"Constructing Knowledge" Actively in Bacterial Genetics Using Synthetic Biology

Resource Type: Article: Focus on Microbiology Education **Publication Date:** 9/29/2006

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Abstract *Dr. Rios-Velazquez completed a Ph.D. in 2000 in Bacteriology at the University of Wisconsin—Madison, analyzing molecularly and biochemically c-type cytochrome maturation in purple nonsulfur anoxyphototrophs. He completed postdoctoral studies at the National Institutes of Dental and Craniofacial Research analyzing toxins and toxin-producing microbes. Dr. Rios-Velazquez is currently an Associate Faculty member in the Biology Department at the University of Puerto Rico (UPR) at Mayagüez, and Co-director of the Center for Hemispherical Cooperation in Research and Education in Engineering and Applied Science.*

He is a member of the executive committee of the Industrial Biotechnology Program, and since 2001 has been counselor of the Industrial Biotechnology Students Association at UPR—Mayagüez. He is involved as co-principal investigator in a National Science Foundation-funded Microbial Observatory at Cabo Rojo Salterns, where microbial mats are molecularly analyzed both to understand phototrophic bacterial diversity and to generate metagenomic libraries to find new genes and activities with medical and biotechnological applications.

Dr. Rios-Velazquez has taught courses in General Biology and Microbiology, and advanced courses in Microbial Physiology, Bacterial Genetics, and Prokaryotic Molecular Biology and Gene Regulation. The Microbial Biotechnology and Bioprospecting laboratory developed by Dr. Rios-Velazquez at UPR—Mayagüez has trained about 180 undergraduate and four graduate (Masters) students.

Article

Fall *FOME* 2006 - Volume 13 No. 1, p 10-12

Last summer I participated as a visiting faculty at the Computational and System Biology Initiative at the Massachusetts Institute of Technology where faculty member Drew Endy showed me the importance, applications, and future implications of an emerging discipline named Synthetic Biology. I realized the importance of bringing that information not only to graduate or upper-level students, but to teachers and students at the K-12 level as well. Here I describe an educational strategy that can be applied to different academic levels, and in introductory courses such as General Biology, General Microbiology, Genetics, and advanced microbiology courses like Microbial Physiology and Bacterial Genetics. I have been able not only to introduce the concept, definition, and application of Synthetic Biology, but also to use it to allow students to have a versatile way of actively understanding gene organization, operons, and gene regulation.

Synthetic Biology has been defined as the combination of science and engineering (sometimes called bioengineering) to design new biological functions, or the redesigning of known biological functions to generate new problem-solving applicable systems. Synthetic Biology was originally described as just the generation of transgenic organisms (by genetic manipulation); now it is seen as the development of active or functional systems with a "nonbiological version" in real life. In order to simplify complex systems and to take advantage of the modular nature (made out of monomers at different organizational levels) of bio-molecules such as nucleic acids and proteins, a series of what are called abstractions hierarchies have been created. Examples of abstractions hierarchies are **parts**, **biological parts, or biological construction units** (a nucleotide sequence with a specific function), **devices** (x-number of combined parts with a testable novel emerging function), and **systems** (combining of devices). For simplicity I have used in class only parts and devices and have asked the students to model functional prototypes using geometrical figures (we use Legos) as manipulatives.

First, the definition and description of a biological part and device are given to the students. Second, the students receive the basic information about the genetic elements to be taught. Finally, a list of parts with their functions and a group of interchangeable geometrical figures assigned to each part are given to each student or team (Fig. 1).

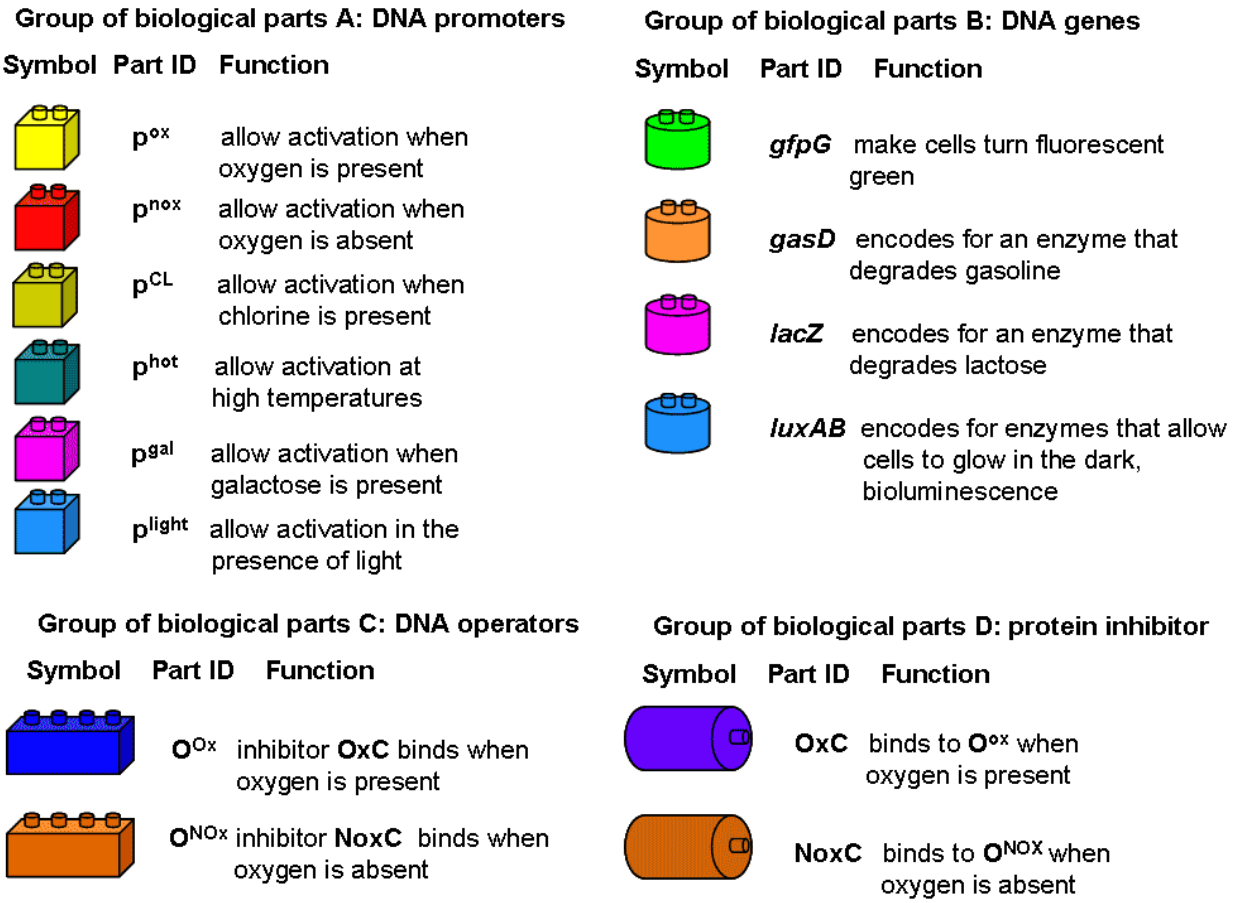

FIG. 1. Biological parts representations and their specific descriptions.

Here I describe examples of premises to develop prototypes. First, students are to design a representation of a genetic prototype that will generate an *Escherichia coli* that can act as an aerobic biosensor of contamination that will turn fluorescent green if there are chlorine compounds in a sample. Students also present the prototype once the conditions become anoxic.

The teams receive all of the "genetic parts," and they have to decide which parts to use, and the correct order for assembly to have a testable prototype (Fig. 2A). The parts used in this activity can vary based on the academic level. At the beginning, the parts do not need to represent real or known genes (parts actually can be combined), but the exercise can serve as an introduction to a general or known operon structure and function and to gene regulation.

In a second example, where students need to generate devices that interact with each other, the groups are also presented with testable conditions and a premise (hypothesis driven) to predict and prove the functionality of the device. Students design a representation of two genetic

prototypes (two devices; Fig. 2B) where the first prototype will degrade lactose anaerobically at high temperatures; the device will allow cells to become blue in X-gal (a substrate that hydrolyzes beta-galactosidase to form a blue precipitate) and will activate a second device which will make cells "glow" in the dark.

Testable conditions. The culture media will contain lactose and X-gal. The cells should be incubated anaerobically at high temperatures.

Prediction. If the cells break lactose into glucose and galactose (due to the device 1), then the galactose produced by the first device will serve as an inducer to activate the second device. The cells will turn blue in X-gal media and will glow in the dark (Fig. 2B, device 2).

