Multi-scale modelling of aneurysm formation - linking continuum mechanics and adaptation to signalling events

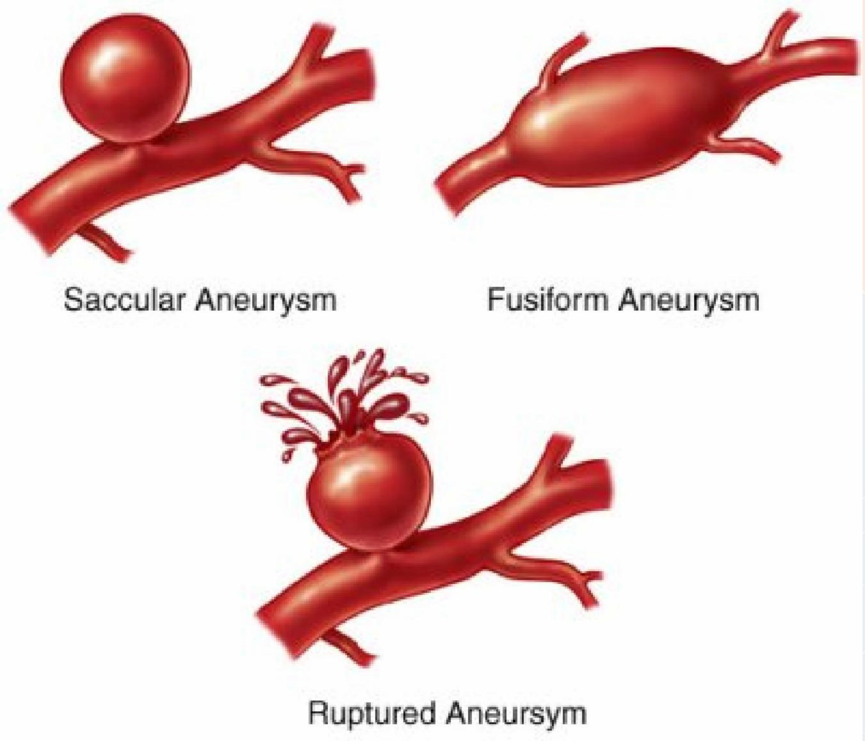
H. Schmid[1], M.Cooling[2] P.N. Watton[3], P. Hunter[2] and M. Itskov[1]

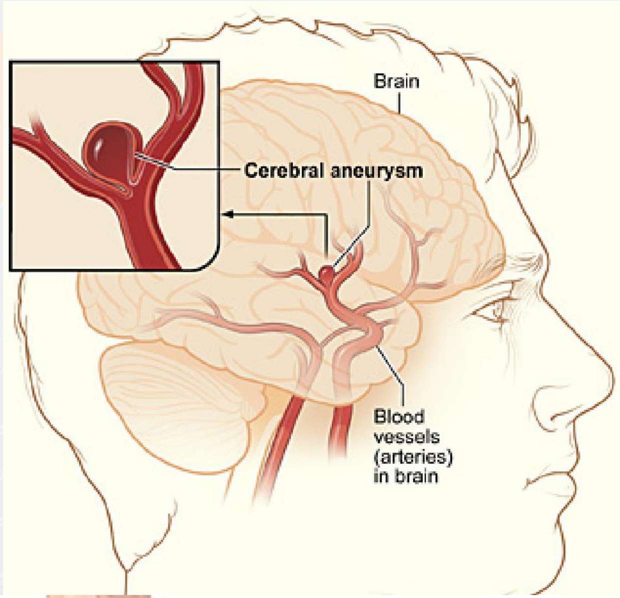
[1]Department of Continuum Mechanics, RWTH Aachen University, Germany
[2]Auckland Bioengineering Institute, University of Auckland, New Zealand
[3]Department of Computational Biology, University of Oxford, Oxford, United Kingdom

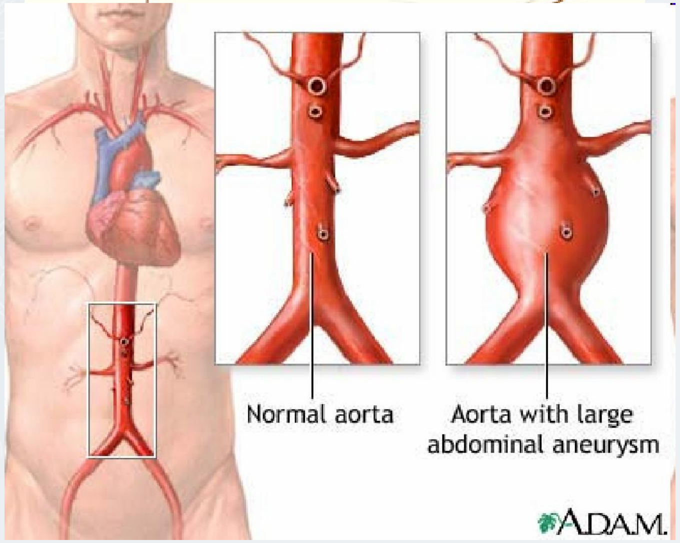
26th January, 2010, CellML meeting Auckland

