Symbolic Systems Technology

Using formal systems and and reasoning tools to

- Understand how things work; why things don’t work
- Design, analyze, adapt complex systems

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SRI Fellows Meeting

2011 October 26

Plan

- About formal systems, formal modeling
- Some examples
- Challenges & Opportunities

Complex systems -- a small sample

- Communicating processes
  - dissemination of messages/knowledge (routing protocols)
  - security protocols
  - business processes/regulations
- Collaborations
  - emergency response
  - surveillance
- Cellular systems
  - signaling (intra, inter) -- regulation, decision making
  - metabolism
  - resilience, fault tolerance

Modeling Step One

- What questions do you want the model answer?
- What can you observe/measure?
- What questions do you ***really*** want the model answer?
- What does that mean?
- Explain it to a computer!

What is a formal system?

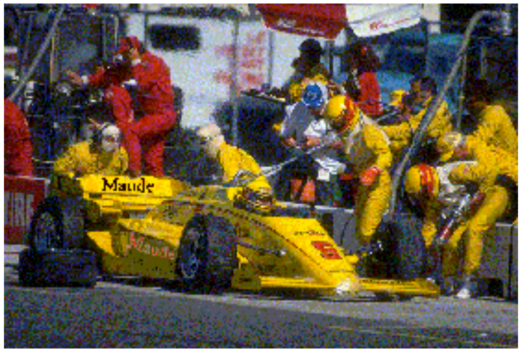
- Language: to describe things and properties
- Semantics: thing satisfies property
- Reasoning principles: proving/disproving properties of things
- [Reflection: to model and reason about models and reasoning]
- Executable formal models (model train, airplane, ...)
  - System state: collections of entities (name,location,knowledge,resources..)
  - State transition rules
  - Execution: application of rules
  - Properties of states (P,Q) and executions (ϕ: P until Q, eventually P)
  - Watch it run, poke it, analyze it

Symbolic analysis -- answering questions

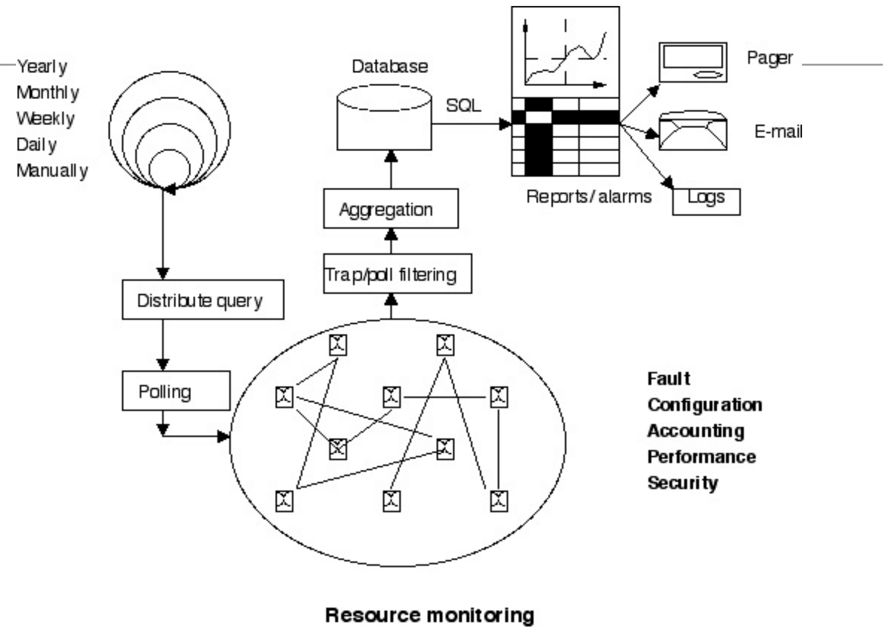
- Forward collection -- upper bound on possible states
- Backward collection -- initial states leading to states of interest
- Search -- for state of interest
- Model checking -- do all executions satisfy ϕ, find counter example
- Constraint solving -- steady state analysis

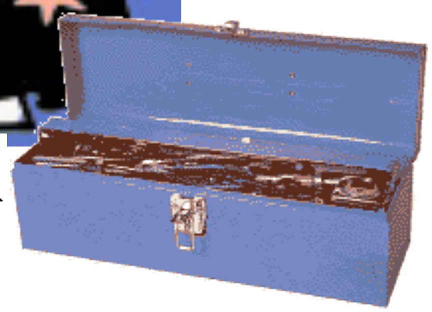
Rewriting Logic & Maude

- Rewriting logic is a simple logic designed to model concurrent and distributed systems,
  - System states described by equational theories, behavior described by local rules
- Maude is modeling environment based on rewriting logic, featuring
  - a high speed rewriting modulo axioms
  - built in search, model-checking, unification
  - reflection



