

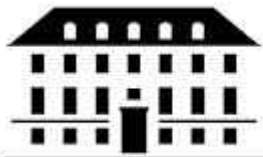


The migration of biological cells

Folkeuniversitetet: News from NBIA
Lecture 1

Niels Bohr Institute
28 October 2013

Søren Vedel



The Niels Bohr
International Academy

Outline

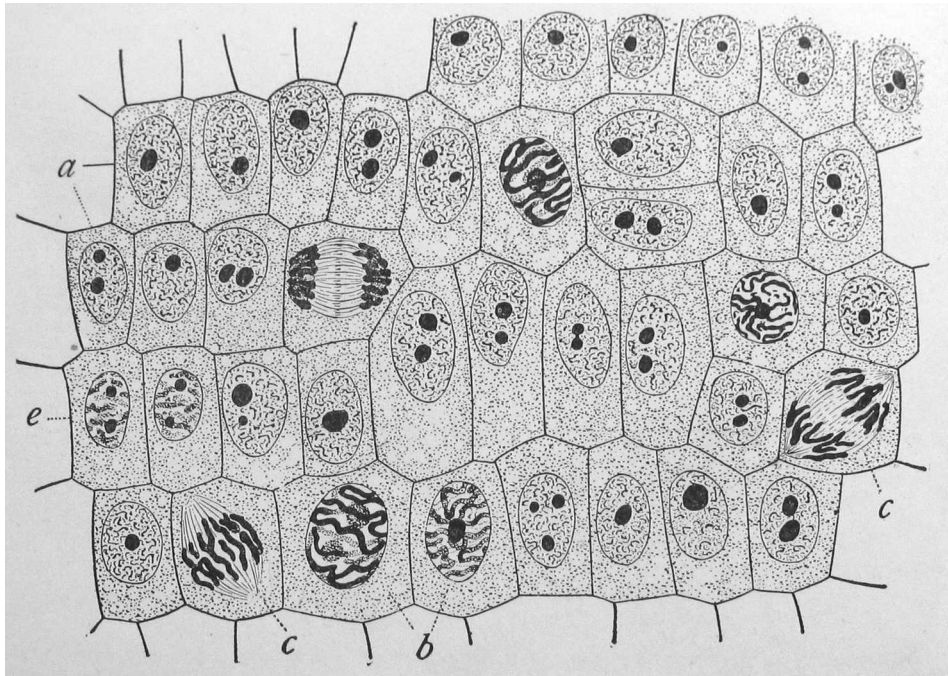
Physics in biology

Migration (movement) of single cells

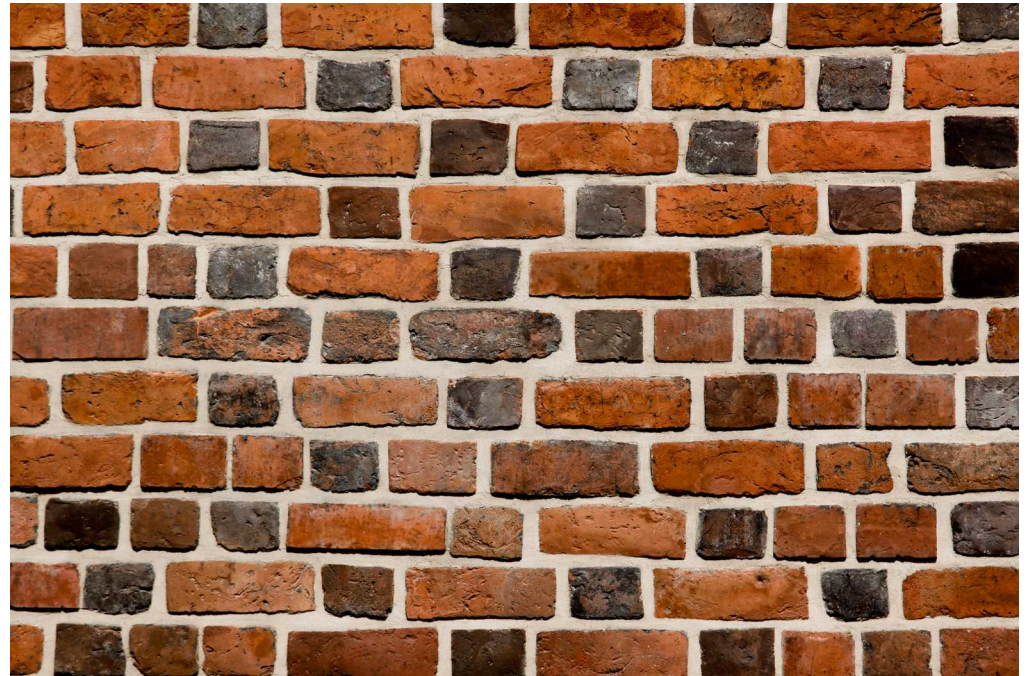
Collective migration

Physics in biology

Biological cells: the bricks of life

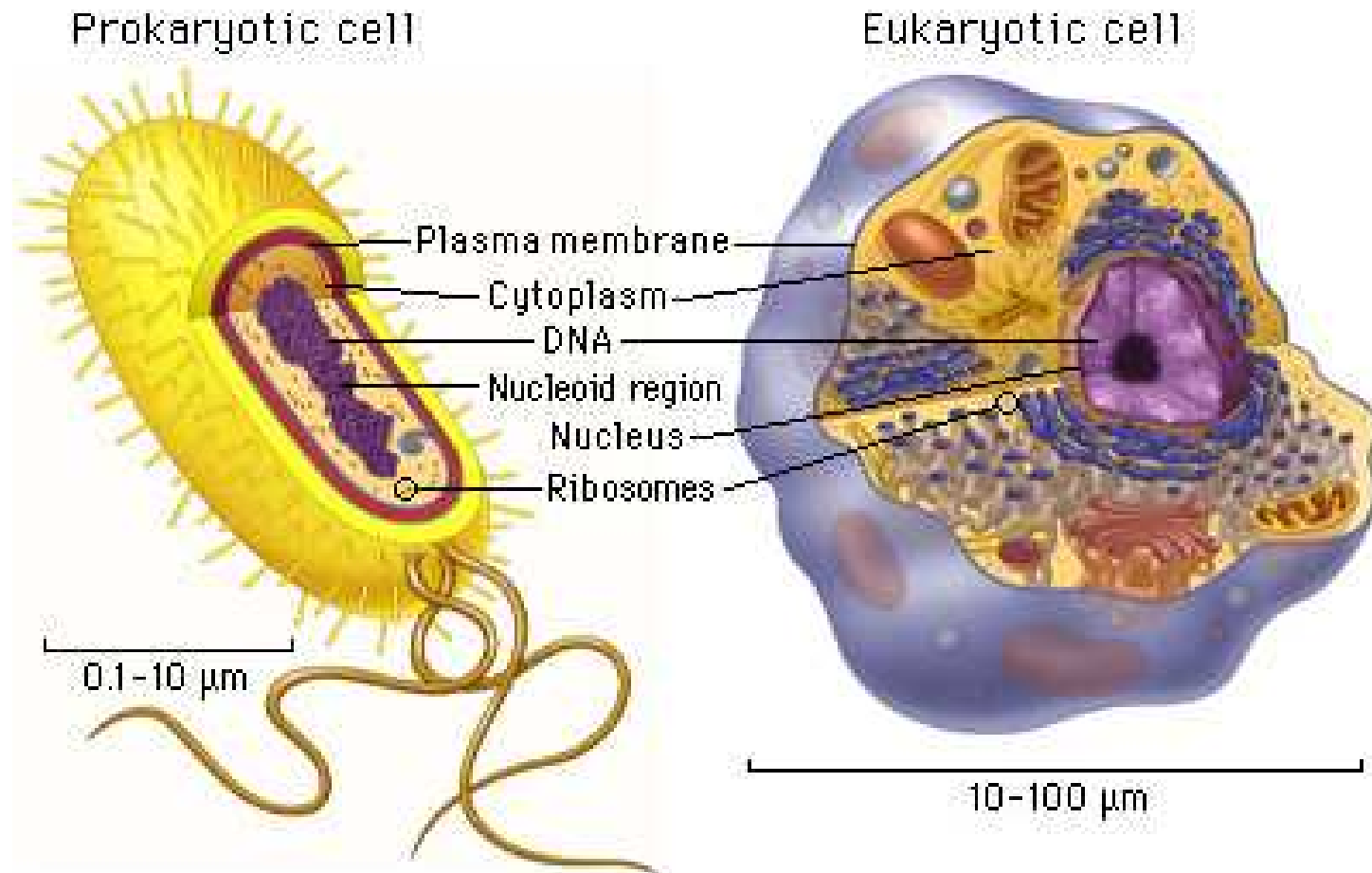


Wilson, Edmund B. (1900) The cell in Development and Inheritance (second edition ed.), New York: The Macmillan Company



http://upload.wikimedia.org/wikipedia/commons/d/d1/Brick_wall_close-up_view.jpg

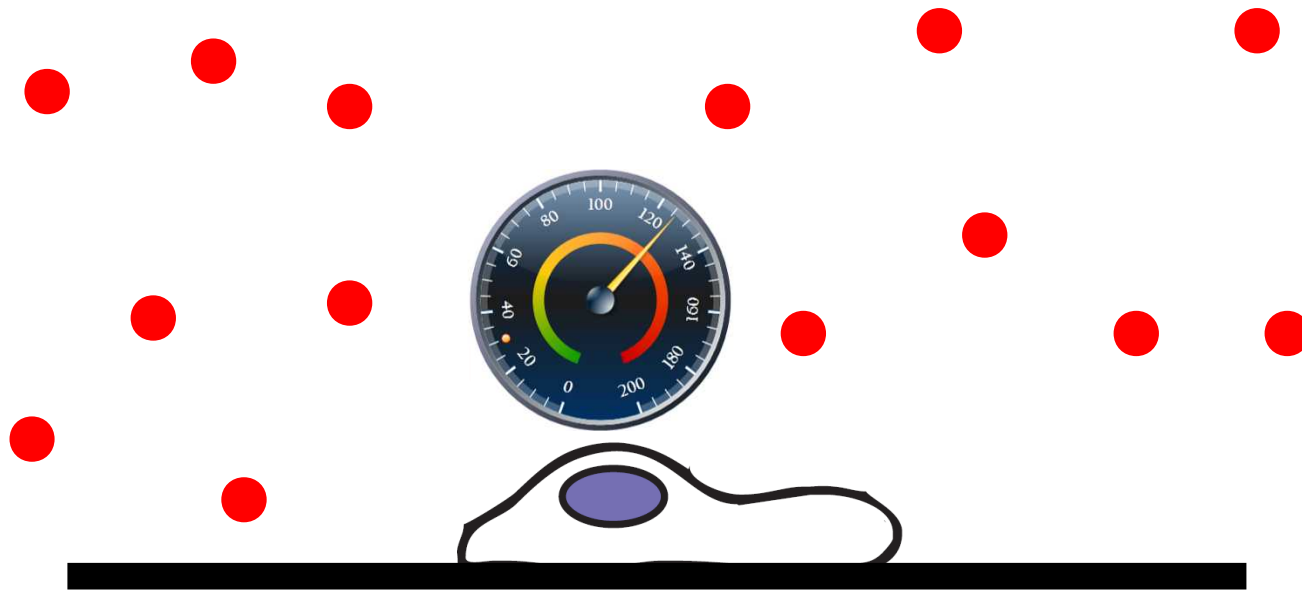
What is a cell?



http://www.phschool.com/science/biology_place/biocoach/images/cells/allcell.jpg

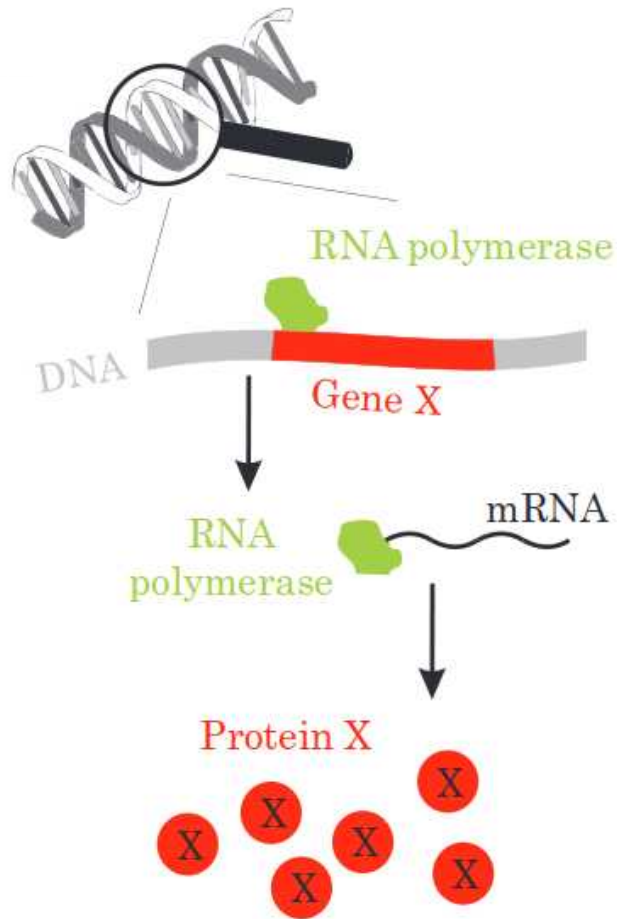
Cells are constantly doing something: sensing and reacting

