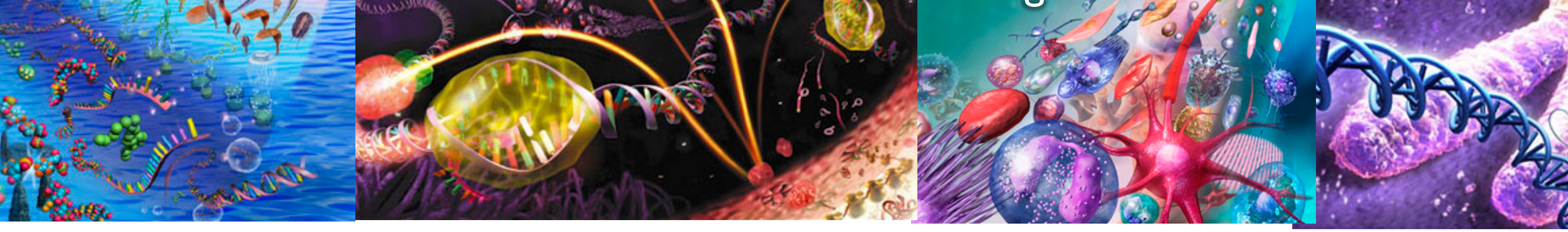

Recent Activities of Biological Function Group for HA-PACS Project

Yasuteru Shigeta

Center for Computational Sciences
University of Tsukuba

1. QM/MM studies on several Enzymes

2. Large-scale MD Simulation with HA-PACS

3. Substrate Binding & Folding Analyses

4. Toward Large-scale First-principles MD

By Prof. Shigeta

5. Implementation of Fragment Molecular Orbital method for GPU based systems

By Dr. Umeda

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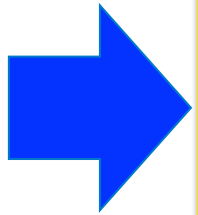
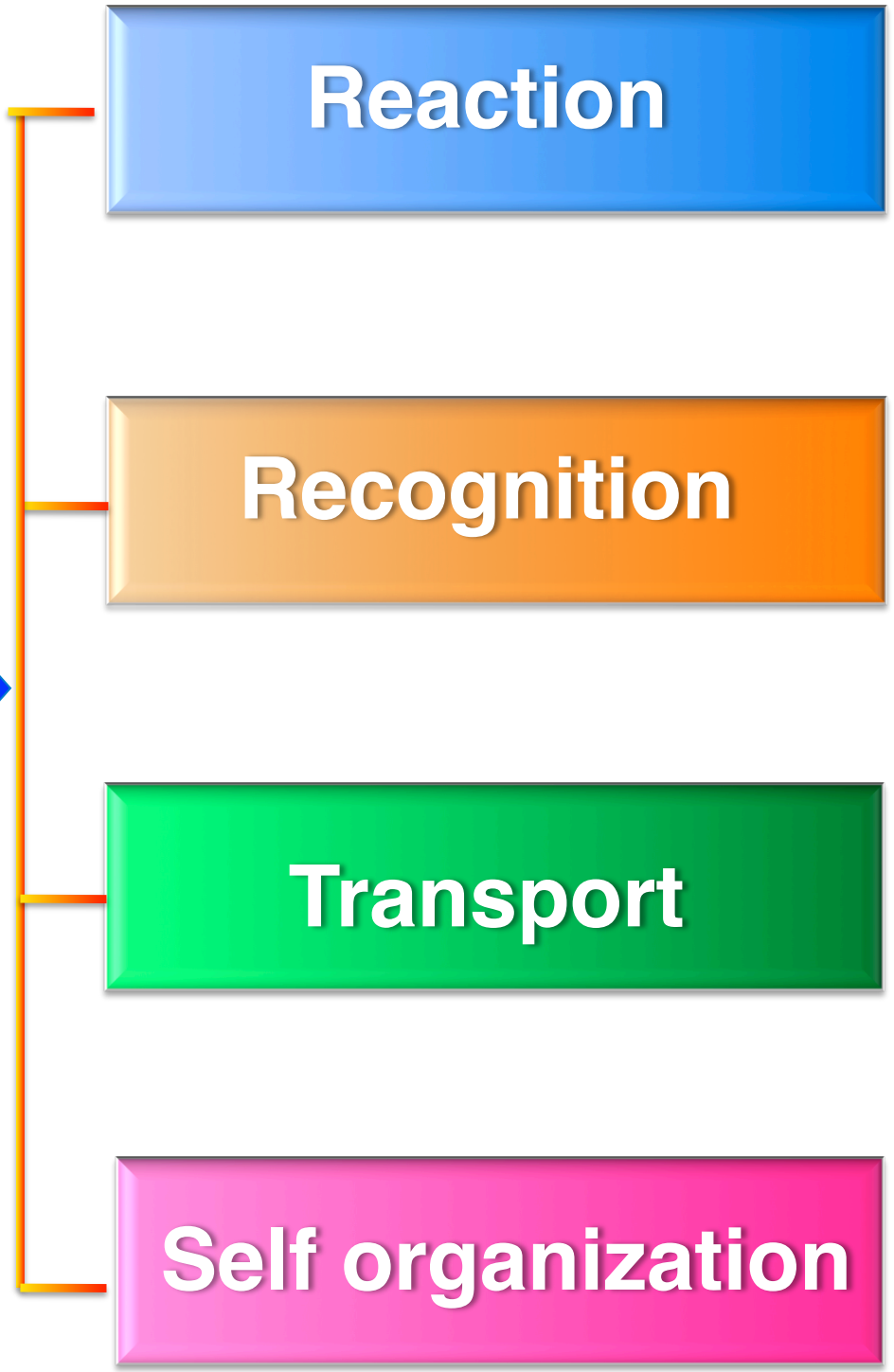




Origin of Biomolecules, De
Life
Many Enzymatic Reactions
Synthetase, Ligase, Hydrase
Peptitase, Lyase, and so on.

Enzyme-Substrate interactio
Substrate and Environment
selectivity, Signal transport

Proton transfer, Electron transfer, Ion transport, Mole
transport, Protein transport, S
transport

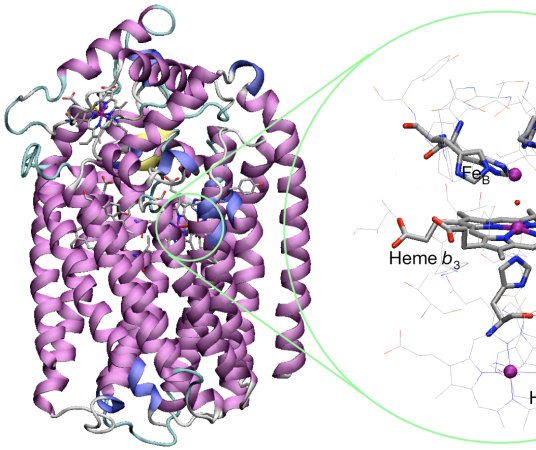
Entropy-driven effects (some
cases), Dynamic order/disord
transition,
Non-equilibrium phenomena

ll topics are of great importance to know bio function

Fragment MO

By Dr. Umeda

Analyses on
Interaction energy



By Myself
Prof. M. Boero(France)

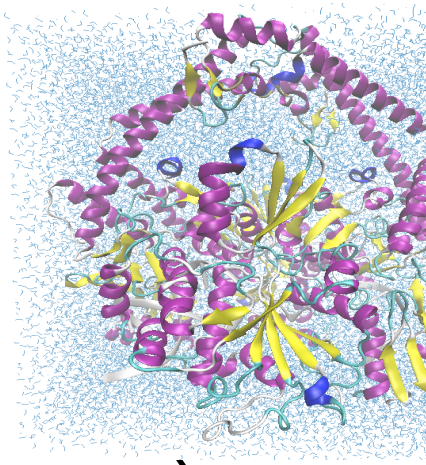
RSCPMD/PWCPMD

Dynamics on
Enzymatic reactions

By Prof. Shoji
Prof. Kayanuma

QM/MM

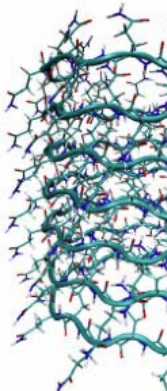
Static Enzymatic
Reaction Analyses



By Prof. Takano (Osaka U)

MD

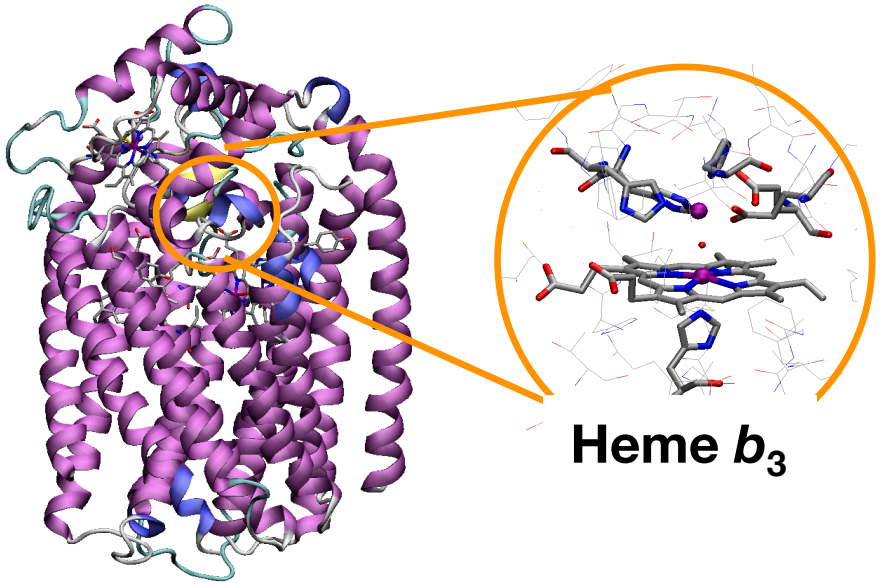
Analyses on structures, large amplitude motion, etc.



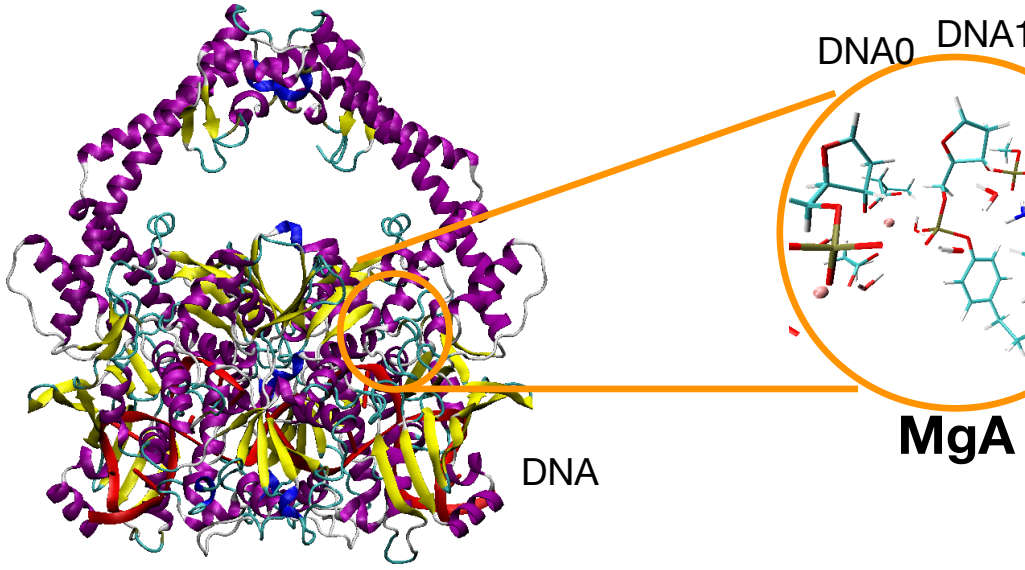
By Dr. Harada **Coarse-grained/ Accelerated MD**

Protein-Protein, Protein-Enzyme complex formation

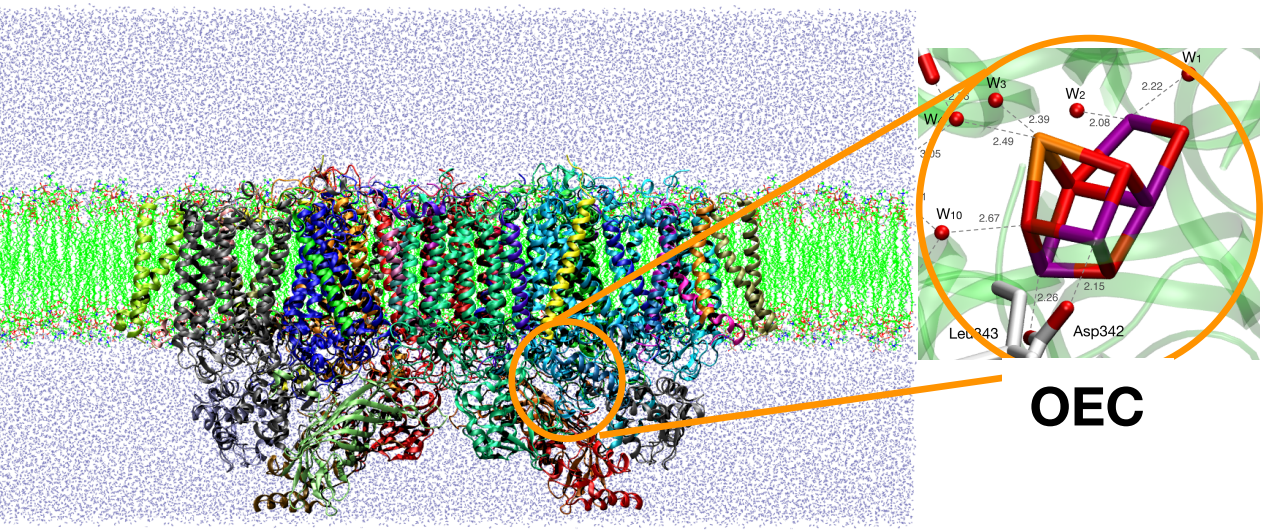
Quantum Mechanics/Molecular Mechanics (QM/MM) method



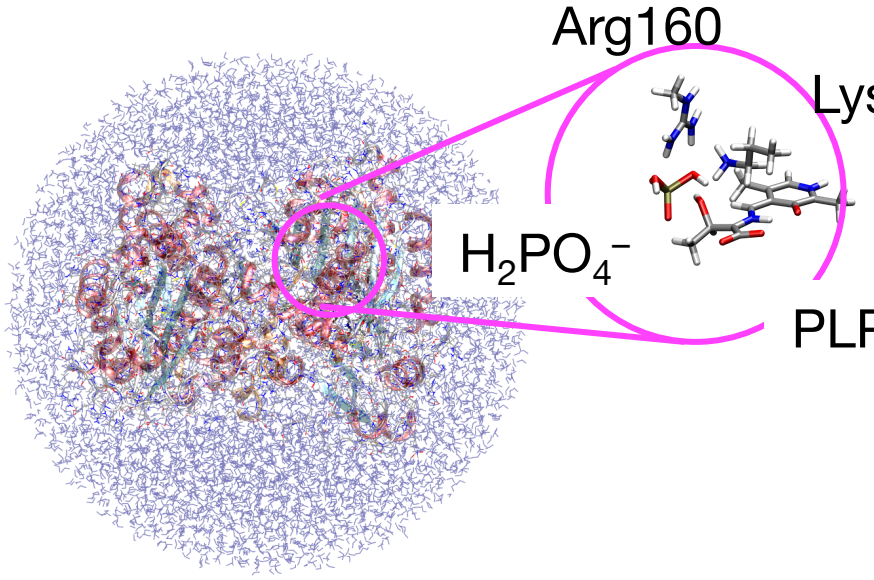
Nitric oxide reductase (NOR) [1]



Topoisomerase (Topo) [2]



gen Evolving Complex in Photosystem II[4]

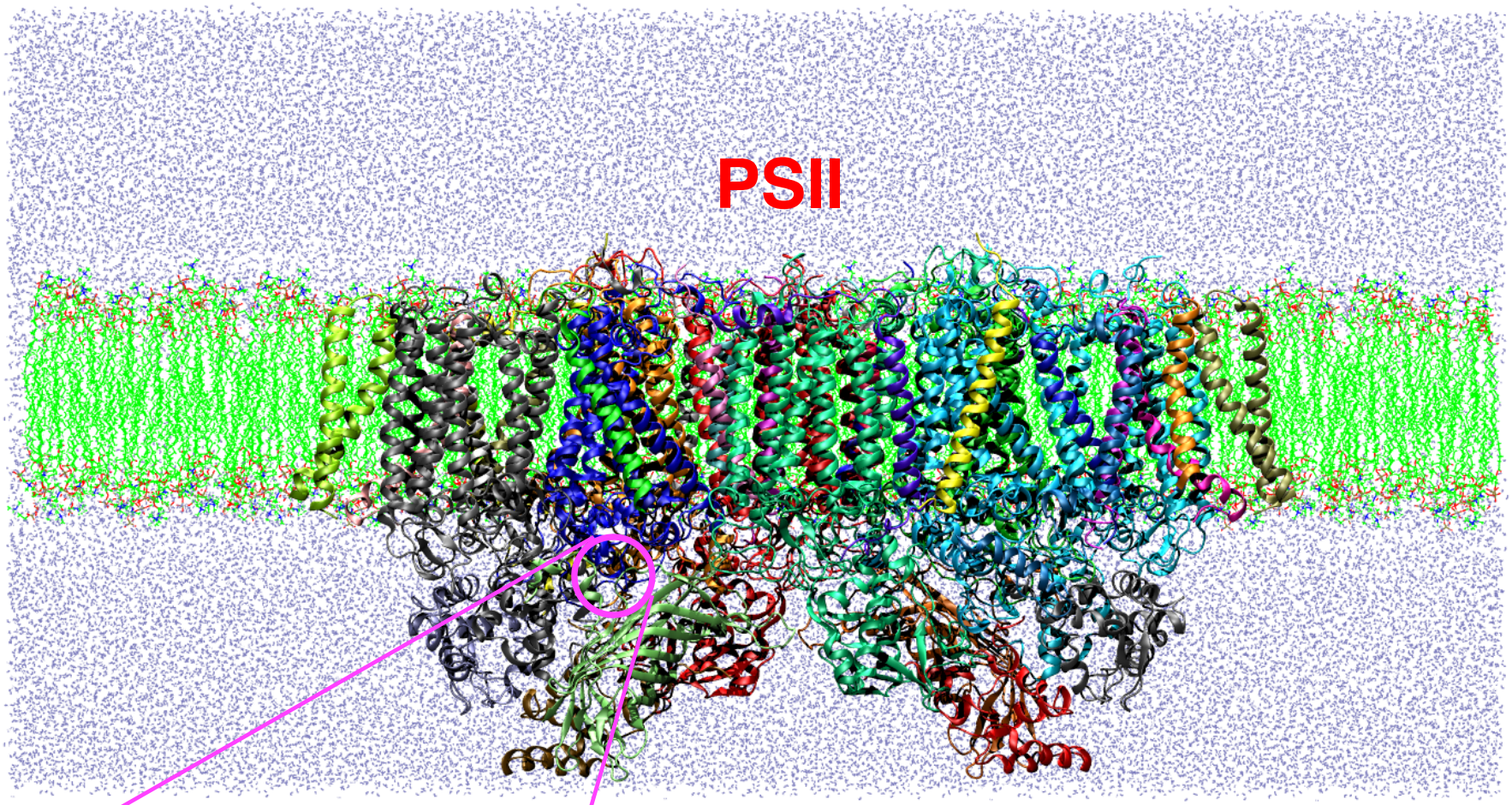


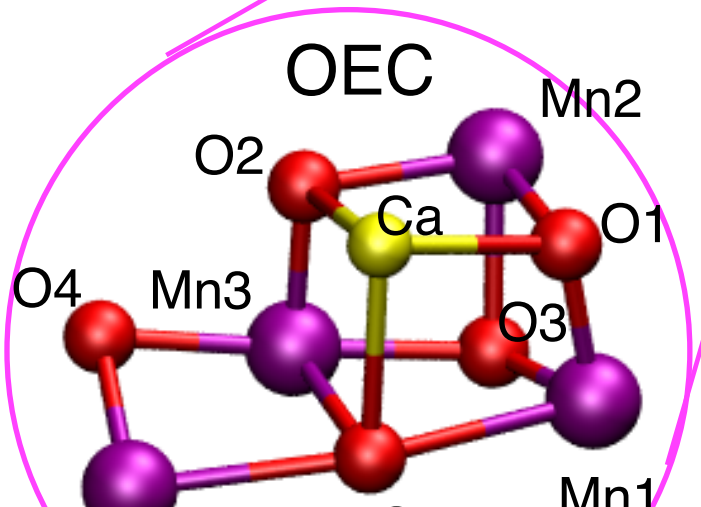
Threonine Synthase [5]

eoretical study on a calculation

[1] M. Shoji et al, Mol. Phys. 112, 393(2013).
[2] K. Hanaoka et al, J. Bio. Struct. & Dyn., accepte

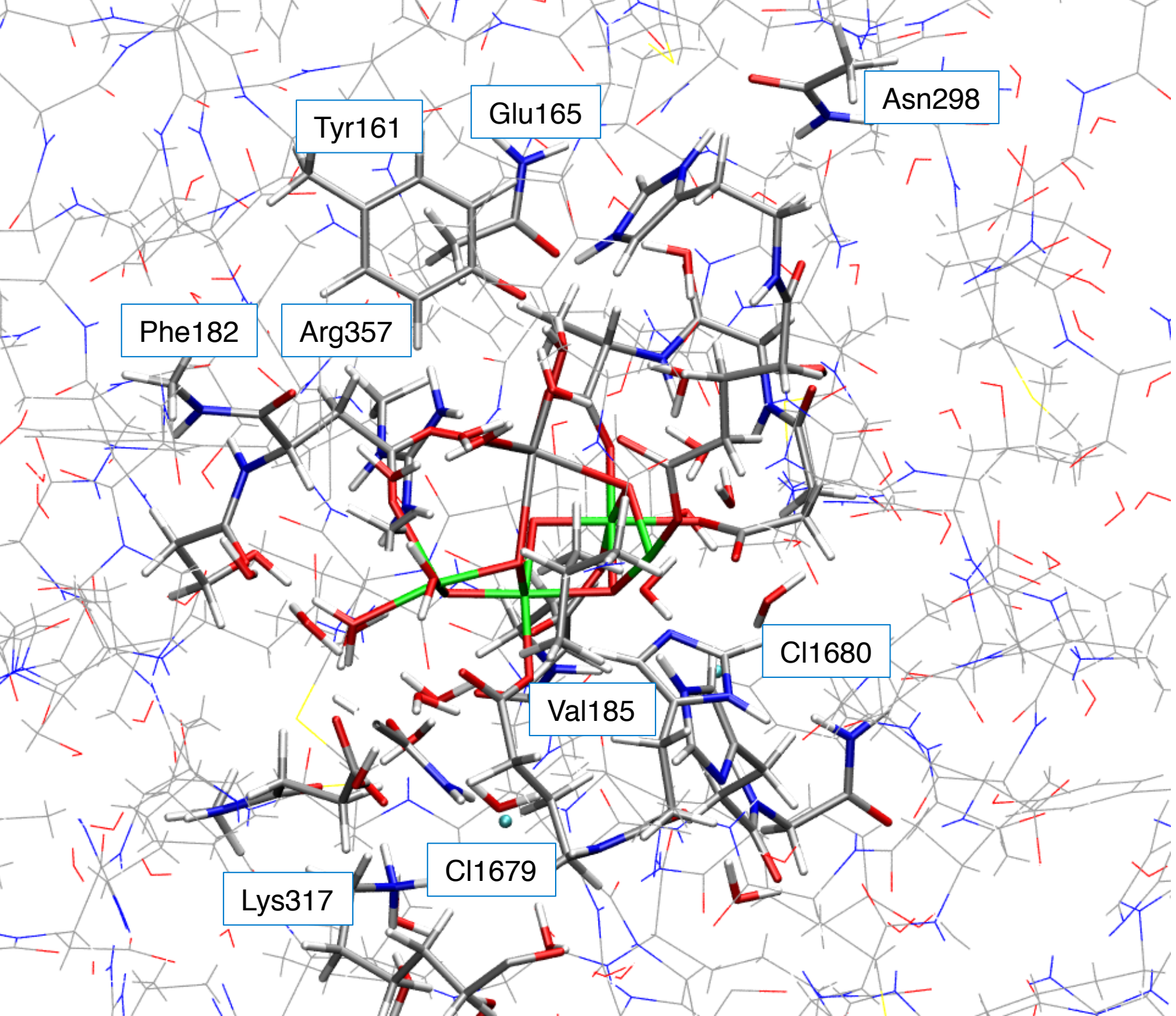
Oxygen-evolving complex (OEC)





• OEC reaction: $2H_2O \rightarrow O_2 + 4H^+ + 4e^-$

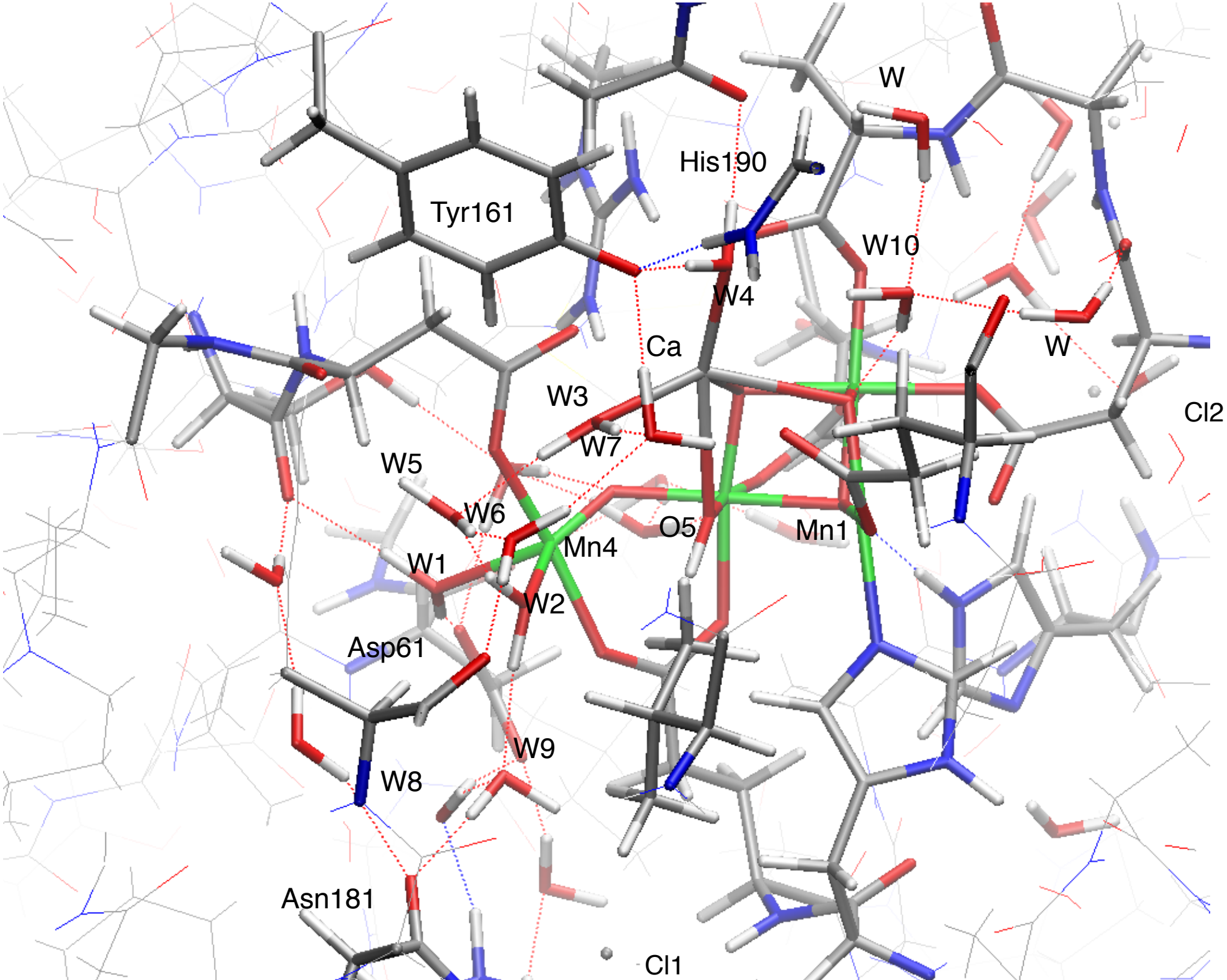
• A 1.9Å resolution X-ray structure of PSII was sol
[1]. - Clear OEC structure and surrounding water
molecules were identified.

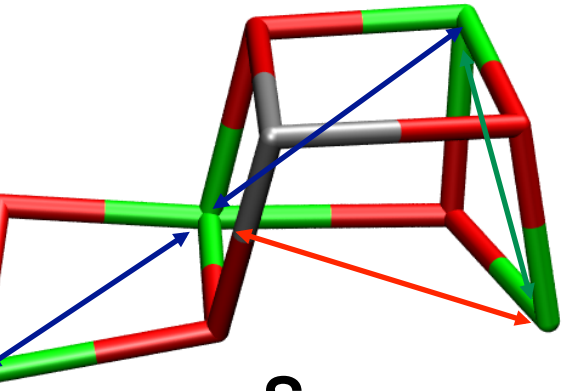


$CaMn_4O_5$(H
Ser169-Asp
Glu189-His
Asp342-Ala
His332-Glu
Glu354

$14H_2O$
Asp61
His337
Arg357

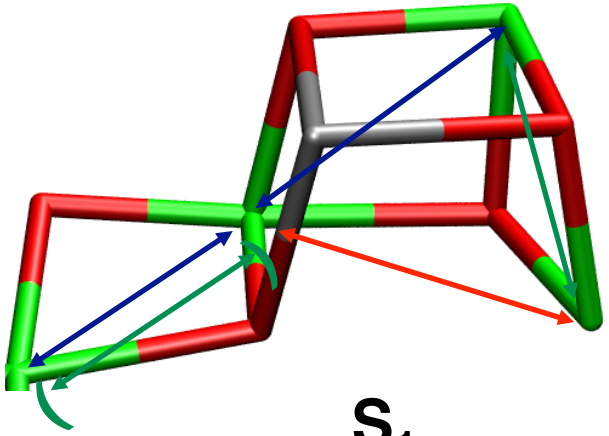
Tyr161
Glu165
Asn181
Phe182
Val185
Asn298
Lys317
Cl1679
Cl1680
+Min2


W
His190
Tyr161
W10
W4
Ca
W
Cl2
W3
W7
W5
W6
O5
Mn1
Mn4
W1
W2
Asp61
W9
W8
Asn181
Cl1



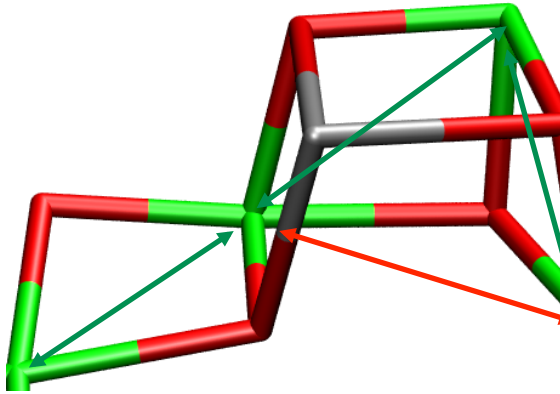
S_0

(III, IV,III, III)



S_1

(III, IV, IV, III)



