



JOHNS HOPKINS  
WHITING SCHOOL  
*of* ENGINEERING

# Cell and Tissue Engineering

Morphogenesis

Part 2: Mechanisms of Development

# Virchow's Principle

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*“omnis cellula e cellula”*

*all cells come from  
cells*

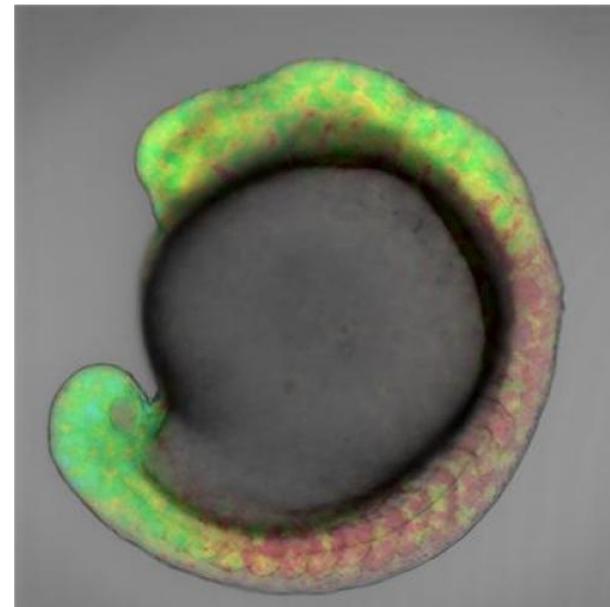


# Mechanism of development

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- Chemical Regulation
  - Morphogens
  - Migration
- Mechanical Regulation
  - Shape
  - Adhesion
  - Migration

FRET used to show gradients of retinoic acid in the zebrafish

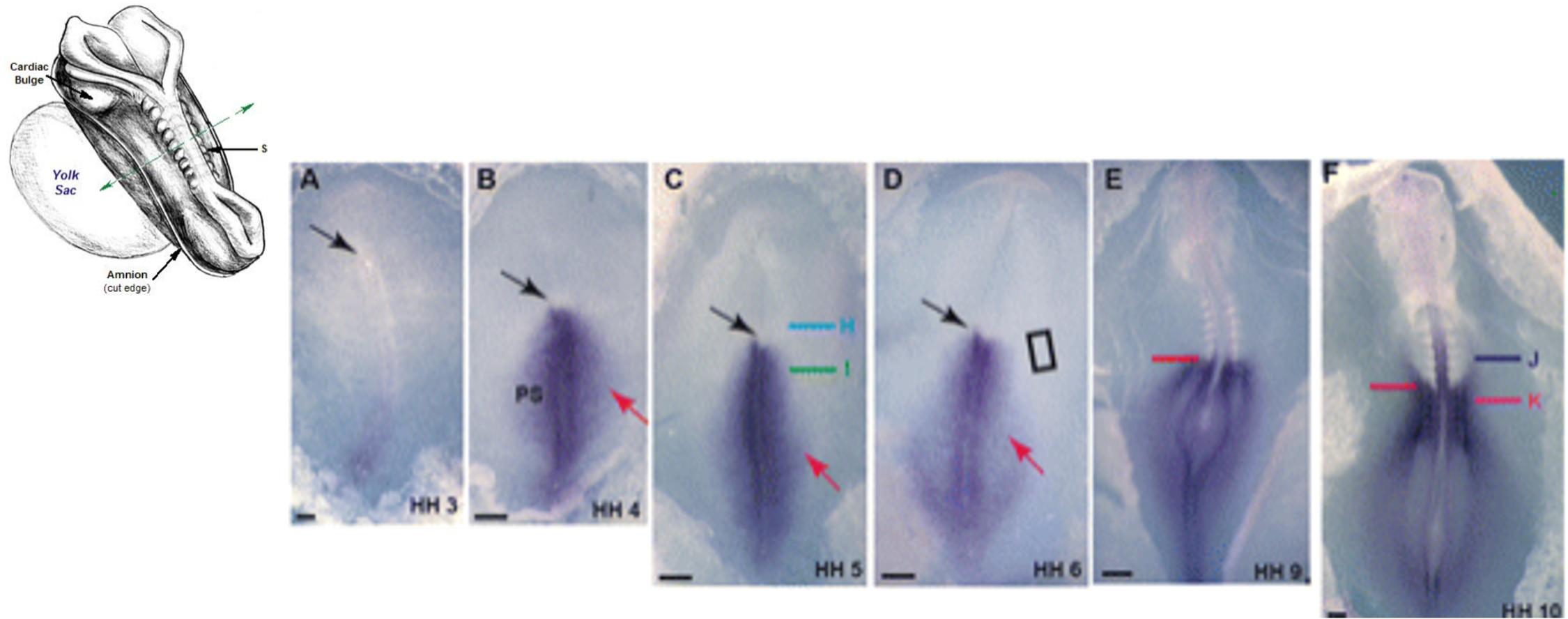


Shimozono et al. Nature 2013

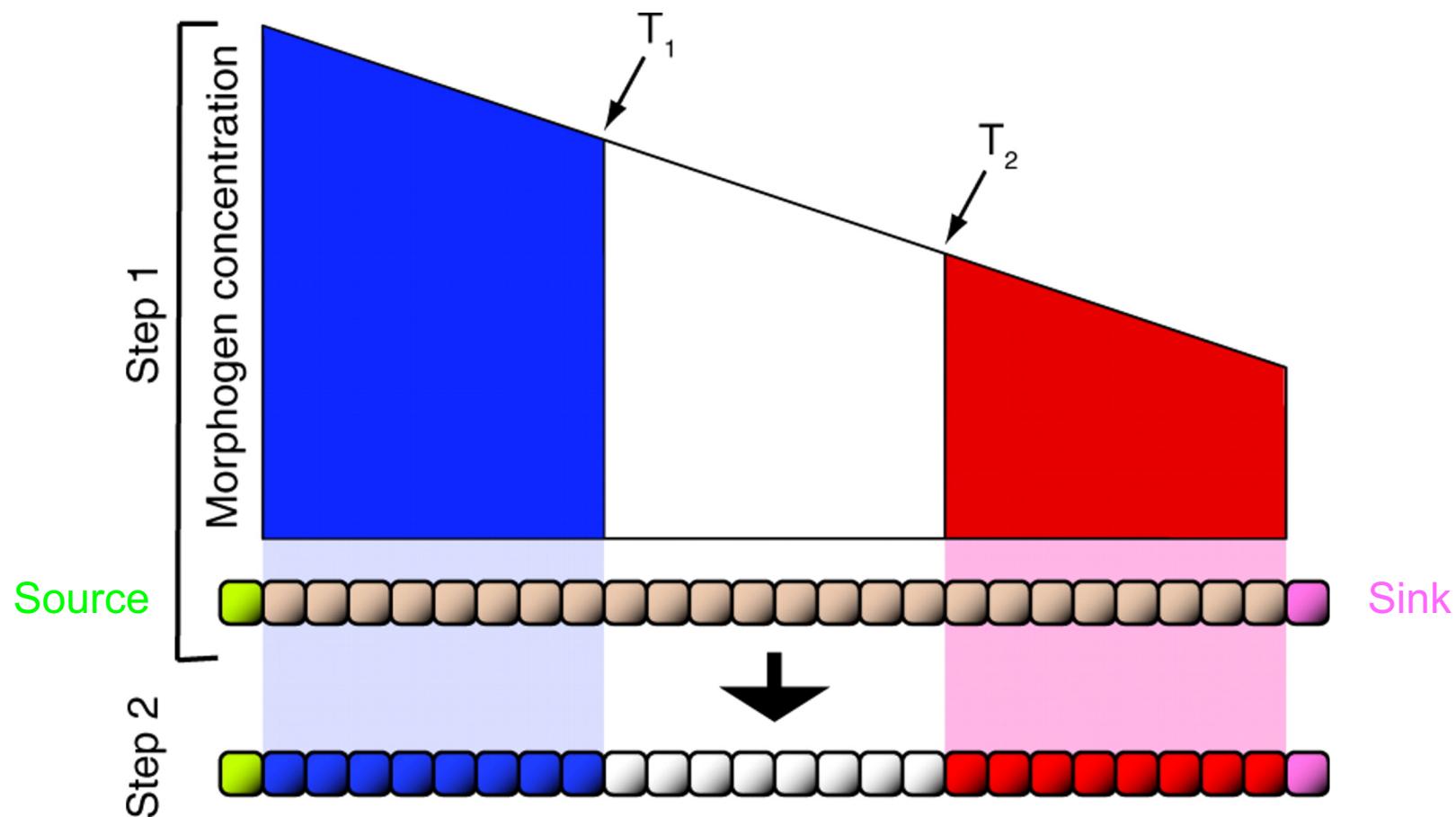
**DIRECTED  
DIFFERENTIATION**

**DIRECTED  
MIGRATION**  
**CHEMOTAXIS**  
**DUROTAXIS**  
**HAPTOTAXIS**

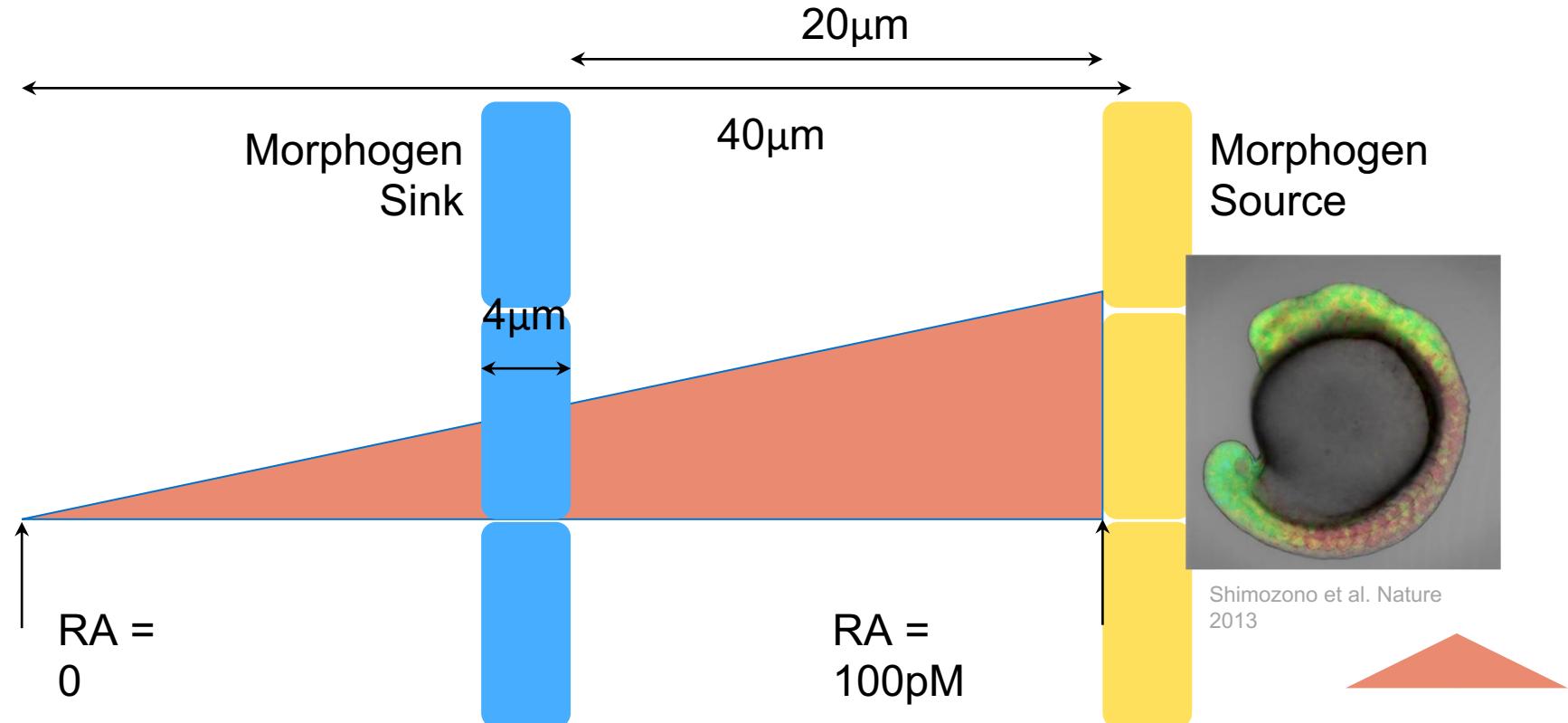
# Chemical Control: Morphogen Gradients (1)



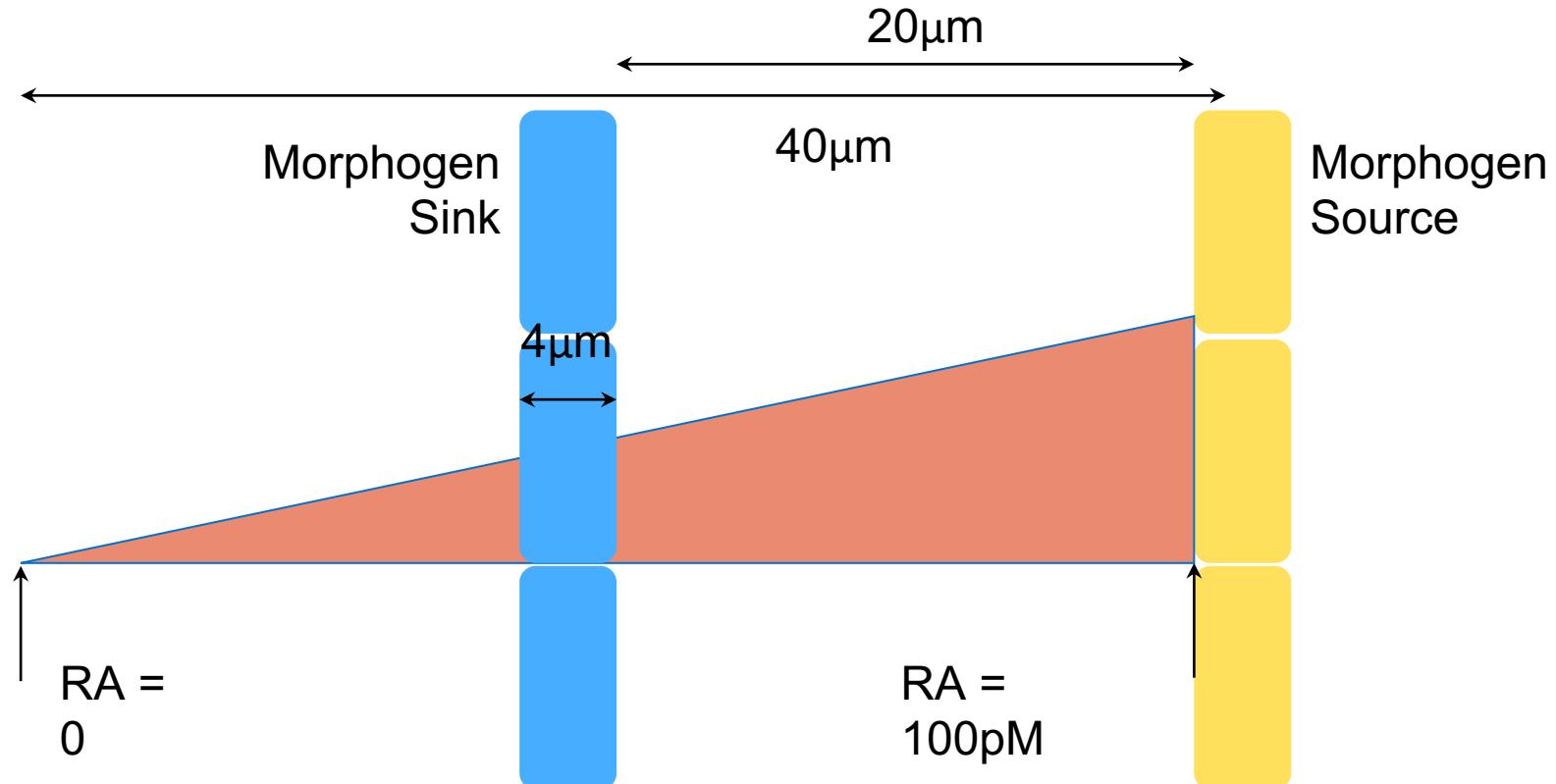
# Chemical Control: Morphogen Gradients (2)



# Chemical Control: Morphogen Gradients (3)

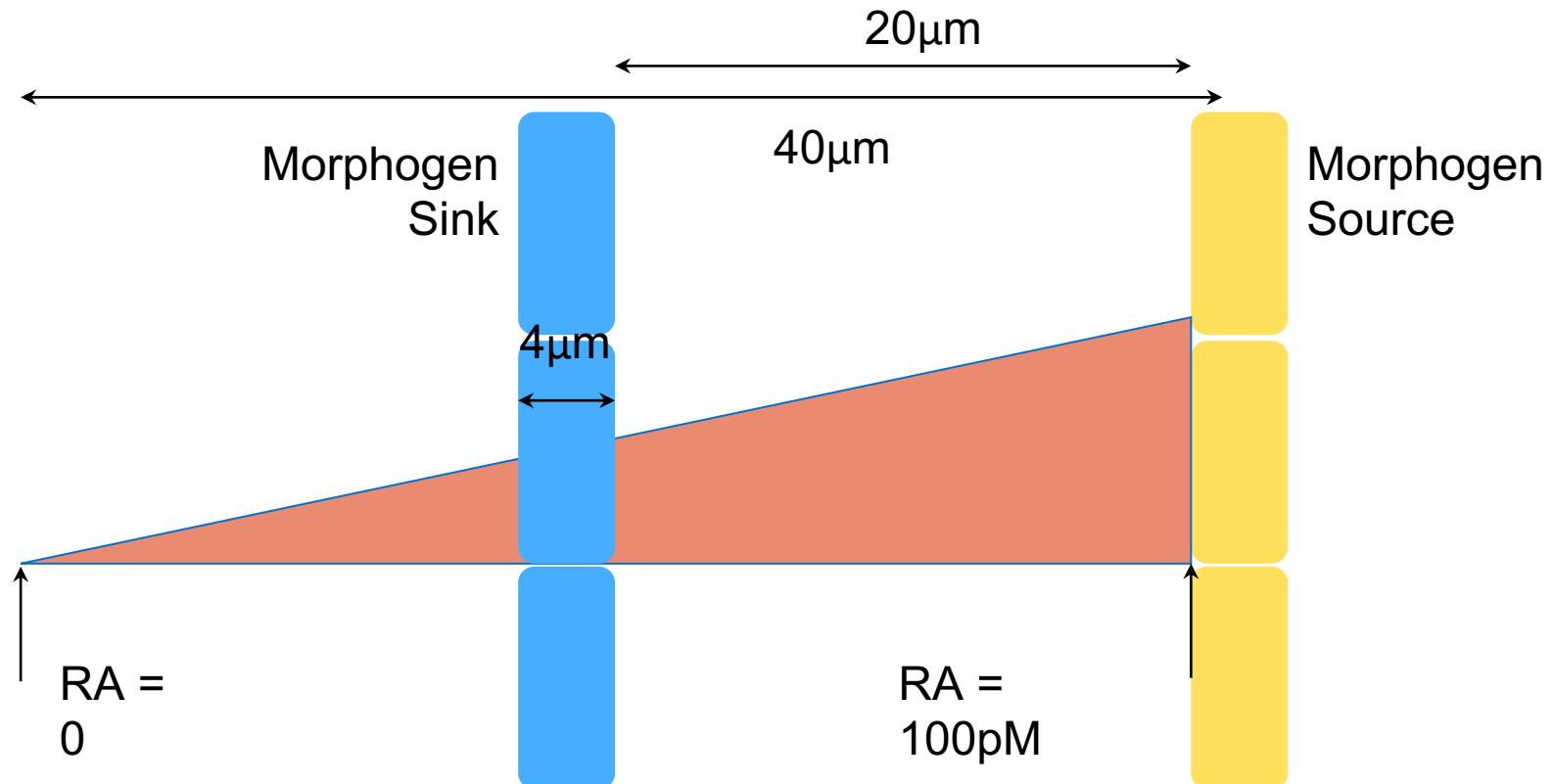


# Chemical Control: Morphogen Gradients (4)



$$\text{Overall Gradient} = \frac{100 \text{ pM}}{40 \mu\text{m}} = 2.5 \text{ pM}/\mu\text{m}$$

# Chemical Control: Morphogen Gradients (5)

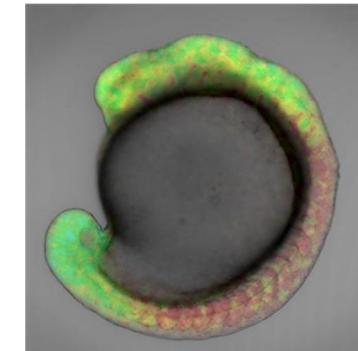
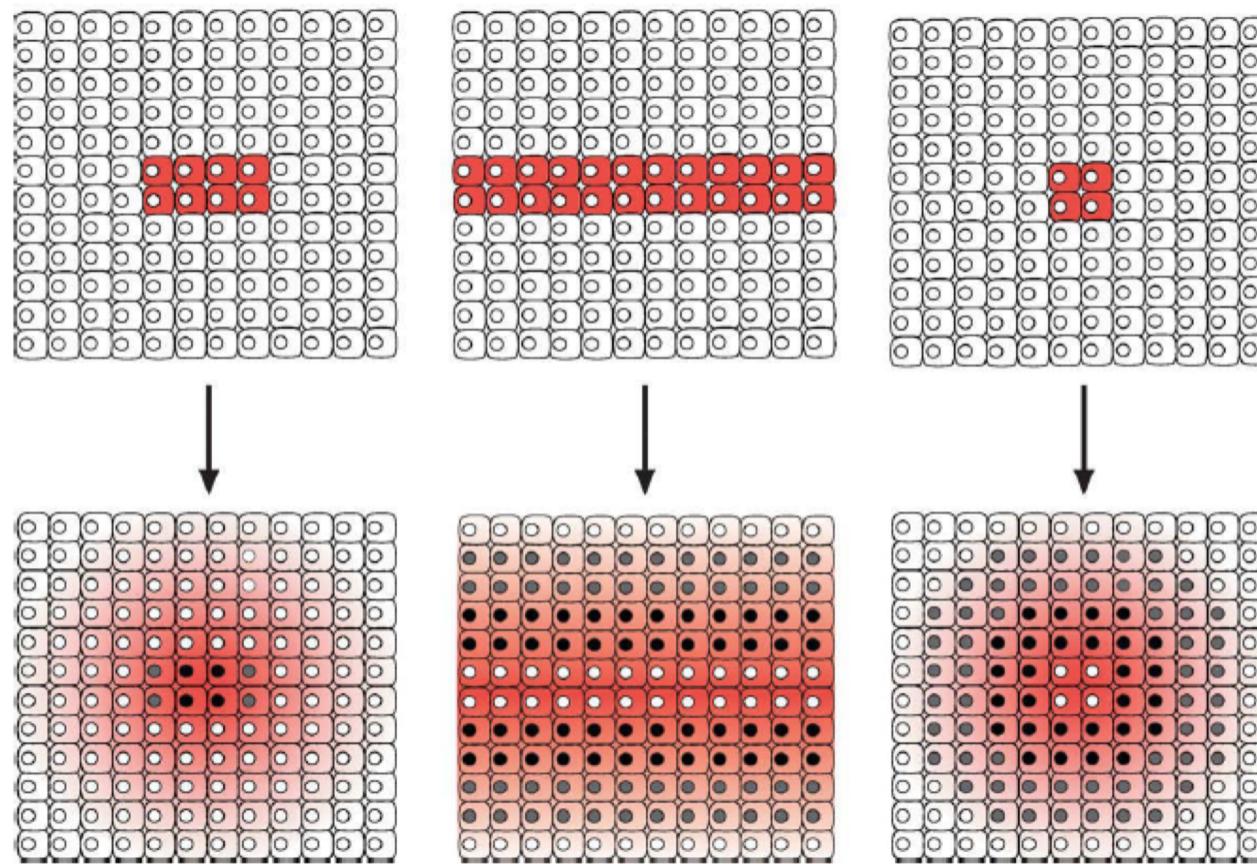


$$\text{Overall Gradient} = \frac{100 \text{ pM}}{40 \mu\text{m}} = 2.5 \text{ pM}/\mu\text{m}$$

$$\text{Gradient seen by the cell} = \frac{[Ra]_{front} - [Ra]_{back}}{[Ra]_{back}} = \frac{[50] - [40]}{[40]} = 25\%$$

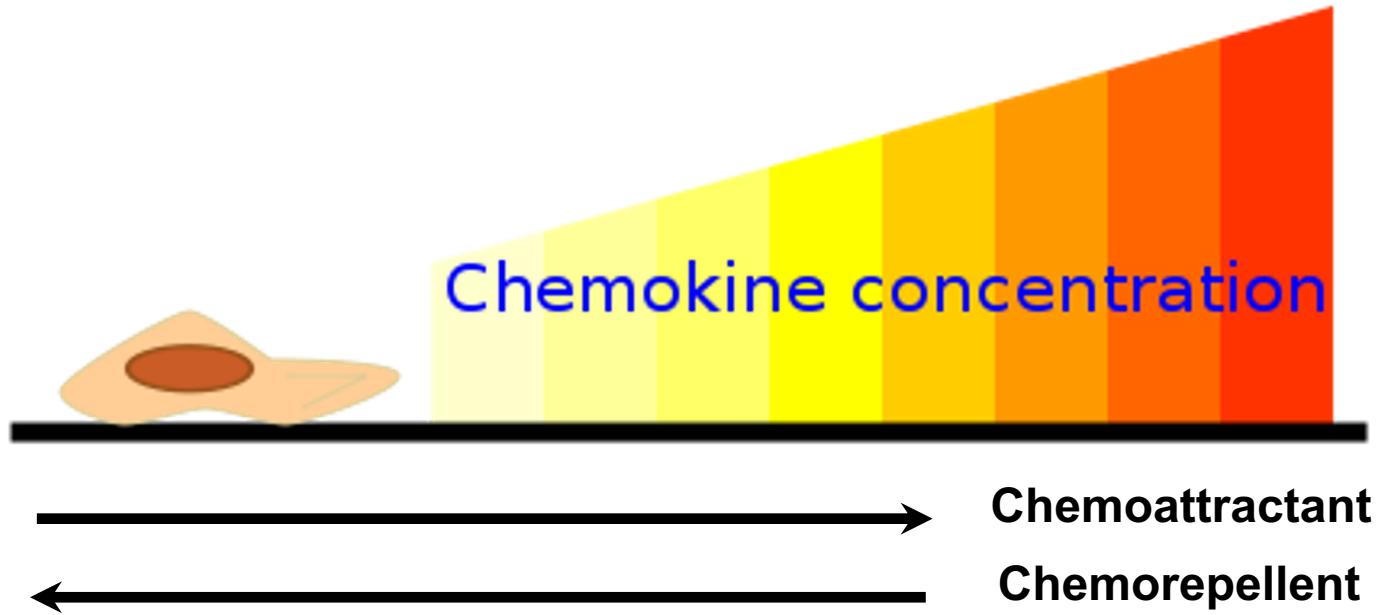
or = (50-40) = 10 pM per cell

# Chemical Control: Morphogen Gradients (6)

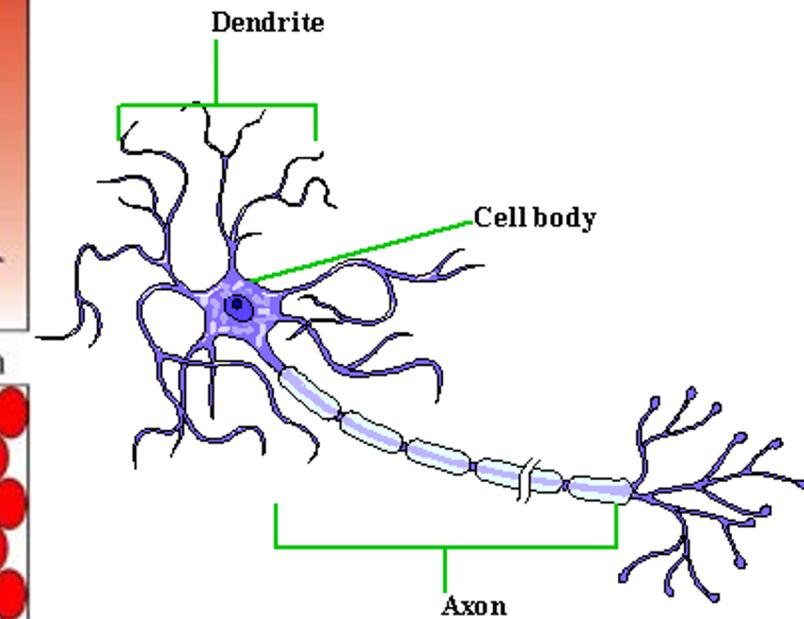
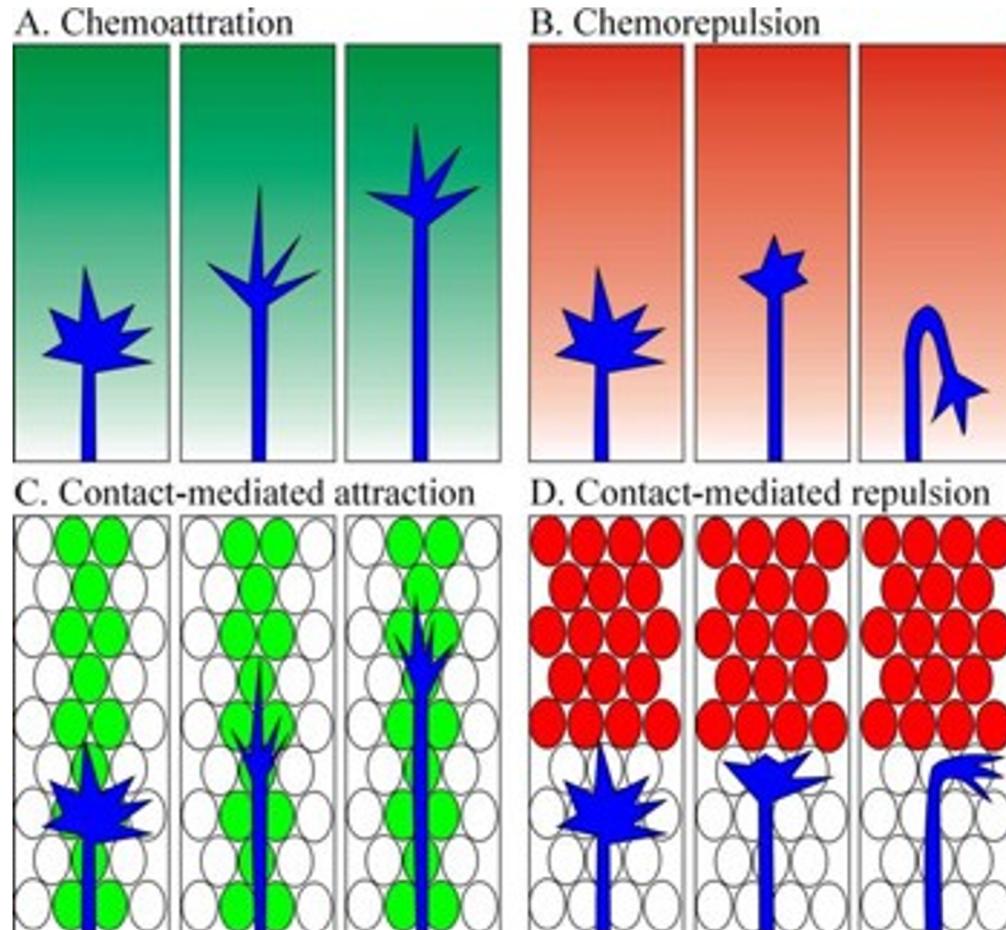


