# Competing growth mechanisms in the development of saccular aneurysms

## Stress-driven growth and control laws

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The Geometry and Mechanics of Growth in Living Systems

Cargèse, July 14-26, 2008

# Outline

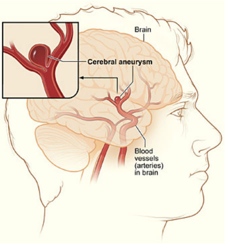

1. Histology and pathology
2. Mechanical model
   - Geometry & kinematics
   - Working & balance
   - Constitutive issues
   - Discussion
3. Multiple growth mechanisms
   - Mechanical model
   - Biomechanical characterisation
4. Numerical simulations

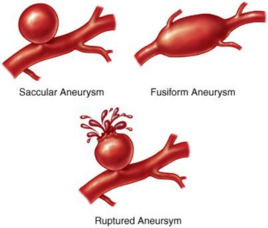
# Part I

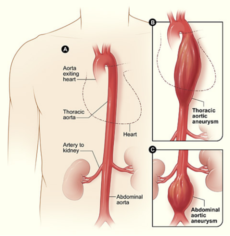
# Saccular aneurysms

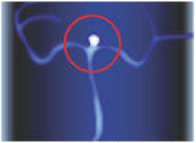
1 Histology and pathology

# Aneurysms

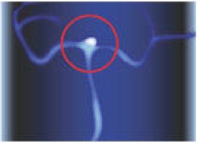


Saccular (sac-like), with a well-defined neck.

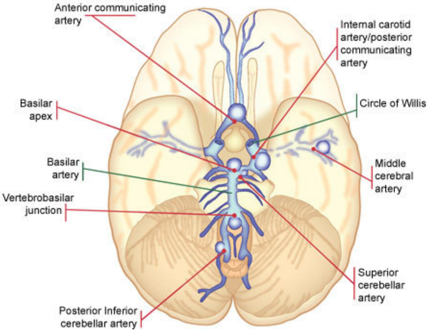


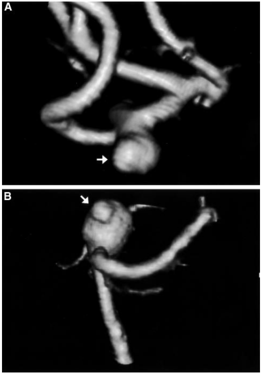
Broad-based with a wide neck.

Fusiform (spindle shaped) without a distinct neck.

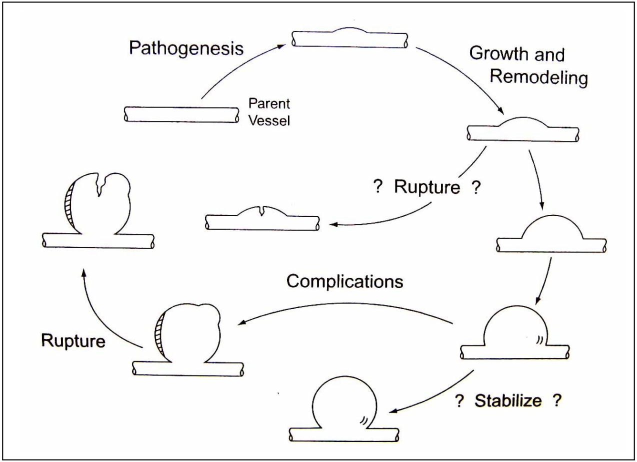
# Aneurysms

Intracranial saccular aneurysms are pouches of the arterial wall.



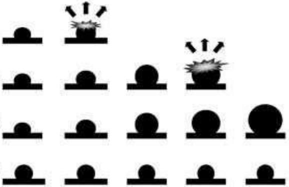



# Aneurysms




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

# Aneurysms




| | Multiple (148 aneurysms) | Single (232 aneurysms) | With SAH (30 aneurysms) | Total (380 aneurysms) |
|---|---|---|---|---|
| | Clinical presentation | | | |
| 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

## Mechanical model

2. Mechanical model
   - Geometry & kinematics
   - Working & balance
   - Constitutive issues
   - Discussion

# Growth mechanics

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

*ex vivo* | zero-load | zero-stress (?)

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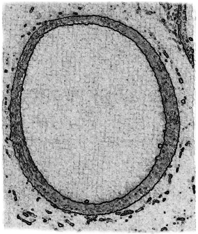

[Y. C. Fung, *Biomechanics: Mechanical Properties of Living Tissues*, 1993]

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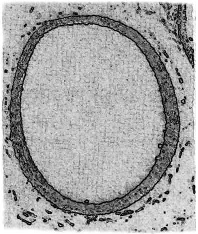

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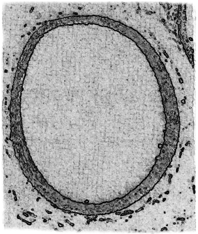
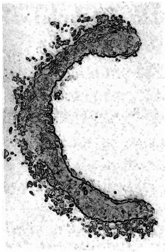


zero-load

zero-stress (?)



