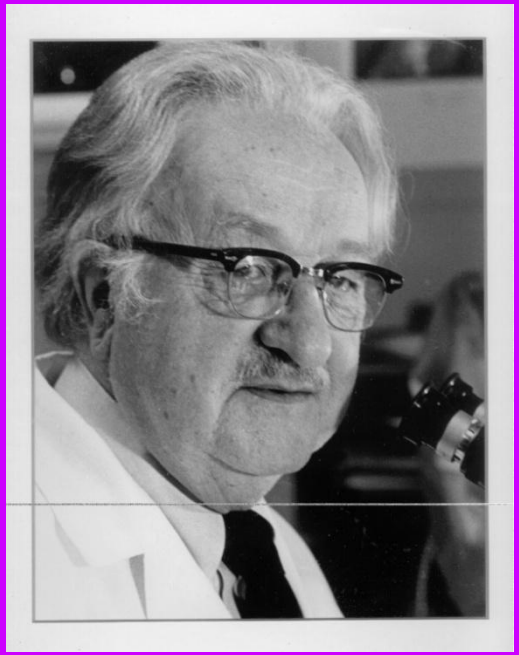
Regeneration and Patterning

Regeneration: pp. 560-571

Modeling: pp. 116-117; 697-698

Regeneration

- “I’d give my right arm to know the secret of regeneration”
  -Oscar Schotté

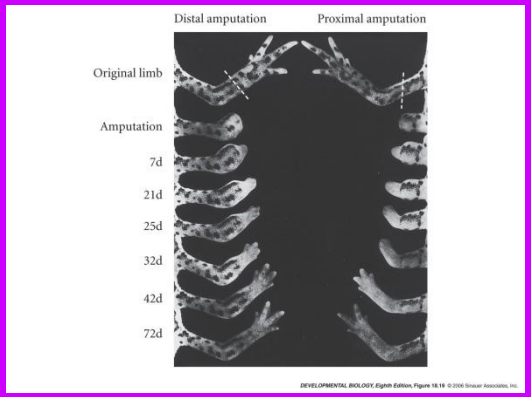


- Making a new organ when one is removed
  - salamander limb
  - starfish “arms”
  - flatworms and hydra
  - vertebrate liver

Regeneration Terminology

- Epimorphosis (e.g. limb, *Hydra*)
  - growth
  - dedifferentiation and respecification
- Morphallaxis (e.g. flatworm)
  - no growth
  - repatterning of existing tissues
- Compensatory (e.g. liver)
  - cell division
  - no dedifferentiation

Limb Regeneration



- Epimorphic
- Wound heals forming an ectodermal cap
- Cells beneath dedifferentiate forming a blastema
- Cell division in blastema followed by redifferentiation into muscle, cartilage and bone, etc.

Limb

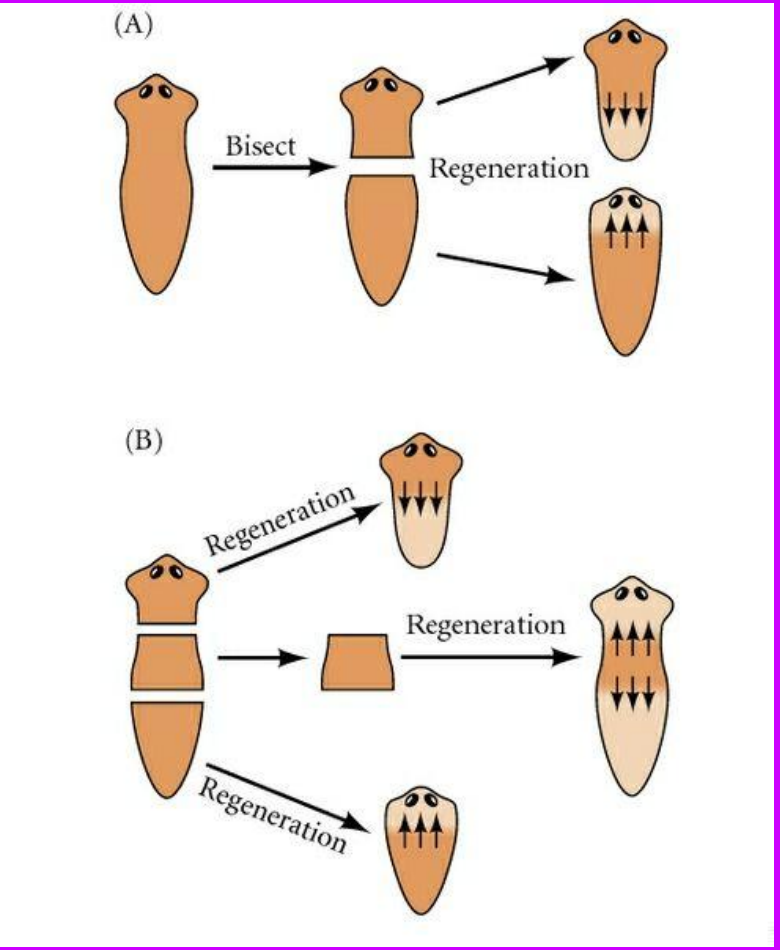
- Blastema re-patterns limb like a new progress zone
  - requires enervation to make growth factors stimulating cell division
  - retinoic acid made by wound epidermis plays a role in specification
- Same order: proximal to distal

