COURSE COMPUTATIONAL BIOLOGY 2025

http://www-binf.bio.uu.nl/BINF

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Theoretical Biology and Bioinformatics Group UU

Aims

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

Lectures (Tuesday, Thursday 10.00-12.45)
Tutorials (Tuesday, Thursday 13.15-17.00)
Review tutorials (Monday afternoons (13.15-15.00)
Background Litterature (Monday and ..)
Mini-project (model study, report (incl litt)
Litterature Seminar

Preliminaries.....

- —— "De leerdoelen van de cursus"

the "art" of biological modeling
Basic modeling skills
understanding modeling results: insights and limitations
ability to read/understand present day modeling litterture
Knowledge of Biological Theory

- —— " Plaats in het curriculum (studiepaden bijvoorbeeld)"

Core course Computational Biology / Biocomplexity (Bsc & Msc)

- —— " De manier van beoordeling"

Written Exam (+ adequate miniproject and seminar)

- —— " Aanwezigheids- en inspanningseisen"

written report on computational project
litterature seminar
No mandatory presence requirements, except at seminars

BUT....

Biological systems are

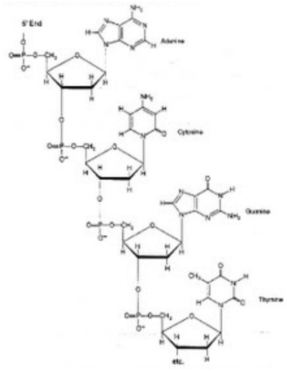
complex multilevel systems, which have come

about by evoution

and are evolving:

(how to) study them as such....

"models should be as simple as possible but not more so...
(Einstein)"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Adenine
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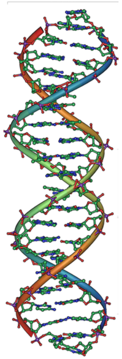
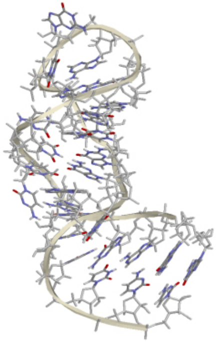
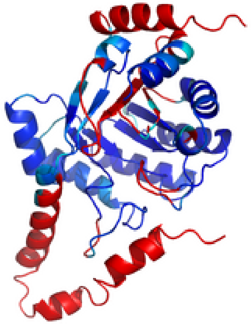
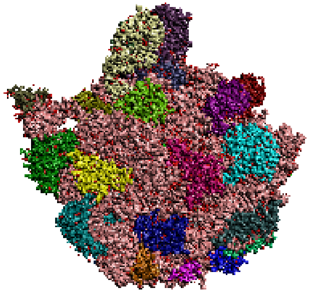
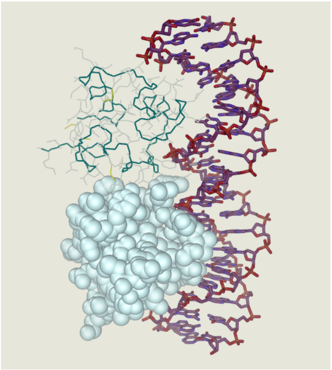
etc.

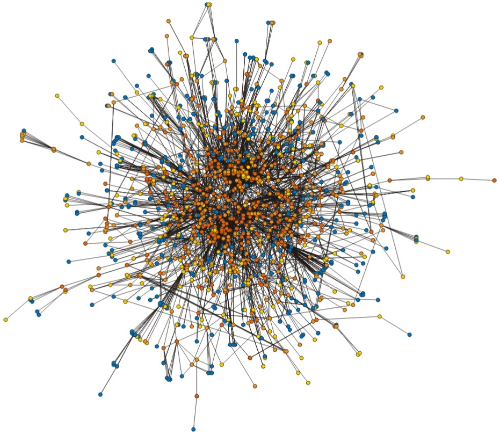


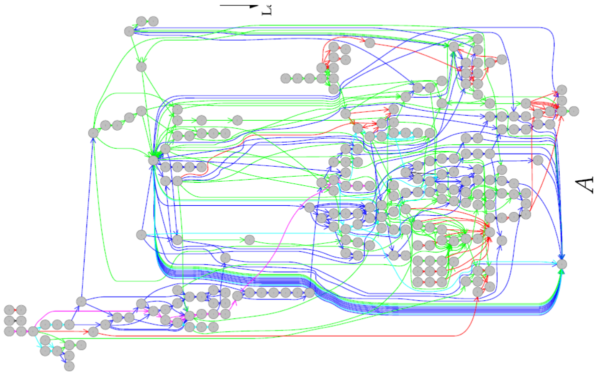








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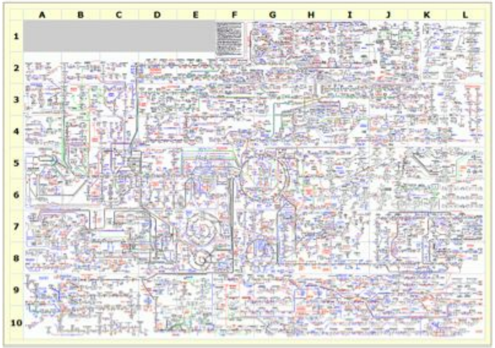
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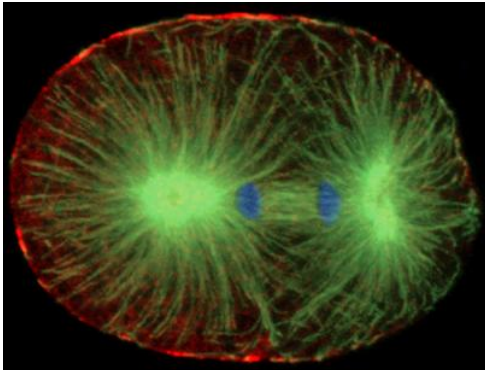
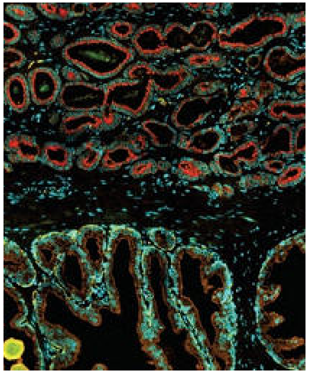
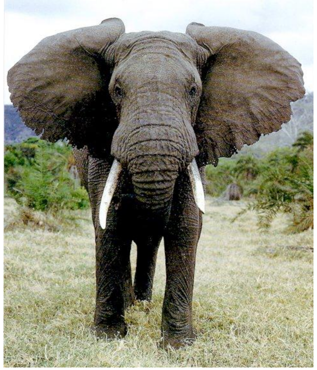







Minor Groove
Major Groove
One Turn = 10 Base Pairs = 34 Ångströms
Diameter = 20 Ångstroms

Computational Biology for Studying of informatic processes in biotic systems (Bioinformatics (Hesper & Hogeweg 1970))

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

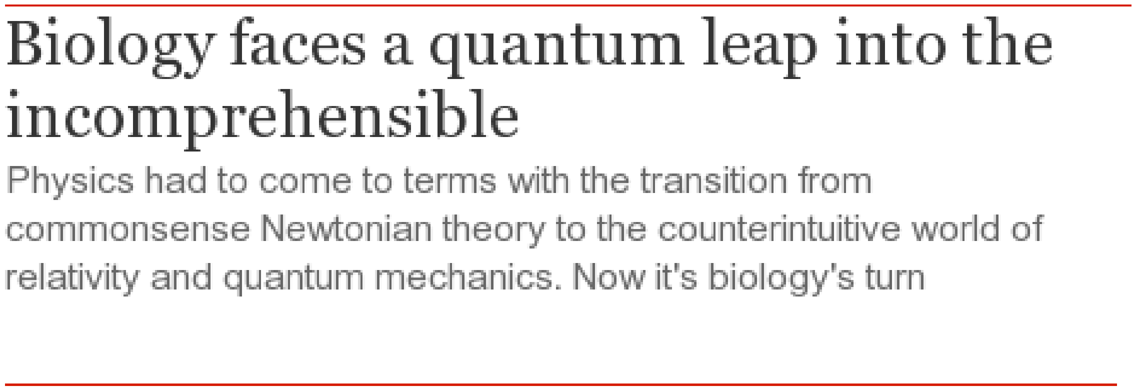
Self-organization

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

Structure of the course

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

- **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

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

A is a model of B when...

By studying A when can gain insight into B.

by exploring, debugging, generation prior/novel idea's

exposing gaps in our understanding etc.

A should not be maximally similar to B (then better study B)

A should not be as general as possible (many B's) (Ashby: "Rock of Gibaltrar")

"as simple as possible but not more so"

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)

State: what is needed to get unique nextstate/output

Unique next state function $- >$
attractor(s)
garden of eden states

Can be specified as table

Input	State	Nextstate	Output
I_1	S_1	S_x	O_j
I_1	S_2	S_y	O_k
.	.	.	.
.	.	.	.
I_2	S_1	S_z	O_l
.	.	.	.
.	.	.	.
.	.	.	.
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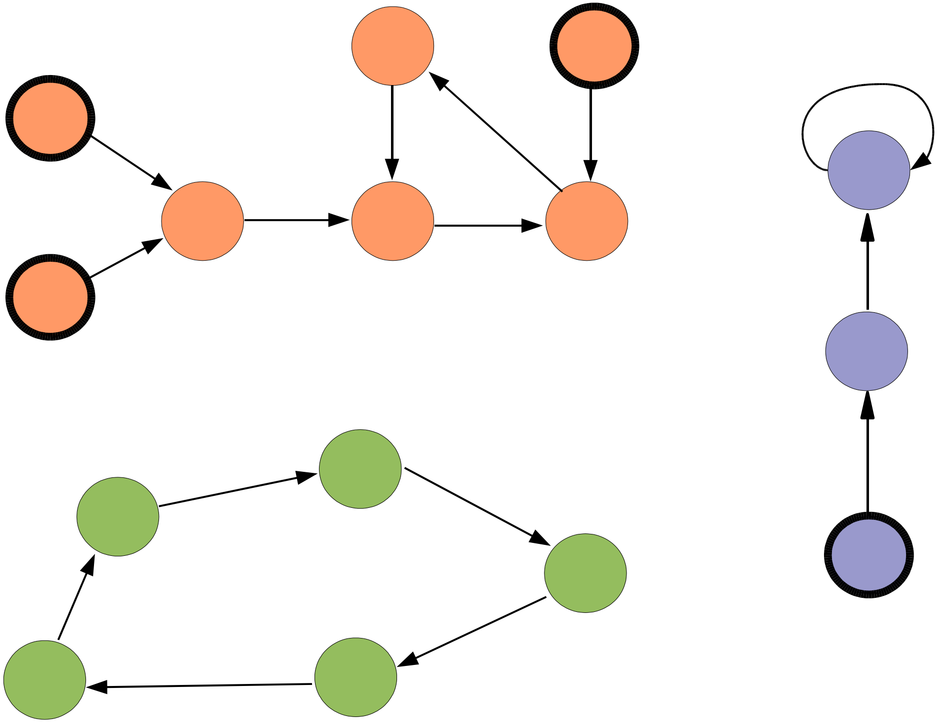
an autonomous FSM



“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

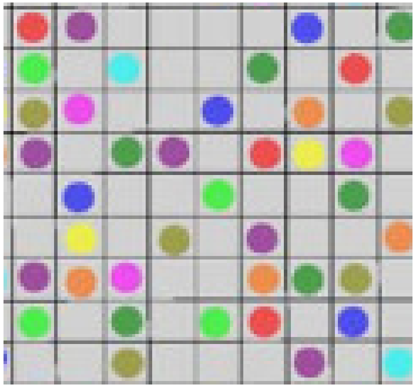
examples:

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

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*

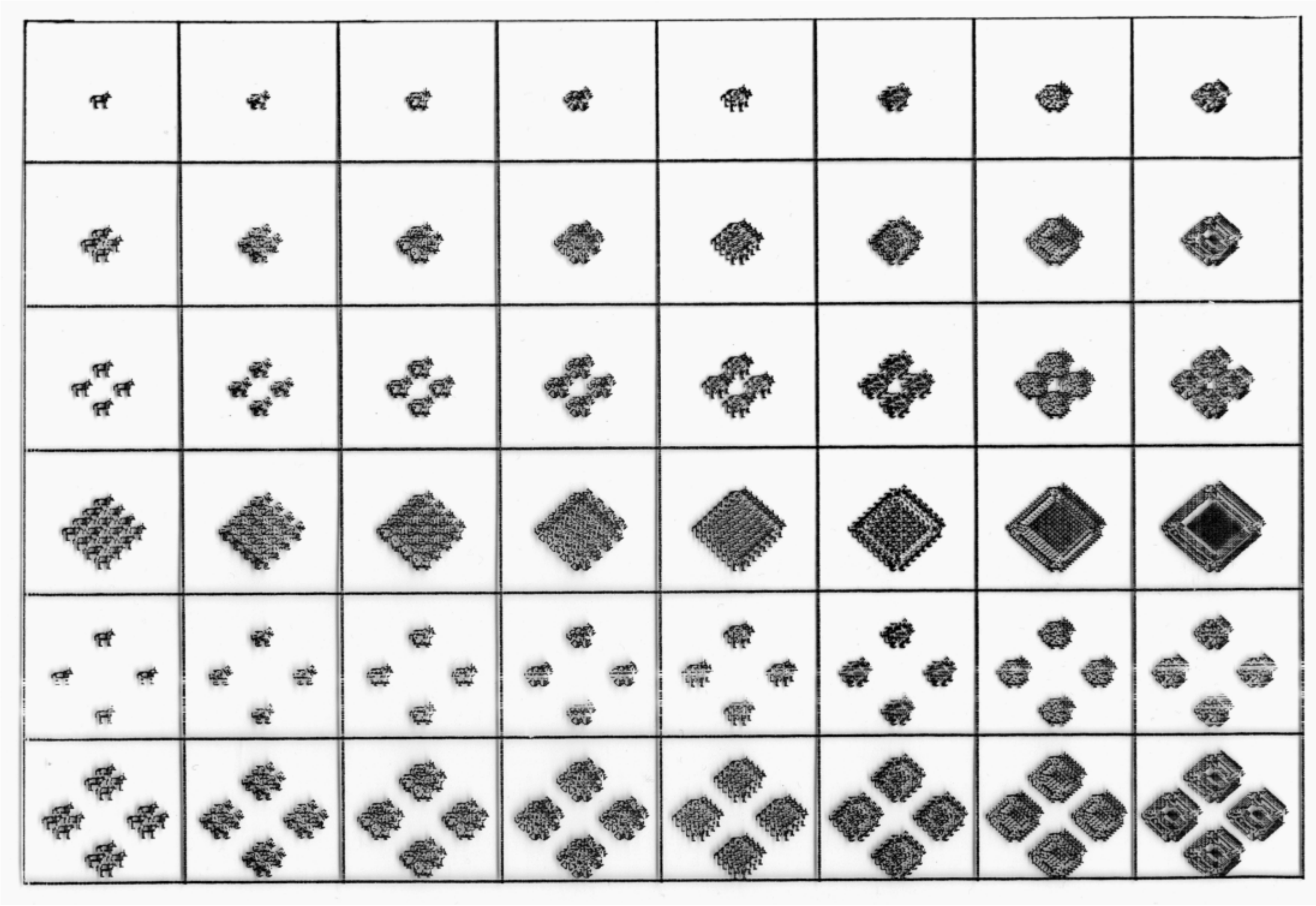


collectively again FSM

“speed of light”

MESOSCALE PATTERNS

Example CA: Modulo Prime



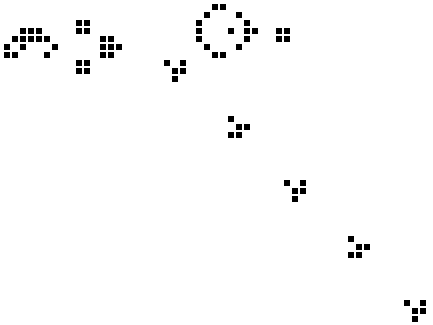
Classical examples of Cellular automata
(2) Game of life

Birth: if # Neighbours is 3 then S = 1

Survival: if in state 1

and # 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

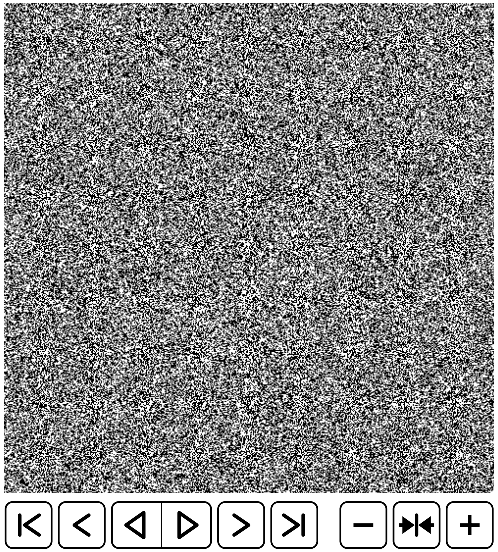
proof of fundamental principle

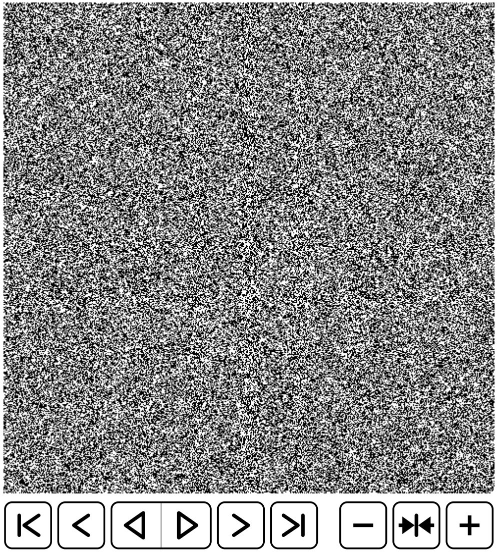
(not model of “something”)

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!

Mesoscale patterns (higher level entities) with a dynamics of their own

Example: Multilevel description of ECA54
(cf Crutchfield et al.)

REVIEW PAPER:

Cellular automata, emergent phenomena in

JE Hanson - Computational Complexity, 2012 - Springer

ECA 54, the rule under consideration here:

$$\phi(\eta) = \begin{cases} 0, & \eta \in \{111, 110, 011, 000\} \\ 1, & \eta \in \{101, 100, 010, 001\} \end{cases}$$

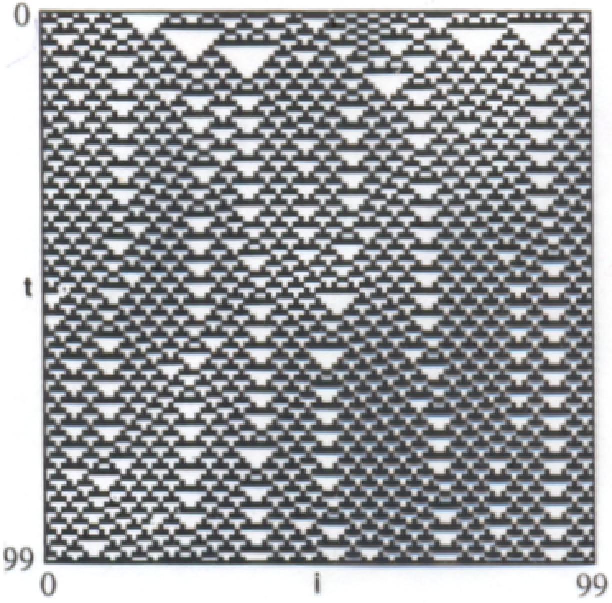


Figure 1. Space-time diagram of ECA 54, starting from an arbitrary initial condition. Boundary conditions are periodic. White squares are cells with value $s_t^i = 0$; black squares are cells with $s_t^i = 1$.

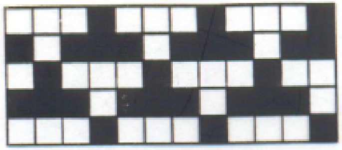


Figure 2. A portion of fig. 1 showing the domain Λ_{54}. Note the spatial phase shift of 2 cells every two iterations.

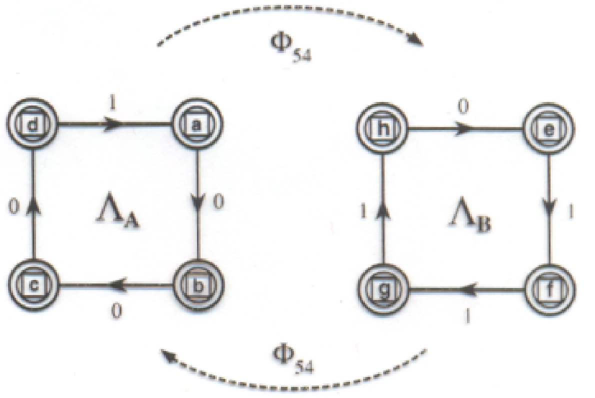


Figure 3. Process graph of ECA 54's domain Λ_{54}. The component on the left is Λ_A; on the right is Λ_B. As the dotted lines indicate, they are mapped onto one another by the CA ensemble evolution operator, Φ_{54}. In this and all following graphs of machines, inscribed circles and squares denote start and accept states, respectively.

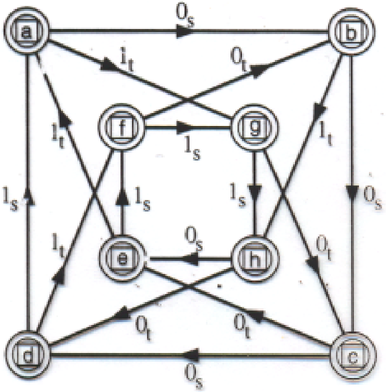


Figure 4. The process graph of $M_{ST}(\Lambda_{54})$, the space-time machine for Λ_{54}. States are labelled to correspond to those in the (purely spatial) domain machine $M(\Lambda_{54})$ in fig. 3.

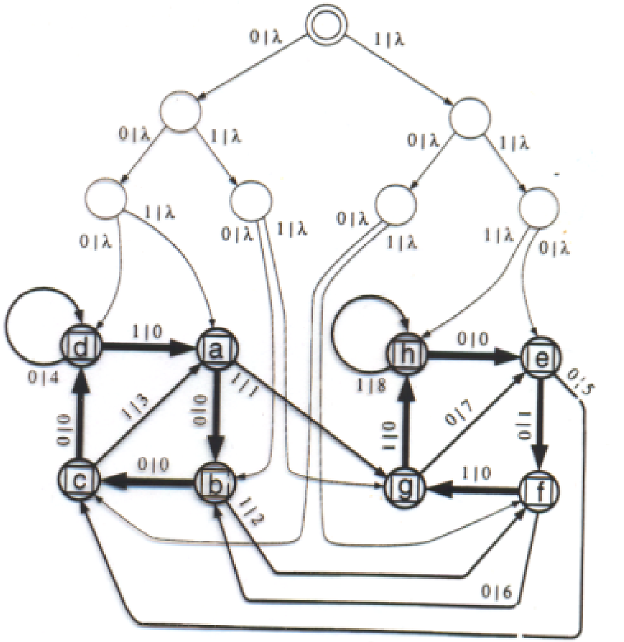


Figure 5. ECA 54's domain filter T^0_{54}, which maps sites in the domain to 0 and each defect to a unique output in $\{1, \ldots, 8\}$. Labelled machine states correspond to the domain states of fig. 3.

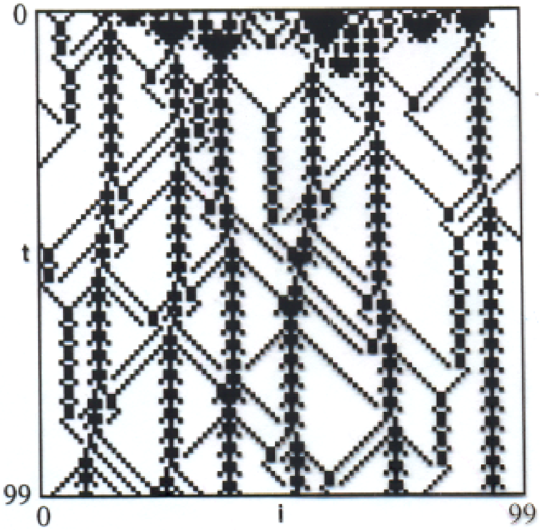


Figure 6. Space-time data of fig.1, filtered with the domain transducer T^0_{54} of fig. 5. White cells correspond to sites participating in Λ_{54}; black cells, to sites with values

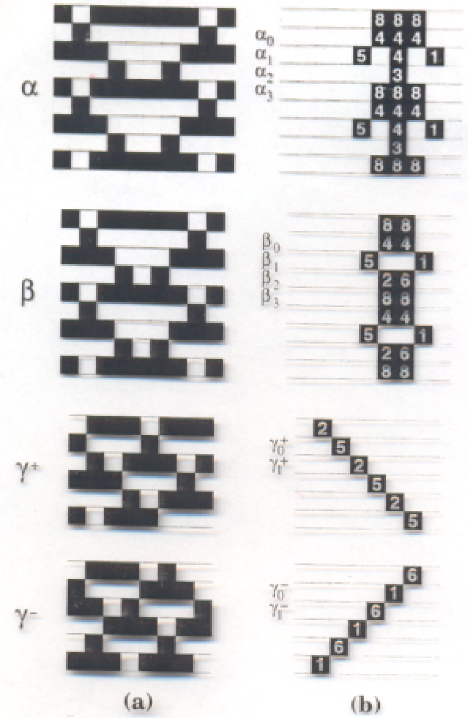


Figure 8. Basic wall structures ("fundamental particles") in space-time patterns of ECA 54. (a) Unfiltered space-time diagrams of the three types of particle α, β, and γ described in the text. (b) Filtered diagrams of the same data, produced by T^0_{54}. Domain symbols are white cells. All defects are shown in black, with the defect symbol inscribed in white. The temporal phases of the particles, chosen by convention, are printed alongside the filtered strings.

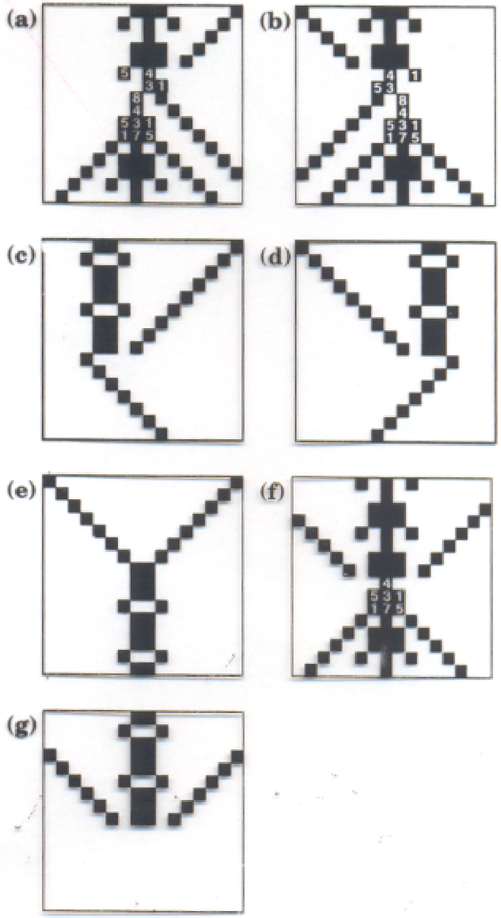


Figure 9. Filtered space-time diagrams of the fundamental interactions among ECA 54's fundamental particles, as listed in table 1. (a)—(e) are two-particle collisions; (f) and (g) are three-particle collisions. Filtering was done with the first version of particle filter T^1_{54} described in the text. The domain is shown as white, the particles $\{\alpha, \beta, \gamma^+, \gamma^-\}$ are shown in black. Defects not corresponding to any of the particles are shown in black and have the corresponding T^0_{54} output symbols inscribed in white.

(a)	$\alpha + \gamma^- \rightarrow \gamma^- + \alpha + 2\gamma^+$
(b)	$\gamma^+ + \alpha \rightarrow 2\gamma^- + \alpha + \gamma^+$
(c)	$\beta + \gamma^- \rightarrow \gamma^+$
(d)	$\gamma^+ + \beta \rightarrow \gamma^-$
(e)	$\gamma^+ + \gamma^- \rightarrow \beta$
(f)	$\gamma^+ + \alpha + \gamma^- \rightarrow \gamma^- + \alpha + \gamma^+$
(g)	$\gamma^+ + \beta + \gamma^- \rightarrow \emptyset$

Table 1. Fundamental interactions among ECA 54's particles. Interactions (a) and (b) induce a spatio-temporal shift in the incident particles, as discussed in the text. Note that the spatial arrangement of input and output particles is respected by the interaction notation. $\emptyset$ *denotes no particles.*

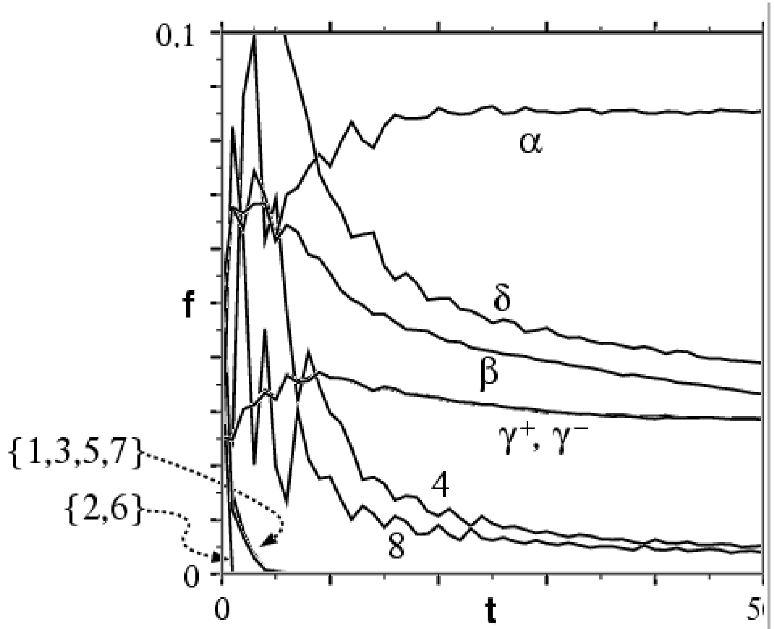


Figure 11. Fraction of the CA lattice devoted to the fundamental particles ($\alpha, \beta, \gamma^+, \gamma^-$)*, to* α-γ *interactions* (δ)*, and to unrecognized defects* $\{1, \ldots, 8\}$ *versus time.*

conclusions

Detection of mesoscale entities
WITH A DYNAMICS OF THEIR OWN

Description of system in variable set of
interacting higher level entities (individual based models)
("beyond dynamical systems")

Description in terms of populations of these entities