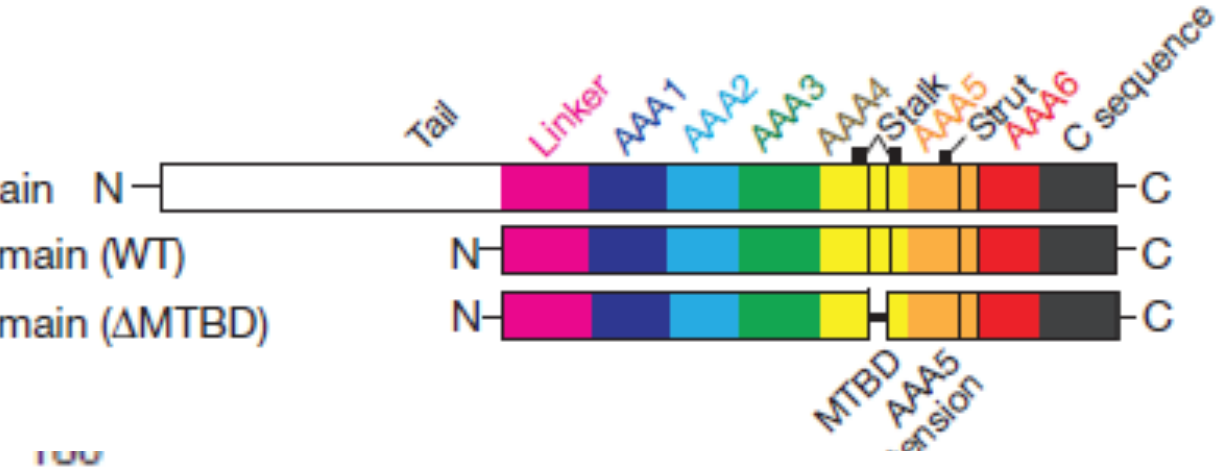
S_2

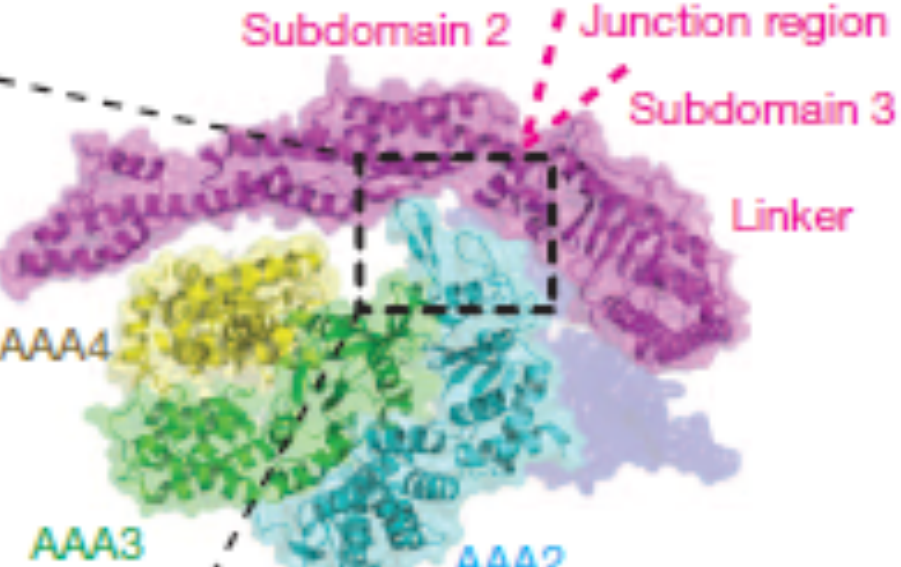
(III, IV, IV, IV)

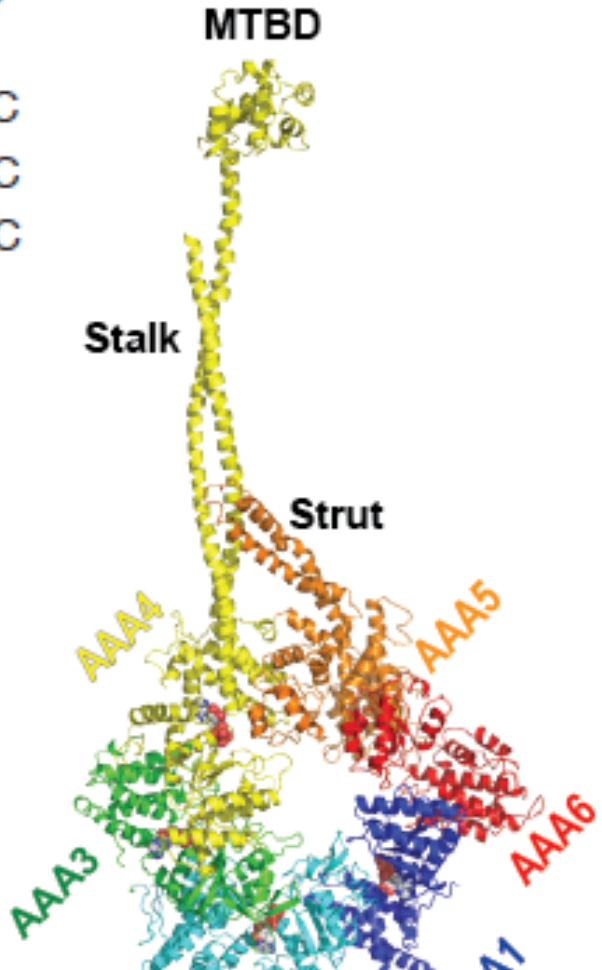
		S0				S1				S2		
		QMMM		EXAFS*		QMMM		EXAFS *		QMMM		EXAFS
		R	N	R	N	R	N	R	N	R	N	R
Mn-O	shorter	1.86	9	1.91	9	1.83	9	1.86	7.8	–	–	1.84
	longer	2.26	2	2.26	3	2.05	2	2.05	4.2	–	–	1.97
Mn-Mn	shorter	2.72	1	2.68	1	2.68(2.72)	1(2)	2.71	2	2.83	3	2.74
	longer	2.90	2	2.77	2	2.77(2.77)	2(1)	2.79	1			
	longest	3.18	1	3.30	1	3.22(3.20)	1	3.27	1	3.38	1	3.30
Mn-Ca	shorter	3.45	3	3.36	3	3.45	3	3.36	3	3.58	3	3.36
	longer	4.00	1	3.99	1	3.71	1	3.99	1	4.01	1	3.99

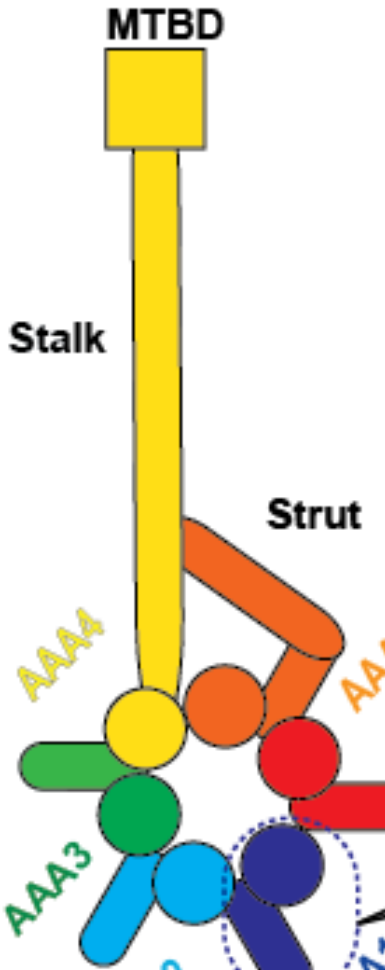
* C. Gloeckner et al. , JBC

motor domain of dynein consists of the linker, a shaped six ATPases called AAA+ modules A1-AAA6), the stalk with microtubule binding ain (MTBD) and the strut.