Liver

- Compensatory regeneration
- Hepatocyte growth factor stimulates cell division of remaining cells
- Each liver cell type retains its character but enters the cell cycle
- Many are arrested in G2 and can rapidly enter mitosis

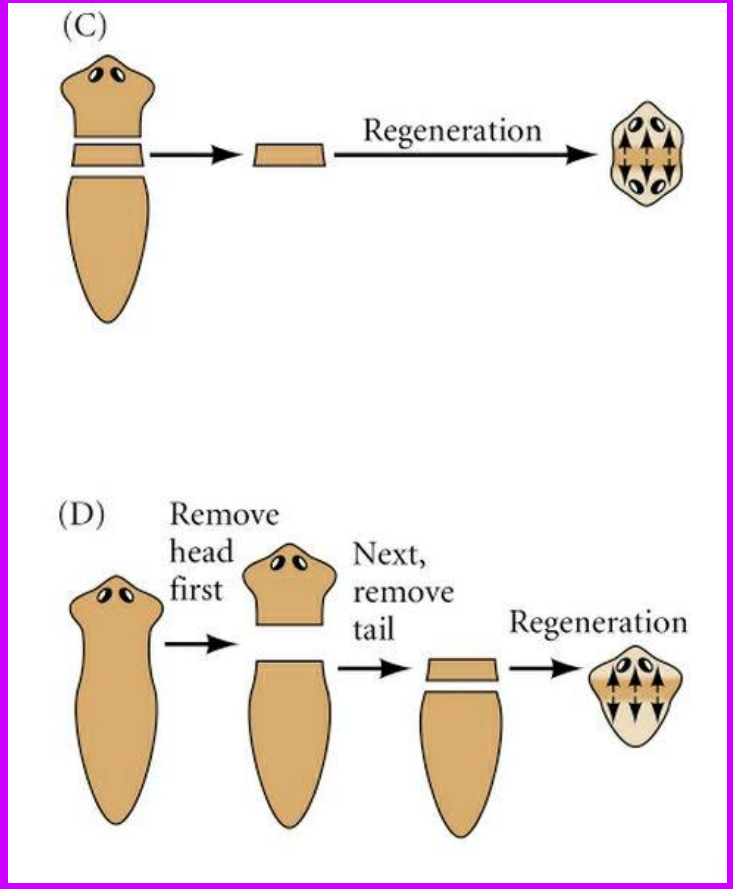
Flatworm Regeneration

- Morphallactic
- Bisect
  - maintains polarity
- Trisect
  - same
- Same tissue can make head or tail



Flatworm Regeneration

- Small piece may show no polarity
- Given time it develops a gradation
- Head commitment at the first cut
- Try some in lab!



Hydra

- Fresh water coelenterate
- Reproduces sexually and also by budding
- Epimorphic
- Regeneration experiments suggest morphogen gradients

Hydra

- Abraham Trembley (1740)
- Is it a plant or animal?
- Moves, eats, so if you cut it up, it should die
  - wrong!
- Parlor games of the 18th century
  - (before TV)
  - music
  - science

Historical Comment

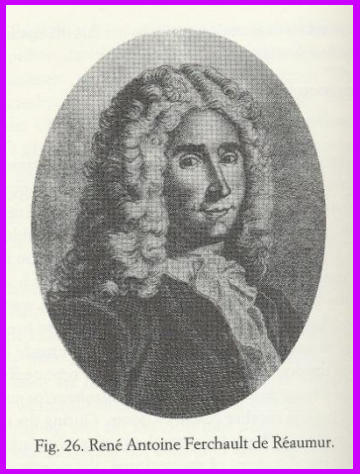
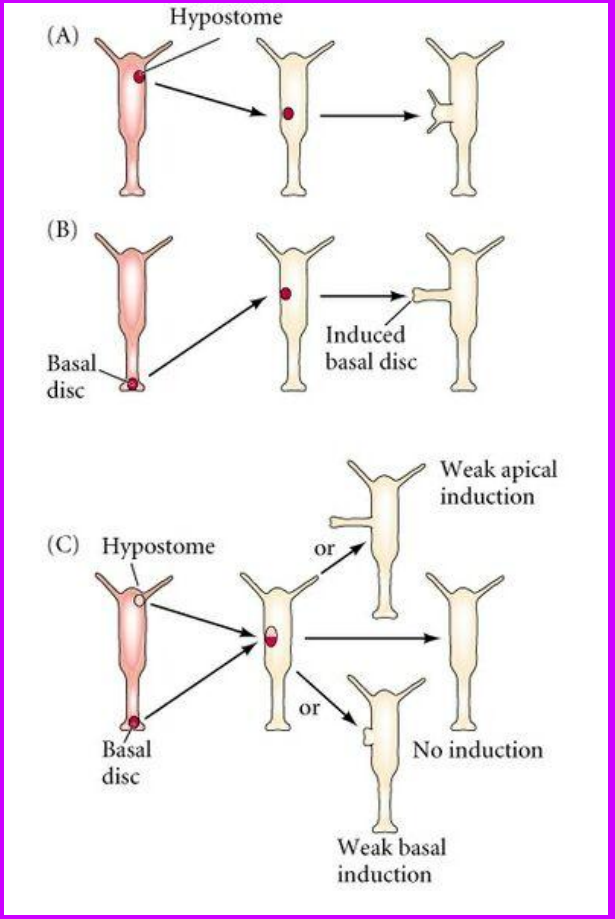


Fig. 26. René Antoine Ferchault de Réaumur.

