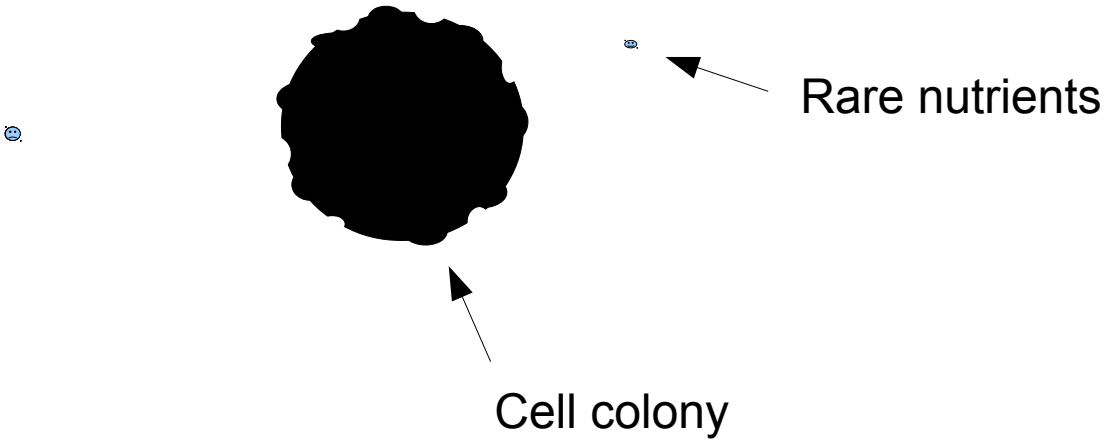
Extra slides for workshop 7

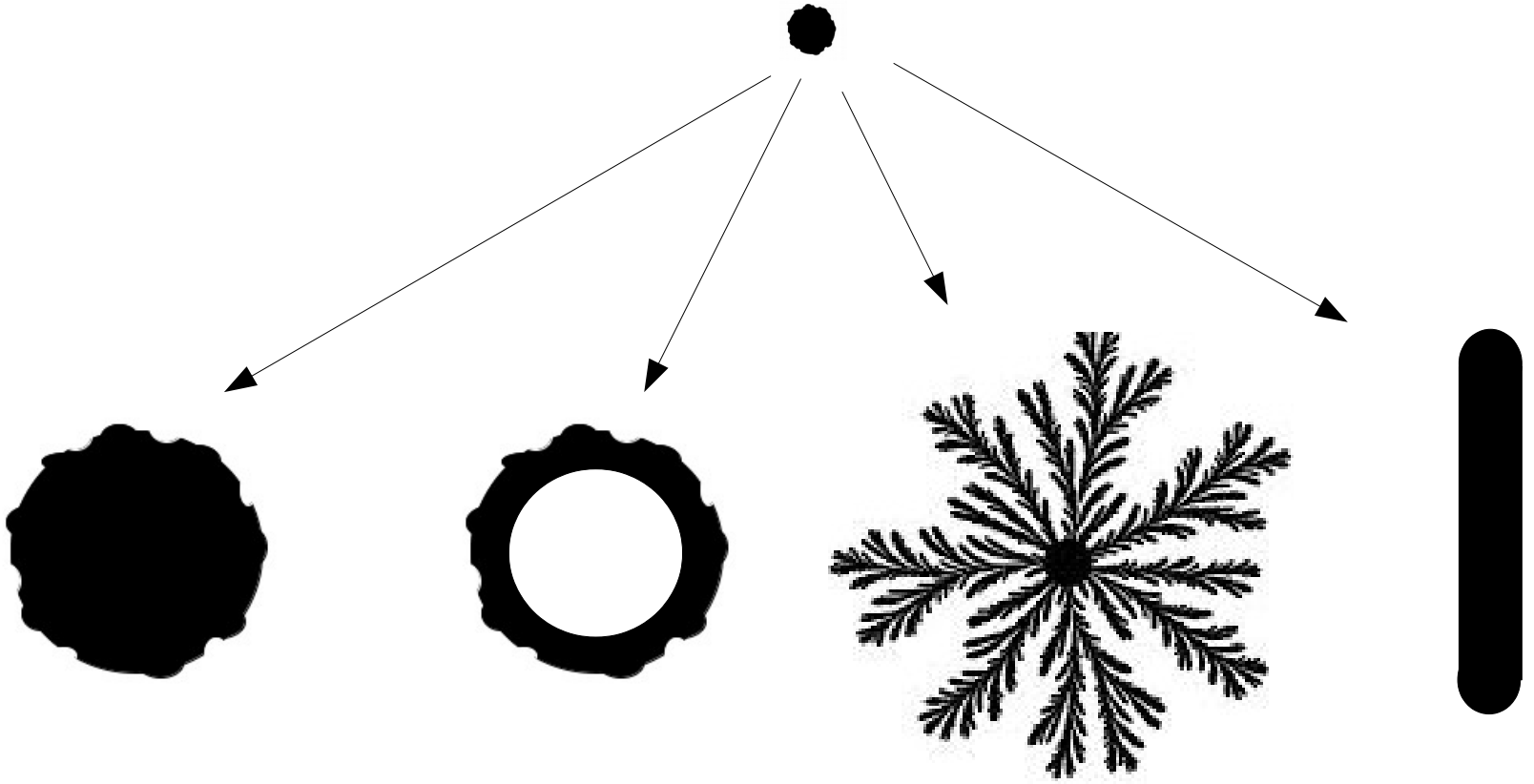
(These are drawn from other courses I teach, MBChB and a new 2nd year BSc course: they may not reflect exactly the diagrams we draw on whiteboards but may still be useful)

Environmental control of growth can directly drive morphogenesis.

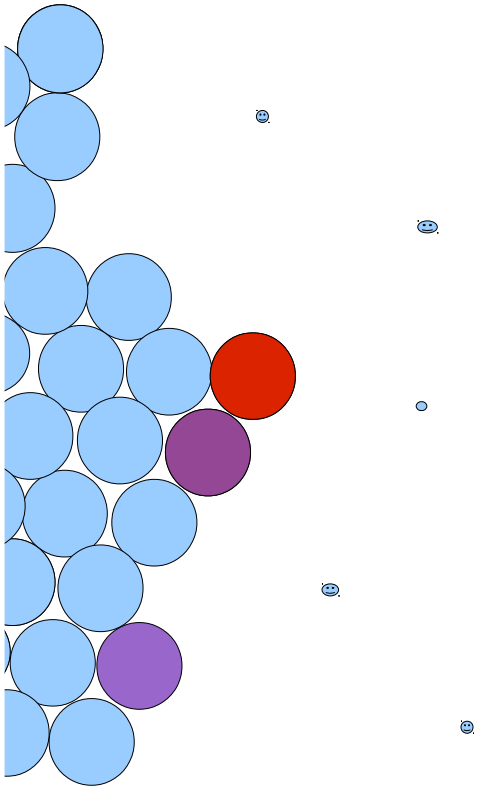
Consider a colony of cells whose growth/proliferation is limited by availability of diffusible nutrients:



Which of the following shape will the colony become?



