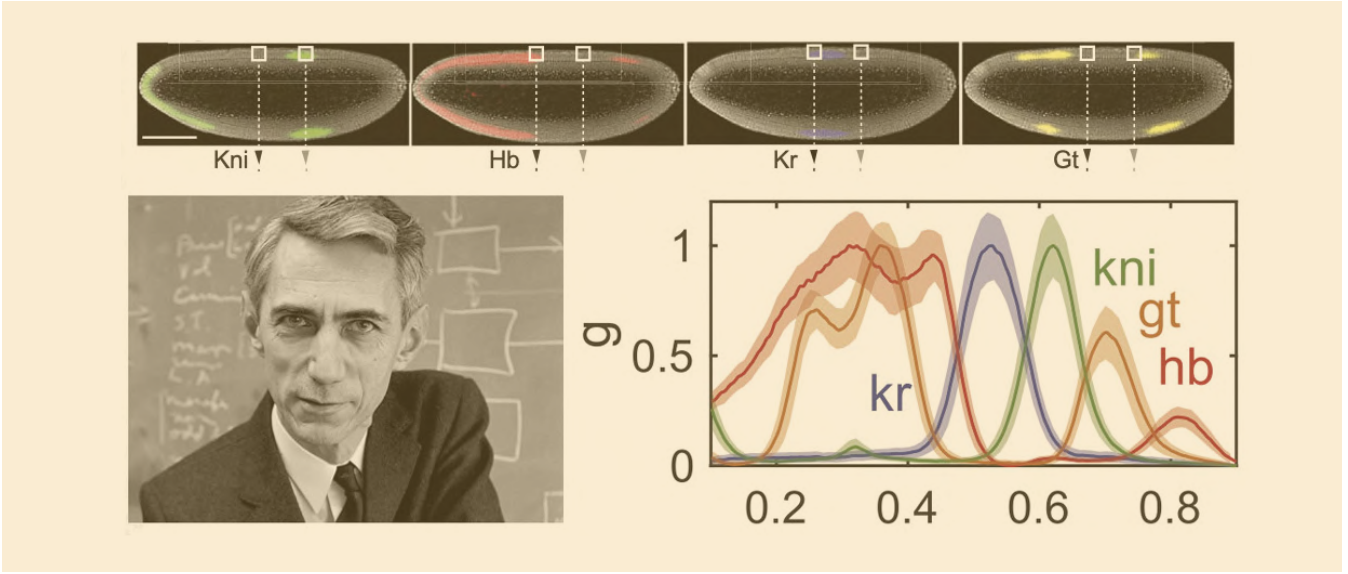
What is biological information?



Course 3: Encoding, Decoding and Representations of *Space*

Thomas Lecuit

chaire: Dynamiques du vivant

COLLÈGE DE FRANCE
1530

« Biological codes »: summary

- From letters (chemical species) to « words »: *sequences* and *combinations*
- *Balance between diversity and specificity*
  - **Genetic code**: deterministic, requires mechanisms for error minimisation (**proofreading and « smooth encoding »**)
  - **Transcriptional code**: **smooth encoding**, but also **combinatorial encoding** and integration relaxes constraints on 1-to-1 specificity, and increases repertoire of context-dependent regulation.
  - **Signalling code:** Promiscuous binding and **combinatorial encoding** increase cellular addressing compared to 1-to-1 L/R signalling. Also allows signal computation.
  - **Adhesion code**: biased stochastic processes rather than deterministic encoding. Many small contribution rather than few, selective, deterministic molecular codes.

« Biological codes »: summary

- From letters (chemical species) to « words »: sequences and combinations
- Balance between diversity and specificity

  - **Coding theory** provides a framework to understand constraints on code evolution (error load, diversity and cost). **Smooth encoding.**

  - **Combinatorial encoding** increases specific « addressing » (cell identity, cell responses)

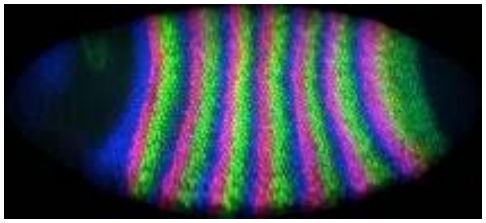
  - **Deterministic use of code**: genetic code
  - **Stochasticity and Algorithmic encoding**: more consistent with self-organisation.

- From « words » to patterns of words (in space and time), ie. « sentences ».

Spatial patterns across scales

- Embryo segmentation

0.5 mm – 1 hour



Shinji Takada

- Plumage/pigmentation pattern

0.5 mm – 2 days

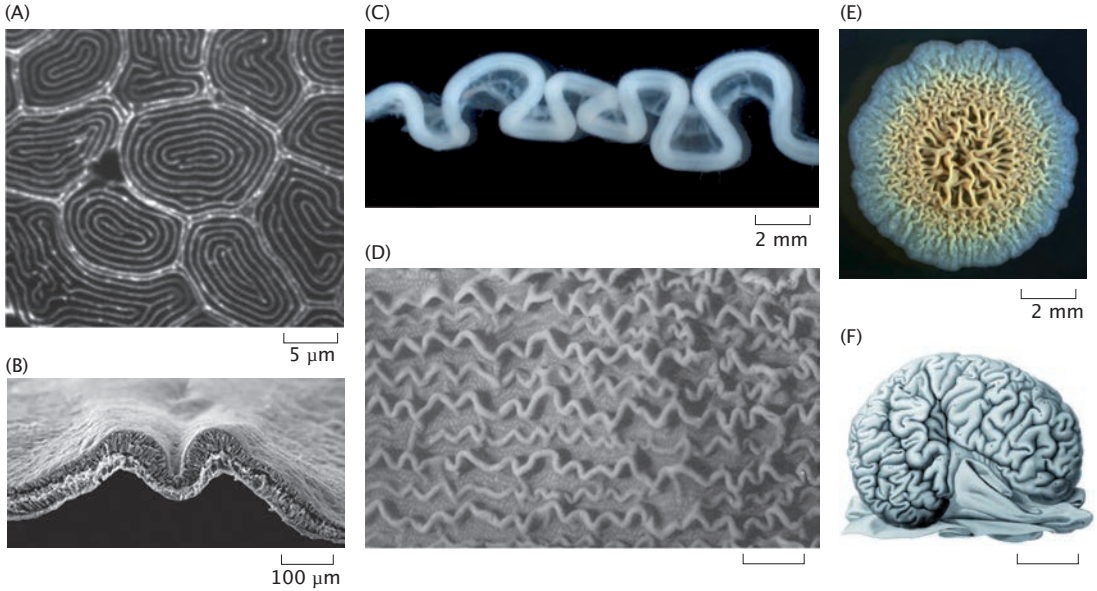
Interface Focus (2012) 2, 433–450 doi:10.1098/rsfs.2011.0122

Tony Hisgett/Wikipedia

5 mm – 10 days

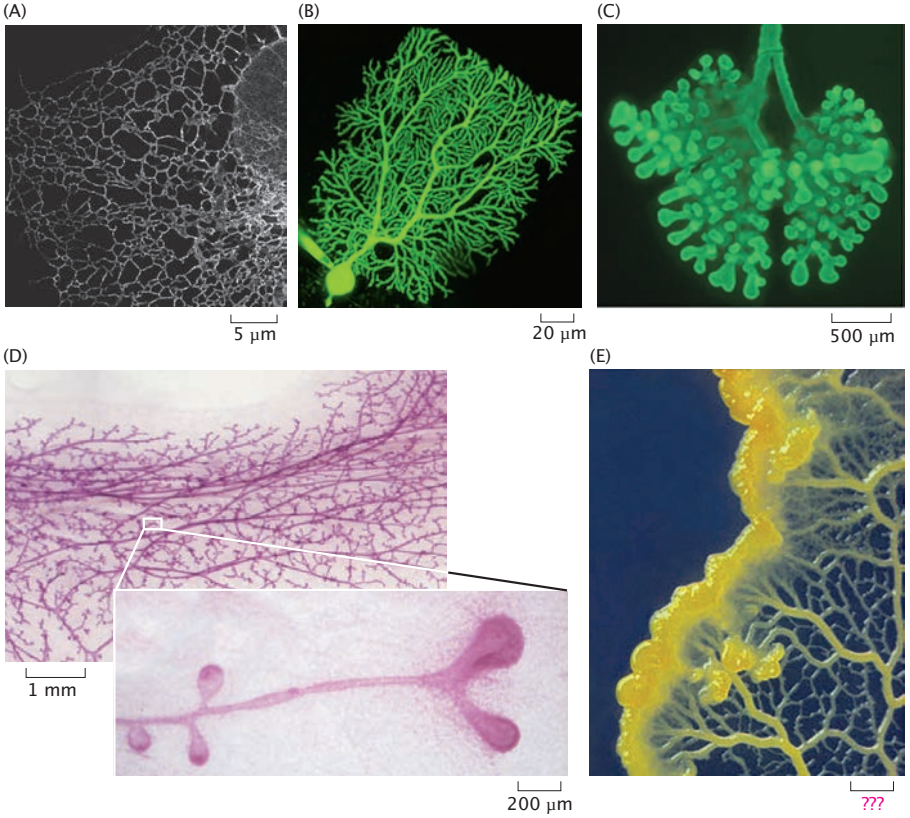
Spatial patterns across scales

- Folding patterns



0.5 mm – 10 days

- Branching patterns



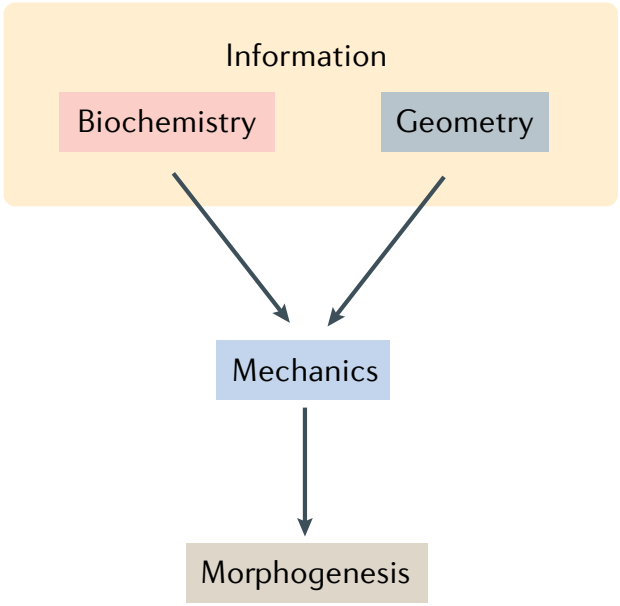
Plan

1. Length scales in biological systems
2. Positional Information (PI) and Morphogens
3. Shannon information theory
4. Encoding and Decoding space with PI
5. Beyond PI: generalisation

Deterministic spatial patterning

PROGRAM

- hierarchy
- modularity
- heredity (biased initial & boundary conditions)
- deterministic rules

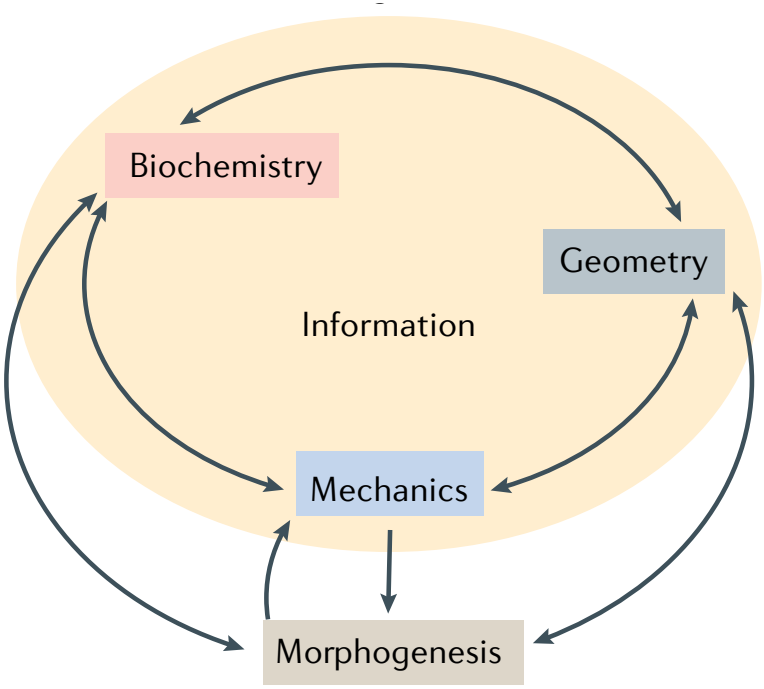


Collinet C. & Lecuit T. *Nature Rev. Mol. Cell Biol.*, 2021
doi.org/10.1038/s41580-020-00318-6

Self-organised spatial patterns

SELF-ORGANIZATION

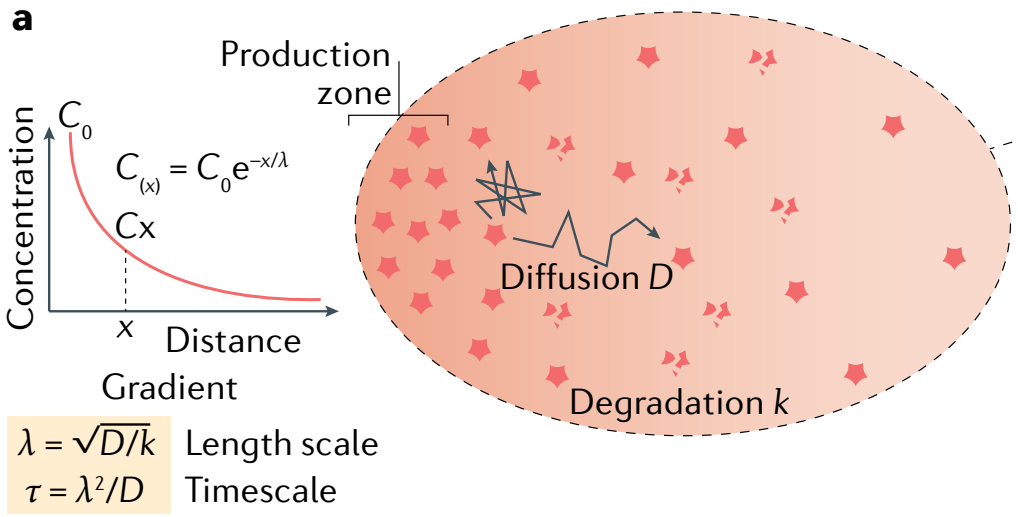
- no hierarchy
- stochastic processes/ statistical rules
- feedbacks



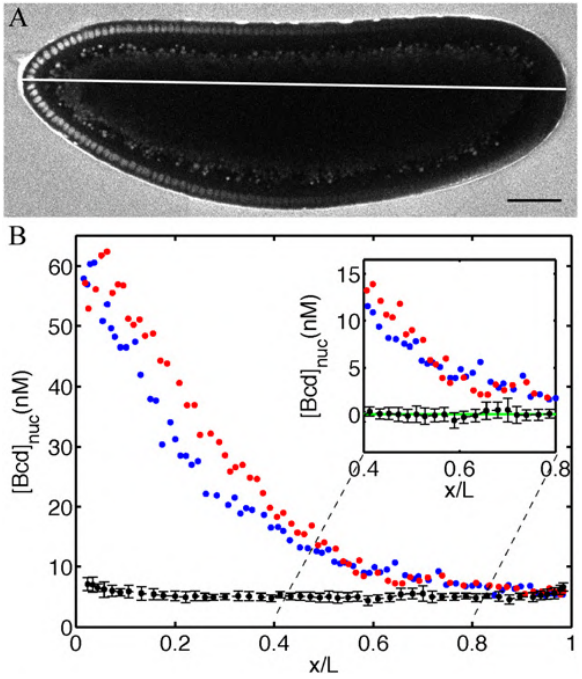
Collinet C. & Lecuit T. *Nature Rev. Mol. Cell Biol.*, 2021
doi.org/10.1038/s41580-020-00318-6

Defining length scales - deterministic models

- Biochemical processes, Diffusion and Morphogen gradients



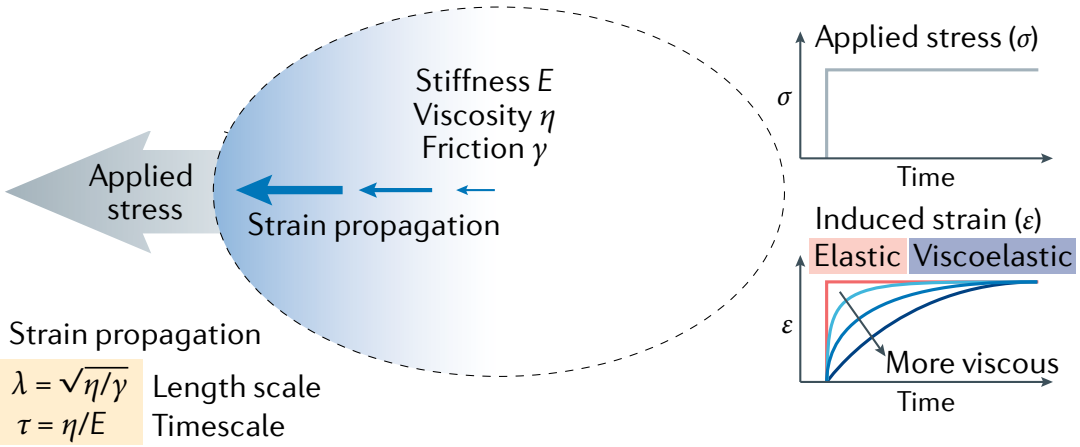
Collinet C. & Lecuit T. *Nature Rev. Mol. Cell Biol.*, 2021
doi.org/10.1038/s41580-020-00318-6



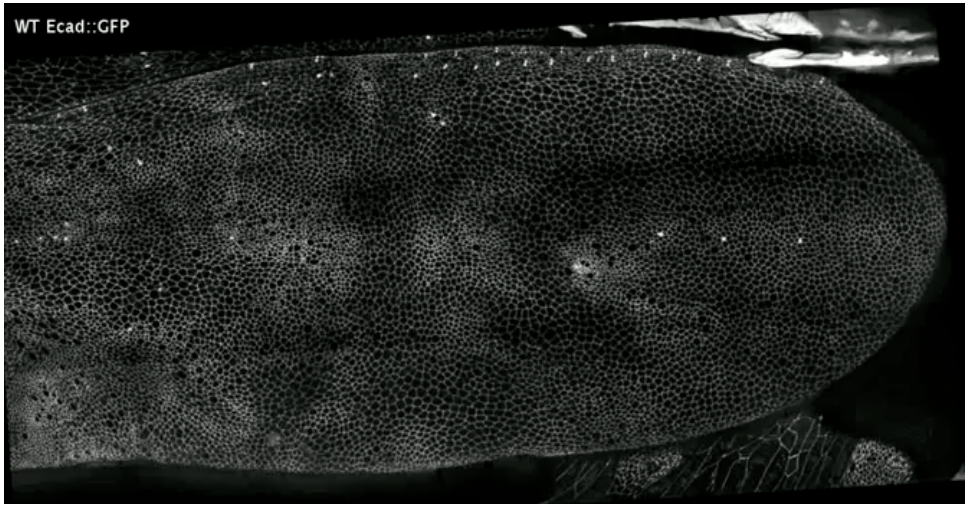
Thomas Gregor, D. Tank, E. Wieschaus and B. Bialek
Cell 130:153 (2007)

Defining length scales - deterministic models

- Mechanical processes



Collinet C. & Lecuit T. *Nature Rev. Mol. Cell Biol.*, 2021
doi.org/10.1038/s41580-020-00318-6



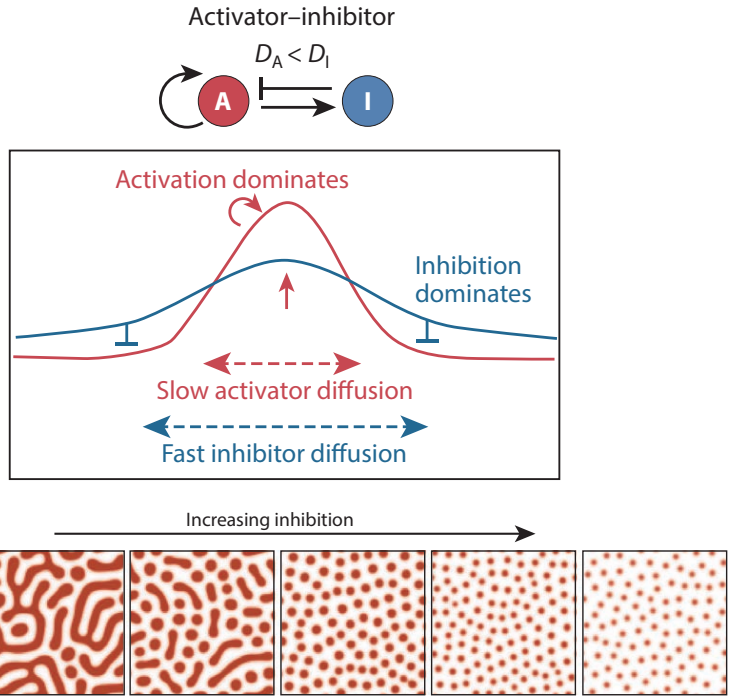
Etournay R, et al. and Jülicher F, Eaton S.
Elife. 4:e07090. (2015)

