How is life (and its origin) organized?

Pietro Speroni di Fenizio, Naoki Matsumaru, Florian Centler, Christoph Kaleta and Peter Dittrich

Bio Systems Analysis Group

FSU Jena

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Bio Systems Analysis Group

Use computational approaches to explain complex *dynamical* phenomena found in living systems

ESIGNET – Evolving Cell Signalling Networks *in silico*
(T. Hinze, T. Lenser, EU)

Systems Analysis of the Cell Cycle
(B. Ibrahim, DAAD)

Chemical Network Theory and Simulation
(P. Speroni d.F., F. Cenler, BMBF)

Organic Computing: Chemical Prgramming
(N. Matsumaru, DFG)

Semantics of Biological Models
(Ch. Knüpfer, RLS)

Autonomous Experimentation
(N. Matsumaru, BMBF)

How is life (and its origin) organized?

2. What is the bio-chemical organization of an organism?

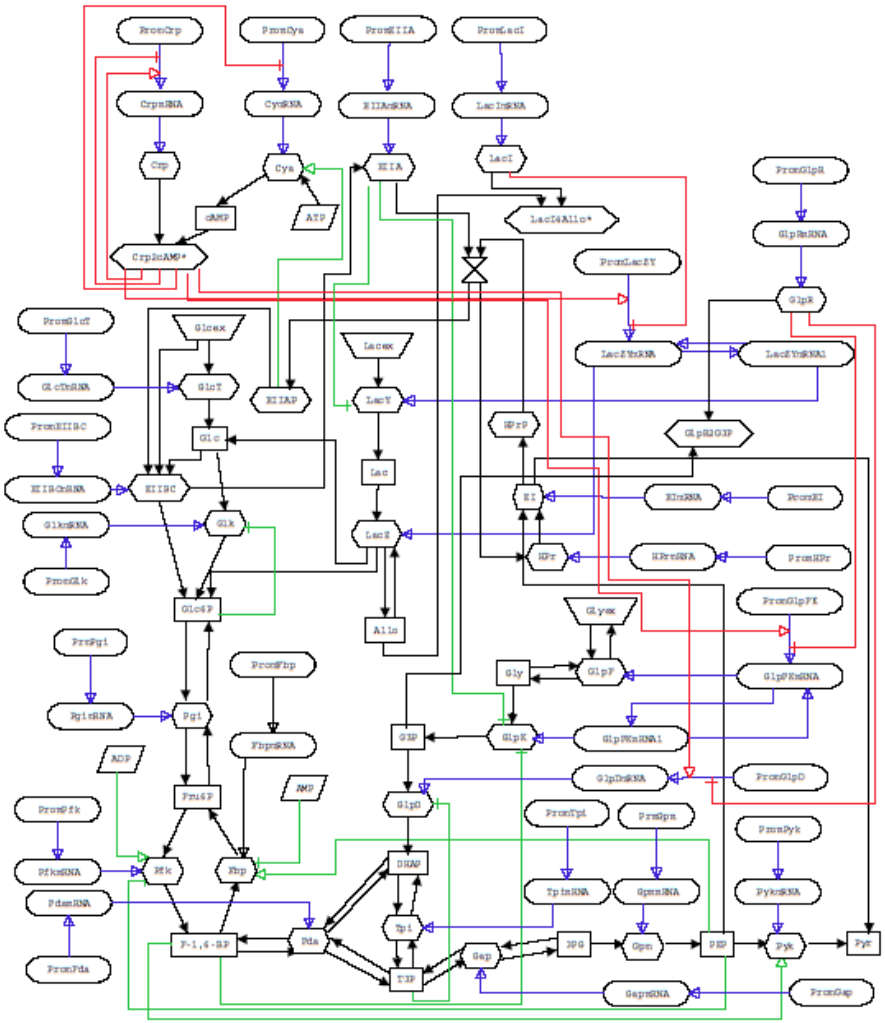
4. How did the bio-chemical organization of the pre-prebiotic soup evolved?

Q1

How does the lattice of organizations of an organism looks like?

lattice of organizations = organizational structure

What is an answer ?



[Source: Puchalka/Kierzek (2004) *Biophys. J.* **86**, 1357]

„Chemical Organization“

There is no reaction producing any other molecules than the member of the set.

Organization :=
a set of molecules that is (algebraically) closed and self-maintaining

Within the set, all molecules consumed by a reaction can be reproduced by a reaction.

[Speroni di Fenizio/Dittrich (2005/7)
inspired by **Fontana**, Buss, Kauffman, Maturana, Varela, Uribe]

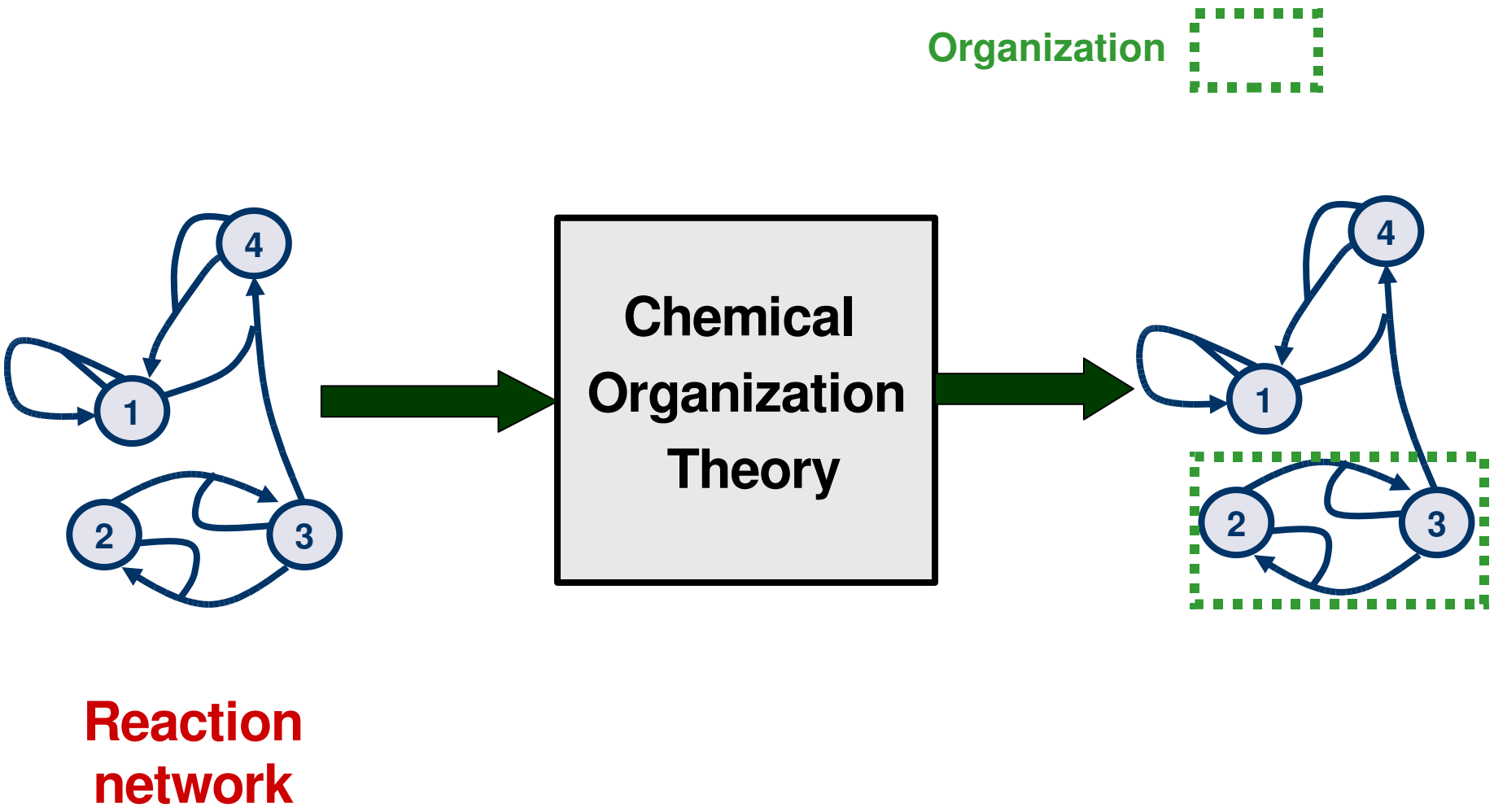
Fixed Point and Organization

Theorem

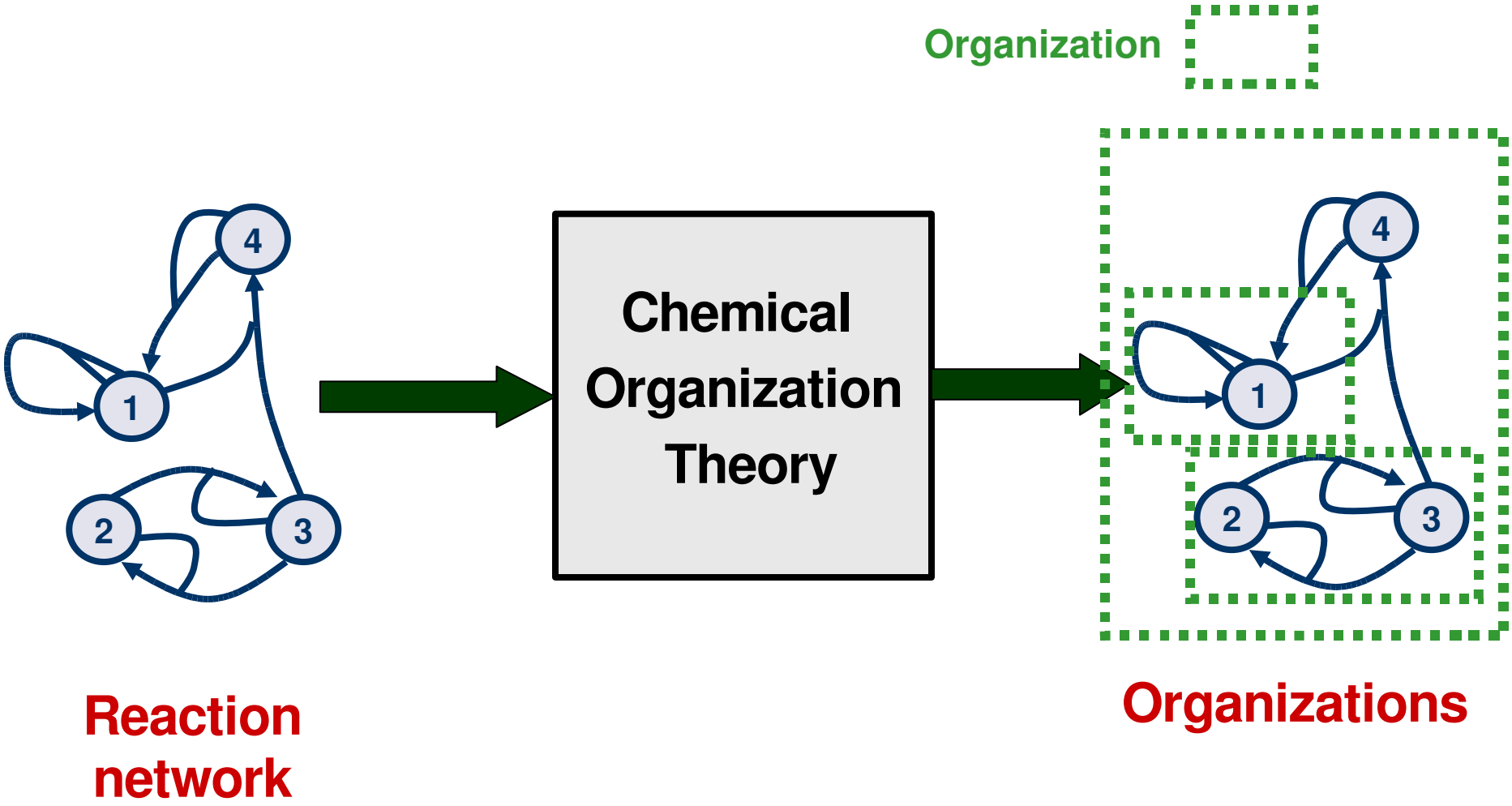
Given a fixed point of the ODE describing the dynamics of a reaction system, then the set of molecules represented by that fixed point is an organization.