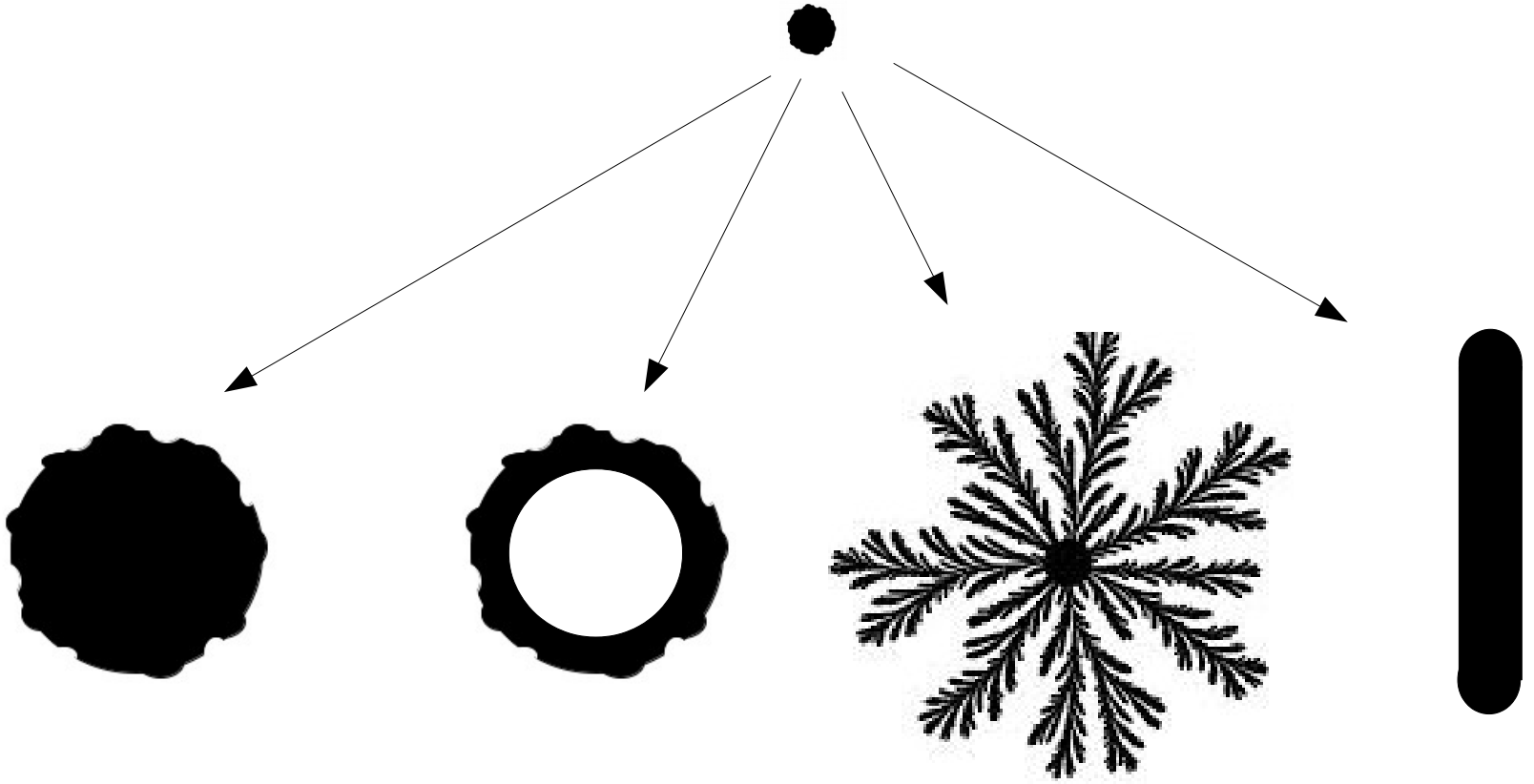
Close-up of outer edge



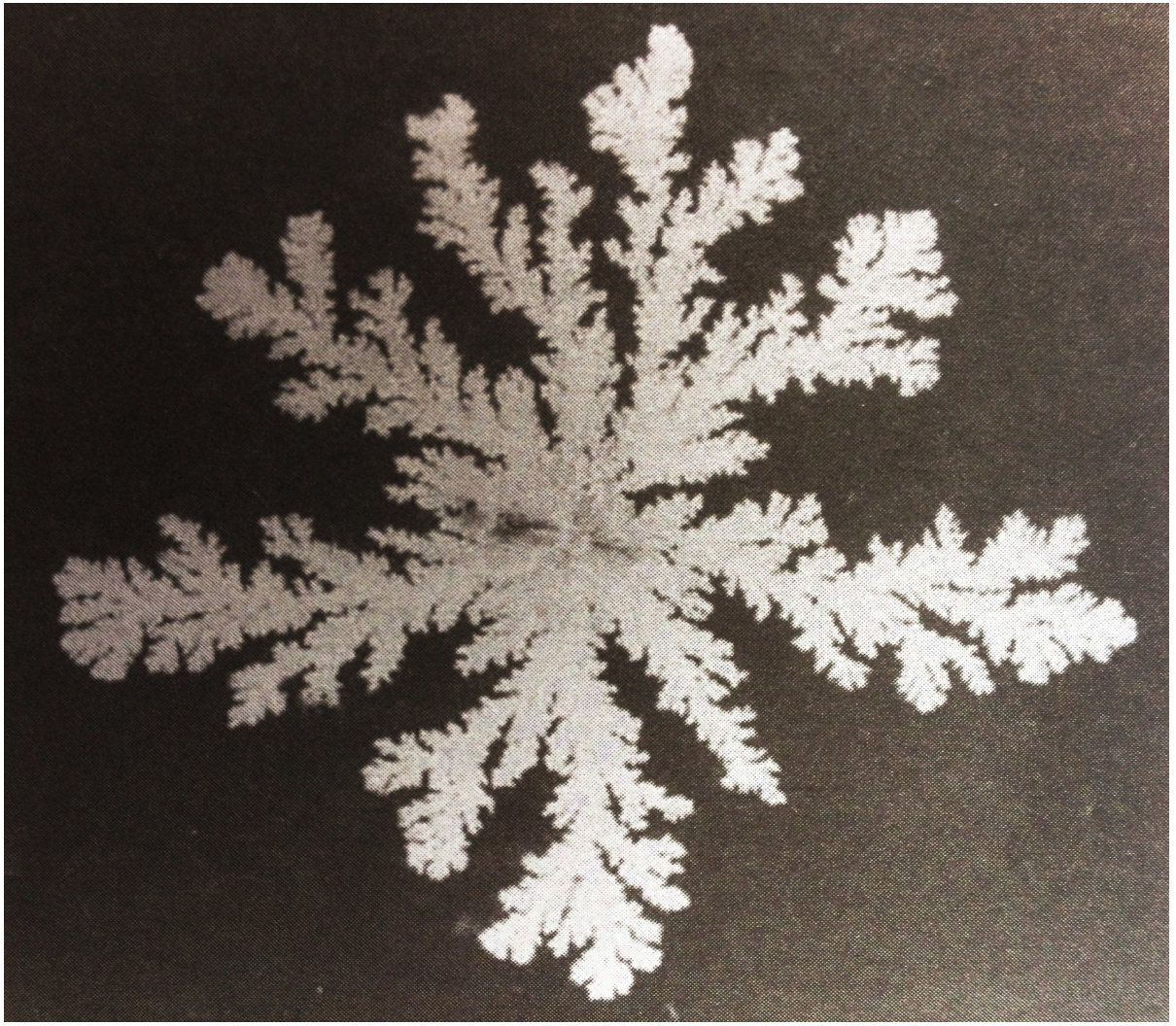
Which cells will be better fed on average?

So...

Which of the following shape will the colony become?

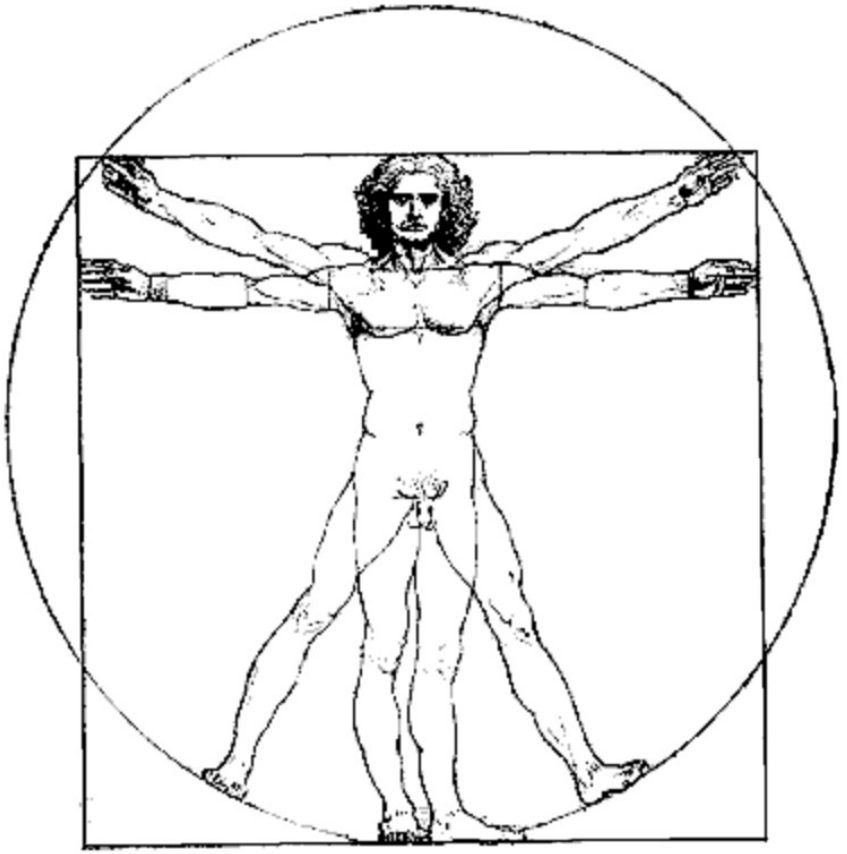


This is the reality of *Bacillus subtilis* growing on agar:



(Ignore the 'pixels': these are just from photographing the printed image: Ball P, *Branches)*