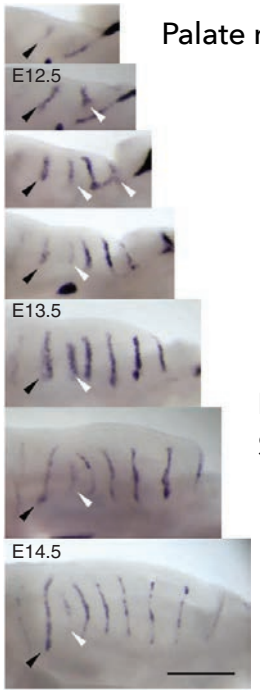
Defining length scales - self-organised instabilities

- Turing chemical instabilities (reaction diffusion)

Local positive feedback - Long range inhibition

The length scales of patterns depend on the details of interaction strengths and diffusivities





Palate ridges

FGF: activator
Shh: inhibitor

Economou AD, et al. & JBA. Green *Nat Gene*t. 44(3):348–51 (2012)

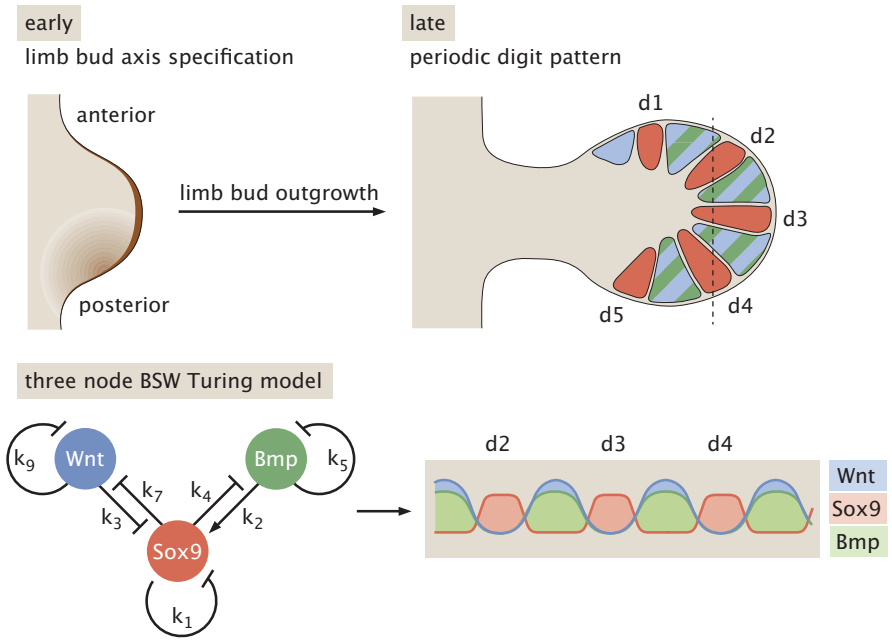
Bailles A, Gehrels EW, Lecuit T. *Annu Rev Cell Dev Biol*. 38:321-347 (2022)

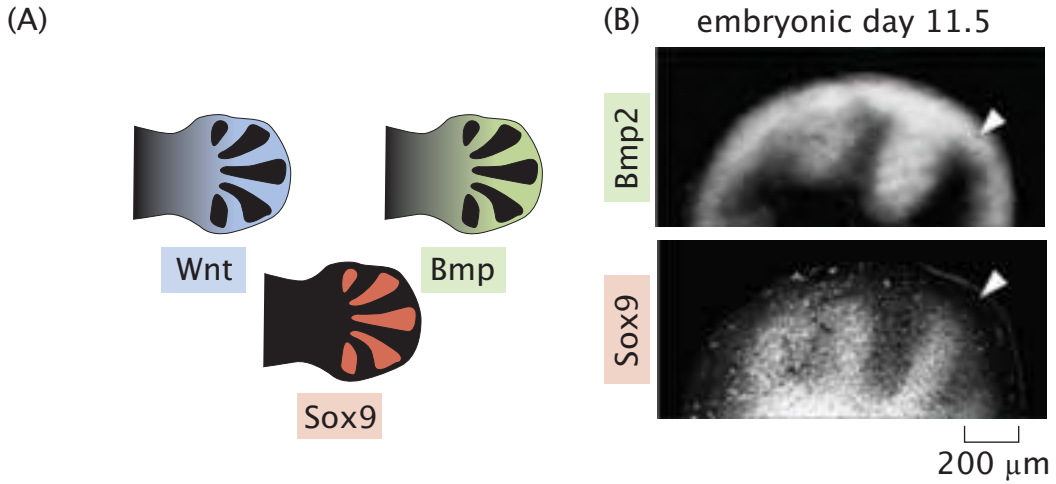
Defining length scales - self-organised instabilities

- Turing chemical instabilities (reaction diffusion)

Local positive feedback - Long range inhibition

The length scales of patterns depend on the details of interaction strengths and diffusivities





J. Raspopovic et al. and J. Sharpe. *Science* 345, 566 (2014)

Rob Phillips and Christina Hueschen, *The restless cell Continuum theories of living matter.* 2024, Princeton Univ. press.

Defining length scales - self-organised instabilities

Local positive feedback - Long range inhibition

- Turing-like mechanical instabilities

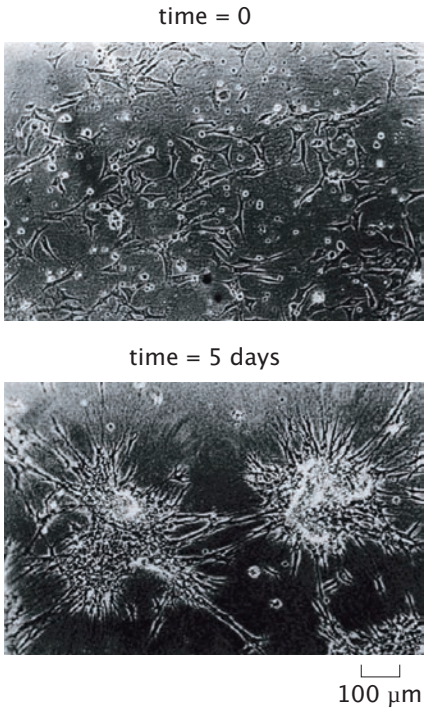
J. Embryol. exp. Morph. 80, 1–20 (1984)
Printed in Great Britain © The Company of Biologists Limited 1984

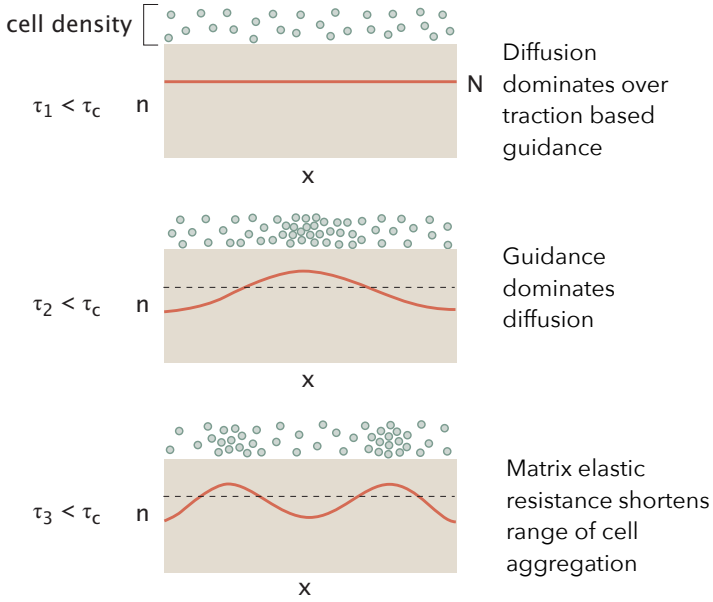
Generation of spatially periodic patterns by a mechanical instability: a mechanical alternative to the Turing model

By ALBERT K. HARRIS[1], DAVID STOPAK[2] AND PATRICIA WARNER[1]

[1] Department of Biology, Wilson Hall (046A), University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27514, U.S.A.

[2] Department of Biological Sciences, Stanford University, Stanford, Carolina 94305-2493, U.S.A.





force balance

$$\nabla \cdot \left[\sigma_{viscous} + \sigma_{elastic} + \sigma_{traction}\right] = 0$$

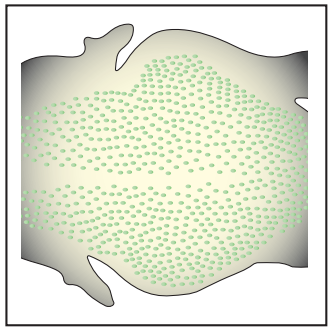
Dimensionless traction parameter (~ratio of traction and ECM stiffness)

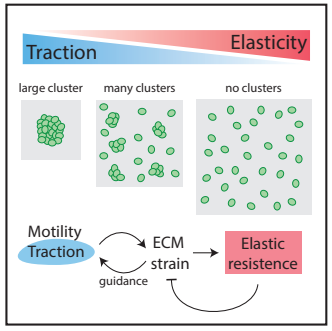
$$\tau^* = \tau \rho_0 N(1+\nu)/E$$

A.K Harris, D. Stopak and P. Warner. *J. Embryol exp. Morph.* 1984. 80:1-20

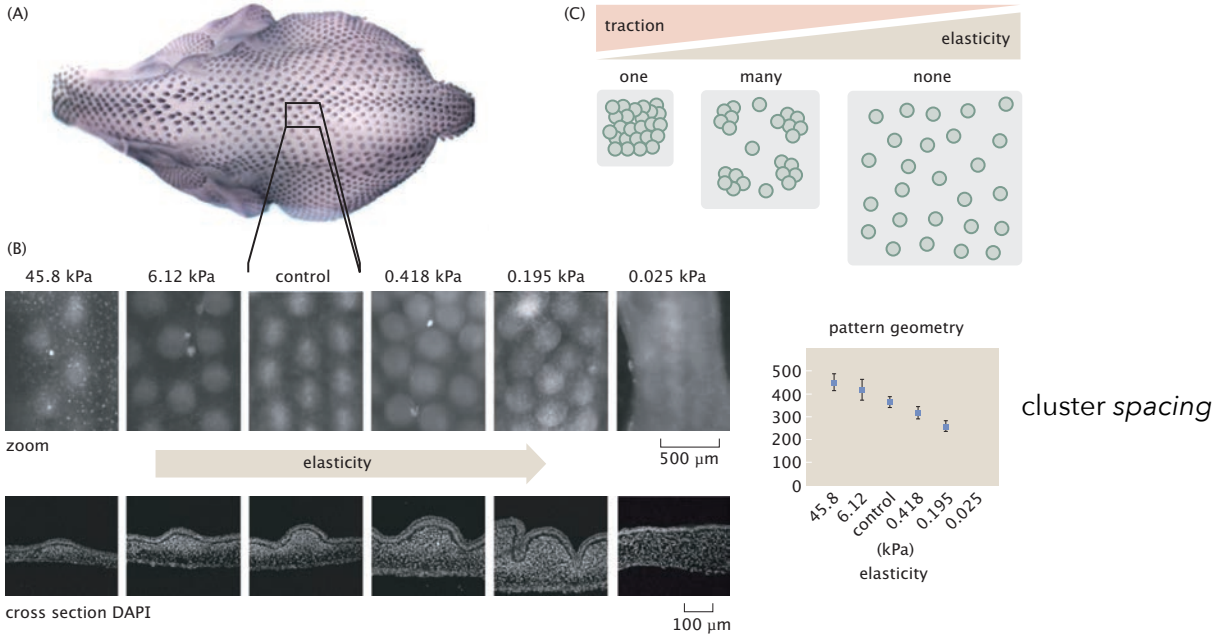
Defining length scales - self-organised instabilities

Local positive feedback - Long range inhibition





- Turing-like mechanical instabilities



cluster *spacing*

G.F. Oster, J.D. Murray, and A.K. Harris. *J. Embryol. esp. Morph.* 1983. 78:83-125

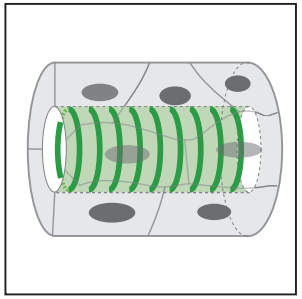
J.D. Murray, G.F. Oster and A.K. Harris. *J. Math. Biology* 1983. 17:125-129

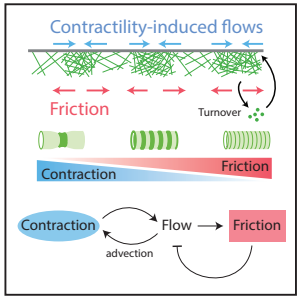
A. Shyer et al, R. Harland. *Science* 357: 811-815 (2017)

Collinet C. & Lecuit T. *Nature Rev. Mol. Cell Biol.*, 2021
doi.org/10.1038/s41580-020-00318-6

Defining length scales - self-organised instabilities

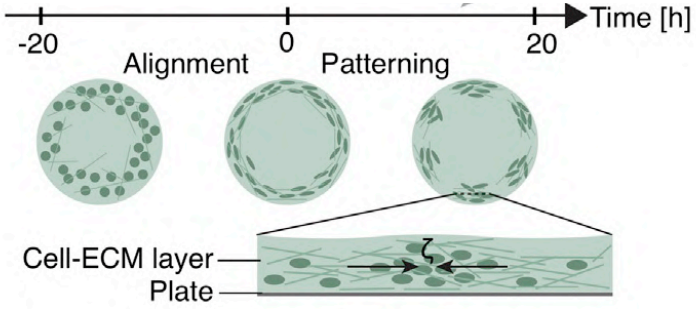
Local positive feedback - Long range inhibition

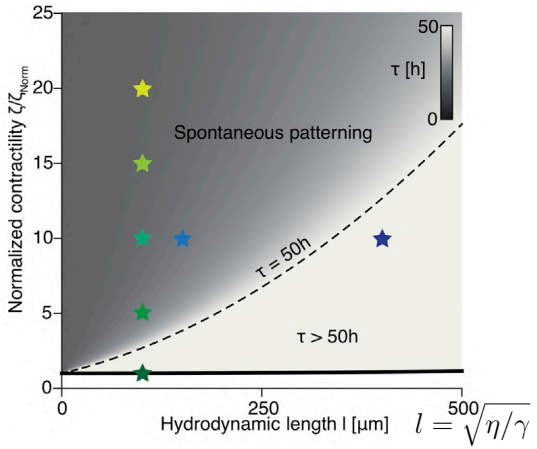




E. Hannezo et al S. Hayashi and J-F. Joanny. *PNAS* 112:8620–8625 (2015)

- Turing-like mechanical instabilities





Constitutive relations and force balance eq.

$$j = -D\frac{\partial \rho}{\partial s} + \rho v. \quad \sigma = \eta\frac{\partial v}{\partial s} + \sigma_{\mathrm{A}}. \quad 0 = \gamma v - \frac{\partial \sigma}{\partial s},$$

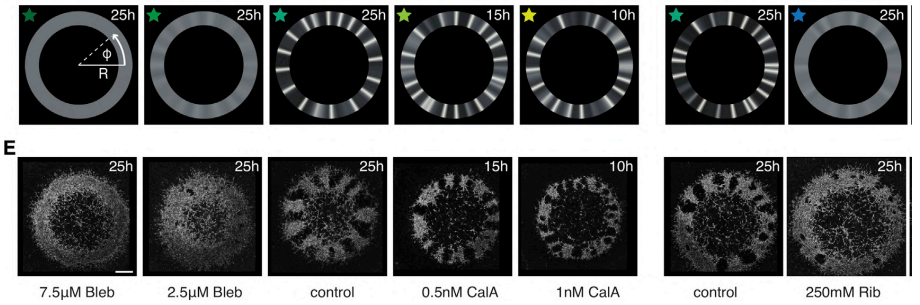
$l = \sqrt{\eta/\gamma}$

At steady state:

$$\delta\rho = \delta\rho_0 \exp(\omega t + iks),$$

$$\omega = Dk^2\left(\frac{\mathrm{Pe}}{1+l^2k^2} - 1\right).$$

ω_{max} for $k_{\max} = \frac{1}{l}\sqrt{\sqrt{\mathrm{Pe}} - 1},$



Pe:Peclet number (ratio of transport by convection/advection versus diffusion) : ζ/ζ_{norm}

Palmquist et al,, *Cell* 185, 1960–1973, 2022

Original theory: J. Bois, F. Jülicher and SW. Grill. *PRL*. 2011. 106, 028103

Plan

1. Length scales in biological systems
2. Positional Information (PI) and Morphogens
3. Shannon information theory
4. Encoding and Decoding space with PI
5. Beyond PI: generalisation

Coordinate systems

- 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)

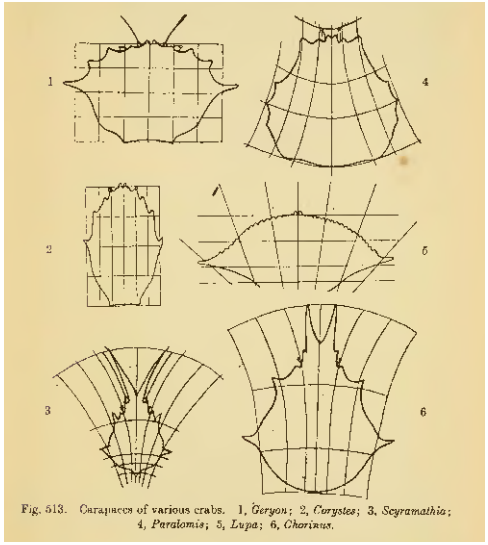


Fig. 513. Carapaces of various crabs. 1, *Geryon*; 2, *Corystes*; 3, *Scyramathia*; 4, *Paralomis*; 5, *Lupa*; 6, *Chorinus*.

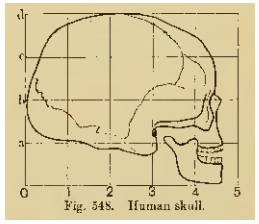


Fig. 548. Human skull.

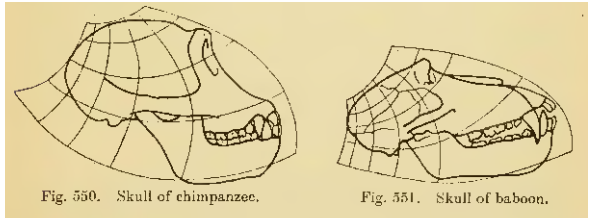


Fig. 550. Skull of chimpanzee.

Fig. 551. Skull of baboon.

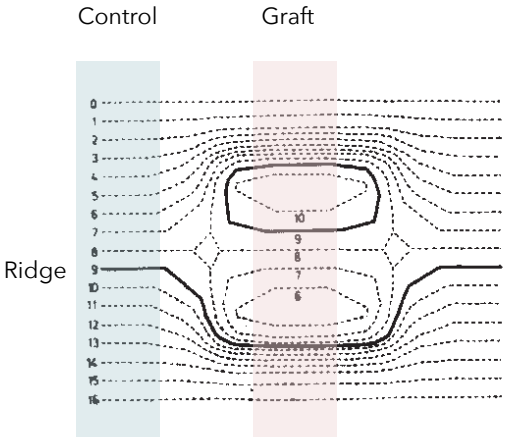
d'Arcy W Thompson, *On Growth and Form*, 1917

Evidence that cells « compute » their distance from a reference *in vivo*

Mechanism by which Cells estimate their Location within the Body

H. F. Stumpf

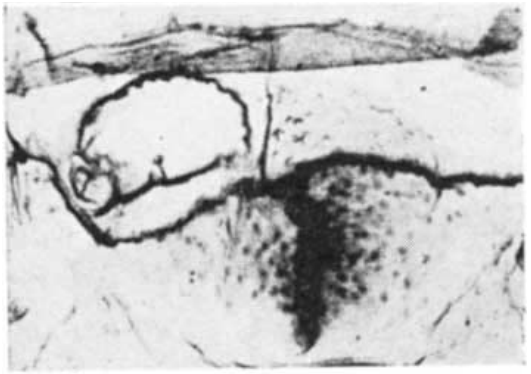
It can thus be concluded that a specific concentration of the gradient substance is responsible for the cell forming a rib. The concentration gradient, the existence of which is confirmed by these results, obviously has two functions: (1) to orient the scales by its direction, (2) to supply the cells by its absolute values (or ranges of concentration) with the necessary information about their distance from the segment margins and to induce the corresponding cuticular structures.



b

Fig. 2.

