Growth and remodelling of soft biological tissues

Competing remodelling mechanisms in saccular aneurysms

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French-Italian meeting on

Mathematics & Biology

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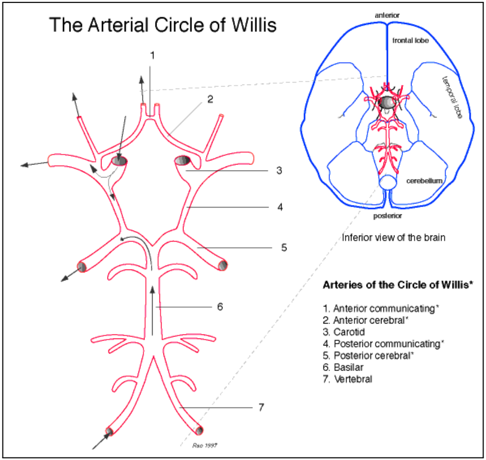
Outline

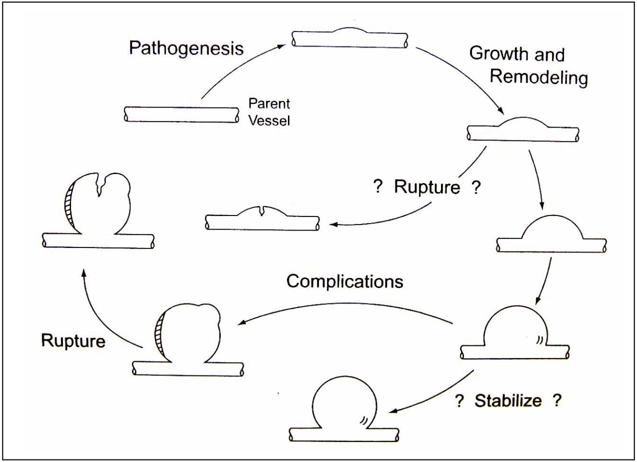
1. Histology of saccular aneurysms
2. A mechanical model of saccular aneurysms
   - Geometry & kinematics
   - Working & balance
   - Constitutive issues
   - Multiple remodelling mechanisms
3. Numerical simulations
   - Natural histories
   - Passive slipping, recovery, null tissue apposition
   - Passive slipping, slow recovery, tissue apposition

Part I

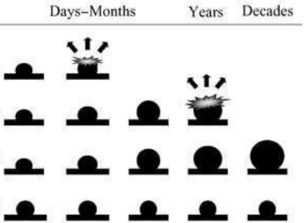
Aneurysms

Intracranial saccular aneurysms are dilatations of the arterial wall.





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



Time scale of development	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]

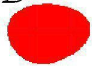
Part II

A mechanical model

Growth mechanics

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

$\mathcal{D}$



p :	*gross placement*
$\nabla\mathrm{p}$:	*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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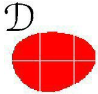

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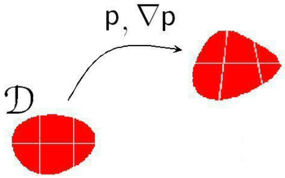

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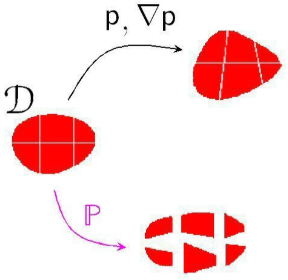

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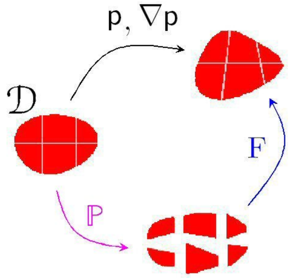

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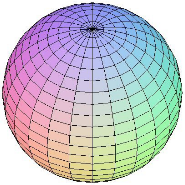
$$(x, \tau) \mapsto (\mathrm{p}(x,\tau), \mathbb{P}(x,\tau))$$

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

Saccular aneurysms

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

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



spherical coordinates

$$\widehat{\xi}(x), \widehat{\vartheta}(x), \widehat{\varphi}(x)$$

spherically symmetric vector fields

$$\mathrm{v}(x) = v(\xi)\, \mathbf{e}_r(\vartheta, \varphi)$$

spherically symmetric tensor fields

$$\mathrm{L}(x) = \mathrm{L}_r(\xi)\, \mathrm{P}_r(\vartheta, \varphi) + \mathrm{L}_h(\xi)\, \mathrm{P}_h(\vartheta, \varphi)$$

orthogonal projectors

$$\mathrm{P}_r := \mathbf{e}_r \otimes \mathbf{e}_r$$
$$\mathrm{P}_h := \mathrm{I} - \mathrm{P}_r$$

