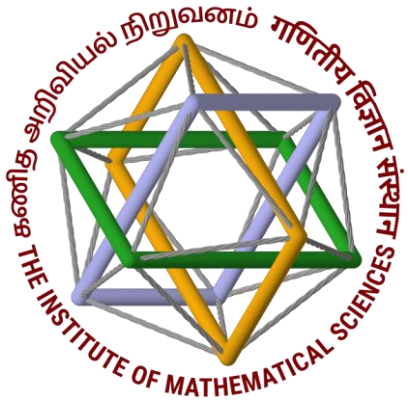
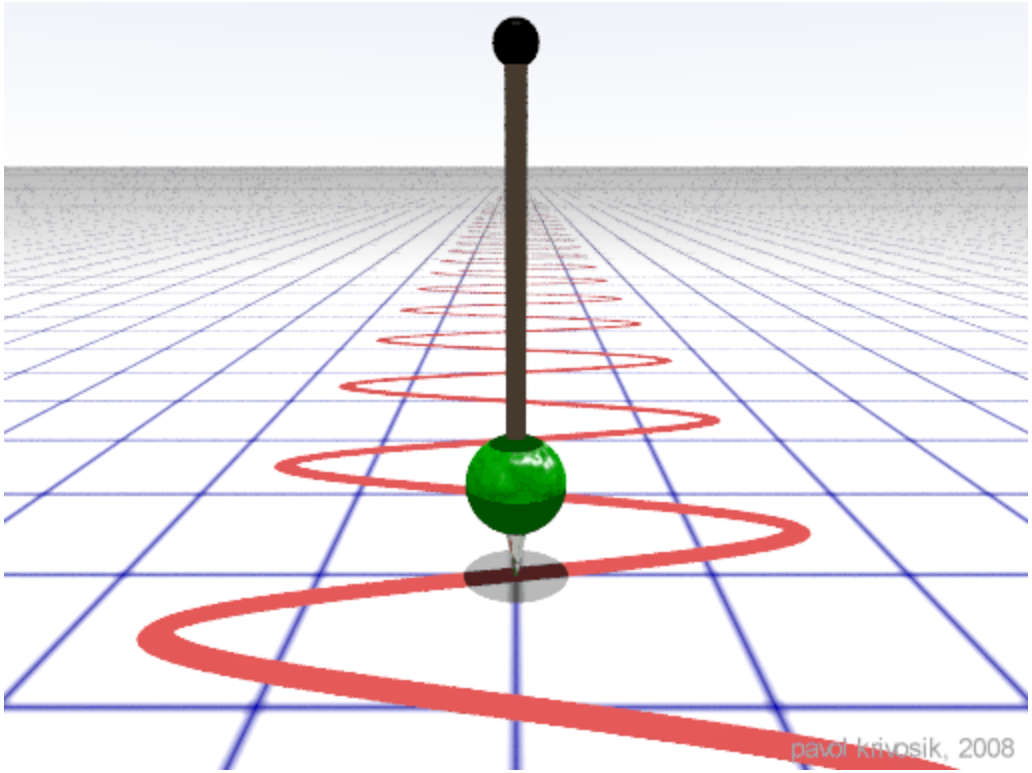


Waves … of life & death

Sitabhra Sinha

The Institute of Mathematical Sciences, Chennai

What is an oscillator ?



Any system exhibiting periodic variation of one or more observables about a central value

Oscillator as a dynamical system

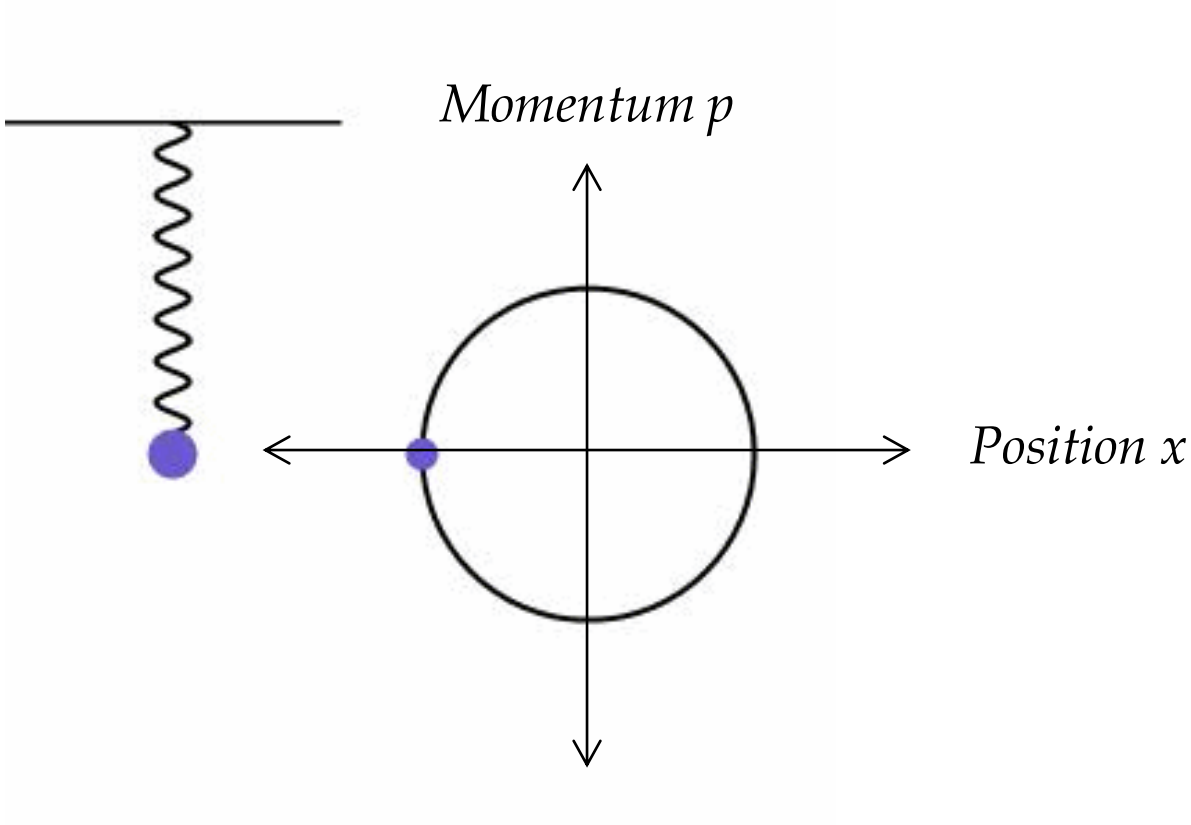


Image: gifer.com

Phase space description

Oscillators around us: desirable

Image: dribbble.com

Oscillators around us: undesirable

https://www.youtube.com/watch?v=XggxeuFDaDU

Video: British Pathe

But wait a minute … Isn't what we seeing are waves ?

What's the relation between waves and oscillators ?

