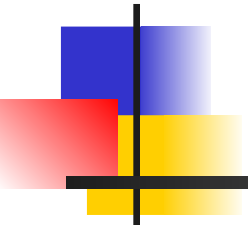
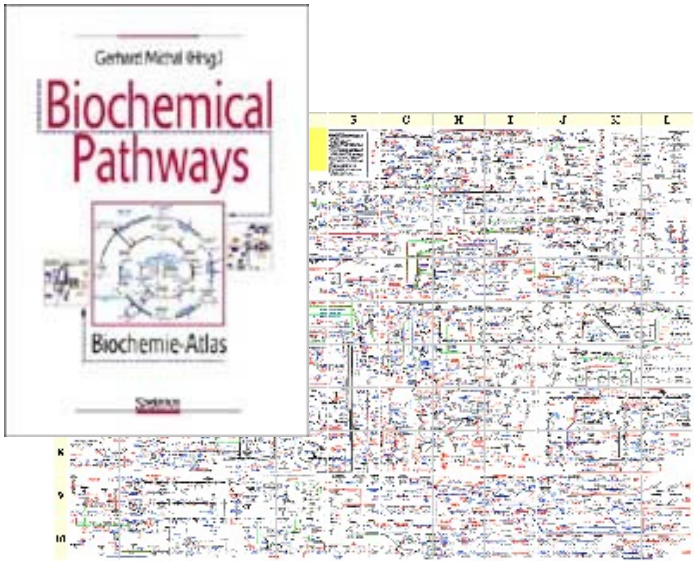


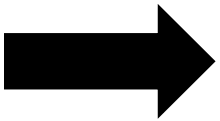
BioPath

Visualization of Biochemical Pathways

Franz J. Brandenburg,
Michael Forster, Andreas Pick,
Marcus Raitner, Falk Schreiber

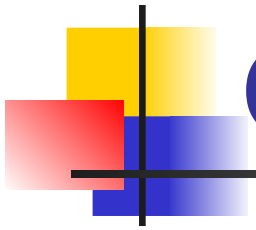
BioPath Project





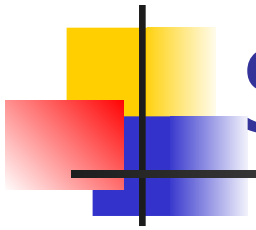
Electronic version
BioPath

Project partners: University of Erlangen
University of Mannheim
University of Passau
Spektrum Verlag Heidelberg



Overview

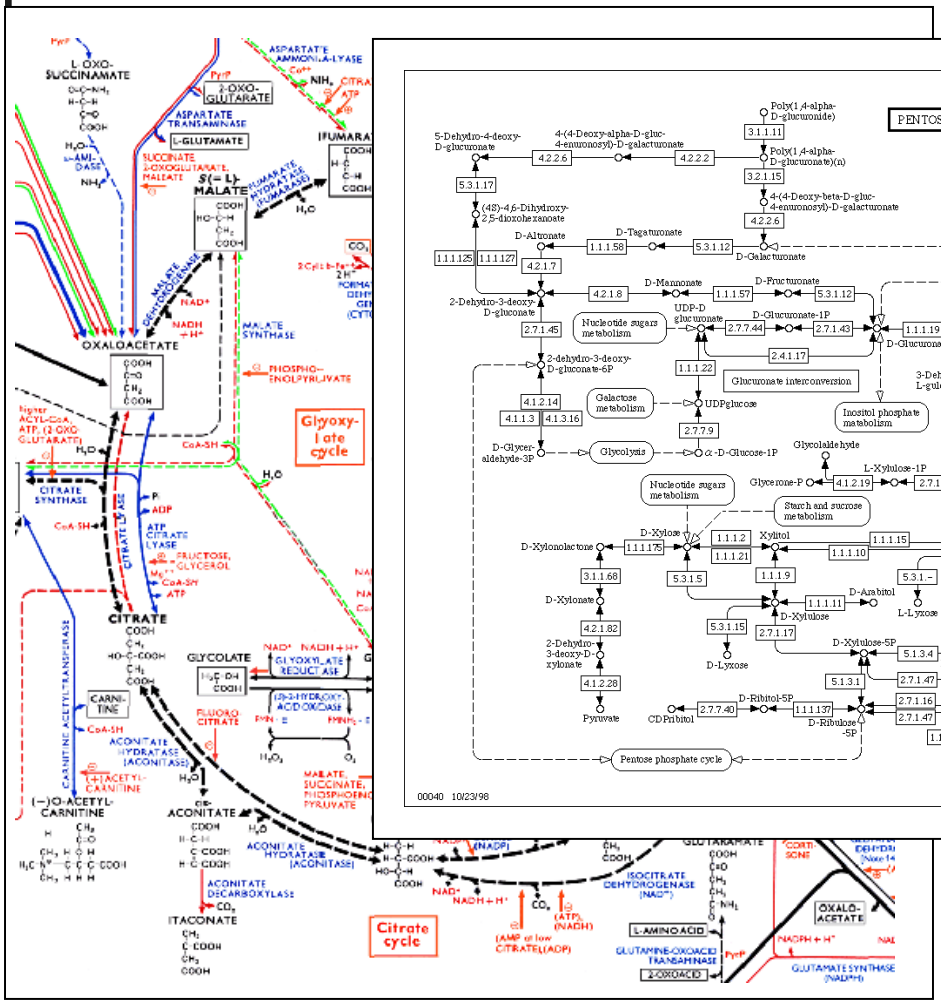
- Visualization of Pathways
  - Static vs. dynamic visualization
  - Requirements
  - Solutions: Modeling & Algorithms
  - Results
- BioPath Prototype
  - System architecture
  - Screenshots
- Perspectives

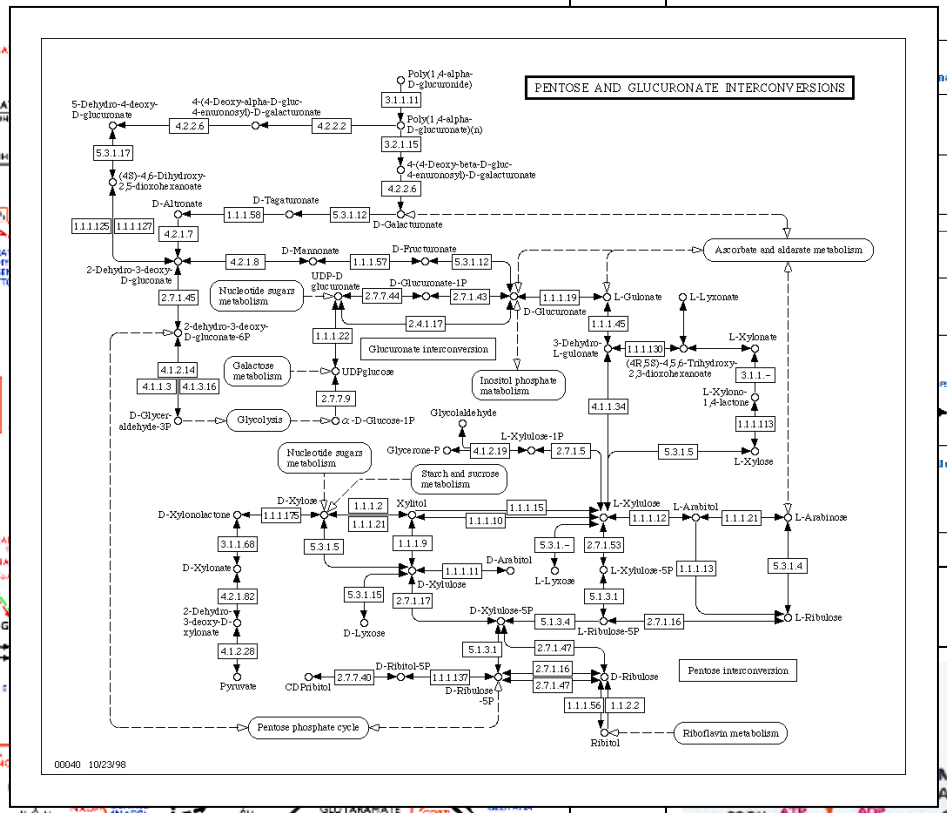


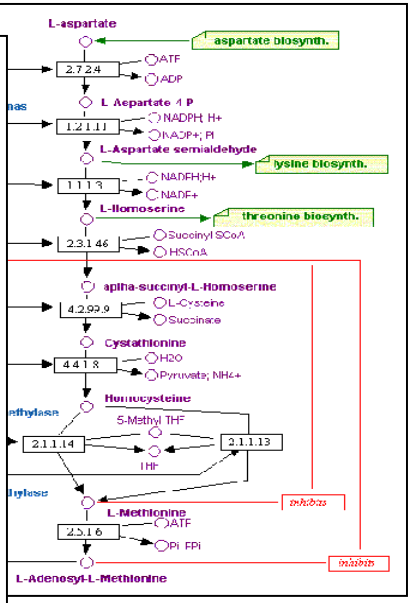
State of the Art

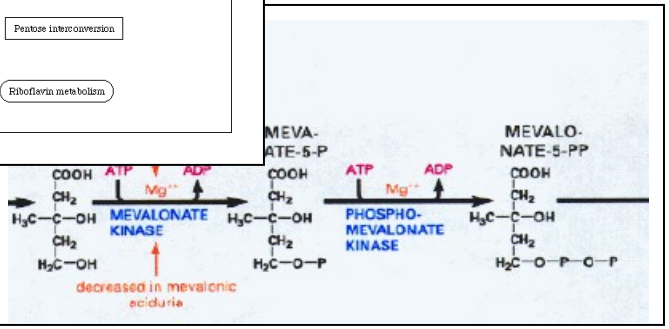
- Static visualization
- Manually produced drawings
  - Produced once
  - Used many times
  - Not changeable
- Used in
  - Biochemistry books
  - Boehringer Poster “Biochemical Pathways”
  - Electronic systems (KEGG, ExPASy, PUMA)

