# COURSE COMPUTATIONAL BIOLOGY 2018-2019
# http://www-binf.bio.uu.nl/BINF


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## Aims

- HOW TO use modeling to gain insights in biotic systems
- Biological insights(theory) obtained through modeling

Lectures (Tuesday, Thursday mornings)
Tutorials (Tuesday, Thursday afternoons)
Review tutorials Monday afternoons
Background Litterature (Monday and ..)
Mini-project (model study, report (incl litt)(Dec/Jab 2018/19)
Litterature Seminar (Jan 2019)

## Preliminaries.....

- —— "De leerdoelen van de cursus"

*Basic modeling skills*
*understanding modeling results: insights and limitatiojs*
*ability to read/understand present day modeling litterture*
*Knowledge of Biological Theory*

- —— Plaats in het curriculum (studiepaden bijvoorbeeld)

*Core course Computational Biology (Bsc & Msc)*

- —— De manier van beoordeling

*Written Exam*
*grade rounded by performance computational project*
*and litterature seminar*

- —— Aanwezigheids- en inspanningseisen

*written report on computational project*
*litterature seminar*
*No mandatory presence requirements BUT....*

# Computational Biology

## Sir Paul Nurse: Organisms are information networks

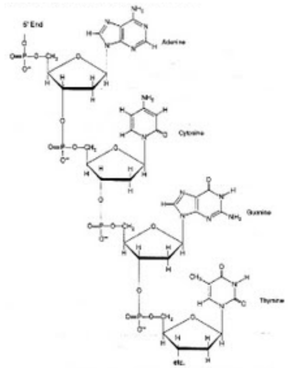
Speaking at the Royal Institution earlier this year, cell biologist and Nobel prizewinner **Paul Nurse** predicts that the complexity of life's networks will take us into a strange and counterintuitive world

guardian.co.uk, Friday 12 November 2010

## Biology faces a quantum leap into the incomprehensible

Physics had to come to terms with the transition from commonsense Newtonian theory to the counterintuitive world of relativity and quantum mechanics. Now it's biology's turn

**counterintuitive - BUT through computational modeling potentially comprehensible**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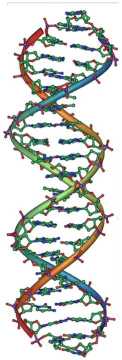
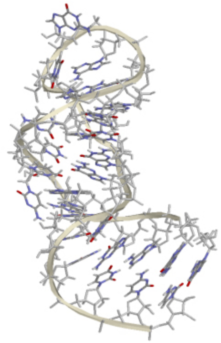
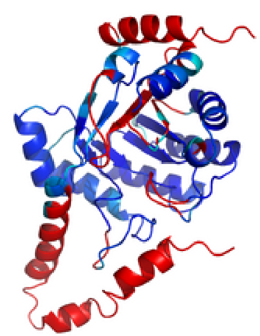
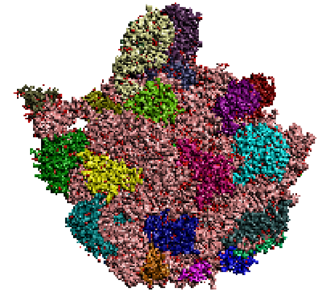
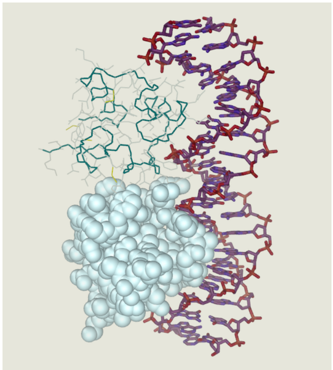
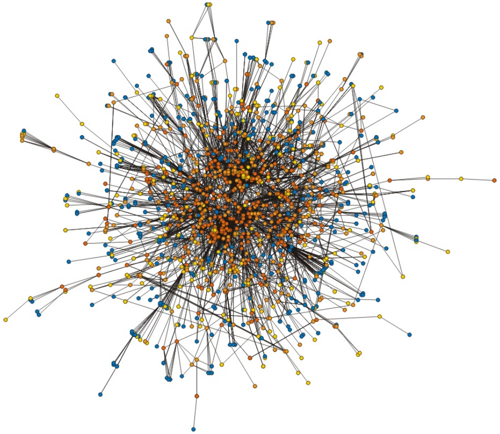
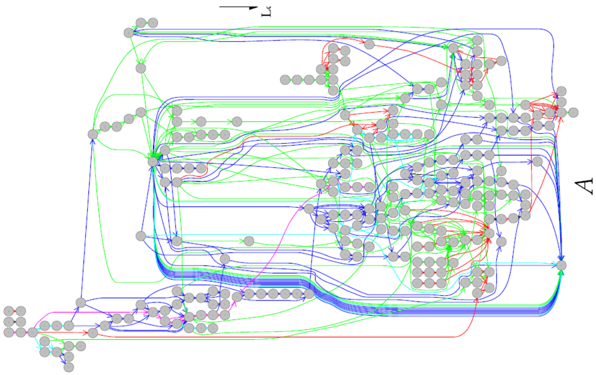
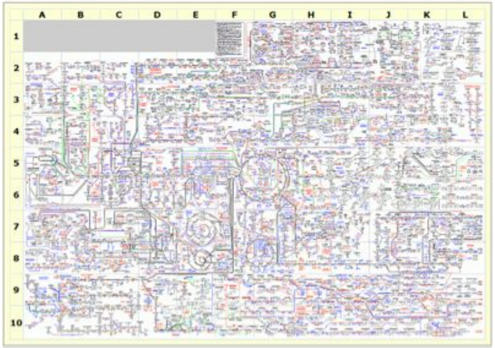
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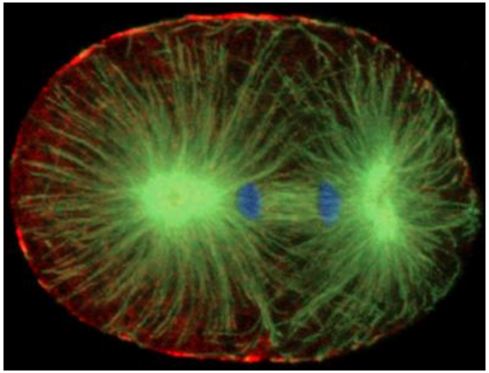
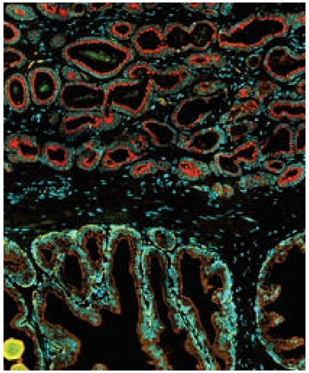
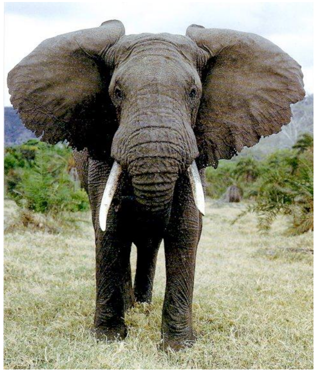





# Computational Biology for Studying of informatic processes in biotic systems (Bioinformatics)

Biotic system are multilevel systems: study them as such.
*information transmision, transformation between levels and over multiple timescales*

Given known (or assumed) interaction at the micro level what are the (counterintuitive) consequences?

*simple local iteractions* $->$ *complex behaviour*

*other names:*
*Complex systems, Biocomplexity, Bioinformatics*
*Systems biology, Theoretical biology*

## Biological systems as complex systems

*Hallmark of complex systems:*
*Emergence /Emergent phenomena*

Structures/ Patterns/ Behavior which is:
not predefined
arise and persist for some time
Unexpected and often counter-intuitive
at space/time scales different from the 'rules'
"mesoscale patterns with a dynamics of their own"
Needs new concepts/words to describe

*simple local rules to complex behavior*

*Self-organization*

# Structure of the course

- **Introduction:**
  - models and model formalisms: FSM, CA, Event-based, IOM, MAPS, ODE, PDE
  - basic modeling concepts: mesoscale patterns
  - examples: ecology, gene regulation networks, morphogenesis

- **Ecoevolutionary dynamics**
  - from population dynamics to multilevel evolutionary processes
  - spatial pattern formation and new levels of selection

- **Evolution of coding structures (genome/ regulome)**
  - genotype-phenotype mapping:
    RNA folding, regulatory networks
  - neutrality and robustnesss, information integration
  - evolution of evolvability (EVOEVO)
  - evolution as modeling tool

- **Multilevel modeling of Development**
- **Individual based models of behaviour**
- **Large scale models**

# Models are (often) caricatures...

Given complexity of (biotic) systems
drastic simplification is needed AND desirable

(needed to make them doable
desirable to be understandable)

Need of multiple different “points of view”

Multiple models

Multiple model formalisms

*Thinking in the most interesting simplifications*

## model requirements: fully specified

Prototype : Finite State Machine

$$< I, S, O, \Sigma, \Omega >$$

and subsets

Input-Output = Simulus Response: $< I, O, \Omega >$

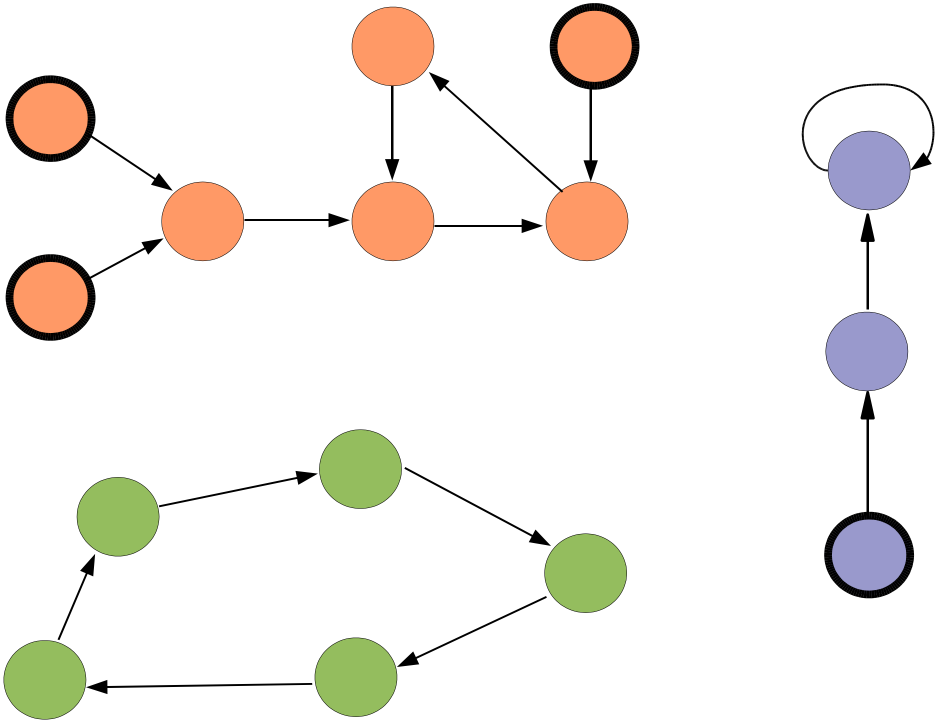
Autonomous systems: $< S, \Sigma >$ (or with output)

*Unique next state function* $->$

*attractor(s)*

*garden of eden states*

# an autonomous FSM



## “short cuts” on full transition table specification modeling formalisms (heuristics)

1. Decomposition in many simple subsystems
(each specified by transition table/ transition function)

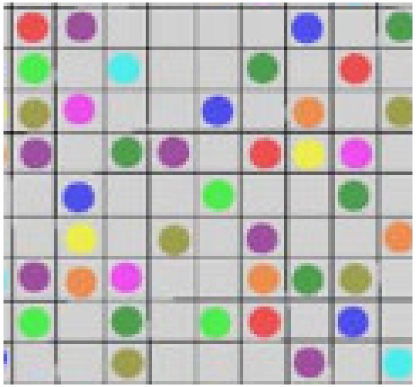
- collective behavior of simple entities
- IO relations between *some* entities

examples:

Cellular automata CA
(Boolean Networks)
Individual/agent based models (IMB/IOM)

# Cellular Automata

prototype for:
simple local information processing leading to
complex “emergent” behaviour
Definition: (in)finite tesselation of ’simple’ FSM



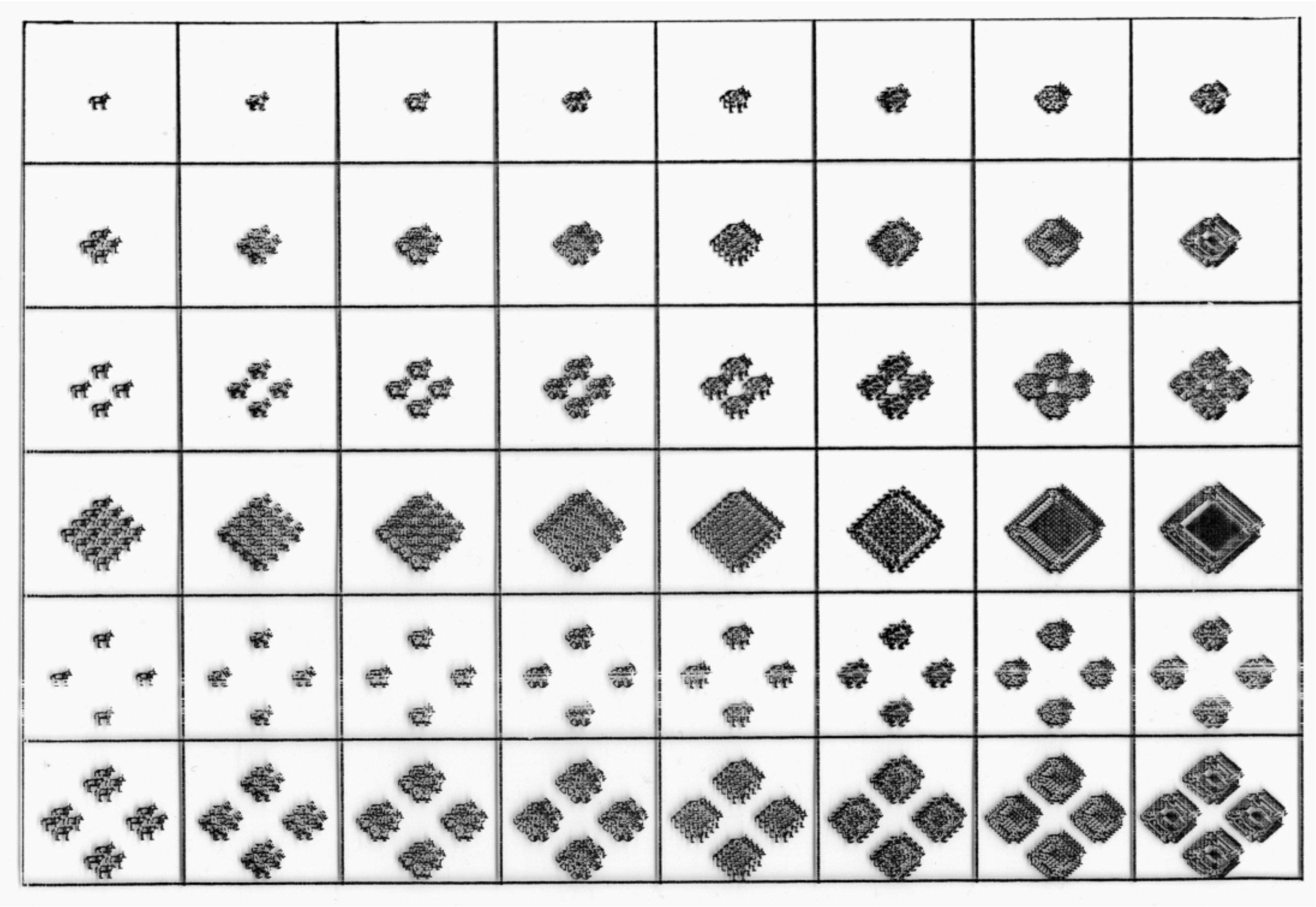
’simple’ FSM:
- small number of states (2)
- output == state
- input from local neighbourhood
- *synchronous updating next state function*

**collectively again FSM**

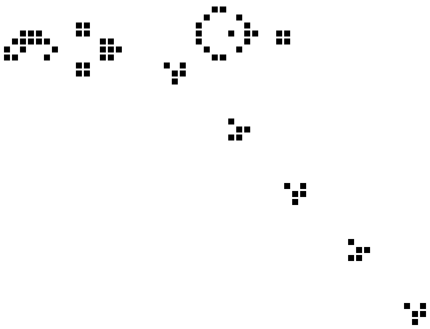
*“speed of light”*

**MESOSCALE PATTERNS**

# Example CA: Modulo Prime



# Classical examples of Cellular automata
# (2) Game of life



Birth: if # Neighbours is 3 then S = 1

Survival: if # Neighbours is 2 or 3 then S = 1

Death: if # Neighbours $< 2$ or $> 3$ then S = 0

*emergence of*
*mesoscale patterns*
*long range signaling*

Conway: “life is universal”

(i.e. game of life can simulate unversal Turing machine)

No machine can “predict” fate of every intitial configuration

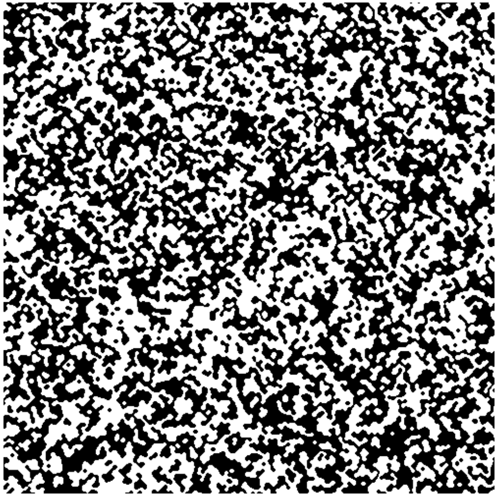
no shortcutes : let it live its life

**proof of fundamental principle**
**(not model of “something”)**

# Classical examples of Cellular automata
## (3) Majority rule

Moore 9 neighbourhood

if $<=4$ Neighours in state 1 nextstate=0; else nextstate=1;



default random .5

**Model for (too?) Many "somethings"**

e.g. Physics: Ising model, social sicience: voting, biology...

## Emergence
## Mesoscale patterns with a dynamics of their own

Sometimes paraphrased as:

*“the whole is more than the ’sum’ of its parts(?)*

HOWEVER

This is because of a *constraint* of the possible states.

$-->$

the whole is LESS than the sum of its parts

MOREOVER:

Emergent patterns not just WOW!