Some open questions for Origlife...

PARMENIDES
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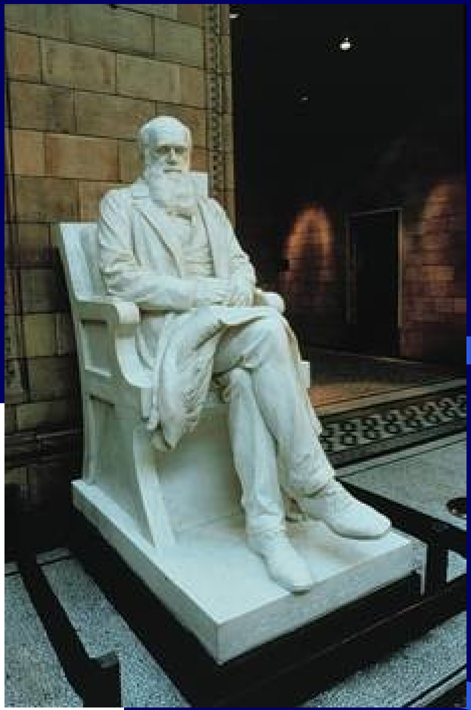
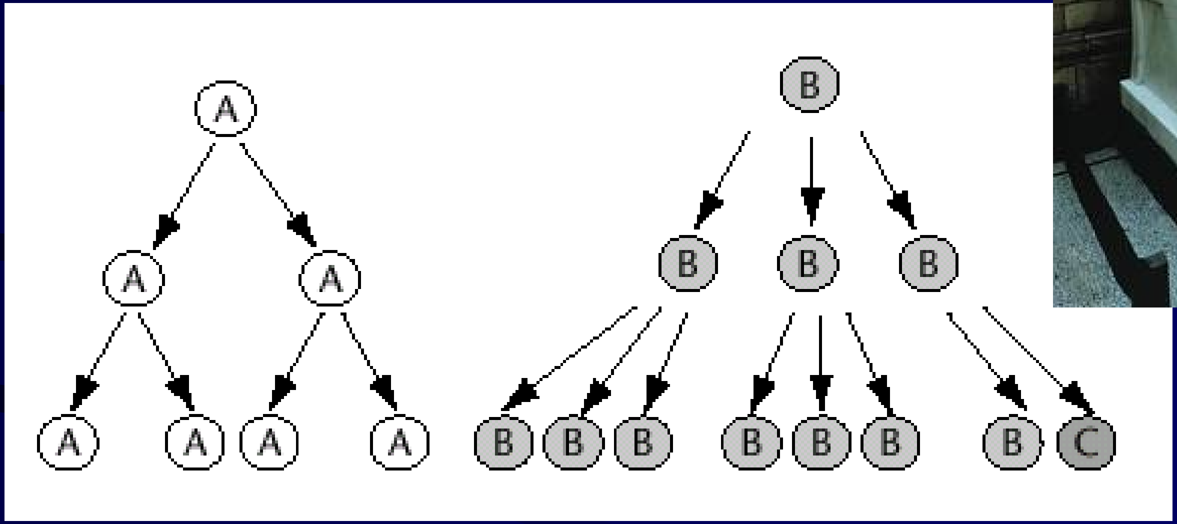
Units of evolution





1. multiplication
2. heredity
3. variation

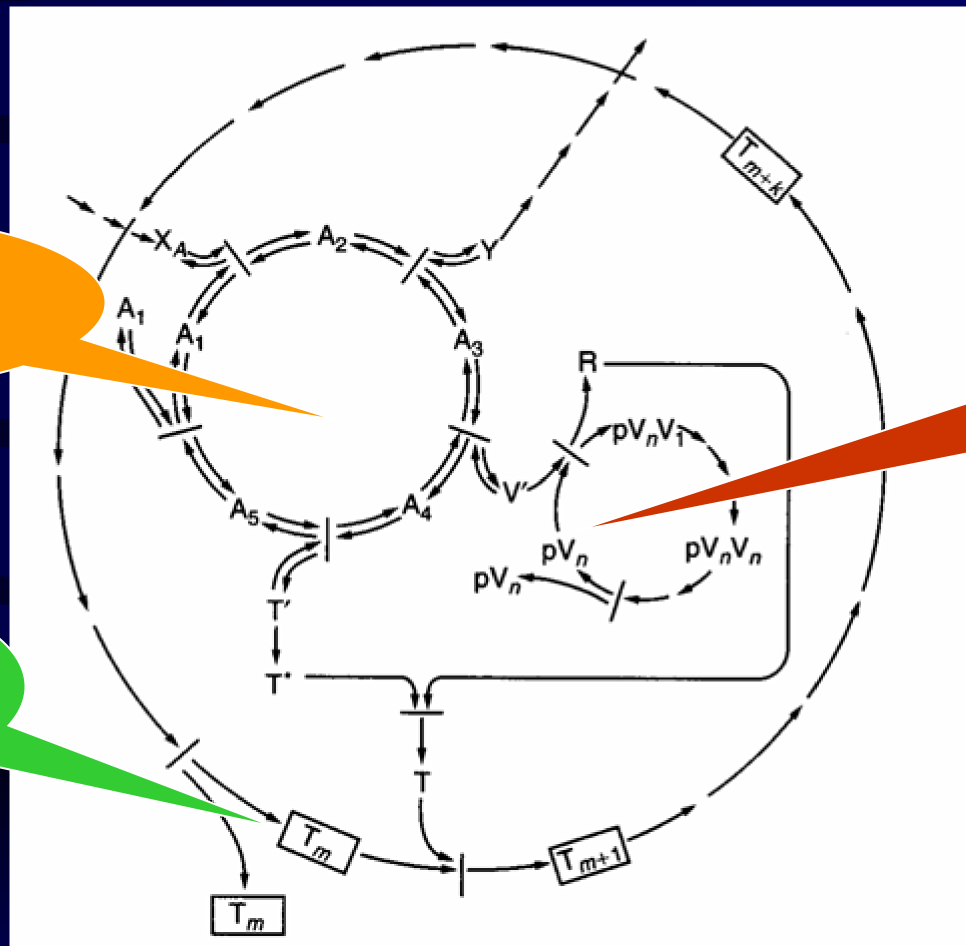
hereditary traits affecting survival and/or reproduction

