Evolution and Analysis of Metabolic Networks
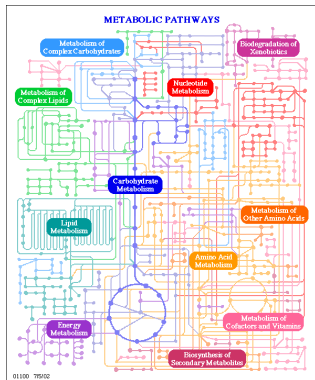
Alexander Ullrich

Chair for Bioinformatics
University of Leipzig

Herbstseminar, Vysoka Lipa, Oktober 22

Metabolism

Enzymes, Metabolites, Reactions, Pathways
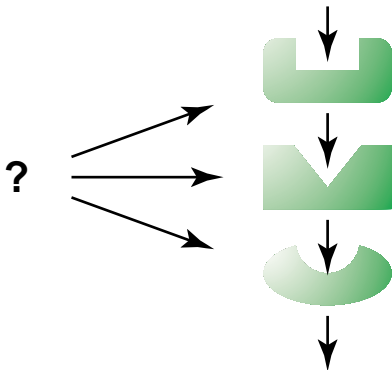
Application

- Functional Genomics
    - Behavior under different external Conditions
    - Drug-Response, Immune-Response
    - Response Networks
- Metabolic Engineering
    - Pathway Analysis, Optimization
    - Production of Pharmaceuticals, Food, Fuel, ...
- General Understanding of Complex Systems
    - Manipulating biological Systems
    - Generating artificial Systems

Evolution

- Enzyme Evolution
  - Neutral Evolution
  - Evolutionary Transitions
- Pathway Evolution
  - Development of Pathways
- Network Evolution
  - Global Properties
  - Dynamic Behavior
- Tools
  - Random Neutral Walk
  - in silico Evolution (stochastic Simulation, Toy-Model of Metabolism)
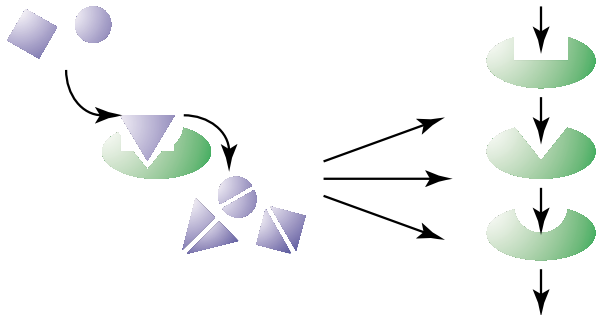 - Metabolic Pathway Analysis

Pathway Evolution

De-novo Scenario

spontaneuous Evolution of Enzymes
Example: tRNA Synthetases

Pathway Evolution

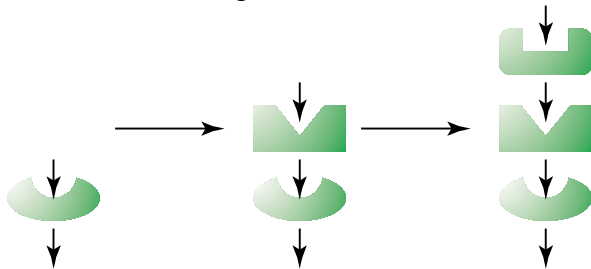Specialization from a multi-functional Enzyme

Duplication and Diversification
Example: Carbomyl phosphate synthetase
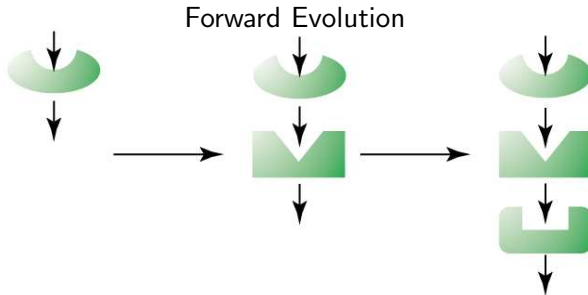
Pathway Evolution

Retrograde Evolution

End-product can be derived from moreand more distant
metabolites
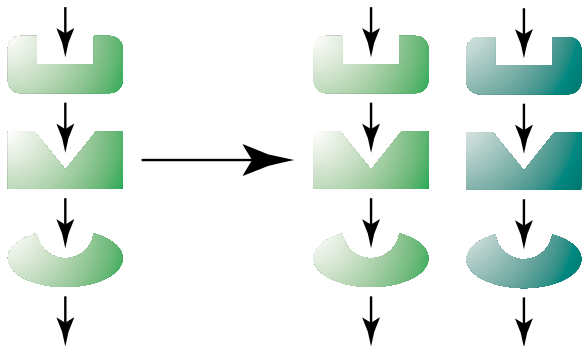Example: glycolytic pathway

Pathway Evolution

Forward Evolution

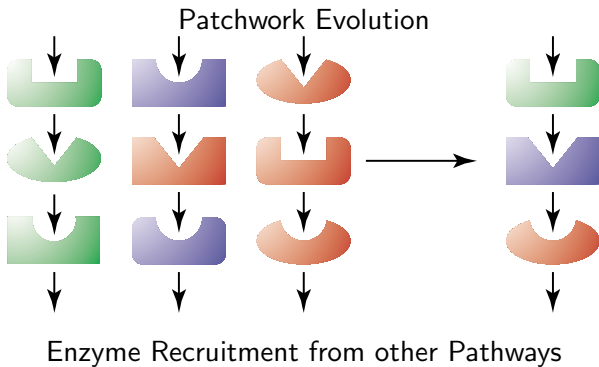more efficient extraction through deeper break-down of metabolites

Pathway Evolution

Pathway Duplication

Duplication and Diversification
Example: tryptophane and histidine biosynthesis

Pathway Evolution

Patchwork Evolution

Enzyme Recruitment from other Pathways

Pathway Evolution

Comparison
red = older, blue = younger

Retrograde Evolution

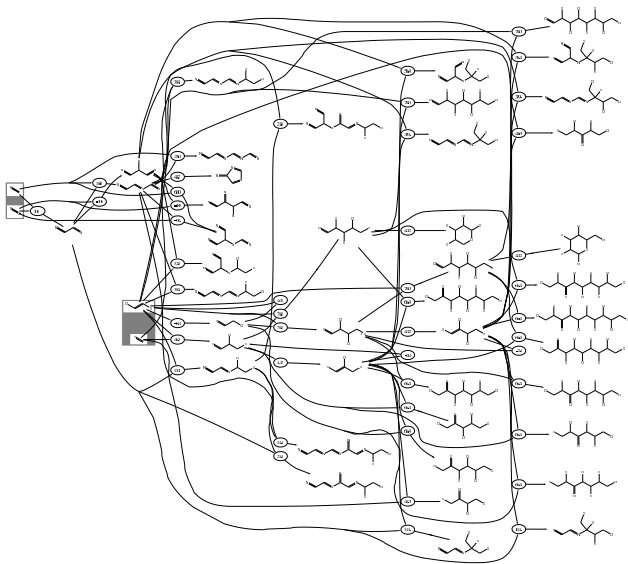Forward Evolution

Patchwork Evolution

in silico Evolution

- Molecules
- Enzymes
- Reactions
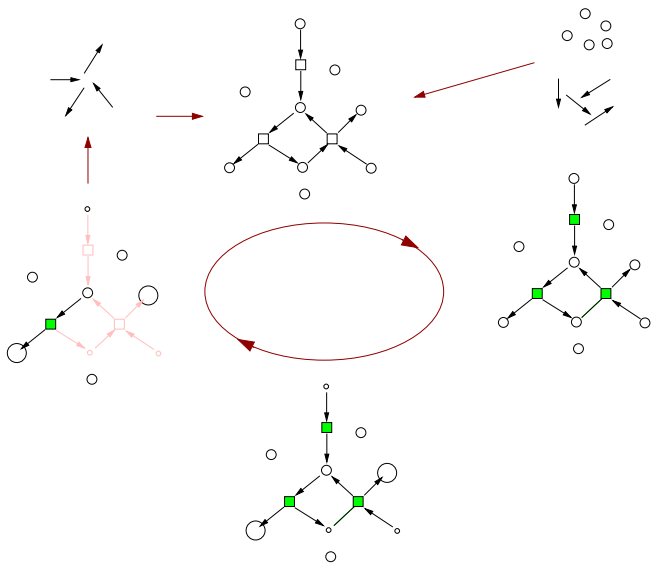- Challenges

Schema of Reaction Network Model
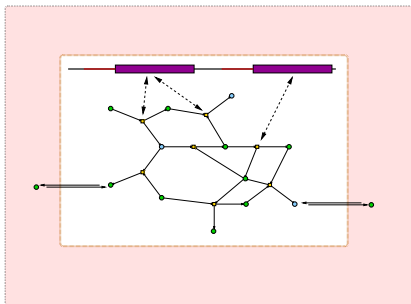
- Bag of ribozymes.
- Algebraic chemistry model.
- Exchange of molecules with the environment.
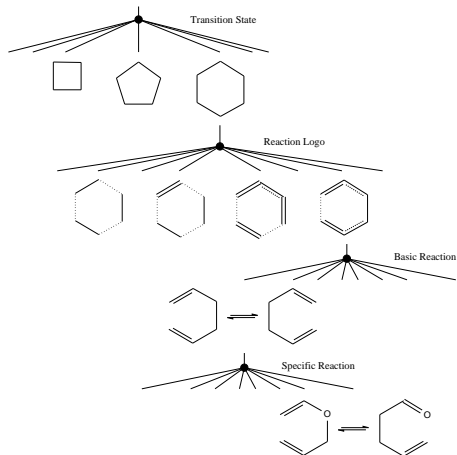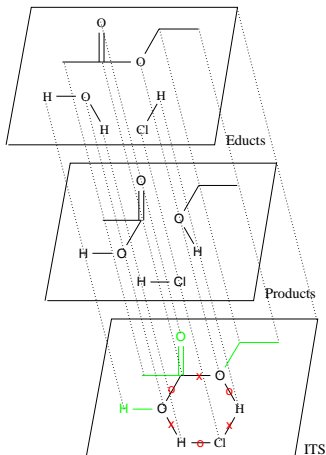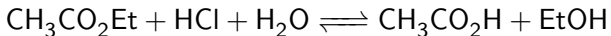
Iterating the Graph Grammar
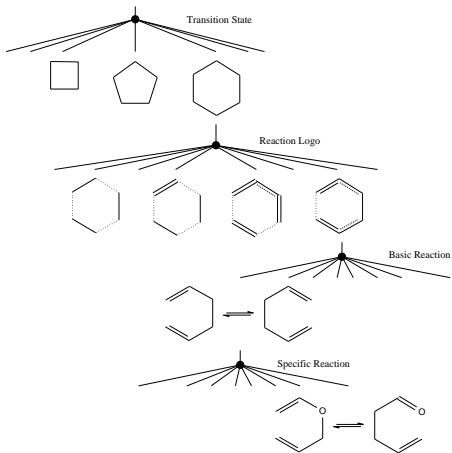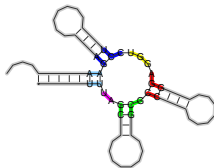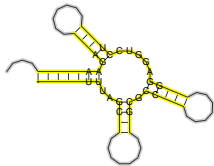

