Embryo Segmentation: a Mechano-Genetical Model

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By
Vincent Fleury
Laboratoire Matière et Systèmes Complexes
CNRS-Université Paris-Diderot
Vincent.Fleury@univ-paris-diderot.fr

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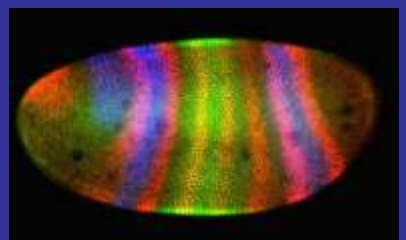
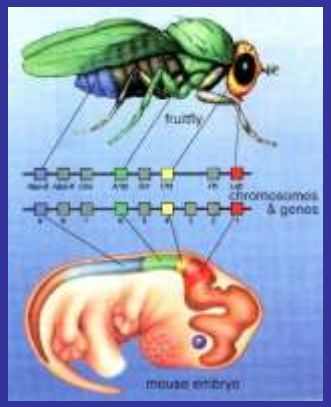
Vincent Fleury
Laboratoire Matière Systèmes Complexes
Université Paris Diderot
Vincent.fleury@univ-paris-diderot.fr

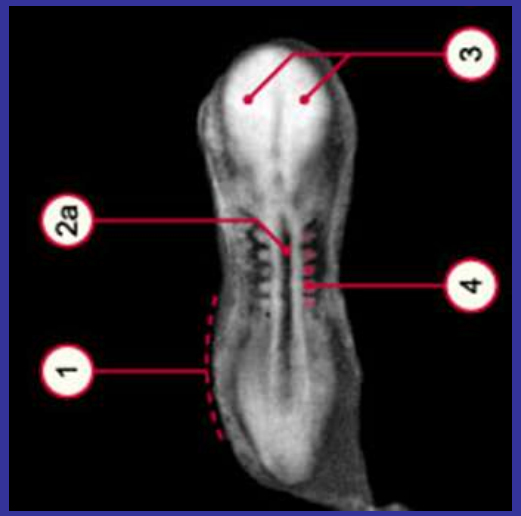
(most images from the copyrighted paper :
V. Fleury Clarifying tetrapod embryogenesis, EPJ 2009)

Segmentation : not a fundamental concept
The embryo « segments »
(unlike the embryo « falls »)

Seems quite different in insects (syncitium stage) and in vertebrates (embryo stage)







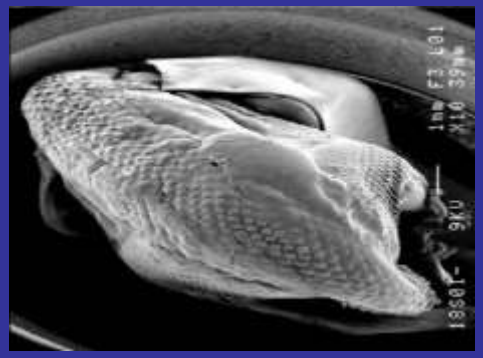
Confusion between the existence of segments and the fate of the segments :

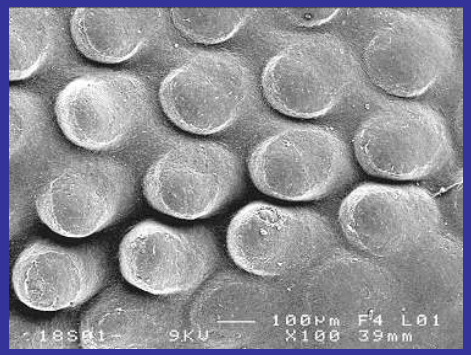
Hox genes and signalling molecules of many sorts do not specify the segments, only subtle differences between already existing segments

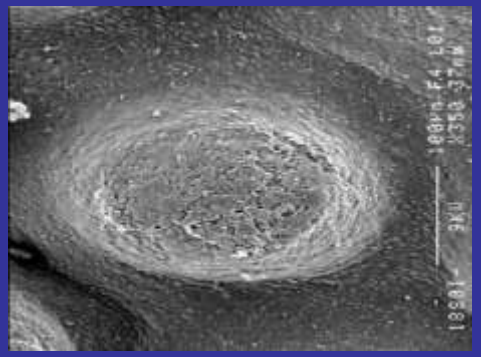
Mathematics of « segmentation » : extremely ordinary, casual :

-Turing models => no furrows (chemical fields)
-Mullins Sekerka instability=>no genes
-Rayleigh Taylor instability=> no genes
-Rayleigh-Bénard=> no genes
-Bénard-Marangoni=> no genes
-Clock and wavefront=> oscillation is a locking mode
-fibroblast instability inside collagen scaffolds=> no ectoderm
etc.

Spatial competition between two « things », or « states » or « energies »







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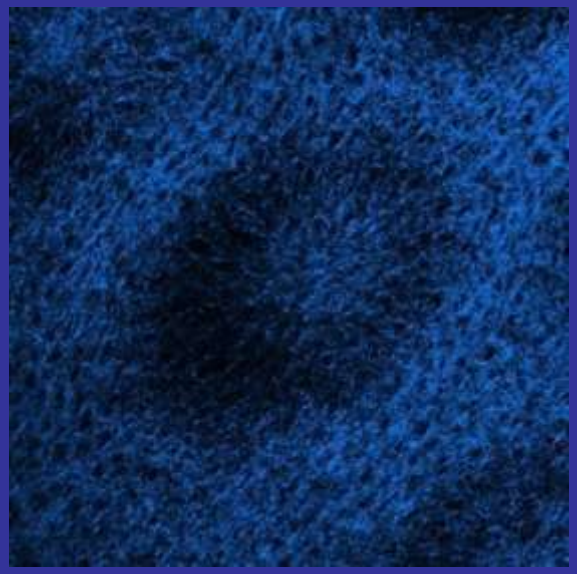


Not truly segments

but almost

Example of instability : very simple modes

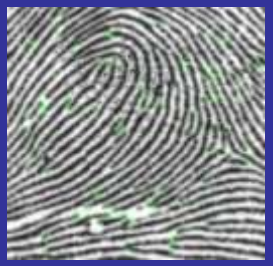
Importance of cell mechanics evident in cell orientation

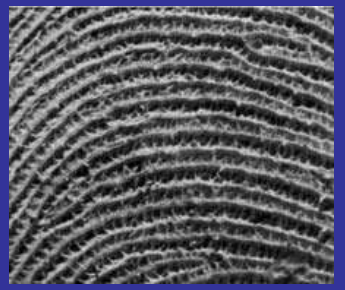
Another simple example of instability : formation of body folds of the embryos

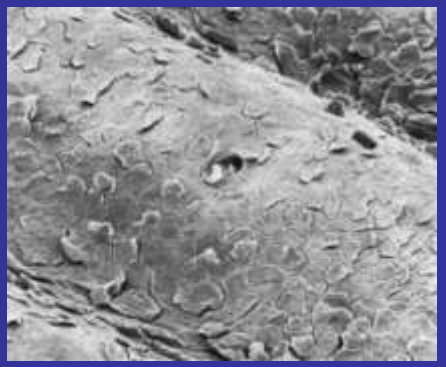
Meier and Packard (1984)

