Abduktivní logické programování a modelování metabolických sítí

Abduction

- *Abductive reasoning* is a form of logical inference which goes **from an observation to a theory** which accounts for the observation, ideally seeking to find the simplest and most likely explanation.
  - copied from Wikipedia

ABL

- Abductive logic theory: *(P, A, IC)*
  - P – logický program v běžném smyslu
  - A – množina predikátů „abducible predicates“
  - IC – „integrity constraints“, množina formulí prvního řádů. Typicky ve formě:
    - false :- A1,...,An, not B1, ..., not Bm.

Úloha ABL

- Given an abductive logic theory *(P, A, IC)*, an abductive explanation for an observation *O,* is a set, Δ, of ground abducible atoms on the predicates *A*, such that:
  - $P \cup \Delta \models O$
  - $P \cup \Delta \models IC$
- Konsekvent ⊨ má stejnou sémantiku jako v logickém programování.

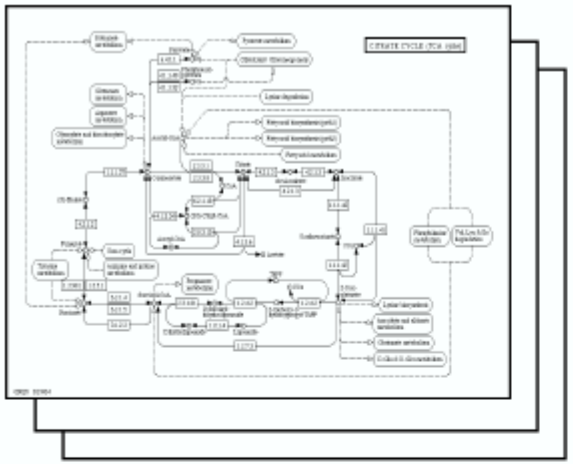
Příklad

- P =

  X is a citizen if X is born in the USA.
  X is a citizen if X is born outside the USA and X is a resident of the USA and X is naturalized.
  X is a citizen if X is born outside the USA and Y is the mother of X and Y is a citizen and X is registered.
  Mary is the mother of John.
  Mary is a citizen.

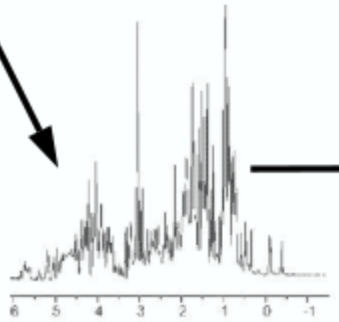
- A = {"is born in the USA", "is born outside the USA", "is a resident of the USA", "is naturalized", "is registered"}
- IC = {false if John is a resident of the USA.}
- O = {John is citizen}
  - Δ_1 = {John is born in the USA}
  - Δ_2 = {"John is born outside the USA", "John is registered"}

Aplikace – modelování inhibice

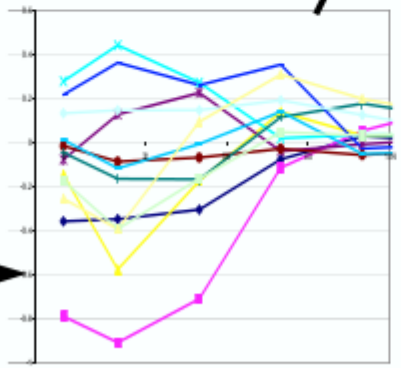


Metabolic diagrams (KEGG)

