Technology Brief 31
Synthetic Biology

Whether amplifying, sensing, computing, or communicating, all of the circuits discussed in this book manipulate electric charge to process information. Voltage levels and current intensities all represent the collective properties of charges inside metals, insulators and semiconductors. The processing of information, however, can be accomplished in other media as well. Mechanical circuits (like the Babbage Engine, described in Technology Brief 1), optical circuits (where computation is accomplished by manipulating light), and chemical circuits (where the operators are the reactants and products of chemical reactions) all have been demonstrated or in use for many years. Recently, engineers have begun to make synthetic information processing circuits inside biological cells. This new branch of engineering grew out of biochemical engineering and is called ***synthetic biology***. It promises to revolutionize the way we interact with biological systems.

In order to understand why synthetic biology is so powerful, and why it is so closely related to electrical engineering, we need to understand how biological cells process information. A cell, whether a free swimming bacterium or a human liver cell, is constantly transducing, storing and processing information from its environment. Cells produce molecules called ***proteins***, each of which can perform a specific function on a specific molecule. They can be thought of as little molecular robots. For example, certain proteins on a cell's membrane act as sensors, detecting the presence of molecules in the liquid around the cell. These surface proteins can change the state of other proteins inside the cell, which in turn affect other proteins, and so on. These chains of chemical reactions are called ***biochemical pathways***, and in this way the cell can adjust what molecules it produces based on what molecules are in its environment. If, say, the environment contains glucose, the cell's sensors can

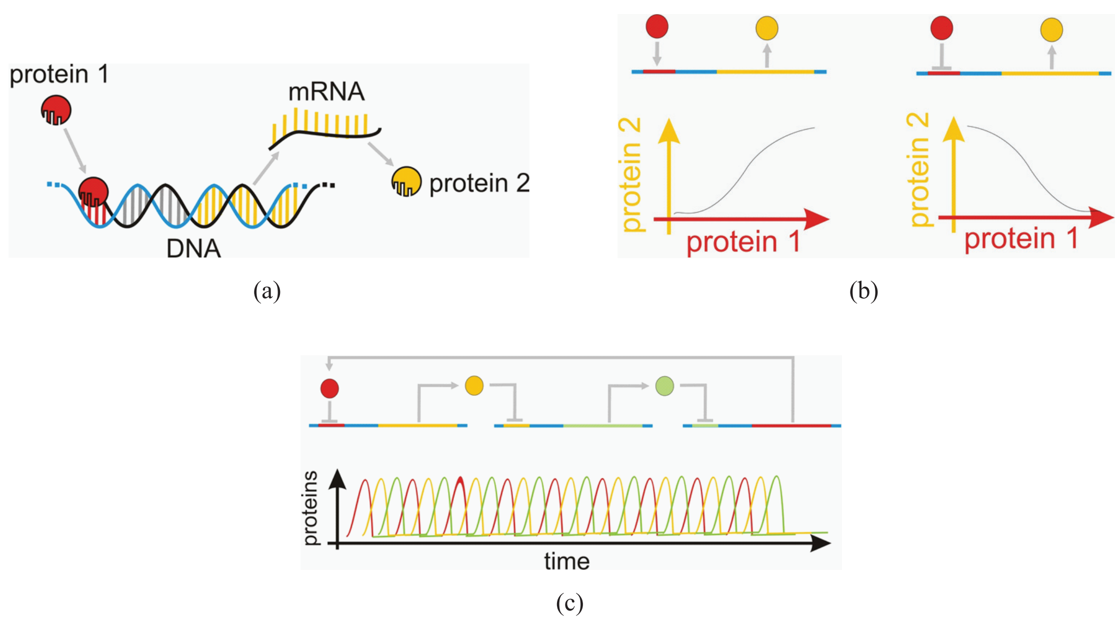

Figure TF31-1: *Building functions with genes and proteins.* (a) Consider a protein (red circle) which can bind to a certain, specific section of DNA within a cell. Upon binding to this sequence (shown in red), the production of another protein (Protein 2, in yellow) is affected; the gene which encodes for Protein 2 is shown as yellow base pairs in the DNA. In this example, increasing the amount of Protein 1 increases the production (and thus the amount) of Protein 2 in the cell. This motif is encountered often in cells. Cells ranging from bacteria to mammals contain relationships like these between proteins and genes. (b) The example on the left shows a simplified representation of (a) along with a plot showing how the amount of Protein 1 affects the amount of Protein 2 in the cell. The example on the right shows a similar cartoon, except in this case Protein 1 *inhibits* the production of Protein 2 (more Protein 1 in the cell causes less Protein 2). Notice how this right example behaves as a rudimentary protein-protein ***inverter***. (c) An example of a synthetic gene circuit in which three of the inverters in (b) are linked so that a protein produced by one gene inhibits the production of the next gene. This produces a chemical oscillator known as a ***repressilator***.

Figure TF31-2: By introducing new genes into ***E. coli***, the bacteria were made sensitive to light. In this example, by a team from the University of Texas at Austin and the University of California, San Francisco, a thin film of bacteria was grown in a Petri dish and exposed to patterns of light with the message "Hello World." Each bacterium in the film responded by changing color depending on the light level it was exposed to.

detect this and begin producing proteins that enable the cell to use glucose as fuel.

A key component of this regulation process depends on the ***genes*** the cell possesses. Although a discussion of genes is well beyond the scope of this book, for our purposes a cell contains a set of molecules called genes, which store descriptions of all the proteins it can make; a given gene will usually ***encode*** a single type of protein. In many ways, you can think of the genes as the cell's software. When we say a cell ***expresses*** a gene, we mean it has used the information in that gene to make the gene's protein. What is important here is that the biochemical pathways determine which genes are expressed. Thus, the surface proteins that detect glucose, for example, cause the cell to express the genes that encode the proteins that consume glucose. A single cell can make thousands of different proteins, which can interact with each other as well as with the cell's genes.

With the advent of modern molecular biology, our knowledge of the cell's pathways has expanded dramatically. In the latter half of the 20th century, biochemical engineers put this information to work by growing cells from many different species and modifying them to perform many useful functions. Waste water treatment, drug production, food additive production, and many other useful chemical processes are now carried out using cells.

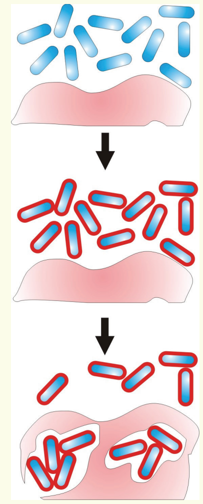

Figure TF31-3: Researchers at the University of California, Berkeley, and the University of California, San Francisco have devised synthetic pathways that may one day allow engineered bacteria to invade and kill tumors. (***top***) Modified ***E. coli*** bacteria at normal cell densities or oxygen conditions behave normally. (***middle***) Upon encountering low oxygen environments (associated with tumors) or high cell densities, the modified bacteria express invasin, a molecule that adheres to tumor cells and tricks the cells into absorbing the bacteria. (***bottom***) Once inside the tumor, the bacteria begin to invade and destroy it.

Even more recently, synthetic biologists have begun to build ***information processing*** circuits into cells (**Fig. TF31-1**). These engineers hope to design components and circuits that perform many of the same functions you have studied in this book, using the cell's biochemical pathways! Amplification, logical functions, clocks, memory, multi-channel communication, sensing, and even rudimentary "software" programs are all being developed using cells, proteins, and genes instead of circuit boards and solid-state materials. If these efforts succeed, our ability to interact and guide the behavior of existing cells and to build entirely new types of cells with human-made programs will have a profound impact on the world of science and technology (**Fig. TF31-2** and **Fig. TF31-3**). Along with these challenges comes a great responsibility to understand how our inventions can affect the natural world. What is very exciting is that synthetic biologists are realizing that many of the concepts electrical engineers developed for their electric circuits—noise, bandwidth, linear analysis, circuit diagrams, etc.—are proving useful for designing biological circuits!