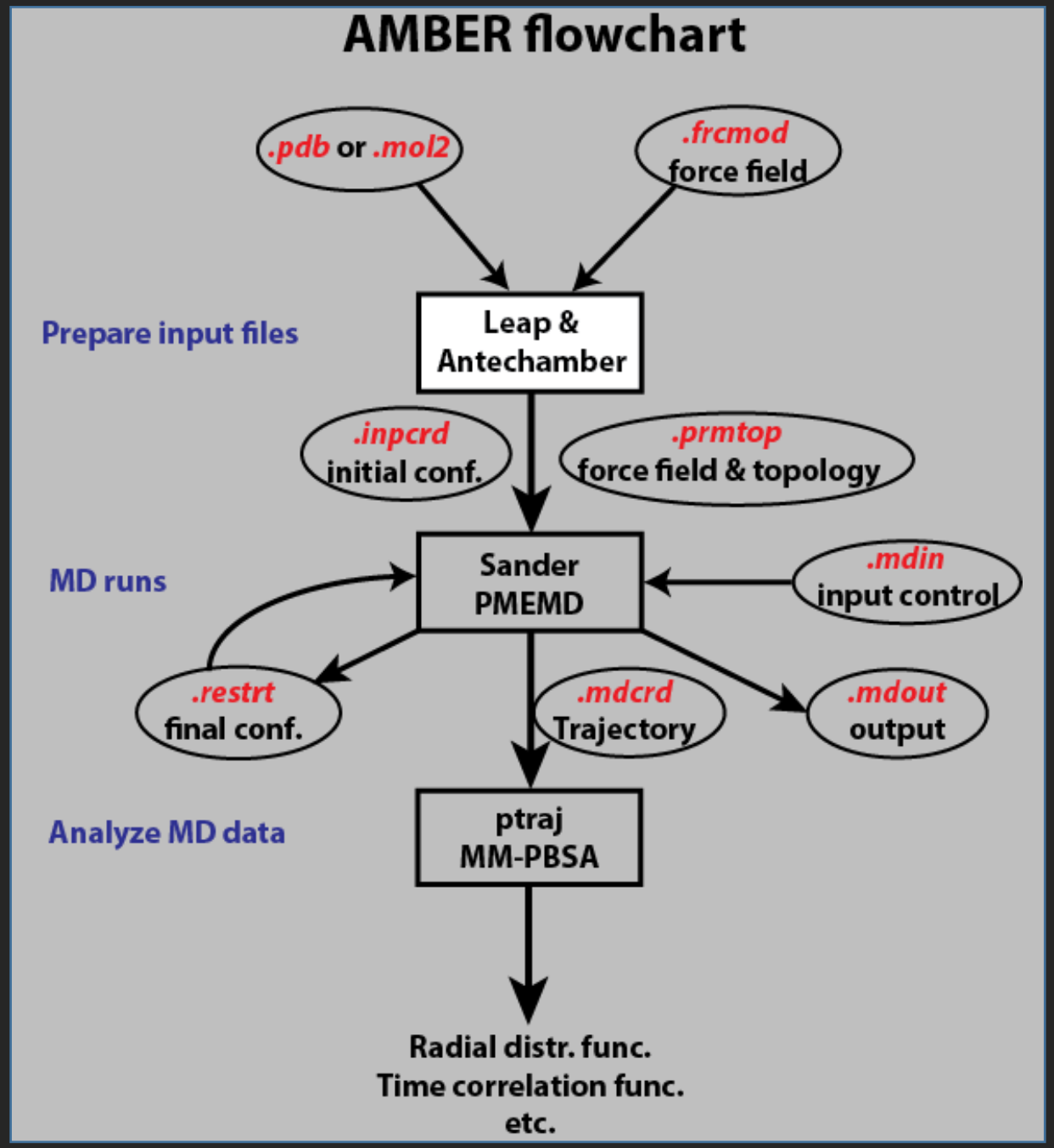


Simplified schematic of the molecular dynamics algorithm

Give atoms initial $\boldsymbol{r}^{(i=0)}$ and $\boldsymbol{v}^{(i=0)}$, set $\boldsymbol{a} = 0.0$, $t = 0.0$, $i = 0$, choose short Δt

