What can BioBricks™ do for you?

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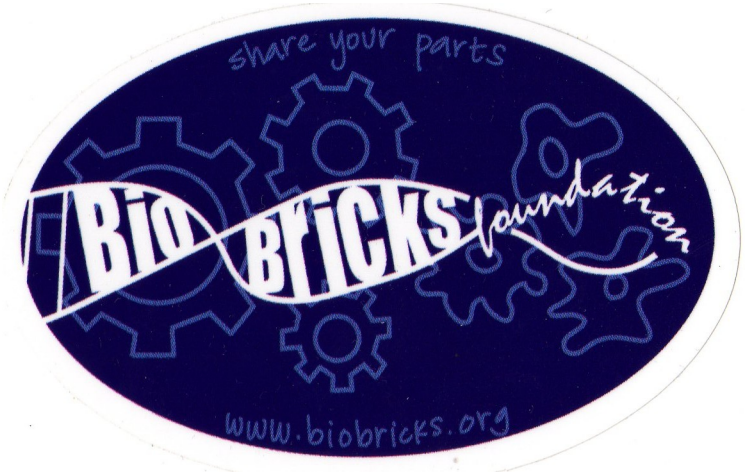
Not Just an experimental tool, but a whole lifestyle...

- The BioBrick™ format
- The Registry of Standard Biological Parts
- iGEM competition
- The BioBricks™ Foundation
- OpenWetware



What is Synthetic Biology?

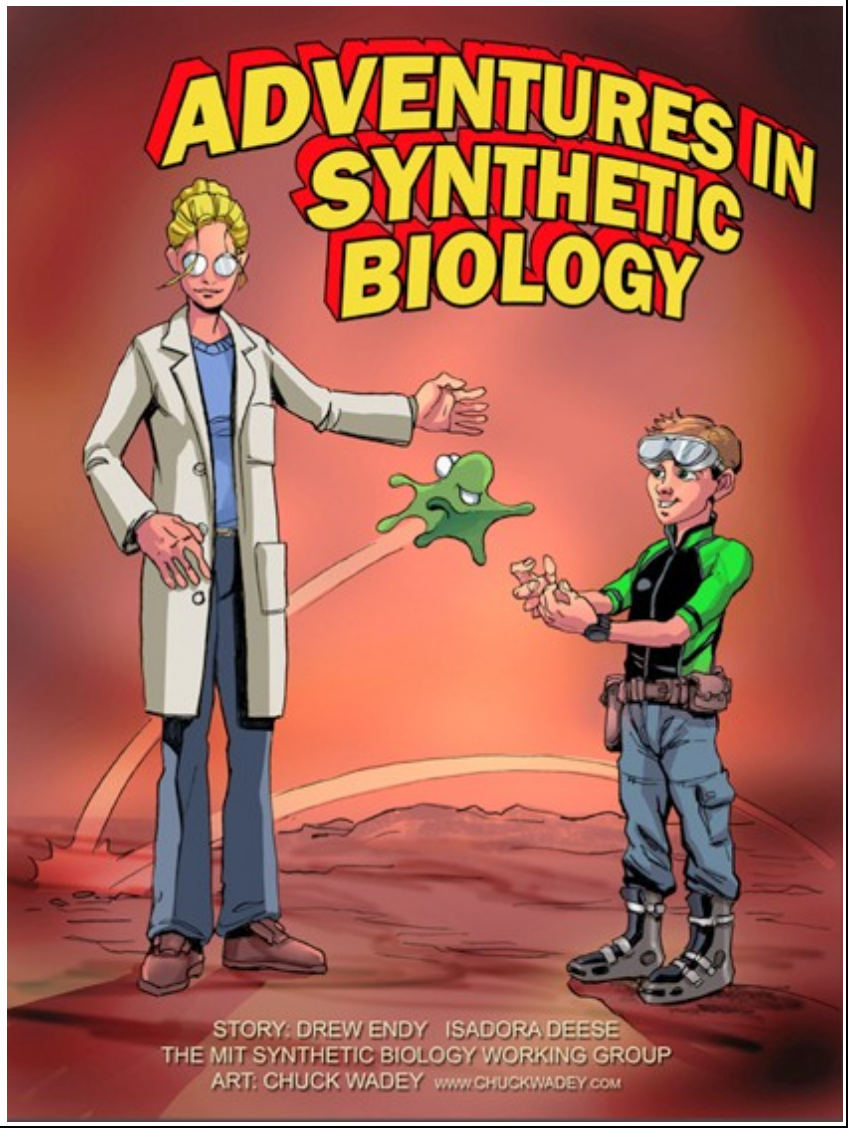
- ‘Genetic engineering on steroids’ (Action Group on Erosion, Technology and Concentration)

- ‘Insane arrogance’ (Pope Benedict XVI, Good Friday address, 2006, as interpreted by Newsweek)

What is Synthetic Biology?

- Constructing biological ‘systems’ from component parts.

- Application of concepts from engineering and computer science to analysis and reconstruction of biological systems.



The problem of design

- “What genetic engineers do isn’t really engineering. The engineering equivalent of what genetic engineers do is to throw a load of steel and concrete into a river, and then if someone manages to walk across it, call it a bridge” (Simon Munnery, *New World Order*).

Applying Engineering Concepts

- Modularity: standard interchangeable parts.
- Abstraction: parts are assembled to make devices, devices are assembled to make systems.Work only at the appropriate level.
- Mathematical analysis of design prior to assembly.
- **Many biologists are highly sceptical about this.**

Rough stones

↓

Shaped stones

↓

Standard sized shaped stones

↓

Bricks

↓

Reinforced concrete, composite materials…

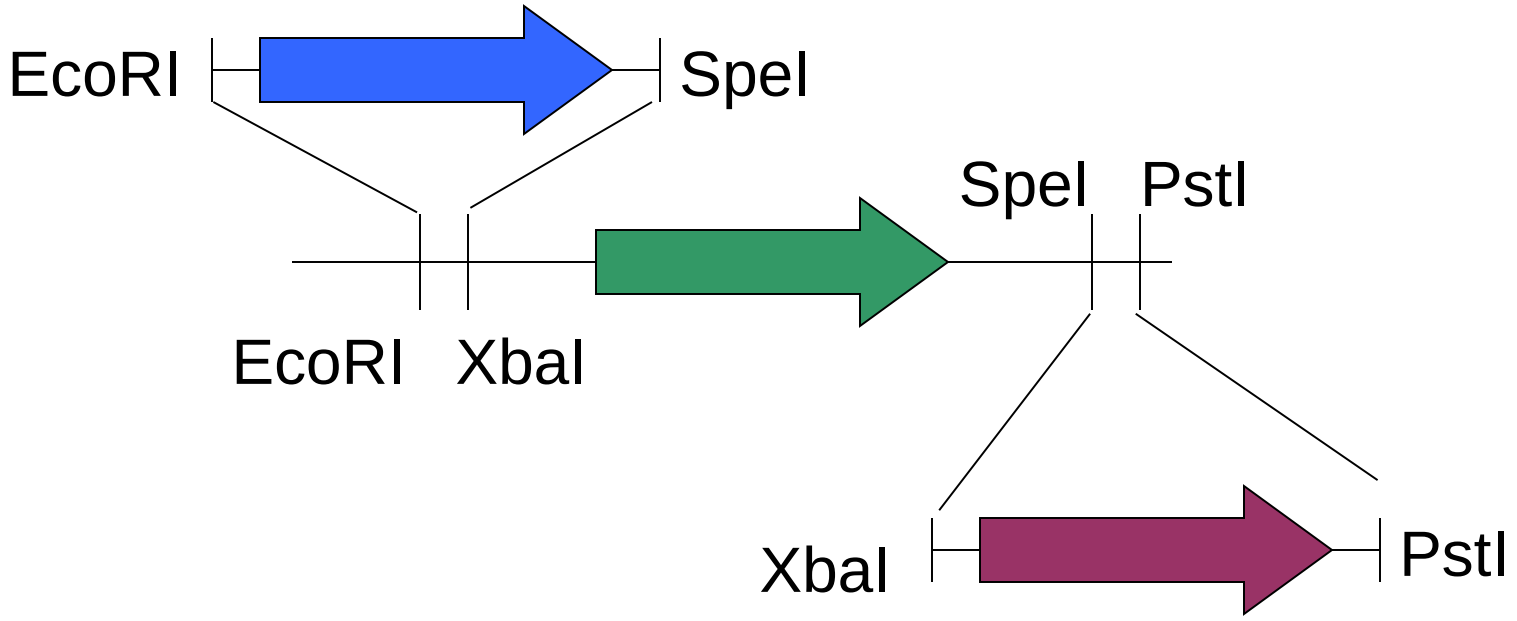
Source of image: wikipedia

Modularity: the BioBrick standard

- Tom Knight, MIT
- ‘Genetic lego’
- Any two BioBricks can be combined in either order to generate a new BioBrick.
- BioBricks made by PCR or synthesis.

What are BioBricks™?

- Modular DNA components with standard ends.
- Any 2 BioBricks™ can be joined together in either order to make a new BioBrick™.

