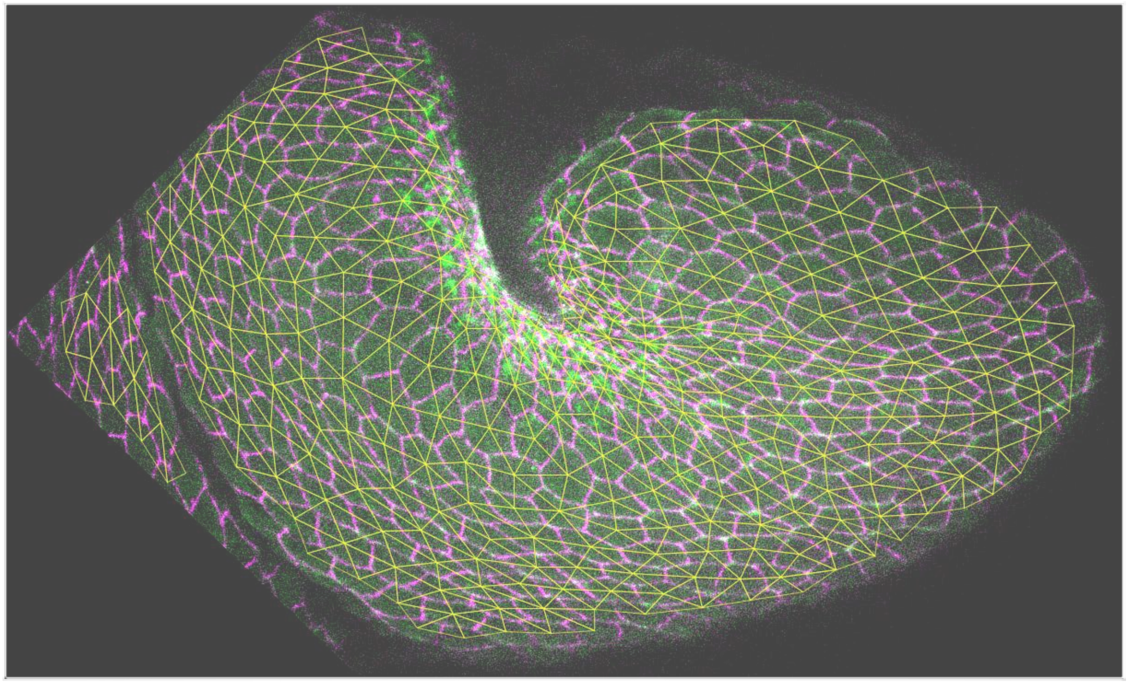
Morphogenesis: space, time, information



Course 1: Introduction — Control and Self-Organisation

Thomas Lecuit
chaire: Dynamiques du vivant

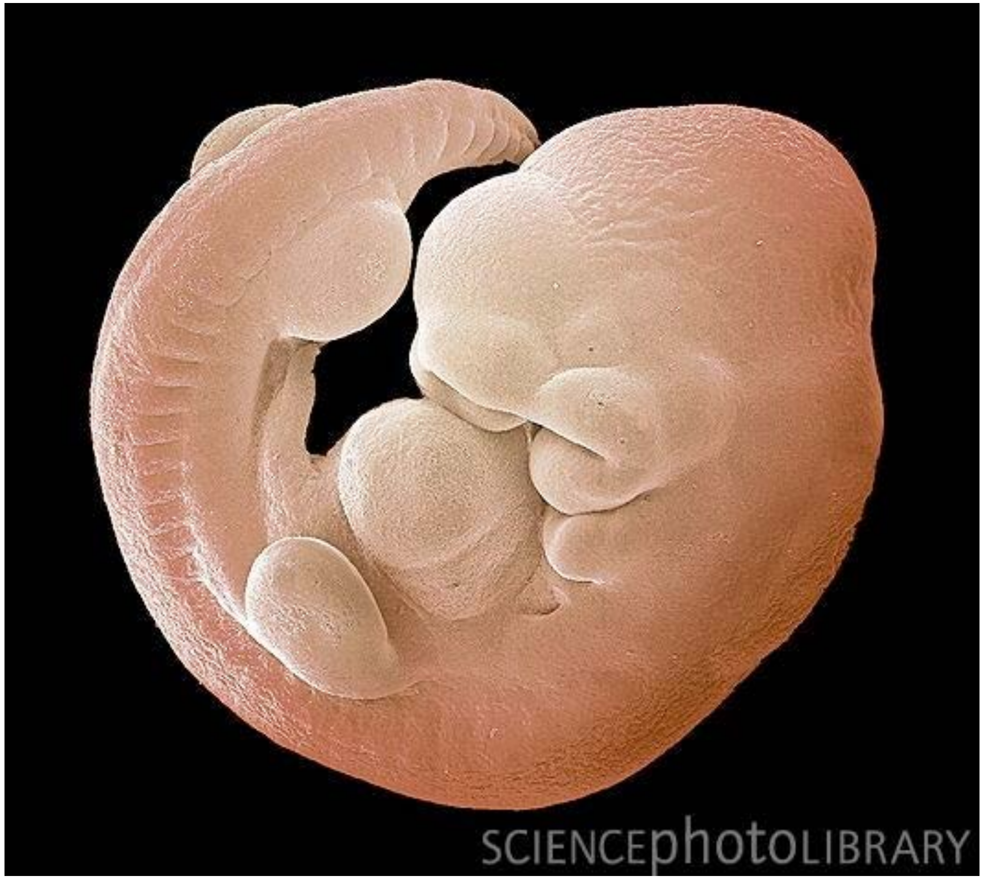
COLLÈGE DE FRANCE
1530

How to account for the emergence of complex shapes?

- Stability of forms
- Intrinsic dynamics
- Information

→

Growth
Shape
Control

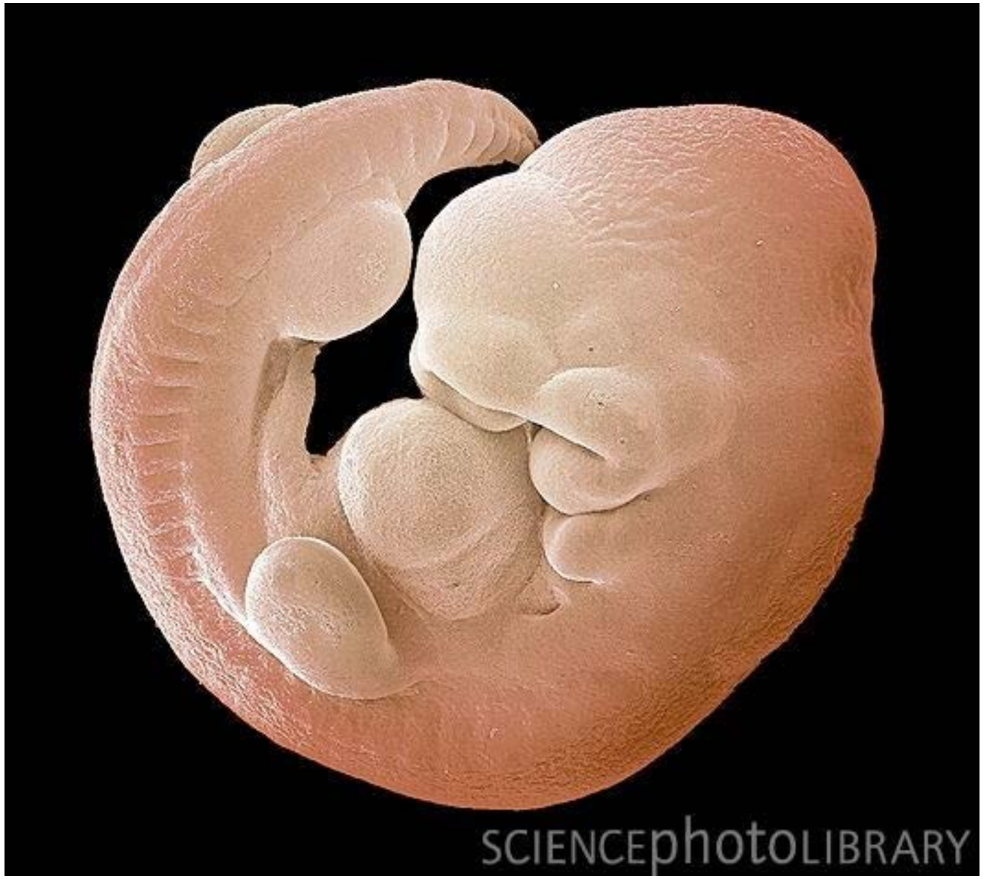


How to account for the emergence of complex shapes?

2017
- Stability of forms
- Intrinsic dynamics

2018
- Information: mechano-chemical

Growth
Shape
Control

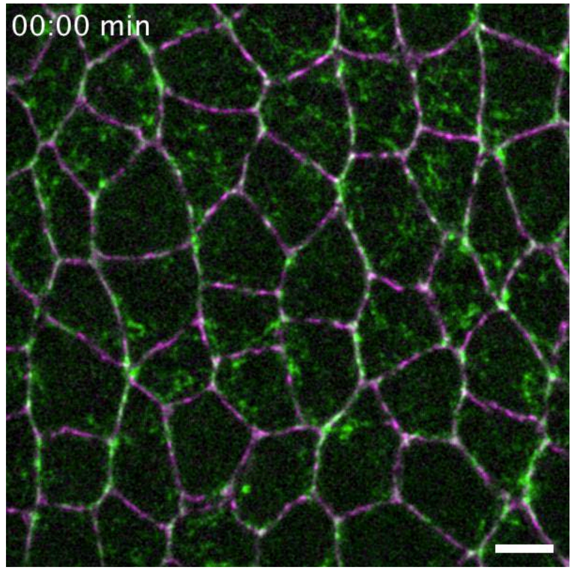


Key notions from last year

Tissue mechanics: principles

- Stability of forms
- Intrinsic dynamics

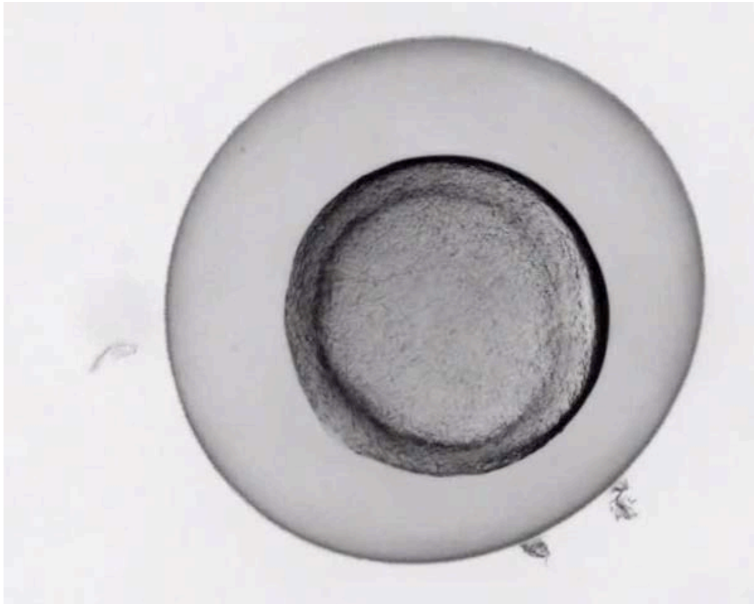
- Tissue cohesion and plasticity
- Properties of cell interactions: adhesion and tension
- Cell connectedness (adhesion) varies across tissues
- **Cell-cell Adhesion:** an active process
  1. Equilibrium models: from affinity to the description of tissues as fluids with surface tension
  2. Adhesion as an active, out-of-equilibrium process: role of coupling to contractile actomyosin networks.
  3. Importance of dissipation: irreversibility.
- **Cellular tension:** also an active process
  4. Membrane tension
  5. Cortical tension
- Interplay between adhesion and tension underlies balance between cohesion and plasticity: tension reinforces or remodels adhesive interfaces (shear versus tensile stress?)



E-cadherin::GFP Myosin-II::Cherry

Development: Cell behaviours are organised in space and time

Sea Urchin Embryo



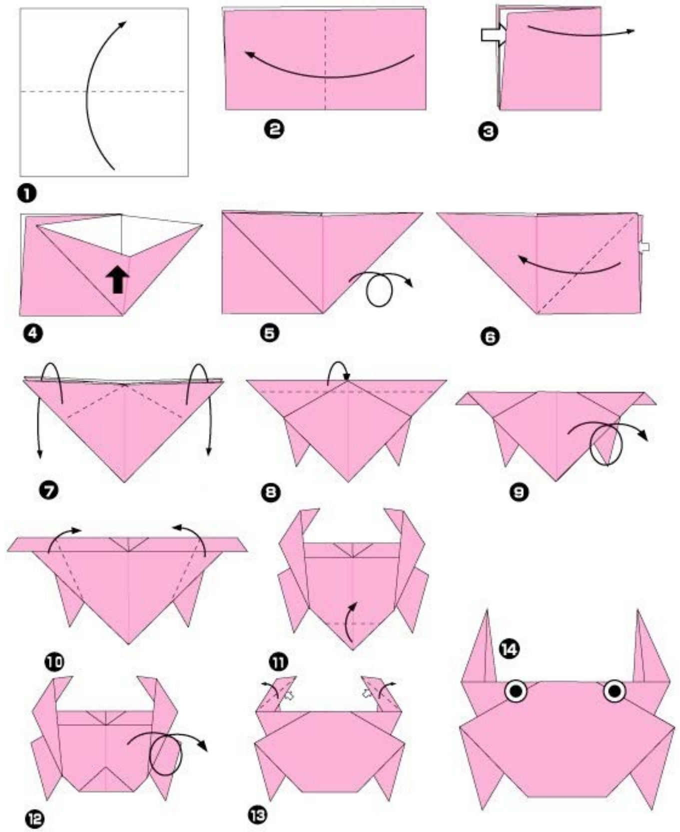
Zebrafish Embryo

A simplistic metaphor

Information

Mechanics

Suggests:
hierarchical organisation
(top-down control)

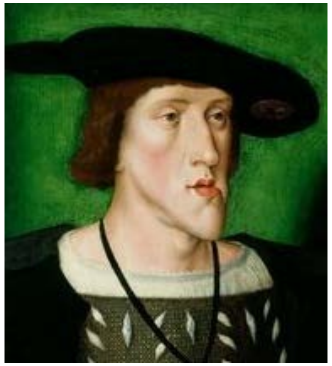


But:

- Information is intrinsic
- What is the nature of developmental information?

Information underlies the stability of forms

- Stability of forms in spite of perpetual current of matter and recycling
- Stems from persistence of information during development and from generation to generation



Charles Quint (1530)

Philippe IV (1630)

Charles II (1685)

Erwin Schrödinger *What is Life?* 1948

10^2 years

10^7 years

Concept of « developmental information »: Historical overview

- 18th century: towards a materialist model
- Buffon.

  3 key notions explain the form of animals and plants.

  - « molécules organiques »: biological particles (molecules or cells)
  - « forces pénétrantes »: forces acting upon particles following the model of newtonian gravitational forces
  - « moule intérieur »: notion of volumic mould that informs the organisation in 3D of the particles. Abstract notion.

Histoire naturelle, générale et particulière.
ChapIII. *De la nutrition et du développement* (1749-1789)

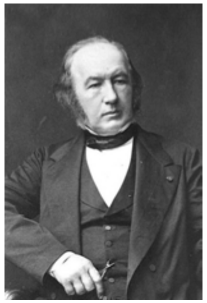
- Maupertuis.

  Affinity: Qualitative (ie. intrinsic) properties of particles underly the self-assembly (auto-organisation) of particles into organs

Vénus physique (1745)
Essai sur la formation des corps organisés 1754

- 19th century:
- Claude Bernard:

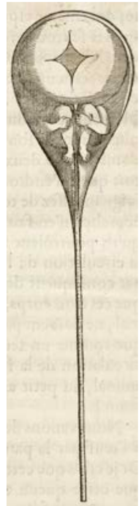
  - physico-chemical forces govern living matter
  -« morphological forces » govern the formation of living organisms



Définition de la vie 1875

Concept of « developmental information »: Historical overview

- The slow path towards a mechanical model of epigenesis: genetic information



  - Preformation and mechanics:

Development is an unfolding (entwicklung, déploiement) process, associated with growth. The unfolding and growth is explained mechanically
Forms are not mechanically explained (creationism)

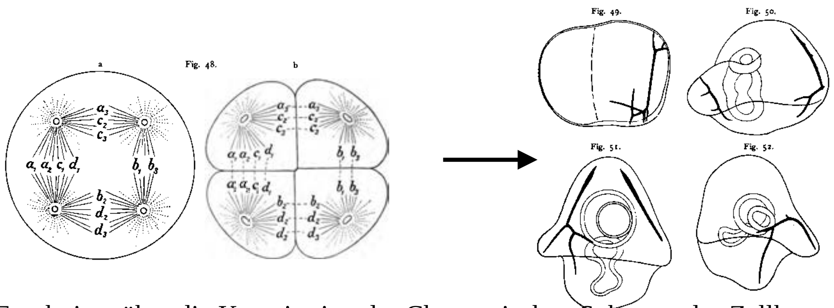
  - Epigenesis and vitalism:

William Harvey (XVIIth century). Gradual elaboration of biological forms.
Follows a finalist, vitalist philosophy (inspired form Aristotelian entelechy)

  - Mechanical model of epigenesis:

Descartes attempted but failed.
Biological information is intrinsic, materialised in the form of chemical molecules, and heritable
Required the chromosomic theory of heredity by Sutton and Boveri.

