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Q - a MD program

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Today's focus

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

Q

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



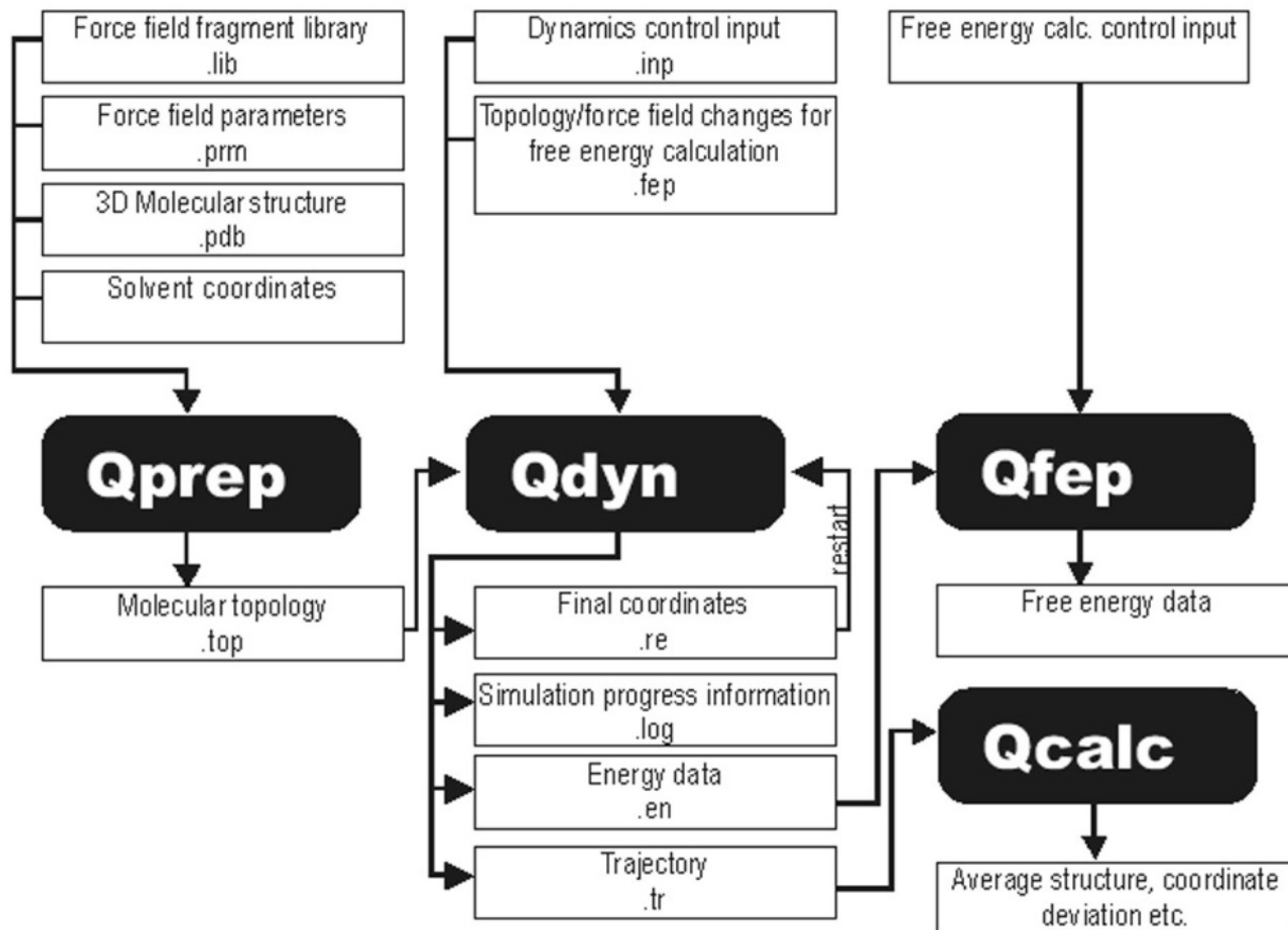
Q: A molecular dynamics program for free energy calculations and empirical valence bond simulations in biomolecular systems

