



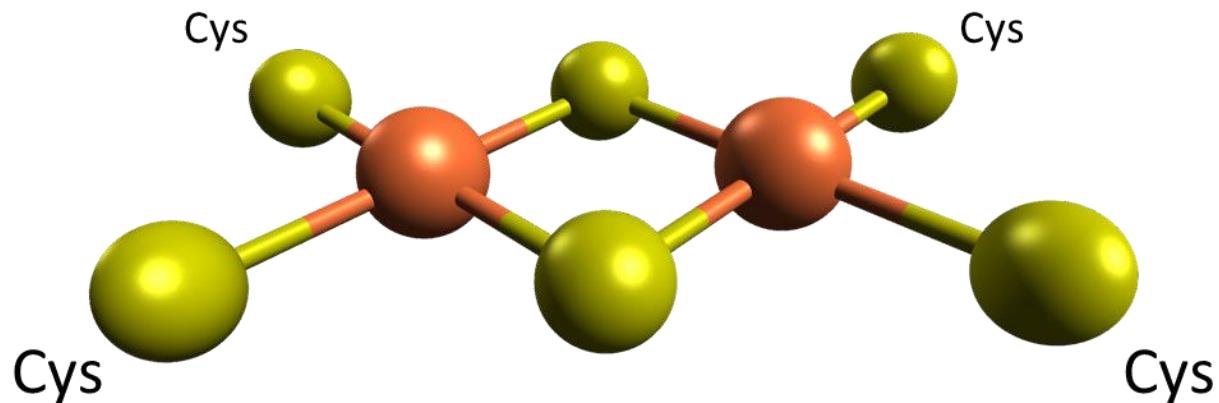
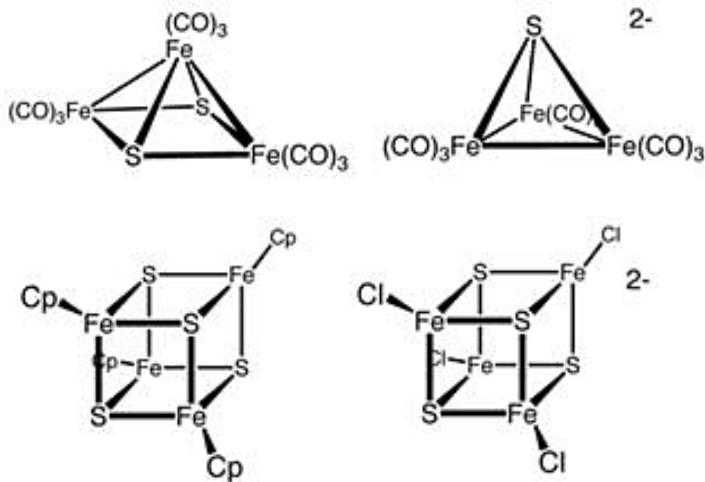
Molecular modeling of protein systems

dr Magdalena Anna Mozolewska



Role of Fe–S clusters protein

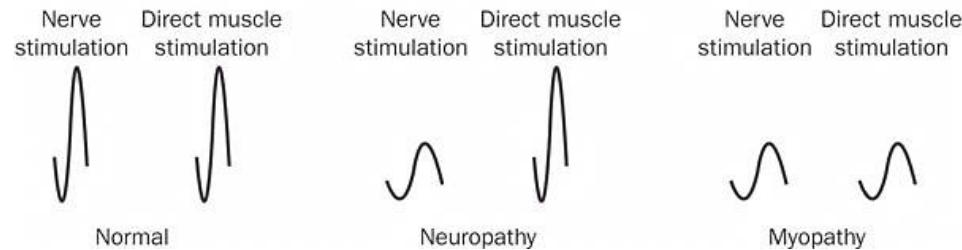
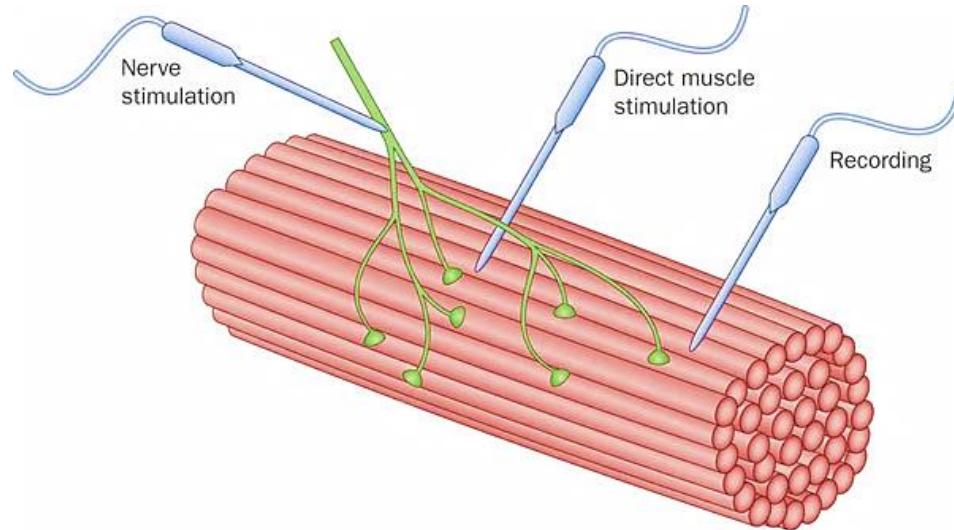
Oxidation – reduction reactions
Regulation of gene expression
Amino acid synthesis
Citric acid cycle
Cofactor biosynthesis



Translation initiation
tRNA modification
Receptor signaling

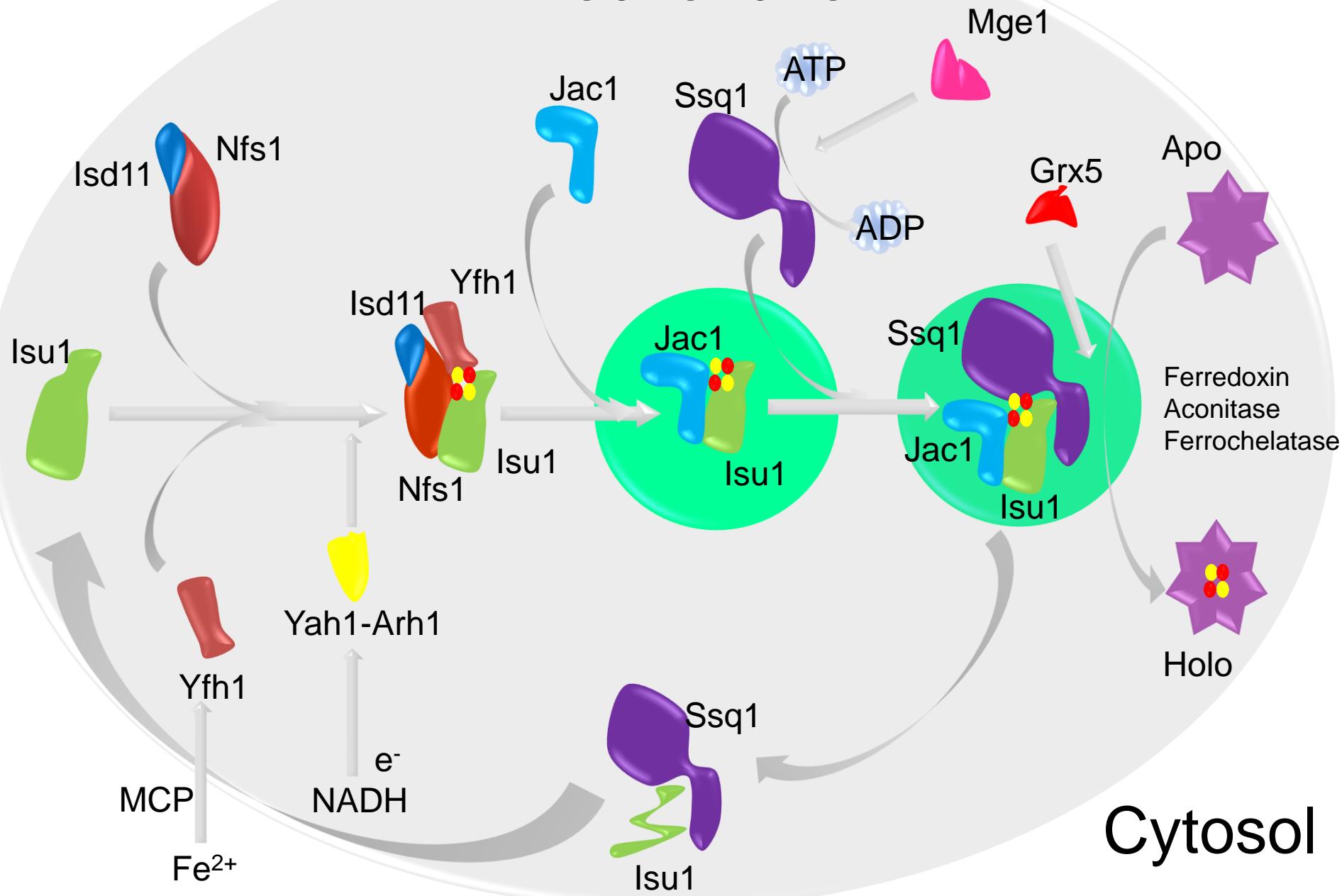
3 Malfunctions of Fe–S clusters proteins

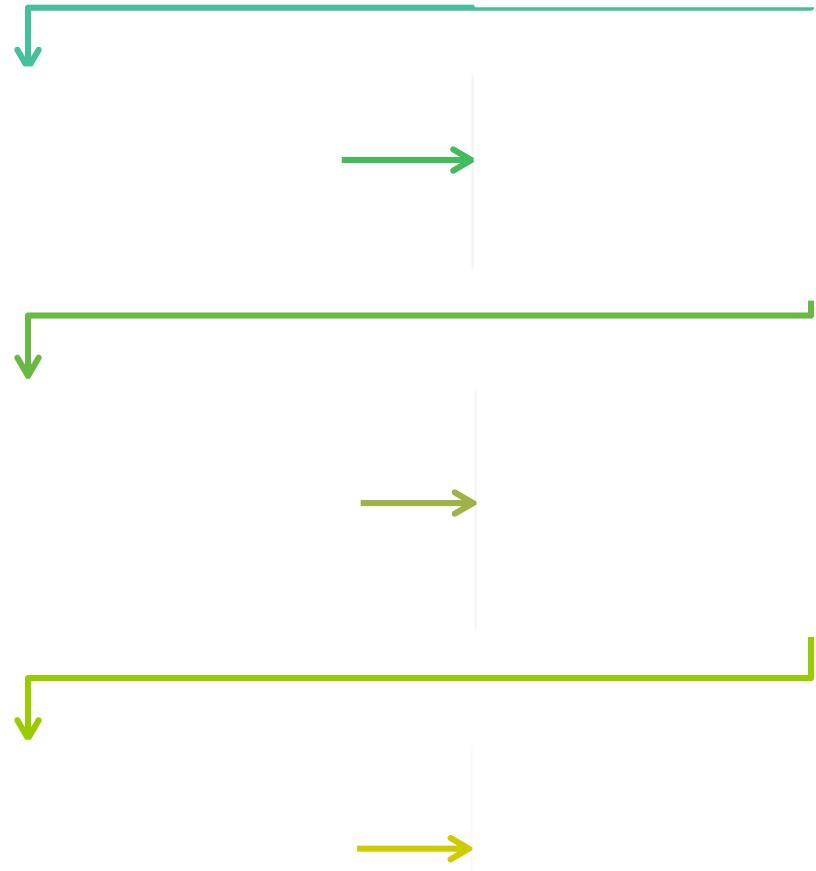
Cerebellar ataxia
Friedreich's Ataxia
Fanconi anemia
Myopathy
Microcytic anemia



Wolfgang Zink, Rainer Kollmar & Stefan Schwab, Critical illness polyneuropathy and myopathy in the intensive care unit, *Nature Reviews Neurology* 5, 372-379

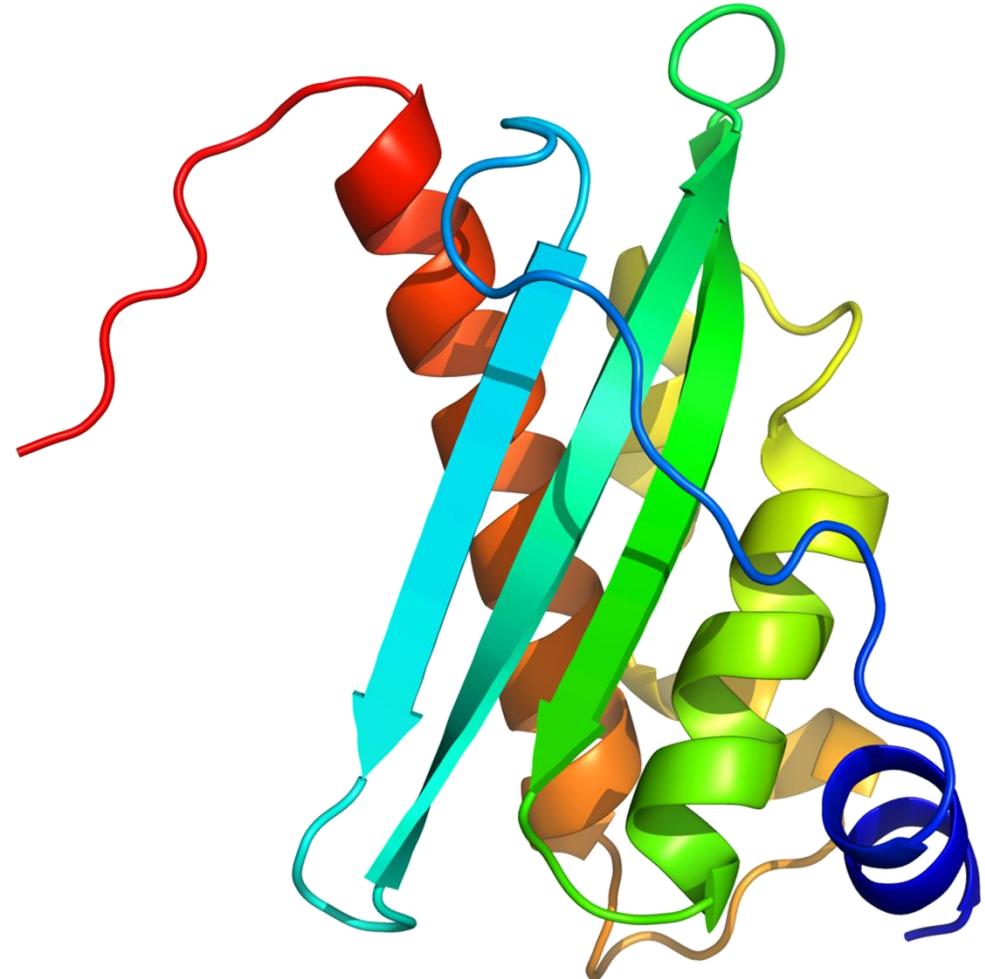
Mitochondrion



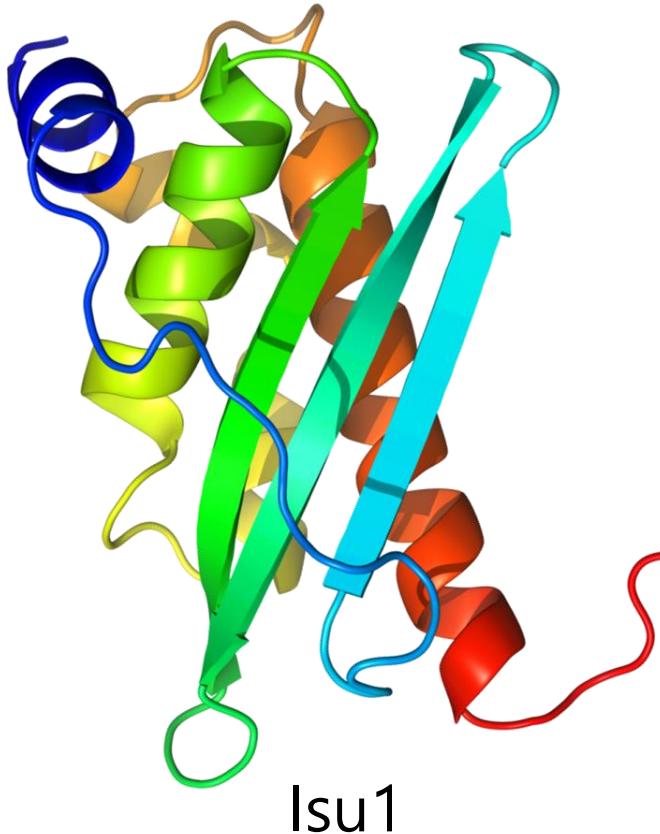


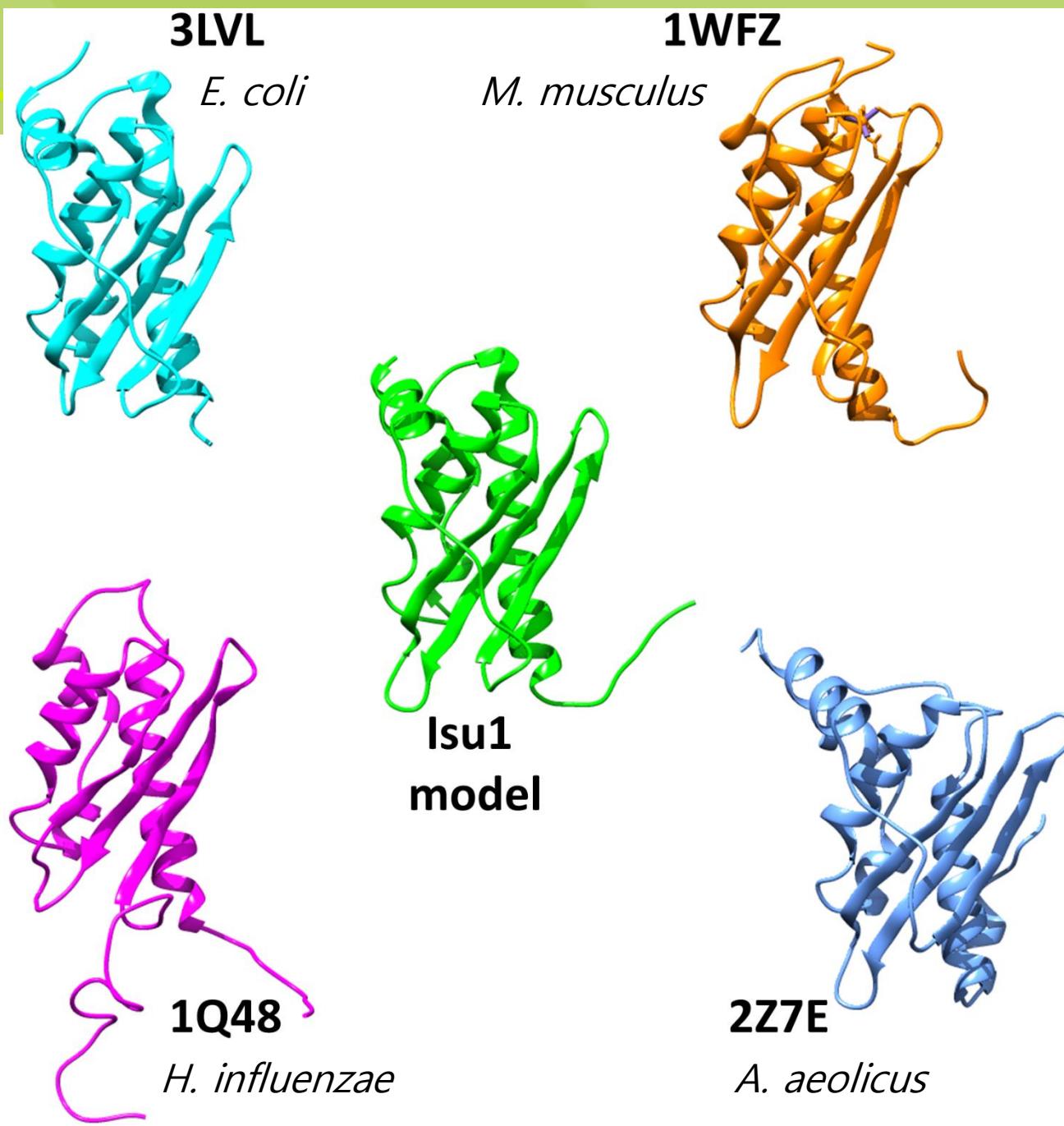
Homology modeling of lsu1

	Z-score
Dihedrals	0.207
1D-packing	-0.192
3D-packing	-0.318
Overall	-0.193



Homology modeling

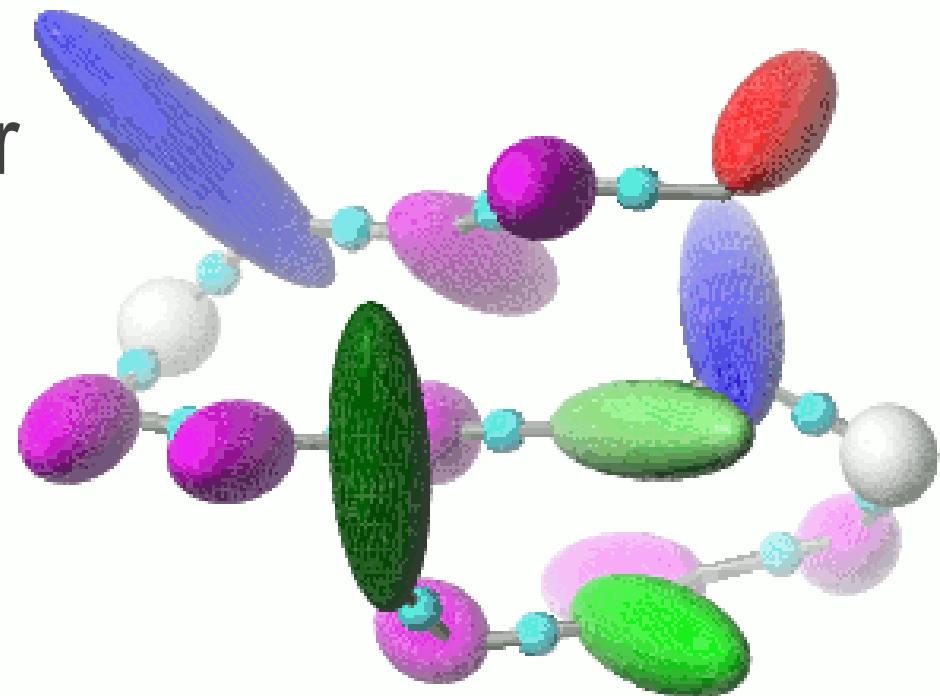




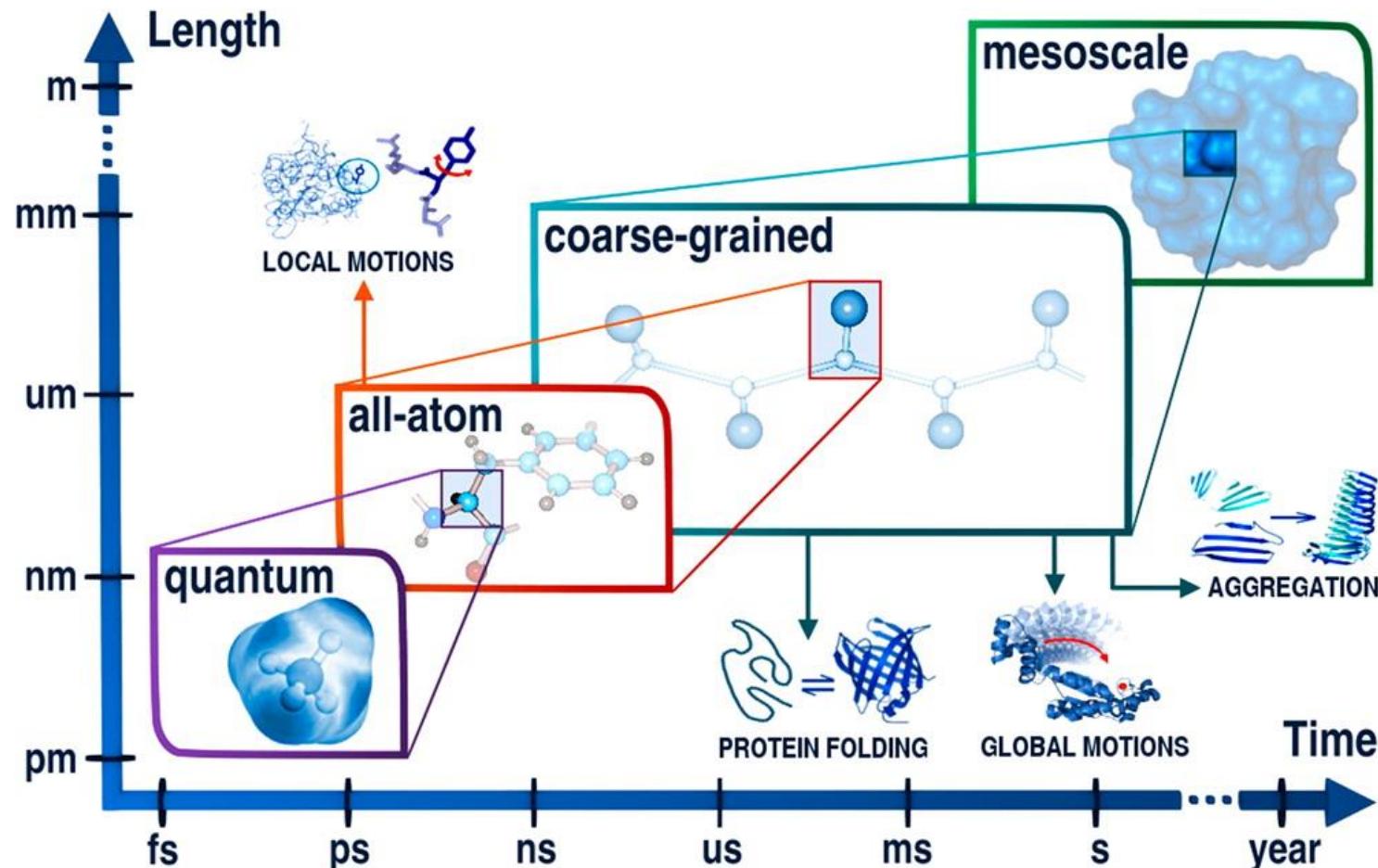
Homology modeling of Isu1

Simulations

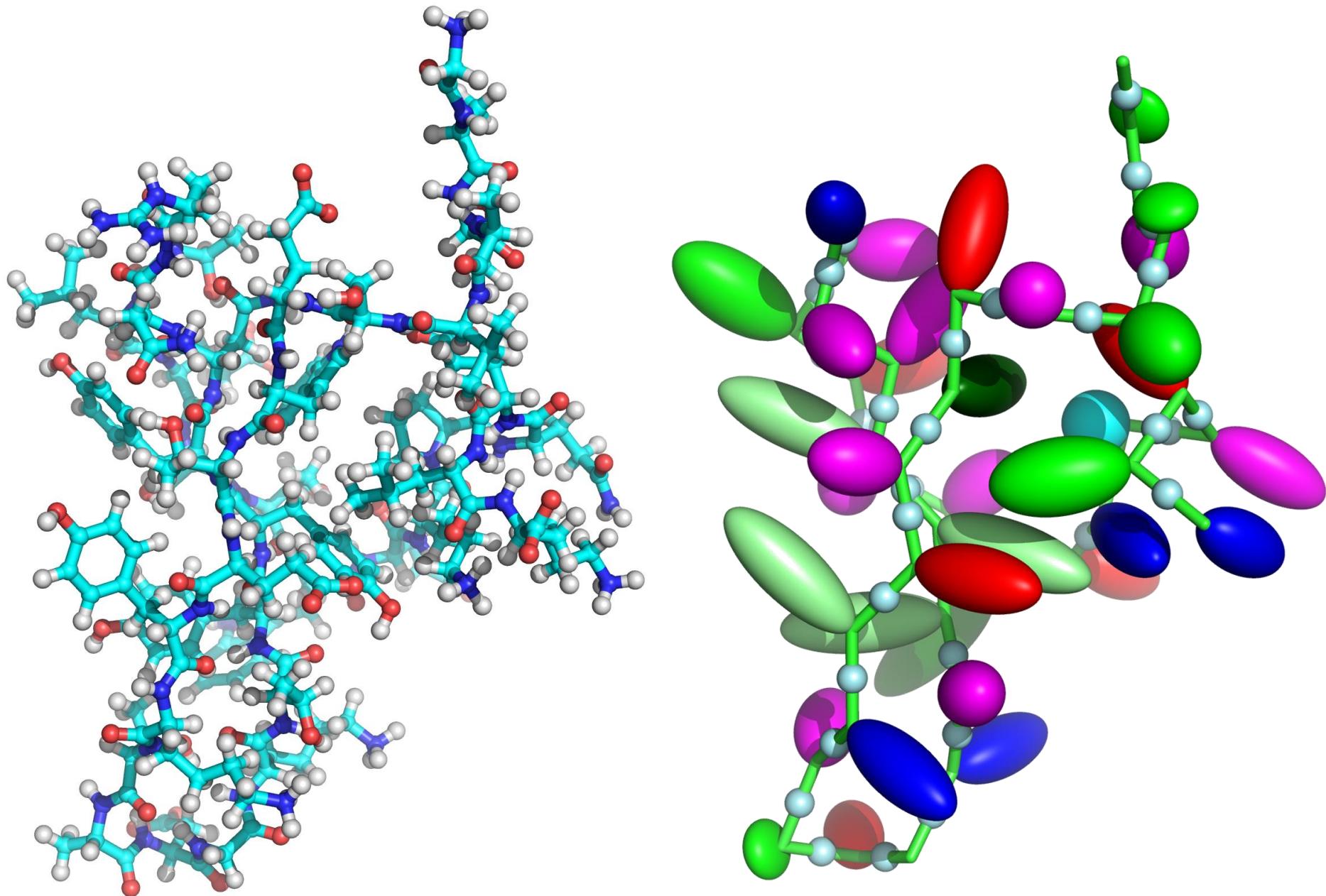
- Minimisations
- MD (Molecular dynamics)
 - All atom
 - CG

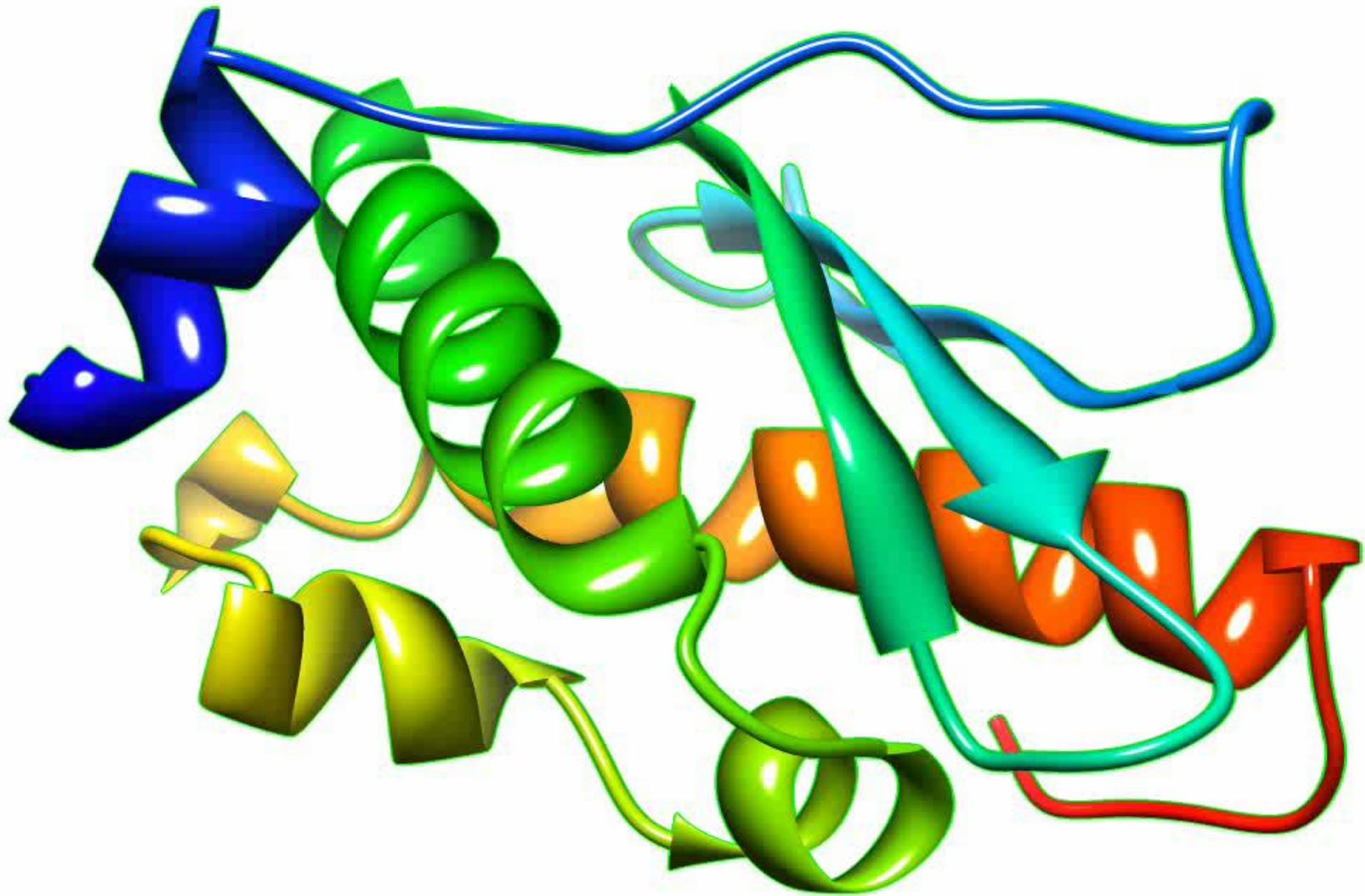


Coarse-grained force fields

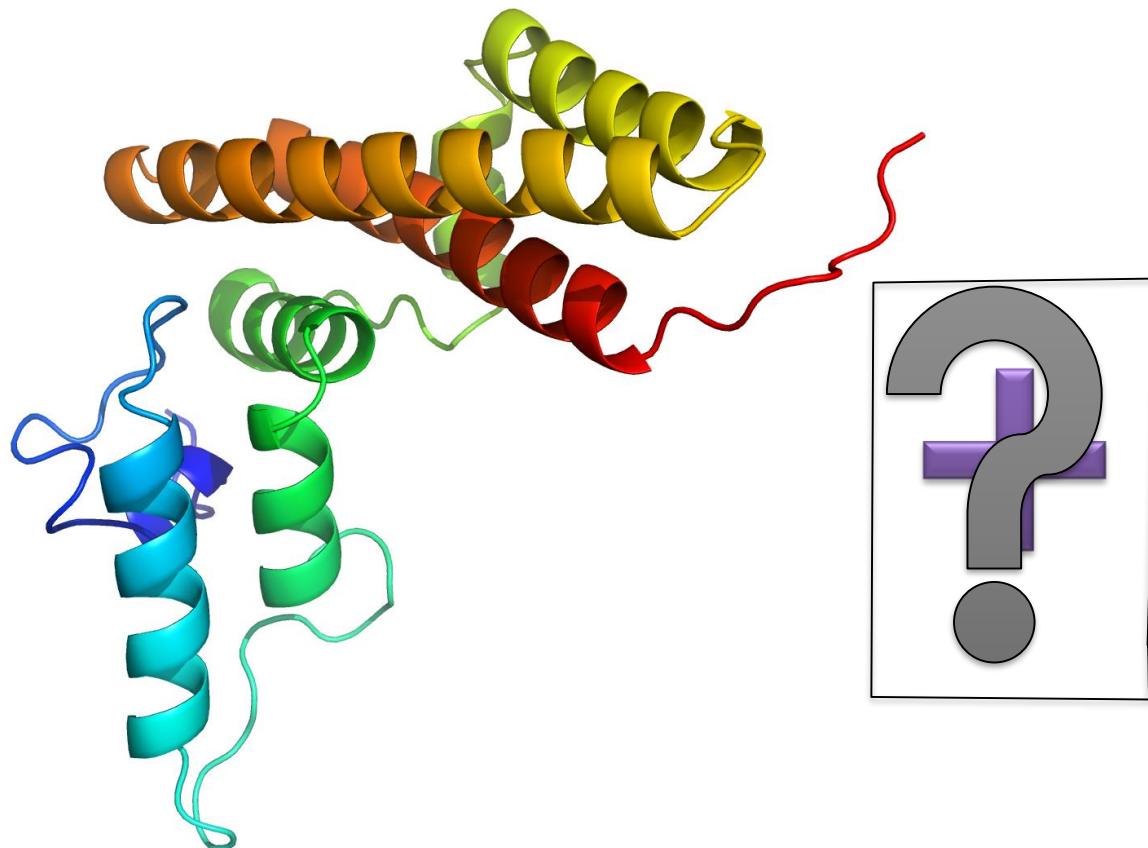


UNRES model of 1E0L

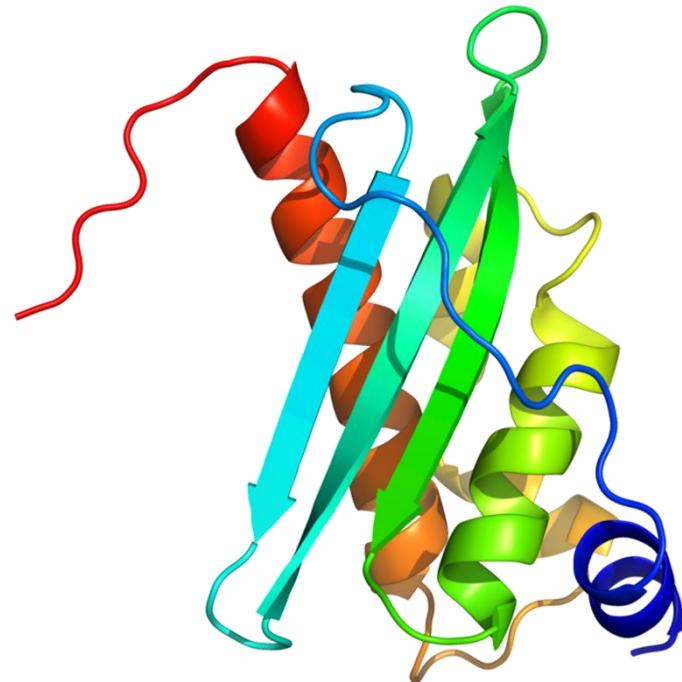




Docking



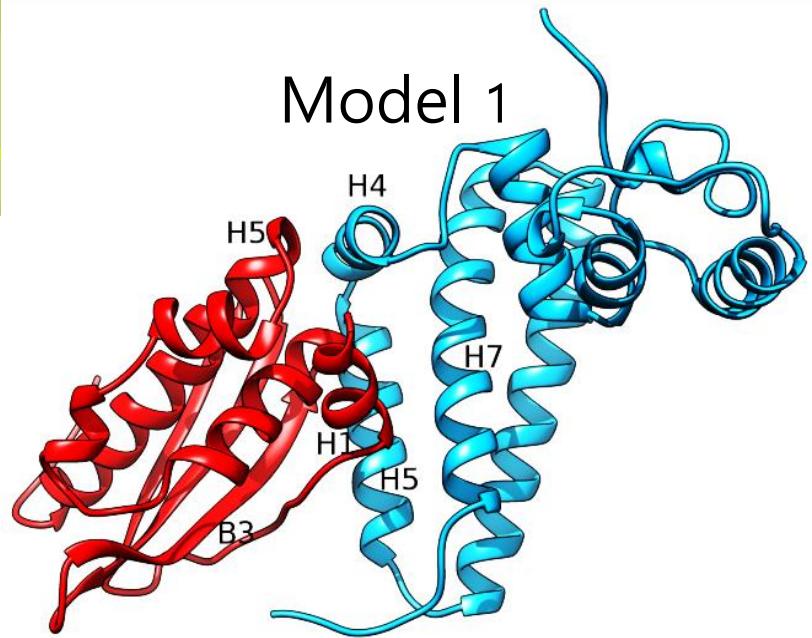
Jac1



lsu1

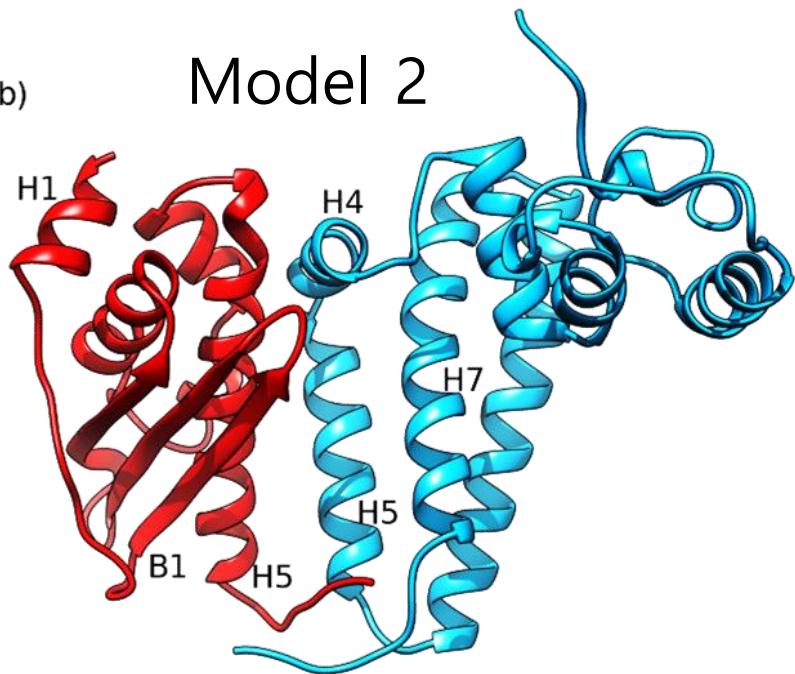
Local docking ZBS IPI PAN

Model 1

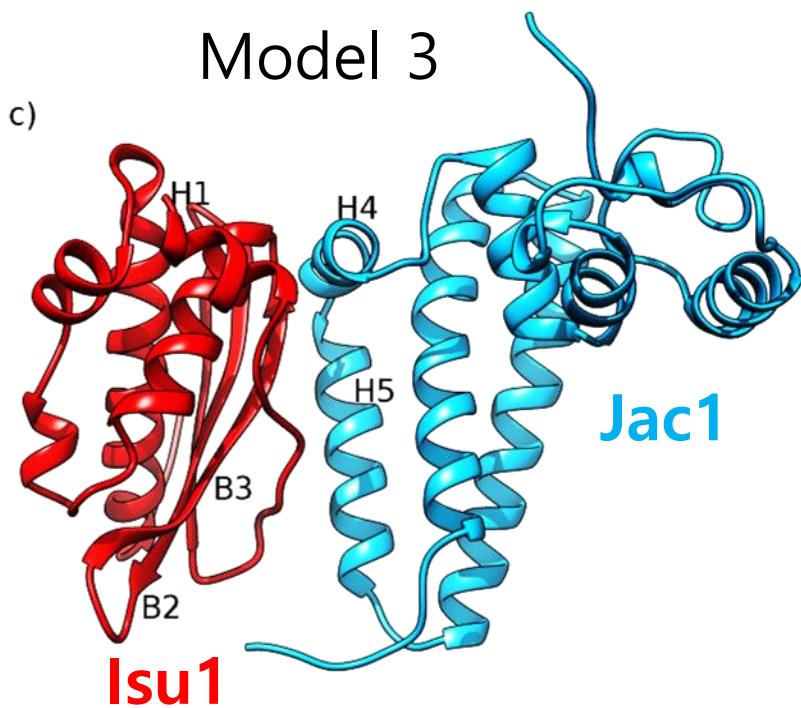


b)

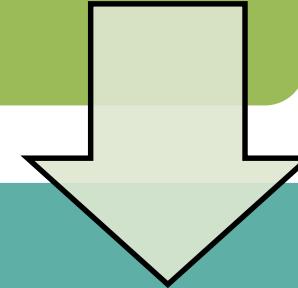
Model 2



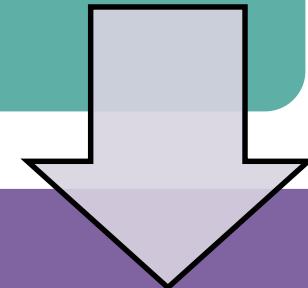
Model 3



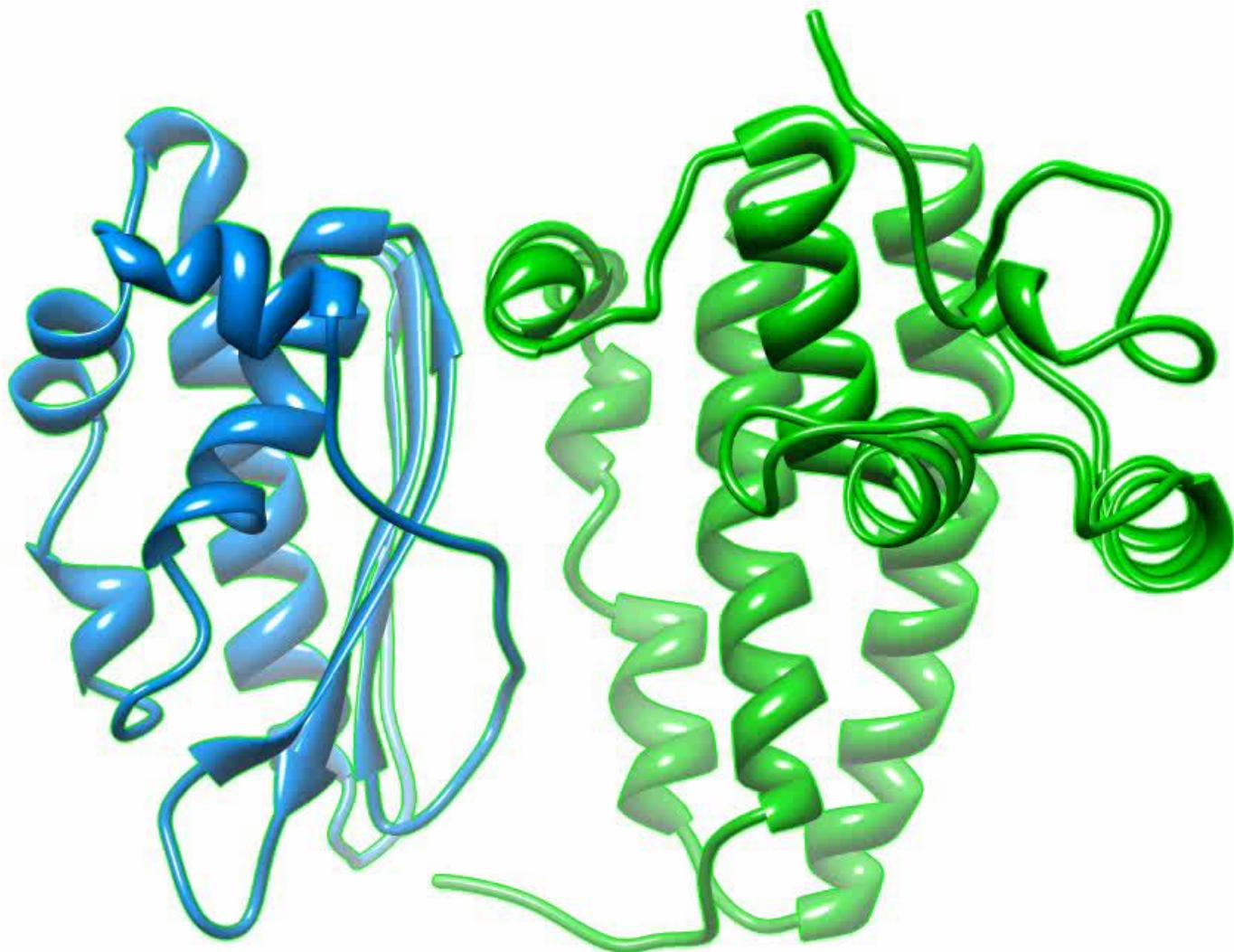
UNRES MD simulations from 3
initial conformations (16
trajectories each)



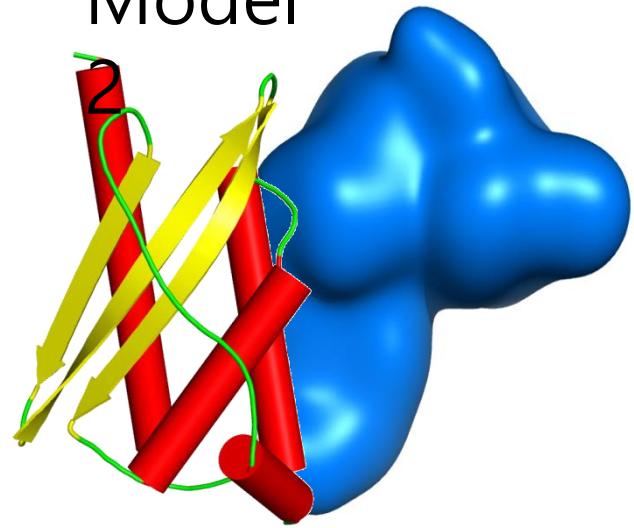
Clustering of all trajectories
from each simulation by RMSD



