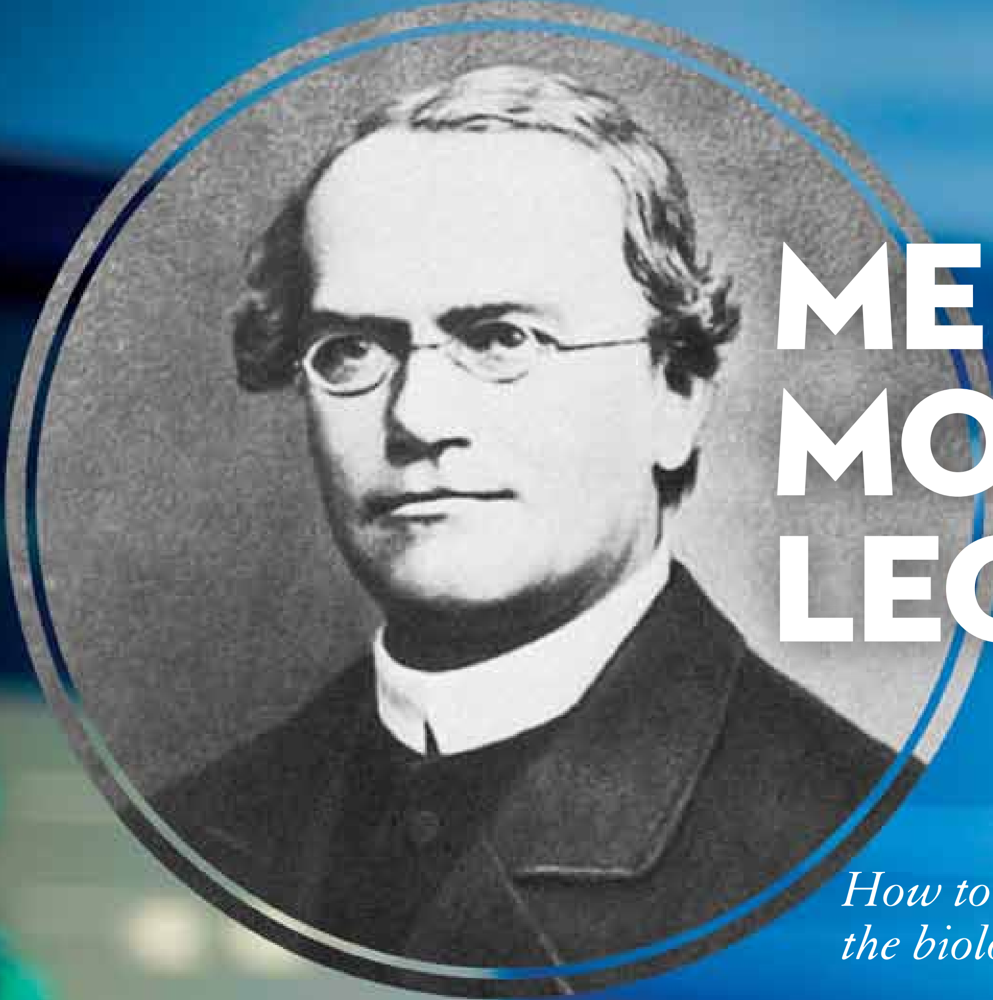


MENDEL'S MODERN LEGACY

How to incorporate engineering in the biology classroom

James Dixon and Natalie Kuldell

Ask science teachers if engineering concepts should be taught in the science classroom, and most will say yes. But even though teachers may agree with guidelines for engineering education, such as those of the *National Science Education Standards* and *A Framework for K–12 Science Education* (NRC 1996, 2011), many will wonder: "When would we have time?" "Are freshman physics students sophisticated enough?" "How do we teach engineering to students with weak math skills?"

As their physics, chemistry, and mathematics colleagues wrestle with these questions, biology teachers often watch from afar, rarely including engineering in their own courses. Yes, genetic engineering is taught in biology but as a scientific tool and not as a means to explore engineering design. Biomedical engineering is another entry point, but it relies heavily on mechanical engineering (and math) and thus often falls to the physics teacher. At least, that has been the norm.

Yet, given the clever behaviors and patterns that can be found when examining living systems, biology classes seem well positioned to teach foundational engineering design principles (Kuldell 2007). This article examines a new, open-access curriculum designed to do just that: BioBuilder (see "On the web") is the product of collaboration between the Massachusetts Institute of Technology's (MIT) Department of Biological Engineering and local high school teachers. It draws from the relatively new field of synthetic biology (Lucks et al. 2008), an engineering approach to the design of novel living systems or the redesign of existing ones. Just as physics teachers have students create functioning electrical circuits or robotic systems, biology teachers can have students safely design, construct, and analyze engineered biological systems.

Synthetic biology

Synthetic biology applies lessons from engineering disciplines, such as electrical and mechanical engineering, to biology. If we think of cells as molecular machines and of biology as technology, we can genetically program living systems to address global challenges in health care, food production, and medicine. For example, synthetic biologists have engineered new bacteria that can change color upon contact with toxins and produce a drug to fight malaria.

In synthetic biology, biological technologies like PCR (polymerase chain reaction), restriction enzymes, and genomic sequence analysis are complemented with foundational engineering tools such as standardization (a series of assembly and characterization rules), modeling, and

SCILINKS
THE WORLD'S A CLICK AWAY

Keywords: Mendelian Genetics
at *www.scilinks.org*
Enter code: TST021201

computer-aided design. Students gain experience using the engineering paradigm of "design, build, and test" in the context of living systems. Synthetic biologists use DNA and genes, instead of bricks and steel, as their raw material. As a student wrote after completing a BioBuilder lab: "Synthetic biology tries to use biological parts such as genes in order to develop machines that can be used to facilitate life."

The BioBuilder curriculum

BioBuilder transforms cutting-edge research projects into teachable modules that students and teachers can investigate together. These modules begin with a collection of three- to five-minute animated videos that explain biology and engineering concepts and set up a challenge. The modules then move offline to the classroom or lab setting.

The freely available BioBuilder curriculum includes laboratory investigations, essay assignments, design assignments, and links to teacher and student resources. There is no story line connecting the videos, so students and teachers can explore topics in any order. For example, one video explains the engineering principle known as *abstraction,* a process borrowed from software engineers that simplifies inherently complex living systems by hiding some information. Another animation discusses the molecules and DNA sequences needed for bacterial gene expression.

The videos explain concepts through conversations between laboratory scientist Systems Sally and a curious young learner, Device Dude. Colorful one-page Bioprimers supplement the animations (Figure 1). These comic book–style stories direct students to lab or classroom activities they can perform with their teacher.