cyanide, formaldehyde glycol; aldolcondensation, tautomerization
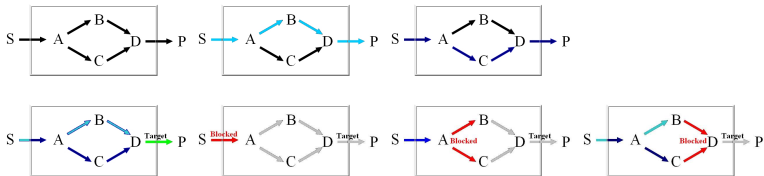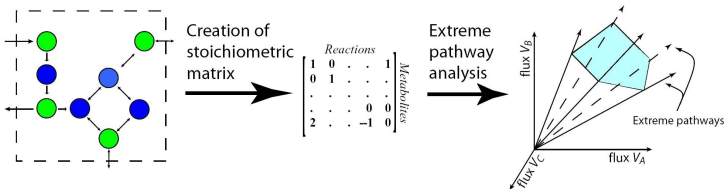
Way to avoid the Combinatorial Explosion

Faulon, J-L, (2001) J Chem Inf Comput Sci 41:894-908

Reaction Classification

$$CH_3CO_2Et + HCl + H_2O \rightleftharpoons CH_3CO_2H + EtOH$$

Fujita, Hendrickson, …

The structure-to-function map

Metabolic Pathway Analysis

Random neutral walk
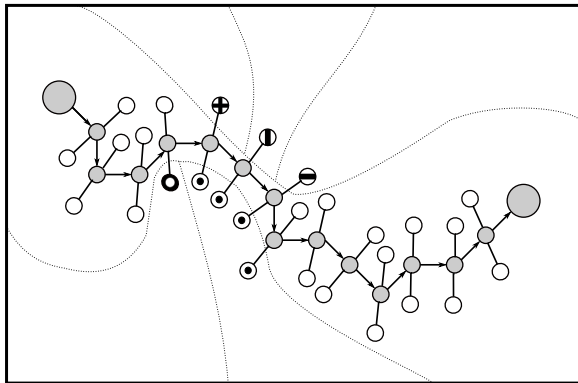
Encountered Phenotypes (length=100)
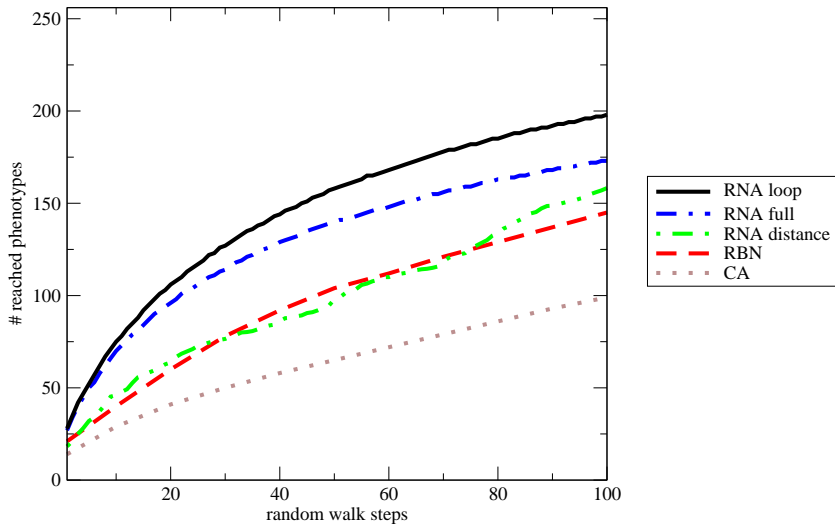
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