Synthetic Biology – a brief overview

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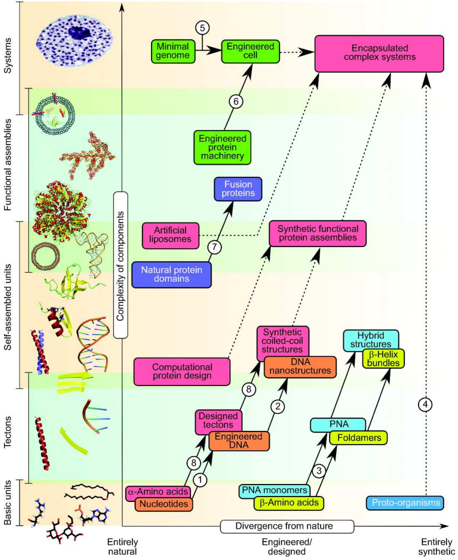
What is Synthetic Biology?

An emerging field at the interface between biology and engineering.

Goals of Synthetic Biology

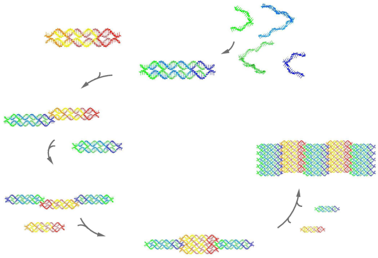
1. The design and construction of new biological parts, devices and systems that do not exist in the natural world.
2. The redesign of existing biological systems to perform specific tasks.
3. Design biological systems in the same way engineers design electronic or mechanical systems.

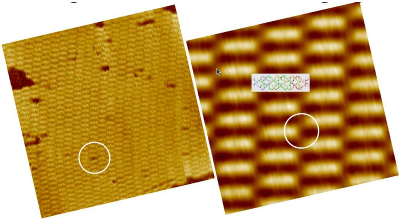
The Synthetic Biology Space



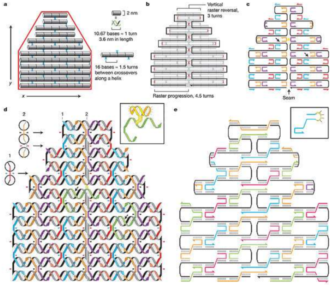
Bromley EHC et al 2008, ACS Chem. Biol. 3(1):38-50; doi:10.1021/cb700249v

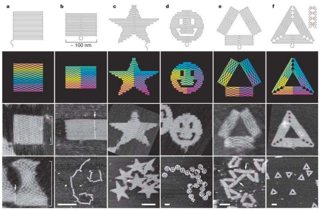
DNA self-assembly





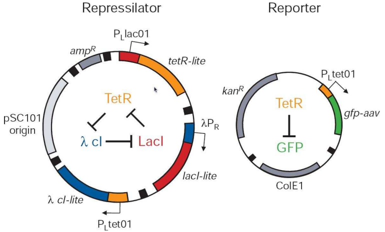
Winfree E et al 1998, Nature 394:539-544;
doi:10.1038/28998

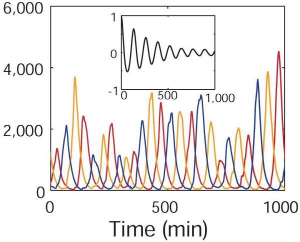


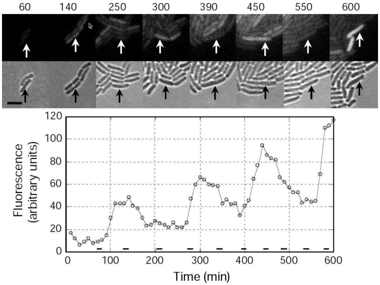


Rothemund PWK 2006, Nature 440:297-302;
doi:10.1038/nature04586

1st generation Genetic Circuits



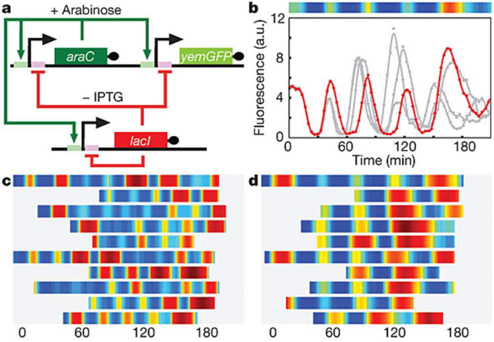




1. Design principle: negative feedback loops.
2. Oscillators lacked robust and damped rapidly.
3. Oscillators were not hereditary.
4. Oscillator frequencies and amplitudes can not be adjusted.

Elowitz MB & Leibler S 2000, Nature 403(6767):335-338; doi:10.1038/35002125

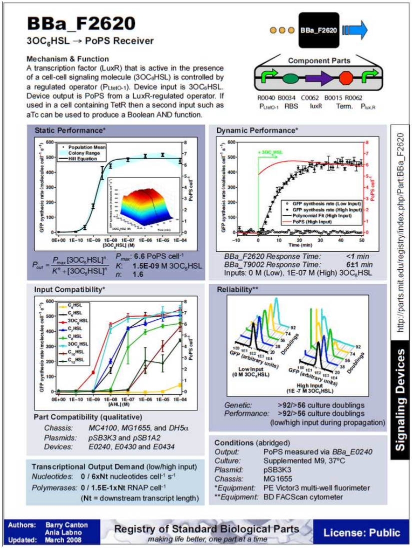
2nd generation Oscillators



1. Design principle: positive & negative feedback loop.
2. Robustness is due to transcription/translation delay.
3. Frequency is tunable with IPTG concentration.
4. No synchronization over the cell population.

Stickler J et al 2008, Nature 456:516-520; doi:10.1038/nature07389

Standardization of Synthetic Parts and Devices



1. Static performance.
2. Dynamic performance.
3. Input compatibility.
4. Reliability.
5. Part compatibility.
6. Conditions.

BioBricks `http://partsregistry.org/`

Canton B et al 2008, Nature Biotechnology 26(7):787-793; doi:10.1038/nbt1413

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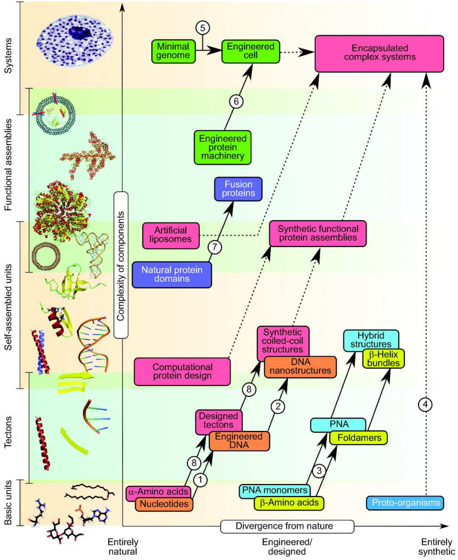
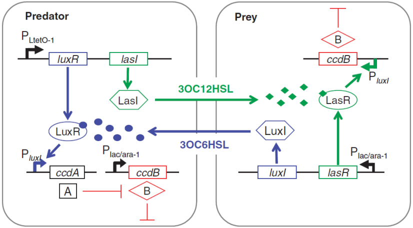
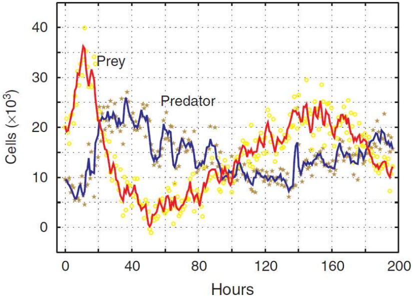


Bromley EHC et al 2008, ACS Chem. Biol. 3(1):38-50; doi:10.1021/cb700249v

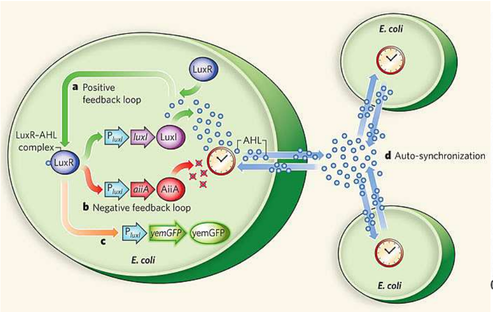
A synthetic predator-prey ecosystem

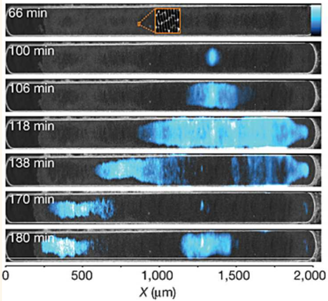


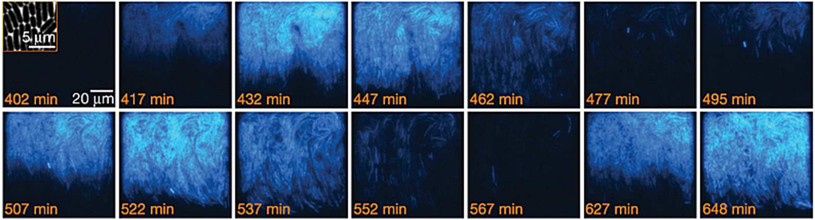


Balagaddé et al 2008, Mol Syst Biol 4:187; doi:10.1038/msb.2008.24

3rd generation Oscillators



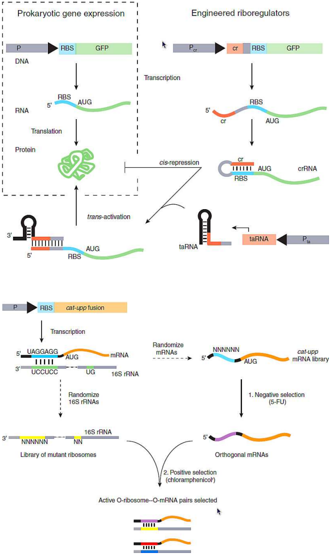




Danino T et al 2010, Nature 463:326-330; doi:10.1038/nature08753

RNA synthetic biology?!?

Class	Mechanism	Activity
Antisense	Prokaryotic Eukaryotic (AAAAA(A)n)	Active in *trans* Binding represses translation
Riboregulators	+ / –	Active in *trans* Binding may repress or activate translation
Ribozymes		Active in *cis* or *trans* Activity (cleavage) in *cis* will repress translation Activity (cleavage) in *trans* may repress or activate translation
Riboswitches	Transcriptional Translational Metabolite-binding ribozyme	Active in *cis* Ligand binding may repress or activate transcription Ligand binding may repress or activate translation
Small interfering RNA (siRNA)	AAAAA(A)n	Active in *trans* Binding represses translation
MicroRNA (miRNA)	AAAAA(A)n	Active in *trans* Binding represses translation



Isaacs FJ et al 2006, Nature Biotech 24(5):545-554; doi:10.1038/nbt1208

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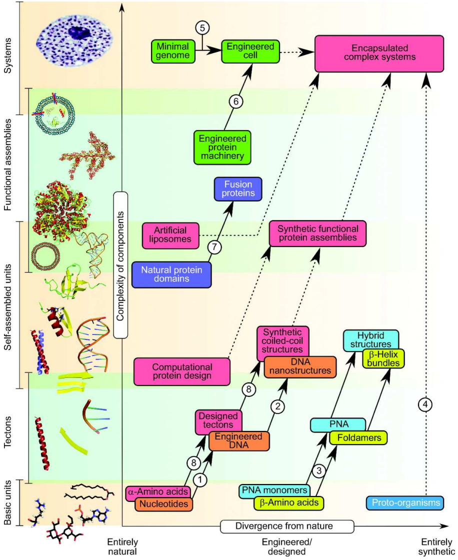

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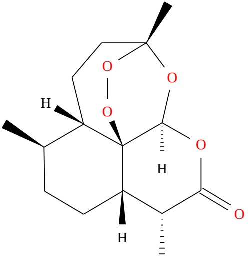
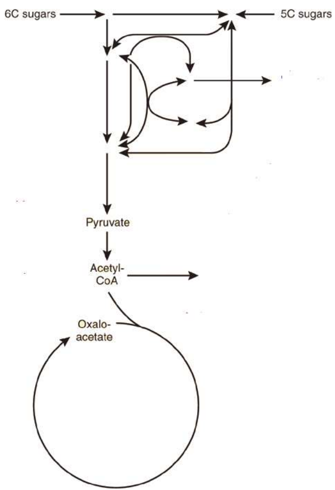
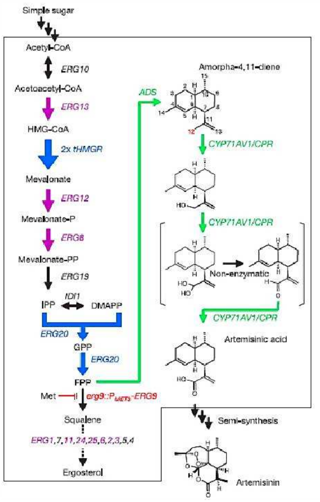
Anti Malaria Drug Artemisinin



