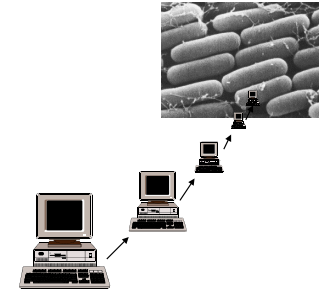


Programming Biological Cells

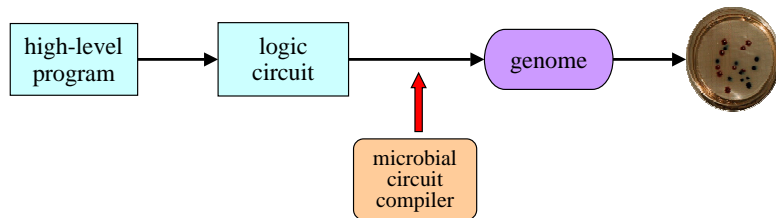
Ron Weiss, George Homsy, Radhika Nagpal
Tom Knight, Gerald Sussman, Nick Papadakis
 MIT Artificial Intelligence Laboratory

Motivation

- ✂ Goal: program biological cells
- ✂ Characteristics
 - ◆ small (*E.coli*: $1 \times 2 \mu\text{m}$, $10^9/\text{ml}$)
 - ◆ self replicating
 - ◆ energy efficient
- ✂ Potential applications
 - ◆ “smart” drugs / medicine
 - ◆ agriculture
 - ◆ embedded systems



Approach

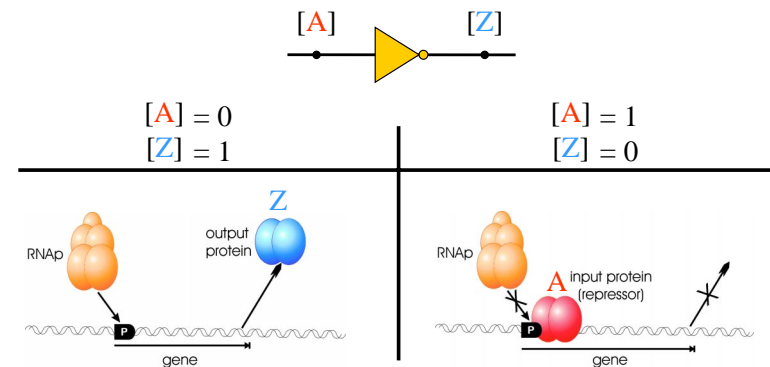


Outline:

- ✂ Building biological digital circuits
 - ◆ compute, connect gates, store values
- ✂ High-level programming issues

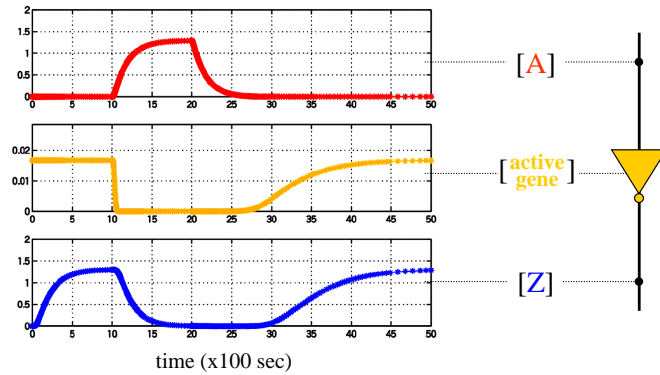
Compute: Biological Inverter

- ✂ signal = protein concentration level
- ✂ computation = protein production + decay



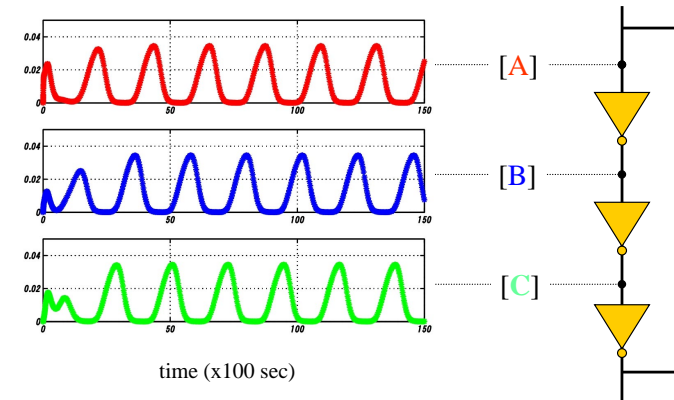
Inverter Behavior

Simulation model based on λ phage biochemistry

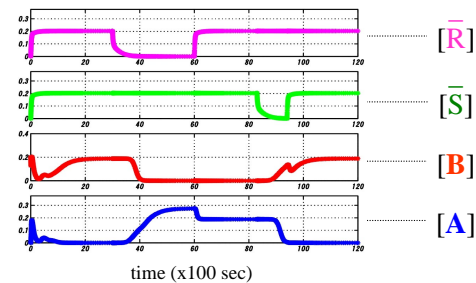
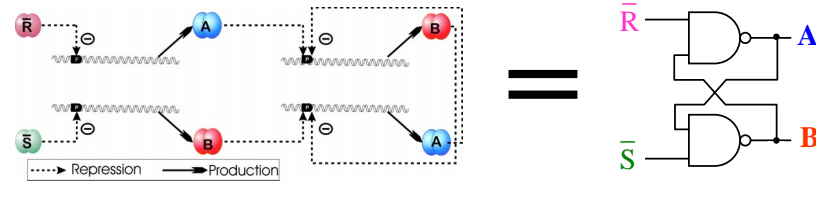


Connect: Ring Oscillator

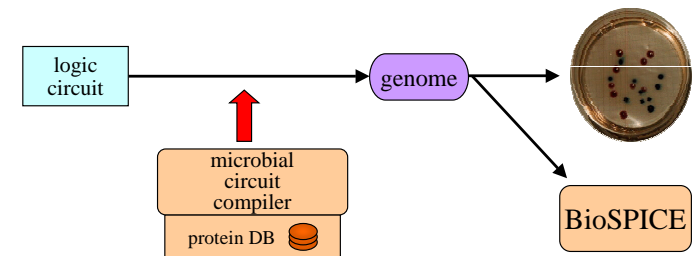
Connected gates show oscillation, phase shift



Memory: RS Latch



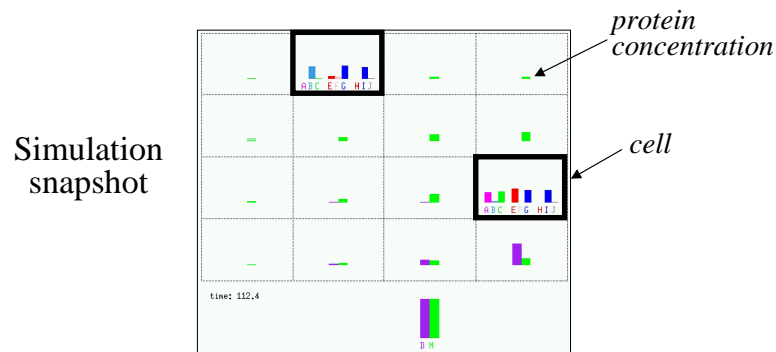
Microbial Circuit Design



- Assigning proteins is hard.
- BioSPICE: Simulate a colony of cells

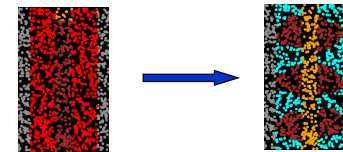
BioSPICE

- ✂ Prototype protein level simulator
 - ◆ intracellular circuits, intercellular communication



High Level Programming

- ✂ Requires a new paradigm
 - ◆ colonies are amorphous
 - ◆ cells multiply & die often
 - ◆ expose mechanisms cells can perform reliably
- ✂ Microbial programming language
 - ◆ example: pattern generation using aggregated behavior



Conclusions + Future Work

- ✂ Biological digital gates are plausible
- ✂ Now:
 - ◆ Implement digital gates in *E. coli*
- ✂ Also:
 - ◆ Analyze robustness/sensitivity of gates
 - ◆ Construct a protein kinetics database
 - ◆ Study protein \leftrightarrow protein interactions for faster logic circuits