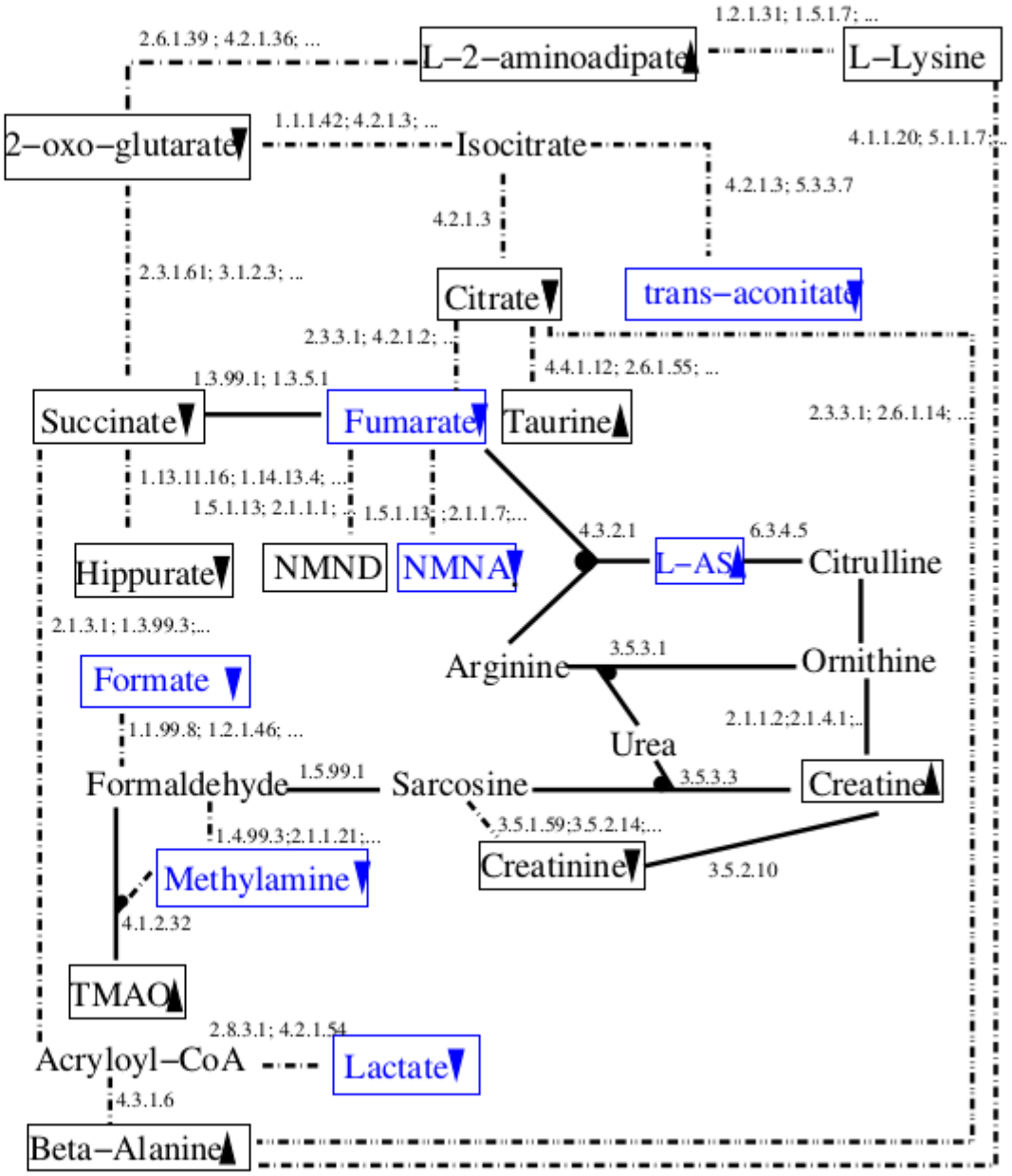
NMR spectrometer



NMR spectra



Concentrations of Metabolites



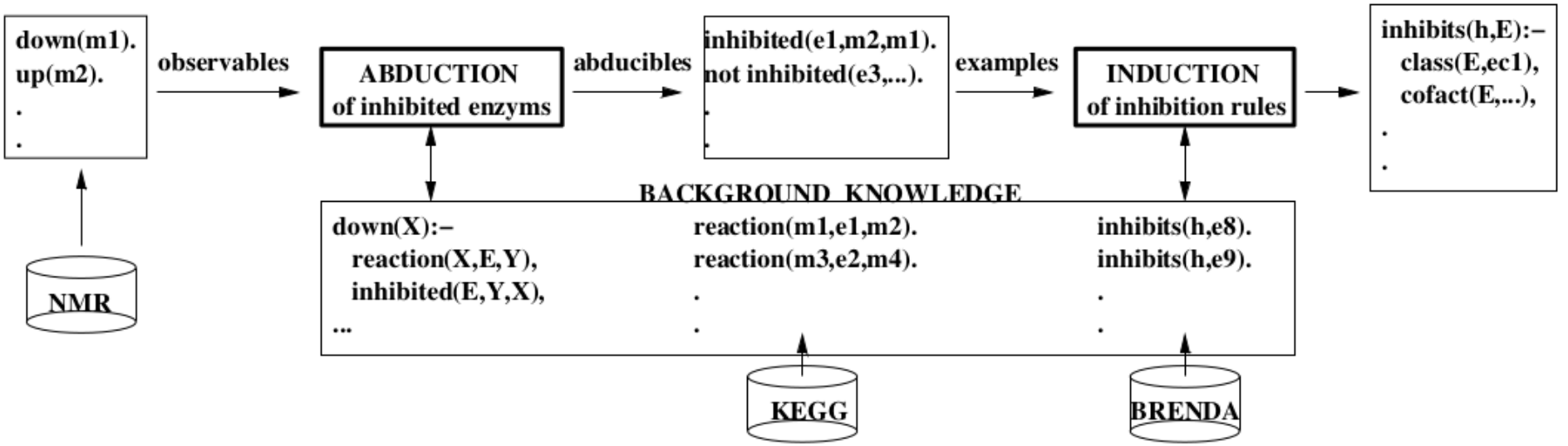
Modelování inhibice

- 1 observable predicate: *concentration(Metabolite, Level), Level ∈ {up, down}*
- Background predicates: *reactionnode(Metabolites1,Enzymes,Metabolites2)* e.g. *reactionnode(l-2-aminoadipate, 2.6.1.39, 2-oxo-glutarate).*
- Abducible predicate: *inhibited(Enzyme, Metabolites1, Metabolites2).*
- Rules in *P* (examples):
  - *concentration(X, down) :- reactionnode(X,E,Y), inhibited(E,Y,X).*
  - *concentration(X, down) :- reactionnode(X,E,Y), not inhibited(E,Y,X), concentration(Y, down).*
- Integrity constraints:
  - *false :- concentration(X, down), concentration(X, up).*

Příklad

