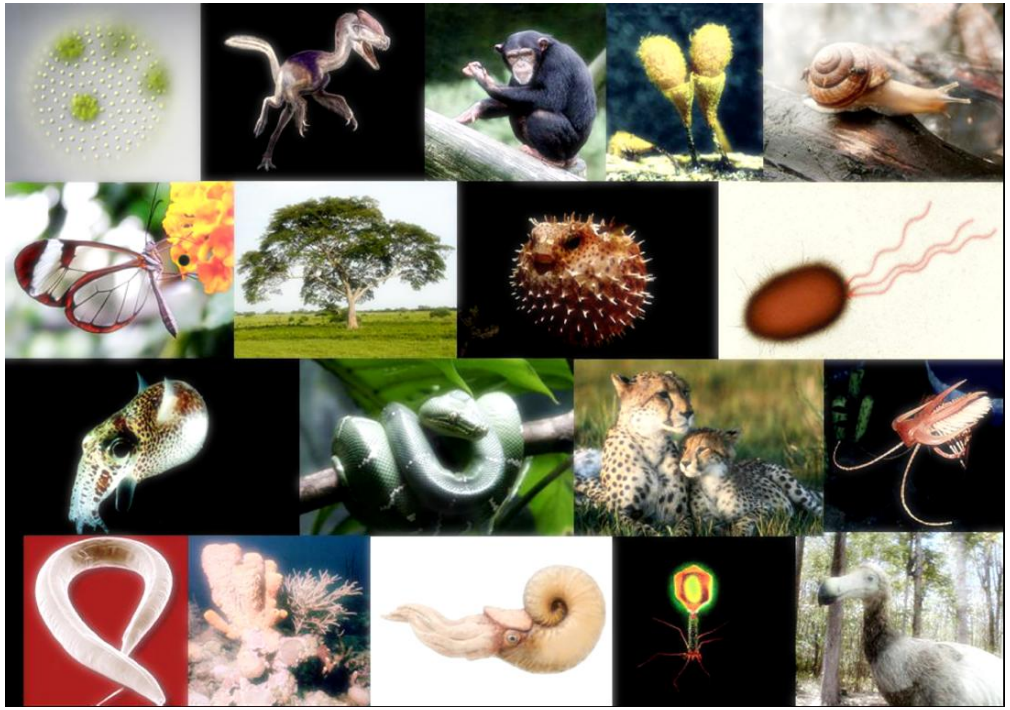
Applications of synthetic biology

Anne Meyer
May 6, 2014

How to implement a new application:

1. Find your parts of interest in nature.



How to implement a new application:

1. Find your parts of interest in nature.

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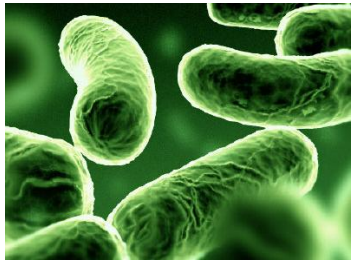
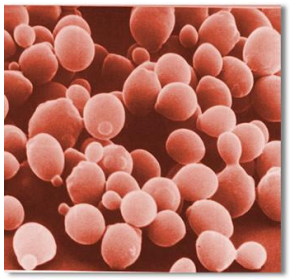
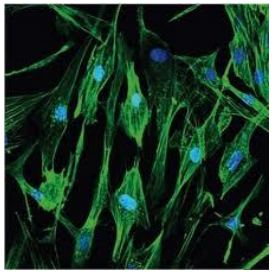






How to implement a new application:

1. Find your parts of interest in nature.

2. Express them in your new chassis.

3. Improve!

Affordable malaria drugs

Make a product

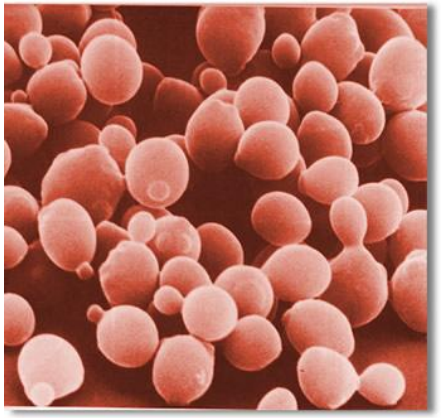
Affordable malaria drugs: borrow plant pathways

Make a product

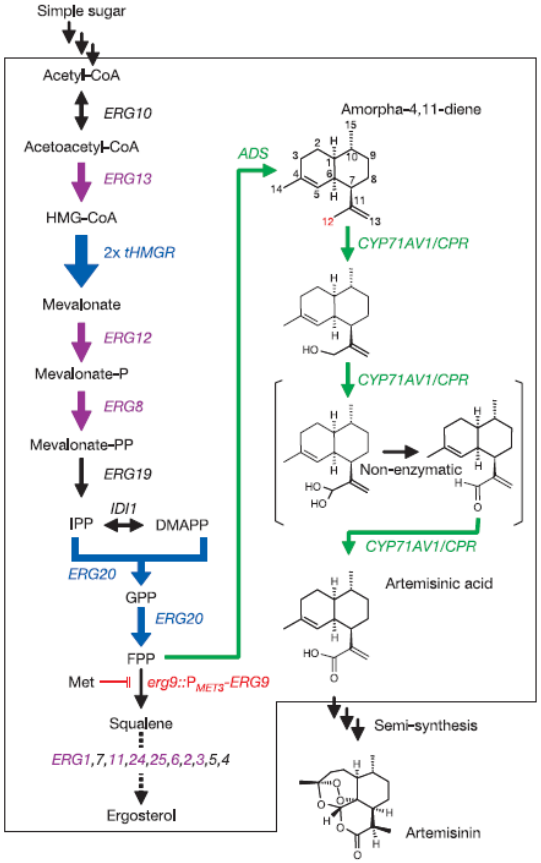
Production of the antimalarial drug precursor artemisinic acid in engineered yeast

Dae-Kyun Ro[1]*, Eric M. Paradise[2]*, Mario Ouellet[1], Karl J. Fisher[6], Karyn L. Newman[1], John M. Ndungu[3], Kimberly A. Ho[1], Rachel A. Eachus[1], Timothy S. Ham[4], James Kirby[2], Michelle C. Y. Chang[1], Sydnor T. Withers[2], Yoichiro Shiba[2], Richmond Sarpong[3] & Jay D. Keasling[1,2,4,5]

Artemisia annua



S. cerevisiae



Ro, Nature 2006

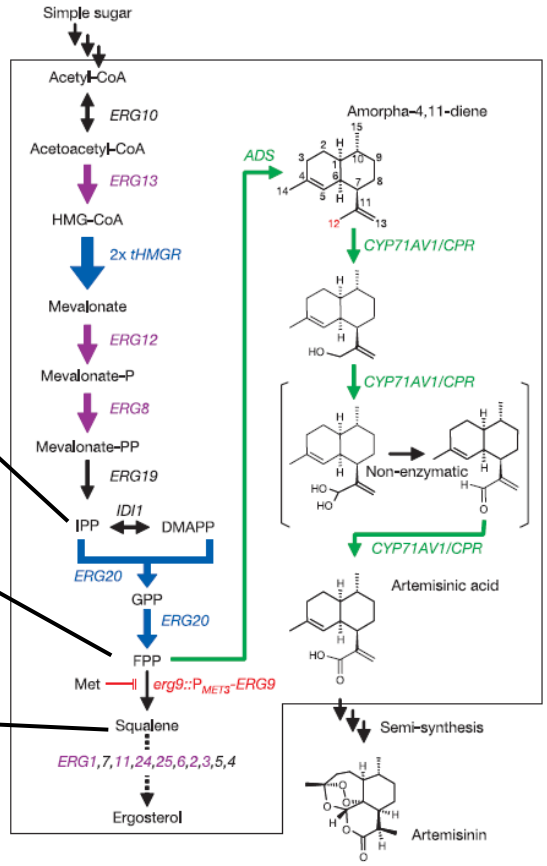
Bioproduction pathways have versatile uses