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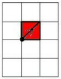
$\mathcal{D}$



| | |
|---|---|
| $\mathrm{p}$ : | *gross placement* |
| $\nabla \mathrm{p}$ : | *gradient of the gross placement* |
| $\mathbb{G}$ : | *growth* |
| $\mathrm{A}$ : | *warp* (*purely elastic*) |
| $(\mathrm{p}, \mathbb{G})$ : | *refined motion* |

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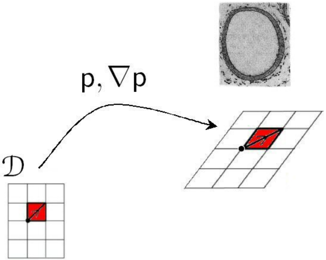


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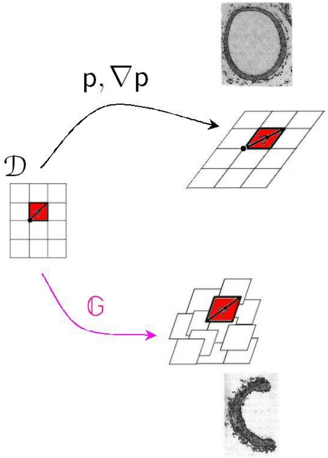


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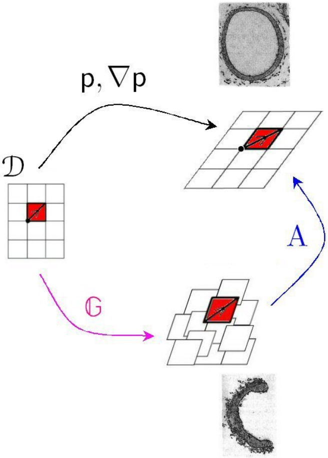


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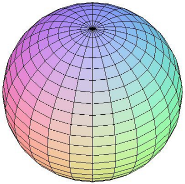
# Saccular aneurysms

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

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



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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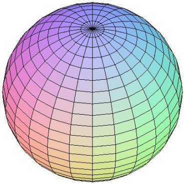

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# Geometry & kinematics

*gross placement*

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

*gradient of the gross placement*

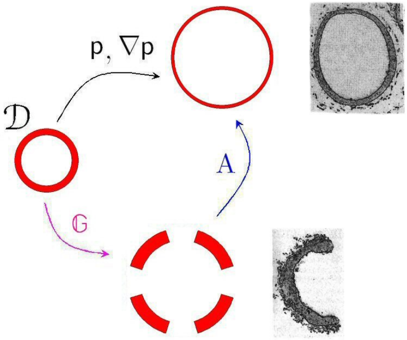
$$\nabla \mathrm{p} = \rho'\, \mathrm{P}_r + \frac{\rho}{\xi}\, \mathrm{P}_h$$

*growth*

$$\mathbb{G} = \gamma_r\, \mathrm{P}_r + \gamma_h\, \mathrm{P}_h$$

*warp*

$$\mathbb{A} := (\nabla \mathrm{p})\, \mathbb{G}^{-1} = \alpha_r\, \mathrm{P}_r + \alpha_h \mathrm{P}_h$$



# Geometry & kinematics

*refined motion*: $(\mathrm{p}, \mathbb{G})$

*refined velocity*: $(\dot{\mathrm{p}}, \dot{\mathbb{G}}\,\mathbb{G}^{-1})$

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

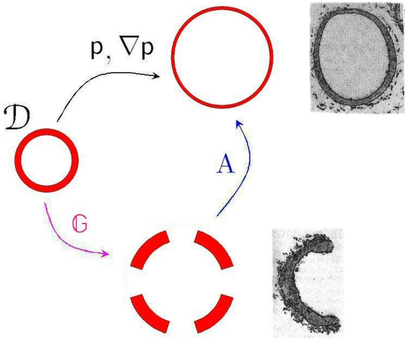
$$\dot{\mathbb{G}}\,\mathbb{G}^{-1} = \frac{\dot{\gamma}_r}{\gamma_r}\,\mathrm{P}_r + \frac{\dot{\gamma}_h}{\gamma_h}\,\mathrm{P}_h$$

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

$$\mathrm{v} = v\,\mathbf{e}_r$$

$$\mathbb{V} = \mathrm{V}_r\,\mathrm{P}_r + \mathrm{V}_h\,\mathrm{P}_h$$

(*gross* and *growth* velocity)



# Working

*Goal:*

- To describe the energetic balance of growth

*Working*

- (brute) elasticity

$$\int_{\mathcal{D}} -\mathrm{S} \cdot \nabla \mathrm{v} + \int_{\partial\mathcal{D}} \mathrm{t}_{\partial\mathcal{D}} \cdot \mathrm{v}$$