↓

Predictor stage: predict next atom positions:
Move atoms: $\boldsymbol{r}^{p} = \boldsymbol{r}^{(i)} + \boldsymbol{v}^{(i)}\,\Delta t + {}^{1}\!/_{2}\,\boldsymbol{a}\,\Delta\, t^{2}$ + more accurate terms
Update velocities: $\boldsymbol{v}^{p} = \boldsymbol{v}^{(i)} + \boldsymbol{a}\,\Delta t$ + more accurate terms

↓

Get forces $\boldsymbol{F} = -\nabla V(\boldsymbol{r}^{p})$ or $\boldsymbol{F} = \boldsymbol{F}(\Psi(\boldsymbol{r}^{p}))$ and $\boldsymbol{a} = \boldsymbol{F}/m$

↓

Corrector stage: adjust atom positions based on new $\boldsymbol{a}$:
Move atoms: $\boldsymbol{r}^{(i+1)} = \boldsymbol{r}^{p}$ + some function of $(\boldsymbol{a}, \Delta t)$
Update velocities: $\boldsymbol{v}^{(i+1)} = \boldsymbol{v}^{p}$ + some function of $(\boldsymbol{a}, \Delta t)$

↓

Apply boundary conditions, temperature and pressure control as needed

↓

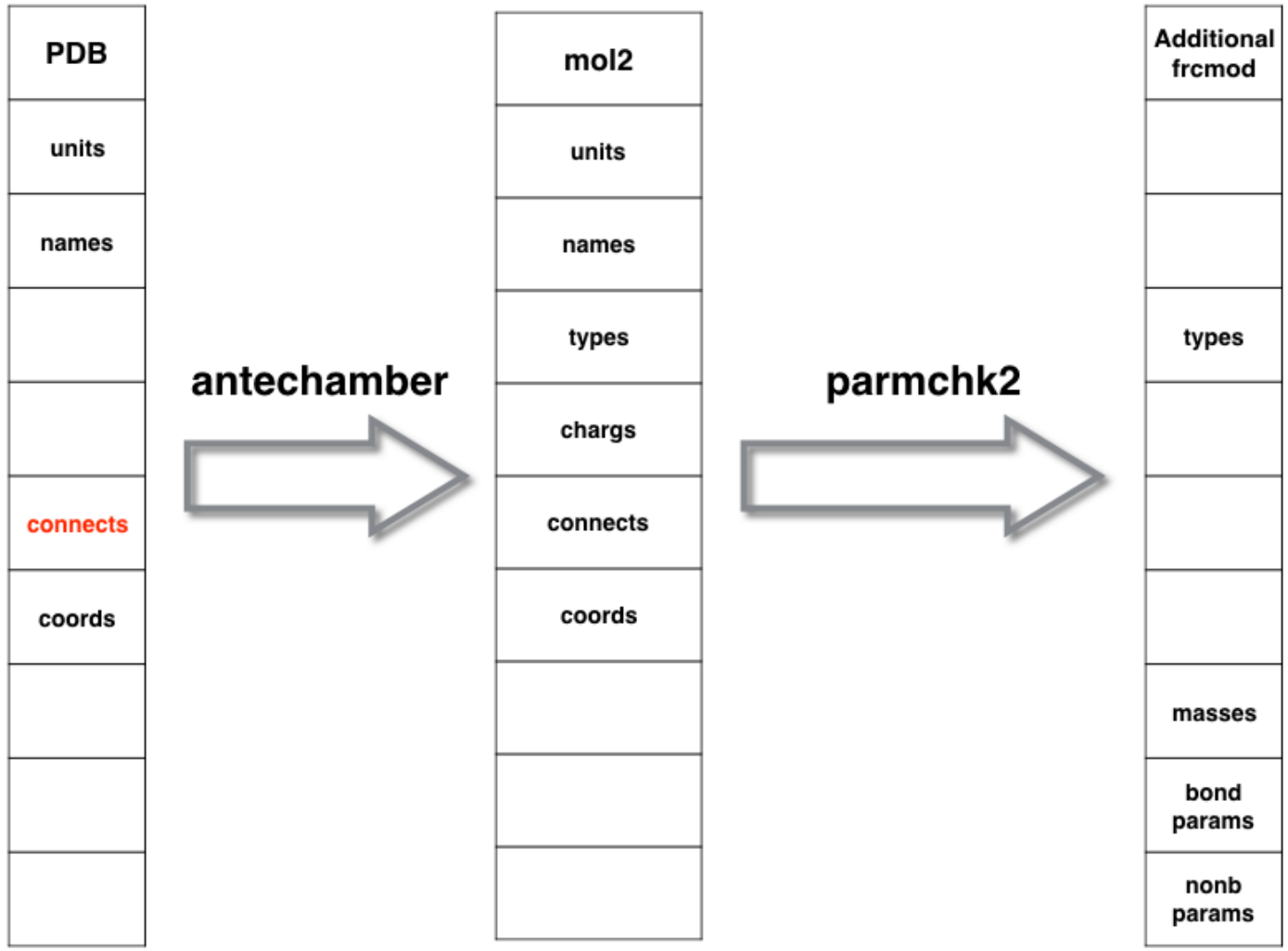
Calculate and output physical quantities of interest