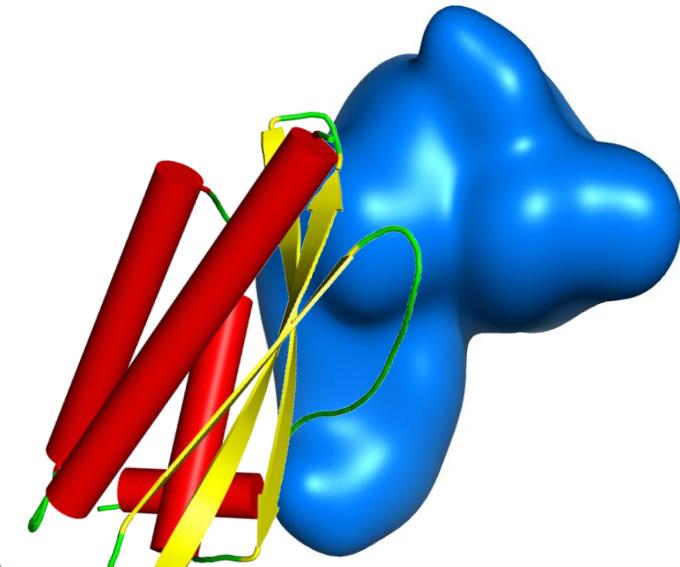
Clustering of all simulations by
protein orientation



Model

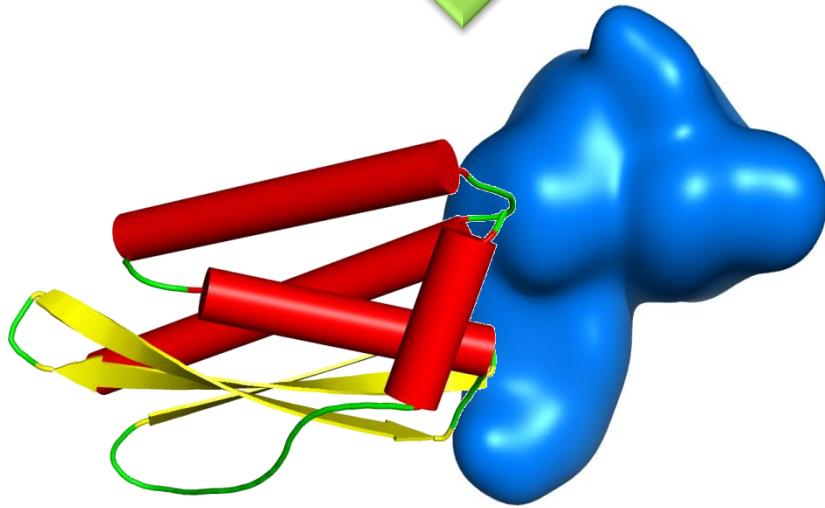
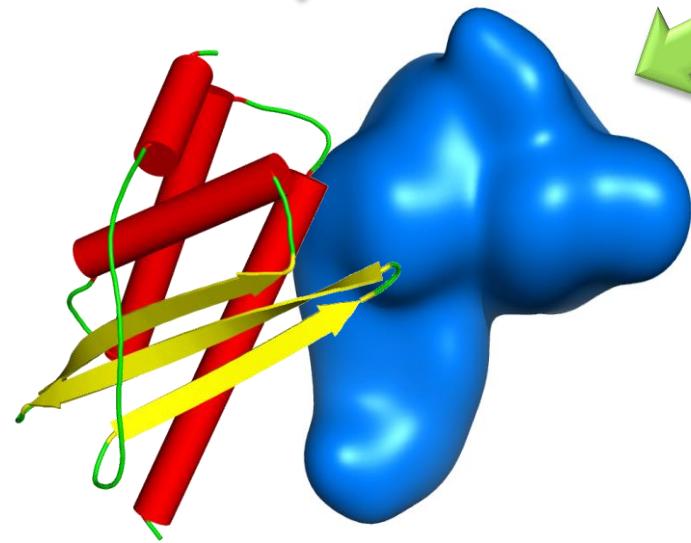