Signal

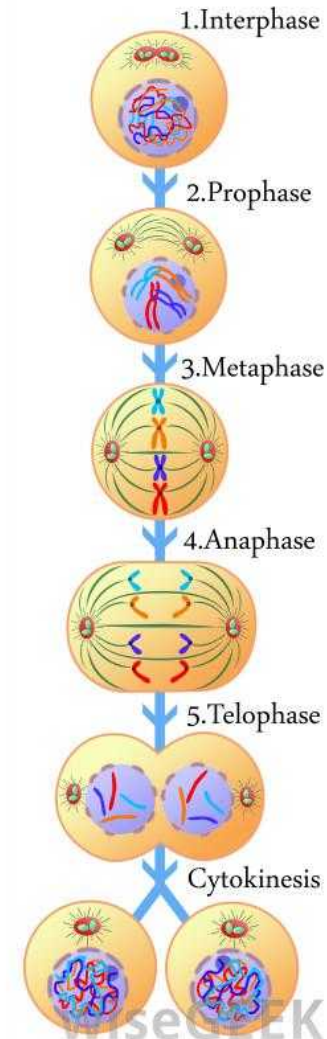


Cells are constantly doing something: “Housekeeping”

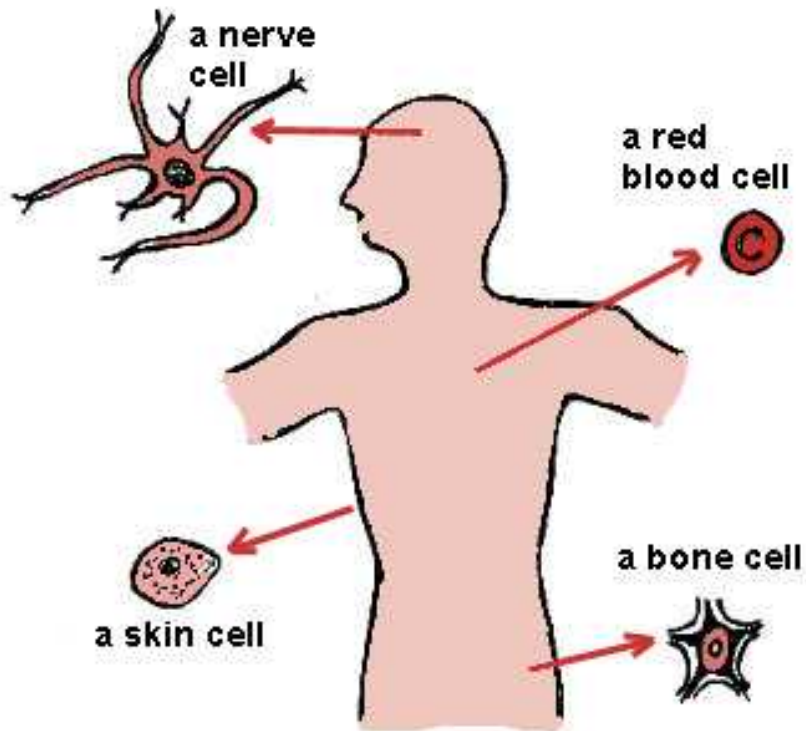
Making new proteins



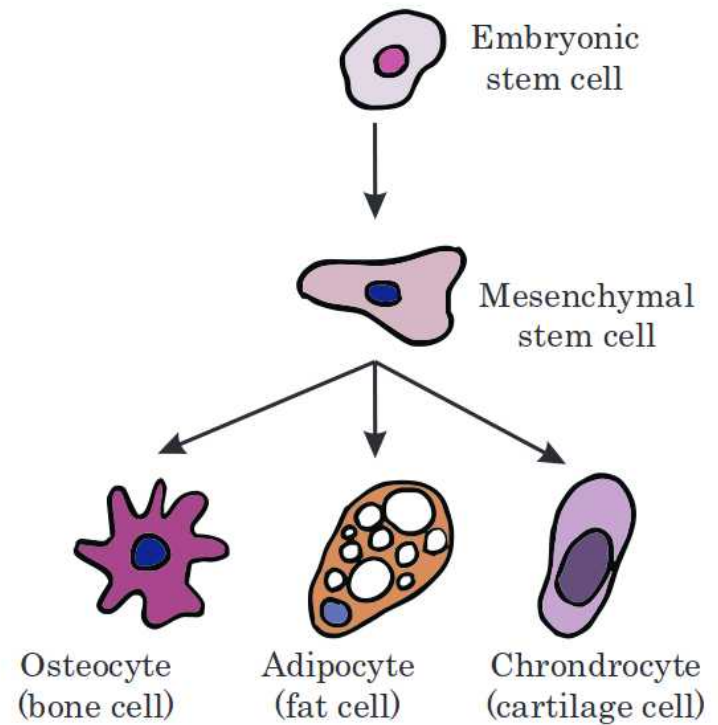
Cell division



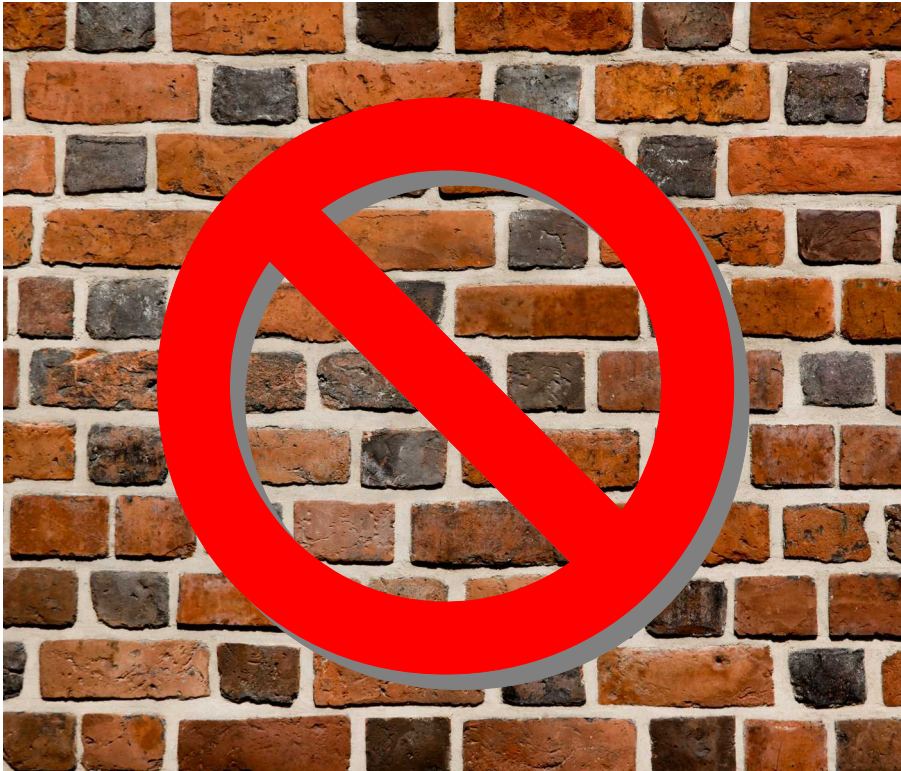
Cells coordinate their function in multicellular organisms



<http://www.saburchill.com/chapters/chap0107.html>



Biological system → House built of interacting computers



http://upload.wikimedia.org/wikipedia/commons/d/d1/Brick_wall_close-up_view.jpg



<http://www.voont.com/files/images/slideshow/20-mindblowing/4.jpg>

Typical numbers in a human

Starts from a single cell!

~ 5×10^{10} cells

~ 10^{14} divisions during life time

~ 200 different cell types

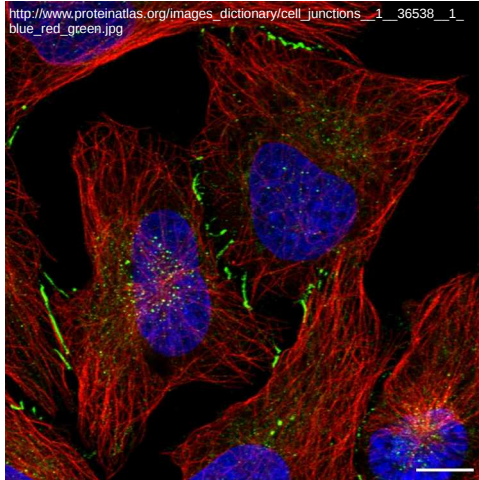
~ 2×10^4 genes

~ 10^8 mutations during life time



Recent explosion in biological data by technological advances

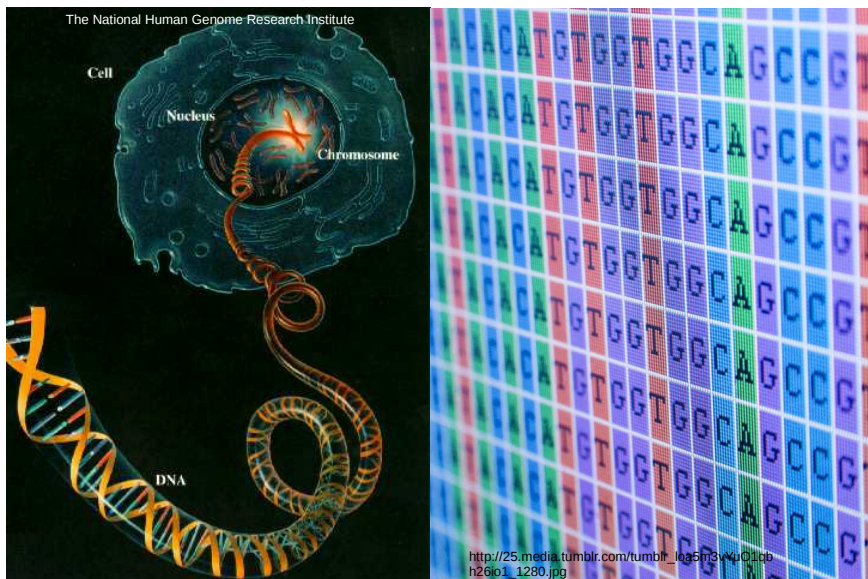
Fluorescent tags



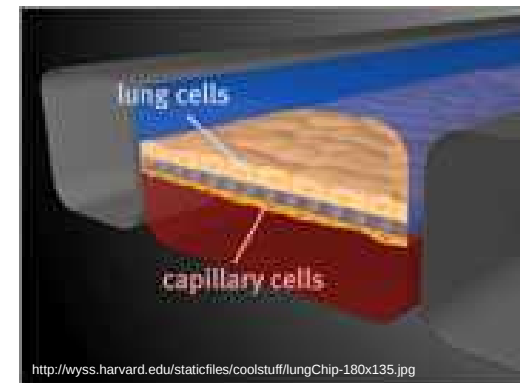
Molecular “snapshots” of what the cell is doing



DNA sequencing



Well-controlled experiments

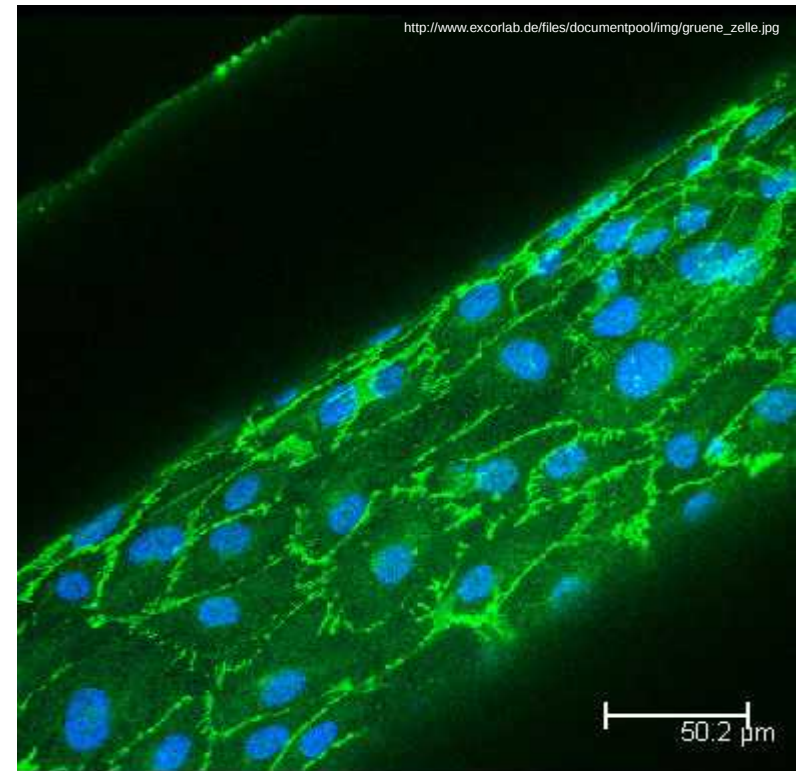


Is life a chemical phenomenon?

