Redirecting Evolution

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“Ask not what you can do for evolution, ask what evolution can do for you”
A salty solution
Biology has much more to offer...

Courtesy: Calvin J. Hamilton
Grand applications
Decoding complexity

genome... → ...parts... → ...circuits

Modified from Innovech WordPress
Acquisition of complexity:
Conditionally activated control inside genes

Koide, Reiss, et al. (2009) MSB
Genetic information processing is dynamic.

- **Genotype**
  - DNA
  - RNA
  - Protein
  - Metabolites
  - Phenotype

**ENVIRONMENT**
Systems Approach: Perturb, Observe and Model

Parts of a system

INPUT(S) → Genes/Proteins → OUTPUT(S)

Environmental Perturbations → Phenotypes → NEW INPUT(S) → NEW OUTPUT(S)
Consequences of small changes resonate throughout the network

Baliga NS, Science (2008)
Tagkopolous et al., Science (2008)
Constrained Evolution

I. Interlocked architecture

II. Few dominant states

Anticipation of linked changes

65 genes: 21.1 hrs (anoxic)

45 genes: 18.5 hrs (oxic)

Whitehead et al., PLoS One (2008); Kaur et al., MSB (2010)
Explosion of technologies
System wide data: looking at the same phenomenon through different lenses
Reverse engineering biological circuits

- Gene Expression
  - Transcriptome, proteome, metabolome
- Protein-DNA interactions (ChIP-chip)
- Gene function annotation
- Phosphorylation
- Protein-DNA interactions
- TE/BRAIN
- Regulatory networks
- Gene expression

Reiss et al., BMC Bioinformatics (2006), Bonneau et al., Genome Biology (2006)
De novo discovery of a subcircuit
Inferelator: Learning regulatory influences

Bonneau et al Genome Biology (2006)
Data-driven discovery of a biological sub-circuit

Bonneau et al, Cell, 2007
Predicting new cellular behaviors

Tracking individual cells

0.85mM CuSO4 + 0.01mg/mL SR101
Dura3::pygX::GFP1044

0 500 1000 1500
Time (min)
Mean Fluorescence

Single cell pygX (via GFP)
Copper (via tracer)
Tracking individual cells

0.85 mM CuSO4 + 0.01 mg/mL SR101
Dura3::PygX-GFP1044

Mean Fluorescence

Time (min)

Multiple single cells yvgX (via GFP)

Copper (via tracer)
Rational Systems Re-engineering

Reengineer circuits
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http://baliga.systemsbiology.net

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Classes of cis-regulatory motifs
Acquisition of complexity: I. Gene Family Expansion

Turkarslan et al. in preparation; Facciotti et al., (2007) PNAS
Snapshots of regulons
Ensembles of networks
Snapshots of a regulon
Ensemble networks