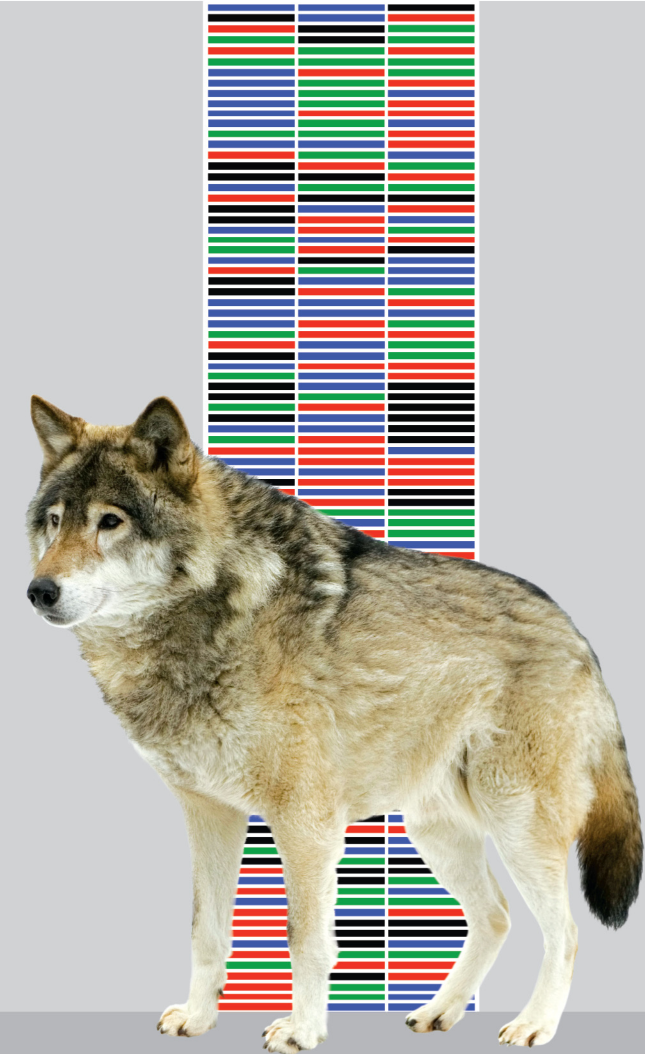

# USING BIOINFORMATICS: *Genetic Research*

ADVANCED

Grades 9–12 | First Edition

NWABR.ORG
Northwest Association for Biomedical Research

# Credits

## Credits/Funding Source

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# Overview

## Unit Overview

This curriculum unit explores how bioinformatics is used to perform genetic research. Specifically, the bioinformatics tools BLAST, ORFinder, ClustalW2/JalView, and Cn3D are used to analyze genetic sequences and molecular structures. The cytochrome c oxidase subunit 1 (*COI*) gene is introduced as the "DNA barcoding" gene that allows for identification of animal species. Students examine DNA sequences from different animal species, investigate the relationship between protein structure and function, and explore evolutionary relationships among eukaryotic organisms. The unit concludes with an optional authentic student research project, sequencing the *COI* genes from samples they collect themselves or samples obtained through partnerships with the National Oceanographic and Atmospheric Association (NOAA) and the Seattle Aquarium, both based in Seattle. Throughout the unit, students are exposed to a number of career options where bioinformatics tools are either developed or used. The career lesson near the end of the unit culminates with resume and cover letter writing activities and a mock job interview.

## Essential Understandings

1. Biological molecules store and process information.
2. The structure of molecules is closely related to their function. Changes in structure can often impact function.
3. Acquisition of biological information has many societal and ethical implications; students need tools to evaluate and decide how information should be used.
4. Technology influences how science is done; bioinformatics gives us new tools to understand biological information.
5. Bioinformatics is used in many areas of life sciences and related fields.

## Unit Objectives

1. Students will be able to explain how bioinformatics tools are useful in analyzing biological sequence and structure information.
2. Students will be able to use sequence analysis tools to identify and explore evolutionary relationships between organisms.
3. Students will use molecular modeling to investigate and identify foreign substances bound to the active site of cytochrome c oxidase.
4. Students will be able to identify and critically evaluate the ethical implications of public funding for genetic research.
5. Students will be able to design and conduct a research study to isolate and analyze the genetic information of an unknown species or specimen using DNA barcoding techniques and bioinformatics tools (For optional *Wet Lab*).
6. Students will evaluate the use of bioinformatics in the life sciences and describe how bioinformatics tools could be used in various careers.

