

Fast Relax...

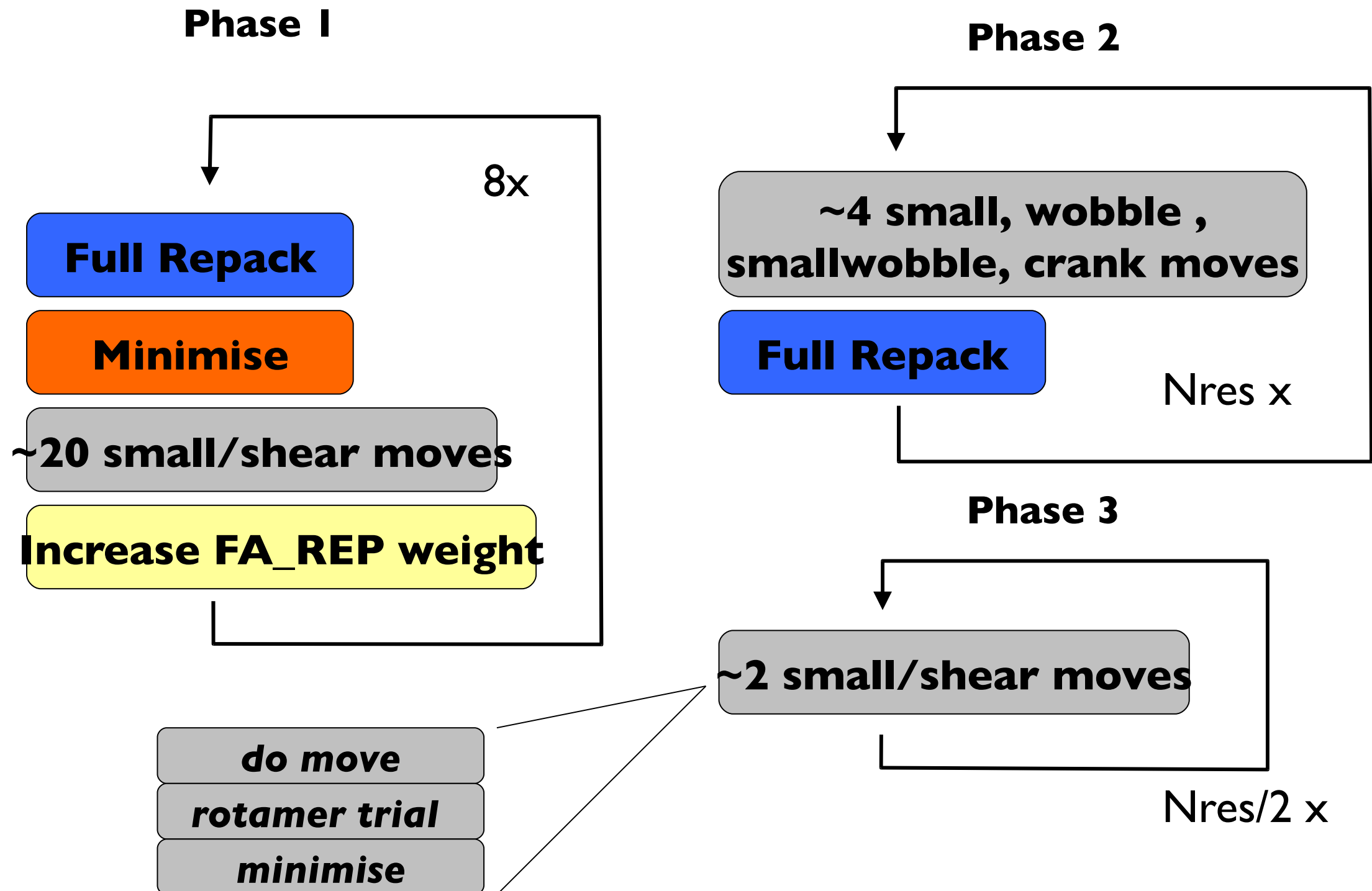
.... and its uses.

Mike Tyka

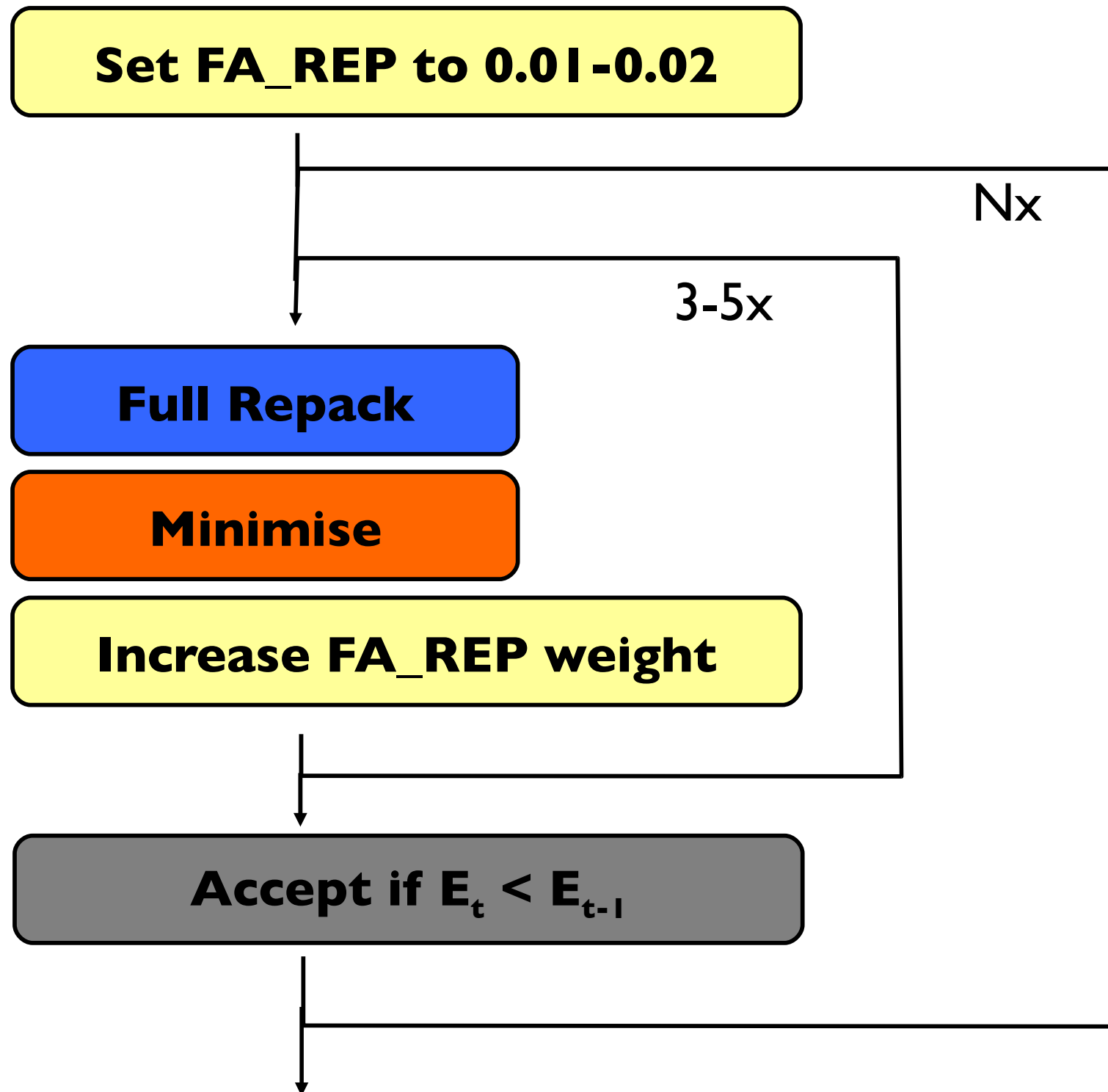
Baker Lab

6th August 2009

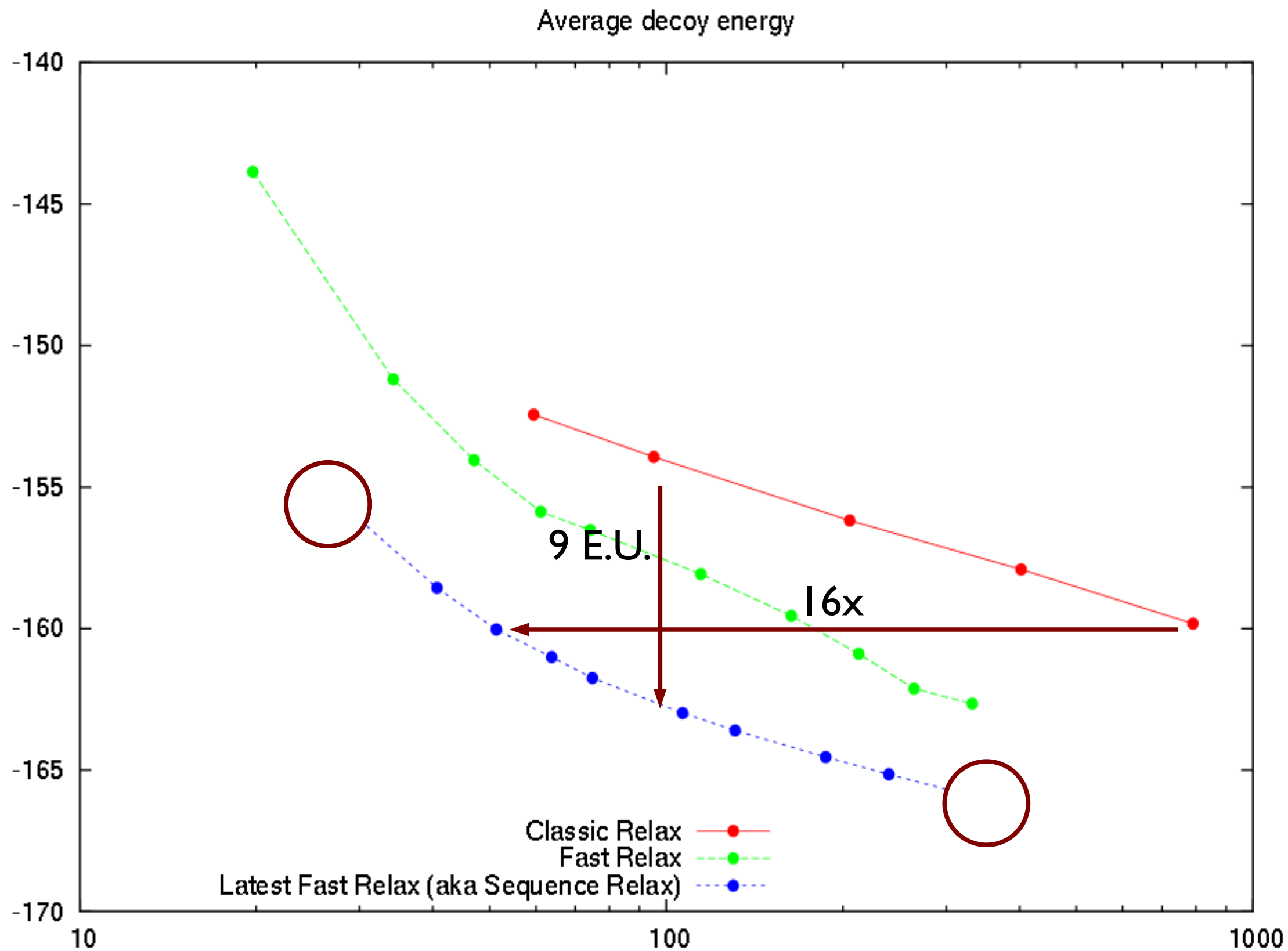
Classic Relax



Fast Relax



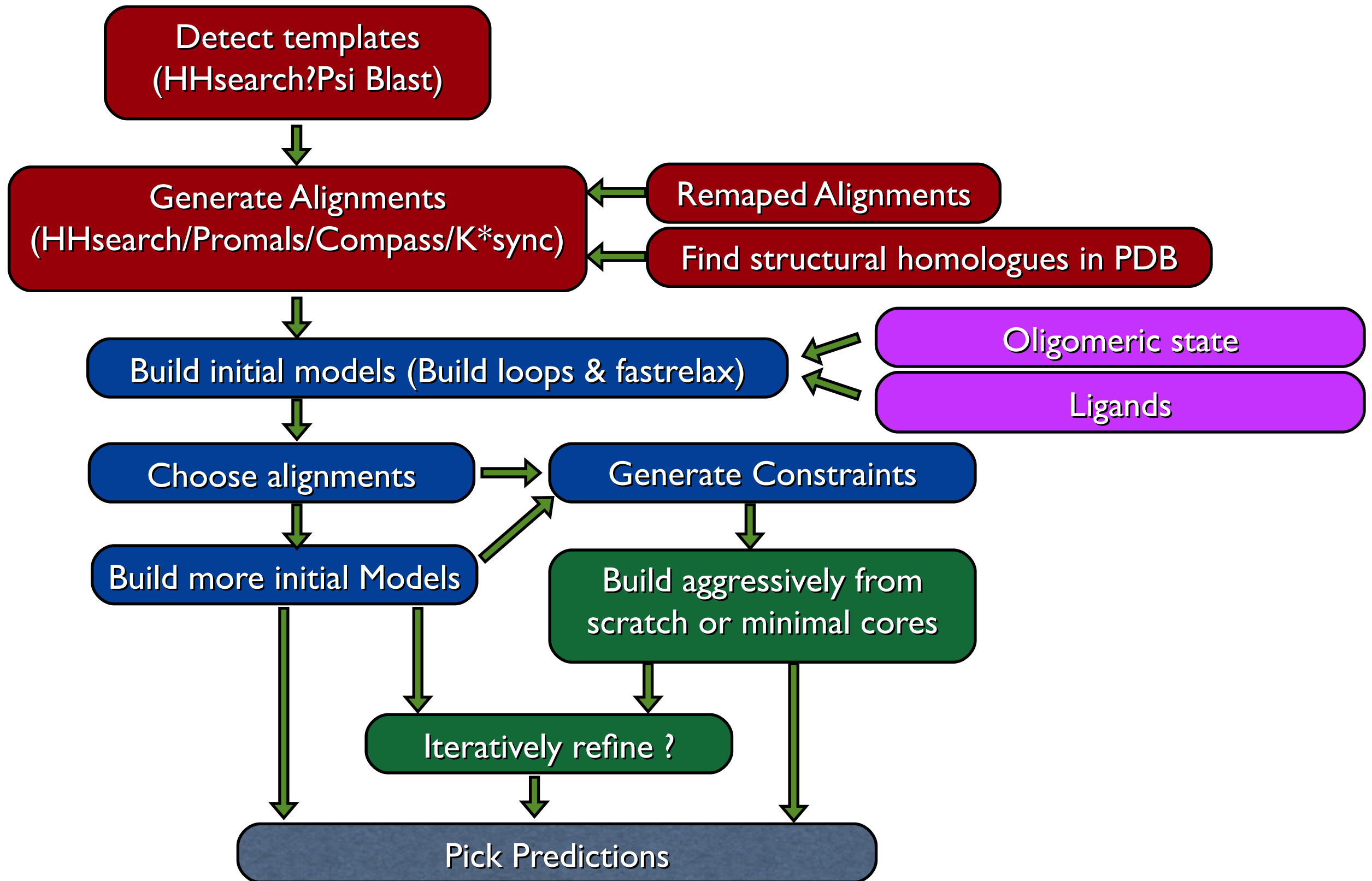
Better Relax...



