USING TECHNOLOGY TO UNDERSTAND CELLULAR AND...

NATIONAL INSTITUTE OF HEALTH.

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Using Technology to Study

Cellular and Molecular Biology

under a contract from the

National Institutes of Health

National Center for Research Resources

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The structure of the oncogene H-Ras p21 protein complexed with

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GTP on the cover photograph was taken from the Protein Data

Pat Leffas, Multimedia Programmer

Bank (PDB) (*http://www.pdb.org*), protein number PDB ID: 121P.

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(Source: Wittinghofer, F., U. Krengel, J. John, W. Kabsch, E.F. Pai.

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1991. Three-dimensional structure of p21 in the active conforma-

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tion and analysis of an oncogenic mutant. *Environmental Health*

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Perspectives, 93: 11.)

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This material is based on work supported by the National Institutes

Abdellah Bougrine, Web Developer/Section 508 Specialist

of Health under Contract No. 263-00-C-0039. Any opinions, find-

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ings, conclusions, or recommendations expressed in this publica-

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tion are those of the authors and do not necessarily reflect the view

of the funding agency.

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NIH Publication No. 05-5170

ISBN: 1-929614-14-4

Contents

Foreword

This curriculum supplement, from *The NIH*
ties promote active and collaborative learning
Curriculum Supplement Series, brings cutting-
and are inquiry-based to help students develop
edge medical science and basic research dis-
problem-solving strategies and critical thinking.
coveries from the laboratories of the National
Institutes of Health (NIH) into classrooms.
Each curriculum supplement comes with a
As the largest medical research institution in
complete set of materials for both teachers and
the United States, NIH plays a vital role in the
students, including printed materials, exten-
health of all Americans and seeks to foster
sive background and resource information,
interest in research, science, and medicine-

and a Web site with interactive activities. The
related careers for future generations. NIH's
supplements are distributed at no cost to teach-
Office of Science Education (OSE) is dedicated
ers across the United States. All materials may
to promoting science education and scientific
be copied for classroom use but may not be
literacy.
sold. We welcome feedback from our users.
For a complete list of curriculum supplements,
We designed this curriculum supplement to
updates, availability and ordering information,
complement existing life science curricula at
or to submit feedback, please visit our Web site
both the state and local levels and to be consis-
at *http://science.education.nih.gov* or write to
tent with *National Science Education Standards*.1
Curriculum Supplements Series
It was developed and tested by a team com-
Office of Science Education
posed of teachers, scientists, medical experts,
National Institutes of Health
and other professionals with relevant subject-
6705 Rockledge Dr., Suite 700 MSC 7984
area expertise from schools and institutes from

Bethesda, MD 20892-7984

across the country; and by NIH scientists and curriculum-design experts from Biological Sci-

We appreciate the valuable contributions of the ences Curriculum Study (BSCS), Edge Inter-

talented staff at BSCS, Edge Interactive, and active, and SAIC. The authors incorporated

SAIC. We are also grateful to the NIH scientists, real scientific data and actual case studies into

advisors, and all other participating profession- classroom activities. A three-year development

als for their work and dedication. Finally, we process included geographically dispersed field

thank the teachers and students who partici- tests by teachers and students.

pated in focus groups and field tests to ensure that these supplements are both engaging and

The structure of this module enables teachers effective. I hope you find our series a valuable

to effectively facilitate learning and stimulate addition to your classroom and wish you a pro-

student interest by applying scientific concepts ductive school year.

to real-life scenarios. Design elements include a conceptual flow of lessons based on BSCS’s 5E

Bruce A. Fuchs, Ph.D.

Instructional Model of Learning, multisubject

Director

integration emphasizing cutting-edge science

Office of Science Education

content, and built-in assessment tools. Activi-

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supplements@science.education.nih.gov

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1 In 1996, the National Academy of Sciences released the *National Science Education Standards*, which outlines what all citizens should understand about science by the time they graduate from high school. The *Standards* encourages teachers to select major science concepts that empower students to use information to solve problems rather than stressing memoriza-tion of unrelated information.

About the National Institutes of Health

Begun as the one-room Laboratory of Hygiene

• biological effects of environmental contami-

in 1887, the National Institutes of Health (NIH)

nants;

today is one of the world's foremost medical

• understanding of mental, addictive, and

research centers and the federal focal point for

physical disorders; and

health research in the United States.

• collection, dissemination, and exchange of

information in medicine and health, includ-

Mission and Goals

ing the development and support of medical

The NIH mission is science in pursuit of funda-

libraries and the training of medical librari-

mental knowledge about the nature and behav-

ans and other health information specialists.

ior of living systems and the application of that

knowledge to extend healthy life and reduce the

Organization

burdens of illness and disability. The goals of

Composed of 27 separate institutes and centers,

the agency are to

NIH is one of eight health agencies of the Pub-

• foster fundamental creative discoveries,

lic Health Service within the U.S. Department

innovative research strategies, and their

of Health and Human Services. NIH encom-

applications as a basis for advancing signifi-

passes 75 buildings on more than 300 acres in

cantly the nation’s capacity to protect and

Bethesda, Md., as well as facilities at several

improve health;

other sites in the United States. The NIH budget

• develop, maintain, and renew scientific

has grown from about $300 in 1887 to more

resources—both human and physical—that

than $27.8 billion in 2004.

will ensure the nation’s ability to prevent disease;

Research Programs

• expand the knowledge base in medical and

One of NIH’s principal concerns is to invest associated sciences in order to enhance the wisely the tax dollars entrusted to it for nation’s economic well-being and ensure a the support and conduct of this research. continued high return on the public invest- Approximately 82 percent of the investment is ment in research; and

made through grants and contracts support-

• exemplify and promote the highest level

ing research and training in more than 2,000 of scientific integrity, public accountability, research institutions throughout the United and social responsibility in the conduct of States and abroad. In fact, NIH grantees are science.

located in every state in the country. These grants and contracts make up the NIH Extra- NIH works toward meeting those goals by pro- mural Research Program.

viding leadership, direction, and grant support to programs designed to improve the health of the nation through research in the

Approximately 10 percent of the budget goes to NIH's Intramural Research Programs, the more than 2,000 projects conducted mainly in its own laboratories. These projects are central to the NIH scientific effort. First-rate intramural scientists collaborate with one another regardless of institute affiliation or scientific discipline and have the intellectual freedom to pursue their research leads in NIH's own laboratories.

- causes, diagnosis, prevention, and cure of human diseases;
- processes of human growth and development;

trious scientists and physicians. Among them are 115 winners of Nobel Prizes for achievements as diverse as deciphering the genetic code and identifying the causes of hepatitis.

These explorations range from basic biology to behavioral research, to studies on treatment of major diseases.

Five Nobelists made their prize-winning discoveries in NIH laboratories. You can learn more

about Nobelists who have received NIH sup-

Grant-Making Process

port at *http://www.nih.gov/about/almanac/nobel/*

The grant-making process begins with an idea

index.htm.

that an individual scientist describes in a writ-

ten application for a research grant. The project

Impact on the Nation's Health

might be small, or it might involve millions of

Through its research, NIH has played a major

dollars. The project might become useful imme-

role in making possible many achievements

diately as a diagnostic test or new treatment, or

over the past few decades, including

it might involve studies of basic biological pro-

• Mortality from heart disease, the number

cesses whose clinical value may not be apparent

one killer in the United States, dropped by

for many years.

36 percent between 1977 and 1999.

• Improved treatments and detection methods

Each research grant application undergoes peer

increased the relative five-year survival rate

review. A panel of scientific experts, primarily

for people with cancer to 60 percent.

from outside the government, who are active

• With effective medications and psychother-

and productive researchers in the biomedi-

apy, the 19 million Americans who suffer

cal sciences, first evaluates the scientific merit

from depression can now look forward to a

of the application. Then, a national advisory

better, more productive future.

council or board, composed of eminent scien-

• Vaccines are now available that protect

tists as well as members of the public who are

against infectious diseases that once killed

interested in health issues or the biomedical sci-

and disabled millions of children and adults.

ences, determines the project’s overall merit and

• In 1990, NIH researchers performed the

priority in advancing the research agenda of the

first trial of gene therapy in humans. Scien-

particular NIH funding institutes.

tists are increasingly able to locate, identify,

and describe the functions of many of the

About 38,500 research and training applications

genes in the human genome. The ultimate

are reviewed annually through the NIH peer-

goal is to develop screening tools and gene

review system. At any given time, NIH supports
therapies for the general population for can-
35,000 grants in universities, medical schools,
cer and many other diseases.
and other research and research training institu-
tions, both nationally and internationally.
For more information about NIH,
visit http://www.nih.gov.

NIH Nobelists

The roster of people who have conducted NIH
research or who have received NIH support over
the years includes some of the world's most illus-

About the National Center for
Research Resources

The National Center for Research Resources
NIH-supported investigators and others special-
(NCRR) is a component of the National Insti-
ized research environments that are profession-
tutes of Health (NIH), one of the world's fore-
ally staffed, have state-of-the-art technologies
most biomedical research organizations. The
and Web-based networks, and provide col-
institutes and centers that compose NIH fund
laborative research opportunities. NCRR also

biomedical research to uncover new knowl-
supports networks of National Gene Vector Lab-
edge that will lead to better health for everyone
oratories and Human Islet Cell Resource Cen-
in the nation. Among the NIH institutes and
ters, a resource for normal and diseased human
centers, NCRR has a unique role. Rather than
tissue for research, and science education for
supporting studies of specific diseases or dis-
K−12 students and the public.
orders, NCRR supports programs that ensure
that essential tools, materials, specialized facili-
Comparative Medicine: Animal models and
ties, and resources for infrastructure and man-
colonies (mammalian and nonmammalian),
power development are accessible to biomedical
genetic stocks, and biological materials—such
researchers throughout the nation. In this way,
as cell lines, tissues, and organs—help meet
NCRR enables research in many areas of health
NIH-supported investigators' resource needs. In
and complements the missions of the NIH
particular, the NCRR network of eight National
categorical institutes. NCRR's diverse array of
Primate Research Centers is a valuable resource

resources is concentrated in four divisions:

for investigations of human health and disease.

Biomedical Technology Research and Research

Research Infrastructure: Diverse grant programs

Resources: A large network of Biomedical Tech-

help build, expand, and strengthen the nation's

nology Resource Centers provides the research

biomedical research environment by developing

community nationwide with the newest and

research infrastructure and faculty capacity at

most advanced technologies and techniques.

minority institutions that award doctorates in

Core scientists at these centers collaborate in

the health or health-related sciences; improving

multidisciplinary investigations and train vis-

biomedical and behavioral research through an

iting researchers to apply these technologies

NIH-wide program of matching grants for con-

and techniques to basic and clinical studies. In

struction and renovation of research facilities;

addition, NCRR provides institutional grants to

and increasing competitiveness of institutions

purchase expensive state-of-the-art and high-

from states with limited NIH support.

end instrumentation to be used by a number of

investigators on a shared basis.

For more information about research resources and resource-related funding opportunities, visit the National Center for Research Resources Web site at *http://www.ncrr.nih.gov.* *Clinical Research Resources:* A national network of General Clinical Research Centers offers

Introduction to

Using Technology to Study

Cellular and Molecular Biology

The abilities to develop and use technology are
us and provides the foundation for improv-
inherent human characteristics. We recognize
ing our choices about our personal health and
problems and look for solutions. Technology
the health of our community. With this mod-
makes our lives easier and more comfortable.
ule, students experience how science provides
At the same time, critical research technolo-
evidence that can be used to understand and
gies have advanced scientific discovery. Where
treat human disease. The National Center for
scientists once gazed in awe at individual cells
Research Resources believes that education is an
and microorganisms, we now can view the elec-
important way to accomplish its mission, which
tron clouds of individual atoms and reconstruct
includes helping the public understand the
detailed three-dimensional structures of biologi-
importance of technology use and development
cal molecules, such as proteins, and biological
to health.

structures, such as ribosomes. As the depth and breadth of scientific knowledge have increased, The lessons in this module encourage students human health and our quality of life have to think about the relationships among knowl- improved.

edge, choice, behavior, and human health in this way:

What Are the Objectives of the Module?

Using Technology to Study Cellular and Molecu-

Knowledge (what is known and not known)

lar Biology has several objectives. The first is to

+ Choice = Power

help students understand that technology is a means of solving a problem. As a consequence,

Power + Behavior = Enhanced Human Health

students realize that technologies affect all facets of our lives and that technology relates to The final objective of this module is to encourmore than computers.

age students to think in terms of these relationships now and as they grow older.

The second objective is to allow students to investigate how technology is used to deepen

Why Teach the Module?

and broaden our knowledge of cellular and
High school biology classes offer an ideal setting
molecular biology. Lessons in this module help
for integrating many areas of student interest.
students sharpen their skills in observation,
In this module, students participate in activities
critical thinking, experimental design, and data
that integrate inquiry science, human health,
analysis. They also make connections to other
mathematics, and the interweaving of science,
disciplines such as English, history, mathemat-
technology, and society. The real-life context
ics, and social science.
of the module's classroom lessons is engaging
for students, and the knowledge gained can be
The third objective is to convey to students the
applied immediately to students' lives.
purpose of scientific research. Ongoing research
affects how we understand the world around
"Lesson 3 was a great inquiry experience. Students

enjoyed the activity and at the same time, learned
In addition, the module provides a means for
how to apply what they know about technology.

professional development. Teachers can engage
The scale activity really got students thinking
in new and different teaching practices like
about the size of the cell and what is in the cell.
those described in this module without com-
This was a wow activity."—Field-Test Teacher
pletely overhauling their entire program. In
Designing Professional Development for Teachers
"The activities made us think. We figured out
of Science and Mathematics, the authors write
things ourselves, and we actually did stuff instead
that replacement modules such as this one
of just reading."—Field-Test Student
"offer a window through which teachers get a
glimpse of what new teaching strategies look
What's in It for the Teacher?
like in action."16 By experiencing a short-term
Using Technology to Study Cellular and Molecu-
unit, teachers can "change how they think
lar Biology meets many of the criteria by which
about teaching and embrace new approaches
teachers and their programs are assessed.
that stimulate students to problem solve, rea-
• The module is **standards based** and meets
son, investigate, and construct their own mean-

science content, teaching, and assessment
ing for the content." The use of a supplemental
standards as expressed in the *National Sci-*
unit such as this module can encourage reflec-
ence Education Standards. It pays particular
tion and discussion and stimulate teachers to
attention to the standards that describe
improve their practices by focusing on student
what students should know and be able to
learning through inquiry.
do with respect to **scientific inquiry**.
• It is an **integrated** module, drawing most
The following table correlates topics often
heavily from the subjects of science, social
included in the high school biology curriculum
science, mathematics, and health.
with the major concepts presented in this mod-
• The module has a Web-based **technology**
ule. This information is presented to help teach-
component on which there is an interactive
ers make decisions about incorporating this
database and simulations.
material into the curriculum.
• The module includes built-in **assessment**
tools, which are noted in each of the les-

If you have any questions about the supple-

sons with an assessment icon.

ment, please contact the NIH Office of Science

Education at *supplements@science.education.*

nih.gov.

Correlation of *Using Technology to Study Cellular and Molecular Biology* to High School Biology Topics

Topics	
Lesson 1	
Lesson 2	
Lesson 3	
Lesson 4	
The development of new	
technologies is continuous,	
✔	
✔	
and the ability to develop	
new technologies is char-	
acteristic of humans.	
Technology provides a	
means of solving a	
✔	
✔	
✔	
✔	

problem.

Biological structures differ

in size.

✔

Different technologies

are used to study biologi-

✔

✔

cal structures of different

sizes.

Biologists use microscopes

to study cells.

✔

✔

Proteins are important

biological molecules. Their

✔

✔

structure is related to their

function.

Science and technology

influence, and are influ-

✔

✔

enced by, society.

3

Introduction

Implementing the Module

The four lessons in this module are designed

What Are the Science Concepts and How

to be taught in sequence for approximately one

Are They Connected?

week as a replacement for a part of the standard

The lessons are organized into a conceptual

curriculum in high school biology. The follow-

framework that allows students to move from

ing pages offer general suggestions about using

what they already know about technology, some

these materials in the classroom; you will find

of which may be incorrect, to gaining a scien-

specific suggestions in the procedures provided

tific perspective on the nature of technology

for each lesson.

and its importance to science and to their lives.

Students begin learning about technology by

What Are the Goals of the Module?

developing their own definition of it and learn-

Using Technology to Study Cellular and Molecular

ing about scale (*What Is Technology?*). Students

Biology is designed to help students reach these

continue to explore the concept of scale and

major goals associated with scientific literacy:

investigate resolution (*Resolving Issues*). An

• to understand a set of basic scientific prin-

investigation of how technologies can be used

ciples related to the nature and role of

to solve scientific problems related to human

technology in biological science and to the

health (*Putting Technology to Work*) allows

effects of technology on human health;

students to gain a deeper understanding of

• to experience the process of scientific inquiry

technology's importance to our lives. The final

and develop an enhanced understanding of the

lesson, *Technology: How Much Is Enough?* , allows

nature and methods of science;

students to consider the current state of tech-

• to recognize the role of science in society

nology and design new technologies to answer

and the relationship between basic science

questions of relevance to cellular and molecular

and human health; and

biology. The following two tables illustrate the

• to help prepare high school biology students

science content and conceptual flow of the class-

for the technological world they will inherit.

room lessons.

Science Content of the Lessons

Lesson

Science Content

Lesson 1

Technology; scale

Lesson 2

Resolution

Lesson 3

Microscopy; X-ray crystallography; using technology to understand and solve health-related problems

Lesson 4

History of technology development; development of new technologies

5

Using Technology to Study Cellular and Molecular Biology

Conceptual Flow of the Lessons

Lesson

Learning Focus*

Major Concept

Lesson 1

Engage

Technology is a body of knowledge used to create tools,

What Is

Explore

develop skills, and extract or collect materials. It is also the

Technology?

Explain

application of science (the combination of the scientific method and material) to meet an objective or solve a problem. Scale is a way to represent the relationship between the actual size of an object and how that size is characterized, either numerically or visually.

Lesson 2

Explore

It is important to identify the right tool (technology) for the

Resolving

Explain

job. An important consideration is technology's ability to

Issues

resolve structural details of biological objects. Two objects can be resolved if they are illuminated with radiation (that is, a probe) of wavelength (that is, size) that is not larger than the distance separating the objects. Generally, the smaller the probe used, the greater the structural detail, or resolution, that results. Detailed structural knowledge about biological objects requires information obtained in three dimensions, not just two.

Lesson 3

Explore

Technologies differ in their resolving capabilities, thus provid-

Putting

Explain

ing different information about an object. Solving a problem

Technology to

Elaborate

requires an appropriate technology or series of technologies.

Work

Technology provides valuable tools for solving scientific prob-

lems of relevance to human health.

Lesson 4

Evaluate

New technologies are developed, and old technologies are

Technology:

improved and refined, continuously. This must be done to

How Much Is

meet the demands created by new and existing problems.

Enough?

*See *How Does the 5E Instructional Model Promote Active, Collaborative, Inquiry-Based Learning?* on page 9.

How Does the Module Correlate to the

National Science Education Standards (*NSES*).

***National Science Education Standards*?**

The content of the module is explicitly stan-

Using Technology to Study Cellular

dards based. Each time a standard is addressed

and Molecular Biology supports

in a lesson, an icon appears in the margin along

you in your efforts to reform sci-

with the applicable standard. The following

ence education in the spirit of the

chart lists the specific content standards that

National Research Council's 1996

this module addresses.

Content Standards: High School

Standard A:

Correlation to

As a result of activities in grades 9–12, all students should develop

Using Technology to

Study Cellular and

Molecular Biology

Abilities necessary to do scientific inquiry

• Identify questions and concepts that guide scientific investigations.

Lessons 1, 2, 3, 4

• Design and conduct a scientific investigation.

Lesson 3

• Use technology and mathematics to improve investigations and

Lessons 2, 3, 4

communications.

• Formulate and revise scientific explanations and models using logic

Lesson 3

and evidence.

• Recognize and analyze alternative explanations and models.

Lessons 1, 3

• Communicate and defend a scientific argument.

Lessons 3, 4

Understandings about scientific inquiry

• Scientists usually inquire about how physical, living, or designed

Lessons 3, 4

systems function.

• Scientists conduct investigations for a wide variety of reasons, such as Lesson 3

to discover new aspects of the natural world, to explain observed

phenomenon, or to test conclusions of prior investigations or predic-

tions of current theories.

• Scientists rely on technology to enhance gathering and manipulating

Lessons 2, 3, 4

data.

• Mathematics is essential in all aspects of scientific inquiry.

Lessons 1, 4

• Scientific explanations must adhere to criteria.

Lesson 3

• New knowledge and methods emerge from different types of investi-

Lessons 3, 4

gations and public communication among scientists.

Standard B:

As a result of their activities in grades 9–12, all students should develop understanding of

Structure and properties of matter

• The physical properties of molecules are determined by the structure

Lesson 3

of the molecule.

Standard C:

As a result of their activities in grades 9–12, all students should develop understanding of

The cell

• Cells have particular structures that underlie their functions.

Lesson 3

Standard E:

As a result of their activities in grades 9–12, all students should develop understanding of

Abilities of technological design

• Identify a problem or design an opportunity.

Lessons 1, 2, 3, 4

• Implement a proposed solution.

Lessons 2, 3

• Evaluate the solution and its consequences.

Lessons 2, 3, 4

• Communicate the problem, process, and solution.

Lessons 1, 2, 3, 4

Understandings about science and technology

• Many scientific investigations require contributions from different

Lessons 1, 2, 3, 4

disciplines, including engineering.

• Science often advances with new technologies.

Lessons 1, 4

• Creativity, imagination, and a good knowledge base are all required in Lessons 1, 4

the work of science and engineering.

• Scientific inquiry is driven by the desire to understand the natural

Lessons 1, 4

world, and technological design is driven by the need to meet human

needs and solve human problems.

Standard F:

As a result of their activities in grades 9–12, all students should

develop understanding of

Science and technology in local, national, and global challenges

• Science and technology are essential social enterprises.

Lessons 1, 4

• Progress in science and technology can be affected by social issues

and challenges.

