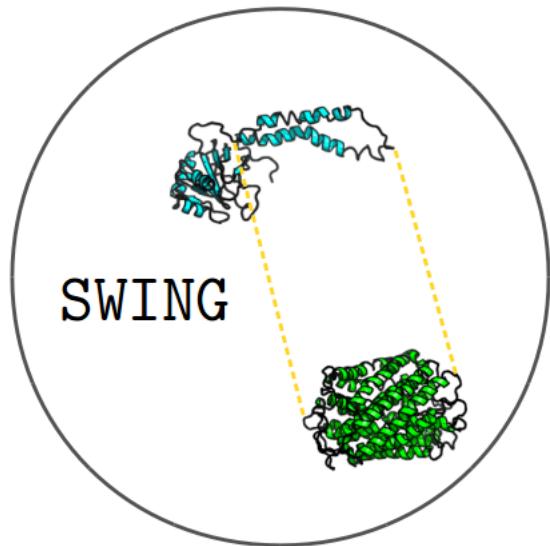


Meet - U



SWING (SAMPLING WITH INTEROLOG)

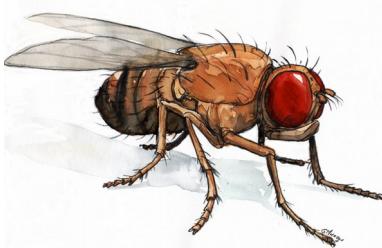
Master 2 Bioinformatique
Université Paris-Sud

Equipe 10
De Azevedo Kévin
Duhamel Marine
Yao Hua-Ting

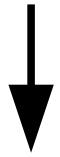
SWING

PRINCIPLE

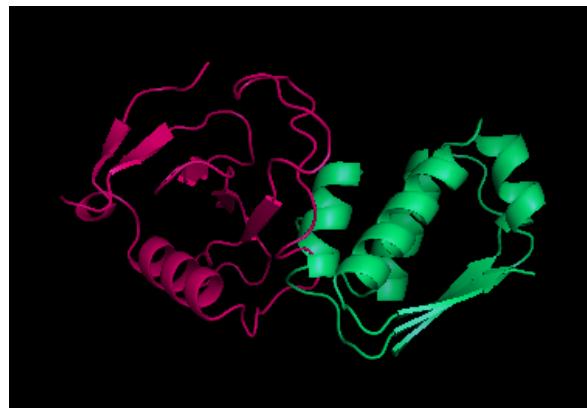
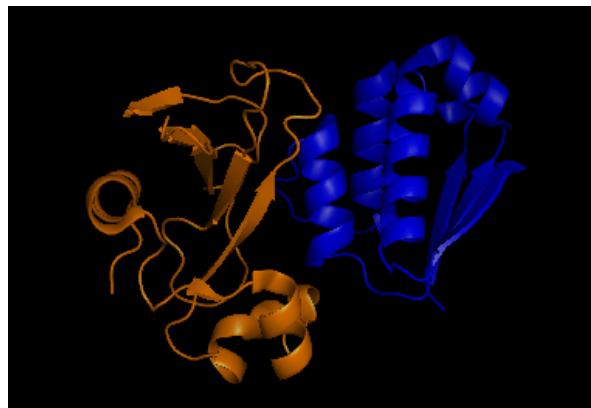
The original idea



Homology between R
and R' and L and L'



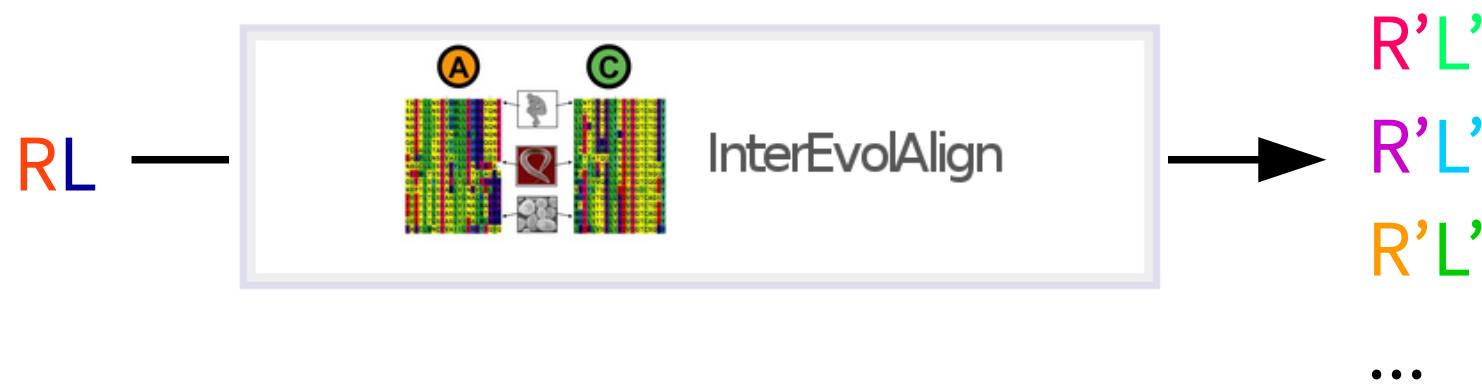
→ RL and R'L' are
interologs



SWING

PRINCIPLE

Interolog research



SWING

PRINCIPLE

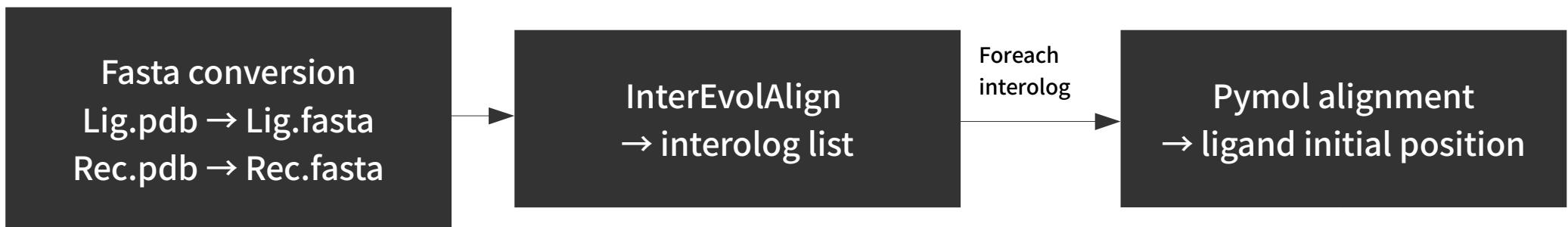
Fasta conversion
Lig.pdb → Lig.fasta
Rec.pdb → Rec.fasta



InterEvolAlign
→ interolog list

SWING

PRINCIPLE



SWING

PRINCIPLE

Initial position setup

1QDL

Receptor

Ligand



SWING

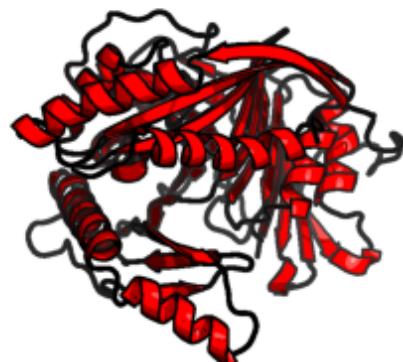
PRINCIPLE

Initial position setup

1QDL

Receptor

Ligand

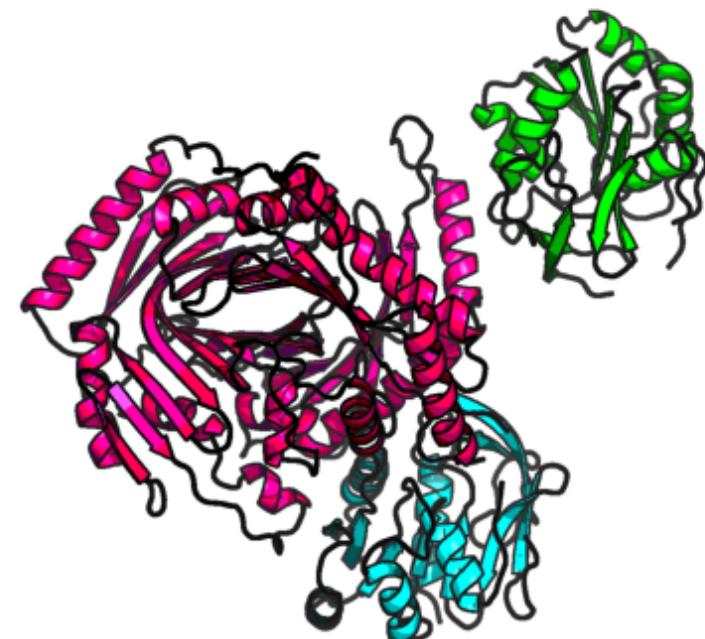


1i1q

Receptor

Ligand 1

Ligand 2



SWING

PRINCIPLE

Initial position setup

1QDL

Receptor

Ligand



1i1q

Receptor (aligned)

Ligand 1

SWING

PRINCIPLE

Initial position setup

1QDL

Receptor

Ligand

(aligned)



1i1q

Receptor (aligned)

Ligand 1

SWING

PRINCIPLE

Initial position setup

1QDL

Receptor

Ligand

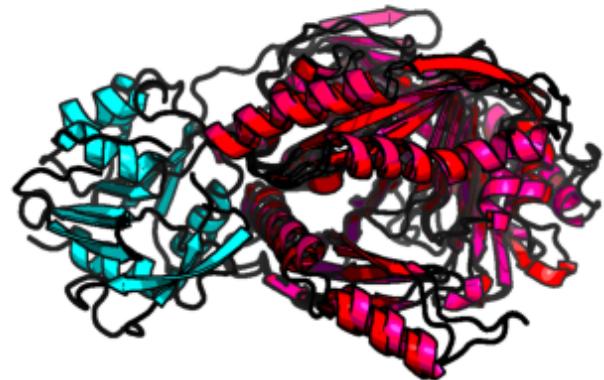
position 1



SWING

PRINCIPLE

Initial position setup



1QDL

Receptor

Ligand

1i1q

Receptor (aligned)