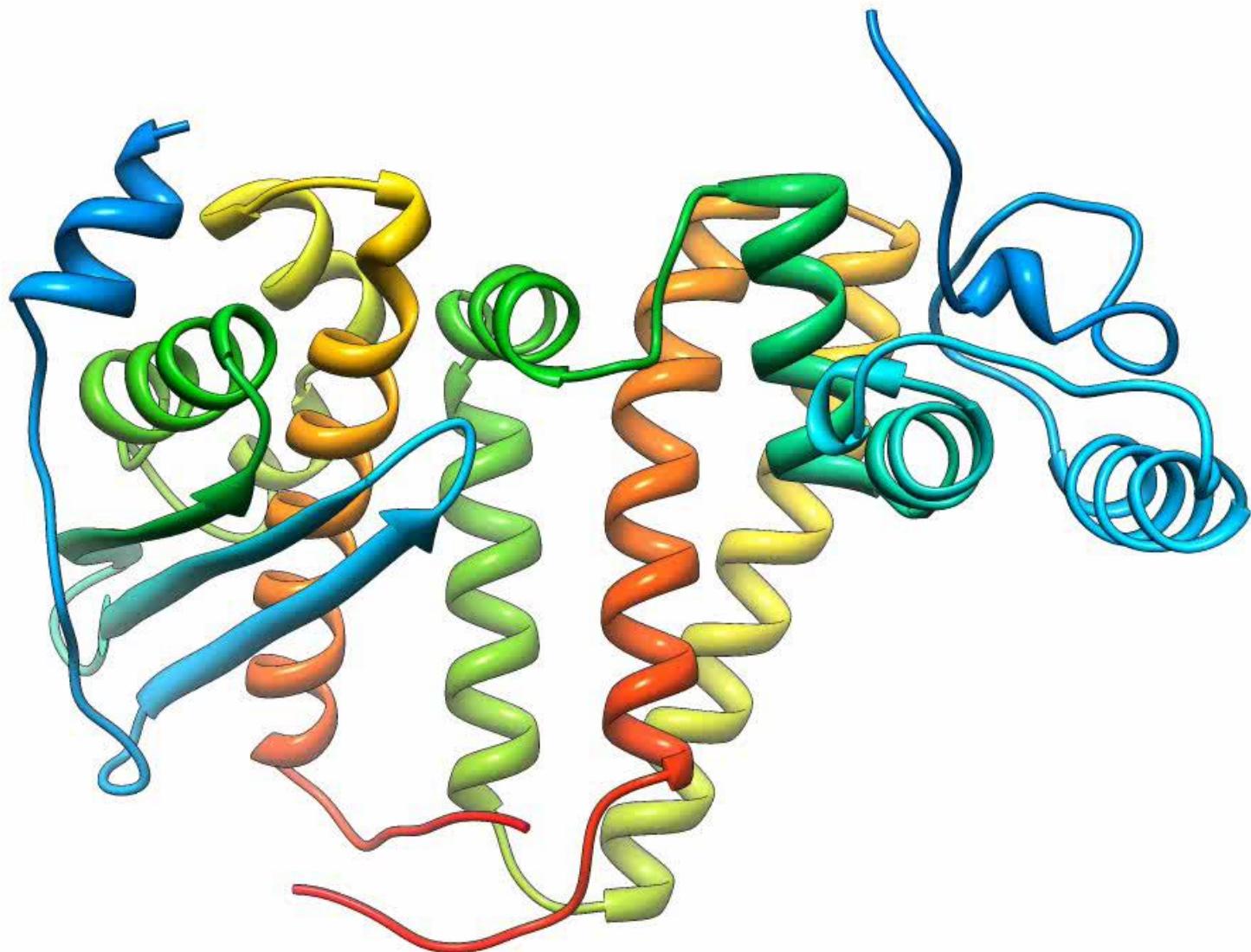
Model 3



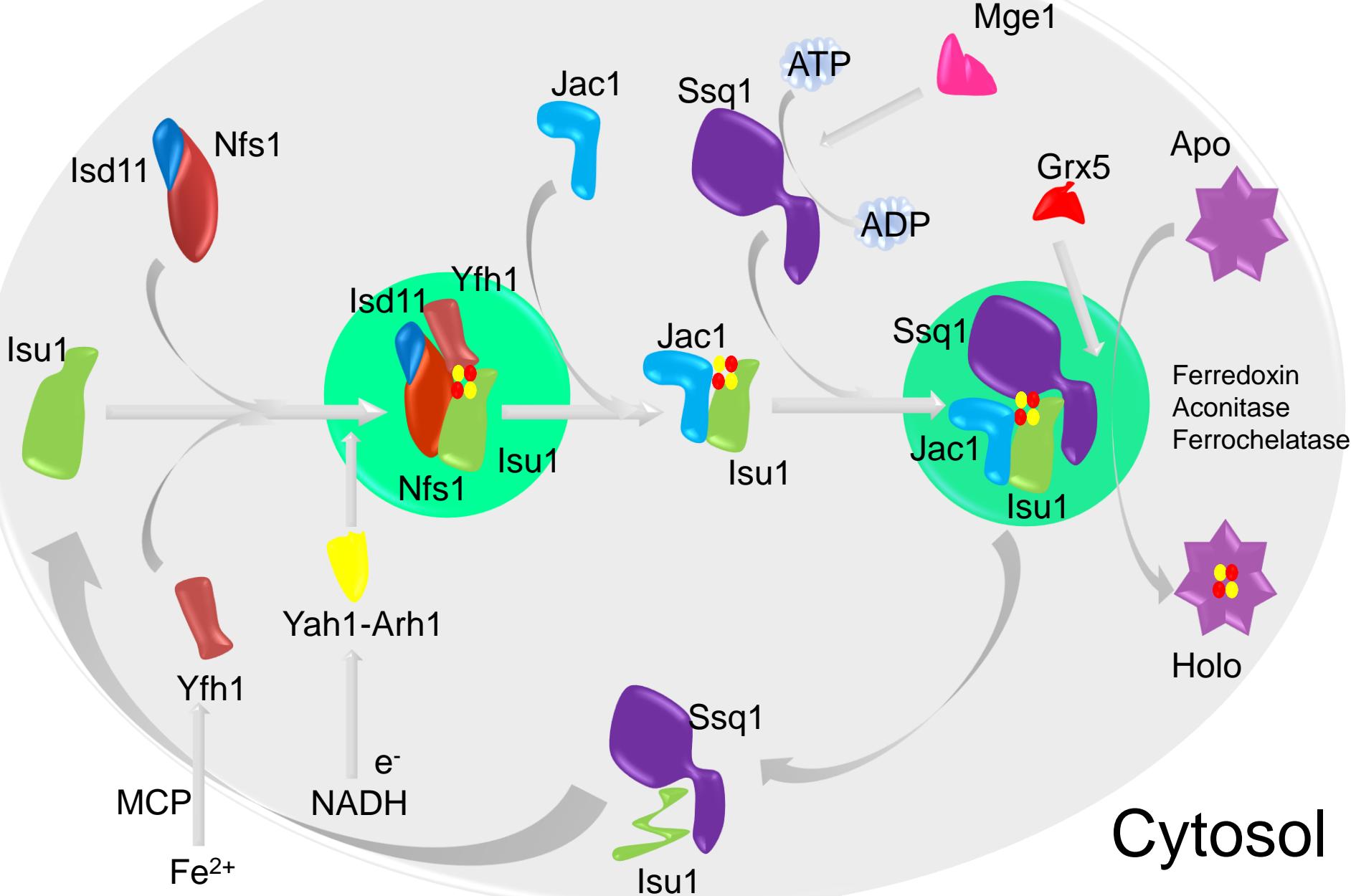
LLY
LL, Mut_all

Y
Mut_all

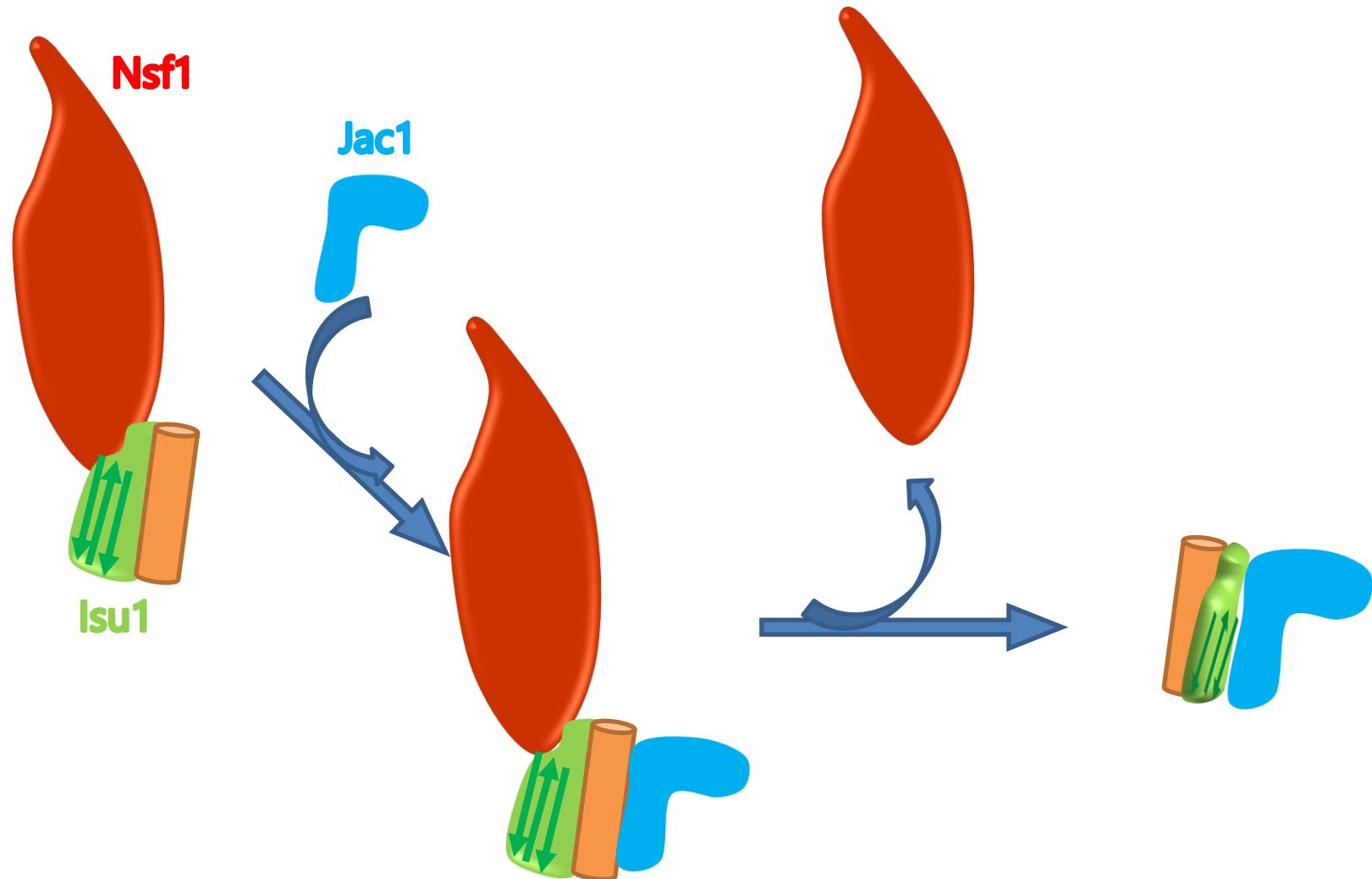




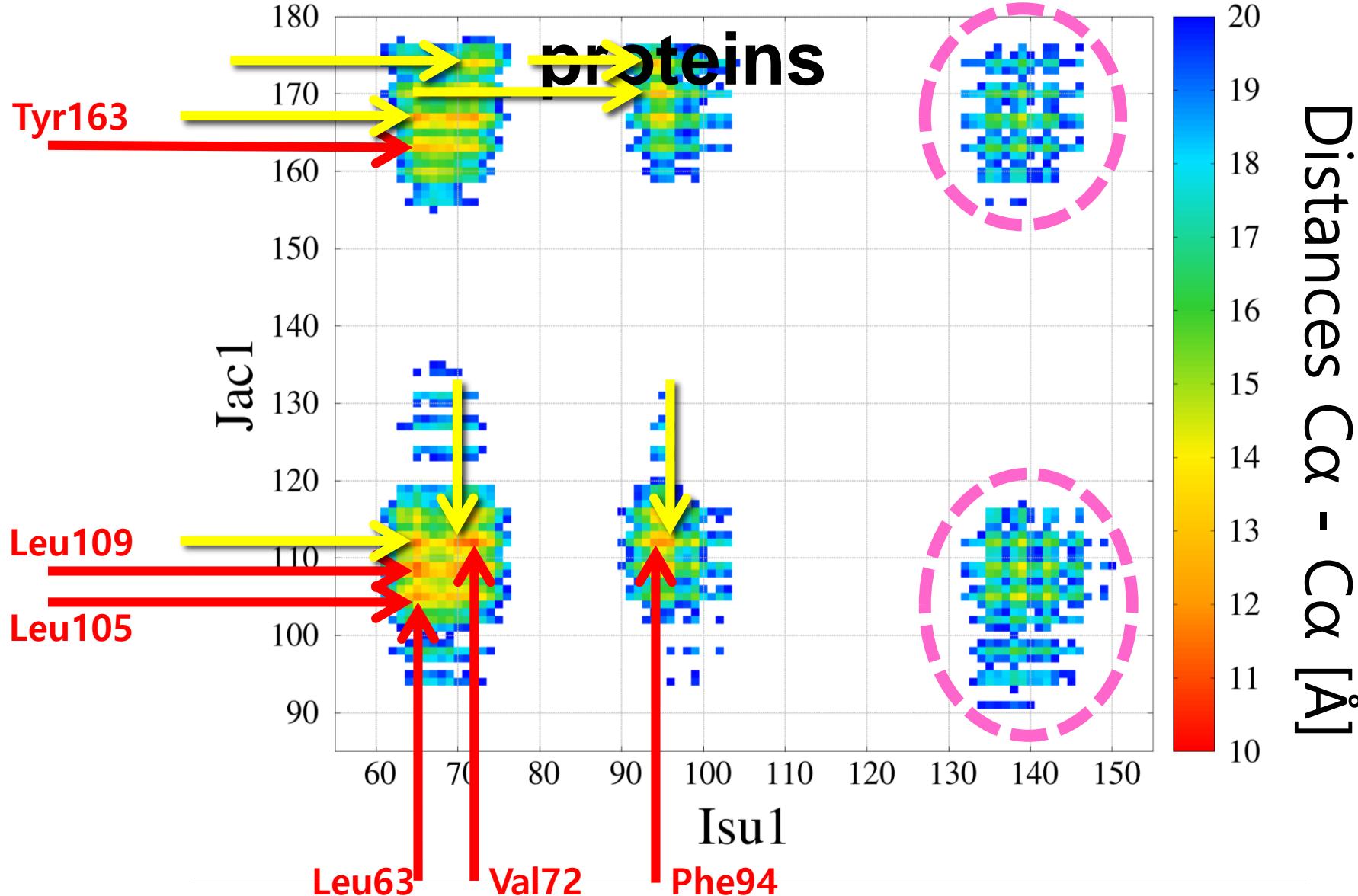
Mitochondrion



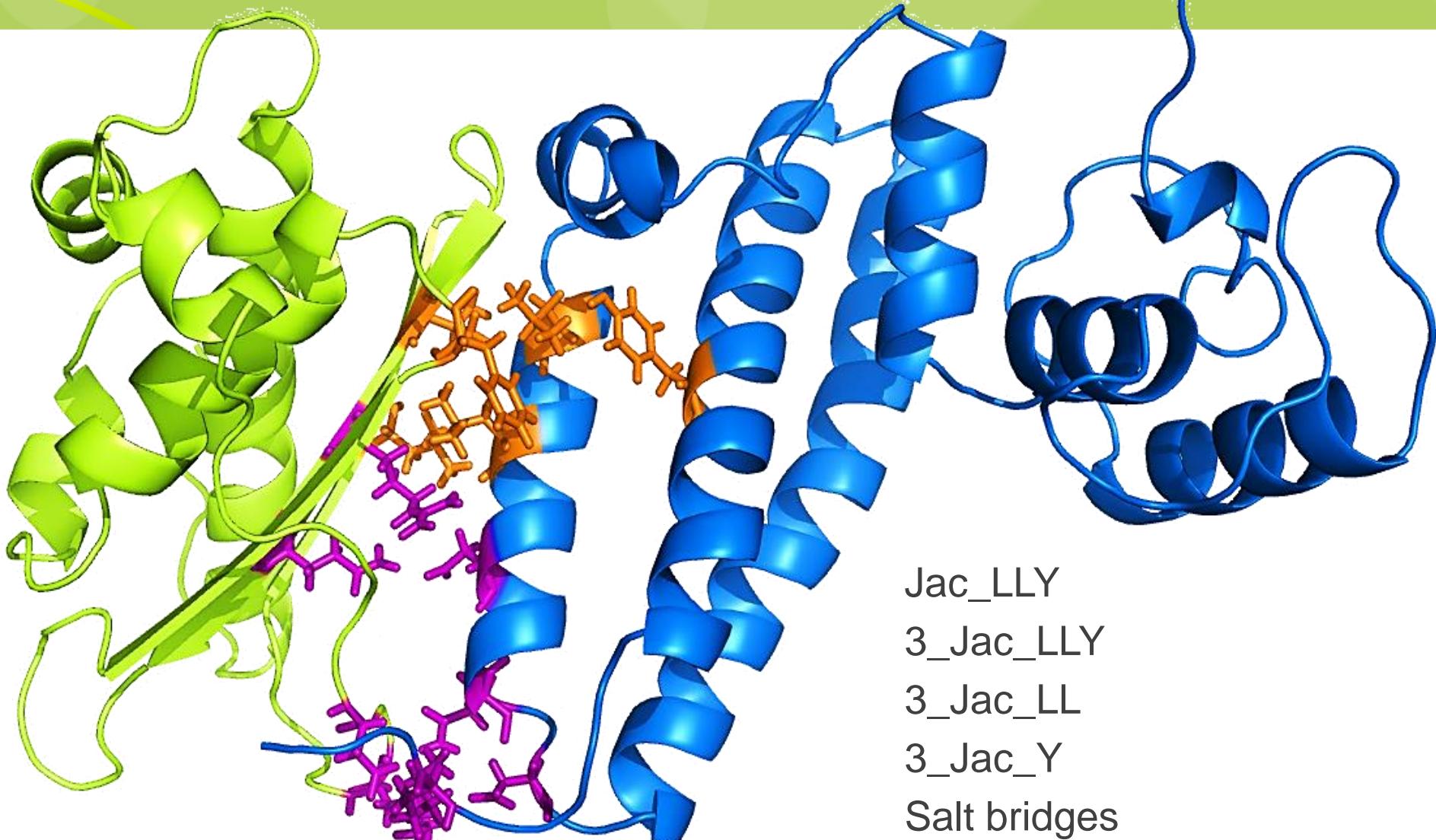
Hypothesis