John Marelus, 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

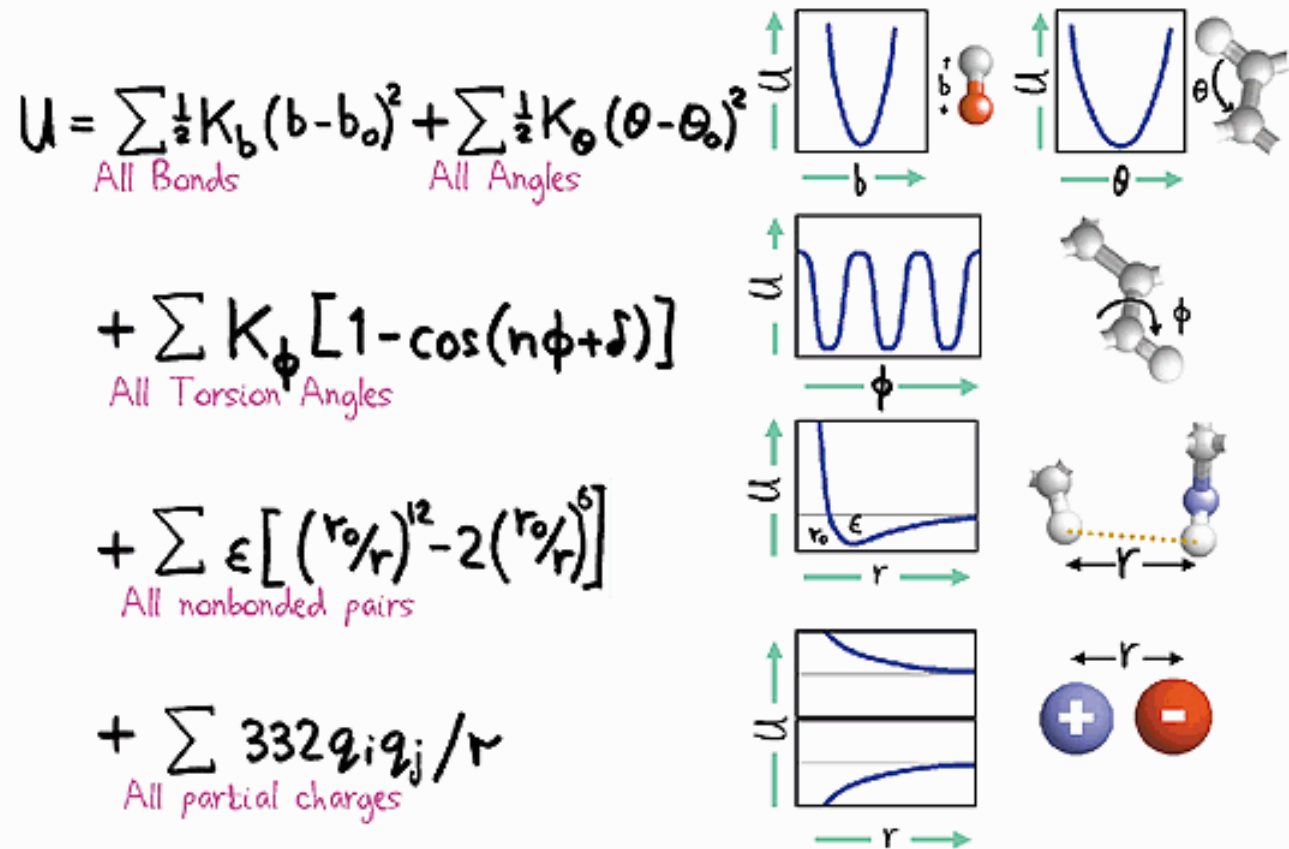


Qprep - creating topology

- 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

Odn - input

[MD]:Basic simulation data.