Gene → function?



Very well-coordinated
multicellular function?



Example of biological complexity

Mouse



http://bioweb.uwlax.edu/bio203/s2009/smith_meg2/images/House%20Mouse.jpg

~30.000 genes

Rice



http://upload.wikimedia.org/wikipedia/commons/7/79/Oryza_sativa_Rice_sprouts_ja01.jpg

~51.000 genes

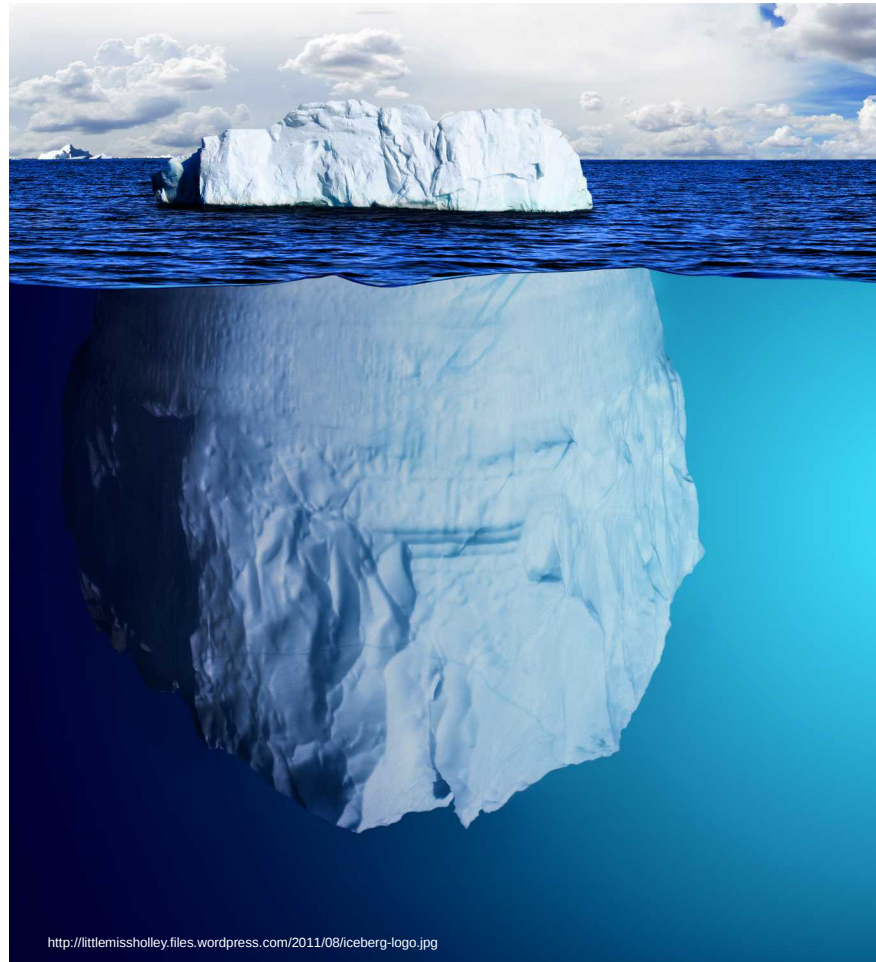
Human being



http://upload.wikimedia.org/wikipedia/commons/thumb/6/6d/Niels_Bohr.jpg/250px-Niels_Bohr.jpg

~20.000 genes

We're only SEEING the tip of the iceberg



<http://littlemissholley.files.wordpress.com/2011/08/iceberg-logo.jpg>

Biology is more than the sum of its parts

“The collapse of the doctrine of one gene for one protein, and one direction of causal flow from basic codes to elaborate totality, marks the failure of reductionism for the complex system that we call biology. . . The key to complexity is not more genes, but more combinations and interactions generated by fewer units of code and many of these interactions [...] cannot be predicted from the separate underlying parts alone.”

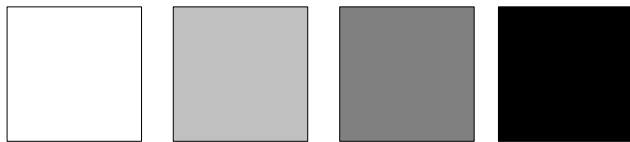
- Stephen Jay Gould, *Humbled by the genome's mysteries*, New York Times , Feb. 19 (2001).

$$1 + 1 \geq 2$$

Emergent properties from interactions

The observed behavior at the system level is a function of the interactions among the units rather than a function inherent to each unit.

Their combination is not just the average



=

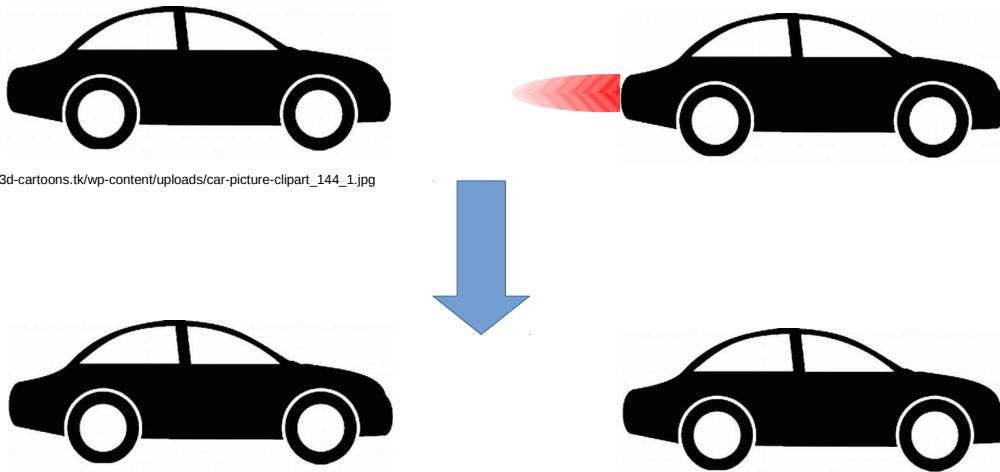


http://i.telegraph.co.uk/multimedia/archive/01529/marilyn_1529599i.jpg

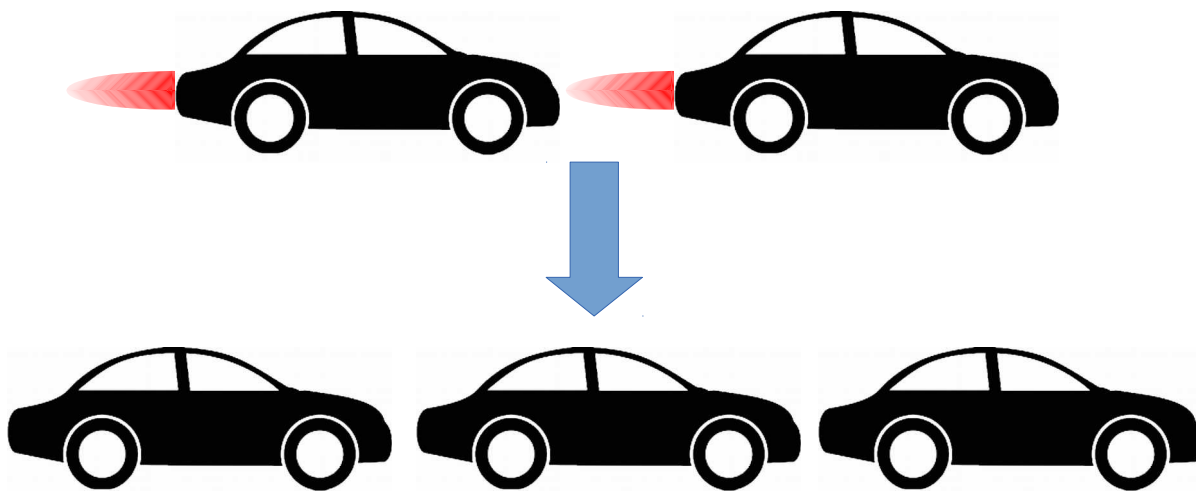
Combination mildly dependent on unit properties

Example of emergent properties: traffic jam

Proper safety distance → no traffic jam



Improper safety distance → traffic jam

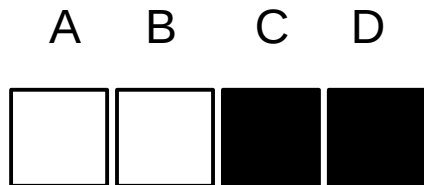


Physics in biology

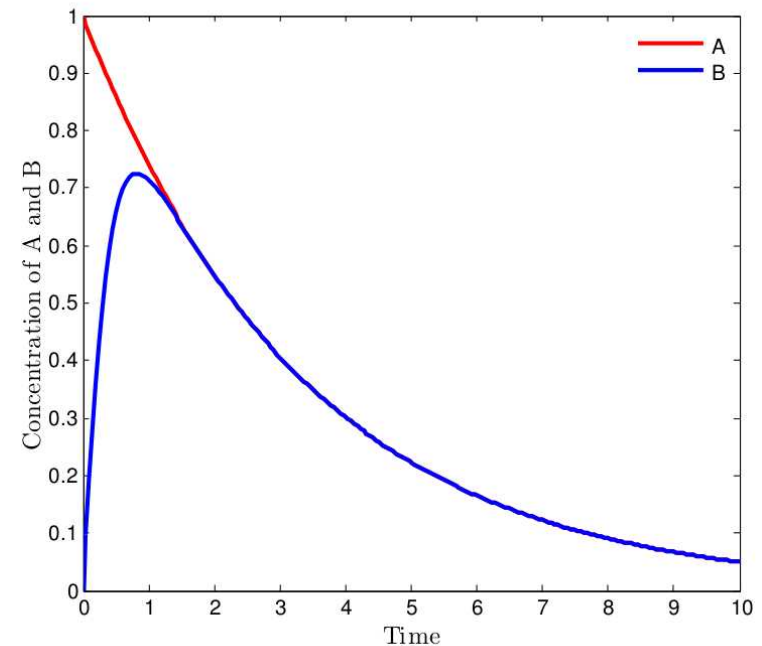
Molecular biologist:
binary information



or

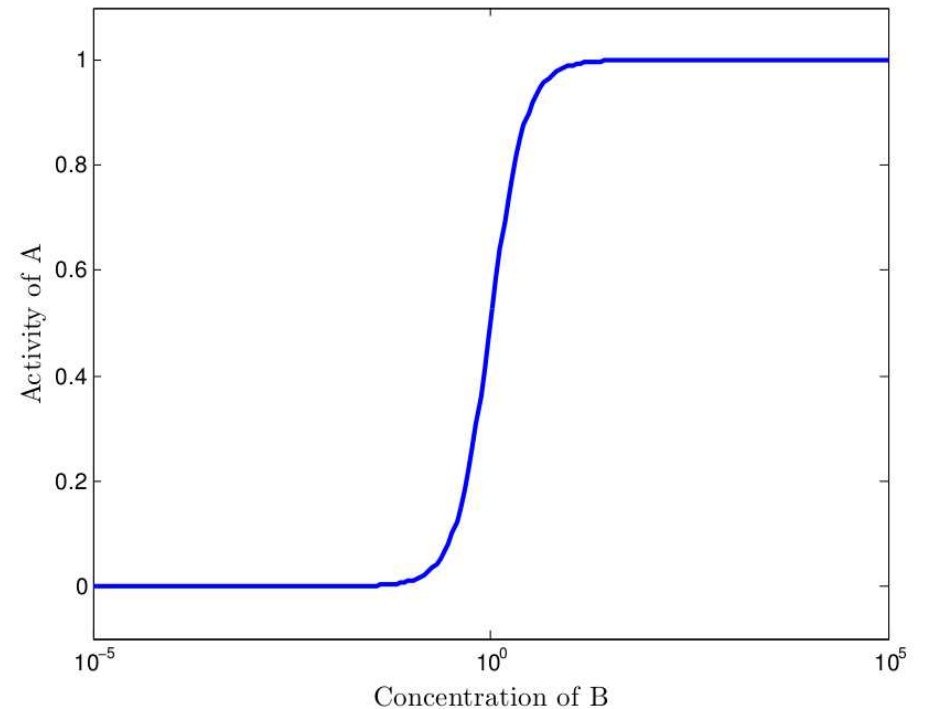
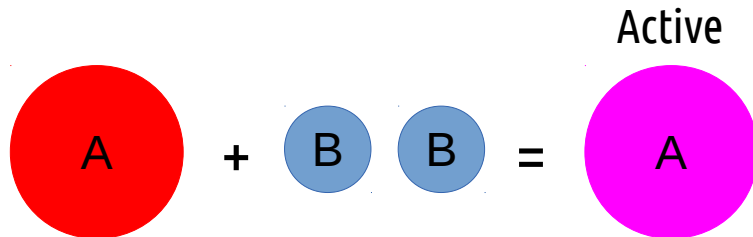


Physicist:
Dynamical information
out of interactions



Emergent properties in biology: From dynamics to function

A molecular switch



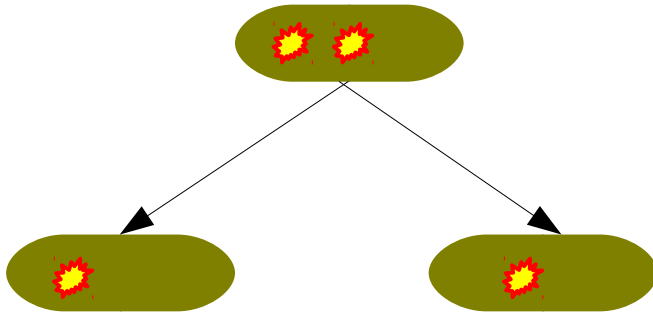
Interactions of molecules form functional entities or modules

Emergent properties in biology: From dynamics to function, continued

A population survival strategy

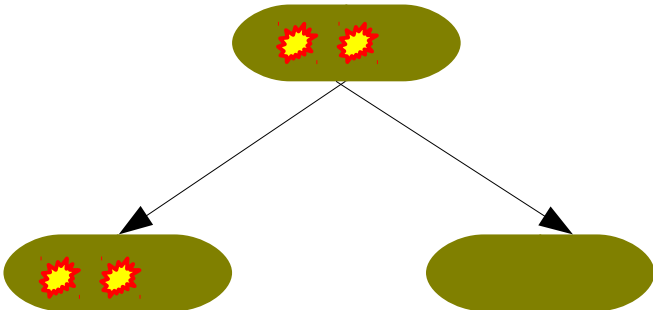


Symmetric damage division



Everybody has the same level of damage.
No variation within population.

