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# Q - a MD program

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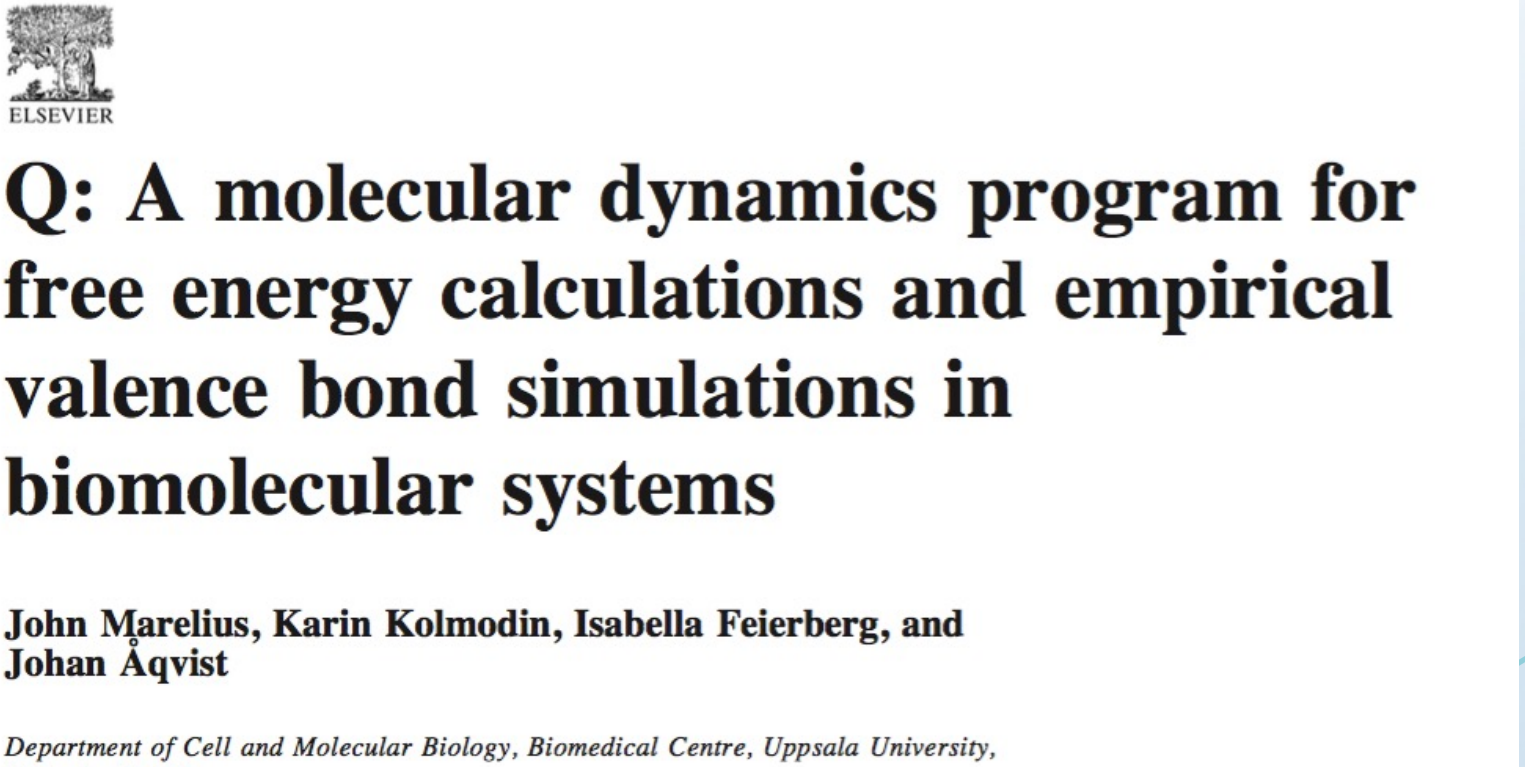
UNIVERSITY OF TROMSØ

# Todays focus

- Molecular dynamics program: Q
- Graphical user interface to Q: Qgui

# Q

- Publication: Marelius, J., Kolmodin, K., Feierberg, I., & Åqvist, J. (1998). Journal of Molecular Graphics & Modelling, 16, 213–225.



ELSEVIER

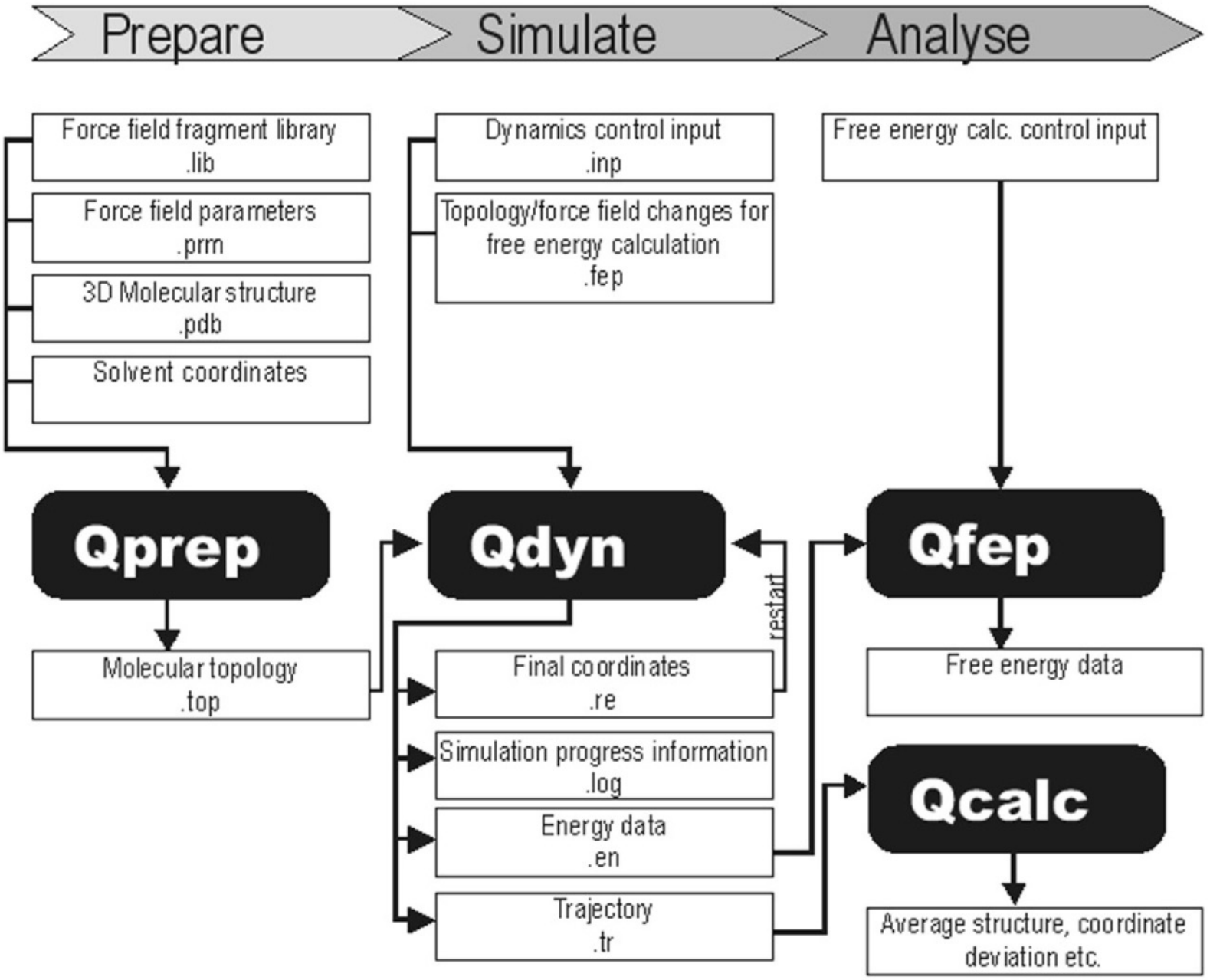
**Q: A molecular dynamics program for free energy calculations and empirical valence bond simulations in biomolecular systems**