Gánti’s chemoton model (1974)

metabolism

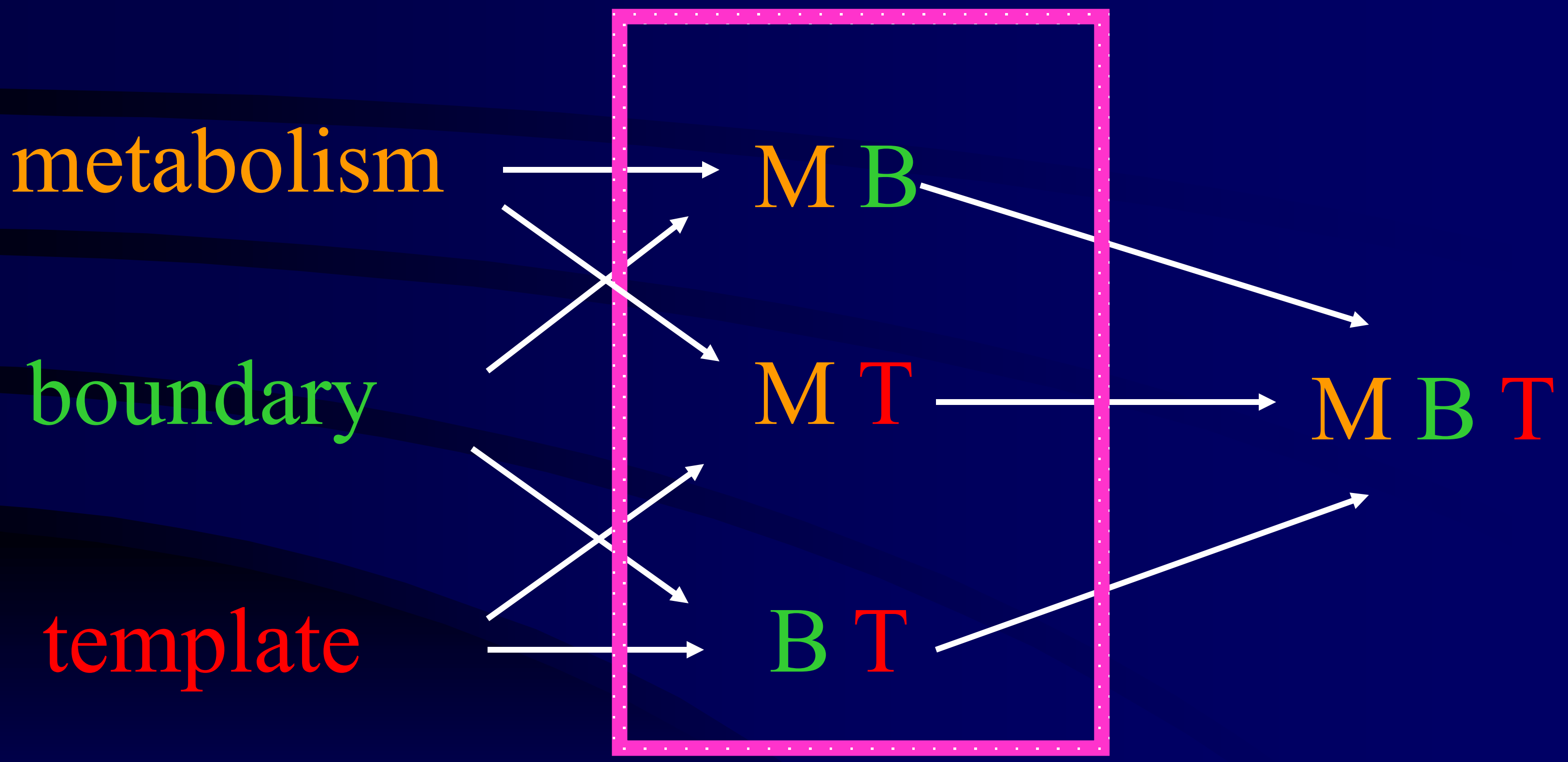
template copying

membrane growth



ALL THREE SUBSYSTEMS ARE AUTOCATALYTIC

Pathways of supersystem evolution



INFRABIOLOGICAL SYSTEMS

A crucial insight: Eigen's paradox (1971)

- Early replication must have been error-prone
- Error threshold sets the limit of maximal genome size to <100 nucleotides
- Not enough for several genes
- Unlinked genes will compete
- Genome collapses
- Resolution???

Simplified error threshold

$$dx/dt = xKQ - x\Phi,$$
$$dy/dt = yk + xK(1-Q) - y\Phi,$$

$$\Phi = xK + yk$$

$$x + y = 1$$

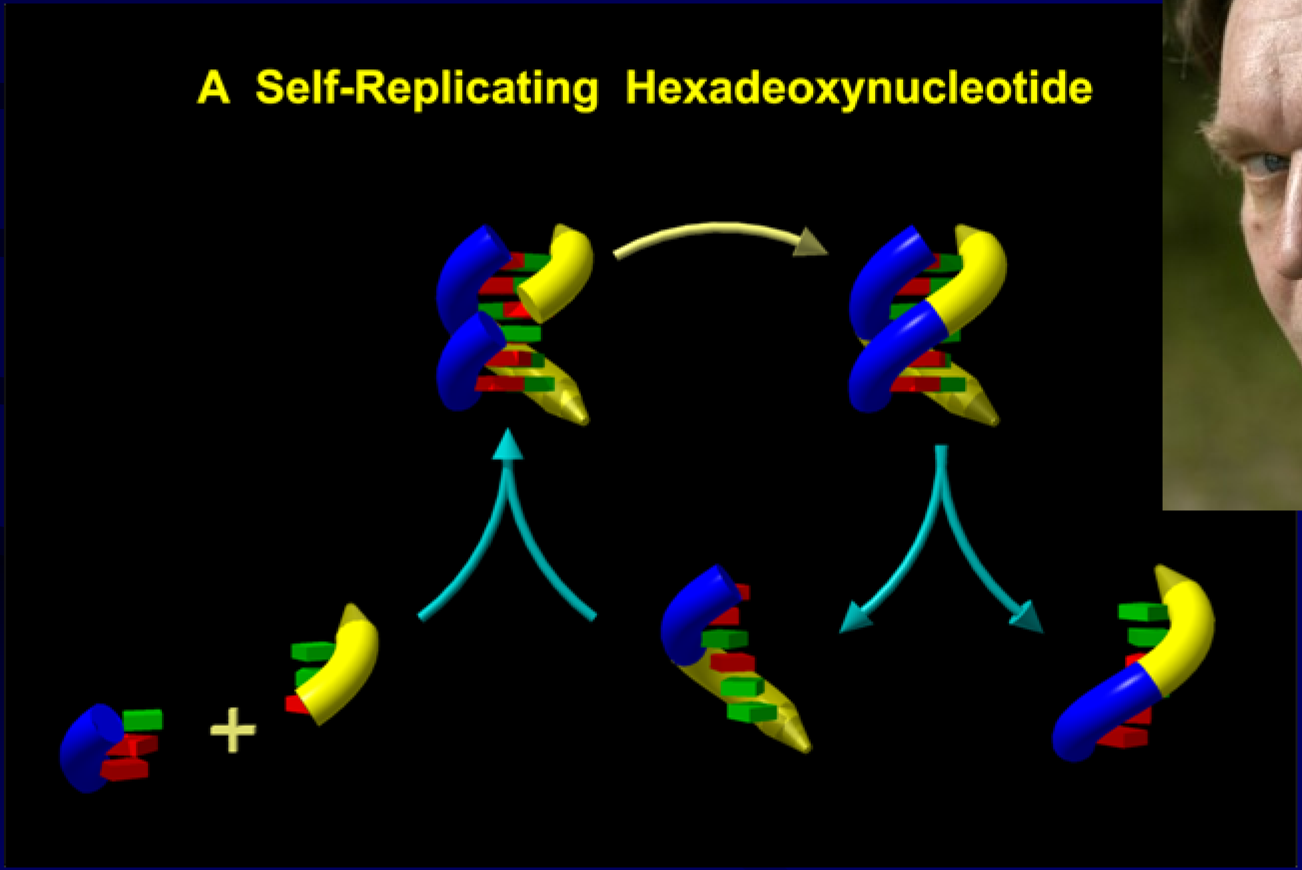
$$x = \frac{(KQ-k)}{(K-k)}$$

$$Q = q^{\nu}$$

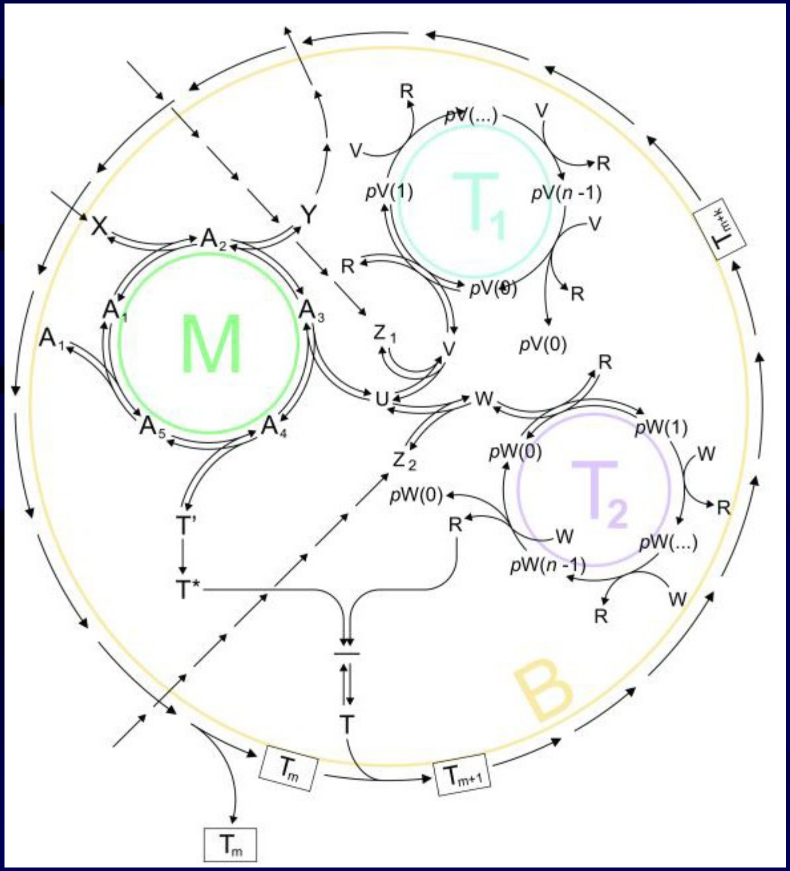
$$e^{-\nu(1-q)}$$

$$\nu < \frac{\ln(K/k)}{(1-q)}$$

Von Kiedrowski's replicator



A more complex chemoton



- Submitted to *Plos One*
- A stochastic simulation

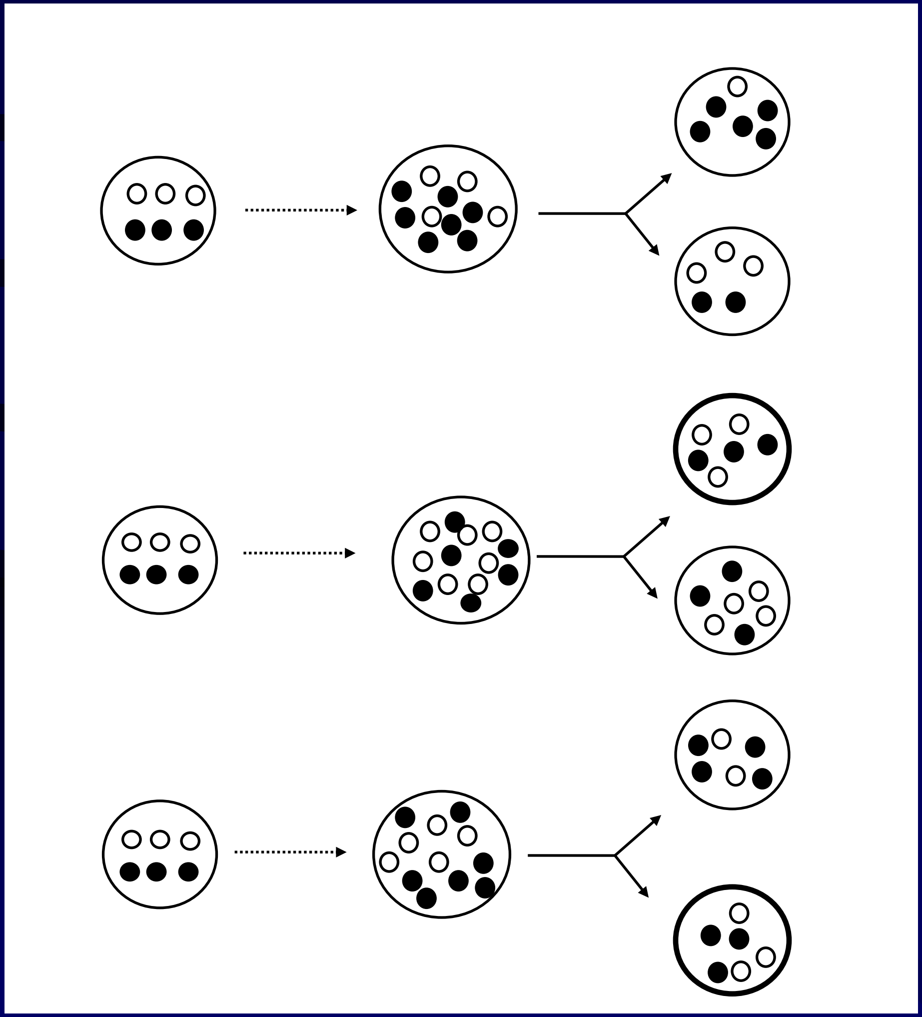
A radically new look at the paradox

- Stochastic simulation of the chemoton with two different templare monomers
- Found coexistence of templates that were thought to be competitors
- Dynamical coexistence is *sequence-dependent*
- Carries over to deterministic solutions of the chemoton, and even to simplifed systems (metabolism and templates in flow reactor)

Solution of the paradox requires systematic search and insight

- Numerical solutions take a lot of time
- It is important to see how this carries over to long templates
- CERN computing welcome

The stochastic corrector model for compartmentation



Szathmáry, E. & Demeter L. (1987) Group selection of early replicators and the origin of life. *J. theor Biol.* **128,** 463-486.

Grey, D., Hutson, V. & Szathmáry, E. (1995) A re-examination of the stochastic corrector model. *Proc. R. Soc. Lond.* B **262,** 29-35.

Dynamics of the SC model

- Independently reassorting genes
- Selection for optimal gene composition between compartments
- Competition among genes within the same compartment
- Stochasticity in replication and fission generates variation on which natural selection acts
- A stationary compartment population emerges

What is the limit of genome size in the SCM?

- It is about a dozen unlinked genes
- Selection for chromosomes
- Requires evolutionary increase in *replication accuracy*
- Calls for evolution of better-than-random *segregation mechanisms*

This is surprisingly linked to the origin of enzyme specificity

- Imagine a pathway to be enzymatized
- Is there selection from a few, inefficient, multifunctional enzymes to many, efficient, highly specific enzymes (Kacser question)
- The answer is negative in the SCM due to the assortment load (if one gene is lacking, others can do the work)

Chromosomes favour metabolic evolution

- Because genes are not lost due to reassortment
- Highly specific enzymes evolve
- *If there selection againts side reactions!*
- Further work needed with better chemical model
- *To be submitted soon*
- Requires CERN resources

The origin of metabolism

- Is a hard question
- Coevolution with other subsystems is likely
- One can generate some pre-insights, but this does not replace detailed simulations

The problems of phylogenetic reconstruction (top-down)

- LUCA was too advanced
- Reconstructions (e.g. Delaye *et al. OLEB* in press) cannot reach deep enough
- The fact that metabolic enzymes are not well conserved does not mean that they were not there!
- Scaffolds (pre-RNA, primitive metabolic reactions) may have disappeared without leaving a trace behind!!!
- A more synthetic approach is needed
- General evolutionary mechanisms must be sought

Two contrasting modes of enzymatic pathway evolution

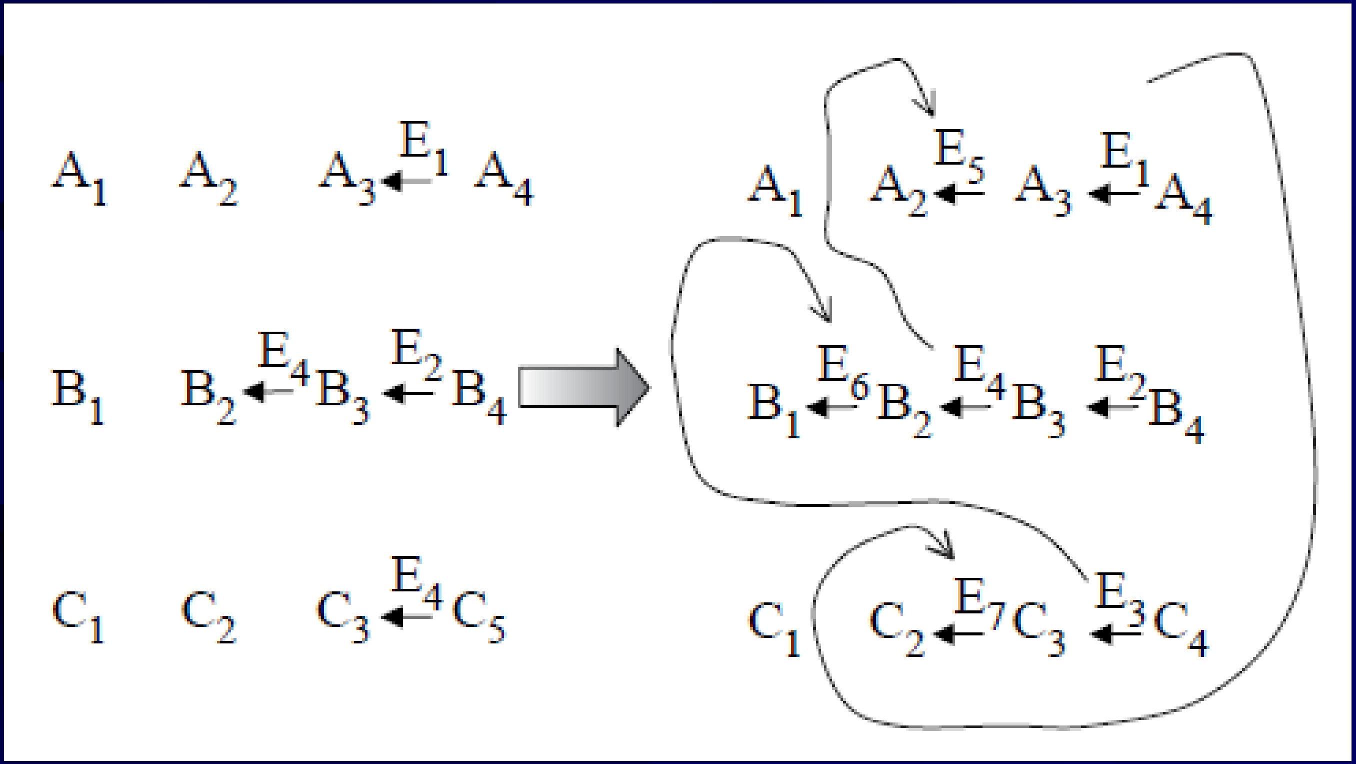
Horowitz (1945) : **retroevolution**

- Ancient non-enzymatic pathway:
- A → B → C → D
- Progressive depletion of D, then C, then B, then A
- Selection pressure for enzyme appearance in this order
- Homologous enzymes will have different mechanisms

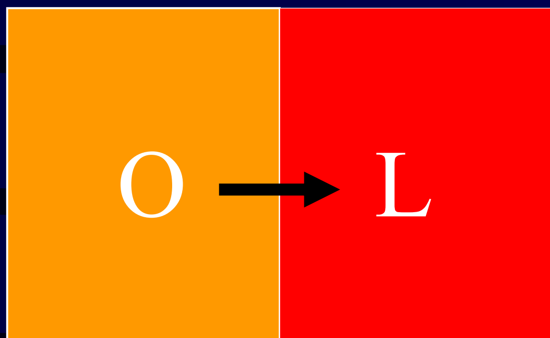
Jensen (1976) **enzyme recruitment (patchwork)**

- One possible mechanism: ambiguity and progressive evolution of specificity
- Homologous enzymes will have related **mechanisms**
- Enzyme recruitment from anywhere (opportunism)

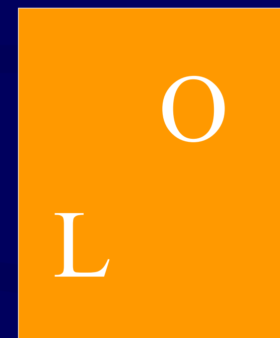
The two views are not necessarily in contradiction



Some elementary considerations



- Autotrophy impossible
- Enzymatic pathways are likely to be radically new inventions



- Autotrophy possible
- Enzymatic pathways may resemble non-enzymatic ones

Organic synthesis

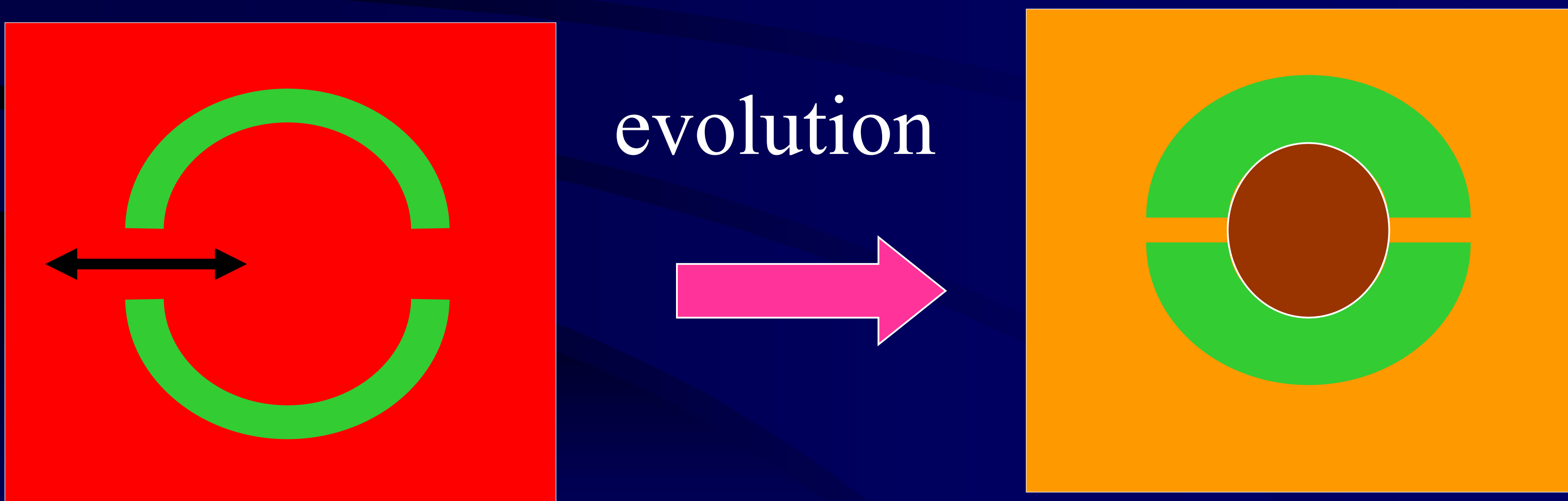
Life

Environment 1

Environment 2

Further complication of supersystem organization

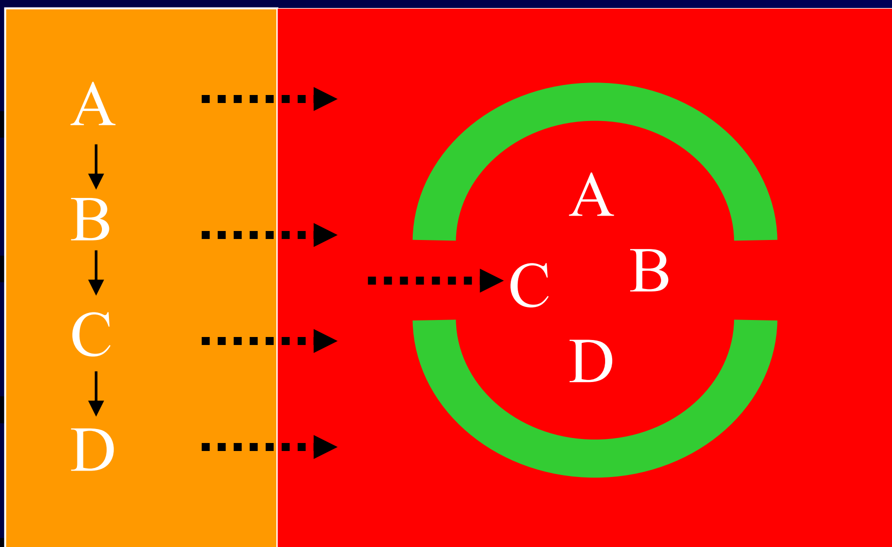
- The example of the Template/Boundary system: progressive distinction from the environment

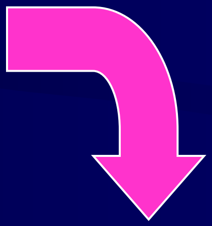


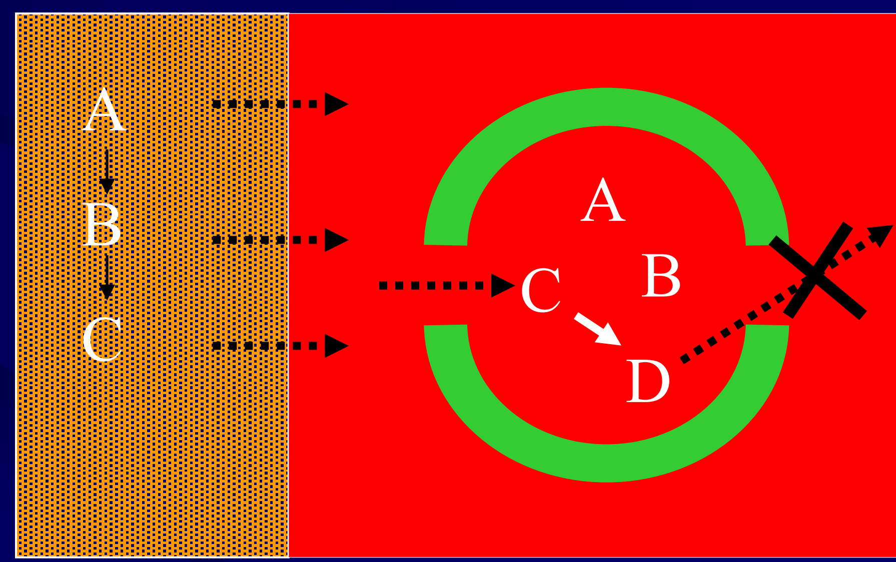
Metabolites pass freely

Metabolites are hindered

Evolution of metabolism: primitive heterotrophy with pathway innovation





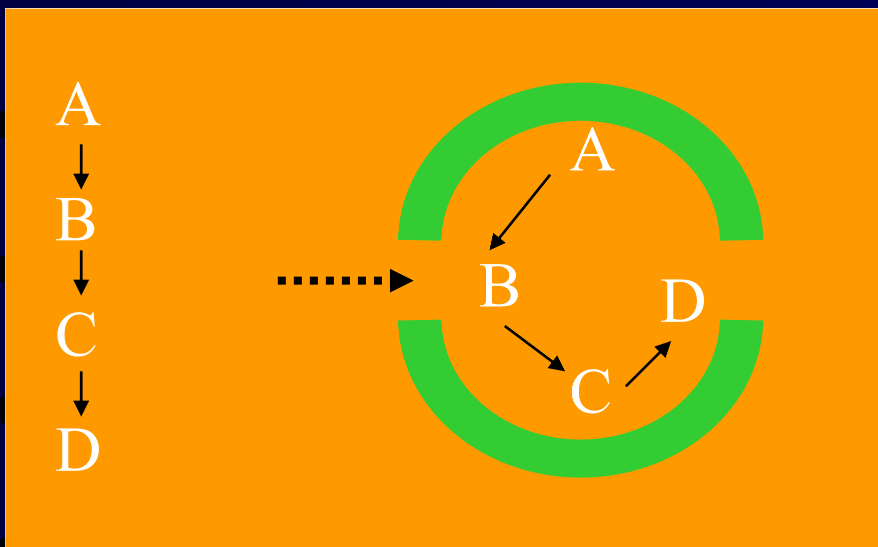


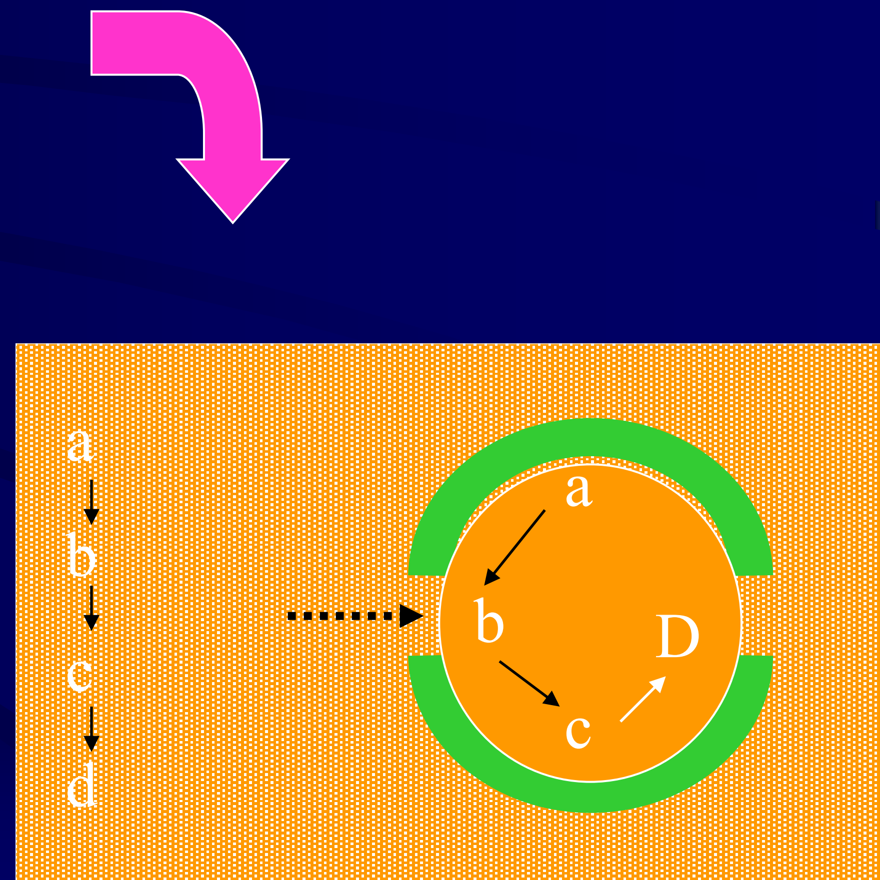
→ Evolved enzymatic reaction

Necessarily heterotrophic protocell

Assume D is the most complex

Evolution of metabolism: primitive autotrophy with pathway retention





Retroevolution is also likely because of membrane coevolution

Progressive sequestration

- Initially only templates are kept in
- They can evolve catalytic properties
- Carriers and channels can also evolve
- Membrane permeability can become progressively restrictive
- Finally, only a very limited sample of molecules can come in
- Inner and outer environments differentiate
- Membrane and metabolism coevolve gradually

All these ingredients (and more) must be put together

- Supersystem evolution
- Changing environments
- Progressive sequestration
- Duplication and divergence of enzymes
- Selection for cell fitness
- Network complexification
- The platform by Christoph Flamm
- Computational resources of CERN!