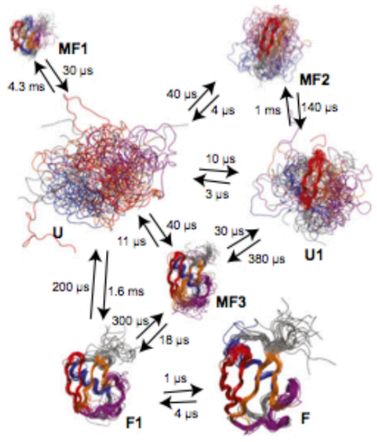
課題代表者氏名（所属）原田 隆平（筑波大学計算科学研究センター）

研究課題名 カスケード型超並列シミュレーションに立脚した遷移経路探索法の開発

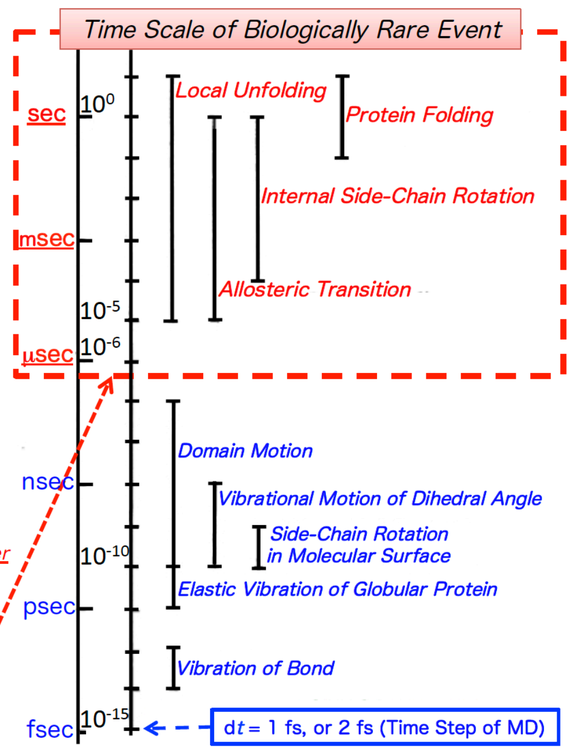
Background: *Biologically Rare Event*

◆*Brute-Force Molecular Dynamics (MD)*
by a Special Purpose Supercomputer
(ex. *ANTON from D. E. Shaw Research*)

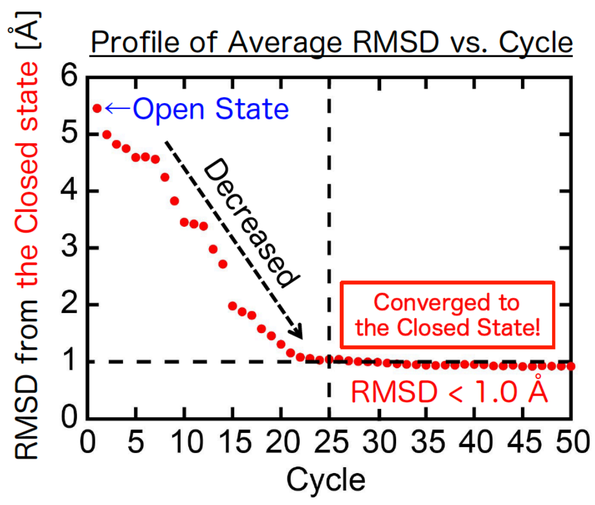


Millisecond-order Folding Simulation of Ubiquitin in Explicit Water
by a Brute-Force MD. (*PNAS*, **110**, 5915, (2013). **Fig. 1**)

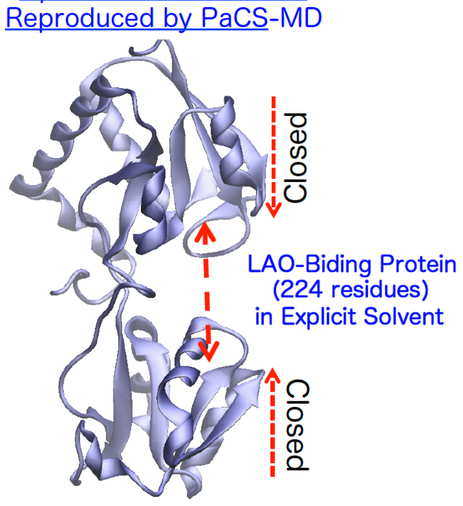
The accessible timescale of normal MD simulation is far from the timescale of rare events.



