Model organisms and developmental biology

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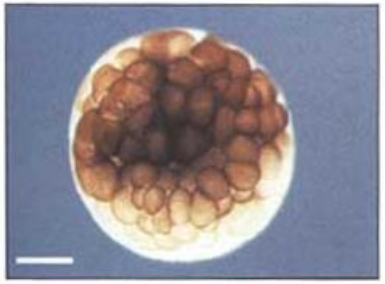
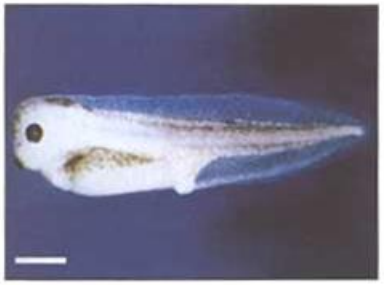
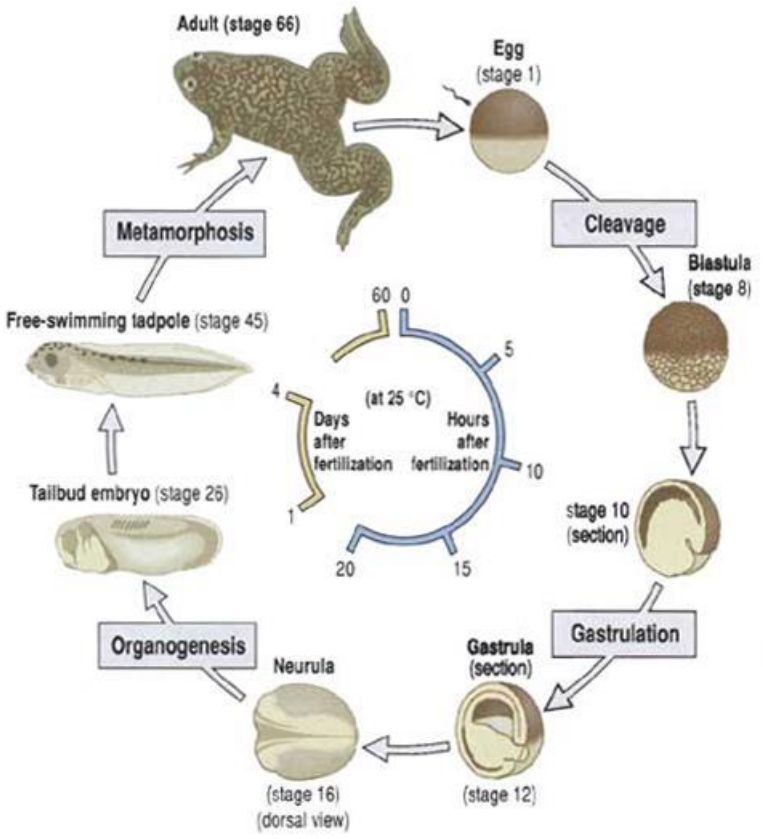
Xenopus laevis (African clawed frog)







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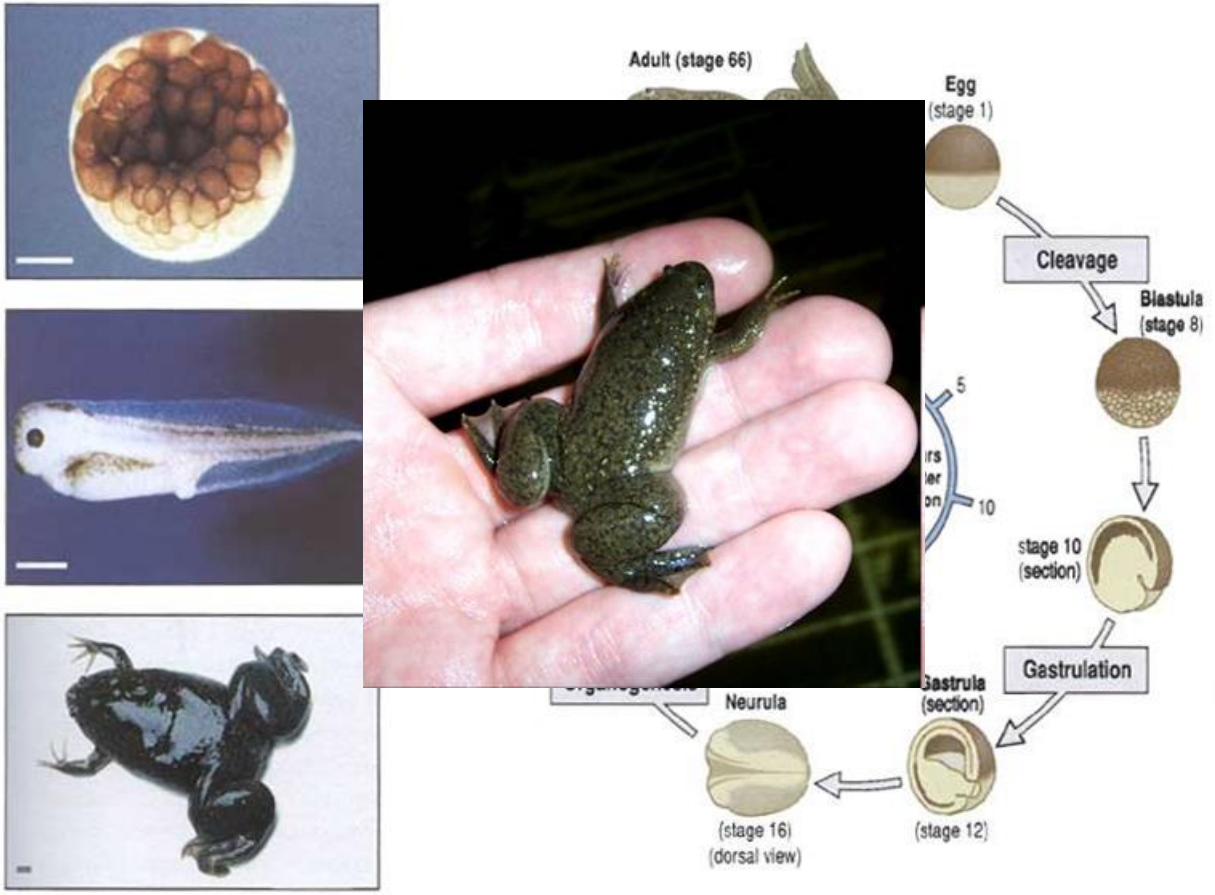


Advantage

- Easy to raise, tap water.
- Easy to obtain eggs and sperms, inject human hormone chorionic gonadotropin (绒毛膜促性腺激素).
- Large eggs, ~1.2 mm, easy to manipulate.
- Robust, highly resistant to infection after surgery.

Cloned frogs

These 19 identical male albino frogs were prepared by nuclear transplantation into unfertilized eggs of the dark green female frog.

Gurdon and Colman, *Nature*, 1999

The Nobel Prize in Physiology or Medicine 2012

Photo: U. Montan
Sir John B. Gurdon

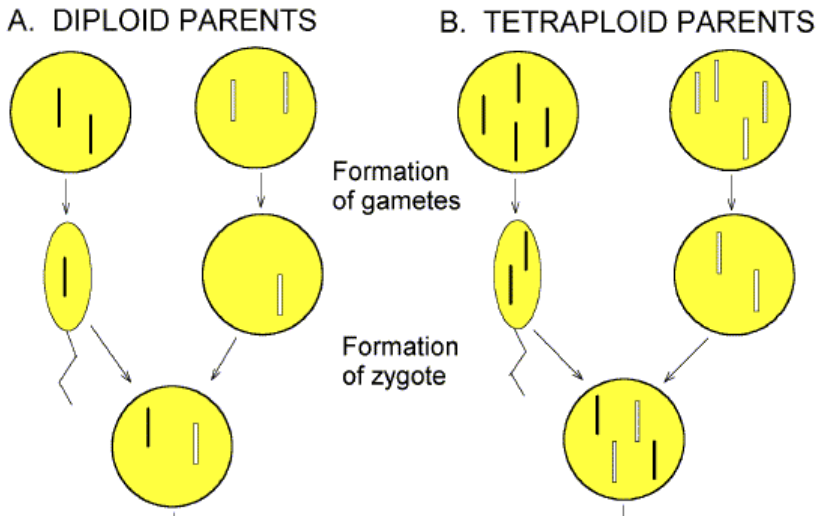
Photo: U. Montan
Shinya Yamanaka

The Nobel Prize in Physiology or Medicine 2012 was awarded jointly to Sir John B. Gurdon and Shinya Yamanaka ***"for the discovery that mature cells can be reprogrammed to become pluripotent"***

Photos: Copyright © The Nobel Foundation

Disadvantage

- Long life cycle, 1 to 2 years to reach sexual maturity
- Tetraploid, hard to do genetics



How did *Xenopus laevis* become a model organism

- Roux and other experimental embryologists used European local frog, initially the frog *Rana*.
- *Xenopus laevis* was first described by a French naturalist François Marie Daudin in 1802.
- During the early twentieth century, *Xenopus* continued to be imported occasionally for research, and increasingly also for hobby aquaria in Europe.
- Lancelot Hogben showed in principle that *Xenopus* might be used as an indicator of the presence of gonadotrophins in the urine of pregnant women.

- The first reliable laboratory pregnancy test had just been invented in Berlin in 1928 by the gynaecologist Bernhard Zondek and the chemist Selman Aschheim and was then very widely discussed. It involved injecting five immature female mice twice a day for three days with morning urine, and then killing them to see if the ovaries were enlarged and congested.