Elastic fish

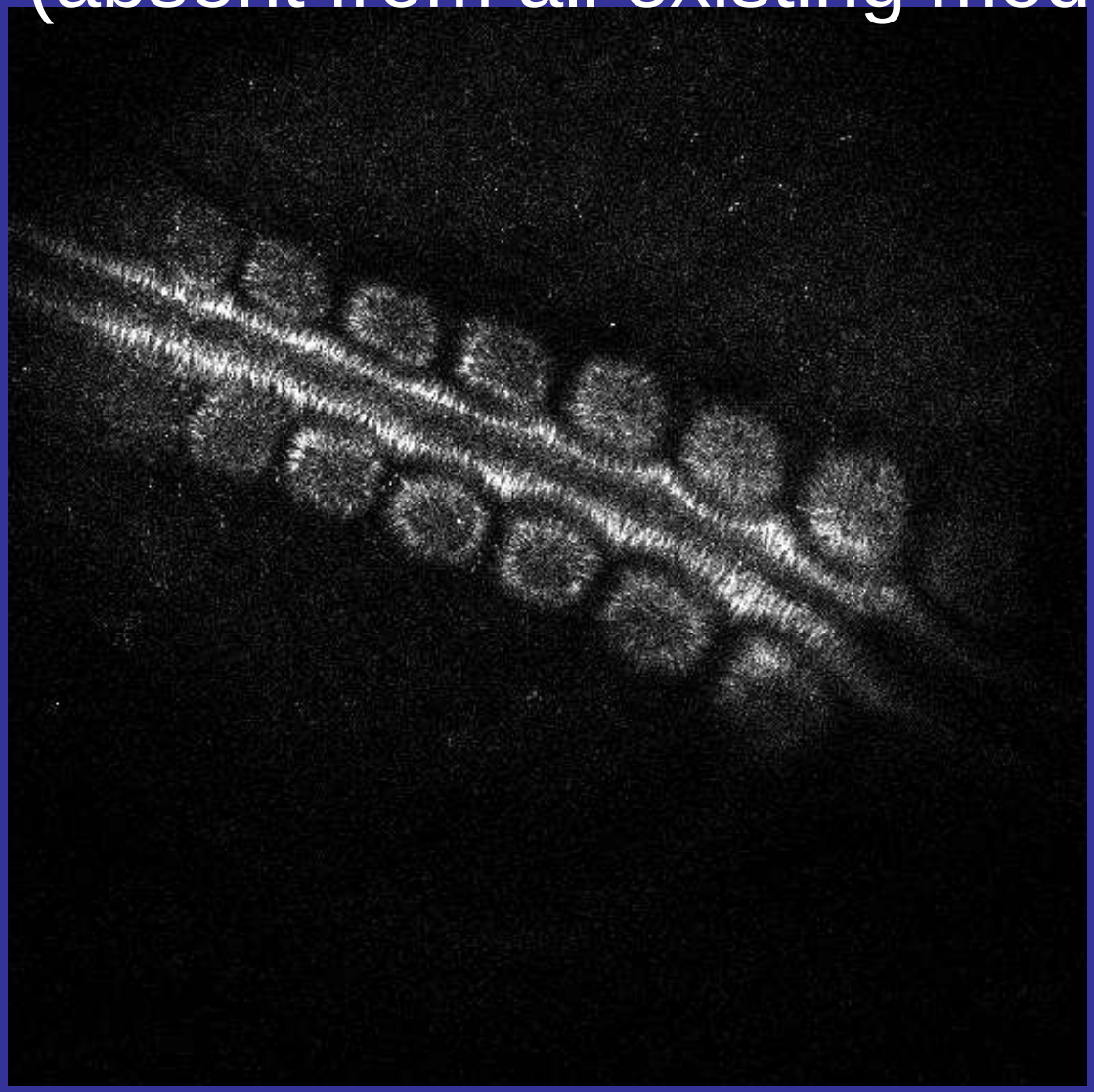
Also : fingerprints





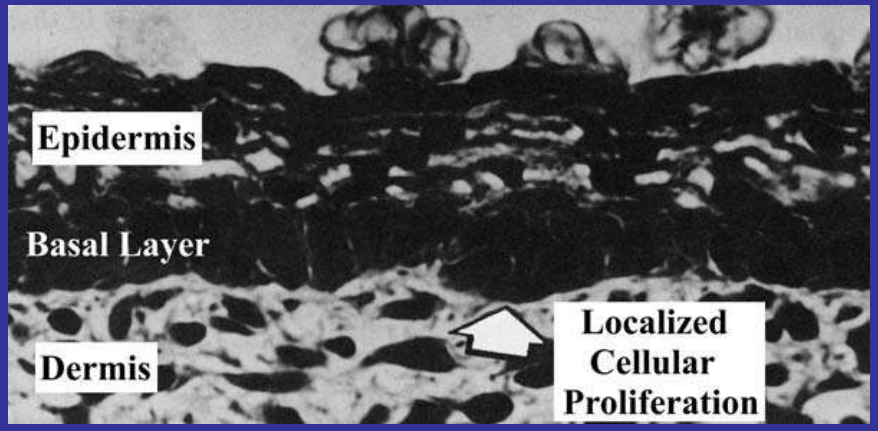


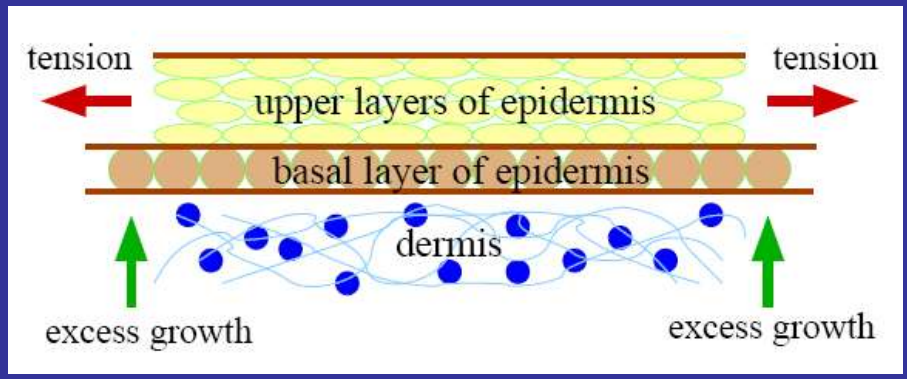
And cells and ECM re-align in the local stress (absent from all existing models)

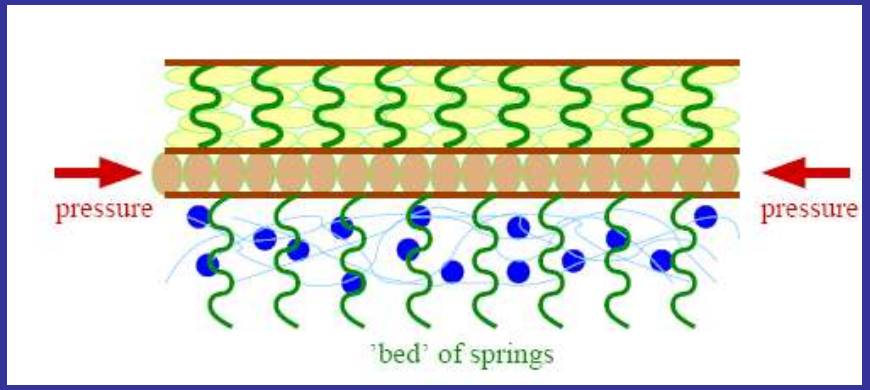


Y. Legrand, C. Odin,
V. Fleury, A. Al-Kilani
Unpublished

In the case of the friction skin (dermatoglyphs): physics of in-plane buckling of the skin (Kuecken and Newell 2005)