Standard G:

As a result of their activities in grades 9–12, all students should

develop understanding of

Science as a human endeavor

• Individuals and teams have contributed and will continue to contribute Lessons 1, 2, 3, 4

to the scientific enterprise.

• Scientists have ethical traditions that value peer review, truthful

Lesson 3

reporting about methods and investigations, and making public the

results of work.

• Scientists are influenced by societal, cultural, and personal beliefs.

Lessons 1, 4

Science is a part of society.

Nature of scientific knowledge

• Science distinguishes itself form other ways of knowing and from

Lesson 3

other bodies of knowledge through the use of empirical standards,

logical arguments, and skepticism.

• Scientific explanations must meet certain criteria such as consistency

Lesson 3

and accuracy.

• All scientific knowledge is subject to change as new evidence

Lessons 1, 4

becomes available.

Teaching Standards

these opportunities for assessment and provide

The suggested teaching strategies in all the les-

answers to questions that can help you analyze

sons support you as you work to meet the teach-

student feedback.

ing standards outlined in the *National Science*

Education Standards. This module helps you plan

How Does the 5E Instructional Model

an inquiry-based science program by provid-

Promote Active, Collaborative, Inquiry-

ing short-term objectives for students. It also

Based Learning?

includes planning tools such as the Conceptual

Because learning does not occur through a pro-

Flow of the Lessons chart and the Suggested

cess of passive absorption, the lessons in this

Timeline for teaching the module. You can

module promote active learning. Students are

use this module to update your curriculum in

involved in more than listening and reading.

response to your students' interest in this topic.

They are developing skills, analyzing and evalu-

The focus on active, collaborative, and inquiry-

ating evidence, experiencing and discussing, and

based learning in the lessons helps you support

talking to their peers about their own under-

the development of student understanding and

standings. Students work collaboratively with
nurture a community of science learners.
others to solve problems and plan investiga-
tions. Many students find that they learn better
The structure of the lessons in this module
when they work with others in a collaborative
enables you to guide and facilitate learning. All
environment than when they work alone in a
the activities encourage and support student
competitive environment. When all this active,
inquiry, promote discourse among students,
collaborative learning is directed toward inquiry
and challenge students to accept and share
science, students succeed in making their own
responsibility for their learning. Using the 5E
discoveries. They ask questions, observe, analyze,
Instructional Model, combined with active, col-
explain, draw conclusions, and ask new ques-
laborative learning, allows you to respond effec-
tions. These inquiry experiences include both
tively to the diversity of student backgrounds
those that involve students in direct experimenta-
and learning styles. The module is fully anno-
tion and those in which students develop expla-
tated, with suggestions for how you can encour-

nations through critical and logical thinking.

age and model the skills of scientific inquiry,

as well as foster the curiosity, openness to new

This view of students as active thinkers who

ideas and data, and skepticism that characterize

construct their own understanding out of inter-

successful study of science.

actions with phenomena, the environment, and

other individuals is based on the theory of **con-**

Assessment Standards

structivism. A constructivist view of learning

You can engage in ongoing assessment of your

recognizes that students need time to

teaching and of student learning using the vari-

• express their current thinking;

ety of assessment components embedded within

• interact with objects, organisms, substances,

the module's structure. The assessment tasks are

and equipment to develop a range of experi-

authentic; they are similar to tasks that students

ences on which to base their thinking;

will engage in outside the classroom or in which

• reflect on their thinking by writing and

scientists participate. Annotations guide you to

expressing themselves and comparing what

they think with what others think; and

• interact with materials and ideas through

• make connections between their learning

classroom and Web activities;

experiences and the real world.

• consider different ways to solve a problem or

answer a question;

This module provides a built-in structure for

• acquire a common set of experiences with

creating a constructivist classroom: the 5E

their classmates so they can compare results

Instructional Model. This model sequences the

and ideas;

learning experiences so that students have the

• observe, describe, record, compare, and

opportunity to construct their understanding of

share their ideas and experiences; and

a concept over time. The model takes students

• express their developing understanding of

through five phases of learning that are easily

technology by analyzing and interpreting

described using five words that begin with the

data and by answering questions.

letter *E*: Engage, Explore, Explain, Elaborate,

and Evaluate. The following paragraphs illus-

Explain

trate how the 5Es are implemented across the

The Explain lessons provide opportunities for

lessons in this module.

students to connect their previous experiences

and to begin to make conceptual sense of the

Engage

main ideas of the module. This stage also allows

Students come to learning situations with prior

for the introduction of formal language, scien-

knowledge. This knowledge may or may not

tific terms, and content information that might

be congruent with the concepts presented in

make students' previous experiences easier to

this module. Engage lessons provide the oppor-

describe and explain.

tunity for teachers to find out what students

already know or think they know about the

In the Explain lessons in this module, Lesson 1:

topic and concepts to be covered.

What Is Technology? , Lesson 2: *Resolving Issues*,

and Lesson 3: *Putting Technology to Work*, students

The Engage lesson in this module, Lesson 1:

• explain concepts and ideas about technology

What Is Technology? , is designed to

(in their own words);

• pique students' curiosity and generate interest;

• listen to and compare others' explanations of

• determine students' current understanding

their results with their own;

about technology;

• become involved in student-to-student dis-

• invite students to raise their own questions

course in which they explain their thinking

about technology;

to others and debate their ideas;

• encourage students to compare their ideas

• revise their ideas;

with the ideas of others; and

• record their ideas and current understanding;

• enable teachers to assess what students do

• use labels, terminology, and formal language;

or do not understand about the stated out-

and

comes of the lesson.

• compare their current thinking with what

they previously thought.

Explore

In the Explore portions of the module, Lesson

Elaborate

1: *How Low Can You Go?* (Activity 2), Les-

In the Elaborate lesson, Lesson 3: *Putting Tech-*

son 2: *Resolving Issues*, and Lesson 3: *Putting*

nology to Work, students apply or extend impor-

Technology to Work, students investigate scale,

tant concepts in new situations and relate their

resolution, and the utility of technology to solve

previous experiences to new ones. Students

scientific problems, including those relevant to

make conceptual connections between new and

human health. These lessons require students to

former experiences. In this lesson, students

make observations, evaluate and interpret data,

• connect ideas, solve problems, and apply

and draw conclusions. Students

their understanding in a new situation;

• use scientific terms and descriptions;

• demonstrate what they understand about

• draw reasonable conclusions from evidence

technology and how well they can apply

and data;

their knowledge to solve a problem;

• add depth to their understanding of con-

• share their current thinking with others;

cepts and processes; and

• assess their own progress by comparing

• communicate their understanding to others.

their current understanding with their prior

knowledge; and

Evaluate

• ask questions that take them deeper into a

The Evaluate lesson is the final stage of the

concept.

instructional model, but it only provides a

“snapshot” of what the students understand

To review the relationship of the 5E Instruc-

and how far they have come from where they

tional Model to the concepts presented in the

began. In reality, the evaluation of students’

module, see the Conceptual Flow of the Lessons

conceptual understanding and ability to use

chart, on page 6.

skills begins with the Engage lesson and contin-

ues throughout each stage of the instructional

When a teacher uses the 5E Instructional Model,

model, as described in the following section.

he or she engages in practices that are very dif-
Combined with the students' written work and
ferent from those of a traditional teacher. In
performance of tasks throughout the module,
response, students also participate in their learn-
however, the Evaluate lesson can serve as a
ing in ways that are different from those experi-
summative assessment of what students know
enced in a traditional classroom. The following
and can do.
charts, What the Teacher Does and What the
Students Do, outline these differences.
The Evaluate lesson in this module, Lesson 4:
Technology: How Much Is Enough? , provides an
opportunity for students to

What the Teacher Does	
Stage	
That is ***consistent*** with	That is ***inconsistent*** with
the 5E Instructional Model	
the 5E Instructional Model	
Engage	
• Piques students' curiosity and	
• Introduces vocabulary	
generates interest	

• Explains concepts

• Determines students' current under-

• Provides definitions and answers

standing (prior knowledge) of a

• Provides closure

concept or idea

• Discourages students' ideas and

• Invites students to express what they questions

think

• Invites students to raise their own

questions

Explore

• Encourages student-to-student

• Provides answers

interaction

• Proceeds too rapidly for students to make

• Observes and listens to the students sense of their experiences

as they interact

• Provides closure

• Asks probing questions to help

• Tells the students that they are wrong

students make sense of their

• Gives information and facts that solve the

experiences

problem

• Provides time for students to puzzle • Leads the students step-by-step to a

through problems

solution

11

Teacher Background

Implementing the Module

Using Technology to Study Cellular and Molecular Biology

Explain

• Encourages students to use their

• Neglects to solicit students' explanations

common experiences and data from • Ignores data and information students

the Engage and Explore lessons to

gathered from previous lessons

develop explanations

• Dismisses students' ideas

• Asks questions that help students

• Accepts explanations that are not

express understanding and

supported by evidence

explanations

• Introduces unrelated concepts or skills

• Requests justification (evidence) for

students' explanations

• Provides time for students to com-

pare their ideas with those of others

and perhaps to revise their thinking

• Introduces terminology and alterna-

tive explanations after students

express their ideas

Elaborate

• Focuses students' attention on con-

• Neglects to help students connect new

ceptual connections between new

and former experiences

and former experiences

• Provides definitive answers

• Encourages students to use what

• Tells students that they are wrong

they have learned to explain a new

• Leads students step-by-step to a solution

event or idea

• Reinforces students' use of scientific

terms and descriptions previously

introduced

• Asks questions that help students

draw reasonable conclusions from

evidence and data

Evaluate

• Observes and records as students

• Tests vocabulary words, terms, and

demonstrate their understanding of

isolated facts

concept(s) and performance of skills • Introduces new ideas or concepts

• Provides time for students to com-

• Creates ambiguity

pare their ideas with those of others • Promotes open-ended discussion

and perhaps to revise their thinking

unrelated to the concept or skill

• Interviews students as a means of

assessing their developing under-

standing

• Encourages students to assess their

own progress

What the Students Do

Stage

That is ***consistent*** with

That is ***inconsistent*** with

the 5E Instructional Model

the 5E Instructional Model

Engage

• Become interested in and curious

• Ask for the “right” answer

about the concept/topic

• Offer the “right” answer

• Express current understanding of a

• Insist on answers or explanations

concept or idea

• Seek closure

• Raise questions such as, What do I

already know about this? What do

I want to know about this? How

could I find out?

Explore

• “Mess around” with materials and

• Let others do the thinking and exploring

ideas

(passive involvement)

• Conduct investigations in which they • Work quietly with little or no interaction observe, describe, and record data

with others (only appropriate when

• Try different ways to solve a problem exploring ideas or feelings)

or answer a question

• Stop with one solution

• Acquire a common set of experi-

• Demand or seek closure

ences so they can compare results

and ideas

• Compare their ideas with those of

others

Explain

• Explain concepts and ideas in their

• Propose explanations from “thin air” with

own words

no relationship to previous experiences

• Base their explanations on evidence • Bring up irrelevant experiences and

acquired during previous investiga-

examples

tions

• Accept explanations without justification

• Record their ideas and current

• Ignore or dismiss other plausible

understanding

explanations

• Reflect on and perhaps revise their

• Propose explanations without evidence to

ideas

support their ideas

• Express their ideas using appropriate

scientific language

• Compare their ideas with what scien-

tists know and understand

Elaborate

• Make conceptual connections

• Ignore previous information or evidence

between new and former experi-

• Draw conclusions from “thin air”

ences

• Use terminology inappropriately and

• Use what they have learned to

without understanding

explain a new object, event,

organism, or idea

• Use scientific terms and descriptions

• Draw reasonable conclusions from

evidence and data

• Communicate their understanding to

others

13

Implementing the Module

Using Technology to Study Cellular and Molecular Biology

Evaluate

• Demonstrate what they understand

• Disregard evidence or previously accepted

about the concept(s) and how well

explanations in drawing conclusions

they can implement a skill

• Offer only yes-or-no answers or mem-

• Compare their current thinking with

orized definitions or explanations as

that of others and perhaps revise

answers

their ideas

• Fail to express satisfactory explanations in

• Assess their own progress by com-

their own words

paring their current understanding

• Introduce new, irrelevant topics

with their prior knowledge

• Ask new questions that take them

deeper into a concept or topic area

How Does the Module Support Ongoing

How Can Controversial Topics Be Handled

Assessment?

in the Classroom?

Because teachers will use this module in a vari-

Teachers sometimes feel that the discussion of

ety of ways and at a variety of points in the

values is inappropriate in the science classroom

curriculum, the most appropriate mechanism

or that it detracts from the learning of “real” sci-

for assessing student learning is one that occurs

ence. The lessons in this module, however, are

informally at various points within the four les-

based on the conviction that there is much to

sons, rather than something that happens more
be gained by involving students in analyzing
formally just once at the end of the module.
issues of science, technology, and society. Society
Accordingly, integrated within the four lessons
expects all citizens to participate in the demo-
in the module are specific assessment compo-
cratic process, and our educational system must
nents. These “embedded” assessment oppor-
provide opportunities for students to learn to deal
tunities include one or more of the following
with contentious issues with civility, objectivity,
strategies:
and fairness. Likewise, students need to learn that
• performance-based activities (for example,
science intersects with life in many ways.
developing graphs or participating in a dis-
cussion of health effects or social policies);
In this module, students have a variety of oppor-
• oral presentations to the class (for example,
tunities to discuss, interpret, and evaluate basic
presenting experimental results); and
science and health issues, some in the light of
• written assignments (for example, answer-
values and ethics. As students encounter issues

ing questions or writing about demonstra-
about which they feel strongly, some discus-
tions).
sions might become controversial. How much
controversy develops will depend on many fac-
These strategies allow the teacher to assess a
tors, such as how similar the students are with
variety of aspects of the learning process, such
respect to socioeconomic status, perspectives,
as students' prior knowledge and current under-
value systems, and religious preferences. In addi-
standing, problem-solving and critical-thinking
tion, the language and attitude of the teacher
skills, level of understanding of new informa-
factor into the flow of ideas and the quality of
tion, communication skills, and ability to syn-
exchange among the students.
thesize ideas and apply understanding to a new
situation.

The following guidelines may help you facilitate
discussions that balance factual information

An assessment icon and an anno-
with feelings.
tation that describes the aspect of

• Remain neutral. Neutrality may be the single

learning that teachers can assess

most important characteristic of a successful

appear in the margin beside each

discussion facilitator.

step in which embedded assessment occurs.

• Encourage students to discover as much

information about the issue as possible.

see whether other students recognize the

• Keep the discussion relevant and moving

inappropriate comment and invite them to

forward by questioning or posing appropri-

respond.

ate problems or hypothetical situations.

• Create a sense of freedom in the classroom.

Encourage everyone to contribute, but do

Remind students, however, that freedom

not force reluctant students to enter the dis-

implies the responsibility to exercise that

cussion.

freedom in ways that generate positive

• Emphasize that everyone must be open to

results for all.

hearing and considering diverse views.

• Insist upon a nonhostile environment in the

• Use unbiased questioning to help the stu-
classroom. Remind students to respond to
dents critically examine all views presented.
ideas instead of to the individuals presenting
• Allow for the discussion of all feelings and
those ideas.
opinions.
• Respect silence. Reflective discussions often
• Avoid seeking consensus on all issues. The
are slow. If a teacher breaks the silence, stu-
multifaceted issues that the students dis-
dents may allow the teacher to dominate the
cuss result in the presentation of divergent
discussion.
views, and students should learn that this is
• At the end of the discussion, ask the stu-
acceptable.
dents to summarize the points that they and
• Acknowledge all contributions in the same
their classmates have made. Respect students
evenhanded manner. If a student seems to
regardless of their opinion about any contro-
be saying something for its shock value,
versial issue.

Using the Student Lessons

The heart of this module is a set of four class-

• **Web-Based Activities** tells you which of the

room lessons that allow students to discover

lesson's activities use the *Using Technology*

important concepts related to technology and

to Study Cellular and Molecular Biology Web

its role in developing our understanding of cel-

site as the basis for instruction.

lular and molecular biology. To review these

• **Photocopies** lists the paper copies and

concepts in detail, refer to the Conceptual Flow

transparencies that need to be made from

of the Lessons chart, on page 6.

masters that are provided after Lesson 4, at

the end of the module.

Format of the Lessons

• **Materials** lists all items other than photo-

As you review the lessons, you will find that all

copies needed for the activities in the lesson.

contain common major features.

• **Preparation** outlines what you need to do to

be ready to teach the activities in the lesson.

At a Glance offers a convenient summary of the lesson.

Procedure provides a step-by-step approach

• **Overview** provides a short summary of stu-

for conducting each activity in the classroom.

dent activities.

It includes implementation suggestions and

• **Major Concepts** presents the central ideas

answers to discussion questions.

that the lesson is designed to convey.

• **Objectives** lists specific understandings or

Within the Procedure section, annotations pro-

abilities students should derive from com-

vide additional commentary.

pleting the lesson.

• **Tip from the field test** details suggestions

• **Teacher Background** specifies which por-

from field-test teachers for teaching strate-

tions of the background section, *Information*

gies, class management, and module imple-

about Using Technology to Study Cellular and

mentation.

Molecular Biology, relate directly to the les-

• **Assessment** provides strategies for gauging

son. This reading material provides the sci-

student progress throughout the module,

ence content that supports the key concepts

and is identified by an assessment icon (see

covered in the lesson. The information

page 18).

provided is not intended to form the basis

• **Icons** identify specific annotations:

of lectures to students nor is it intended

as a direct resource for students. Rather, it

identifies teaching strategies that

enhances your understanding of the content

address specific science content

so that you can facilitate class discussions,

standards as defined by the *National*

answer student questions, and provide addi-

Science Education Standards.

tional examples.

identifies when to use the Web site

In Advance provides instructions for collecting

as part of the teaching strategy.

and preparing materials required to complete

Instructions in the Procedure sec-

the activities in the lesson.

tion tell you how to access the Web

site and the relevant activity. Infor-

each activity and includes icons that denote

mation about using the Web site can

where in each activity masters, transparencies,

be found in *Using the Web Site* (see

and the Web site are used. The lesson organizer

page 19). A print-based alternative

is intended to be used only after you become

to each Web activity is provided for

familiar with the lesson materials. It can be a

classrooms in which Internet access

handy resource during lesson preparation as

is not available.

well as during classroom instruction.

identifies a print-based alternative

Masters to be photocopied are found after Les-

to a Web-based activity to be used

son 4, at the end of the module.

when computers are not available.

Timeline for the Module

identifies when assessment is

The timeline below outlines the optimal plan

embedded in the module's structure.

for completing the four lessons in this module.

An annotation suggests strategies

The plan assumes you will teach the activities

for assessment.

on consecutive days. If your class requires more

time for discussing issues raised in this module

Lesson Organizer provides a brief summary

or for completing activities, adjust your time-

of the lesson. It outlines procedural steps for

line accordingly.

Suggested Timeline

Timeline

Activity

3 weeks ahead

Reserve computers

Check performance of Web site

1 week ahead

Make photocopies and transparencies

Gather materials

Day 1

Lesson 1

Monday

Activity 1: *Technology—What's It All About?*

Activity 2: *Searching for Scale*

Day 2

Lesson 2

Tuesday

Activity 1: *Probing for Answers*

Activity 2: *More than Meets the Eye*

Day 3

Lesson 3

Wednesday

Activity 1: *Putting Technology to Work*;

Part 1, some of Part 2

Day 4

Part 2 (conclude), Part 3, and Part 4 (print version only)

Thursday

Day 5

Lesson 4

Friday

Activity 1: *Time Travel*

Activity 2: *Is That All There Is?*

Day 6

Activity 2: *Is That All There Is?* (conclude)

Monday

18

Using the Web Site

The *Using Technology to Study Cellular and*

puters. Links to download the Macromedia

Molecular Biology Web site is a wonderful tool

Flash plug-in are provided on the Web site's

that can engage student interest in learning,

Getting Started page. *This plug-in is required for*

enhance the student's learning experience,

the activities to function properly. The recom-

and orchestrate and individualize instruction.

mended hardware and software requirements

The Web site features simulations that articu-

for using the Web site are listed in table below.

late with two of this unit's lessons. To access

Although your computer configuration may dif-

fer from those listed, the Web site may still be

the Web site, type the following URL into

functional on your computer. The most impor-

your browser: *http://science.education.nih.gov/*

tant items in this list are current browsers and

supplements/technology/student. Click on the

plug-ins.

link to a specific lesson under *Web Portion of*

Student Activities. If you do not have computer

or Internet access, you can use the print-based

Downloading and Installing Macromedia

alternative provided for each Web activity. Text

Flash Player

pertaining only to Web-based activities is lightly

To experience full functionality of the Web site,

shaded.

Macromedia Flash Player, version 6.0 or higher,

must be downloaded and installed on the hard

Hardware/Software Requirements

drive of each computer that will be used to

The Web site can be accessed from Apple

access the site. The procedure for downloading

Macintosh and IBM-compatible personal com-

and installing Macromedia Flash Player is out-

lined below.

Recommended Hardware/Software Requirements for Using the Web Site*

CPU/Processor (PC Intel, Mac)

Pentium III, 600 MHz; or Mac G4

Operating system (DOS/Windows, Mac OS)

Windows 2000 or higher; or Mac OS 9 or newer

System memory (RAM)

256 MB

Screen setting

1024 × 768 pixels, 32 bit color

Browser

Netscape Communicator 7.1 or Microsoft Internet

Explorer 6

Browser settings

JavaScript Enabled

Free hard drive space

10 MB

Connection speed

56 kbps modem or high-speed Internet connection

Plug-ins, installed for your Web browser

Macromedia Flash Plug-In, version 6 or better; or

Apple QuickTime Plug-In, version 6 or better

Audio

Sound card with speakers

*For users of screen-reader software, a multichannel sound card such as Sound Blaster® Live!™ is recommended.

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Using Technology to Study Cellular and Molecular Biology

• Open a Web browser.

actual real-life experience than print-based

• Access the main page of the Web site at

resources can offer;

http://science.education.nih.gov/supplements/

• provide teachers with support for experi-

technology/teacher.

menting with new instructional approaches

• Click on the “Getting Started” section.

that allow students to work independently or

• Click on the link to “Macromedia Flash.”

in small teams and that give teachers increased

This will bring up the Macromedia Flash

credibility among today’s technology-literate

Player Download Center Web site.

students; and

• The Download Center Web site should

• increase teachers’ productivity by helping

present you with the option of installing the

them with assessment, record keeping, and

latest version (highest number) of Macro-

classroom planning and management.

media Flash Player. As of August 2004, this

should be at least version 7.0.

The ideal use of the Web site requires one com-

• Click on the button marked “Install Now,” or

puter for each student team. However, if you
“Download Now.” Clicking this button will
have only one computer available, you can still
allow Macromedia’s Web site to download and
use the Web site. For example, you can use a
install Flash Player on your computer’s hard
projection system to display the monitor image
drive. If you are using Internet Explorer, the
for the whole class to see. Giving selected stu-
installation will happen automatically after
dents in the class the opportunity to manipulate
clicking the “Install Now” button. If you are
the Web activities in response to suggestions
using Netscape, you will have to download
from the class can give students some of the
and run the installation file. Follow the on-
same autonomy in their learning that they
screen instructions provided.
would gain from working in small teams. Alter-
• Your Web browser may present you with
natively, you can rotate student teams through
a Security Dialog Box asking if you would
the single computer station.
like to install and run Macromedia Flash
Player. Click “Yes.”

Collaborative Groups

• After a minute or so, you should once again

Many of the activities in the lessons are

see the Macromedia Download Center Web

designed to be completed by teams of students

page on your browser. There will be a box

working together. Although individual students

toward the top of the page containing click-

working alone can complete these activities,

able text. The appearance of this box in

this strategy will not stimulate the types of

your browser window indicates that you

student-student interactions that are part of

have successfully downloaded and installed

active, collaborative, inquiry-based learning.

Macromedia Flash Player.

Therefore, we recommend that you organize

collaborative teams of two to four students

Getting the Most out of the Web Site

each, depending on the number of computers

Before you use the Web site, or any other piece

available. Students in teams larger than this will

of instructional software in your classroom, it

have difficulty organizing student-computer

may be valuable to identify some of the benefits

interactions equitably. This can lead to one or

you can expect the software to provide. Well-

two students' assuming the primary responsibil-

designed instructional multimedia software can

ity for the computer-based work. Although this

• motivate students by helping them enjoy

type of arrangement can be efficient, it means

learning and want to learn more because

that some students will not have the opportu-

it enlivens content that students otherwise

nity to experience the in-depth discovery and

might find uninteresting;

analysis that the Web site was designed to stim-

• offer unique instructional capabilities

ulate. Team members not involved directly may

that allow students to explore topics in

become bored or disinterested.

greater depth and in ways that are closer to

We recommend that you keep students in the

Web Activities for Students with

same collaborative teams for all the activities

Disabilities

in the lessons. This will allow each team to

The Office of Science Education (OSE) is com-

develop a shared experience with the Web site
mitted to providing access to the Curriculum
and with the ideas and issues that the activities
Supplement Series for individuals with dis-
present. A shared experience will also enhance
abilities, including members of the public and
your students' perceptions of the lesson as a
federal employees. To meet this commitment,
conceptual whole.
we will comply with the requirements of Sec-
tion 508 of the Rehabilitation Act. Section 508
If your student-to-computer ratio is greater than
requires that individuals with disabilities who
four to one, you will need to change the way
are members of the public seeking these materi-
you teach the module from the instructions in
als will have access to and use of information
the lessons. For example, if you have only one
and data that are comparable to those provided
computer available, you may want students to
to members of the public who are not individu-
complete the Web-based work over an extended
als with disabilities. The online versions of this
time period. You can do this several ways. The
series have been prepared to comply with Sec-

most practical way is to use your computer

tion 508.

as a center along with several other centers at

which students complete other activities. In this

If you use assistive technology (such as a Braille

approach, students rotate through the computer

reader or a screen reader) and the format of

center, eventually completing the Web-based

any material on our Web sites interferes with

work you have assigned.

your ability to access the information, please let

us know. To enable us to respond in a manner

A second way to structure the lessons if you

most helpful to you, please indicate the nature

have only one computer available is to use a

of your accessibility problem, the format in

projection system to display the desktop screen

which you would like to receive the material,

for the whole class to view. Giving selected stu-

the Web address of the requested material, and

dents in the class the opportunity to manipulate

your contact information.

the Web activities in response to suggestions

from the class can give students some of the

Contact us at

same autonomy in their learning they would

Curriculum Supplement Series

have gained from working in small teams.

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21

Using the Web Site

Using the

Using T Web Site

echnology to Study Cellular and Molecular Biology

Using Technology to Study Cellular and Molecular Biology **508-Compliant Web Activities** Lesson

For Students with Hearing

For Students with Sight Impairment

Impairment

Lesson 2, both activi- No special considerations are required. There is no equivalent alternative to these ties

activities for students with sight impair-

ments. Students should be involved in the

group discussions of these activities and

be asked for their perspective.

Supervision is recommended.

Lesson 3, Parts 1

No special considerations are required. Students using screen-magnification or

and 3

screen-reading software can choose an alternate, text-based version of the activity. The content of the alternate activity is equivalent to the original's, but it's in a text format. The activity is based on the print version of the lesson. Images within the reference manual are kept to a minimum. The print version of the activity should be kept handy for reference.

Note: Students using a screen magnifier may prefer the original version of the activity.

When the activity loads, students press a button to proceed to the original version or the screen-reader-friendly version of the activity.

Use the "Teacher Administration" link to generate login codes for your students. You will need one code for each student using this version of the activity. You may request up to 100 codes at one time.

The "Progress Map" at the bottom of each page keeps track of each student's progress. If a student closes the activity and

returns later, he will resume where he left off. The last page of the activity provides a summary of all the student's answers. To edit their responses, students can use the Progress Map to return to any page they have completed.

The computer the students use must be linked to a printer.

Supervision is recommended.

Lesson 3, Part 2

No special considerations are required. This activity has been incorporated into the print version of Lesson 3.

2

Information about Using Technology to Study Cellular and Molecular Biology

1 Introduction

scientific community in 1985. Biology teach-

For society to gain the most from **technology**,

ers became aware of the technique through

the public must be able to understand scientific

stories in the media and wanted to learn more

issues and consider them rationally. This point

about it. It was not until 1990, however, when

is made in the *National Science Education Stan-*
PCR inventor Kary Mullis published an article
dards: “Because molecular biology will continue
about the technique in *Scientific American*, that
into the 21st century as a major frontier of sci-
teachers found an accessible treatment of this
ence, students should understand the chemi-
important technology. It took another few years
cal basis of life, not only for its own sake, but
for PCR to be mentioned in most high school
because of the need to take informed positions
biology textbooks. This curriculum supplement,
on some of the practical and ethical implica-
Using Technology to Study Cellular and Molecu-
tions of humankind’s capacity to tinker with the
lar Biology, will help short-circuit the usually
fundamental nature of life.”
lengthy process by which technology makes its
way to the classroom.

A molecular genetic perspective affords teach-
ers an opportunity to help integrate many of

2 Major Preconceptions

biology’s subdisciplines. This integrative process

Preconception 1. Study in one field proceeds

began with the advent of recombinant-DNA

without contributions from, or connections to,

technology and is now being propelled by the

other fields.

new areas of **bioinformatics** and genomic biol-

This belief occurs, in part, because scientific

ogy. According to the *National Science Education*

disciplines are treated as isolated subjects in

Standards, molecular and evolutionary biology

most schools. Most science educators, however,

are among the "small number of general prin-

recognize the many connections among biol-

ciples that can serve as the basis for teachers

ogy, chemistry, and physics, and understand

and students to develop further understanding

the need for an integrated approach to science

of biology." A similar point is made in a medi-

teaching. For example, molecular biology is a

cal context by the new *Standards for Technol-*

hybrid discipline, drawing upon concepts and

ogy Literacy, which recognizes that "the use of

techniques from physics, chemistry, and biology.

technology has made numerous contributions

This hybrid nature explains in part why high

to medicine over the years. Scientific and tech-

school students may find the study of molecular

nological breakthroughs are at the core of most biology challenging. They are confronted by a diagnostic and treatment practices."12 science that is abstract and seems far removed from classical biology. Moreover, many students When teachers try to relate advances in tech- are introduced to the subject at a point in their nology to biology, they may be frustrated by education where they have yet to take a formal the fact that there is a lag, measured in years, course in either chemistry or physics. Without between scientific advance and its inclusion in this scientific foundation, they are ill-prepared the curriculum. For example, the polymerase to undertake the study of life at its most funda- chain reaction (PCR) was introduced to the mental level.

Preconception 2. Most of what students are exposed to in science classes is about science, not technology.

Preconception 4. Structure and function are independent and unrelated concepts.

This supplement can build a foundation to

Additionally, technology is about computers address this preconception and to help students rather than about a way of adapting or a pro- understand the interdependence of structure cess for solving a problem. It is important for and function. With this supplement, students students to learn that each of the technologies will explore concepts to help them under- covered in this supplement is a tool applied to a stand that technologies provide scientists with specific task. The supplement will help students essential information about structure. The recognize the type of scientific information that relationship between structure and function can be obtained from various techniques and may be easier for students to understand at a gain an appreciation for and an understanding macroscopic level, and students may struggle to of the role technology has played in advancing understand this relationship at the abstract level our understanding of biological systems.

of molecules. Inquiry-based activities will allow students to learn what structure is and at how

Preconception 3. Students are likely to have pre- many levels structure can be defined. Through

conceptions about the contributions that a range

these activities, students will learn how devel-

oping structural information at various tiers

of technologies has made to science and medi-

provides increasingly greater information about

cine, that is, about the problem-solving capacity

function. Structure-function relationships are

of technology.

critical to understanding normal cellular pro-

For example, students have probably looked at

cesses, as well as those associated with disease.

a specimen with a light microscope, and they

Such intimate knowledge of biomolecules

have seen photomicrographs in textbooks.

promises to expand the range of drug targets,

However, students have limited experience

shift the discovery effort from direct screen-

evaluating the information conveyed at the

ing programs to rational **target-based drug**

microscopic level and placing it in the proper

design, and usher in a new era of personalized

context. Consequently, it will be important in

medicine. One of the activities that follows—in

this supplement to help students gain a per-

Lesson 3, *Putting Technology to Work*—gives stu-

spective of the relative sizes of cellular and

dents insight into these scientific developments.

molecular structures. The concepts of **resolu-**

tion and **scale** can help students appreciate that

3 Scale and Resolution

structures invisible to the unaided eye, such

3.1 Scale

as mitochondria, ribosomes, viruses, and pro-

How big is “big”? How small is “small”? It

tein molecules, have vastly different sizes and

depends, of course, on one’s point of refer-

require different technologies for study. It is

ence. An insect such as a bee (about 12 mm in

important that this supplement help students

length) is very small compared with a human

understand the need to obtain information from

(perhaps 1.7 to 2 meters in height). However, a

more than one technique to solve a problem.

bee is very large compared with one of the pol-

len grains it gathers (about 30 µm, or 0.03 mm,

in diameter). While it may be easy to discern

The concepts of resolution and scale

the relative sizes of some objects, such as those

can help students appreciate that struc-

we can see with the naked eye, it is far more

tures invisible to the unaided eye, such

difficult to imagine the size of things that are

as mitochondria, ribosomes, viruses,

very large or very small. For instance, how large

and protein molecules, have vastly dif-

is a lightyear? Can we conceive of the difference

ferent sizes and require different tech-

between 10 lightyears and 100 lightyears? What

nologies for study.

is the distance across a cell? A virus? A protein

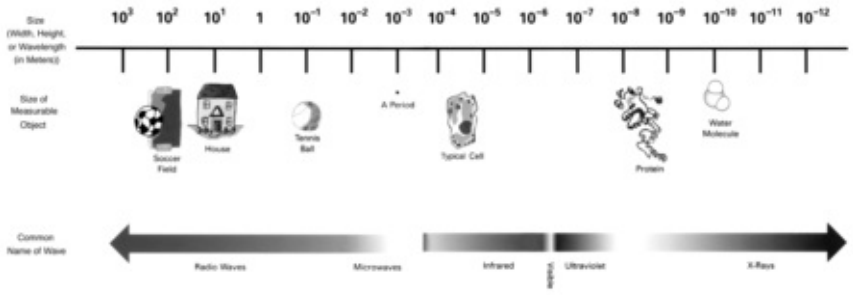


Figure 1. Size of some familiar objects and energy waves on a logarithmic scale.

molecule? How much larger are these than the

in understanding how living systems function.

distance between two adjacent carbon atoms

How do muscles contract? How do enzyme

in a sugar molecule? Importantly, where do we

reactions occur? How are metabolic pathways

humans fit into the picture?

regulated? How are molecules transported from

one site to another? How do antibodies recog-

To understand the continuum from small to
nize antigens? We want answers to so many
large, we need a way to represent the relation-
questions related to how living systems func-
ship between the actual size of an object (for
tion that require us to understand molecular
example, its length or mass) and how that size
structure first. Why? A molecule’s function is
is characterized either numerically or visu-
determined by and is dependent on its struc-
ally. We need a scale, a series of ascending and
ture. So, how do we get information about the
descending steps to assess the relative or abso-
structure of biological molecules? Consider the
lute size of some property of an object. Scales
following:
can have upper and lower values, as required.
They may be linear, or, when the distance
As we look down a street in a residential neigh-
between upper and lower values is very large,
borhood, we note individual houses because
they may be logarithmic. Figure 1 presents the
we are capable of distinguishing the space
size of some familiar objects and energy waves
between the houses. We accomplish this feat

on a logarithmic scale.

using our visual system to detect visible light. In other words, visible light is the **probe** we use to resolve these discrete structures. In a general sense, we can think of resolving power as a measure of the ability of a system to form separate and distinct images of two objects of a given angular separation. This relationship is derived from the laws of optics. What does this mean to the study of cellular and molecular biology? In the laws of optics, two objects can be resolved if they are illuminated with radiation of wavelength that is not larger than the distance separating the objects. Visible light is not small enough to resolve the fine details of the molecules that make up living systems, and of molecular interactions. We are interested

Without some notion of scale, a water molecule might appear to be as large as a house if both are drawn to occupy the same physical space on a piece of paper.

3.2 Resolution

In cellular and molecular biology, we are interested in resolving structural details of organs and tissues at the cellular level, of the intricacies that form the intracellular environment,

has a **wavelength** of 4,000 to 7,000 **angstroms**

25

Information about Using Technology to Study Cellular and Molecular Biology Using Technology to Study Cellular and Molecular Biology

(Å; 1 Å = 10–8 cm = 10–10 m), or 4 to 7 × 10–7

a brief survey of some technologies important

m, and is a great probe for viewing a portion

to the study of cellular and molecular biology.

of our world. We can resolve much with the

It presents a sampling of current research in

naked eye and even more, such as cells and cell

cellular and molecular biology, showing that

organelles, with a light microscope. However,

techniques that have been around for decades

its wavelength makes it unusable as a probe for

continue to be refined and put to new uses,

resolving much smaller objects, such as mol-

sometimes in combination with other tech-

ecules and atoms. Other probes with smaller

niques.

wavelengths are required for this task.

4.1 Microscopy

4 Major Techniques in the Study of

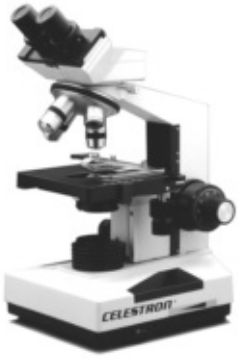
The development of the microscope allowed us

Cellular and Molecular Biology

to extend our view to things not visible to the

There is a reciprocal relationship between tech-
naked eye. Consider what our view of biologi-
nology and the process of science. Improve-
cal systems would be if we had no knowledge
ments in technology enable scientists to
of cells and cell structure. Figure 2 depicts the
investigate questions that were previously dif-
development of three major types of microscopy
ficult, or even impossible, to address. At the
over time.
same time, scientific curiosity often provides
the impetus for refining an existing technology
The line for each type of microscopy shows
or developing a new one. This section provides
how improvements in technology have

Figure 2. Development and resolution of three major types of microscopy over time.



increased the resolution available with each
pighi proved the controversial theory that blood
technique. Higher resolution means being able

circulates in a circular motion from the heart around the body and back to the heart. Also about this time, Robert Hooke is credited with discovering the cell, the basic unit of life. Antonio van Leeuwenhoek improved the lenses used in microscopes, allowing an increase in maximum magnification from 50× to 200×. Because of this, Leeuwenhoek was the first scientist to view bacteria, protozoa, and sperm cells. There were additional improvements to optical microscopy over the next 200 to 300 years, which ultimately allowed optical microscopes to distinguish objects as small as 200 **nanometers** (nm; 2 × 10–7 m). This resolution is a physical limit dictated by the wavelength of light (see section 3.2).

Electron microscopy. The first electron microscope was built in 1933 by Ernst Ruska, who was awarded the 1986 Nobel Prize in Physics for his achievements in electron optics. To break the 200-nm optical-resolution barrier, Ruska used accelerated electrons instead of

Figure 3. Optical microscope.

Optical microscopy. The first microscopes were

optical microscopes, which used glass lenses
light and magnetic coils instead of glass lenses
to focus and magnify light. The first optical
to make an image. Electrons have a wavelength
microscope was constructed around 1695 by
that is 104 to 105 times smaller than the wave-
Hans and Sacharias Janssen, but it wasn’t until
length of light. This allows electron micro-
60 to 80 years later that major discoveries were
scopes to resolve objects that are 103 times
made with this technology. By viewing capillar-
smaller than the smallest resolvable object in a
ies under a microscope in 1660, Marcello Mal-
light microscope.

Figure 4. Resolution of three major types of microscopes.

Using Technology to Study Cellular and Molecular Biology

Interestingly, although the design and physical appearance of electron microscopes have changed over the years, the essential characteristics remain the same. All electron microscopes require a high vacuum in which to form an electron beam and high voltage to control this

beam. Electromagnetic lenses then focus the electron beam onto the specimen and viewing screen.

Figure 5 shows a typical transmission electron microscope (TEM). Note the much larger physical size compared with a standard light microscope, which fits comfortably on a laboratory bench. TEMs are patterned after standard transmission light microscopes and yield similar information about the size, shape, and arrangement of particles that make up a specimen, albeit at much higher resolution and with a magnification range of about 1,000× to 300,000×.

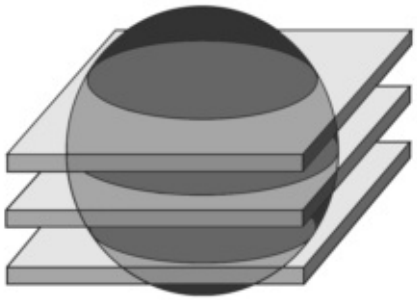
Figure 6. High-resolution TEM.

Figure 5. A typical transmission electron microscope (TEM).

The state-of-the-art TEM is the high-resolution TEM (Figure 6), which can magnify a sample up to 50,000,000 times and provide a resolution of 0.1 nm. It can produce information that com-

Figure 7. Scanning electron microscope.

plements data obtained from **X-ray** techniques (see section 4.2).



In addition to the TEM, the other most com-
moving through the cell interior, can create a
mon electron microscope is the scanning elec-
chemical map of the cell. One disadvantage of
tron microscope (SEM; Figure 7). The SEM
the technique is that it takes many minutes to
provides information about the surface features
produce an image, which limits its ability to
of an object. We learn about an object's appear-
visualize rapid changes within the cell.
ance, texture, and detectable features to within
a resolution of several nanometers. Interest-
Another technique, called Fourier transform
ingly, we do not learn this information by view-
infrared microspectroscopy (FTIR) combines
ing biological specimens directly. Biological
microscopy with **spectroscopy** to provide
specimens have low contrast and are difficult
chemical information about the sample being
to see in the SEM. Consequently, high-contrast
visualized. Samples can be analyzed wet or

heavy atoms, such as osmium, are used to stain
dry, in air, at room temperature, and at normal
specimens and provide an indirect image of the
pressure. FTIR is limited for analysis of living
underlying biological structures.
specimens because samples must be very thin.
It has proven useful in studies of pathogenesis,
Resolution can be improved by modifica-
however. Biochemical studies of disease often
tions of the sample-preparation procedure. In
fail to detect chemical compounds associ-
a technique called cryo-electron microscopy
ated with **pathology** because the chemicals are
(cryo-EM), specimens are rapidly frozen with-
diluted during their analysis. FTIR can be used
out formation of ice crystals that can distort
to pinpoint areas of disease and identify com-
the specimen’s structure. It is then possible to
pounds in individual cells, providing insights
construct two- and three-dimensional models
into disease progression. The technique is cur-
of the sample by using a computer program
rently being developed for objective evaluations
that averages many electron **micrographs** taken
of pap smears.

from different angles. When the technique was first applied to the structure of the ribosome in 1991, the resolution was just 45 Å. Still, it was possible to see the two ribosome subunits and the triangular space between them. In recent years, scientists have used cryo-EM techniques to image the ribosome to 4 Å.6–8 Studies with these techniques have revealed the surface topography of the ribosome for the first time and helped crystallographers interpret the ribosome's diffraction patterns.

Other microscopic techniques. Despite the long history of light microscopy, it is still being improved. For example, a new way to image living cells without disturbing their biochemistry has been developed. Called coherent anti-Stokes Raman scattering, the technique directs two **laser** beams into the cell. The frequencies of the lasers differ by exactly the frequency at which a particular chemical bond in the cell vibrates.

Figure 8. Laser confocal microscopes produce optical sections of biological specimens one plane at a time.