Vitruvian Man



span of the out-stretched arms = height

distance from hairline to chin = 10% height

elbow to the tip of the hand = 25% height

length of foot = 1/6 height,

length of an ear = 1/3 length of the face

etc, etc

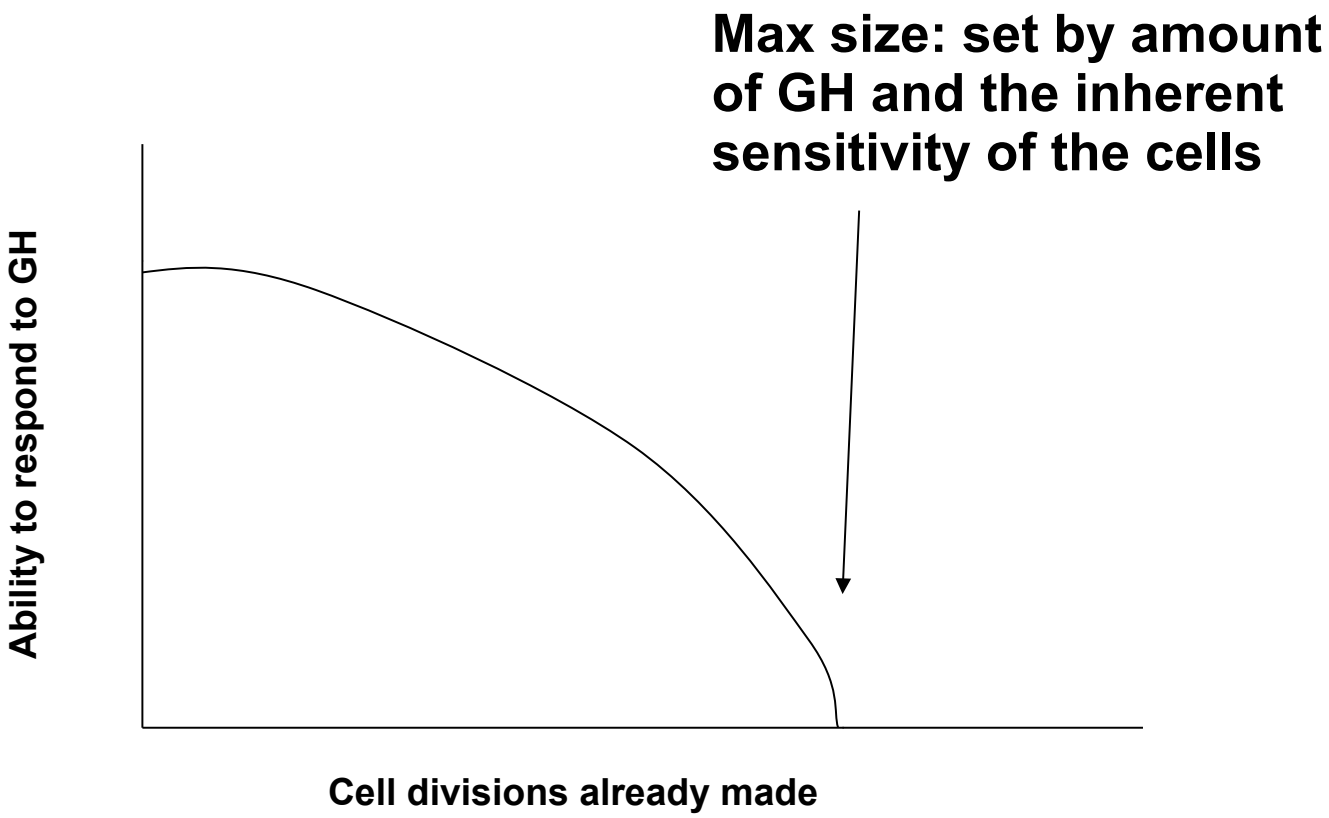
Rabbit leg experiment

- Inhibit the growth of *one* leg of a young rabbit
- Contralateral leg grows normally (-> lop-side bunny)
- Release the inhibition -> inhibited leg catches up (faster growth than the other).

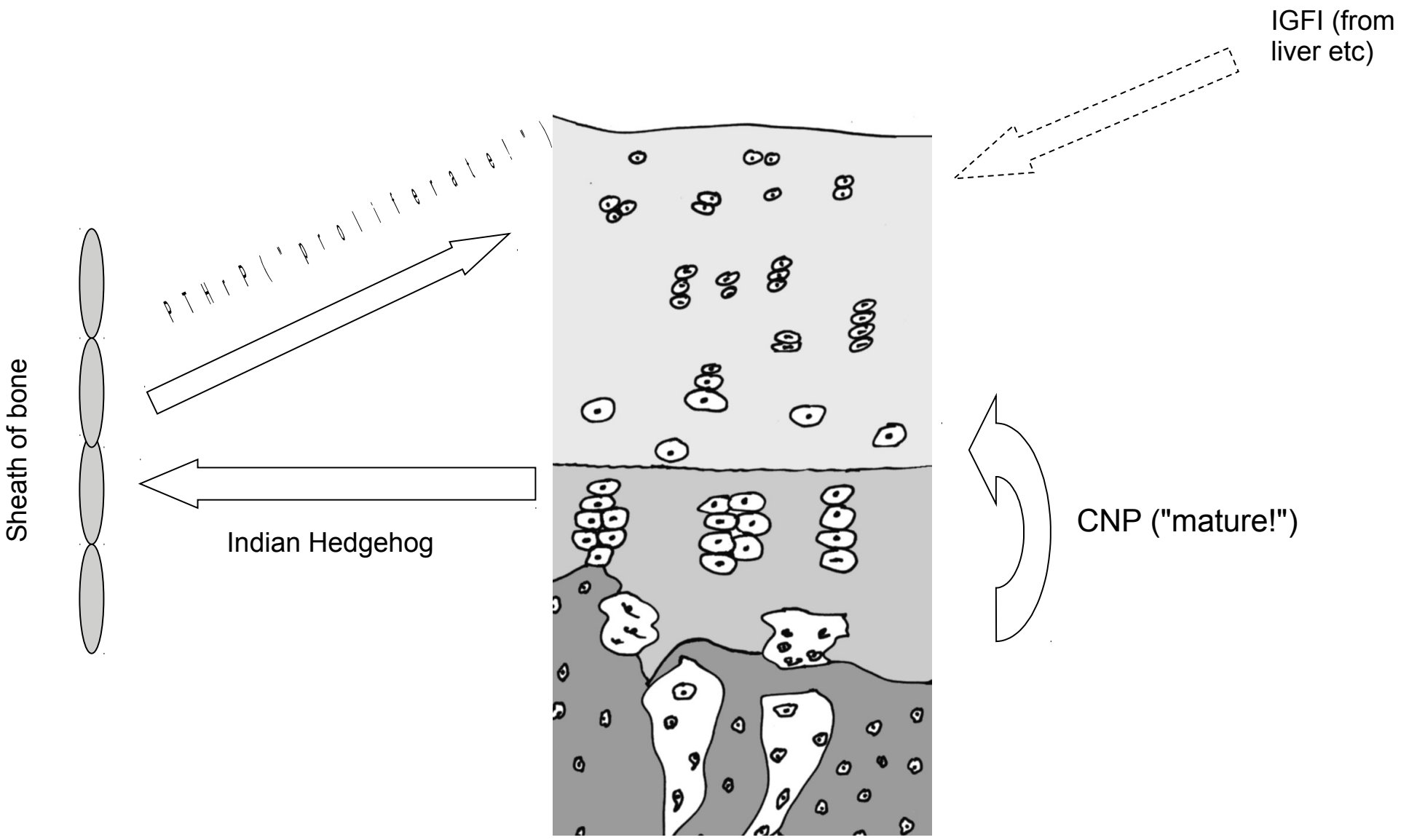
Possible explanation

- The ability of the growth plate of the long bone to respond to GH declines with the number of cell divisions it has made.

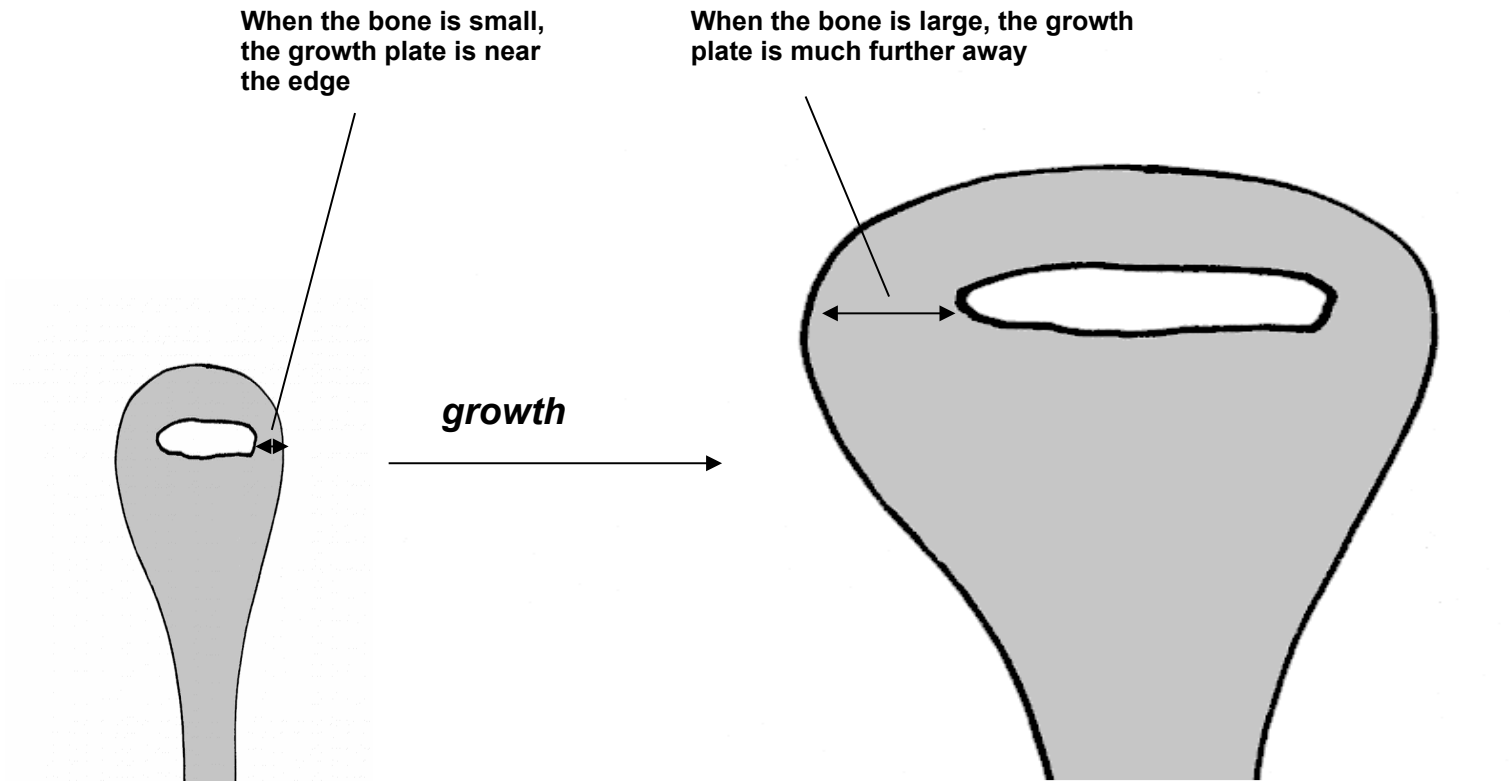
(the stalled leg made fewer divisions early, so retained the ability to "listen to" GH and catch up.)