Modeling Methodology



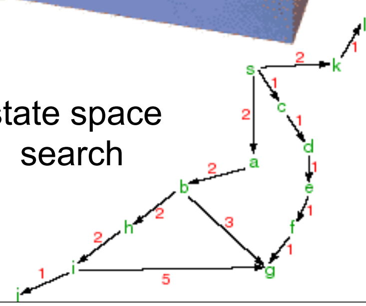


$S \models \Phi$

model checking

rapid prototyping

state space search

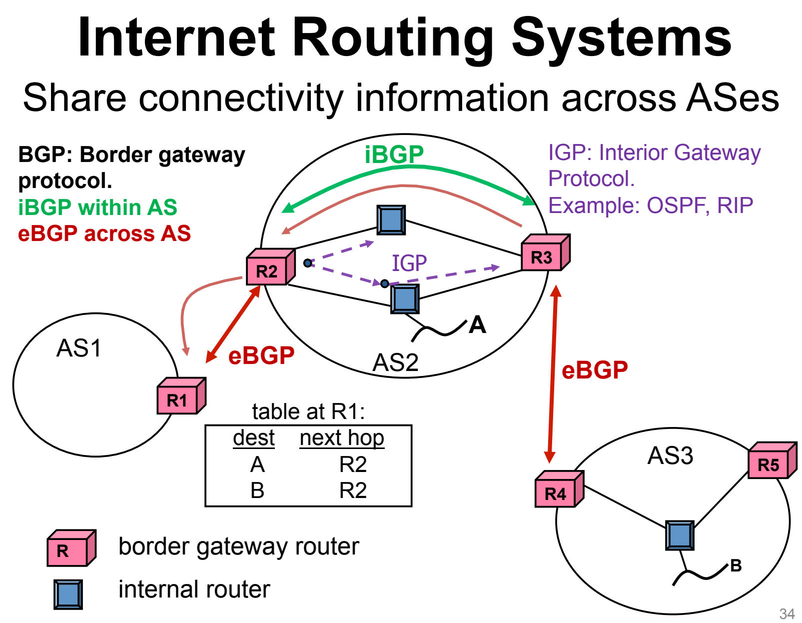


Finding Bugs in Complex Systems

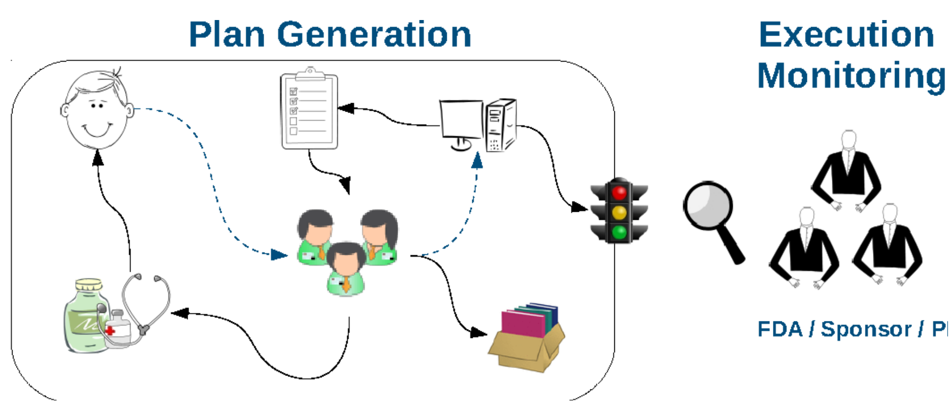
- AER/NCA active network reliable multicast protocol
  - Is the nominee (chosen responder) aware?
  - Do the agents come to agreement within time t?
  - Poor timer setting leads to bad behavior
- Secure service broker via proxies
  - Is the service from a trusted provider
  - Is it the requested service
- Security issues in IE (Meseguer et. al.)
  - found nine status bar types of spoofing attacks and four address bar spoofing attack types

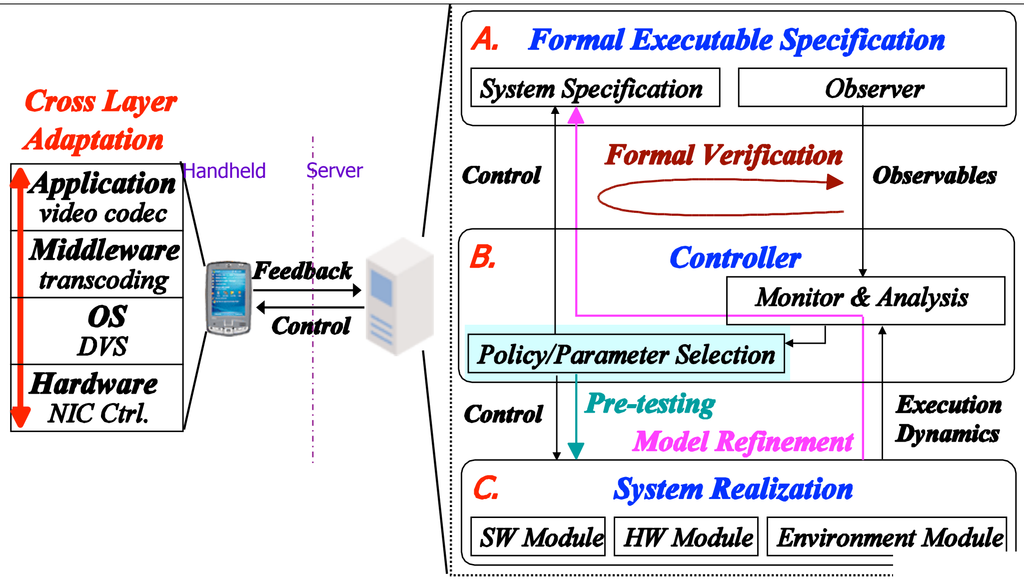
More Applications

- Border Gateway Protocol Analysis (Anduo Wang, Boon Tau Loo, Andre Scedrov UPenn)
  - looping -- fail to find route
  - inconsistency -- intra vs inter

