Building Reliable Genetic Devices Using Unreliable Ones

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Synthetic Biology

- Design and deploy protein circuits that live inside cells and solve problems.
- Exemplary Application : Cancer Treatment
  - Engineer bacteria to seek out and invade cancer cells
  - Do no harm to healthy cells
  - Method: design a sensor/actuator that will kill a cell if certain proteins exceed a threshold.
- Other Applications
  - Smarter drugs, biofactories, biofuel cells, ...
  - Market for synthetic biology in 2013 expected as over $2.4 billion (BCCC research, June 2009)

Our Approach

- Use information theory to create more reliable biocircuits
  - Biocircuits designed using electrical circuit analogy
  - Extremely wireless (no direct connection).
  - Building blocks: biological logic gates, clocks, amplifiers . . .
- Eventual goal: Compiler from logical circuit to biological logic gates with reliability guarantees.

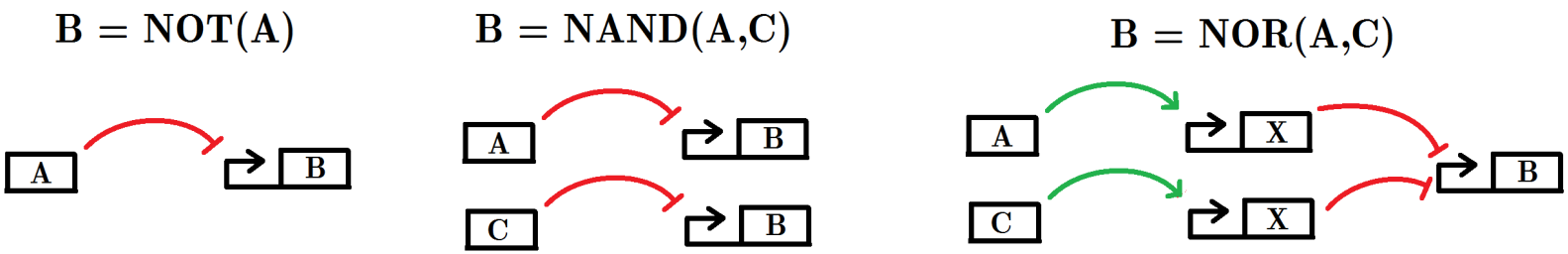


Figure: *Some simple biocircuits*

Motivational Example: Genetic Switch

- Genetic Switch: $\mathcal{X} \longrightarrow \mathcal{Y}$

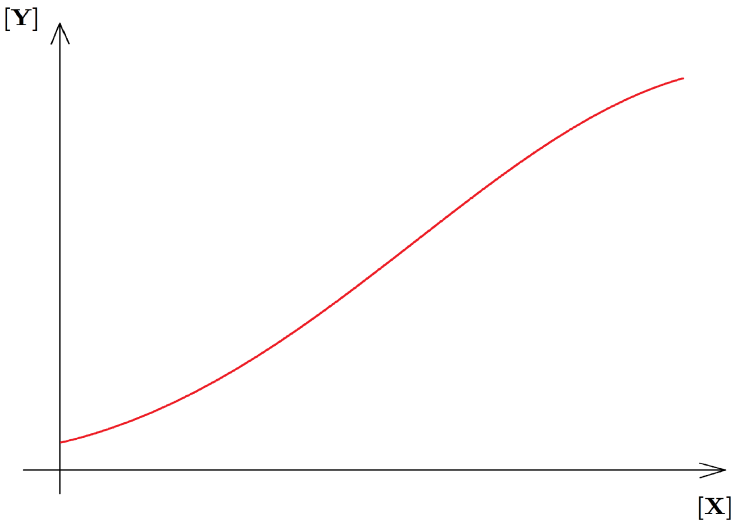
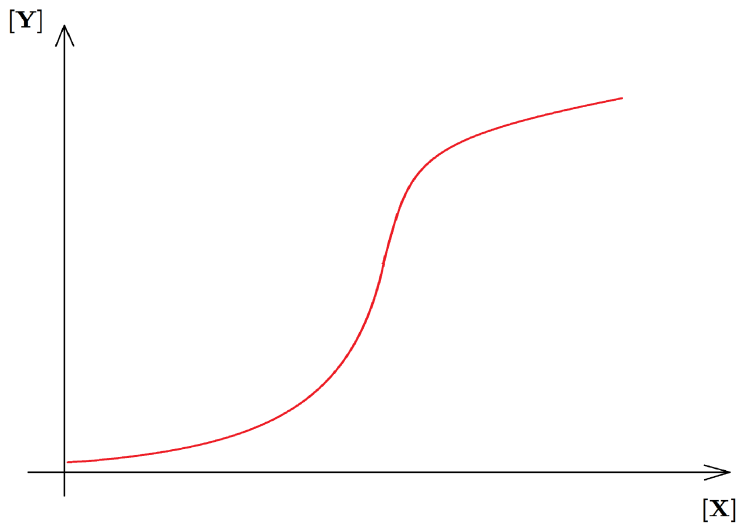


Figure: *Unreliable response*



Reliable response

Motivational Example: Cancer

- *Anderson et al*: Cancer indicator $\Rightarrow$ Invade cell
- Low immune function/nutrient dense:
  - Bacteria naturally congregate around cancer
  - E. Coli engineered to transmit indicator chemical to determine colony density
  - If indicator concentration passing threshold , activate surface protein invasin and invade surrounding cells
- Low oxygen:
  - Bacteria change to anaerobic metabolism in low oxygen environments indicative of cancer
  - Production of invasin linked to production of anaerobic metabolic protein

Motivational Example: Cancer

- *"In this work individual promoters communicate an input signal to an output response. Genetic logic circuits or response regulatory networks could integrate multiple inputs to achieve more accurate environmental sensing. However, engineering the necessary artificial fusions between sensory promoters and output genes is complicated by mismatches in rates of transcription and translation, especially as the complexity of the system increases."*
  - *Anderson, J. Christopher, et al. "Environmentally controlled invasion of cancer cells by engineered bacteria." Journal of molecular biology 355.4 (2006): 619-627.*

External Funding

- NSF
  - Communication and Information Foundations
    - Information theory, including emerging applications to biology
- NIH
  - Smart and Connected Health