Max size: set by amount of GH and the inherent sensitivity of the cells
Ability to respond to GH
Cell divisions already made

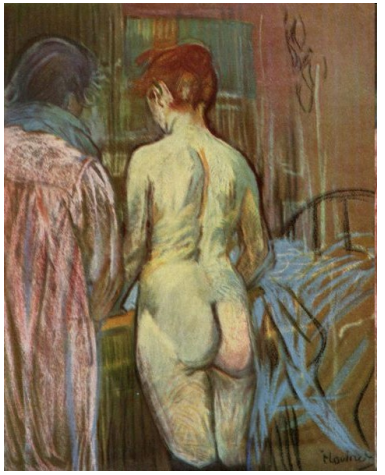
The growth plate maintains itself using internal and external signals

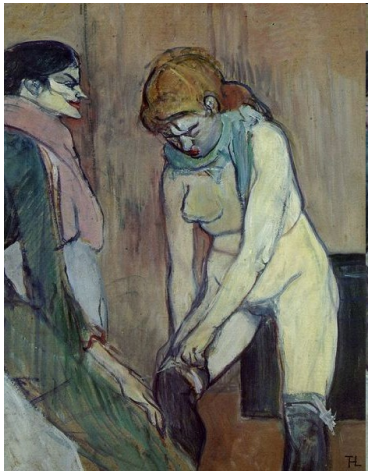


A possible explanation for rate of growth falling away with size

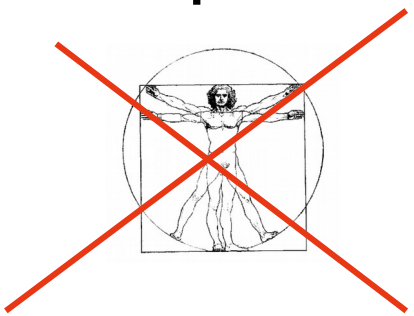


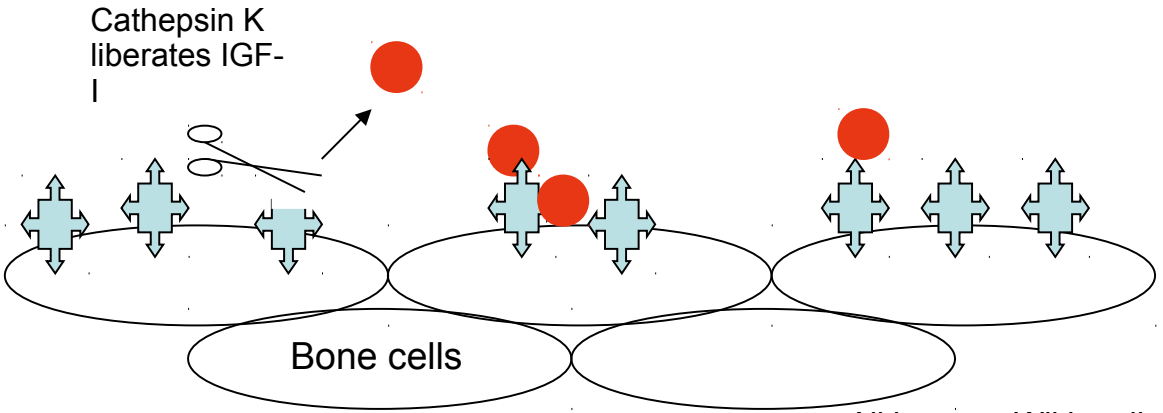
Henri de Toulouse-Lautrec





Pycnodystosis: mutant Cathepsin K





All images: Wikimedia commons

This kind of mutation makes two points;

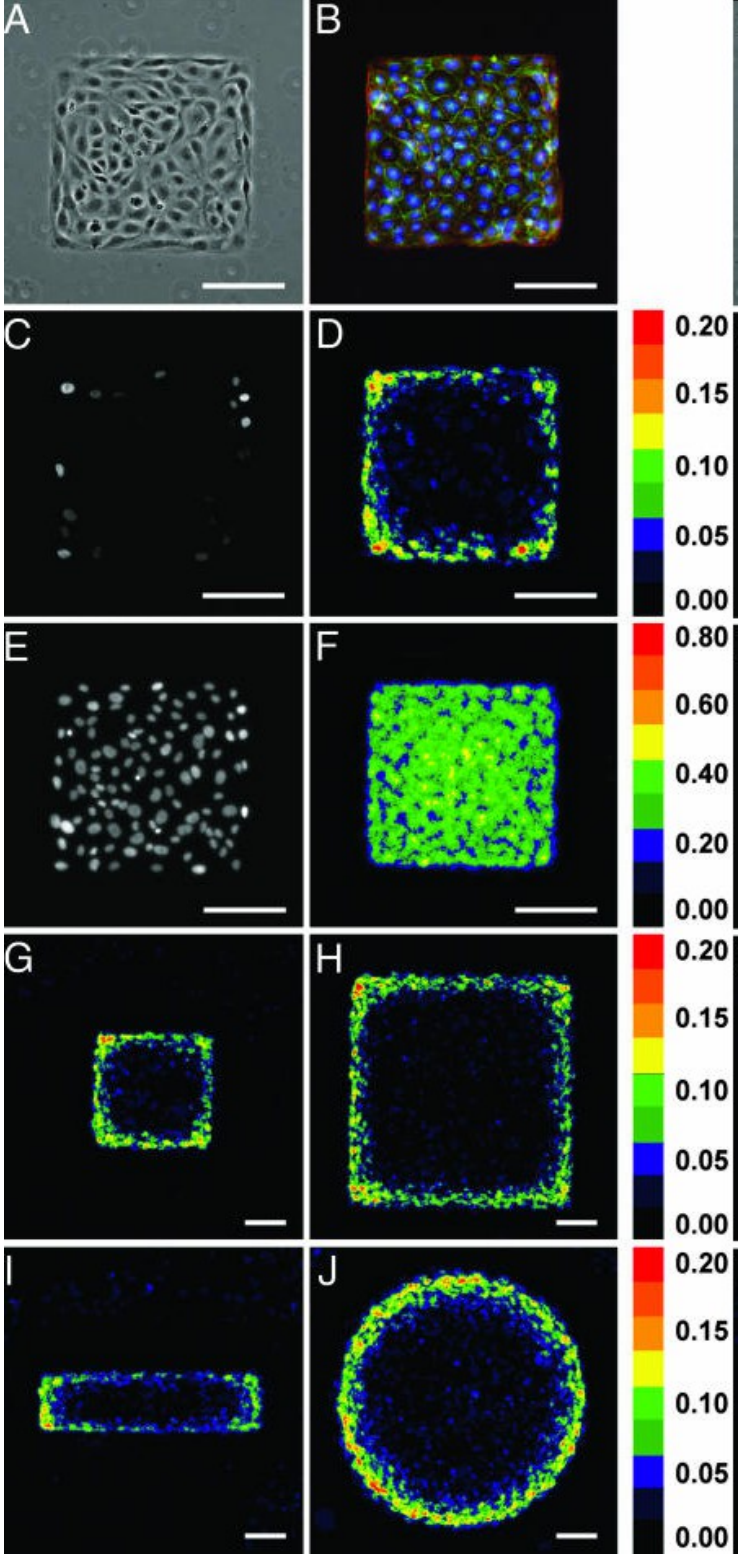
1) **Some parts of the body keep growing anyway (so it is *not* that every part keep up with every other part)**

2) **The amount of skin, tendon, muscle, etc is still correct for a peculiar shortened limb, so tissues cannot be independent for each other.**