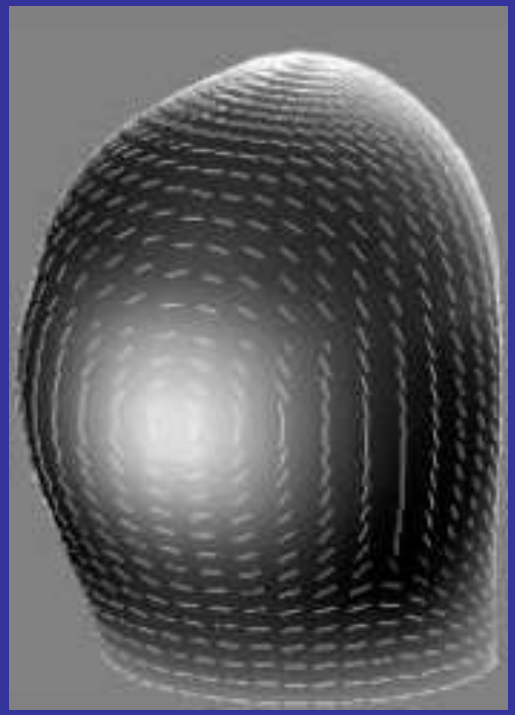


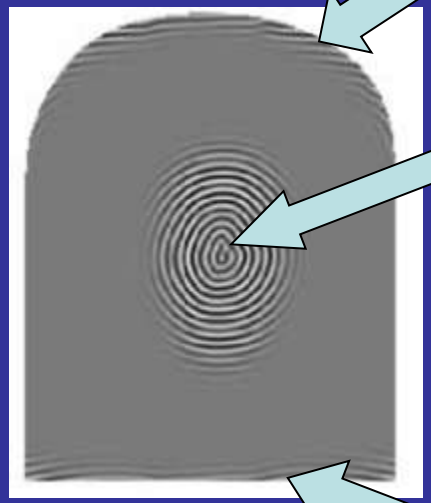




In plane stresses generate folds

Mathematical modelling: von Karman with an in-plane stress in the finger (embryo)





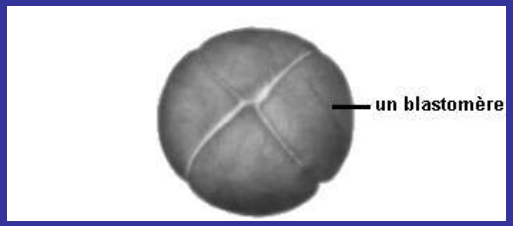
Principal stress
in the finger (smooth)

Onset of buckling

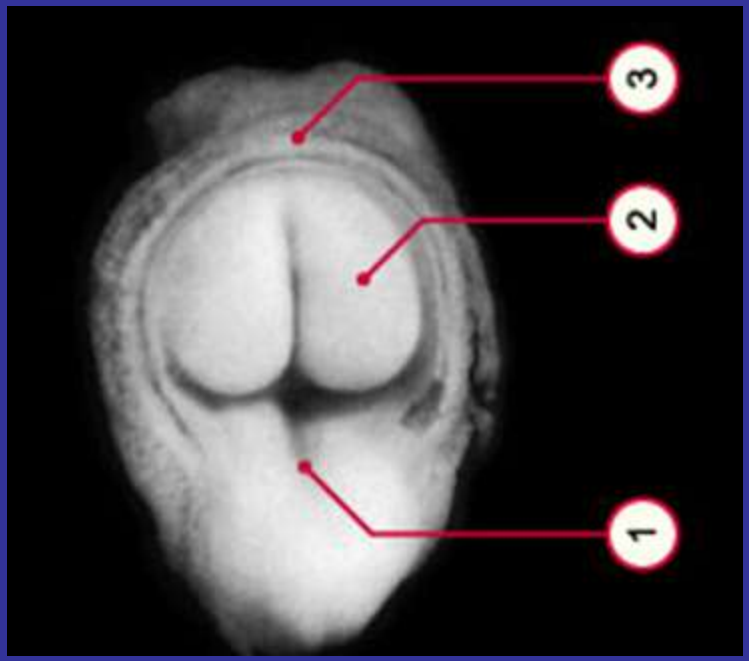
Visco-elastic buckling:

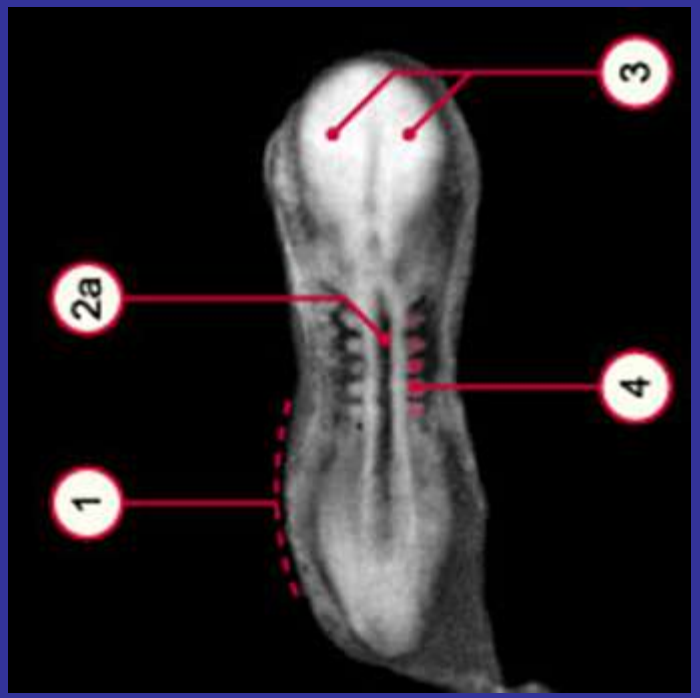
Bifurcation (forking)

furrows tend to be orthogonal to the principal stress



In the case of embryos



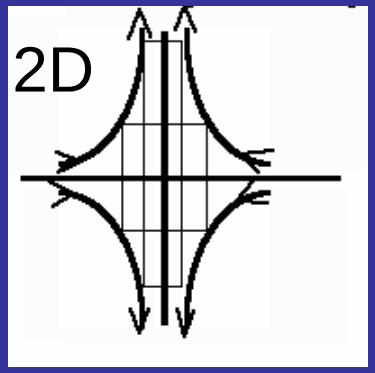


Folds seem to form in the most constricted part
=> influenced by stress; genetics *and* mechanics

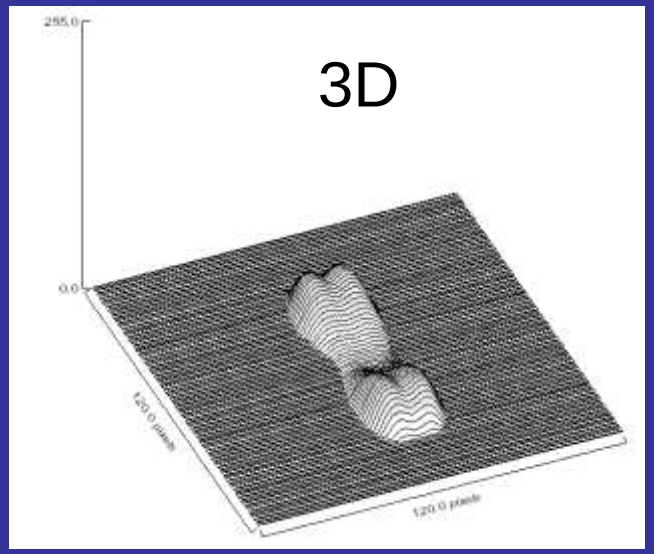
The body may form by a mechanism of buckling in a hyperbolic flow

The stress is :
$P(x,y) \sim X^2 - Y^2$

Cell flow map



Hyperbolic flow

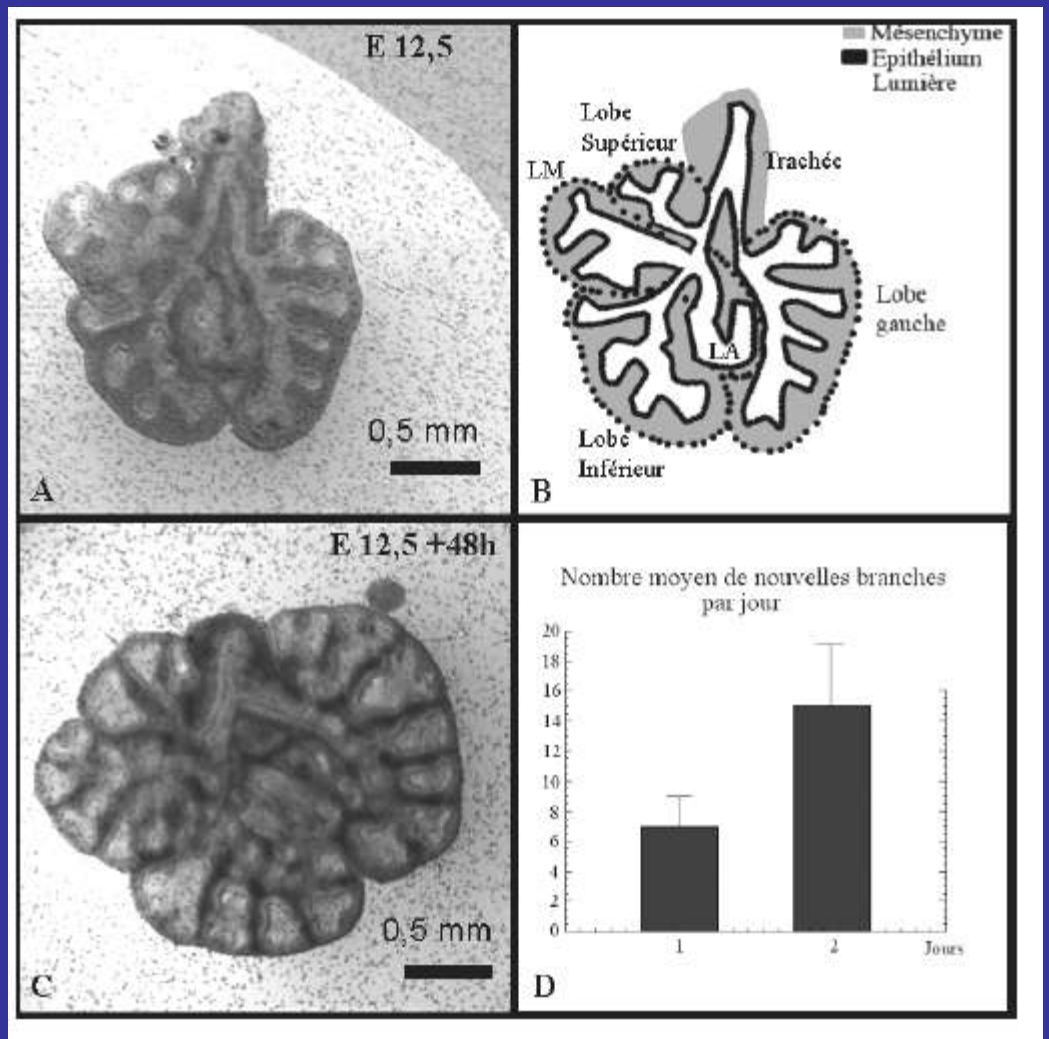


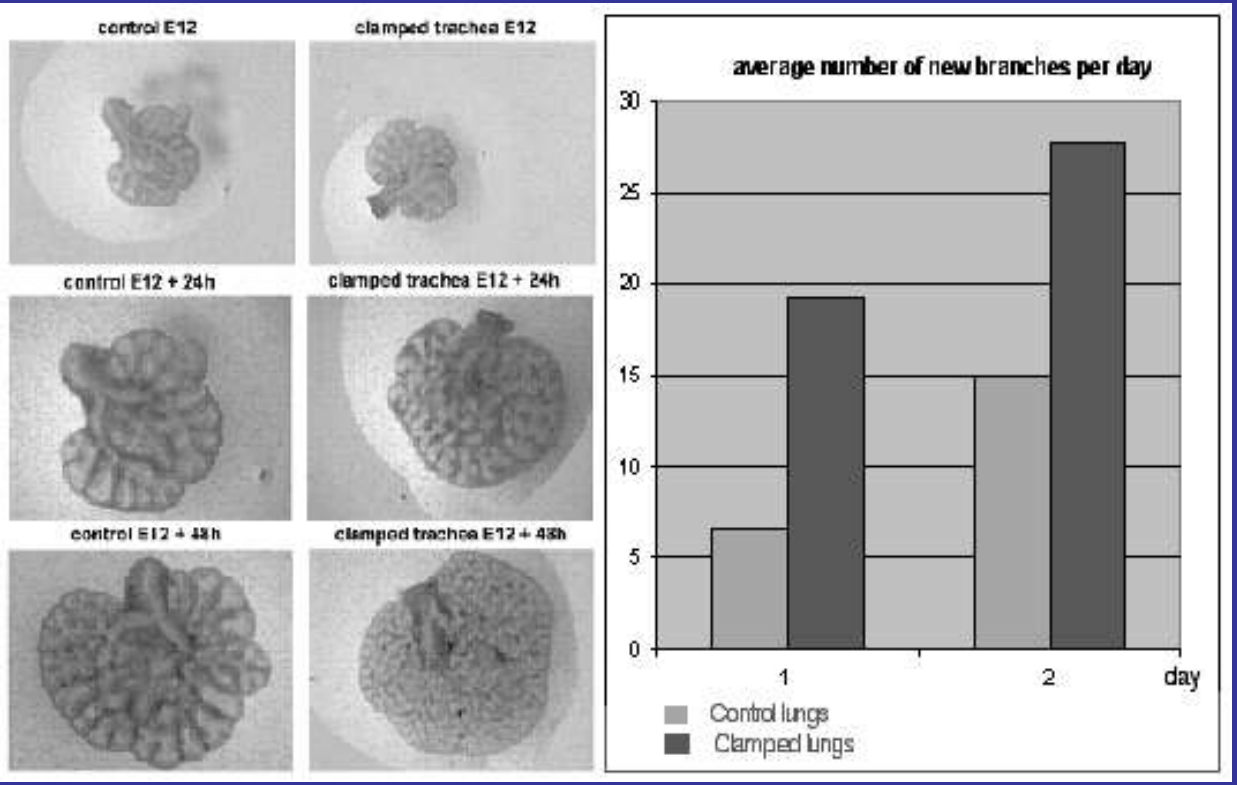
A body, but not yet segmented
What should we add?

Quite reminiscent of lung growth

2 days of lung development (Unbekandt et al.)

