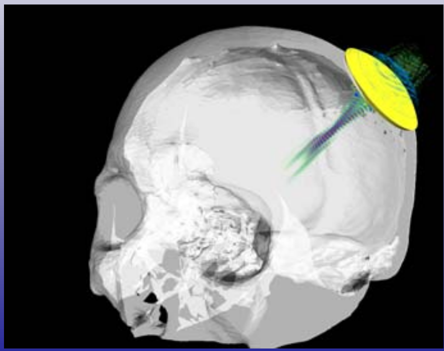
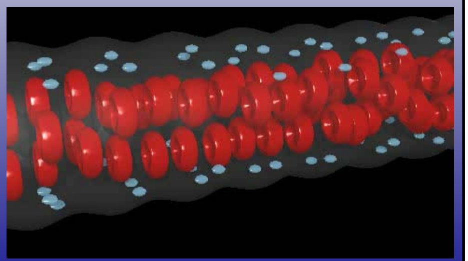
予測医療に向けたマルチスケール人体シミュレータの開発

東京大学　高木　周





予測医療に向けた階層統合シミュレーション

一人一人が健康で活き活きとして社会

↓

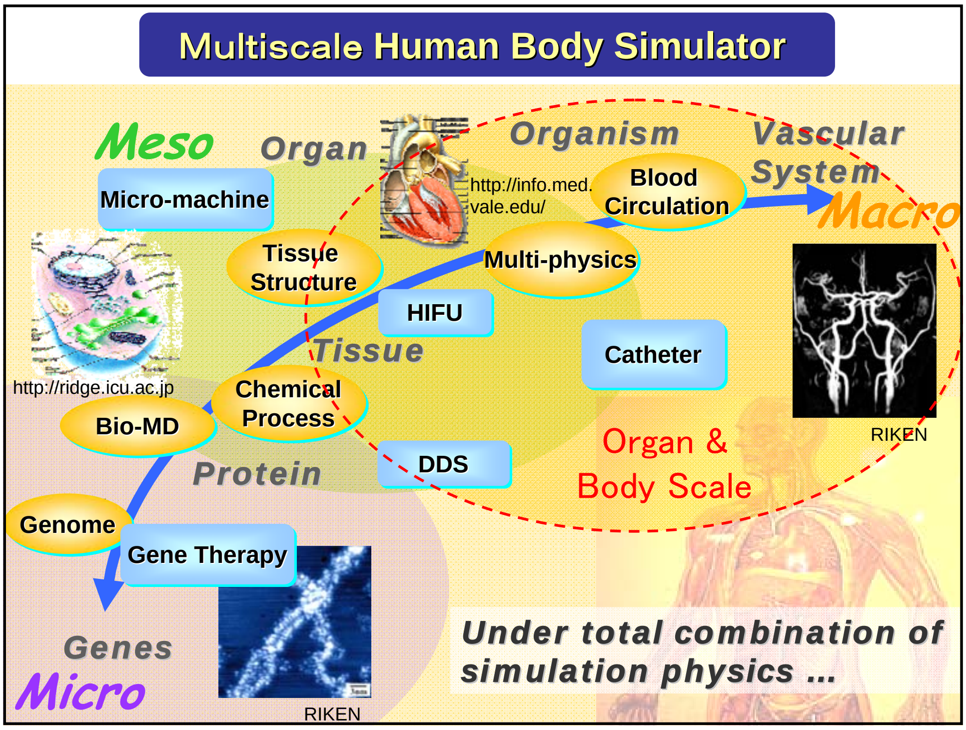
疾患の早期発見・早期治療

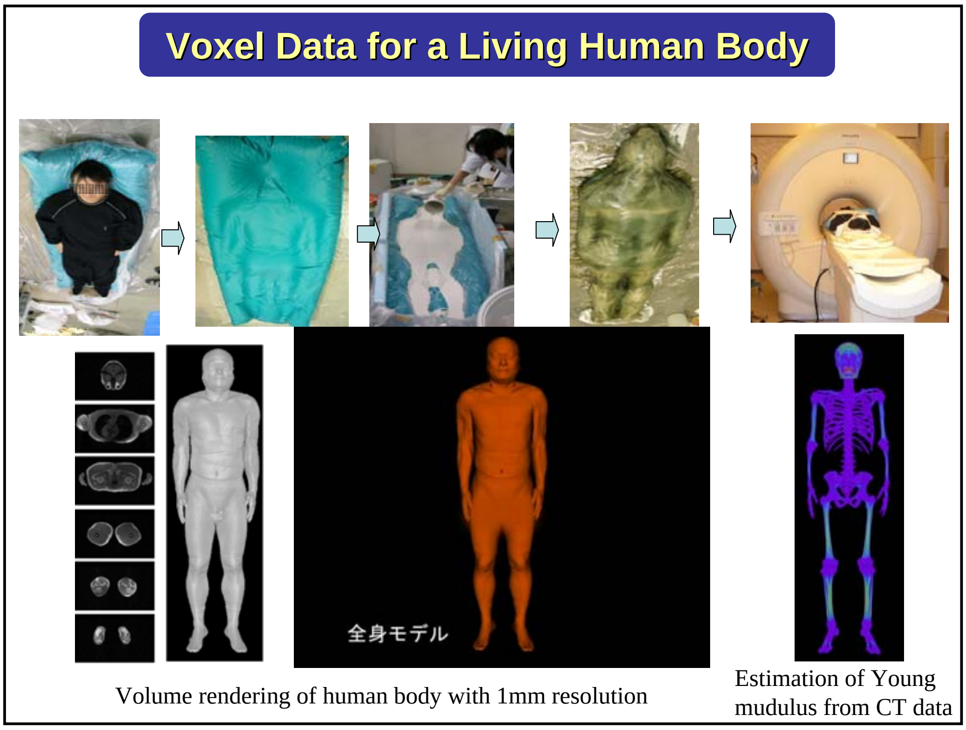
↓

シミュレーションによる
病態の早期予測と治療支援

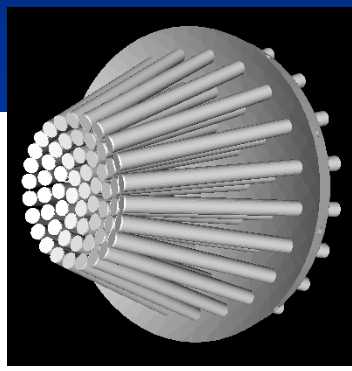
↓

次世代スーパーコンピュータによる
新しい予測医療の構築


Multiscale Human Body Simulator
Meso
Organ
Organism
Vascular System
Macro
Micro-machine
http://info.med.vale.edu/
Blood Circulation
Tissue Structure
Multi-physics
http://ridge.icu.ac.jp
HIFU
Tissue
Catheter
Chemical Process
Bio-MD
RIKEN
Organ & Body Scale
DDS
Protein
Genome
Gene Therapy
Genes
Micro
RIKEN
Under total combination of simulation physics …


Voxel Data for a Living Human Body
全身モデル
Volume rendering of human body with 1mm resolution
Estimation of Young mudulus from CT data

ULTRASOUND THERAPY



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[2]The University of Tokyo, Japan
[3]RIKEN, Japan

RIKEN

THE UNIVERSITY OF TOKYO

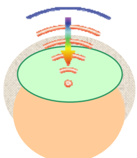
High Intensity Focused Ultrasound therapy

- Prostate cancer
- Breast cancer

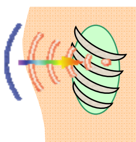
http://www.prostatecancercentre.co.uk/treatments/hifu.html

HIFU therapy has been developed for the treatment of deeply-placed cancer.

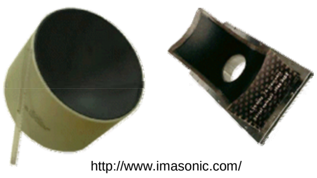
Brain cancer



Liver cancer



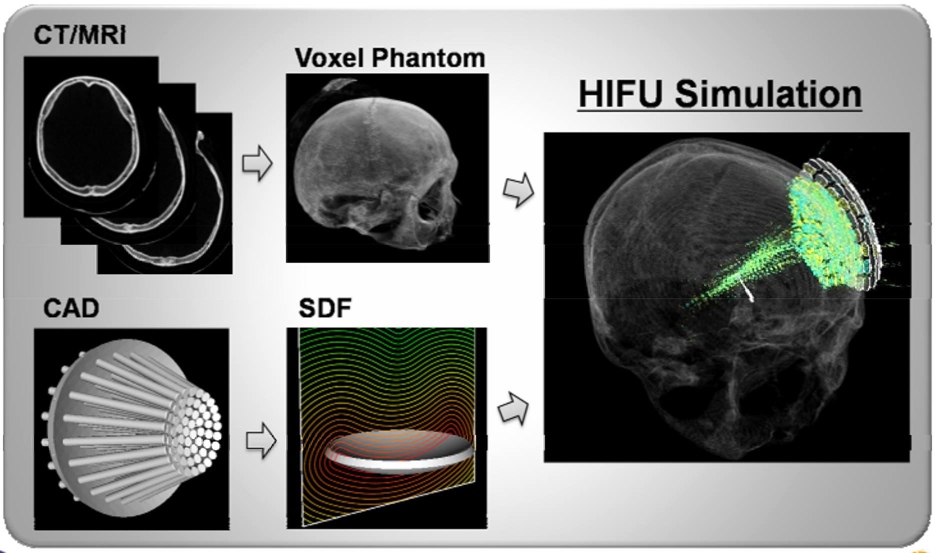
Displacement of focal point due to the reflection and refraction of ultrasound at the interfaces of bones



http://www.imasonic.com/

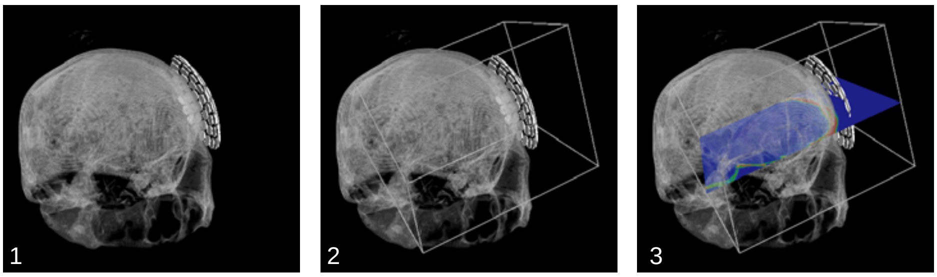
Control of the focal point by an array transducer