# Chemical Control: Chemotaxis

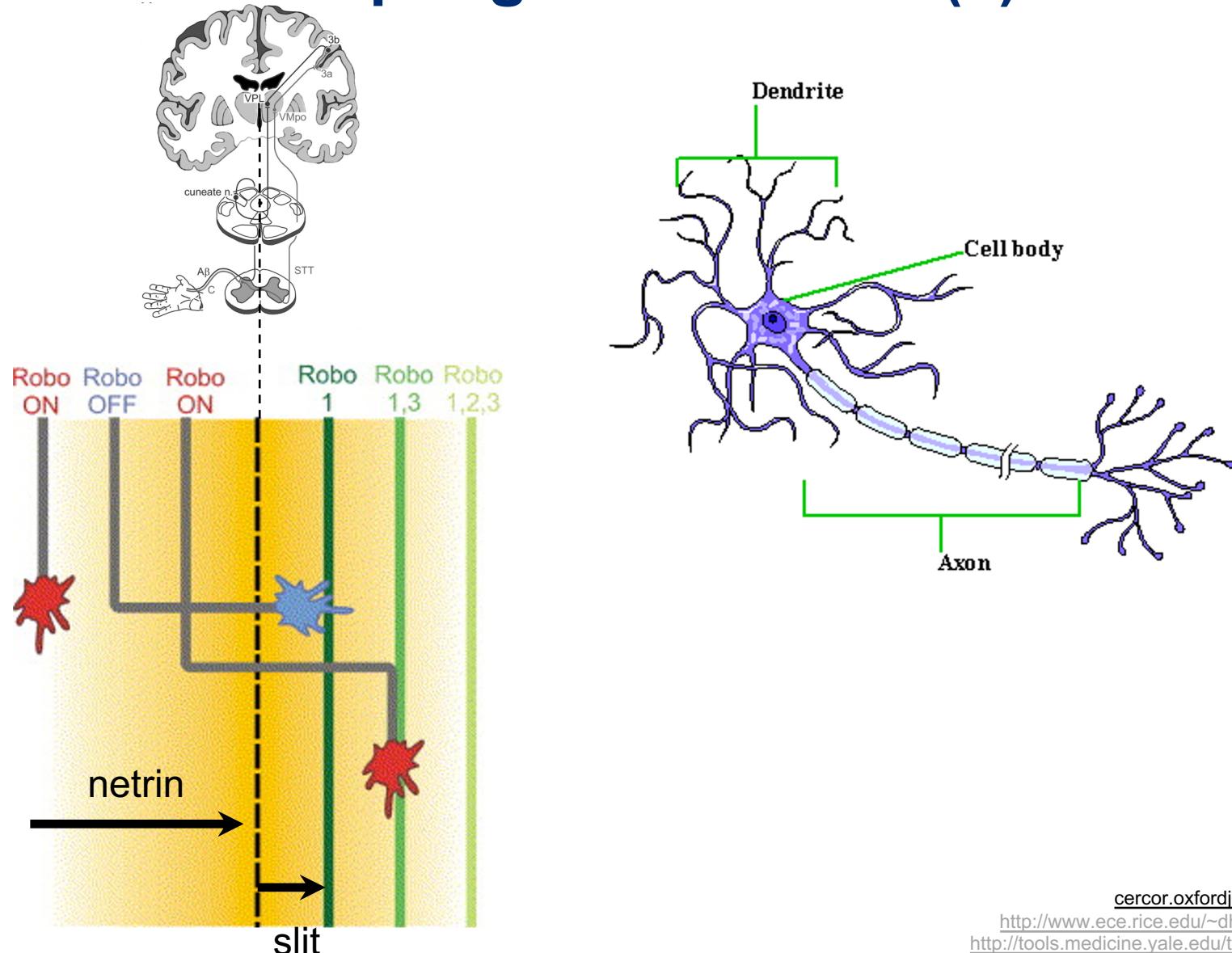
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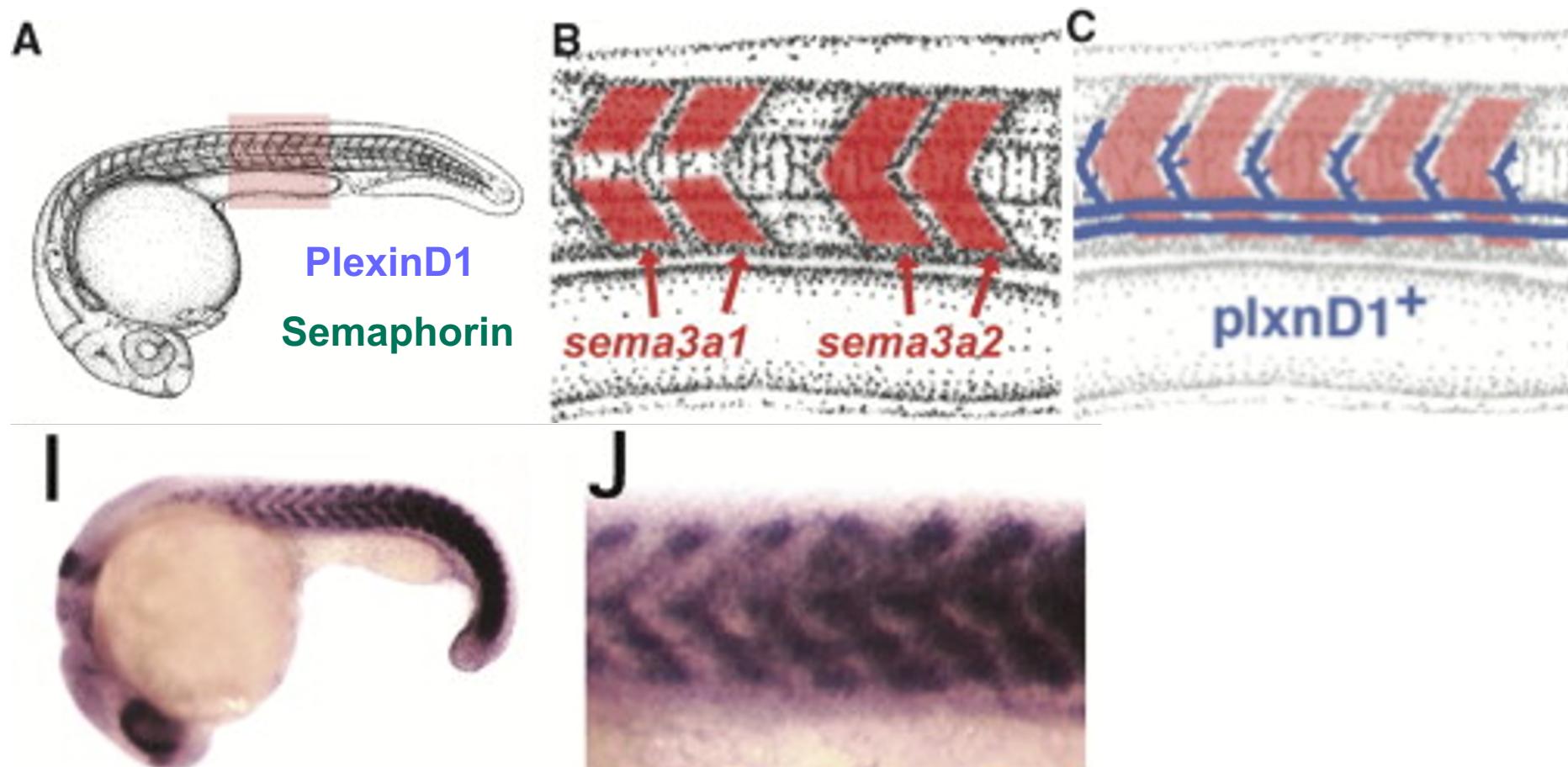
# Chemical Control: Morphogen Gradients (7)



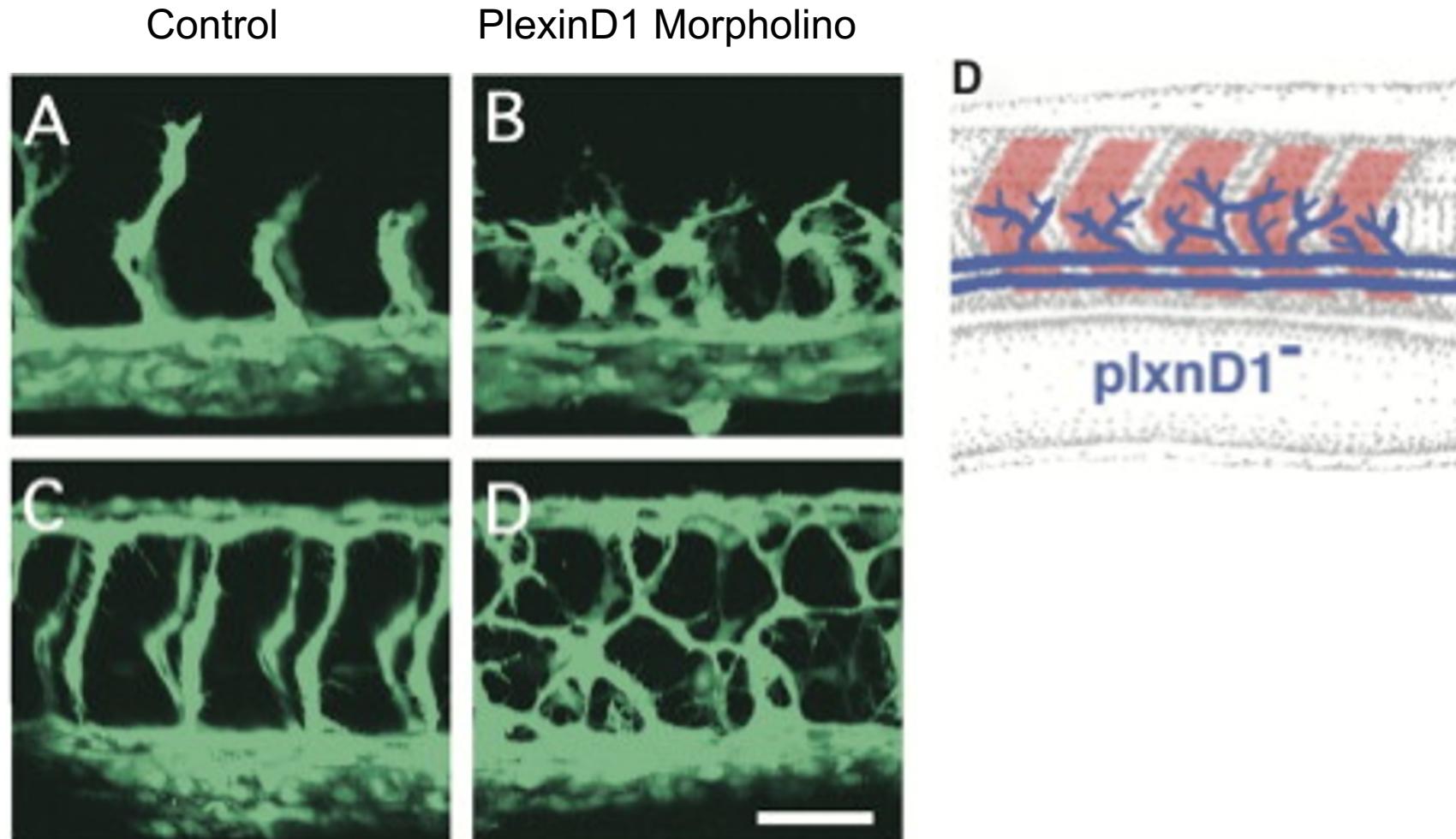
# Chemical Control: Morphogen Gradients (8)



# Chemical Control: Morphogen Gradients (9)

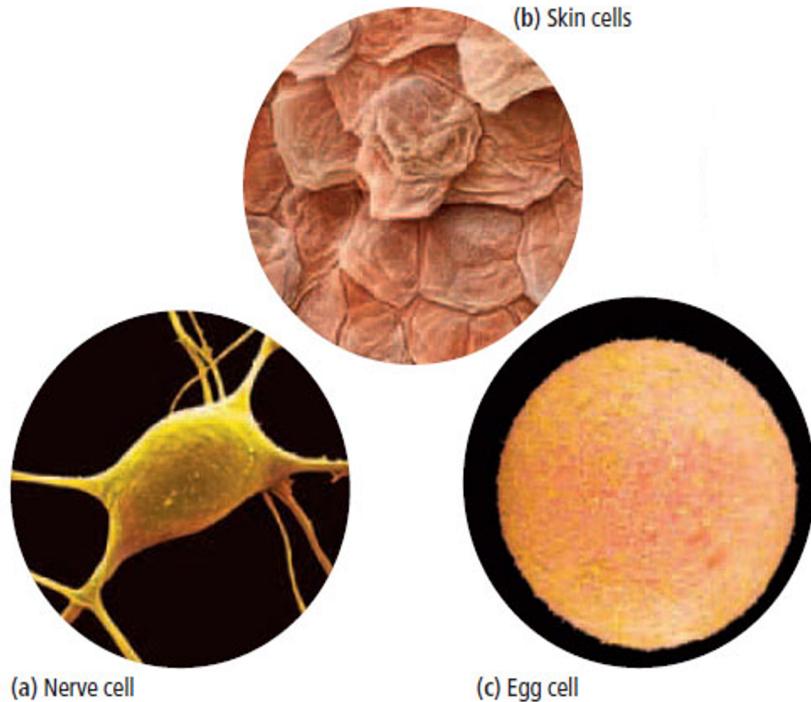


# Chemical Control: Morphogen Gradients (10)

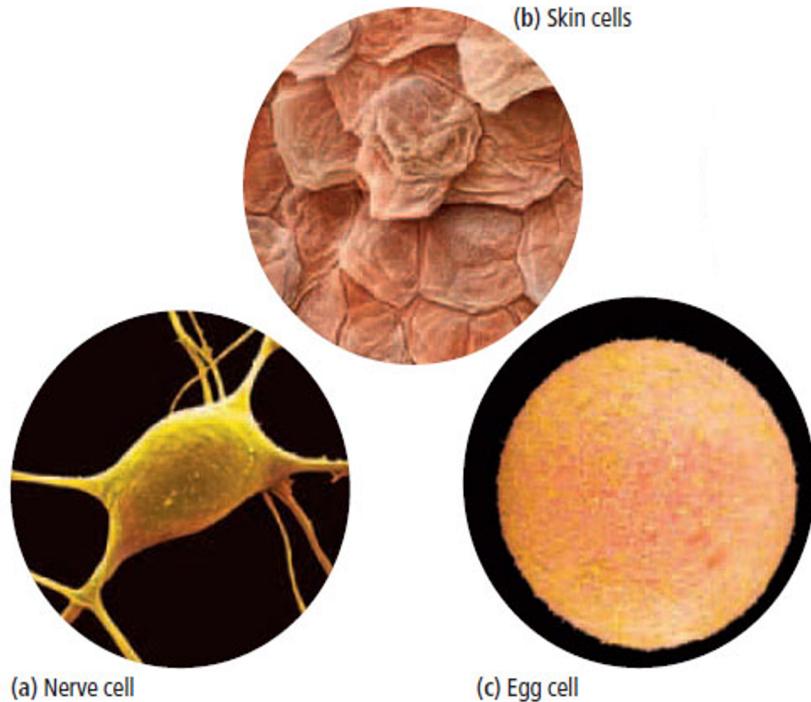


# Mechanical Controls: Shape (1)

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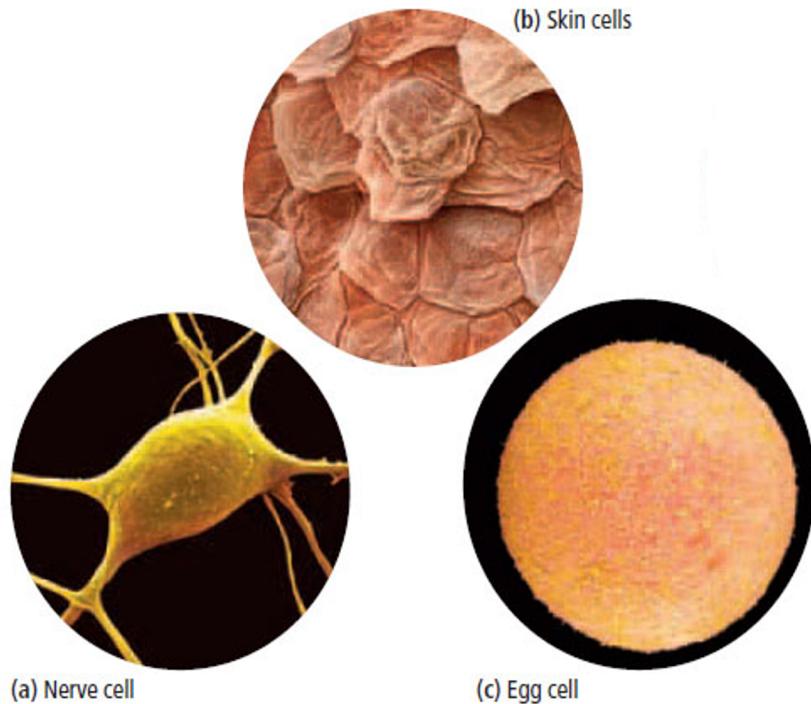


# Mechanical Controls: Shape (2)

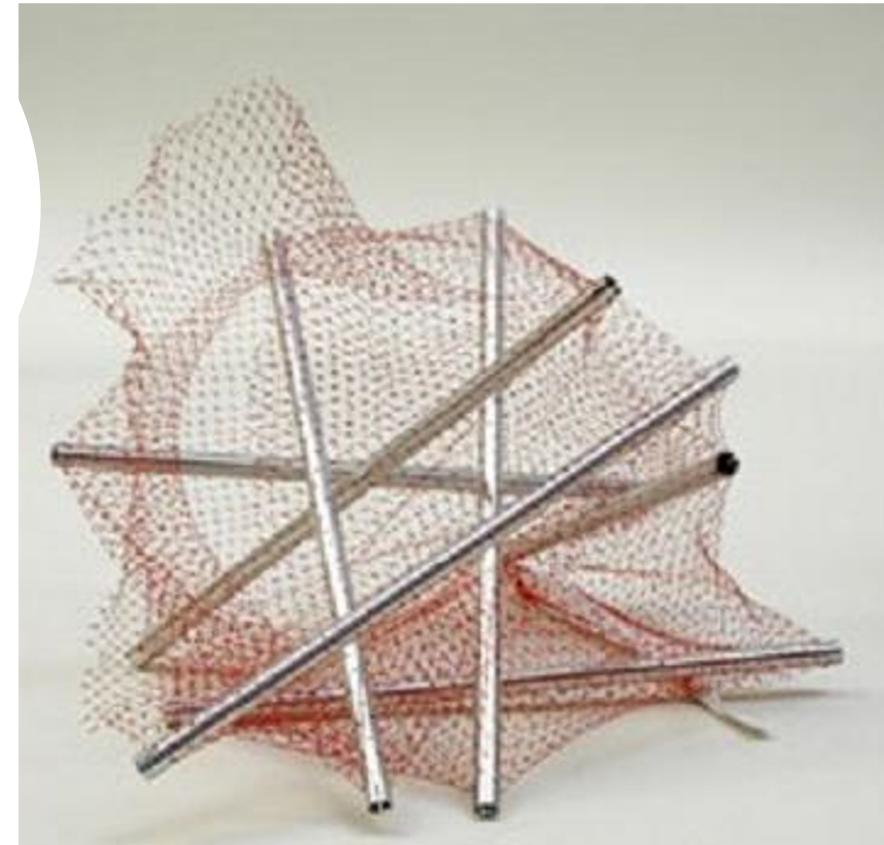


Plasma membrane  
Cytoplasm

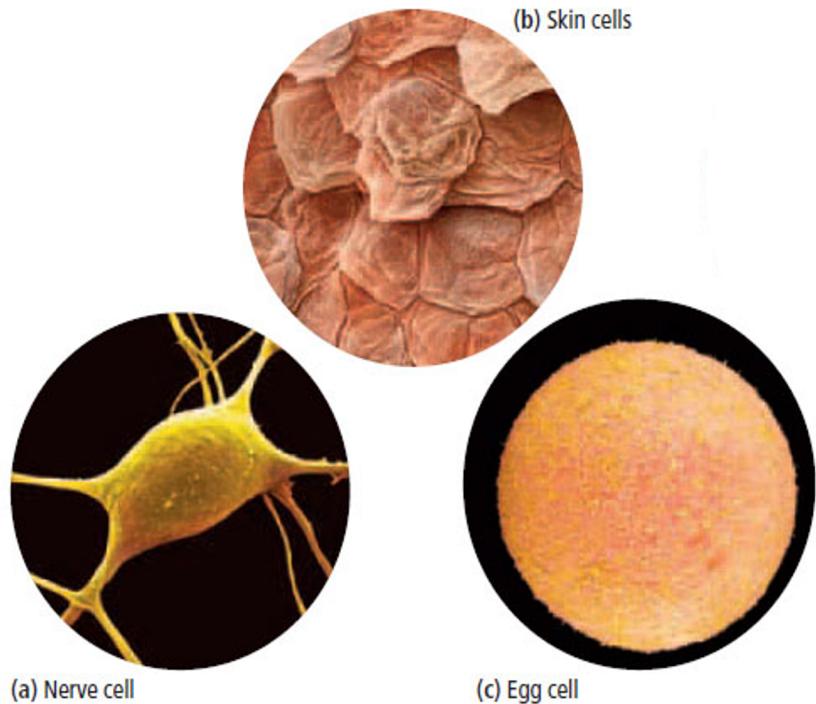
# Mechanical Controls: Shape (3)



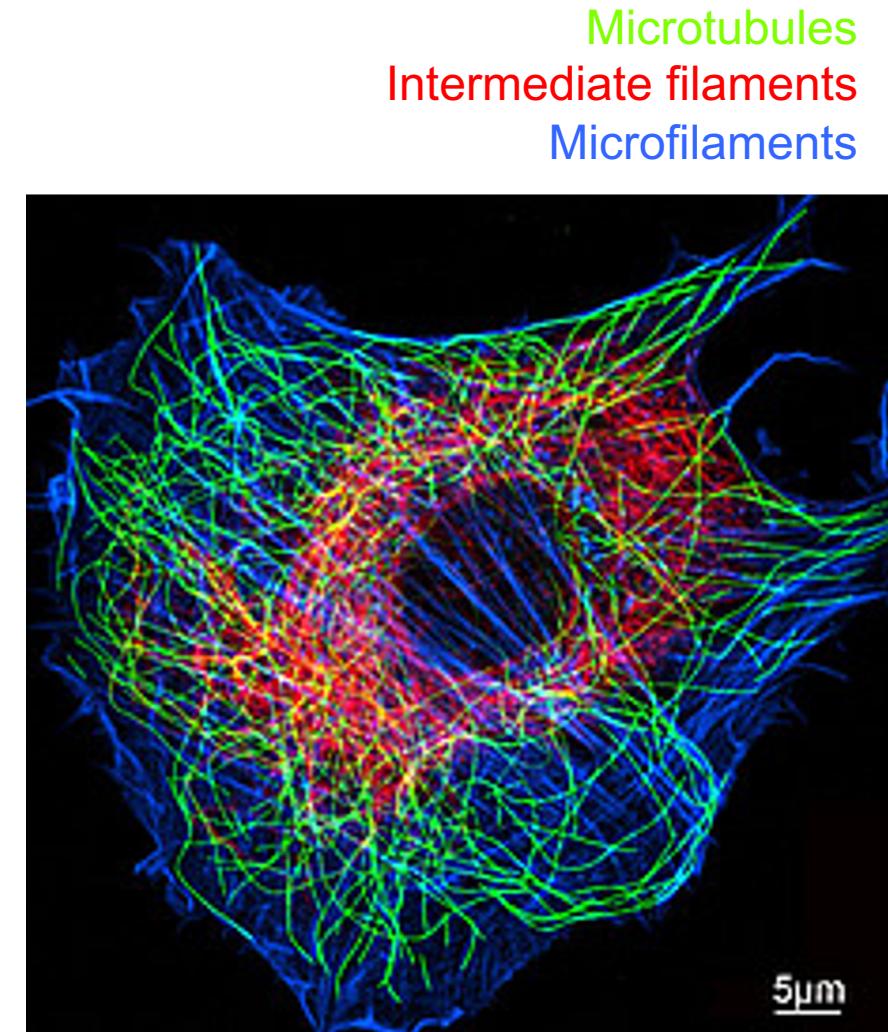
Plasma membrane  
Cytoplasm  
**Cytoskeleton**



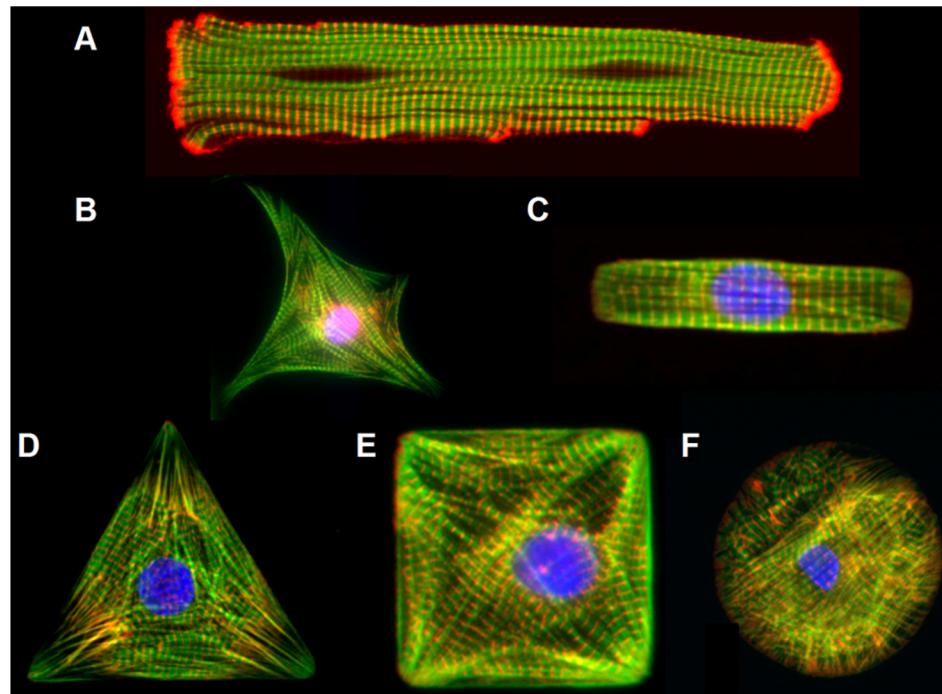
# Mechanical Controls: Shape (4)



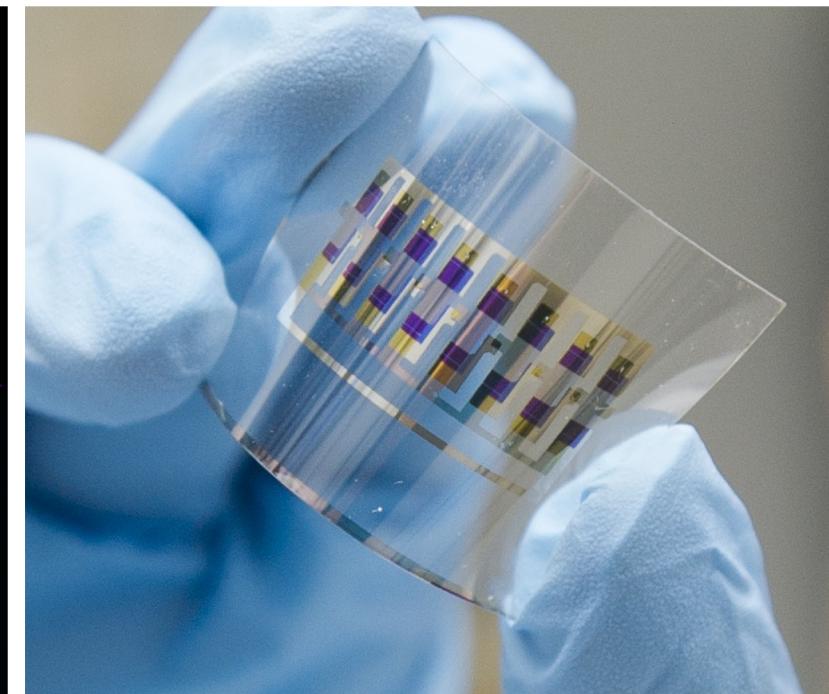
Plasma  
membrane  
Cytoplasm  
**Cytoskeleton**



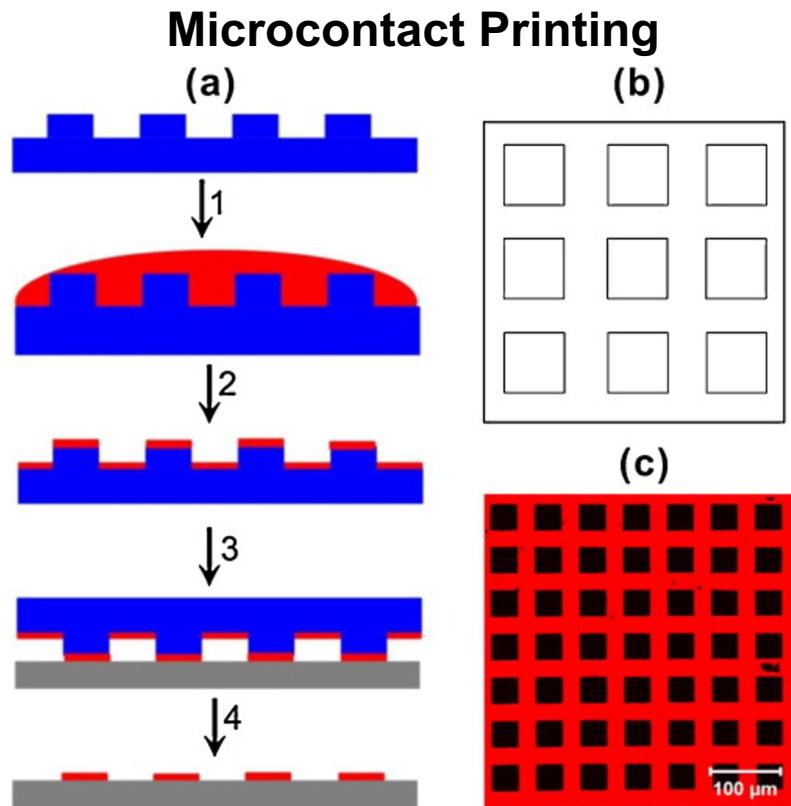
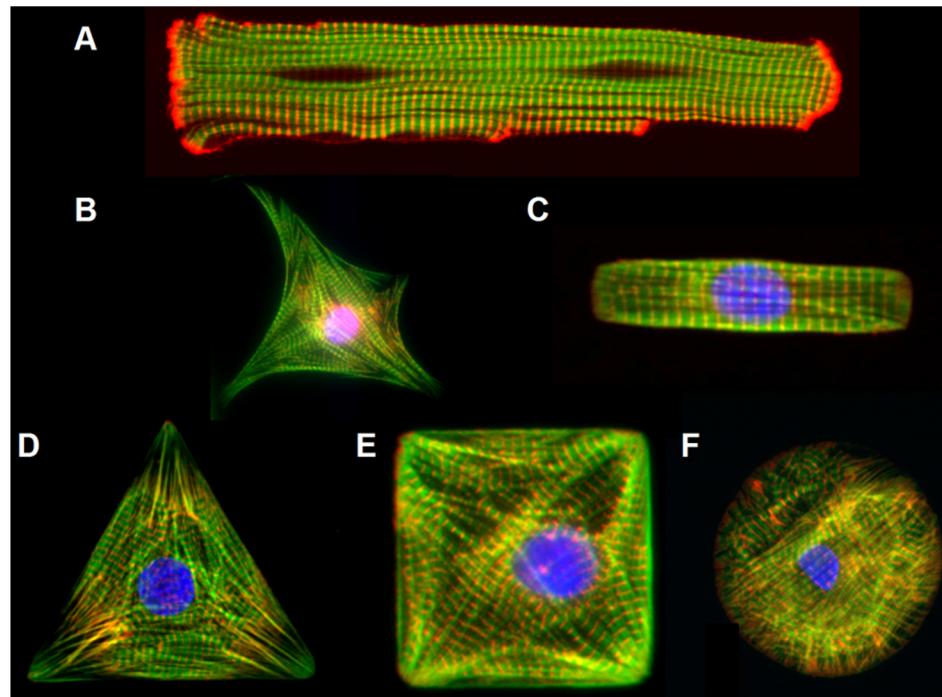
# Mechanical Controls: Shape (5)



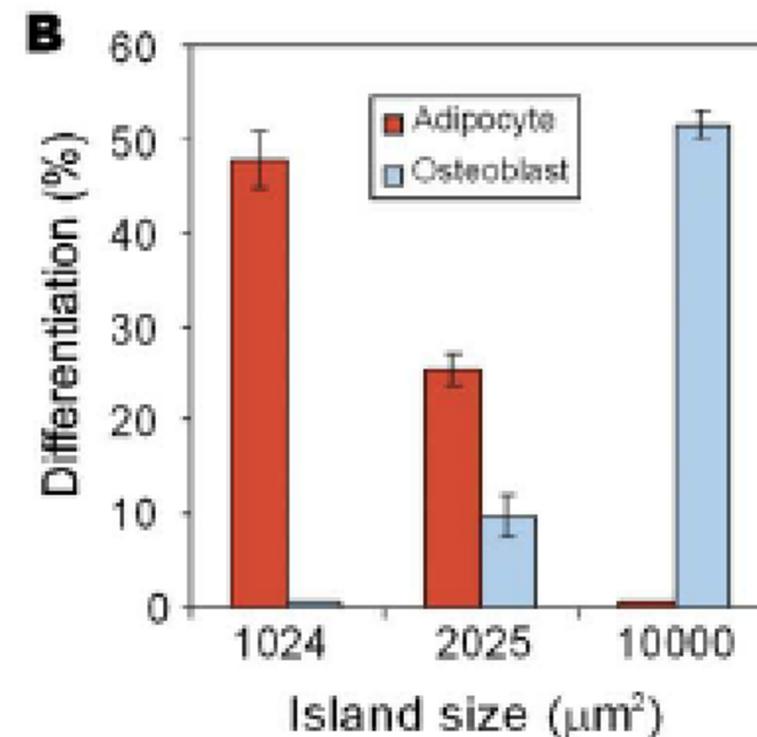
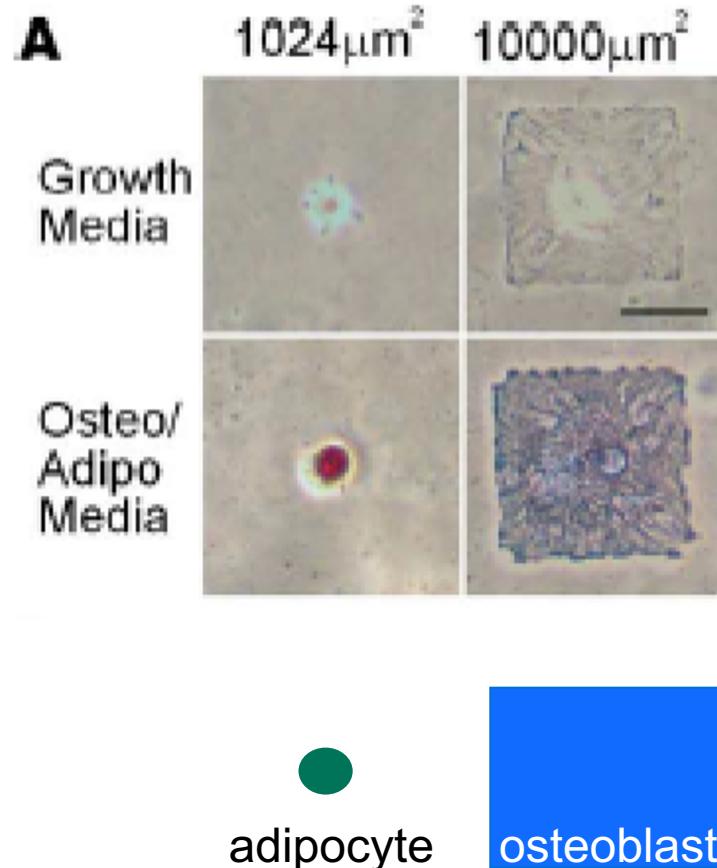
Microcontact Printing



# Mechanical Controls: Shape (6)

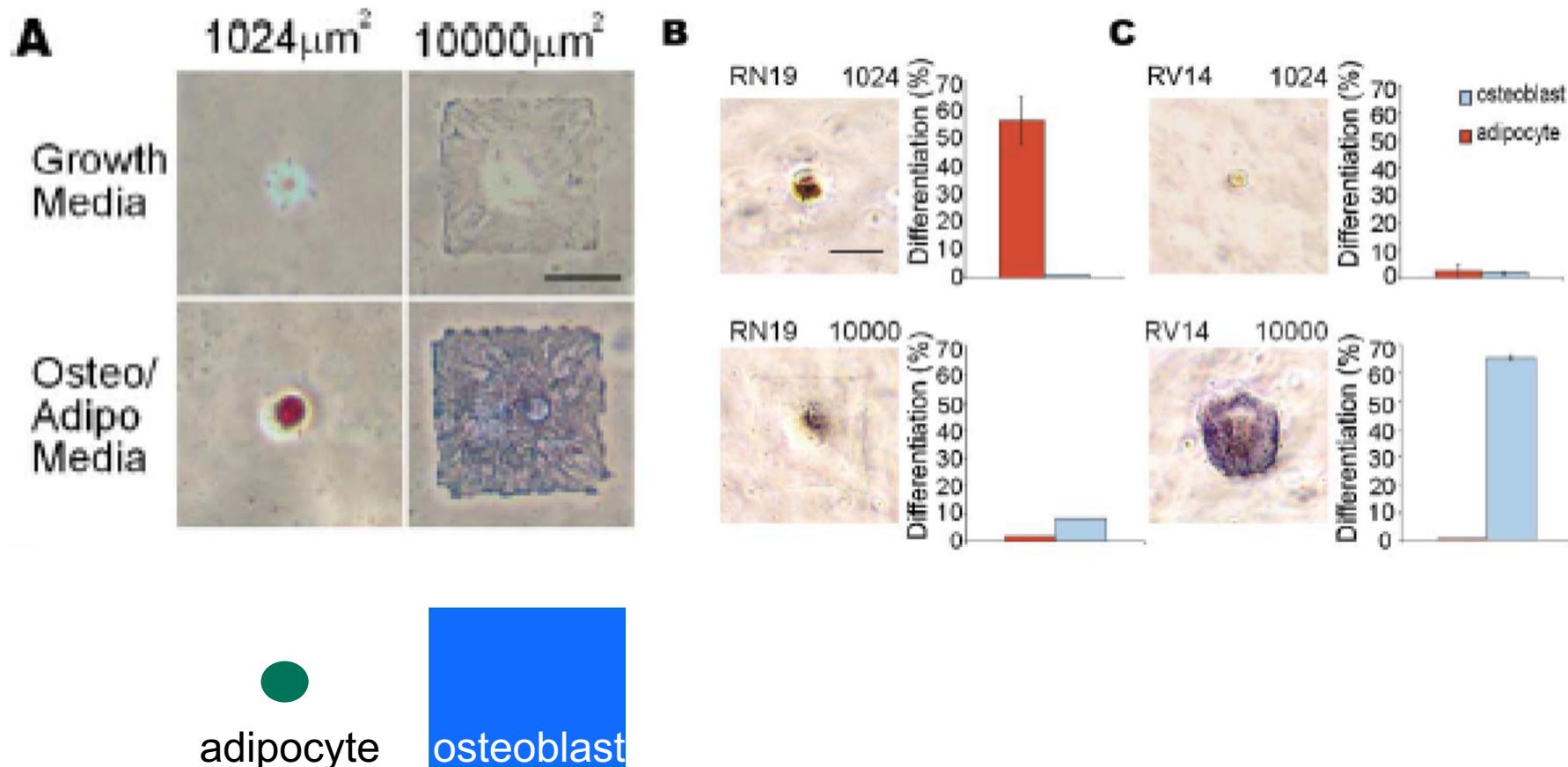


# Mechanical Controls: Shape (7)

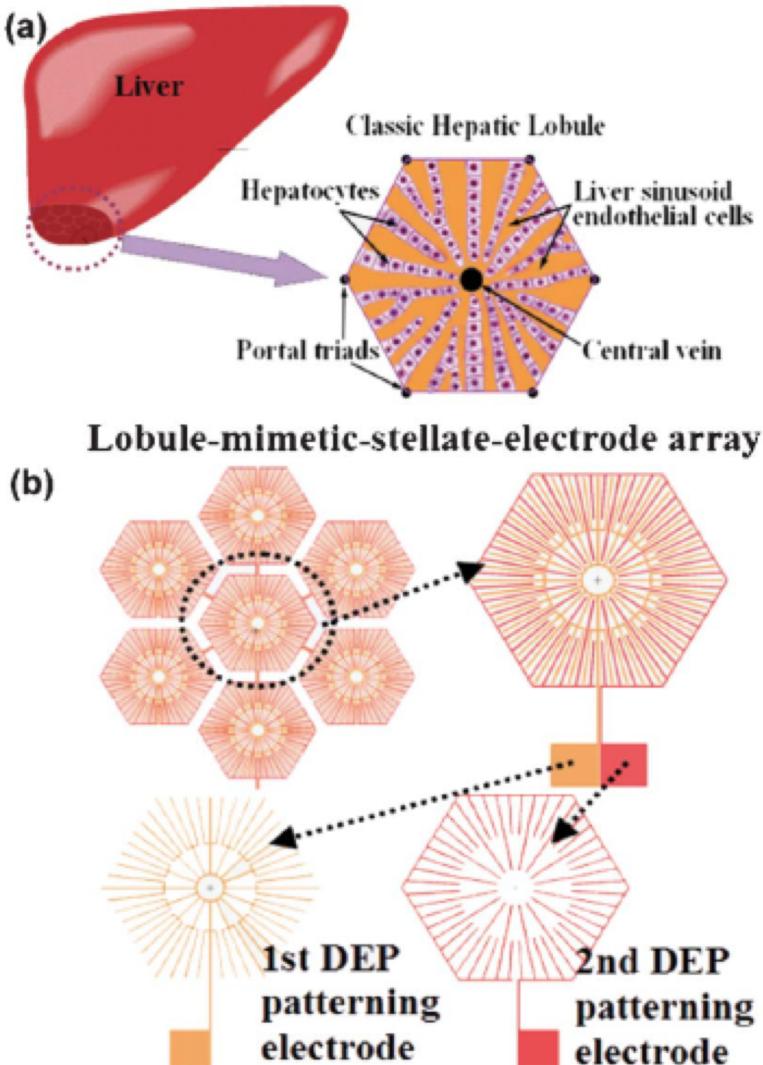


# Mechanical Controls: Shape (8)

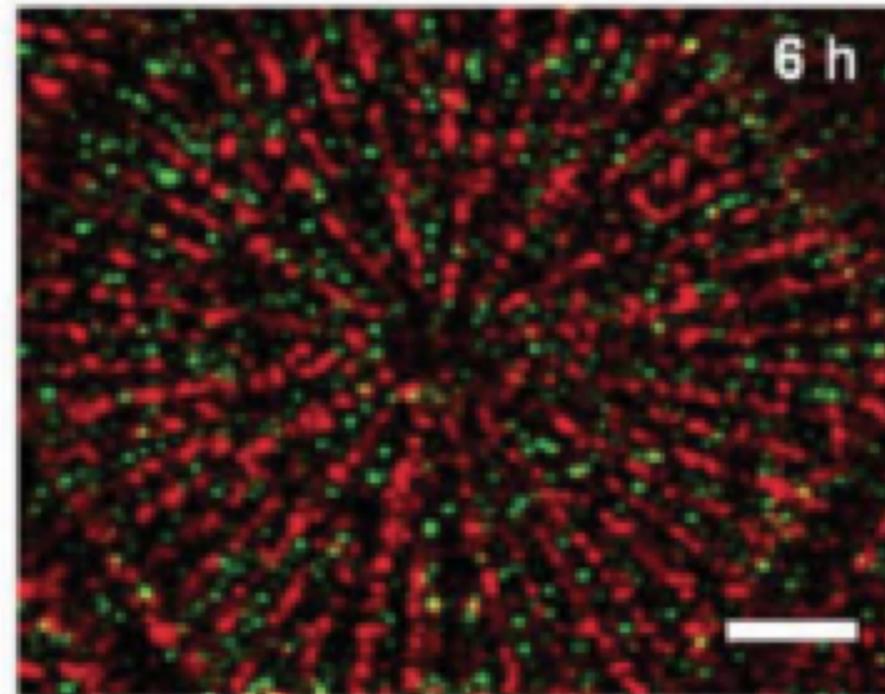
RN19: Dominant negative RhoA  
RV14: Constitutively active RhoA



