仮説を立てて考えてみよう
Let's Hypothesize and Reason!

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何がわかる？

Intelligent machines ---

Thinking like human being.

Automated discovery of scientific knowledge, in particular biological knowledge.

どんな研究？

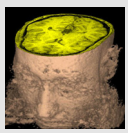
Automated hypothesis-finding through deductively complete methods.

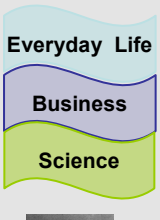
Induction of causal laws in action theories, and applications to systems biology.

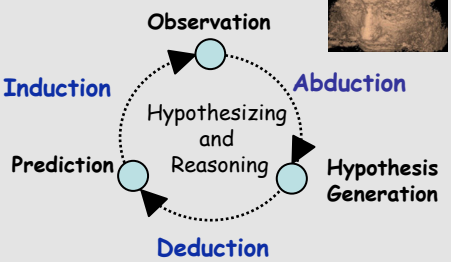
Web-based ILP system.

Background

How Human Beings Think ?







The genius people are able to mix these three fundamental modes of reasoning.

How Intelligent Machines Think ?

Induction
Abduction
Deduction

Diagnosis
Design
Characterization
Discovery
Verification

Combination of Induction and Abduction → One of the most powerful theoretical answers for the next generation of Intelligent Machine (Inoue 2001,2004)

Logic and Computation

Abduction and Induction: Logic

Input:
B : background theory
E : examples ／observations

Output:
H : hypothesis satisfying that

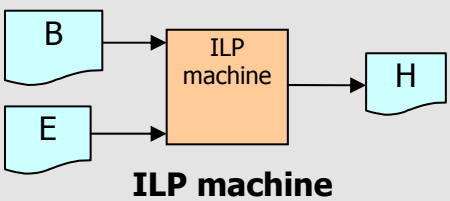
1. $B \wedge H \models E$,
2. $B \wedge H$ is consistent.

Inverse Entailment (IE)

Computing a hypothesis H can be done deductively by:

$$B \wedge \neg E \models \neg H$$

We have good tools for this inverse computation.



ILP machine

IE for Abduction

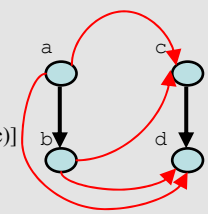
- **SOLAR** (Nabeshima, Iwanuma & Inoue 2003)
  - B: full clausal theory
  - E: conjunction of literals ($\neg E$ is a clause)
  - H: conjunctions of literals ($\neg H$ is a clause)

Example: graph completion problem – *pathway finding*

Find an arc which enables a path from a to d.

Axioms: [¬node(X),¬node(Y), ¬arc(X,Y), path(X,Y)].
[¬node(X), ¬node(Y), ¬node(Z), ¬arc(X,Y), ¬path(Y,Z), path(X,Z)].
[node(a)]. [node(b)]. [node(c)]. [node(d)].
[arc(a,b)]. [arc(c,d)].
Negated Observation: [¬path(a,d)].
Production_field: [¬arc(_,_)].

SOLAR outputs four consequences:
[¬arc(a, d)] , [¬arc(a, c)], [¬arc(b, d)], [¬arc(b, c)]



IE for Induction

- **CF-induction** (Inoue 2004: Yamamoto, Ray & Inoue 2007)
- **fc-HAIL** (Inoue & Ray 2007)
  - B, E, H: full clausal theory

Note: CF-induction is the only existing ILP system that is complete for full clausal theories.

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推論による仮説発見とシステム生物学への応用
Inference-based Hypothesis-Finding for System Biology

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何がわかる？

Discover hidden rules in systems biology.

Explain the relationships between causes and effects from genotype to phenotype.