Make a product

Used to make tire material

Used to make jet fuel

Used in cosmetics

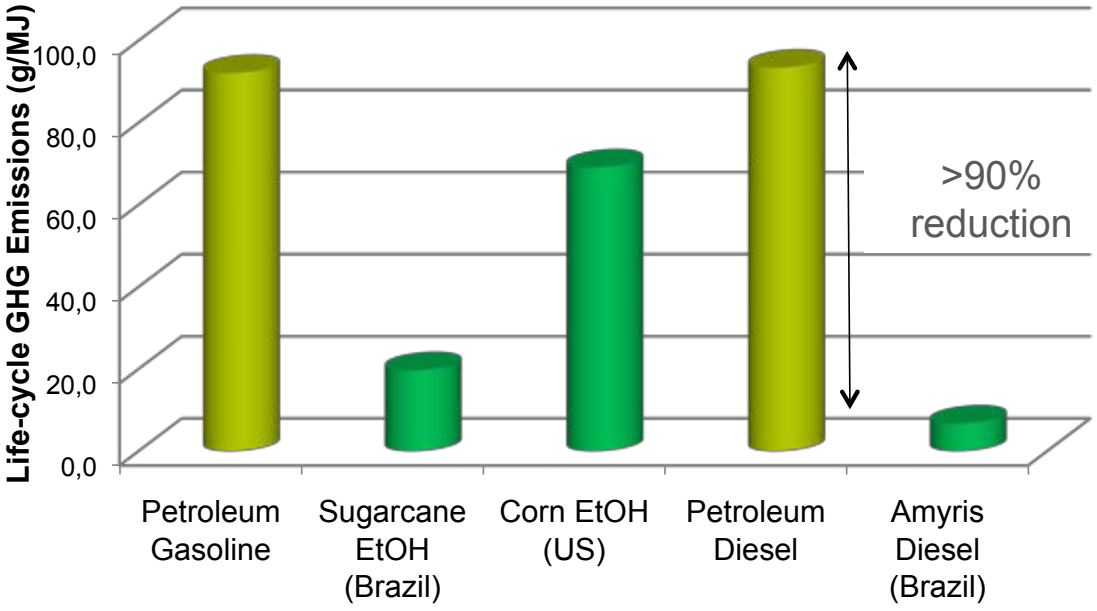


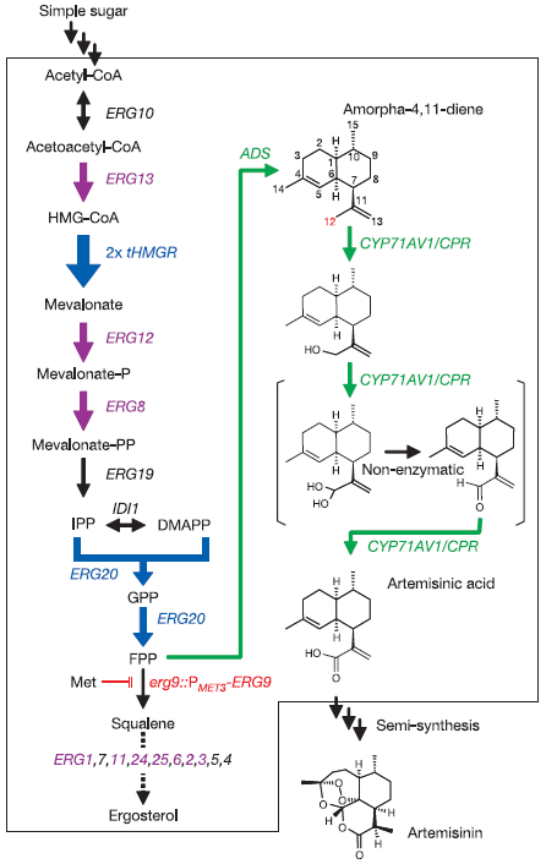
Ro, Nature 2006

Bioproduction pathways have sustainable uses

Make a product

Amyris Diesel shows a reduction in GHG's, even vs. sugarcane ethanol…

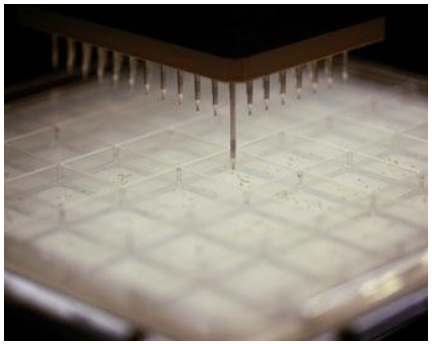




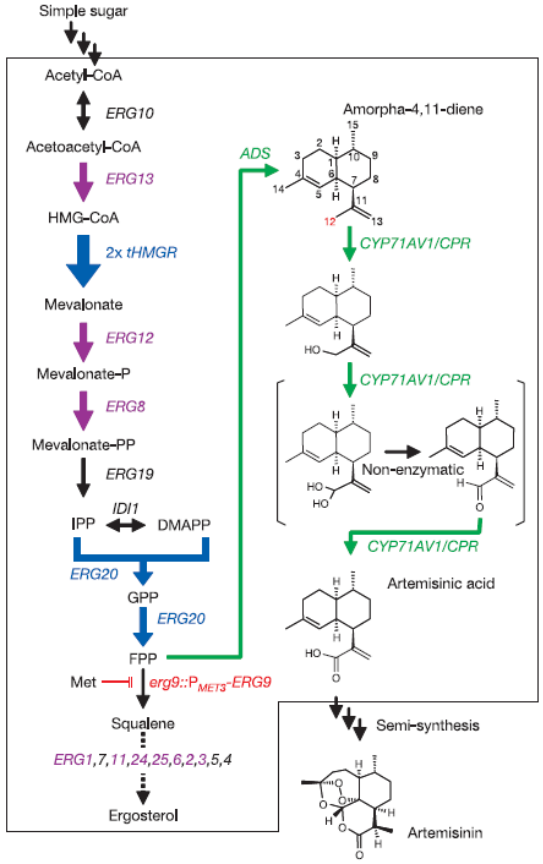
Ro, Nature 2006

Bioproduction pathways require reprogramming

Make a product



Test thousands of strains a day to:



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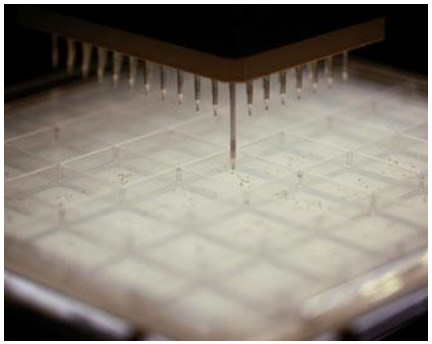

