2020高中生物教師研習營：細胞通訊的語言

Cell communication: Development system

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How is such elaborate pattern generated from a single cell?

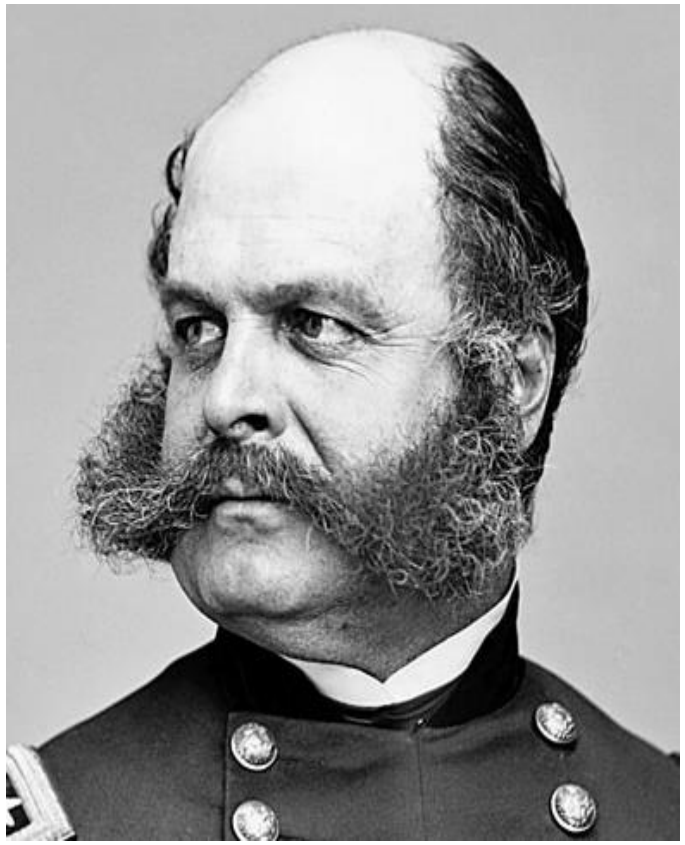
We learn from nature's variations

- Breeding: based on natural variations
- Suggests only a few genes are involved in the variations




http://www.pigeonmad.com/guide_to_fancy_pigeon_breeds.php

Not simply basic biology. Can be applied with great value.



Distribution; growth; loss/removal; texture; color; orientation; hormone/age

Epithelial derivatives: hair, scale, horn; nail, feather

$$$

- 當產品有問題時，才意識到製造過程　How to control number and position of body parts?
- Always question the data!

http://news2.onlinenigeria.com/news/general/293795-meet-the-woman-with-three-breasts-photos.html

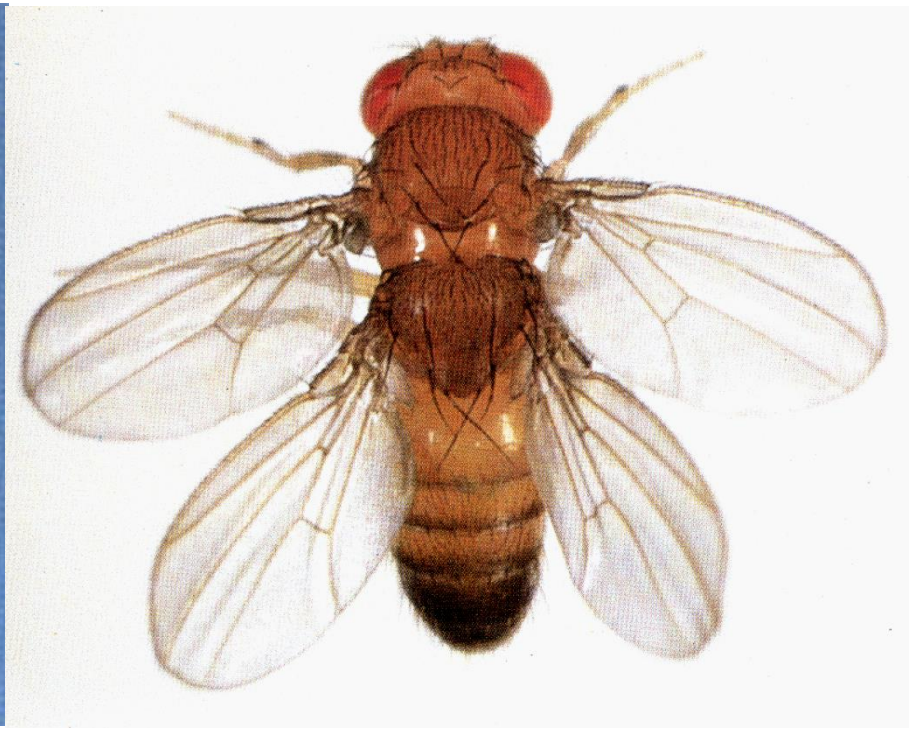
http://simplypimped.com/engine/print.php?newsid=58&news_page=1