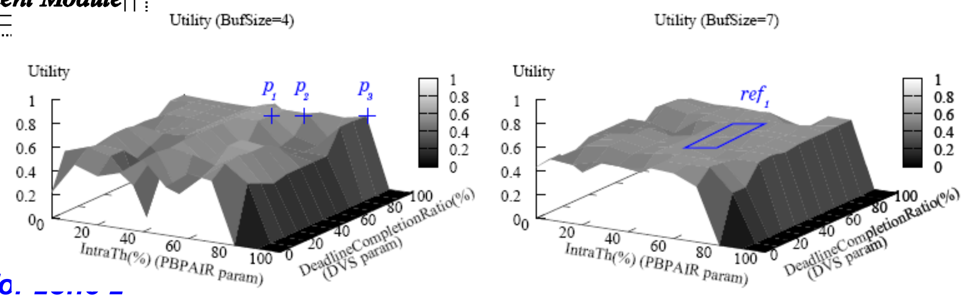


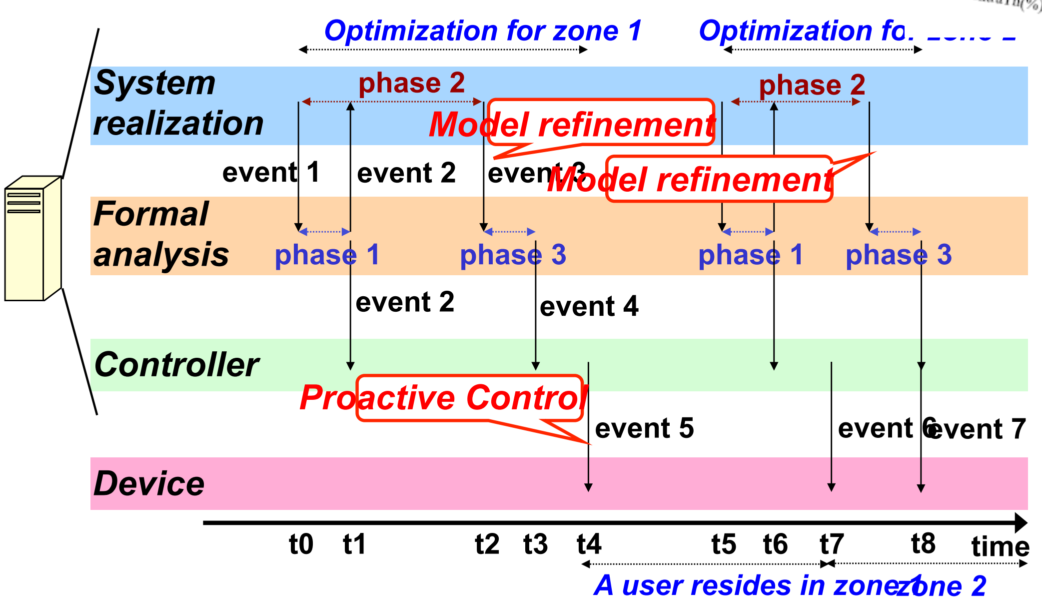
- Modeling Regulations for Clinical Trials (Andre Scedrov (UPenn), Vivek Nigam (Munich), ...
  - Federal regulations, clinical protocol
  - Events and obligations
  - Runtime monitoring
  - Situation aware plan generation
  - Post trial inspection





Xtune
cross layer adaptation

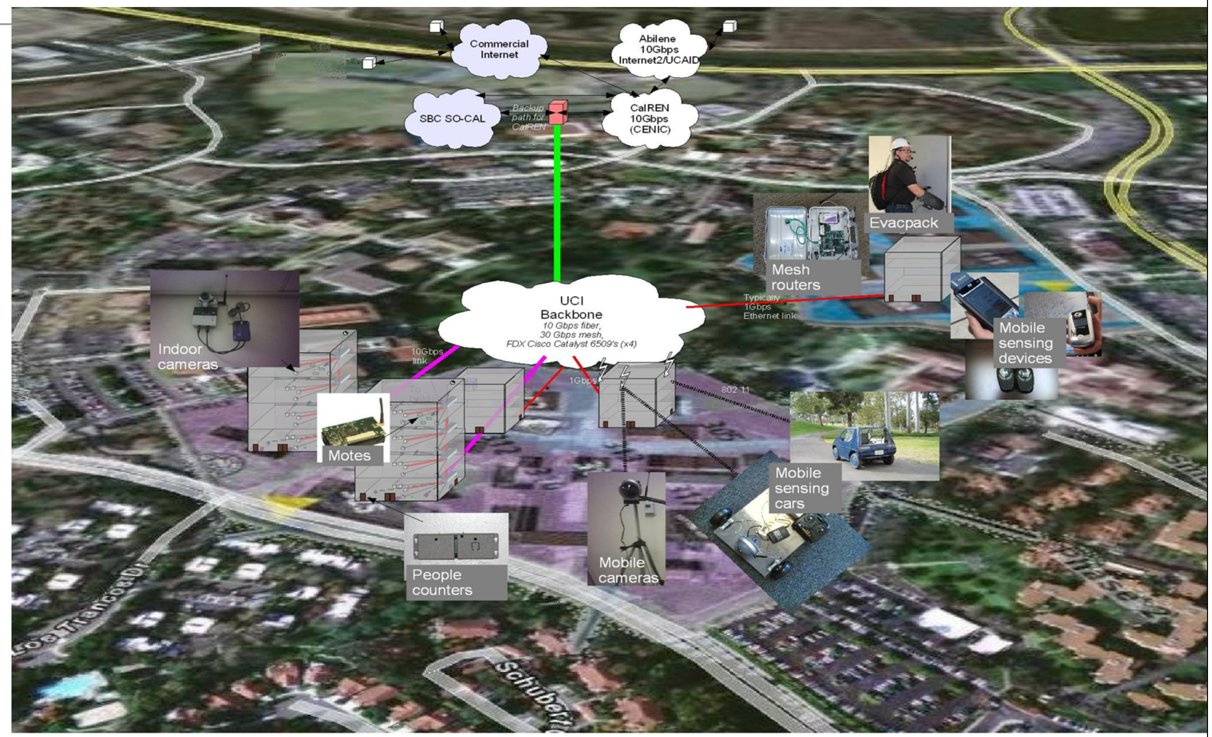




Constraint refinement

Dependability Techniques for Instrumented Cyber-Physical Spaces

- Principles / techniques for infrastructure and data resilience
- Formal models and cross-layer tuning
- Middleware services
- Pervasive space testbed



