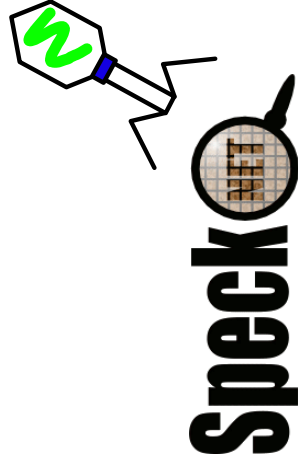


# Towards Biospecks

September 2005



**Marc Blenkiron**

*Supervisors*

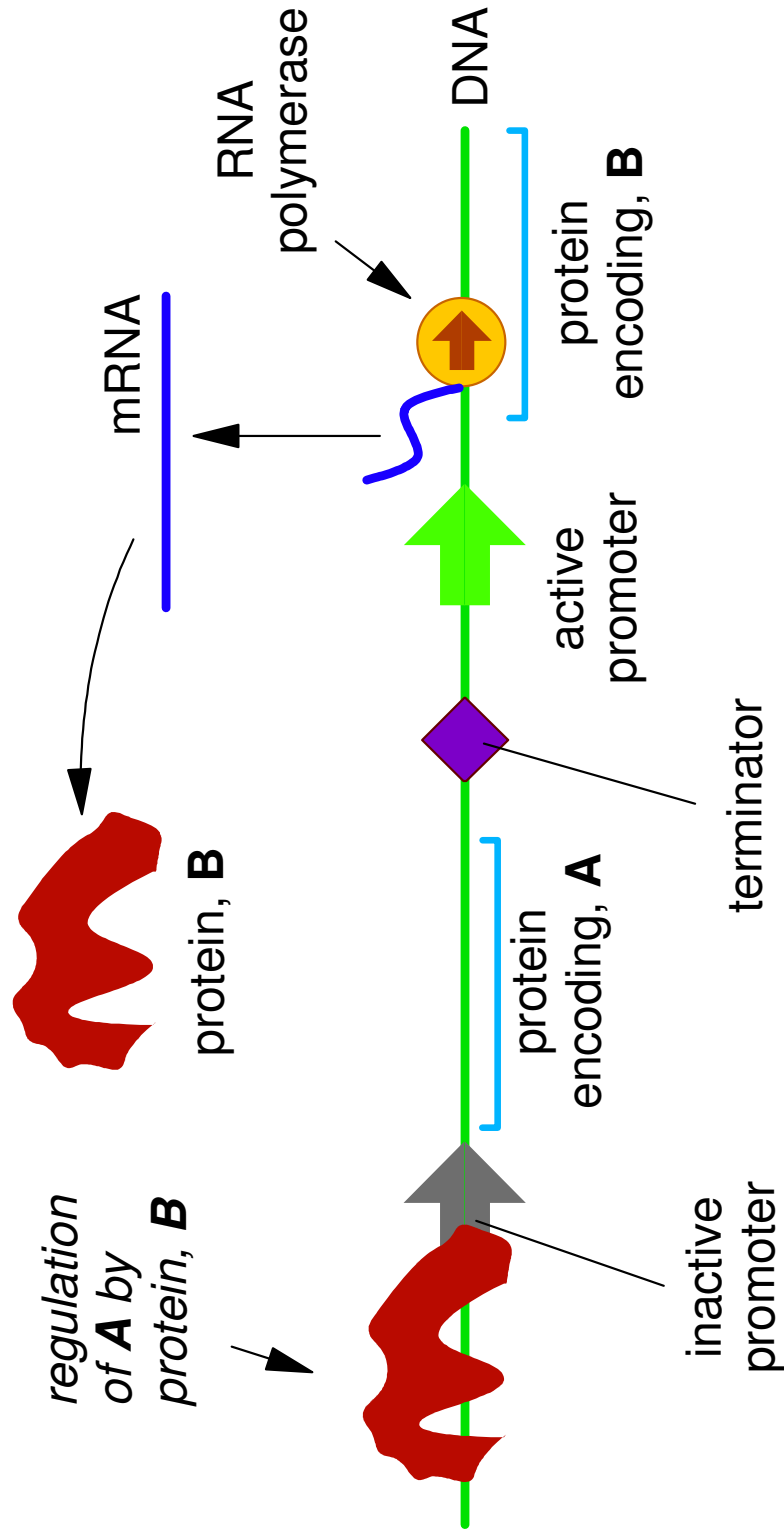
**D.K. Arvind & Jamie Davies**



# Overview

- Synthetic Biology
  - ▶ Storage and Processing
  - ▶ Communications
- Reprogrammable DNA (*my project*)
  - ▶ Computer Simulation
  - ▶ Biological Demonstration
- Towards Biospecks
  - ▶ Integration
  - ▶ Beyond Sensors