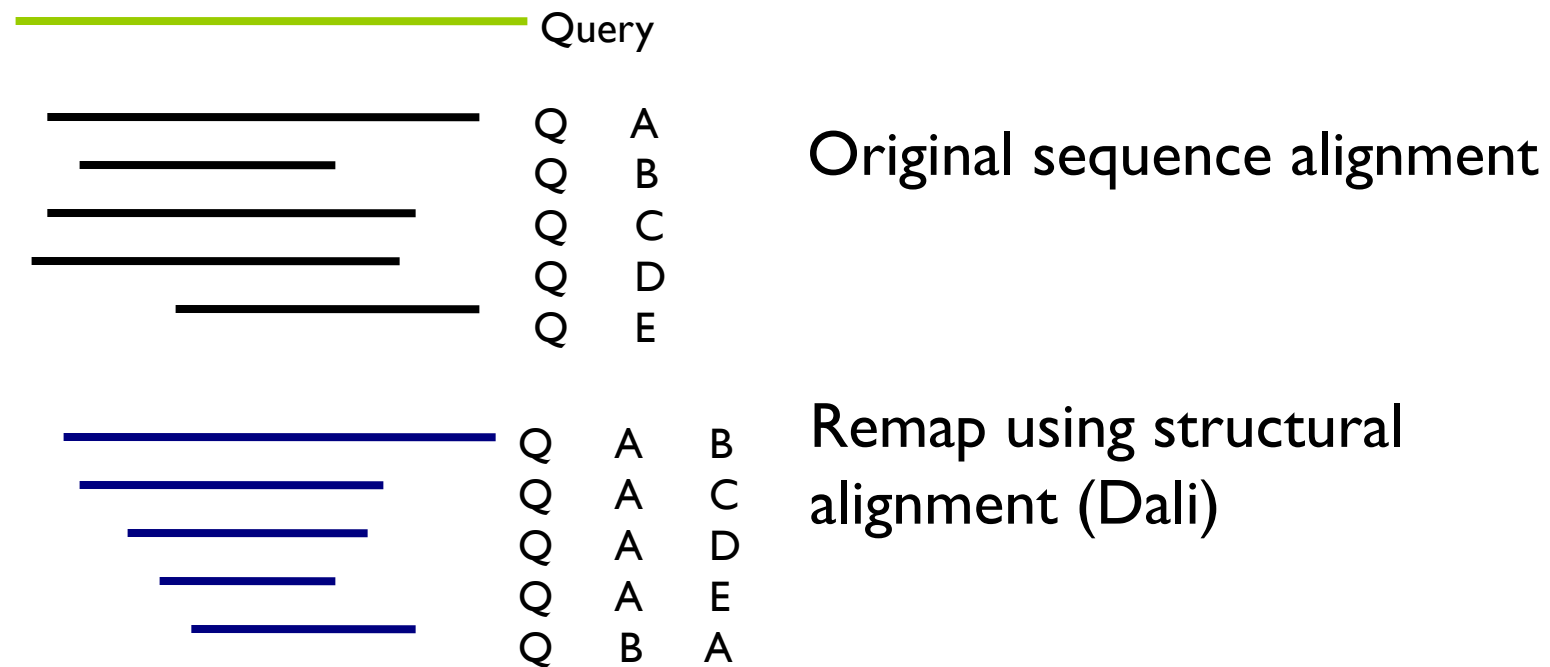
Case 1: Homology Modelling – Template selection

Case 2: Energy Landscape Exploration

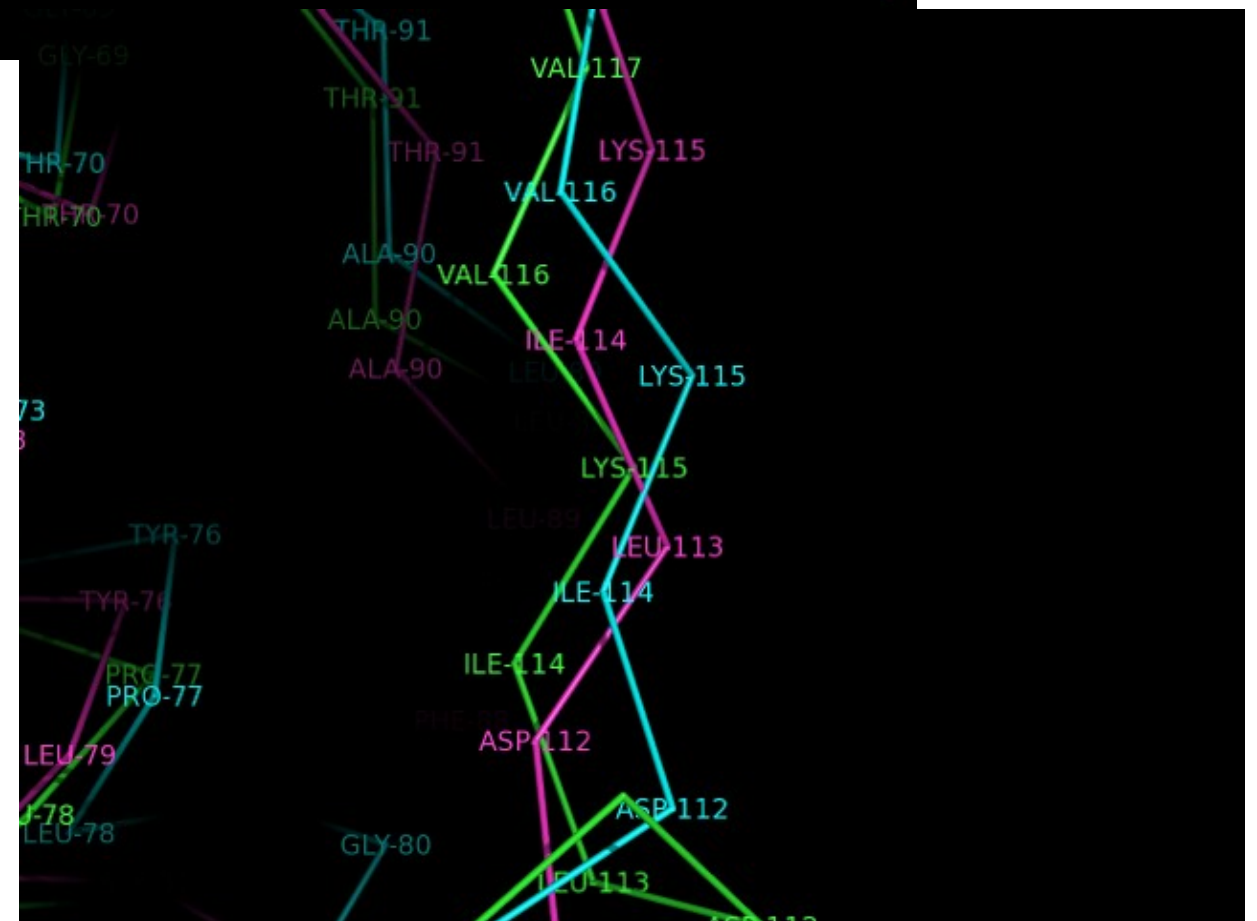
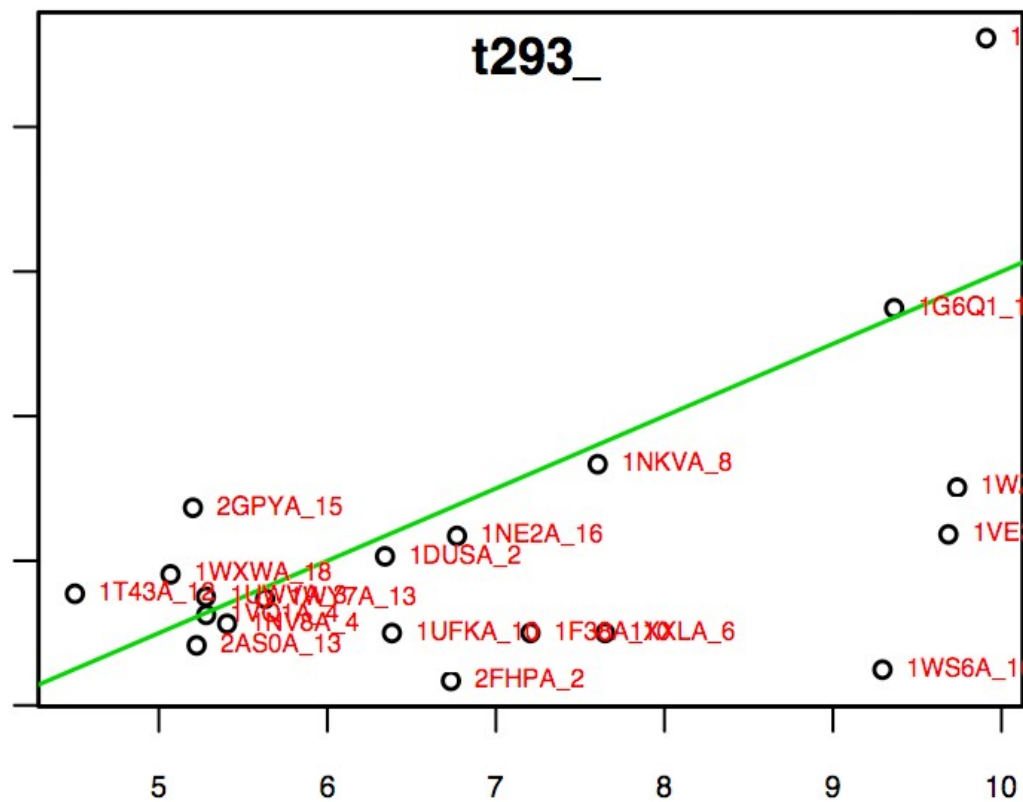
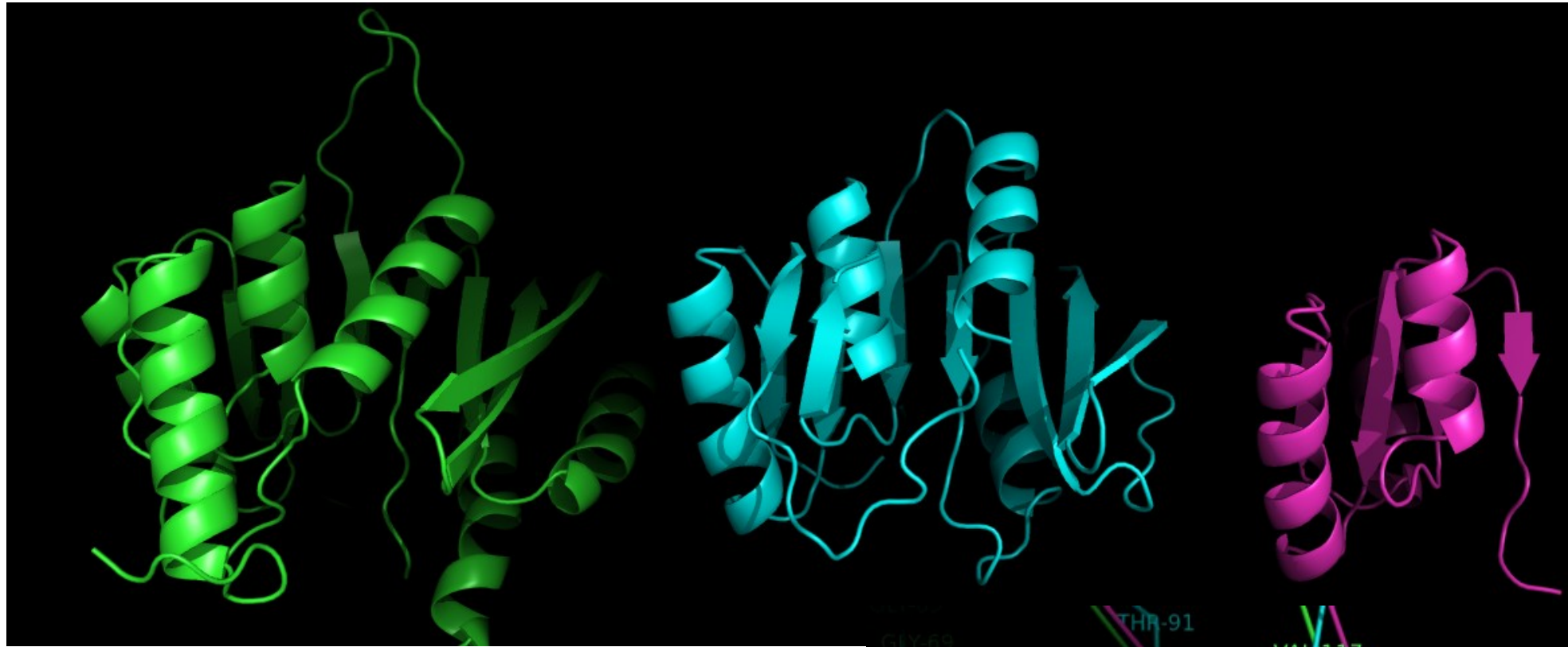
Homology Modelling: Outline for CASP9



