

# DIFFERENTIATION

HOW CAN AN IDENTICAL SET OF GENETIC INSTRUCTIONS PRODUCE DIFFERENT TYPES OF CELLS?

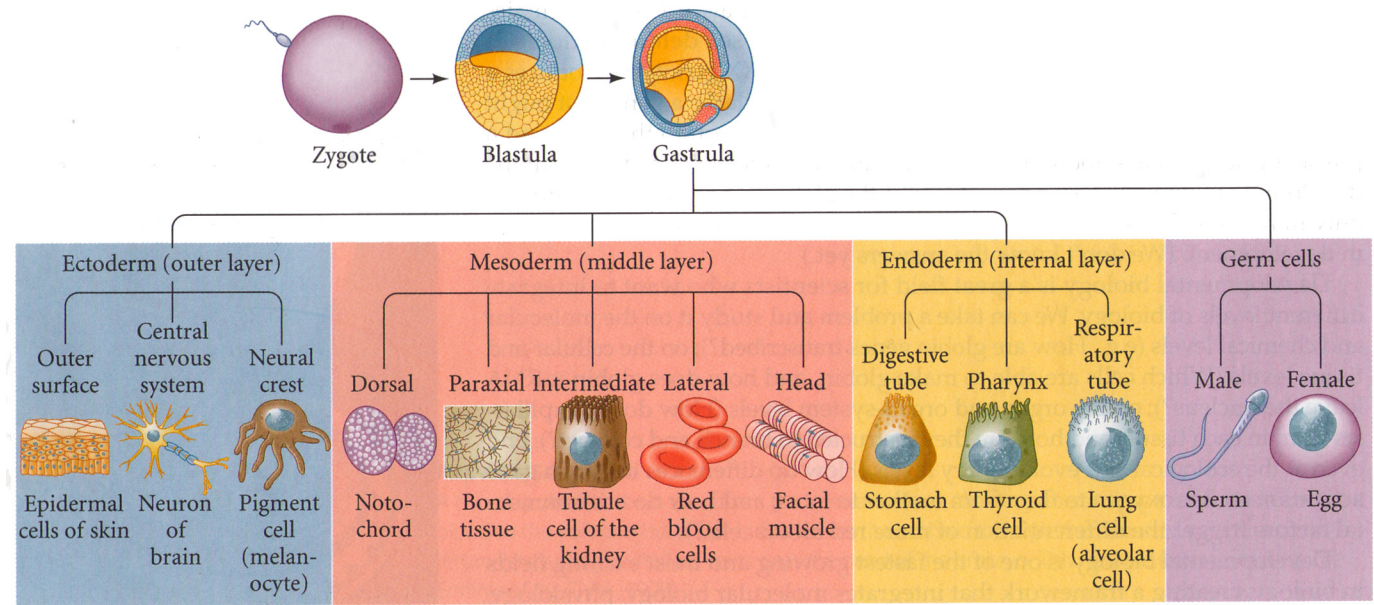
# MORPHOGENESIS

HOW CAN CELLS FORM ORDERED STRUCTURES?

# GROWTH

HOW DO OUR CELLS KNOW WHEN TO STOP DIVIDING AND WHEN TO DIE?





# DIFFERENTIATION

## DIFFERENTIAL GENE TRANSCRIPTION

regulates which genes are allowed to be transcribed into RNA

## SELECTIVE NUCLEAR RNA PROCESSING

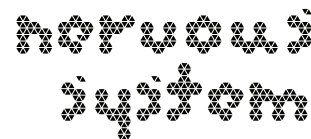
regulates which RNAs are allowed to enter the cytoplasm

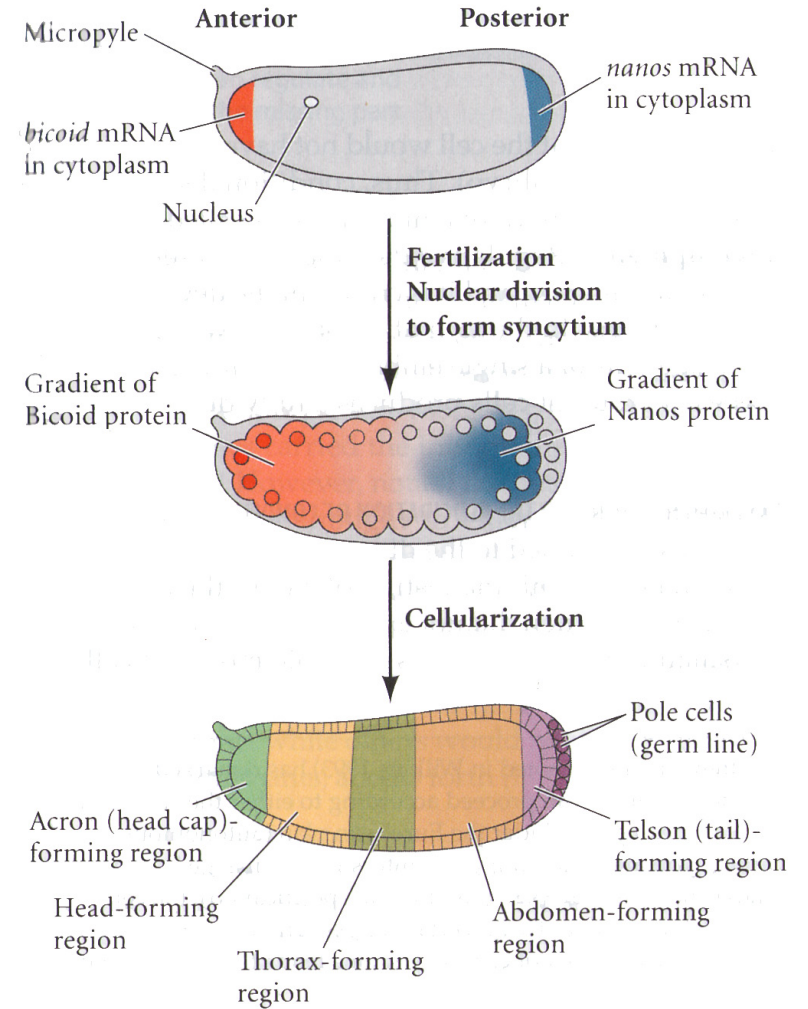
## SELECTIVE MESSENGER RNA TRANSLATION

regulates which mRNAs in the cytoplasm are translated into proteins

## DIFFERENTIAL PROTEIN MODIFICATION

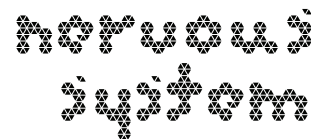
regulates which proteins are allowed to remain and function in the cell