Laser confocal microscopy is a valuable tool for obtaining high-resolution images and three-

The lasers cause the chemical bond to vibrate

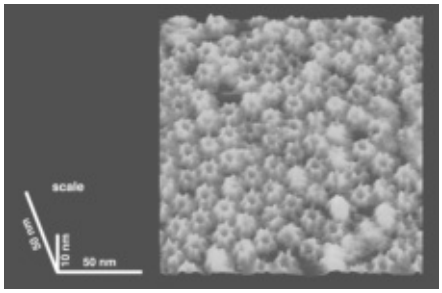
dimensional reconstructions of biological speci-

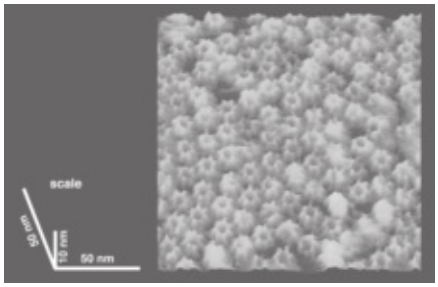
and emit its own characteristic optical signal.

mens. This technique’s major value is its ability

The lasers can focus on tiny volumes and, by

to produce optical sections of a biological





specimen that contain information from only
Research indicates that proteins move rapidly
one focal plane. By moving the focal plane of
throughout the nucleus in an energy-indepen-
the microscope step by step through the thick-
dent manner. Studies such as these are helping
ness of a specimen, a series of optical sections
scientists understand nuclear architecture and
can be obtained. The source of light for this
how nuclear processes are organized in the cell.
technique is a laser, because it can produce very
high intensities. The biological specimens are
While electron microscopes require that sam-
stained with a fluorescent probe to make a spe-
ples be carefully prepared and examined in
cific structure or structures visible in the pres-
a vacuum, a new family of microscopes can
ence of the laser light.
achieve electron microscope resolution in air or
even liquid, and they require much less sample

preparation. They have even been used to study living cells. These are called scanning probe microscopes (SPMs). These instruments use a microscopic needle-like probe (3 to 50 nm at the tip) that is scanned back and forth across a surface. A three-dimensional image is constructed from the recorded interactions between the probe and the atoms in the sample. The SPM has the ability to operate on a scale from micrometers to nanometers. It can magnify an object up to 10,000,000 times. In the laboratory under ideal conditions, the SPM can be used to look at individual atoms. Furthermore, SPMs can measure properties that other microscopes cannot, such as thermal properties, friction, hardness, magnetic properties, and extent of chemical binding.

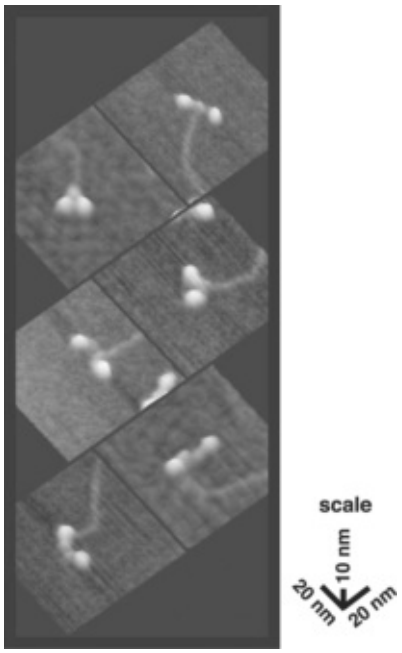
Figure 9. Laser confocal microscope.

Confocal microscopes are not large instruments. They consist of a microscope containing a confocal attachment. In the example in Figure 9, the confocal attachment is mounted on top of the upright microscope. It contains the compli-

cated optics package. Also necessary are a large box containing electronics, a laser, and a computer for collecting and analyzing data.

Laser confocal microscopy is being used now to study the spatial and temporal organization of the DNA-transcription apparatus. Three-dimensional reconstructions suggest that splicing factors are stored in specific areas of the nucleus. When DNA templates are introduced, these factors are recruited to sites of transcription in an intron-dependent fashion. The movement of proteins within the nucleus is also being studied using confocal microscopy.20

Figure 10. Molecules of the protein GroEL viewed with a scanning probe microscope (SPM). (Reprinted here with permission from Zhifeng Shao, University of Virginia. Posted at http://www.people.virginia.edu/~zs9q/zsfig/random.html *.)*



Resolving the structure of biomolecules requires visualizing individual atoms, which are only 1 to 3 Å apart when joined to form molecules. Therefore, resolving carbon, oxygen, and nitrogen atoms requires a probe with a wavelength of less than 2 Å. Light, with a wavelength of 4,000 to 7,000 Å, cannot be used for this task. However, the wavelengths of X-rays (like electrons) are short enough that the X-rays are scattered by the electron clouds of molecules and can be used to reveal the shape of a molecule. Furthermore, X-ray techniques have some advantages over electron microscopy for determining the structure of biomolecules, such as proteins. For instance, the electron beam damages its target after a short exposure because it is powerful enough to break chemical bonds.

Electron microscopy is limited to resolving biomolecules to no greater than about 7 Å, whereas X-ray crystallography can be used to resolve biomolecular structures to greater than 1 Å in some cases.

In X-ray crystallography, X-rays, with wavelengths of the same order of magnitude as the spacing between atoms, are directed through a crystal of the substance under study (Figure 12). The X-rays are bent (or **diffracted**) by the electrons surrounding the atoms in the crystal. Each diffracted X-ray is represented as a spot, whether recorded on film or electronically by a detector.

Figure 11. Myosin molecules viewed with an SPM. (Reprinted here with permission from Zhifeng Shao, University of Virginia. Posted at http://www.people.virginia.edu/~zs9q/zsfig/myosin.html *.)*

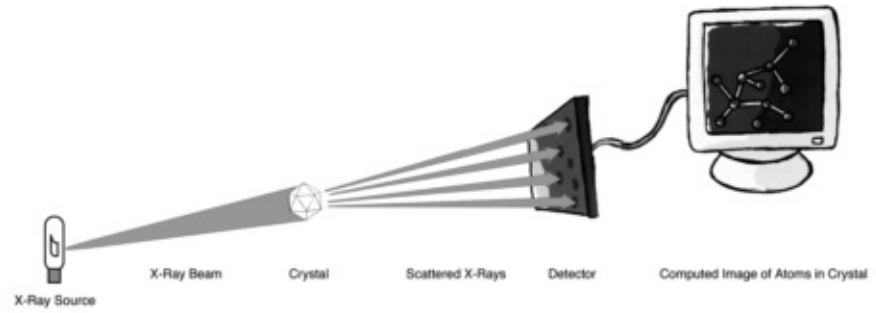
A single molecule will not produce a detectable diffraction pattern, so crystals containing many millions of identical molecules in a regular pattern are used to amplify the signal.

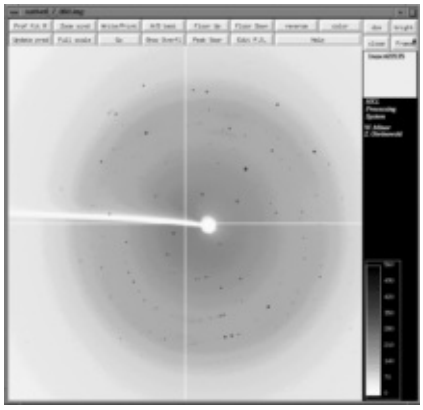
4.2 X-ray crystallography

X-ray crystallography of proteins is a perfect

example of the multidisciplinary approach to
After measuring the positions and intensities
technology development, since it is a combina-
of the diffraction spots, these data can be used
tion of chemistry, physics, and biology. It was
to calculate an electron density map. There are
designed to determine protein structure and, in
thousands of spots to analyze, so sophisticated
so doing, provide some information about how
computer programs and high-speed computers
proteins actually function in cells. This technol-
are needed to convert the patterns of different
ogy, like the microscopic techniques described
intensity spots into electron density maps. The
above, continues to evolve. While it provides
maps display contour lines of electron density,
detailed information about protein structure, X-
thus producing an image of the electron clouds
ray crystallography is also being used to design
of the molecule being studied. Because elec-
better medicines for treating serious diseases.

trons surround atoms more or less uniformly,





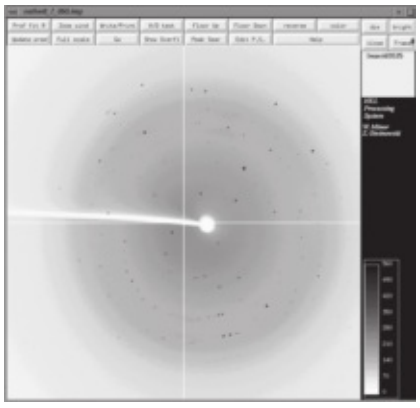


Figure 12. The X-ray crystallography process.

it is possible to determine where atoms are

One of the most striking advancements has

located by looking at these maps. By rotating

been the use of **synchrotron** X-rays, which are

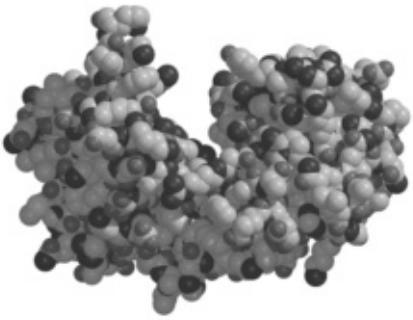
the crystal and generating an electron density

produced by the bending of particle beams gen-
map for each angle of rotation, it is possible to
erated by large accelerators. In a synchrotron,
produce a three-dimensional model of the mol-
charged particles, such as electrons or posi-
ecule. If the amino acid sequence of a protein
trons, are orbited around a path nearly a mile
is known, an accurate model of the protein can
in circumference, which must be maintained
be generated by fitting the atoms of the known
in a vacuum. Understandably, synchrotrons are
sequence into the electron density map.
quite expensive to build and to maintain, and
Figure 13 shows a typical diffraction pattern for
a single orientation of a protein crystal through
which an X-ray beam has been passed. Note
the different positions and intensities of the
spots, which mark the locations where scattered
X-rays have struck the detector. The image is
divided into quadrants because the detector was
composed of four separate, adjacent modules.
The white circle to the right of center with the
white line extending to the left is a shadow
resulting from a “beamstop.” The beamstop is a
small piece of lead mounted on a metal arm. It

prevents the intense beam of unscattered X-rays from impinging on and damaging the detector. Figure 14 shows a three-dimensional model of a protein that was crystallized and then analyzed by X-ray crystallography.

Figure 13. A typical X-ray−diffraction pattern for a single orientation of a protein crystal through which an X-ray beam has been passed.

Equipment used in X-ray crystallography continues to undergo development and refinement.



synchrotron radiation. A modern synchrotron source can reduce total data collection to just 30 minutes, as compared with weeks using earlier X-ray–diffraction equipment.

Determining structures by **X-ray diffraction** continues to add to our understanding of DNA replication and protein synthesis. For example, scientists recently studied the crystal structures of a bacterial DNA polymerase I that had DNA primer templates bound to its active site.13

The enzyme was catalytically active, which allowed for direct observation of the products of several rounds of nucleotide incorporation. The polymerase was able to retain its ability to distinguish between correctly and incorrectly paired nucleotides in the crystal. By comparing the structures of successive complexes, it was possible to determine the structural basis for sequence-independent recognition of correctly formed base pairs.13

Figure 14. Three-dimensional structure of the DNA-repair protein MutY as determined by X-ray crystallography. Graphic was produced from information available at http://www.rcsb.org/pdb/ .

there are fewer than 20 in the world. Because synchrotron X-ray beams are many orders of magnitude brighter than the usual laboratory X-ray sources, data for single crystal orientations can be collected with exposures of a minute or less, rather than exposures of several minutes to several hours. Results, with resolutions as high as 2.4 Å, have helped establish the locations of the 27 proteins and the 2,833 bases of ribosomal (rRNA) found

Ribosomes are the largest asymmetric structures to be solved by X-ray crystallography so far.

an hour.

within the ribosome.4 The structure also shows

that contacts between the two ribosome sub-

The completion of the Human Genome Proj-

units are limited, which helps explain why the

ect has provided the foundation for explosive

ribosome subunits dissociate so readily.

growth in structural biology. Technological

advances in X-ray crystallography have greatly

Some biomolecules or biomolecular complexes

reduced the time and effort required to solve

are not suitable for diffraction analysis because

structures. In addition to synchrotron X-

they cannot be crystallized. Scientists, however,

rays, advances include faster X-ray detectors,

are optimistic about developing techniques to

improved computational methods for process-

deal effectively with noncrystalline materials.18

ing data, and robotics for growing and handling

This will make it possible to image everything

crystals. Structure determinations that used to

from cells to individual protein molecules.

involve a 20-person, yearlong effort now con-

stitute a single chapter in a graduate student’s

4.3 Nuclear magnetic resonance (NMR)

thesis. The Protein Structure Initiative, remi-

spectroscopy

niscent of the Human Genome Project, aims to

Most people know of magnetic resonance imag-

produce the three-dimensional structures for

ing (MRI) as an important diagnostic tool in

the estimated 1,000 to 5,000 distinct spatial

medicine that can produce incredible images

arrangements assumed by polypeptides found

of soft tissues. Less well known is that MRI

in nature. Such high-throughput data collection

represents only a limited area of NMR. NMR

is best suited to X-ray crystallography using

depends on the fact that atomic nuclei having

an odd number of protons, neutrons, or both
in plants. This enzyme functions as a molecular
have an intrinsic spin. When such a nucleus is
motor that uses an internal rotary mechanism.
placed in a **magnetic field**, it can align either in
NMR has been used to reveal structural changes
the same direction as the field or in the oppo-
in a protein subunit of the enzyme that may
site direction. A nucleus aligned with the field
explain how the rotation is driven.20
has a lower energy than one aligned against it.
NMR spectroscopy refers to the absorption of
Many see the successful Human Genome Project
radiofrequency radiation by nuclei in a strong
as providing a foundation for a major initiative
magnetic field. Absorption of energy causes the
in structural biology in which NMR will play
nuclei to realign in the higher-energy direction.
a critical role.5 Informal groups of scientists in

The nuclei then emit radiation and return to
the United States are proposing the creation of
the lower-energy state. The local environment
10 regional “collaboratories,” each with power-
around each nucleus will distort the magnetic
ful new-generation NMR spectrophotometers
field slightly and affect its transition energy.
to assist with high-throughput structure deter-
This relationship between transition energy and
minations. Universities, too, are interested in
an atom’s position within a molecule allows
establishing collaborative centers in genomics
NMR to provide structural information.
and proteomics.9 At Stanford, Nobel Prize–
winning physicist Steven Chu and biochemist
One advantage of NMR spectroscopy over X-ray
James Spudich are leading an effort to create
crystallography and electron microscopy is that
an interdisciplinary research center housing 50
it can be applied to the study of movement at
faculty members, while Princeton University is
the molecular level. NMR studies are providing
planning to add an interdisciplinary genomics
a growing list of cases where conformational
institute to its molecular biology department.

dynamics correlate with protein-protein interaction on surfaces. For example, the enzyme ATP

4.4 Laser technology

synthase catalyzes the formation of ATP from

When the laser made its first appearance in

ADP and phosphate during oxidative phosphor-

the 1950s, it was a tool without a task. Since

ylation in animals and photophosphorylation

then, the laser has been put to myriad uses in

our everyday lives—from scanning prices at the

supermarket to playing music and printing text.

Similarly, in scientific research, the laser has

found many applications. It is like a Swiss Army

knife, having many blades with a variety of uses.

Combining lasers and microscopy has greatly

expanded our ability to image cellular and

molecular structures. Cells, or parts of cells,

can be exposed to antibodies or nucleic acid

probes labeled with fluorescent dyes. When

excited by laser light of the appropriate wave-

length, specific areas of the cell, or regions of

a chromosome, can be visualized. The resolu-

tion of optical microscopy is limited by physical

laws. Diffraction prevents the laser beam (and

therefore the spot of fluorescence) from being

focused any finer than about 200 nm. However, a new approach is overcoming this limit. It uses a combination of two laser beams, one to illuminate and image the sample, and a second that shapes the first beam and reduces the effects of diffraction. The technique has been used to distinguish crystals only 100 nm apart and is still undergoing improvement.

Lasers, together with magnets, are being used to develop technologies for manipulating single molecules. Investigators are now able to examine how DNA interacts with the various protein molecules that cut, paste, and copy it. DNA is an ideal choice for single-molecule studies. It

Figure 15. Equipment for high-resolution nuclear magnetic resonance (NMR) spectroscopy.

The amount of genetic data available and the rate of acquisition are astonishing by any measure.

The use of computers to model protein folding is one of the primary efforts in the postsequencing phase of the Human Genome Project. In the 1970s, when the first proteins were modeled, the structures generated were *in vacuo* (in a vac-

is a very large molecule (the longest human
uum), with no other molecules interacting with
chromosome stretches to 9 centimeters) and
the protein. Of course, each protein in a living
quite robust. For example, scientists have suc-
cell is surrounded by thousands of water mol-
ceeded in using lasers as optical tweezers to tie
ecules, and these have an important effect on
knots in single DNA molecules.2 Results indi-
the protein’s conformation. Indeed, research has
cate that knotted DNA is stronger than actin, a
demonstrated that the water-containing models
major muscle protein. Although tying DNA into
of proteins are much better predictors of how
knots may not seem particularly useful, it does
the proteins look and function within a cell.10
provide insight into the molecule’s mechanical
properties, which are critical to understanding
The importance of protein folding was recently
how enzymes interact with it.
recognized by IBM, which announced that it
would spend $100 million to build a supercom-

4.5 Simulations and computations

puter called Blue Gene. The five-year IBM initia-
The explosion of data produced by the Human

tive will involve modeling how proteins take on
Genome Project led to the creation of a new
their three-dimensional shapes. A major aim is
discipline, bioinformatics, whose focus is on
to help drug researchers identify drug targets for
the acquisition, storage, analysis, modeling, and
treating diseases. Protein folding is a daunting
distribution of the many types of information
problem. Even Blue Gene, which will be 500
embedded in DNA and protein-sequence data.14
times faster than the current fastest computer,
Biologists are familiar with the terms *in vivo* and
will require about one year to simulate the com-
in vitro, used to describe processes that occur
plete folding of a typical protein. The stakes,
in the body and in the test tube, respectively.
however, are huge. Approximately one-third
Now they are becoming acquainted with a new
of the genes identified in the newly sequenced
term, *in silico*, used to describe a new branch
human genome are of unknown function and
of biology that requires little more than a com-
are therefore of particular academic and com-
puter and a connection to the Internet. As more
mercial interest. New companies are formed

and more DNA and protein sequence data find
on a monthly basis to take part in this genetics
their way into computer databases, the ability
sweepstakes.
of bioinformatics to address biological ques-
tions becomes more powerful. The amount of
5 Technology and the Origins of
genetic data available and the rate of acquisition
Molecular Biology
are astonishing by any measure. According to
This section provides a brief history of the ori-
Francis Collins, head of the National Human
gins of molecular biology. It addresses the gene's
Genome Research Institute, it took four years
chemical nature, organization, and behavior.
to obtain the first 1 billion base pairs of human
Despite molecular biology's narrow focus on
sequence and just four months to get the second
DNA, it is readily apparent that many of the
billion.16
most important advances in the field have relied

heavily on technology-based contributions from
unaware of the important one-gene–one-enzyme

chemistry and physics. This is addressed in the work of George Beadle and Edward Tatum from *National Science Education Standards*. The His- the early 1940s), the book has been credited tory and Nature of Science Content Standard with influencing a generation of physicists to G states, “As a result of activities in grades 9 to consider biological questions.
12, all students should develop understanding of . . . historical perspectives.” It further states, Soon, the ranks of the Phage Group began to “Occasionally, there are advances in science and grow. It included other physicists, such as Leo technology that have important and long-lasting Szilard, holder of the patent for the nuclear effects on science and society.”
chain reaction and a participant in the Man- hattan Project, and Thomas Anderson, one Science historians often attribute the origins of of the first American electron microscopists. molecular biology to the Phage Group, which Micrographs obtained by Anderson and Roger first met in 1940 at Cold Spring Harbor Labora- Herriott showed that phage begin the infection tory in Long Island, N.Y. At the center of the

process by attaching to bacteria by their tails.

group were three scientists. Max Delbrück, a

Later, empty phage “ghosts” could be seen on

German physicist working at Vanderbilt Uni-

the bacterial surface.

versity, and Salvador Luria, an Italian biologist

working at Indiana University, had fled to the

Hershey and his colleague Martha Chase used

United States from Nazi Europe. They were

phage to examine the molecular nature of the

joined at Cold Spring Harbor by Alfred Hershey,

gene.11 They took advantage of radioactive iso-

an American biologist working for the Carnegie

topes that became available as a consequence

Institution’s Department of Genetics.

of work on the atomic bomb. Despite the ear-

lier work of Oswald Avery and his colleagues

Bacteriophage, also called phage, are viruses

demonstrating that DNA was the hereditary

that infect bacteria.1 These were discovered in

substance,3 many scientists continued to believe

1916 by the English microbiologist F.W. Twort

that genes could only be made of protein. Her-

and, independently, two years later by the

shey and Chase began their experiment by

French-Canadian F. d’Herelle. It was d’Herelle
using radioactive phosphorous to label phage
who came up with the name *bacteriophage*.
DNA and radioactive sulfur to label phage pro-
Phage became an important area of research in
tein. They tried to detect which radiolabel went
the 1920s, when scientists hoped they could be
inside the bacterium to direct synthesis of new
used to treat bacterial diseases. When this hope
phage particles after the bacterium was infected.
failed to materialize, phage research fell out of
At first, they could not effectively detach the
favor until the Phage Group resurrected it.22
phage particles from the surfaces of the bacte-
rial cells, but then an unexpected technology
In 1944, Delbrück organized a summer course
came to their aid. They used a Waring blender,
at Cold Spring Harbor Laboratory to introduce
originally designed to mix cocktails, to disrupt
other scientists to the quantitative methods for
the attachments of the phage to the bacterial
studying phage that he and Luria had devel-
cells. The radioactive phosphorous went into
oped. In that same year, the great Austrian
the bacterial cells, while the radioactive sulfur

physicist Erwin Schrödinger published a book
remained outside with the phage ghosts, con-
titled *What Is Life?* that discussed heredity from
firming that DNA, and not protein, contains the
a physics perspective.19 Schrödinger reasoned
genetic information. This work set the stage for
that although living things obey the laws of
the contribution of the youngest member of the
physics, they also might be governed by undis-
Phage Group, James Watson.
covered physical laws. Although biologists of
that time regarded Schrödinger's book as roman-
Watson came to the Cavendish Laboratory at
tic and a bit naive (for example, he seemed
Cambridge University in 1951, ostensibly to

study the three-dimensional structures of pro-
Samples of cells were removed before the switch
teins. He quickly fell in with Francis Crick, a
to the light-isotope growth medium (genera-
British physicist, who had developed an inter-
tion 1) and from the first two generations fol-
est in heredity after reading Schrödinger's *What*
lowing the switch (generations 2 and 3). DNA
Is Life? The pair formed a collaboration that

samples extracted from the cell samples were
resulted two years later in the proposal of the
centrifuged through a solution of cesium chlo-
double helix model of DNA.23 Although Watson
ride that forms a density gradient during cen-
and Crick relied on model building to solve
trifugation (for 20 hours at 40,000 revolutions
DNA’s structure, they could not have succeeded
per minute). DNA molecules form a discrete
without help from two other scientists at Cam-
band at a position where their density equals
bridge, Maurice Wilkins and Rosalind Franklin.
that of the cesium chloride gradient. The DNA
Wilkins first, and then Franklin, used X-ray
samples taken from generation 1 contained a
diffraction to study the structure of DNA. In
single heavy band, since both DNA strands con-
the case of DNA fibers, the diffraction patterns
tained the 15N isotope. Samples from generation
suggested that the molecule was some type of a
2 displayed a single band of medium density,
helix with a diameter of 20 Å and a repeat of 34
since each DNA molecule consisted of one
Å. Near the end of the paper that describes the
heavy (15N) parental strand and one light (14N)

double helix, Watson and Crick included the complementary strand. Finally, samples from statement, “It has not escaped our notice that generation 3 displayed bands of two different the specific pairing we have postulated immedi- densities. One band of medium density again ately suggests a possible copying mechanism for consisted of a heavy parental strand and a new the genetic material.”