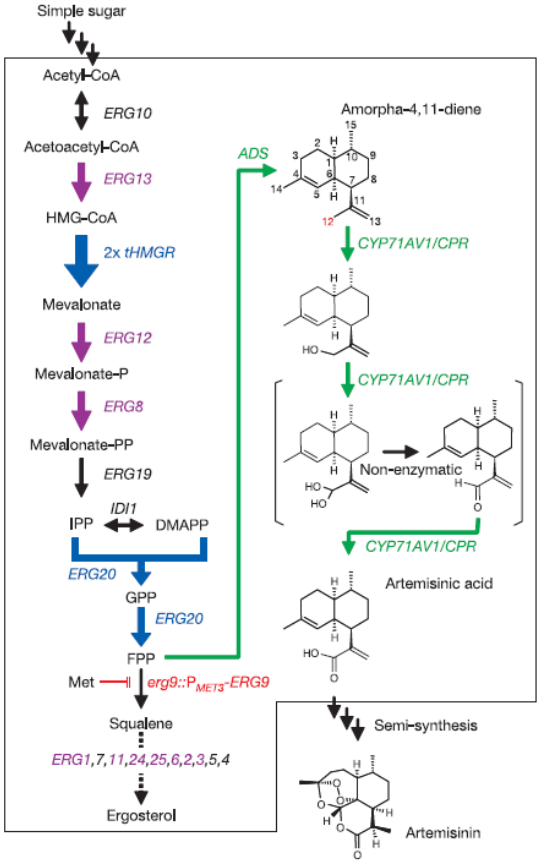

Test thousands of strains a day to:
1. Increase supply of precursors
2. Help folding of plant enzymes
3. Upregulate expression of enzymes within the pathway
4. Downregulate expression of enzymes that catalyze competing reactions

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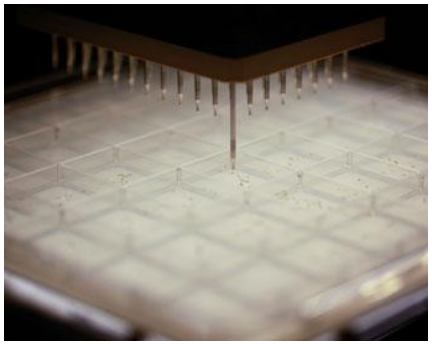

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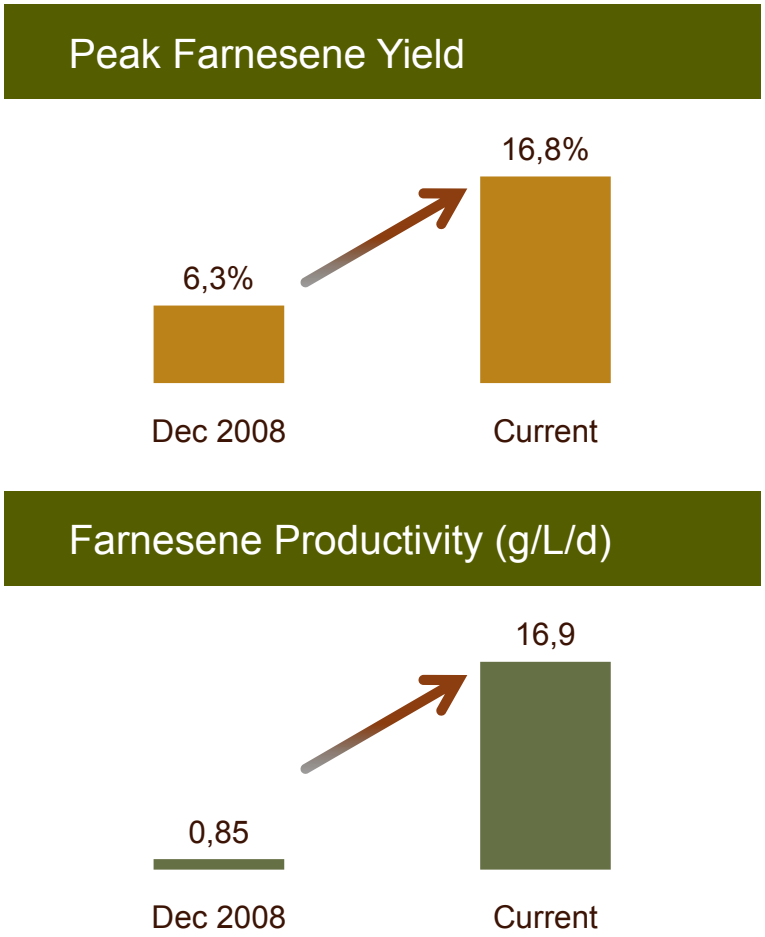
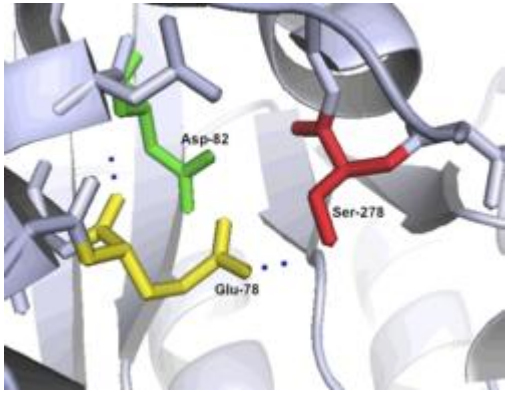


Novel products by design: gluten destruction

Make a product



Want a drug active at low pH:
Check an acidophilic bacteria!

UW iGEM
MAKE IT OR BREAK IT

Novel products by design: gluten destruction

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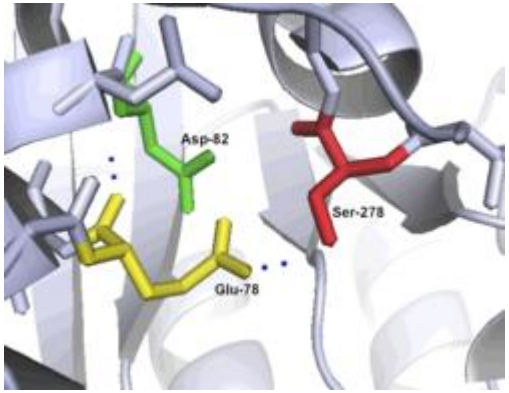