- growth + elasticity

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

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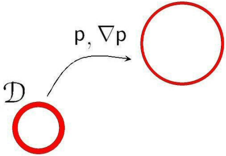
# Balance laws

balance of *(brute) stress*

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




balance of *accretive stress*

$$\mathrm{Q_r^i}(\xi) - \mathrm{Q_r^o}(\xi) = 0$$
$$\mathrm{Q_h^i}(\xi) - \mathrm{Q_h^o}(\xi) = 0$$

# Balance laws

balance of *(brute) stress*

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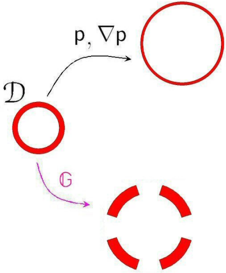
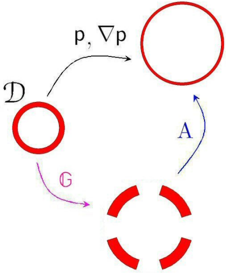


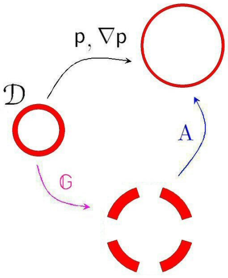
# Characterising the passive mechanical response

- Energetics
- Dissipation principle



# Energetics

$$\Psi(\mathscr{P}) = \int_{\mathscr{P}} \mathrm{J}\,\psi\,, \qquad \mathrm{J} := \det(\mathbb{G}) > 0$$




$(\mathrm{H1}_1)$: the value of $\psi(x)$ depends solely on the value of the warp $\mathrm{A}(x)$

$$\psi(x) = \phi\,(\,\alpha_{\mathrm{r}}(\xi), \alpha_{\mathrm{h}}(\xi); \xi\,)$$

$(\mathrm{H1}_2)$: incompressible elasticity

$$\det \mathrm{A} = \alpha_{\mathrm{r}}\, {\alpha_{\mathrm{h}}}^2 = 1$$

Fung strain energy density

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

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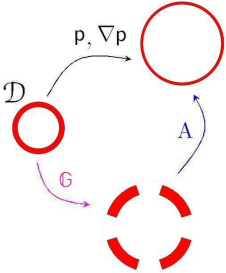


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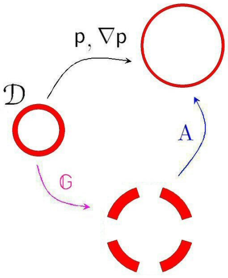


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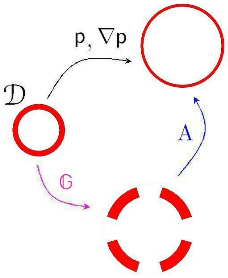


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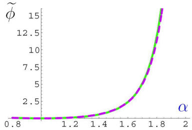

# Dissipation principle

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

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

*consistency*

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

*reduced dissipation inequality*

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

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

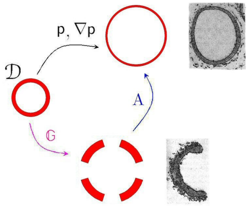
*reduced dissipation inequality*

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

# Mechanical model

## Kinematics

| | | | |
|---|---|---|---|
| *gross placement* | $\mathrm{p}$ | $=$ | $x_o + \rho\, \mathbf{e}_r$ |
| *growth* | $\mathbb{G}$ | $=$ | $\gamma_r \mathsf{P}_r + \gamma_h \mathsf{P}_h$ |
| *warp* | $\mathrm{A}$ | $=$ | $\alpha_r \mathsf{P}_r + \alpha_h \mathsf{P}_h$ |




## Working

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

## (Reduced) dissipation inequality

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

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

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

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

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

*But...*

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

*How to explain that?*
*How to deal with that?*

# Part III

## Multiple growth mechanisms

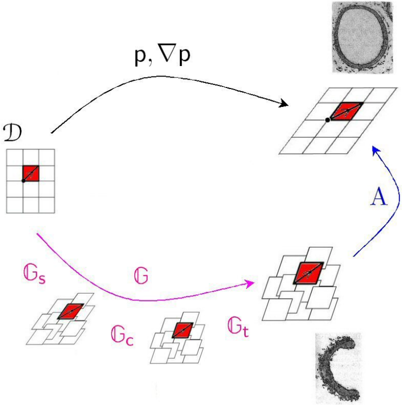
3. Multiple growth mechanisms
   - Mechanical model
   - Biomechanical characterisation

# Multiple (competing) growth mechanisms

(s) *slipping*, (c) *recovery*, and (t) *tissue apposition/resorption*

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

- s sliding of tissue constituents
  passive
- c any action directly contrasting the slipping
  active
- t fiber deposition/removal, cell proliferation/destruction
  active



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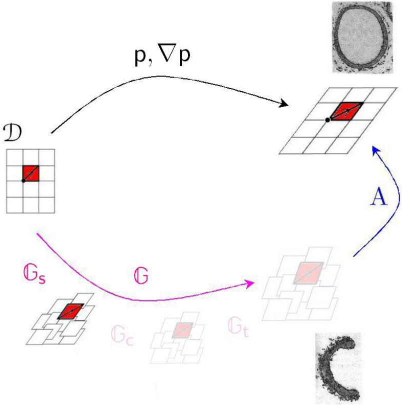

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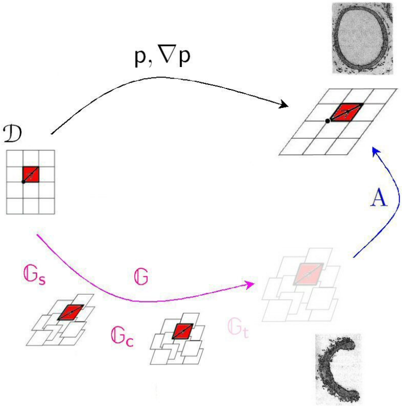

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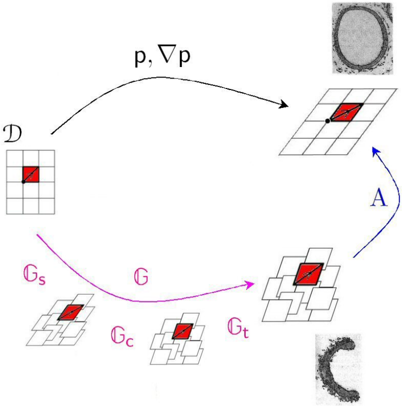

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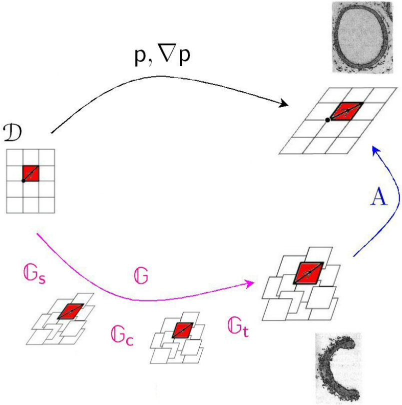

# Multiple (competing) growth mechanisms

(s) *slipping*, (c) *recovery*, and (t) *tissue apposition/resorption*

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

*growth velocity*

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

*test velocity*

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

*working*

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

# Dissipation principle

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

*consistency*

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

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

*reduced dissipation inequality*

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

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# Multiple (competing) growth mechanisms

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*growth velocity*

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*test velocity*

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

*working*

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

# Characterising the accretive couples

| | **Inner** | **Outer** | |
| --- | --- | --- | --- |
| "stress" | $\mathbb{Q}^i_t \,, \mathbb{Q}^i_c \,, \mathbb{Q}^i_s$ | $\mathbb{Q}^o_t \,, \mathbb{Q}^o_c \,, \mathbb{Q}^o_s$ | active control |
| | $\Uparrow$ | $\vdots$ | |
| | $\mathbb{G}_t \,, \mathbb{G}_c \,, \mathbb{G}_s$ | | |
| | $\overset{+}{\mathbb{Q}}{}^i_t \,, \overset{+}{\mathbb{Q}}{}^i_c \,, \overset{+}{\mathbb{Q}}{}^i_s$ | | |

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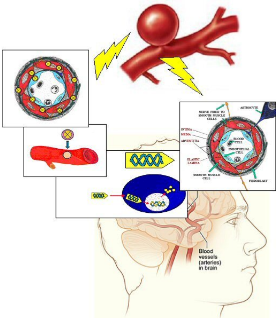

# Characterising the growth mechanisms

(H2$_1$): We assume that only $\mathbb{G}_t$ changes volume, while neither $\mathbb{G}_s$ nor $\mathbb{G}_c$ affects volume

(H2$_2$): We assume that tissue apposition is only radial

$$\mathbb{G}_t = \gamma_r^t \mathsf{P}_r + \mathsf{P}_h$$

$$\mathbb{G}_c = \gamma_r^c \mathsf{P}_r + \gamma_h^c \mathsf{P}_h \qquad \gamma_r^c (\gamma_h^c)^2 = 1$$

$$\mathbb{G}_s = \gamma_r^s \mathsf{P}_r + \gamma_h^s \mathsf{P}_h \qquad \gamma_r^s (\gamma_h^s)^2 = 1$$

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$$\mathbb{G}_s = \gamma_r^s \, P_r + \gamma_h^s \, P_h \qquad \gamma_r^s (\gamma_h^s)^2 = 1$$

# Characterising the dissipation

($H3_1$): We assume that dissipation is only due to growth

($H3_2$): Linear viscous dissipation

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

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

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

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

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

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

# Evolution equations

*growth*

$$D^{t}\,\dot{\gamma}^{t}_{r}/\gamma^{t}_{r} = (\mathrm{T}_{r} - \widetilde{\phi}) + \mathrm{Q}^{t}$$
$$D^{c}\,\dot{\gamma}^{c}_{h}/\gamma^{c}_{h} = (\mathrm{T}_{h} - \mathrm{T}_{r}) + \mathrm{Q}^{c}$$
$$D^{s}\,\dot{\gamma}^{s}_{h}/\gamma^{s}_{h} = (\mathrm{T}_{h} - \mathrm{T}_{r}) + \mathrm{Q}^{s}$$