Average distances between C α atoms for obtained conformations of the Isu1-Jac1



Mutations of Jac1



Jac_LLY

3_Jac_LLY

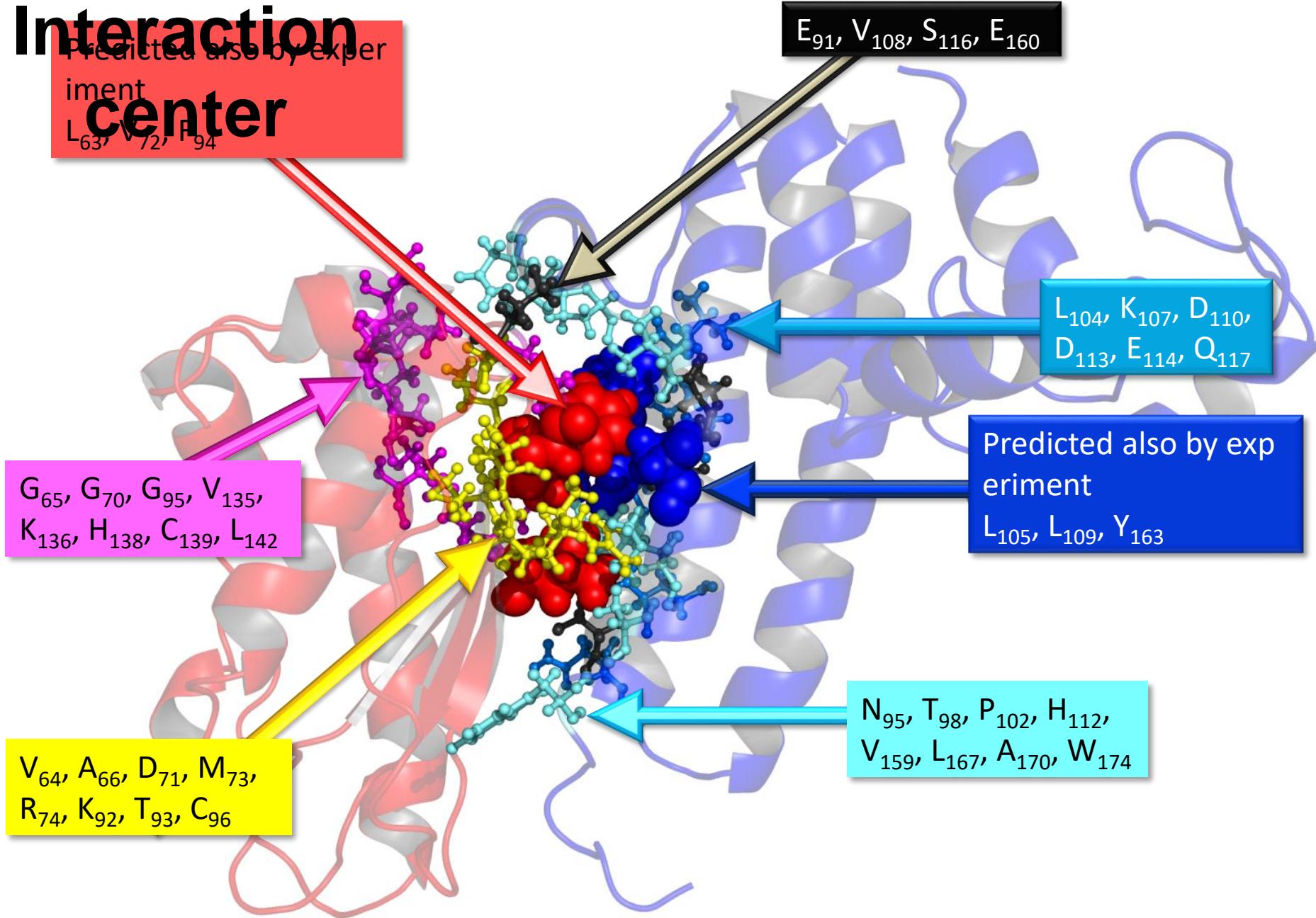
3_Jac_LL

3_Jac_Y

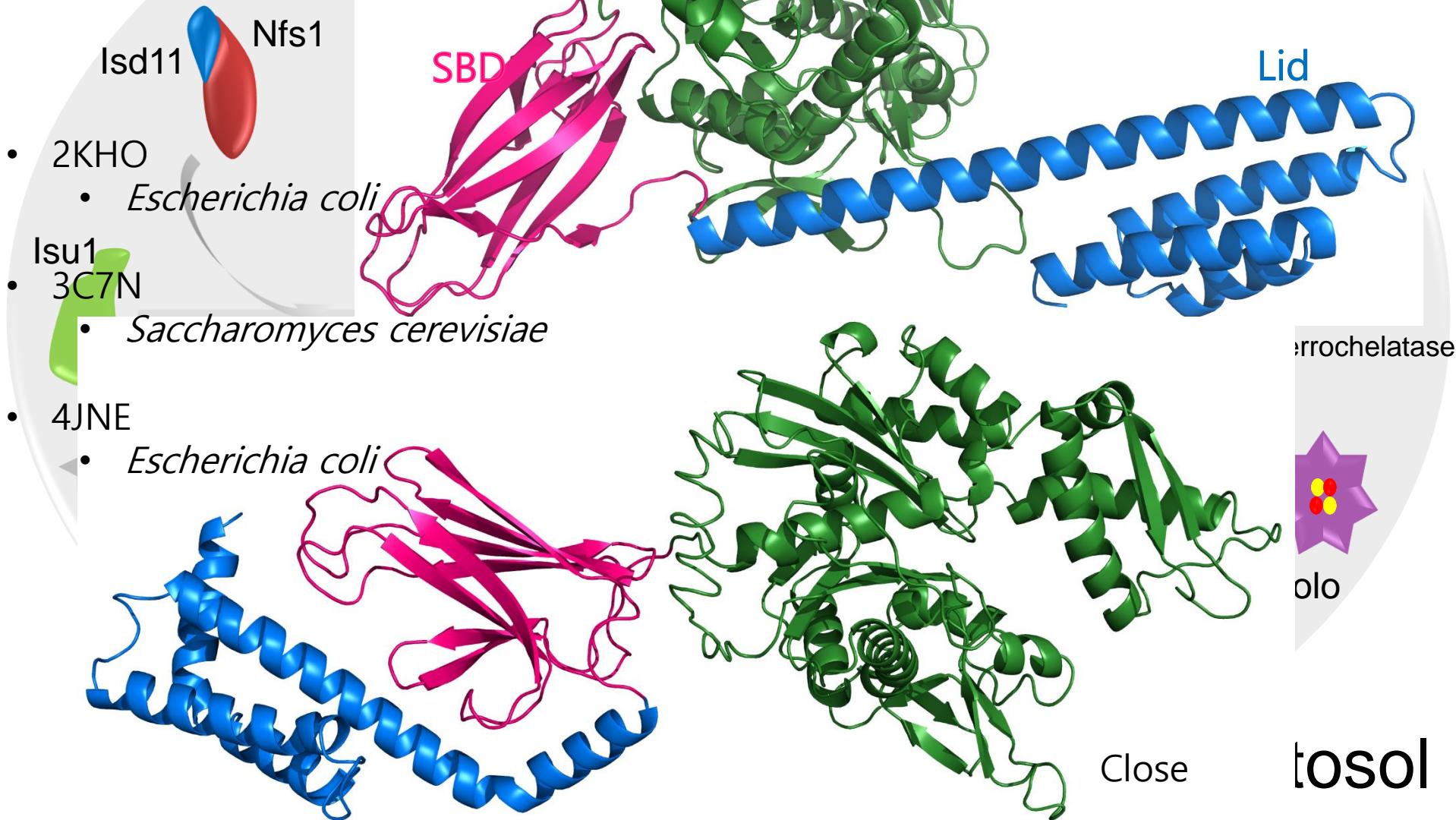
Salt bridges

Mut_all

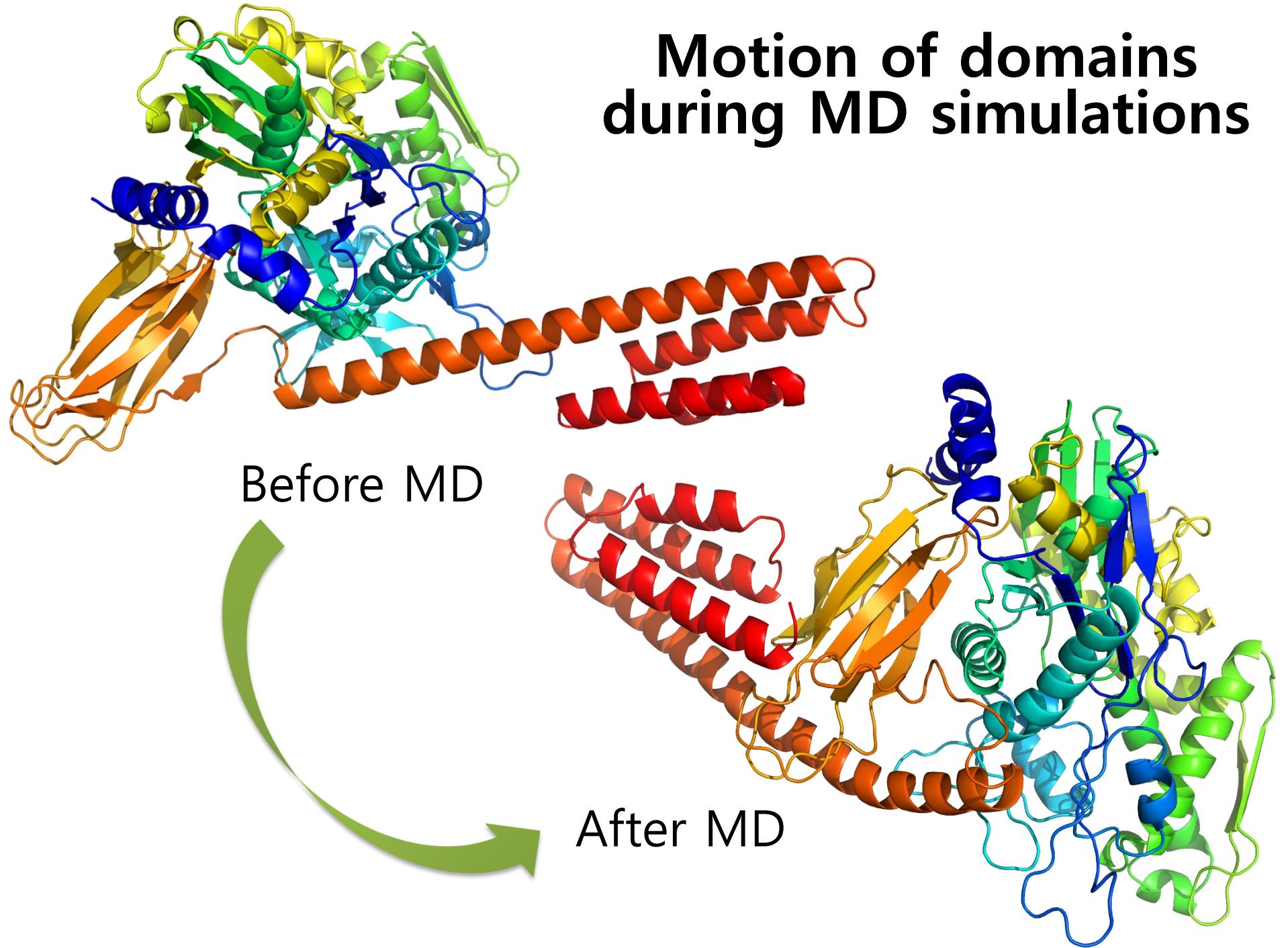