Static Visualization Examples



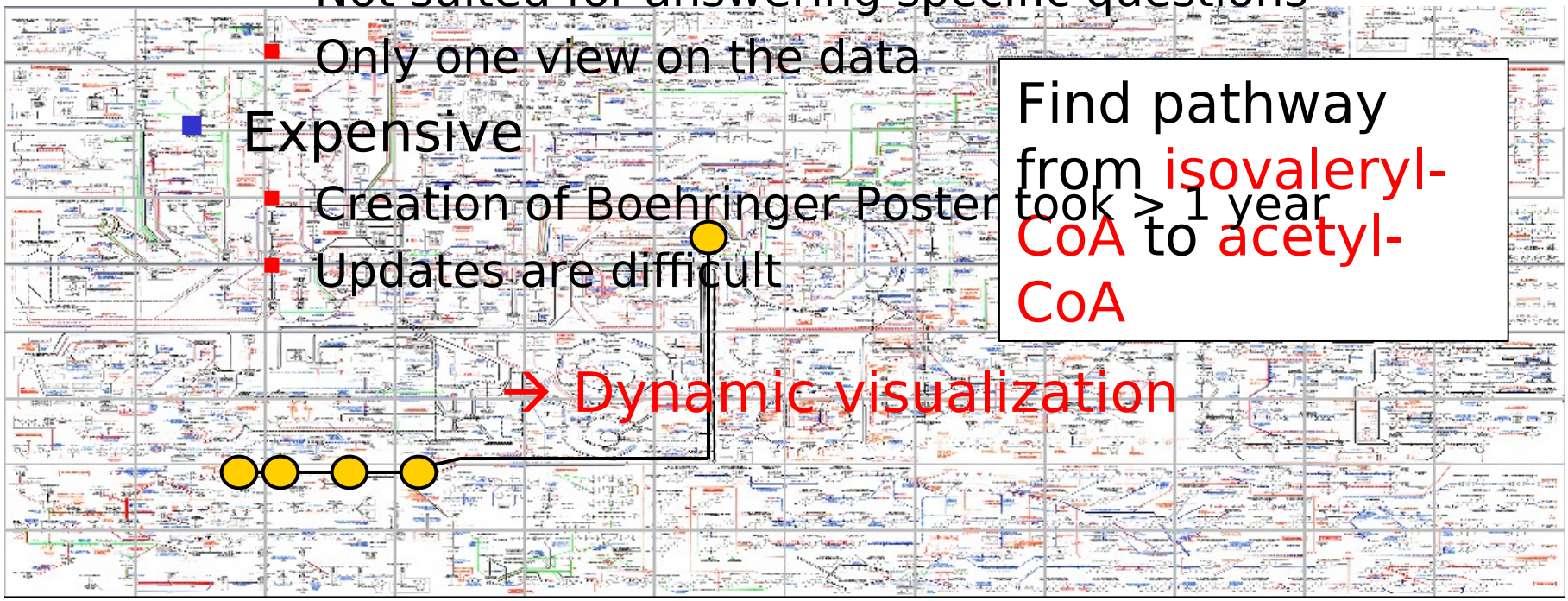


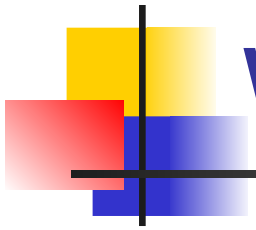




Static Visualization Problems

- Very complex
  - Information overflow
  - Hard to find information (even with an index)
  - Not suited for answering specific questions
  - Only one view on the data
- Expensive
  - Creation of Boehringer Poster took > 1 year
  - Updates are difficult

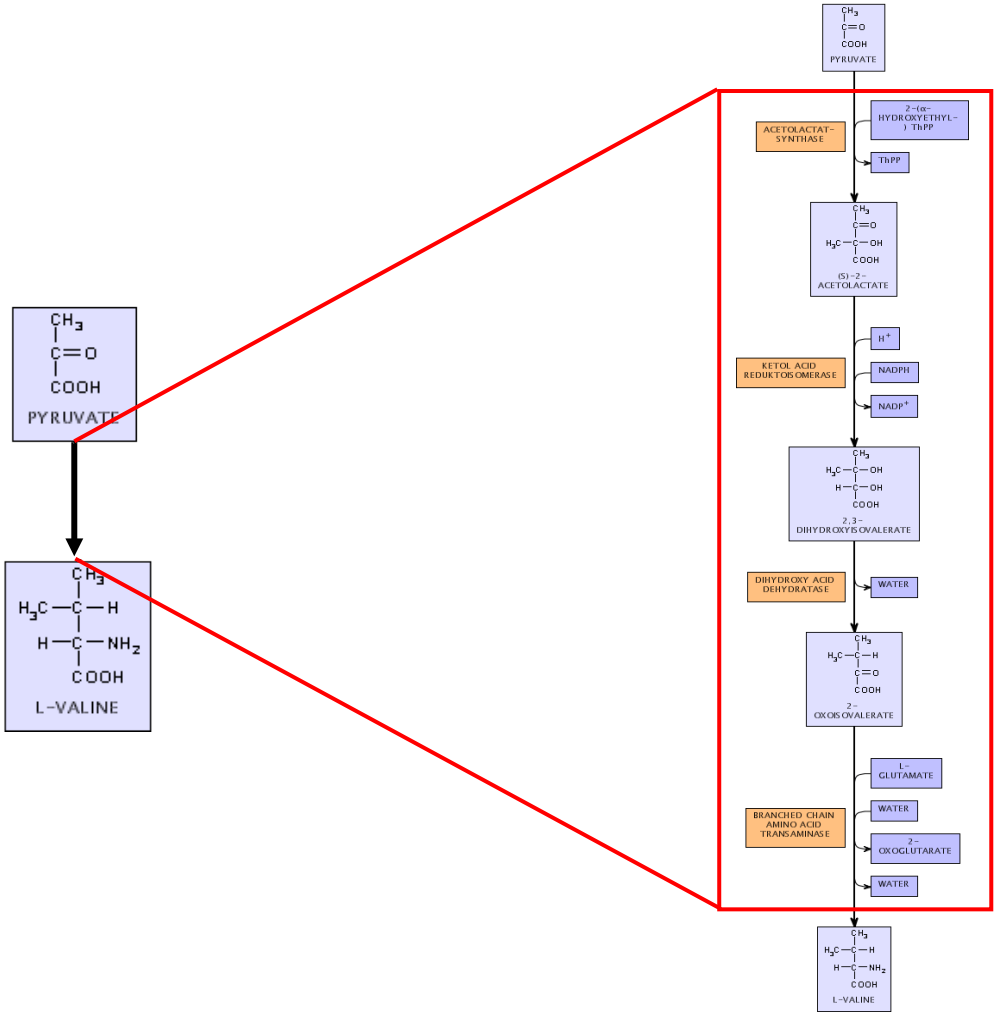




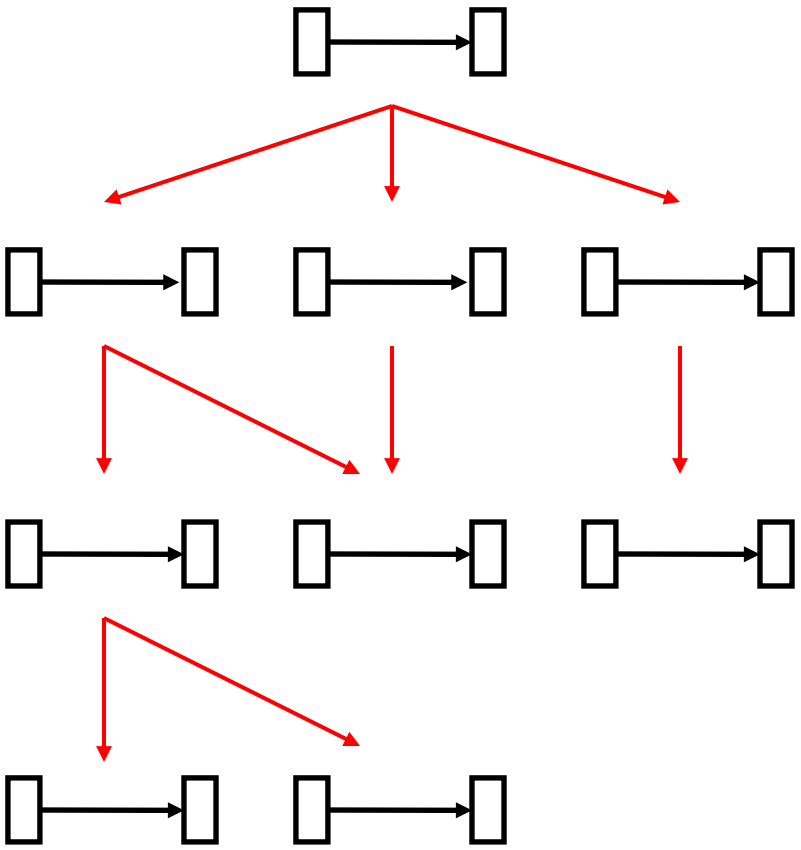
Wishes

- Interactive Navigation
- Arbitrary views on the data
  - Part of the network
  - Part of the available information
  - Different levels of detail

Pathway Hierarchy



Pathway Hierarchy



Metabolism

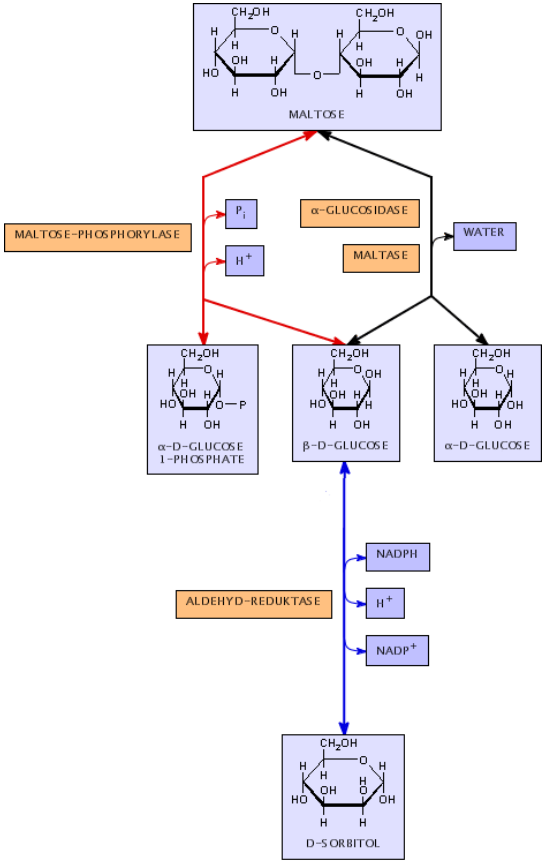
Pathways

Reactions

Reaction mechanisms

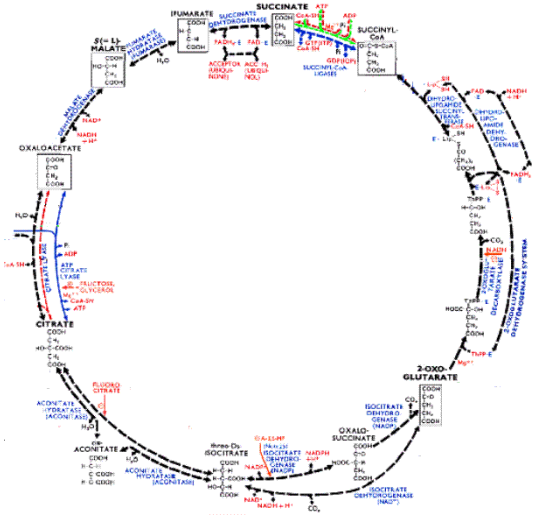
Visualization Requirements

- Substances, co-substances, enzymes
  - Text and/or images
- Reactions
  - Substances: start/end of reaction arrow
  - Enzymes: along reaction arrow
  - Co-substances: along reaction arrow, according to chemical order
- Reaction networks
  - Distinct Direction
  - Predefined layout of special pathway structures