- Réaumur
  - "During the summer of 1741, lizards, frogs, worms, snakes, eels, crabs, butterflies, and lobsters were threatened by dangers to which they had never been exposed before."
  - "When I saw for the first time two polyps form little by little from the one I had cut in two, I could hardly believe my eyes: and it is a fact which I am not at all accustomed to seeing, after having seen it over again hundreds and hundreds of times."

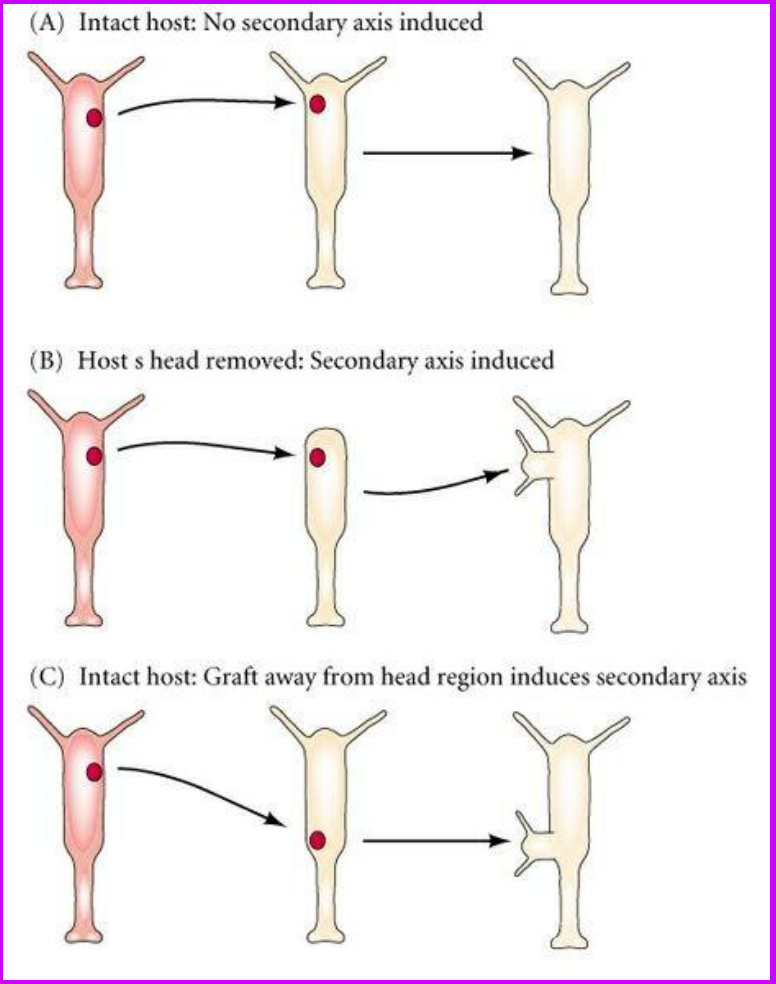
Head and Base Activating Regions

- Head or region near head induces outgrowth from host
- Base induces base
- Each “neutralizes” the other