體節命運的決定

單一基因的改變，使T3轉型成T2

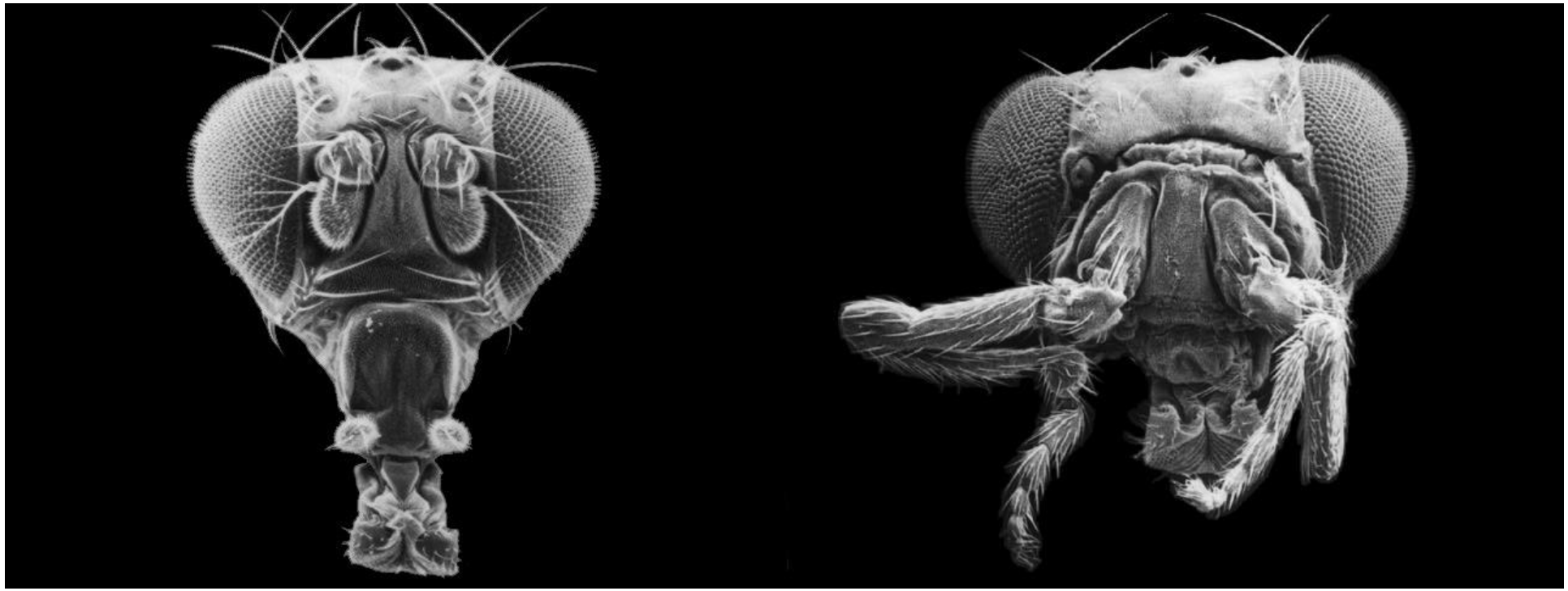
Wild type（野生型）

Ubx 突變



體節命運的決定

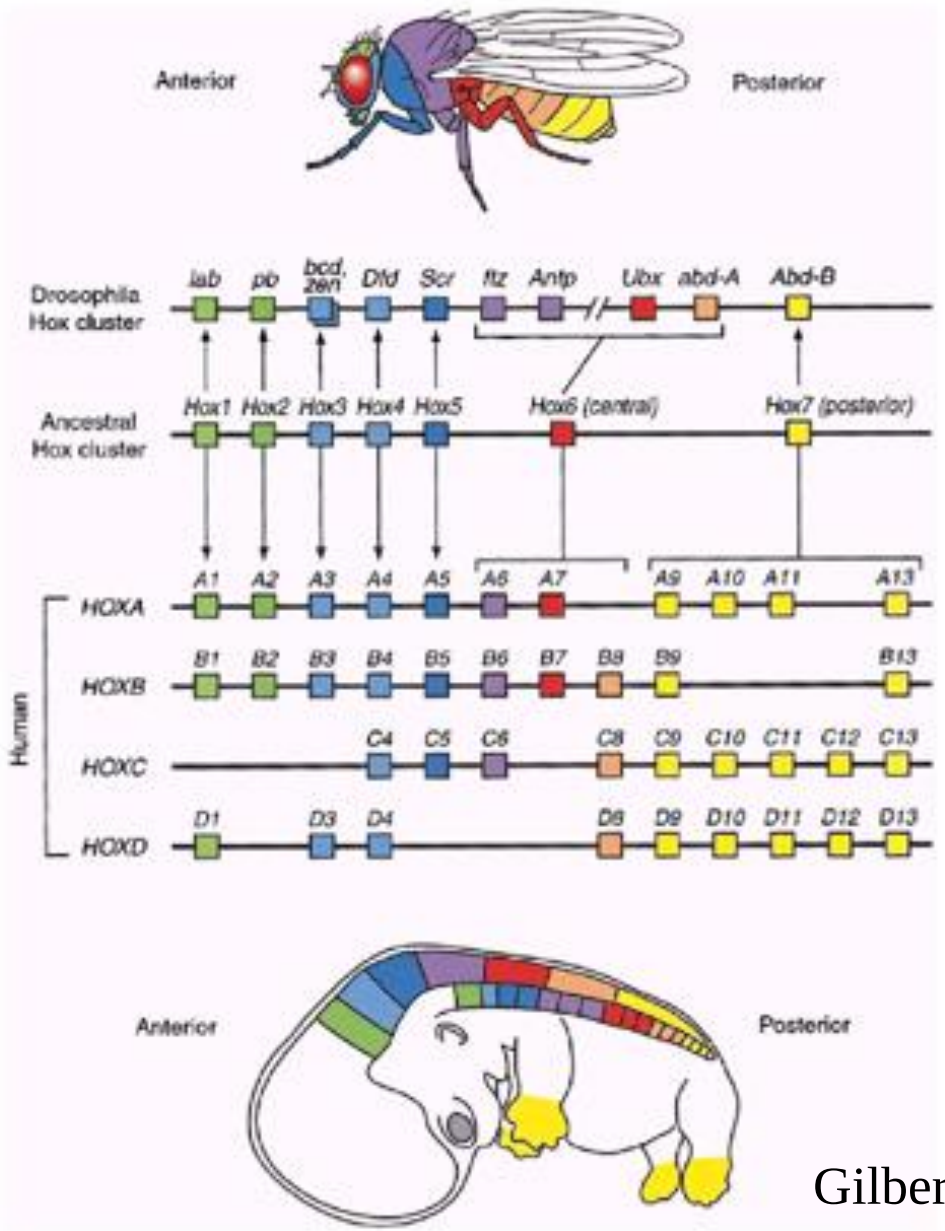
單一基因的改變，使觸角轉型成腿



WT

Antennapedia

HOX 基因：從果蠅到人

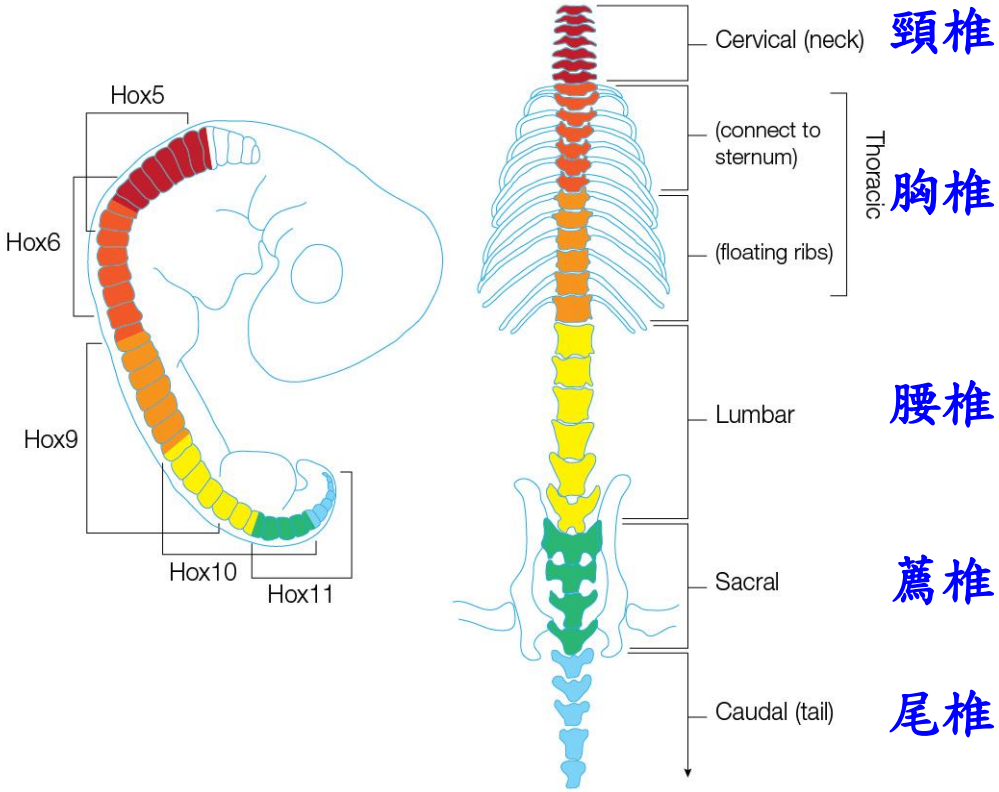


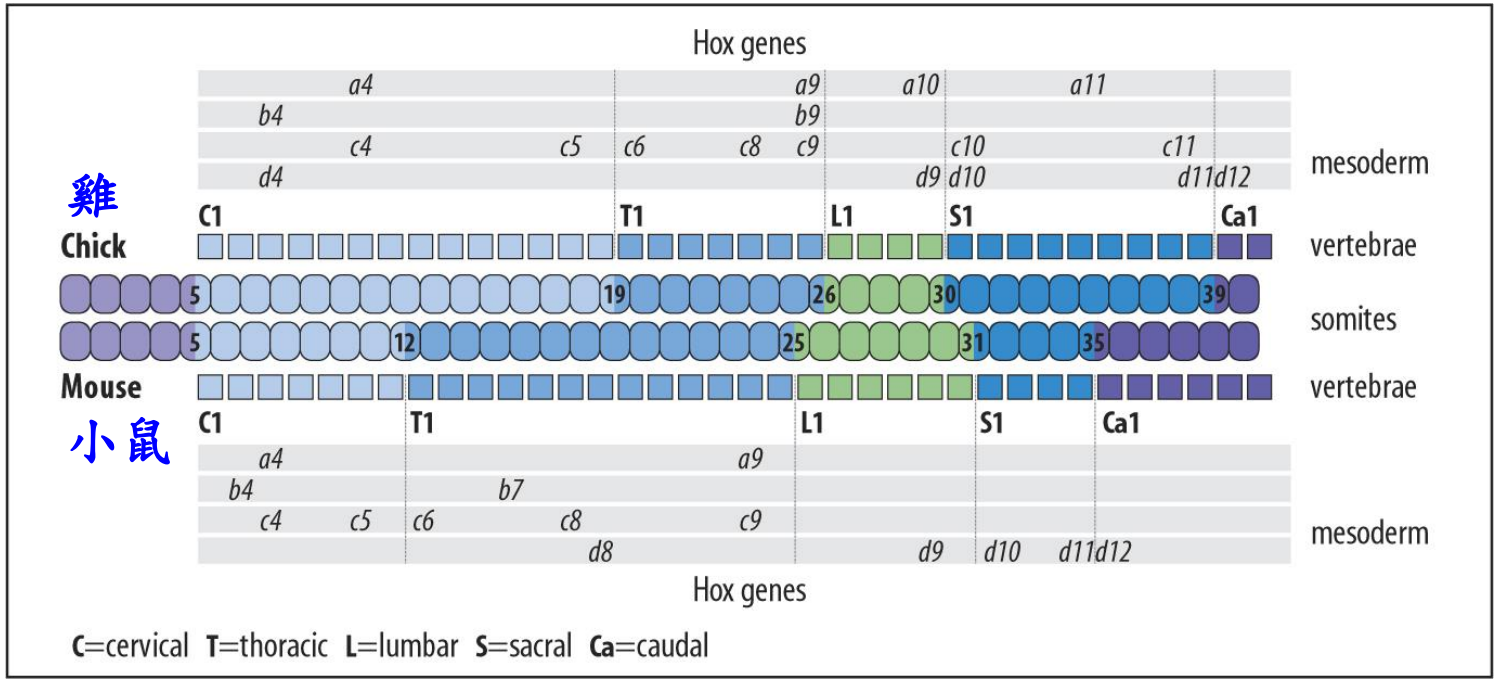
果蠅

小鼠、人

Gilbert, 2000, Developmental Biology, 6ed

HOX 基因影響脊椎發育

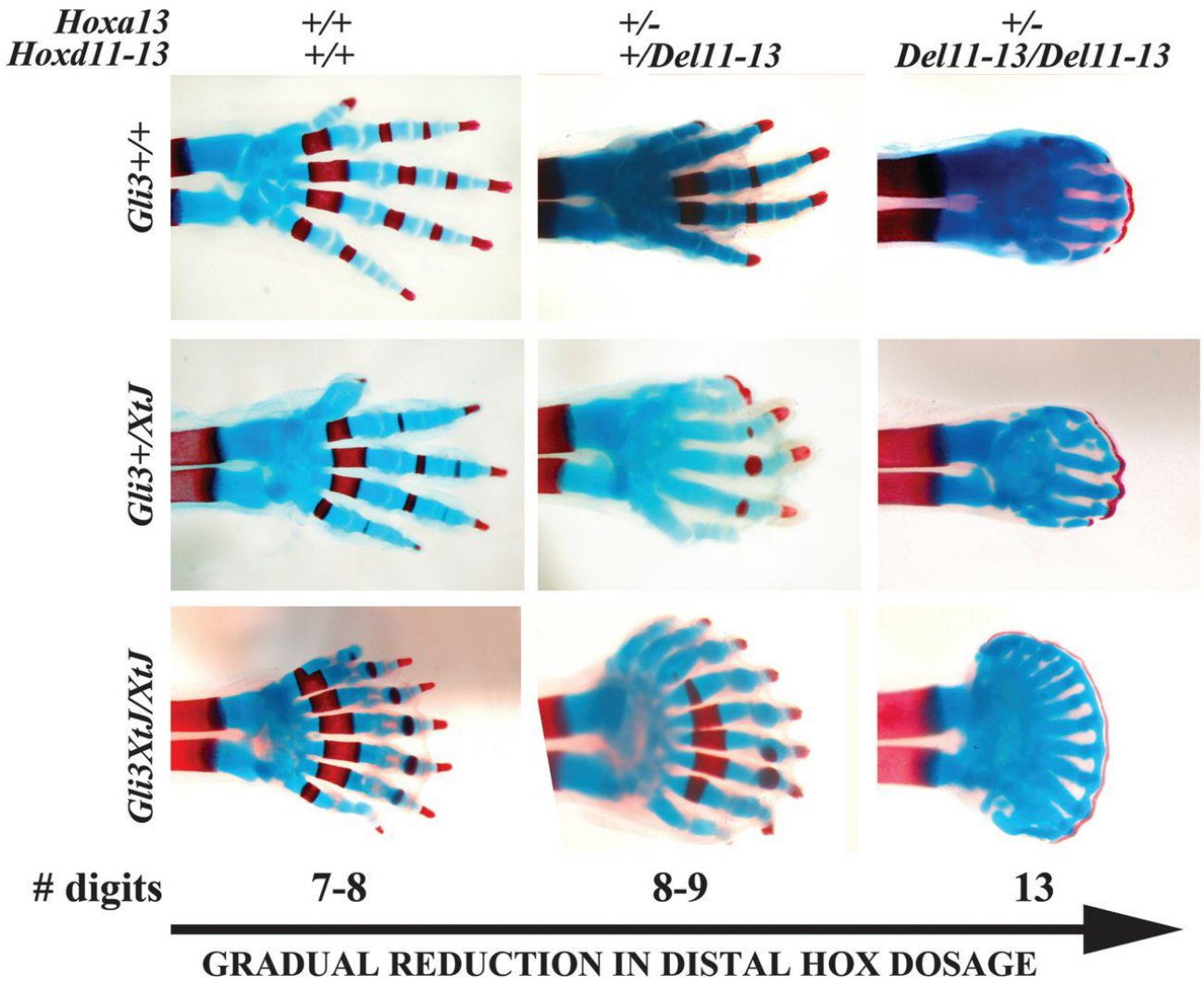




http://learn.genetics.utah.edu/content/basics/hoxgenes/

http://www.mun.ca/biology/desmid/brian/BIOL3530/DEVO_05/devo_05.html

HOX 基因影響指節發育



http://www.devbio.biology.gatech.edu/?page_id=7140

基因控制發育

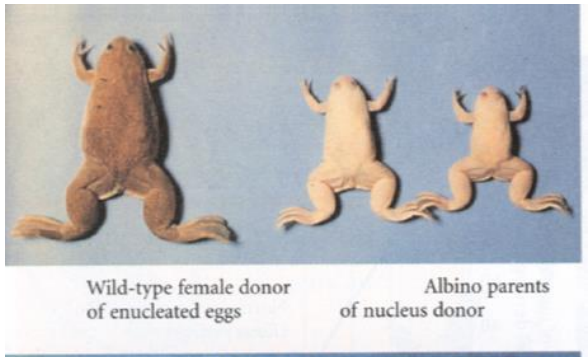
但，每個細胞都帶有同樣的基因，

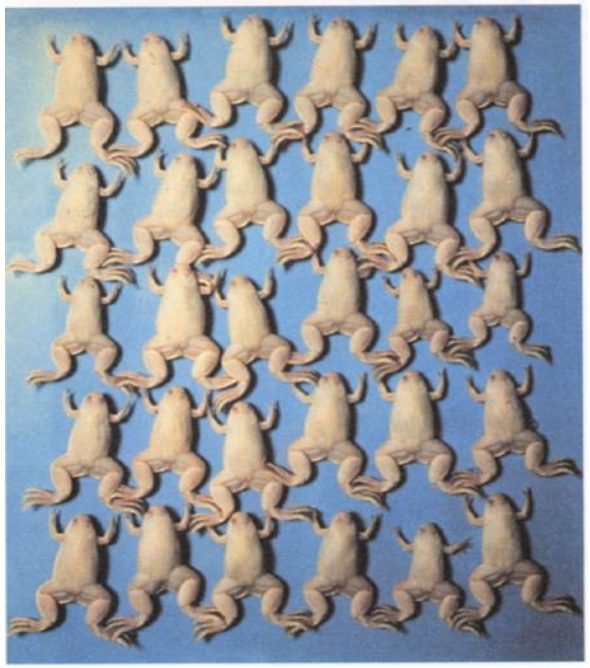
為何細胞有所不同？

Nuclear totipotency of differentiated cells

卵 donor

核 donor





- Plant regeneration from tissue culture cells
- Nuclear transplant in amphibian
- Nuclear transplant in mammals (Dolly)

Exceptions: lymphocytes

Briggs and King (1952) PNAS **38**: 455–463.
Transplantation of Living Nuclei From Blastula Cells into Enucleated Frogs' Eggs.

Gurdon et al. (1958) *Nature*. **182**: 64–65.
Sexually Mature Individuals of Xenopus laevis from the Transplantation of Single Somatic Nuclei.

Dolly (1996-2003)

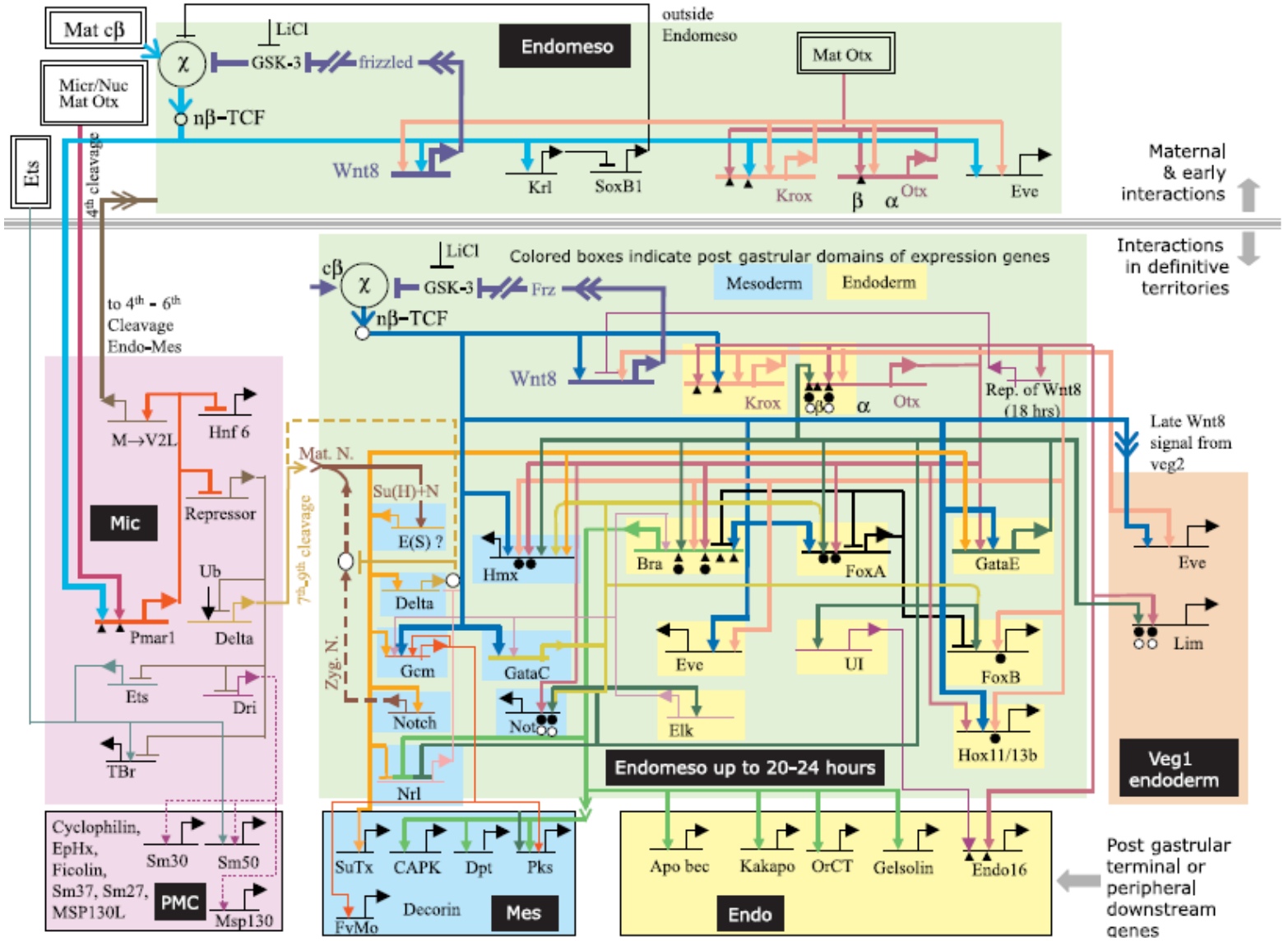
Bonnie

Campbell et al (1996) *Nature*. **380**: 64–6.
Sheep cloned by nuclear transfer from a cultured cell line.