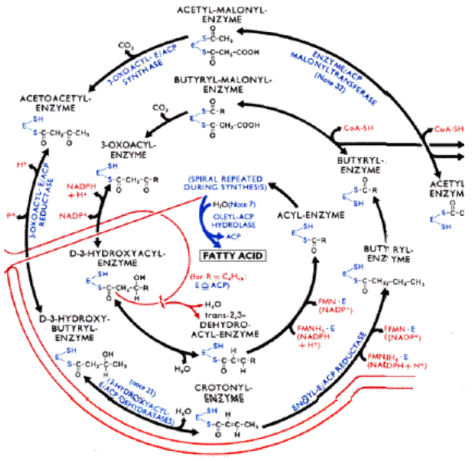


Special Pathway Structures

- Closed Cycles
  - Sequence of related reactions
  - Product is equal to educt

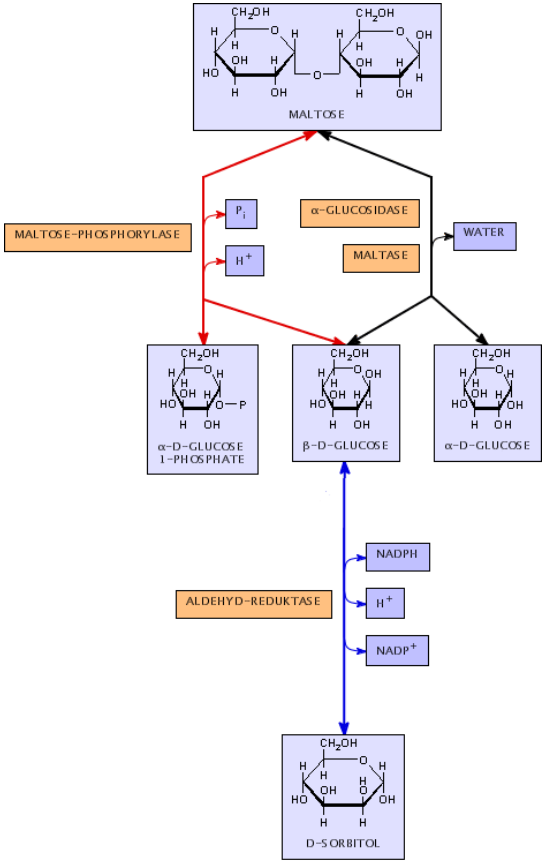


- Open Cycles
  - Sequence of related reactions
  - Product is similar to educt

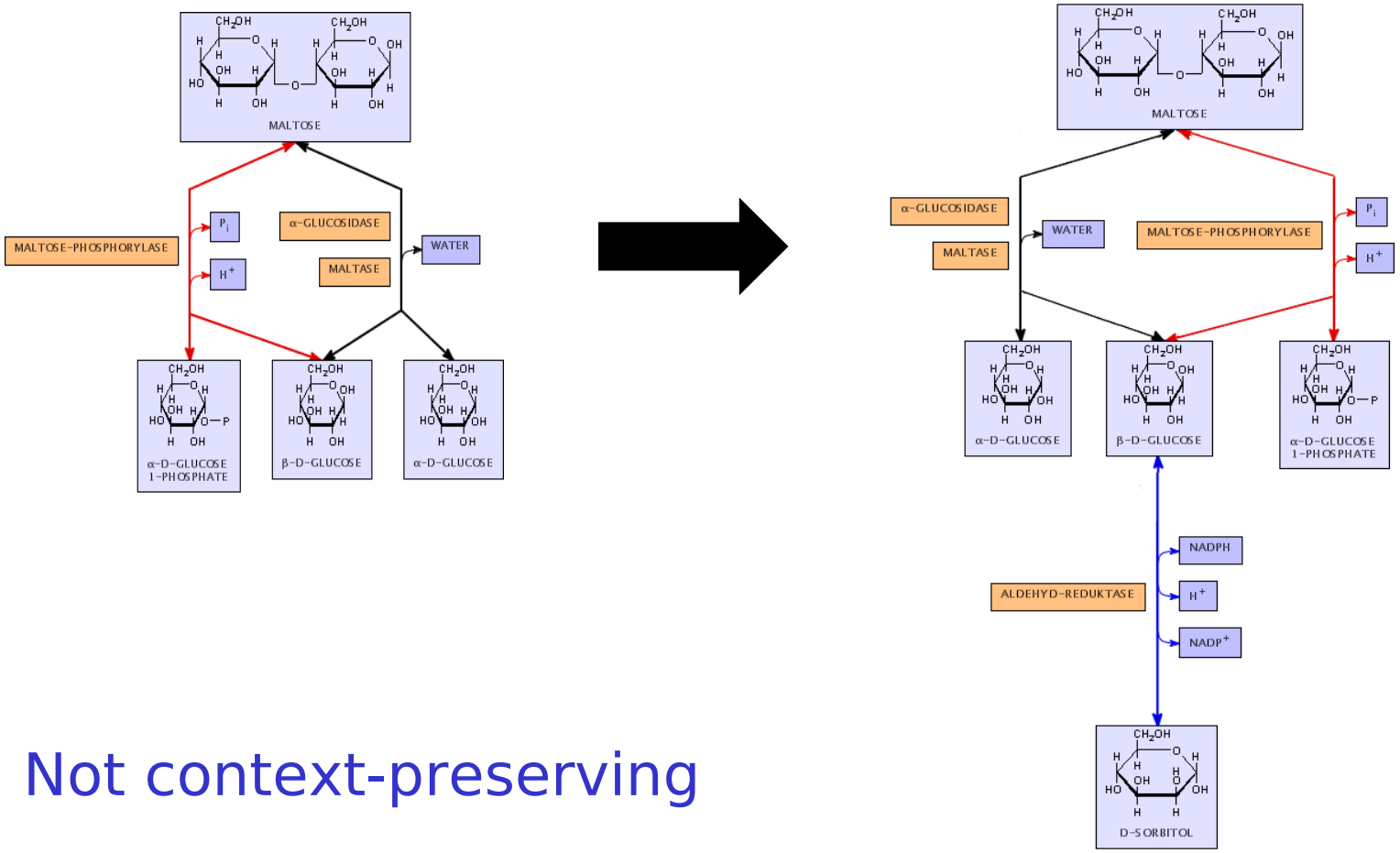


Drawing Conventions

- Substances, co-substances, enzymes
  - Text and/or images
- Reactions
  - Substances: start/end of reaction arrow
  - Enzymes: along reaction arrow
  - Co-substances: along reaction arrow, according to chemical order
- Reaction networks
  - Distinct Direction
  - Predefined structures of special pathway structures (e. g. citrate cycle)
- Sequences of networks
  - Context-preserving layouts