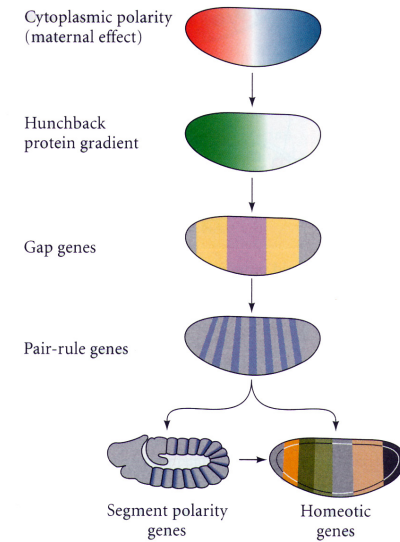
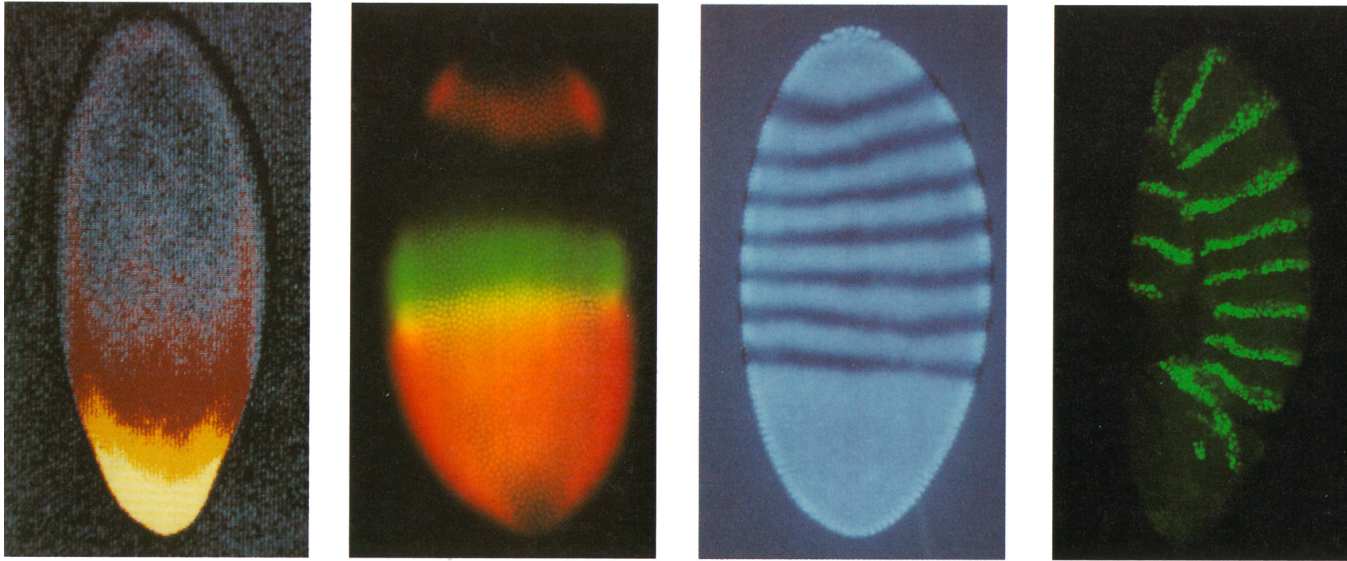




# protein gradients

the ratio of Bicoid to Nanos forms a coordinate system that distinguishes each position along the axis from any other position. when division occurs the amount of each protein present differentially activates transcription of various genes that specify the segmental identities of the fly

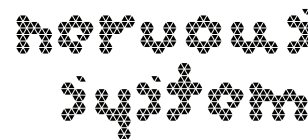




# *morphegenetic fields*

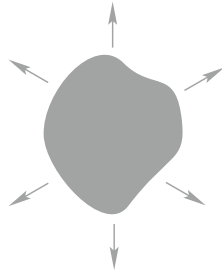
“FIELDS OF ORGANIZATION”  
“CELLULAR ECOSYSTEMS”

a group of cells able to respond to discrete, localized biochemical signals leading to the development of specific morphological structures or organs. The spatial and temporal extent of the embryonic fields are dynamic, and within the field is a collection of interacting cells out of which a particular organ is formed. As a group, the cells within a given morphogenetic field are constrained — i.e. cells in a limb field will become a limb tissue, those in a cardiac field will become heart tissue. However, the specific cellular programming of individual cells in a field is flexible: an individual cell in a cardiac field can be redirected via cell-to-cell signaling to replace specific damaged or missing cells.