[Dittrich/Speroni di Fenizio, (2005,2007)]

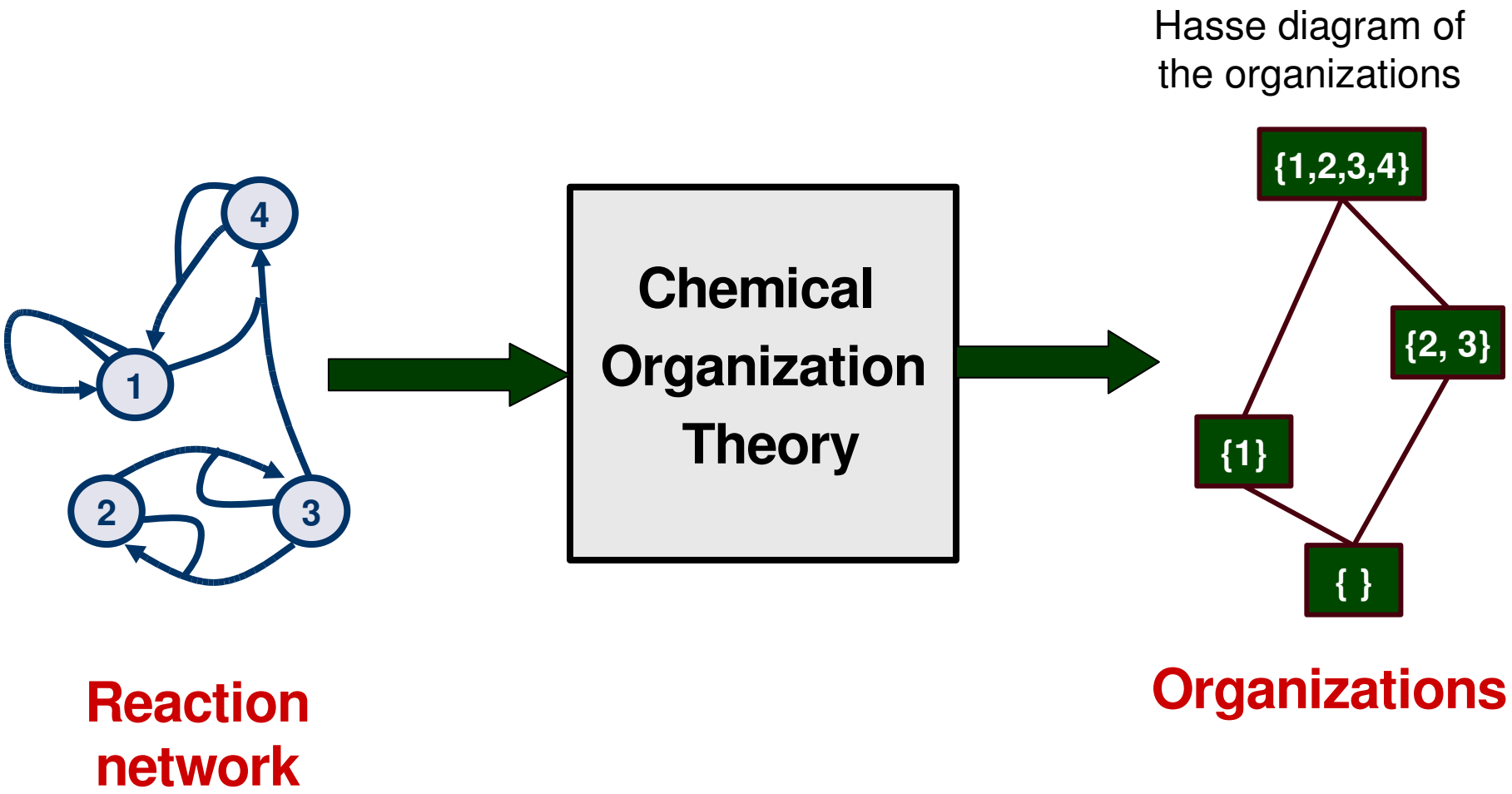
Practical View



All Organizations

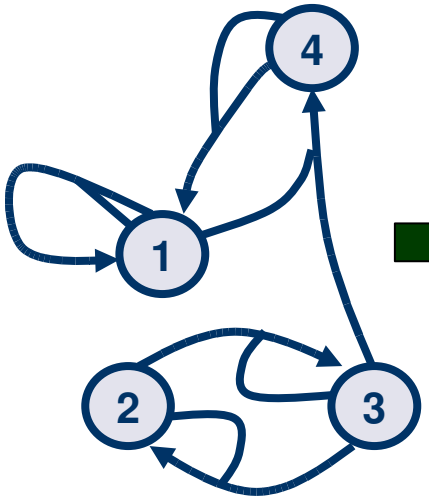


Lattice of Organizations

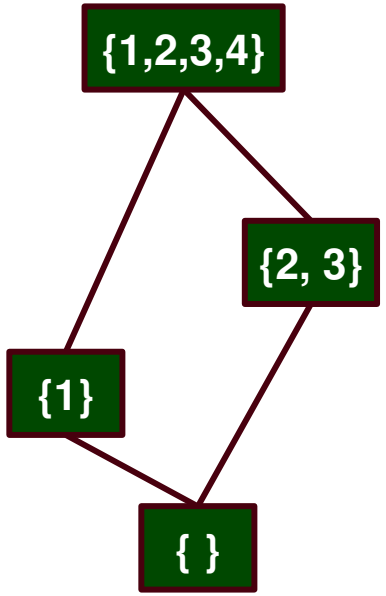


Generate Organization

Hasse diagram of the organizations



Chemical Organization Theory



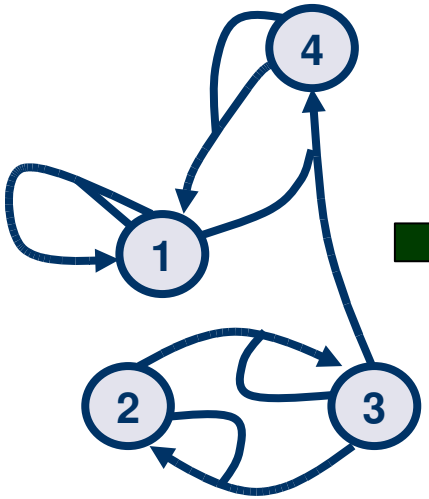
Reaction network

$G_O(\{3, 4\}) = ?$

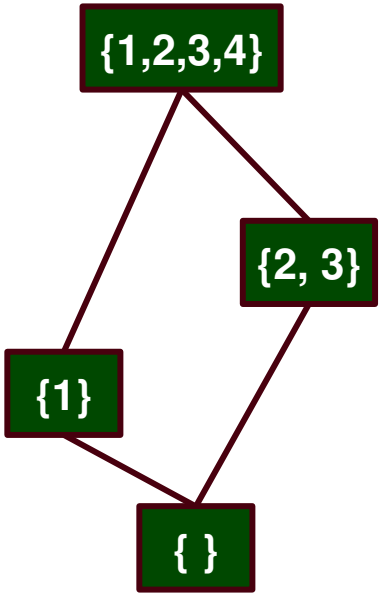
Organizations

Generate Organization

Hasse diagram of the organizations



Chemical Organization Theory

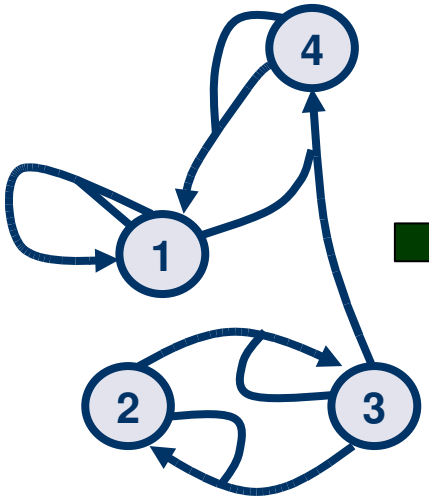


Reaction network

$G_{Org}(\{3, 4\}) = \{1\}$

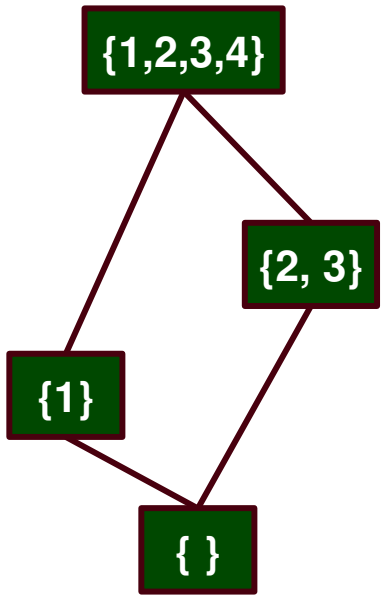
Organizations

Union of Organizations



Chemical Organization Theory

Hasse diagram of the organizations



Reacti **zations**
netwo

$G_{Org}(\{3, 4\}) = \{1\}$

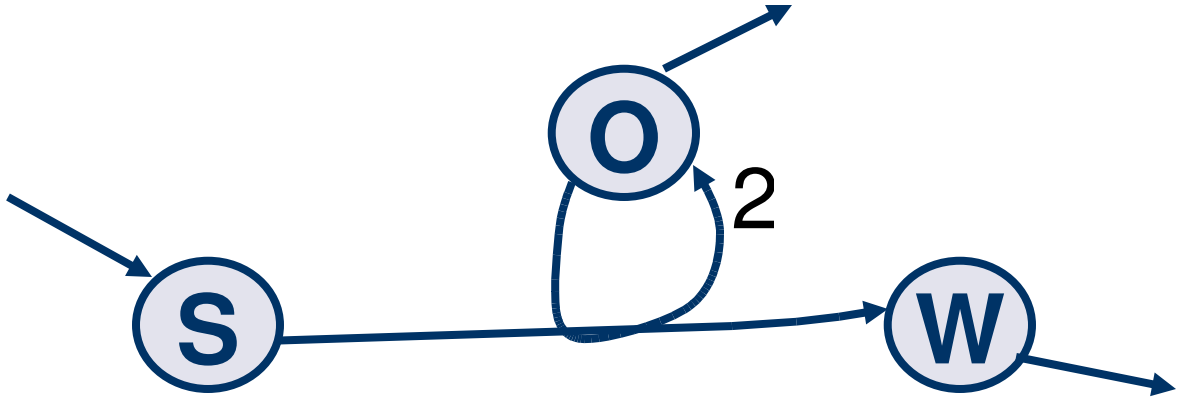
$\{1\} \cup_O \{2, 3\} := G_{Org}(\{1\} \cup \{2,3\})$

Q1

How does the lattice of organizations of an organism looks like?

organizational structure = lattice of organizations

Trivially, all organisms have at least one organization

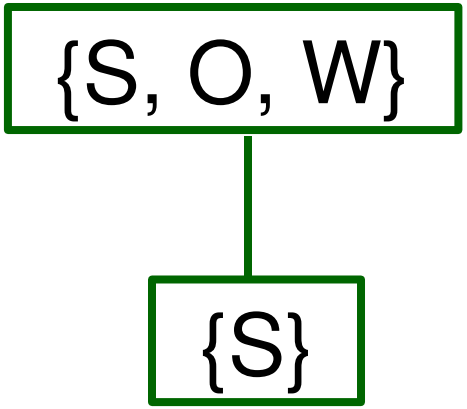


S + O →2O + W

→S

O→

W→



Is there more?