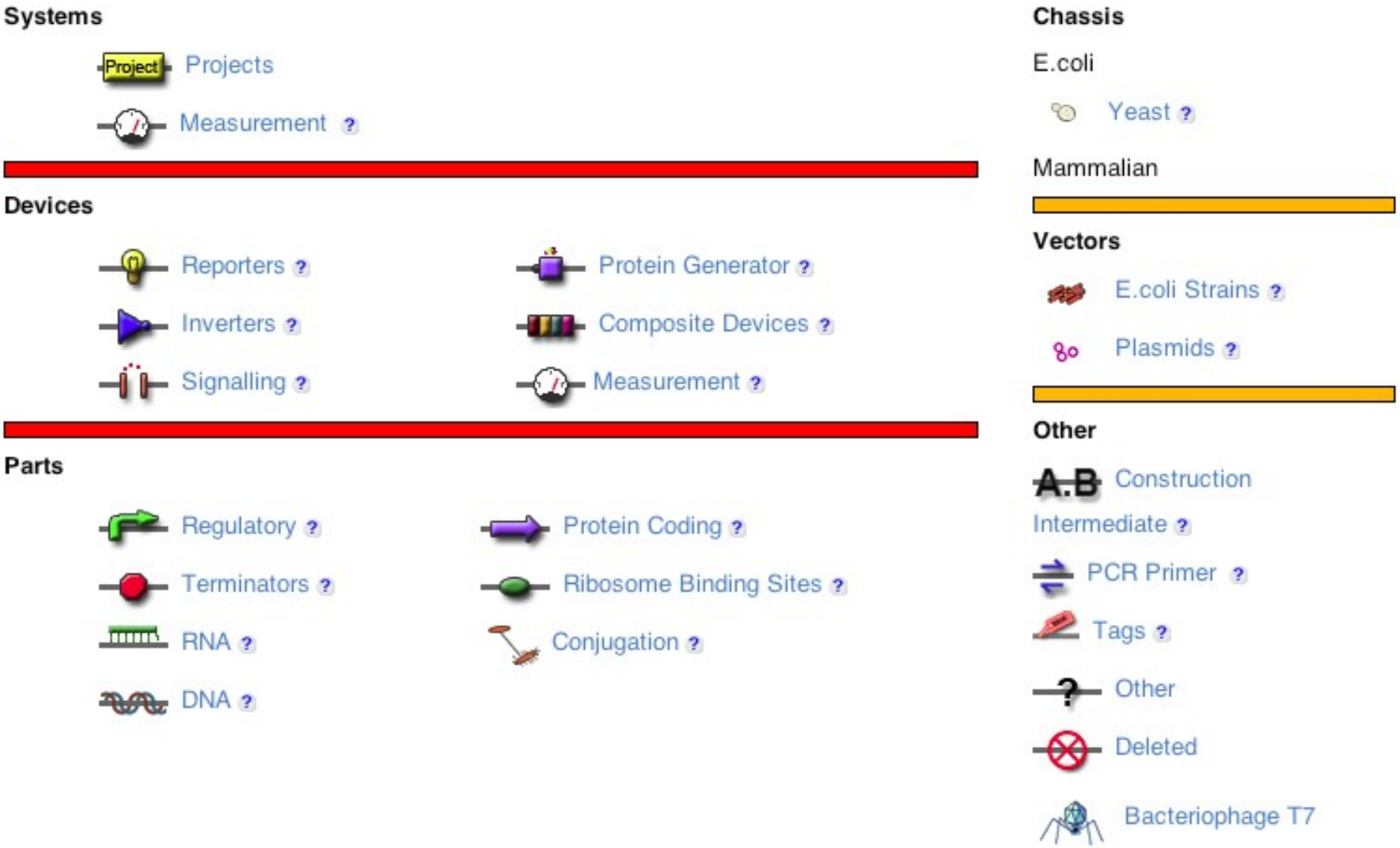


The BioBrick™ 1.0 Format

- Standard prefix: gaattcgcggccgcttctagag...
- Coding sequence prefix: gaattcgcggccgcttctag ATG
- Standard suffix: ...tactagtagcggccgctgcag
- Fusion scar: tactagag OR tactagATG
- Insert must not contain EcoRI, XbaI, SpeI, PstI sites (but NotI is OK).