Development as a process of temporally and spatially coordinated differential gene expression

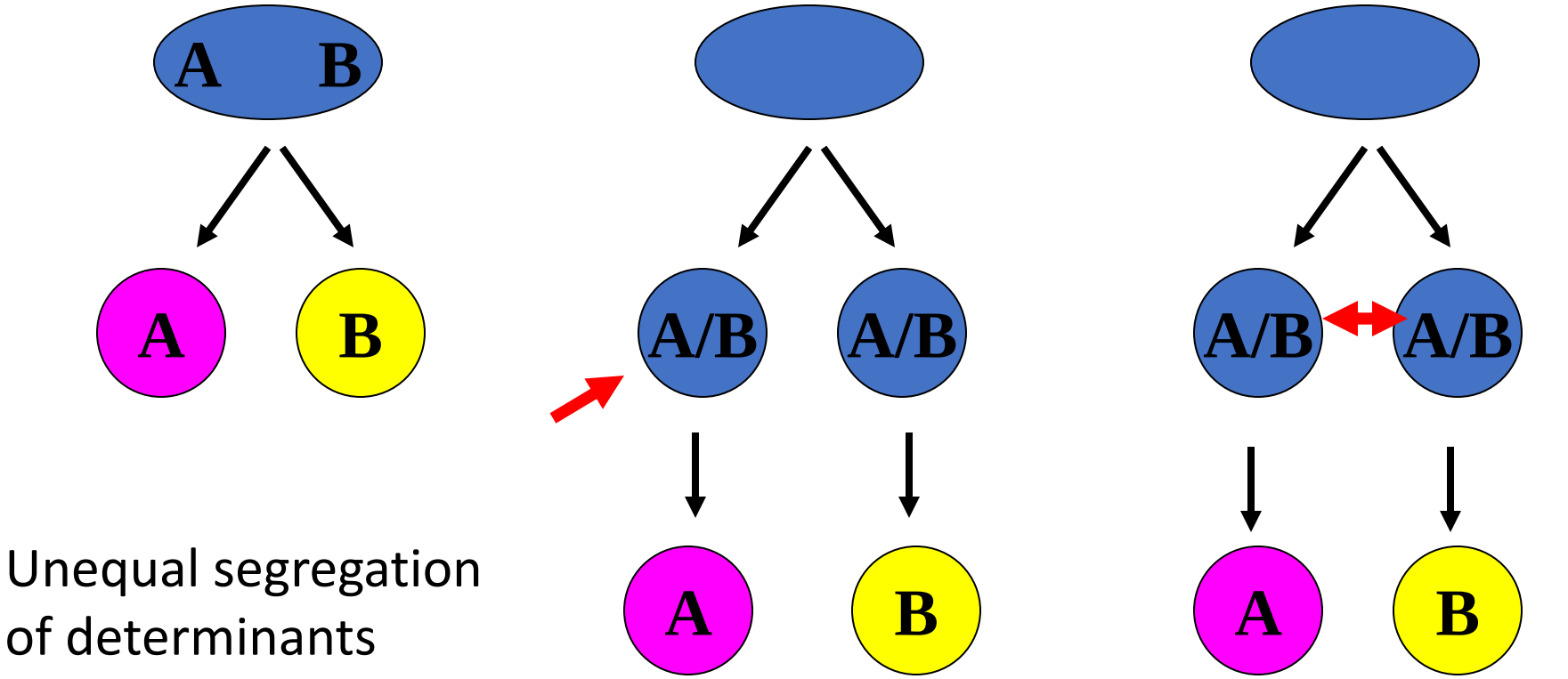
- Cells are different in their gene expression
- Reduced to molecular biology: gene regulation
- Hierarchy (circuits) of gene regulation
- Cellular interactions

Gene regulatory network



- ~ electrical circuit
- Describes relationships among genes
- Need to describe temporal changes
- Need to describe spatial relationships (among different cells)

How to create asymmetry ?
(Two B's or not two B's?)

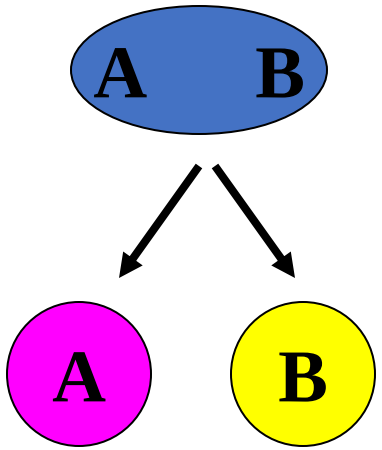


Unequal segregation of determinants

External signals

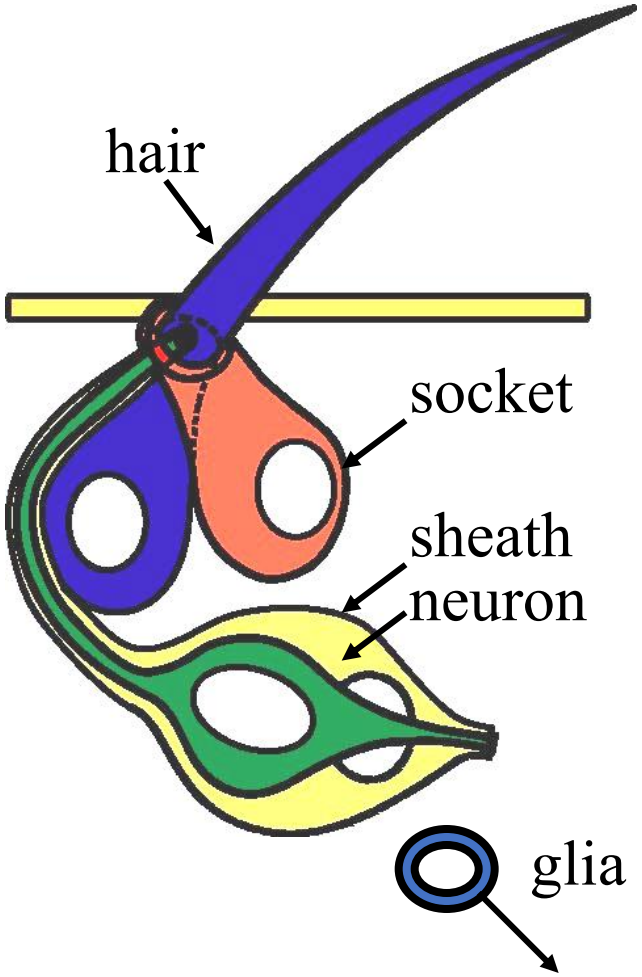
Cellular interaction

Horvitz & Herskowitz (92) Mechanisms of asymmetric cell division: two Bs or not two Bs, that is the question. Cell 68:237-55.

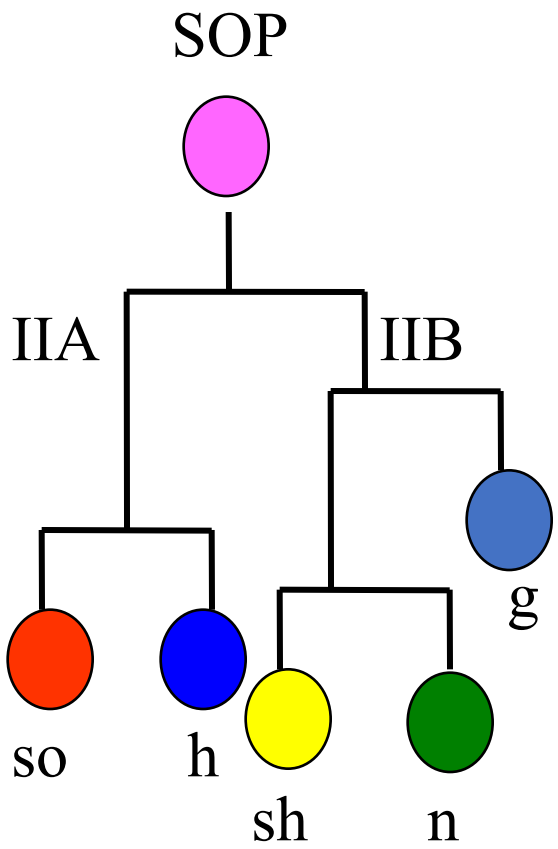


Unequal segregation
of determinants

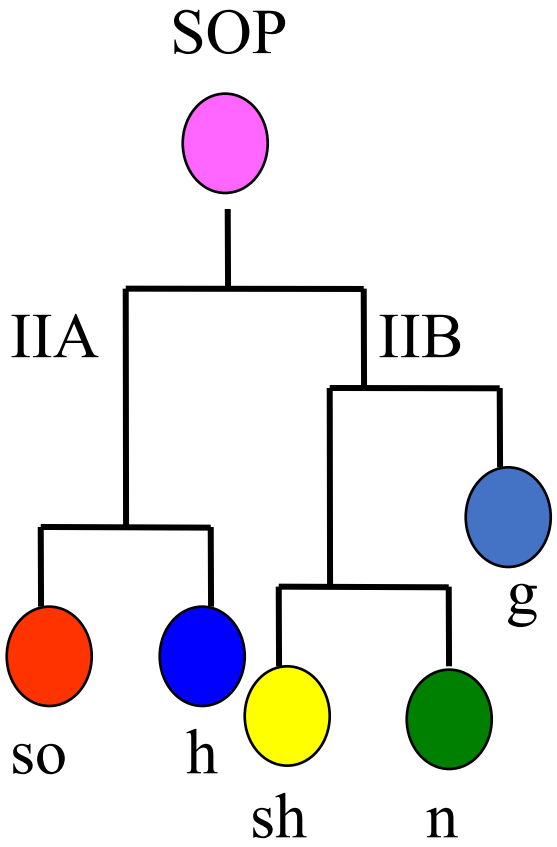
External Sensory (ES) organs in Drosophila