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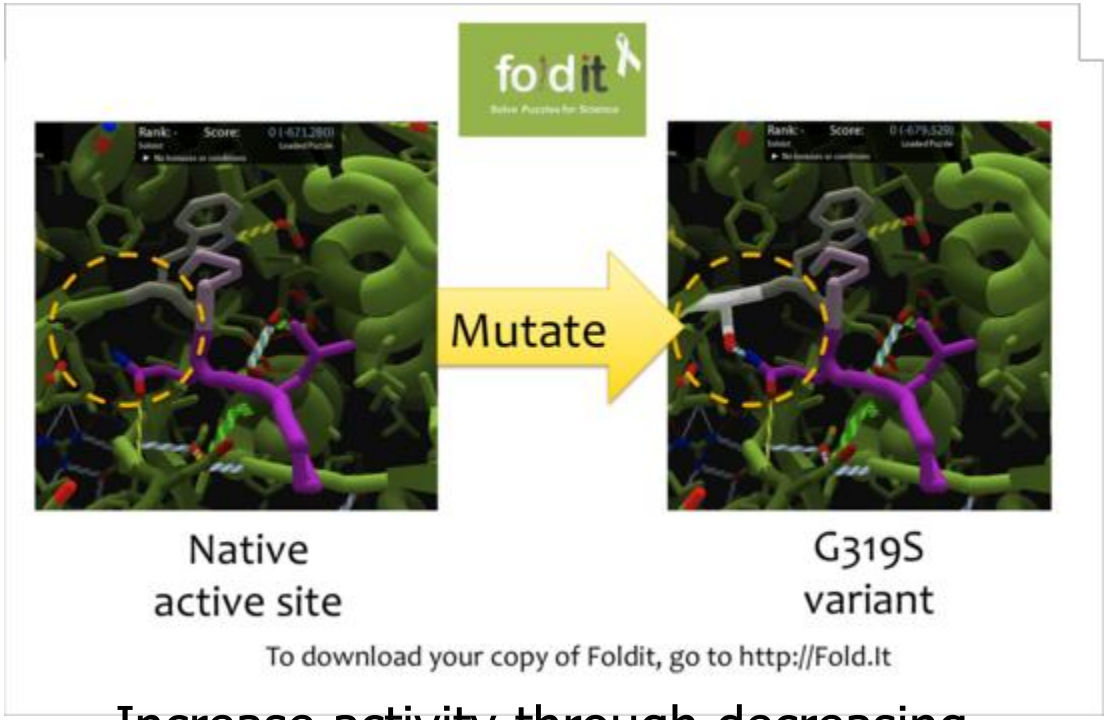

Increase activity through decreasing free energy of the system.

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MAKE IT OR BREAK IT

Novel products by design: gluten destruction

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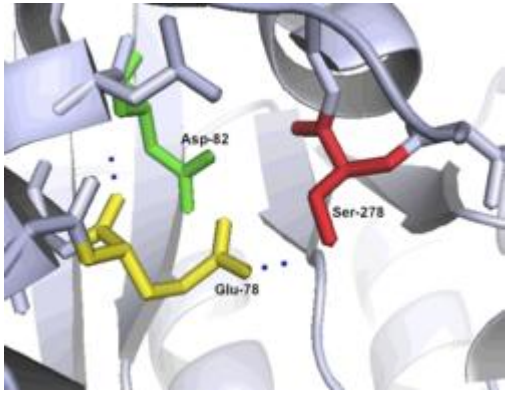
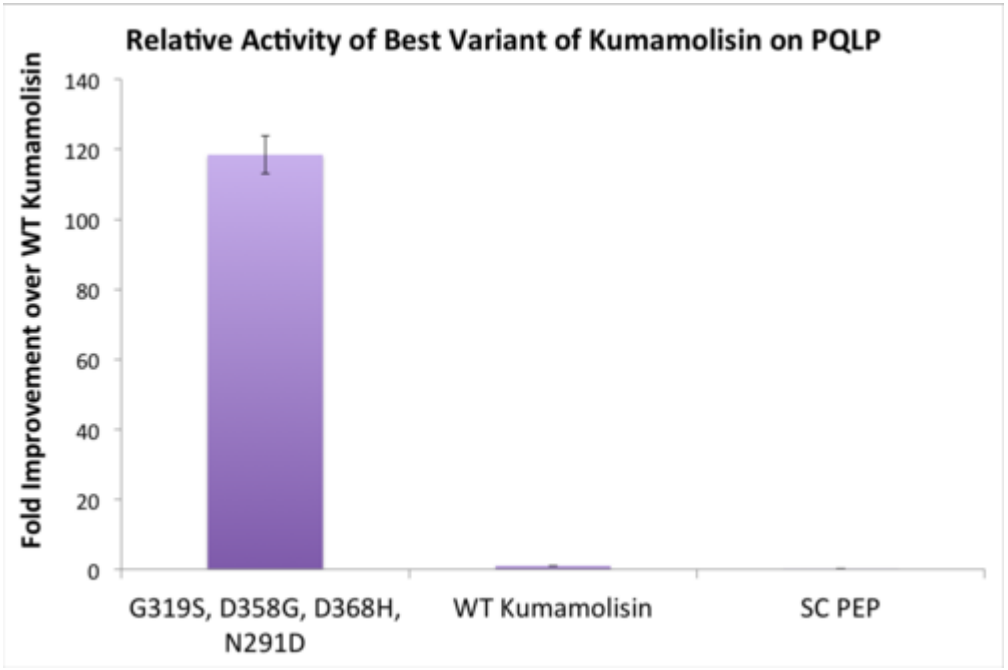




Want a drug active at low pH:
Check an acidophilic bacteria!

Increase activity through decreasing free energy of the system: 100-fold.

UW iGEM
MAKE IT OR BREAK IT

Could bacteria replace conventional lighting?

Make a product

New behaviors

Borrow genes from luminescent organisms:

Hawaiian bobtail squid and *Vibrio fischeri*

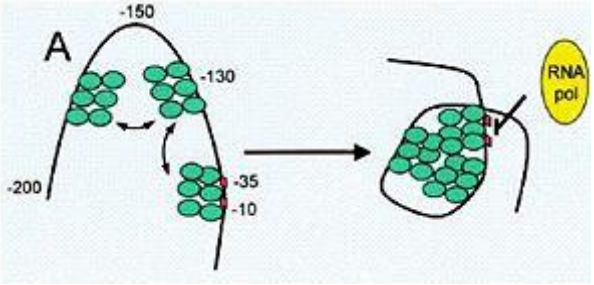
Firefly species

Could bacteria replace conventional lighting?

Make a product

New behaviors

Introduce into *E. coli* and improve output:



Relieve transcriptional repression by decreasing DNA curvature

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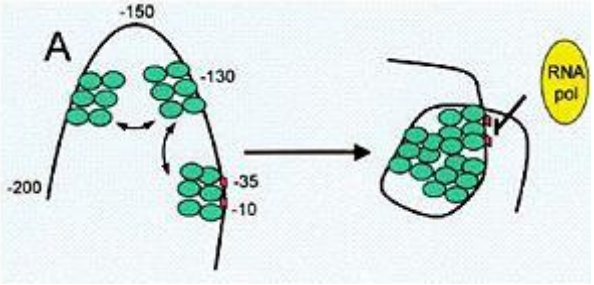

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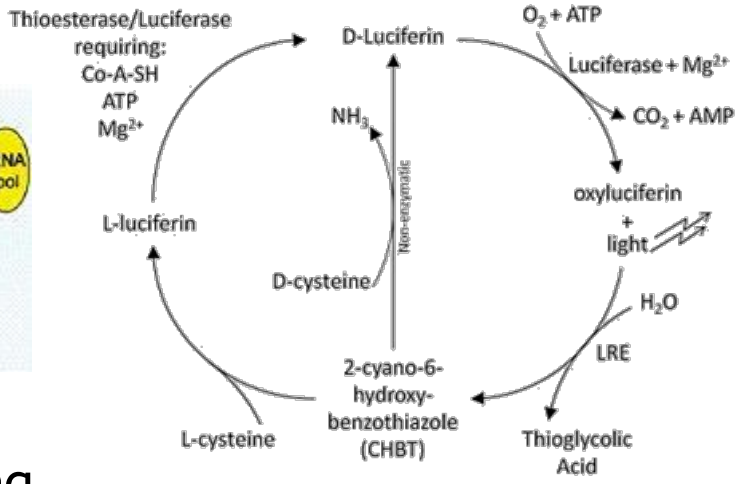

Regeneration of luciferin substrates

Could bacteria replace conventional lighting?