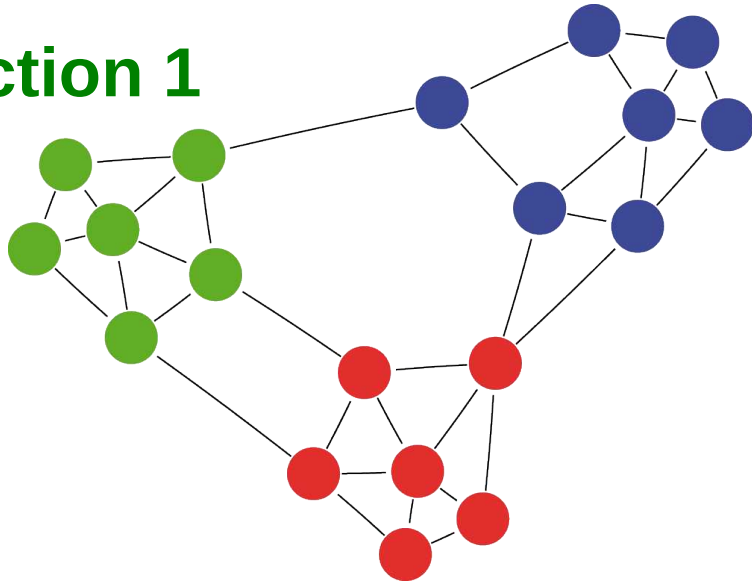
Asymmetric damage division



Different levels of damage dependent on lineage.
Average damage lower than for symmetric division.

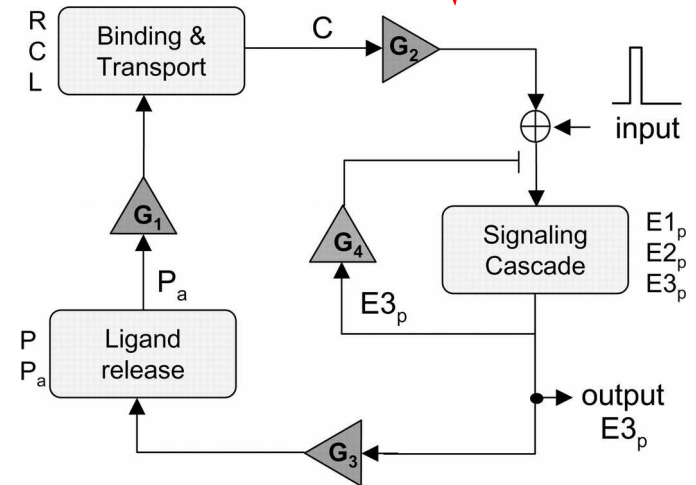
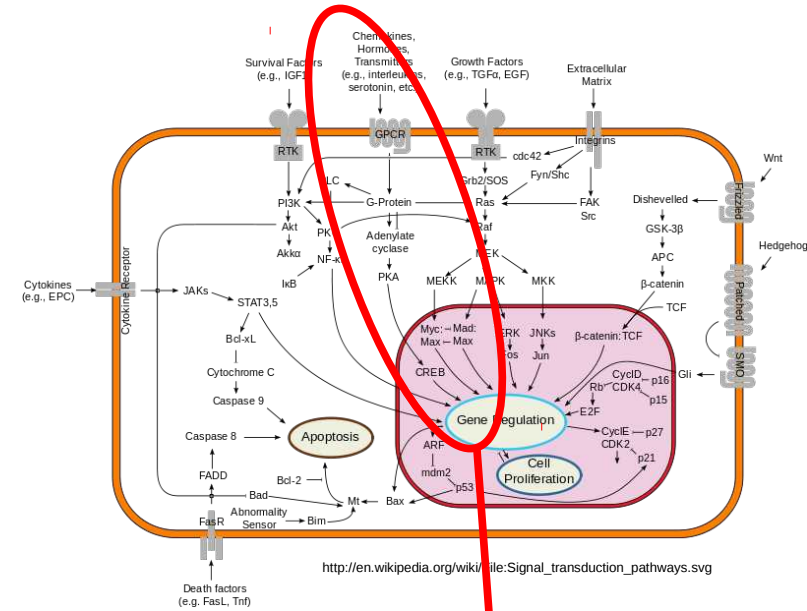
From single function to "behavior" → from unit to system

Function 1



Function 2

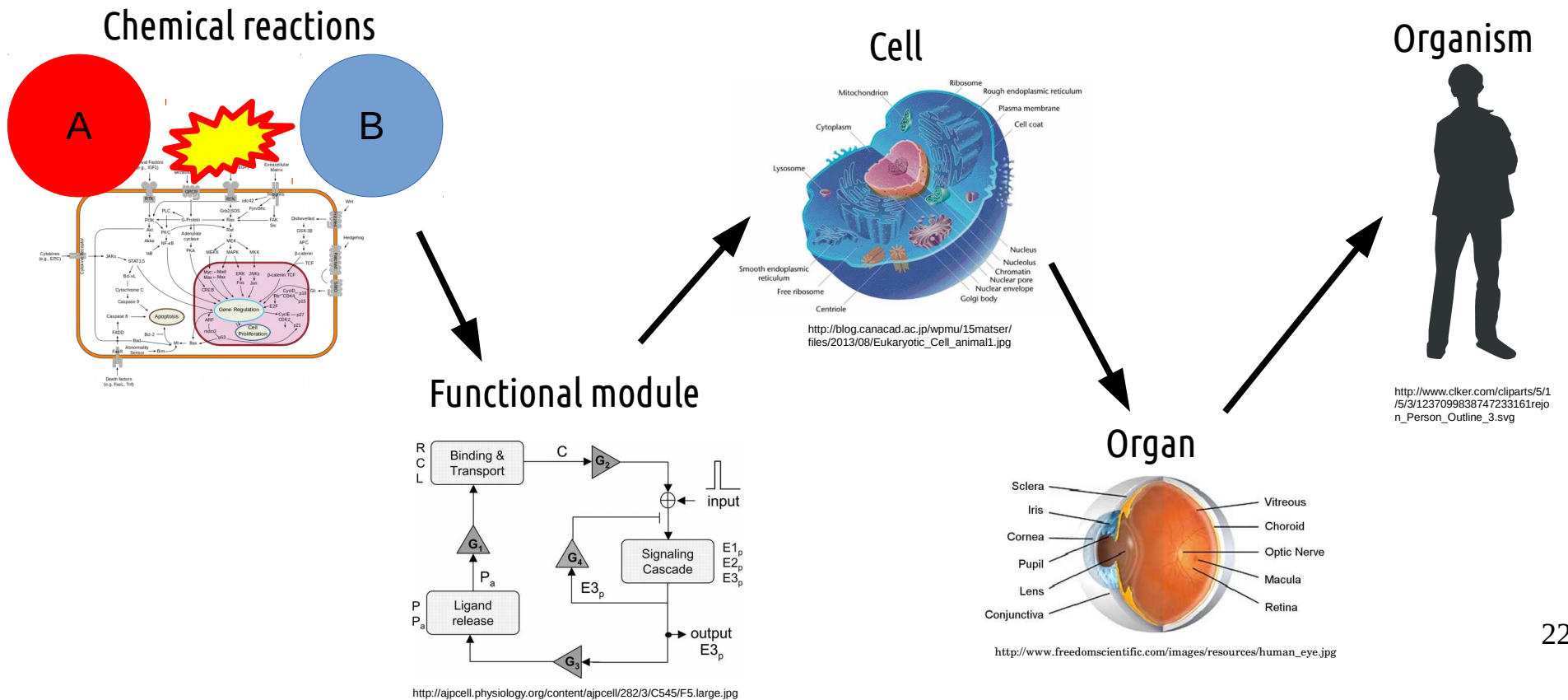
Function 3



Life is physics?

Chemistry is underlying most biological behavior, but seems to be a means of transmitting and processing information →

Behavior arises from the interactions at each level



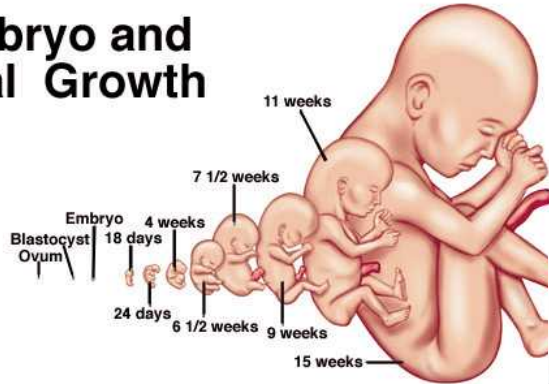
Migration of single cells

Physiological situations of cell migration

Embryonic development

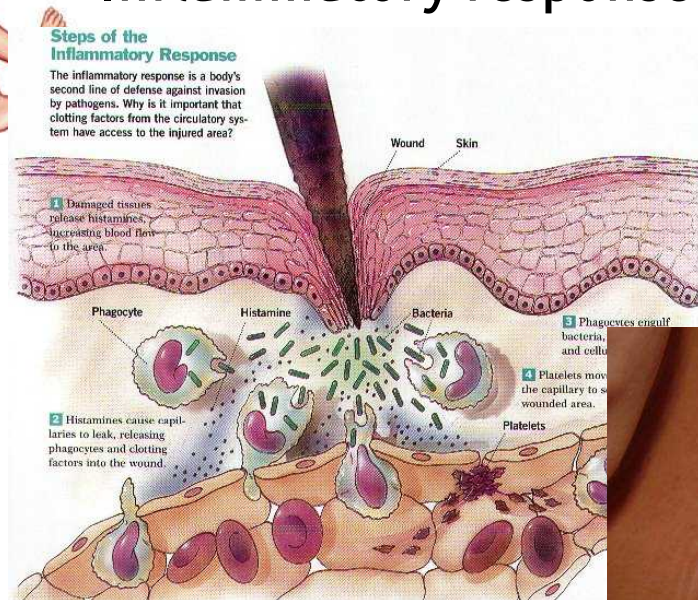
Byer/Shainberg/Galliano *Dimensions Of Human Sexuality*, 5e. Copyright © 1999. The McGraw-Hill Companies, Inc. All Rights Reserved.

Embryo and Fetal Growth



Inherently "social"

Inflammatory response



<http://www.inflammationreliefguide.com/wp-content/uploads/2011/10/Inflammatory-Response.jpg>

Wound healing

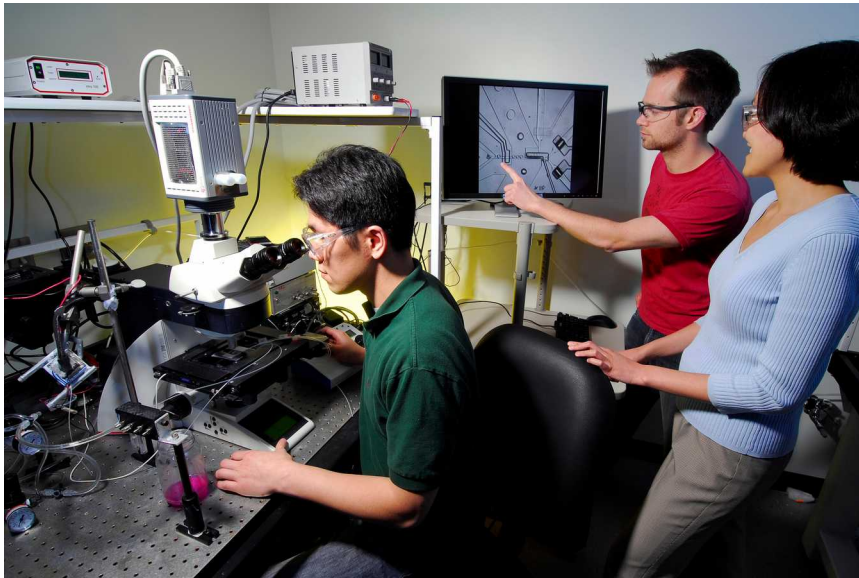


http://www.todaysplanet.com/pg/beta/lizardlover/pic/vikki_big_bite_wound.jpg

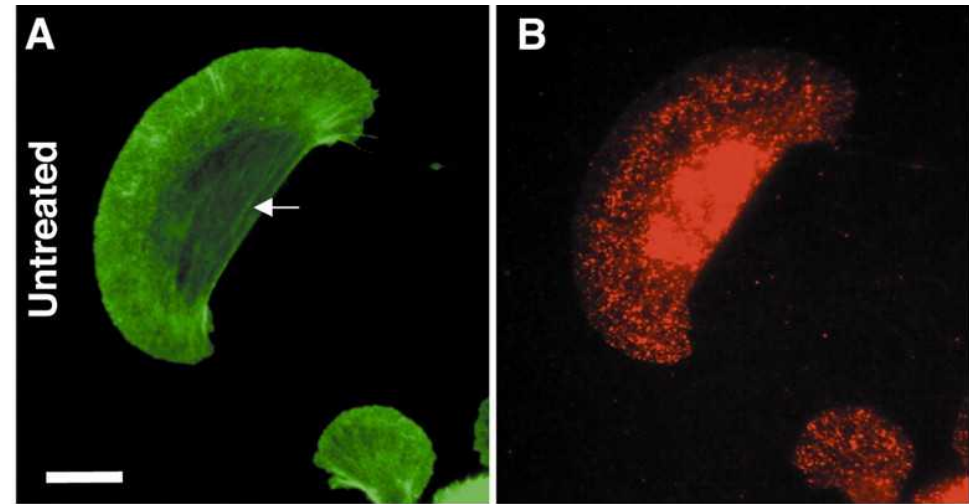
Experiments

Microscopy w/ special device for cells

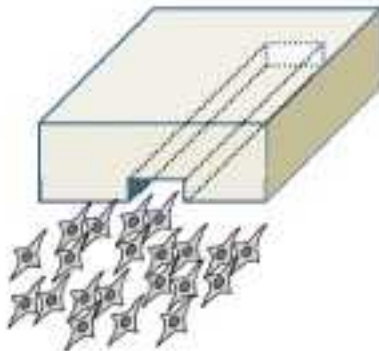
Cell lines, sometimes fluorescent tags



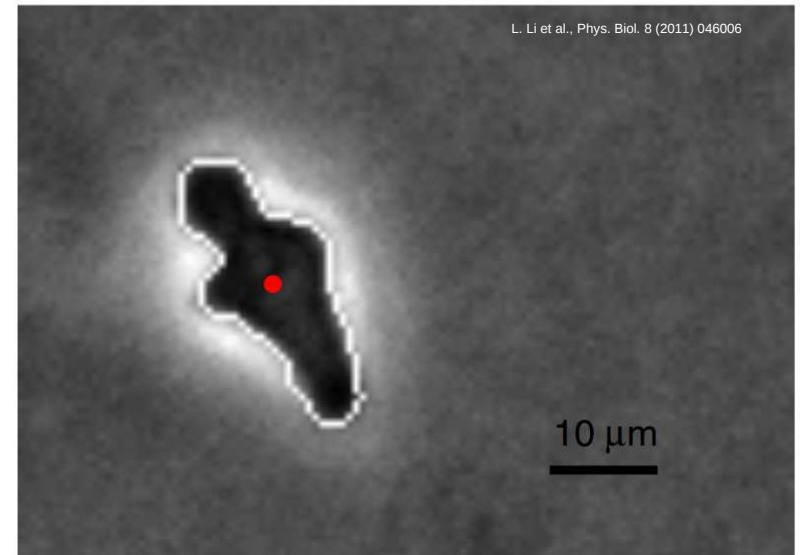
http://www.gtresearchnews.gatech.edu/wp-content/uploads/2009/11/microchipP095_hires.jpg?phpMyAdmin=387c4b701e2at54367afa



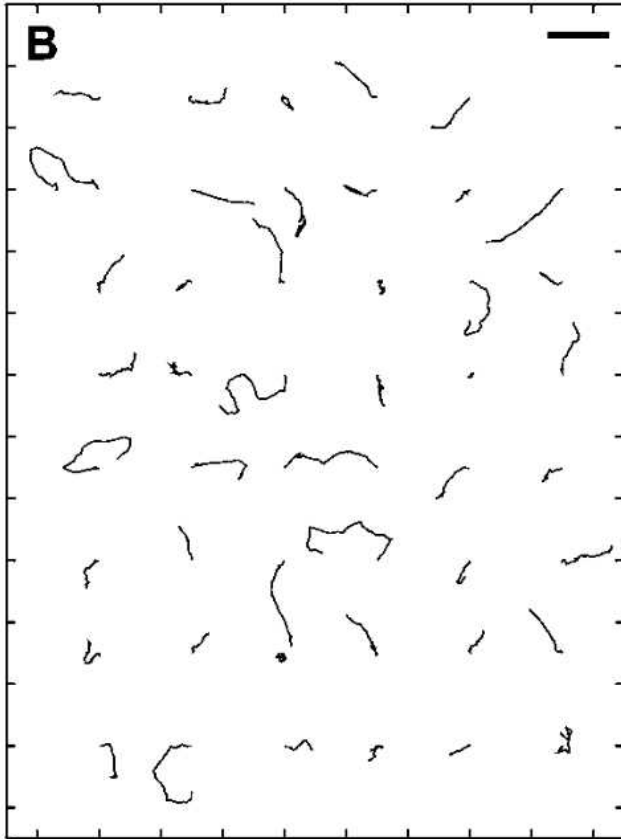
A. D. Doyle & J. Lee, *J. Cell Sci.*, 2005 *J Cell Sci* 118, 369-379.



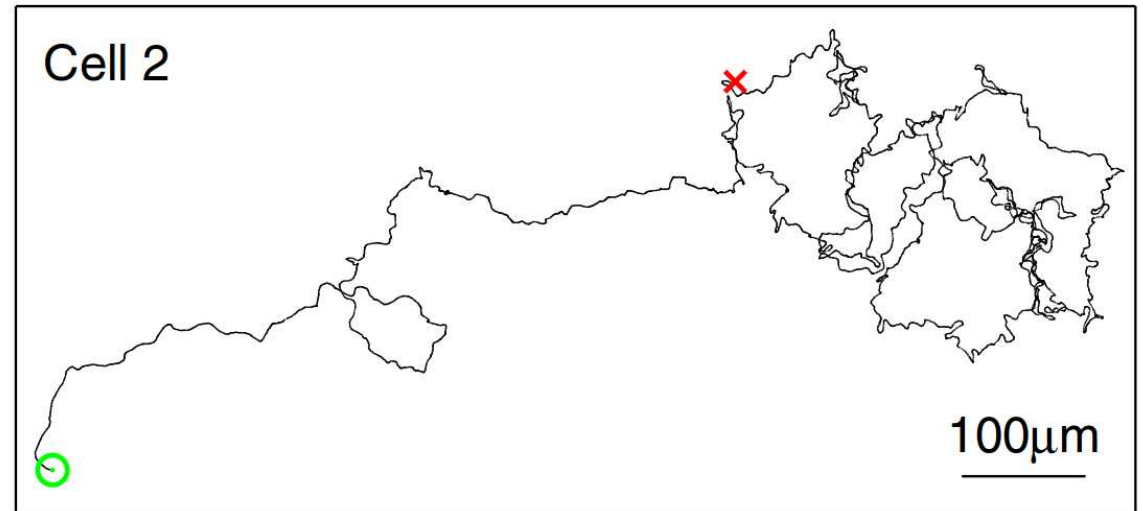
K. Uto et al (2012) *Sci. Technol. Adv. Mater.* 13 064207



Experimental examples



D. Selmecki et al., Biophys. J., 89 (2005), 912-931



L. Li et al., Phys. Biol. 8 (2011) 046006

Single-cell migration characteristics

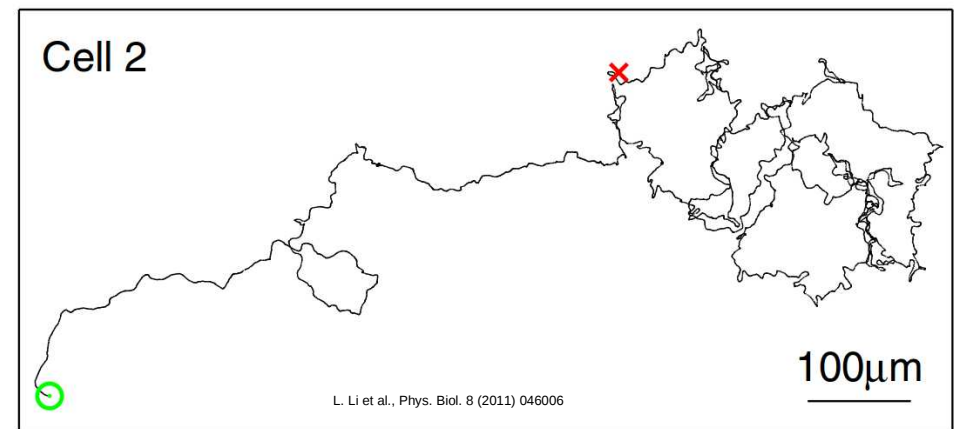
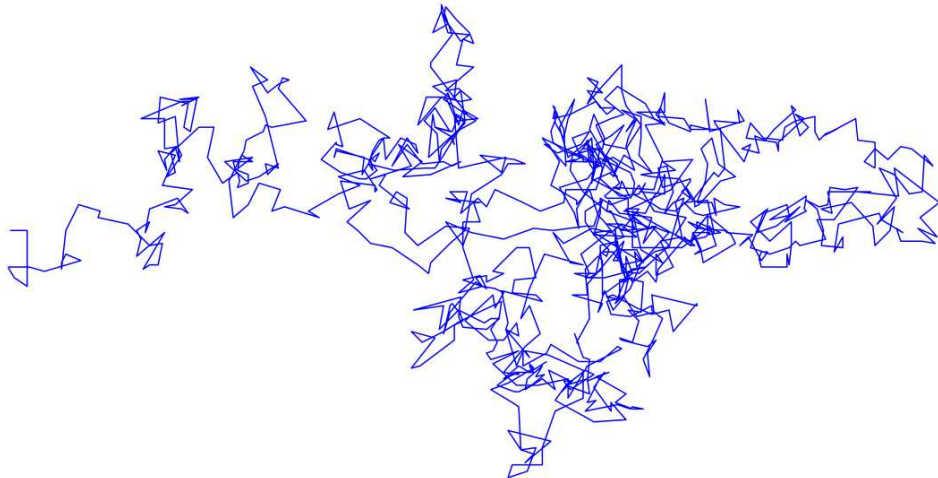
Seemingly random

Directional stability:

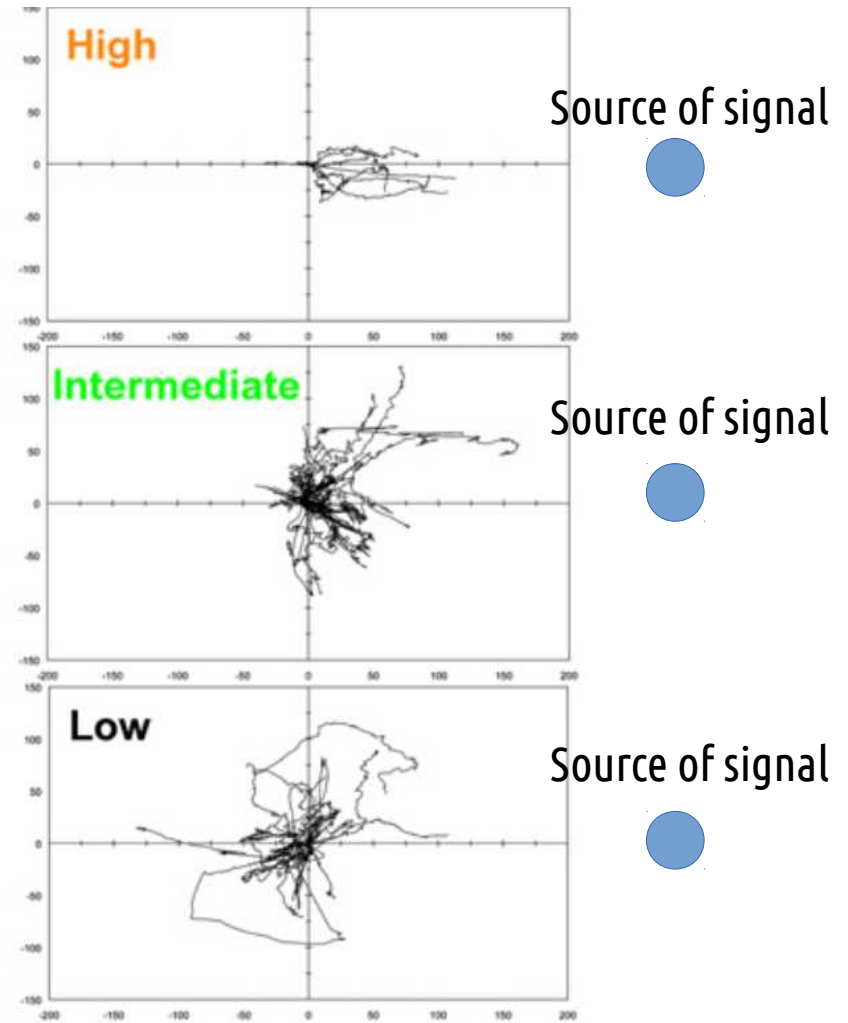
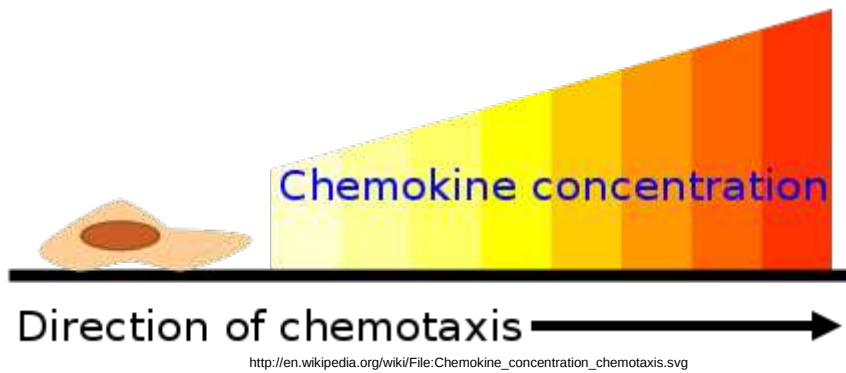
The cell maintains its direction for some time (~ 30 min – 1 h)

Otherwise no apparent biases (what's the reason for this movement?)

Unbiased random walk



Chemotaxis: chemical signals bias cell movement



A. T. Melvin et al., Biophys. J., 100, 1893-1901 (2011)

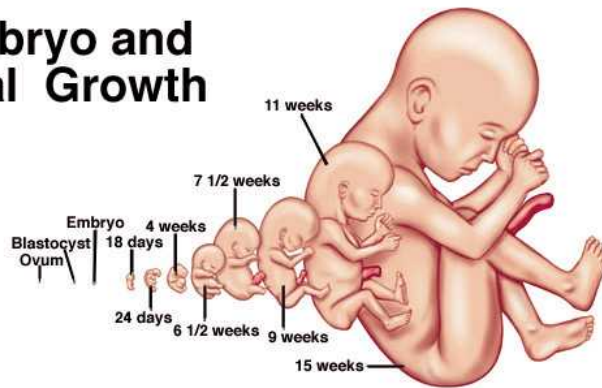
Collective migration

Will present two examples

Development

Byer/Shainberg/Galliano *Dimensions Of Human Sexuality*, 5e. Copyright © 1999. The McGraw-Hill Companies, Inc. All Rights Reserved.

Embryo and Fetal Growth



Wound healing



http://www.todaysplanet.com/pg/beta/lizardlover/pic/vikki_big_bite_wound.jpg

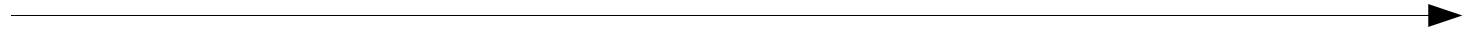
Example I: Collective migration of keratocytes