complementary light strand. A second band of light density consisted of two strands of light Experimental support for a copying mechanism DNA, one an inherited light parental strand and suggested by the double helix structure came in the other, a new complementary light strand. 1958 from Matthew Meselson and Frank Stahl, then working at the California Institute of Tech- Around the time that Meselson and Stahl were nology. In what some have called “the most performing their experiments, Crick theorized elegant experiment in molecular biology,” they that genetic information flow resided in DNA, demonstrated that DNA replicates in a semicon- passed through an RNA intermediate, and servative fashion, during which one parental

became expressed as a sequence of amino acids. DNA strand serves as the template for the syn- Using the electron microscope, it was possible thesis of a new complementary strand.17 Their to visualize DNA and RNA molecules that first ingenious approach involved using a heavy had been stained with heavy metals. Using isotope of nitrogen and the ability of density extracts from bacteria, scientists were able gradient centrifugation to distinguish this heavy to glimpse Crick's "central dogma" in action. form (15N) from the normal light form (14N). Micrographs were obtained that showed newly synthesized RNA molecules branching off from Meselson and Stahl grew *Escherichia coli* in a transcribed region of DNA. Furthermore, a nutrient medium containing only 15N as a ribosomes could be seen already attaching to source of nitrogen. DNA replication introduced the growing RNA chains. Not only did electron the heavy isotope of nitrogen into the bacterial microscopy provide this comprehensive view of DNA. After 14 generations, the bacteria were gene expression, it also was about to produce placed into a medium that contained only 14N

critical insight into gene organization.

as a nitrogen source. During the subsequent

replication, the light isotope was incorporated

In 1977, the laboratories of Phillip Sharp

into the bacterial DNA.

and Richard Roberts independently used the

electron microscope to make a fundamental

Information about Using Technology to Study Cellular Teacher

and

Background

Molecular Biology

Information

Using T

about Energy

echnology to

Balance

Study Cellular and Molecular Biology

discovery about gene organization and expres-

to a manipulative one. In a similar way, the rise

sion. First in adenovirus, and later in eukary-

of structural biology is helping propel biology

otic DNA, it was shown that some genes are

toward another paradigm shift. Currently, over

interrupted by stretches of DNA that are not

500,000 human DNA sequences are contained
represented in the messenger RNA (mRNA).
in genetic databases. It is estimated that these
For example, DNA containing the gene for
may give rise to 160,000 targets for drug devel-
ovalbumin was denatured and hybridized to
opment.
ovalbumin mRNA. Electron micrographs of the
hybrid revealed regions of heteroduplex forma-

6 The Goal of This Supplement

tion alternating with a series of seven loops that
The goal of this curriculum supplement is to
corresponded to regions of genomic DNA that
help prepare high school biology students for
have complementary sequences in the mRNA.
the technological world they will inherit. This
The regions of a gene found in the mRNA are
is consistent with the *National Science Education*
called exons, because they are expressed in the
Standards. For example, Science and Technol-
gene product. Regions not found in the mRNA
ogy Content Standard E states, “As a result of
are called introns, because they are located in
activities in grades 9 to 12, all students should
between the exons.

develop . . . understandings about science and technology." A fundamental concept that underlies this standard is that science advances with technology. The origins and early development of molecular biology would not have been possible without the introduction of new technologies, and solving technological problems results in new scientific knowledge. New technologies also extend scientific understandings and introduce new areas of research.

These techniques, along with others, continue to be refined and extended to new areas of biology. As biology becomes more data intensive, it relies increasingly on biophysical techniques. The technologies presented in this supplement are new to most high school students. Very few students will have had much exposure to chemistry or physics, and students in your classes will be spending only about a week with this biophysical techniques such as X-ray diffraction, electron microscopy, and isotope labeling.

The completion of the Human Genome Project marks the end of the effort to decode the entire set of human genes. It also marks the unofficial start of the next phase of our continuing

supplement. A detailed understanding of each
quest to understand how genetics contrib-
technique should *not* be the primary objective of
utes to human health and well-being. Biology
the supplement. Rather, students should come
underwent a paradigm shift more than 30 years
away from it with an appreciation of some of the
ago after the discovery of restriction enzymes.
applications and implications of technology in
These enzymes are just tools, yet they helped
the study of cellular and molecular biology.
shift biology from a largely descriptive science

Glossary

angstrom: Unit of measurement defined as
probe: An exploratory device, especially one
1 × 10–10 meter and represented by the symbol
designed to investigate and obtain information
Å; a sheet of paper is about 1,000,000 Å thick.
about an unknown region or object.
bacteriophage: Viruses that infect bacteria.
radiofrequency radiation: Electromagnetic
waves with a wavelength of 1 millimeter to
bioinformatics: The study of the inherent struc-
30 meters.

ture of biological information and biological systems. It brings together biological data from

rational drug design: See target-based drug design.

genome research with the theory and tools of mathematics and computer science.

resolution: A measure of the ability of a system to form separate and distinct images of two

infectious agent: A living organism that enters objects of a given angular separation.

and multiplies in a host (that is, produces an infection); the infection can be without symp-

scale: A series of ascending and descending toms, or it can produce disease.

steps to assess the relative or absolute size of some property of an object. Scales can be linear

laser: A device that produces a narrow, power- or logarithmic.

ful beam of light.

spectroscopy: The study of the distribution of

magnetic field: A region in space created by a characteristic of a system or phenomenon, moving electrons (that is, an electric current); especially the distribution of energy emitted by this produces a force that causes other electrons

a system or the distribution of atomic or sub-

to move, thus creating another electric current.

atomic particles in a system.

micrograph: A graphic reproduction of the

striated muscle: Muscle tissue, such as skel-

image of an object formed by a microscope.

etal muscle, that is made up of long fibers and

is characterized by alternating light and dark

nanometer: Unit of measurement defined as

bands.

1 × 10–9 meter and represented by the abbrevia-

tion nm.

synchrotron: A name given to X-rays or light

produced by electrons circulating at nearly the

pathogen: An agent, such as bacteria, viruses,

speed of light. These can be used to investigate

and fungi, that produces disease.

atomic and molecular structure.

pathology: The study of disease or any condi-

target-based drug design: Also called rational

tion that affects the length or quality of life.

drug design, an approach based on the

development of molecules (potential drugs) to

X-ray: Electromagnetic energy having a wave-
interact specifically with a biological structure
length in the approximate range from 0.01 to
involved in disease. The biological structure
10 nanometers.
may be a pathogen, a product of the pathogen
(such as a protein), or a molecule (such as a
X-ray diffraction: The scattering of X-rays by
protein or other disease-causing molecule) of
crystal atoms that produces a pattern that yields
a host cell that interacts with a pathogen or a
information about the structure of the crystal.
pathogen product.
The wavelengths of X-rays are comparable in
size to the distances between atoms in most
technology: A body of knowledge used to cre-
crystals. X-ray diffraction is the basis of X-ray
ate tools, develop skills, and extract or collect
crystallography.
materials; the application of science (the combi-
nation of the scientific method and material) to
meet an objective or solve a problem.
wavelength: The distance between one peak of
a wave of light, heat, or other energy and the
next corresponding peak.

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4

Lesson 1

Engage

Explore

What Is Technology?

Explain

Overview

At a Glance

This lesson consists of two activities linked by classroom discussion. Its purpose is to engage students in the general topic of technology. The first activity involves classroom discussion and a short scenario to allow students to develop a sense of what technology is and to dispel the notion that technology relates mostly to computers. The second activity introduces students to the concept of scale by using the classroom to represent a cell and other smaller objects to represent subcellular components.

Major Concepts

Technology is a body of knowledge used to create tools, develop skills, and extract or collect materials. It is also the application of science (the combination of the scientific method and material) to meet an objective or solve a problem. Scale is a way to represent the relationship between the actual size of an object and how that size is characterized, either numerically or visually.

Objectives

After completing this lesson, students will

- be able to explain what technology is,
- recognize that human intervention is the common bond among technologies, and
- describe the use of **scale** to distinguish between objects of different size.

Teacher Background

See the following sections in Information about Using Technology to Study Cellular and Molecular Biology:

1 Introduction *(page 23)*

2 Major Preconceptions *(pages 23–24)*

3.1 Scale *(pages 24–25)*

43

Using Technology to Study Cellular and Molecular Biology

In Advance

Web-Based Activities

Activity

Web Version

1

No

2

No

Photocopies

Activity 1

none

Activity 2

Master 1.1, *Searching for Scale*, 1 copy per student

Materials

Activity 1

none needed

• meter stick

Activity 2

• rulers

• objects of various sizes (see Teacher note on page 49)

Preparation

Activity 1

No preparations needed.

Activity 2

No preparations needed.

Activity 1: ***Technology—What's It All About?***

Procedure

Tip from the field test: Activities 1 and 2 can be conducted in several ways. You can engage the class as a whole in discussion as directed. Alternatively, you can divide the class into groups of three to five students each, ask each group to consider the questions you ask, and then have each group provide its responses. It is also possible to have student groups consider only a limited number of the questions and then handle the remainder with the whole class. If you choose either of the last two approaches, you should limit the time allotted for groups to consider each question to several minutes. Field-testing indicated that no approach was superior to another.

Assessment: This activity is designed to engage students in learning about technology and to help the teacher assess the students'

1.

Begin by asking the class, “How do you define *technology*?”

prior knowledge of the

subject.

Accept all answers and write student responses on the board. Do not attempt to have students refine their definitions of technology at this point. They will revisit their definitions and refine them in

Step 5. Students, like older individuals, may harbor the preconception that technology relates mostly to computers. Through advertisements and media articles, they are familiar with the terms *information technology* and *computer technology*.

Teacher note: Asking this question requires students to call on their prior knowledge, and it engages their thinking. At this point, do not critique student responses. Appropriate teacher comments are short and positive, such as “good” and “what else?” Other appropriate teacher responses include, “Why do you believe that?” or “How do you know that?” Questions such as these allow the teacher to assess students’ current knowledge about the subject and to adjust lessons accordingly. They also provide a springboard to “Let’s find out” or “Let’s investigate.” In general, it is time to move forward when the teacher sees that thinking has been engaged.

2.

Ask students, “In general, what does technology do for us?”

This question may help students understand that technology helps

us solve problems, makes our lives easier, and extends our abilities to do things. Technology is used to develop skills or tools, both in our daily lives and in our occupations.

3.

Focus discussion on technologies that are relevant to each student's life. Ask students to look around the room. What technologies do they see? How do these technologies solve problems and make their lives easier?

Accept all responses and write them on the board. Students may mention any number of items. Some may be school-related, such as binders, backpacks, pens, pencils, paper, and paper clips. Other items may be more personal, such as water bottles, personal stereos, and hair clips. Students may neglect items such as shoelaces, zippers, buttons, fabric, eyeglasses or contact lenses, makeup, and bandages. Discussion should reinforce the notion that humans develop technology with a specific objective in mind. A related concept is that a given task requires the right tool or tools.

4.

Pick a technology that students have mentioned. Ask them what types of knowledge were required to develop that technology.

Students may not realize that technologies are generally developed by applying knowledge from multiple disciplines. For example, producing today's audio devices, such as a portable CD player, requires knowledge obtained from engineering, physics, mathematics, chemistry, and computer science.

5.

On the basis of previous discussions, ask students to rethink and refine their definition of technology (from Step 1).

Students should mention that technology is a way of solving problems through the application of knowledge from multiple disciplines.

6.

Tell students to imagine that they live in the Stone Age. Their only garment has been ripped and requires mending. How would they do it?

Students first should recognize that the ripped garment is a problem requiring a solution. They should consider what technologies they have available. The Stone Age was a period early in the development of human cultures when tools were made of stone and bone. Clothing consisted of animal skins or fabrics woven from threads derived from plant fibers. Bones and sharp reeds were used to make needles.

7.

Ask students how their approach to mending the garment would change as time advanced from the Stone Age to the present. What new knowledge would allow the development of new technology?

Student responses will vary, and some students may want to jump directly from the Stone Age to the modern sewing machine. Slow them down and have them consider incremental changes in knowledge that is driven by the need

Content Standard E:

Technological design

edge and technologies. They may cite the use of metals to fashion

to meet human needs

repair tools, like knives and finer needles. New knowledge of met-

and solve human

als and chemistry would help here. Later advances in engineer-

problems.

ing and mechanics would lead to the development of human-run

machines for assisting with repairs. Eventually, advances in physics

(electricity) and engineering led to the invention of modern sewing

machines. Similarly, advances in agriculture, chemistry, and engi-

neering produced better fabrics and threads. Students should derive

an understanding that technology advances through interactions

among multiple disciplines. While a problem may remain basically

the same over time (for instance, the need to make or repair cloth-

ing), advances in technology change how the problem is solved.

8.

Write the words *problem* and *technology* on the board. Ask students to use arrows to draw a graphic that represents the

relationship they believe exists between a problem and the tech-

nology to solve it.

Assessment:

Listening to students’

They can use arrows of any kind, and they should be prepared to

responses wil help you

defend their suggestions. The graphic should illustrate that a

assess their understand-

ing of the relationship
between problems and
technology.

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problem does not drive technology unidirectionally, nor does technology exist solely in search of a problem to solve. Rather, these two areas exist to support and drive one another. Solving problems does require the development of new technologies, which can then be applied to other problems. A graphic to depict this indicates the cyclic relationship between the two:

Activity 2: *Searching for Scale*

1.

Biological molecules are small, but how small *is* "small"? Ask students these two questions:

a.

How do biological structures, such as cells, organelles, bacteria, and viruses, compare in size with one another?

b.

How do molecules compare in size with biological structures such as cells, organelles, bacteria, and viruses?

Accept all responses and write them on the board. Students will explore these size relationships in the next steps.

2.

Tell students that they will now investigate the relative sizes of different biological structures and see how close their estimates of relative size were.

3.

Give each student a copy of Master 1.1, *Searching for Scale*. Work with the class to complete column 3, Size relative to cell.

The table with column 3 completed is as follows:

Biological

Actual

Size

Object

Mea-

Size

Structure Diameter Relative to Cell

Used to

sured

Relative

(in

Model

Size of to Model

Meters)

Biological Model Cell (the

Structure

Object

Room)

Cell

1 × 10–5

1 × 10–5

Room

10 m

10

= 1

= 1

1 × 10–5

10

Bacterium 1 × 10–6

1 × 10–6

Desk

1 m

= 1

1 = 1

1 × 10–5

10

10 10

Mitochon- 5 × 10–7

5 × 10–7

0.5 m

= 1

drion

1 × 10–5

20

Virus

1 × 10–7

1 × 10–7

0.1 m

= 1

1 × 10–5 100

(10 cm)

Ribosome 1 × 10–8

1 × 10–8

0.01 m

= 1

1 × 10–5 1,000

(1 cm)

Protein

5 × 10–9

5 × 10–9

0.5 cm

= 1

1 × 10–5 2,000

Glucose

1 × 10–9

1 × 10–9

0.1 cm

=

1

molecule

1 × 10–5 10,000

(1 mm)

H2O

1 × 10–10 1 × 10–10

0.1 mm

=

1

molecule

1 × 10–5 100,000

4.

Tell students that the information in columns 2 and 3 each can

be used to construct *scales* to describe the sizes of the different biological structures in the table. Ask students to define *scale*.

Accept all answers and write them on the board. Guide discussion

Content Standard A:

so that students realize that scale is a way to represent the relation-

Mathematics is essen-

ship between the actual size of an object (for example, its length or

tial in all aspects of

mass) and how that size is characterized either numerically or visu-

scientific inquiry.

ally. A scale is a series of ascending and descending steps to assess

either some relative (column 3) or absolute (column 2) property of

an object. In this case, the property being investigated is size.

5.

Ask students to try to visualize the 100,000-fold difference in size between a cell and a water molecule. Can they do it? How could they demonstrate this large size difference more easily?

Master 1.1, *Searching for Scale* provides the necessary clues for students, since the heading of column 4 is *Object used to model biological structure*. Students can use larger structures, such as a room, to model smaller ones, such as a cell, to make size differences more apparent and bring them into the realm of common experience.

6.

Ask two students to use a meter stick to mark approximately 10 m along both the length and width of the classroom.

It is okay if the classroom does not allow 10 m to be measured in either or both directions. A distance of 7 to 9 m will still make the point visually. However, for ease of calculations to follow, use room dimensions of 10 m even if the actual dimensions are smaller than that.

7.

Tell students that the space defined by 10 m wide, 10 m in

length, and the height of the room now represents a cell. In other words, this space is now a *model* for a typical cell.

8.

Organize students into pairs and give each pair a ruler.

9.

Tell students that they will be searching the classroom for objects that model the biological structures on Master 1.1,

Content Standard A:

Searching for Scale.

Recognize and analyze alternative explana-

Explain that they will be looking for objects that have the same size relative to the model cell (the room) that the actual biological structure has to a real cell.

tions and models.

10. Ask students to look at the last three columns on Master 1.1, *Searching for Scale*. As an example, a desk measuring 1 meter high is provided as a model for a bacterium. Important points are as follows:

Assessment:

Circulate around the room, noting whether

1

a.

A bacterium is the size of an actual cell (column 3).

10

students understand

1

b.

Similarly, the desk is

10 the size of the model cell, the

the mathematics

room (1 m compared with 10 m; columns 4 and 5).

involved in scaling

objects for this activity.

c.

Because it is of the correct scale, the desk can be used to

model a bacterium if a cell is modeled by a room 10 m

across.

11. Instruct student pairs to locate items in the classroom that can

be used to model the biological structures listed on Master 1.1,

***Searching for Scale*. They should enter their results in columns 4,** Assessment:

5, and 6 of the master. Allow 15 minutes for this activity.

Listening to student

responses will help

Students may approach this activity in different ways. Some may

you assess their under-

find it useful to determine the size of the object they are looking

standing of scale and

for first by multiplying the ratio in column 3 by 10 m. Some stu-

modeling. Collecting

dents may begin by locating objects, measuring them, and then

their completed tables

determining whether they meet the size requirements.

(Master 1.1, *Search-*

ing for Scale) allows

Teacher note: It is helpful to have objects available in the class-

a more formal oppor-

room that will meet the size requirements for modeling the bio-

tunity to evaluate stu-

logical structures in Master 1.1. Objects, such as erasers, marbles,

dents' understanding.

fine- and ultrafine-tip pencils or pens, pieces of candy, an inflated

balloon, balls of different sizes, and other easily obtained materi-

als, ensure that students will be able to find something to serve as a

model for each structure.

12. Ask student pairs to share some of their results with the class.

Students should realize that the size ratios in columns 3 and 6 are

the same. In other words, modeling allows *relative* sizes to be stud-

ied, although the *actual* sizes of the real biological structure and its

model differ quite a bit.

Discussion Questions

1.

If a cell of 1 × 10–5 m (10 × 10–6 m, or 10 µm) diameter is represented by a room 10 m across, what distance would represent a human 2 m tall?

First, as in column 3 of Master 1.1, *Searching for Scale*, derive the relationship between the size of the human and the size of the cell:

2 meters ÷ (1 × 10–5 meter) = 2 × 105.

Thus, a 2-m-tall individual is 2 × 105 times larger than a cell 1 × 10–5 m in diameter.

If the cell is represented by a distance of 10 m, the 2-m-tall individual would be represented by a distance of

10 m × (2 × 105) = 2 × 106 m (2,000 km, or 1,250 miles)

As a reference, this distance is the same as that from Boston to Miami, Kansas City to Boston, or Los Angeles to Dallas. This calculation is intended to provide a "wow" for the students, and they derive an understanding of the difference in size between a human and a molecule (in this example, the difference between 2,000,000 m for the human and 2 to 5 mm for a protein). This should help students understand the need for specialized technologies for studying living systems at the cellular and molecular levels.

2.

As a lead-in to Lesson 2, write the following terms on the board in random order: Eye; Light Microscopy; Electron Microscopy; X-ray Techniques. Ask students to speculate on which technology (or technologies) could provide useful information about the

objects on Master 1.1, *Searching for Scale*. What would make one technology more useful than another in any given situation?

Students should realize that naked-eye observation is useful only for relatively large objects and is not useful at all for discerning cellular and subcellular objects. They also will realize that light microscopy is useful for looking at cells and resolving some

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organelles, like the nucleus and vacuoles. Students should know from material in their texts that electron microscopy is used to provide details about cells and subcellular structures. Some may have seen electron micrographs of DNA. Most students know little about X-ray technologies, although they may have heard of X-ray crystallography as a technique that was used to help resolve the structure of DNA. If students have ideas about why certain technologies are better for some tasks than others, write those responses on the board. Indicate that the reason for having the right tool for the right task is addressed in Lesson 2.