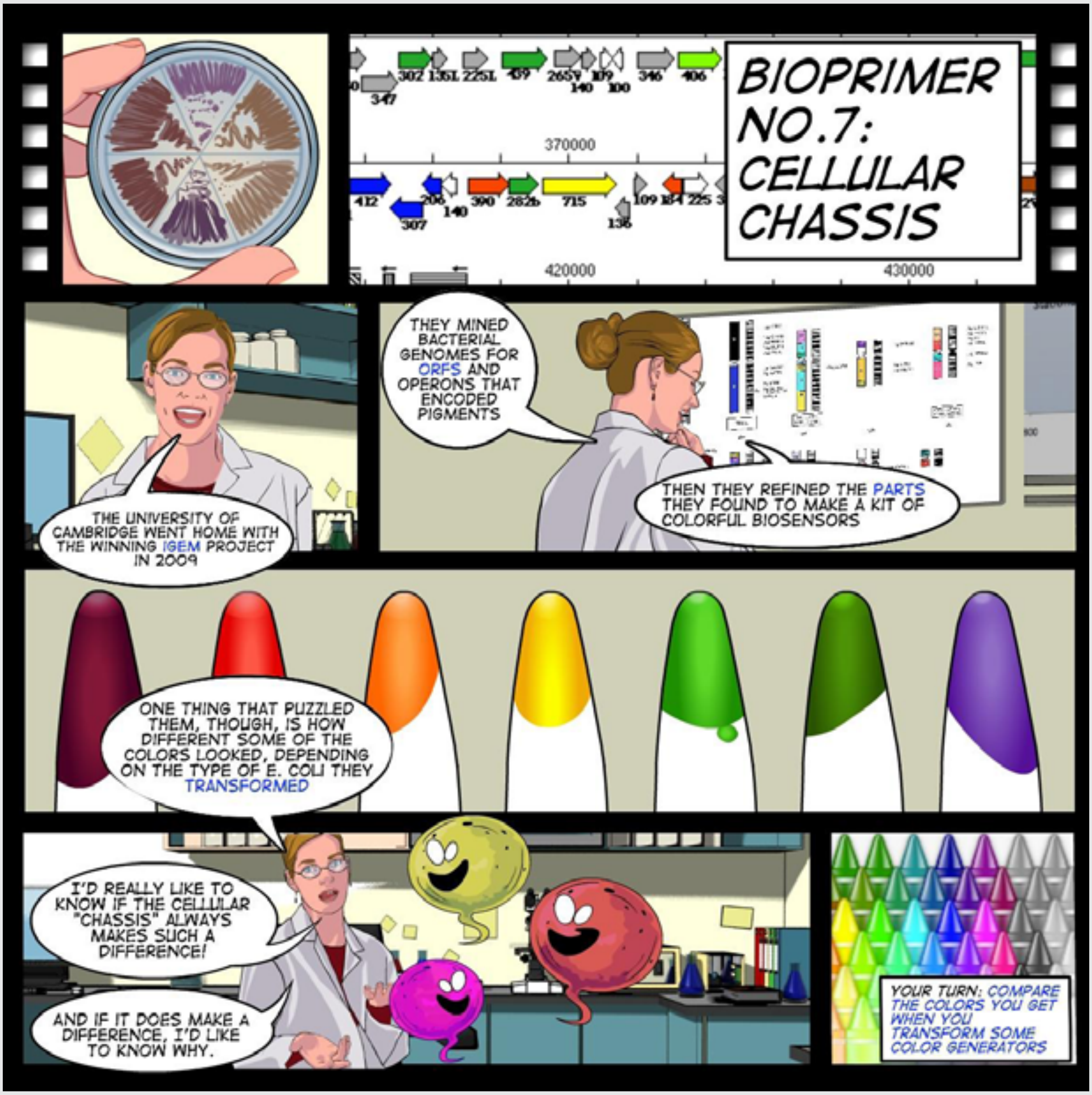
BioBuilder provides introductions and instructions for students and a teacher portal that includes laboratory workflow guidance and grading rubrics. The activities are based on current research and projects by undergraduate design teams in the annual International Genetically Engineered Machine (iGEM) competition (see "On the web"), yet they use equipment and materials available in most high school biology laboratories. After completing the lab and classroom work, students and teachers return to BioBuilder's online forums to upload their findings and compare their results.

Each lab activity in the BioBuilder curriculum focuses on different, but related, aspects of both biology and synthetic

FIGURE 1

Sample BioPrimer.

Through the narrative established with this Bioprimer, the embedded animations, and the associated laboratory activity, students explore the role of the bacterial chassis in the expression of a color-generating genetic program.



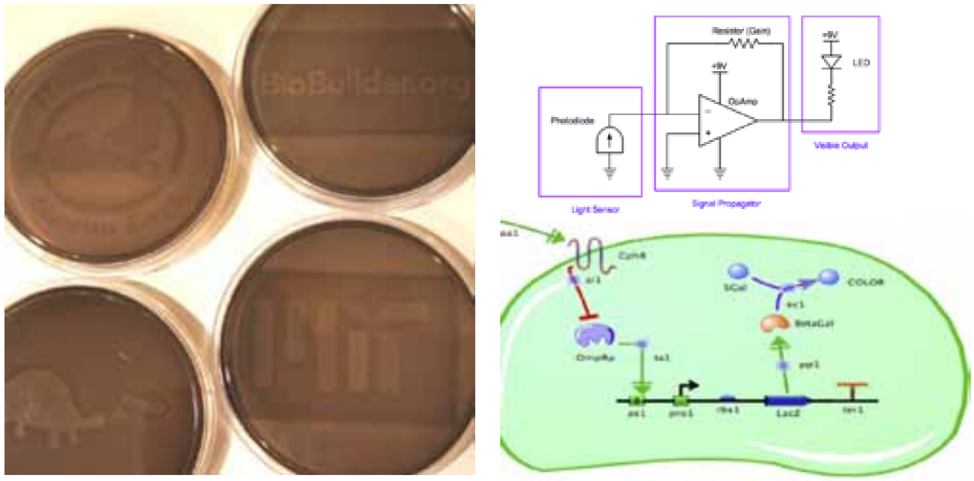
ALL IMAGES COURTESY OF THE AUTHORS

biology. Each investigation includes an introduction to genetics and engineering principles, a detailed procedure, a lab report or other assignment, rubrics, and score sheets. The website also includes video of experimental techniques and connections to National Science Education Standards (NRC 1996).

FIGURE 2

Bacterial "photography."

Bacteria were engineered to serve as pixels in a living photograph (left). The genetic circuitry that underlies this behavior is explored through a computer-aided design tool (bottom right) and the building of an electronics circuit (top right) in the "Picture This" lab.



"Eau That Smell"

"Eau That Smell" is a lab exercise that compares two genetic designs that use different genetic elements to reach the same outcome: the smell of bananas. The exercise is based on a 2006 MIT iGEM team project in which *E. coli* bacteria were engineered to smell like bananas during their stationary growth phase. In the BioBuilder lab, students measure changes in the bacterial population over one or more laboratory periods and compare the intensity of the banana smell.

The lab allows students to practice microbiological techniques (e.g., plating, maintaining cultures, using spectrophotometers) while learning about gene expression and bacterial growth. It also provides an opportunity to investigate and discuss the relative merits of quantitative and qualitative measurements. Students explore these biology concepts and techniques in the context of engineering concepts such as standardization and reference measurements (Dixon and Kuldell 2011). "A lot of times, the biology we learn is simplified for our convenience," one student said after the lab activity, "but [the BioBuilder] experiments show complications that aren't expressed in textbooks."

"The iTune Device"

"The iTune Device" lab examines the performance of standardized genetic "parts"—such as promoters (DNA sequences where transcription of RNA is initiated) and ribosome-binding sites (RBS) (RNA sequences where the ribosome binds and translation to protein is initiated)—and the predictable design of genetic devices. Students practice microbiologically sterile techniques and perform enzymatic activity reactions to measure the cell's output (of the enzyme β-galactosidase). They learn these laboratory procedures to evaluate a matrix of promoters and RBS parts that in combination "tune" the cell's enzyme production.

Though the efficiencies of the genetic parts can be evaluated bioinformatically, students see that these individual bits of sequence information don't automatically enable the rational assembly of the parts into more complex, predictable devices and systems. Through the lens of basic biology (e.g., homeostasis, regulated gene expression) and engineering (e.g., digital vs. analog behavior of systems), students learn that a system shouldn't always be tuned to "maximal output." Thus, this activity encourages students to consider the useful recombination of a cell's genetic machinery to engineer a system to specification.

"Picture This"

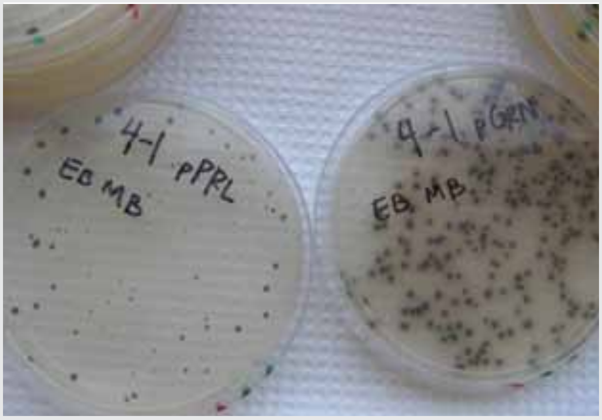
"Picture This" consists of three activities that focus on circuit design and modeling. Students first learn about a synthetic genetic system in which bacteria serve as pixels in a living photograph (Figure 2). When the engineered cells are grown in the dark, they express β-galactosidase and convert an indicator compound in the media to a dark-color precipitate (Levskaya et al. 2005), allowing students to create a living "photograph."

This charismatic system is a useful point of departure for several biology and engineering lessons. One teaching direction uses this lab to reinforce the scientific content related to signaling (communication among cells), cellular differentiation, and gene expression. Another opportunity

FIGURE 3

Results from BioBuilder's "What a Colorful World" lab.