A Rapid Test for Pregnancy on *Xenopus lævis*

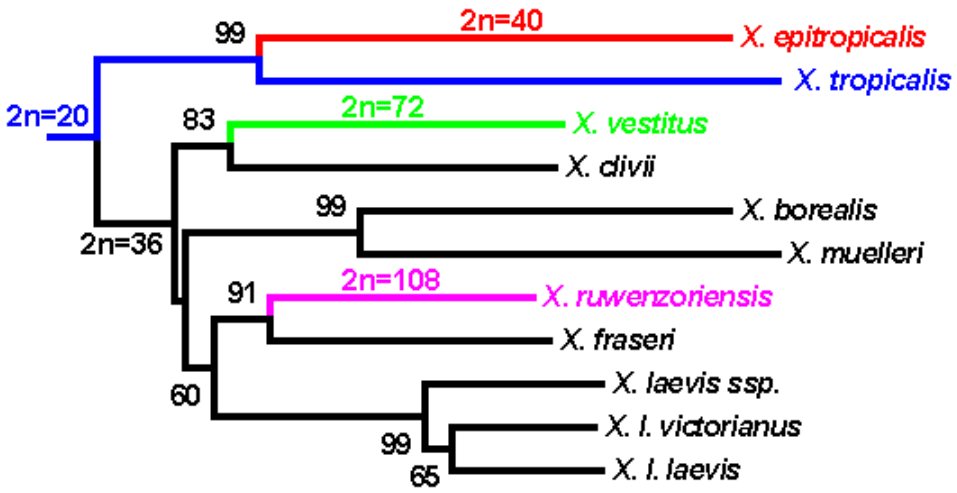
In a recent communication Bellerby (1933)[1] has shown that injection of acid or alkaline extracts of bovine anterior lobe of the pituitary gland into female South African clawed toads (*Xenopus lævis*) produces extrusion of ova through the cloaca within 18 hours.

Shapiro and Zwarenstein , 1934, Nature

- The Utrecht zoologist Pieter D. Nieuwkoop played a key role in making *Xenopus* an effective tool in embryology.

- Its dominance over other amphibia was ensured by scientists with primarily biochemical, cellular, and/or genetic interests who in the 1960s were increasingly entering the field.

X. tropicalis, a cousin of *X. laevis*



X. tropicalis, 2n=20; *X. laevis*, 4n=36

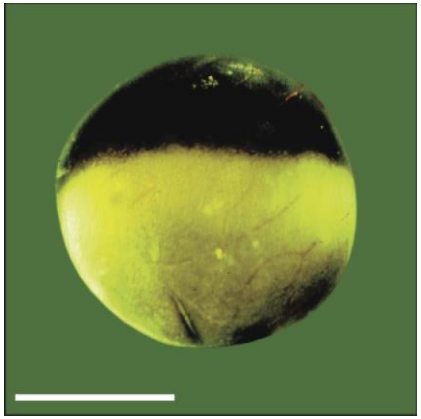
X. tropicalis, a cousin of *X. laevis*

X. tropicalis, 2n=20; *X. laevis*, 4n=36

X. laevis early embryogenesis

Fertilization — Cleavage — Blastula — Gastrula — Neurula
受精 卵裂 囊胚 原肠胚 神经胚

Gastrulation

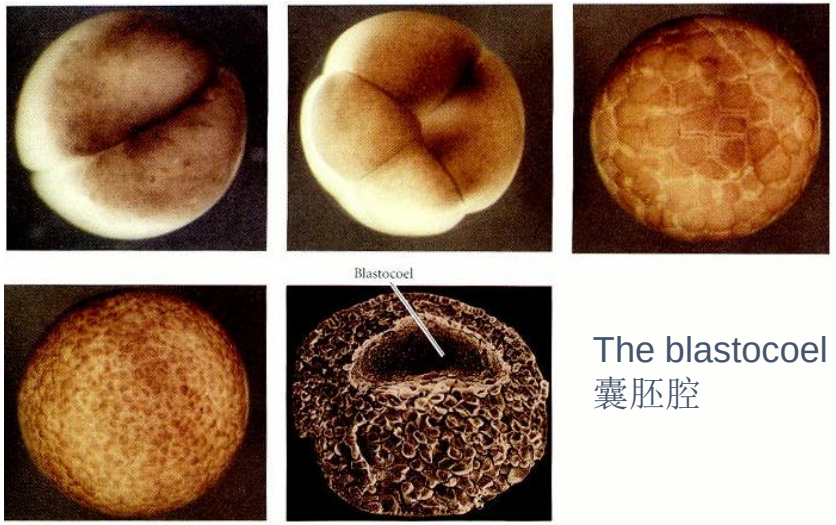


Cleavage and blastula

Cleavage is a special mitosis, in which cells do not grow between each division, so producing small daughter cells.

Dark, animal pole

Pale, vegetal pole



The blastocoel
囊胚腔

A blastula contains about 4k cells (12-round division).

Gastrulation

Gastrulation is the process in which blastula cells move to form three germ layers: ectoderm, mesoderm, and endoderm.

- Ectoderm: brain, spinal cord, skin
- Mesoderm: heart, blood vessel, bone, muscle
- Endoderm: gut, liver, pancreas, lung

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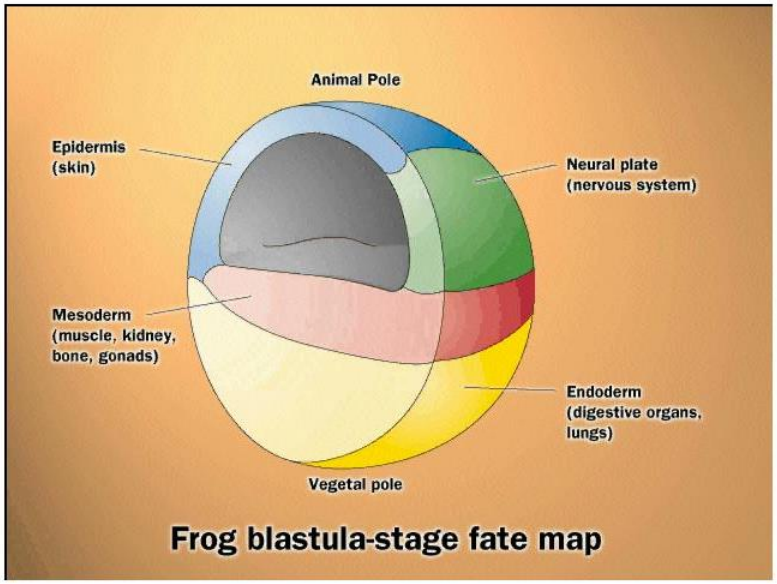
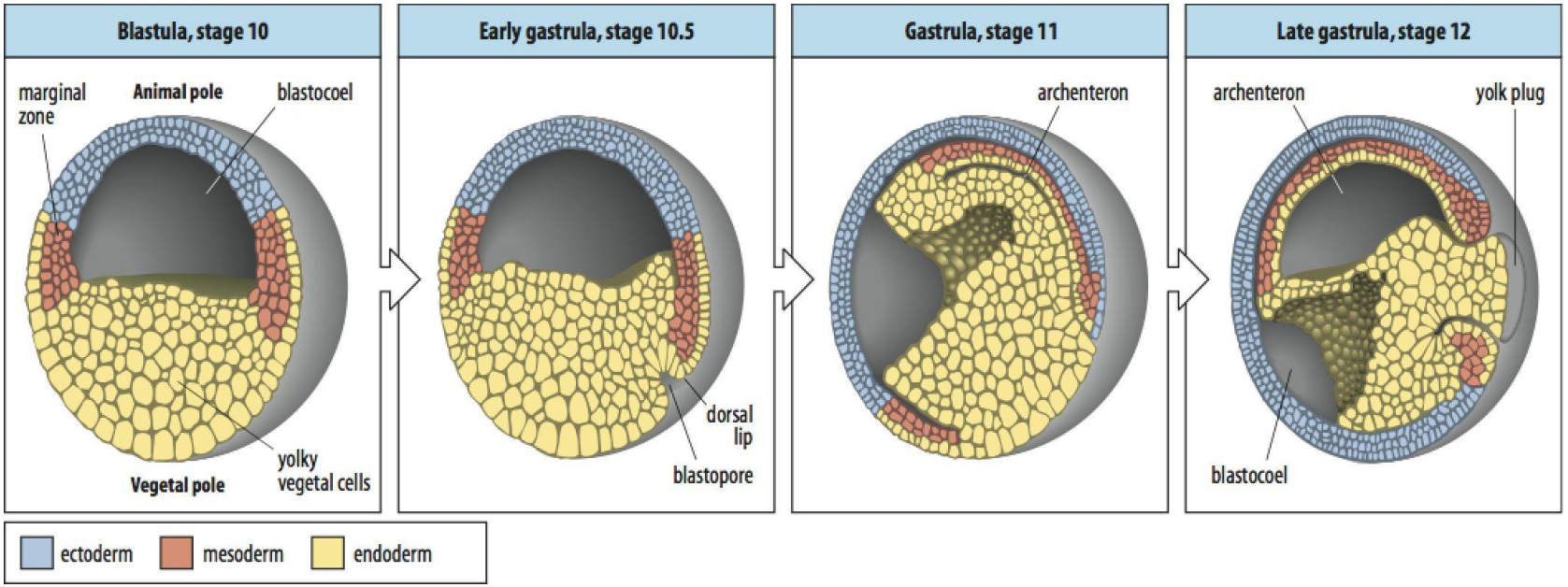
"It is not birth, marriage, or death, but **gastrulation**, which is truly the most important time in your life." Lewis Wolpert (1986)

