Competing growth mechanisms in the development of saccular aneurysms

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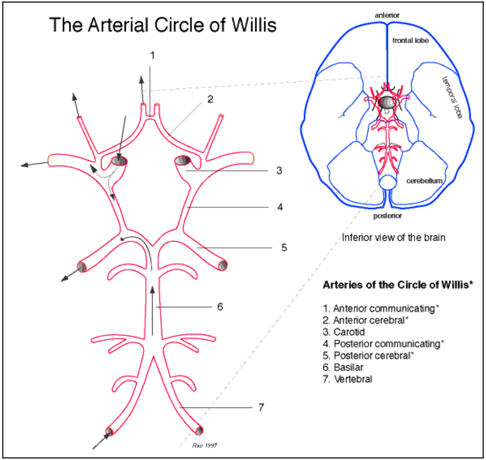
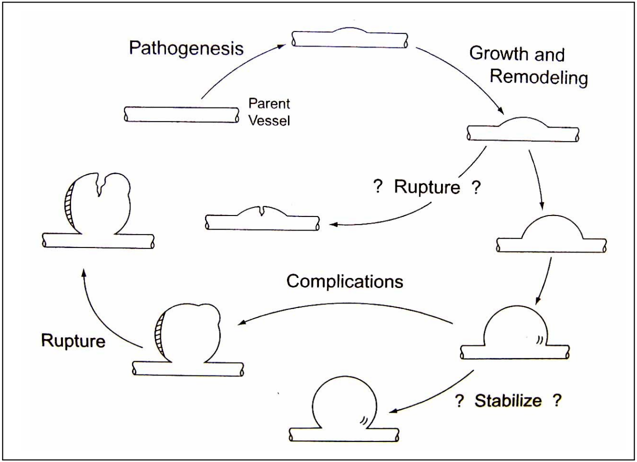
Rencontres de Modélisation en Physiopathologie

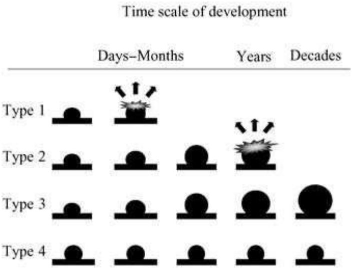
ENS Cachan, June 16-17, 2008

Intracranial saccular aneurysms are dilatations of the arterial wall.





[J.D. Humphrey, *Cardiovascular Solid Mechanics*, 2001]



	Clinical presentation			
	Multiple (148 aneurysms)	Single (232 aneurysms)	With SAH (30 aneurysms)	Total (380 aneurysms)
	Mean follow up (months)			
	13.3	11.8	14.2	13.8
Type 1				
Type 2	3 (2.0%)	1 (0.4%)		4 (1.0%)
Type 3	9 (6.1%)	9 (3.9%)	4 (13.3%)	18 (4.7%)
Type 4	136 (91.9%)	222 (95.7%)	26 (86.7%)	358 (94.2%)

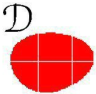
[M. Yonekura, *Neurologia medico-chirurgica*, 2004]

Part II

Biomechanical model

Growth mechanics

Growth as *change in the zero-stress reference state.*



p : *gross placement*

∇p : *gradient of the gross placement*

$\mathbb{P}$: *prototype*

F : *warp* (*Kröner-Lee decomposition*)

refined motion

$$(\mathrm{p}, \mathbb{P}) : \mathcal{D} \times \mathscr{T} \to \mathscr{E} \times (\mathrm{V}\mathscr{E} \otimes \mathrm{V}\mathscr{E})$$
$$(x, \tau) \mapsto (\mathrm{p}(x, \tau), \mathbb{P}(x, \tau))$$

($\mathcal{D}$: reference shape, $\mathscr{T}$: time line)

Growth mechanics

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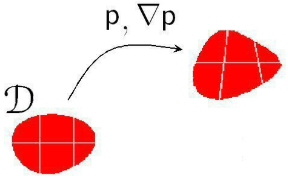

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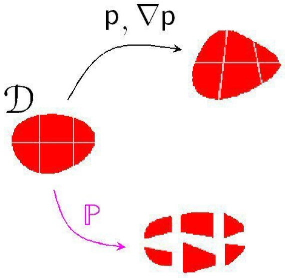

