Stress/Diffusion Dependent Morphogenesis

Presented in the Embryo Physics Course http://www.embryophysics.org
May 19, 2010
By

Laboratori de Càlcul Numèric (LaCàN)
Dep. App. Mathemtics III
Universitat Politècnica de Catalunya
Barcelona, Spain
http://www-lacan.upc.es, j.munoz@upc.edu

Stress/diffusion dependent morphogenesis

Jose J Muñoz

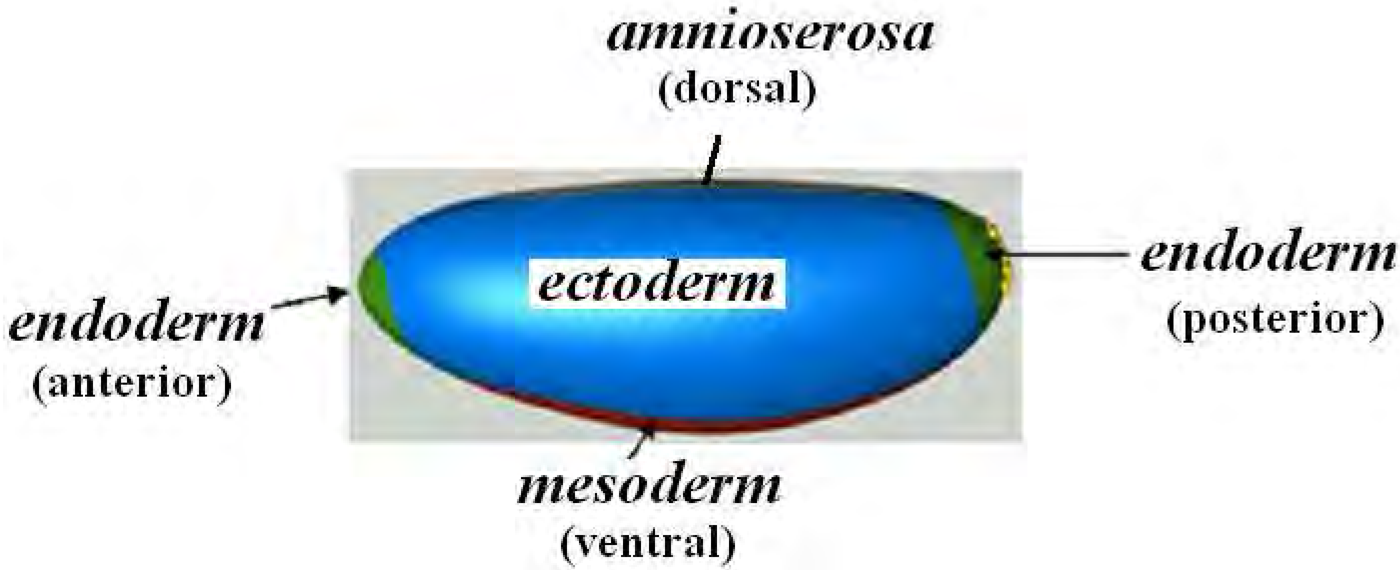
Laboratori de Càlcul Numèric (LaCàN)
Dep. App. Mathemtics III
Universitat Politècnica de Catalunya
Barcelona, Spain
www-lacan.upc.es

Outline

- Morphogenesis in embryo development
- The biomechanical perspective:
  - Driving mechanisms
  - Signalling
- Modelling:
  - Deformation decomposition
  - Kinematically driven forces
  - Stress-controlled model

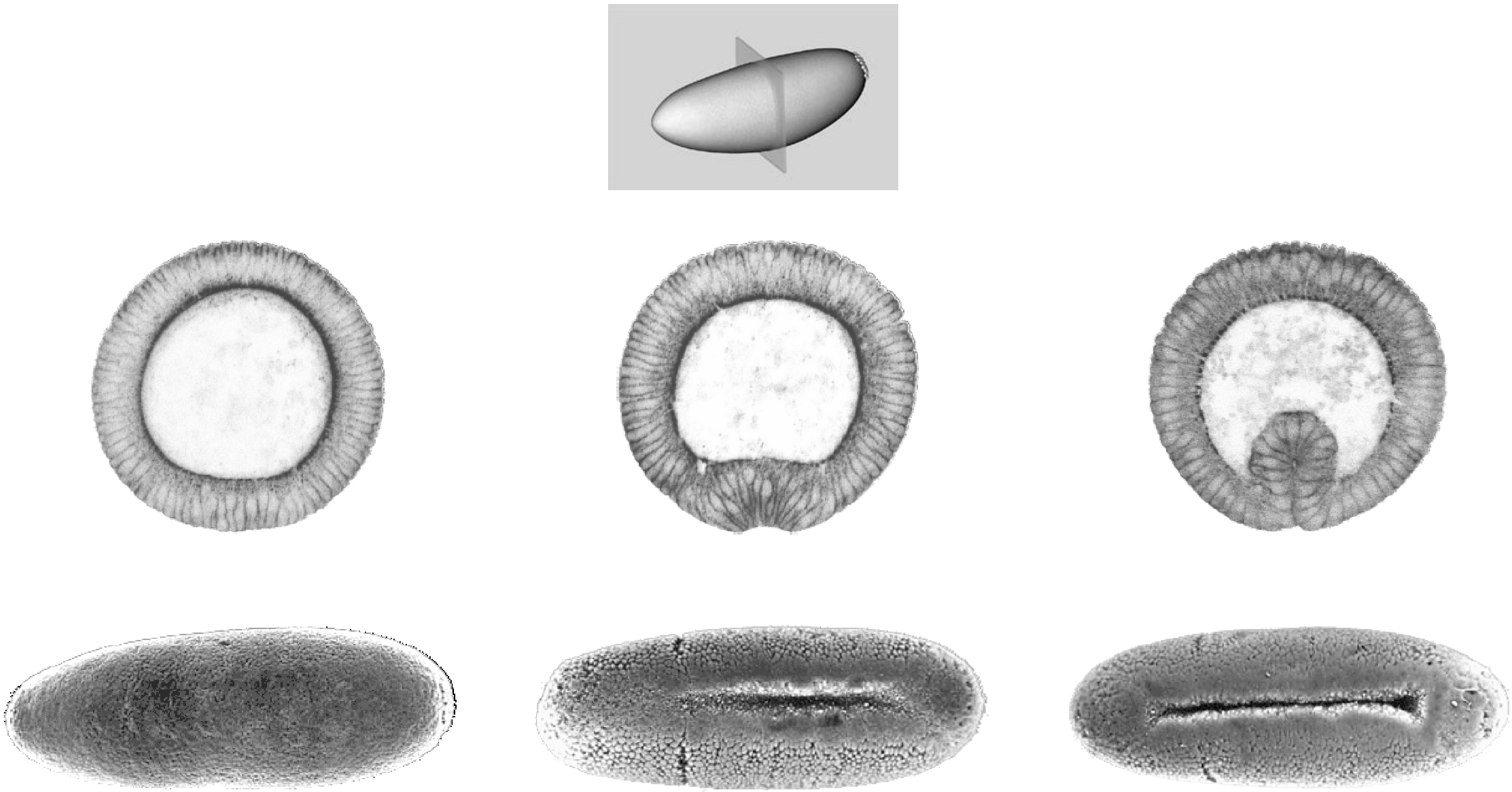
Morphogenesis in embryo development

- Gastrulation:
  - After cellularisation and formation of the blastocel
  - Cell fate differentiation and polarisation
  - First large displacements and deformation of epithelium