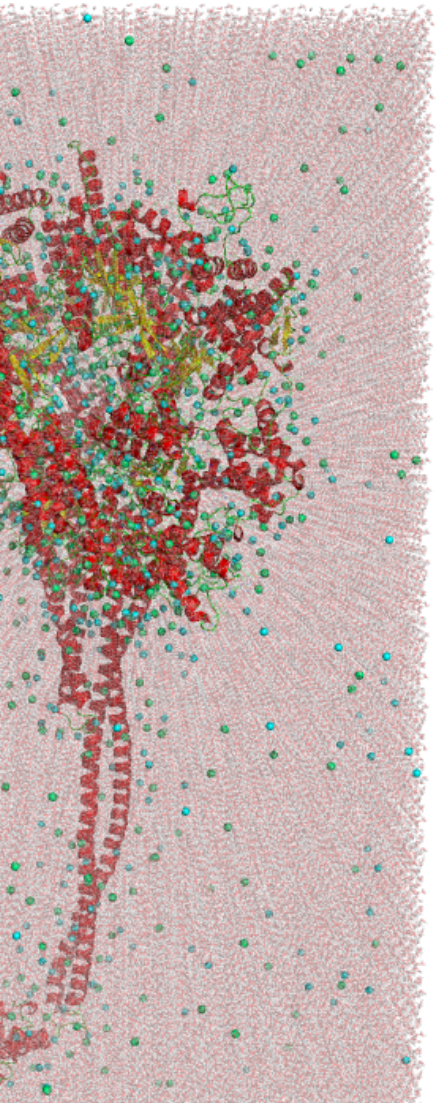


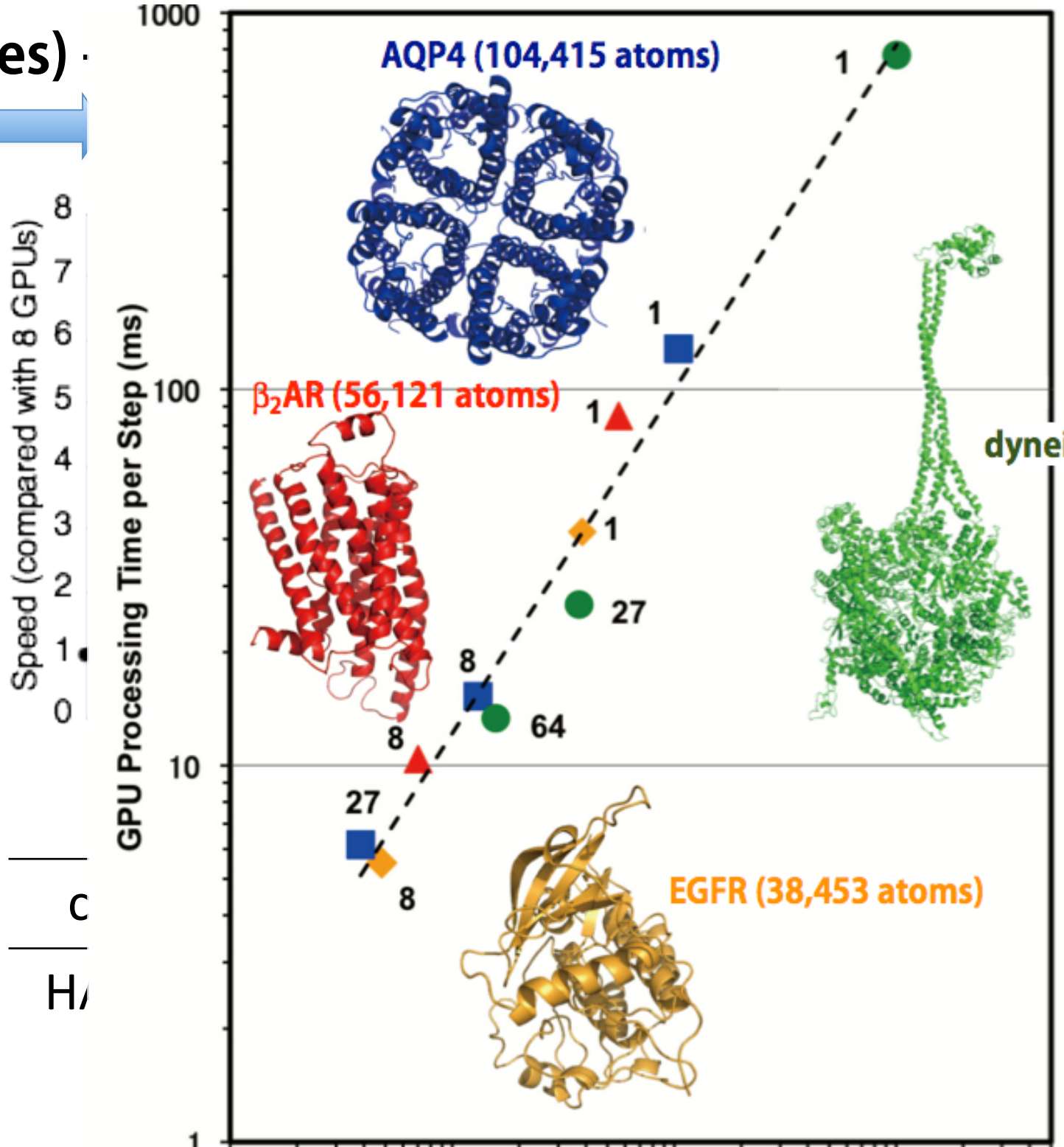






n(3,322 residues) ·
a⁺ + 528 Cl⁻





BP wa
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Takan
Osaka U

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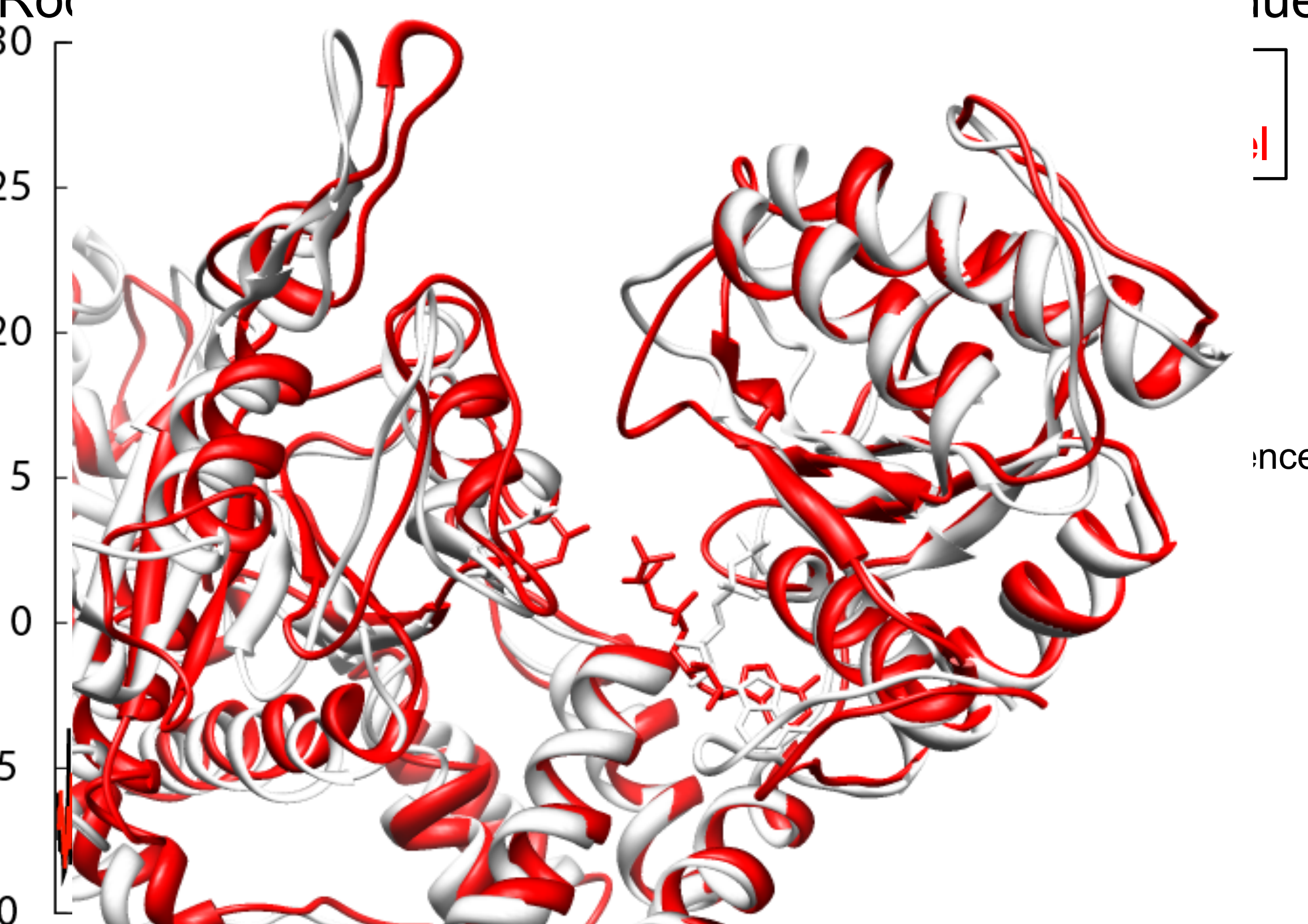
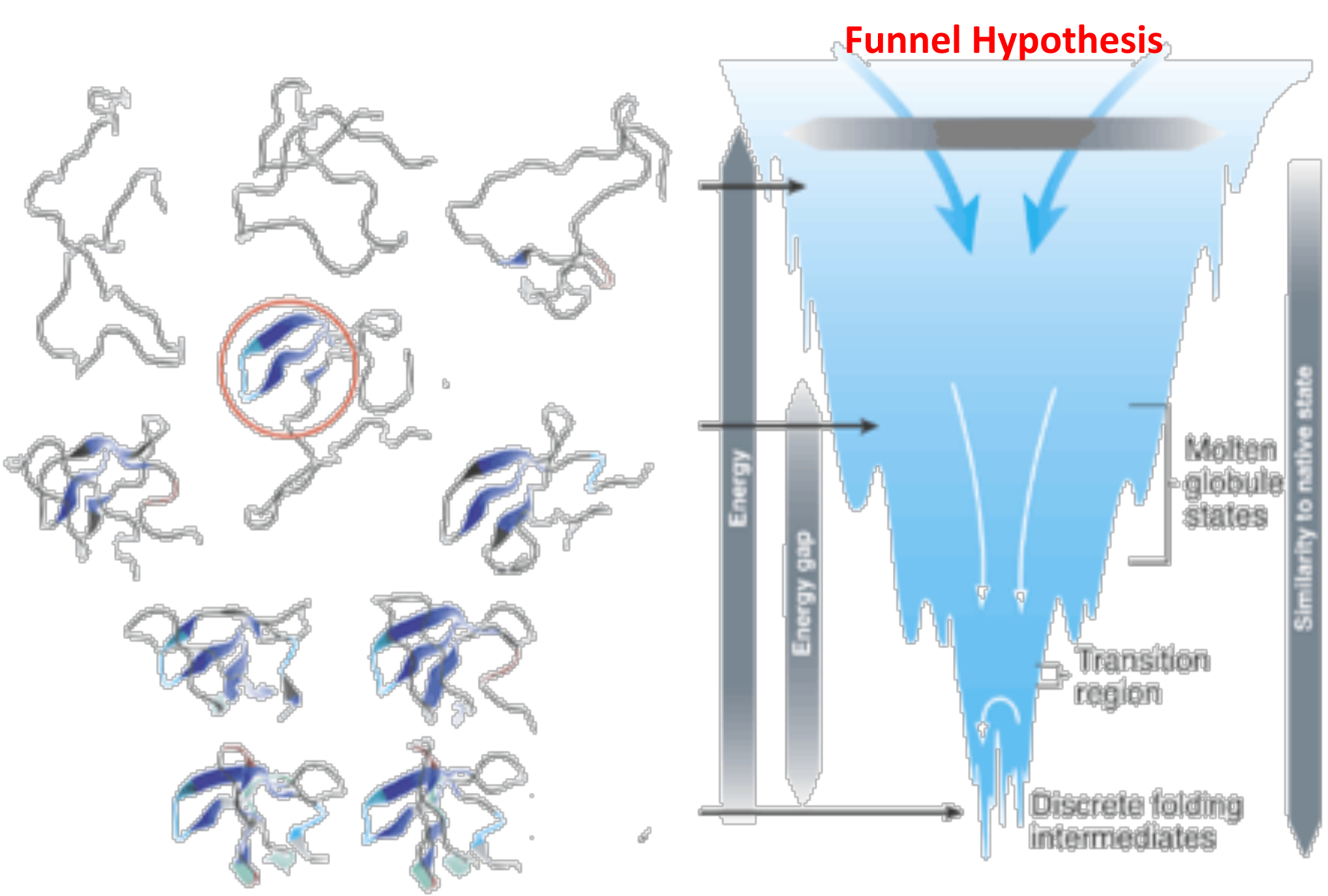
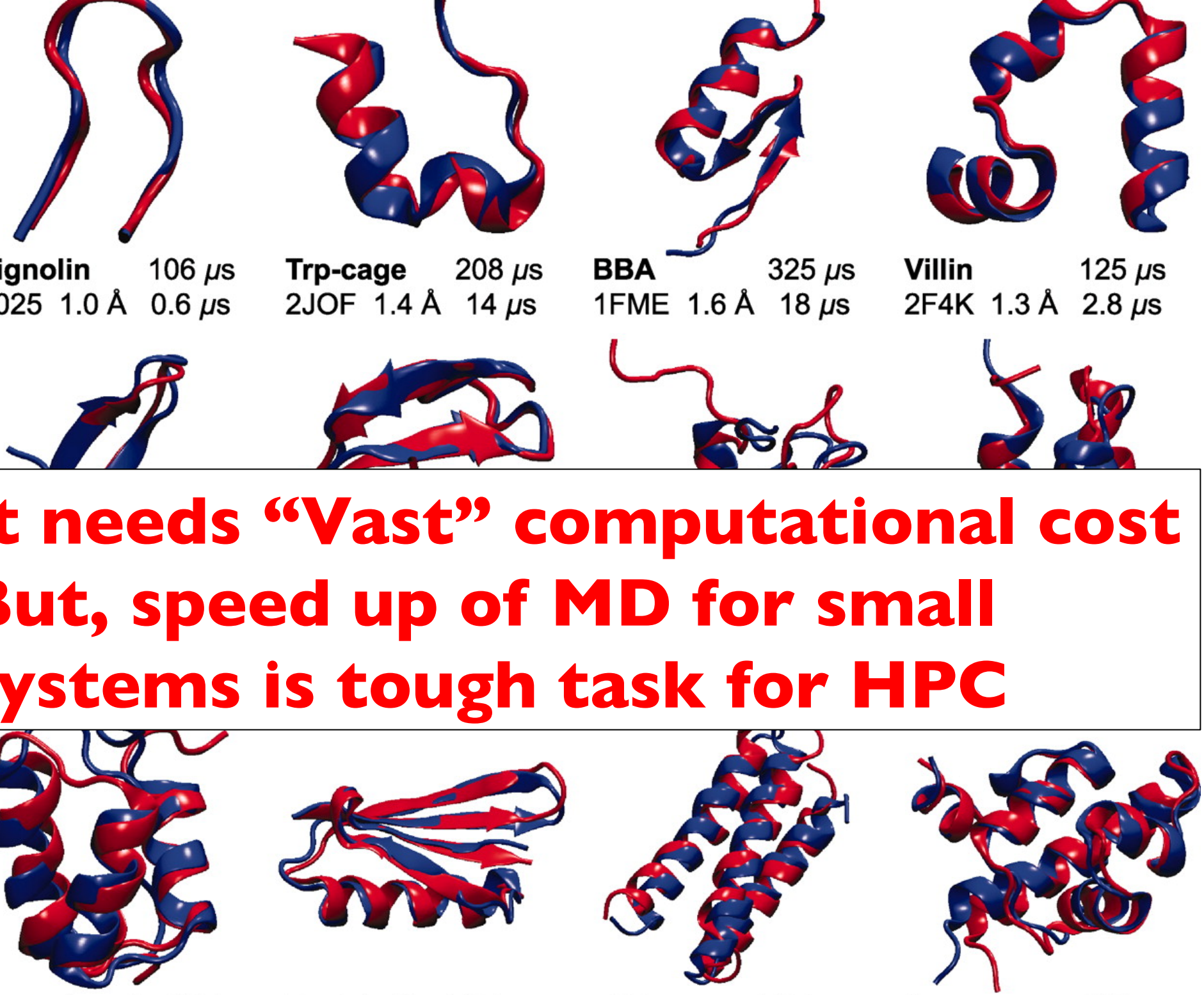
faster