If Synthetic Biology is defined as using biological parts or components to seek the generation of nonnatural biological active systems, I have used a very simplified version of the work done by Levskaya et al. (5) in order to make an "*E. coli* bacterial lawn to smile." The premise is stated as follows: generate a bacterial lawn capable of showing a happy face with blue eyes and mouth for at least one hour.

Testable conditions. The culture media will contain X-gal. The cells should spread on the plate, let them start growing in the dark, place a cut cardboard filter (with eyes and a mouth) on top of the plate, place the plate under light, and remove the cardboard or filter after a few hours.

Prediction. If the cells have a device that activates with light and allows the cells to degrade X-gal, then the cells will turn blue only in the areas exposed to the light and will form a happy face with blue eyes and mouth. Notice that in this case a nonbiological component (cardboard happy face) needs to be added for the device to be testable and functional (Fig. 2C).

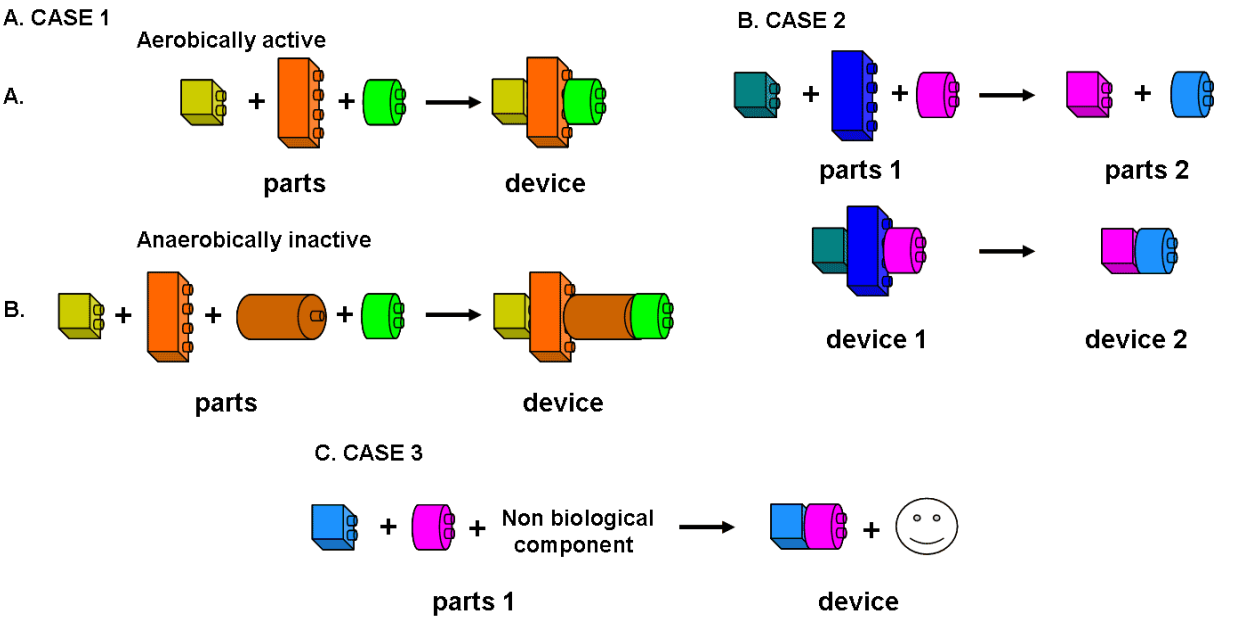

FIG. 2. Examples of assigned cases and the device generation based on the chosen parts.

Just recently (July 2006), I tested this educational strategy with secondary students and teachers in the BETTeR-IC Summer Camp (Biotechnology for Educational Training in Teams through Research and Interdisciplinary Centers)**.** Four situations were given to each educational team (four teams of five students and two teachers) asking them to solve only one. At the end of the workshop, all of the teams accomplished the assigned devices, and 75% of them wanted to try additional situations.

I have done the same exercise with undergraduate and graduate students and it is just positively addictive. It is analytical, creative, dynamic, challenging, and a perfect instrument to develop critical thinking, allowing the use of Bloom's taxonomy's highest hierarchies (e.g., analysis, synthesis, and evaluation).

In the workshops I used "gigantic Legos," but you can use anything from construction paper to a piece of paper and a few markers, or just a pen or a pencil. Depending on the basic objective of the activity, one can let the students design their own parts, based on previous knowledge of other genetic systems.

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