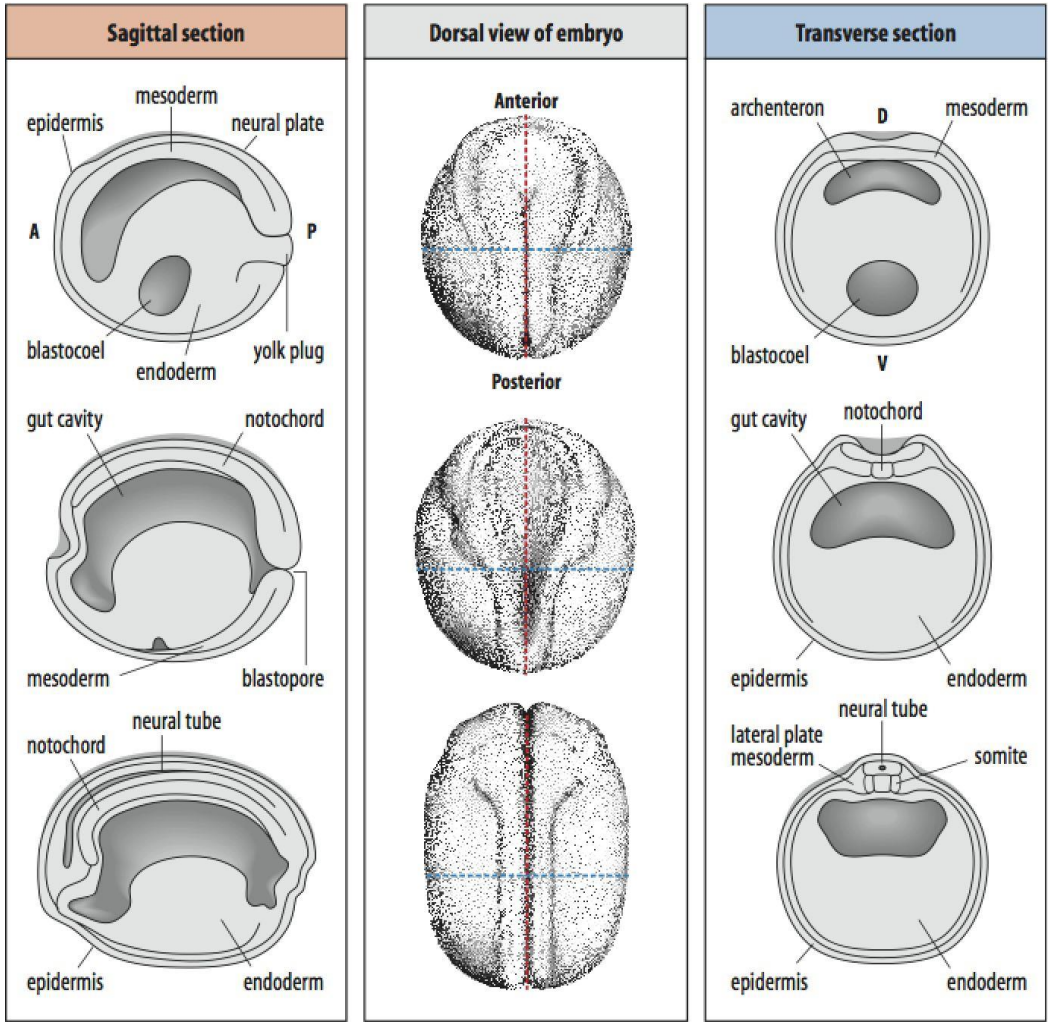
Gastrulation of *X. laevis*



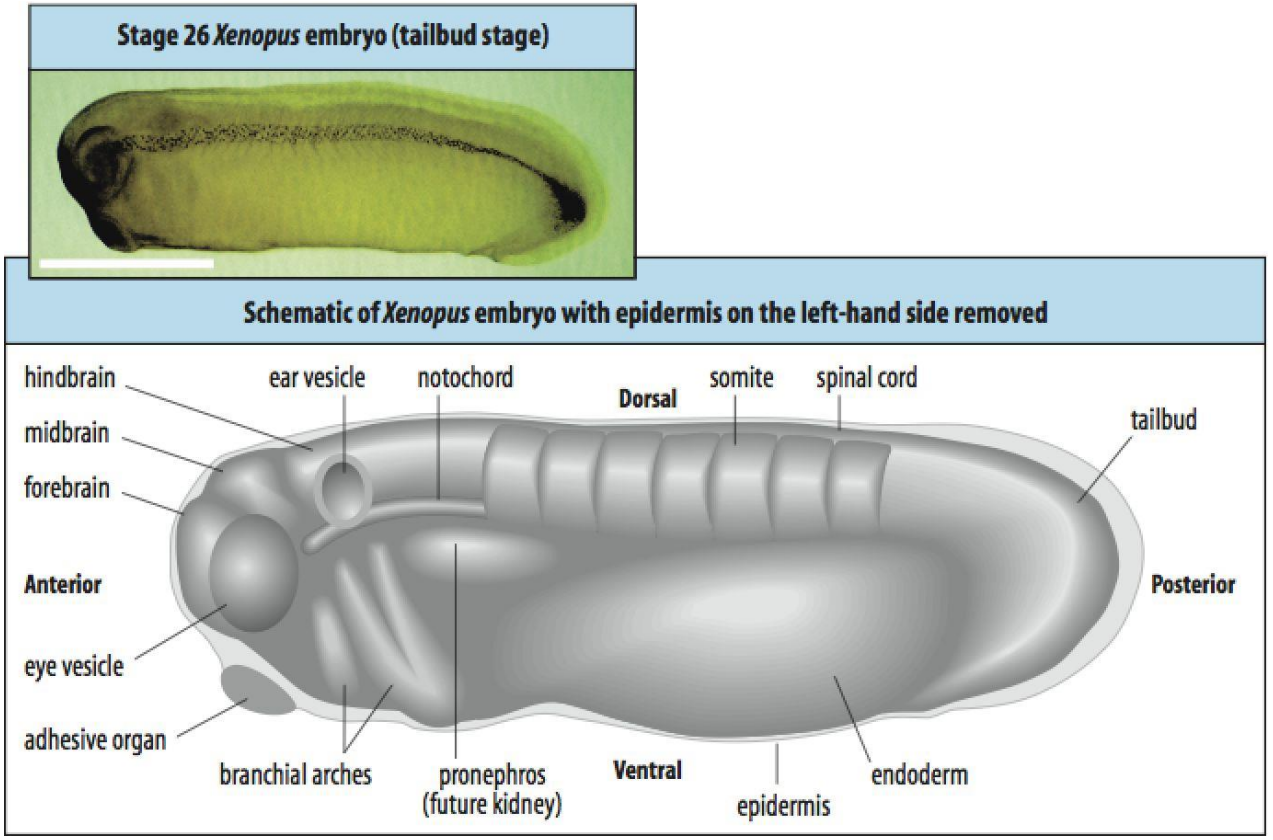
Gastrulation of *X. laevis*



Neurulation



The early tailbud stage of a Xenopus embryo

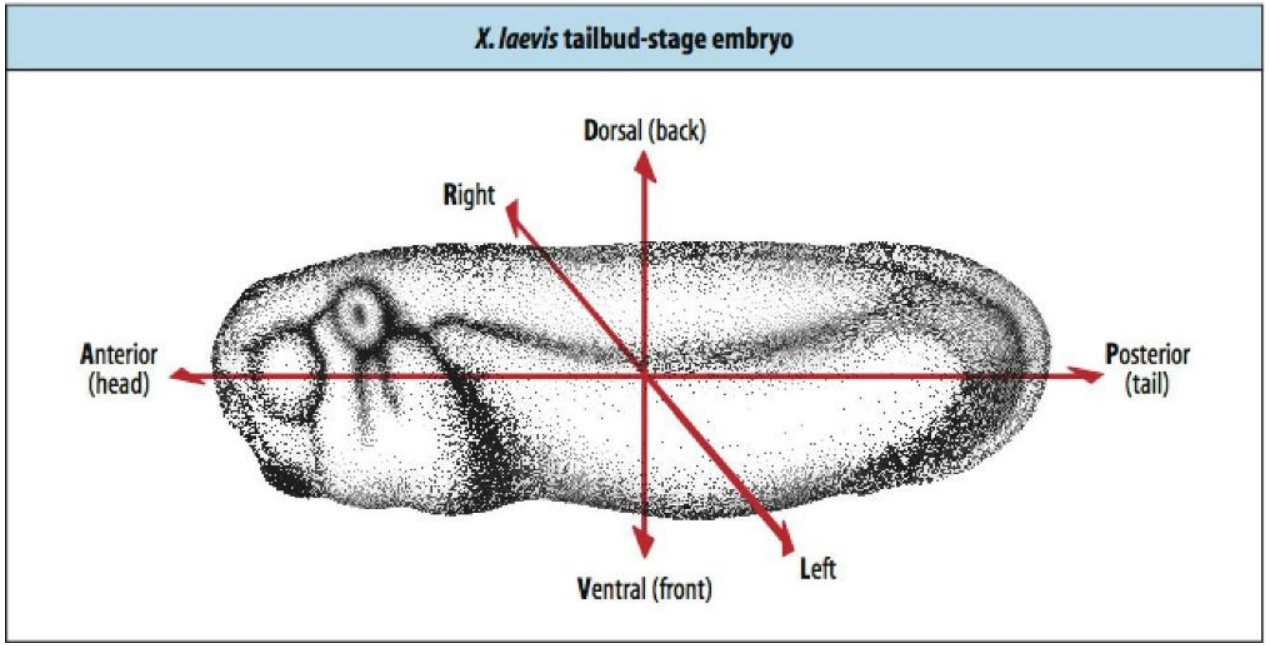


A conceptual tool kit

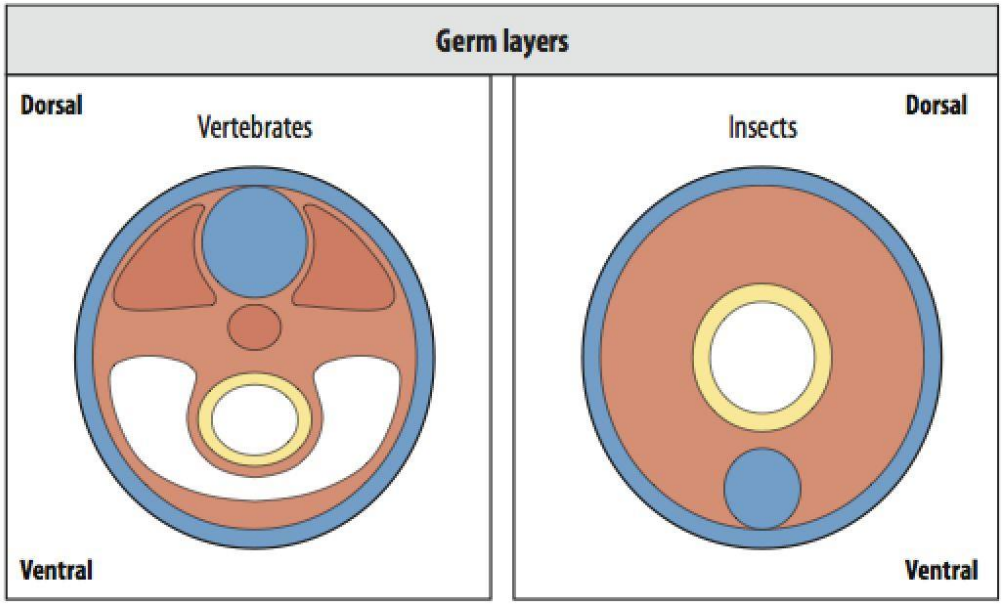
- Development involves pattern formation, morphogenesis, cell differentiation, and growth.
- Pattern formation – large range, eg. three germ layers.
- Morphogenesis – organ or tissue, some kind of recognizable structure.
- Cell differentiation – change on cell level.
- Growth – increase in size and volume.
- These processes are intertwined with each other.