c	comm
H/	44.8
	15.6

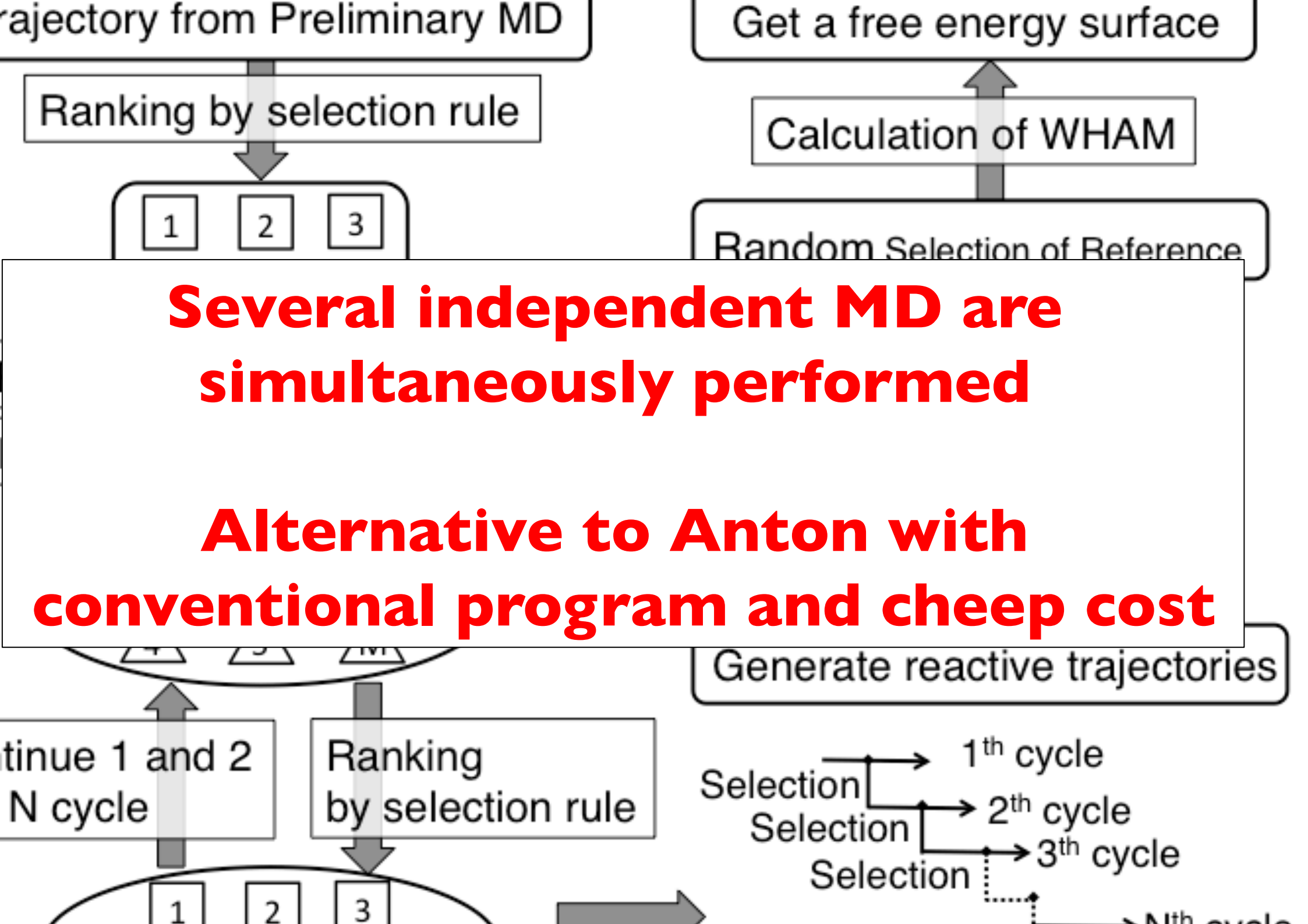

30
25
20
5
0
5
0

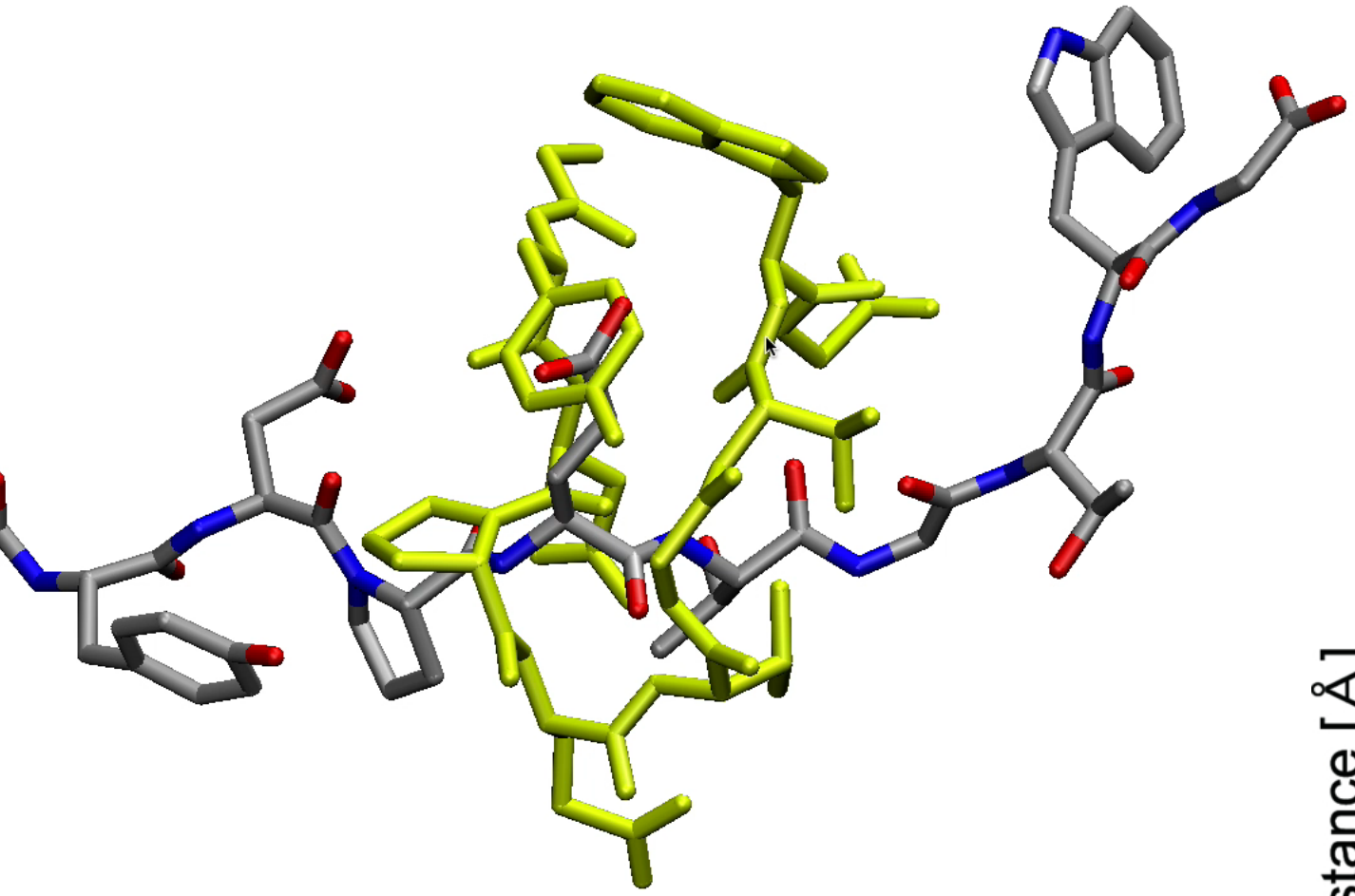


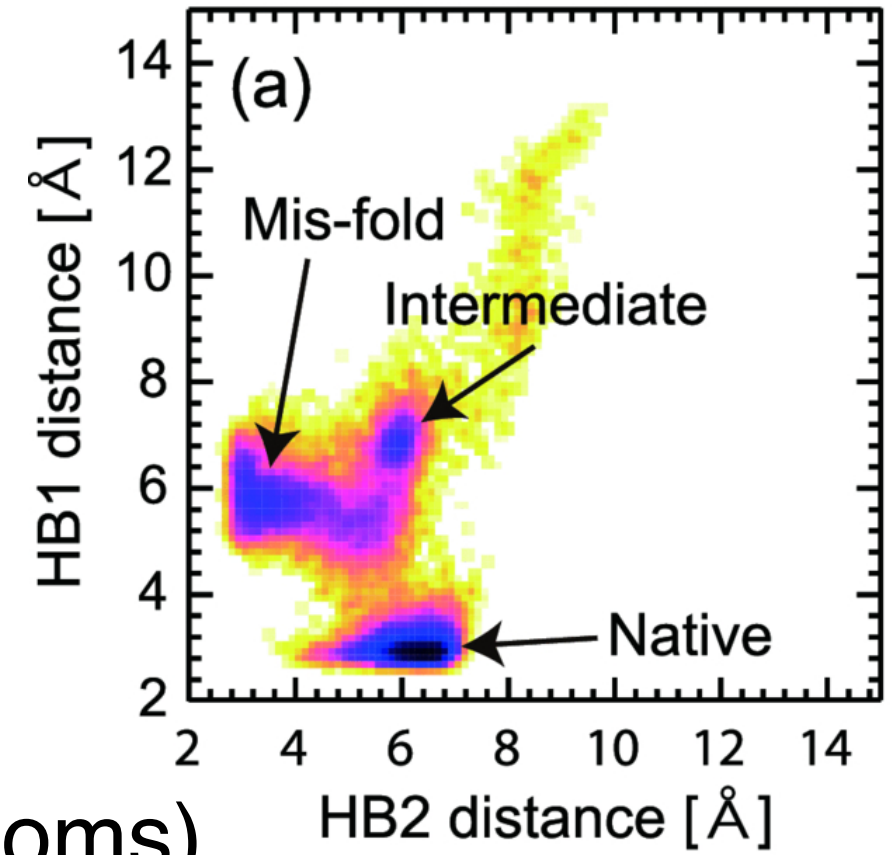
Large amplitude motion takes long time and folding occurs as a stochastic proce
so it is difficult to accomplish with available MD simulations.
(Except now for long time dynamics done by David Shaw with Anton)