- Pro síť uvedenou výše pozorujeme:
  - concentration(2-oxo-glutarate, down)
- Abduktivní vysvětlení (některá):
  - Δ_1 = {inhibited(2.3.1.61, succinate, 2-oxo-glutarate)}
  - Δ_2 = {inhibited(2.6.1.39, l-2-aminoadipate, 2-oxo-glutarate)}
  - Δ_3 = {inhibited(1.1.1.42, isocitrate, 2-oxo-glutarate)}
  - ...

Modelling framework

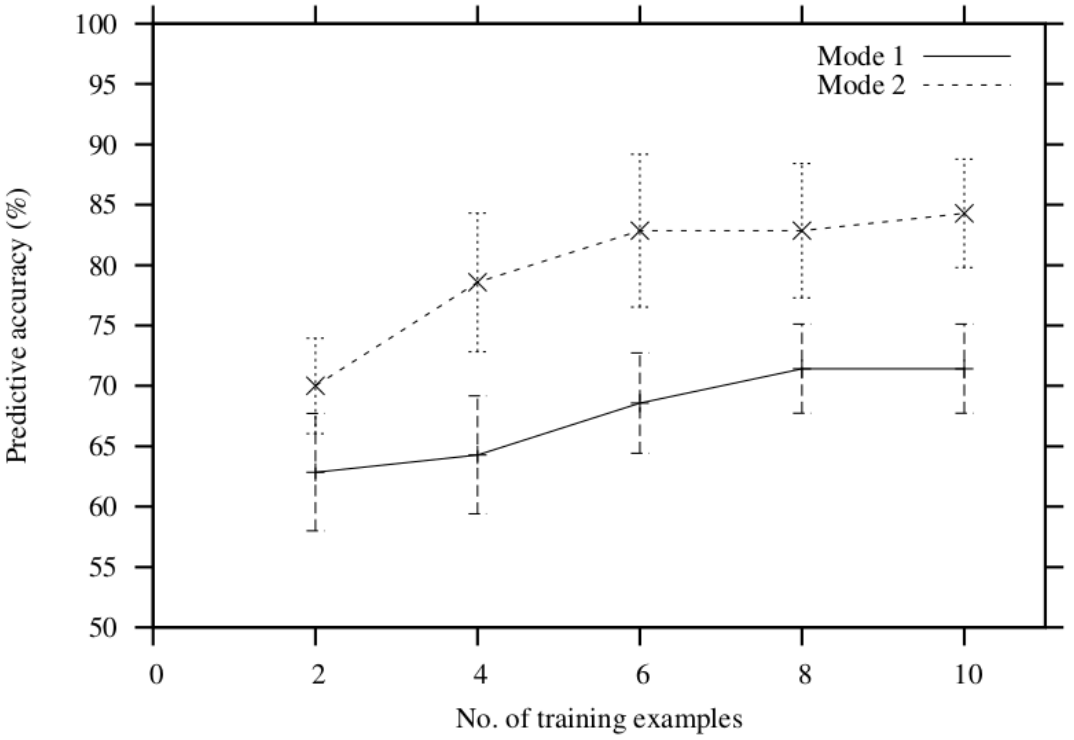


Příklad - pokračování

- Pro síť uvedenou výše pozorujeme:
  - concentration(2-oxo-glutarate, down)
  - concentration(isocitrate, down) (Δ_3 nekonzistentní)
  - concentration(l-2-aminoadipate, up)
- Abduktivní vysvětlení:
  - Δ_2 = {inhibited(2.6.1.39, l-2-aminoadipate, 2-oxo-glutarate)}
  - Δ'_2 = {inhibited(2.6.1.39, l-2-aminoadipate, 2-oxo-glutarate), inhibited(1.2.1.31, l-2-aminoadipate, l-lysine)}