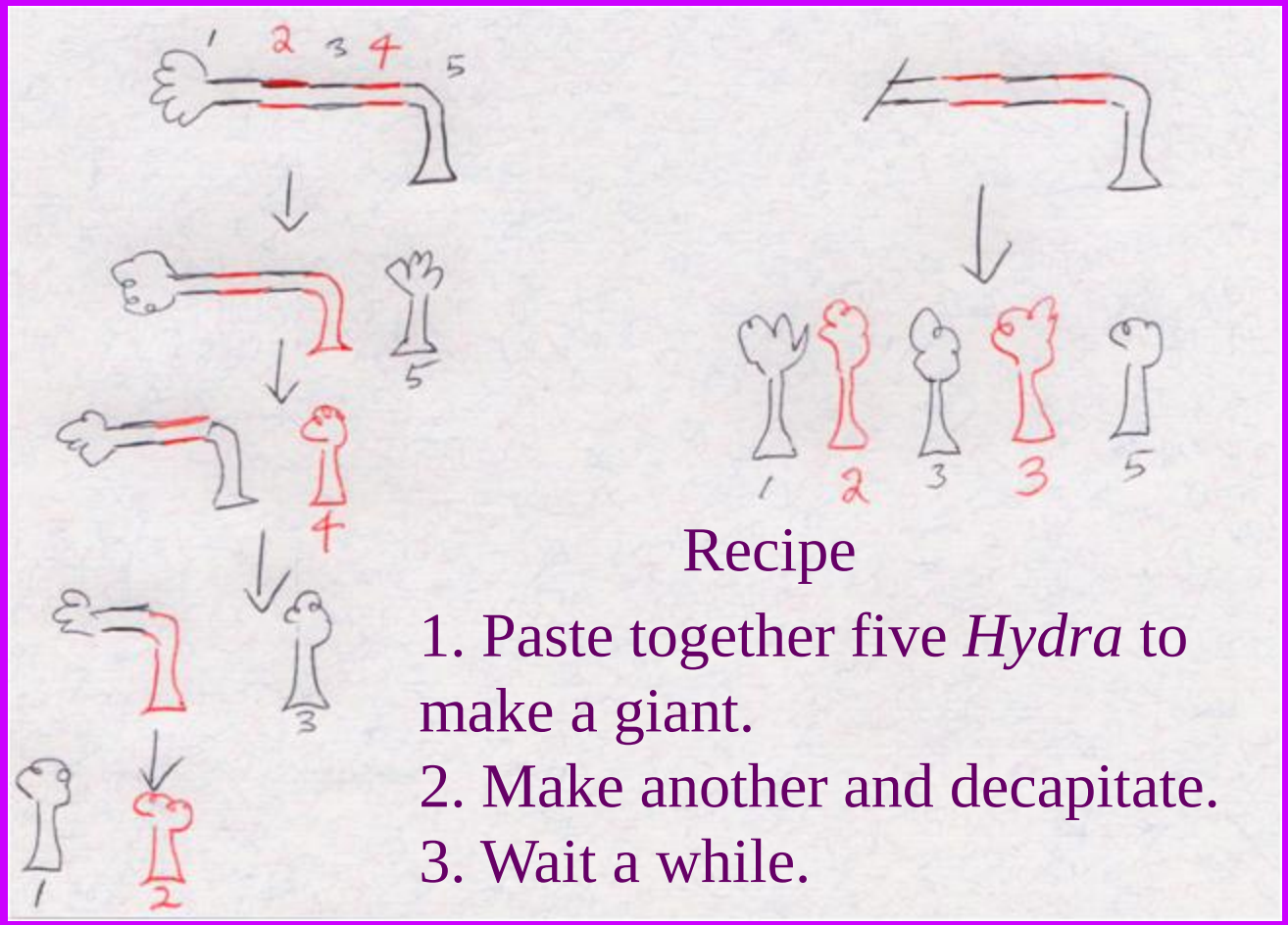


Head Inhibition of Heads

- Head induces almost anywhere
- Subhead does not induce if near head
- Remove head allows induction
- Gradient of inhibition