Galleria mellonella



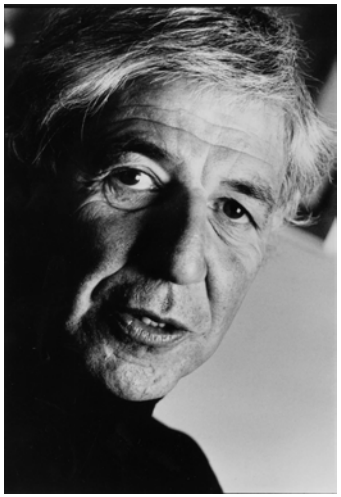
b

Fig. 3.

Rotation 180° of piece of cuticle leads to deformation of ridge and to reorientation of cuticular patterns

Hildegard F. Stumpf, *Nature*, 212, 430-431. (1966)

Positional information: an intrinsic coordinate system



Lewis Wolpert
(1929-2021)

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

The problem of pattern is considered in terms of how genetic information can be translated in a reliable manner to give specific and different spatial patterns of cellular differentiation. Pattern formation thus differs from molecular differentiation which is mainly concerned with the control of synthesis of specific macromolecules within cells rather than the spatial arrangement of the cells. It is suggested that there may be a universal mechanism whereby the translation of genetic information into spatial patterns of differentiation is achieved. The basis of this is a mechanism whereby the cells in a developing system may have their position specified with respect to one or more points in the system. This specification of position is positional information. Cells which have their positional information specified with respect to the same set of points constitute a field. Positional information largely determines with respect to the cells' genome and developmental history the nature of its molecular differentiation. The specification of positional information in general precedes and is independent of molecular differentiation. The concept of positional information implies a co-ordinate system and polarity is defined as the direction in which positional information is specified or measured. Rules

It is too often implicit in embryological thinking that each step in development is a unique or special phenomenon with little general significance. One might, for example, view development as a sequential process involving the synthesis of a large number of different proteins, the essential feature of each stage being dependent on the nature of the proteins synthesized

I would like to suggest that such a view is quite misleading and that there is good reason for believing that there are a set of general and universal principles involved in the translation of genetic information into pattern and form.

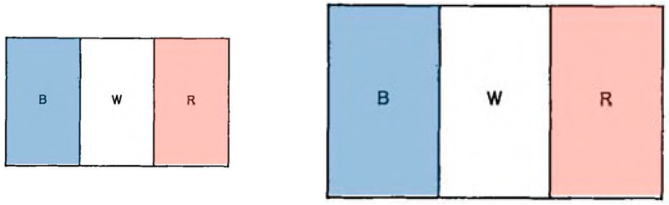
- An intrinsic **coordinate systems specifies positional identity (information)**
- Interpret the positional information to produce structures and differentiate
- **Uncouples *information* and *interpretation* at cellular and tissue levels:**

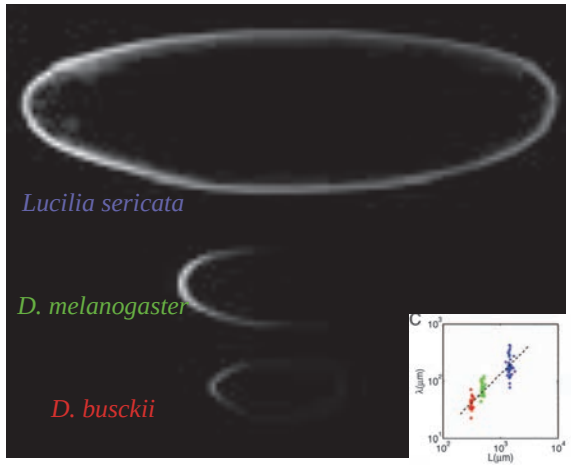
  based on the discovery of scaling property of developmental processes (e.g. Hans Driesch's observation of « regulative » development in sea urchin: cells are not pre-specified, and generate their own coordinate system)

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

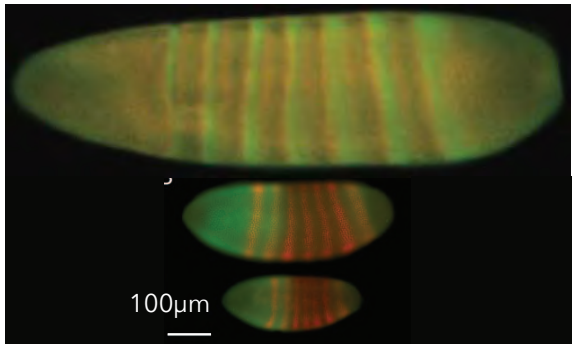
Positional information: an intrinsic coordinate system

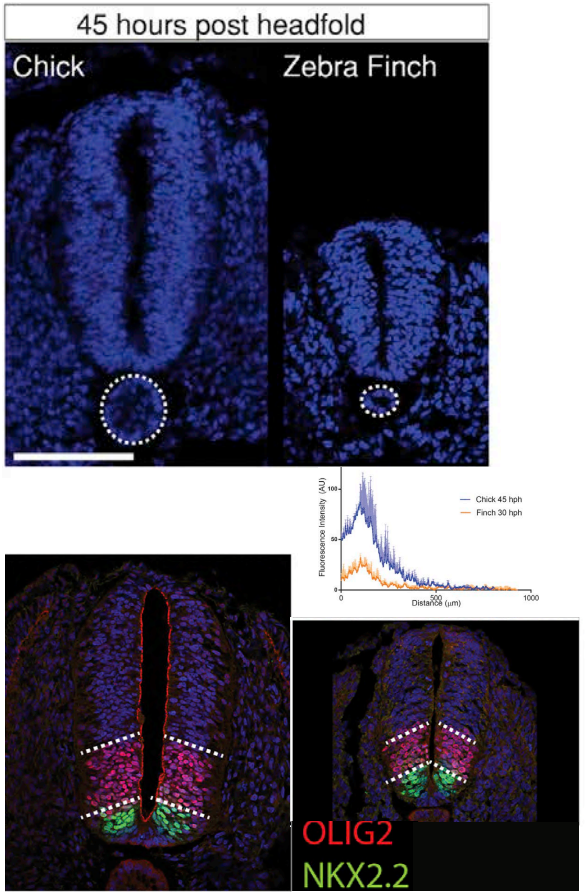
- The French Flag Problem
- Regenerative potential of a tissue with scale invariant pattern
- Requires (i) a mechanism for specifying polarity; (ii) a mechanism for the differential response of the cells, such as thresholds; and (iii) at least one spontaneous self-limiting reaction (Wolpert, 1968).





T. Gregor, W. Bialek et al, E. Wieschaus. *PNAS*, 51, 18403-18407 (2005)



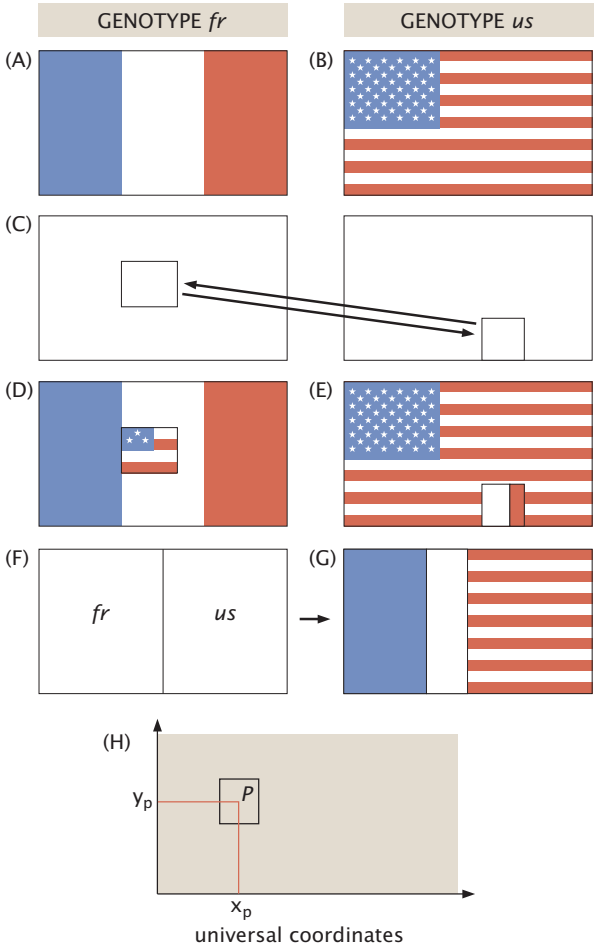


Uyghur A. Et al, and J. Briscoe, C. Tabin. *Developmental Cell* 37, 127–135

Positional information: an intrinsic coordinate system

- The French Flag Problem
- Regenerative potential of a tissue with scale invariant pattern
- Requires (i) a mechanism for specifying polarity; (ii) a mechanism for the differential response of the cells, such as thresholds; and (iii) at least one spontaneous self-limiting reaction (Wolpert, 1968).

- Implications of the universality of positional information



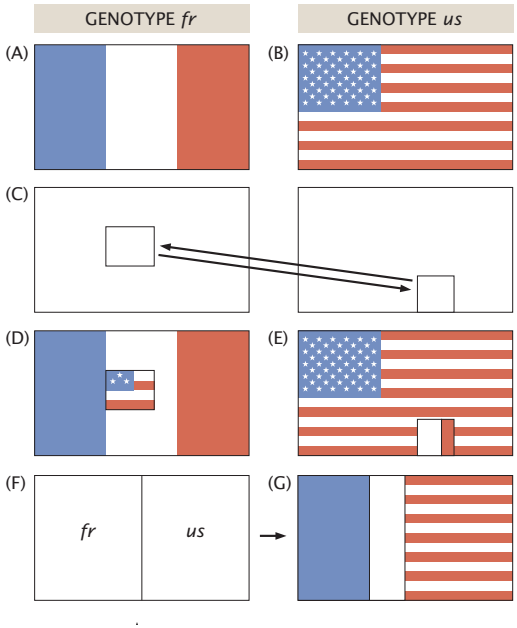
- Same positional information system
- Genotype specifies interpretation

FIG. 5. Some examples to show some possible implications of the universality of positional information. Consider a rectangular field and two different genotypes. Genotype *fr* results in the interpretation of the positional information so that a French Flag is formed (a) while genotype *us* results in the Stars and Stripes (b). If, at an early stage, two pieces are interchanged as in (c), and if positional information in the two fields is the same, then the results shown in (d) and (e) will follow: that is the cells behave according to their genotype and position and are indifferent to the nature of the surrounding tissue. Similarly, if two halves of different genotypes are joined as in (f) a mosaic as in (g) will form (B is blue, W is white, R is red).

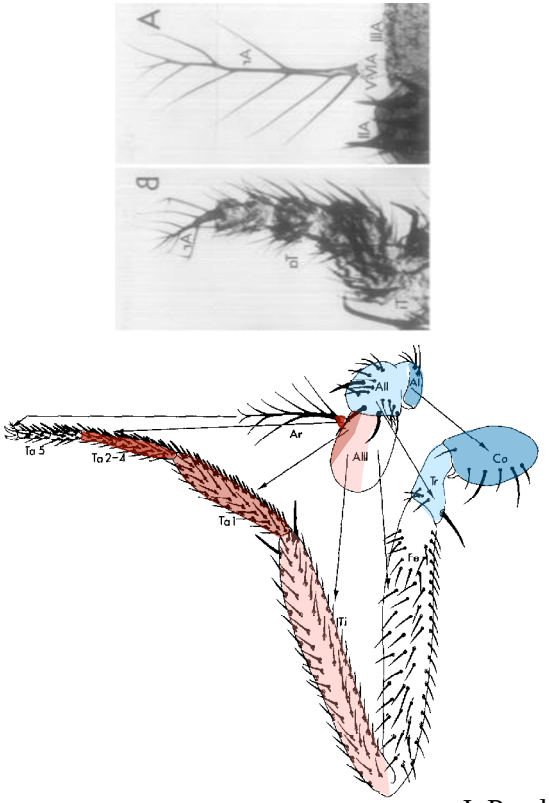
Lewis Wolpert, *J. Theoret. Biol.* (1969) 25: 1-47

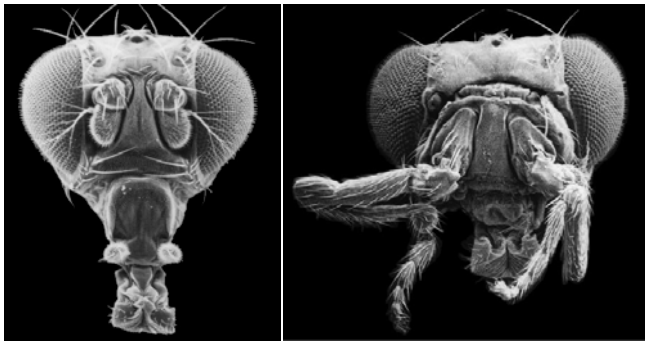
Positional information: an intrinsic coordinate system

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



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





wild type *Antennapedia*

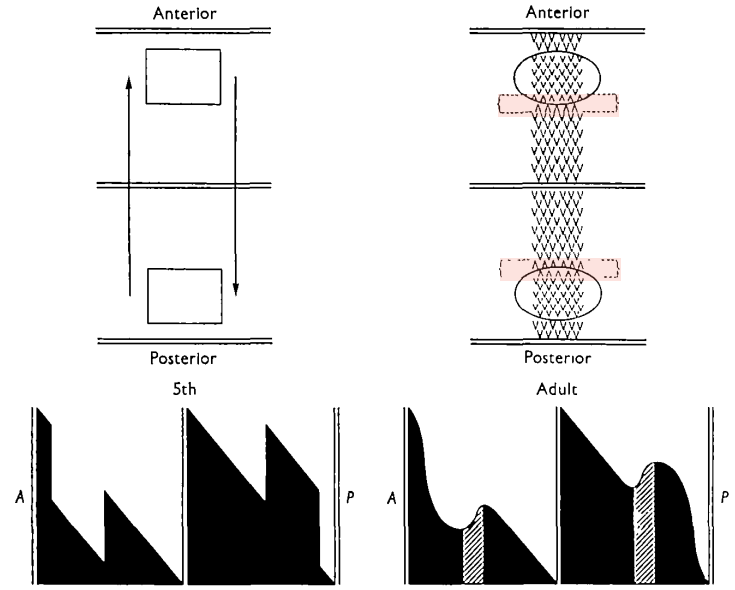
J. Postlethwait and H. Schneiderman, *Dev. Biol.* (1971) 25:606-640

Evidence that cells respond to gradients of positional information

- Graft experiments on the cuticle of insects (*Rhodnius*) induce reorientations of hairs in cells at the boundary of the graft
- This is consistent with this orientation being set up by the **slope of a gradient of positional information (slope defined by the position of a source)**

A GRADIENT OF POSITIONAL INFORMATION IN AN INSECT, *RHODNIUS*

P. A. LAWRENCE, F. H. C. CRICK AND M. MUNRO
Medical Research Council, Laboratory of Molecular Biology, Hills Road, Cambridge, CB2 2QH England



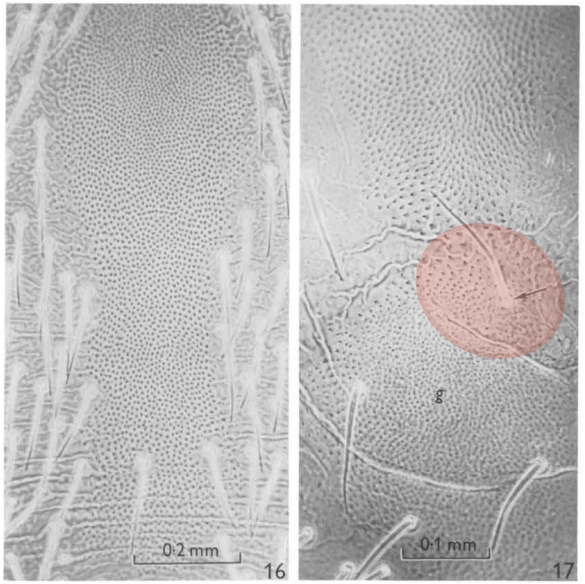
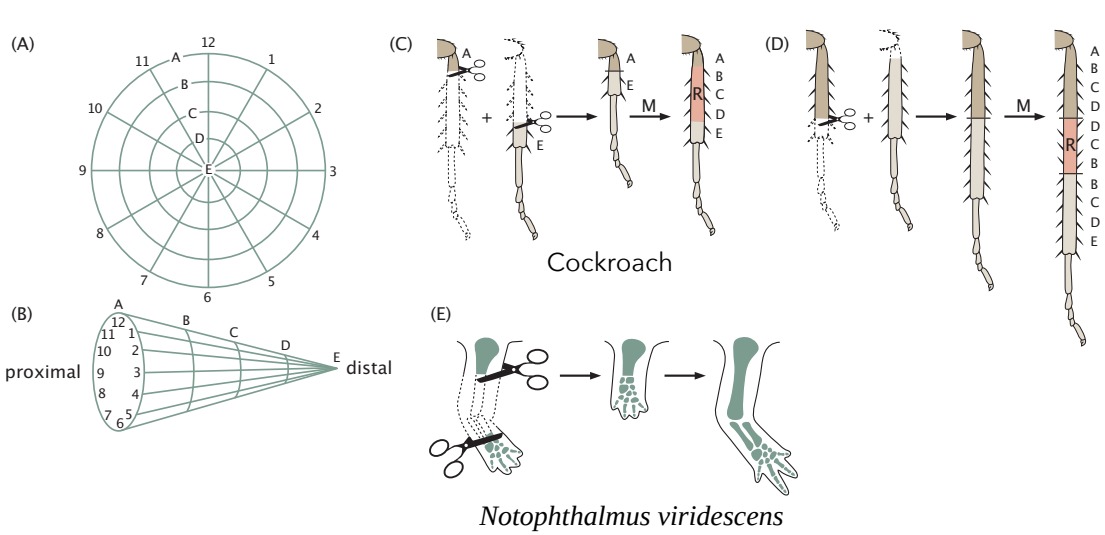


Fig. 3. Experiment illustrating the dependence of polarity on the direction of gradient slope. The operation was performed on the sternite of a 5th-stage larva (left) and the result shown diagrammatically on the right. Cross-sections of the gradient landscapes are indicated below. Note the regions where the gradient slope is reversed as a result of local diffusion. Brackets indicate where the oriented tubercles point towards the anterior margin (*A*) instead of towards the posterior (*P*). (Compare Figs. 16, 17.)

J. Cell Sci. **11**, 815–853 (1972)

Positional information as Coordinate systems

- Regeneration experiments and positional information



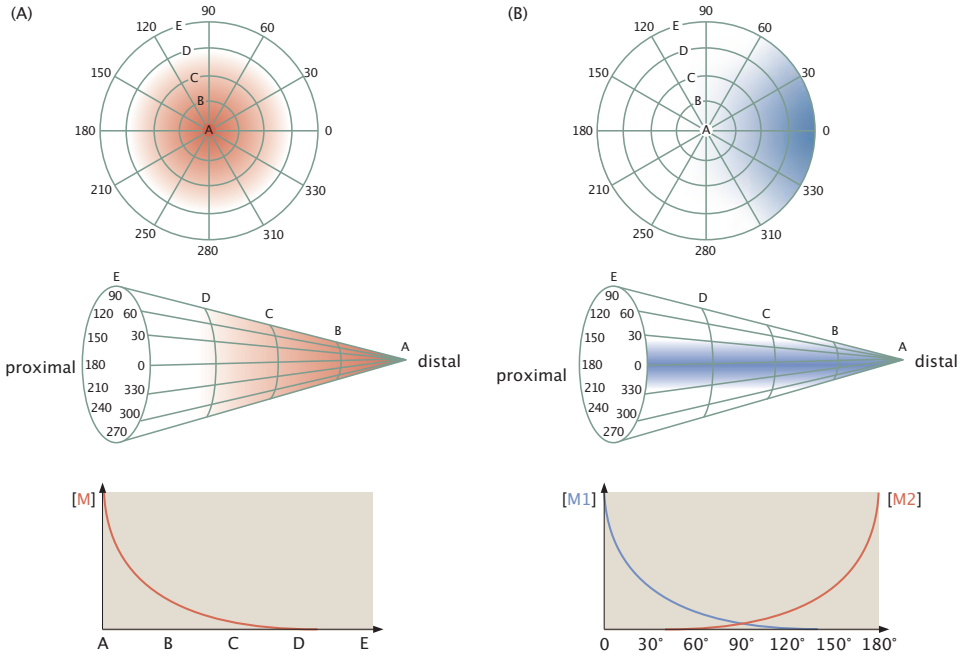
S.V. Bryant , V. French, and P.J. Bryant *Science* (1981). 212::993-1002

V. French, P.J. Bryant and S.V. Bryant *Science* (1976). 193::969-981

The Polar Coordinate Model

We begin from Wolpert's (*3*) idea that spatial patterns result from cells acquiring information about their physical positions in the developing cell population.