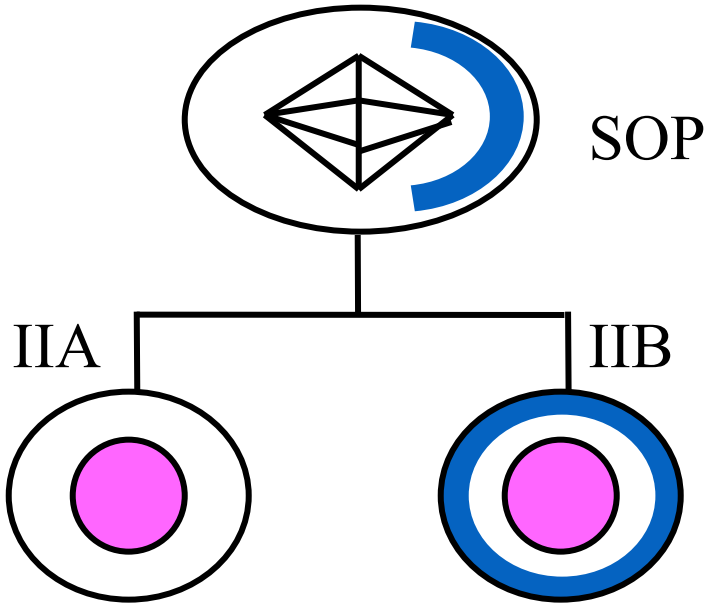
Asymmetric cell divisions



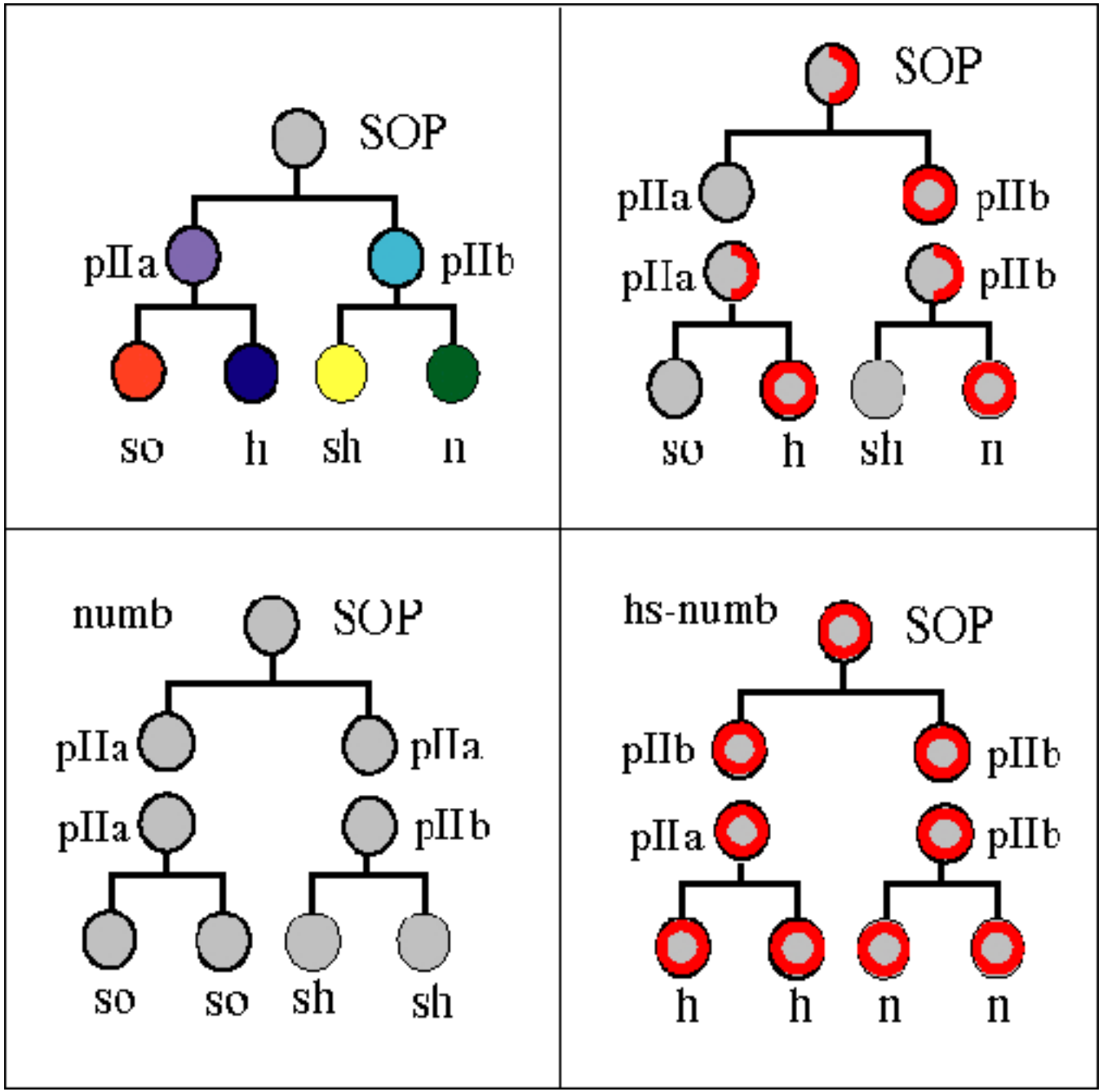
Generation of Asymmetry (I)



Numb protein localization

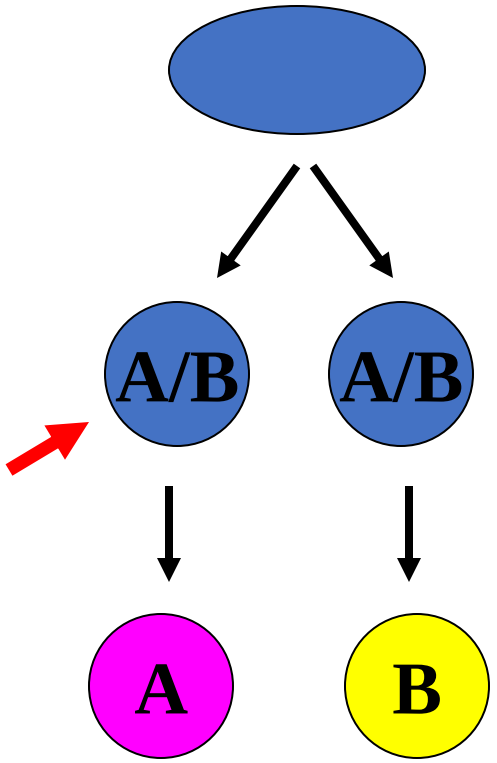


Asymmetric cell divisions


SOP
pIIa
pIIb
so
h
sh
n
SOP
pIIa
pIIb
pIIa
pIIb
so
h
sh
n
numb
SOP
pIIa
pIIa
pIIa
pIIb
so
so
sh
sh
hs-numb
SOP
pIIb
pIIb
pIIa
pIIb
h
h
n
n

Numb

Generation of Asymmetry (II)



External signals

Totipotent up to 8-cell stage

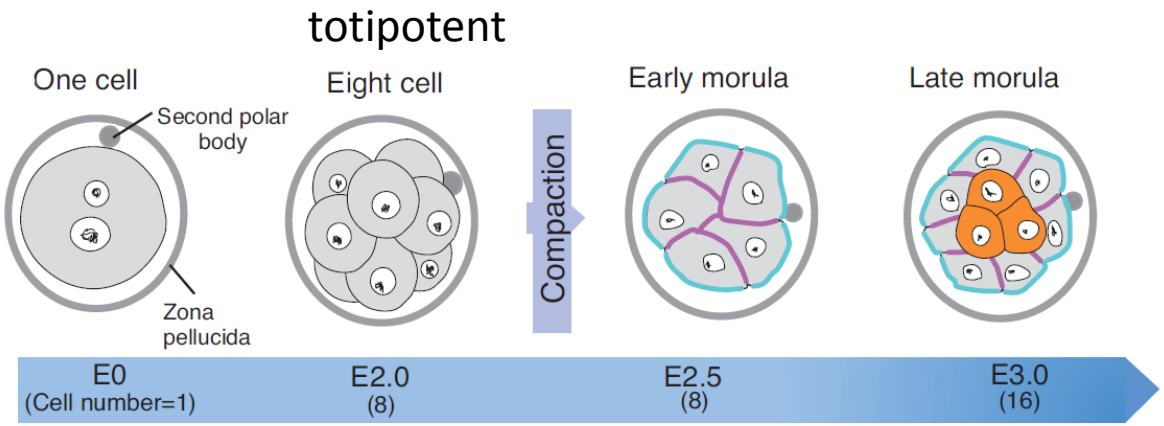
同卵五胞胎

http://ymiit.com/0n79393n

同卵四胞胎
Nine-banded armadillo

https://www.pinterest.com/teresawordgirl/armadillos/?lp=true

Compaction generates the first asymmetry

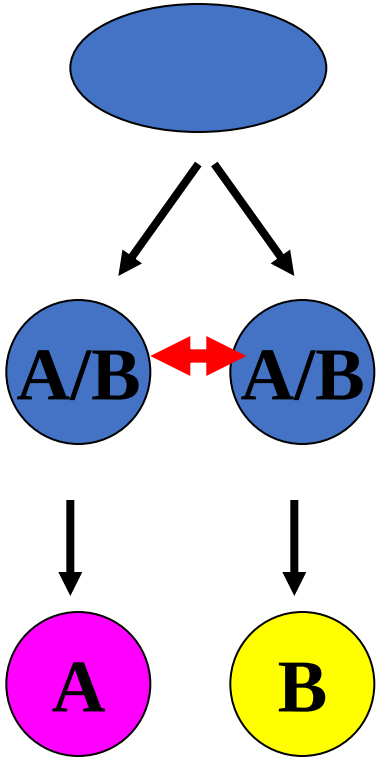


- Apical-basal polarity in 8-cell stage
- Further divisions creates inner and outer cells

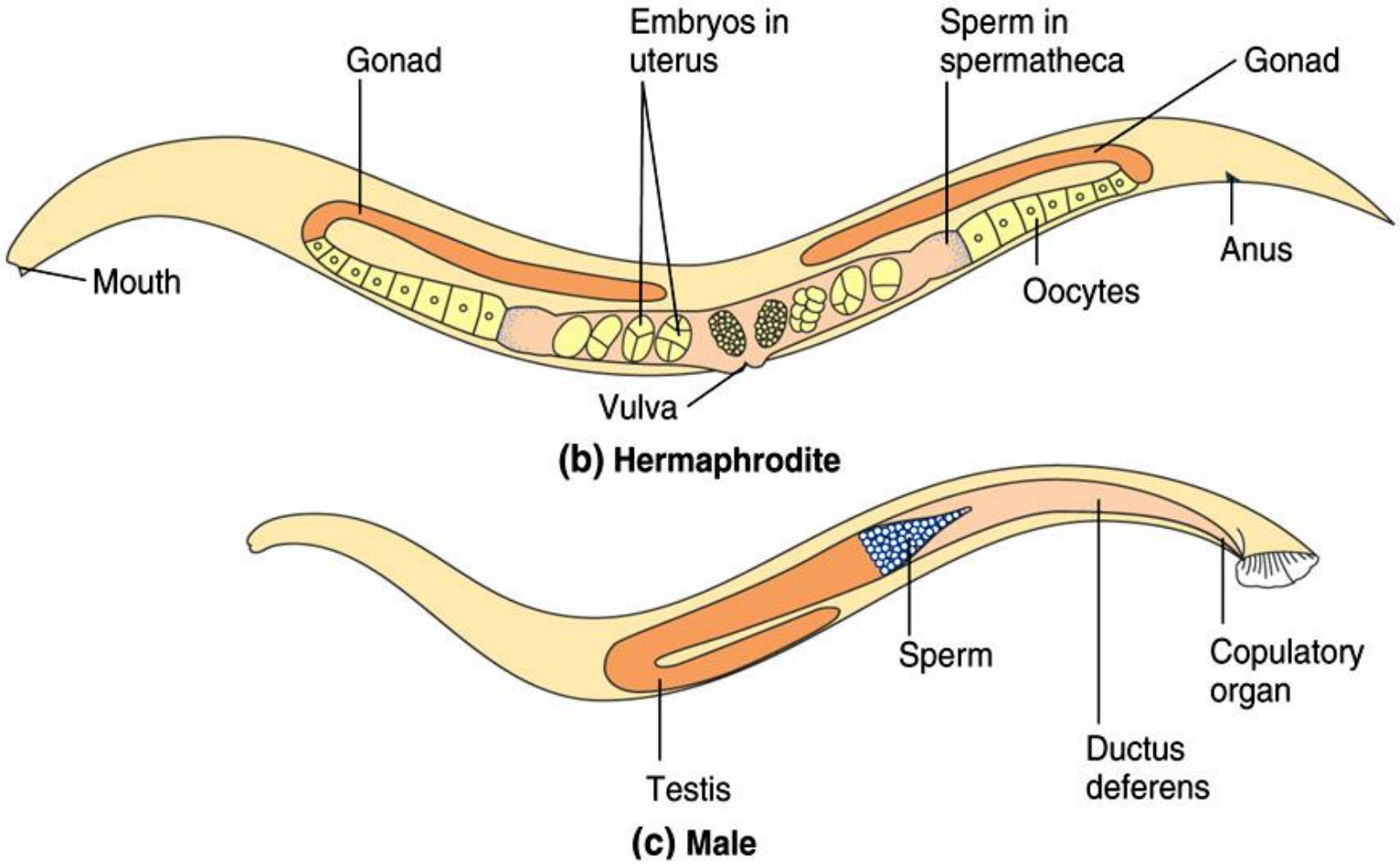
Takaoka and Hamada (2012) Development 139, 3-14

Generation of Asymmetry (III)

signaling/interaction between equipotential cells



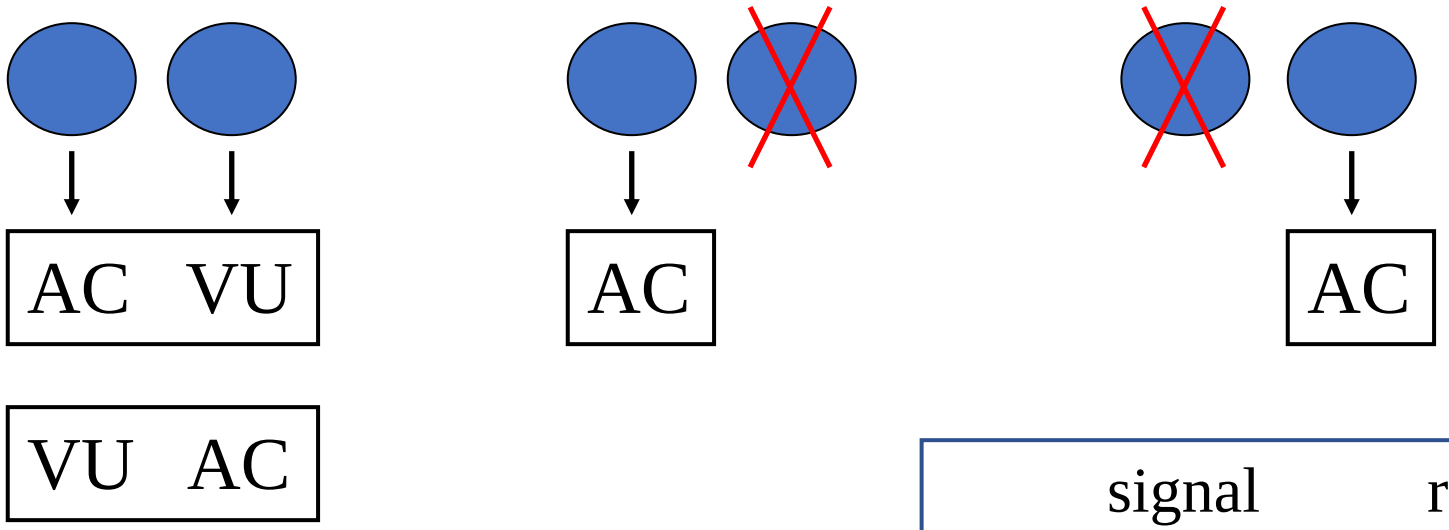
Caenorhabditis elegans

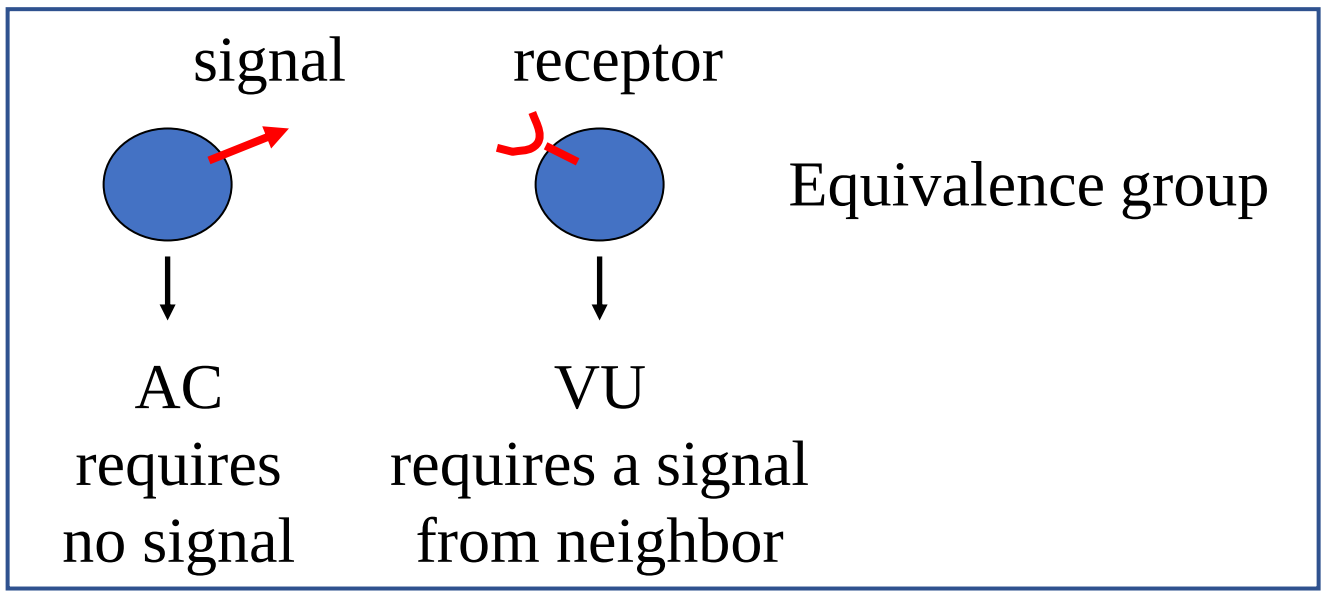


Hemaprhodite: 959 somatic cells + variable germ cells

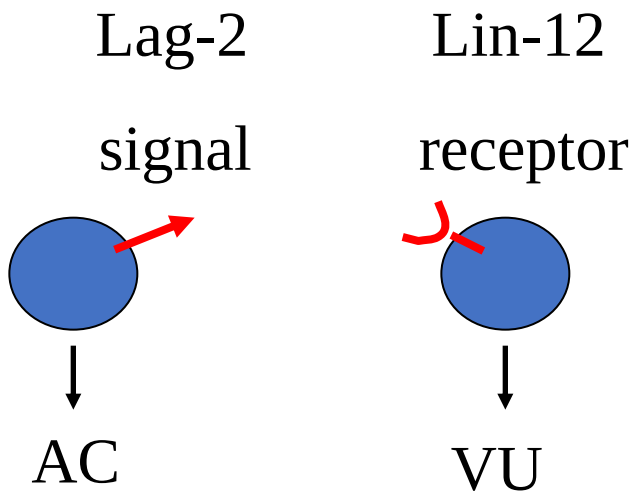
Cell-cell interactions for developmental fate decisions

Z1.ppp Z4.aaa
(different lineage)





Comparison of Lin-12 activity determines VU



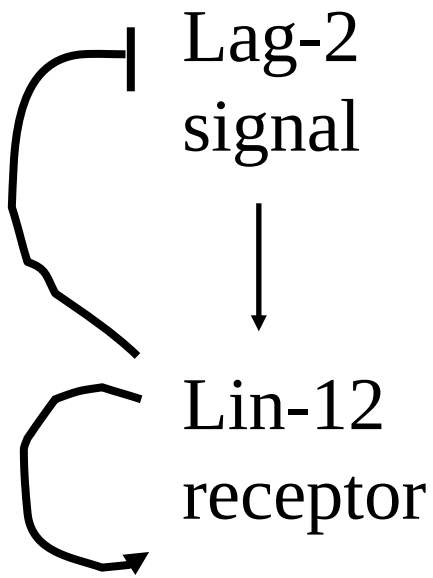
***lin-12*$^{-}$**	AC	AC
***lin-12*^{act}**	VU	VU

***lin-12*$^{+}$**	***lin-12*$^{-}$**
↓	↓
VU	AC

***lin-12*$^{+}$**	***lin-12*^{act}**
↓	↓
AC	VU

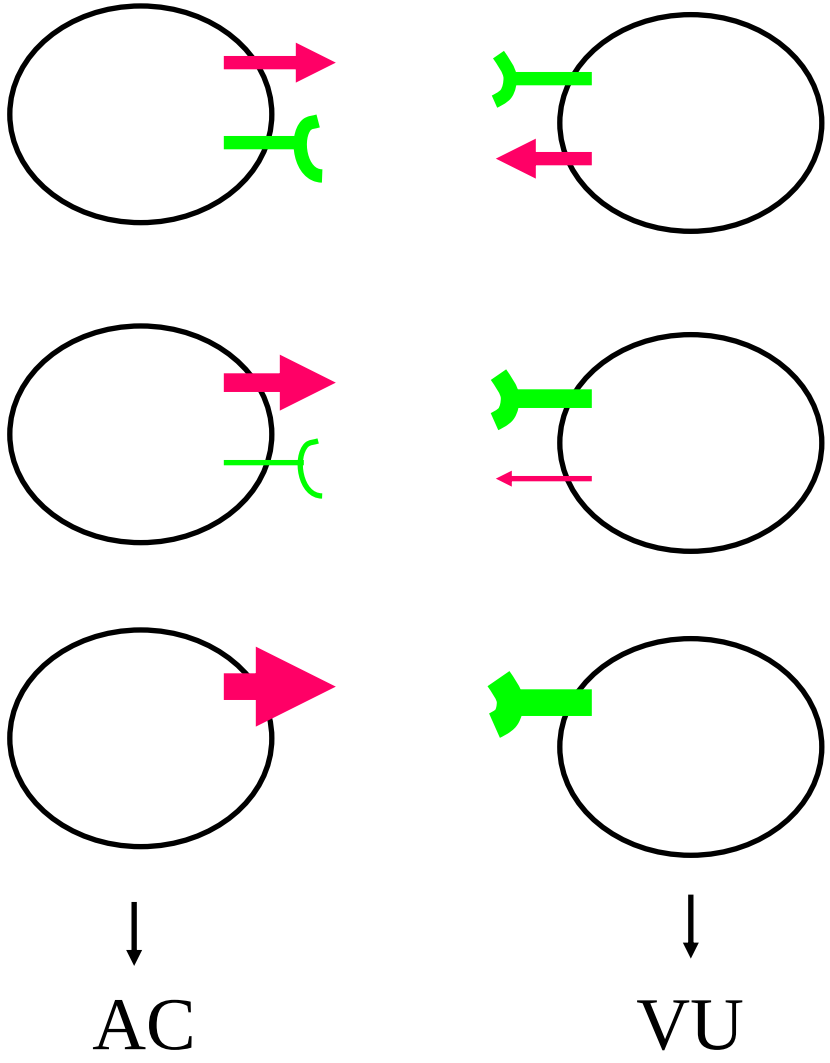
Bistable switch of developmental fates

Lateral inhibition



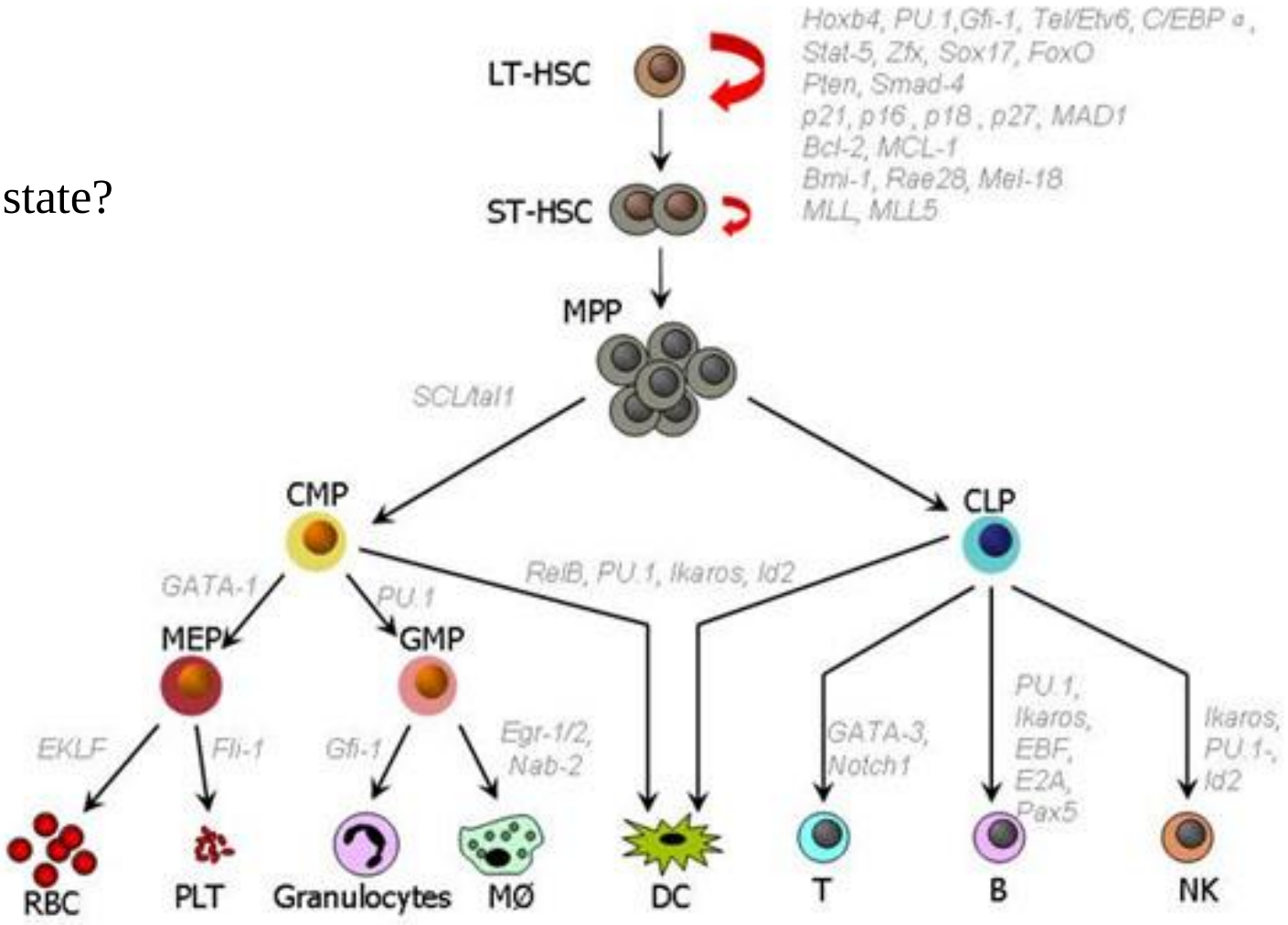
Self enhancement

Initial difference: stochastic



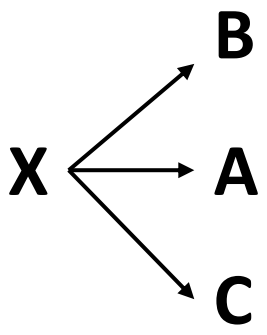
細胞的逐步分化

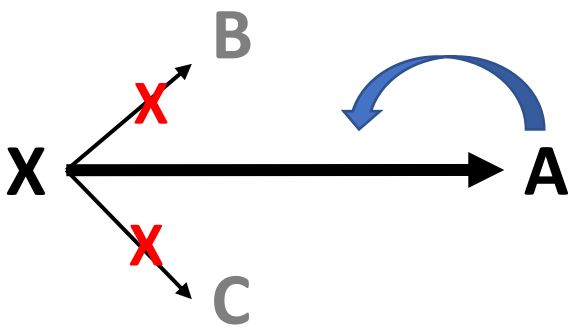
- 如何知道是逐步分化？
- How does one cell state change to another state?
  - Intrinsic mechanism
  - External signals
- Coordination (pattern formation)



http://www.gene-knockout.com.cn/en/research.html

Progressive differentiation



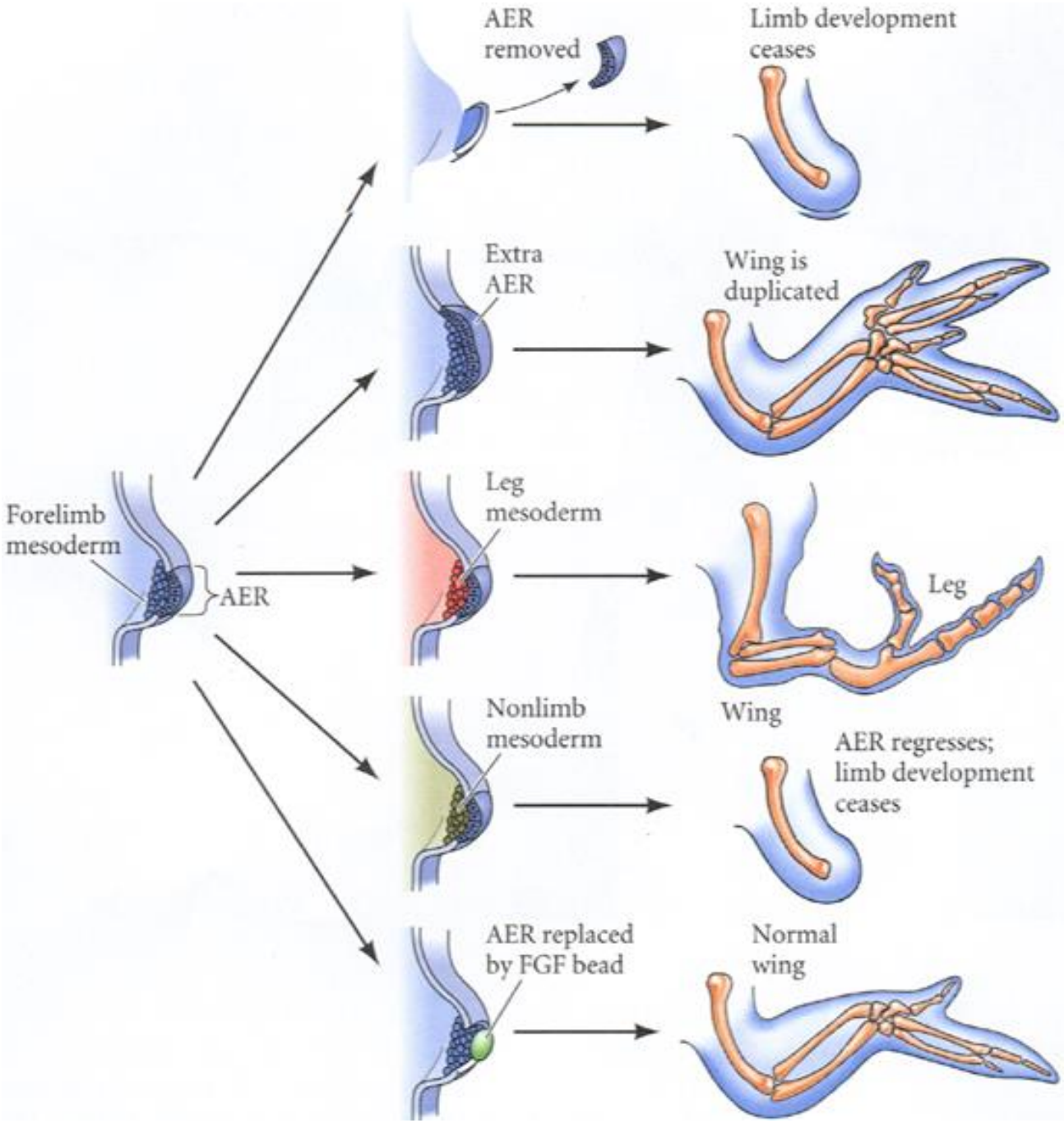


- Select among limited options

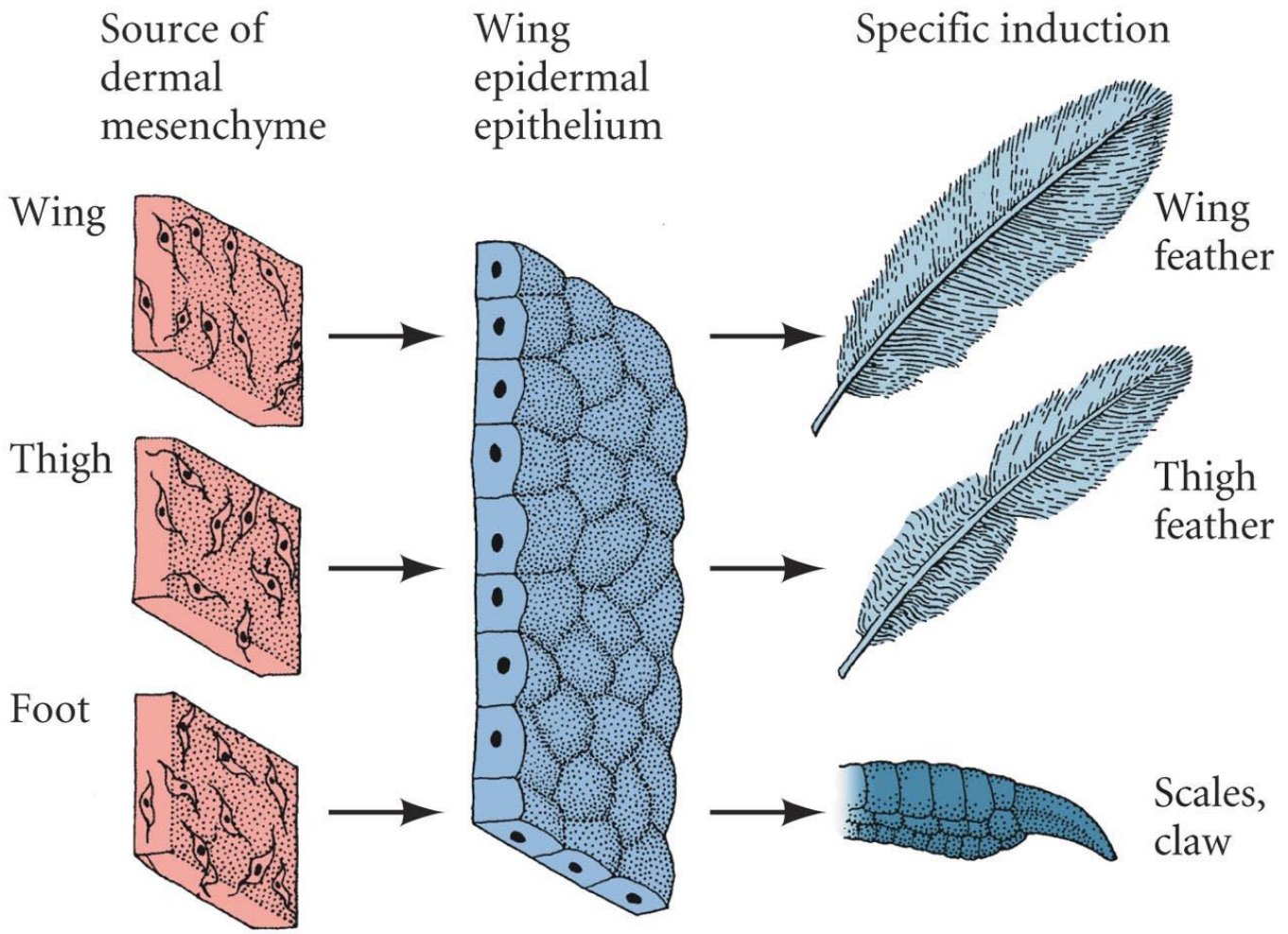
- Positive feedback
- Amplify preference
- Self maintenance
- Block other pathways
- Restricted potential

- Plasticity
- External signal (S)
- Feedbacks
- Change of fate

Induction

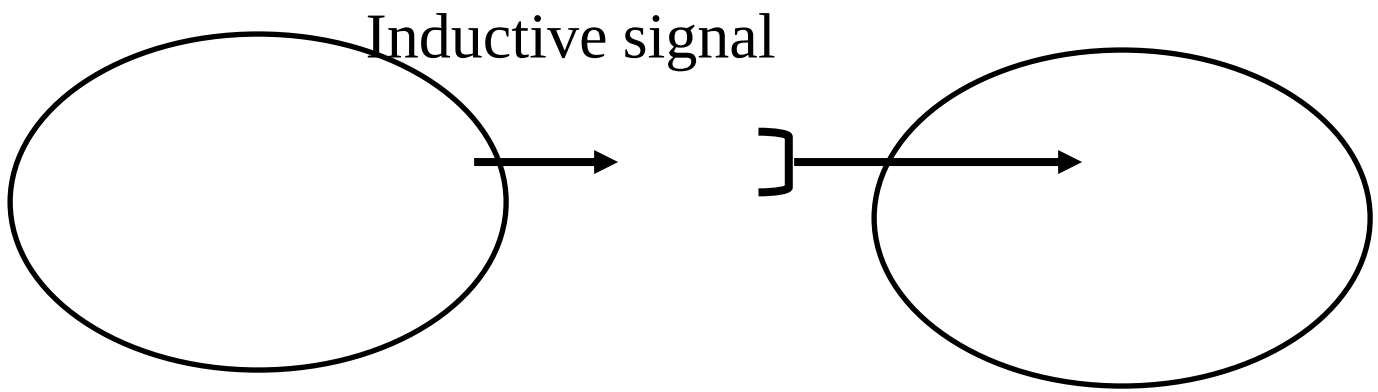

AER removed
Limb development ceases
Extra AER
Wing is duplicated
Forelimb mesoderm
AER
Leg mesoderm
Leg
Wing
Nonlimb mesoderm
AER regresses; limb development ceases
AER replaced by FGF bead
Normal wing

same responding tissue
difference in signal (diff molecules, concentration, etc.)

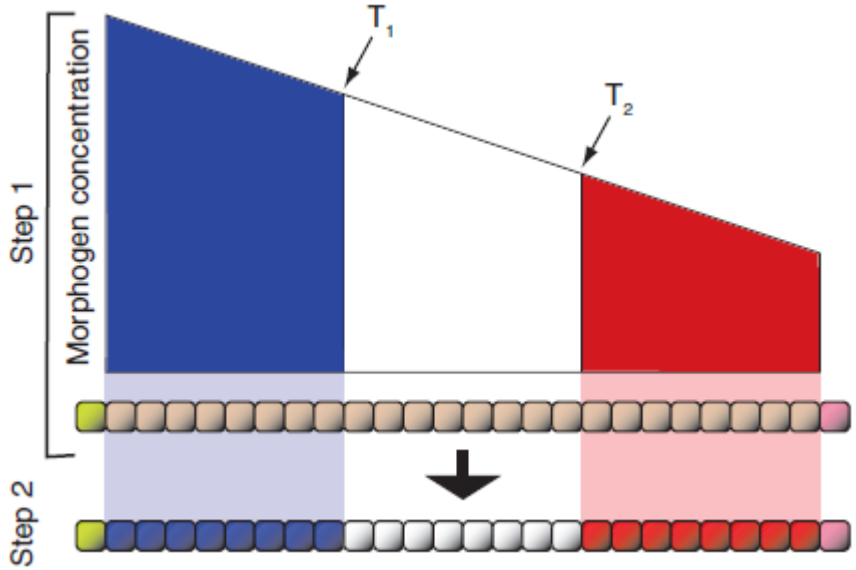


DEVELOPMENTAL BIOLOGY, Seventh Edition, Figure 6.7 Sinauer Associates, Inc.

Cell-cell communication



The French Flag Model (Lewis Wolpert, 1968)



Morphogen 的條件:

- Gradient distribution
- Dose-dependent activity
- Effect on morphogenesis

Provides spatial coordination

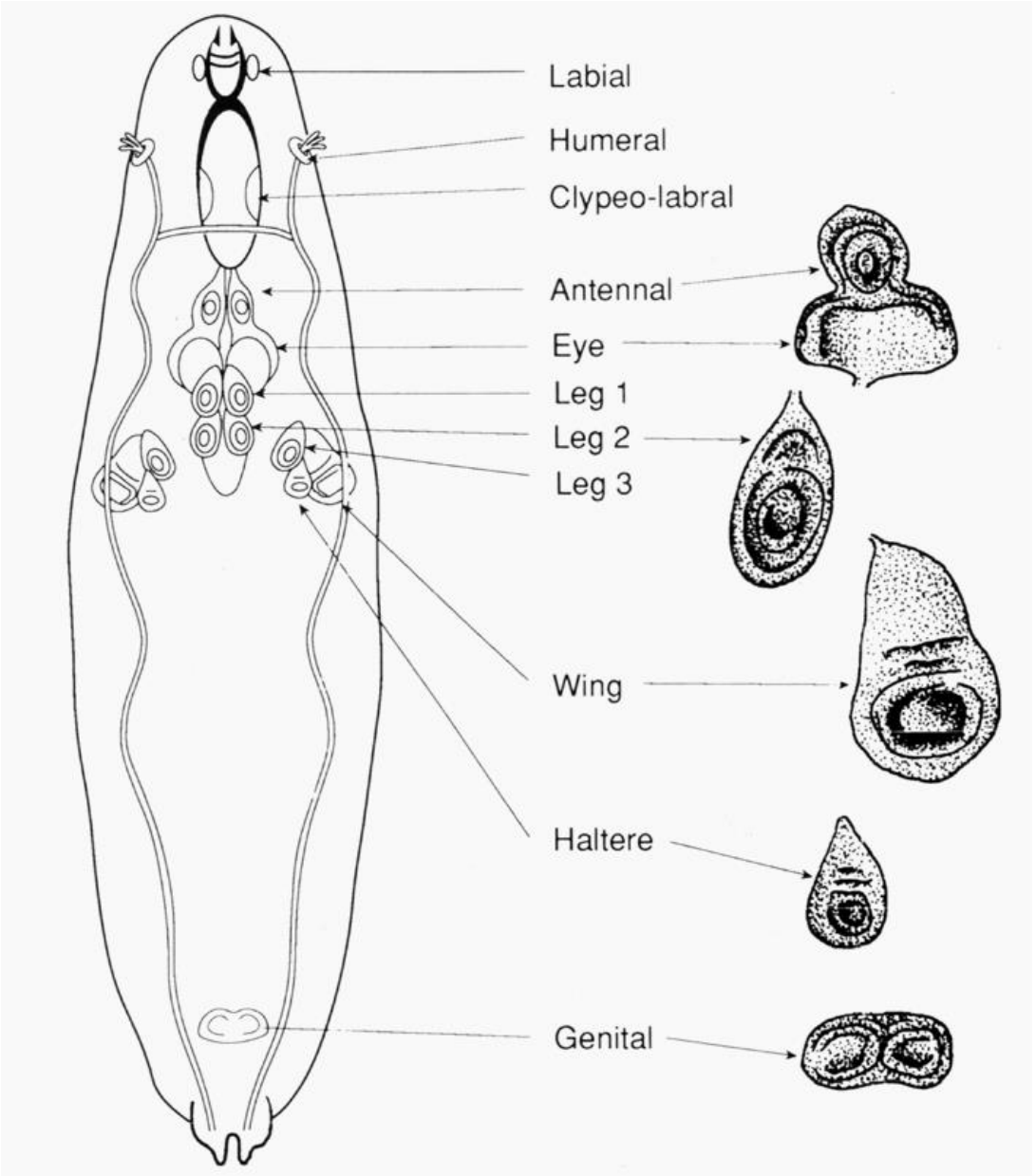
Simple model:

•Localized source of morphogen

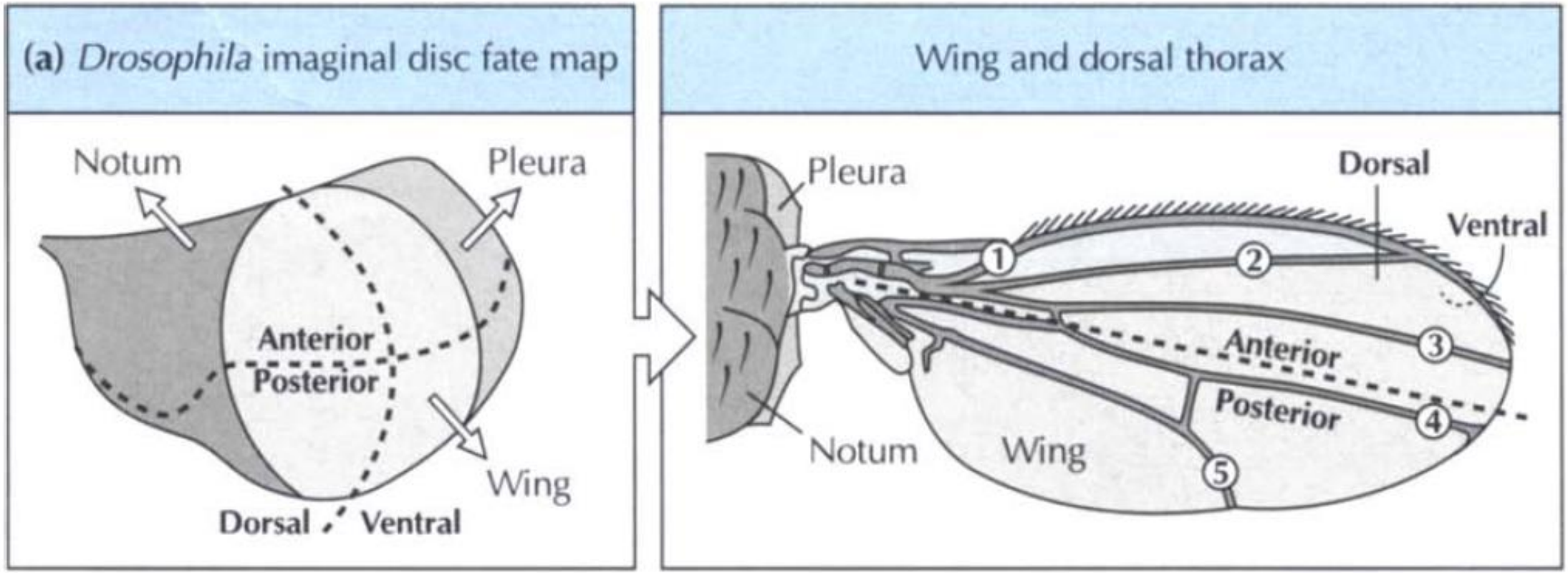
•Diffusion

•Generalized degradation

Imaginal discs in *Drosophila* larva

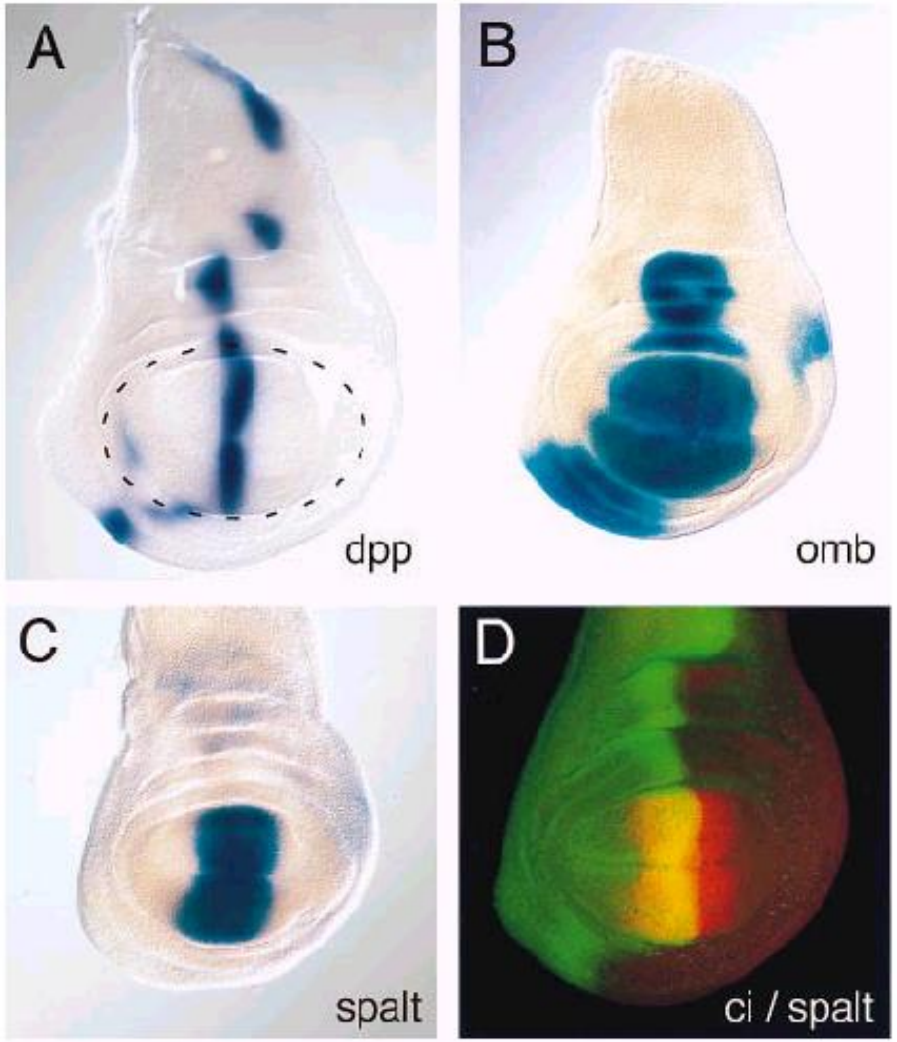


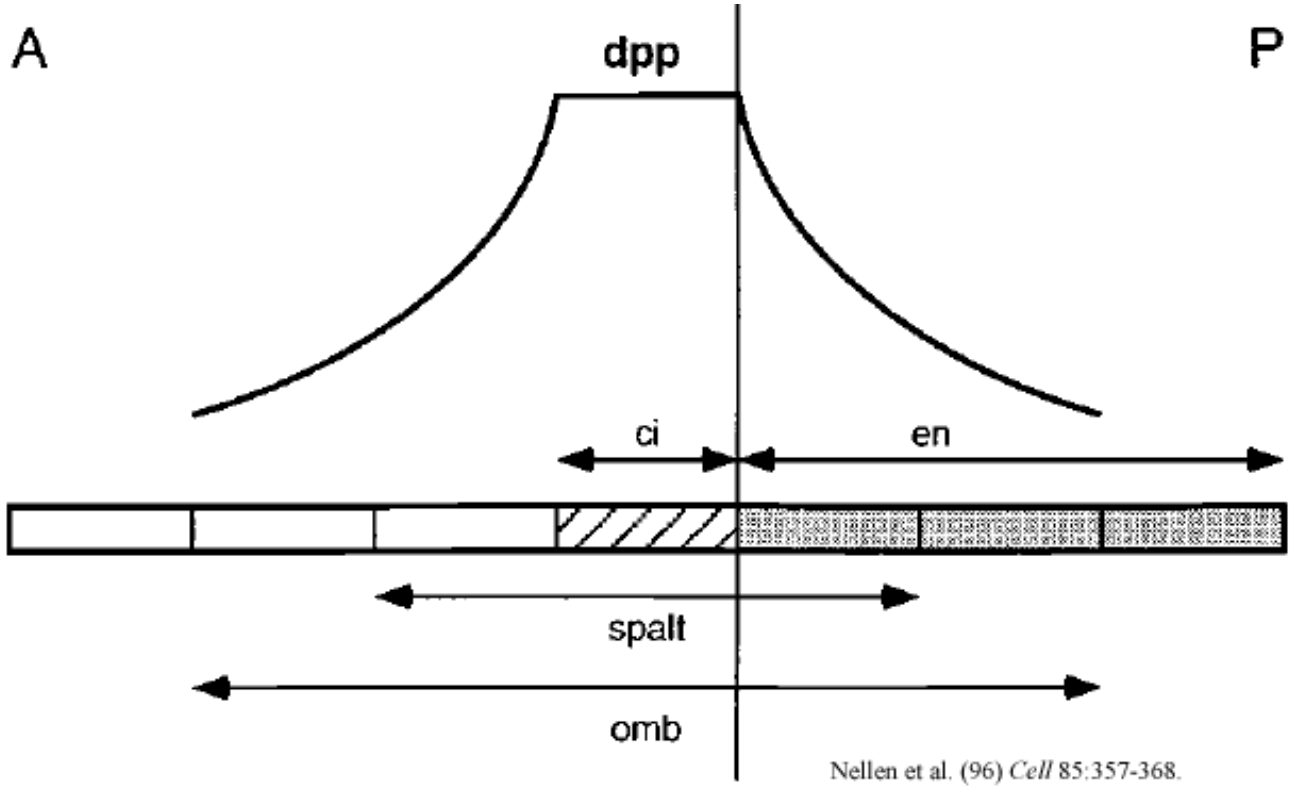
Wing disc



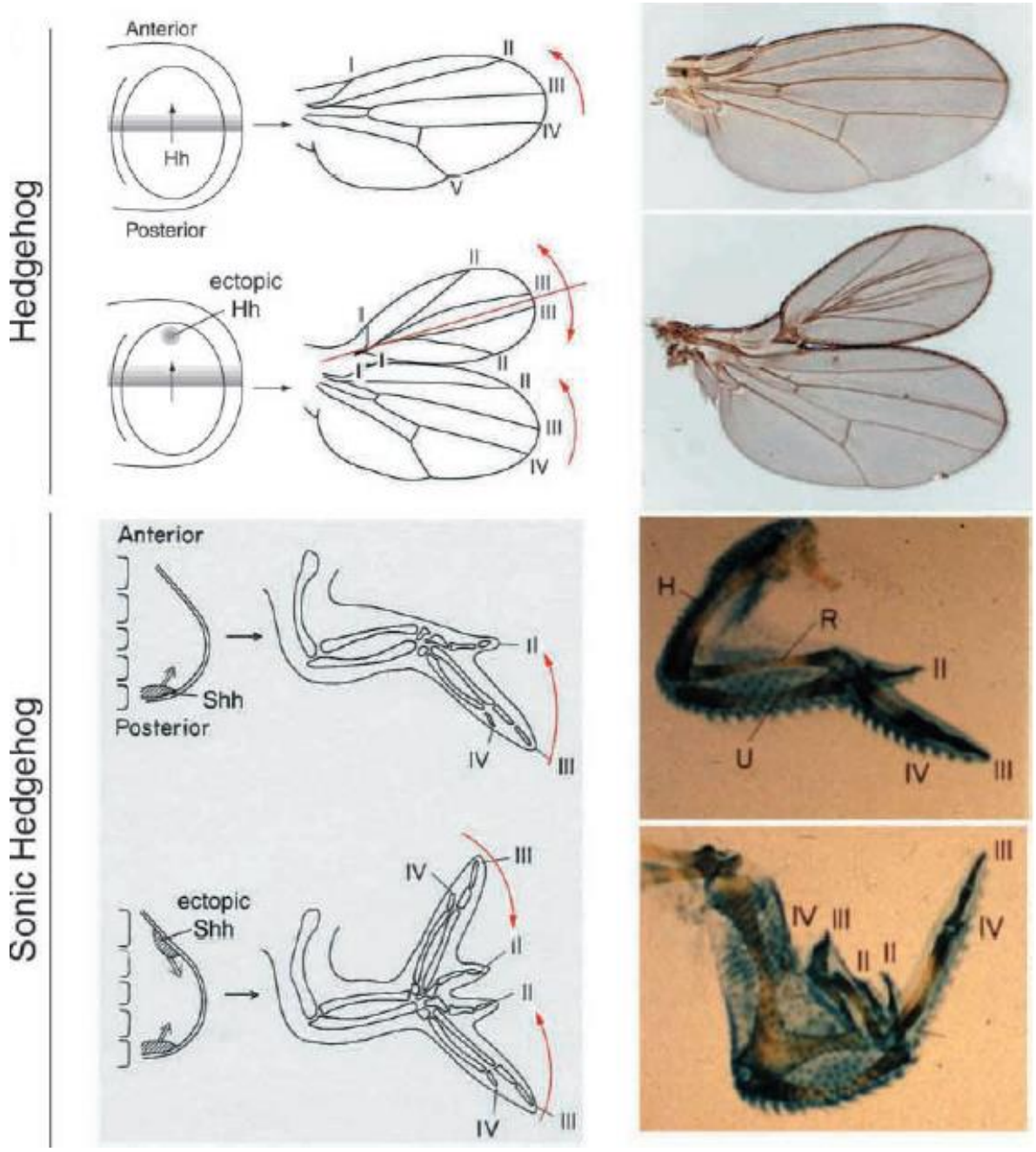
North and French (1994) Curr. Biology 4:611-614

DPP as a morphogen





Nellen et al (1996) Cell 85, 357–368



Tabata and Takei (2004) Development 131: 703-712

Polydactyly: extra digits

Six toes in prehistorical rock art

Infant with eight toes

Hemingway cat with six toes

Zeller et al (09) Nature Rev Genetics 10:845-858

絲羽烏骨雞 Silkie bantam

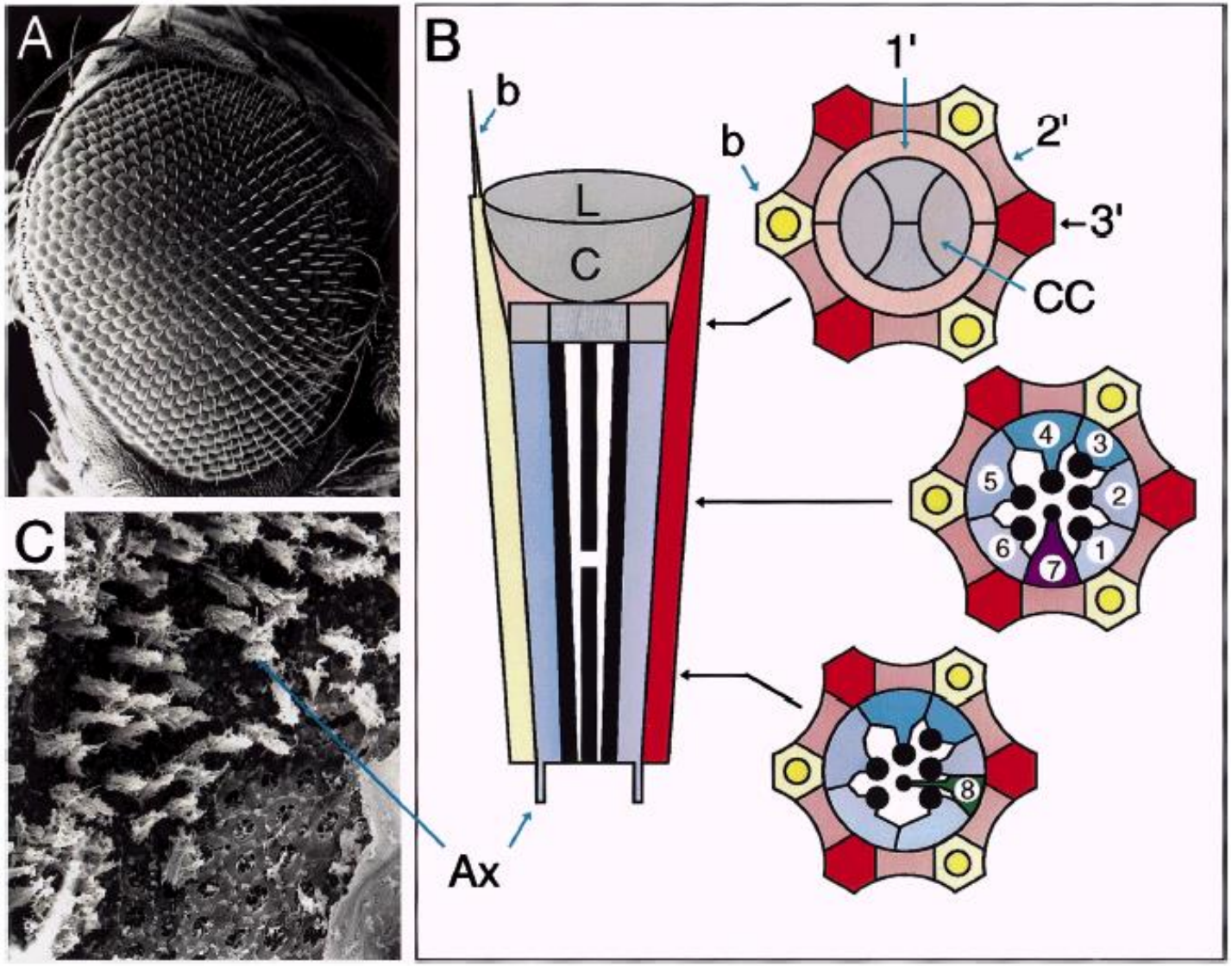
- 起源：江西省泰和縣
- 唐高宗
- 最早紀錄：Marco Polo

Shh ectopic expression (chick, human, mouse)

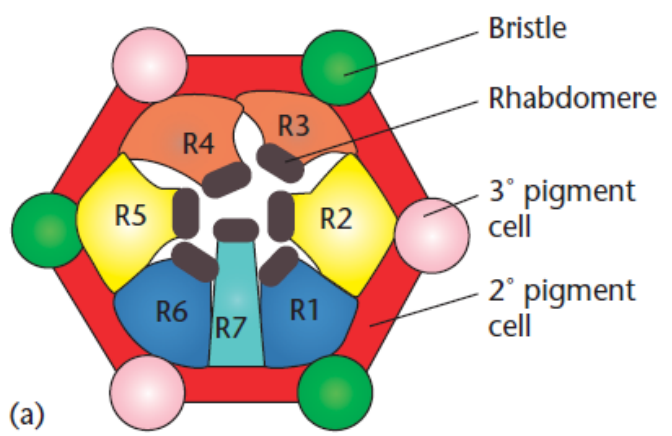
十全：紫冠、綠耳、白絲毛、藍縷子、鬍子、五爪、毛腳、烏皮、烏骨、烏肉

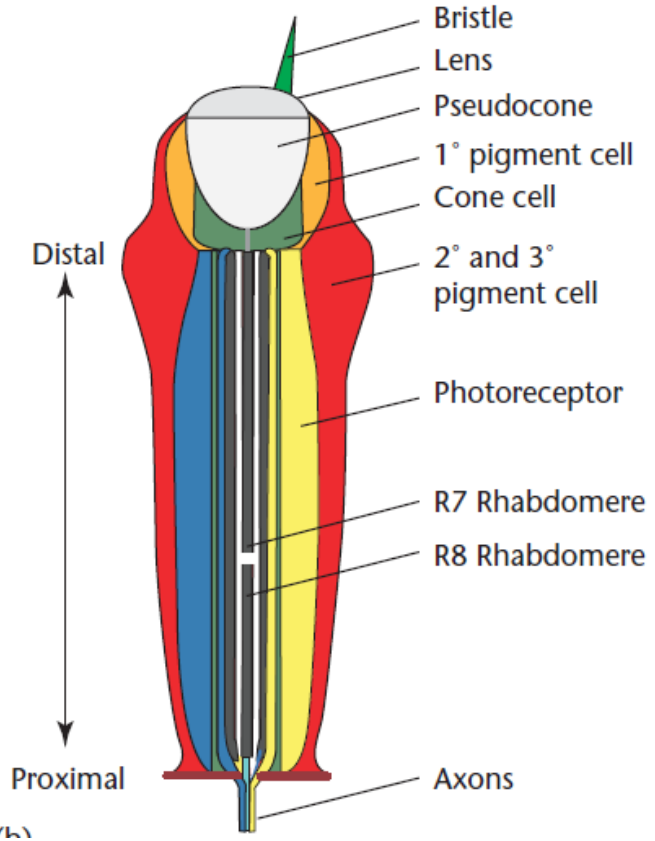
台灣畜產種原知識庫

Drosophila compound eye



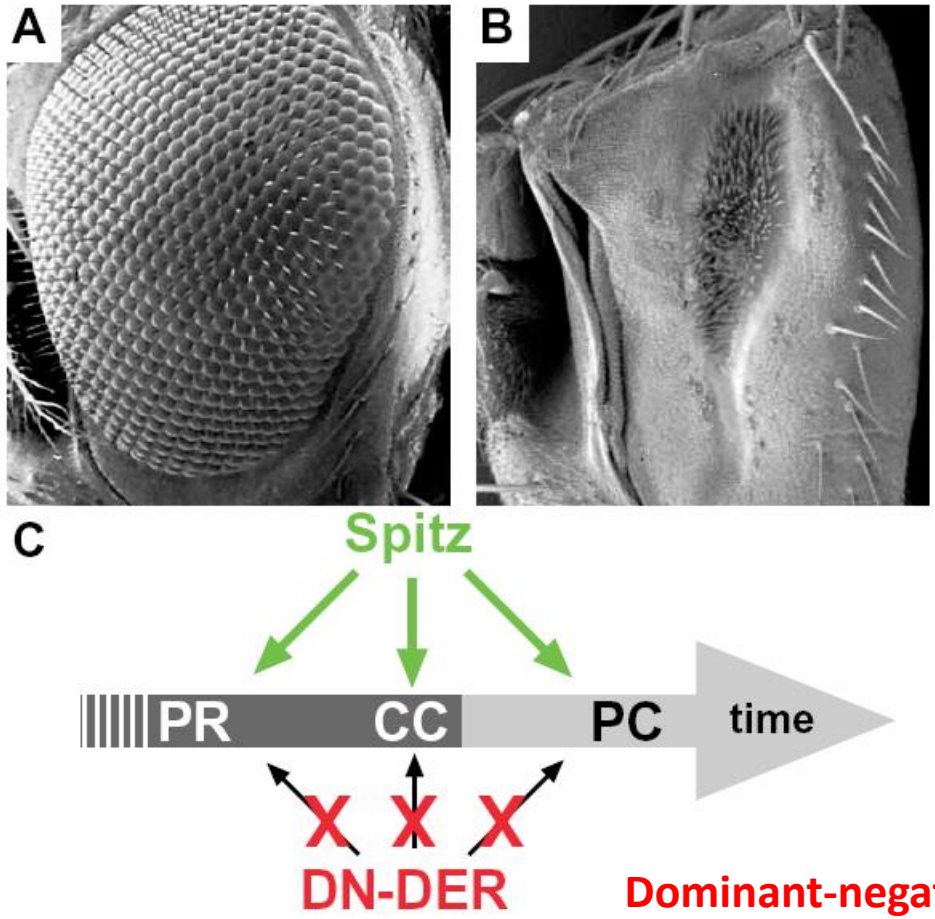
Brennan & Moses (00) *Cell. Mol. Life Sci*. 57:195-214.





Şahin and Çelik (2013) eLS. John Wiley & Sons, Ltd: Chichester.
DOI: 10.1002/9780470015902.a0001147.pub2

Drosophila EGF Receptor (DER) is involved in all retinal cell development



$GMR>DER^{DN}$

Dominant-negative (non-functional)

Spitz (EGF)

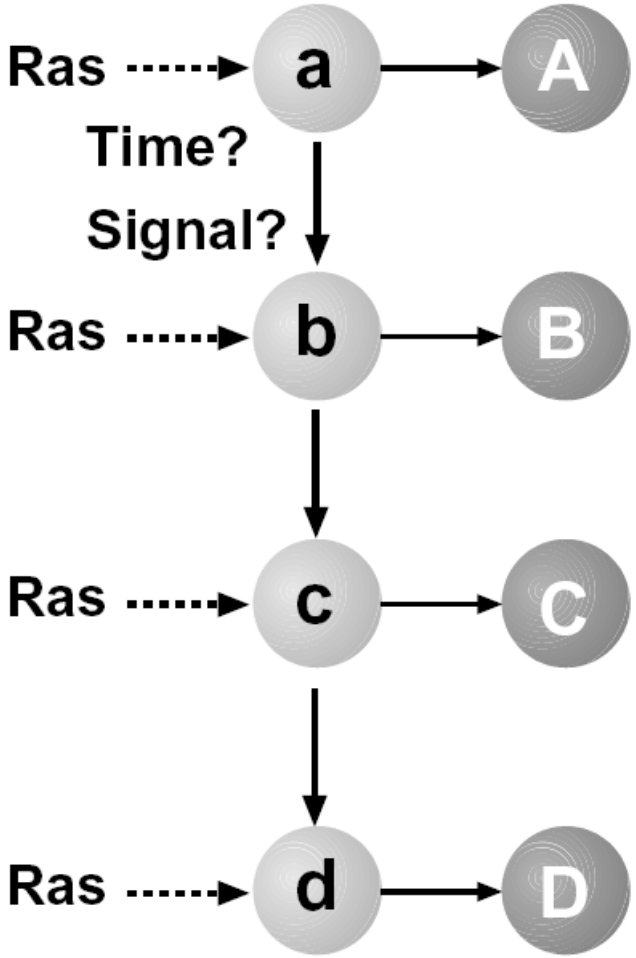
↓

DER (Drosophila EGF receptor)

photoreceptors, cone cells, pigment cells

Freeman (97) Development 124, 261-270

EGFR signaling may be a permissive signal



- EGFR (Receptor tyrosine kinase, RTK) signaling just turns ON (gives a green light) a nuclear factor already waiting.
- Which fate to adopt is predetermined by the cell's history (gene expression).

Signaling

Instructive vs. Permissive

Freeman (97) Development 124, 261-270