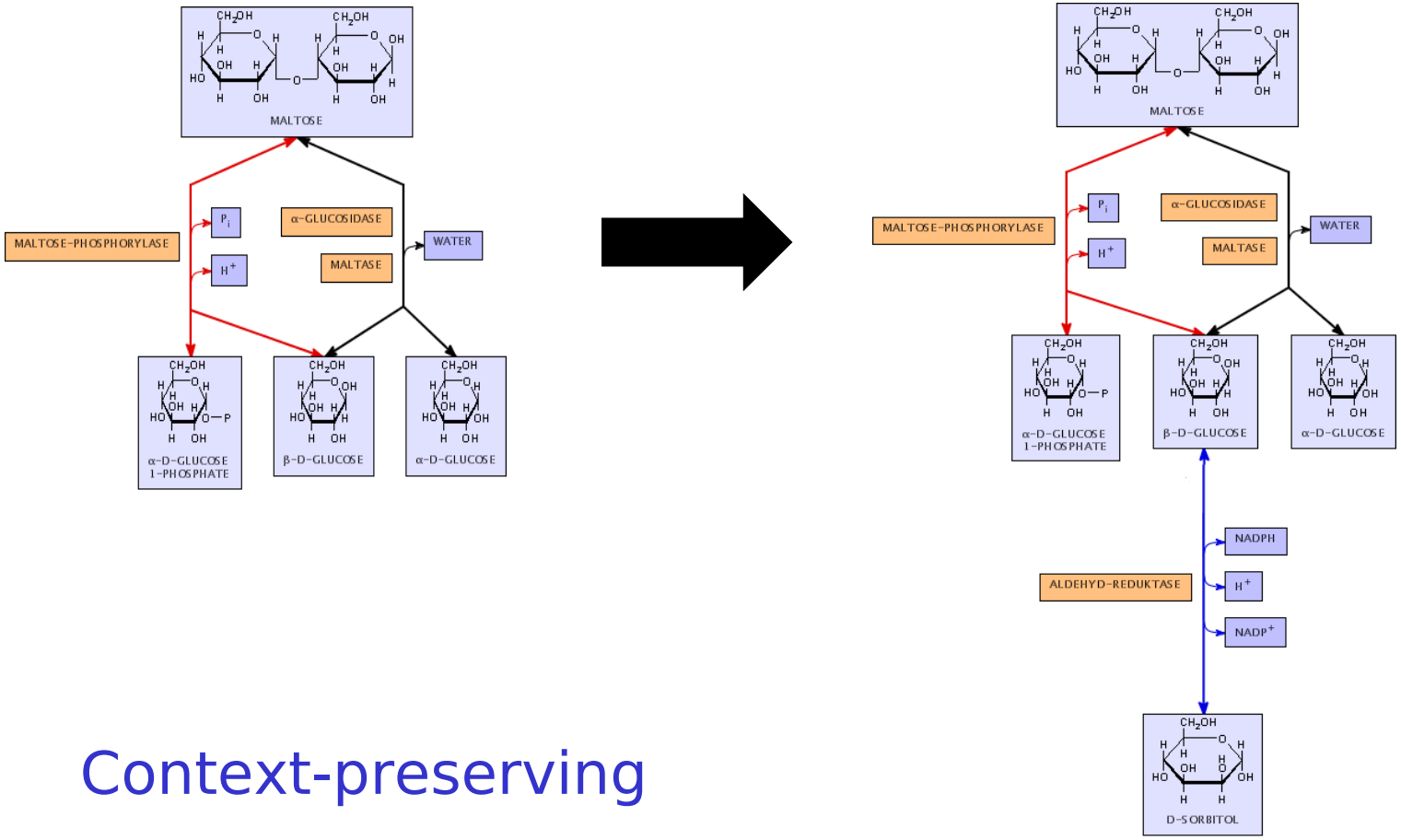


Context Preservation



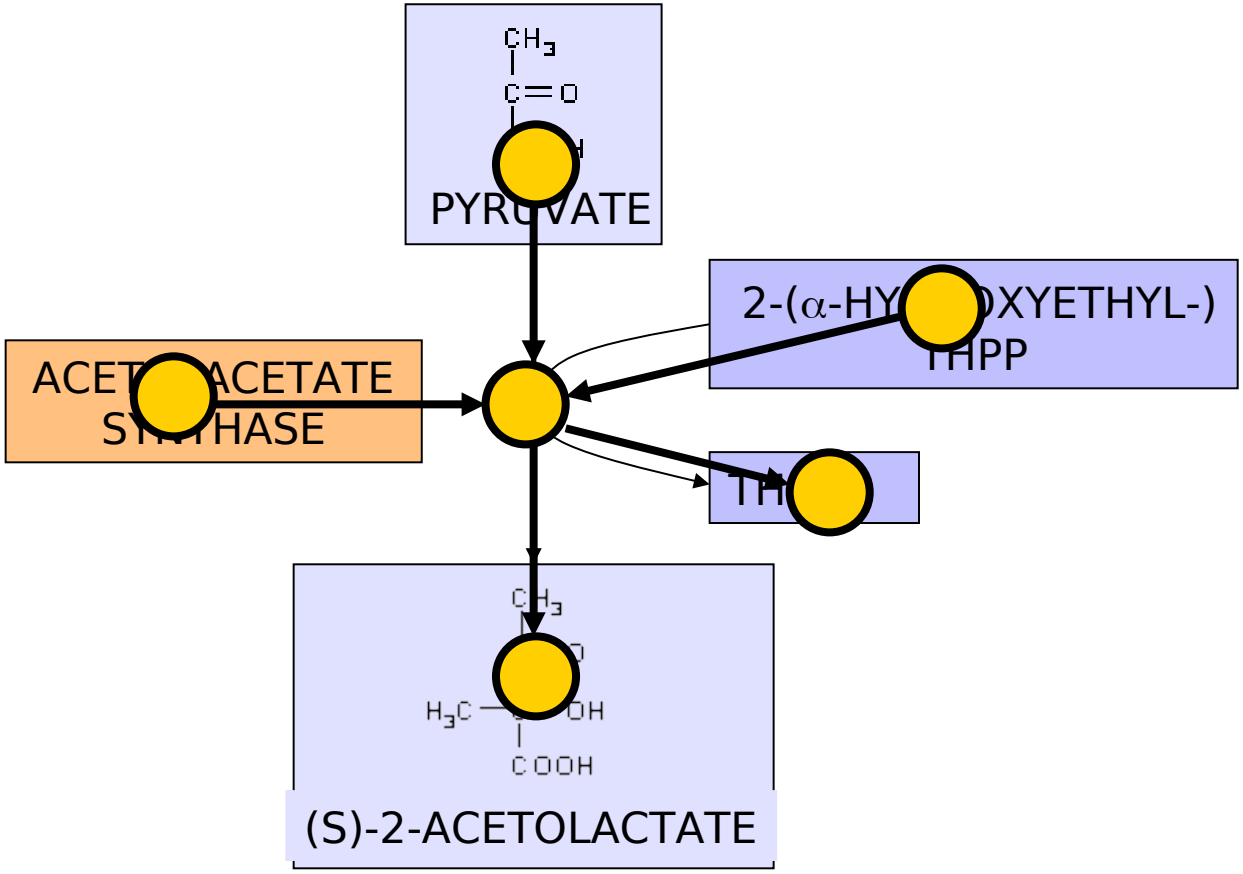
Not context-preserving

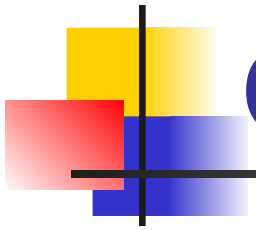
Context Preservation



Context-preserving

Modeling of Reactions

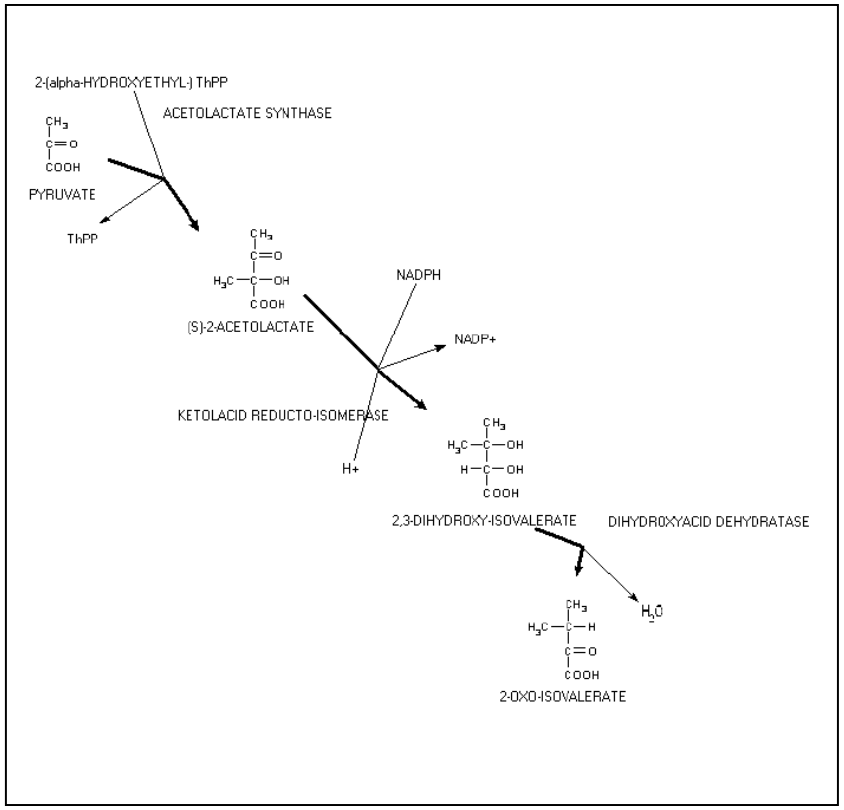


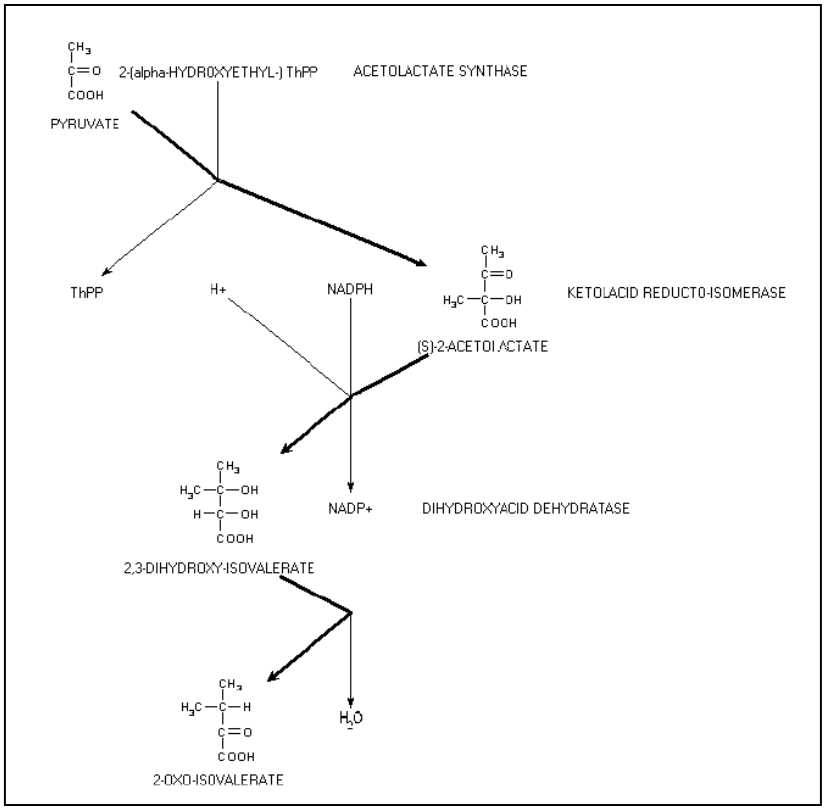


Graph Drawing

- Given: Graph
- Wanted: “Nice” Drawing
  - Node positions
  - Edge routing
- Several standard algorithms
  - Force directed (Spring Embedder)
  - Hierarchical (Sugiyama)
  - Specialized Algorithms for
    - Trees
    - Planar Graphs
    - Other special classes of graphs