Instrumented UCI Campus

Biology

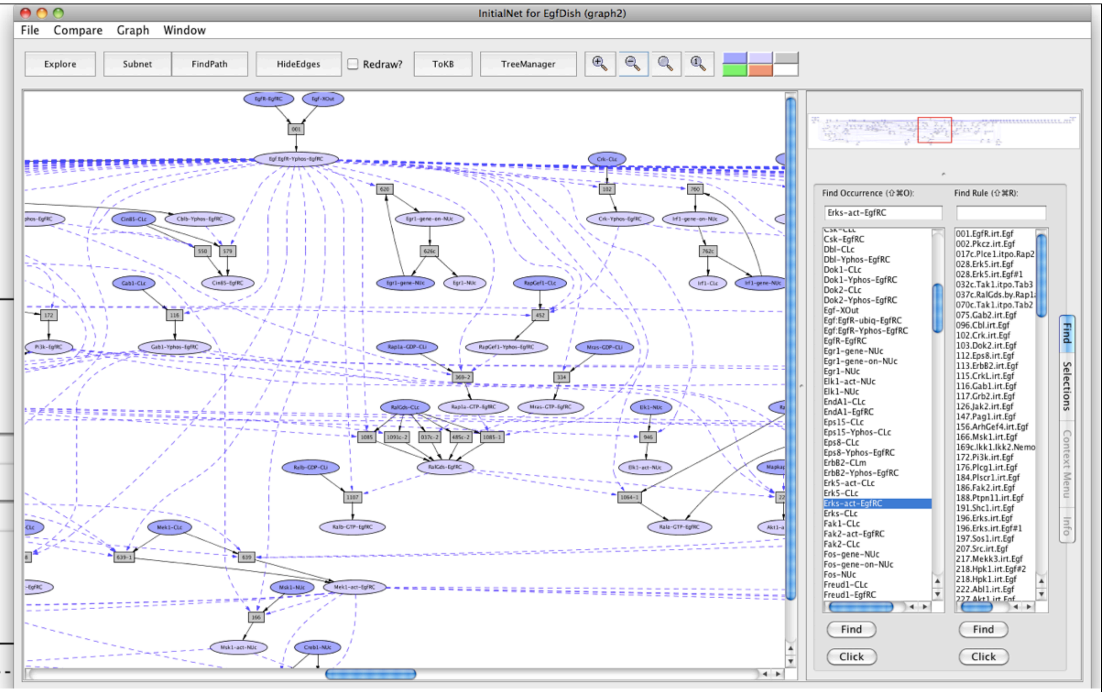
- Pathway Logic
- Combining Pathways and Cheminformatics
- Diet Planning

Pathway Logic (PL) http:pl.csl.sri.com

- The essence
  - Formal models of experimental findings
  - Executable models of biological processes
  - Pathways (sets of biomolecules that function to gether) and regulation effects discovered by asking questions (answered by formal reasoning)
- Sample models
  - Mammalian intra cellular signaling
  - Bacterial protease interactions
  - TB mycolic acid synthesis
  - Function of sleep

Signaling response to Egf (AMK)

Datum query



Predicates

subject | entity | matches | Erk

assay | type | is a | ActivationAssay

Add a predicate Remove all predicates

50 of 407 Results

Export all results to txt or csv

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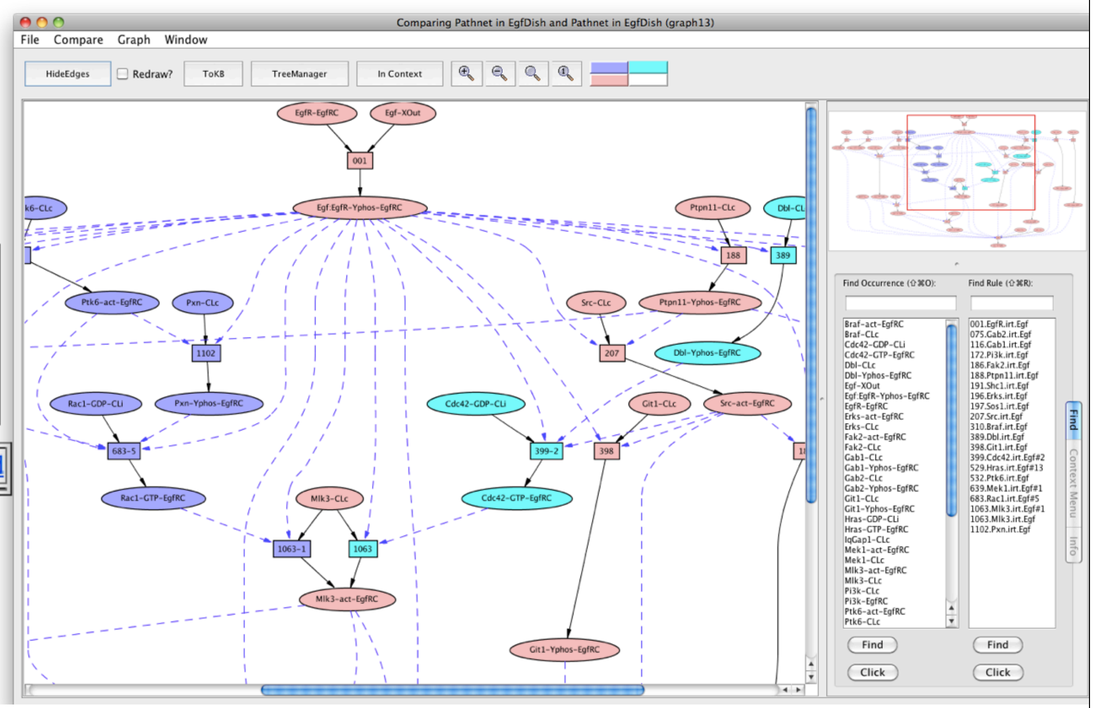
Expand All | Collapse All

Erks[Ab]IP IVKA(MBP)[32P-ATP] is increased irt Lps (times) Expand

- cells: mPECs in BMS
- times: 0 7+ 15+ 30 60 90 min
- partially reqs: Irak1 [KO]
- source: 10754329-Fig-3c

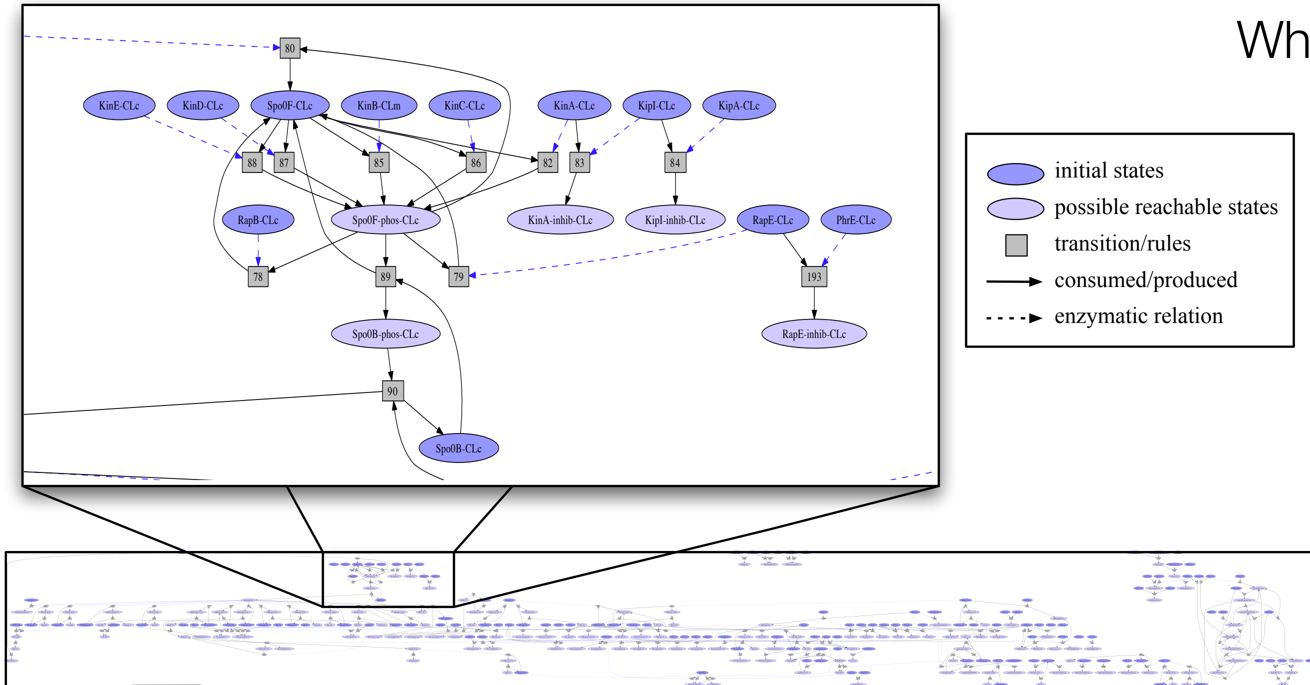
Erks[Ab]IP IVKA(Elk1)[32P-ATP] is increased irt Lps (30 min) Expand



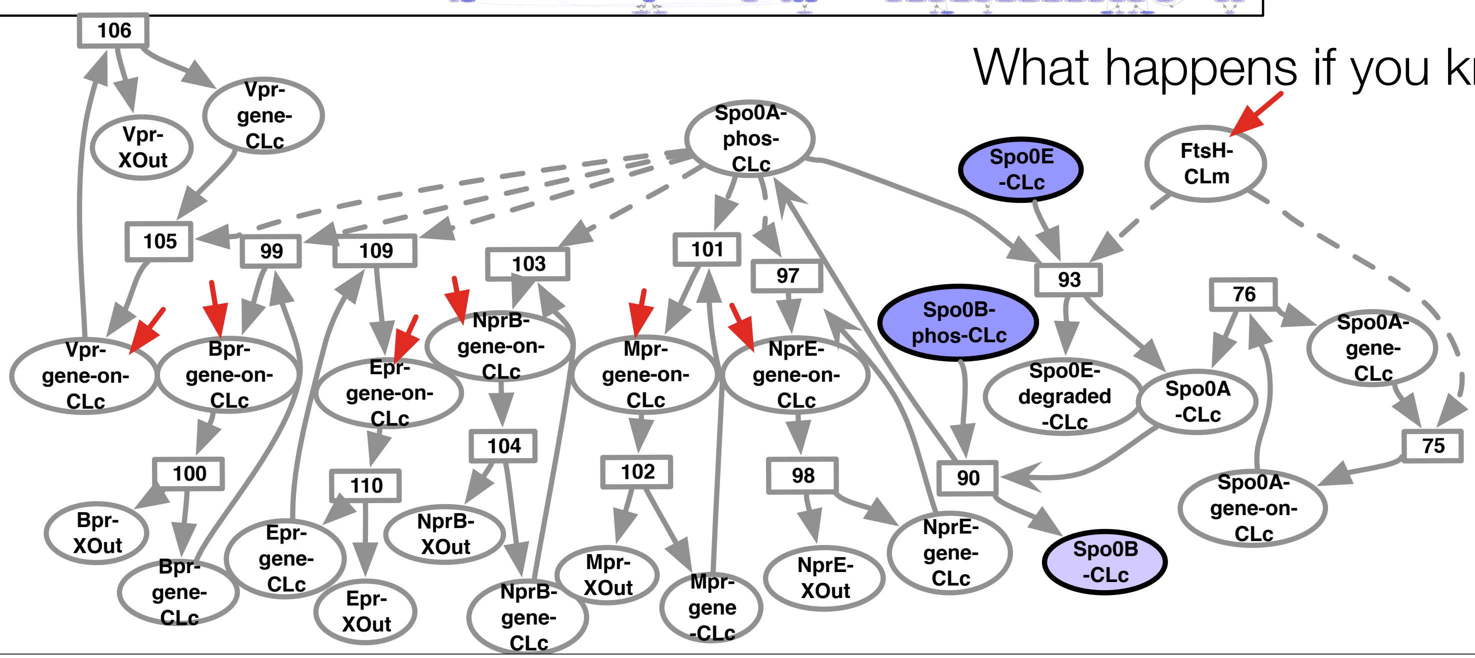
Two ways to activate Erk

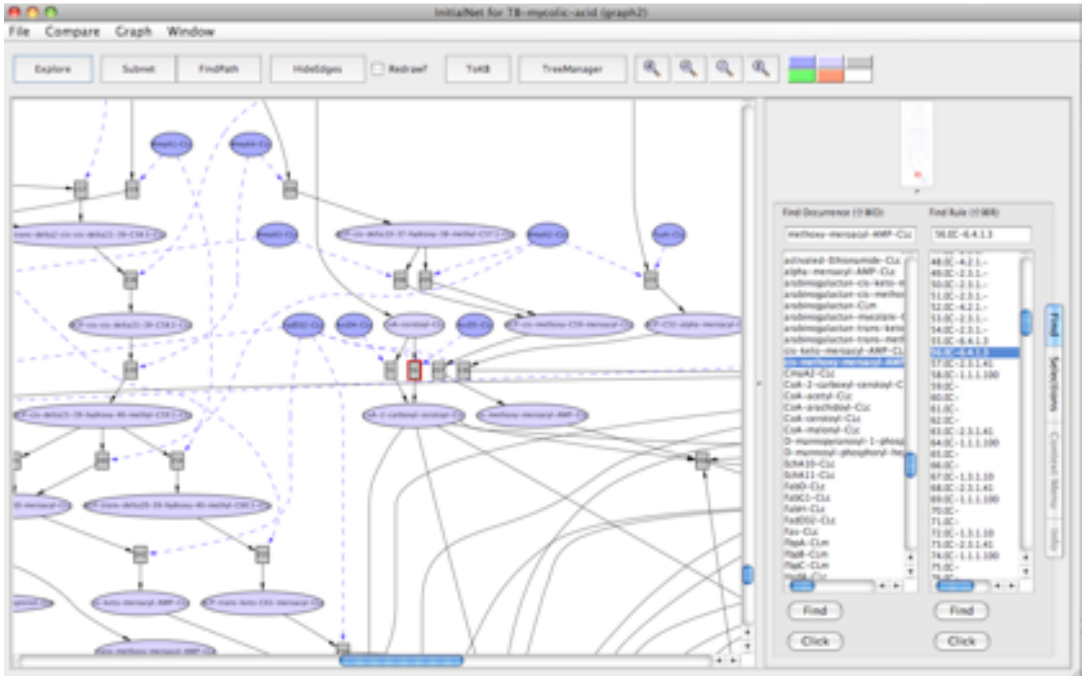
Protease interaction network (Gram Positive Bacteria) (Anupama)

What regulates a protease, what does it regulate



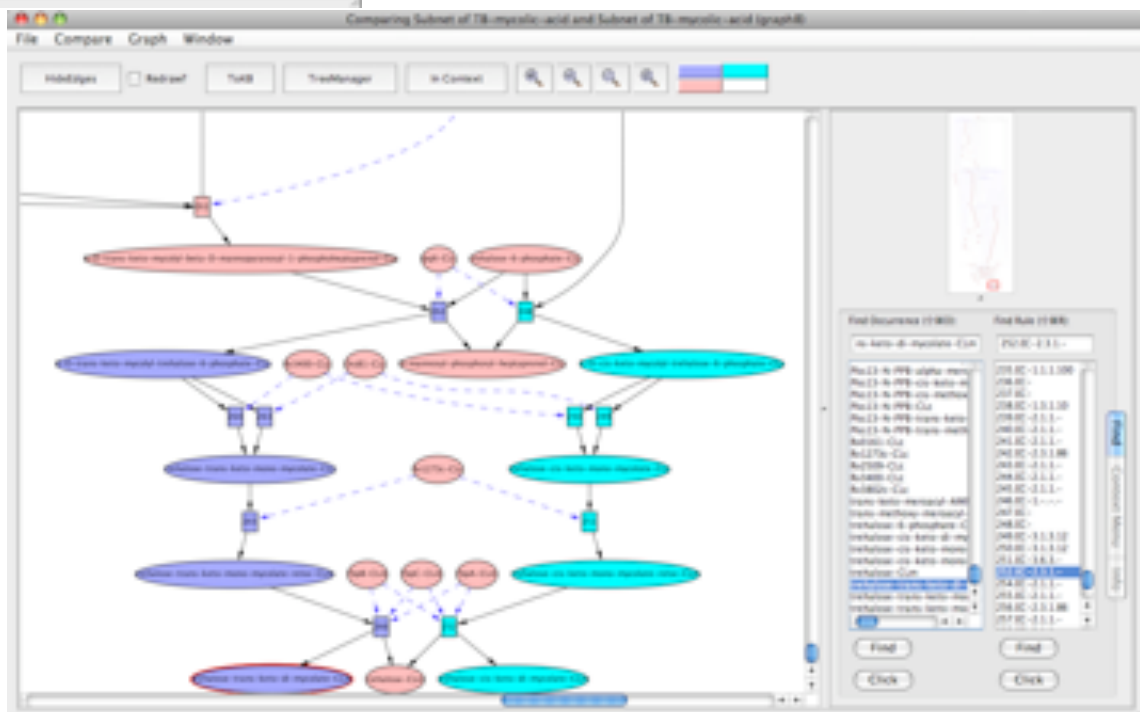
What happens if you knockout FtsH?



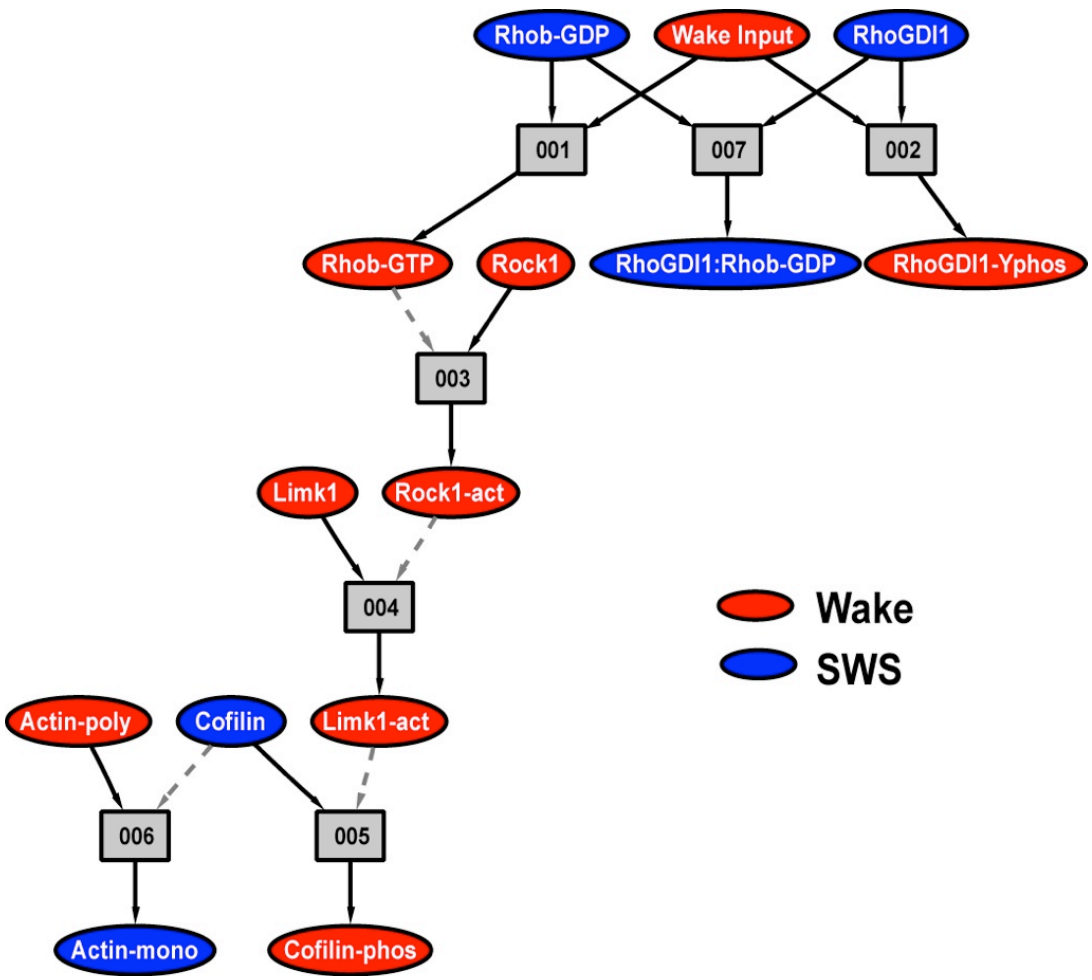


TB-mycolic-acid synthesis
(Malabika)

Multiple synthesis routes



A HypotheticaL Model Pathway Relating State and Synaptic Plasticity



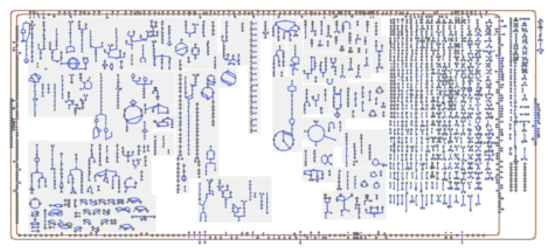
Wake state:
unknown signal(s)
=> phosphorylation of Rock1
=> activation of Limk1
=> phosphorylation of cofilin
=> increase in polymerized actin
(Phosphorylated cofilin is unable to depolymerize actin)

SWS:
RhoDG11 binds Rhob-GDP
(is not phosphorylated)
=> Rock1, Limk1, and cofillin would not be phosphorylated and
=> actin depolymerization
=> decrease in synaptic weight

Diet planning for Ecoli
(aka finding minimal nutrient sets)

- Metabolic network, transportables, and growth conditions, represented as constraints.
- Find all minimal nutrient set solutions
- OOPS there are ~8560
- Partition nutrients into equivalence classes (replacable)
- 19 sets with 12 classes
- Surprise! E.Coli can grow on cyanate (and several other novel nutrient sets).

A.

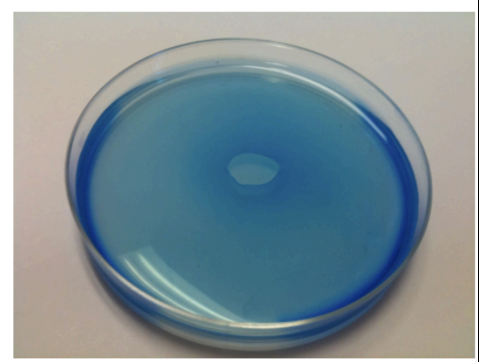


B.

	reaction 1	reaction 2
A	-1	0
B	-1	1
C	1	-1
D	1	0
E	0	1
F	0	-1

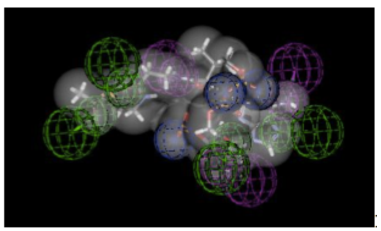
C.