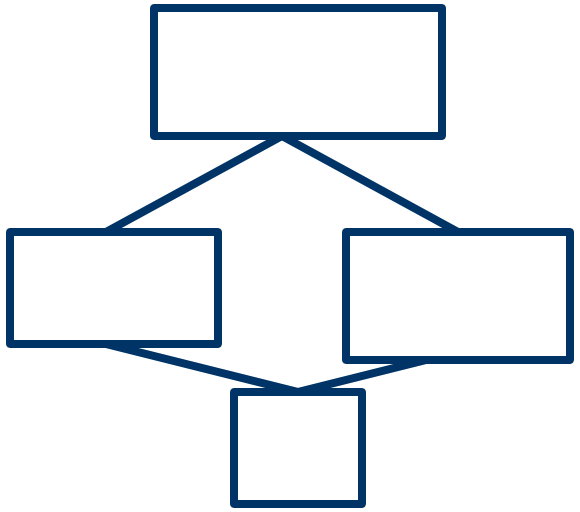
$S + O_1 \rightarrow 2O_1 + W$

$S + O_2 \rightarrow 2O_2 + W$

$\rightarrow S$

$O \rightarrow$

$W \rightarrow$



Is there more?

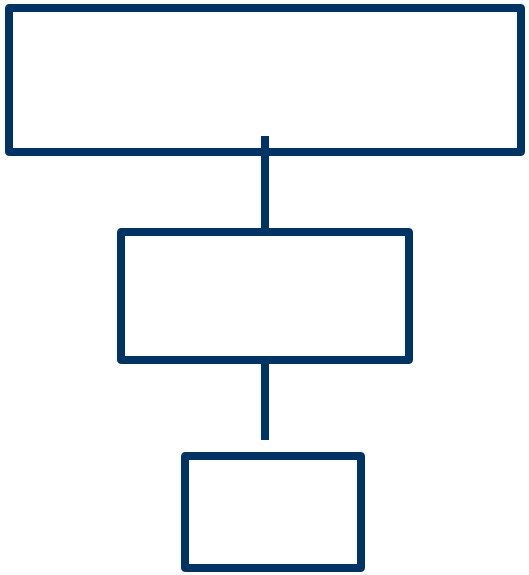
$$S + O_1 \rightarrow 2O_1 + W$$

$$S + O_1 + O_2 \rightarrow 2O_2 + W$$

$$\rightarrow S$$

$$O \rightarrow$$

$$W \rightarrow$$



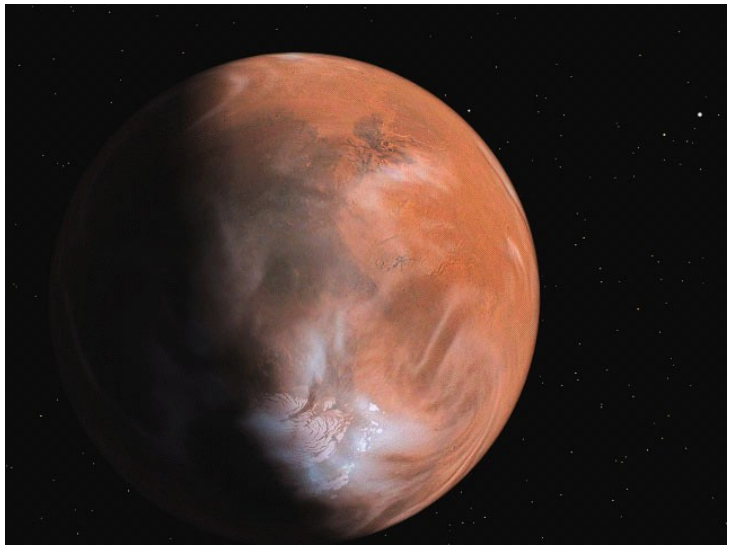
How does the lattice organizations in an organism looks like?

- number?
- hight?
- size distribution?

We looked at a couple of network models of "real" systems

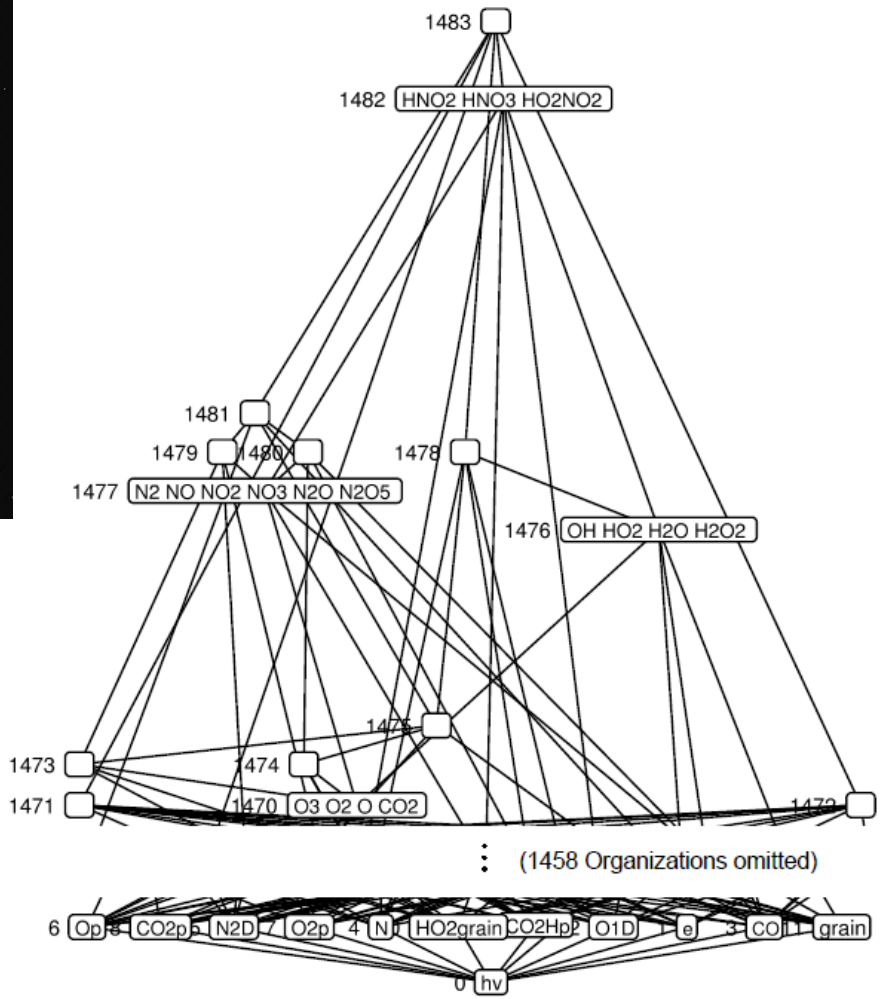
- photochemistries
  (dead, closed but not isolated systems)
- metabolism
- regulated metabolism
- lambda-phage
- HIV - immunesystem

Photochemistry



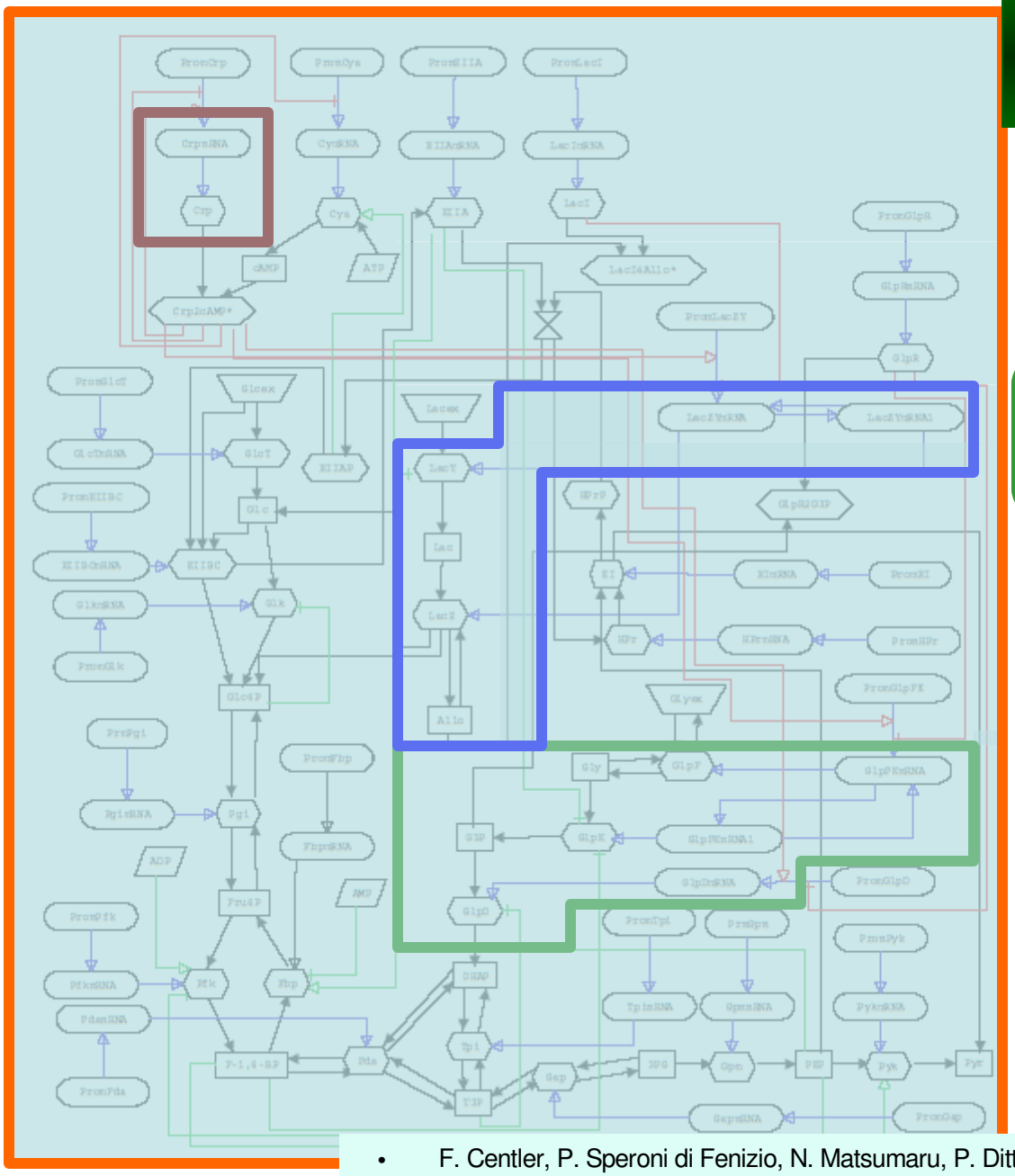
http://www.fpsoftlab.com/images/screenshots/mars-640x480-1.jpg

