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GENERAL USE OF Science in the Classroom

Student Learning Goals:
“One fundamental goal for K-12 science education is a scientifically literate person who can understand the nature of scientific knowledge.”¹

The U.S. National Academy of Sciences defines science as: “Any new finding requires independent testing before it is accepted as scientific knowledge; a scientist is therefore required to honestly and openly report results so that they can readily be repeated, challenged, and built upon by other scientists. Proceeding in this way over centuries, the community effort that we call science has developed an increasingly accurate understanding of how the world works. To do so, it has had to reject all dogmatic claims based on authority, insisting instead that there be reproducible evidence for any scientific claim.”

An important student learning goal, central to any understanding of “the nature of scientific knowledge,” is to give each student an appreciation of how science is done.

This includes knowing why:
- Scientists must be independent thinkers, who are free to dissent from what the majority believes.
- Science can deal only with issues for which testable evidence can be obtained.
- All scientific understandings are built on previous work.
- It is to be expected that one scientist’s conclusions will sometimes contradict the conclusions of other scientists.
- Science is a never-ending venture, as the results from one study always lead to more questions to investigate.

Using This Resource

Learning Lens:

The Learning Lens tool can be found on the right sidebar of each resource and is the source of annotations. Click on the headings to highlight portions of the text of the corresponding research article. A subsequent click on the highlighted text will produce a text box containing more information about that particular piece of text. Below is an example of the Glossary function of the Learning Lens.

**ABSTRACT**

White-Nose Syndrome (WNS) is an emerging disease affecting hibernating bats, spurring mortality and precipitous population declines in winter. *Hibernacula* First discovered spreading rapidly across eastern North America and currently affects several species, a regional population collapse and is predicted to lead to regional extinction of the little brown myotis (*Myotis lucifugus*), previously one of the most common bat species in North America. Novel diseases can have serious impacts on native wildlife populations, which in turn can have substantial impacts on ecosystem integrity.

**REPORT**

Emerging infectious diseases are increasingly recognized as direct and indirect agents of extinction of free-ranging wildlife 

1-4. Introductions of disease into native wildlife populations have led to serious declines or local extinctions of different species in the past few decades, including amphibians from *Pseudogymnodexys* (5, 6), rabbits from myxomatosis in the United Kingdom (7), Tasmanian devil from infectious cancer (8), and birds in North America from West Nile virus (9). Here we demonstrate that White-Nose Syndrome (WNS), an emerging infectious disease, is causing unprecedented mortality among hibernating bats in eastern North America and has caused a population collapse that is threatening regional extinction of the little brown myotis (*Myotis lucifugus*), a once widespread and common bat species.

WNS is associated with a newly described psychrophilic fungus, *Geomyces destructans* that grows on exposed tissues of hibernating bats, apparently causing premature arousals, aberrant behavior, and premature loss of critical fat reserves (9, 10) (Fig. 1). The origin of WNS and its host-pathogen, *G. destructans*, is uncertain (5). A plausible hypothesis for the origin of this disease in North America is introduction via human trade or travel from Europe, based on recent evidence that *G. destructans* has been observed on at least one hibernating bat species in Europe (11). Anthropogenic spread of invasive pathogens in wildlife and domestic animal populations, so-called pathogen pollution, poses substantial threats to biodiversity and ecosystem integrity, and is of major concern in conservation efforts (1, 2).

An example of the resource with the Glossary, Previous Work, Author’s Experiments, News and Policy Links, and References and Notes tools turned on. The Glossary tool is in use.
Learning Notes:

Learning Notes accompany each figure and are designed to help students deconstruct the methods and data analysis contained within each figure.

Fig. 1. Spatial distribution of head scales. (A) Head scales in most snakes (here, a corn snake) are polygons (two upper panels) with stereotyped spatial distribution (two lower panels); left (yellow) and right (red) scale edges overlap when reflected across the sagittal plane (blue). (B) Polygonal head scales in crocodiles have a largely random spatial distribution without symmetrical correspondence between left and right. (C) Head scales from different individuals have different distributions of scales’ sizes and localizations (blue and red edges from top and bottom crocodiles, respectively).