**John Marelius, Karin Kolmodin, Isabella Feierberg, and Johan Åqvist**

*Department of Cell and Molecular Biology, Biomedical Centre, Uppsala University,*

# Q

- Consists of:
  - Qprep - used to create topology
  - Qdyn - used to run MD
  - Qfep - used to post-process data
  - Qcalc - used to analyze data

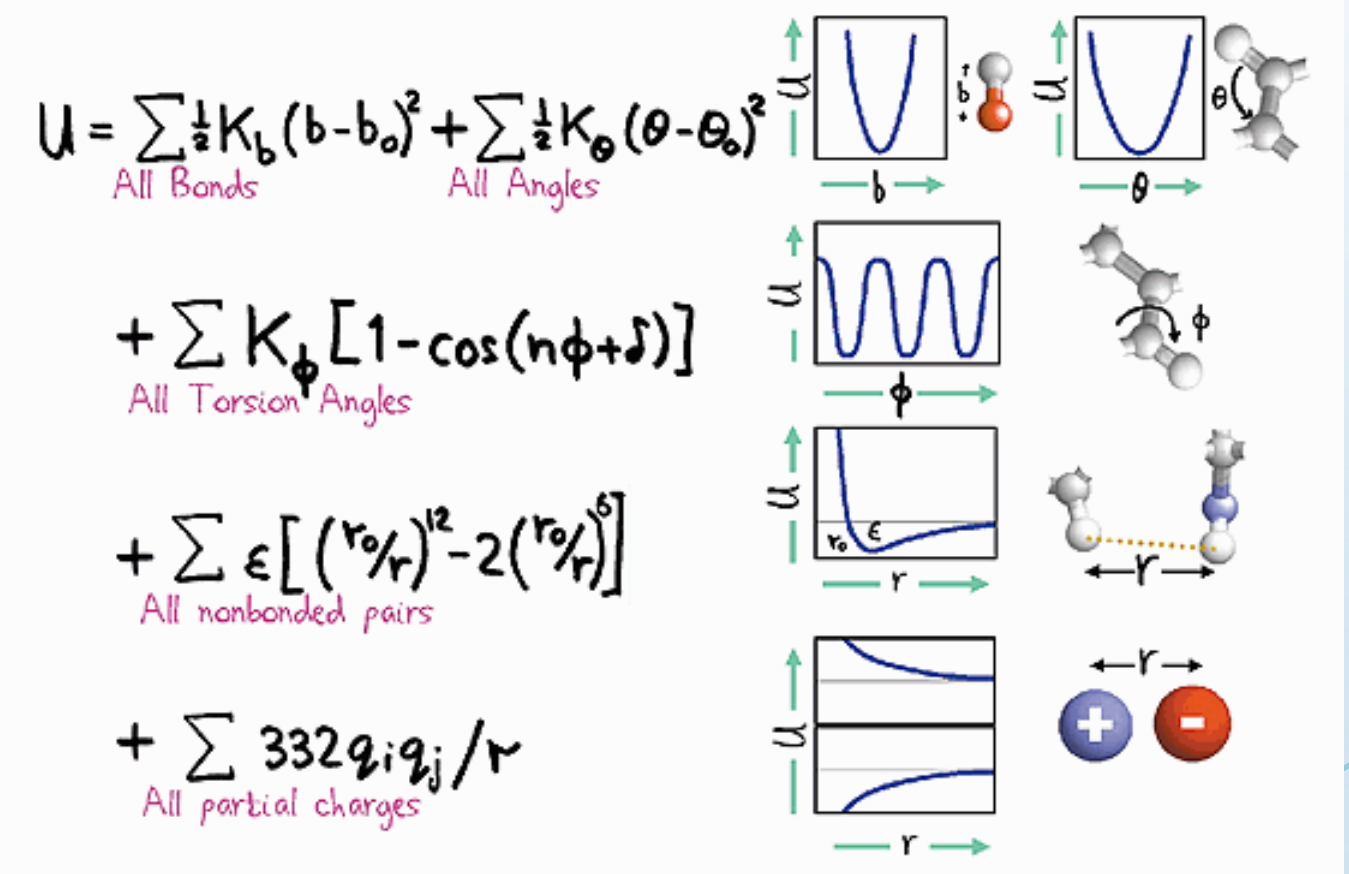

Prepare
Simulate
Analyse
Force field fragment library
.lib
Force field parameters
.prm
3D Molecular structure
.pdb
Solvent coordinates
Dynamics control input
.inp
Topology/force field changes for free energy calculation
.fep
Free energy calc. control input
Qprep
Qdyn
Qfep
Molecular topology
.top
Final coordinates
.re
restart
Free energy data
Simulation progress information
.log
Energy data
.en
Qcalc
Trajectory
.tr
Average structure, coordinate deviation etc.

# Qprep - creating topology

- Topology describes the connectivity of the molecules
- Atomic charges is included in topology
- Force field parameters must be specified

# Qprep - creating topology

- Levitt: Nature Structural Biology 8, 392 - 393 (2001)



# Qprep - creating a topology

- Atomic coordinates of the system must be provided (PDB file)
- H-atoms are automatically added if missing
- Library file: describes the residues
- Parameter file: describes the force field terms

# Qprep

Library file format:

```
{ALA}                  ! Alanine
    [info]
        SYBYLtype  RESIDUE     !SYBYL substructure type
    [atoms]
         1 N        N           -0.5000 !At. no., name, type, charge
         2 H        H            0.3000
         3 CA       CT           0.1400
         4 HA       HC           0.0600
         5 CB       CT          -0.1800
         6 HB1      HC           0.0600
         7 HB2      HC           0.0600
         8 HB3      HC           0.0600
         9 C        C            0.5000
        10 O        O           -0.5000
    [bonds]                   !connect i -- j
       N    H
       N    CA
       CA   HA
       CA   CB
       CB   HB1
       CB   HB2
       CB   HB3
       CA   C
       C    O
    [connections]   !tail and head connections
        head     N
        tail     C
    [impropers]
        H    N    -C    CA
        O    C    CA    +N
    [charge_groups] !charge groups, with switch atom first
        N    H    CA    HA
        CB   HB1  HB2   HB3
        C    O
*-------------------------------------------------------------
```

# Qprep - creating a topology

- Parameter file format:
  - [atom_types]
  - [bonds]
  - [angles]
  - [torsions]
  - [impropers]