Pattern formation - Organization in time and space in large range

- Body plan, establishment of axes (antero-posterior, dorso-ventral, left-right), and germ layers.



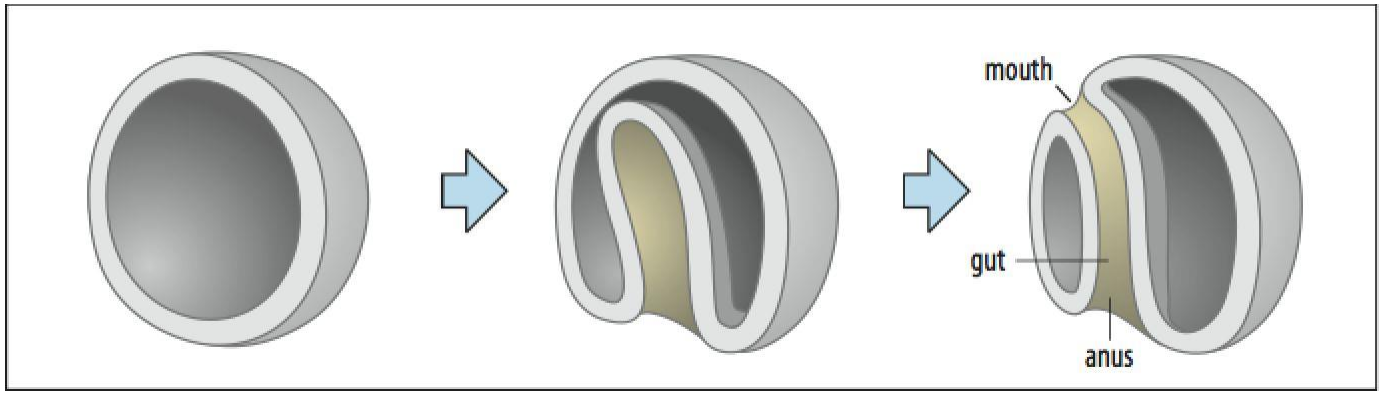
Formation of three germ layers - the earliest differentiation



Germ layers	Organs	
Endoderm	gut, liver, lungs	gut
Mesoderm	skeleton, muscle, kidney, heart, blood	muscle, heart, blood
Ectoderm	skin, nervous system	cuticle, nervous system

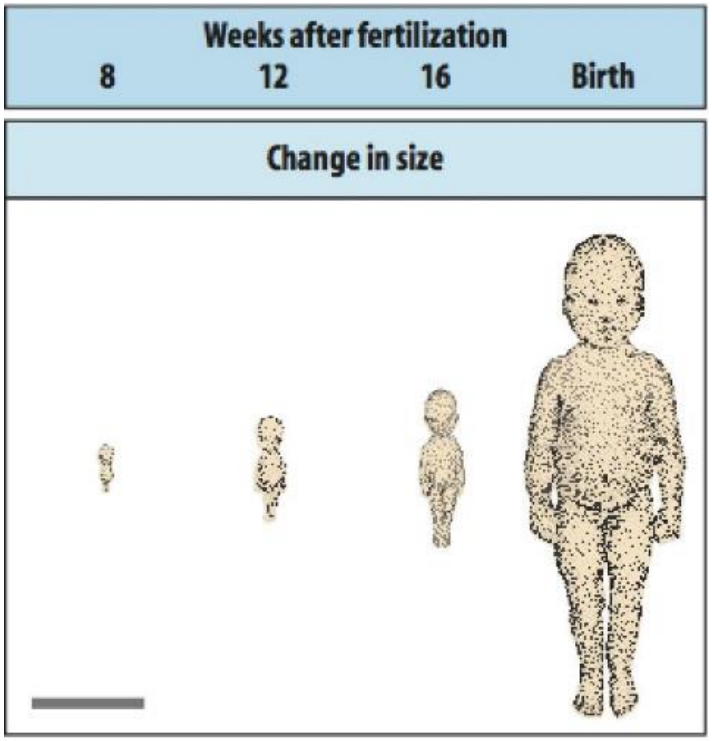
Morphogenesis – change in form

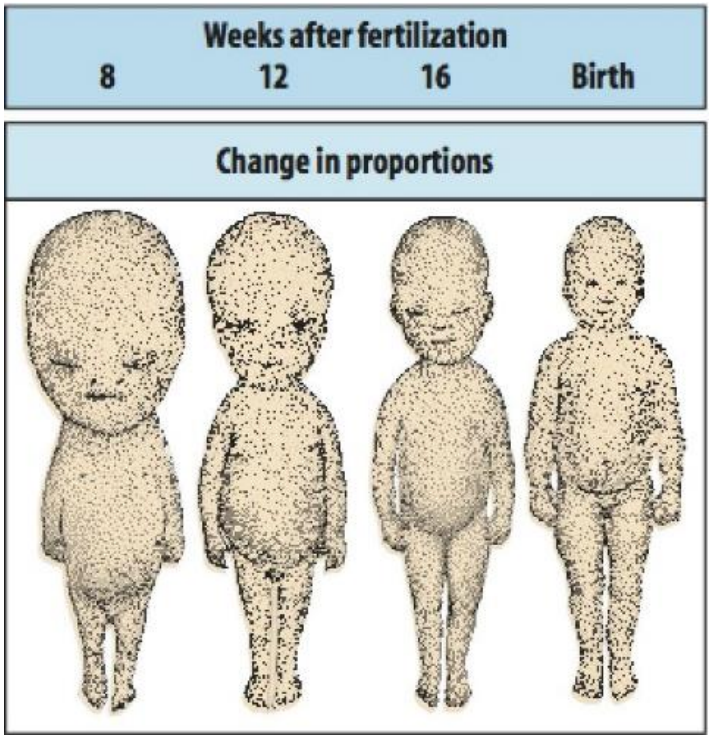
Gastrulation in the sea urchin



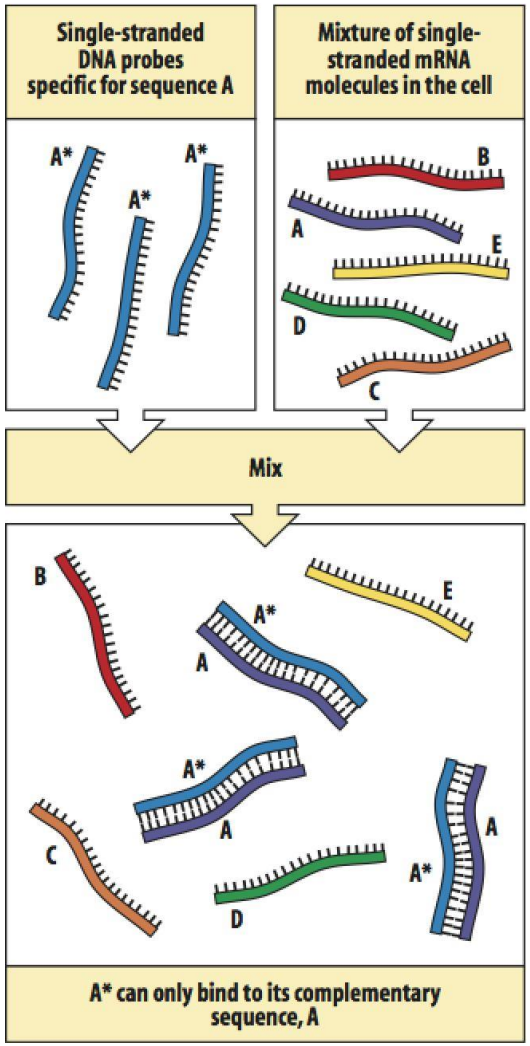
By gastrulation, the three germ layers are formed.