Method: 3D geometry and color-texture reconstruction

The authors took 120 color pictures of each animal to create detailed, three-dimensional models of reptile heads. Watch this video in which the authors further explain their modeling methods:

http://www.sciencemag.org/content/suppl/2012/11/29/science.1226265.DC1/1...
References:

The Reference section of each resource is annotated with a short statement about how or why each reference relates to the current research study.

10. Gaemers, B. Behr, G. Kempermann, A. Shoot strategies. Proc. Natl. Acad. Sci. U.S.A. 109, E14 (2012). This paper showed that while both physical activity, like running, and living in an enriched environment can result in the generation of new hippocampal neurons in mice, a combination of the two activities leads to even greater rates of neurogenesis.
17. Lewejohann et al., Environmental bias: Effects of housing conditions, laboratory environment and experimenter on behavioral tests. Genes Brain Behav. 5, 64 (2006).
28. K. L. Jang, R. R. McClue, A. Arigle, R. Riemann, W. J. Livesley, Heritability of face-level traits in a cross-cultural twin
Thought Questions

Thought Questions are located above the Learning Lens in the right sidebar of each resource. These questions were written to be universal and applicable to any primary research paper. Thought questions do not have a single answer, or a correct answer for that matter, and can be used to stimulate discussion among students.
Suggestions for Classroom Use:

In addition to the thought questions discussed above, other resources are provided for use in the classroom. These can be found toward the end of the teacher guides associated with each specific article and include:

1. Discussion questions specific to the article, related to the standards, and/or associated with the figures.

2. Activities tied to the articles.

Some ways to use the *Science* in the Classroom articles:

1. Assign to student groups to read and discuss during class.

2. Assign small sections of the article to student groups to read and discuss during class, with the expectation that they will present or use jigsaw to teach the entire class what is in their part of the article.

3. Assign to individual students to complete during class or as homework.

4. Assign reading as an extra credit project.

Some ideas for interactive student engagement after reading the article:

1. Students write answers to discussion questions (for example, those linked to the standards or those linked to the diagrams).

2. Go over the abstract, as well as information about the purpose and structure of an abstract, and have students write their own abstracts for the articles in language that could be understood by their peers.

3. Have students edit the article, or parts of the article, to a simpler reading level.

4. Have students, alone or in small groups, use the annotated list of references to explain how the scientists who wrote this article built on the published work of at least one independent group of scientists in making their discoveries. In the process, did they produce data that supports the findings of the earlier publication that they have cited in the text? In what way does this article support the statement that scientific knowledge is built up as a “community effort”? 
5. Use the article and discussion questions linked to the standards and the diagrams for a teacher-led classroom discussion. The discussion can focus on the nature of science and scientific research, as well as on the science in the article itself.

6. Have students give a classroom presentation about the article, parts of the article, or their answers to discussion questions.
ARTICLE-SPECIFIC MATERIALS

Connections to the nature of science from the article

- How do scientists investigate how components of the molecular machinery are spatially controlled during organ formation and disease using optical microscopy?
- What physical and chemical principles are considered when designing new microscopy methods?

The importance of this scientific research

- Provides a novel combination of physical and chemical tools that enable scientists to gain greater subcellular insights into organ development and diseases through optical microscopy.

The actual science involved

- Physics
- Engineering
- Mathematics
- Neurobiology
- Cell biology
**Connect to Learning Standards:**

*The Next Generation Science Standards*

- Science and Engineering Practice 4: Analyzing and interpreting data

*The AP Biology Standards*

- Practice 2: Students will be able to derive and apply the expansion factor for estimating the lateral and axial resolution.
- Practice 7: The ExM method enables students to appreciate the biological insights of neuron structure and function across engineering, biology, and physical sciences.

*Common Core English Language Arts*

- 11-12.3: Follow precisely a complex multistep procedure when carrying out experiments, taking measurements, or performing technical tasks; analyze the specific results based on explanations in the text.
- 11-12.4: Determine the meaning of symbols, key terms, and other domain-specific words and phrases as they are used in a specific scientific or technical context relevant to grades 11-12 texts and topics.

*Common Core Statistics and Probability*

- ExM resolved clathrin-coated pits as a function of SR-SIM resolved clathrin-coated pits have a linear relationship.
- Evaluating random processes and statistical experiments
Summary of the Article for the Teacher:

It is recommended that this not be used by students in place of reading the article.

General Overview:

For more than 300 years, scientists have made incremental steps toward visualizing the molecular action of important chemical interactions inside the cell: the building block of multicellularity and mammalian tissues. One of the optical tools, such as light microscopy, has been limited by the diffraction limit of light: just over 250 nanometers to resolve two points in space. This optical limitation was a major hurdle until the development of superresolution microscopy, a technique that earned the 2014 Nobel Prize in Chemistry. However, the ability for superresolution microscopy to cover large swaths of tissues, such as the developing brain, has hampered the recent goal of mapping neuronal brain connections, or connectomics. In January 2015, a team of scientists at the Massachusetts Institute of Technology in Cambridge reported a series of physical and chemical tools that enable fluorescently labeled mammalian brain neurons to be expanded using conventional fluorescent light microscopy that can reveal lateral resolution of molecular objects close to 70 nanometres over hundreds of microns of brain tissue.

Topics Covered:

- Diffraction and optical resolution limits (Abbe’s Theory)
- Biophysical polymer behavior
- Linear transformations, Gaussian distribution, error calculation estimation
- Pre- and postsynaptic protein localization
- Molecular components of vesicle trafficking and cytoskeletal dynamics

Why this research is important:

The tour-de-force series of chemical and physical methods in ExM will enable neuroscientists to map vast networks of neurons embedded within mammalian brains at exquisite subcellular resolution. These insights would provide clues for treating neurologic diseases, such as patients living with Parkinson’s and autism.
Methods used in the Research:

- Superresolution, confocal, and widefield fluorescent microscopy approaches
- Immunostaining methods for detecting pre- and postsynaptic components in neurons in the hippocampus
- Mathematical and statistical methods, such as linear transformations, Gaussian distribution, deconvolution, and error calculation estimation
- Utilizing transgenic mice with neurons labeled with genetically encoded yellow fluorescent protein

Conclusions:

- Defined a method called ExM that enables fluorescently labeled and expanded brain tissues amenable for imaging large volumes of hippocampal regions of the mouse brain at nanoscale resolution.
- Expanded fluorescently labeled embryonic kidney cells using ExM that had comparable resolution of cellular components of endocytosis and cytoskeleton.
- ExM also had the added benefit of minimizing light scattering of fluorescently labeled brain slices. This enables the use of additional imaging methods, such as light-sheet microscopy.

Areas of Further Study:

- Modulating physical properties of ExM polymer may provide greater axial or lateral resolutions that may go beyond 70 nanometers in fluorescently labeled cells and tissues.
Discussion Questions:

1. Figure 1D:
   What are the chemical components of the fluorescent tag that enabled it to be used in ExM?

2. Supplemental Figure 3 and Figure 2C.
   How did the authors quantify the isotropy of tissues processed with ExM?

3. Figure 2O:
   What is the relationship between the radius of clathrin-coated pits imaged using a superresolution method versus ExM?

4. Figure 3:
   What is the relationship between measurement length and root-mean-square (RMS) error pre- versus post-ExM of fluorescently labeled brain neurons?

5. Why did the authors show the nanometer separation distribution of synapses between Bassoon and Homer1?

6. Figure 4:
   Why is a “scalable” 3D superresolution microscopy of ExM-processed mouse brain significant?

7. What neuronal structures were resolved in ExM processed dentate gyrus? How did it compare with these neuronal structures using electron microscopy in the previous paper by Rollenhagen and Lubke?