DESIGNS IN LIVING SYSTEMS

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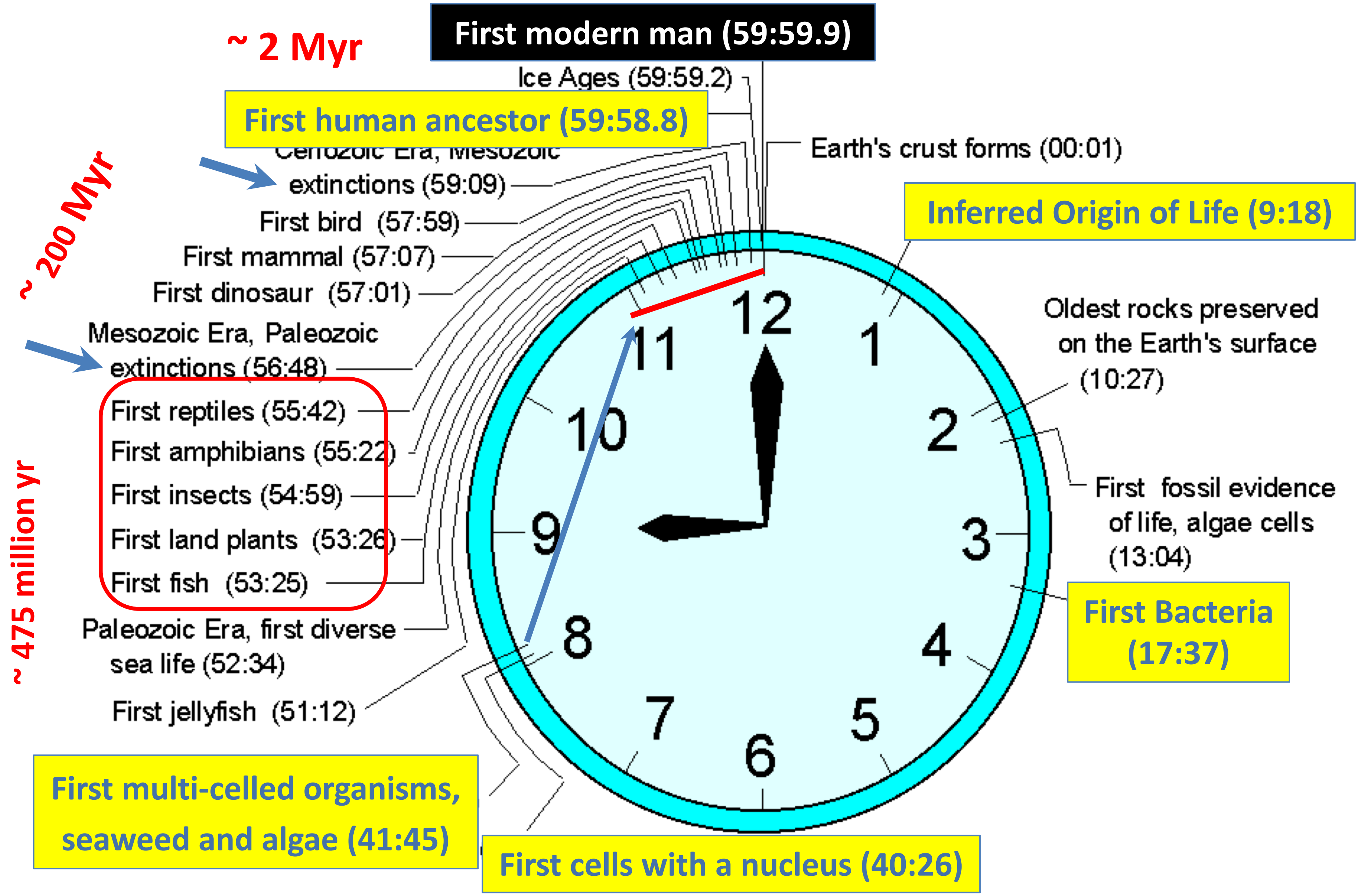


4.6 billion years in one hour

Adapted from
https://letstalkaboutscience.wordpress.com/tag/analogies/

Evolution of tissue-specific expression of ancestral genes across vertebrates and insects.

F Mantica et al. (Centre for Genomic Regulation, Barcelona).

Nature Ecology & Evolution, 15 April 2024.

700 million years ago, through a **whole genome duplication event**, an animal emerged which had a front and a back, a top and a bottom. This was a ground-breaking adaptation at the time, and one which laid down the basic body plan which most complex animal, including humans, would eventually inherit.

The last common ancestor of bilaterian, a vast supergroup of animals including vertebrates (fish, amphibians, reptiles, birds and mammals), and invertebrates (insects, arthropods, mollusks, worms, etc.).

More than 7000 groups of genes can be traced back to the last common ancestor of bilaterians.

Repurposing of genes in specific parts of the body.

DESIGN & PATTERN can have different meanings depending on the context.

but generally -

Pattern refers to a recurring or repeating theme, structure, or arrangement. more elaborate, complex, level of details, scale of applicability with colour, motifs, details.

Design refers to the intentional planning and arrangement and arrangement of elements to achieve a specific goal or purpose.

Plan, Sketch, Outline, blueprint, map.

Design is a broader term

Body plan of an animal phylum is a set of morphological features common to many members, the basic shape of its members – **the general structure each individual assumes as it develops.**

The vertebrates share one body plan, while invertebrates have many.

Blueprint encompasses aspects such as, symmetry, layers, segmentation, nerve, limb, gut, etc.

Evolutionary developmental biology seeks to explain the origins of diverse body plans.

No all-encompassing definition of life

"Life is a self-sustained chemical system capable of undergoing Darwinian evolution

(John Bernal, Eugene Wigner, John Avery, J D Watson, F. Crick, …)

In 1964, James Lovelock was requested by NASA to make a "theoretical life detection system" to look for life on Mars during the upcoming space mission.

"I'd look for an entropy reduction, since this must be a general characteristic of life."

...living matter, while not eluding the "laws of physics" as established up to date, is likely to involve "other laws of physics" hitherto unknown, which however, once they have been revealed, will form just as integral a part of science as the former. **Schrödinger**

Joyce, G. F. (1995). The RNA world: life before DNA and protein. Cambridge University Press

S Kauffman (2004): "Autonomous agents"; Barrow, et al, . Cambridge University Press

J E Lovelock. A Physical Basis for Life Detection Experiments. Nature (1965)

J Krissansen-Totton et al. Understanding planetary context to enable life detection on exoplanets and test the Copernican principle. Nature Astronomy (2022)

Erwin Schrödinger. "What Is Life? The Physical Aspect of the Living Cell" (1944)

PROPERTIES CHARACTERISTIC OF LIVING SYSTEMS

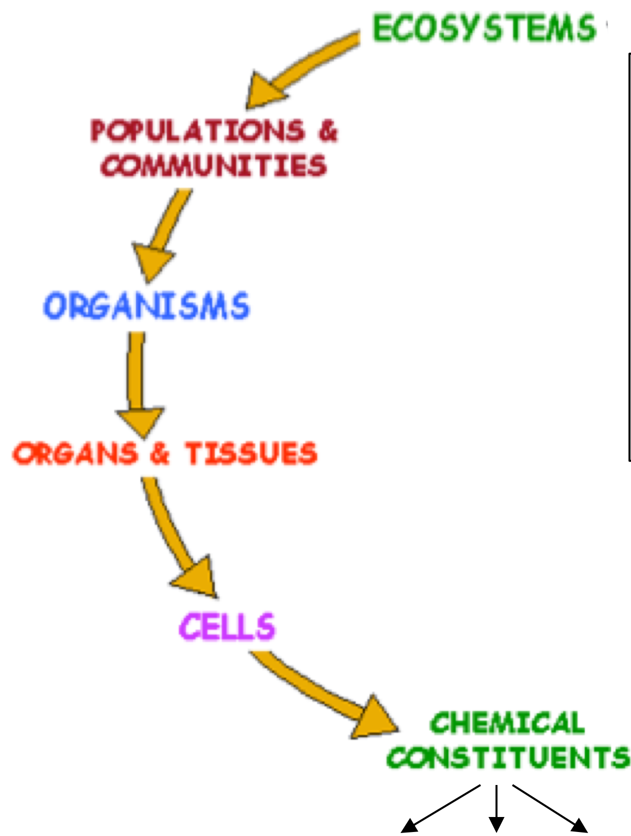
- ***Homeostasis:*** ***Regulation of the internal environment to maintain a constant state;***
- ***Organization:*** ***Being structurally composed of one or more cells (basic units of life)***
- ***Metabolism:*** ***Transformation of energy by converting chemicals and energy into cellular components (anabolism) and decomposing organic matter (catabolism).***
- ***Growth:*** ***Maintenance of a higher rate of anabolism than catabolism***
- ***Adaptation:*** ***The ability to change over time in response to the environment***
- **Response to *Stimuli; Reproduction***

These complex processes (physiological functions), have underlying physical and chemical bases, as well as signaling and control mechanisms that are essential to maintaining life

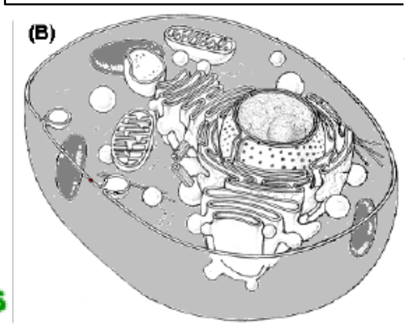
Different Levels of Biological Organisation

Enormous range of time and length scales

REDUCTIONIST APPROACH



Isolation and characterisation of all organelles and molecules that make up a cell only gives a "part list".



DNA, RNA, Proteins, Lipid bilayer, mitochondria, etc

Macroscopic biological system behaviour at any level is determined by microscopic interaction rules involving the lower level constituents

Multi-level and Multi-Scale Description

SYSTEM ORGANISATION

A structural or functional "**whole**" that is made up of lower level entities that interact according to certain "**rules and patterns**" which, in turn, can also modulate the constituent entities' behaviour.

Information plus regulation

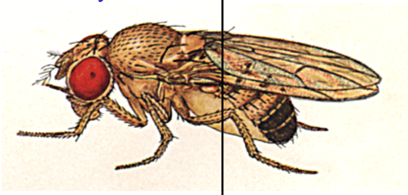
System organisation is limited by the communication between the subsystems

Difference between Physical and Biological systems

- **Greater complexity of the parts**:
  small molecules, genes, cells, ants, populations;
- **Nature of rules** governing interactions among system components

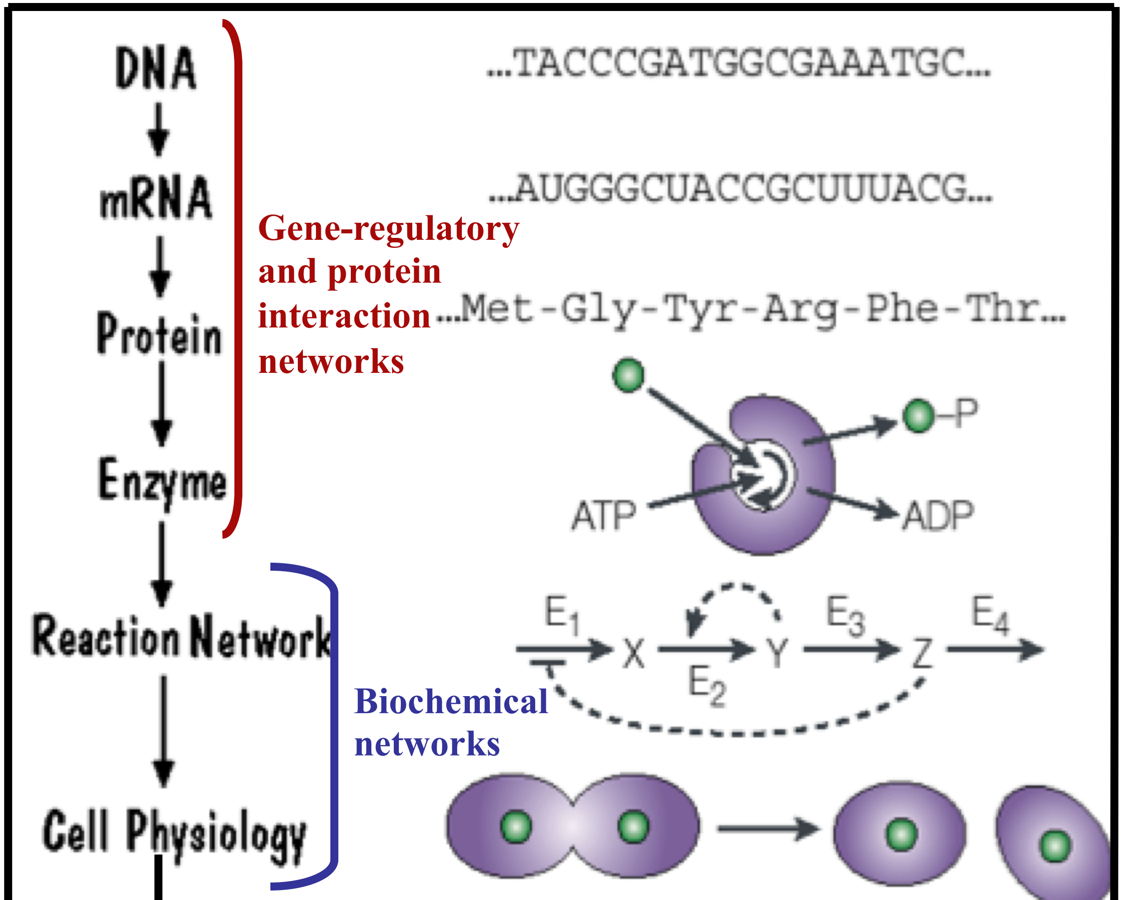
Biological system:

- *Physical laws, (surface tension, viscosity, gravity)*
- *Physiological & Behavioural interactions,*
- *Genetically-controlled properties,*
- *Evolution through natural selection*



Flow of Information in Biology

FLOW of INFORMATION

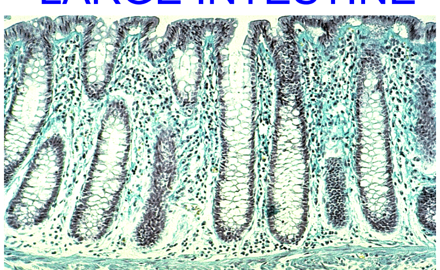


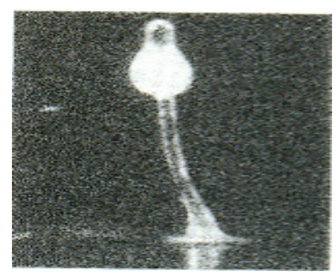
Ecological systems

FOODWEBS, CONTACT NETWORKS IN EPIDEMIOLOGY

Social systems

LARGE INTESTINE





Slime mold

Multicellular systems

DESIGNS IN LIVING SYSTEMS

Pattern Formation

Formation of a **regular or logical form, order or arrangement of parts** in space and time

Coat marks, Heart beats, Calcium waves

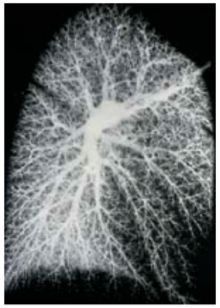
Morphogenesis

Development of form in organisms starting from near homogeneous initial condition (egg/cell mass)

involves orchestrated cell division, movement, & differentiation

Self-organization:

Systematize form (different elements) into an organic whole through intrinsic interactions.



Self-Organization

a) Pattern at the global level emerges solely from interaction among the lower level components of the system

b) Rules specifying interactions among the components of the system are executed using only local information without reference to the global pattern

Pattern is an emergent property of the system that arises from interactions among system components

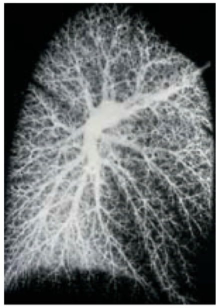
Bird Flock, Bacterial Swarm, Fish School, Animal Herd

Patterns can be produced through

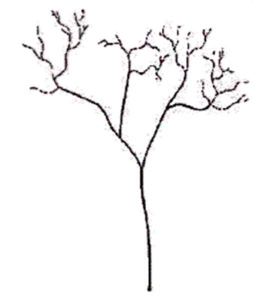
<u>extrinsic influences</u>

a) **Order by the leader:** *Pace-maker*

c) **Pre-existing patterns (templates)**



Pattern Formation

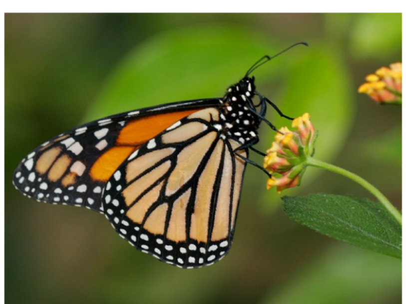


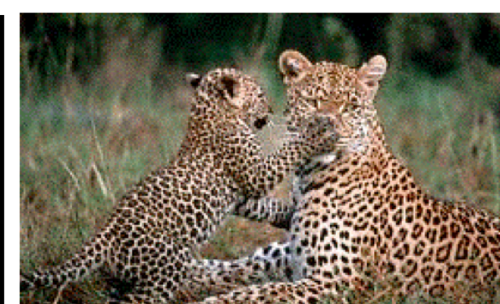
SPATIAL,

TEMPORAL

&

SPATIO-TEMPORAL





Spatiotemporal patterns in biological systems are manifestations of the activities of underlying non-linear interacting processes at varied space and time scales

Molecular reactions during gene expression,
enzyme reactions,
transport processes in cells
signaling processes,
cell movement,
migration in populations,
social interactions,
gene interactions at evolutionary scale.

Normal pattern can be altered
Mutations, Pathological conditions, or Environmental changes

Understand and identify mechanisms that yield specific patterns can help control pathology or regulate as per requirement

Through modelling we can explore the role of non-linearity, coupling, feedback and other biologically realistic properties that contribute to the evolution and maintenance of pattern in space and time

SPATIAL, TEMPORAL, & SPATIO-TEMPORAL PATTERNS in STRUCTURE, FUNCTION, REGULATION, INTERACTION & PROCESSES

ECOSYSTEMS

POPULATIONS & COMMUNITIES

Fairy circles: barren round patches that dot the grasslands of Namibia. They can persist as long as 75 years, but their cause has been hotly debated.

Tiny termites create this amazing spatial patterning that could go for hundreds and sometimes thousands of kilometers, that can be seen from space? **What drives that?**

Turing-type pattern

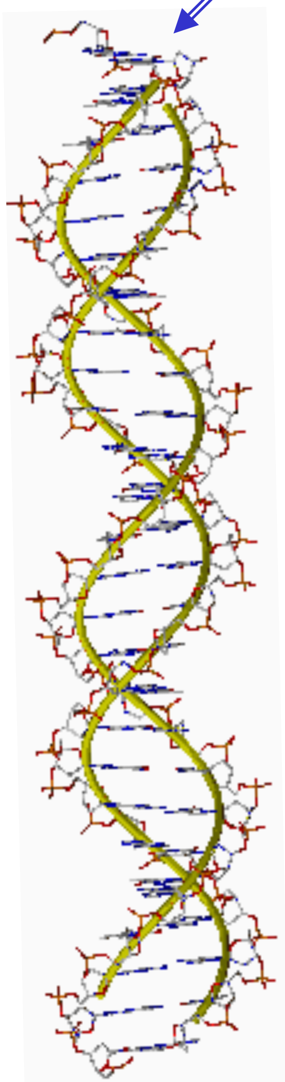
Strong competition for resources

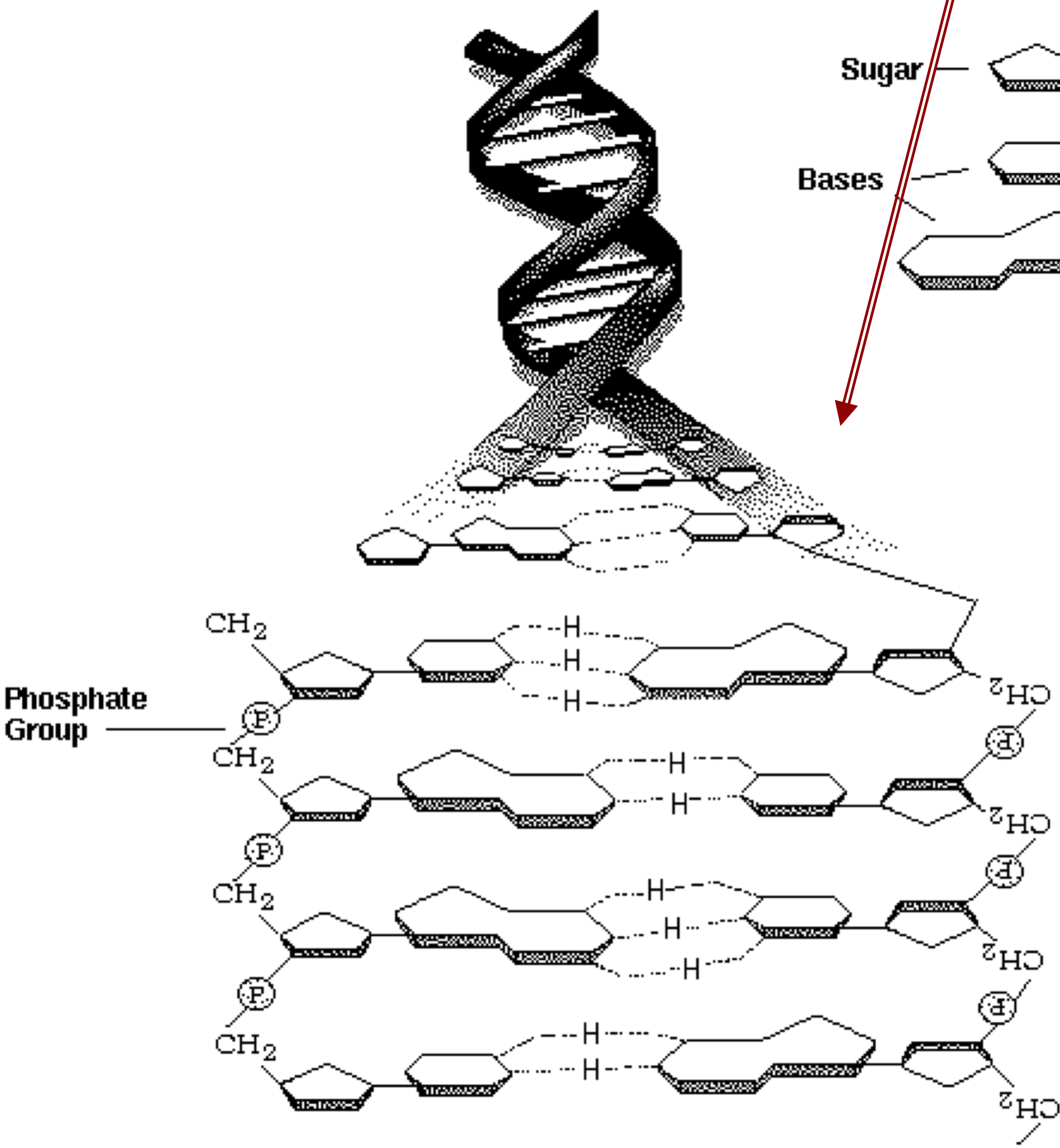
If two different colonies run into each other, they will fight to the death. They like to be separated from each other, and so they create this hexagonal, honeycomb-type pattern.

Corina Tarnita (Harvard) deciphers bizarre patterns in the soil created by competing life-forms.

https://www.quantamagazine.org/a-mathematician-who-decodes-the-patterns-stamped-out-by-life-20171220/

Double Helical Structure of DNA facilitates its replication





Similar pattern in sequences indicate functional motifs

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ORGANISMS                          AA Sequence

sso_SSO1145    IFMVRTSYYAKPYRKYMMQMYGAEVHPSPSDLTEFGRQLLAKD-SNHPGSLGIAISDAVE
sto_ST1567     IFMVRTSYYAKPYRRYLMQMYNAQVHPSPSEFTRYGREVLAKD-PNTPGSLGIAISEAVY
tvo_TVG0983765 IFMVRTSFYAKPYRKYMMYMYGAHPHPSPSEFTEYGKEVLKKN-PDTPGSLGLAISEAIH
tac_Ta0669     IFMVRTSFYAKPYRKYMMYMYGAHPHPSPSEFTEYGREVLKRM-PDTPGSLGLAISEAIH
pfu_PF1706     IYMGAEDVERQKMNVFRMKLLGANVIPVNSG----------------SRTLKDAINEALR
pab_PAB2048    IYMGAEDVERQKMNVFRMKLLGANVIPVHTG----------------SKTLKDAINEALR
afu_AF1600     IYMGAEDYERQKMNVFRMELLGAKVTAVESG----------------SRTLKDAINEALR
mth_MTH1659    IYMGTEDVERQKLNVFRMEVSGAEVIPVDSG----------------SRTLKDAINEAMR
mja_MJ1037     IYMGAKDVERQKLNVFRMELMGAKVIPVFGG----------------SQTLKDAVNEALR
hal_VNG0307G   IYMGRTDVNRQRPNVFRMRLHDADVNPVTVG----------------SGTLKEAINETMR
               ::*   .   :  .   *   ..   .                    . :*  *: :::

sso_SSO1145    YAHKNG--GKYVVGSVVN------SDIMFKTIAGMEAKKQMELI-GEDPDYIIGVVGGGS
sto_ST1567     YALENG--GKYVVGSVVN------SDILFKTIAGMEAKKQMEMI-GEDPDYIIGVVGGGS
tvo_TVG0983765 YALDNG--GKYIAGSVIN------SDILFKTIAGMEAKKQMEMA-GEDPDYVVGVVGGGS
tac_Ta0669     YALDNG--GKYIAGSVIN------SDILFKTIAGMEAKKQMEMA-GEDPDYIVGVVGGGS
pfu_PF1706     DWVATFEYTHYLIGSVVGPHPYPTIVRDFQSVIGREAKAQILEAEGQLPDVIVACVGGGS
pab_PAB2048    DWVATFEYSHYLIGSVVGPHPYPIIVRDFQSVIGREAREQILEAEGDLPDVIVACVGGGS
afu_AF1600     DWVESFEHTHYLIGSVVGPHPFPTIVRDFQAVIGKEARRQIIEAEGGMPDAIIACVGGGS
mth_MTH1659    DWISNVDDTHYLIGSTMGPHPYPTMVKHFQSVIGREAREQILEVEGELPDTVIACVGGGS
mja_MJ1037     DWTTNVRTTYYLLGSALGPHPYPMMVREFQRVIGKELKEQILEKEGRLPDVIVACVGGGS
hal_VNG0307G   DWATNVADTHYVIGSVVGPHPFPSMVRDFQAIISEELRAQSREQLGELPAAVIACAGGGS
                         *  **.:           .: : . *   *        .   :.  ****

sso_SSO1145    NYAALAYPFLGDELRSG--------KVRRKYIASGSSEVP-KMTKGV-----YKYDYPDT
sto_ST1567     NYAALAYPFLGEELRKG--------KVRRKYIASGAIEVP-KMTKGV-----YKYDYPDT
tvo_TVG0983765 NYAALAFPFLADELQSG--------KVKRTYIASGSKEVP-KMTEGE-----YRYDYPDT
tac_Ta0669     NYAALAFPFLADELSSG--------KIRRTYIASGSKEVP-KMTEGE-----YRYDYPDT
pfu_PF1706     NAMGIFYPFVNDK--------------KVKLVGVEAGGK--GLESGK----HSASLNAGQ
pab_PAB2048    NAMGIFYPFVKDK--------------SVRLIGVEAGGK--GIESGK----HSASLNAGE
afu_AF1600     NAMGIFHPFLND---------------DVRLIGVEAGGE--GIESGR----HSASLTAGS
mth_MTH1659    NAIGIFSAFMDD---------------DVELIGAEGGGE--GIESGN----HGATLSAGS
mja_MJ1037     NAIGAFYEFLDD---------------DVELYAVEAGGK--GIETGM----HGASLCAGE
hal_VNG0307G   NTMGAFGAFVGSASLPGAPAGTHEPAPDVDLLAVEAGGSRLGVDDDAGYAPNSASLSTGT
               .  .    :                       .         .  .            .
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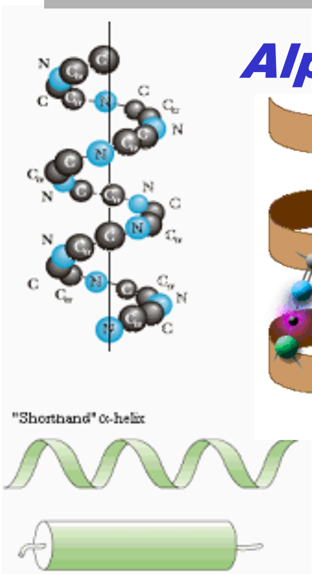
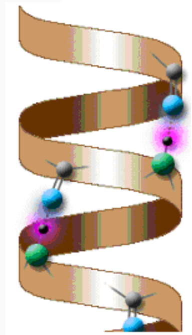
The residues Gly227, Gly228, Gly229, Ser230 are conserved.
The phosphate group of the co-enzyme is highly ligated through hydrogen bonds with the peptide backbone atoms of these residues.

Amino acid sequences in proteins form patterns of specific secondary structures useful for their function

Alpha Helix

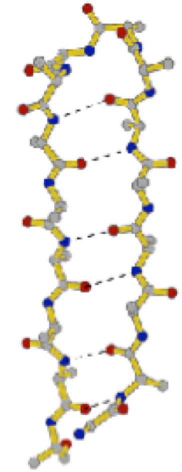


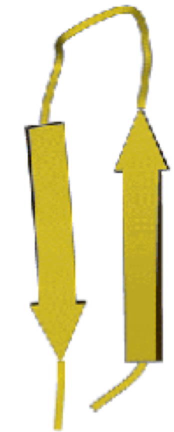


α - Helix
Only the N—C_α—C backbone is represented. The vertical line is the helix axis.

Beta Conformation

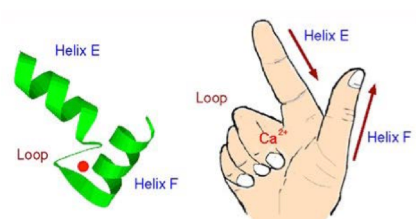
Parallel chains





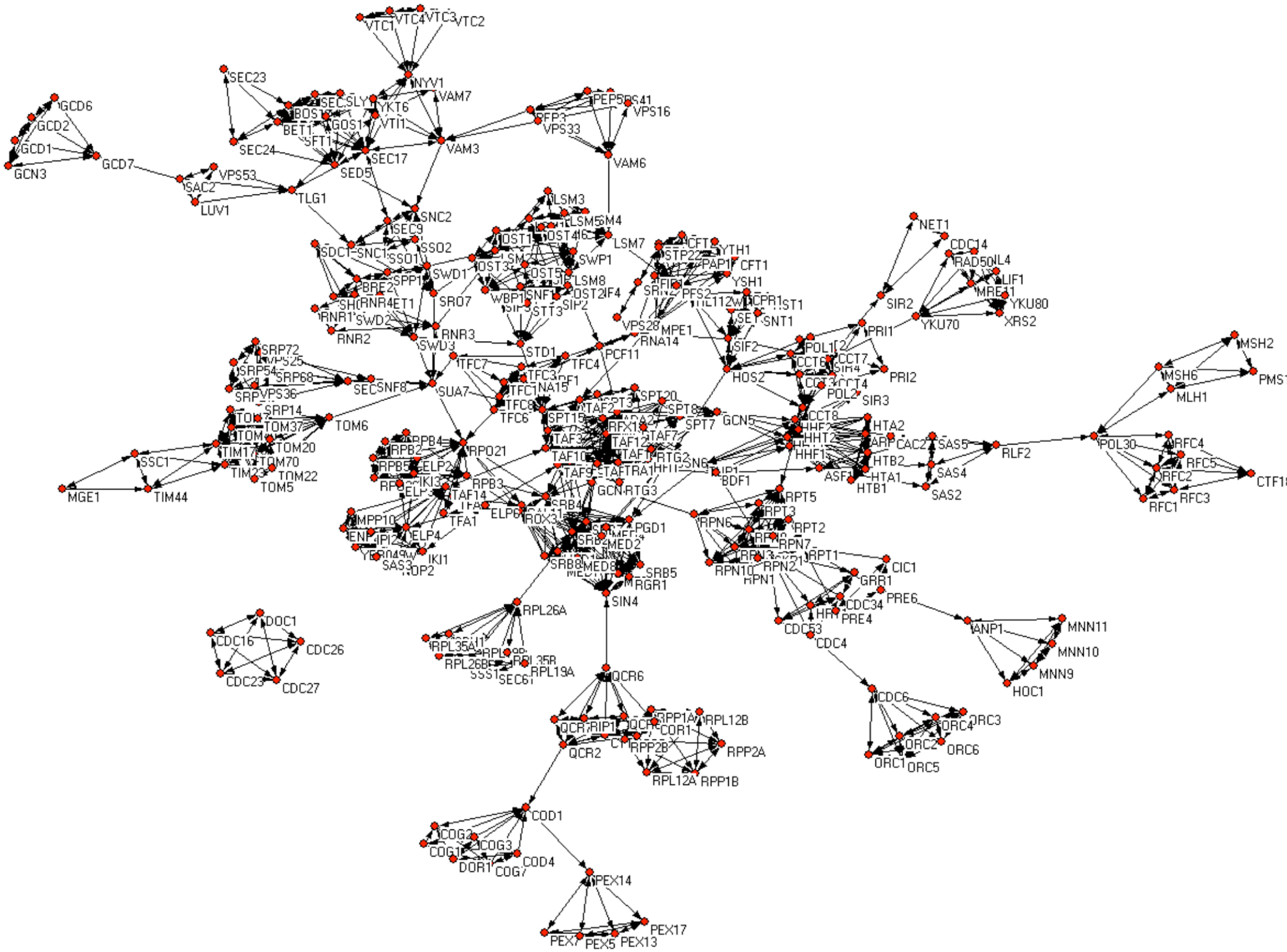
Combinations of secondary structural elements form different patterns of *Super Secondary Structures* (folds) that perform specific functions

TIM *(triose-phosphate isomerase)* **Barrel**
An eight-stranded α/β domain (first found in Triose phosphate isomerase). A central barrel formed by parallel β-strands surrounded by seven or eight α helices which shield the barrel from solvent.



EF Hand : The loop region in Calcium binding proteins are enriched in Asp, Glu, Ser, and Thr.

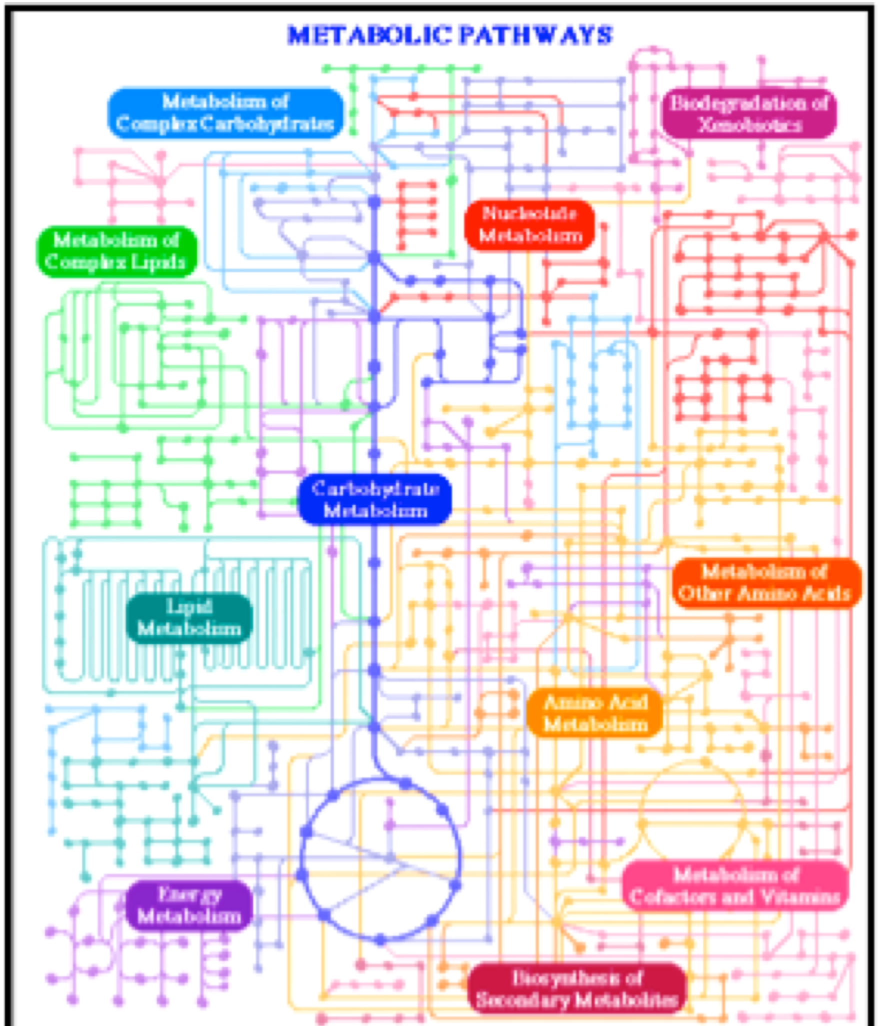
Pattern of contacts in protein interaction network
- *scale free nature*

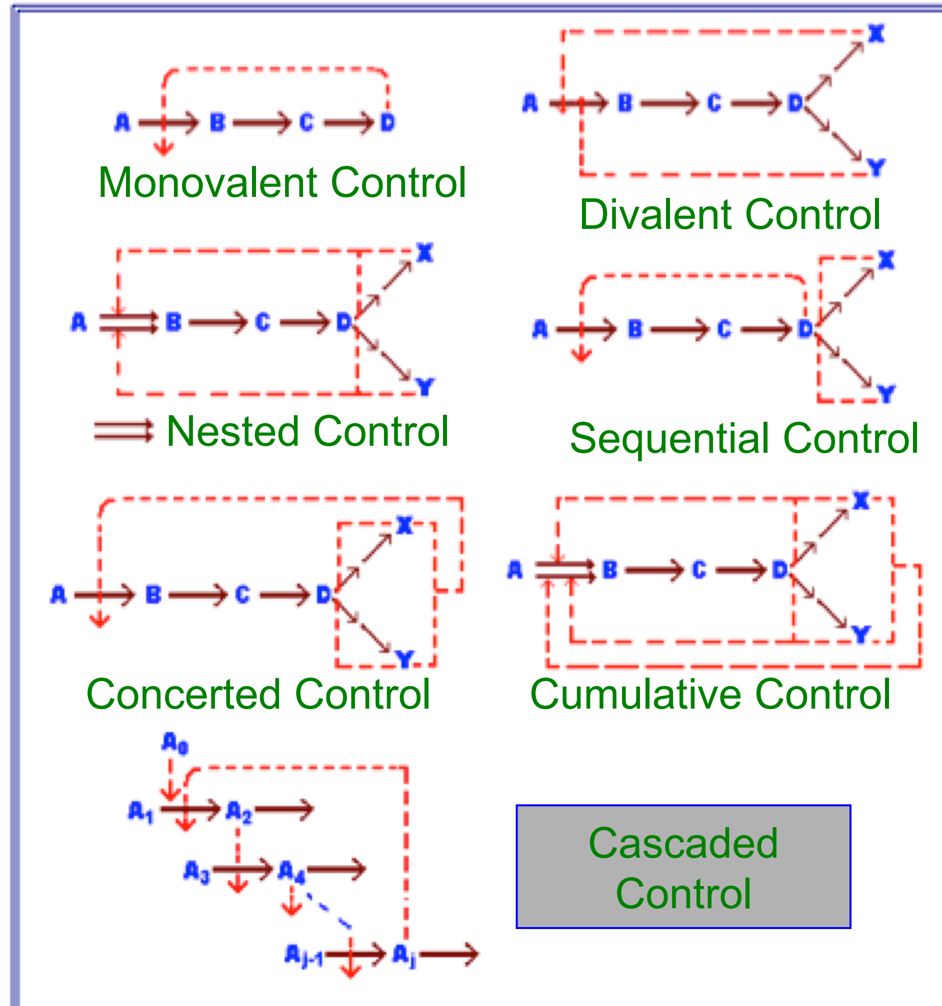


A small part of the budding yeast (*Saccharomyces cerevisiae*) protein-protein interaction network.

Patterns of Regulation in Biochemical Pathways in Cells

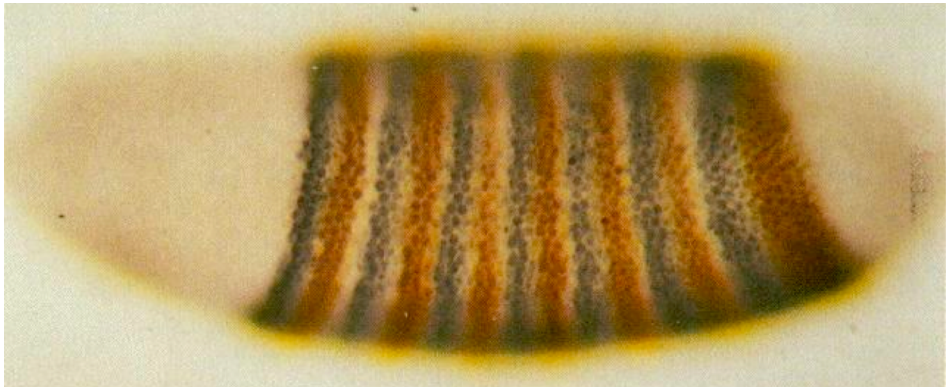
Biochemical reactions are controlled by multiple levels of feedback processes - varied functional requirements



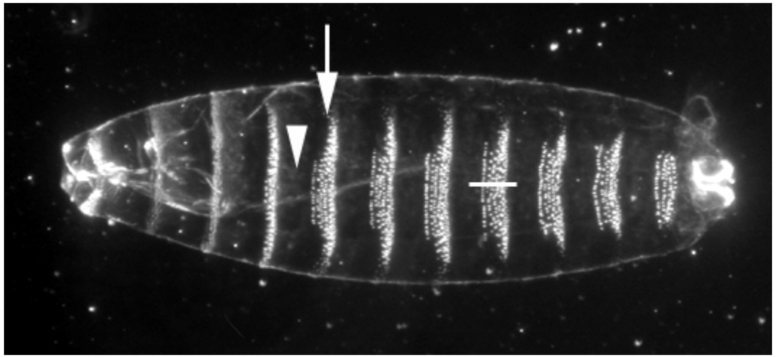


Patterns of Gene Expression give rise to structure

Pattern Formation (Segmentation) in Drosophila Embryo



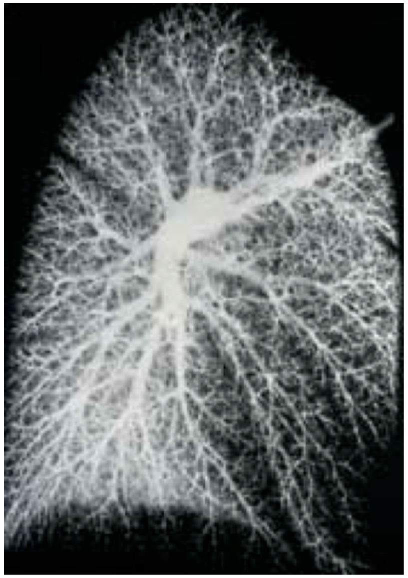
Gene expression pattern

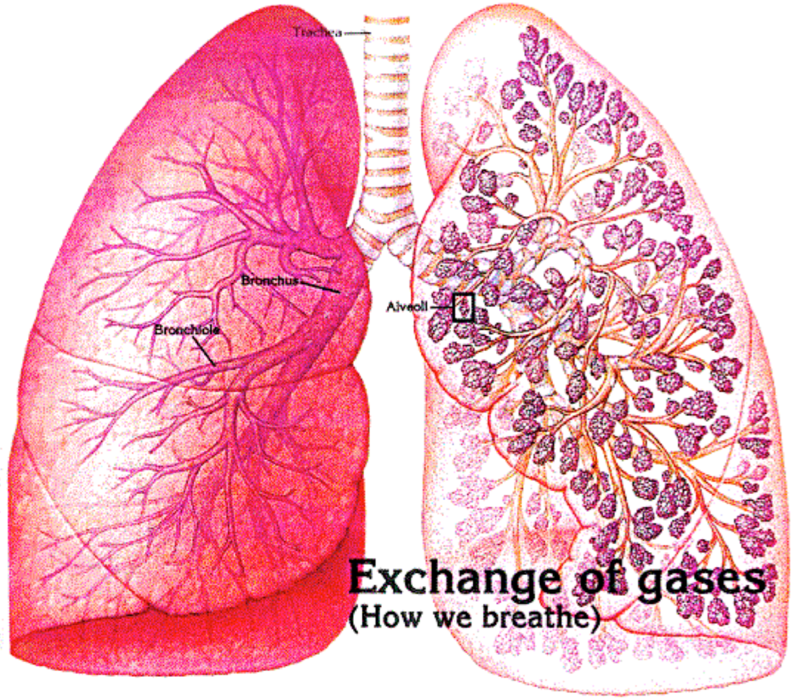


Epidermal pattern

Embryonic body pattern is organized into repeating, segmental units, visible in the cuticle of the first instar larva (ventral view). Smooth cuticle (arrrow head) alternates with bands of "denticles" (arrow) across each segment.

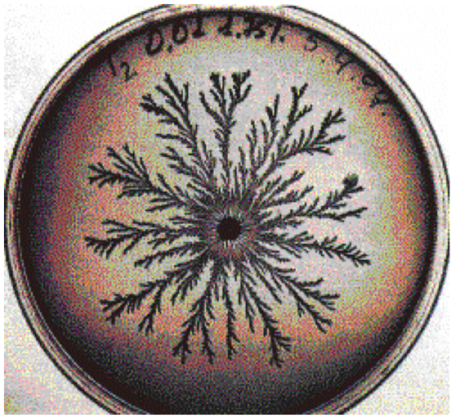
Patterns of tissue or organ structure – aids in cellular functions



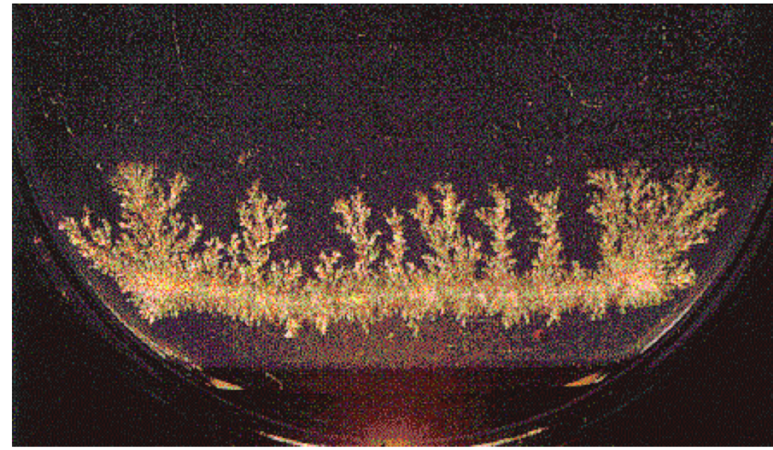


The lungs have an extensive network of blood vessels. This aids in excellent blood supply that is needed to transport oxygen away from the lungs efficiently.

Patterns of Growth under Stressed Environment – aids in survival



Colonies of the bacteria *Bacillus subtilis* under nutrient-limited conditions - cause the bacteria to spread out in complex search patterns – a fractal form.



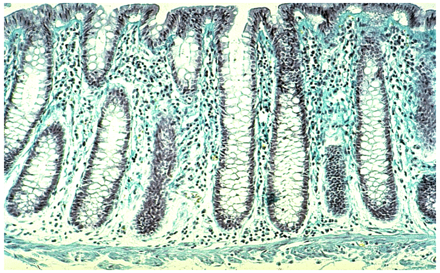
Aspergillus oryzae grown under decreasing nutrient concentrations

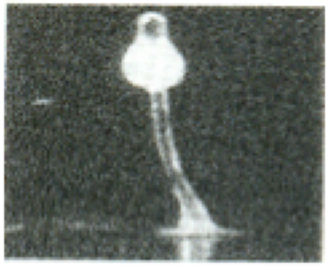
Diffusion-Limited Aggregation, or DLA, is a simple computer simulation of the formation of clusters by particles diffusing through a medium that jostles the particles as they move.

Eshel Ben-Jacob (www.microbialart.com)

Morphological Patterns during Development

LARGE INTESTINE





Slime mold

Clouds are not spheres, mountains are not cones, coastlines are not circles and bark is not smooth, nor does lightning travel in a straight line.

Benoit Mandelbrot

http://www.math.yale.edu/mandelbrot/

Morphological Patterns during Development - alterations

Apetala mutant

Mutant plant makes anthers where it is supposed to make petals.
The mutant has high fertility.

[Brassica oleracea (cabbage, broccoli, cauliflower, etc)]

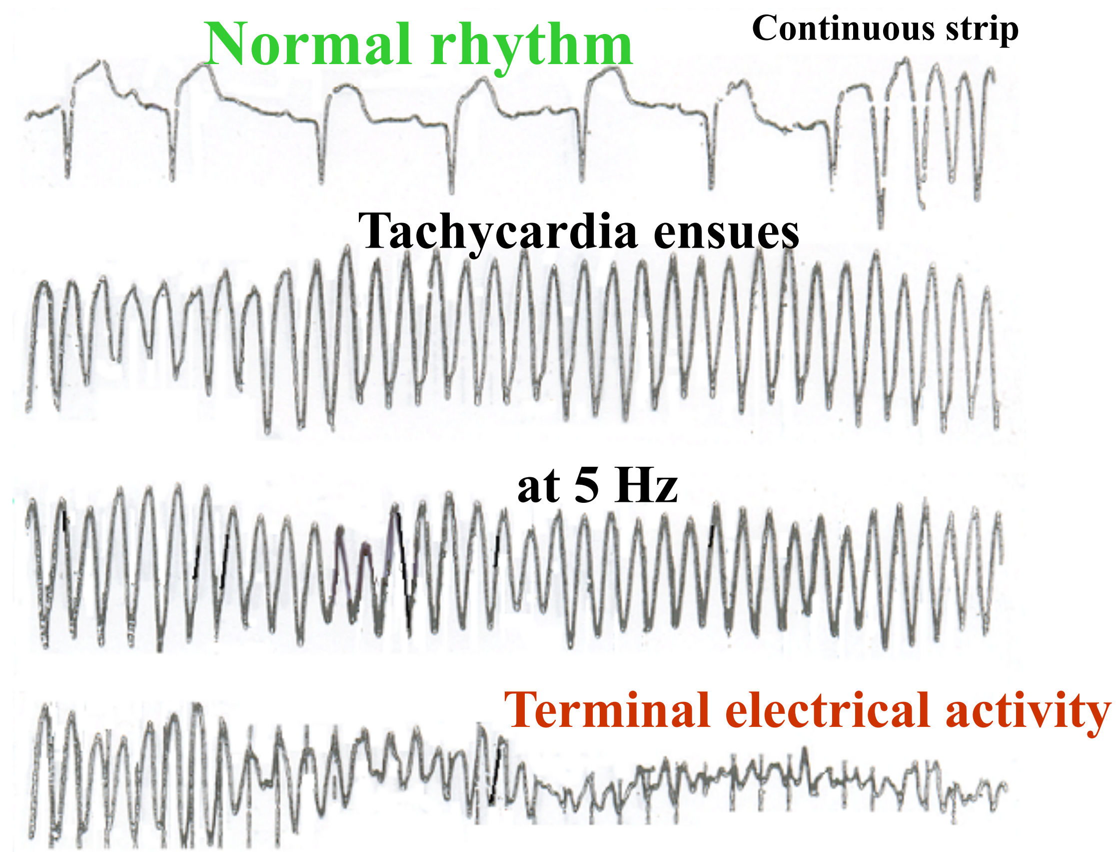
Temporal Patterns - alterations lead to disease

Cell cycle, Circadian rhythm, Calcium oscillations, Flashing of fireflies in unison, Recurrence pattern of disease, etc

ECG during sudden cardiac death

Normal sinus rhythm ~ 1 sec

Change in the type of rhythm during disease



Phase synchronisation of coupled oscillators - *Statistical Physics*

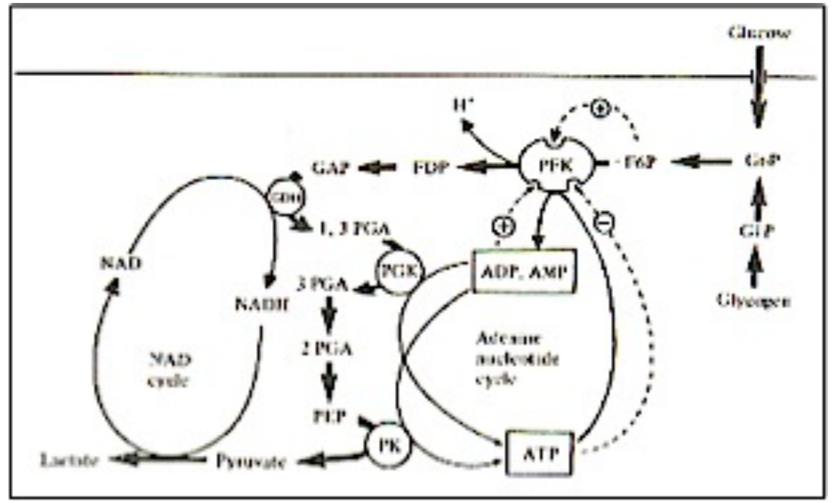
(Oscillator death !)

Temporal Patterns - Driven by external agents

Control structure of glycolytic pathway

Material transport ———

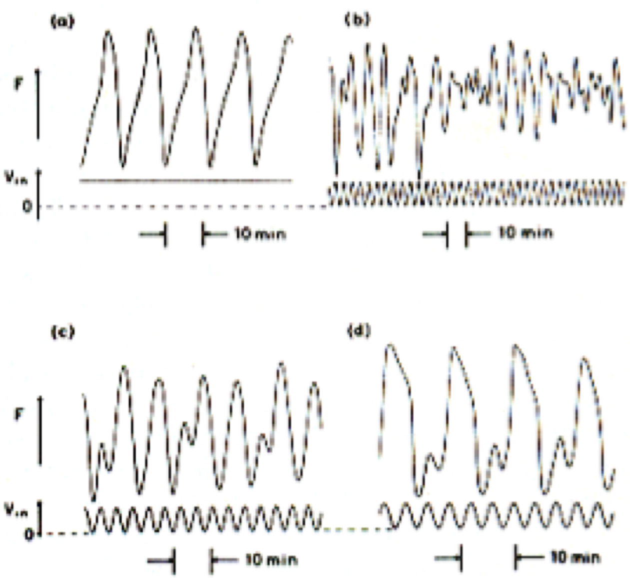
Control loops -----



Glucose

Experiments on cell-free yeast extracts:

NADH Fluorescence



Glucose input

measurements of NaDH fluorescence (Y axis) with time for different glucose input

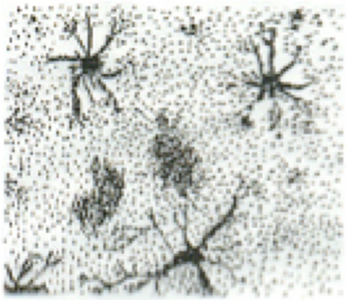
Constant input → oscillations
Periodic input → chaos
1:5 entrainment
1:3 entrainment

Spatio-Temporal Patterns

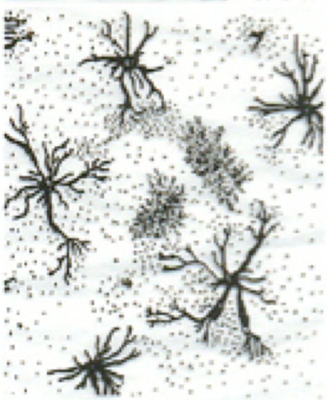
change lead to developmental irregularities

social amoebae

Free-living cells - eat and reproduce



Cells aggregate (signal (cAMP) relay)



Large aggregation centres formed

Mound of cells form slug

Fruiting body with stalk and spore cells

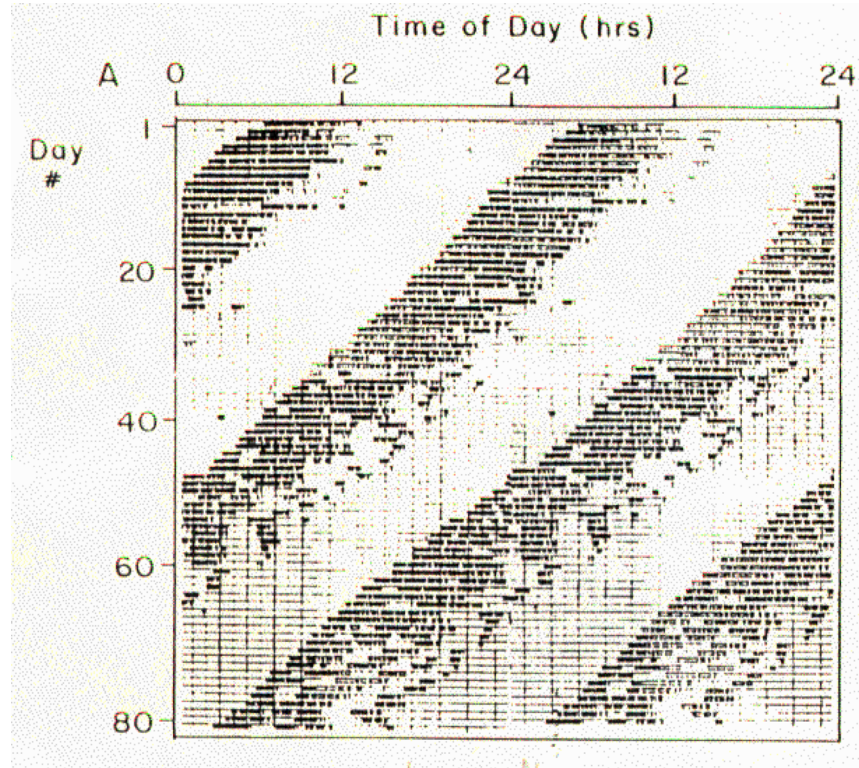
Active communication and interaction among the cells in a population leads to development of pattern

Patterns in Processes

Activity Pattern

Free-running activity pattern of mouse. Free running inherent rhythm T<24hr.

Entrainment happens as soon as environmental cue is given



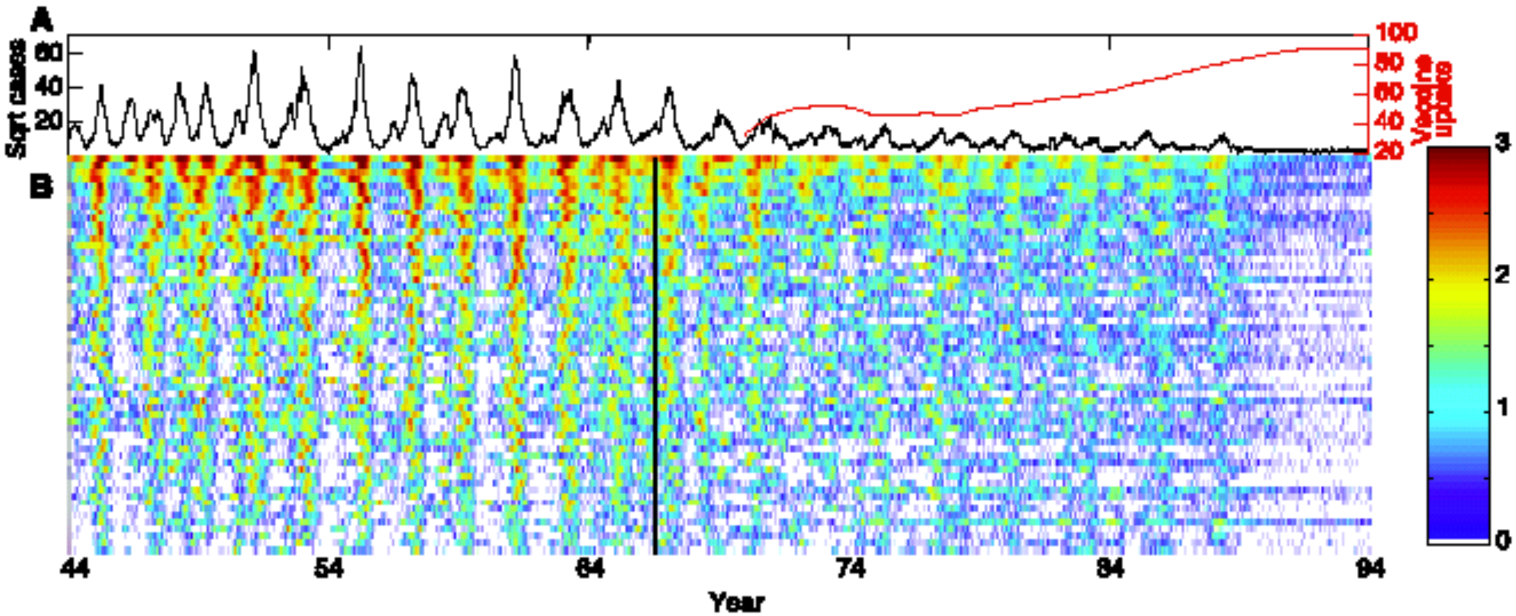
Ant Foraging Trails

As the colony size (number of ants) increases these trail networks increase in size.

Holldobler and Wilson *The Ants* (1990)

Patterns in Processes – *effect of intervention*

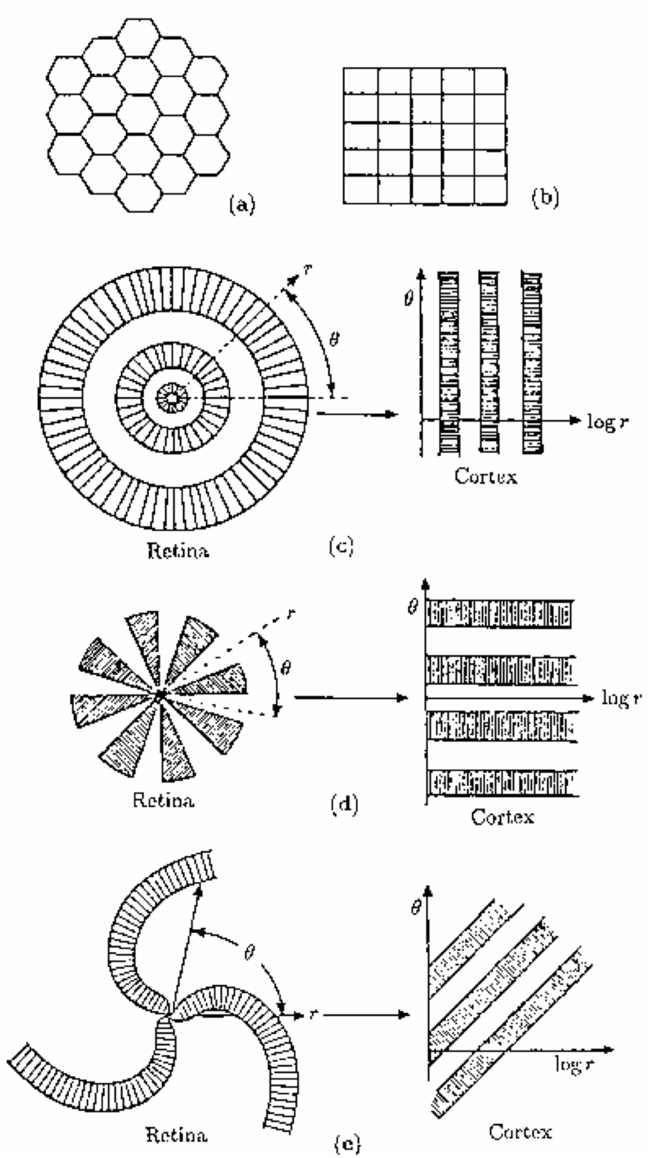
Measles and whooping cough notifications in England and Wales from 1944 to 1994



(A) Time series for measles in London (**black line**) and vaccine uptake levels (percentage of infants vaccinated) for England and Wales, starting in 1968 (**red line**).

(B) The spatial distribution of log10 (1 + measles cases) with cities arranged in descending order of population size (from top to bottom) and colors denoting epidemic intensity (white regions highlight periods with no reported cases).

The vertical black line represent the onset of vaccination.



Patterns in Processes

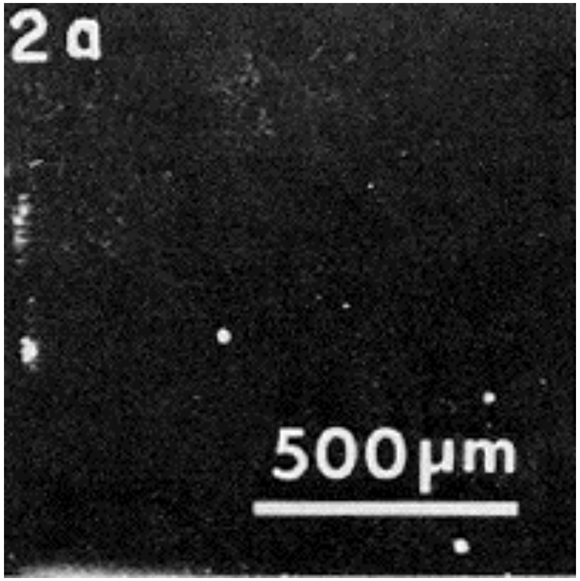
Drug induced hallucinations

Patterns under visuo-cortical transformation –

Hallucination patterns (left) Cortical images (right)

(Ermentrout & Cowan, 1979)

Spatio-Temporal Patterns - waves

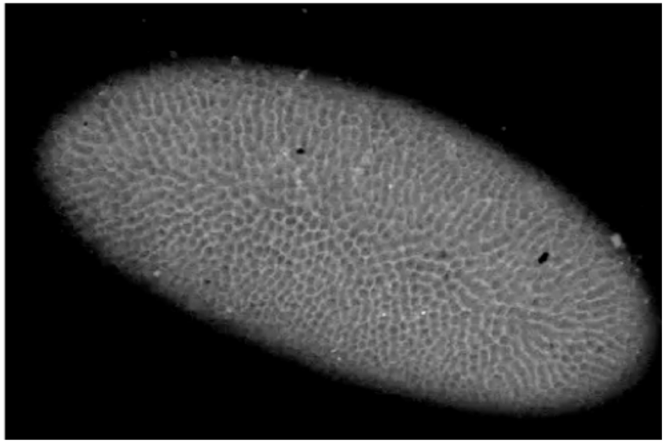


A free calcium wave propagating across a sperm-activated medaka egg

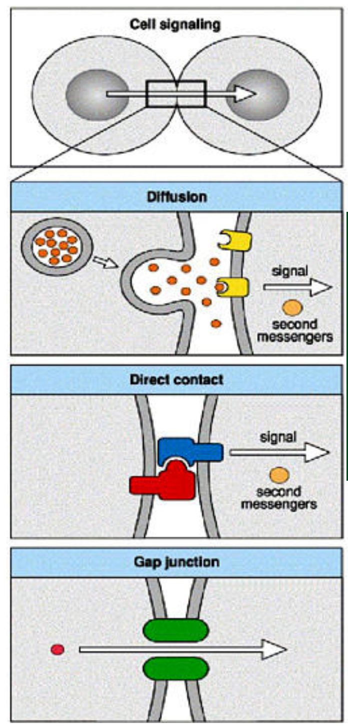
Successive photographs are 10 s apart.
Egg axis horizontal with sperm entry point to the left.

(Gilkey et al, J. Cell Biol. 1978)

Cell movement is a major process underlying formation of spatiotemporal patterns in biological systems.



Lewis Wolpert:
"It is not birth, marriage, or death, but gastrulation, which is truly the most important time in your life."



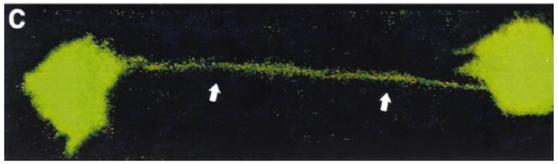
CELL-MATRIX CONTACT

Cell-to-cell communication is crucial for collective behaviour, and for the development and maintenance of multi-cellular organisms.

Diverse mechanisms of intercellular exchange of information are known and being discovered !

Types of Contacts in Multi-cell Systems

1. **Nearest-neighbour,**
2. **Long range,**
3. **Transient connections**



O. Renaud and P. Simpson. Developmental Biology 240, 361–376 (2001)

Types of Movement *(Cells, Organisms, etc.)*

Convection/Advection — Transport equation

(MASS TRANSFER)

- Moving in a fluid (e.g., blood)
- Matrix-mediated movement *(cells on moving substrate)*

Diffusion — Diffusive motion

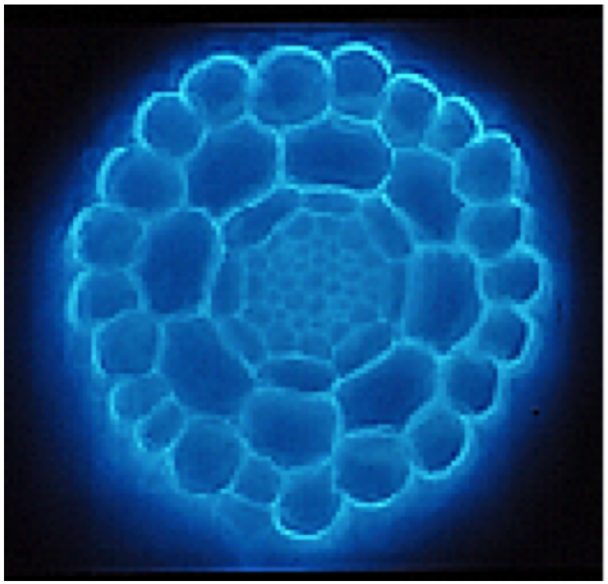
Transport associated with **random motions** in a fluid/substrate

Attraction/Repulsion — Field equation

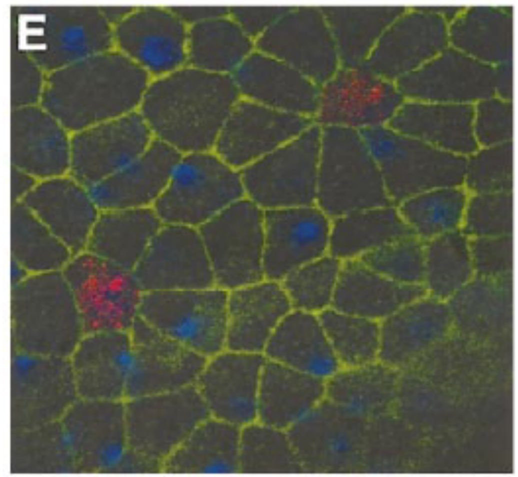
- Moving towards light source – phototaxis
- Moving along chemical gradient – chemotaxis
- Avoiding overcrowding

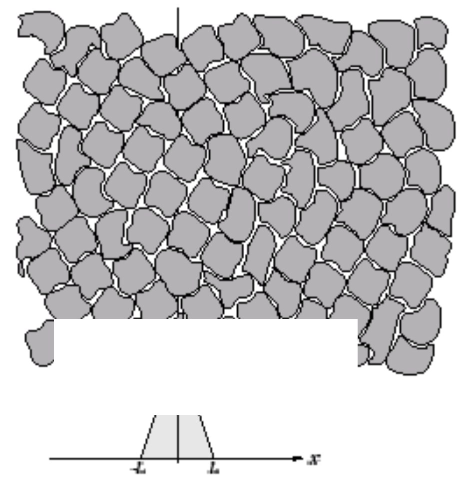
Tissue as a spatially-extended systems

Arabidopsis Root cells stained with DAPI (blue).

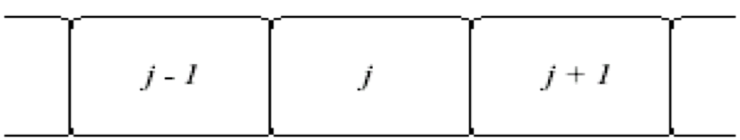


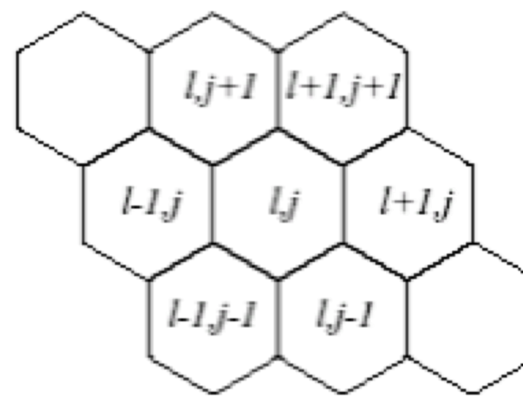
Epithelium of a 15-h *Drosophila* pupa stained for **Sca**, ***D*E-cadherin**, and **DAPI**.





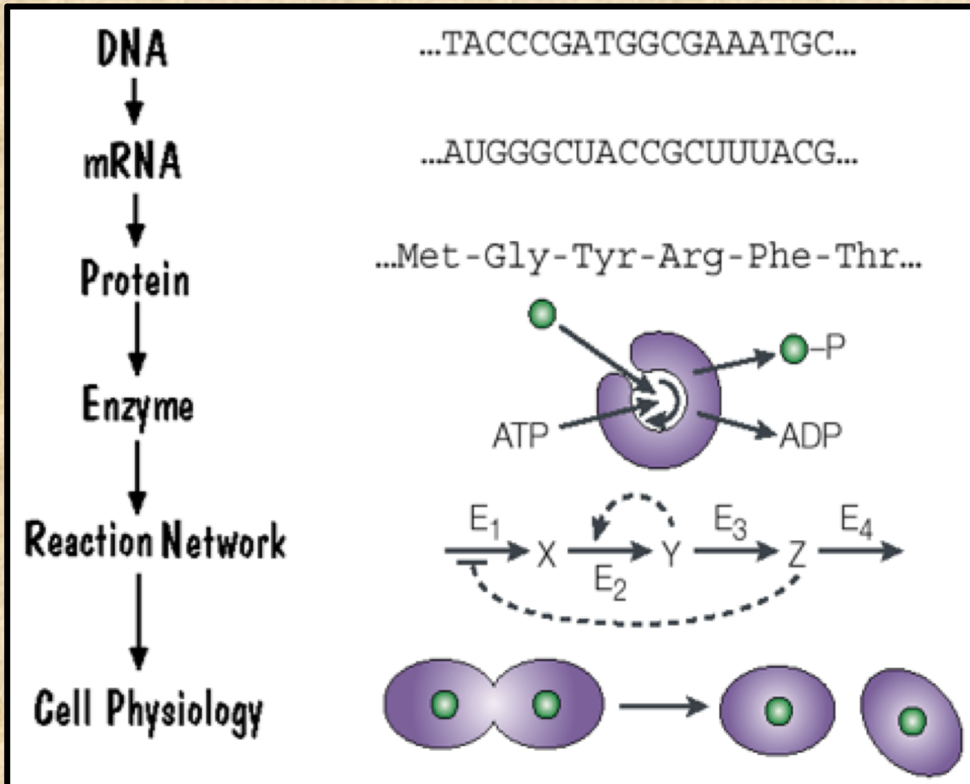
Labelling scheme used for cells in
One (linear or circular) and Two-dimensional arrays





Theoretical Approaches

FLOW of INFORMATION



Information in nucleotide strings

Dynamic Programming, Probabilistic methods, Algorithms

Gene Networks – Boolean models

Protein Structure & Folding

Molecular Dynamics, Stat. Phys, Quantum Mech., Electrostatics, Network Theory

Biochemical Pathways

Dynamical Systems Theory Network Theory, Differential Eqns, Boolean Algebra, Topology

Tissue pattern formation

Dynamical Systems Theory Differential Eqns, Partial Diff. Eqns, Coupled map lattices, Agent-based models, Graph Theory, Topology

Ecology, Epidemiology

Dynamical Systems Theory Network Theory, Discrete and Differential Eqns, ABM

Some Pioneers

August Weismann's Keimplasmtheorie (**Theory of Germ-Plasm 1892**), which held that differentiation in development results from the specific partitioning of the genetic material.

Hans Driesch (1894) - Analytical theory of development one of the great and influential books in the history of developmental biology. *Driesch started his research with the goal to explain development on the basis of physics and mathematics. Self-regulation and scaling during development. He also introduced the concept of "Positional Information" 75 years before Lewis Wolpert did it in 1969.*

Wilhelm Roux (1914) had coined the term Entwicklungsmechanik (Developmental Mechanics). Driesch's observation of self-regulation and scaling during development.

D'Arcy W. Thompson's monumental **On growth and form (1917)**, a work which would become influential for all subsequent researchers addressing problems of morphogenesis and pattern formation.

Hans Spemann, and Hilda Mangold demonstrated (1924) that animal bodies develop from a pattern-less single cell, rather than growing from a microscopic, preformed version of the adult body — in humans, the 'homunculus'.

Some Pioneers

Developmental biologists today investigate how molecular determinants and forces exerted by cells control embryonic patterning

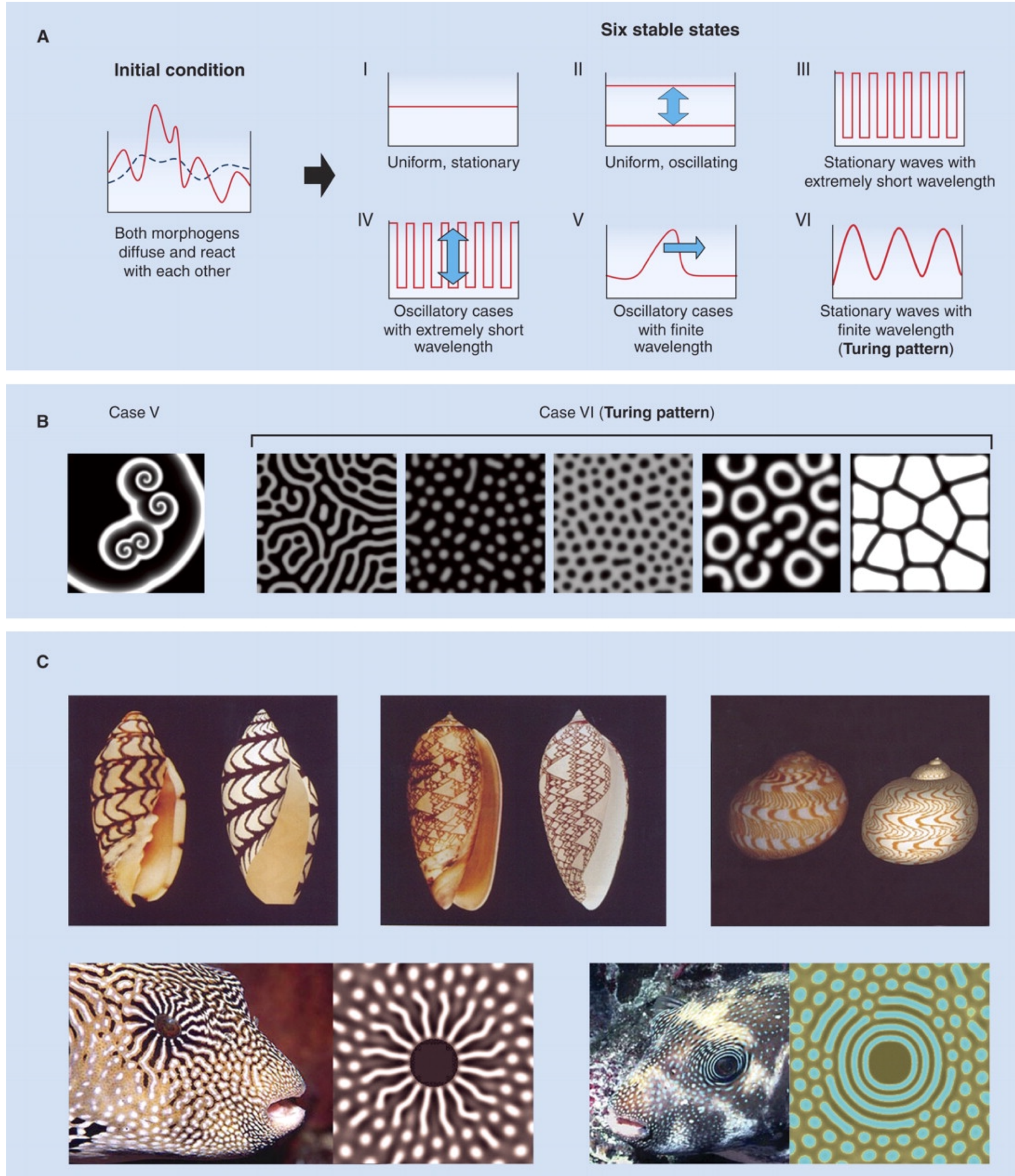
Waddington CH (1940) Organisers and genes. Cambridge University Press, Cambridge

'The chemical basis of morphogenesis' **(1952),**
Alan Turing showed that a pattern can indeed form *de novo*.
Turing's focus was on chemical patterns
He coined the term '**morphogen**' as an abstraction for a molecule capable of inducing tissue differentiation later on.
(The protein products of the *HOX* gene cluster, for example, which are essential for body patterning throughout the animal kingdom, are morphogens in Turing's sense.)

Ilya Prigogine and co-workers (**1947-1967**), attempted to extend non-equilibrium thermodynamics to situations far from equilibrium.

At the heart of pattern-making is symmetry-breaking.

TURING PATTERNS



In the early 1960s, **Alfred Gierer** his group in Tubingen, Germany shifted to developmental biology (from Physics), focusing on hydra as a model system which allowed them to study regeneration and self-regulation. In 1971, **Hans Meinhardt** joined the group. Influenced by ideas from cybernetics, they formulated their theory of local self-activation and lateral inhibition.

By combining a local deviation-amplifying process with lateral inhibition, Gierer and Meinhardt (1972) could explain how **structure formation was possible starting from a homogeneous state**.
Key aspects of the kinetics were **non-linear autocatalysis of the activator and, as in Turing's model, differences in the diffusion rates of the components**. The short-range action of the activator resulted from a small diffusion constant, the long-range effect of inhibitor action resulting from a large diffusion constant.

Models of biological pattern formation (Meinhardt 1982)

ELSEVIER

Developmental Biology

Volume 154, Issue 1, November 1992, Pages 218-222

Brief note

Perturbations in morphogen gradients induce budding in hydra

Somdatta Sinha[2], Sivatosh Mookerjee*

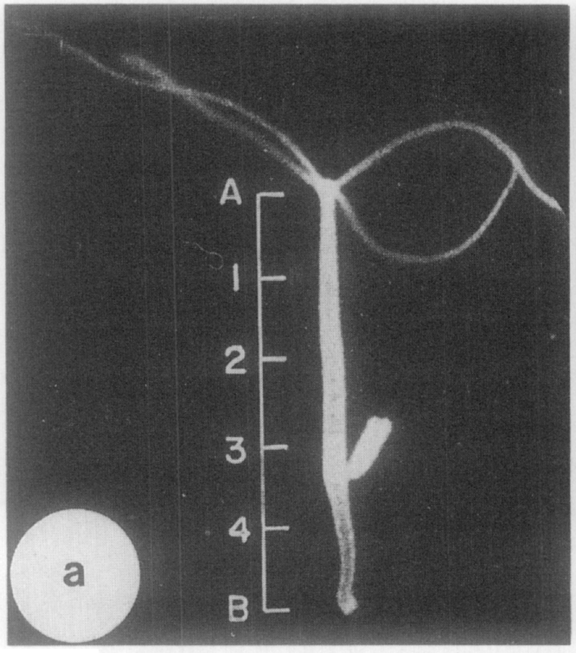
Roux's Arch Dev Biol (1984) 194:56–60

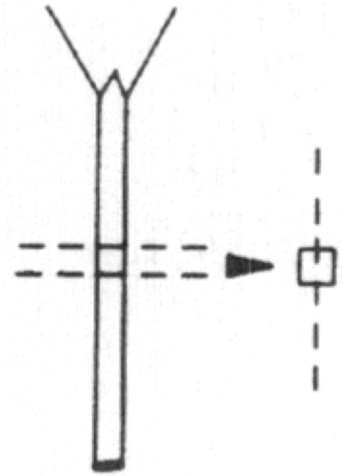
Roux's Archives of Developmental Biology

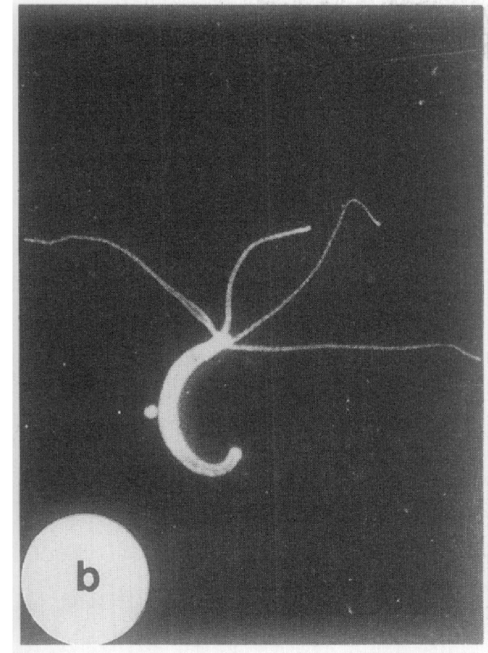
Hydra pattern is controlled by two distinct but interacting morphogen sets

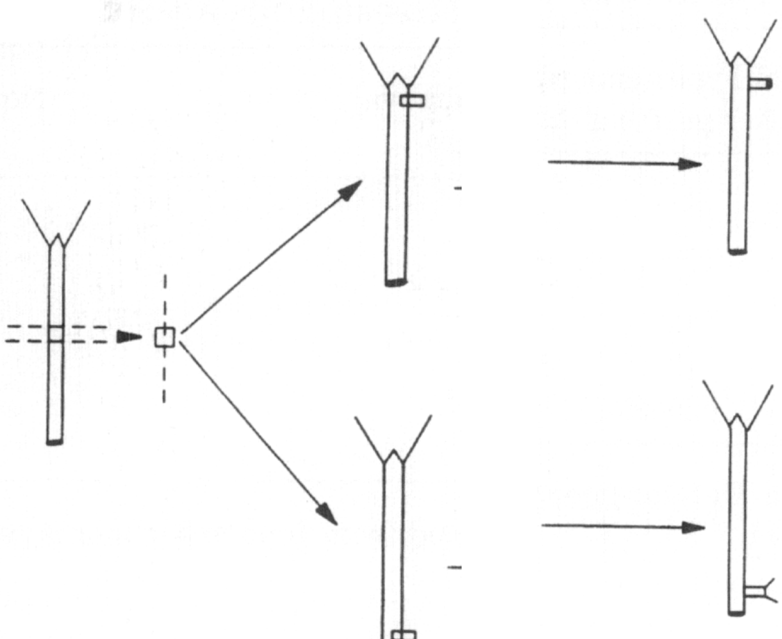
Somdatta Sinha* and Sivatosh Mookerjee

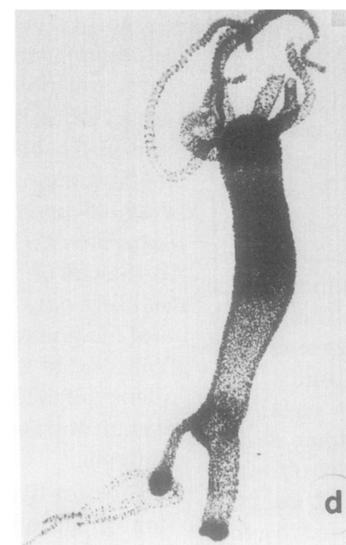
School of Environmental Sciences and School of Life Sciences, Jawaharlal Nehru University, New Delhi, India











Sinha S, et al. (1984) A four-variable model for the pattern-forming mechanisms in Hydra. Biosystems

To explain these results, it is necessary to consider **interactions between the head- and foot-forming processes**. We simulated the experiment of apical midpiece grafting in a simple **Gierer-Meinhardt type lateral inhibition model with weak cross-reaction between the head and foot inhibitors**, and the simulated chimera showed **two foot activator peaks at the two ends of the animal** with the head activation peak near the mid-region. This shows that *this model can not explain the coexistence of two terminal structures unless constraints are put on the ranges and details of interactions between the head- and foot-specific morphogens.*

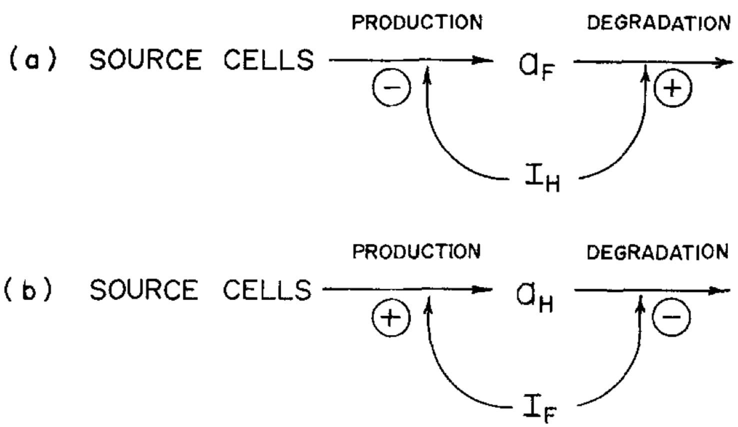


Fig. 5a, b. A possible scheme of interaction between the activators and inhibitors