D.

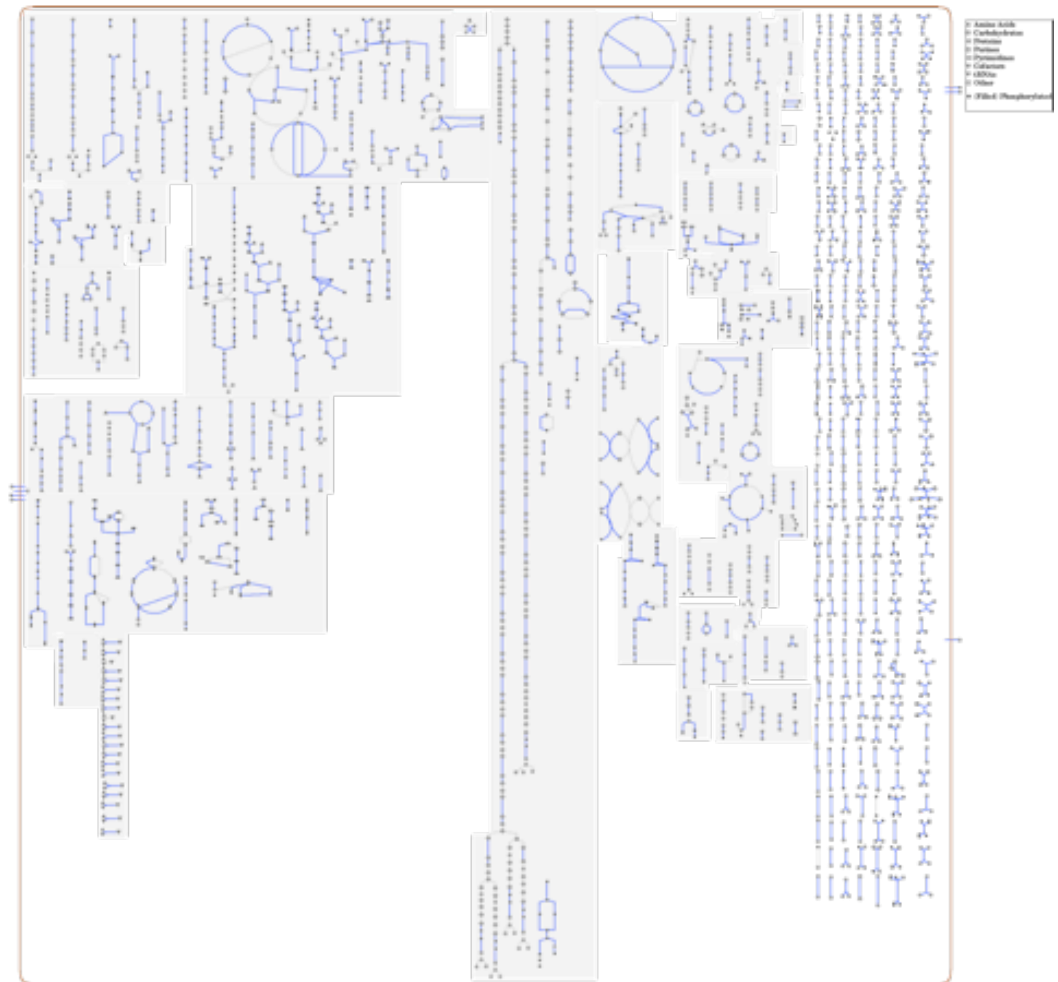


Combining Cheminformatics and Pathway Analysis
Finding TB drug candidates
NIH STTR with Collaborative Drug Design (CDD)

- Identify essential genes/enzymes
- Select substrates of highly connected enzymes
- Generate pharmcophores (abstract model of metabolite)



- Look for matches in drug catalog
- Predicted 30 candidate drugs, tested 20, 3 had activity
- Phase II STTR submitted.



Challenges and Opportunities

- Cyberphysical Systems
- Communicating cellular processes

Networked cyber-physical systems

- Networked Cyber-Physical Systems (NCPS) consist of networked hard- and software components embedded in the physical world and interacting with it through sensors and actuators.
- Increasingly large numbers of *heterogeneous* and potentially *resource-constrained* and *unreliable* components
- Need to work in challenging environments with unreliable/intermittent connectivity
- Need to operate in the entire spectrum between autonomy and cooperation
- Decisions based on local knowledge and knowledge dissemination
- **Opportunity :** General principles and tools for building robust, effective NCPS using individual cyber-physical devices as building blocks.

Communicating Cellular Systems

- For example the immune system, or neuron system, or combination ...
- All the NCPS challenges are relevant to modeling and understanding how these systems work:
  - What are the right abstractions?
  - What are the essential rules/balances that ensure correct/robust operation?
    - What are the underlying *distributed, reactive* control principles
  - What makes learning and adaptation work (or not)?

Principles and Foundations for NCPS

- **Problem:** Current models are too abstract by not taking into account fundamental physical limitations and hence are not efficiently implementable or scalable
- Once explicitly represented, physical limitations can be overcome to some degree (e.g. probabilistically)
- Diversification, redundancy, and randomization can offset many physical limitations
- Distribution is a source of redundancy and diversification and can be turned from an obstacle into an advantage

Vision

- Bringing together the cyber and the physical
- New insights for design and modification
  - synthetic biosystems; training colonies to do useful things
- New coordination/control laws
  - new ways to control the immune system
  - on-the-fly self-assembling/organizing systems

The end! (The beginning?)