↓

Move time and iteration step forward: $t = t + \Delta t$, $i = i + 1$

↓

Repeat as long as you need


PDB
units
names
connects
coords
antechamber
mol2
units
names
types
chargs
connects
coords
parmchk2
Additional frcmod
types
masses
bond params
nonb params

Terms	Abbreviation
Molecule and residue information	units
Atom names	names
Atom types	types
Atomic charges	chargs
Atomic connectivities	connects
Atomic coordinates	coords
Atomic masses	masses
Bonded parameters (bond, angle, dihedral)	bond params
Nonbonded parameters (electrostatic, VDW)	nonb params

Terms	Input Files		Force Field Files		Output Files	
	PDB	mol2	lib/mol2	dat/frcmod	topology	coordinate
units	✔	✔	✔		✔	
names	✔	✔	✔		✔	
types		✔	✔	✔	✔	
chargs		✔	✔		✔	
connects	✔	✔	✔		✔	
coords	✔	✔	✔			✔
masses				✔	✔	
bond params				✔	✔	
nonb params				✔	✔	

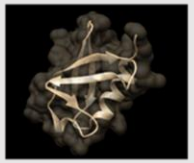
First, an overview of creating ensembles of MD training sets in DROIDS 3.0 (Detecting Relative Outlier Impacts in Dynamic Simulation)

begin with a typical comparison of protein dynamics…

A) before/after mutation or chemical modification
B) bound/unbound state or protein to DNA, another protein, drug, signaling molecule, toxin etc.
C) two temperature states (i.e. analyze stability)

Here we introduce DROIDS 2.0 free software for comparative protein dynamics

Reference MD run

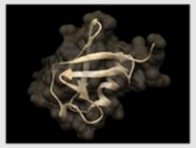


energy minimize heating

long equilibration MD run

sampling MD runs = random time spacer to mitigate chaotic dynamics + fixed time data production run

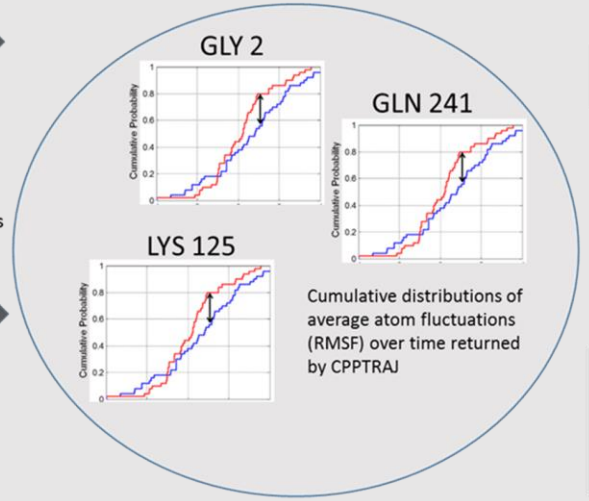
Query MD run



energy minimize heating

long equilibration MD run

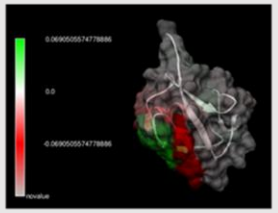
Two sets of molecular dynamic (MD) simulations to be compared



Cumulative distributions of average atom fluctuations (RMSF) over time returned by CPPTRAJ

2 sample KS tests on MD of each residue backbone

Colors = delta values, p values, or KS D values



Light gray = no difference or no significance

Dark gray = no homology between structures

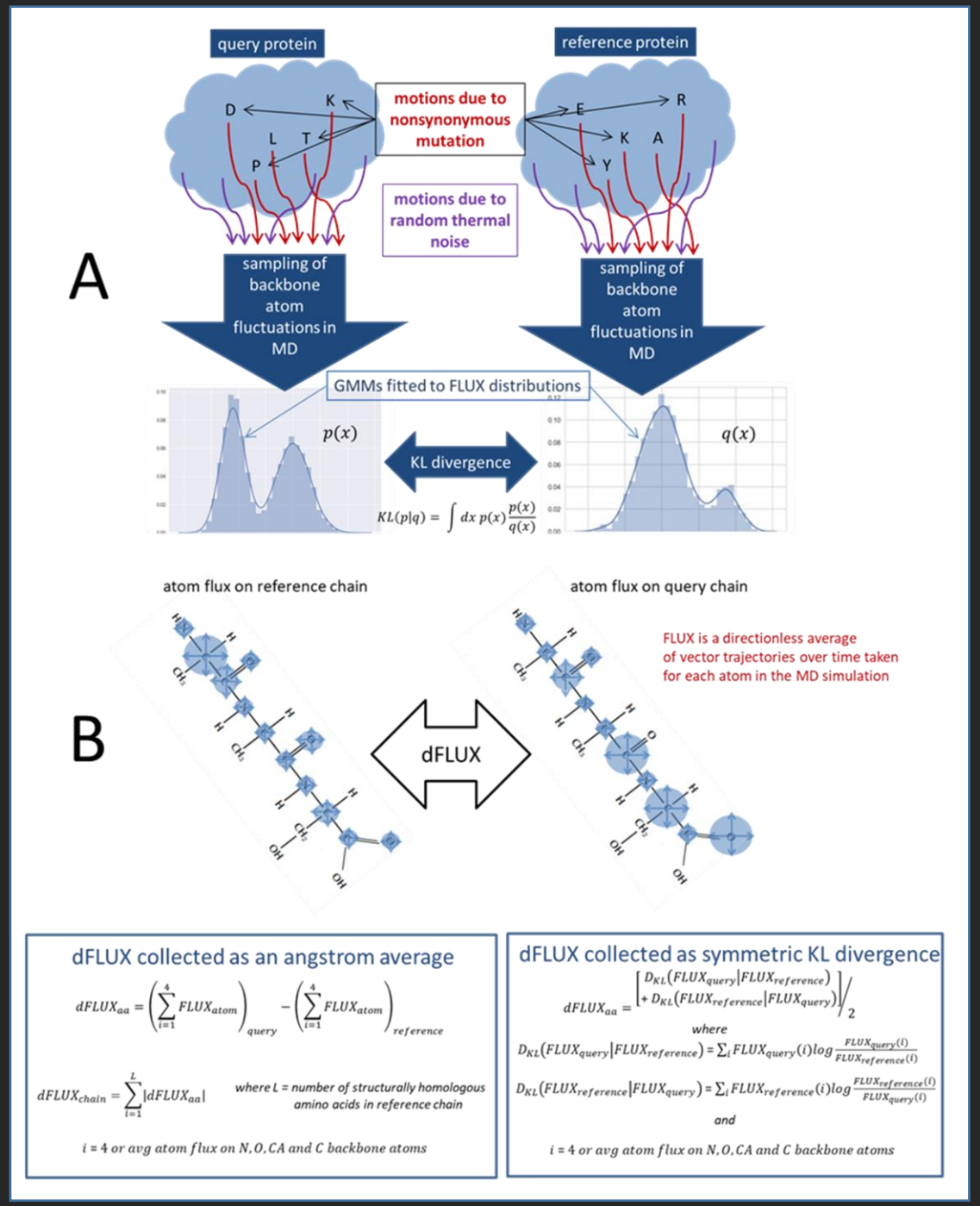
results are color mapped onto reference MD movie

DROIDS allows sampling and subsequent statistical comparison of many individual molecular dynamics runs on two different homologous protein files of interest to the researcher

DROIDS is freely downloadable from GitHub and requires AMBER 16/18 (licensed by the University of CA) and UCSF Chimera (visualization freeware) running on the Linux PC installed with modern Nvidia GPU and CUDA libraries

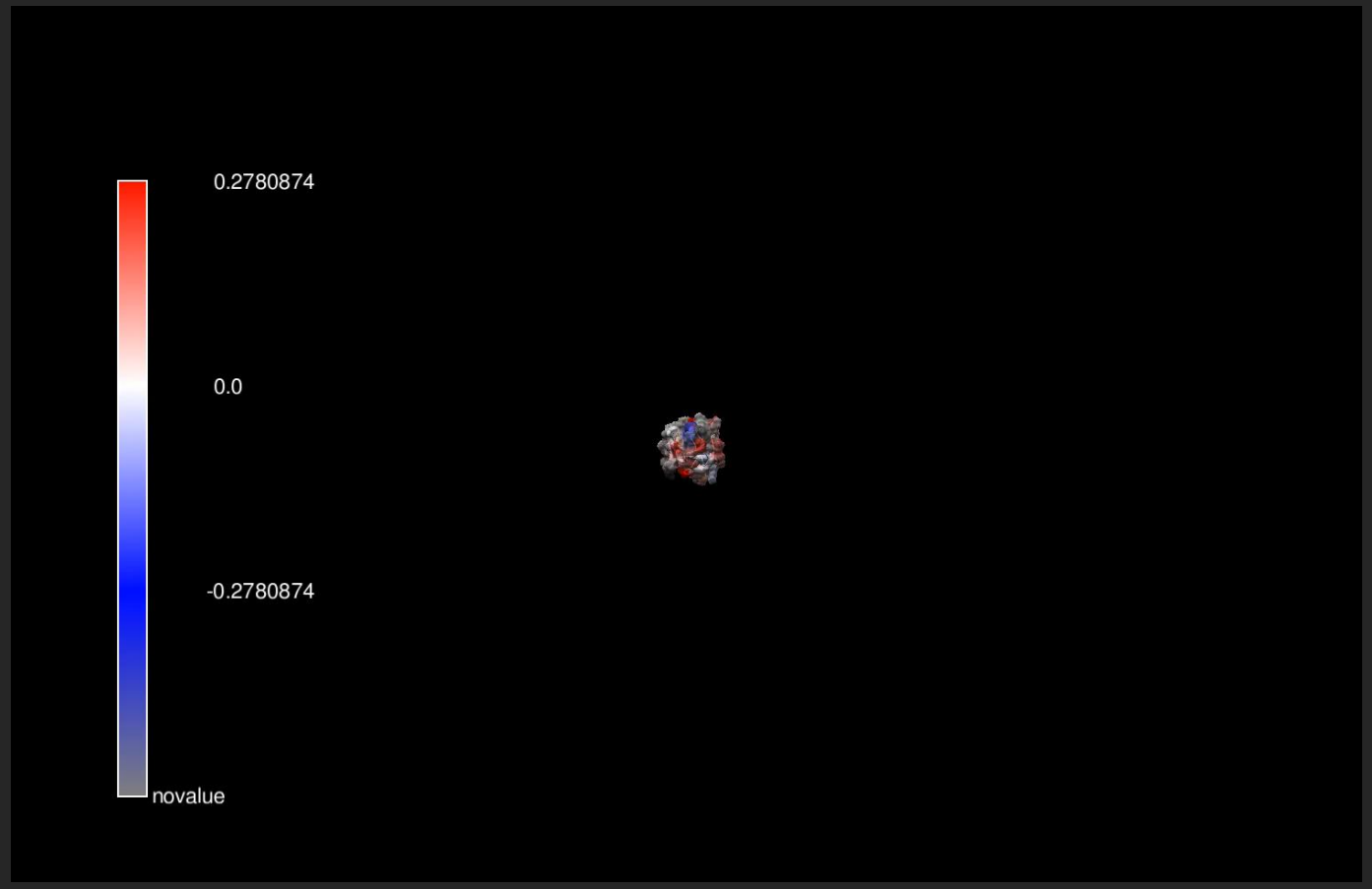
Some mathematical details….