51

Student

Student L

L essons

esson 1

How Your

Using T Brain Understands

echnology to Study What Your

Cellular Ear

and Hears

Molecular Biology

Lesson 1 Organizer

Activity 1: *Technology—What's It All About?*

What the Teacher Does

Procedure Reference

Ask students,

Pages 44–45

• "What is technology?"

Steps 1–2

• "In general, what does technology do for us?"

Focus discussion of technologies relevant to each student's life.

Pages 45–46

• Ask students to look around the room; what technolo-

Steps 3–5

gies do they see?

• How do these technologies solve problems and make

their lives easier?

• Pick a technology mentioned. Ask students what types of

knowledge were required to develop that technology.

• After discussion, ask students to rethink and refine their

definition of technology.

Tell students to imagine that they live in the Stone Age. Their

only garment is ripped and requires mending. Ask,

Steps 6–7

• “How would you mend the garment?”

• “How would your approach to mending the garment change as time advanced from the Stone Age to the present?”

• “What new knowledge would allow the development of new technology?”

Write the words *problem* and *technology* on the board. Ask

Page 46

students to use arrows to draw a graphic that represents the

Step 8

relationship they believe exists between a problem and the technology needed to solve it.

Activity 2: *Searching for Scale*

What the Teacher Does

Procedure Reference

Ask students,

Page 47

• “How do biological structures, such as cells, organelles,

Step 1

bacteria, and viruses, compare in size with one another?”

• “How do molecules compare in size with biological structures such as cells, organelles, bacteria, and viruses?”

Tell students that they will investigate the relative sizes of differ-

Pages 47–48

ent biological structures.

Steps 2–5

• Give each student a copy of Master 1.1, *Searching for Scale.*

• Work with the class to complete column 3, Size relative to cell.

• Ask students to define *scale* based on the information in columns 2 and 3.

• Ask students if they can visualize the 100,000-fold difference in size between a cell and a water molecule. How could they demonstrate this large size difference?

• Ask two students to measure and mark approximately

Pages 48–49

10 m along both the length and width of the classroom.

Steps 6–7

• Tell students that the space defined by 10 m wide, 10 m in length, and the height of the room is a model for a typical cell.

Organize students into pairs.

Pages 49–50

• Give each pair a ruler.

Steps 8–11

• Tell students that they will be searching the classroom for objects that model the biological structures on Master 1.1, *Searching for Scale.*

• Tell students to use the information provided in the last three columns of Master 1.1 to help in their search.

• Instruct students to complete the last three columns of Master 1.1 as they locate appropriate objects.

Ask students to share some of their results with the class.

Page 50

Step 12

= Involves copying a master.

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Student Lesson 1

Lesson 2

Explore

Explain

Resolving Issues

Overview

At a Glance

This lesson consists of two activities linked by classroom discussion. In the first activity, which is similar to the game Battleship, students investigate the concept of resolution and the relationship between probe size and resolution. The second activity incorporates results from the first activity and classroom observation and discussion. Students discover that

in order to understand the complete structure of an object, it is necessary to have information in three dimensions rather than just two.

Major Concepts

Doing research in cellular and molecular biology requires scientists to identify the right technology (tool) for the job. An important consideration is the technology's ability to resolve structural details of biological objects. Two objects can be resolved by using a probe (radiation) of a size (wavelength) that is not larger than the distance separating the objects. Generally, the smaller the probe, the greater the structural detail, or resolution, that results. Detailed structural knowledge about biological objects requires information obtained in three dimensions.

Objectives

After completing this lesson, students will

• be able to define resolution,

• be able to explain the relationship between probe size and resolution, and

• be able to explain why information in three dimensions is necessary to describe the structure of an object.

Teacher Background

See the following sections in Information about Using Technology to Study Cellular and Molecular Biology:

3.1 Scale *(pages 24–25)*

3.2 Resolution *(pages 25–26)*

In Advance

Web-Based Activities

Activity

Web Version

1

No

2

Yes

Photocopies

Activity 1 • Master 2.1, *Probing for Answers Score Sheet*, 1 copy per 2

students; 1 transparency for classroom demonstration

• Master 2.2, *Probes*, 1 copy per 12 students (see

Preparation)

• Masters 2.3 to 2.8, *Probing for Answers—Levels 1–6*,

1 copy of each per 12 or fewer students; 2 copies of each

for 13–24 students; 3 copies of each for 25–36 students

Activity 2

• Master 2.9, *Solution to Probing for Answers*, 1 transparency

(*print version* only)

Materials

Activity 1 manila folders (1 per group, optional)

Activity 2

• 2 hard-crusted bread rolls, unsliced

• knife to slice bread

• food coloring

• syringe with needle, or 1-mL pipette

Preparation

Activity 1

From Master 2.2, *Probes*, cut out each 3 × 3, 2 × 2, and 1 × 1 square (1 copy produces 6 of each size of probe).

Activity 2

Just before the class period in which students will do this activity, inject a small amount of colored food dye into two locations in each of two unsliced, hard-crusted bread rolls. One location should be to the right of center and the other, to the left of center. The same or different dye colors can by used. Injecting the dye can be accomplished several ways to meet the primary objective, which is to color the inside and not the outside of each roll. Use either a syringe with a needle long enough to reach well into the roll or a carefully inserted 1-mL pipette. Wipe the outside surface of the needle or pipette to remove any dye solution before inserting it into the roll. It may help to use a sharp object, such as the sharp, pointed portion of a compass, to make a small hole before inserting a pipette containing dye. Try not to leave traces of the dye on the outside of the rolls.

If you have Internet access, have at least one computer at the URL *http://science.education.nih.gov/supplements/technology/student.* This is a main menu page from which you can access this activity.

Activity 1: *Probing for Answers*

Procedure

1.

Begin by stating or writing on the board, “Technology is a means of extending human potential or of extending human senses.” Ask students to raise their hands if they agree with this statement.

2.

Ask students to provide justification for their responses. Can students relate specific technologies to the extension of specific

Assessment:

human attributes or senses?

Steps 1 to 5 are intended to be a quick method to assess students’ prior conceptions about the use of technology in biological science.

Students will generally agree that technology extends human potential. Obvious examples include the wheel and other transportation innovations that extend our potential for movement, and electronic devices, such as TV, radio, and telephones, that extend our ability to communicate. Microscopes, telescopes, eyeglasses, and contact lenses extend and enhance our sense of vision. Computers and written materials can be seen as ways to extend memory. There are many other examples.

Tip from the field test: Some students correctly pointed out that technology is also used to extend animal potential.

3.

Ask students to consider only technologies that have increased our understanding of living systems. Do they extend any human attributes? If they do, which attributes are extended?

Students will probably focus on those that extend vision, since they are the easiest to recognize. Examples could include radar, eyeglasses, contact lenses, and telescopes. Students also know that microscopes allow us to see objects that we cannot see with the naked eye. Students should be familiar with the light microscope, and many may have heard of electron microscopes. Through figures in textbooks, they may know X-ray crystallography as a technology that helped us "see" the structure of DNA. Other technologies might be mentioned. Accept all responses and write them on the board. This is an opportunity to identify students' current understanding of these technologies.

A Gary Larson Far Side cartoon, "Early Microbiologists," can be used to engage students. Pictured is a caveman "laboratory," in which several cavemen peer intently into Petri dishes filled with agar. Since they do not have microscopes, they hold the dishes in various ways, such as very close to the face. One of the cavemen

imitates binoculars by holding his hands to his eyes. (The cartoon can be found in several published works, including *The Prehistory of the Far Side,* by Gary Larson, copyright 1989 by FarWorks, Inc., distributed by Universal Press Syndicate, published by Andrews McMeel, Kansas City, Kansas.)

4.

Ask students to focus on technologies as tools that allow us to "see" biological objects (the eye, microscopes of all kinds, and X-ray techniques). *One at a time,* ask the following questions:

a.

What technologies would you use to study a whole (intact) organism and why?

b.

What technologies would you use to study cells and why?

c.

What technologies would you use to study molecules and why?

Accept all reasonable responses, but challenge those that are incorrect. Students should understand that no single technology is useful at all levels of organization of biological organisms. In other words, no single technology is able to resolve structural details from the intact organism to the molecules that make up that organism. This discussion introduces students to the idea that there is a right tool for the job.

5.

Ask students why a single technology cannot provide information at all levels of organization of biological organisms.

You might remind students that at the conclusion of Lesson 1, they were asked to speculate on what would make one technology more useful than another in a given situation. If students need prodding, you can ask whether they would use a microscope to study a whole organism, or whether they would use their eyes alone to study molecules. While a microscope is required to study single-celled organisms, such as bacteria and protists, most multicellular organisms can be observed with the unaided eye. High-resolution technologies, such as X-ray crystallography, are required for investigations of molecular structure.

Content Standard A:
Identify questions and concepts that guide scientific investigations.

6.

Tell students that what makes some technologies better than others for a given job relates to the concept of "resolution." Ask them what *resolution* means.

Tip from the field test: Students generally had no concept of resolution as it relates to technologies used in biological science. Responses often related to resolution of computer monitors, personal resolve, or New Year's resolutions.

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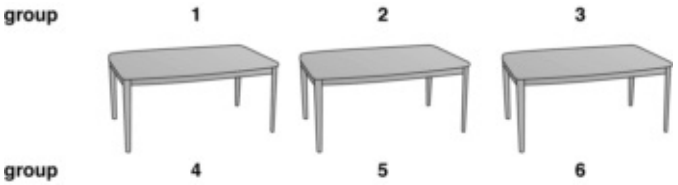

7.

Tell students that they will investigate resolution. Organize the class into groups of two and then pair two groups.

This activity works best if you have a minimum of six groups so that each can receive one of the six Masters 2.3 through 2.8.

8.

Ask groups to arrange their seating so that one is directly opposite another:

Allow sufficient room between tables so that groups do not interfere with one another.

9.

Explain to the class that this activity resembles the game Battleship, with which some of them might be familiar. Each group's task is to locate and define the shape of an object or objects on the master held by the opposing group.

Tip from the field test: Field-testing indicated the need to point out that this activity is not exactly like Battleship. Students do not "sink" or "destroy" an opposition's force. Rather, they use the Battleship strategy to locate and define the shape of a shaded region or regions on the master held by an opposing group.

10. Give each group a copy of Master 2.1, *Probing for Answers Score Sheet.*

Students use this sheet to record hits and misses as they probe for the location of the opposing group's shaded region(s).

11. Randomly color several regions on a transparency of Master 2.1, *Probing for Answers Score Sheet*. Use this transparency and a 3 × 3 probe from Master 2.2, *Probes*, to demonstrate how this activity is done.

a.

Use this probe to locate areas 3 squares by 3 squares on the transparency. To save time, you may instruct students to probe only the nine nonoverlapping 3 × 3 regions, as shown on the following diagram:

b.

One group begins by calling out the location of the 3 × 3 area they wish to probe, such as A-C, 1-3.

c.

If the opposing group's Master (2.3, 2.4, 2.5, 2.6, 2.7, or 2.8) has a shaded square within the area called, they indicate this as a hit; if not, a miss.

d.

The first group records the result on their score sheet. Draw an X in 3 × 3 squares that are misses, and put an O in the 3 × 3 squares that are hits.

e.

It is then the opposing group's turn to select an area to probe, which is then recorded as a hit or a miss.

f.

Groups take turns trying to locate the opposing group's shaded squares.

12. Give each group a copy of *one* master selected from Masters 2.3 to 2.8. Instruct groups to hide this master from their opposing group.

Make sure that each of these six masters is used by at least one group. In larger classes, the same master may be used by more than one group. You may choose to place each master in a manila folder. Students can use the folder in various ways (for instance, opened and stood on its edge) to keep their master from being seen by the opposing group.

13. Give each group a 3 × 3 probe from Master 2.2, *Probes*. Instruct students to use this probe to locate areas 3 squares by 3 squares that contain the opposing group's shaded area(s).

Limit the time allowed for this portion of the activity to no more than five minutes.

14. Ask students whether they believe they have gathered enough information to specify the *exact* shape(s) and location(s) of the opposing group's shaded object(s).

Make sure students in opposing groups do not share information about their shaded patterns. Students should realize from look-

ing at their own shaded pattern that the 3 × 3 probe is too large to identify the shape and location of smaller objects; that is, the large probe cannot resolve the size and shape of the smaller objects.

15. Ask students what would help them define the shape and location of the opposing group's shaded object(s).

A smaller probe is required.

Tip from the field test: Field-testing indicated the importance of having students come to this conclusion on their own.

16. Next, give each group a 2 × 2 probe. Groups are to focus on those areas that were determined to be hits with the larger probe.

Students are to repeat with this probe what they did earlier (see Step 13 above) and try to determine the structure and location of the opposing group's shaded pattern. Limit the time allowed for this portion of the activity to no more than several minutes.

17. Ask students whether they believe they now have enough information to specify the exact shape(s) and location(s) of the opposing group's shaded object(s).

Make sure students in opposing groups do not share information about their shaded patterns. At this point, some students may believe they have sufficient information to predict the pattern held by the opposing group. Ask those willing to speculate on the opposing group's pattern to provide their justification, especially how they know that all four squares in a 2 × 2 "hit" region are shaded.

18. Next give each group a 1 × 1 probe.

Students should focus only on those areas determined to be hits with the 2 × 2 probe. They should continue to define the structure and location of the opposing group's shaded pattern. Limit the time allowed for this portion of the activity to no more than several minutes.

19. Ask students if they believe they now have gathered enough information to specify the exact shape(s) and location(s) of the opposing group's shaded objects. Do they need another probe to complete the task?

Students should justify their responses. Students cannot know for sure what the opposing group's pattern looks like, even though they see that their own pattern is composed of 1 × 1 squares. If they speculate that the opposing group's pattern is constructed similarly, then no additional probes are required, since the objects

being resolved (the 1 × 1 squares, both shaded and unshaded) are the same size as the final probe. Importantly, the final probe is not larger than the objects being resolved. If students believe that additional probes are required, they should justify this based on what they believe to be the size of the objects being resolved (shaded and unshaded). Their suggestion for an additional probe should indicate a probe size no larger than that of the objects being resolved. No matter what the response, ensure that students derive a general relationship between probe size and the size of the objects being resolved before proceeding. They should be able to explain that the size of the probe should be no larger than the objects being resolved.

20. Have opposing groups confirm that after using the series of three probes, they were able to determine the correct pattern on one another's master.

Assessment:

Listening to students explain their answers, defend their reasoning, and modify their responses after listening to other students

Discussion Questions

1. Why not use the smallest probe first?

explain their logic will

A similar question is, Is there an advantage to using larger probes

help you assess stu-

first and then using smaller probes? The larger probes allowed the

dents' understanding

students to quickly identify the general location of the object(s)

being investigated. In some cases, even information about struc-

of resolution.

ture, albeit crude, can be obtained. Remind students of the pro-

cedure they follow when using a light microscope. They first use

the lowest magnification to locate the object of interest and then

switch to a higher magnification to gain more information. Using

the smallest possible probe first can be time consuming and expen-

sive. In some cases, using the smallest available probe also can be

inappropriate; for example, when the probe is very much smaller

than the objects being resolved. As an example, consider the time

and expense involved in using an electron microscope rather than a

light microscope to count yeast cells or to assess fruit fly traits in a

genetics experiment.

2.

On the board, write these wavelengths:

- **visible light, 4 to 7 × 10–7 m;**
- **electrons, 2.7 to 0.9 × 10–10 m; and**

•

X-rays, 1 × 10–8 to 1 × 10–11 m.

Refer to Master 1.1, *Searching for Scale,* and ask students which 62

6

of these they think would be appropriate probes (that is, provide the appropriate level of resolution) for the objects listed.

Visible light could be used to resolve cells, bacteria, and mitochondria. Longer-wavelength electrons are potential probes for viruses, small cell organelles such as ribosomes, and large molecules such as proteins. Shorter-wavelength electrons and short-wavelength X-rays are potential probes for molecules, even small ones like glucose. They also may be used to resolve adjacent atoms in molecules (which requires probes smaller than 2 × 10–10 m).

Teacher note: Whether or not a probe is useful in a given situation also depends on whether the technology actually exists to make use of the probe. For instance, are appropriate sample-preparation techniques available? Are appropriate sample handling technologies available (for example, can the sample be rotated if necessary, and in a way that does not interfere with the rest of the procedure)? Can the probe be focused sufficiently? Is there technology to view and evaluate the results of such analyses?

Activity 2: *More Than Meets the Eye*

1.

Begin by holding one of the bread rolls up to the class. Make sure that no dye is showing. Ask students to describe what they see.

Students will recognize the object, and they may describe it by noting its color, shape, and apparent external texture. They should indicate that the roll is a three-dimensional object.

2.

Do students have maximum information about the roll? Is there anything they do not know about the bread roll from just looking at it?

Student responses will vary from, “Is it tasty?” and “Where does it come from?” to “What is inside?” Some students may realize that although they might have made an assumption about the roll’s interior (for example, it is just plain bread), they actually know nothing about what is under the crust.

3.

Focus discussion on what is inside the bread roll. Ask students how they would get that information.

Students will suggest cutting or tearing the roll.

4.

Slice the roll to reveal the presence of dye in one of the two dye locations. Hold the roll so the class can see

the two cut edges. Do the students now feel they have complete information about this object? If not, what questions do they have?

Even though they know there is a dyed region inside the roll, students should realize that they do not know what this region looks like. What is the shape of the dyed region and how far does it extend in any given direction? Is there only a single dyed region, or are there multiple regions? If there is more than one dyed region, is it the same color as the region they can see?

Tip from the field test: Some students suggested cutting the roll as one would if making a sandwich. The second bread roll is helpful if this possibility is raised.

5.

Ask students how they could obtain information to answer these questions.

A simple approach would be to make additional slices in the roll. Students may suggest more exotic means (for example, use a fiber optic light source connected to a minivideo device to view the roll's interior on a remote screen). If suggestions fall in the latter category, congratulate students for their ingenuity. Ask them to think about how to gain the information required quickly and using

simple, available technology. In the end, focus student attention on increasing the number of slices. This requires only a knife and can be done quickly.

6.

Ask the students how many slices would be required to define the dyed region(s) in the roll's interior. What are their considerations in providing an answer to this question?

The actual number of slices that the students believe is correct is not the important issue. If students do provide a specific answer, ask them to justify it. It is important for them to understand the following. First, multiple slices *are* required to define the object's properties. The *size* of the slices will determine the resolution used to define the object's properties. Thicker slices will provide less resolution, just as the 3 × 3 probes provided low resolution in Activity 1. Thinner slices will provide greater resolution, just as the 1 × 1 probes did in Activity 1.

7.

Ask students to have their group's Master 2.3 to 2.8 available. Explain that the "level" designation below the grid (Level 1, 2, 3, 4, 5, or 6) on the master indicates the location of a slice through an object.

Level 1 is the top slice, followed by 2, 3, 4, 5, and 6 (at the bottom).

8.

Ask students to visualize their pattern in three dimensions by imagining that their shaded pattern represents the top of a stack of gray blocks. Their level is a slice two blocks thick.

9.

Ask the groups to share their data (that is, the location of the shaded regions) and try to reconstruct the three-dimensional object that has been cut into six slices.

Do not provide additional guidance. Give students about five minutes to do this. Students may or may not be able to reconstruct the object in this time.

For those using the* Web version *of this activity, proceed as follows:

10. Were students able to arrive at a solution? What might have made the task of reconstructing the object in three dimensions easier?

Content Standard E:

Identify a problem or

Students might suggest that a computer could provide the technol-

design an opportunity.

ogy to make reconstruction easier.

Content Standard E:

11. Have students proceed to the URL *http://science.education.nih.gov/*

Implement a proposed

***supplements/technology/student*. Students should then click on the** solution.

link to "Lesson 2—Solution to Probing for Answers." This brings

up the unit's desktop, from which students can access this activity. Content Standard A: **12. Students can enter their data by first selecting a level (1 to 6) and** Scientists rely on tech-then clicking on the squares they determined to be shaded. The

nology to enhance

reconstructed object will appear as data are entered.

gathering and manipu-

lating data.

It may be easier and less time consuming for the teacher to enter

the data provided by the students.

For those using the* print version *of this activity, proceed as

follows:

10. Show students a transparency of Master 2.9, *Solution*

***to Probing for Answers*. Were they able to arrive at this**

Content Standard E:

solution? What might have made their task easier?

Identify a problem or

design an opportunity.

Some students do well thinking in three dimensions, and others do

not. Many may recognize the need for additional technology, such

as a computer and appropriate software, to make the job of recon-

struction easier. Even a simple technology, such as wooden blocks

or Legos, could have been used to construct a three-dimensional

model of the intact object.

Student

Student L

L essons

esson 2

How Your

Using T Brain Understands

echnology to Study What Your

Cellular Ear

and Hears

Molecular Biology

Discussion Question

1.

As a follow-up, ask students, “Have these activities expanded your understanding of technology? If they have, how?”

Assessment:

Activity 1 demonstrates the use of multiple probes to achieve dif-

This question allows

ferent levels of resolution. It also demonstrates that the right tool,

students to integrate

in this case a probe of appropriate size, must be selected to solve a

the information they

problem (resolving the structure of an unknown object). Therefore,

have learned in the

students should realize that there is an appropriate technology for

first two lessons and

a given problem (that is, the right tool for the job). Activity 2 dem-

refine their under-

onstrates that solutions to a problem may involve more than one

standing of what tech-

technology (the use of slices to determine the structure of a three-

nology is.

dimensional object and technologies to collect and analyze the data).

Lesson 2 Organizer: Web Version

Activity 1: *Probing for Answers*

What the Teacher Does

Procedure Reference

State or write on the board, “Technology is a means of extend-

Pages 57–58

ing human potential or of extending human senses.”

Steps 1–3

• Ask students if they agree with this statement.

• Ask students to provide justification for their responses.

Can they relate specific technologies to the extension of

specific human attributes or senses?

• Ask students to consider technologies that have

increased our understanding of living systems.

o Do they extend any human attributes?

o If they do, which attributes are extended?

Ask students to focus on technologies (the eye, microscopes,

Page 58

X-ray techniques) that allow us to see biological objects. Ask,

Steps 4–6

• “What technologies would you use to study a whole organism and why?”