31 molecular species,
103 reactions



Y. L. Yung and W. B. DeMore (1999)
Photochemistry of Planetary Atmospheres, *Oxford University Press*

E. coli Model (I)



All 92 Species
Glucose + Glycerol + Lactose

78 + 8 = 86 Species
Glucose + Glycerol

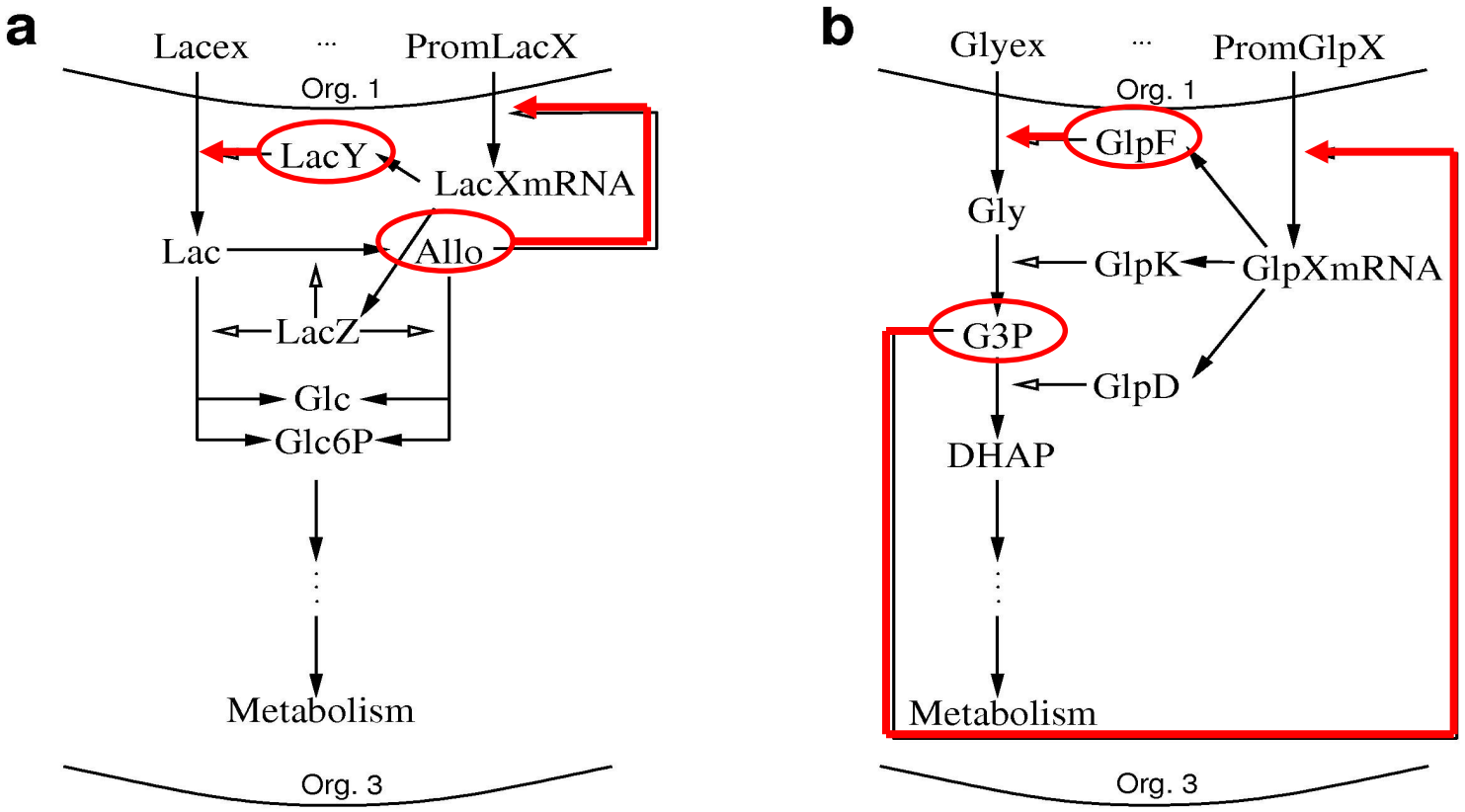
78 + 6 = 84 Species
Glucose + Lactose

76 + 2 = 78 Species
Glucose

76 Species, incl.
28 Input
Glucose

- F. Centler, P. Speroni di Fenizio, N. Matsumaru, P. Dittrich (2007); in: Modeling and Simulation in Science Engineering and Technology, Post-proceedings of ECMTB 2005, Dresden (in print)

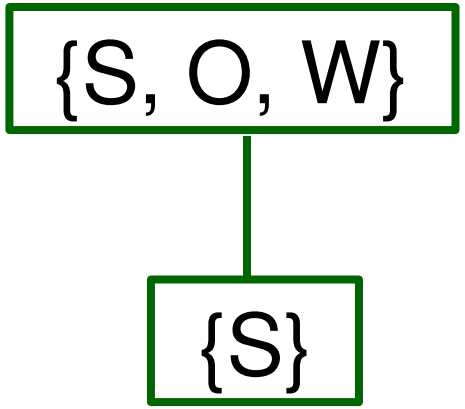
E. coli Model (I)



- F. Centler, P. Speroni di Fenizio, N. Matsumaru, P. Dittrich (2007); in: Modeling and Simulation in Science Engineering and Technology, Post-proceedings of ECMTB 2005, Dresden (in print)

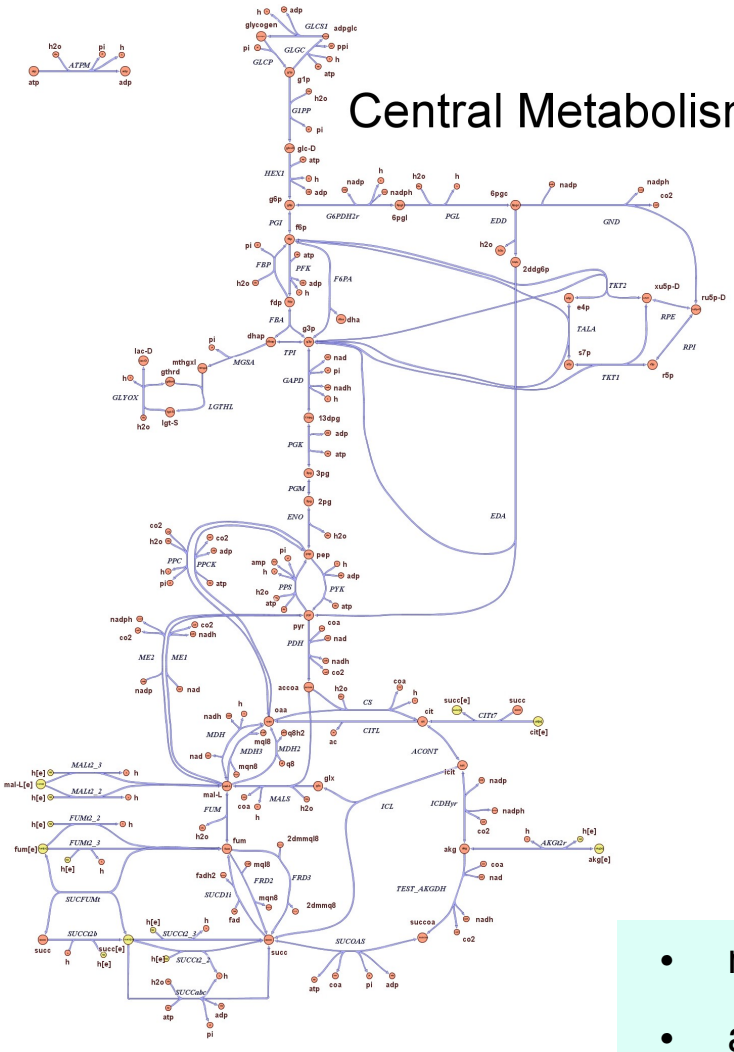
E. coli Model (II) – Regulated Network

- Palsson/Covert
- Organization theory is able to predict growth phenotypes of various mutants quite nicely
- But the organizational structure is simple



- C. Kaleta, F. Centler, P. Speroni di Fenizio, P. Dittrich (2007), submitted

E. coli Model (III)



- network from Palsson et al (?)
- analysis by C. Kaleta 2006

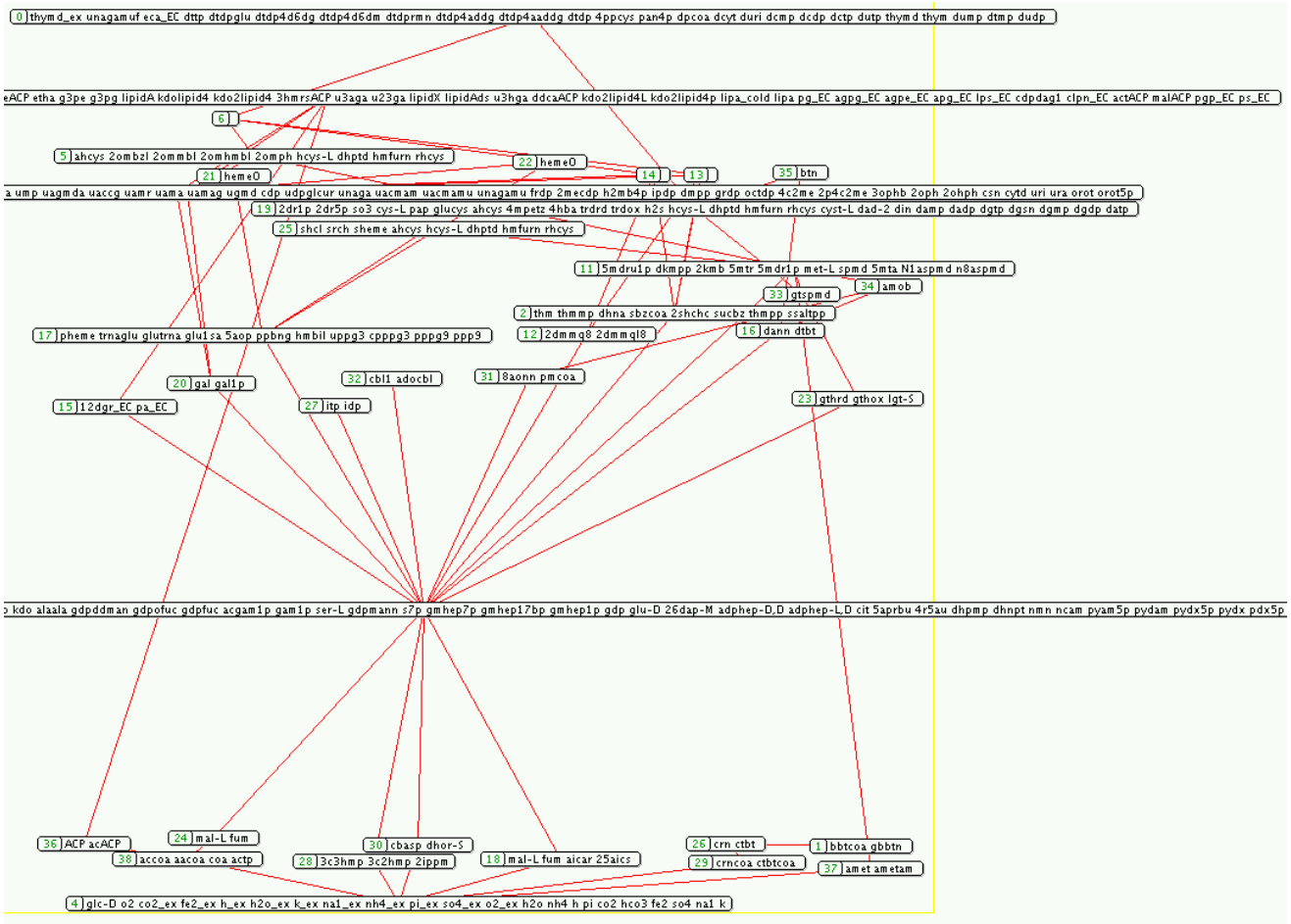
E. coli Model (III)

synthesis of some dNTPs

lipid synthesis
ACP or hmrsACP

pyrimidine nucleotide synthesis
q8 (quinone)

