Beating heart simulation driven by three dimensional molecular dynamics model

Takumi Washio (UT-Heart Inc.)
Ryo Kanada (RIKEN)
Xiaoke Cui (UT-Heart Inc.)
Seiryo Sugiura (UT-Heart Inc.)
Yasushi Okuno (Kyoto Univ.)
Toshiaki Hisada (UT-Heart Inc.)

Heart + Cell + Motor proteins Multiscale Challenge on K-computer (2012)

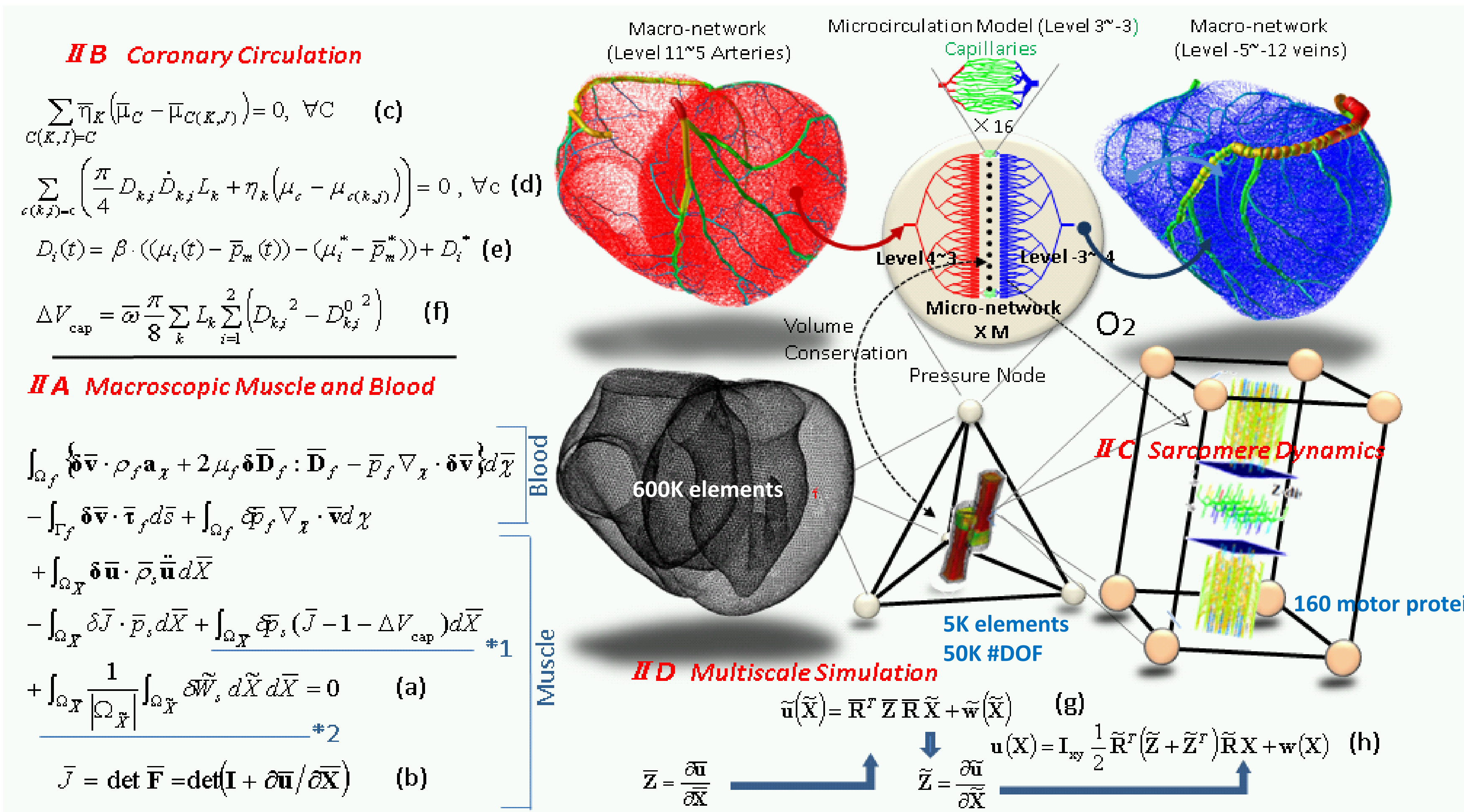
FEM FEM MonteCarlo

Model size

macro	#myocardial elements	659456
micro	#myofibril elements of a cell	5796
	NDOF of a cell	49245
	NDOF of a z disk	230
	#motor proteins	160

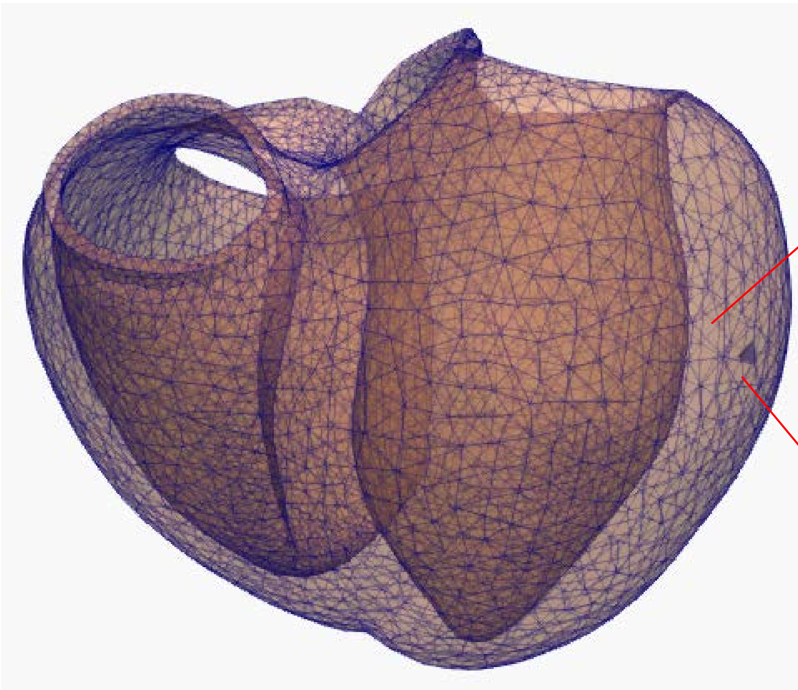
Performance

	Pflop/s			% of peak		
model\#nodes	20736	41472	82944	20736	41472	82944
49KDOF	0.72	1.39	2.74	28.10	27.43	27.72



Conventional Multiscale Approach

Heart –Sarcomere Coupling Model



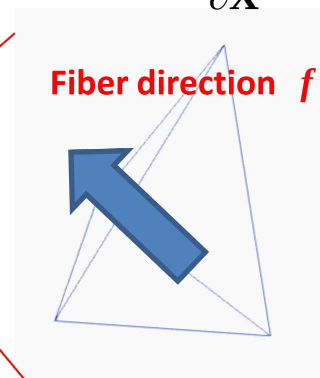
Strain tensor

$${}^{t}\mathbf{F} = \frac{\partial\, {}^{t}\mathbf{x}}{\partial \mathbf{X}}$$

Length change in the fiber direction *f*

Sarcomere length

$${}^{t}SL = SL_0 \left\| {}^{t}\mathbf{F}\mathbf{f} \right\|$$



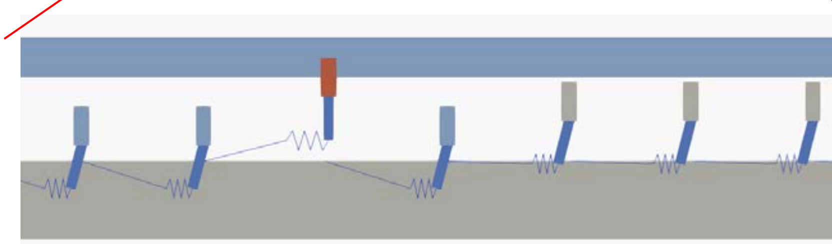
Sarcomere model

Stress tensor

$${}^{t}\boldsymbol{\Pi}_{act} = \frac{C\,T_S}{\left\| {}^{t}\mathbf{F}\mathbf{f} \right\|}\mathbf{f} \otimes \mathbf{f} \cdot {}^{t}\mathbf{F}^{T}$$

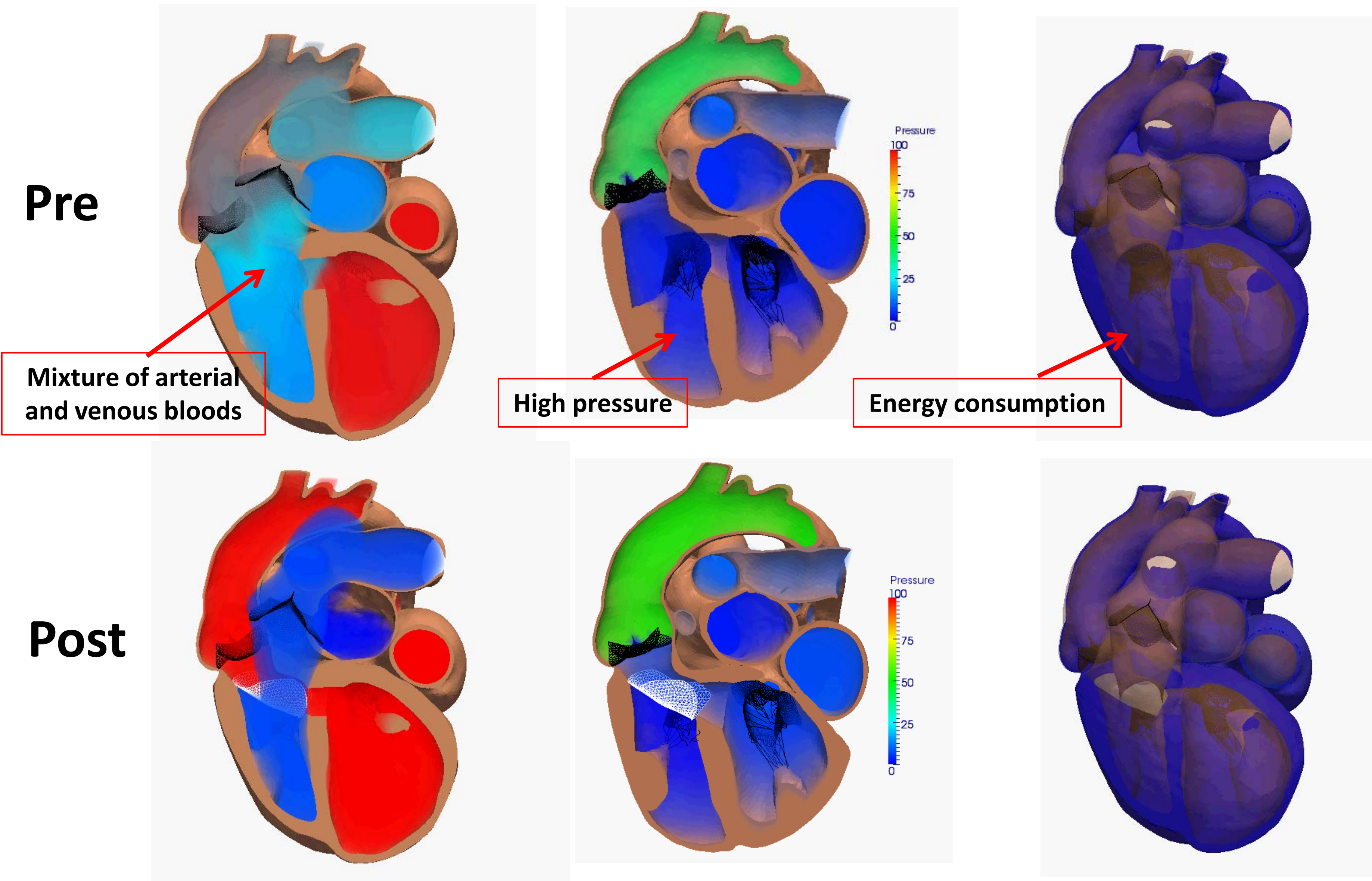
$${}^{t}T_S = \sum_{i=1}^{n} \delta_{A,i} k_M\, {}^{t}x_i$$

Contraction force



Filament sliding changes the mechanical load, thereby affects the lever arm swing and the detachment .

Application: Prediction of post-operation



Improvement of SPO2

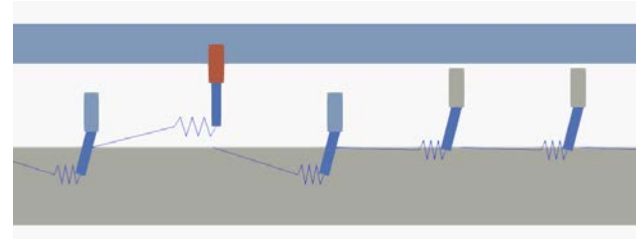
Load reduction
(RV blood pressure)

Energy saving
（RV energy consumption)

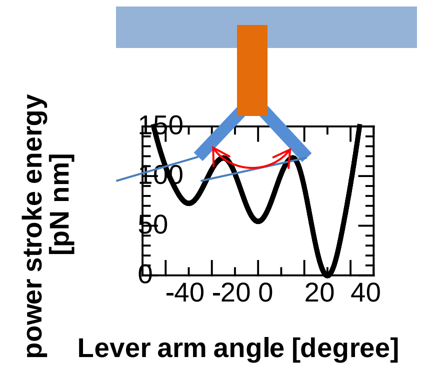
Research directions for Post-K ： from 1d MC to 3d MD

K

1D Monte Carlo
Load dependent state Transition



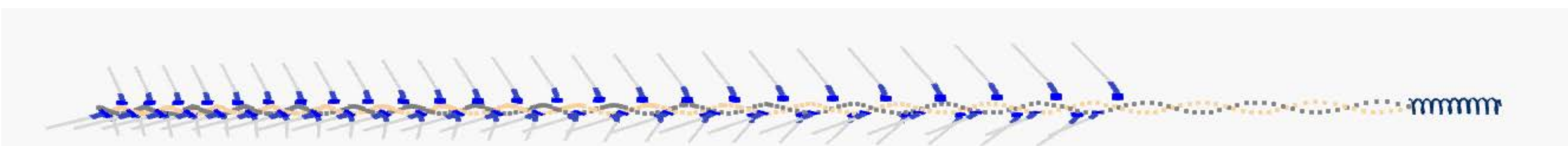
3D Molecular Dynamics
Deformation potentials



Post-K

Super Coarse grained (UT-Heart Inc.)

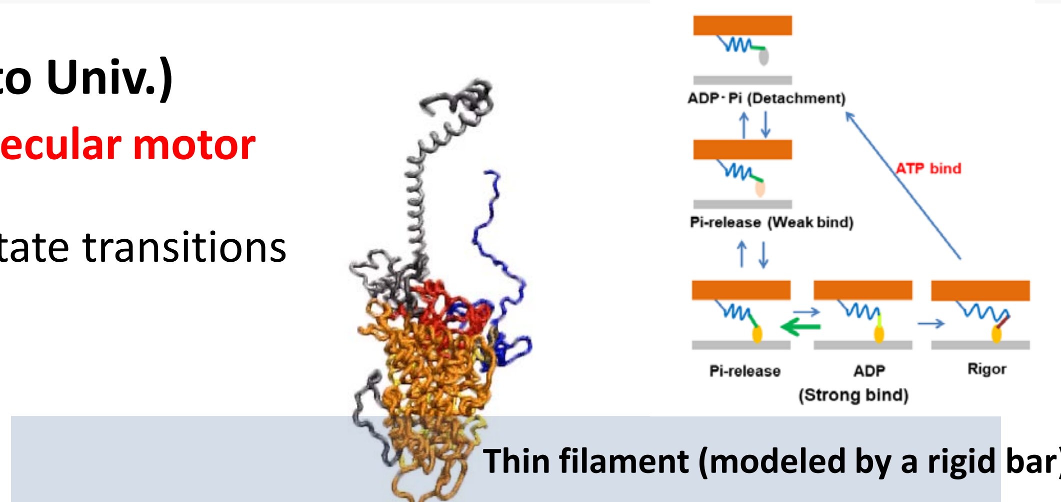
Focusing on 3D sarcomere structure



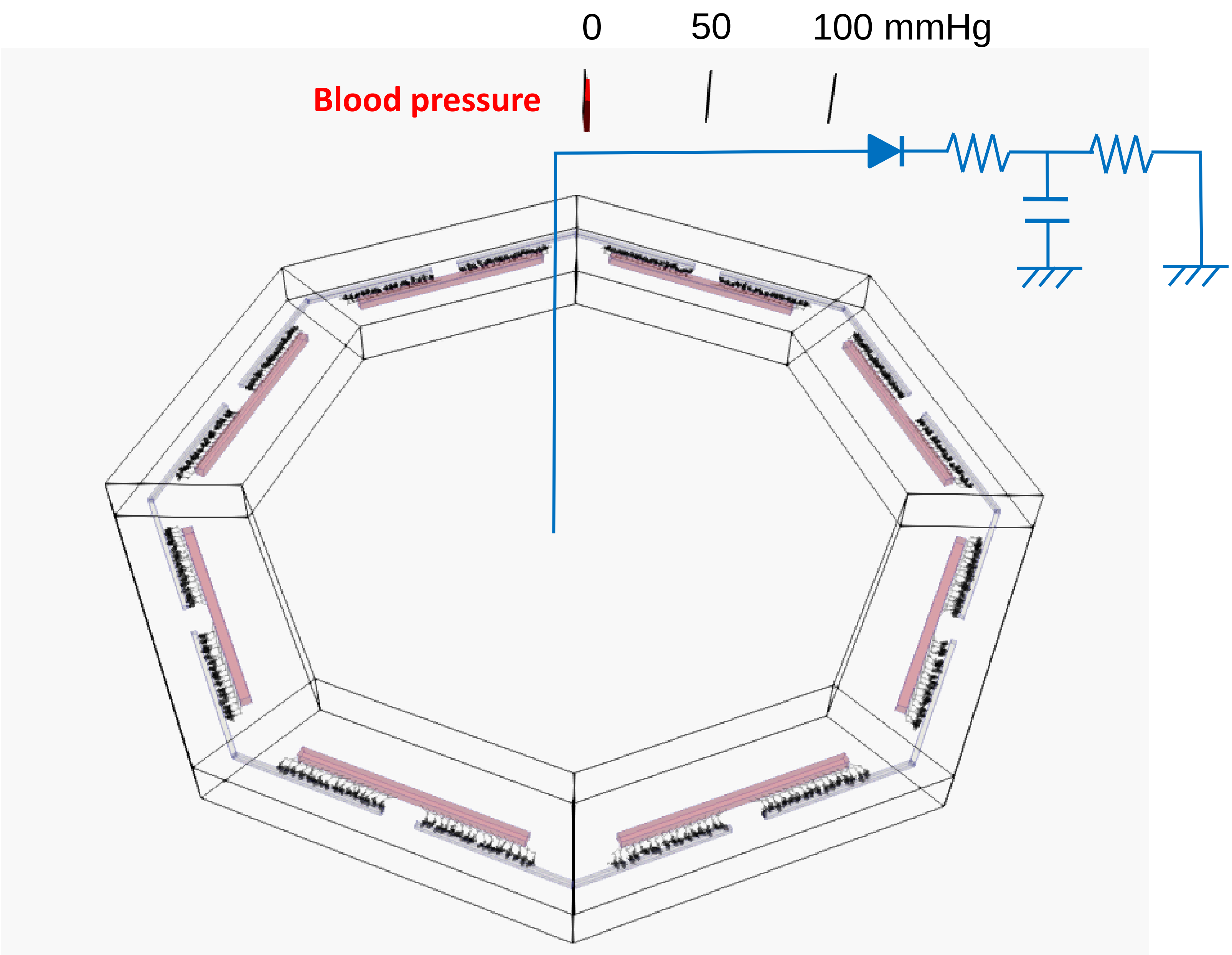
Cafemol (Takada Lab., Kyoto Univ.)

Focusing on inside of the molecular motor

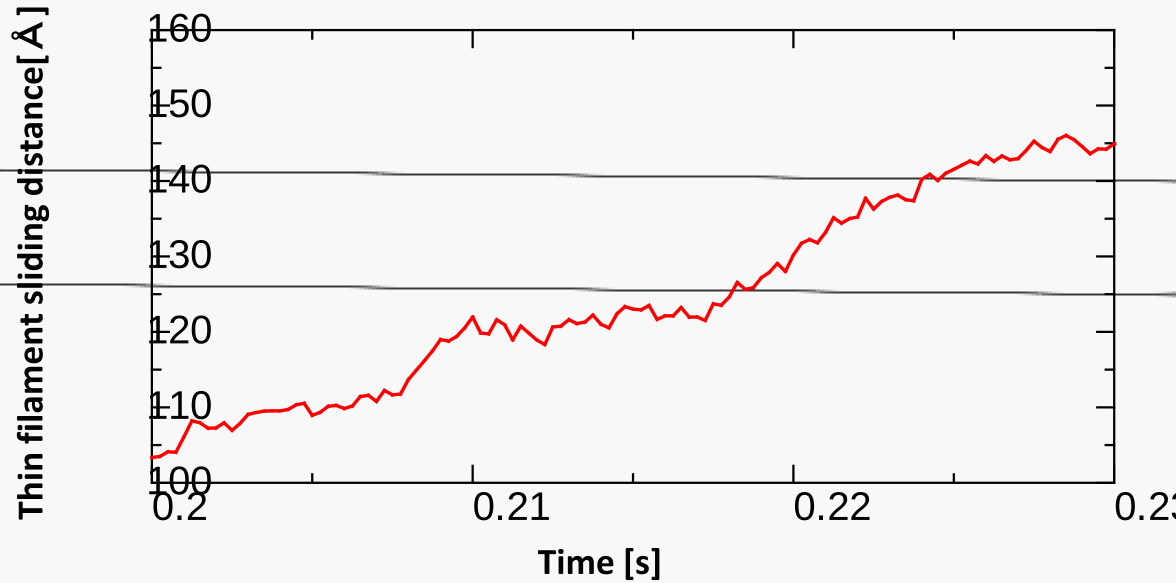
Switch the potentials at the state transitions



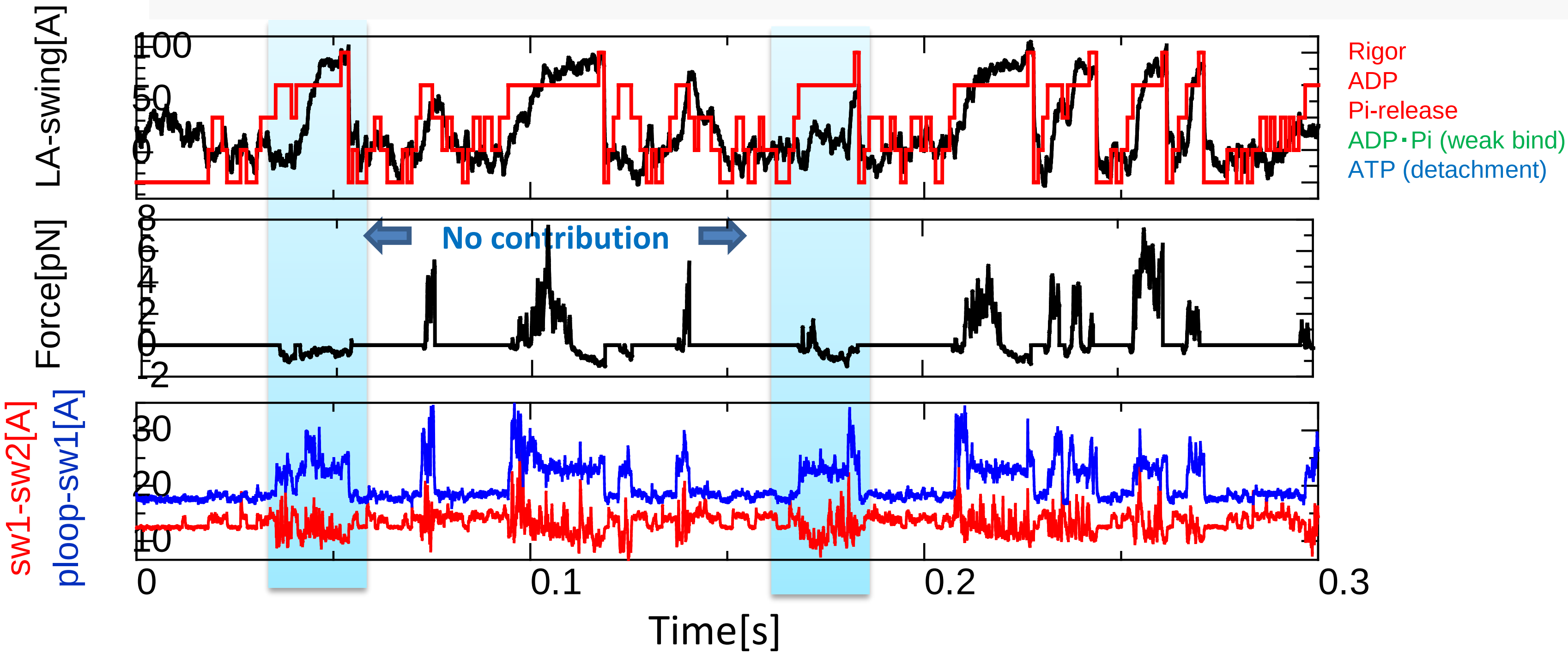
Preliminary test using Cafemol-Ring Coupling model



Micro-Macro interaction through the thin filament sliding



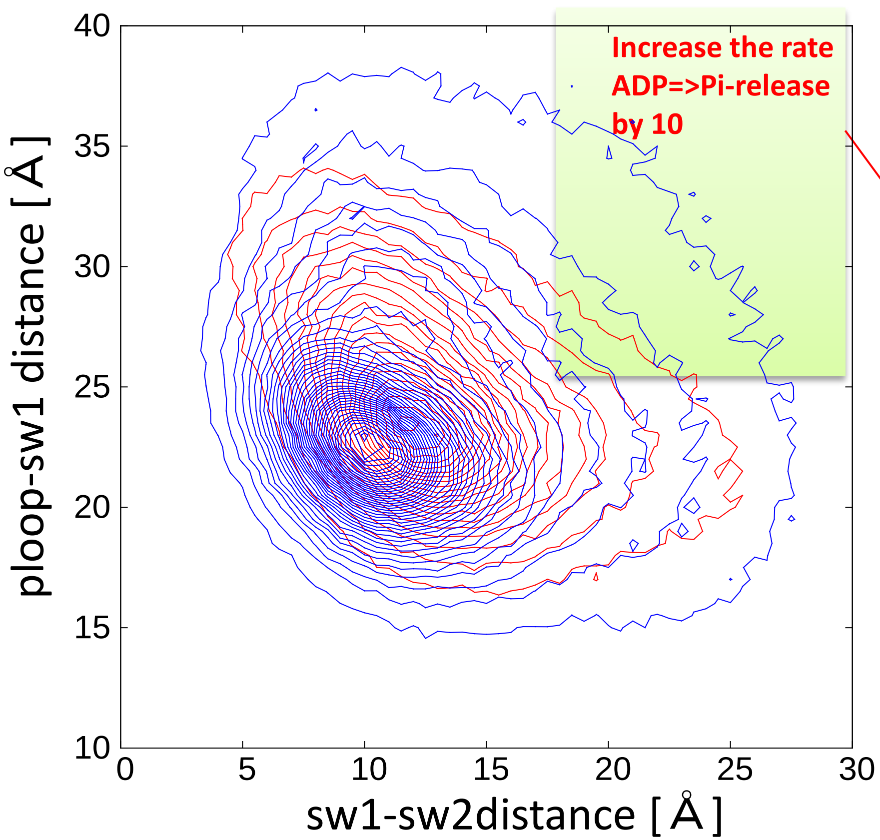
Behavior of the molecular motor under physiological condition

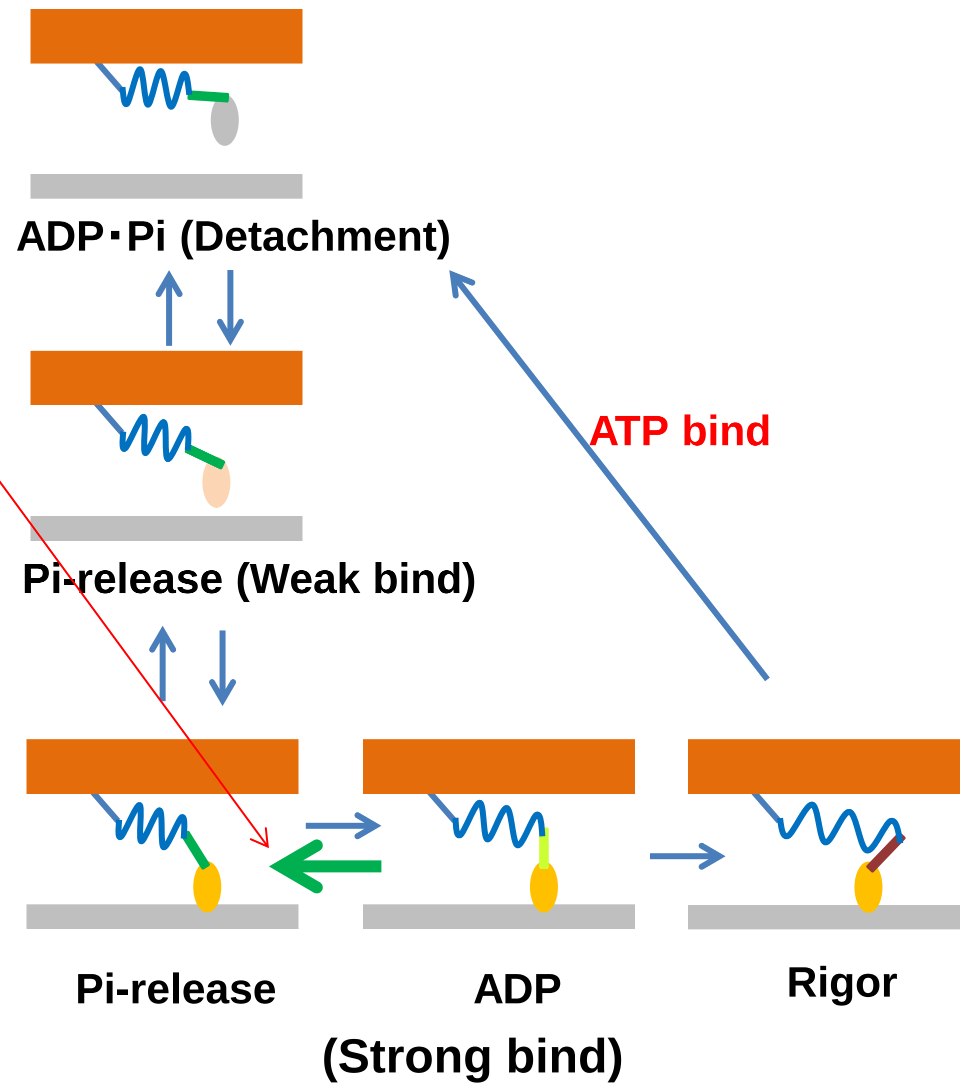


Verification of Pocket Deformation Feedback Model

Contour of the pocket deformation of the basic model

Red: : successful cycles
Blue : unsuccessful cycles



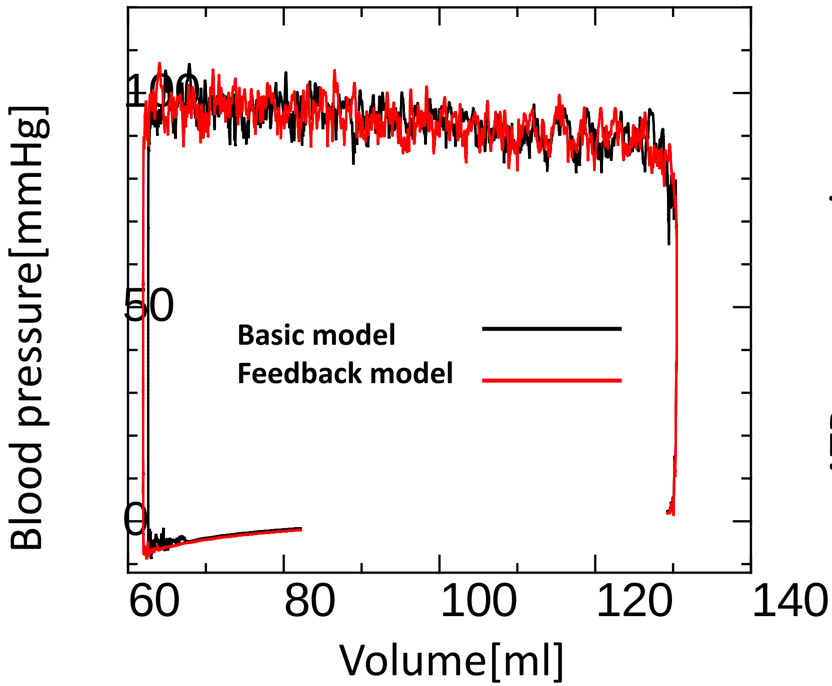


Verification of Pocket Deformation Feedback Model

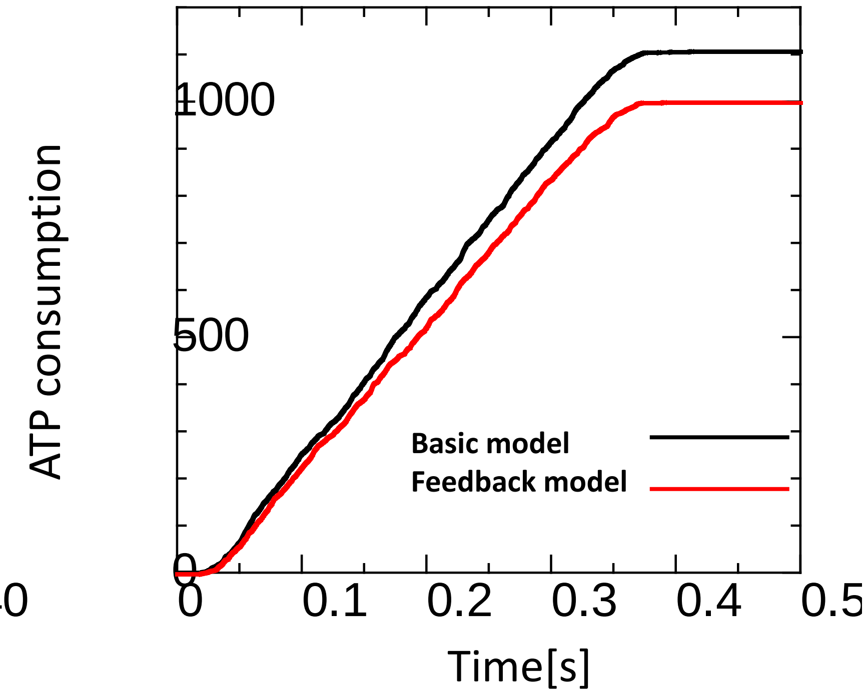
Benefits of the feedback mechanism

1. **3% increase of blood ejection**
2. **10% reduction of ATP consumption**

Pressure Volume loop

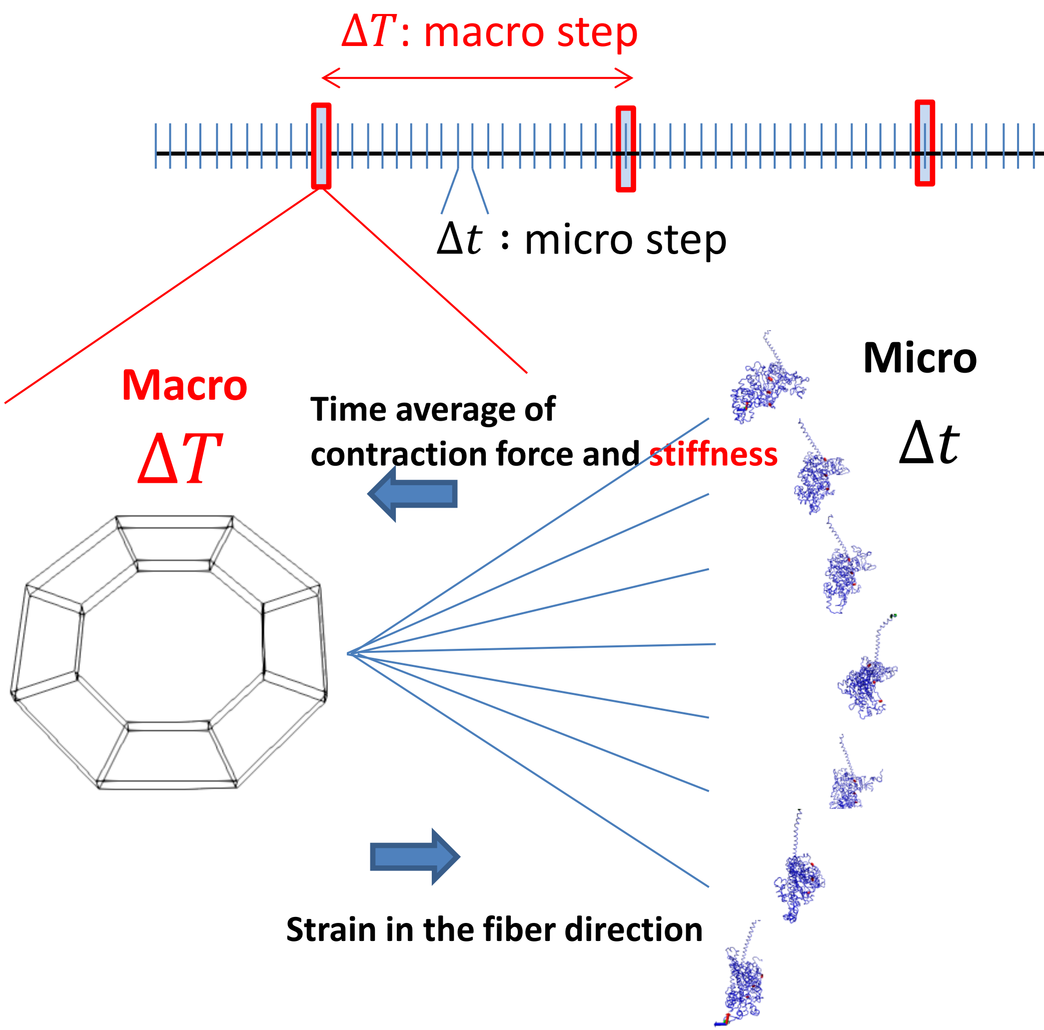


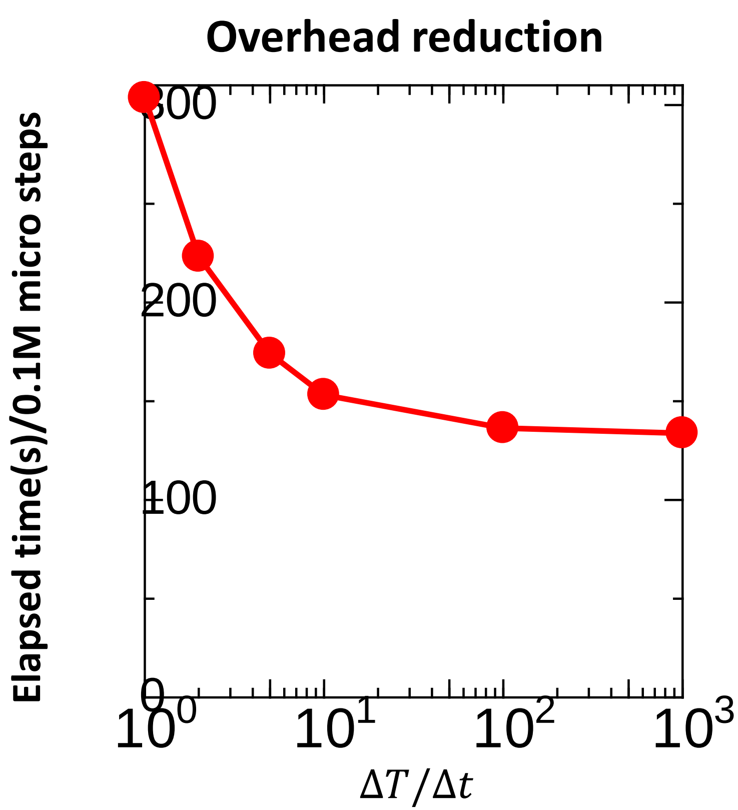
Energy consumption



Coupling technique : Efficiency & Stability

1. Reduction of communication overheads by the multiple time step method
2. Stability by taking the active stiffness





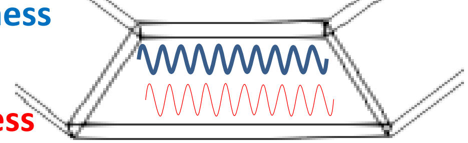
Coupling technique : Efficiency & Stability

1. Reduction of communication overheads by the multiple time step method
2. Stability by taking the active stiffness

Macro

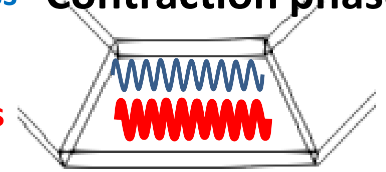
Relaxation phase

Passive stiffness
>
Active stiffness

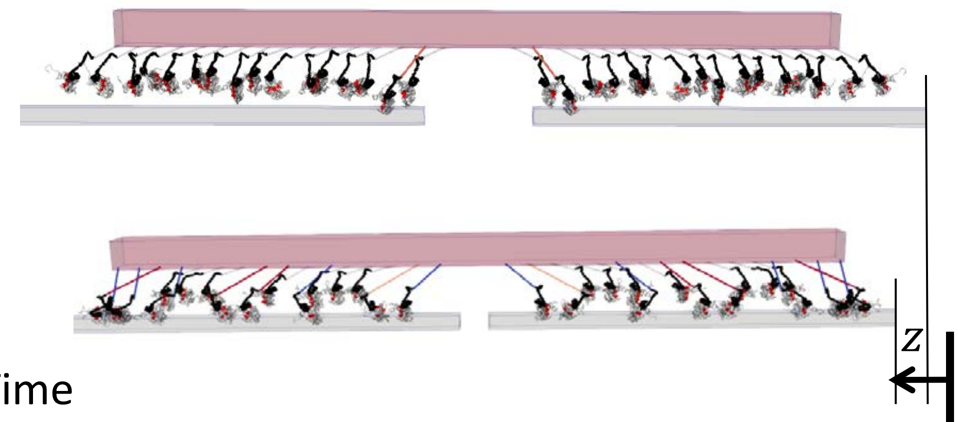


Contraction phase

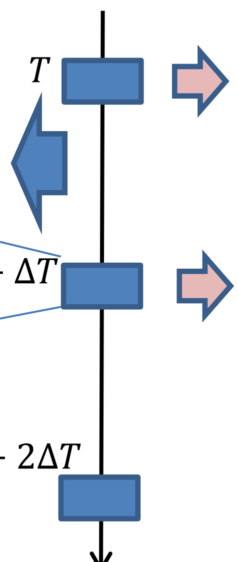
Passive stiffness
<<
Active stiffness



Micro



Time



Force ${}^{T,\Delta T}\overline{\boldsymbol{F}}_{act}$

Stiffness ${}^{T,\Delta T}\overline{\boldsymbol{K}}_{act}$

$$\boldsymbol{C}\frac{{}^{T+\Delta T}\boldsymbol{u}-{}^{T}\boldsymbol{u}}{\Delta T} = \boldsymbol{F}_{pas}({}^{T+\Delta T}\boldsymbol{u})+\boldsymbol{F}_{act}({}^{T+\Delta T}\boldsymbol{u})$$

$$\boldsymbol{F}_{act}\left({}^{T+\Delta T}\boldsymbol{u}\right) = {}^{T,\Delta T}\overline{\boldsymbol{F}}_{act}+{}^{T,\Delta T}\overline{\boldsymbol{K}}_{act}\left({}^{T+\Delta T}\boldsymbol{u}-{}^{T}\boldsymbol{u}\right)$$

Strain in the fiber direction ${}^{T}\epsilon$

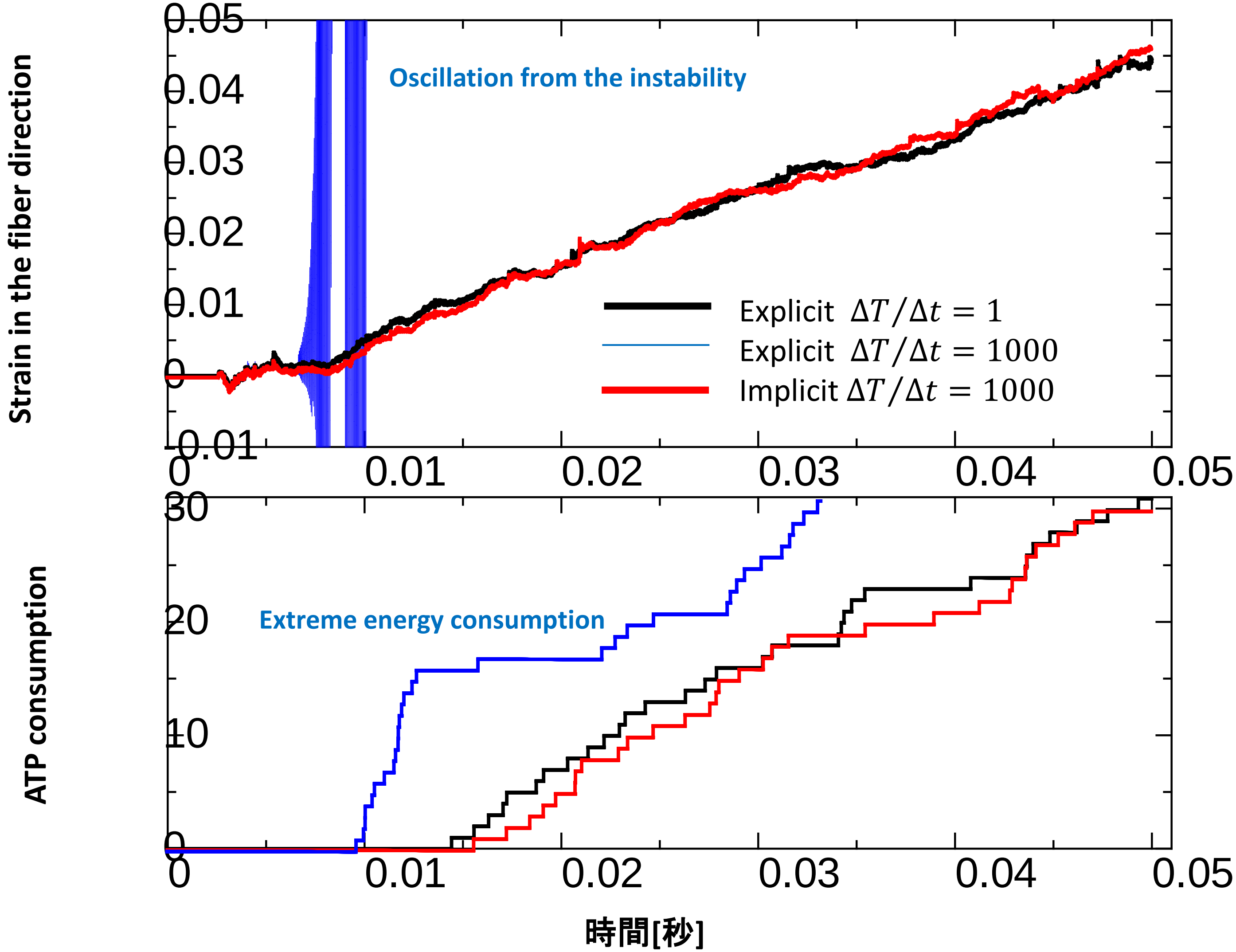
$${}^{T-\Delta T+\omega\Delta T}Z = \frac{SL_0}{2}\left((1-\omega){}^{T-\Delta T}\epsilon+\omega{}^{T}\epsilon\right)$$

Strain in the fiber direction ${}^{T+\Delta T}\epsilon$

$${}^{T+\omega\Delta T}Z = \frac{SL_0}{2}\left((1-\omega){}^{T}\varepsilon+\omega{}^{T+\Delta T}\epsilon\right)$$

Coupling technique : Efficiency & Stability

1. Reduction of communication overheads by the multiple time step method
2. Stability by taking the active stiffness



Concluding Remarks

We constructed a multiscale platform that enables us to analyze the stochastic dynamics of motor proteins under the condition :

that is generated by the protein motors themselves

that can't be made from artificial boundary conditions

Big data & AI

- Huge numerical simulation data of the molecular behavior
- Seeking correlations between the functional parts in the protein motors
- Optimization of parameters of numerical models