HIFU simulator



Analysis based on CT data

Preprocessing in the numerical analysis



1. Place a transducer in the voxel modeled body based on CT data (voxel pitch : 0.976x0.976x0.5[mm])
2. Place a numerical domain around transducer
3. Copy the data of body to the numerical domain

Basic Equations

•The mass conservation:

$$\frac{1}{\rho_m c_{sm}^2}\frac{\partial p}{\partial t} + \nabla\cdot \boldsymbol{u} = -\frac{f_p}{\rho_L}\frac{\partial \rho}{\partial E}\bigg|_{T,p}\frac{\partial E}{\partial t}$$

Volume change of piezoelectric device due to the change of electric potential $\frac{\partial \rho}{\partial E}\Big|_{T,p} < 0$

where $\frac{1}{\rho_m c_{sm}^2} = \frac{f_p}{\rho_p c_{sp}^2} + \frac{f_L}{\rho_L c_{sL}^2} + \frac{f_B}{\rho_B c_{sB}^2}$ and $f_p + f_L + f_B = 1$

•The momentum conservation:

$$\rho_m \frac{\partial \boldsymbol{u}}{\partial t} = -\nabla p \qquad \rho_m = f_p\rho_p + f_L\rho_L + f_B\rho_B$$

•The equation of state: $\rho_L = \rho_L(p)$

Tait equation for EOS of water

$$\frac{p+B}{p_\infty + B} = \left(\frac{\rho_L}{\rho_{L\infty}}\right)^n \qquad p_\infty = 0.1[MPa], \rho_\infty = 1000[kg/m^3]$$

$$B = 304.9[MPa], n = 7.15$$

Numerical Method

- Finite Difference Method
  - Orthogonal mesh
  - Staggered arrangement
  - 4th-central difference method for spatial derivatives
  - 2step explicit method for time marching as follows

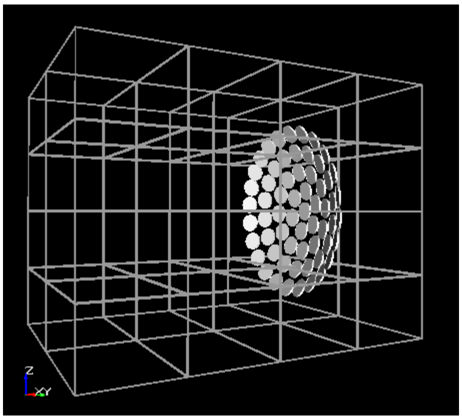
Step 1. update velocity vector $\frac{\boldsymbol{u}^{(n+1)} - \boldsymbol{u}^{(n)}}{\Delta t} = -\frac{1}{\rho_m^{(n)}}\nabla p^{(n)}$

Step 2. update pressure by the updated velocity vector

$$\frac{1}{\rho_m^{(n)} c_{sm}^{(n)2}}\frac{p^{(n+1)} - p^{(n)}}{\Delta t} + \nabla\cdot\boldsymbol{u}^{(n+1)} = -\frac{f_{pi}}{\rho_p}\frac{\partial \rho}{\partial E}\bigg|_{T,p}\frac{\partial E_i}{\partial t}$$

- Boundary condition
  - Perfectly Matched Layer is employed for non-reflecting boundary condition

Numerical Settings



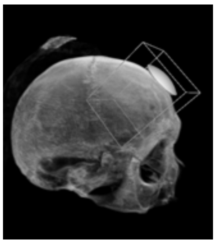
- ➤Parameter of Transducer
  - •Size 10mm x 61 elements
  - •Focus distance 85mm
- ➤Frequency 1MHz (λ~1.5mm in water)

- ➤3-dimensional orthogonal mesh
- ➤Numerical domain 120x160x120(mm)
- ➤Grid number 600x800x600
- ➤PML region 30 grids
- ➤Total time step=10000Δt ($\Delta t=0.1\Delta x/c_s$)

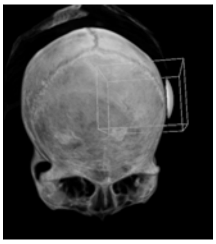
- ➤Ambient pressure 0.1MPa

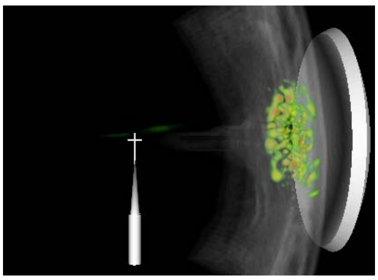
Simulation of Ultrasound Propagation in Skull

Irradiation from the Front



from the Side

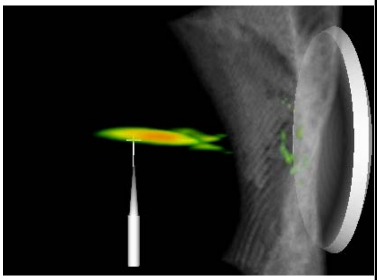




Pressure Distribution

0 2

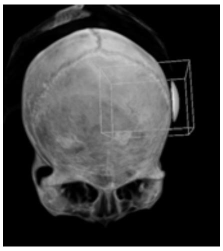
Pressure [MPa]

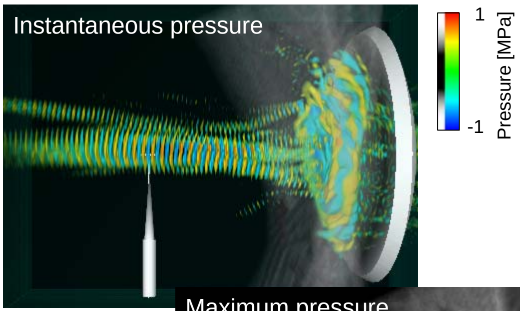


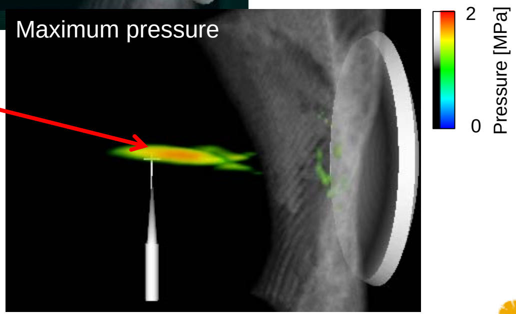
Insufficient intensity at the focal point.

Sufficient Intensity near the focal point

Shift of Focal Point

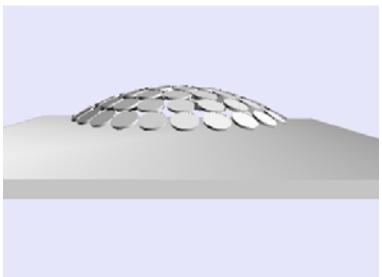




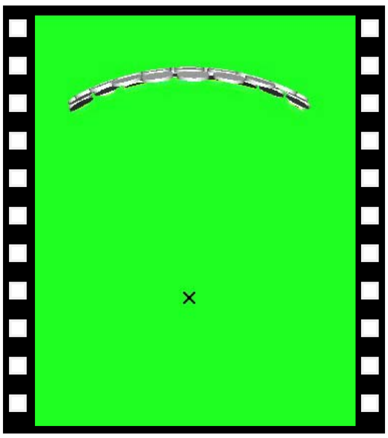


Displacement of the focal point !

US through a bone plate

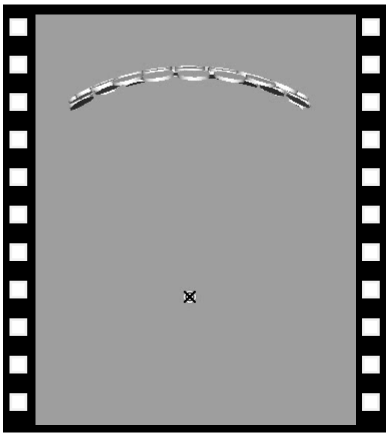


Properties of the bone plate
•Density 1380 kg/m^3
•Impedance 3.75 x 10^6 kg/m^2.s