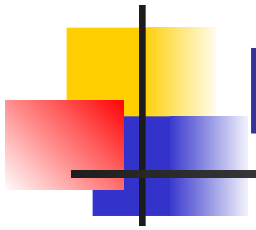
Standard Algorithms





Spring Embedder

Sugiyama

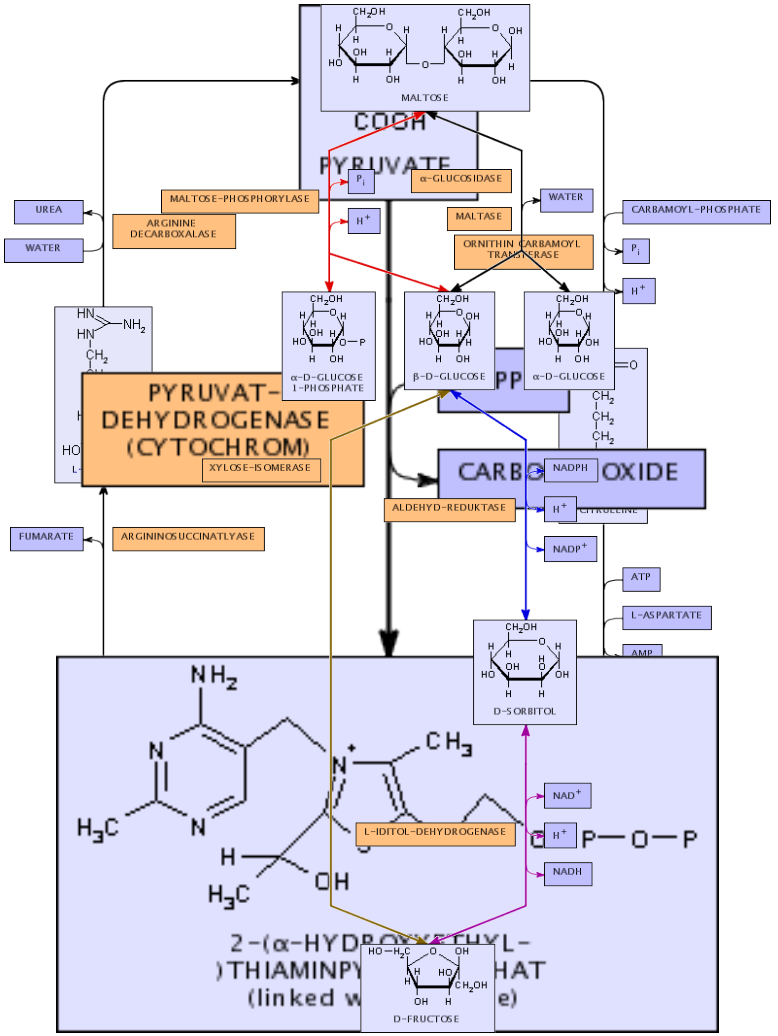


New Algorithm

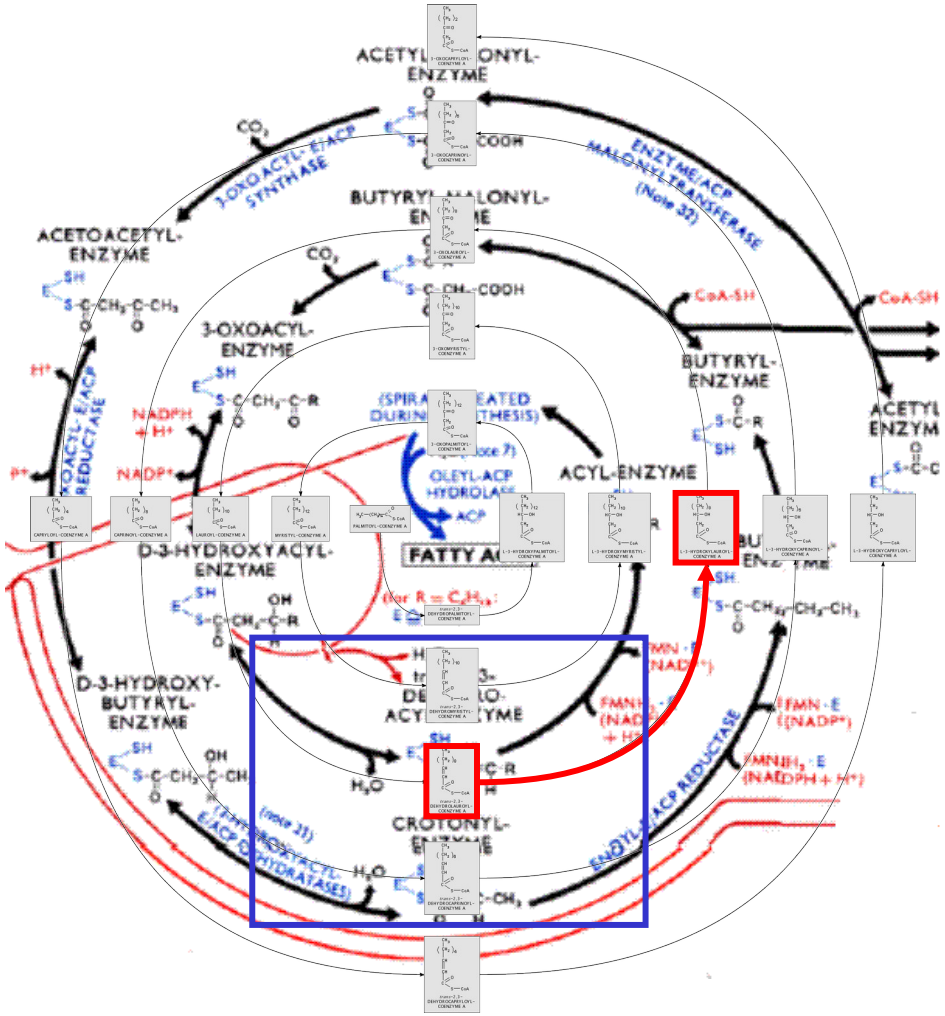
- Too technical for presentation here
  - Several problems proven to be NP-hard
  - Efficient heuristics
- Extension of Sugiyama algorithm
  - Arbitrary node sizes
  - Layout constraints
    - Special pathway structures
    - Context preservation

Results

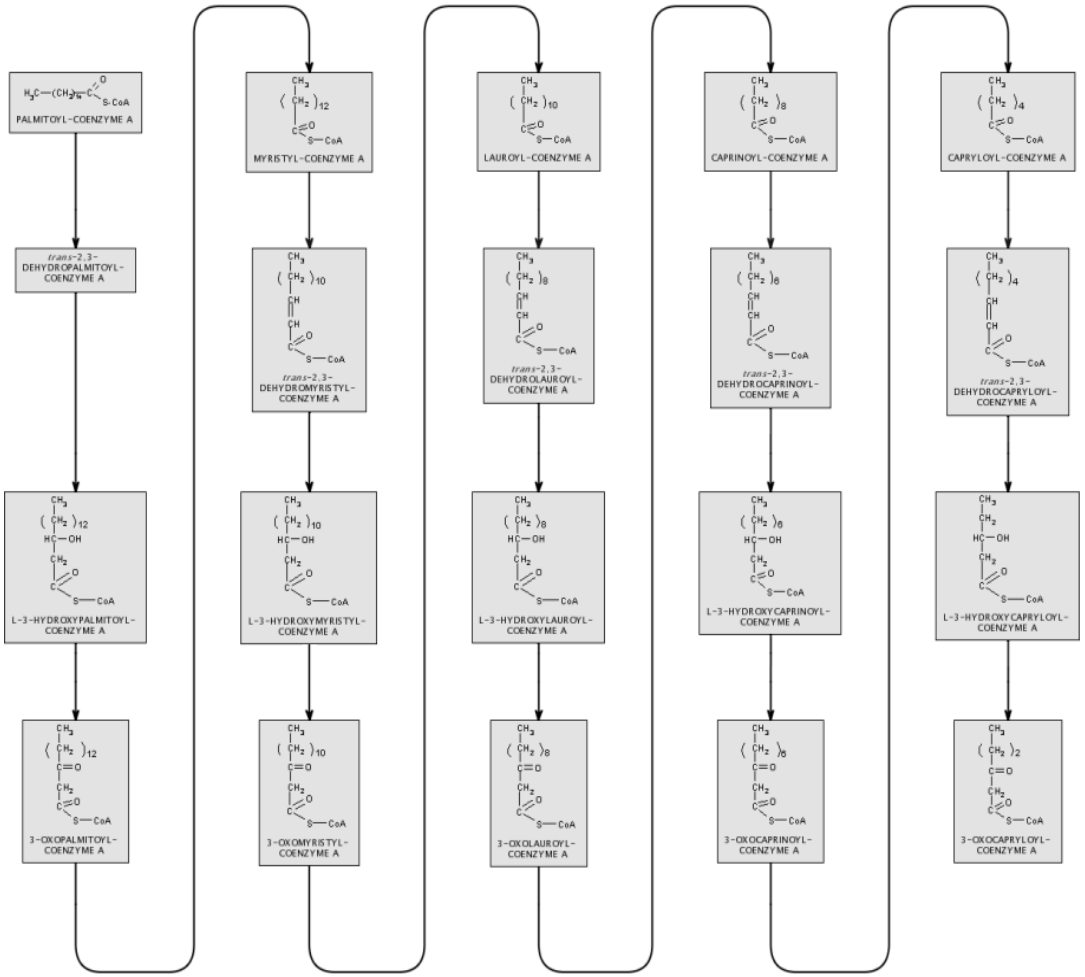
- Reactions
- Reaction networks
  - closed cycles
  - open cycles