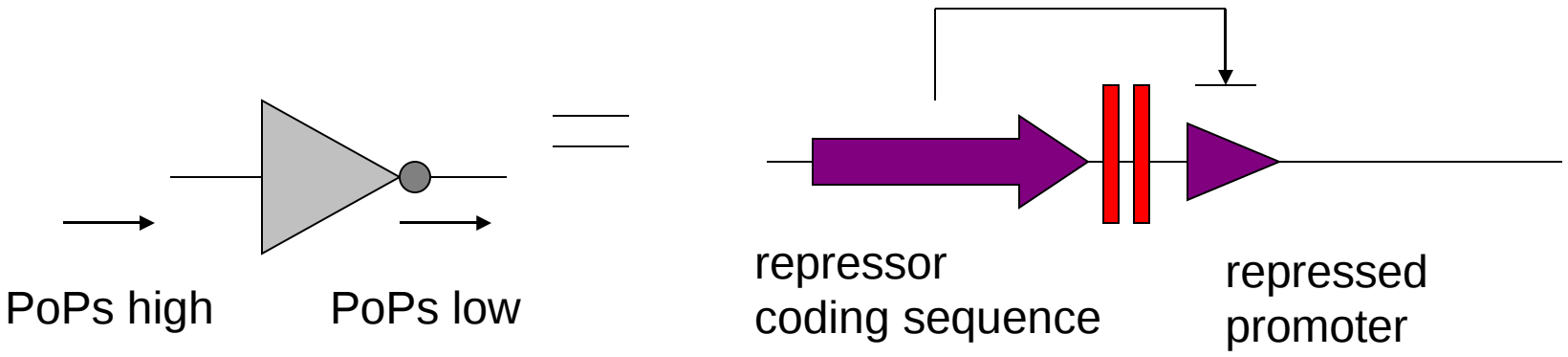
Registry of Standard Biological Parts

- Randy Rettberg, MIT: http://partsregistry.org/Main_Page



What's in the Registry?

- Constitutive and inducible promoters
- Ribosome binding sites
- Coding sequences: repressors, activators, enzymes
- Composite parts: reporters, protein generators
- Devices: inverters, oscillators, logic gates

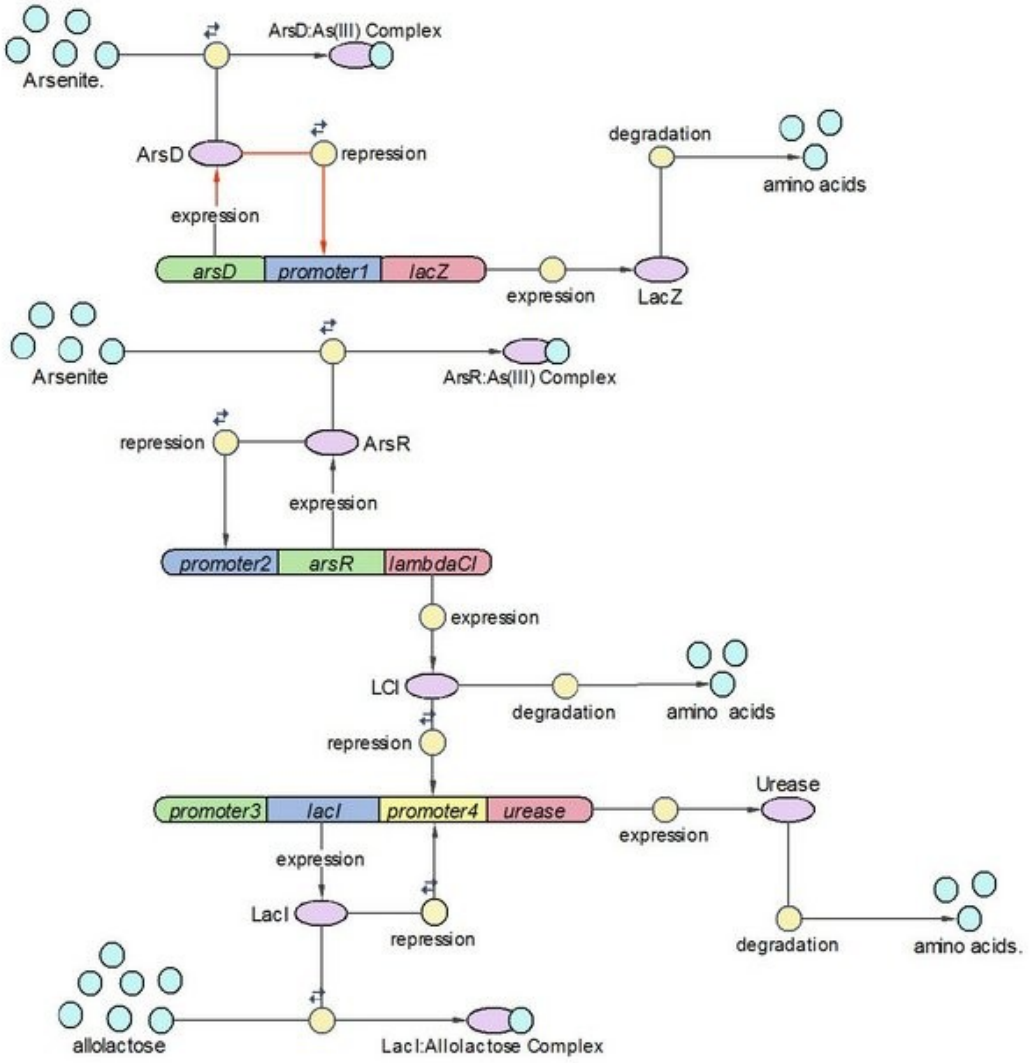


iGEM

iGEM 2008

- International Genetically Engineered Machine competition, run from MIT.
- 2003: MIT summer course.
- 2004: 5 teams from US universities.
- 2005: 17 teams including Cambridge and ETH Zurich.
- 2006: 37 teams including Edinburgh, Cambridge, ICL.
- 2007: 55 teams competed.
- 2008: 85 teams registered.
- http://2008.igem.org/Main_Page