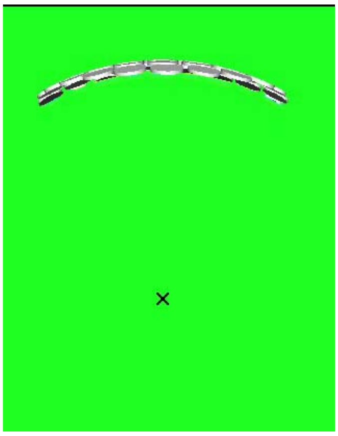


Simulation Assist Time Reversal Method

1. Simulate and Record the ultrasound emitted from the target

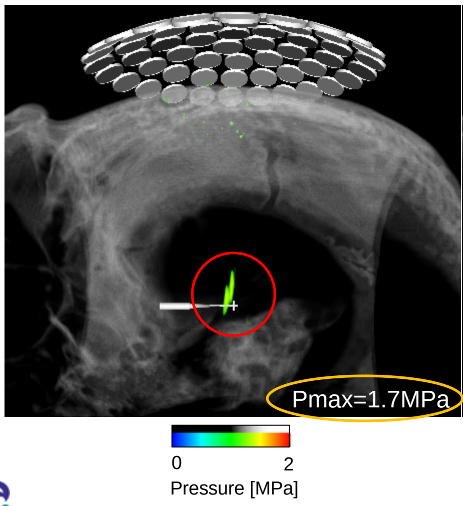


2. Focusing toward the taget

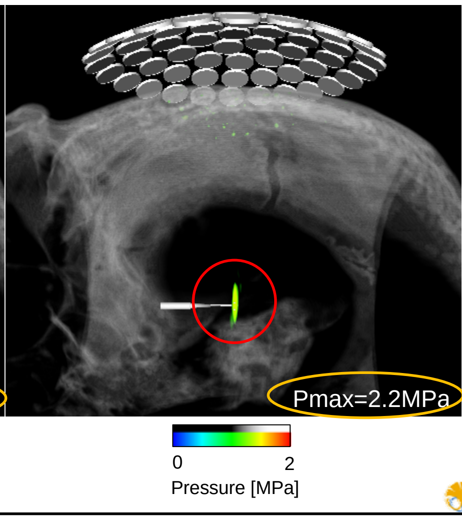


Comparison of the focal point

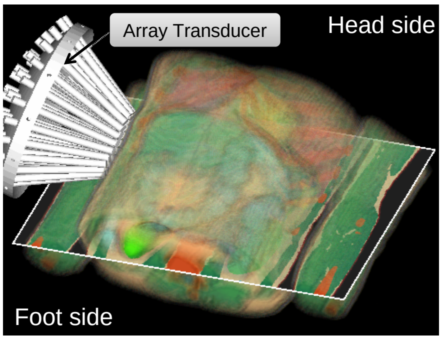
Without phase delay



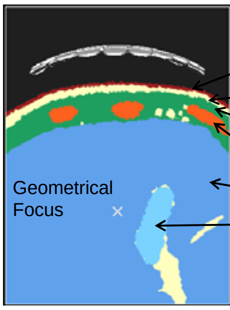
With phase delay



Simulation for Lever Cancer Treatment



Tissues on the path of US propagation



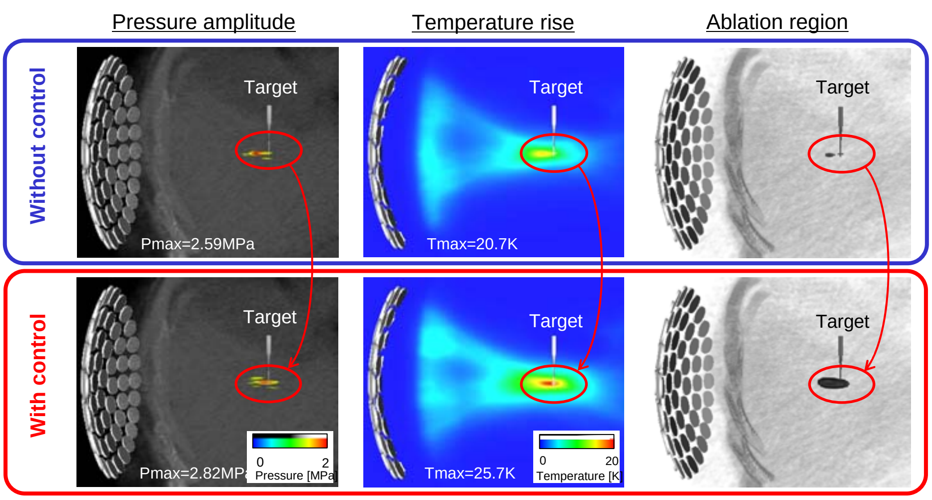
Tissue	Acoustic Impedance [10^6 kg/m^2.s]
Skin（皮膚）	1.76
Adipose(脂肪）	1.38
Muscle（筋肉）	1.66
Bone（骨）	6.98★
Liver（肝臓）	1.69
Gallbladder（胆嚢）	1.48

➢Array transducer
- •Size 10mm x 61 piezo elements
- •Focal distance 85mm
- •Frequency 1MHz

➢Numerical domain
- •Size 120x160x120(mm)
- •3-dimensional orthogonal mesh with 600x800x600 = 288 M grid points

➢Volume data of human body
- Based on CT & MRI data
- Including ID of tissues
- Constructed by RIKEN Computational Biomechanics Project

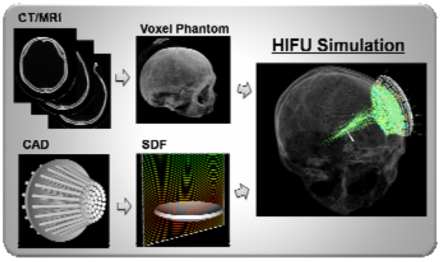
Focus control and ablation region

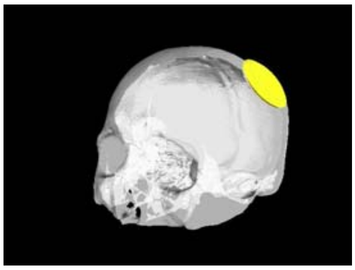


Pmax is 9% UP and Temperature is 25% UP by the control.

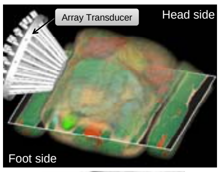
Tissue is effectively ablated.

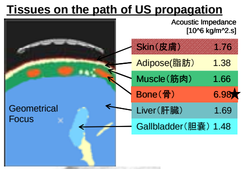
超音波治療器開発に向けたシミュレーションツールの整備



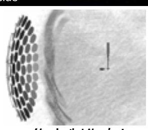


医用画像データとCADデータを直接利用するHIFUシミュレータ

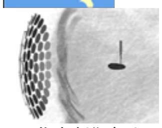




実機設計のための詳細シミュレーション



焦点制御なし



焦点制御あり

時間反転法による肝腫瘍焼灼シミュレーション

現状：低解像度・ミリ秒スケール超音波伝播シミュレーション

「京」では：高解像度・実機設計用詳細計算＆秒スケール腫瘍焼灼シミュレーション

Finite Difference Approach for FSI using Eulerian Description

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1. Organ and Body Scale Team, CSRP, RIKEN
2. Dept. of Mechanical Engineering, The University of Tokyo

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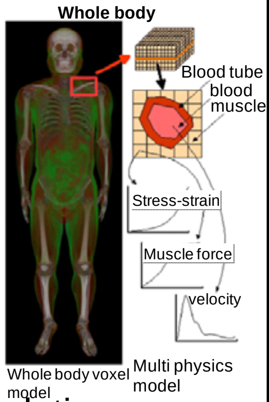
Background

Fluid-Structure coupling analysis of living body



Diagnostic image (CT, MRI)

⇩

Voxel data (**Volume Fraction of Constituents**)
representing multi-component geometry

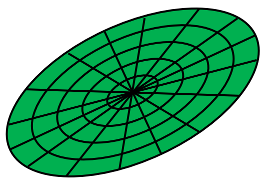
⇩ **without Mesh Generation**

(Finite-Difference or Finite-Element) Simulation
on Eulerian frame

Objective

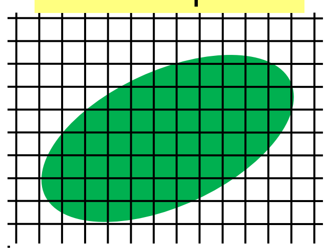
To develop a numerical simulation method
for fluid-structure coupling problems
based on full Eulerian formulation
using a Finite Difference scheme.

Lagrangian points



sit on Material

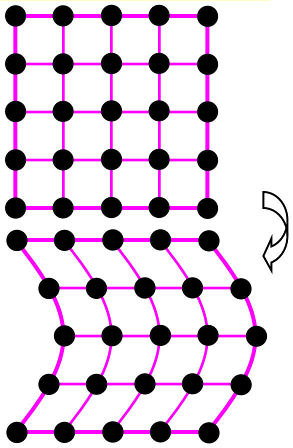
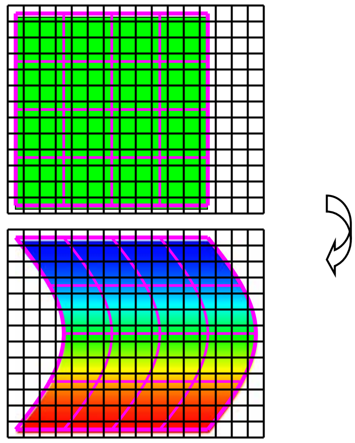
Eulerian points



sit on Laboratory

for Fluid-Solid Interaction Problems

How is the solid deformation described?