It needs "Vast" computational cost
But, speed up of MD for small systems is tough task for HPC


rajectory from Preliminary MD
Ranking by selection rule
1
2
3
Get a free energy surface
Calculation of WHAM
Random Selection of Reference
Several independent MD are simultaneously performed
Alternative to Anton with conventional program and cheep cost
Generate reactive trajectories
tinue 1 and 2
N cycle
Ranking
by selection rule
1
2
3
Selection
1th cycle
Selection
2th cycle
Selection
3th cycle



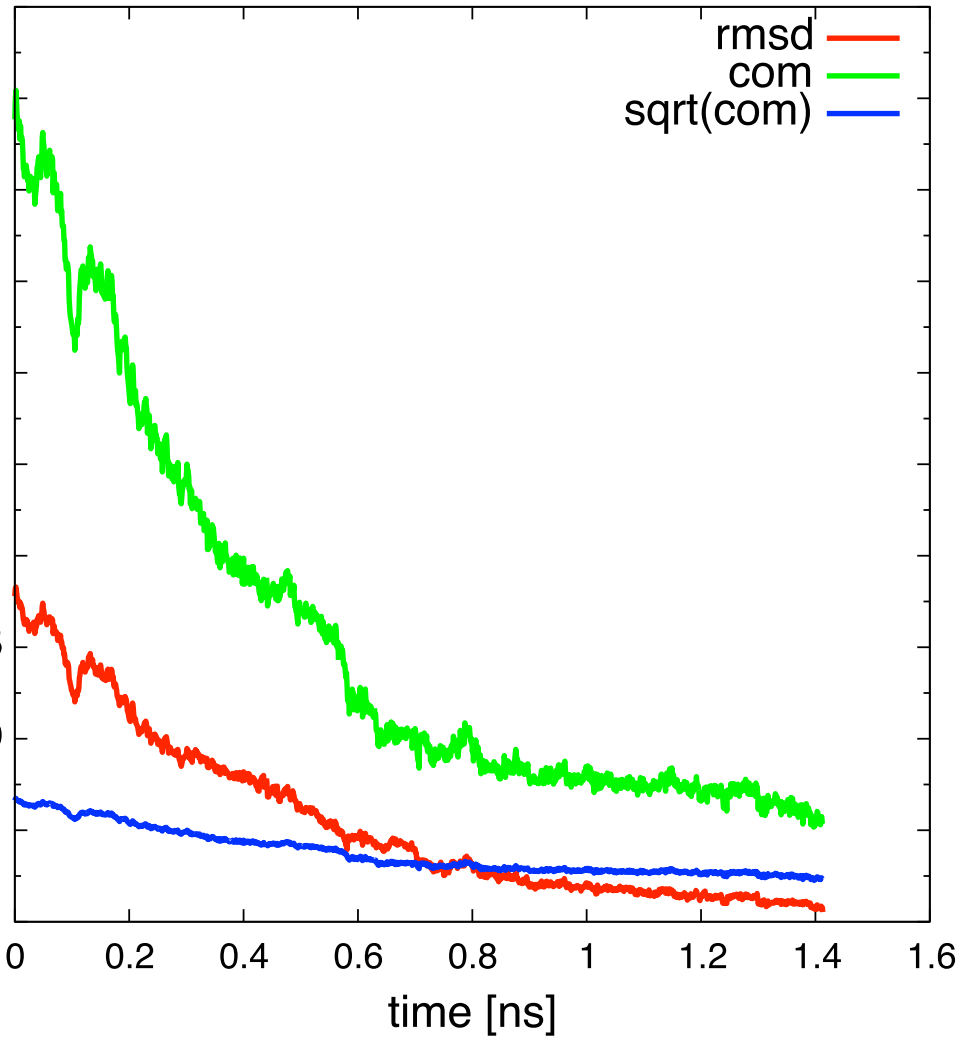


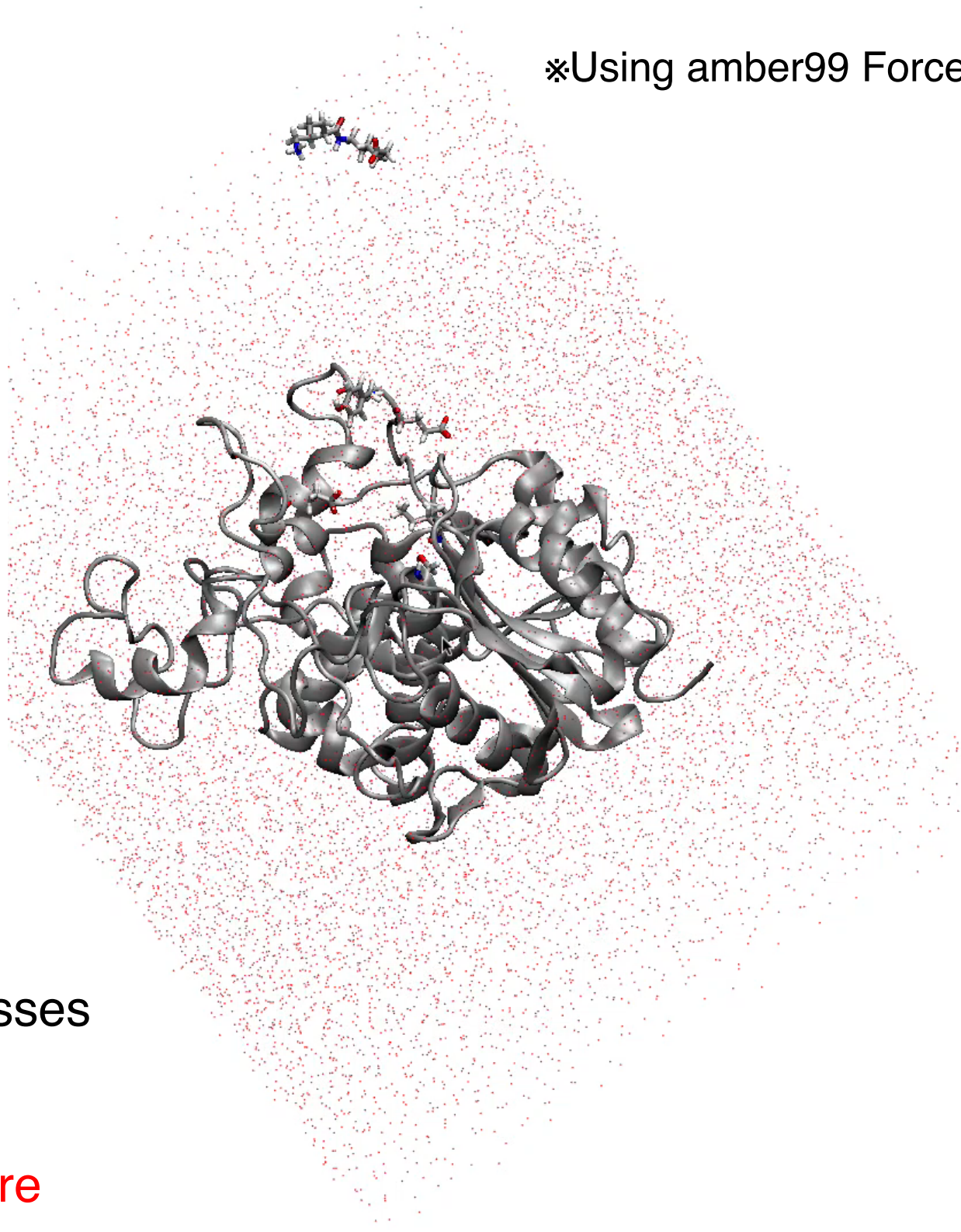
◆Chignolin (Artificial Protein)

esidue with folded structure(138 atoms)

ith Generalized Born Solvent Model

※Using amber99 Force





: Distance bw two Center-of-Masses

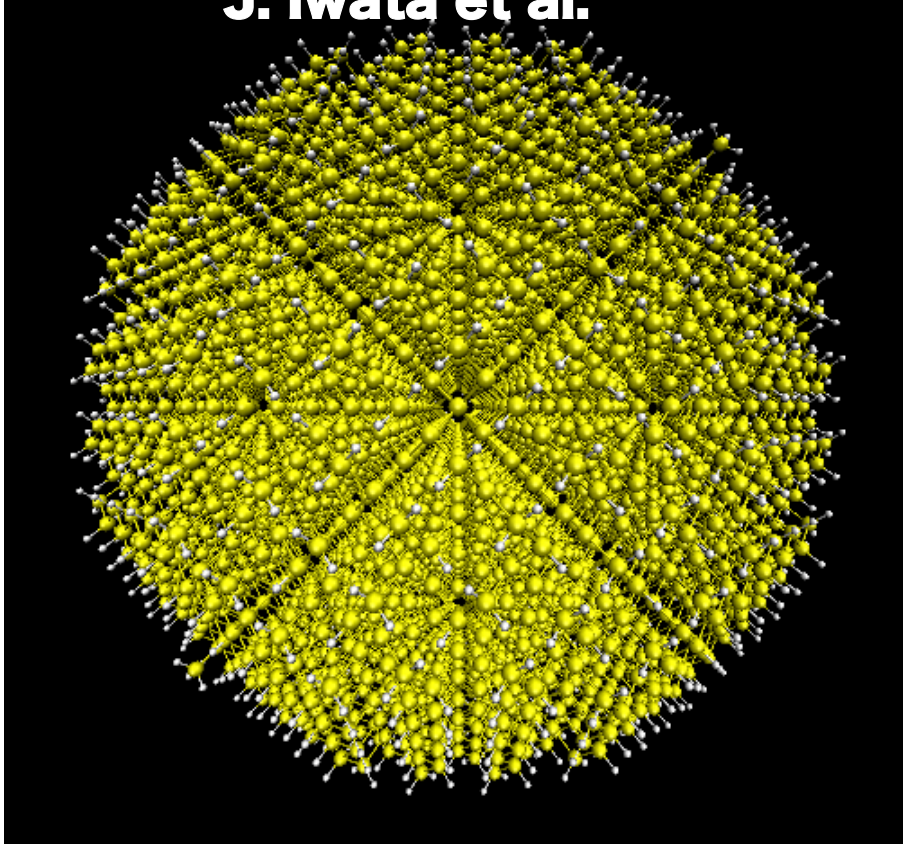
SD : RMSD toward X-ray Structure

e can precisely predict X-ray Structure

Massively Parallel Density Functional Theory code

Finite Difference Less FFTs

Gordon Bell Prize in 2011 For 10^5 atom Si Nano wire



Si Nano dot d=6.6nm ($Si_{7055}H_{1}$

- Troullier-Martins pseudopotetial
- LDA
- Mesh size = 0.847 (a.u.) (~14Ry)

程式 (finite-difference eq.)

$$+ v_{HXC}[\rho](\mathbf{r}) + v_{Ion}(\mathbf{r}) \phi_n(\mathbf{r}) = \varepsilon_n \phi_n(\mathbf{r})$$

-order finite difference

$$\psi_n(x,y,z) \approx \sum_{m=-6}^{6} C_m \psi_n(x+m\Delta x, y, z)$$

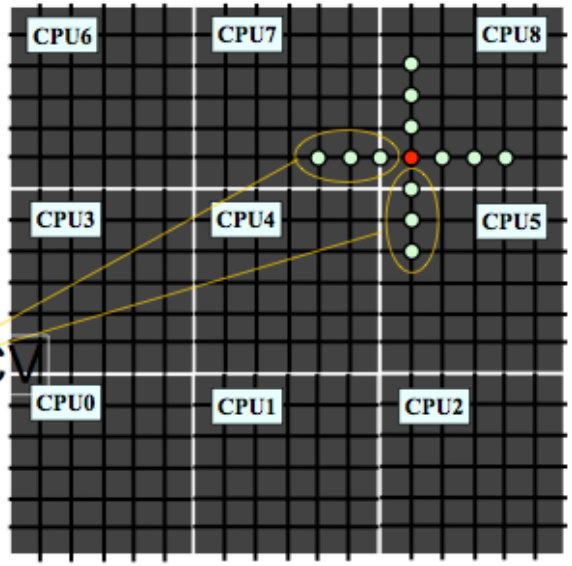
MPI_ISEND, MPI_IRECV
(隣接通信)

ration

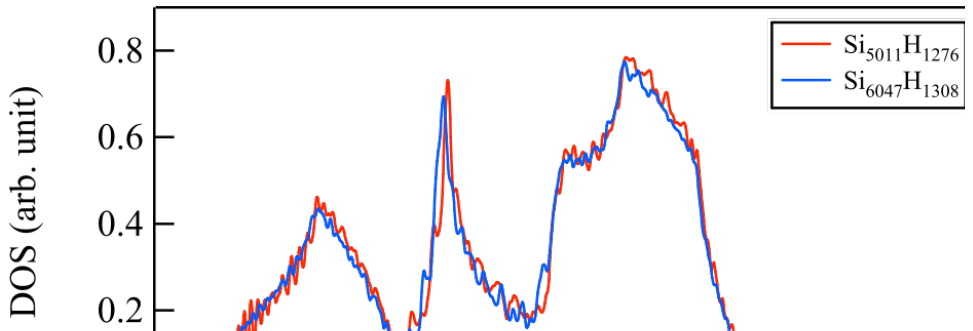
$$(\mathbf{r})\psi_n(\mathbf{r})d\mathbf{r} \approx \sum_{i=1}^{Mesh} \psi_m(\mathbf{r}_i)\psi_n(\mathbf{r}_i)\Delta x \Delta y \Delta z$$

MPI ALLREDUCE

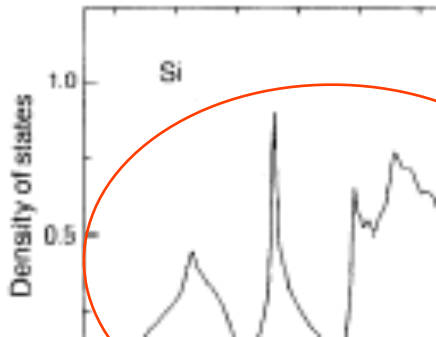
3D grid is divided by several regions for parallel computation.



Cluster model



Bulk Si



ext target is First-nciples Molecular namics Simulation,

Cut off 20Ry Hybrid parallelization at K-computer

	grid	grid/band
1024MPI-8192 core (sec)	4.43	3.50
512MPI-4096 cores (sec)	6.94	4.33
8MPI-64 core (sec)	175.41	175.41
64-8192 Performance(%)	30.9	39.2
64-4096		

```
ix=a1b/(ML1/np1); iy=a2b/(ML2/np2); iz=a3b/(ML3/np3);
 icolor=iy+iz*np2
 call mpi_comm_split(comm_grid,icolor, 0, comm_fftx, ierr)
 icolor=iz+ix*nprocs;
 call mpi_comm_split(comm_grid,icolor, 0, comm_ffty, ierr)
 icolor=iy+ix*nprocs;
 call mpi_comm_split(comm_grid,icolor, 0, comm_fftz, ierr)
```

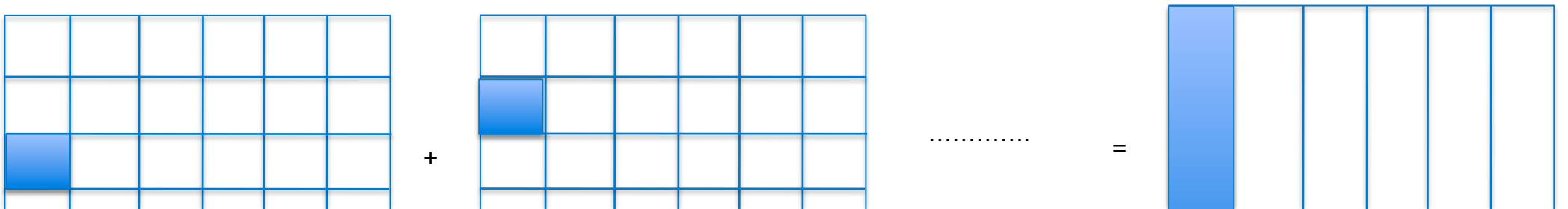
We split communicator into 3 parts (X,Y,Z) (setting)

```
do i1~i3=a1b~a3b, b1b~b3b
    zwork1(i1,i2,i3)=zwork0(i1,i2,i3)
end do
call mpi_allreduce(zwork1,zwork2,ML1*(b2b-a2b+1)*(b3b-a3b+1),
                   mpi_complex16,mpi_sum,comm_fftx,ierr)
```

hrow processes for X direction and use only Y, Z directions (same process number as gri

(**FFTE is parallelized into 2 direction**)

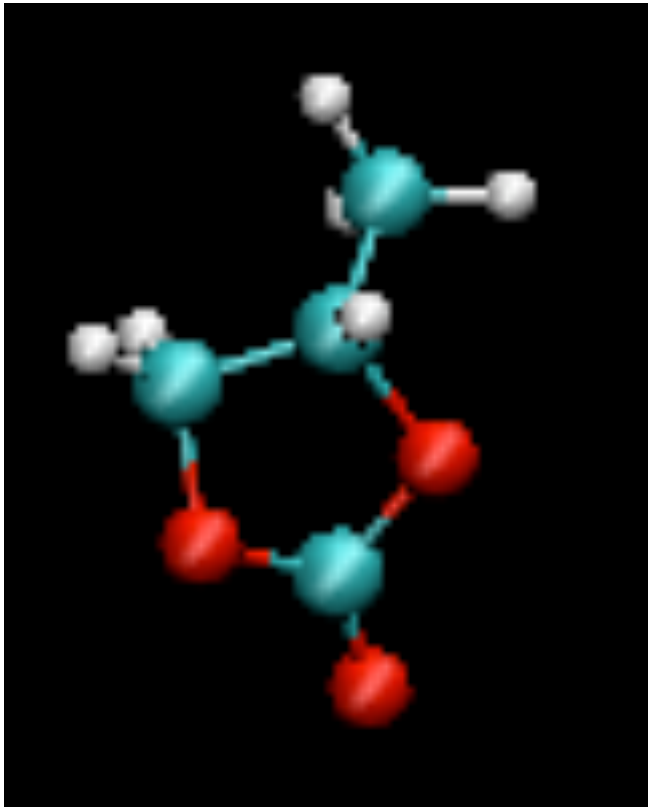
Para

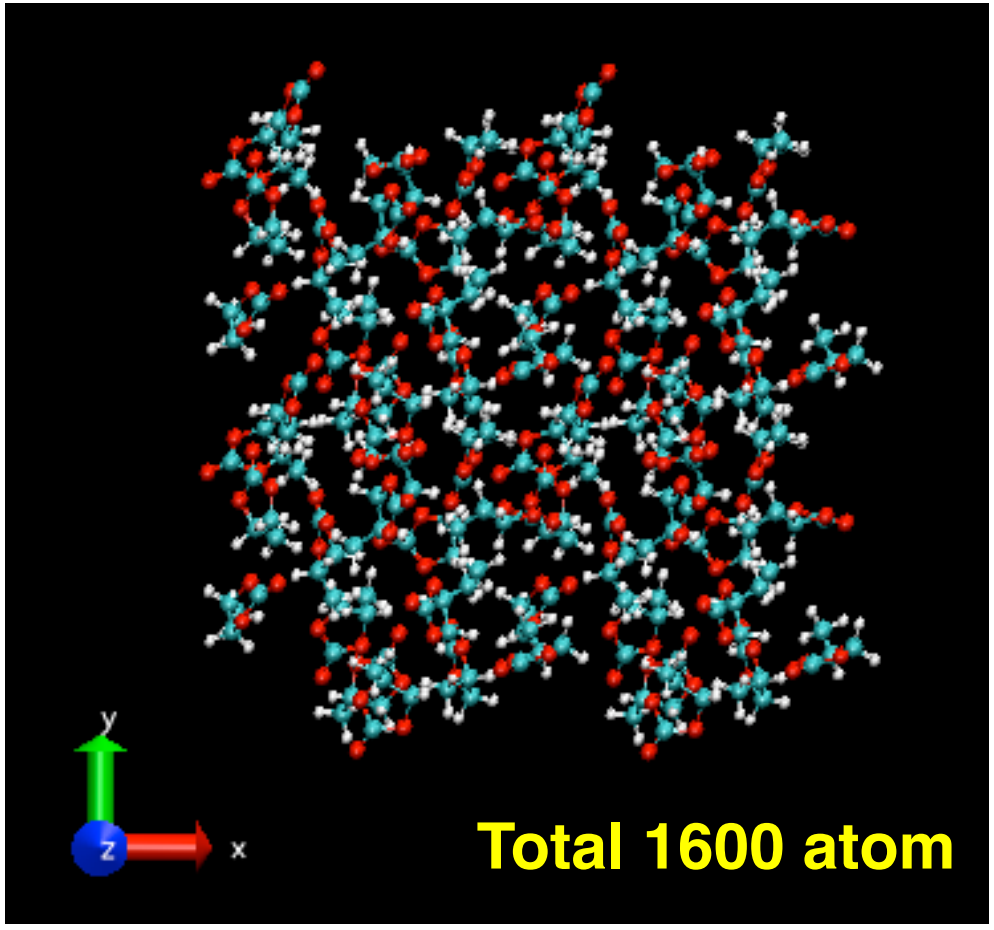


PC 128 by PW-CPMD : 11.9 sec (512MPI-8OMP=4096 cores)

	8192 cores	4096 cores	2048 cores
Hybrid 8OMP	7.37	9.46	14.18
with FFTE	**6.12**	-	-

Molecular fluid 83.2Ry (128 molecules)





Cut off 20Ry Hybrid parallelization at K-computer

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64-4096		

c.f. 3

1. QM/MM studies on several Enzymes

・ Substrate binding and protein folding processes we
simulated with newly developed MD algorithm

2. Large-scale MD Simulation with HA-PACS

・ Large amplitude motion of Dynein upon ATP/ADP
binding is extracted from brute force MD simulation.

3. Substrate Binding & Folding Analyses

・ Substrate binding and protein folding processes we
simulated with newly developed MD algorithm

4. Toward Large-scale First-principles MD

・ Real-space density functional theory-based
Car-Parrinello Molecular Dynamics (RS-CPMD)