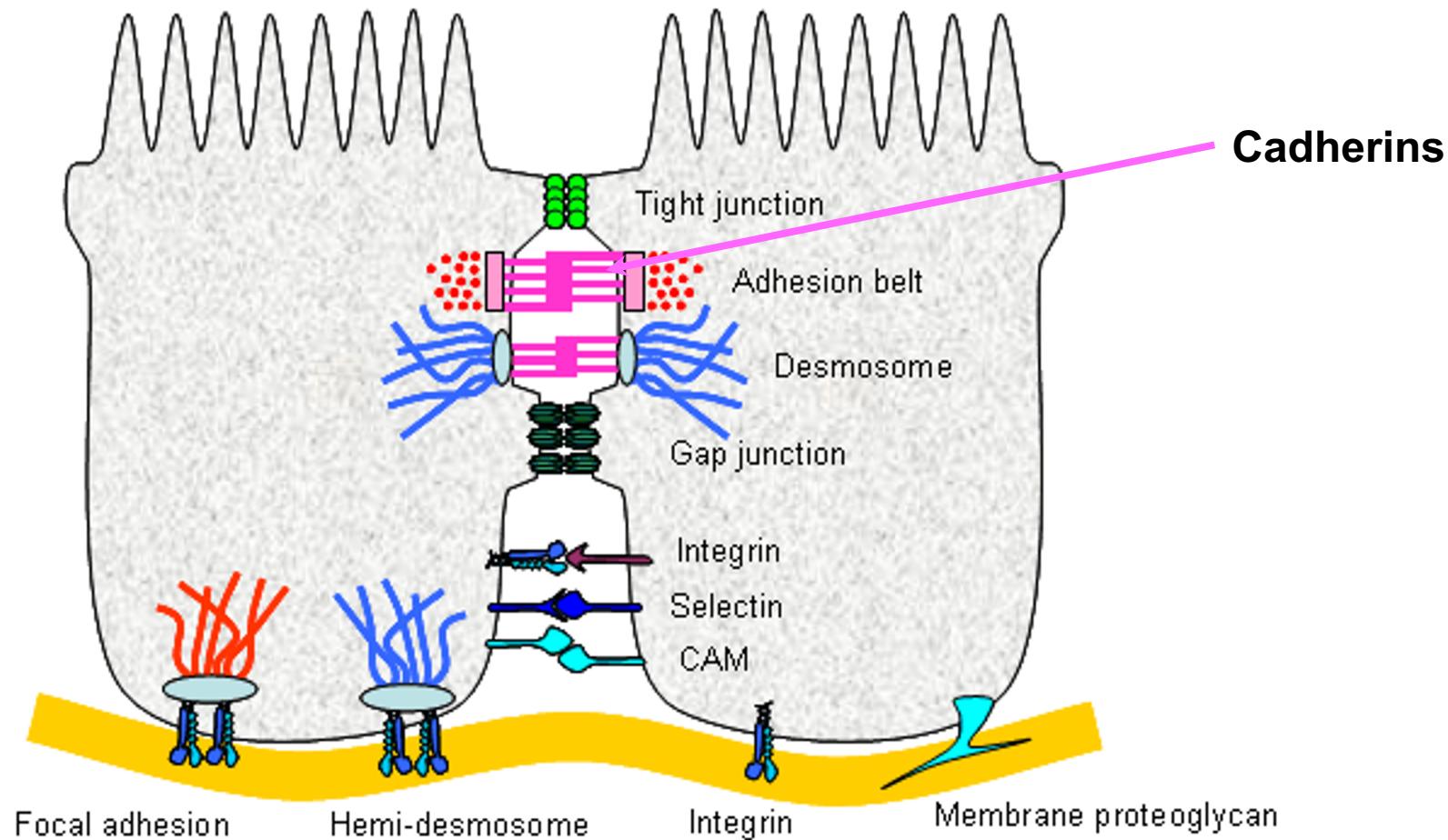
# Mechanical Controls: Shape (9)



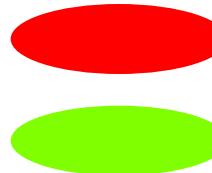
Microcontact Printing



# Mechanical Controls: Adhesion (1)



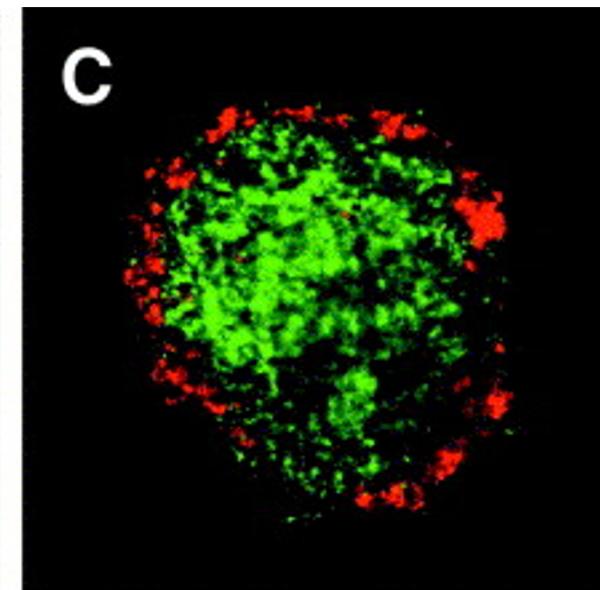
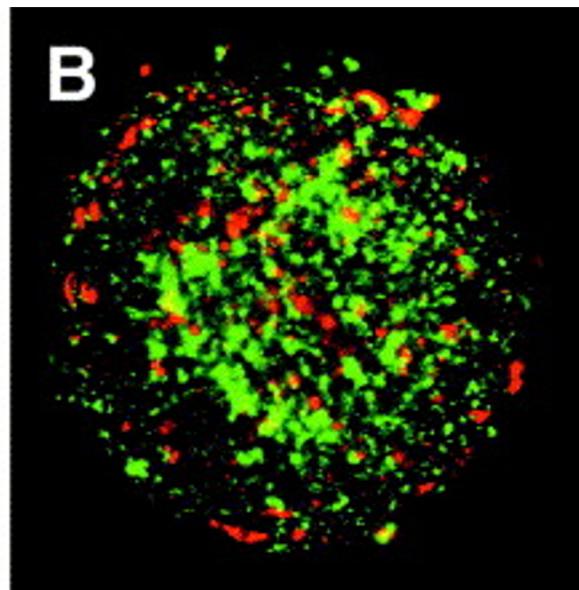
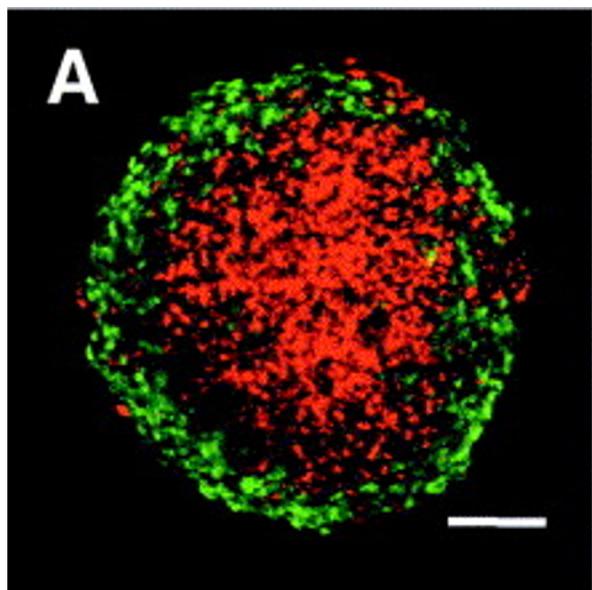
# Mechanical Controls: Adhesion (2)



Standard levels

More or less cadherin

**Spontaneous sorting based  
on cadherin expression**

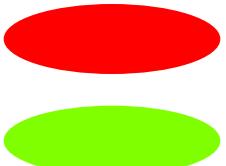
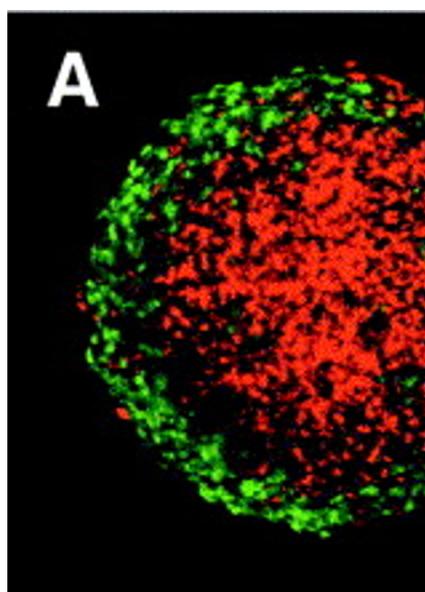


less



more

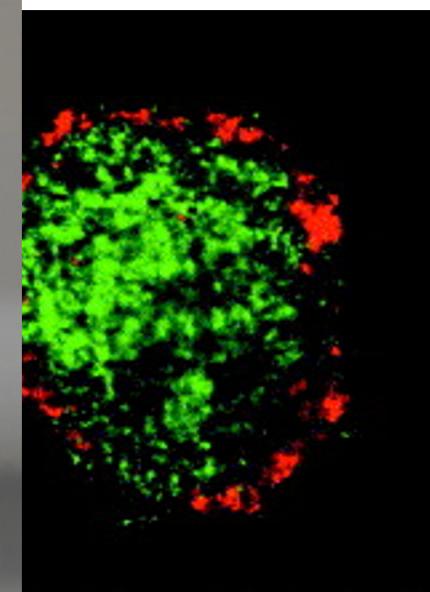
# Mechanical Control



Standard level  
More cadherin



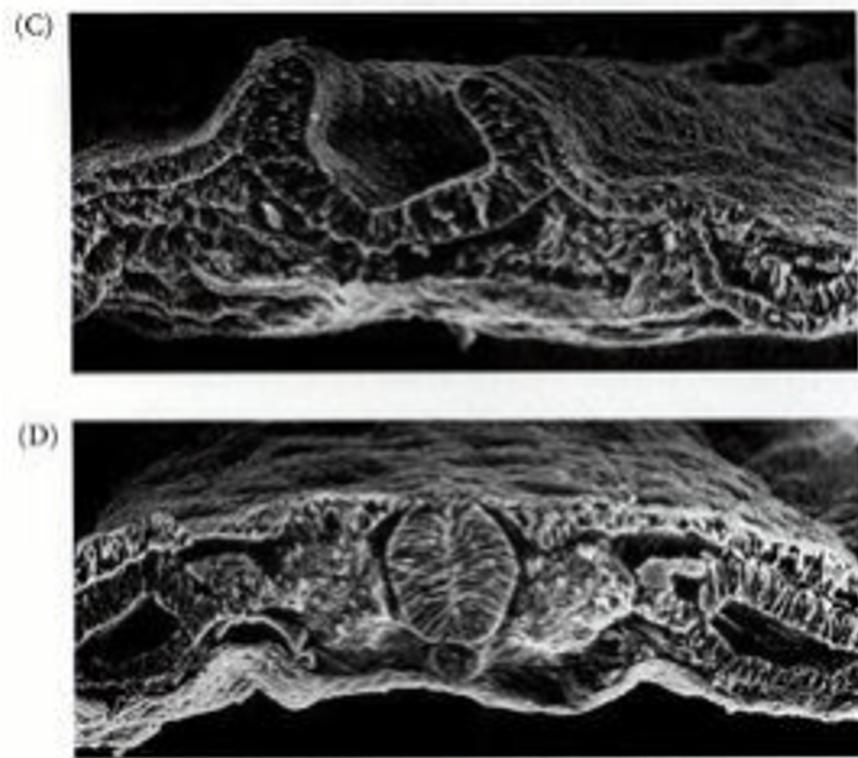
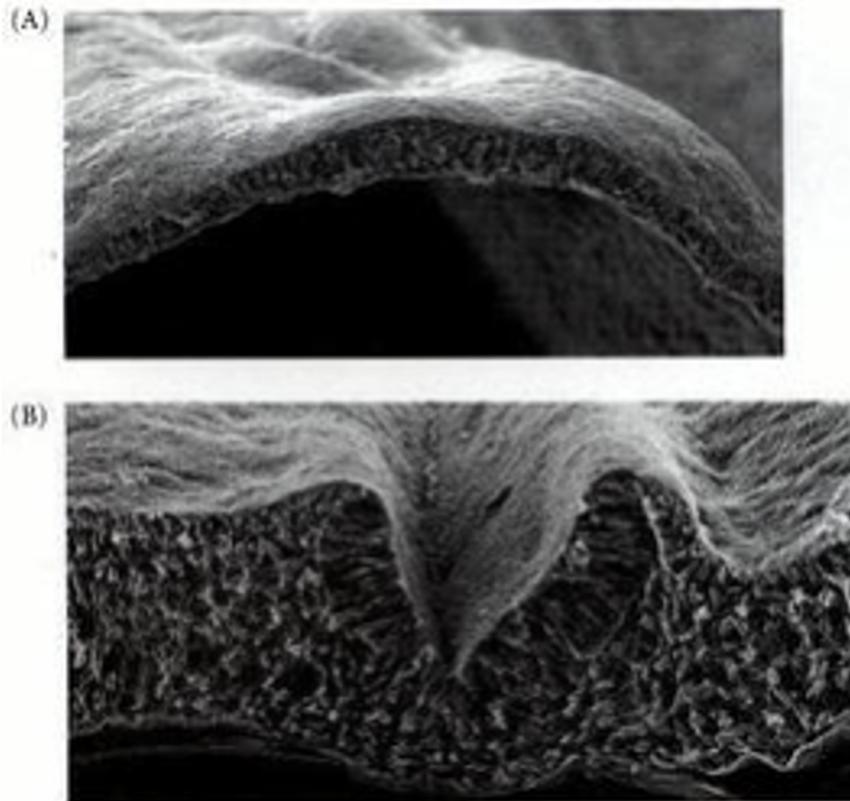
Based  
pression



more

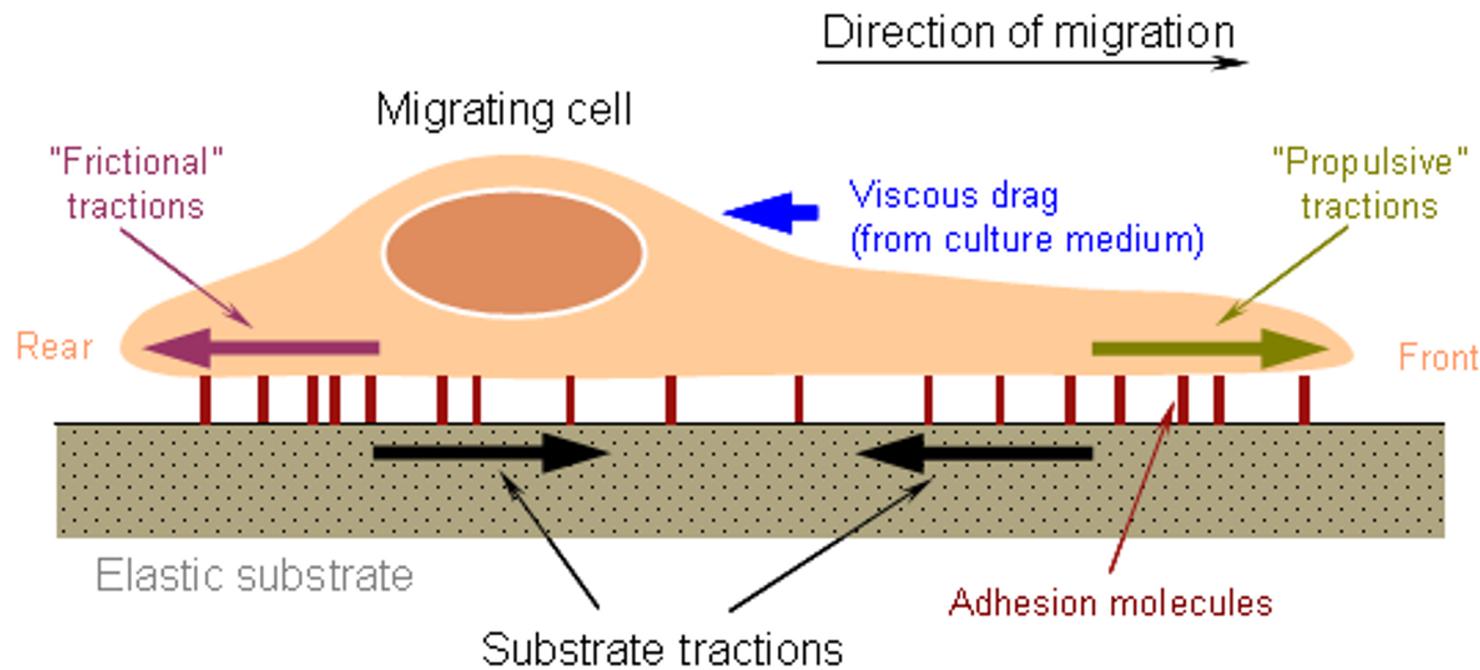
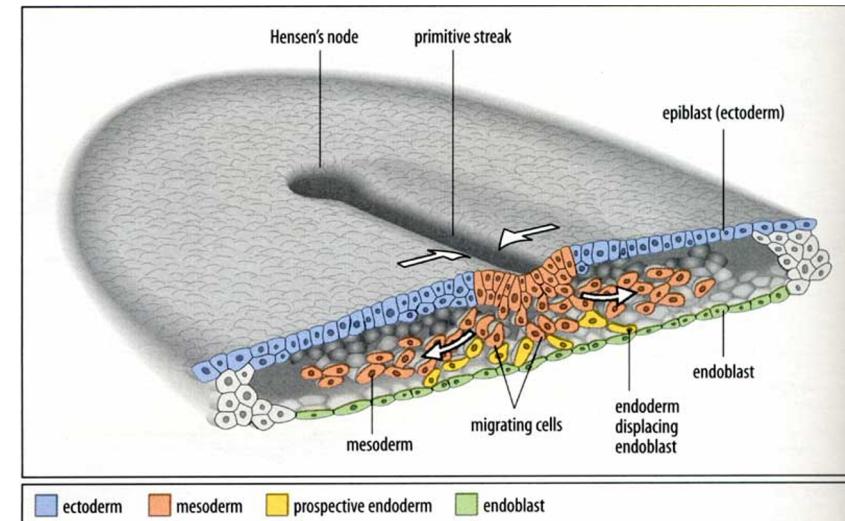
# Mechanical Controls: Adhesion (4)

Neural plate      Epidermis



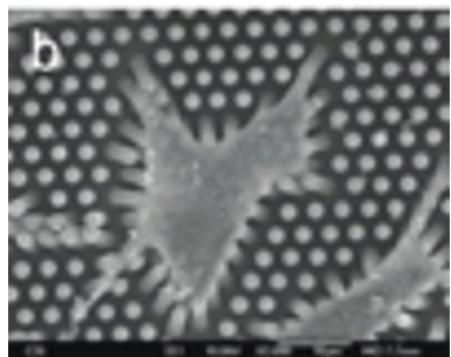
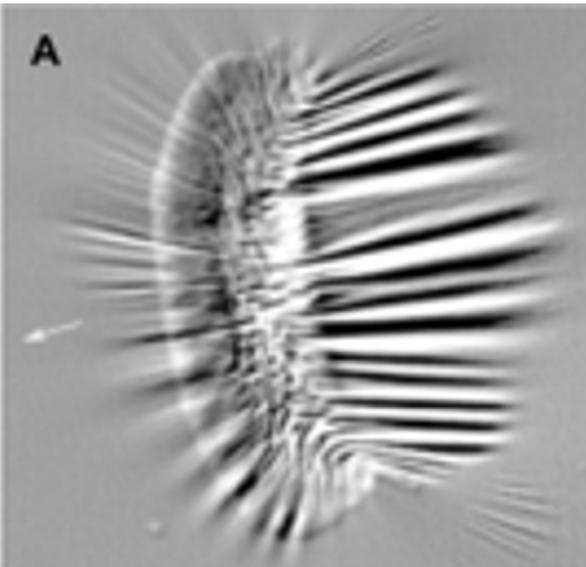
Neural tube

# Mechanical Controls: Migration



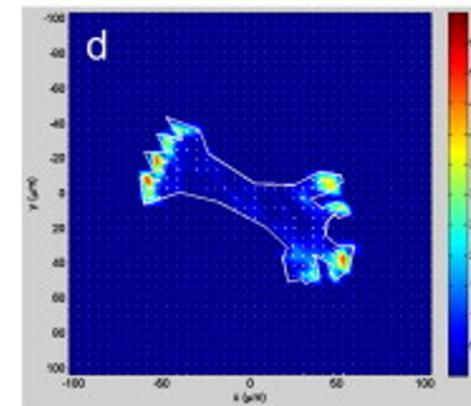
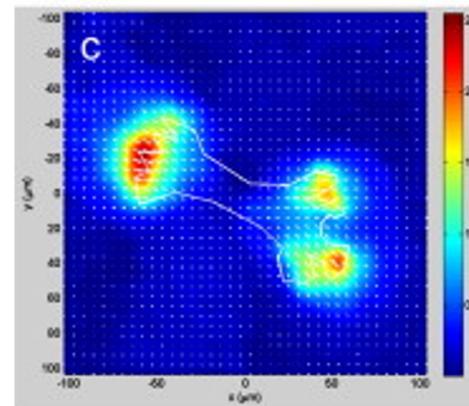
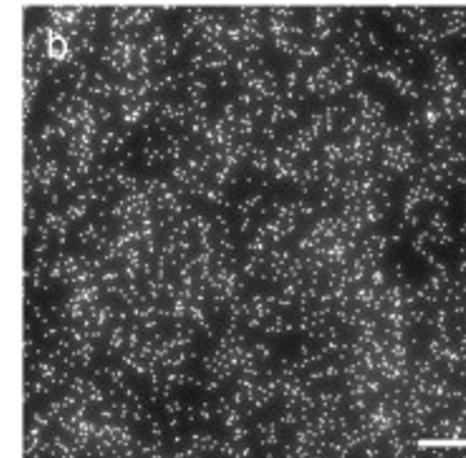
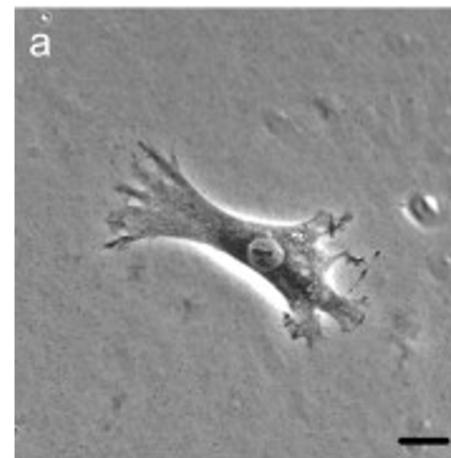
# Mechanical Controls: Migration (cont)

Wrinkle Assay

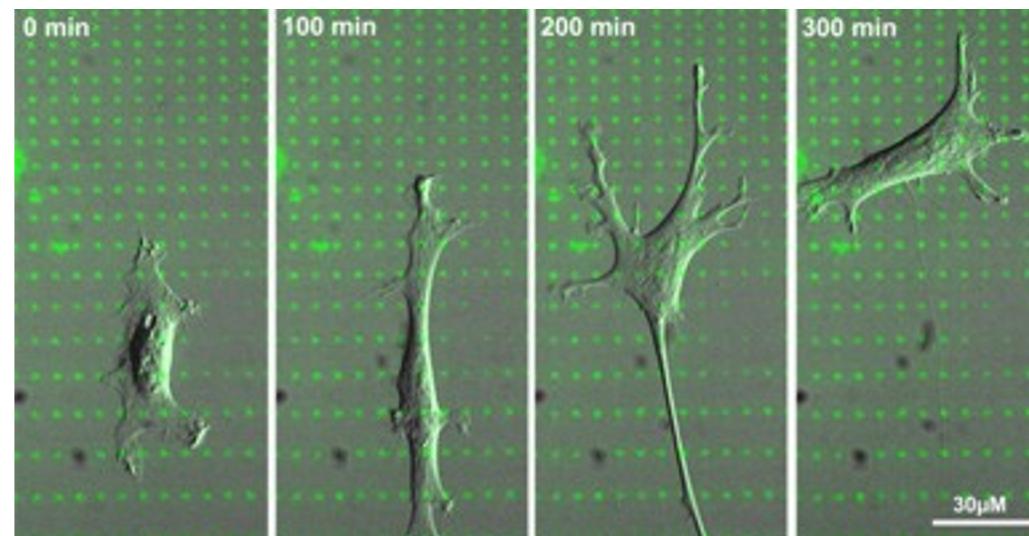
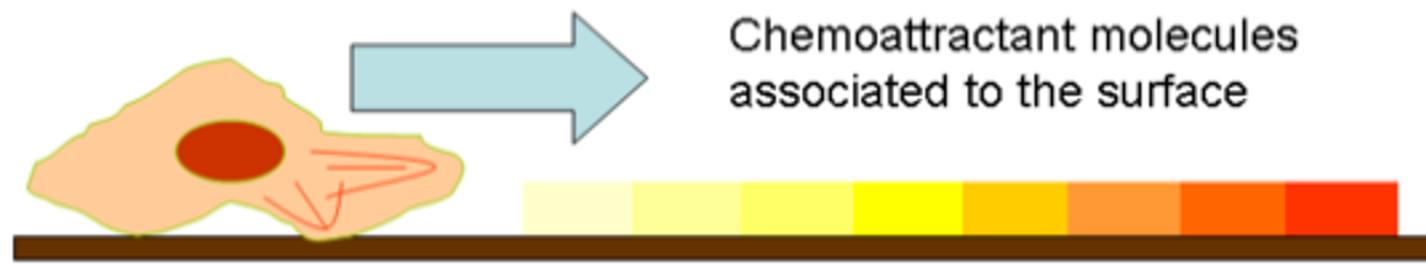


Microneedles

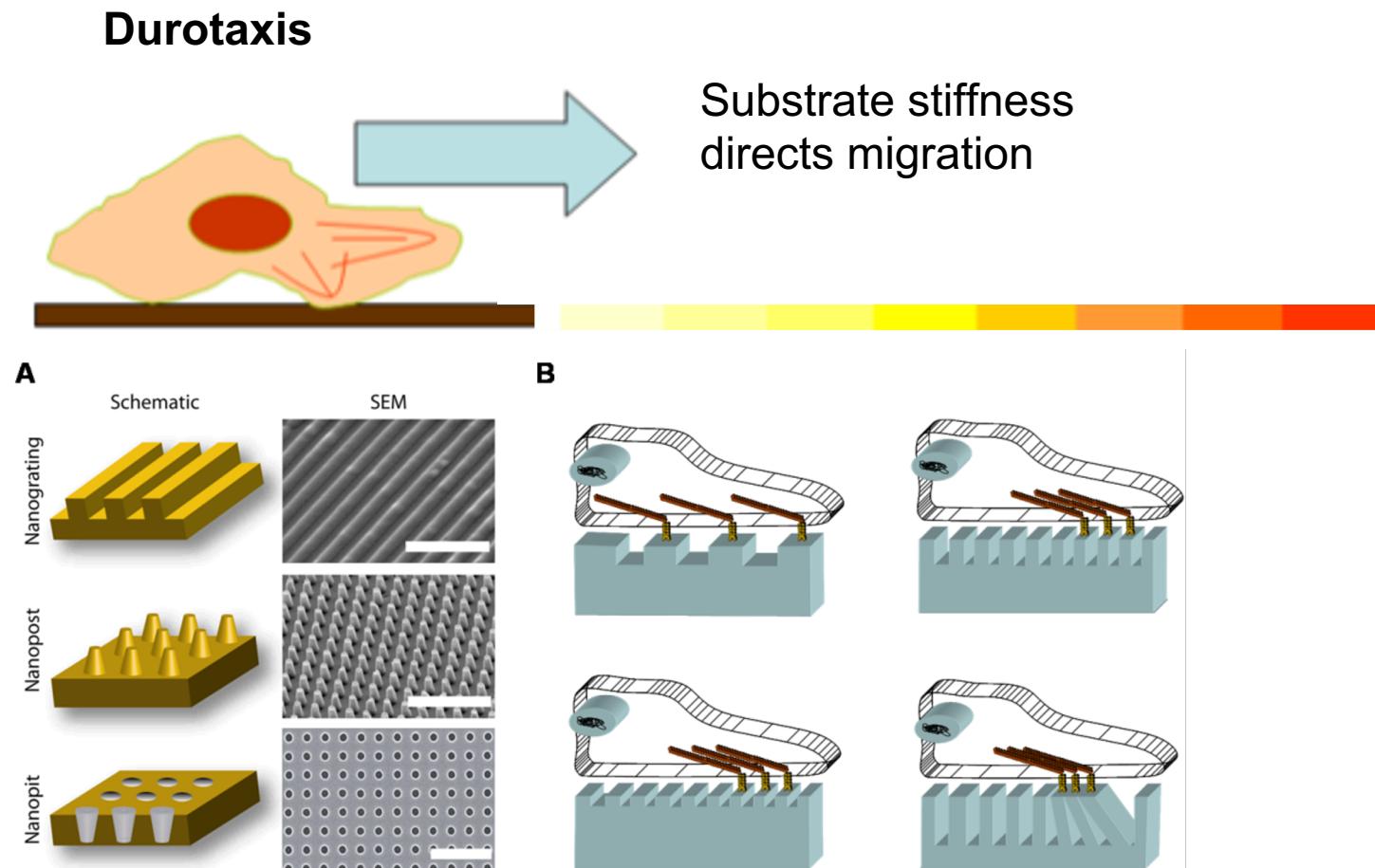
Traction Force Microscopy



# Mechanical Control: Haptotaxis

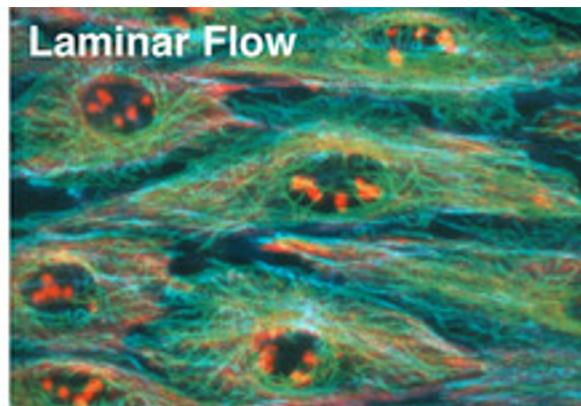
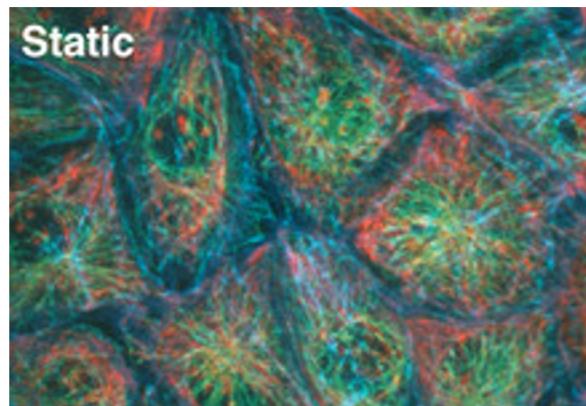
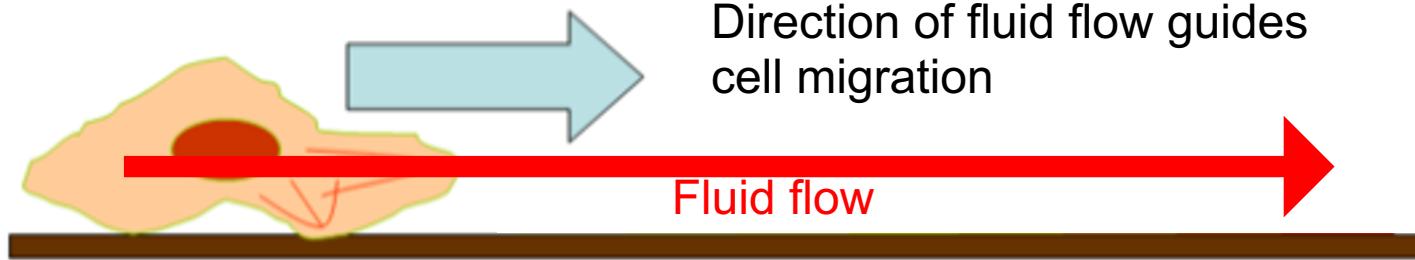