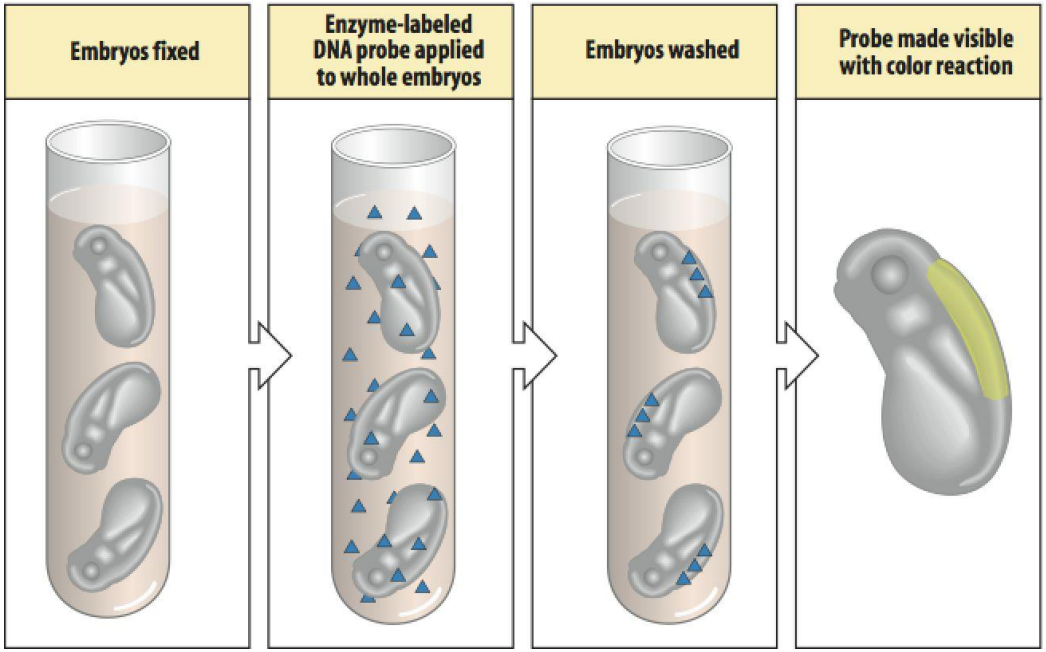
Growth happens in later stage



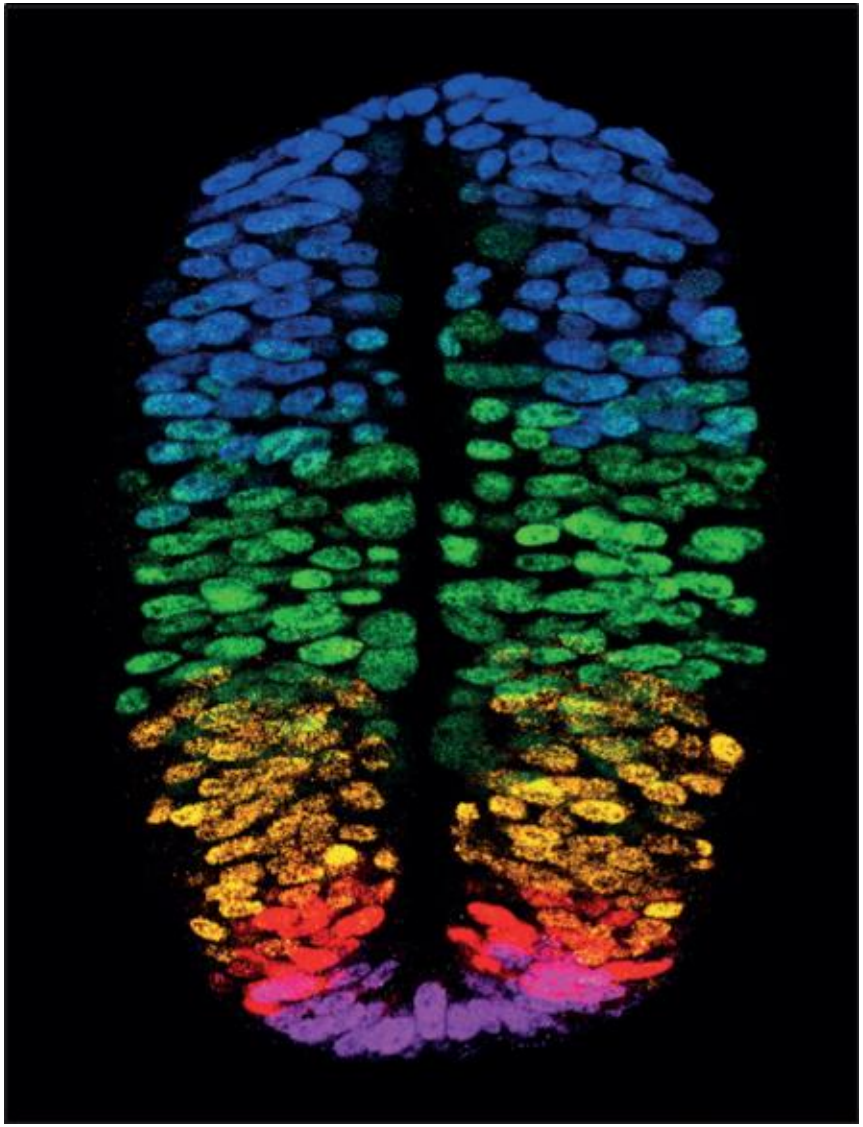


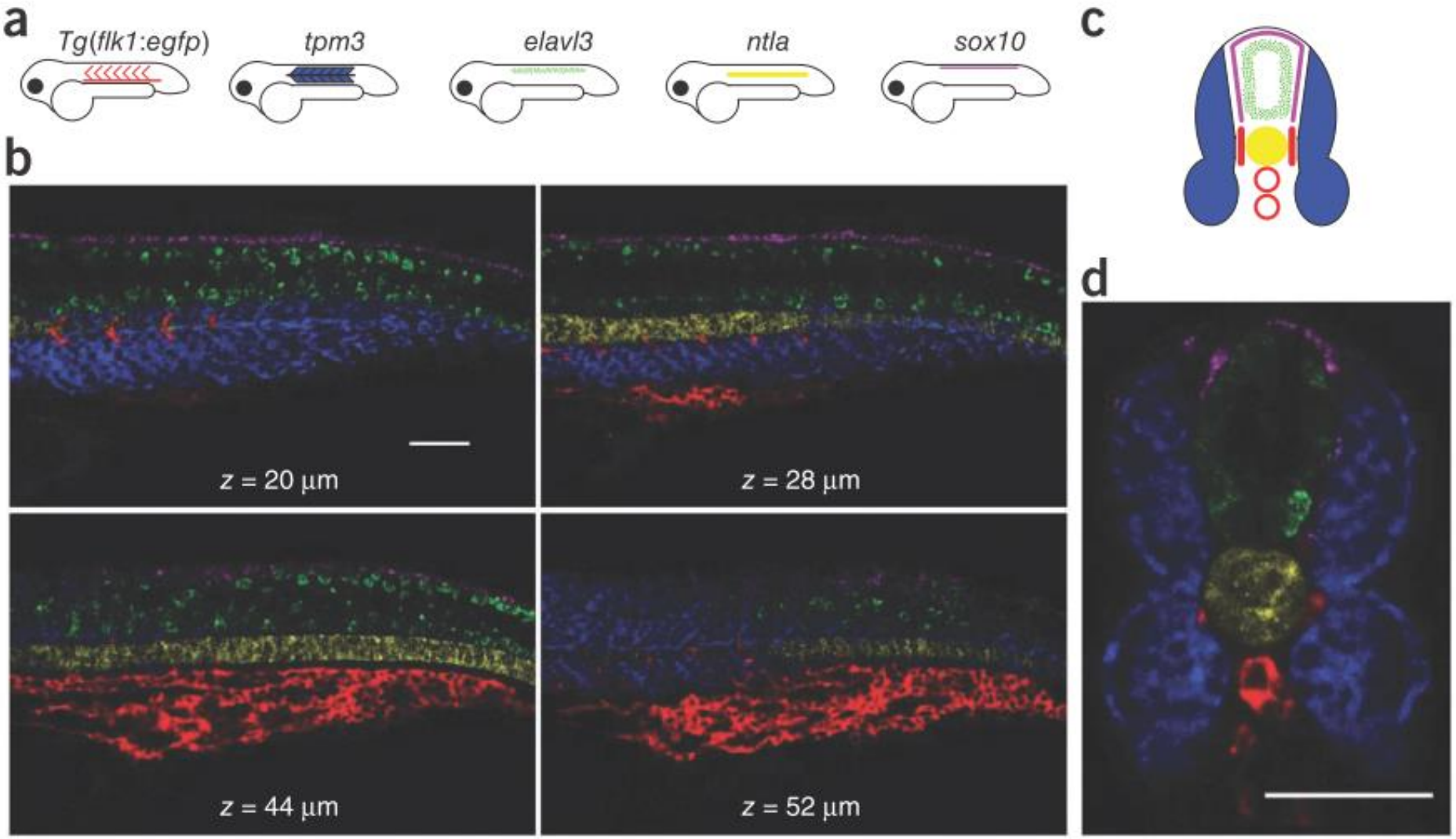
Gene expression is tightly regulated in time and space