# Preparing coordinates

- Q reads the PDB file format
- Need to add missing residues
- Hydrogens does not need to be provided
- Disulphide bonds must be specified
- Protonation states must be given
- You need to tell the program about His/Hid/Hie/Hip residues

# Preparing coordinates

- Typically done in other programs
  - Maestro
  - ICM
  - …
- You must be able to map your atom names and residue names to the molecular library file

# Creating the topology file

When you are ready with:

- PDB file prepared
- Molecular library files describing all components of your system
- You need to specify solvent and add this to your system (done in Qprep)
- Choose a simulation center and size of your system

# Qdyn - running MD simulations

- Qdyn is the part of Q that actually carries out the simulations
- Gives you
  - log files
  - dcd files (trajectories)
  - en(e) files (energies)
  - re files (restart)

# Qdyn - input

- Topology is needed to start the MD simulations
- You will also need a fep file
  - Q-atoms
  - FEP protocol

# Odyn - input

[**MD**]:Basic simulation data.

| **keyword** | **value** | **comment** |
|---|---|---|
| steps | Number of MD steps. | Required. |
| stepsize | MD stepsize ($\Delta$t) (fs). | Required. |
| temperature | Target temperature (K). | Required. |
| bath_coupling | Temperature bath relaxation time T (fs)[30]. | Optional, default 100 fs. Must be $\geq$ stepsize. |
| separate_scaling | Enable (on) or disable (off) separate temperature scaling of solute and solvent. | Optional, default on. |
| random_seed | Integer value to seed the random number generator. | Optional. Used only for random velocities. Change number to get a different set of velocities. |
| initial_temperature | Temperature (K) of Maxwellian distribution for random velocities. | Optional except when no restart file is used. Use *only* when velocities should be randomised! |
| shake_solvent | Enable (on) or disable (off) shake constraining of bonds and angles of water. | Optional, default on. We recommend the use of shake for water. |
| shake_solute | Shake constraining of solute bonds on or off. | Optional, default off. |

# Qdyn - a minimal input file

| Data | | Description |
|---|---|---|
| [MD] | | Basic data for the simulation |
| steps | 2000 | Number of steps |
| stepsize | 1.0 | Step size (fs) |
| temperature | 1 | Temperature (K) |
| initial_temperature | 1 | Temperature (K) for Maxwell-distributed initial velocities |
| [files] | | File names for input and output |
| topology | molecule.top | Topology file |
| final | molecule.re | Restart to write at end of simulation |

# Qfep - analyzing free energies

- Qfep allows free energies to be calculated based on the energy files

| Line | Data | Description |
|---|---|---|
| 1 | 11 | Number of energy files |
| 2 | 2 0 | Number of states, number of predefined off-diagonal elements (from .fep-file, 0 means redefine) |
| 3 | 0.596 100 | kT, number of points to skip in each energy file |
| 4 | 40 | Number of gap bins |
| 5 | 20 | Minimum number of points per bin |
| 6 | 12.3 | Energy shift $\Delta\alpha_{ij}$ (for states≠1) |
| 7 | 1 | Number of off-diagonal elements ≠0 |
| 7.1 | 1 2 18.1 0.32 0.0 2.0 | i, j, $A_{ij}$, $\mu_{ij}$, $\eta_{ij}$, $r0_{ij}$ |
| 8 | 1 -1 | Linear combination of states defining the reaction coordinate $(\varepsilon_1 - \varepsilon_2)$. |
| 9 | md_00.ene | List of energy files |
| 10... | md_01.ene | |
| ...19 | md_10.ene | |

# Qcalc - analyzing structural features

- Qcalc will allow you to examine more specific details of your simulations as a function of time
  - H-bond distance
  - RMSF
  - RMSD
  - Entropy
  - …

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# Qgui - a graphical interface to Q