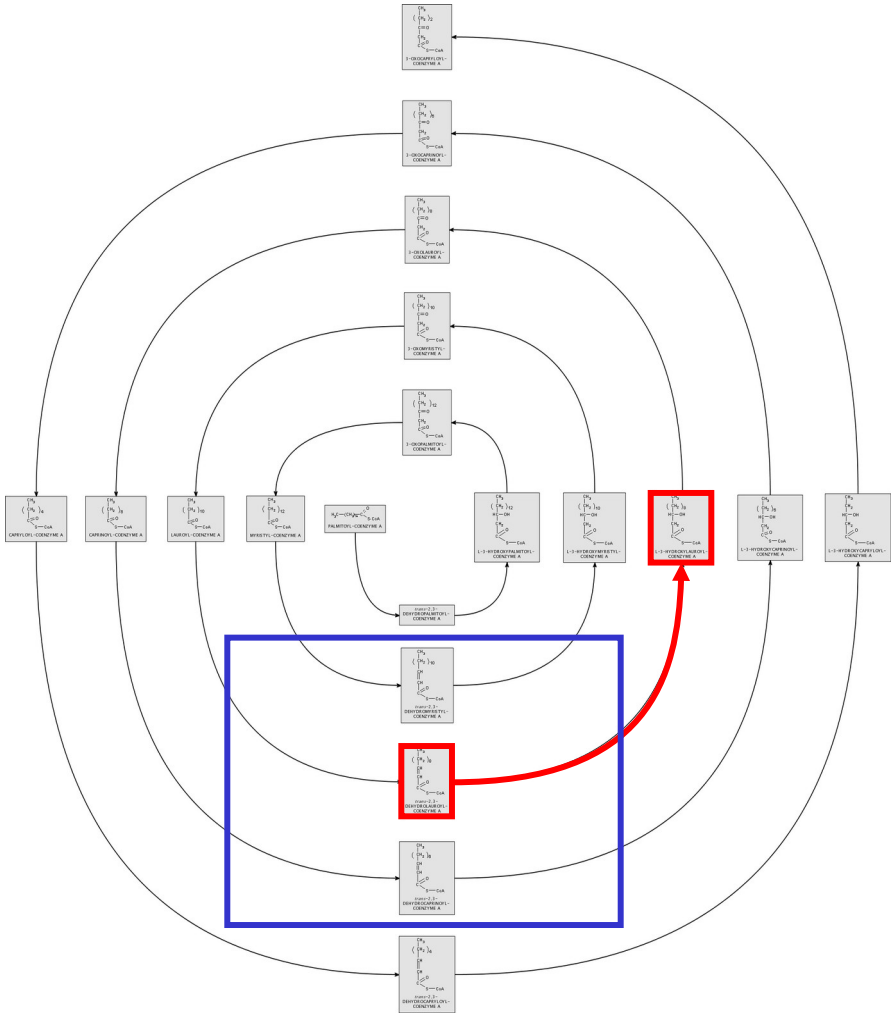
Results - Open Cycles

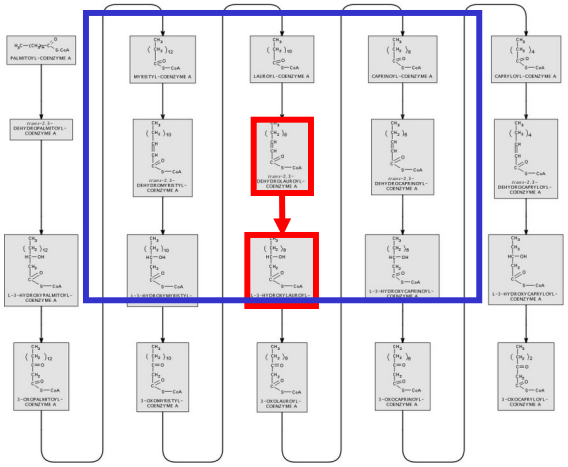


Results - Open Cycles



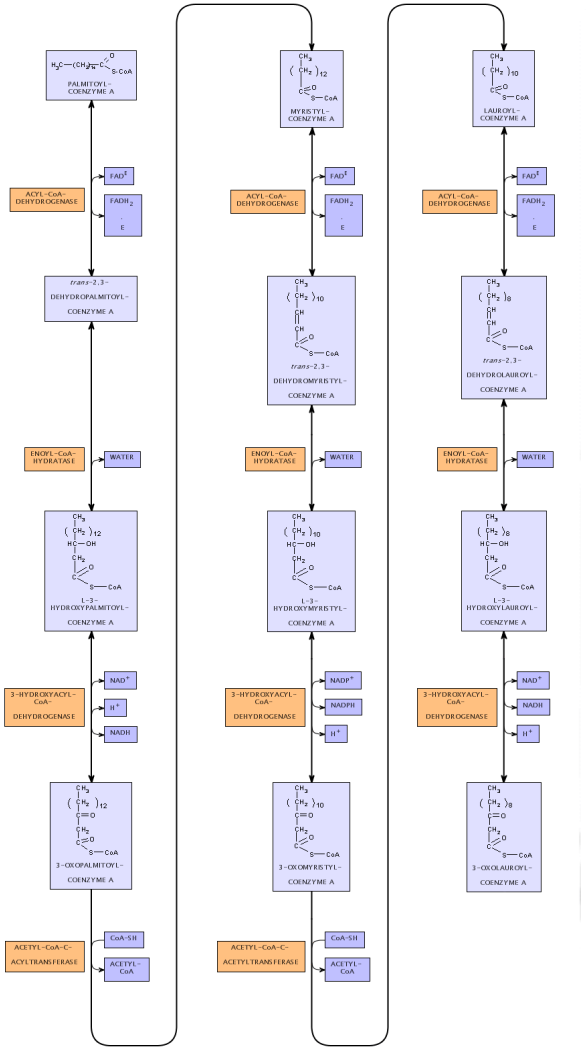
Results - Open Cycles





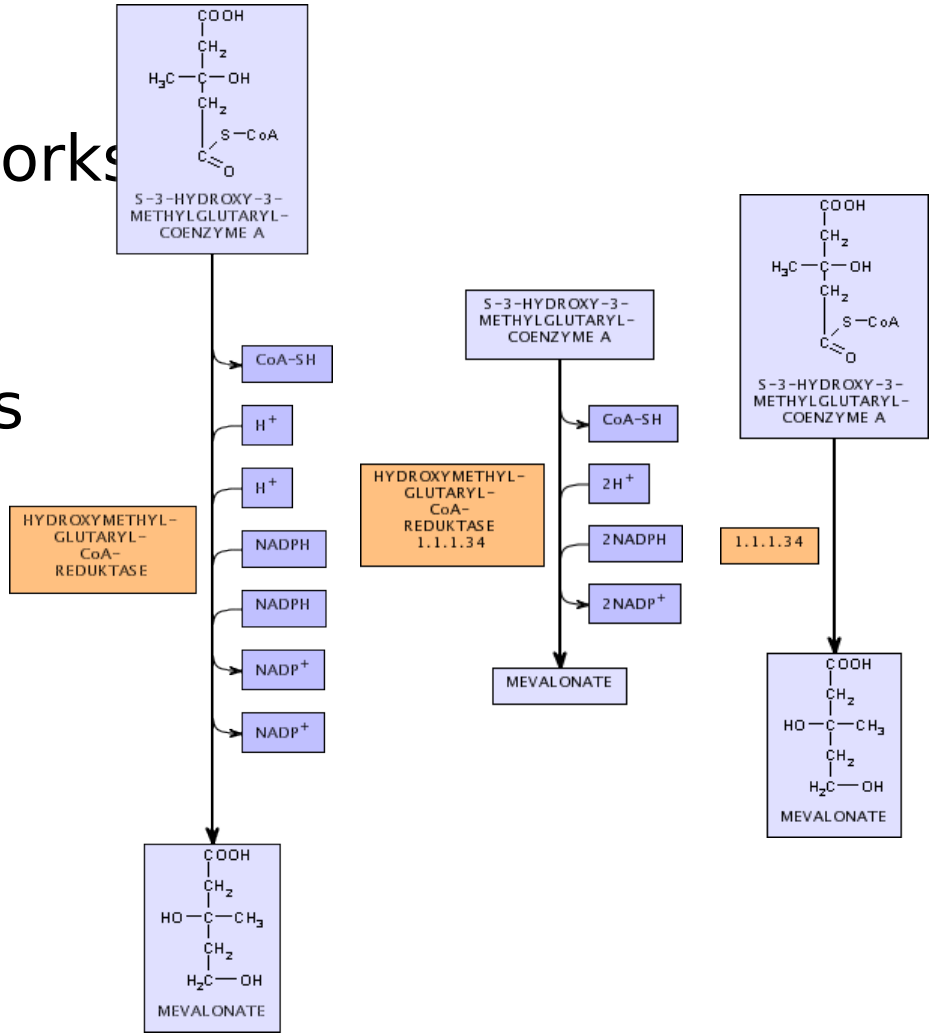
Results

- Reactions
- Reaction networks
  - closed cycles
  - open cycles



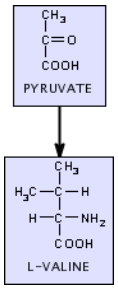
Results

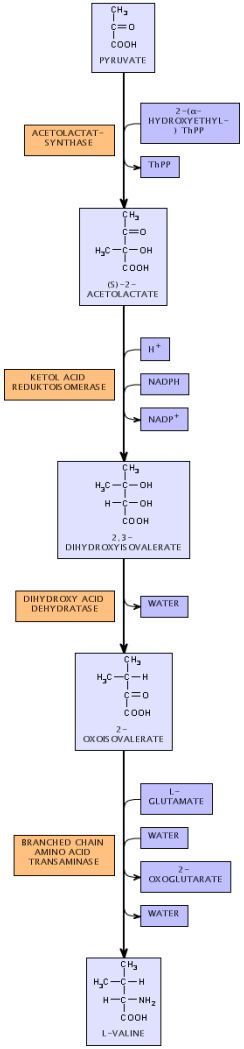
- Reactions
- Reaction networks
  - closed cycles
  - open cycles
- Different views



Results

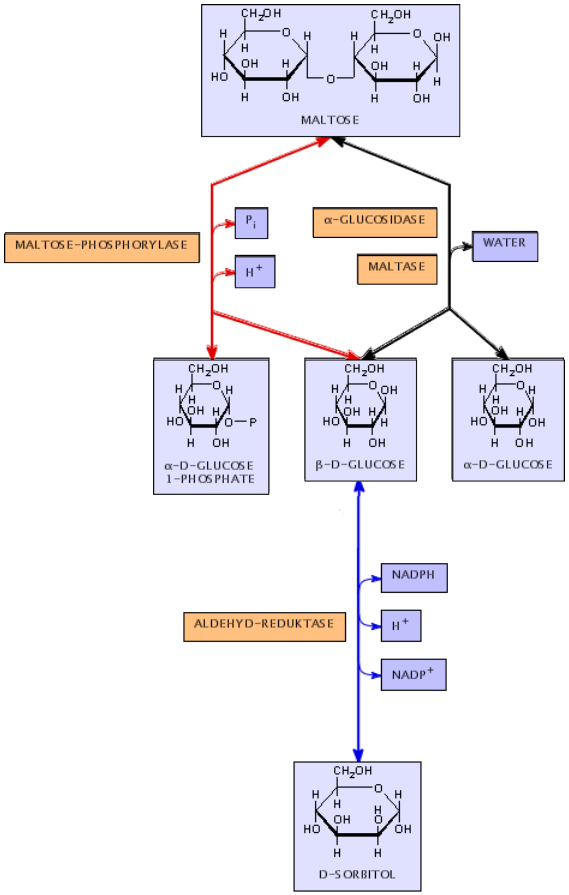
- Reactions
- Reaction networks
  - closed cycles
  - open cycles
- Different views
- Different levels of detail





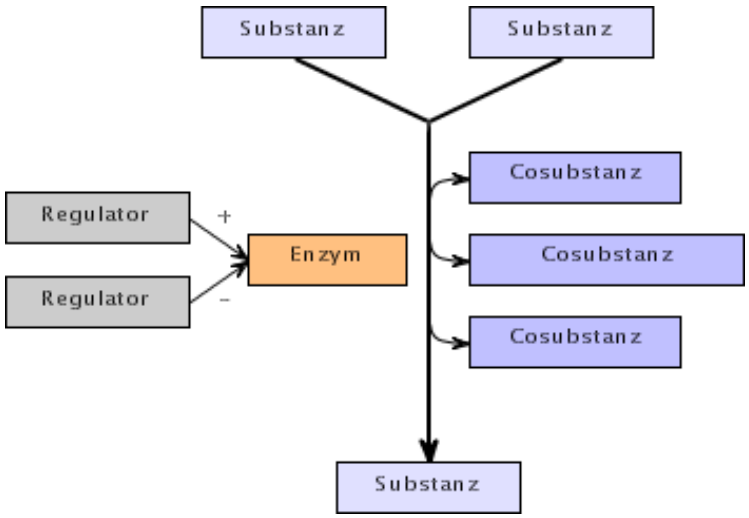
Results

- Reactions
- Reaction networks
  - closed cycles
  - open cycles
- Different views
- Different levels of detail
- Preserving the context