Biological information is an intrinsic property of living matter: DNA on chromosomes.



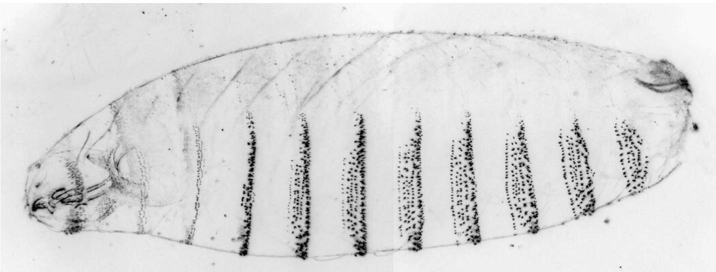
Ergebnisse über die Konstitution der Chromatischen Substanz des Zellkerns. Theodor Boveri, 1904

Spatial patterns during Development

- Macroscopic patterns (>mm) emerge from molecular interactions (nm-µm)

  Regularities: symmetries, repetition of units (segments), characteristic lengths, …

  Are there general principles underlying the development of patterns?

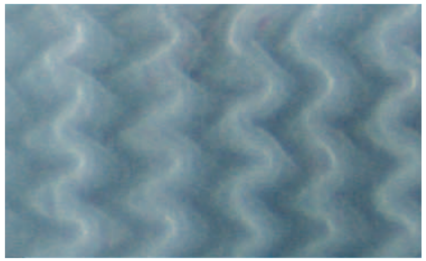


Interface Focus (2012) 2, 433–450 doi:10.1098/rsfs.2011.0122

Shinji Takada

Tony Hisgett/Wikipedia

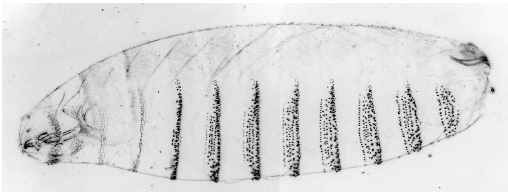
Shiyer et al, and Mahadevan, C. Tabin 2011

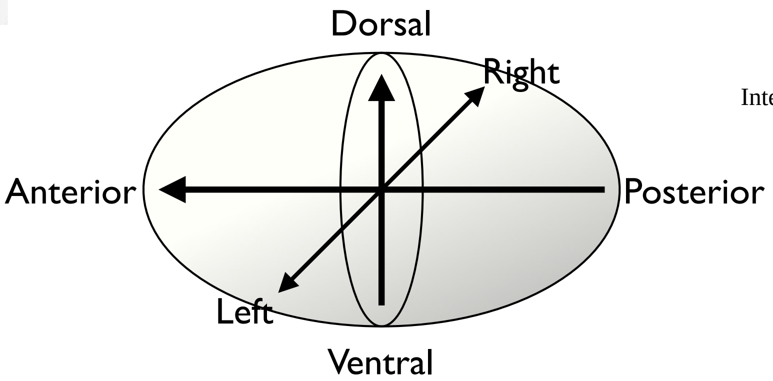


Shiyer et al, and Mahadevan, C. Tabin 2013

Spatial patterns: axis specification and coordinate systems

- Macroscopic patterns (>mm) emerge from molecular interactions (nm-µm)





Interface Focus (2012) 2, 433–450 doi:10.1098/rsfs.2011.0122

Shinji Takada

Tony Hisgett/Wikipedia

Coordinate systems as a descriptive task

- Theory of transformation from d'Arcy Thompson

1. System of coordinates
2. Transformation between related species via deformation of the coordinate system.
3. Mechanical forces (stress) induce deformations (strain)

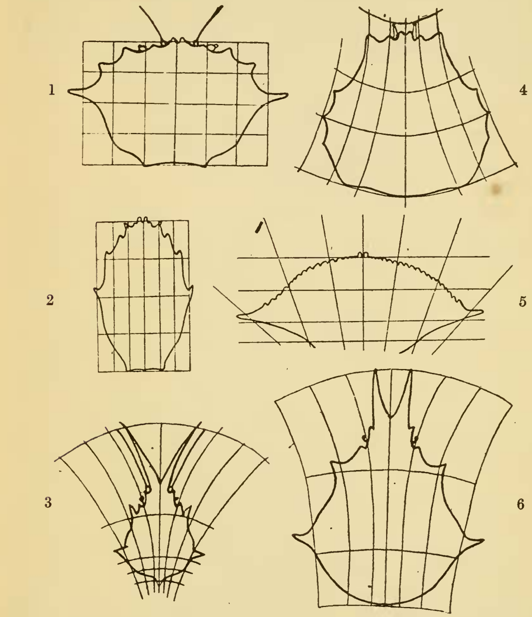


Fig. 513. Carapaces of various crabs. 1, *Geryon*; 2, *Corystes*; 3, *Scyramathia*; 4, *Paralomis*; 5, *Lupa*; 6, *Chorinus*.

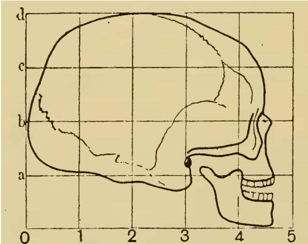


Fig. 548. Human skull.

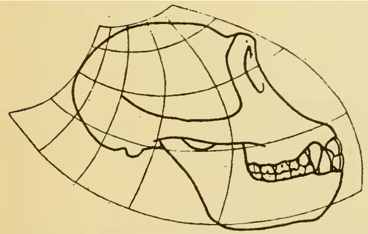


Fig. 550. Skull of chimpanzee.

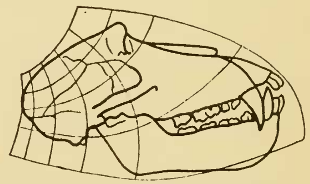
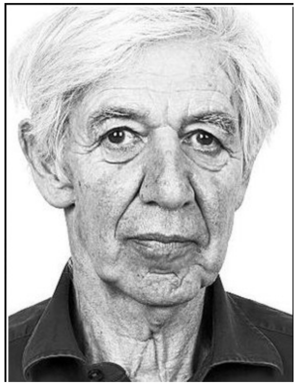


Fig. 551. Skull of baboon.

d'Arcy W Thompson, *On Growth and Form*, 1917

Positional information: an intrinsic coordinates system

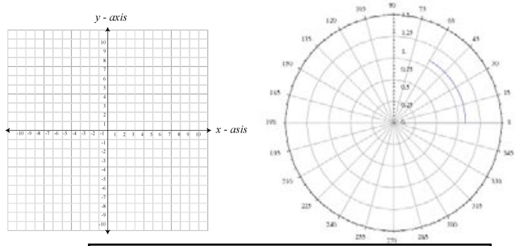


Positional Information and the Spatial Pattern of Cellular Differentiation†

L. WOLPERT

Department of Biology as Applied to Medicine, The Middlesex Hospital Medical School, London, England

J. Theoret. Biol. (1969) **25,** 1–47



Information

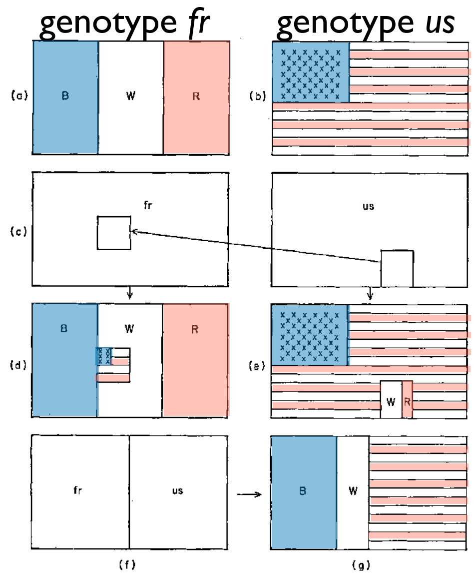
↓

Mechanics

- Set up a coordinate systems to specify positional identity (information)
- Interpret the positional information to produce structures and differentiate
- Uncouples information and interpretation at cellular and tissue levels

  based on the discovery of scaling property of developmental processes (e.g. Hans Driesch's observation of « regulative » development in sea urchin: cells are not pre-specified, and generate their own coordinate system)

- Mechanisms of positional information are potentially general: (ie. may be used in different contexts)



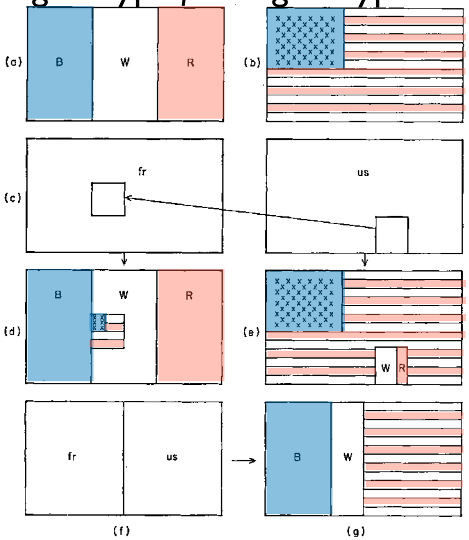
« Universality » of positional information

Lewis Wolpert, *J. Theoret. Biol.* (1969) 25: 1-47

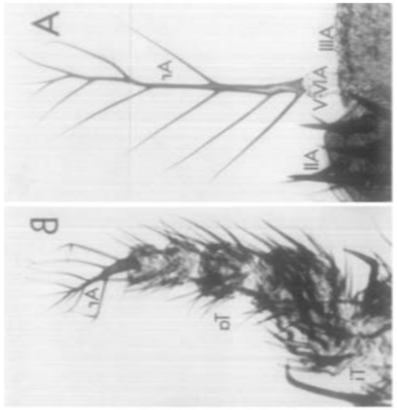
Positional information: an intrinsic coordinates system

- Clones of cells carry the *Antennapedia* mutation
- Cell identity (namely antenna or leg identity) is changed autonomously: see selector gene.
- Invariant property: position along the proximo-distal axis.
- There is an equivalence of different relative positions along limb axis: positional information

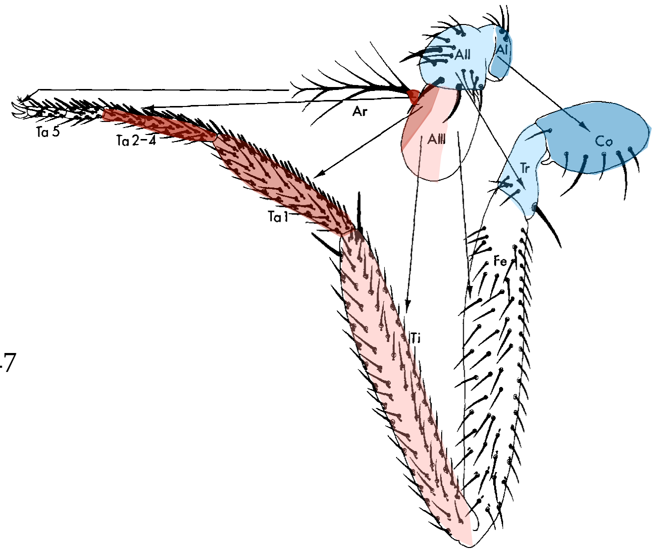
genotype *fr* genotype *us*

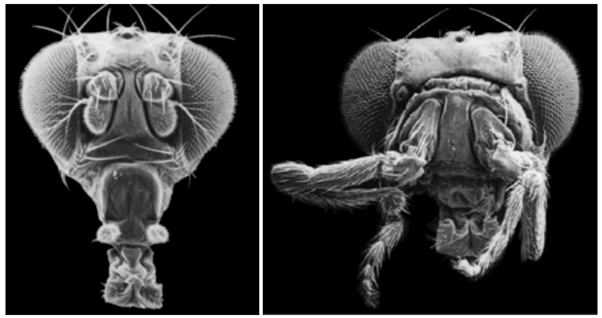


Lewis Wolpert, *J. Theor. Biol.* (1969) 25:1-47



Information
↓
Mechanics



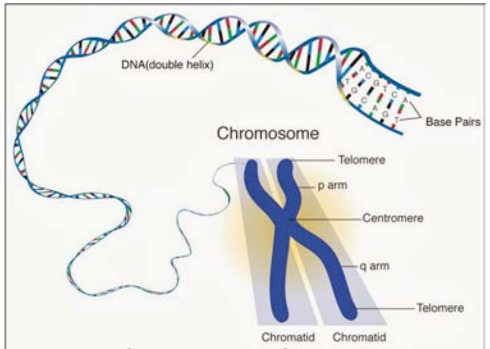


wild type *Antennapedia*

J. Postlethwait and H. Schneiderman, *Dev. Biol.* (1971) 25:606-640

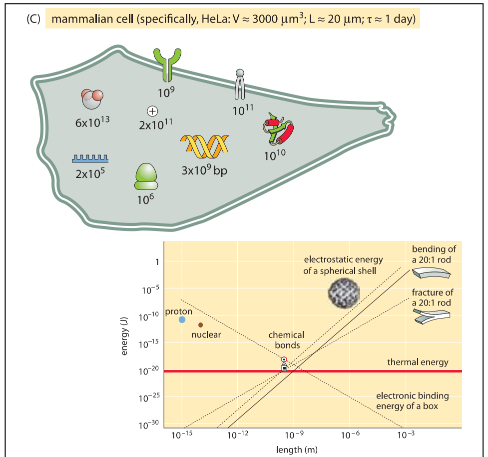
What is the nature of « morphogenetic information »?

- Genetic information: DNA sequence on chromosomes
  1. Not a simple « blueprint ». More akin to a « recipe » (contains the rules of agency/interaction) or to an « operating system » than to a « hard disc »: contains a prescription of the sequence of operations to be conducted in a finite amount of time.
  2. Genetic information acts upon itself (recursion) and encodes the means to read itself: an algorithmic machine?



National Genome Research Institute

- but also:
- physics: Genetic information does not contain a prescription of every molecular or cellular position.
  1. Information deployment depends on the nature of the physical world (chemical composition),
  2. length and time scales, nano-world properties (role of energy conversion and of thermal fluctuations),
  3. physical constraints imposed by physical laws acting within cells and across tissues, organisms (mechanics, thermodynamics).



