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？

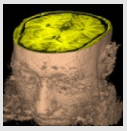
- **Intelligent machines:**
  Thinking like human being.
- **Automated discovery of scientific knowledge, in particular biological knowledge.**

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 → Diagnosis, Design, Characterization
Abduction → Discovery
Deduction → 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

IE for Abduction

- **SOLAR**

(Nabeshima, Iwanuma and Inoue 2003)
(Nabeshima, Iwanuma, Inoue and Ray 2010)
B : full clausal theory, E: conjunction of literals
H : conjunction of literals

IE for Induction

- **CF-induction**

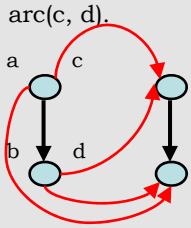
(Inoue 2004: Yamamoto, Ray and Inoue 2007)
B : full clausal theory, E : full clausal theory
H : full clausal theory

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).
Observation: path(a, d).
Abducibles: arc(_, _).

SOLAR outputs four hypotheses.
arc(a, d), arc(a, c), arc(b, d), arc(b, c).



Distributed Abduction

- **Learner-Critic Protocol**

(Bourgne, Maudet and Inoue 2010)
N agents $a_0, \ldots, a_n$, each having his own knowledge (B_i, E_i)
$B = \cup_i B_i$: full clausal theory, $E = \cup_i E_i$: conjunction of literals
H : conjunction of literals

Learner:
1. Compute local hypothesis (and context)
2. Interact with critics (propose)

Critic:
1. Consistency check (context computation)
2. Explainabilty check (uncovered examples)
3. Admissibility check

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

どんな研究？

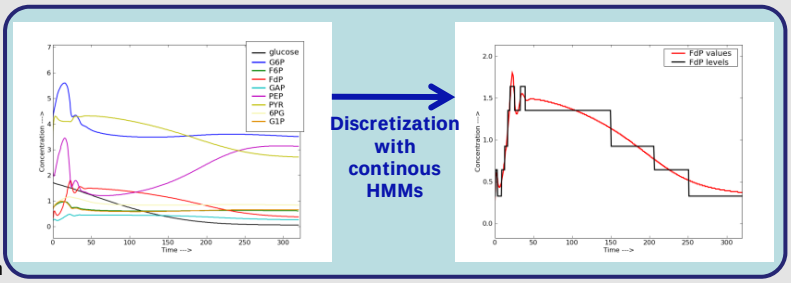
- **Development of a framework for knowledge discovery from biological databases using logic-based AI.**
- **Clarification of the principles of hypothesis formation and hypothesis evaluation and their efficient implementation.**
- **Bridge between biologists and computer scientists**

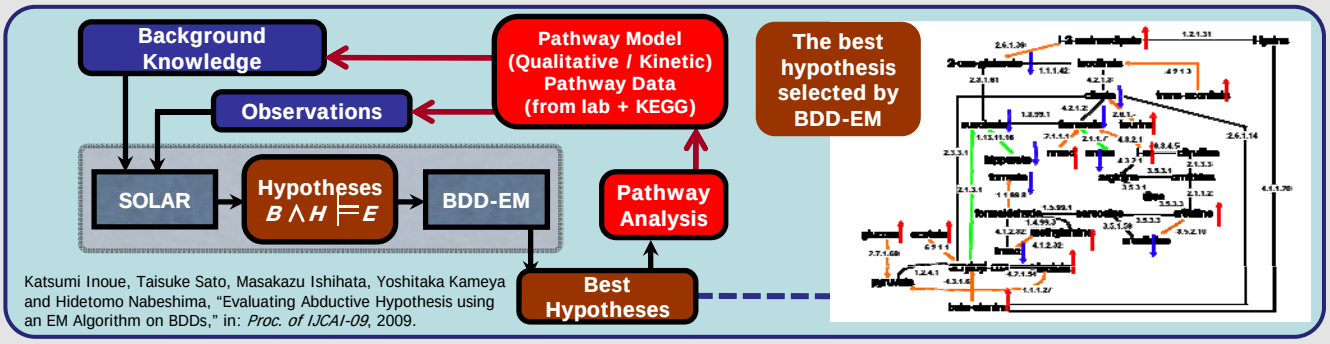
Closed-loop Architecture for Biological Inference