1. Drug is derived from a herb used in Chinese traditional medicine.
2. Sesquiterpene lactone with an endoperoxide bridge.
3. Drug used to treat multi-drug resistant strains of *falciparum malaria*.
4. Proposed mechanism of action: causes oxidative stress.
5. Drug is extracted from *A. annua* (∼0.16% dry weight).
6. Access to the purified drug and the plant is restricted by the Chinese government.

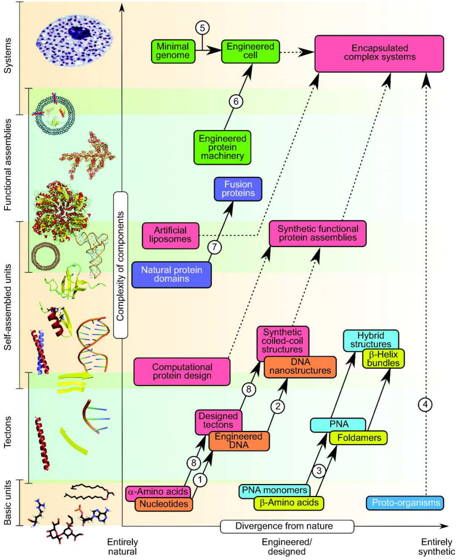
Engeneering yeast for *Artemisinic acid* production.





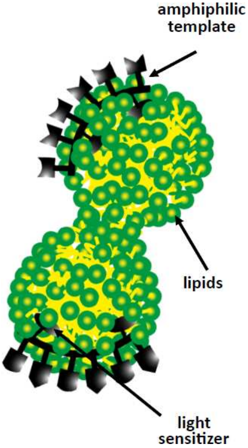
Ro D-K et al 2006, Nature 440:940-943; doi:10.1038/nature04640

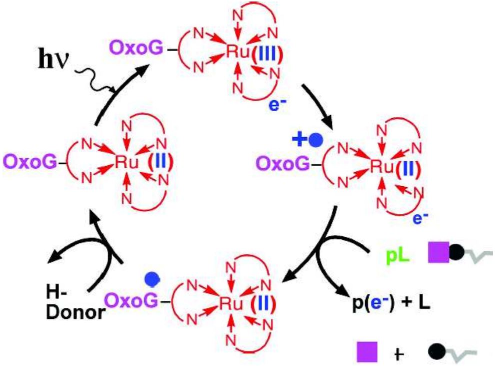
The Synthetic Biology Space



Bromley EHC et al 2008, ACS Chem. Biol. 3(1):38-50; doi:10.1021/cb700249v

Minimal Proto-Cell: bottom-up approach





Rasmussen S et al 2004, Science 303:963-965; doi:10.1126/science.1093669

Conclusion

1. Synthetic Biology is an emerging and exciting area.
2. Success of Synthetic Biology rests only on our imagination and ability to synthesize new molecules.
3. Synthetic Biology is a rigorous test of our understanding of Biology.

For Further Reading

Mukherji S, van Oudenaarden A
Synthetic biology: understanding biological design from synthetic circuits.
Nature Reviews Genetics (2009) 10, 859-871 | doi:10.1038/nrg2697

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Chemical synthesis using synthetic biology.
Curr Opin Biotechnology (2009), 20(4):498-503 | doi:10.1016/j.copbio.2009.08.001

Agapakis CM, Silver, PA
Synthetic biology: exploring and exploiting genetic modularity through the design of novel biological networks.
Molecular BioSystems (2009) 5:704-713 | doi: 10.1039/b901484e

Purnick PE, Weiss R
The second wave of synthetic biology: from modules to systems.
Nature Reviews Molecular Cell Biology (2009) 10:410-422 | doi:10.1038/nrm2698

Martin CH, Nielsen DR, Solomon KV, Prather KL
Synthetic Metabolism: Engineering Biology at the Protein and Pathway Scales.
Chemistry & Biology (2009) 16(3):277-286 | doi:10.1016/j.chembiol.2009.01.010