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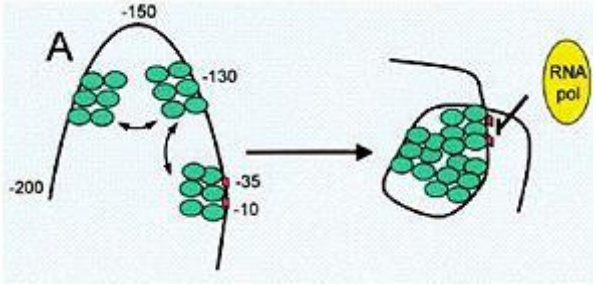

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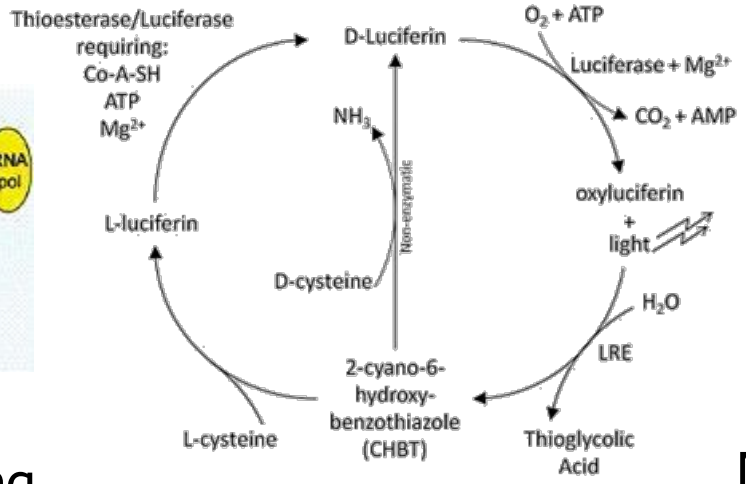


Regeneration of luciferin substrates

New colors through targeted mutagenesis

Could bacteria replace conventional lighting?

Make a product

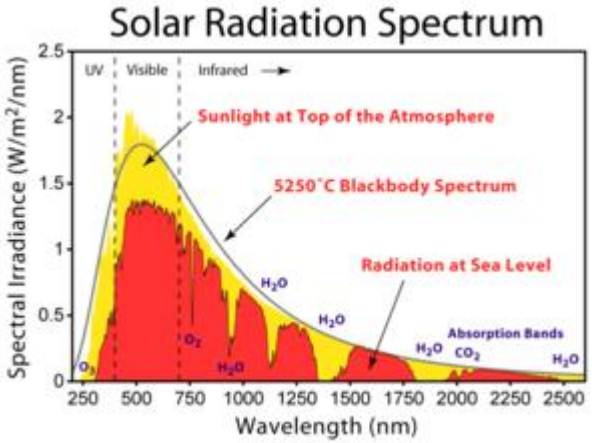
New behaviors

How bright is it?

Could bacteria replace conventional lighting?

Make a product

New behaviors



Radiation in

How feasible is it to have bacterial street lamps?

"If we choose the least bright street lamp (**X=210**) and hypothesise a projected area of **A=30m²**, and a **day:night ratio 14:10** then we find that the efficiency must be roughly **0.02%**. This means that 0.02% of the total energy which the tree absorbs in photosynthesis must be converted eventually into light output, a potentially achievable target."

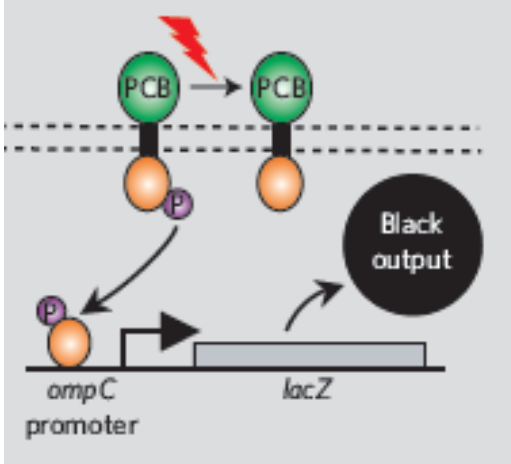
Edge detection: Bacterial photograph

Make a product

New behaviors

Engineering *Escherichia coli* to see light

These smart bacteria 'photograph' a light pattern as a high-definition chemical image.



Levskaya, Nature 2005

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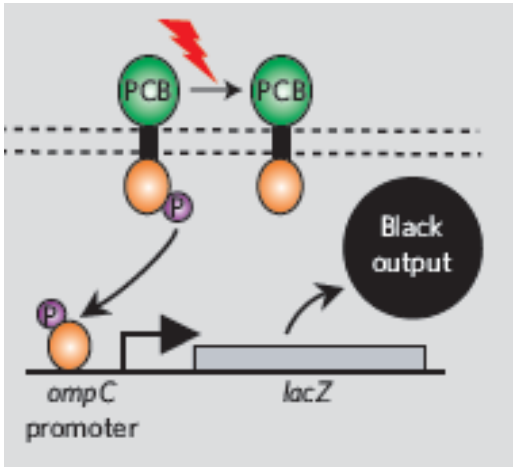
nature



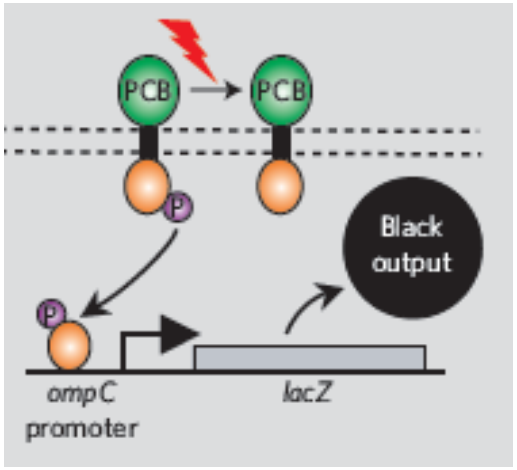
Levskaya, Nature 2005

Edge detection: Bacterial photograph

Make a product

New behaviors

Tuning: Trial and error



To create the chimaera, we aligned members of the phytochrome family with EnvZ and identified potential functional crossover points between the *Synechocystis* phytochrome Cph1 and EnvZ. (For methods, see supplementary information.) The length and composition of the peptide that links a photoreceptor to its response-regulator can affect signal transduction[5,6], and we therefore constructed a series of chimaeras with variable linker lengths. The

Individual Cph1–EnvZ chimaeras were then activated at 37 °C for 4 h with broad-spectrum light and assayed for expression of the *lacZ* reporter. The chimaera Cph8 (BBa_I15010) produced a particularly strong response to light (Fig. 1b).

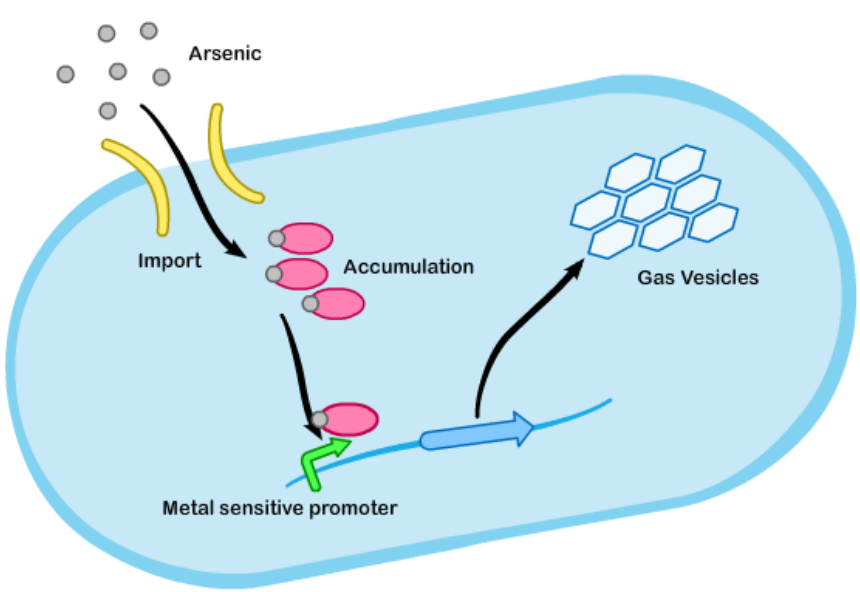
Levskaya, Nature 2005

Arsenic scavengers

Make a product

New behaviors

Interact with the environment



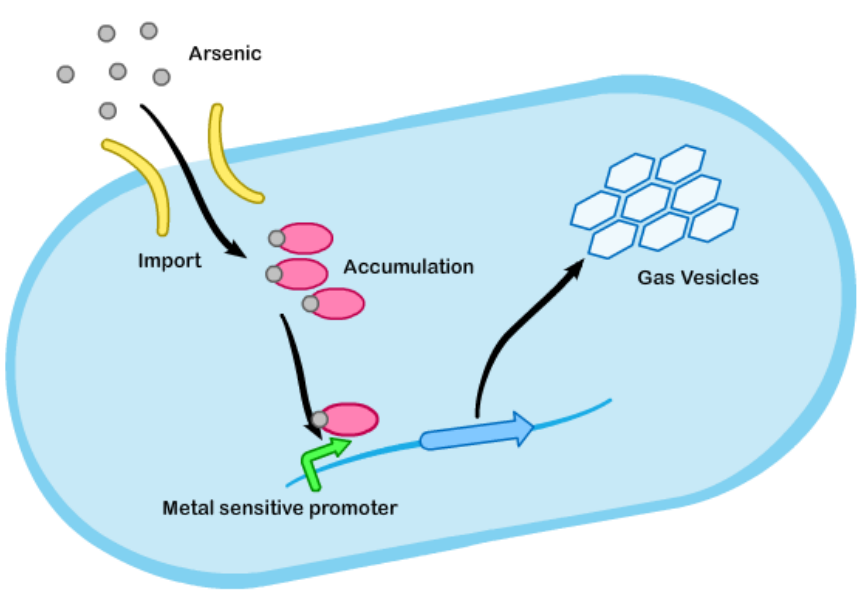
1. Overexpress arsenic transporter from *E. coli*

Arsenic scavengers

Make a product

New behaviors

Interact with the environment



1. Overexpress arsenic transporter from *E. coli*
2. Introduce a metallothionein from a macroalgae to store arsenic

Arsenic scavengers

Make a product

New behaviors

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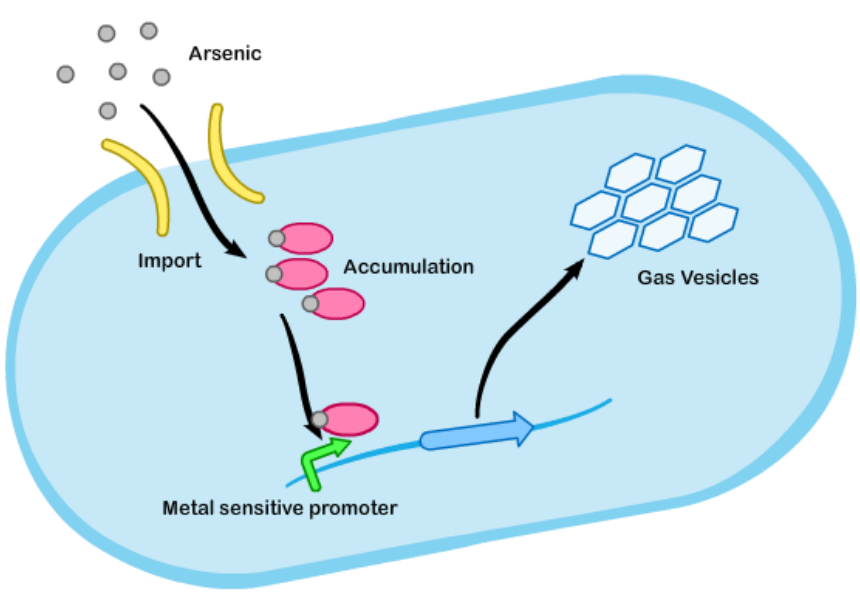

1. Overexpress arsenic transporter from *E. coli*
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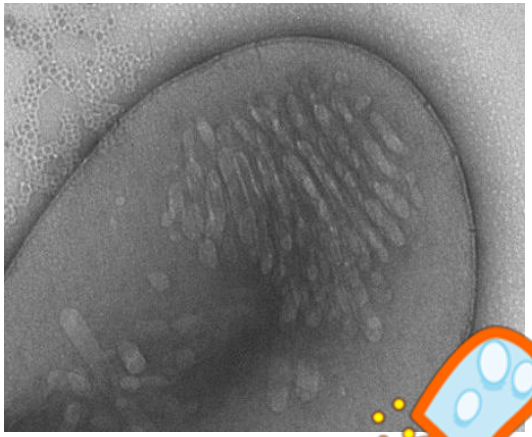
3. Use an arsenic-inducible promoter from *E. coli* to drive the production of gas vesicles from *B. megaterium*

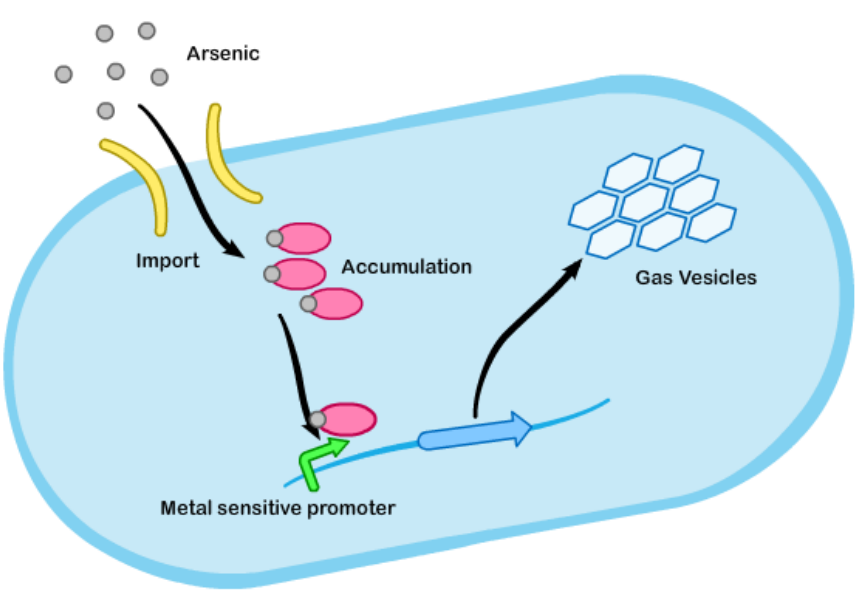


Arsenic scavengers

Make a product

New behaviors

Interact with the environment



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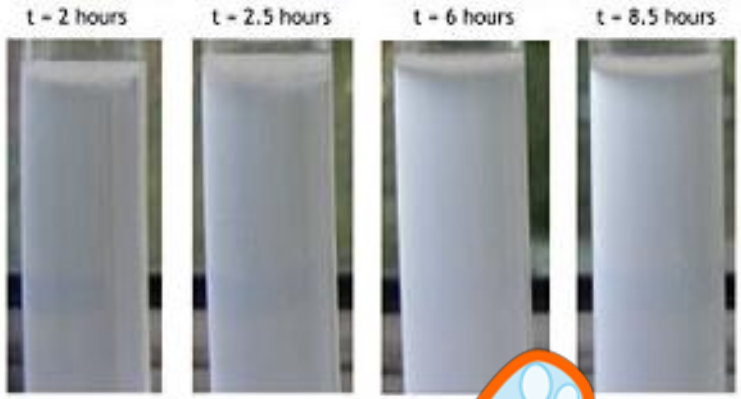
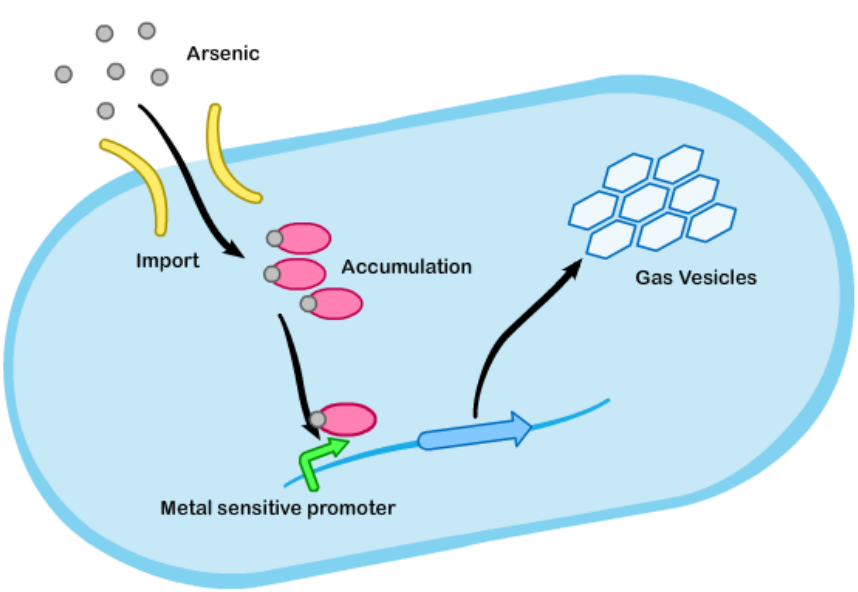


Arsenic scavengers

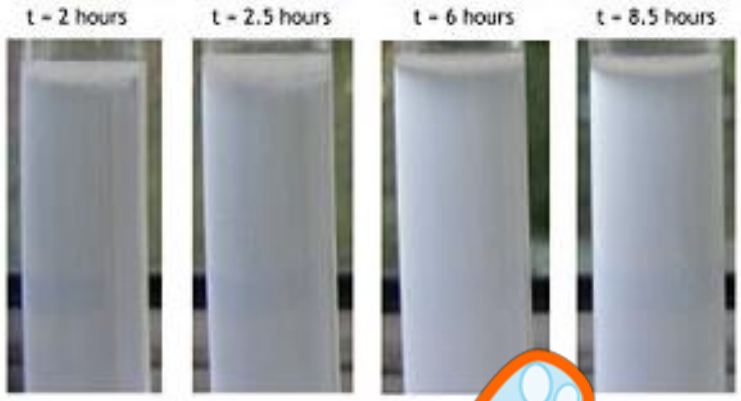
Make a product

New behaviors

Interact with the environment



How would you select for greater buoyancy?



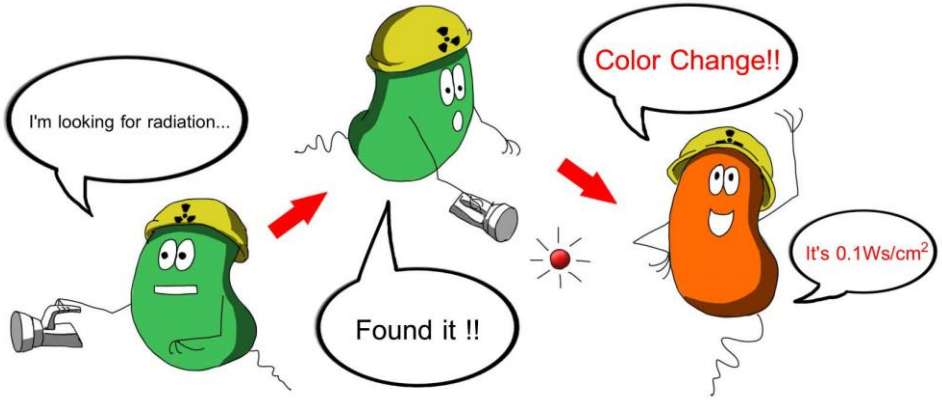
Other examples

Make a product

New behaviors

Interact with the environment

- Oil degradation (TU Delft iGEM 2010)
- Bio-dosimeter (Osaka iGEM 2011)