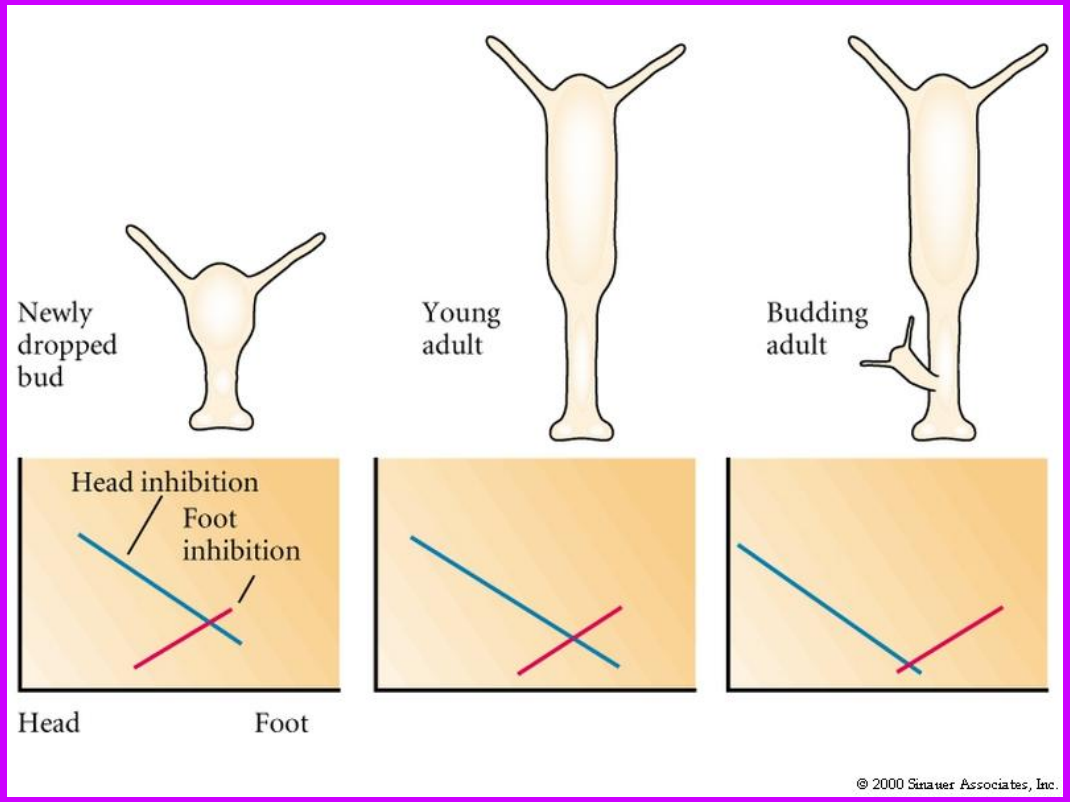
Long Distance Inhibition



Recipe

1. Paste together five *Hydra* to make a giant.
2. Make another and decapitate.
3. Wait a while.

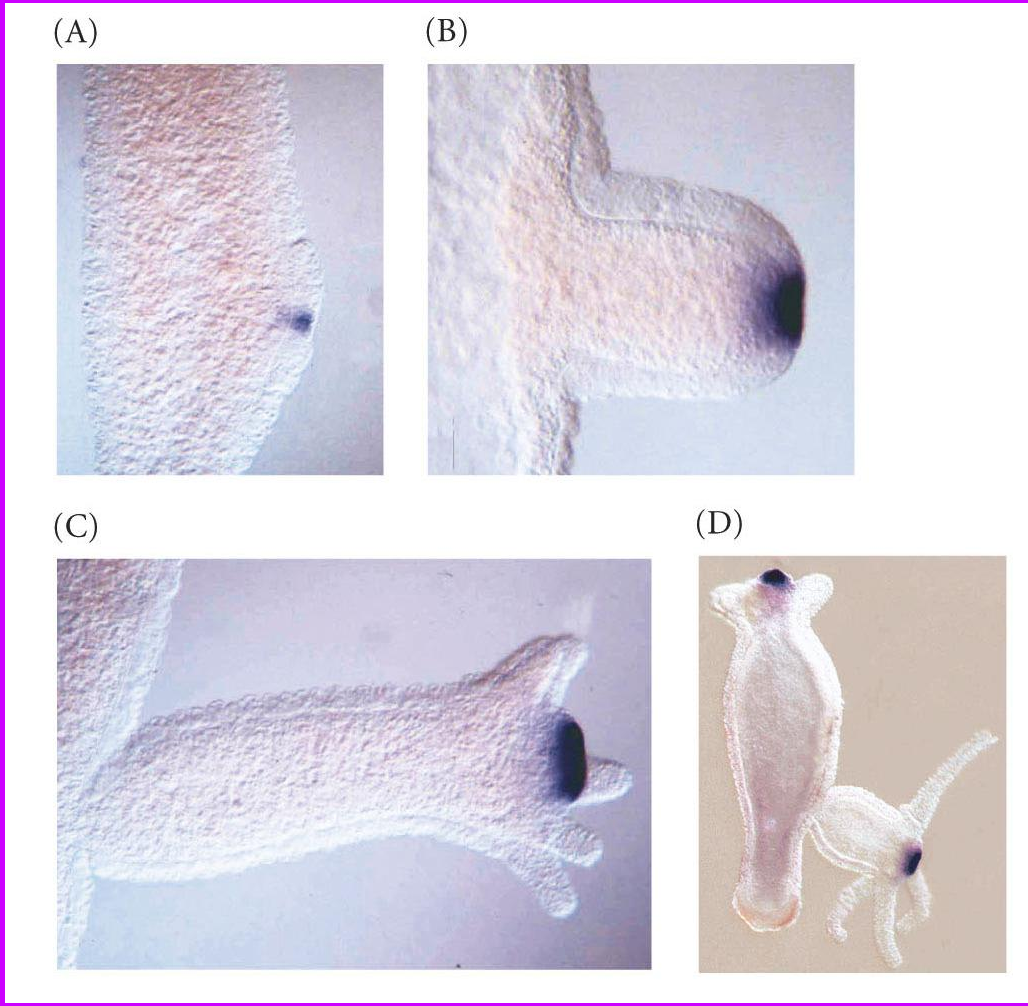
Model of Function of Inhibitor in Budding