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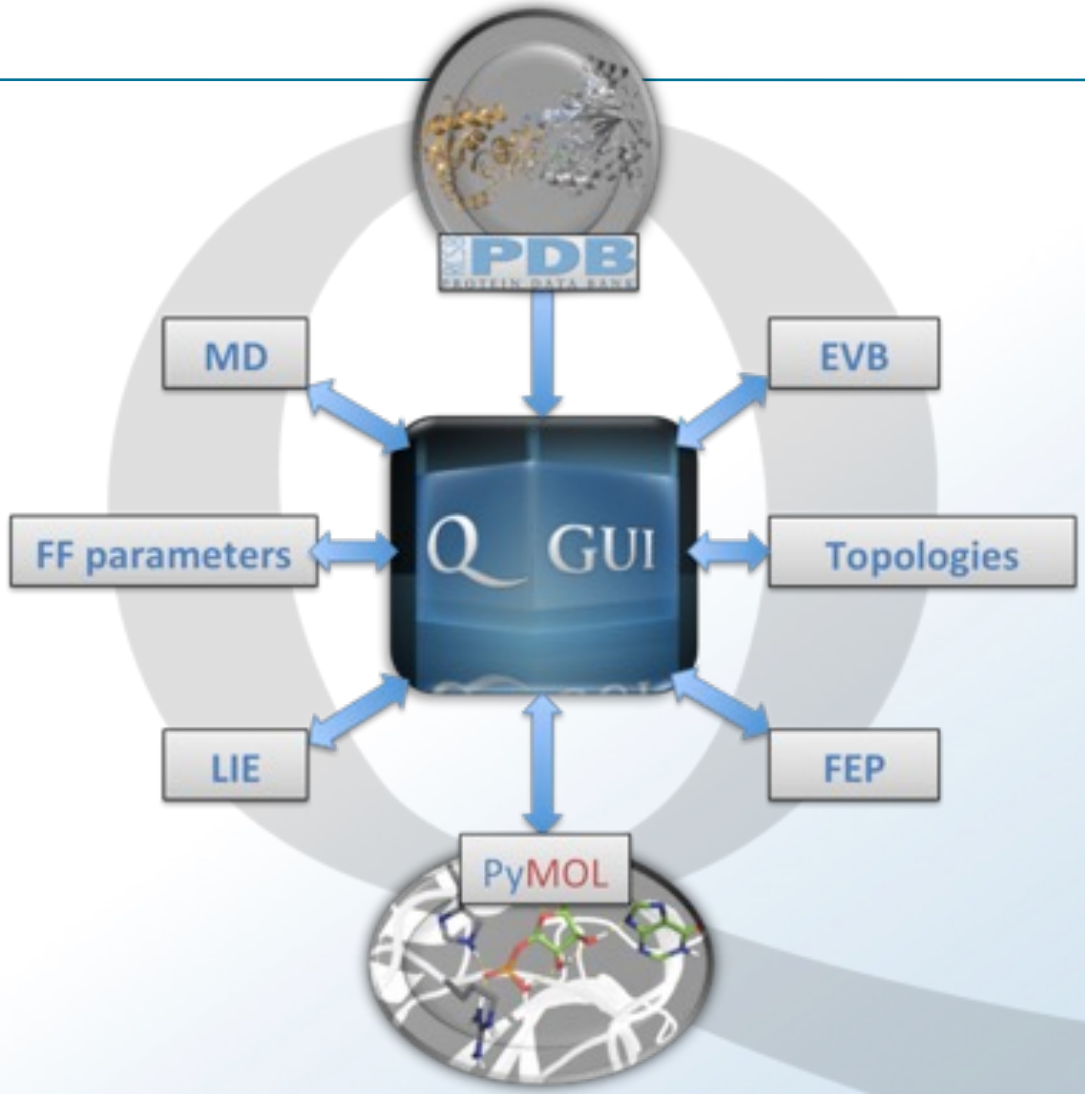
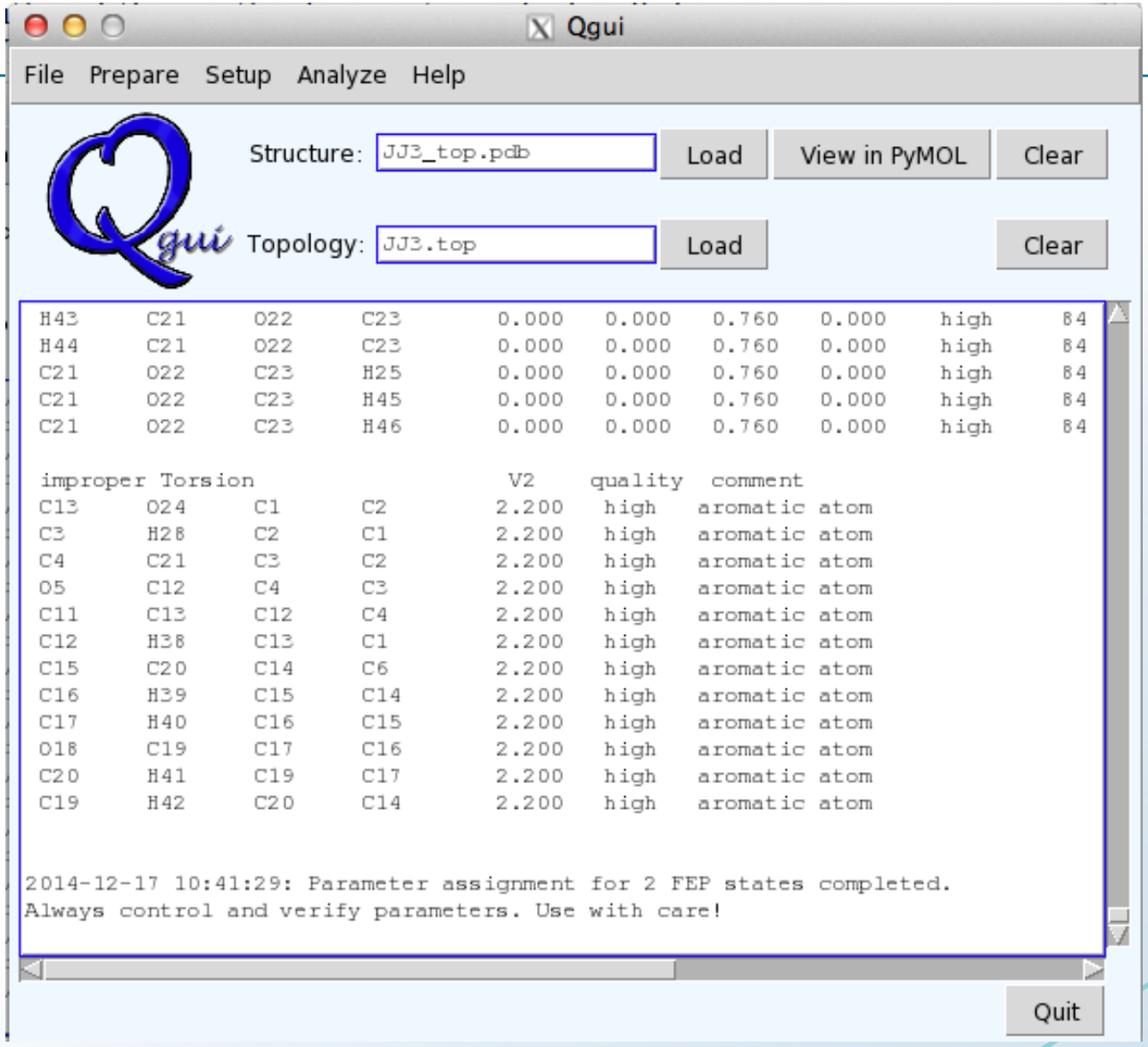
# Qgui

- Written in Tkinter (python)
- Runs on all operating systems
- It is located in your bin (home/username/bin)
- There is a hidden fold in your home folder:
  - .qgui
  - contains settings and submission details

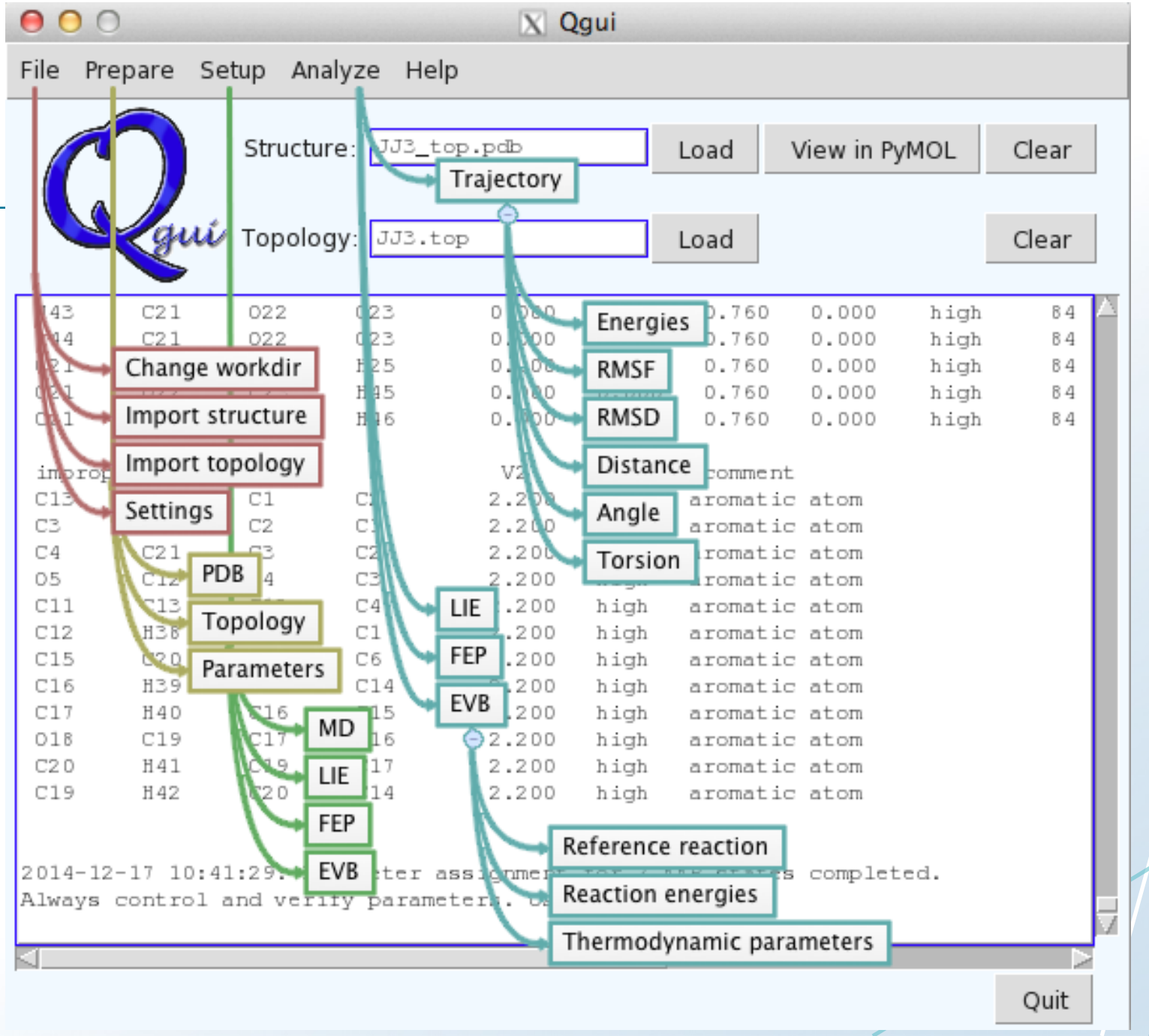
# Qgui



# Qgui - main window



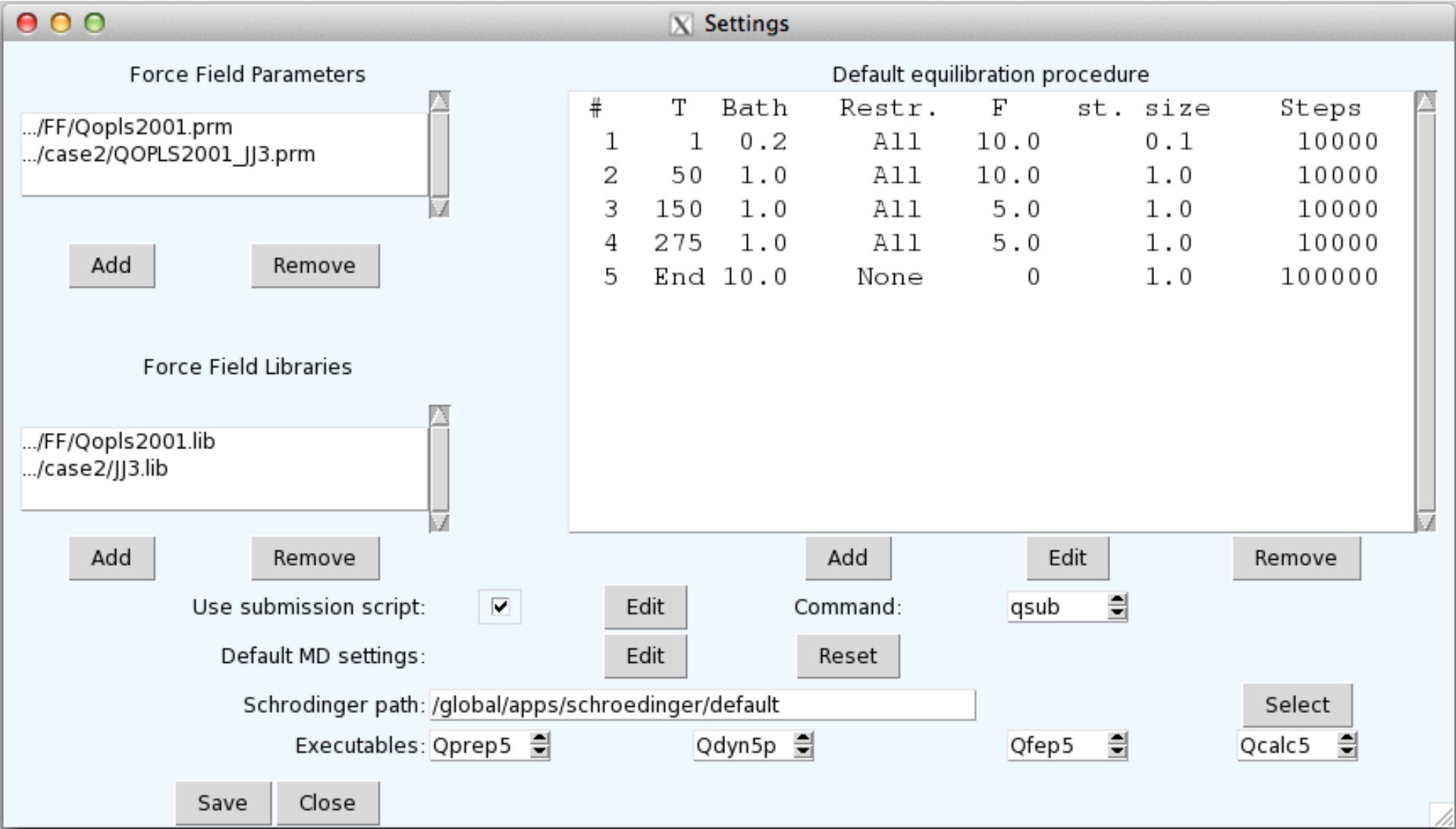
# Qgui


Qgui
File
Prepare
Setup
Analyze
Help
Structure:
JJ3_top.pdb
Load
View in PyMOL
Clear
Trajectory
Topology:
JJ3.top
Load
Clear
Change workdir
Import structure
Import topology
Settings
PDB
Topology
Parameters
MD
LIE
FEP
EVB
Energies
RMSF
RMSD
Distance
Angle
Torsion
LIE
FEP
EVB
Reference reaction
Reaction energies
Thermodynamic parameters
Always control and verify parameters.
Quit