Lagrangian frame	Eulerian frame
	
by the displacement of material points themselves	by left Cauchy-Green deformation tensor

Basic equations

$$\frac{\partial v_i}{\partial x_i}=0,\quad \rho_m\left(\frac{\partial v_i}{\partial t}+v_j\frac{\partial v_i}{\partial x_j}\right)=-\frac{\partial p}{\partial x_i}+\frac{\partial \sigma'_{m,ij}}{\partial x_j}+f_i,$$

Cauchy 's stress tensor $\sigma'_{m,ij}=(1-\phi_s)\sigma'_{f,ij}+\phi_s\sigma'_{s,ij},$

$$\sigma'_{f,ij}=2\eta D_{ij},$$

$$D_{ij}=\frac{1}{2}\left(\frac{\partial v_i}{\partial x_j}+\frac{\partial v_j}{\partial x_i}\right),$$

strain rate (D_{ij})

$$\frac{\mathrm{D}\phi_s}{\mathrm{D}t}=0,$$

solid volume fraction (ϕ_s)

$$\frac{\mathrm{D}\tilde{B}_{ij}}{\mathrm{D}t}-\frac{\partial v_i}{\partial x_k}\tilde{B}_{kj}-\frac{\partial v_j}{\partial x_k}\tilde{B}_{ki}=0,$$

$$\tilde{B}_{ij}=\begin{cases}\phi_s^{\alpha}B_{ij} & \text{for } \phi_s\ge\phi_{\min}\\ 0 & \text{for } \phi_s<\phi_{\min}\end{cases}$$

$$\tilde{B}_{ij}=\phi_s^{1/2}\delta_{ij}\quad \text{at } t=0,$$

left Cauchy-Green deformation tensor (B_{ij})

$$\mathbf{B}=\mathbf{F}\cdot\mathbf{F}^T,\quad F_{ij}=\frac{\partial x_i}{\partial X_j},$$

Hyperelastic solid stress:

St. Venant-Kirchhoff model: $\phi_s\boldsymbol{\sigma}'_s=G(\phi_s^{1-2\alpha}\tilde{\mathbf{B}}\cdot\tilde{\mathbf{B}}-\phi_s^{1-\alpha}\tilde{\mathbf{B}})'.$

(Linear) Mooney-Rivlin model: $\phi_s\boldsymbol{\sigma}'_s=G\phi_s^{1-\alpha}\tilde{\mathbf{B}}'+2c_2\phi_s^{1-2\alpha}\left(\mathrm{tr}(\tilde{\mathbf{B}})\tilde{\mathbf{B}}-\tilde{\mathbf{B}}\cdot\tilde{\mathbf{B}}\right)'.$

Algorithm

(based on SMAC method)

1. compute VOF and modified left Cauchy-Green deformation

$$\phi_s^{N+1} = \phi_s^N - (\Delta t)\left(\frac{3}{2}\mathbf{v}^N \cdot \nabla \phi_s^N - \frac{1}{2}\mathbf{v}^{N-1} \cdot \nabla \phi_s^{N-1}\right),$$

$$\tilde{\mathbf{B}}^{N+1} = \tilde{\mathbf{B}}^N - (\Delta t)\left\{\frac{3}{2}\left(\mathbf{v}^N \cdot \nabla \tilde{\mathbf{B}}^N - \mathbf{L}^N \cdot \tilde{\mathbf{B}}^N - \tilde{\mathbf{B}}^N \cdot \left(\mathbf{L}^T\right)^N\right) - \frac{1}{2}\left(\mathbf{v}^{N-1} \cdot \nabla \tilde{\mathbf{B}}^{N-1} - \mathbf{L}^{N-1} \cdot \tilde{\mathbf{B}}^{N-1} - \tilde{\mathbf{B}}^{N-1} \cdot \left(\mathbf{L}^T\right)^{N-1}\right)\right\},$$

$$\phi_f^{N+1} = 1 - \phi_s^{N+1}, \quad \rho_m^{N+1} = \rho_s \phi_s^{N+1} + \rho_f \phi_f^{N+1},$$

2nd-order Adams-Bashforth
5th-order WENO

2. predict velocity and stress

2nd-order Adams-Bashforth
+2nd-order Crank-Nicolson,
2nd-order central difference

$$\mathbf{v}^* = \mathbf{v}^N - (\Delta t)\nabla \tilde{P}^N - (\Delta t)\left(\frac{3}{2}\mathbf{v}^N \cdot \nabla \mathbf{v}^N - \frac{1}{2}\mathbf{v}^{N-1} \cdot \nabla \mathbf{v}^{N-1}\right) + \frac{2(\Delta t)}{\rho_m^{N+1} + \rho_m^N}\left(\frac{1}{2}\nabla \cdot \boldsymbol{\sigma}^* + \frac{1}{2}\nabla \cdot \boldsymbol{\sigma}^N + f\right)$$

$$\boldsymbol{\sigma}^* = \eta \phi_f^{N+1}\left(\nabla \mathbf{v}^* + (\nabla \mathbf{v}^*)^T\right) + G(\tilde{\mathbf{B}}^{N+1} \cdot \tilde{\mathbf{B}}^{N+1} - \left(\phi_s^{N+1}\right)^{1/2} \tilde{\mathbf{B}}^{N+1}),$$

3. solve pressure equation

$$\nabla^2 \varphi = \frac{\nabla \cdot \mathbf{v}^*}{(\Delta t)}, \quad \tilde{P}^{N+1} = \tilde{P}^N + \varphi, \quad \text{(where } \nabla \tilde{P} \equiv \frac{1}{\rho_m}\nabla p \text{)}$$

4. modify velocity and stress

$$\mathbf{v}^{N+1} = \mathbf{v}^* - (\Delta t)\nabla \varphi,$$

$$\boldsymbol{\sigma}^{N+1} = \boldsymbol{\sigma}^* - 2\eta(\Delta t)\phi_f^{N+1}\nabla\nabla \varphi,$$

Lid-driven cavity

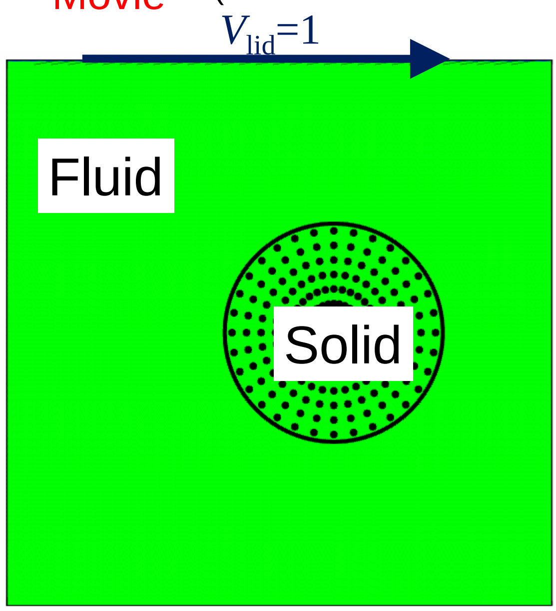
Movie (solid motion in fluid flow)

$\rho_s = \rho_f = L_s = L_f = 1$, $\mu = 10^{-2}$, $G = 0.1$

neo-Hookean

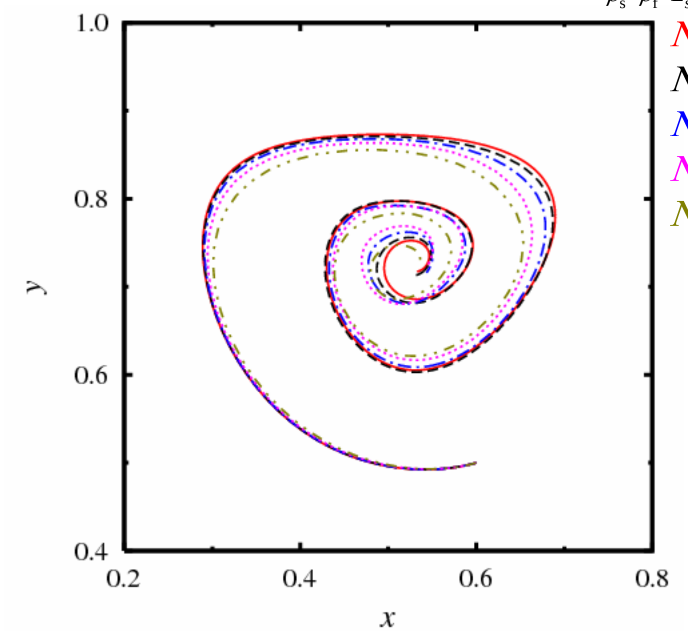
● material points (tracers)

vector: velocity
closed curve: interface
contour: vorticity (spin)



Trajectory of the centroid

$\rho_s=\rho_f=L_s=L_f=1$, $\mu=10^{-2}$, $G=0.1$



N_xxN_y=512x512

N_xxN_y=256x256

N_xxN_y=128x128

N_xxN_y=64x64

N_xxN_y=32x32

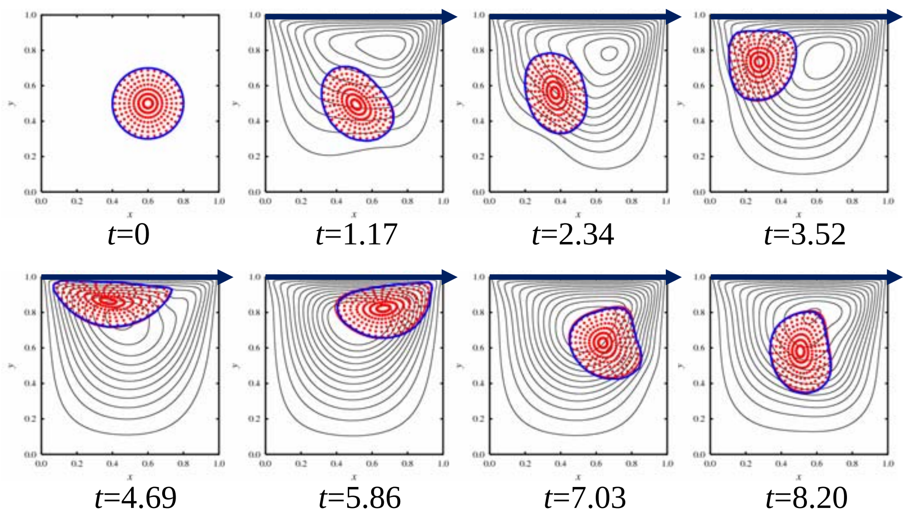
Comparison with Zhao, Freund & Moser (JCP 2008)

N_xxN_y=512x512

$\rho_s=\rho_f=L_s=L_f=1$, $\mu=10^{-2}$, $G=0.1$

– Zhao *et al.* (Lagrangian for solid)

– Present (full Eulerian)

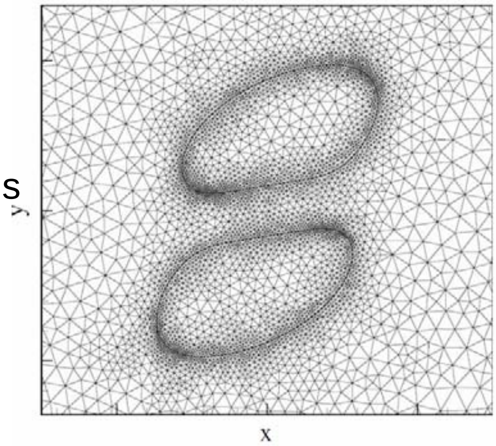


Another comparison with available numerical data

Gao & Hu (2009)
J. Comput. Phys. **228,** 2132.