Research Goals
- Modeling, explaining and predicting metabolic pathways

Target Problems
1. Predicting the inhibitory effect of toxins including hydrazine with qualitative modeling
2. Explaining dynamic behavior of *E. coli* pathways with kinetic modeling

Approaches
- Hypothesis generation by SOLAR
- Hypothesis evaluation by an EM algorithm on BDDs
- Modeling with discretization and the Michaelis-Menten equation





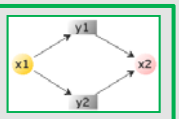
Katsumi Inoue, Taisuke Sato, Masakazu Ishihata, Yoshitaka Kameya and Hidetomo Nabeshima, "Evaluating Abductive Hypothesis using an EM Algorithm on BDDs," in: *Proc. of IJCAI-09*, 2009.

Identifying Necessary Reactions in Large Metabolic Pathways

Target Problem
- Identifying necessary reactions in metabolic pathways.

Approaches
- Translating reaction laws to propositional formulas.
- Computing minimal models of the translated formulas.

Example.



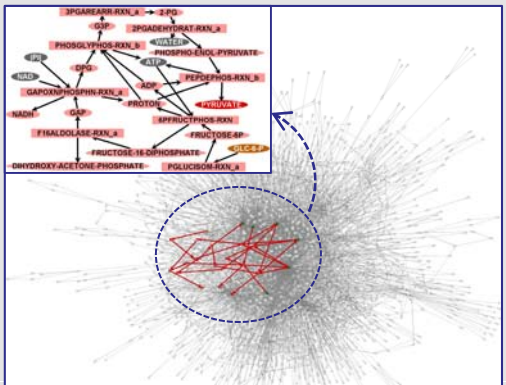
Source condition $m_{x1,0}$, $\neg m_{x2,0}$
Target condition $m_{x2,2}$
Reaction Laws

$m_{x1,0} \rightarrow m_{x1,1}$, $m_{x1,1} \rightarrow m_{x1,2}$, $m_{x2,0} \rightarrow m_{x2,1}$, $m_{x2,1} \rightarrow m_{x2,2}$

$r_{y1,1} \rightarrow m_{x1,0}$, $r_{y1,1} \rightarrow m_{x2,1}$, $\neg r_{y1,1} \rightarrow (\neg m_{x2,0} \rightarrow \neg m_{x2,1})$

$r_{y2,2} \rightarrow m_{x1,0}$, $r_{y2,2} \rightarrow m_{x2,2}$, $\neg r_{y2,2} \rightarrow (\neg m_{x2,1} \rightarrow \neg m_{x2,2})$

Reaction Name	a	b	c	d	e	f	g	EcoCyc
2.7.1.121-RXN					x			
2PGADEHYDRAT-RXN				x	x	x	x	x
3PGAREARR-RXN				x	x	x	x	x
6PFRUCTPHOS-RXN			x				x	x
6PGLUCONOLACT-RXN	x							
DLACTDEHYDROGNAD-RXN		x	x					
F16ALDOLASE-RXN			x				x	x
F16BDEPHOS-RXN								x
GAPOXNPHOSPHN-RXN				x	x	x	x	x
GLU6PDEHYDROG-RXN	x							
GLYOXIII-RXN		x	x					
KDPGALDOL-RXN	x							
METHGLYSYN-RXN		x	x					
NAD-KIN-RXN	x							
PEPDEPHOS-RXN				x			x	x
PEPSYNTH-RXN					x			x
PGLUCISOM-RXN		x	x	x	x	x	x	x
PGLUCONDEHYDRAT-RXN	x							
PHOSGLYPHOS-RXN				x	x	x	x	x
RXN0-313		x		x	x	x		
RXN0-4401					x	x		
TRIOSEPISOMERIZATION-RXN		x						x



Pathway: A whole metabolic pathway of *E. coli* consisting of 1777 reactions and 1073 metabolites (from EcoCyc version 13.6).
Initials: PROTON, WATER, ATP, ADP, |pi| and NAD.
Source: GLC-6-P. **Target**: PYRUVATE.

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