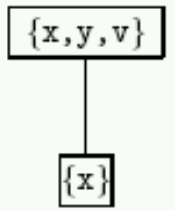
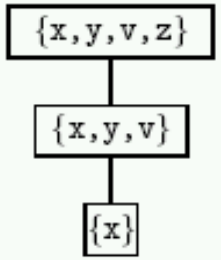
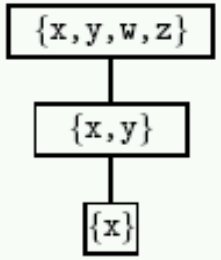
central metabolism+



Minimal growth scenario:
D-Glucose, O_2, Fe_2, NH_4, H^+, Pi, SO_4

- analysis by C. Kaleta, F. Centler, 2006

HIV Models

ODE Model	Reaction Network Model	Organizational Structure
A: (M. A. Nowak, C. R. M. Bangham: *Science 272*, 5258 (1996), 74–79.) $\dot{x} = \lambda - dx - \beta xv$ $\dot{y} = \beta xv - ay$ $\dot{v} = ky - uv$	$\emptyset \to x$ $x \to \emptyset$ $y \to \emptyset$ $v \to \emptyset$ $x + v \to y + v$ $y \to y + v$	
B: (M. A. Nowak, C. R. M. Bangham: *Science 272*, 5258 (1996), 74–79.) $\dot{x} = \lambda - dx - \beta xv$ $\dot{y} = \beta xv - ay - pyz$ $\dot{v} = ky - uv$ $\dot{z} = cyz - bz$	$\emptyset \to x$ $x \to \emptyset$ $y \to \emptyset$ $v \to \emptyset$ $z \to \emptyset$ $x + v \to y + v$ $y + z \to z$ $y + z \to y + 2\,z$ $y \to y + v$	
C: (D. Wodarz, M.A. Nowak: *PNAS 96*, 25 (1999), 14464–14469.) $\dot{x} = \lambda - dx - \beta xy$ $\dot{y} = \beta xy - ay - pyz$ $\dot{w} = cxyw - cqyw - bw$ $\dot{z} = cqyw - hz$	$\emptyset \to x$ $x \to \emptyset$ $y \to \emptyset$ $w \to \emptyset$ $z \to \emptyset$ $x + y \to 2\,y$ $y + z \to z$ $y + w \to y + z$ $x + y + w \to x + y + 2\,w$	

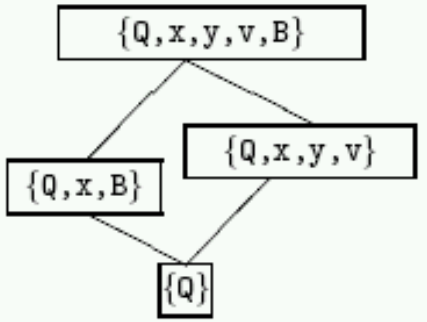
- N. Matsumaru, F. Centler, P. Speroni di Fenizio, P. Dittrich (2006); *it - Information Technology*, **48**(3):1-9,

HIV Models

D: (D. S. Callaway, A. S. Perelson: *Bull. Math. Biol. 64* (2002), 29–64.)

$$
\begin{aligned}
\dot{Q} &= \xi - fQ - \theta(v+B)Q \\
\dot{x} &= s\theta(v+B)Q - dx \\
&\quad -(1-\kappa)\beta xv \\
\dot{y} &= (1-\kappa)\beta xv - ay \\
\dot{v} &= N_T\delta y - uv
\end{aligned}
$$

$$
\begin{aligned}
\emptyset &\rightarrow \mathtt{Q} \\
\mathtt{Q} &\rightarrow \emptyset \\
\mathtt{x} &\rightarrow \emptyset \\
\mathtt{y} &\rightarrow \emptyset \\
\mathtt{v} &\rightarrow \emptyset \\
\mathtt{x} + \mathtt{v} &\rightarrow \mathtt{y} + \mathtt{v} \\
\mathtt{y} &\rightarrow \mathtt{y} + N_T\mathtt{v} \\
\mathtt{Q} + \mathtt{v} &\rightarrow s\mathtt{x} + \mathtt{v} \\
\mathtt{Q} + \mathtt{B} &\rightarrow s\mathtt{x} + \mathtt{B}
\end{aligned}
$$



E: (A.S. Perelson, *et al.*: *Science 271*, 5255 (1996), 1582–1586.)

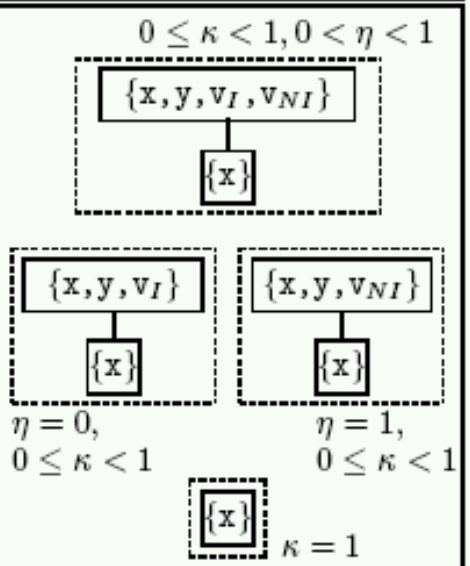
$$
\begin{aligned}
\dot{x} &= \lambda - dx - (1-\kappa)kv_I x \\
\dot{y} &= (1-\kappa)kv_I x - \delta y \\
\dot{v}_I &= (1-\eta)N_T\delta x - cv_I \\
\dot{v}_{NI} &= \eta N_T\delta y - cv_{NI}
\end{aligned}
$$

$P = 1 - \eta$

$$
\begin{aligned}
\emptyset &\rightarrow \mathtt{x} \\
\mathtt{x} &\rightarrow \emptyset \\
\mathtt{v}_I &\rightarrow \emptyset \\
\mathtt{v}_{NI} &\rightarrow \emptyset \\
\mathtt{x} + \mathtt{v}_I &\rightarrow \mathtt{y} + \mathtt{v}_I \\
\mathtt{y} &\rightarrow \mathtt{y} + \mathtt{v}_I
\end{aligned}
$$

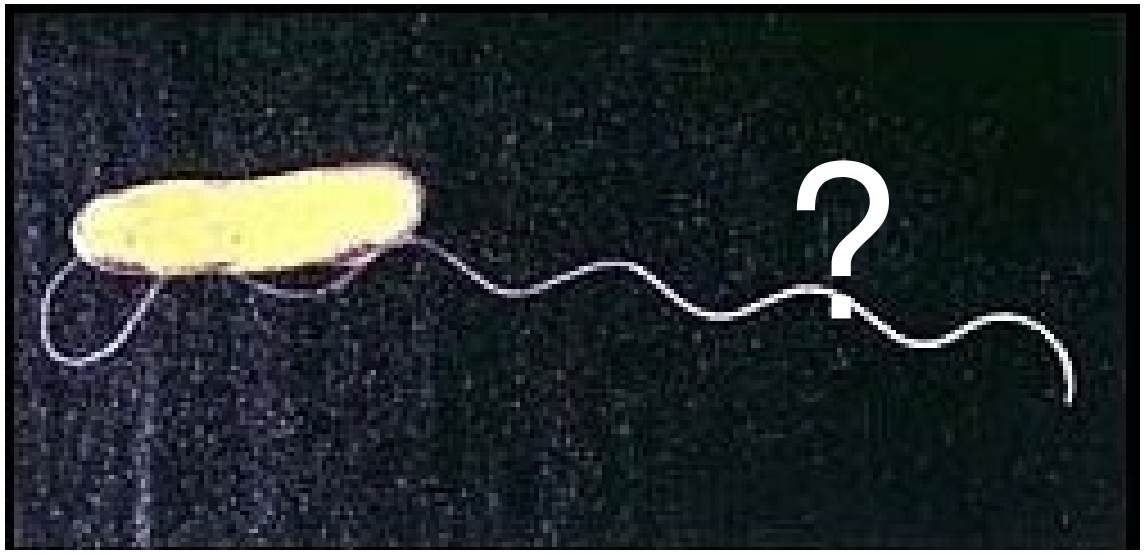
$P = \eta$

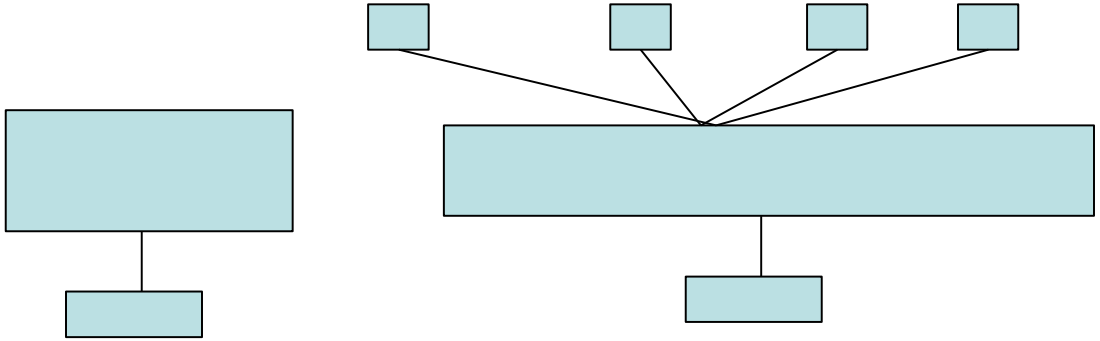
$$
\begin{aligned}
\emptyset &\rightarrow \mathtt{x} \\
\mathtt{x} &\rightarrow \emptyset \\
\mathtt{v}_I &\rightarrow \emptyset \\
\mathtt{v}_{NI} &\rightarrow \emptyset \\
\mathtt{x} + \mathtt{v}_I &\rightarrow \mathtt{y} + \mathtt{v}_I \\
\mathtt{y} &\rightarrow \mathtt{y} + \mathtt{v}_{NI}
\end{aligned}
$$

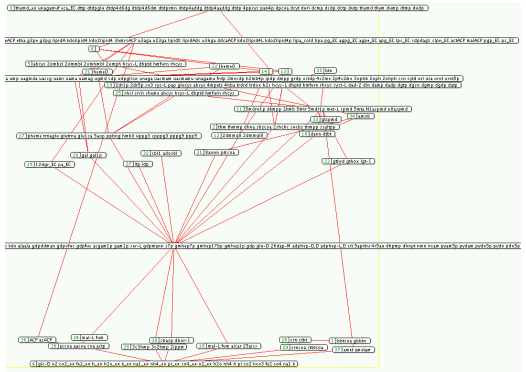


- N. Matsumaru, F. Centler, P. Speroni di Fenizio, P. Dittrich (2006); *it - Information Technology*, **48**(3):1-9

How does the lattice of organizations of an organism looks like?





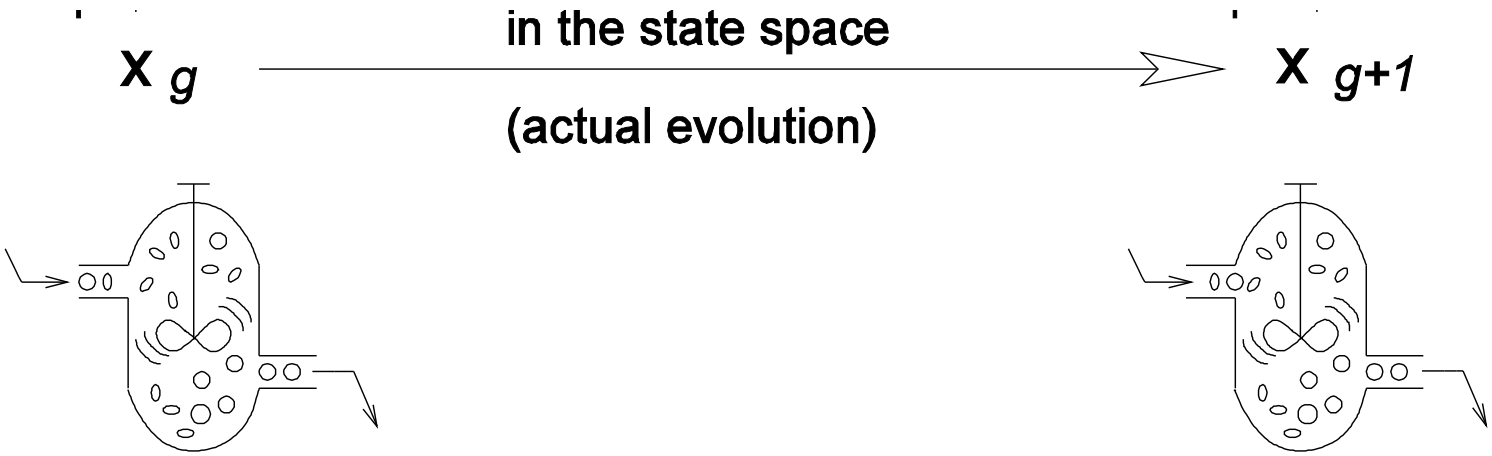


Q2

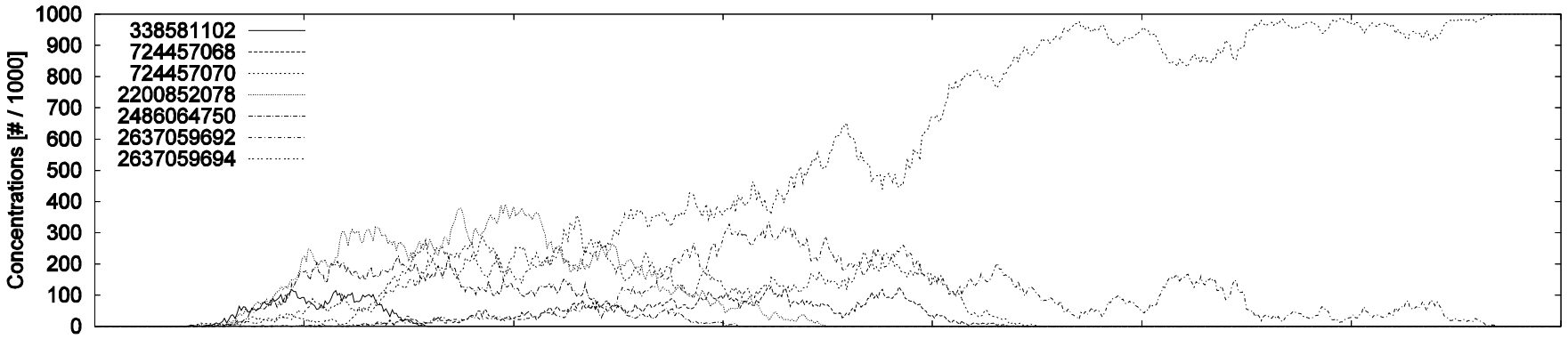
How did the bio-chemical organization of the pre-prebiotic soup evolved?

What is the characteristics of the organizational evolution?
upward? downward? ...

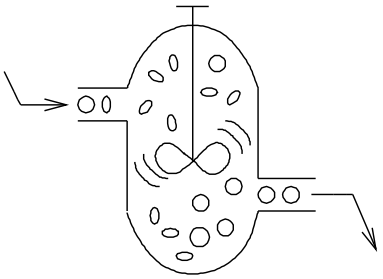
A View of Chemical Evolution

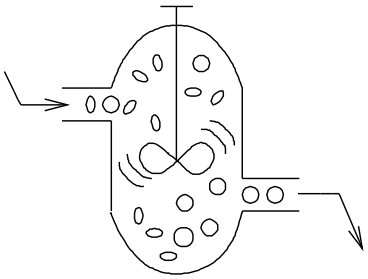


Actual Evolution

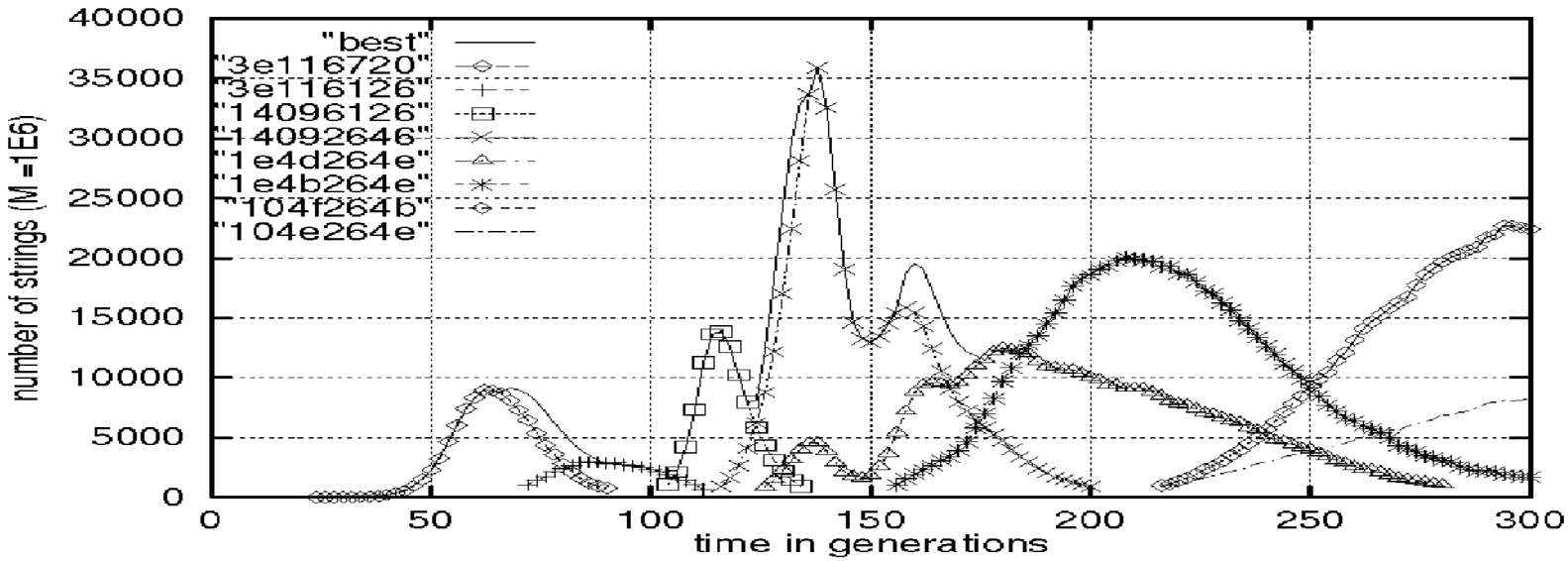


x_g —— in the state space (actual evolution) ——▷ x_{g+1}

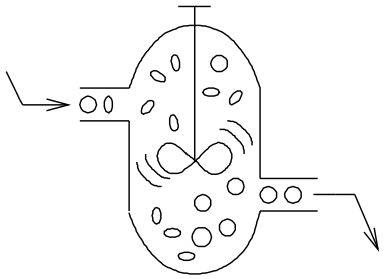


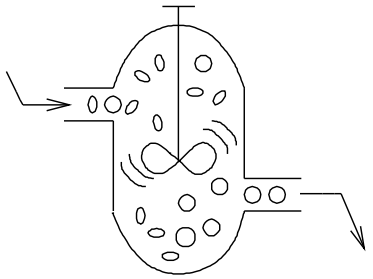


Actual Evolution



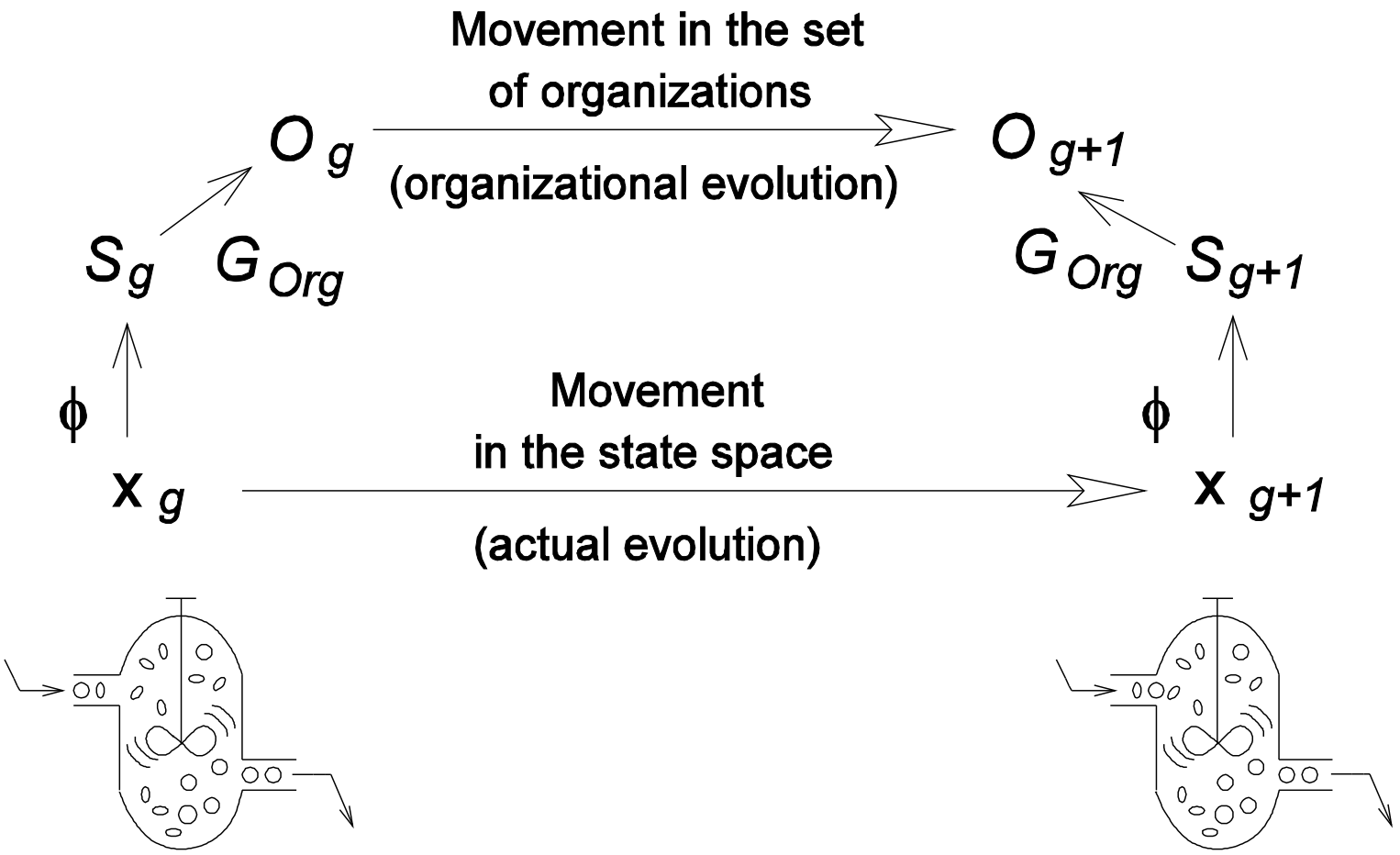
x_g — in the state space (actual evolution) → x_{g+1}





Actual Evolution
vs.
Organizational Evolution

Organizational Evolution

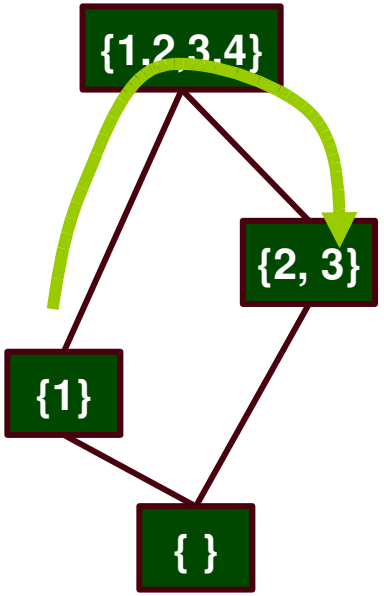


Organizational Evolution

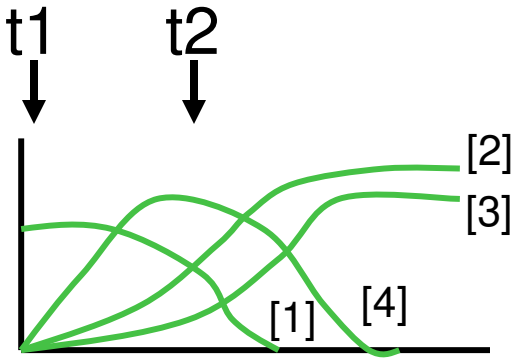
1. Upwards [t1—t2]

$$O_{t1} \subset O_{t2}$$

Hasse diagram of organizations



Organizations



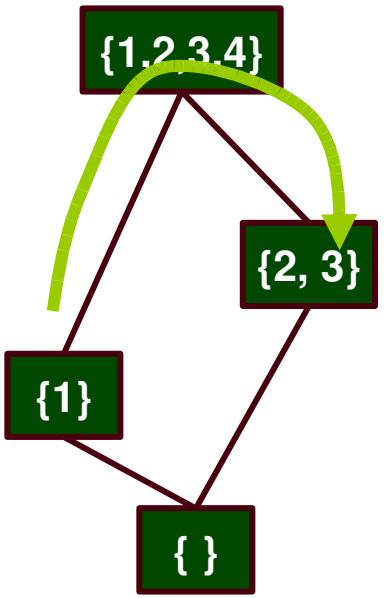
Dynamics

Organizational Evolution

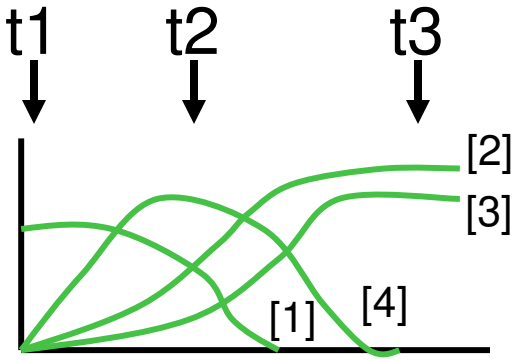
1. Upwards [t1—t2] $O_{t1} \subset O_{t2}$

3. Downwards [t2—t3] $O_{t2} \supset O_{t3}$

Hasse diagram of organizations



Organizations

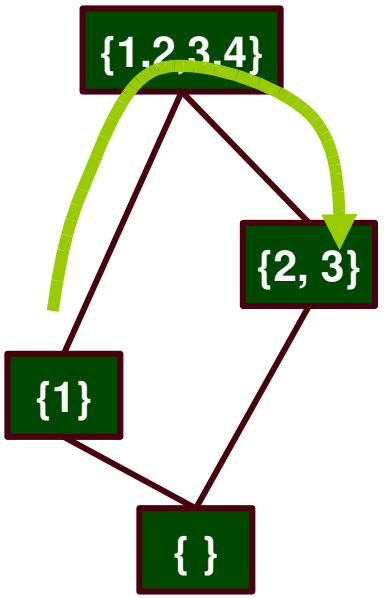


Dynamics

Organizational Evolution

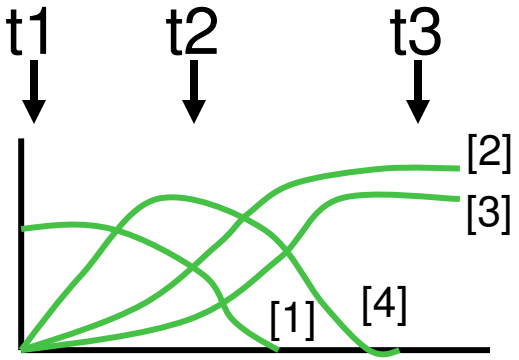
1. Upwards [t1—t2] $O_{t1} \subset O_{t2}$
3. Downwards [t2—t3] $O_{t2} \supset O_{t3}$
5. Sidewards [t1—t3] $otherwise$

Hasse diagram of organizations



Organizations

A set of existing species and an organization are not equivalent. *e.g.*, {2,3,4}



Dynamics

Theoretical vs. Practical

- Theoretically:
  - Every possible species is known.
  - Entire reaction network is given.

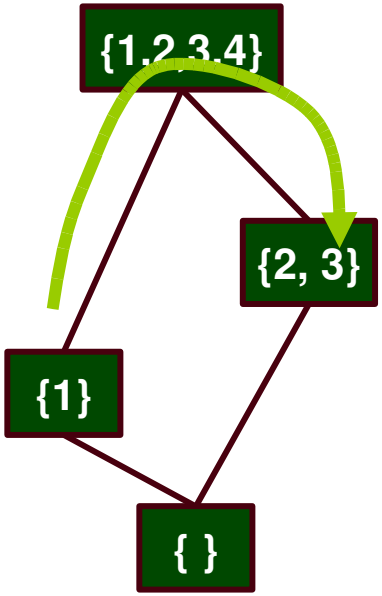
  →Every possible organization can be calculated.

  →It is possible to define the dynamics on the ODE
- Practically:
  - **NOT** every possible species is known.
  - the entire network is **NOT** given.

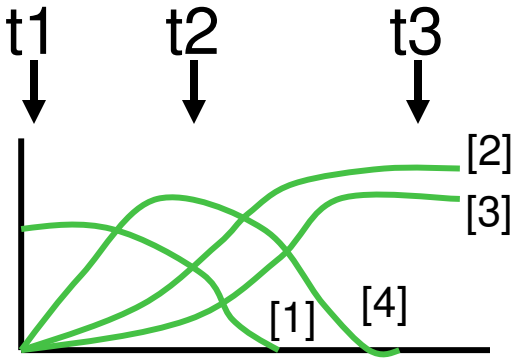
  →**NOT** evey possible organization can be calculated.

Perspective Change

Hasse diagram of the organizations

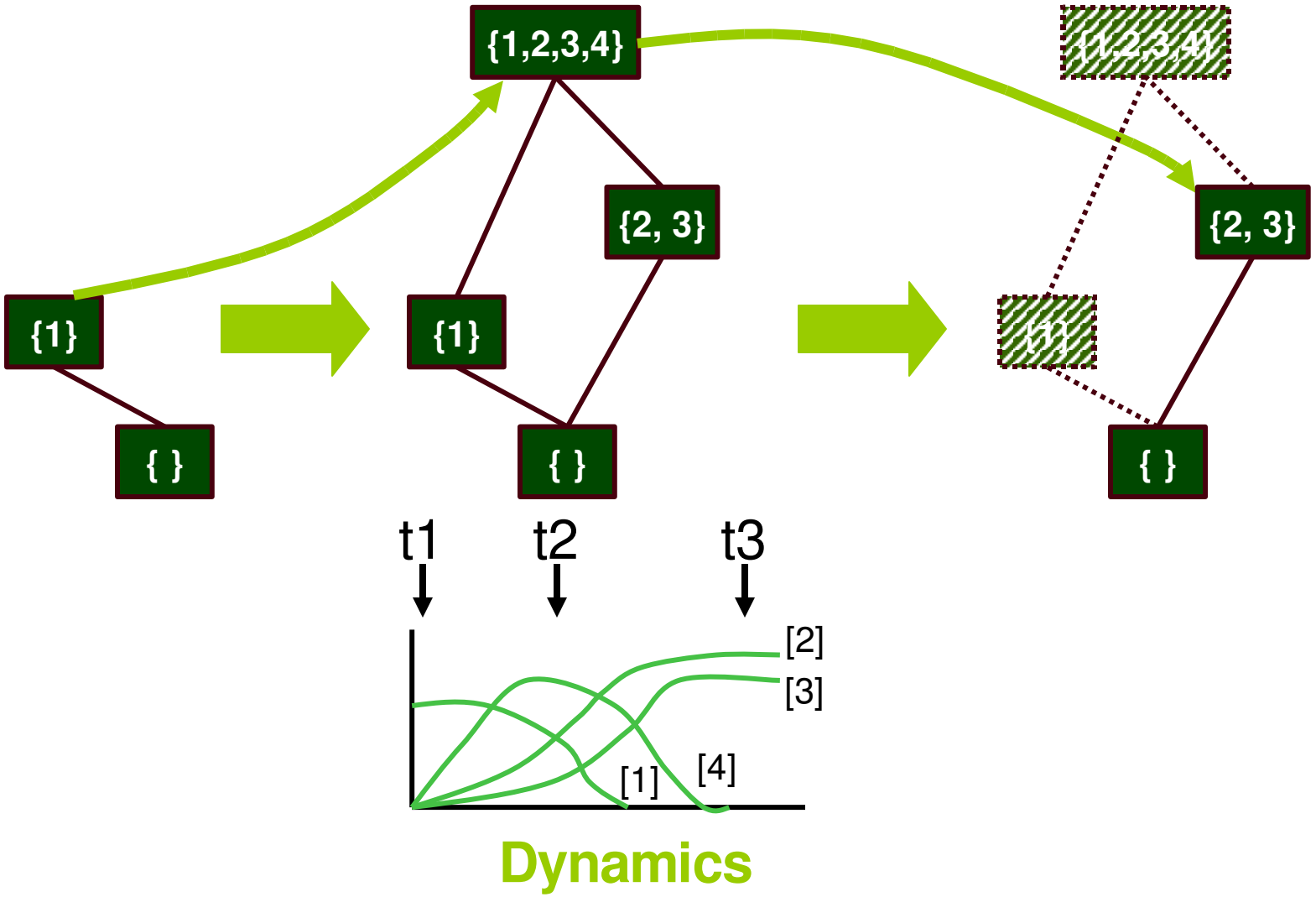


Organizations

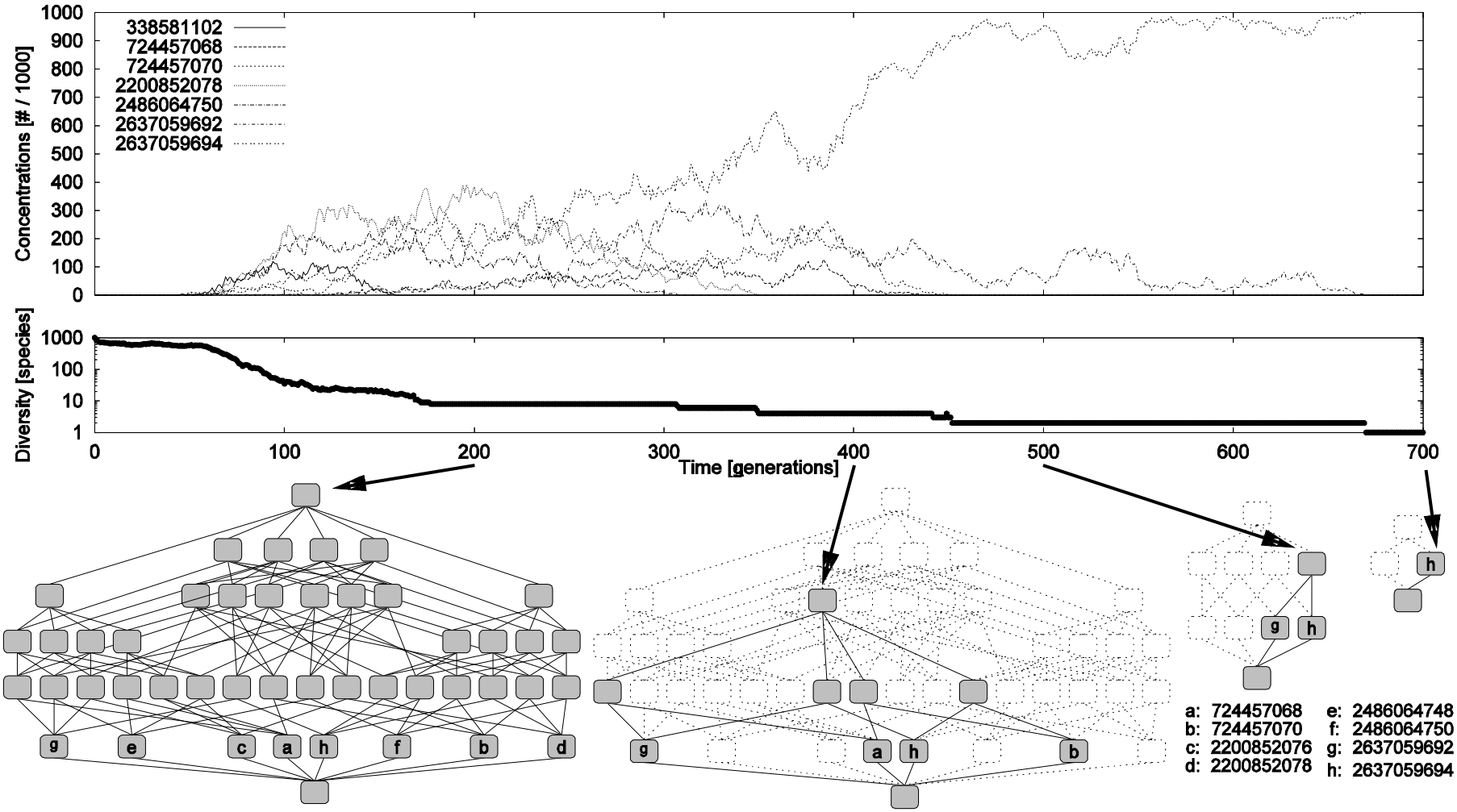


Dynamics

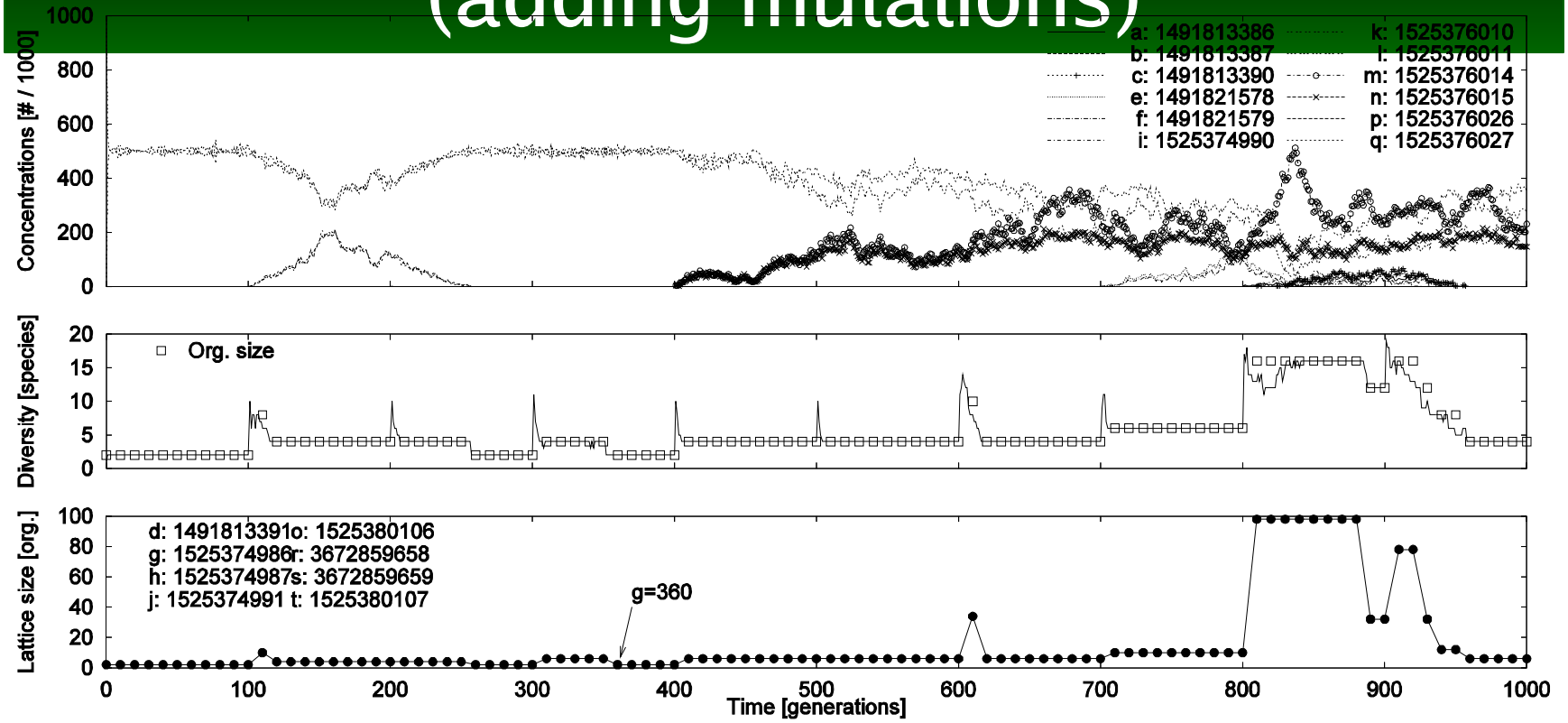
Perspective Change

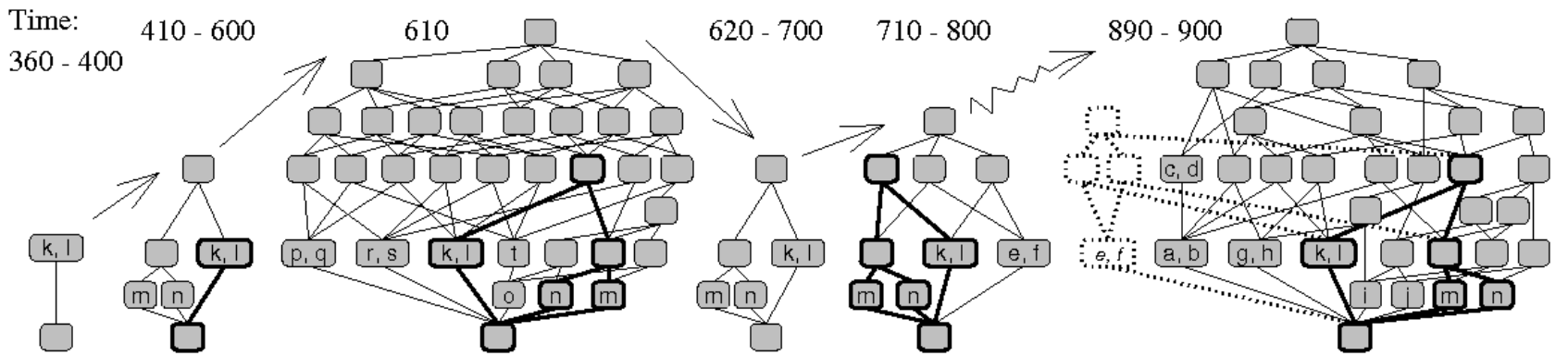


Downward movement



Upward Movements (adding mutations)





Q2

How did the bio-chemical organization of the pre-prebiotic soup evolved?

What is the characteristics of the organizational evolution?
upward? downward? ...

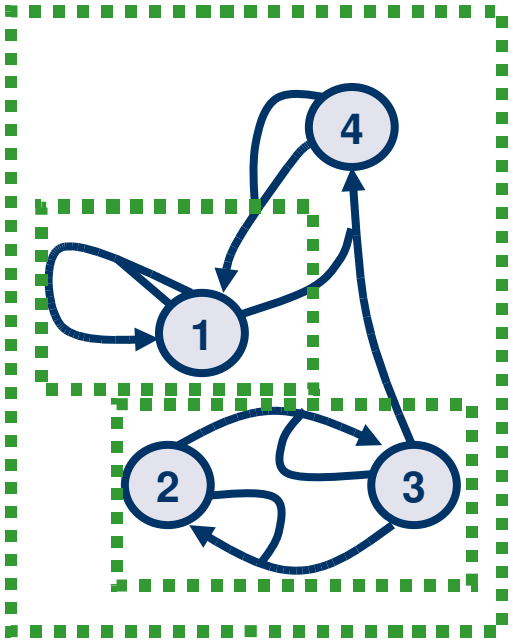
Q2 - Notes

- There are two levels of chemical evolution.
  - Actual evolution
    (the actual vessel)
  - Organizational evolution
    (upward, downward, sideward movements)
- These levels are different.
- If the organizations are complex, a downward movement (organizational level) can lead to a state with a higher diversity (actual evolution).

beauty of mathematics

vs.

unaccesibilty of the real world



vs.

Http://www.mbl.edu/Astrobiology/Riley/image/E.coli.gif

crule abstraction of mathematics

vs.

beauty of the real world

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