particle-particle interactions in a shear flow

full Lagrangian

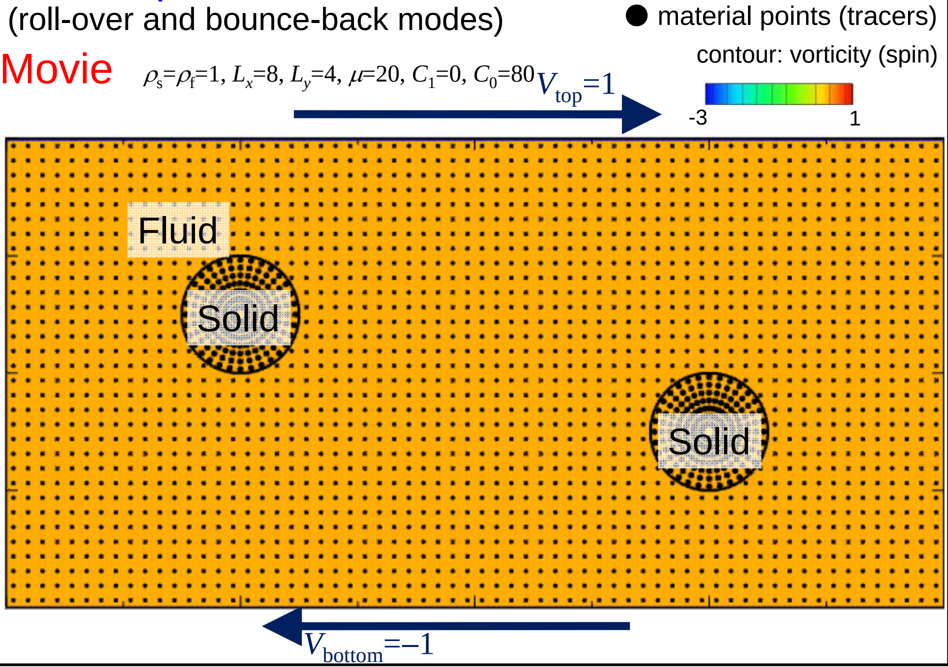


Particle-particle interactions in a shear flow

(roll-over and bounce-back modes)

Movie

$\rho_s = \rho_f = 1$, $L_x = 8$, $L_y = 4$, $\mu = 20$, $C_1 = 0$, $C_0 = 80$

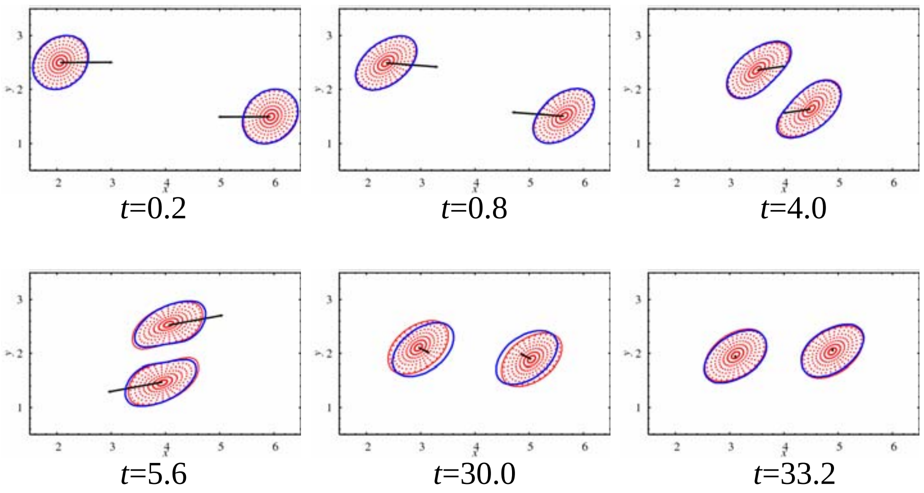


Comparison with Gao & Hu (JCP2009)'s results

– Gao & Hu (full Lagrangian)

– Present (full Eulerian)

N_xxN_y=1024x512



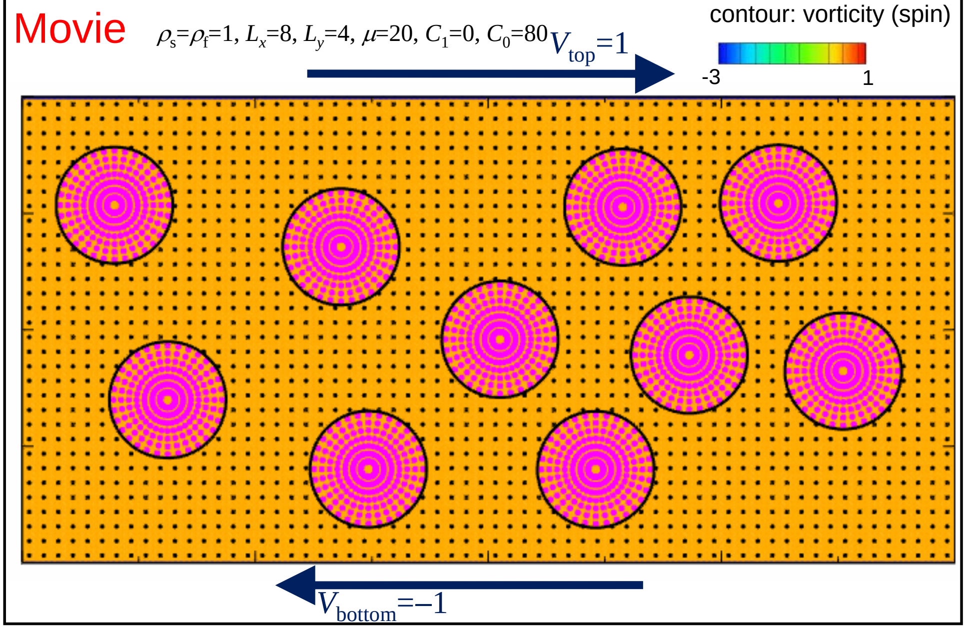
Extension to 10-particle system

● material points (tracers)

contour: vorticity (spin)

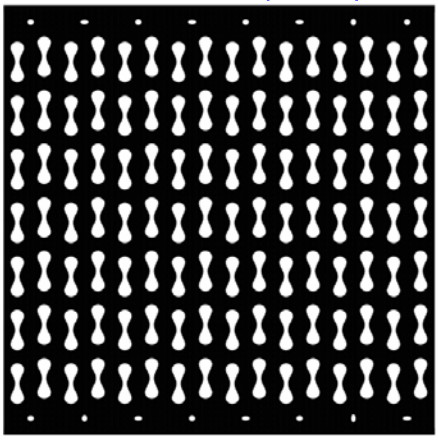
Movie

$\rho_s=\rho_f=1$, $L_x=8$, $L_y=4$, $\mu=20$, $C_1=0$, $C_0=80$

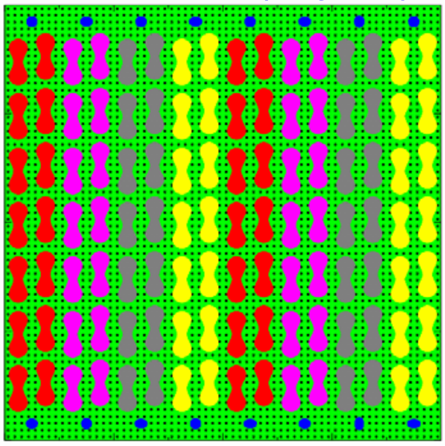


Toward the Thrombus Simulator

Voxel data (virtual)



Fluid-Structure coupling analysis



WITHOUT mesh generation procedure

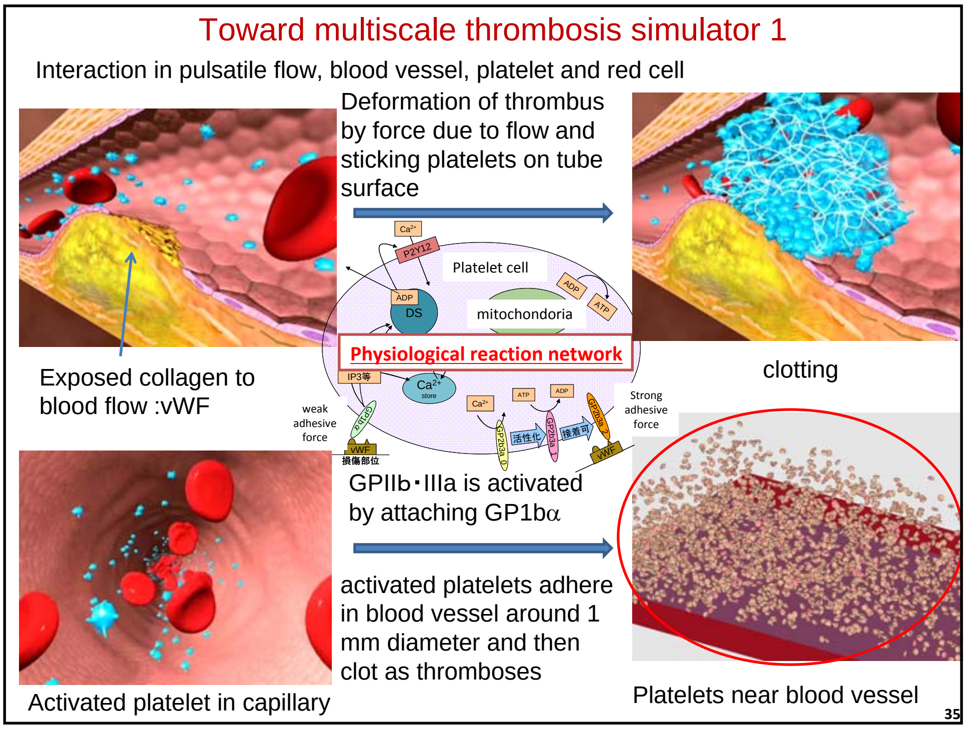
Development of Multiscale Thrombus simulator

