NORCIA
LUGLIO 2005

AUTOPOIESIS AND THE DEFINITION OF THE LIVING

(AN OVERVIEW OF THE ORIGINAL BIOLOGICAL AUTOPOIESIS, AND ITS RELATIONSHIP
WITH COGNITION)

PIER LUIGI LUISI

What is life?

THE MOST COMMON NOTION OF LIFE:

LIFE AT THE LEVEL OF POPULATION GROWTH AS A GENETIC FLUX OF INFORMATION FROM GENERATION TO GENERATION

WHICH IMPLIES THE HISTORICAL DIMENSION OF EVOLUTION

THE THREAD WHICH LINKS ALL LIVING BEING TO ONE ANOTHER FROM THE VERY BEGINNING OF LIFE

BUT ALSO:
LIFE AT THE INDIVIDUAL LEVEL,
LIFE HERE AND NOW
A DEFINITION WITHOUT THE CONSTRAINS OF GENETICS

Valid more in general
When you do not know or cannot establish the genetic heritage
For synthetic systems
For unknown (e.g. exobiology) systems...

a surprisingly acute definition given by F. Engels
(yes, the Engels of Karl Marx memory) written in 1894 (!):

Life is the existence form of proteic structures, and this existence form consists essentially in the constant self-renewal of the chemical components of these structures.

This is indeed surprising, given the early time and the fact that Friedrich Engels certainly was not a great biologist, and acted in a time where nobody had a clear notion of what proteins really were.

M. Perret, who in the early fifties wrote a definition that was again taken by D. Bernal in **1965:**

Life is a potentially self–perpetuating system of linked organic reactions, catalyzed stepwise and almost isothermally by complex and specific organic catalysts
which are themselves produced by the system.

Alexander I. Oparin gave a description of life based on six properties:

(1) capability of the exchange of materials with the surrounding medium;
(2) capability of growth;
(3) capability of population growth (multiplication);
(4) capability of self-reproduction;
(5) capability of movement;
(6) capability of being excited.

He also added some additional properties, such as the existence of a **membrane** (a cardinal principle for him); and the interdependency with the **milieu**

An important milestone in this regard is the so called "NASA definition of life". This was originally simply an operational perspective used by the Exobiology Program within the National Aeronautics and Space Agency - a general working definition. However the community of people working in the origin of life uses it often as a definition of life. This working definition - used earlier by Horowitz and Miller (1962) - goes as follows (Joyce, 1994):

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

the adherents to the RNA-world would be satisfied by
a definition of minimal life summarized in the following terms:

life appears at a population of RNA molecules (a quasi-species) which is able to self-replicate and to evolve in the process.

THE GAME OF THE TWO LISTS

LIST OF THE **LIVING**
The fly
The tree
The mule
The baby
The mushroom
The amoeba

LIST OF THE **NON-LIVING**
The radio
The automobile
The robot
The crystal
The moon
The computer

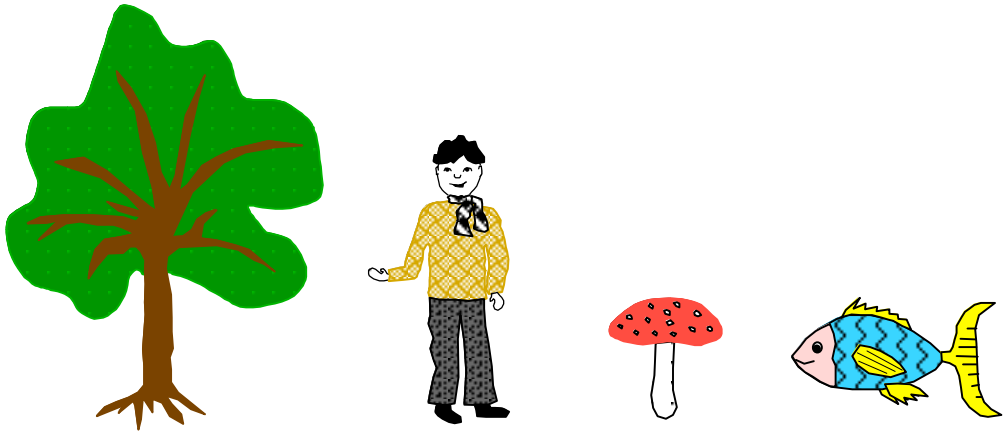
QUESTION: What discriminates the living from the non-living?

IN OTHER WORDS: What is the quality (or qualities) which is present in all members of the "living list" and which is not - and cannot - be present in any of the elements of the "non-living" list?

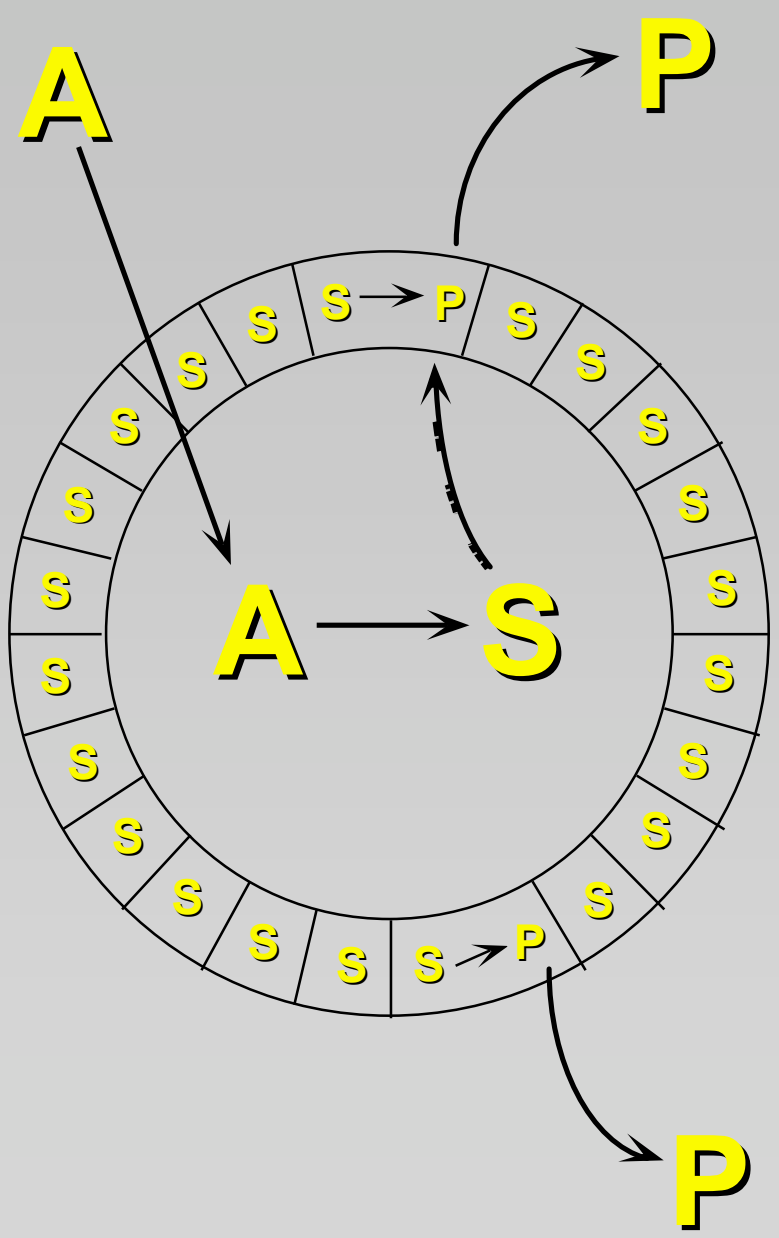
(

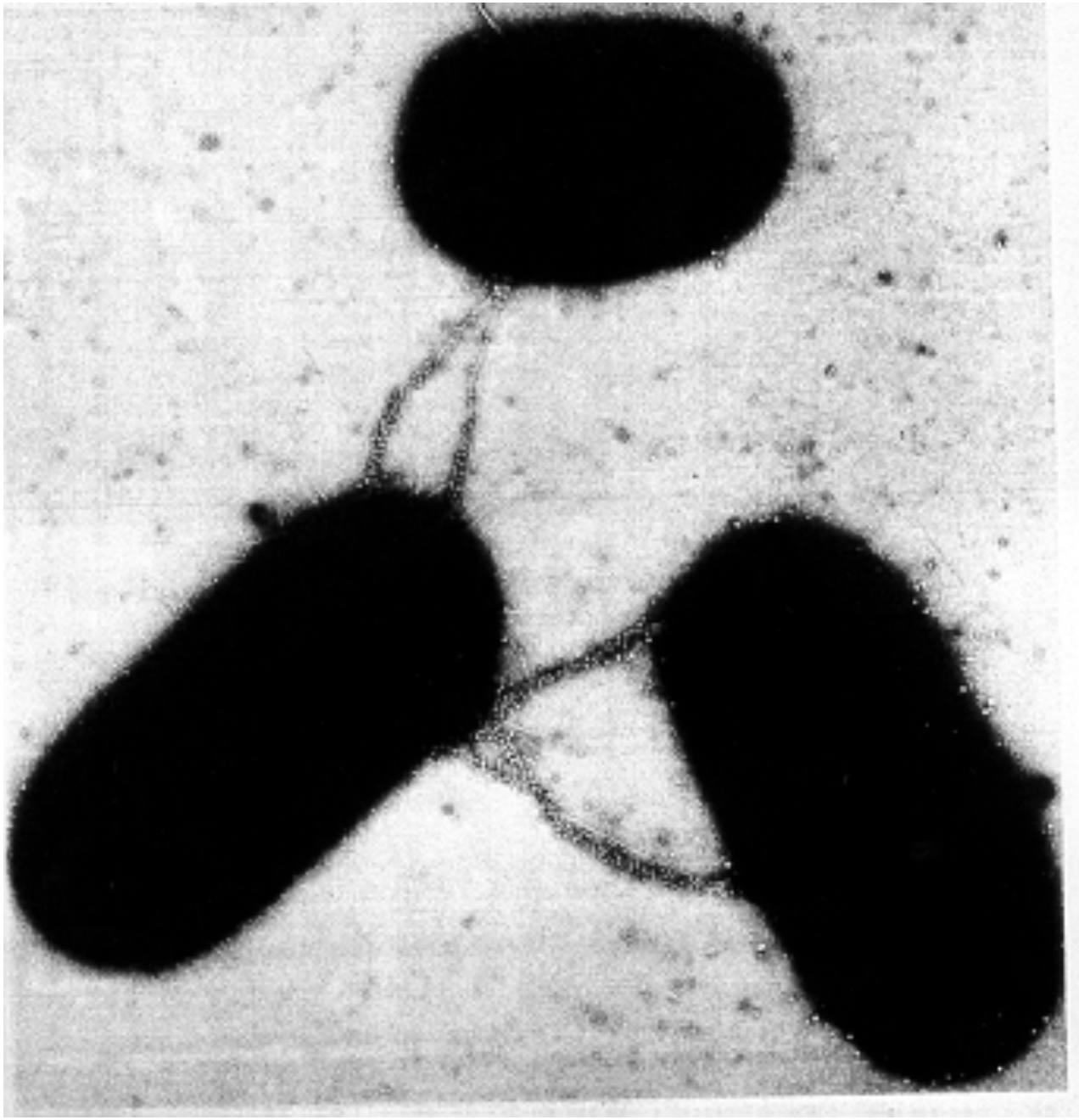
What is life ?
A common sense definition at individual level
(LIFE " HERE AND NOW ")