- Polar and cartesian coordinate systems



Graded substances during early development

- 1901: **Thomas Hunt Morgan postulated that gradients of "formative stuff"** underlie regeneration events

We might make an appeal to the hypothesis of formative stuffs, and assume that there are certain substances present in the head, and others in the tail, of such a sort that they determine the kind of differentiation of the new part; but this view meets also with serious objections. In the first place, it gives only the appearance of an explanation because it assumes both that such stuffs are present, and that they can produce the kind of result that is to be explained. Until such substances have been found and until it can be shown that this kind of action is possible, the stuff-hypothesis adds nothing to the facts themselves, and may withdraw attention from the real solution of the problem.

- 1901: **Theodor Boveri proposed that gradients of substances pattern the embryo** along the animal vegetal axis (working on sea urchins)

- 1905: **Edwin Conklin**

Vol. VIII. *March, 1905.* *No. 4*

BIOLOGICAL BULLETIN

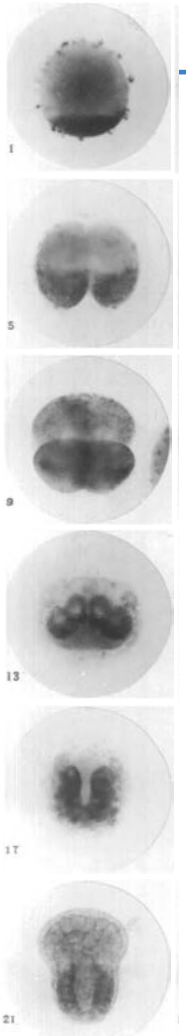
ORGAN-FORMING SUBSTANCES IN THE EGGS OF ASCIDIANS.

EDWIN G. CONKLIN.

Recent experimental work on some of these forms confirms and extends these conclusions and proves that even in the egg before cleavage begins different substances may be present which are destined in the course of development to enter into specific parts of the embryo.

egg. Here the different substances of the egg are strikingly dissimilar; they are localized in their definitive positions at a remarkably early period, and they may be traced with ease and certainty

These facts point to the conclusion that the complex organization of an egg, such as that of an ascidian, has not arisen through the "reflection of adult characters upon the egg," but rather that this organization is primary. Furthermore they seem to indicate that evolution has taken place, not through modifications of adult structure, but through changes in germinal organization; modifications of this organization, however produced, are probably the real causes of evolution.

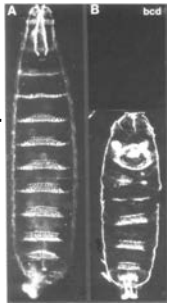


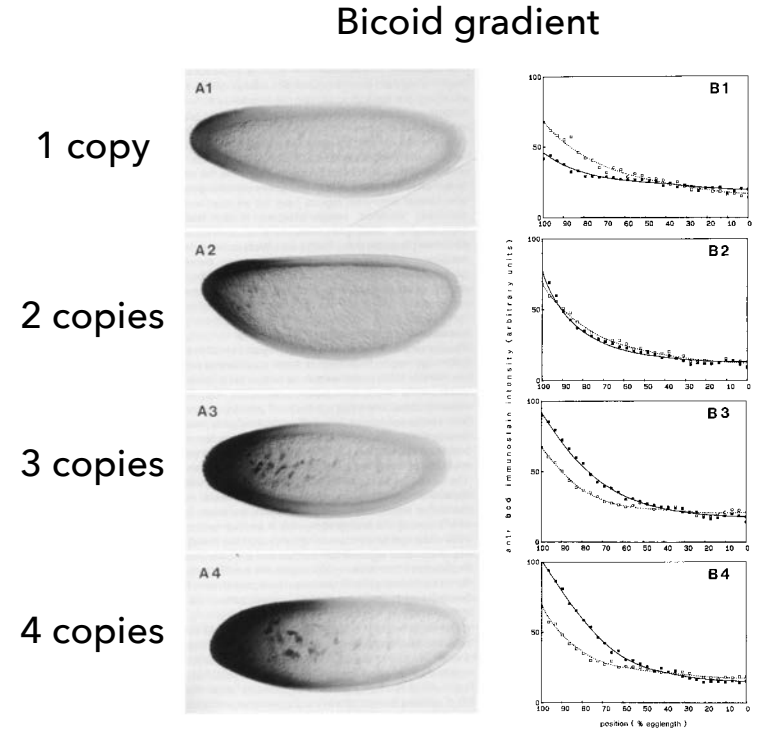
Cynthia (Slyela) partita

Discovery of gradients of morphogens - case study: Bicoid

The *bicoid* Protein Determines Position in the Drosophila Embryo in a Concentration-Dependent Manner

- Increasing the gene copy number of *Bicoid* increases the length scale of the Bicoid gradient distribution
- And modifies the embryo pattern and morphology consistent with Bicoid specifying the anterior (head) region.
- Bicoid is required for the head region



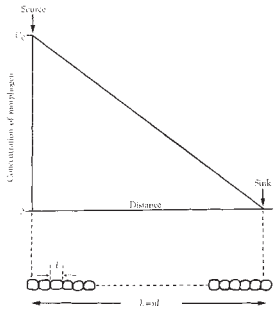


W. Driever and C. Nüsslein-Volhard *Cell* 54, 95-104 (1988)

Discovery of gradients of morphogens - case study: Bicoid

Diffusion in Embryogenesis

by
FRANCIS CRICK
Medical Research Council
Laboratory of Molecular Biology,
Hills Road, Cambridge



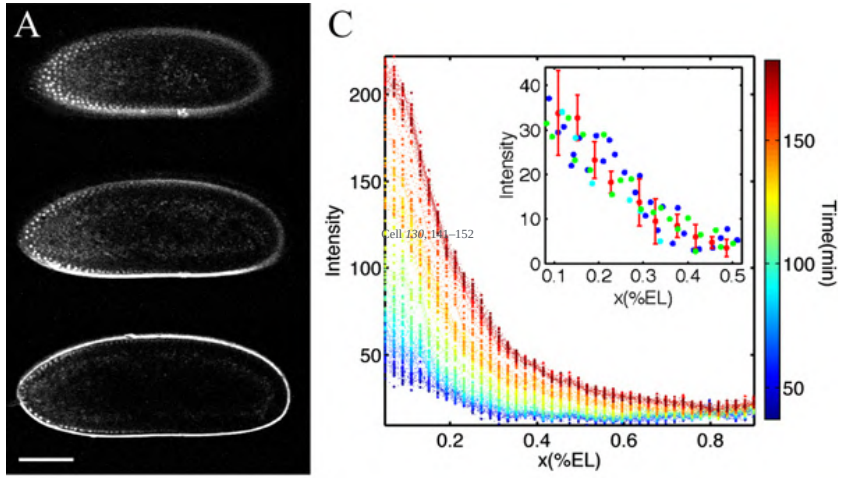
$$t = \frac{A\ (nl)^2}{D}$$

n~70 cells

A simple order-of-magnitude calculation suggests that diffusion may be the underlying mechanism in establishing morphogenetic gradients in embryonic development.

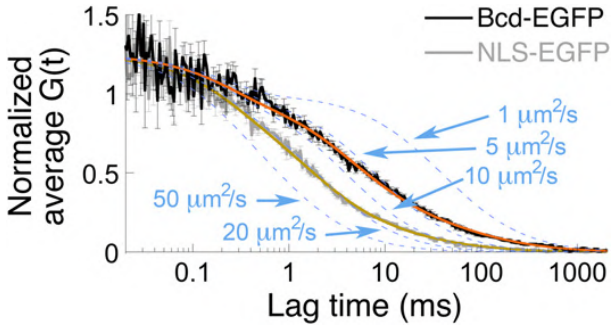
F. Crick *Nature* 1970

Bcd::GFP



T. Gregor et al and D. Tank. *Cell* 130, 141–152 (2007)

Measures of Bcd diffusivity:
Using FCS, in the range of D~7μm²/s



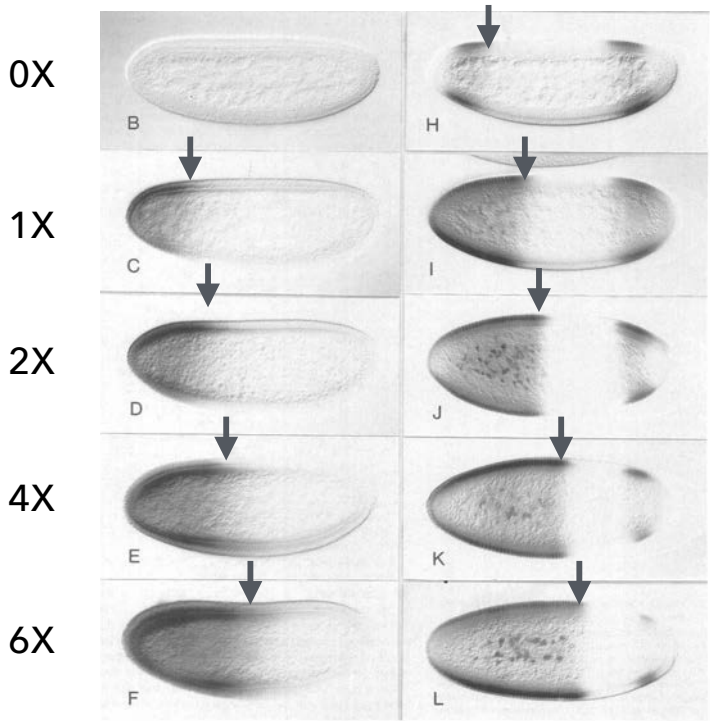
This value is large enough to explain the stable establishment of the Bcd gradient simply by diffusion before the onset of zygotic transcription.

$\lambda \sim 125\ \mu m \qquad \tau \sim \lambda^2/D \sim 40$ min

A. Abu-Arish, et al, N. Dostatni and C. Fradin. *Biophysical Journal* 99(4) L33–L35, 2010

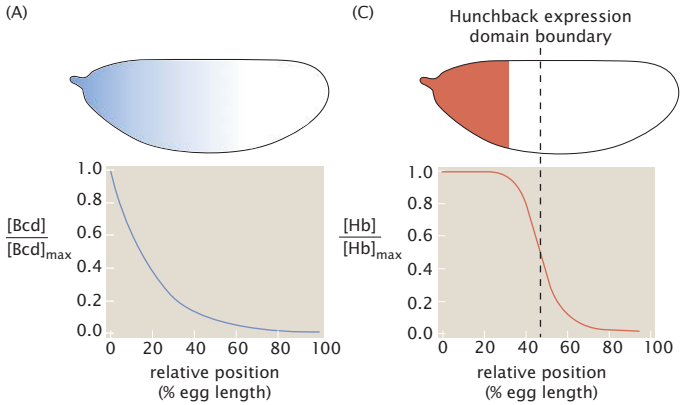
Discovery of gradients of morphogens - case study: Bicoid

- Bcd is a concentration dependent transcriptional activator
- Concentration threshold for gene activation



Bicoid *hb-lacZ* Hb protein

G. Struhl, K. Struhl and P. MacDonald *Cell* 57, 1259-1273 (1989)

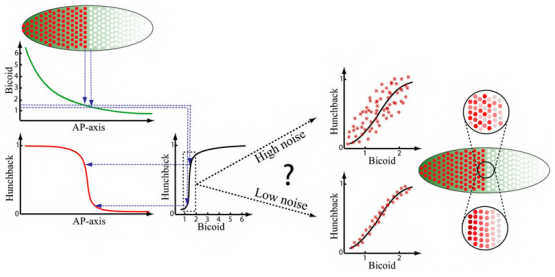


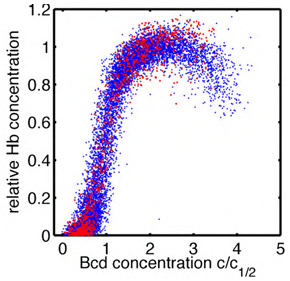
R. Phillips, J. Kondev, J. Thériot & H. Garcia. *Physical Biology of the Cell (Garland Science)* 2012

Discovery of gradients of morphogens - case study: Bicoid

How precise is Bicoid/Hunchback system?

- Bcd may be noisy and the system compensates via averaging or through properties of network.
- Bcd may be precise and downstream steps maintain or increase this precision up to physical limits.





13,366 nuclei in 9 embryos

T. Gregor et al and W. Bialek. *Cell* 130, 153–164, 2007

- Precision:
- **Expectations** for spatial discrimination of adjacent nuclei *in vivo:*

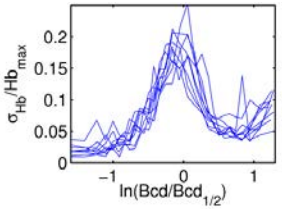
$$\frac{\Delta c(x)}{c(x)} = \frac{1}{c(x)}\left|\frac{dc(x)}{dx}\right|\Delta x = \frac{\Delta x}{\lambda} \sim 0.1.$$

$\Delta x \sim 8\mu m$
$\lambda \sim 100\ \mu m$

Measurement precision [Bcd] ~10%
(70 molecules at 50% embryo length)

- **Physical limit**: Berg & Purcell $\frac{\delta c}{c} \sim \frac{1}{\sqrt{DacT}}$, T~20 min for 10% precision (D~7μm²/s)

- **Data**: Does Hb read Bcd with such precision?
  Yes, within 10% precision.

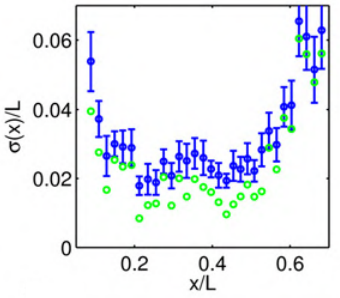


- Reproducibility:
- The reproducibility of the Bcd gradient profile from embryo to embryo and from one cycle of nuclear division to the next within one embryo is at the 10% level.

Converting the measured rms in concentration profile into rms of spatial coordinate (positional error)

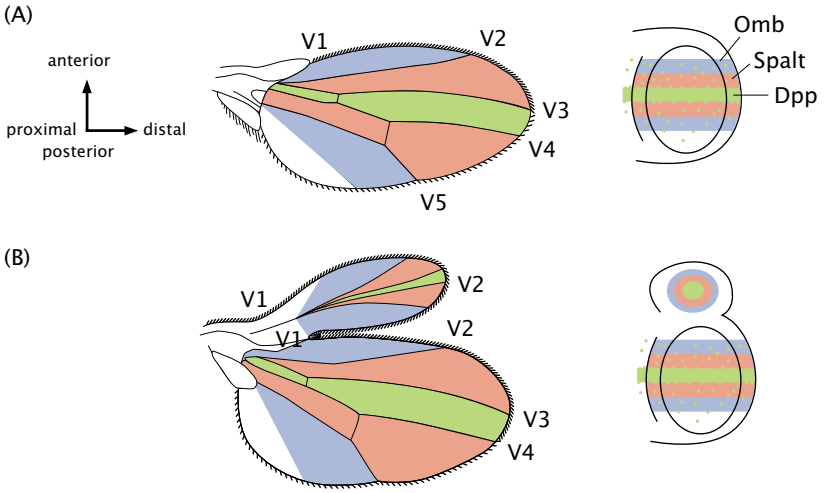
$$\sigma(x) = \delta c(x)\left|\frac{d\bar{c}(x)}{dx}\right|^{-1}.$$

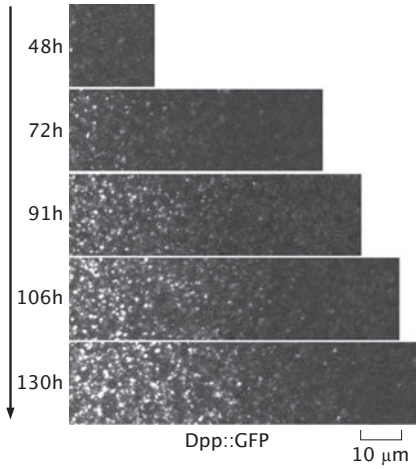
~1-2% of embryo length after correcting for measurement noise

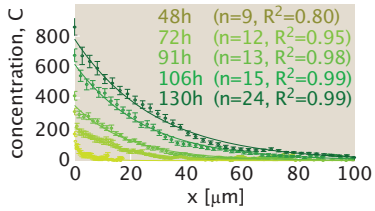


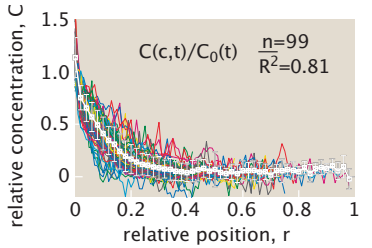
Discovery of gradients of morphogens - in growing tissues

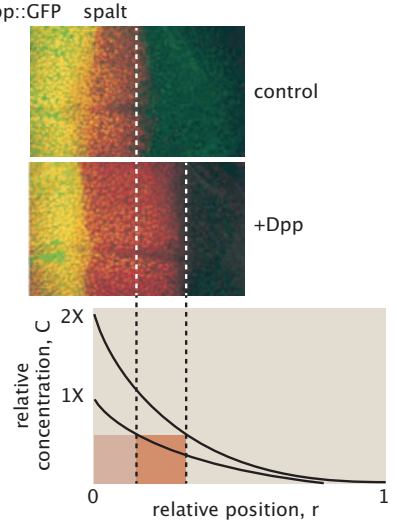
Diffusible morphogens and spatial patterning in growing tissues











$D = 0.10 \pm 0.05\ \mu m^2/s$

$k = 2.52 \times 10^{-4} \pm 1.29 \times 10^{-4}\ s^{-1}$

$j_0 = 3.98 \pm 2.34$ molecules/(µm × s)

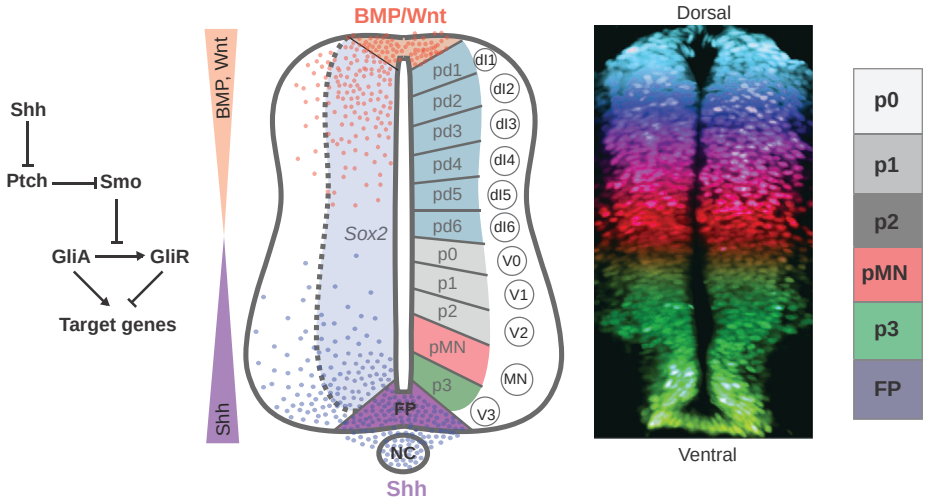
mass conservation	$\partial_t C = D\nabla^2 C - kC + 2j_0\delta(x)$ (degradation; diffusion; production)
steady state solution	$C(x) = C_0 e^{-\frac{x}{\lambda}}$
decay length	$\lambda = \sqrt{D/k}$
source concentration	$C_0 = j_0\sqrt{D/k}$

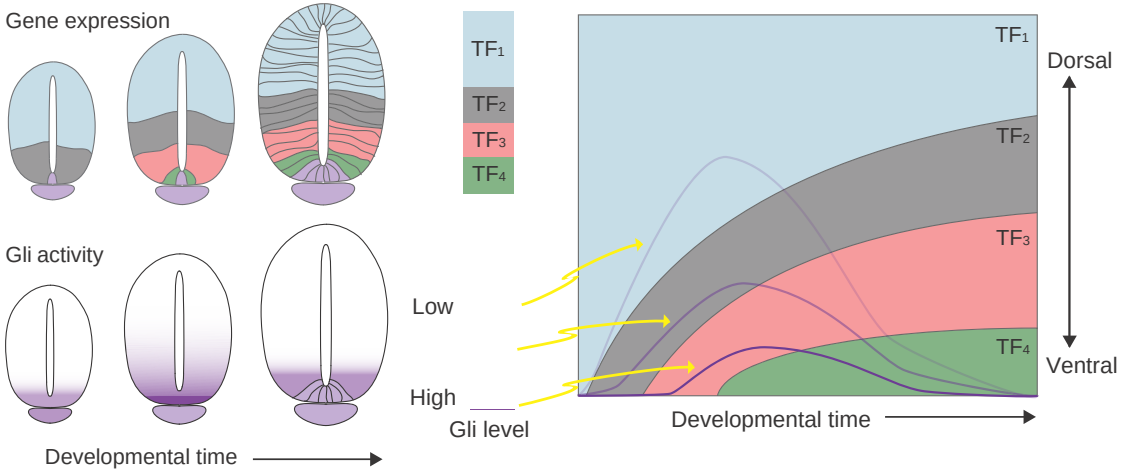
T. Lecuit et al, *Nature* 1996
D. Nellen et al *Cell* 1996
A. Kicheva et al, *Science* 2000
A. Teleman et al, *Cell* 2000

Discovery of gradients of morphogens - in growing tissues

Diffusible morphogens and spatial patterning in growing tissues

- Opposing gradients generate patterns
- Temporal integration and network properties are required for spatial patterning





Reviewed in: J. Briscoe and S. Small. *Development* (2015) 142, 3996-4009 doi:10.1242/dev.129452

Need for a quantitative theory of positional information

- The concept of Information is *generally qualitative* (causal power)

(1) Semantophoretic molecules or semantides—molecules that carry the information of the genes or a transcript thereof. The genes themselves are the primary semantides (linear "sense-carrying" units). Messenger-RNA molecules are secondary semantides. Polypeptides, at least most of them, are tertiary semantides.