• “What technologies would you use to study cells and why?”

• “What techniques would you use to study molecules and why?”

• “Why can’t a single technology provide information at all levels of organization of biological organisms?”

Introduce the concept of resolution. Ask students what resolution means.

Tell students that they will investigate resolution. Organize the

Pages 59–60

class into groups of two and then pair two groups.

Steps 7–11

• Arrange seating so that one group sits opposite the other.

• Explain that the activity resembles the game Battleship.

• Each group’s task is to locate and define the shape of an object or objects on the master held by the opposing group.

• Give each group a copy of Master 2.1, *Probing for*

Answers Score Sheet.

• Use a transparency of this master to demonstrate how

the activity is done.

67

Student

Student L

L essons

esson 2

How Y

Using our

T Brain Understands

echnology to Study What Your

Cellular Ear

and Hears

Molecular Biology

Begin the activity.

Pages 60–62

• Give each group one master selected from Masters 2.3

Steps 12–20

to 2.8, *Probing for Answers—Levels 1–6.*

• Give each group a 3 × 3 probe from Master 2.2, *Probes*.

Instruct students to use this probe to locate areas 3

squares by 3 squares that contain the opposing group's

shaded object(s).

• After five minutes, ask students if they have enough

information to specify the exact shape(s) and location(s) of the opposing group's shaded object(s).

• Ask students what would help them define the shape and location of the opposing group's shaded object(s).

• Give each group a 2 × 2 probe and ask them to refine their search with this probe.

• After several minutes, ask students if they believe they now have enough information to specify the exact shape(s) and location(s) of the opposing group's shaded object(s).

• Give each group a 1 × 1 probe and ask them to refine their search with this probe.

• After several minutes, ask students if they believe they now have enough information to specify the exact shape(s) and location(s) of the opposing group's shaded object(s). Do they need another probe to complete their task?

• Have opposing groups confirm that after using the series of three probes, they were able to determine the correct pattern on one another's master. Proceed to discussion questions.

Activity 2: *More Than Meets the Eye*

What the Teacher Does

Procedure Reference

Hold a bread roll into which you have inserted food dye up to

Pages 63–64

the class.

Steps 1–6

• Ask students to describe what they see.

• Is there anything about the roll they do not know from just looking at it?

• Focus discussion on what is inside the roll and ask students how they would get that information.

• Slice the roll to reveal the dye.

• Ask students if they feel that they now have complete information about the object.

• What additional questions do they have and how could they get the answers?

• How many slices are required to define the dyed region(s) in the roll's interior? Focus discussion on resolution.

68

Ask students to have their Master 2.3 to 2.8 available.

Pages 64–65

• Explain that the "level" designation on the master indi-

Steps 7–10

cates the location of a slice through an object (1 at the top to 6 at the bottom).

• Ask students to visualize their pattern in three dimensions by imagining that their shaded pattern represents

the top of a stack of grey blocks. Their level is a slice two blocks thick.

• Ask the groups to share their data (that is, the location of the shaded regions) and try to reconstruct the three-dimensional object that has been cut into six slices.

• Ask if students were able to arrive at a solution. What might have made their task easier?

Have students click on “Lesson 2—Solution to Probing for

Answers” and then click on the link to “Solution to Probing Steps 11–12 for Answers.” Have students enter their data to reconstruct the object.

= Involves copying a master.

= Involves using the Internet.

= Involves using a transparency.

Student

Student L

L essons

esson 2

How Y

Using our

T Brain Understands

echnology to Study What Your

Cellular Ear

and Hears

Molecular Biology

Lesson 2 Organizer: Print Version

Activity 1: *Probing for Answers*

What the Teacher Does

Procedure Reference

State or write on the board, “Technology is a means of extend-

Pages 57–58

ing human potential or of extending human senses.”

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• Ask students if they agree with this statement.

• Ask students to provide justification for their responses.

Can they relate specific technologies to the extension of

specific human attributes or senses?

• Ask students to consider technologies that have

increased our understanding of living systems.

o Do they extend any human attributes?

o If they do, which attributes are extended?

Ask students to focus on technologies (the eye, microscopes,

Page 58

X-ray techniques) that allow us to see biological objects. Ask,

Steps 4–6

• “What technologies would you use to study a whole

organism and why?”

• “What technologies would you use to study cells and why?”

• “What techniques would you use to study molecules and why?”

• “Why can’t a single technology provide information at all levels of organization of biological organisms?”

Introduce the concept of resolution, Ask students what resolution means.

Tell students that they will investigate resolution. Organize the class into groups of two and then pair two groups.

Pages 59–60

Steps 7–11

• Arrange seating so that one group sits opposite the other.

• Explain that the activity resembles the game Battleship.

• Each group’s task is to locate and define the shape of an object or objects on the master held by the opposing group.

• Give each group a copy of Master 2.1, *Probing for Answers Score Sheet.*

• Use a transparency of this master to demonstrate how the activity is done.

Begin the activity.

Pages 60–62

• Give each group one master selected from Masters 2.3

Steps 12–20

to 2.8, *Probing for Answers—Levels 1–6*.

• Give each group a 3 × 3 probe from Master 2.2, *Probes*. Instruct students to use this probe to locate areas 3 squares by 3 squares that contain the opposing group's shaded object(s).

• After five minutes, ask students if they have enough information to specify the exact shape(s) and location(s) of the opposing group's shaded object(s).

• Ask students what would help them define the shape and location of the opposing group's shaded object(s).

• Give each group a 2 × 2 probe and ask them to refine their search with this probe.

• After several minutes, ask students if they believe they now have enough information to specify the exact shape(s) and location(s) of the opposing group's shaded object(s).

• Give each group a 1 × 1 probe and ask them to refine their search with this probe.

• After several minutes, ask students if they believe they now have enough information to specify the exact shape(s) and location(s) of the opposing group's shaded object(s). Do they need another probe to complete their task?

• Have opposing groups confirm that after using the series of three probes, they were able to determine the correct pattern on one another's master. Proceed to discussion questions.

Activity 2: *More Than Meets the Eye*

What the Teacher Does

Procedure Reference

Hold a bread roll into which you have inserted food dye up to

Pages 63–64

the class.

Steps 1–6

• Ask students to describe what they see.

• Is there anything about the roll they do not know from just looking at it?

• Focus discussion on what is inside the roll and ask students how they would get that information.

• Slice the roll to reveal the dye.

• Ask students if they feel that they now have complete information about the object.

• What additional questions do they have and how could they get the answers?

• How many slices are required to define the dyed region(s) in the roll's interior? Focus discussion on resolution.

Student

Student L

L essons

esson 2

How Y

Using our

T Brain Understands

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Cellular Ear

and Hears

Molecular Biology

Ask students to have their Master 2.3 to 2.8 available.

Pages 64–65

• Explain that the “level” designation on the master indi-

Steps 7–10

cates the location of a slice through an object (1 at the top to 6 at the bottom).

• Ask students to visualize their pattern in three dimensions by imagining that their shaded pattern represents the top of a stack of grey blocks. Their level is a slice two blocks thick.

• Ask the groups to share their data (that is, the location of the shaded regions) and try to reconstruct the three-dimensional object that has been cut into six slices.

• Show students a transparency of Master 2.9, *Solution to*

Probing for Answers.

• Ask if students were able to arrive at this solution. What might have made their task easier?

= Involves copying a master.

= Involves using a transparency.

72

Lesson 3

Explore

Explain

Putting Technology

Elaborate

to Work

Overview

At a Glance

This lesson consists of a single activity with three parts in the Web version and four parts in the print version. It will take two days to complete. The lesson provides an opportunity for students to investigate some technologies that have advanced our understanding of cellular and molecular biology. Probe size, resolution, and using the right tool for the job are emphasized. Students are presented with a fictitious scenario involving the discovery of a muscle-wasting disease. As members of a medical and scientific team, they must choose a technology to use—light microscopy, transmission electron microscopy, cryo-electron microscopy, or X-ray crystallography—to investigate the disease. They answer questions such as, What is the infectious agent, how does the infectious agent cause dis-

ease, and is there a drug to treat or prevent the disease?

Major Concepts

Technologies that differ in their resolving capabilities provide different information about the structure of an object. Solving a problem requires an appropriate technology or series of technologies. Technology provides valuable tools for solving scientific problems relevant to human health.

Objectives

After completing this lesson, students will

• be able to explain the use of technologies based on their resolving power,

• be able to explain how technologies are used to solve scientific and health-related problems,

• be able to explain the concept of using the right tool for the job, and

• be able to develop a multistep research plan in which hypotheses are formulated, data are gathered and interpreted, and new questions are asked.

Teacher Background

See the following sections in Information about Using Technology to Study Cellular and Molecular Biology:

3 Scale and Resolution *(pages 24–26)*

4 Major Techniques in the Study of Cellular and Molecular Biology *(pages 26–35)*

In Advance

Web-Based Activities

Activity

Web Version

1

Yes

Photocopies

For class- • Master 3.1, *Memo from the Director, Global Science and*

rooms

Health Organization, 1 copy per group

using the • Master 3.2, *Research Plan*, 1 copy per student and

Web

1 transparency

version

• Master 3.3, *Example of a Research Plan*, 1 transparency

of this

• Master 3.4, *Drug Discovery Evaluation Form*, 1 copy per

activity:

student

• Master 3.1, *Memo from the Director, Global Science and*

For class- *Health Organization*, 1 copy per group

rooms

• Master 3.2, *Research Plan*, 1 copy per student or

using the 1 transparency for class

print

• Master 3.3, *Example of a Research Plan*, 1 transparency

version

• Master 3.5, *Available Technologies*, 1 transparency

of this

• Master 3.6, *Science Reference Manual*, 1 copy per group

activity:

• Master 3.7, *Muscle Protein Structures Determined by X-Ray*

Crystal ography, 1 copy per group or 1 transparency for class

Materials

Activity 1 none required

Preparation

For classrooms using the* Web version *of this activity:

Verify that computer lab is reserved for two consecutive class periods or

that classroom computers are ready to use. To save time, have comput-

ers at the URL *http://science.education.nih.gov/technology/student*. This is a main menu page from which this activity can be accessed.

For classrooms using the* print version *of this activity:

No preparations needed.

Procedure

For classrooms using the* Web version *of this activity.

Teacher note: This activity allows students to enter a virtual

laboratory in which they use microscopic techniques and X-

ray crystallography to solve a problem. The activity requires students to

view and interpret data. An essential part of it is having students develop

a logical research plan based in part on what they learned earlier in this

module about scale and resolution. They should formulate hypotheses

that can be tested with the technologies available to them.

Part 1, Solving the Problem

1.

Divide the class into groups of two students each, and give each group a copy of Master 3.1, *Memo from the Director, Global Science and Health Organization.*

2.

Ask students to read the memo and note the questions they are instructed to answer.

This memo also appears when students access the activity on the Web. Students can retain the printed memo to remind themselves of the questions they are to answer.

3.

Explain that students will begin by formulating a research plan. They will develop hypotheses that can be tested in their virtual laboratory.

If necessary, remind students that hypotheses are statements that predict a result and are testable experimentally.

4.

Ask students to proceed to *http://science.education.nih.gov/supplements/technology/student.* They should click on the link to "Lesson 3—Putting Technology to Work." This brings up the unit's desktop, from which this activity can be accessed.

After clicking on the activity link on the desktop, the memo from the director appears. After students close the memo, each of the

four available technologies is highlighted. **Note:** Students should not yet click on a technology.

5.

Explain that students have resources available to them, including various technologies and reference materials. Ask students to click on the link to "Reference Manual."

Briefly review the contents of the Reference Manual with the students.

Tip from the field test: Field-testing has indicated that it is very useful for teachers to introduce students to the Science Reference Manual early in this activity (see Teacher note 1 on page 79). This resource contains valuable information to help students formulate their hypotheses, including the sizes of biological structures and resolution limits of various technologies, as well as details about

unfamiliar technologies, blood cells, muscle cells, and pathogens and how they cause disease. At a minimum, you should introduce students to the table of contents of the Science Reference Manual,

point out which topics are links to more information, and use one link to show students the kind of information provided.

6.

Ask students how they will begin their studies. What should they do first? Encourage student participation and accept all responses.

Teacher note: Even though students are in pairs, work with the class as a whole through Step 15 to help them understand the process.

This question is purposely vague. Its intent is to engage the students and initiate creative thinking. Student responses may vary considerably. Some students may suggest beginning at the lowest level of resolution, the eye, and visually confirming the presence of ill individuals. They may suggest talking with healthy and ill individuals to gain clues about the nature of the disease. They may want more details about symptoms. Indicate to students that while gaining additional information by talking with affected and unaffected individuals might be helpful, there is no time to travel. They need to get down to business and begin investigating the issues raised in the director's memo.

7.

Direct students to the first question in the director's memo. Choosing from the available technologies and using tissue samples from affected and unaffected individuals, how can they confirm the presence of disease at the cellular level in the affected

population?

Students have muscle and blood samples available for study. Students should reason that light microscopy can be used to look for the presence of abnormal muscle cells in affected individuals. Unaffected individuals should have normal muscle cells. Students should provide a reason for wanting to look at any other tissue samples.

8.

Ask students, "Why would you use light microscopy to confirm the presence of disease?"

Students should know that cells are too small to be seen by the naked eye, although they can be seen easily with a light microscope. If necessary, ask students to think about the information on Master 1.1, *Searching for Scale* (the size of a cell) and what they discovered in Lesson 2, Activity 1: *Probing for Answers* (start with the largest probe, in this case visible light).

9.

After deciding on a starting point (light microscopy), students should begin constructing their detailed research plan. Give each student a copy of Master 3.2, *Research Plan*.

Master 3.2 presents an example of how a research plan can be organized. It is important for students to see how information flows

Identify questions and

as an investigation proceeds and how what is done at one step

concepts that guide

depends on results from previous steps.

scientific investiga-

tions.

10. Use the transparency of Master 3.2 to demonstrate how the research plan is constructed. Use Master 3.3, *Example of a*

Content Standard A:

***Research Plan*, as your guide.**

Design and conduct a

scientific investigation.

11. In the space next to the statement, "To answer the question," write the question, Is there evidence of disease at the cellular level (in muscle cells)? Ask students to help you determine which technology to use to answer this question.

Students should choose to begin their studies with light micros-

copy to look for the presence of abnormal cells in the muscle tissue

of affected individuals. Write this response in the space next to the

statement, "I will use this technology."

12. Ask students to respond to the statement, "I chose this technology because."

Students should have reasoned that cells are too small to be seen

with the naked eye but can be seen easily using a light microscope.

In other words, the resolution of a light microscope is sufficient to

see individual cells. Record the response on the transparency.

13. Ask students to state a hypothesis.

There is (or is not) evidence of disease in muscle cells.

14. Ask students what two results they would expect.

Either abnormal muscle cells will be seen in affected individuals or they will not. Record this response on the transparency.

15. Ask students what question they would answer next if they observe abnormal muscle cells in affected individuals.

They would proceed to Question 2 on Master 3.1, *Memo from the Director*, Is the disease caused by an infectious agent? Record this response on the transparency.

16. Ask students what question they would answer next if they do not observe abnormal muscle cells in affected individuals.

There is no single response to this question. Students can use their imagination.

Encourage students to use the Science Reference Manual to learn about muscle and blood cells. Examples of normal muscle and blood cells

are included in the reference material. Information about the size of cells, bacteria, and viruses is also provided, as well as the various technologies students will investigate in this activity.

17. Ask students to complete all tasks except those dealing with discovery of a drug to treat the disease (Question 6 on Master 3.1, *Memo from the Director, Global Science and Health Organization*).

18. Instruct students to begin their studies. They should make careful observations at each step and record all of their observations. They should follow their research plan.

Circulate among groups as students work. Ensure that students are proceeding according to a rational plan they have developed. You may want to quiz students about why they selected a specific technology, what they hoped to see, how they interpret what they did see, or why a technology is appropriate for solving a specific problem.

Teacher notes:

1. Selecting a technology activates a short animation. For example, after clicking on the light microscope, the animation changes from a view of the whole instrument to the view students would have looking through the eyepiece. Then, a small window opens over an interactive screen. This window contains information about the samples available for investigation, such as what the sample is (for instance, tissue or protein), and the source of the sample (that is, from a person with the disease or from an unaffected individual). Samples are coded, and students should record the coding information.

2. The light microscope and the transmission electron microscope are

interactive. Students should begin by selecting a sample and adjusting the brightness by moving the brightness slider. Magnification of the sample can be changed. Students can move most cell and tissue images up and down and to the left and right. Students may take a snapshot of a field they are viewing by clicking on the “View Snapshots.” Clicking on an individual snapshot produces a larger image that can be compared with another on-screen image (that is, an image on the microscope or an image in the Reference Manual). The “View Snapshot” window may be moved to allow easier comparison of images. Up to 12 snapshots may be stored.

3. Using the cryo-EM, students should click on “Affected” and “Unaffected.” They should record their observations of what appears in the

electron microscope (left monitor) and in the three-dimensional reconstruction (right monitor).

4. After clicking on “X-ray Crystallography,” students see a detailed animation of the process. We indicate that the data were obtained from three different orientations of the protein crystal, which is far fewer than the thousands of different orientations actually used in a research laboratory. Students begin by making observations of the X-ray crystallography patterns that appear on screen. All that students—or scientists, for that matter—can judge at this point is that the patterns for the affected and unaffected proteins are different from one another for each orientation. Making sense of these data requires processing by high-speed computers

using specialized software. Finally, students compare three-dimensional models of the affected and unaffected proteins. They should use the slider to rotate the proteins and record their observations of the differences and similarities of the proteins' structures.

19. When students have completed their work and answered Questions 1 through 5 on Master 3.1, *Memo from the Director, Global Science and Health Organization*, reconvene the class.

20. One at a time, have groups share their findings with the rest of the class.

Content Standard A:

Formulate and revise

Presentations need not be long. However, students should demon-

scientific explanations

strate an understanding of scale, resolution, and selecting the right

and models using

tool for the job. Members of each group should share the respon-

logic and evidence.

sibilities of presenting the group's information. Students should be

encouraged to question the hypotheses, research plans, and inter-

Content Standard A:

pretations of others. Remind students that science is a collaborative Recognize and analyze process in which scientists must be able to support their ideas.

alternative explana-

tions and models.

Teacher notes:

Content Standard A:

1. The Science Reference Manual contains information that is very help-

Communicate and

ful to students, and they should consult it early in their investigations.

defend a scientific

For instance, students can view light micrographs of normal muscle.

argument.

They will also find information on two common pathogens, bacteria and viruses, thus limiting the pathogens they search for. Additionally, key information about technologies is presented.

2. Students should reason that light microscopy can be used to look for the presence of abnormal muscle cells in affected individuals. Students generally know that cells are too small to be seen by the naked eye, although they can be seen easily with a light microscope. If necessary, ask students to think about the information on Master 1.1, *Searching for Scale*, (the size of cell) and what they discovered in Lesson 2, Activity 1: *Probing for Answers* (start with the largest probe, in this case visible light). In this activity, unaffected individuals have normal muscle cells.

Individuals susceptible to disease have abnormal muscle cells.

3. The Science Reference Manual lists two common pathogens: bacteria and viruses. Students should focus on the 10- to 100-fold difference in size between bacteria and viruses. Light microscopy can be used to resolve bacteria, but not viruses. Students should understand that they are following a plan analogous to the one developed in Lesson 2. They are starting with the largest probe available (visible light) to find out about the largest possible structures that can be resolved.

4. No bacteria are visible in either muscle or blood samples. Therefore, students should use transmission electron microscopy to see whether viruses are present in any of the tissue samples. Viruses are readily visible with this technique, which uses a probe (electrons) that is smaller than the probe they used initially (visible light).

5. Transmission electron microscopy demonstrates the presence of viruses in blood and muscle tissue samples from one affected and one unaffected individual. A second set of unaffected blood and muscle samples does not contain viruses. This observation is a key finding for this activity, although it may be confusing to some students. How do students interpret the presence of virus and the absence of disease? How might this relate to how the virus produces disease in susceptible individuals? They can consult their Science Reference Manual for helpful information. A possible reasoned scenario is 1) virus is present in muscle tissue of both affected and unaffected individuals because the virus binds to a protein receptor in that tissue, 2) the virus nucleic acid codes for a protein produced by the muscle cells, 3) the virus protein binds to a key muscle

protein in cells of affected individuals, which causes the disease, 4) the virus protein does not bind to the muscle protein in cells of unaffected individuals, 5) the *affected* muscle protein has a different structure from the unaffected protein, and 6) this difference in structure allows the *affected* muscle protein to interact with the virus protein.

6. On the basis of the scenario presented above, a hypothesis might be as follows: the structure of the affected muscle protein is different from that of the unaffected muscle protein. An extension of this hypothesis is that the virus protein binds to the affected muscle protein and not the unaffected muscle protein because of differences in structure between the two muscle proteins.

7. On the basis of the scenario presented above, students can use cryo-EM to generate a three-dimensional reconstruction of the virus attached to the muscle to see whether the virus attaches to affected muscle fibers and not unaffected muscle fibers, and they can use X-ray crystallography to compare the structures of affected and unaffected muscle proteins.

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8. To students—and to trained scientists, as well—the X-ray crystallography patterns are a collection of spots that do not themselves present a clear and obvious picture of a molecule’s structure. Students can note that the patterns differ from one another in spot location and intensity. They should understand that each pattern is unique because the structure being investigated is unique; that is, different patterns are produced both by different orientations of the same molecule and by different molecules.

Students should also see the value of computer technology in providing three-dimensional molecular structure from a series of X-ray crystallography patterns. Please note that many more than three X-ray crystallography patterns are required to produce a three-dimensional structure. The process has been simplified for this activity.

9. Students should evaluate how the structure of the affected muscle protein compares with the unaffected muscle protein. The only visible difference between the two proteins is seen in the view along the z-axis (that is, from the top looking down). The affected muscle protein has an opening that is not present in the unaffected muscle protein.

Part 2, Applying Technology . . . Again

1.

On behalf of the Global Science and Health Organization, thank students for their efforts. They have provided answers to some important questions. However, one very important question remains: Is there a drug to treat or prevent the disease?

Content Standard A:

Scientists conduct

2.

