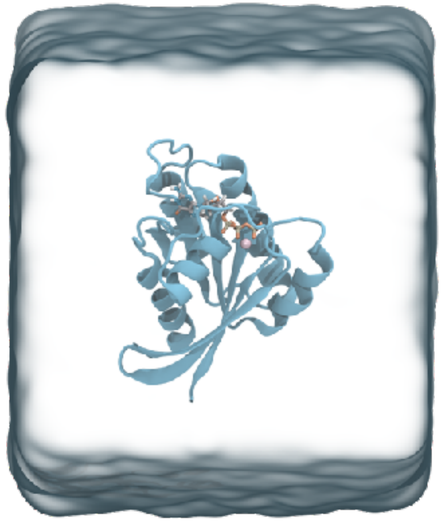


Implicit Solvent

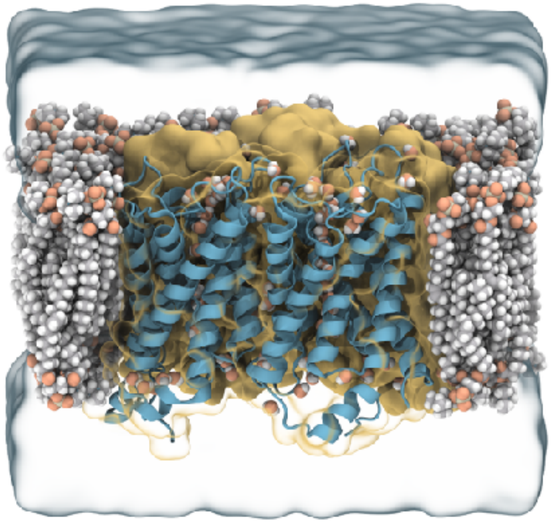
Simulation Environment

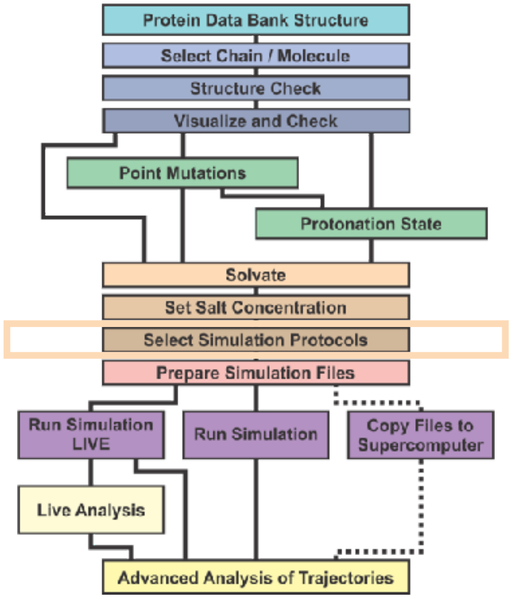
- Solvent Model
- Salt Concentration
- Water Box Size
  - Reduced Volume Available
- Membrane Protein Insertion

Explicit Solvent



Explicit Solvent + Membrane



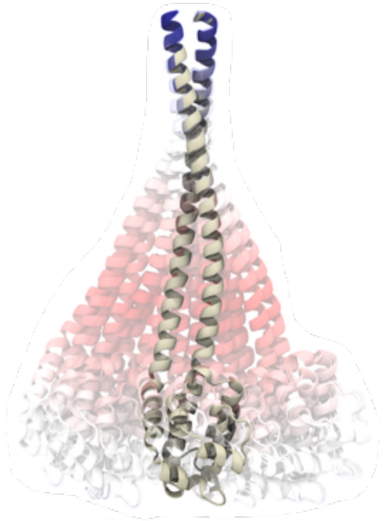


Simulation Protocols

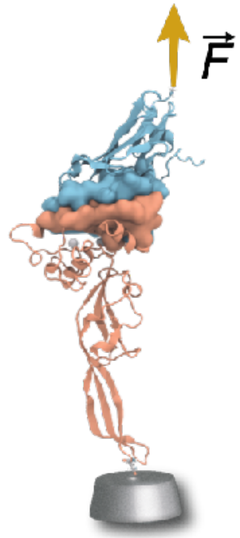
Simulation Protocol

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

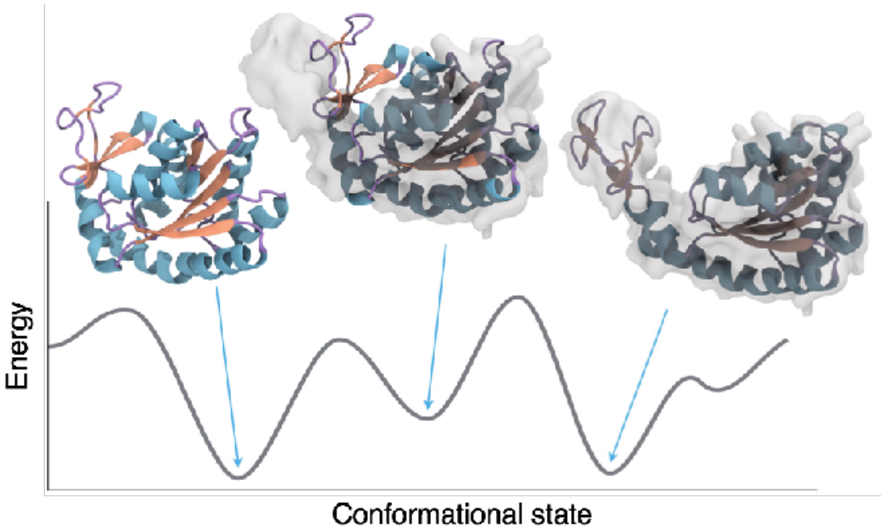
Molecular Dynamics



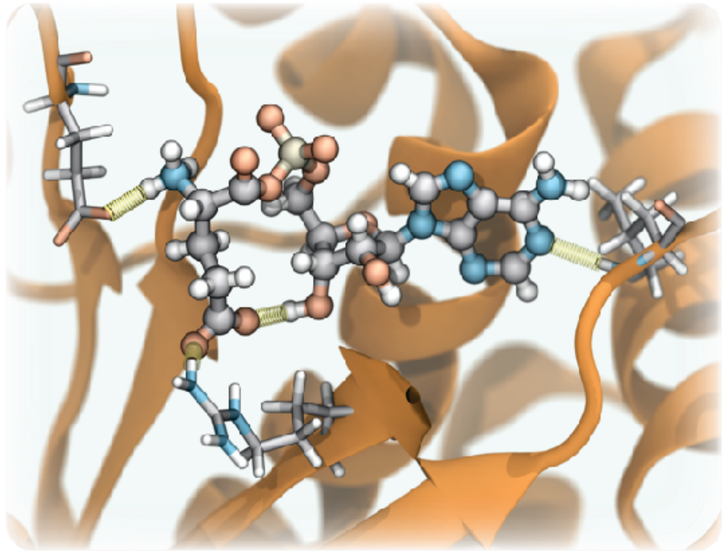
Steered MD



MDFF



QM/MM

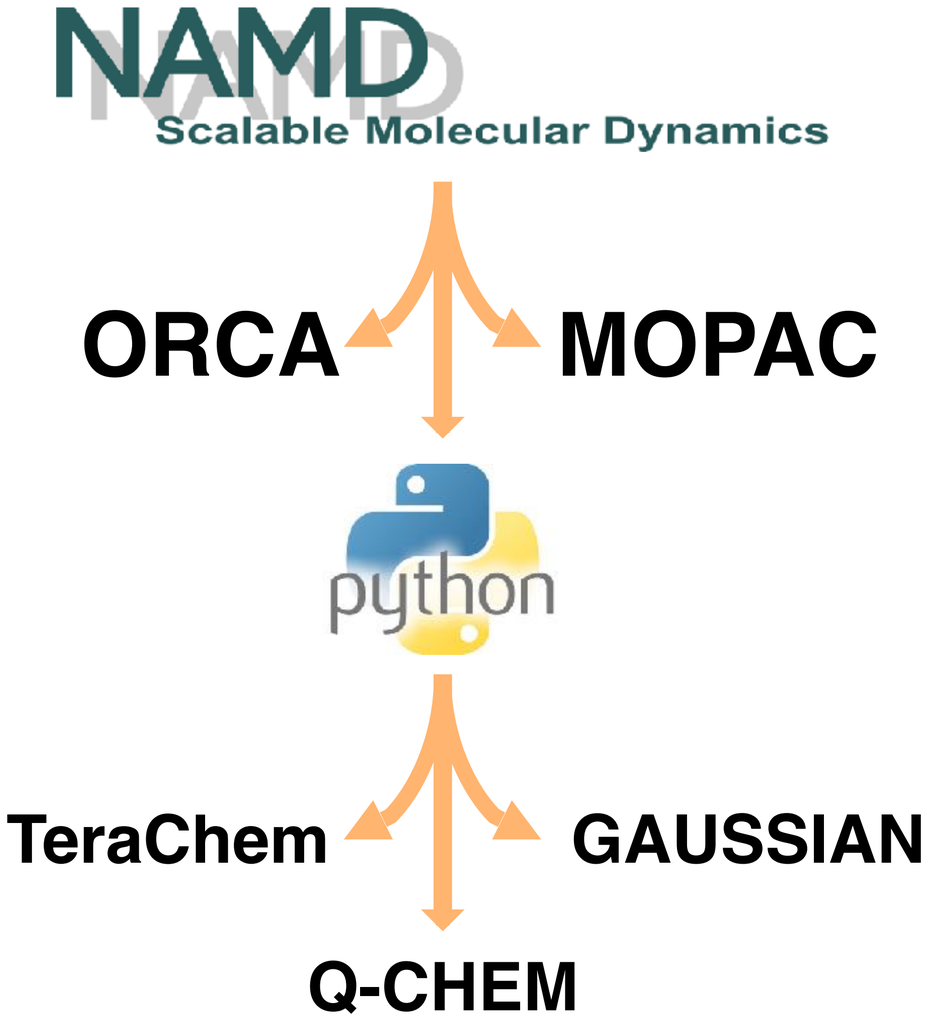


NAMD QM/MM Interface

http://www.ks.uiuc.edu/Research/qmmm/

QwikMD Interface

- QM Region Definition:
  - VMD Atom Selection
  - Point-and-Click
- Multiple Independent QM Regions
- Prevent QM Region Definition Errors
- Detection and Definition of QM/MM Bonds from Protein and Nucleic Acid residues
- QM Orbitals and Energies Analysis



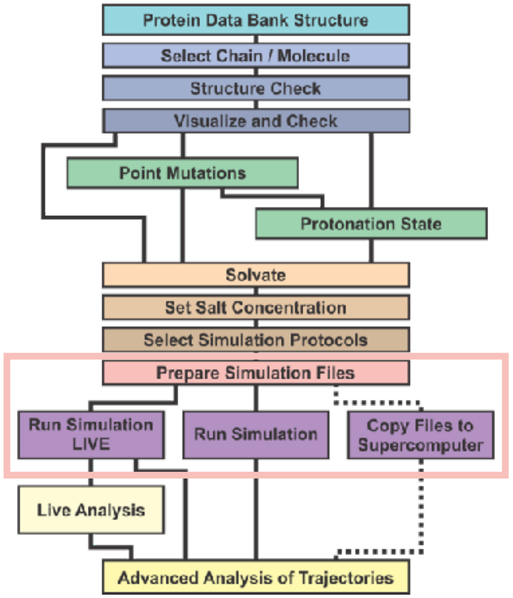
Full Control of QM Package Execution:

- Execution Command Lines as Arguments (ORCA & MOPAC)
- Wrapper Scripts
- Flexible Definition of QM Regions and QM/MM Bonds scheme

Nature Methods 2018

NAMD goes quantum: an integrative suite for hybrid simulations

Marcelo Melo, Rafael Bernardi, Till Rudack, Maximilian Scheurer, Christoph Riplinger, James Phillips, Julio Maia, Gerd Rocha (MOPAC), João Ribeiro, John Stone, Frank Neese (ORCA), Klaus Schulten, Zaida Luthey-Shculten



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)

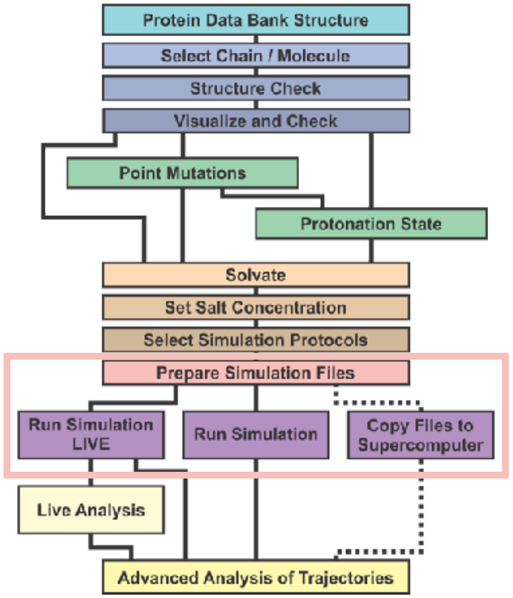
Setup Folder

- 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
- Loading Script and Text Log Files
- Reproduce and/or Share the Process and the End Result

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 Na
mdtime,0 5.0 mdtime,1 4.0 currenttime,0 {} currenttime,1 {} solvent,0
Explicit }
array set QWIKMD::advGui {live 0 currenttime {Completed 0.000 of 0.000 n
plength 10.0 desktop white temperature,0 27 temperature,1 27 saltconc,0
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```

"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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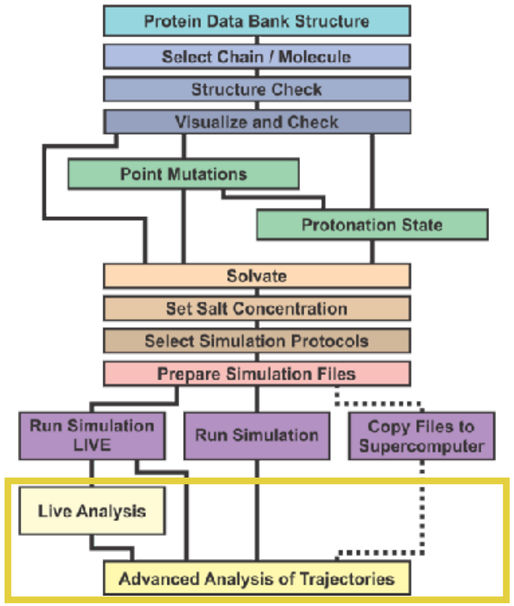
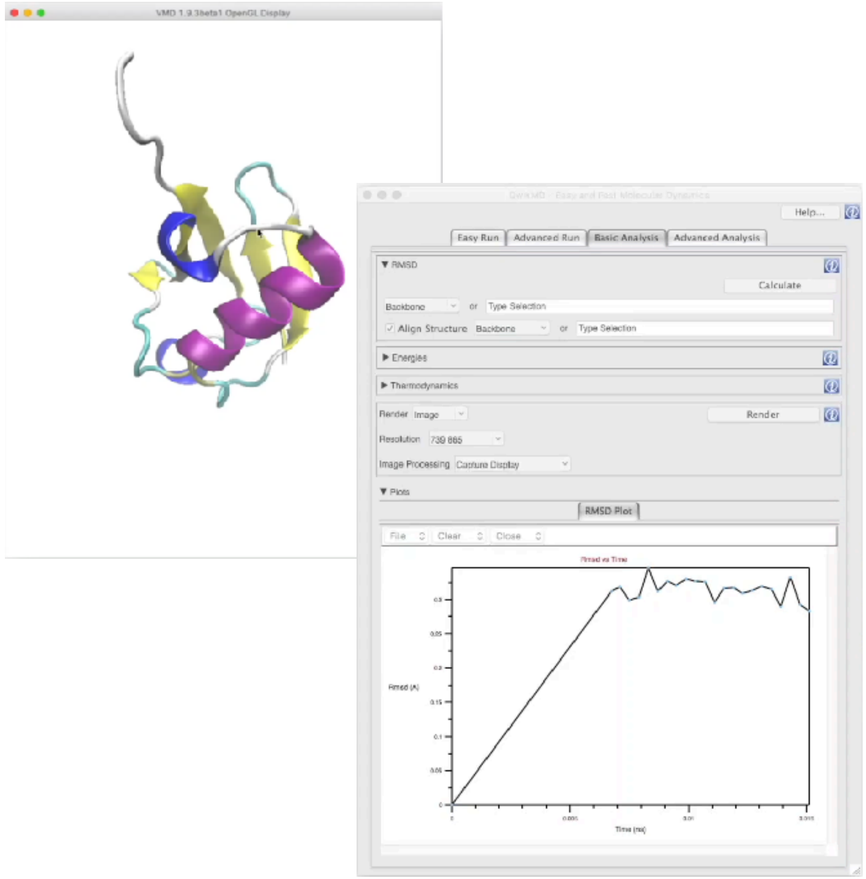
Load Simulation Trajectories and Analysis



Live Simulation and After Load Analysis



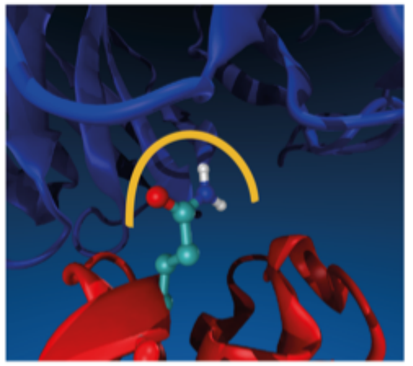
Analyses Available:

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

Contact Area

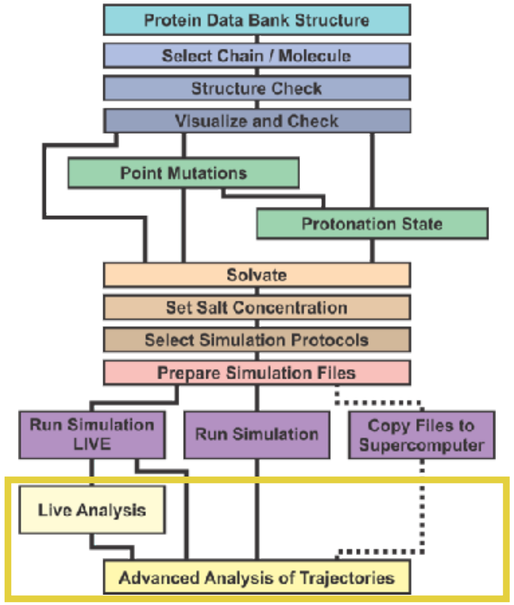
First Implemented in CompASM as Hot Spots Filter