Plate cells on to shaped islands

Emergent patterns of growth controlled by multicellular form and mechanics

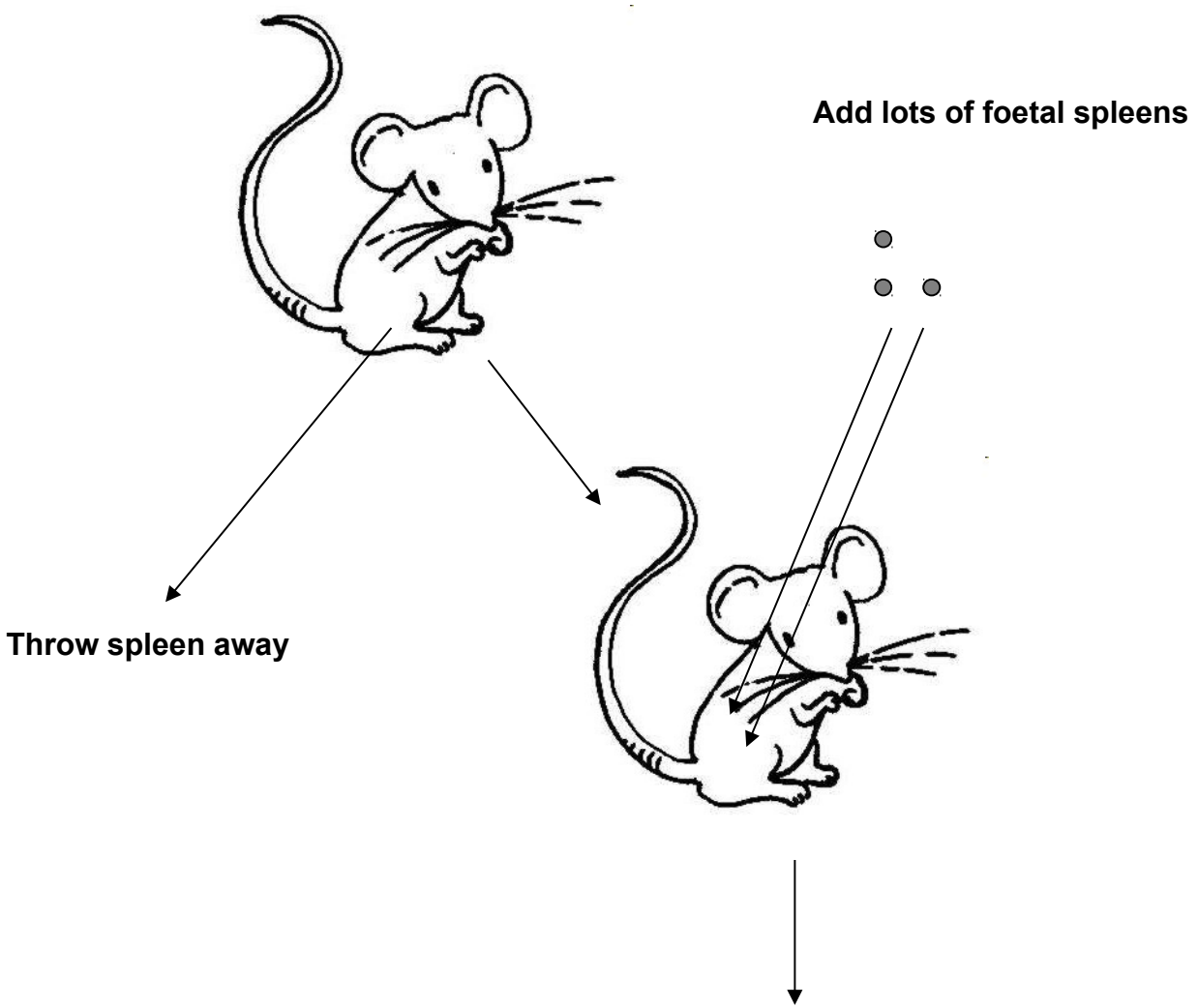
Celeste M. Nelson*†, Ronald P. Jean*, John L. Tan*, Wendy F. Liu*, Nathan J. Sniadecki*, Alexander A. Spector*, and Christopher S. Chen*†‡



How about 'mechanically isolated' organs?

Spleen:

TOTAL mass = mass of one normal spleen.

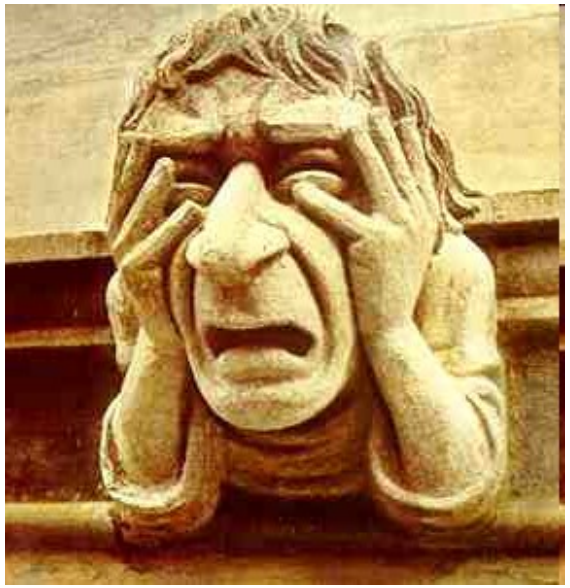


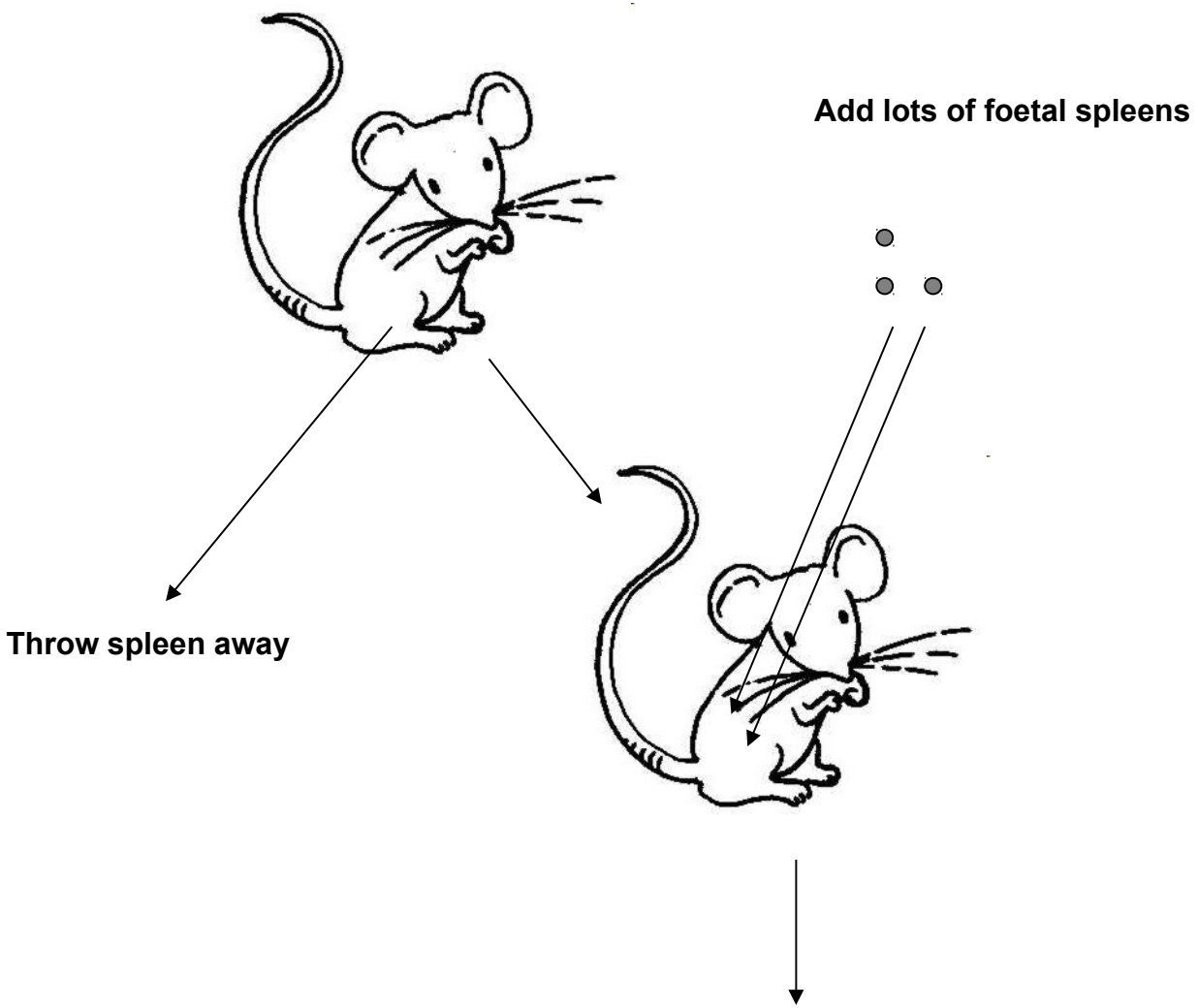
How about 'mechanically isolated' organs?

Spleen:

TOTAL mass = mass of one normal spleen.