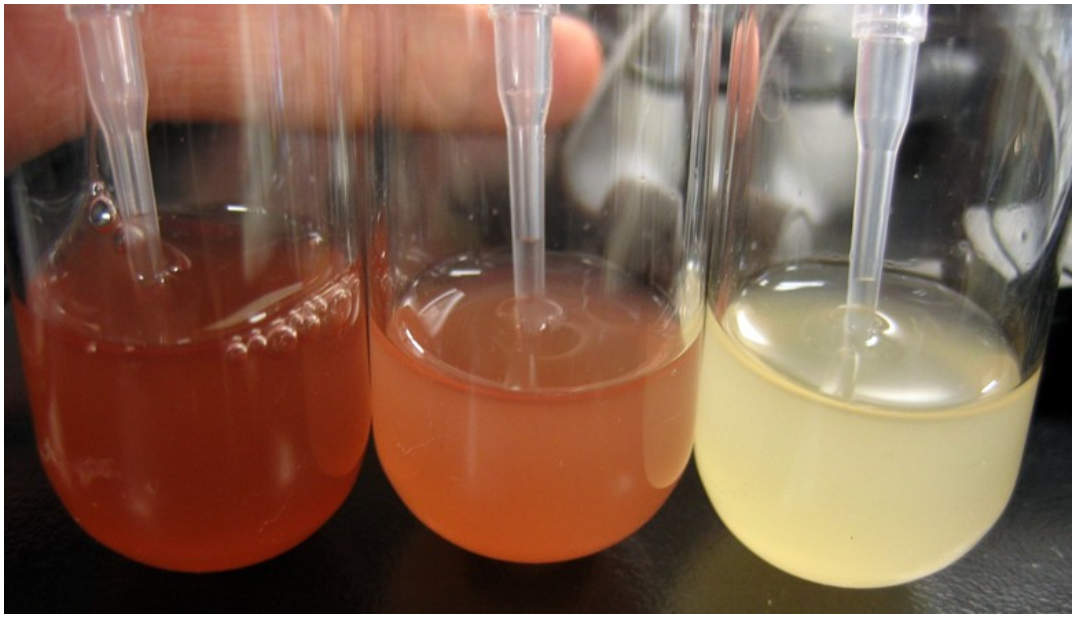
Biosensors



- Edinburgh iGEM 2006: biosensor to detect arsenic in groundwater.
- Original design had three-level pH output.
- First prize for Best Real World Application, third prize for Best Device.

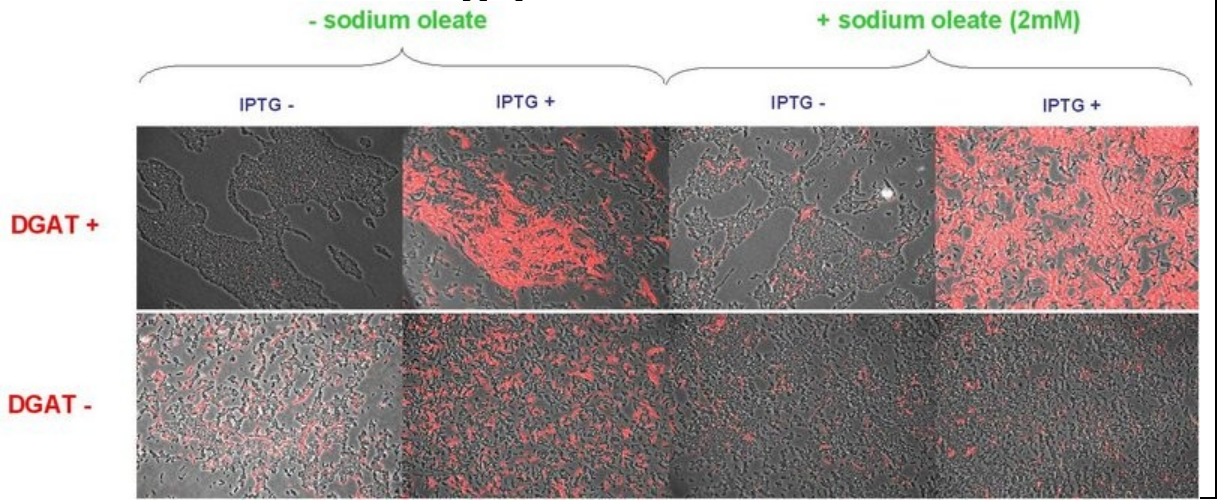
The weird and wonderful

- Bacterial photography (UCSF 2005)
- Bacteria that smell of bananas (MIT 2006)
- Artificial blood made from bacteria (Berkeley 2007)