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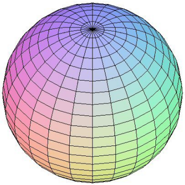

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orthogonal projectors

$$\mathrm{P}_\mathrm{r} := \mathbf{e}_\mathrm{r} \otimes \mathbf{e}_\mathrm{r}$$
$$\mathrm{P}_\mathrm{h} := \mathrm{I} - \mathrm{P}_\mathrm{r}$$

Geometry & kinematics

gross placement

$$p = x_o + \rho \, \mathbf{e}_r$$

gradient of the gross placement

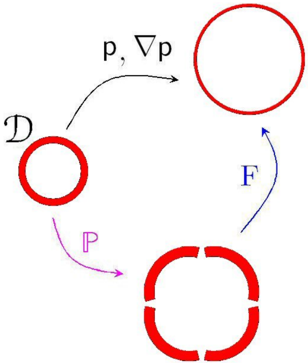
$$\nabla p = \rho' \, P_r + \frac{\rho}{\xi} \, P_h$$

prototype

$$\mathbb{P} = \alpha_r \, P_r + \alpha_h \, P_h$$

warp

$$\mathrm{F} := (\nabla p) \, \mathbb{P}^{-1} = \lambda_r \, P_r + \lambda_h P_h$$



Refined motion

Refined motion: $(\mathrm{p}, \mathbb{P})$

Refined velocity: $(\dot{\mathrm{p}}, \dot{\mathbb{P}}\,\mathbb{P}^{-1})$

$$\dot{\mathrm{p}} = \dot{\rho}\,\mathbf{e}_{\mathrm{r}}$$

$$\dot{\mathbb{P}}\,\mathbb{P}^{-1} = \frac{\dot{\alpha}_{\mathrm{r}}}{\alpha_{\mathrm{r}}}\,\mathrm{P}_{\mathrm{r}} + \frac{\dot{\alpha}_{\mathrm{h}}}{\alpha_{\mathrm{h}}}\,\mathrm{P}_{\mathrm{h}}$$

Test velocity: $(\mathrm{v}, \mathbb{V})$

$$\mathrm{v} = v\,\mathbf{e}_{\mathrm{r}}$$

$$\mathbb{V} = \mathrm{V}_{\mathrm{r}}\,\mathrm{P}_{\mathrm{r}} + \mathrm{V}_{\mathrm{h}}\,\mathrm{P}_{\mathrm{h}}$$

(*gross velocity* and *growth velocity*)

Working

The basic balance structure of a mechanical theory is encoded in the way in which forces expend *working* on a general test velocity.

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

Balance laws

$$\left.\begin{array}{rcl} 2\big(\mathrm{S_r}(\xi)-\mathrm{S_h}(\xi)\big)+\xi\,\mathrm{S}'_{\mathrm{r}}(\xi) & = & 0 \\ \mathrm{A^i_r}(\xi)-\mathrm{A^o_r}(\xi) & = & 0 \\ \mathrm{A^i_h}(\xi)-\mathrm{A^o_h}(\xi) & = & 0 \end{array}\right\}\quad(\xi_-<\xi<\xi_+)$$

$$\mp\mathrm{S_r}(\xi_\mp) = t_\mp$$

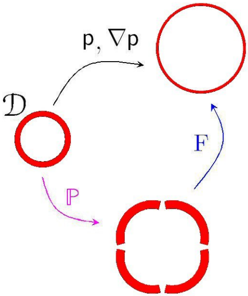
Energetics

$$\Psi(\mathscr{P}) = \int_{\mathscr{P}} \mathrm{J}\,\psi\,, \qquad \mathrm{J} := \det(\mathbb{P}) = \alpha_{\mathsf{r}}\,\alpha_{\mathsf{h}}{}^2 > 0$$

ψ free energy per unit *prototypal* volume
$\mathrm{J}\,\psi$ free energy per unit *paragon* volume