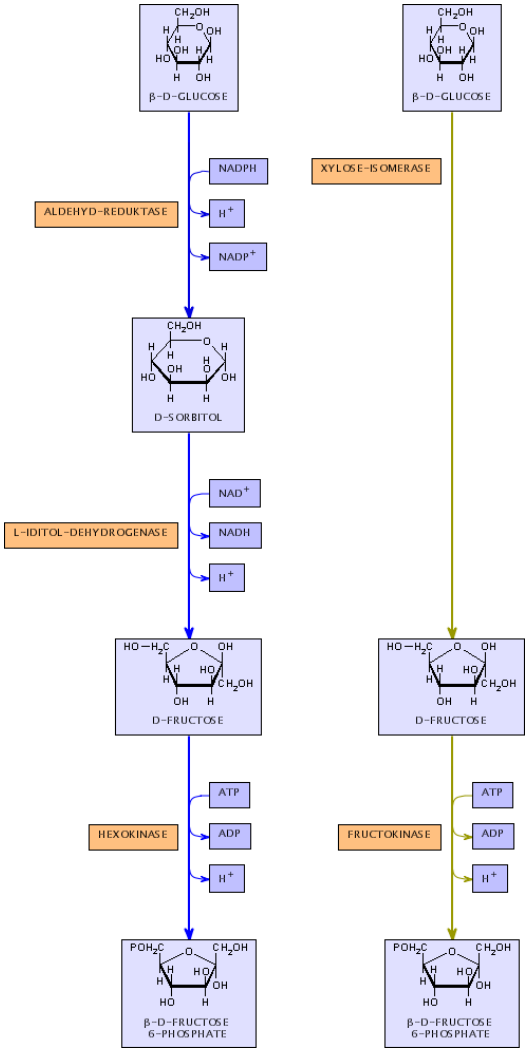
Results

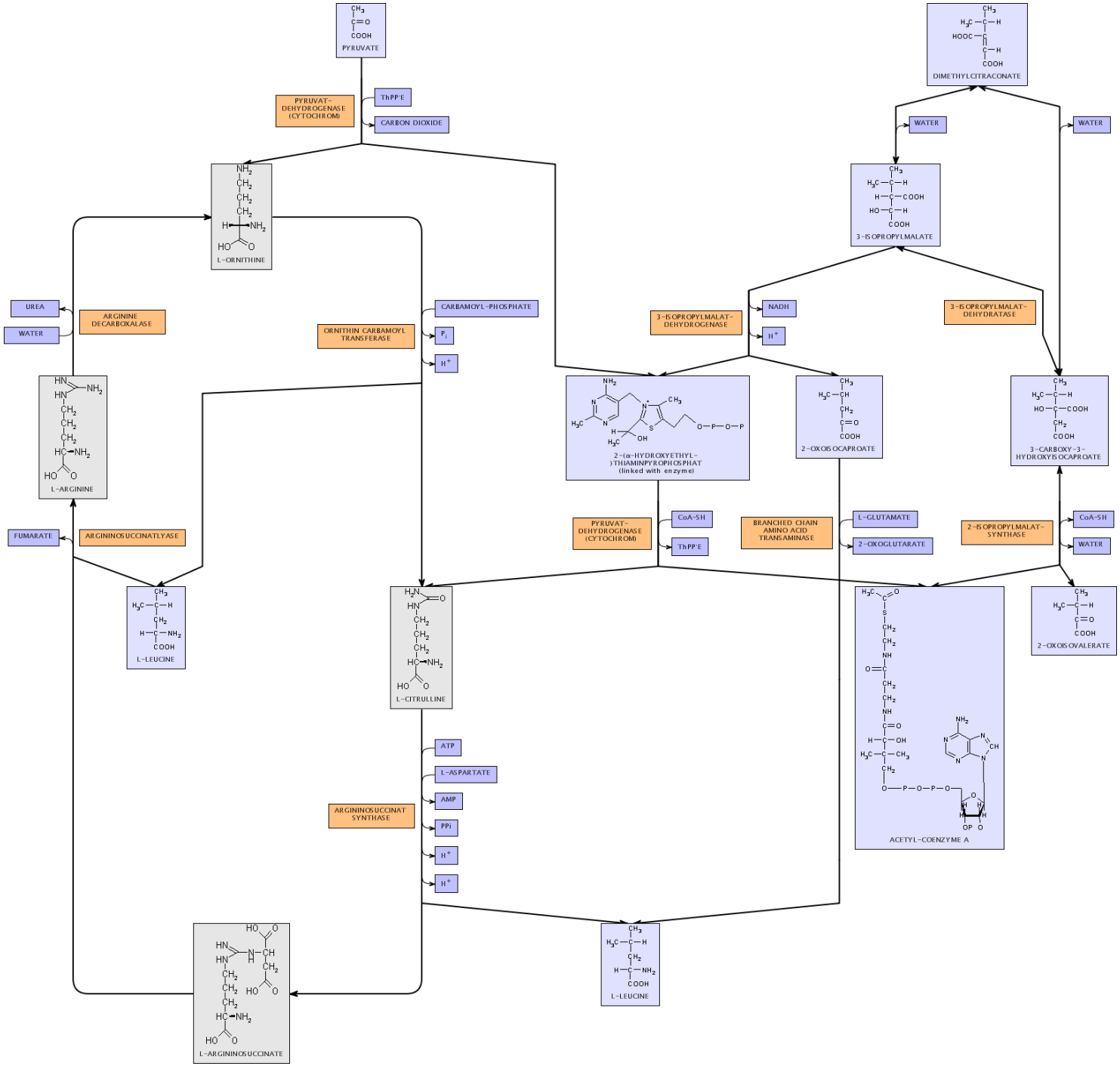
- Reactions
- Reaction networks
  - closed cycles
  - open cycles
- Different views
- Different levels of detai
- Preserving the context
- Extensible
  - new information



Results

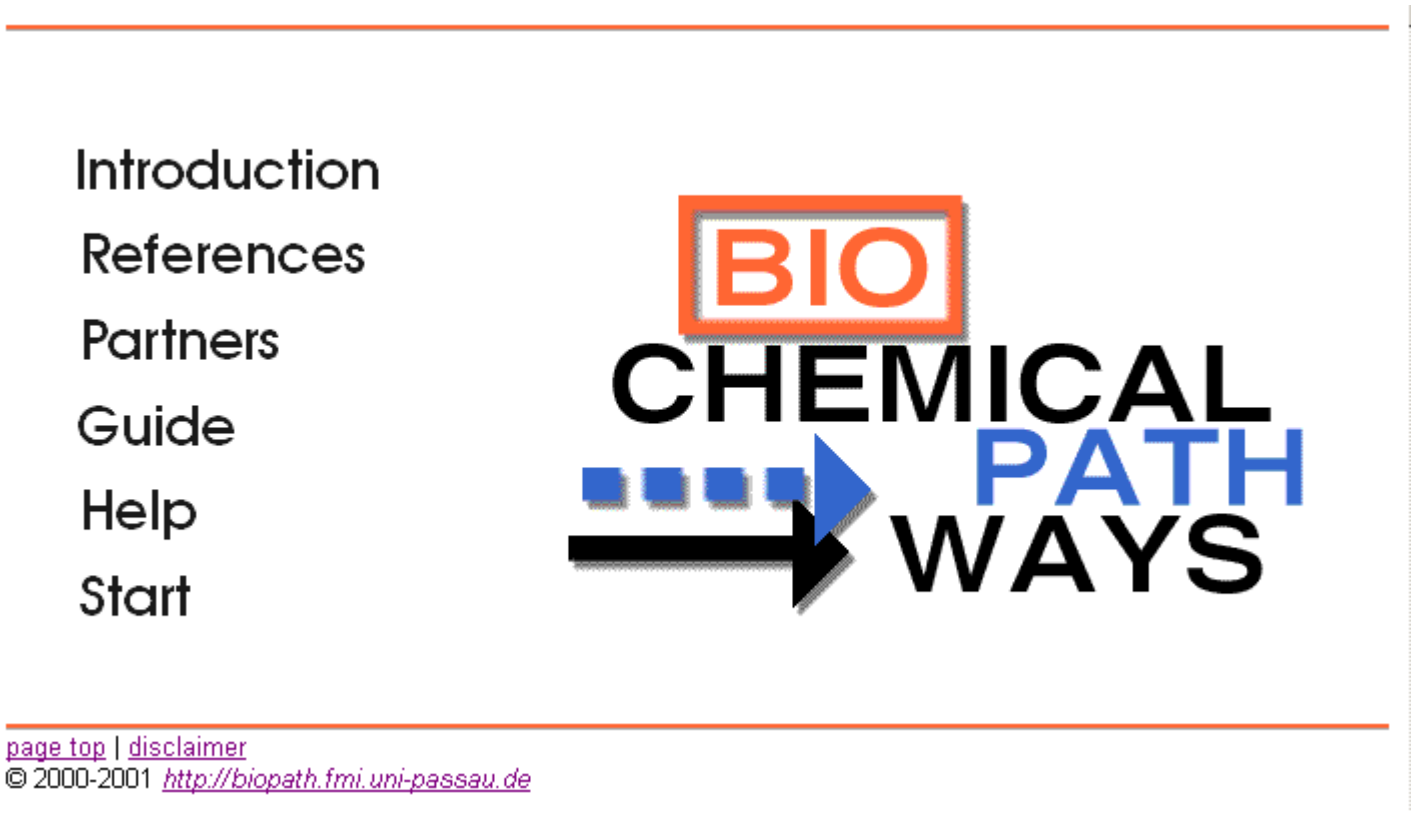
- Reactions
- Reaction networks
  - closed cycles
  - open cycles
- Different views
- Different levels of detail
- Preserving the context
- Extensible
  - new information
  - new applications



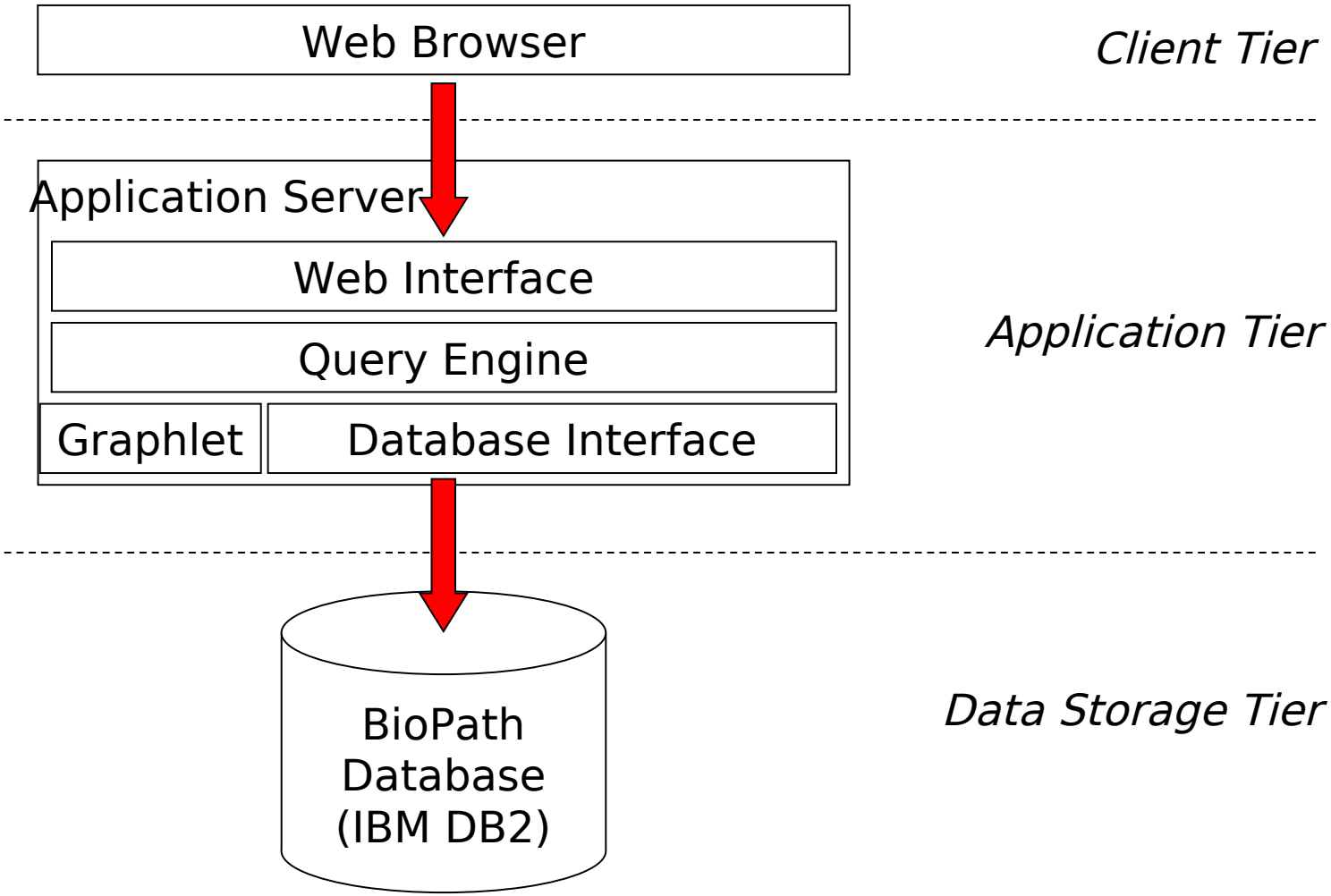

PYRUVATE
PYRUVAT-DEHYDROGENASE (CYTOCHROM)
ThPP'E
CARBON DIOXIDE
L-ORNITHINE
UREA
WATER
ARGININE DECARBOXALASE
L-ARGININE
FUMARATE
ARGININOSUCCINATLYASE
L-LEUCINE
CARBAMOYL-PHOSPHATE
ORNITHIN CARBAMOYL TRANSFERASE
Pi
H+
L-CITRULLINE
ATP
L-ASPARTATE
AMP
ARGININOSUCCINAT SYNTHASE
PPi
H+
H+
L-ARGININOSUCCINATE
DIMETHYLCITRACONATE
WATER
WATER
3-ISOPROPYLMALATE
3-ISOPROPYLMALAT-DEHYDROGENASE
NADH
H+
3-ISOPROPYLMALAT-DEHYDRATASE
2-(α-HYDROXYETHYL-)THIAMINPYROPHOSPHAT (linked with enzyme)
2-OXOISOCAPROATE
3-CARBOXY-3-HYDROXYISOCAPROATE
PYRUVAT-DEHYDROGENASE (CYTOCHROM)
CoA-SH
ThPP'E
BRANCHED CHAIN AMINO ACID TRANSAMINASE
L-GLUTAMATE
2-OXOGLUTARATE
2-ISOPROPYLMALAT-SYNTHASE
CoA-SH
WATER
2-OXOISOVALERATE
ACETYL-COENZYME A
L-LEUCINE