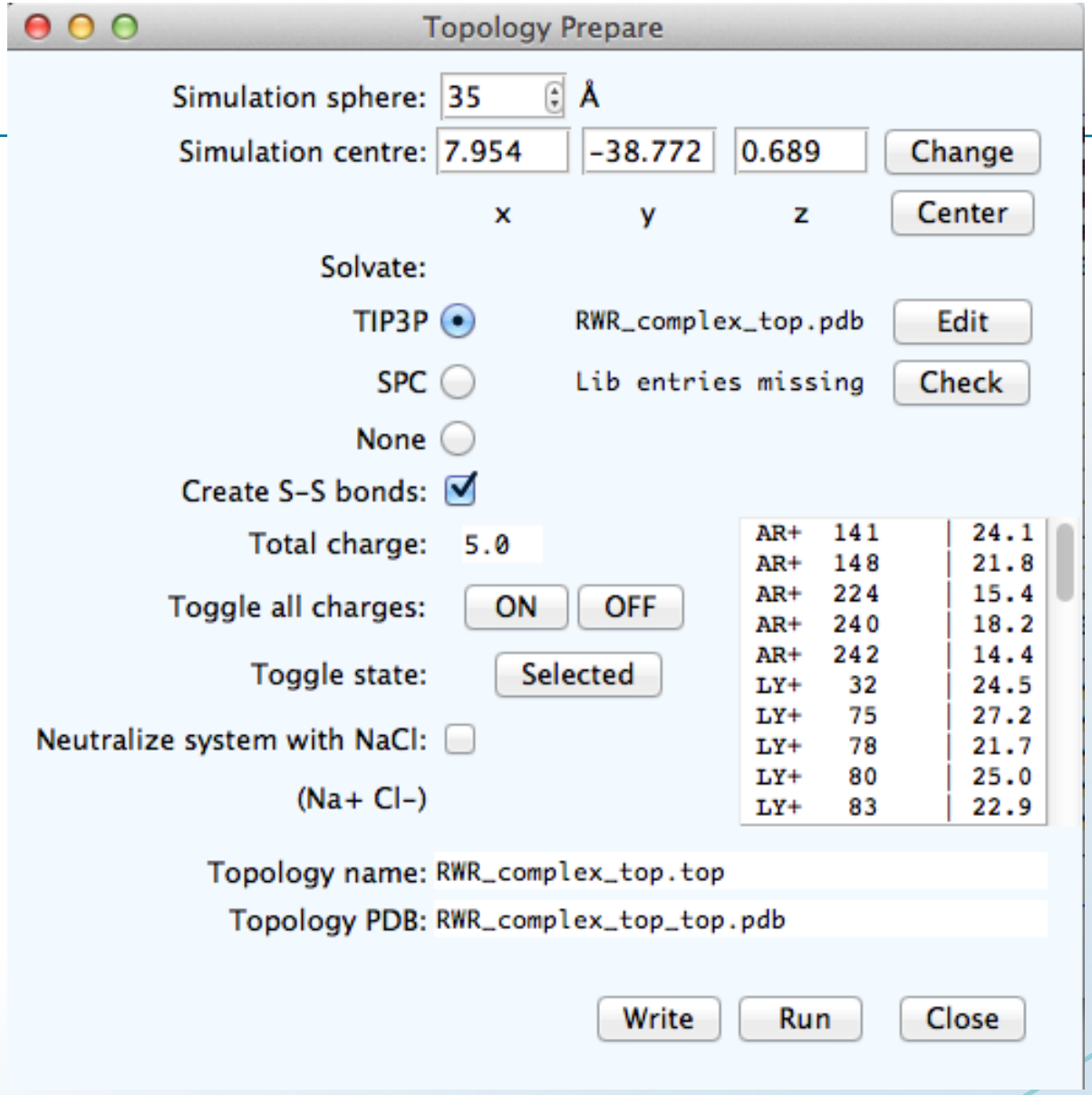
# Qgui - loading structures

- Qgui can load pdb files directly from PDB by typing their pdb code.
- After the PDB has been loaded - you can then prepare missing parameters and library files
- Remember to add additional prm and lib files in the settings menu.