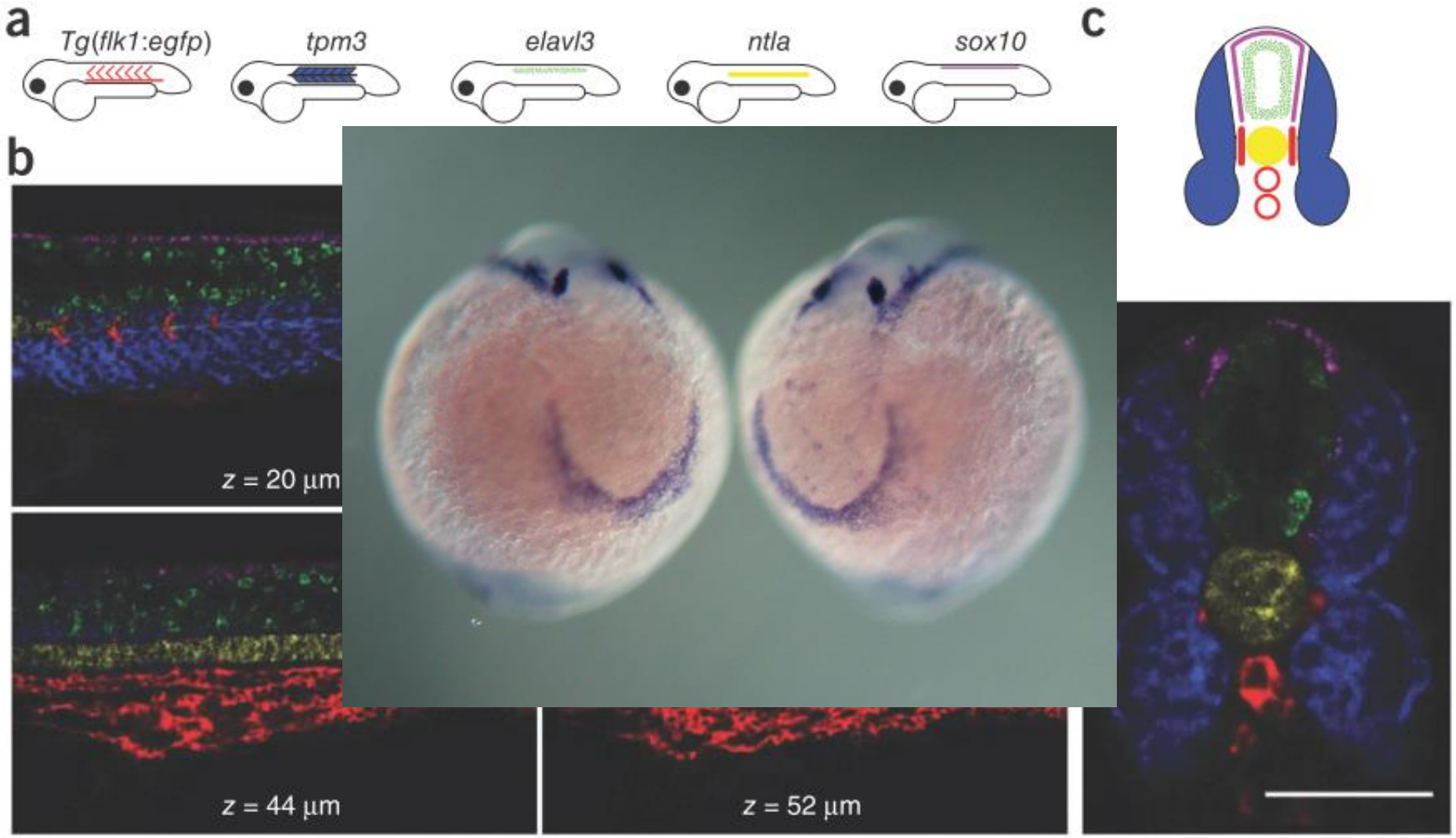




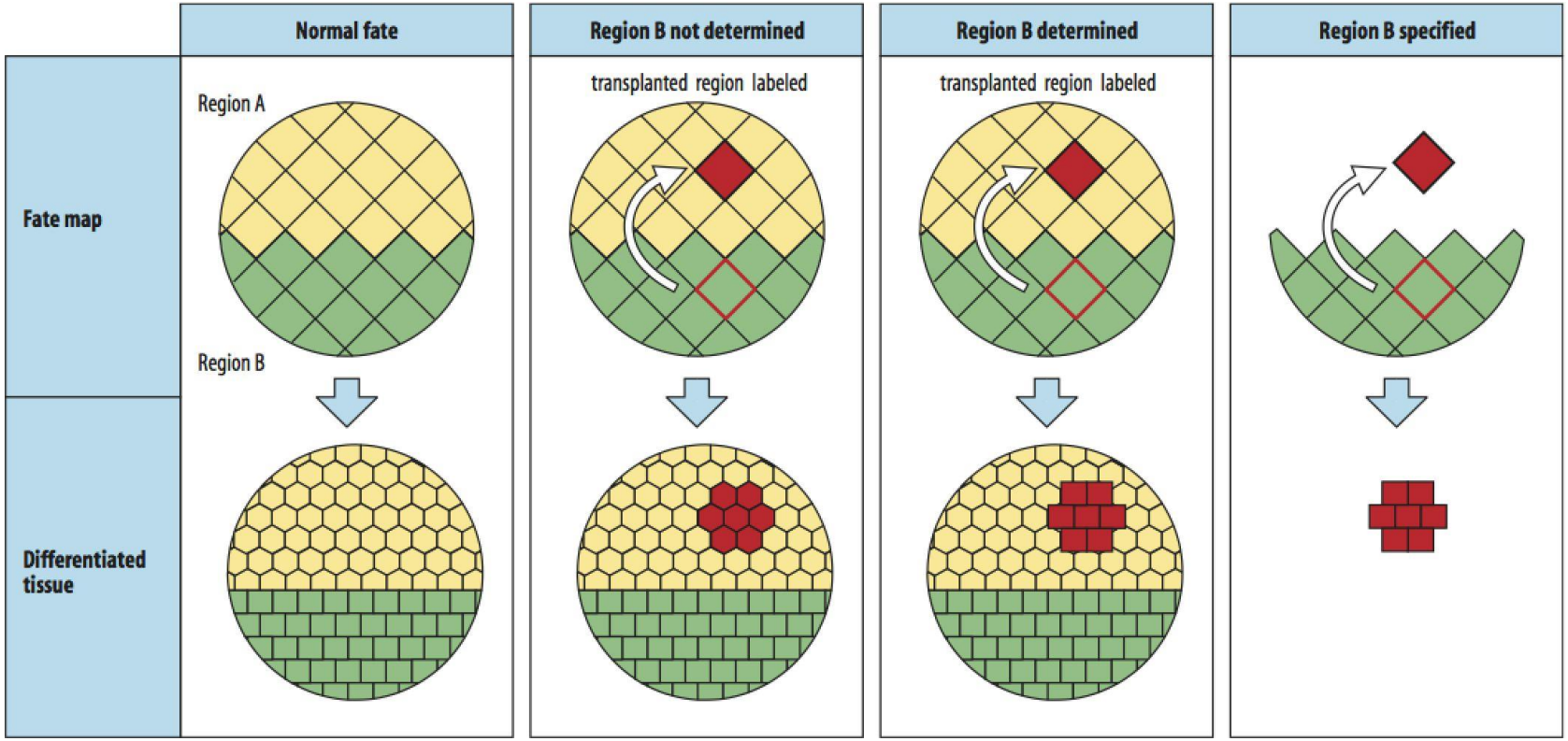
In situ hybridization



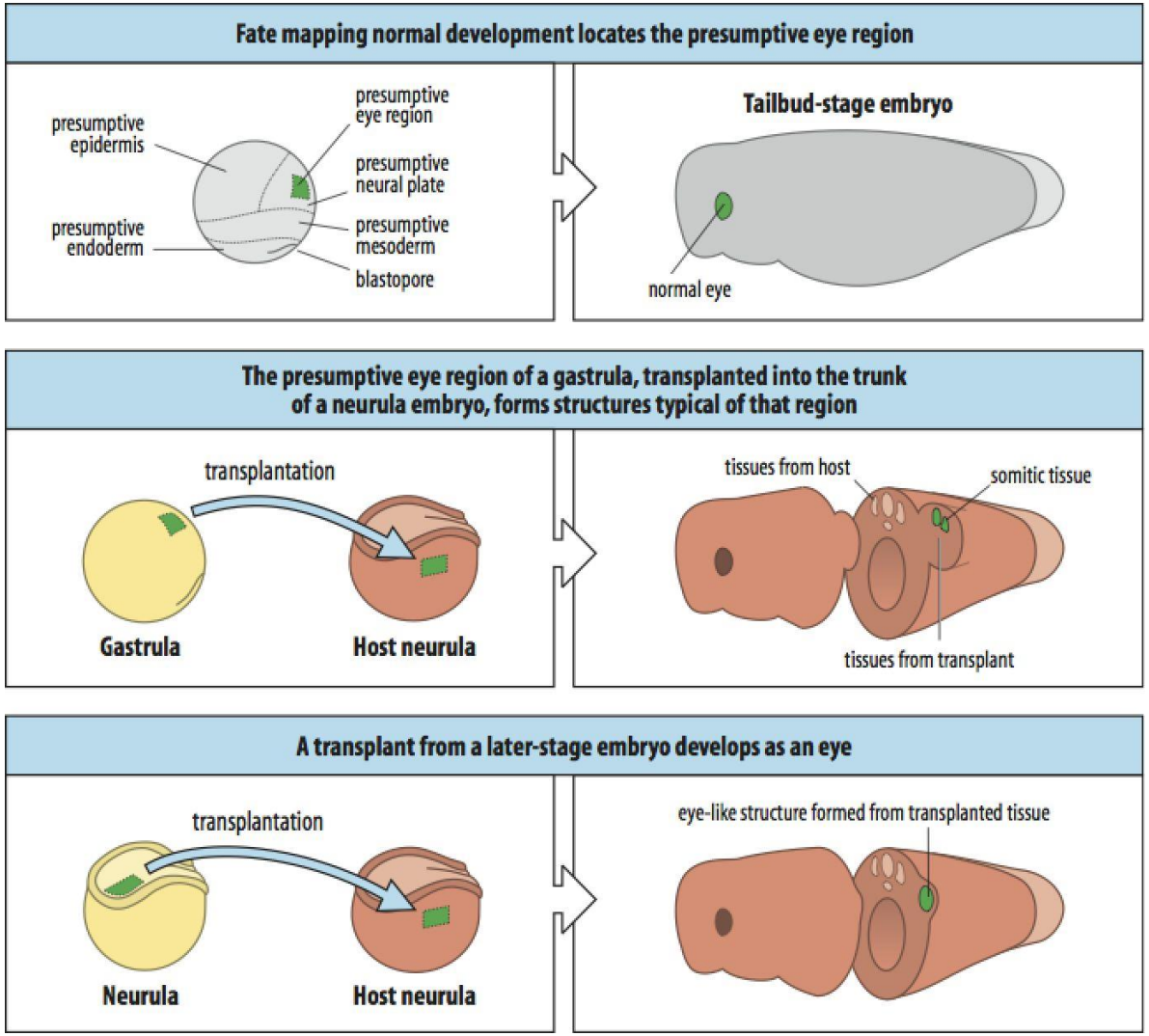

a
Tg(flk1:egfp)
tpm3
elavl3
ntla
sox10
b
z = 20 µm
z = 28 µm
z = 44 µm
z = 52 µm
c
d