# Quick Introduction: How Cells "Read" DNA



# Synthetic Biology

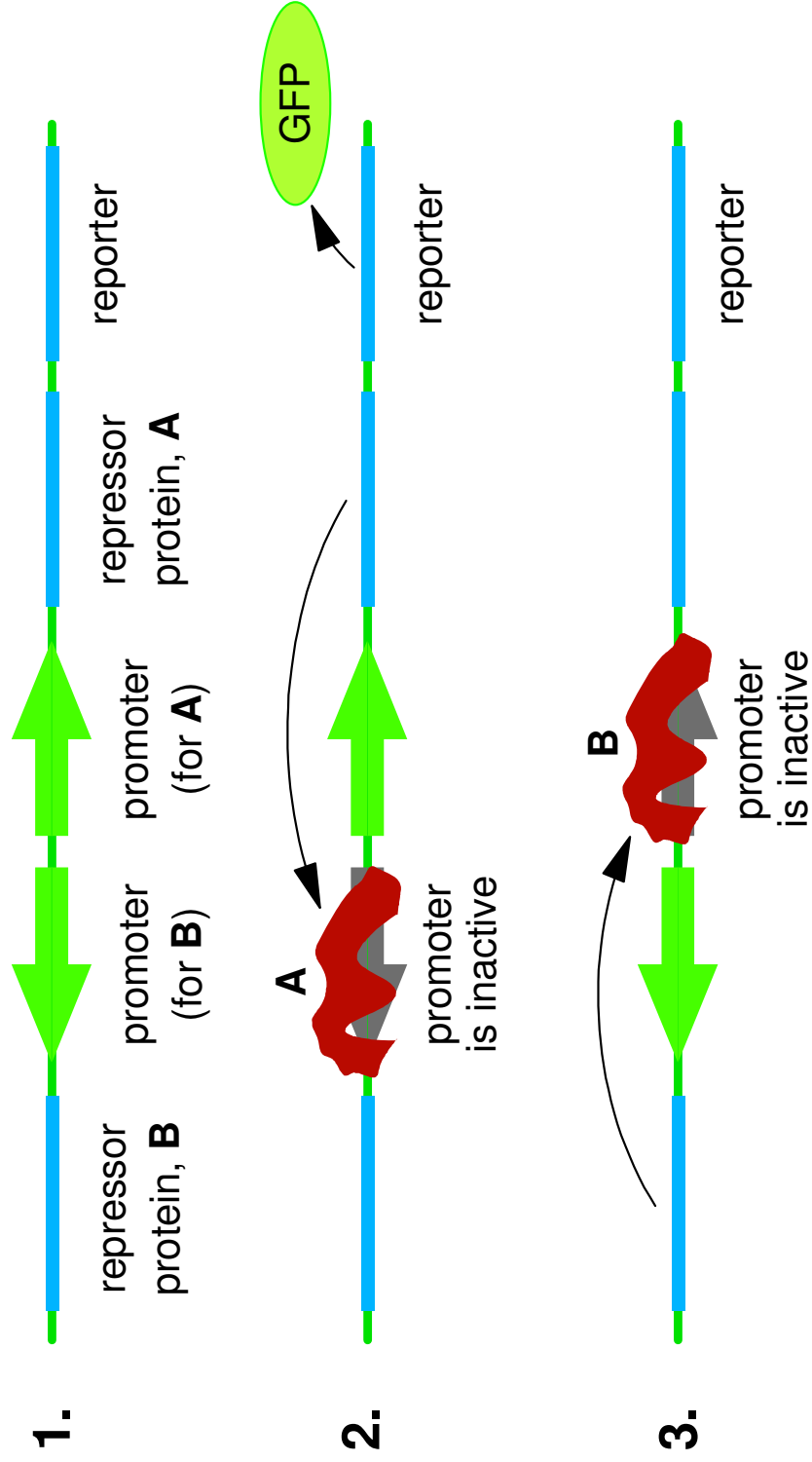
## ■ Storage and Processing

- ▶ Flip-flop
- ▶ Clock
- ▶ Gates

## ■ Communications

- ▶ Laser
- ▶ Broadcast
- ▶ Colour

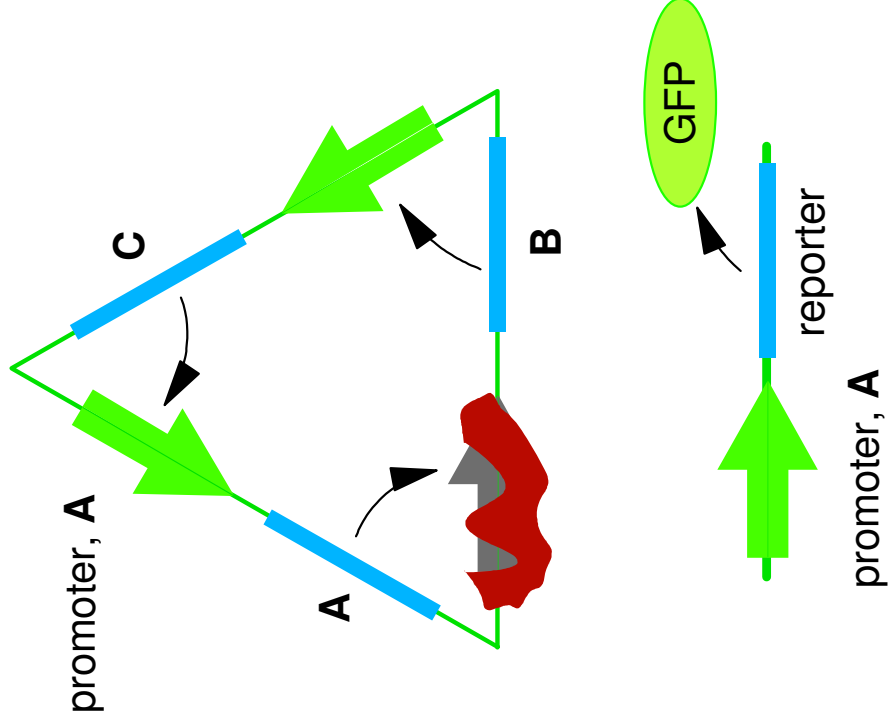
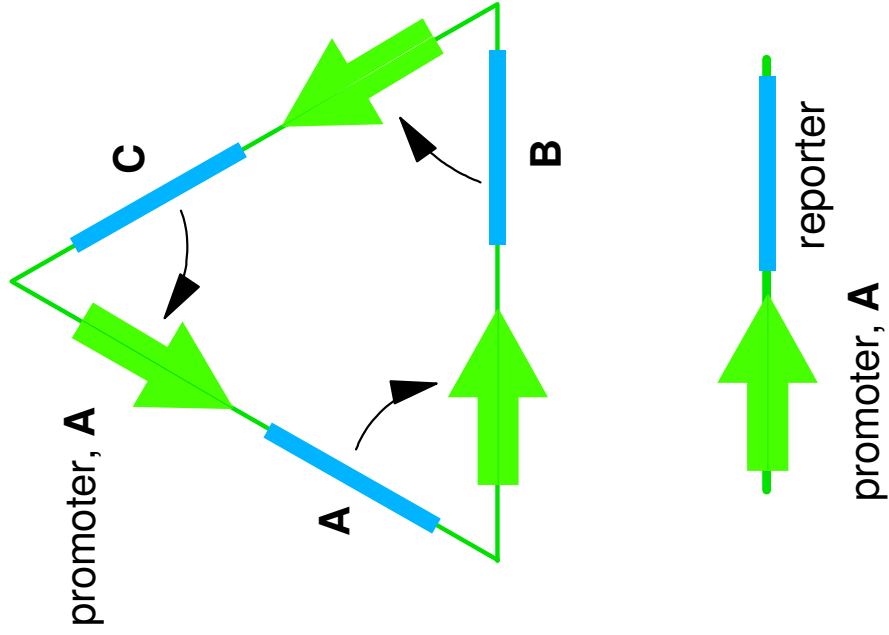
# Flip-Flop



*Toggle Switch*

Gardener, Cantor and Collins

# Clock



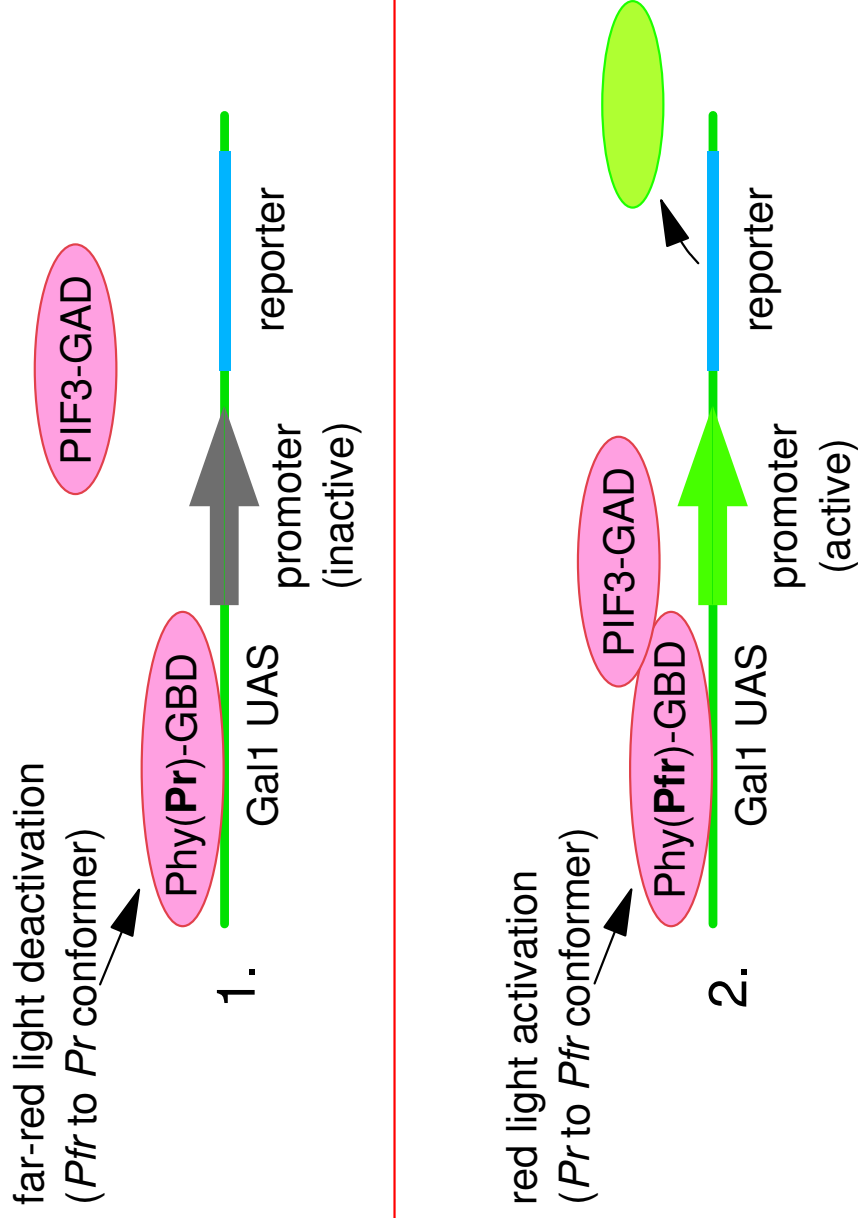
*The Repressilator*

Elowitz and Leibler

# Gates

- Logic
  - ▶ Invertor
  - ▶ And
  - ▶ Or
- Analogue
  - ▶ Pulse Detection

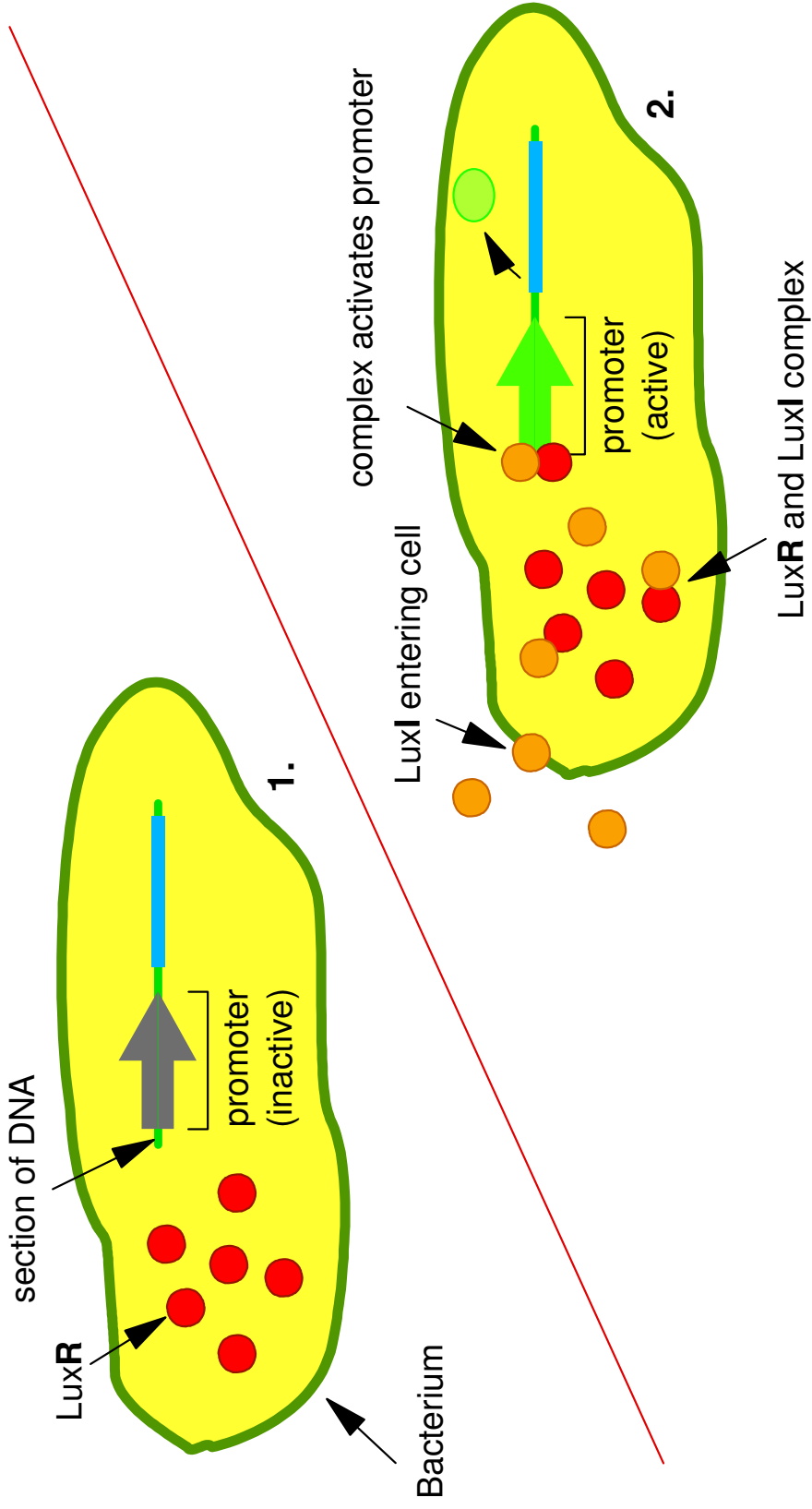
# Laser



*Light Switch Promoter*

Shimizu-Sato et al.

# Broadcast

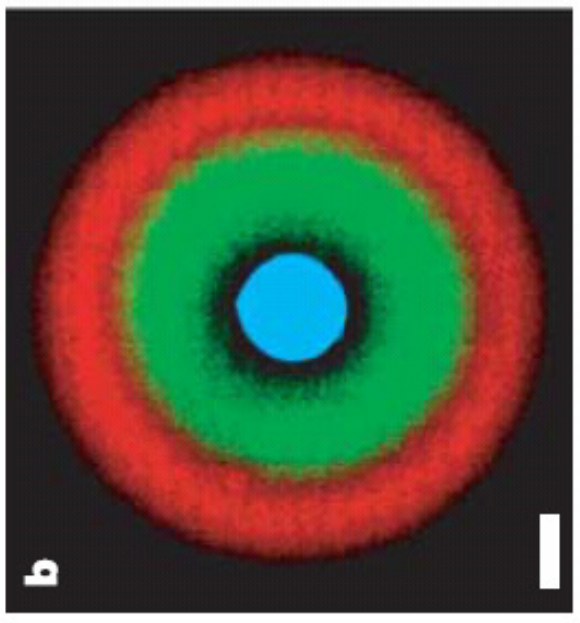


*Quorum Sensing Bacteria*

# Broadcast, Colour



Photograph



Fluorescence Microscope

*Programmed Pattern Formation*

*Basu et al.*

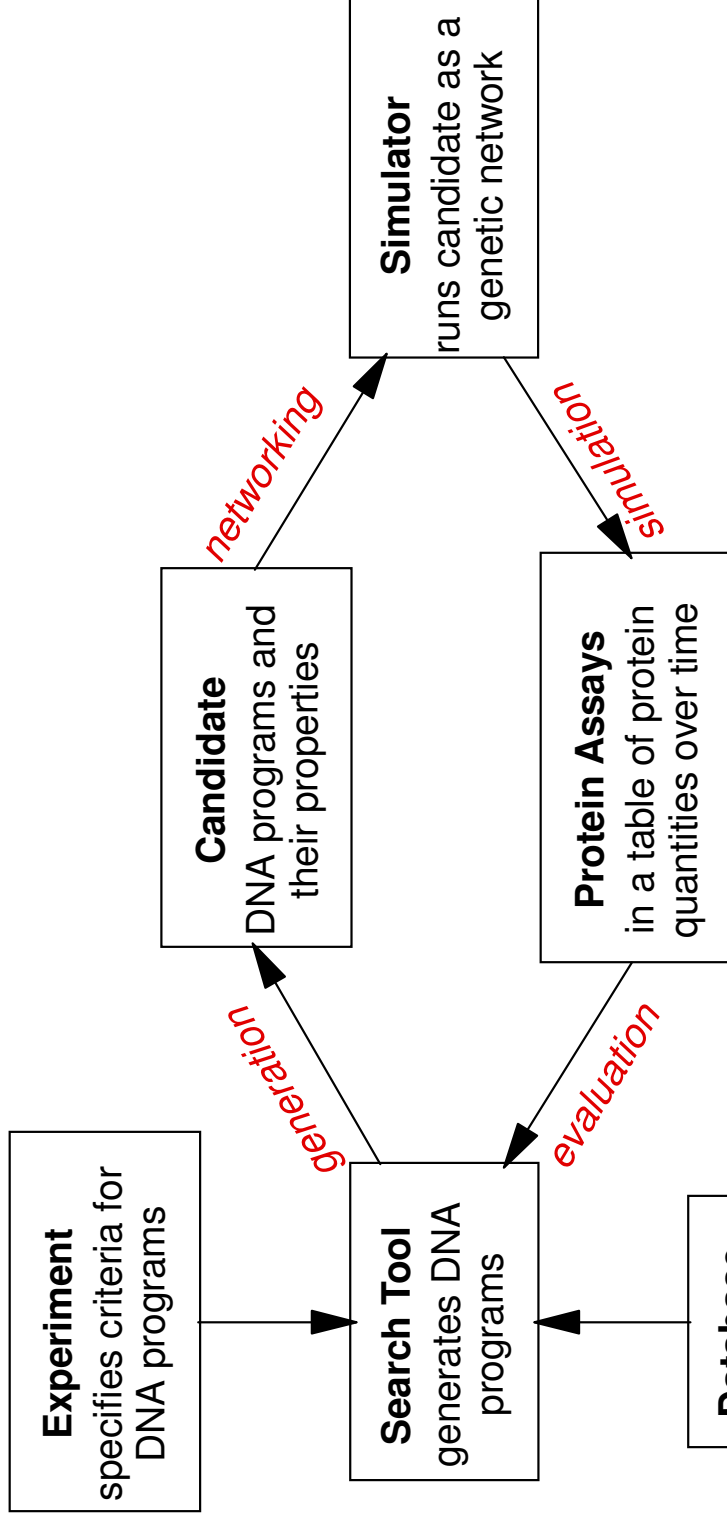
# Reprogrammable DNA (In Vivo)

- Computer Simulation
  - ▶ Purpose
  - ▶ Design
  - ▶ Example
- Biological Demonstration
  - ▶ Overview
  - ▶ Results
  - ▶ Characteristics

## Simulation: Purpose

- Investigate *In Vivo* Reprogrammable Operations
  - ▶ Potential Scalability
  - ▶ DNA "programs" are reprogrammed while running
  - ▶ Find a Good Candidate for Biological Demonstration
- Ideally...
  - ▶ Given A Set of Input/Output Requirements
  - ▶ A Database of DNA Sites
  - ▶ Compose DNA to Fulfill Requirements

# Simulation: Design



# Simulation: Example

Trial: first

Send 0.03 units of rnap from 0:00 to 8:00.

Check gfp at 8:00 is much more than bfp at 8:00.

Check gfp at 8:00 is more than 0.

Trial: second

Send 0.05 units of IPTG from 0:30 to 4:00.

Send 0.03 units of rnap from 0:00 to 8:00.

Check bfp at 8:00 is more than gfp at 8:00.

Check bfp at 8:00 is more than 0.

Send reset at 8:30.

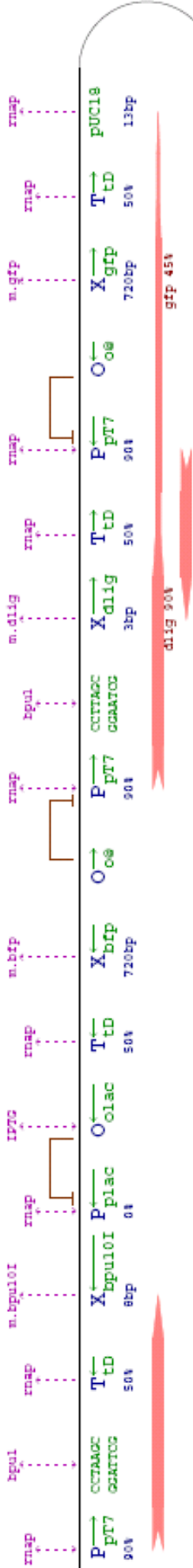
Send 0.03 units of rnap from 9:00 to 16:00.

Check bfp at 16:00 is much more than gfp at 16:00.

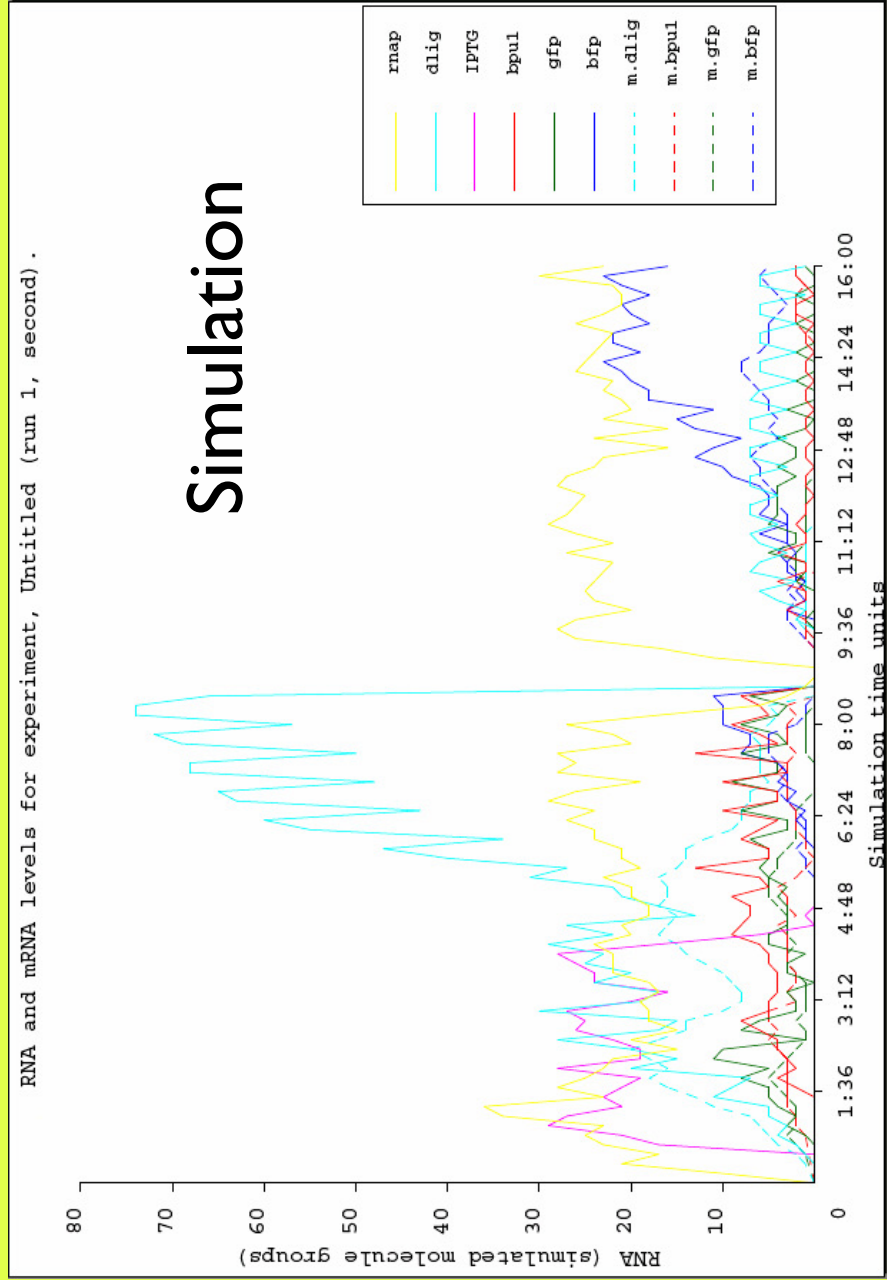
Check bfp at 16:00 is more than 0.

Check dna at 16:00 with bfp is circular (very important).

DNA illustration of Untitled (run 1, second) at time 0:01.



# Composition



# Simulation

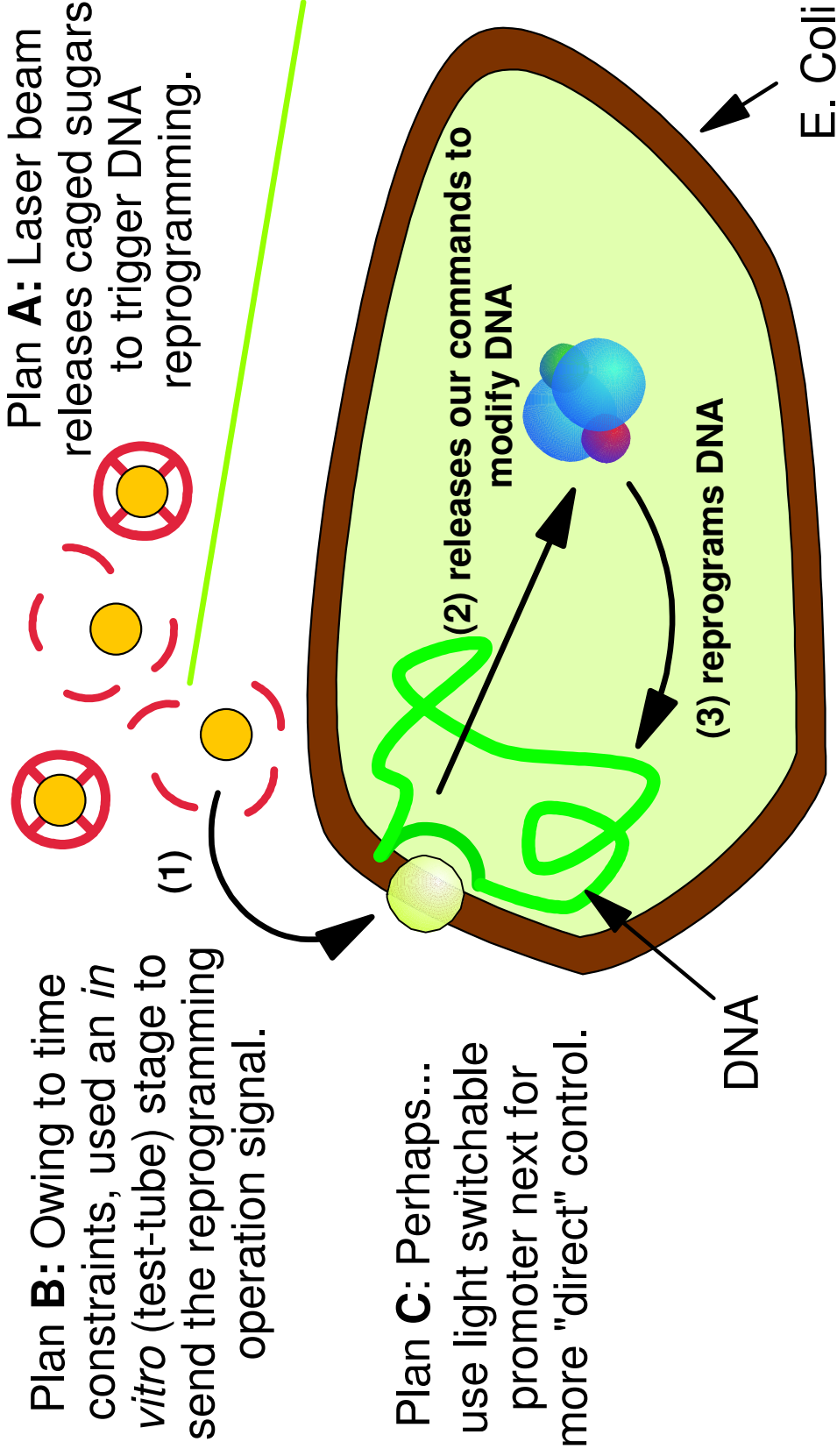
RNA and mRNA levels for experiment, Untitled (run 1, second).