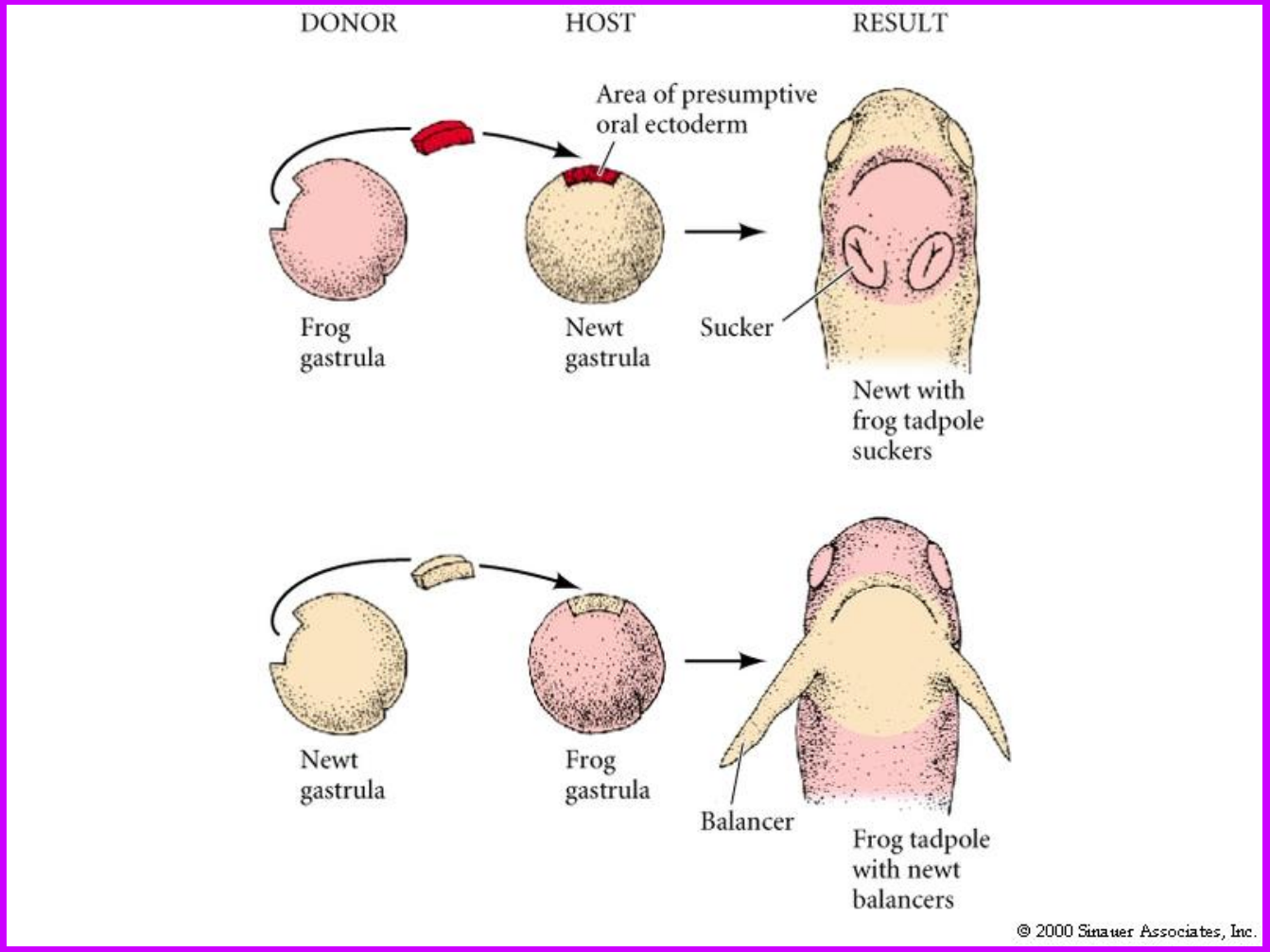
Loss of distal inhibition upon growth

Wnt Expression

- Wnt signals mark the future head region



Recall Schotté's Experiment: Positional Information

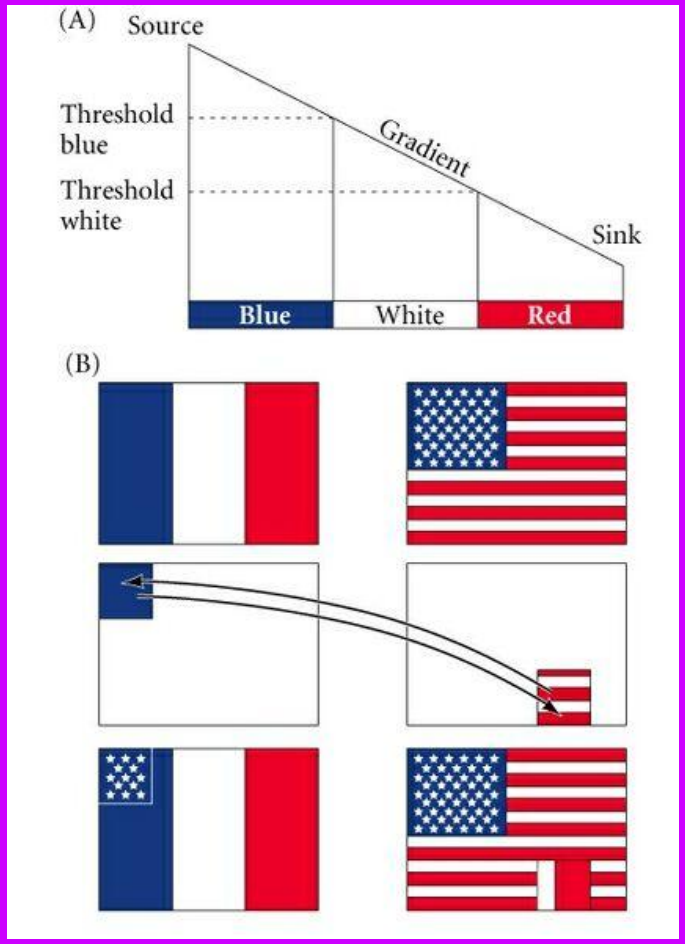


Positional Information

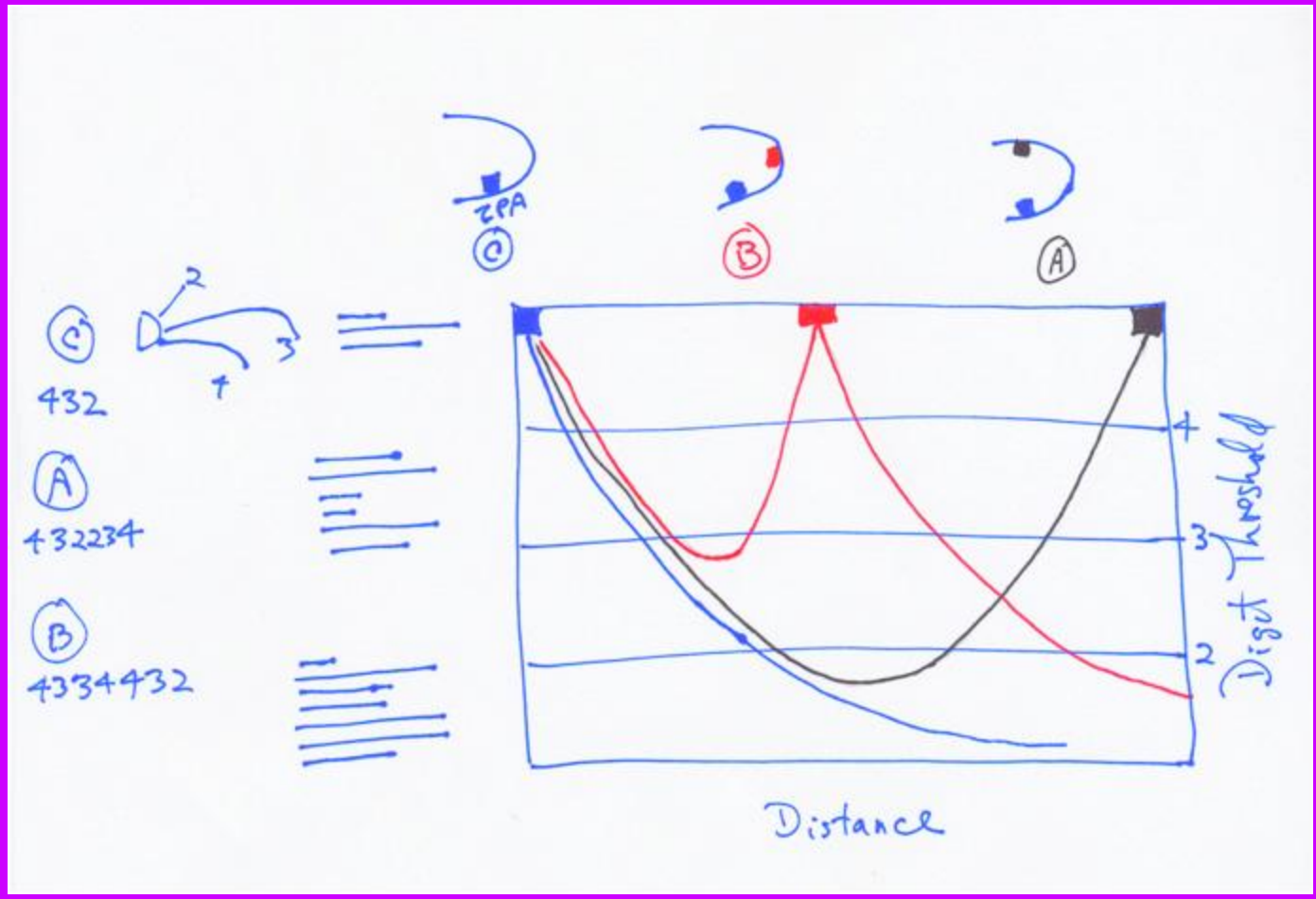
- One interpretation
  - There is information specifying only relative position
  - What a cell makes depends on how it reads the signal
  - This depends on
    - its capabilities
      - its genes
      - and its history

Wolpert's French Flag