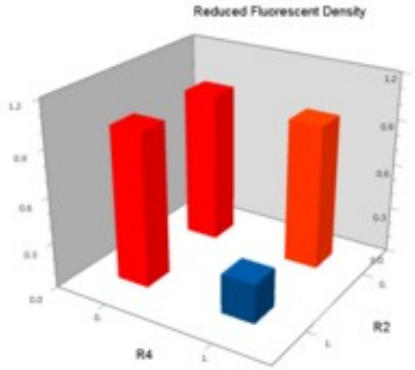
Paris 2007

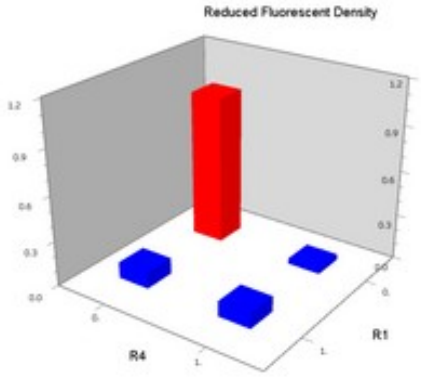
- Artificial multi-cellular bacteria
- Auxotrophic ‘germline’ cells (need dap) differentiate into protrophic ‘somatic’ cells which feed them with dap, but can’t reproduce (*ftsK*).
- Differentiation controlled by recombinase-mediated excision; frequency controllable by induction of *cre*.
- Test: somatic cells accumulate triglycerides.

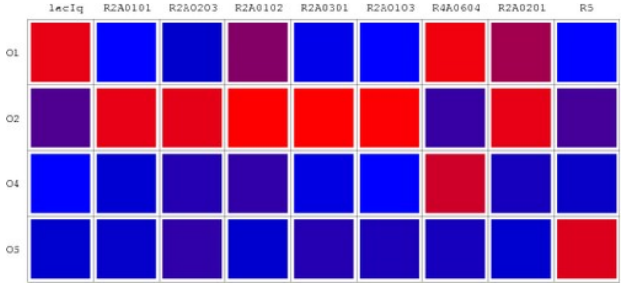


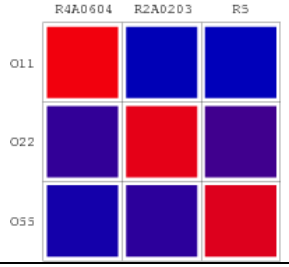
USTC 2007

- Logic switches in bacteria.
- Tested combinations of promoters and operator sites to find NOR and NAND switches with good operating characteristics.
- Tested many combinations of artificially mutated *lac* repressors and binding sites to find multiple pairs that would not ‘cross-talk’: analogous to insulated wires.



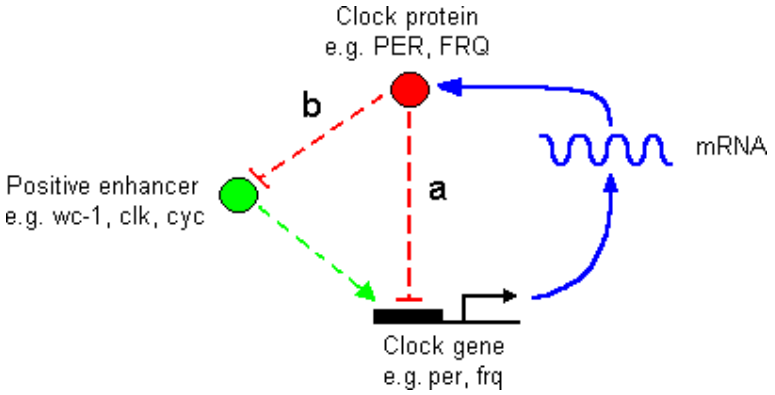






What else are BioBricks good for?

- Validating theoretical models - **just because something makes sense doesn't mean it's true!**
- Allows us to address a large class of biological problems by synthesis rather than analysis.

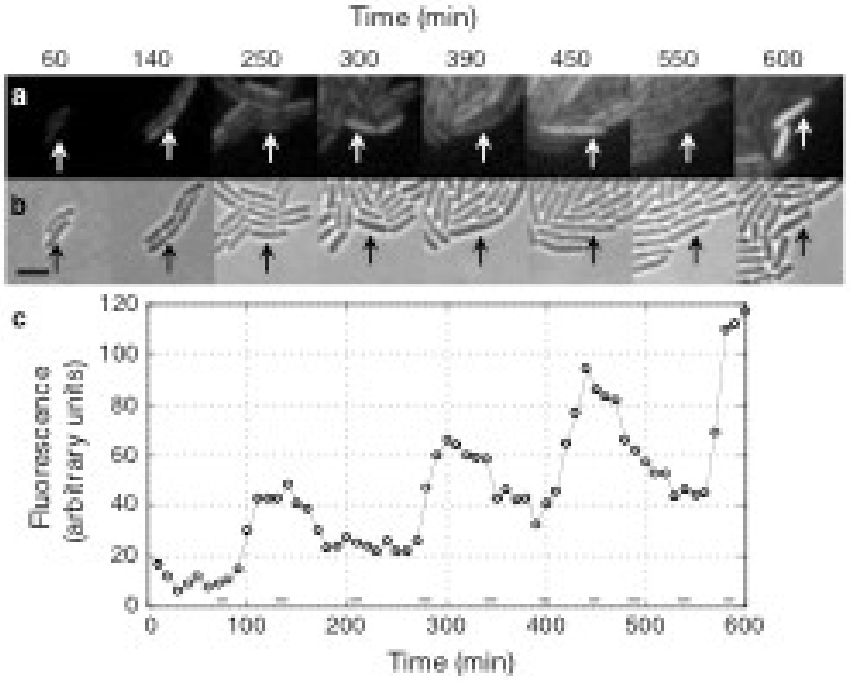


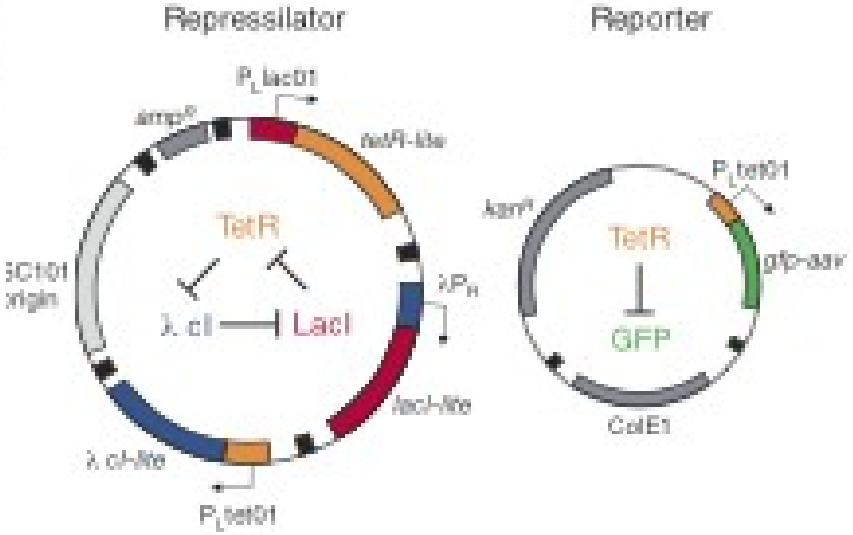
$$\frac{d\phi_1}{dt} = \frac{d}{dt}\left(\frac{n_1}{V_1}\right) = \frac{1}{V_1}\frac{dn_1}{dt} + n_1\left(\frac{-1}{V_1^2}\right)\left(\frac{dV_1}{dt}\right)$$

$$\frac{d\phi_1}{dt} = \frac{1}{V_1}\left[\frac{1}{2}\left(\frac{N_c V_0}{\tau_0}\right)\left(\frac{n_2}{V_2} - \frac{n_1}{V_1}\right) - \frac{n_1}{V_1}\frac{d}{dt}\left(N_c V_c\right)\right]$$

Analogues of electrical systems

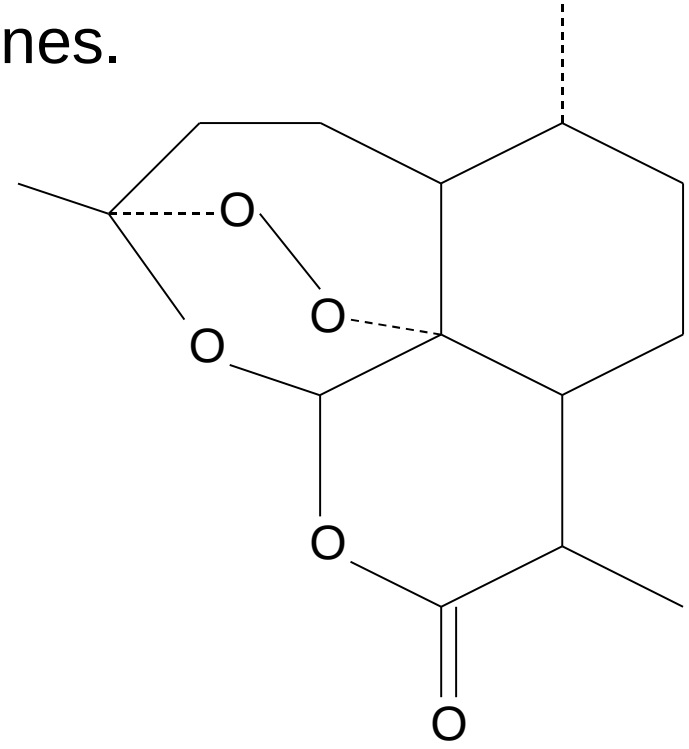
- toggle switch (Jim Collins, Boston)
- repressilator (Mike Elowitz, Caltech)
- binary counter (ETH Zürich iGEM team)
- Band filter, tristable switch,inverters, amplifiers...