Cell Biology by the Numbers R Milo and R Phillips

- **environment and history**: the outcome of **interaction** between Genetics and Physics
  1. Geometry/Organisation: how information flows in a cell or a tissue.
     - The cell is not a simple 3D, isotropic solvent. It is **organised** (discontinuities, dimensionality…)
  2. Epigenetic information: environment (cell composition-chemistry, organism physiology…)
  3. History: e.g. cell organisation in the egg at fertilisation and in organism that hosts the egg, evolutionary history embedded in DNA sequence

Modes of biological organisation in space and time

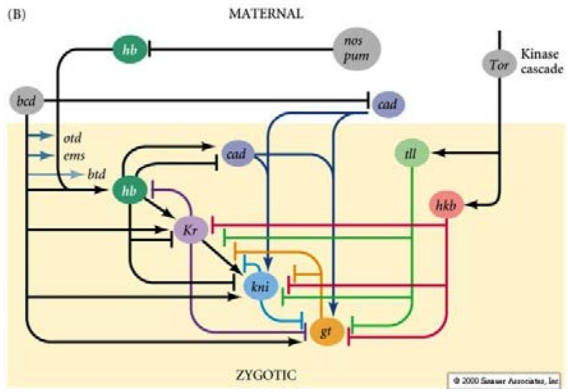
- Two modalities of information flow during morphogenesis

Programme

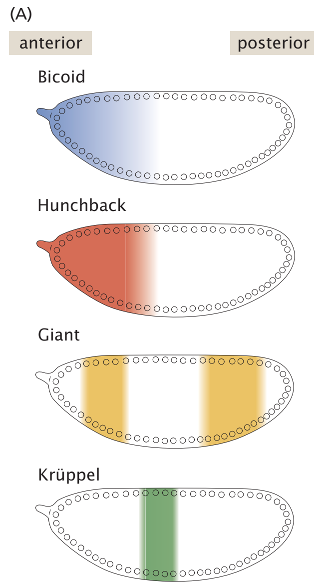
Self-organization

Programme

- hierarchical, indirect interactions
- modular
- long and short range interactions
- high-wired
- multiple parameters



http://courses.biology.utah.edu/bastiani/3230/DB%20Lecture/Lectures/b10FlyZygotic.html



✓ The amount of information required to model/ encode is very large

Rob Philipps, Jane Kondev, Julie Theriot, Hernan G. Garcia.
illustration: Nigel Orme
Physical Biological of the Cell (Garland Science)

Programme

- hierarchical, indirect interactions
- modular
- long and short range interactions
- high-wired
- multiple parameters

DROSOPHILA DEVELOPMENT

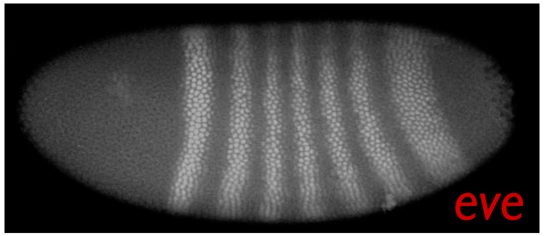
Making stripes inelegantly

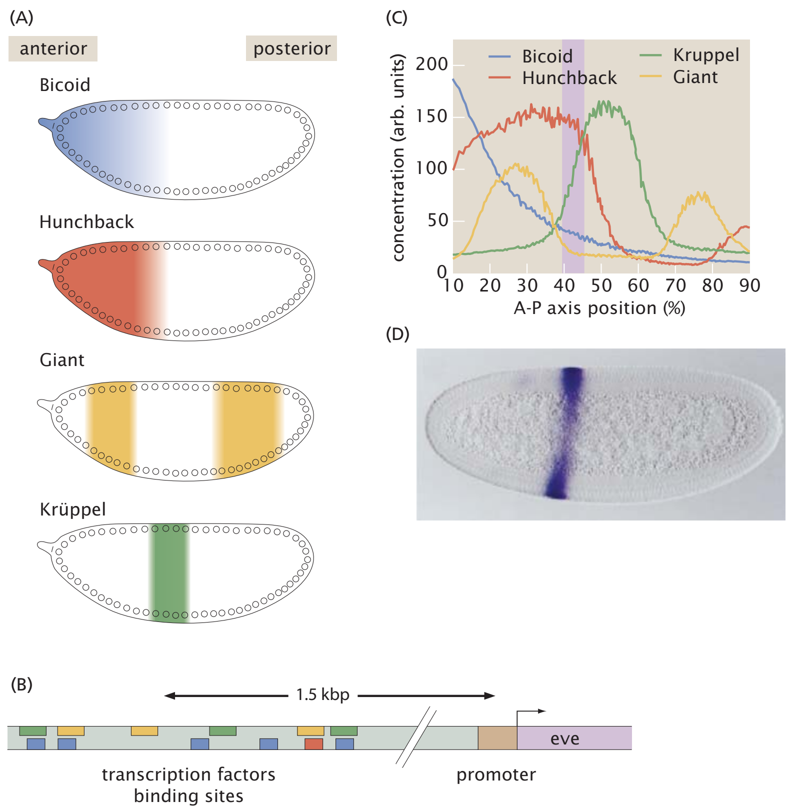
Michael Akam

NATURE · VOL 341 · 28 SEPTEMBER 1989

Turing & Meinhardt

Periodicity might be generated in one of two ways. An elegant mechanism, favoured by model builders[3,4], would use an intrinsically periodic pattern-generating system, comprising the pair-rule genes and their products. This would only need to be triggered by local stimuli from the gap genes. Alternatively, unique instructions could be generated by the gap-gene proteins to define the position of each pair-rule stripe.

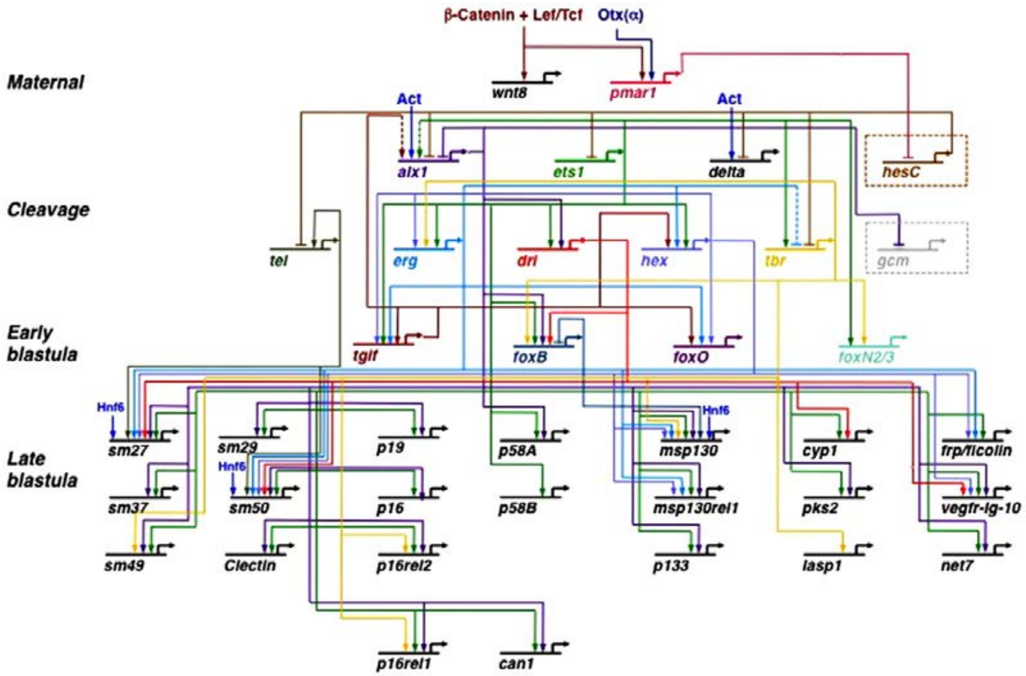




Rob Philipps, Jane Kondev, Julie Theriot, Hernan G. Garcia.
illustration: Nigel Orme
Physical Biological of the Cell (Garland Science)

Programme: gene regulatory networks

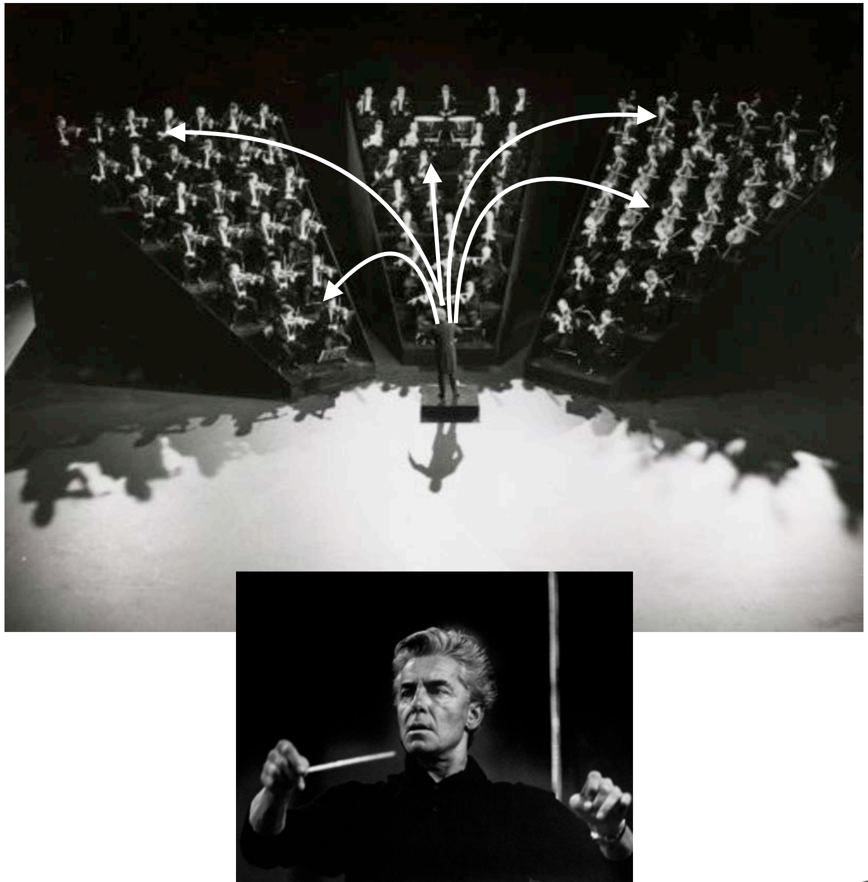
- hierarchical, indirect interactions
- modular
- long and short range interactions
- high-wired
- multiple parameters



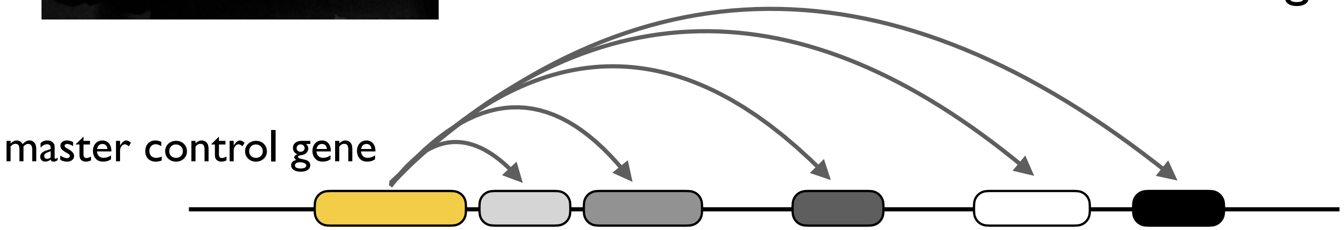
Kiran Rafiq, Melani S. Cheers, Charles A. Ettensohn
Development 2012 139: 579-590; doi: 10.1242/dev.073049

Programme

- « *Conductors* »: organiser, master control gene, selector genes, morphogens etc



The score: « genomic recipe »

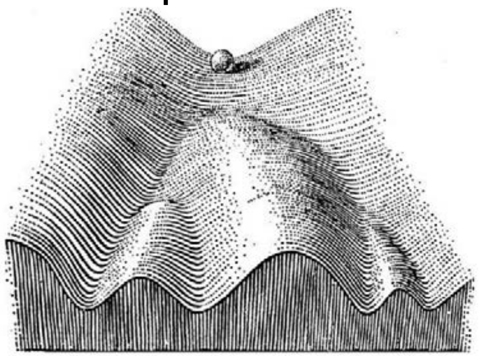


Genes control cellular decisions: epigenetic landscape

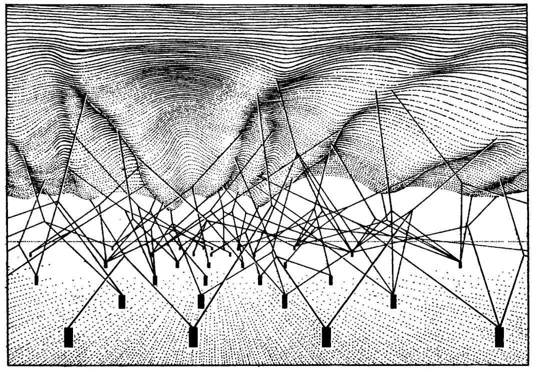
- Differential gene regulation underlies cellular differentiation pathways during development

The epigenetic landscape of Development

Cell determination and differentiation pathways during development (creodes)



The strategy of the genes. 1957

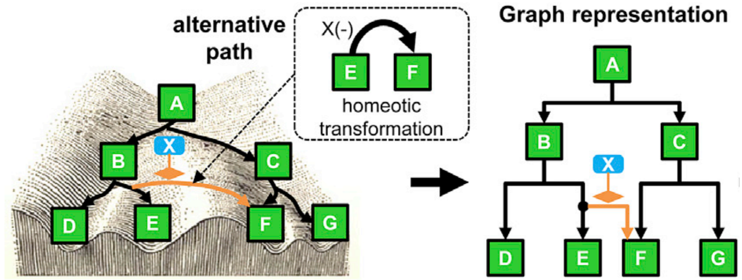


The complex system of interactions underlying the epigenetic landscape. The pegs in the ground represent genes; the strings leading from them the chemical tendencies which the genes produce. The modelling of the epigenetic landscape, which slopes down from above one's head towards the distance, is controlled by the pull of these numerous guy-ropes which are ultimately anchored to the genes.

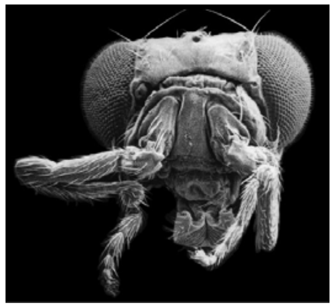
Conrad Waddington

Gene activity moulds the landscape

Differentiation Landscape



Zhuo Du, et al, Zhirong Bao . *Dev Cell* (2015) 34: 1-16



Antennapedia: Homeotic transformation antenna to leg

Development as a tree of decisions: selector gene

- Differential gene regulation underlies cellular differentiation pathways during development

- Garcia Bellido: distinction between *selector* genes, and *cytodifferentiation* genes

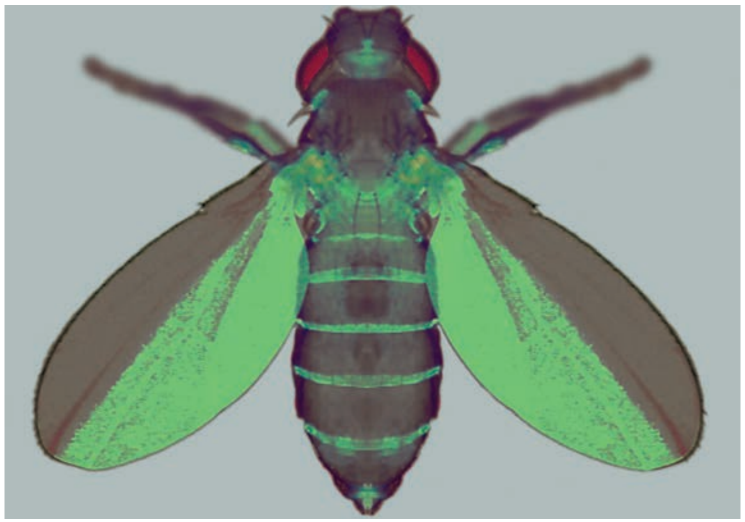
« Genes of a first group (***cyto-differentiation genes***) would include those controlling cell behaviour relevant to morphogenesis and common to most developing systems: mitotic rate, mitotic orientation, cell recognition and cuticular differentiation.
Those of a second group (***selector genes***) **seem to control developmental pathways** and share several operational characteristics. A functional scheme is advanced showing how selector genes may become activated and control development. We postulate that inductor molecules interfere with the products of activator genes which are selector specific. In this way signals extrinsic to the genome become translated into genetic ones. The activation, or repression, of selector genes occurs once in development and remains clonally irreversible ». García-Bellido A. *Ciba Found Symp.* 1975;0(29):161-82.

Information
↓
Mechanics
Differentiation

- The embryo as a *genetic and cellular automata*: each cell division marked by decision to activate or repress gene expression

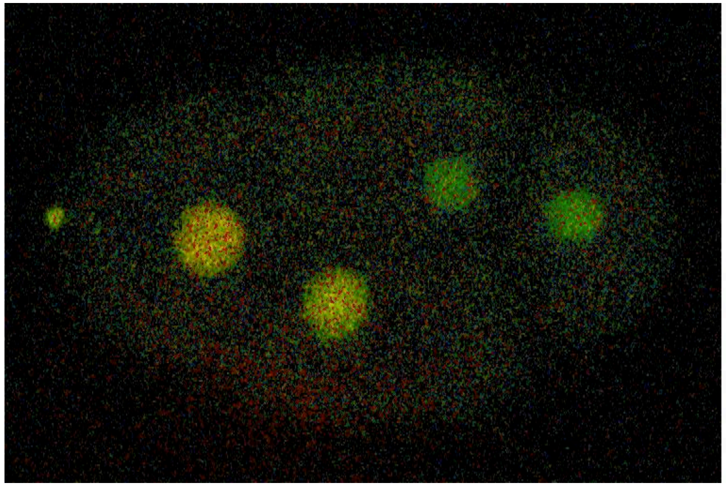
embryo
Engrailed

→



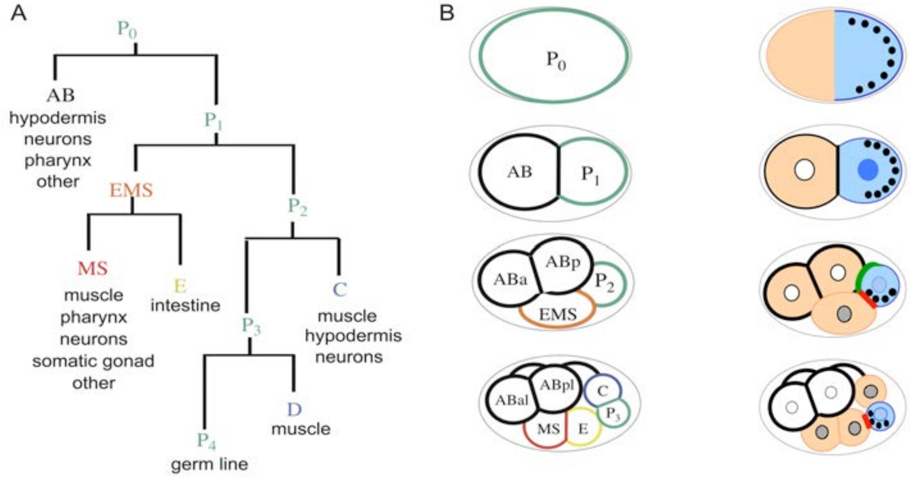
adult *Drosophila*
Engrailed

Development as a tree of decisions

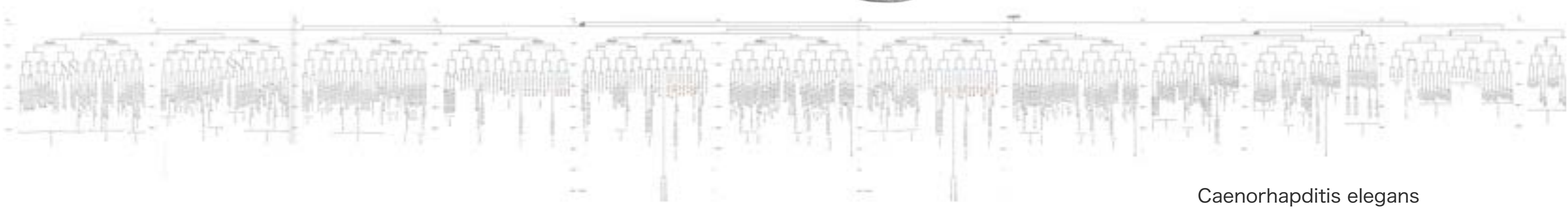


http://waterston.gs.washington.edu/lineaging.htm

Asymmetric cell fate segregation at cell division



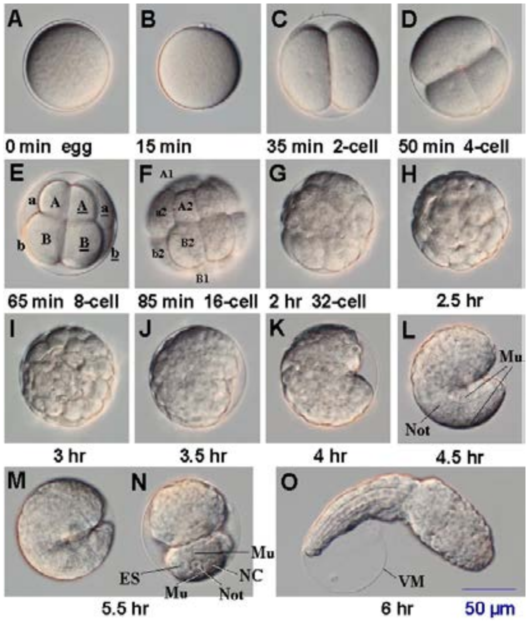
WormBook

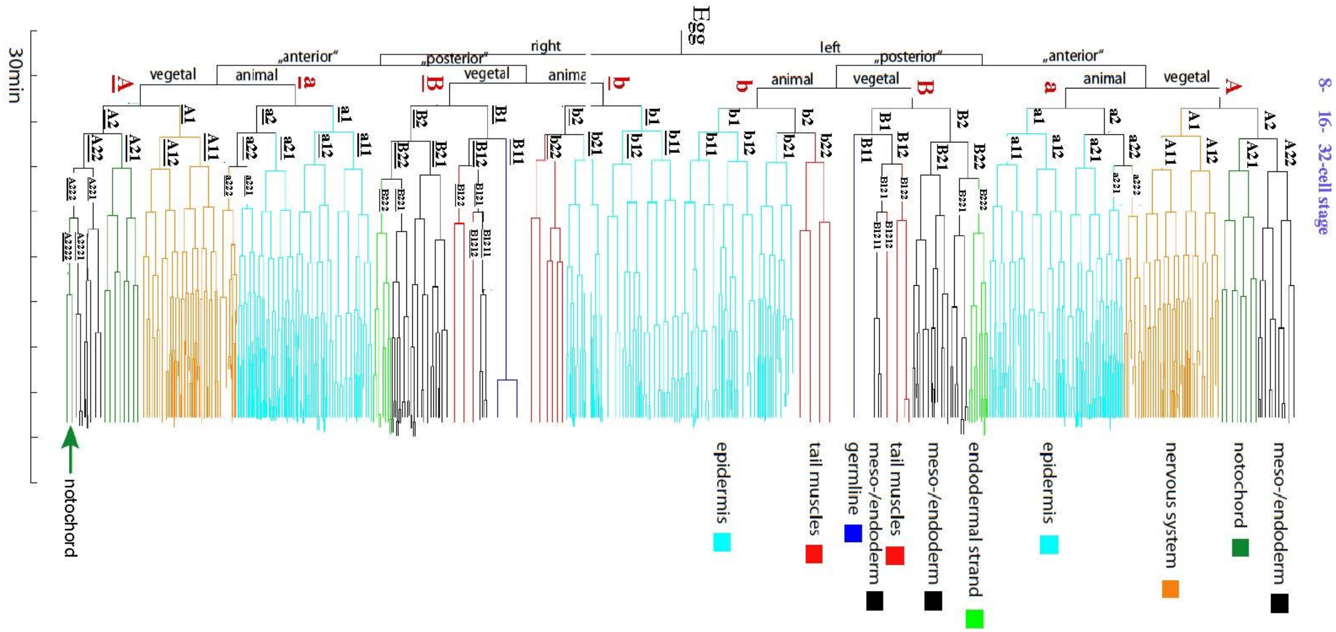


Caenorhapditis elegans

J .E. Sulston, E. Schierenberg, J. G. White, J. N. Thomson
http://www.wormatlas.org/celllineages.html

Development as a tree of decisions





Oikopleura dioica (Tunicate, Urochordate)

Hiroki Nishida

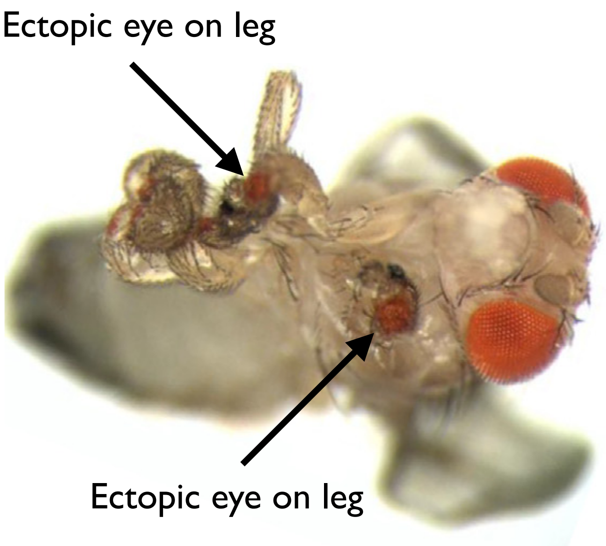
Master control gene: organogenesis

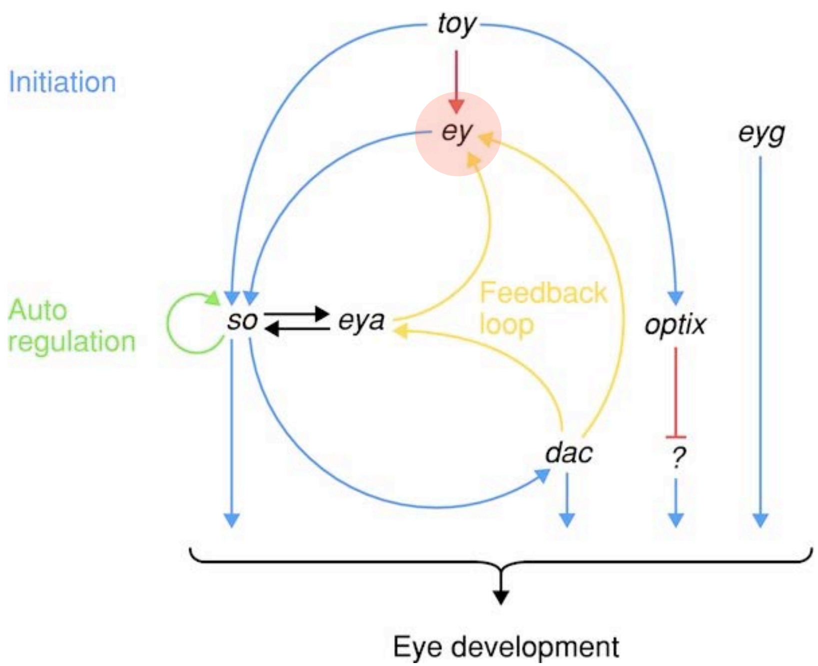
- Misexpression of a single gene (Eyeless/Pax6) can elicit formation of a complete new eye.

(Necessary and Sufficient)

Information

Mechanics





Halder G, Callaerts P, Gehring WJ. *Science*. (1995) 267(5205):1788-92.

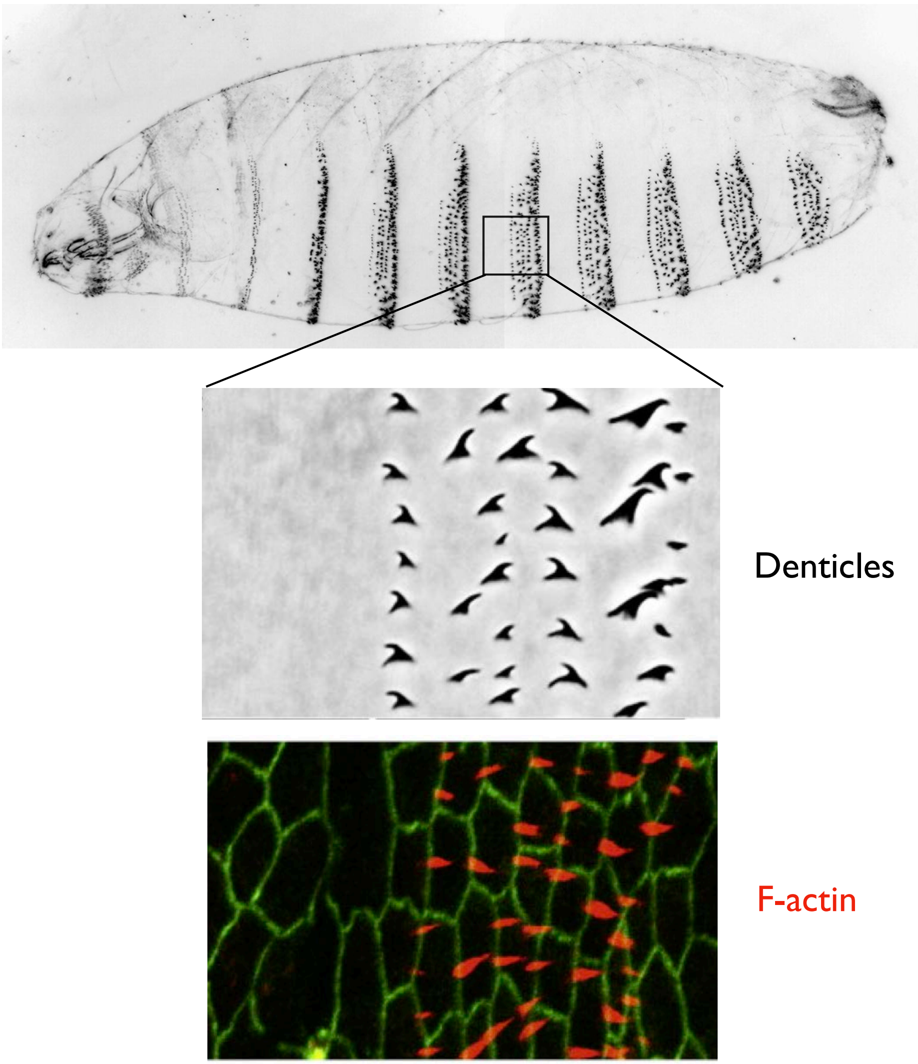
Master control gene: cell differentiation

- Expression of a single gene (Svb) induces a complete differentiation program (denticle formation)

(Necessary and Sufficient)

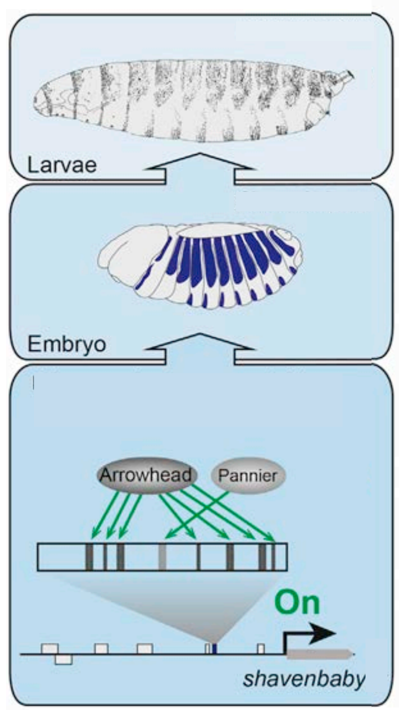
Information

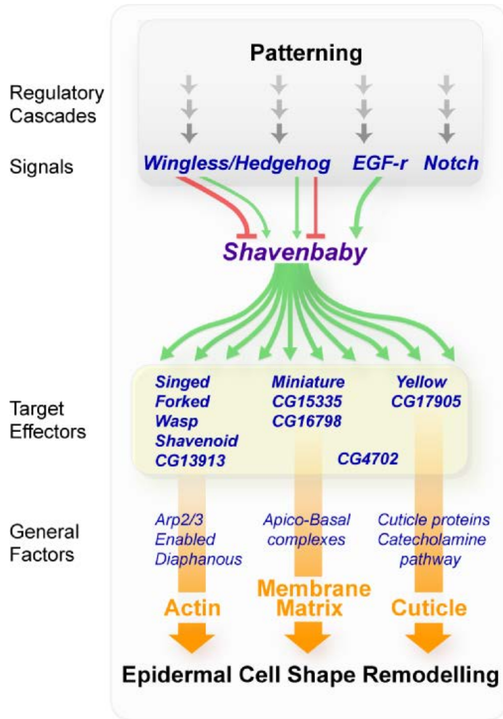
Mechanics



Denticles

F-actin



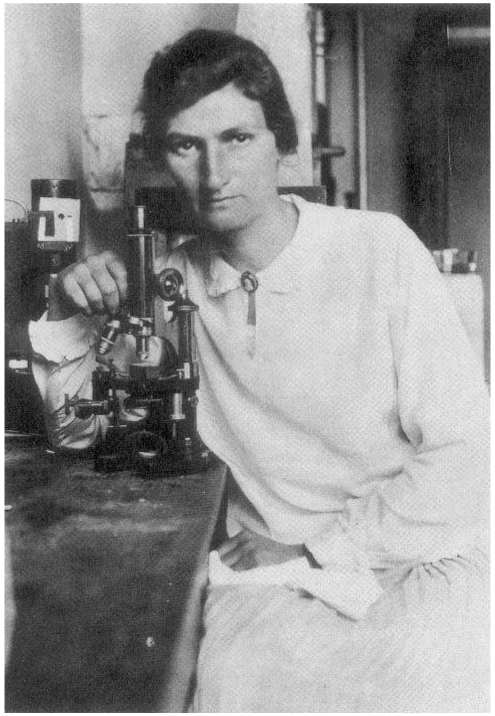


Chanut-Delalande H, Fernandes I, Roch F, Payre F, Plaza S (2006). *PLoS Biol* 4(9): e290.

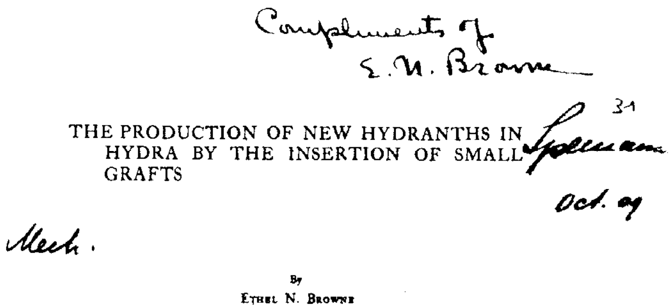
Preger-Ben Noon et al., 2016, *Developmental Cell* 39, 572–584

The concept of Organiser: inspiration

- Developmental « stimulation » can be triggered by certain tissues in Hydra

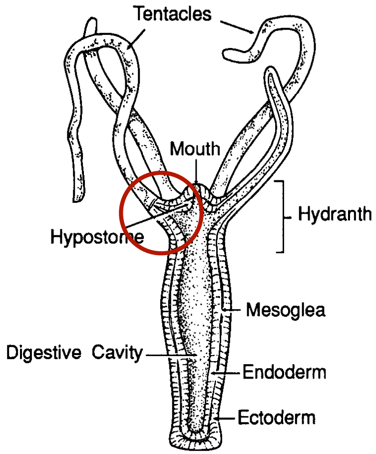


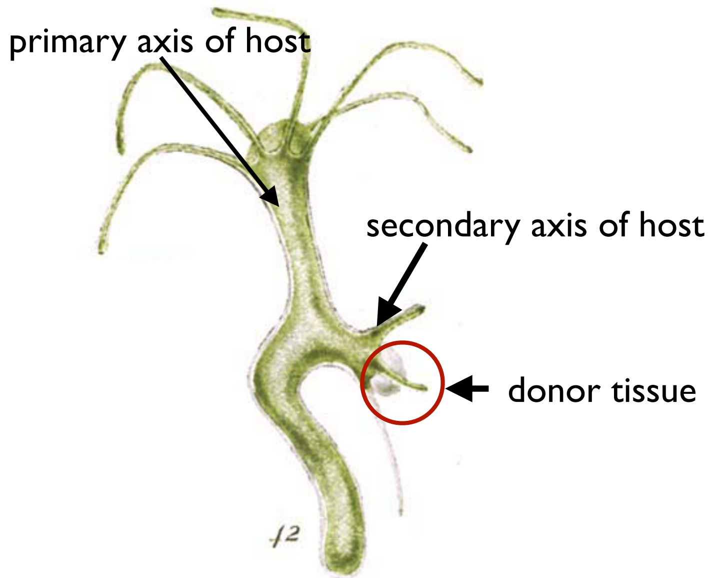
Ethel Browne (1885-1965)


Compliments of
E. N. Browne
31
Spemann
Oct. 09
Mech.

THE PRODUCTION OF NEW HYDRANTHS IN HYDRA BY THE INSERTION OF SMALL GRAFTS

By
ETHEL N. BROWNE

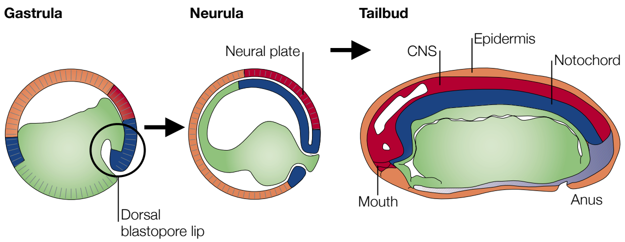




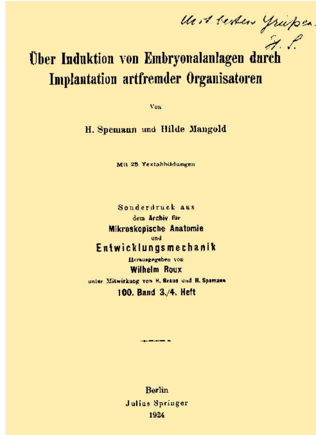
4. A new hydranth can be stimulated to grow out from a hydra by (1) the graft of the peristome tissue at the base of the tentacle, with or without the tentacle itself, and by (2) the graft of the material of a regenerating hydranth and by (3) the graft of the material of a bud. Neither a wound nor the graft of any other kind of tissue will stimulate the stock to send out a new hydranth.

The concept of Organiser: axis duplication

- Embryonic axis duplication is induced by a graft from the dorsal region of an amphibian embryo



Hilde Mangold Hans Spemann



Über Induktion von Embryonalanlagen durch Implantation artfremder Organisatoren

Von

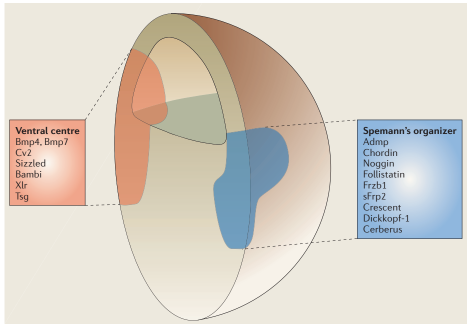
H. Spemann und Hilde Mangold

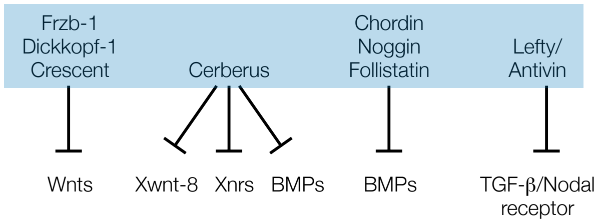
Mit 25 Textabbildungen

Sonderdruck aus
dem Archiv für
Mikroskopische Anatomie
und
Entwicklungsmechanik
Herausgegeben von
Wilhelm Roux
unter Mitwirkung von H. Braus und H. Spemann
100. Band 3./4. Heft

Berlin
Julius Springer
1924

1924



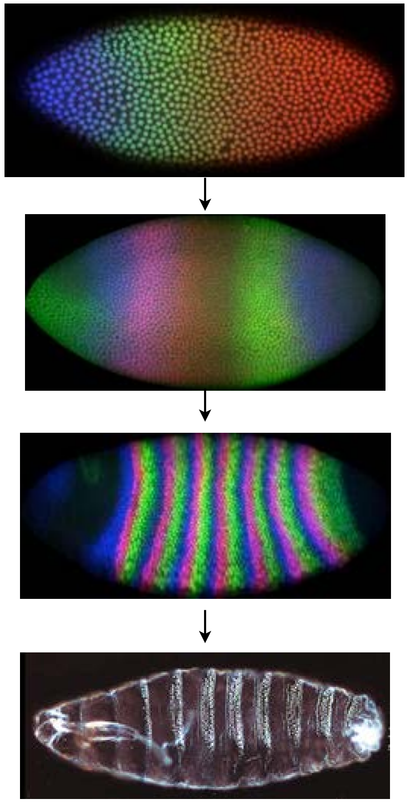


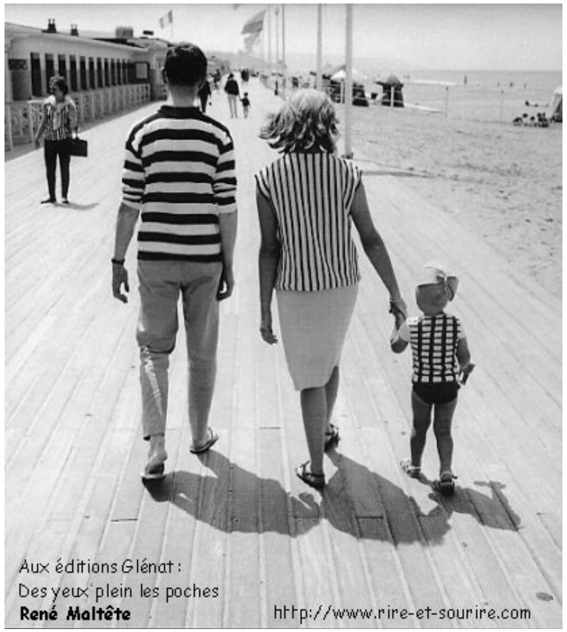
The Spemann's organiser produces inhibitors of several signalling pathways

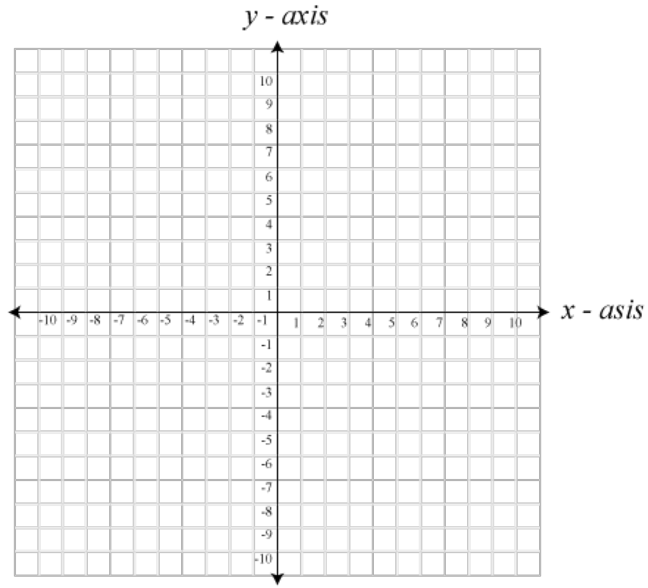
E. de Robertis. *Nature Rev. Mol. Cell Biol.* (2006) 7:297-302.

Specification of positional information by morphogens

- Case study: antero-posterior axis specification in the *Drosophila* embryo

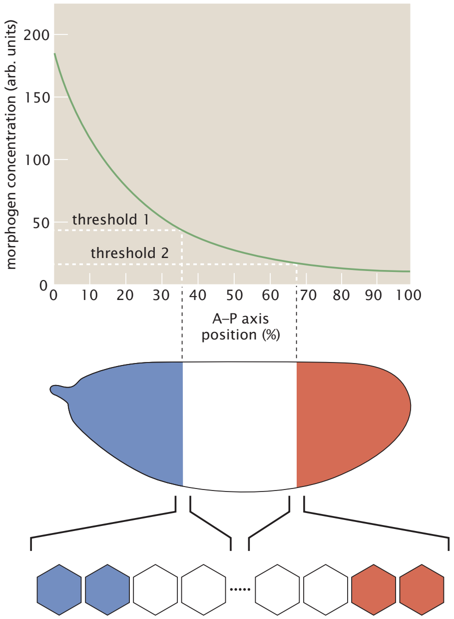






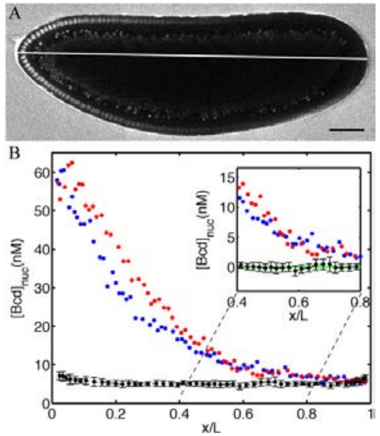
Positional information: Morphogen gradient

- Gradient of concentration/activity of a molecule
- Activity thresholds induce gene transcription at different position
- Concentration of morphogen is a positional information

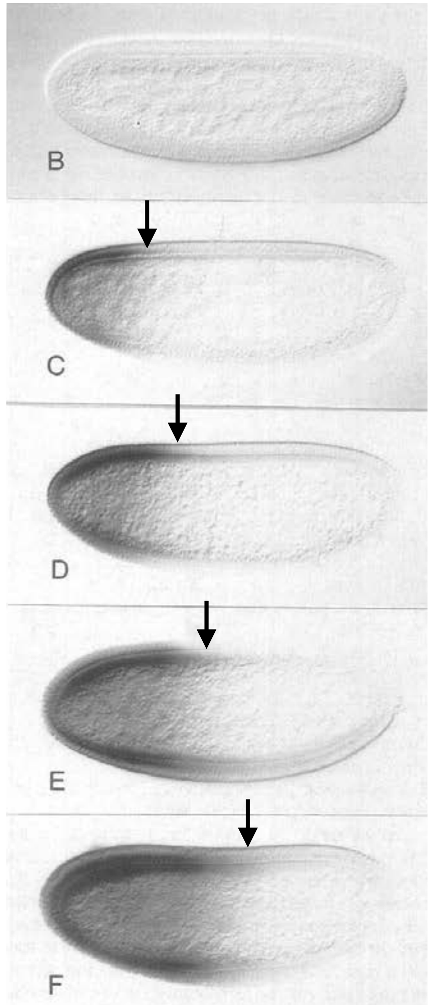


R. Philipps, J. Kondev, J. Theriot, H. G. Garcia (ill. N. Orme)
Physical Biological of the Cell (Garland Science)

Lewis Wolpert, *J. Theoret. Biol.* (1969) 25: 1-47



Thomas Gregor, D. Tank, E. Wieschaus and B. Bialek
Cell 130:153 (2007)



0x Bcd

1x Bcd

2x Bcd

4x Bcd

6x Bcd

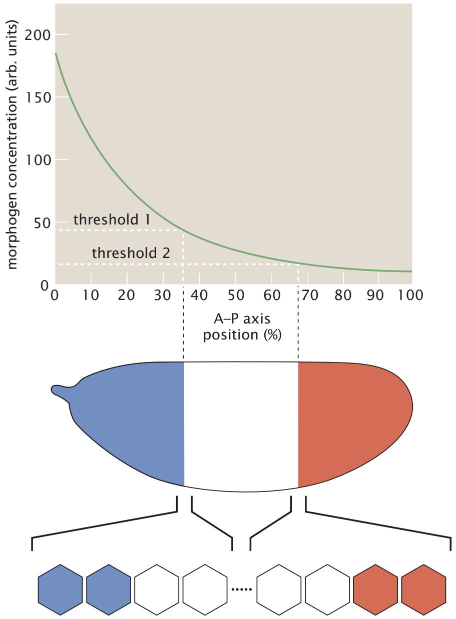
W. Driever and C. Nüsslein-Volhard *Cell* (1988)
G. Struhl, K. Struhl and P. MacDonald *Cell* (1989)

Positional information: Morphogen gradient concentration

- Position specific expression of morphogen target:

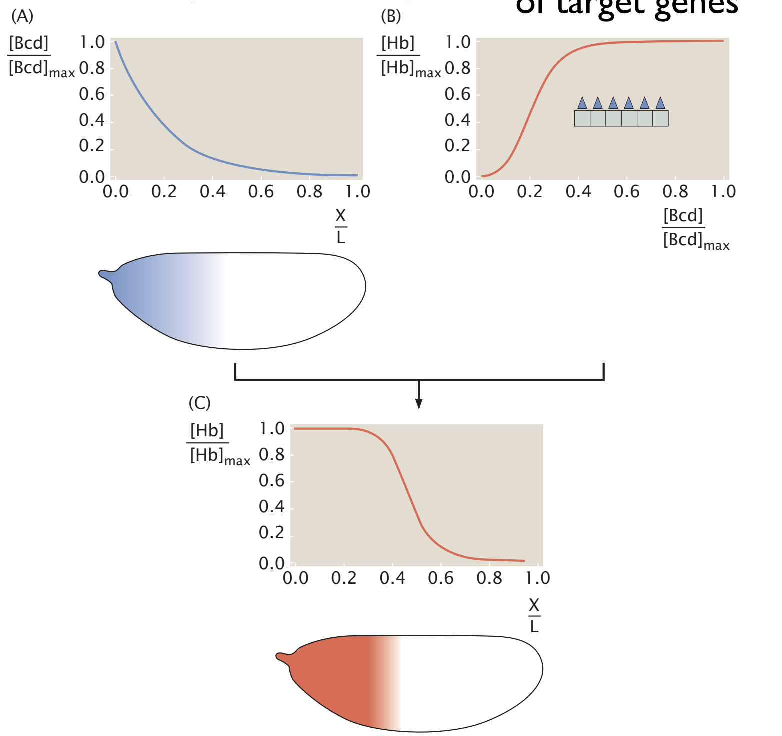
$$\frac{\partial[\mathrm{Bcd}]}{\partial t} = D\frac{\partial^2[\mathrm{Bcd}]}{\partial x^2} - \frac{1}{\tau}[\mathrm{Bcd}].$$

$$[\mathrm{Bcd}] = [\mathrm{Bcd}]_{\mathrm{max}} e^{-x/\lambda} \qquad \lambda = \sqrt{D\tau}$$



Gradient exponential decay

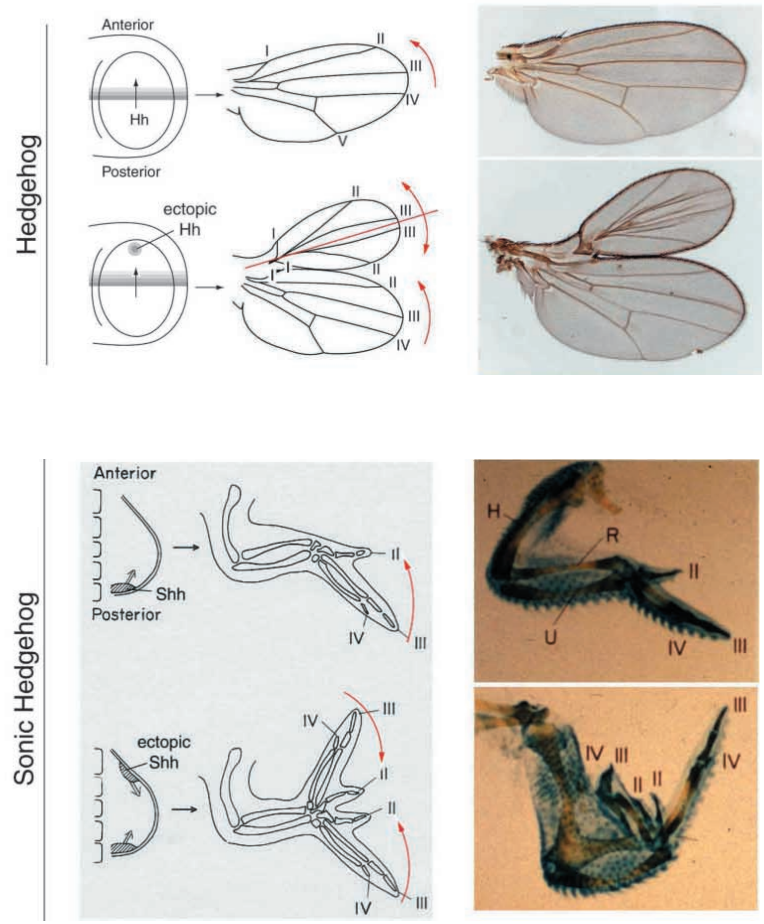
Non-linear induction of target genes



R. Philipps, J. Kondev, J. Theriot, H. G. Garcia (ill. N. Orme)
Physical Biological of the Cell (Garland Science)

The concept of Organiser: axis duplication

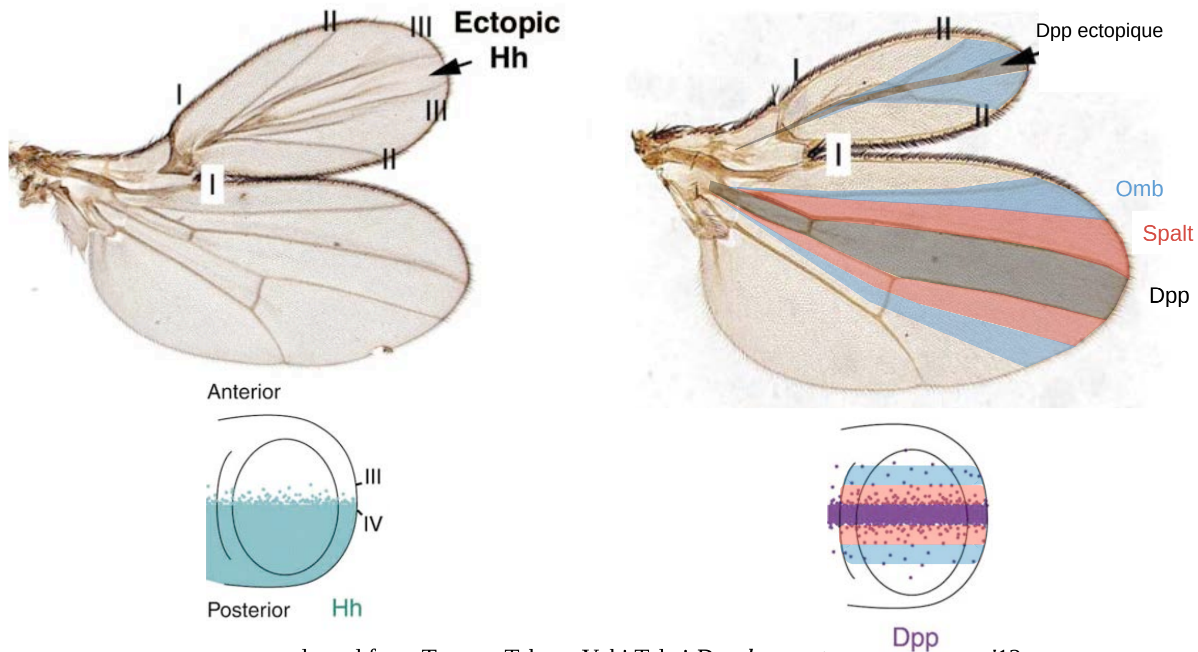
- Axis duplication in limbs can induced by specific secreted molecules
- The developmental induction acts non-autonomously: it influences cells at a distance (>100µm)



Tetsuya Tabata, Yuki Takei *Development* 2004 131: 703-712
T. Tabata and T. Kornberg. *Development* 1994

Mode of organisation: Morphogen gradient

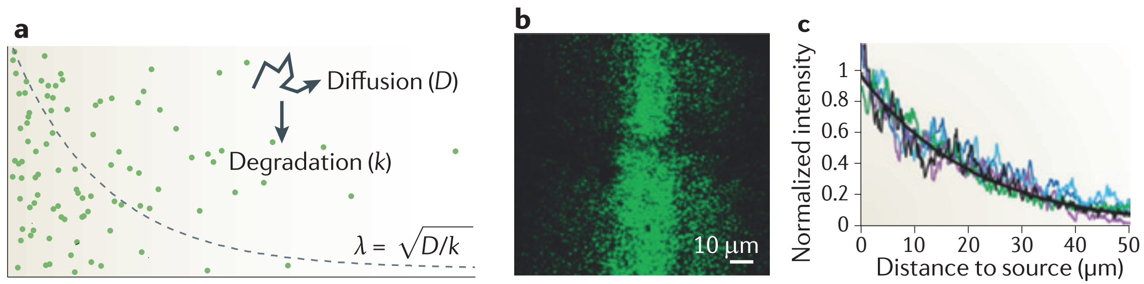
- Gradient of concentration/activity of a molecule
- Activity thresholds



adapted from Tetsuya Tabata, Yuki Takei *Development* ’12
M. Zecca et al. and K. Basler. *Dev* 1995
D. Nellen et al. and K. Basler. *Cell* 1996
T. Lecuit et al. and S. Cohen. *Nature* 1996

Information

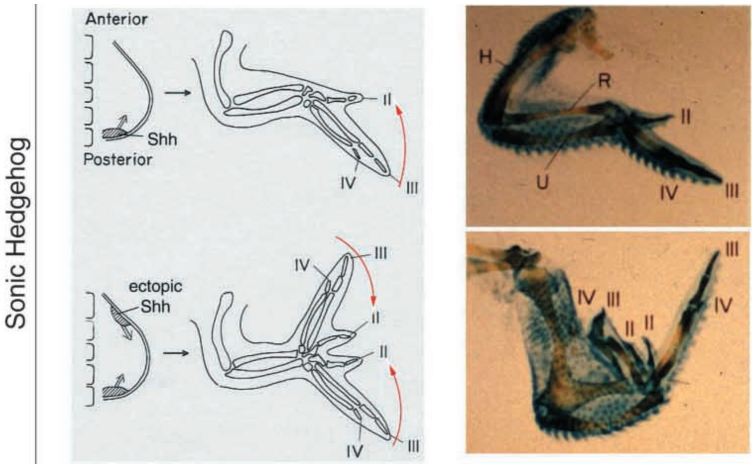
Mechanics
(differenciation and
morphogenesis)



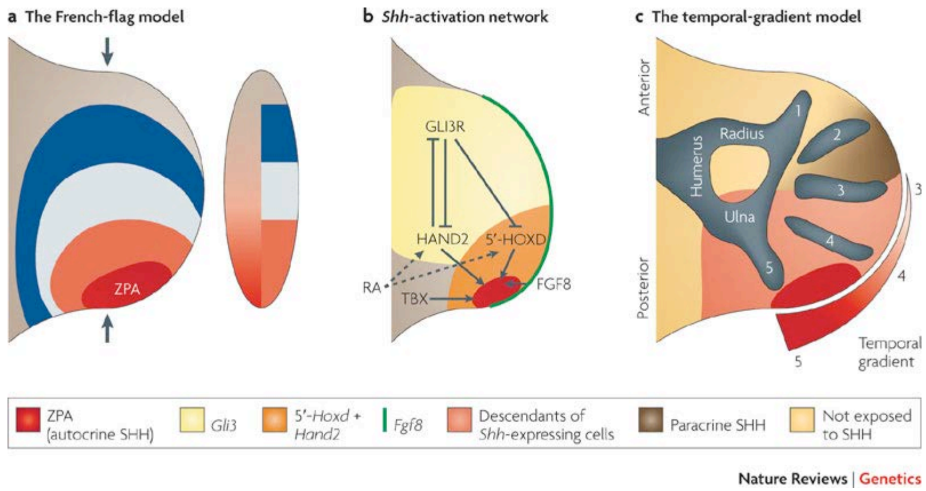
Kicheva et al, M. Gonzalez Gaitan, Science (2007) 315:521

Mode of organisation: Morphogen gradient

- Gradient of concentration/activity of a molecule (Shh)
- Activity thresholds



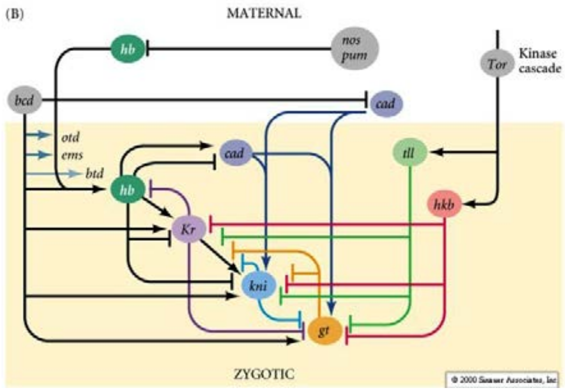
Tetsuya Tabata, Yuki Takei *Development* 2004 131: 703-712



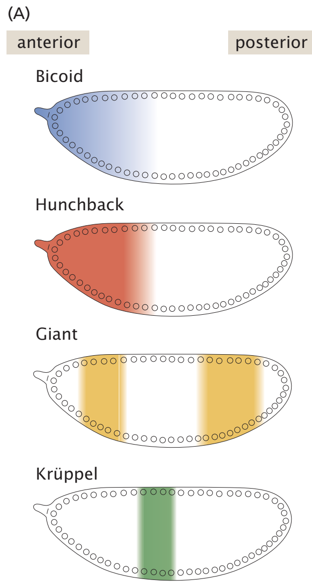
Rolf Zeller et al. *Nature Reviews Genetics* **10**:45–858 (2009)

Programme

- hierarchical, indirect interactions
- modular
- long and short range interactions
- high-wired
- multiple parameters



http://courses.biology.utah.edu/bastiani/3230/DB%20Lecture/Lectures/b10FlyZygotic.html



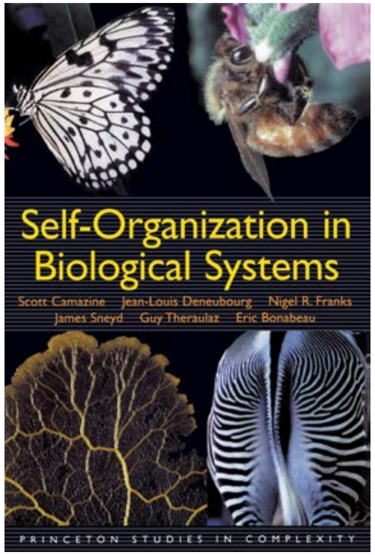
✔ The amount of information required to model/encode is very large

Rob Philipps, Jane Kondev, Julie Theriot, Hernan G. Garcia.
illustration: Nigel Orme
Physical Biological of the Cell (Garland Science)

Self-organization

- local and direct interactions
- few rules and parameters

✓ Complexity emerges from very simple rules
The amount of information required to model/encode is very small

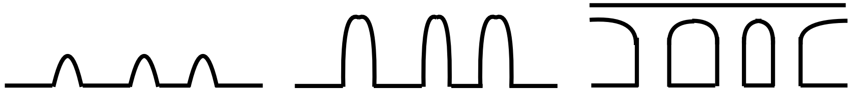


Scott Camazine, J-L Deneubourg, NR. Franks, J. Sneyd, G. Theraulaz and E. Bonabeau
Self-Organisation in Biological Systems
Princeton University Press

Self-organization

- local and direct interactions
- few rules and parameters

- Ants (*Lasius niger*) form pellets, move them around and deposit them.
- The form pillars evenly spaced
- Once pillars reach a certain height, ants form roofs that bridge pillars.



Anaïs Khuong et al, and Guy Theraulaz. *PNAS* 113:1303-1308. 2016

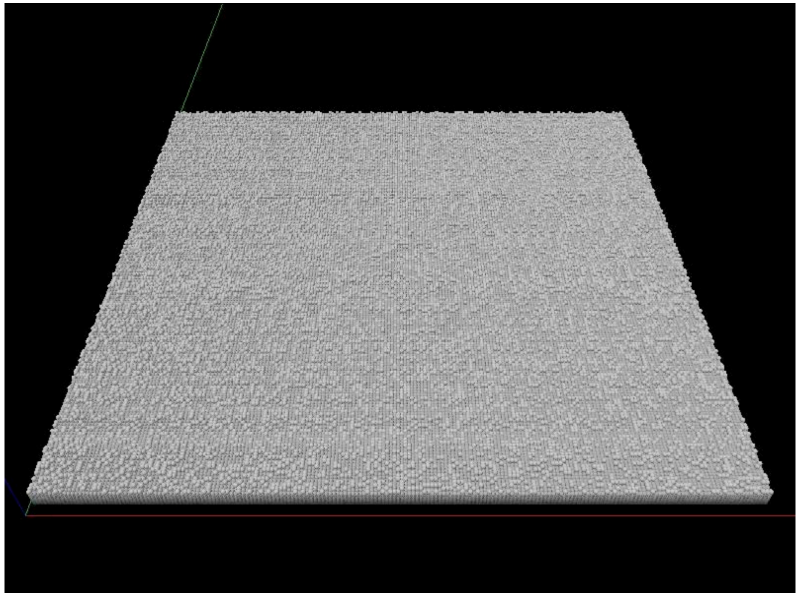
Self-organization

- local and direct interactions
- few rules and parameters

Two kinds of **local and direct** interactions:

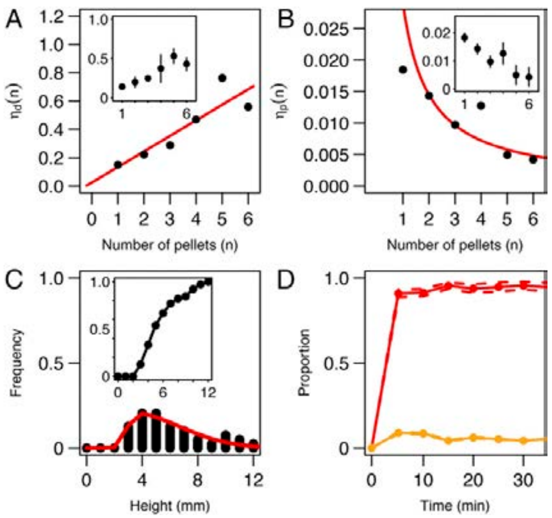
1. **stigmergic-based interactions:** local amplification of soil deposition is dependent on pheromone concentration added by ants. Pheromone life-time depends on temperature
   > controls the spacing of pillars

2. **template-based interaction** between ant's body and built structure: depends on length of animal
   >controls the height of roof



- Model constrained by data (interactions)
- Only free parameter is pheromone life time

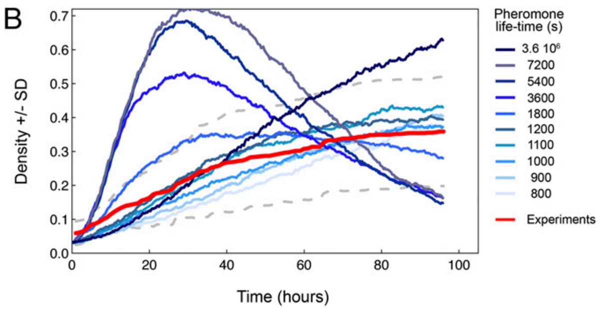
p(deposit I n)



p(pick I n)

pilar manipulated by ants

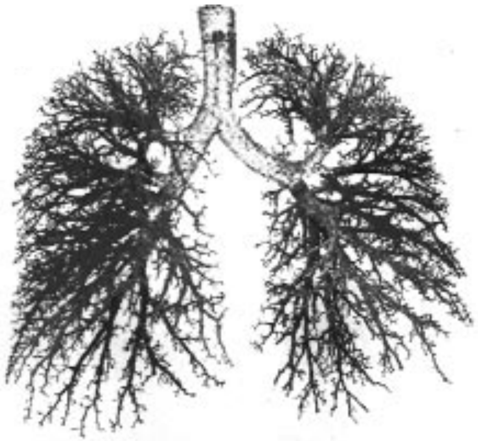
pilar not in contact with ants

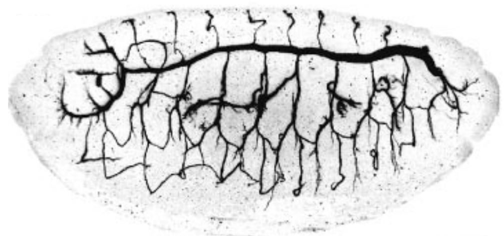


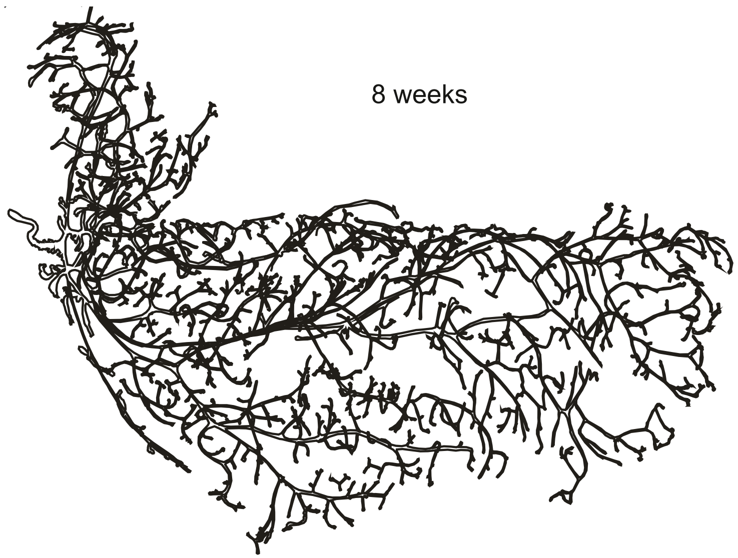
Anaïs Khuong et al, and Guy Theraulaz. *PNAS* 113:1303-1308. 2016

Self-organization vs Programme in development

- Case study: branching morphogenesis



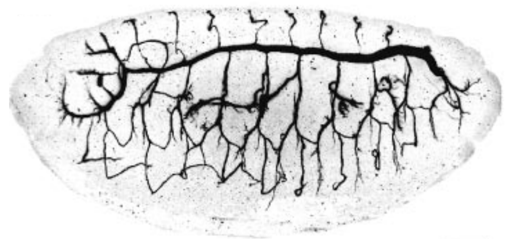


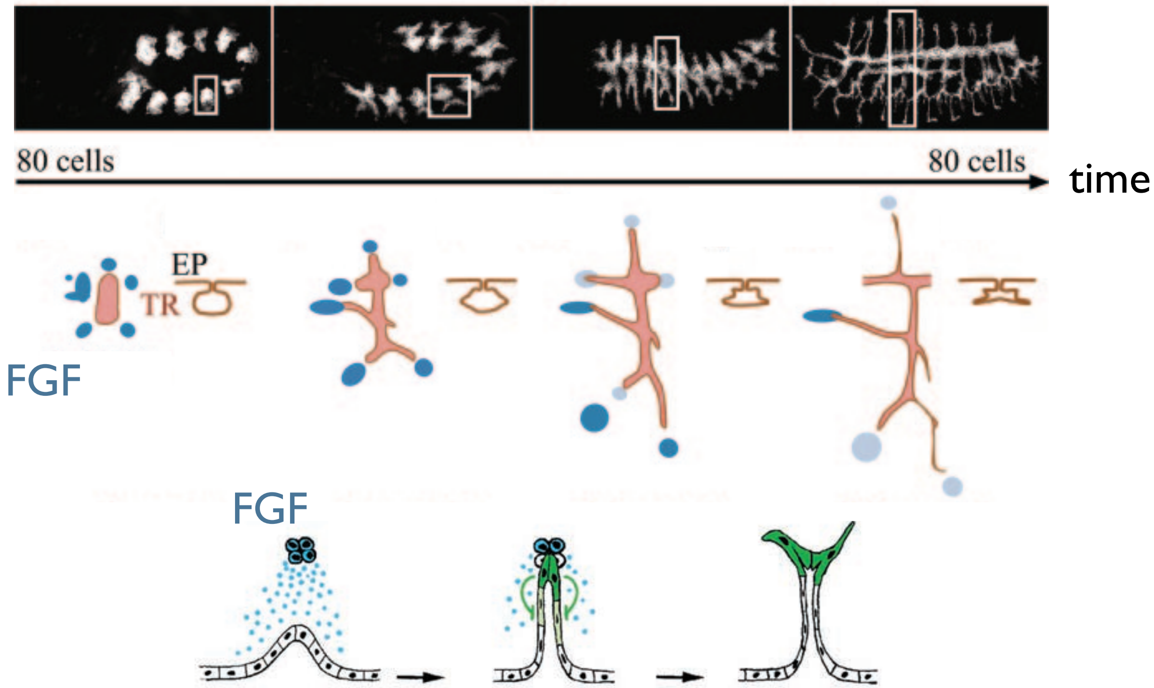


Self-organization vs Programme in development

- Branching morphogenesis as a controlled programme

1. Stereotypical sequence of branching
2. Tube growth driven by FGF signalling
3. Dynamic pattern of FGF expression controls branching
4. FGF expression under complex upstream control





Clemens Cabernard, M. Neuman and Markus Affolter. *J Appl Physiol* 97: 2347–2353, (2004)

R. Metzger and M. Krasnow, *Science* 1999.

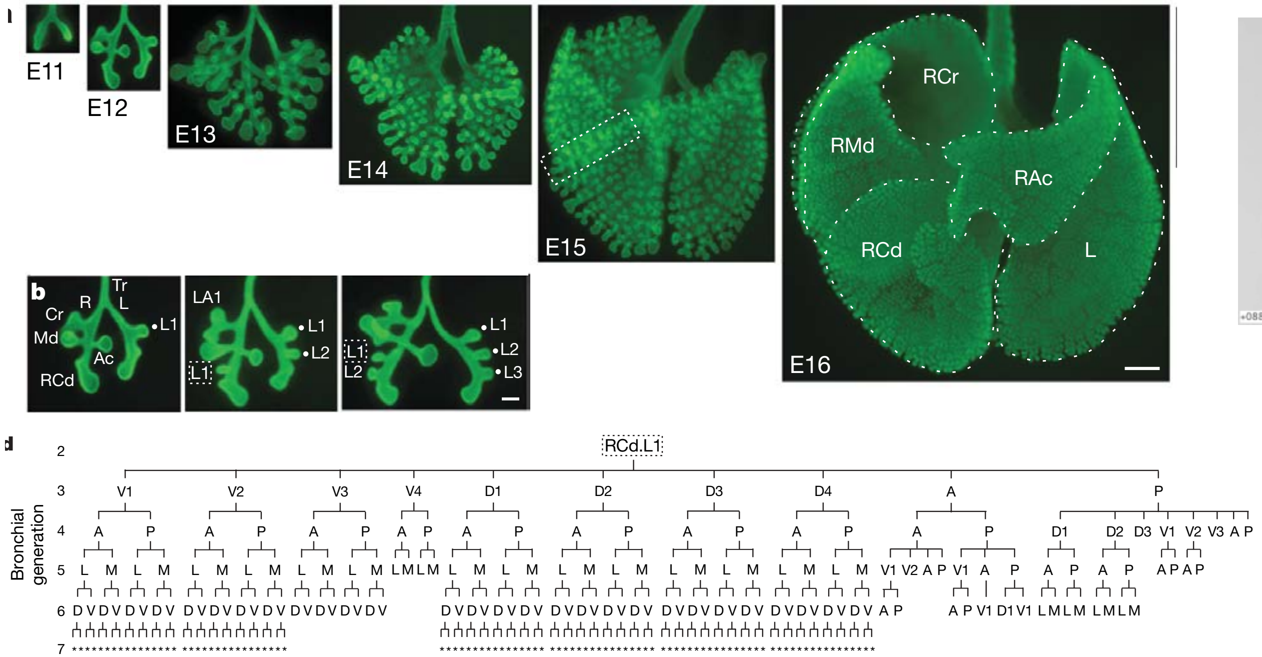
Self-organization vs Programme in development

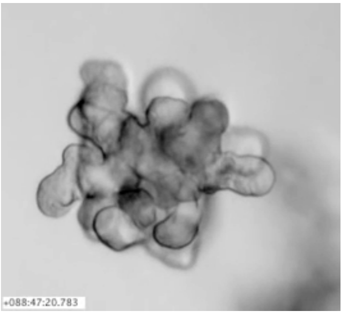
- Branching morphogenesis as a controlled programme

- Stereotypical branching pattern

The branching programme of mouse lung development

Ross J. Metzger[1]†, Ophir D. Klein[2]†, Gail R. Martin[2] & Mark A. Krasnow[1]





Thomas LECUIT 2018-2019

R. Metzger et al., G. Martin, M. Krasnow. *Nature* 453:745. 2008

Self-organization vs Programme in development

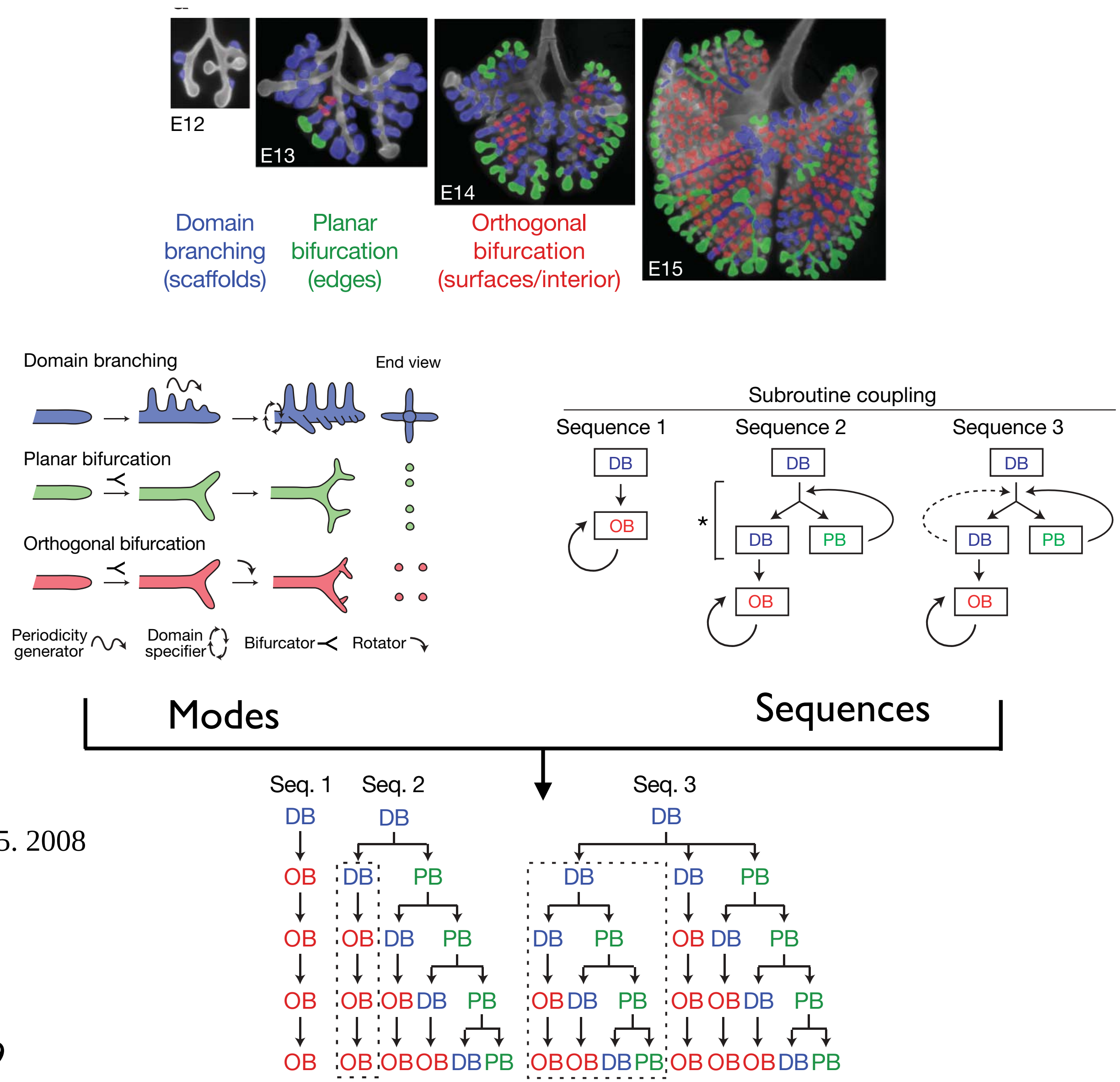
- Branching morphogenesis as a controlled programme

1. Stereotypical branching pattern comprising:
2. 3 **modes** of branching
3. organised in 3 **sequences** (order)

4. Suggests a **deterministic** programme,
5. with a **hierarchical** and **modular** organisation

6. Propose that this is **controlled by a genetically encoded subroutine** and a global **master routine**

7. Space-filling strategy



R. Metzger et al., G. Martin, M. Krasnow. *Nature* 453:745. 2008

COLLÈGE DE FRANCE 1530

Thomas LECUIT 2018-2019

Self-organization vs Programme in development

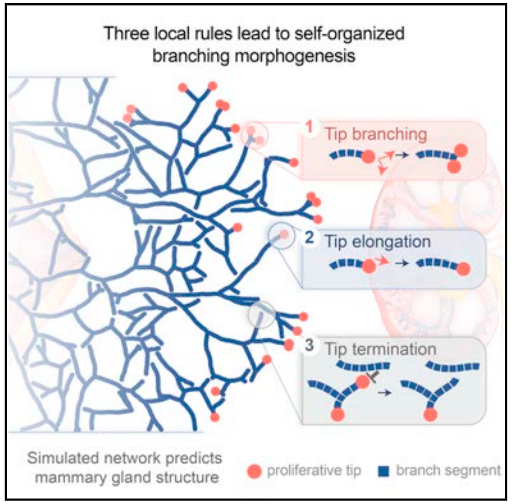
- Branching morphogenesis as a self-organised process

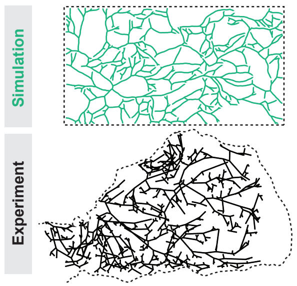
1. Tip of growing branches follow local rules: tip branching, tip elongation or tip termination.
2. Statistical rules operating at the population level, but not local deterministic rule: no exponential growth but balance of tip bifurcation by tip termination.
3. Phenomenology well predicted by a Branching Annihilating Random Walk.

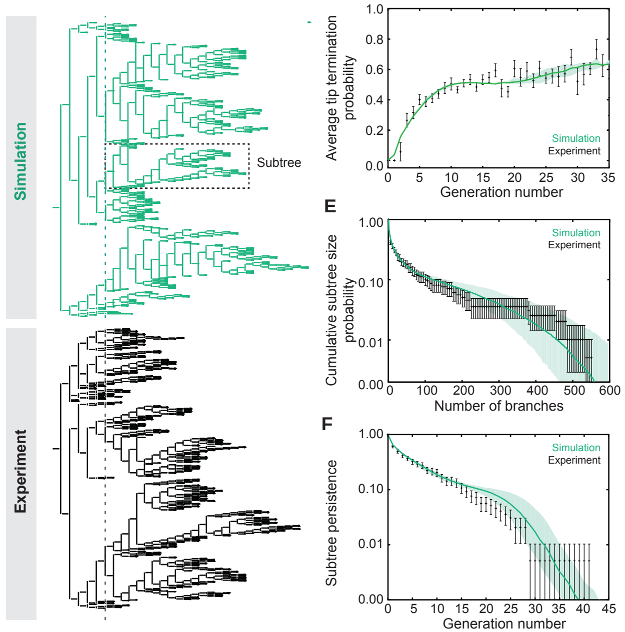
$a(x,t)$ active tip
$i(x,t)$ inactive tip

$$\begin{cases} \partial_t a = D\nabla^2 a + r_b a\left(1 - \dfrac{a+i}{n_0}\right) \\ \partial_t i = r_e a + \dfrac{r_b}{n_0} a(a+i) \end{cases},$$

4. Gives rise to a density dependent feedback (→)



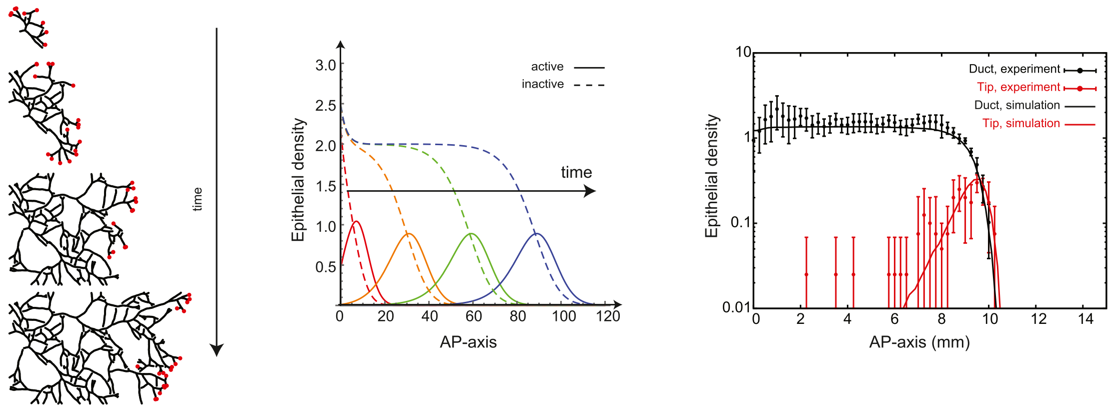




E Hannezo et al. B. Simons. *Cell* (2017) 171, 242–255

Self-organization vs Programme in development

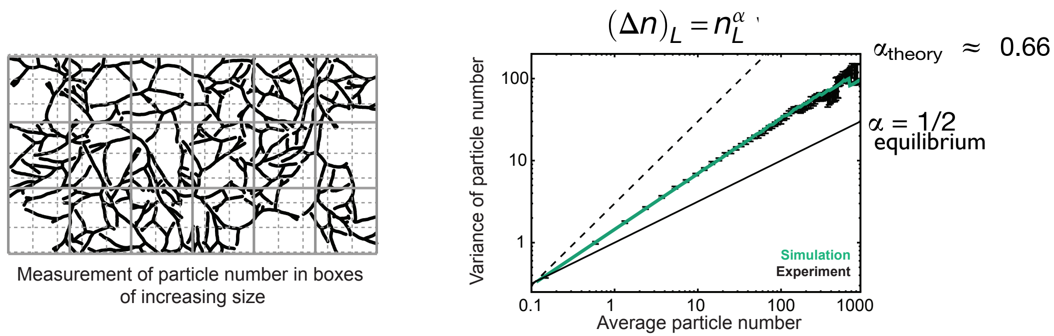
- Branching morphogenesis as a self-organised process

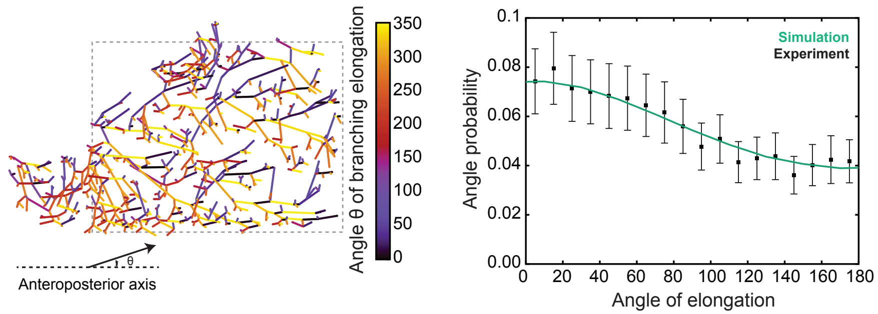


- The Branching Annihilating Random Walk model predicts:

1. Pulse of active tips at front and steady concentration of ducts behaind.
2. Fluctuation scaling law (giant fluctuations) characteristic of non-equilibrium. $(\Delta n)_L = n_L^{\alpha}$ $\alpha > ½$
3. Intrinsic polarity of growing network from isotropic local statistical rule (due to density dependent feedback).

4. There is no need for genetically encoded deterministic sequence of a programme
5. Strategy that optimises expansion rate of network (at the expense of space filling).



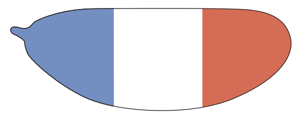


E Hannezo et al. B. Simons. *Cell* (2017) 171, 242–255

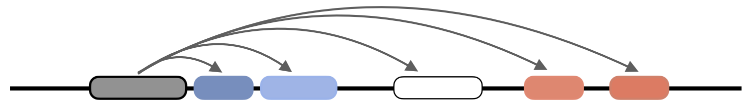
What is specified by morphogenetic information?

- Genetics/Biochemistry

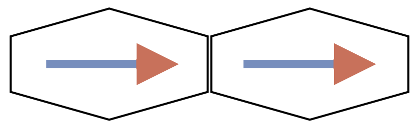
  1. **Where**: function of regionalisation



  2. **When**: temporal sequence
  3. **How fast:** rate of change



  4. **Direction**: polarisation



  5. **How much**: amplitude

[X]

  6. **Specificity**: molecular affinity

$R + L \rightleftharpoons RL$

$K_d = k_{off}/k_{on}$

  7. **Antagonistic activities:** activators/inhibitors

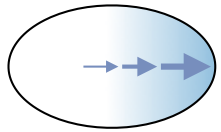
- Output: length scale and time scale

  - **diffusion:** $\lambda = \sqrt{D.\tau}$ D: diffusion coefficient
  - **Transport:** $\ell = v.\tau$ v: velocity of motor

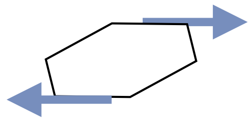
What is specified by morphogenetic information?

- Mechanics: stresses and material properties specify deformations

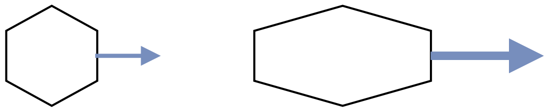
1. **Where**: depends on distribution of stresses (e.g. active stresses) and/or on stiffness E.
   Friction (γ) affects gradient of stress. $\partial\sigma / \partial x = \gamma . v$



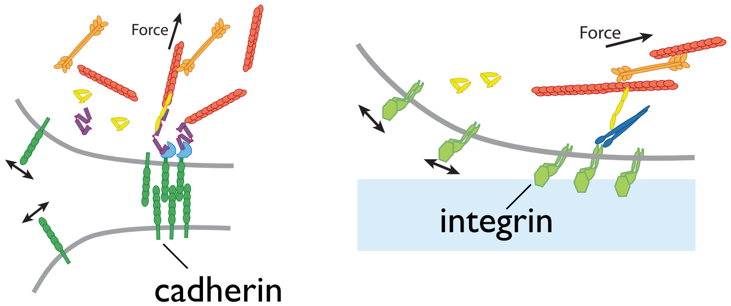
2. **How fast**: rate of deformation depends on viscosity η
   When: deformations governed by mechanical properties of cells



3. **Direction**: isotropic/anisotropic stress, tensile versus shear stress,
4. **How much**: amplitude



5. **Specificity**: molecular specificity of mechanotransduction (Integrin, Cadherin etc)
6. **Antagonistic activities:** e.g. active vs elastic
   or active stress vs friction



- Output: length scale and time scale
  - **propagation of deformation:** $\tau = \eta / E$
  - **hydrodynamic length:** $\ell = \sqrt{\eta / \gamma}$

Mechano-chemical information

Biochemistry ⇄ Mechanics

Biochemistry

- Sets mechanical parameters (stiffness: actin crosslinkers, viscosity: turnover)
- Regulates stresses (eg. activation of motors)

Mechanics

- affects transport of molecules: advection by flow
- elicits mechanotransduction: stress/strain dependent effect
- affects geometry of environment: polarity

- **diffusion:** $\lambda=(D.\tau)^{1/2}$
- **transport:** $\ell = v.\tau$

D: diffusion coefficient
v: velocity of motor + processivity

- **propagation of deformation:** $\tau = \eta / E$
- **hydrodynamic length:** $\ell = (\eta/\gamma)^{1/2}$

E: stiffness
η : viscosity
γ : friction

Information
(genetics/biochemistry)
↓
Mechanics

Information
(mechano-chemistry)

Self-organisation with mechano-chemical information

Information
(genetics/biochemistry)

Mechanics

Information
(mechano-chemistry)

Colloque: le 22 Mars 2019

Controlled and Self-organised Morphogenesis

Karen Alim (MPI Göttingen)
Suzanne Eaton (MPI Dresden)
Jérôme Gros (Institut Pasteur)
Edouard Hannezo (IST Vienna)
Maria Leptin (EMBL)
Jean-Léon Maître (Institut Curie)
Edwin Munro (Univ. Chicago)
Ewa Paluch (UCL)
Olivier Pourquié (Harvard Medical School)
Guillaume Salbreux (Crick Institute)
Cliff Tabin (Harvard Medical School)
Marie-Hélène Verlhac (Collège de France)

Plan

1. Self-organisation: spatial and temporal instabilities

    11. Turing like instabilities (mechano-chemical)
    12. Excitability, oscillations etc
    13. Trigger waves

    Courses 2 & 3 — 27 Nov , 4 Dec

2. Tissue deformations: control and self-organisation

    21. Folding, invagination, branching — Course 4 — 11 Dec

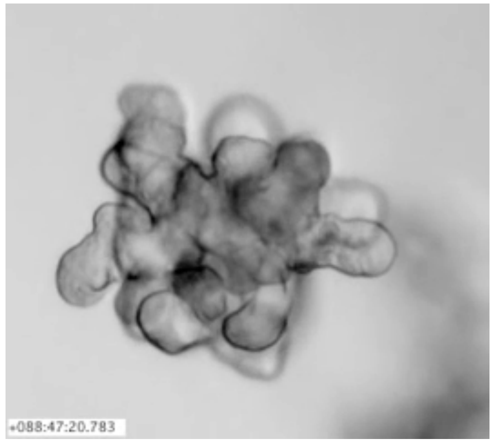
    22. Extension, flow — Course 5 — 18 Dec

1. Tissue folding , looping, branching

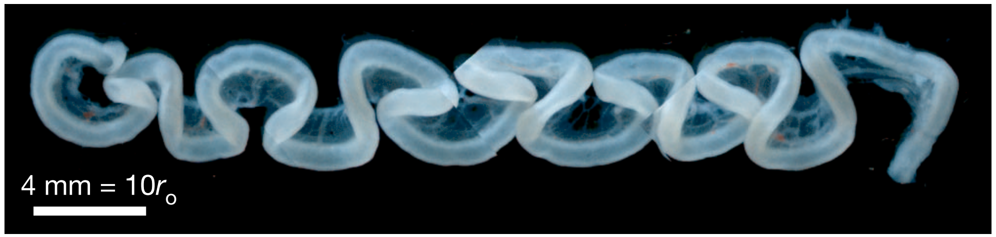
Course 4 — 11 Dec

Cortex convolution

Gut villi

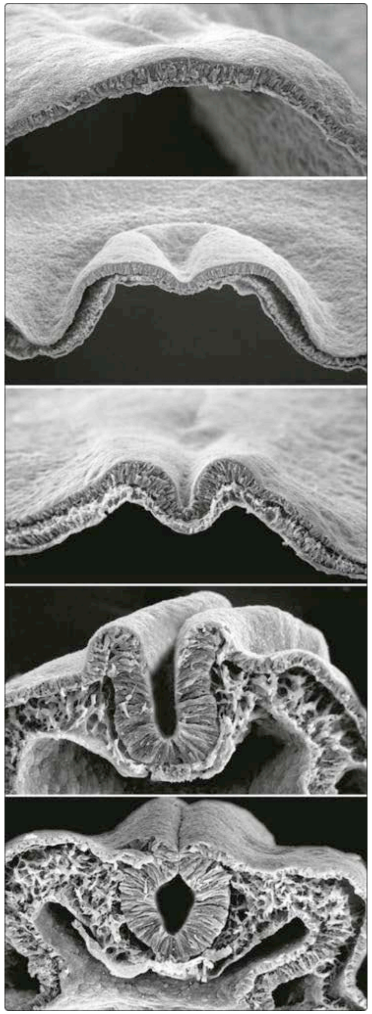


lung branching



Tissue deformations: control and self-organisation

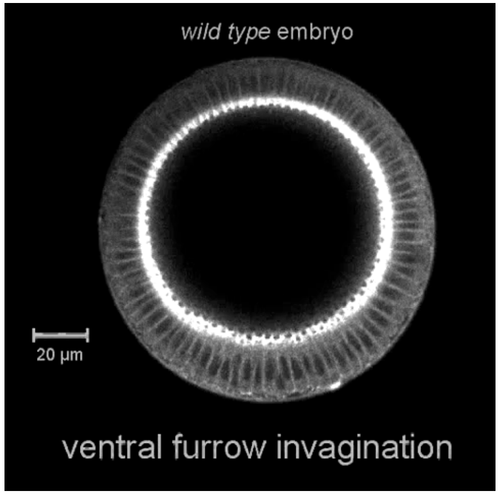
2. Tissue invagination   Course 4 — 11 Dec



G. Schoenwolf U. Utah School of Medicine

Chick neural tube

Sea Urchin endoderm

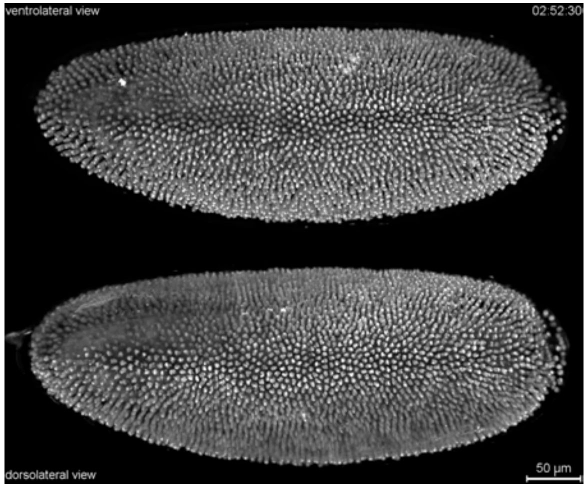


Drosophila mesoderm

Tissue deformations: control and self-organisation

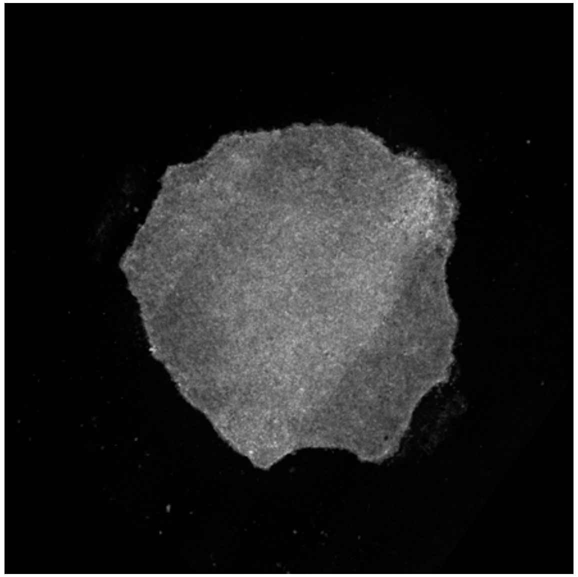
3. Cellular flow and tissue extension, rotation

Course 5 — 18 Dec

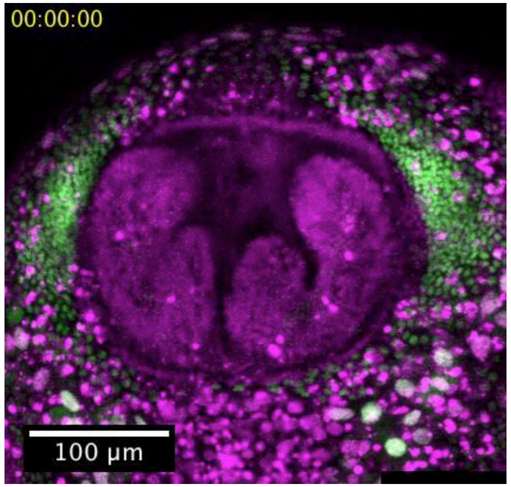


Patrick Keller (Janelia Campus)

Drosophila germband extension



Chick gastrulation



Drosophila genitalia rotation