Boundary conditions : « inside out »



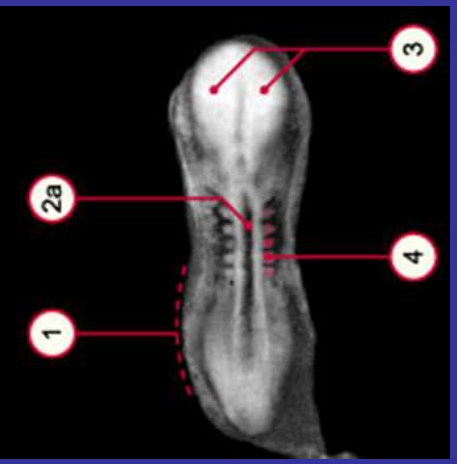


Effect of tracheal occlusion (thesis Mathieu Unbekandt, see website VF)

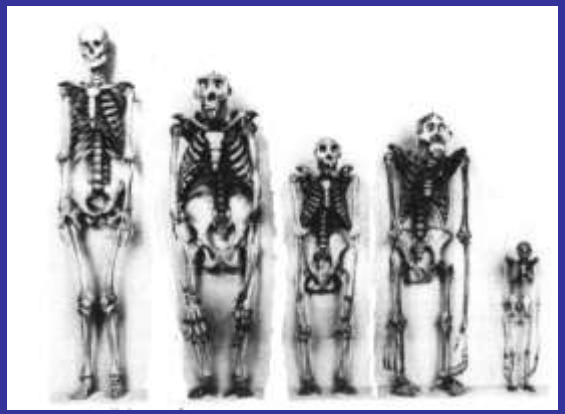
PCR of cDNA (mRNA of cells)

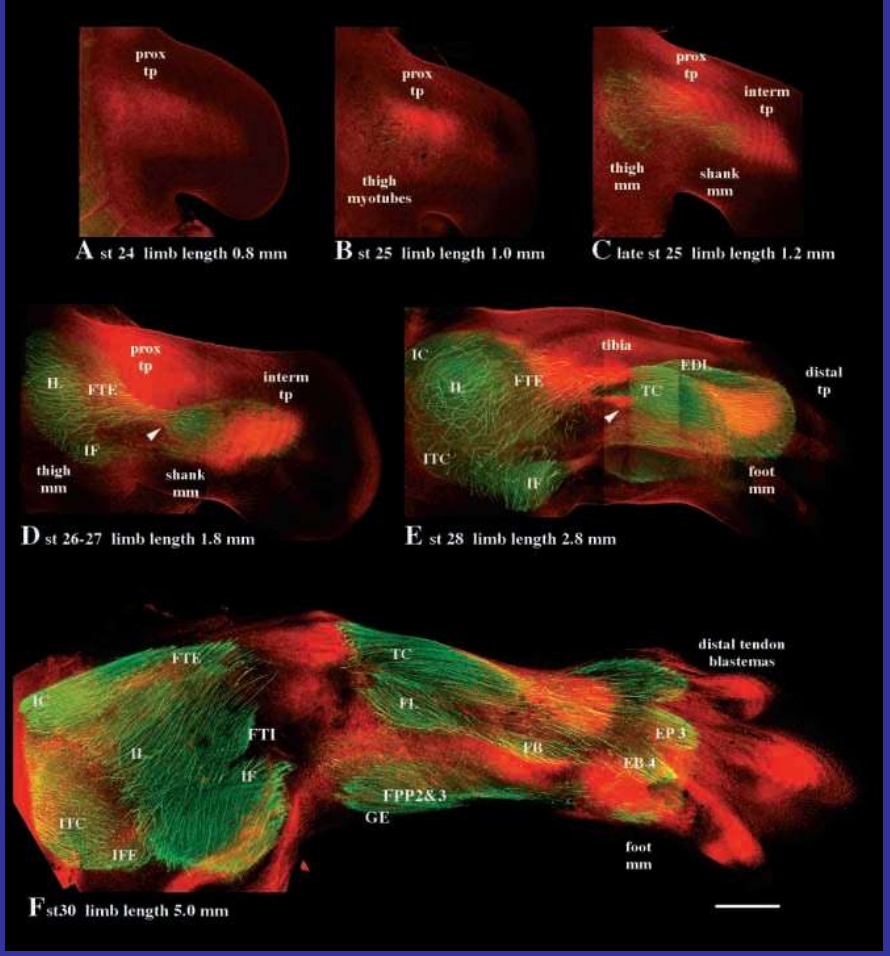
Developmental genes are mechanosensitive

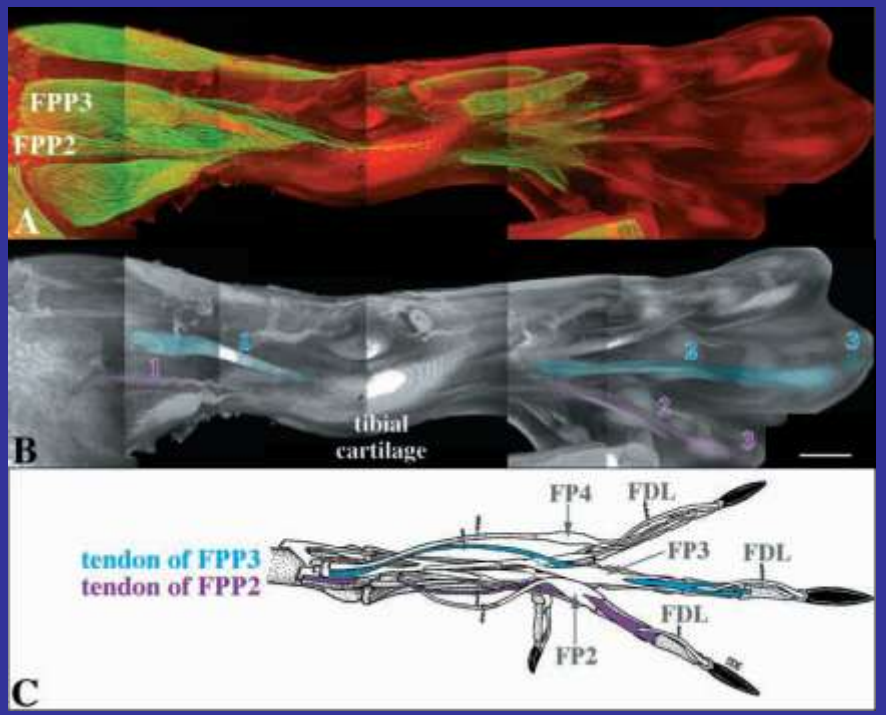
Formation of segments : a wave propagating inside a hyperbolic buckling, with mode lockings