(H1): the value of the free energy $\psi(x)$ depends solely on the value of the warp $\mathrm{F}(x)$

$$\psi(x) = \phi\,(\,\lambda_{\mathsf{r}}(\xi), \lambda_{\mathsf{h}}(\xi); \xi\,)$$



Characterising the passive mechanical response

(H2): incompressible elasticity

$$\det \mathrm{F} = \lambda_r \, {\lambda_h}^2 = 1 \quad \Longleftrightarrow \quad \lambda_r = 1/{\lambda_h}^2 \, .$$

$$\widetilde{\phi} : \lambda \mapsto \phi\,(\,1/\lambda^2,\, \lambda\,)$$

Fung strain energy density

$$\widetilde{\phi}(\lambda) = (c/\delta)\, \exp\big((\Gamma/2)\,(\lambda^2 - 1)^2\big)$$

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

Dissipation principle

$$\mathrm{S} \cdot \nabla \dot{\mathsf{p}} - \mathbb{A}^{\mathsf{i}} \cdot \dot{\mathbb{P}}\, \mathbb{P}^{-1} - (\mathrm{J}\,\widetilde{\phi})^{\cdot} \geq 0$$

$$\left(\mathrm{S}\,\mathbb{P}^{\top} - \mathrm{J}\,\frac{\mathrm{d}\widetilde{\phi}}{\mathrm{dF}}\right) \cdot \dot{\mathrm{F}} - \left(\mathbb{A}^{\mathsf{i}} - \mathrm{F}^{\top}\mathrm{S}\,\mathbb{P}^{\top} + \mathrm{J}\widetilde{\phi}\,\mathsf{I}\right) \cdot \dot{\mathbb{P}}\,\mathbb{P}^{-1} \geq 0$$

consistency

$$\mathrm{S} = \mathrm{J}\,\frac{\mathrm{d}\widetilde{\phi}}{\mathrm{dF}}\,\mathbb{P}^{-\top} + \overset{+}{\mathrm{S}}, \quad \mathbb{A}^{\mathsf{i}} = \mathrm{F}^{\top}\mathrm{S}\,\mathbb{P}^{\top} + \mathrm{J}\widetilde{\phi}\,\mathsf{I} + \overset{+}{\mathbb{A}^{\mathsf{i}}}$$

reduced dissipation inequality

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

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

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In this framework, in a homeostatic state ($\mathbb{P} = \mathrm{I}$), 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*

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

growth velocity

$$\dot{\mathbb{P}} \, \mathbb{P}^{-1} = \dot{\mathbb{P}}_t \, \mathbb{P}_t^{-1} + \dot{\mathbb{P}}_c \, \mathbb{P}_c^{-1} + \dot{\mathbb{P}}_s \, \mathbb{P}_s^{-1}$$

test velocity

$$\mathbb{V} = \mathbb{V}_t + \mathbb{V}_c + \mathbb{V}_s$$

working

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

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test velocity

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$$\int_{\mathcal{D}} \left(\mathbb{A}_t^i \cdot \mathbb{V}_t + \mathbb{A}_c^i \cdot \mathbb{V}_c + \mathbb{A}_s^i \cdot \mathbb{V}_s - \mathrm{S} \cdot \nabla \mathrm{v} \right)$$

$$+ \int_{\mathcal{D}} \left(\mathbb{A}_t^o \cdot \mathbb{V}_t + \mathbb{A}_c^o \cdot \mathbb{V}_c + \mathbb{A}_s^o \cdot \mathbb{V}_s \right) + \int_{\partial\mathcal{D}} \mathrm{t}_{\partial\mathcal{D}} \cdot \mathrm{v}$$

Dissipation principle

$$\mathrm{S} \cdot \nabla \dot{\mathsf{p}} - \left(\mathbb{A}^{\mathsf{i}}_{\mathsf{t}} \cdot \dot{\mathbb{P}}_{\mathsf{t}} \, \mathbb{P}_{\mathsf{t}}^{-1} + \mathbb{A}^{\mathsf{i}}_{\mathsf{c}} \cdot \dot{\mathbb{P}}_{\mathsf{c}} \, \mathbb{P}_{\mathsf{c}}^{-1} + \mathbb{A}^{\mathsf{i}}_{\mathsf{s}} \cdot \dot{\mathbb{P}}_{\mathsf{s}} \, \mathbb{P}_{\mathsf{s}}^{-1} \right) - (\mathrm{J}\,\psi)^{\cdot} \geq 0$$