E. Zuckerkandl and L. Pauling *J. Theoret. Biol.* (1965) 8, 357-366

The type of molecules that have been called informational macromolecules (68) or semantides (75) (DNA, RNA, proteins) has a unique role in determining the properties of living matter

E. Zuckerkandl and L. Pauling (1966)
doi.org/10.1016/B978-1-4832-2734-4.50017-6

- Yet positional information calls for a *quantitative measure of information*

- This requires a quantitative theory of information in order to:
  – define *how much* information is encoded, transmitted and decoded?
  – understand how information may be reliably transmitted in the face of internal and external noise.

Plan

1. Length scales in biological systems
2. Positional Information (PI) and Morphogens
3. Shannon information theory
4. Encoding and Decoding space with PI
5. Beyond PI: generalisation

Towards a theory of information

- Harry Nyquist – *Transmission of Intelligence* 1924
- Bell labs and telecommunication in US

BELL SYSTEM TECHNICAL JOURNAL

Certain Factors Affecting Telegraph Speed[1]

By H. NYQUIST

SYNOPSIS: This paper considers two fundamental factors entering into the maximum speed of transmission of intelligence by telegraph. These factors are signal shaping and choice of codes. The first is concerned with the best wave shape to be impressed on the transmitting medium so as to permit of greater speed without undue interference either in the circuit under consideration or in those adjacent, while the latter deals with the choice of codes which will permit of transmitting a maximum amount of intelligence with a given number of signal elements.

THEORETICAL POSSIBILITIES USING CODES WITH DIFFERENT NUMBERS OF CURRENT VALUES

The speed at which intelligence can be transmitted over a telegraph circuit with a given line speed, *i.e.*, a given rate of sending of signal elements, may be determined approximately by the following formula, the derivation of which is given in Appendix B.

$$W = K \log m$$

Where W is the speed of transmission of intelligence,
m is the number of current values,
and, K is a constant. (ie. the number of current values sent/unit of time)

- The number of current values is the number of characters in the code that are used, ie. the number of letters in the alphabet, or 0/1 in binary signal.
- The larger number of values to choose from, the fewer need to be sent to convey a given intelligence, because the larger the density of intelligence in each value.

Towards a theory of information

- **Ralph Hartley** – *Transmission of information* 1928
- Constructs a quantity to measure the information transmitted which is independent of psychological considerations (meaning).
- Information is a **measure of uncertainty** about an outcome.
- **The Hartley function quantifies the information gained when a sample is picked randomly from a finite set,** considering that all outcomes have **same probability** of occurence.

Ralph Hartley (1888-1970)

BELL SYSTEM TECHNICAL JOURNAL

Transmission of Information[1]

By R. V. L. HARTLEY

SYNOPSIS: A quantitative measure of "information" is developed which is based on physical as contrasted with psychological considerations. How the rate of transmission of this information over a system is limited by the distortion resulting from storage of energy is discussed from the transient viewpoint. The relation between the transient and steady state viewpoints is reviewed. It is shown that when the storage of energy is used to restrict the steady state transmission to a limited range of frequencies the amount of information that can be transmitted is proportional to the product of the width of the frequency-range by the time it is available. Several illustrations of the application of this principle to practical systems are included. In the case of picture transmission and television the spacial variation of intensity is analyzed by a steady state method analogous to that commonly used for variations with time.

Towards a theory of information

- Ralph Hartley – 1928
- The Hartley function H quantifies the information gained when a sample is picked randomly from a finite set, considering that all outcomes have **same probability** of occurence.

n selections among s symbols
The number of distinguishable sequences is s^n.
This measure of information would increase exponentially with sequence length.
Need of measure of transmitted information which is *proportional* to sequence length.

$$H = n \log s$$

$$= \log s^n.$$

$$H(A) := \log_b(|A|).$$

For a particular system let the amount of information associated with n selections be

$$H = Kn, \tag{4}$$

where K is a constant which depends on the number s of symbols available at each selection. Take any two systems for which s has the values s_1 and s_2 and let the corresponding constants be K_1 and K_2.

$$s_1^{n_1} = s_2^{n_2},$$

$$H = K_1 n_1 = K_2 n_2,$$

$$\frac{K_1}{\log s_1} = \frac{K_2}{\log s_2}.$$

This relation will hold for all values of s only if K is connected with s by the relation

$$K = K_0 \log s, \tag{8}$$

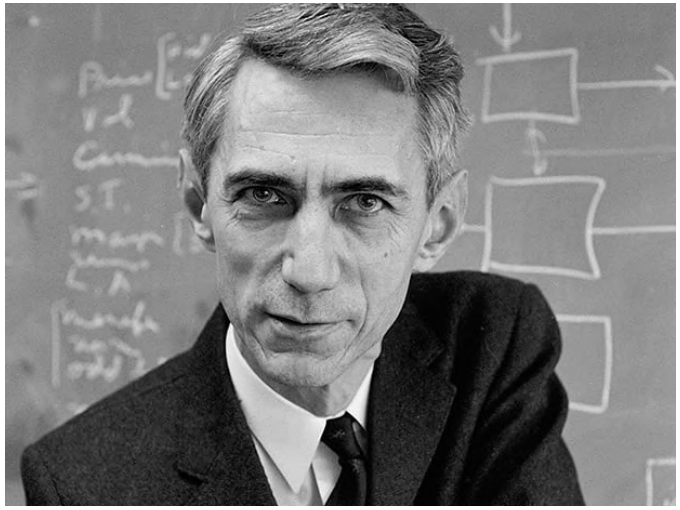
where K_0 is the same for all systems. Since K_0 is arbitrary, we may omit it if we make the logarithmic base arbitrary. The particular base selected fixes the size of the unit of information. Putting this value of K in (4),

$$H = n \log s \tag{9}$$

$$= \log s^n. \tag{10}$$

Mathematical theory of Information and Communication

- **Claude Shannon – 1948**
- Extends and generalises the work of Hartley:
  - – semantic is not relevant
  - – probabilistic nature of information
  - – considers non uniform frequency of « events » and statistics of the message



Claude Shannon (1916-2001)

The Bell System Technical Journal

Vol. XXVII *July, 1948* *No. 3*

A Mathematical Theory of Communication

By C. E. SHANNON

INTRODUCTION

THE recent development of various methods of modulation such as PCM and PPM which exchange bandwidth for signal-to-noise ratio has intensified the interest in a general theory of communication. A basis for such a theory is contained in the important papers of Nyquist[1] and Hartley[2] on this subject. In the present paper we will extend the theory to include a number of new factors, in particular the effect of noise in the channel, and the savings possible due to the statistical structure of the original message and due to the nature of the final destination of the information.

The fundamental problem of communication is that of reproducing at one point either exactly or approximately a message selected at another point. Frequently the messages have *meaning*; that is they refer to or are correlated according to some system with certain physical or conceptual entities. These semantic aspects of communication are irrelevant to the engineering problem. The significant aspect is that the actual message is one *selected from a set* of possible messages. The system must be designed to operate for each possible selection, not just the one which will actually be chosen since this is unknown at the time of design.

If the number of messages in the set is finite then this number or any monotonic function of this number can be regarded as a measure of the information produced when one message is chosen from the set, all choices being equally likely. As was pointed out by Hartley the most natural choice is the logarithmic function. Although this definition must be generalized considerably when we consider the influence of the statistics of the message and when we have a continuous range of messages, we will in all cases use an essentially logarithmic measure.

The logarithmic measure is more convenient for various reasons:

1. It is practically more useful. Parameters of engineering importance

[1] Nyquist, H., "Certain Factors Affecting Telegraph Speed," *Bell System Technical Journal*, April 1924, p. 324; "Certain Topics in Telegraph Transmission Theory," *A. I. E. E. Trans.*, v. 47, April 1928, p. 617.

[2] Hartley, R. V. L., "Transmission of Information," *Bell System Technical Journal*, July 1928, p. 535.

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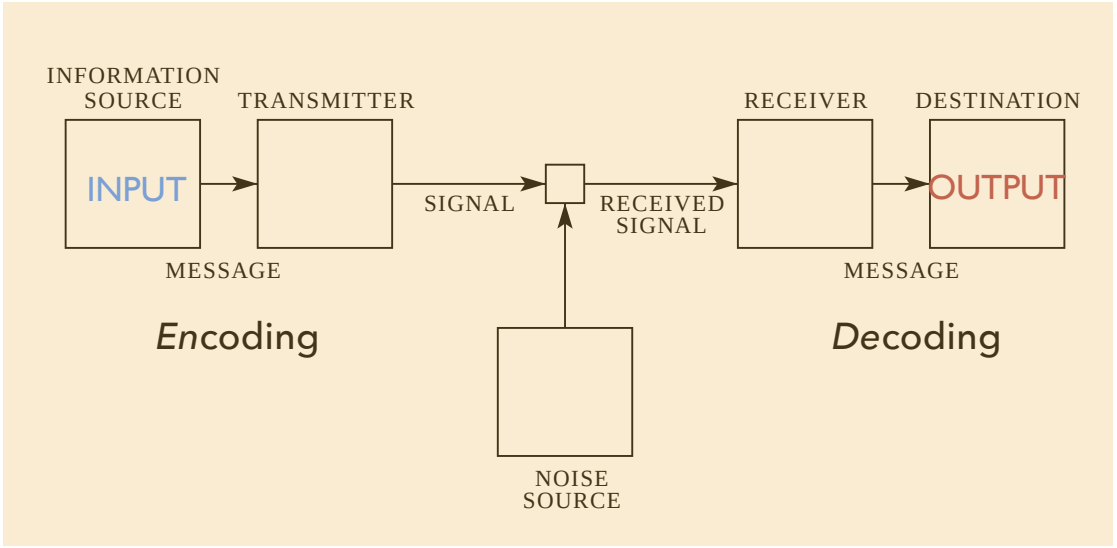
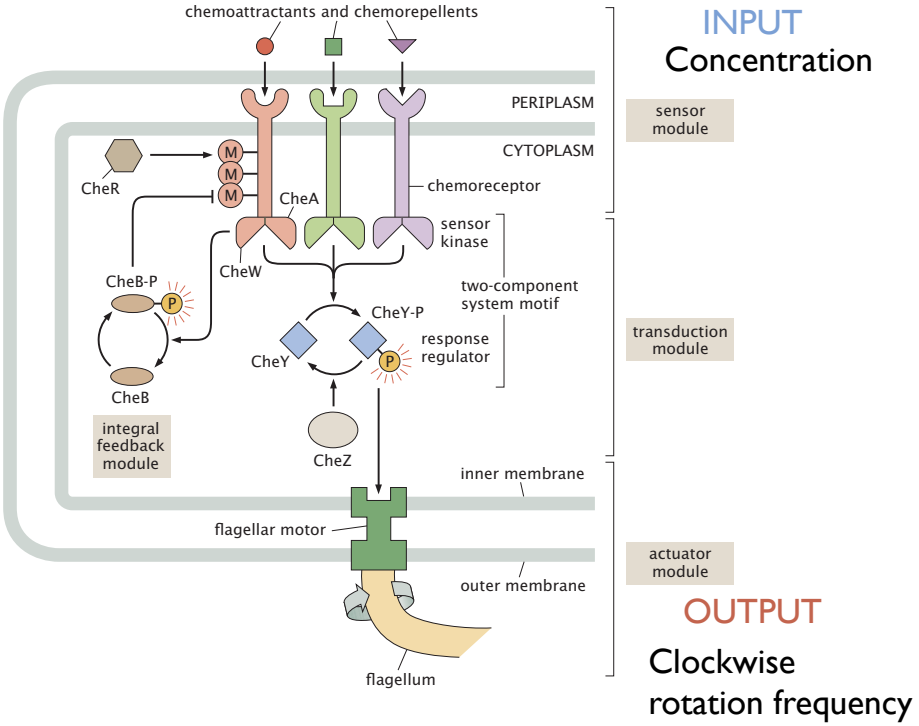
Theory of Information and Communication

« The fundamental problem of communication is that of reproducing at one point either exactly or approximately a message selected at another point. »

- Basic architecture of a communication system



- Biology

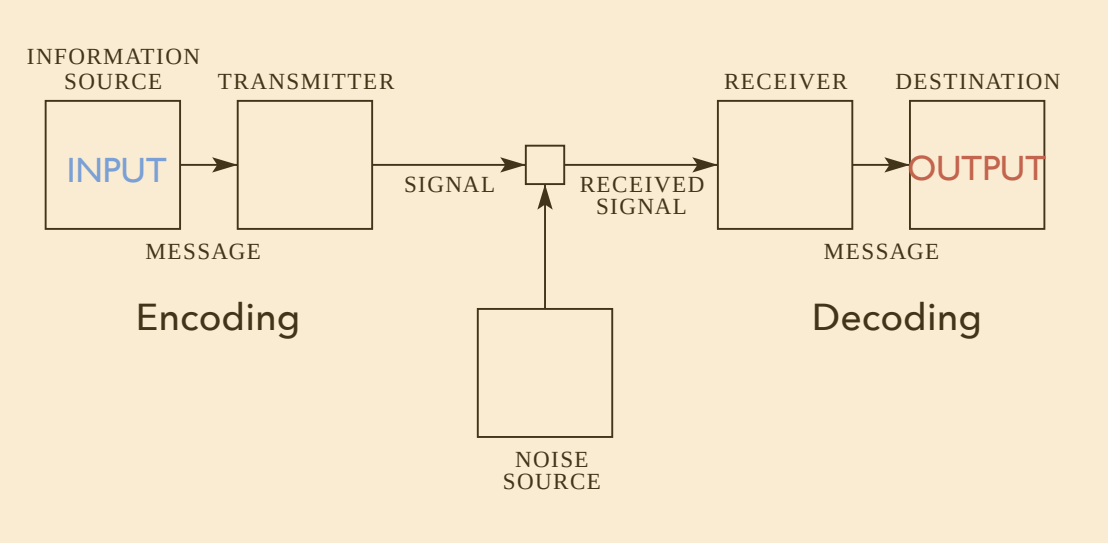


R. Phillips, The Molecular Switch: signaling and allostery. *Princeton Univ. Press.* 2020

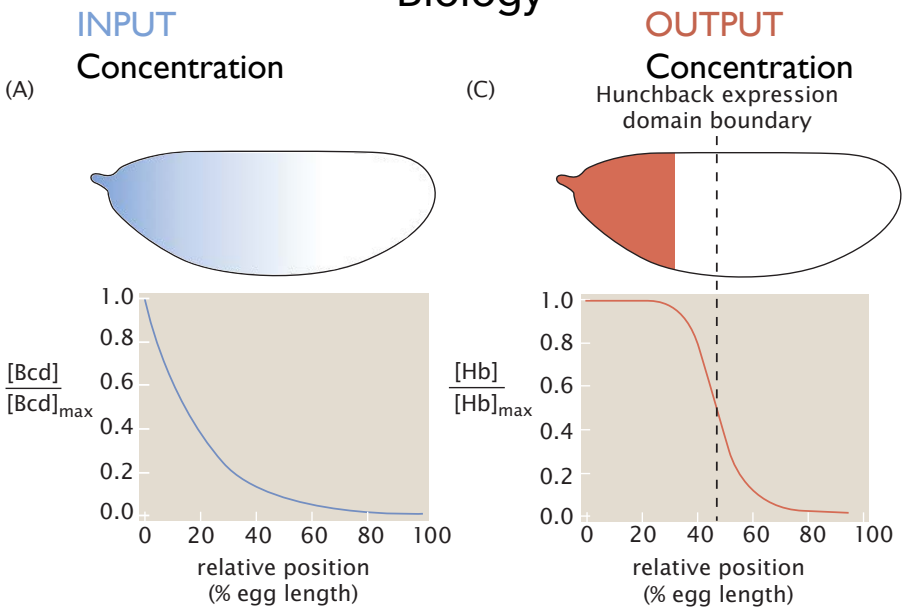
Theory of Information and Communication

« The fundamental problem of communication is that of reproducing at one point either exactly or approximately a message selected at another point. »

- Basic architecture of a communication system



- Biology



R. Phillips, J. Kondev, J. Thériot & H. Garcia.
Physical Biology of the Cell (Garland Science) 2012

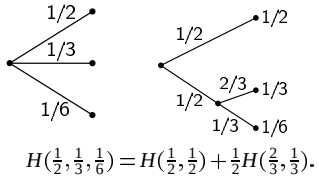
Theory of Information and Communication

- Consider a set of discrete events i with probability of occurence p_i.
- What is a **measure** H of how much « choice » is involved in the selection of the event or **of how uncertain one is of the outcome?**

Expected properties:

H continuous in p_i

If $p_i=1/n$ then H is a monotonic function of n as there is more uncertainty when there are more possible events



$$H(\tfrac{1}{2},\tfrac{1}{3},\tfrac{1}{6}) = H(\tfrac{1}{2},\tfrac{1}{2}) + \tfrac{1}{2}H(\tfrac{2}{3},\tfrac{1}{3}).$$

$$H = -\sum p_i \log p_i$$

- H **is a measure of choice or uncertainty or information.** The more uncertainty the greater the information gained per choice (surprise)
- H **has the form of entropy** (ie. $S = k_B \log W$).
- H is a number, with unit *bit* (binary integer) with $\log_2$ base.

- Can be extended to continuous distributions with probability density distribution $p(x)$: $H = -\int_{-\infty}^{\infty} p(x)\log p(x)\,dx.$

Or $S[P_x(x)] = -\int dx\, P_x(x)\log_2\left[P_x(x)\right],$

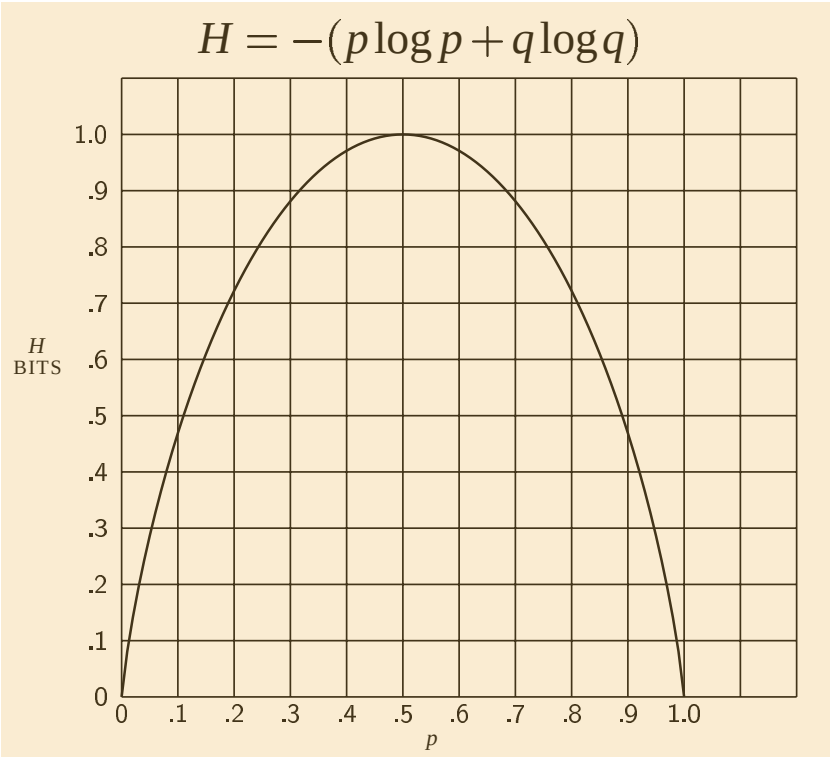


Fig. 7—Entropy in the case of two possibilities with probabilities p and $(1-p)$.