keyword	value	comment
steps	Number of MD steps.	Required.
stepsize	MD stepsize (Δt) (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 <i>only</i> 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 $\neq 1$)
7	1	Number of off-diagonal elements $\neq 0$
7.1	1 2 18.1 0.32 0.0 2.0	i, j, A_{ij} , μ_{ij} , η_{ij} , r_{0ij}
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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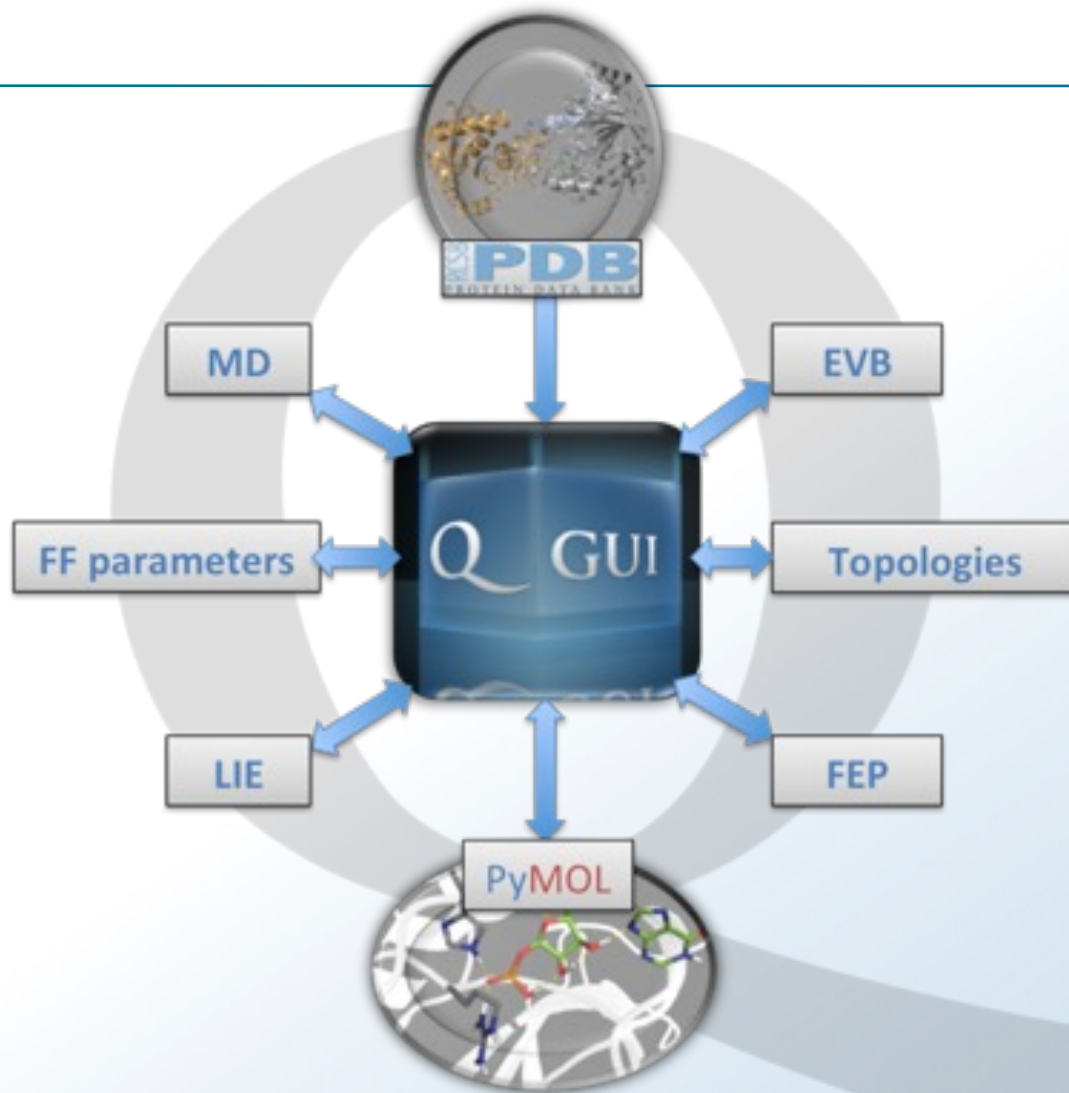
bjorn-olav.brandsdal@uit.no