Image: Leybold Shop

A wave machine

Demo using Cellotape and Pencils

Example: Mexican Wave

Video: Andy Webb

https://www.youtube.com/watch?v=hq387m0PRac

Example: Mexican Wave in classroom

Video: Childline

https://www.youtube.com/watch?v=BBPlTa64Aeg

Biological analog: In the embryo, mitotic waves which dictate cell division

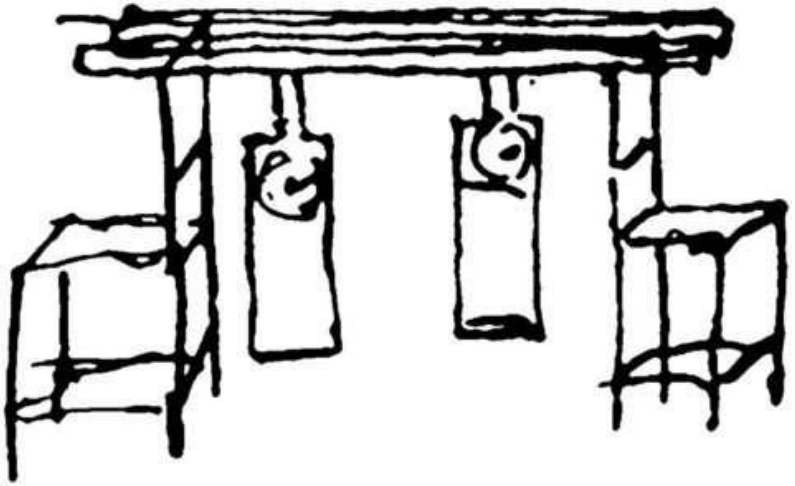
Mitotic waves

cycles of synchronous nuclei divisions in waves from posterior to anterior ends

Mitotic waves (cycles of nuclei divisions) and gastrulation in *Drosophila melanogaster*

https://brunovellutini.com/posts/mitotic-waves-gastrulation-fly-embryo/

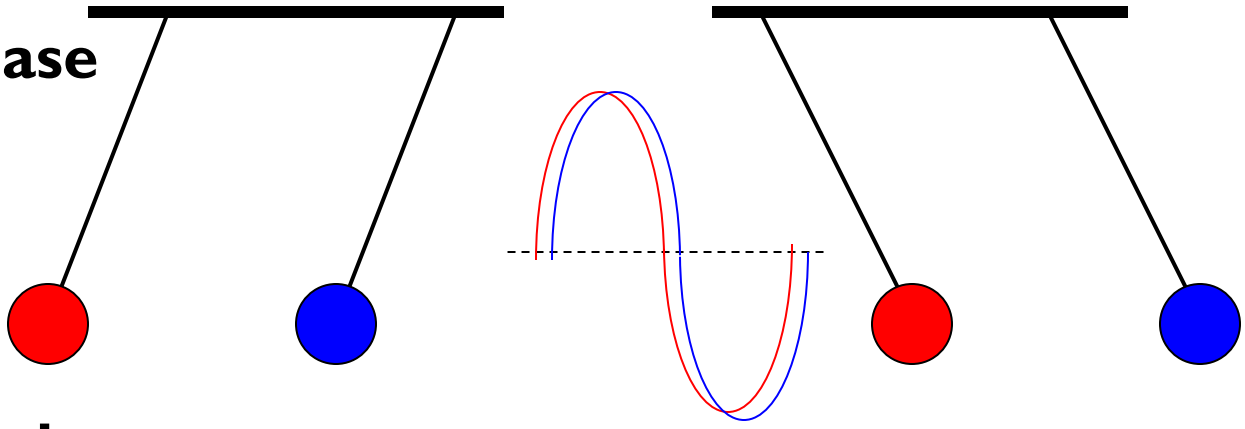
Synchronization of Coupled Oscillators



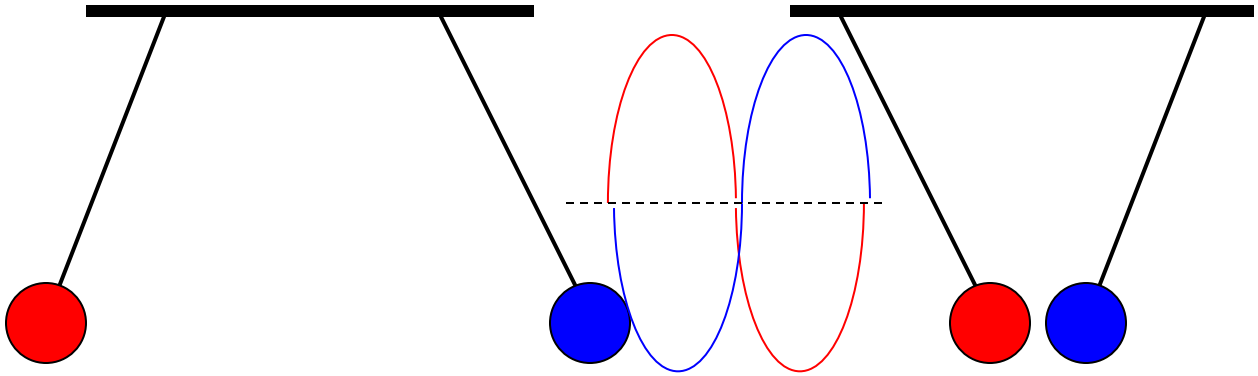
Feb 1665: Huygens observed phase-locking between two pendulum clocks hung side by side

Christiaan Huygens
(1629-1695)

In-phase



Anti-phase



Demo of spontaneous synchronization using metronomes

https://www.youtube.com/watch?v=T58IGKREubo

Video: uclaphysicsvideo

If you are interested do please watch the documentary

The Surprising Secret of Synchronization in YouTube

https://www.youtube.com/watch?v=t-_VPRCtiUg

Video: Veritasium

A spectacular demonstration of spontaneous synchronization in nature

Image source: Scientific American

Male Fireflies flashing in unison

Each insect has its own rhythm – but the phase alters based on seeing its neighbors lights, resulting in synchronous flashing of almost all the insects in a tree

For a video clip showing the emergence of this synchronization, see the episode "Talking to strangers" in the BBC series *The Trials of Life: The Natural History of Behaviour* (1990) by David Attenborough

Synchronicity Experiment in mangrove forests of Thailand

Thousands of live fireflies are made to synchronize their flashes with a few computer controlled LEDs

https://www.youtube.com/watch?v=ZGvtnE1Wy6U&t=1s

Video: Robin Meier

Honeybees Defensive Wave

https://www.youtube.com/watch?v=8bNKU8GRYmU

The Question

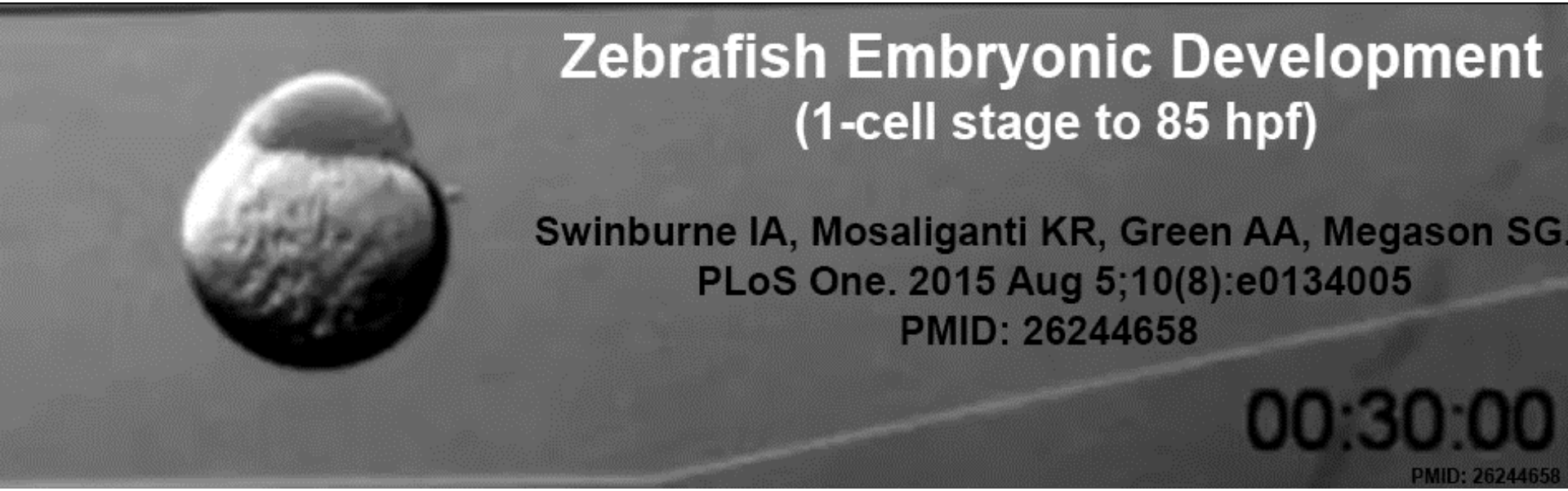
?