But if you do it with a THYMUS, each one grows normal size

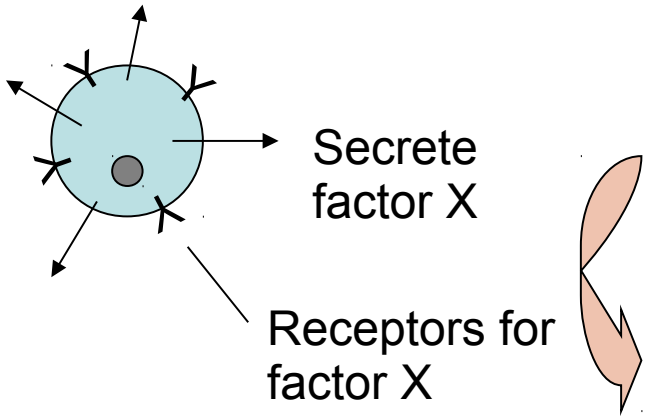


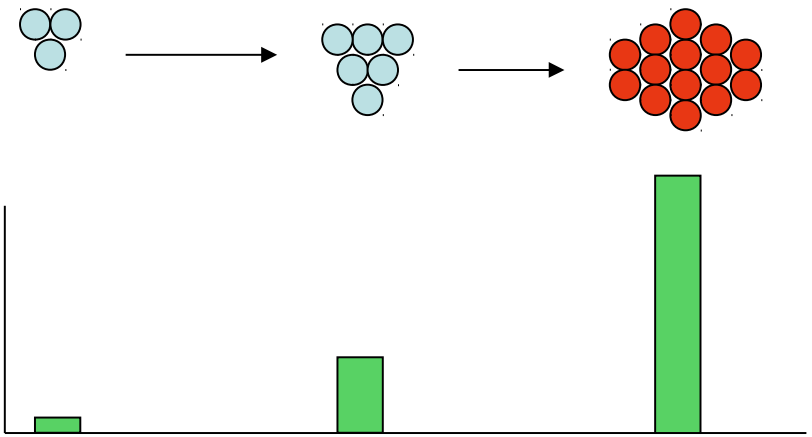


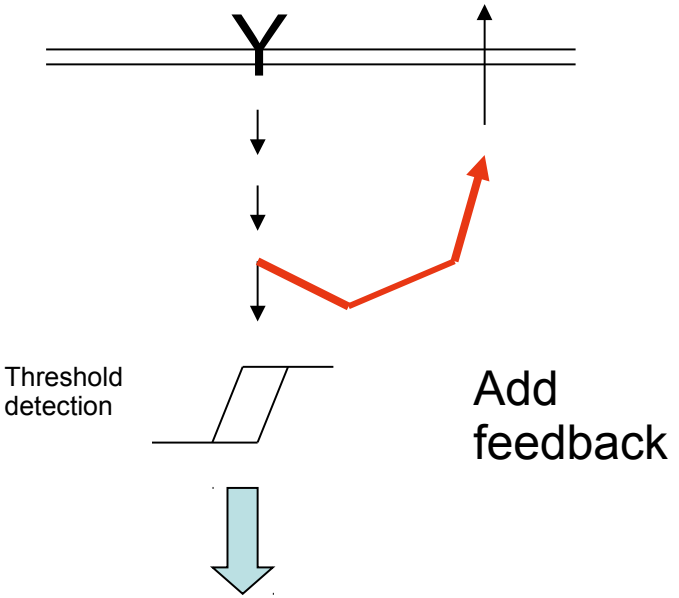
How big do they grow??

Quorum-sensing

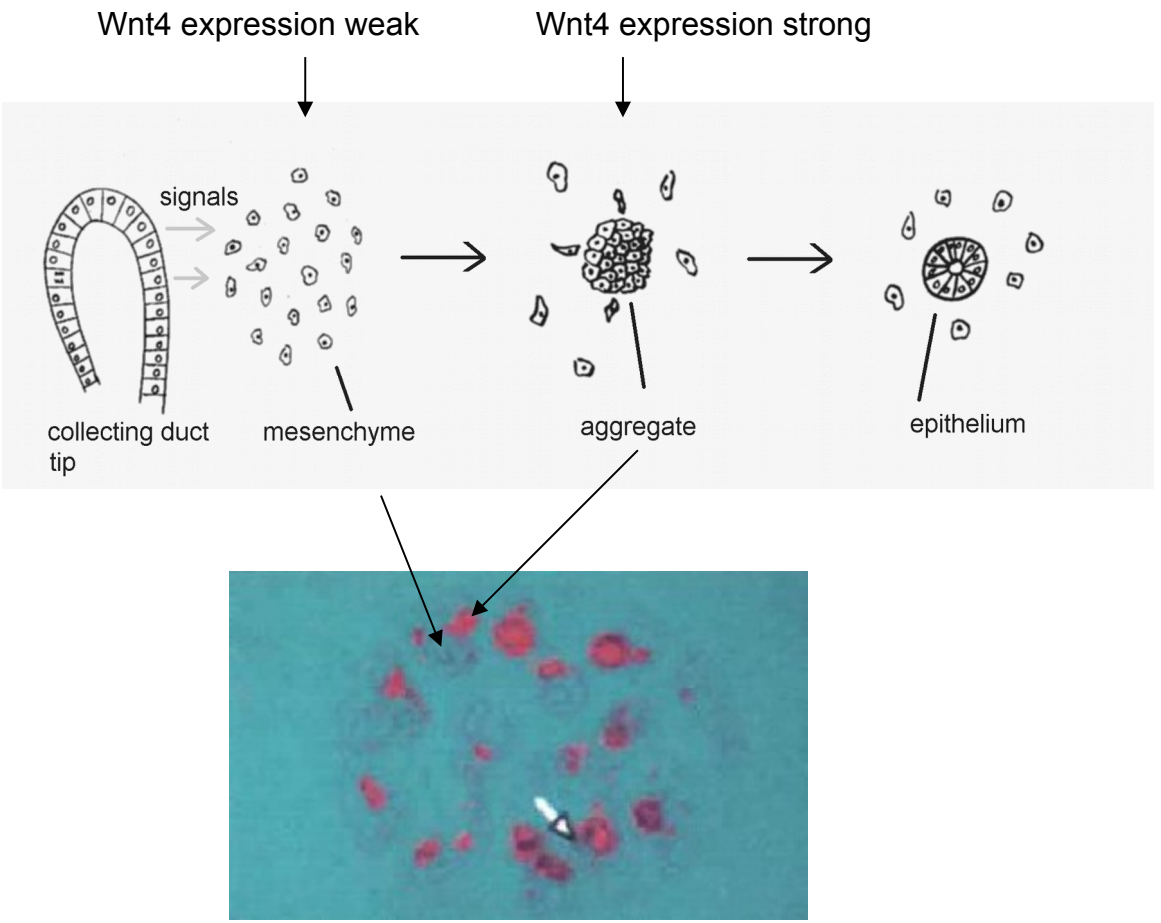
Paracrine signalling:





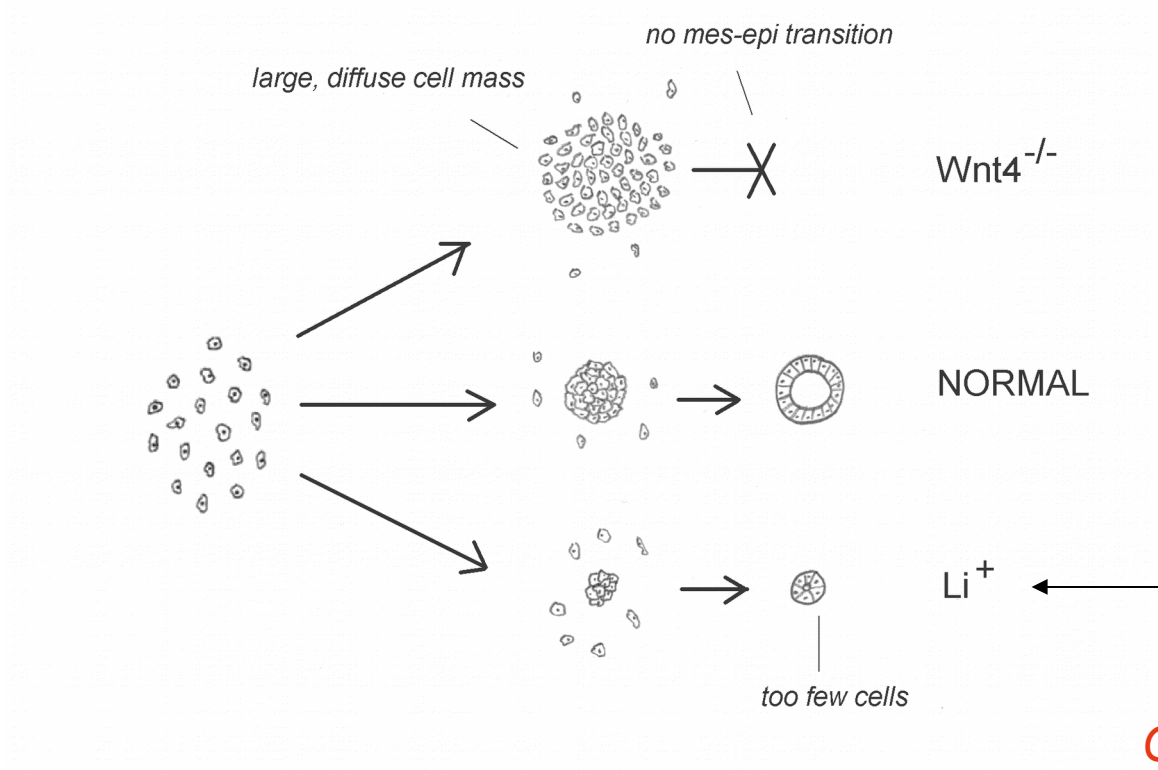


Evidence for quorum sensing: the kidney



Ref: Davies JA (2005) *Mechanisms of morphogenesis*

Evidence for quorum sensing: the kidney



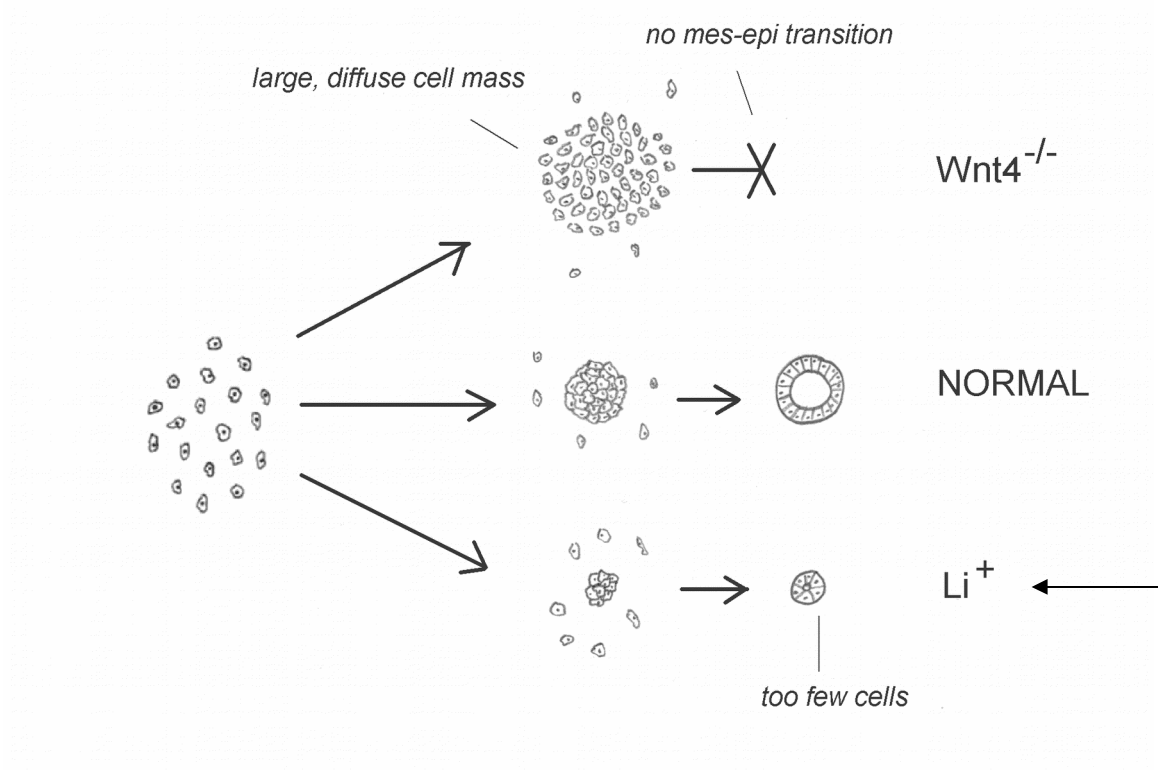
Cells have no way of knowing they have made a big enough aggregate

This mimics Wnt signalling even in the absence of Wnts

Cells think the aggregate is already big

Ref: Davies JA (2005) *Mechanisms of morphogenesis*

Evidence for quorum sensing: the kidney



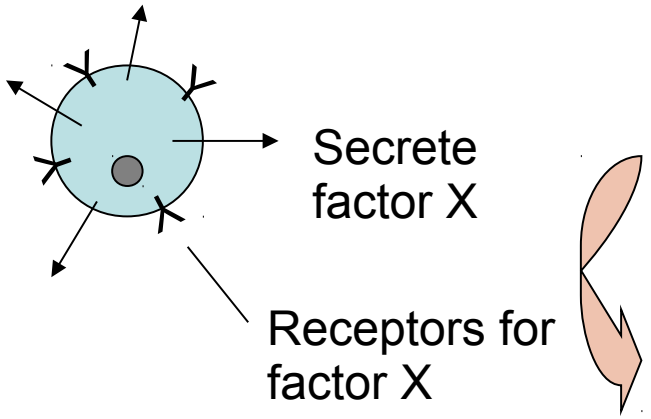
These cells show only a low level of Gal4 Wnt-replacing reporter

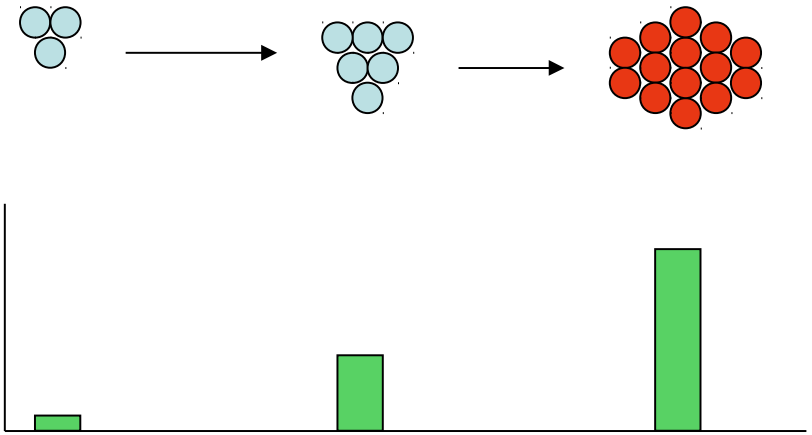
This mimics Wnt signalling even in the absence of Wnts

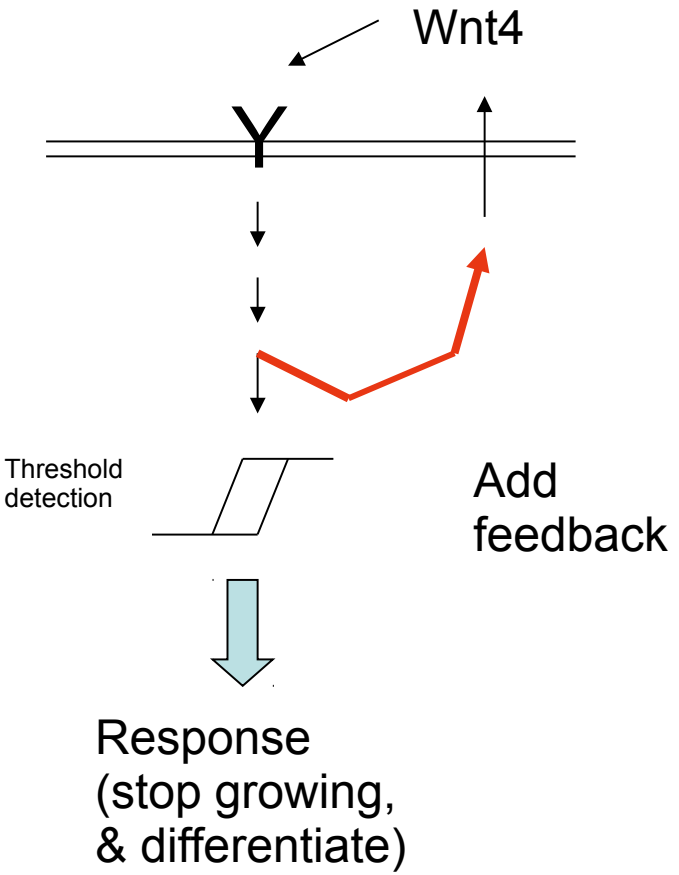
Ref: Davies JA (2005) *Mechanisms of morphogenesis*

Kidney model

Paracrine signalling:





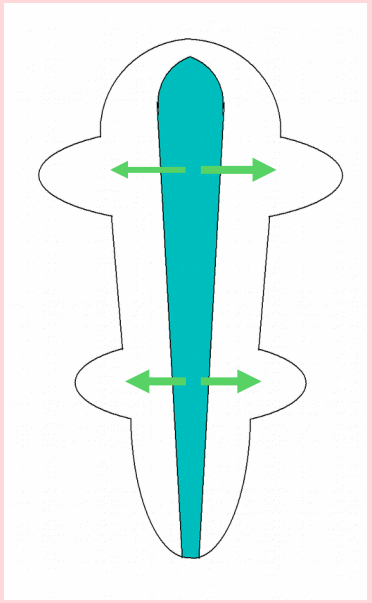


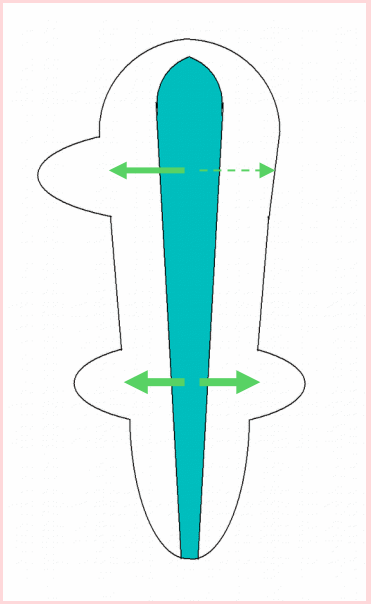
"Are we big enough for that other tissue?"