The same wave gives different local outcomes

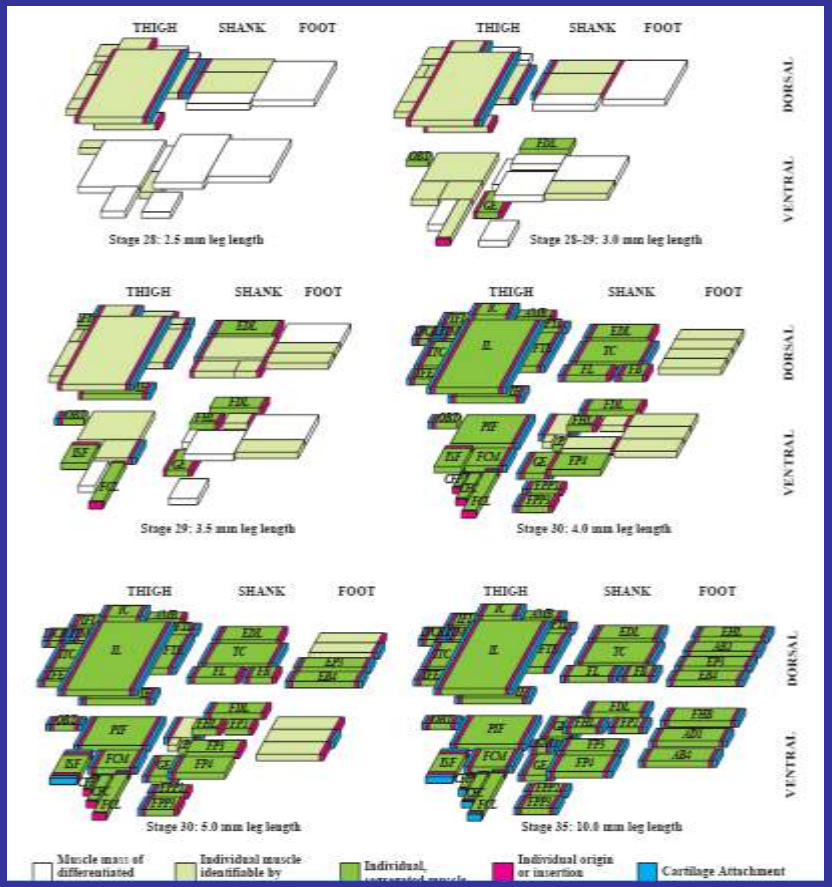


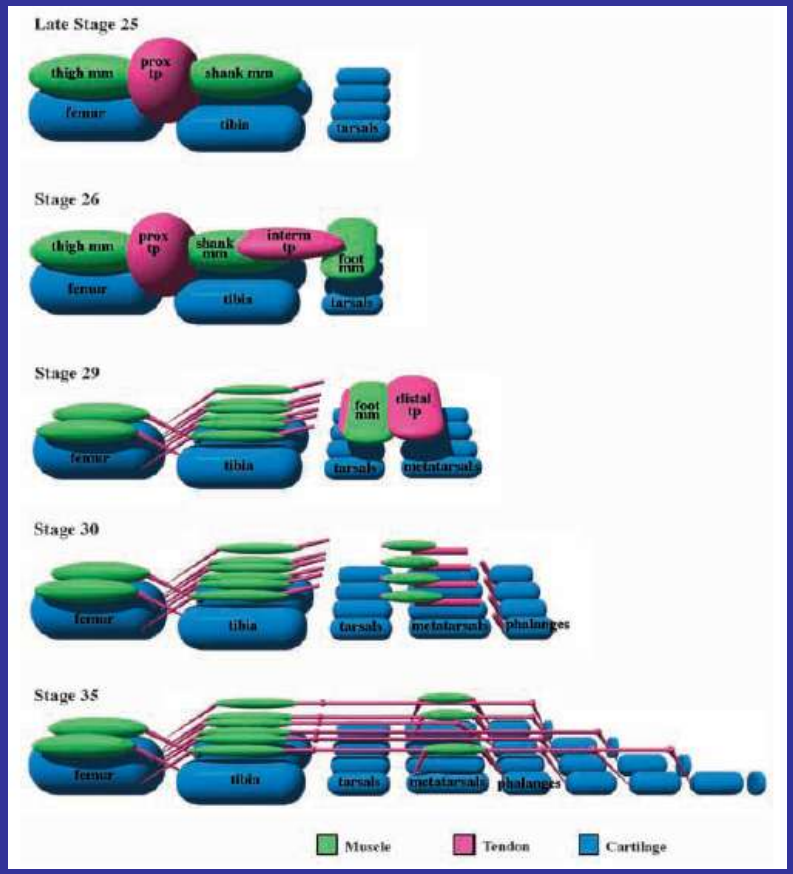




Kardon, Development 1998.

SOFT tissues self-organize on the segmented pattern (russian doll top down)

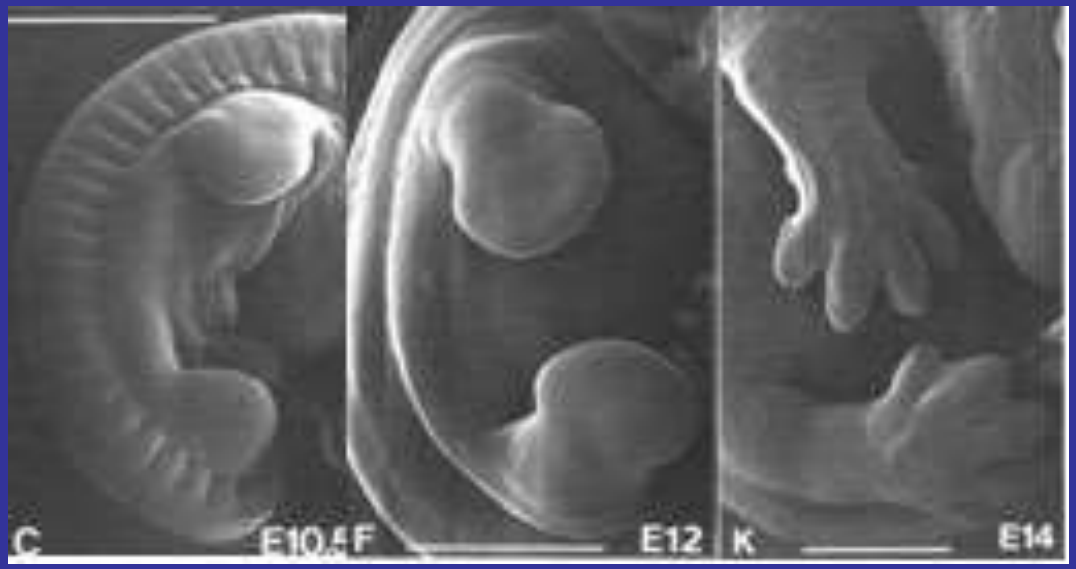




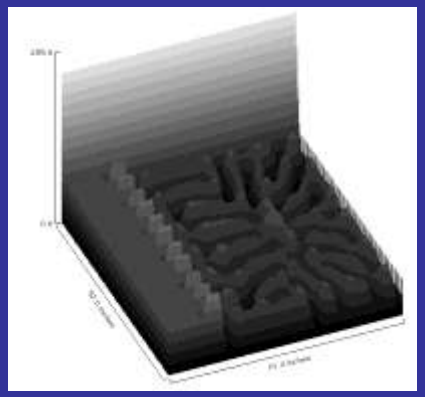
Top down cascade « automatic »

Already visible on jellyfish: coupling of a segmentation wave with any topology

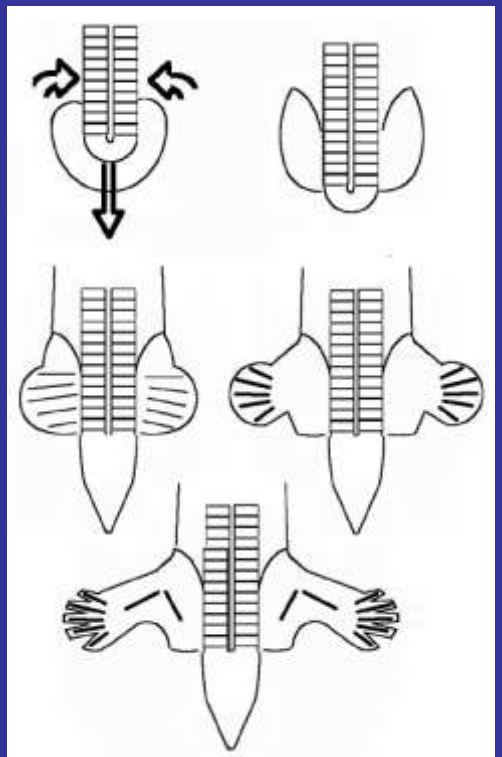
Mode locking of hands and vertebrae



A single mutation causes almost a doubling of finger count (gène Gli3-/-) and vertebrae change



Finger formation is an instability, with
Mode locking onto vertebrate count



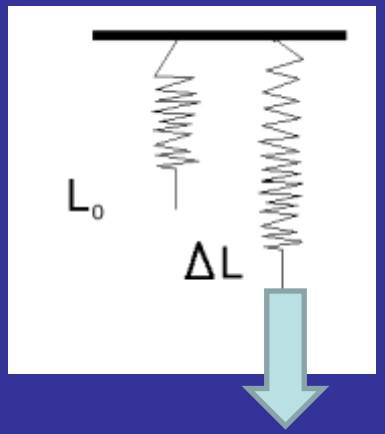
A fish with leg-like fins

- von Karman equation =
  buckling of elastic plates

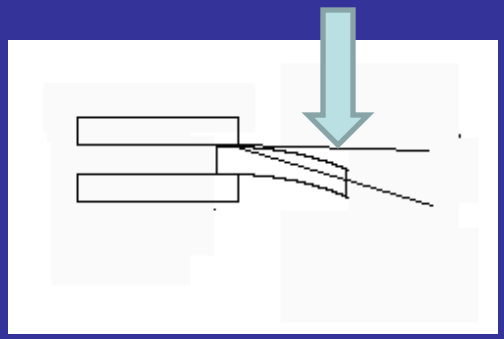
- Géneralization of Euler equation for thin plates buckling

- What is it?

Solids may resist in tension (stretching)



Solids may resist in flexure (bending)



- Combination of bending and streching

$$EI\Delta^4 h+\sigma\Delta h=0$$

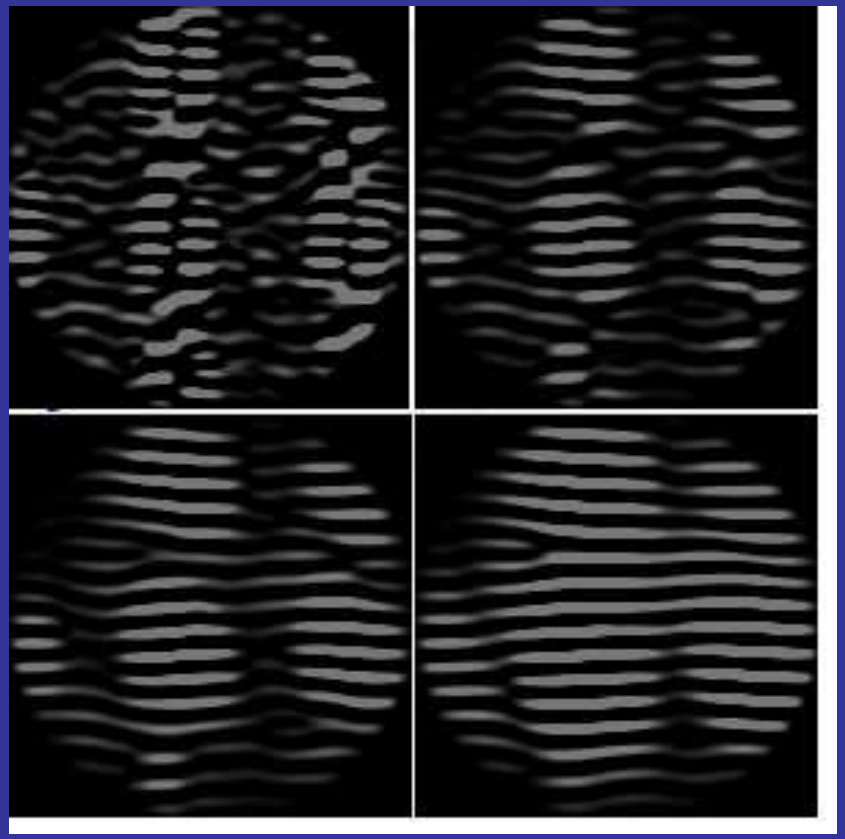
Flexures, torques : order 4
« plate» : bilaplacian

Tensions, forces - order 2
« membrane »: laplacian operator

E bending modulus, I geometrical factor,
σ is the in plane stress

h is the local deformation

Example of propagation of folds : true « segments » (actual physical furrow) Used for fingerprints, brain convolutions etc.



But what about genes?

What about biology?

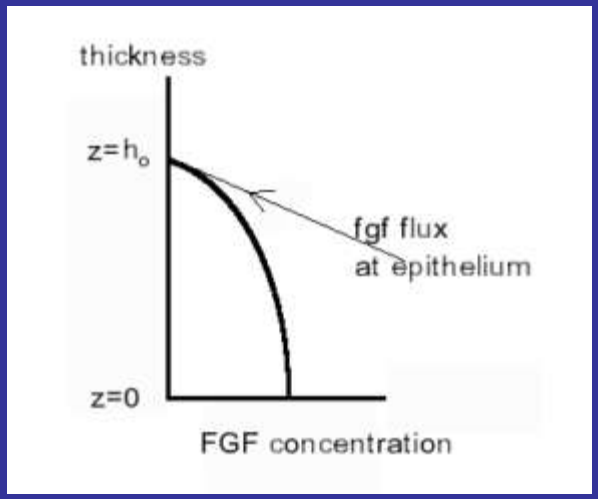
Black is a valley, white is a hill

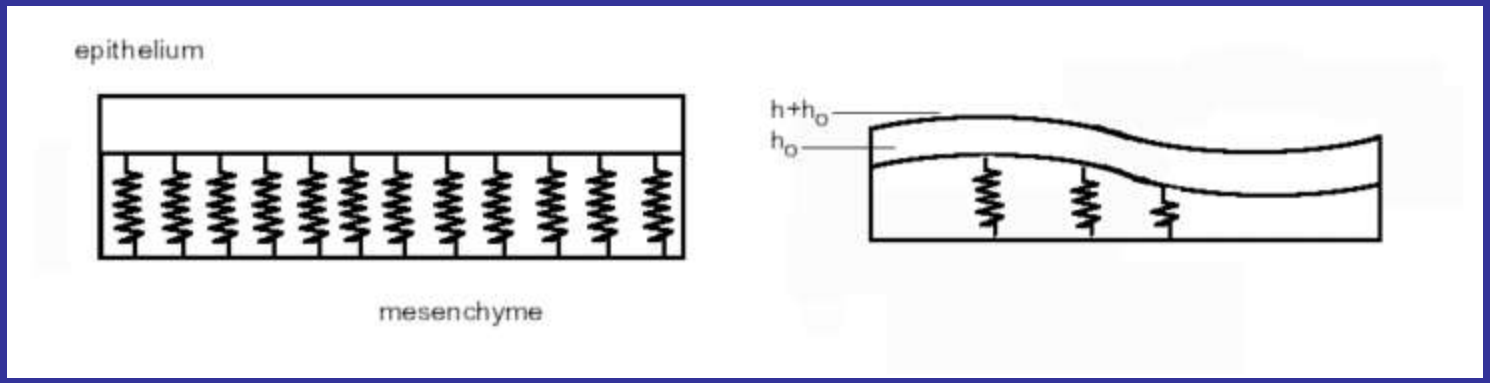
Introduce mechanosensitive growth factors

In plane stress at the epithelium is proportional to

h(h+h0)

Flux of growth factor





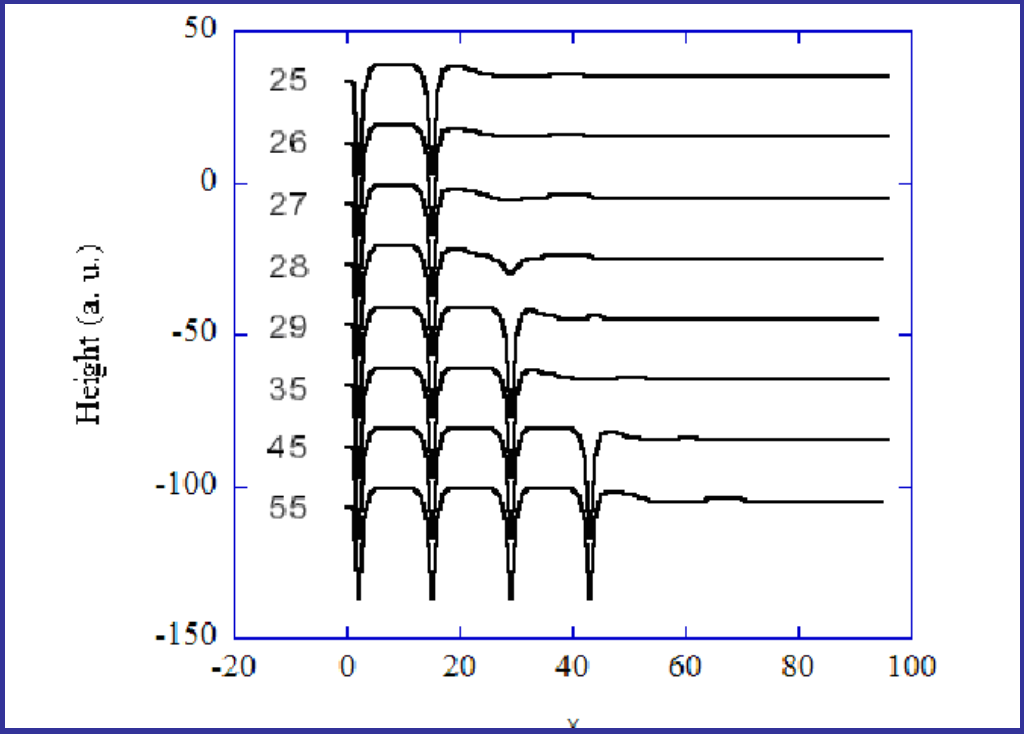
$$\kappa \partial h(x)/\partial t = D\partial^4 h(x)/\partial x^4 - (2\alpha h(h+h_0)/\Xi)\,\partial^2 h(x)/\partial x^2$$

Plate flexure

Stress growth

What does the non linearity $h(h+h_0)$ means?? =>
Very simple: there are two no-growth states=>
either cells are not stressed
or there are no cells

The maximal growth rate is achieved at $h_0/2$ where the force x (number of cells) is maximum.

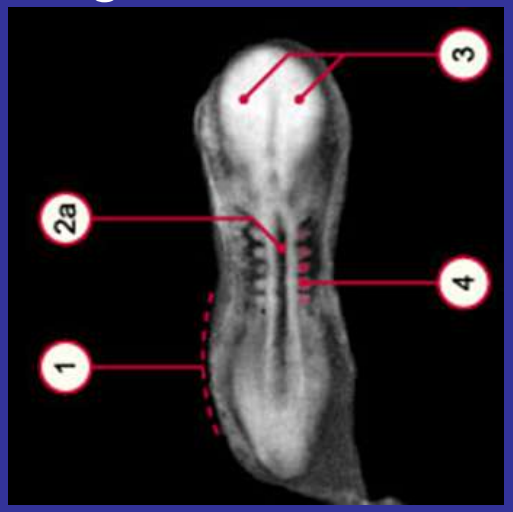


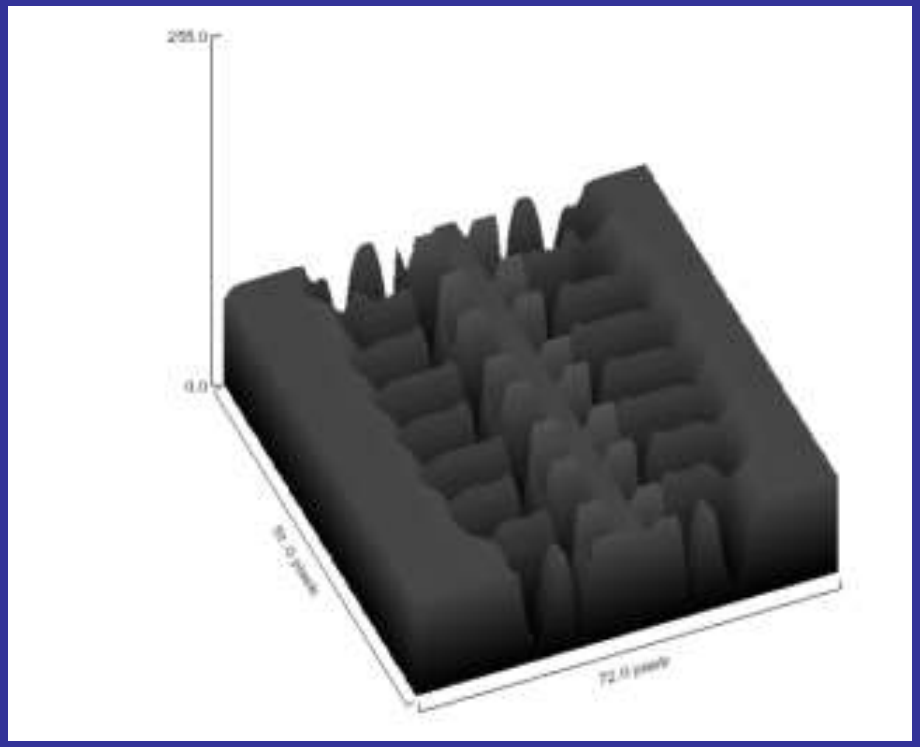
There is a Threshold

« induction »

Result : flat areas, without stress, deep « joints » without cells

The segmentation starts in the stressed areas (as observed)





Analogy with the electrocapillary effect also known as Lippmann effect, the surface tension is a quadratic function of potential: charges repell each other=> reduced surface tension

$\gamma=\gamma_0-CV^2$

Comes from charge=V/C

And $\partial\gamma/\partial V$=-charge

Interest of a negative surface tension??

Spontaneous production of work??

Surface may increase indefinitely all by itself??

=> instabilities, lung growth etc.

Possibility of locking onto a prepattern (calcium waves in the ovocyte).

Possibility of locking onto the clock and wavefront thing

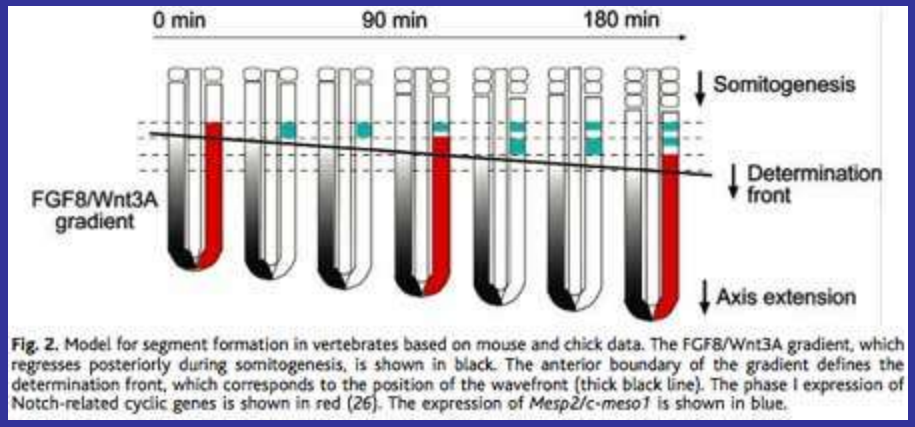


Fig. 2. Model for segment formation in vertebrates based on mouse and chick data. The FGF8/Wnt3A gradient, which regresses posteriorly during somitogenesis, is shown in black. The anterior boundary of the gradient defines the determination front, which corresponds to the position of the wavefront (thick black line). The phase I expression of Notch-related cyclic genes is shown in red (*26*). The expression of *Mesp2/c-meso1* is shown in blue.