Plant Bioinformatics, Systems and Synthetic Biology Summer school

Nottingham, 27-31 July 2009

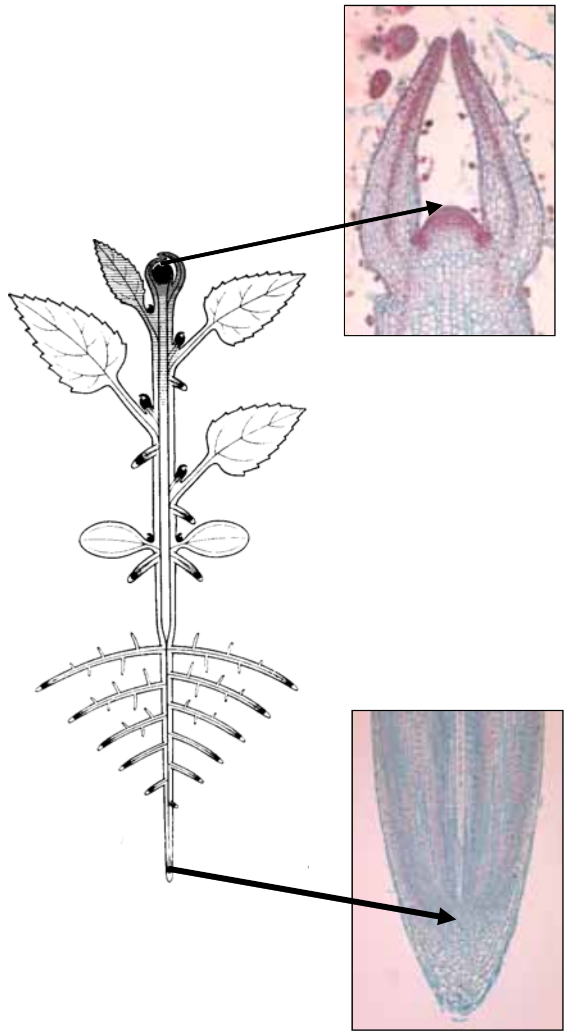
Components of a virtual tissue

Christophe Godin

INRIA Project-team

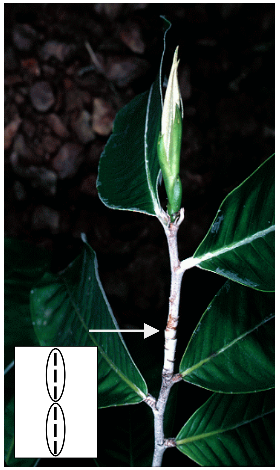
Virtual Plants

Growth areas in plants



Phyllotaxy

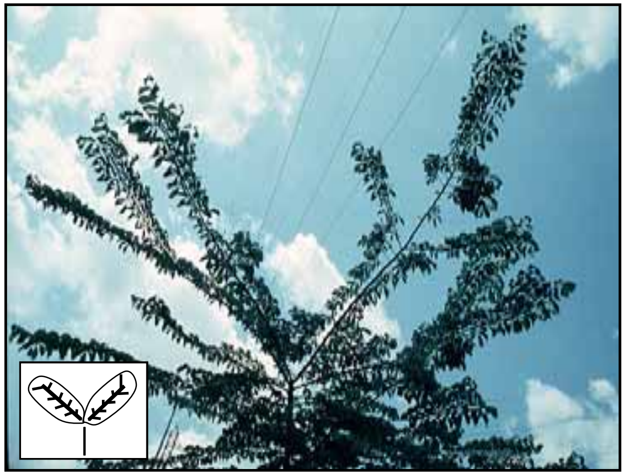
Architectural diversity and plasticity



Couepia,
(Ph. Y.Caraglio)

Kleinia,
(Ph. F. Hallé)

Fagrea,
(Ph. F. Hallé)



Elme tree,
(Ph. Y. Caraglio)

Parinari
(Ph. Y. Caraglio)

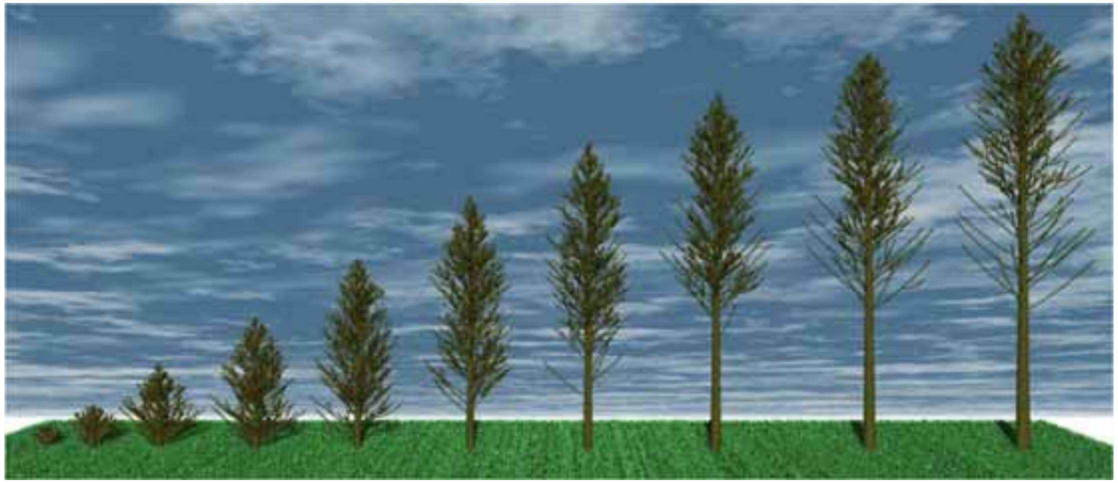
Effect of the environment:

Araucaria (Ph. X. Grosfeld)

→ *Hypotheses on meristem functioning*

Two main approaches

- Descriptive

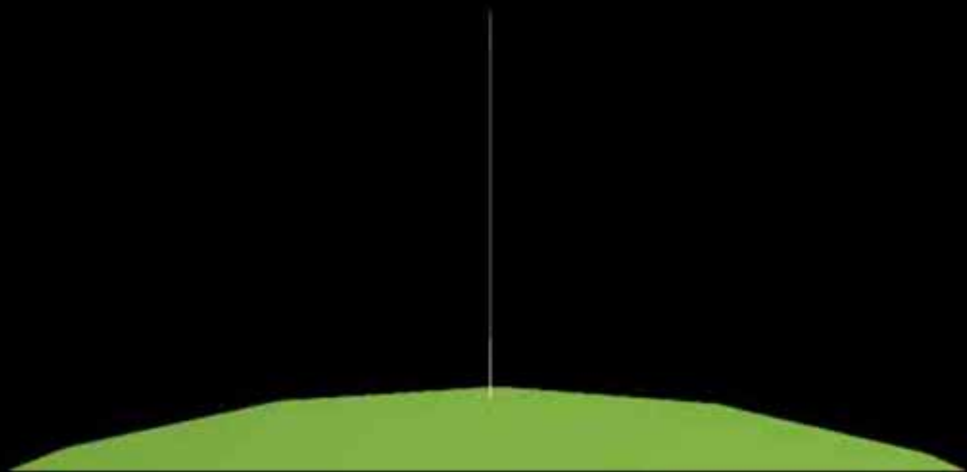


(Caraglio et al., 2000)

- Mechanistic

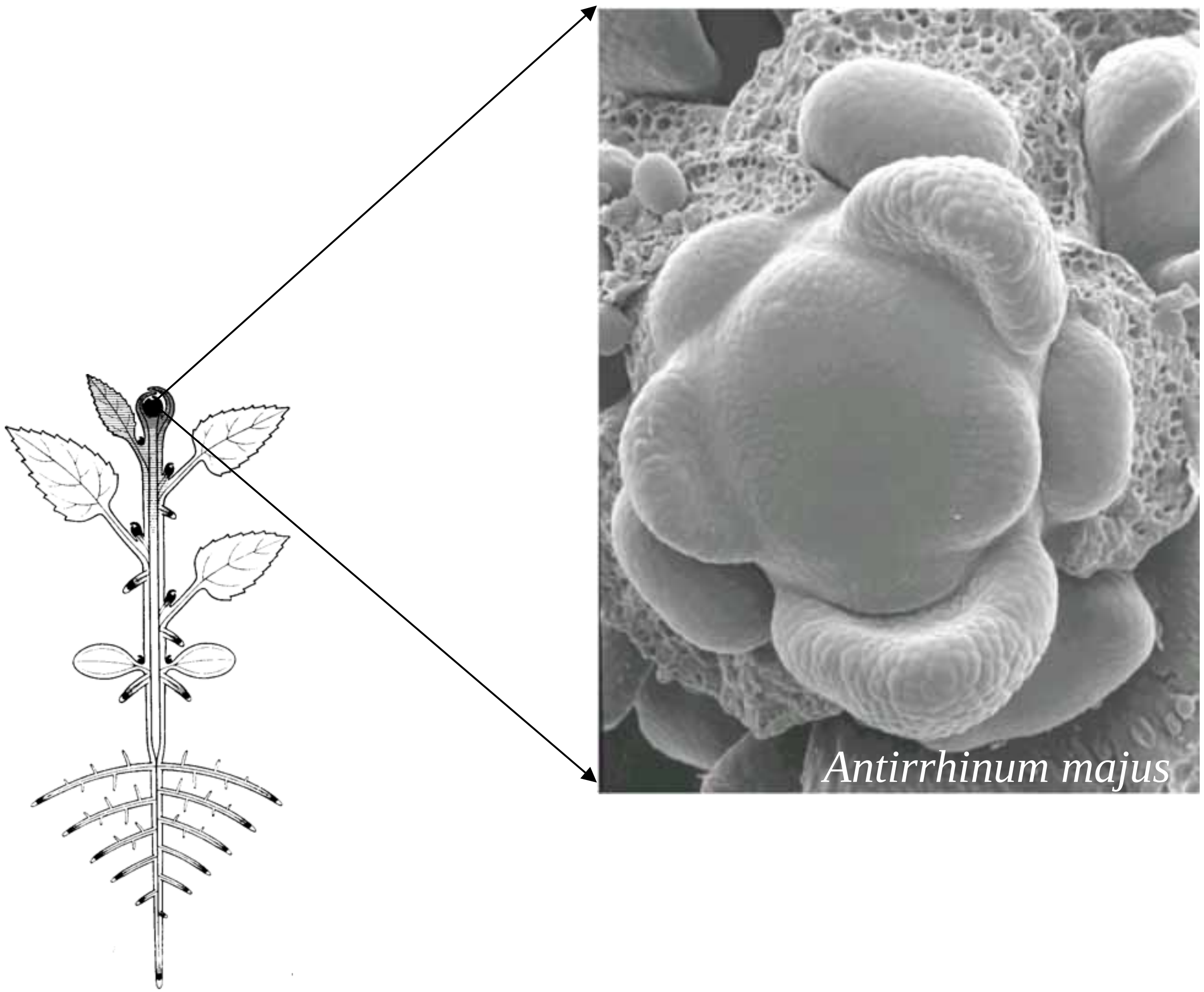
(Renton et al., 2005)

Mixed stochastic/mechanical model

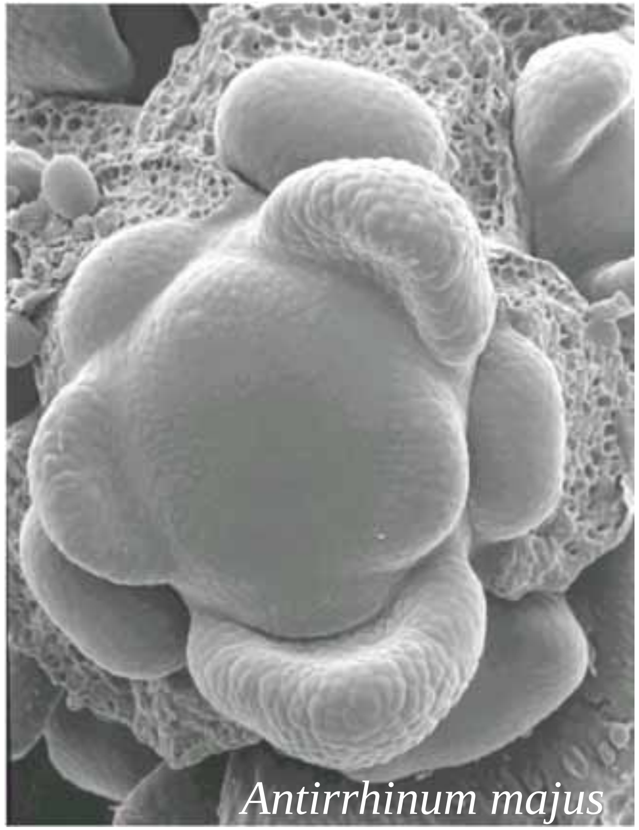


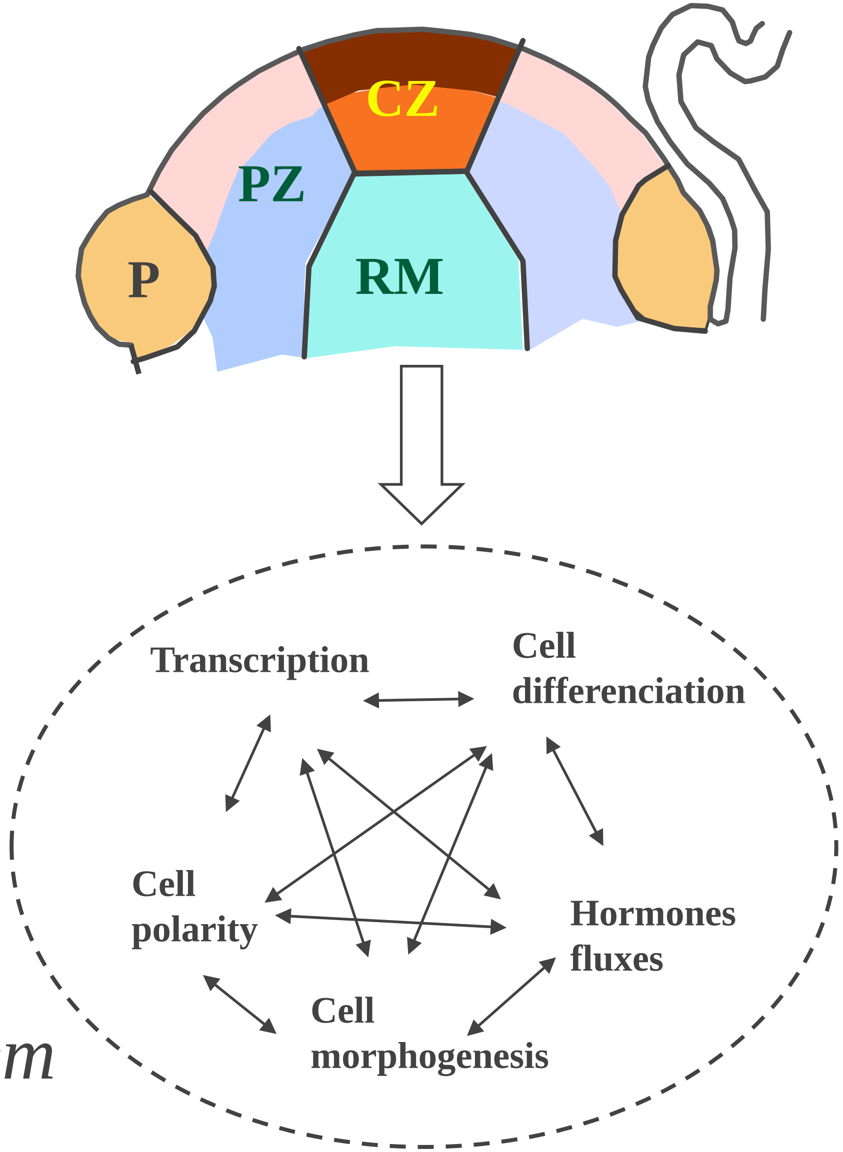
(Costes et al., J. Exp Bot, 2006)

Meristem



Shoot apical meristem

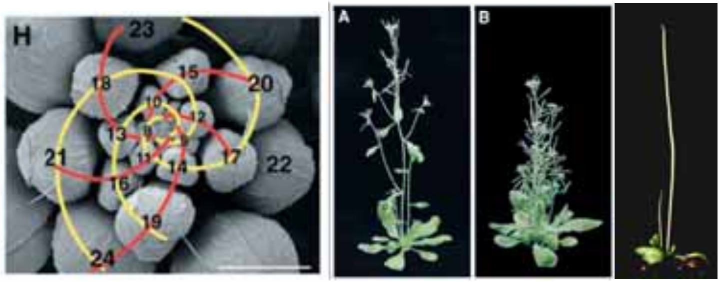




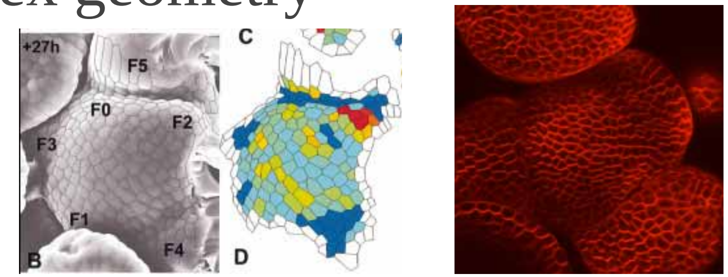
→ *Complex dynamical system*

What do we know about meristem growth?

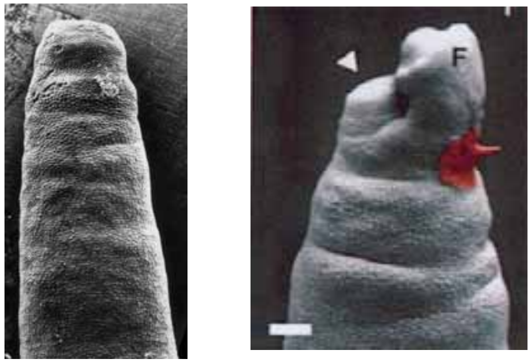
- Phyllotaxy / Phenotypes



- Apex geometry

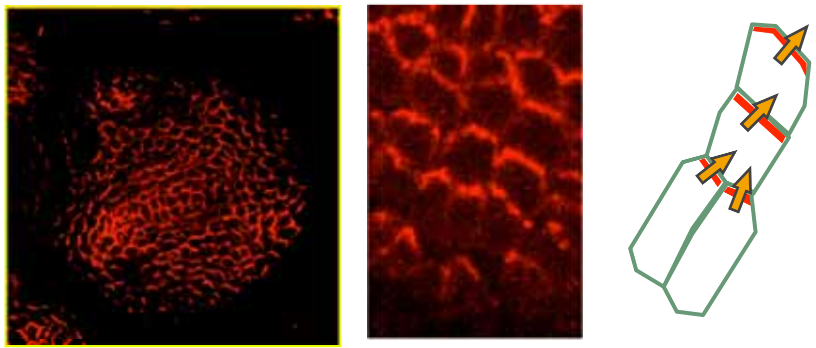


- Auxin as a morphogene



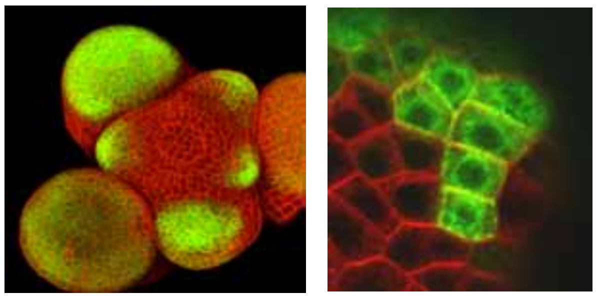
Organ generation in the *pin*1 mutant

- Auxin is transported actively

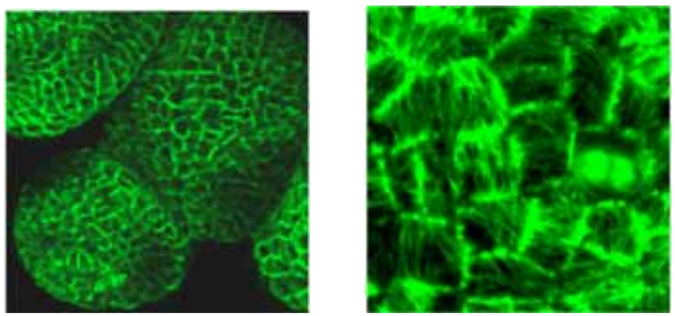


Immunolabelling of PIN-FORMED1 protein

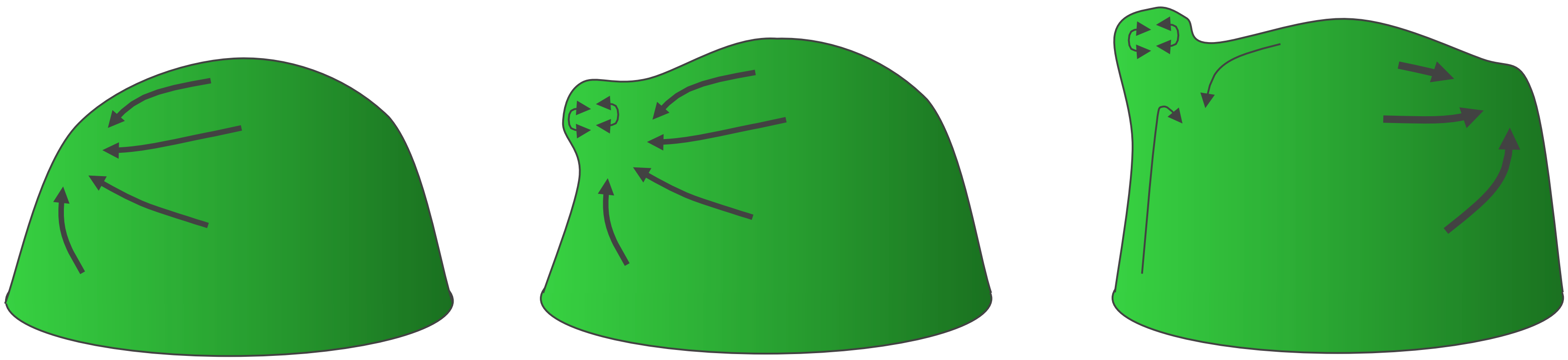
- Gene activity / cell identity



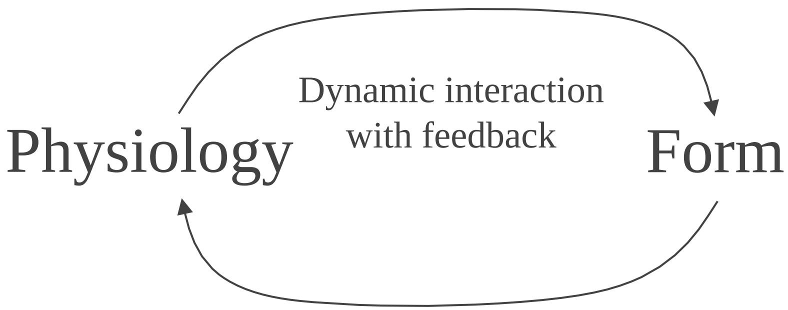
- Mechanical properties



A complex dynamic system with dynamic structure $(DS)^2$

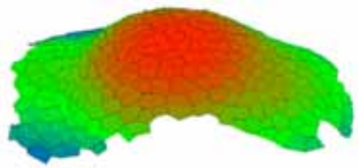


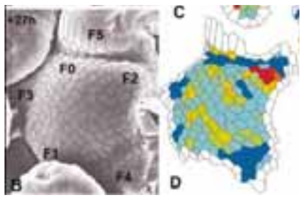
Physiology… changes Form… which changes Physiology…



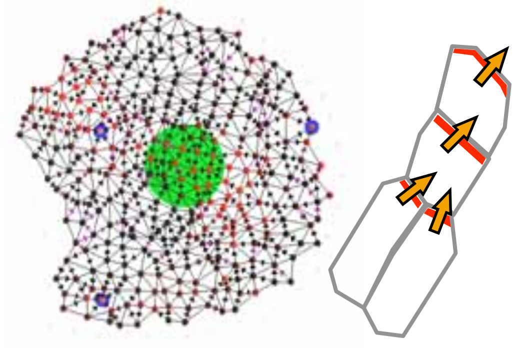
Building of a virtual meristem

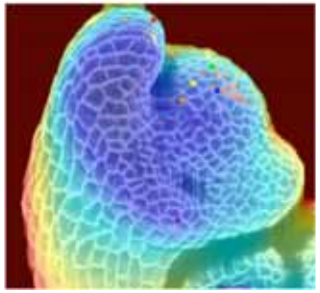
1 – Geometric Model



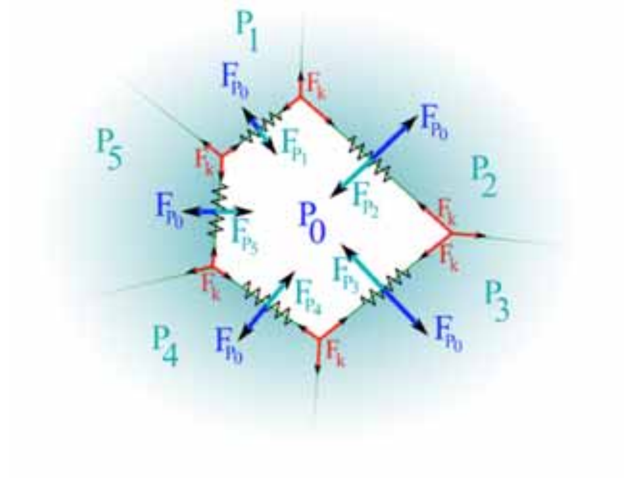


2 – Transport model



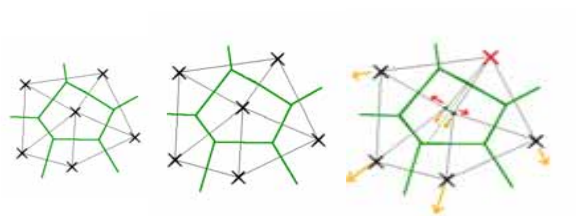


3 – Physical model

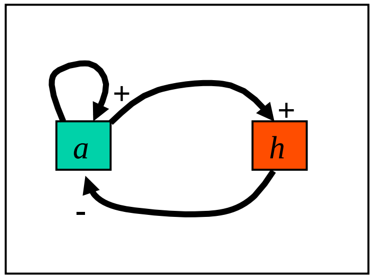


4 – Cell model

Division and Growth

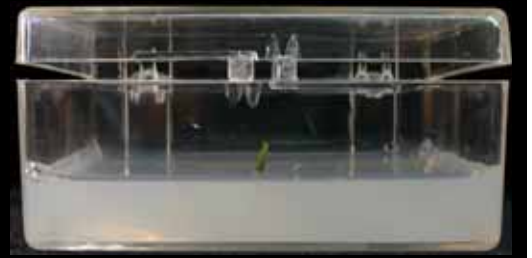


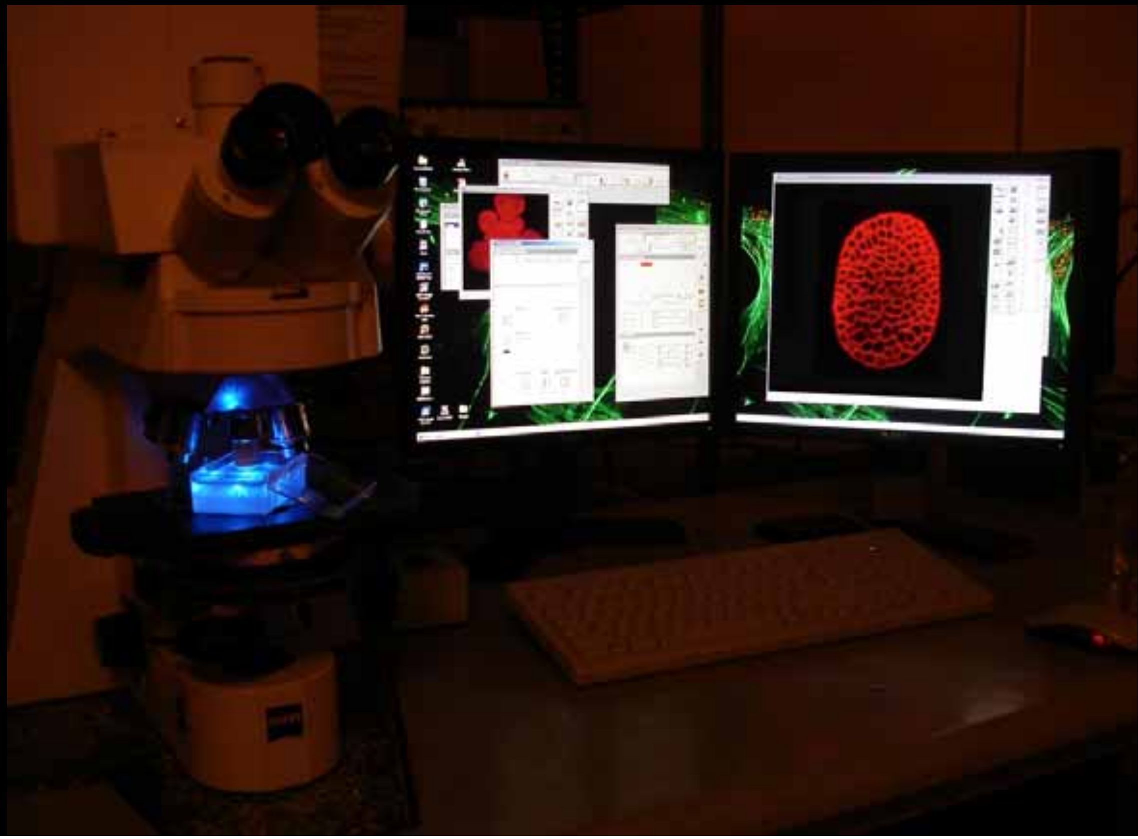
Interaction network



Real-time live-imaging confocal microscopy

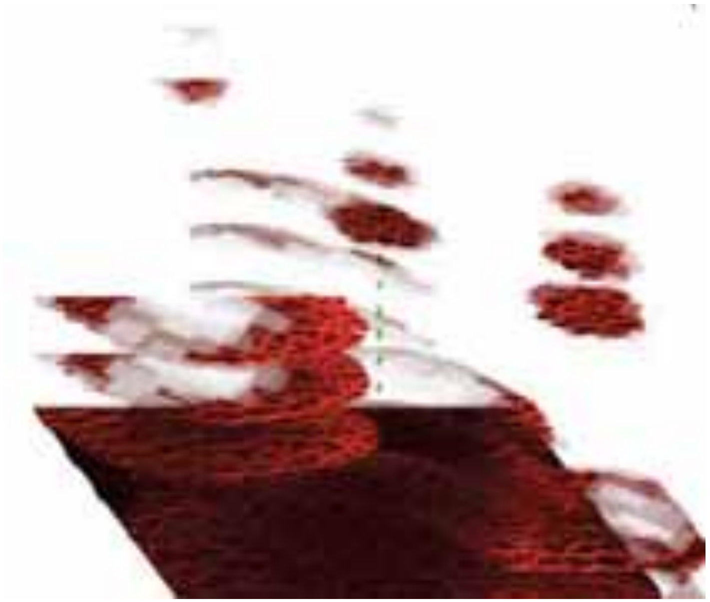
- Plant is grown on soil
- Apical meristem is placed on growth medium
- Older flowers are removed
- Imaged on a confocal

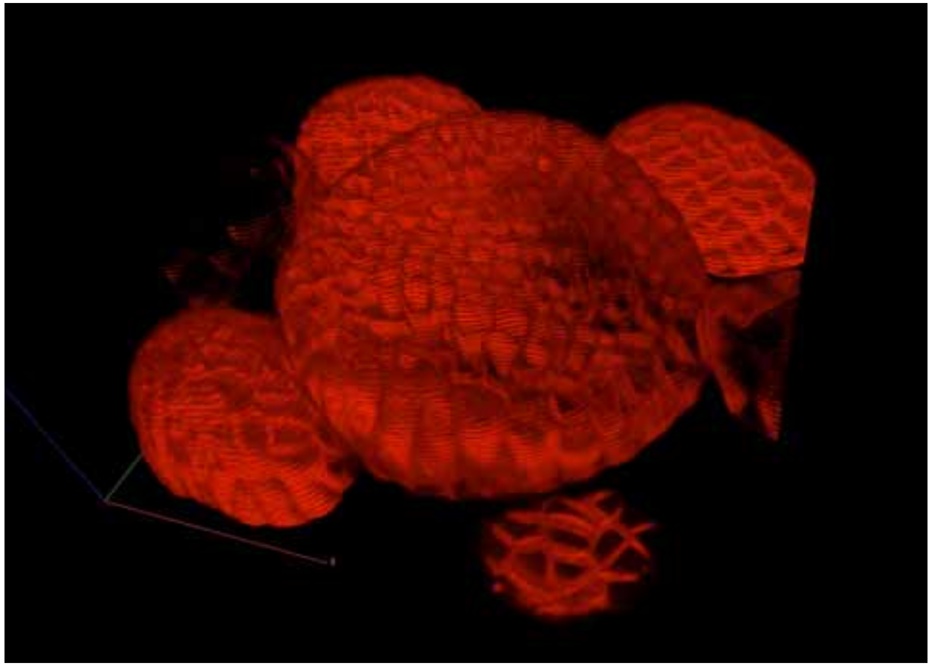




3D meristem reconstruction

3D restitution of a stack of images : a set of “voxels”

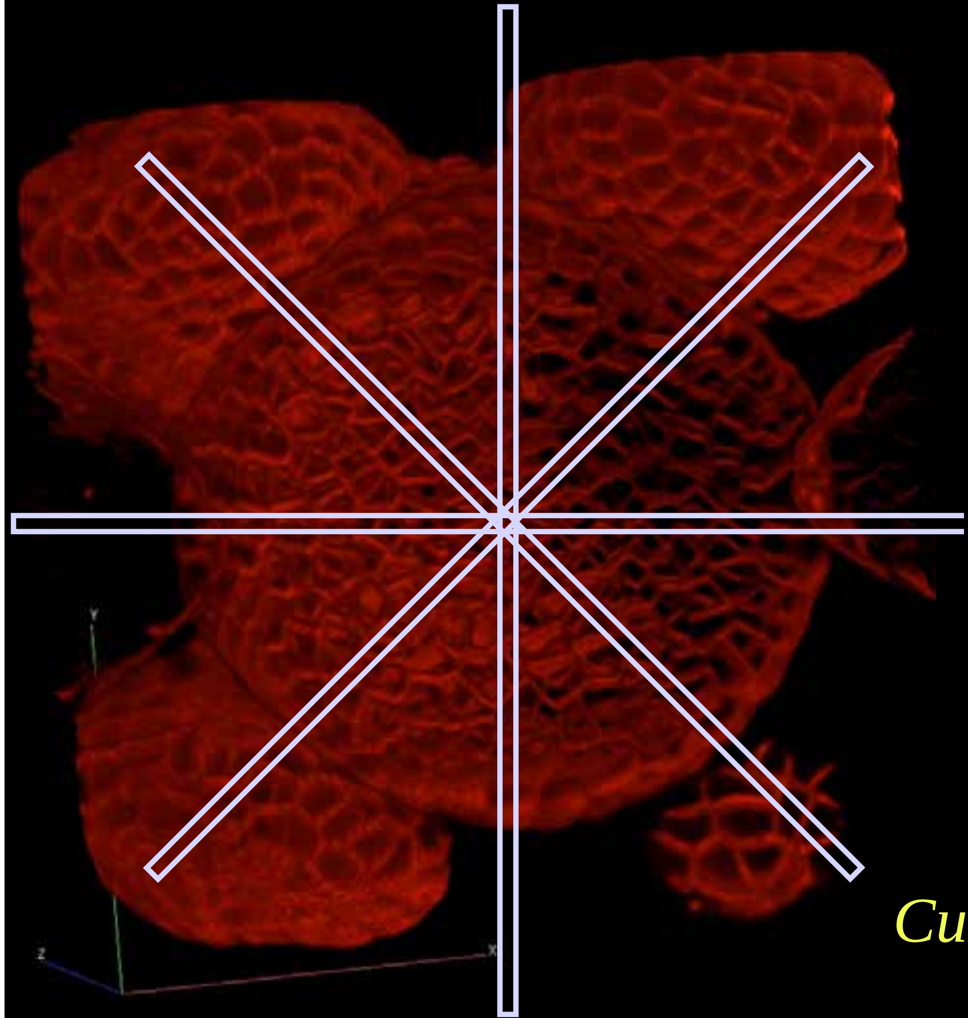




J. Traas (ENS-Lyon)

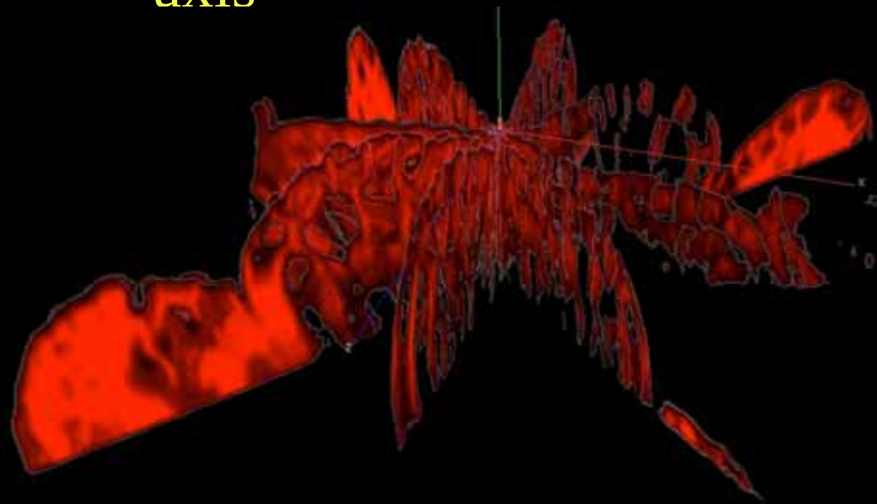
- *Automatic labelling of meristem cells*
- *Automatic identification of cell lineage*
- *Building a geometric model of the tissue*

Building a surface representation

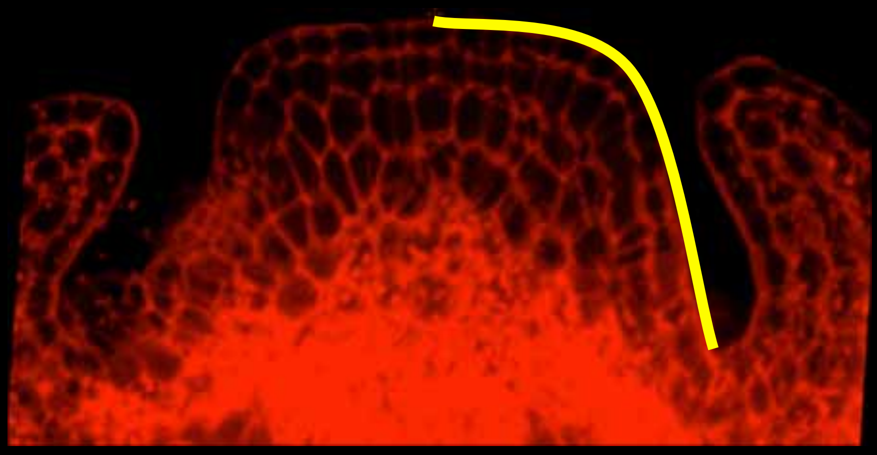


Cuts

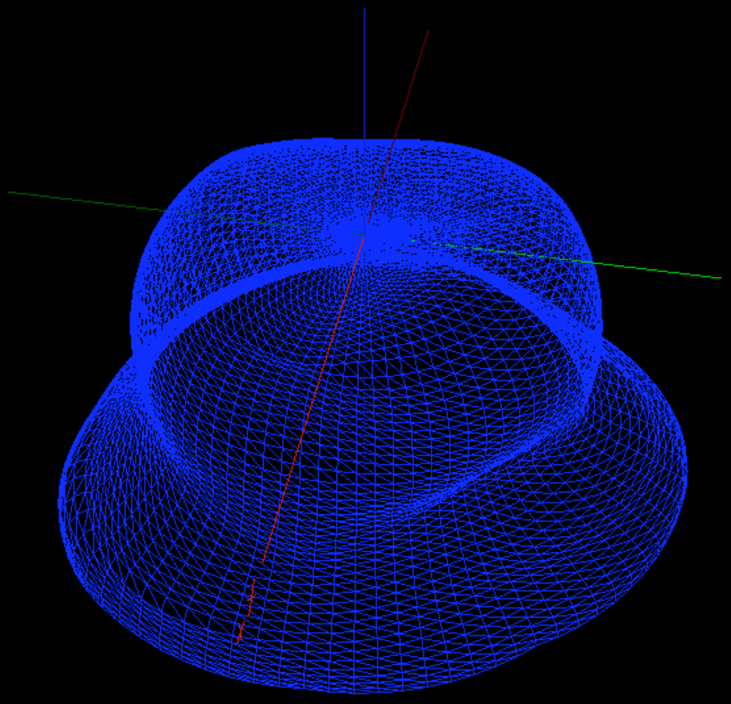
- Cuts along the vertical axis



Parametric model of the surface

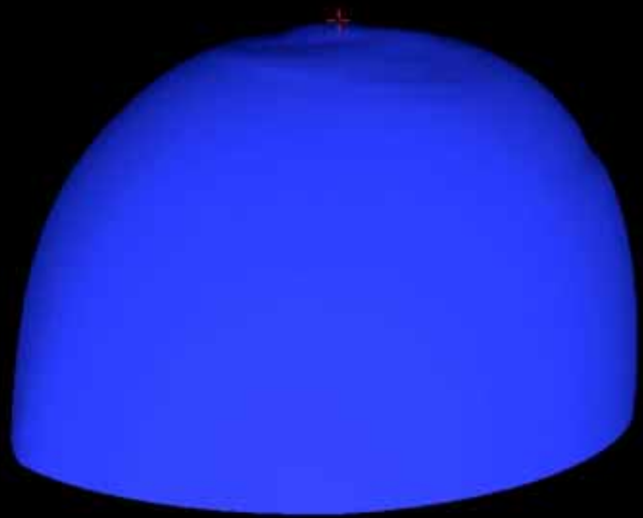


Parametric envelope of each cut



Swung Nurbs interpolated
from all vertical cuts

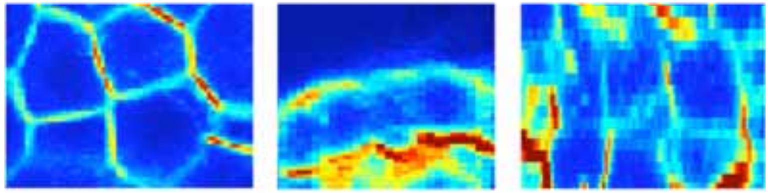
Carpel development first stages (1-7)
(Continuous model of the surface)

