Rewirable Circuits
An elegant means of system integration

Introduction

- **Goals**
  - Challenges:
    - Crosstalk: regulators may interact with each other’s targets leading to errors in the desired operation.
    - Host overload: the synthetic circuits may compete with natural parts that maintain the normal cellular processes for limited resources.

- **A new concept we proposed**
  - Rewirable circuit. To implement more functions, jamming in more modules is not the only way. We propose an alternative: Make full use of similar structures, and rewire the regulatory relationships.

- **Advantages of our idea**
  1. Circuit becoming adaptable: specific modules come into function only when they are needed.
  2. Reducing cell workload: parallel modules now share the same structures.
  3. No crosstalk between processing modules: parallel modules no longer parallel in space, but in function.

Methods

We constructed two circuits to prove our concept. The one is an integrated module of two classical circuits, a repressilator and a toggle switch. The other is a quorum-sensing module that sometimes performs positive feedback control and sometimes carries out negative feedback control.

Proof of our concept

- **Characterization**
  - We estimated and adjusted some parameters in our systems.

- **Results**
  - We added a GFP under the control of luxP to test our quorum-sensing module.

- **Improvement in I/O module**
  - Input module
    - To ameliorate the leakage problem of the recombinease, we utilized an engineered riboregulator to implement post-transcriptional control.
  - Output module
    - Sometimes the fluorescent proteins accumulate and are not very efficient to monitor the real-time processes. We synthesized RNA aptamers and monitored the fluorescence at RNA level.

Design principles of rewirable circuits

How to customize your own rewirable circuits? Here are the general steps:

- Design fitness functions
- Scan the topological space
- Match topological structures
- Sort and select

Policy & Practices

- **Intellectual Property Law**
  - "What if rewire goes haywire?"—despite scientists’ greatest effort, why would the public always fear the worst? We find its origin in psychological archetypes: God and Lucifer.
  - A 4-Dimension Model to help iGEmers think.

- **Economics**
  - If a basic assumption which underlines all economics analysis fails, where does that leave policies, which are based on this analysis?

- **Outreach**
  - Public Outreach: We held activities such as Future Scientists, iGEM Talks, and had videos on mainstream media.
  - Collaboration: We held the 1st Central China iGEMers’ Meetup, initiated the Central China iGEMers’ Consortium, helped each other, and reached outside China!

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References: