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Title: DNA through the looking glass

Abstract: Have you ever looked in a mirror and noticed that if you lift your left hand, your mirror-image raises their right hand? Like your hands, a molecule and its reflection can be different, a property called "chirality" (from the Greek word for hands), and most of the molecules that make up our bodies are chiral. This lesson looks at the chirality of DNA, the molecule that makes our genes, and how the "handedness" of DNA determines its structure and behavior. This module is best presented after students have learned about the chemical structure of DNA, base-pairing, and the double-helix. Students can further expand their understanding of DNA's structure and function by learning how natural, "right-handed" DNA and its unnatural mirror image, "left-handed" DNA, look different at a chemical level, and then use a simple origami method to build three-dimensional models of "right-handed" and "left-handed" DNA. By studying these models, they will learn how molecular chirality determines the higher-order structure of DNA (the "double-helix"), and how these differences determine how DNA interacts with itself by base-pairing, and how it interacts with the enzymes which read DNA. By the end of the lesson, students should understand how the fundamental chemical concept of chirality relates to biology, why "homochirality" is a defining feature of life, and have the opportunity to discuss how this relates to the origin of life on Earth and what "alien" life might look like if we found it on other planets.

What standard(s) does this address?

NGSS Performance Expectation	<p>HS-LS1-1 All cells contain genetic information in the form of DNA molecules. Genes are regions in the DNA that contain the instructions that code for the formation of proteins, which carry out most of the work of cells.</p> <p>HS-LS3-1 Each chromosome consists of a single very long DNA molecule, and each gene on the chromosome is a particular segment of that DNA. The instructions for forming species' characteristics are carried in DNA. All cells in an organism have the same genetic content, but the genes used (expressed) by the cell may be regulated in different ways. Not all DNA codes for a protein; some segments of DNA are involved in regulatory or structural functions, and some have no as-yet known function.</p>
Common Core Math	
Common Core English (<i>found w/ NGSS</i>)	<p>RST.11-12.1 Cite specific textual evidence to support analysis of science and technical texts, attending to important distinctions the author makes and to any gaps or inconsistencies in the account.</p> <p>WHST.9-12.2.a-e Write informative/explanatory texts, including the narration of historical events, scientific procedures/experiments, or technical processes.</p> <p>RST.11-12.9 Synthesize information from a range of sources (e.g., texts, experiments, simulations) into a coherent understanding of a process, phenomenon, or concept, resolving conflicting information when possible.</p>

Keywords: Chirality, DNA, mirror-image, alien life, abiogenesis, synthetic biology.

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Learning Objectives: What will the students be able to do or demonstrate after this lesson?

After completing this lesson, students will be able to:

- Express the definition of chirality and how it relates to mirror-image reflection, and identify the handedness of DNA nucleotides and a DNA double-helix.
- Explain how molecular chirality of DNA nucleotides determines the larger scale handedness of the double-helix.
- Describe biological homochirality as it applies to DNA and proteins, evaluate how homochirality is important for the structure and function of living things, and assess whether different forms of life could use chiral molecules differently.

Lesson plan outline:

Learning E	Teacher Does / Says	Student Does
Engage (5 minutes) How can I get students interested in this?	<i>T: Asks students to consider how their left and right sides are flipped in a mirror, wonder if the cells and molecules in their bodies can also flip right and left.</i>	<i>S: Compares right and left hands and their reflections in a mirror. Watch "Give us a Hand - what's chirality" OxfordSparks video (link in appendix)</i>
Explore (5 minutes) What tasks / questions can I offer to have students puzzle through this?	<i>T: Explain to students they will look at the chirality of DNA, as described in the video. Review the structure of DNA, base pairing, and the double helix as necessary.</i>	<i>S: Work through attached worksheet, pages 1-2, Q1. Draw/differentiate between a DNA nucleotide and its mirror-image.</i>
Explain (10 minutes) How can I help students make sense of their observations? - let them try to explain first	<i>T: Introduce concept of biological homochirality, natural "right-handed" D-DNA and unnatural "left-handed" L-DNA. Guide students through pages 3-4 of the worksheet.</i>	<i>S: Complete Q2 of worksheet, compare and discuss answers. Speculate on how handedness of DNA strands will affect the double-helix shape.</i>

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<p>Elaborate (20 minutes)</p> <p>How can my students apply their new knowledge to other situations?</p>	<p><i>T: Guide students through construction of their origami DNA double helix. Explain how this models how base-paired DNA folds into a double helix in cells (page 5 of the worksheet). Guide comparison between different student's origami structures.</i></p>	<p><i>S: Identify if their origami sheet is D- or L-DNA (Q3). Fold the origami into a double helix and identify its handedness (Q4). Make comparisons between handedness of helices made from D- or L-DNA (Q5).</i></p>
<p>Evaluate (10 minutes)</p> <p>How can I help my students self-evaluate and reflect on their learning?</p>	<p><i>T: Have students assess how handedness of DNA helix will affect DNA base pairing and interactions with proteins. Assess student's understanding of the roll DNA structure has on its function in cells.</i></p>	<p><i>S: Write or state answers to Q6-8. Work as pairs or larger teams, as questions require comparing D- and L-DNA helices. Students should be able to explain how chirality of nucleotides determines the shape of the double helix, and how that shape can affect its function.</i></p>