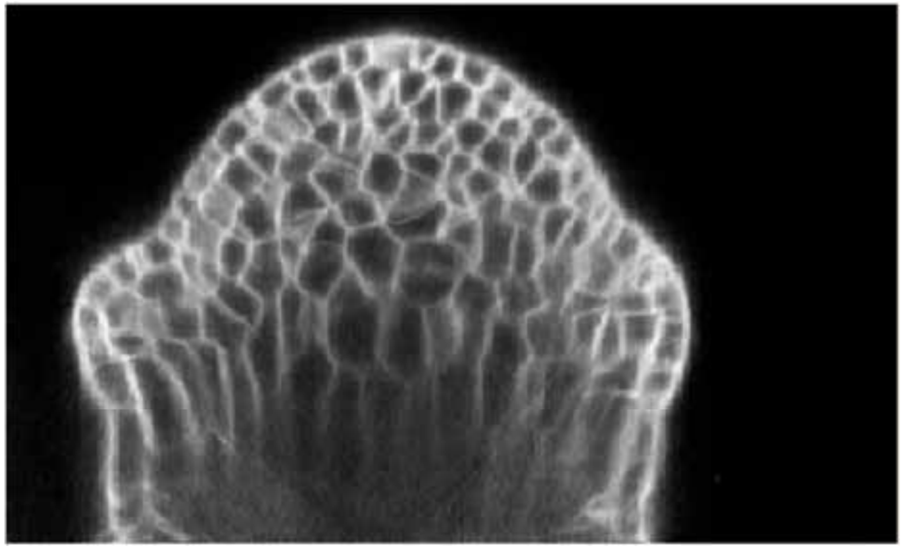


Automatic reconstruction at cell resolution

- 2 problems:
  - Microscope anisotropy
  - Tissue thickness

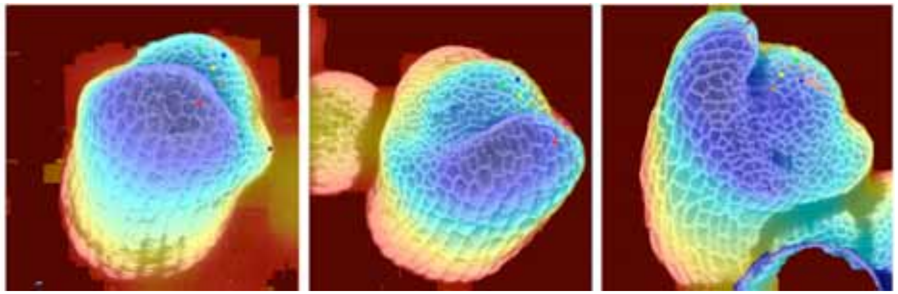
Romain Fernandez PhD programme





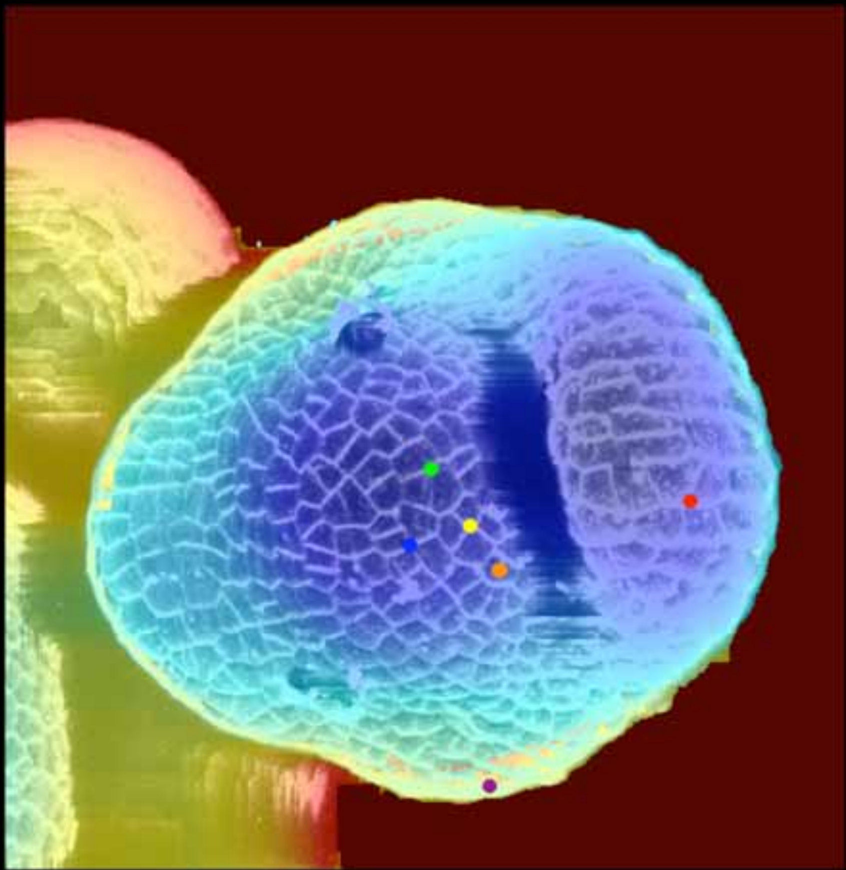
- Images taken from different angles

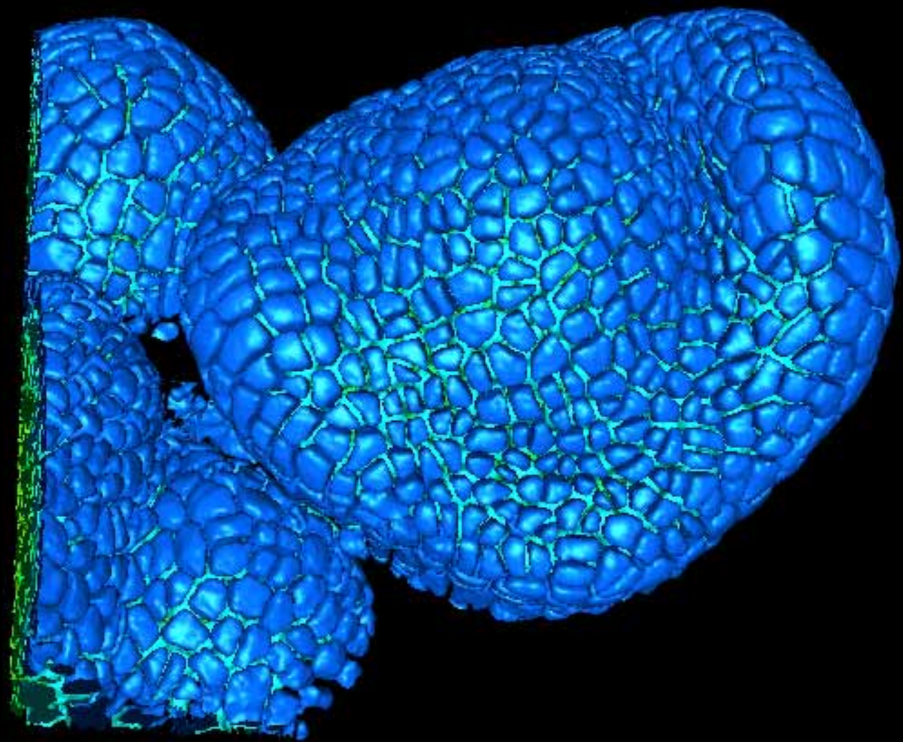
→ *Algorithms to merge the images*



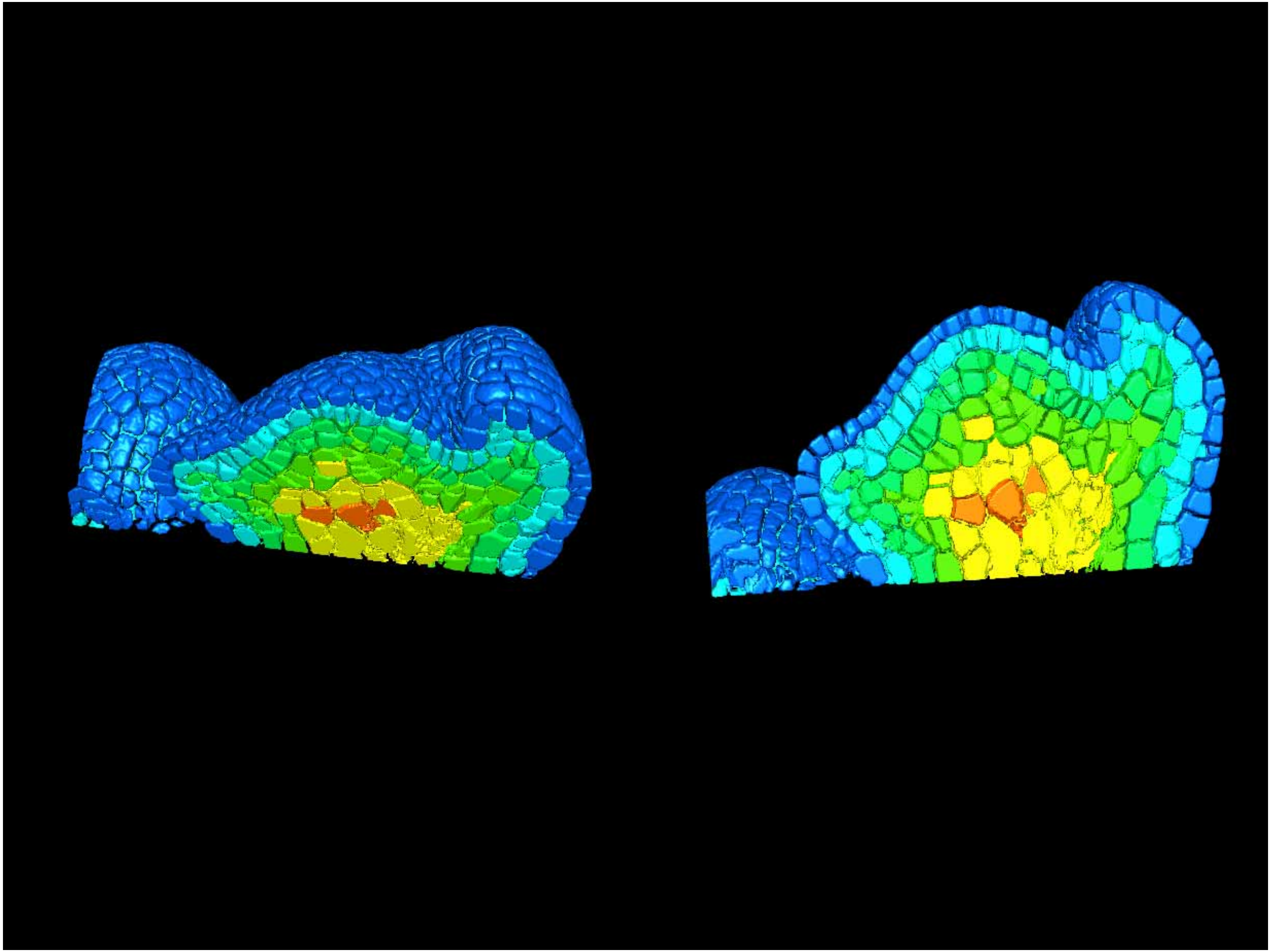
3D reconstruction of meristem

-3D registration
- watershed (with automatic seedling of cells)

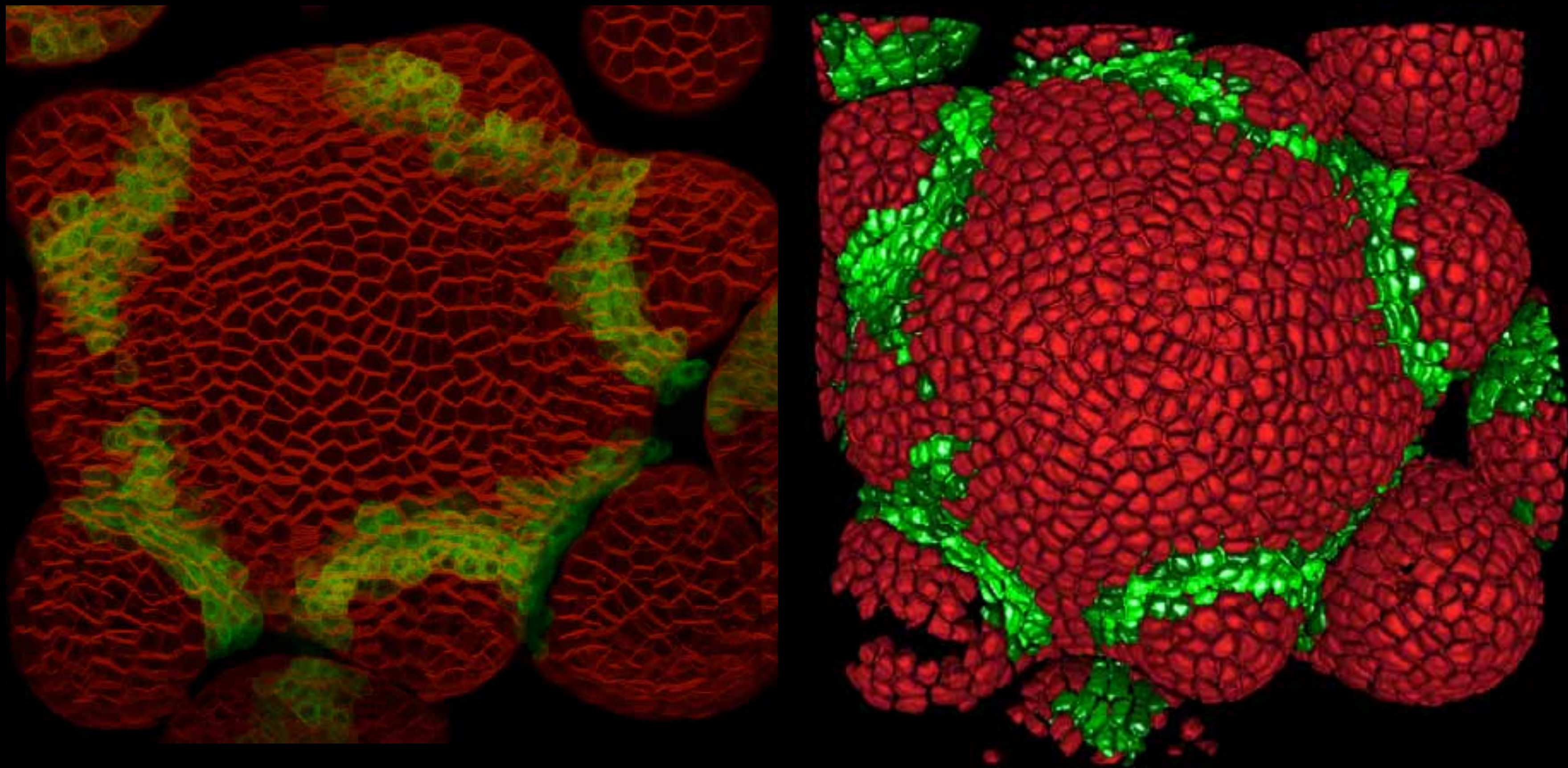




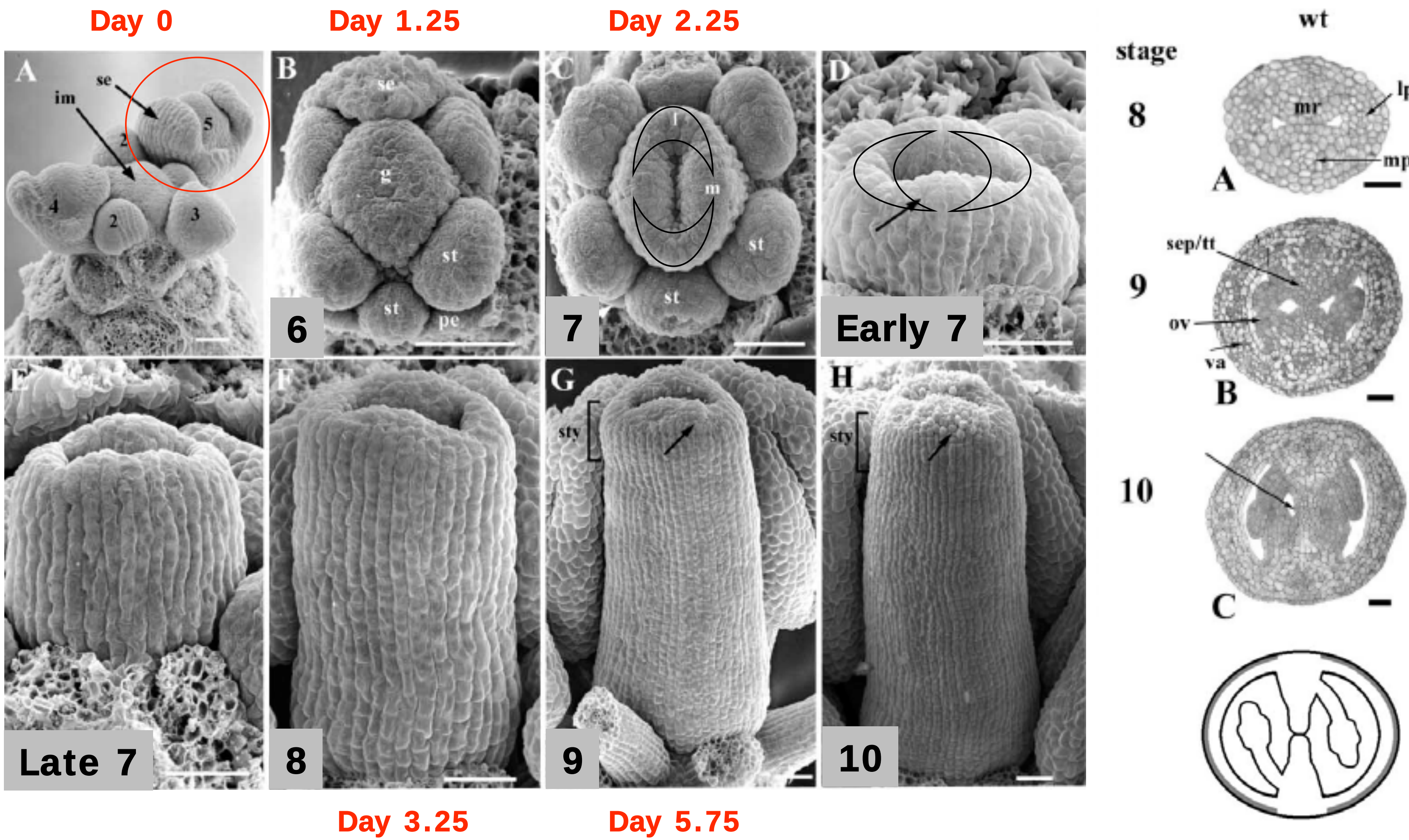
Collab. *EPI Asclepios (G. Malandain)*
Arabidopsis, ENS-Lyon (J. Traas, P. Das)



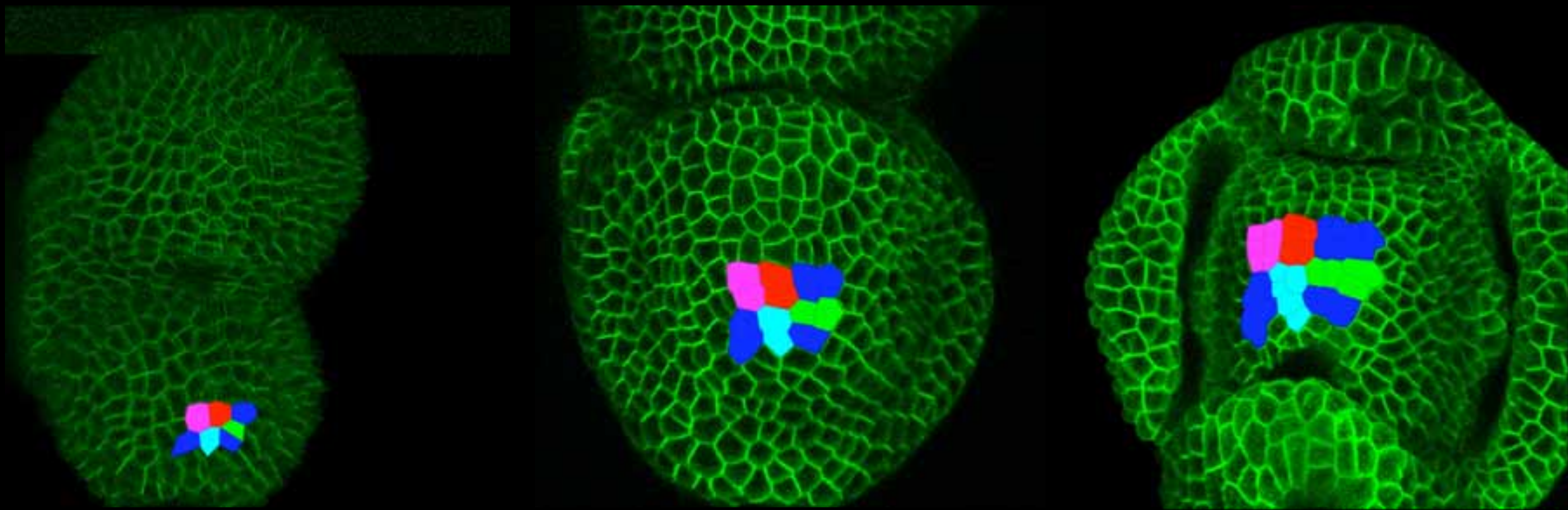
Extracting labelled cells (GFP)



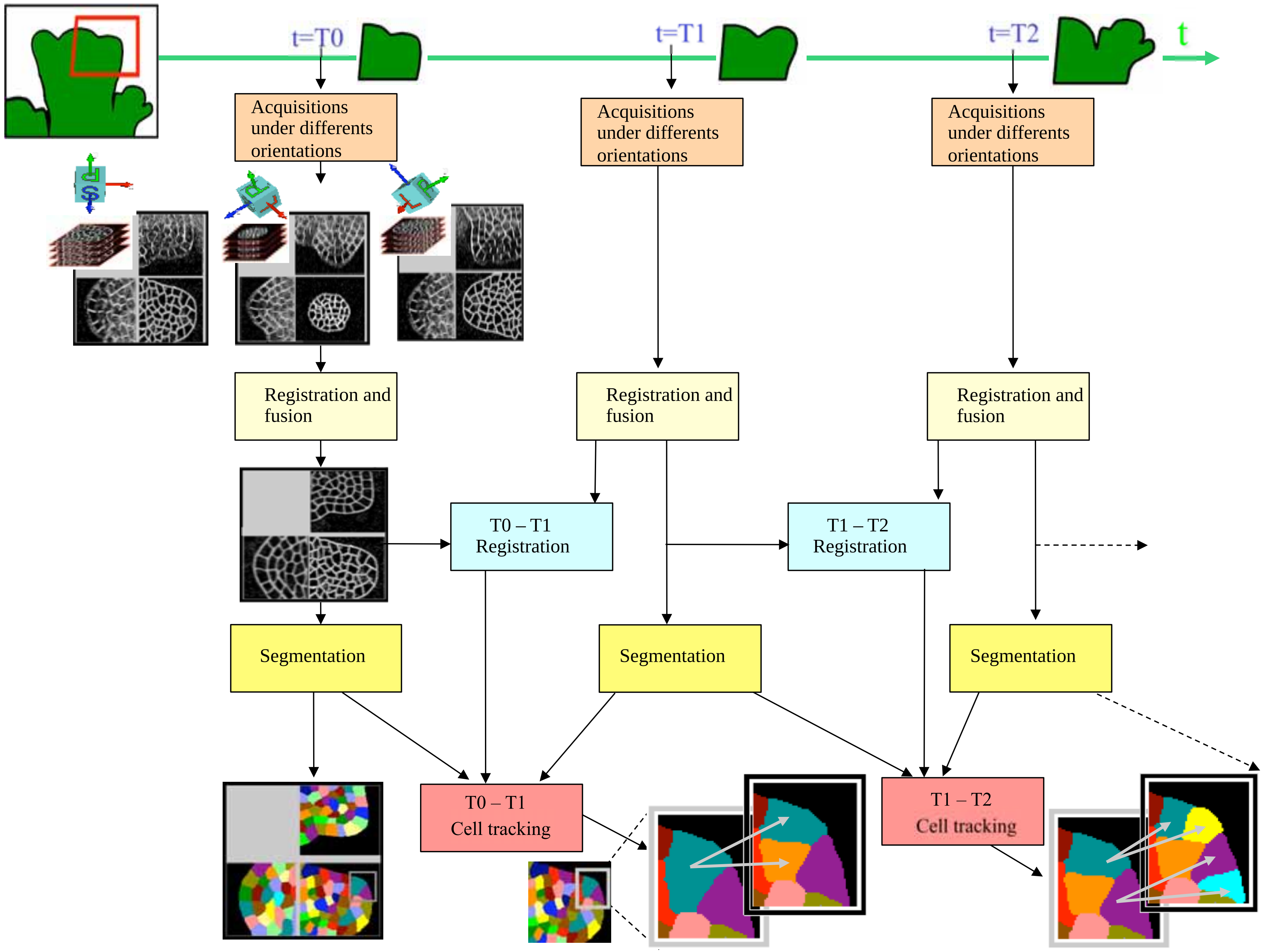
Quatification of shape development



Automatic segmentation and cell lineage

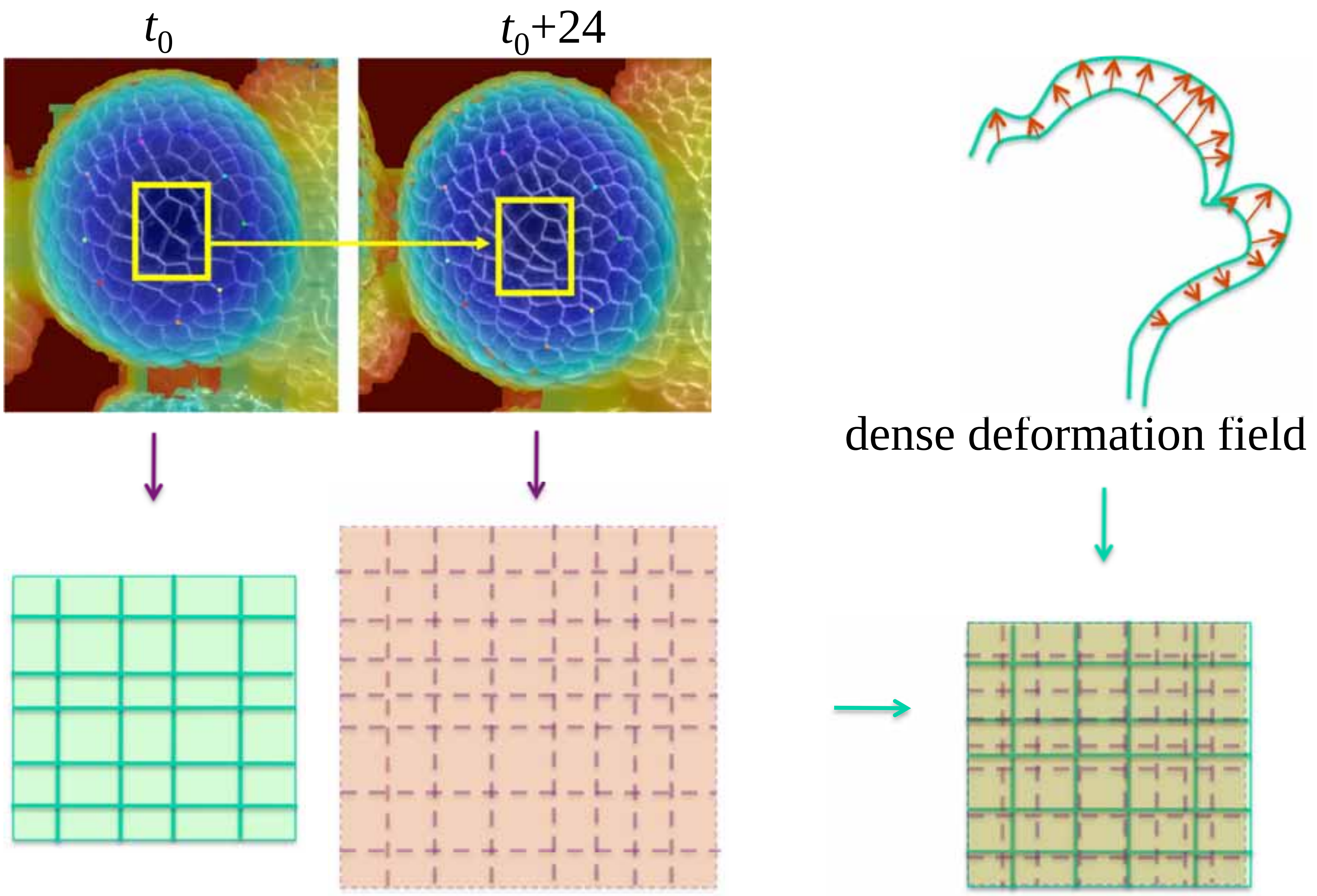


(PhD Work of Romain Fernandez)

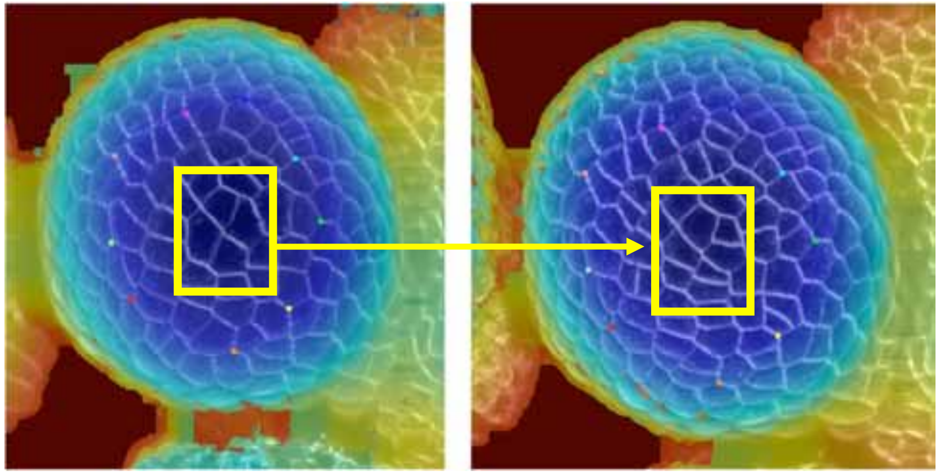


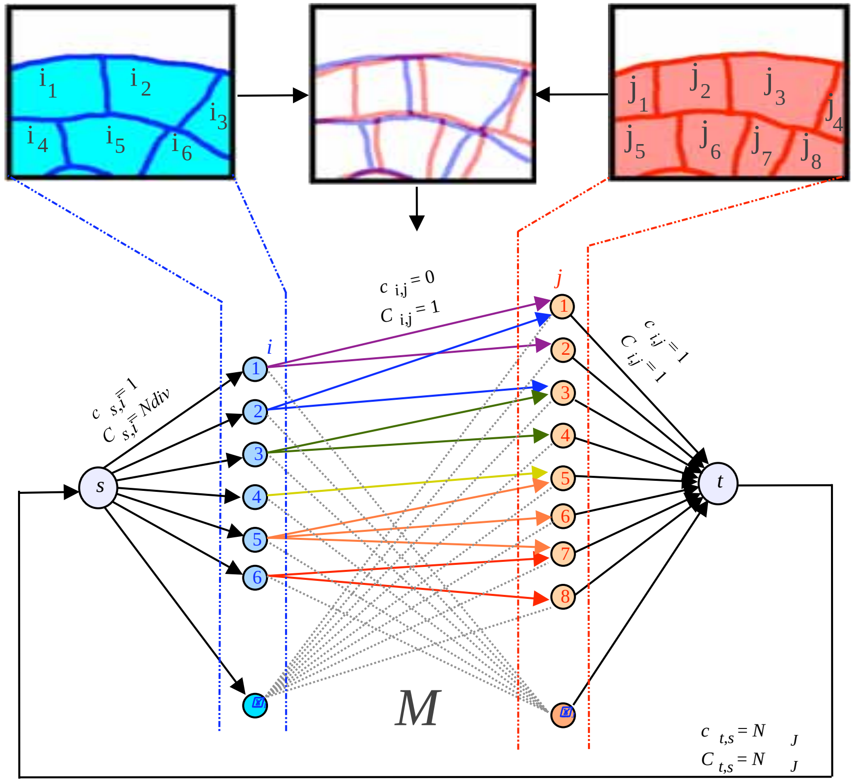
t=T0
t=T1
t=T2
t
Acquisitions under differents orientations
Acquisitions under differents orientations
Acquisitions under differents orientations
Registration and fusion
Registration and fusion
Registration and fusion
T0 – T1 Registration
T1 – T2 Registration
Segmentation
Segmentation
Segmentation
T0 – T1 Cell tracking
T1 – T2 Cell tracking

Automatic detection of cell lineage



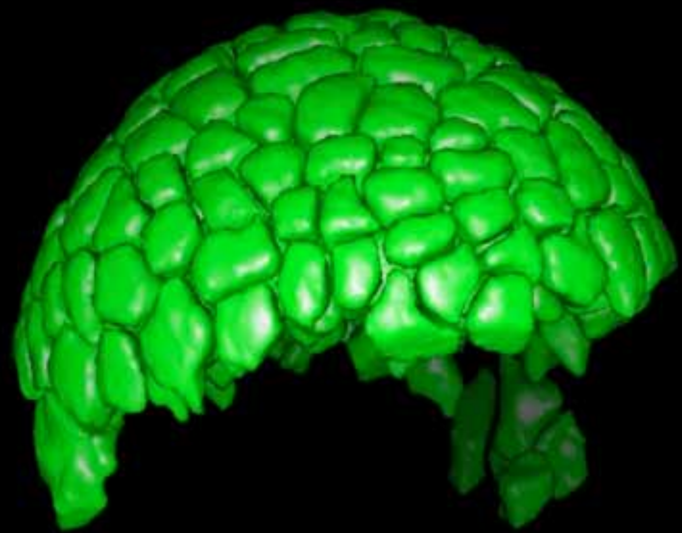
Automatic detection of cell lineage





$$\Gamma(M) = \sum_{M} \gamma_{ij} + \sum_{\bar{I}_M} \gamma_I + \sum_{\bar{J}_M} \gamma_J$$

$$M^* = \underset{M\ valid}{\arg\min}\, \Gamma(M)$$

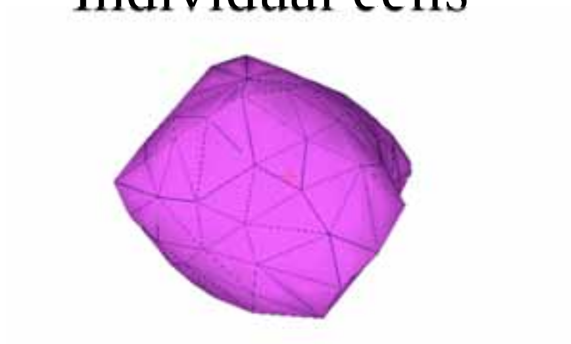


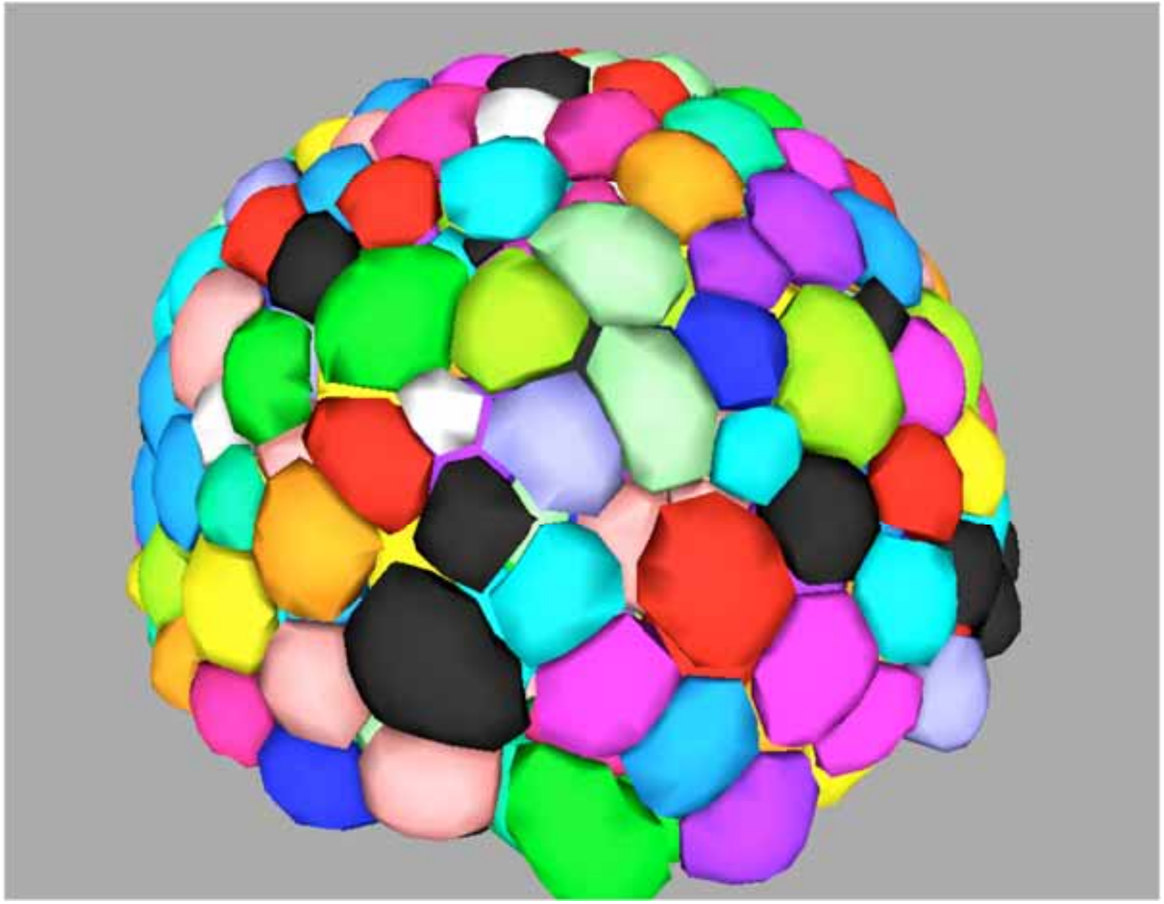
PhD Romain Fernandez (col. Asclepios INRIA, ENS-Lyon, CIRAD-DAP)

Building mesh representations from segmented images

(J. Chopard, R Fernandez)

Individual cells

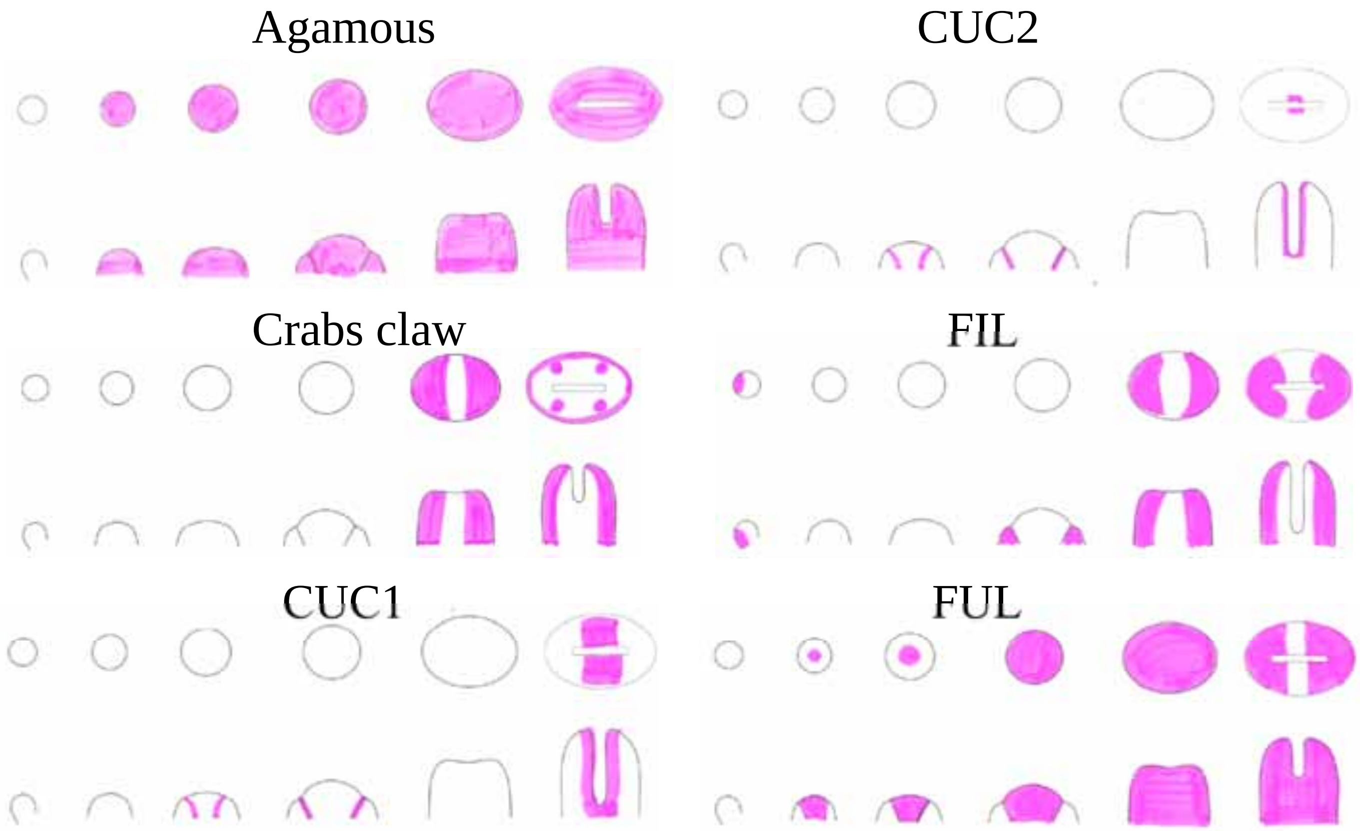




Reconstructed 3D mesh

Building virtual maps

immunolabelling



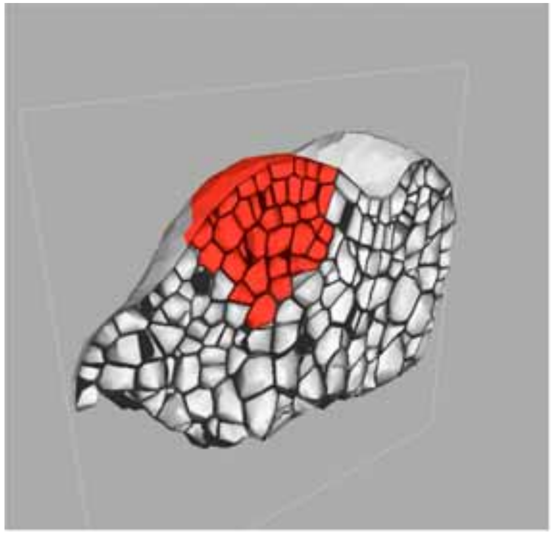
• • •

Coll. ENS-Lyon (J. Traas, F Monéger)

Definition of a querying language

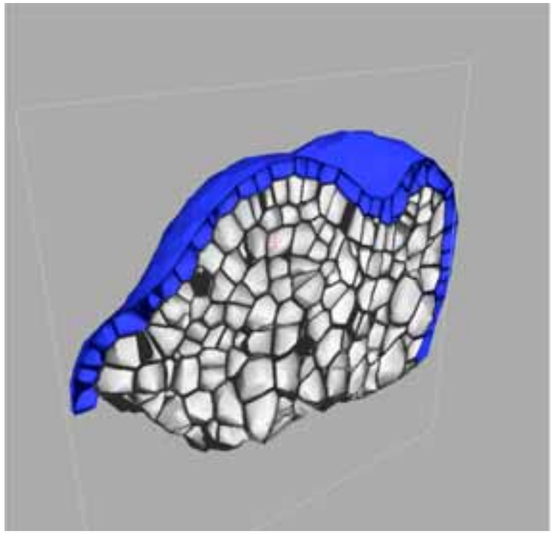
(J. Chopard)

Definition of zones:



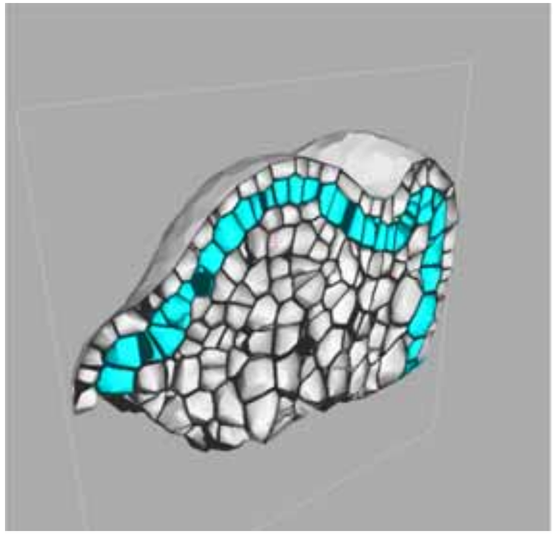
Geometry:

CZ = Sphere(« top »,
(4, « cells »))



Fixed:

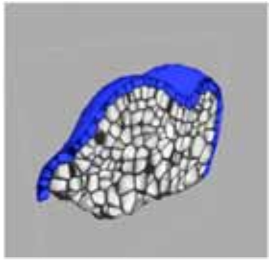
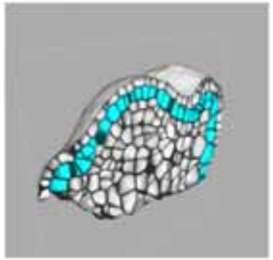
L1 = [cell1, …, cellN]



Topology:

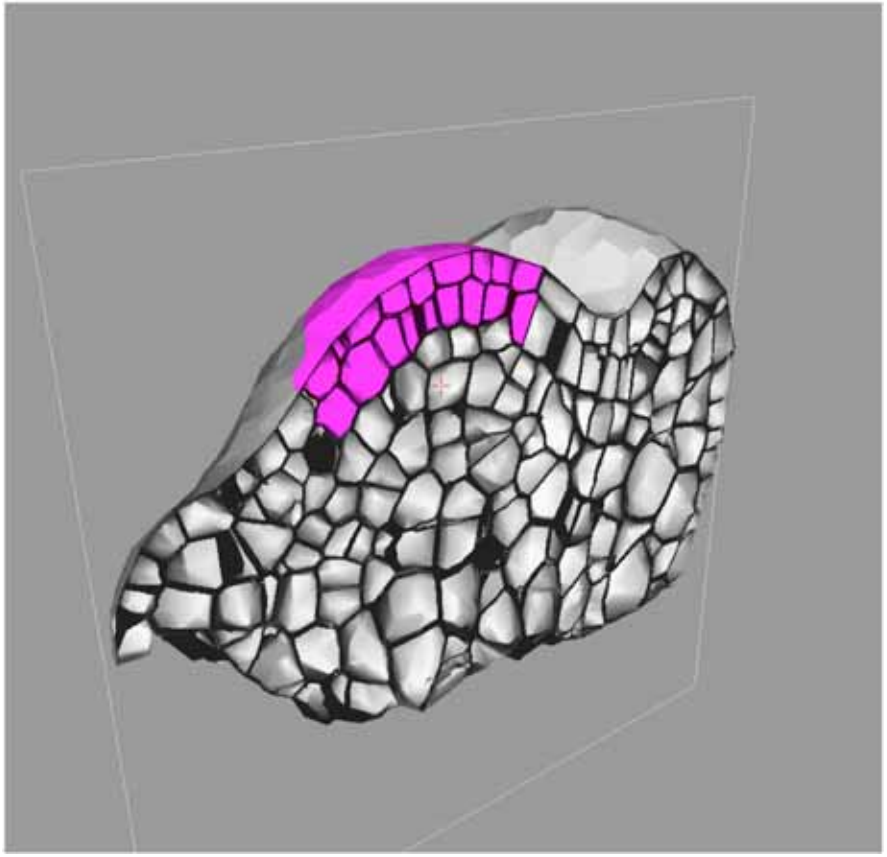
L2 =
Expand(L1) – L1

Pattern definition

 & ( + )

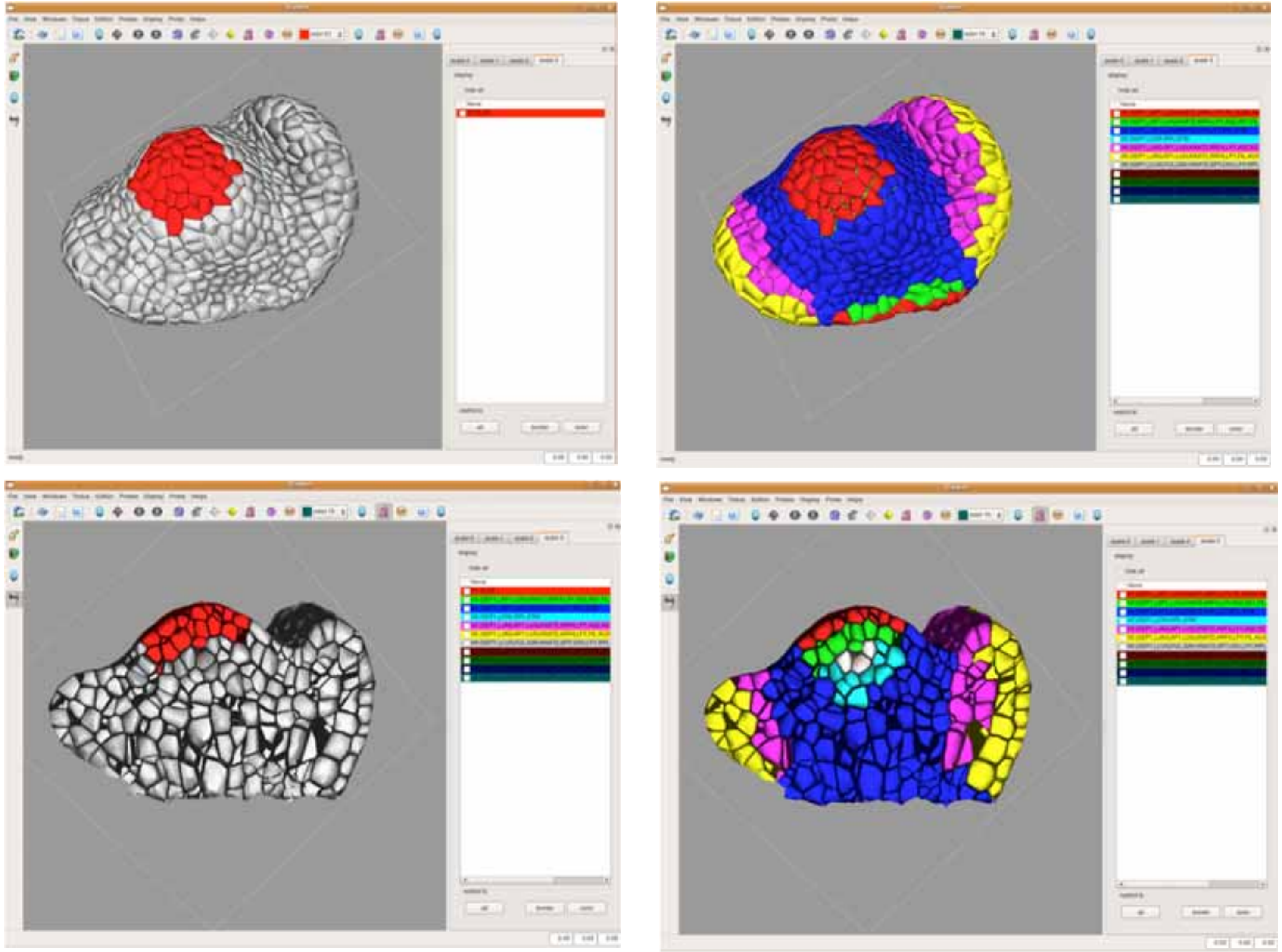
Python code:

```
def pattern_CLV3 (stade) :
    if stade == 3 :
        return CZ & (L1 + L2)
```



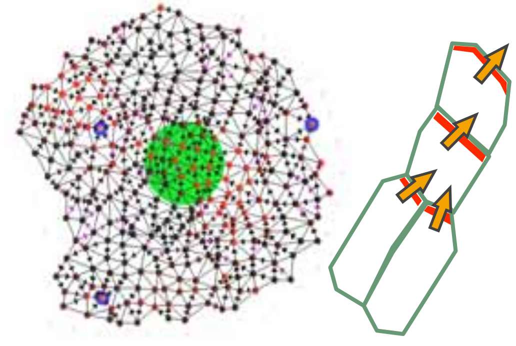
Building virtual maps (atlases)

Post-doc J. Chopard

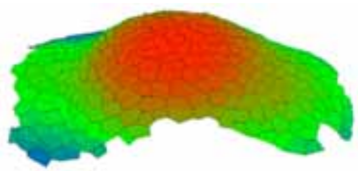


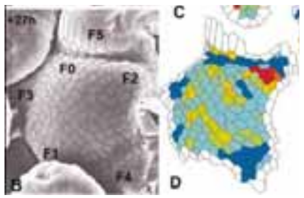
Building of a virtual meristem

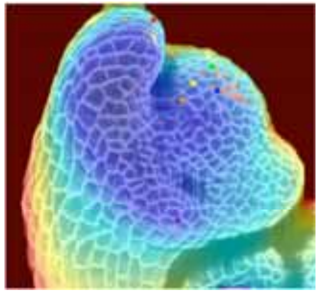
2 – Transport model



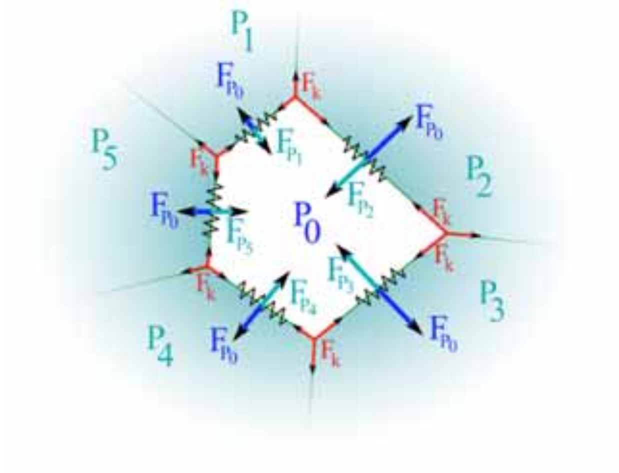
1 – Geometric model





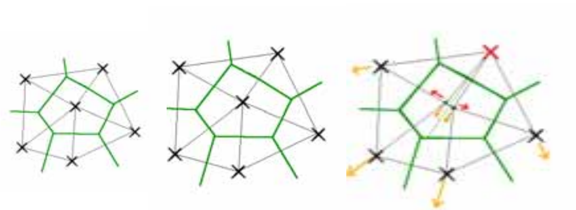


3 – Physical model

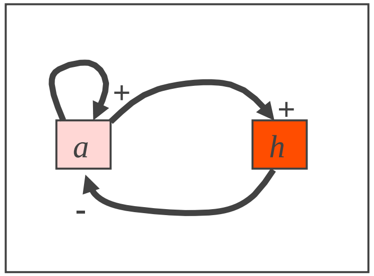


4 – Cell model

Division and Growth



Interaction network



Organ phyllotaxy at the SAM

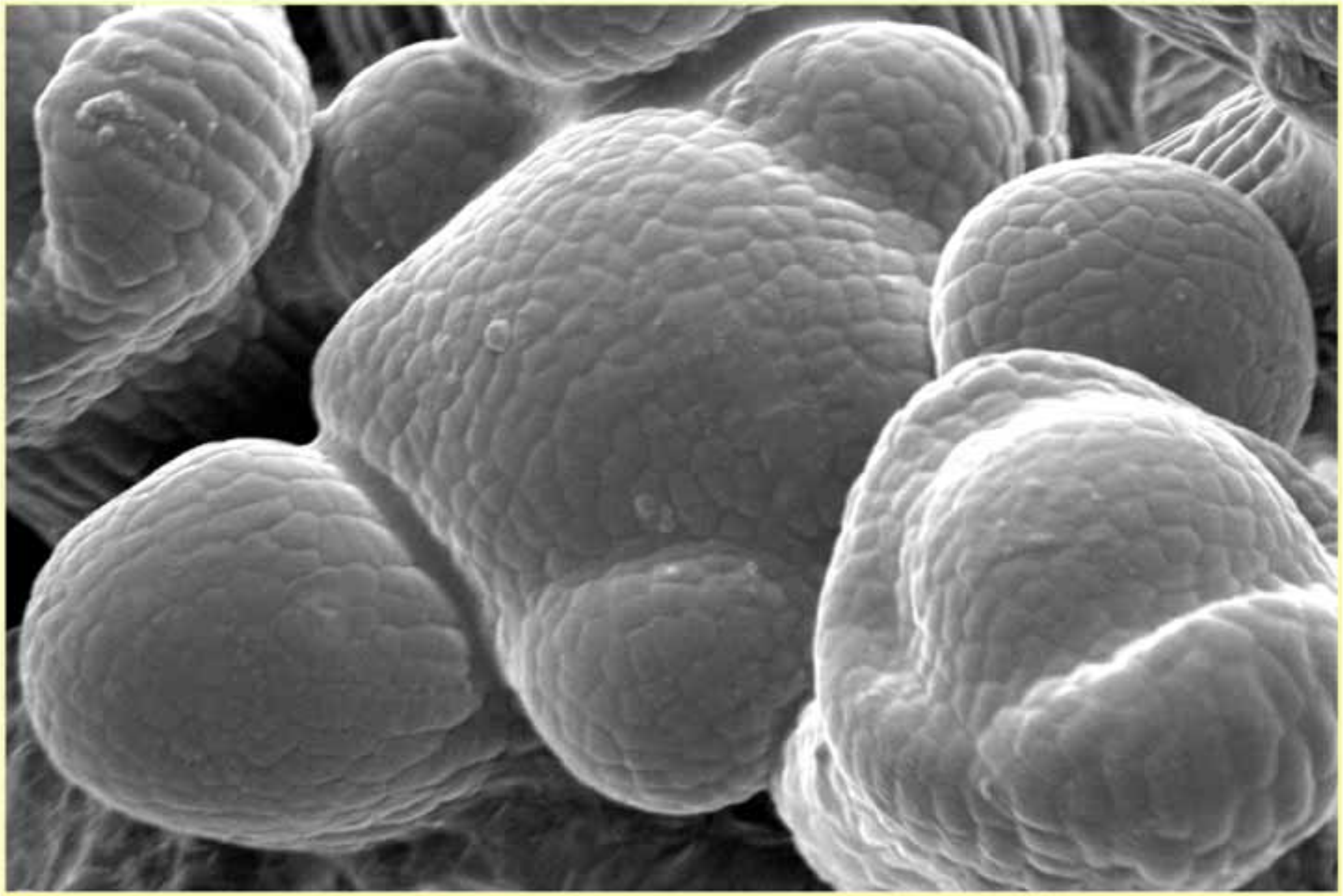
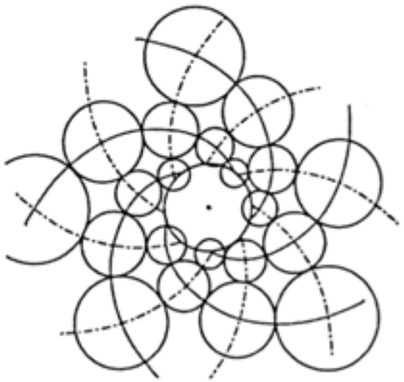


Photo: Jan Traas

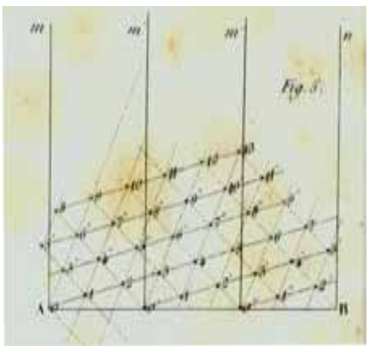
Phyllotaxis models

- Three kinds of approaches

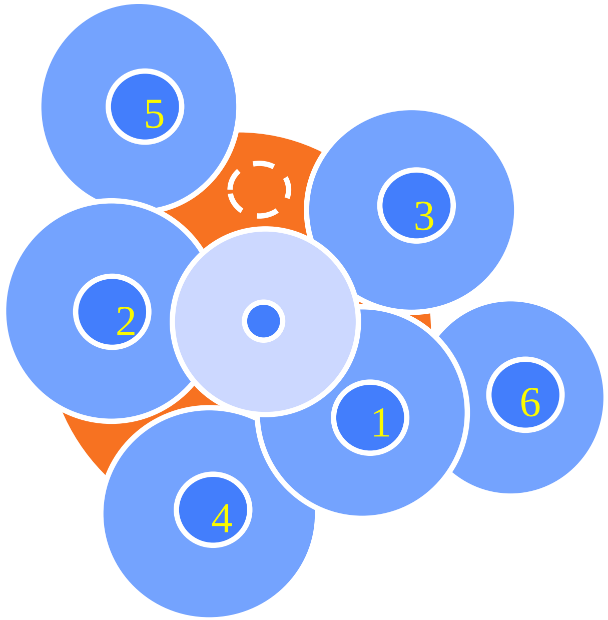
Geometrical



(Bravais & Bravais,1837)



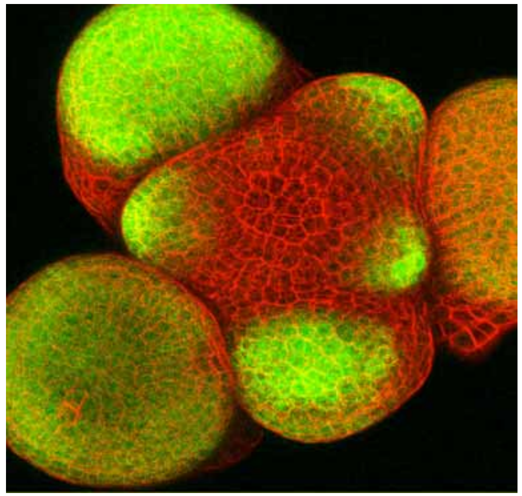
Dynamical



(Hofmeister, 1868)

(Snow and Snow, 1962)

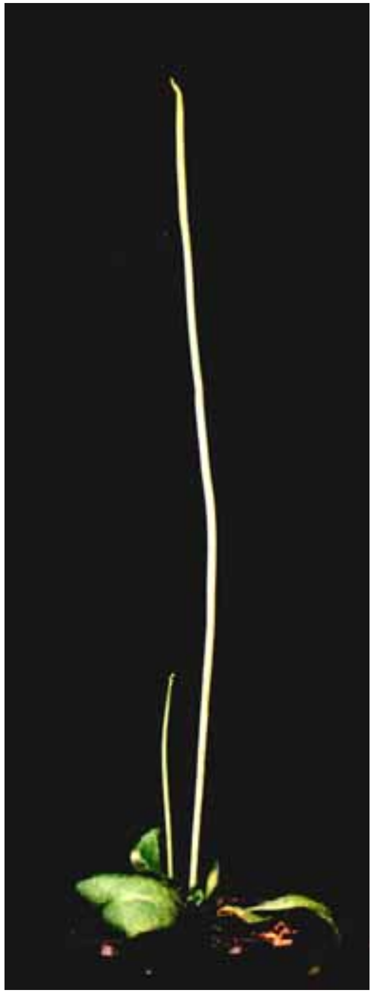
Physiological



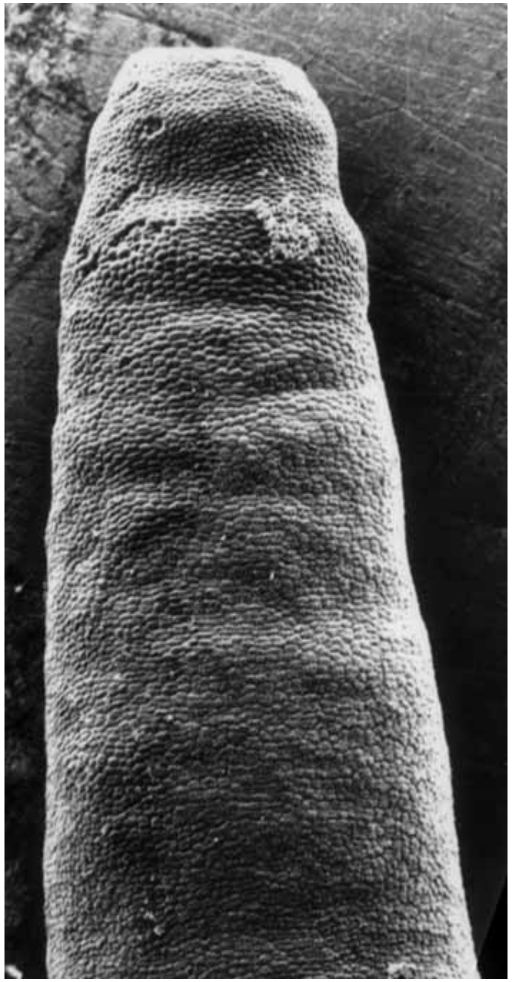
Auxin transport perturbation

Perturbed auxin transport is correlated with perturbed organ formation in the *pin-formed1* mutant

wild type
of *Arabidopsis*

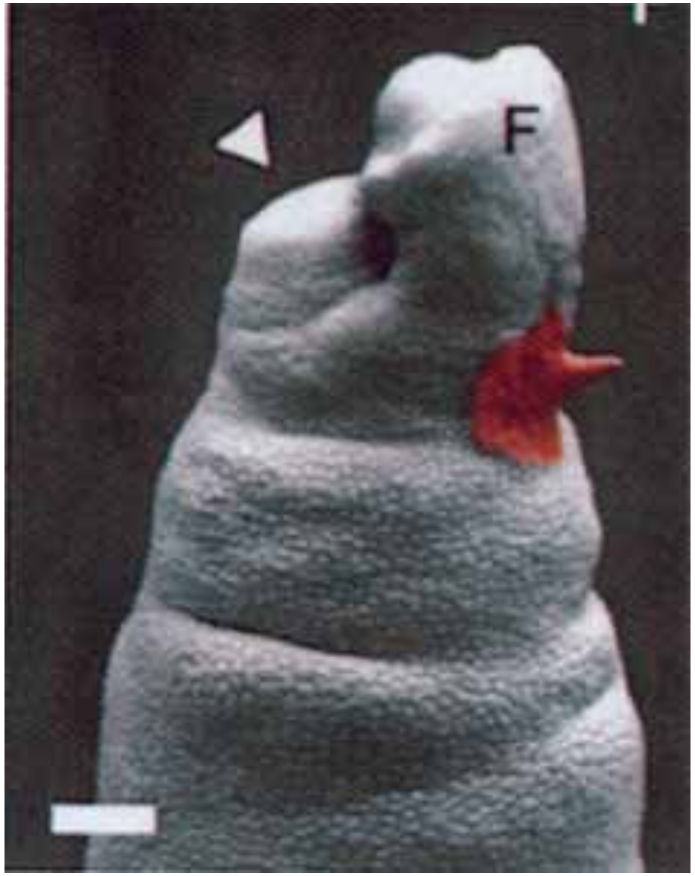


pin 1



pin 1

The local application of auxin induces organ formation in pin1

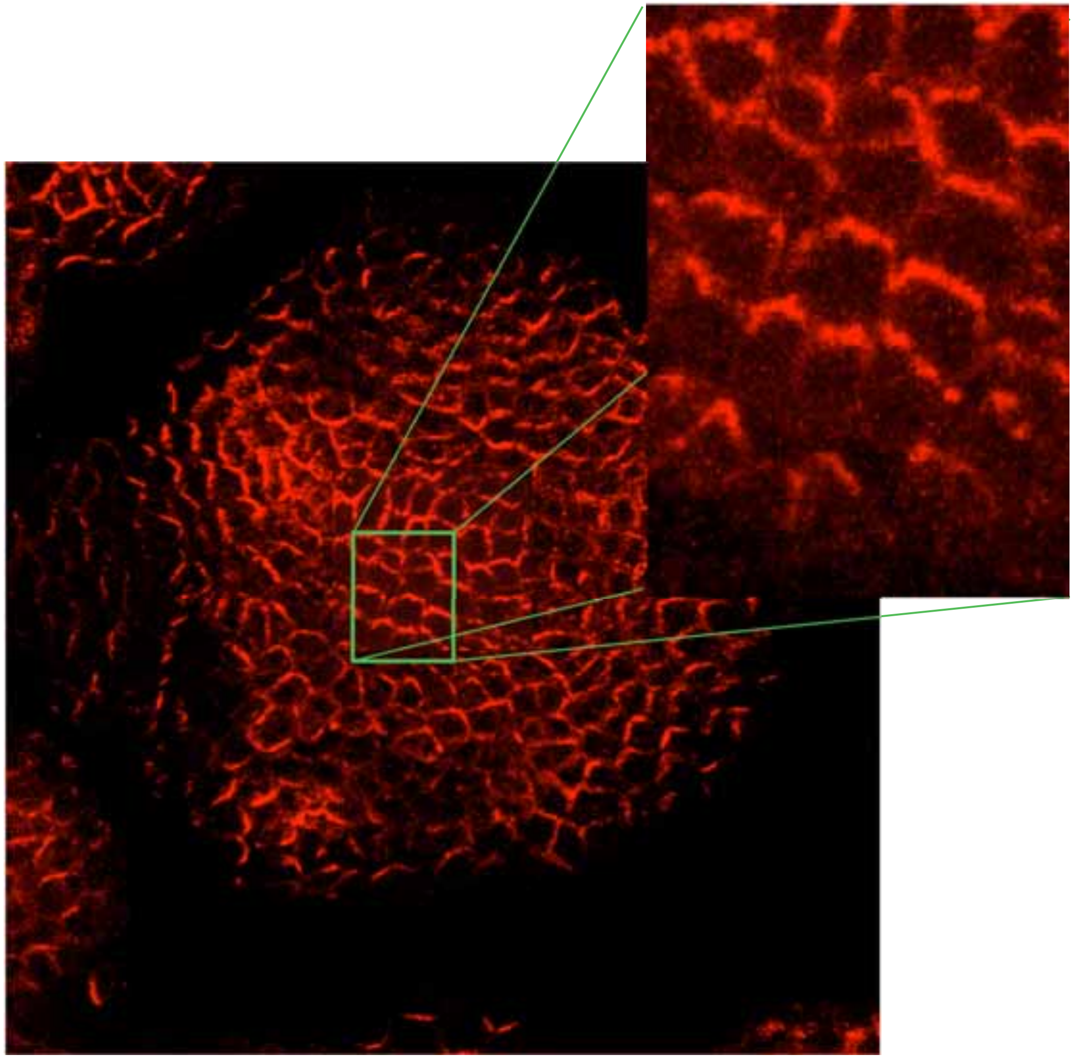


(Reinhardt et al. 2000)

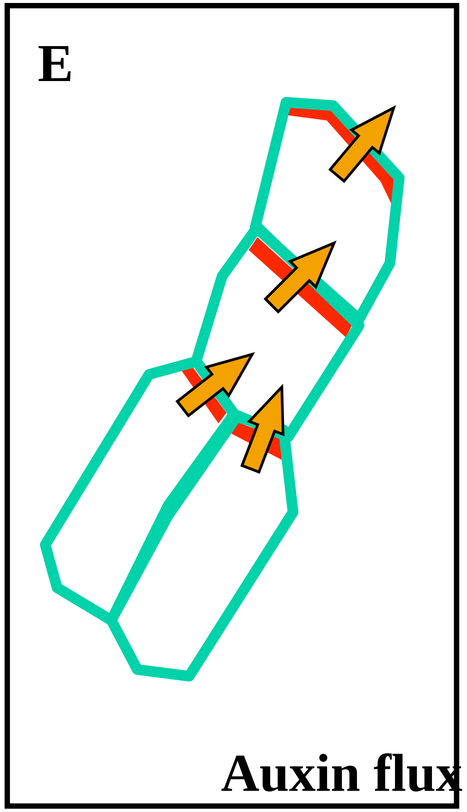
High concentrations of auxin induce organ initiation

Active transport of Auxin

The PIN-FORMED1 protein (PIN1) is an efflux carrier

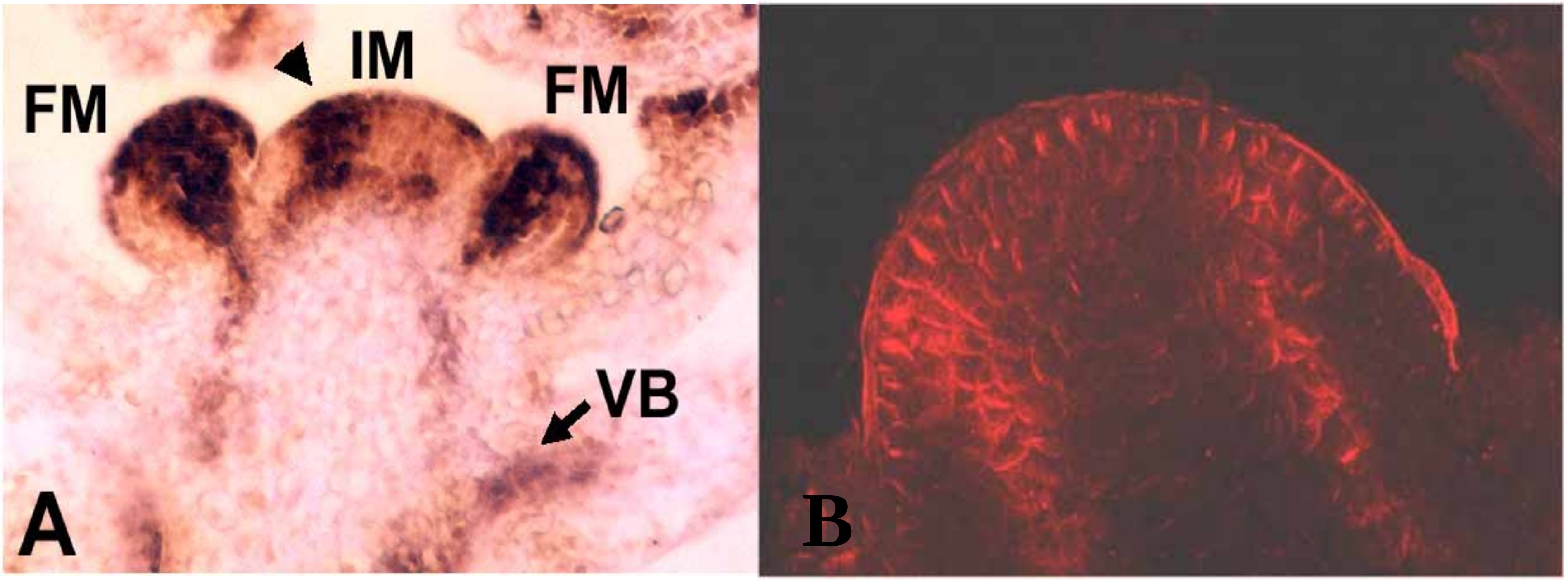


Immunolabelling of
PIN1 protein



(Gälweiler et al. 1998)
(Steinmann et al. 1999)

Expression pattern and protein distribution of PIN1



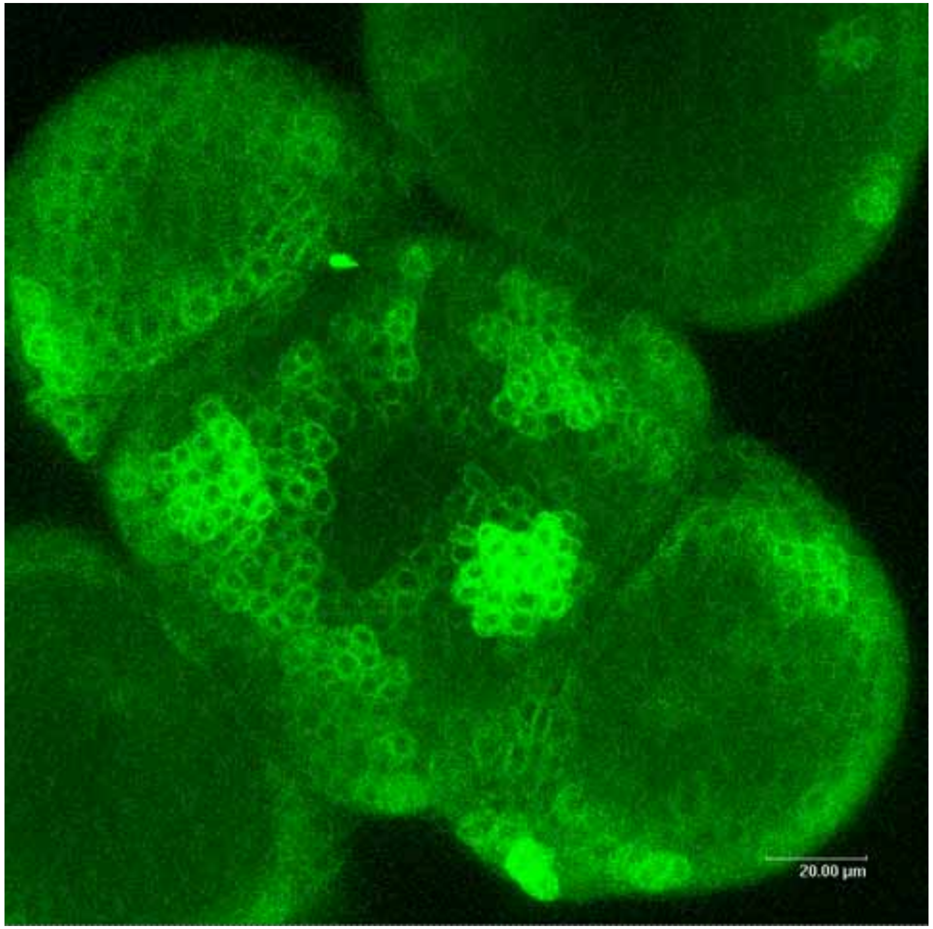
mRNA (Vernoux et al. 2000)

PIN1 antibody (anti-peptide) (Traas)

PIN1 is present in the L1 layer throughout the meristem and in the (pro)vascular strands of the young primordia

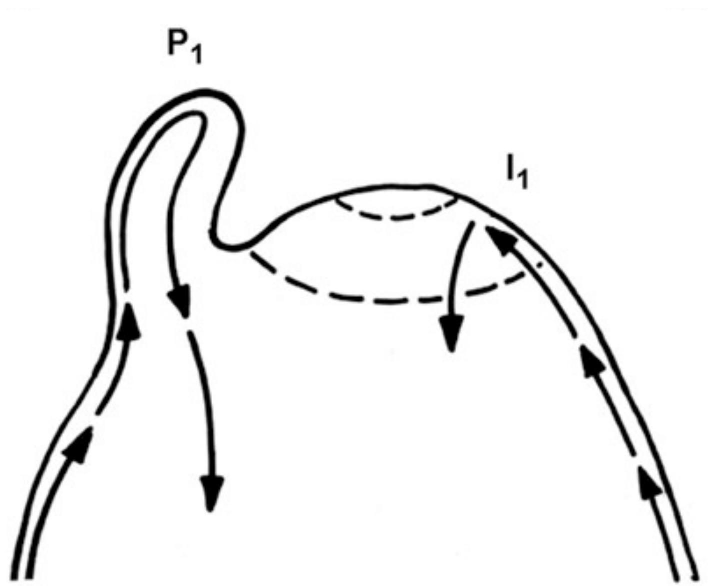
Indirect sensing of auxin by DR5::GFP

Promoter activated by auxin responsive transcription factors



Bright green : DR5::GFP

Qualitative model of auxin transport at the SAM

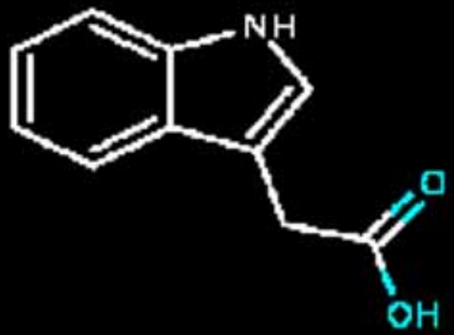


(Reinhardt et al. 2003)

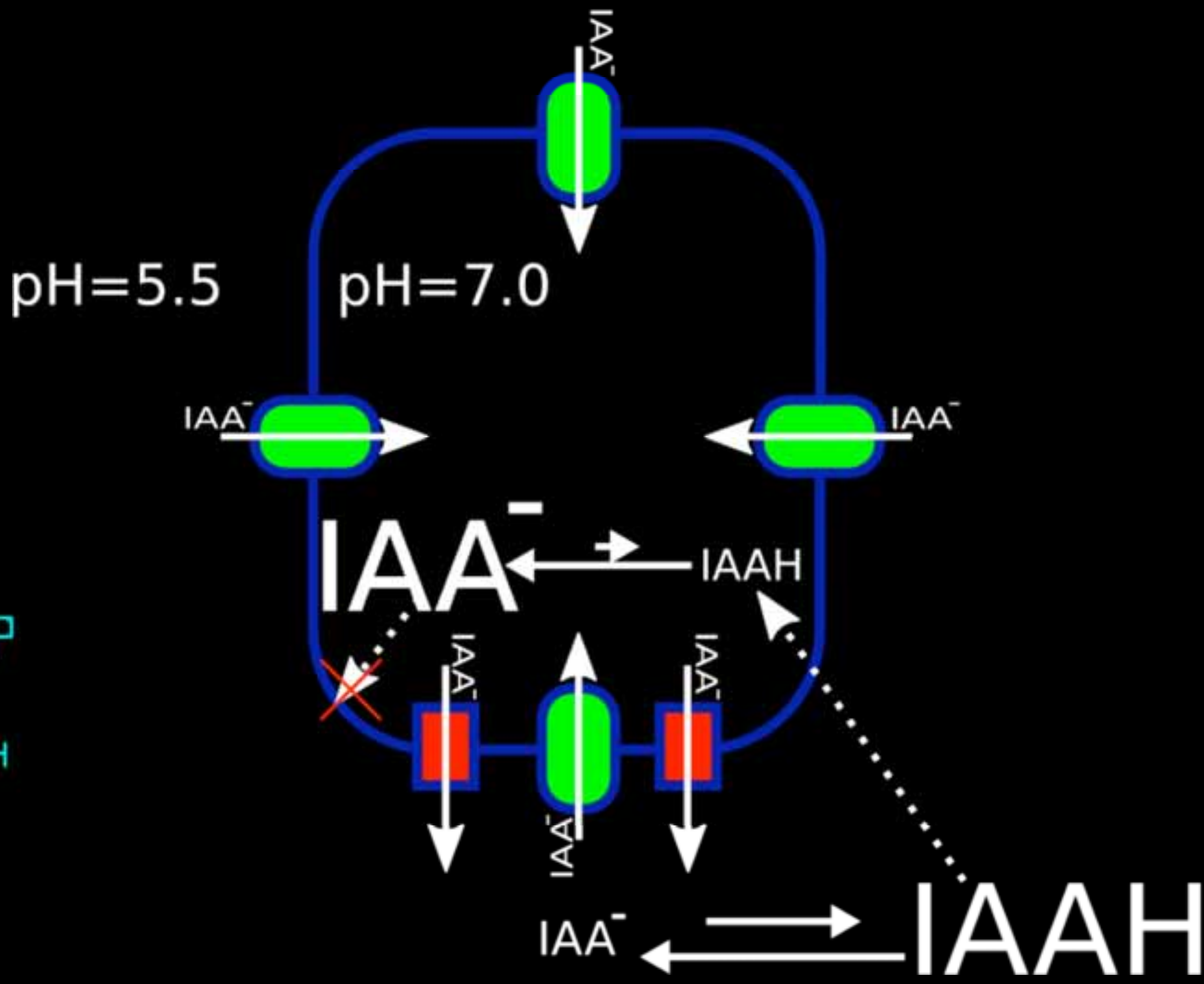
Chemosmotic model of auxin transport

AUX

PIN

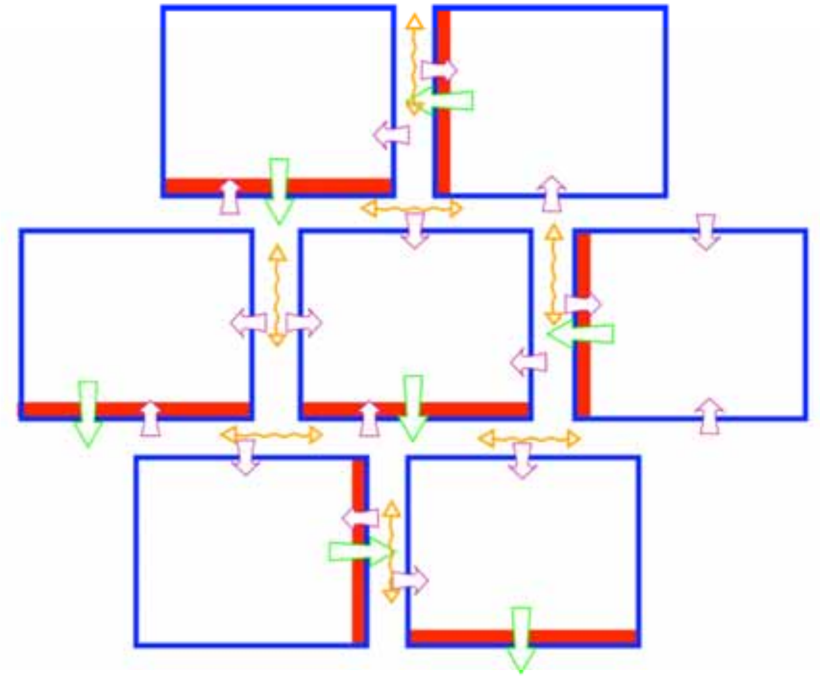


AUXIN: Indole-3-acetic-acid (IAA)

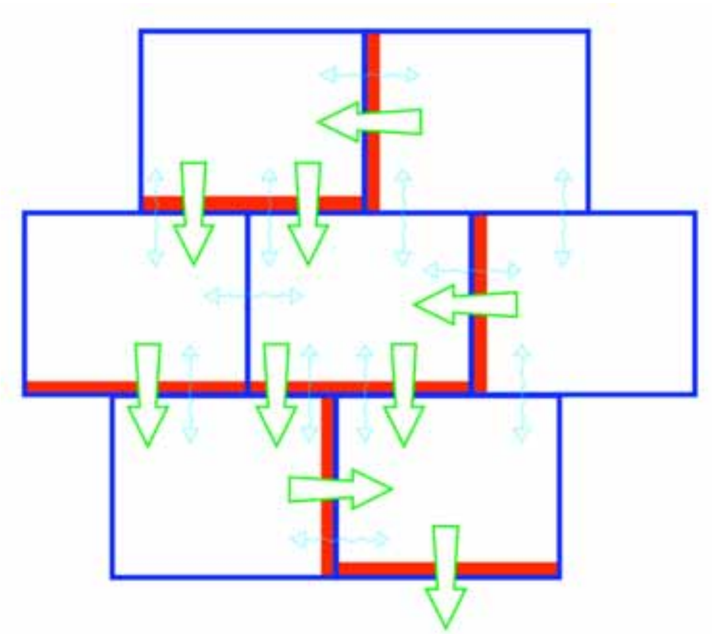


Simplified model of auxin transport

- No AUX/LAX influx transporter
- No apoplastic compartment



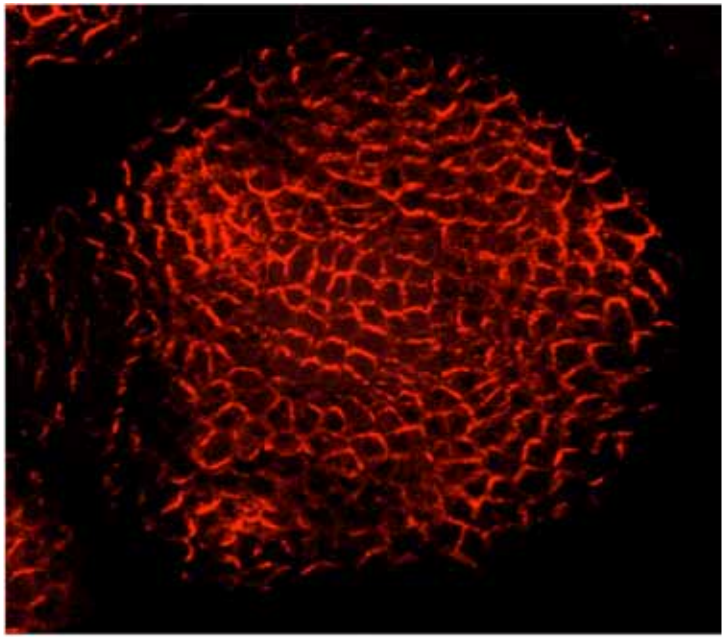
Chemosmotic transport model



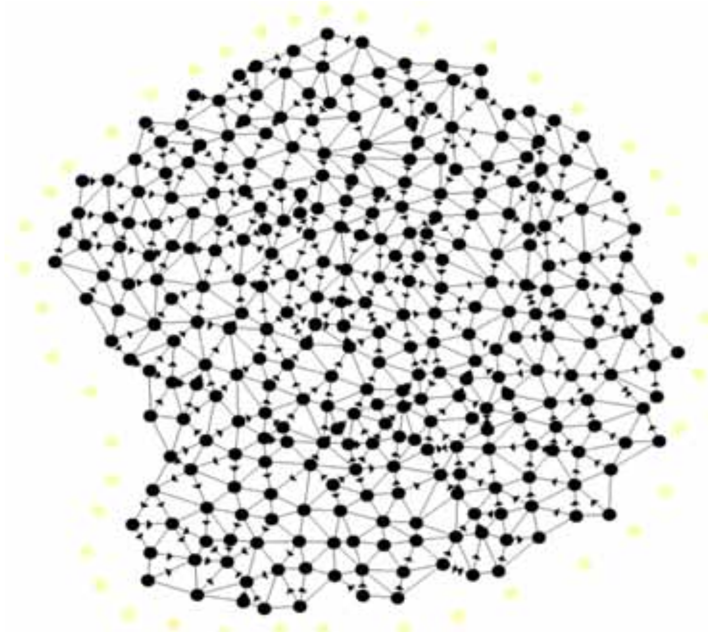
Simplified transport model

Modelling auxin transport at the SAM

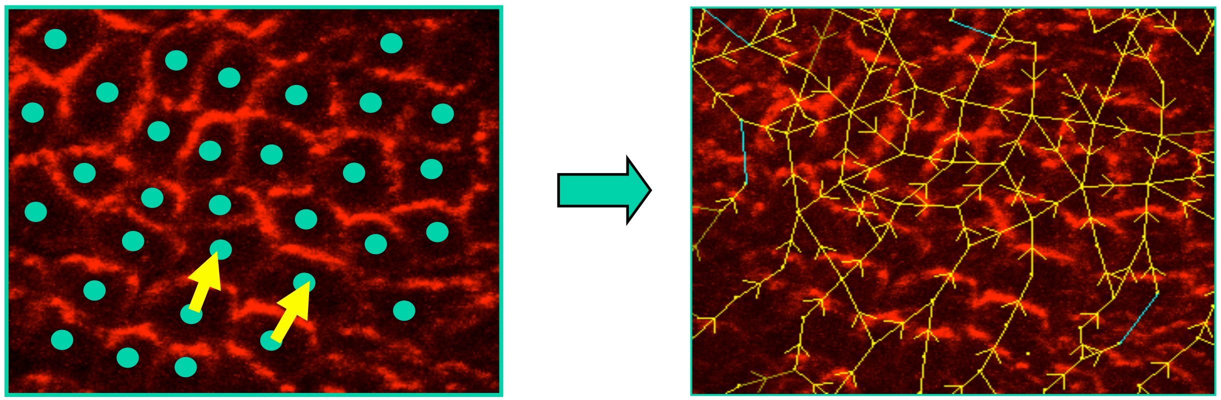
(Barbier de Reuille, PNAS, 2006)



Original image

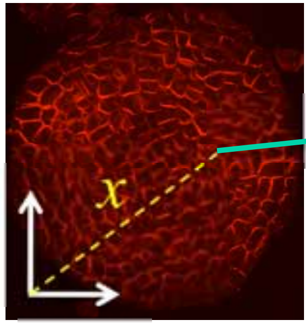


Network of “pumps”



Modeling transport

Description of the spatial variation of a quantity u(x,t):



$u(x,t)$?

Local conservation equation:

Change in local **concentration** per unit time	=	Rate of local **creation**	-	Rate of **destruction**	+	Rate of **net exchange** with environment

$$\frac{\partial u(x,t)}{\partial t} = \delta - \gamma u(x,t) + f(x,y,t)_{y \in V(x)}$$

(*Partial Differential Equation, PDE*)

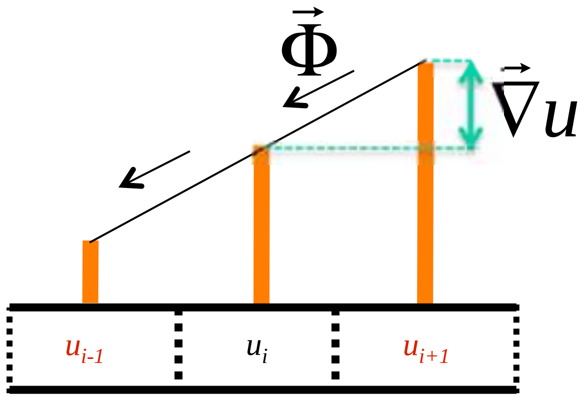
Diffusion equation

Flux:

$\vec{\Phi}(x,t)$ # particles crossing a unit area at *x* per unit time

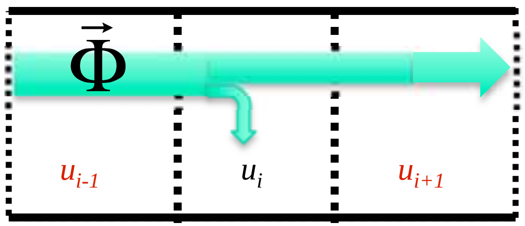
Fick's law (eg. Heat, Osmotic diffusion):

$$\vec{\Phi}(x,t) = -\alpha \frac{\partial u(x,t)}{\partial x} = -\alpha\, \vec{\nabla} u$$



Conservation equation:

local variation of concentration = spatial variation of flux



$$\frac{\partial u}{\partial t} = -\frac{\partial \Phi}{\partial x}$$

$$= -\frac{\partial}{\partial x}\left(-\alpha \frac{\partial u}{\partial x}\right) = \alpha \frac{\partial^2 u}{\partial x^2} = \alpha\, \Delta u$$

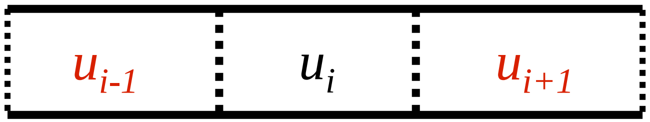
Diffusion: passive transport

Diffusion equation

$$\frac{\partial u}{\partial t} = \alpha \, \Delta u$$

Geometric interpretation :

1 dimension: $\dfrac{\partial u}{\partial t} = \alpha \dfrac{\partial^2 u}{\partial x^2}$



$$\frac{u_i(t+k) - u_i(t)}{k} = \alpha \frac{\left(u_{i+1}(t) + u_{i-1}(t) - 2u_i(t)\right)}{h^2}$$

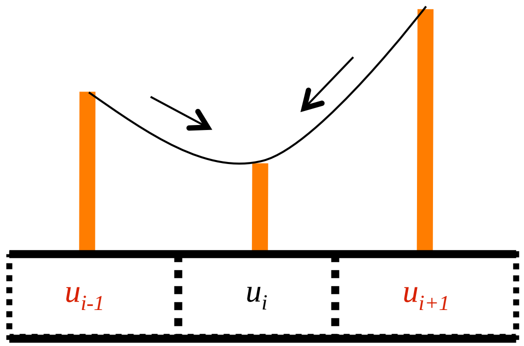
Δu measures the difference between:

-the average value over the neighborhood of a point P

-the value at point P

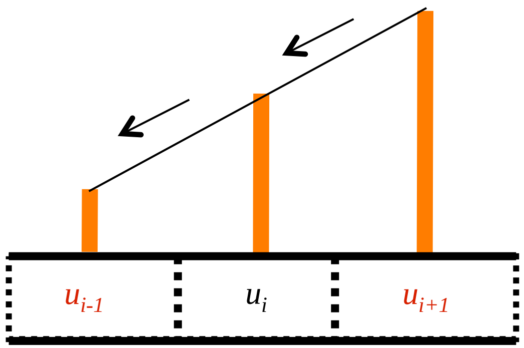
Net input > 0

$\Delta u > 0$



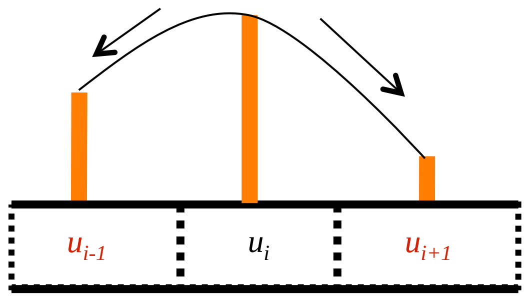
Net input = 0

$\Delta u = 0$



Net input < 0

$\Delta u < 0$



Diffusion in 2D

Diffusion equation (eg. Heat, Osmotic diffusion)

$$\frac{\partial u}{\partial t} = \alpha \, \Delta u$$

Geometric interpretation (2 Dimensions)

2 dimensions: $\frac{\partial u}{\partial t} = \alpha \left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} \right)$

	$u_{i,j+1}$	
$u_{i-1,j}$	$u_{i,j}$	$u_{i+1,j}$
	$u_{i,j-1}$	

$$\frac{u_{i,j}(t+k) - u_{i,j}(t)}{k} = \alpha \frac{\left(u_{i-1,j}(t) + u_{i+1,j}(t) + u_{i,j-1}(t) + u_{i,j+1}(t) - 4u_{i,j}(t)\right)}{h^2}$$

$$= \frac{\alpha}{h^2} \sum_{n \in V(m)} (u_n - u_m)$$

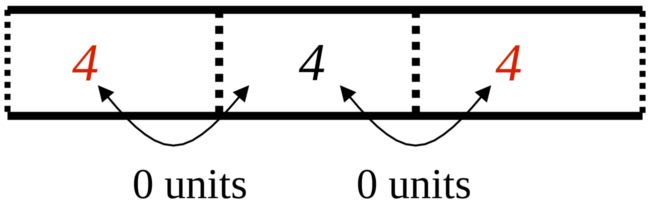
Why is there a « second » derivative in the diffusion equation?

2 cases of stationarity !

$$\frac{\partial u}{\partial t} = 0$$

1 dimension :

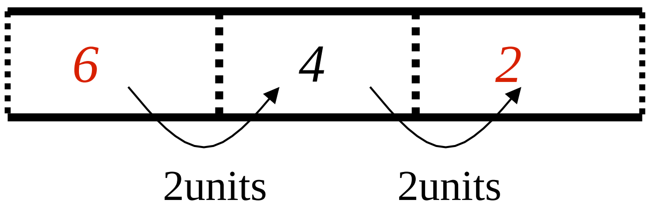
2 dimensions :



$$\vec{\nabla} u = \vec{0}$$

$$\Delta u = 0$$

	6	
6	6	6
	6	



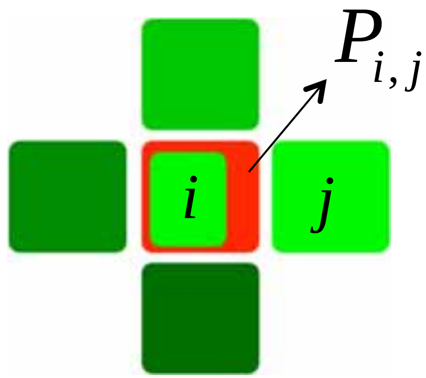
$$\vec{\nabla} u \neq \vec{0}$$

$$\Delta u = 0$$

	10	
3	6	6
	5	

Active transport

$P_{i,j}$ Strength of the PIN transporter in membrane *i* to *j*



auxin molecules *imported* during *dt* from cell *j* into cell *i* :

$$\alpha P_{j,i} a_j(t)$$

auxin molecules *exported* during *dt* from cell *i* to *j* :

$$\alpha P_{i,j} a_i(t)$$

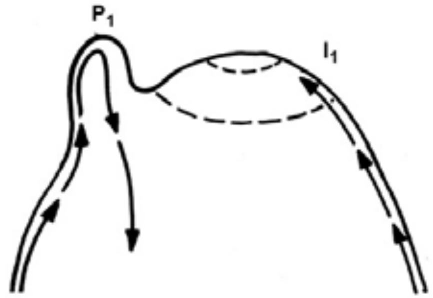
Net result of active transport :

$$\frac{\partial a_i(t)}{\partial t} = \alpha \sum_{j \in V(i)} (P_{j,i} a_j(t) - P_{i,j} a_i(t))$$

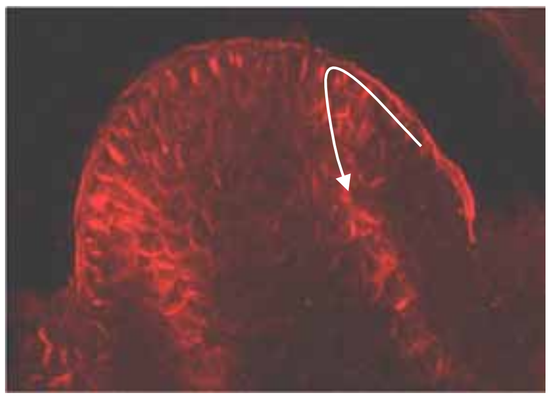
Auxin transport hypotheses

- Active and passive transport

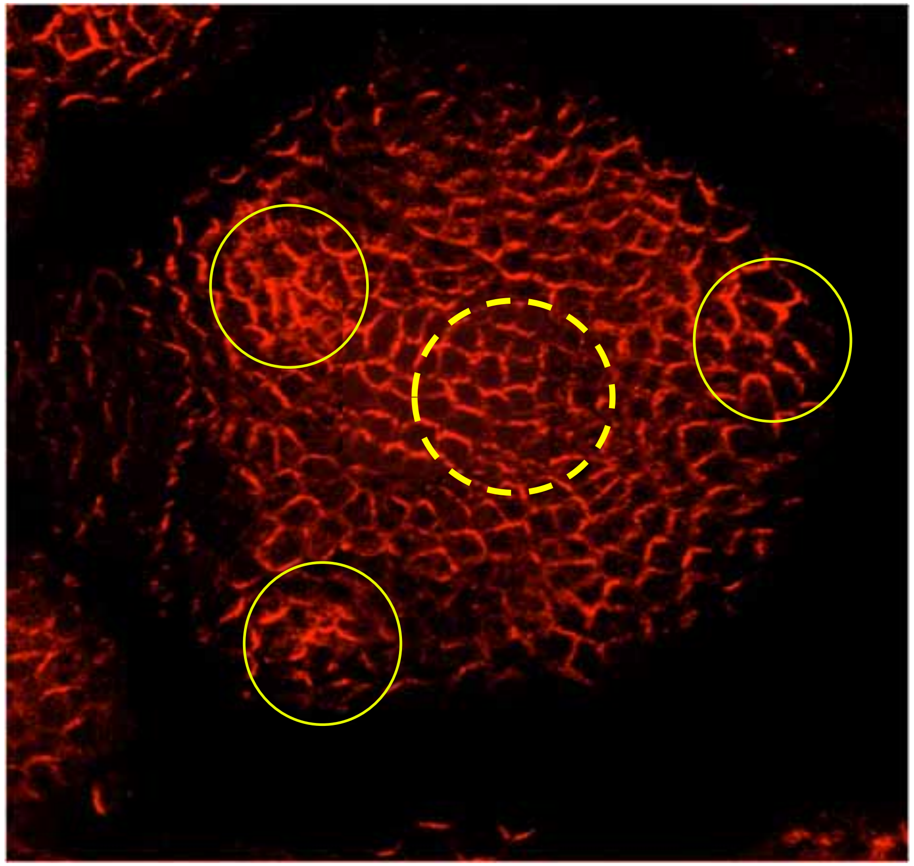
$$\frac{\partial a_i(t)}{\partial t} = \underbrace{D\Delta a_i(t)}_{\text{Diffusion}} + \underbrace{\alpha \sum_j (P_{j,i} a_j(t) - P_{i,j} a_i(t))}_{\text{Active transport}} \underbrace{- \gamma a_i(t)}_{\text{Degradation}} + \underbrace{\delta}_{\text{Production}}$$

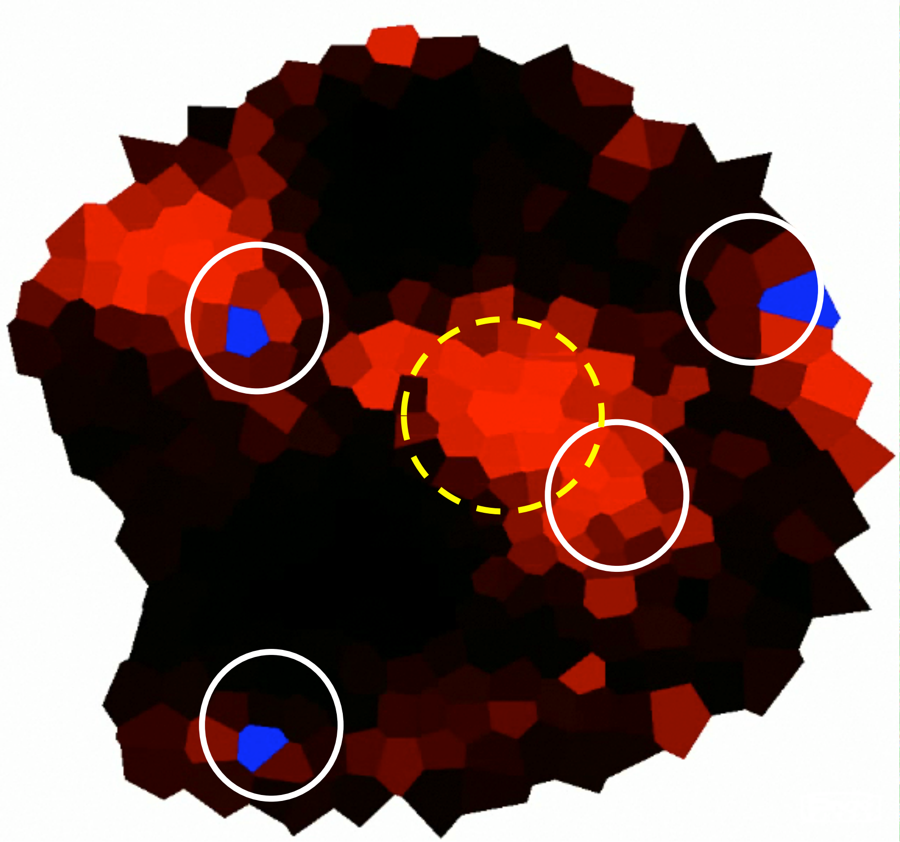


- Auxin enters the meristem at the periphery via L1 (Reinhardt et al. 2003) and/or is produced locally
- PIN1 is localized in L1, except at the level of primordia where it is also present in provascular tissues (Vernoux et al. 2000)
- Above a given threshold, auxin accumulation in the competence zone triggers the formation of primordia
- Above a given concentration, auxine is evacuated in the inner layers at the level of primordia through the provascular tissues, (Reinhardt et al. 2003)



Result of virtual auxin transport on digitized PIN1 maps



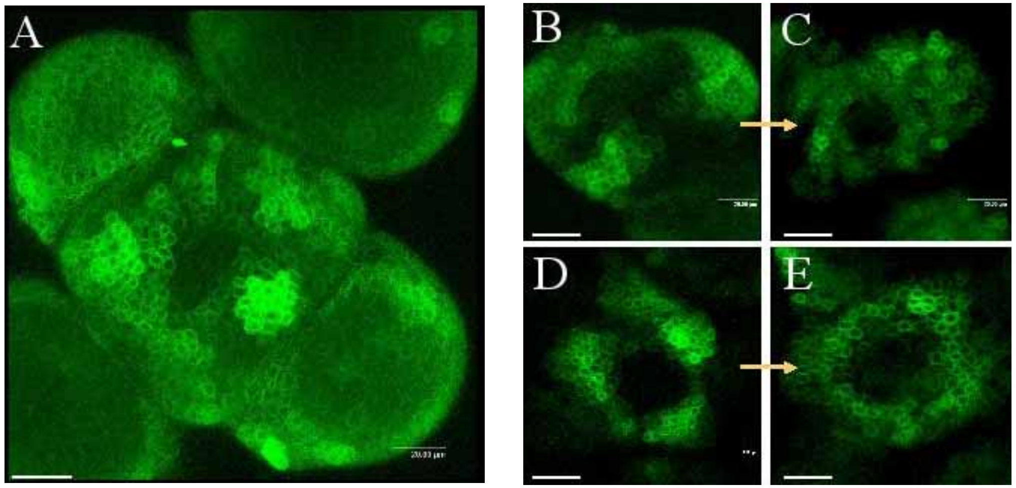


- Auxin accumulates at the primordia locations
- Auxin accumulates at the initium location
- Auxin accumulates in the center
- Accumulation patterns do not depend on the location of auxin production

Back to experiment …

1. The center is not sensitive to auxin

$t = 0$ $t = 22\text{h}$



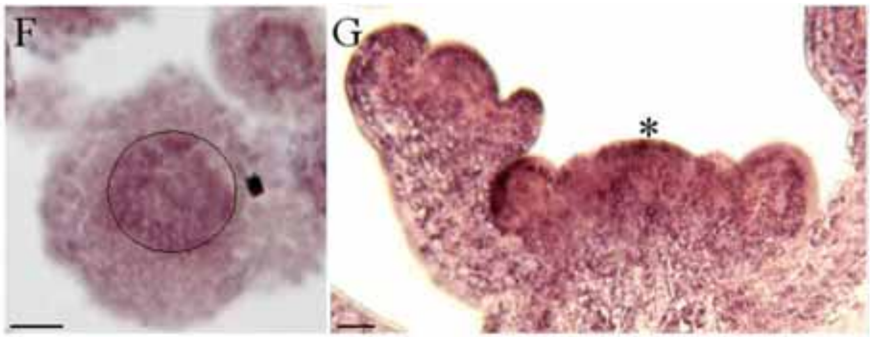
NPA

with NPA

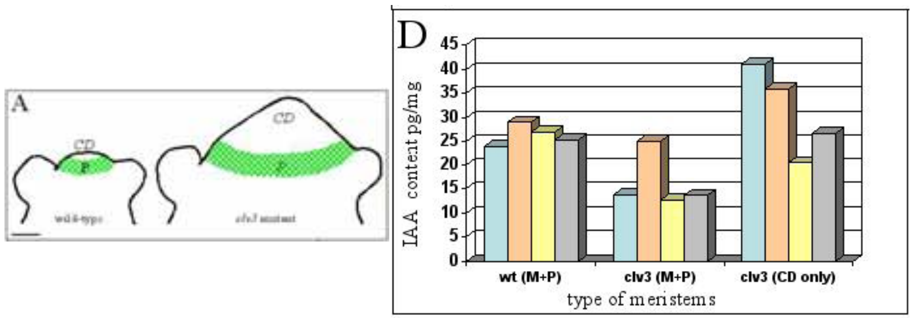
DR5::GFP

Addition of auxin

2. Anti-auxin immunolabelling



3. High levels of auxin observed in the CZ of the clv3 mutants



What drives the polarization of PIN pumps ?

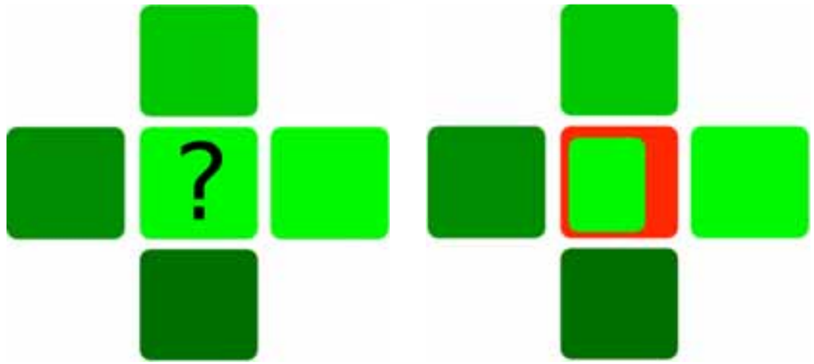
Integrating dynamics of tissue development

Allocation of PIN to membranes

$$\frac{\partial a_i(t)}{\partial t} = D\Delta a_i(t) + \alpha \sum_j (P_{j,i} a_j(t) - P_{i,j} a_i(t)) - \gamma a_i(t) + \delta$$

- **Hypothesis 1**:
  - Pumps are oriented so that local auxin spots are amplified (***concentration-based hypothesis***)

    (Jönsson et al. 06, Smith et al., PNAS, 06)



$$P_{i,j} = P_i \frac{s_{i,j} \beta^{a_j(t)}}{\sum_j s_{i,j} \beta^{a_j(t)}}$$

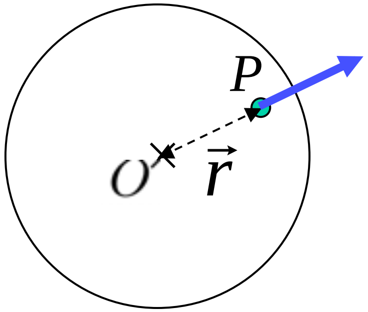
(Smith et al., 06)

P_i Available amount of PINs in cell *i*

$s_{i,j}$ Surface between cell *i* and *j*

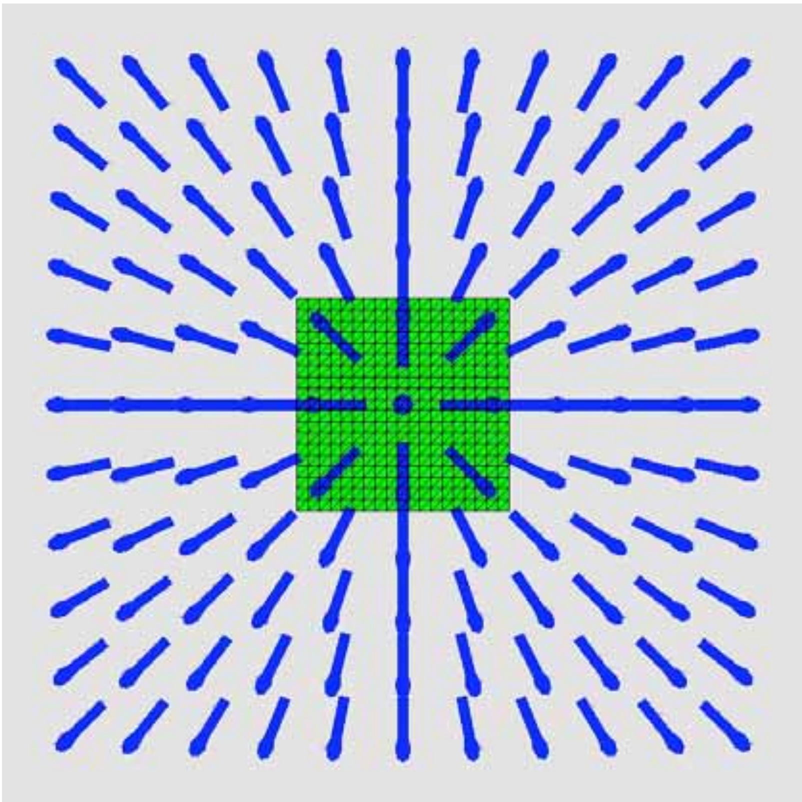
Simulating tissue growth

Velocity field:

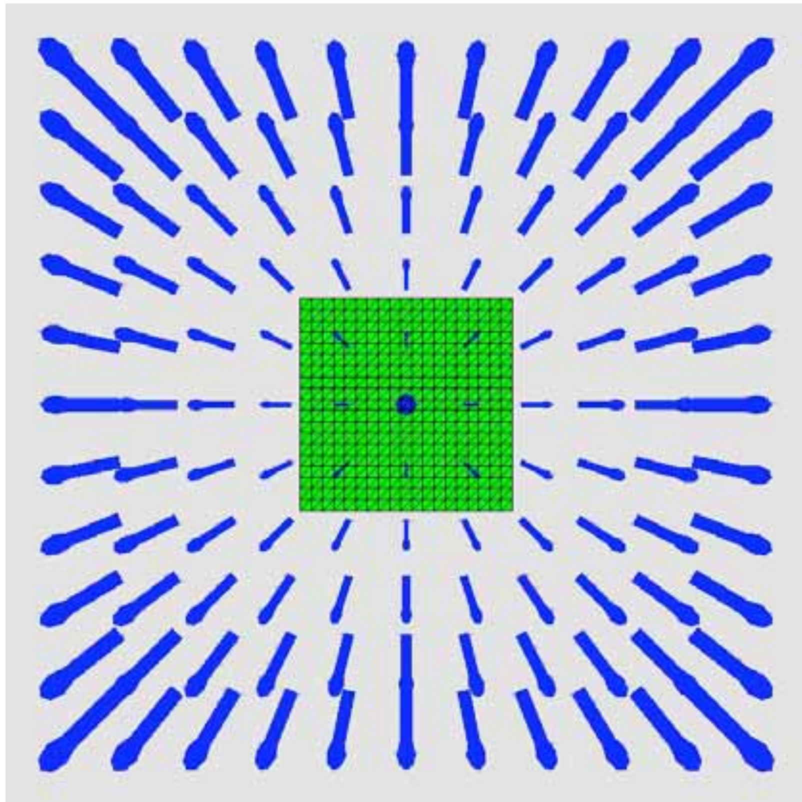


$$\vec{V} = \frac{d\vec{r}}{dt} = \alpha\vec{r}$$

α : relative elementary rate of growth



Constant speed

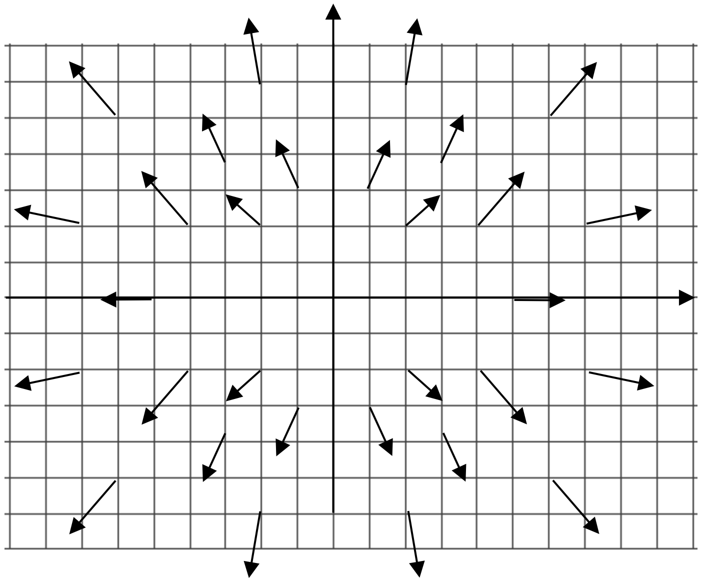


Linear speed

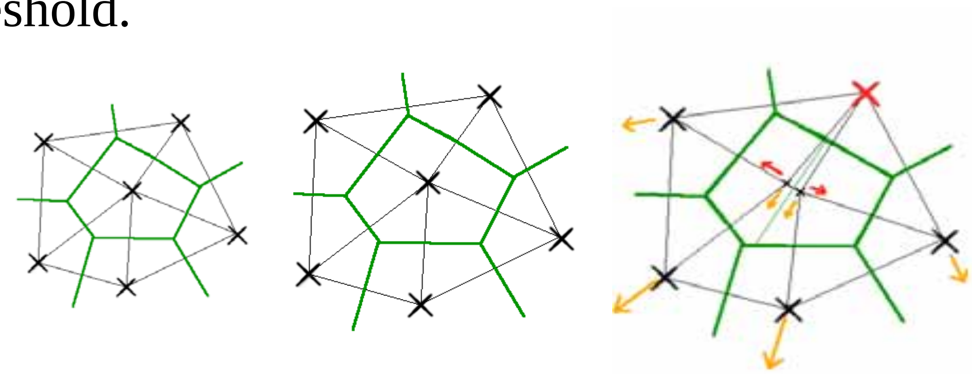
Simulating tissue growth

- **Velocity Field**

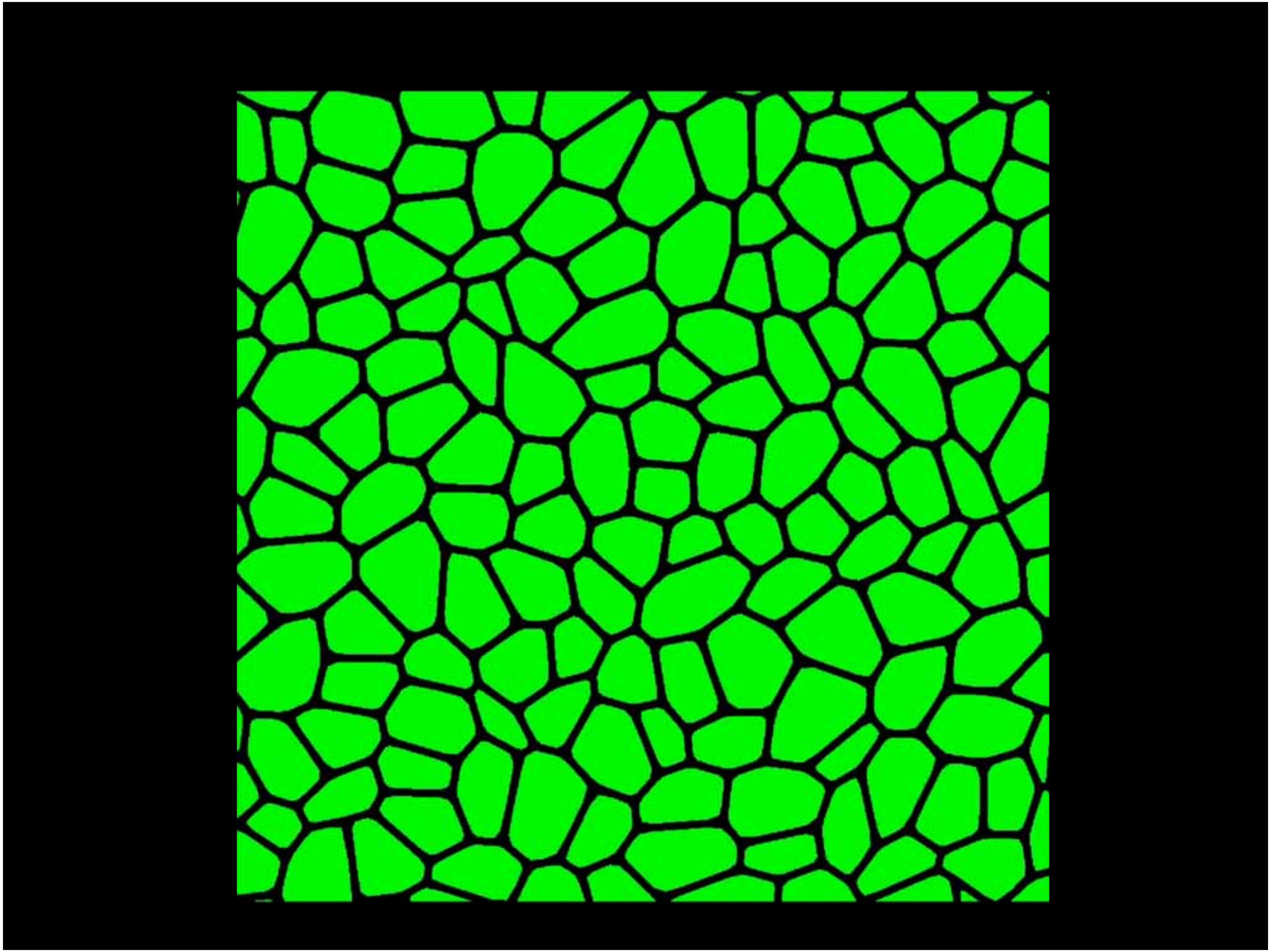
$$\vec{V} = \frac{d\vec{r}}{dt} = f(\vec{r}, t)$$



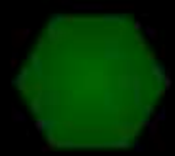
- **Division rules** (Nakielski, …)
  - Volume > threshold.