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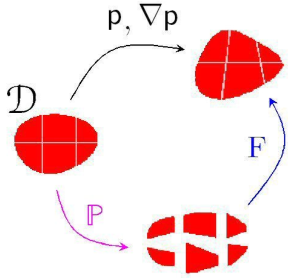

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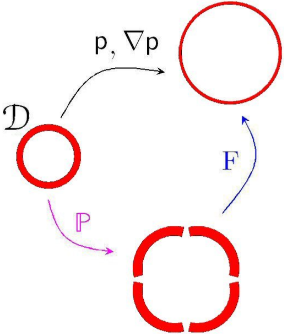
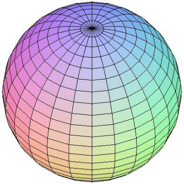
Saccular aneurysms





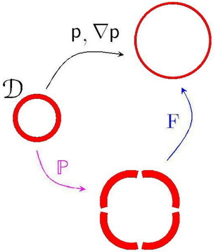
paragon shape $\mathcal{D}$ of the vessel

$$\mathcal{B}(x_\circ, \xi_+) - \bar{\mathcal{B}}(x_\circ, \xi_-)$$

Mechanical model

Kinematics

gross placement	p	$=$	$x_o + \rho\, \mathbf{e}_r$
prototype	$\mathbb{P}$	$=$	$\alpha_r\, \mathsf{P}_r + \alpha_h\, \mathsf{P}_h$
warp	F	$=$	$\lambda_r\, \mathsf{P}_r + \lambda_h \mathsf{P}_h$



Working

$$\int_{\mathcal{D}} \left(\mathbb{A}^i \cdot \mathbb{V} - \mathrm{S} \cdot \nabla \mathrm{v} \right) + \int_{\mathcal{D}} \mathbb{A}^o \cdot \mathbb{V} + \int_{\partial\mathcal{D}} \mathrm{t}_{\partial\mathcal{D}} \cdot \mathrm{v}$$

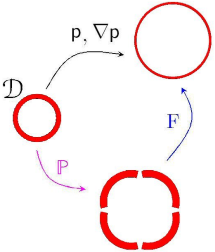
(Reduced) dissipation inequality

$$\overset{+}{\mathrm{S}}\, \mathbb{P}^\top \cdot \dot{\mathrm{F}} - \overset{+}{\mathbb{A}^i} \cdot \dot{\mathbb{P}}\, \mathbb{P}^{-1} \geq 0$$

Mechanical model

Kinematics

gross placement	p	$=$	$x_o + \rho\, \mathbf{e}_r$
prototype	$\mathbb{P}$	$=$	$\alpha_r\, P_r + \alpha_h\, P_h$
warp	$\mathbb{F}$	$=$	$\lambda_r\, P_r + \lambda_h P_h$



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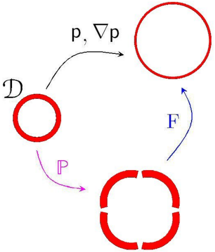
Mechanical model

Kinematics

gross placement $\quad \mathsf{p} = \mathsf{x_o} + \rho\, \mathbf{e}_\mathsf{r}$

prototype $\quad \mathbb{P} = \alpha_\mathsf{r}\, \mathsf{P_r} + \alpha_\mathsf{h}\, \mathsf{P_h}$

warp $\quad \mathrm{F} = \lambda_\mathsf{r}\, \mathsf{P_r} + \lambda_\mathsf{h}\, \mathsf{P_h}$



Working

$$\int_{\mathfrak{D}} \left(\mathbb{A}^{\mathrm{i}} \cdot \mathbb{V} - \mathrm{S} \cdot \nabla \mathrm{v} \right) + \int_{\mathfrak{D}} \mathbb{A}^{\mathrm{o}} \cdot \mathbb{V} + \int_{\partial \mathfrak{D}} \mathrm{t}_{\partial \mathfrak{D}} \cdot \mathrm{v}$$

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$$\overset{+}{\mathrm{S}}\,\mathbb{P}^{\top} \cdot \dot{\mathrm{F}} - \overset{+}{\mathbb{A}}{}^{\mathrm{i}} \cdot \dot{\mathbb{P}}\,\mathbb{P}^{-1} \geq 0$$