## Instructional Components

**The Curriculum:** The *Using Bioinformatics: Genetic Research* curriculum consists of seven sequential lessons, an eighth lesson that focuses on careers that make use of bioinformatics tools, and a ninth lesson offering instruction in DNA sequence analysis. *Lesson Six* is provided as an assessment of the skills obtained in the first five lessons. An optional *Wet Lab* is also included.

Throughout this curriculum, a variety of resources are provided. These materials include:

- Student "Handouts" that are designed to be printed or copied and given to each student as a "worksheet." Answers to lesson activity and/or homework questions may be completed on the handouts, on separate sheets of paper, or in lab notebooks, as directed by the teacher.
- "Class Sets" that contain lesson activity instructions for students and are designed to be printed or copied and re-used as class sets. Questions that students should answer on their handout, piece of paper, or lab notebook are indicated with an icon.

- Teacher "Resources" that include teacher demonstrations and additional information.
- Teacher Answer "Keys" that provide suggested answers and scoring information.

**Time Commitment:** Each lesson requires a minimum of one 50 minute class session. Some lessons require two class sessions, in addition to homework assignments. The entire unit (nine lessons) is expected to take 16–20 class periods of 50 minutes each. The optional wet lab requires an additional 4–6 class periods of 50 minutes each. For a detailed overview of the unit time commitment with and without the optional wet lab, as well as suggested lesson orders, see the *Overview* section *Wet Lab Component* and the summary tables following the *Lesson Overview*.

**Prior Knowledge Needed:** This curriculum is not designed to introduce students to the "Central Dogma of Molecular Biology" (that information in DNA is transcribed into mRNA and then translated into protein), but to reinforce that concept. Students should already be familiar with DNA replication, transcription, and translation. Student understanding of these processes will be deepened through the use of this curriculum. In addition, this curriculum relies on concepts in taxonomy. An introduction to taxonomy before instruction is beneficial.

The Bio-ITEST Introductory curriculum, *Using Bioinformatics: Genetic Testing*, is not a required prerequisite for this curriculum, but it is strongly recommended. The Introductory curriculum develops foundational skills in the bioinformatics programs BLAST and Cn3D, while introducing concepts like sequence alignments.

## Career Component

Most lessons in the curriculum are accompanied by a PowerPoint slide highlighting a person in a career that uses bioinformatics, followed by a slide providing job information about that career. Student Handout—*Careers in the Spotlight* is given to students during the first lesson. Students are expected to take daily notes on this handout at the beginning and end of the class for the duration of the unit.

*Lesson Eight* focuses entirely on careers that use bioinformatics tools. Students consult interview transcripts from professionals, conduct internet research on a specific career, and review the information they have collected on Student Handout—*Careers in the Spotlight*. Students then update their resume (developed in the Bio-ITEST Introductory curriculum *Using Bioinformatics: Genetic Testing*) and learn how to create a cover letter. The lesson ends with a mock job interview.

Although bioinformatics is a career choice in itself, there are also a wide variety of careers that use bioinformatics tools. This curriculum highlights a broad range of career paths, even if the use of bioinformatics is not central to that career.

## Wet Lab Component

An optional *Wet Lab* lesson is included in the Bio-ITEST curriculum. This series of four lab experiments is designed to provide students with hands-on experience in DNA barcoding, through classroom laboratories or as part of an independent research project. The four lab experiments include:

- DNA purification
- Polymerase chain reaction (PCR)
- Agarose gel electrophoresis
- Preparation of samples for DNA sequencing

Samples for barcoding could include meat or fish from local grocery stores, markets, or restaurants; samples collected from local parks or other ecosystems; or samples obtained through partnerships with NWABR, zoos, or aquariums.

**Lesson Order:** The *Wet Lab* lesson is designed to be modular and can be inserted throughout the curriculum as time permits. Many teachers find it best to provide students with a general overview of DNA barcoding (i.e., *Lesson One*), followed by the *Wet Lab*, then *Lessons Two* through *Eight*, and finally, complete the unit with *Lesson Nine*. This allows students to complete the DNA sequence analyses in *Lesson Nine* with their own DNA sequence data. This lesson order should allow sufficient time for classes to send their DNA samples for sequencing and receive their data while completing the other Bio-ITEST lessons. Alternatively, the *Wet Lab* could be used to start or end the unit.

For classes that will not complete the *Wet Lab*, a collection of sequence data for *Lesson Nine* has been obtained through partnerships with the Seattle Aquarium and the National Oceanographic and Atmospheric Administration (NOAA), and is available under the "Resources" tab on the Bio-ITEST advanced bioinformatics webpage at: http://www.nwabr.org/curriculum/advanced-bioinformatics-genetic-research.

The Bio-ITEST program will provide PCR primers for DNA barcoding of animal samples. For contact information, visit http://www.nwabr.org.

## Technology Requirements

Detailed information regarding computer equipment, files, software, and media requirements can be found in the *Materials* section at the beginning of each lesson.

For all nine lessons and the optional *Wet Lab*, teachers will need to be able to project PowerPoint slides for the class to see. If this is not possible, teachers can print the PowerPoint slides onto transparencies, which can be displayed with an overhead projector.

*Lessons One*, *Two*, *Five*, *Nine*, and the optional *Wet Lab* require the capability to show online streaming videos to the class. *Lesson One* includes an optional video from the Howard Hughes Medical Institute, "Sanger Method of DNA Sequencing." *Lesson Two* includes the video "Barcode of Life: Global Diversity Challenge," produced by the International Barcode of Life Project Biodiversity Institute of Ontario (available on YouTube), and/or the NWABR animation "DNA Barcoding" (available under the "Resources" tab on the Bio-ITEST advanced curriculum webpage at: http://www.nwabr.org/curriculum/advanced-bioinformatics-genetic-research). *Lesson Five* requires the capability to show the online streaming video, "Electron-Transport Chain," produced by Garland Sciences (available on YouTube). The Howard Hughes Medical Institute's "Sanger Method of DNA Sequencing" is also recommended for *Lesson Nine*. The optional *Wet Lab* includes a number of recommended online streaming videos to supplement instruction.

*Lessons One* through *Six*, *Lesson Eight*, and *Lesson Nine* require students to use computers with internet access and a search engine such as Mozilla Firefox. Students may also need a text editing program such as Microsoft® Notepad or TextEdit for saving their "unknown" DNA sequences (optional, see *Lessons Two* and *Nine*). Students are encouraged to use a word processing program (Microsoft® Word) for writing the *Student Research Report* (*Lesson Six*), for creating their resume and cover letter (*Lesson Eight*), and for answering homework questions. *Lesson Seven* does not require computer use except for answering homework questions (optional); no internet is required.

*Lesson Five* requires the Cn3D program to be downloaded and installed on all student computers. The program can be downloaded from: http://www.ncbi.nlm.nih.gov/Structure/CN3D/cn3d.shtml. Instructions are also available in the *Teacher Resource* at the end of *Lesson Five*.

*Lesson Nine* requires the program FinchTV to be downloaded and installed on all student computers. The program can be downloaded from: http://www.geospiza.com/Products/finchtv.shtml. Instructions are also available in the *Teacher Resource* at the end of *Lesson Nine*.

## Before Beginning the Unit

**Set Classroom Discussion Norms:** It is especially important to foster a safe classroom atmosphere when discussing ethical issues about funding research for rare genetic diseases (*Lesson Seven*) that may involve conflicting moral choices. Please review or create classroom discussion ground rules (norms) before proceeding. Instructions for doing this can be found in the *Appendix*.

**Install Cn3D and FinchTV on all Computers:** Contact your school administrator or IT support staff to be sure these programs have been downloaded and installed on all student computers for *Lessons Five* (Cn3D) and *Nine* (FinchTV). Instructions for downloading each of these programs can be found in the *Teacher Resources* sections of each corresponding lesson (*Lesson Five* and *Lesson Nine*).

## Additional Resources

**DNA Structure:** *Exploring DNA Structure* by Dr. Sandra Porter contains information on the discovery and structure of DNA, along with hands-on activities that students can use to explore the structure of DNA first-hand. Students determine where molecules bind to DNA, investigate base-pairing, examine the phosphodiester backbone, and study the interaction between DNA strands. *Exploring DNA Structure* is also available on a CD together with 76 DNA structures, Cn3D, and the textbook. For more information, see http://www.digital-world-biology.com.

**Ethics:** Additional information about ethical theories and perspectives can be found in *An Ethics Primer: Lesson Ideas and Ethics Background* by Jeanne Ting Chowning and Paula Fraser, produced through the Northwest Association for Biomedical Research. The complete *Ethics Primer* is available free for download from http://www.NWABR.org.

**Molecular Structures:** Have you ever wanted to find molecular structures that you can use as class examples? *A Beginner's Guide to Molecular Structure*, by Dr. Sandra Porter, navigates through the NCBI databases to help teachers determine whether structures come from normal or mutant proteins, and to identify the parts of the protein that are found in the structure. Activities include superimposing influenza structures to see why one strain could become resistant to Tamiflu, working with green fluorescent protein, and more. For more information, see http://www.digital-world-biology.com.

## Lesson Overview

**Lesson One: The Process of Genetic Research**

In this lesson, students are introduced to the process of genetic research. The lesson begins with a Think-Pair-Share activity designed to introduce students to the types of research questions people in different career fields might answer using bioinformatics tools. After a short background explanation provided by the teacher about how genetic research is done, students make their own hypotheses and predictions about the relatedness of canine species, and align paper DNA sequences to evaluate their hypotheses. The lesson concludes with a group activity introducing students to pairwise comparisons of DNA sequences, which will be explored more fully in later lessons. In *Lesson One*, students learn how ***DNA sequencing core lab managers*** might use bioinformatics tools in their career.

**Lesson Two: DNA Barcoding and the Barcode of Life Database (BOLD)**

In this lesson, students will receive an "unknown" DNA sequence and use the bioinformatics tool Basic Local Alignment Search Tool (BLAST) to identify the species from which the sequence came. Students then visit the Barcode of Life Database (BOLD) to obtain taxonomic information about their species and form taxonomic groups for scientific collaboration. The lesson ends with each student generating a hypothesis about the relatedness of the species within each group. In *Lesson Two*, students learn how ***postdoctoral scientists in DNA and history*** might use bioinformatics tools in their career.

**Lesson Three: Using Bioinformatics to Study Evolutionary Relationships**

In this lesson, students learn how to use bioinformatics tools to analyze DNA sequence data and draw conclusions about evolutionary relationships. Students collaborate with their group members by pooling their DNA sequences from *Lesson Two: DNA Barcoding and the Barcode of Life Database (BOLD)* to perform and analyze multiple sequence alignments using the computer programs ClustalW2 and JalView. After comparing relatedness among and between the species within their group, students use their sequence alignment to generate a phylogenetic tree, which is a graphical representation of inferred evolutionary relationships. This tree is used to draw conclusions about their research question and hypothesis. In *Lesson Three*, students learn how ***microbiologists*** might use bioinformatics tools in their career.

**Lesson Four: Using Bioinformatics to Analyze Protein Sequences**

In this lesson, students perform a paper exercise designed to reinforce student understanding of the complementary nature of DNA and how that complementarity leads to six potential protein reading frames in any given DNA sequence. They also gain familiarity with the circular format codon table. Students then use the bioinformatics tool ORFinder to identify the reading frames in their DNA sequence from *Lesson Two* and *Lesson Three*, and to select the proper open reading frame to use in a multiple sequence alignment using their protein sequences. In *Lesson Four*, students learn how ***biological anthropologists*** might use bioinformatics tools in their career.

**Lesson Five: Protein Structure and Function—A Molecular Murder Mystery**

Prior to this lesson, students learned how the cytochrome c oxidase subunit 1 (*COI*) gene is used to barcode animals. In this lesson, students learn more about the cytochrome c oxidase protein and its three-dimensional structure. In particular, students learn how to identify the active site in cytochrome c oxidase. Once they can find this site, they look at aligned structures (one of which contains a poison) and then determine the identity of a foreign substance that acts as a poison by binding to the active site. This lesson allows students to explore the use of the molecular visualization program Cn3D to learn more about cytochrome c oxidase, a ubiquitous and important protein. In *Lesson Five*, students learn how ***molecular diagnostics researchers*** might use bioinformatics tools in their career.

**Lesson Six/Assessment: Writing Research Reports**

In this lesson, students compile and synthesize what they have learned in the preceding lessons by writing a research report. The research report includes ***Introduction***, ***Methods***, ***Results***, ***Discussion***, and ***References*** sections. Emphasis is placed on relating previous lesson activities to the original research question and hypothesis. Extensions and lesson alternatives include instructions for creating a scientific poster, writing a scientific abstract, or writing a science-related magazine article. In *Lesson Six*, students learn how ***science and technical writers*** might use bioinformatics tools in their career.

**Lesson Seven: Who Should Pay? Funding Research on Rare Genetic Diseases**
In this lesson, students learn about Leigh's disease, a rare form of Subacute Necrotizing Encephalomyelopathy (SNEM) that can be caused by a deficiency in cytochrome c oxidase (complex IV). Deficiencies in the large, 13-subunit cytochrome c oxidase complex can result from defects in one of several proteins, including cytochrome c oxidase subunit 1, the protein encoded by the DNA barcoding gene, and examined in *Lesson 5*. Without the COI protein, cells are unable to harness usable energy from glucose. This is a jigsaw exercise. Students are assigned or choose one of four stakeholder parties. They meet in "like" interest groups to become more familiar with that stakeholder's position and concerns. Afterwards, they meet in "mixed" groups with a representative from each of the stakeholder groups. Students identify areas of agreement and disagreement, and propose a compromise to recommend to Congress regarding funding for rare disease research. In *Lesson Seven*, students learn how ***pediatric neurologists*** might use bioinformatics tools in their career.

**Lesson Eight: Exploring Bioinformatics Careers**
In this lesson, students synthesize the information they have learned throughout the unit about people in various careers who use bioinformatics. Students then have the opportunity to perform independent research about a career of interest before developing a resume to use when applying for a bioinformatics-related job. Students also learn about writing cover letters. Optional extensions include peer-editing of resumes and a mock interview for a job related to a career of interest.

**Lesson Nine: Analyzing DNA Sequences and DNA Barcoding**
DNA sequencing is performed by scientists in many different fields of biology. Many bioinformatics programs are used during the process of analyzing DNA sequences. In this lesson, students learn how to analyze DNA sequence data from chromatograms using the bioinformatics tools FinchTV and BLAST. Using data generated by students in class or data supplied by the Bio-ITEST project, students learn what DNA chromatogram files look like, learn about the significance of the four differently-colored peaks, learn about data quality, and learn how data from multiple samples are used in combination with quality values to identify and correct errors. Students use their edited data in BLAST searches at the NCBI and the Barcode of Life Database (BOLD) to identify and confirm the source of their original DNA. Students then use the bioinformatics resources at BOLD to place their data in a phylogenetic tree and see how phylogenetic trees can be used to support sample identification. Learning these techniques will provide students with the basic tools for inquiry-driven research.

**Wet Lab: DNA Barcoding—From Samples to Sequences**
In this lesson, students perform the wet lab experiments necessary for DNA barcoding. Beginning with a small tissue sample, students purify the DNA, perform the polymerase chain reaction (PCR) using *COI*-specific primer pools, and analyze their PCR products by agarose gel electrophoresis. PCR reactions that result in products of the correct size are purified and submitted for DNA sequencing. This DNA sequence data can be used in *Lesson Nine*, or as part of an independent project.

**Suggested Lesson Order with Optional Wet Lab**

| Lesson | 1 | Wet Lab | 2 | 3 | 4 |
|---|---|---|---|---|---|
| **Topic** | What is genetic research? | DNA purification, PCR, gel electrophoresis, submit samples for sequencing | Introduce barcoding databases | DNA alignments | Protein reading frames and alignments |
| **Day(s) per lesson** | 2 | 4–6 | 1 | 1 | 2 |
| **Cumulative Days** | 2 | 6–8 | 7–9 | 8–10 | 10–12 |

| Lesson | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|
| **Topic** | Protein structure | Writing research reports | Bioethics | Careers | DNA sequence analysis (using DNA data from *Wet Lab*) |
| **Day(s) per lesson** | 1 | 3–5 | 1 | 2–4 | 3 |
| **Cumulative Days** | 11–13 | 14–18 | 15–19 | 17–23 | 20–26 |

**Suggested Lesson Order without Optional Wet Lab**

| Lesson | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| **Topic** | What is genetic research? | Introduce barcoding databases | DNA alignments | Protein reading frames and alignments | Protein structure |
| **Day(s) per lesson** | 2 | 1 | 1 | 2 | 1 |
| **Cumulative Days** | 2 | 3 | 4 | 6 | 7 |

| Lesson | 6 | 7 | 8 | 9 |
|---|---|---|---|---|
| **Topic** | Writing research reports | Bioethics | Careers | DNA sequence analysis (using DNA data from *Bio-ITEST*) |
| **Day(s) per lesson** | 3–5 | 1 | 2–4 | 3 |
| **Cumulative Days** | 10–12 | 11–13 | 13–17 | 16–20 |

## National Science Education Standards

The nine lesson plans in this curriculum are aligned to the National Research Council's National Science Education Standards, as shown in the following table:

| | Lesson 1 | Lesson 2 | Lesson 3 | Lesson 4 | Lesson 5 | Lesson 6 | Lesson 7 | Lesson 8 | Lesson 9 |
|---|---|---|---|---|---|---|---|---|---|
| ***Science as Inquiry*** | | | | | | | | | |
| Abilities necessary to do scientific inquiry | • | • | • | • | • | • | | | • |
| Understandings about scientific inquiry | • | • | • | • | • | • | • | • | • |
| ***Science and Technology*** | | | | | | | | | |
| Abilities of technological design | • | • | | • | • | • | | | • |
| Understandings about science and technology | • | • | • | • | • | • | • | • | • |
| ***Science in Personal and Social Perspectives*** | | | | | | | | | |
| Personal health and community health | • | • | • | • | • | • | • | • | • |
| Science and technology in local, national, and global challenges | • | • | • | • | • | • | • | • | • |
| ***History and Nature of Science*** | | | | | | | | | |
| Science as a human endeavor | • | • | • | • | • | • | • | • | • |
| Nature of scientific knowledge | • | • | • | • | • | • | • | | • |

Source: National Research Council. (1996). *National Science Education Standards*. Washington, D.C.: National Academies Press.

## Next Generation Science Education Framework

| | Lesson 1 | Lesson 2 | Lesson 3 | Lesson 4 | Lesson 5 | Lesson 6 | Lesson 7 | Lesson 8 | Lesson 9 |
|---|---|---|---|---|---|---|---|---|---|
| ***Scientific Practices*** | | | | | | | | | |
| 1. Asking Questions | • | • | • | • | • | • | | | • |
| 2. Developing and Using Models | • | • | • | • | • | | | | • |
| 3. Planning and Carrying out Investigations | • | • | • | • | | | | | |
| 4. Analyzing and Interpreting Data | • | • | • | • | • | • | • | | • |
| 5. Using Mathematics, Information and Computer Technology, and Computational Thinking | • | • | • | • | • | • | | | • |
| 6. Constructing Explanations | • | • | • | • | • | • | • | | • |
| 7. Engaging in Argument from Evidence | • | • | • | • | • | • | • | | |
| 8. Obtaining, Evaluating, and Communicating Information | • | • | • | • | • | • | • | • | • |
| ***Crosscutting Concepts*** | | | | | | | | | |
| Patterns | • | • | • | • | • | | | | • |
| Cause and Effect: Mechanisms and Explanation | • | • | • | • | • | | | | • |
| Scale, Proportion, and Quantity | | | • | • | • | | | | |
| Systems and System Models | • | • | • | • | • | | | | • |
| Structure and Function | | | | • | • | | | | |
| Stability and Change | • | • | • | • | • | | | | |
| ***Core Ideas: Life Sciences*** | | | | | | | | | |
| LS 1: From Molecules to Organisms: Structures and Processes | | | | | • | | | | |
| LS 3: Heredity: Inheritance and Variation of Traits | • | | • | • | | | • | | |
| LS 4: Biological Evolution: Unity and Diversity | • | • | • | • | • | | | | |

Source: Committee on Conceptual Framework for the New K-12 Science Education Standards, National Research Council. (2011). *A Framework for K-12 Science Education: Practices, Crosscutting Concepts, and Core Ideas*. Washington, D.C.: National Academies Press.