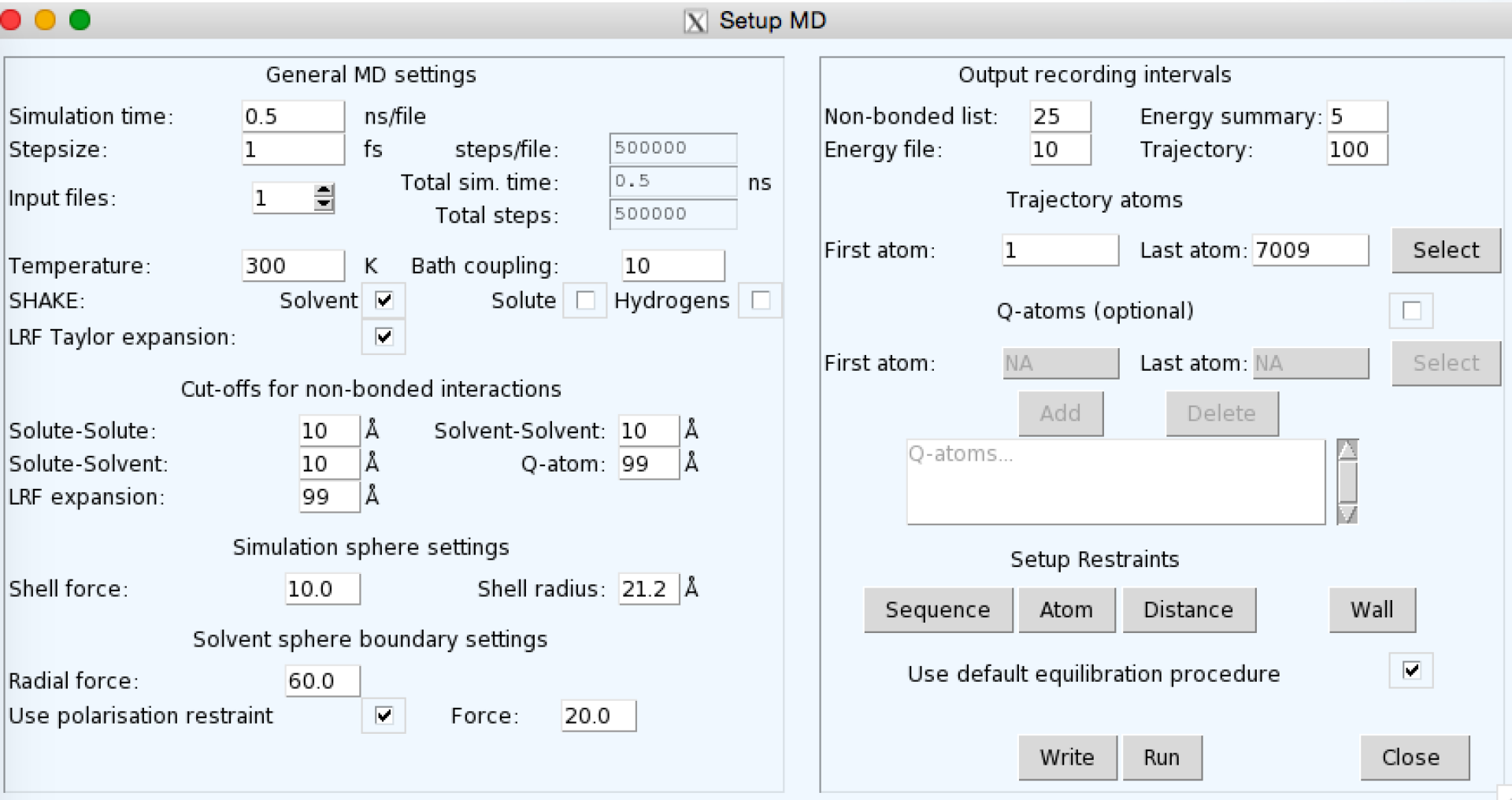
# Qgui - settings window



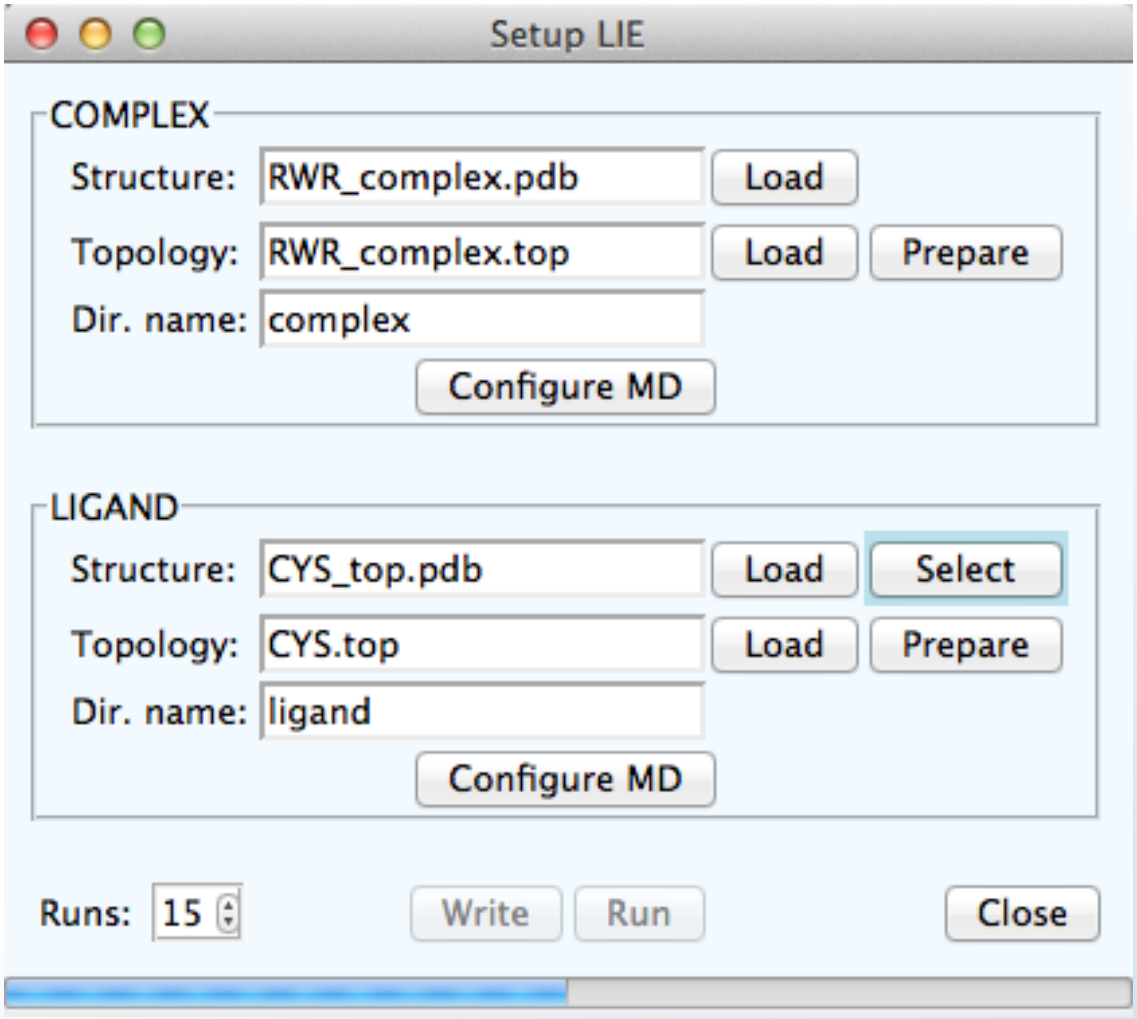
# Qgui - preparing topology

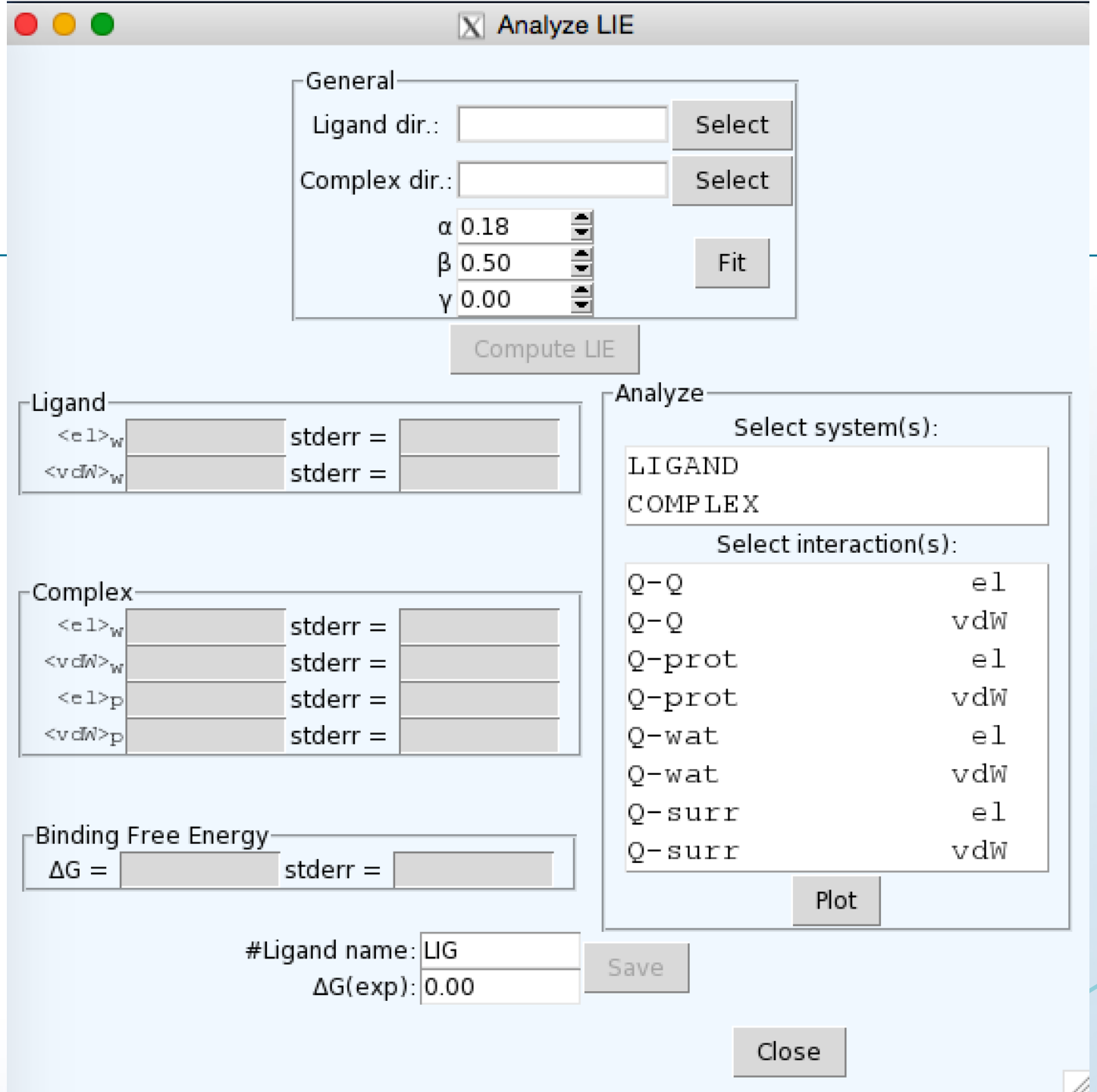


# Qgui – MD setup



# Qgui - Setup LIE




Analyze LIE
General
Ligand dir.:
Select
Complex dir.:
Select
α 0.18
β 0.50
γ 0.00
Fit
Compute LIE
Ligand
<el>w
stderr =
<vdW>w
stderr =
Complex
<el>w
stderr =
<vdW>w
stderr =
<el>p
stderr =
<vdW>p
stderr =
Binding Free Energy
ΔG =
stderr =
Analyze
Select system(s):
LIGAND
COMPLEX
Select interaction(s):
Q-Q el
Q-Q vdW
Q-prot el
Q-prot vdW
Q-wat el
Q-wat vdW
Q-surr el
Q-surr vdW
Plot
#Ligand name: LIG
ΔG(exp): 0.00
Save
Close