# Mechanical Controls: Mechanotaxis (1)



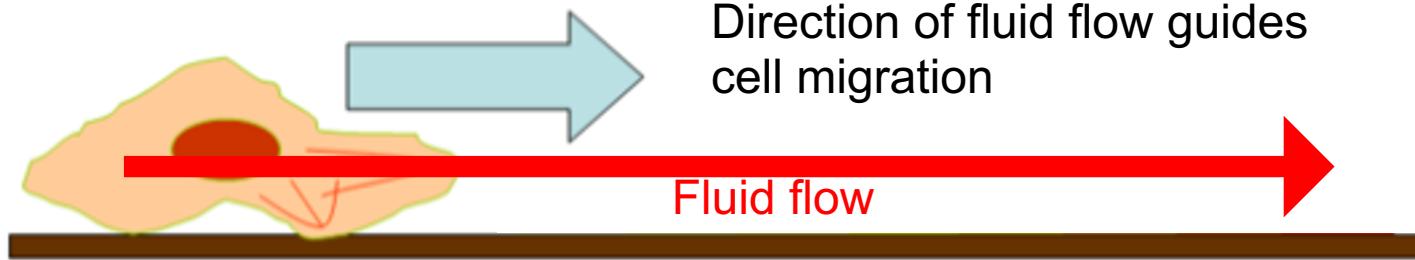
# Mechanical Controls: Mechanotaxis (2)

## Fluid-mediated motility



# Mechanical Controls: Mechanotaxis (3)

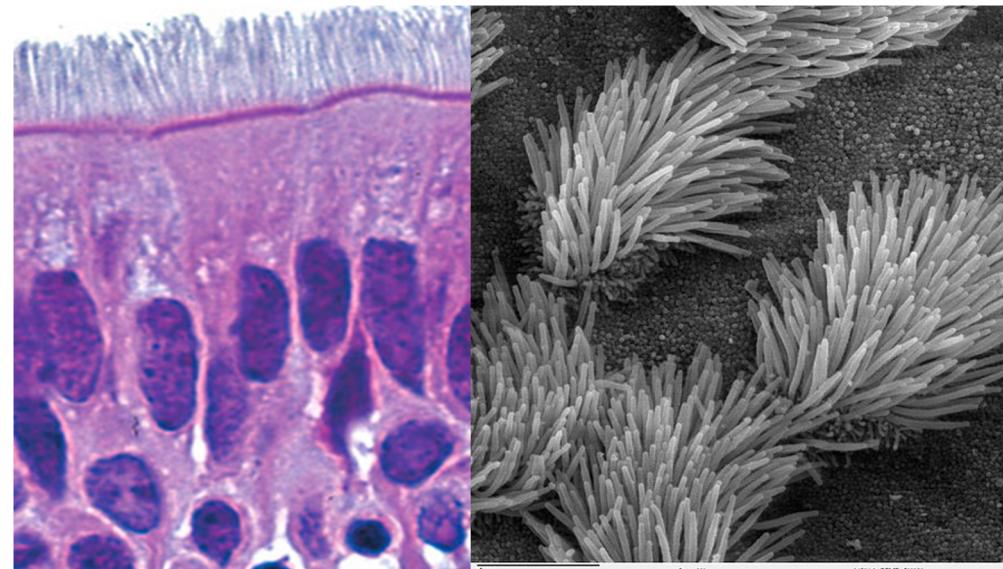
## Fluid-mediated motility



### Kartagener's Syndrome

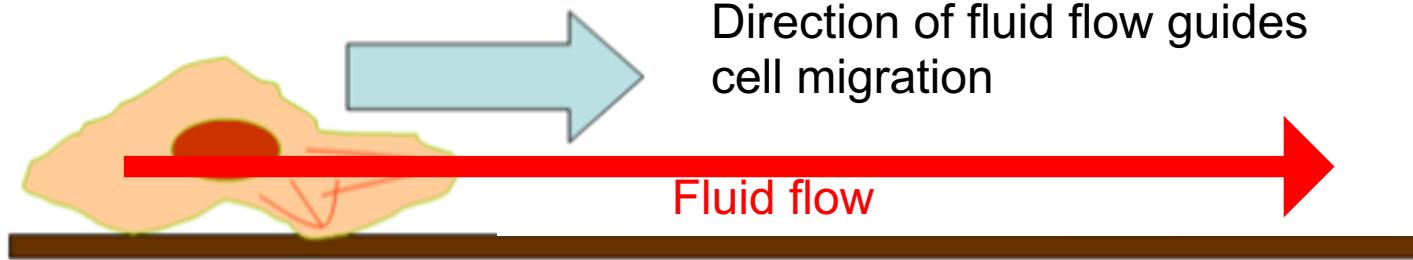
Situs Inversus

Primary ciliary dyskinesia



# Mechanical Controls: Mechanotaxis (4)

## Fluid-mediated motility

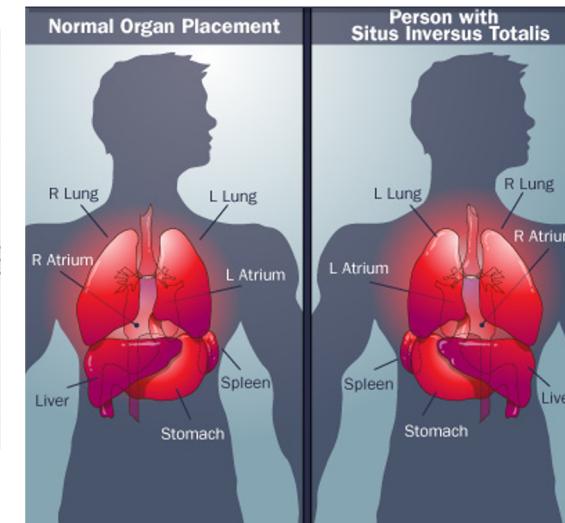
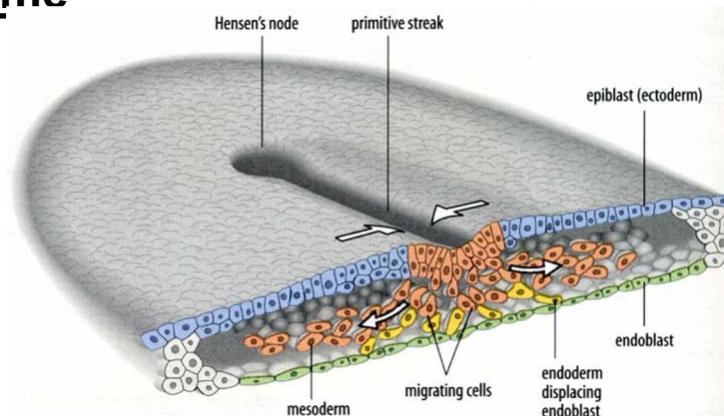
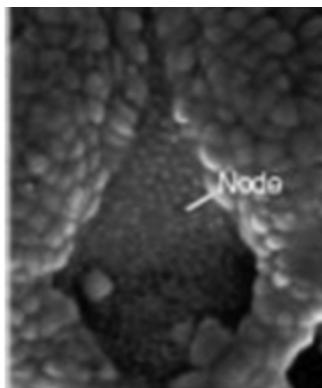


Direction of fluid flow guides  
cell migration

## Kartagener's Syndrome

Situs Inversus

Primary ciliary dyskinesia



<http://en.wikipedia.org/>

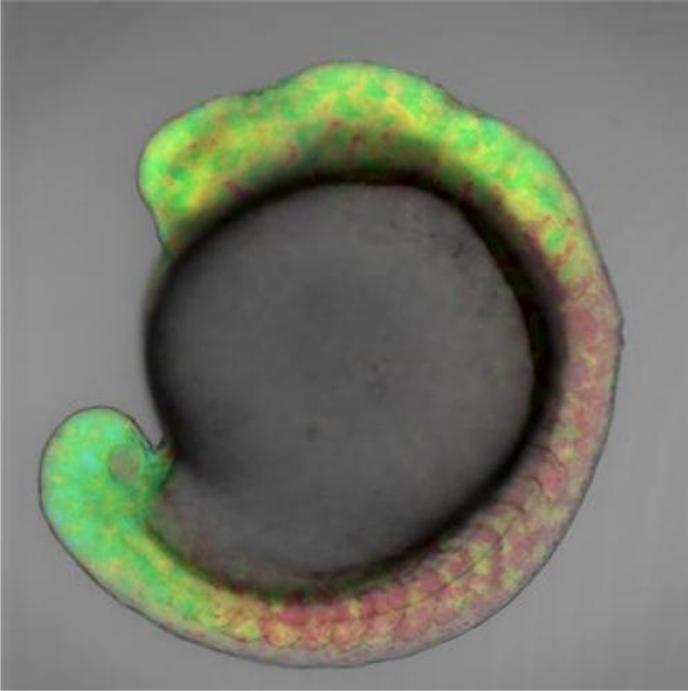
Cartwright et al, HFSP, 2008.

<http://science.howstuffworks.com/life/human-biology/reversal-of-organ1.htm>

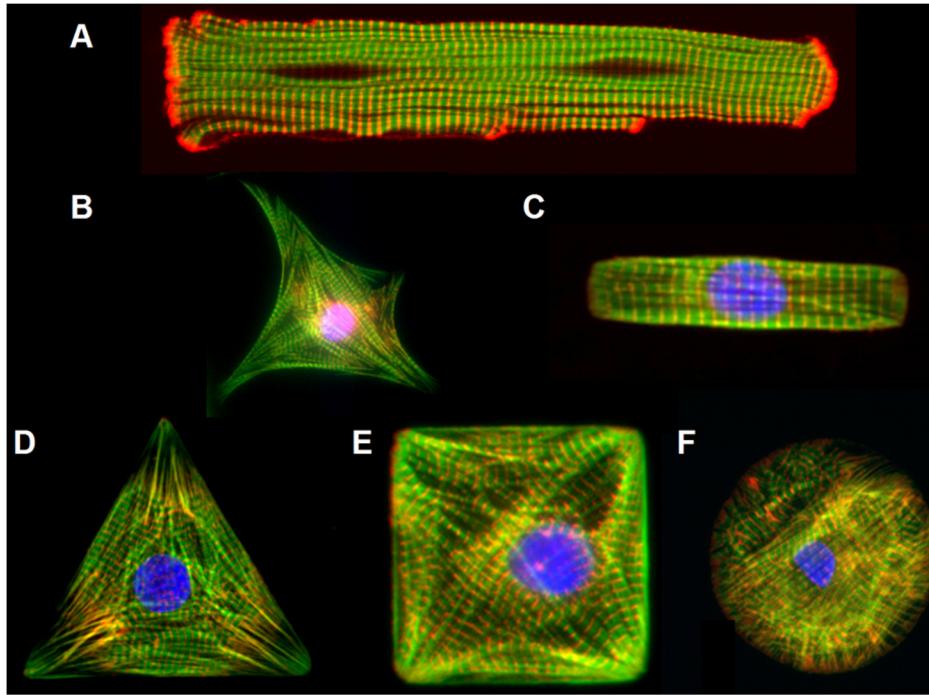
## Part 2 Review

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**Chemical Regulators**



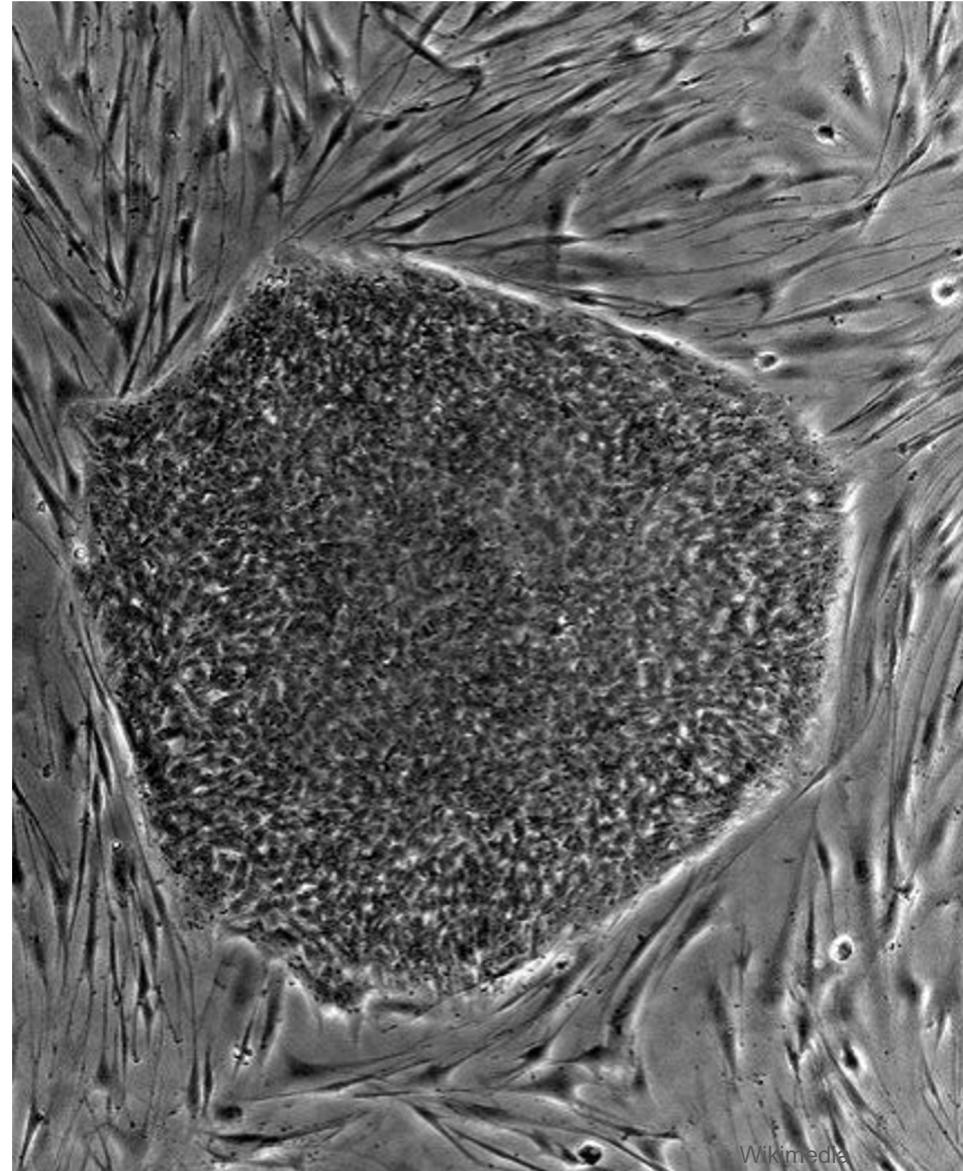
**Mechanical Regulators**



# Next Module

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- Cell Numbers, Growth and Kinetics



Wikimedia  
Commons



# JOHNS HOPKINS

## WHITING SCHOOL *of* ENGINEERING