Interaction center



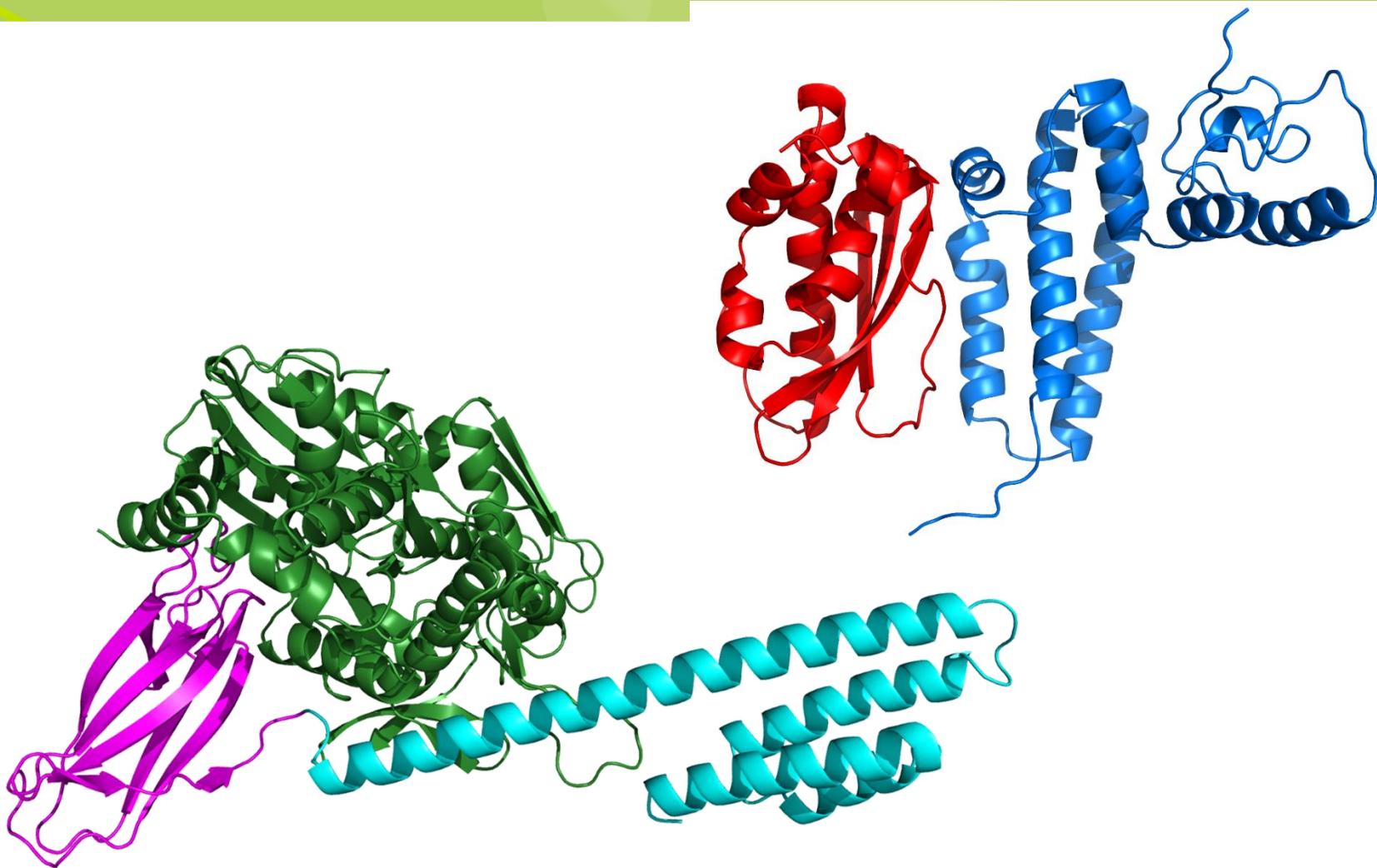
Homology modeling of Ssq1 protein



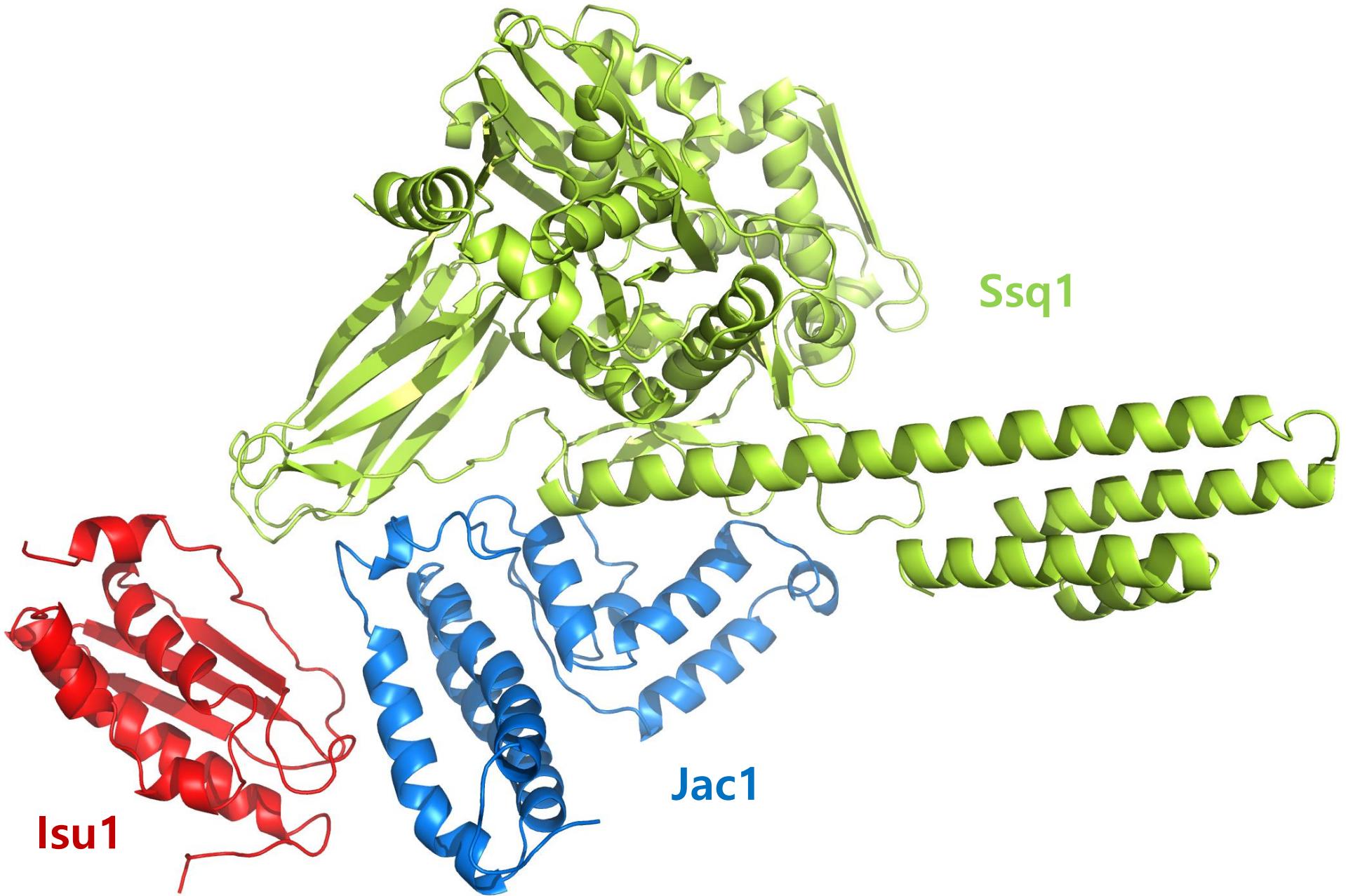
Motion of domains during MD simulations



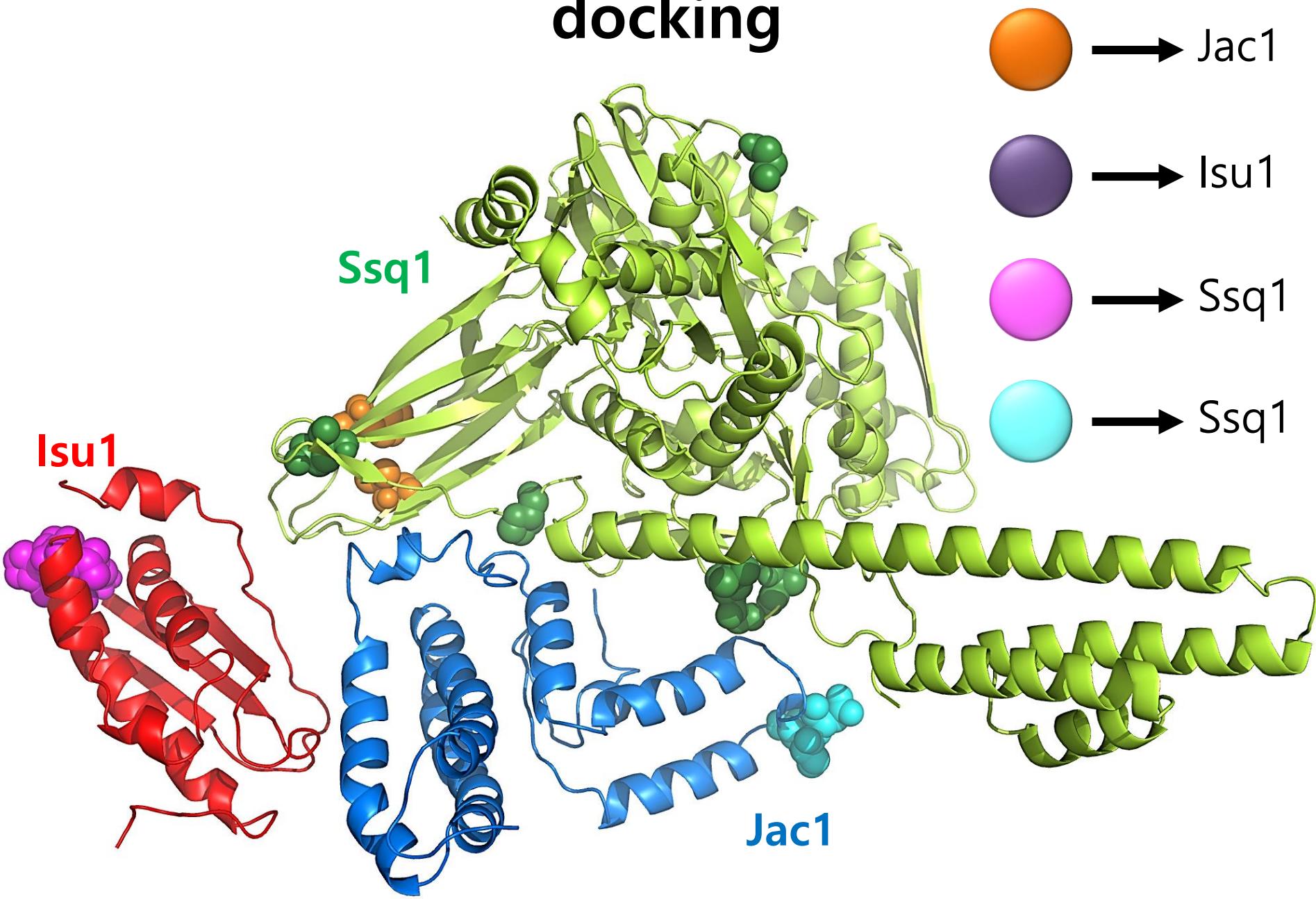
Docking of three proteins



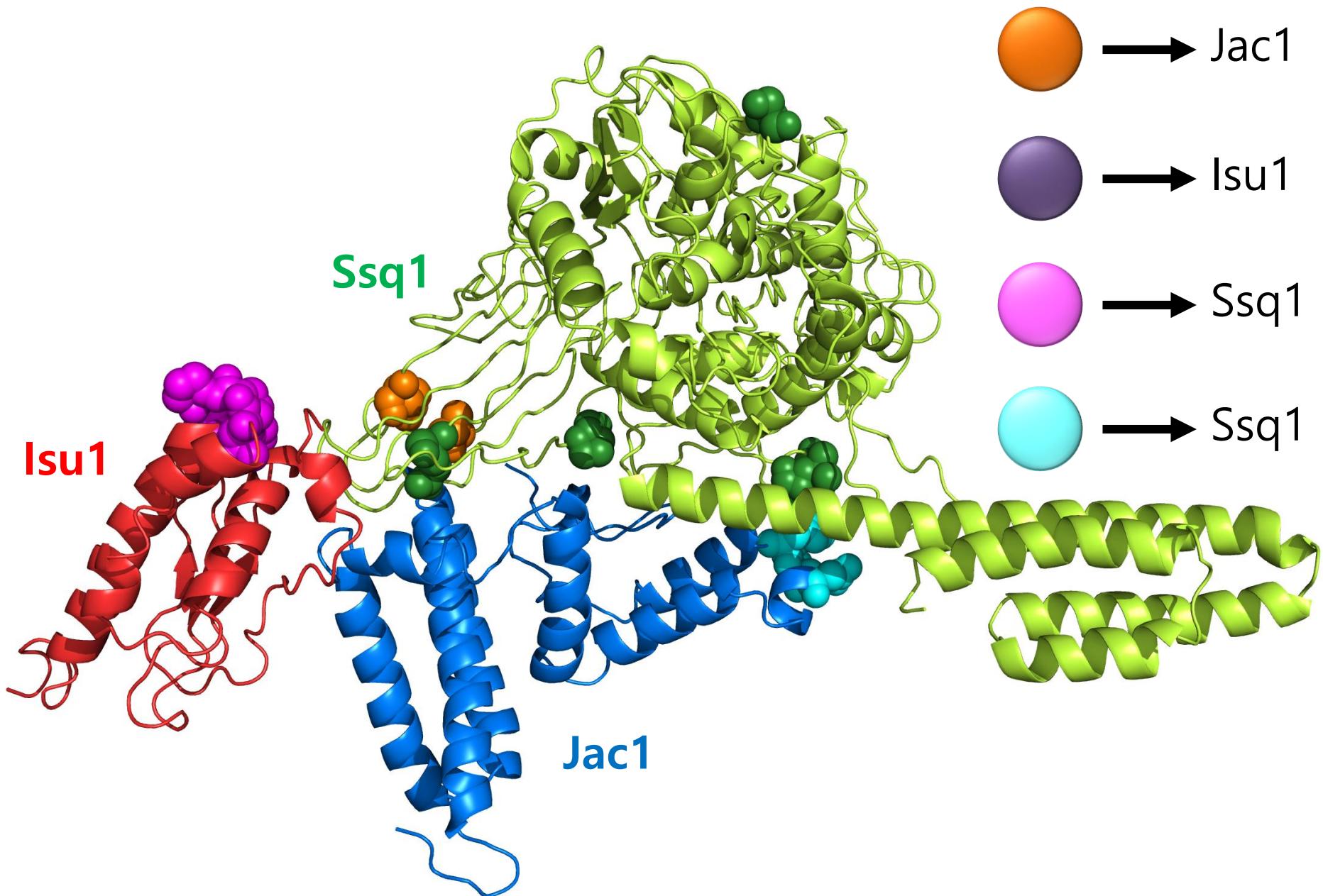
Conformation after docking



Conformation of Isu1-Jac1-Ssq1 after docking



Conformation of Isu1-Jac1-Ssq1 after MD



Acknowledgements

Prof. Adam Liwo, UG

Prof. Harold Scheraga, Cornell University

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Thank you for
your attention!