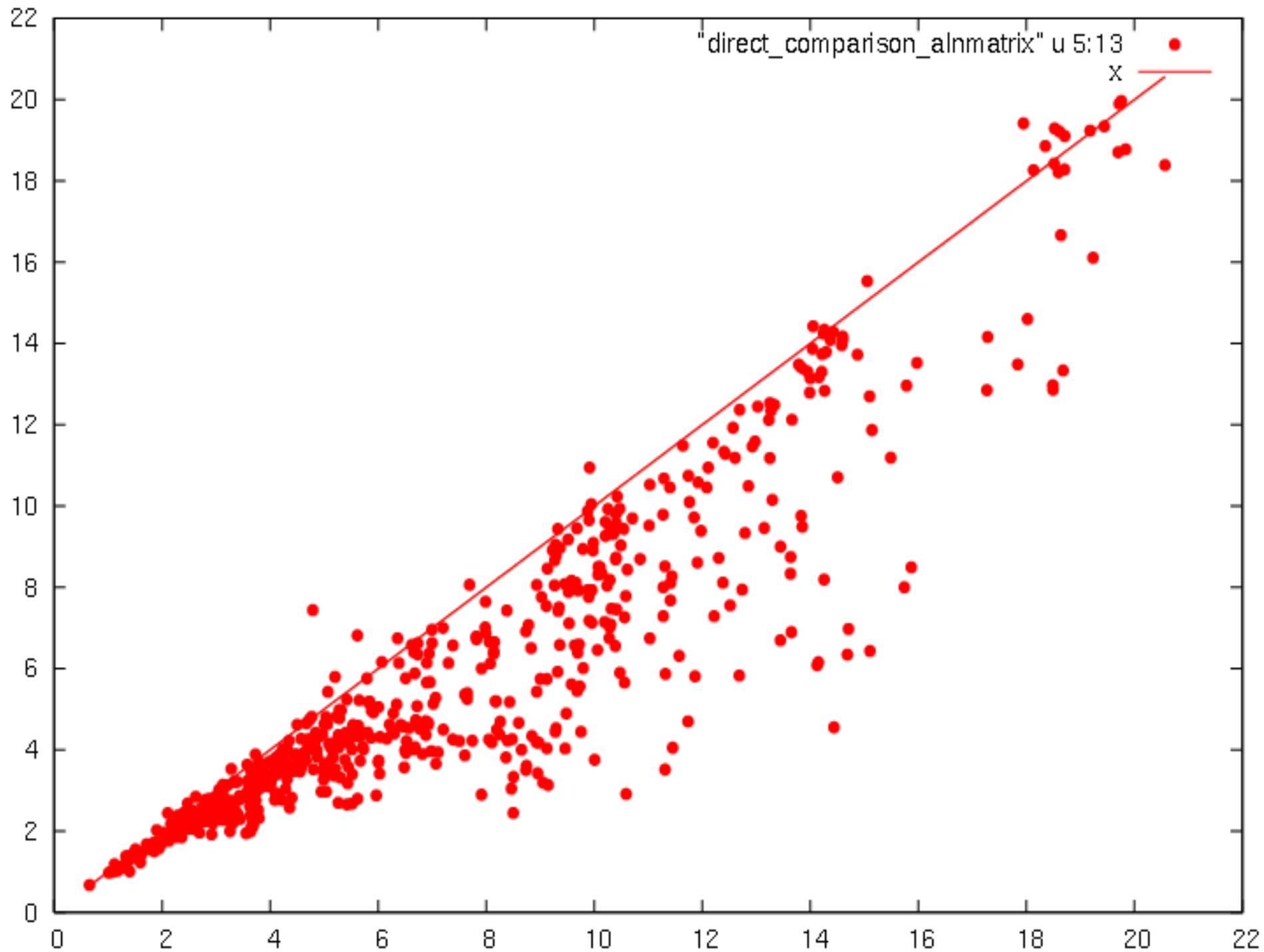
Remapping of alignments



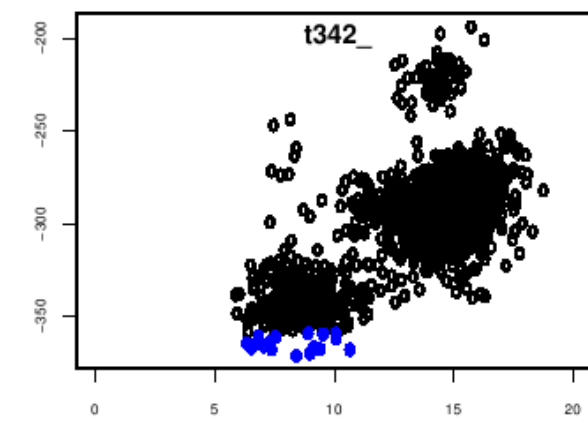
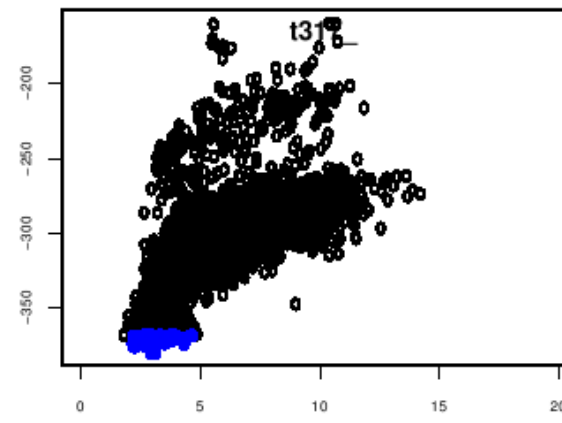
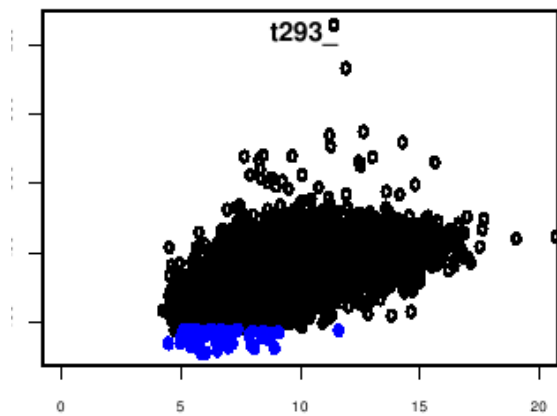
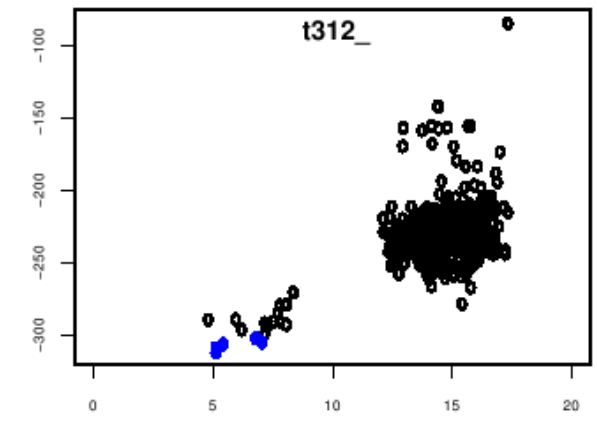
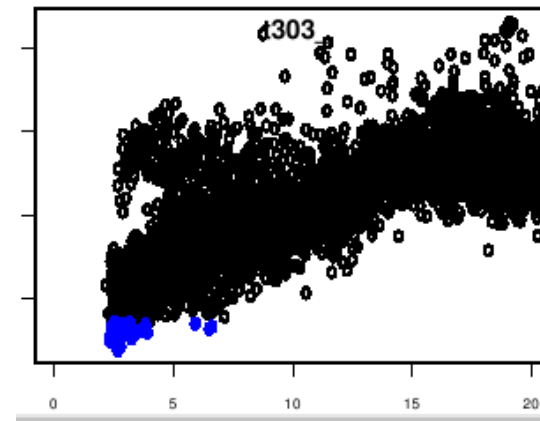
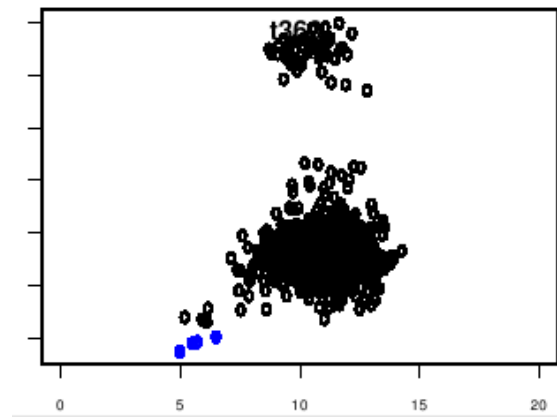
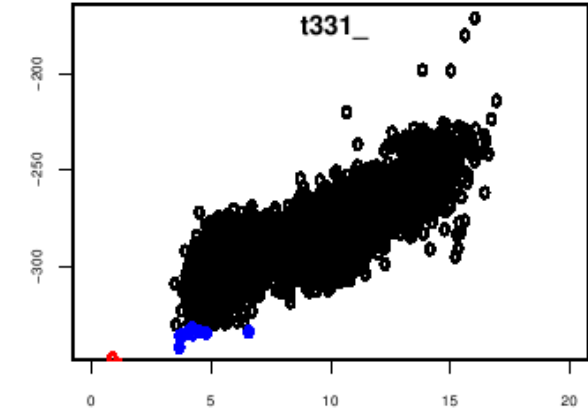
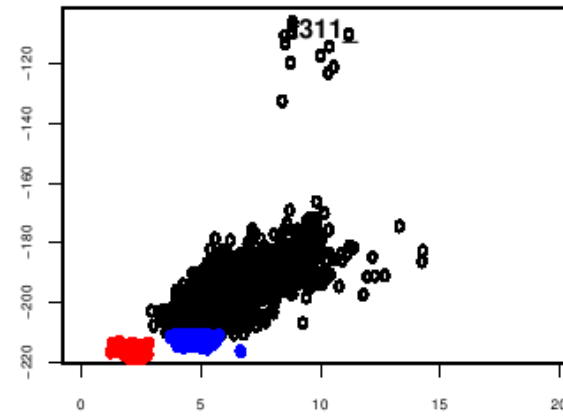
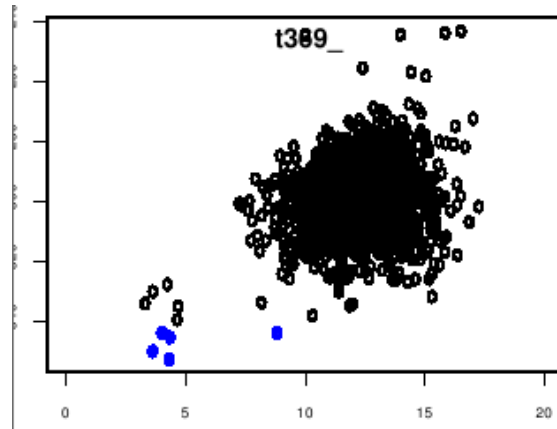
Remapping can improve alignments considerably.



Remapping can improve alignments considerably.



Choosing good alignments – quick CCD looprebuild and fast relax.



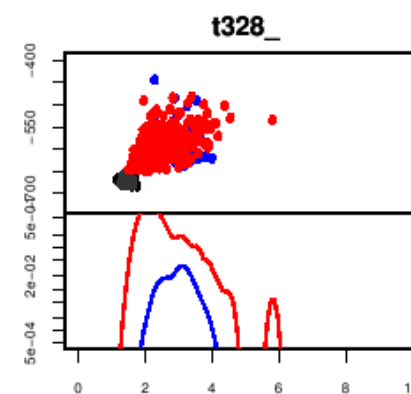
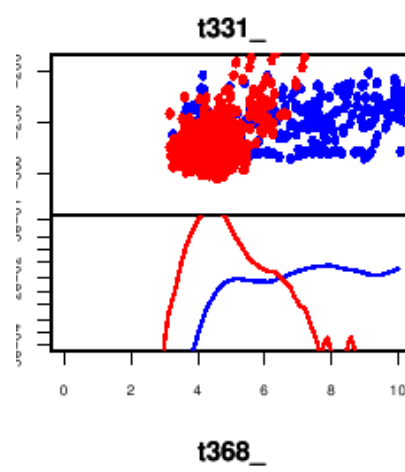
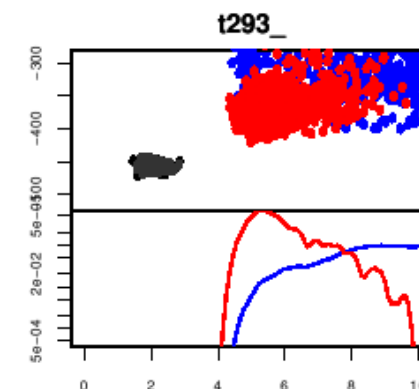
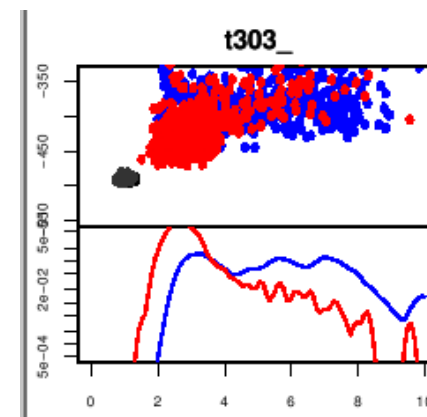
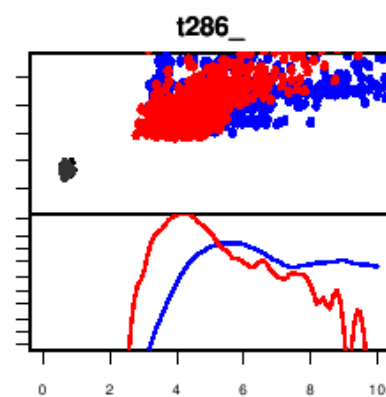
Why the fuzz ? Resampling!

LoopRebuilding

Choose best aln

Constraints

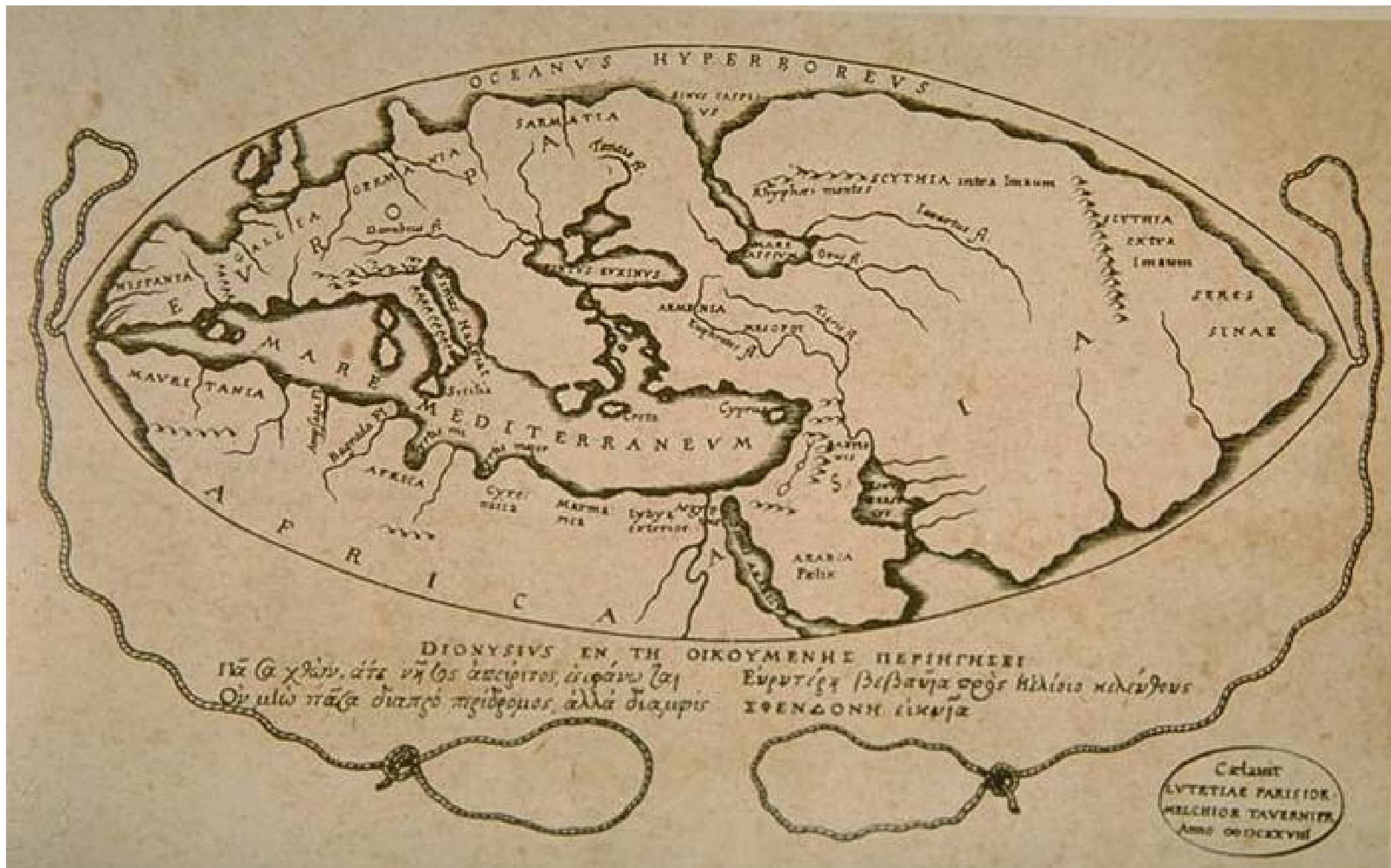
Build up from
minimal core +
constraints