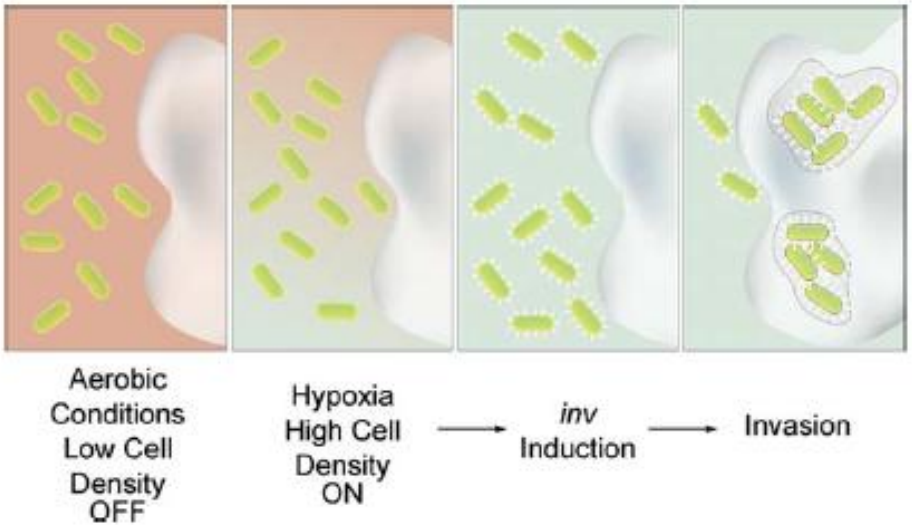
Invade cancer cells

Make a product

New behaviors

Interact with the environment

Interact with other organisms



1. Introduce the *inv* gene from *Y. pseudotuberculosis* into *E. coli* to promote invasion of mammalian cells.

Anderson, JMB 2006

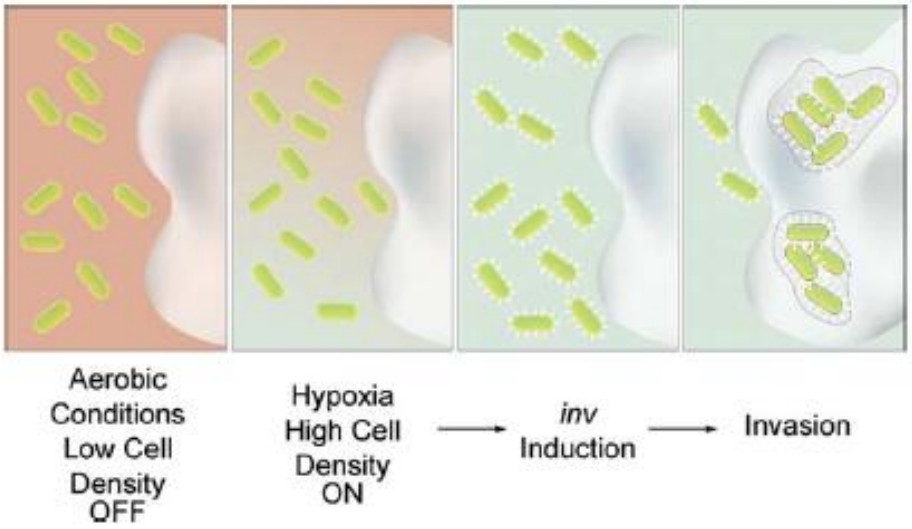
Invade cancer cells

Make a product

New behaviors

Interact with the environment

Interact with other organisms



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2. Express *inv* under (A) the control of a hypoxia-inducible promoter (from *E. coli)* or (B) a cell density-inducible promoter, along with a quorum-sensing circuit (from *Vibrio fischeri*).

Anderson, JMB 2006

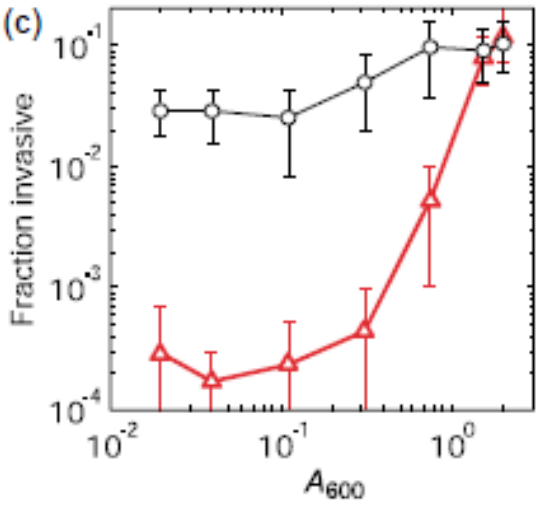
Invade cancer cells

Make a product

New behaviors

Interact with the environment

Interact with other organisms



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Invade cancer cells

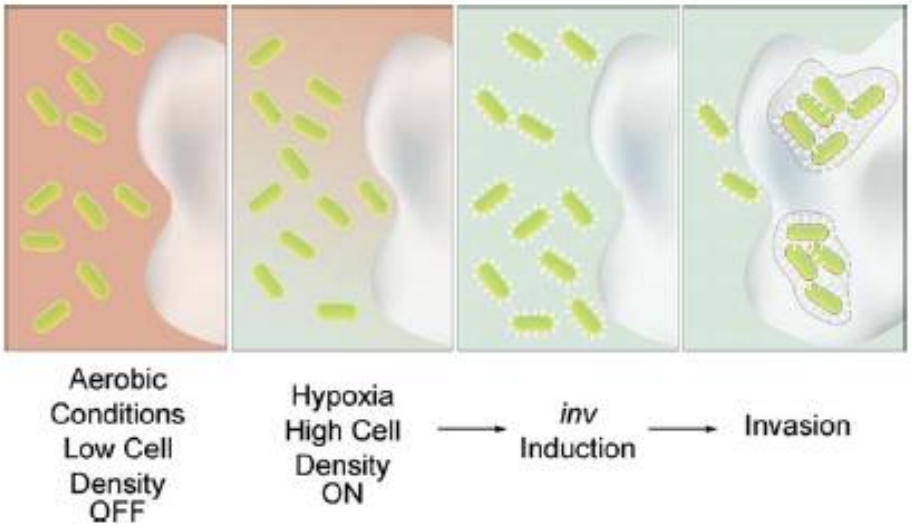
Make a product

New behaviors

Interact with the environment

Interact with other organisms

How would you select for stronger invasiveness?



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Anderson, JMB 2006

Other examples

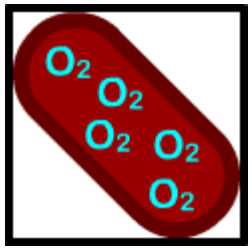
Make a product

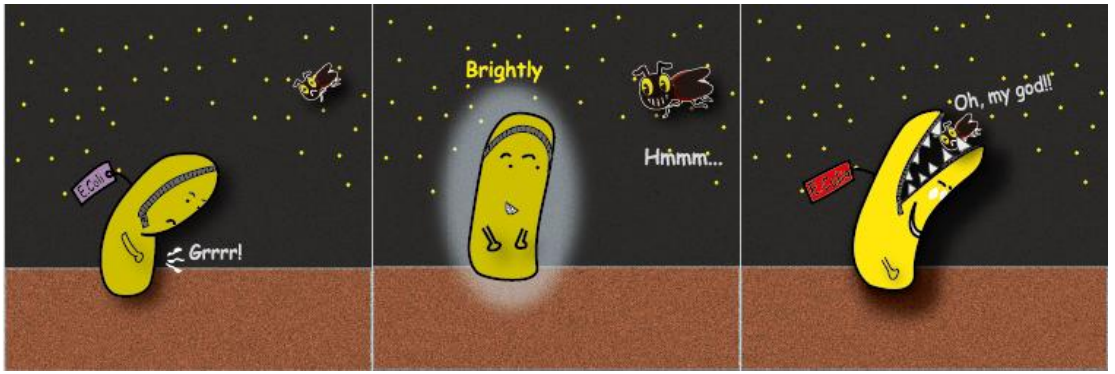
New behaviors

Interact with the environment

Interact with other organisms

- Carnivorous *E. coli* (Kyoto iGEM 2011)
- Bactoblood (Berkeley iGEM 2007)
- Synthetic predator-prey interactions





DIY: Workflow of a synthetic biology project

- Think of a **problem**.
- What **functions** do you need to solve that problem?
- What **organisms** do that function? (try Google, Google Scholar, or the Parts Registry)
- Are these functions caused by one (or a few) defined **genes**? Cite your sources.
- Pick a **chassis**. (*E. coli*? *S. cerevisiae*?)
- How should the organism **regulate** these genes or have the functions **interact**?
- How can you apply **selection or tuning** to improve the organisms's performance?