Ligand 2



SWING PRINCIPLE

Initial position setup



1QDL

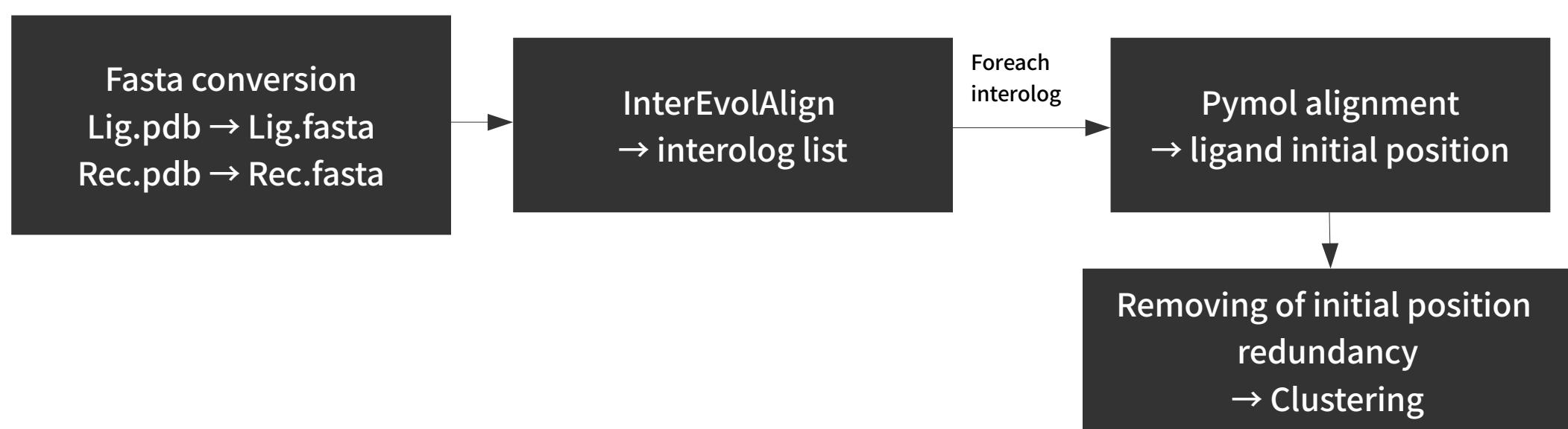
Receptor

Ligand position 1
position 2

→ 2 initial positions

SWING

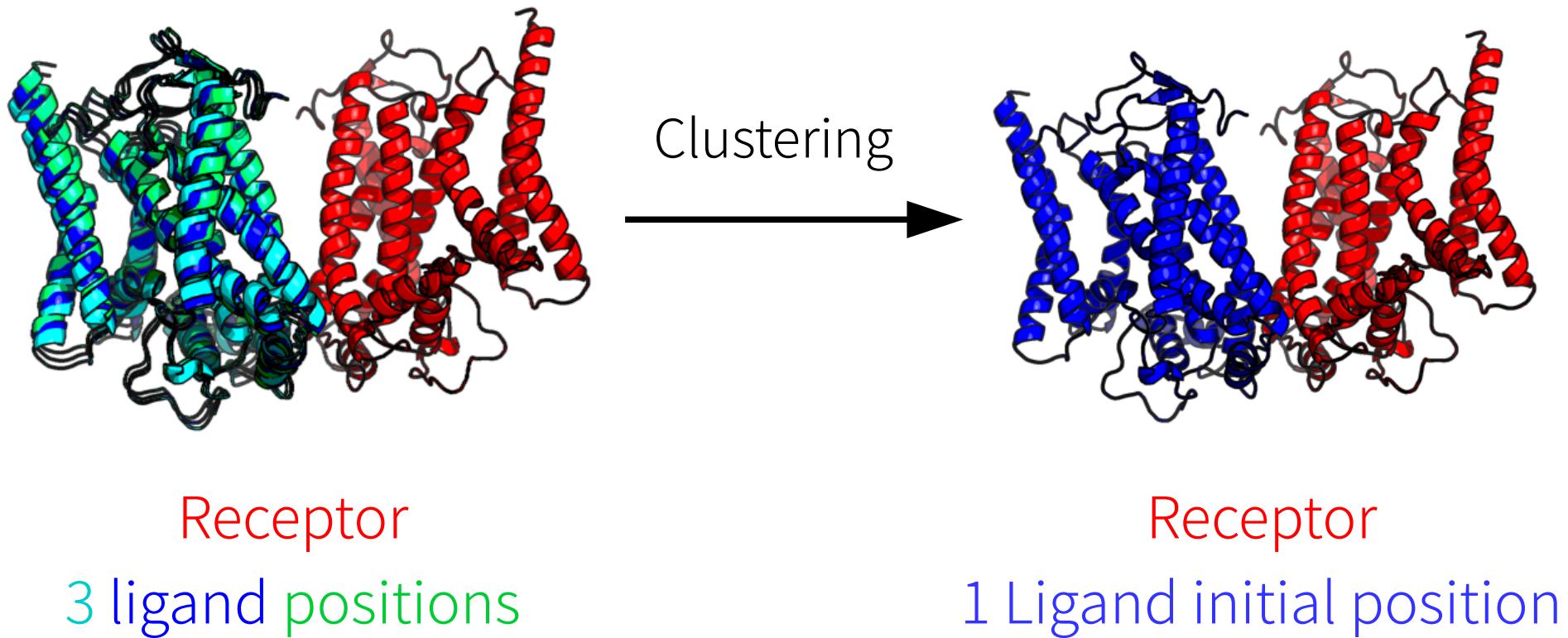
PRINCIPLE



SWING

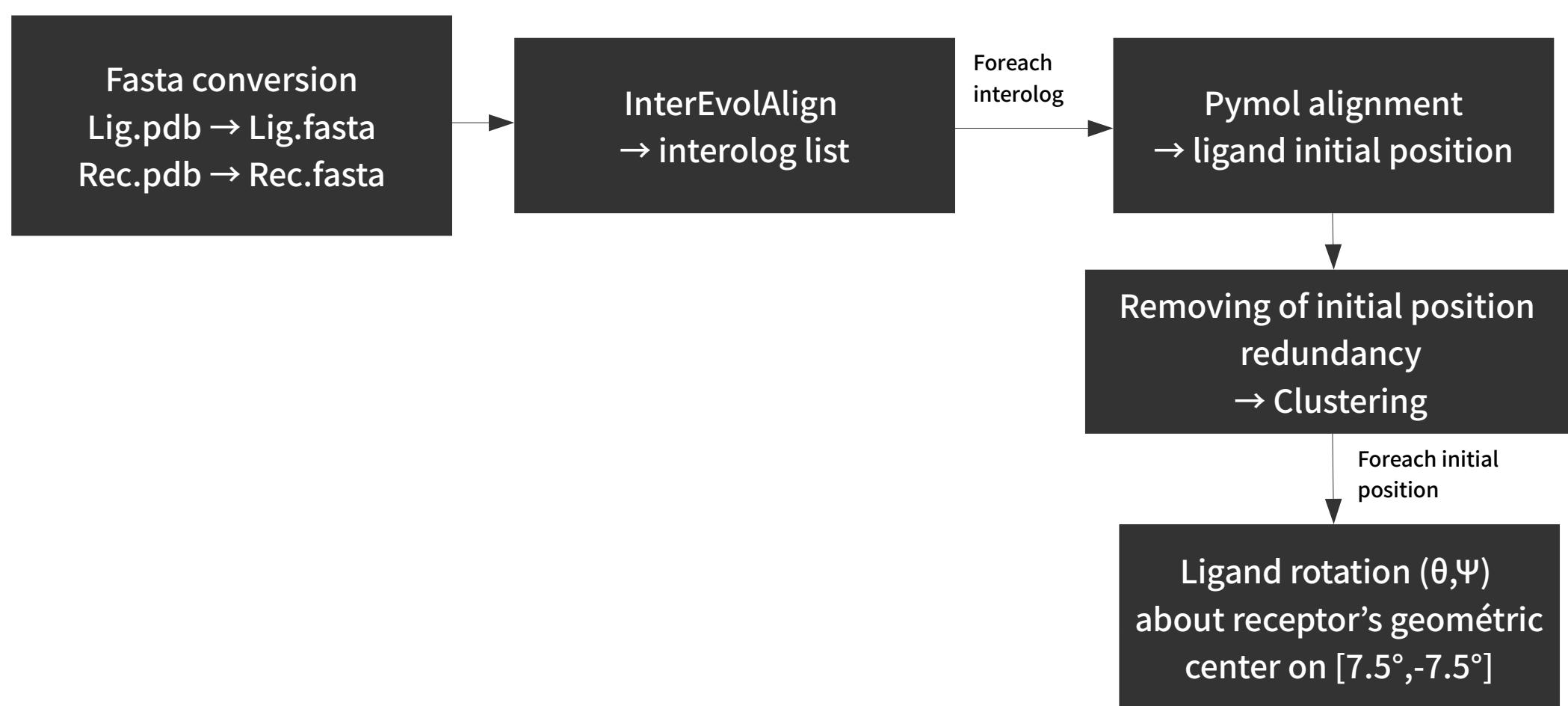
PRINCIPLE

1PPJ (CP)