- French and American flags have different "genetics" or rules
- Gradient of positional information can be the same left to right
- Rules of interpretation different



Applied to Chick Wing ZPA



Patterning Models

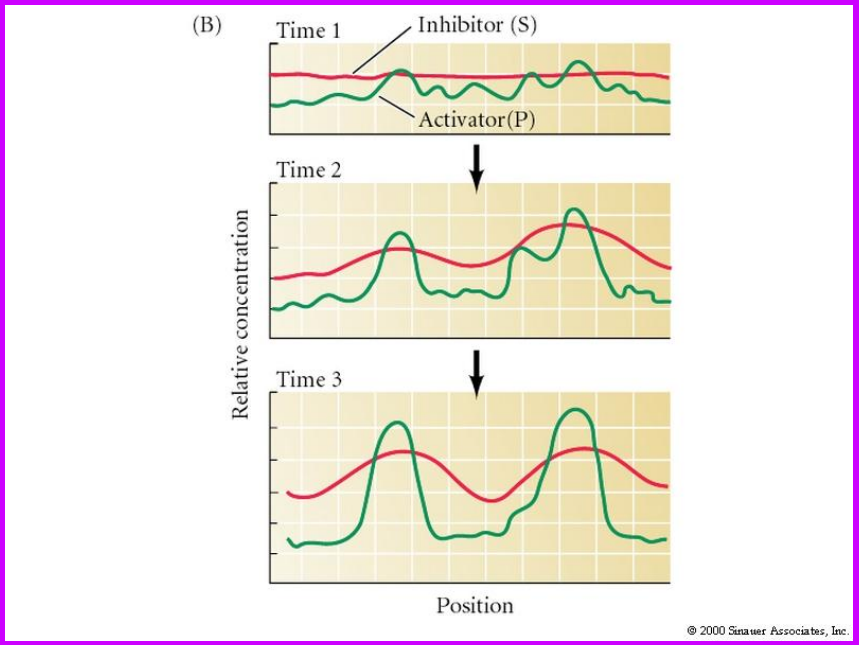
- Where does the gradient come from?
  - Could be preformed
    - could be gradient of receptor concentrations on cell surface or a source of localized source of morphogen diffusing through tissue
    - begs the question?
  - Could be generated
    - but what could generate a gradient of positional information from an initially homogeneous field?