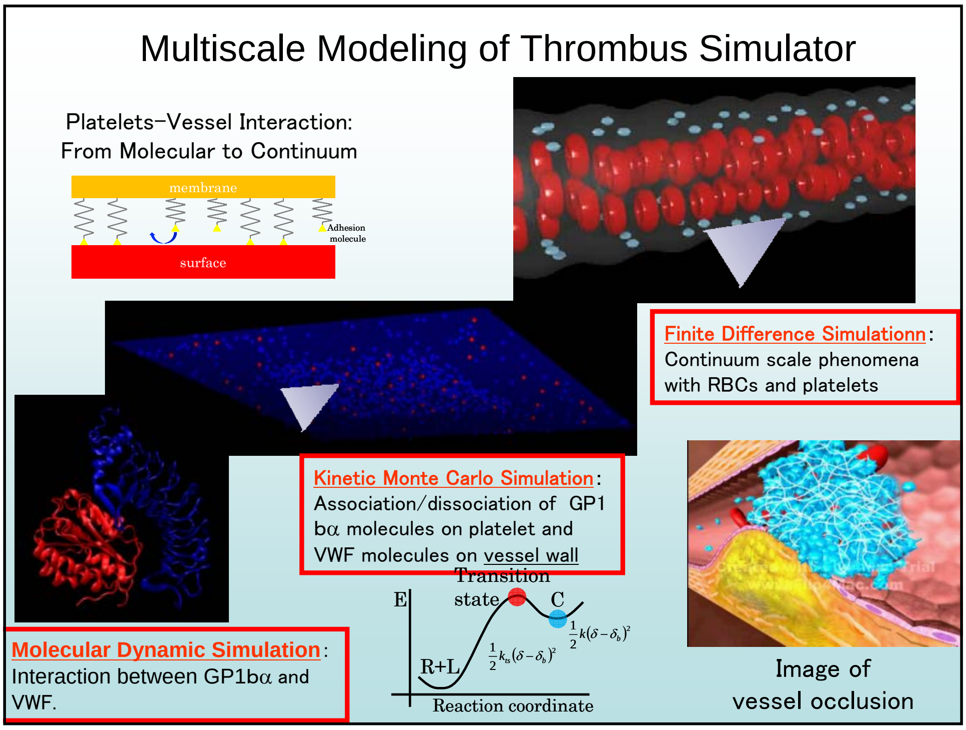
Kazuyasu Sugiyama[2], Satoshi II[2],
Seiji Shiozaki[1], Shinya Goto[3], Shu Takagi[1,2]

1. Organ and Body Scale Team, CSRP, RIKEN
2. Dept. of Mechanical Engineering, The University of Tokyo
3. School of Medicine, Tokai University

RIKEN

THE UNIVERSITY OF TOKYO


Toward multiscale thrombosis simulator 1
Interaction in pulsatile flow, blood vessel, platelet and red cell
Deformation of thrombus by force due to flow and sticking platelets on tube surface
Platelet cell
mitochondoria
Physiological reaction network
Exposed collagen to blood flow :vWF
weak adhesive force
Strong adhesive force
clotting
GPIIb･IIIa is activated by attaching GP1bα
activated platelets adhere in blood vessel around 1 mm diameter and then clot as thromboses
Activated platelet in capillary
Platelets near blood vessel
35


Multiscale Modeling of Thrombus Simulator
Platelets-Vessel Interaction:
From Molecular to Continuum
membrane
Adhesion molecule
surface
Finite Difference Simulationn: Continuum scale phenomena with RBCs and platelets
Kinetic Monte Carlo Simulation: Association/dissociation of GP1bα molecules on platelet and VWF molecules on vessel wall
Transition state
E
C
R+L
Reaction coordinate
Molecular Dynamic Simulation: Interaction between GP1bα and VWF.
Image of vessel occlusion

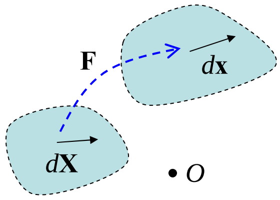
Basic description*,**

*Skalak *et al.*, *Biophys. J.*, 13 (1973) 245.
**Barthés-Biesel *et al.*, *J. Fluid Mech.*, 113 (1981) 251.

$\mathbf{X}$: reference configuration

$\mathbf{x}$: current configuration

$\mathbf{F} = \dfrac{\partial \mathbf{x}}{\partial \mathbf{X}}$: deformation gradient tensor



$\mathbf{P} = \mathbf{I} - \mathbf{nn}$: surface projection tensor in $\mathbf{x}$

$\mathbf{P}_R = \mathbf{I} - \mathbf{n}_R\mathbf{n}_R$: surface projection tensor in $\mathbf{X}$

$\mathbf{F}_s = \mathbf{P}\cdot\mathbf{F}\cdot\mathbf{P}_R$: surface def. gradient tensor $(\mathbf{n}\cdot\mathbf{F}_s = \mathbf{F}_s\cdot\mathbf{n}_R = \mathbf{0})$

$\mathbf{B}_s = \mathbf{F}_s\cdot\mathbf{F}_s^T = \mathbf{P}\cdot\mathbf{F}\cdot\mathbf{P}_R\cdot\mathbf{F}^T\cdot\mathbf{P} \rightarrow \mathbf{P}\cdot\mathbf{G}_s\cdot\mathbf{P}$: surface left C.-G. def. tensor

$\mathbf{G}_s = \mathbf{F}\cdot\mathbf{P}_R\cdot\mathbf{F}^T$

$$\frac{D\mathbf{P}_R}{Dt} = \mathbf{0},\quad \frac{D\mathbf{F}}{Dt} = \nabla\mathbf{v}^T\cdot\mathbf{F} \longrightarrow \boxed{\frac{D\mathbf{G}_s}{Dt} = \nabla\mathbf{v}^T\cdot\mathbf{G}_s + \mathbf{G}_s\cdot\nabla\mathbf{v}}$$

Membrane stress

*Barthés-Biesel *et al.*, *J. Fluid Mech.*, 113 (1981) 251.
**Skalak *et al.*, *Biophys. J.*, 13 (1973) 245.
***Pozrikidis, *J. Fluid. Mech.*, 440 (2001) 269.

$\boxed{\boldsymbol{\tau} + \mathbf{qn}}$

In-plane stress

$$\boldsymbol{\tau} = \frac{2}{\sqrt{c_2}}\left(\frac{\partial W_s}{\partial c_1}\mathbf{B}_s + c_2\frac{\partial W_s}{\partial c_2}\mathbf{P}\right)$$

$$c_1 = \mathrm{tr}(\mathbf{B}_s) - 1,\quad c_2 = \frac{1}{2}\left(\mathrm{tr}(\mathbf{B}_s)^2 - \mathrm{tr}(\mathbf{B}_s{}^2)\right)$$

(Neo-Hookean model*)

$$W_s = \frac{E_s}{6}\left(c_1 + \frac{1}{c_2} - 2\right)$$

(Skalak model**)

$$W_s = \frac{E_s}{8}\left(c_1{}^2 + \alpha c_2{}^2 - 2(\alpha+1)c_2 + \alpha + 1\right)$$

Bending stress***

$\mathbf{q} = (\mathbf{P}\cdot\nabla\cdot\mathbf{m})\cdot\mathbf{P}$: transverse shear tension

$\mathbf{m} = E_b\left(\boldsymbol{\kappa} - \kappa_R\mathbf{P}\right)$: bending moment with linear constitutive law

$\boldsymbol{\kappa} = -\mathbf{P}\cdot\nabla\mathbf{n}$: Cartesian curvature tensor

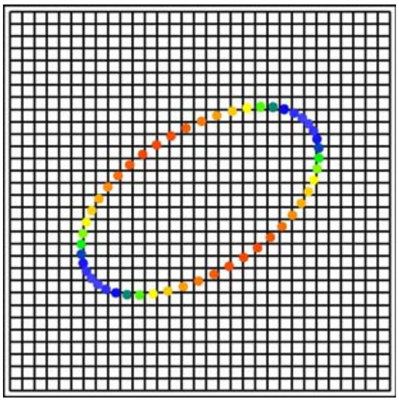
$\kappa_R = -\dfrac{1}{2}\mathrm{tr}(\mathbf{P}_R\cdot\nabla\mathbf{n}_R)$: reference mean curvature

How to treat the membrane?

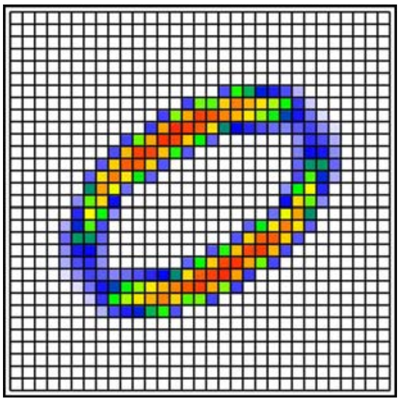
* Peskin, J. Comput. Phys., 10 (1972) 252-271.