In this framework, in a homeostatic state ($\mathbb{P} =$ stat.), no dissipation is associated with the remodelling.

$$\overset{+}{\mathrm{S}}\,\mathbb{P}^{\top}\cdot\dot{\mathrm{F}}-\overset{+}{\mathbb{A}}{}^{\mathrm{i}}\cdot\dot{\mathbb{P}}\,\mathbb{P}^{-1}\geq 0$$

In this framework, in a homeostatic state ($\mathbb{P}=$ stat.), no dissipation is associated with the remodelling.

But...

Even if the relaxed configuration does not evolve, some energy may be dissipated.

How to explain that?
How to deal with that?

Multiple (competing) remodelling mechanisms

(s) *slipping*, (c) *recovery*, and (p) *tissue apposition*

$$\mathbb{P} = \mathbb{P}_t \, \mathbb{P}_c \, \mathbb{P}_s$$

working

$$\int_{\mathcal{D}} \left(\mathbb{A}^i_t \cdot \mathbb{V}_t + \mathbb{A}^i_c \cdot \mathbb{V}_c + \mathbb{A}^i_s \cdot \mathbb{V}_s - \mathrm{S} \cdot \nabla \mathrm{v} \right) + \int_{\mathcal{D}} \left(\mathbb{A}^o_t \cdot \mathbb{V}_t + \mathbb{A}^o_c \cdot \mathbb{V}_c + \mathbb{A}^o_s \cdot \mathbb{V}_s \right) + \int_{\partial\mathcal{D}} \mathrm{t}_{\partial\mathcal{D}} \cdot \mathrm{v}$$

reduced dissipation inequality

$$\overset{+}{\mathrm{S}} \, \mathbb{P}^\top \cdot \dot{\mathrm{F}} - \overset{+}{\mathbb{A}}{}^i_t \cdot \dot{\mathbb{P}}_t \, \mathbb{P}_t^{-1} - \overset{+}{\mathbb{A}}{}^i_c \cdot \dot{\mathbb{P}}_c \, \mathbb{P}_c^{-1} - \overset{+}{\mathbb{A}}{}^i_s \cdot \dot{\mathbb{P}}_s \, \mathbb{P}_s^{-1} \geq 0$$

Multiple (competing) remodelling mechanisms

(s) *slipping*, (c) *recovery*, and (p) *tissue apposition*

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working

$$\int_{\mathcal{D}} \left(\mathbb{A}^i_t \cdot \mathbb{V}_t + \mathbb{A}^i_c \cdot \mathbb{V}_c + \mathbb{A}^i_s \cdot \mathbb{V}_s - \mathrm{S} \cdot \nabla \mathrm{v} \right) + \int_{\mathcal{D}} \left(\mathbb{A}^o_t \cdot \mathbb{V}_t + \mathbb{A}^o_c \cdot \mathbb{V}_c + \mathbb{A}^o_s \cdot \mathbb{V}_s \right) + \int_{\partial\mathcal{D}} \mathrm{t}_{\partial\mathcal{D}} \cdot \mathrm{v}$$

reduced dissipation inequality

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Characterising the remodelling mechanisms

(H1$_1$): We assume that only $\mathbb{P}_t$ changes volume, while neither $\mathbb{P}_s$ nor $\mathbb{P}_c$ affects volume

(H1$_2$): We assume that tissue apposition is only radial

$$\mathbb{P}_t = \alpha_r^t \, P_r + P_h$$

$$\mathbb{P}_c = \alpha_r^c \, P_r + \alpha_h^c \, P_h \qquad \alpha_r^c (\alpha_h^c)^2 = 1$$

$$\mathbb{P}_s = \alpha_r^s \, P_r + \alpha_h^s \, P_h \qquad \alpha_r^s (\alpha_h^s)^2 = 1$$