Keratocytes = fish scale cells

Experiments

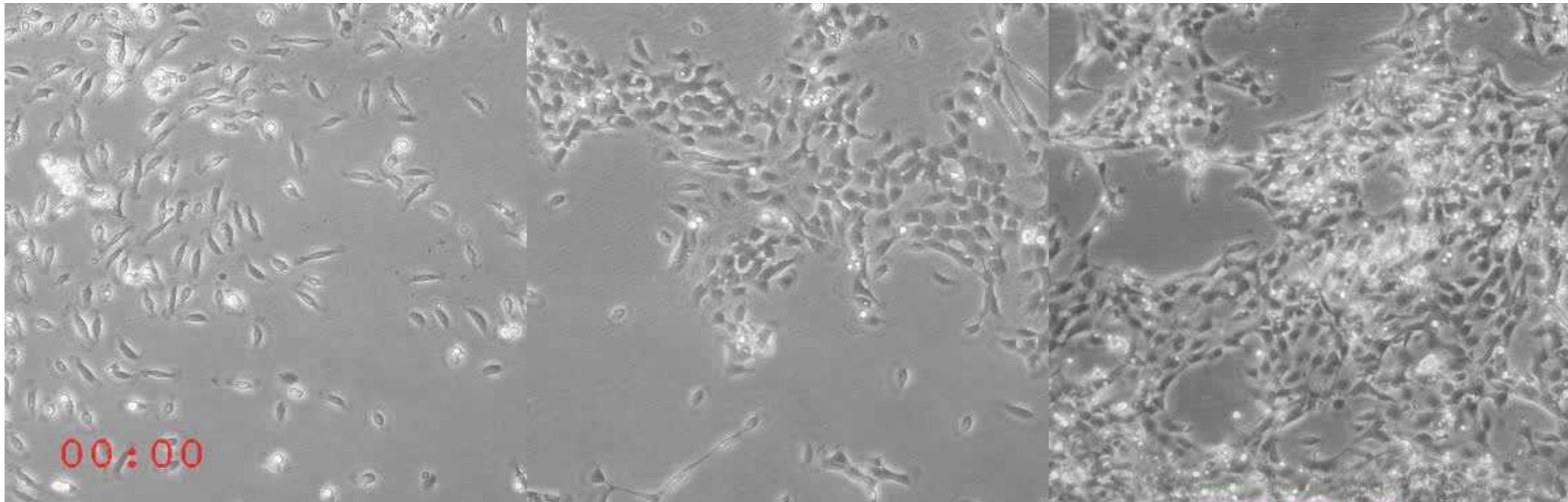
Cell density



Low

Medium

High

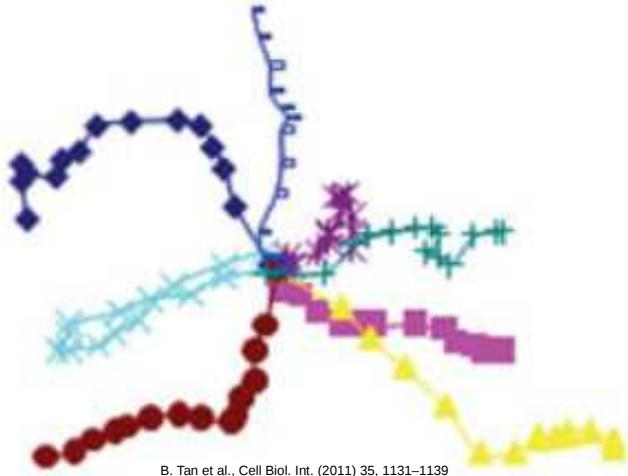


B. Szabó et al., Phys. Rev. E 74, 061908 (2006)

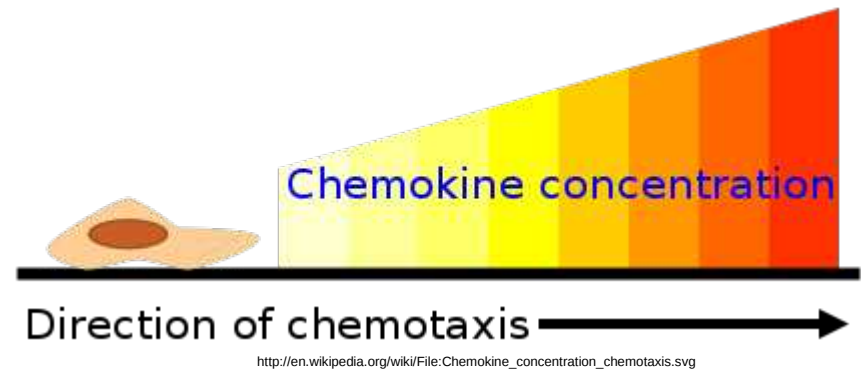
$V \approx 10 \mu\text{m}/\text{min}$

Characteristics

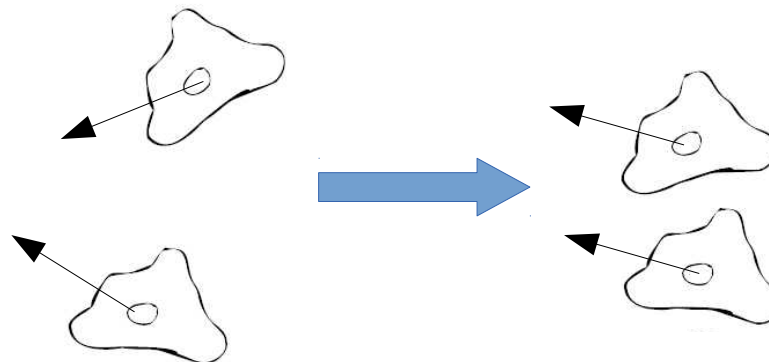
Persistent random motion



Attraction by chemical signal

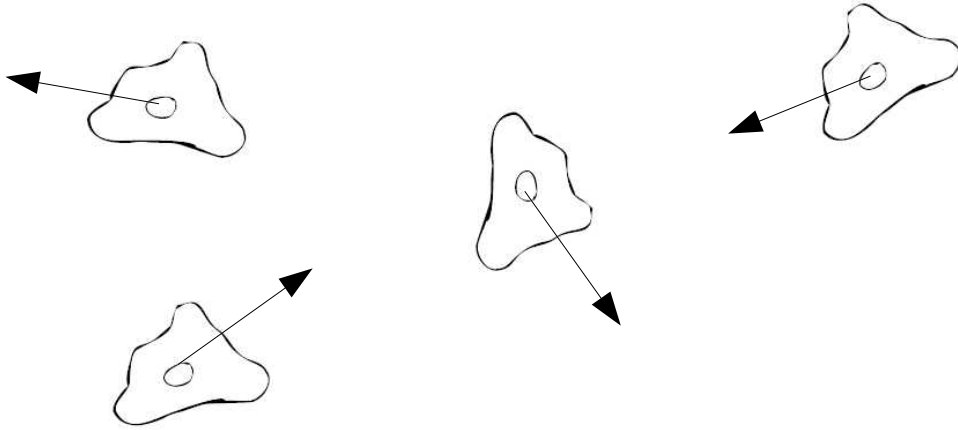


“Stickiness” and alignment

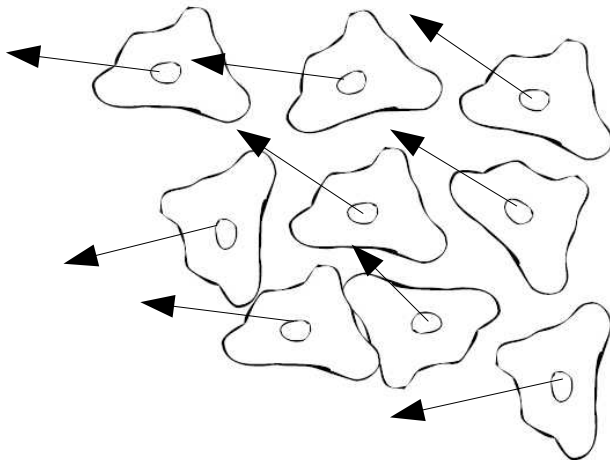


Emergent property: ordered group motion by increasing density

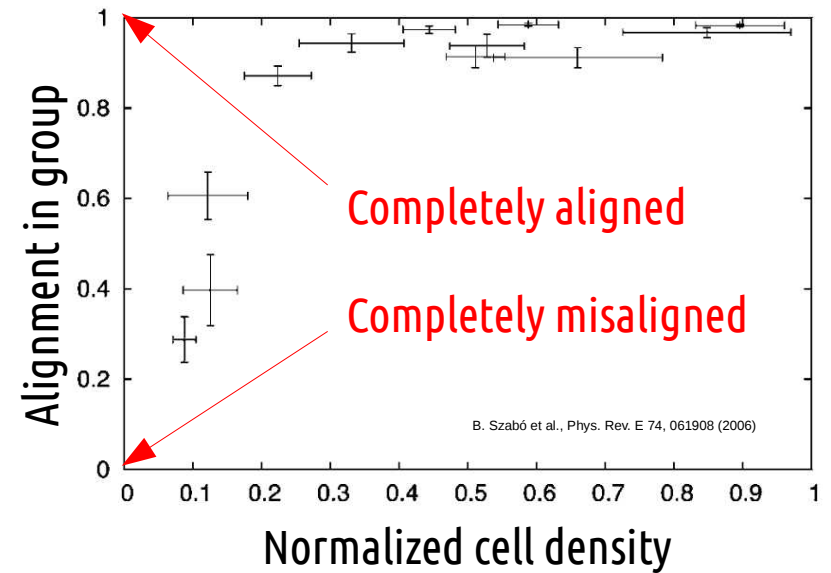
Low density



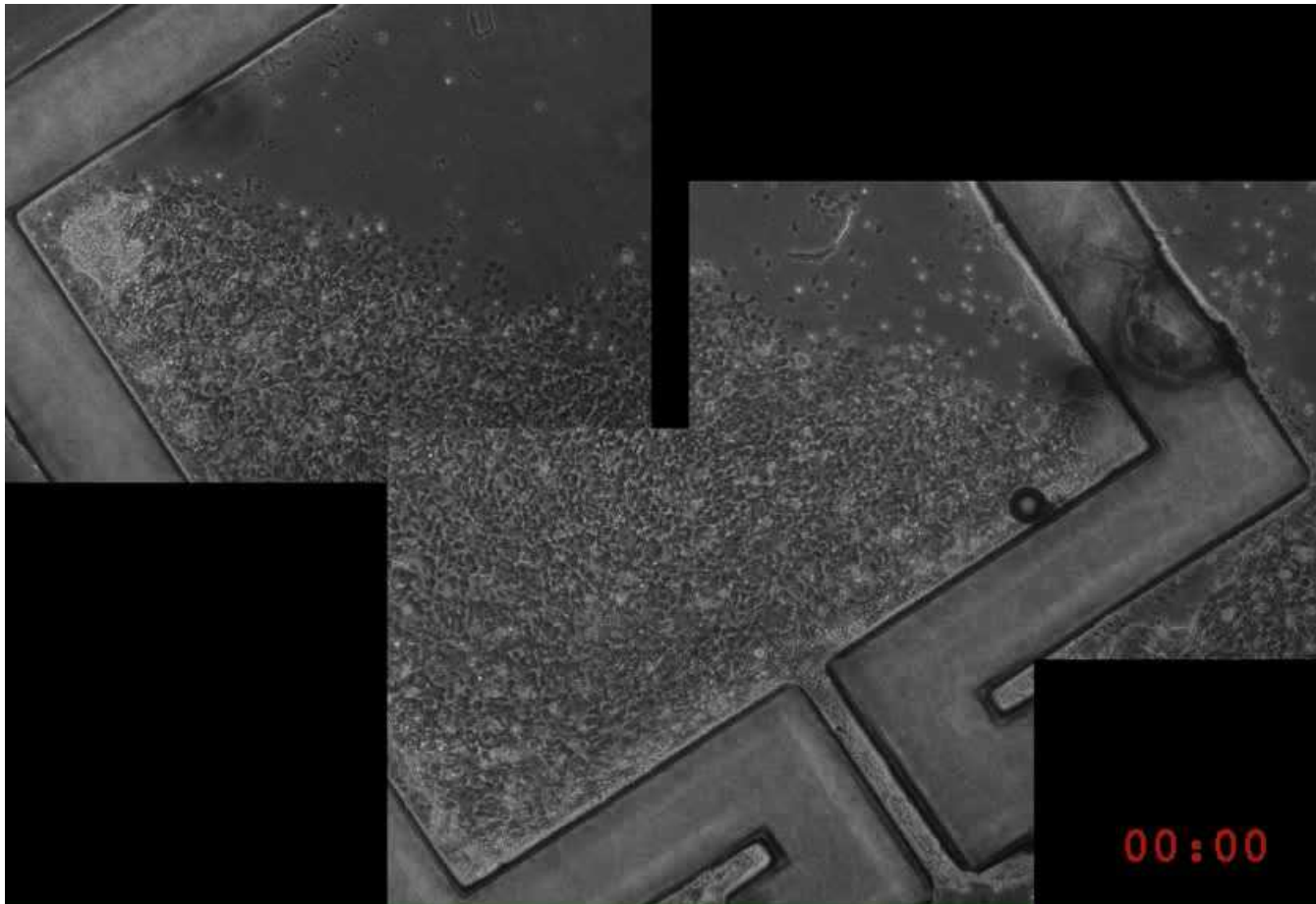
High density



Experimental evidence



Emergent property: unidirectional group motion



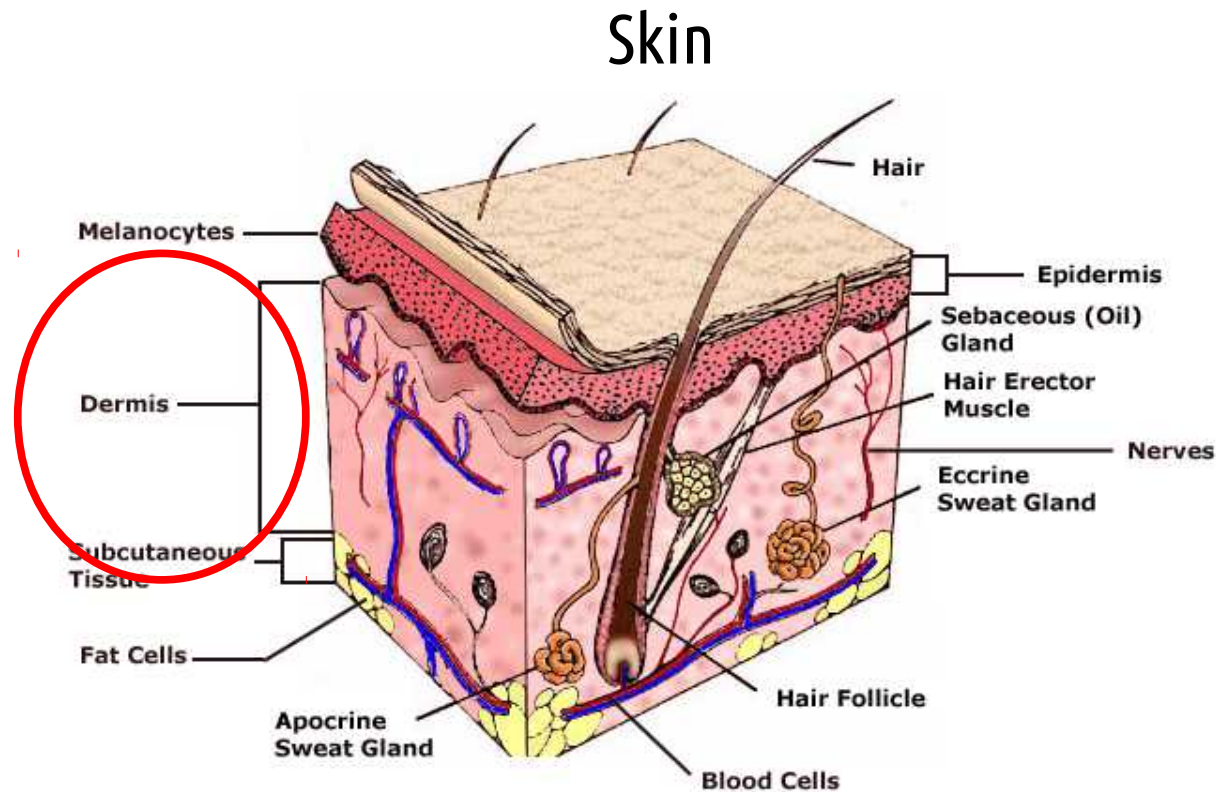
B. Szabó et al., Phys. Rev. E 74, 061908 (2006)

To grow a fish scale, you only need to set
the initial cells in the right direction

Marching desert locusts



Example II: Collective migration of fibroblasts



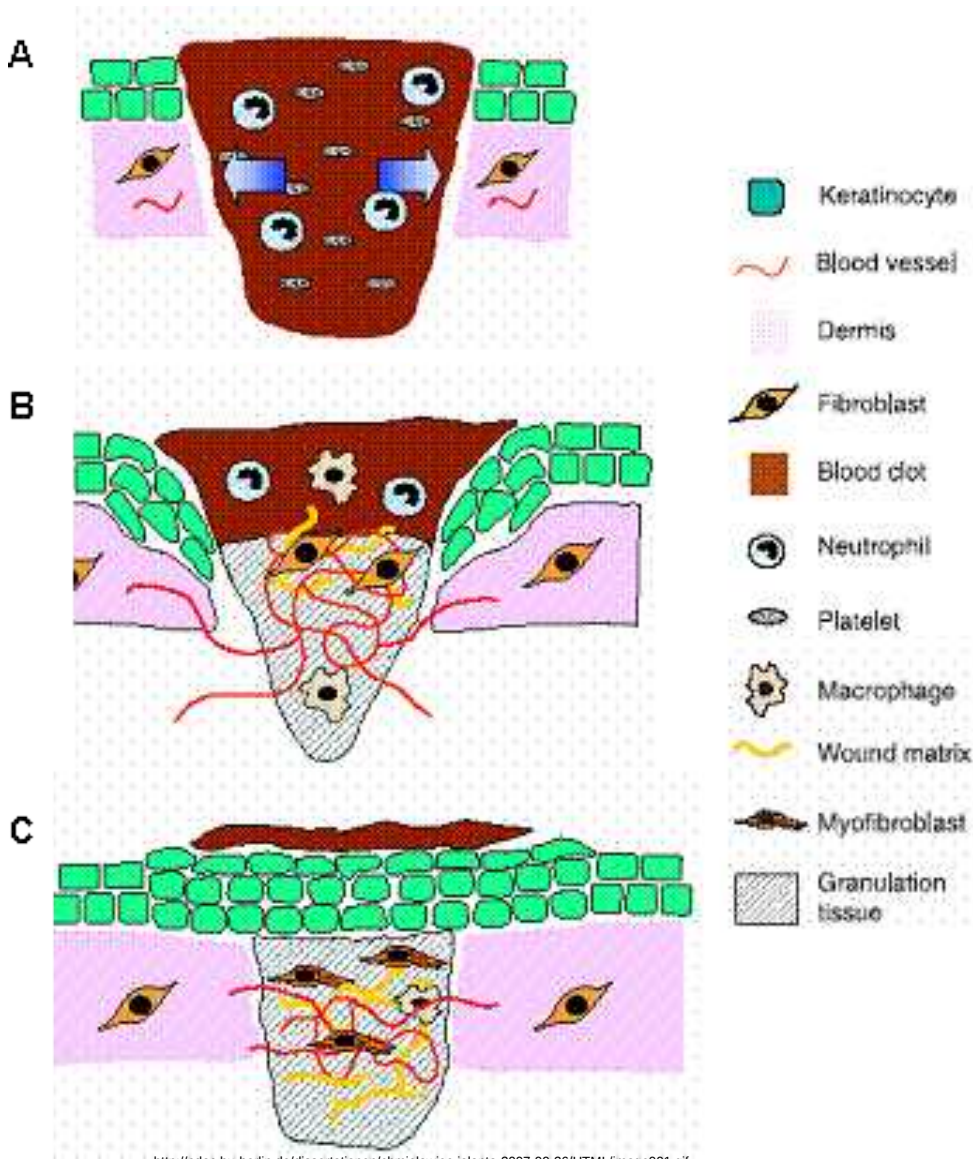
http://www.americanskin.org/resource/images/scp_img1.gif

Fibroblasts and wound healing

Wound healing

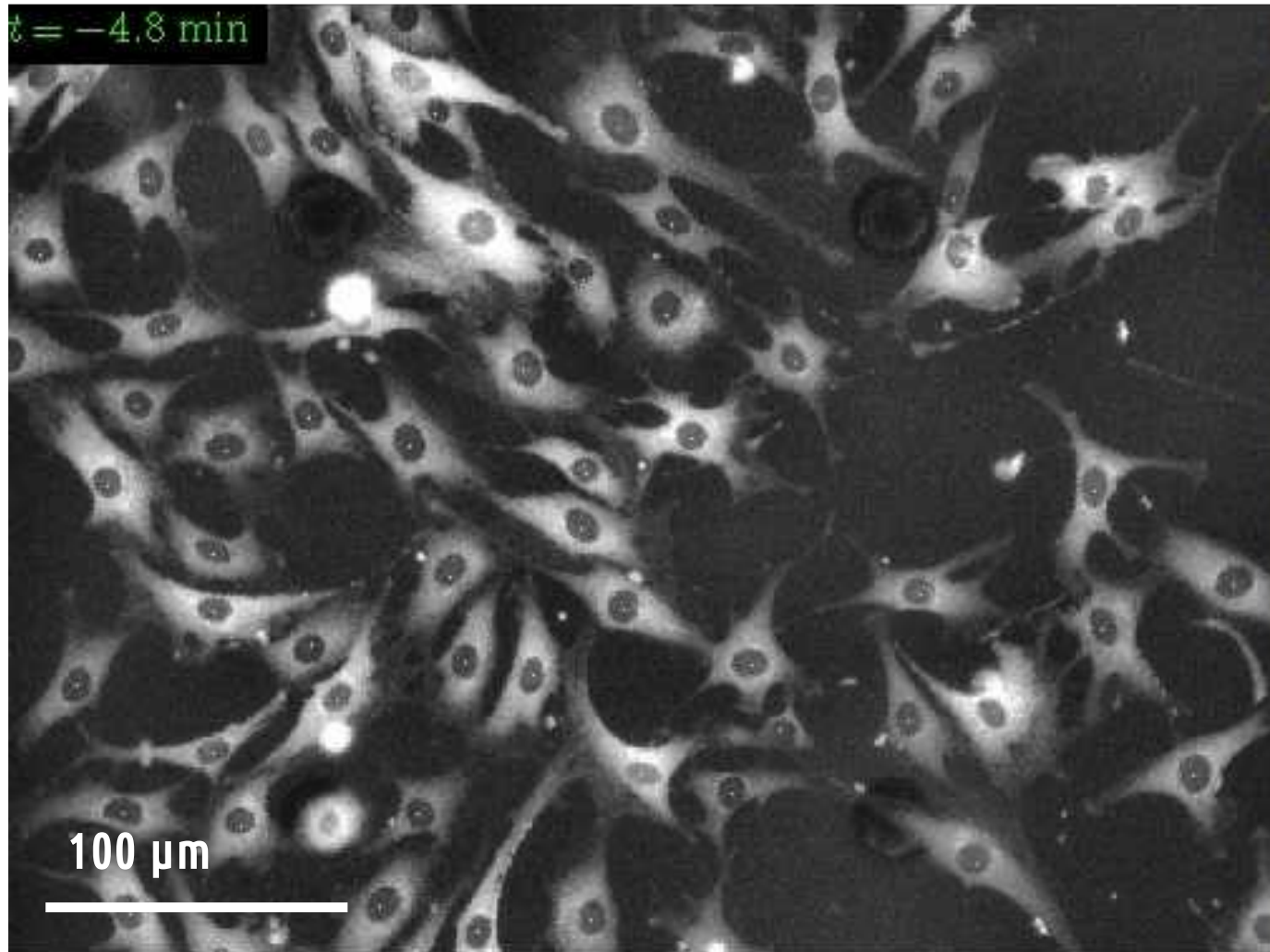


http://www.todaysplanet.com/pg/beta/lizardlover/pic/vikki_big_bite_wound.jpg



<http://edoc.hu-berlin.de/dissertationen/chmielowiec-jolanta-2007-09-26/HTML/image001.gif>

Fibroblast experiments

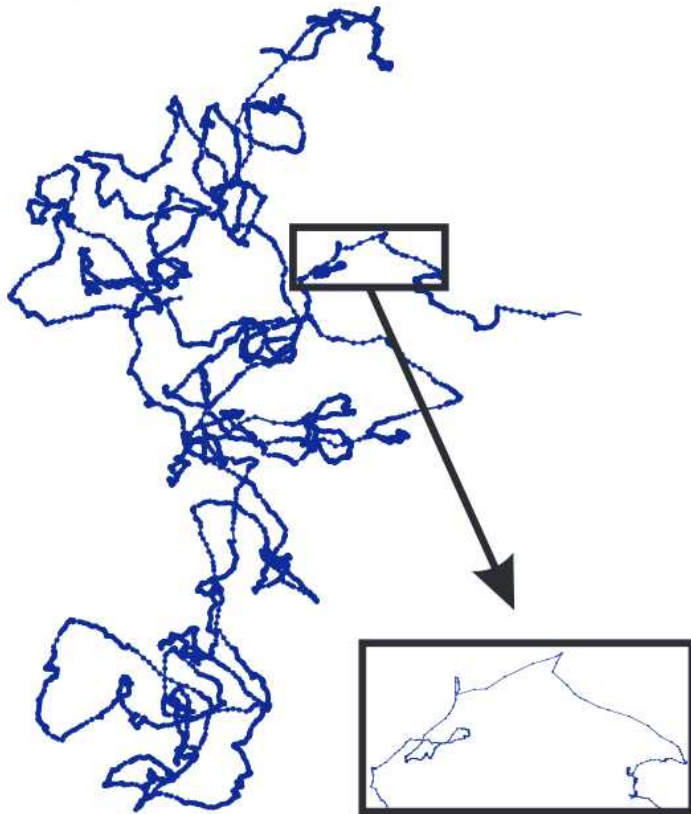


Data courtesy of Savaş Tay, ETH Zürich

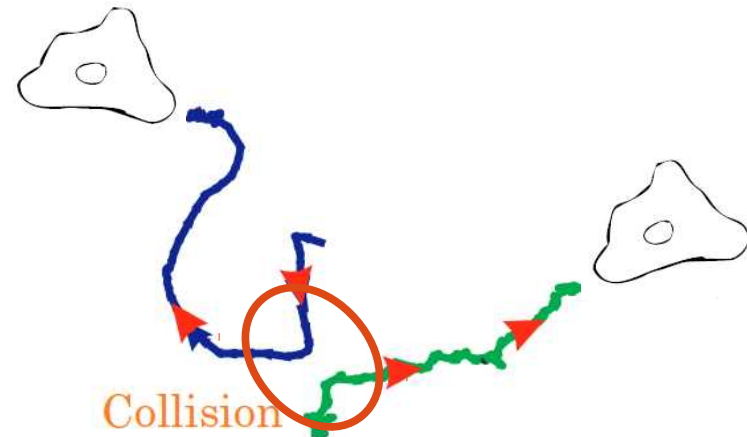
$$V \approx 0.3 \mu\text{m}/\text{min}$$

Characteristics

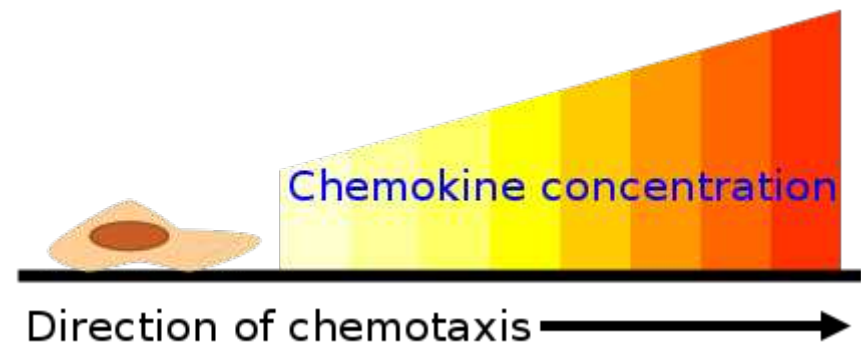
Persistent random motion



Repulsion at collision



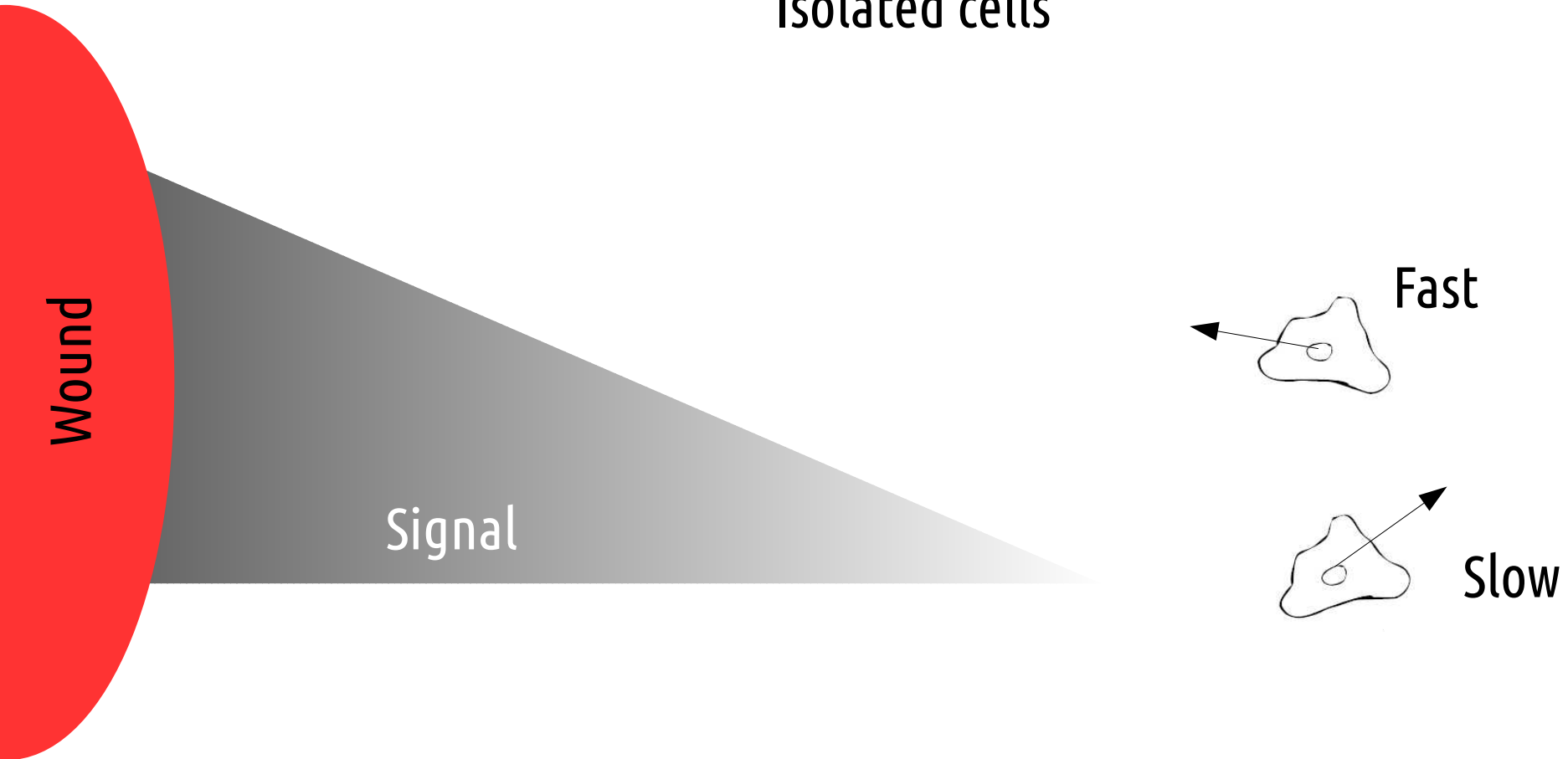
Attraction by chemical signal



http://en.wikipedia.org/wiki/File:Chemokine_concentration_chemotaxis.svg

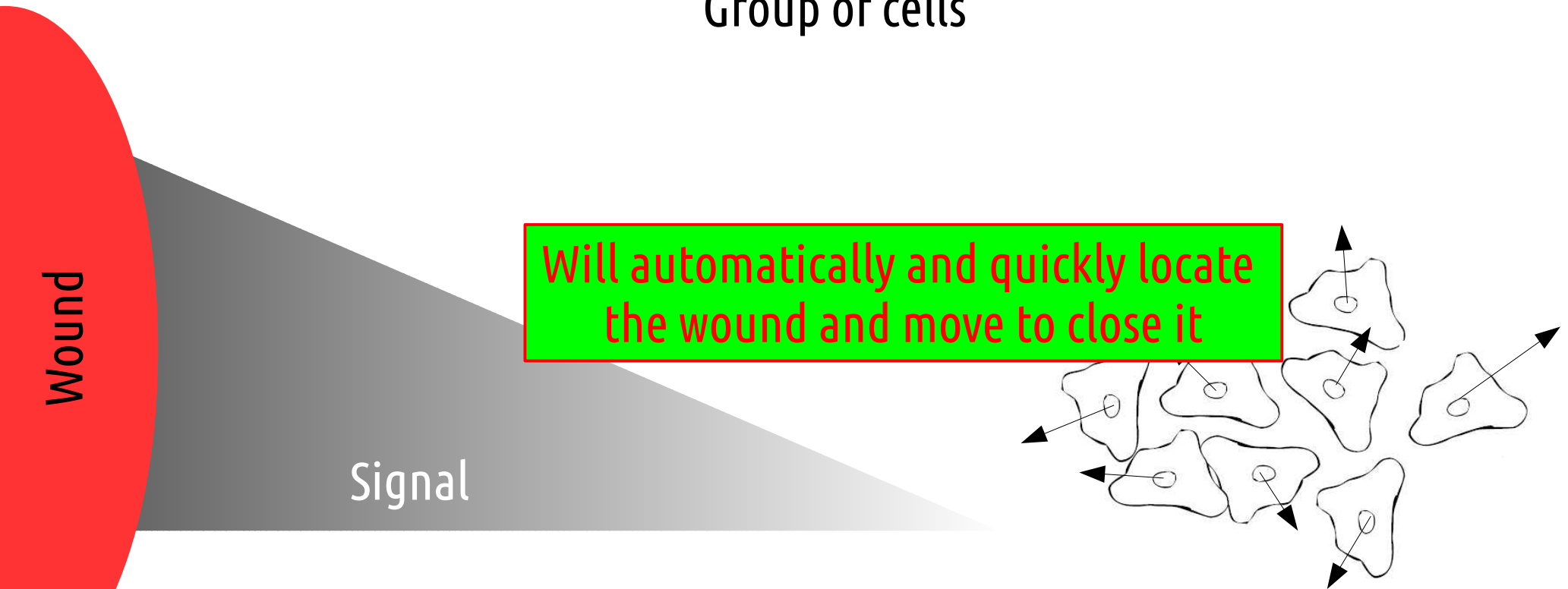
Emergent property: fast, adaptive and isotropic directional sensor for wound healing

Isolated cells



Emergent property: fast, adaptive and isotropic directional sensor for wound healing

Group of cells



- Outer cells always moving away → directed towards any signal
- Group randomizes directions of all cells
- Will (eventually) bring whole group to wound

Thank you for attending *News from NBIA*

We hope to see you again in the future...