A living system is a system defined by a physical boundary which allows the assimilation of nutrients / energy from the outside, and which is able to self-maintenance and self-generation owing to the activity of the system from within the boundary.

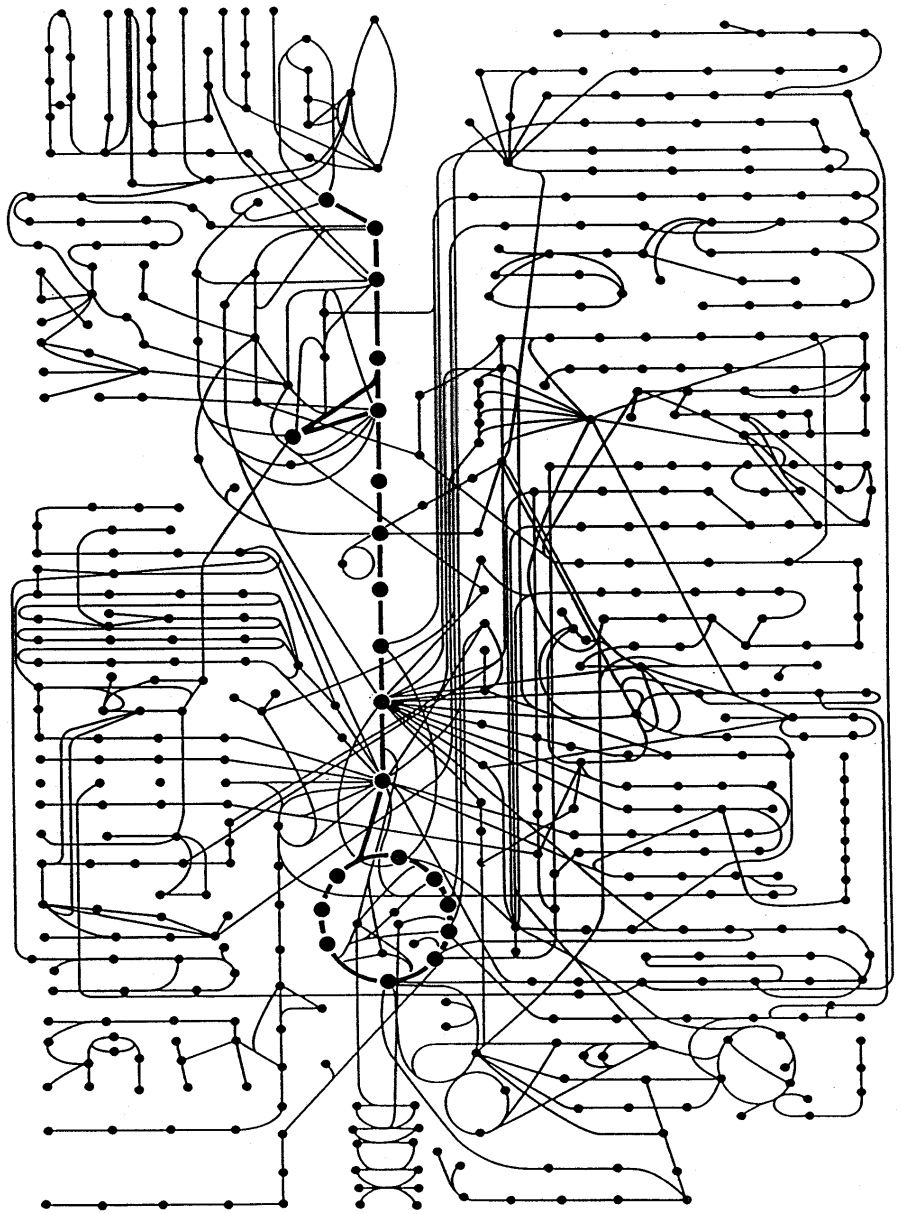


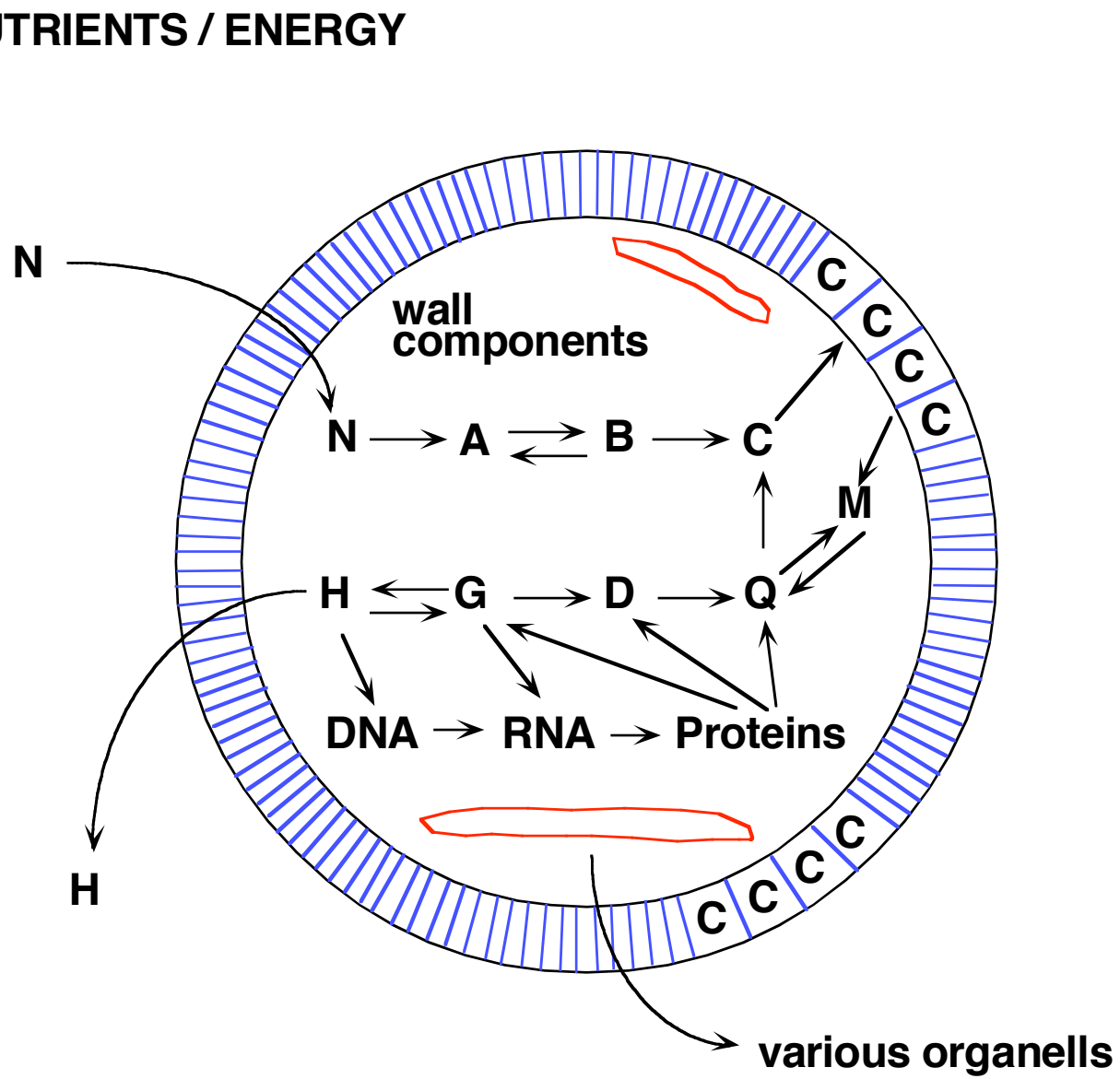
Notice that for this first-level definition no scientific knowledge on cellular structure or molecular biology is needed.
Notice also that self-reproduction or evolution are at this first-level (life here and now) not necessary.


A
P
S → P
A → S
S → P
P



A maze illustrating the chemical reactions that interconvert small molecules in cells.




NUTRIENTS / ENERGY
N
wall
components
N
A
B
C
M
H
G
D
Q
DNA
RNA
Proteins
H
C
C
C
C
C
C
C
various organells

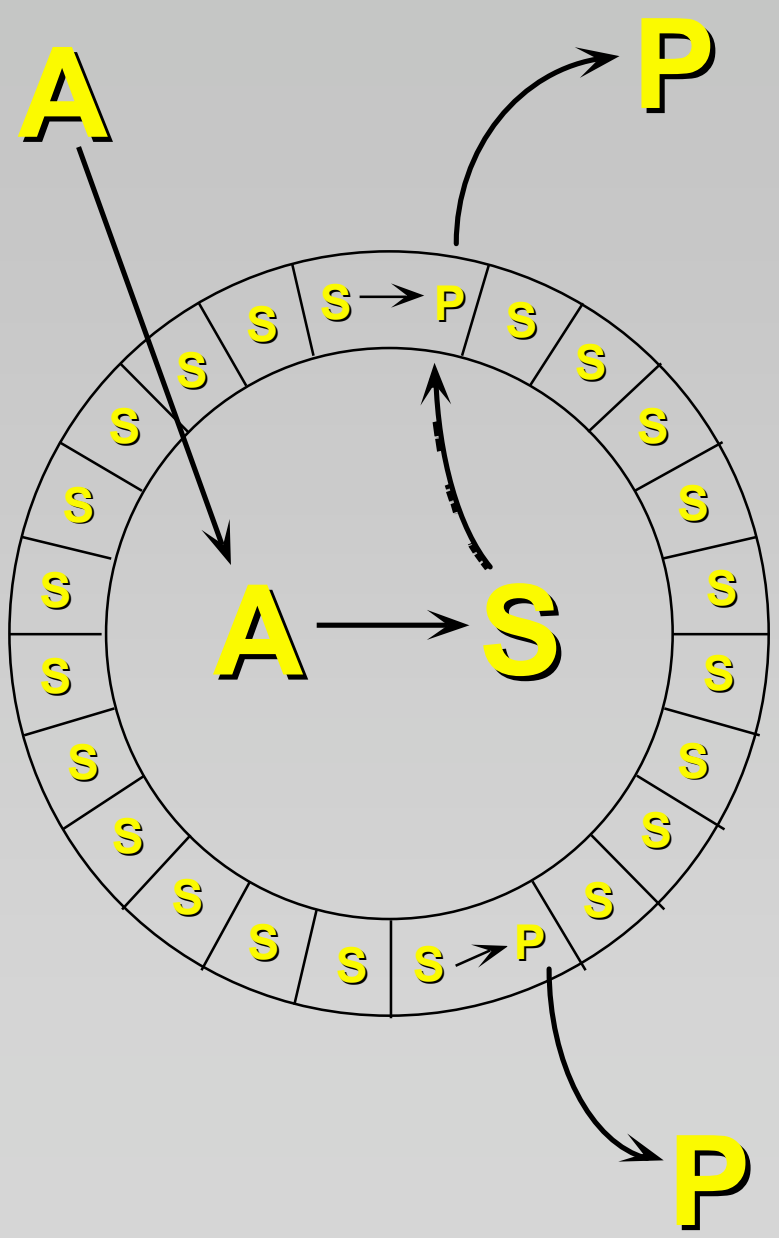
how does a cell work ?

- a semipermeable membrane discriminates “self” from “non-self” & allows energy / nutrients in and byproducts out

- and determines a particular microenvironment which induces a specific reaction network

- by which several components are transformed and continuously replaced

- so that the cell maintains its own identity (“self”) in the face of an on-going series of transformations


A
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S → P
A → S
S → P
P

THE CELL MAIN ACTIVITY IS

TO MAINTAIN ITS OWN IDENTITY

(SELF-MAINTENANCE)

DESPITE THE ENORMOUS NUMBER OF TRANSFORMATIONS

AND THE CELL DOES SO

THANKS TO A PROCESS OF
RE-GENERATION FROM WITHIN

The cellular definition of life:

A system spatially defined by a boundary of ist own making and that is self-sustaining by re-generating all system‘s components from the inside

GENERALIZING ALL THIS

AND GIVING A GENERAL THEORY:

AUTOPOIESIS

AUTO POIESIS
(SELF PRODUCING)

Maturana & Varela, 1970 .....

→ **Varela, Maturana, Uribe**
Biosystems 5 (1974) 187

→ **F. Varela, Principles of biological autonomy**
north Holland 1979

→ **G. Fleischhaker**
Biosystems 22 (1988) 37

→ **P.L. Luisi in "Thinking about Biology"**
W. Stein + F. Varela editors
Addison-Wesley, 1993

autopoietic unity = minimal life

" an autopoietic unity is able to self-generate owing to a reaction network taking place within its own boundary "

(the reaction network makes all components of the unit, including the boundary.)

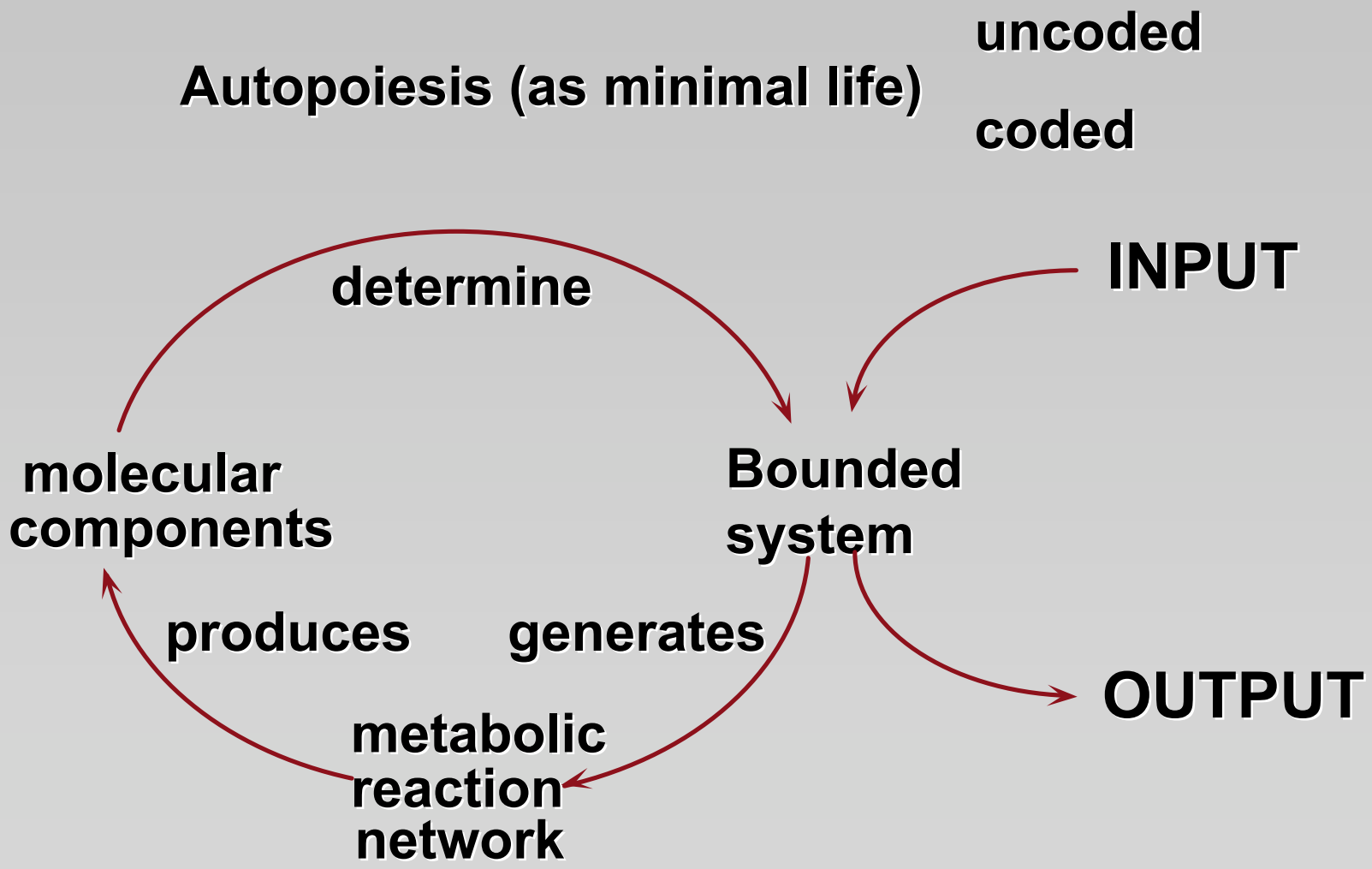
Varela et al., Biosystems, 5 (1974) 187

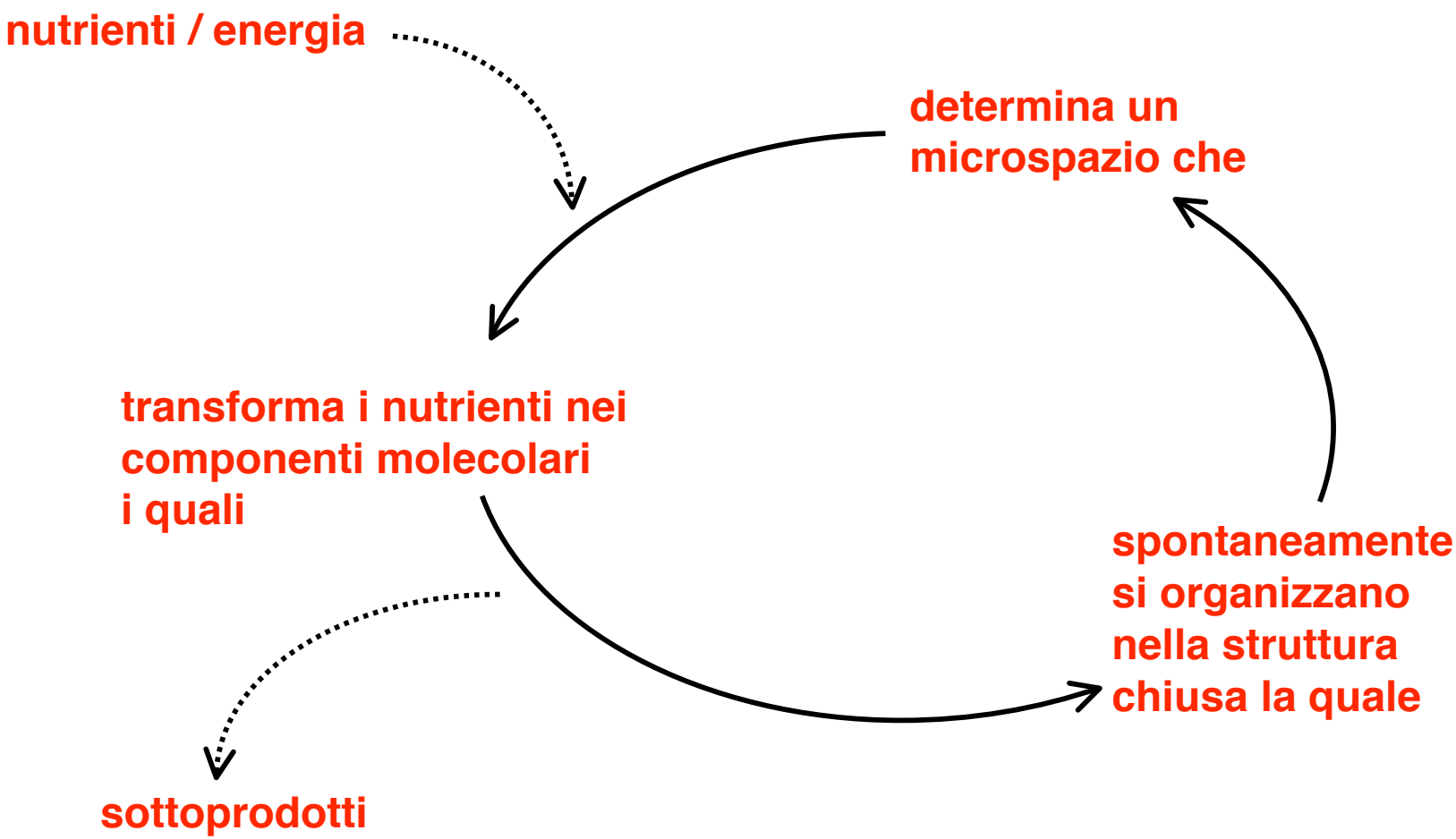
" self-generate" → self-maintenance or self-reproduction

in general

self-reproduction ≠ self-replication

Autopoiesis is the most general pattern of minimal life. It does not specify the actual structures and their mechanistic processes.





LA DEFINIZIONE CICLICA
DEL "SELF"
(...la vita ubbidisce ad una logica ciclica...)

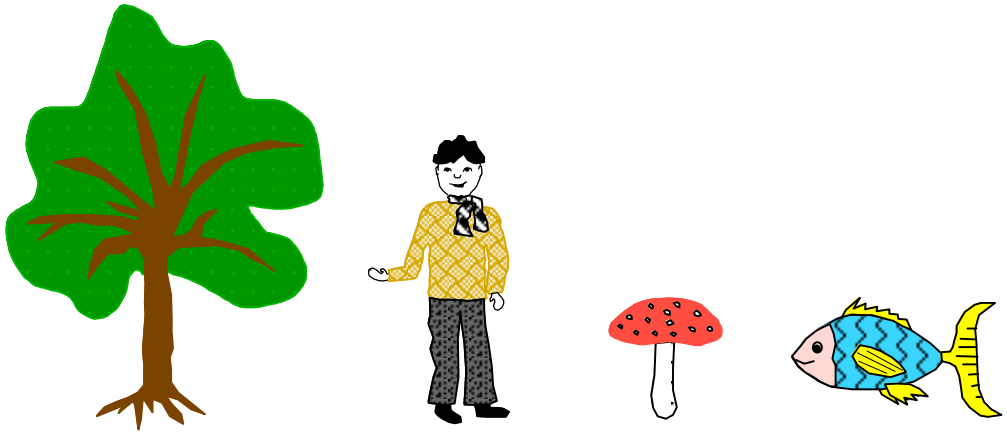
**self-maintenance from within,
due to a dynamic network of
interactions,
which are defined and
constructed
by the system itself"**

A DISCOVERY: THE CELLULAR (AUTOPOIETIC) DEFINITION OF LIFE ALSO APPLIES

TO MULTICELLULAR, MACROSCOPIC LIFE

What is life ?
A common sense definition at individual level
(LIFE " HERE AND NOW ")

A living system is a system defined by a physical boundary which allows the assimilation of nutrients / energy from the outside, and which is able to self-maintenance and self-generation owing to the activity of the system from within the boundary.



Notice that for this first-level definition no scientific knowledge on cellular structure or molecular biology is needed.
Notice also that self-reproduction or evolution are at this first-level (life here and now) not necessary.

three criteria of autopoiesis

applications of these criteria permits one to discriminate between the living and the non-living. Only if you answer yes three times is the system autopoietic and therefore living.

1. ***Self-boundary:***
   Does the system have a boundary of its own making?

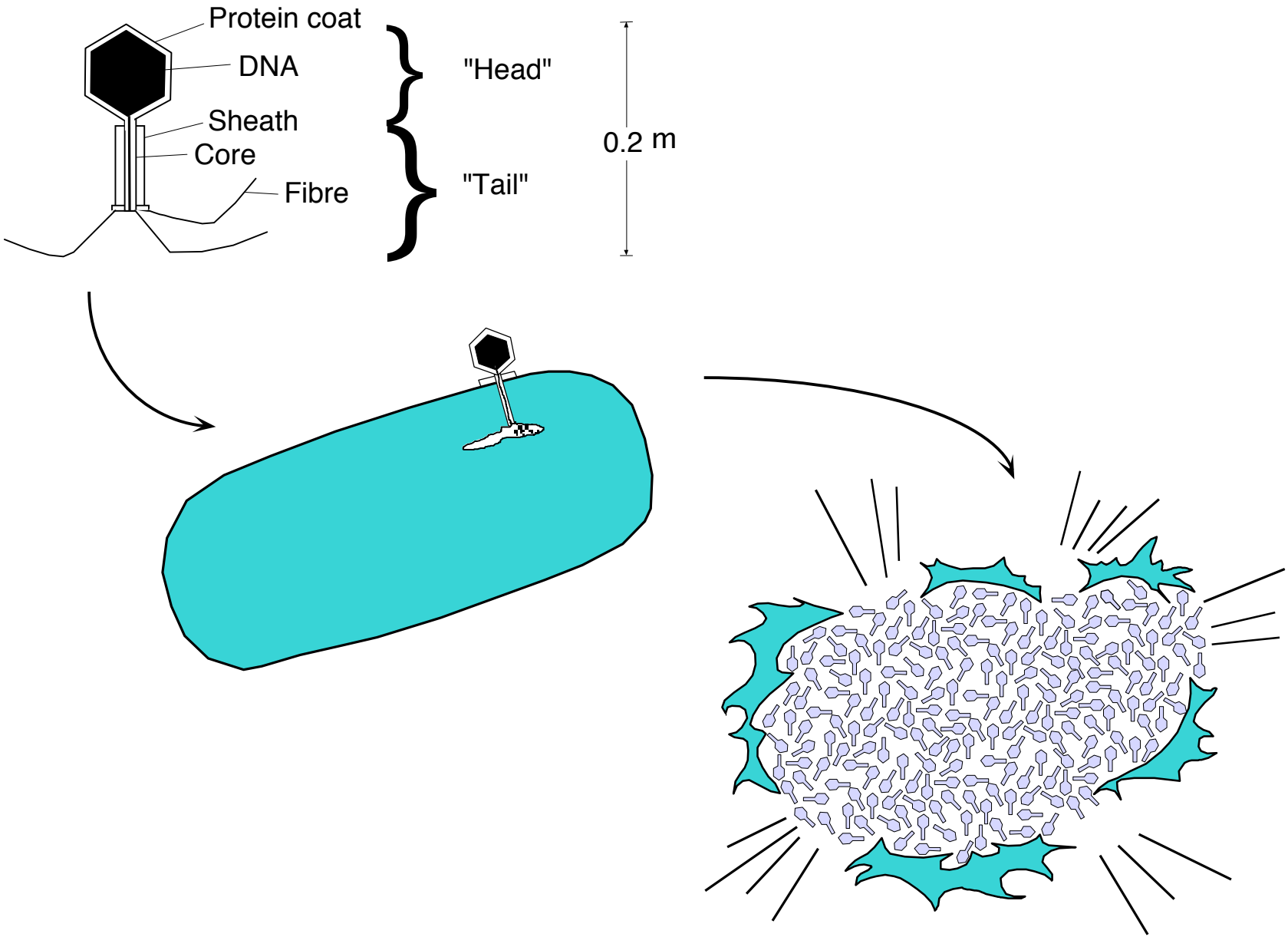
2. ***Self-maintenance:***
   Is the system capable of maintaining its own identity via dynamic processes, i.e. those components which are being used up are made anew by the system itself?

3. ***Self-generation:***
   does this happen throughout a network of reactions which are generated by the system itself?

Consider a growing crystal:
Is it living?

Apply the criteria of autopoiesis

..AND A COMPUTER VIRUS?


Protein coat
DNA
Sheath
Core
Fibre
"Head"
"Tail"
0.2 m

..the same for a computer virus

The virus per se‘ does nothing
It is just information
Does not reproduce alone
it needs a host cell (hardware computer)

CONCEPTS RELATED TO AUTOPOIESIS

BOUNDARY
ORGANIZATION AND STRUCTURE
EMERGENCE
HOMEOSTASIS

SELF-MAINTENANCE; SELF-GENERATION
AUTONOMY; SELF-IDENTITY

CODED AND UNCODED LIFE
DISSIPATIVE STRUCTURES

STRUCTURAL COUPLING
SYSTEM'S HISTORY
SOCIAL AUTOPOIESIS

COGNITION
MIND AND MATTER
CONSCIOUSNESS

what autopoiesis does not contain :

origin of life
evolution / mutation

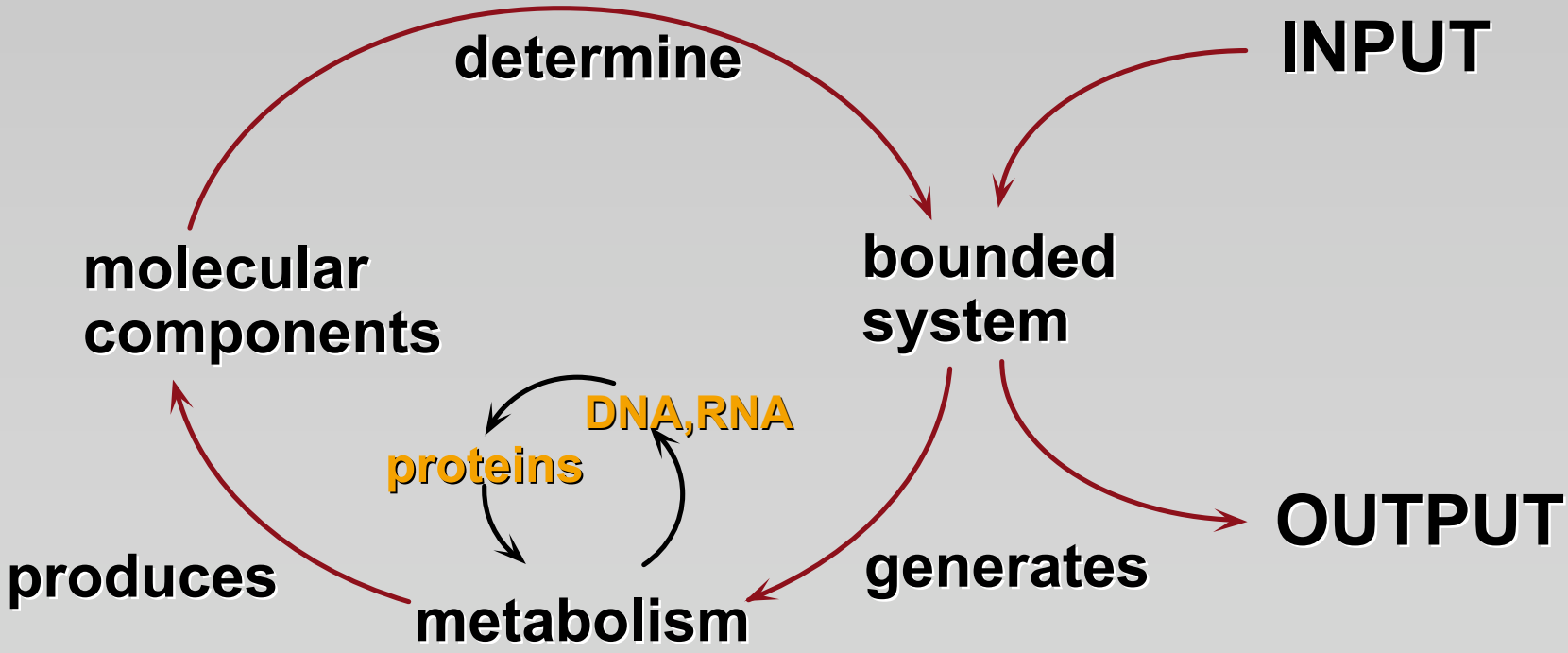
1) ...because autopoiesis is primarily interested in defining life here & now

2) and also because the above properties are easily implemented in an actual operating autopoietic system.

Notabene :
cellular evolution is a consequence of life - not its cause....
The autopoietic unit must preceed its own evolution.

LIFE IS

a system confined by a chemical boundary and which contains a network of nucleic acid - protein - based reactions which is able to transform external energy / nutrients into self-maintainance and self-generation.



But ! ...

if something exhibits autopoietic production, that "something" is living.

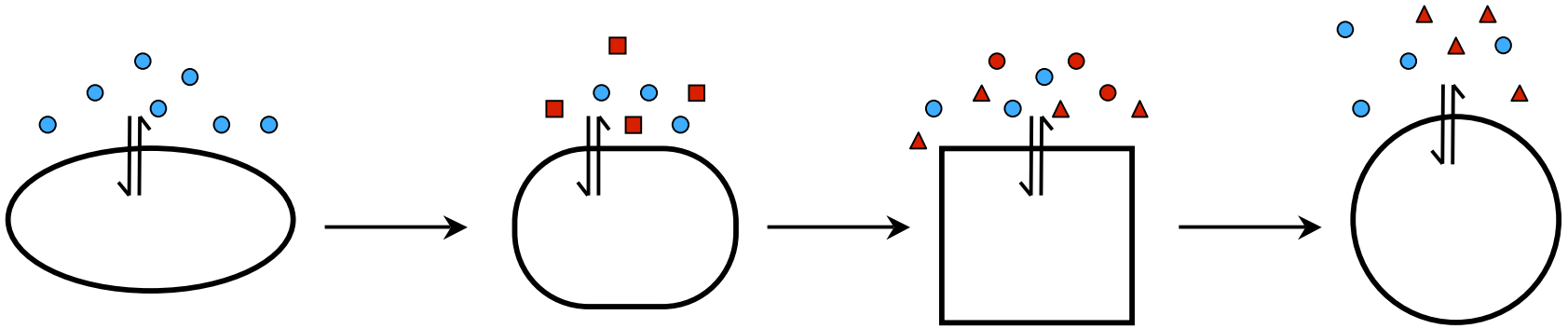
Autopoiesis is a minimal definition, in that autopoietic organization is the one phenomenon which is common to every member of life's kingdoms on earth - and yet does not exist among the constituents of their non-living surroundings.

... if some hitherto inconceivable entity were to exhibit autopoietic organization, that alone would suffice to distinguish it as living ...

Fleischaker (1990)

AUTOPOIESIS AND EVOLUTION

evolution:
the history of coupling interactions



a living organism as the
depositary of a long history
of adaptive changes

THE VAGARIES OF EVOLUTION:

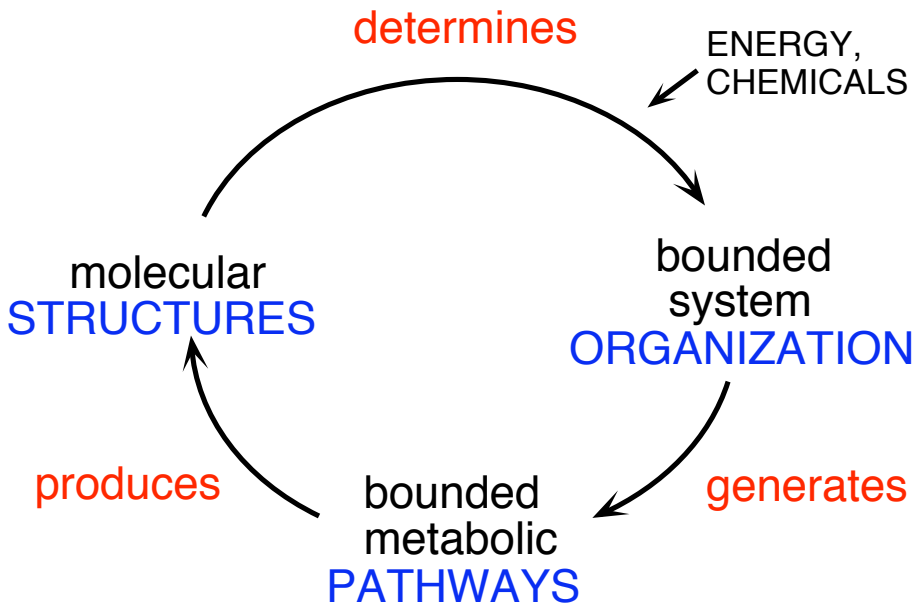
WARUM IST DIE BANANA KRUMM?

THE MAIN DRIVING FORCE OF THE LIVING IS SELF-MAINTENANCE.

WHEN EVOLUTION HAS TO OCCURR-BECAUSE OTHERWISE THE ORGANISM WOULD DIE-
THE LIVING STRUCTURES WILL MAKE THE SMALLEST POSSIBLE ADJUSTMENT-
SO AS TO
REMAIN AS MUCH AS POSSIBLE WHAT THEY WERE

**self-maintenance from within,
due to a dynamic network of
interactions,
which are defined and
constructed
by the system itself"**

The circular of " self " in autopoietic self-production



In their operational relationships, molecular strucures determine system organization which generates pathways whose operation produces molecular structures that determine system organization which generates pathways *et cetera ad infinitum....*
The autopoietic " self " is the active on - goingness of this unitary circular operation.

The autopoietic " product " is pathway generation :
creation of a network of molecular relationship that establishes continuity of metabolic operation.

Fleischaker (1990)

It is perhaps proper at this point to cite a recent definition by Maturana himself (in Poerksen, 2004):

"When you regard a living system you always find a network of processes or molecules that interact in such a way as to produce the very network that produced them and that determine its boundary. Such a network I call autopoietic. Whenever you encounter a network whose operations eventually produce itself as a result, you are facing an autopoietic system. It produces itself. The system is open to the input of matter but closed with regard to the dynamics of the relations that generate it."

From all the above it is apparent that autopoiesis belongs epistemologically to systems theory, according to which it is the organization of the components that characterizes the quality of the system. Thus, the life of a cell is a global property, and cannot be ascribed to any single component.

(Maturana and Varela, 1998):

“*In order to reproduce something, the unit must first be constituted as a unit, with an organization that defines this unit itself. This is simple common sense logics.”*

(Varela 2000)

“*A living organism can also exist without being capable of self-reproduction.”*

Autopoiesis, Emergence, and Biological Autonomy

…..the threefold relationship between autopoiesis, emergence, and biological autonomy. The autopoietic cycle in fact suggests an example of emergence, since the new properties of the bounded structure arise only when the components assemble together. Life itself can be seen as an emergent property, something that the individual components do not display, and that occurs only at the level of the organized, distributed ensemble. On the other hand, once this particular emergent properties of life are actualized, we have a case for biological autonomy, one system that is capable of specifying its own rules of behavior. According to Varela and Maturana, autopoiesis is the mechanism that imparts autonomy to the living

(Varela, 2000).

….from the epistemological point of view, the notion of biological autonomy is equivalent to the notion of auto-referentiality (Varela, 2000, Varela et al. 1991) and, in turn, auto-referentiality is related to the concept of operational closure. This is a process of circular and reflexive interdependency, whose primary effect is its own production. Operational closure must not be viewed as a lack of contact with the environment-as already stressed, any living system must be seen as an open system from the thermodynamic point of view. The relation between autopoiesis and autonomy and self-referentiality is treated in the specialized literature, see for example Marks-Tarlow et al (2002) and Weber (2002).

Questions to the reader chapter two

1. Do you believe in the utility of the attempt to give a definition of life?

   If not, how would you go for answering the following questions?

2. Is an apple – hanging on a tree – living?
   And when it falls to the ground – is it still living?

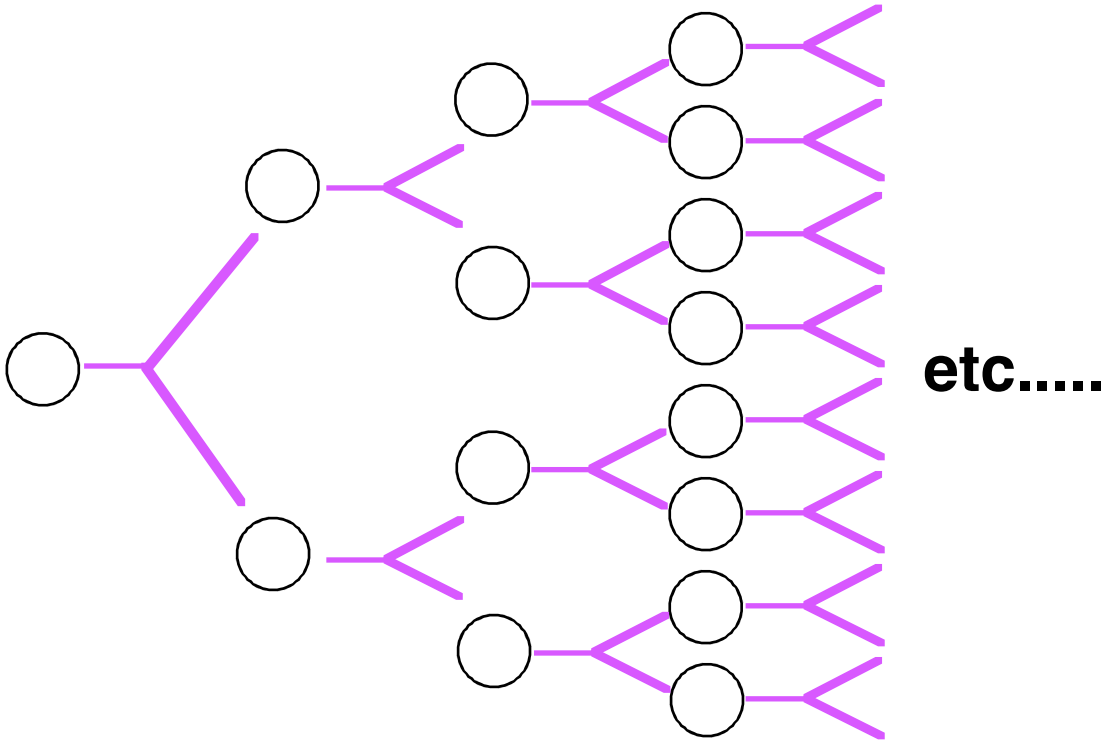
3. What is the difference between a living horse and a one which just died? They have the same amount of RNA, DNA, and all nucleic acid reactions are working for a while. Why the dead horse is dead?

4. Do you accept the definition (operational description) of life given by the Greenman; and in particular the statement that it could have been given also a few centuries ago?

WHAT IS DEATH?

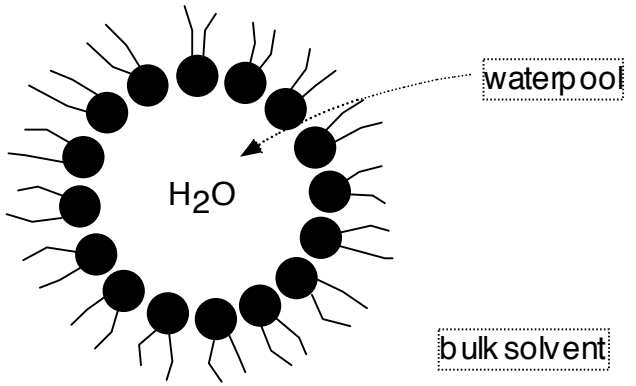
CHEMICAL AUTOPOIESIS

SELF-REPRODUCING MICELLES, LIPOSOMES & CHEMICAL AUTOPOIESIS



SELF - REPLICATING MICELLES

a



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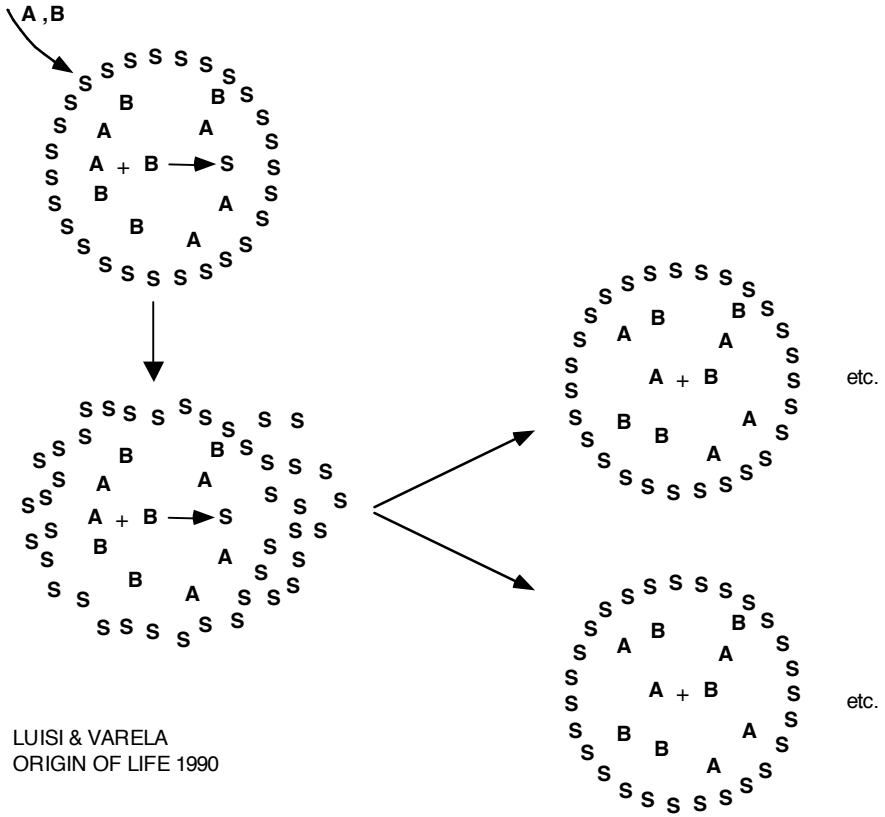

LUISI & VARELA
ORIGIN OF LIFE 1990

caprylate 

or

oleate $CH_3(CH_2)_7$ -CH = CH-$(CH_2)_7COO^-$

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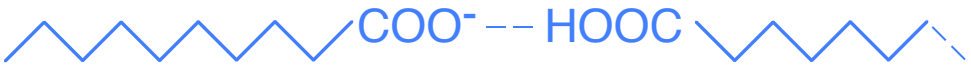
form micelles at alkaline pH

(Deamer, 1976)

vesicles at pH=7-8

(pH ≃ pk)



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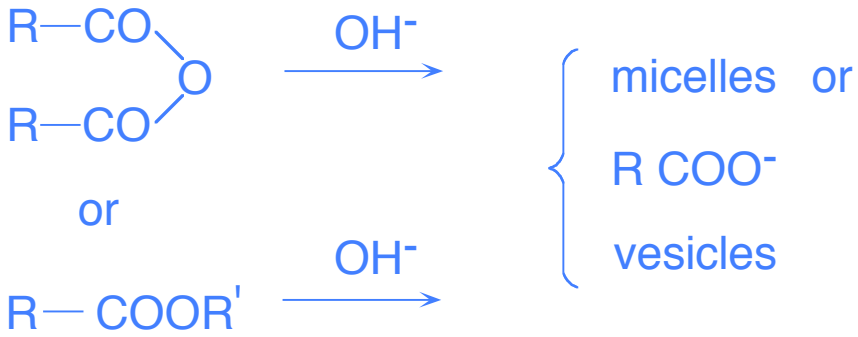
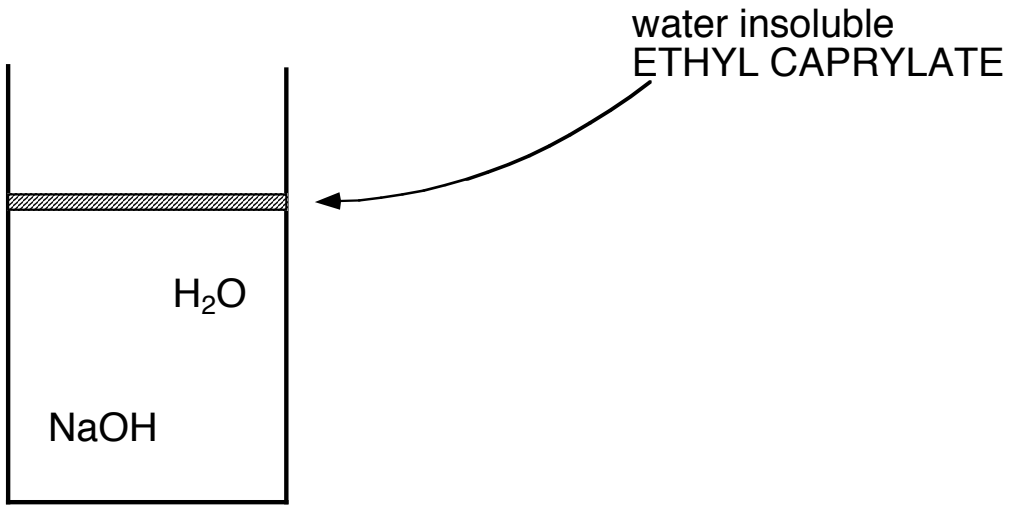
precursors (water insoluble!)

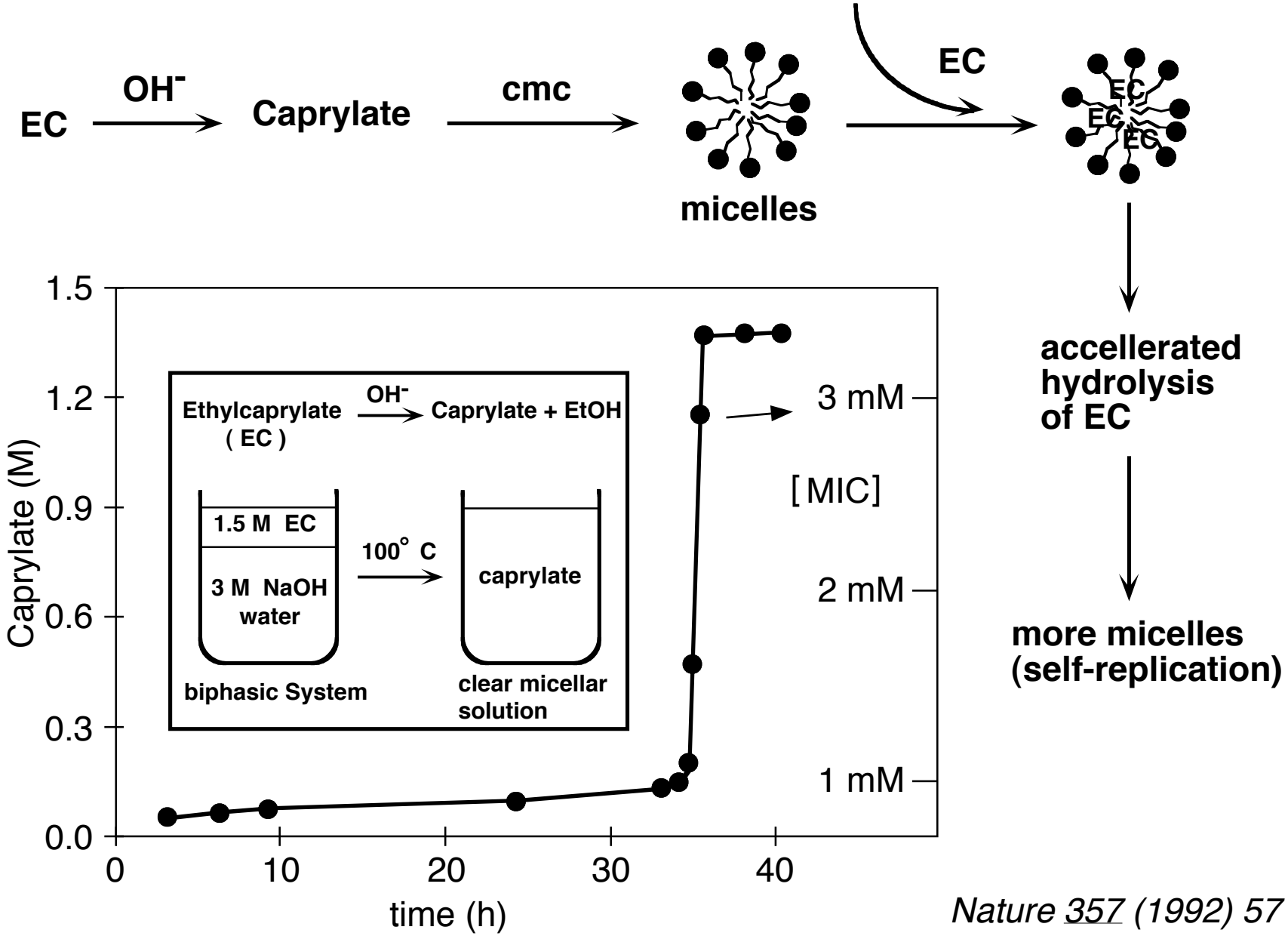


... a reaction which creates its own microenvironment for self-replication....



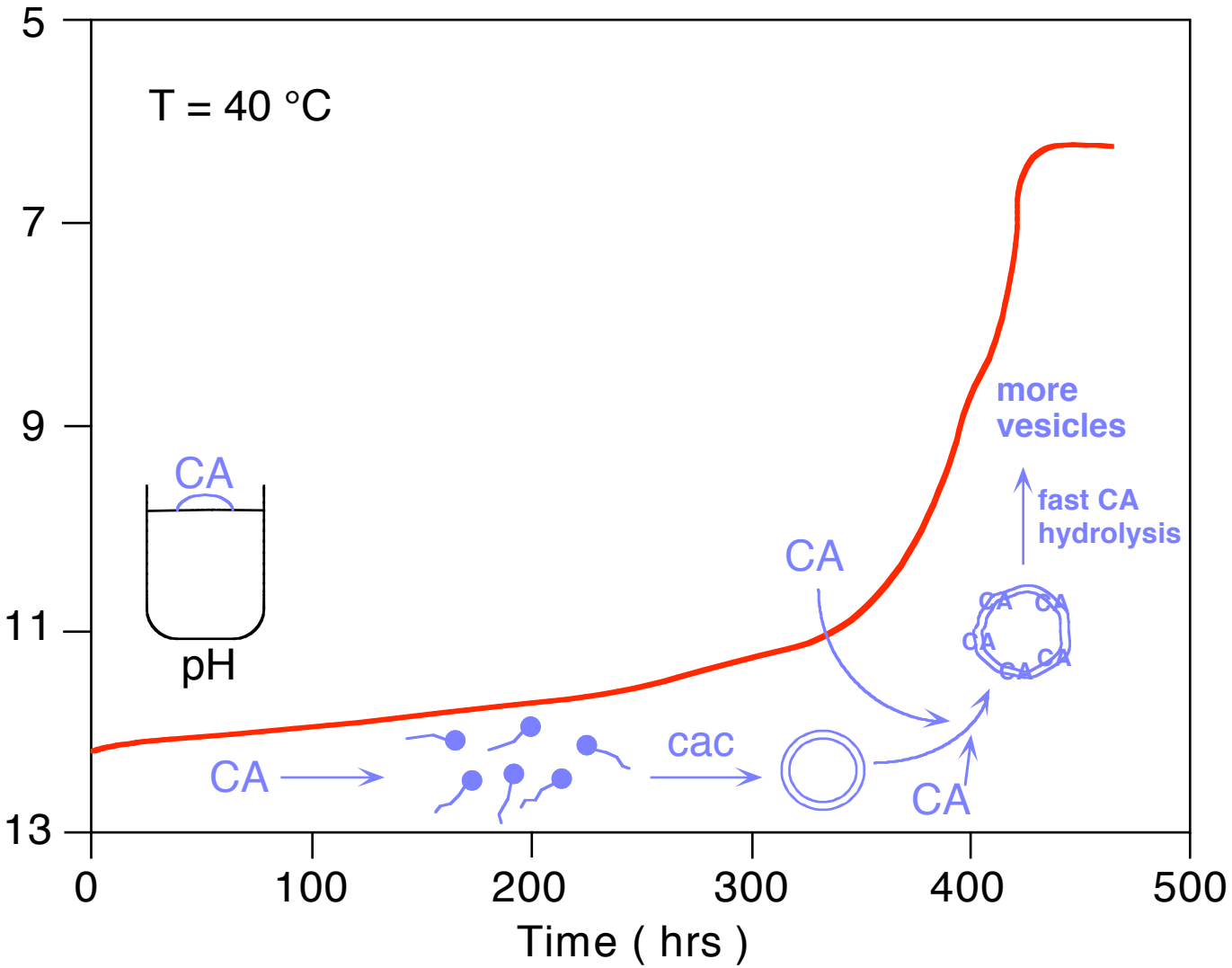
Ethylcaprylate $\xrightarrow{OH^-}$ caprylate $\xrightarrow{cmc}$ micelles in water (pH ~ 10)

or vesicles (pH ~ 7 - 8)
(start with anhydride)



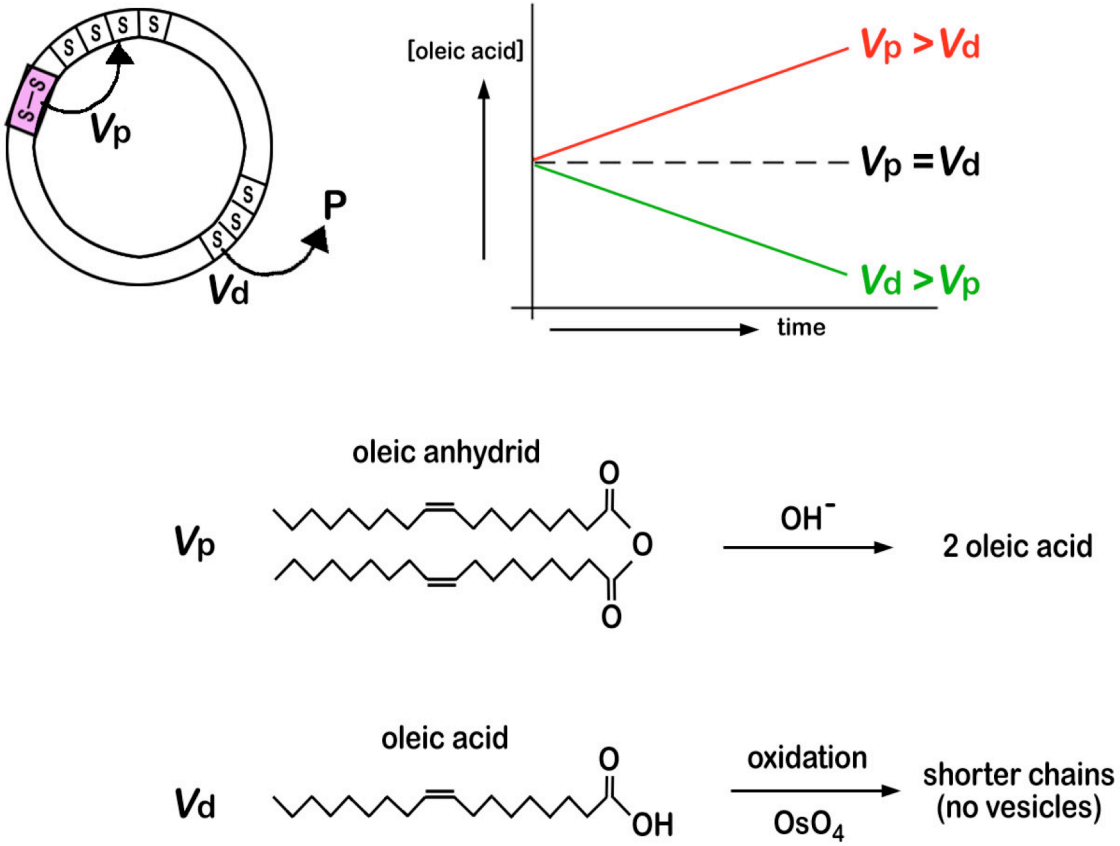
Nature 357 (1992) 57

Hydrolysis of Caprylic anhydride



a simple experimental model of chemical homeostasis

Zepik et al., Angew. Chem. 40 (2001) 199-202

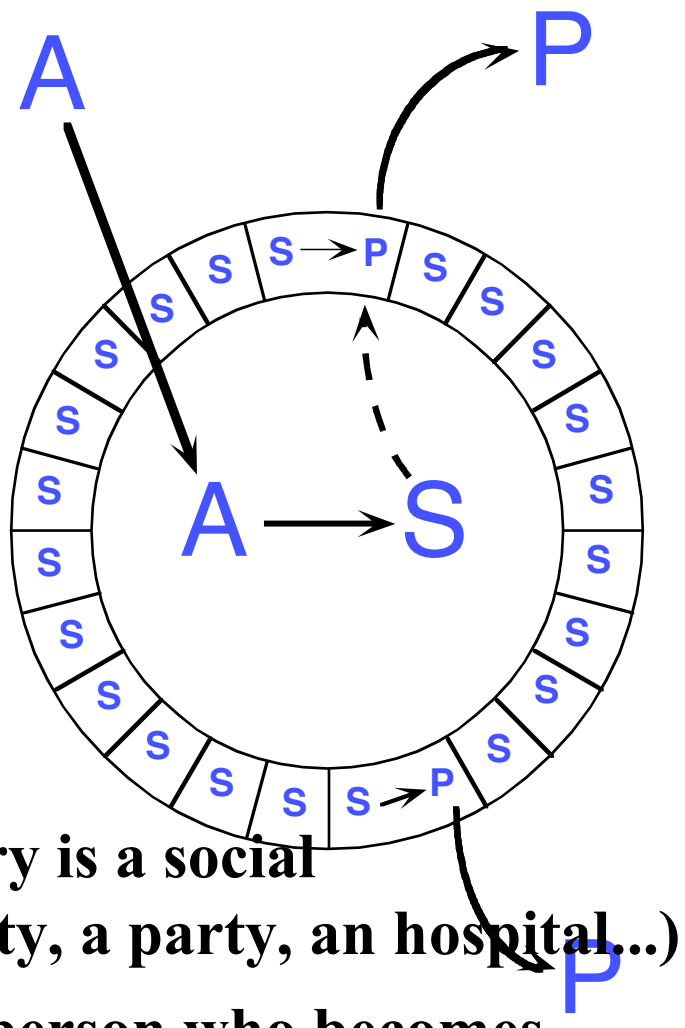


The experimental implementation of the autopoietic model of figure 8.2 with two competitive reactions. Here one reaction forms new oleate surfactant from the hydrolysis of the anhydride and another reaction destroys oleate via oxidation of the double bond. Depending on whether the two velocities are equal or not, different pathways for the systems are obtained: homeostasis (which corresponds to an autopoietic self-maintenance system), growth and self-reproduction, or decay and death (Luisi 1993, 1996, Luisi et al. 1966)

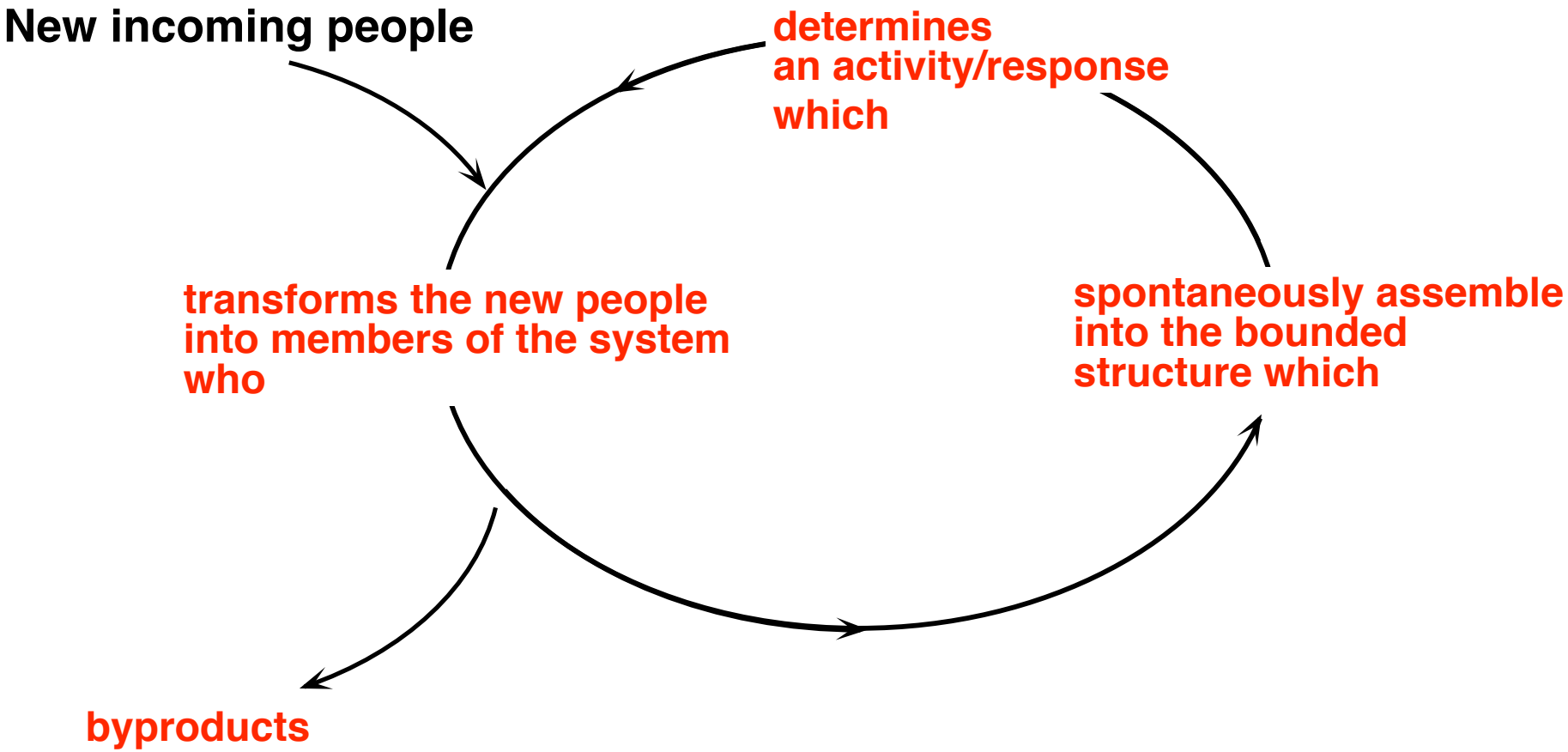
reaction destroys oleate via oxidation of the double bond.

Figure 8.5. *The experimental implementation of the autopoietic model of figure 8.2 with two competitive reactions. Here one reaction forms new oleate surfactant from the hydrolysis of the anhydride and another reaction destroys oleate via oxidation of the double bond. Depending on whether the two velocities are equal or not, different pathways for the systems are obtained: homeostasis (which corresponds to an autopoietic self-maintenance system), growth and self-reproduction, or decay and death (Luisi 1993, 1996, Luisi et al. 1966)*

Towards social autopoiesis



If the boundary is a social structure(a city, a party, an hospital...) and A a new person who becomes a member (S)....



Towards social autopoiesis

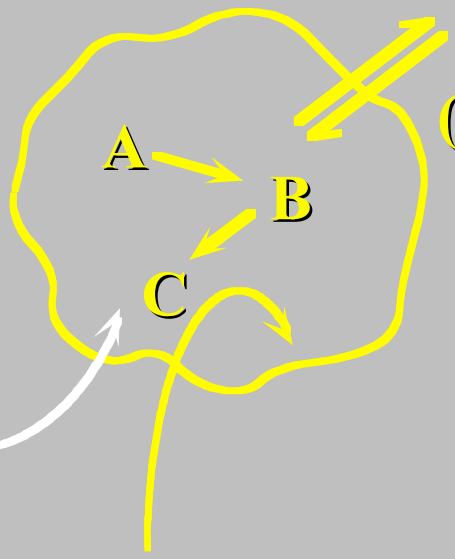
SOCIAL AUTOPOIESIS (?)

- a nation
- a political party
- religion
- family
- one city
- any social system ?
- Gaia

} ructure & rganization

coupling interactions

(+ history)



(substructures or individuals) which are being reproduced from within

boundary defined (and created) from within .....

" self-maintenance from within, due to a dynamic network of interactions, which are defined and constructed by the system itself "

Varela remained somewhat skeptical about these extensions of autopoiesis. He says in this regard (Varela, 2000):

"These ideas are based, in my opinion, on an abuse of language. In autopoiesis, the notion of boundary has a more or less precise meaning. When, however, the net of processes is transformed into one 'interaction among people', and the cellular membrane is transformed into the limit of a human group, one falls into an abuse, as I expressly said)"

ECOLOGY

the interaction between organisms and their environment is part of the more general scenario of ecology. It has been in fact stated that living organisms make and continuously change the environment in which they live, and vice versa, so that every act of consumption is also an act of production; also, that we must forget the idea that there is a constant and fixed world – as we are constantly changing it and cannot live without changing it. (Lewontin, 1991). From that, the difficulty of finding a healthy equilibrium that preserves as much as possible the identity of the living.

**self-maintenance from within,
due to a dynamic network of
interactions,
which are defined and
constructed
by the system itself"**