consistency

$$\mathrm{S} = \mathrm{J}\,\frac{\mathrm{d}\widetilde{\phi}}{\mathrm{dF}}\,\mathbb{P}^{-\top} + \overset{+}{\mathrm{S}}$$

$$\mathbb{A}^{\mathsf{i}}_{\bullet} = \left(\mathrm{F}^{\top}\mathrm{S}\,\mathbb{P}^{\top} - \mathrm{J}\,\phi\,\mathsf{I} \right) + \overset{+}{\mathbb{A}}{}^{\mathsf{i}}_{\bullet}\,, \qquad \bullet \in \{\mathsf{s}, \mathsf{c}, \mathsf{t}\}$$

reduced dissipation inequality

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

Characterising the remodelling forces

	Inner	**Outer**	
remodelling	$\mathbb{A}^{i}_{t}\,,\,\mathbb{A}^{i}_{c}\,,\,\mathbb{A}^{i}_{s}$	$\mathbb{A}^{o}_{t}\,,\,\mathbb{A}^{o}_{c}\,,\,\mathbb{A}^{o}_{s}$	control
	$\Uparrow$		
	$\mathbb{P}_{t}\,,\,\mathbb{P}_{c}\,,\,\mathbb{P}_{s}$		
dissipation	$\overset{+}{\mathbb{A}}{}^{i}_{t}\,,\,\overset{+}{\mathbb{A}}{}^{i}_{c}\,,\,\overset{+}{\mathbb{A}}{}^{i}_{s}$		

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	$\Uparrow$		
	$\mathbb{P}_t\,,\,\mathbb{P}_c\,,\,\mathbb{P}_s$		
dissipation	$\overset{+}{\mathbb{A}}{}^i_t\,,\,\overset{+}{\mathbb{A}}{}^i_c\,,\,\overset{+}{\mathbb{A}}{}^i_s$		

Characterising the remodelling mechanisms

($H3_a$): We assume that only $\mathbb{P}_t$ changes volume, while neither $\mathbb{P}_s$ nor $\mathbb{P}_c$ affects volume

$$J := \det(\mathbb{P}) = \det(\mathbb{P}_t)\,, \quad \det(\mathbb{P}_c) = 1\,, \quad \det(\mathbb{P}_s) = 1$$

($H3_b$): We assume that tissue apposition is only radial

$$\mathbb{P}_t = \alpha^t_r\, P_r + P_h$$

$$\mathbb{P}_c = \alpha^c_r\, P_r + \alpha^c_h\, P_h \qquad \alpha^c_r(\alpha^c_h)^2 = 1$$

$$\mathbb{P}_s = \alpha^s_r\, P_r + \alpha^s_h\, P_h \qquad \alpha^s_r(\alpha^s_h)^2 = 1$$

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

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

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

Characterising the dissipation

(H4): We assume that dissipation is only due to remodelling

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

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

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

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

Evolution equations

remodelling laws

$$\mathrm{D}^{\mathsf{t}}\,\dot{\alpha}^{\mathsf{t}}_{\mathsf{r}}/\alpha^{\mathsf{t}}_{\mathsf{r}} = (\mathrm{T}_{\mathsf{r}} - \widetilde{\phi}) + \mathrm{Q}^{\mathsf{t}}$$

$$\mathrm{D}^{\mathsf{c}}\,\dot{\alpha}^{\mathsf{c}}_{\mathsf{h}}/\alpha^{\mathsf{c}}_{\mathsf{h}} = (\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{r}}) + \mathrm{Q}^{\mathsf{c}}$$

$$\mathrm{D}^{\mathsf{s}}\,\dot{\alpha}^{\mathsf{s}}_{\mathsf{h}}/\alpha^{\mathsf{s}}_{\mathsf{h}} = (\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{r}}) + \mathrm{Q}^{\mathsf{s}}$$