Appendix:

- This video, made by Oxford University in the UK, is a great 5 minute introduction to the concept of chirality in nature, including in DNA.
https://www.youtube.com/watch?v=OL_VCvjfX3I
- If your students are already familiar with chemical structures and bonds, this Ted-Ed video is a great introduction to chirality as understood from a chemical process, and could connect students' understanding of chemistry and biology. The latter half of the video, about optical rotation, is not particularly relevant to this lesson, however.
<https://www.youtube.com/watch?v=71GjsRnsol8>
- After students answer Q8, there is an opportunity to connect their conclusions to some of the ideas about the origins of biological homochirality and the origin of life that are brought up at the end of the "Give us a Hand - what's chirality" video above. Students can watch a brief video about the discovery of chiral molecules in space (https://www.youtube.com/watch?v=s3uVI_0QYHQ) or read about how scientists at Scripps Research (here in San Diego) have started testing some of the hypotheses mentioned in the "Give us a Hand" video (<https://cen.acs.org/biological-chemistry/origins-of-life/New-evidence-against-popular-t>

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heory/97/web/2019/09). Students can also discuss what it would be like if we discovered life on another planet that used L-DNA and how it would interact with life from Earth.

- The origami DNA idea uses the template and instructions provided by yourgenome.org (<https://www.yourgenome.org/activities/origami-dna>), which were made by Alex Bateman and based off of Thoki Yenn's design. The models have been modified for this lesson plan in the following ways:
 - PDF files were changed to fit standard US 8.5"x11" paper, the originals were designed for European A4 paper.
 - The left-handed version is a mirror image of the right-handed version made by Bateman. If you follow the same instructions, this reflected version should fold into a left-handed helix.
 - Models of the appropriate DNA molecule (L- or D-DNA) have been added to each, to make the relationship between DNA's molecular structure and its double-helix more clear to students when making the origami structure.
- Folding the origami should be straight forward but there are a few ways to get confused. The instructor should practice folding the origami before the lesson at least once, and have a pre-folded version of both the L- and D-DNA structures on hand during the lesson.
- Cutting the origami in half to study L- and D-DNA pairing together (Q6) can be tricky. Again, the instructor should practice this before-hand, and be prepared to assist students, or alternatively demonstrate the concept to the class as a group, rather than have students attempt it themselves.
- The following materials are provided for the lesson in a zip file ("chiralDNA.zip"):
 - "Chiral DNA Worksheet" - the main handout for students, or can alternatively be used by the instructor to guide verbal instruction
 - "Chiral DNA Answer Key" - correct answers to Q1-8 in the worksheet
 - "OrigamiDNA-instructions" - instructions for folding origami DNA, from [yourgenome.org/Alex Bateman](http://yourgenome.org/Alex%20Bateman)
 - "origamiDNA-right" - origami sheet for folding D-DNA into a right-handed double helix.
 - "origamiDNA-left"- origami sheet for folding L-DNA into a left-handed double helix.
 - 6 PDF files sized for index cards are provided as alternatives to instruction through the worksheet. These show L- and D-DNA nucleotides and base-paired L- and D-DNA, and can be printed onto index cards or included in a slide presentation as an alternative way of presenting and discussing the material.
 - "D-DNA-nucleotide" and "L-DNA-nucleotide" - unlabeled structures of individual right and left-handed DNA nucleotides
 - "right_hand_DNA" and "left_hand_DNA" - labeled structures of individual right and left-handed DNA nucleotides shown cupped in the palm of a

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right or left hand, to help students understand how to differentiate the two chiral forms.

- "DNA_basepairs_right(D)" and "DNA_basepairs_left(L)" - structures of two base-paired strands of D- or L-DNA.
- This lesson is designed for in person instruction, but should be adaptable to a virtual classroom. Students can have the origami sheets mailed to them, picked up, or sent electronically and printed out. Alternatively, the instructor can demonstrate the origami process over video for students who don't have access to a printed version of the origami sheets. The rest of the materials can easily be shared electronically, and questions 6-8, which require comparisons between right- and left-handed DNA helices, can be demonstrated for the whole class, or handled in smaller groups by break-out sessions. Keep in mind that some video cameras on laptops record a reflected, mirror-image version of the presenter, which can cause confusion when comparing left- and right-handed structures. To make sure everyone is seeing the same kind of image, have everyone raise their right hand at the same time early in the lesson to identify anyone who is sending/receiving a mirrored image.