Image: Wikipedia,

Image: a-z-animals.com

Pattern formation in development

Zebrafish development from 1-cell stage to 85 hours post fertilization



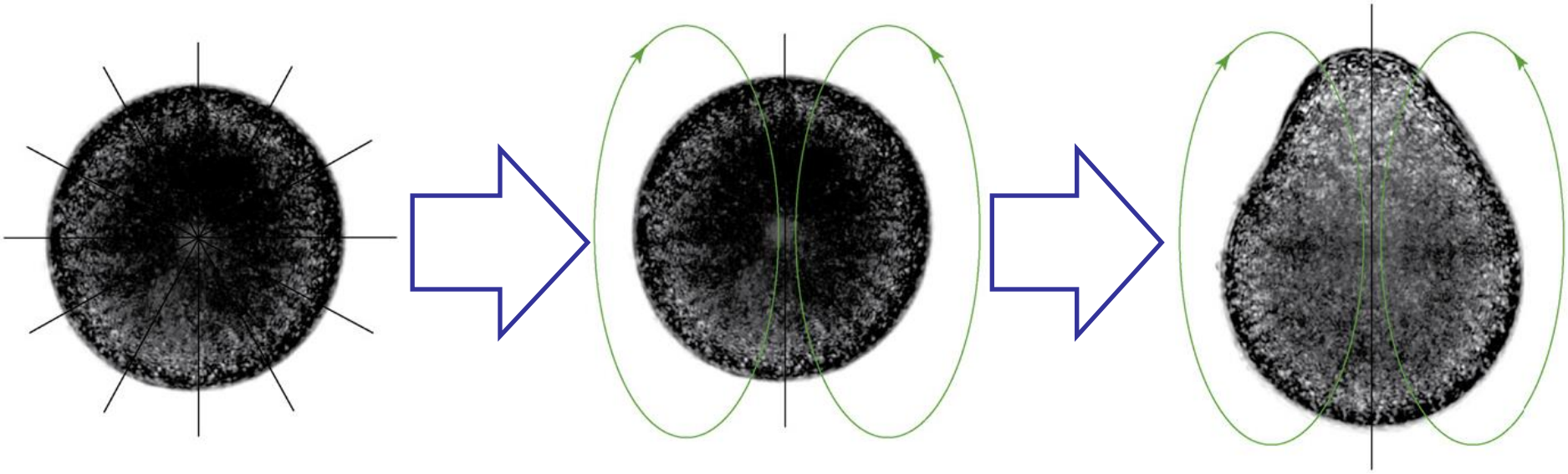
https://embryology.med.unsw.edu.au/embryology/index.php/Zebrafish_Development_Movie

Frames are every 40 seconds of developmental time from 30 minutes to 12 hpf,
every 80 seconds of developmental time from 12–24 hpf, and
every 160 seconds of developmental time from 24 hpf to end of movie.

Fundamental Question:

How are the symmetries of the initial state broken ?

How to break symmetry ?



Spherical symmetry of an unfertilized *Fucus serratus* egg

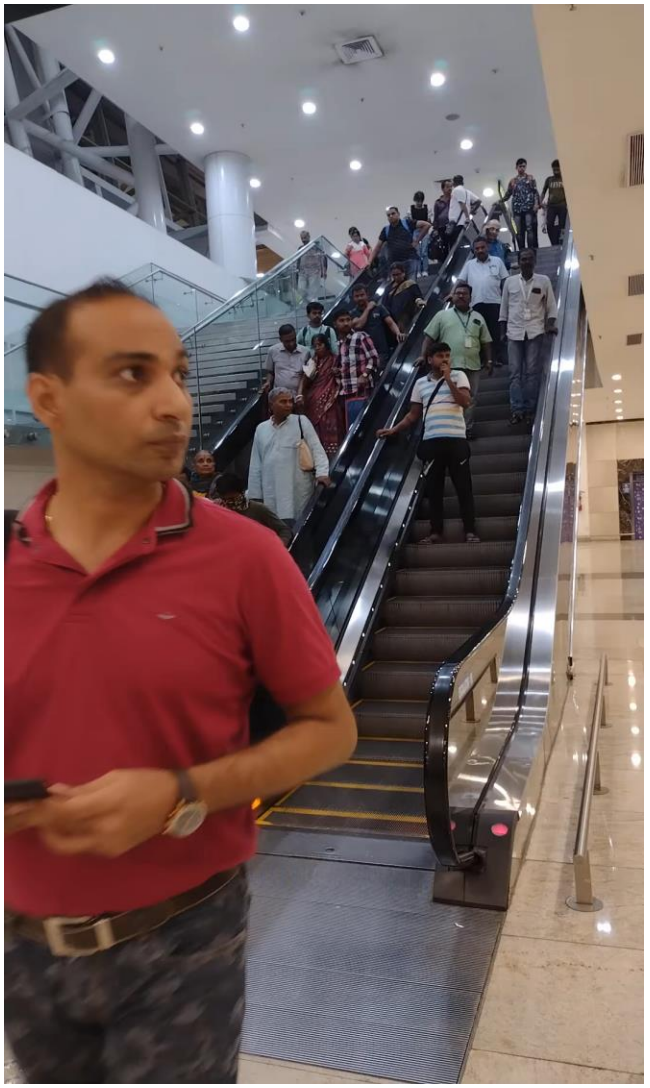
Few minutes after fertilization, symmetry broken by Ca^{2+} transcellular current flow

16 hours later, morphological changes exhibit the broken symmetry

Image: Homble & Leonetti, *Trends in Plant Sciences* (2007)

How to break symmetry ?

First, we need the possibility of
choosing between multiple possibilities



Video: Sitabhra Sinha

How to break symmetry ?

Second, we need some way by which to choose one possibility over the others

Video: Sitabhra Sinha

This qualitative change in the property or behaviour of the system is an example of

Bifurcation

e.g., the proverbial straw that broke the camel's back

Unlike the calculus of Leibniz and Newton

Continuous change in the stimulus (independent variable) can result in discontinuous change in the response (dependent variable)

Question

How do the cells at different positions know their correct fates, i.e., what type of cell they should differentiate into ?

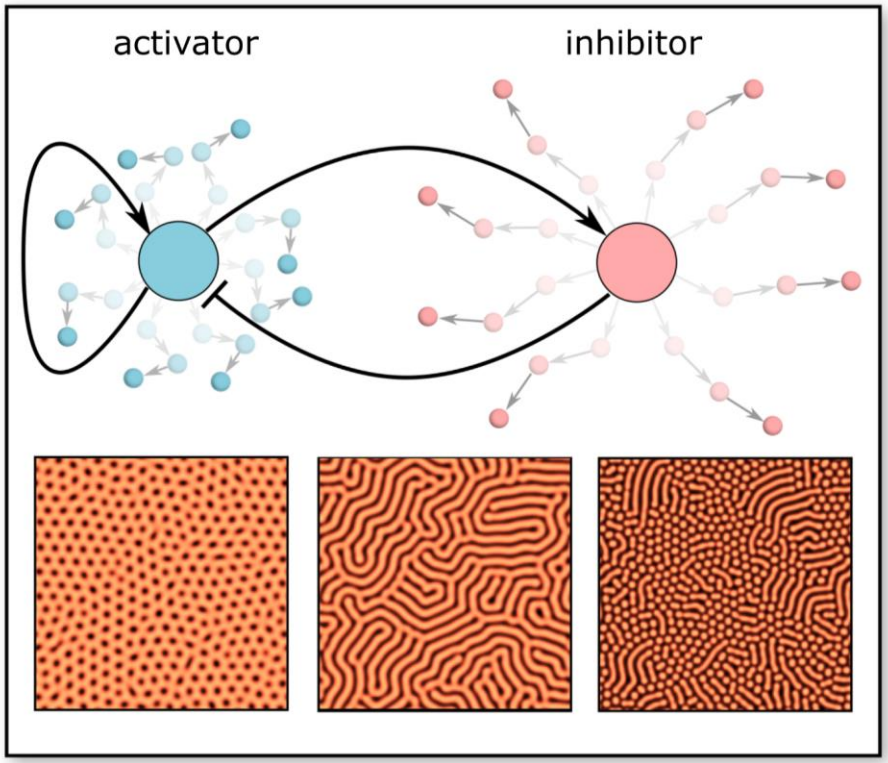
Otherwise you could have eyeballs sprouting on your toes

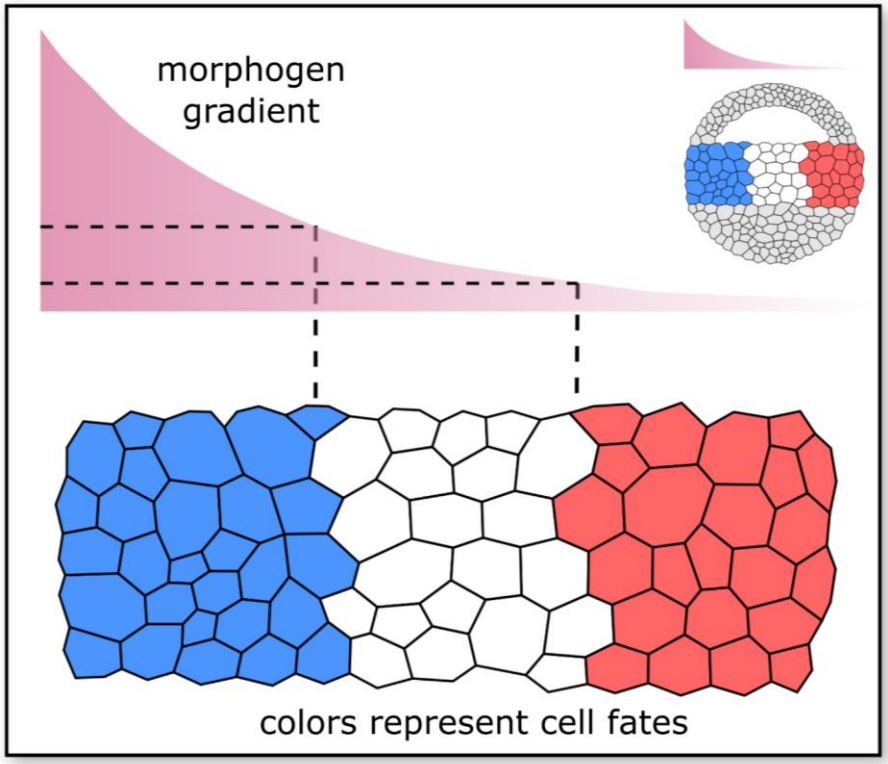
But how are the characteristic patterns formed ?

an initially homogeneous domain exhibits patterns of varying concentrations of molecular species (morphogens)

Two principal theoretical mechanisms of pattern formation

Self-organized vs Boundary-organized





Boundary organized pattern formation

Positional Information

- Cells receive external cues to identify their positions (with respect to boundaries)
- Cells interpret this information to achieve distinct states.

These two processes need not be related → same positional information can be interpreted to yield different patterns, depending on the genetic program inherent to the cells.

A simple mechanisms for specifying positional information → an external chemical gradient ("morphogen")

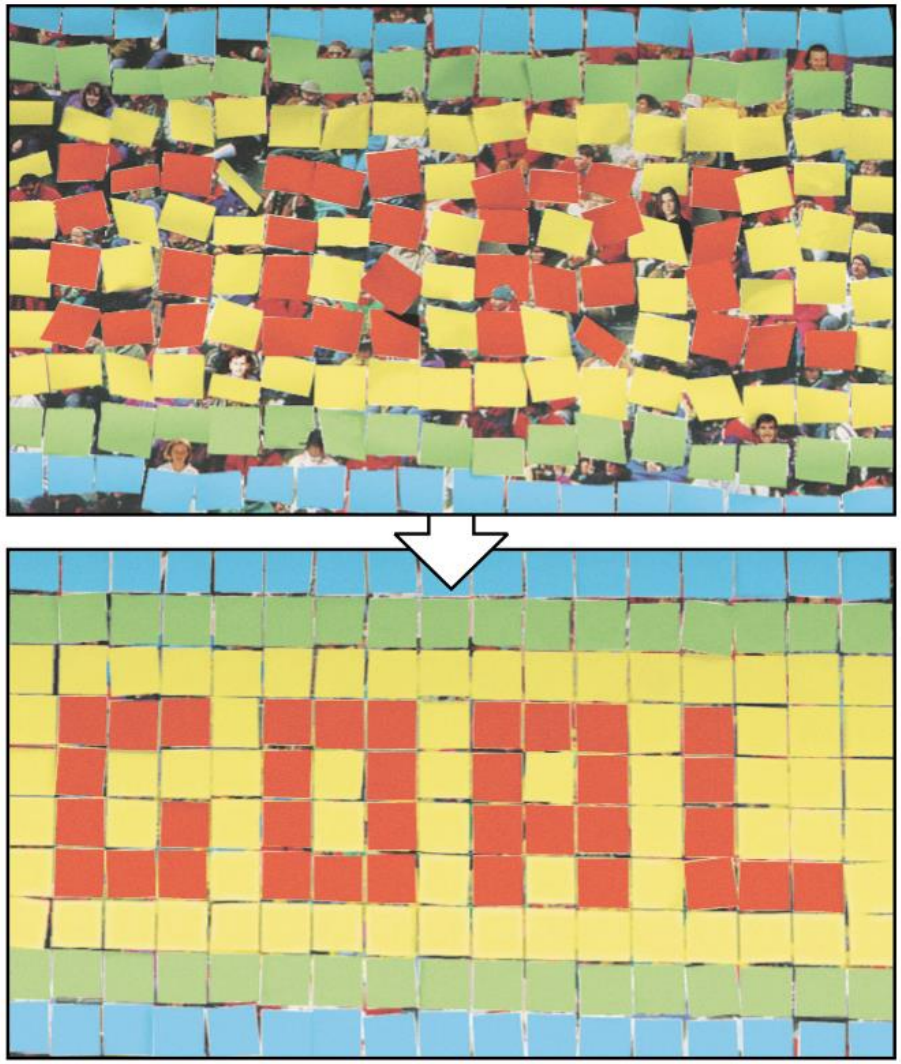


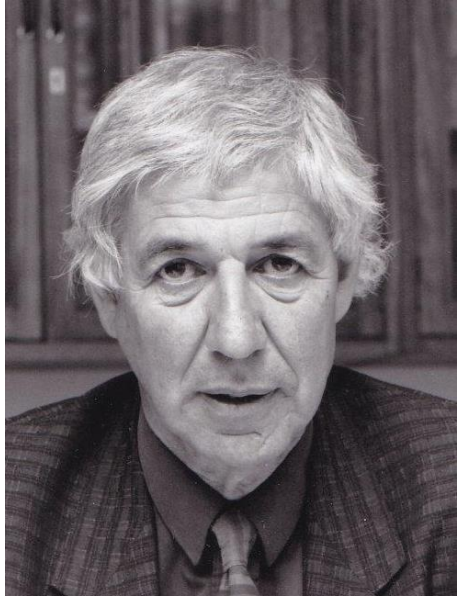
Image: L. Wolpert, C. Tickle, A. M. Arias, Principles of Development, 6th ed (2019).

Demo

Image: Varuni Prabhakar

Source: Youtube

The human LED screen: Arirang Mass Games North Korea



Lewis Wolpert (1969)

French flag model

Morphogen: a signaling molecule eliciting specific cellular responses

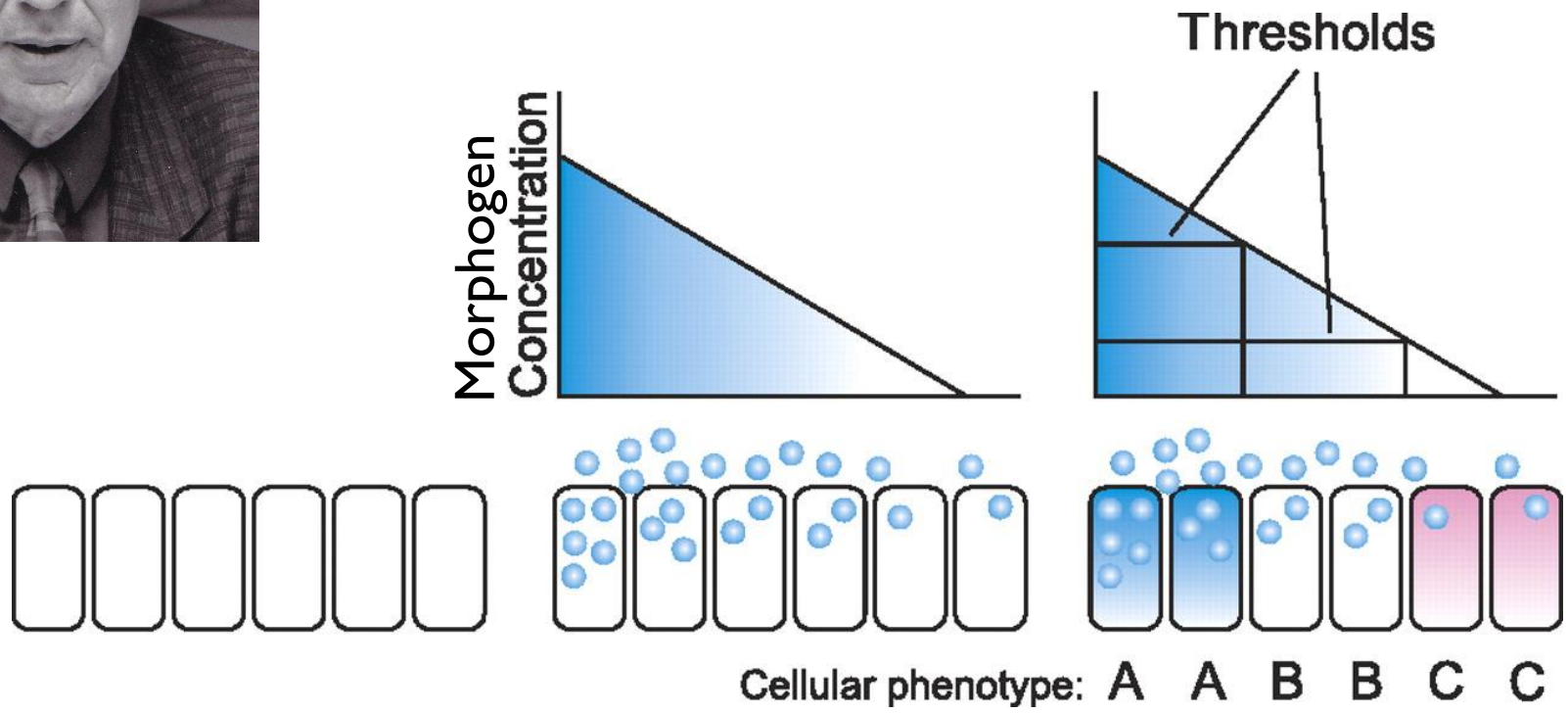


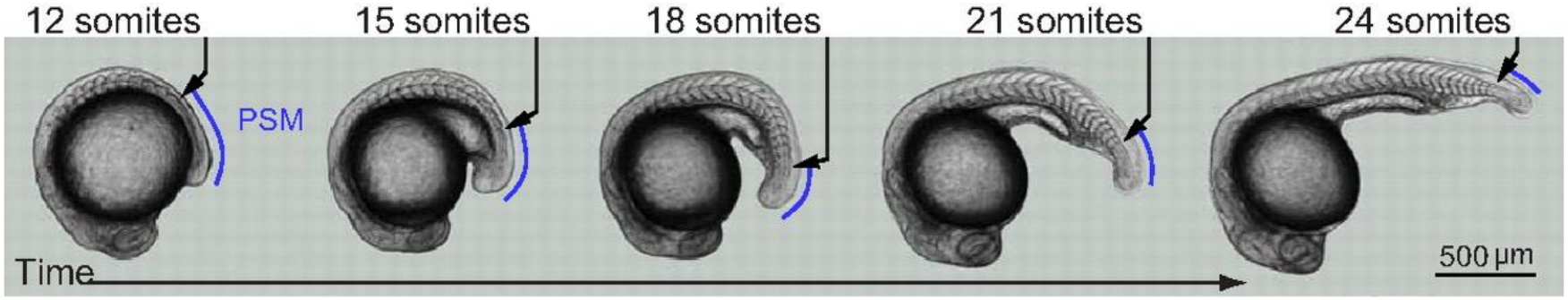
Image: van den Brink G R *Physiol Rev* 2007;87:1343

Undifferentiated cells can choose three different cell fates (blue, white, or red) specified in a cell position-dependent manner by localized production of a morphogen

Cells respond to different thresholds of morphogen concentration depending on their distance from the source.

Explaining Somitogenesis

The process by which body segmentation occurs during embryonic development in all vertebrates.



A. Oates et al., *Development* **139**:625-639 (2012)

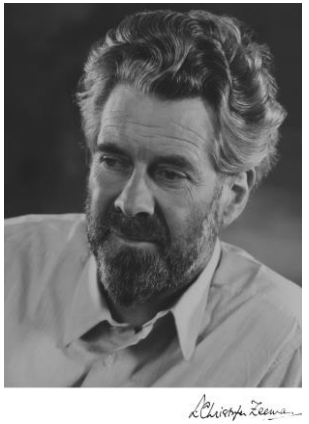
Somites → modular building blocks of vertebrate bodies
formed in the paraxial, or pre-somitic, mesoderm (PSM) of developing embryos as the body axis elongates

Experiments → oscillatory expression of segmentation clock genes underpins the emergent spatial patterns.

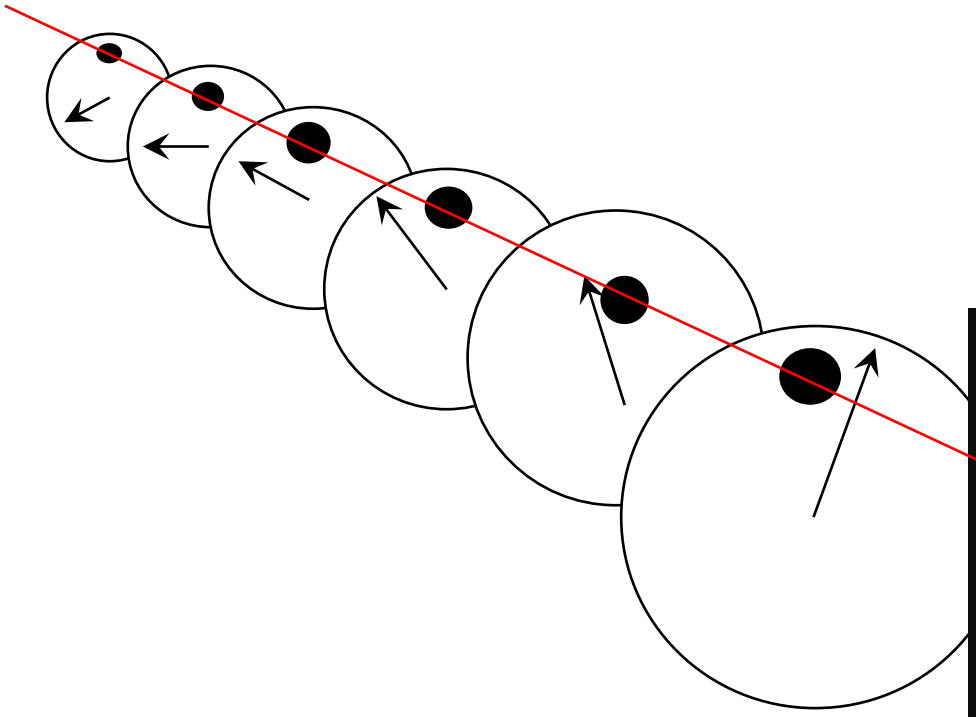
The "Clock-and-wavefront" scheme

Converting temporal pattern into spatial pattern

Cooke and Zeeman (1976)



Autonomous cellular oscillators ("clocks")
arrested by a moving "wavefront" of activity



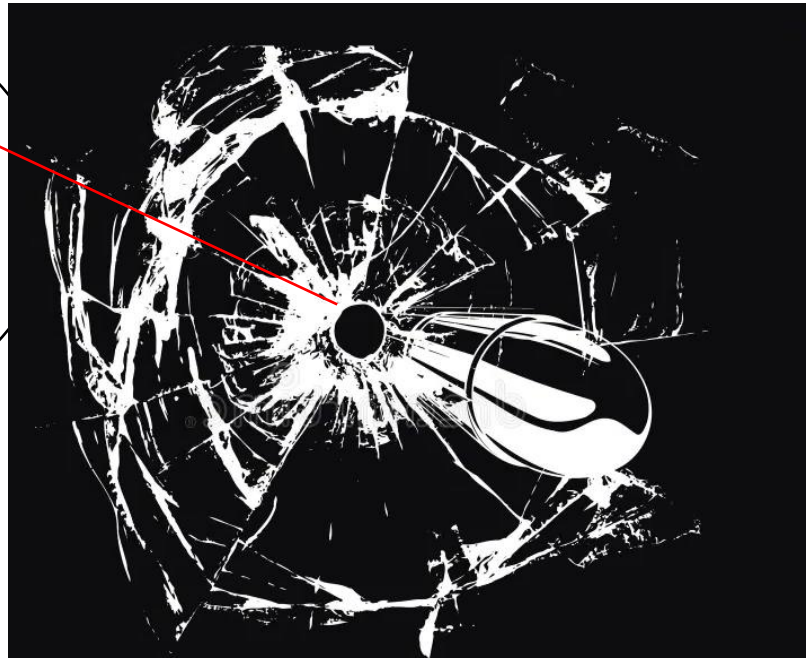
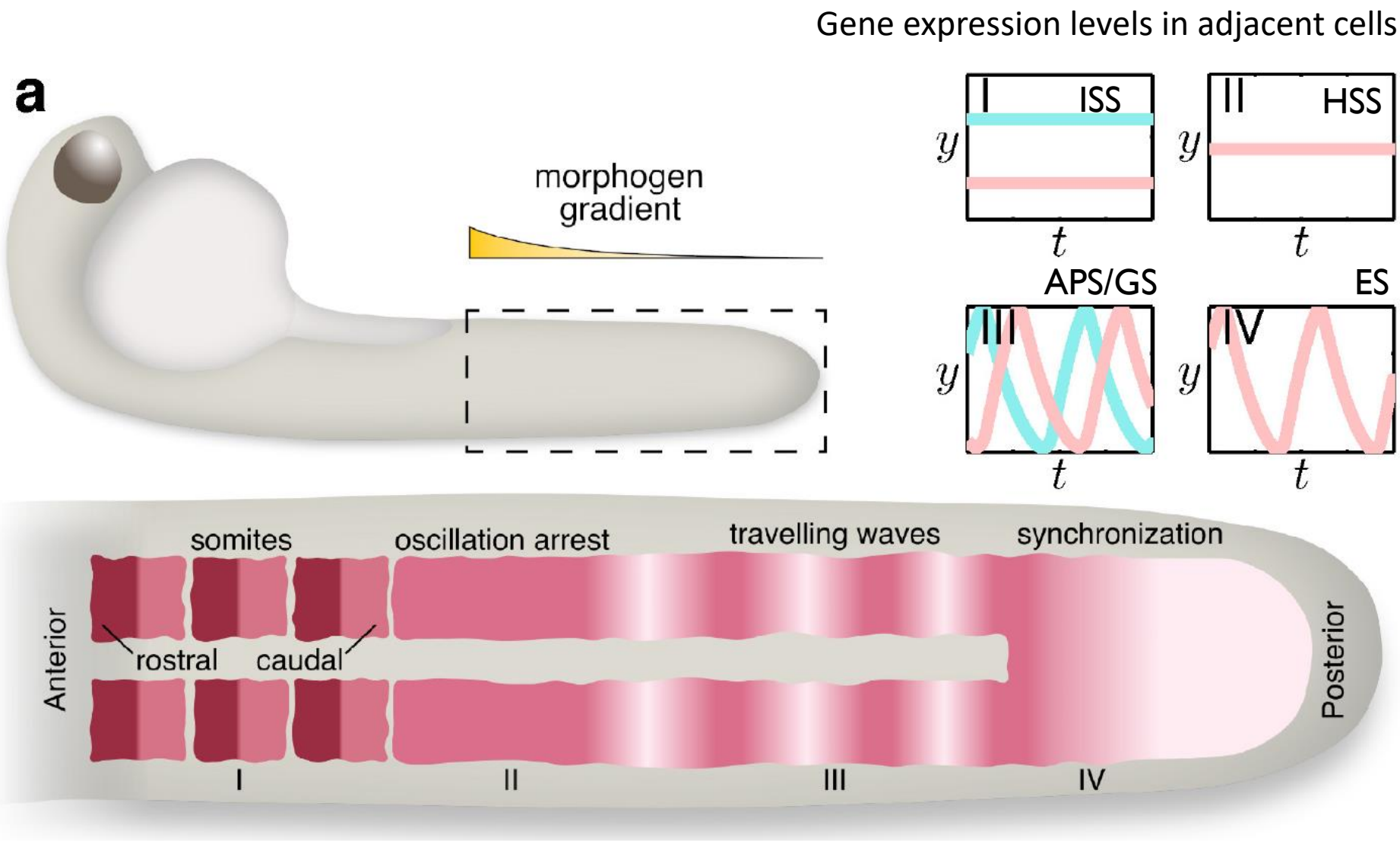


Image: Nabeel Zytoon, Dreamstime.com

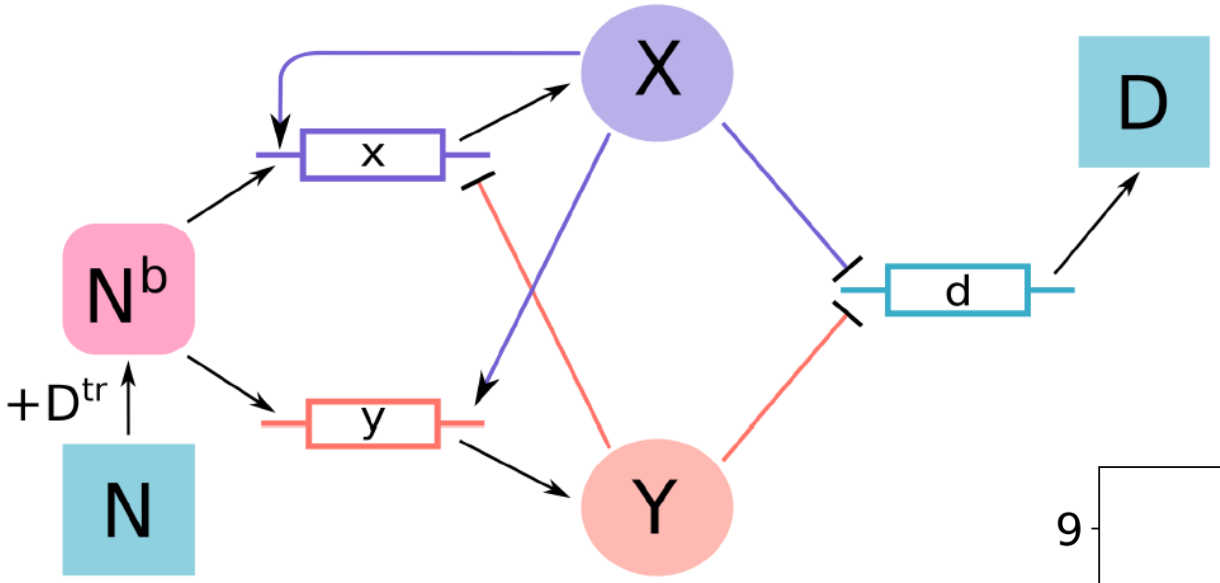
A bullet going through a series of clocks
arresting them at various phases

The Zebrafish presomitic mesoderm



Genetic oscillator model

From activator-inhibitor interactions



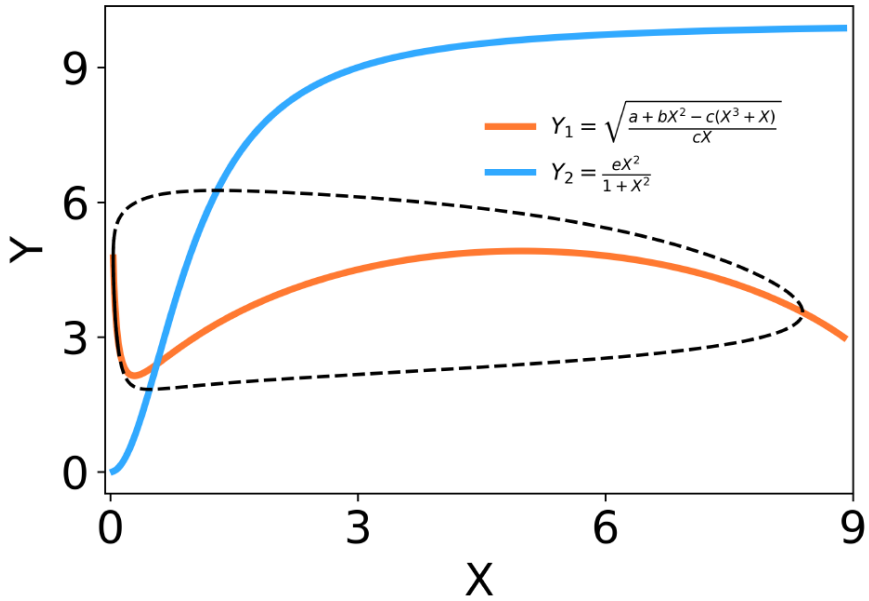
X activator gene product

Y inhibitor gene product

N free Notch

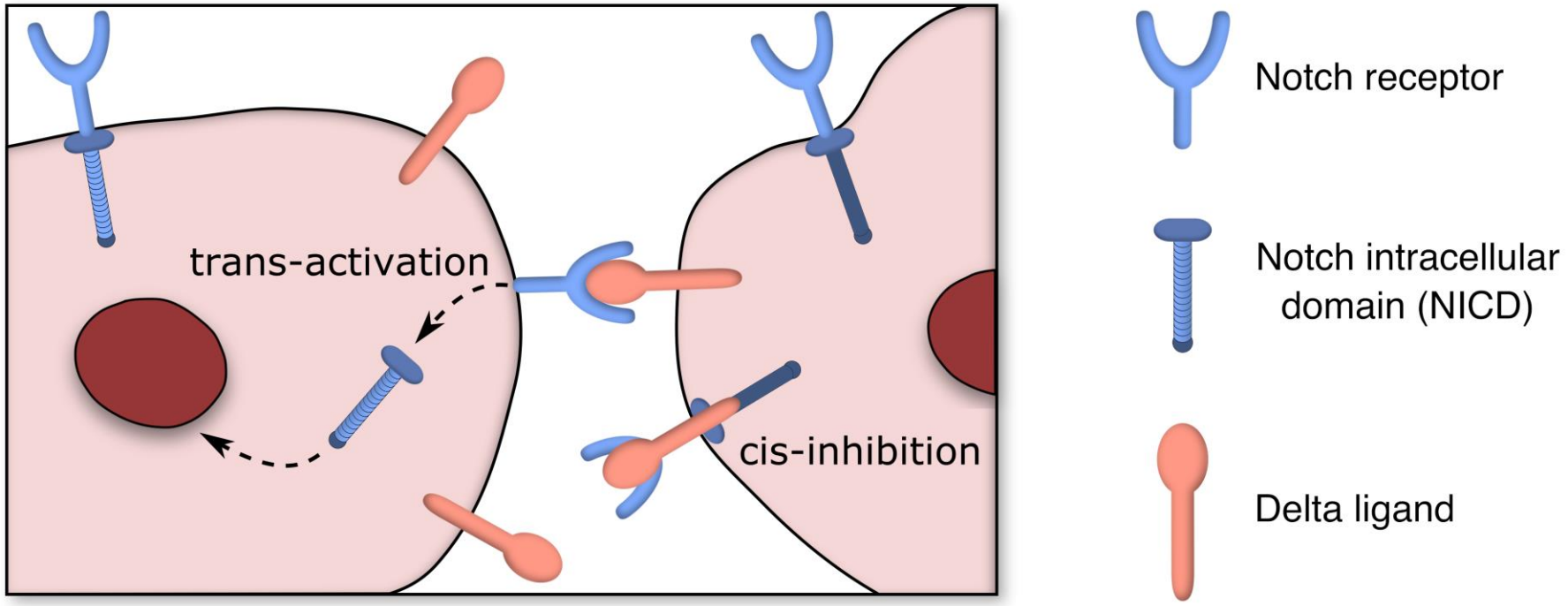
N^b bound Notch

D free Delta



Inter-cellular receptor-ligand coupling mechanism: Notch-Delta signalling pathway

plays a major role in somitogenesis



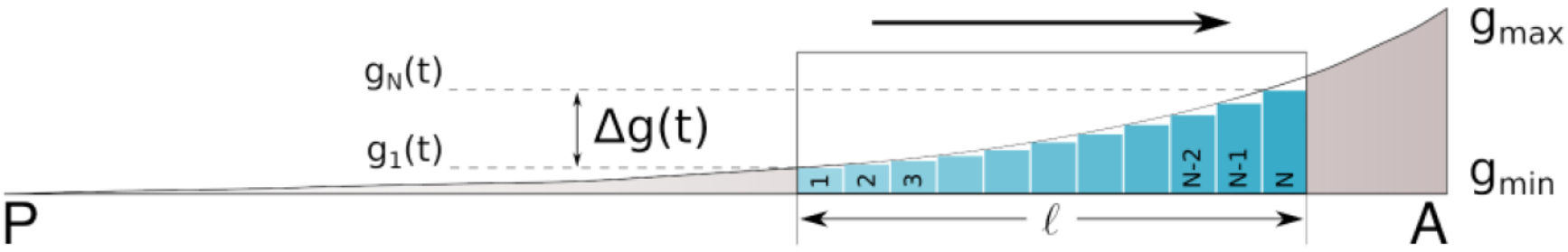
downstream targets include *cyclic genes* that underpin the segmentation clock

Introducing a morphogen gradient

Multiple gradients of morphogens belonging to the FGF, RA and Wnt families along the anteroposterior (AP) axis of the PSM that diffuse from anterior to posterior.

As new cells are continually added to the tail, PSM expands along the AP axis.

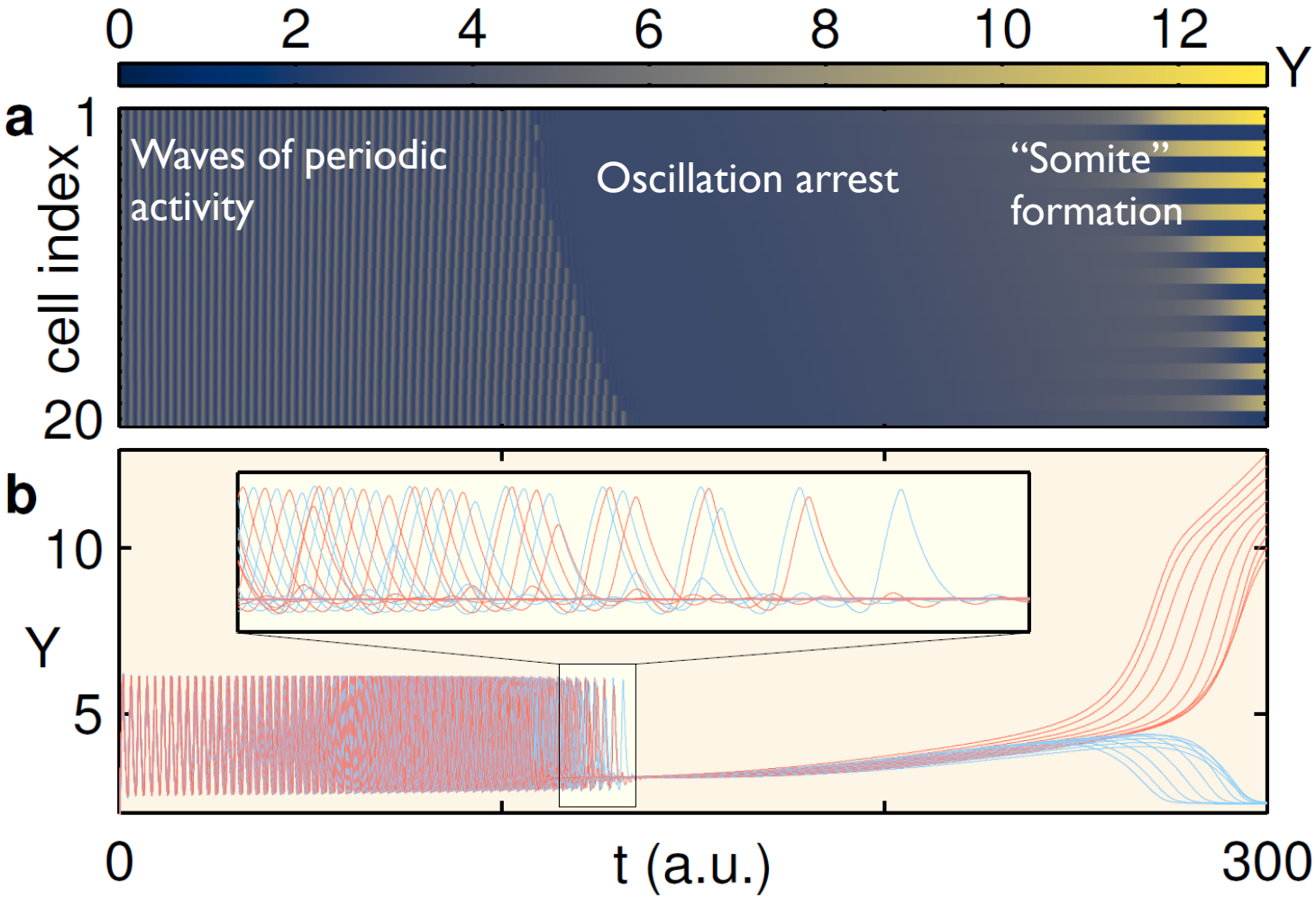
From reference frame of a contiguous block of cells on the PSM, the morphogen gradients appear to vary over time ⇒ we consider a time-varying exponential gradient of morphogen concentration



Incorporating a morphogen gradient by varying the Notch-Delta coupling parameter *g* of adjacent oscillators

Collective dynamics of a segment of cells "flowing up" a morphogen gradient

To confirm that the observed dynamical transitions can be obtained in a spatially extended system, we consider a one dimensional array of coupled cells experiencing a morphogen gradient that decays exponentially from anterior to posterior



The system exhibits the same three distinct collective dynamical states over time, eventually arriving at a steady state pattern resembling alternating rostral and caudal halves of somites

Thanks

Funding