a
Tg(flk1:egfp)
tpm3
elavl3
ntla
sox10
b
z = 20 µm
z = 44 µm
z = 52 µm
c

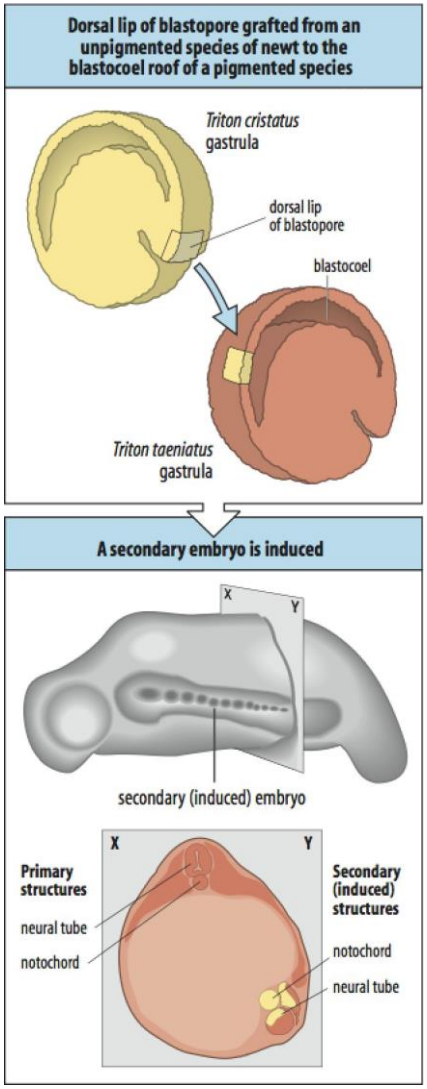
Cell fate, determined and specified

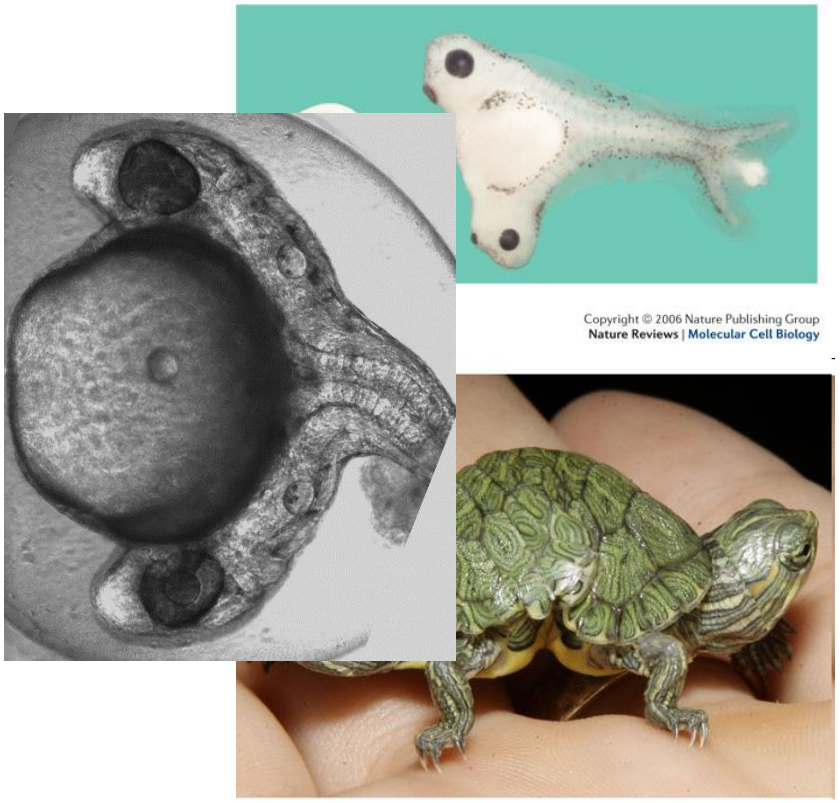


Transplantation is used to demonstrate the state of determination

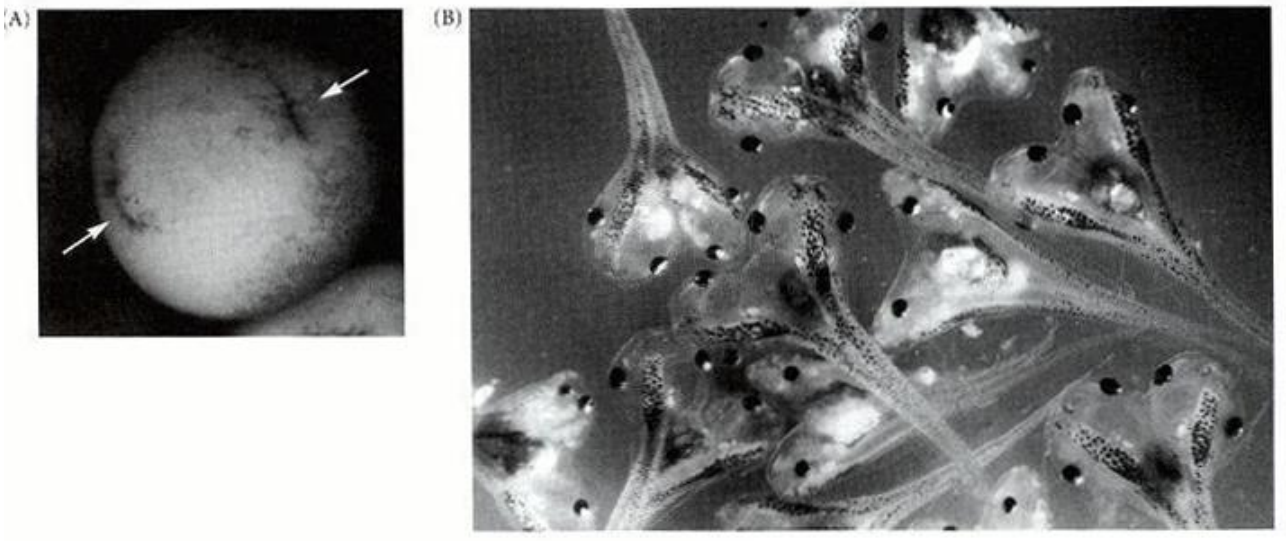


Dorsal lip, an example of induction

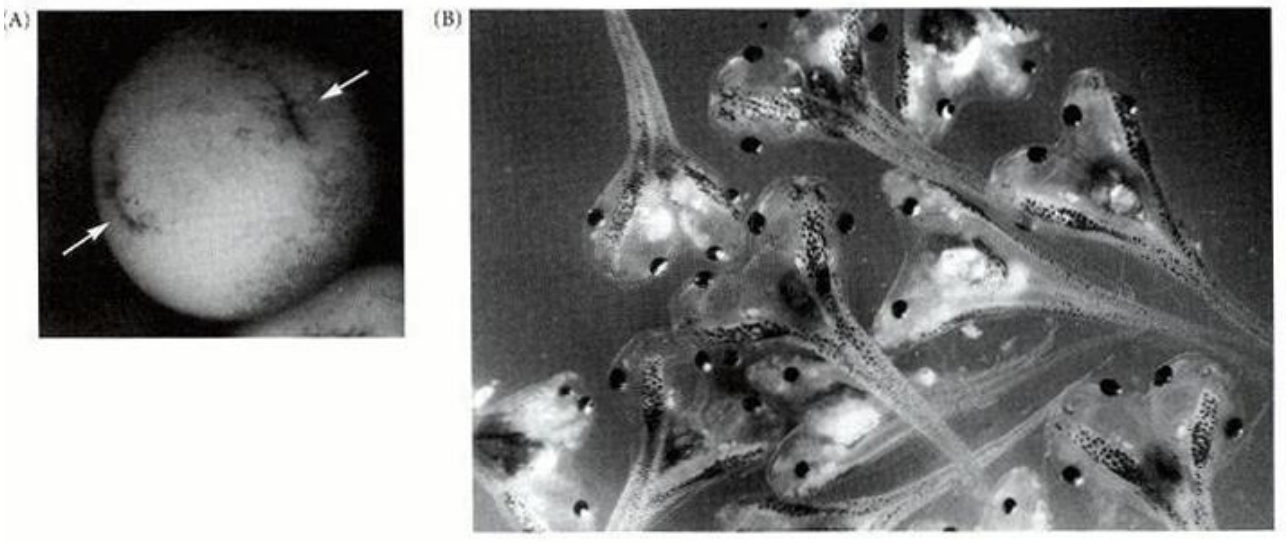




Rearrangement of the Egg Cytoplasm



Rearrangement of the Egg Cytoplasm



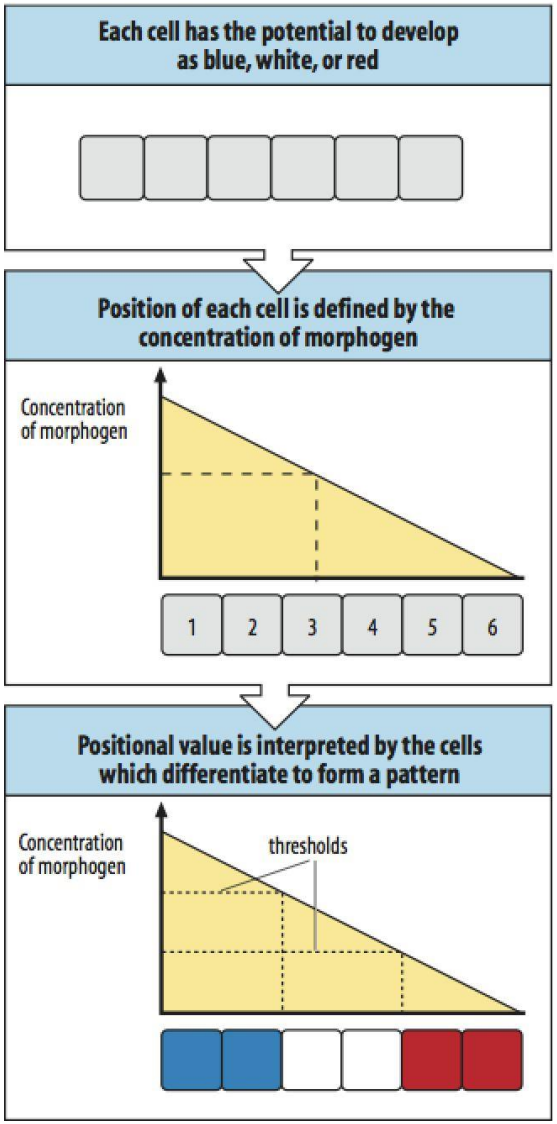
After the initial sperm-directed rotation occur, fertilized eggs were mounted in gelatin and rotated.