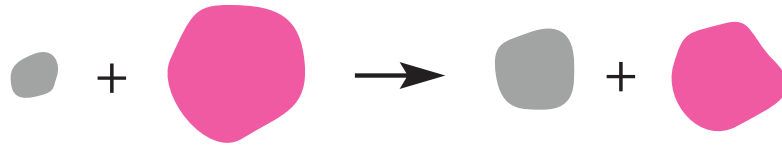
# REACTION-DIFFUSION

Diffusion



Molecules naturally spread to areas of less density

Reaction

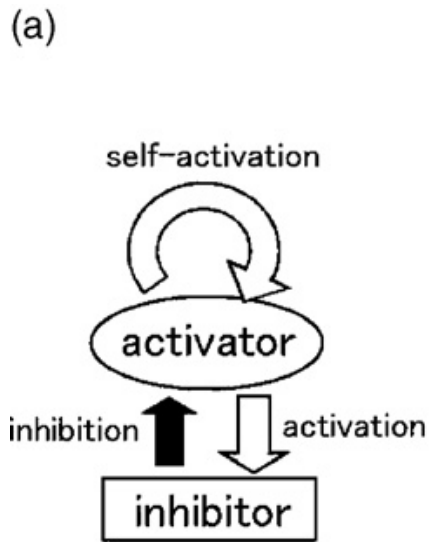


Chemicals recombine, synthesize, degrade changing quantities

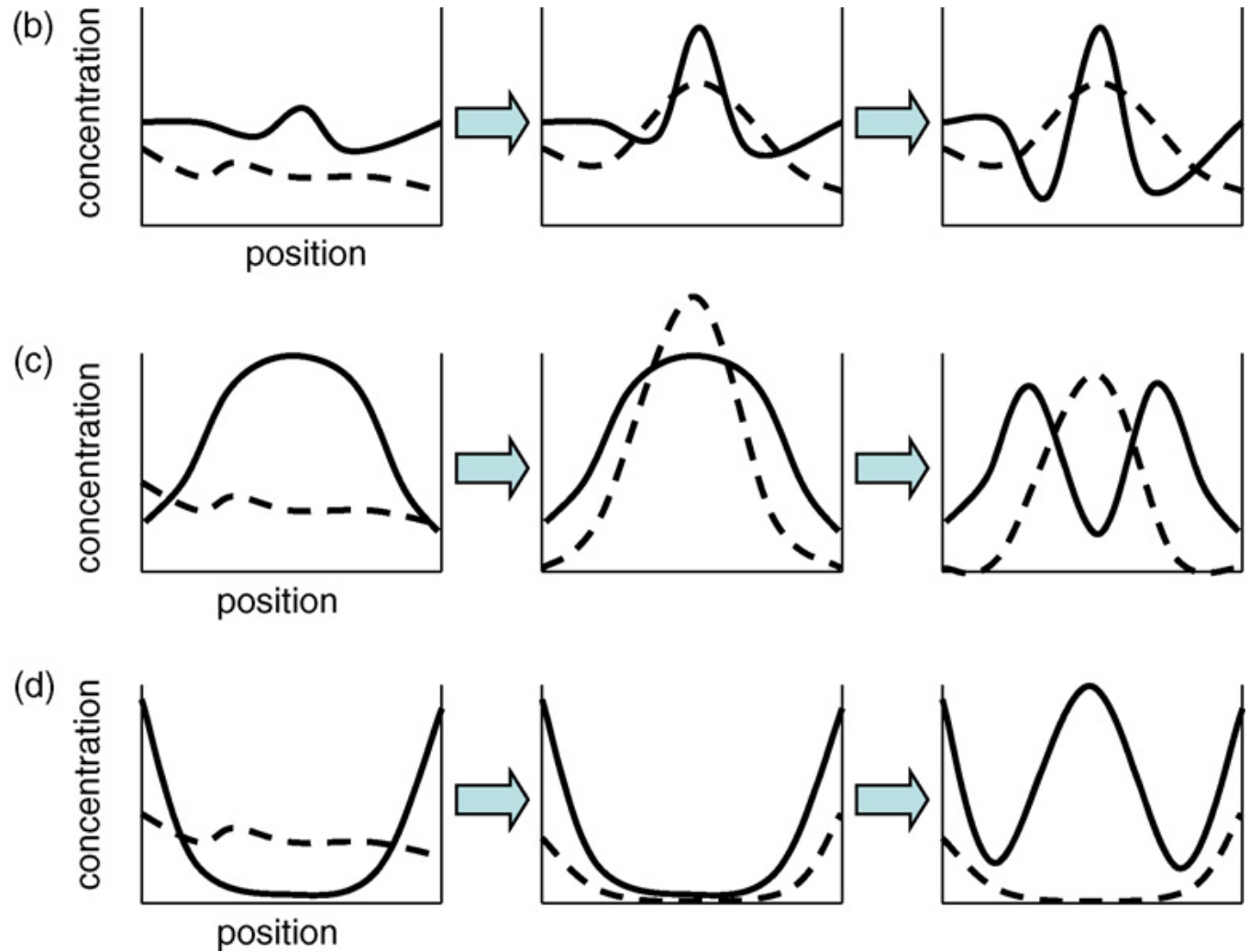
Reaction  
Diffusion



Combining these processes patterns emerge and stabilize



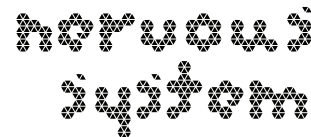
— Activator  
 - - - inhibitor

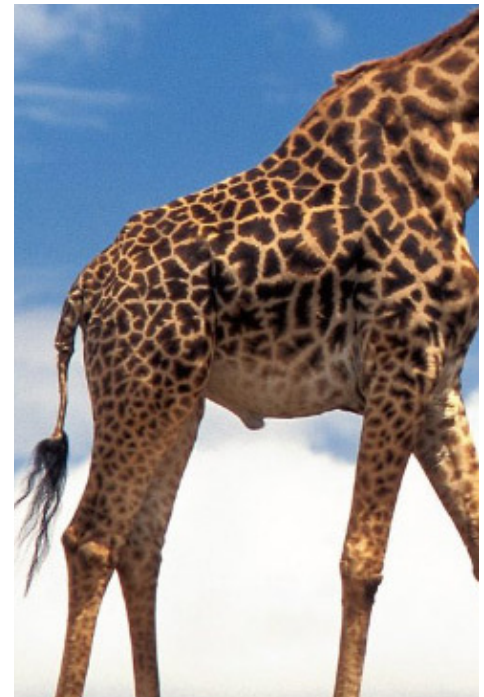
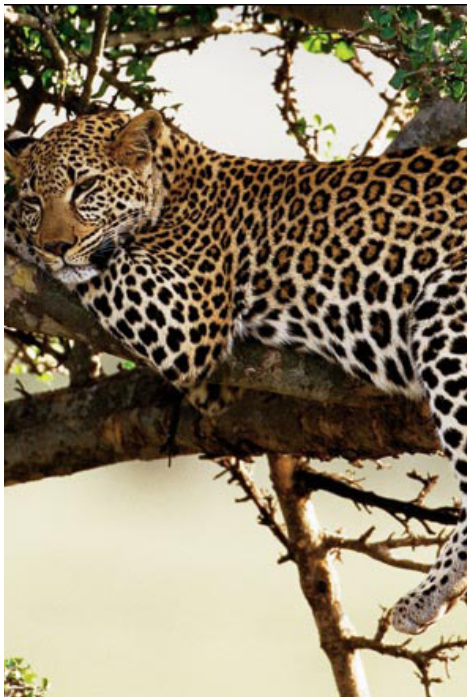
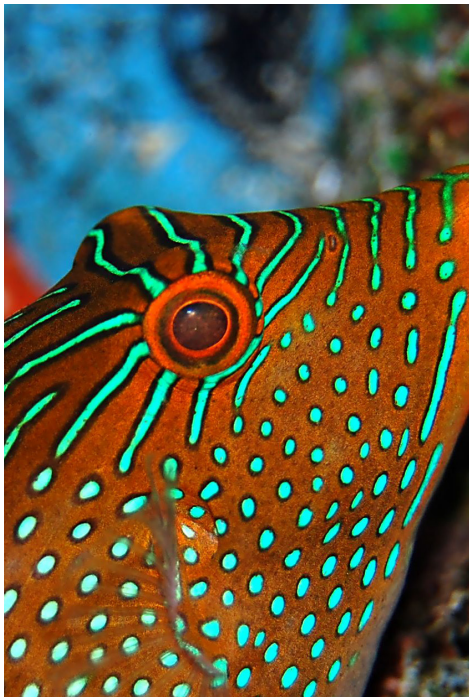
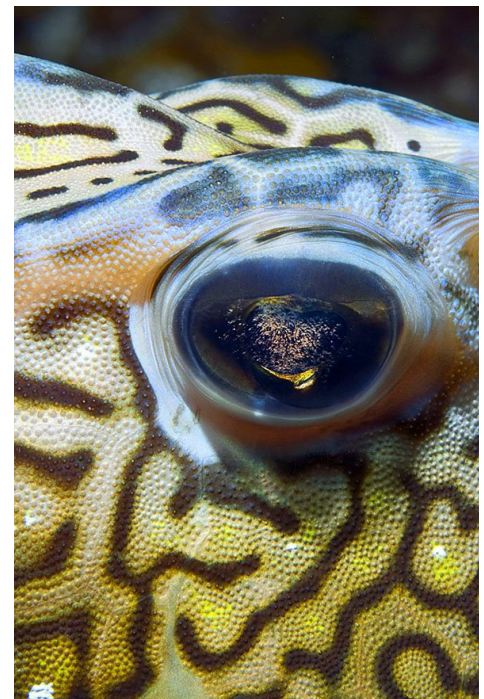
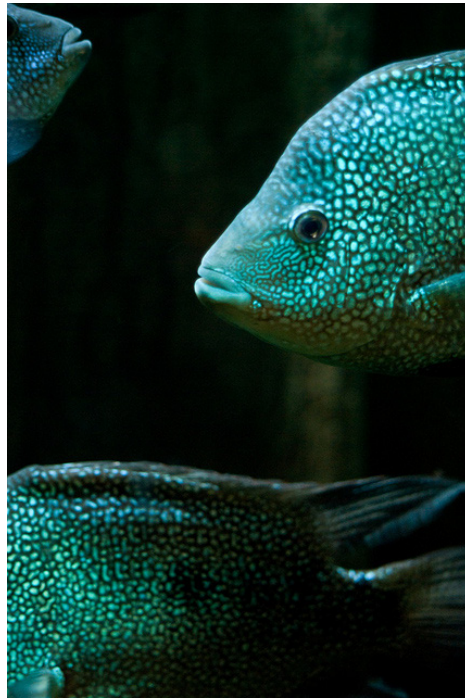


local amplification

lateral inhibition

inhibitor diffuses more quickly than activator





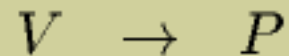
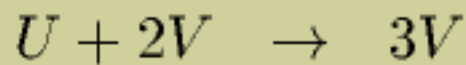
Норвежская  
система

## Equations:

$$\frac{\partial u}{\partial t} = r_u \nabla^2 u - uv^2 + f(1 - u)$$

$$\frac{\partial v}{\partial t} = r_v \nabla^2 v + uv^2 - (f + k)v$$

## Chemical Reaction:



U and V and P are chemical species.

u and v represent their concentrations.

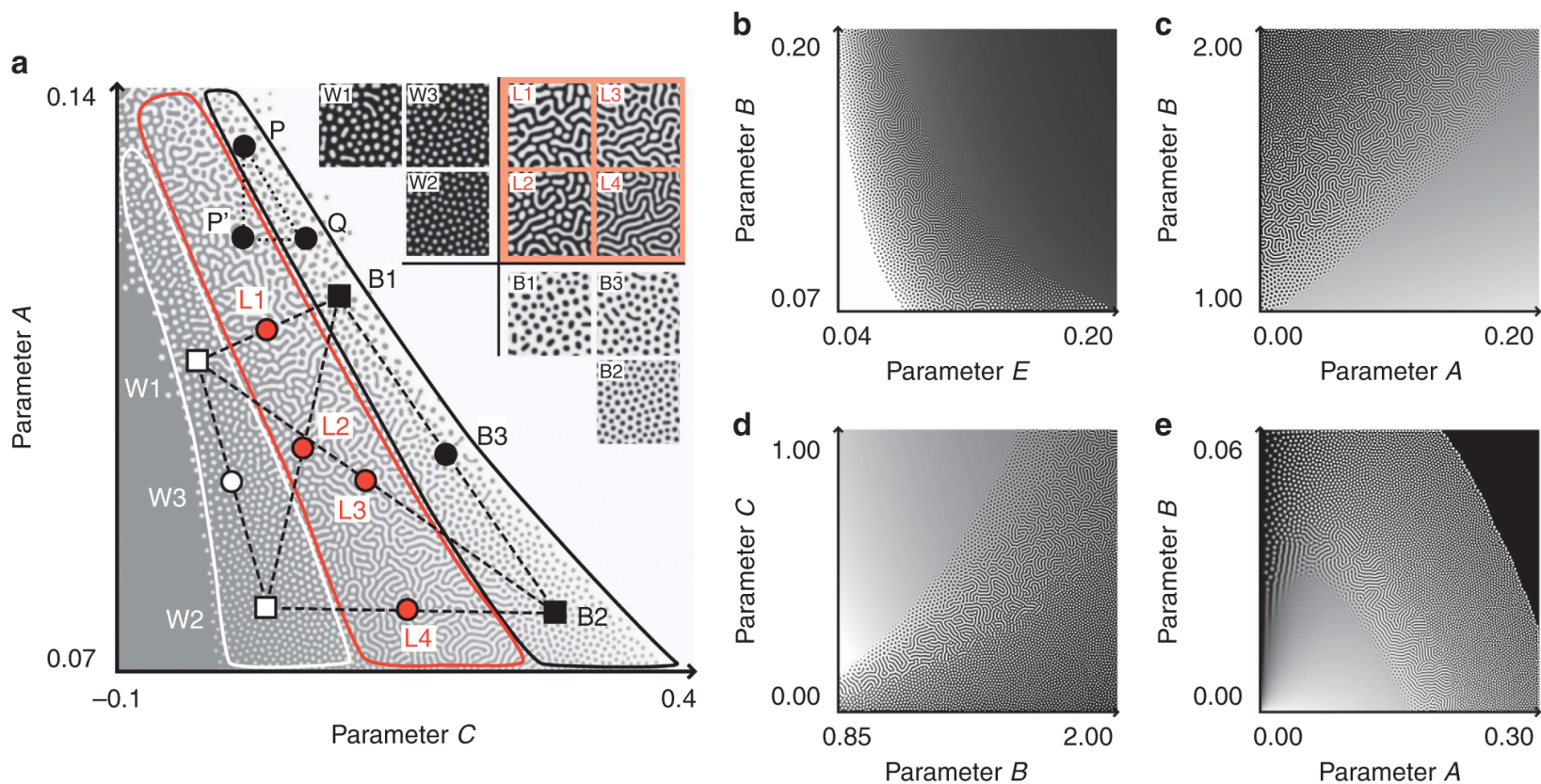
$r_u$  and  $r_v$  are their diffusion rates.

k represents the rate of conversion of V to P.