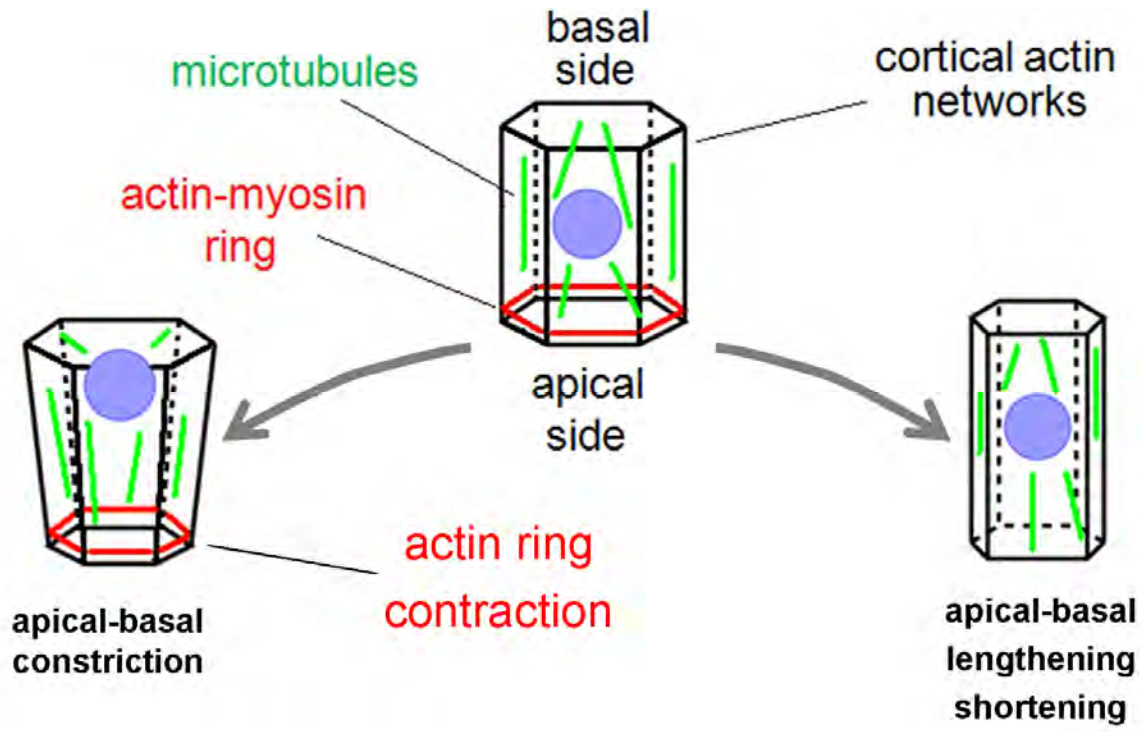
Morphogenesis in embryo development

•Concurrent movements: ventral and cephalic furrow invagination, germ band extension (GBE)



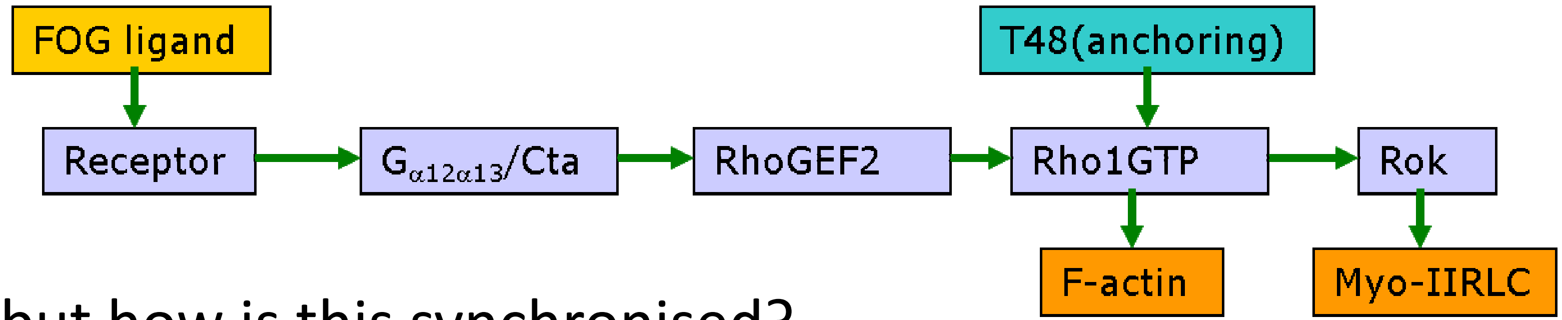
The biomechanical perspective

- •Mechanical components :
  - •Cytoskeleton: microtubulines, actin filaments, intermediate filaments
  - •Cytoplasm, yolk: fluids(nearly-incompressbile and fully incompressible)
- •Observed deformations:



The biomechanical perspective

- Main genes involved:
  - ***twist*****:** flattening, synchronisation, snail expression.
  - ***snail***: apico-basal constriction, elongation, repression of ectoderm
  - ***huckebein,tailless*****:** define region of twist and snail expression
  - ***bnt*****:** Repressiono of cephallic furrow
- Pathway[1]:



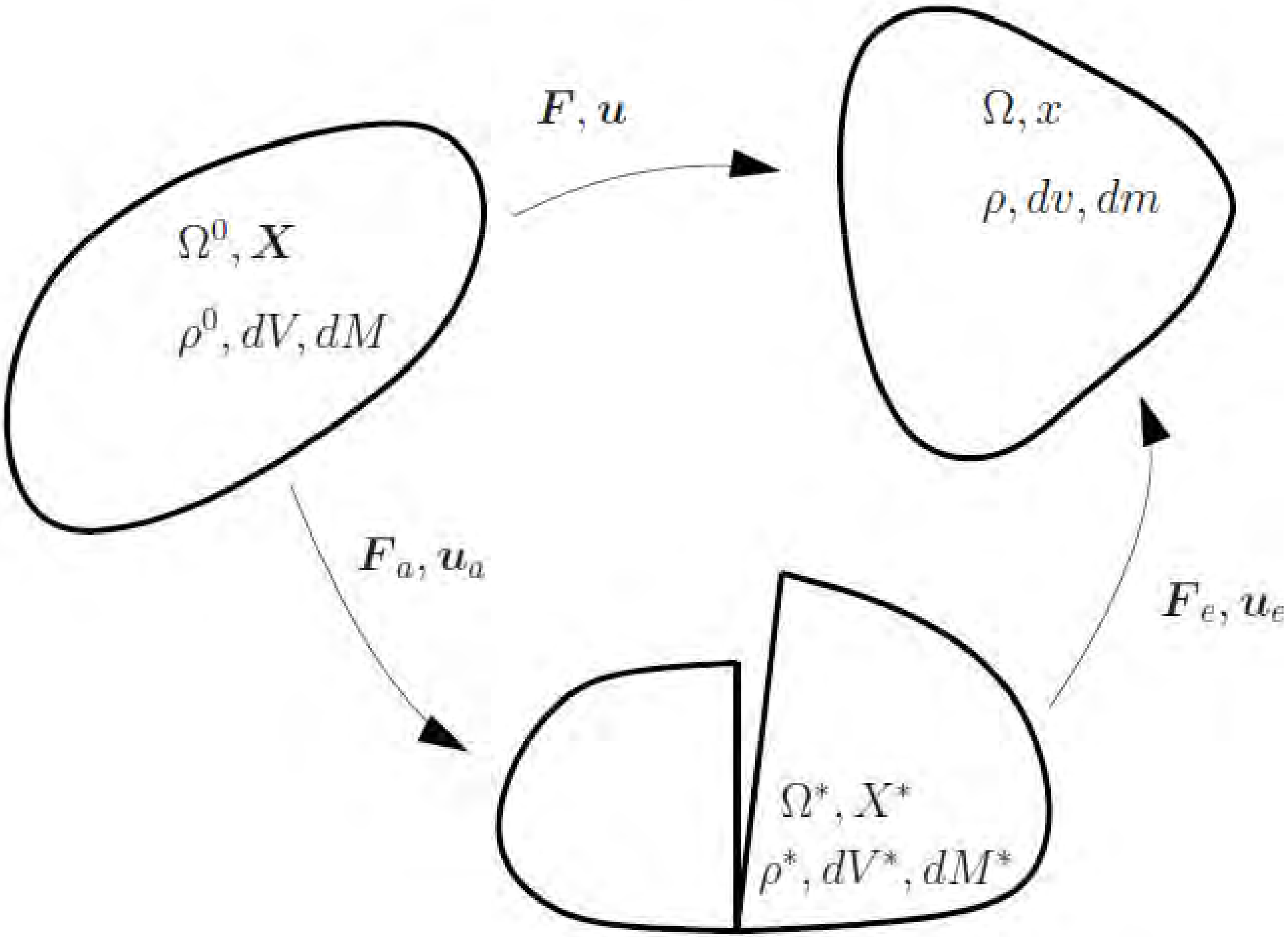
…but how is this synchronised?
- stresses
- morphogen diffusion (fgf8, Dpp,,…)

[1] T Lecuit and PF Lenne. Nature Reviews, 8:633-644 (2007)

Modelling: active deformations

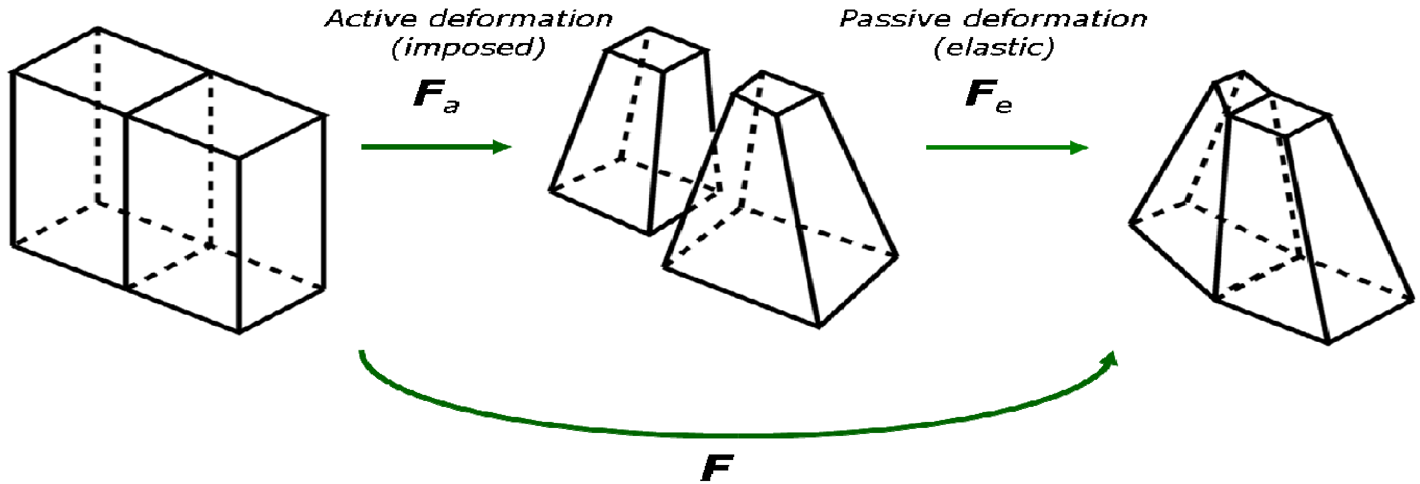
- Decomposition of deformation:

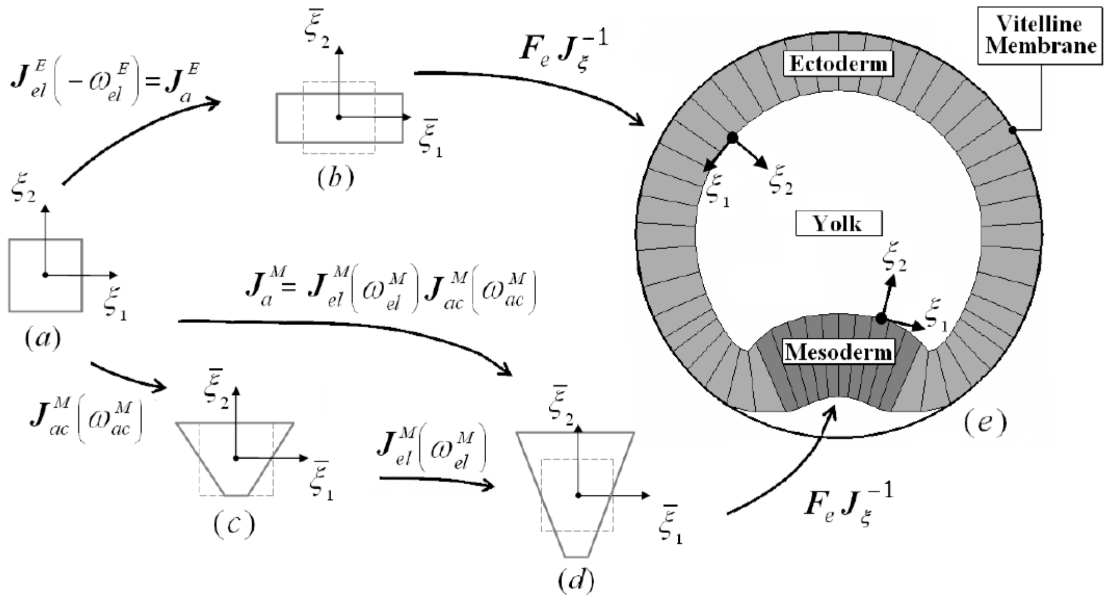
$$\boldsymbol{F} = \boldsymbol{F}_e \boldsymbol{F}_a$$



Modelling: active deformations

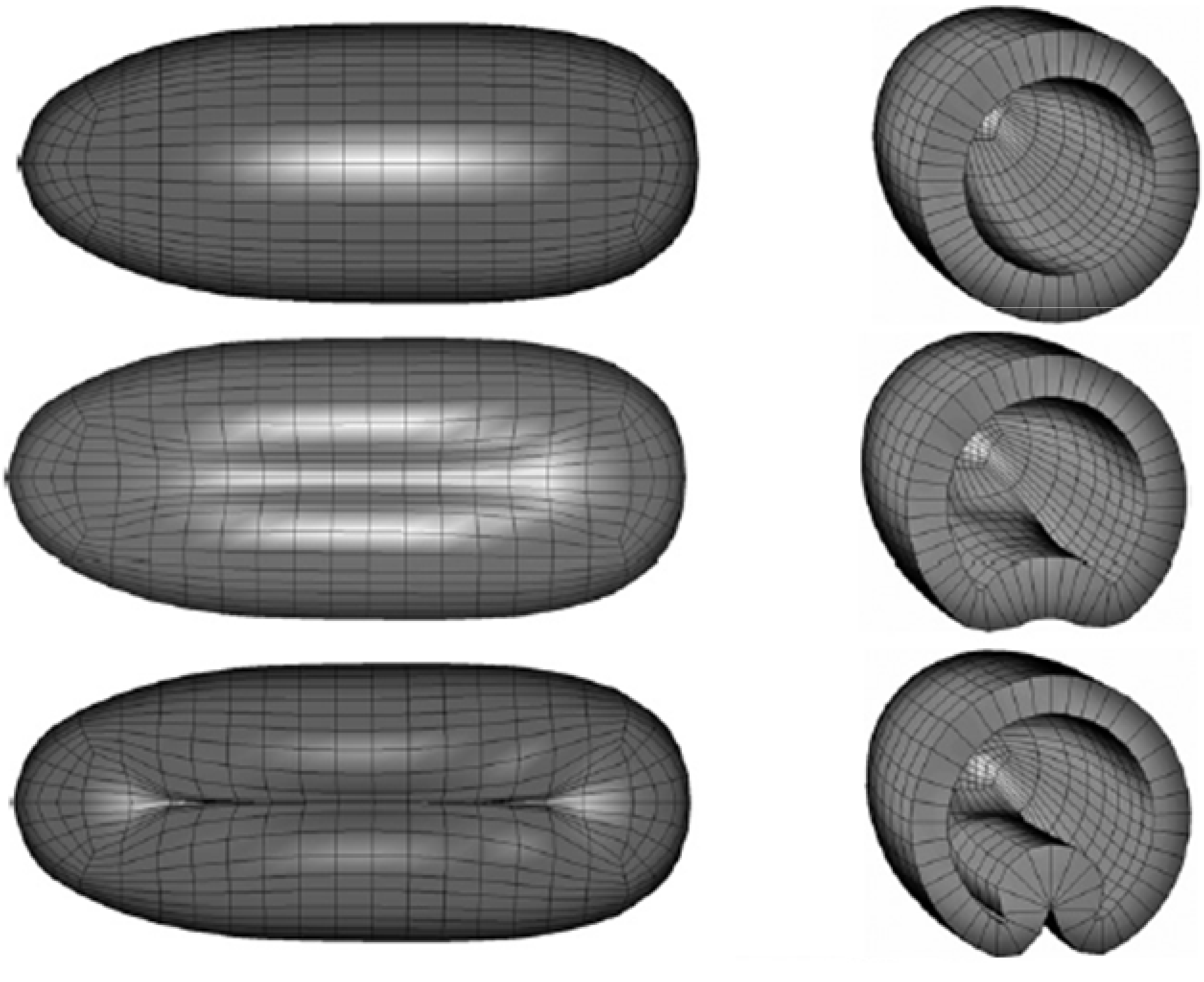
- Applying active displacements:





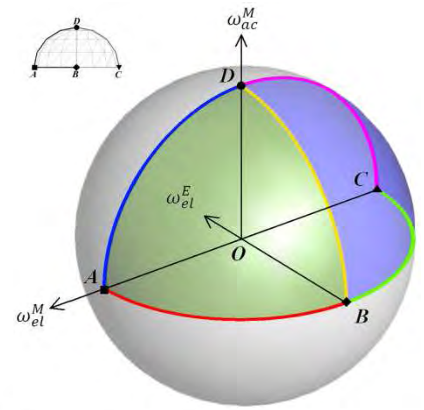
Modelling: active deformations

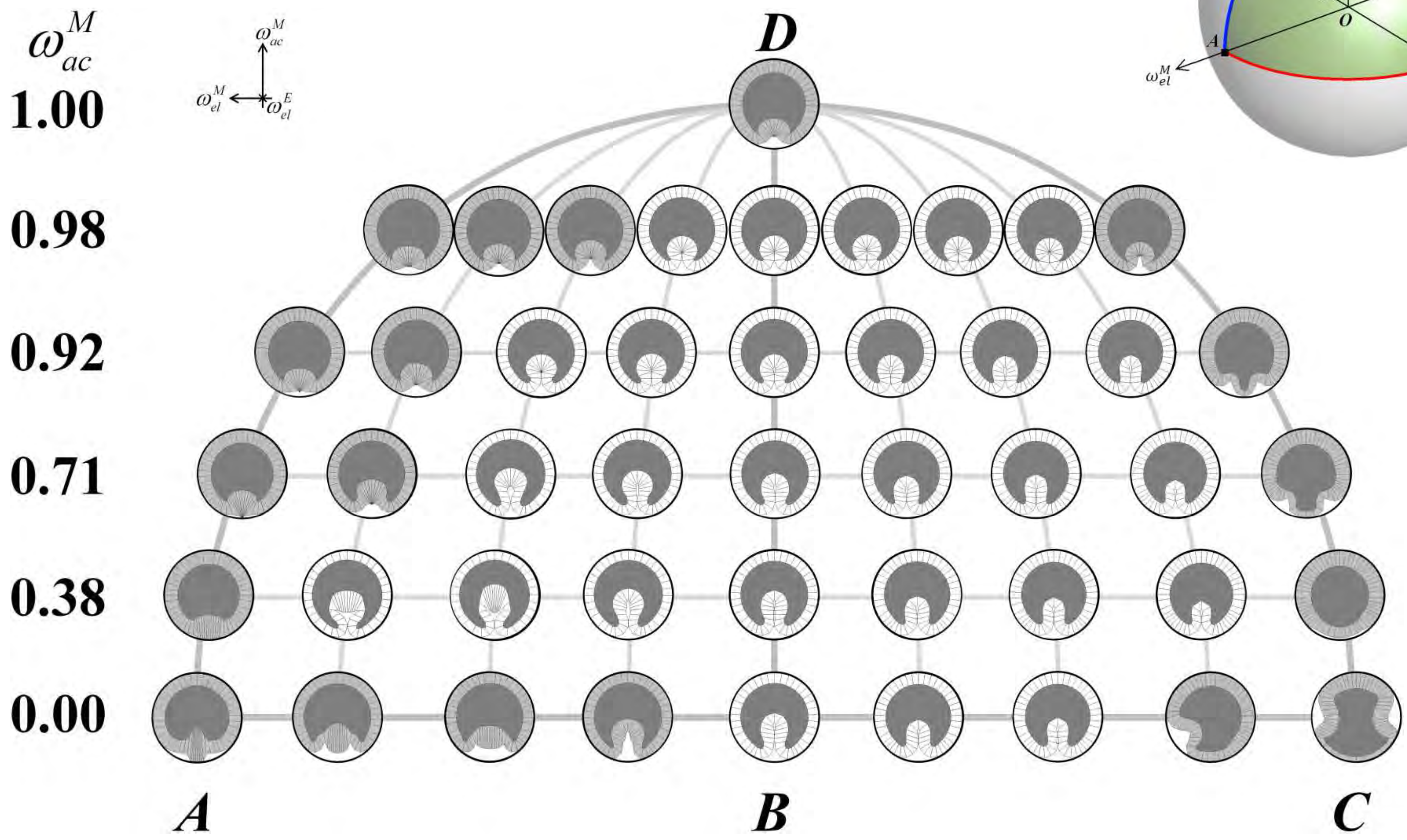
- No viscosity, applied deformation:



Modelling: kinematically driven forces

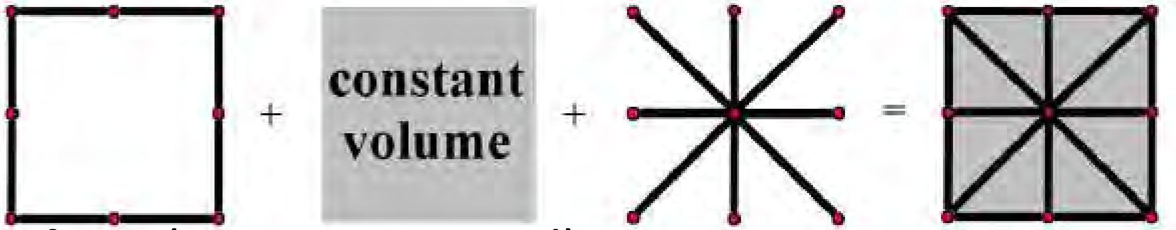
- Stability and robustness analysis:





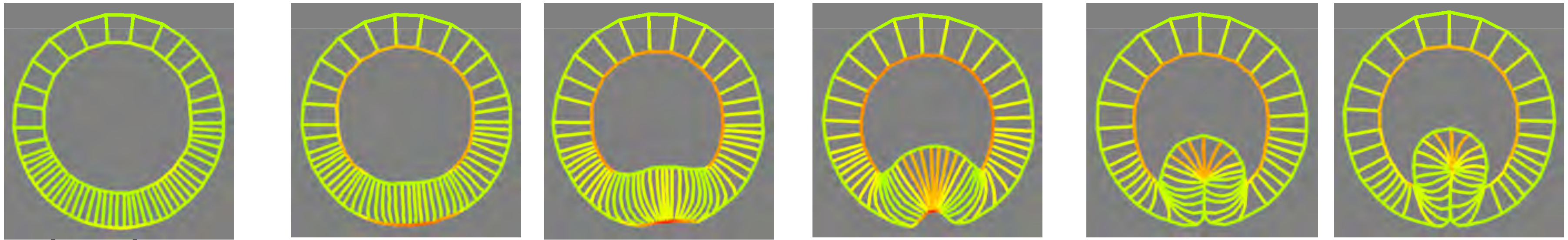
Modelling: inverse analysis

•Applying forces at the boundary.

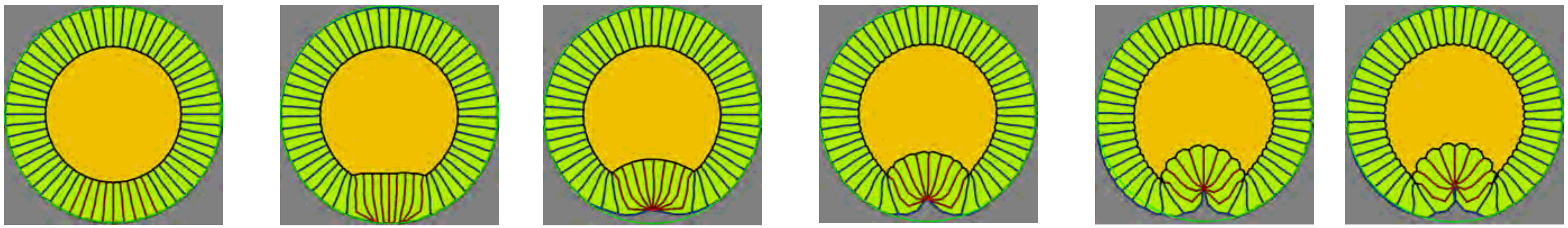


•**Inverse analysis** (viscous material):

In vivo:



In silico:

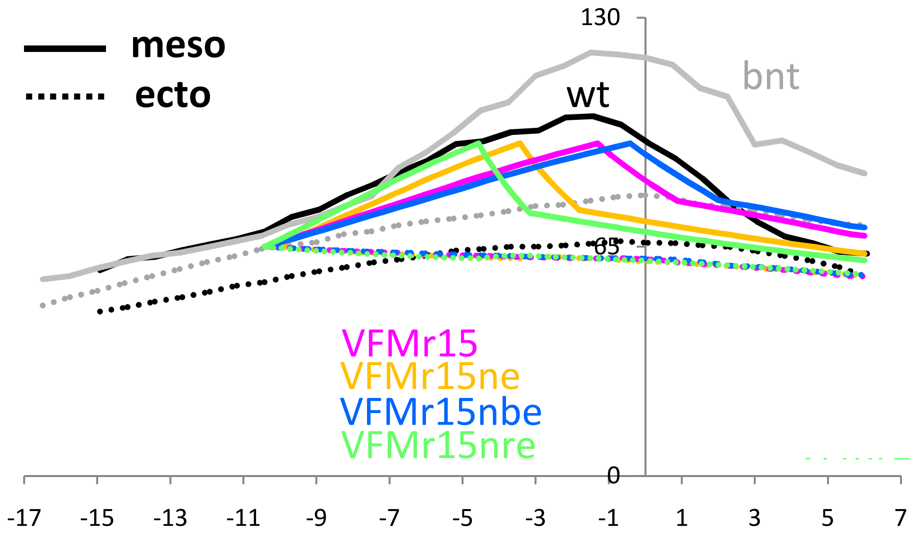


[1] G. W Brodland, V Conte, P. G Carnston, J Veldhuis, S Narasimhan, M. S Hutson, A Jacinto, ,FUlrich, B Baum, M Miodownik. Submitted.

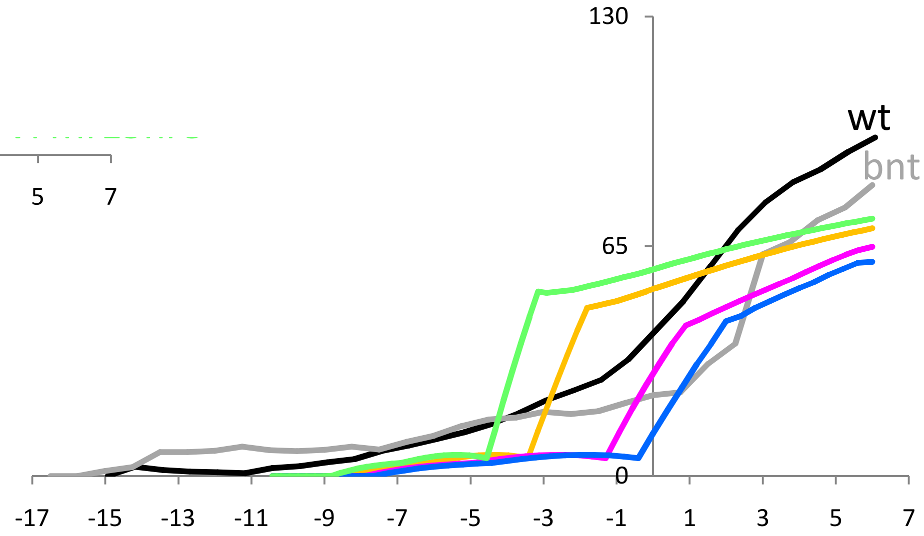
Modelling: applied forces

•Accurate deformation ***throughout*** process:

radial thicknesses



height of the furrow



Modelling: stress-driven forces

- Experimental observations: some phenotypes are mechanically induced [1,2].
    - After some laser ablation or physical cuts, invagination may be disrupted.
    - Similar situation to cardiovascular biomechanics, but with larger deformations.

- Morphogens have a profile that agrees with a diffusion governing law [3]

[1] E Farge, E. Current Biol. 13: 1365-1377, 2003.

[2] E Brouzés, W Supatto and E Farge. Biol. Cell 96: 471-477, 2004.

[3] S R Yu1, M Burkhardt, M Nowak, J Ries, Z Petrasek, S Scholpp, P Schwille and M Brand. Nature, 461:533-537, 2009.