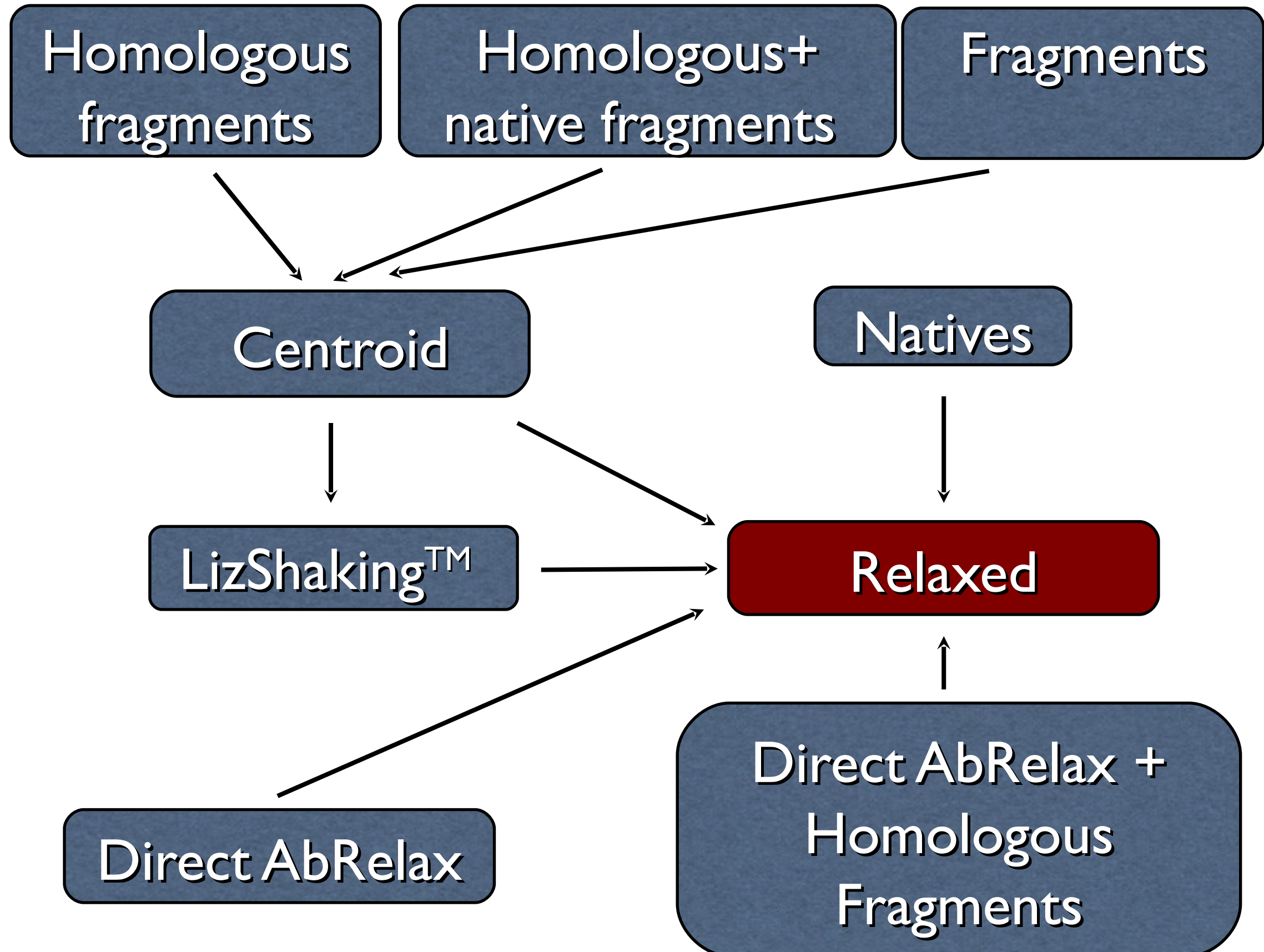
Looprebuilding

Rebuilding from minimal core

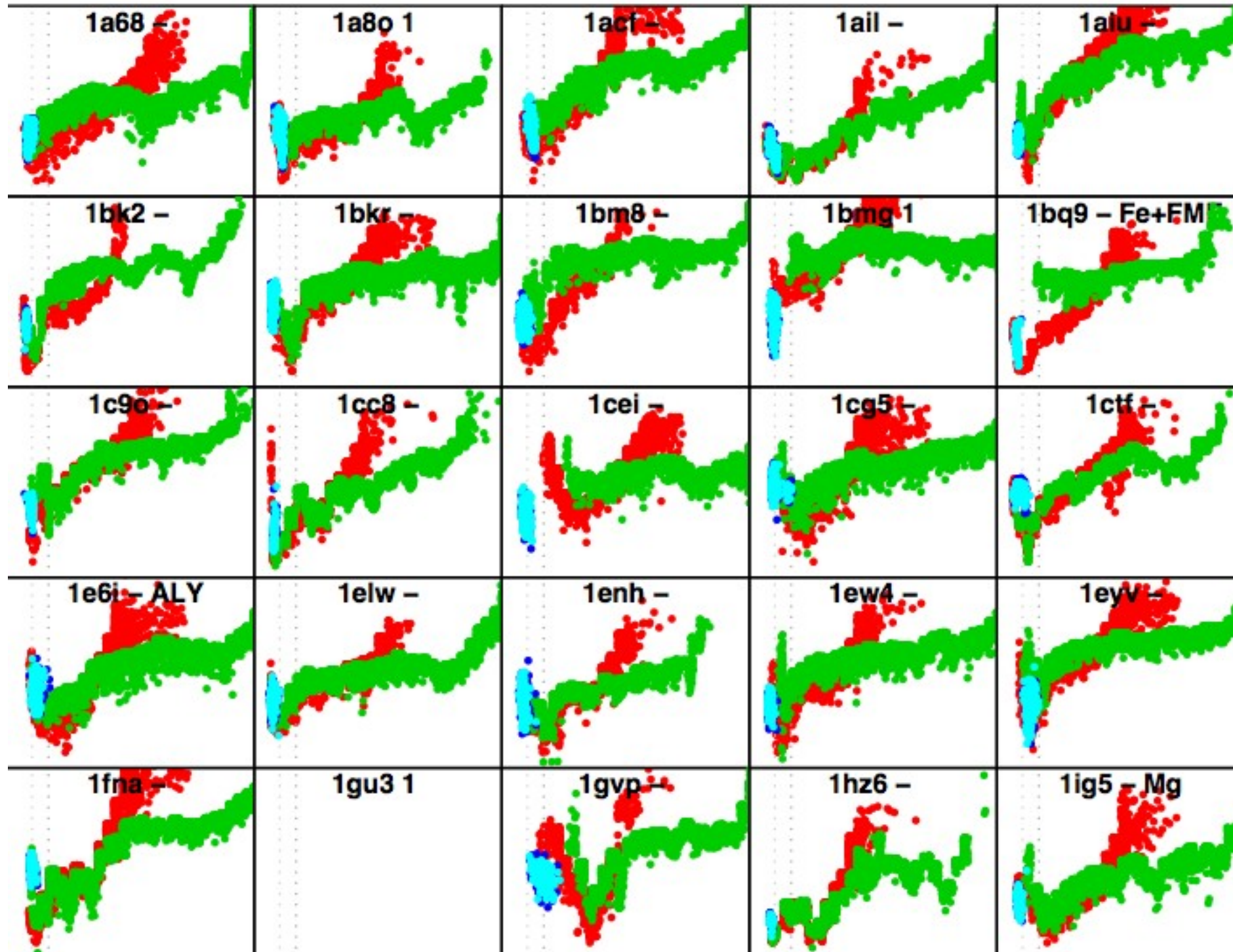
Case 2: Energy Landscape Exploration



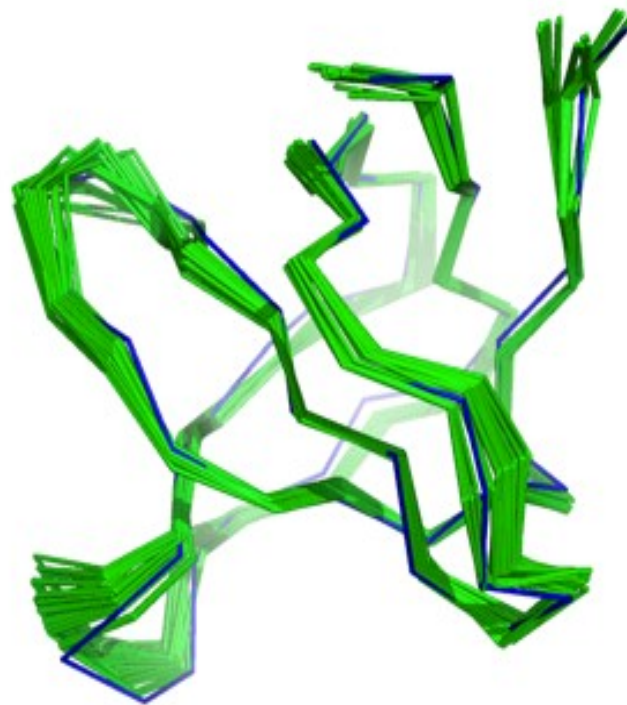
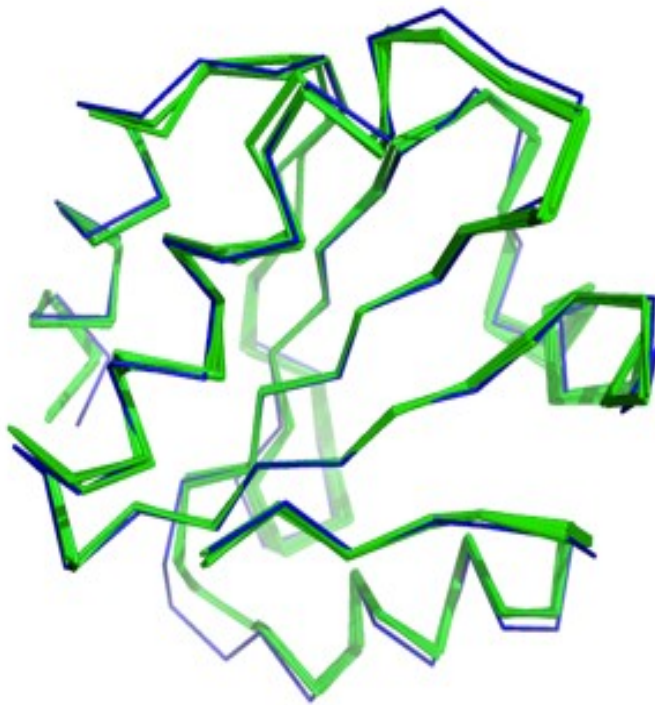
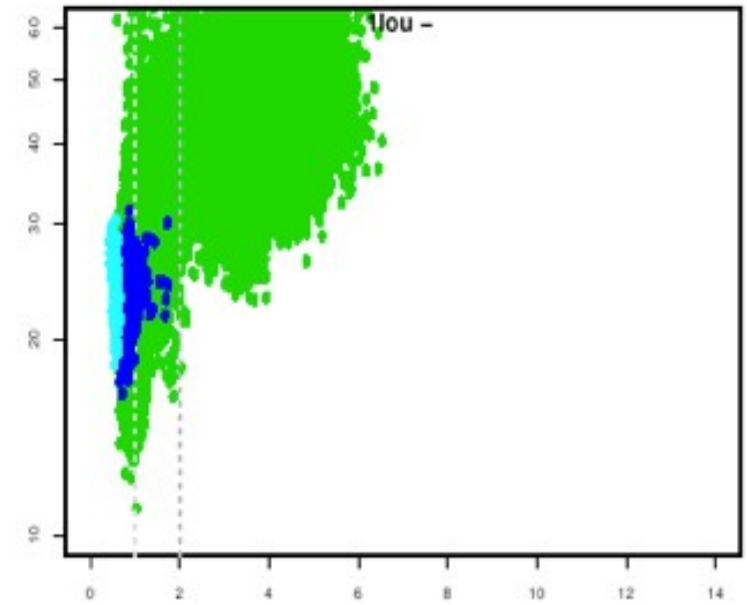
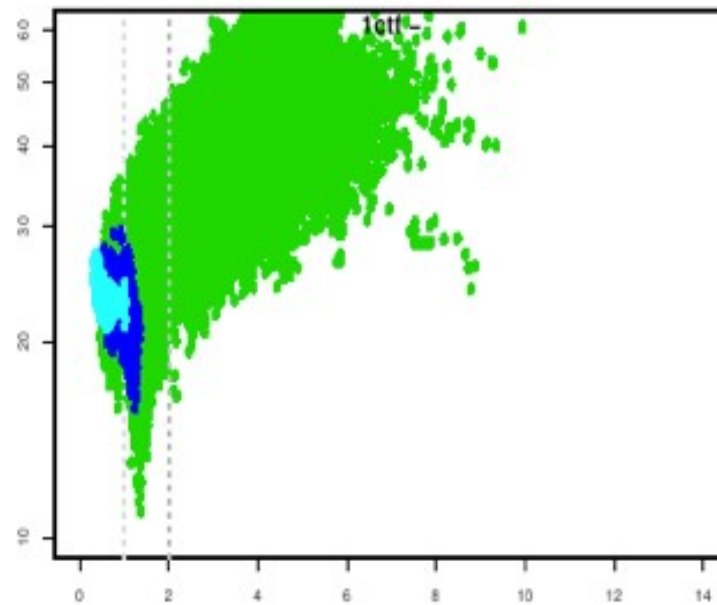
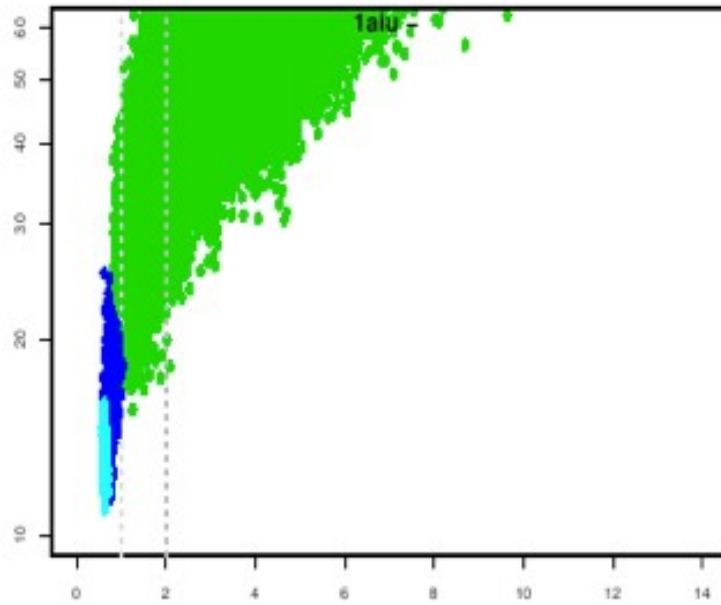
Generating Decoys from many different angles



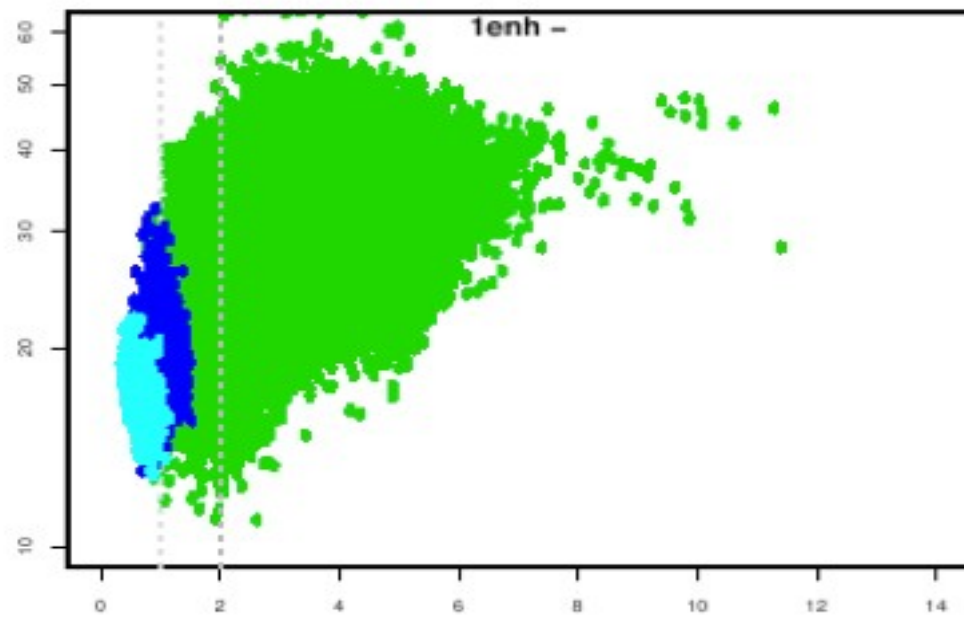
I) In almost all cases, Rosetta's global energy minimum is v. close to the native state



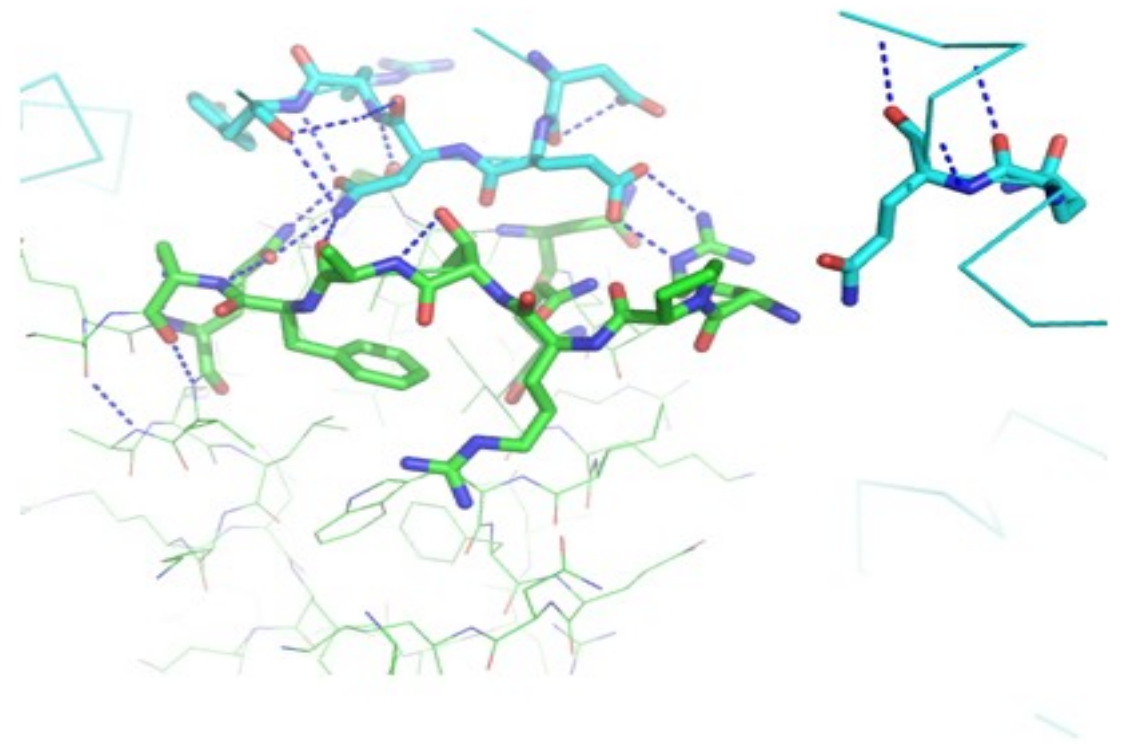
2) In almost all cases there are small deviations.



