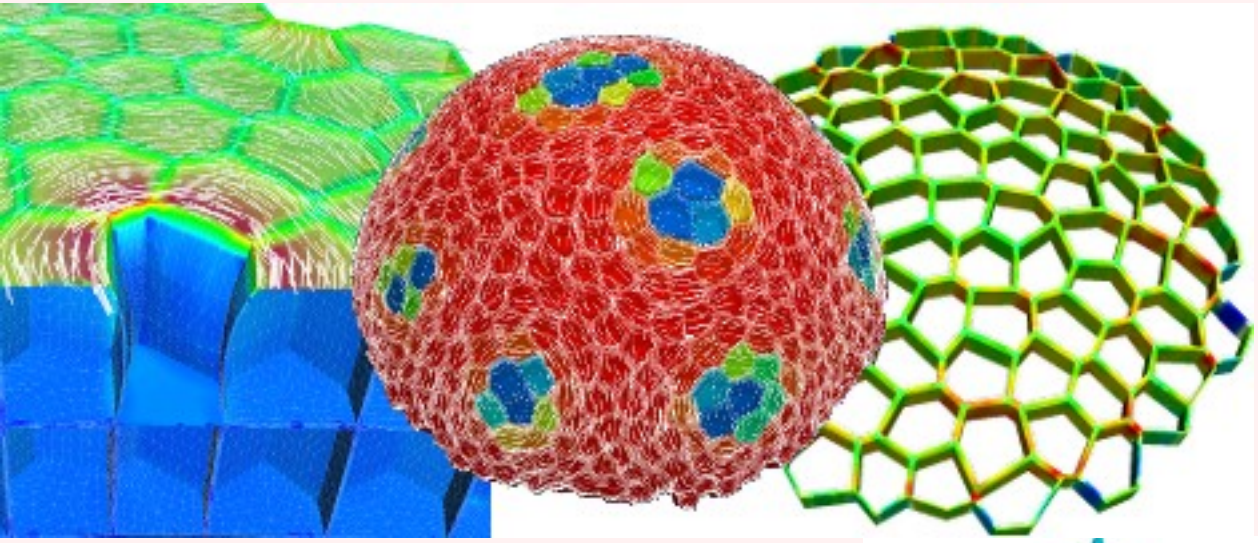
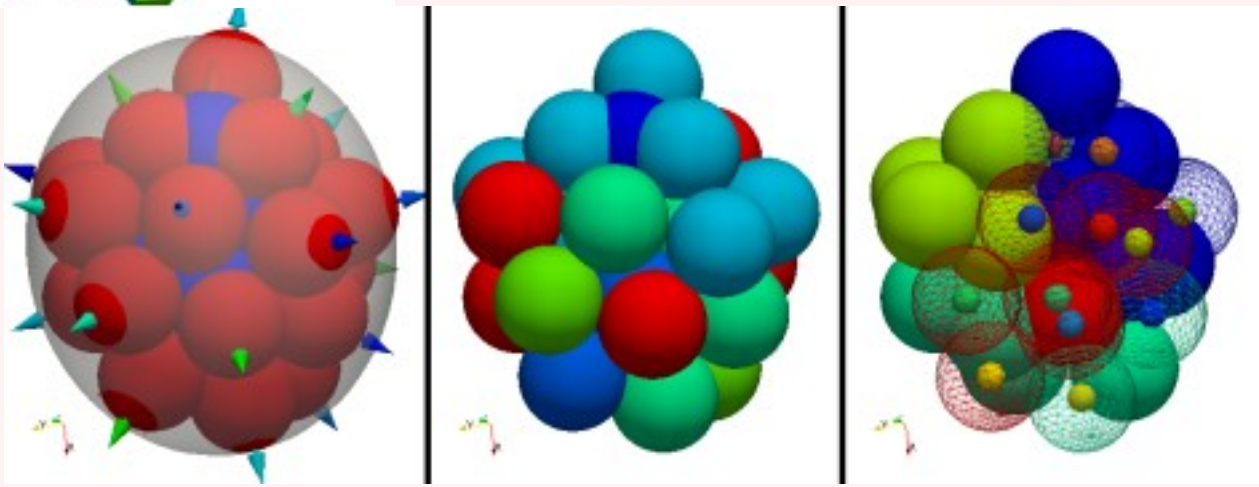
Biomechanics of cells and their interactions – models for plants and animals



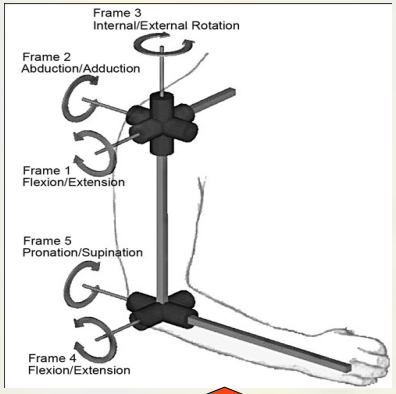
Pawel Krupinski

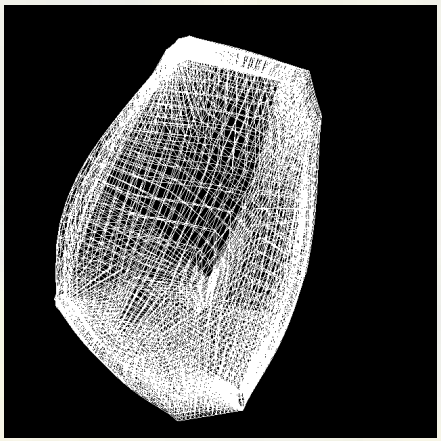


Computational Biology & Biological Physics
Lund University

Mechanics at different scales

- Organisms – tissues – cells
- Form reflects function
- Complex system



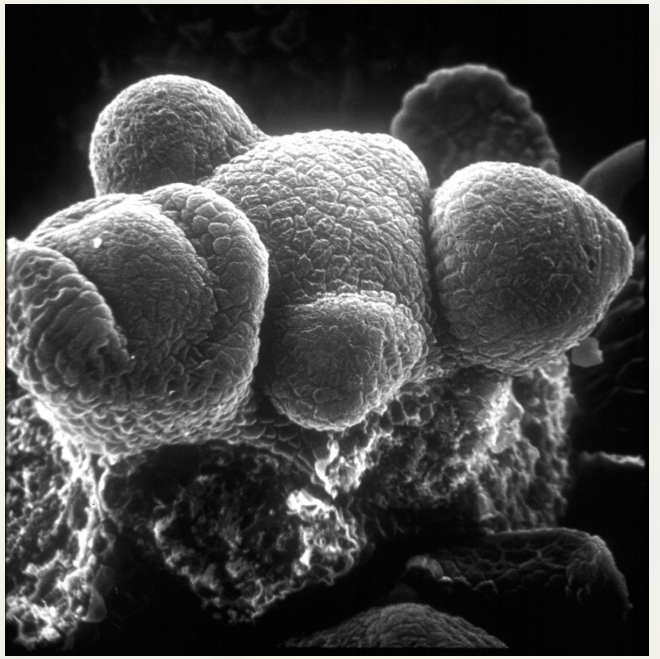


Resolution of the model

- Type of processes studied
- Time scales
- Tissue – medical simulation
- Cellular – signaling
- Subcellular – mRNA polarization, intracellular transport
- Multiscale models

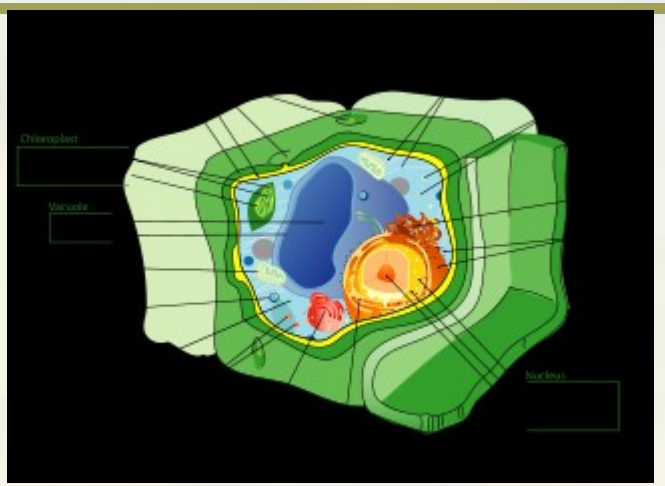
Mechanics in morphogenesis

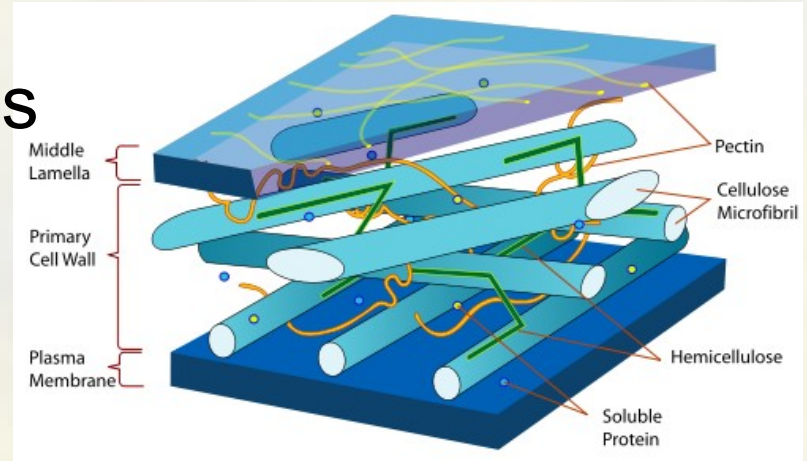
- Creation of new organs – change of shape – large deformations
- Cellular scale
- Cell growth and division
- Conditions change in the cell
- Regulation of mechanical properties
- Mechanotransduction



Plant cells

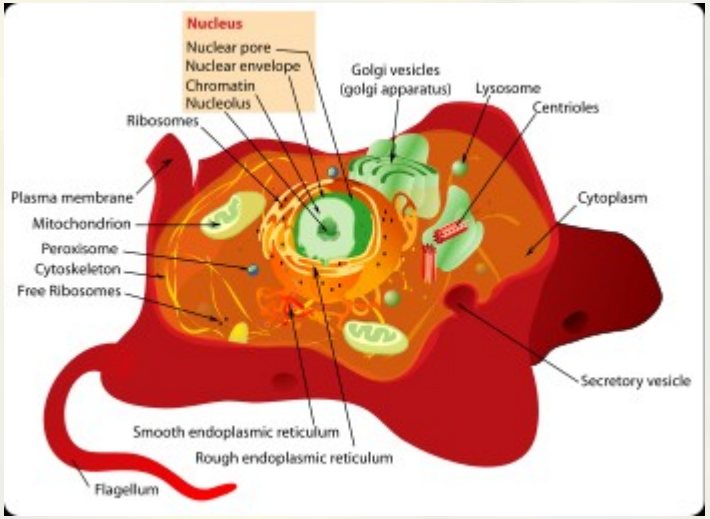
- Rigid walls
- Turgor pressure
- Transport
- Simplastic growth
- Anisotropy – cellulose microfibrils
- Cortical microtubules





Animal cells

- Cell membrane – no cell wall
- Can move with respect to each other
- Cytoskeleton – scaffold of a cell
- Adhesion
- Specialized junctions

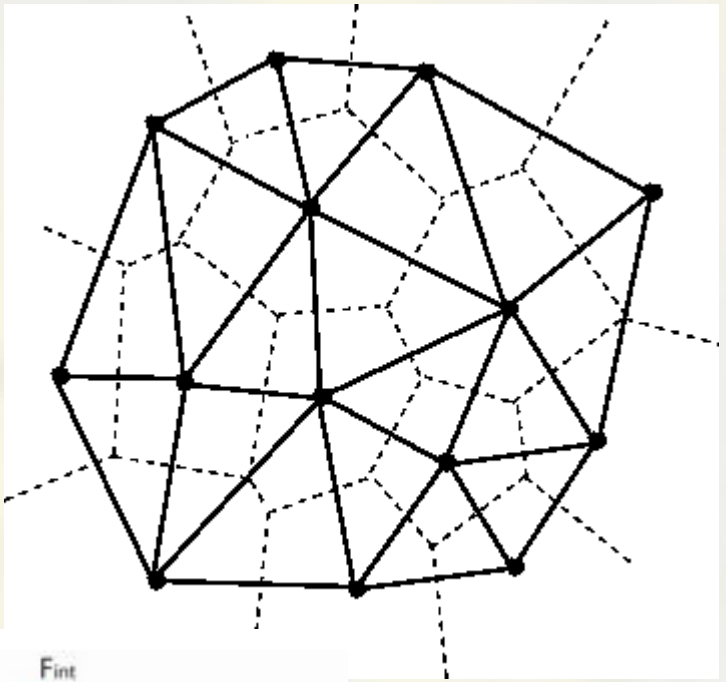


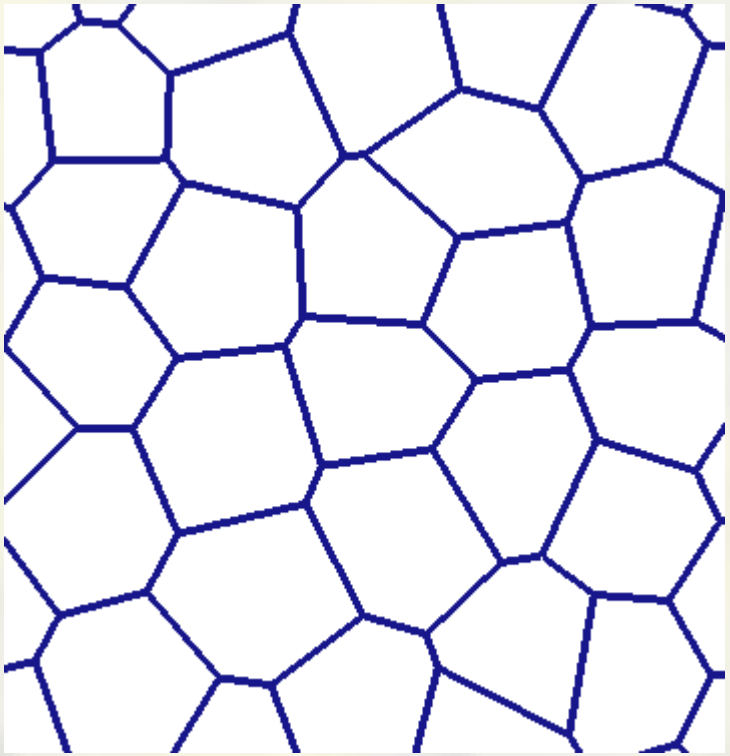
Cellular models

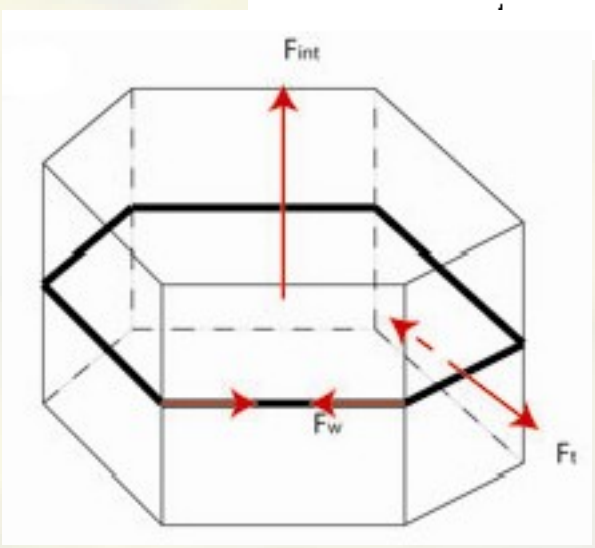
- Mass spring models
- Vertex dynamics
- Cellular Potts
- FEM models
- Particle models
- Tensegrity

Mass spring models

- Cells as point masses or...
- Plant walls as the springs
- Easy cell growth and division



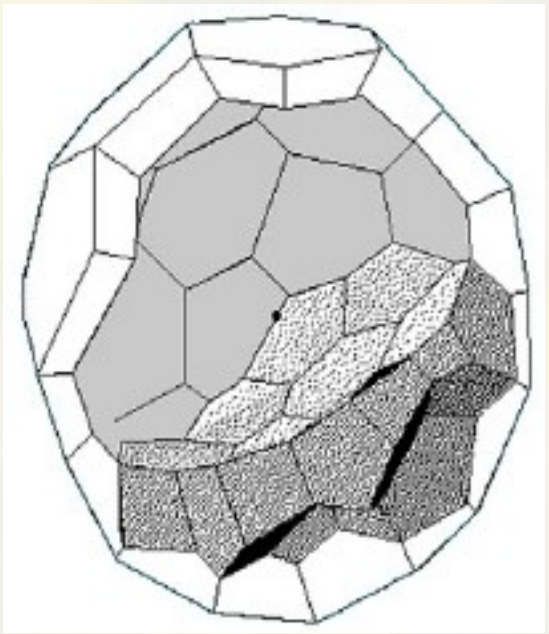


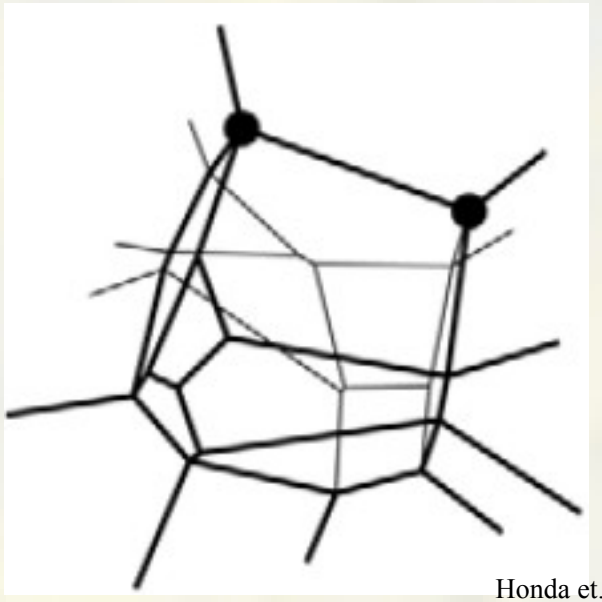


Vertex dynamics models

- Vertices → Potential function of cells and walls
- Solve equations of motion for all vertices

$$m\ddot{r}_i + \eta \dot{r}_i = -\nabla_i U$$





Honda et.al 2008

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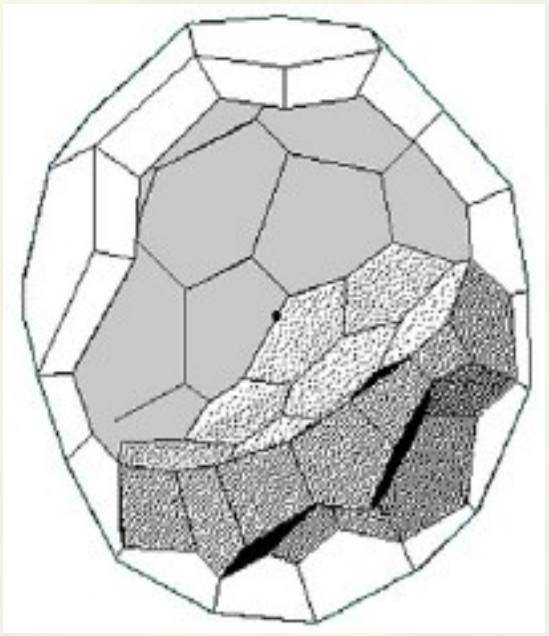

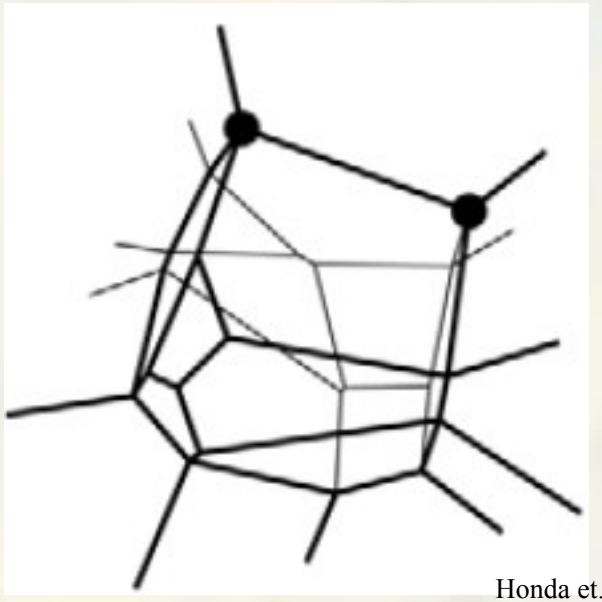

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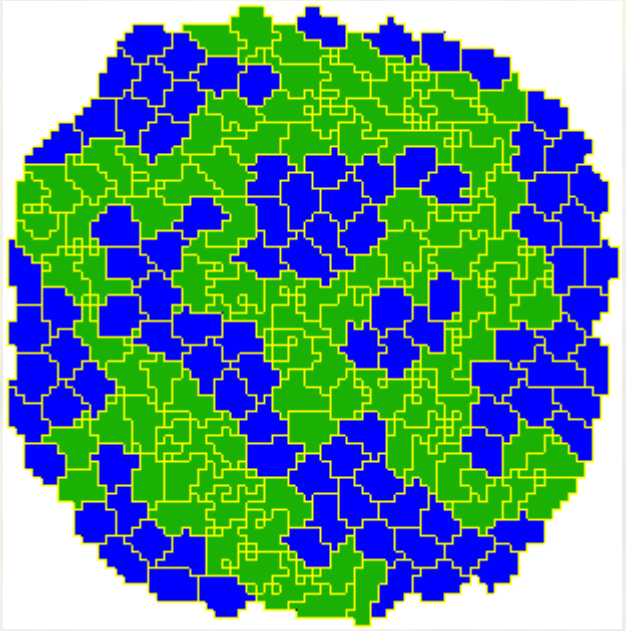
Cellular potts models

- Lattice based
- Monte Carlo updates
- Hamiltonian defines probabilities

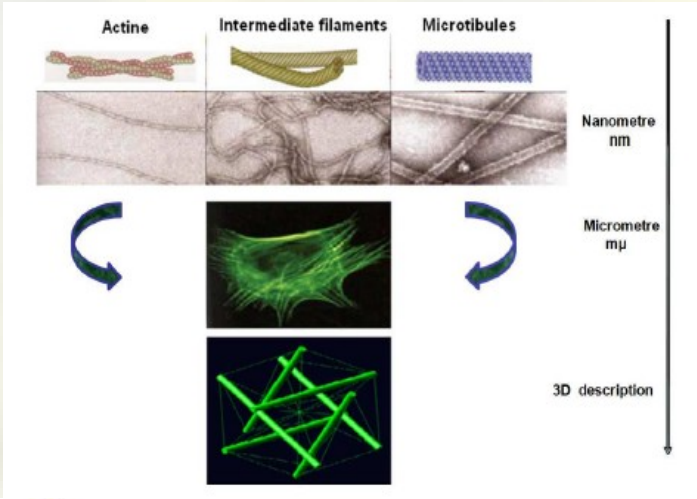


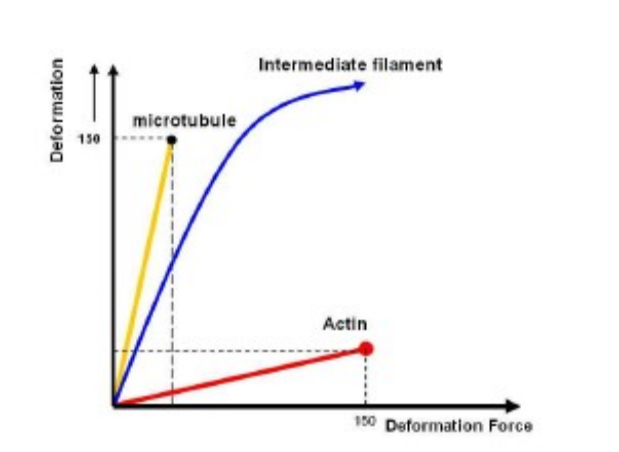
CompuCell 3D

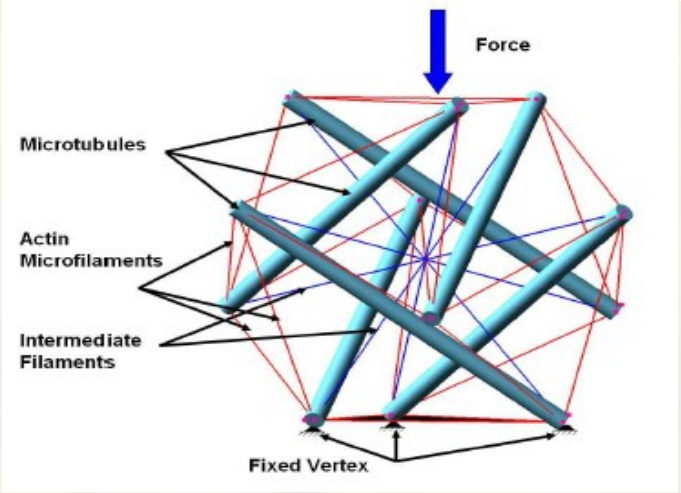
$$P\left(s_{i,j} \rightarrow s'_{i,j}\right) = \exp\left\{-\Delta H / kT\right\}$$

Tensegrity models

- Aims to reproduce internal structure
- Different response of elements







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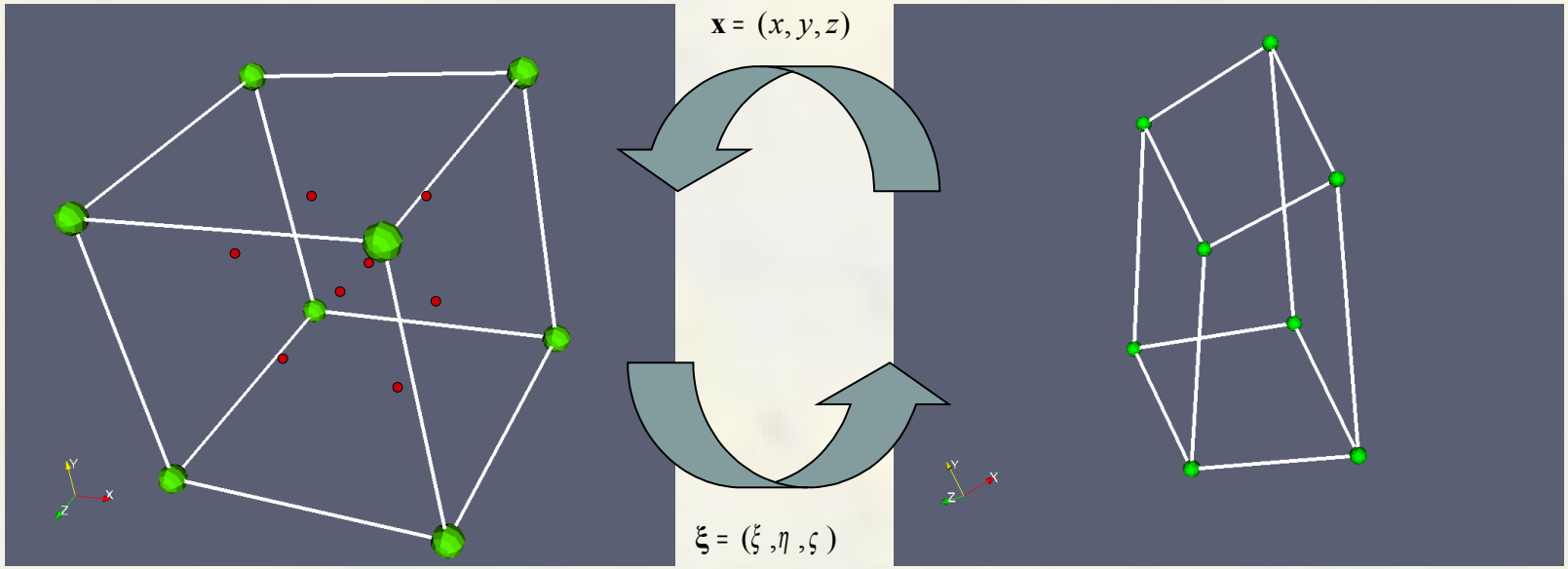
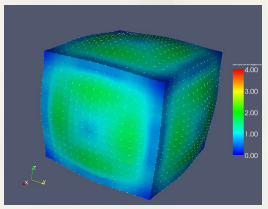
Finite Element Method

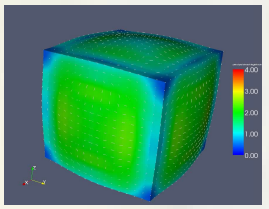
- Boundary value problem on complicated geometries
- Variational formulation
- Division of domain to simple elements

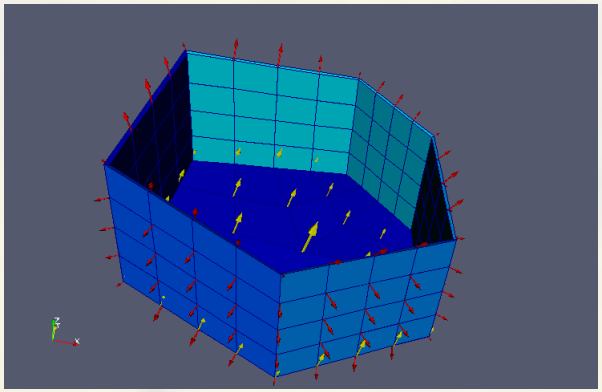


FEM for biological tissues

- Anisotrophy
- Growth, divisions
- Viscoelasticity







FEM for biological tissues

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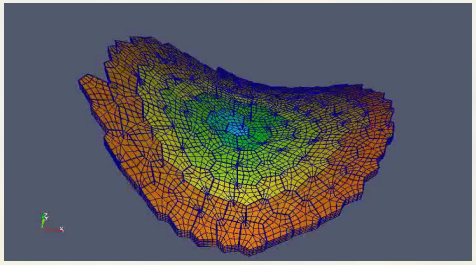
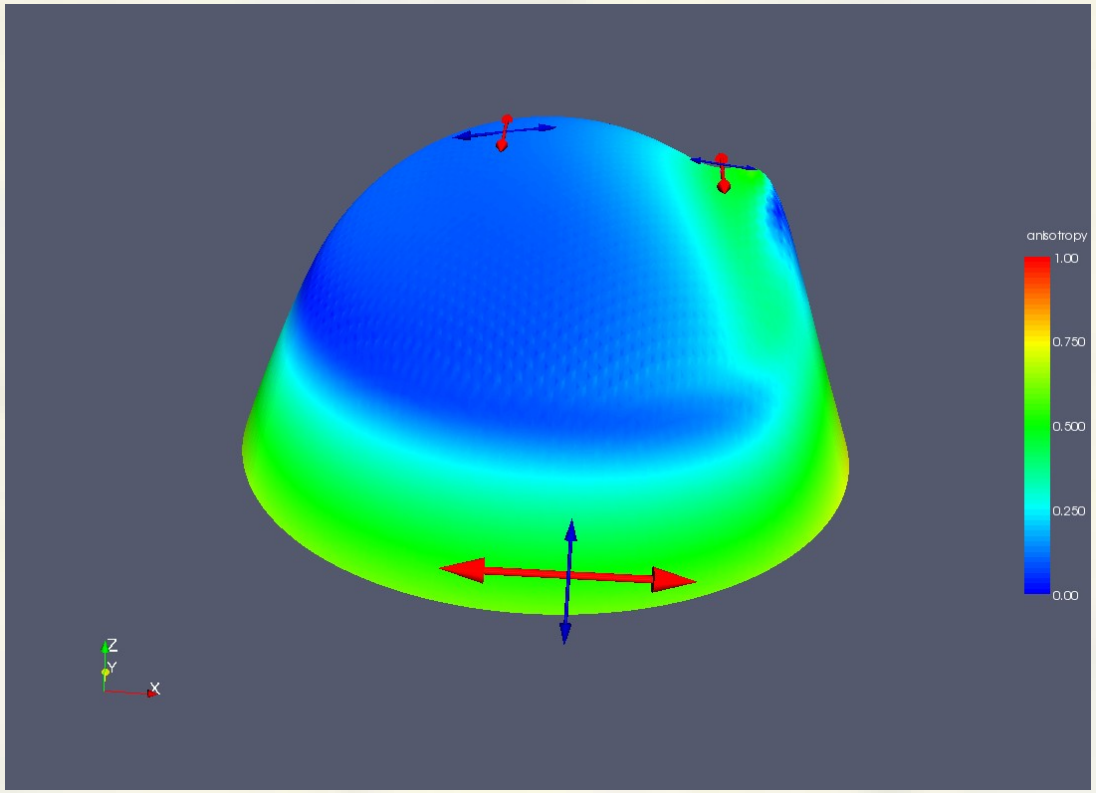


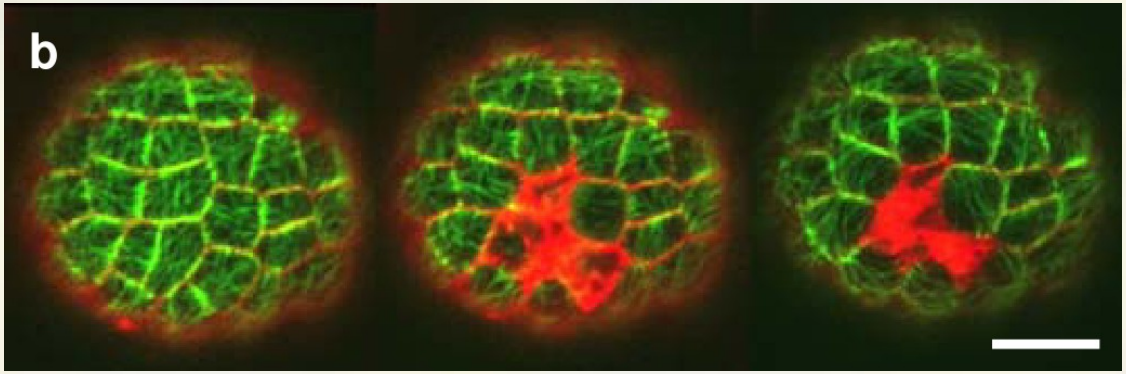
Microtubules – stress

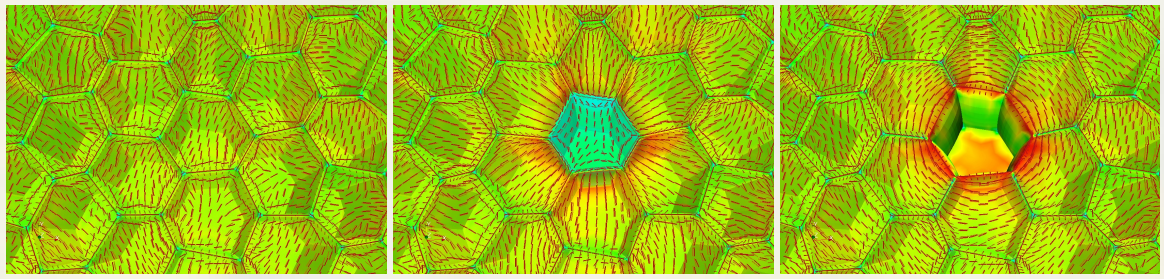
- Microtubules direction correlates with max principal stress direction

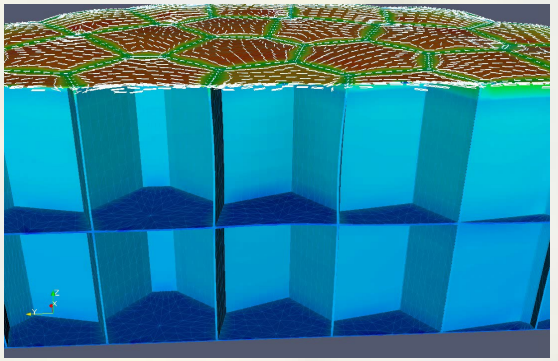


Microtubules – stress

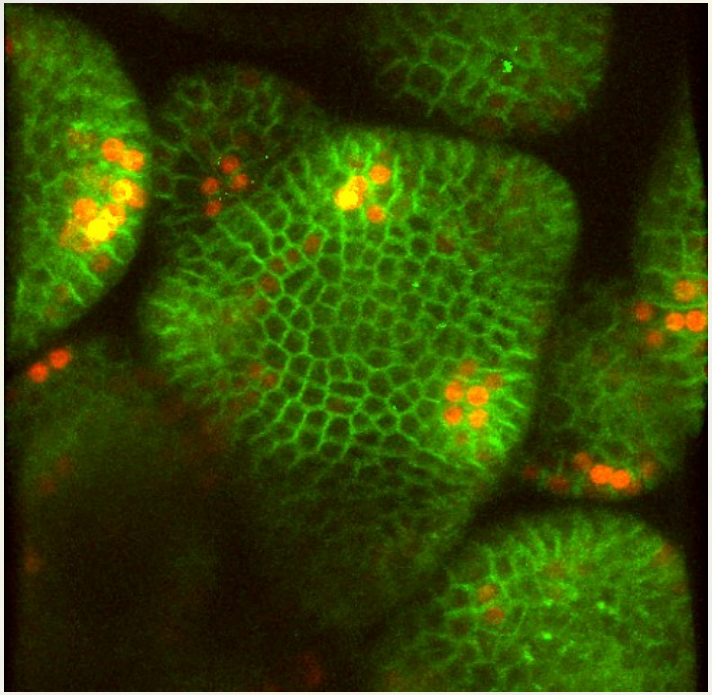
- Cell ablation induces changes in microtuble arangement

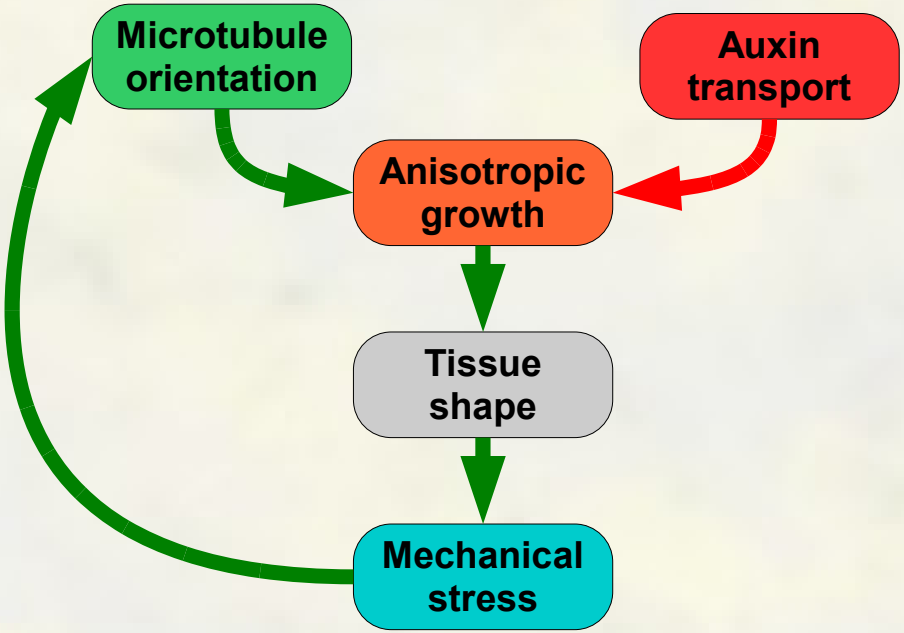






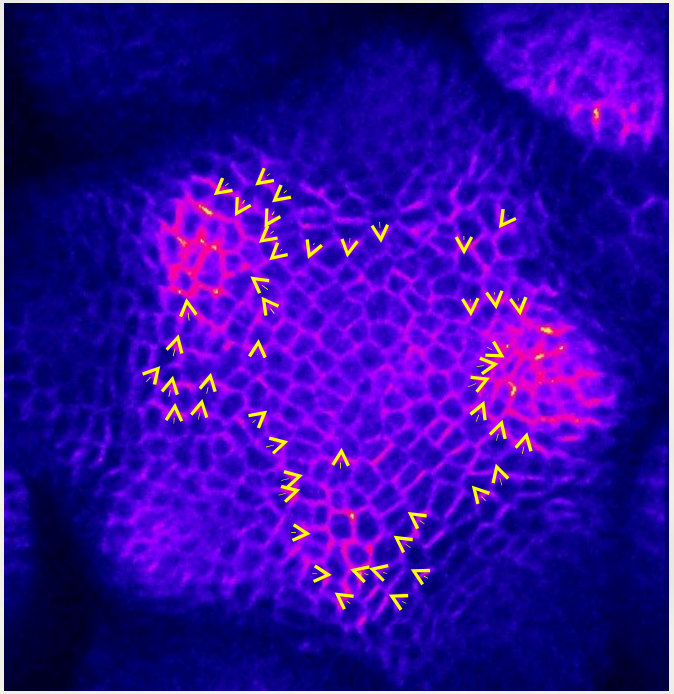
Auxin transport

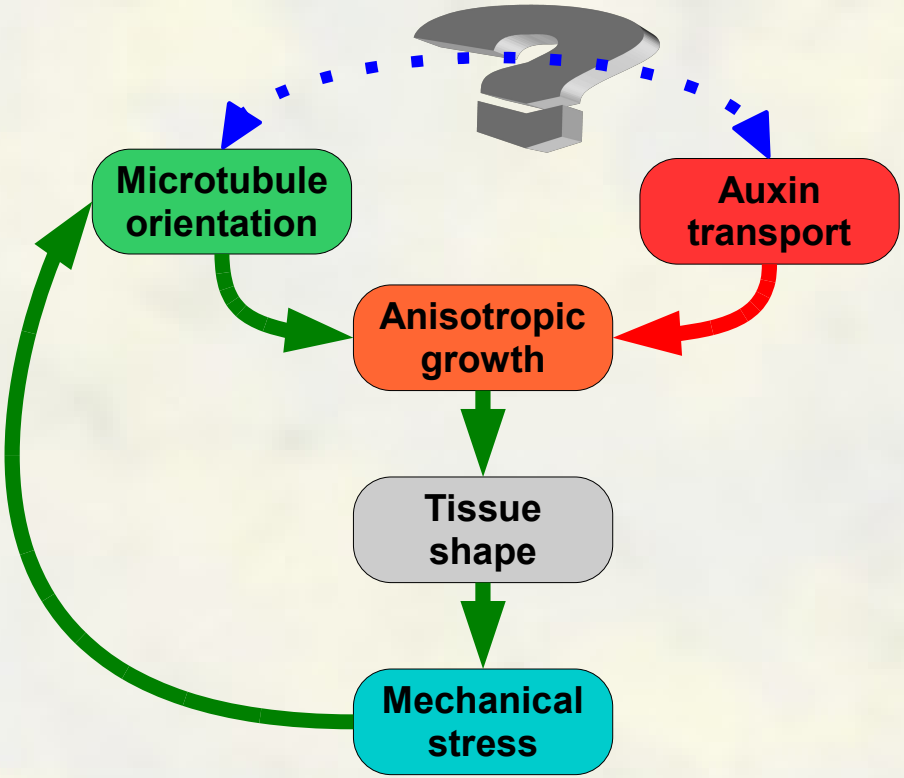




Auxin transport

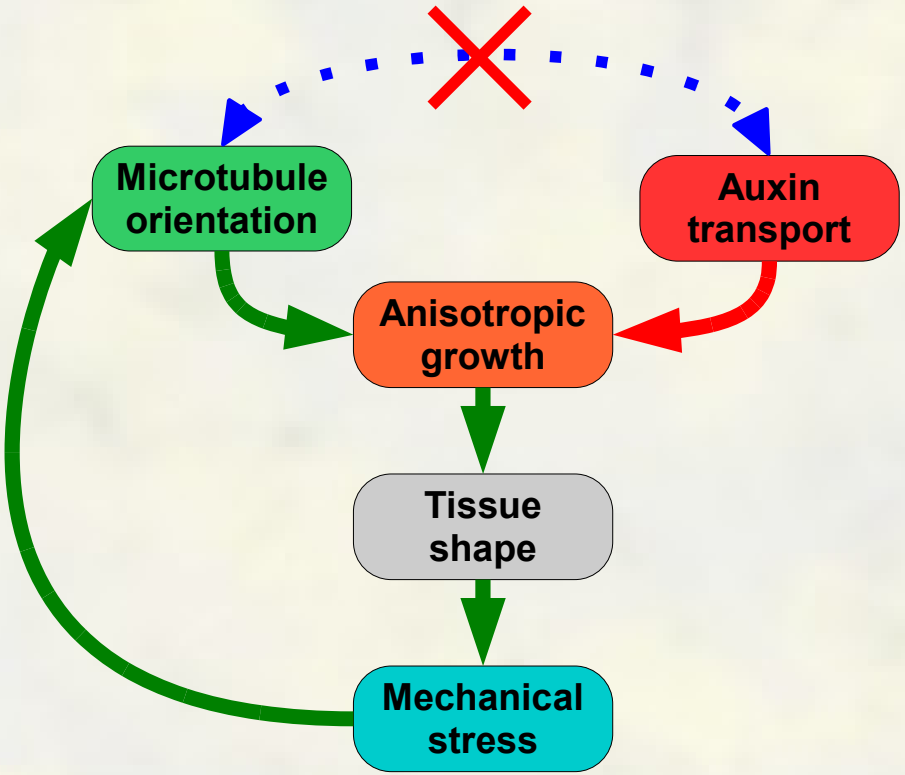
- PIN1 correlates with microtubules





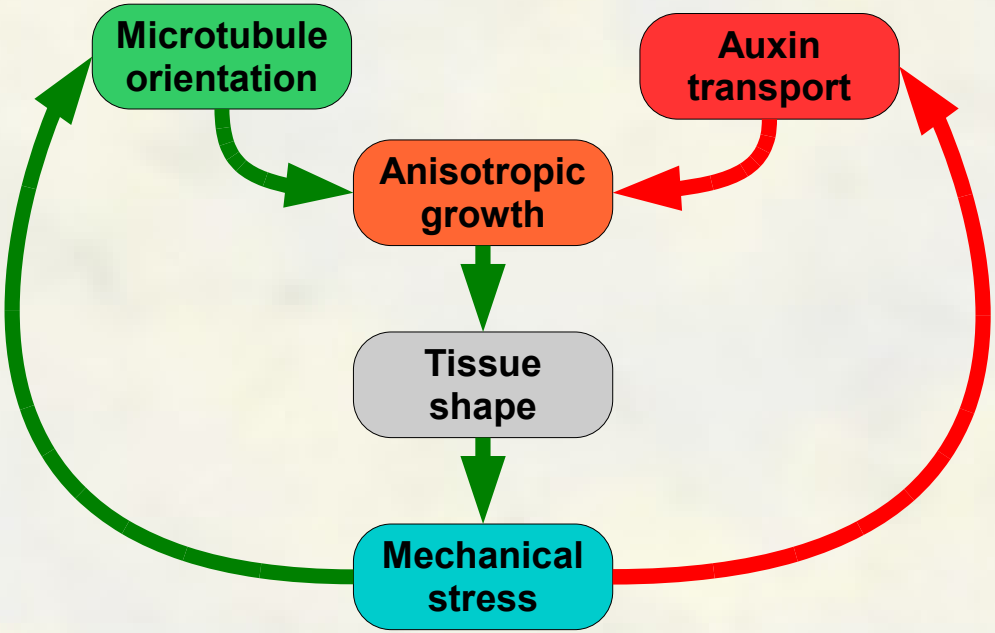
Auxin transport

- No direct connection between PIN1 and microtubules

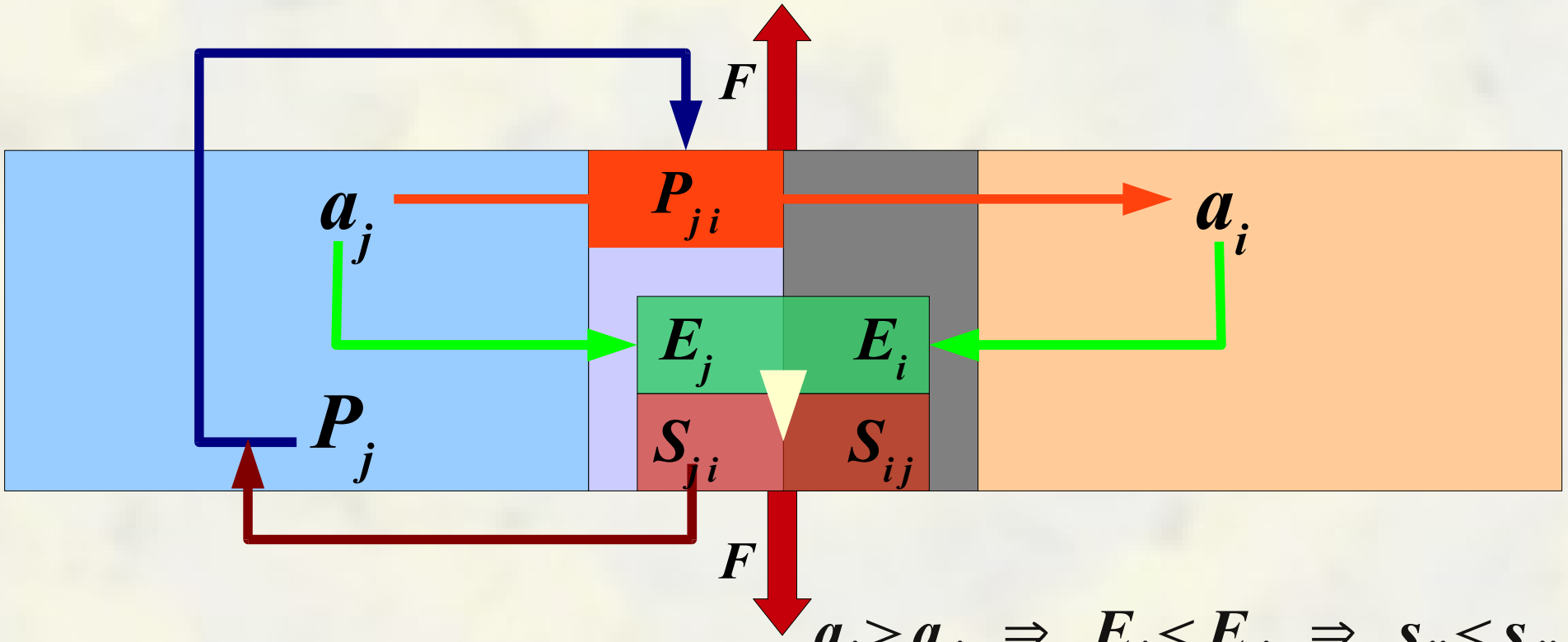


Auxin transport

- Hypothesis: stress regulates both microtubules and auxin transport



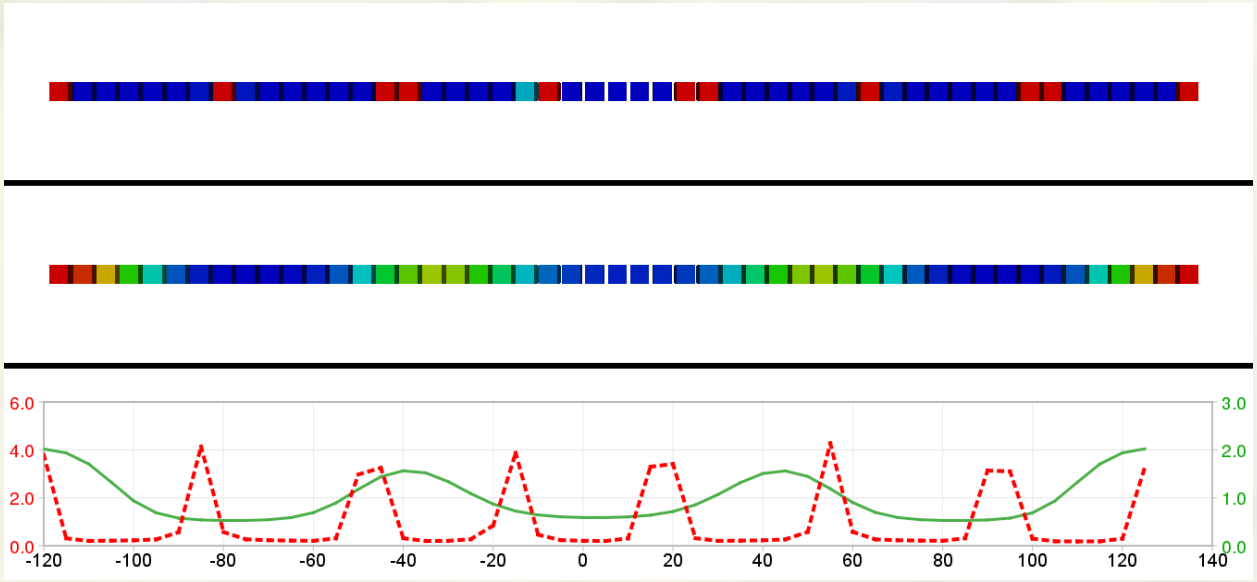
Auxin transport

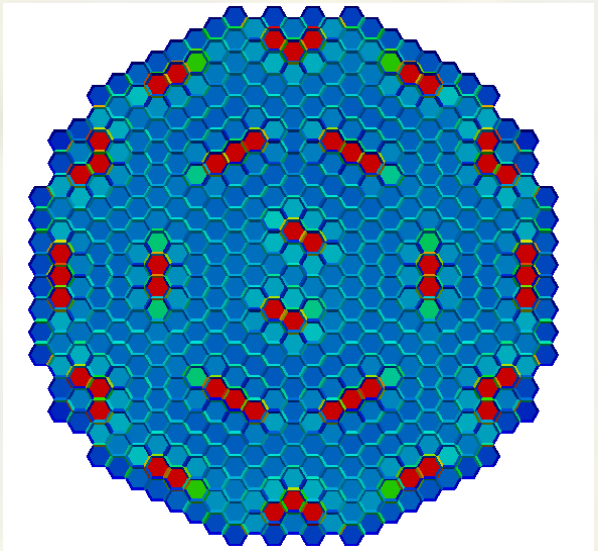


$$a_i > a_j \Rightarrow E_i < E_j \Rightarrow s_{ij} < s_{ji}$$

Auxin transport

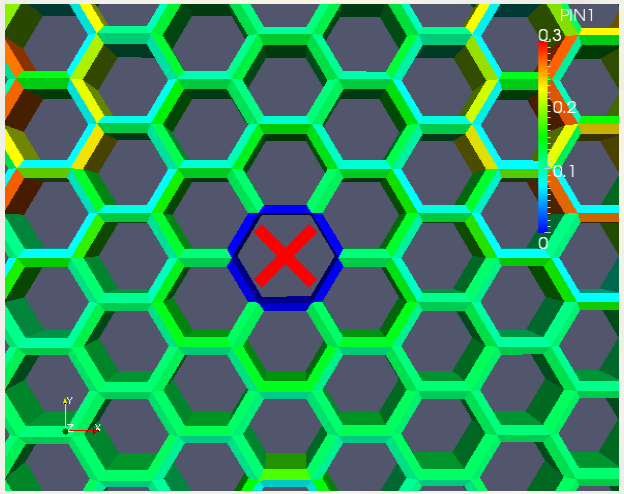
- Spontaneus pattern formation

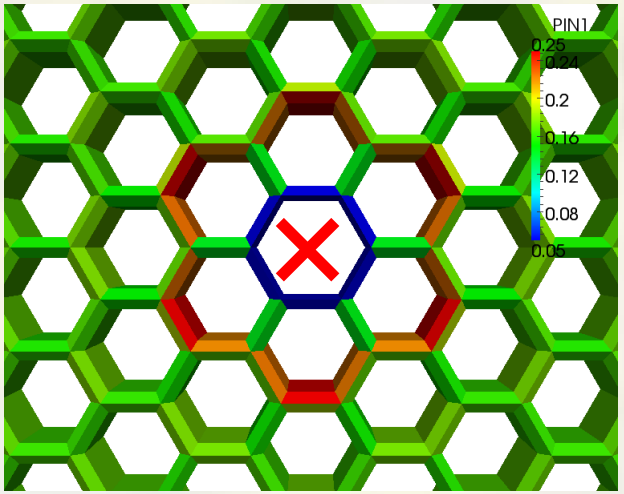




Auxin transport

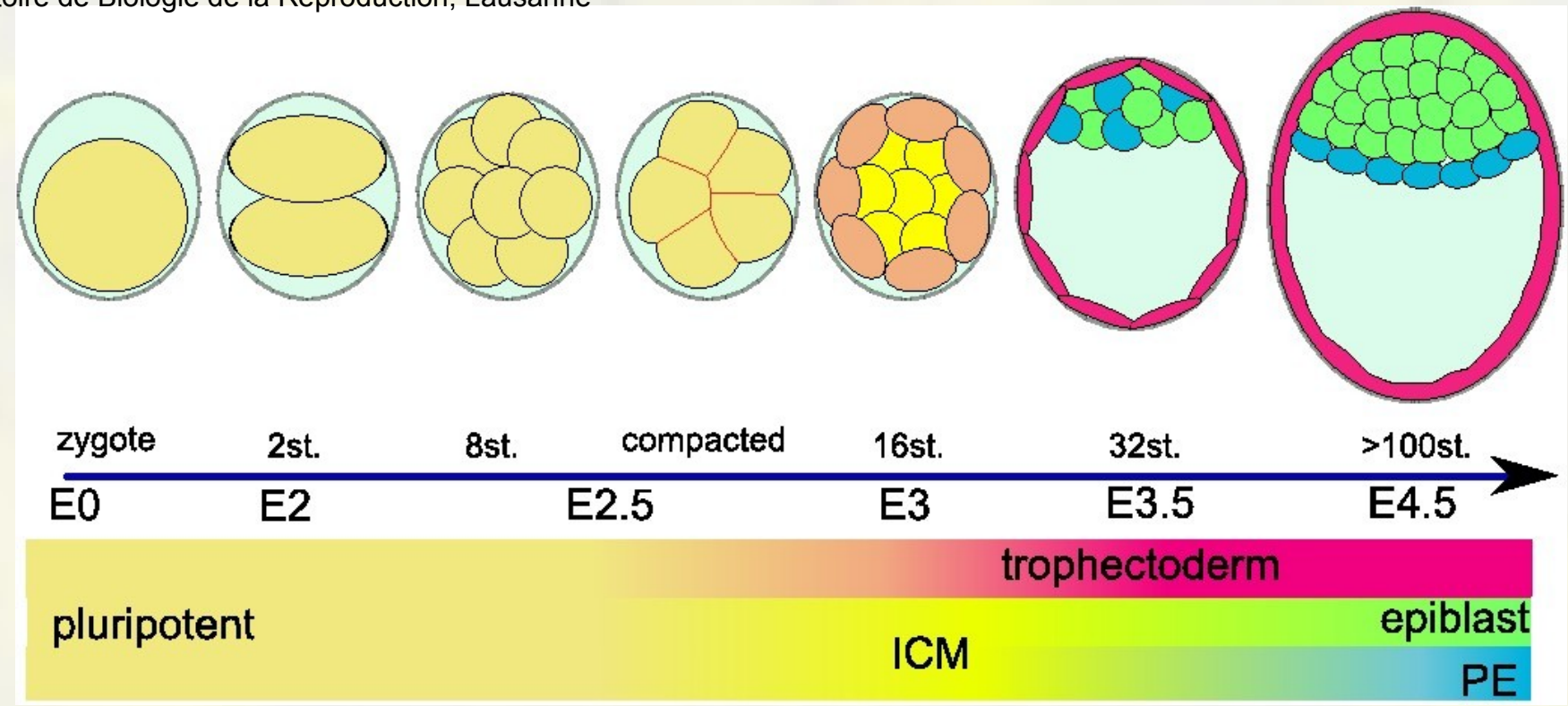
- Ablation
- PIN1 polarizes away from ablated cell





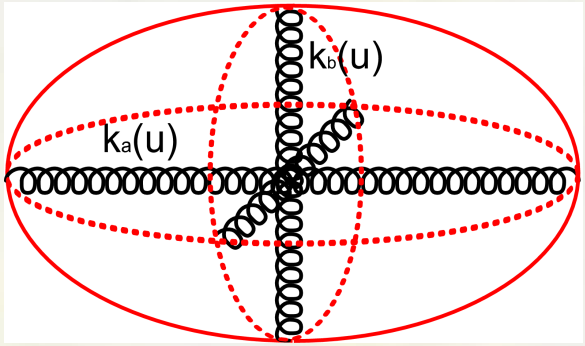
Mechanistic model of embryogenesis

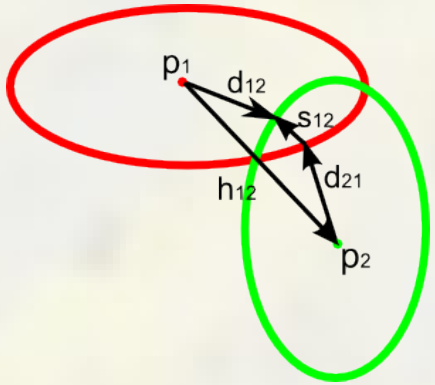
Laboratoire de Biologie de la Reproduction; Lausanne



Mechanistic model of embryogenesis

- Elastic response lumped to principal axes
- Elastic, adhesion and drag forces
- Each cell has a set of internal data (concentration of proteins, cell cycle length, etc)





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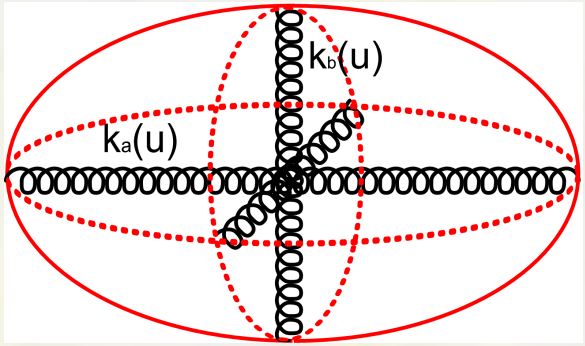
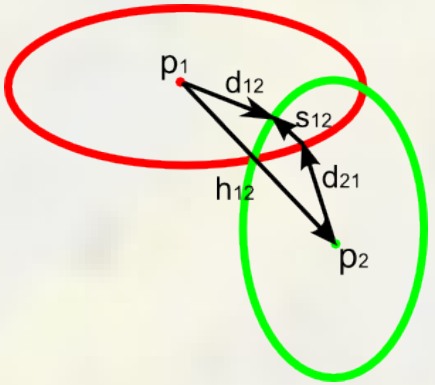
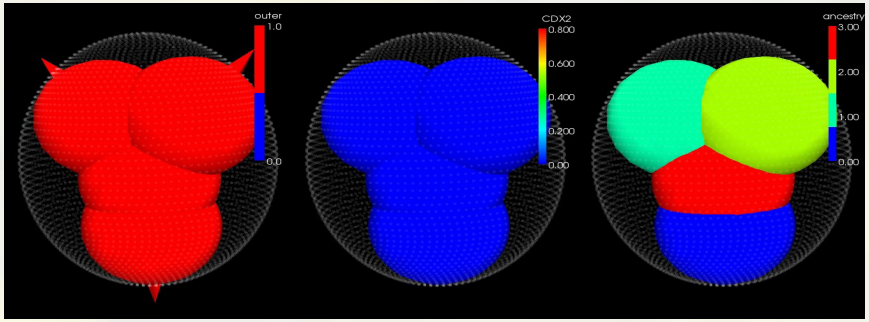
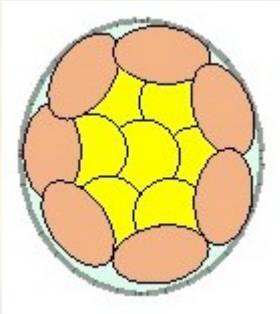


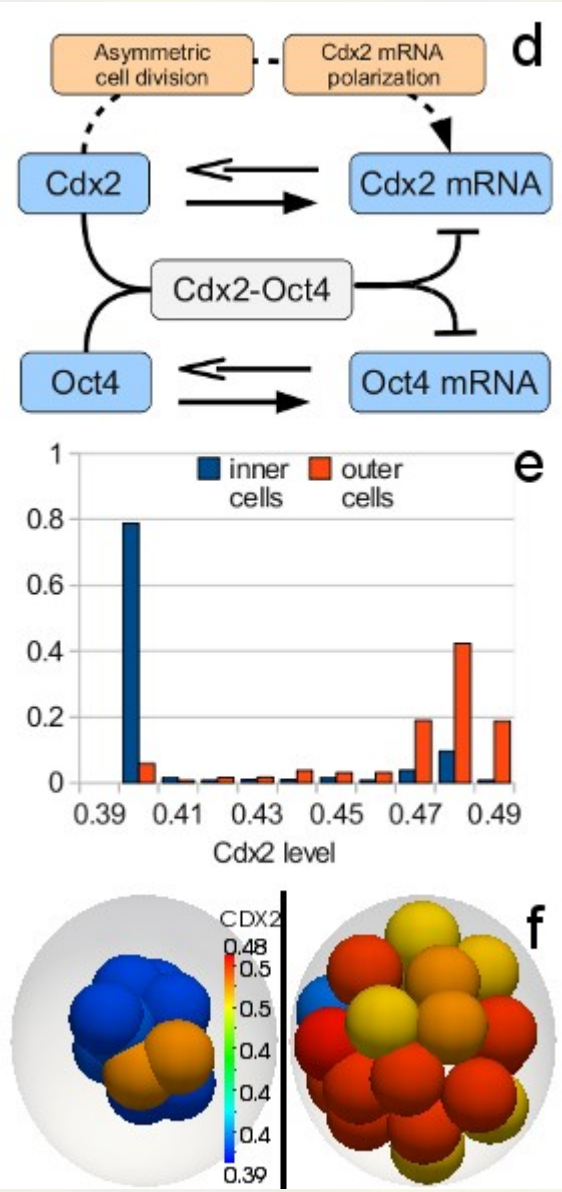




Trophectoderm formation

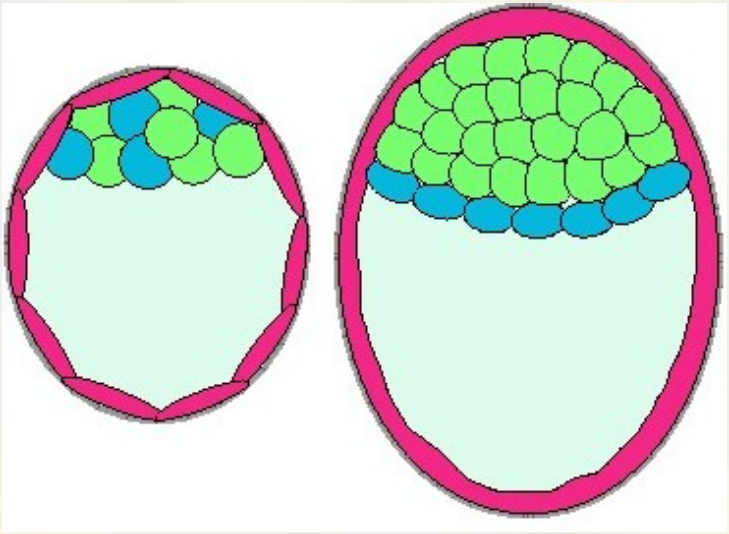
- Cdx2 – Oct4 antagonism
- Polarity based model
  - Cdx2 mRNA divides asymmetricaly
  - Asymmetric division more probable for low Cdx2 cell
- Inside-outside separation of Cdx2 levels





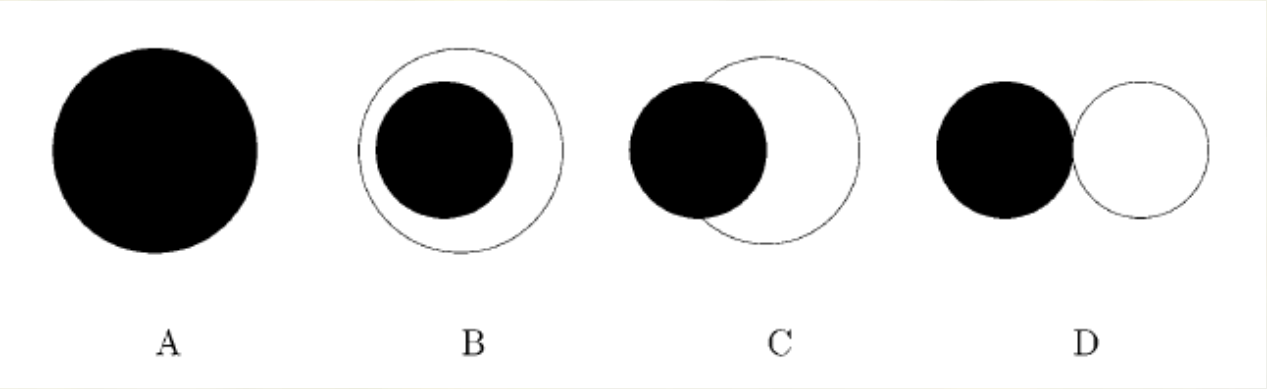
Endoderm formation

- Gata6 – Nanog expression specified early
- Spacial sorting



Differential adhesion

- Differences in adhesion strength lead to spacial sorting



$(A)\ C > \frac{S_1 + S_2}{2}$

$(B)\ S_1 < C < S_2$

$(C)\ C < S_1,\ C < S_2$

$(D)\ C = 0$

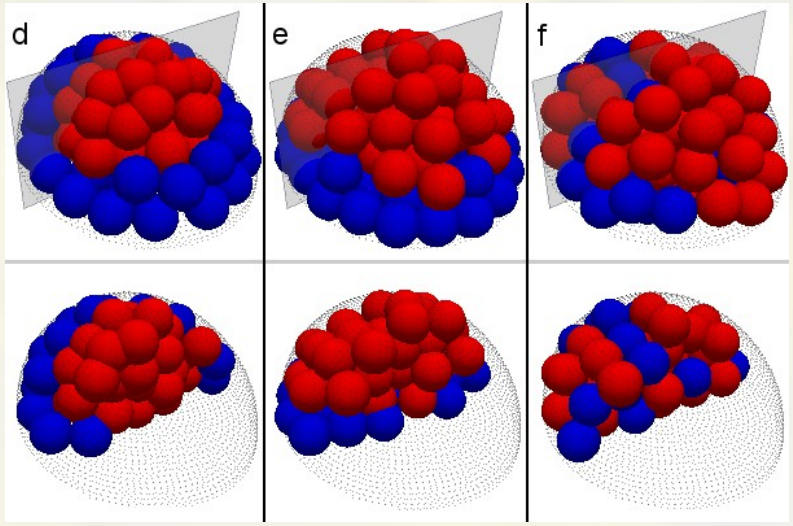
C – cross-adhesion

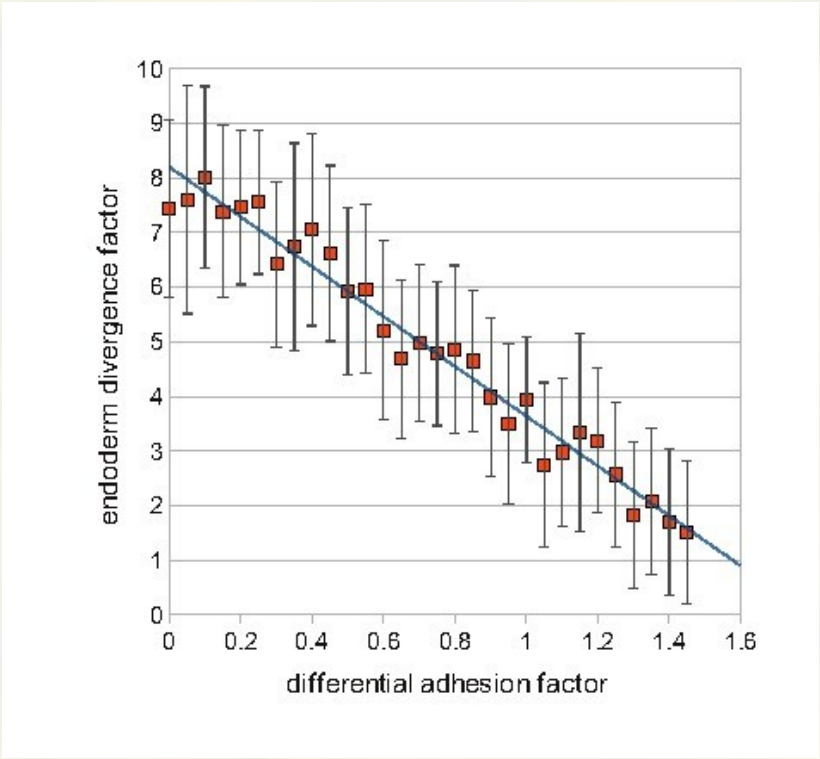
S_1 – white “species” adhesion

S_2 – black “species” adhesion

Endoderm formation

- Differential adhesion + directional basal movement





Summary

- Can't escape mechanics on cellular level
- Integral part of morphogenesis
- Connected to molecular integrations

Acknowledgments

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