✓Fluid field is obtained on the fixed Cartesian mesh

✓Lagrangian frame
(immersed boundary method*)



✓Eulerian frame



Color: deformation quantity $\mathrm{tr}\left(\mathbf{B}_S\right)$

Eulerian fluid-membrane interaction model*

* Ii *et al.*, *Commun. Comput. Phys.*, submitted (2010).

$$\frac{\partial \phi}{\partial t} + \mathbf{v} \cdot \nabla \phi = 0$$

$$\nabla \cdot \mathbf{v} = 0$$

$$\rho \left(\frac{\partial \mathbf{v}}{\partial t} + \mathbf{v} \cdot \nabla \mathbf{v} \right) = -\nabla p + \nabla \cdot (\mu (\nabla \mathbf{v} + \nabla \mathbf{v}^T)) + \mathbf{f}$$

$$\frac{\partial \mathbf{G}_s}{\partial t} + \mathbf{v} \cdot \nabla \mathbf{G}_s = \nabla \mathbf{v}^T \cdot \mathbf{G}_s + \mathbf{G}_s \cdot \nabla \mathbf{v}$$

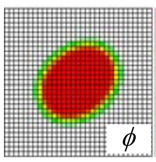
$$\frac{\partial \kappa_R}{\partial t} + \mathbf{v} \cdot \nabla \kappa_R = 0$$

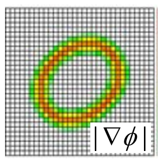
$$\mathbf{f} = |\nabla \phi| \nabla \cdot (\boldsymbol{\tau}(\mathbf{B}_s) + \mathbf{q}(\kappa_R)\mathbf{n})$$

$$\mathbf{n} = \frac{\nabla \phi}{|\nabla \phi|}, \quad \boldsymbol{\kappa} = -\nabla \mathbf{n},$$

$$\mathbf{B}_s = (\mathbf{I} - \mathbf{nn}) \cdot \mathbf{G}_s \cdot (\mathbf{I} - \mathbf{nn})$$

- ϕ : VOF function
- $\mathbf{v}$: velocity vector
- p : pressure
- ρ : density
- μ : dynamic viscosity
- κ_R : reference mean curvature
- $\mathbf{n}$: unit normal vector
- $\boldsymbol{\kappa}$: current Cartesian curvature tensor
- $\mathbf{B}_s$: surface left C.-G. def. tensor
- $\boldsymbol{\tau}$: membrane in-plane stress
- $\mathbf{q}$: transverse shear tension





Validation

Membrane capsule in shear flow

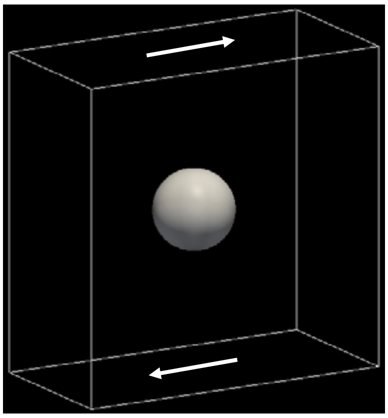
Spherical membrane
(neo-Hookean model)

$[-4,4]\times[-2,2]\times[-4,4]$

density: $\rho = 1$
radius: $a = 1$
shear rate: $\dot{\gamma} = 1$

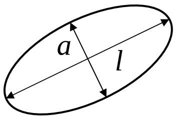
Reynolds number: $\mathrm{Re} = \dfrac{\rho a^2 \dot{\gamma}}{\mu} = 0.01$

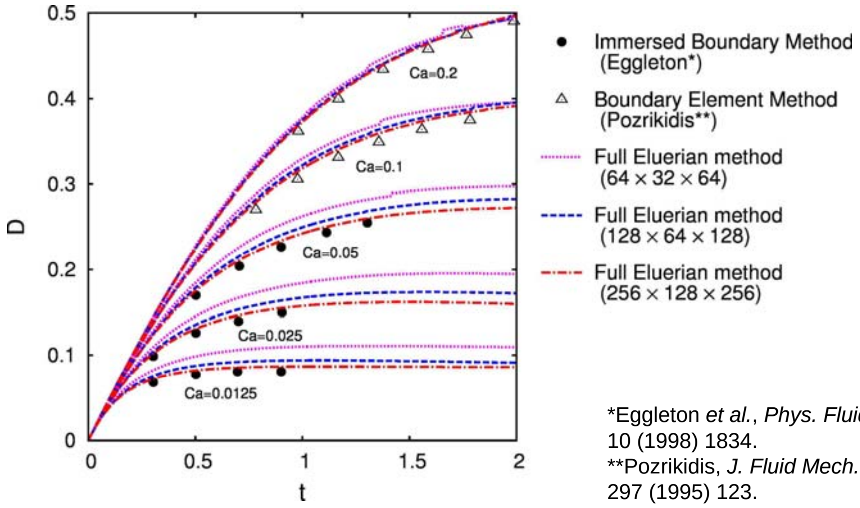
Capillary number: $\mathrm{Ca} = \dfrac{\mu a \dot{\gamma}}{E_s}$



Time history of the deformation parameter *D*

$$D = \frac{l-a}{l+a}$$





*Eggleton *et al.*, *Phys. Fluids,* 10 (1998) 1834.
**Pozrikidis, *J. Fluid Mech.,* 297 (1995) 123.

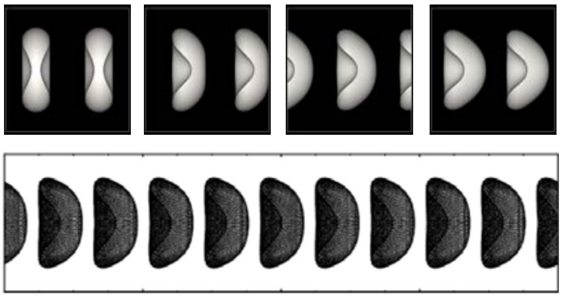
Comparison with an existing result*

*Gong *et al.*, *J. Biomech. Eng.*, 131 (2009) 074504.

case 1

Present

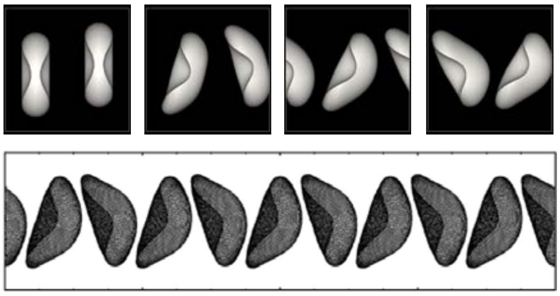
Reference*



case 2

Present

Reference*

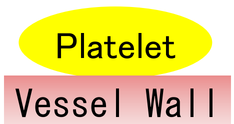


Kinetic Monte Carlo Simulation of Cell adsorption/desorption on vessel wall

Jianrong Li, et. al(2009)

$$R+L \underset{k_r}{\overset{k_f}{\rightleftarrows}} C$$

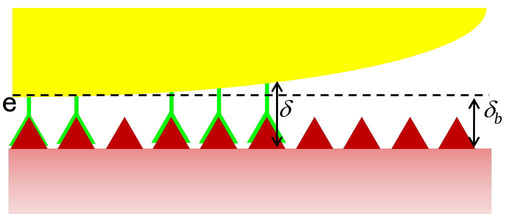
R: Receptor
L: Ligand
C: R–L complex
k_f: Binding React. Rate Cnst.
k_r: Dissosc. React. Rate Cnst.



$$\frac{dC}{dt} = k_f RL - k_r C$$

Receptor—Ligand Bind. Force

$$f_b = k\left(\delta - \delta_b\right)$$



kinetic Monte Carlo

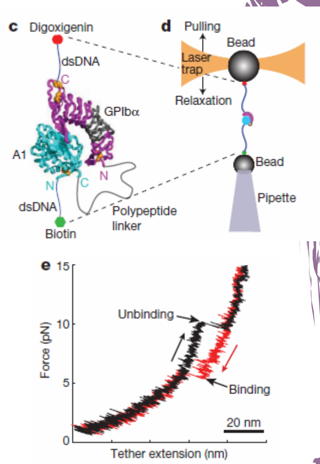
Events for kMC (M. Dembo, 1987)

- association

$$k_f = k_f^0 \exp\left[-\frac{k_{ts}\left(\delta-\delta_b\right)^2}{2k_BT} \right]$$

- dissociation

$$k_r = k_r^0 \exp\left[\frac{\left(k-k_{ts}\right)\left(\delta-\delta_b\right)^2}{2k_BT} \right]$$



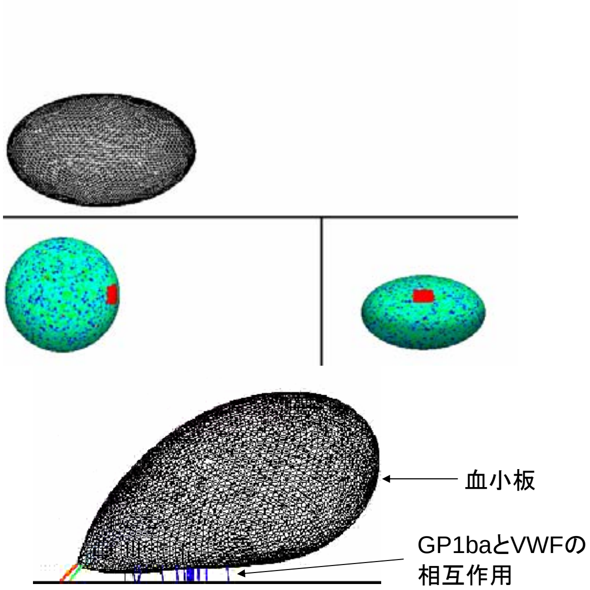
J. Kim, Nature, 2010.