Contents

Aneurysm, forms & location:





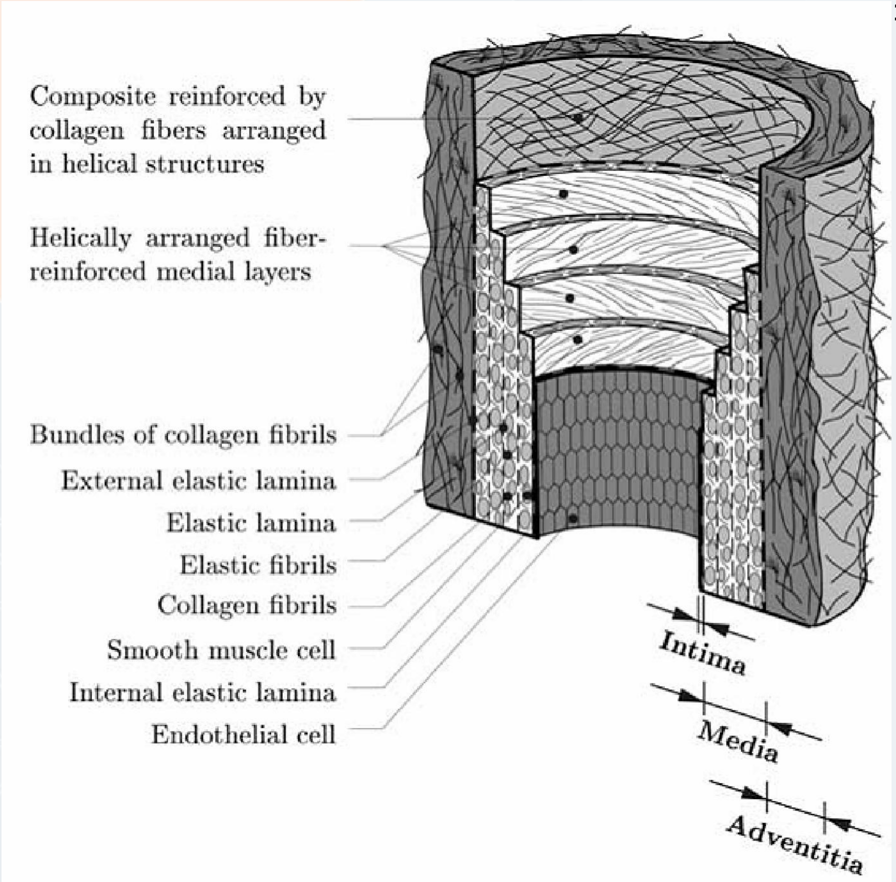


Aneurysm: potentially pathological dilatation of arterial wall

Images from: www.aarp.org

Arterial wall, structure:

- Mechanical components:
  - smooth muscle cells
  - collagen
  - elastin
- Passive & active response



[1]Holzapfel et al., 2000

Remodelling framework[1]:

e.g. endothelial shear stress

signalling pathway model

composition of tissue

e.g. constrained mixture

rule of mixtures

material law

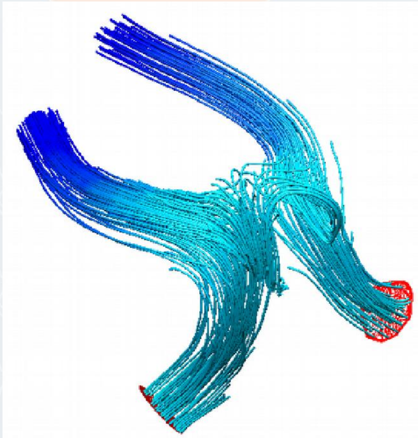
mechanical properties of tissue

FEM analysis

fluid structure interaction

aneurysm shape

CFD analysis



CFD analysis
Circle of Willis[2]

[1]Schmid et al, 2008

[2]Ho et al, 2009

How to link micro- and macro-scale?

signalling pathway model

?

composition of tissue

e.g. constrained mixture

rule of mixtures

material law

mechanical properties of tissue

FEM analysis

fluid structure interaction

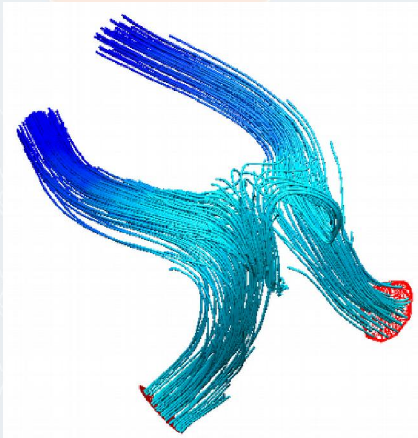
aneurysm shape

?

CFD analysis

e.g. endothelial shear stress

?

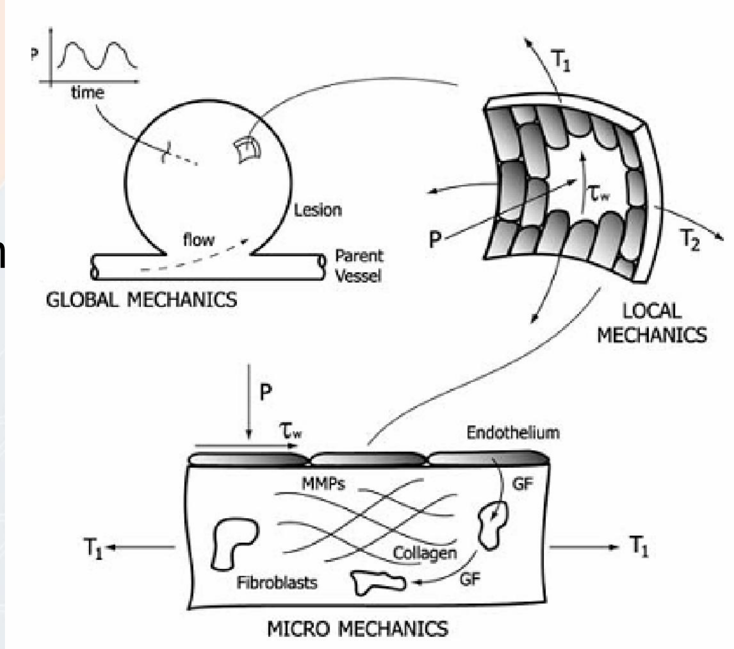


CFD analysis
Circle of Willis[2]

[2]Ho et al, 2009

Remodelling:

- **Mechanical factors** for altered signal transduction pathways due to change in:
  - wall shear stress (**WSS**) from blood flow
  - pressure – biaxial stretch of **endothelium**
  - axial tension of artery



- Possible **mechanical responses** to altered environment:
  - active: vasoconstriction (sec ~ min)
  - passive: **remodelling**: change of reference configuration (days ~ months)
  - passive: **growth**: increase of constituents (days ~ months)

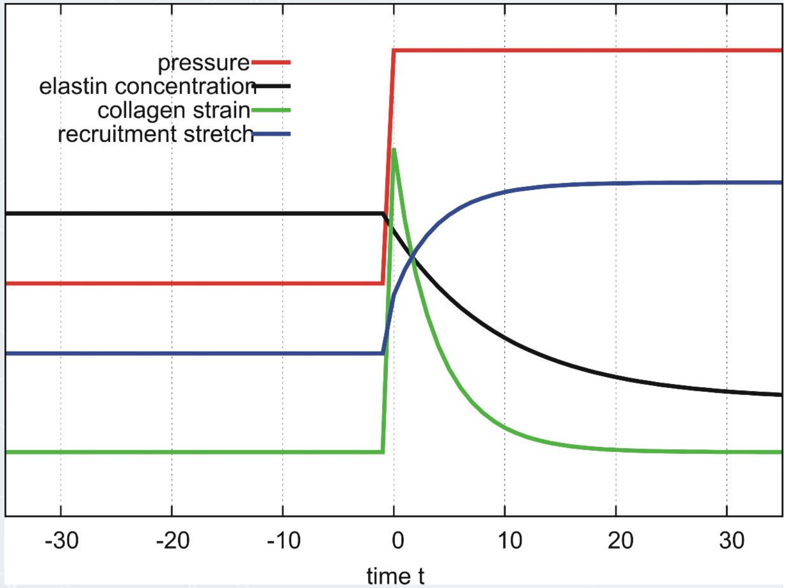
[1]Humphrey & Rajagopal, 2003

Current approach – just solid mechanics

$$f_e(t) = f_e(0)\, c_{\min}^{\frac{t}{T}}$$

$$\frac{\partial \lambda_{rec}}{\partial t} = \alpha (E_c - E_a)$$

$$\frac{\partial f_c}{\partial t} = \beta\, f_c (E_c - E_a)$$



Future ideas – first step, coupling to hemodynamics

$$f_e(t) = F_{fluid}(\tau, E_{endoth})$$

$$\frac{\partial \lambda}{\partial t} = \alpha(E_c - E_a)$$

$$\frac{\partial f_c}{\partial t} = \beta\, f_c(E_c - E_a)$$

Future ideas – second step, coupling to signalling

$$f_e(t) = F^{e}_{sign}(\tau, E_{endoth})$$

$$\frac{\partial \lambda}{\partial t} = F^{\lambda}_{sign}(\tau, E_{endoth})$$

$$\frac{\partial f_c}{\partial t} = F^{c}_{sign}(\tau, E_{endoth})$$

Challenges

- Vastly differing time scales (sec ~ years)
- Computational cost (CFD, FEM and signalling)
- How to implement it into CMISS?
  - Mechanical stress strain relationship is also implemented via CellML
  - Problem with storage between different solution procedures
- How can we use both: the mechanical and signalling models in one integrated model?

Thank you very much for your attention!

Special thanks to

- Peter
- Catherine
- Chris
- Mike
- Admin team