Students discover that transformation of the purple-color generator and the green-color generator plasmids behave differently in different cellular contexts (i.e., "chassis").



dovetails with engineering efforts common to physics classrooms: BioBuilder provides step-by-step instructions for an electronics kit to recapitulate the biological circuitry using a breadboard (circuitry model). It also provides instructions for using a downloadable biodesign program called *TinkerCell.* This program enables students to model the genetic system and vary experimental parameters to simulate the system's response to those changes (Chandran, Bergmann, and Sauro 2009).

Asked how the availability of a computer-aided design tool will affect her teaching, one teacher responded: "Every student in my school has a computer to use, and TinkerCell is a wonderful way to get them to see the role computers play in biology." She continued: "A number of my students have individualized education programs and are English language learners. I can see how the lab will allow me to pique their interest and learn some science."

"What a Colorful World"

"What a Colorful World" examines the role of the cellular chassis in system performance, asking students to consider system integration, a challenging aspect of synthetic biology. This BioBuilder lab uses a streamlined protocol to transform two "flavors" of *E. coli* (a K12 strain and B-type strain) with the same genetic devices. These devices—engineered genetic constructs composed of a promoter and protein coding sequences that are carried into the cells on a plasmid—were originally designed for the *E. chromi* project (see "On the web") as part of the 2009 iGEM competition. They are intended to generate purple and green pigments in the bacteria.

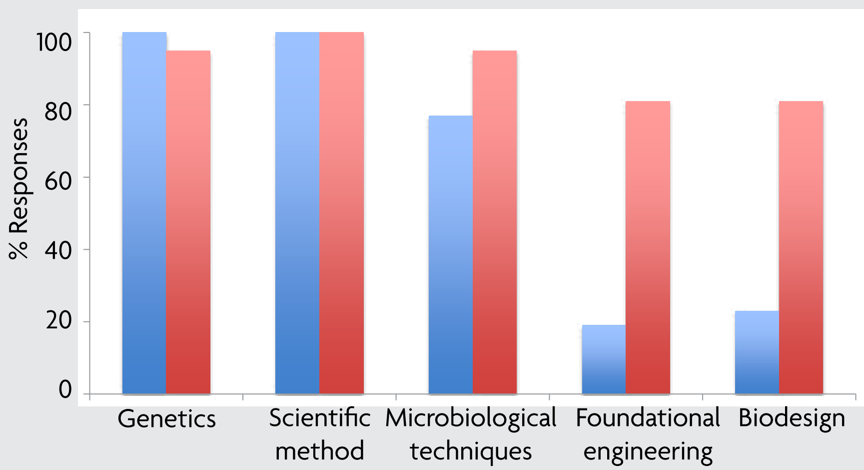
Students find that the system's behavior depends not only on the DNA plasmid they transform but also on the cell type that provides the raw materials for its expression (Figure 3). Differences in the intensity of the colors generated and in the number of transformants lead students to ask additional questions about how the cell background explains these differences. Unexpected outcomes create teachable moments. One teacher reported: "The students were surprised to see the different patterns of growth between the two strains."

This BioBuilder lab is similar to the bacterial transformation labs frequently conducted in biotechnology and Advanced Placement Biology courses, but a teacher, using this engineering framework, can simultaneously cover the techniques of transformation; data analysis for scientific inquiry; and the design, build, and test cycle of engineering. These labs use basic equipment found in most advanced biology classrooms

FIGURE 4

Effect of BioBuilder on teaching core concepts.

Teachers were asked how often they taught these concepts before learning the BioBuilder curriculum. The blue bars indicate those who answered "often" or "always." After running the BioBuilder lab activities, participants indicated how likely they were to teach these concepts. The red bars measure those who answered "likely" or "certain."



and safe strains of *E. coli* that can be easily disposed of using directions found on the BioBuilder website.

Classroom projects

Beyond the four lab activities are two other classroom projects: The bioethics essay requires students to consider the potential and risks of biological engineering, such as the introduction of synthetic living systems into the environment. In the design assignment, students identify a problem that can be effectively addressed with synthetic biology and then specify a living system they believe could meet the challenge.