- H=0 when one is certain of outcome (all p_i are zero but one, and the last one =1)
- H has a maximum when all p_i are equal. There is maximum uncertainty

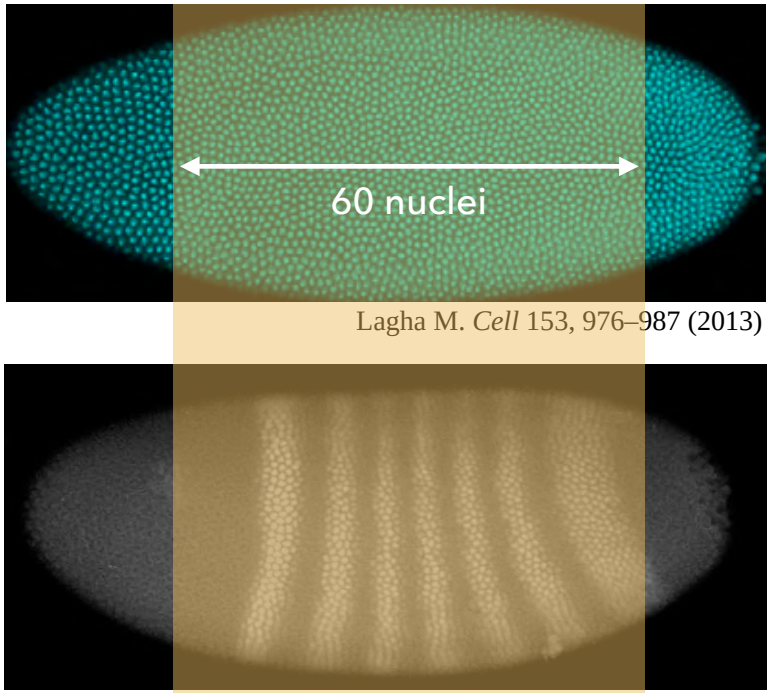
Theory of Information and Communication

- A device with **two stable positions**, such as a relay can store **one bit of information**.
- *N* such devices can store *N* bits, since the total number of possible states is 2^N.

- It takes 1 bit of information to discriminate between 2 states
- N bits are needed to discriminate with zero error between 2^N states, or **Log_2N bits to discriminate between N states.**
- Example: chain of letters and space (27 options). If letters were equiprobable, the entropy of 1 letter would be $Log_2 27 \sim 4.75$. The transmission of each letter requires 4-5 bits.

- **Shannon entropy can be interpreted as the number of Yes/No questions required to fully resolve the uncertainty about a state (discriminate between N possible states).**

5.9 bits needed to determine with zero error cell position



Lagha M. *Cell* 153, 976–987 (2013)

Thomas Gregor lab

Mutual information

- Consider two variables x, y of a system occurring at probability $p(x)$ and $p(y)$:
- For the joint event, with probability $p(x,y)$, the Shannon entropy is:

$$H(x,y) = -\sum_{i,j} p(i,j) \log p(i,j)$$

- Furthermore $H(x,y) \leq H(x) + H(y)$, with equality if x, y are independent
- Conditional entropy, $H_x(y)$, measures how uncertain we are of y on average when we know x. defined as the average of the entropy of y for each value of x, weighted according to the probability of getting that particular x:

$$H_x(y) = -\sum_{i,j} p(i,j) \log p_i(j)\,.$$

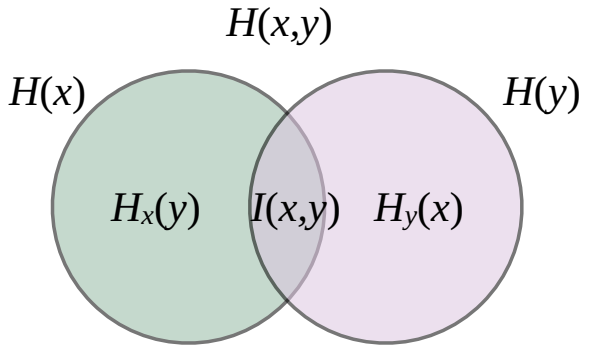
- From this we deduce that: $\boxed{H(x,y) = H(x) + H_x(y).}$
- The knowledge of x increases knowledge of y, unless they are independent variables: $H(y) \geq H_x(y)$.

Mutual information

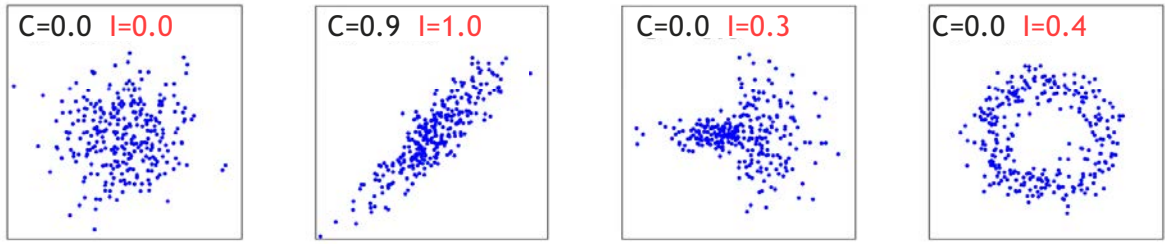
- Consider two variables x, y of a system occurring at probability $p(x)$ and $p(y)$
- x, y are not independent variables: a change to x leads to change to y with certain probability. In other words, x and y can be said to « share information ».
- Quantifying the degree of shared information would allow to infer y when we know x or vice versa.
- Definition of mutual information, as a function of entropy:

$$I(x,y) = H(x) + H(y) - H(x,y)$$

or equivalently: $I(x,y) = H(x) - H_y(x) = H(y) - H_x(y)$



- It captures the non-linear dependence between variables (generalizes linear regression)



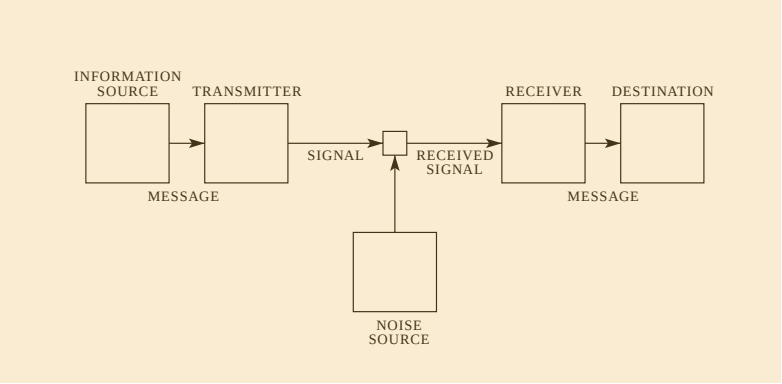
G. Tkacik & T. Gregor. *Development* (2021) 148, dev176065. doi:10.1242/dev.176065

Information across a noisy channel

- If a noisy channel is fed by a source there are two statistical processes at work: the source and the noise.
- We conciser the entropy $H(x)$ at the source (input), the entropy of the output of the channel, $H(y)$. In the noiseless case $H(y) = H(x)$.
- The joint entropy of input and output is $H(x,y)$. There are two conditional entropies $H_x(y)$ and $H_y(x)$, the entropy of the output when the input is known and conversely.

$$H(x,y) = H(x) + H_x(y) = H(y) + H_y(x).$$

- We want to estimate the rate of information in this noisy channel. We have no knowledge of when some information is lost.



Capacity of noisy channel:

$$C = \mathrm{Max}\left(H(x) - H_y(x)\right) = \mathrm{Max}\ I(x,y)$$

The effective rate of transmission of information R:

$$\begin{aligned} R &= H(x) - H_y(x) \\ &= H(y) - H_x(y) \\ &= H(x) + H(y) - H(x,y). \end{aligned}$$

ie. the amount of information sent less the uncertainty of what was sent

ie. the amount of information received less the part due to noise

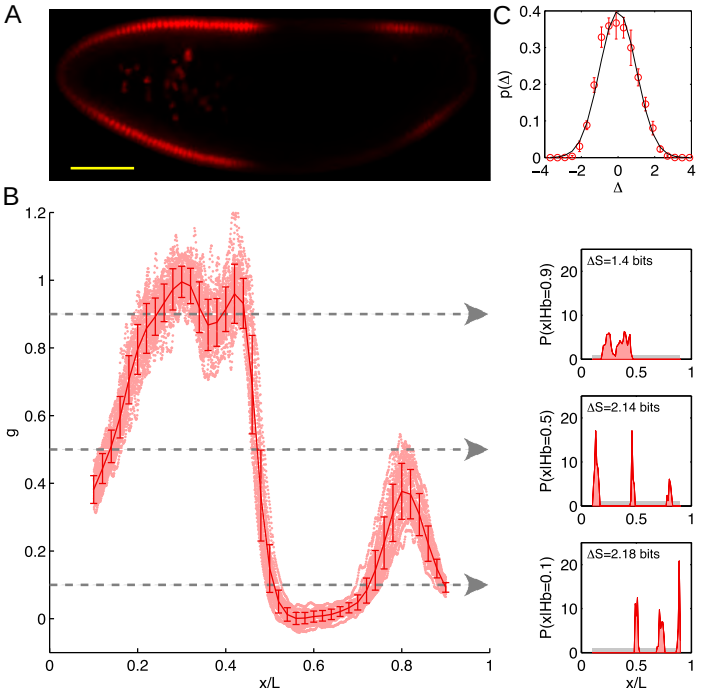
ie. the sum of the two information less the joint entropy. This is in a sense the number of bits per second common to the two (mutual information)

Back to positional information

- Positional information calls for a *quantitative measure of information:*
  – we now have this

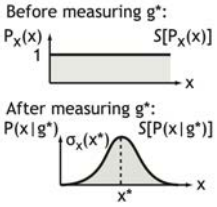
- This requires a quantitative theory of information in order to:
  – define *how much* information is encoded, transmitted and decoded?
  – understand how information may be reliably transmitted in the face of internal and external noise.

Mutual information as Positional Information



- Without any information about gene expression then there is no information about position *x*, ie, position *x* is drawn from distribution $P_x(x)$ (which is uniform $P_x(x) = 1/L$)
- When we measure *g*, then there is still some uncertainty in *x*, but this is reduced significantly. The conditional probability $P(x/g)$ has a narrower distribution but reflects also the effect of noise.
- We define the corresponding entropies: $S[P_x(x)] = -\int dx\, P_x(x)\log_2[P_x(x)]$,

$$S[P(x|g)] = -\int dx\, P(x|g)\log_2[P(x|g)].$$



For $P_x(x) = 1/L$, $S[P_x(x)] = \log_2(L)$

Therefore $S[P(x/g)]$ is smaller than $S[P_x(x)]$.

- The reduction in entropy when we measure g compared to before measuring is the measure of information that g provides about x, measured in bits. $I(g) = S[P_x(x)] - S[P(x|g)]$.

$$I_{g\to x} = \int dg \int dx\, P(g,x)\log_2\left[\frac{P(g,x)}{P_g(g)P_x(x)}\right]$$

- This is symmetric $I_{g\to x} = I_{x\to g}$ and is the mutual information between *g* and x

The mutual information is the positional information $I_{g\to x} = \int dx\, P_x(x)\left(S[P_g(g)] - S[P(g|x)]\right)$.

Dubuis, J. O., Tkacik, G., Wieschaus, E. F., Gregor, T. and Bialek, W. Positional information, in bits. *PNAS* 110, 16301-16308 (2013)

Mutual information as Positional Information

- Mutual information linking position *x* and morphogen concentration *g*, is the proper formalisation of PI

- Definition: $PI = I(g;x) = H(g) + H(x) - H(g,x) = H(g) - H_x(g)$

  PI is the sum of the two information (entropy) less the joint entropy.

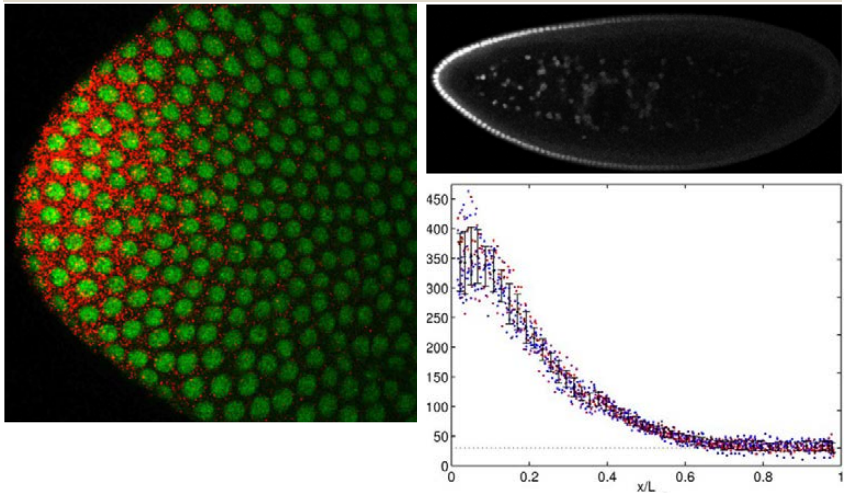
  PI is in a sense the number of bits common to the two informations

  Ex: If information associated with Bcd concentration along the antero-posterior axis, and information about the position are independent, then *I*(*Bcd; x*)= 0 and there is indeed no PI.

- PI and channel concepts do not depend on the underlying mechanisms, but only on statistical dependence between x and g
- Determines how much a change in concentration *g* can be used to interpret as a change in position *x*.
- PI can be used for any combination of input concentrations

1) *Encoding*
Mechanisms of Bcd gradient formation

2) *PI* in *I*(Bcd;x)



G. Tkacik and T. Gregor. *Development* (2021) 148, dev176065. doi:10.1242/dev.176065

Plan

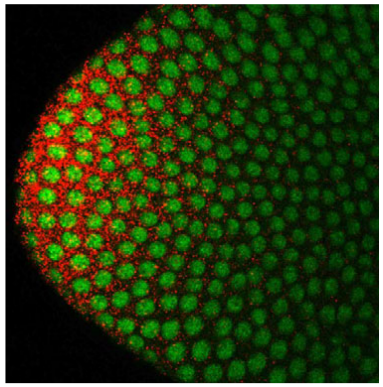
1. Length scales in biological systems
2. Positional Information (PI) and Morphogens
3. Shannon information theory
4. Encoding and Decoding space with PI
5. Beyond PI: generalisation

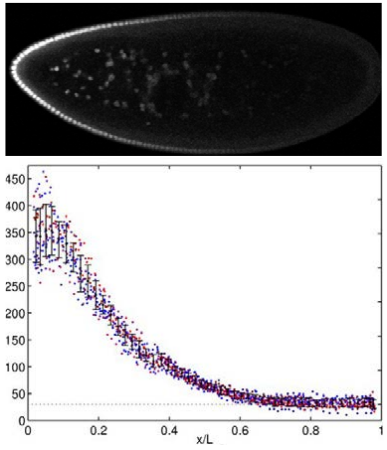
Mutual information as Positional Information

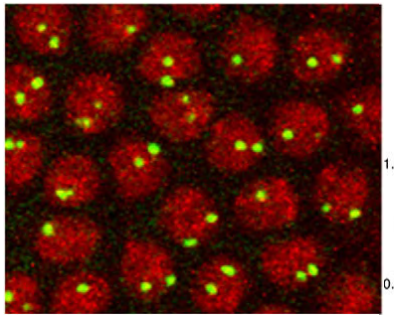
- **Positional information can be recoded and yield a new representation**
  (Maternal gradients -> Gap genes -> Pair rule genes)

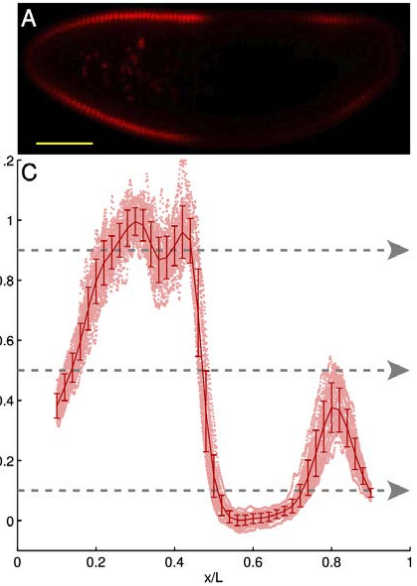
Establishment | **Representation**

1) *Encoding*	2) *PI* in *I*(Bcd;x)	3) *Recoding*	4) *PI* in *I*(Hb;x)
Mechanisms of Bcd gradient formation		Mechanisms of Hb regulation by Bcd	









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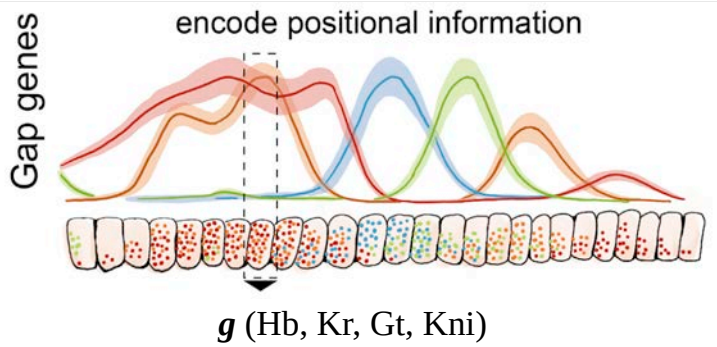
Mutual information as Positional Information

- How many bits of information are required to discriminate every cell/nuclear position?

  $Log_2 60$ = 5.9 bits needed to determine with zero error all cell position

- What is the amount of PI associated with Bcd and the downstream gap gene network?

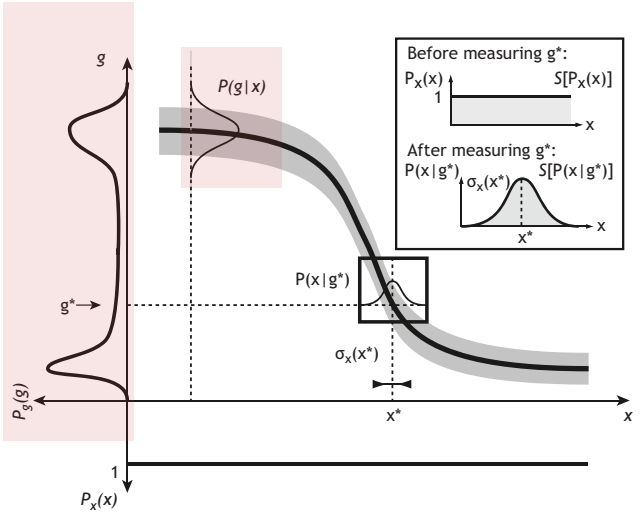
In a continuous form: $I(\boldsymbol{g};x) = \underbrace{\left\langle \int dg\ P(\boldsymbol{g}|x)\ \log_2 \frac{P(\boldsymbol{g}|x)}{P_g(\boldsymbol{g})} \right\rangle_x}_{H(g) - H_x(g)}.$



$P(\boldsymbol{g}|x)$ is measured from experimental data.

$P_g(\boldsymbol{g})=\langle P(\boldsymbol{g}|x)\rangle_{\boldsymbol{x}}$

This is the average of the distribution of morphogen concentrations across all positions x; it represents the probability that a particular combination of concentrations, $\boldsymbol{g}$, can be seen anywhere in the embryo.



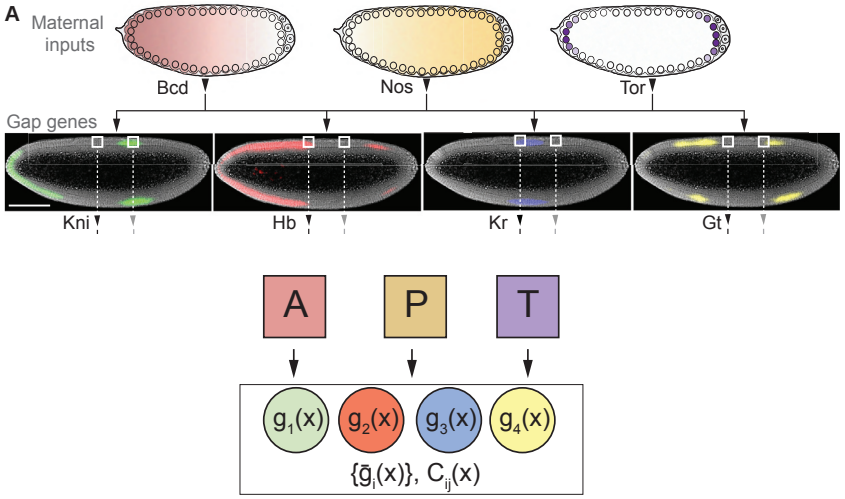
Mutual information as Positional Information

- **How many bits of information are required to discriminate every cell/nuclear position?**

  $Log_2 60$ = 5.9 bits needed to determine with zero error all cell position (60 cells)

- **How much information is actually used to determine with precision cell fate in the embryo?**
- Some cells are determined with precision: position of the cephalic furrow has 1% accuracy.

- **What is the amount of PI conveyed by the gap gene network?**



Petkova, M.D., et. al. *Cell* 176, 844-855 (2019)

- Based on: $I(\boldsymbol{g};x) = \left\langle \int dg\ P(\boldsymbol{g}|x)\ \log_2 \frac{P(\boldsymbol{g}|x)}{P_g(\boldsymbol{g})} \right\rangle_x$.