Characterising the dissipation

(H2$_1$): We assume that dissipation is only due to remodelling

(H2$_2$): Linear viscous dissipation to remodelling

$$\overset{+}{\mathrm{S}} = 0$$

$$\overset{+}{\mathbb{A}}{}^{i}_{t} = -\mathrm{J}\, D^{t}_{r}\, \dot{\alpha}^{t}_{r}/\alpha^{t}_{r}\; \mathrm{P}_{r}$$

$$\overset{+}{\mathbb{A}}{}^{i}_{c} = -\mathrm{J}(D^{c}_{r}\, \dot{\alpha}^{c}_{r}/\alpha^{c}_{r}\; \mathrm{P}_{r} + D^{c}_{h}\, \dot{\alpha}^{c}_{h}/\alpha^{c}_{h}\; \mathrm{P}_{h})$$

$$\overset{+}{\mathbb{A}}{}^{i}_{s} = -\mathrm{J}(D^{s}_{r}\, \dot{\alpha}^{s}_{r}/\alpha^{s}_{r}\; \mathrm{P}_{r} + D^{s}_{h}\, \dot{\alpha}^{s}_{h}/\alpha^{s}_{h}\; \mathrm{P}_{h})$$

Characterising the controls

($H3_s$): null control on slipping mechanism

$$Q^s = 0$$

($H3_c$): recovery tuned with respect to slipping

$$Q^c \sim G^c (T_h - T_r) + (1 - G^c)(T_h^\diamond - T_r^\diamond)$$

($H3_t$): radial apposition driven by hoop stress

$$Q^t \sim G^t (T_h - T_h^\diamond)$$

$T_h^\diamond$, $T_r^\diamond$: “target” values.

Evolution equations

$$2\big(\,\mathrm{S_r}(\xi) - \mathrm{S_h}(\xi)\big) + \xi\,\mathrm{S}'_\mathrm{r}(\xi) = 0$$
$$\mp\mathrm{S_r}(\xi_\mp) = t_\mp$$

$$\dot{\alpha}_\mathrm{h}/\alpha_\mathrm{h} = \gamma_\mathrm{h}\,(\Delta\mathrm{T_h} - \Delta\mathrm{T_r})$$
$$\dot{\alpha}_\mathrm{r}/\alpha_\mathrm{r} = -2\dot{\alpha}_\mathrm{h}/\alpha_\mathrm{h} + \gamma_\mathrm{r}\,\Delta\mathrm{T_h}$$

$\Delta\mathrm{T_h} := \mathrm{T_h} - \mathrm{T_h^\diamond}$

$\gamma_\mathrm{h} := (1/\mathrm{D^c} + 1/\mathrm{D^s})\,(1 - \mathrm{G^c})$

$\Delta\mathrm{T_r} := \mathrm{T_r} - \mathrm{T_r^\diamond}$

$\gamma_\mathrm{r} := \mathrm{G^t}/\mathrm{D^t}$

Part III

Numerical simulations

Simulated natural histories

- Let us assume that an aneurysm, subjected to a constant intramural pressure $p^\diamond$, has reached a spherical shape in a homeostatic state with hoop and radial stress:

$$\mathrm{T}^\diamond_{\mathsf{h}}\,, \qquad \mathrm{T}^\diamond_{\mathsf{r}}\,.$$

  Let $Q^\diamond$ be the value of the control Q^{c} necessary to maintain this homeostatic state:

$$Q^\diamond \sim \mathrm{T}^\diamond_{\mathsf{h}} - \mathrm{T}^\diamond_{\mathsf{r}}\,.$$

- Thus, the intramural pressure experiences a short-time bump:

$$p(t) = p^\diamond + \delta p(t)\,.$$

Simulated natural histories

- Inefficient *vs.* Efficient recovery
- Negligible *vs.* Non-negligible tissue apposition

History ♯1: slow recovery, null apposition

1. Q^{c} is held fixed to the previous value for the rest of the time:

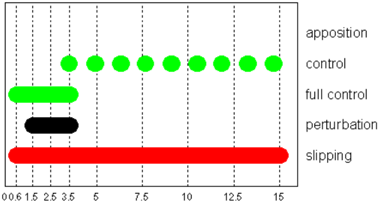
$$\mathrm{Q}^{\mathsf{c}} = Q^{\diamond} \sim \mathrm{T}^{\diamond}_{\mathsf{h}} - \mathrm{T}^{\diamond}_{\mathsf{r}}$$

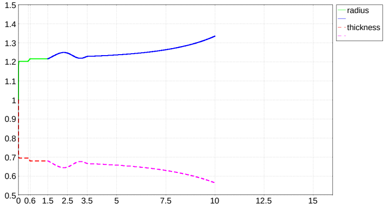
   simulating the inability of the recovery control to keep pace with a sudden perturbation;

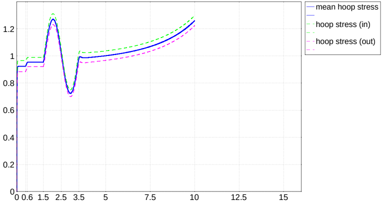
2. negligible tissue apposition:

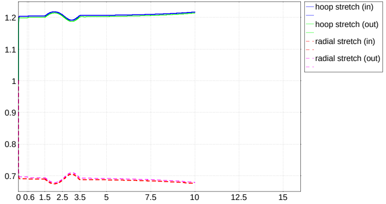
$$\mathrm{Q}^{\mathsf{t}} \sim 0$$

SLOW RECOVERY ($\mathrm{G^c} = 0$), null tissue apposition









History ♯2: fast recovery, null apposition

1. Q^c is set to a full recovery control:

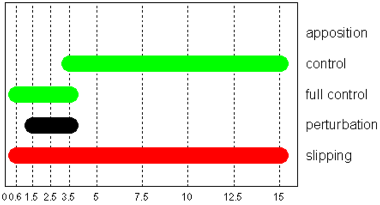
$$\mathrm{Q}^c \sim \mathrm{T}_h - \mathrm{T}_r$$

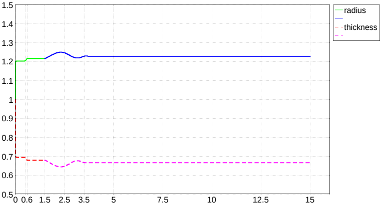
simulating the capability of the recovery control to immediately keep pace with a sudden perturbation;

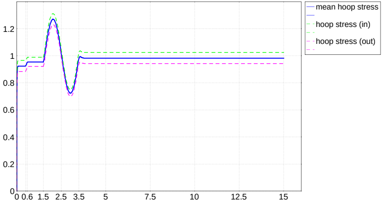
2. negligible tissue apposition:

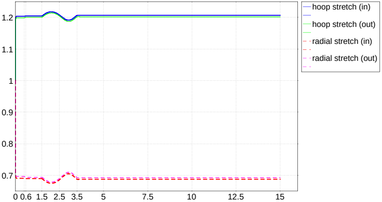
$$\mathrm{Q}^t \sim 0$$

FAST RECOVERY ($\mathrm{G}^{\mathrm{c}} = 1$), null tissue apposition









History ♯3: delayed recovery, null apposition

1. Q^c is a fraction of the full recovery control:

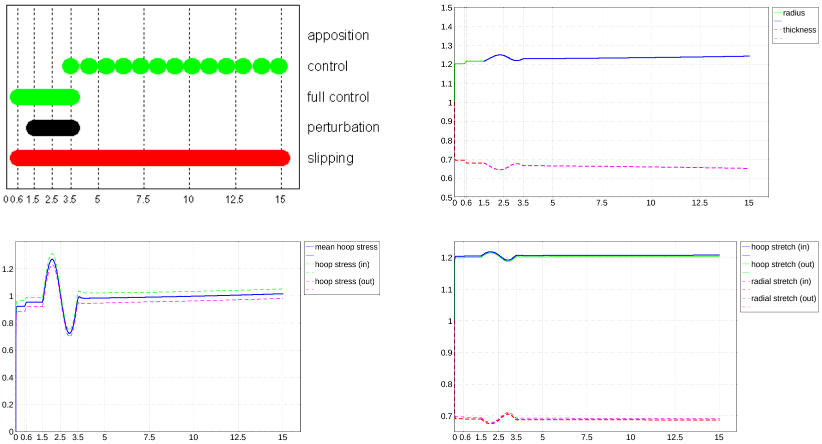
$$\mathrm{Q}^{\mathsf{c}} \sim \mathrm{G}^{\mathsf{c}}\,(\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{r}}) + (1 - \mathrm{G}^{\mathsf{c}})\,(\mathrm{T}_{\mathsf{h}}^{\diamond} - \mathrm{T}_{\mathsf{r}}^{\diamond})$$

which is meant to simulate an impaired recovery control.

2. negligible tissue apposition:

$$\mathrm{Q}^{\mathsf{t}} \sim 0$$

DELAYED RECOVERY ($G^c = 0.8$), null tissue apposition



History ♯4: slow recovery, tissue apposition

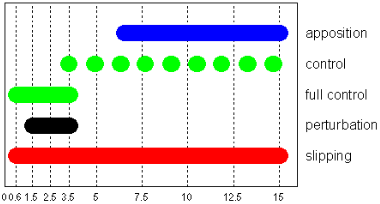
1. Q^{c} is held fixed to the previous value for the rest of the time:

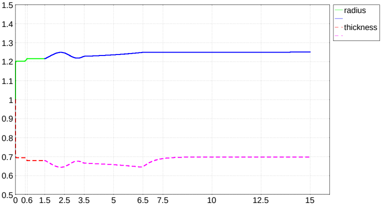
$$\mathrm{Q}^{\mathsf{c}}(t) = Q^{\diamond}$$

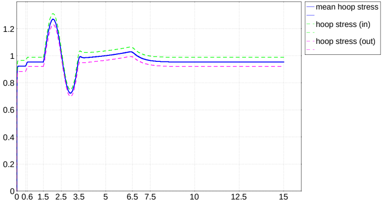
2. radial tissue apposition goes into action through a stress-driven control law:

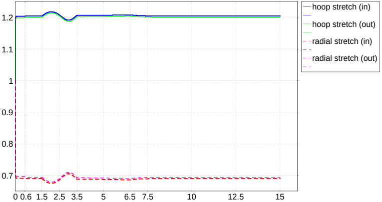
$$\mathrm{Q}^{\mathsf{t}} \sim \mathrm{G}^{\mathsf{t}}(\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{h}}^{\diamond})$$

Slow recovery ($G^c = 0$), FAST TISSUE APPOSITION ($G^t \gg$)

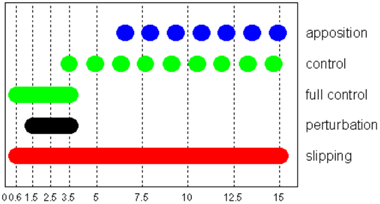


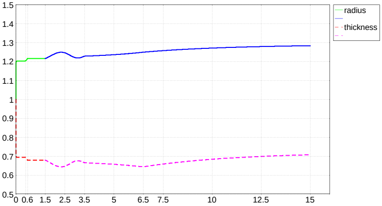


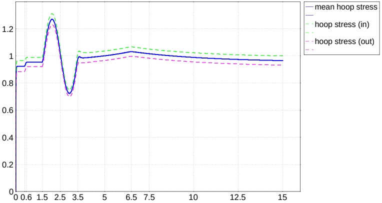


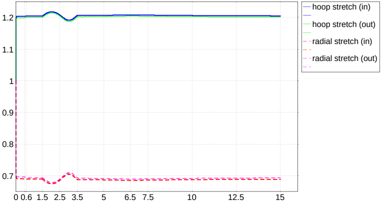


Slow recovery ($G^c = 0$), SLOW TISSUE APPOSITION ($G^t \ll$)









Summary

- Growth of saccular aneurysms
  - elastic deformation;
  - change of relaxed configuration.
- Multiple remodelling mechanisms
  - *slipping*: only passive;
  - *recovery*: slow/fast control;
  - *tissue apposition*: hoop stress driven control.
- Numerical evidence
  - only recovery control is unable to keep the aneurysm in a homeostatic state;
  - control on tissue apposition plays a central role.

References

- A. DiCarlo, V. Sansalone, A. Tatone, and V. Varano, Living Shell-Like Structures, in *Applied and Industrial Mathematics In Italy - II*, World Scientific, 2007.

Open problems

- Better characterisation of material properties
  - evolution of elastic stiffness;
  - non uniform remodelling parameters.
- Weaker assumptions on symmetry
- Quantitative calibration and model validation