Experiment - Learning ground hypotheses

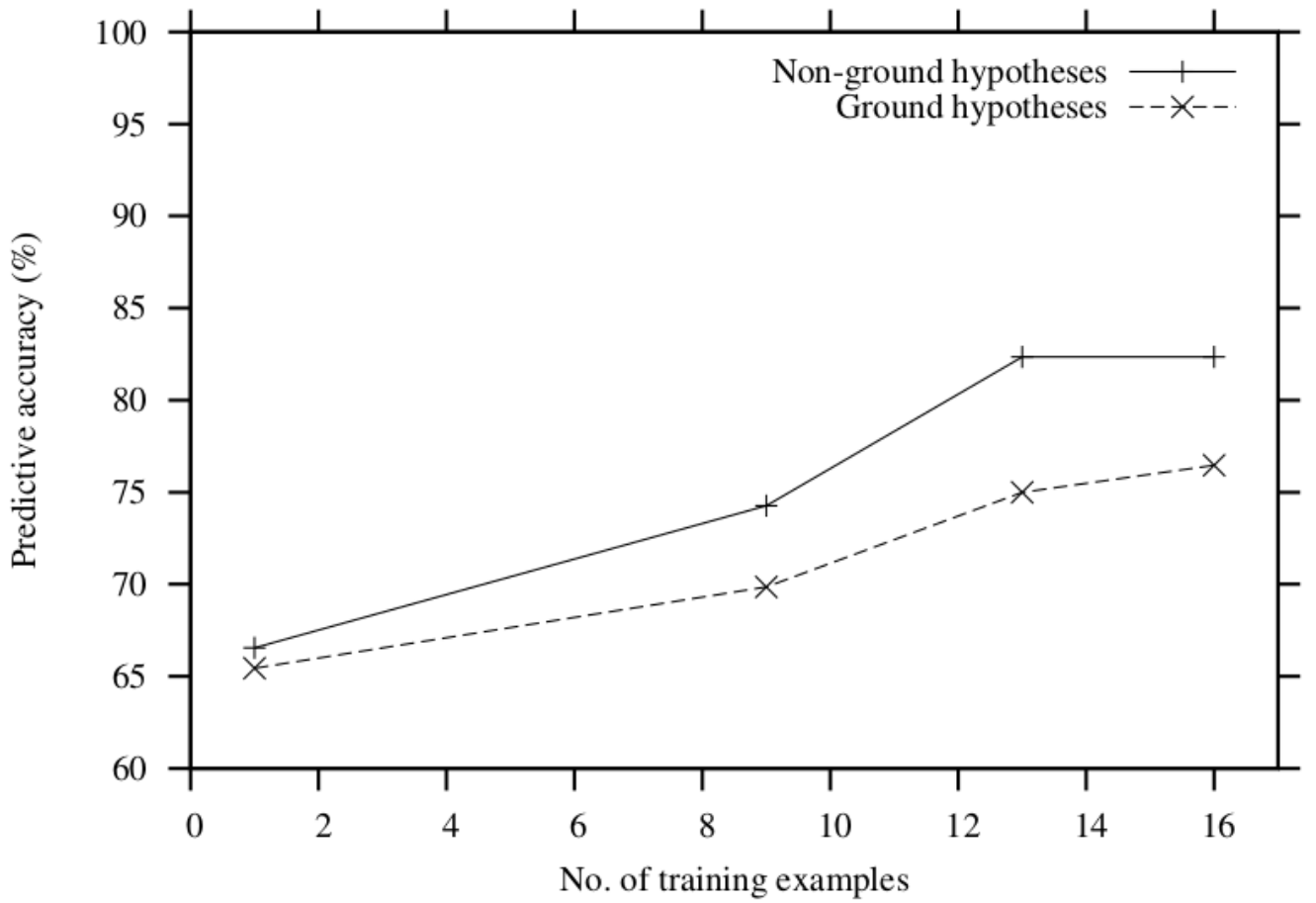
- Výsledky
  - Inhibited(2.6.1.39, l-2-aminoadipate, 2-oxo-glutarate)
  - not inhibirted(2.3.1.61, 2-oxo-glutarate, succinate)
  - and more…
- 7 such hypotheses → correctly predicts concentrations of six of the seven new (blue = testing) metabolites.



Experiment 2 – learning non-ground hypotheses

- Idea: Existují informace o podobnostech enzymů (BRENDA, LIGAND)
- Do background knowledge přidáme třídy enzymů
- Příklad indukcí naučeného pravidla: inhibited(E, M1,M2) :- reactionnode(M2,E,M1), class(E, 2.6.1).

Srovnání výsledků experimentů



Literatura

- Modelling inhibition in metabolic pathways through Abduction and Induction, (Alireza Tamaddoni-Nezhad, Antonis Kakas, Stephen Muggleton, Florencio Pazos)