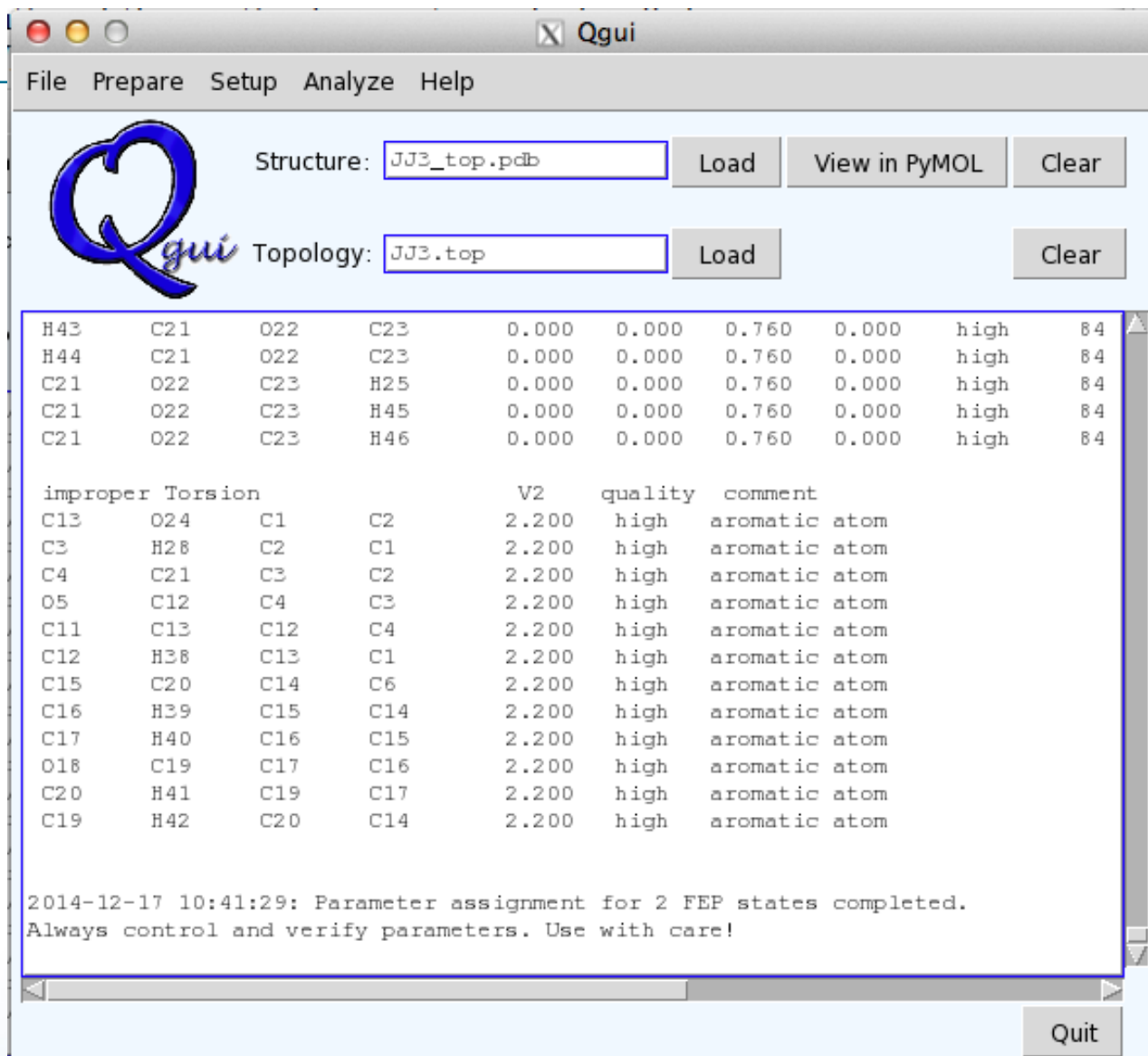
Qgui

- 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

The screenshot shows the Qgui application window with a menu bar (File, Prepare, Setup, Analyze, Help) and a main workspace. A large blue 'Q' logo with 'gui' in script is in the top left. The interface is annotated with several colored boxes and arrows indicating different functional areas:

- File Management (Red Arrows):** Arrows point from the 'File' menu to 'Change workdir', 'Import structure', 'Import topology', and 'Settings'.
- Structure and Topology (Green Arrows):** Arrows point from the 'Prepare' menu to 'PDB', 'Topology', and 'Parameters'.
- Analysis (Blue Arrows):** Arrows point from the 'Analyze' menu to 'Trajectory', 'Energies', 'RMSF', 'RMSD', 'Distance', 'Angle', 'Torsion', 'LIE', 'FEP', 'EVB', 'Reference reaction', 'Reaction energies', and 'Thermodynamic parameters'.
- Simulation (Green Arrows):** Arrows point from the 'Setup' menu to 'MD', 'LIE', 'FEP', and 'EVB'.