- The trophic theory

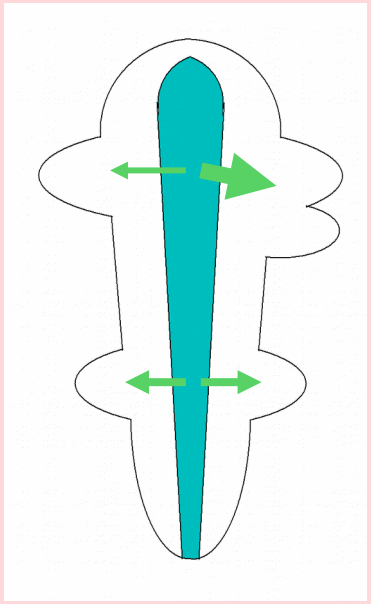
Innervation of chick limbs:

Hamburger V (1934) J Exp Zool 68: 449-494; Hamburger V (1939) Physiol Zool 12: 268-284



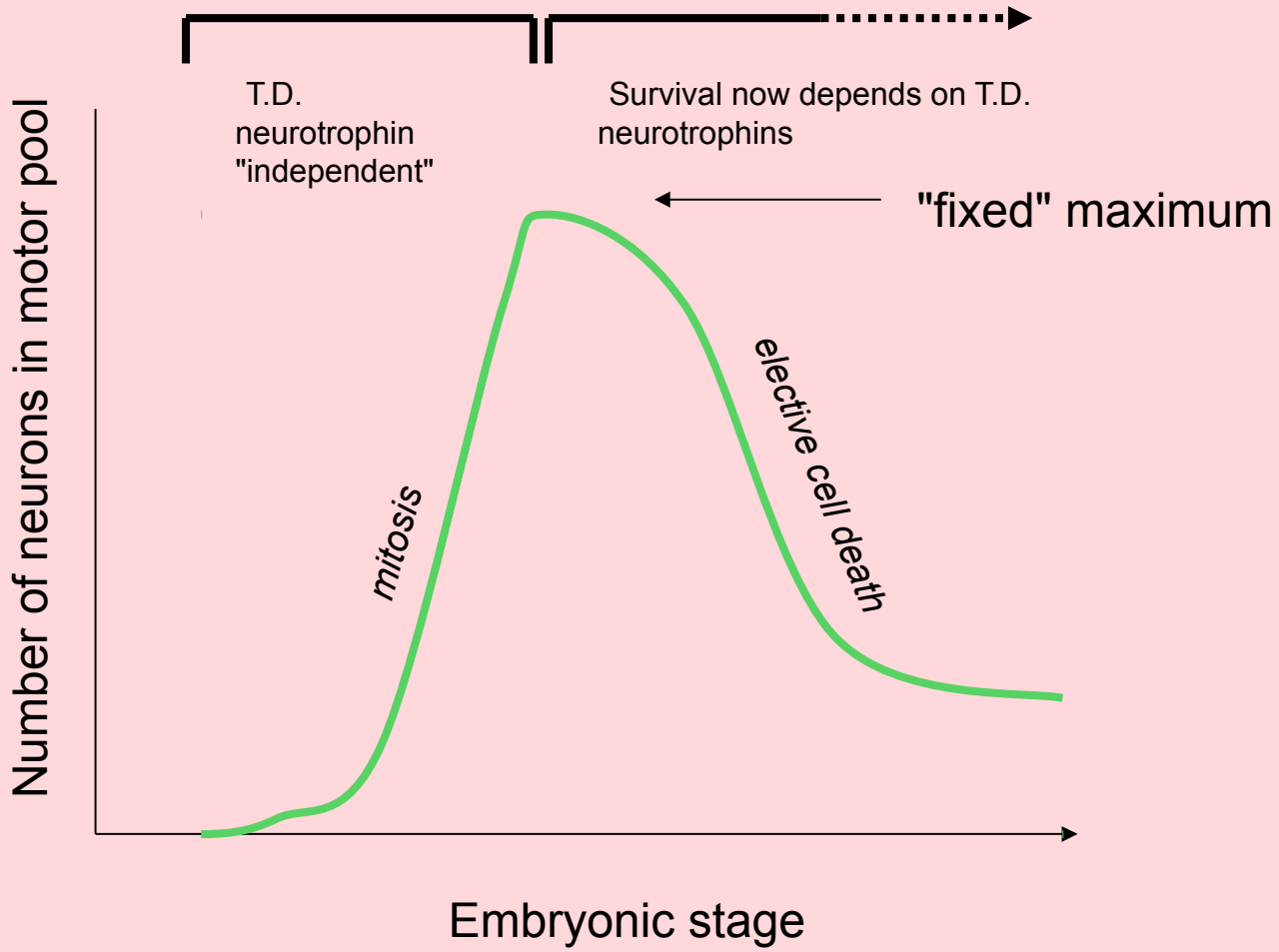


Fewer neurons when target field is reduced



More neurons when target field is increased

Time course of neuronal development:

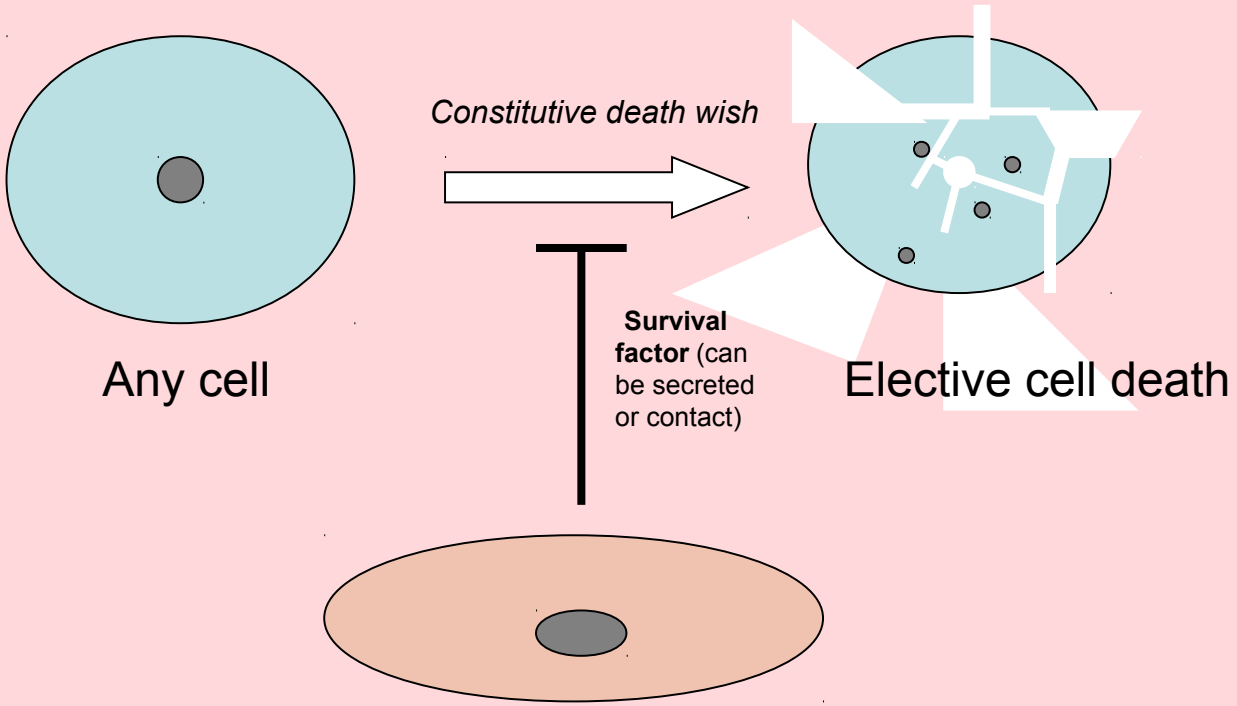


Neurotrophins:

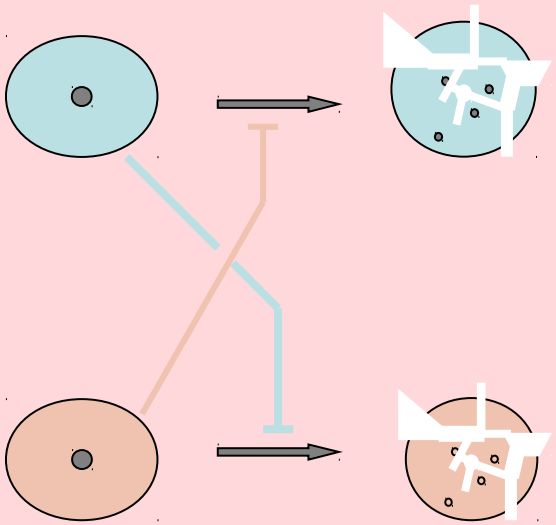
- NGF
- BDNF
- NT-3
- GDNF
- CNTF
- HGF

This is not just a neuronal story…

The Trophic Theory: (Martin Raff)



Within a tissue:



Component 1

Component 2

Between tissues: