粗視化生体分子シミュレータ CafeMol

検崎博生[1],
古賀信康[1], 藤原慎司[1], 堀直人[1], 金田亮[1],
李 文飛[1,2], 岡崎圭一[1], 姚 新秋[1], 高田彰二[1,2]
[1]京都大学理学研究科生物物理学教室
[2] JST-CREST

CafeMol (www.cafemol.org)

Kenzaki

- CafeMol 1.0
  source & manual released

- Features are;
  - Various CG protein models
    multiple basin model
    accurate CG model
  - Simulating protein-at-work
    “switching”

- Under development
  DNA/RNA, lipid

Overview of CafeMol

- General-purpose coarse-grained (CG) biomolecular modeling and simulation software
  - Protein: 1 bead / 1 amino acid
  - Nucleic acid: 3 beads (sugar, nucleotide, phosphate) / nucleotide
  - Lipid: ~3 beads / lipid
- Written by FORTRAN90 with MPI and Open MP
- Large-scale simulation
  - ～”millisecond” event by K-computer
- Version 1.0 is released (only protein) (2010/12/27)

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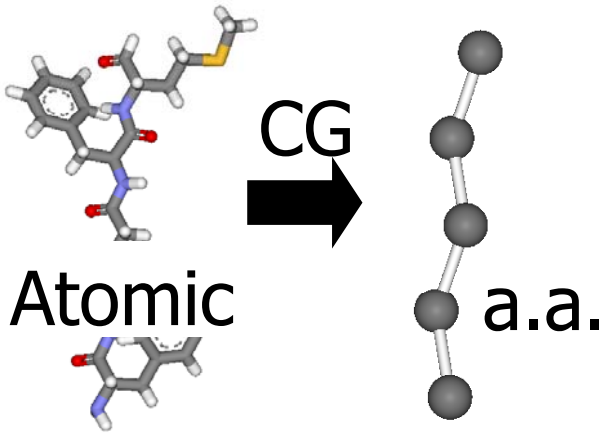
Models and energy functions



1 beads / 1 amino acid

A. Off-lattice Go model
B. Atomic interaction based CG model
C. Multiple basin model
D. Elastic network model
E. Electrostatic and hydrophobic interactions
F. Explicit and implicit ligands

Off-lattice Go model

C. Clementi, H. Nymeyer, and J.N. Onuchic, J. Mol. Biol. (2000)

Based on the energy landscape theory

Structure based

$$V_{protein} = V_{local} + V_{go} + V_{ex}$$

$$V_{local} = K_b \sum_i \left(r_{i,i+1} - r_{0i,i+1} \right)^2 + K_\theta \sum_i \left(\theta_i - \theta_{0i} \right)^2$$

$$+ K_\phi^1 \sum_i \left(1 - \cos\left(\phi_i - \phi_{0i} \right) \right) + K_\phi^3 \sum_i \left(1 - \cos 3\left(\phi_i - \phi_{0i} \right) \right)$$

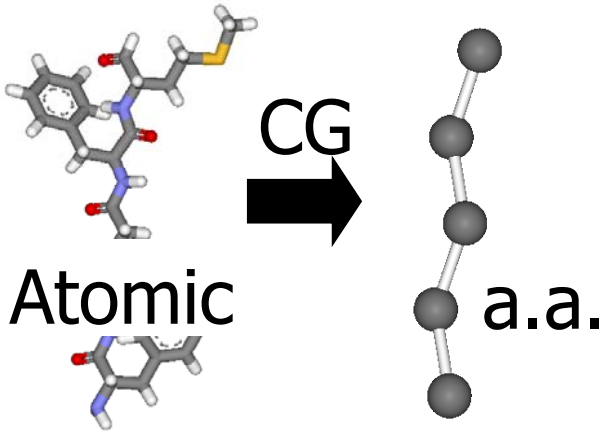
$$V_{go} = \varepsilon_{go} \sum_{i,j}^{native} \left[5 \left(\frac{r_{0ij}}{r_{ij}} \right)^{12} - 6 \left(\frac{r_{0ij}}{r_{ij}} \right)^{10} \right]$$

$$V_{ex} = \varepsilon_{ex} \sum_{i,j}^{nonnative} \left(\frac{\sigma}{r_{ij}} \right)^{12}$$

θ: bond angle
ϕ: dihedral angle
(0 means native state)

$K_b = 100\varepsilon$
$K_\theta = 20\varepsilon$
$K_\phi^1 = \varepsilon$
$K_\phi^3 = 0.5\varepsilon$
$\varepsilon_{go} = 0.18\varepsilon$
$\varepsilon_{ex} = \varepsilon$
σ= 4A
ε=1.0kcal/mol

Atomic interaction based CG (AICG) model



$$V = \sum_i k_b^i (r^i - r_0^i)^2 + \sum_i k_a^i (\theta^i - \theta_0^i)^2$$
$$+ \sum_i \{\varepsilon_{\phi,1}^i [1 - \cos(\phi^i - \phi_0^i)] + \varepsilon_{\phi,3}^i [1 - \cos 3(\phi^i - \phi_0^i)]\}$$
$$+ \sum_{i>j-3}^{native} \varepsilon^{ij} [5(r_0^{ij}/r^{ij})^{12} - 6(r_0^{ij}/r^{ij})^{10}] + \sum_{i>j-3}^{non-native} \varepsilon (C/r^{ij})^{12}$$

Wenfei Li

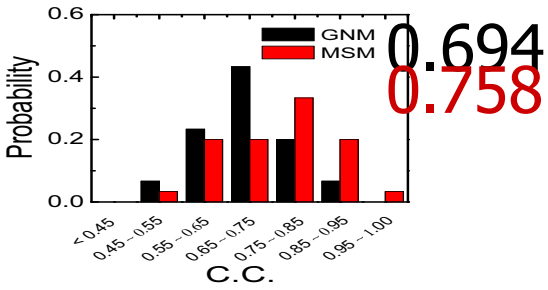
1) Contact energy ε_{ij} from pairwise all-atom (AA) energy

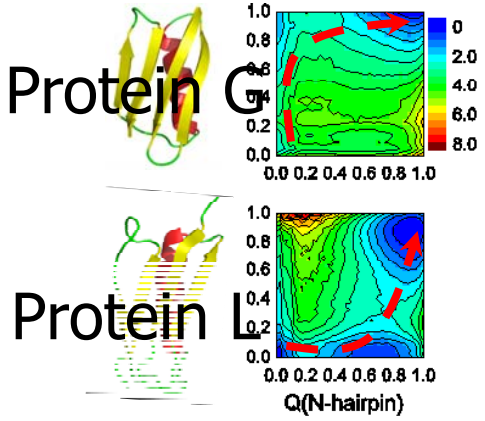
$$E^{IJ}(R_{IJ}) = \sum_{i \in I} \sum_{j \in J} u_{AA}(r_{ij}) \qquad u_{AA}(r) = V(r) + \Delta G_{pol}^{GB}(r) + \Delta G^{SA}(r)$$

2) Coefficients fitted by AA-derived fluctuation (23 proteins)

param	K_b	K_a^G	k_a^H	k_a^E	k_a^T	k_a^C	ε_ϕ^G	ε_ϕ^H	ε_ϕ^E	ε_ϕ^T	ε_ϕ^C	ε_{nloc}
Av.	109.94	13.40	40.03	17.32	19.35	11.70	0.29	1.76	1.32	0.82	0.81	0.37

Test for fluctuation, structural change, & folding





Multiple-basin model for proteins

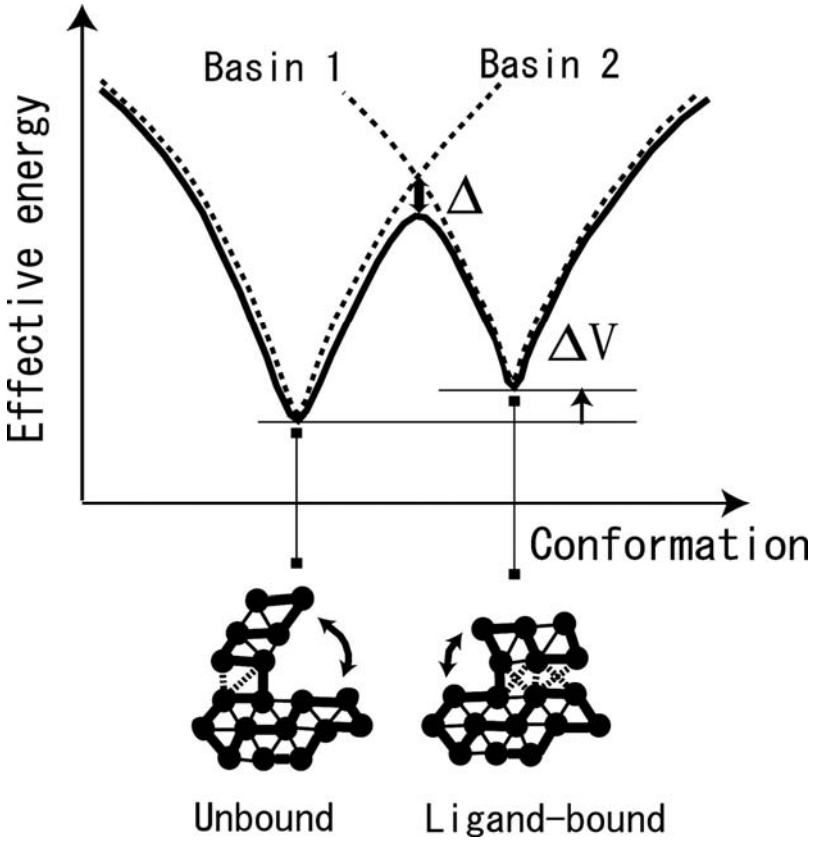
K. Okazaki, N. Koga, S. Takada, J.N. Onuchic, and P.G. Wolynes, PNAS (2006)

Use of 2 references

$$\begin{pmatrix} V(R|R_1) & \Delta \\ \Delta & V(R|R_2)+\Delta V \end{pmatrix}\begin{pmatrix} c_1 \\ c_2 \end{pmatrix} = V_{MB}\begin{pmatrix} c_1 \\ c_2 \end{pmatrix}$$

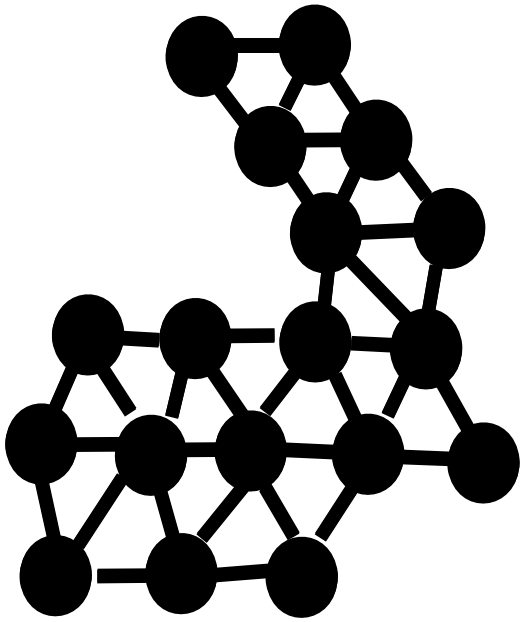
$$V_{MB} = \frac{V(R|R_1)+V(R|R_2)+\Delta V}{2} - \sqrt{\left(\frac{V(R|R_1)-V(R|R_2)-\Delta V}{2}+\Delta \right)}$$

$$\chi = \log\left(\frac{c_2}{c_1}\right)$$

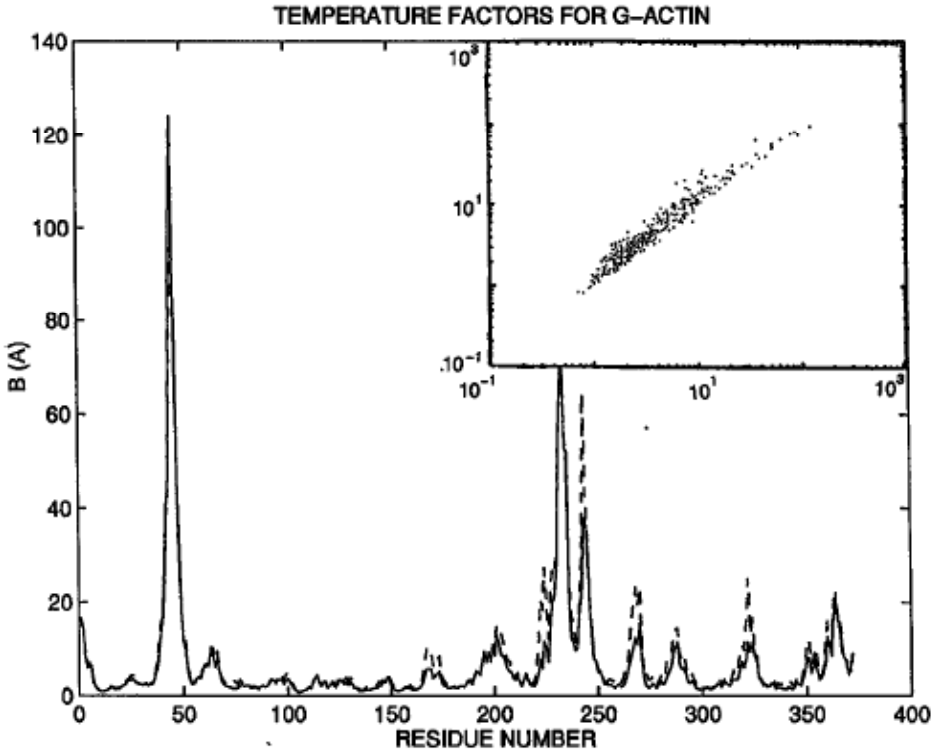


Elastic network model

$$E = \sum_{ij, s.t. r_{ij}^0 < r_c} K(r_{ij} - r_{ij}^0)^2$$



Atomic fluctuation reproduced by ENM (Tirion96)



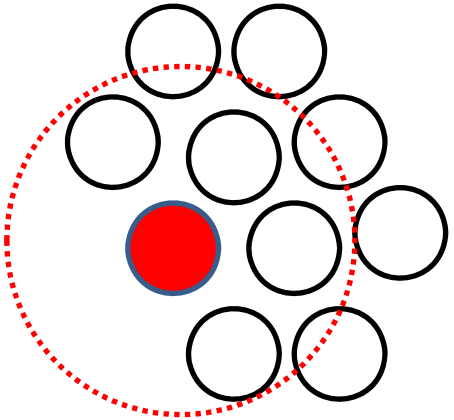
Electrostatic and hydrophobic interactions

Debye-Huckel form for electrostatics

$$V_{\text{ele}} = \sum_{i<j}^{N} \frac{q_i q_j}{4\pi\epsilon_0\epsilon_k r_{ij}} e^{-r_{ij}/\kappa_D}$$

HP interactions analogous to ASA

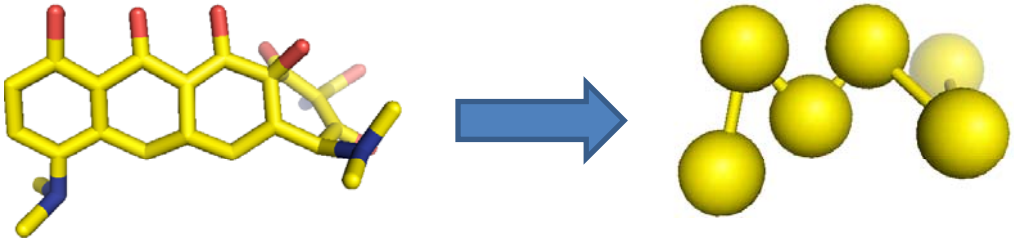
$$V_{\text{HP}} = -c_{\text{HP}} \sum_{i\in\text{HP}} \epsilon_{\text{HP},A(i)} S_{\text{HP}}(\rho_i)$$



Count coordination number
for each hydrophobic particle

Explicit and Implicit ligands

Explicit ligand; as a rigid molecule



Implicit ligand; MD-MC scheme with ligand-mediated contact

$$V_{protein} \underset{k_{off}}{\overset{k_{on}}{\rightleftharpoons}} V_{protein} + V_{imp-lig}$$

$$V_{imp-lig} = \sum_{\substack{ligand-mediated \\ contact-pairs}} -c_{lig}\varepsilon_{go} \exp\left[-\frac{(r_{ij}/r_{0ij}-1)^2}{2(\sigma/r_{0ij})^2}\right]$$

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Simulation method

- Dynamics
  - Newtonian dynamics with Berendsen thermostat
  - Langevin dynamics
- Time integration
  - velocity Verlet algorithm
- Run mode
  - Constant temperature simulation
  - Simulated annealing
  - Auto-search of Tf
  - Replica exchange method
  - Potential “switching”

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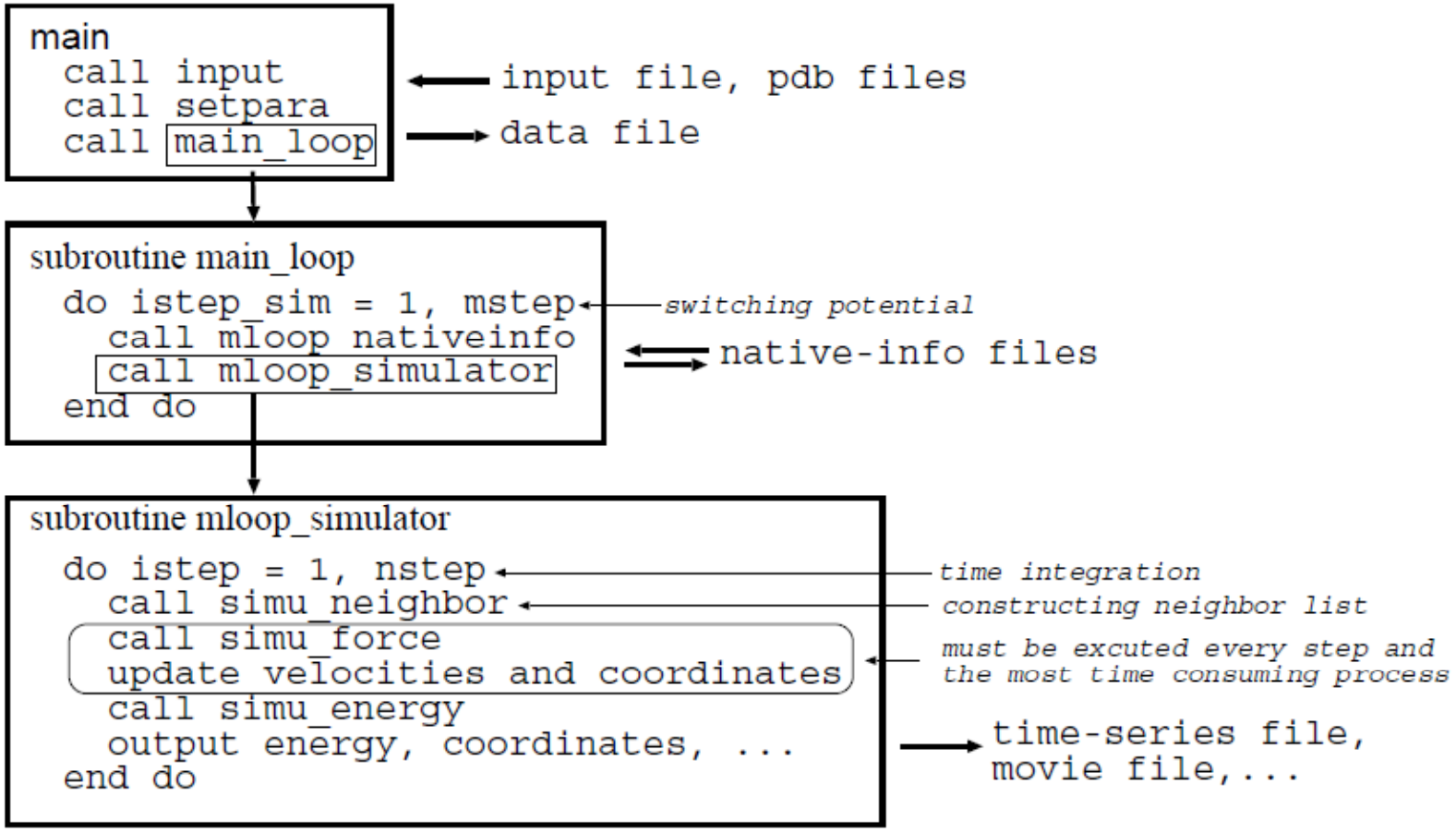
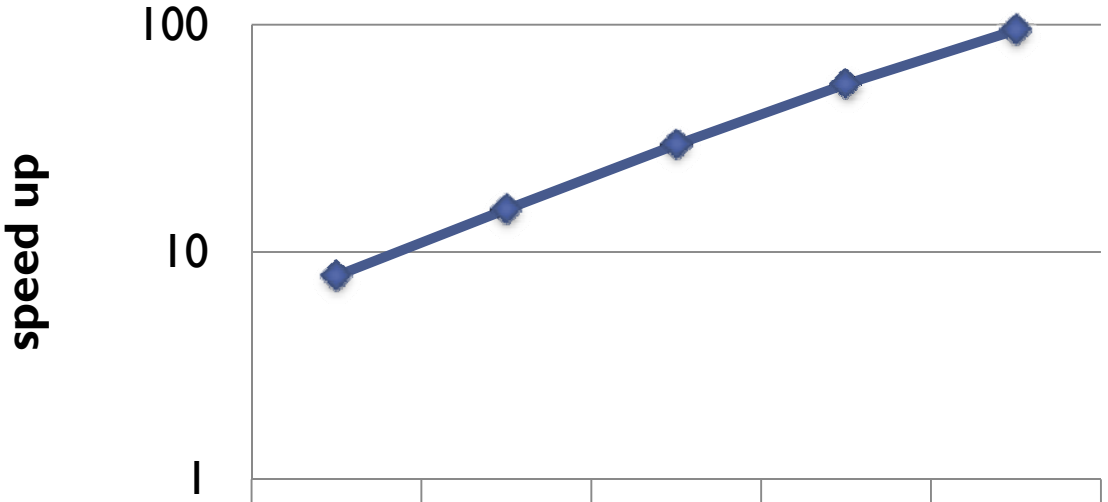
CafeMol code



- Parallelization
  - neighboring list, force, energy
    →hybrid(MPI+Open MP)
  - replica exchange
    →MPI(temperature/Hamiltonian REMD)

Performance of MPI parallelization

1300 base pairs DNA (7798 particles)
BG/L at Riken



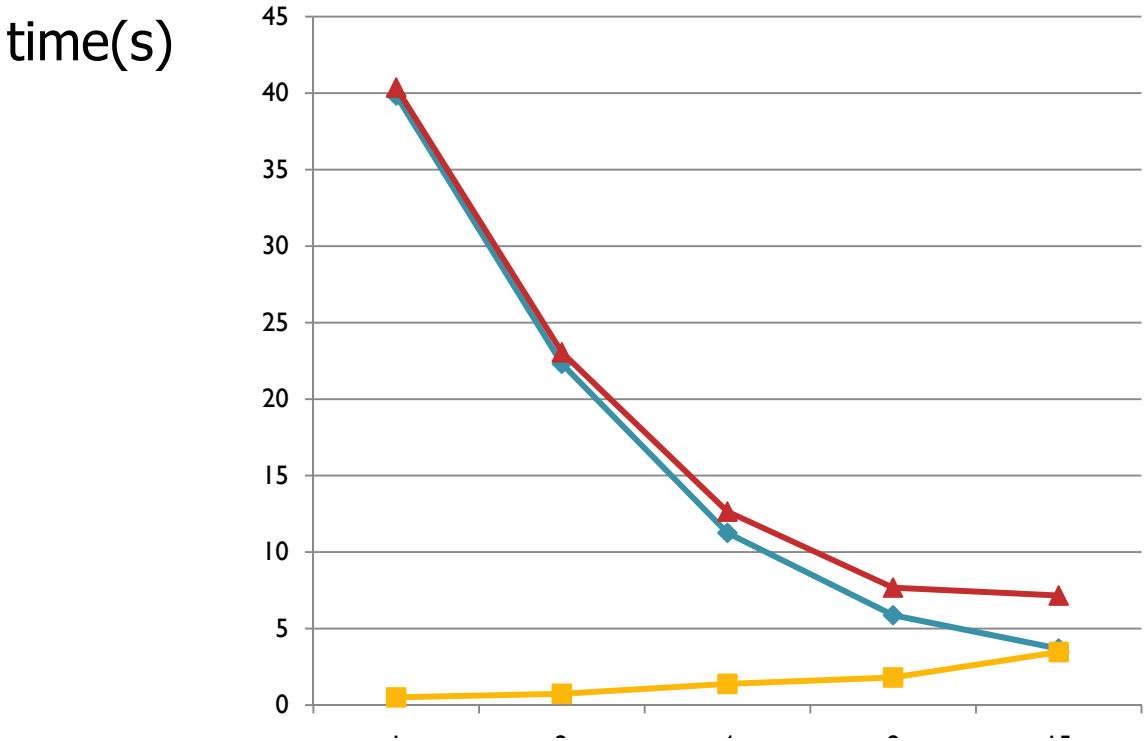
	8	16	32	64	128
speed up	7.85	15.38	29.64	54.76	94.65

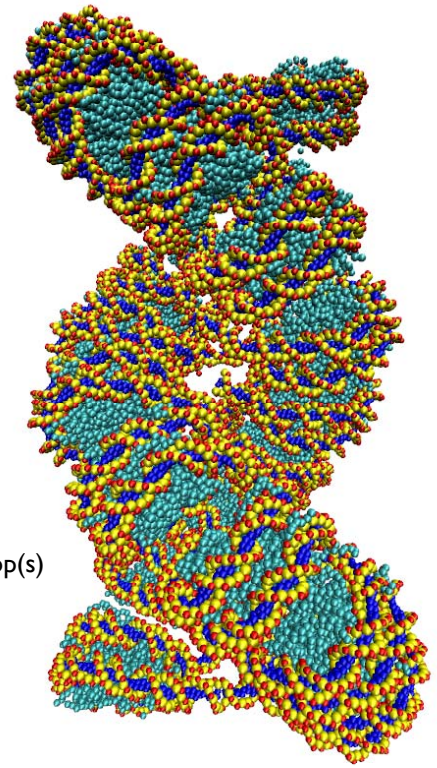
ope(s)	328.62	164.64	82.65	42.18	22.01
mpi(s)	5.44	5.90	5.84	5.71	5.70

High parallelization efficiency

Performance of hybrid parallelization (MPI and Open MP)

20 nucleosomes (35918 particles)
RICC at Riken





OMP(force)	8	8	8	8	8
MPI(force)	1	2	4	8	15
MPI(replica)	64	64	64	64	64
speed up	1	1.75	3.19	5.26	5.64

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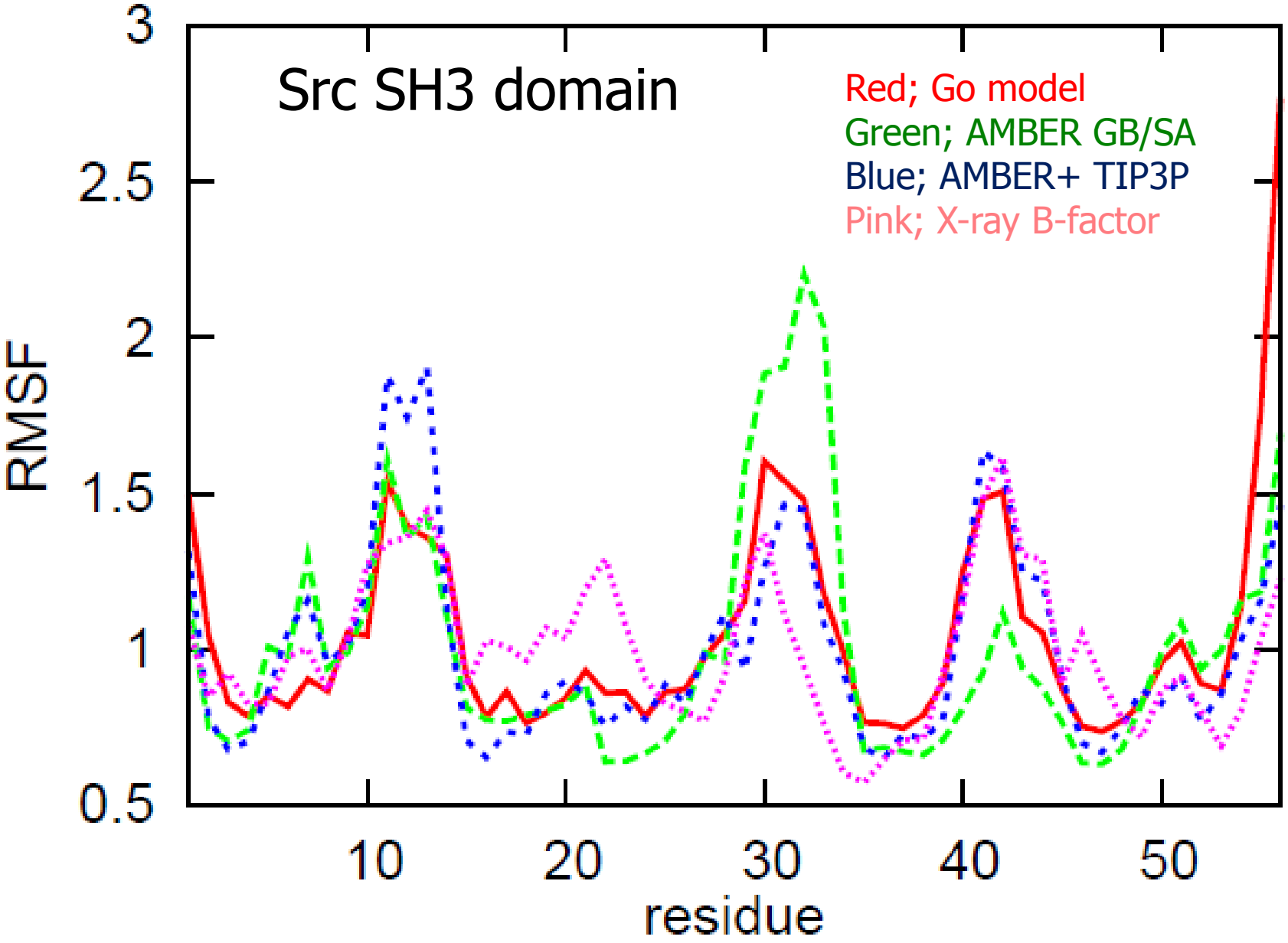
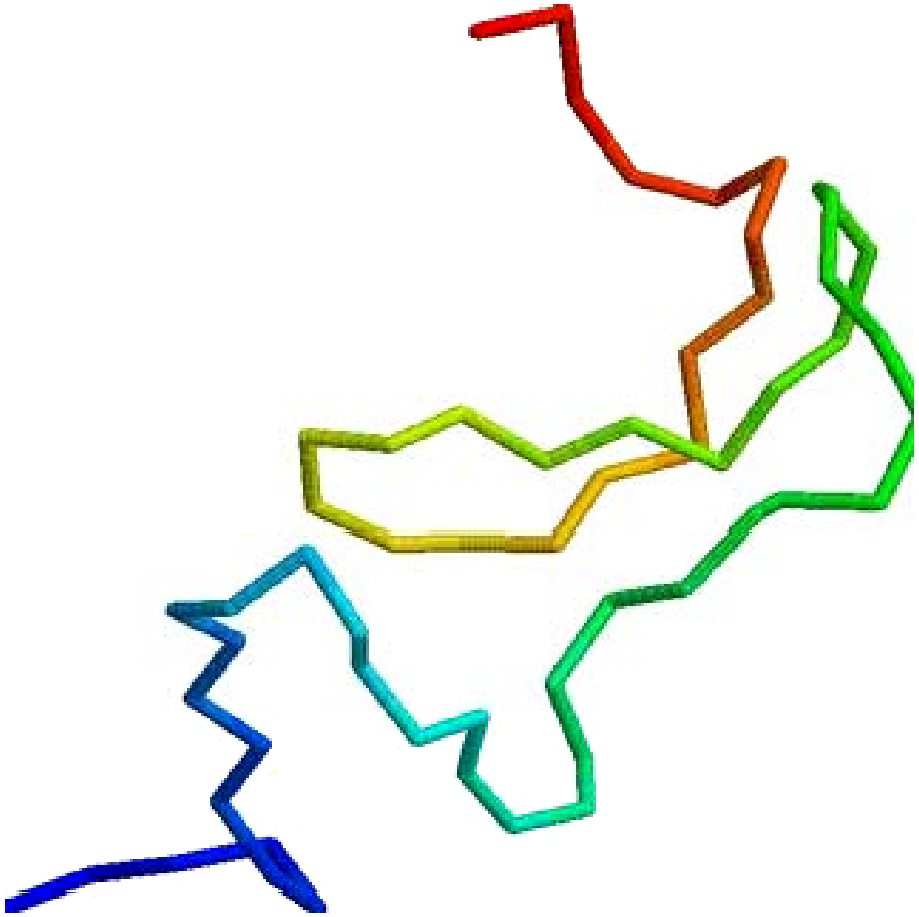
Native fluctuation by off-lattice Go model

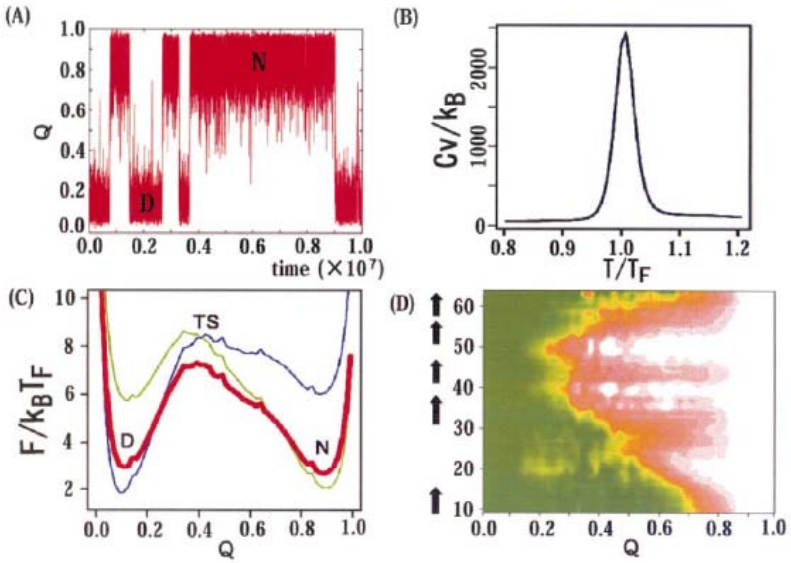


Folding simulation of src SH3 domain

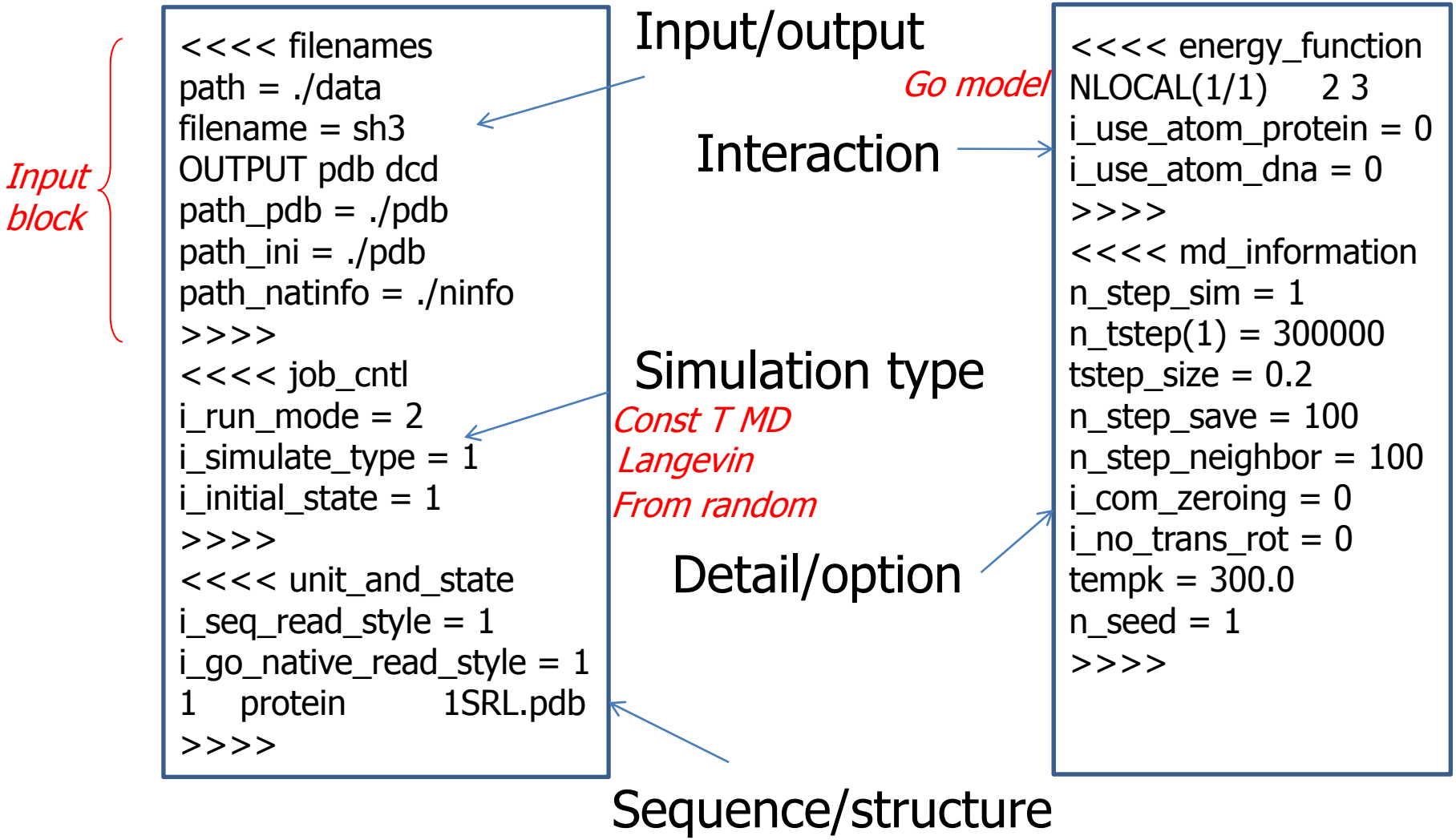


N. Koga, and S. Takada, J. Mol. Biol. (2001)

computed ϕ–values experimental ϕ–values



Example of input file (folding simulation of src SH3)



Folding temperature of src SH3 (Auto-search of Tf)

Bi-section method

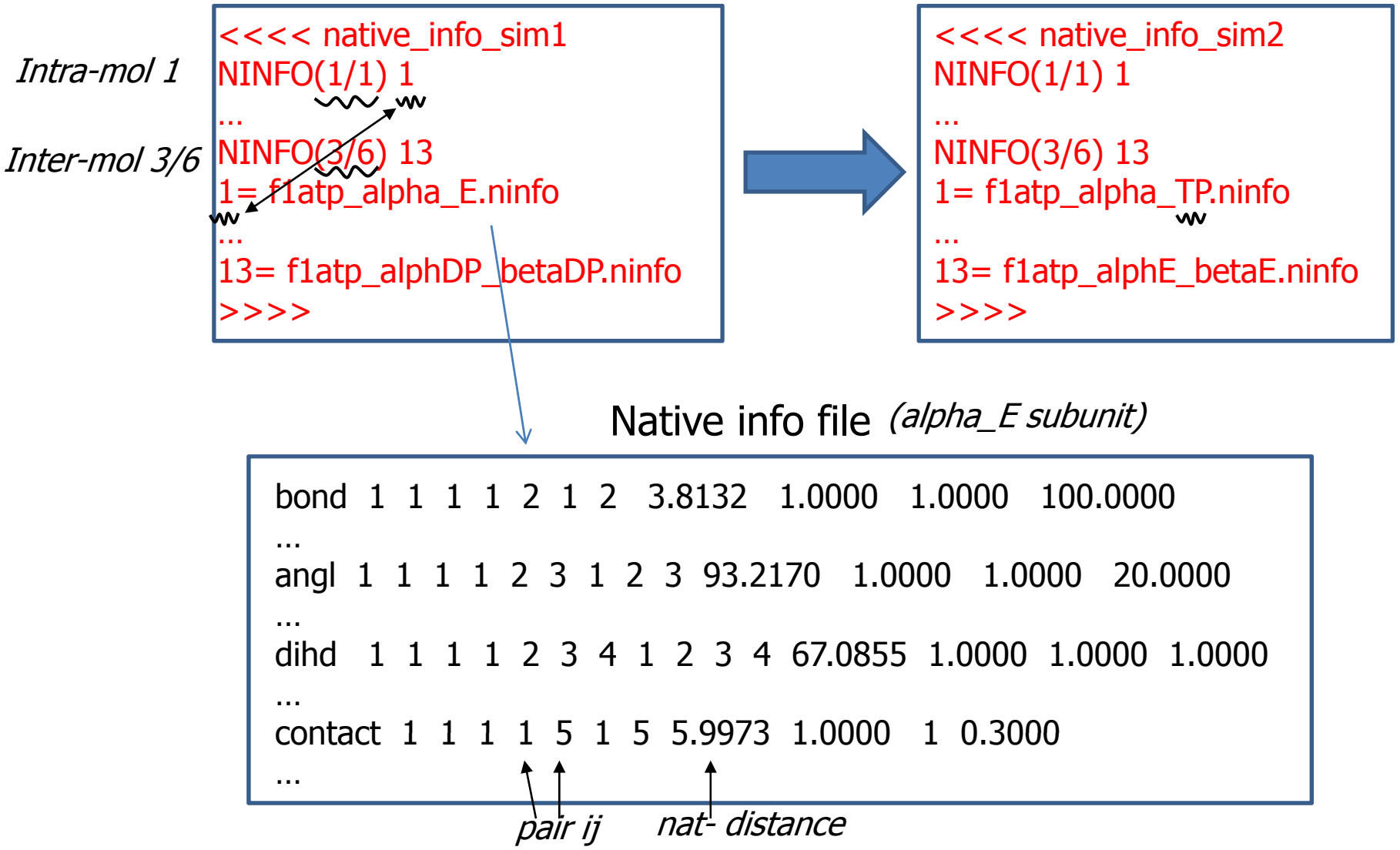
```
<<<< job_cntl
i_run_mode = 4
i_simulate_type = 1
i_initial_state = 1
>>>>
<<<< searching_tf
tempk_upper = 500.0
tempk_lower = 100.0
>>>>
```

```
**********************************
tf_out   tempk n_state d_state p_trans
tf_out 300.000     995       5       1
**********************************
tf_out   tempk n_state d_state p_trans
tf_out 400.000       1    1000       0
**********************************
tf_out   tempk n_state d_state p_trans
tf_out 350.000     166     835      78
**********************************
tf_out   tempk n_state d_state p_trans
tf_out 325.000     953      48      19
**********************************
...
...
**********************************
tf_out   tempk n_state d_state p_trans
tf_out 341.406     638     363      98
**********************************
```

Folding temperature of some proteins

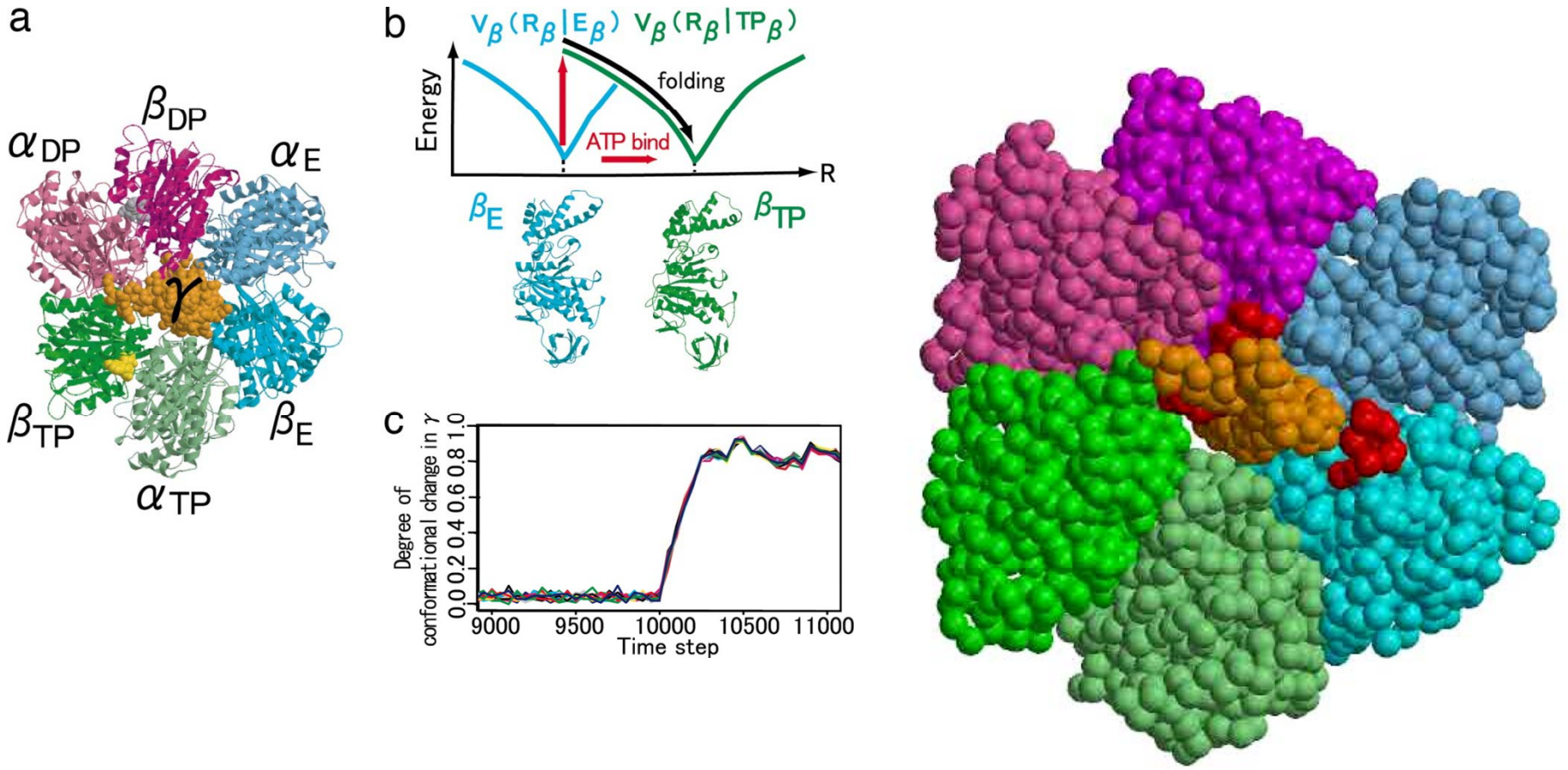
Protein	Number of amino acid	Folding temperature(K)
albumin binding domain	53	380.4
src SH3 domain	56	342.9
protein G	56	338.2
α-spectrin SH3 domain	57	360.1
Sso7d	64	332.0
protein L	78	374.2
Im9	86	382.0
cytochrom B562	106	352.2

“Switching” simulation



Rotation mechanism of F_1-ATPase by switching Go model

N. Koga, and S. Takada, PNAS (2006)



Conformational change by MBP

K. Okazaki, N. Koga, S. Takada, J.N. Onuchic, and P.G. Wolynes, PNAS (2006)

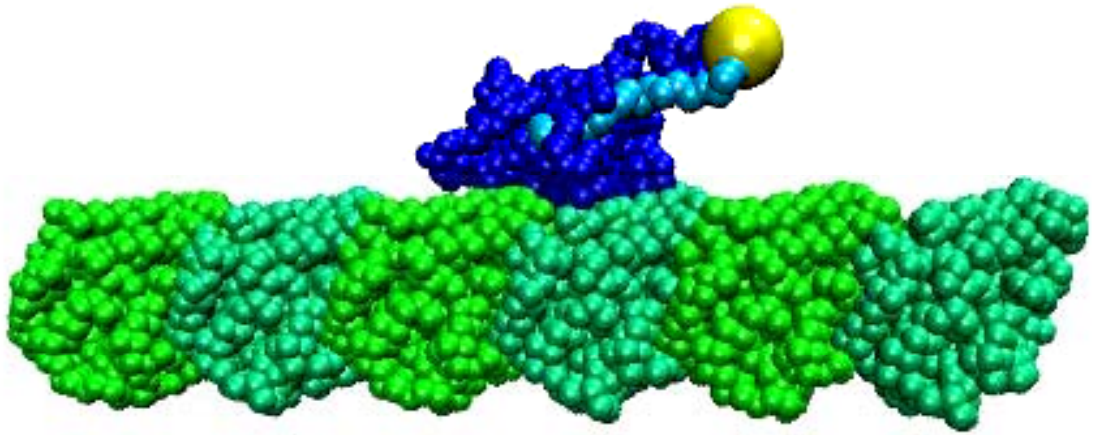
```
<<<< unit_and_state
i_seq_read_style = 1
i_go_native_read_style = 1
1a     protein        1GGG_2.pdb
1b     protein        1WDN_2.pdb
>>>>
<<<< energy_function
NLOCAL(1a/1a)     2 3
NLOCAL(1b/1b)     2 3
MULTIGO_SYSTEM(1a)   1a/1a
MULTIGO_SYSTEM(1b)   1b/1b
i_use_atom_protein = 0
i_use_atom_dna = 0
>>>>
<<<< multiple_go
bdemax_mgo = 100.0
baemax_mgo = 1.0
dihemax_mgo = 0.5
ENEGAP(1)(1)  0.0   -1.8
DELTA(1ab)    28.0
>>>>
```

Sliding movement of KIF1A

R. Kanada, et al unpublished data

1 phase: multiple-basin (T, D)
2 phase: go(D)
3 phase: multiple-basin(D, phi)
4 phase: go(phi)
5 phase: go(T)

KIF1A:blue
tubulin:green
carge:yellow



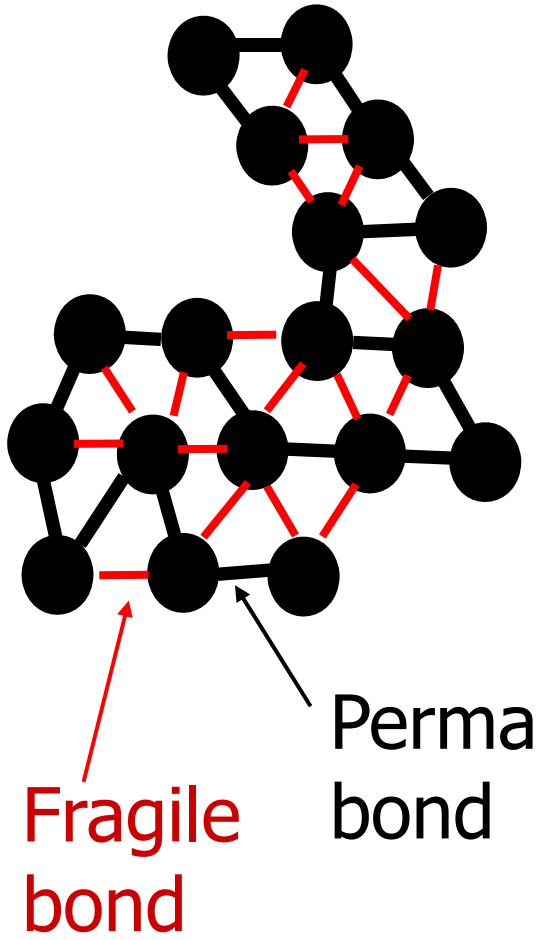
Wenfei Li

Frustration, specificity & nonlinearity in large-amplitude motion of allosteric proteins

Li, Wolynes, & Takada, PNAS 2011

Off-lattice Go model
(merge of Go model & ENM)

Clementi, Nymeyer, & Onuchic 200(



$$V(\mathbf{R}|\mathbf{R}_0)=\sum_{\text{bonds}}\mathrm{K_r}(b_i-b_{i0})^2+\sum_{\text{angles}}K_\theta(\theta_i-\theta_{i0})^2+$$

$$\sum_{\text{dihedral}}\{K_\phi^1[1-\cos(\phi_i-\phi_{i0})]+K_\phi^3[1-\cos(3(\phi_i-\phi_{i0}))]\}+$$

$$\sum_{i<j-3}^{\text{natcontact}}\varepsilon_1\left[5\left(\frac{r_{0ij}}{r_{ij}}\right)^{12}-6\left(\frac{r_{0ij}}{r_{ij}}\right)^{10}\right]+\sum_{i<j-3}^{\text{non-nat}}\varepsilon_2\left(\frac{D}{r_{ij}}\right)^{12}$$

Subscript 0 means
the value at native

K_r = 100e $K_\theta{}^1$ = 20e $K_\phi{}^3$= 1.0e K_ϕ= 0.5e

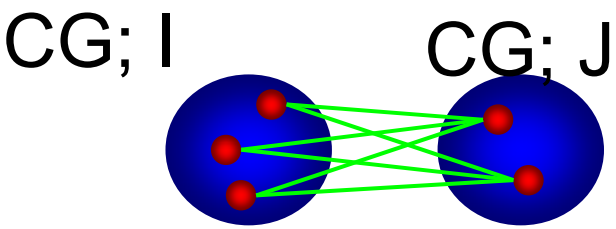
$\varepsilon_1=\varepsilon_2$=0.17e D=0.45(Å)

Atomic interactions in allosteric proteins:
Energy decomposition

Analysis of residue-pairwise energy from atomic force fielc

$$E^{IJ}(R_{IJ}) = \sum_{i \in I} \sum_{j \in J} u_{AA,ij}(r)$$

Gohlke et al., JMB, 2003, 330, 891



E^{IJ}: coarse grained contact energy

$u_{AA,ij}$: All atom energy between atom pair (i, j)

$$U_{AA}(r) = V(r) + \Delta G^{GB}_{pol}(r) + \Delta G^{SA}(r)$$

Using LCPO (pair wise)

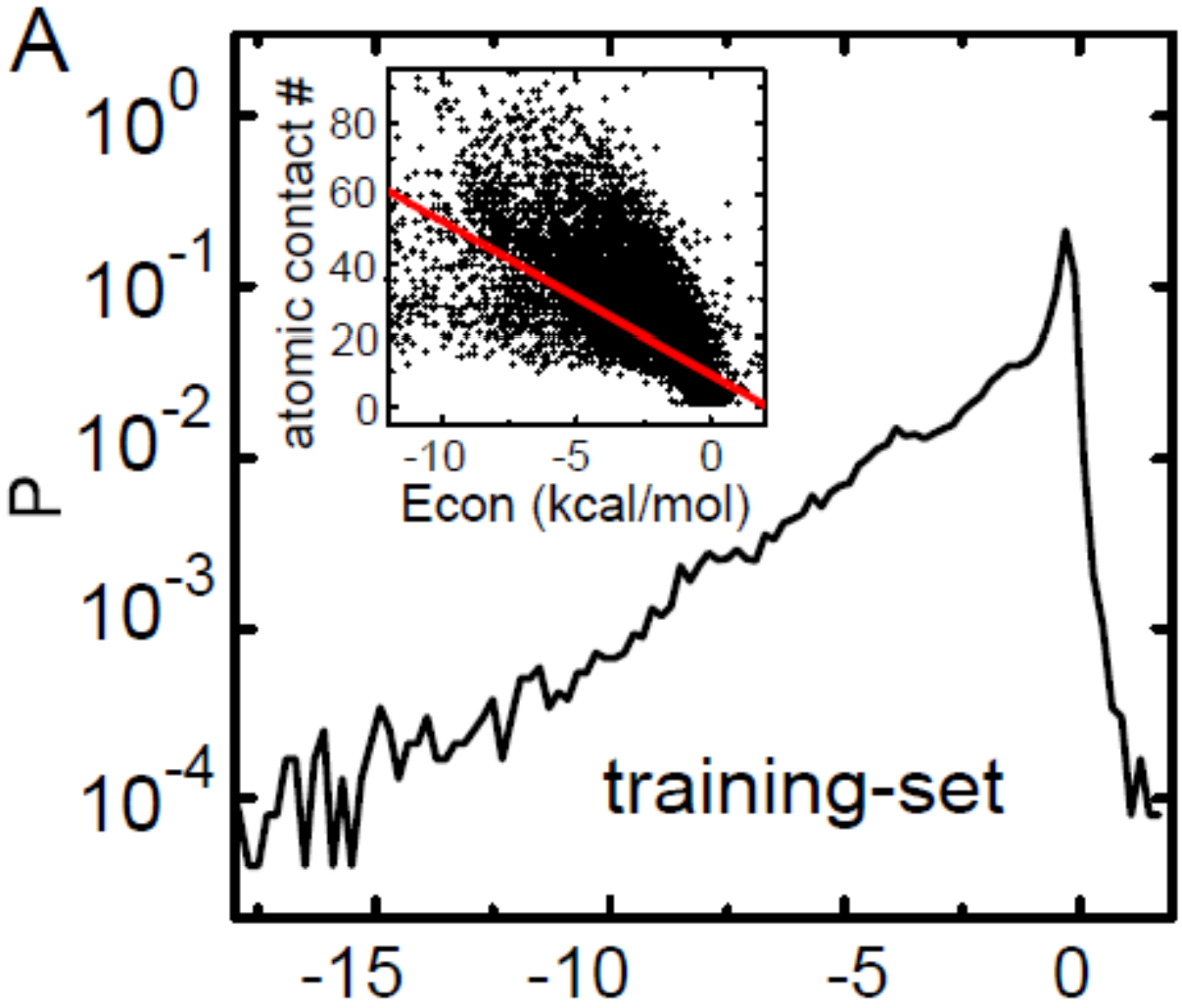
AA energy include vacuum part and solvation part, by AMBER99SB force field.

Case et al. AMBER10, 2008
Weiser et al, JCC, 1999, 20,217

Contact energies in single-domain proteins

Energy decomposition

Exponential law!!

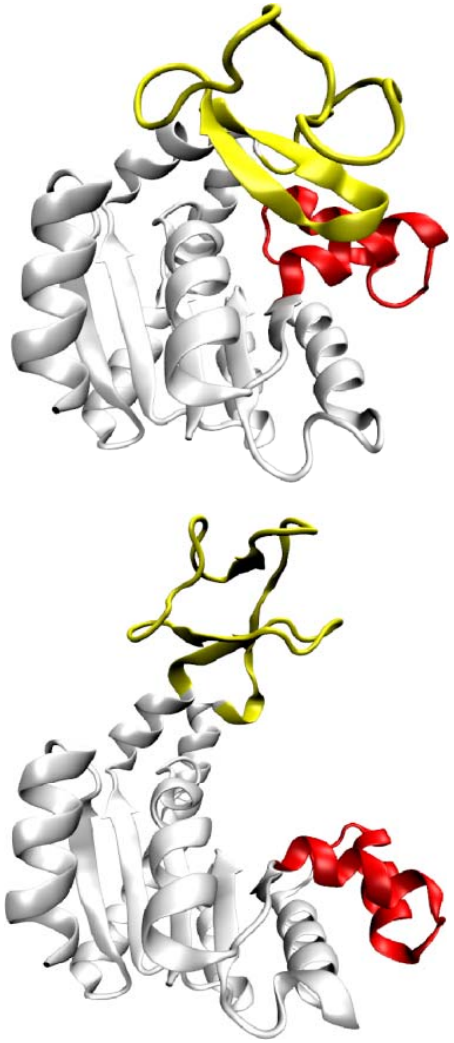


Contact energies in allosteric proteins:

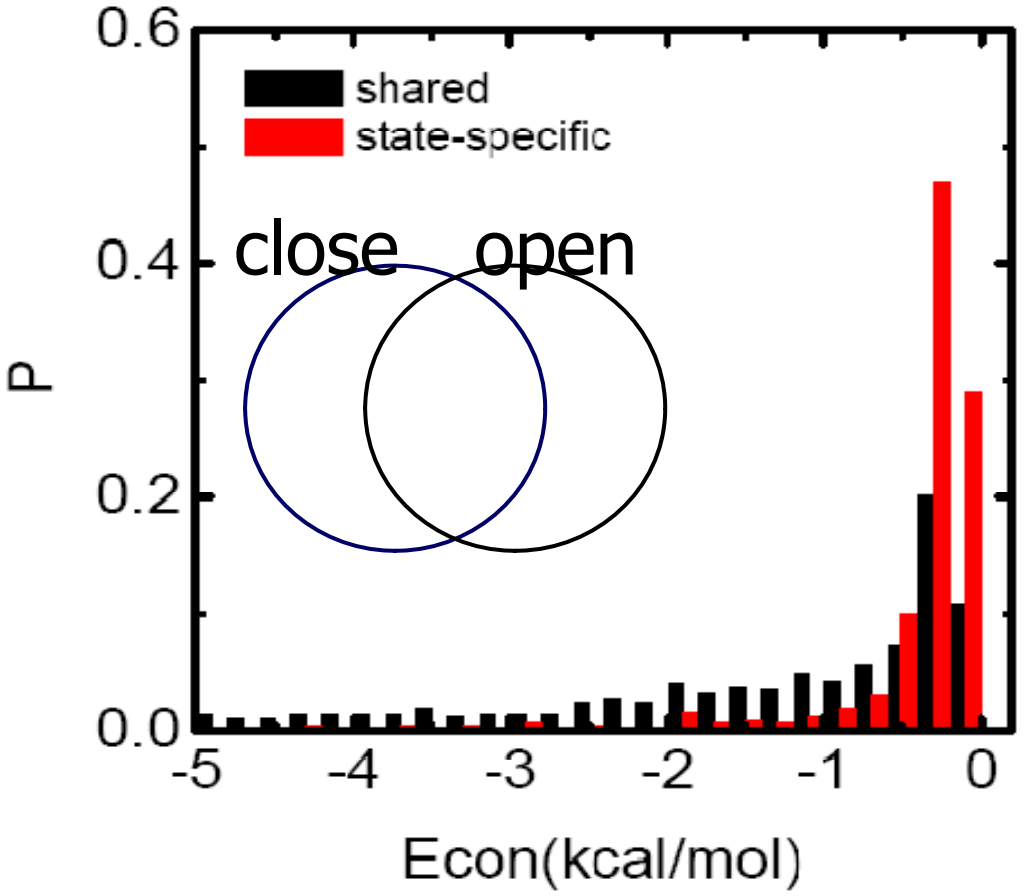
Energy decomposition

1ake
close

4ake
open



Adenylate kinase

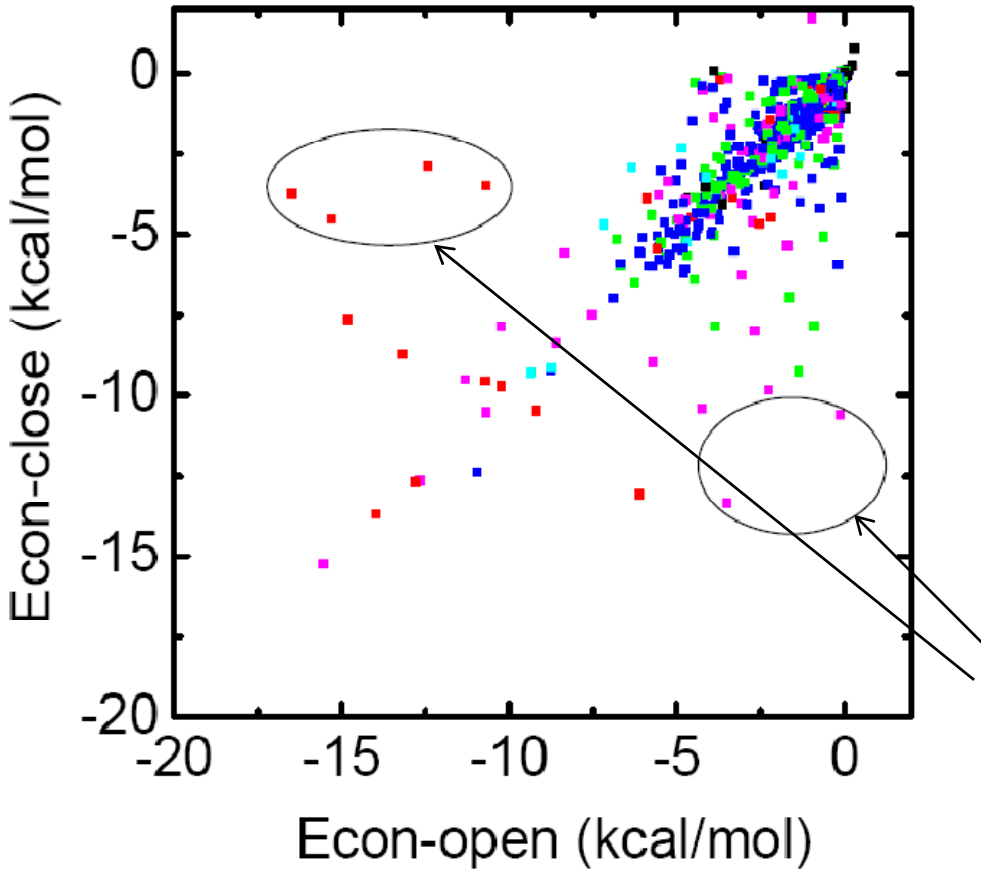


- Diverse
- Diff bet. classes

Atomic interactions in allosteric proteins:

Energy decomposition

Adenylate kinase



Red: oppositely charged

Pink: charged+polar

Green:charged+apolar

Cyan:polar+polar

Green:polar-apolar or polar+apolar

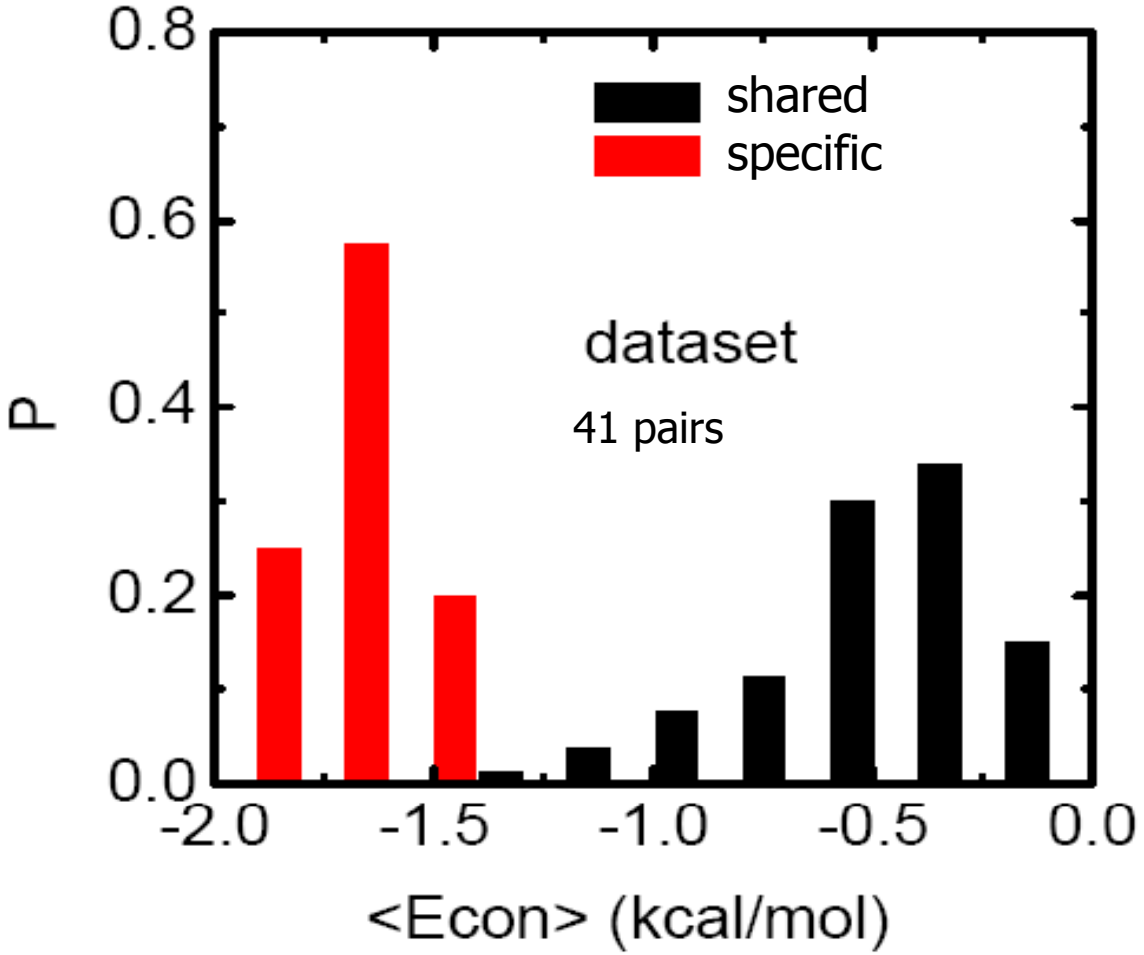
Black: identically charged

D54, K200, D158, E167, E162, K50 and D61

Atomic interactions in allosteric proteins:
Energy decomposition

41 allosteric proteins in pdb

Comp of class-average for each protein



Atomic interaction based CG (AICG) model

Deriving parameters

$$V(R|R^0) = \sum_i k_b^i (r^i - r_0^i)^2$$
$$+ \sum_i k_a^i (\theta^i - \theta_0^i)^2$$
$$+ \sum_i \{\varepsilon_\phi^i [1 - \cos(\phi^i - \phi_0^i)]$$
$$+ \varepsilon_\phi^i [1 - \cos 3(\phi^i - \phi_0^i)]/2\}$$
$$+ \sum_{i>j-3}^{native} \varepsilon^{ij} [5(r_0^{ij}/r^{ij})^{12} - 6(r_0^{ij}/r^{ij})^{10}]$$
$$+ \sum_{i>j-3}^{non-native} \varepsilon (C/r^{ij})^{12}$$

Multiscale strategies:

Chu and Voth, 2006
Li et al., 2010,
See also
Trylska et al
Gohlke et al., 2003,

❖Energy decomposition →

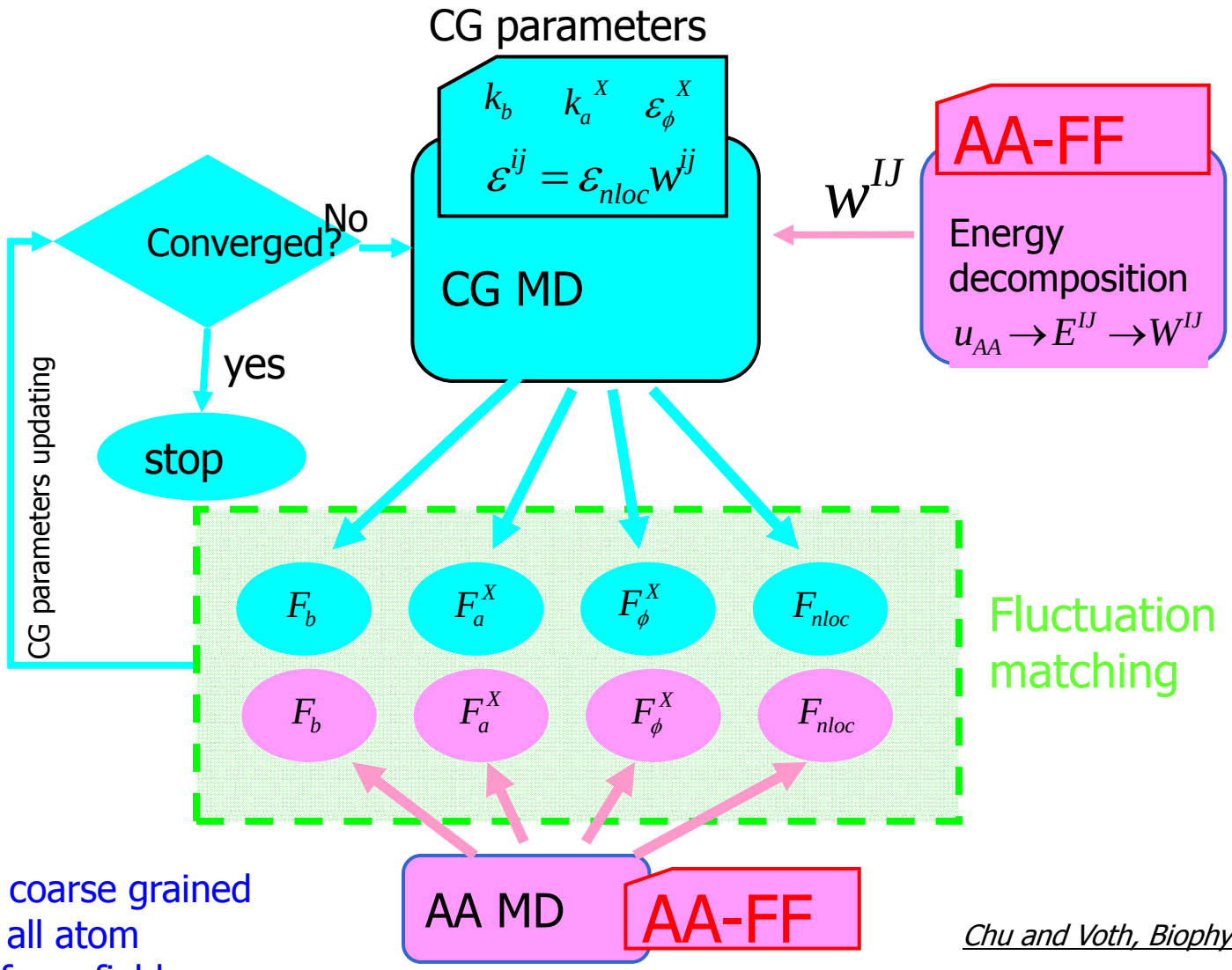
relative weight of contact energies

❖ Match rmsf bet. AA and CG→

scale local & tertiary interactions

For 23 training proteins

--- Flow chart



CG: coarse grained
AA: all atom
FF: force field

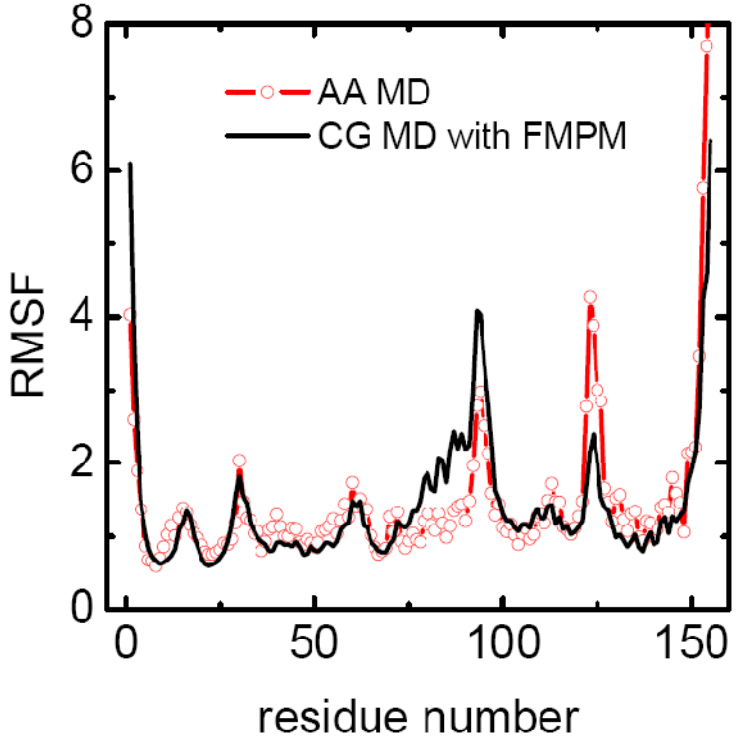
Chu and Voth, Biophys. J., 2006,90,1572

F: mean square fluctuations

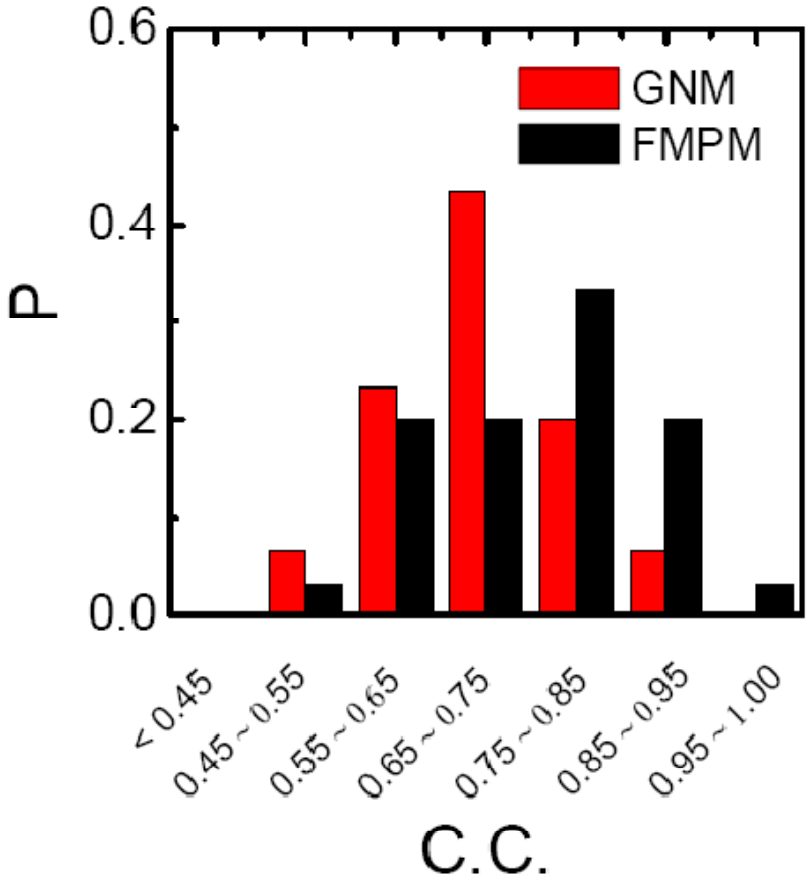
AICG model for mean fluctuations

Near native fluctuation (RMSFs)

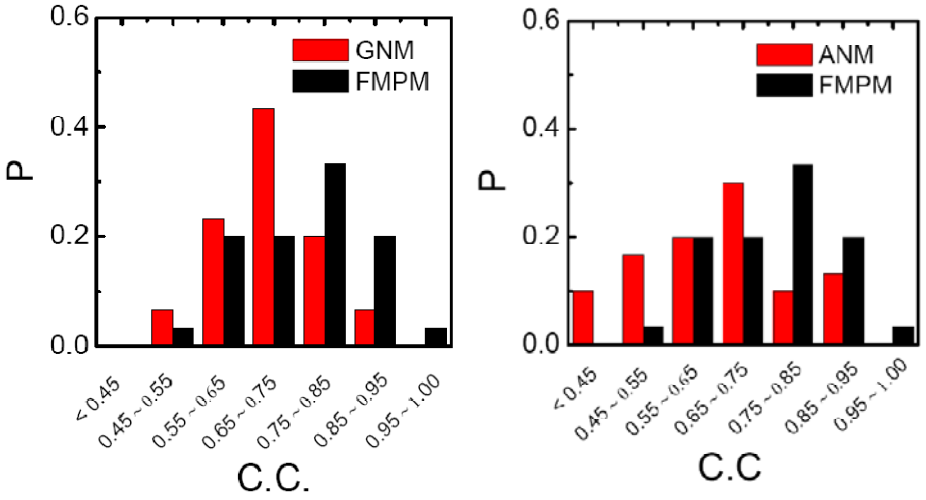
Comp against AA MD



Stat for 30 proteins



AICG model for mean fluctuations



30 proteins

Fujitsuka et al, 2006, *Proteins*
Yang et al, 2007, *Structure*

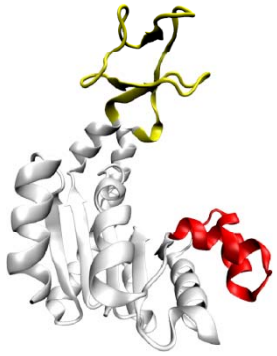
Table 3. Average correlation coefficients (C.C.) and standard errors (S.E.) between the rmsfs derived by AA model and by different CG models based on the proteins of testing set.

	ENM		AICG model		
Models	GNM	ANM	hete	homo	hete-nloc
C.C.	0.694	0.648	**0.758**	0.722	0.738
S.E.	0.018	0.031	0.021	0.027	0.031

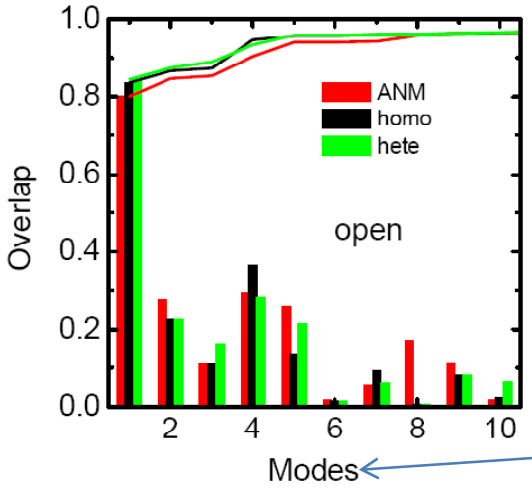
hete: heterogeneous model.
homo: homogeneous model.
hete-nloc: only the nonlocal interactions are heterogeneous.

AICG model for predicting structural change

adenylate kinase



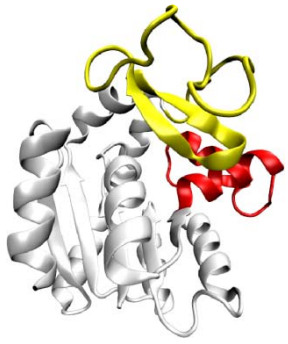
$V(R \mid R^{open})$



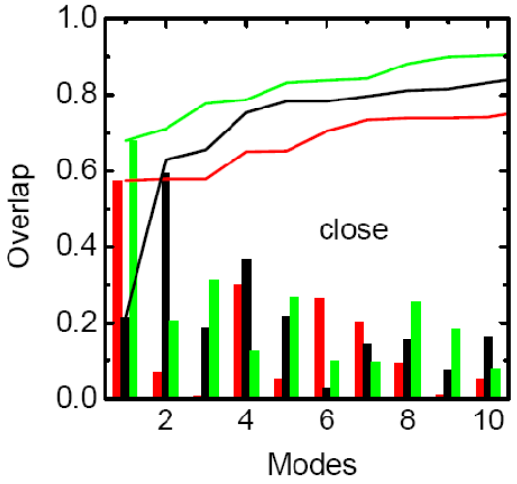
$$\vec{d} = (\vec{R}^o - \vec{R}^c) / | \vec{R}^o - \vec{R}^c |$$

$$overlap(i) = \vec{v}^i \cdot \vec{d}$$

PCA for Go model,
NM for ANM



$V(R \mid R^{close})$



AICG model for predicting structural change

Correlation w. structure change

41 struct pairs of allosteric proteins

Gerstein, NAR1998

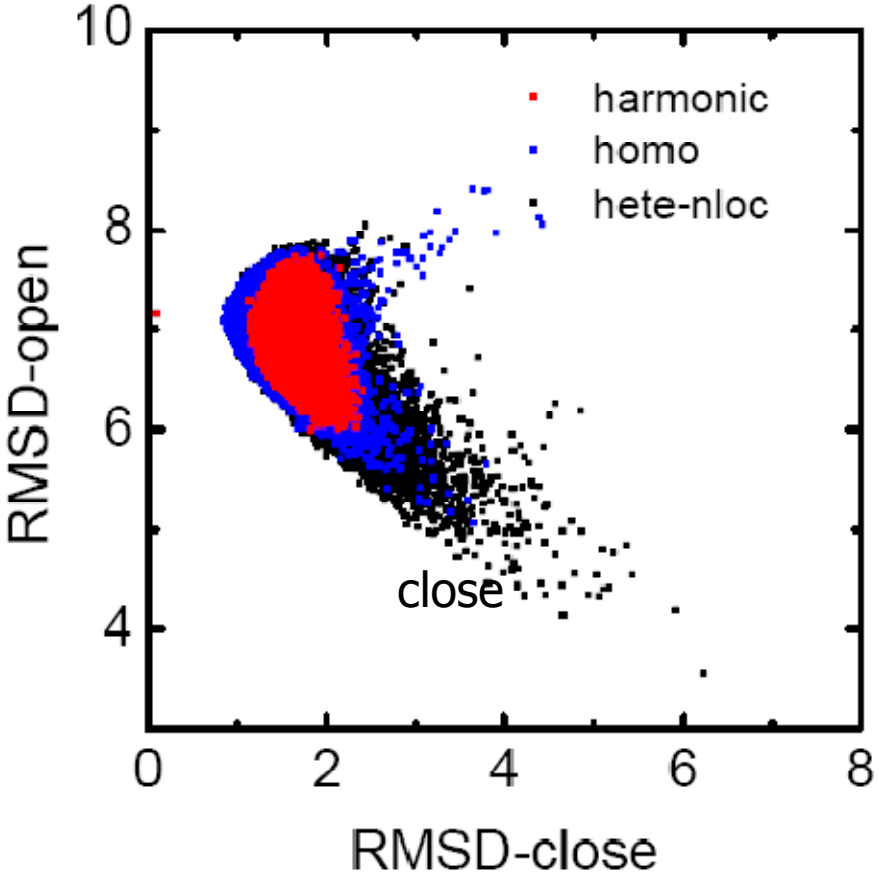
		ENM	New model		
Models		ANM	hete	homo	hete-nloc
open→close $V(R \mid R^{open})$	M.O.	0.480 (0.037)	0.540 (0.037)	0.511 (0.038)	0.518 (0.040)
	C.O.	0.600 (0.040)	0.657 (0.039)	0.628 (0.040)	0.626 (0.042)
close→open $V(R \mid R^{close})$	M.O.	0.421 (0.032)	0.517 (0.036)	0.475 (0.036)	0.512 (0.038)
	C.O.	0.556 (0.037)	0.638 (0.038)	0.608 (0.038)	0.631 (0.039)

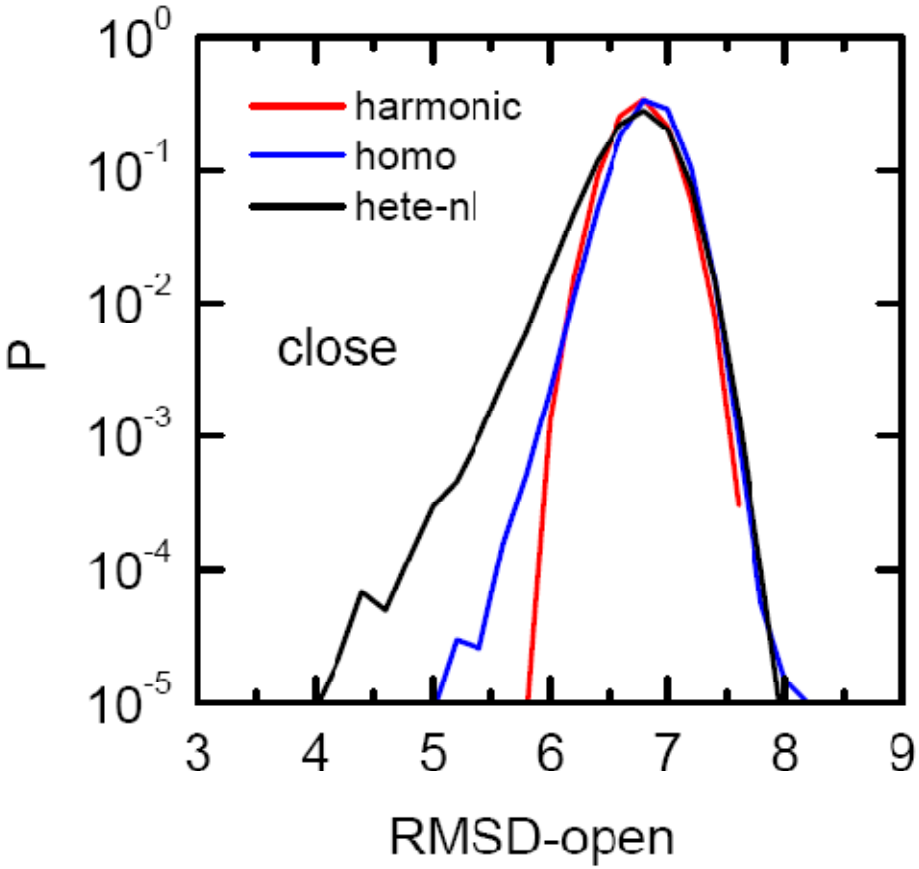
Both the interaction heterogeneity and anharmonicity are important for predicting the conformational change.

Large-amplitude fluctuation

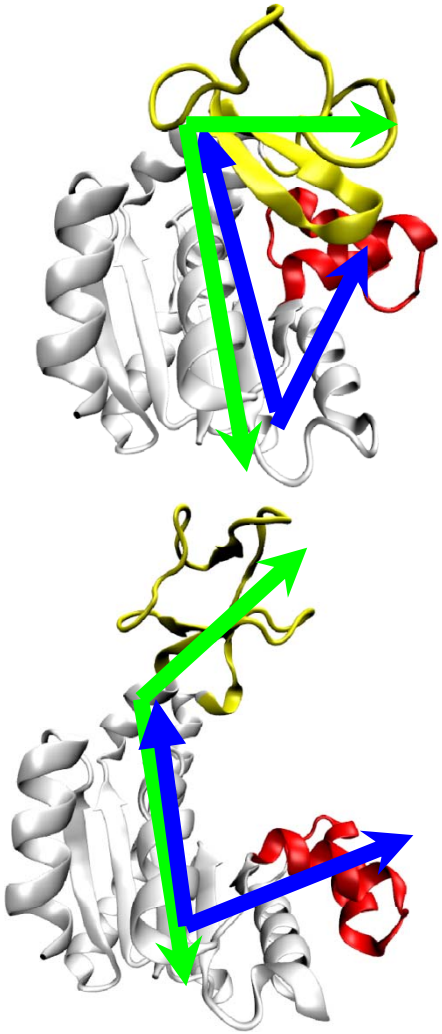
adenylate kinase

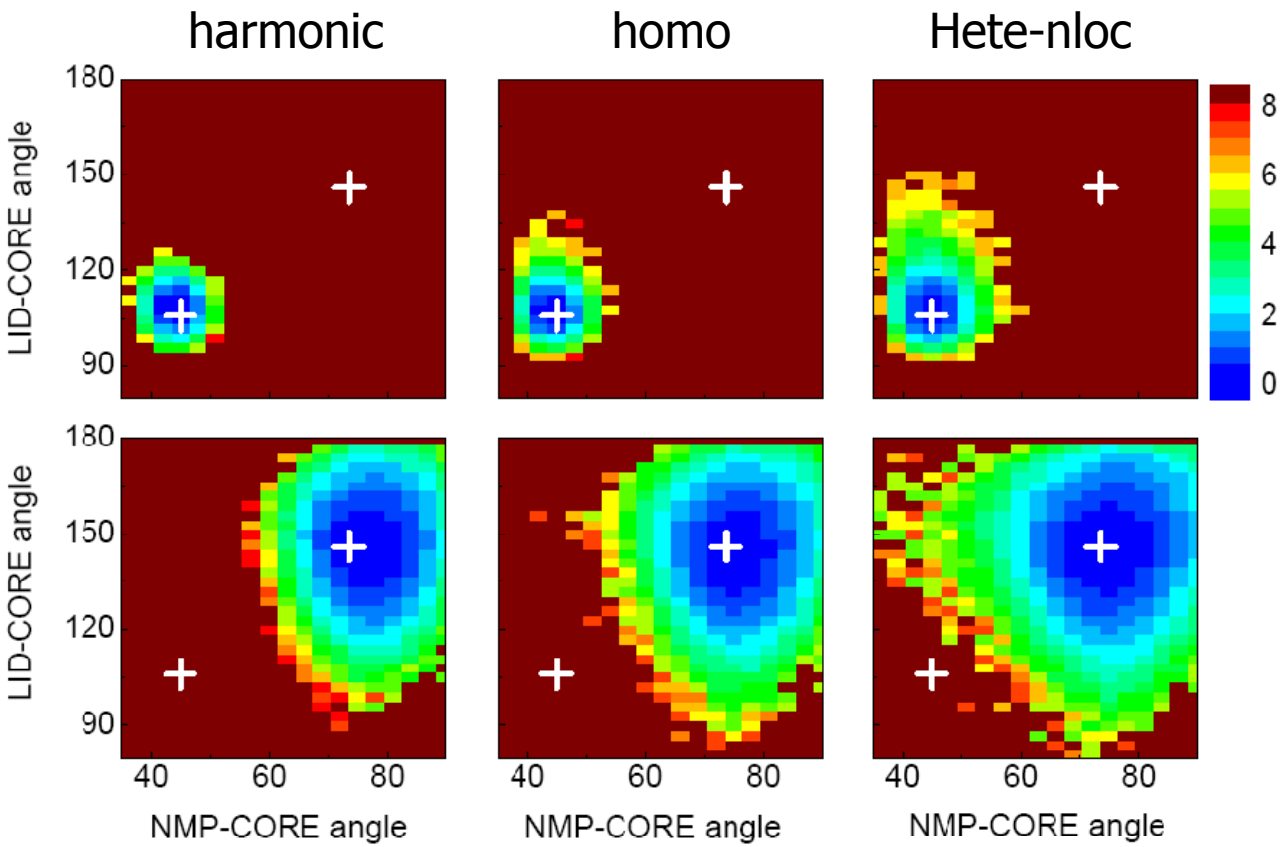
$V(R \mid R^{close})$ Fluctuation in close state





Large-amplitude fluctuation in AKE

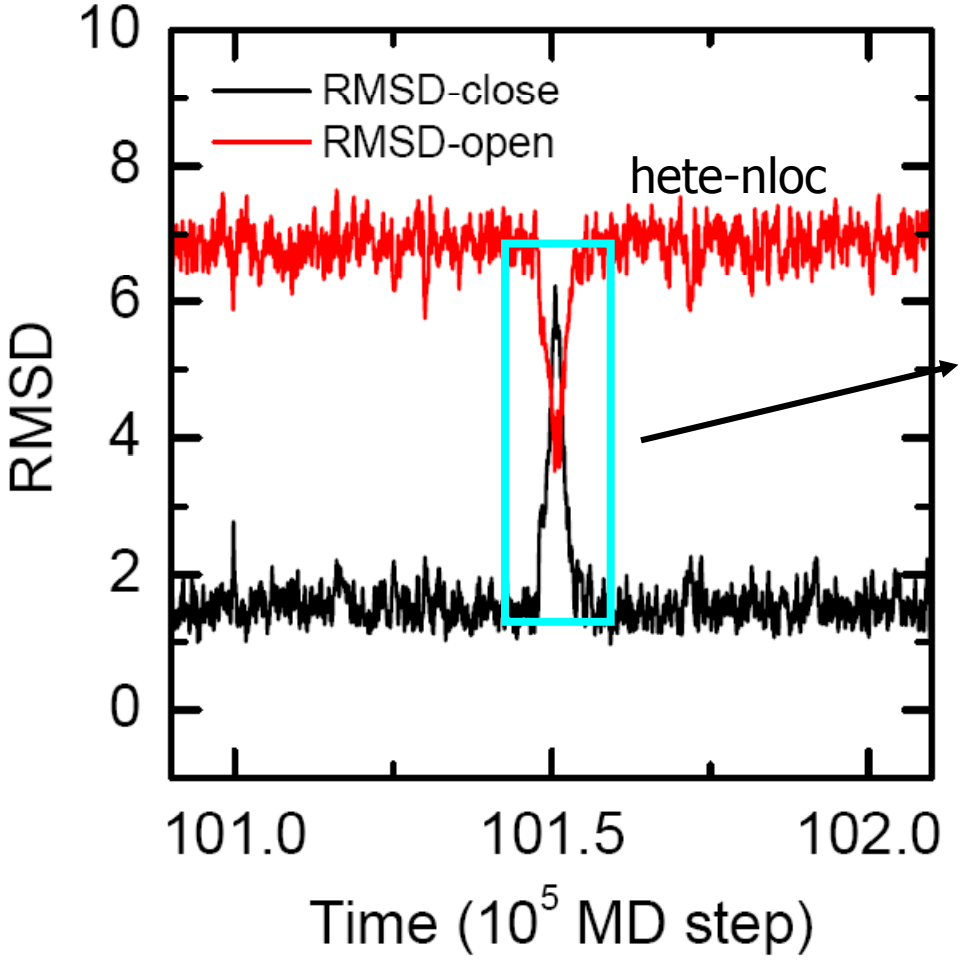


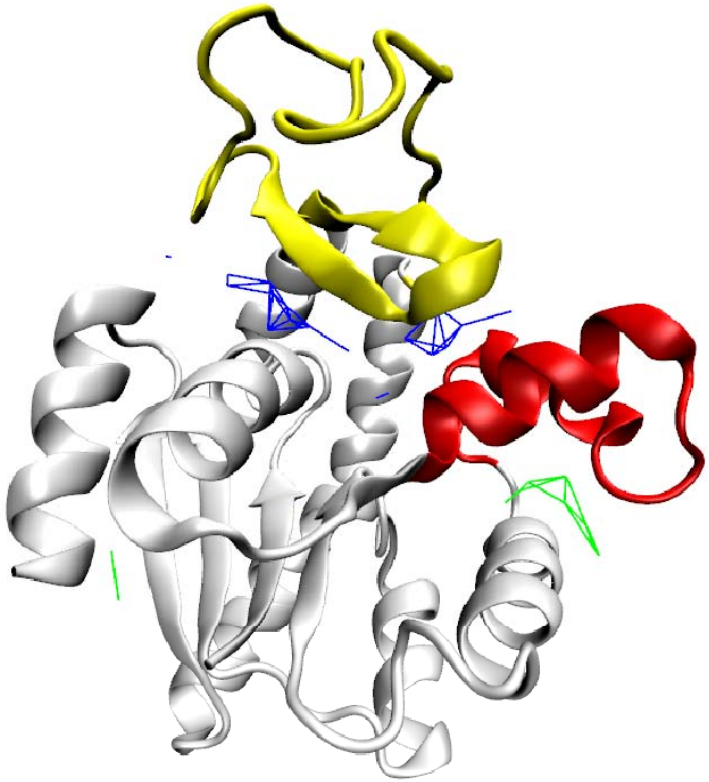


LID domain has higher mobility than the NMP domain.

Interaction heterogeneity enhances the collective motions.

Large-amplitude fluctuation in AKE





Very rare event in a long trajectory

Menu

Models

Simulation methods

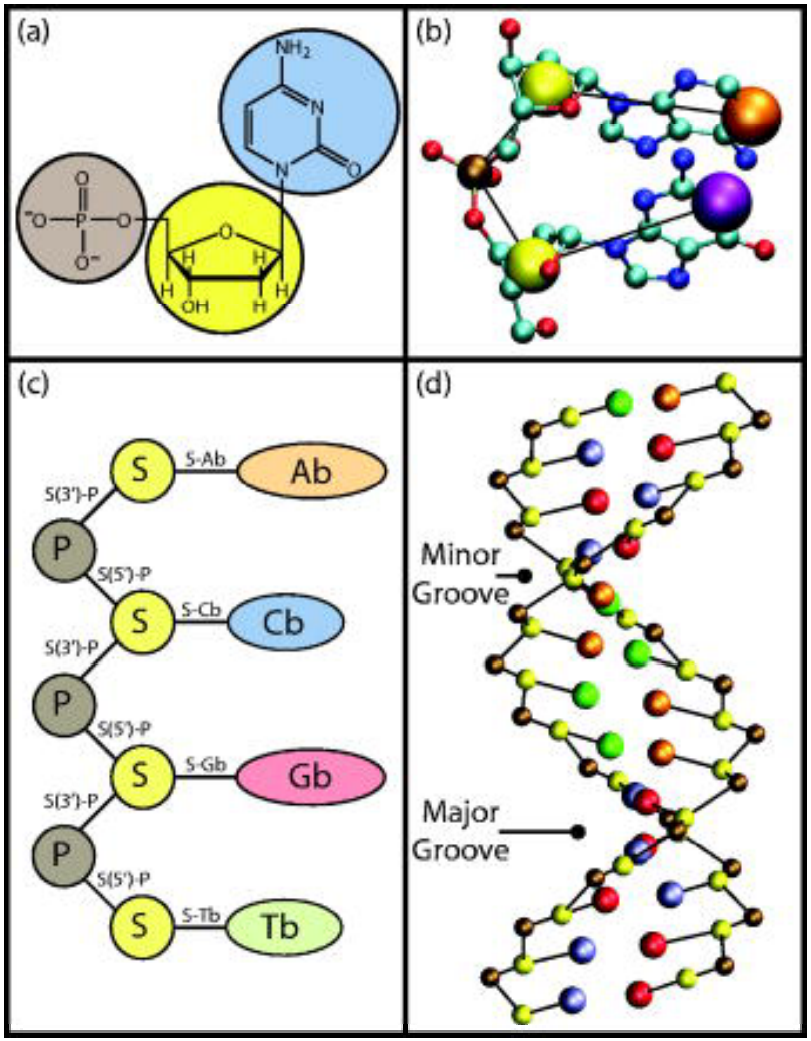
Implementation

Selected applications

In-progress models & methods

CG DNA model

- Three interactions sites
  - Phosphate
  - Sugar
  - Base
- Reproduce various DNA behavior
  - Salt-dependent melting
  - Bubble formation
  - Mechanical properties



T.A. Knotts IV, N.Rathore, D.C. Shwartz, and J.J. Pablo, J. Chem. Phys. (2007)

3SPN.1 force field

E.J. Sambrisiki, D.C. Schwartz, and J.J. de Pablo,Knotts, Biophys J. (2009)

$$V_{dna} = V_{local} + V_{stack} + V_{bp} + V_{ex} + V_{qq} + V_{solv}$$

$$V_{local} = K_{b1}\sum_i \left(r_{i,i+1} - r_{0i,i+1}\right)^2 + K_{b2}\sum_i \left(r_{i,i+1} - r_{0i,i+1}\right)^4$$

$$+ K_\theta \sum_i \left(\theta_i - \theta_{0i}\right)^2 + K_\phi \sum_i \left(1 - \cos\left(\phi_i - \phi_{0i}\right)\right)$$

$$V_{stack} = 4\varepsilon_1 \sum_{i,j}^{Nst} \left[\left(\frac{\sigma_{0ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{0ij}}{r_{ij}}\right)^{6} \right]$$

$$V_{bp} = \sum_{i,j}^{Nbp} 4\varepsilon_{bpi} \left[5\left(\frac{r_{0ij}}{r_{ij}}\right)^{12} - 6\left(\frac{r_{0ij}}{r_{ij}}\right)^{10} \right]$$

$$V_{ex} = 4\varepsilon_1 \sum_{i,j}^{Nex} \left[\left(\frac{\sigma_0}{r_{ij}}\right)^{12} - \left(\frac{\sigma_0}{r_{ij}}\right)^{6} \right] + \varepsilon_1 \ (if\ \ r_{ij} < d_{cut}),$$

$$= 0 \ (if\ \ r_{ij} > d_{cut})$$

θ: bond angle
ϕ: dihedral angle
(0 means B-type DNA)

Go type interaction

$K_{b1} = 1\varepsilon$
$K_{b2} = 100\varepsilon$
$K_\theta = 1400\varepsilon$
$K_\phi = 28\varepsilon$
$\varepsilon_{bpGC} = 2.532\varepsilon$
$\varepsilon_{bpAT} = 2.0\varepsilon$
ε =0.1839kcal/mol

3SPN.1 force field (electrostatic and solvation interaction)

$$V_{qq} = \sum_{i,j}^{N} \left(\frac{q_i q_j}{4\pi\varepsilon_0 \varepsilon(T,C) r_{ij}} \right) e^{-r_{ij}/\kappa D}$$

← Debye-Huckel theory

$$\varepsilon(T,C) = \varepsilon(T) a(C)$$

$$\varepsilon(T) = 249.4 - 0.788 T/K + 7.20 \times 10^{-4} (T/k)^2$$

$$a(C) = 1.000 - 0.2551 C/M$$

$$+ 5.151 \times 10^{-2} (C/M)^2 - 6.889 \times 10^{-3} (C/M)^3$$

$$V_{solv} = \sum_{i<j}^{Nsolv} \varepsilon_s \left[1 - e^{-a(r_{ij} - r_s)} \right]^2 - \varepsilon_s$$

$$\varepsilon_s = \varepsilon_N A_I$$

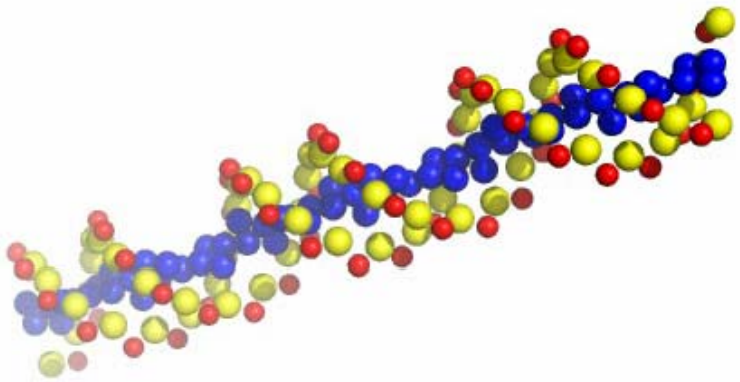
$$e_N = e_0 (1 - [1.40418 - 0.268231 N_{nt}]^{-1})$$

$$A_I = 0.474876 (1 + \{0.148378 + 10.9553 [Na^+]\}^{-1})$$

α^{-1} = 5.333A
r_s = 13.38A
$\varepsilon_0 = 0.504982\varepsilon$

DNA duplex

- 30 bp oligomer of DNA
- Langevin dynamics (300K)
- [Na^+] = 69mM



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i_seq_read_style = 2
i_go_native_read_style = 3
1-2    dna          sequence
>>>>
<<<< energy_function
NLOCAL(1-2/1-2)    7 11
i_use_atom_protein = 0
i_use_atom_dna = 0
>>>>
<<<< electrostatic
cutoff_ele = 20.0
ionic_strength = 0.069
diele_water = 78.0
>>>>
<<<< in_box
xbox = 120.0
ybox = 120.0
zbox = 120.0
boxsigma = 4.0
>>>>
```

DH

3SPN.1

Intra mol 1,2

Inter mol 1-2

Simulation of nucleosome

1KX5.pdb

- Electrostatic interaction + Go potential

$\varepsilon_{go}^{\text{pro-dna}} = 0.5\varepsilon_{go}^{\text{pro}}$

$[Na^+]$ = 50mM

$\varepsilon_{go}^{\text{pro-dna}}$:coefficient of protein-DNA Go potential

```
<<<< energy_function
NLOCAL(1-2/1-2)    7 11
NLOCAL(1-2/3-10)   2 3 7
NLOCAL(3-10/3-10)  2 3
i_use_atom_protein = 0
i_use_atom_dna = 0
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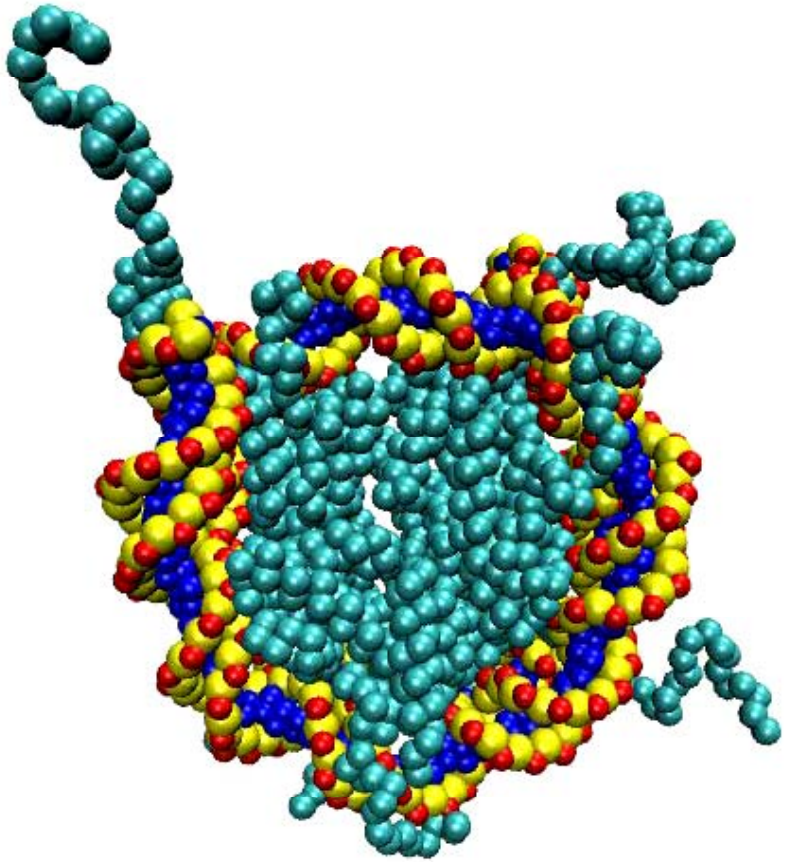
<<<< electrostatic
cutoff_ele = 20.0
ionic_strength = 0.05
diele_water = 78.0
>>>>
```

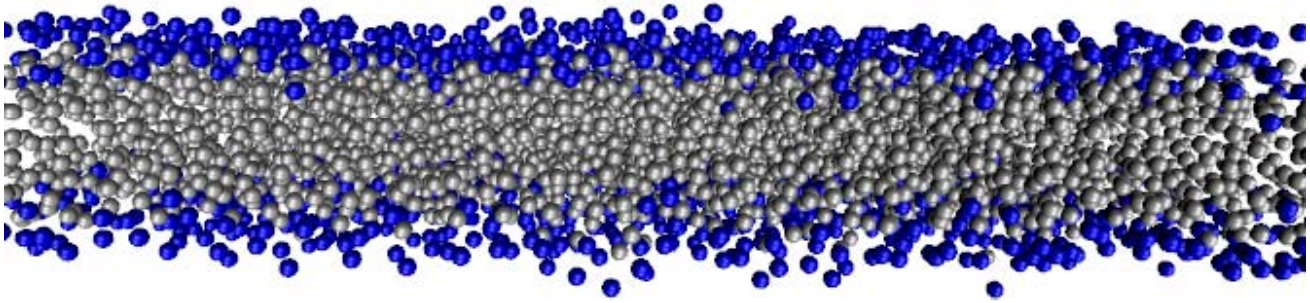


H. Kenzaki, et al unpublished data

CG lipid model

H. Noguchi, and M. Takasu, Phys. Rev. E (2001)

- i th lipid molecule:
  - 1 hydrophilic particle (j=1, blue)
  - 2 hydrophobic particles (j=2,3, gray)
- Self-assemble bilayer structure



CG lipid model

$$V_{lip} = V_{local} + V_{rep} + V_{hydro}$$

θ: bond angle

$$V_{local} = K_b \sum_{i,j=1,2} \left(r_{(i,j),(i,j+1)} - r_{0(i,j),(i,j+1)} \right)^2 + K_\theta \sum_i \cos\theta_i$$

$$V_{rep} = \varepsilon \sum_{i \neq i',j}^{Nst} \exp\left[-20 \left\{ \frac{r_{(i,j),(i',j')}}{\sigma} - 1 \right\} \right]$$

$$V_{hydro} = \varepsilon \sum_{i,j=2,3} \begin{cases} -0.5\rho & (\rho_{i,j} < \rho_j^* - 1) \\ 0.25(\rho_{i,j} - \rho_j^*)^2 - c_j & (\rho_j^* - 1 \le \rho_{i,j} < \rho_j^*) \\ -c_j & (\rho_j^* \le \rho_{i,j}) \end{cases}$$

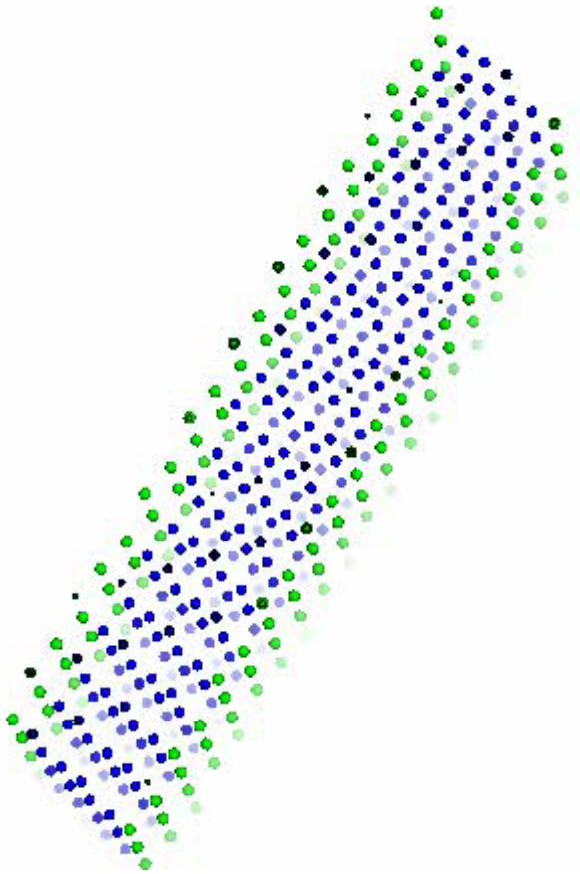
$$\rho_{i,j} = \sum_{i \neq i',j'=2,3} \frac{1}{\exp\left[20 \left(\frac{r_{(i,j),(i',j')}}{s} - 1.9 \right) \right] + 1}$$

$K_b = 500\varepsilon$
$K_\theta = 500\varepsilon$
$\varepsilon = 0.6594$kcal/mol
$\sigma = 7.5$A
$\rho_2^* = 10$
$c_2 = 4.75$
$\rho_3^* = 14$
$c_3 = 6.75$

Density dependent attraction

Formation of vesicle

S. Fujiwara, et al unpublished data



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i_go_native_read_style = 3
1    lipid     sequence
>>>>
<<<< initial_lipid
nmp_transverse_lipid = 20
nmp_longitudinal_lipid = 20
nlayer_lipid = 1
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z_coord_lipid(1) = 1.0
>>>>
<<<< energy_function
NLOCAL(1/1)    17 19
i_use_atom_protein = 0
i_use_atom_dna = 0
>>>>
```

Acknowledgement

CafeMol development has been supported by Research and Development of the Next-Generation Integrated Simulation of Living Matter, a part of the Development and Use of the Next-Generation Supercomputer Project of the Ministry of Education, Culture, Sports, Science and Technology.