Open-Closed Transitions of Protein Reproduced by PaCS-MD

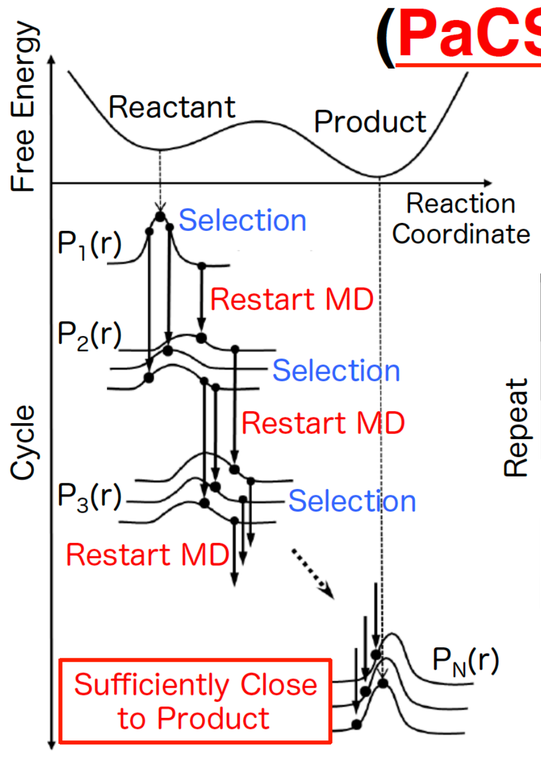


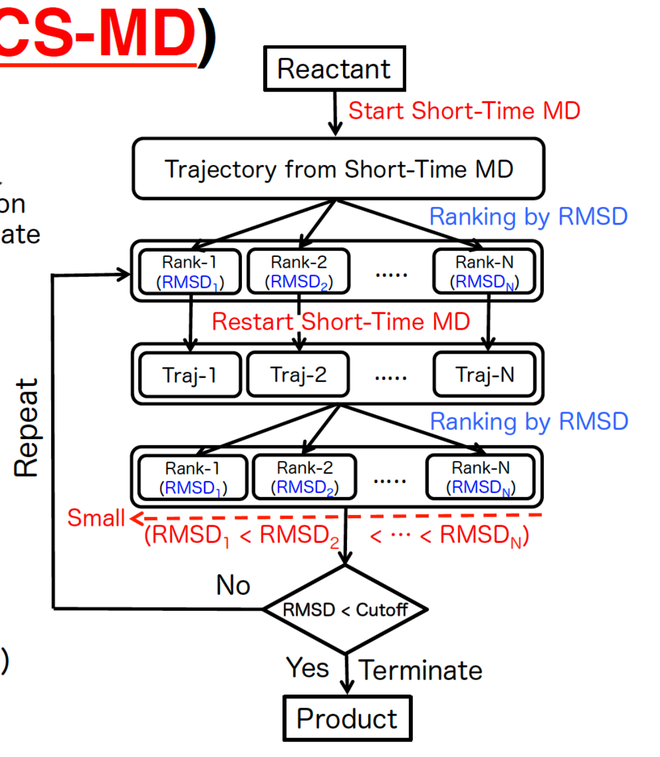
Open-Closed Transition
Reproduced by PaCS-MD



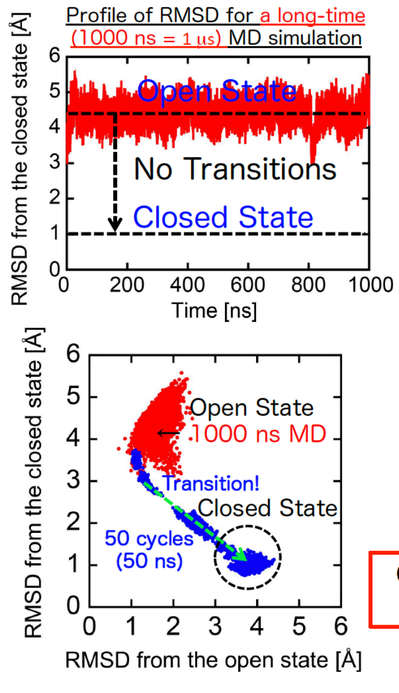
∗ Short-time (100 ps) MD simulation × 10 initial structures / cycle: 1 ns / cycle
Totally simulation time after the 50th cycle: 50 ns
∗ $RMSD_{closed}$ < 1.0 Å → Terminate PaCS-MD.

Parallel Cascade Selection MD (PaCS-MD)

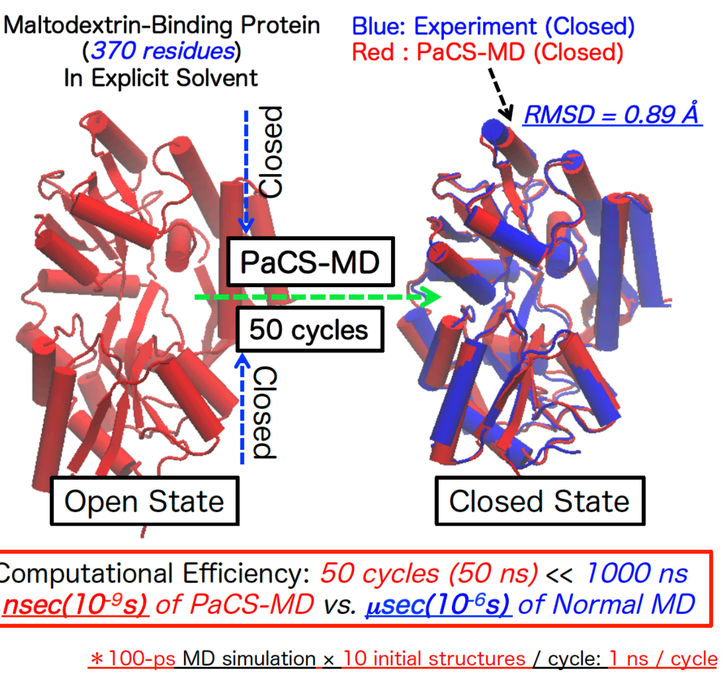




Computational Efficiency of PaCS-MD



Maltodextrin-Binding Protein
(*370 residues*)
In Explicit Solvent

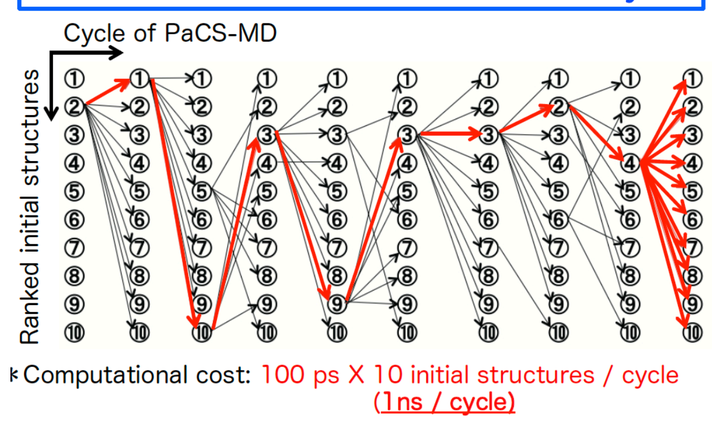


Computational Efficiency: *50 cycles (50 ns)* << *1000 ns*
nsec(10^{-9}s) of *PaCS-MD* vs. *μsec(10^{-6}s)* of *Normal MD*

∗100-ps MD simulation × 10 initial structures / cycle: 1 ns / cycle

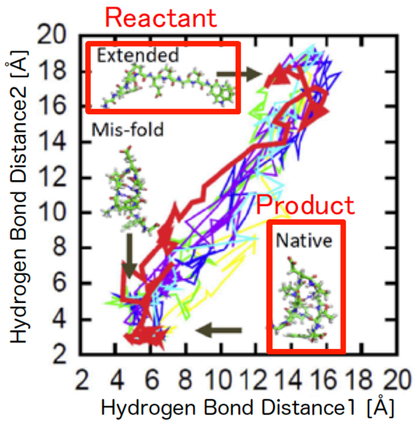
Selections of Initial Structures in PaCS-MD: *Folding of Chignolin*

Selections of Initial Structures at Each Cycle



∗Computational cost: 100 ps X 10 initial structures / cycle
(1ns / cycle)

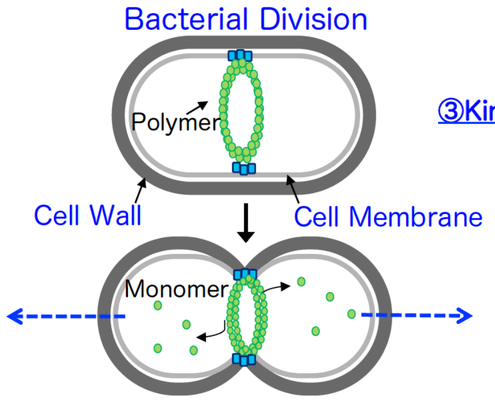
Folding Pathways Reproduced by PaCS-MD



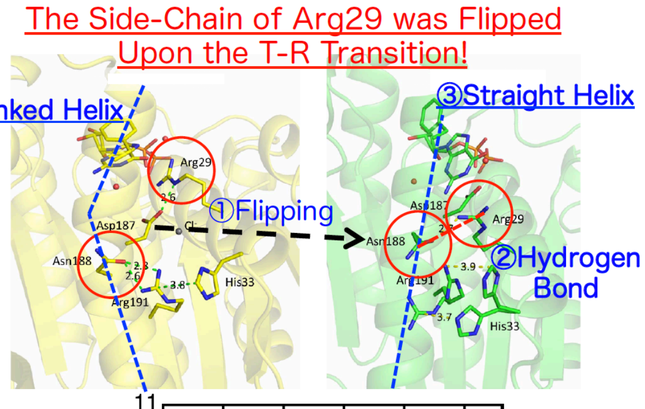
∗ *Snapshots are Ranked with RMSD from Product* at Each Cycle.
∗ *Highly ranked Top Ten Snapshots* were Selected by *low RMSD values*.

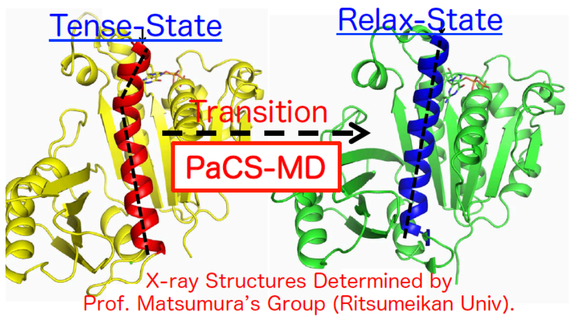
Application: *Structural Transition of FtsZ Monomer*

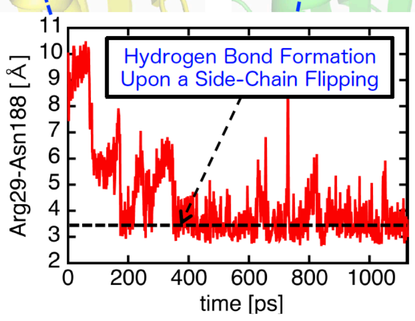
- FtsZ (Monomer)
  Bacterial Division



The Side-Chain of Arg29 was Flipped Upon the T-R Transition!







J.Struc.Biolo., **198**, 65 (2017), *just accepted*.

1. R. Harada and A. Kitao, *J. Chem. Phys.*, **139**, 035103 (2013)
2. R. Harada, Y. Takano, T. Baba, and Y. Shigta, *Phys. Chem. Chem. Phys.*, **17**, 6155 (2015)
3. R. Harada, T. Nakamura, Y. Takano, and Y. Shigeta, *J. Comput. Chem.*, **36**, 97 (2015)