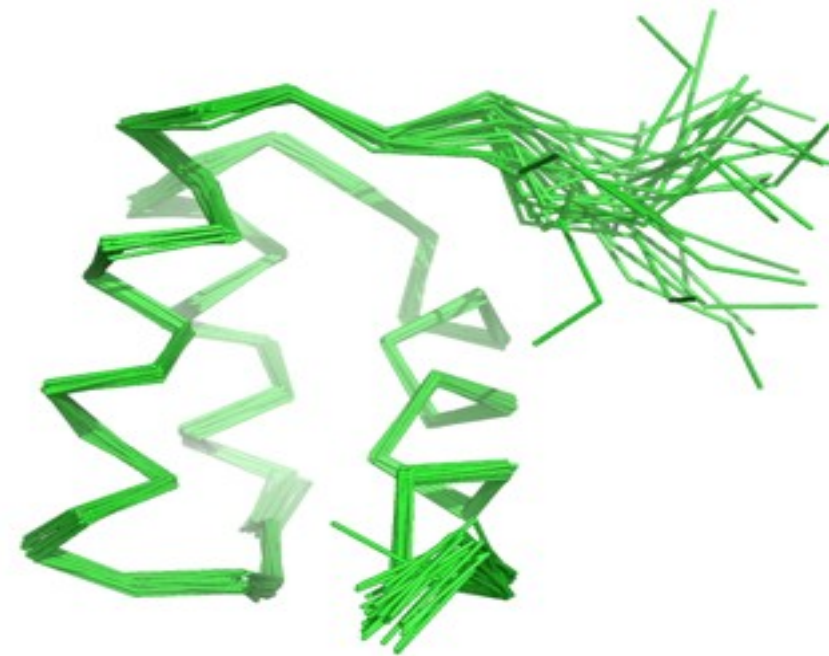
Disorder is very commonly observed



1ENH

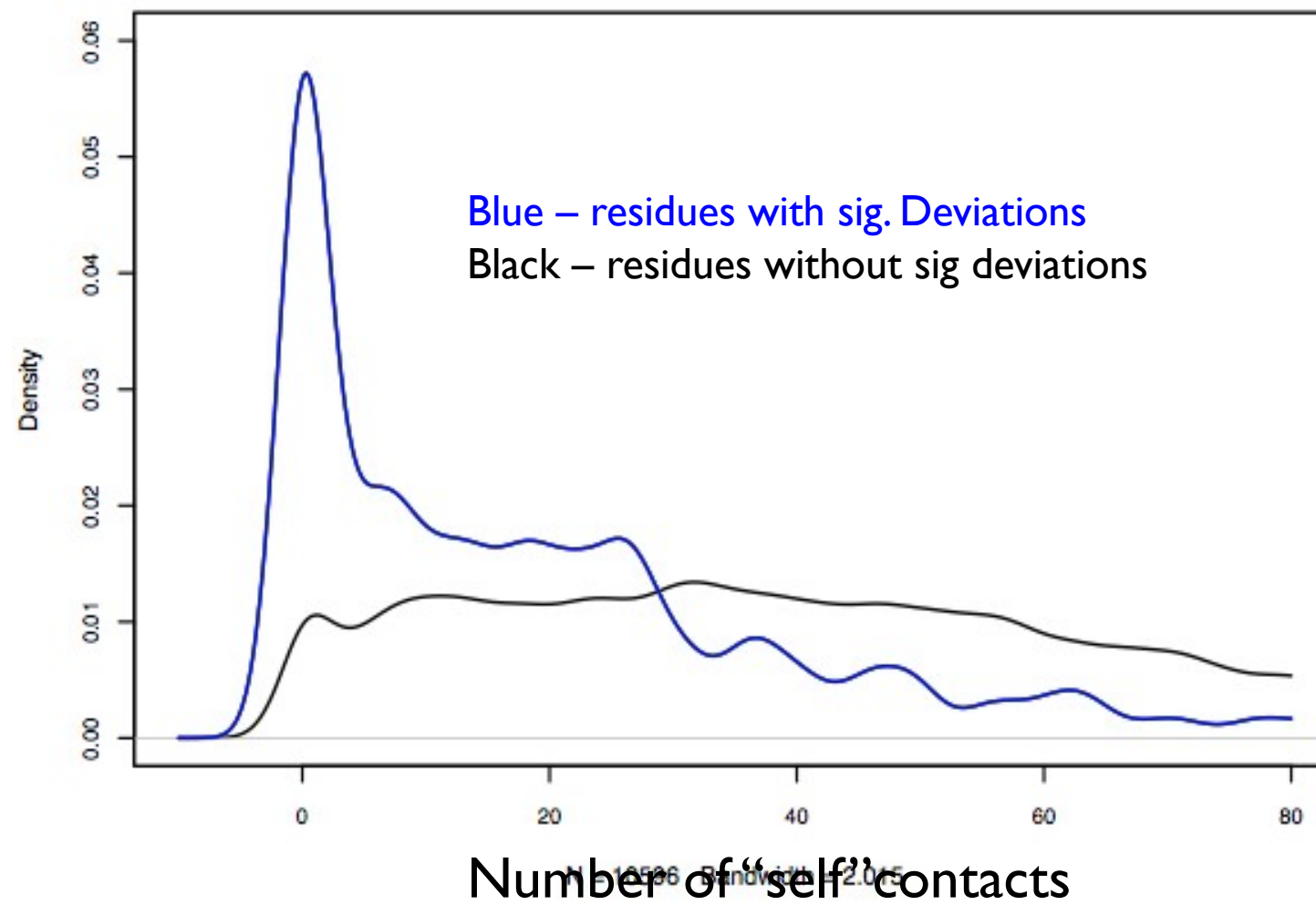


Rosetta Ensemble



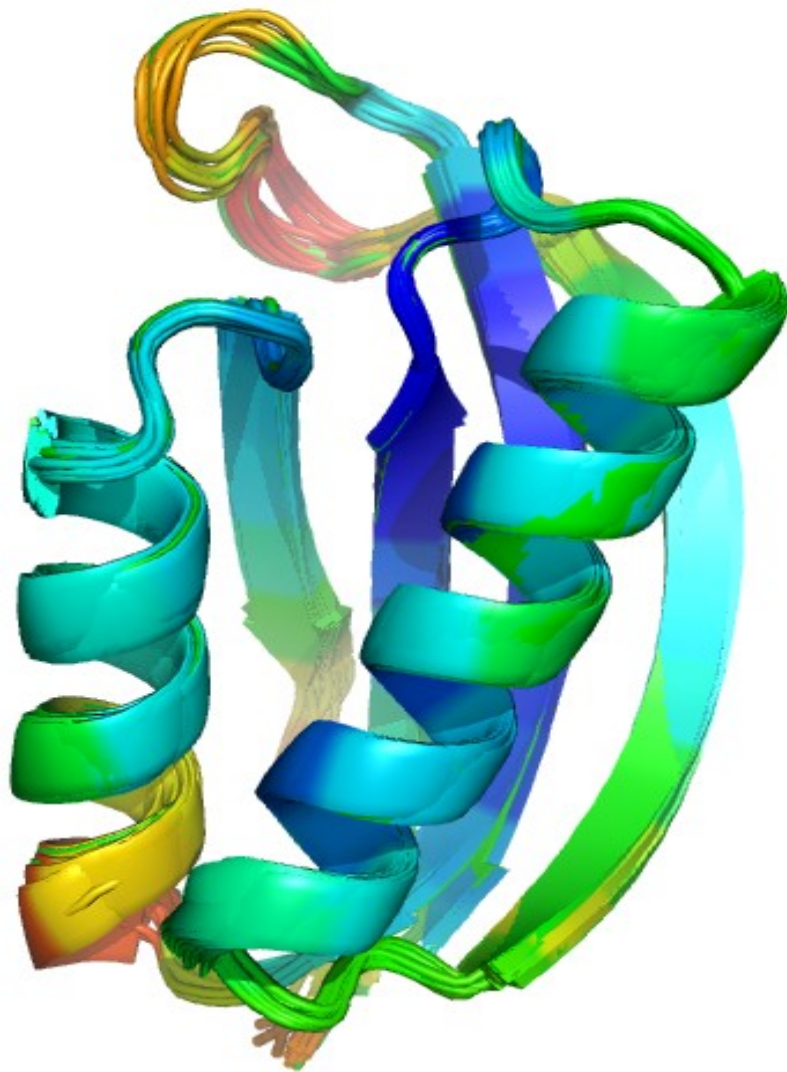
NMR ensemble

Deviations correlate with contact density

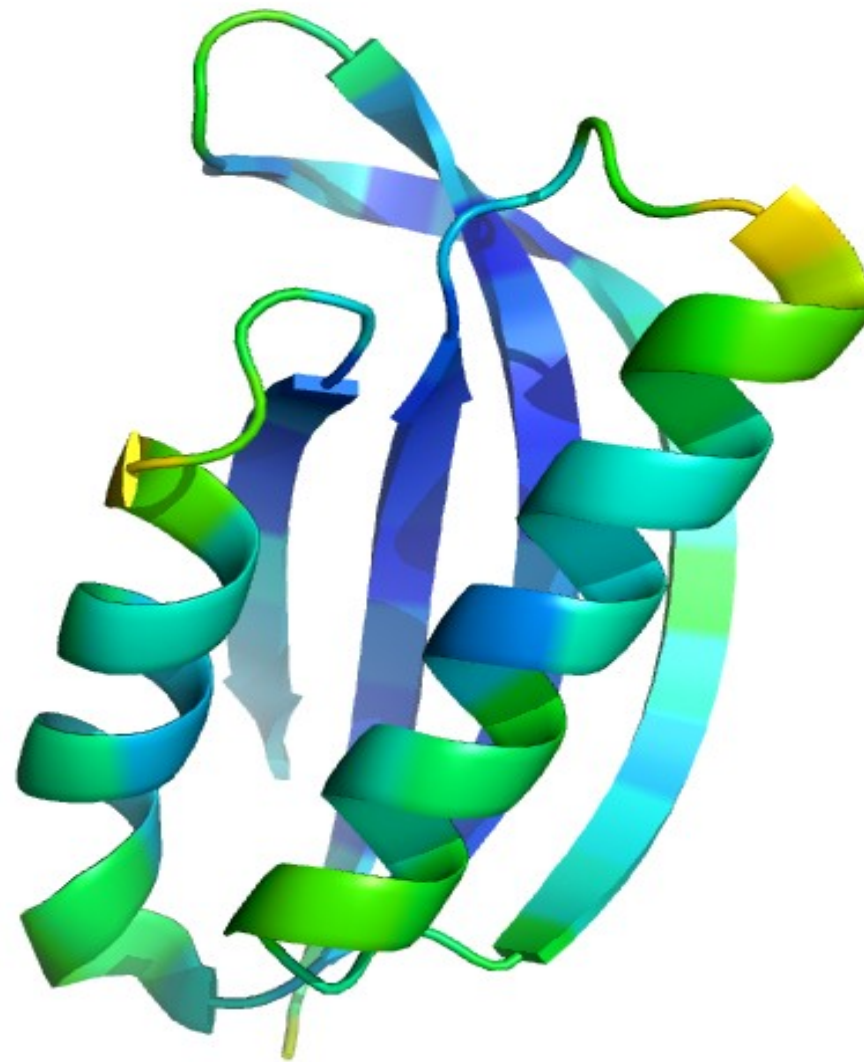


Small deviations tend to correlate with B-Factor

Ilou

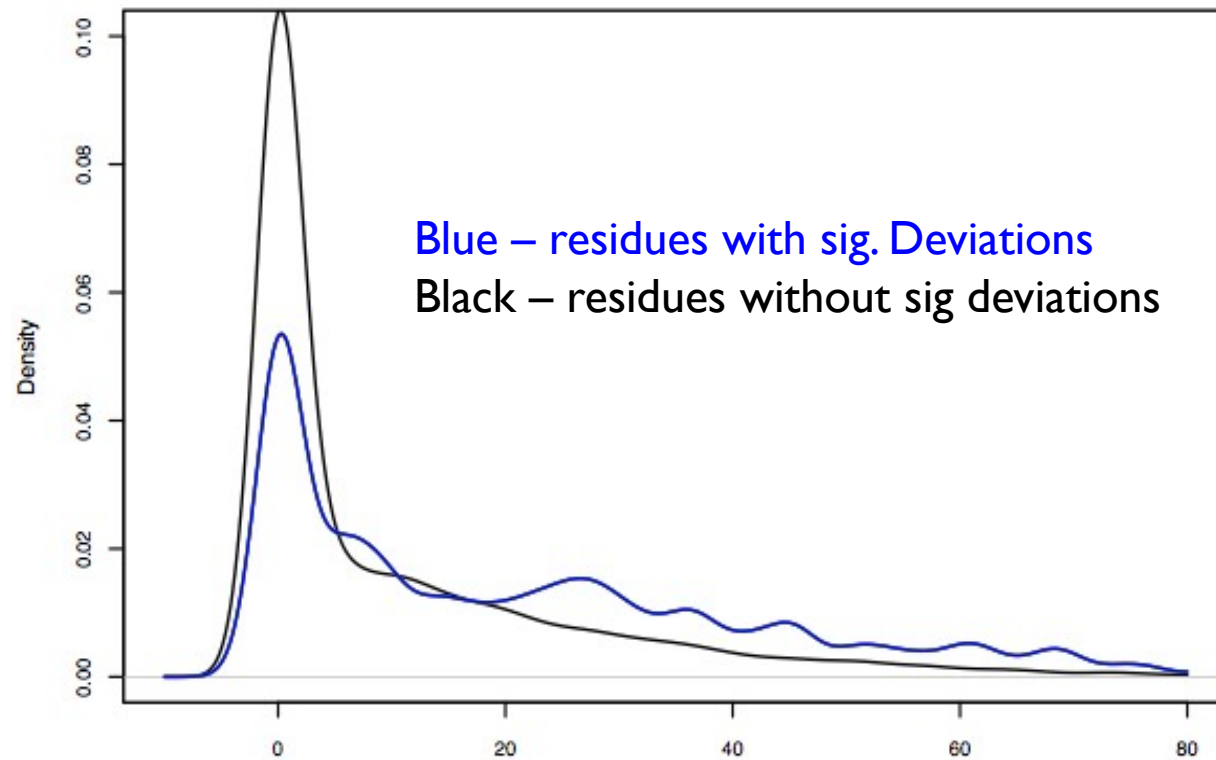


Rosetta Variance

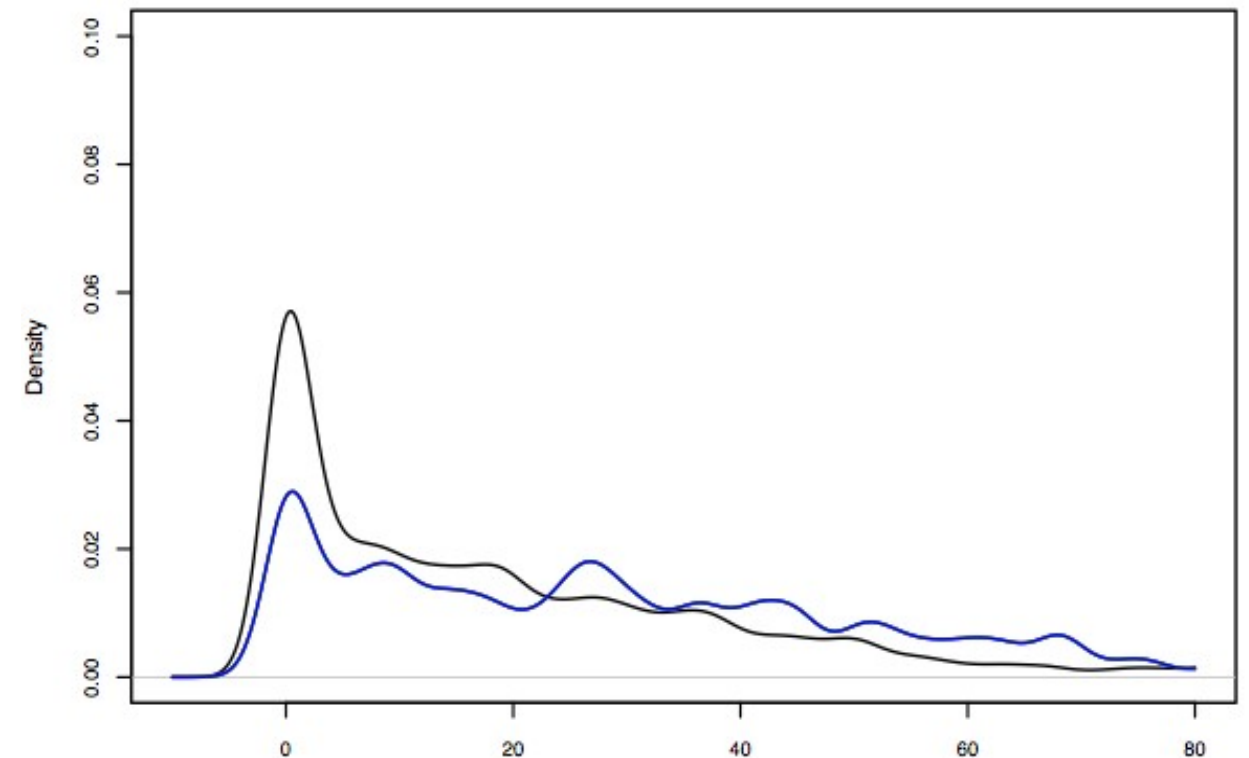


Xtal B-factors