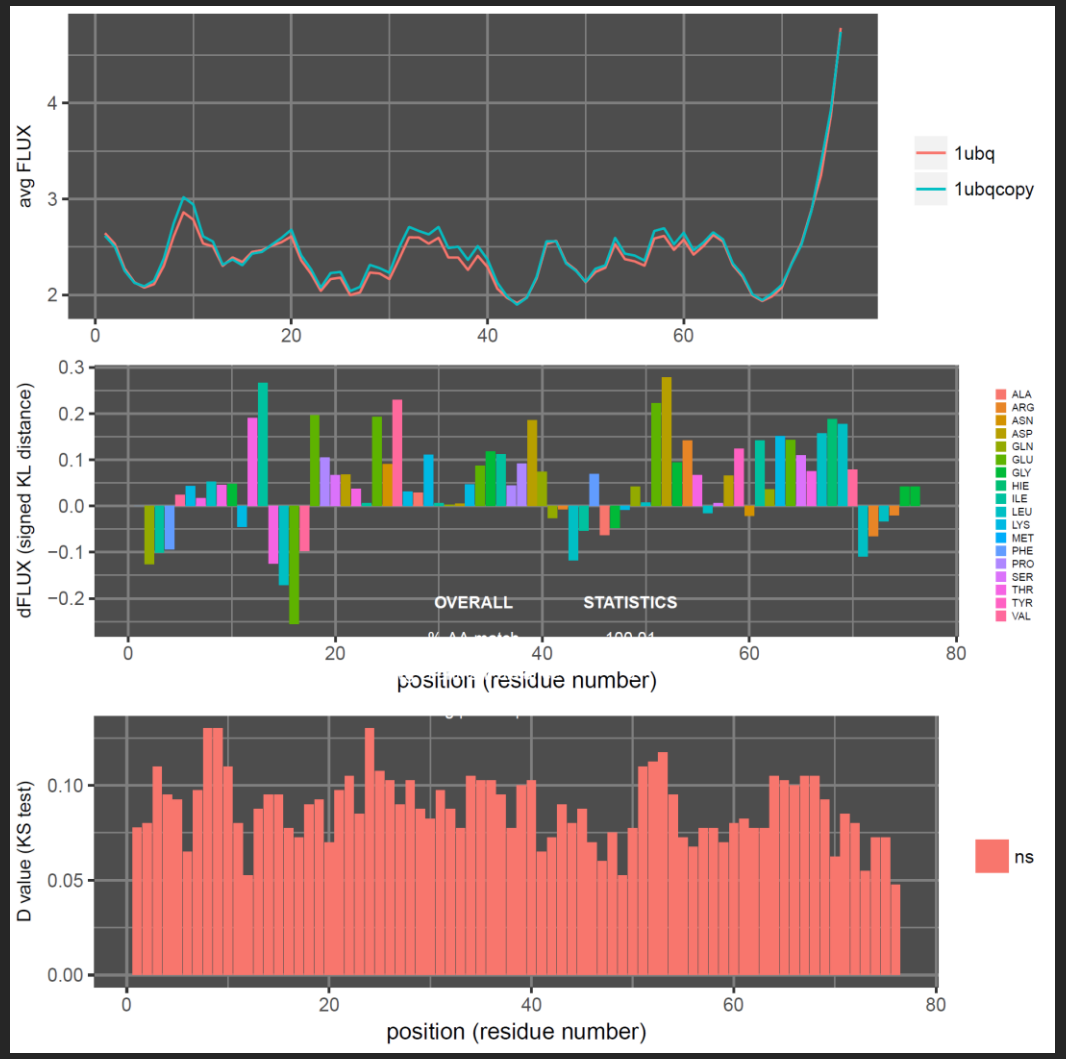
In the following MD ensemble analysis we collect 100 x 0.3ns of dynamics for each state of the comparison using a small stable protein ubiquitin (PDB ID: 1ubq)



Change in RMSF (dFLUX) due to random thermal noise at 300K (i.e. no temp change…no significant change in dFLUX)

red = increased motion, blue = decrease motion





Change in RMSF (dFLUX) due to 50K temperature decrease from 300K

red = increased motion, blue = decrease motion