The main workspace contains a table of atom coordinates and a log window at the bottom.

Atom	X	Y	Z	B	Occupancy	Displacement	Temperature	Weight
143	C21	O22	O23	0.000	0.760	0.000	high	84
144	C21	O22	O23	0.000	0.760	0.000	high	84
121	H25	H25	H25	0.000	0.760	0.000	high	84
121	H45	H45	H45	0.000	0.760	0.000	high	84
121	H46	H46	H46	0.000	0.760	0.000	high	84

Log window output:

```

2014-12-17 10:41:29.123456789 Parameter assignment for the reaction completed.
Always control and verify parameters. Use the 'Verify' button to check the parameters.
  
```


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

Force Field Parameters

.../FF/Qopls2001.prm
.../case2/QOPLS2001_JJ3.prm

Add Remove

Force Field Libraries

.../FF/Qopls2001.lib
.../case2/JJ3.lib

Add Remove

Default equilibration procedure

#	T	Bath	Restr.	F	st. size	Steps
1	1	0.2	All	10.0	0.1	10000
2	50	1.0	All	10.0	1.0	10000
3	150	1.0	All	5.0	1.0	10000
4	275	1.0	All	5.0	1.0	10000
5	End	10.0	None	0	1.0	100000

Add Edit Remove

Use submission script: ☒ Edit

Default MD settings: Edit

Command: qsub

Schrodinger path: /global/apps/schroedinger/default Select

Executables: Qprep5 Qdyn5p Qfep5 Qcalc5

Save Close

Qgui - preparing topology

Topology Prepare

Simulation sphere: 35 Å

Simulation centre: 7.954 -38.772 0.689 Change

x y z Center

Solvate:

TIP3P ☒ RWR_complex_top.pdb Edit

SPC ☐ Lib entries missing Check

None ☐

Create S-S bonds: ☒

Total charge: 5.0

Toggle all charges: ON OFF

Toggle state: Selected

Neutralize system with NaCl: ☐

(Na+ Cl-)

AR+	141	24.1
AR+	148	21.8
AR+	224	15.4
AR+	240	18.2
AR+	242	14.4
LY+	32	24.5
LY+	75	27.2
LY+	78	21.7
LY+	80	25.0
LY+	83	22.9

Topology name: RWR_complex_top.top

Topology PDB: RWR_complex_top_top.pdb

Write Run Close

Qgui - MD setup

Setup MD

General MD settings

Simulation time: 0.5 ns/file
Stepsize: 1 fs steps/file: 500000
Input files: 1 Total sim. time: 0.5 ns
Total steps: 500000
Temperature: 300 K Bath coupling: 10
SHAKE: Solvent ☒ Solute ☐ Hydrogens ☐
LRF Taylor expansion: ☒

Cut-offs for non-bonded interactions

Solute-Solute: 10 Å Solvent-Solvent: 10 Å
Solute-Solvent: 10 Å Q-atom: 99 Å
LRF expansion: 99 Å

Simulation sphere settings

Shell force: 10.0 Shell radius: 21.2 Å

Solvent sphere boundary settings

Radial force: 60.0
Use polarisation restraint ☒ Force: 20.0

Output recording intervals

Non-bonded list: 25 Energy summary: 5
Energy file: 10 Trajectory: 100

Trajectory atoms

First atom: 1 Last atom: 7009

Q-atoms (optional) ☐

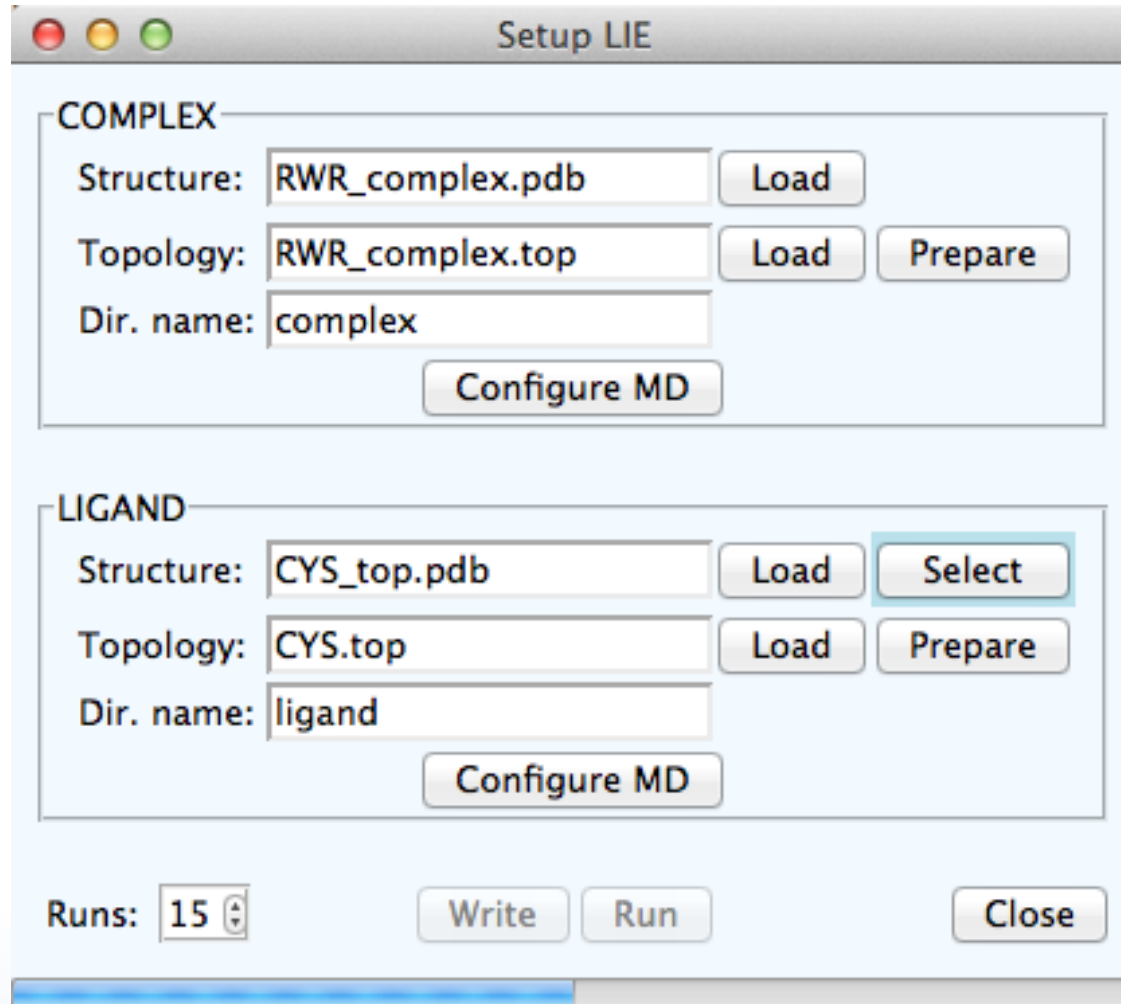
First atom: NA Last atom: NA

Q-atoms...

Setup Restraints

Use default equilibration procedure ☒

Qgui - Setup LIE



The screenshot shows a window titled "Setup LIE" with two main sections: "COMPLEX" and "LIGAND". Each section contains input fields for "Structure", "Topology", and "Dir. name", along with "Load" and "Prepare" buttons. A "Configure MD" button is located below each section. At the bottom, there is a "Runs" field set to 15, and "Write", "Run", and "Close" buttons.

COMPLEX

Structure:

Topology:

Dir. name:

LIGAND

Structure:

Topology:

Dir. name:

Runs:

General

Ligand dir.:

Complex dir.:

α 0.18

β 0.50

γ 0.00

Ligand

$\langle e_l \rangle_w$ stderr =

$\langle v_{dW} \rangle_w$ stderr =

Complex

$\langle e_l \rangle_w$ stderr =

$\langle v_{dW} \rangle_w$ stderr =

$\langle e_l \rangle_p$ stderr =

$\langle v_{dW} \rangle_p$ stderr =

Binding Free Energy

$\Delta G =$ stderr =

#Ligand name:

$\Delta G(\text{exp}):$

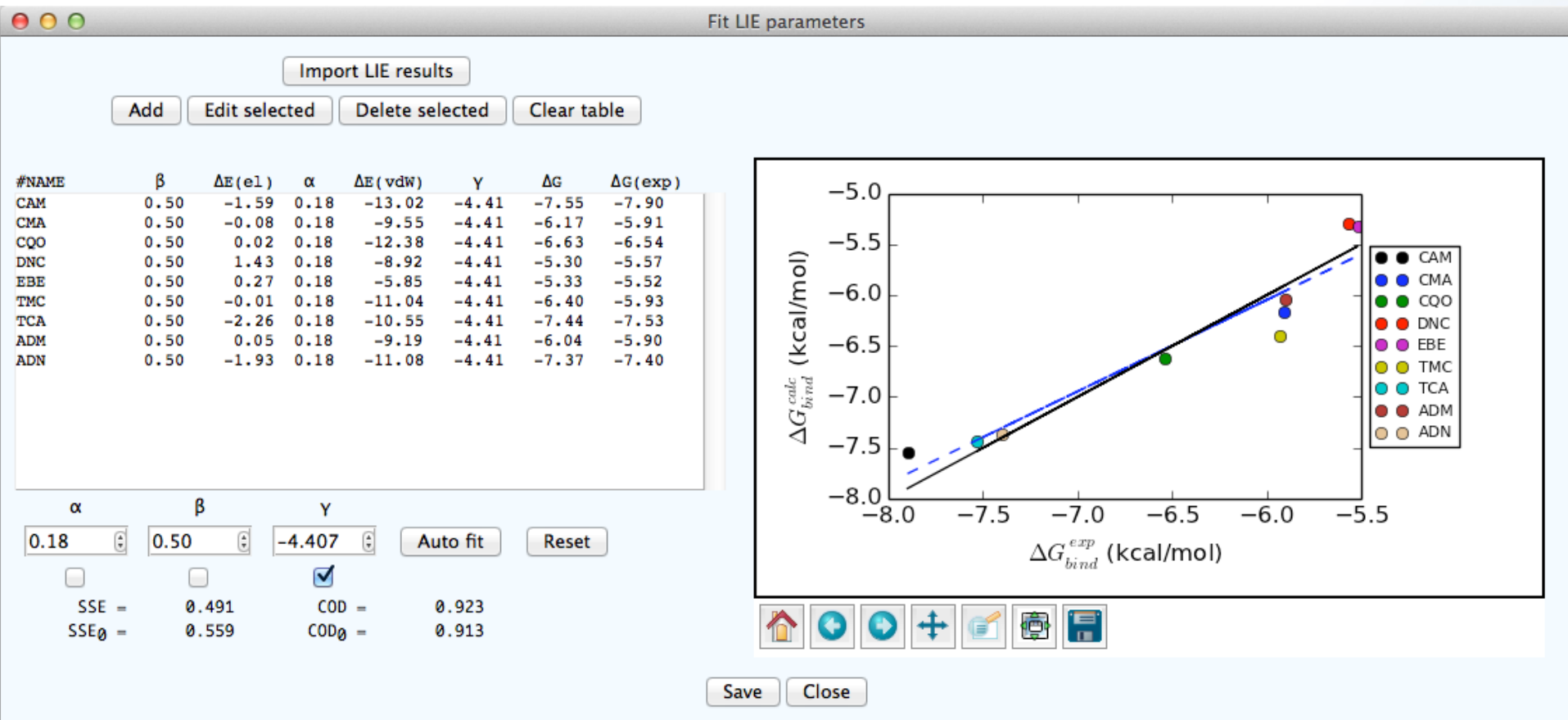
Analyze

Select system(s):

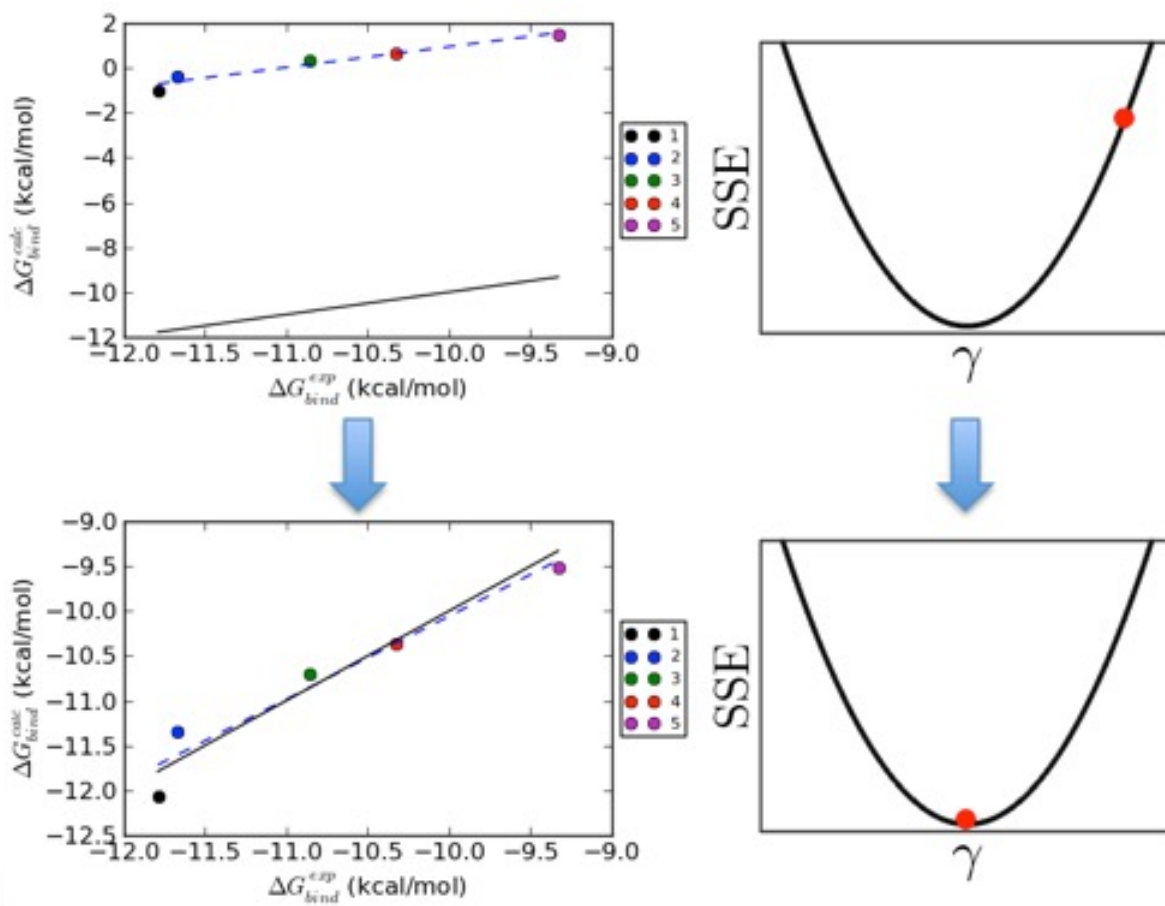
Select interaction(s):

Q-Q	e_l
Q-Q	v_{dW}
Q-prot	e_l
Q-prot	v_{dW}
Q-wat	e_l
Q-wat	v_{dW}
Q-surr	e_l
Q-surr	v_{dW}

Qgui - fitting LIE data



Qgui - fitting LIE data



Qgui - Setup FEP

Q-atoms

Qi	Atom	!Note
----	------	-------

+

-

Note

Fix geom.

Remove atoms

Qi	ϕ 1	ϕ 2	ϕ 3	ϕ 4
----	----------	----------	----------	----------

+

-

ϕ 1

ϕ 2

ϕ 3

ϕ 4

Setup

2 states FEP

Assign

Auto assign

2005

Sync pyMol

☐

selH

☐

Status

Form/Break bonds: WARNING! None selected.
Total simulation time (ns): 0.51
Q-atoms: WARNING! None selected.

Configure MD

Run

Write

Edit FEP

Close

Overwrite existing files ☒