Mathematical Models

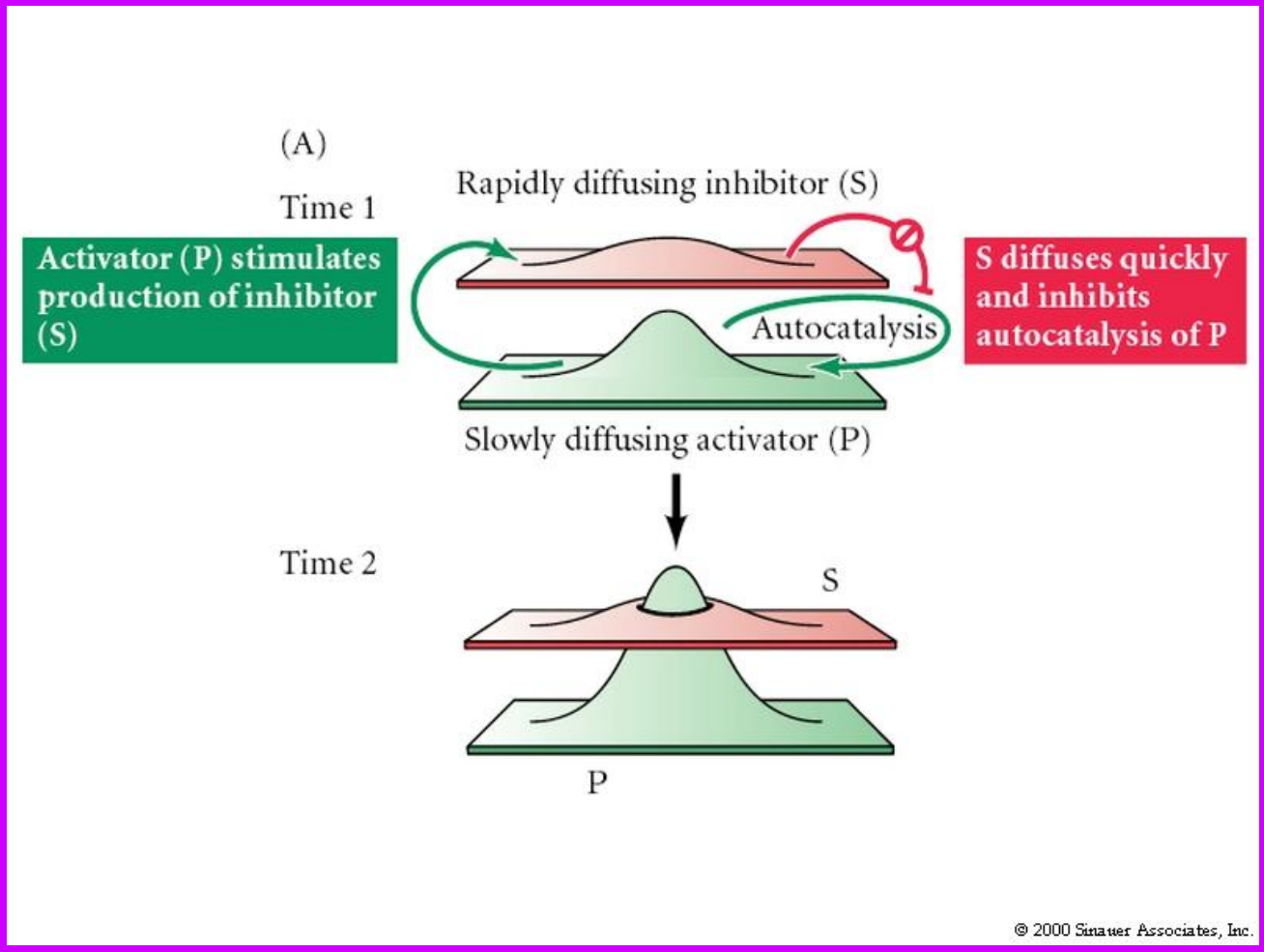
- Turing's reaction diffusion model
  - chemical analogue in oscillating reactions
- Need 2 substances
  - the inhibitor suppresses the other (activator)
  - the activator promotes itself and the inhibitor
  - inhibitor diffuses more rapidly than the activator
- Random fluctuations will generate pattern

Patterning Models

- Initial random fluctuations
- Eventually a series of peaks is generated in a pattern
- Can predict complex patterns



Patterning Models



Patterning Models

- Some people like them, some people don't.