BioPath Prototype

http://biopath.fmi.uni-passau.de/



System Architecture



BioPath Prototype

BIO CHEMICAL PATH WAYS

OVERVIEW | SUBSTANCE | REACTION | REACTION NET | HELP

Search Reaction Net

From: ISOVALERYL-COENZYME A

To: ACETYL-COENZYME A

Pathways:
- ○ Search in one pathway only
- ◉ Search across pathway borders

Search depth: 10

Search Reaction Net

page top | disclaimer

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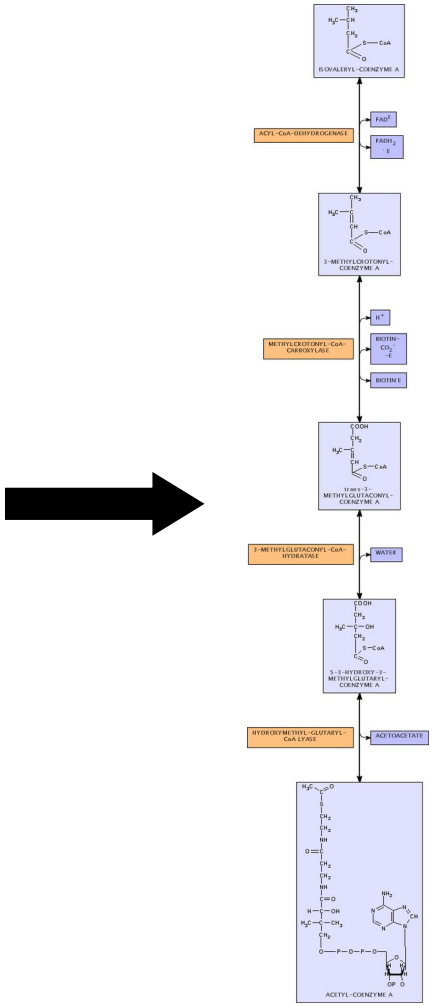
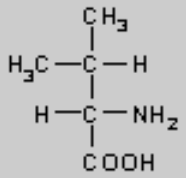
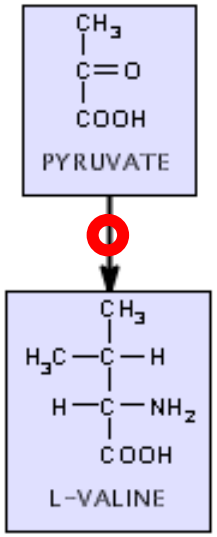


BioPath - Substances

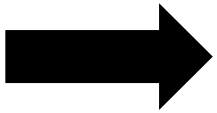
Names	L-VALINE [English] L-VALIN [Deutsch]
Structural Formula	
Empirical Formula	$C_5H_{11}NO_2$
Weight	117.147
Total Charge	0
Reactions	Biosynthesis of L-VALINE Degradation of L-VALINE 2-OXOISOVALERATE ---> L-VALINE {L-VALINE, L-VALYL-tRNA}

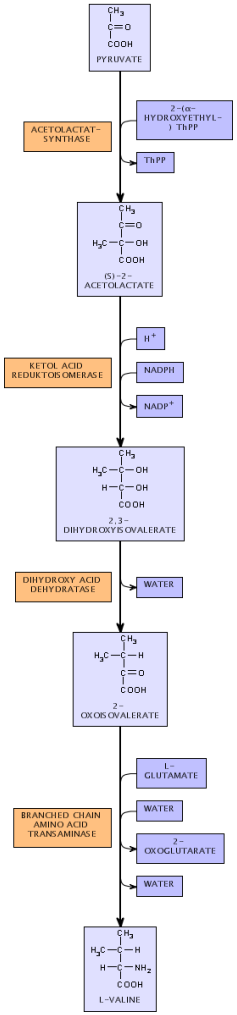
BioPath - Reactions

Names	Biosynthese von L-VALIN [Deutsch] Biosynthesis of L-VALINE [English]
Parents	Branched chain amino acids



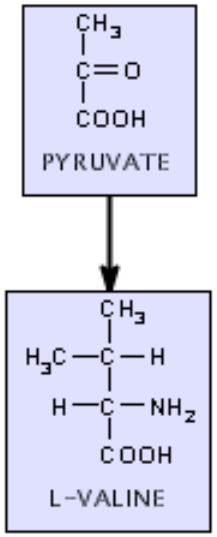
Navigation



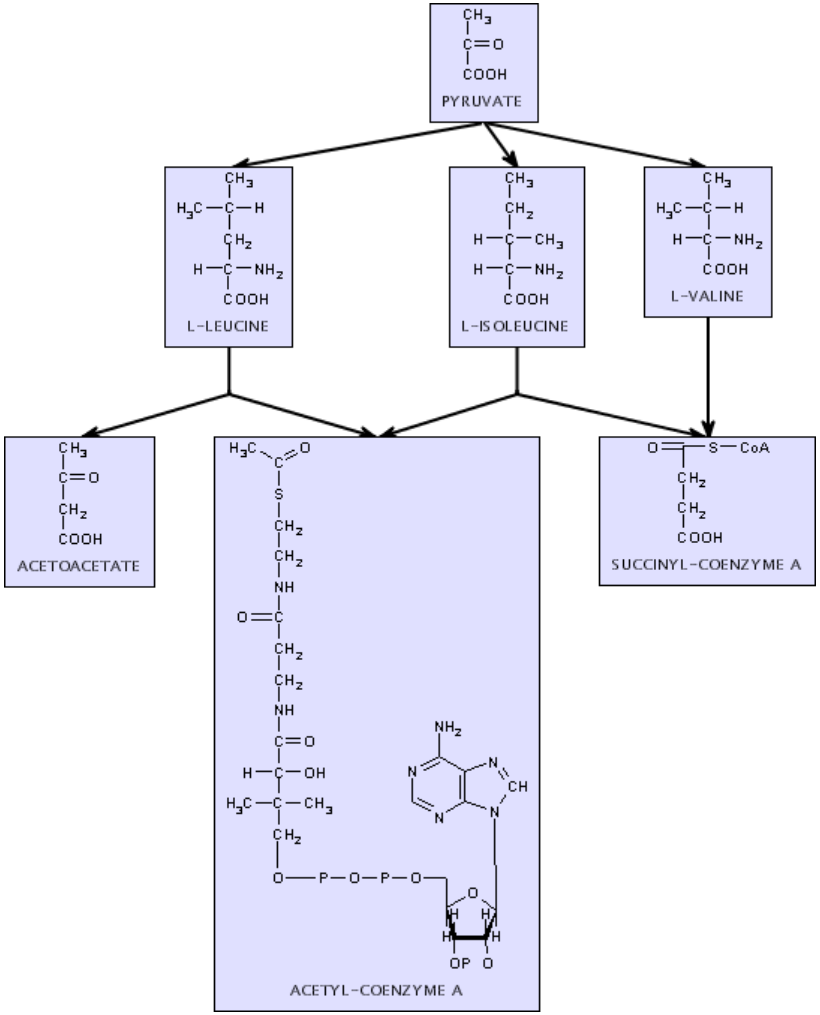


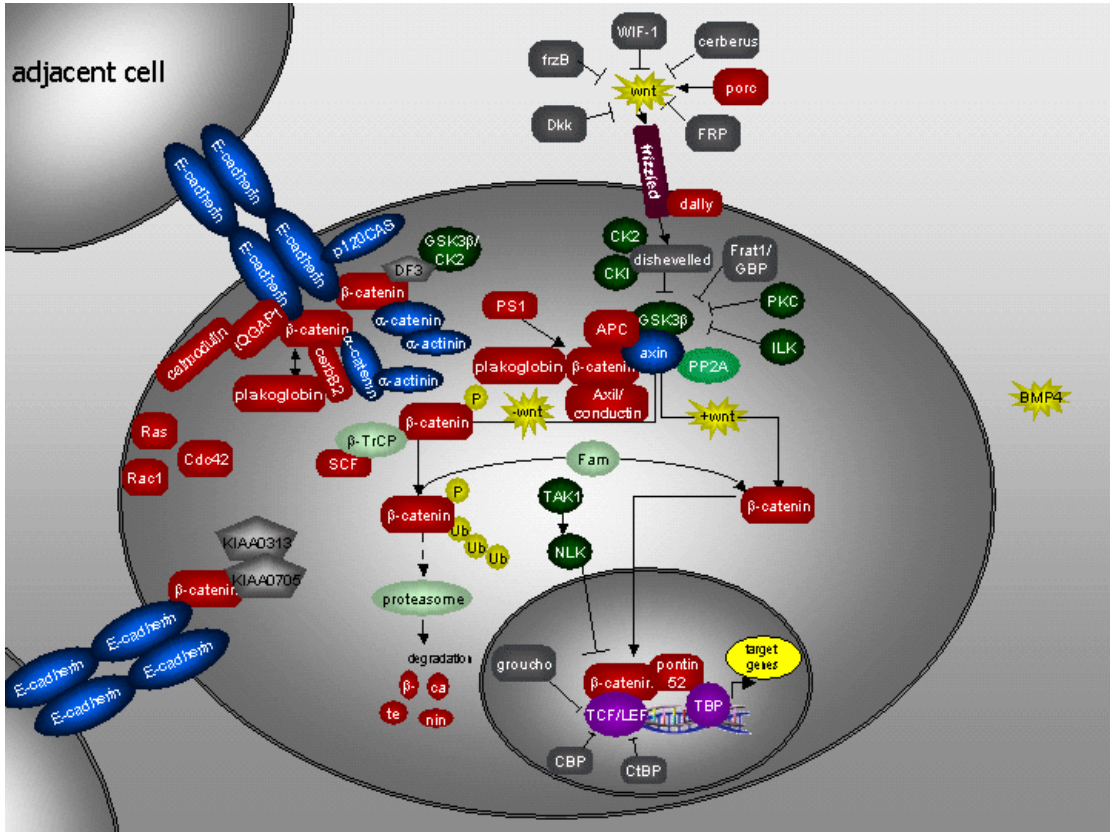
BioPath - Reactions

Names	Biosynthese von L-VALIN [Deutsch] Biosynthesis of L-VALINE [English]
Parents	Branched chain amino acids



Navigation



Perspective

- Signal pathways
- Static visualization example (TRANSPATH