Modelling: stress-driven forces

- Minimisation of total free energy $\int_{\Omega^0} \rho^0 \psi \, d\Omega^0$ yields:

$$\nabla_X \cdot \frac{\partial \psi}{\partial \boldsymbol{F}_a} = \boldsymbol{0}$$

- Use evolution law for the active deformations:

$$\dot{\boldsymbol{F}}_a = \boldsymbol{f}(\boldsymbol{F}_e)$$

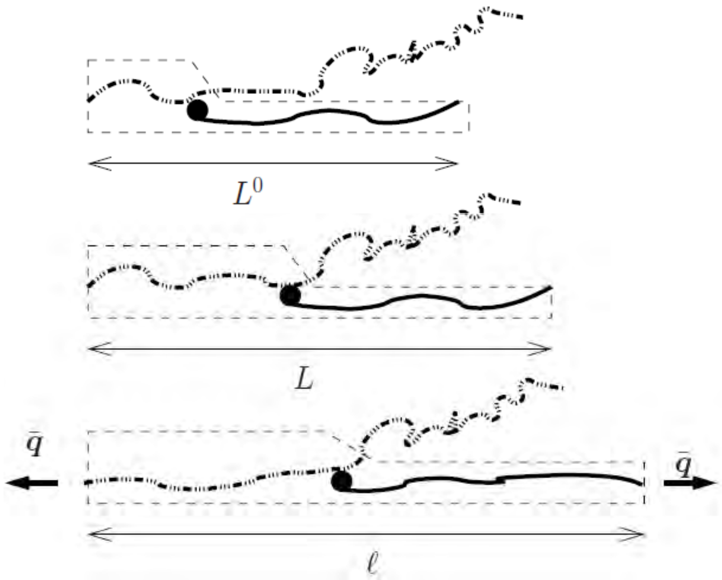
- Resulting equilibrium equation:

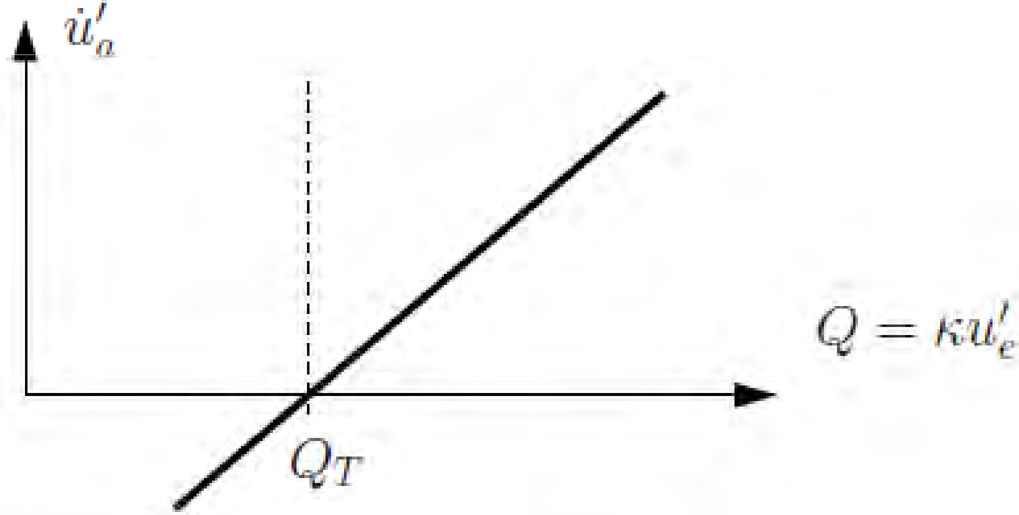
$$\nabla_X \cdot \left(\Delta t (\nabla \boldsymbol{f})^{\mathrm{T}} : \frac{\partial \psi^*}{\partial \boldsymbol{F}_a} \boldsymbol{F}_a^{-\mathrm{T}} + \boldsymbol{P} \right) = \boldsymbol{0}$$

Modelling: stress-driven forces

- Evolution law:

$$\dot{u}'_a = \beta(Q - Q_T) = \beta\left(ku'_e - Q_T\right)$$





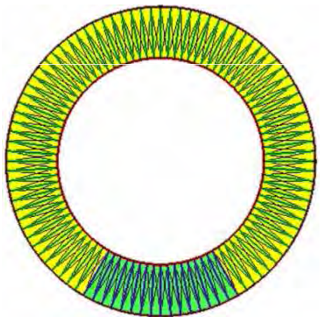
Shortening Elongation

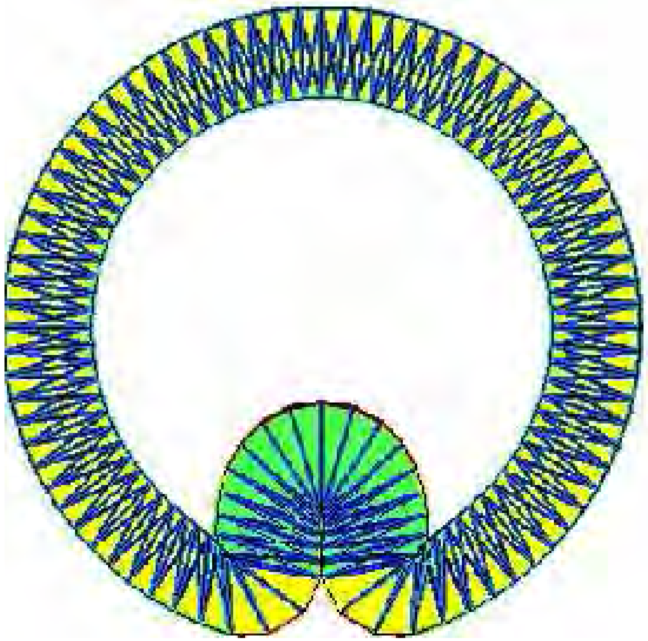
Modelling: stress-driven forces

•Second law of thermodynamics satisfied if, $-(1 + u'_e)Q\beta(Q - Q_T) \geq 0$

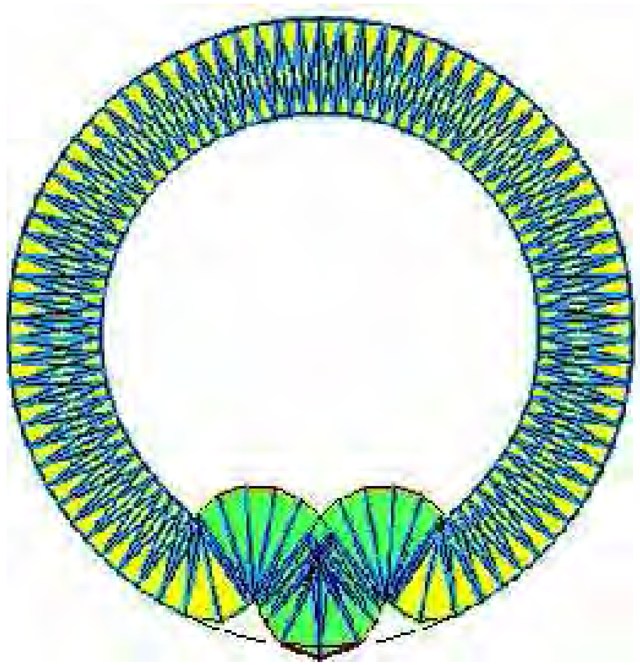
$$Q \geq 0 : Q_T \geq Q$$
$$Q \leq 0 : Q_T \leq Q$$

•Resulting invagination:





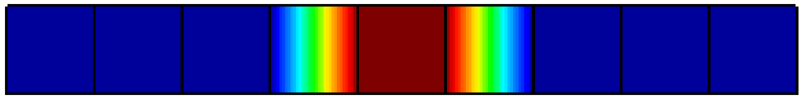
With
Yolk incompressibility
condition

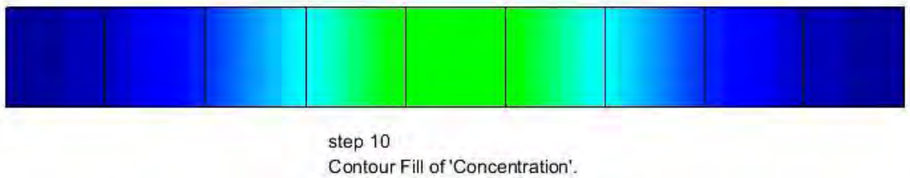


Without
Yolk incompressibility
condition

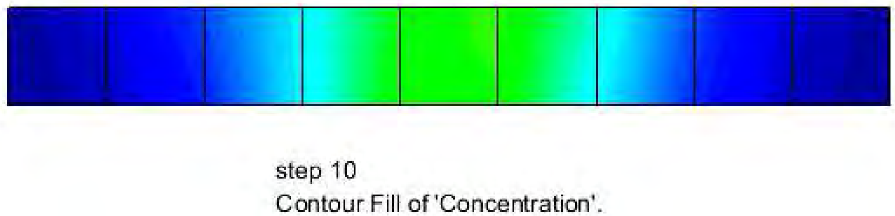
Modelling: diffusion-driven forces

Initial concentration:





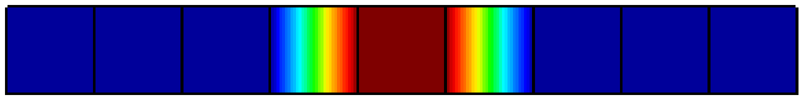
Diffusion on fixed domain

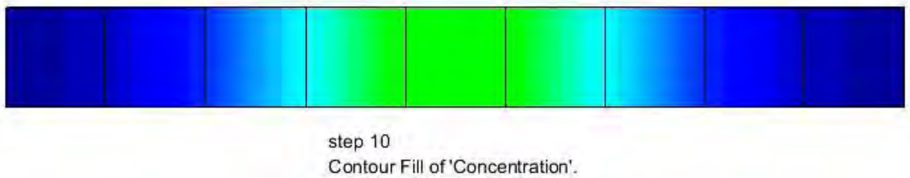


Diffusion on a deforming domain

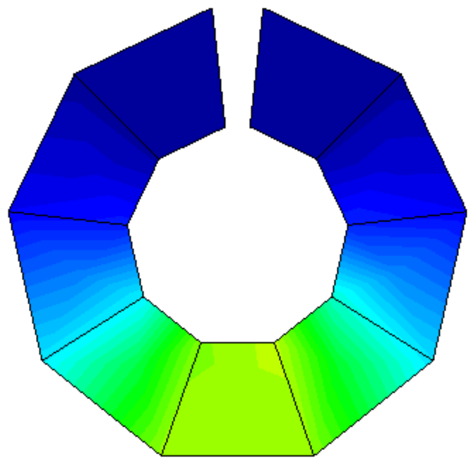
Modelling: diffusion-driven forces

Initial concentration:





Diffusion on fixed domain

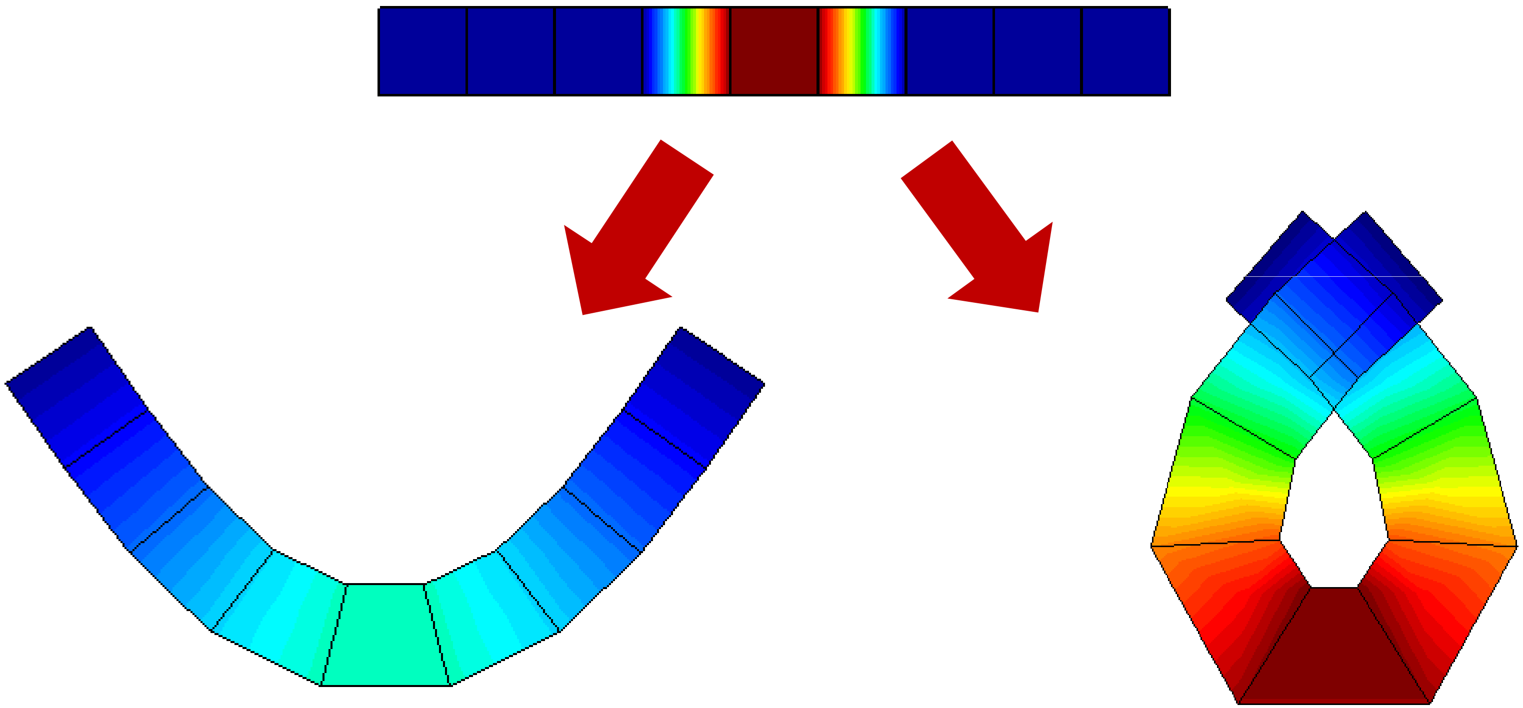


Diffusion on a deforming domain

Modelling: diffusion-driven forces

- Diffusion dependent active deformations

Initial concentration:

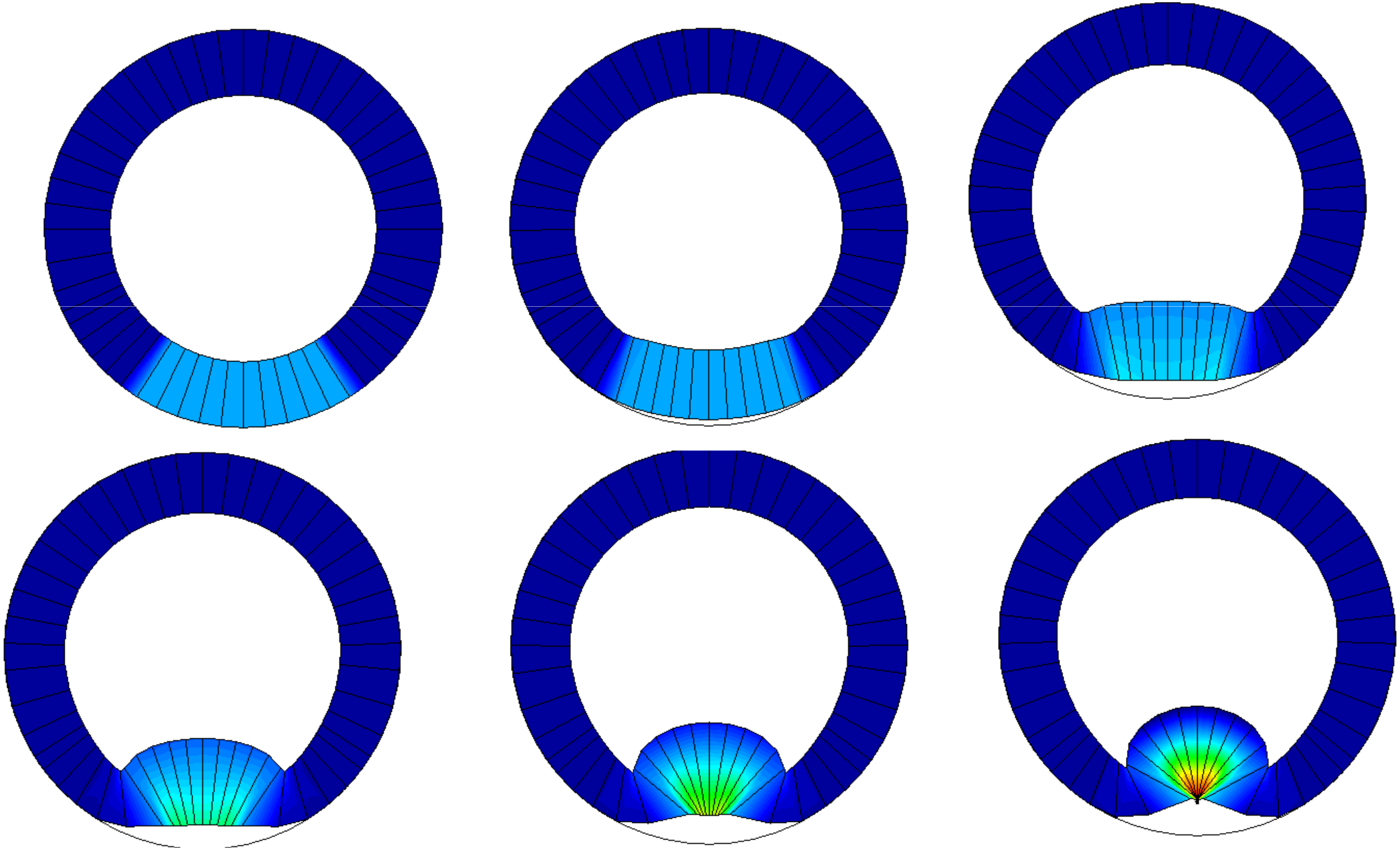


Diffusion

Diffusion
+
Reaction

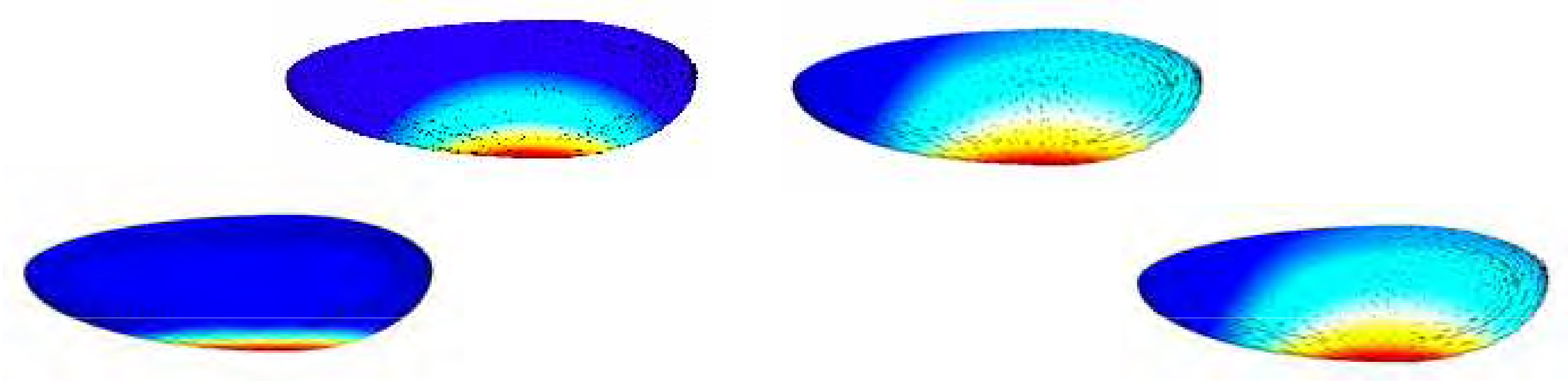
Modelling: diffusion-driven forces

- 2D results:

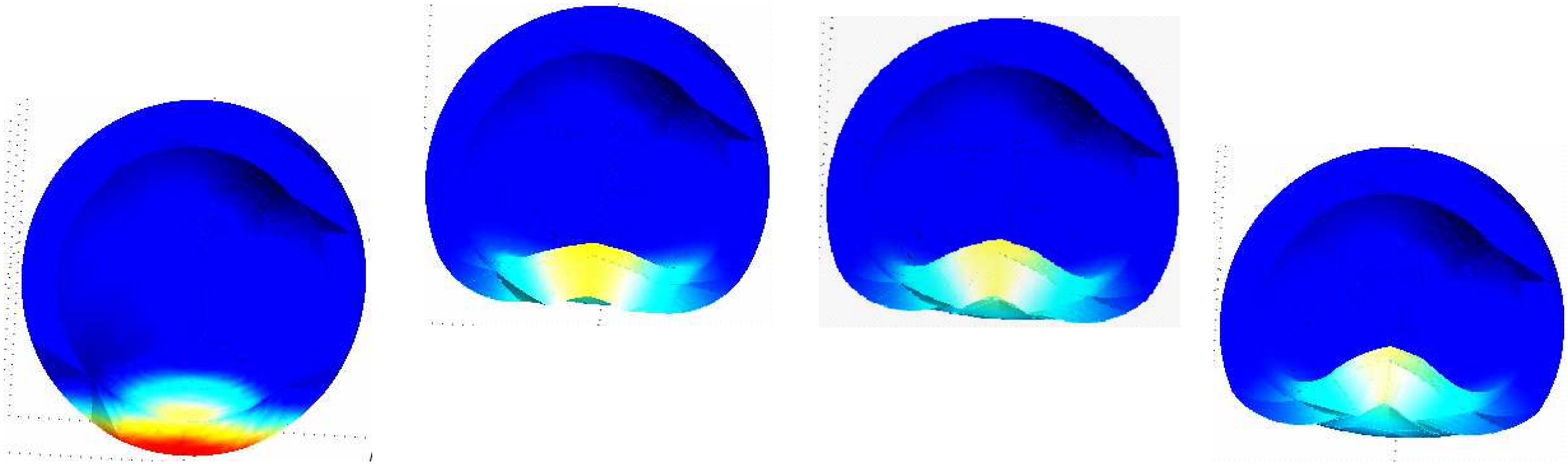


Modelling: diffusion-driven forces

•3D germ band extension:



•3D Ventral Furrow Invagination:



Conclusions

- Cell is a complex mechano-chemical-genetic system: requires multiphysics
- Different singalling may be responsible for the activation of the mechanisms (mechanotransduction)
- The influence of each mechanism must be validated experimentally
- Possibly there is no unique source, but combination of them

Acknowledgements:


Mark Miodownik, King’s College London


Vito Conte, King’s College London


Denis Aubry, Ecole Centrale Paris


Rachele Allena, Ecole Centrale Paris

•Buzz, Baum (LMCB, UCL), Florian Ulrich (NYU) for biological background and data.

•GW Brodland et al. Waterloo University, Canada.