k_r^0 = 0.0027 s^{-1}
k = 0.1 pN/nm
k_{ts} = 0.99 × k

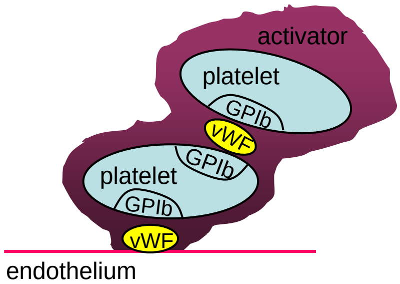
Equilibrium constant:

$$K_{eq} = \frac{k_f^0}{k_r^0} \qquad (10^{-4}\sim10^{9})$$

動的モンテカルロ法と連続体計算の連成による血栓吸着シミュレーション



Toward analysis of Thrombus formation

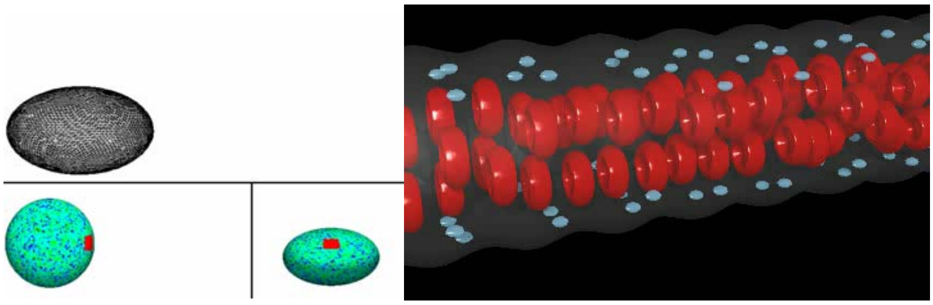


Simple adhesion model

$$\mathbf{F}(C) = \phi_p C\left(f_{0x}\mathbf{e}_x + f_{0y}\mathbf{e}_y + f_{0z}\mathbf{e}_z \right)$$

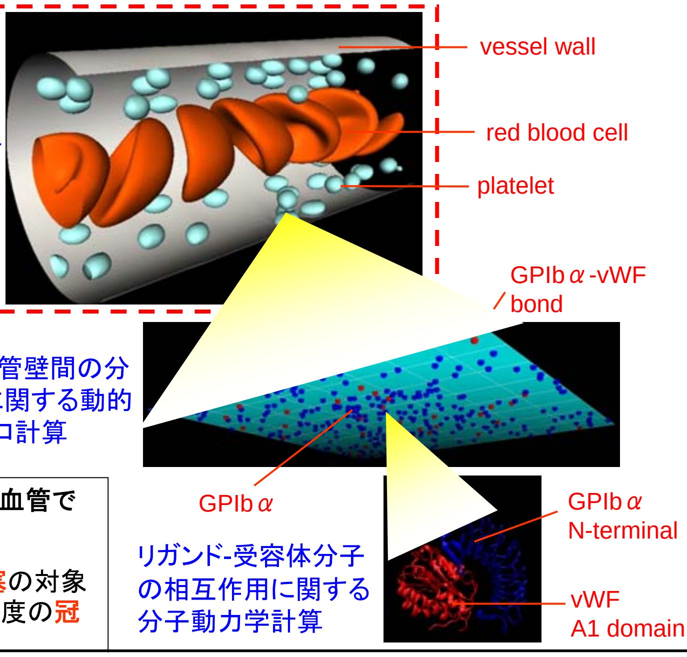
$$\frac{\partial C}{\partial t} = D_c \nabla^2 C - D_d (1-\phi_p) C$$

$$C(\mathbf{x}, t) = 1, \ \ \mathbf{x} \in \Omega_{\text{int.}}(t)$$



血栓症のマルチスケール・マルチフィジックスシミュレーション

多数の赤血球や血小板を含んだ血流計算



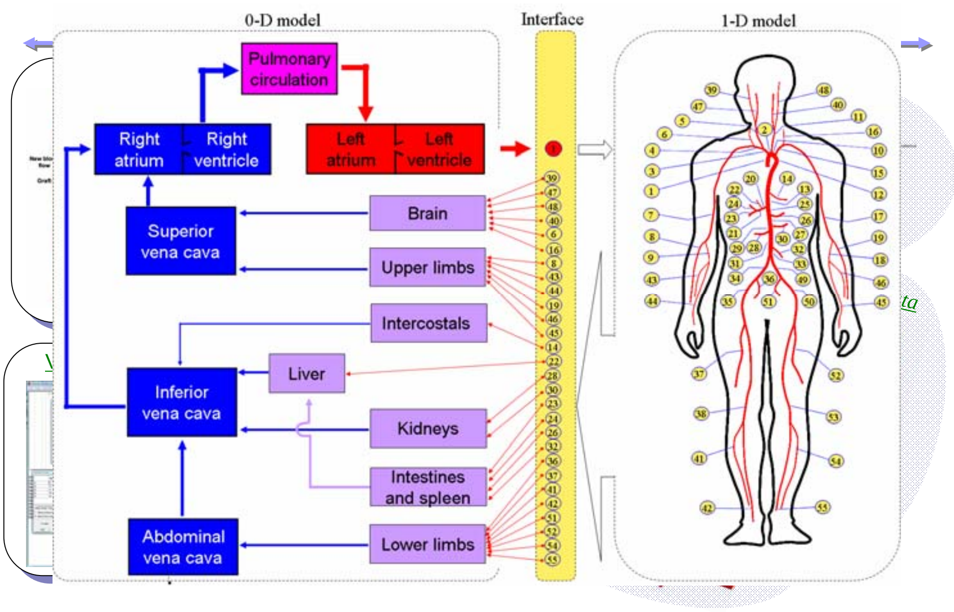
血小板，血管壁間の分子間結合に関する動的モンテカルロ計算

リガンド-受容体分子の相互作用に関する分子動力学計算

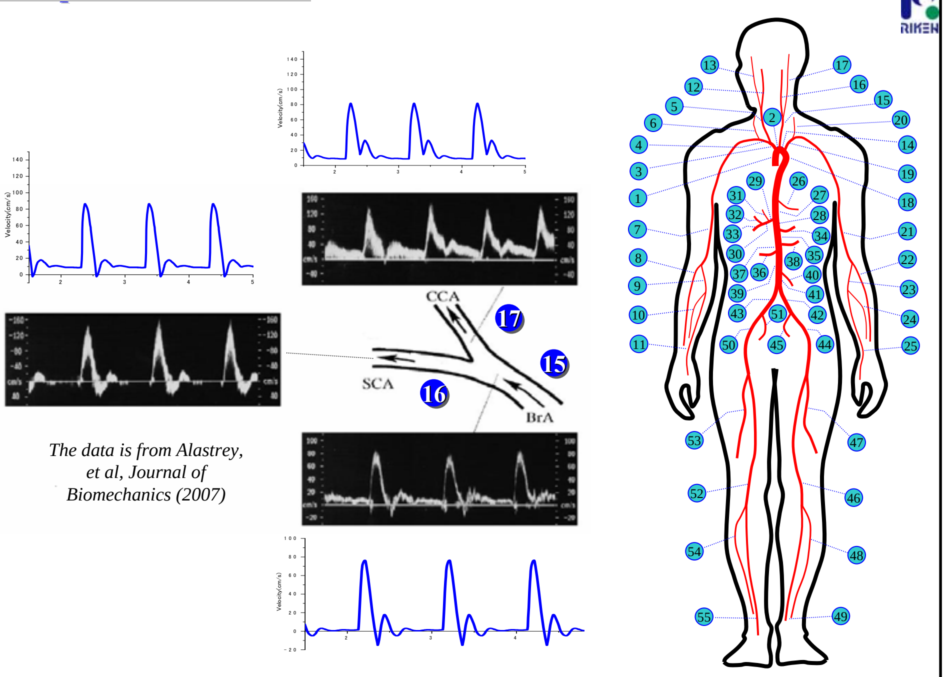
現状：直径20μmの血管で計算

「京」では：**心筋梗塞**の対象となる直径数mm程度の**冠動脈**の計算が可能

Modeling of the Entire Cardiovascular System Based on 0-D, 1-D Coupling

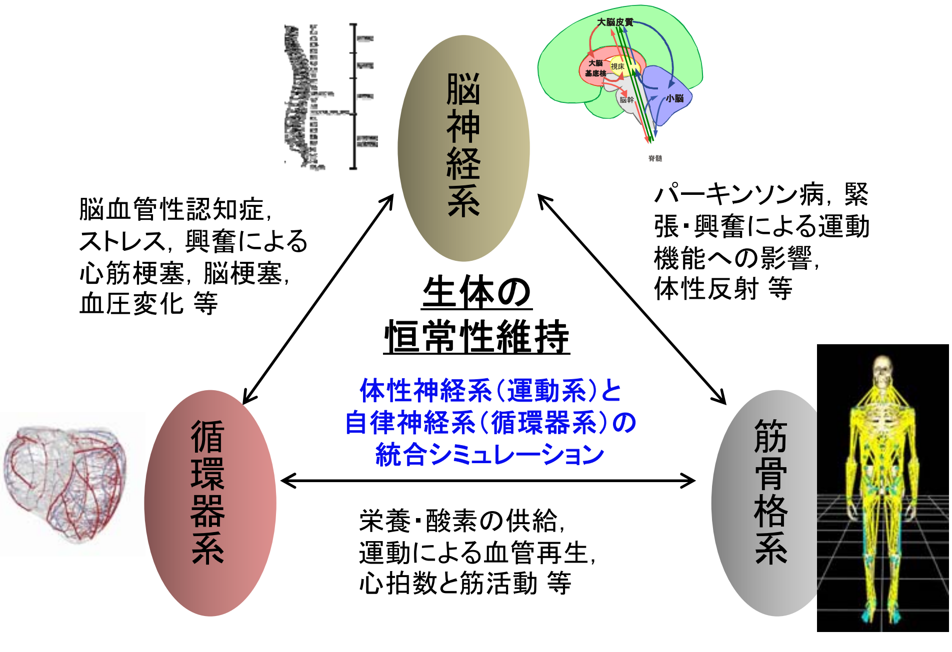


Comparison with data



The data is from Alastrey, et al, Journal of Biomechanics (2007)

筋骨格-神経-循環器系統合シミュレータ



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S. Goto (Tokai Univ.)
K. Doya (OIST)

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