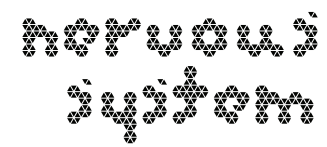
f represents the rate of the process that feeds U and drains U,V and P.

# gray-scott reaction-diffusion





**Figure 3 | 'In silico hybridization' in the two-dimensional parameter space.** (a) Pattern dynamics in the linear model RD system. Each point  $(x, y)$  represents a parameter set ( $C=x, A=y$ ) for the model equations. The labyrinthine pattern zone (outlined by the red border) lies between the white spot zone (white bordered) and the black spot zone (black bordered). Broken line segments joining the coloured squares (W1-2 and B1-2) denote 'in silico hybridization' between distinct parameter sets ('genotypes'). The midpoints of these segments (coloured circles; W3, B3 and L1-4) correspond to the 'hybrids'. The colour patterns calculated using the parameter sets of the indicated points are shown in the insets. (b-e) Pattern dynamics with various parameter sets and models. (b) Linear model, (c, d) the Gierer-Meinhardt model and (e) the Gray-Scott model.





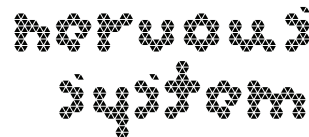
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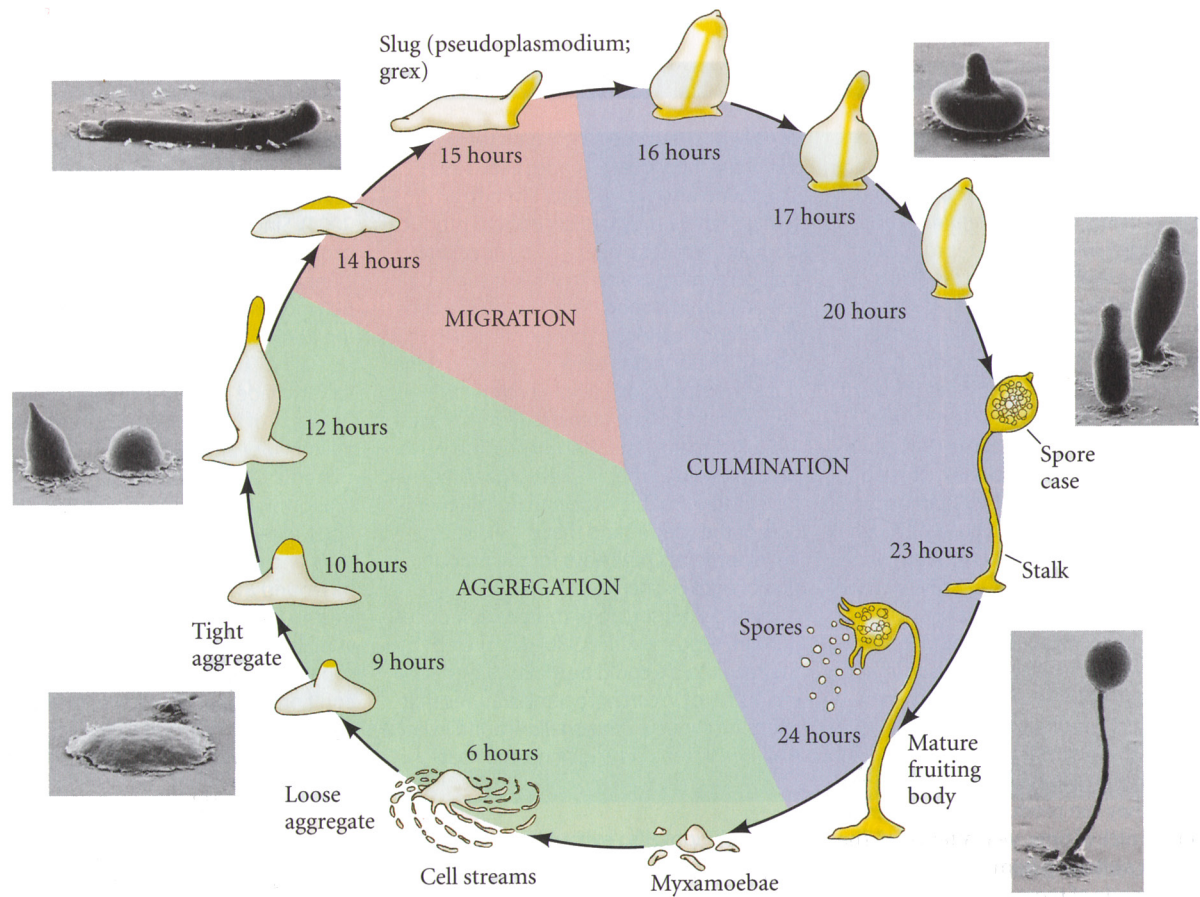


# *hybrid fish experiments*

WHITE-SPOTTED CHARR ( *S. LEUCOMAENIS* ) X MASU SALMON ( *O. MASOU MASOU* )

PECULIAR LABYRINTHINE PATTERNS ARE SEEN IN ALL THE HYBRIDS.

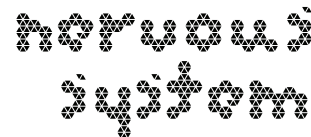




# *the social amoeba*

INDIVIDUAL SLIME MOLD CELLS CAN ACT TOGETHER TO FORM MACROSCOPIC STRUCTURES USING REACTION-DIFFUSION

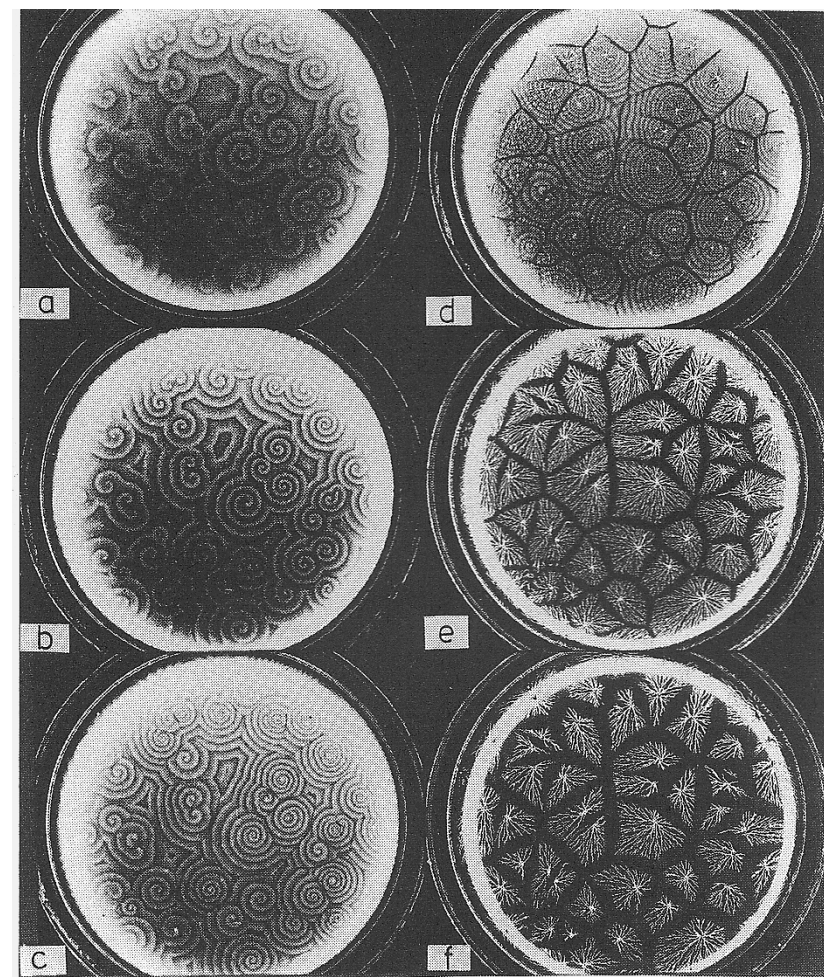
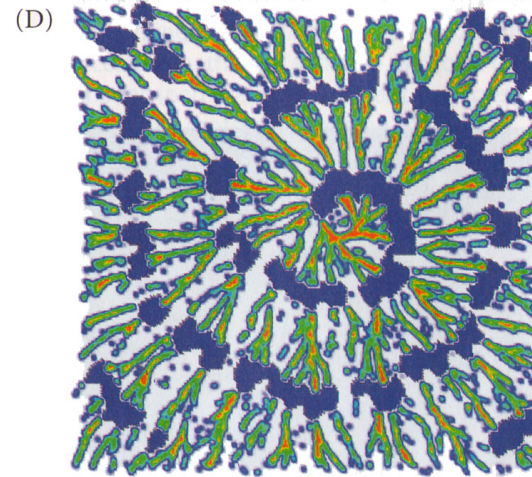
When food is readily available they are individual amoebae, which feed and divide normally. However when the food supply is exhausted, they aggregate to form a multicellular assembly, called a pseudoplasmodium or slug. The slug has a definite anterior and posterior, responds to light and temperature gradients, and has the ability to migrate. Under the correct circumstances the slug matures forming a fruiting body with a stalk supporting one or more balls of spores. These spores are inactive cells protected by resistant cell walls, and become new amoebae once food is available.



CAMP WAVES PRODUCED (B)  
BY AGGREGATING  
DICTYOSTELIUM AS SEEN ON  
FILTER PAPER TAGGED WITH  
RADIOACTIVE CAMP



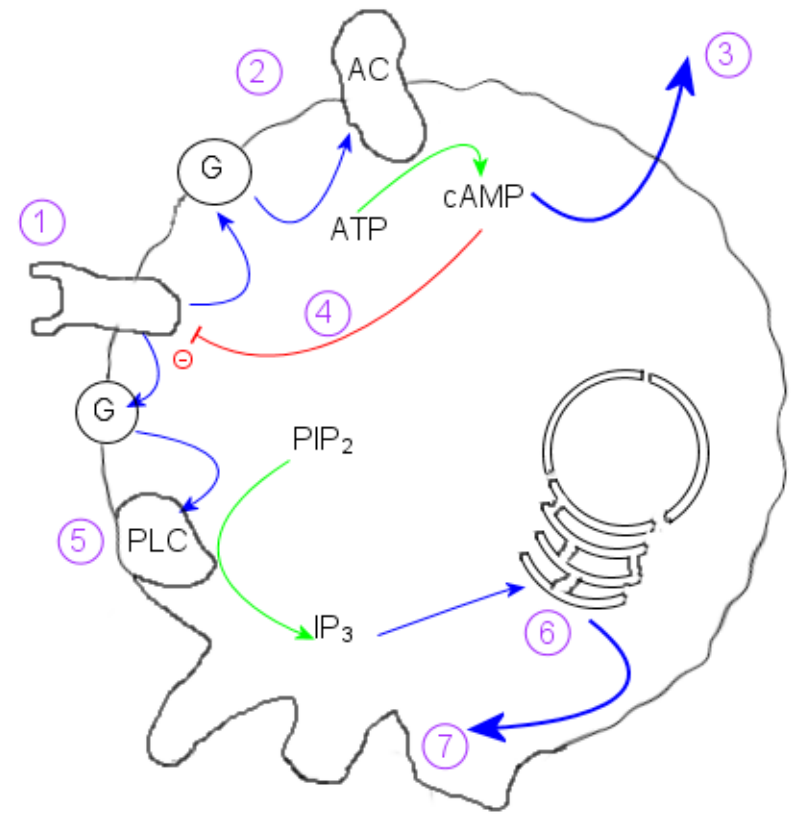
COMPUTER SIMULATION  
MODELING RECEPTION AND  
RELEASE OF CAMP AND  
CHANGES IN CELL DENSITY  
DUE TO CELL MOVEMENT



PHOTOS TAKEN 10 MIN APART OF  $5 \times 10^7$  AGGREGATING  
DICTYOSTELIUM DISCOIDEUM. CELLS APPEAR BRIGHT WHEN MOVING  
AND DARK WHEN STATIONARY

# *Dictyostelium* aggregation

AGGREGATION IS INITIATED AS EACH OF THE SLIME MOLDS BEGIN TO SYNTHESIZE CAMP. THERE ARE NO DOMINANT CELLS THAT BEGIN THE SECRETION OF CONTROL THE OTHERS. INSTEAD THE SITES OF AGGREGATION ARE DETERMINED BY THE DISTRIBUTION OF DICTYOSTELIUM. THE CELLS RESPOND TO CAMP BY INITIATING MOVEMENT TOWARD THE CAMP PULSE FOR ABOUT 1 MINUTE AND THEY RELEASE CAMP OF THEIR OWN. THE CAMP ALSO CAUSES A CHANGE IN CYTOSKELETAL POLARITY WHICH LEADS TO THE MOVEMENT OF THE CELL. AFTER THIS THE CELL IS UNRESPONSIVE TO FURTHER CAMP PULSES FOR SEVERAL MINUTES.



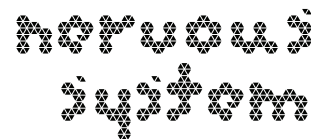
# *Dictyostelium* aggregation

1. cAMP reception at the cell membrane activates a G-protein
2. G protein stimulates Adenylate cyclase
3. cAMP diffuses out of cell into medium
4. Internal cAMP inactivates the external cAMP receptor.
5. A different g-protein stimulates Phospholipase C
6. IP3 induces calcium ion release
7. Calcium ions act on the cytoskeleton to induce the extension of pseudopodia.

Cell signaling/spiral waves in Dictyostelium  
<http://www.youtube.com/watch?v=OX5Yiz38fgY>

John Bonner's slime mold movies  
<http://www.youtube.com/watch?v=bkVhLJLG7ug>

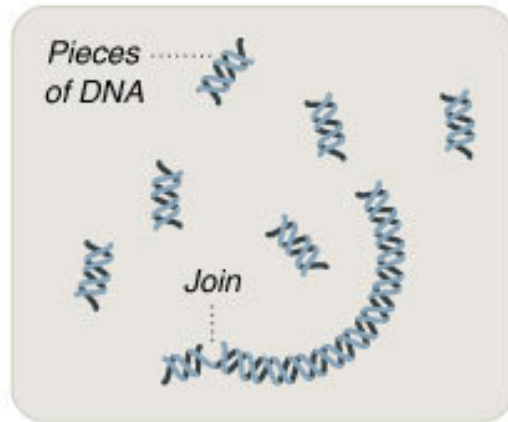
Slime Mold Waltz  
<http://www.youtube.com/watch?v=wwRxoiiGCWY>



May 2010 - the Venter Institute created the first “synthetic” lifeform  
*Mycoplasma laboratorium*

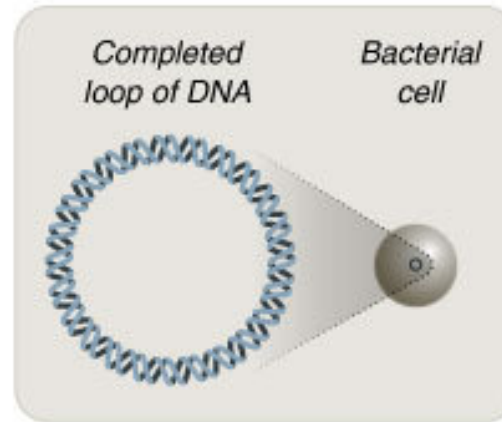
## Synthesizing a Functional Genome

A team led by J. Craig Venter has succeeded in creating a synthetic bacterial genome and using it to control a cell.

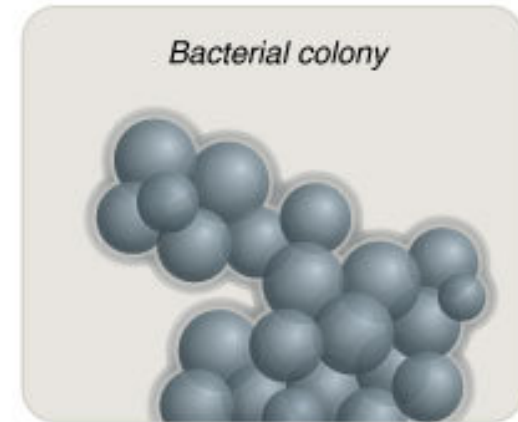


**ASSEMBLY** The team began with small pieces of laboratory-made DNA, then used a new technique to join them together into the largest piece of DNA synthesized so far, a loop one million units in length.

Source: *Science*



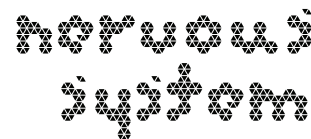
**INSERTION** The loop of DNA was designed to closely replicate the genetic sequence of a species of bacterium. To test the DNA, the team inserted it into an empty cell of a different species of bacterium.



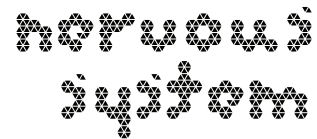
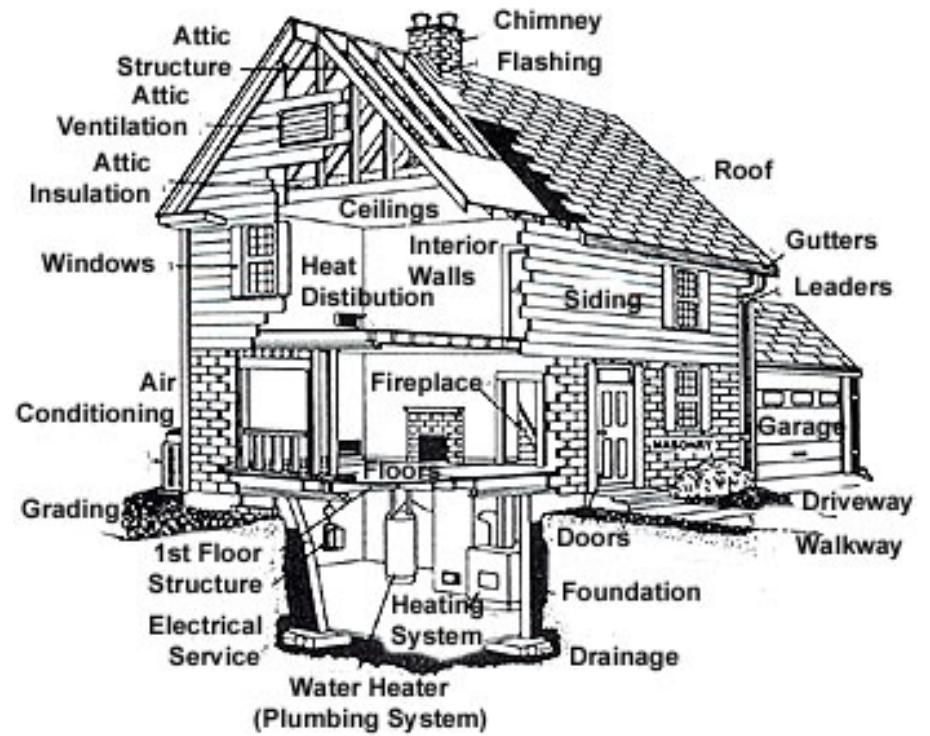
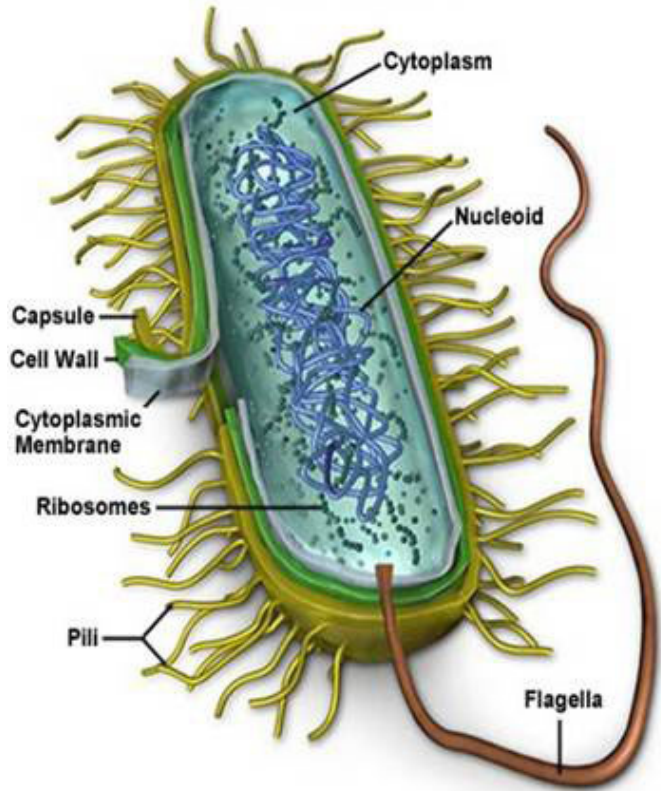
**SELF-REPLICATION** The synthetic DNA proved accurate enough to take over the bacterial cell and substitute for the cell's own DNA. The “synthetic cell” then replicated itself to form a bacterial colony.

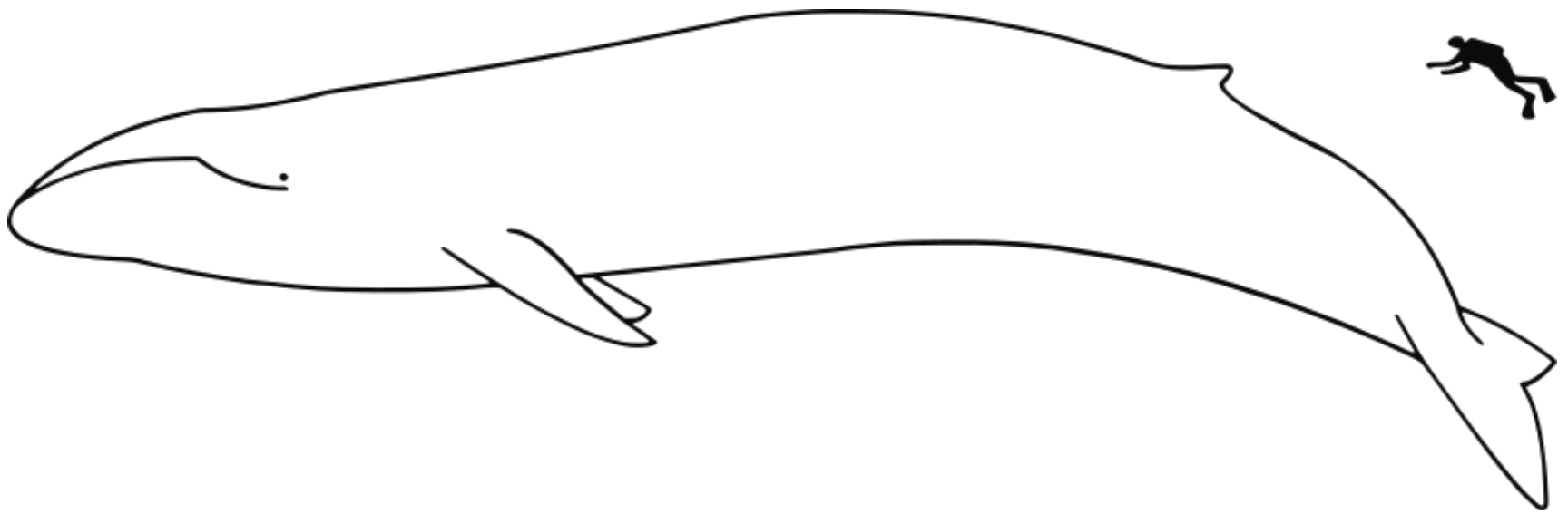
THE NEW YORK TIMES

now what?

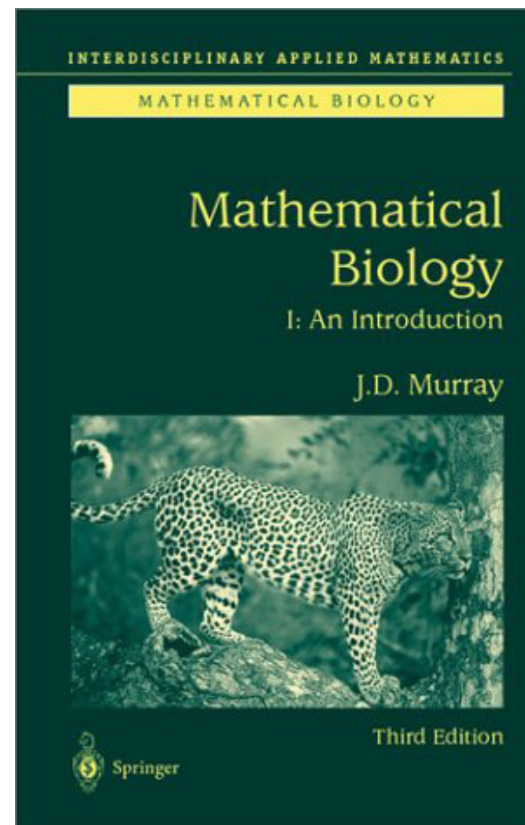
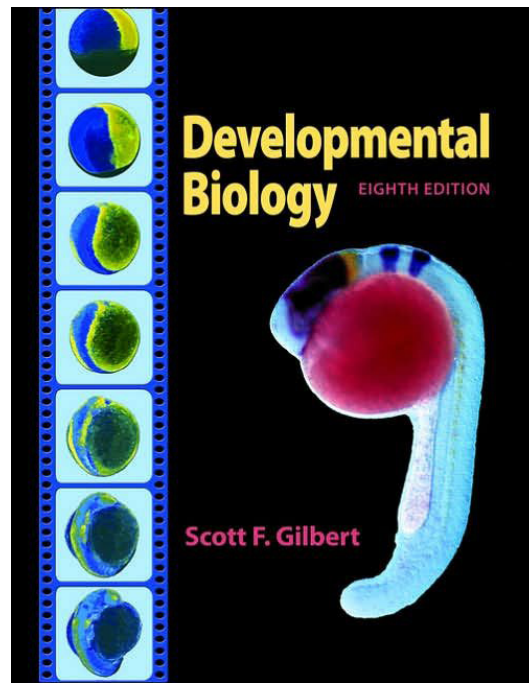


**Cell Structure**









<http://dictybase.org/>

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Slime Mold Waltz  
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