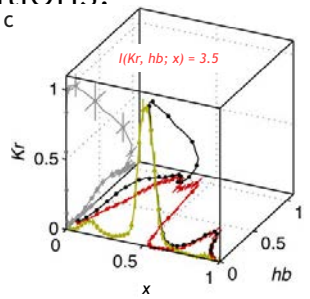
And expression data for all 4 gap genes $\boldsymbol{g}$ at all positions:

$I_{g_{\mathrm{Hb}}\to x} = 2.26 \pm 0.04$ bits

$I_{g_{\mathrm{Kr}}\to x} = 1.95 \pm 0.07$ bits, $I_{g_{\mathrm{Gt}}\to x} = 1.84 \pm 0.05$ bits, $I_{g_{\mathrm{Kni}}\to x} = 1.75 \pm 0.05$ bits.

Which is more than if they were simple on/off switches

When considering all 4 gap genes: $I = 4.1 \pm 0.23$ bits



- **Can information increase?** Bcd vs Gap genes.
- Yes if instantaneous profile, No if considering Bcd dynamics.

Dubuis, J. O. et al. *PNAS* 110, 16301-16308 (2013)

Decoding positional information from concentrations

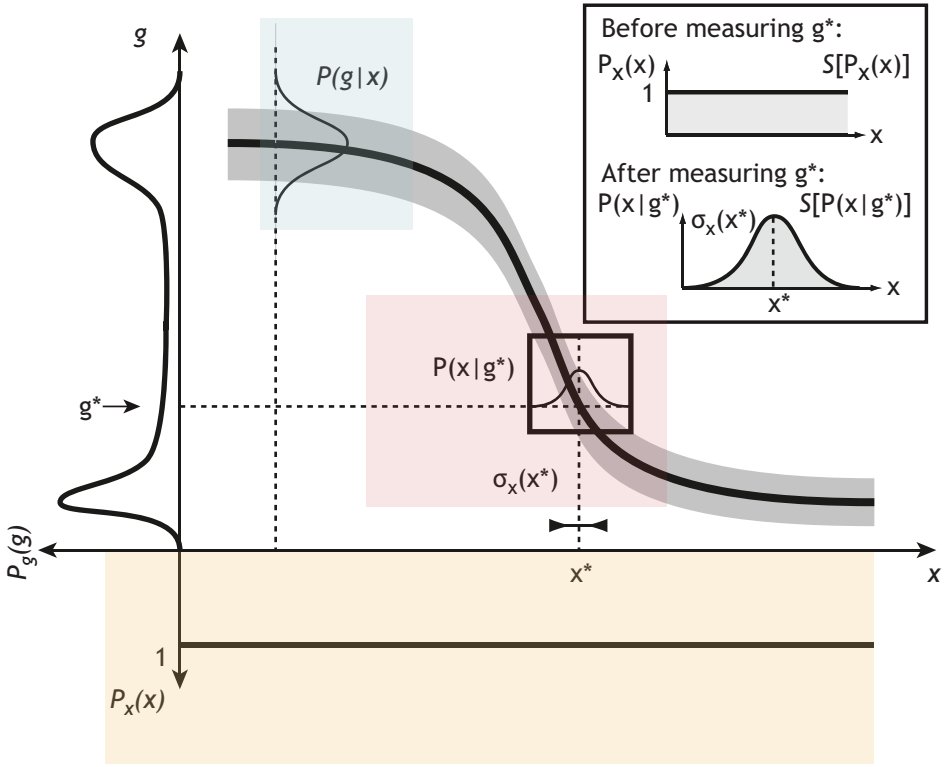
- Bayes' theorem:

$$P(x^*|\boldsymbol{g}) = \frac{1}{Z} P(\boldsymbol{g}|x^*) P_x(x^*).$$

Posterior (Decoded position based on measured concentrations)

Measurements

Prior (A priori position of nuclei to be decoded)



G. Tkacik and T. Gregor. *Development* (2021) 148, dev176065. doi:10.1242/dev.176065

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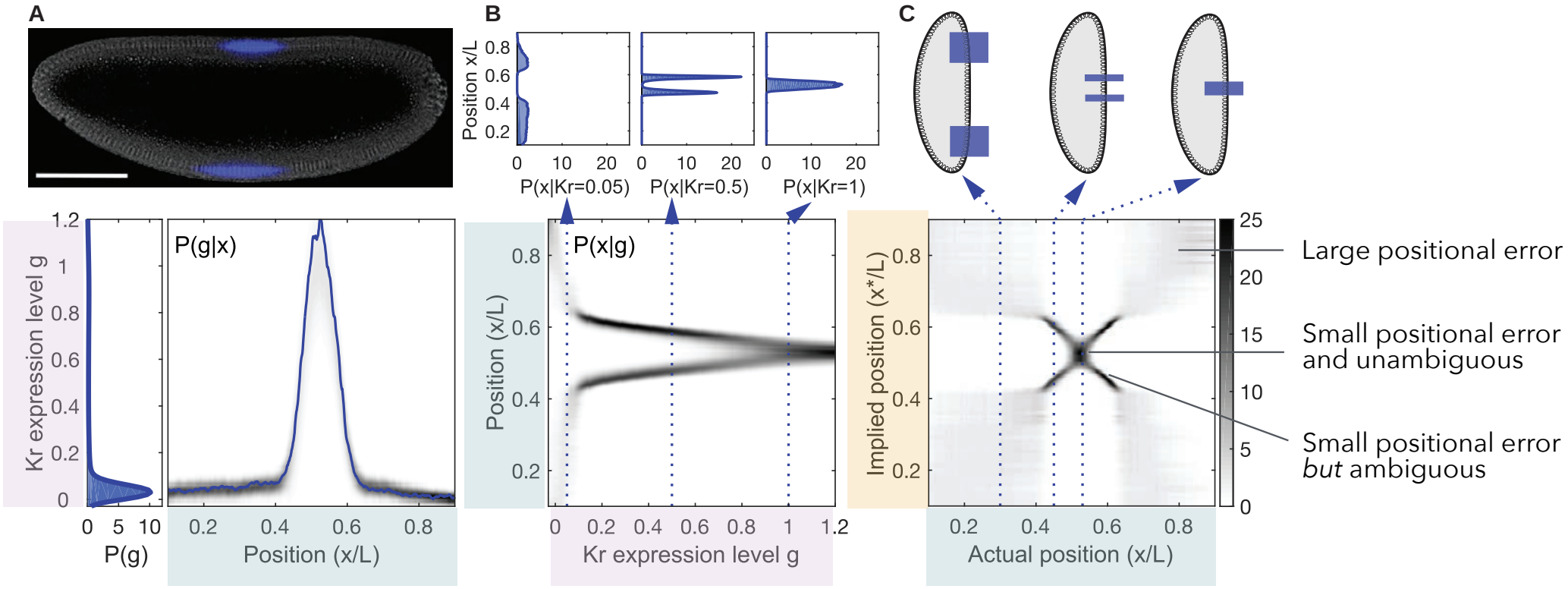


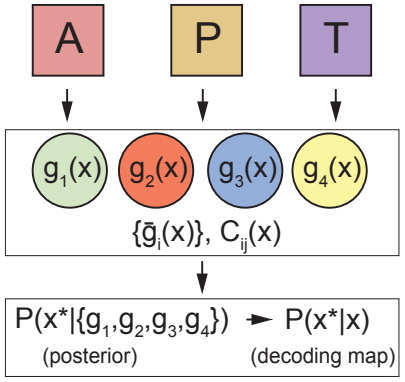
Petkova, M.D., Tkačik,G., Bialek,W., Wieschaus, E.F. and Gregor,T. Optimal decoding of cellular identities in a genetic network. *Cell* 176, 844-855 (2019)

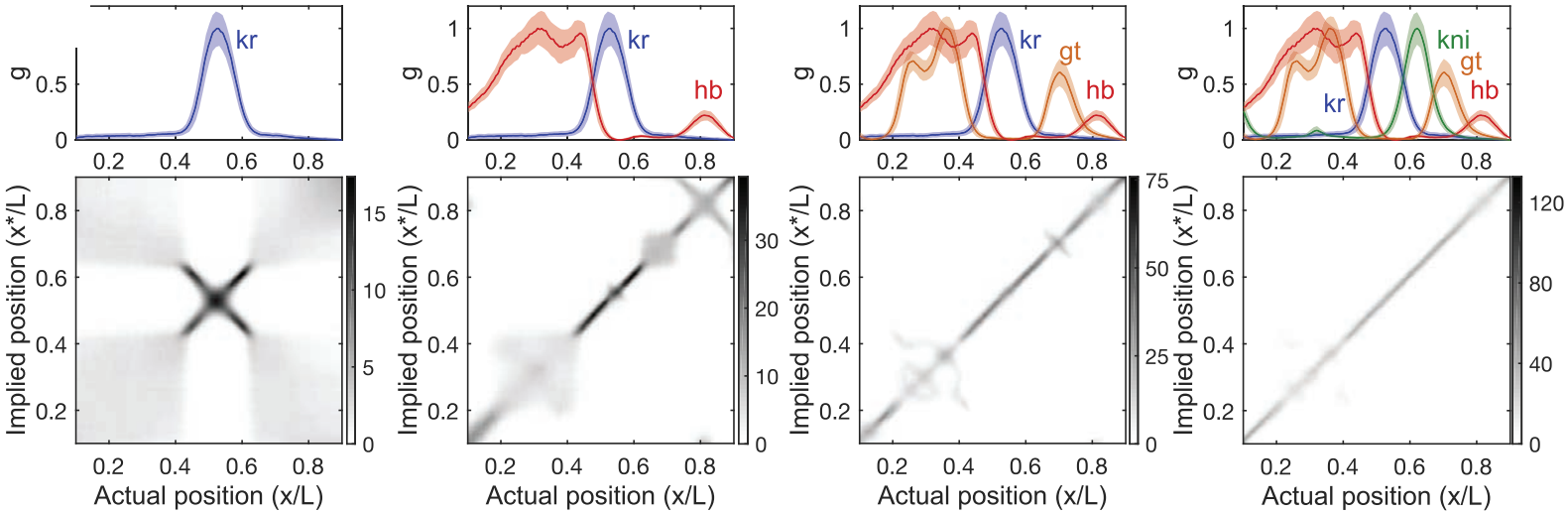
Decoding positional information from concentrations

- Decoding positional information with an increased number of gap genes

$$P(x^*|\boldsymbol{g}) = \frac{1}{Z} P(\boldsymbol{g}|x^*) P_x(x^*).$$

- The complete set of all 4 gap genes provides a uniform precise positional information with a high precision within 1% of embryo length

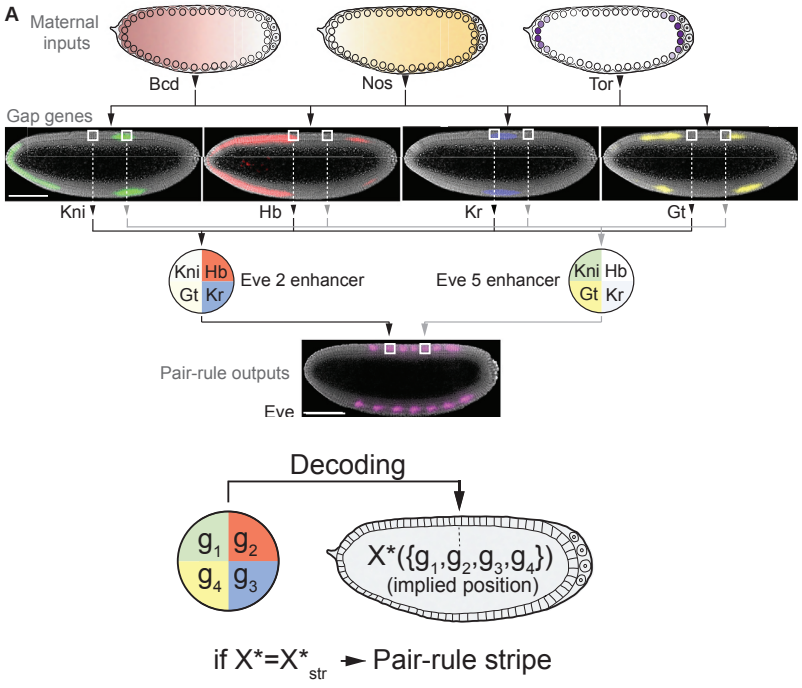


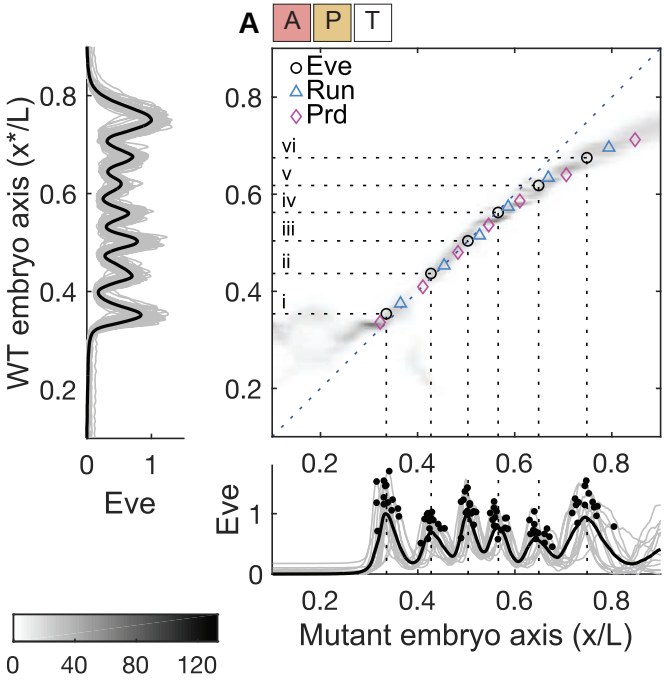


Petkova, M.D., Tkačik,G., Bialek,W., Wieschaus, E.F. and Gregor,T. *Cell* 176, 844-855 (2019)

Decoding positional information from concentrations

- **Is this positional information actually used in the embryo?**
- Comparaison of inferred position based on gap genes PI and actual position of downstream pair rule genes.





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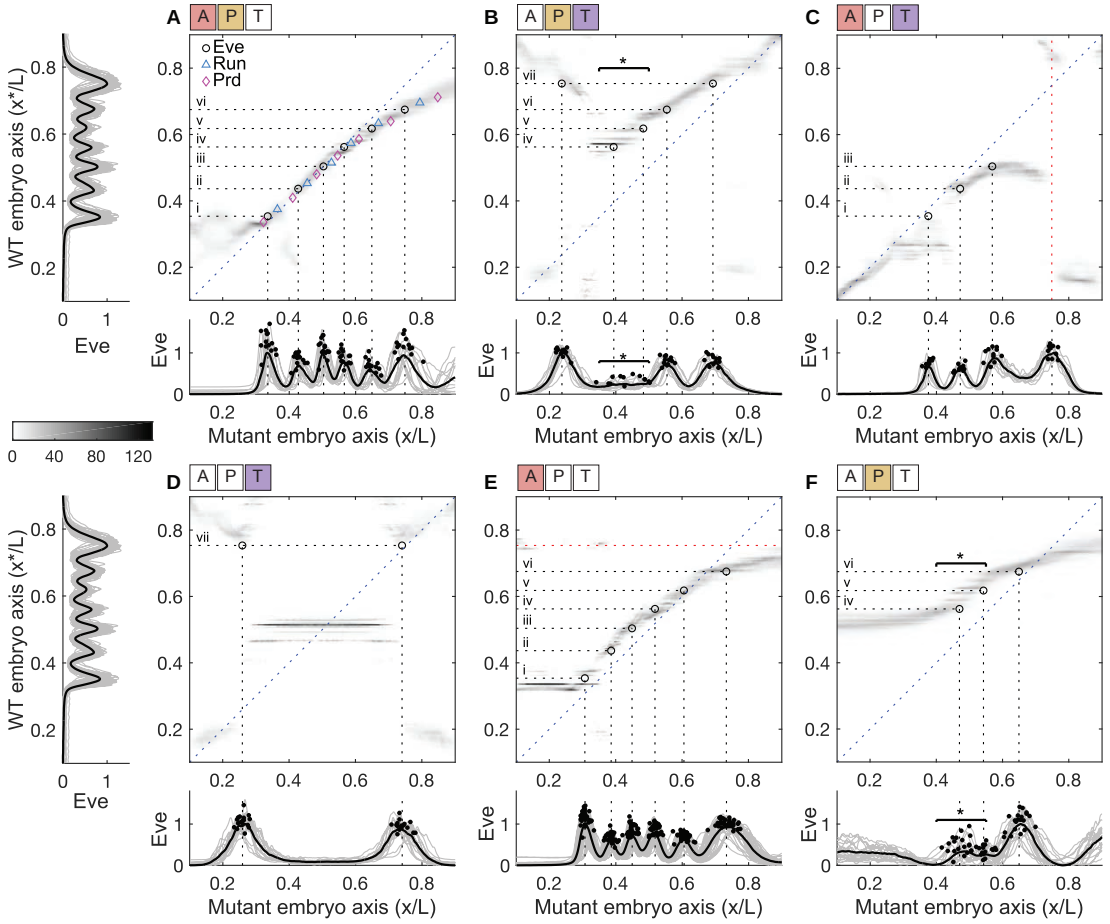
Decoding positional information from concentrations

- **Is this positional information actually used in the embryo?**
- Perturbations of maternal inputs to gap genes, expecting that the same decoding strategy is used as in controls: implied positions are shifted in specific domains.
- Comparaison of implied position based on gap genes PI and actual position of downstream pair rule genes.



Petkova, M.D., Tkačik,G., Bialek,W., Wieschaus, E.F. and Gregor,T. Optimal decoding of cellular identities in a genetic network. *Cell* 176, 844-855 (2019)

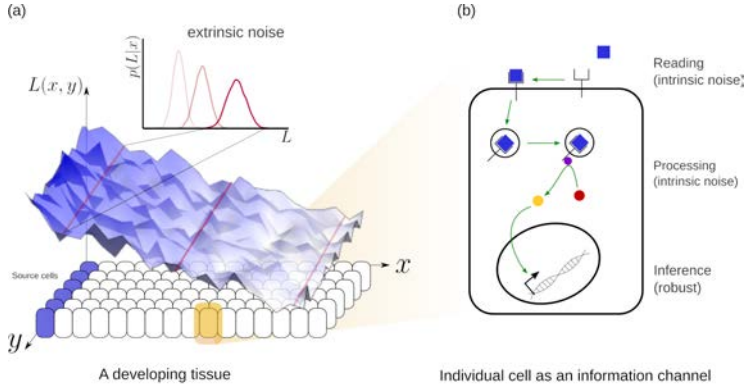
Mutual information as Positional Information

- Morphogens in growing tissues

Cellular compartmentalisation and receptor promiscuity as a strategy for accurate and robust inference of position during morphogenesis

Krishnan S Iyer[1], Chaitra Prabhakara[2], Satyajit Mayor[2]*, Madan Rao[1]*

[1]Simons Center for the Study of Living Machines, National Center for Biological Sciences - TIFR, Bangalore, India; [2]National Center for Biological Sciences - TIFR, Bangalore, India

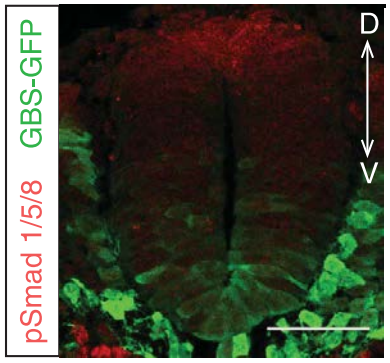


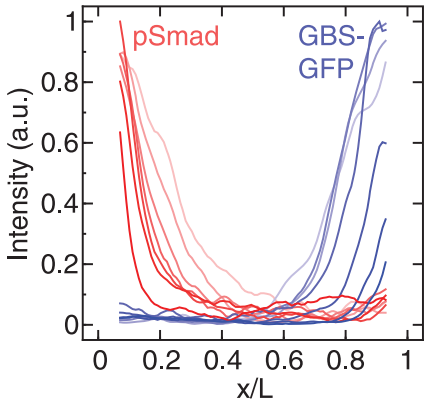
Iyer et al. and M. Rao *eLife* 2023;12:e79257. DOI: https://doi.org/10.7554/eLife.79257

Decoding of position in the developing neural tube from antiparallel morphogen gradients

Marcin Zagorski,[1] Yoji Tabata,[2] Nathalie Brandenberg,[2] Matthias P. Lutolf,[2] Gašper Tkačik,[1] Tobias Bollenbach,[1,3]* James Briscoe,[4]* Anna Kicheva[1,4]*

Like many developing tissues, the vertebrate neural tube is patterned by antiparallel morphogen gradients. To understand how these inputs are interpreted, we measured morphogen signaling and target gene expression in mouse embryos and chick ex vivo assays. From these data, we derived and validated a characteristic decoding map that relates morphogen input to the positional identity of neural progenitors. Analysis of the observed responses indicates that the underlying interpretation strategy minimizes patterning errors in response to the joint input of noisy opposing gradients. We reverse-engineered a transcriptional network that provides a mechanistic basis for the observed cell fate decisions and accounts for the precision and dynamics of pattern formation. Together, our data link opposing gradient dynamics in a growing tissue to precise pattern formation.