# Qgui - fitting LIE data

Fit LIE parameters

Import LIE results

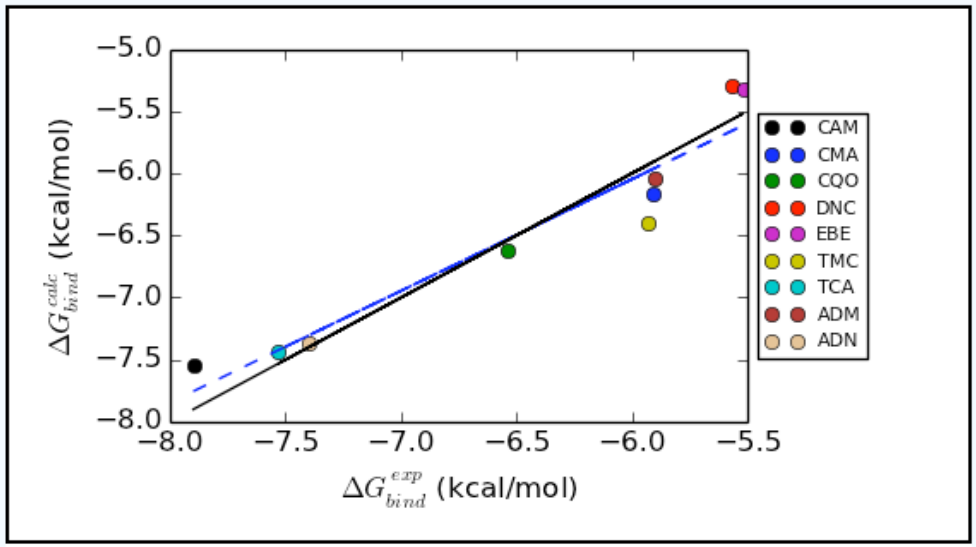
Add | Edit selected | Delete selected | Clear table

| #NAME | β | ΔE(el) | α | ΔE(vdW) | γ | ΔG | ΔG(exp) |
|---|---|---|---|---|---|---|---|
| CAM | 0.50 | -1.59 | 0.18 | -13.02 | -4.41 | -7.55 | -7.90 |
| CMA | 0.50 | -0.08 | 0.18 | -9.55 | -4.41 | -6.17 | -5.91 |
| CQO | 0.50 | 0.02 | 0.18 | -12.38 | -4.41 | -6.63 | -6.54 |
| DNC | 0.50 | 1.43 | 0.18 | -8.92 | -4.41 | -5.30 | -5.57 |
| EBE | 0.50 | 0.27 | 0.18 | -5.85 | -4.41 | -5.33 | -5.52 |
| TMC | 0.50 | -0.01 | 0.18 | -11.04 | -4.41 | -6.40 | -5.93 |
| TCA | 0.50 | -2.26 | 0.18 | -10.55 | -4.41 | -7.44 | -7.53 |
| ADM | 0.50 | 0.05 | 0.18 | -9.19 | -4.41 | -6.04 | -5.90 |
| ADN | 0.50 | -1.93 | 0.18 | -11.08 | -4.41 | -7.37 | -7.40 |

α 0.18 β 0.50 γ -4.407 Auto fit Reset

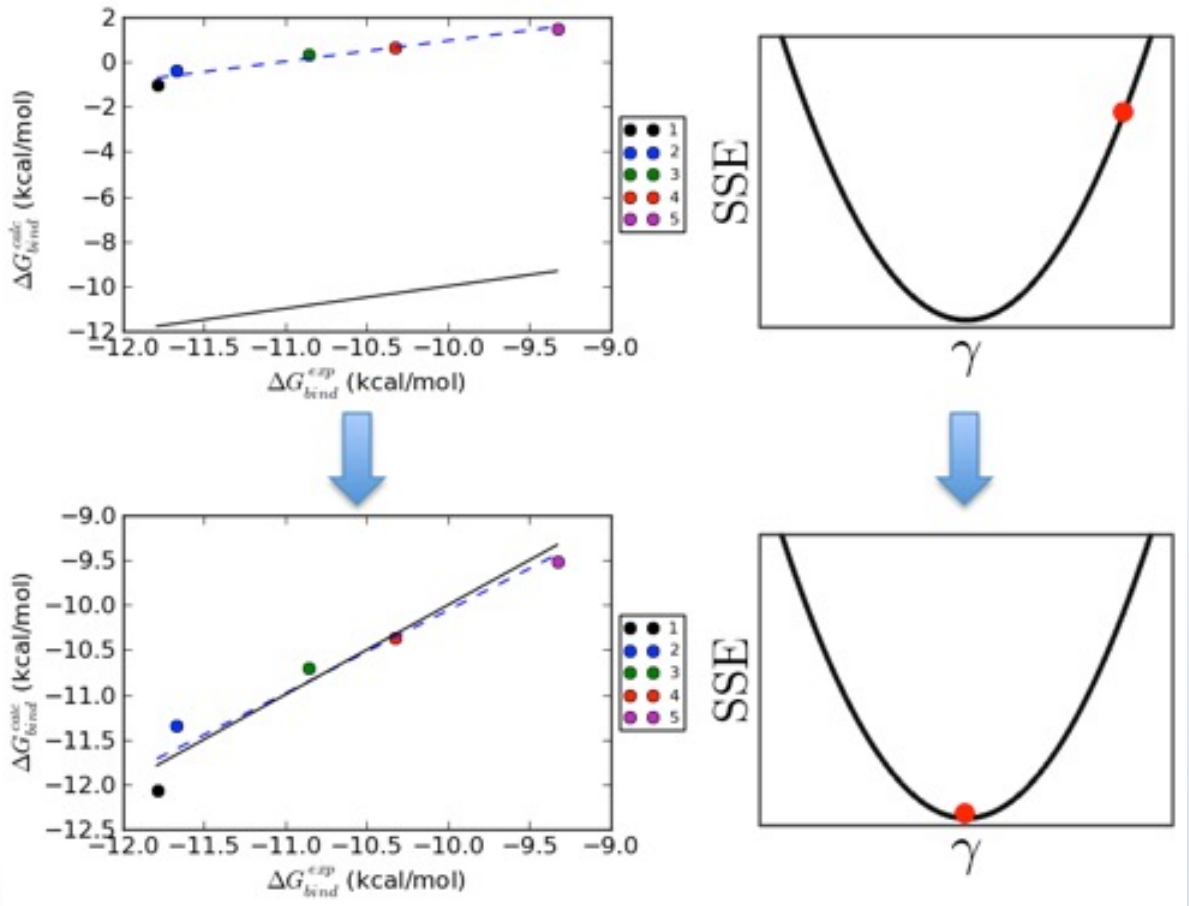
SSE = 0.491 COD = 0.923

SSE$_0$ = 0.559 COD$_0$ = 0.913




Save | Close

# Qgui - fitting LIE data



# Qgui - Setup FEP