$$\mathbb{A}^{o}_{\mathsf{t}}/\mathrm{J} = Q^{\mathsf{t}}_{\mathsf{r}}\,\mathsf{P}_{\mathsf{r}} \qquad \mathbb{A}^{o}_{\mathsf{c}}/\mathrm{J} = Q^{\mathsf{c}}_{\mathsf{r}}\,\mathsf{P}_{\mathsf{r}} + Q^{\mathsf{c}}_{\mathsf{h}}\,\mathsf{P}_{\mathsf{h}} \qquad \mathbb{A}^{o}_{\mathsf{s}}/\mathrm{J} = Q^{\mathsf{s}}_{\mathsf{r}}\,\mathsf{P}_{\mathsf{r}} + Q^{\mathsf{s}}_{\mathsf{h}}\,\mathsf{P}_{\mathsf{h}}$$

$$\mathrm{Q}^{\mathsf{t}} := Q^{\mathsf{t}}_{\mathsf{r}} \qquad \mathrm{Q}^{\mathsf{c}} := (Q^{\mathsf{c}}_{\mathsf{h}} - Q^{\mathsf{c}}_{\mathsf{r}}) \qquad \mathrm{Q}^{\mathsf{s}} := (Q^{\mathsf{s}}_{\mathsf{h}} - Q^{\mathsf{s}}_{\mathsf{r}})$$

$$\mathrm{D}^{\mathsf{t}} := D^{\mathsf{t}}_{\mathsf{r}} \qquad \mathrm{D}^{\mathsf{c}} := (2D^{\mathsf{c}}_{\mathsf{r}} + D^{\mathsf{c}}_{\mathsf{h}}) \qquad \mathrm{D}^{\mathsf{s}} := (2D^{\mathsf{s}}_{\mathsf{r}} + D^{\mathsf{s}}_{\mathsf{h}})$$

$$\mathrm{T}_{\mathsf{r}} = \mathrm{J}^{-1}\mathrm{S}_{\mathsf{r}}\,\alpha_{\mathsf{r}}\,\lambda_{\mathsf{r}} \qquad \mathrm{T}_{\mathsf{h}} = \mathrm{J}^{-1}\mathrm{S}_{\mathsf{h}}\,\alpha_{\mathsf{h}}\,\lambda_{\mathsf{h}}$$

Characterising controls

(H5$_s$): slipping

Q^s

(H5$_c$): recovery

Q^c

(H5$_t$): tissue apposition

Q^t

$\mathrm{T}_h^\diamond$, $\mathrm{T}_r^\diamond$: "target" values.

Slipping

null control on slipping mechanism

$$\mathrm{D}^{\mathsf{s}}\,\dot{\alpha}_{\mathsf{h}}^{\mathsf{s}}/\alpha_{\mathsf{h}}^{\mathsf{s}} = (\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{r}}) + \mathrm{Q}^{\mathsf{s}}$$

1. passive slipping:

$$\mathrm{Q}^{\mathsf{s}}(t) = 0\,,$$

$$\dot{\alpha}_{\mathsf{h}}^{\mathsf{s}}/\alpha_{\mathsf{h}}^{\mathsf{s}} = 1/\mathrm{D}^{\mathsf{s}}\,(\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{r}})\,.$$

Recovery

recovery tuned with respect to slipping

$$\mathrm{D}^{\mathsf{c}}\,\dot{\alpha}^{\mathsf{c}}_{\mathsf{h}}/\alpha^{\mathsf{c}}_{\mathsf{h}} = (\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{r}}) + \mathrm{Q}^{\mathsf{c}}$$

1. sluggish recovery control–*stationary control* ($\mathrm{g} = 0$):

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

$$\dot{\alpha}^{\mathsf{c}}_{\mathsf{h}}/\alpha^{\mathsf{c}}_{\mathsf{h}} = 1/\mathrm{D}^{\mathsf{c}}\,(\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{r}}) + \mathrm{Q}^{\mathsf{c}}/\mathrm{D}^{\mathsf{c}}\,;$$

2. prompt recovery control–*recovery immediately compensates slipping* ($\mathrm{g} = 1$):

$$\mathrm{Q}^{\mathsf{c}}(t) = -\left(1 + \frac{\mathrm{D}^{\mathsf{c}}}{\mathrm{D}^{\mathsf{s}}}\right)(\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{r}})\,,$$

$$\dot{\alpha}^{\mathsf{c}}_{\mathsf{h}}/\alpha^{\mathsf{c}}_{\mathsf{h}} = -1/\mathrm{D}^{\mathsf{s}}\,(\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{r}})\,.$$