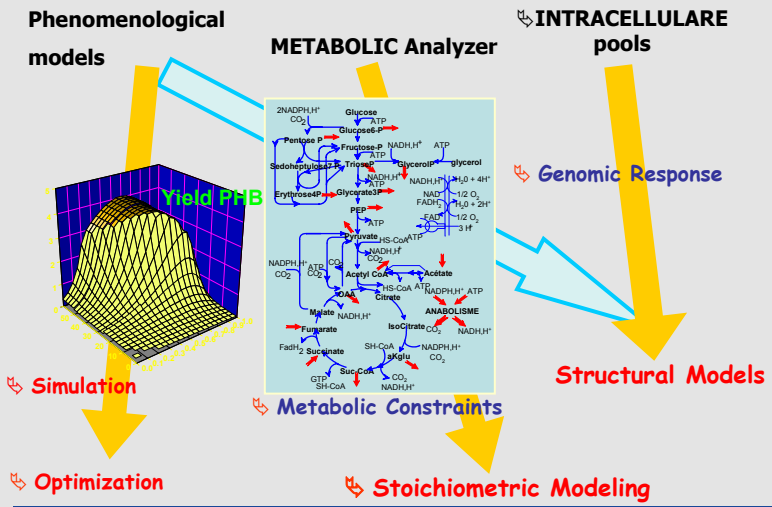
Use generic models in biology, *Saccharomyces Cerevisiae* and *E-coli.*

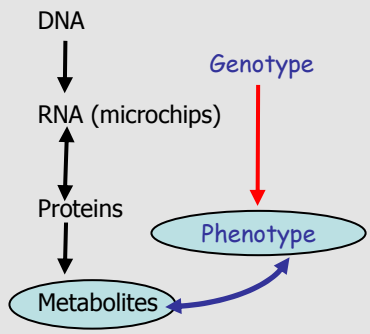
どんな研究？

Use Inductive Logic Programming (ILP).

Bridge between biologists and computer scientists, due to the possibility to represent biologist knowledge in the form of logical formulas.

Modeling





Metabolic pathway: sequences of enzyme-catalyzed reaction steps, converting substrate to a variety of product to meet the needs of the cell.

Flux: the rate at which material is processed trough a metabolic pathway.

Approach

Previously proposed methods

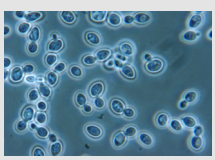
Using the stoichiometric model

- dynamic behavior:

$$\frac{dC}{dt} = v_{in} - v_{out} - \mu C$$

- steady states:
metabolite flux balancing

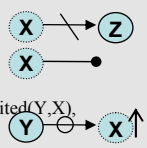
$$v_1 = v_2 + rB$$



- **Using the simple metabolic pathway (Pyruvate)**
- **Results obtained by CF-induction**

B:

reaction(pyruvate, acetylcoa). reaction(pyruvate, acetaldehide).
reaction(glucose, glucosep). reaction(glucosep, pyruvate).
reaction(acetaldehide, acetate). reaction(acetate, acetylcoa).
reaction(acetaldehide, ethanol). concentration(glucose, up).
terminal(ethanol).
blocked(X)←reaction(X,Z), inhibited(X,Z).
blocked(X)←terminal(X).
concentration(X,up) ←reaction(Y,X), ¬inhibited(Y,X), blocked(X).



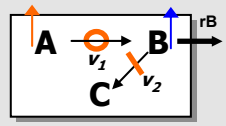
E: concentration(ethanol,up). concentration(pyruvate, up).

Our approach

Using the logical model (causal relations)

Observation: the concentration of B increases.

Background knowledge:
if the concentration of A increases, the reaction A→B is accelerated and the reaction B→C is inhibited, then the concentration of B increases.



Hypothesis:
the concentration of A increases, **the reaction A→B is accelerated** and **the reaction B→C is inhibited**.

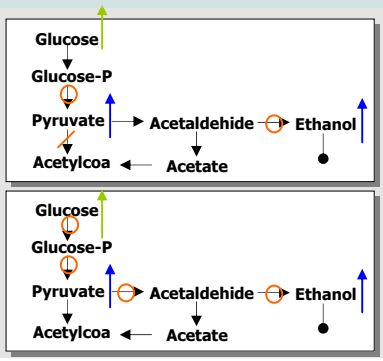
➢ **Not only estimating possible reaction states, but also discovering new pathway rules that are missing in the current background theory**

H_1:

¬Inhibited(glucosep, pyruvate).
¬inhibited(acetaldehide, ethanol).
inhibited(pyruvate, acetylcoa).

H_2:

¬inhibited(glucose, glucosep)
¬Inhibited(glucosep, pyruvate).
¬inhibited(acetaldehide, ethanol).
¬inhibited(pyruvate, acetaldehide).
concentration(X, up)← ¬inhibited(Y, X), concentration(Y, up).



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