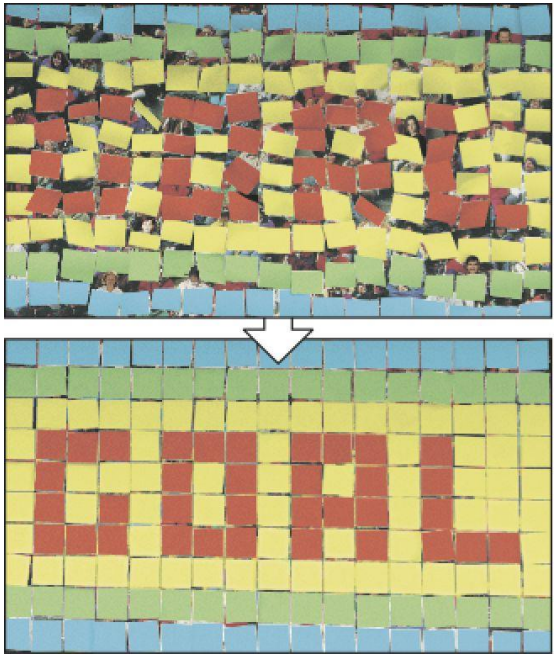
Patterning can involve the interpretation of positional information

- 1. One dimension.
- 2. Positional values has to be related to some boundary or threshold.
- 3. Interpreted by cells.

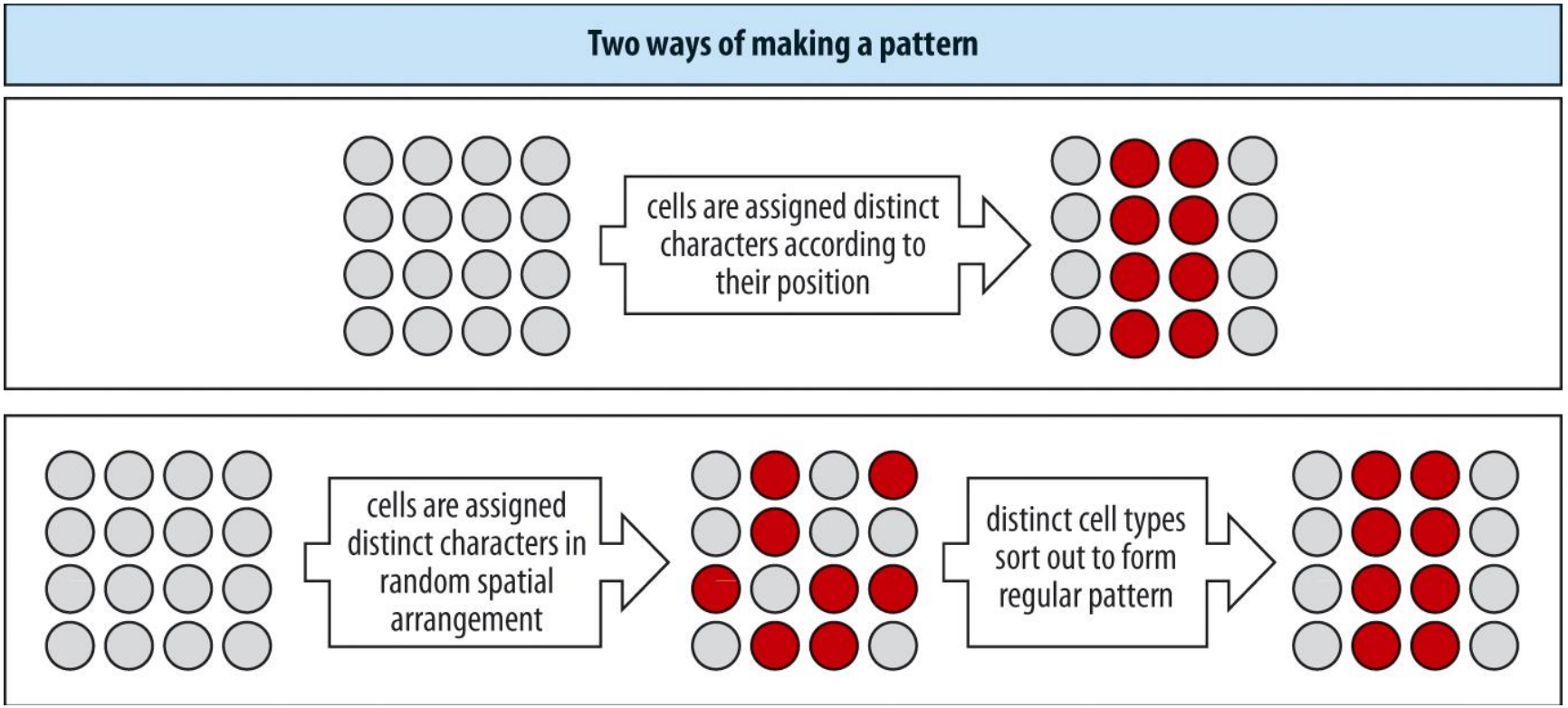
- 4. A gradient is a solution of positional value.
- 5. Such kind of chemical is called morphogen.

Cell responses to a certain gradient.



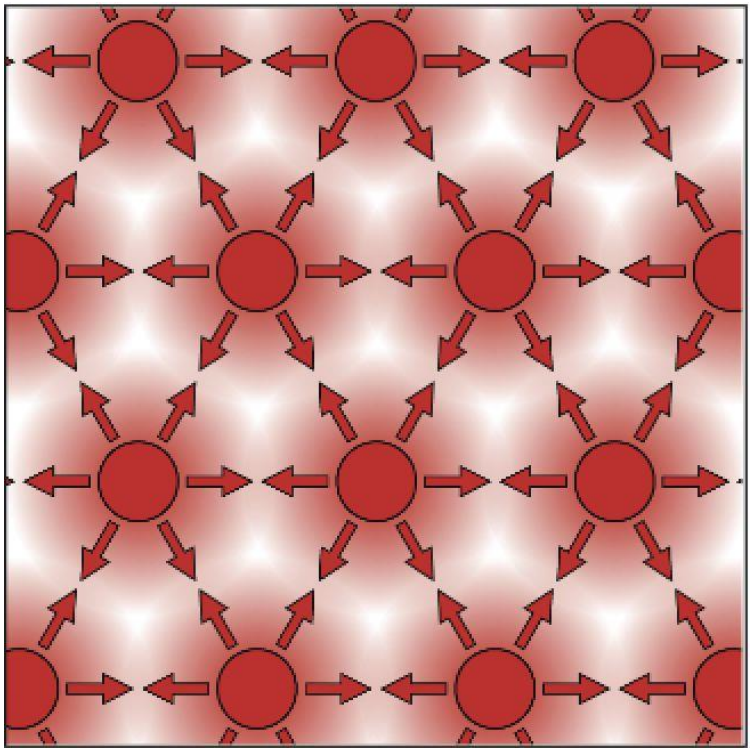


Two ways of making a pattern



A salt-and-pepper fashion

Lateral inhibition can generate spacing patterns



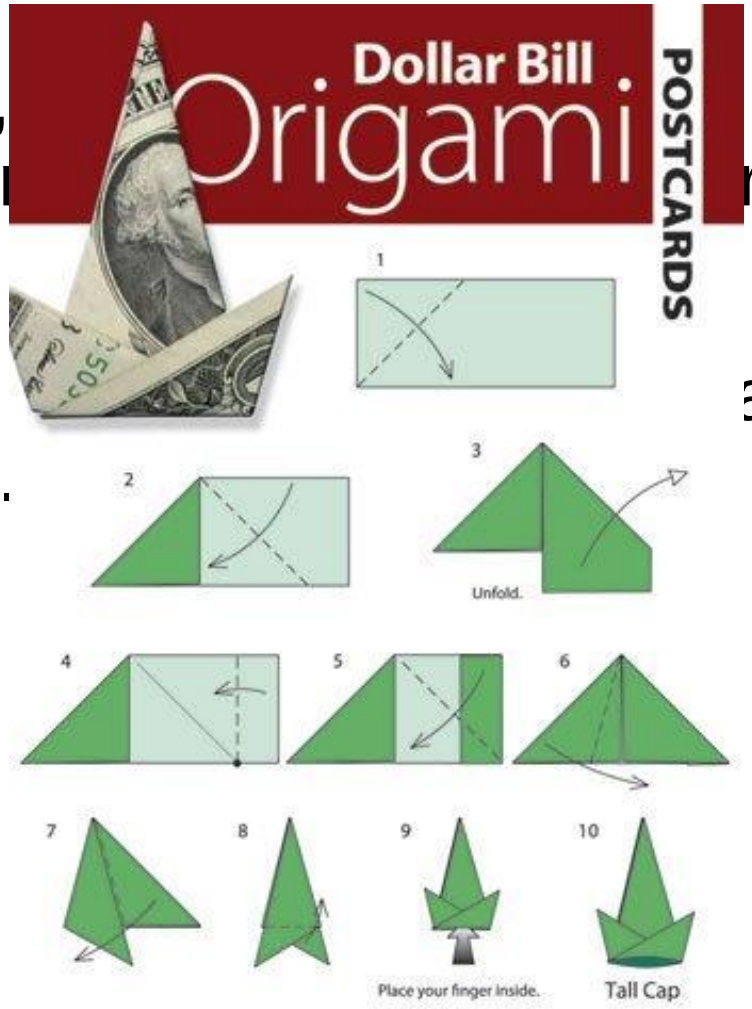
Generative rather than descriptive

- Descriptive, describe in detail, eg, size, position, composition, like a blueprint.

- Generative, instruct how to make an object, like origami.

Generative rather than descriptive

- Descriptive, size, position, co rint.
- Generative, an object, like origami.



How to achieve reliability?

- 1. Redundancy.
- 2. Negative feedbacks.

Thanks!