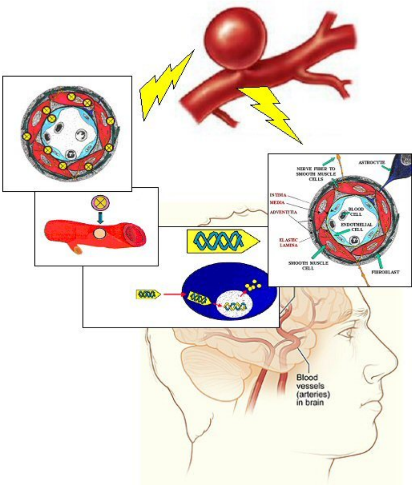
$$\mathbb{Q}^{o}_{t}/\mathrm{J} = Q^{t}_{r}\,\mathrm{P}_{r} \qquad \mathbb{Q}^{o}_{c}/\mathrm{J} = Q^{c}_{r}\,\mathrm{P}_{r} + Q^{c}_{h}\,\mathrm{P}_{h} \qquad \mathbb{Q}^{o}_{s}/\mathrm{J} = Q^{s}_{r}\,\mathrm{P}_{r} + Q^{s}_{h}\,\mathrm{P}_{h}$$

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

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

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

# Characterising the controls




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

# Characterising the controls

(H4$_s$): null control on slipping mechanism

$$Q^s = 0$$

(H4$_c$): recovery tuned with respect to slipping

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

(H4$_t$): radial apposition driven by hoop stress

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

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

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(H4$_t$): radial apposition driven by hoop stress

$$Q^{t} \sim G^{t}\left(T_{h} - T_{h}^{\diamond}\right)$$

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

# Evolution equations

*gross motion*

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

*growth*

$$\dot{\gamma}_\mathsf{h}/\gamma_\mathsf{h} = \kappa_\mathsf{h}\,(\Delta\mathrm{T}_\mathsf{h} - \Delta\mathrm{T}_\mathsf{r})$$
$$\dot{\gamma}_\mathsf{r}/\gamma_\mathsf{r} = -2\dot{\gamma}_\mathsf{h}/\gamma_\mathsf{h} + \kappa_\mathsf{r}\,\Delta\mathrm{T}_\mathsf{h}$$

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

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

# Part IV

# Numerical simulations

4 Numerical simulations
- Natural histories
- Passive slipping, recovery, null tissue apposition
- Passive slipping, slow recovery, tissue apposition

# 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 $Q^{\mathsf{c}}$ necessary to maintain this homeostatic state:

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

- Thus, let the intramural pressure experience a short-time bump:

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

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

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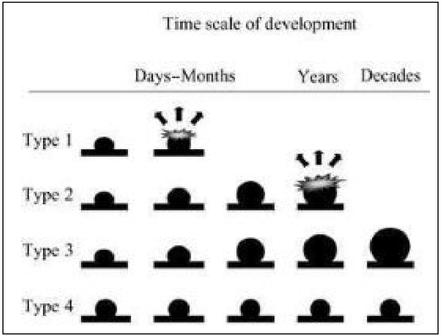
- Thus, let the intramural pressure experience a short-time bump:

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

# 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:

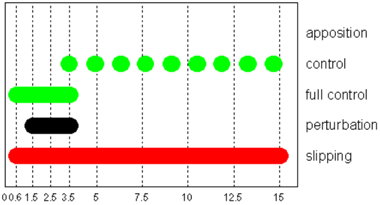
$$\mathrm{Q}^{\mathsf{c}} = Q^{\diamond} \sim \mathrm{T}^{\diamond}_{\mathsf{h}} - \mathrm{T}^{\diamond}_{\mathsf{r}}$$

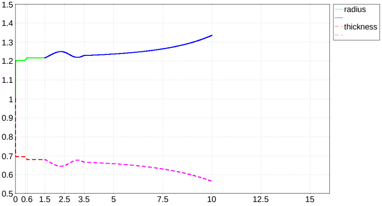
   simulating the inability of the recovery control to keep pace with a sudden perturbation

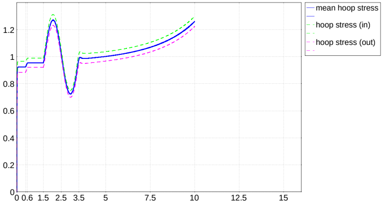
2. negligible tissue apposition:

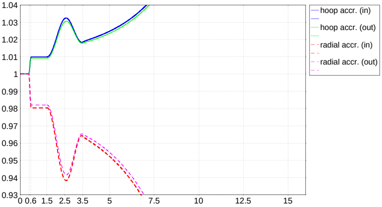
$$\mathrm{Q}^{\mathsf{t}} \sim 0$$

# SLOW RECOVERY ($G^c = 0$), null tissue apposition

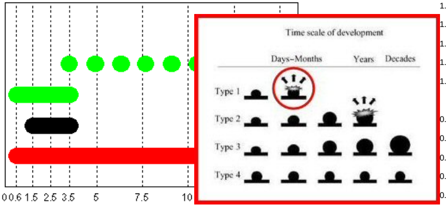


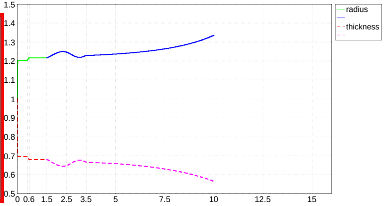



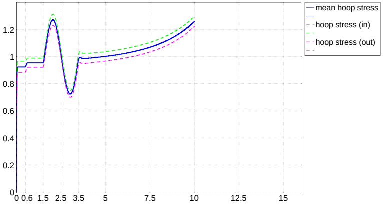



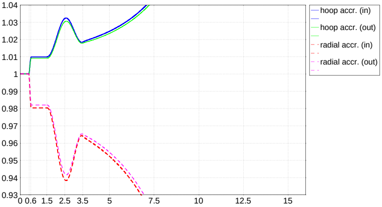



# SLOW RECOVERY ($G^c = 0$), null tissue apposition



# History ♯2: fast recovery, null apposition

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

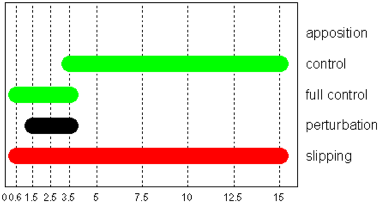
$$\mathrm{Q}^{\mathsf{c}} \sim \mathrm{T}_{\mathsf{h}} - \mathrm{T}_{\mathsf{r}}$$

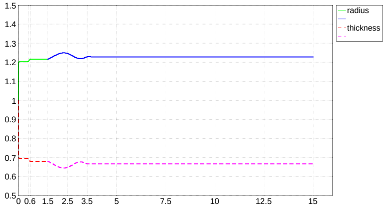
   simulating the capability of the recovery control to immediately keep pace with a sudden perturbation

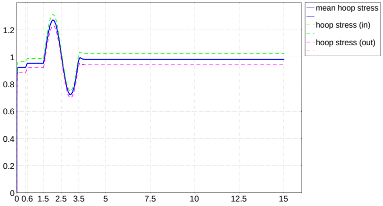
2. negligible tissue apposition:

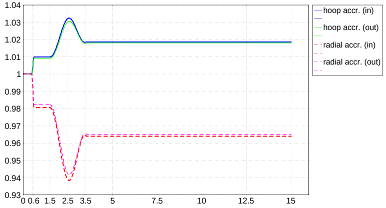
$$\mathrm{Q}^{\mathsf{t}} \sim 0$$

# FAST RECOVERY ($G^c = 1$), null tissue apposition

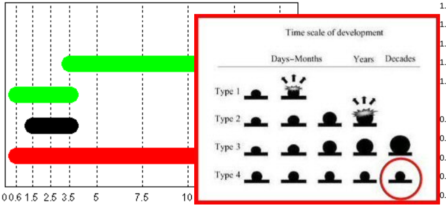


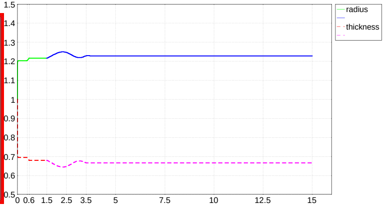



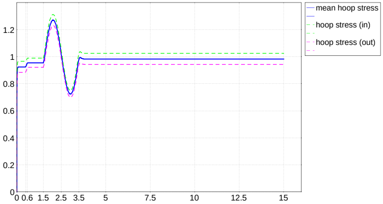



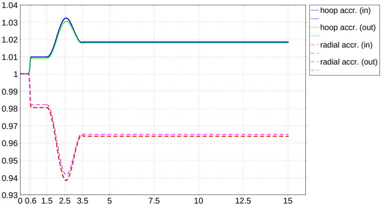



# FAST RECOVERY ($G^c = 1$), null tissue apposition



# History ♯3: delayed recovery, null apposition

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

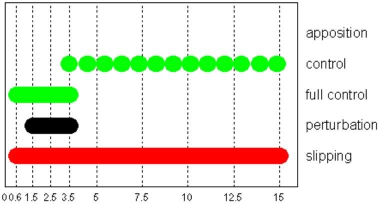
$$\mathrm{Q}^{\,c} \sim \mathcal{G}^c\,(\mathrm{T_h} - \mathrm{T_r}) + (1 - \mathcal{G}^c)\,(\mathrm{T_h^\diamond} - \mathrm{T_r^\diamond})$$

