Modeling Gene Regulatory Networks as Interacting Modules

**Motivation**

An interesting question in Systems Biology is whether a Gene Regulatory Network (GRN) could be decomposed into interacting functional units. This is analogous to the modular design of electrical circuits from Electrical Engineering where complex networks are designed to perform specific tasks. These complex networks can be broken down into smaller functional units, such as amplifiers or mixers, and then these modules can be interconnected in a coherent way to perform their intended function.

**Low-Pass Filter**

- **Reactions**
  \[ J_0 = \alpha \]
  \[ J_1 = \gamma \]
- **System Equation**
  \[ \beta = \frac{1}{2} (\gamma - \alpha) \]
- **Steady State Value**
  \[ S_0 = \beta \]

**Band-Pass Filter**

- **Reactions**
  \[ J_0 = \alpha \]
  \[ J_1 = \gamma \]
- **System Equations**
  \[ \beta = \frac{1}{2} (\gamma - \alpha) \]
  \[ \gamma = \alpha \]
- **Steady State Values**
  \[ S_0 = \beta \]
  \[ S_1 = \gamma \]

**Phase Inverter Module**

- **Reactions**
  \[ J_0 = \alpha \]
  \[ J_1 = \gamma \]
- **System Equations**
  \[ \beta = \alpha \]
  \[ \gamma = -\alpha \]
- **Steady State Values**
  \[ S_0 = \beta \]
  \[ S_1 = \gamma \]

**Results**

We have designed three modules. Each of these modules is a network which contains transcription factors. The gene transcriptions are regulated by some of these transcription factors and the network connectivity which gives rise to interesting dynamics.

The following two modules are defined in terms of the frequency response between the input transcription factor and the output protein concentration.

**Complex Networks**

Using the above modules we designed two networks which are made up of many components.

- **Double Pass Response**
  This network has a frequency response which has two peaks at different frequencies.

**Frequency Tracking Filter**

The network consists of a control system for a biological oscillator whose frequency in mode is twice the frequency of an external oscillatory signal.

**Conclusions**

We have presented a modular approach to designing gene regulatory network models. Such models can be used to design large networks using functional units and these models can be used to design networks to study the similarity or differences. This will allow us to probe the design principles of Gene Regulatory Networks. Our goal is to draw up such a list, design networks and compare them with real networks to study their similarity or differences. This will allow us to probe the design principles of Gene Regulatory Networks.

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**EXAMPLE 1:** Building a Network with maximal responses at two different frequencies

**Introduction**

Building a network which is subject to external stimuli that in some cases are a periodic function of time, is an example of such a design. Simple models show that the external stimulus to the oscillatory system can have significant effects on the frequency and amplitude of the oscillations.

**Characteristics of the Frequency Response**

- **Amplitude in a linear scale**
  \[ 0 \leq \text{Amplitude} \leq 1 \]
- **Amplitude in a logarithmic scale**
  \[ \text{Amplitude} \geq 0 \]
- **Phase**
  \[ -\pi \leq \text{Phase} \leq \pi \]

**EXAMPLE 2:** An Artificially constructed Gene Network for tracking frequency changes in an external source

**Introduction**

We constructed a network that tracks an external signal varying in time. Such a network is widely used, for example, in electronic systems.

**Gene Network Model of the Frequency tracking circuit**

We consider a two gene interaction network which is regulated by a transcription factor and a protein that produces an external signal. The final readout is a gene which has two activations set up from the low and high frequency paths.

**Characteristics of the Frequency Response:**

- **Amplitude in a linear scale**
  \[ 0 \leq \text{Amplitude} \leq 1 \]
- **Amplitude in a logarithmic scale**
  \[ \text{Amplitude} \geq 0 \]
- **Phase**
  \[ -\pi \leq \text{Phase} \leq \pi \]