  - Location and orientation of the new wall
    - Minimal length,
    - Right angle between new and old walls.



Concentration-based hypothesis



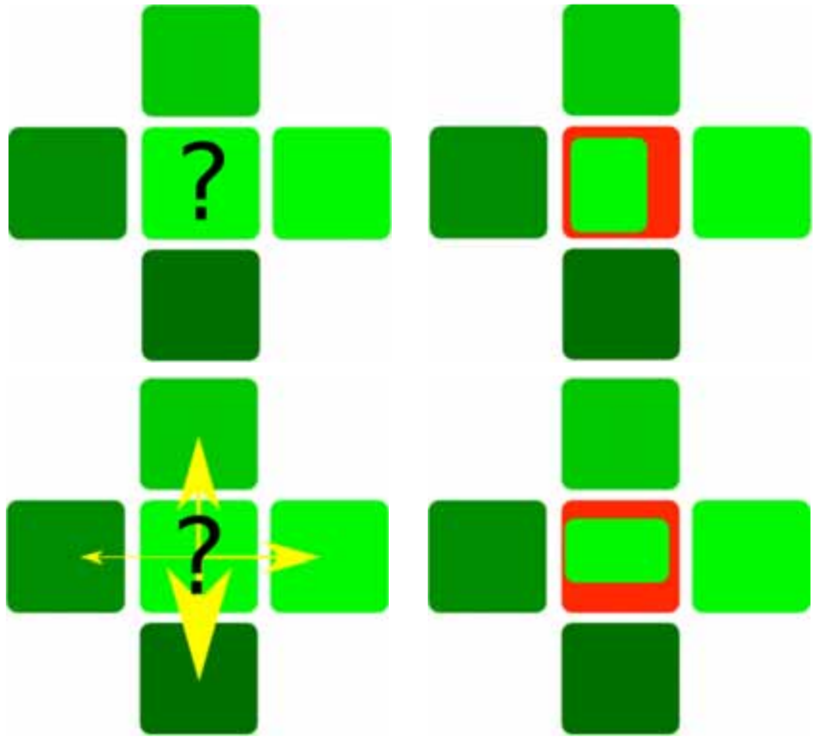
(Smith et al., PNAS, 06)

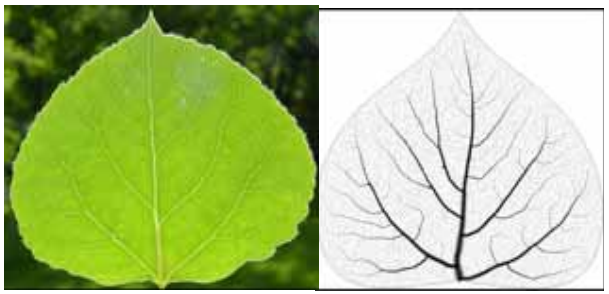
Candidate hypotheses

$$\frac{\partial a_i(t)}{\partial t} = D\Delta a_i(t) + \alpha \sum_j \left(P_{j,i}a_j(t) - P_{i,j}a_i(t)\right) - \gamma a_i(t) + \delta$$

- **Hypothesis 1**:
  - Pumps are oriented so that local auxin spots are amplified (***concentration-based hypothesis***)

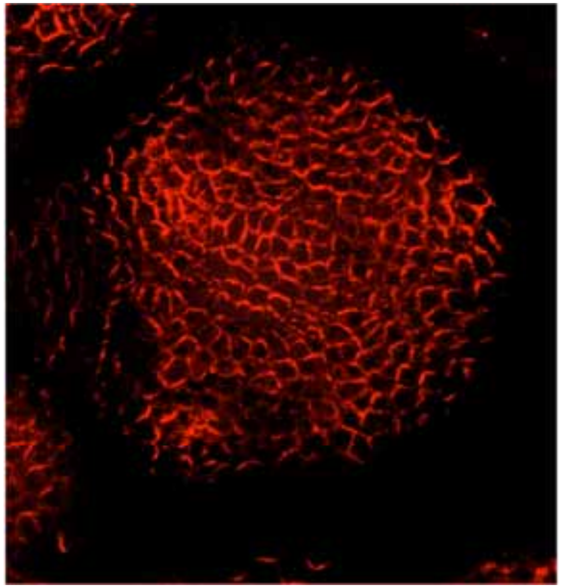
    (Jönsson et al. 06, Smith et al., PNAS, 06)
- **Hypothesis 2**:
  - Pumps are oriented so that fluxes are amplified (***canalization = flux-based hypothesis***) (Sachs 69, Mitchison 81, Feugier et al. 05, Rolland-Lagand et al. 05)





(Runions et al., SIGGRAPH, 05)

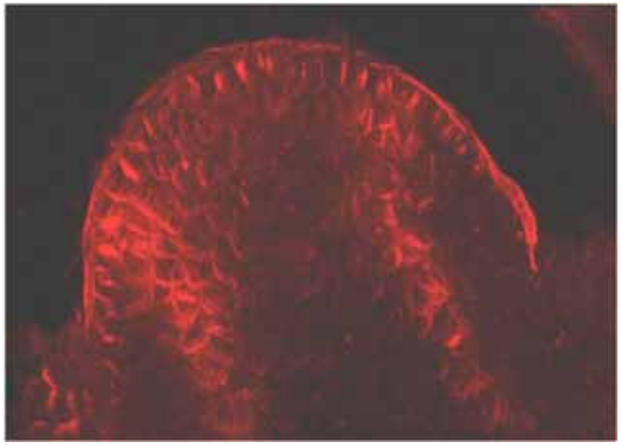
Could canalization explain auxin transport in the L1 layer ?



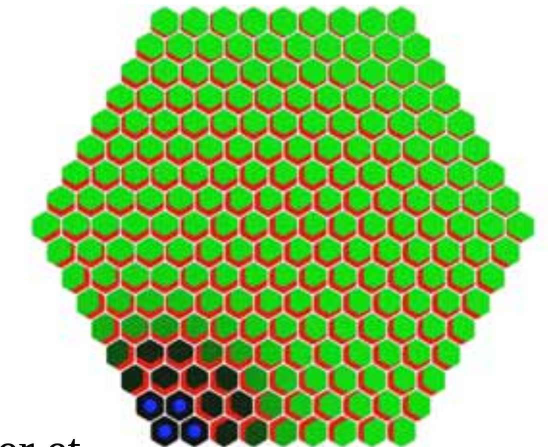
Flux-based hypothesis:

$$\frac{dP_{i,j}}{dt} = f(\phi_{i,j}) - \gamma P_{i,j} + \lambda$$

f = feedback function

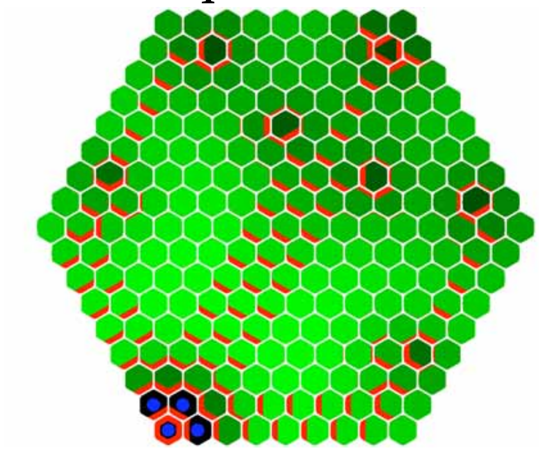


f linear



weak

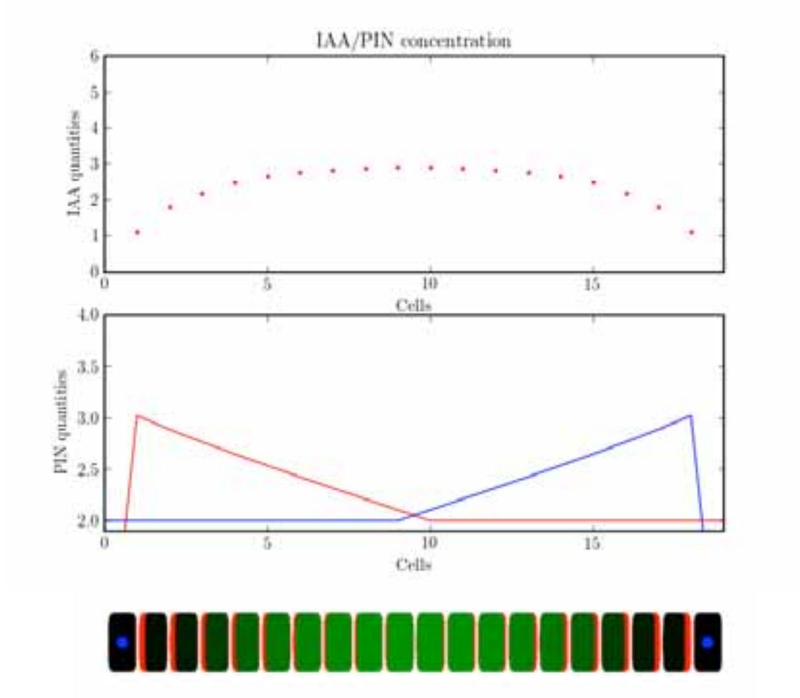
f quadratic



strong (canalization)

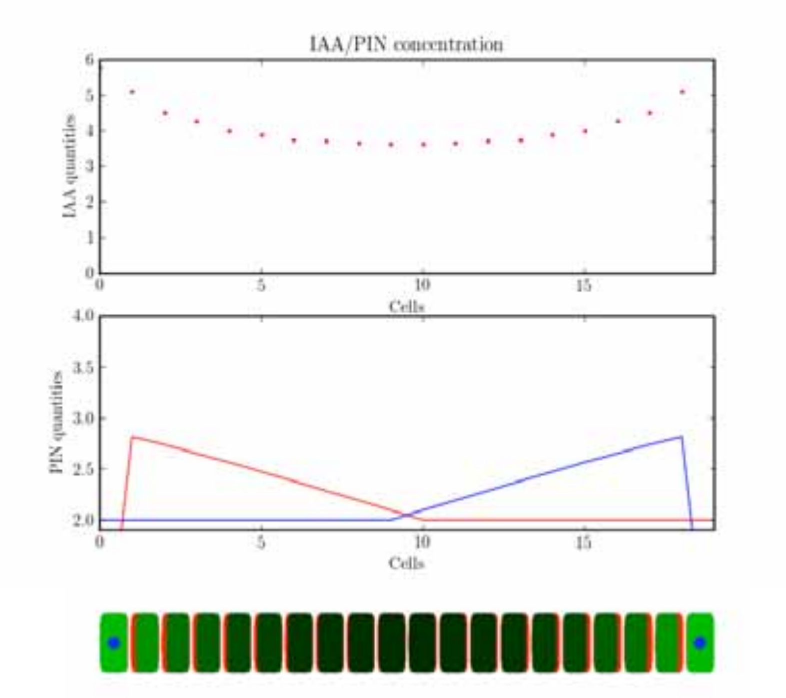
(Feugier et al. JTB, 05)

Flux-based polarization allows pumping *with* or *against* the auxin gradient



Pumping with the gradient

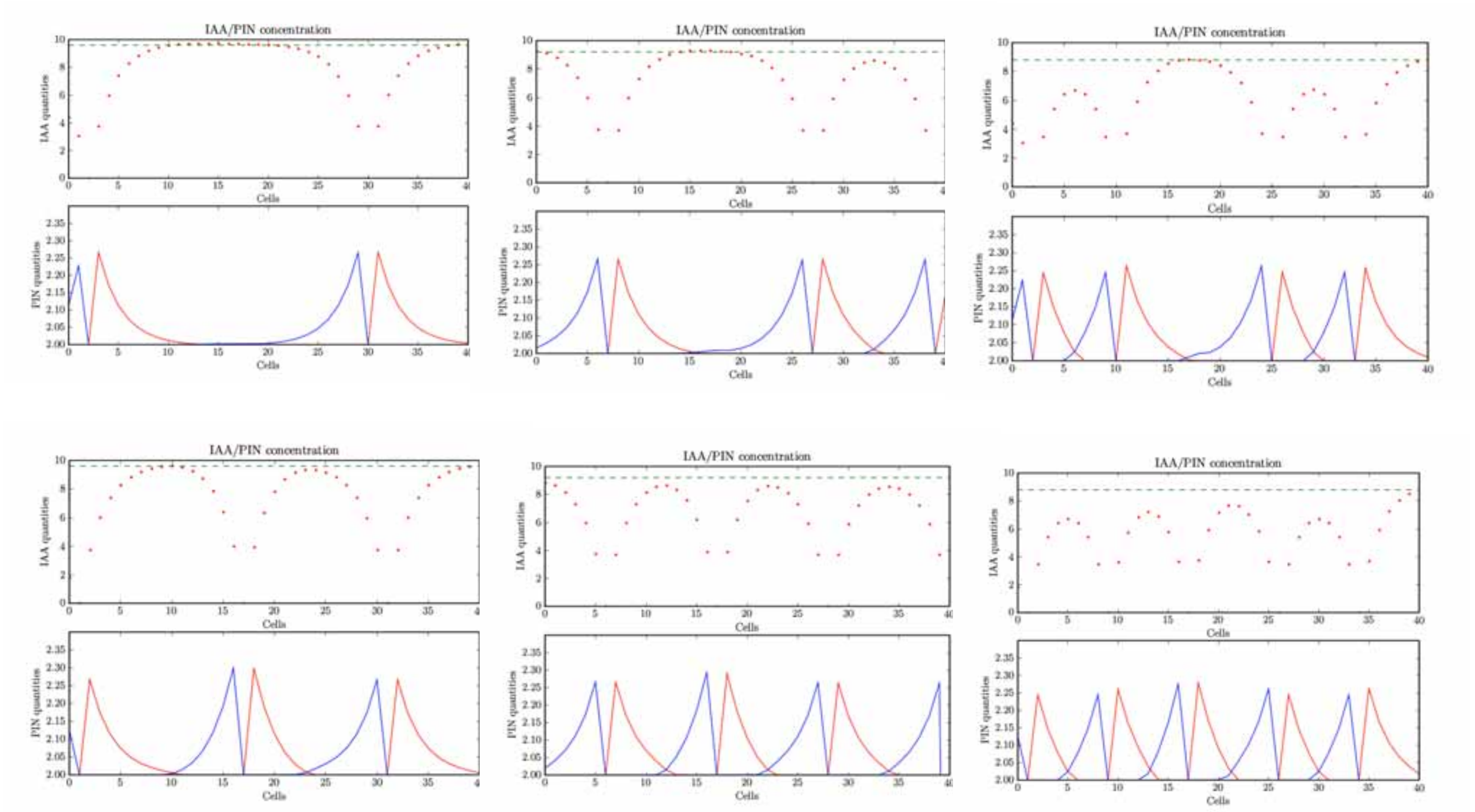
(infinite sink strength)



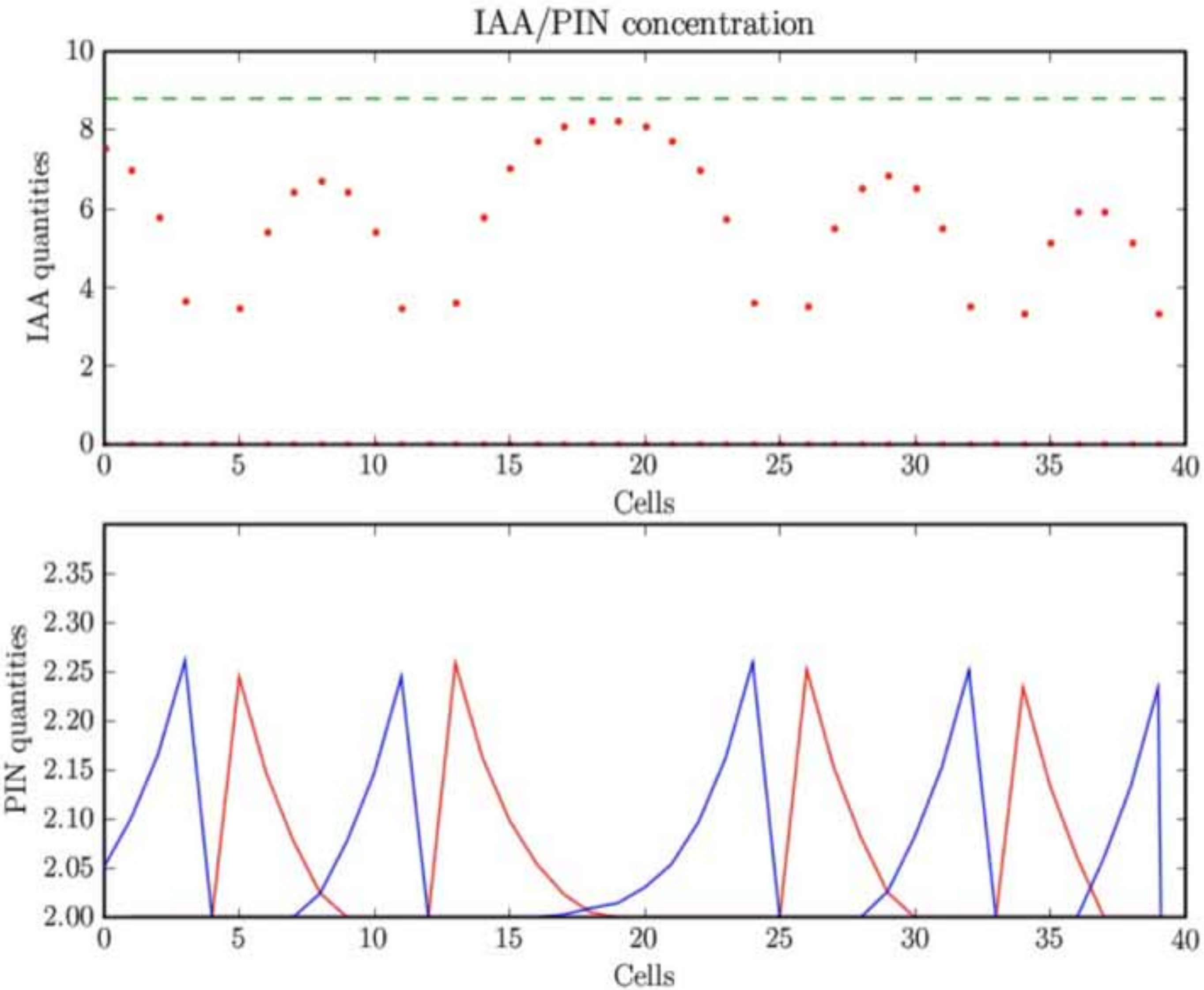
Pumping against the gradient

(finite sink strength)

Flux-based polarization may create dynamic patterning



Decreasing the threshold of primordia initiation

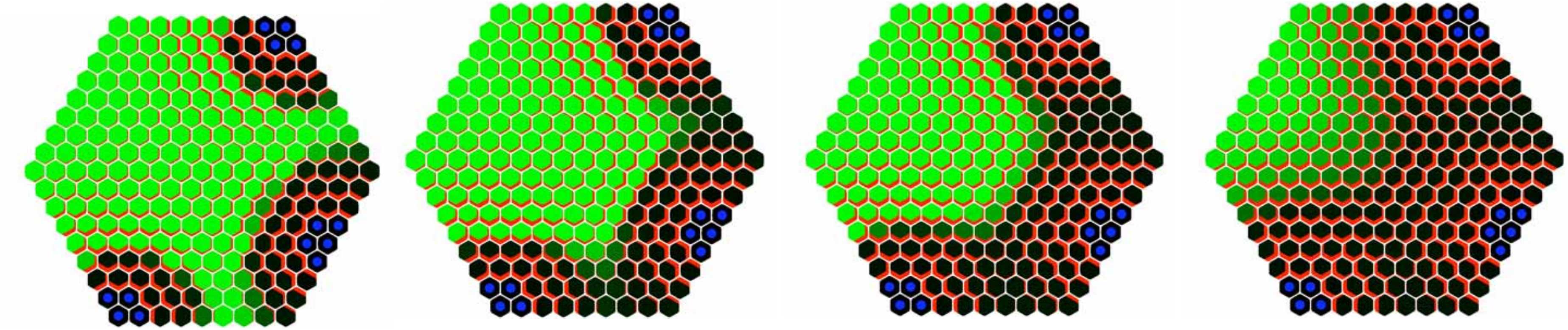


IAA/PIN concentration
IAA quantities
Cells
PIN quantities
Cells

Weak flux-based polarization can create inhibitory fields

The size of the inhibitory field is a function of the feedback parameter (β)

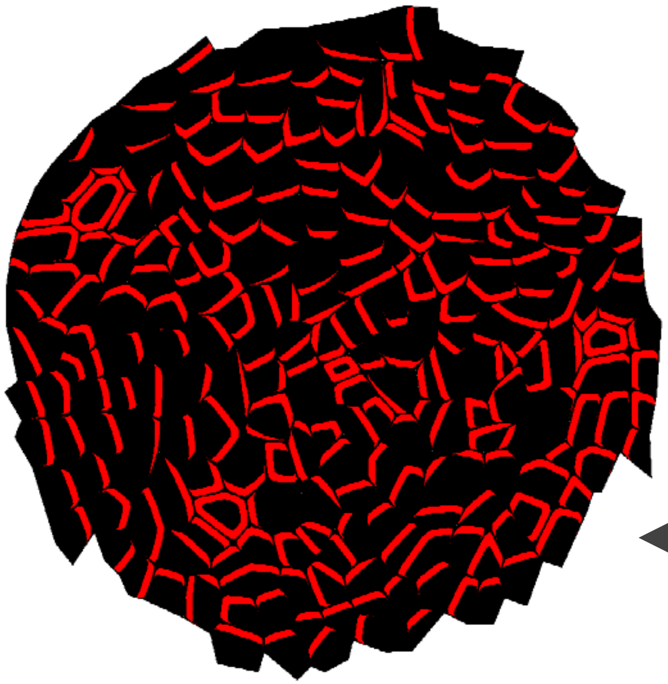
$$\frac{\partial P_{i,j}}{\partial t} = \beta \Phi_{i,j} - \gamma P_{i,j} + \lambda$$



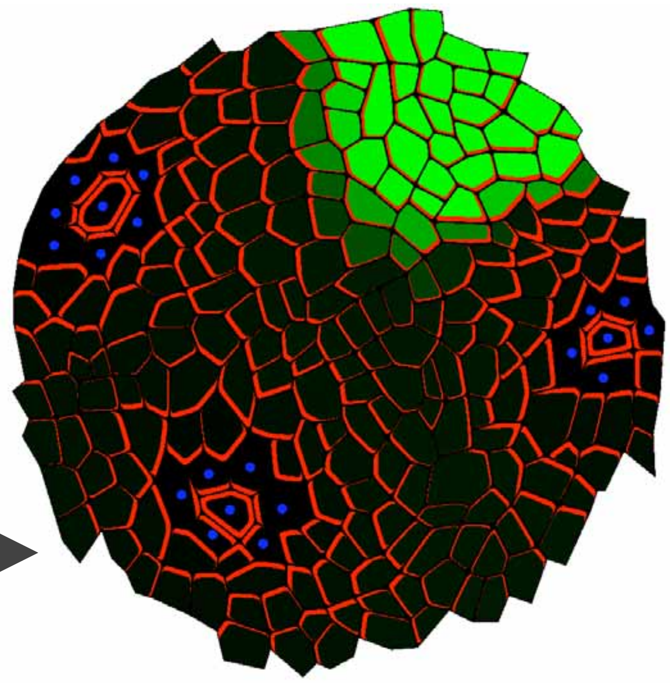
β=1.3 β=1.5 β=1.7 β=2.0

Simulation of auxin fluxes on digitized PIN1 maps

- Auxin is produced and degraded in each cell
- Diffusive and active transport
- Primordia are perfect sinks



?

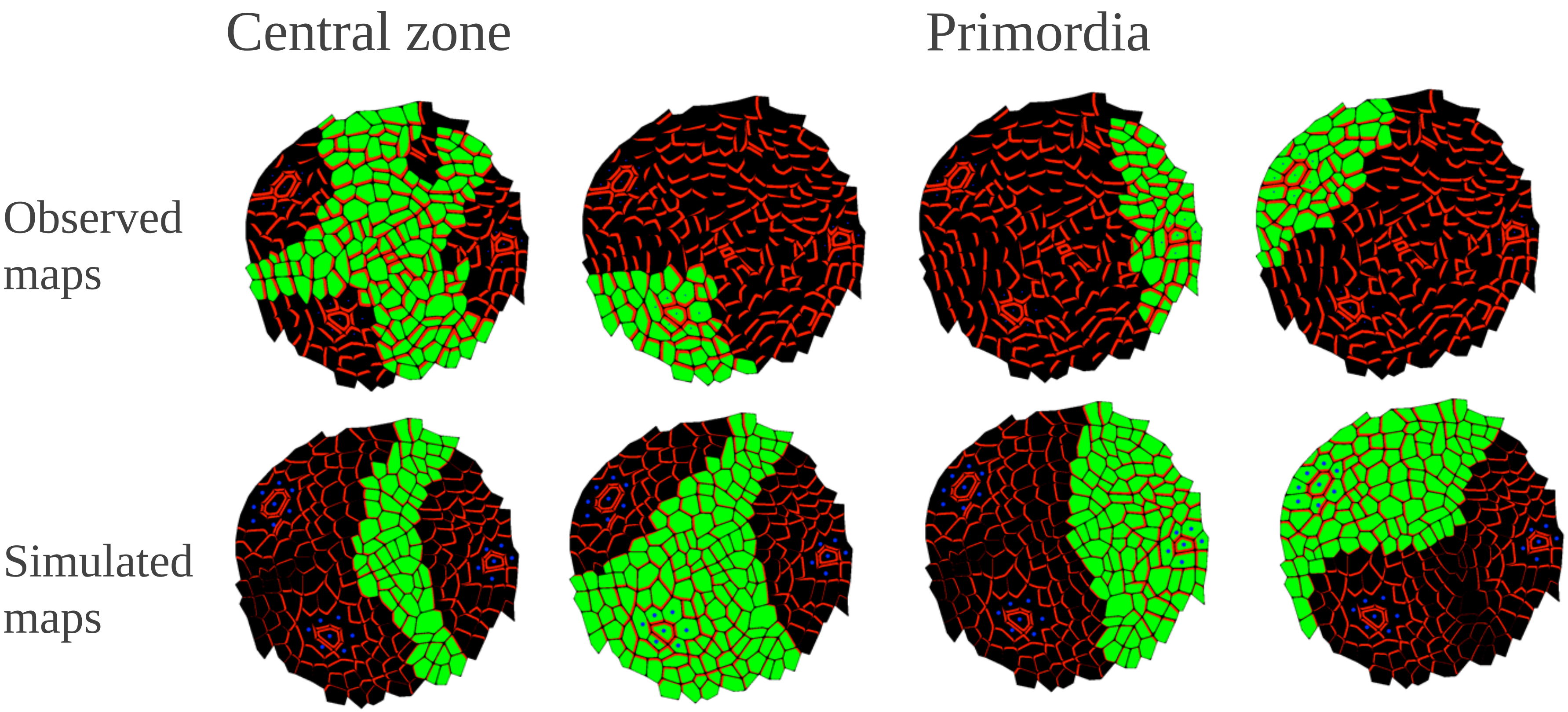


Observed PIN1 maps

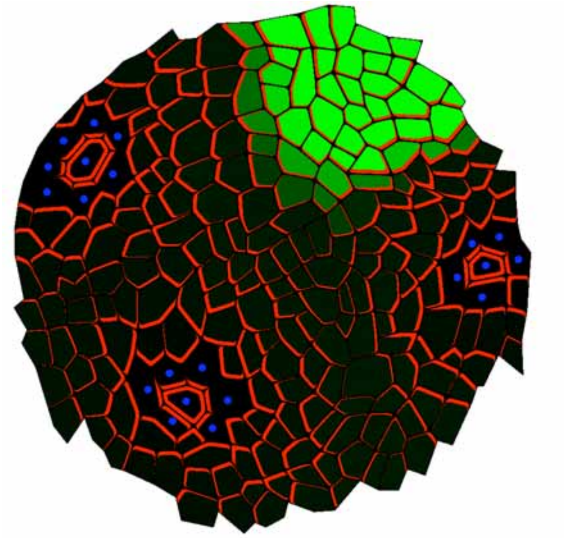
Simulated PIN1 maps
(weak flux-based polarization)

Influence zone of a region

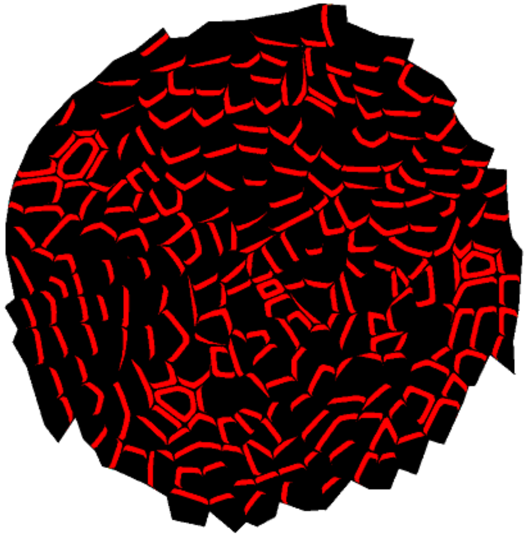
Definition: set of cells connected in the map with cells of a given region by an oriented path of pumps



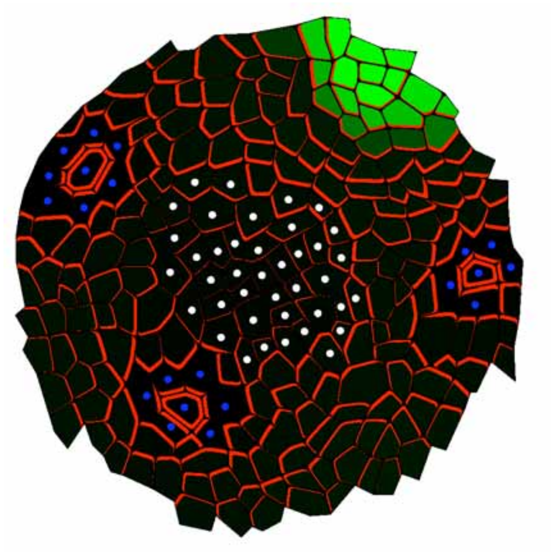
Role of the central zone



Central zone has no distinct behaviour



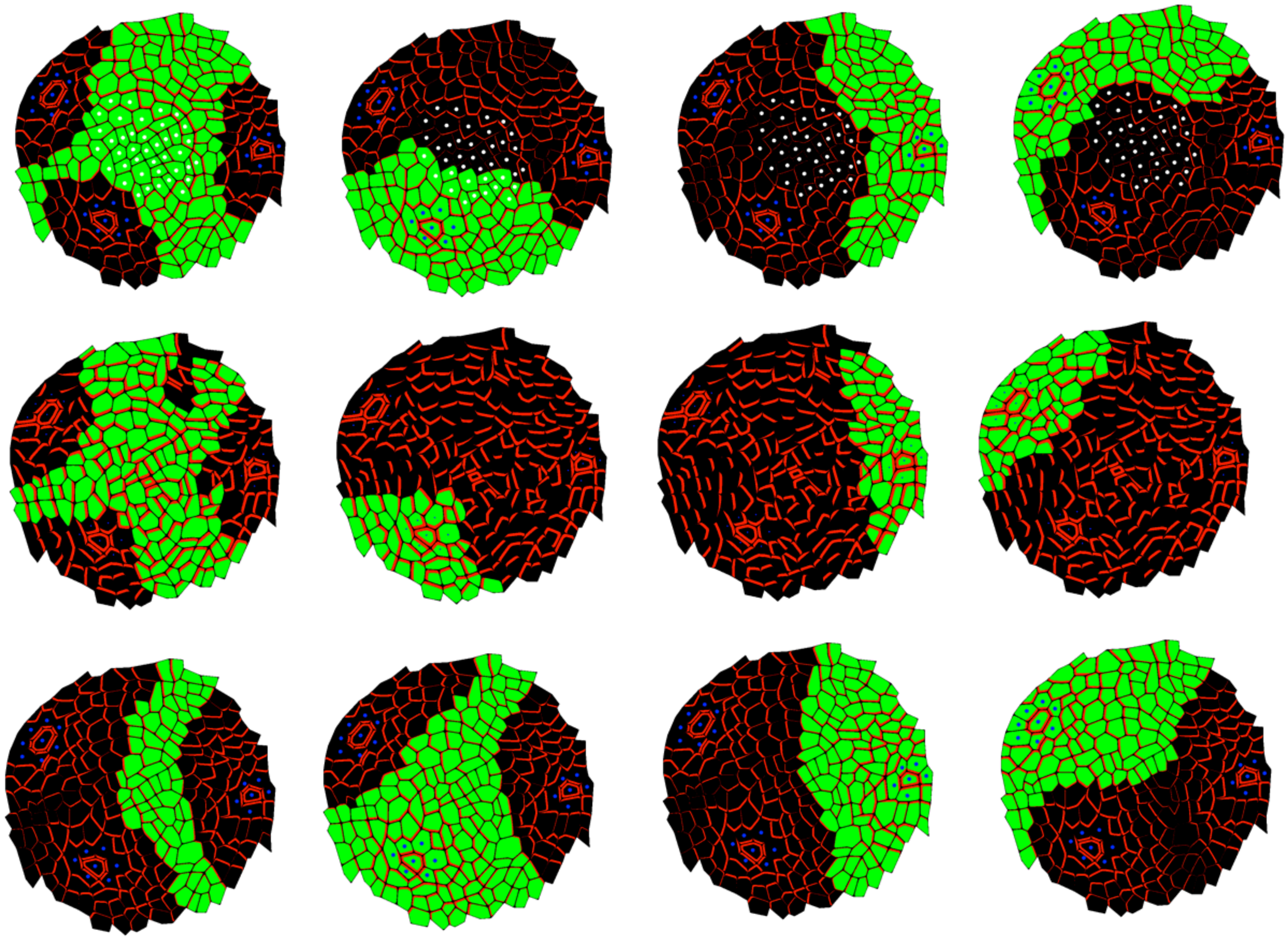
Observed map



Central zone degrades auxin

Comparison of the influence zones

15% more pumps are correctly oriented (78% in total)

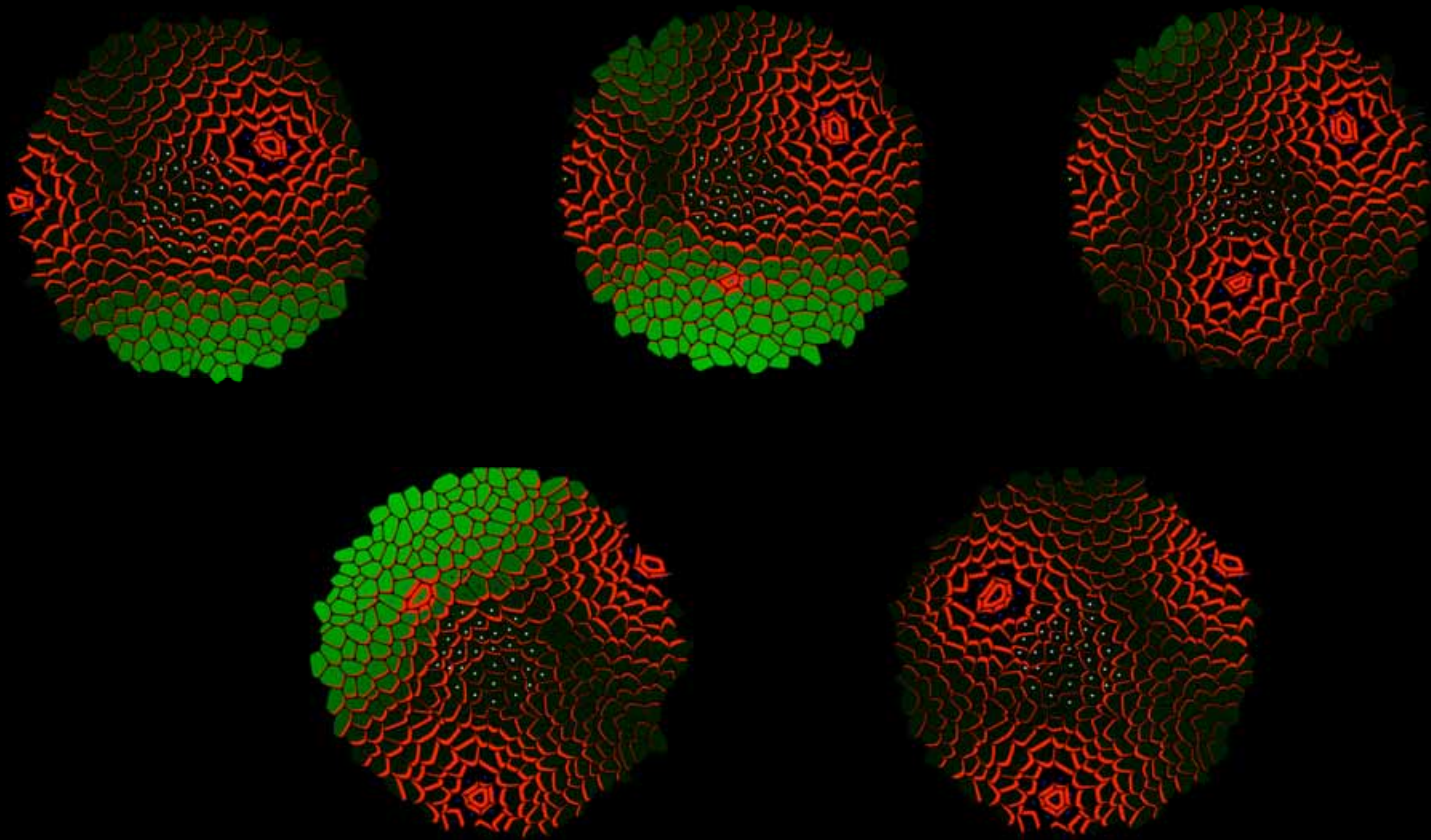


Simulated map with CZ degrading auxin

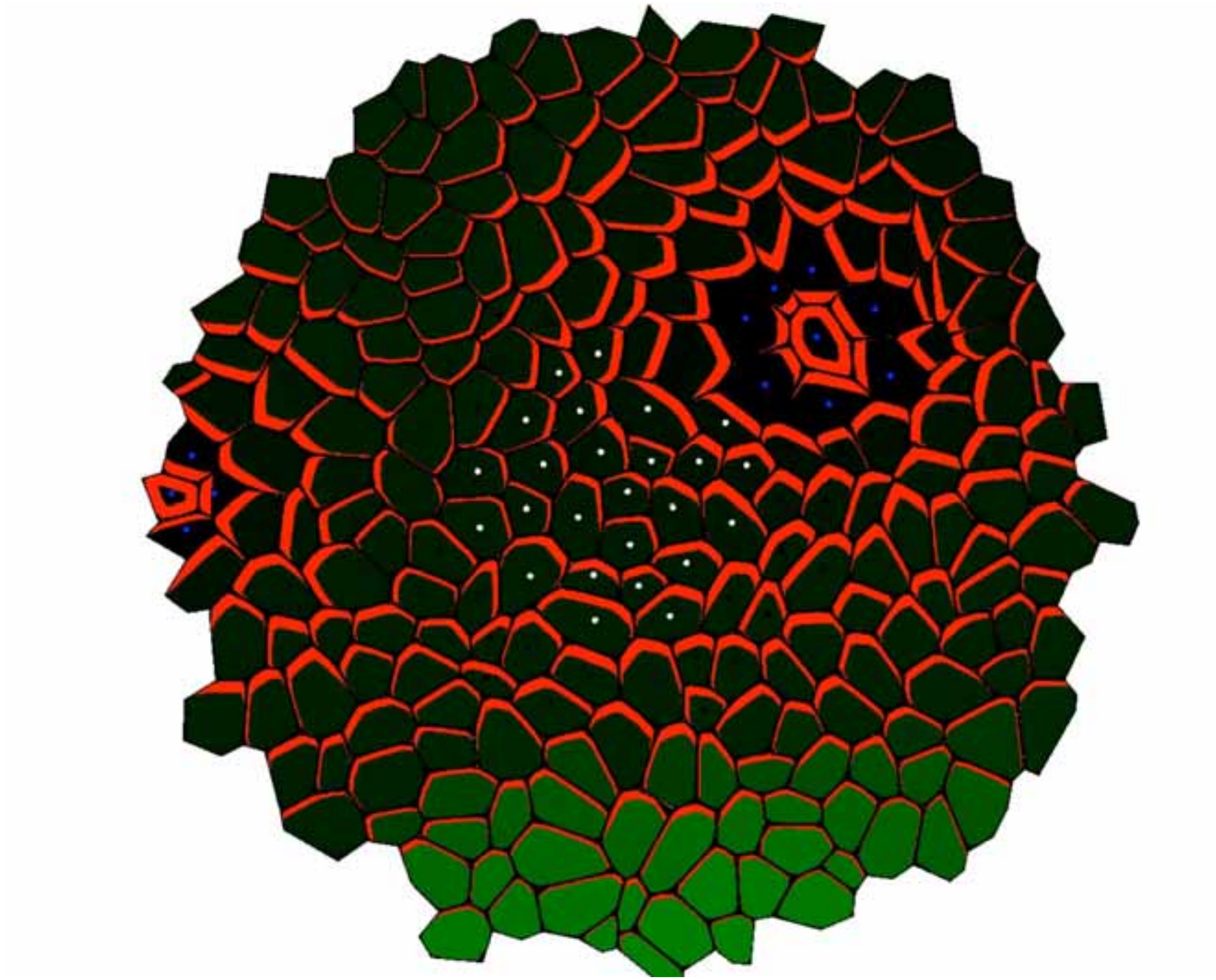
Observed maps

Simulated map without CZ

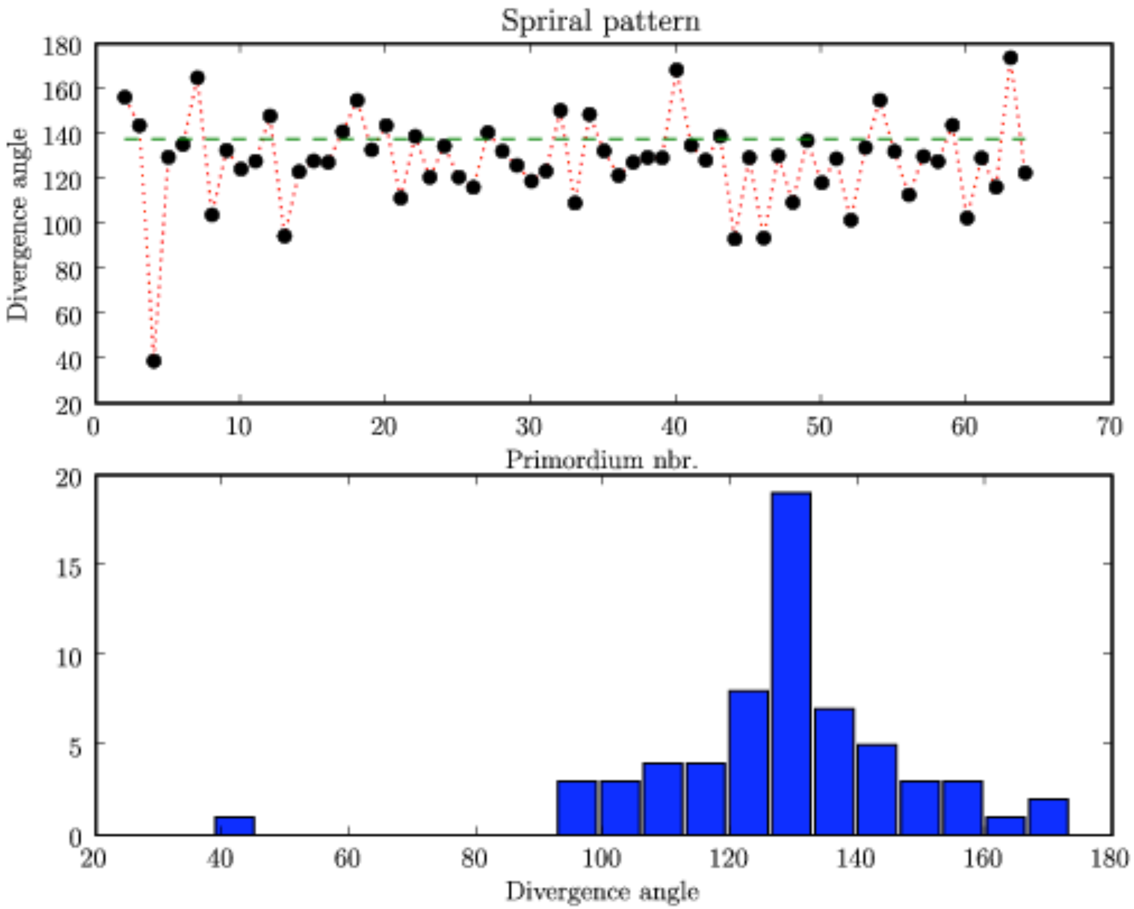
Dynamic simulation of phyllotaxy



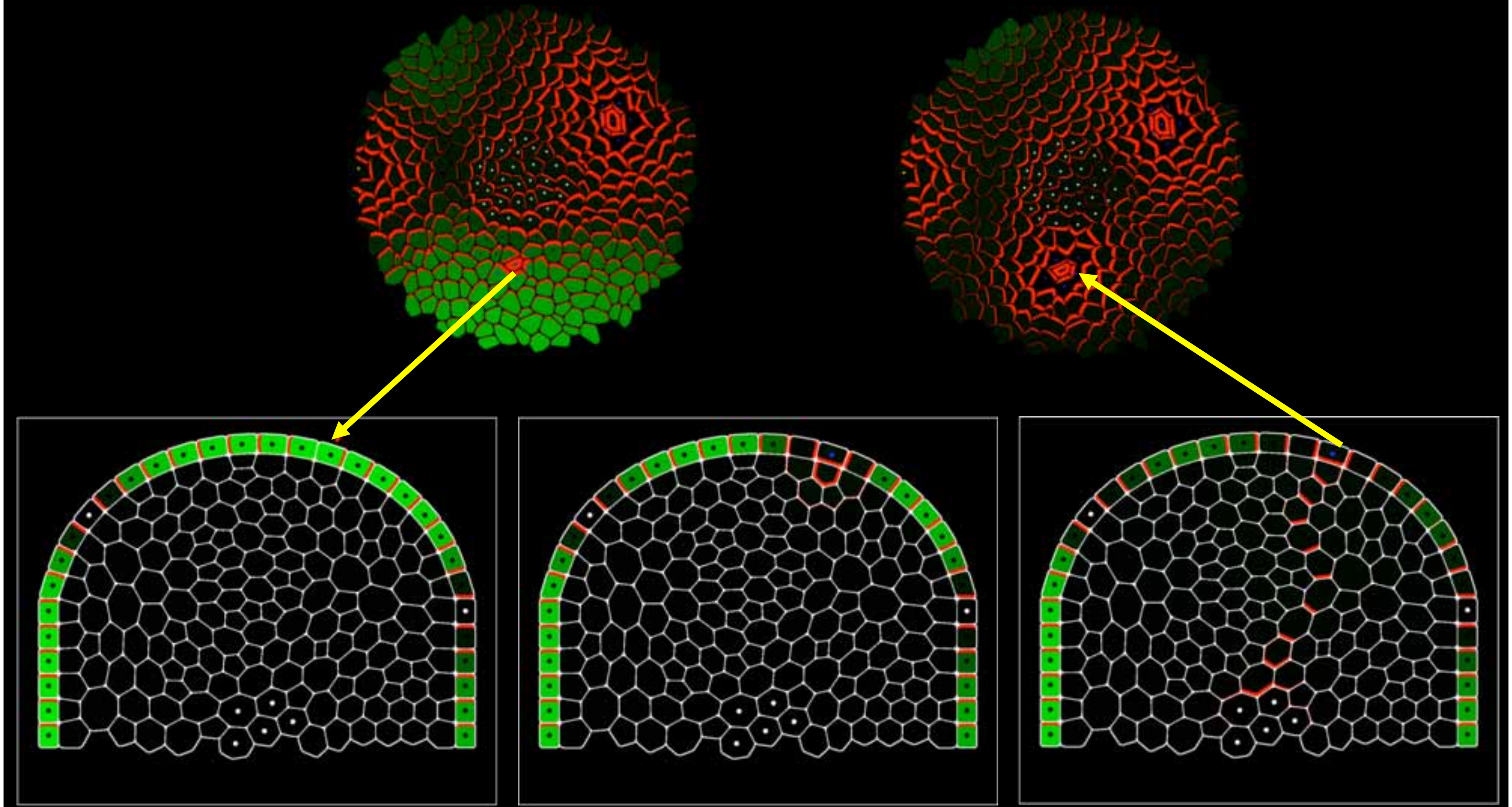
Flux-based simulation of phyllotaxy



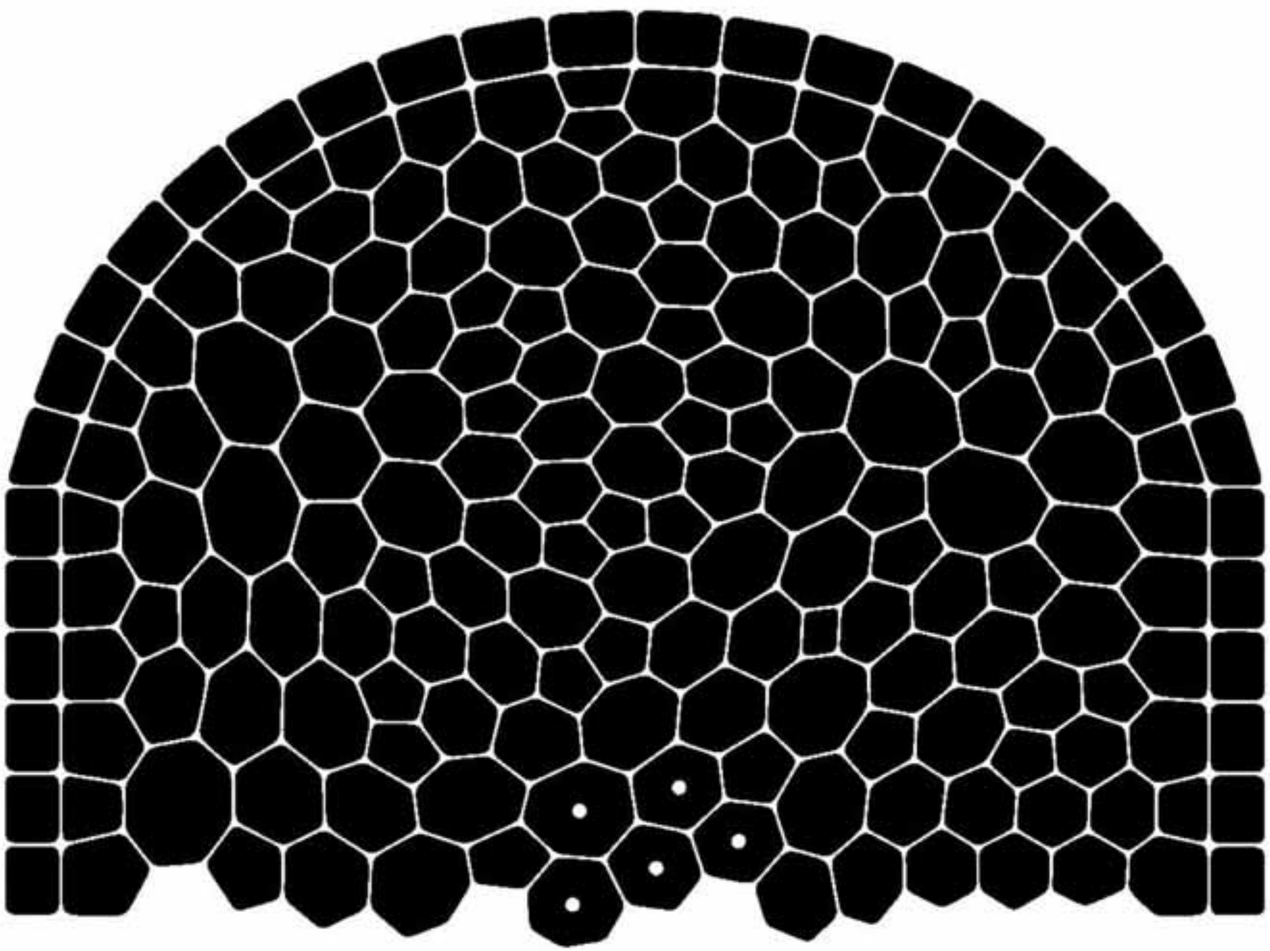
Simulated divergence angle



Simulation of the generation of provascular tissues

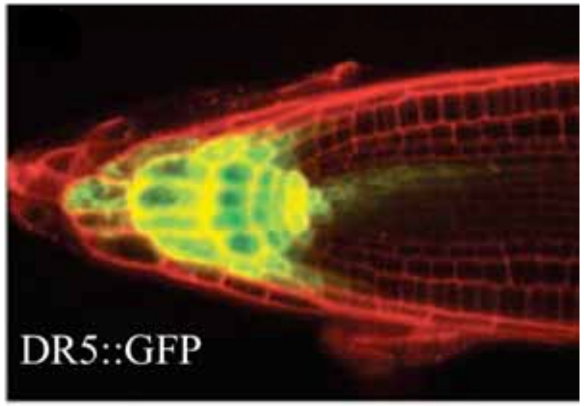


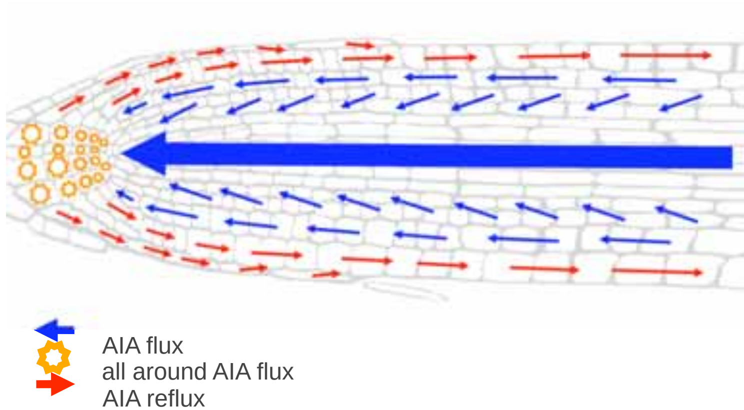
Flux-based simulation of vascularisation

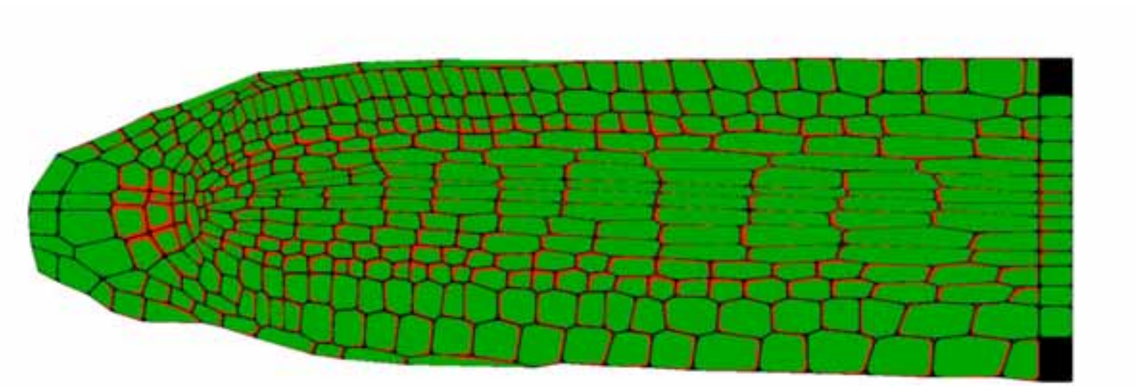


Flux-based polarization makes it possible to pump both with and against the gradient

(Ottenschläger et al. *PNAS*, 03)

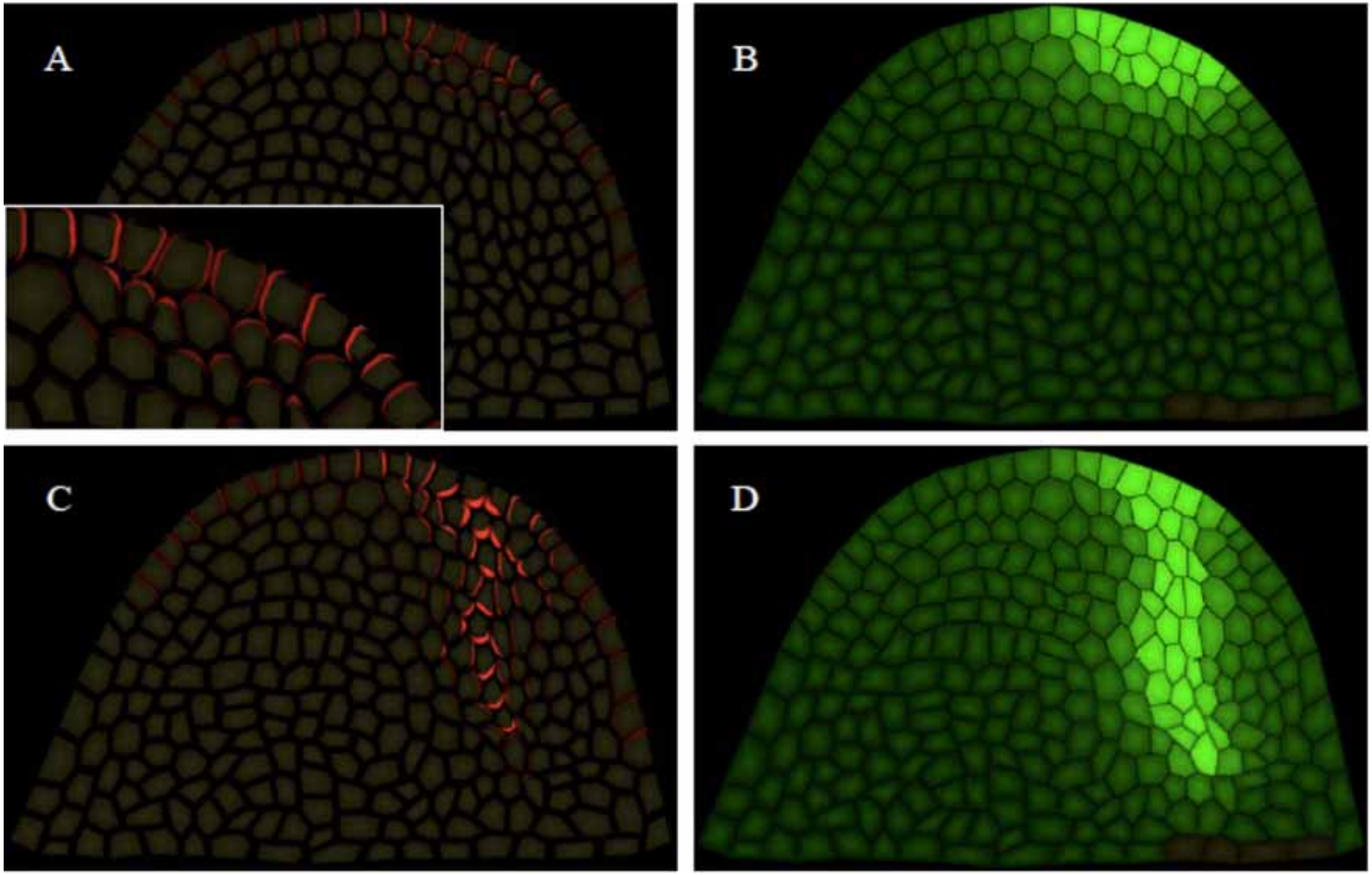






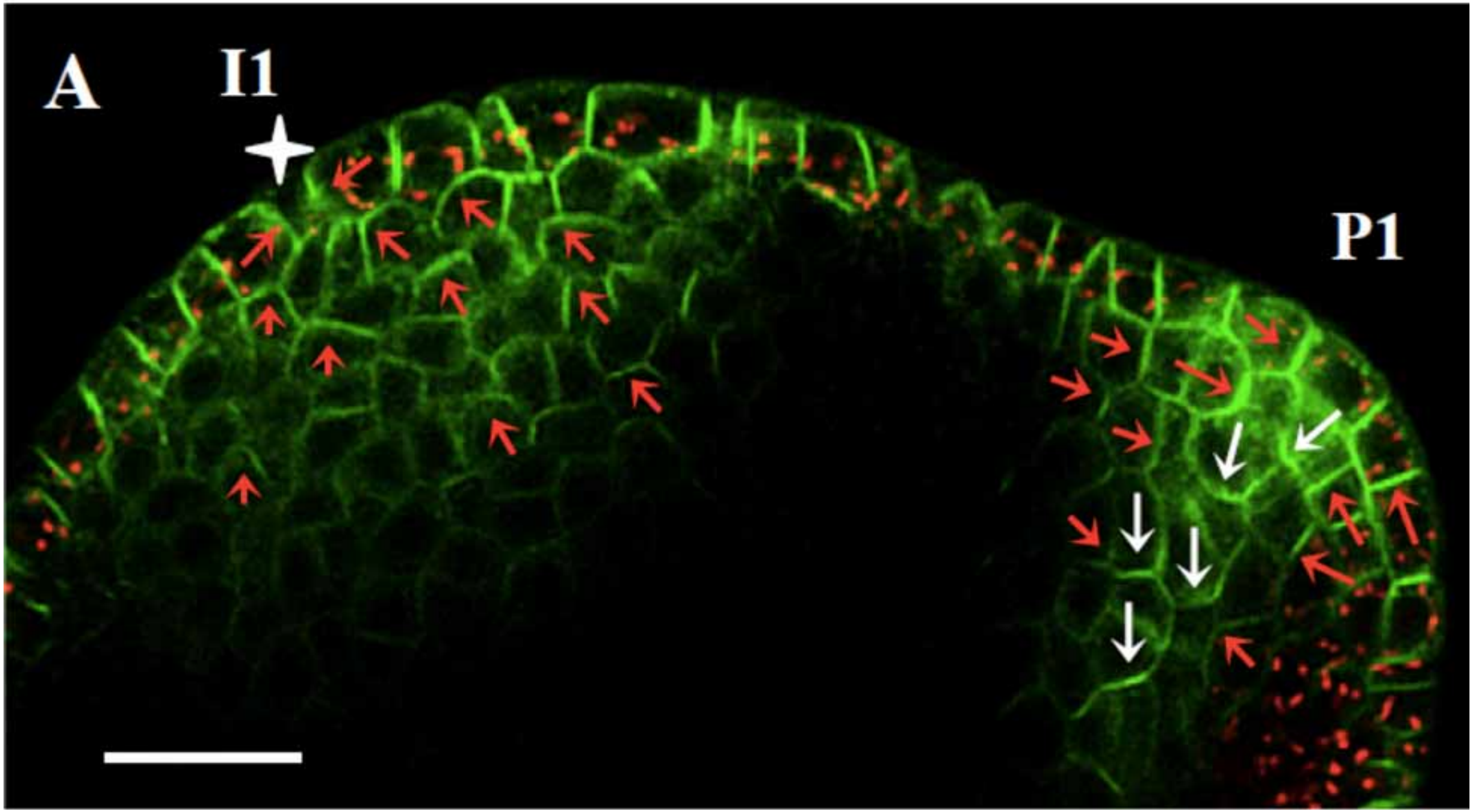
An alternative dual model

(Bayer et al., 2008)



Simulated PIN Simulated Auxin

Experimental verification

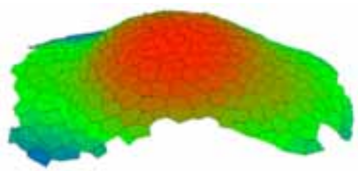


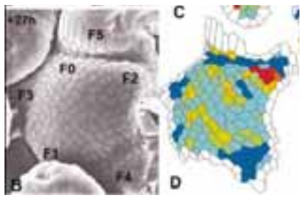
Summary on transport

	Concentration-based polarization	Flux-based polarization
Phyllotaxis	YES (Smith et al. 06, Johnson et al. 06)	YES (weak FBP) (Stoma et al. 08)
Venation patterns	Being investigated/Mixed model (Merks et al. 07), / (Bayer,08)	YES (strong FBP) (Mitchison 81, Rolland-Lagan 06, Runion 06, Feugier 05)
Fountain model (root apex)	?	YES (strong FBP) (Stoma et al. 08)
Molecular interpretation	No	No
Assessment (Phyllotaxis):		
Divergence angles	Ok	Ok
Phyllotactic pattern stability	To improve	To improve
Consistent with observed PIN maps	Partially/qualitative	Fairly consistent / quantitative if center degrades auxin (role?)
Predicted event sequence	Maximum is maintained / Pumps pointing upwards initially	Maximum / leaks / minimum

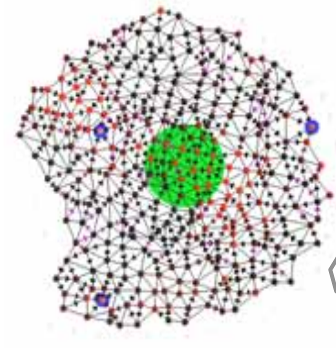
Building of a virtual meristem

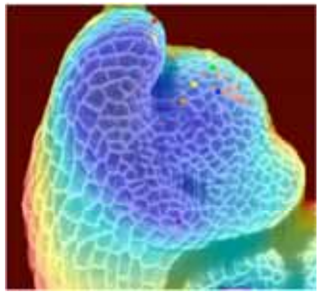
1 – Geometric model



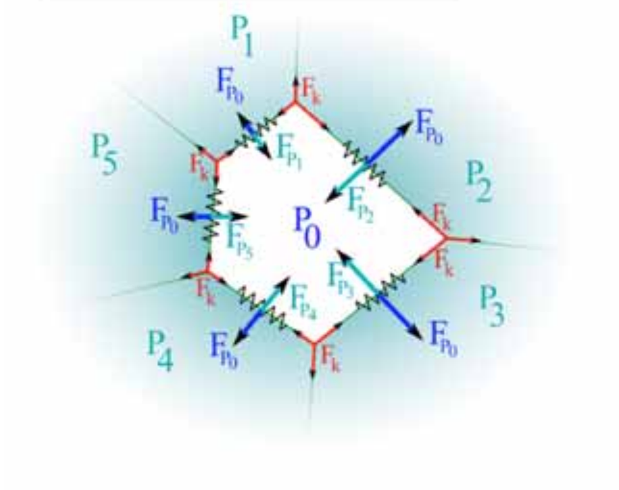


2 – Transport model



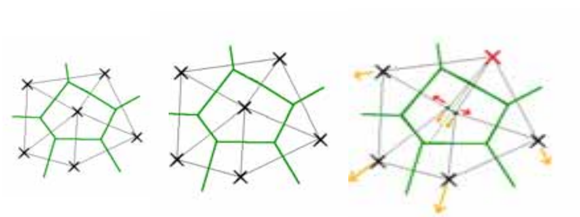


3 – Physical model

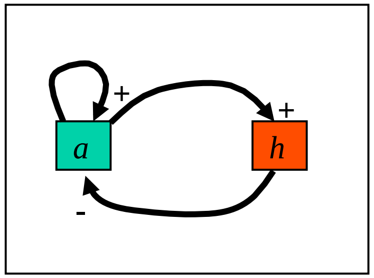


4 – Cell model

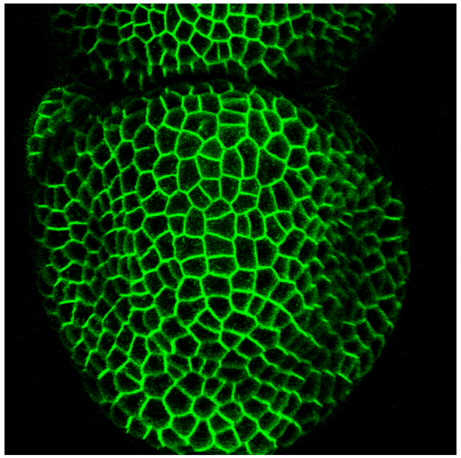
Division and Growth



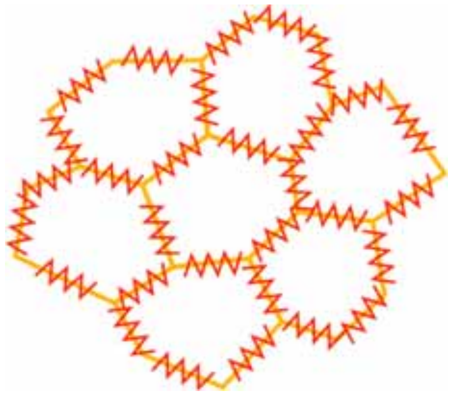
Interaction network

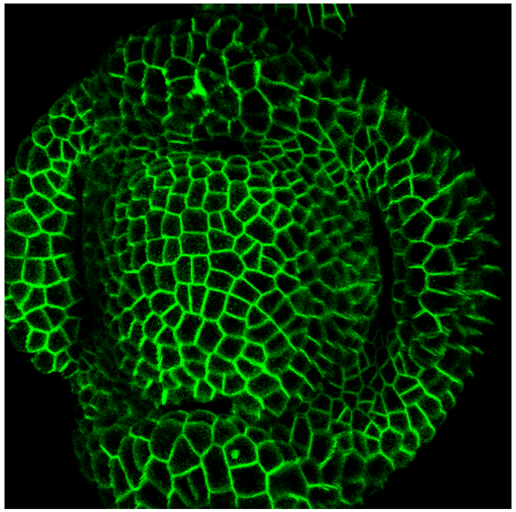


Mechanical aspects of growth



Cell-cell physical interactions ?



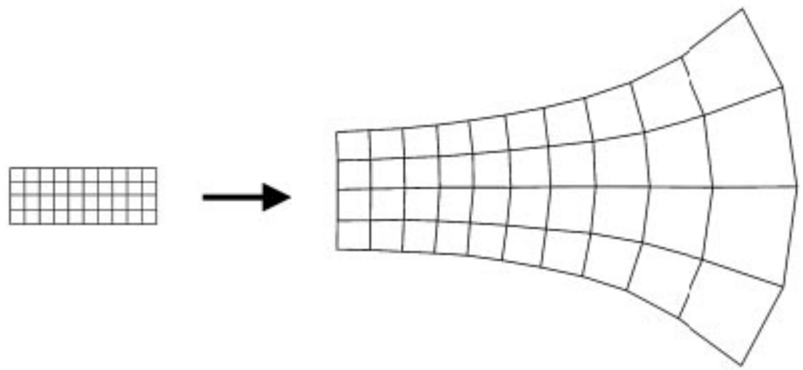


Local/Bottom up specification of growth

« The growing Canvas », *The art of genes*, E. Coen, 1999

« *The genetics of geometry* », (Coen et al, PNAS, 2004)

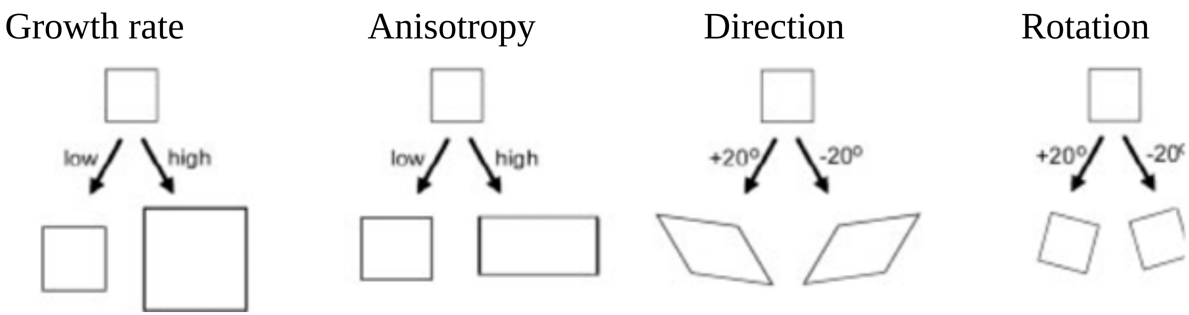
Shape as an emerging property of region growth …



A general conceptual framework

« *The genetics of geometry* », (Coen et al, PNAS, 2004)

Alphabet of elementary geometric transformations :



Local information:

- genes activity,
- hormones
- …

- microtubules,
- …

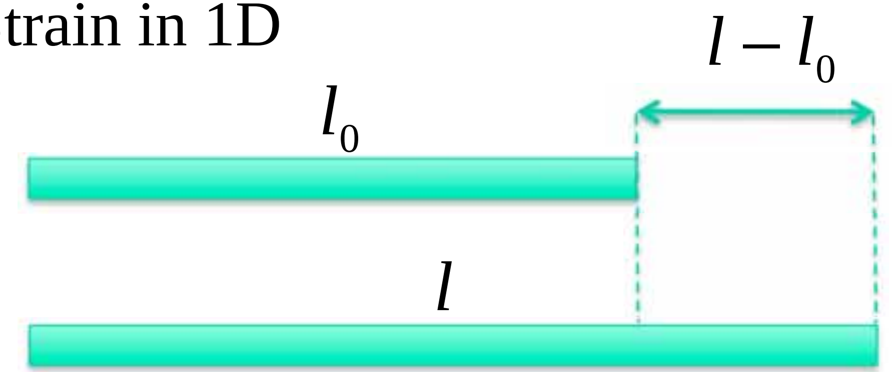
- fluxes,
- stresses,
- …

Global constraints :

- Mechanical forces,

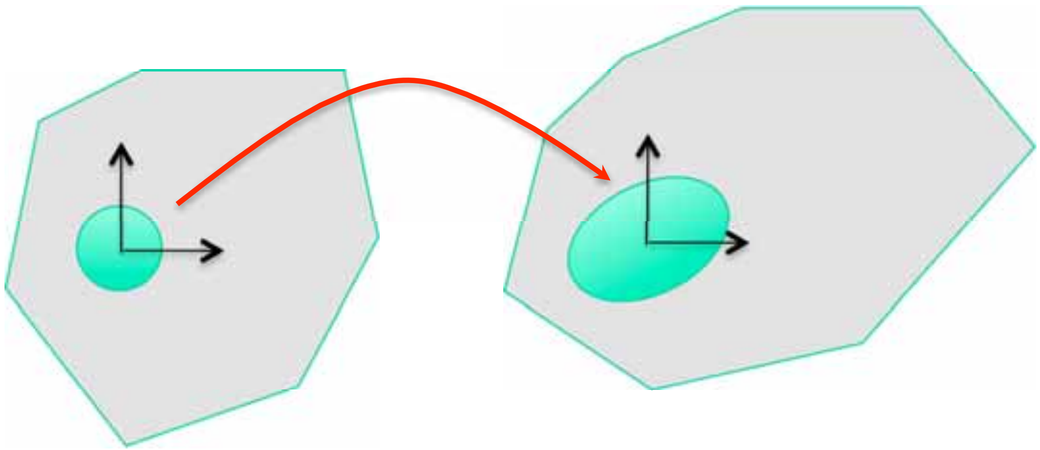
Strain description

- Strain in 1D



$$\varepsilon = \frac{l - l_0}{l_0}$$

- Strain in 2D



$$\varepsilon = \begin{bmatrix} \varepsilon_{xx} & \varepsilon_{xy} \\ \varepsilon_{yx} & \varepsilon_{yy} \end{bmatrix}$$

Strain tensor

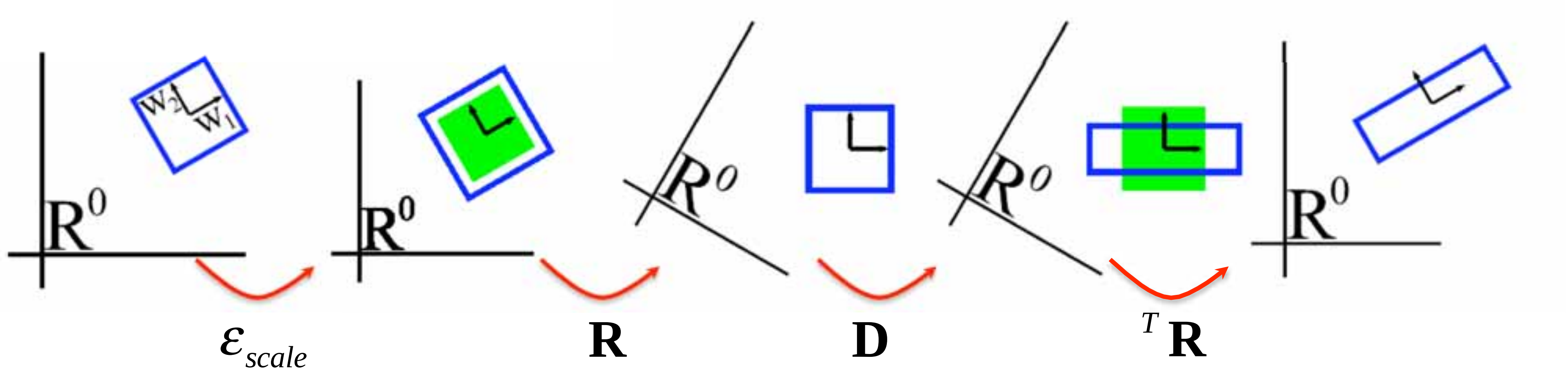
Elementary transforms in mathematical terms

Decomposition of the strain tensor (2D) :

$$\varepsilon = \varepsilon_{scale} . \varepsilon_{ani}$$

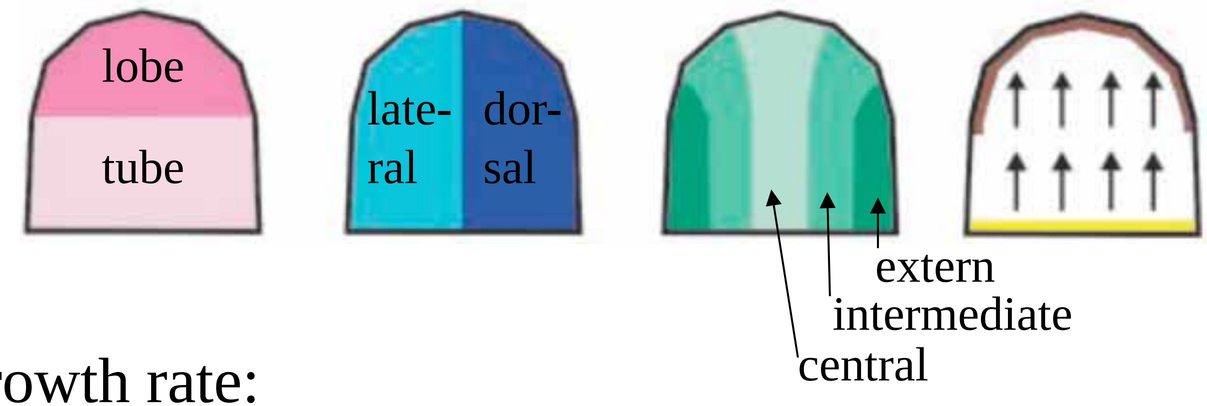
$$\varepsilon_{scale} = \frac{\Lambda}{2}.\mathbf{I} \qquad \Lambda = \frac{V - V_{ref}}{V_{ref}} \approx \lambda_1 + \lambda_2$$

$$\varepsilon_{ani} = {}^{T}\mathbf{RDR} \qquad \mathbf{D} = \begin{bmatrix} \frac{2\lambda_1}{\Lambda} & 0 \\ 0 & \frac{2\lambda_2}{\Lambda} \end{bmatrix}$$

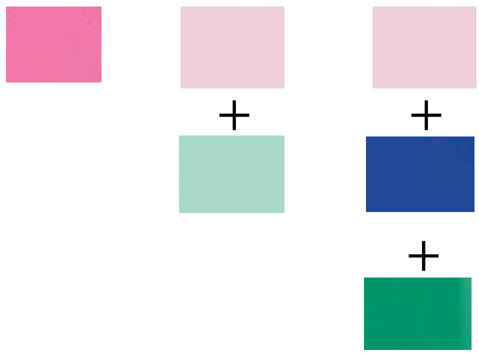


Development controlled by gene expression

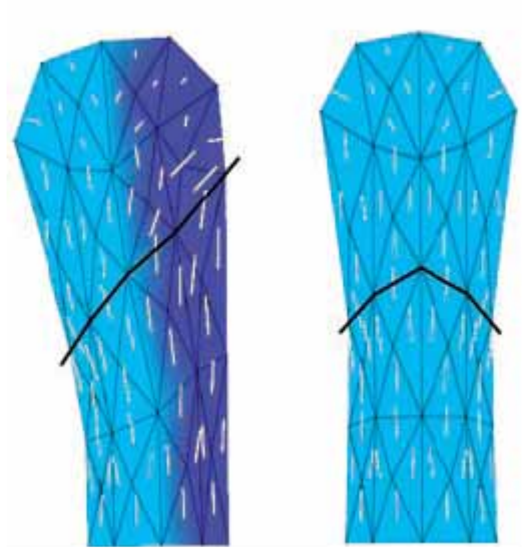
« *The genetics of geometry* », (Coen et al, PNAS, 2004)



- High growth rate:

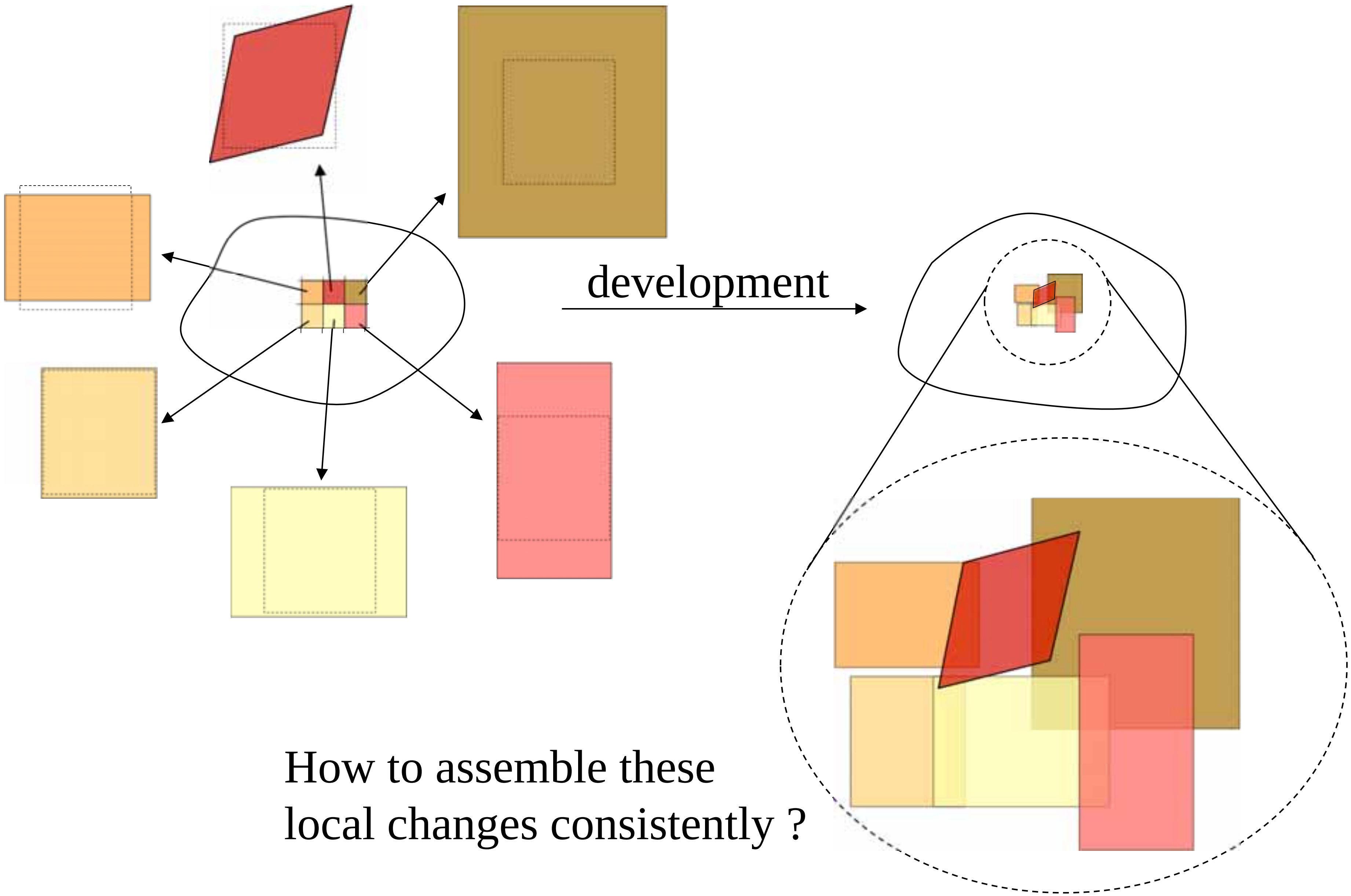


- High anisotropy:



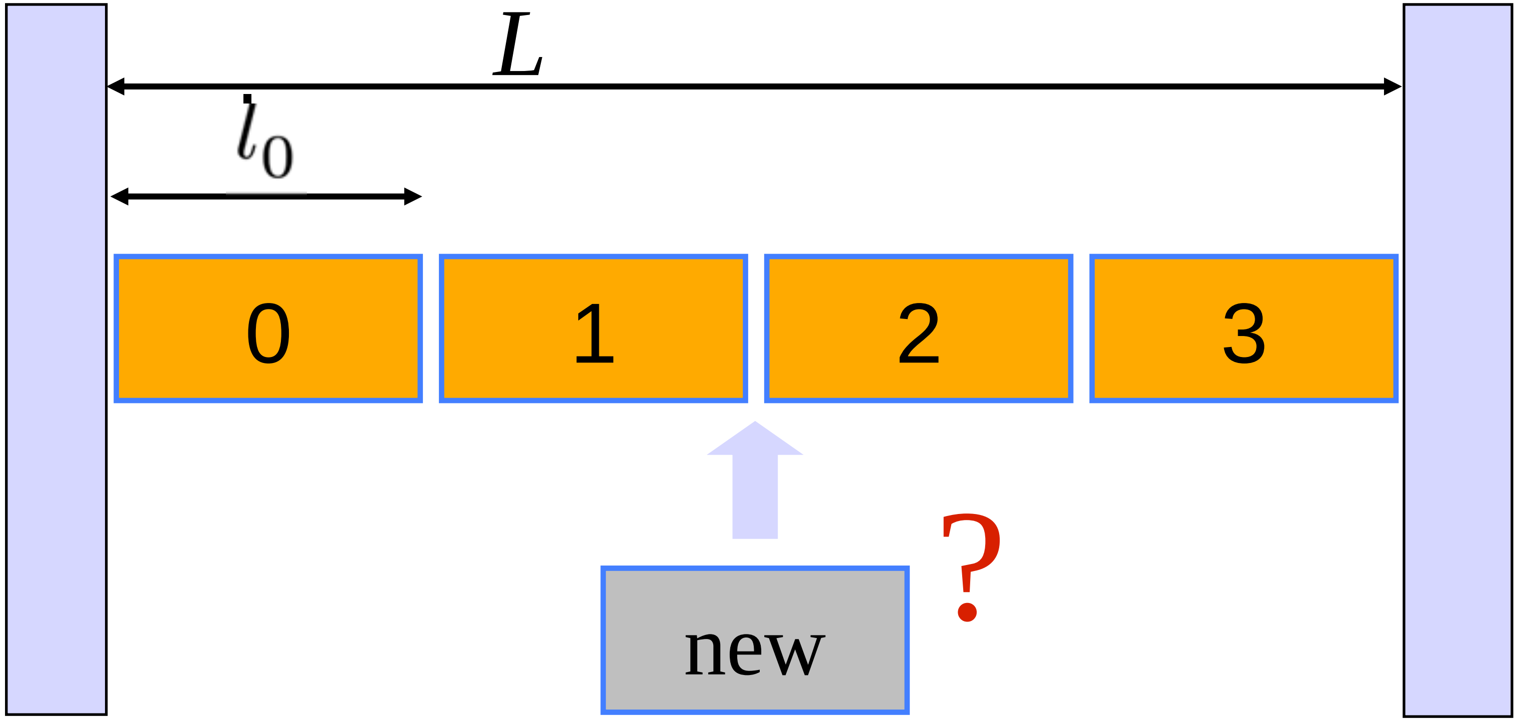
Modeling the growth of a petal shape

Integration of local changes



How to assemble these
local changes consistently ?

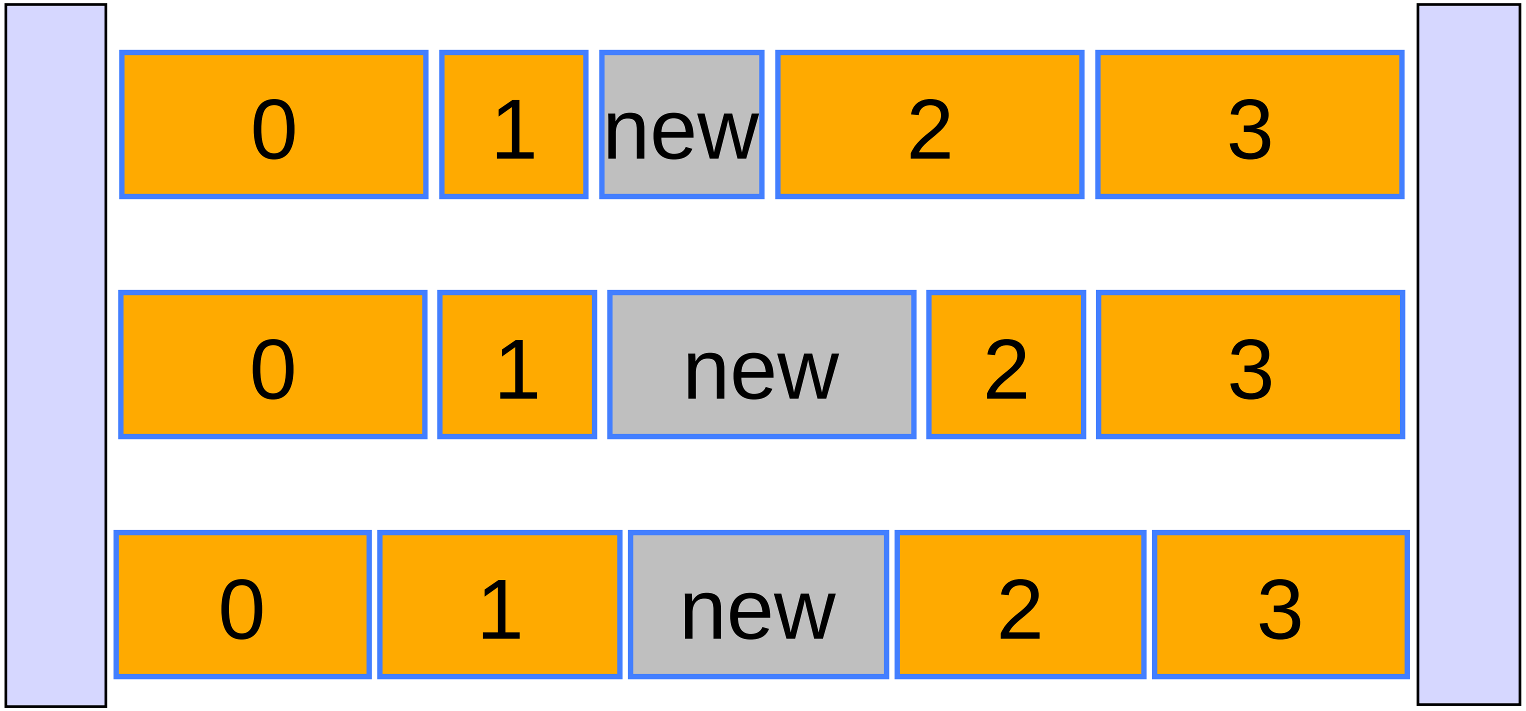
Deformation constraints



Geometric constraint: $$\sum_{i=0}^{n} l_i = L$$

Different admissible solutions

Different combinations:



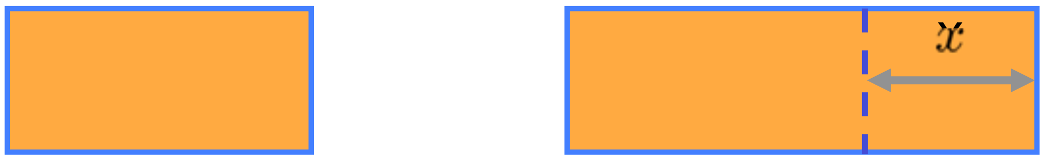
Cost of a deformation
(Energy)

Physical interpretation:

Translation

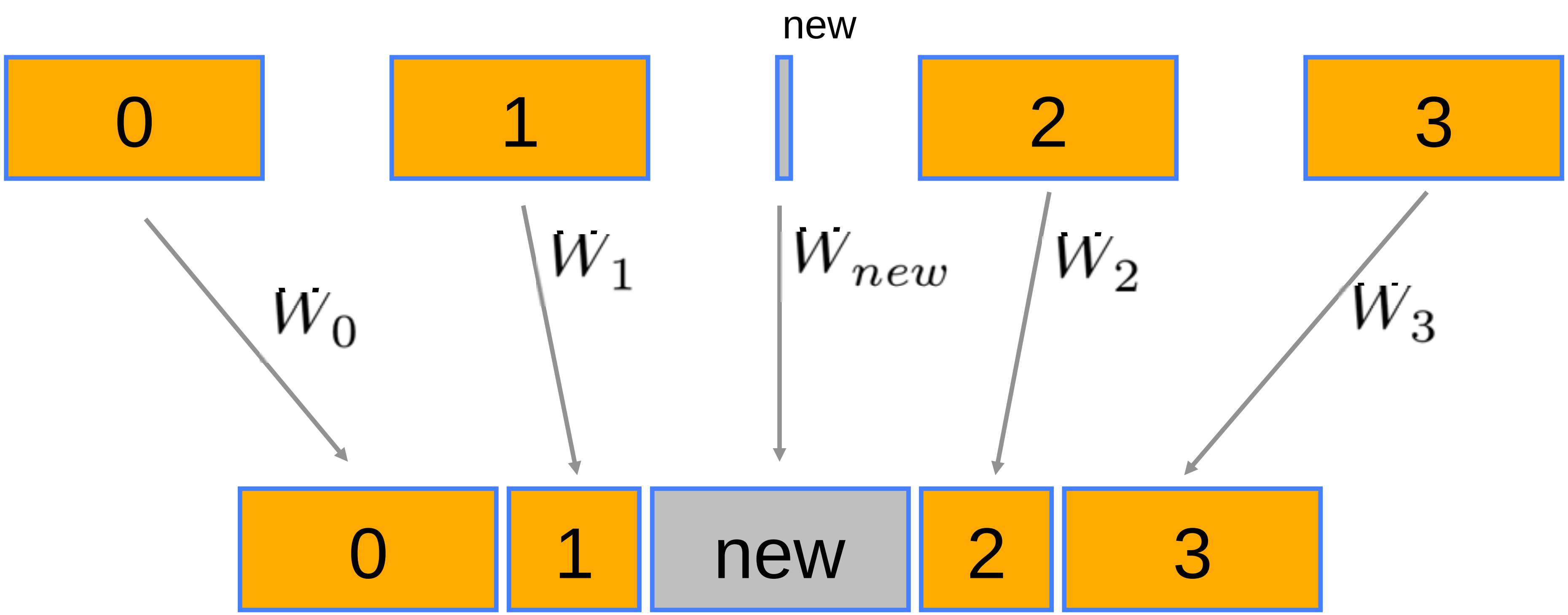
$$W = Mgh$$

Deformation



$$W = \frac{1}{2}kx^2$$

Total energy of a transformation

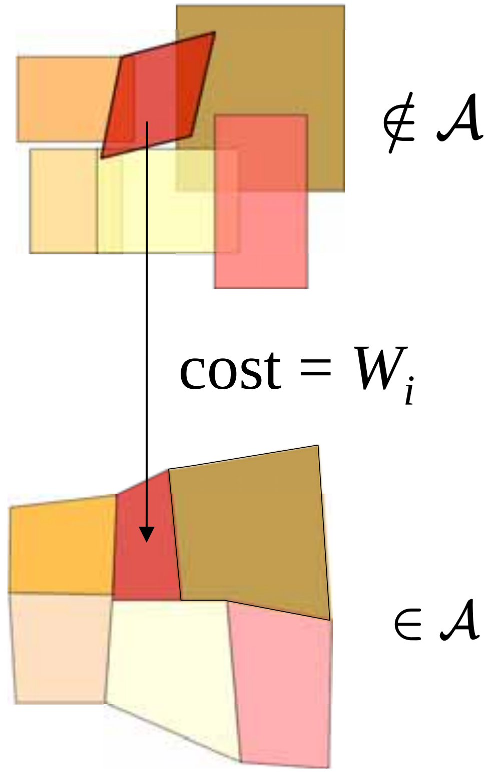


$$\dot{W} = \dot{W}_0 + \dot{W}_1 + \dot{W}_2 + \dot{W}_3 + \dot{W}_{new}$$

Solution : transformation with minimum energy

Integration

- Set of admissible deformations $\mathcal{A}$



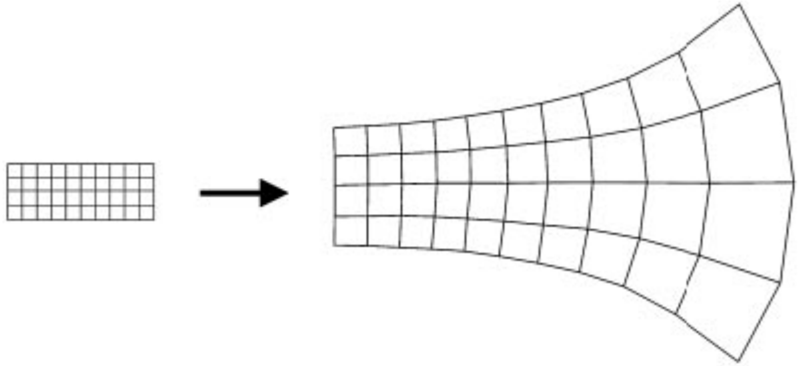
- Energy minimization over $\mathcal{A}$

$$W^* = \min_{a \in \mathcal{A}} \sum_{i \in a} W_i$$

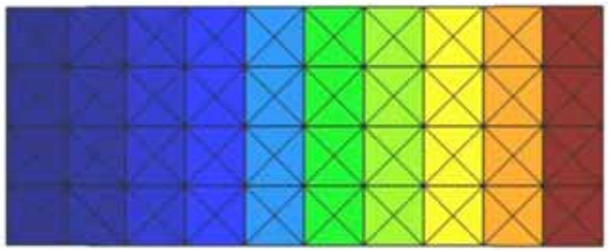
Use of integration methods:

- mass-spring systems
- finite elements

Mechanics and Differential growth



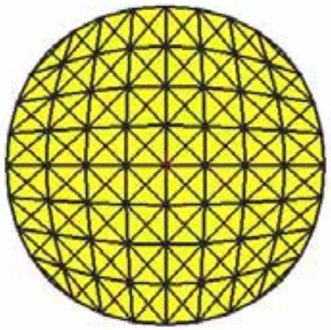
- Each region grows isotropically



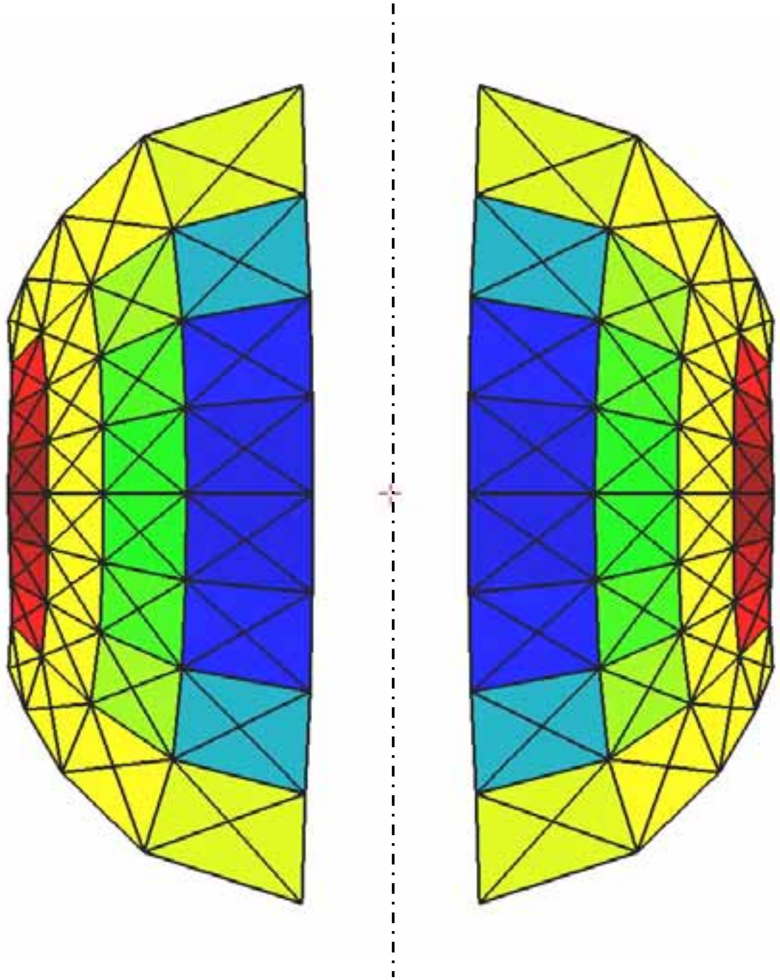
- Geometric anisotropy results from global constraints

Residual stresses

Growing "petal"



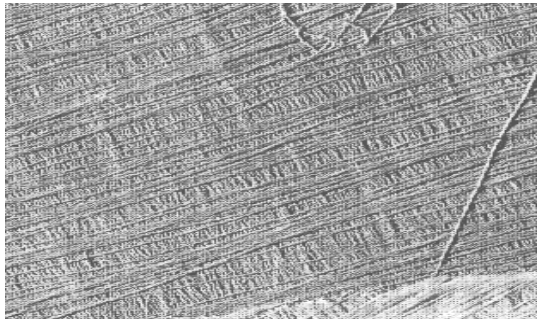
Problem of residual stresses



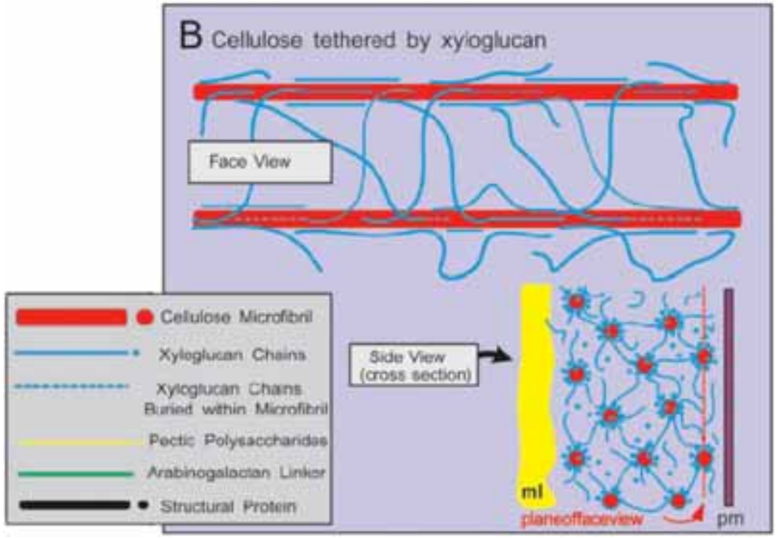
Solution: introduce a feedback of the stress on the growth

Cell wall

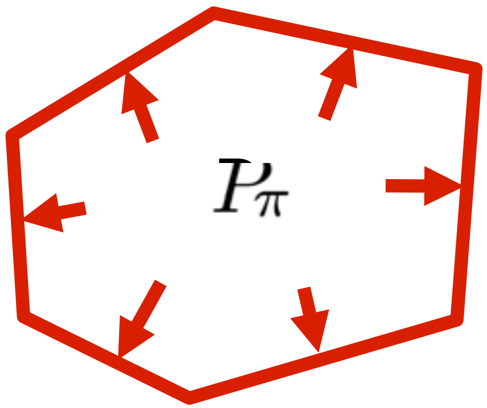
- Cell wall :
  - Main determinant of cell shape
  - Regularly synthesized by the cell
  - Composed of bundles of microfibrils linked together by elastic links



Cosgrove (2001)



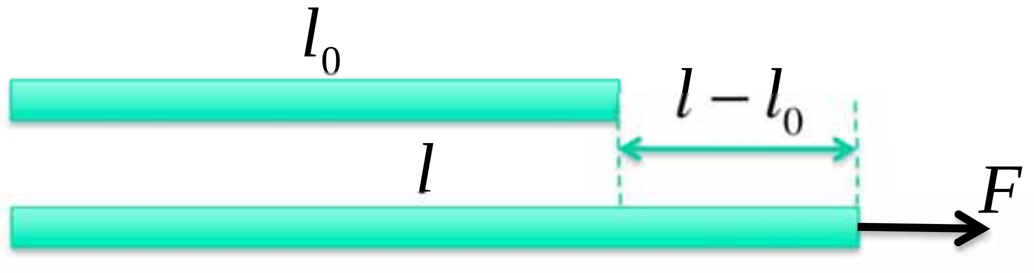
- Mechanical aspects:
  - Each microfibril resist axial load
  - Resistance perpendicular to microfibrils is less important
  - Turgor pressure induces cell wall strain



Individual cell growth

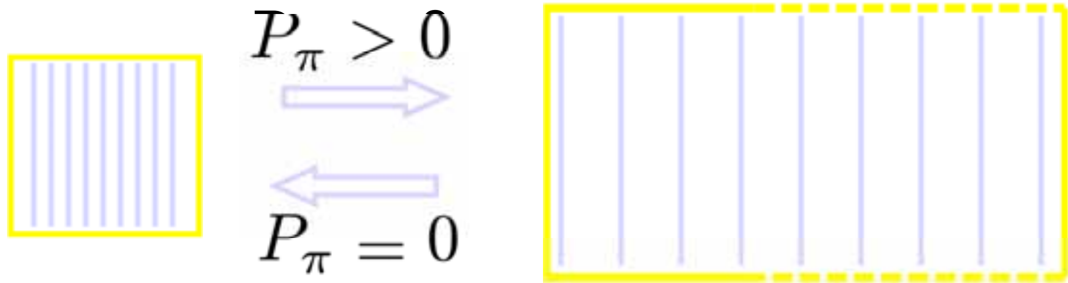
- Elasticity of a rod : Hook's law

$$\varepsilon = \frac{l - l_0}{l_0}$$



$$\sigma = \frac{F}{s} = E\varepsilon$$

- Cell is elastically deformed by turgor pressure



$$\sigma = P_\pi \mathbf{I} = \begin{bmatrix} P_\pi & 0 \\ 0 & P_\pi \end{bmatrix}$$

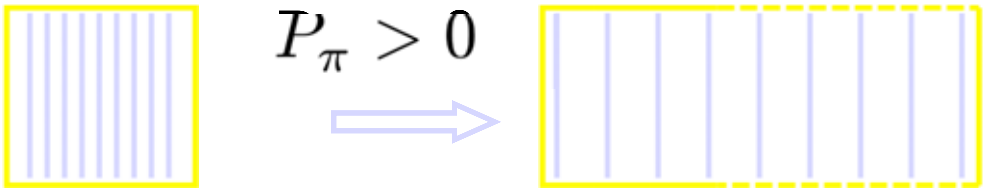
Stress in the region

$$\varepsilon_\pi = \sigma_\pi E^{-1} = P_\pi \begin{bmatrix} \frac{1}{E_x} & 0 \\ 0 & \frac{1}{E_y} \end{bmatrix}$$

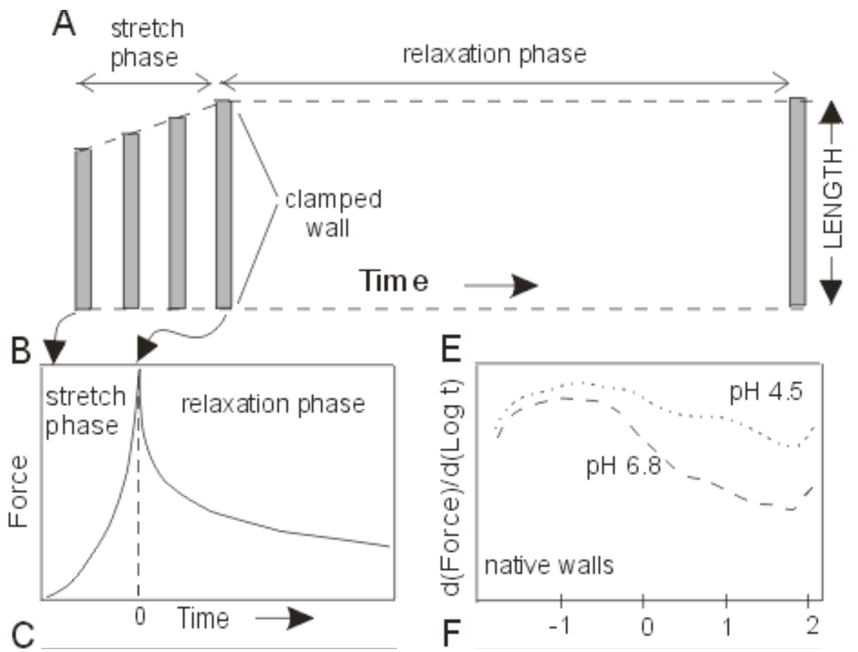
Elastic strain
(Hook's law)

Individual cell growth

- Cell deformation



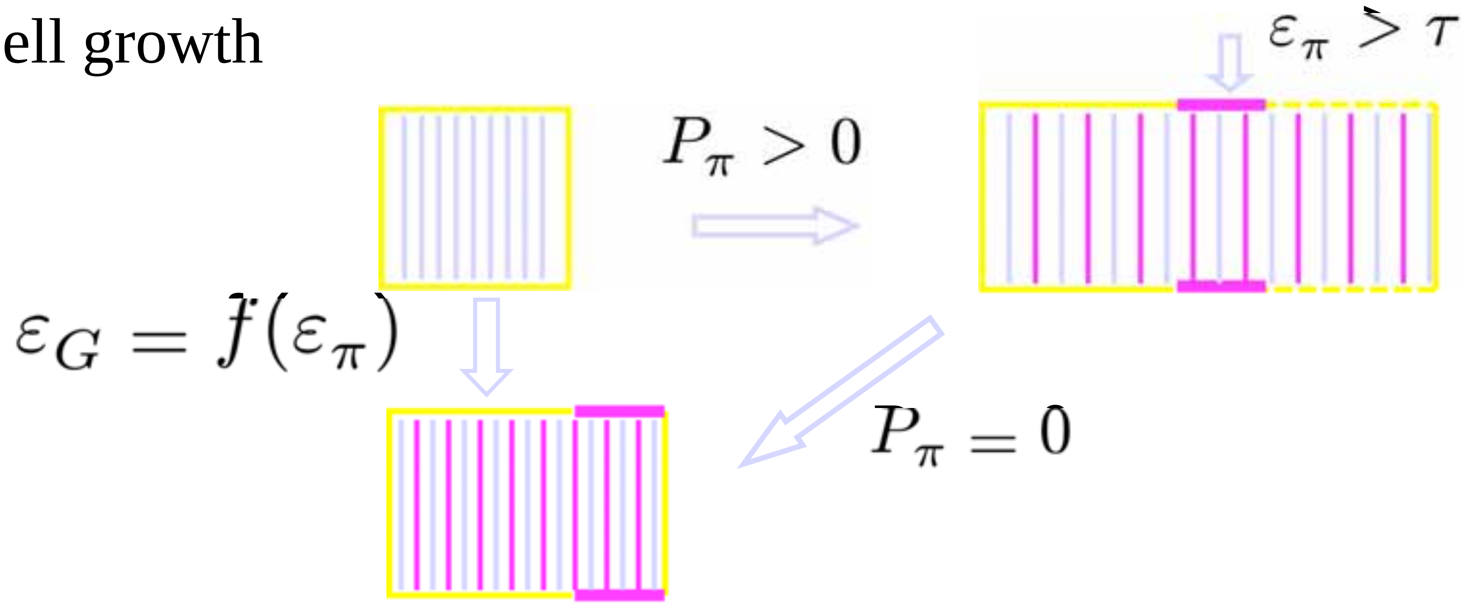
- Growth induces plastic deformations



(Cosgrove 98,01,03,04)

Taking into account cell growth

- Cell growth



Example: $\varepsilon_G = \Gamma \Delta t \; \varepsilon_\pi$

Wall synthesis speed   Elastic strain

$$\varepsilon_G = \Gamma \Delta t \; P_\pi \begin{bmatrix} \frac{1}{E_x} & 0 \\ 0 & \frac{1}{E_y} \end{bmatrix}$$

Mechanical interpretation of growth parameters

Growth strain of the reference configuration:

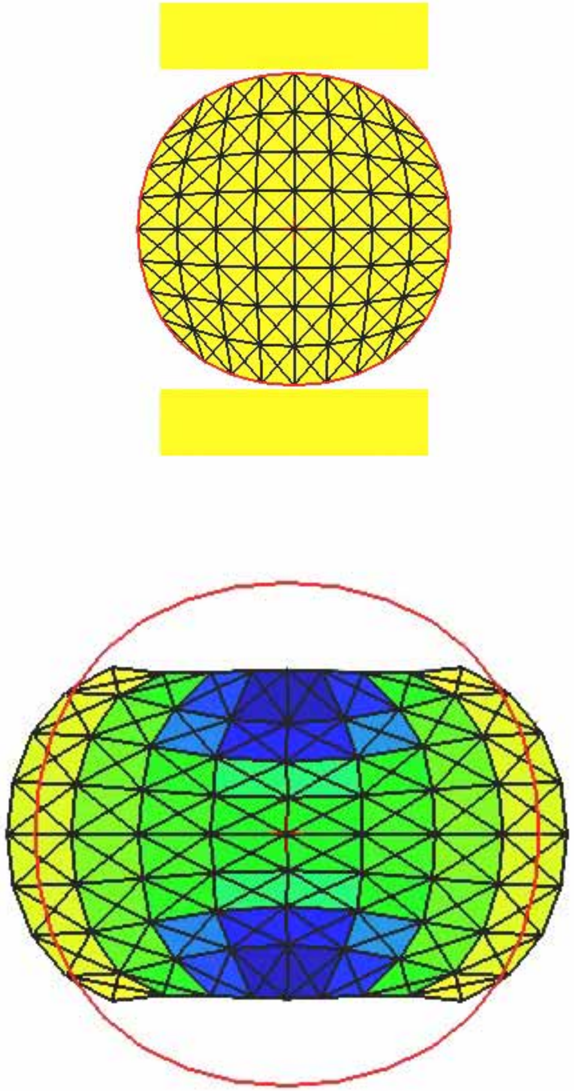
$$\varepsilon_G = \underbrace{\Gamma \Delta t P_\pi \frac{E_x + E_y}{2E_x E_y}}_{\varepsilon_{scale}} \underbrace{\begin{bmatrix} \frac{2E_y}{E_x + E_y} & 0 \\ 0 & \frac{2E_x}{E_x + E_y} \end{bmatrix}}_{\varepsilon_{ani}}$$

- Scaling represents the relative variation of volume $\frac{V - V_{ref}}{V_{ref}}$

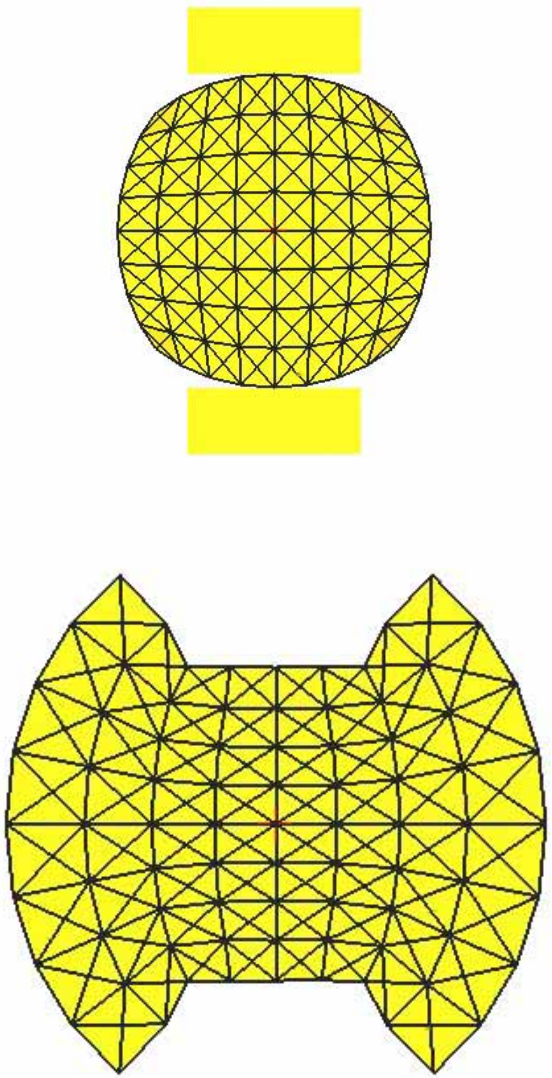
- Anisotropy distributes the growth along the principal axes

Simulation

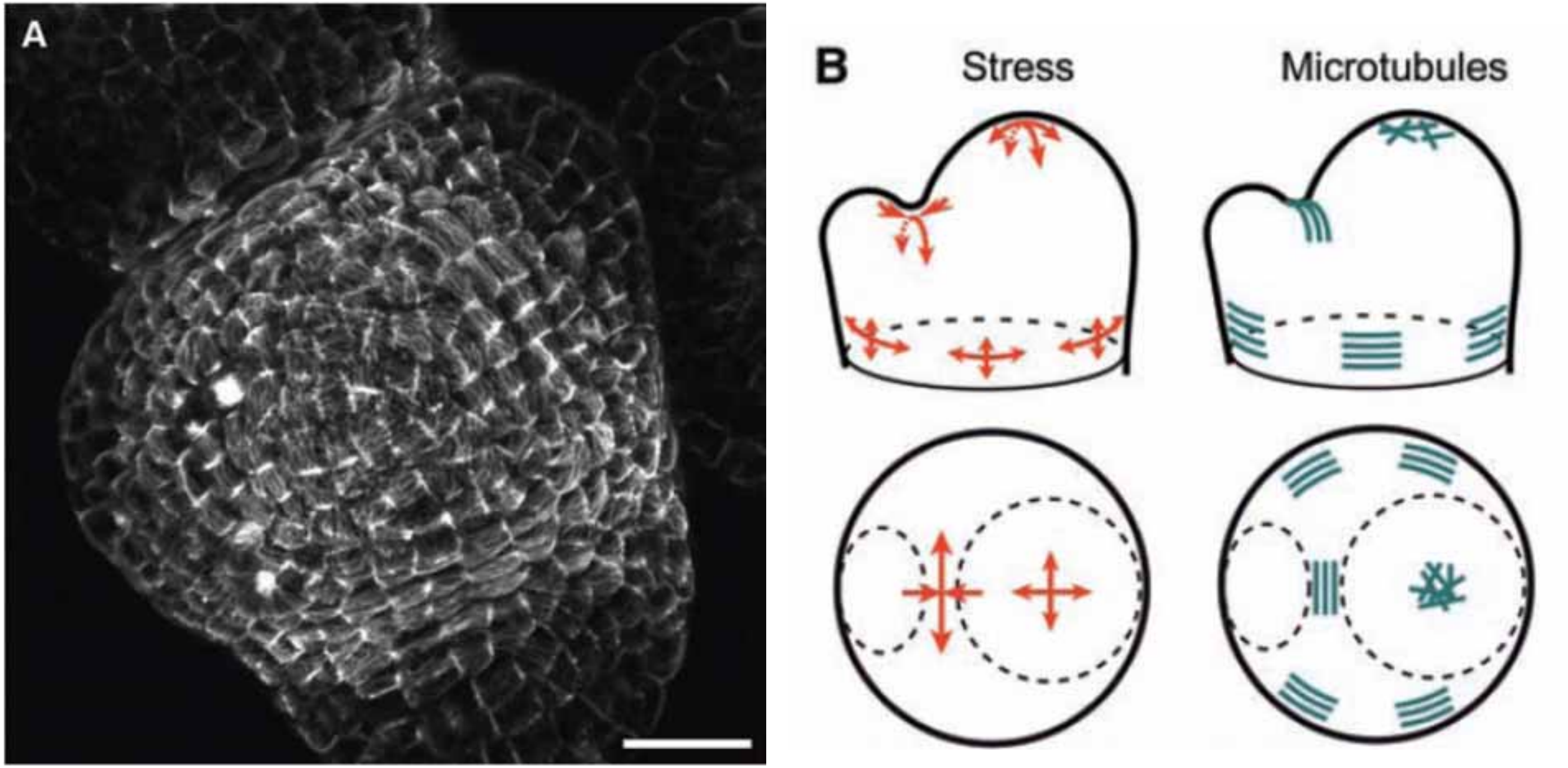
- Without retroaction



- With retroaction



Role of microtubules in growth



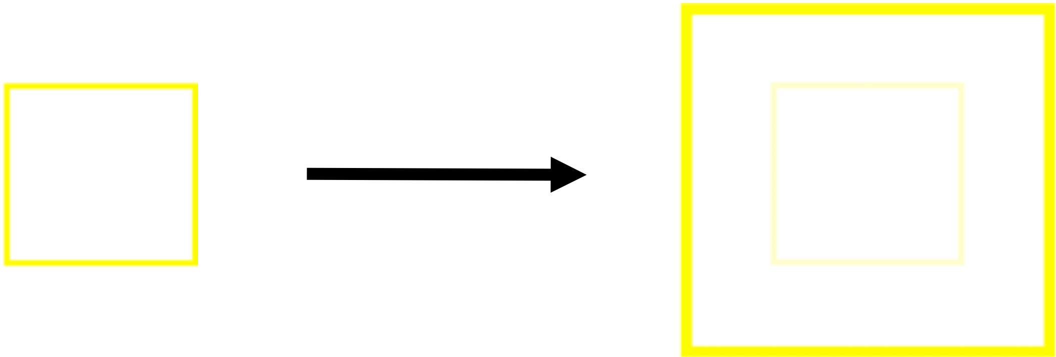
Microtubules re-orient according to main stresses

(Hamant et al., Sience, 2008)

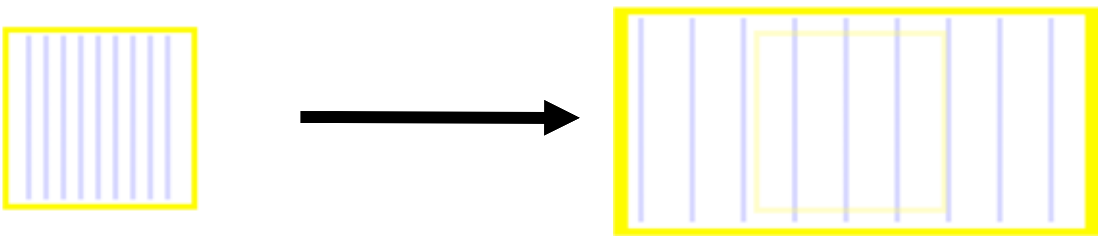
Cell growth decomposition

Cell growth is controled by 2 factors :

• Growth intensity (e.g hormone concentration, gene activity)

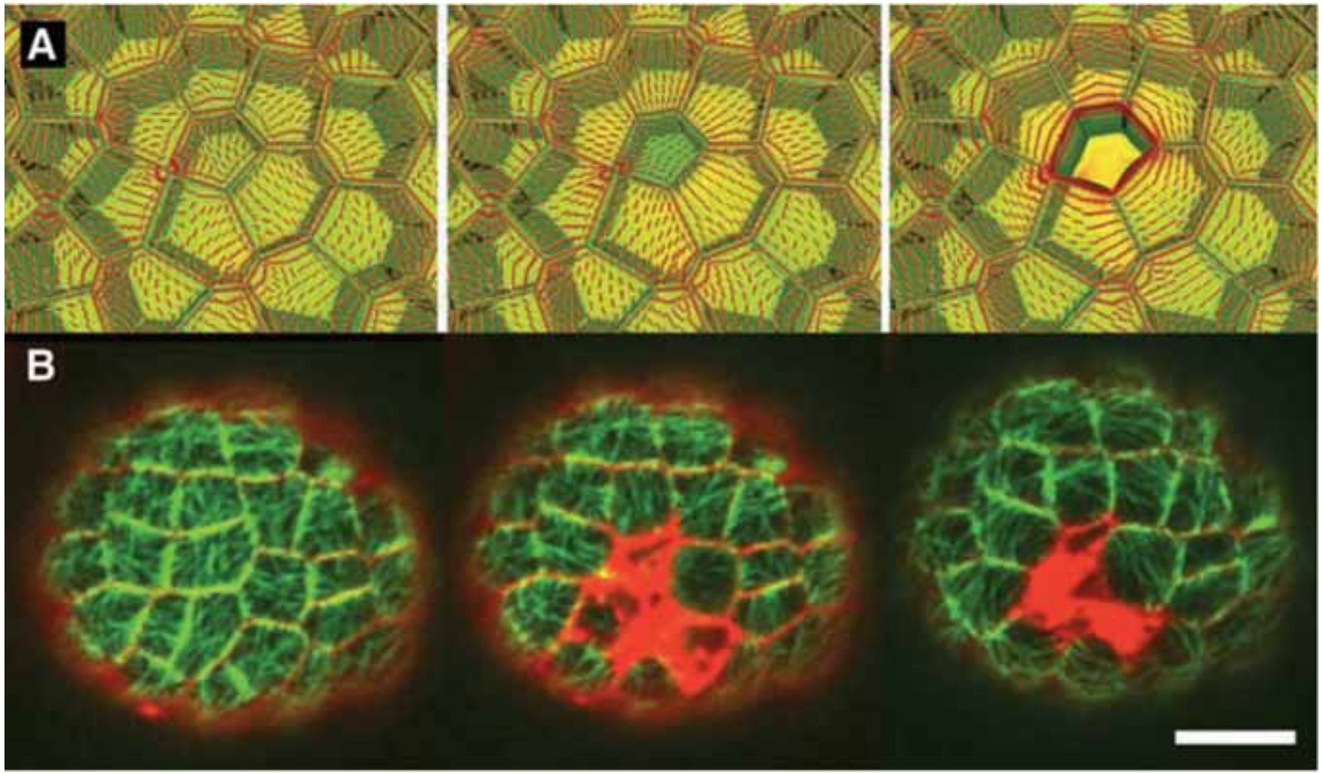


• Growth anisotropy (polarization of microtubules)



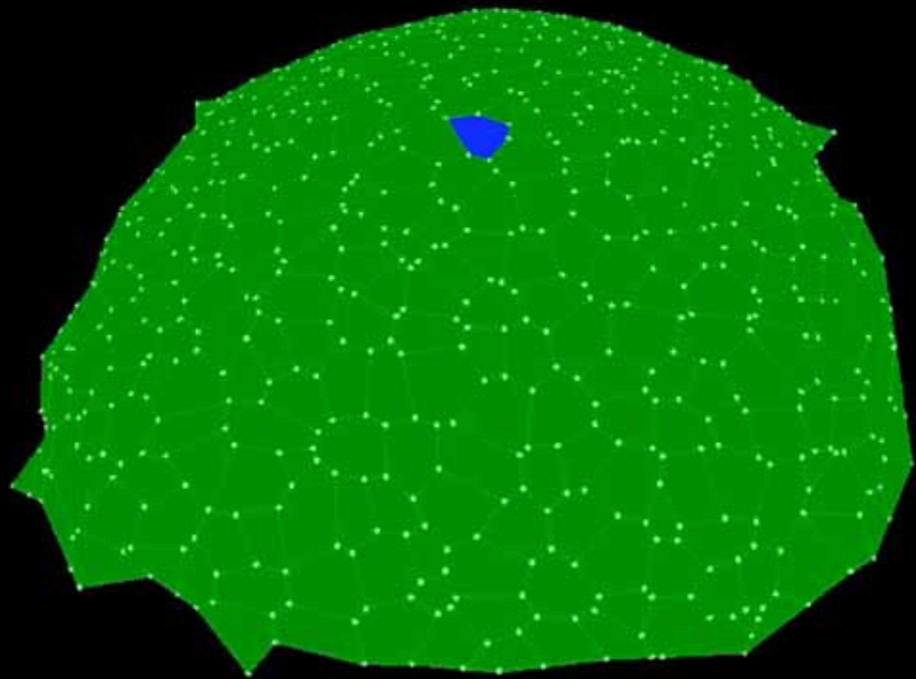
Modeling cell mechanics

Testing the hypothesis: microtubules re-orient according to main stress



(Hamant et al., Science 2008)

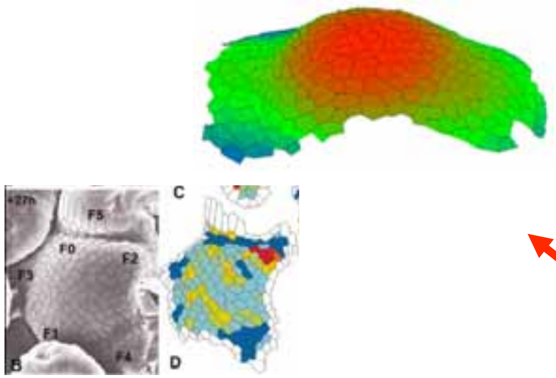
Simulation of the PIN experiment



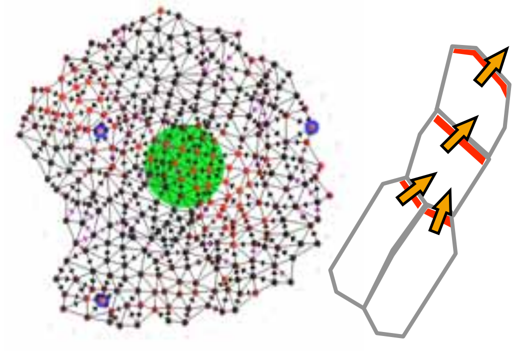
PhD Szymon Stoma

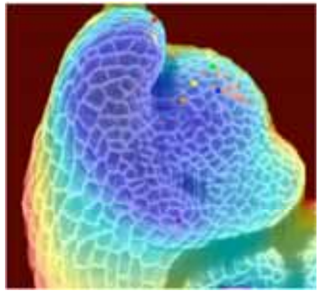
Building of a virtual meristem

1 – Geometric model

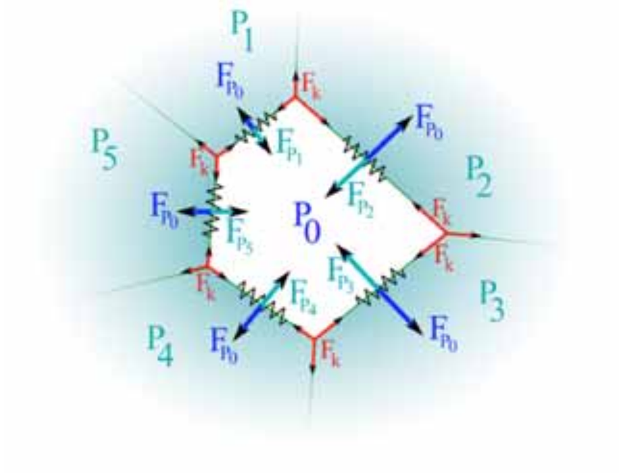


2 – Transport model



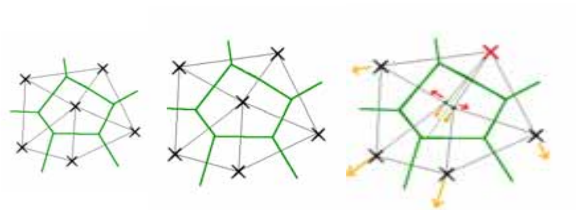


3 – Physical model

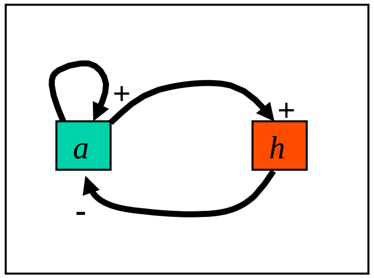


4 – Cell model

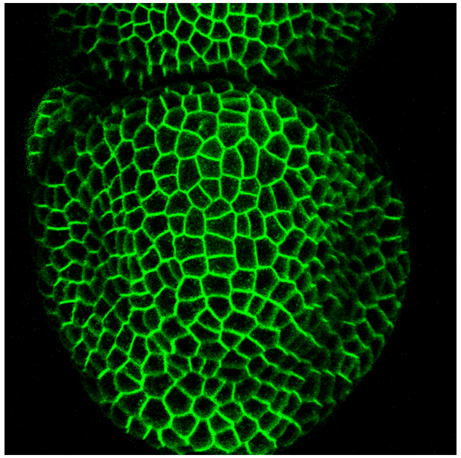
Division and Growth

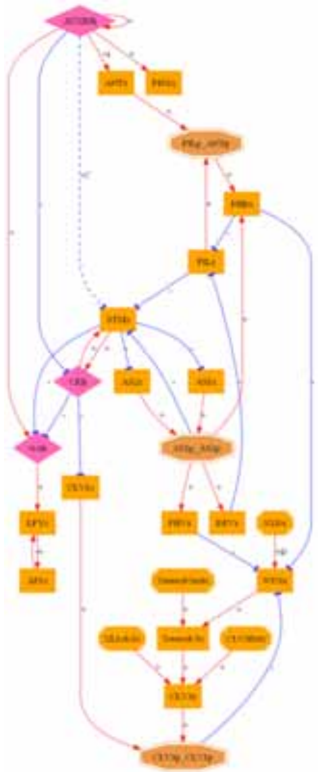


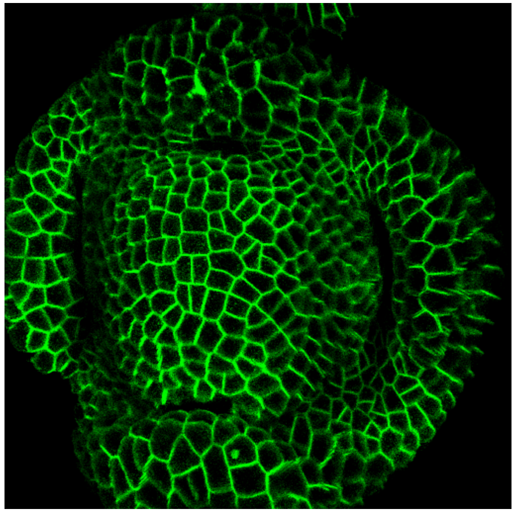
Interaction network



How genes control shape development ?







?

Gene networks

State of a cell: $$X(t) = {}^T[x_0(t), x_1(t), \ldots, x_n(t)]$$

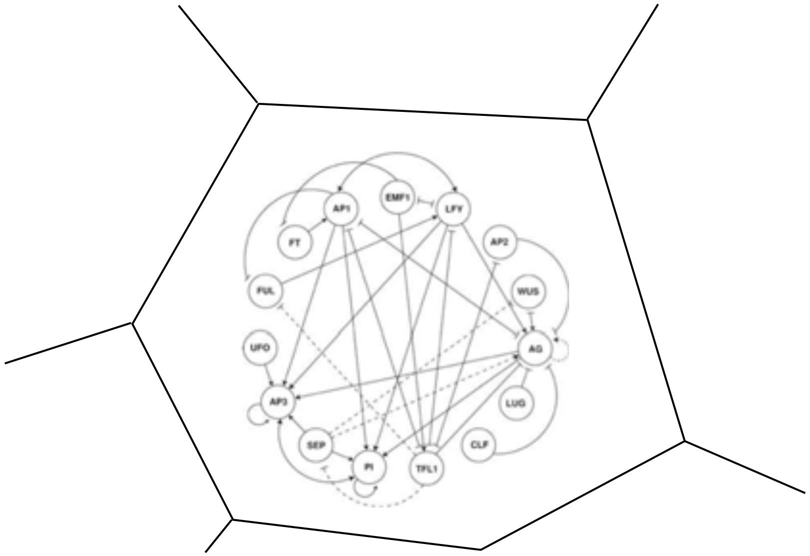
Activity level of gene 0

Activity level of gene 1

Activity level of gene *n*

Gene interaction network:

$$X(t+1) = F(X(t))$$



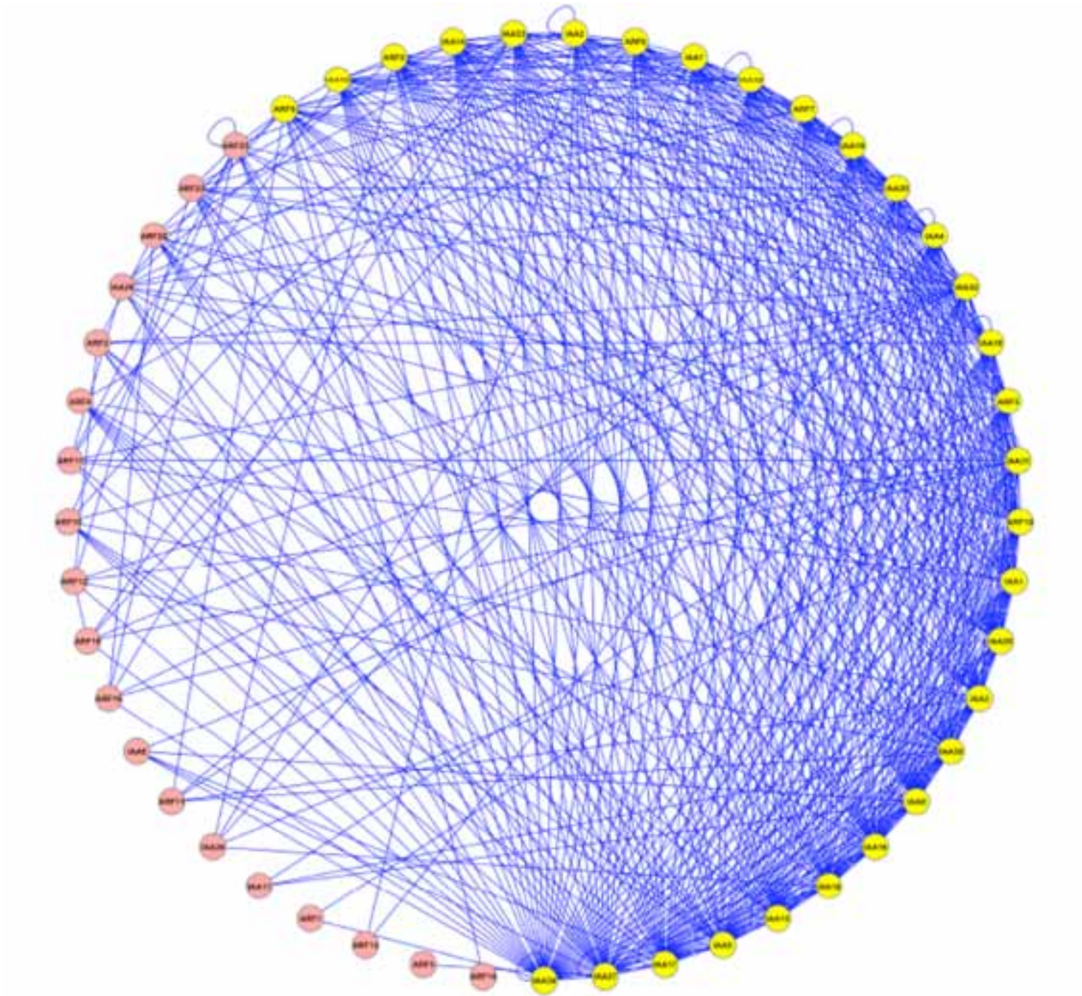
- Stable ?
- Attractors ?

$\boxed{\text{Cell identity = 1 stable state}}$

Gene Regulatory Networks

Example: <u>Auxin perception </u>(collab. T. Vernoux):

Auxin regulates gene expression via a network of protein-protein interactions

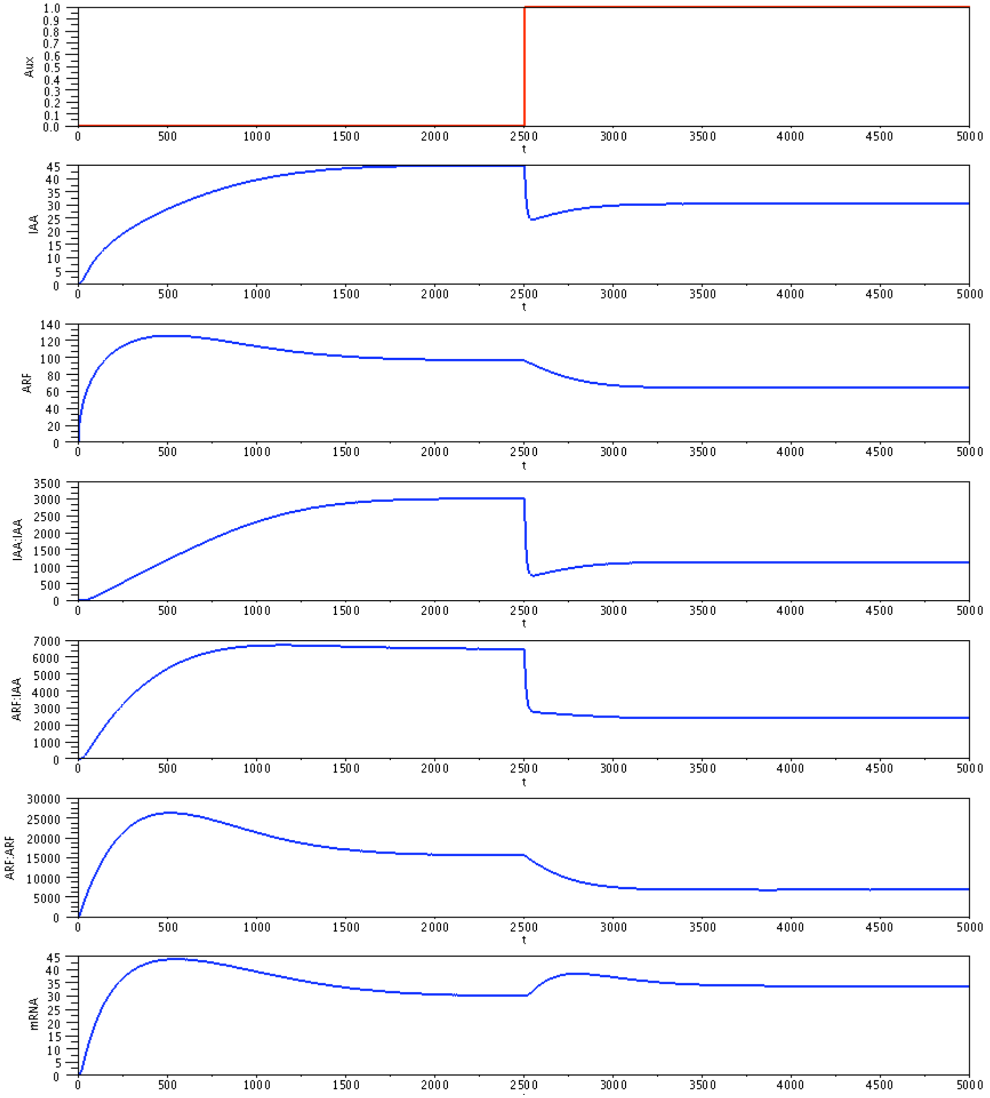


Product variation described by differential equations

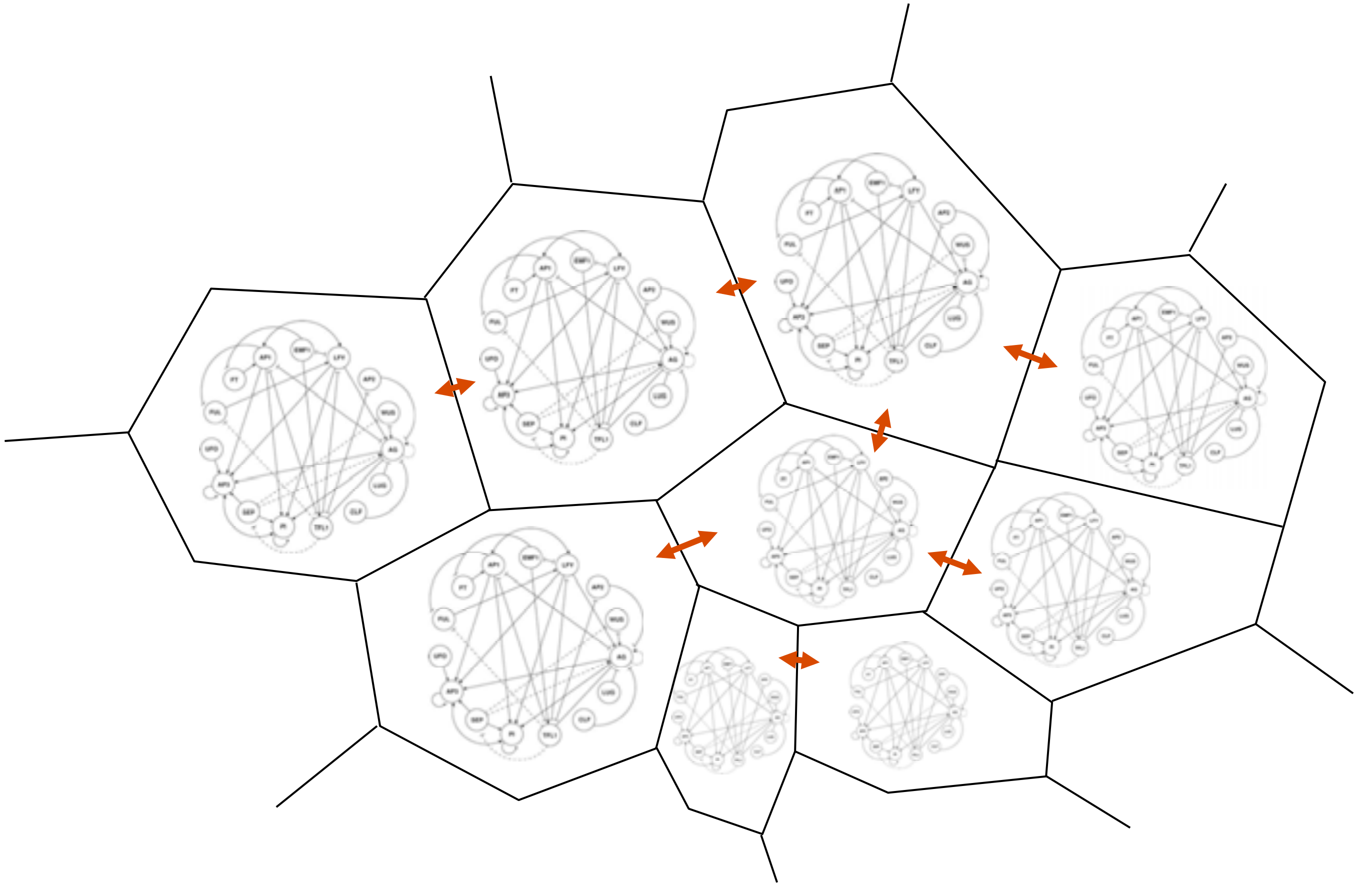
$$\begin{aligned}
\frac{da_1}{dt} &= \pi_1 r + 2k'_{11}d_{11} - 2k_{11}a_1^2 + k'_{12}d_{12} - k_{12}a_1a_2 - \delta_1(x)a_1 \\
\frac{da_2}{dt} &= \pi_2 + 2k'_{22}d_{22} - 2k_2a_2^2 + k'_{12}d_{12} - k_{12}a_1a_2 - \delta_2a_2 \\
\frac{d(d_{11})}{dt} &= k_{11}a_1^2 - (k'_{11} + \delta_{11})d_{11} \\
\frac{d(d_{12})}{dt} &= k_{12}a_1a_2 + \beta'_{12}g_{12} - \beta_{12}gd_{12} - (k'_{12} + \delta_{12})d_{12} \\
\frac{d(d_{22})}{dt} &= k_{22}a_2^2 + \beta'_{22}g_{22} - \beta_{22}gd_{22} - (k'_{22} + \delta_{22})d_{22} \\
\frac{dr}{dt} &= h(g_{22}) - \delta_r r \\
\frac{dg_{22}}{dt} &= \beta_{22}gd_{22} - \beta'_{22}g_{22} \\
\frac{dg_{12}}{dt} &= \beta_{12}gd_{12} - \beta'_{12}g_{12} \\
g &= 1 - g_{12} - g_{22}
\end{aligned}$$

Where : a_1 (resp. a_2) denotes IAA (resp. ARF) concentration, and d_{ij} (resp. g_{ij}) the corresponding free (resp. DNA bound) dimers.
The function h for mRNA (r) production is Michaelis-Menten or Hill like.

Stationary state of differential equations



Scaling up : a network of network

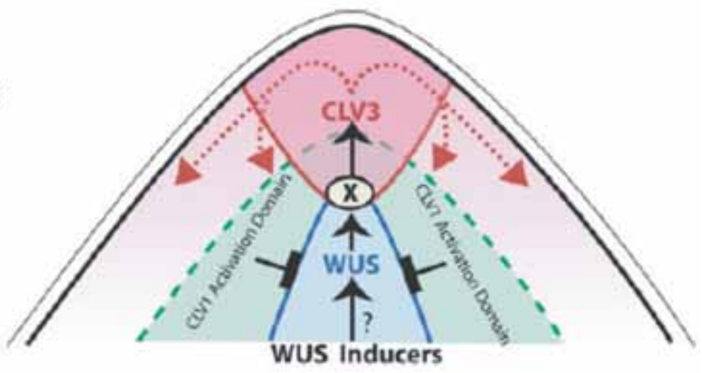


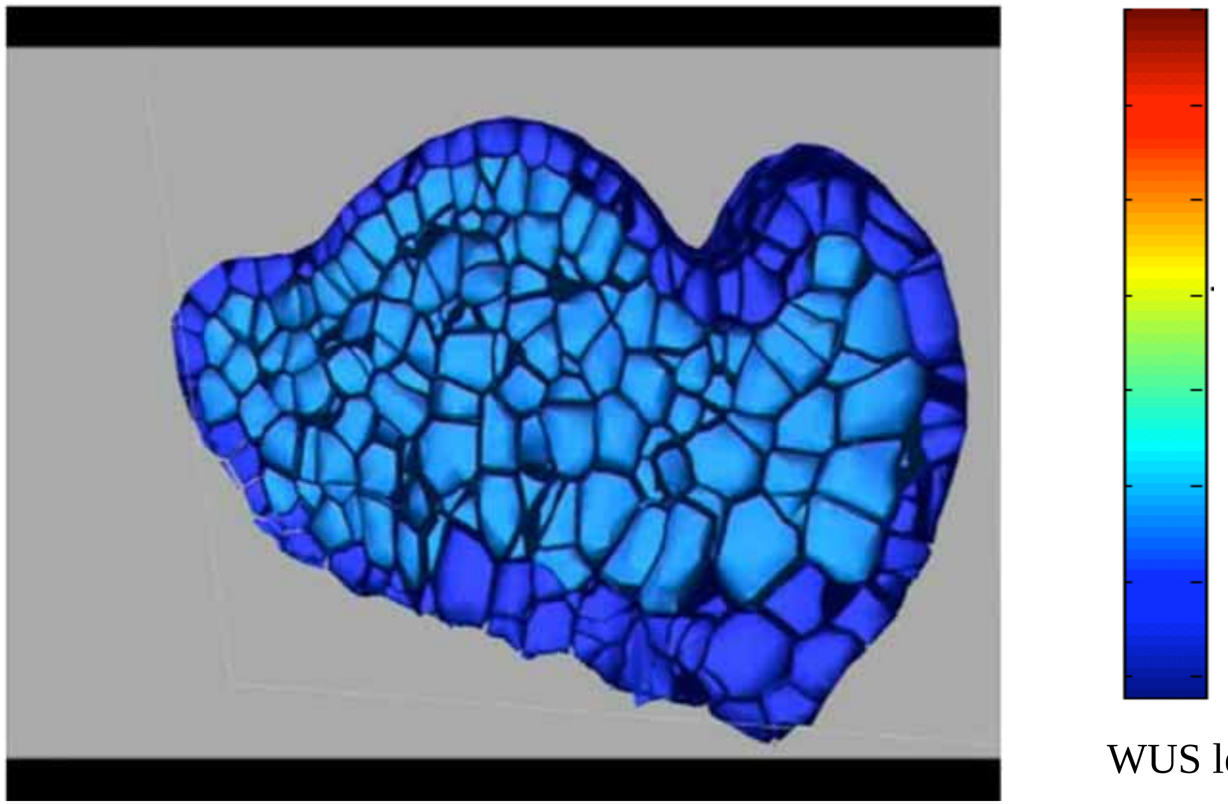
$$X_i(t+1) = F(X_i(t), \{X_j(t)\}_{j \in N(i)})$$

Multiscale Gene Regulatory Networks

Multiscale gene interaction networks (Y. Refahi PhD):

- implementation of 3D simulation tools
- meristem reconstruction & representation

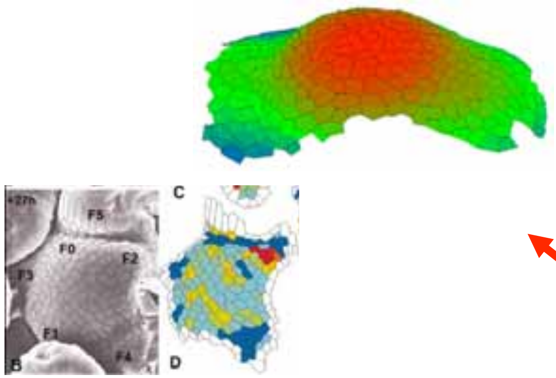




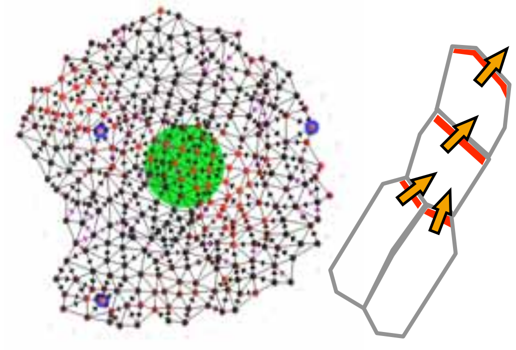
WUS level

Building of a virtual meristem

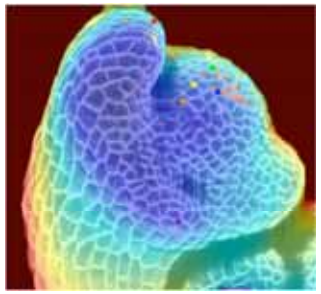
1 – Geometric model



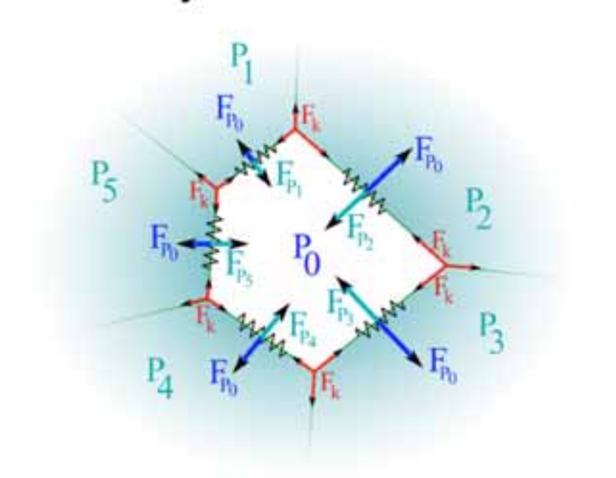
2 – Transport model



5.Integration

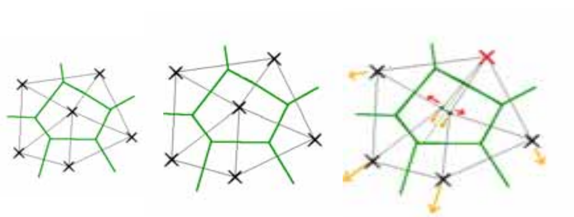


3 – Physical model

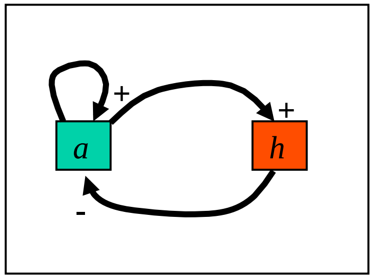


4 – Cell model

Division and Growth



Interaction network



5 – Structure-function integration

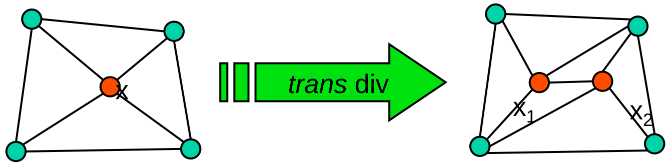
- **Integrate processes at different time scales**

Pin orientation << Auxin flux << cell growth ~ mechanics

- **Dealing with missing information**
  - design choices, bibliography, sensitivity analysis
  - model inversion : $X=M(p)$. For X_0 find p_0 such that $|X_0-M(p_0)|$ is minimum

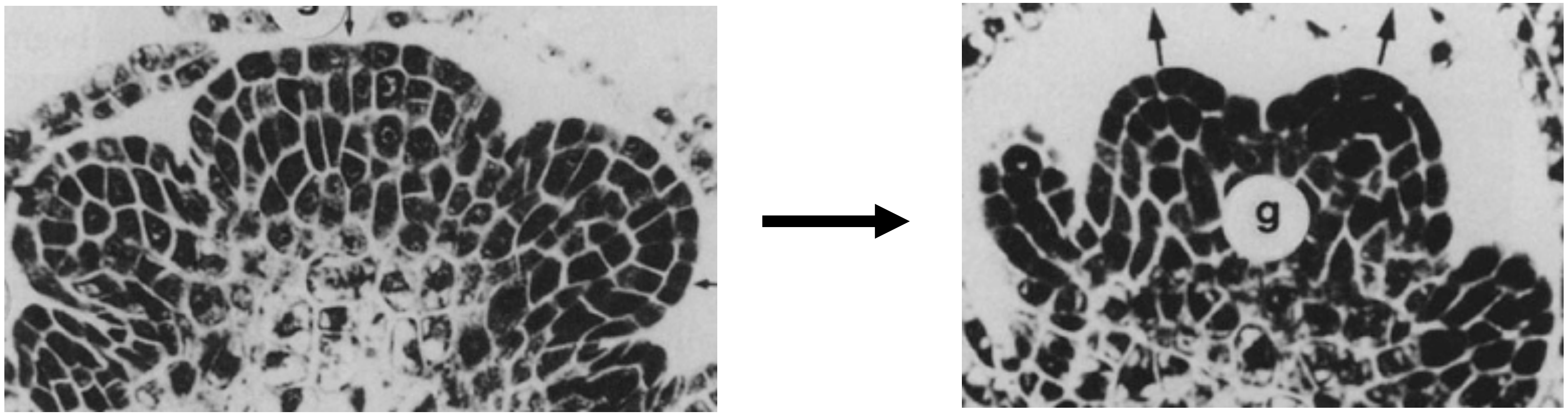
- **Programming language for $(DS)^2$**

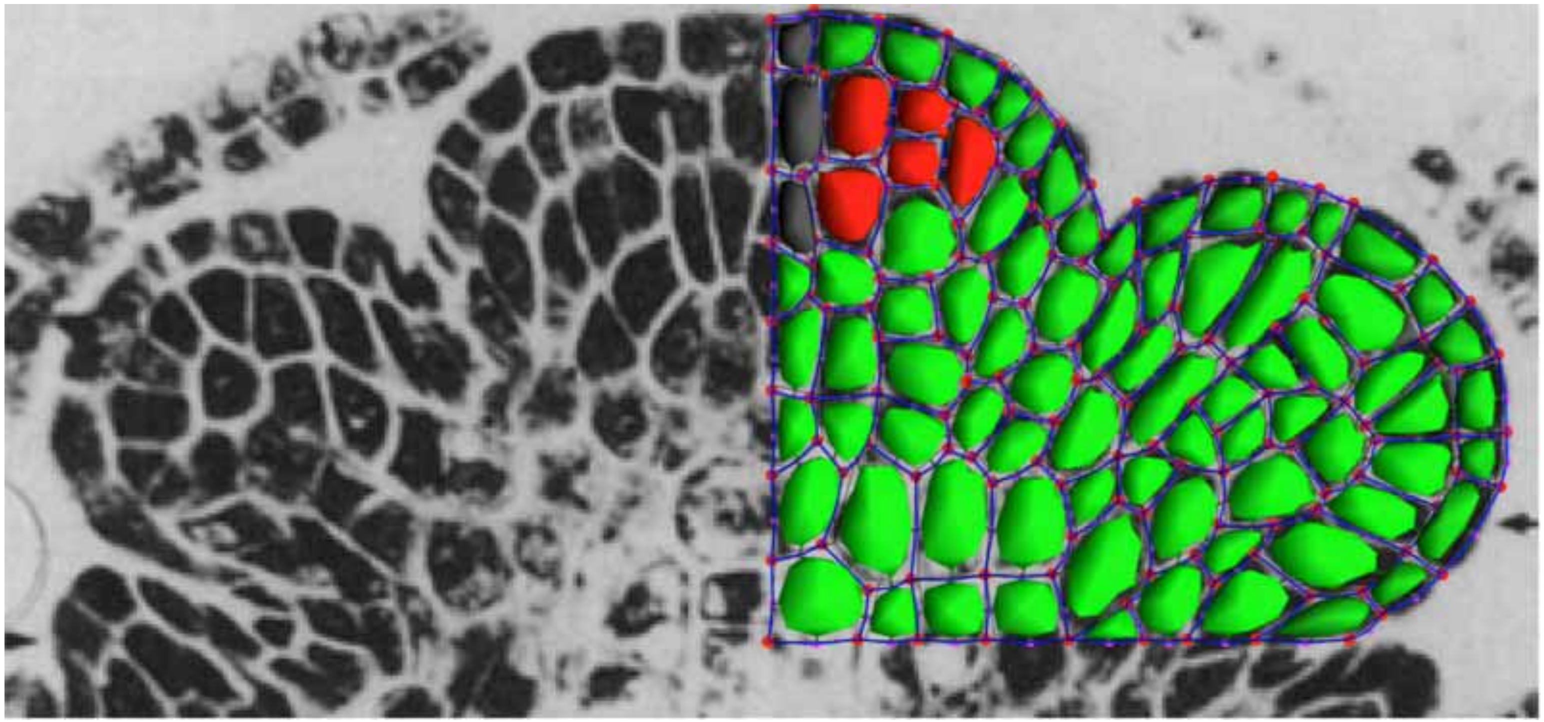
Procedural vs declarative languages (*MGS, L-Systems, VV, …*)



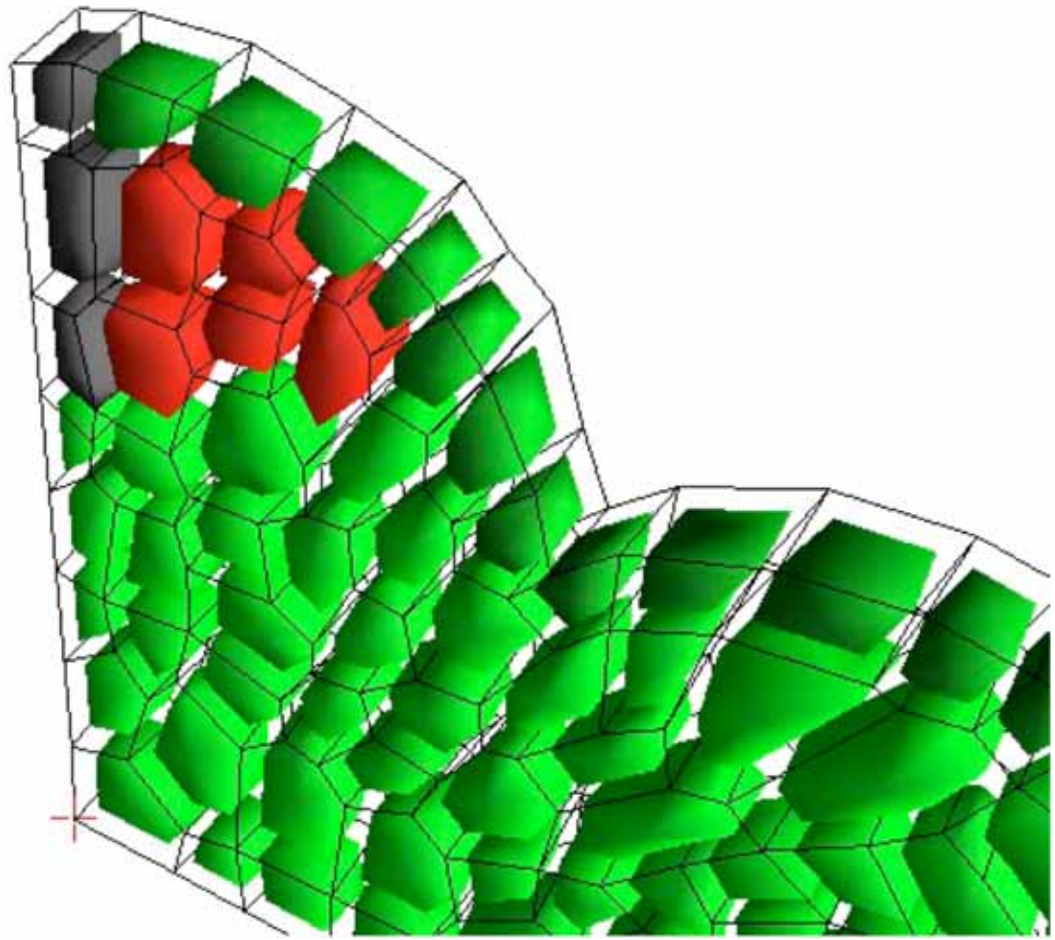
$$trans\ \mathrm{div} = \left\{ x \,/\, dividing(x) \Rightarrow child(x,1), child(x,2) \right\}$$

A first approach of carpel development





Growth Simulation (real time =10h)



Acknowledgements

Virtual Plants (Montpellier):





Etienne Farcot

Jérôme Chopard (Post-doc)

Szymon Stoma (PhD Student)

Mikael Lucas (PhD Student)

Romain Fernandez (PhD Student)

(Pierre Barbier de Reuille)

ENS-RDP (Lyon):

Jan Traas
(ENS-Lyon/INRA)

Pradeep Das
(ENS –Lyon)

Françoise Monéger
(ENS-Lyon)

Olivier Hamant
(INRA)

Teva Vernoux
(CNRS)

INRIA (Sophia-Antipolis) :

Grégoire Malandain
(Asclepios, INRIA Sophia-Antipolis)