Conclusion

The BioBuilder curriculum contains primers, animations, and labs for synthetic biology instruction. There are both student and teacher versions of the labs, which can be printed directly from the website. Teachers who wish to conduct the labs can order material (bacteria and chemical reagents) through the "request reagents" link. So far, 35 schools have requested individual BioBuilder modules, and 27 educators conducted the entire curriculum at an August 2011 pilot workshop at MIT. Afterward, teachers reported they were more likely to teach engineering principles and biodesign (Figure 4). One teacher, Sherry Annee of Brebeuf Jesuit Preparatory School in Indianapolis, Indiana, said:

"The BioBuilder curriculum causes a dramatic paradigm shift. No longer can one be satisfied teaching genetics within the context of [Gregor] Mendel; rather, through a series of hands-on, inquiry-based labs, the BioBuilder curriculum *compels* students to discover Mendel's modern legacy: synthetic biology. The BioBuilder curriculum not only teaches the facts of science but, more importantly, the art of science as students must apply content to engineer intricate systems devised of parts that may or may not work in unison as anticipated."

Synthetic biology advances often make front-page news. Just recently, students may have heard of cells programmed by synthetic DNA and bacteria that have had their codons reconfigured. This work is done by engineers using genes and cells as their materials. The BioBuilder curriculum provides an opportunity for students to learn about this exciting research while improving their understanding of biology and engineering principles. As the BioBuilder project expands, we will use our pilot teachers to gather additional evidence of student learning of engineering and biological concepts. We also wish to provide materials to other teachers who want to use engineering concepts to help teach their biology classes. ■

James Dixon (j_dixon@sharon.k12.ma.us) *is a biology teacher at Sharon High School in Sharon, Massachusetts, and*

Safety note.

Special care needs to be taken to train students in professional best practices in proper Biosafety Level 1 lab techniques. Laboratory safety acknowledgement forms should be reviewed, signed, and returned by students' parents or guardians. Safety procedures should include proper handling of biological and chemical agents, use of required personal protective equipment (e.g., nitrile gloves), appropriate disposal of lab equipment that contacts the *E. coli* plates, autoclaving, proper hand-washing techniques with soap and water, and so on. Never have students use environmental bacteria in petri dish systems. Only use commercial cultures of nonpathogenic bacteria.

Natalie Kuldell (nkuldell@mit.edu) *is a faculty member in the department of biological engineering at the Massachusetts Institute of Technology in Cambridge.*

On the web

BioBuilder: *www.BioBuilder.org*

BioBuilding 2012 workshop: *http://openwetware.org/wiki/BioBuilding2012_workshop_@_UC_Berkeley*

iGEM Competition: *http://igem.org/Main_Page*

iGEM *E. chromi* project: *http://2009.igem.org/Team:Cambridge/Project*

iGEM Eau d'coli project: *http://parts.mit.edu/wiki/index.php/MIT_2006*

References

Chandran, D., F.T. Bergmann, and H.M. Sauro. 2009. TinkerCell: Modular CAD tool for synthetic biology. *Journal of Biological Engineering* 3: 19.

Dixon, J., and N. Kuldell. 2011. BioBuilding using banana-scented bacteria to teach synthetic biology. *Methods in Enzymology* 497: 255–271.

Kuldell, N. 2007. Authentic teaching and learning through synthetic biology. *Journal of Biological Engineering* 1: 8.

Levskaya, A., A.A. Chevalier, J.J. Tabor, Z.B. Simpson, L.A. Lavery, M. Levy, E.A. Davidson, A. Scouras, A.D. Ellington, E.M. Marcotte, and C.A. Voigt. 2005. Synthetic biology: Engineering *Escherichia coli* to see light. *Nature* 438 (7067): 441–442.

Lucks J.B., L. Qi, W.R.Whitaker, and A.P. Arkin. 2008. Toward scalable parts families for predictable design of biological circuits. *Current Opinion in Microbiology* 11 (6): 567–573.

National Research Council (NRC). 1996. *National science education standards.* Washington, DC: National Academies Press.

NRC. 2011. *A framework for K–12 science education: Practices, crosscutting concepts, and core ideas.* Washington, DC: National Academies Press.