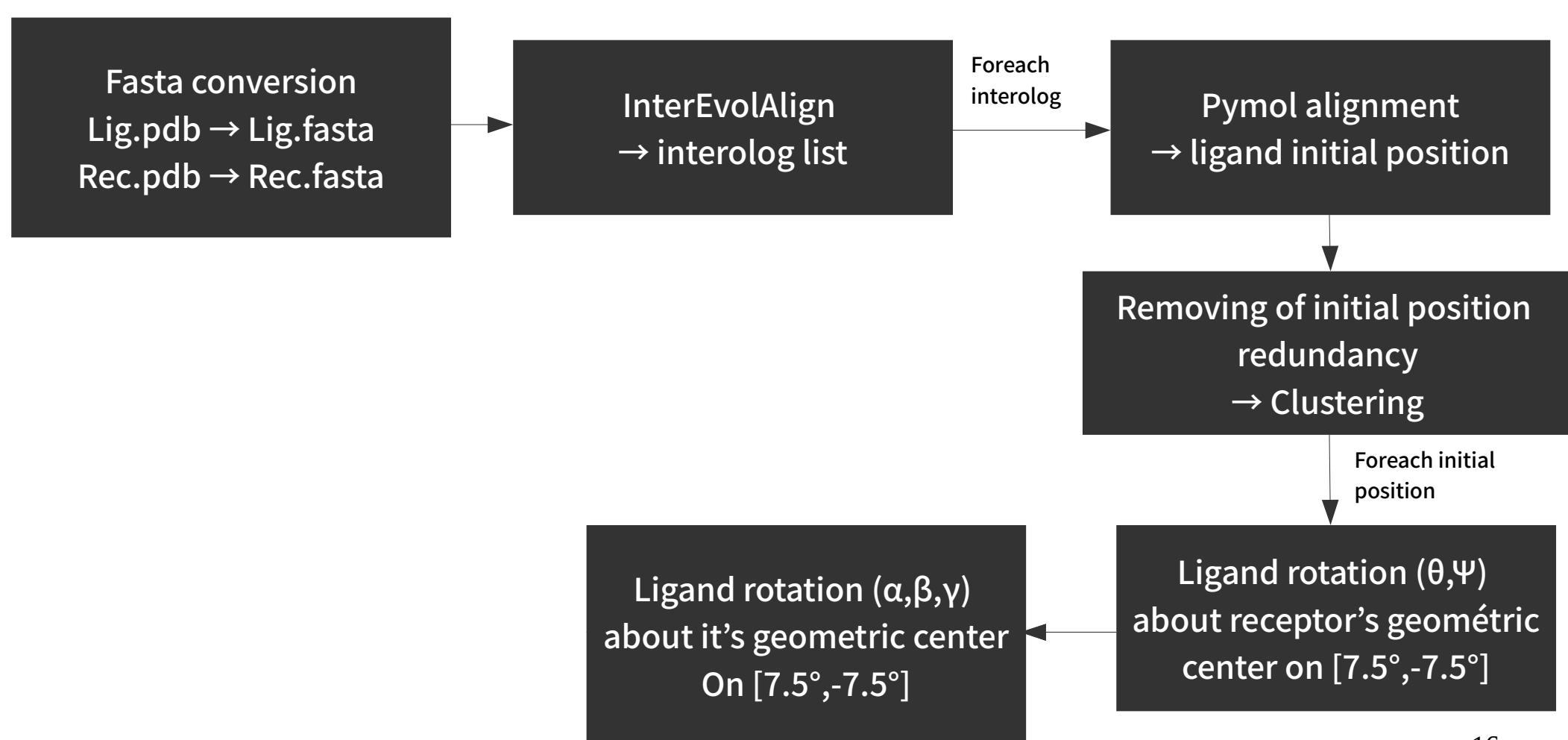
SWING

PRINCIPLE



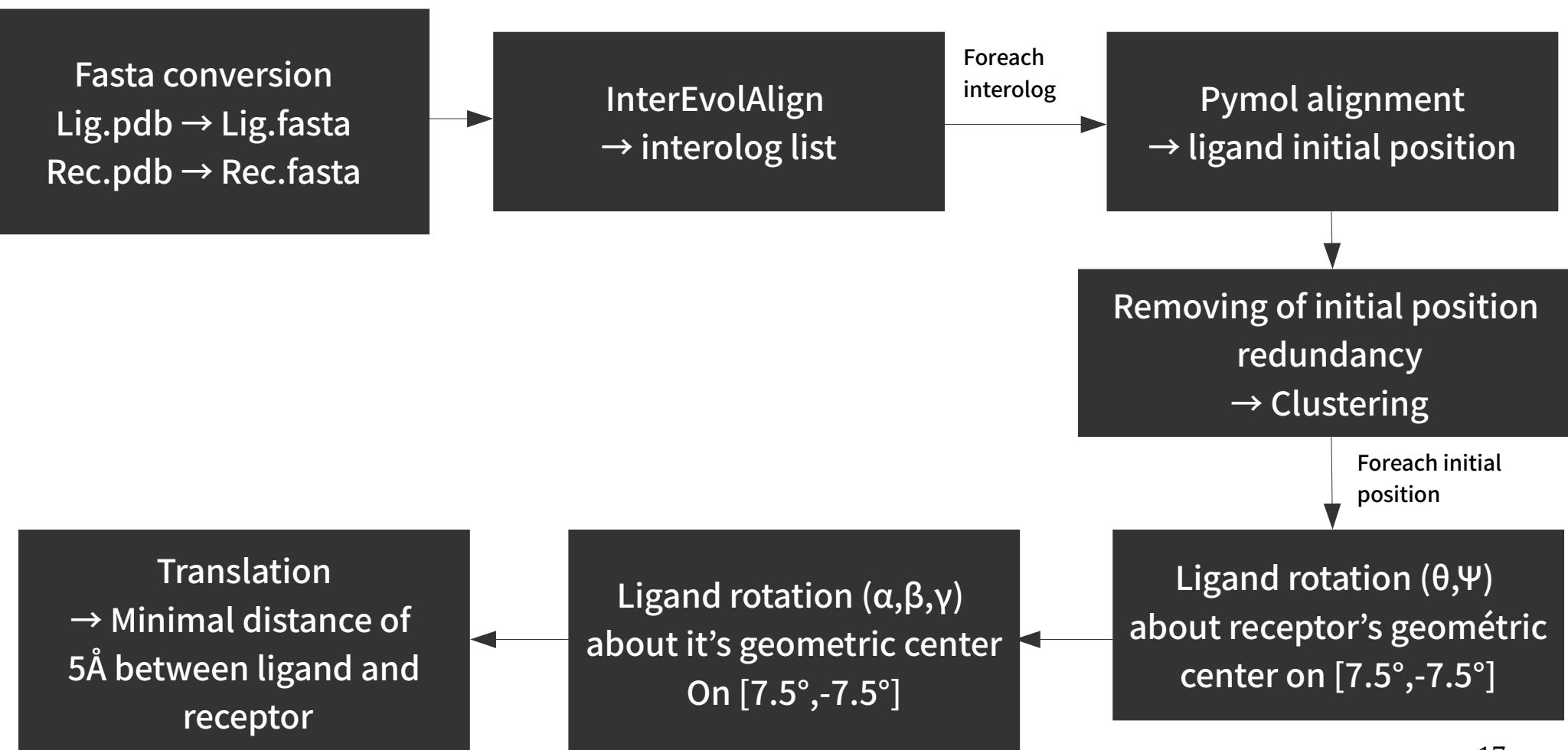
SWING

PRINCIPLE



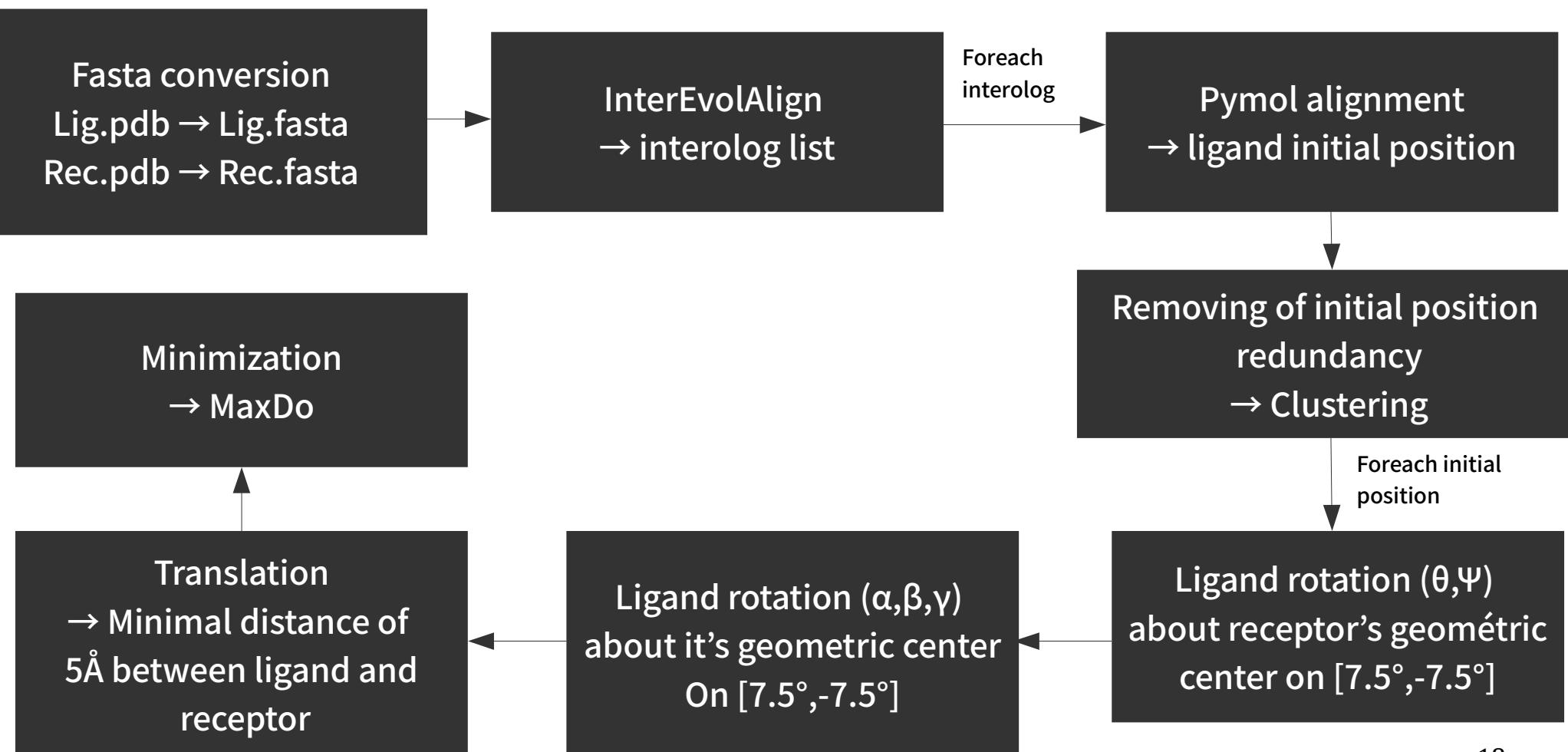
SWING

PRINCIPLE



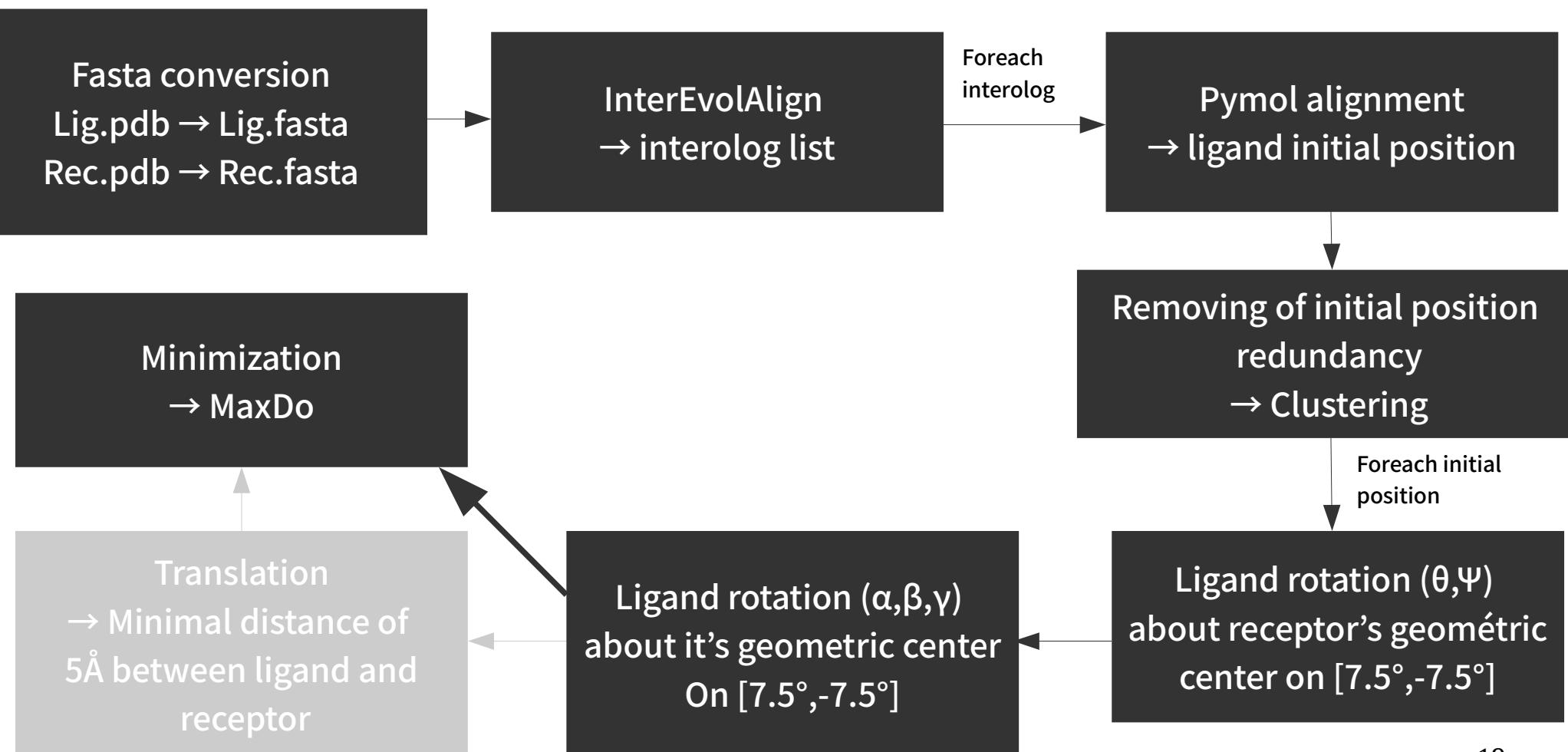
SWING

PRINCIPLE



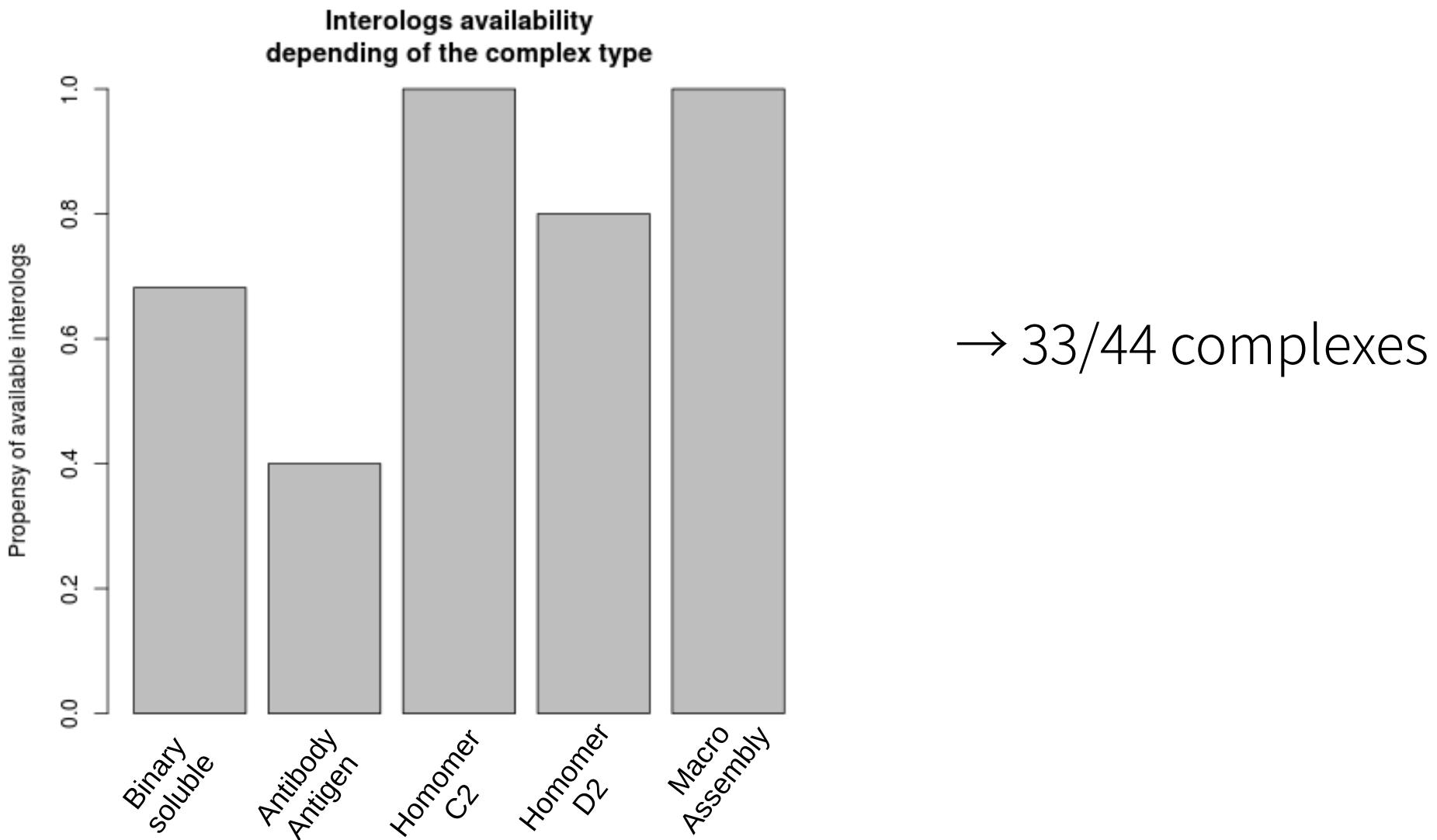
SWING

PRINCIPLE



SWING

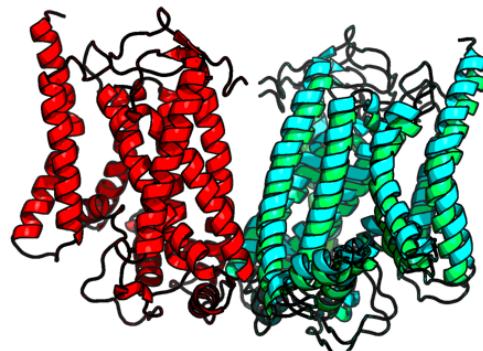
INTEROLOG AVAILABILITY



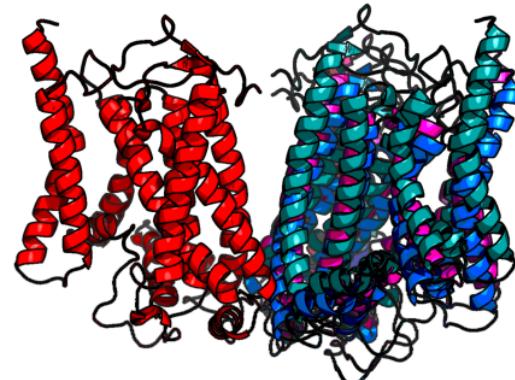
SWING

SAMPLING DISTRIBUTION

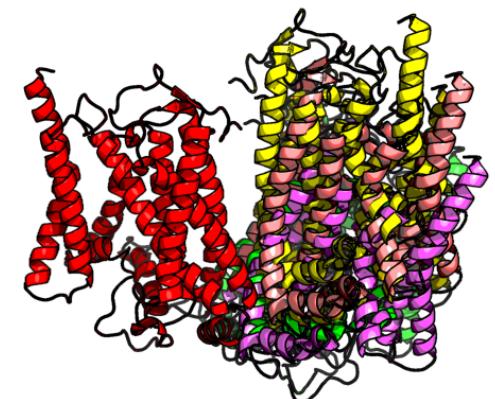
1PPJ (CP)
Before
minimization



7.5° - clustering cutoff 1Å

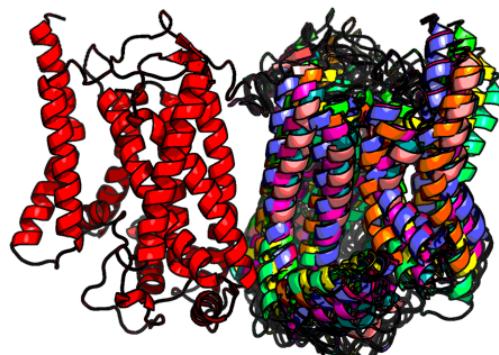


15° - clustering cutoff 1.65Å

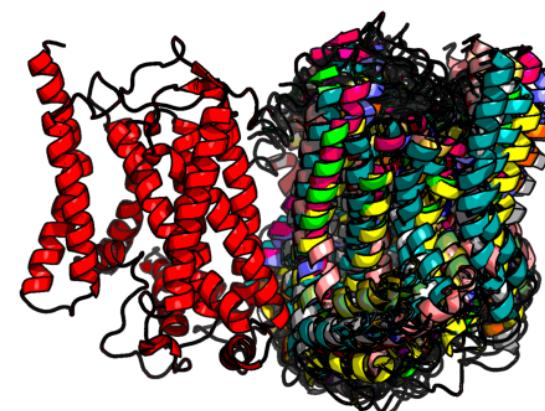


30° - clustering cutoff 4Å

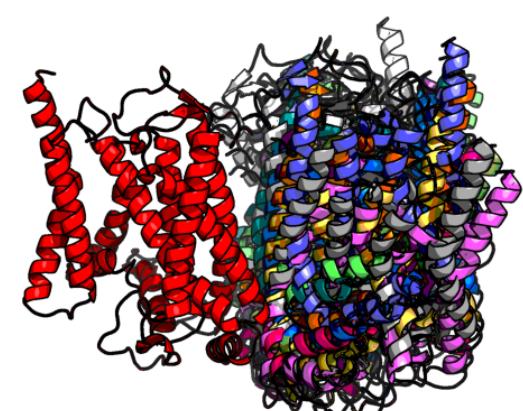
1PPJ (CP)
After
minimization



7.5° - clustering cutoff 1Å



15° - clustering cutoff 1.65Å



30° - clustering cutoff 4Å

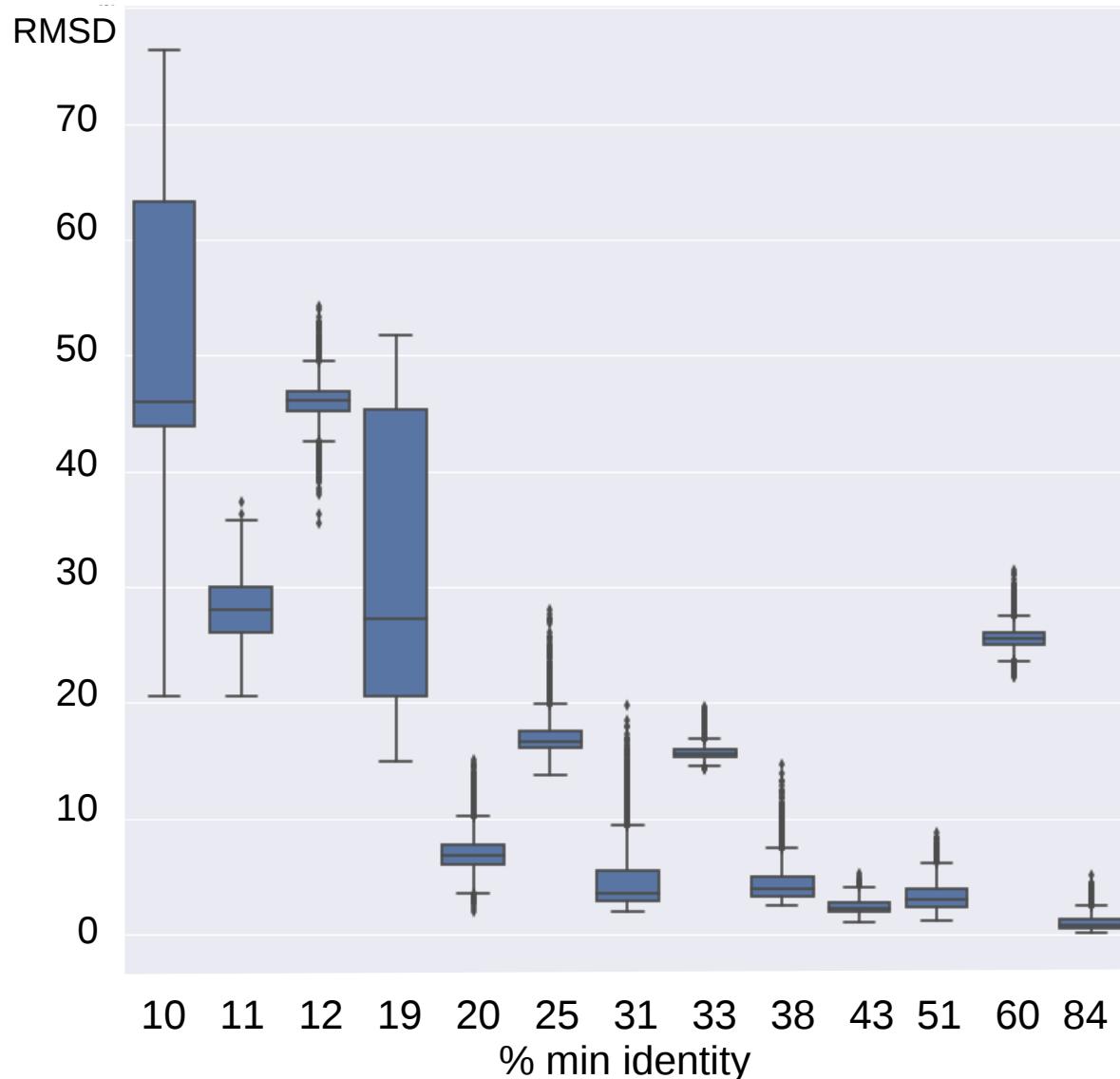
SWING

SAMPLING RESULTS

	Type	# interologs	# initial positions	# conformations	Angle	LRMSD (Å) no minimization	LRMSD (Å) minimization
1CGI	soluble	6	3	1178	7.5°	2.7012	0.5044
3FN1	soluble	15	11	7352	30°	2.4971	0.7707
1AY7	soluble	1	1	716	30°	2.4553	1.3287
1DQJ	AB-AG	3	3	2491	7.5°	0.2370	0.6683
1PPJ (CP)	Macro-assembly	3	1	795	30°	2.0073	1.2939

SWING

INTEROLOG IDENTITY DEPENDENCY



	Native-like (<5Å)	Native-like (>5Å)
Identity < 30 %	258	93439
Identity > 30 %	15887	17745

Chi² test : pvalue < 0.01

	Native (<1Å)	Native (>1Å)
Identity < 30 %	5	93697
Identity > 30 %	3701	33632

Chi² test : pvalue < 0.01²³

SWING

SCORING RESULTS

Complex	Type	angle	score MeetDockOne naccess	score DeNovo energy	score DeNovo stat
1AY7	soluble	30°	4 → 1 * Best : 4.29 Å	0 → 9 * Best : 2.08 Å	0 → 10 * Best : 2.08 Å
1DQJ	AB-AG	30°	N/A → 10 * Best : 1.91 Å	7 → 10 * Best : 0.34 Å	0 → 6 * Best : 3.46 Å

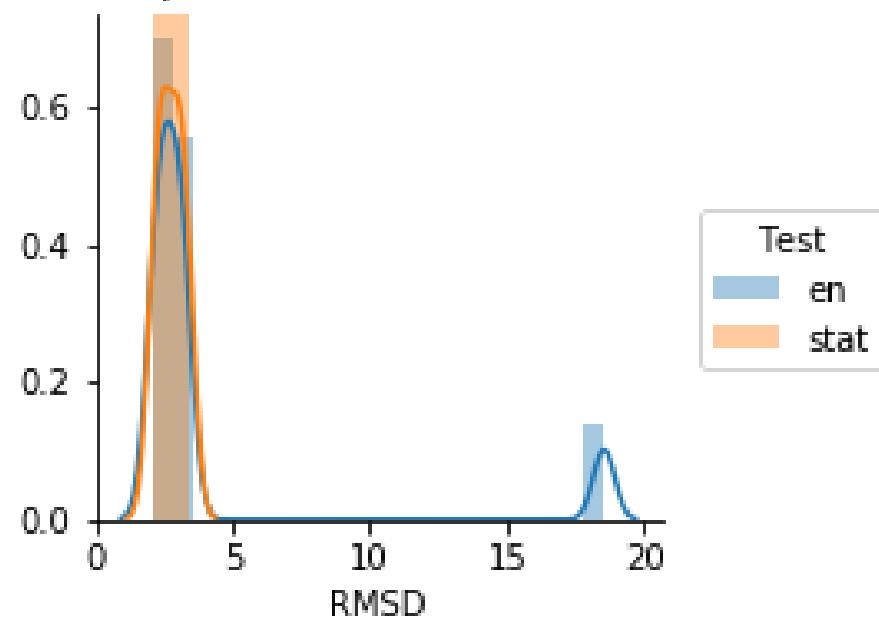
* Native-like in top10 before minimization → after minimization

SWING

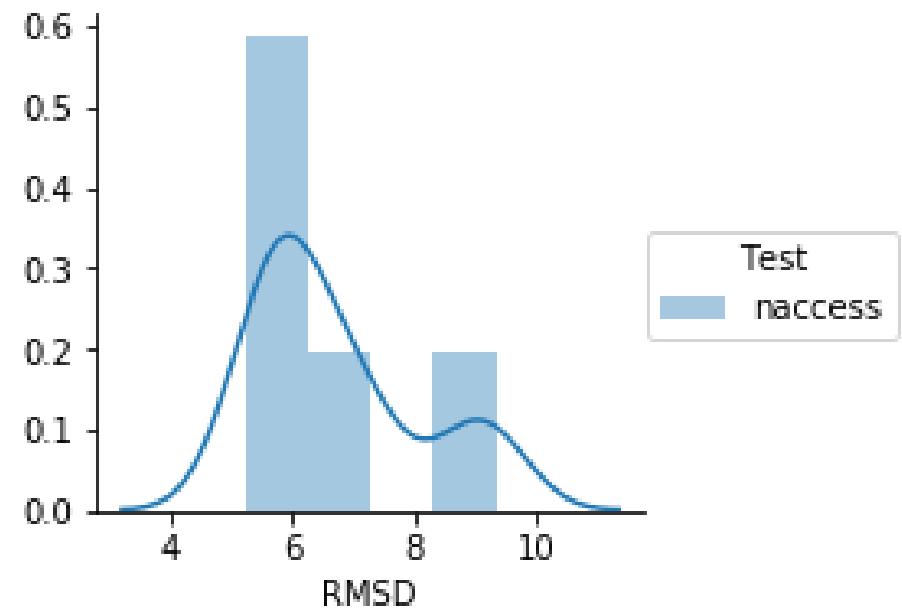
SCORING RESULTS

Minimized and without pushback...

RMSD of Top 10 scored conformations for 1AY7



RMSD of Top 10 scored conformations for 1AY7

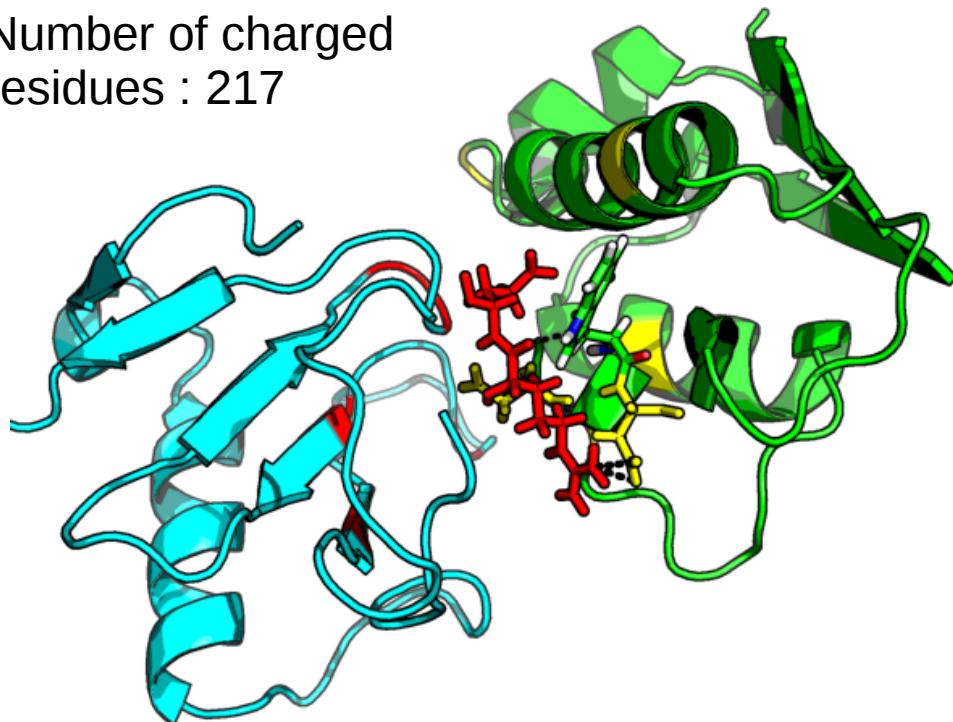


SWING

SCORING RESULTS

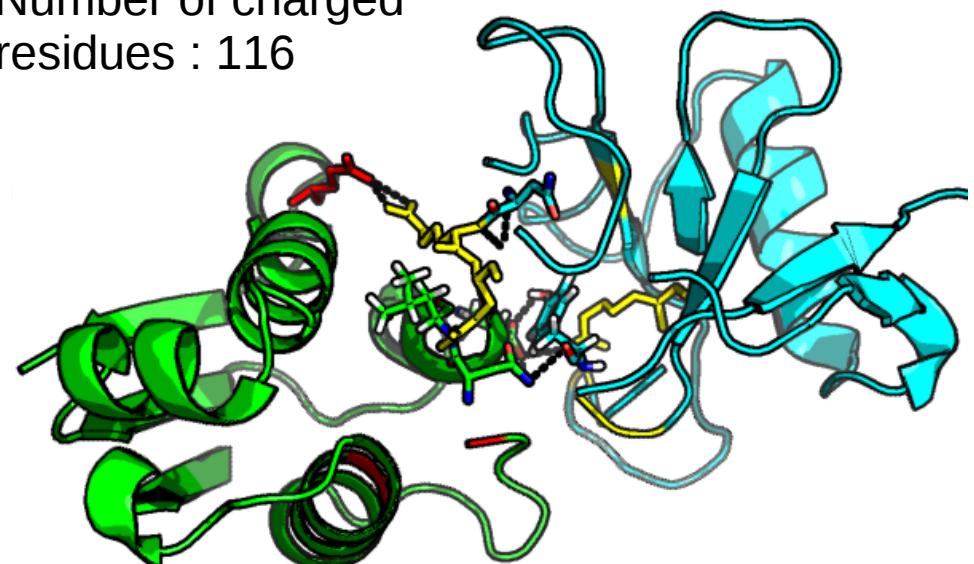
« Best » 1AY7 (IRMSD = 18)

Number of charged residues : 217



Second best 1AY7 (IRMSD = 2)

Number of charged residues : 116



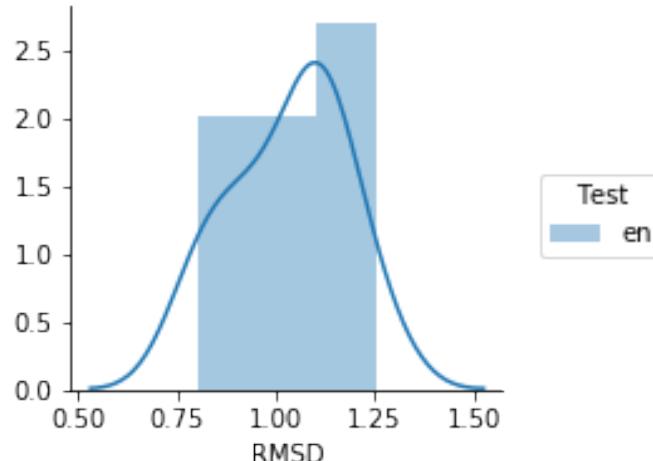
Receptor - charged residues
Ligand - charged residues

SWING

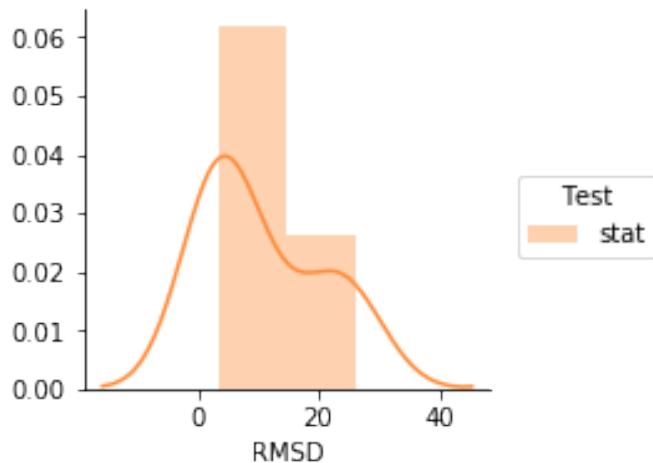
SCORING RESULTS

1DQJ minimized – DeNovo

RMSD of Top 10 scored conformations for 1DQJ

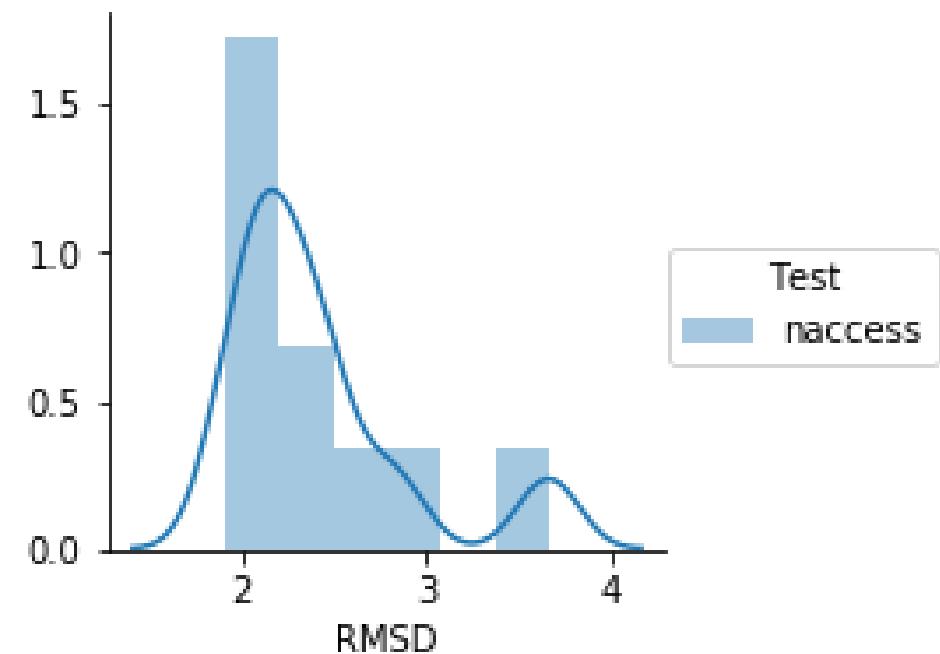


RMSD of Top 10 scored conformations for 1DQJ



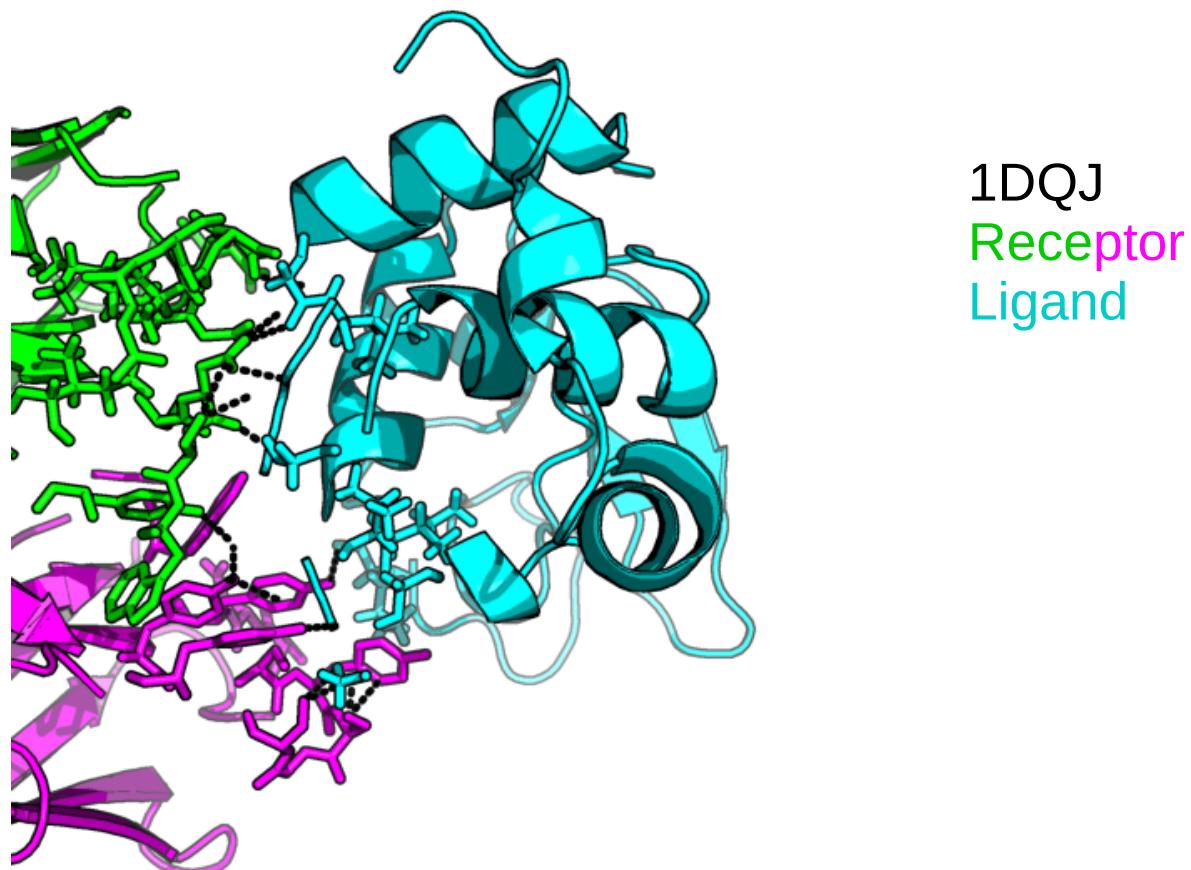
1DQJ minimized - MeetDockOne

RMSD of Top 10 scored conformations for 1DQJ



SWING

SCORING RESULTS



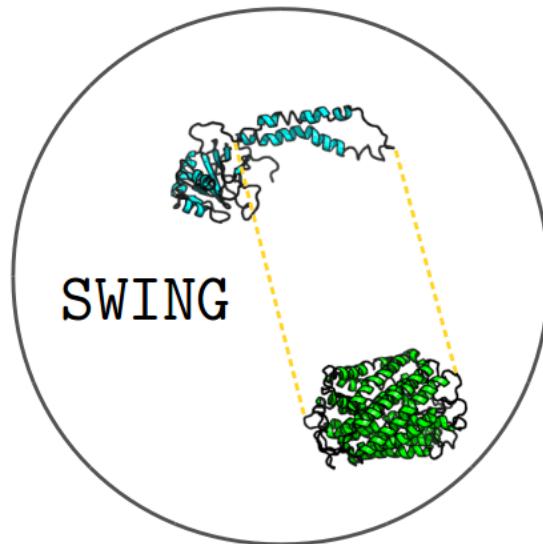
SWING

PERSPECTIVES

- Test on more complexes
- CAPRI ranking
- Iterate sampling with decrease of the rotation range on the best scored ligands
- Cluster ligand structures by score → identify local minima
- Test other setting for interolog search for more distant interologs

SWING

Thank you for your attention !

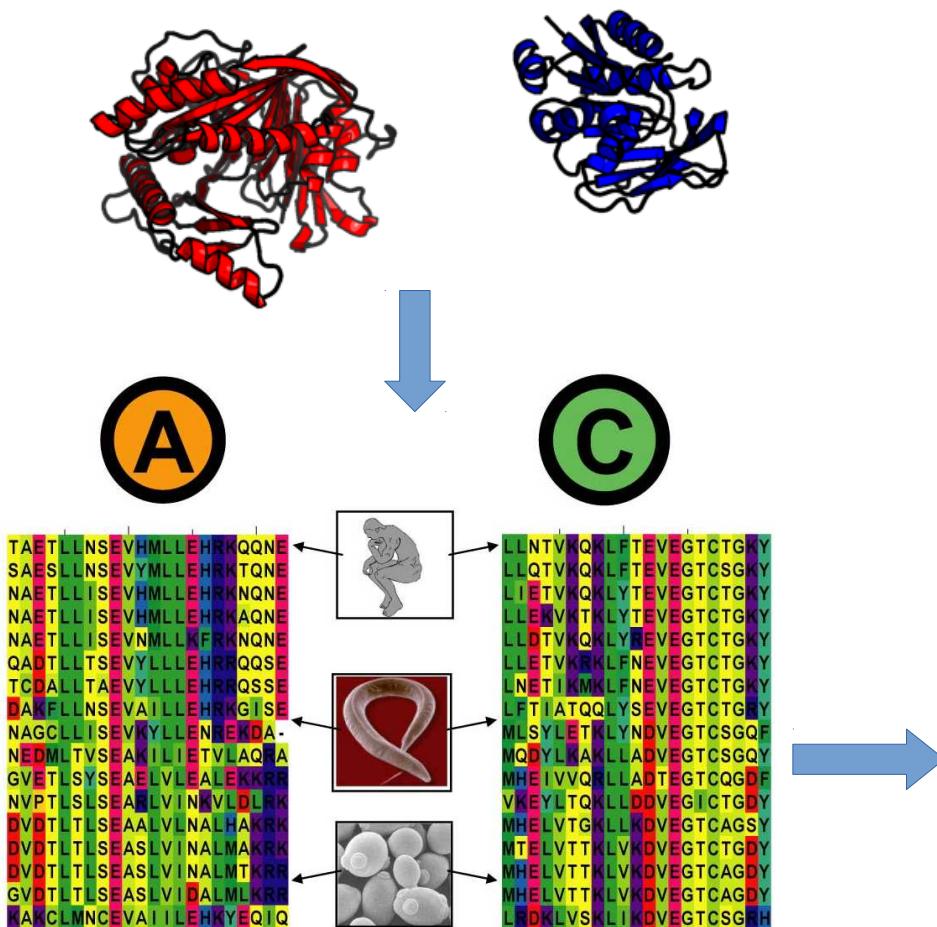


special thanks to our instructors
and scoring teams 1 and 11

SWING

SUPPLEMENTARY FIGURES

1) Multiple sequence alignment and restriction to homologous sequences found in the same species



2) HHSearch against the InterEvol database for structural interologs

Results

Download the multiple sequence alignments of partner 1 and partner 2 :[results.zip](#)

receptor.alig_headersp : 6 homologs

Homolog	Identity	Coverage
1go3_B	19%	73%
2waq_T	20%	56%
2ckz_B	21%	77%
3i4m_F	33%	98%
3h0g_O	44%	91%
2c35_A	90%	91%

Both alignments can be downloaded

ligand.alig_headersp : 8 homologs

Homolog	Identity	Coverage
2nn6_I	13%	52%
2rf4_A	16%	88%
2ckz_A	19%	95%
2pmz_K	24%	98%
1go3_A	25%	97%
3k1f_I	44%	99%
3h0g_P	50%	98%
2c35_B	94%	99%

Columns can be sorted by clicking in the headers

Even remote homology can be retrieved

Hyperlink to the chains in InterEvol

4 interologs

Interaction	Id partner 1	Id partner 2
2ckz_AB	19%	21%
2pmz_KL	24%	20%
1wcm_OP	33%	44%
2c35_AB	90%	94%

Hyperlink to the interfaces in InterEvol

SWING

SUPPLEMENTARY FIGURES

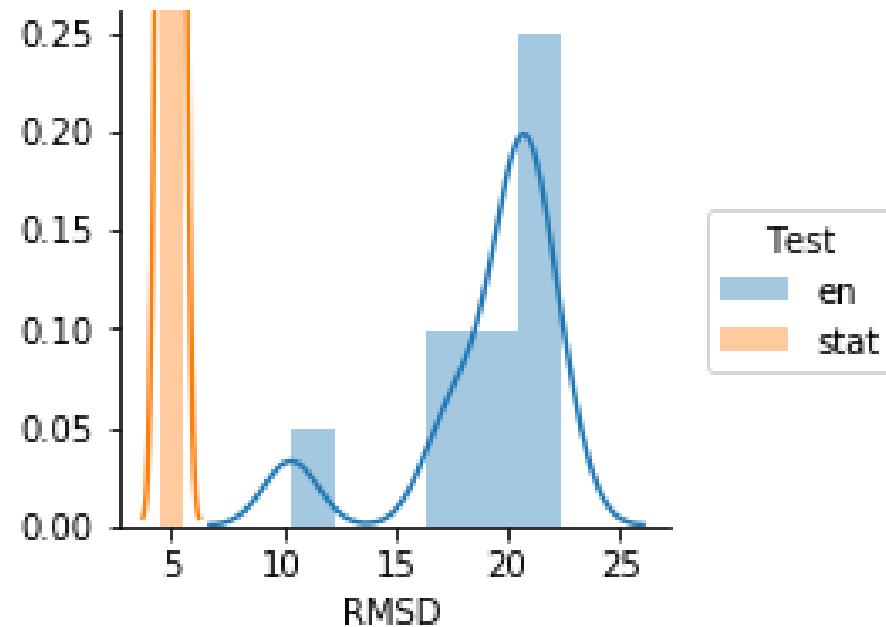
	# structures	Angle	Native (<1Å) structures propensity	Native-like (<5Å) structures propensity	LRMSD (Å) no minimization	LRMSD (Å) minimization	LRMSD (Å) Initial position
1CGI	1178	7.5°	0.13	0.34	2.7012	0.5044	2.972
3FN1	7352	30°	0.01	0.01	2.4971	0.7707	3.6043
1AY7	716	30°	0	0.36	2.4553	1.3287	2.6016
1DQJ	2491	7.5°	0.30	0.28	0.2370	0.6683	0.3708
1PPJ (CP)	795	30°	0	0.01	2.0073	1.2939	2.3671

SWING

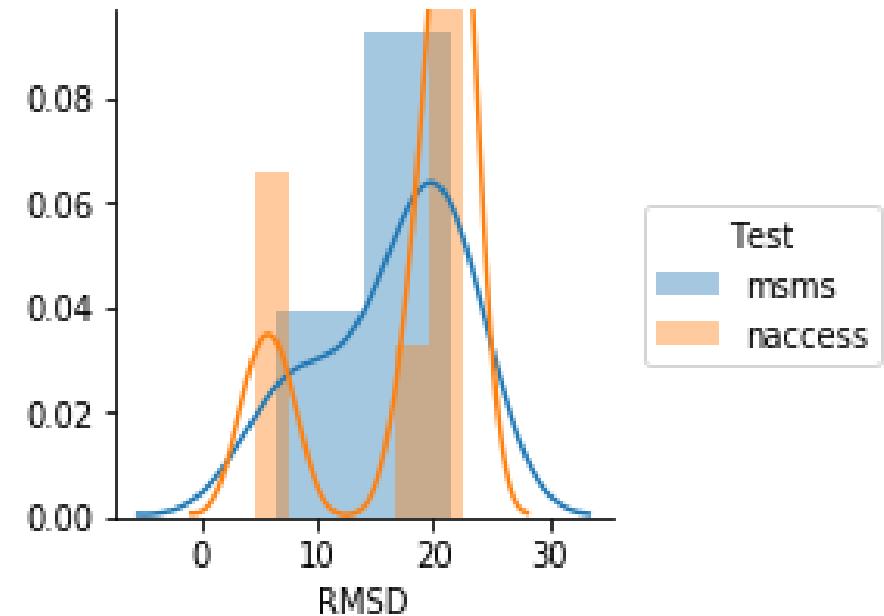
SCORING RESULTS

Minimized conformations

RMSD of Top 10 scored conformations for 1AY7



RMSD of Top 10 minimized conformations of 1AY7

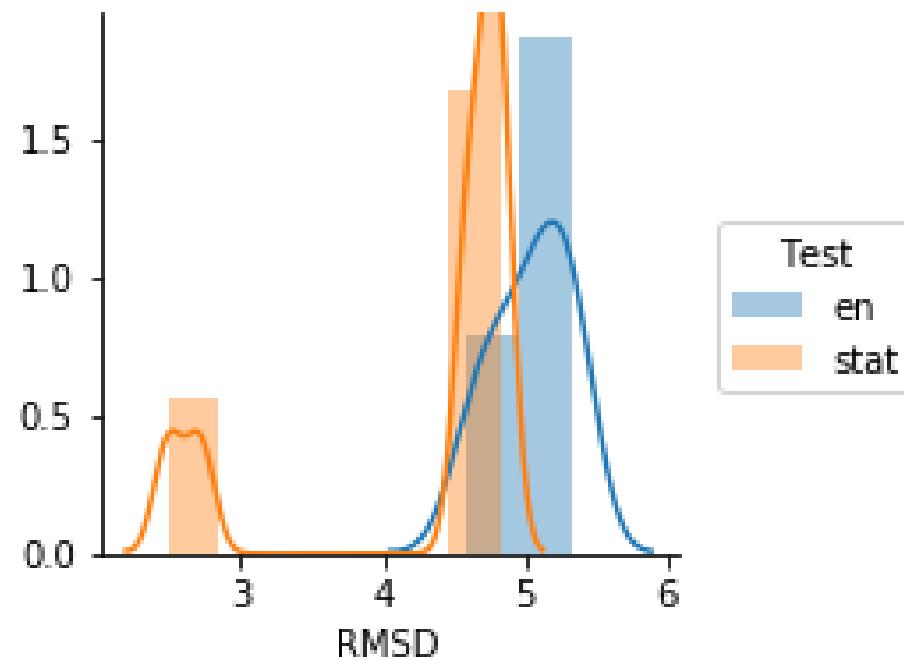


SWING

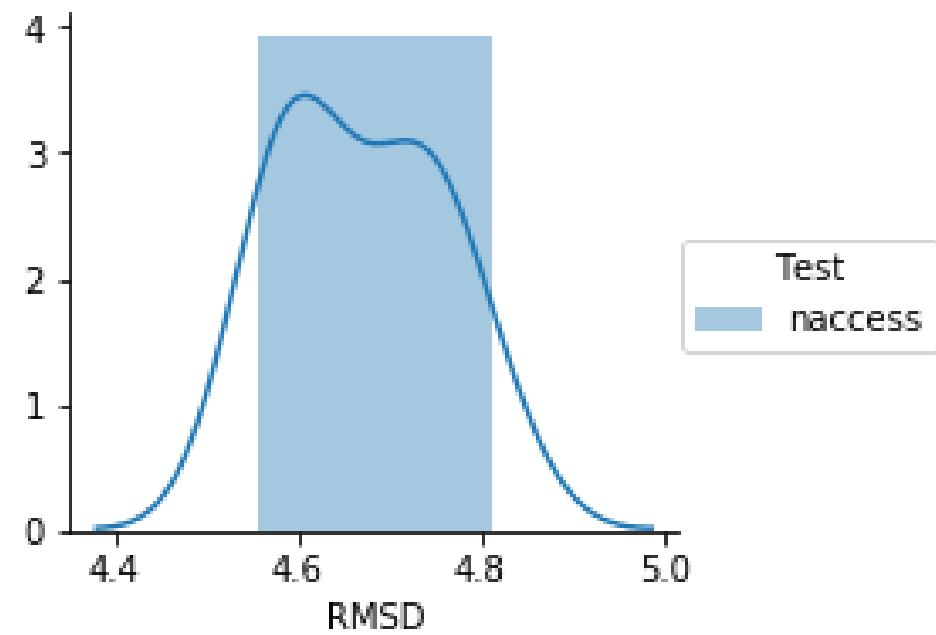
SCORING RESULTS

Non minimized conformations

RMSD of Top 10 scored conformations for 1AY7



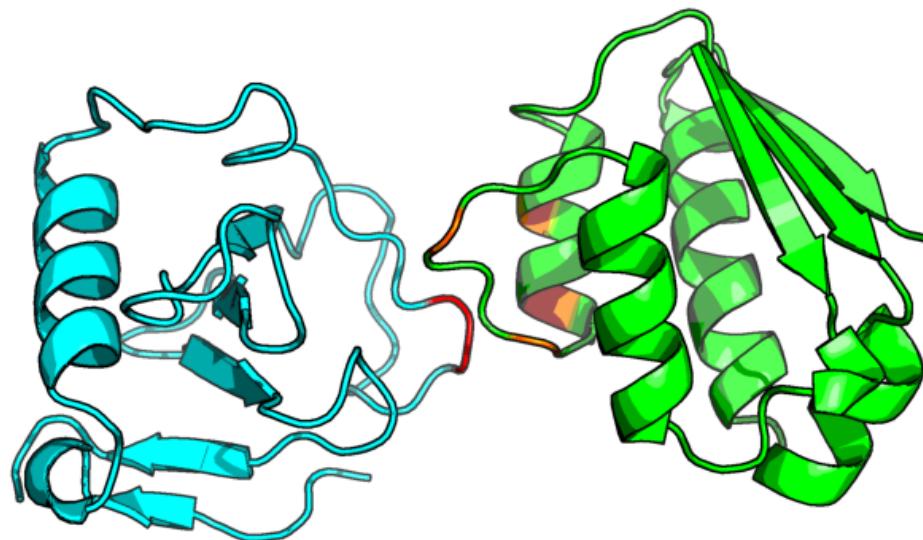
RMSD of Top 10 raw conformations of 1AY7



SWING

SUPPLEMENTARY FIGURES

Number of charged
residues : 54

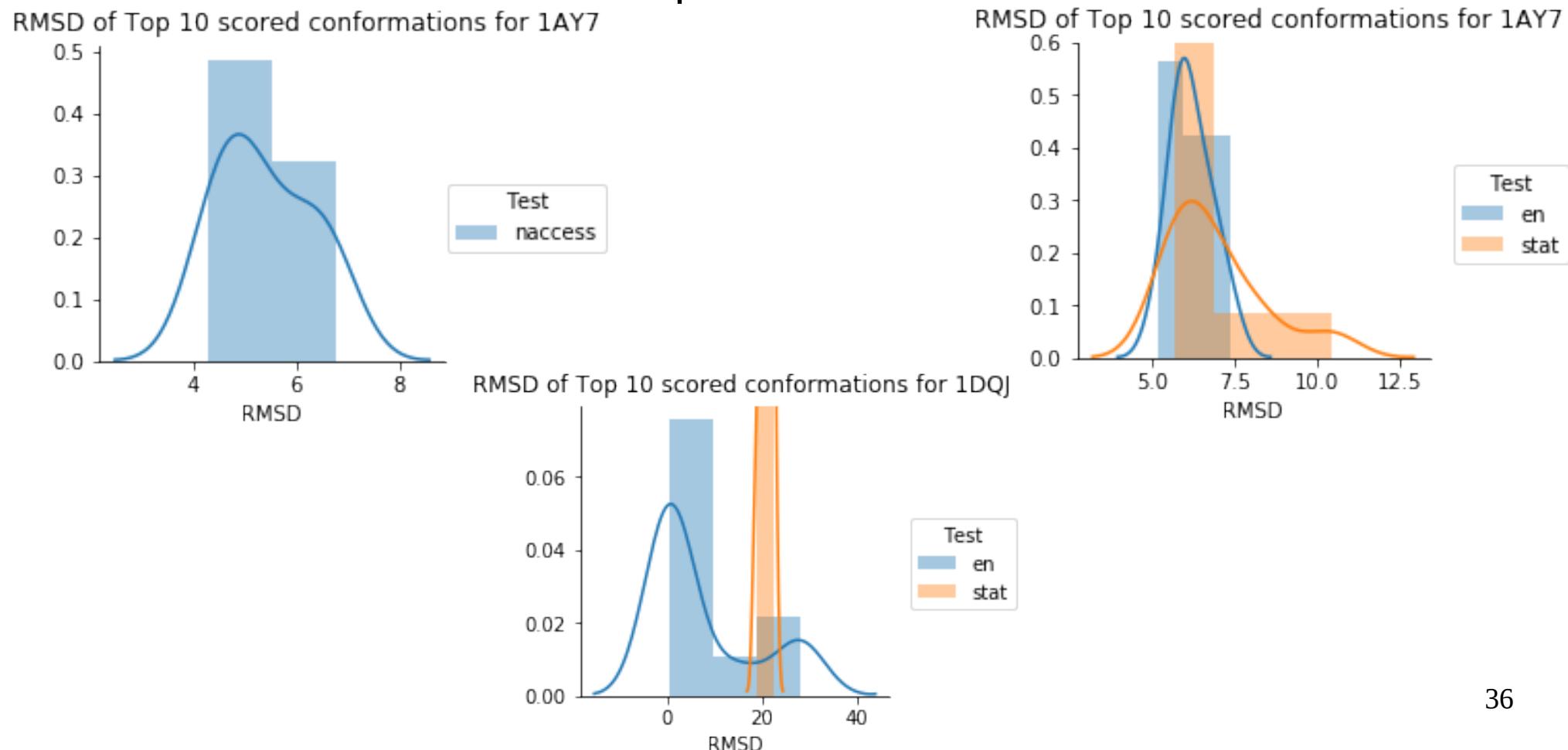


Green = Lig, Blue = Rec,
Orange = charged residues of Lig, Red = charged residue of Rec

SWING

SUPPLEMENTARY FIGURES

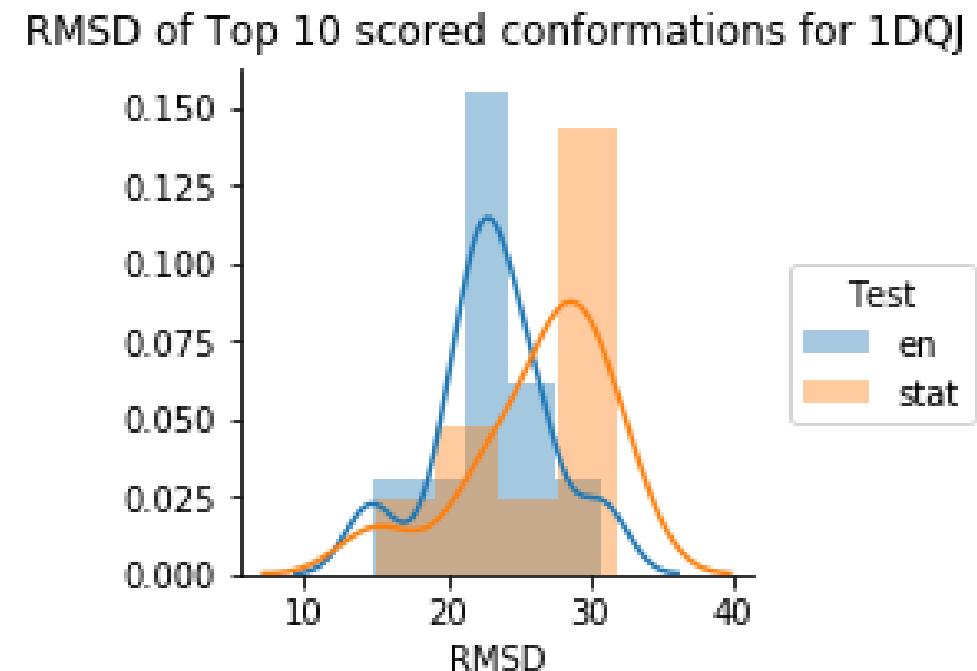
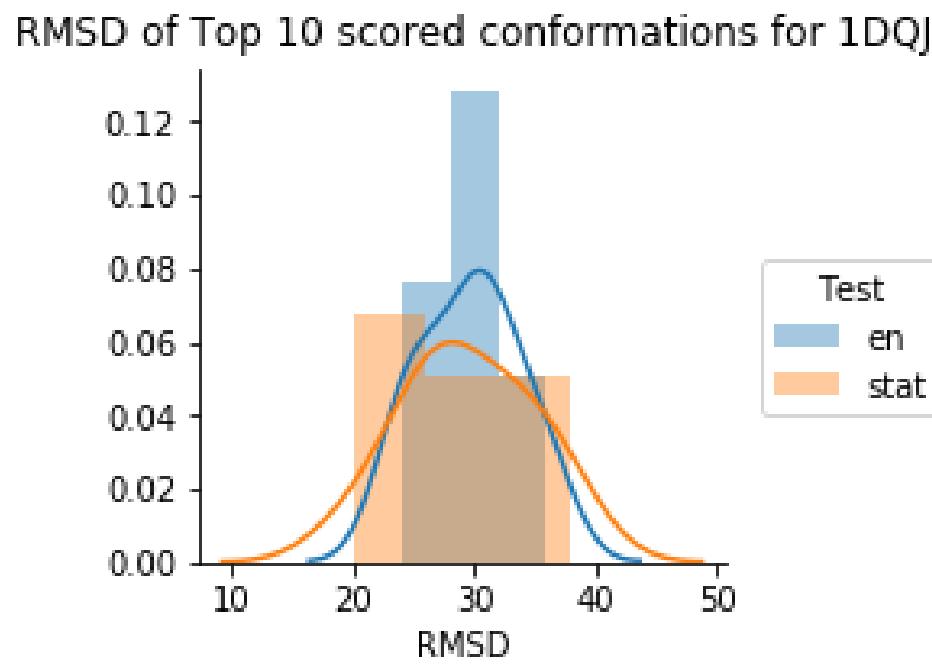
Non minimized and without pushback...



SWING

SUPPLEMENTARY FIGURES

1DQJ before pushback

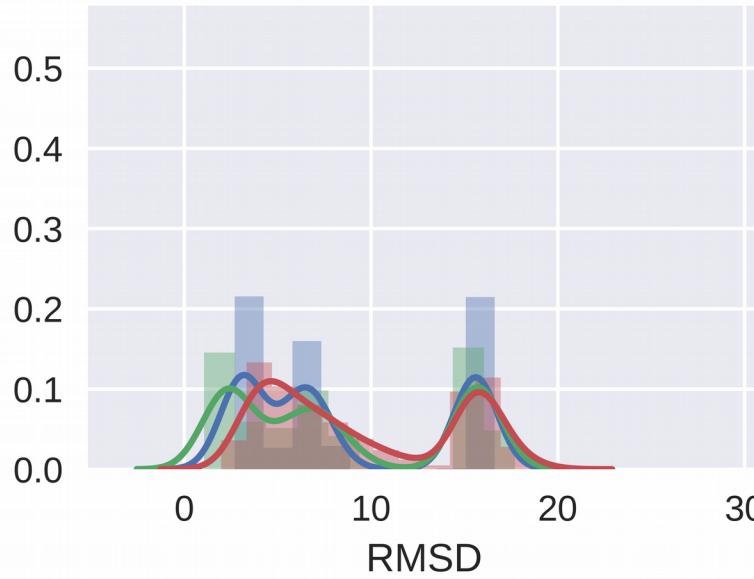


SWING

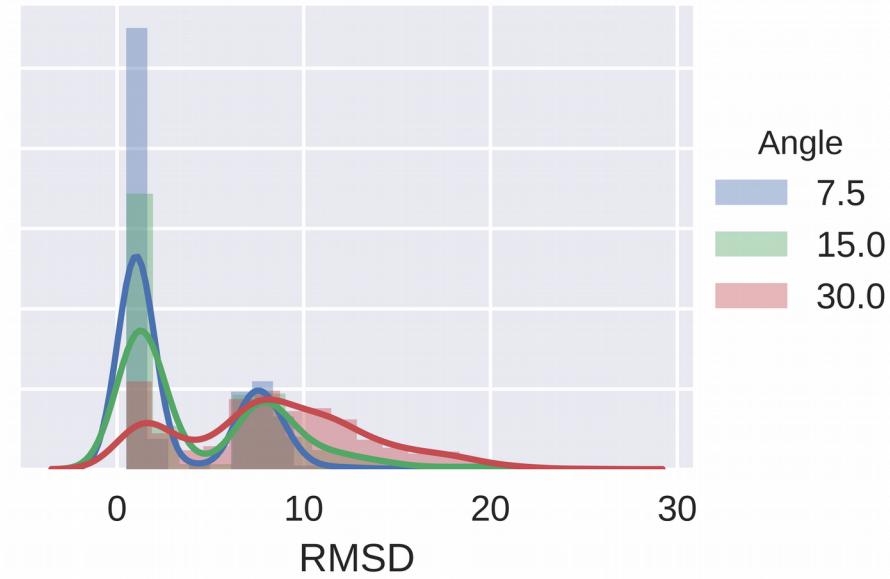
SUPPLEMENTARY FIGURES

RMSD with different angles 1CGI

Minimizer = 0



Minimizer = 1

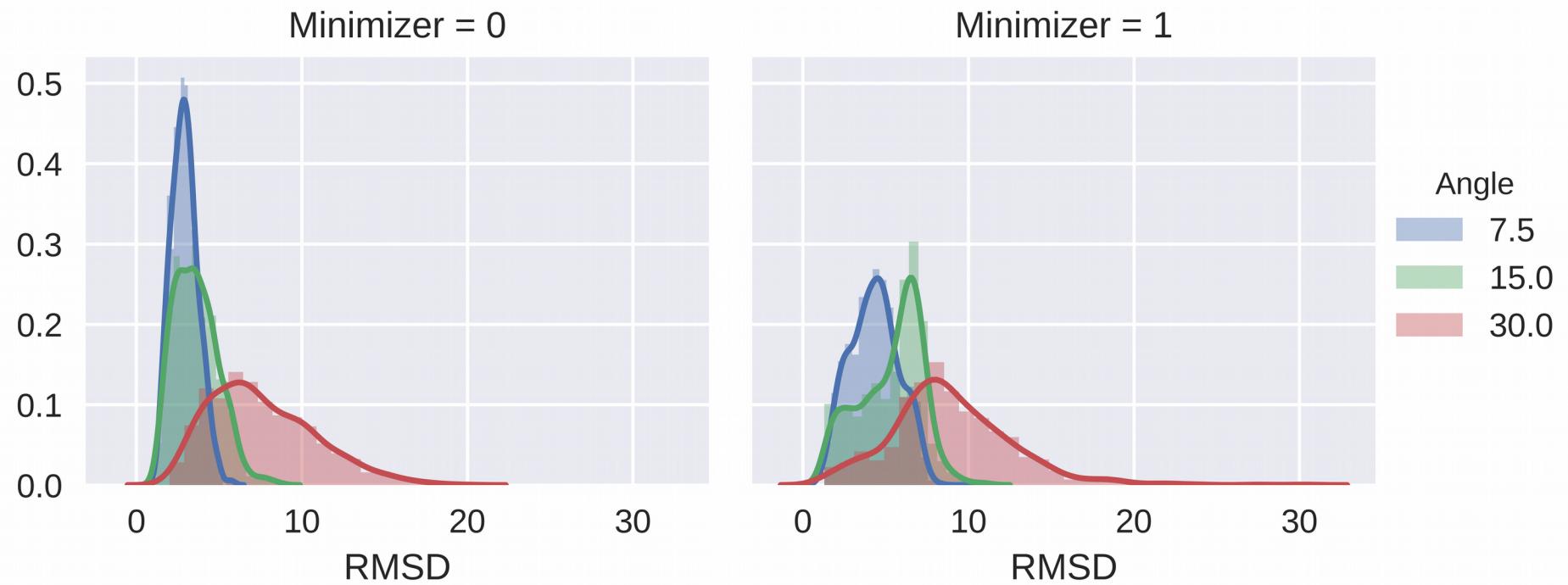


Angle
7.5
15.0
30.0

SWING

SUPPLEMENTARY FIGURES

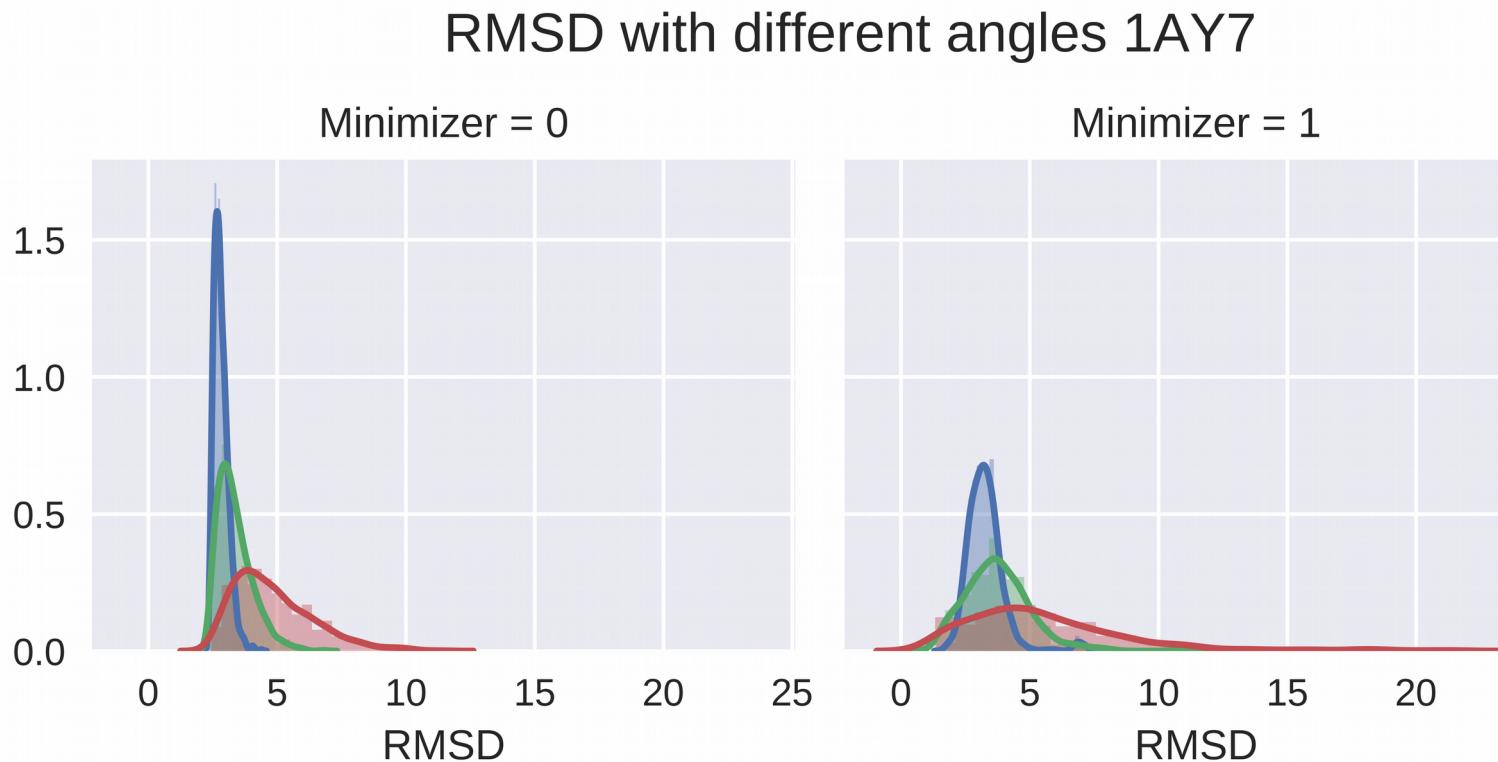
RMSD with different angles 1PPJ_CP



SWING

SUPPLEMENTARY FIGURES

Supplementary Figure showing RMSD distributions for different angles (7.5, 15.0, 30.0) comparing Minimizer = 0 and Minimizer = 1.

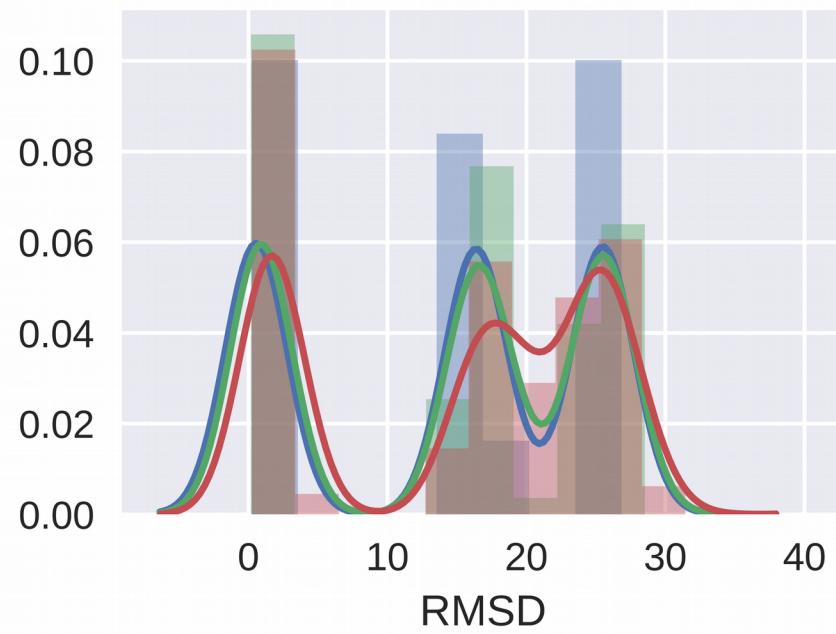


SWING

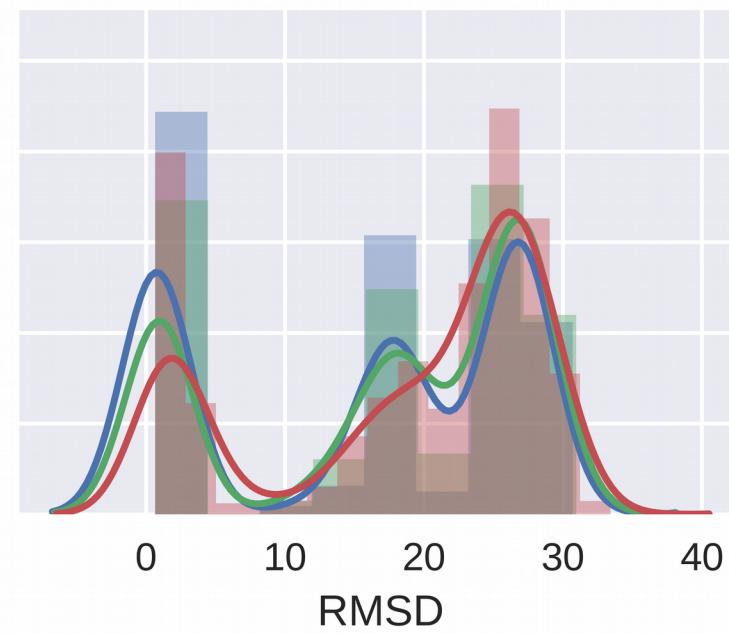
SUPPLEMENTARY FIGURES

RMSD with different angles 1DQJ

Minimizer = 0



Minimizer = 1

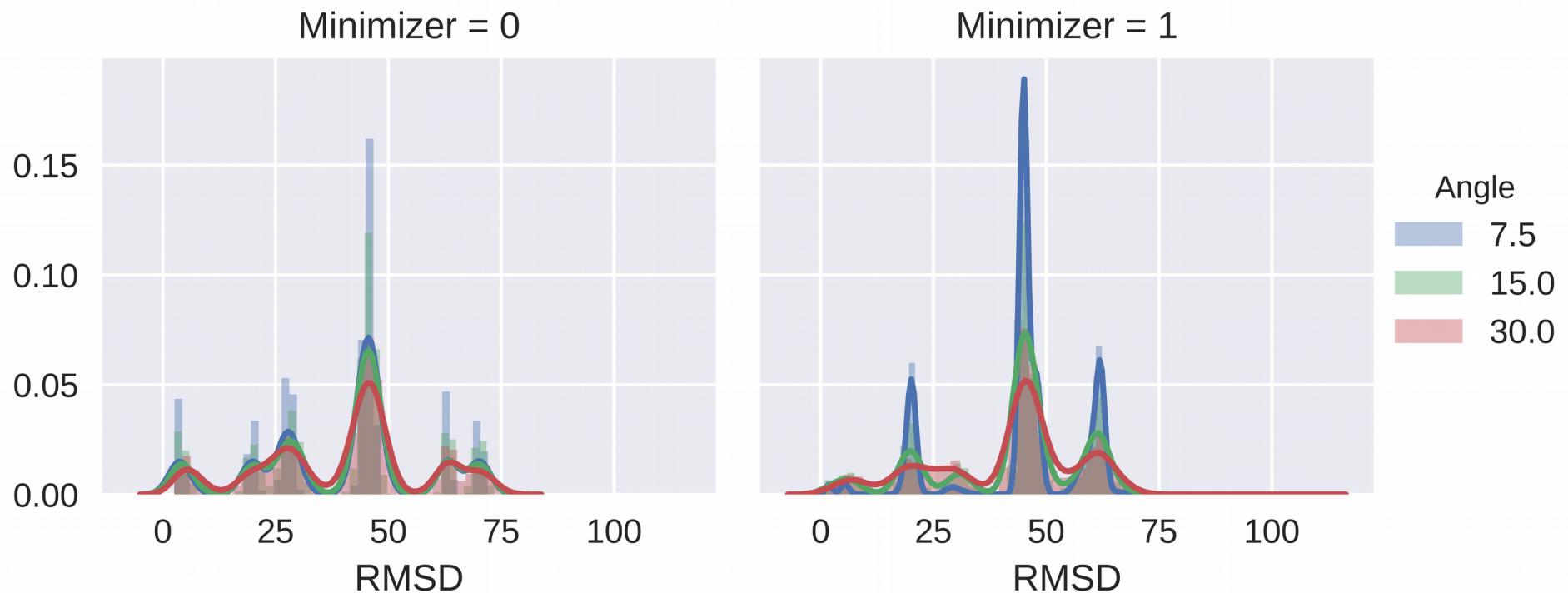


Angle
7.5
15.0
30.0

SWING

SUPPLEMENTARY FIGURES

RMSD with different angles 3FN1

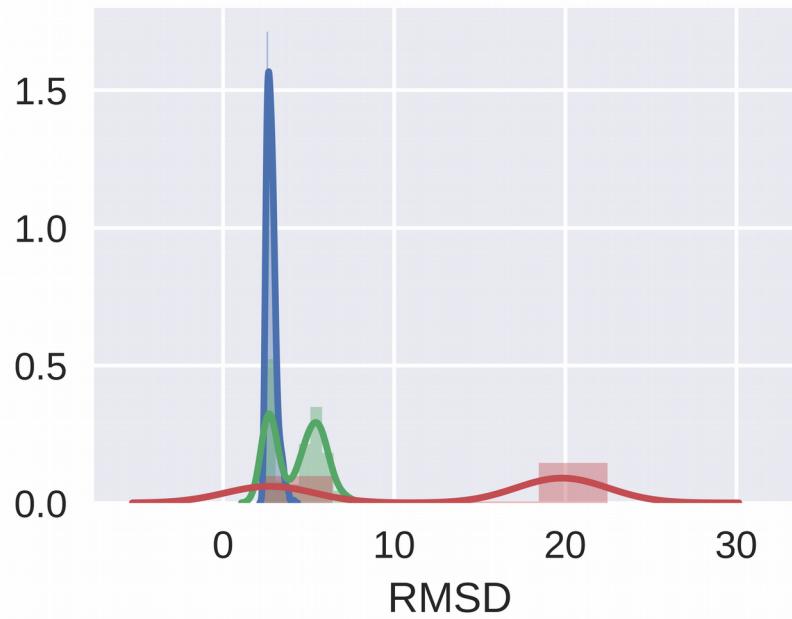


SWING

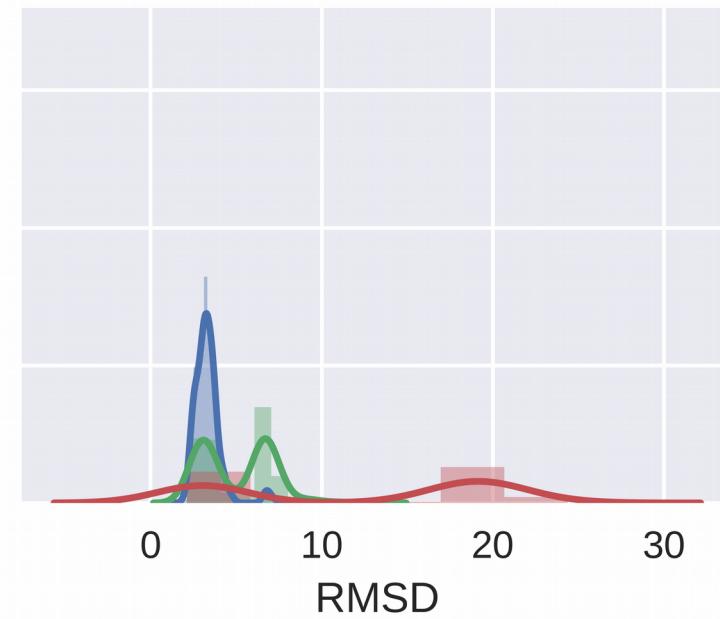
SUPPLEMENTARY FIGURES

RMSD with different move back distance

Minimizer = 0



Minimizer = 1

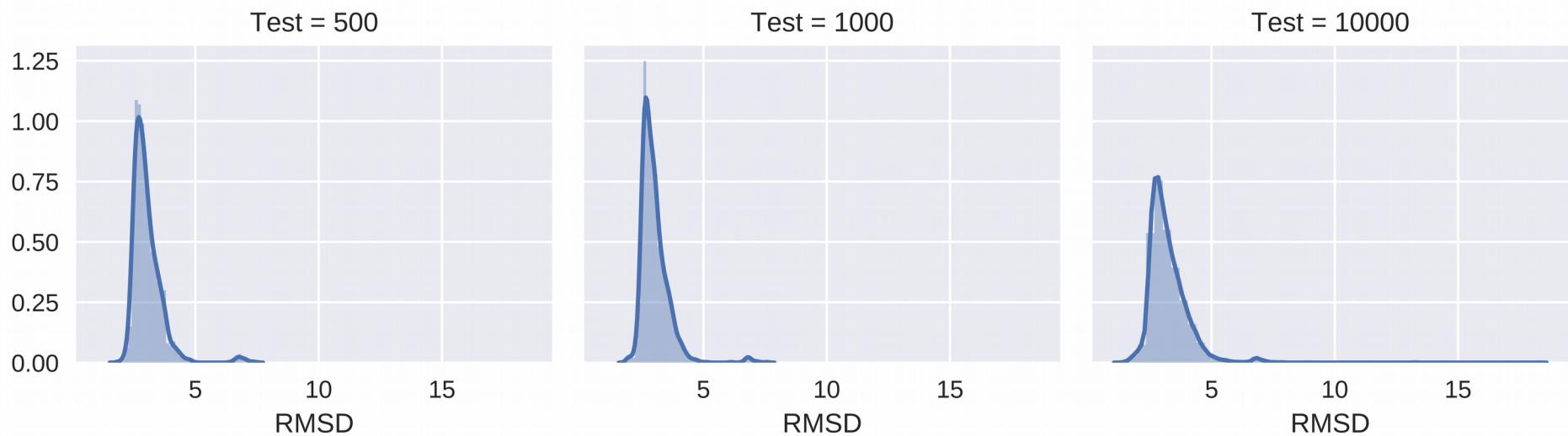


Distance
0
10
25

SWING

SUPPLEMENTARY FIGURES

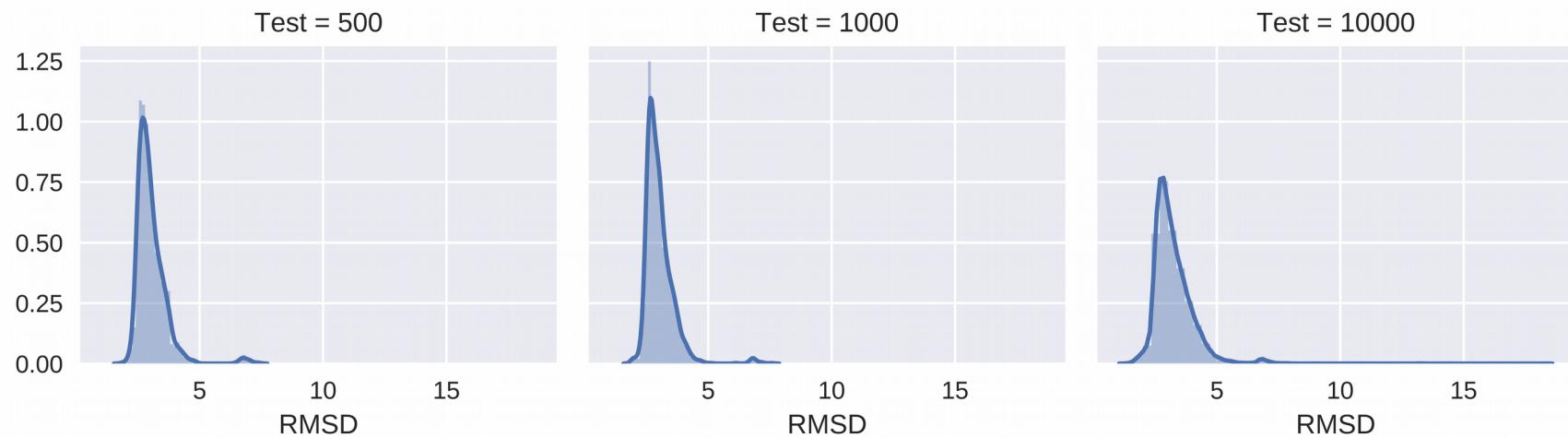
1AY7 RMSD distribution after minimization



SWING

SUPPLEMENTARY FIGURES

1AY7 RMSD distribution after minimization



RMSD Iden_min