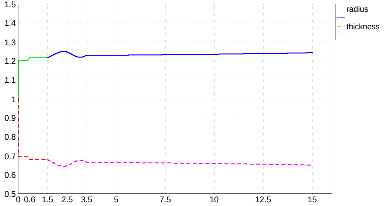
which is meant to simulate an impaired recovery control

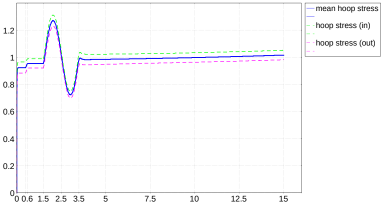
2. negligible tissue apposition:

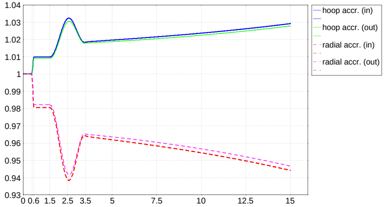
$$\mathrm{Q}^{\,t} \sim 0$$

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

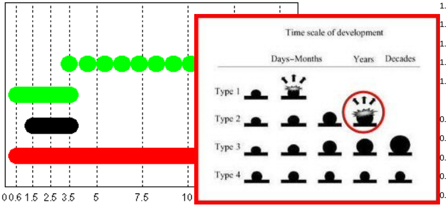


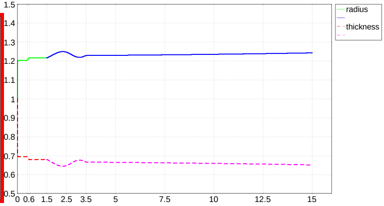



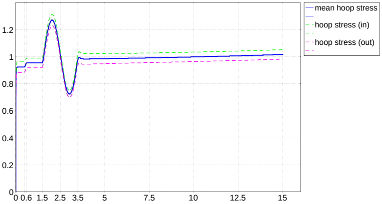



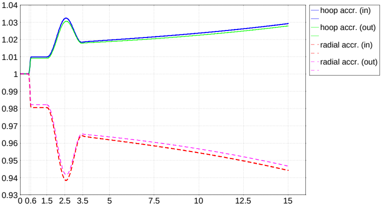



# DELAYED RECOVERY ($G^c = 0.8$), null tissue apposition

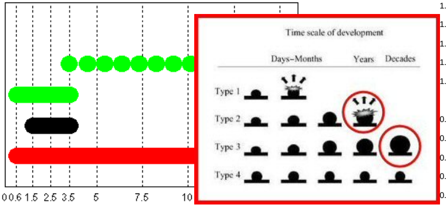


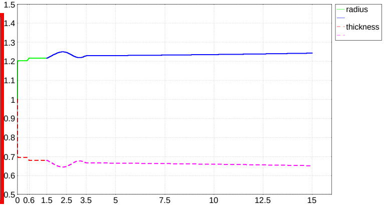



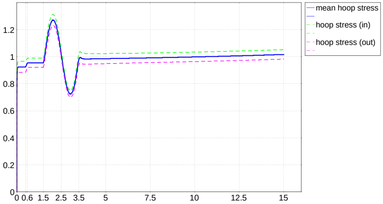



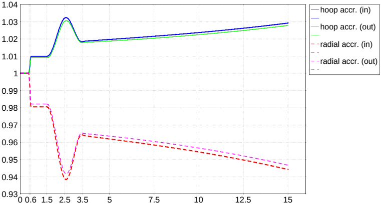



# DELAYED RECOVERY ($G^c = 0.8$), null tissue apposition



# History ♯4: slow recovery, tissue apposition

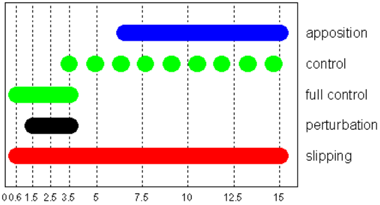
1. $Q^{c}$ is held fixed to the previous value for the rest of the time:

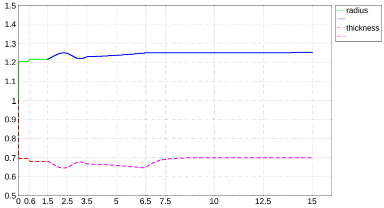
$$\mathrm{Q}^{c}(t) = Q^{\diamond}$$

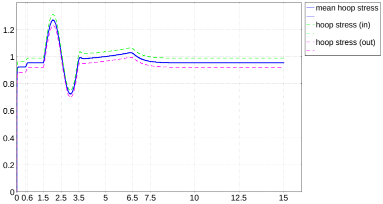
2. radial tissue apposition goes into action through a stress-driven control law:

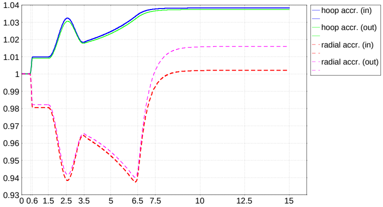
$$\mathrm{Q}^{t} \sim G^{t}\left(\mathrm{T}_{h} - \mathrm{T}_{h}^{\diamond}\right)$$

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

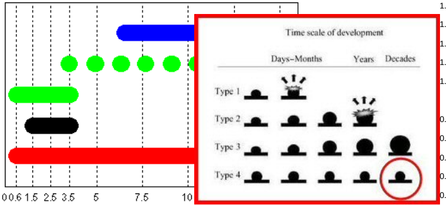


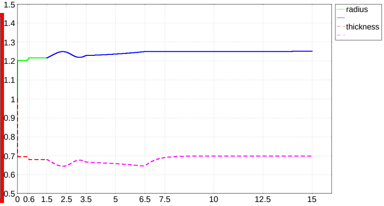



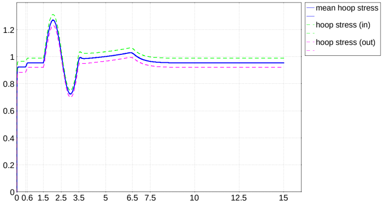



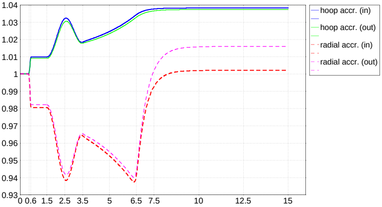



# Slow recovery ($G^c = 0$), FAST TISSUE APPOSITION ($G^t \gg$)

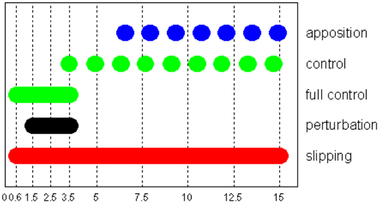


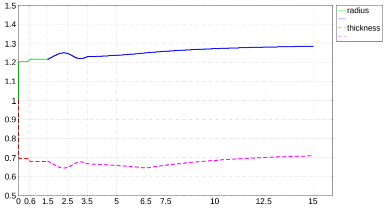



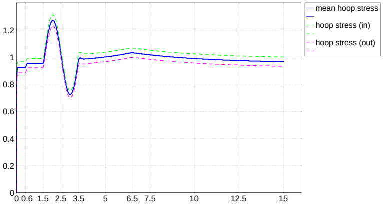



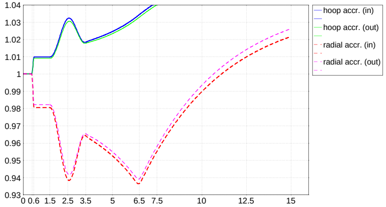



# Slow recovery ($G^c = 0$), SLOW TISSUE APPOSITION ($G^t \ll$)

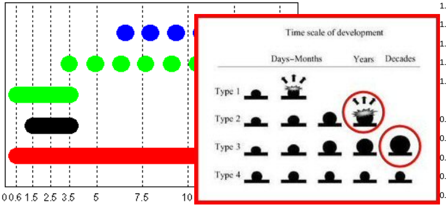


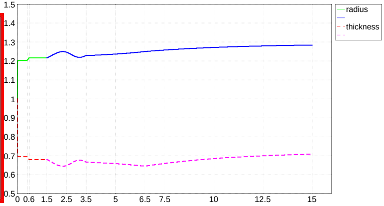



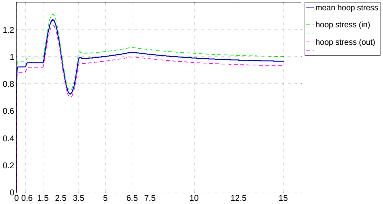



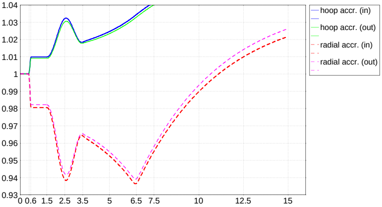



# Slow recovery ($G^c = 0$), SLOW TISSUE APPOSITION ($G^t \ll$)



# Summary

- Evolution of saccular aneurysms
  - elastic deformation;
  - growth, *i.e.* change of relaxed configuration.
- Multiple remodelling mechanisms
  - *slipping*: only passive;
  - *recovery*: slow/fast control;
  - *tissue apposition*: hoop stress driven control.
- Numerical evidence
  - recovery control is unable to maintain homeostatis;
  - tissue apposition plays a central role.

# Future work

- In tight connection with biologists, physicists and clinicians...
- Better characterisation of the biological system
  - description of the growth mechanisms;
  - evolution of elastic properties;
  - non uniform material properties.
- Weaker assumptions on symmetry
- Quantitative calibration and model validation

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# References

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3. V. Sansalone, A. Tatone, V. Varano, and A. DiCarlo, Competing growth mechanisms in the development of saccular aneurysms, *in preparation*. (Ask me for preprint.)

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