Scores  
Justifications

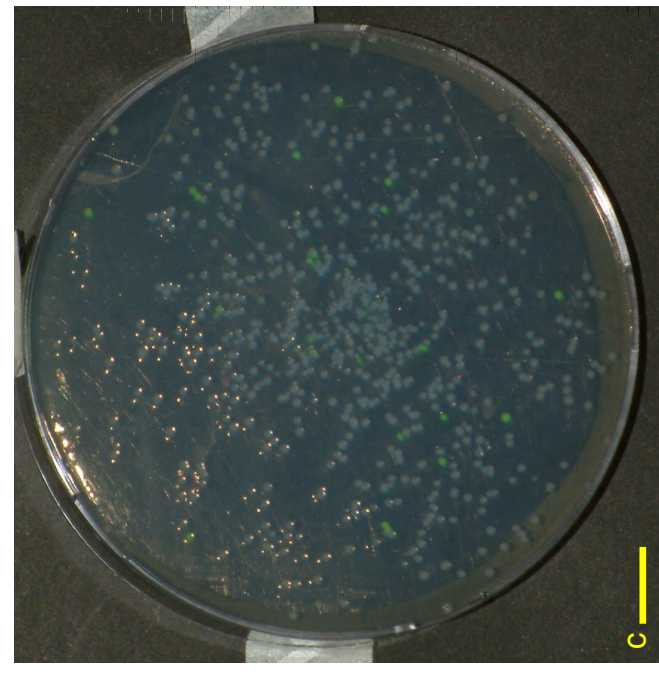
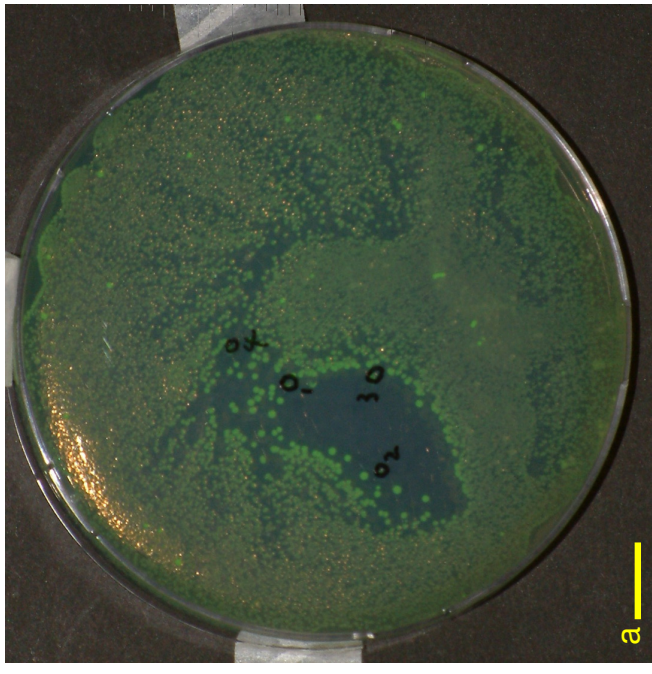
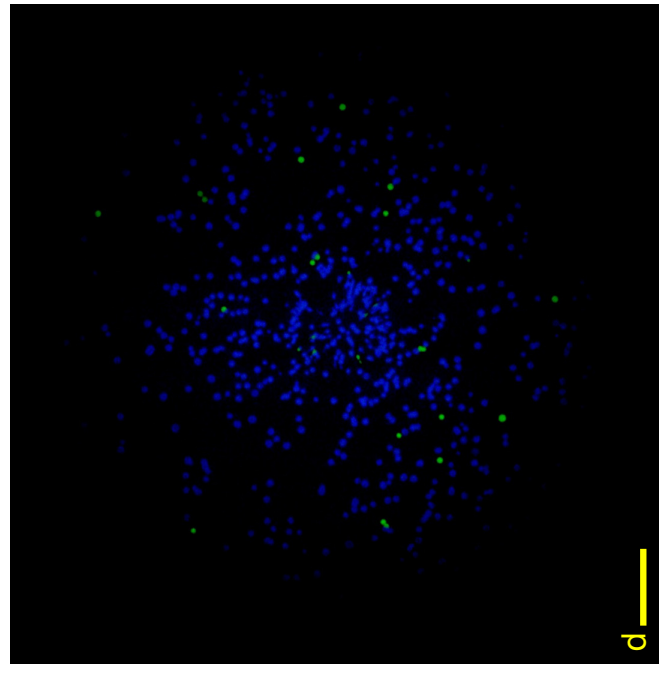
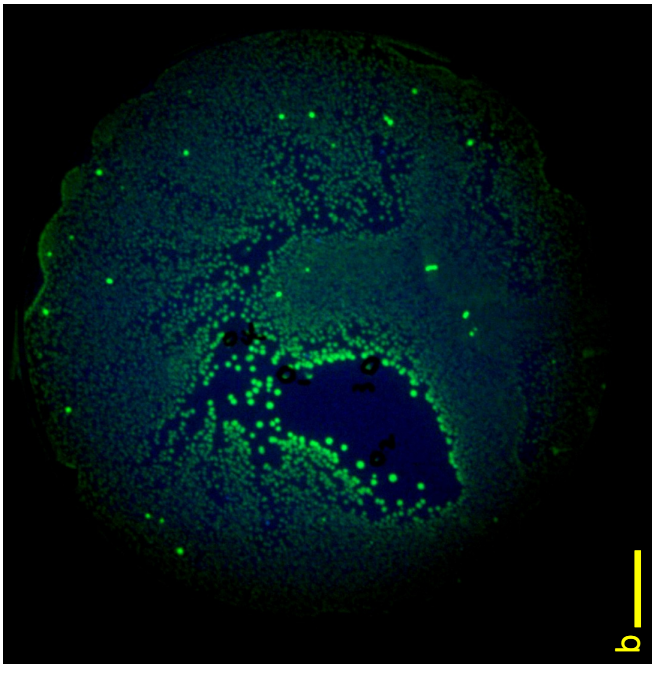
## Biology: Overview

**Plan B:** Owing to time constraints, used an *in vitro* (test-tube) stage to send the reprogramming operation signal.

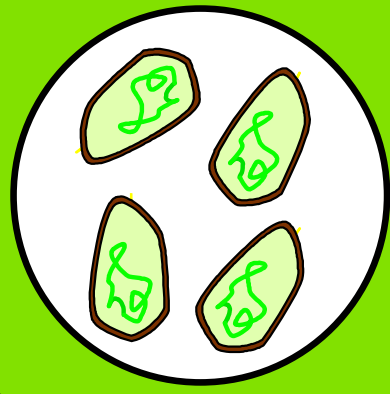
**Plan A:** Laser beam releases caged sugars to trigger DNA reprogramming.



**Plan C:** Perhaps... use light switchable promoter next for more "direct" control.



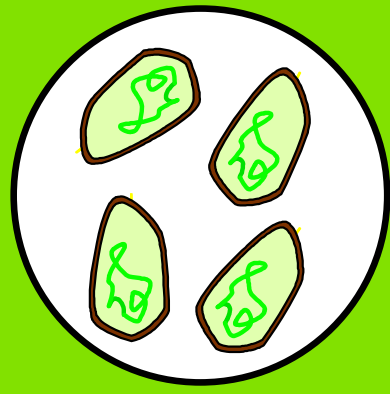
17



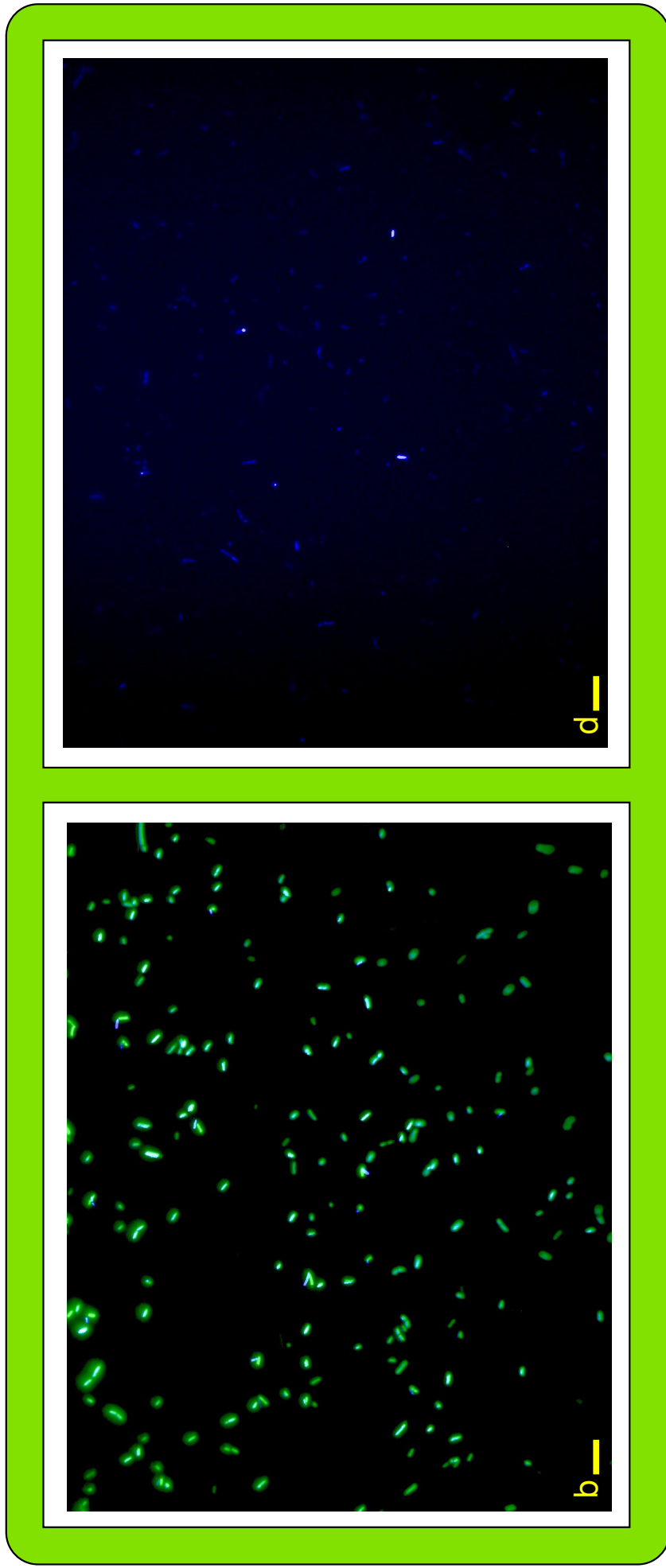
← just grow



→ reprogram and grow



# Biology Results: Close up



## Biology: Characteristics

- Plausibility of Reprogrammable DNA
- Also Found
  - ▶ State is stable across generations of bacteria
  - ▶ State can be stored irreversibly once set
  - ▶ Possible to distinguish states easily (by eye)

# Towards Biospecks

- Integration
  - ▶ Characteristics
  - ▶ I/O with Silicon
- Beyond Sensors
  - ▶ Biosensors with Basic Processing
  - ▶ Silicon "Control" of Cells



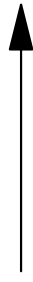
# Towards Biospecks: Characteristics

- Why?
  - ▶ Size (e.g. *E. Coli*, 1-5um)
  - ▶ Power (e.g. glucose, metabolise 17kJ/g)
  - ▶ Hibernation (can slow down if lacking nutrients)
  - ▶ Pre-made Devices (e.g. bacterial "motors")
  - ▶ Sensitivity (e.g. aspartate, 5 OoM, *E. Coli*)
  - ▶ Robustness (e.g. up to boiling point of water)
- Hurdles
  - ▶ Speed (e.g. from 1s to minutes)
  - ▶ Complexity and Other

# Towards Biospecks: I/O with Silicon

Silicon

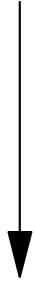
■ LDR



Carbon

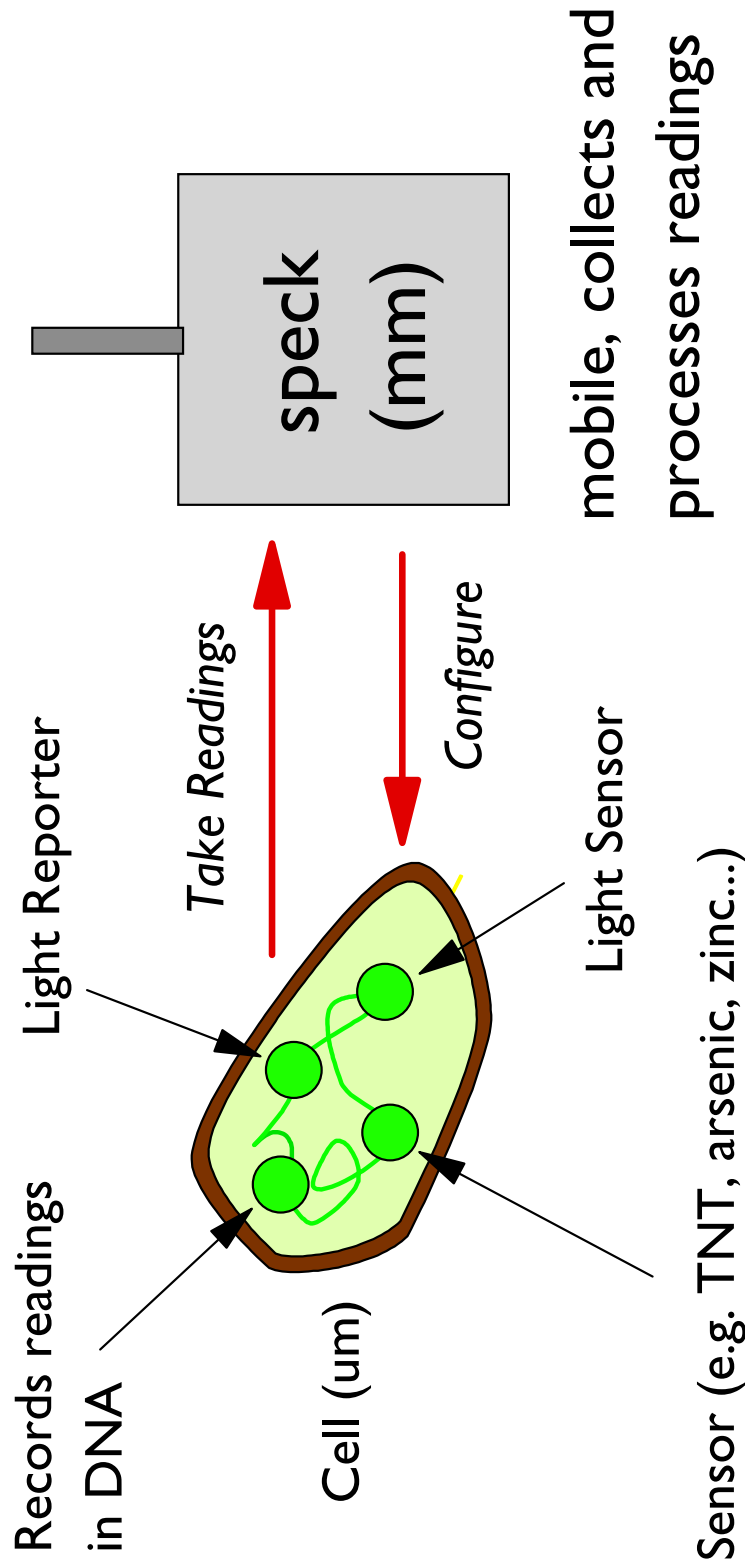
■ Firefly gene

■ Laser

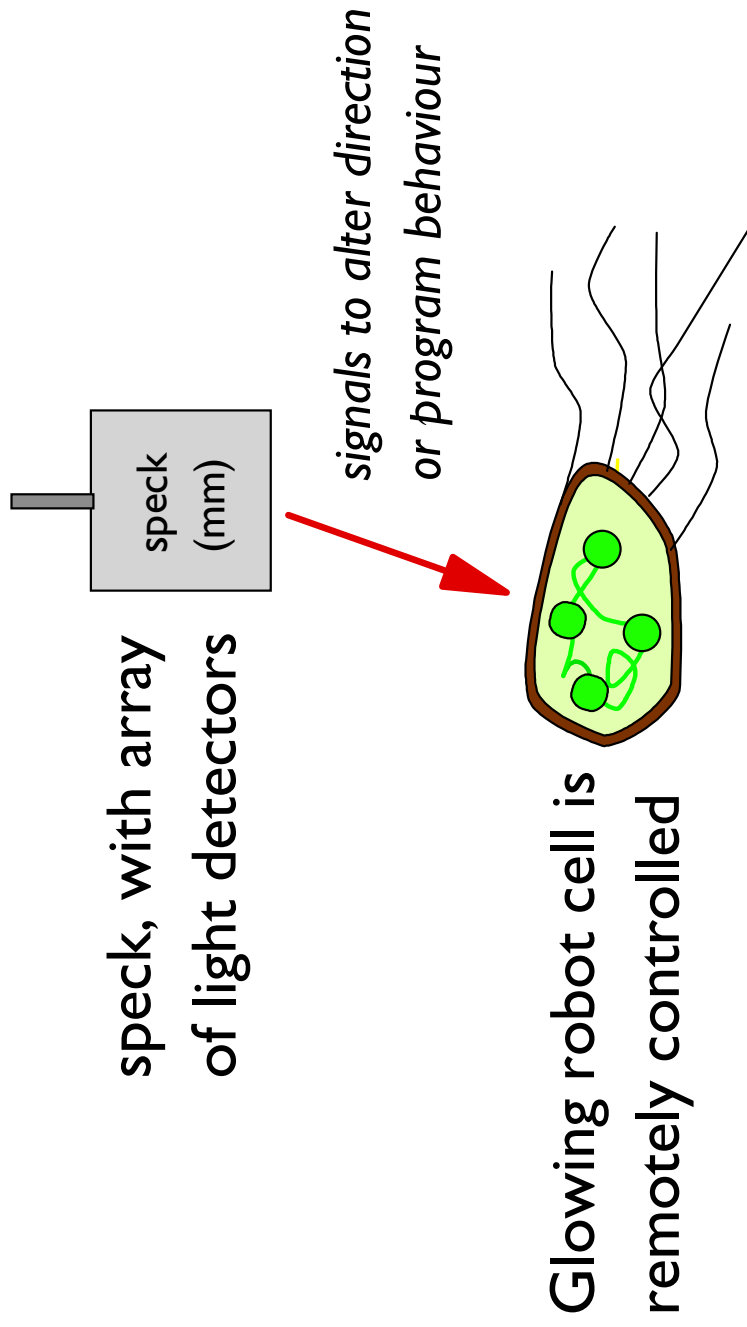


■ Light switch promoter

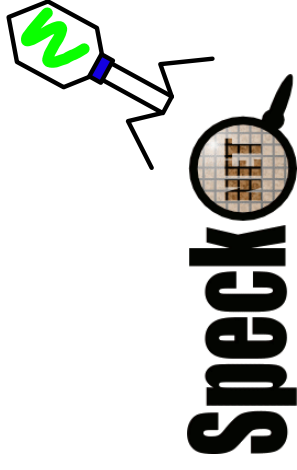
# Towards Biospecks: Biosensors with Basic Processing



# Towards Biospecks: Silicon "Control" of Cells



# Towards Biospecks



**Speck**



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