Tissue apposition

radial apposition driven by hoop stress

$$\mathrm{D}^{\mathsf{t}}\, \dot{\alpha}_{\mathsf{r}}^{\mathsf{t}}/\alpha_{\mathsf{r}}^{\mathsf{t}} = (\mathrm{T}_{\mathsf{r}} - \widetilde{\phi}) + \mathrm{Q}^{\mathsf{t}}$$

1. sluggish apposition control

$$\mathrm{Q}^{\mathsf{t}}(t) = 0\,,$$

$$\dot{\alpha}_{\mathsf{r}}^{\mathsf{t}}/\alpha_{\mathsf{r}}^{\mathsf{t}} = 1/\mathrm{D}^{\mathsf{t}}\,(\mathrm{T}_{\mathsf{r}} - \widetilde{\phi})\,;$$

2. apposition control parameterised by G^{t}:

$$\mathrm{Q}^{\mathsf{t}}(t) = \mathrm{G}^{\mathsf{t}}\big(\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{h}}^{\diamond}\big) - \big(\mathrm{T}_{\mathsf{r}} - \widetilde{\phi}\big)\,,$$

$$\dot{\alpha}_{\mathsf{r}}^{\mathsf{t}}/\alpha_{\mathsf{r}}^{\mathsf{t}} = \mathrm{G}^{\mathsf{t}}/\mathrm{D}^{\mathsf{t}}\,\big(\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{h}}^{\diamond}\big)\,.$$

Characterising controls

($H5_s$): null control on slipping mechanism

$$Q^s = 0$$

($H5_c$): recovery tuned with respect to slipping

$$Q^c = -\left(1 + \frac{D^c}{D^s}\right)\left(g\left(T_h - T_r\right) + \left(1 - g\right)\left(T_h^\diamond - T_r^\diamond\right)\right)$$

($H5_t$): radial apposition driven by hoop stress

$$Q^t = G^t\left(T_h - T_h^\diamond\right) - \left(T_r - \widetilde{\phi}\right)$$

$T_h^\diamond$, $T_r^\diamond$: "target" values.

Evolution equations

$$2\big(\mathrm{S}_\mathsf{r}(\xi) - \mathrm{S}_\mathsf{h}(\xi)\big) + \xi\,\mathrm{S}'_\mathsf{r}(\xi) = 0$$

$$\mp\mathrm{S}_\mathsf{r}(\xi_\mp) = t_\mp$$

$$\dot{\alpha}_\mathsf{h}/\alpha_\mathsf{h} = \gamma_\mathsf{h}\,(\Delta\mathrm{T}_\mathsf{h} - \Delta\mathrm{T}_\mathsf{r})$$

$$\dot{\alpha}_\mathsf{r}/\alpha_\mathsf{r} = -2\dot{\alpha}_\mathsf{h}/\alpha_\mathsf{h} + \gamma_\mathsf{r}\,\Delta\mathrm{T}_\mathsf{h}$$

$\Delta\mathrm{T}_\mathsf{h} := \mathrm{T}_\mathsf{h} - \mathrm{T}_\mathsf{h}^\diamond$ $\quad$ $\Delta\mathrm{T}_\mathsf{r} := \mathrm{T}_\mathsf{r} - \mathrm{T}_\mathsf{r}^\diamond$

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

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:

$$Q^\diamond := -\left(1 + \frac{D^{\mathsf{c}}}{D^{\mathsf{s}}}\right)\left(\mathrm{T}^\diamond_{\mathsf{h}} - \mathrm{T}^\diamond_{\mathsf{r}}\right).$$

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

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

Simulated natural histories

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

History ♯1: slow recovery, null apposition

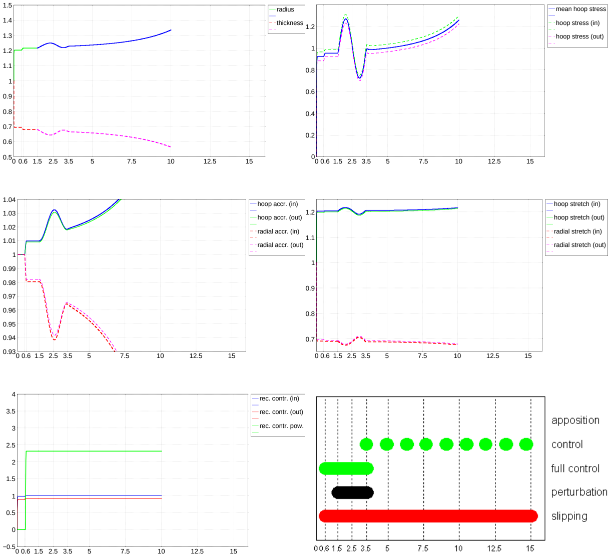
1. Q^{c} is held fixed to the previous value for the rest of the time:

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

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

2. negligible tissue apposition:

$$Q^{\mathsf{t}} = -\left(\mathrm{T}_{\mathsf{r}} - \widetilde{\phi}\right) .$$



SLOW RECOVERY

[case-42-001]

D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	0

A recovery control, held fixed to the previous homeostatic value, is unable to keep the aneurysm in a homeostatic state in response to a perturbation of the intramural pressure.

History ♯2: fast recovery, null apposition

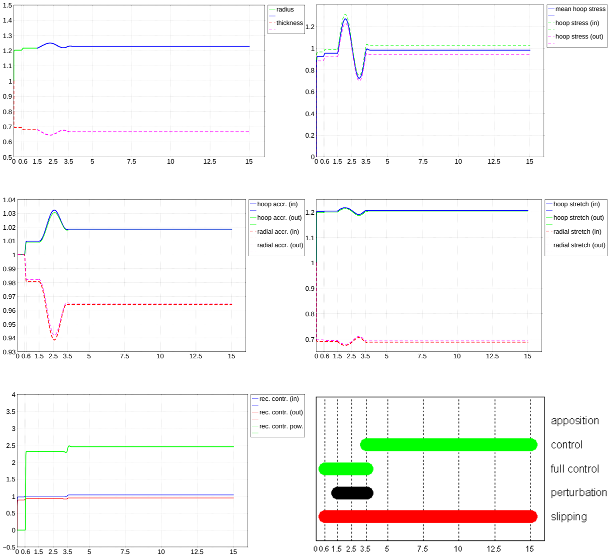
1. Q^{c} is set to a full recovery control:

$$Q^{\mathsf{c}}(t) = -\left(1 + \frac{D^{\mathsf{c}}}{D^{\mathsf{s}}}\right)(\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{r}}),$$

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

2. negligible tissue apposition:

$$Q^{\mathsf{t}} = -\left(\mathrm{T}_{\mathsf{r}} - \widetilde{\phi}\right).$$



FAST RECOVERY

[case-41-001]

D^c / D^s	1000
D^c	0.01
D^s	1e-005
char time	10
δQ^c ampl	0
δQ^c period	0
δp ampl	0.25
δp period	2
Q^c factor g	1

After the end of a short perturbation of the intramural pressure, a full recovery control drives the aneurysm to a new homeostatic state, with a higher hoop stress.

History ♯3: delayed recovery, null apposition

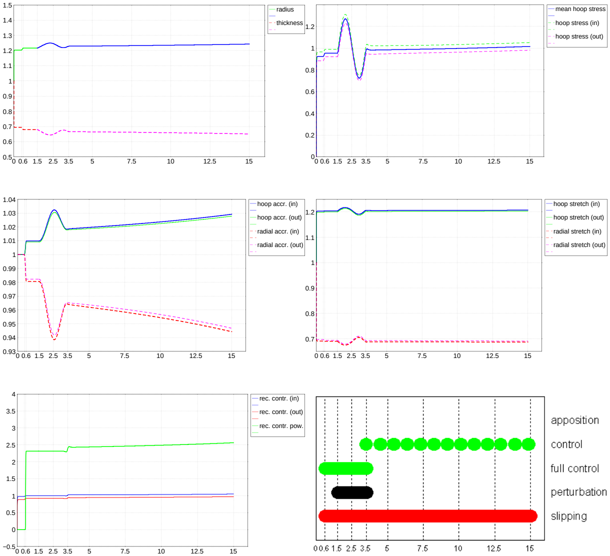
1. Q^{c} is increased to a fraction of the value of a full recovery control:

$$Q^{c} = Q^{\diamond} - \mathrm{g}\left(1 + \frac{D^{c}}{D^{s}}\right)\left(\left(\mathrm{T}_{h} - \mathrm{T}_{h}^{\diamond}\right) + \left(\mathrm{T}_{r} - \mathrm{T}_{r}^{\diamond}\right)\right),$$

which is meant to simulate an impaired recovery control.

2. negligible tissue apposition:

$$Q^{t} = -\left(\mathrm{T}_{r} - \widetilde{\phi}\right).$$



IMPAIRED RECOVERY

[case-41-003]

D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	0.8

After the end of a short perturbation of the intramural pressure, a recovery control, though higher than the previous homeostatic value but lower than the optimal value, cannot prevent the unlimited increase of the radius.

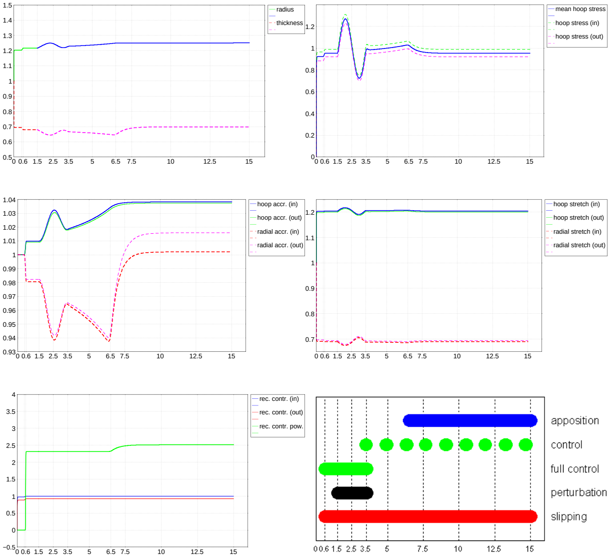
History ♯4: slow recovery, tissue apposition

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

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

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

$$Q^{\mathsf{t}} = G^{\mathsf{t}}\left(\mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{h}}^{\diamond}\right) - \left(\mathrm{T}_{\mathsf{r}} - \widetilde{\phi}\right).$$

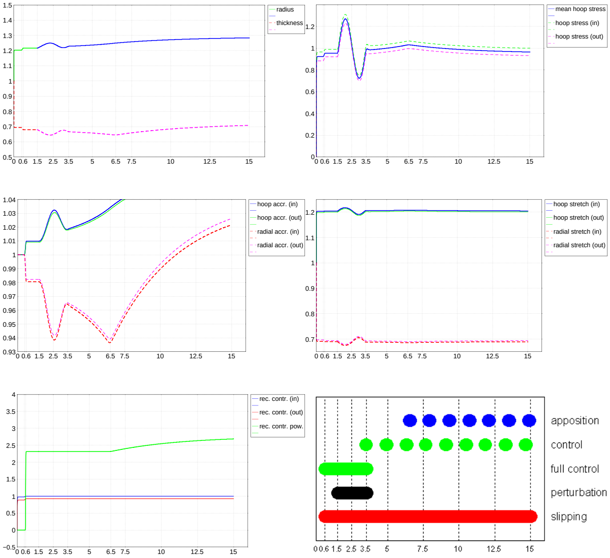


SLOW RECOVERY STRONG APPOSITION

[case-42-004]

D^c/D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	0
G^p D^p	4000 0.002

After the end of a short perturbation of the intramural pressure, radial tissue apposition goes into action making the aneurysm thicken and driving it to a new homeostatic state at the starting value of the hoop stress.



SLOW RECOVERY
WEAK APPOSITION

[case-42-005]

D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	0
G^p D^p	1000 0.002

After the end of a short perturbation of the intramural pressure, a radial tissue apposition goes into action making the aneurysm thicken but failing to drive it quickly to a new homeostatic state.

Summary

- Growth of saccular aneurysms
  - elastic deformation;
  - change of relaxed configuration.
- Multiple remodeling 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.

Future work

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

Background references

1. A. Di Carlo, S. Quiligotti, Growth and balance, *Mechanics Research Communications*, 29, 449–456, 2002.
   - Conceptual framework of growth and remodeling theory.
2. A. DiCarlo, V. Varano, V. Sansalone, and A. Tatone, Living Shell-Like Structures, in *Applied and Industrial Mathematics In Italy - II*, World Scientific, 2007.
   - First ideas concerning the modeling of saccular aneurysms.
3. M. Tringelová, P. Nardinocchi, L. Teresi, and A. DiCarlo, The cardiovascular system as a smart system, in *Topics on Mathematics for Smart Systems*, World Scientific, 2007.
   - Application to modeling of arterial walls.