Intro to Synthetic Biology
Summer HSSP 2020
Week 1 Notes - 7/11/2020
Introduction, Design Principles

Synthetic biology aims to make implementation of new biological functions more reliable, efficient, safe, and transparent. It can solve problems in health, environment, energy, and security. The history of synthetic biology has been marked with important biological techniques, including the development of molecular cloning techniques in the 1970s, DNA sequencing in the 1990s, and biological circuits in the early 2000s, among others. Synthetic biology has useful and far-reaching applications, including CRISPR-Cas9 editing, gene drives, and even air-purifying houseplants.

The pipeline of synthetic biology experiments can be grouped into three phases: design, assembly, and measurement. This course will focus on the design and assembly phases. Today, we will focus on design principles and how they work.

Top-down design:

Top-down design involves systematically breaking down a system to determine the sub-systems and sub-processes that make it up. This is especially important for biology because it helps scientists understand common motifs for solving problems.
It consists of multiple different levels:

- The highest level, the **systems level**, is a biological circuit. This is the description of what happens in general. No implementation details are at this level and we only can make very rough predictions about the behavior of the system.
- The second highest level is the **network level**. A biological circuit is implemented as a network of nodes, where the interactions between the nodes determine how the system behaves. At this level there are more detailed predictions about the system's behavior.
- The last level is the **physical implementation level**. This includes details the specific physical elements (such as actual genes and proteins). Because actual elements are used, there are very detailed predictions that this level can provide.

Gene circuits:

Gene circuits are useful to diagram and chart complex regulatory pathways in biological systems. Different aspects of synthetic biology focus on different parts of a genetic circuit. For instance, pharmaceutical science includes changing sensors and input. For the purposes of our course, we will mostly look at how internal logic can be changed. The main components of any gene circuit are sensors, internal logic circuits, and actuators.

- **Sensors** detect changes in input, which is the molecule that sets the circuit into motion. Input can include small molecules, light, and sound.
- **Internal logic circuits** describe the methodology that cells use to carry out different gene regulatory network. This includes transcription and how it is regulated by the cell. The cell's logic can be modified using outside genome editing techniques, such as CRISPR/Cas9

- **Actuators** are on the receiving end of the gene circuit. They are responsible for interpreting the transcriptional logic of the pathway and converting it into a concrete signal or result.

Gene networks:
Gene networks consist of multiple circuits put together. Many gene networks are complex and consist of various intertwined pathways. They can span over different types of cells or even within different regions of a single cell. The examples we will cover in this course are individual parts of much larger systems.

Parts and compositors:

- A part is a functional unit that is typically used to construct gene circuits. Parts can convert molecules, create new ones, destroy them, or transport them. Specific processes mediate specific transitions between states.
- There are different types of parts:
  - A **basic part** is a single functional unit that cannot be divided further into smaller functional units.
  - A **composite part** is a functional unit of DNA consisting of two or more basic parts assembled together.
  - A **device** is a type of composite part that is capable of conducting an operation in the cell.
- Parts must have certain characteristics:
  - **Consistent** - works the same way in any given genetic context
  - **Specific** - only inputs specified trigger the function of the specific part and nothing else
  - **Non-toxic** - allows the host to grow
  - **Reusable** - the same conceptual part could be re-used in a circuit, although this is harder to achieve in biology because input molecules diffuse and activate all parts with that specific input
  - **Orthogonal** - parts do not crosstalk (interact) with each other and instead act independently
  - **Composable** - can be fused to give composite function
  - **Connective** - can be chained one after the other to propagate a signal
  - **Scalable** - able to extend to complex and larger circuits