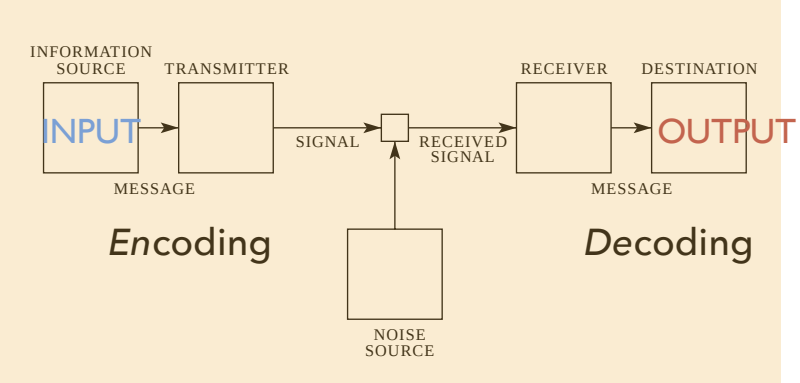




Zagorski et al., *Science* 356, 1379–1383 (2017)

Use of Shannon information theory beyond positional information

- *Mutual information* is independent of details about the biological systems so this could used in a variety of contexts where **statistical correlations between input and output variables could be identified.**
- Requires careful experimental data.
- **Input need not be a concentration, but any function of concentration: eg. scalar or vector.**



Accurate information transmission through dynamic biochemical signaling networks

Jangir Selimkhanov,[1*] Brooks Taylor,[1*] Jason Yao,[2] Anna Pilko,[2] John Albeck,[3] Alexander Hoffmann,[4,5] Lev Tsimring,[4,6] Roy Wollman[2,4,7†]

Selimkhanov et al., *Science* 346, 1371–1373 (2014)

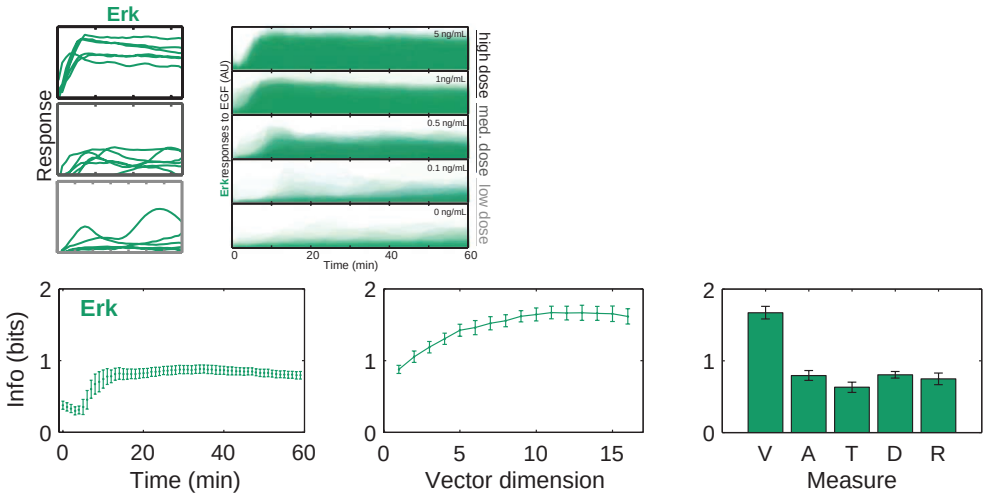
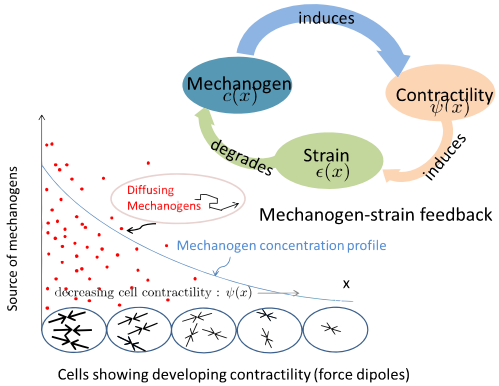
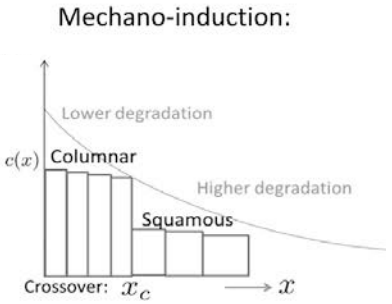


Fig. 2. Information transmission capacity of static and dynamic ERK, Ca^{2+}, and NF-κB responses.

Use of Shannon information theory beyond positional information

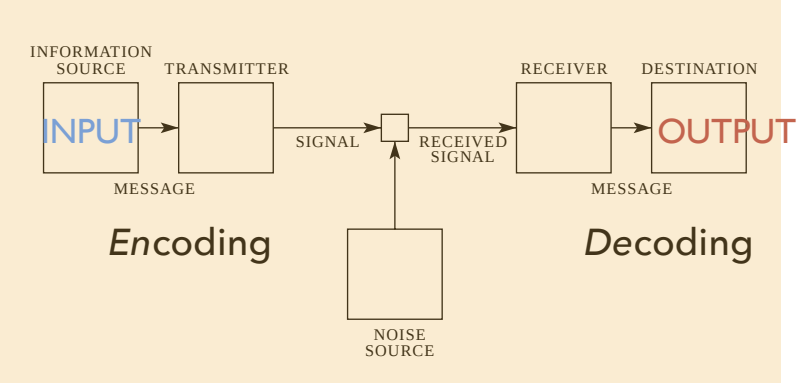
- Could also apply to mechanical input or output (mechanochemical patterning): eg. Mechanogens



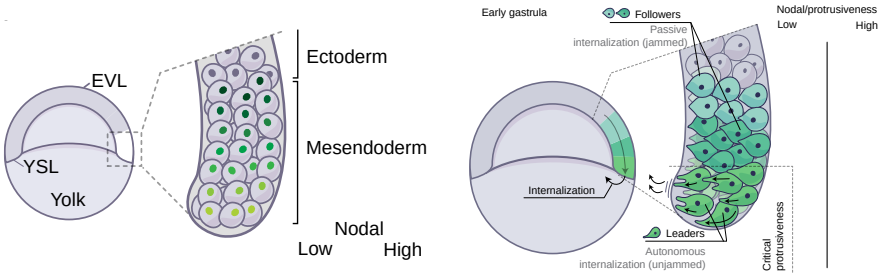


K. Dasbiswas, E. Alster & S. A. Safran (2016) *Scientific Reports* | 6:27692

K. Dasbiswas, E. Hannezo and Nir S. Gov *Biophysical Journal* 114, 968–977 (2018)



- Morphogen (cell fate) and mechanogen (motility driven un-jamming)

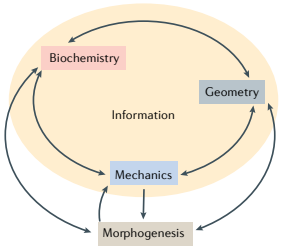


D. Pinheiro, et al, E. Hannezo & CP. Heisenberg *Nature Physics* 18, 1482–1493 (2022)

See also: Yang et al, and A. Shyer and A. Rodrigues. *Science* 382: eadg5579

Information theory and self-organisation

- **What about other situation where there is no clear input? e.g self organisation**
- Constituents of a system interact with each other to create system-wide spatiotemporal patterns.
- No input and initial conditions are difficult to define: components, interactions, noise, boundary conditions
- Self-organised systems exhibit 1) **spontaneous patterns** from homogeneous initial state and **2) reproducibility**

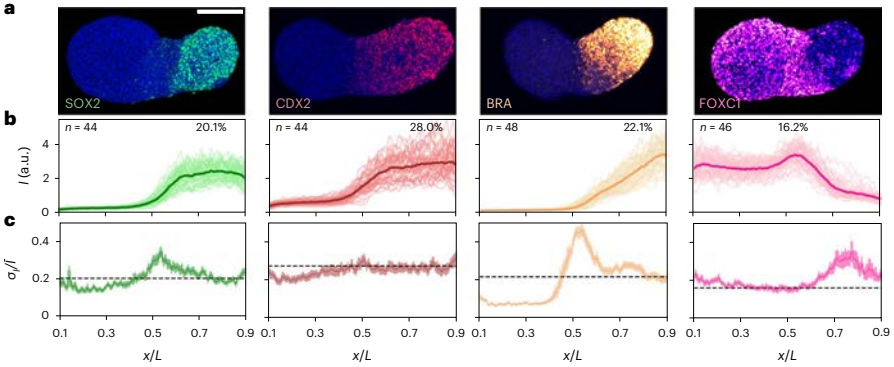


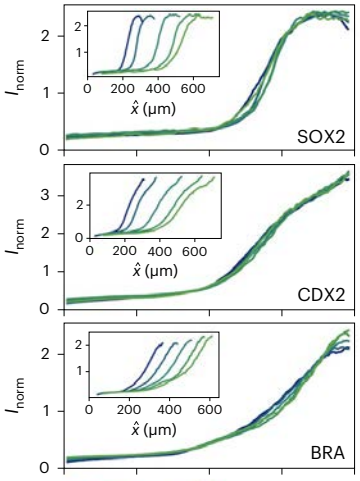
- Scaling

Precise and scalable self-organization in mammalian pseudo-embryos

Gene expression is inherently noisy, posing a challenge to understanding how precise and reproducible patterns of gene expression emerge in mammals. Here we investigate this phenomenon using gastruloids, a three-dimensional in vitro model for early mammalian development. Our study reveals intrinsic reproducibility in the self-organization of gastruloids, encompassing growth dynamics and gene expression patterns. We observe a remarkable degree of control over gene expression along the main body axis, with pattern boundaries positioned with single-cell precision. Furthermore, as gastruloids grow, both their physical proportions and gene expression patterns scale proportionally with system size. Notably, these properties emerge spontaneously in self-organizing cell aggregates, distinct from many in vivo systems constrained by fixed boundary conditions. Our findings shed light on the intricacies of developmental precision, reproducibility and size scaling within a mammalian system, suggesting that these phenomena might constitute fundamental features of multicellularity.

- Precision

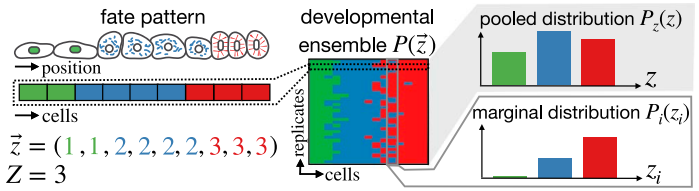




M. Merle et al. and T. Gregor. *Nature Structural & Molecular Biology*, 31, 896–902 (2024)

Information theory and self-organisation

- An information theoretic mathematical formulation for 1) **spontaneous patterning** and 2) **reproducibility**



- Two entropies for reproducibility and patterning

$$S_{\rm rep} = \frac{1}{N} S\left[P(\vec{z})\right] = -\frac{1}{N}\sum_{\vec{z}} P(\vec{z}) \log_2 P(\vec{z}).$$

$$S_{\rm pat} = S[P_z(z)] = -\sum_{z=1}^{Z} P_z(z) \log_2 P_z(z).$$

- Correlation free entropy: $S_{\rm cf}$

entropy of a joint distribution constructed from independent marginals, i.e., $P(\vec{z}) = \prod_{i=1}^{N} P_i(z_i)$ corresponding to a system with no spatial correlations.

- Defining Utility function for self-organised system: minimises $S_{\rm rep}$ and maximises $S_{\rm pat}$. $U = S_{\rm pat} - S_{\rm rep}$.

- Total information: positional information (local) and correlational information (non-local statistical structure)

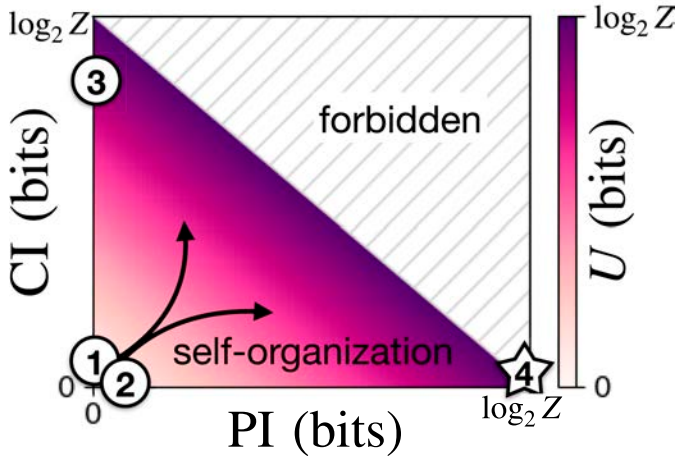
	name	definition
entropies	reproducibility entropy	$S_{\rm rep} = S[P(\vec{z})]/N$
	patterning entropy	$S_{\rm pat} = S[P_z(z)]$
	correlation-free entropy	$S_{\rm cf} = \Sigma_i^N S[P_i(z_i)]/N$
information	utility / total information	$U = S_{\rm pat} - S_{\rm rep}$
	positional information	$\mathrm{PI} = S_{\rm pat} - S_{\rm cf}$
	correlational information	$\mathrm{CI} = S_{\rm cf} - S_{\rm rep}$

$$U = \mathrm{PI} + \mathrm{CI}.$$

D. Brückner a d G. Tkacik. *PNAS* 121, e2322326121

Information theory and self-organisation

- An information theoretic mathematical formulation for 1) **spontaneous patterning** and 2) **reproducibility**



- Defining information: positional information (local) and correlational information (non-local statistical structure)

	name	definition
entropies	reproducibility entropy	$S_{\rm rep} = S[P(\vec{z})]/N$
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	correlation-free entropy	$S_{\rm cf} = \Sigma_i^N S[P_i(z_i)]/N$
information	utility / total information	$U = S_{\rm pat} - S_{\rm rep}$
	positional information	$\mathrm{PI} = S_{\rm pat} - S_{\rm cf}$
	correlational information	$\mathrm{CI} = S_{\rm cf} - S_{\rm rep}$

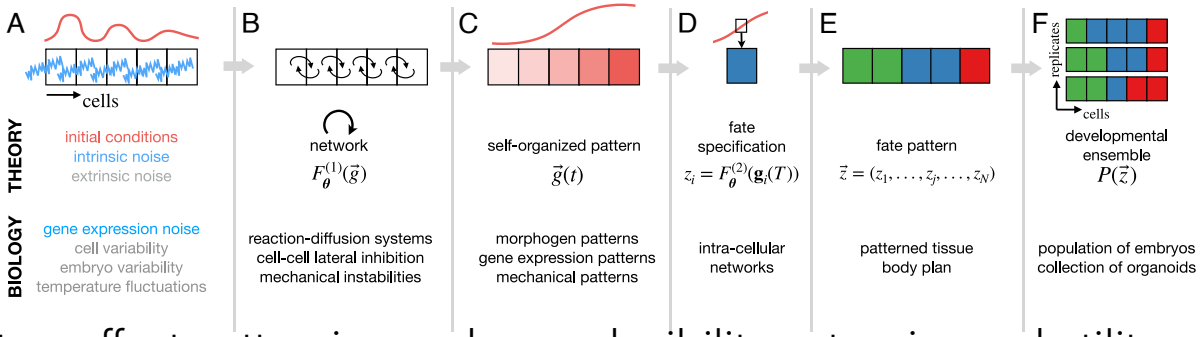
- Self-organization can proceed by 1) setting up correlations of gene expression with position and/or by 2) setting up correlations across positions.

D. Brückner a d G. Tkacik. *PNAS* 121, e2322326121

Information theory and self-organisation

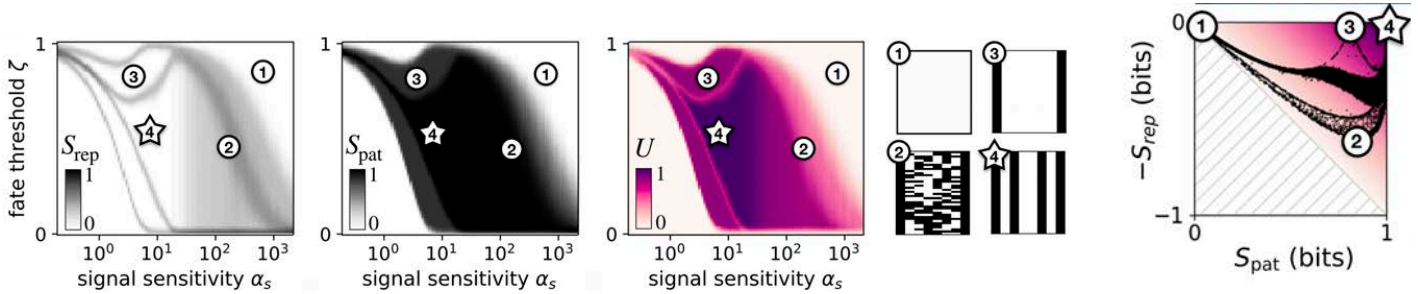
- Hypothesis: **self-organization in developmental systems is a simultaneous maximization of reproducibility and of cell type diversity (ie. utility U is maximised)**

  - Self-Organized Patterning as a Stochastic Dynamical System



- Exploring how parameters affect patterning and reproducibility entropies and utility.
- The utility function can be used as an optimization criterion to select model parameters.

Ex: Lateral inhibition

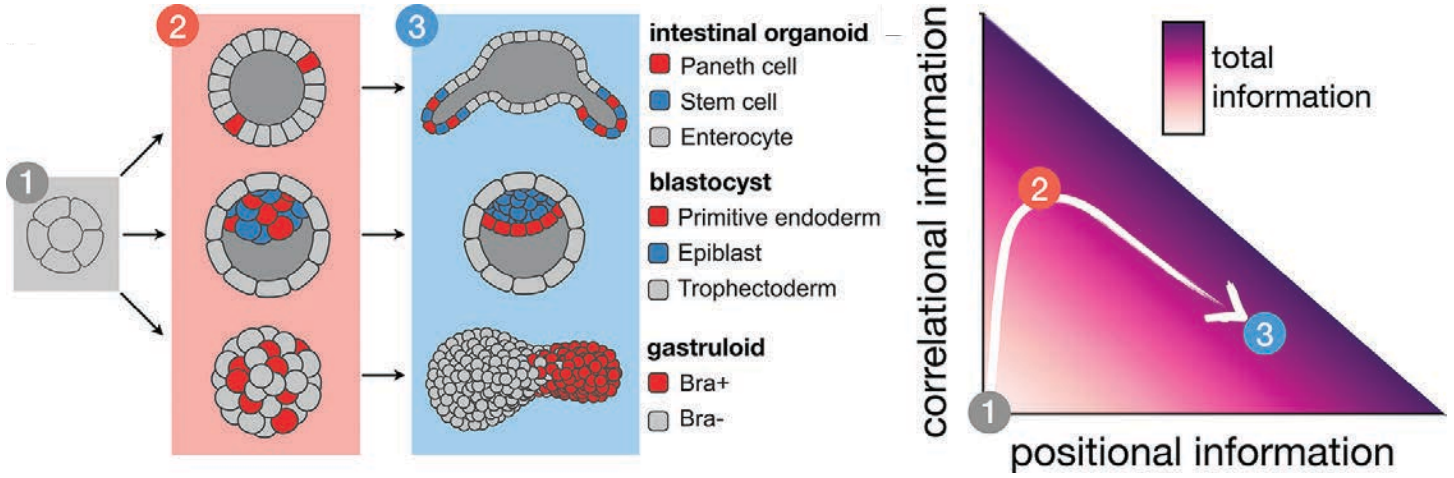


D. Brückner a d G. Tkacik. *PNAS* 121, e2322326121

Information theory and self-organisation

- Hypothesis: **self-organization in developmental systems is a simultaneous maximization of reproducibility and of cell type diversity (ie. utility U is maximised)**

- A possible general trend:
- The systems first break symmetry, giving statistical structure (proportion of cell fates) without spatial pattern (CI)
- The systems later acquires spatial organisation and reproducibility (PI).



D. Brückner a d G. Tkacik. *PNAS* 121, e2322326121

Conclusions

1. ***Shannon information theory*** **provides a powerful framework to:**
   - *Quantify* biological information encoded in a chemical system
   - Assess information transmission in a noisy channel, such as in any input/output system in biology.

2. ***Mutual information*** **provides a measurement of positional information** through the statistical structure of correlations between concentrations of molecules and spatial coordinates.

3. **In self-organised systems, exploration of other means to quantify total information: eg. positional and correlational information.**

4. **Need to consider other parametrizations of space (than spatial coordinates): polarity, nematic order etc.**

Book recommendations as a background