Engineering metabolic pathways

- Jay Keasling, UC Berkeley
- Artemisinin production in yeast.
- Upregulation of terpenoid biosynthesis and addition of plant genes.

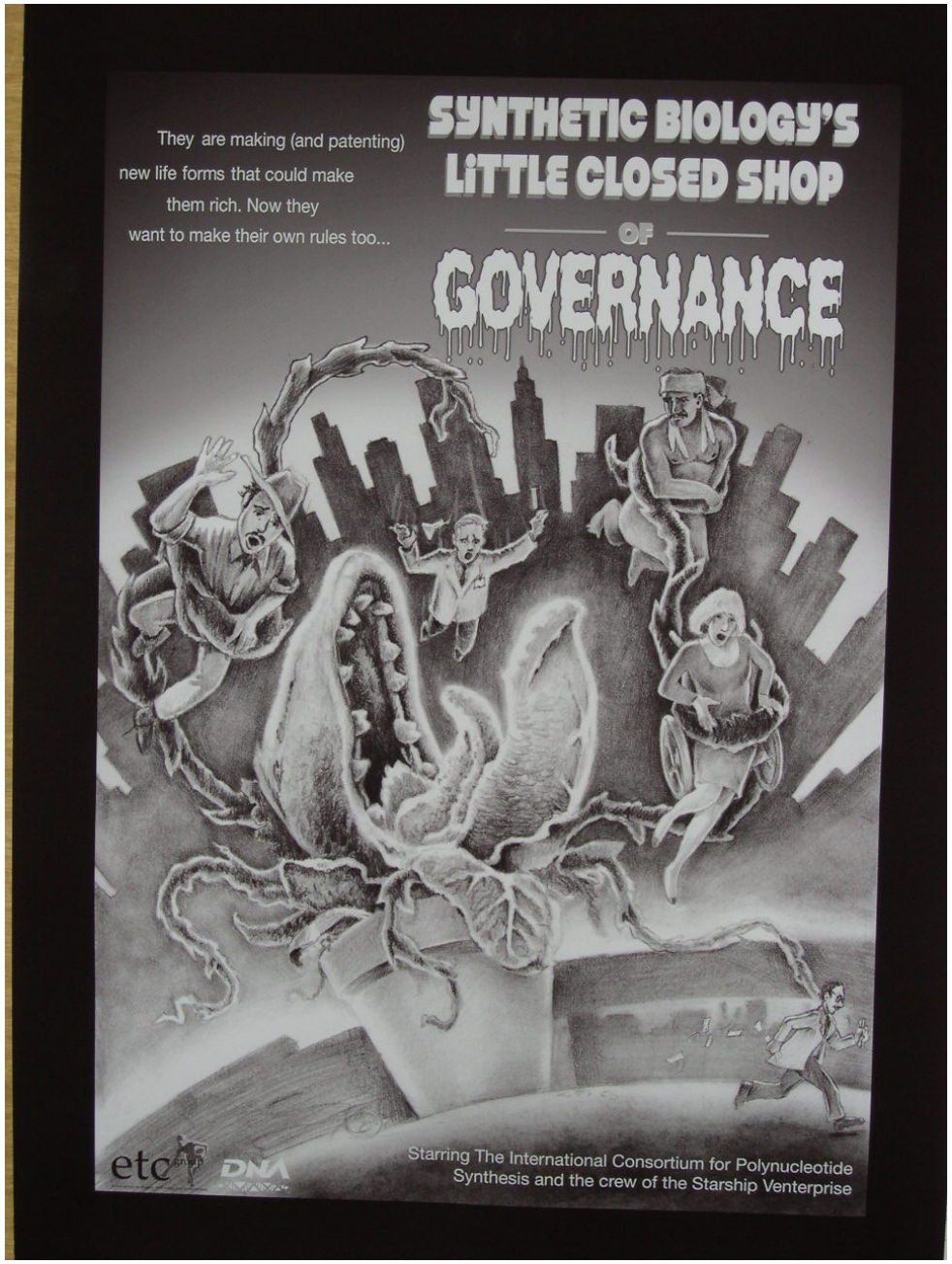


Renewable energy

- Need to combine multiple complex multi-gene phenotypes in one organism:
- Photosynthesis or biomass conversion
- Synthesis of a liquid fuel or other product
- Solvent tolerance.
- Rapid growth and robustness in industrial processes

Is this really a good idea?

- Bioerror or bioterror - raising the chances of a one-million casualty event?
- Biohackers and garagistas: is the world ready for open-source genetic engineering?



Focus on ethics and human practices

- BioBricks Foundation
- Industry Association of Synthetic Biologists
- SynBERC Human Practices component
- EU SYNBIOSAFE project
- Inogen, Genomics Forum

FIN

- That’s All, Folks!