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

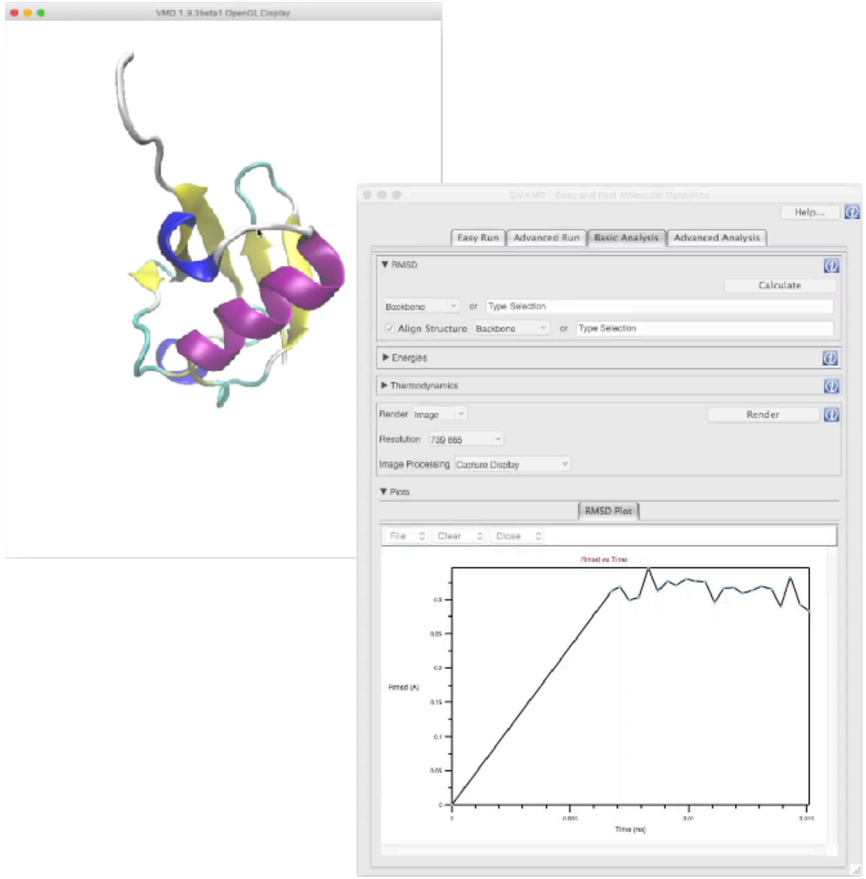


Ligand Exposed/Contact Surface Area

Load Simulation Trajectories and Analysis

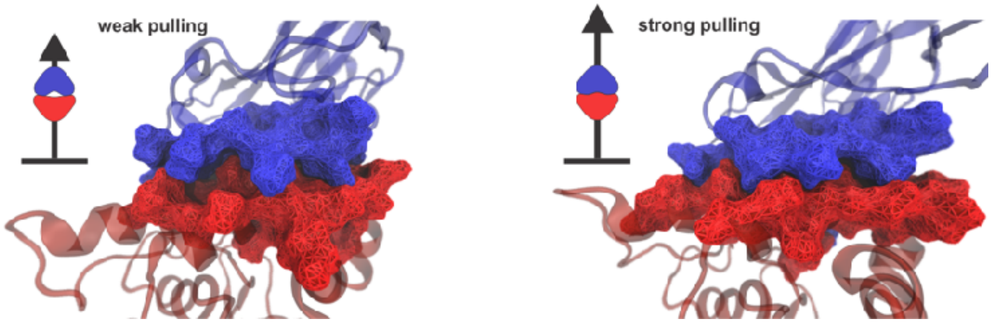


Live Simulation and After Load Analysis



Contact Area

First Implemented in CompASM as Hot Spots Filter

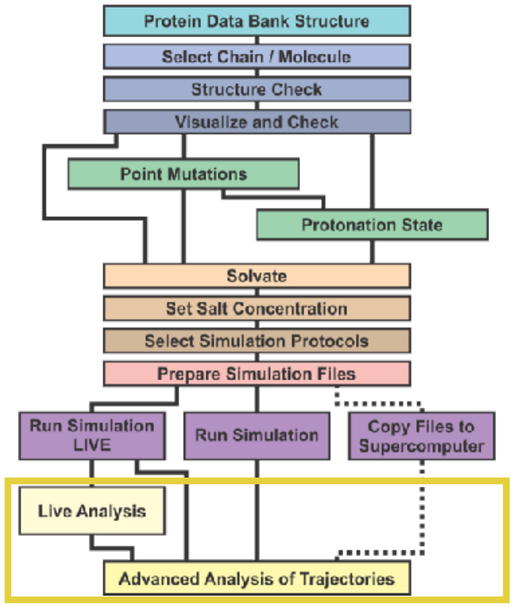


Schoeler C., *et al.*,Ultrastable cellulosome-adhesion complex tightens under load*, Nat. Commun.,* **2014**, 6, 5635.

Analyses Available:

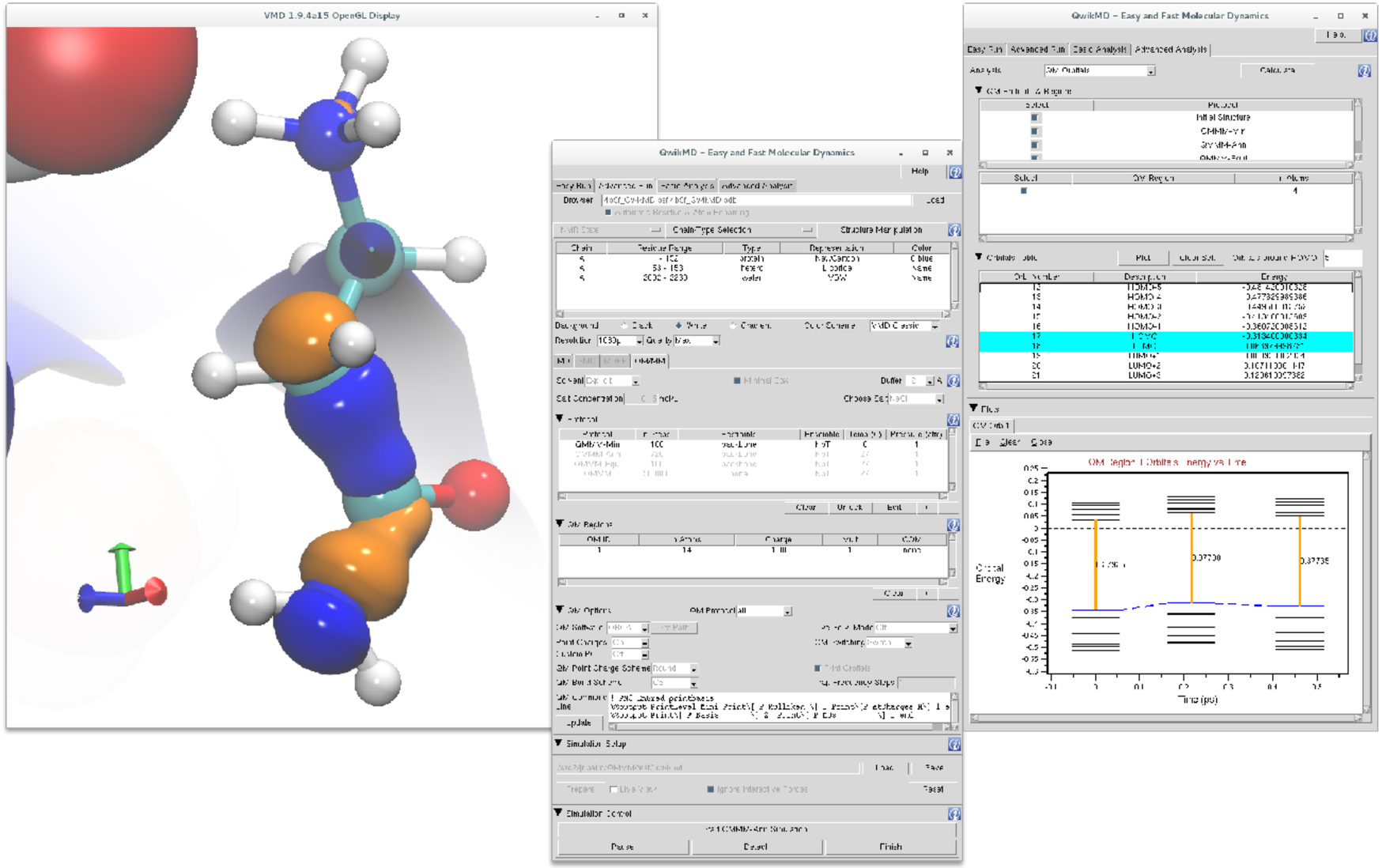
- Energies
- Temperature, Pressure and Volume
- RMSD
- Hydrogen Bonds
- SASA
- **Contact Area**
- QM Energies

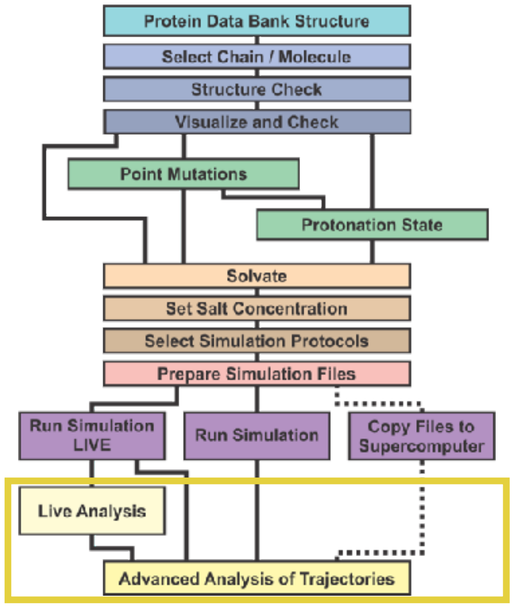
New QM/MM Simulation and Orbitals Visualization



Analyses Available:

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





New QM/MM Simulation and Orbitals Visualization

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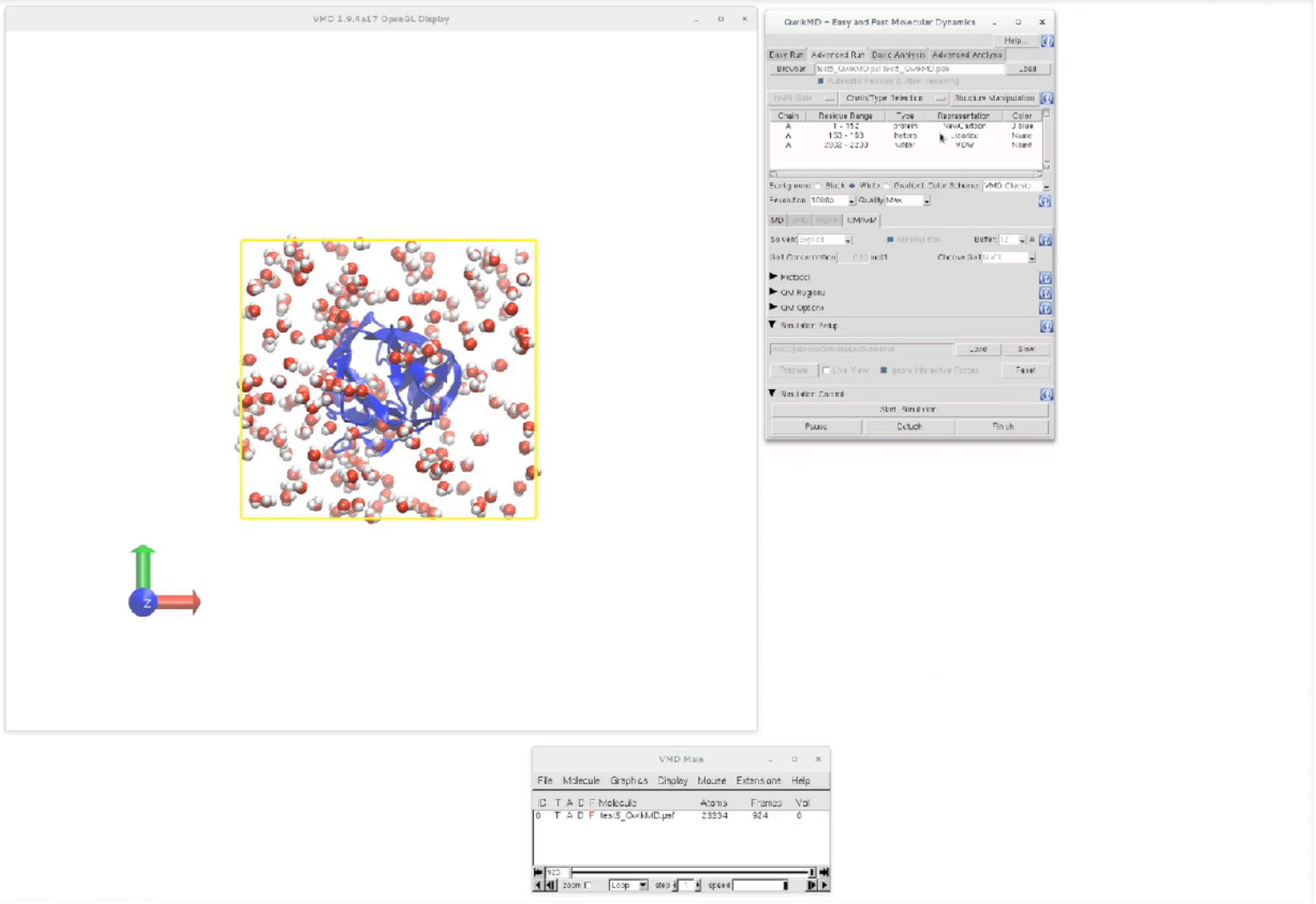
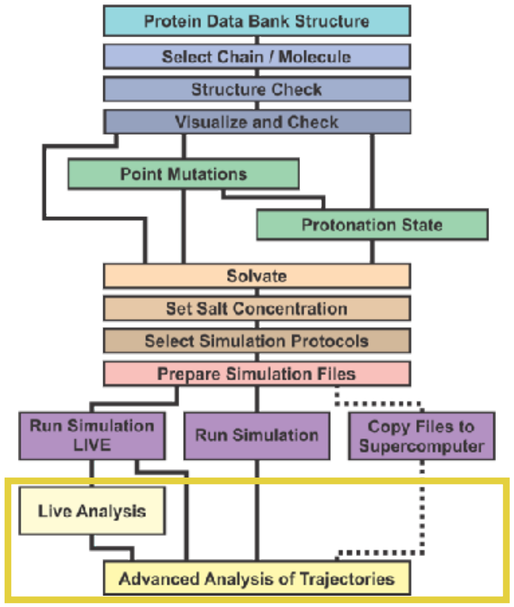
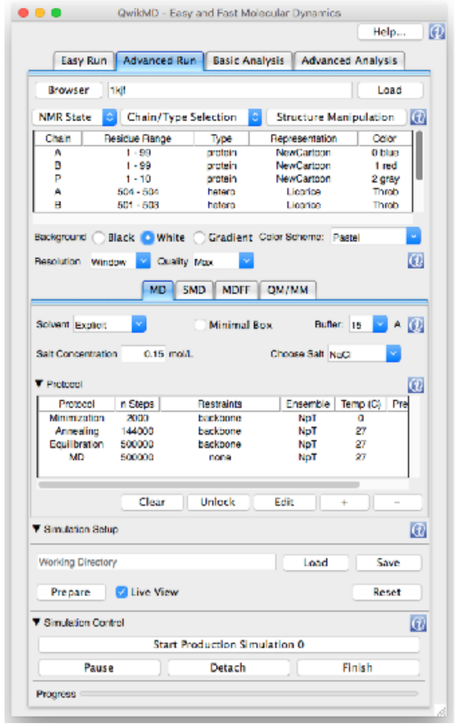
- **QM Orbitals Visualization**
- **Nature Methods 2018**



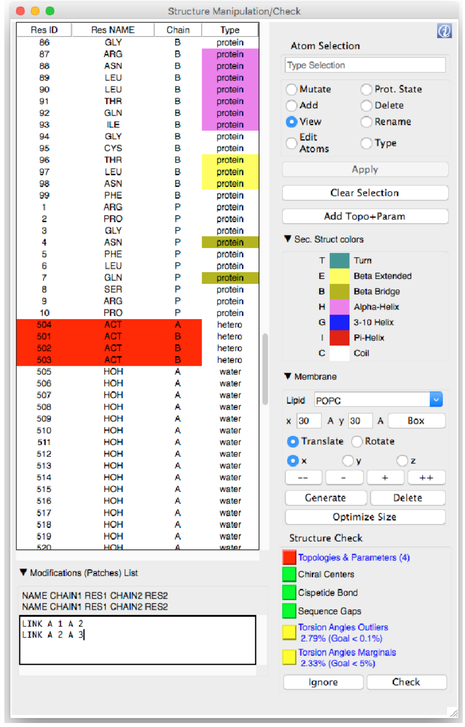


QwikMD Graphical User Interface

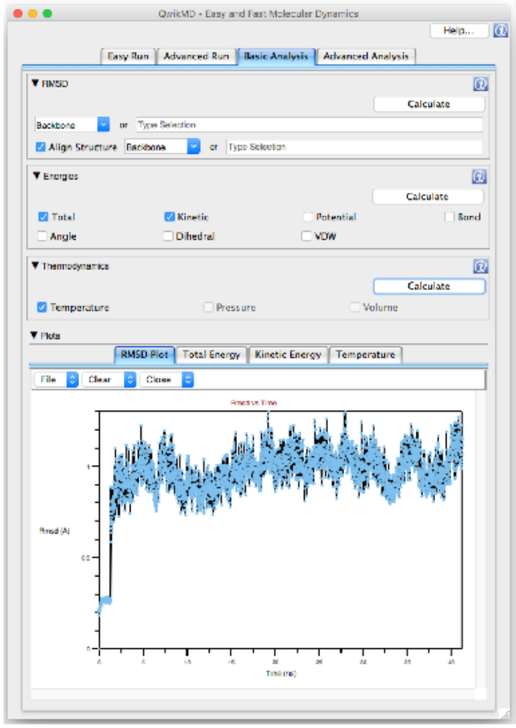
Simulation Preparation



Struct. Manipulation



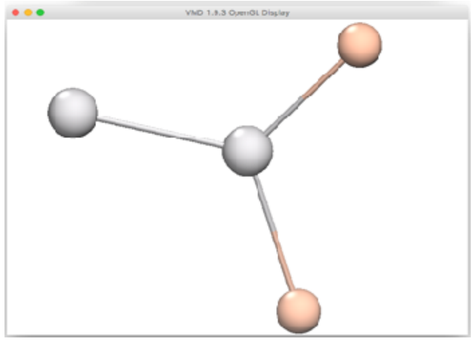
Simulation Analysis

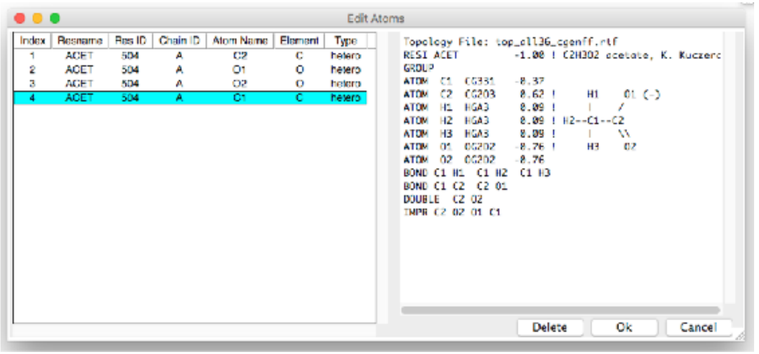


Other Features:

- Info Buttons
- Simulation Controls

Atom Editing

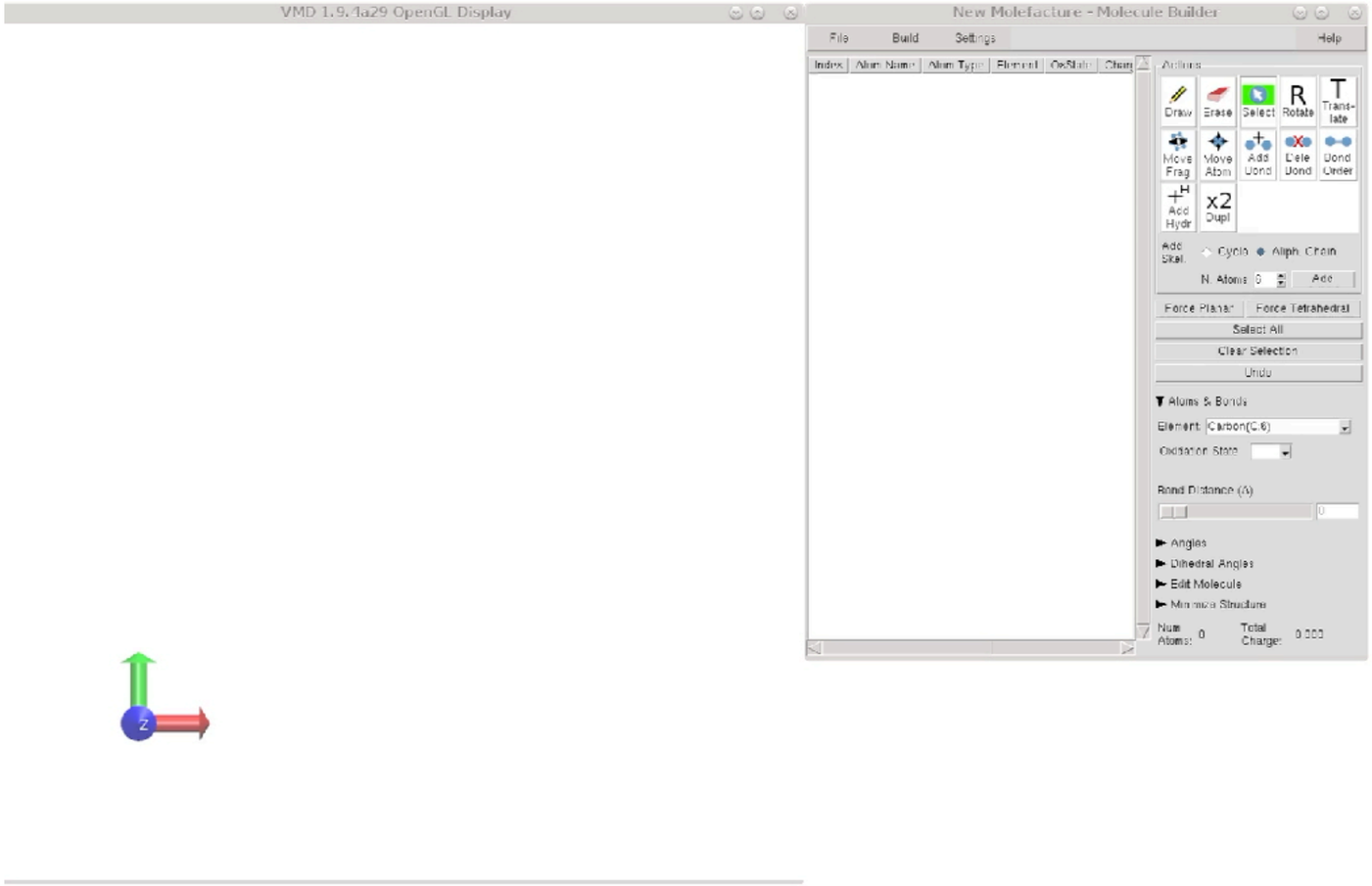




Small Molecules Modeling in VMD

Molefacture Interface

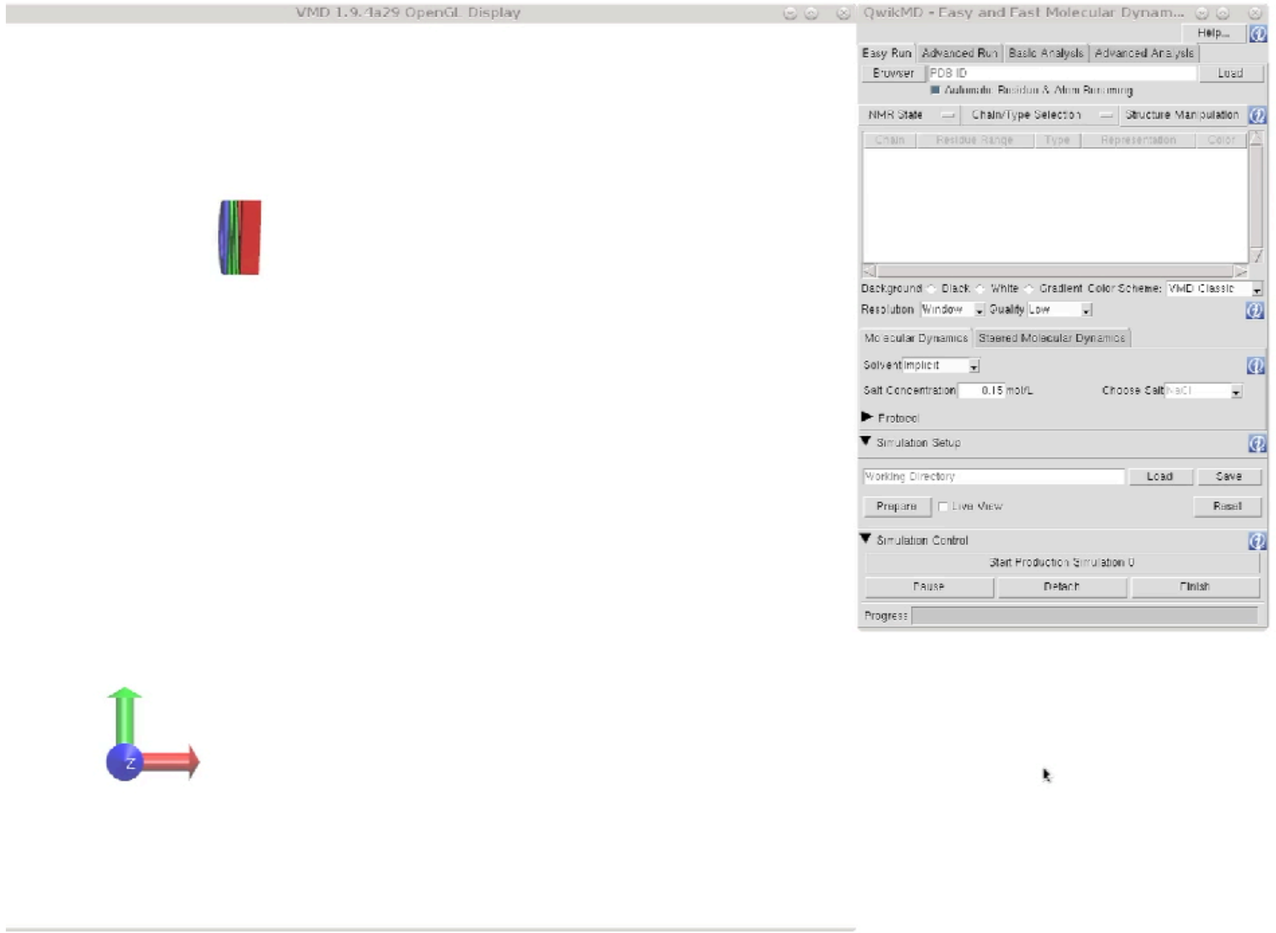
- Design Molecules from Scratch
- Edit Existing Molecules
- Use Templates for Quick Design
- Molecule and Functional Groups Library
- Minimize Structure with NAMD or OpenBabel
- Protein Editor
- Export Structure to:
  - PSF/PDB
  - MOL2
  - XYZ
- **Interface with ffTK and QwikMD**



Integrated Molecular Modeling Environment

Molecular Tools Interface

- Contiguous Use of the Modeling tools
- Direct Communication Between the Tools
- **Easy-to-Use**
- **No Scripting Required**



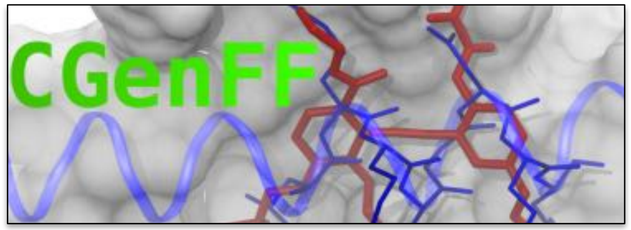
Molecular Modeling Environment

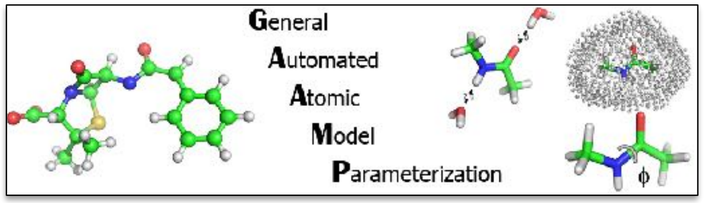
External Tools

Molecular Tools Interface

- Assign Atoms' Type and Parameters with CGenFF Server
- Parameters Refinement with ffTK and GAAMP
- Structure Refinement with MDFF Gui
- VMD Modeling Ecosystem

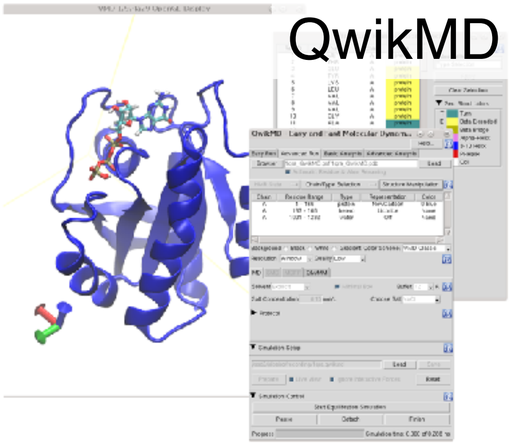
Alex Mackerell – University of Maryland



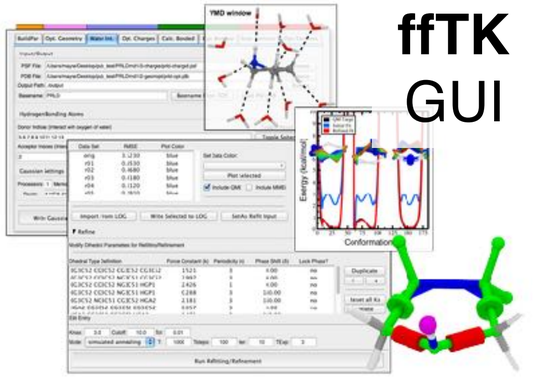


Benoit Roux – University of Chicago

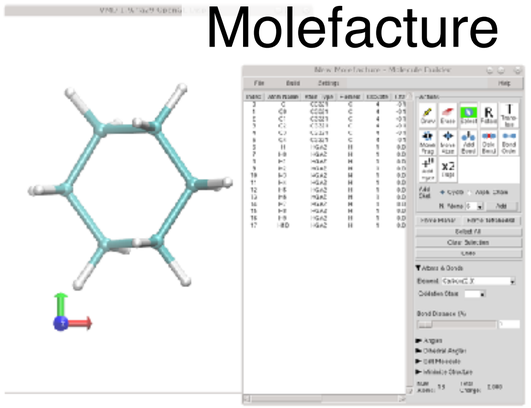
VMD Modeling Tools



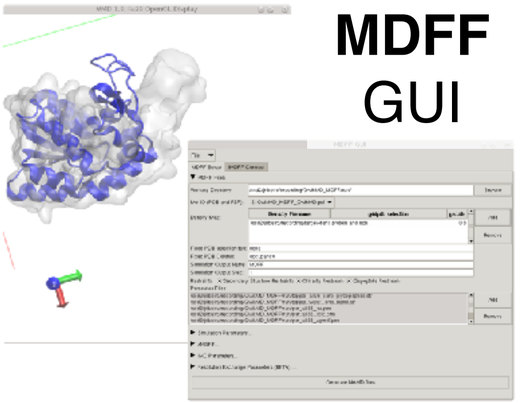
QwikMD



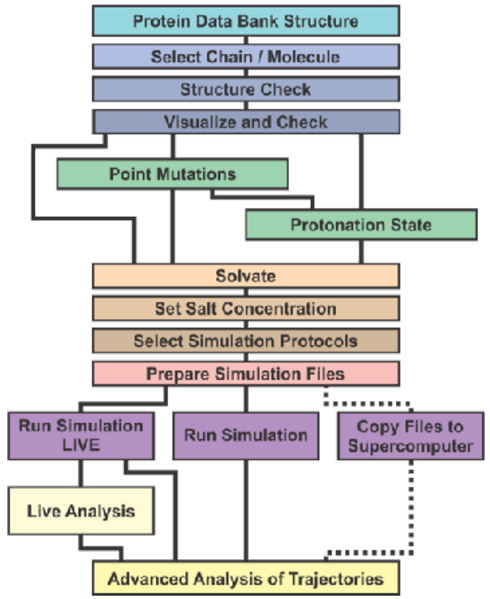
ffTK GUI



Molefacture



MDFF GUI

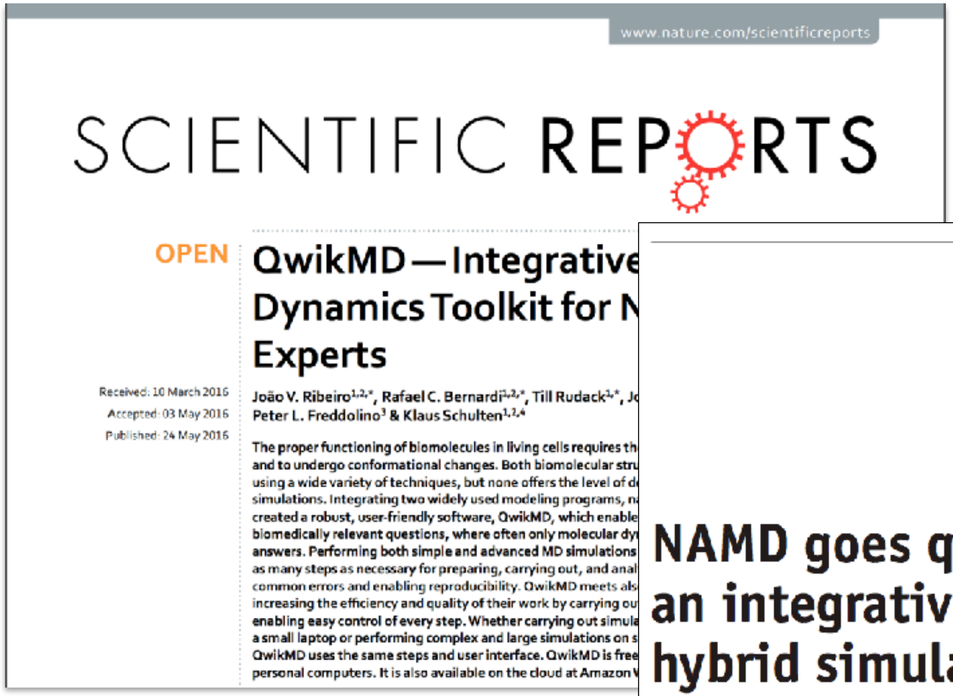


QwikMD Papers

QwikMD:

- Scientific Reports
- BPS 2016
- BPS 2017
- BPS 2018
- ACS 2018
- **ACS 2019 (Fall)**

[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

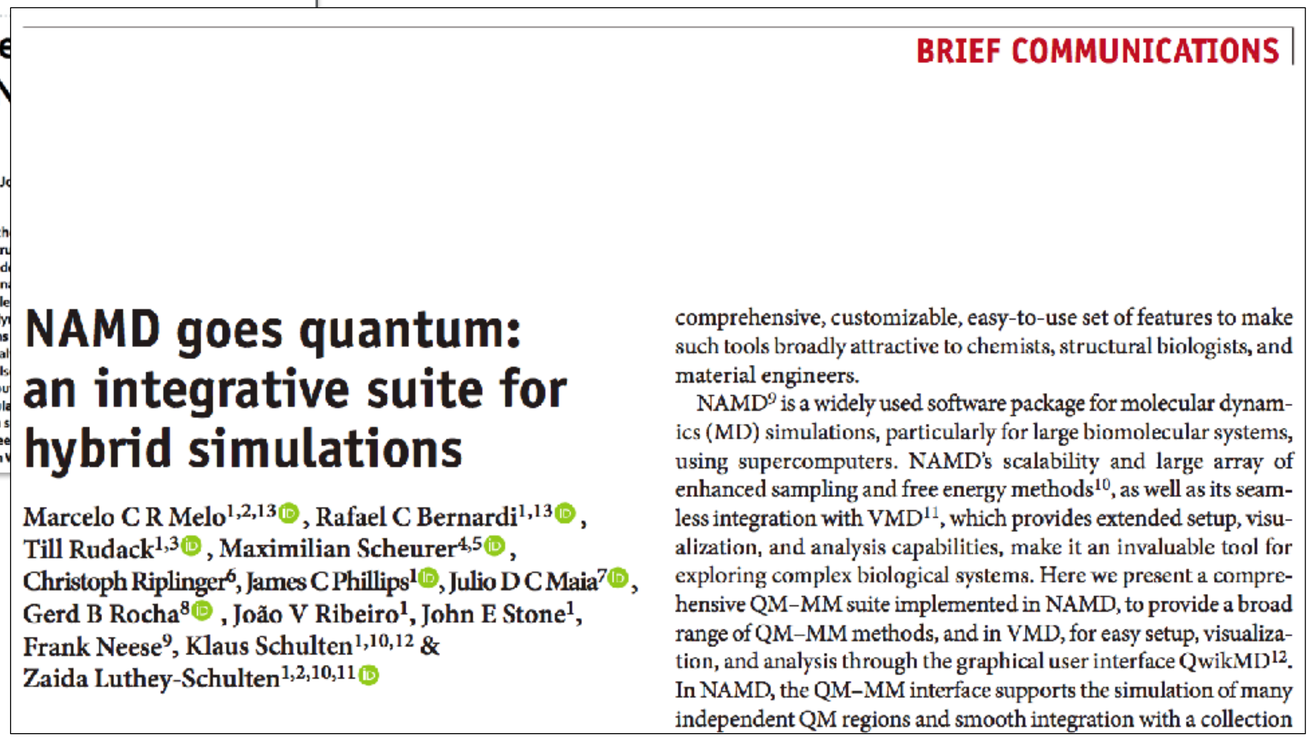
QwikMD—Integrative Dynamics Toolkit for N Experts

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

João V. Ribeiro[1,2,*], Rafael C. Bernardi[1,2,*], Till Rudack[3,*], 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

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

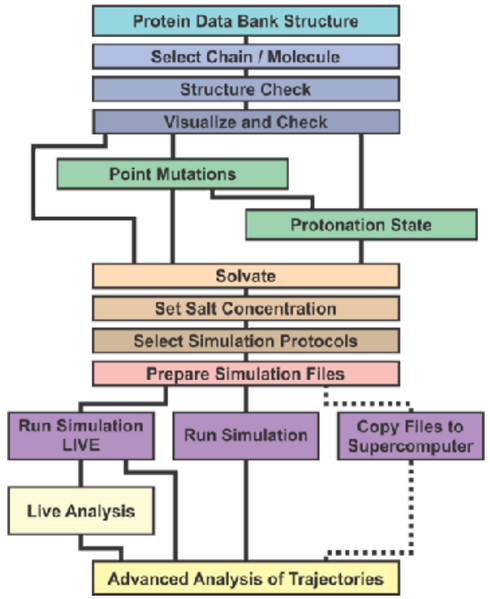

BRIEF COMMUNICATIONS

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



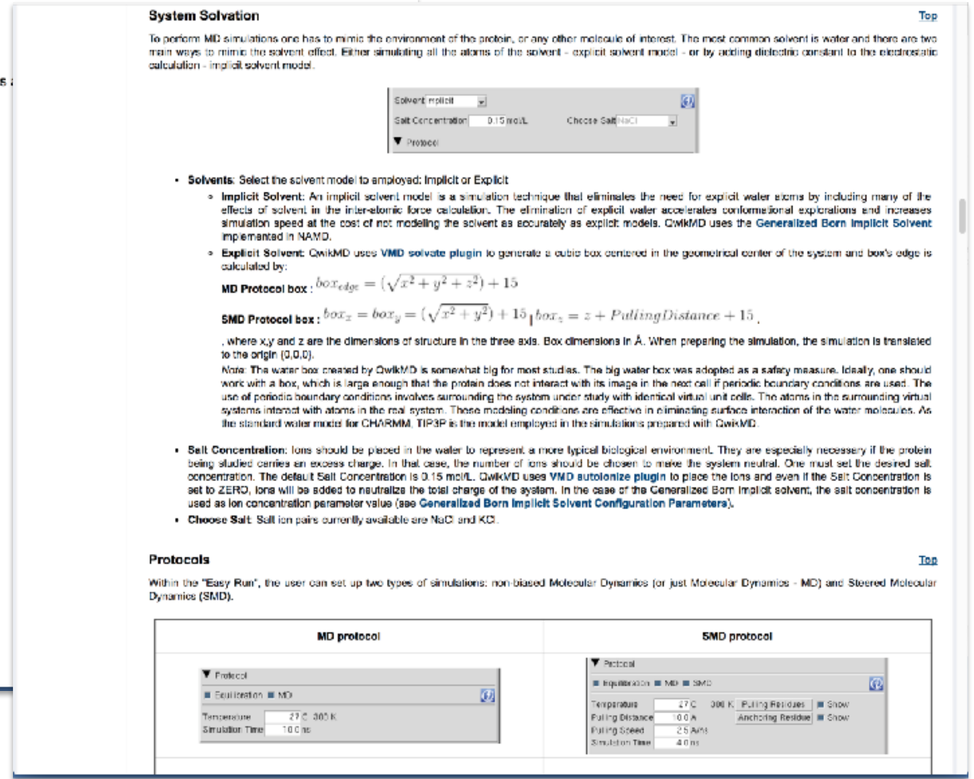
Dissemination, Documentation and User Support

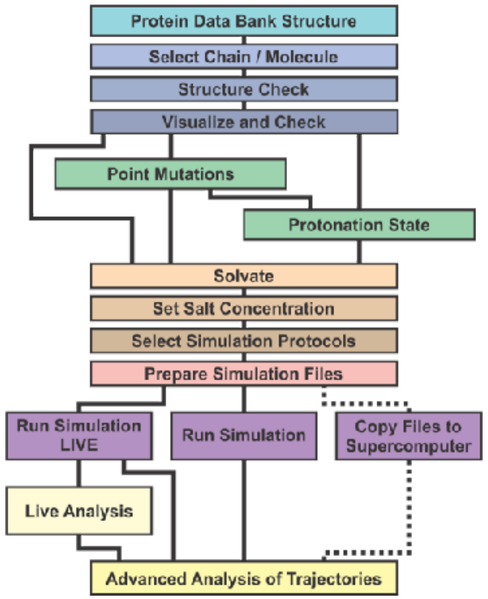
www.ks.uiuc.edu/Research/qwikmd

User's Guide

Webpages:

- Home page
- User's Guide Page



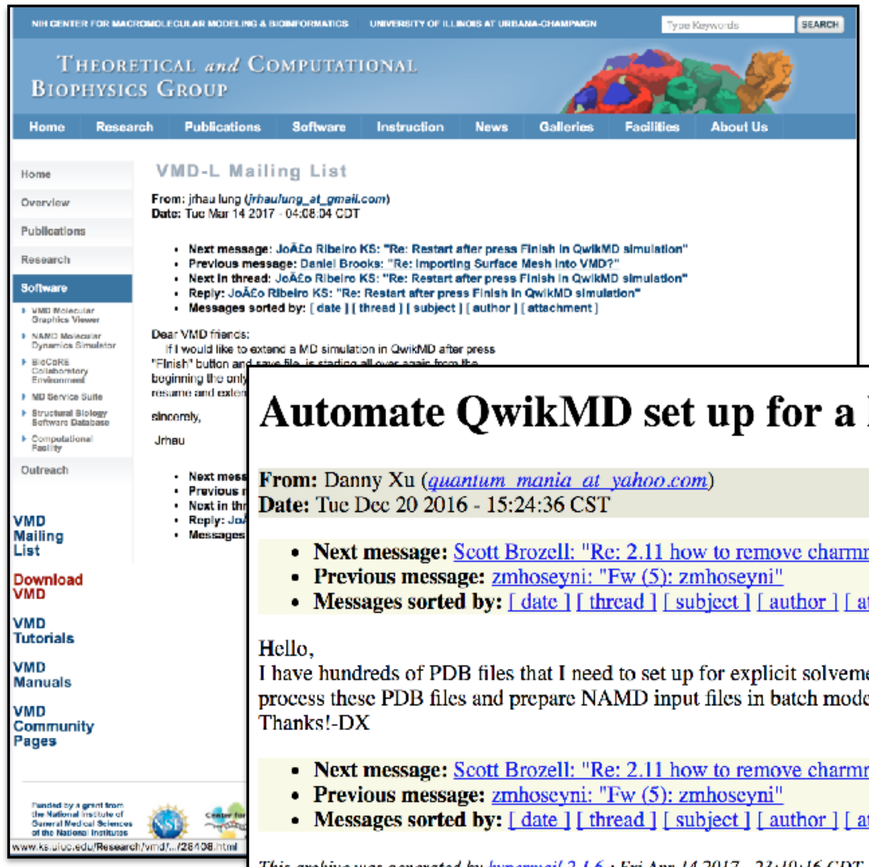


Dissemination, Documentation and User Support

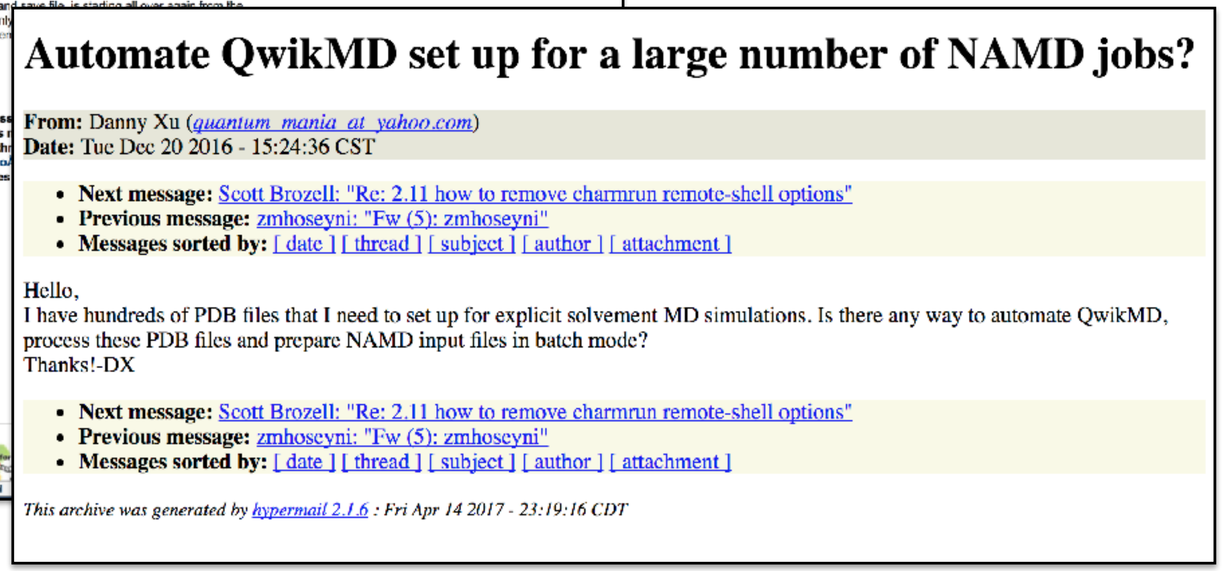
Webpages:

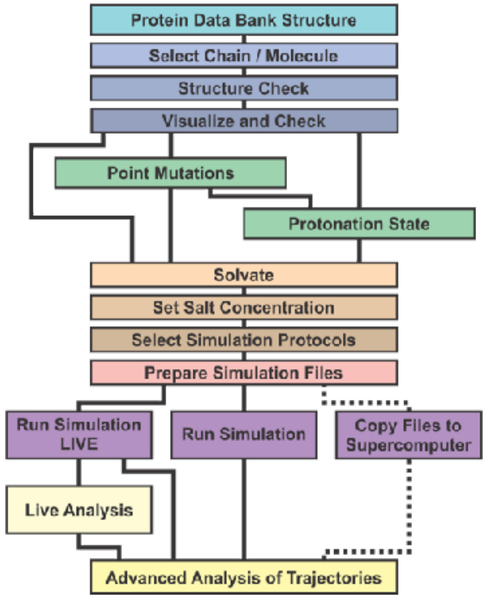
- Home page
- User's Guide Page
- VMD Mailing List
- NAMD Mailing List

vmd-l@ks.uiuc.edu



namd-l@ks.uiuc.edu





QwikMD beta Version – Latest Developments

www.ks.uiuc.edu/Research/qwikmd

QwikMD beta:

- Latest Implementations
- Bug Fixes
- Available Before VMD Release

Availability

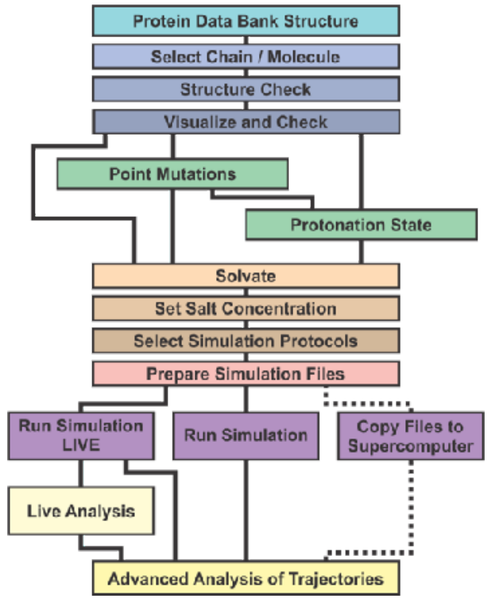
QwikMD is available free of charge on VMD 1.9.3 and newer.

Download VMD for free here

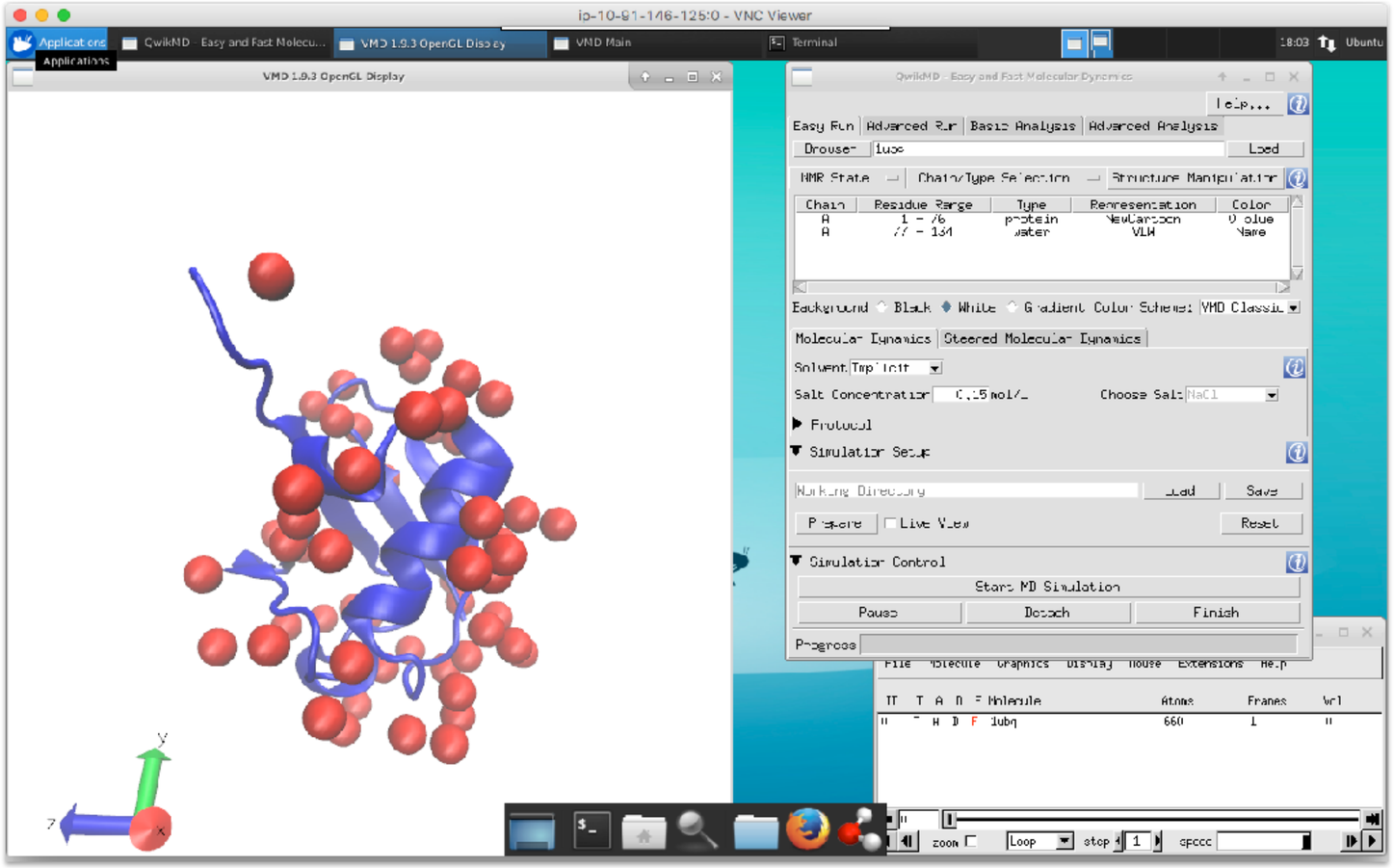
To perform Molecular Dynamics simulations you will also need the widely employed **NAMD** program, which is available free of charge **here**.

QwikMD beta Linux and **QwikMD beta (Windows running VMD 1.9.3)** . The latest version of the QwikMD including the most recent bug fixes can be downloaded **here** **(last update on March 28, 2019)**. 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

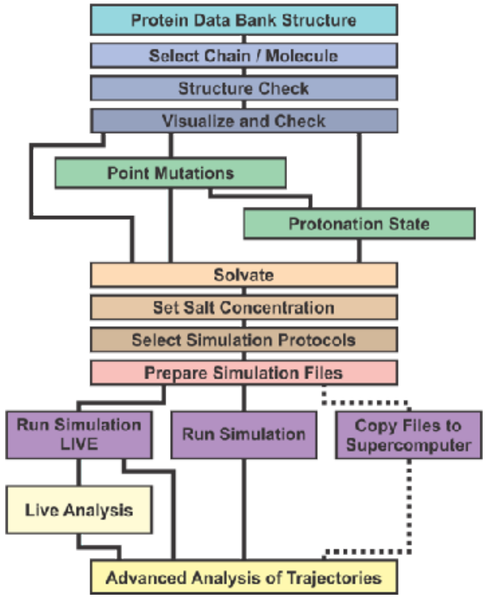


Amazon Web Services:

- 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™

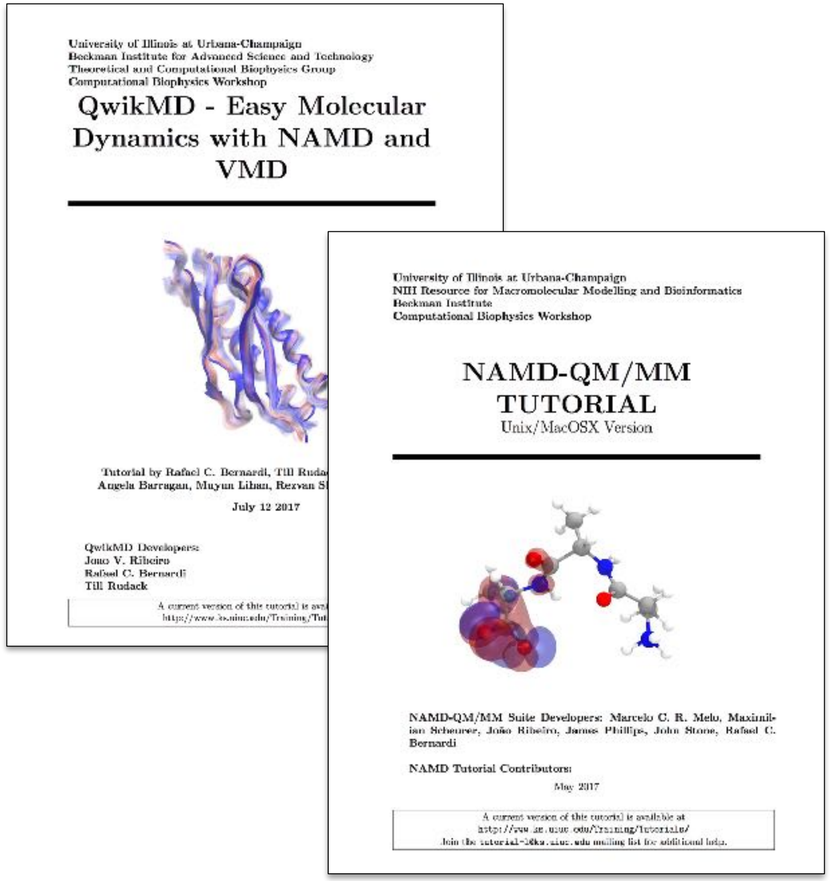


Training others...

Webpages:

- Home page
- User's Guide Page
- VMD Mailing List
- 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

July 12 2017

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Beckman Institute
Computational Biophysics Workshop

NAMD-QM/MM TUTORIAL
Unix/MacOSX Version

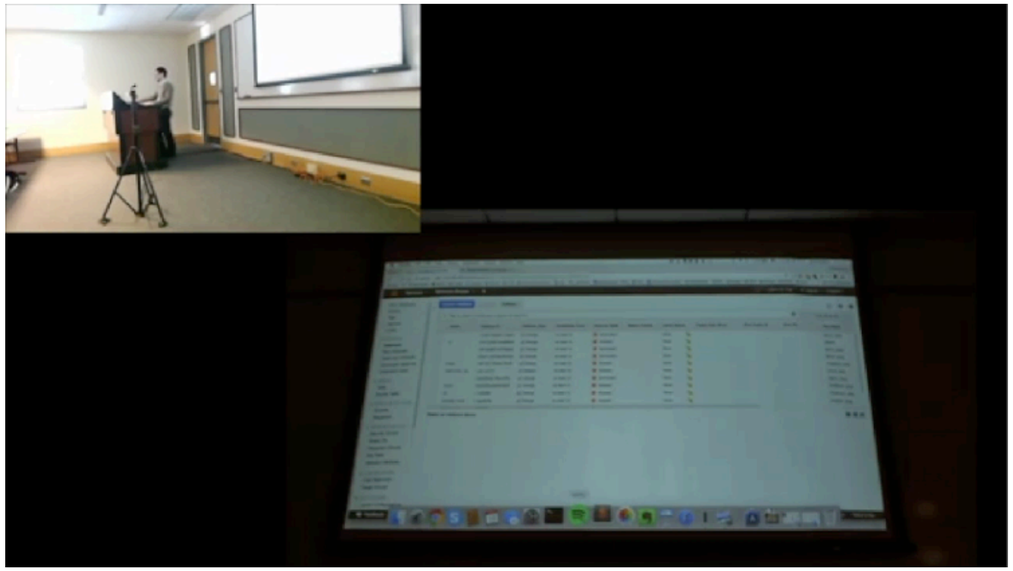
NAMD-QM/MM Suite Developers: Marcelo C. R. Melo, Maximilian Scheurer, João Ribeiro, James Phillips, John Stone, Rafael C. Bernardi

NAMD Tutorial Contributors:

May 2017

QwikMD on Amazon

Workshop Live-Streamed on Facebook



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