Deviations correlate with xtal contacts

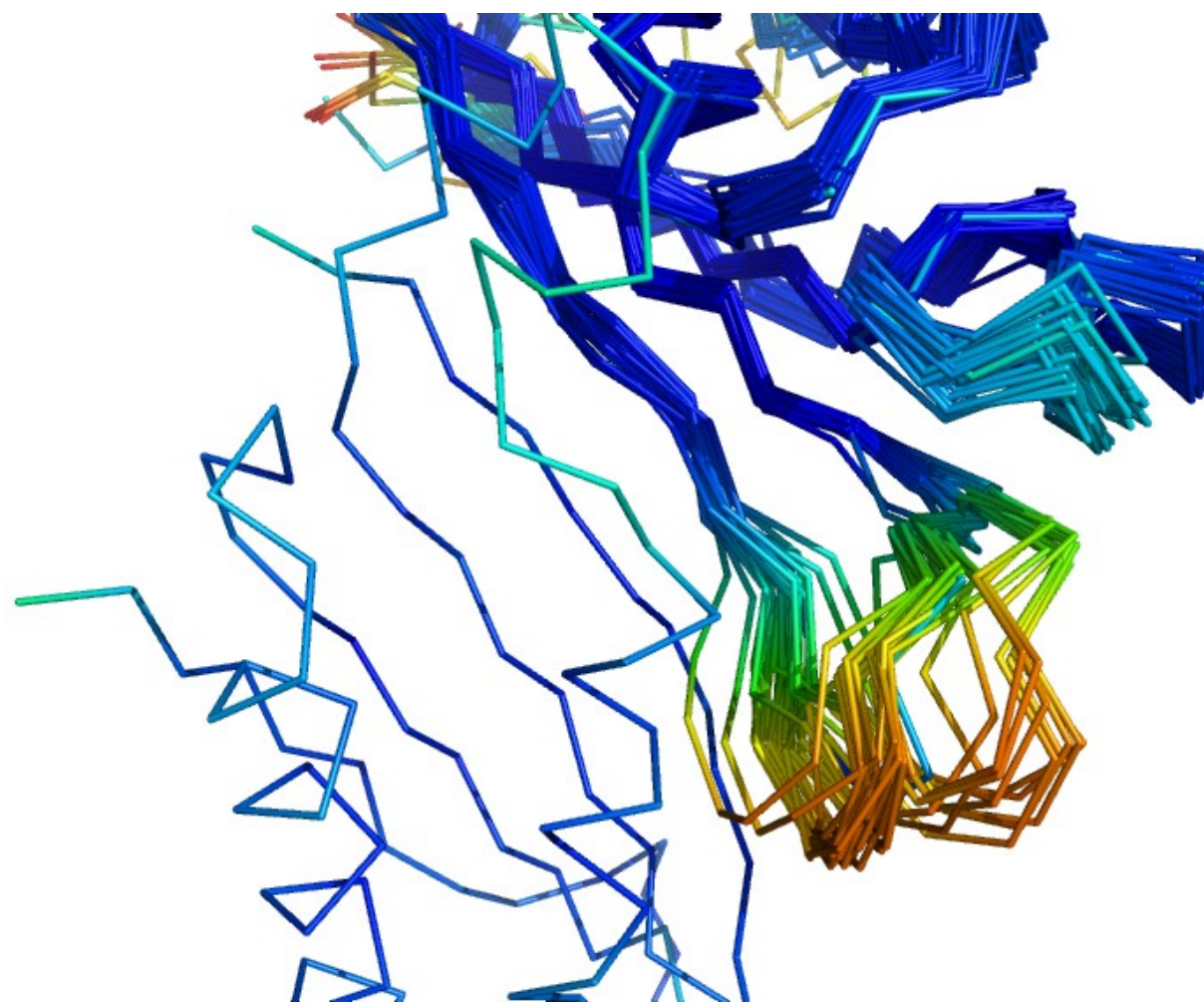


Number of crystal contacts

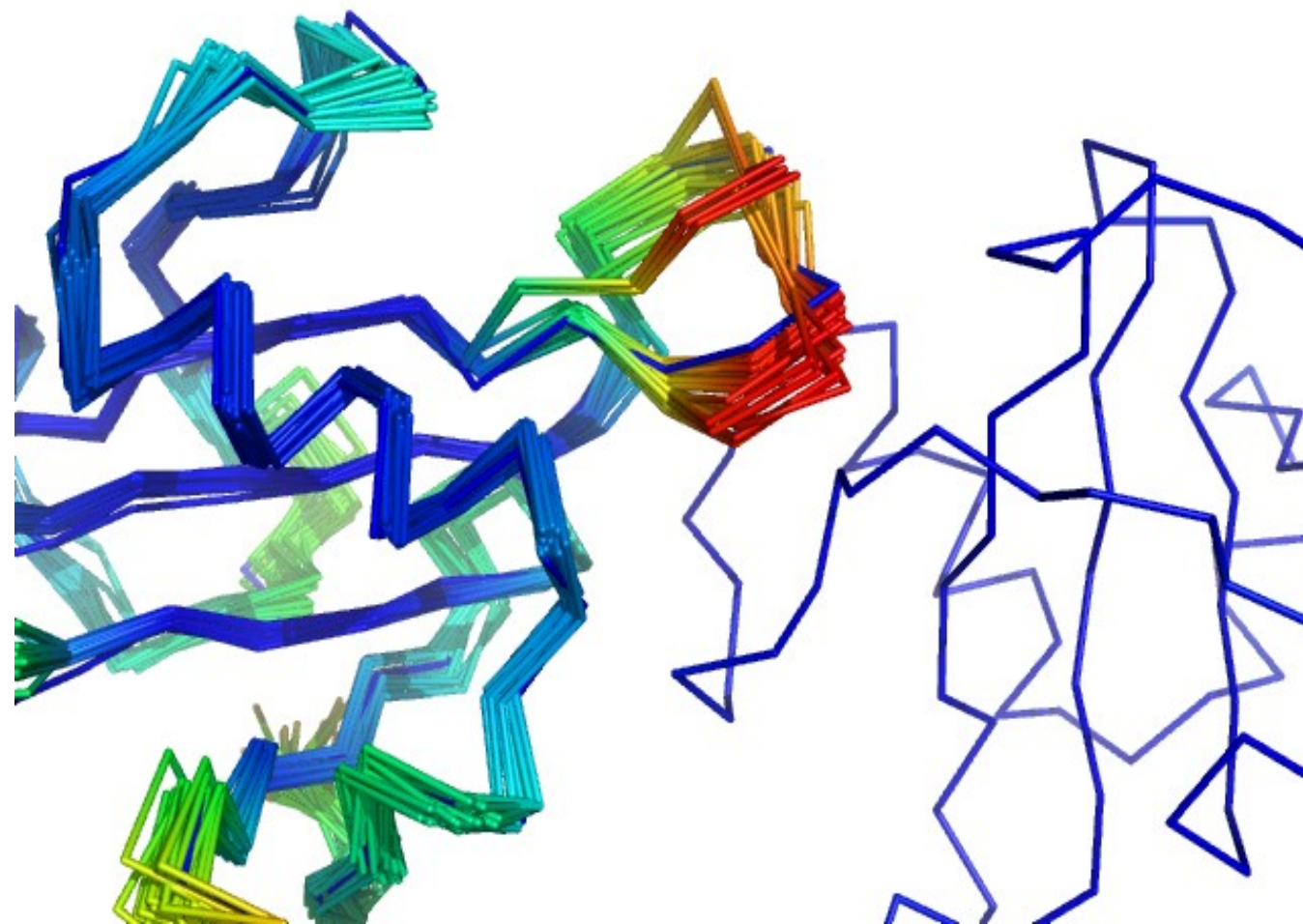


Number of crystal contacts, only for residues with few self contacts (<10)

Examples: Crystal contacts ?



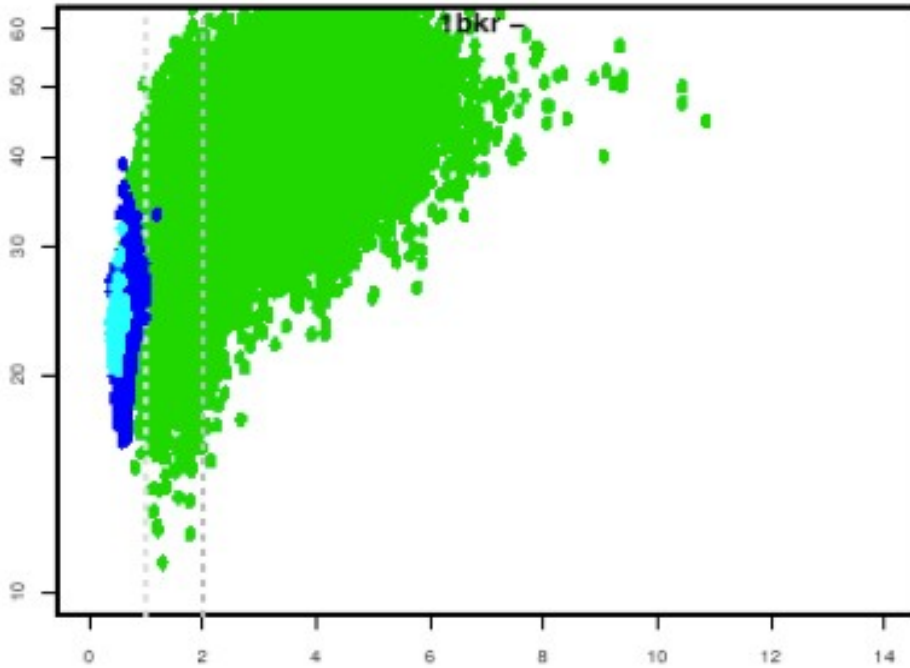
IDHN



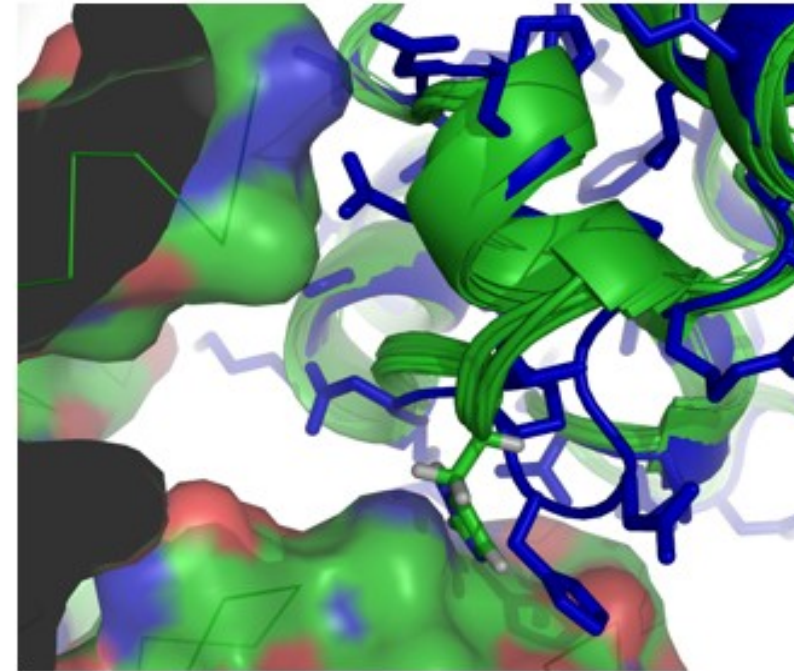
IYNV

Examples: Crystal contacts ?

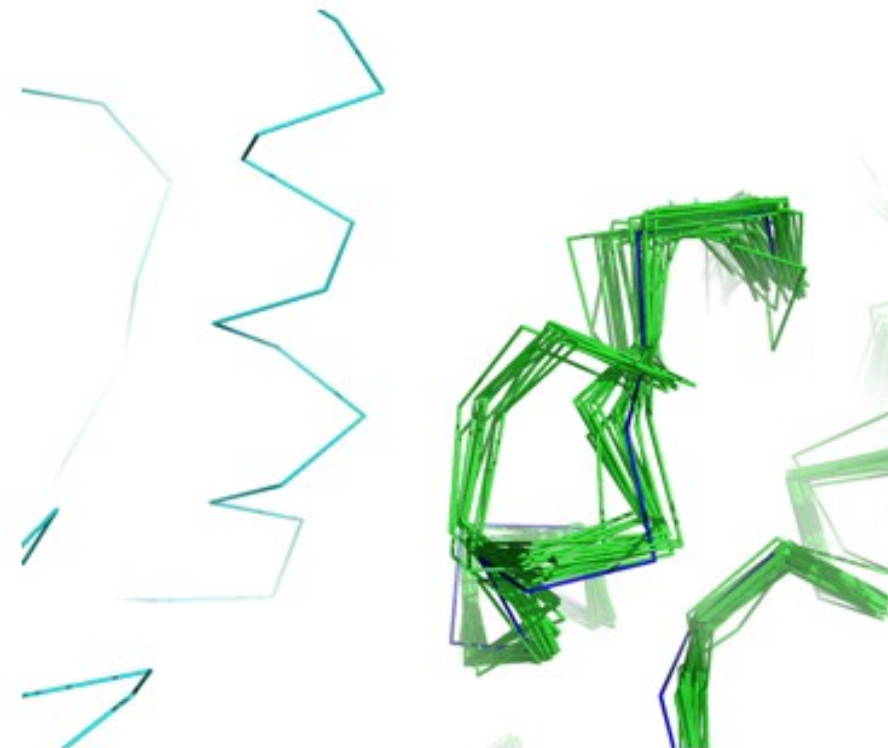
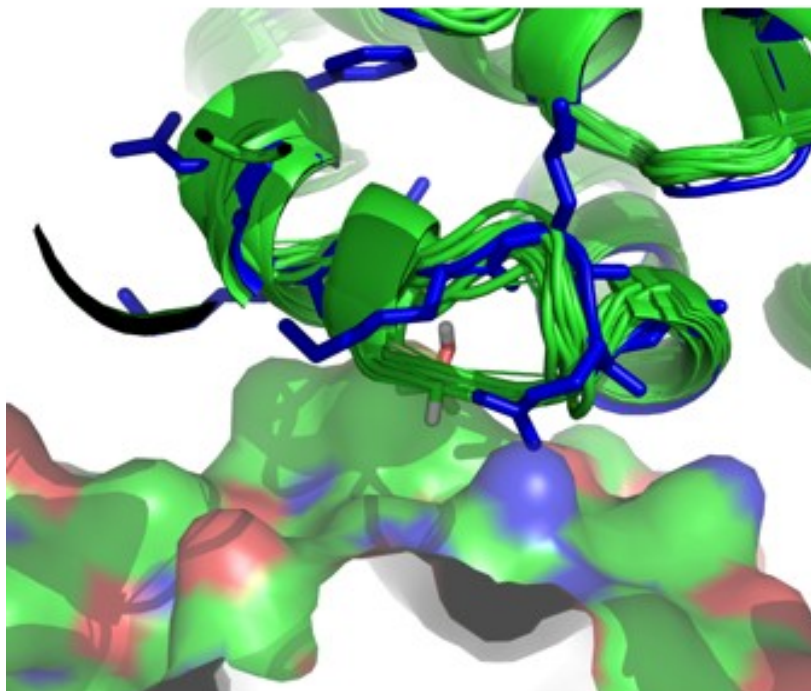
1bkr



