Designing Biological Systems

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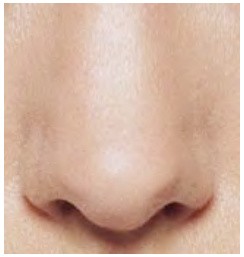
We can use Biology to make useful things

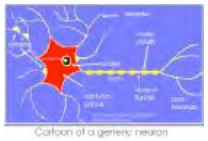
- **Redesign of a system can test our understanding of its components**
- **Biology knows how to make things we can't make**
  - but would like to

When is biology better than engineering?



- Very sensitive

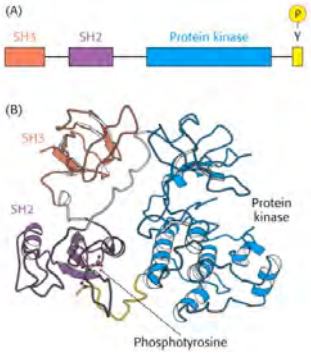
When is biology better than engineering?



Cartoon of a generic neuron

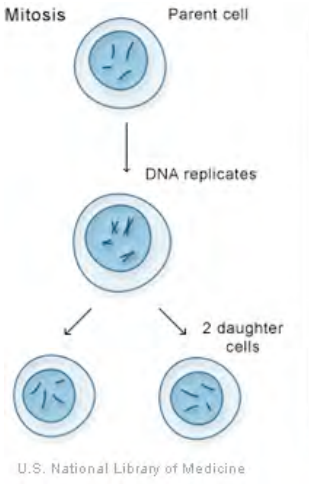
- Very sensitive
- Can send and receive signals

When is biology better than engineering?



- Very sensitive
- Can send and receive signals
- Made of modules

When is biology better than engineering?



- Very sensitive
- Can send and receive signals
- Made of modules
- Capable of easy duplication

Can we make Biology easier to engineer?

- Rapid, inexpensive DNA synthesis
- Sequenced genomes for raw materials
- Information explosion via the internet
- Worldview from computer chip design
  - Appreciation of biological modularity
    eg promoters, genes, proteins

DNA Synthesis is getting faster and cheaper -- just like computer chips

1970s

- **Chemical synthesis of the first gene**

1980s

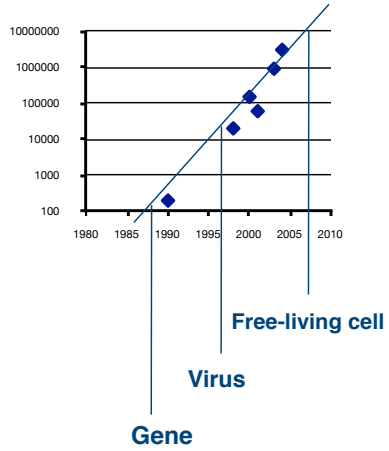
- **Chemical synthesis of a gene encoding an enzyme**

1990s

- **Polymerase chain reaction - PCR**
- **"Liberation of the genome"**
- **Commercial synthesis of short DNAs**

2000 and beyond

- **Synthesis of viruses and bacteriophages**
- **Commercial synthesis of larger DNAs**



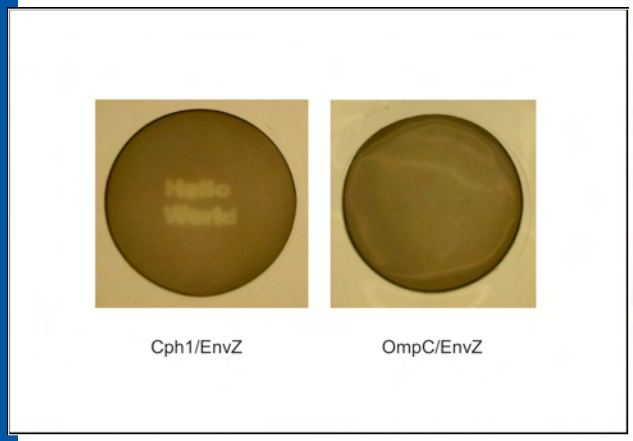
Rob Carlson, U. of Washington

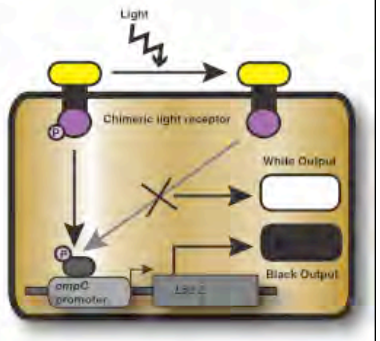
Synthetic Biology Goals

- Whole genome synthesis
- Design or redesign of biological systems
- Logical metabolic engineering
- Reconstruction of self-replicating systems in vitro

Biological Devices - Abstraction

Bacterial Edge Detector





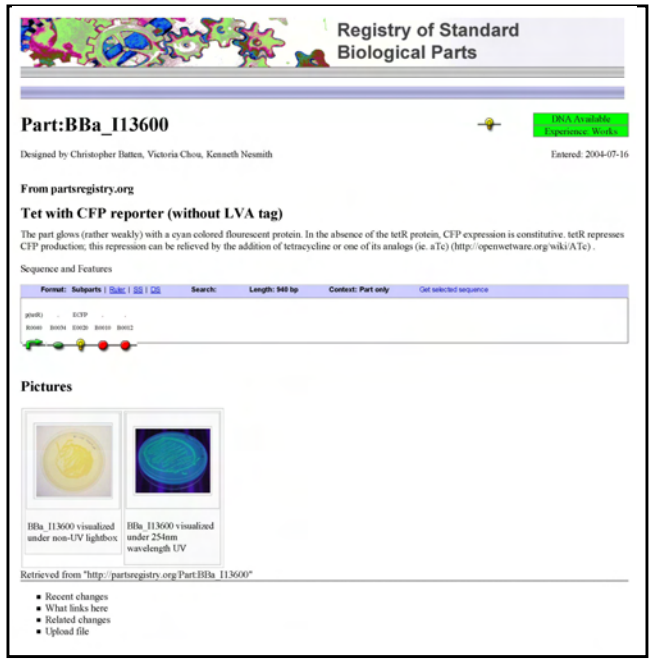
“Coligraph”

Tabor et al

partsregistry.org

Example Part

igem.org



Registry of Standard Biological Parts

Part:BBa_I13600

DNA Available
Experience: Works

Designed by Christopher Batten, Victoria Chou, Kenneth Nesmith

Entered: 2004-07-16

From partsregistry.org

Tet with CFP reporter (without LVA tag)

The part glows (rather weakly) with a cyan colored flouresent protein. In the absence of the tetR protein, CFP expression is constitutive. tetR represses CFP production; this repression can be relieved by the addition of tetracycline or one of its analogs (ie. aTc) (http://openwetware.org/wiki/ATc) .

Sequence and Features

Format: Subparts | Raw | SO | GB Search: Length: 940 bp Context: Part only Get selected sequence

Pictures

BBa_I13600 visualized under non-UV lightbox

BBa_I13600 visualized under 254nm wavelength UV

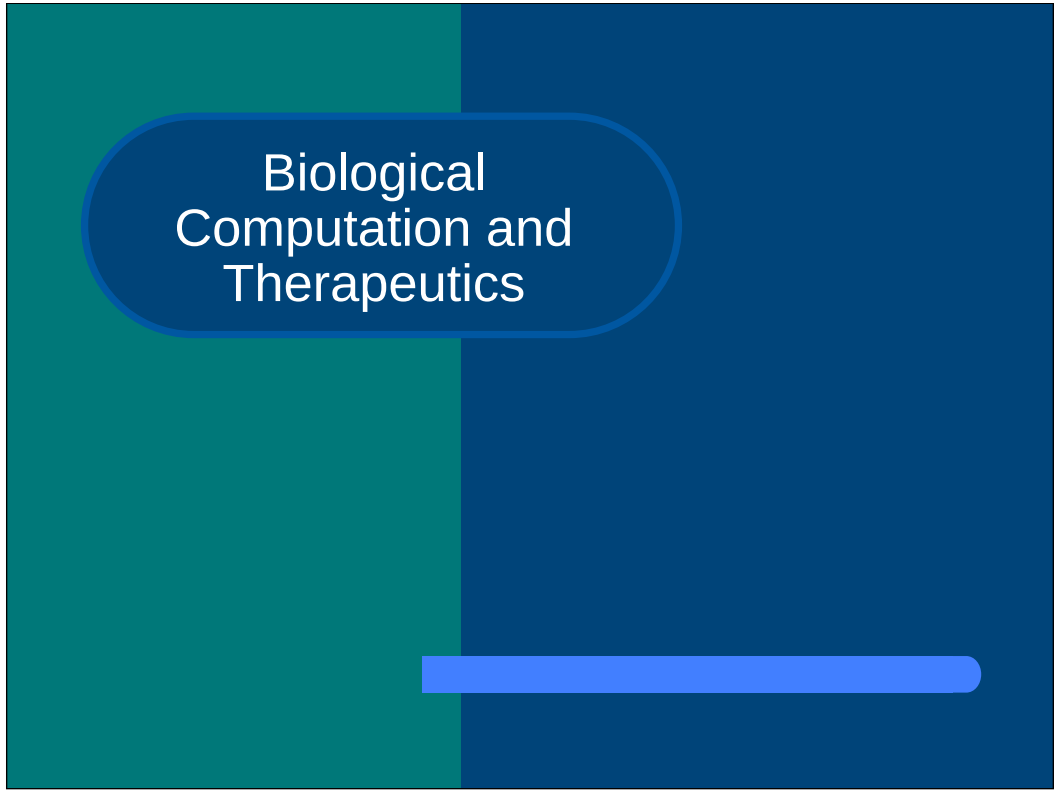
Retrieved from "http://partsregistry.org/Part:BBa_I13600"

- Recent changes
- What links here
- Related changes
- Upload file

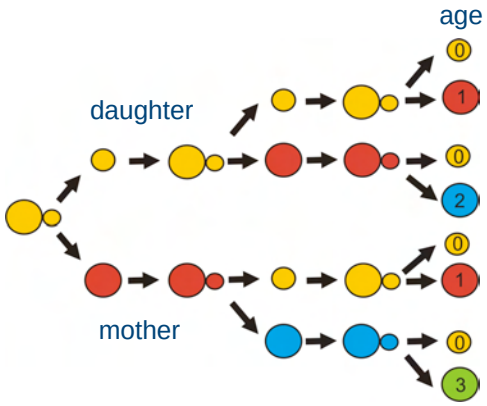
Can we make biological design predictable?

- Standardized parts
- Measurements of behavior
- Mathematical models
- Gene to genome synthesis - when does the ‘experiment’ start?

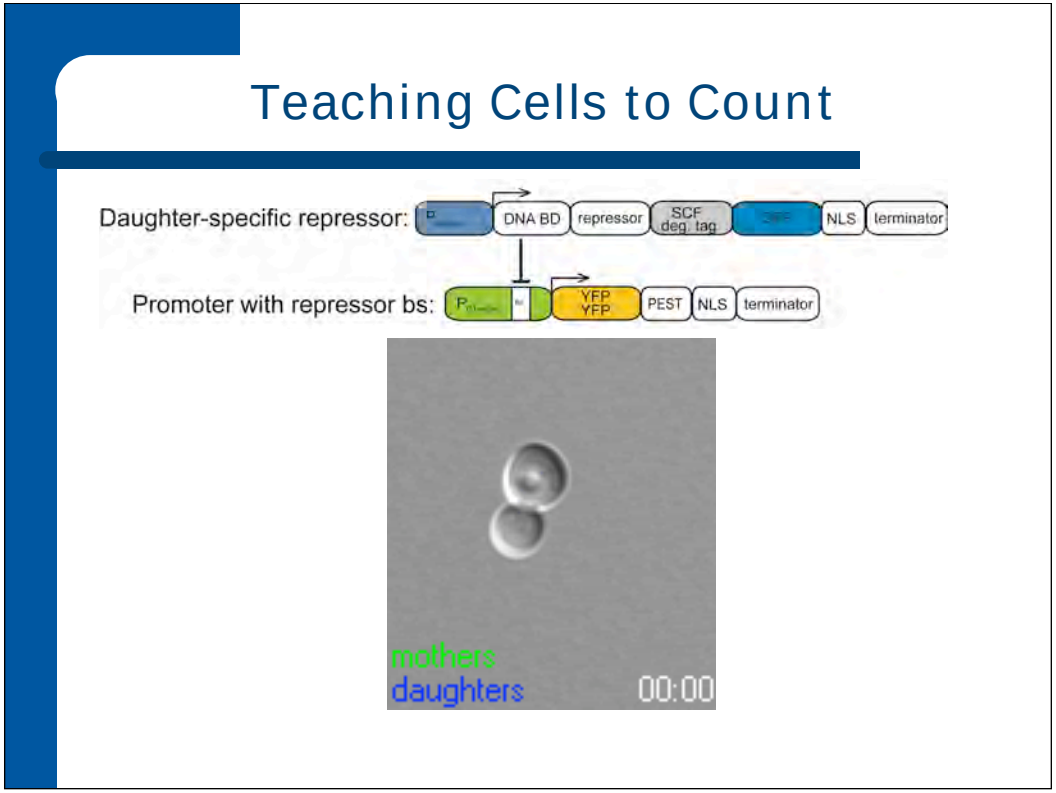
    - Consider the future synthetic biologist……..


Biological
Computation and
Therapeutics

Counting Cell Divisions



- Budding yeast: asymmetric division
- Count mitotic divisions

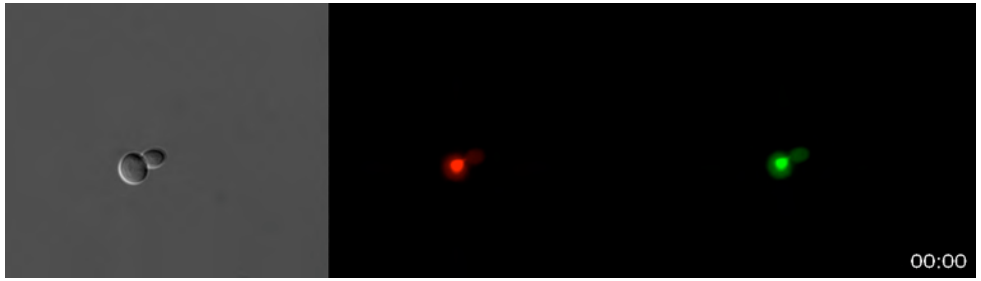


were the cells in exp growth phase?

Yeast strain: DLY4

Cells that Remember

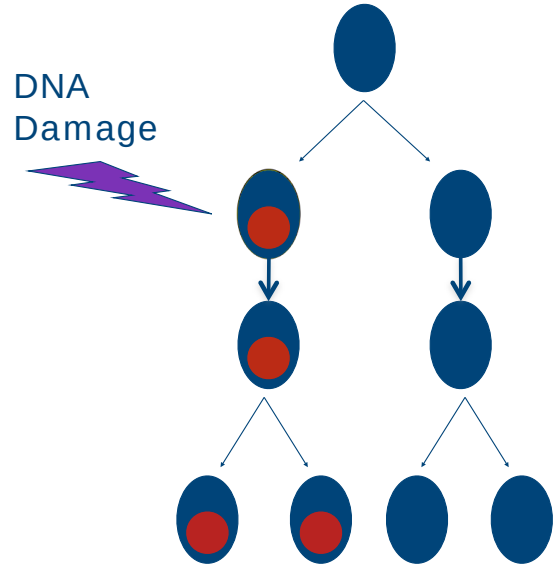
allow to grow



http://www.youtube.com/watch?v=nlqltVI2jSc

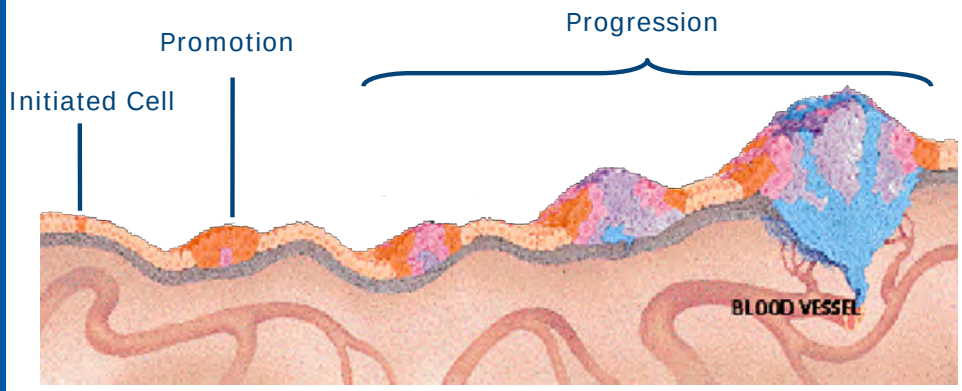
Memory in Cancer Cells

DNA Damage



Could compare responders with non-responders from a single population

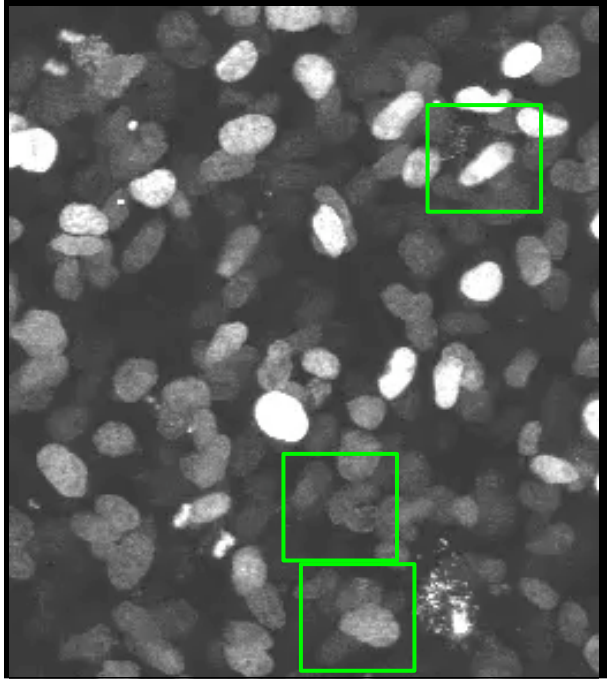
Apply Specific Cell Tracking To Studying Carcinogenesis

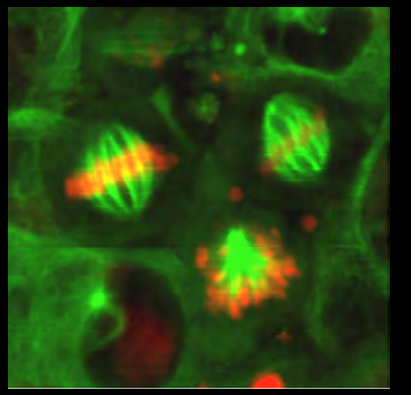


Adapted from: Dana Burns-Pizer

Weinberg RA. (1996). How Cancer Arises. Sci Am 275: 62-70.

Intravital imaging of tumor mitosis





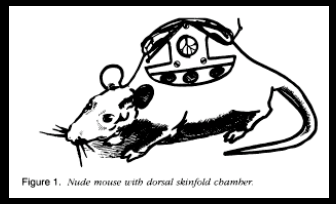
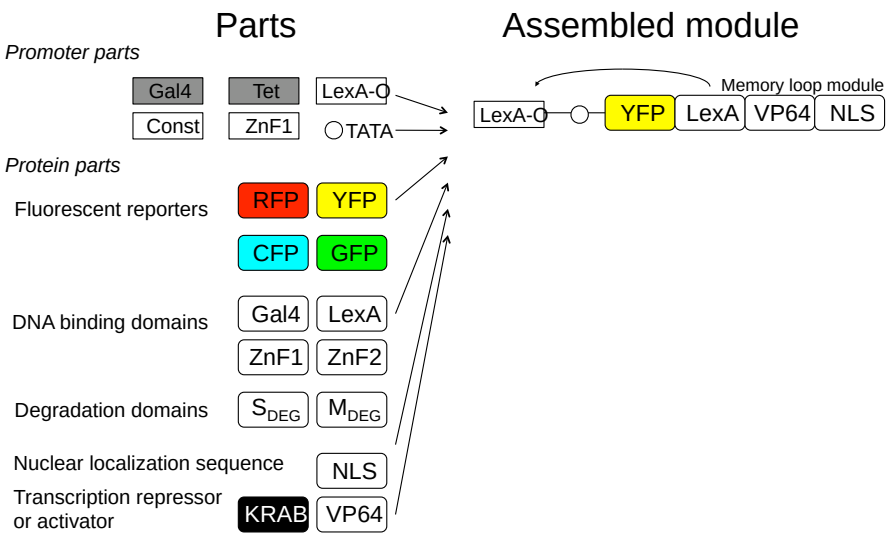
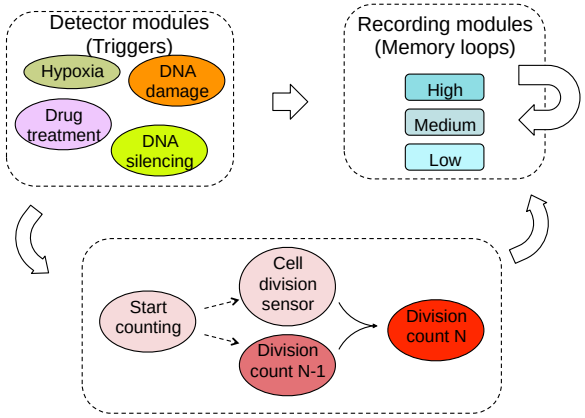


Figure 1. *Nude mouse with dorsal skinfold chamber.*


Parts
Assembled module
Promoter parts
Gal4
Tet
LexA-O
Const
ZnF1
TATA
Protein parts
Fluorescent reporters
RFP
YFP
CFP
GFP
DNA binding domains
Gal4
LexA
ZnF1
ZnF2
Degradation domains
S DEG
M DEG
Nuclear localization sequence
NLS
Transcription repressor or activator
KRAB
VP64
Memory loop module
LexA-O
YFP
LexA
VP64
NLS

Abstraction with multiple devices



The Sun, Bio-Energy and Beyond

Engineering microorganisms for energy production

Conclusions from the JASON report:

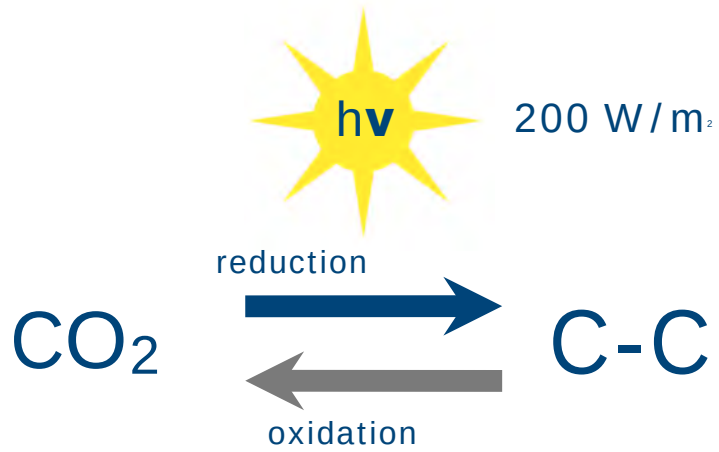
Boosting efficiency of fuel formation form microorganisms is THE major technological application of Synthetic Biology

Engineering fuel production from microbes is a SYSTEMS problem

Successful engineering requires a basic understanding of the system to be engineered (multiple feedback loops, etc)

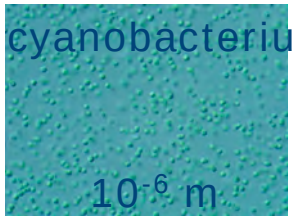
Study Leader Mike Brenner; 6/23/06

Reduction and Oxidation of Carbon is central to our lives



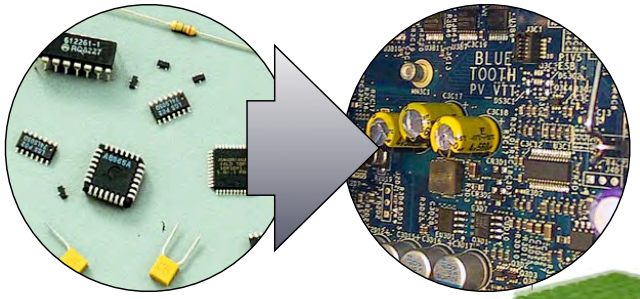
Photosynthetic organisms come in all shapes and sizes

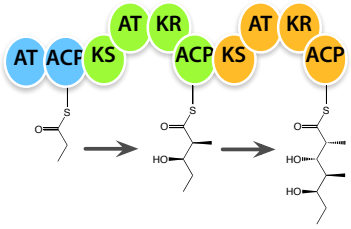
10^2 m

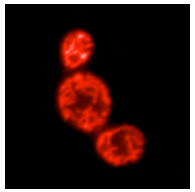


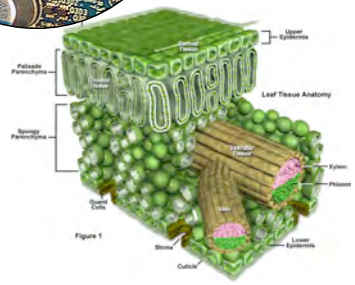
Cyanobacteria are responsible for ~50% of all photosynthesis on earth!

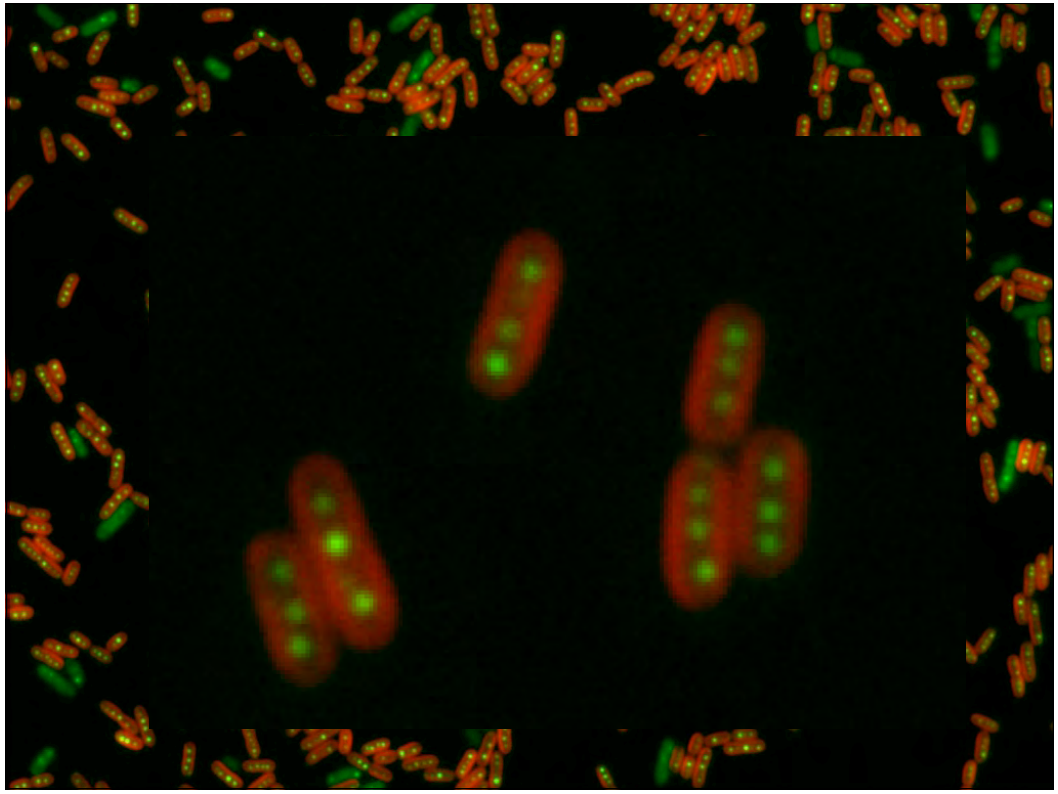
spatial organization is important for engineering and biology





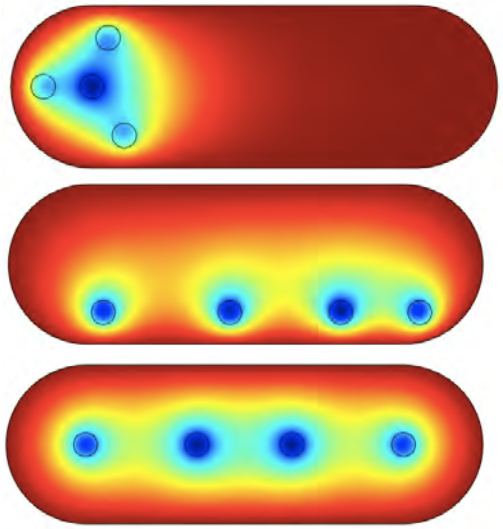


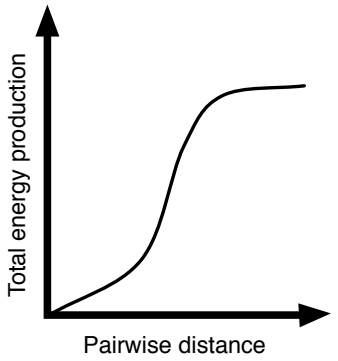




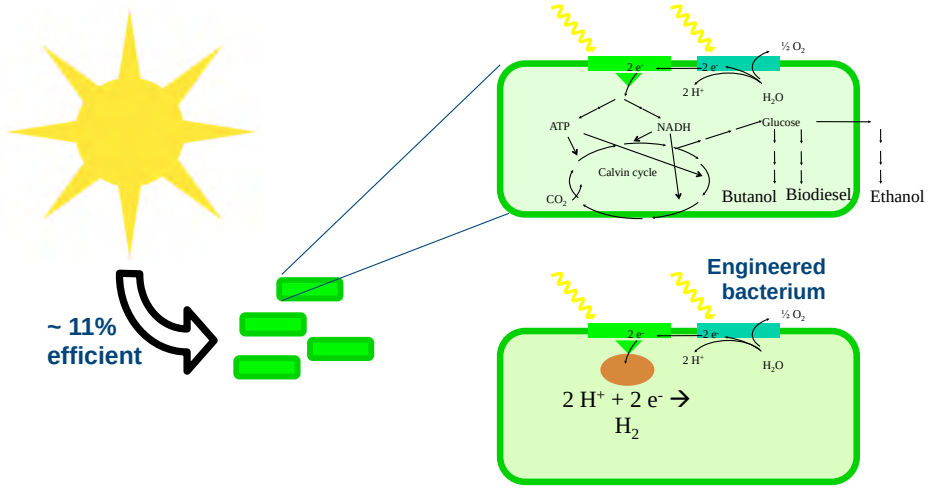
We can improve carbon fixation by engineering

- A diffusion-limited reaction will be susceptible to spatial arrangements

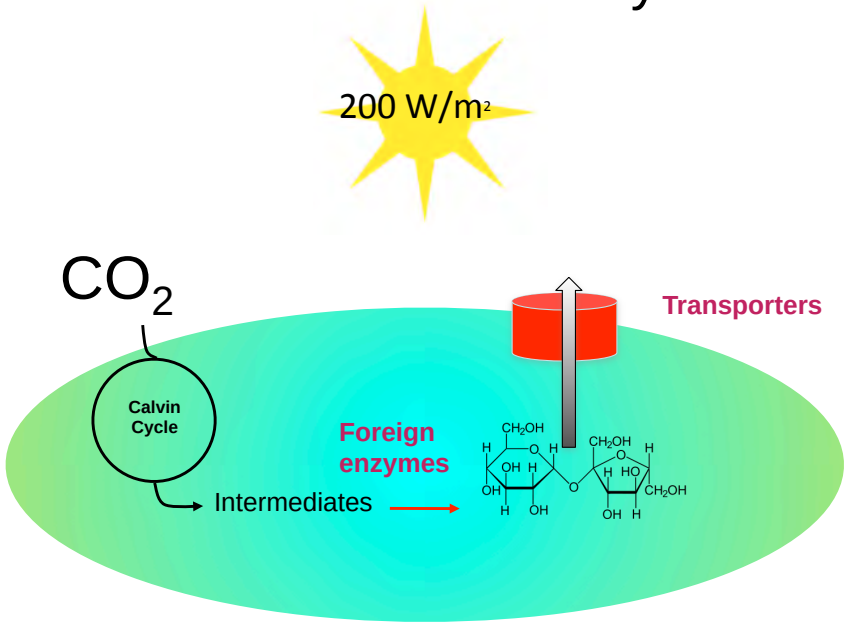




Harnessing Bacterial Photosynthesis

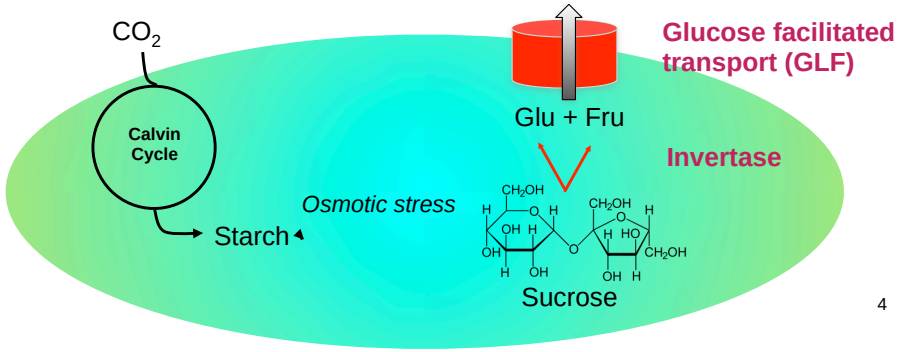


Platform for chemical synthesis

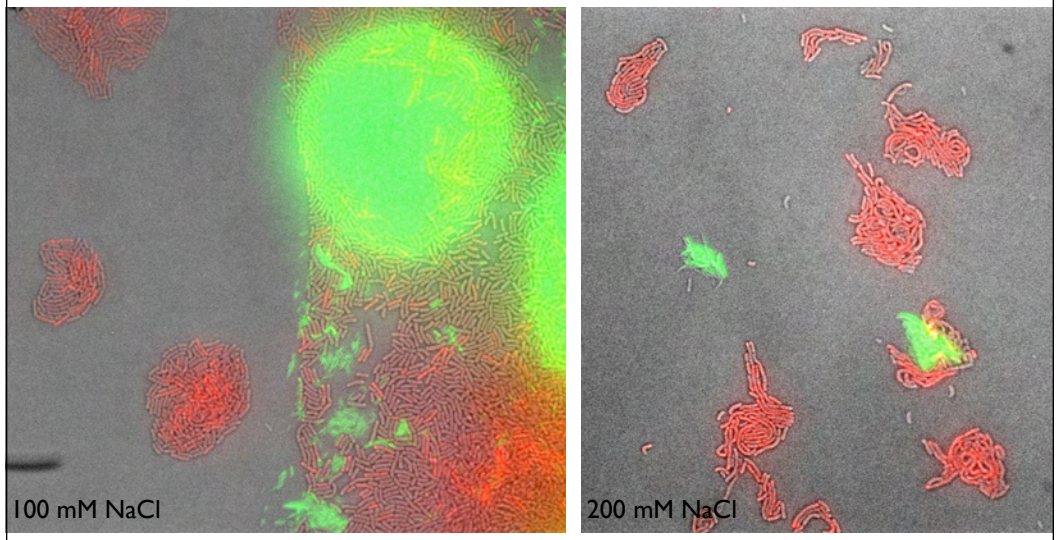


Sugar production in cyanobacteria

- Sugars = feedstock for all metabolic engineering
- Glucose + fructose mixture = ‘high-fructose corn syrup’
- Engineering concept:
  - Induce sucrose production by osmotic stress (natural process)
  - Invertase = enzyme that cleaves sucrose
  - GLF = facilitated diffusion transporter for glucose, fructose



Feeding *E. coli* with light (on plates)



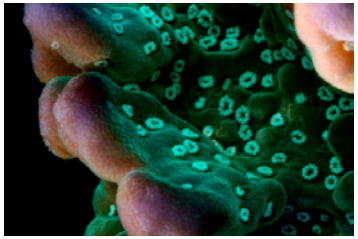
Naturally Photosynthetic Animals

Sea slug

Jellyfish

Clam

Coral



Mammal

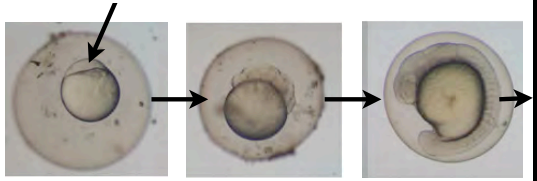
Flatworm

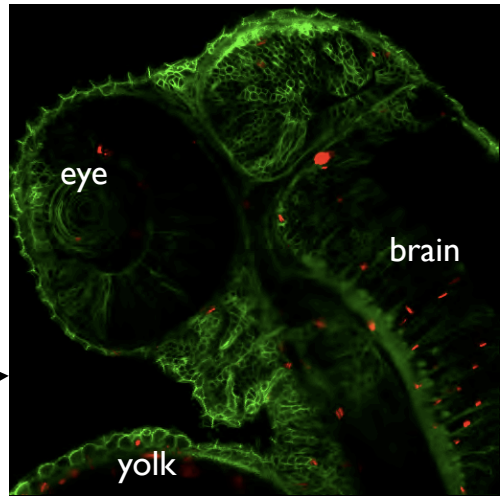
Synthetic Photosynthetic Animals

Making Photosynthetic Fish?

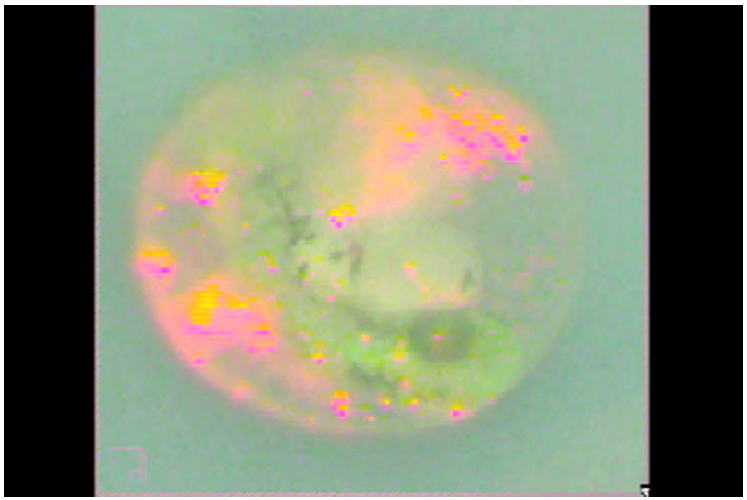
glf + *invA*

microinject engineered *Synechococcus* into zebrafish zygote



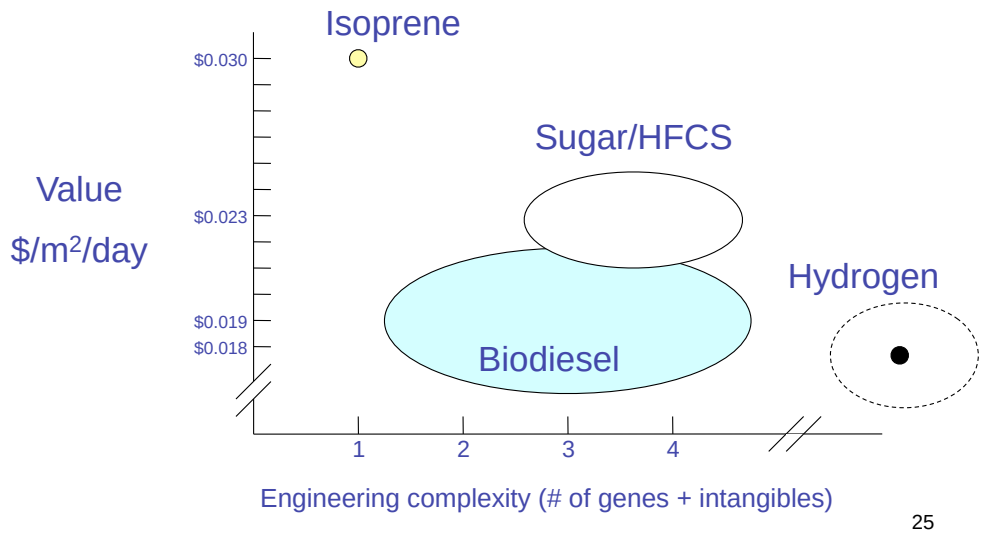


Making Photosynthetic Fish?



for more fun videos check out www.hydrocalypse.com!

Mix of commercial potential and scientific feasibility



Thanks to many people who have contributed to these ideas

Funding:
National Institutes of Health
Department of Energy
Department of Defense
Harvard University Center for the Environment
Wyss Institute of Biologically Inspired Engineering
National Science Foundation Center for Synthetic Biology Research