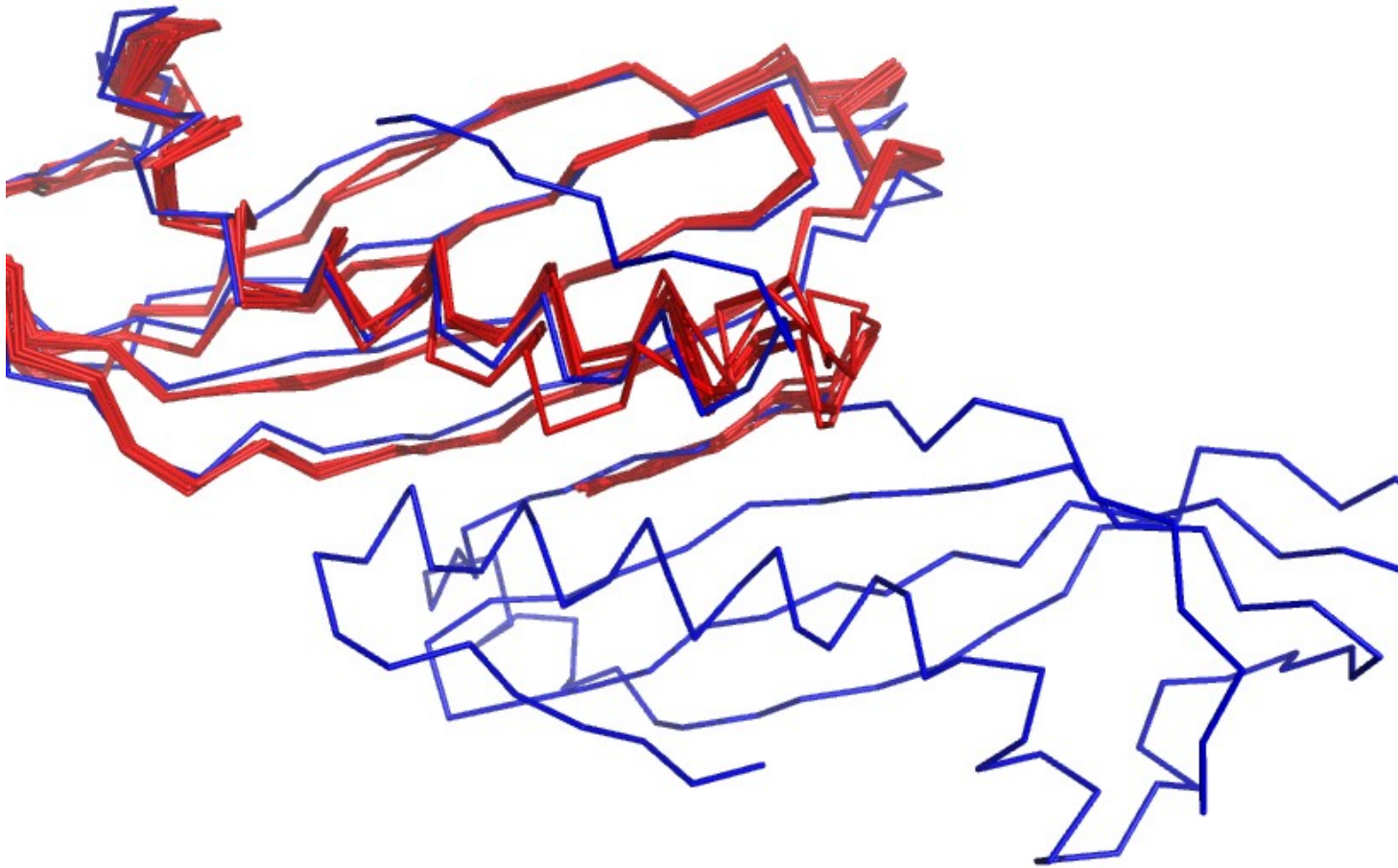
Deviation I



Deviation2

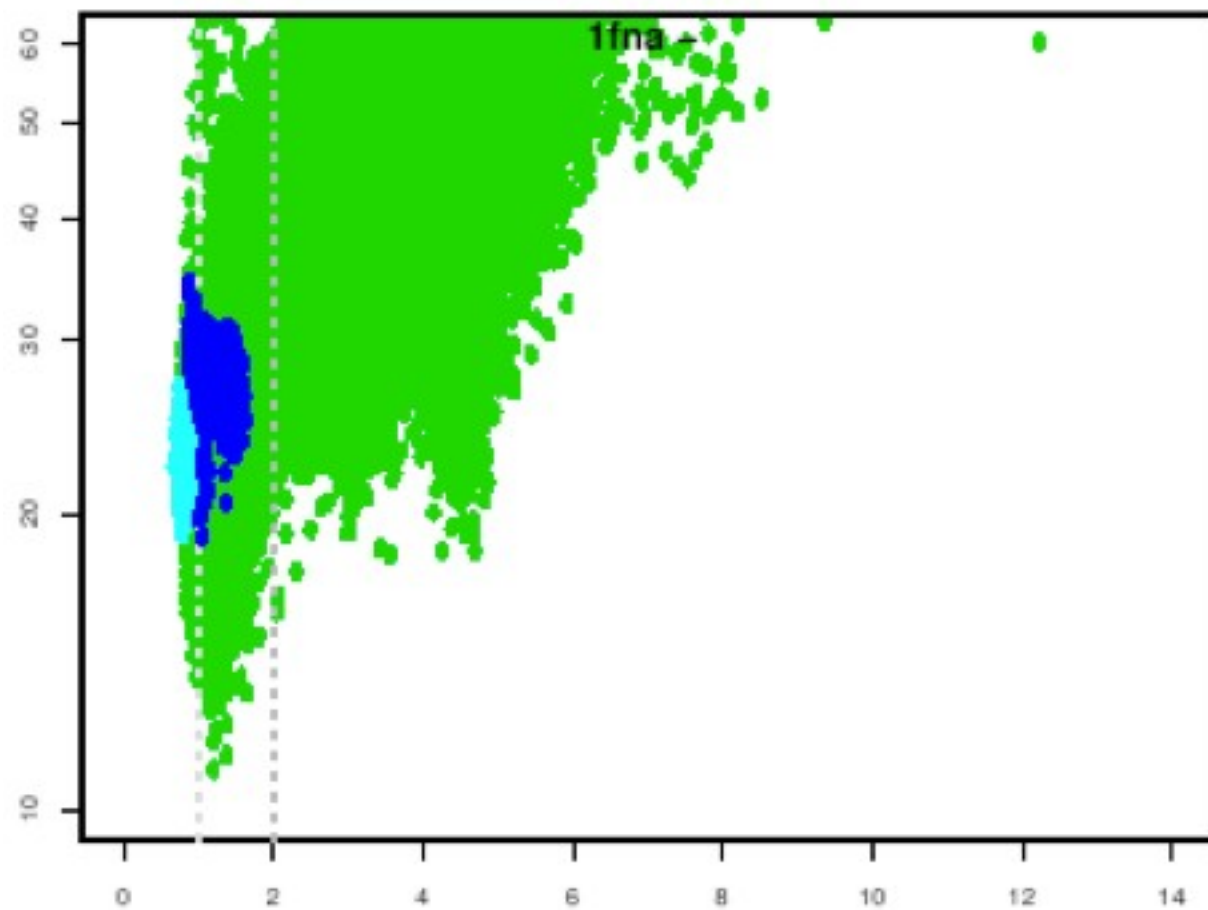


2hng

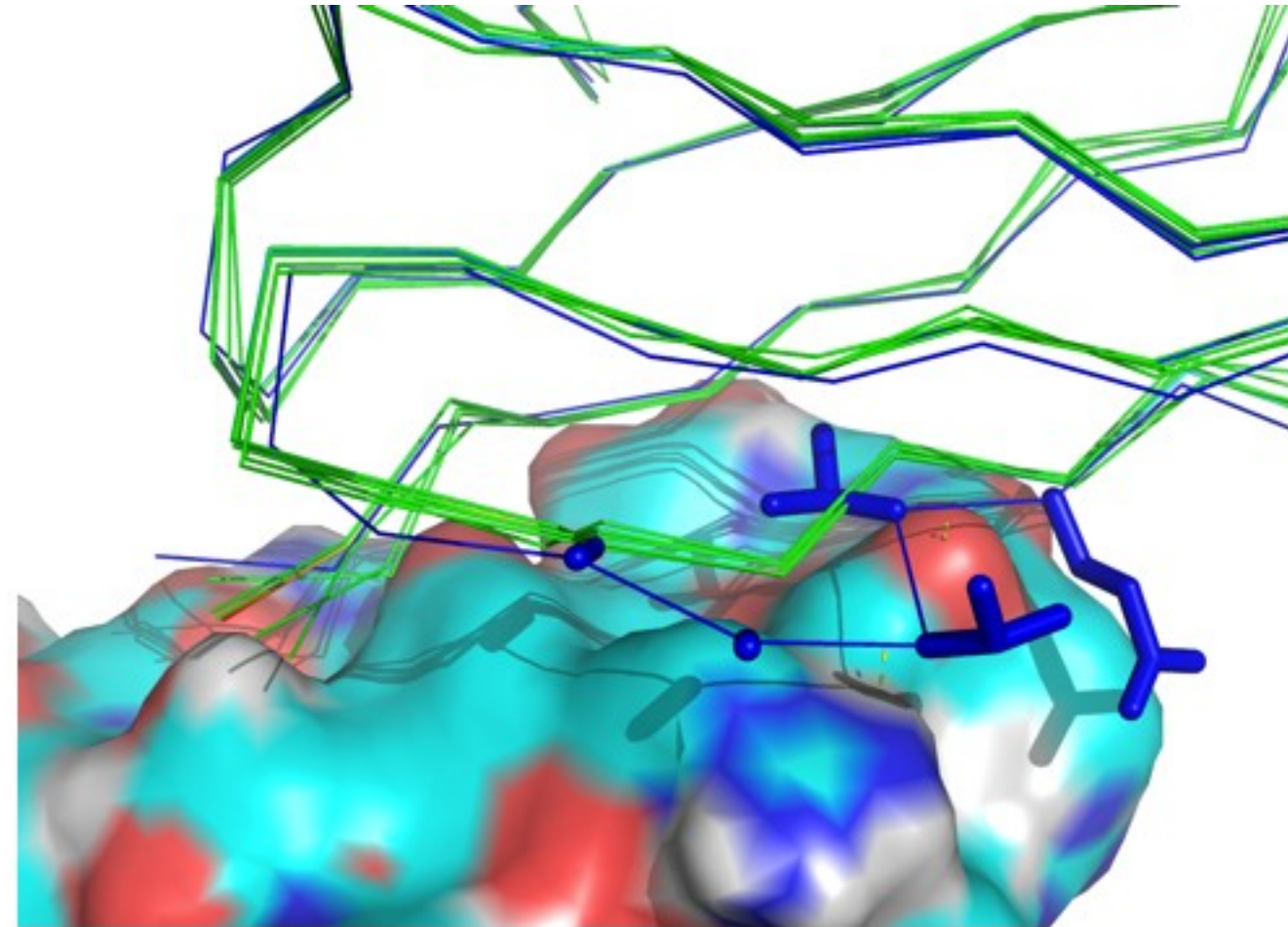


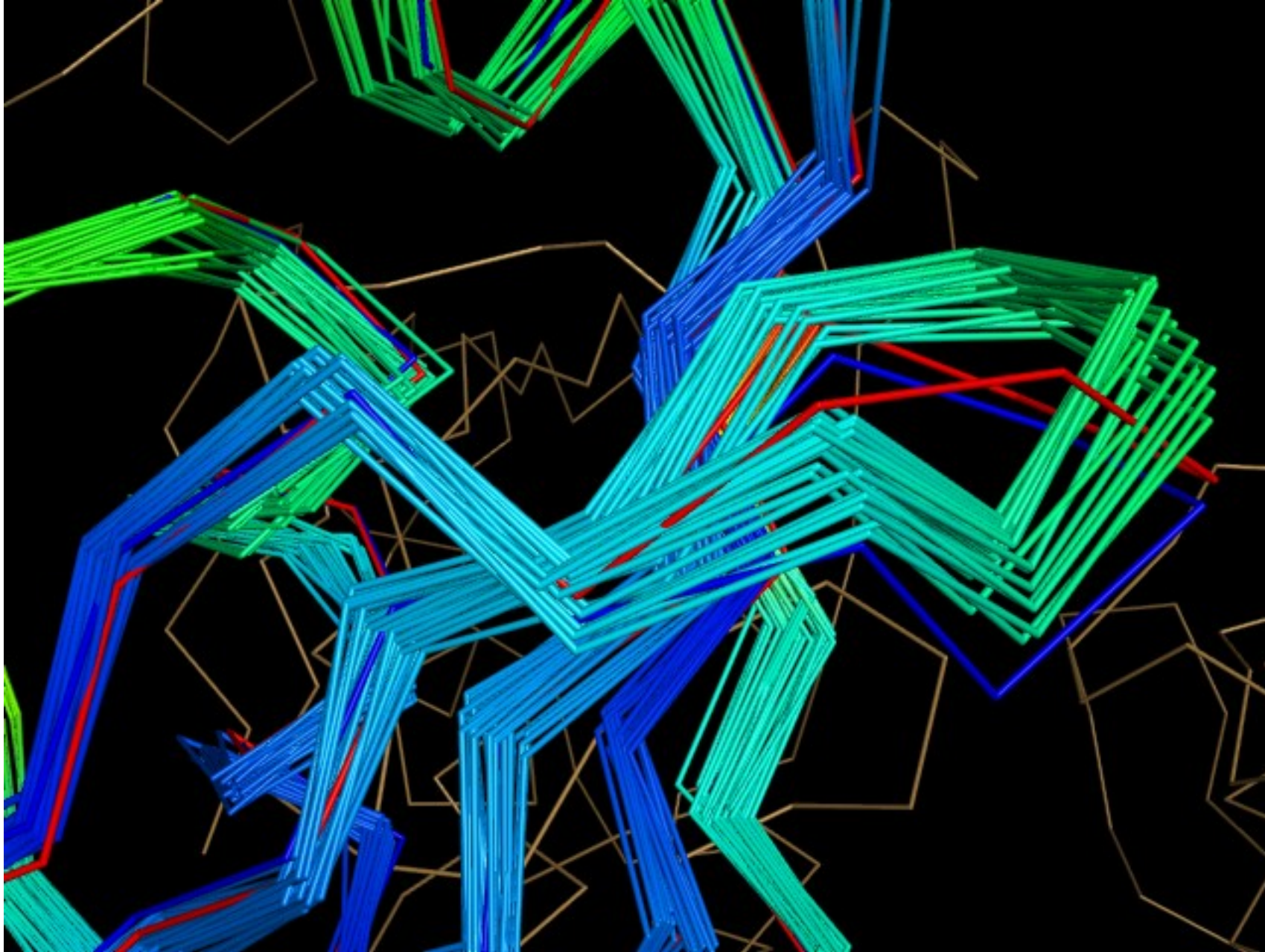
Dimer contact prevents
alternative conformation

l fna



Systematic deviation:

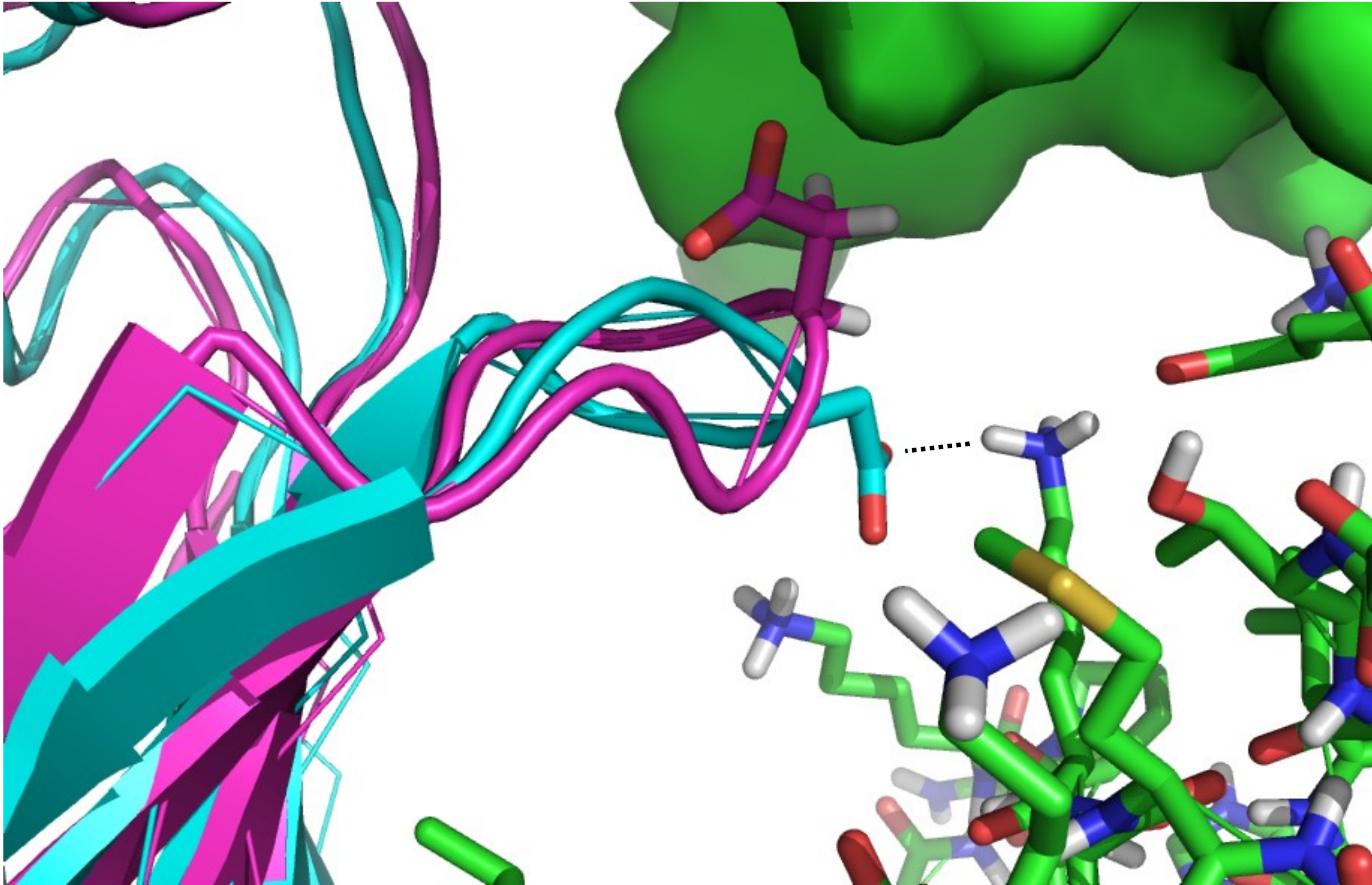




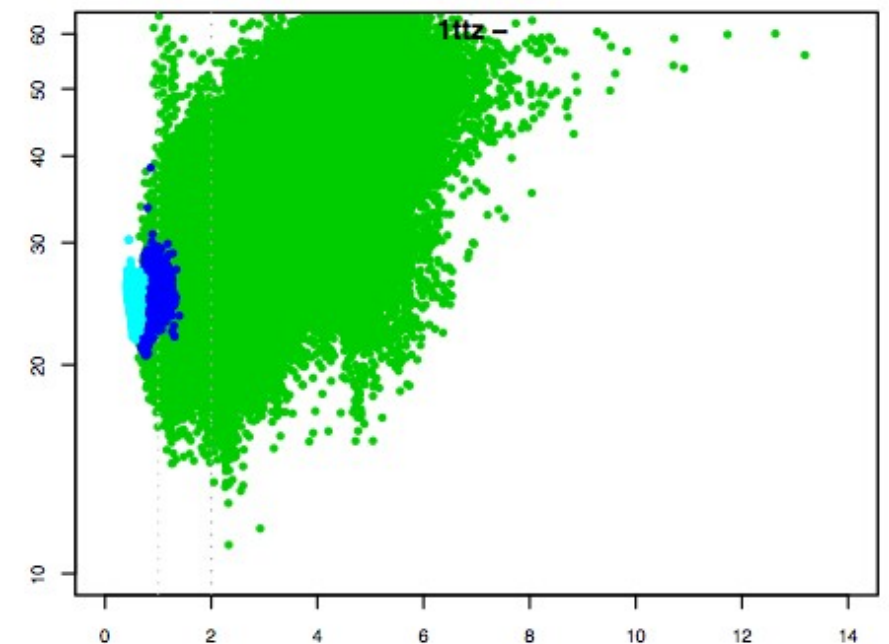
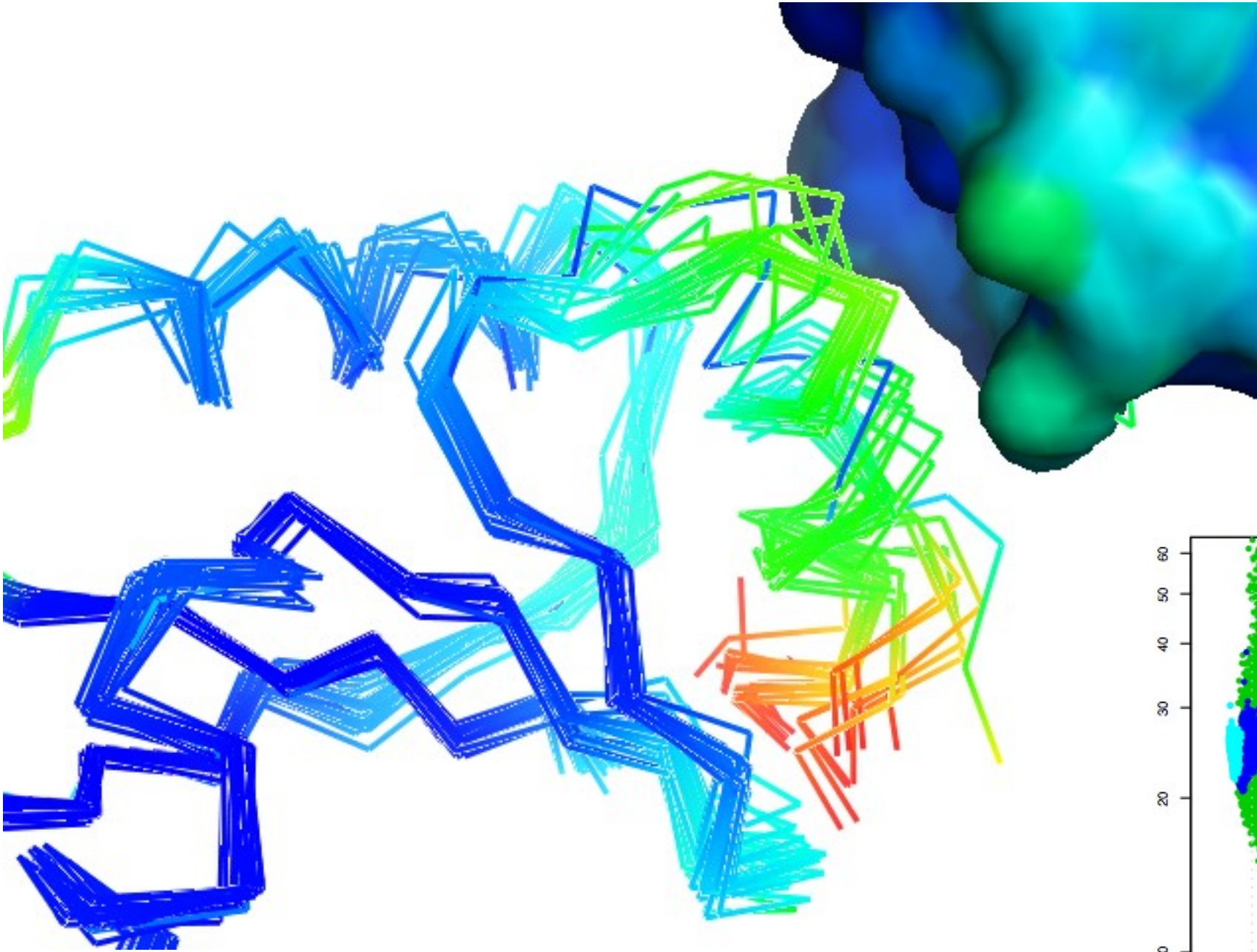
I fkb - Native

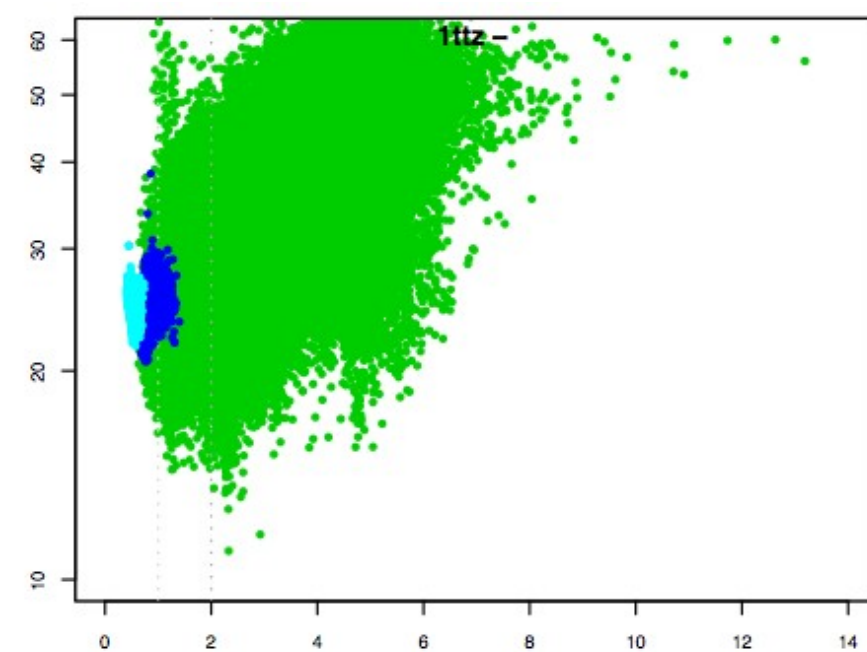
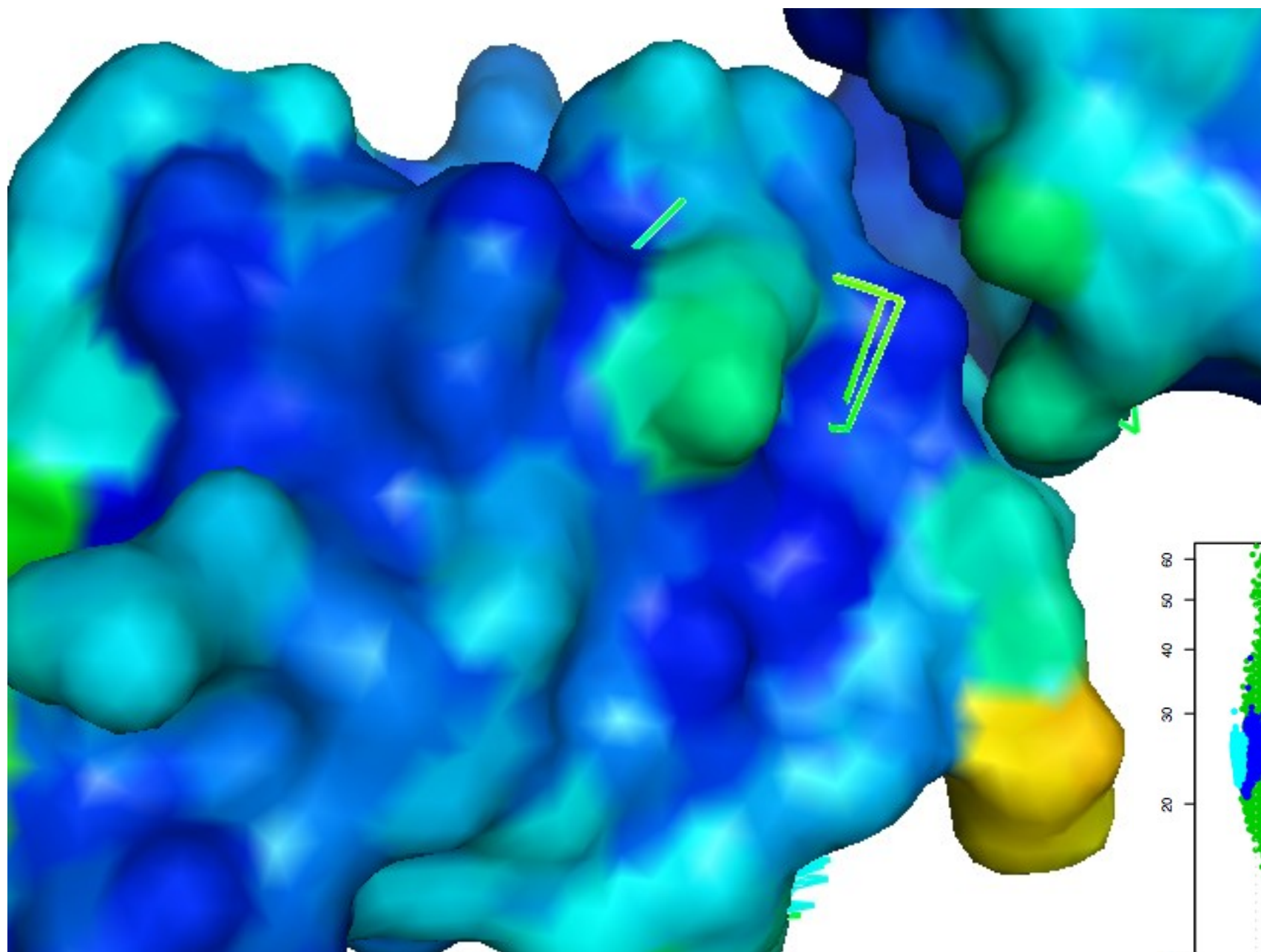
I fkj - 100% Homologue in
different crystal

I fkb vs rosetta model



8) Rosetta gets it wrong
also - a high accuracy metric
for improving the e-function

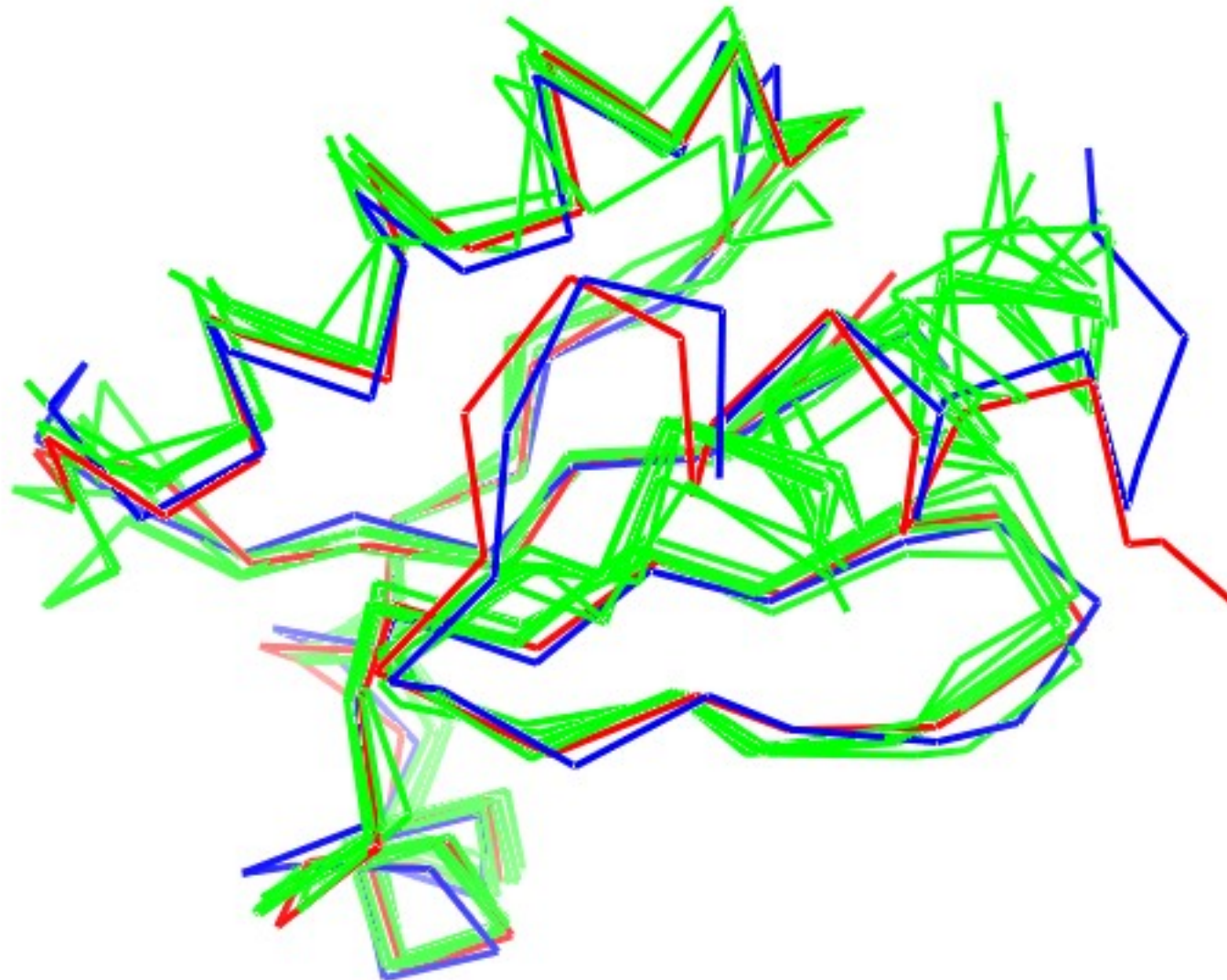




Rosetta

XRay

NMR



Acknowledgements

- Oliver Lange, James Thompson, David Kim, Andrew Leaver-Fay, Grishin Lab
- Daniel Keedy, Yifan Song, Ingemar Andre, Andrew Leaver-Fay, Jane Richardson, Spencer Blivens, Liz Kellogg
- David B & Baker Lab