Ask students how the structural data on the affected and unaf-

investigations for a

fected muscle proteins, obtained by X-ray crystallography, sug-

wide variety of rea-

gest a way that the virus could cause the disease.

sons, such as to dis-

cover new aspects

Accept all responses. It is possible that the affected muscle protein

of the natural world,

can interact with the virus protein because its structure is different

to explain observed

from that of the unaffected muscle protein. Students might wonder

phenomenon, or to

how this interaction could occur. They might speculate that the

test conclusions of

virus protein interacts with parts of the affected muscle protein

prior investigations or

around the opening that exists. It also may be that the virus protein predictions of current interacts with some other region of the affected muscle protein.

theories.

Alternatively, students may hypothesize that the virus causes the

hole in the affected muscle protein. In other words, this action

of the virus produces a muscle protein of changed structure and,

therefore, changed function.

3.

How might a drug be used to treat the disease?

This is another opportunity for students to relate structure to function. They might reason that the affected muscle protein interacts with the virus protein and not the unaffected muscle protein because the two muscle proteins have different structures. This

difference appears to be characterized primarily by an opening in the affected muscle protein. Therefore, perhaps a drug can be developed to change the affected muscle protein's structure to one more like the unaffected muscle protein. A simple possibility is to develop a drug to close the opening. Students may suggest other possibilities as well. Do not limit their thinking or try to guide the discussion one way or another.

4.

Direct student groups to their computers. Tell them that the director of the Global Science and Health Organization has requested that they evaluate four new drugs that are believed to have potential to treat the disease.

5.

Give each student a copy of Master 3.4, *Drug Discovery Evaluation Form*. They should use this form to record their observations and interpretations.

6.

Ask students to click on the link "Drug Discovery Laboratory" on the unit's desktop.

A memo appears that gives students the instructions for this activity. Students compare the unaffected muscle protein with a complex formed by combining a drug molecule with the affected muscle protein. Four different drug molecules are available. When students close the memo, a short animation comes on that leads to a screen on which appear the unaffected protein, the affected protein, and the four drug molecules. Students can make observations about their structures. Clicking on a drug molecule attaches that drug to the affected protein. Students should use the slider to rotate the two proteins and compare their structures.

The instructions to students are purposely general. Students should conclude that the drugs have been designed such that they either do or don't convert the structure of the affected muscle protein to one more like the unaffected protein. Students will observe that none of the drugs interacts with the affected muscle protein to form

a structure that is exactly the same as the unaffected muscle protein. This, too, is purposeful and is intended to stimulate student thinking.

Depending on the class time you have available, you can assign groups all four molecules to evaluate or a limited number of molecules (one or two) to evaluate.

Part 3, Wrapping It Up

1.

Reconvene the class. Ask groups to share their drug evaluations. What were the drugs apparently designed to do? Do any drugs show promise for treating the disease?

This discussion allows students to share thoughts about what they have done. They should focus on results and interpretations. Students should understand that the path to solving a scientific problem is long and complex and that technology plays a key role in the process. They also come to realize that there are not always neat solutions to problems.

2.

Instruct students to prepare a report that summarizes their work. They are to present their group's work, from development of a research plan to drug discovery. It is acceptable for students to add

their own touches to the group effort, based on class discussions

Formulate and revise

and further reflection. They should focus on

scientific explanations

• justifying their choice of technology to solve specific problems,

and models using

• demonstrating an understanding of specimen size and resolu-

logic and evidence.

tion, and

• indicating a logical flow for using technologies of increasing

resolution to solve problems.

For classrooms using the* print version *of this activity

Teacher note: The print version of this activity is a "thought" activity. It does not make use of the graphics found in the Web activity, since these graphics do not always reproduce well. This version of the activity is more open-ended than the Web version. It allows students more latitude in formulating a research plan, since they are not restricted by available resources. Most important in this activity is the students' reasoning. Why do they propose to use a given technology? What results do they expect? How will this lead them to the next step in their plan? Students work in groups to increase interaction and collaboration.

Part 1, What Is It?

1.

Divide the class into groups of three or four students each, and give each group a copy of Master 3.1, *Memo from the Director,*

Global Science and Health Organization.

2.

Ask students to read the memo.

3.

Show students the transparency of Master 3.5, *Available Technologies.*

Tell students that to help them answer the questions raised by the director of the Global Science and Health Organization, the following technologies are available: observation by naked eye, light microscopy, transmission and cryo-electron microscopy, and X-ray crystallography. Remind them (as stated in the memo) that tissue samples from affected and unaffected individuals will be available.

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4.

Give each group a copy of Master 3.6, *Science Reference Manual*.

Explain to students that as scientists, they need reference materials to help them develop a logical and realistic research plan.

Tip from the field test: Field-testing indicated that it is very useful for teachers to introduce students to the Science Reference Manual early in this activity (see Teacher note 1 on page 79). This resource

Content Standard A:

contains valuable information to help students formulate their

Design and conduct a

hypotheses, such as sizes of biological structures and resolution

scientific investigation.

limits of various technologies. It also contains information about unfamiliar technologies, such as X-ray crystallography, as well as about blood cells, muscle cells, and pathogens and how they cause disease. At a minimum, you should introduce students to the Table of Contents of the Science Reference Manual and point out the information provided there.

5.

Ask students how they will begin their studies. What should they do first? Encourage student participation and accept all responses.

Teacher note: Even though students are in smaller groups of three or four, work with the class as a whole through Step 14 to help them understand the process they will follow.

This question to students is purposely vague. Its intent is to engage the students and their imagination. Responses may vary considerably. Some students may suggest beginning at the lowest level of resolution, the eye, and visually confirming the presence of ill

individuals. They may suggest talking with healthy and ill individuals to gain clues about the nature of the disease. They may want more details about symptoms. Indicate to students that while gaining additional information by talking with affected and unaffected individuals might be helpful, there is no time to travel. They need to get down to business and begin investigating the issues raised in the director's memo.

6.

Direct students to the first question in the director's memo. Choosing from the available technologies, and using tissue samples from affected and unaffected individuals, how can they confirm the presence of disease at the cellular level in the affected population?

If students ask what tissue samples are available, ask them to consider which tissue samples they would want and why. Students should reason that light microscopy can be used to look for the presence of abnormal muscle cells in affected individuals. Unaffected individuals should have normal muscle cells. Students should provide a reason for wanting to look at any other tissue samples.

7.

Ask students, "Why would you use light microscopy to confirm the presence of disease?"

Students should know that cells are too small to be seen by the

naked eye, although they can be seen easily with a light microscope. If necessary, ask students to think about the information on Master 1.1, *Searching for Scale* (the size of a cell) and what they discovered in Lesson 2, Activity 1: *Probing for Answers* (start with the largest probe, in this case visible light).

8.

After deciding on a starting point (light microscopy), students should begin to create their detailed research plan. Master 3.2, *Research Plan,* presents an example of how a research plan can be organized.

Either give each student a copy of Master 3.2 or make a transparency of Master 3.2 to show the class. It is important for students to see how information flows as an investigation proceeds and how what is done at one step depends on results from previous steps. The research plan is constructed as a modified decision tree: if I see (result 1), I will do (next task); or, if I see (result 2), I will do (next task).

9.

Use the transparency of Master 3.2, *Research Plan*, to demonstrate how the research plan is constructed. Use Master 3.3, *Example Research Plan*, as your guide.

10. Begin by writing the question, Is there evidence of disease at the cellular level (in muscle cells)?, in the space next to the statement, "To answer the question." Ask students to help you determine which technology to use to answer this question.

Students should begin their studies with light microscopy to look for the presence of abnormal cells in the muscle tissue of affected individuals. Write this response in the space next to the statement, "I will use this technology."

11. Ask students to respond to the statement, "I chose this technology because."

Students should reason that cells are too small to be seen with the naked eye but can be seen easily using a light microscope. In other words, the resolution of a light microscope is sufficient to see individual cells. Record the response on the transparency.

12. Ask students to state a hypothesis.

There is (or is not) evidence of disease in muscle cells.

13. Ask students what two results they would expect.

Either abnormal muscle cells will be seen in affected individuals or

they will not. Record this response on the transparency.

14. Ask students what question they would answer next if they observe abnormal muscle cells in affected individuals.

Students would proceed to Question 2 on Master 3.1, *Memo from the Director*, Is the disease caused by an infectious agent? Record this response on the transparency.

15. Ask students what question they would answer next if they do not observe abnormal muscle cells in affected individuals.

There is no single response to this question. Students can use their imagination.

16. Inform students that they are ready to begin their studies. They should create their research plans in a manner similar to that demonstrated.

17. Inform the class that results indicate the presence of abnormal muscle cells in tissue samples from affected individuals but not in unaffected individuals. First, they will address the question of whether or not the disease is caused by an infectious agent.

Students now begin working in smaller groups.

18. The Science Reference Manual lists two common *pathogens*: bacteria and viruses. How could they identify one or the other as a potential cause of the disease (that is, as being present in affected individuals and not present in unaffected individuals) using the technologies available to them?

They should name the technology they would use, justify their choice based on the size of the objects they are looking for and the resolving power of the technology, and indicate possible results

and what their next step would be. Allow groups no more than five minutes to formulate their plan.

19. Ask a group to present its research plan very briefly.

Students should focus on the 10- to 100-fold difference in size between bacteria and viruses. Light microscopy can be used to resolve bacteria but not viruses. Students should understand that they are following a plan analogous to that developed in Lesson 2. They start with the largest probe available (visible light) to find out about the largest possible structures that can be resolved.

20. Ask whether any groups have a different research plan.

Ask groups with a different research plan to make a brief presentation. Use class discussion to resolve differences or reinforce similarities.

21. Inform the class that light microscopy did not demonstrate the presence of any structures resembling bacteria in tissue samples from affected or unaffected individuals. On the basis of this result, students should now formulate the next step in their research plan.

As before, students should name the technology they would use,

Content Standard A:

justify their choice on the basis of the size of the objects they are

Formulate and revise

looking for and the resolving power of the technology, and indicate

scientific explanations

possible results and what their next step would be. Allow groups

and models.

two to three minutes to confirm their plan.

22. Ask a group to present its research plan very briefly.

Students should use transmission electron microscopy to see whether viruses are present in any of the tissue samples. Viruses are readily visible with this technique, which uses a probe (electrons) that is smaller than the probe they used initially (visible light). Ask students to justify any other approach they suggest.

23. Ask whether any groups have a different research plan.

Ask groups with a different research plan to make a brief presentation. Use class discussion to resolve differences or reinforce similarities.

Part 2, How Does It Work?

1.

Inform the class of the following results:

• transmission electron microscopy demonstrated the pres-

ence of viruses in blood and muscle tissue samples from *both*

affected and unaffected individuals,

• no other tissue samples contained viruses,

• there were more viruses in muscle of affected people than in

unaffected people, and

• the viruses appeared to be associated with actin filaments in

the muscle.

2.

Ask students to consider these results as they develop their plan

to answer Questions 4 and 5 on the director's memo (Master 3.1).

For instance,

• How do students interpret the presence of virus and the absence of disease?

• How might this relate to how the virus produces disease in susceptible individuals?

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This may be a tough issue for students to deal with. It is not important for them to come up with our scenario. It is important for them to reason properly and use the available technologies to solve whatever problem they perceive exists. *They should consult their Science Reference Manuals for helpful information.*

A possible reasoned scenario is 1) virus is present in muscle tissue of both affected and unaffected individuals because the virus binds to a receptor in that tissue, 2) the virus nucleic acid codes for a

protein produced by the muscle cells, 3) the virus protein binds to a key muscle protein in cells of affected individuals, which causes the disease, 4) the virus protein does not bind to the muscle protein in cells of unaffected individuals, 5) the *affected* muscle protein has a different structure from the *unaffected* protein, and 6) this difference in structure allows the *affected* muscle protein to interact with the virus protein.

3.

Ask groups to form a hypothesis based on their assessment of the data presented in Step 1 of Part 2.

On the basis of the sample scenario presented in Part 2, Step 2, one hypothesis might be as follows: the structure of the affected muscle protein is different from that of the unaffected muscle protein. A related hypothesis might be that the virus protein binds to the affected muscle protein and not the unaffected muscle protein because of differences in structure between the two muscle proteins. Another hypothesis is that the virus can attach to affected muscle fibers and not to unaffected muscle fibers. There are many possible hypotheses. It is important that each student hypothesis be a testable statement that predicts a result.

4.

Ask groups to formulate a plan to test their hypothesis. They should use only the techniques available to them.

On the basis of the sample scenario presented in Part 2, Step 2, students might propose to do the following:

• use cryo-EM to generate a three-dimensional reconstruction of the virus attached to the muscle to see whether the virus attaches to affected muscle fibers and not unaffected muscle fibers,

• use cryo-EM to produce three-dimensional reconstructions of both the affected and unaffected muscle proteins to look for differences in structure between the two,

• use X-ray crystallography to compare the structures of affected and unaffected muscle proteins, or

• use either cryo-EM or X-ray crystallography to look at the structure of any virus-muscle protein combination that might form (that is, a virus protein-affected muscle protein combination or a virus protein-unaffected muscle protein combination).

Students might come up with other possibilities depending on the hypothesis they formulate.

5.

Ask a group to present its hypothesis and research plan.

Content Standard A:

Members of each group should share the responsibilities of present- Communicate and ing the group's information. Students should be encouraged to ques- defend a scientific tion the hypotheses and research plans developed by others. Remind argument.

students that science is a collaborative process in which scientists must be able to support their ideas.

6.

Ask whether any groups have a different hypothesis or research plan.

Ask groups with a different research plan to make a brief presentation. Use class discussion to resolve differences or reinforce similarities. On the basis of feedback from their fellow scientists, groups should be allowed to revise their hypotheses and research plans.

Part 3, What Can We Do about It?

tions and models.

1.

Thank students, on behalf of the Global Science and Health Organization, for their efforts so far. They must now think about developing a drug to treat this newly discovered disease.

2.

If the hypothesis students developed in Part 2 of this activity (about how the virus might produce disease) is supported by experimental data, how could students use a drug to treat the disease?

Even though students are still in groups, use this as an opportunity for class discussion. Accept all responses. This question is intentionally vague to stimulate student thinking. If students do not

understand the concept of drug targeting (that is, designing a drug to interact specifically with another molecule, such as a host protein or a molecule produced by a pathogen), direct them to review the final item in Master 3.6, *Science Reference Manual*. The drug-specific molecule can be one associated with the pathogen, such as a bacterial or viral surface protein, or a protein produced by the pathogen. Alternatively, the drug-specific molecule can be one associated with the host, such as a receptor for the pathogen, or a molecule with which a pathogen-produced substance interacts.

3.

Tell students that new data have been obtained. Provide each group with a copy of Master 3.7, *Muscle Protein Structures Determined by X-Ray Crystallography*. Alternatively, use a transparency of this master for the class.

4.

Inform the class that the director of the Global Science and Health Organization wants them to evaluate these structures with

their fellow scientists (the other group members) and answer a series of questions, which you will write on the board.

• How does the structure of the affected muscle protein compare with the unaffected muscle protein? Are there differences?

The one difference between the two proteins is seen in the view along the z-axis. The affected muscle protein has an opening that is not present in the unaffected muscle protein.

• Do these results support a way that the virus could cause the disease?

They could. It is possible that the affected muscle protein can interact with the virus protein because its structure is different from that of the unaffected muscle protein. Students might wonder how this interaction could occur. They might speculate that the virus protein interacts with parts of the affected muscle protein around the opening that exists. It may also be that the virus protein interacts with some other region of the affected muscle protein.

• On the basis of these results, what approach might be taken to develop a drug to treat the disease?

This is another opportunity for students to relate structure to function. They might reason that the affected muscle protein interacts with the virus protein and not the unaffected muscle protein because the two muscle proteins have different struc-

tures. This difference appears to be characterized primarily by an opening in the affected muscle protein. Therefore, perhaps a drug can be developed to change the affected muscle protein's structure to one more like the unaffected muscle protein. A simple possibility is to develop a drug to close the opening. Students may suggest other possibilities as well. Accept any response that students can justify.

• Using the technologies available, how could potential drugs be tested for effectiveness before using them to treat humans?

Responses will depend on the approach taken. For example, X-ray crystallography would be an obvious choice for students who want to demonstrate that a drug has returned the structure of the affected muscle protein to that of the unaffected muscle protein. Accept all responses as long as students justify their use.

5.

Allow groups 10 to 15 minutes to work on their responses. After this time, reconvene the class and ask each group to present their answers.

Part 4, This, Too, Is What Science Is All About

1.

Remind students that reporting their results is also an important part of doing science. That is what they must do now.

Content Standard A:

2.

Instruct students to prepare a report that summarizes the work

Scientists conduct

done within their group.

investigations for a

wide variety of rea-

Students are to present all of their group’s work, from development

sons, such as to dis-

of a research plan to drug discovery. It is acceptable, based on class

cover new aspects

discussions and further reflection, to add their own touches to the

of the natural world,

group effort. Student reports should

to explain observed

• focus on justifying their choice of technology to solve specific

phenomena, or to

problems,

test conclusions of

• demonstrate an understanding of specimen size and resolution,

prior investigations or

and

predictions of current

• indicate a logical flow in which they use technologies of

theories.

increasing resolution to solve problems.

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Lesson 3 Organizer: Web Version

Activity 1: *Putting Technology to Work*

What the Teacher Does

Procedure Reference

Part 1, Solving the Problem

Divide the class into groups of two.

Pages 75–76

• Give each group a copy of Master 3.1, *Memo from the*

Steps 1–5

Director, Global Science and Health Organization.

• Ask students to read the memo.

• Explain that they will begin by formulating a research plan.

• Have students access the activity and click on the link to

the reference manual.

• Briefly review the contents of the reference manual.

Help students develop a research plan.

Pages 76–78

• Ask students how they would begin their studies.

Steps 6–16

• Guide students to the use of light microscopy to confirm the presence of disease at the cellular level in affected people.

• Give each student a copy of Master 3.2, *Research Plan*.

• Use a transparency of Master 3.2 to demonstrate how a research plan is developed.

• With student input, fill in the required information on the transparency. Use Master 3.3, *Example of a Research Plan*, as a guide.

• In the space next to the statement, *To answer the question*, write the question, Is there evidence of disease at the cellular level (in muscle cells)? Ask students to help you determine which technology to use to answer this question.

• Ask students to respond to the statement, I chose this technology because.

• Ask students to state a hypothesis.

• Ask students what two results they would expect.

• Ask students what question they would answer next if

they do not observe abnormal muscle cells in affected

individuals.

92

Instruct students to begin their studies. They should construct

Pages 78–79

their research plans in a manner similar to that demonstrated.

Steps 17–20

They should complete all tasks except the one dealing with drug

discovery (Question 6 on Master 3.1, *Memo from the Director, Global Science and Health Organization*). Have groups share

their findings.

Part 2, Applying Technology . . . Again

Remind students of the final question to be answered: Is there

Page 81

a drug to treat or prevent the disease?

Step 1

Ask students,

Pages 81–82

• how the structural data on the affected and unaffected

Steps 2–3

muscle proteins, obtained by X-ray crystallography, sug-

gest a way that the virus could cause the disease and

• how a drug might be used to treat the disease.

Direct students to computers.

Page 82

• Tell students that they are to evaluate four new drugs

Steps 4–6

that are believed to have potential to treat the disease.

• Give each student a copy of Master 3.4, *Drug Discovery*

Evaluation Form, on which they should record their

observations and interpretations.

• Ask students to click on the link for the Drug Discovery

Laboratory on the unit's desktop and complete the

activity.

Part 3, Wrapping It Up

Reconvene the class. Ask groups to share their drug evaluations.

Pages 82–83

• What were the drugs apparently designed to do?

Step 1

• Do any drugs show promise for treating the disease?

Instruct students to prepare a report that summarizes their

Page 83

work.

Step 2

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Lesson 3 Organizer: Print Version

Activity 1: *Putting Technology to Work*

What the Teacher Does

Procedure Reference

Part 1, What Is It?

Divide the class into groups of three or four.

Pages 83–84

• Give each group a copy of Master 3.1, *Memo from the*

Steps 1–4

Director, Global Science and Health Organization.

• Ask students to read the memo.

• Show students the transparency of Master 3.5, *Available Technologies*.

• Give each group a copy of Master 3.6, *Science Reference Manual*.

Ask students how they will begin their studies. Direct attention

Pages 84–85

to the first question on the director's memo. Ask,

Steps 5–7

• "Choosing from the available technologies and using tissue samples from affected and unaffected individuals, how can you confirm the presence of disease at the cellular level in the affected population?"

• "Why would you use light microscopy to confirm the presence of disease?"

After deciding on a starting point, students should begin con-

Pages 85–86

structing their research plan.

Steps 8–16

• Use the transparency of Master 3.2, *Research Plan*, to demonstrate how the research plan is constructed.

• With student input, fill in the required information on the transparency. Use Master 3.3, *Example of a Research Plan*, as a guide.

• In the space next to the statement, *To answer the ques-*

tion, write the question, Is there evidence of disease at the cellular level (in muscle cells)? Ask students to help you determine which technology to use to answer this question.

• Ask students to respond to the statement, I chose this technology because.

• Ask students to state a hypothesis.

• Ask students what two results they would expect.

• Ask students what question they would next answer if they do not observe abnormal muscle cells in affected individuals.

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Inform the class that results indicate the presence of abnormal

Pages 86–87

muscle cells in tissue samples from affected individuals but not

Steps 17–20

in unaffected individuals.

• The class will first address the question of whether or not the disease is caused by an infectious agent.

• Their science reference manual lists two common pathogens: bacteria and viruses.

• Ask students how they could identify one or the other as a potential cause of the disease using the technologies available to them.

• Ask a group to present its research plan.

• Ask if any groups have a different research plan.

Inform the class that light microscopy did not demonstrate the

Page 87

presence of any structures resembling bacteria in tissue samples

Steps 21–23

from affected or unaffected individuals.

• On the basis of this result, students should now formu-

late the next step in their research plan.

• Ask a group to present its research plan.

• Ask whether any groups have a different research plan.

Part 2, How Does It Work?

Inform the class of the following results:

Page 87

• transmission electron microscopy demonstrated the

Step 1

presence of viruses in blood and muscle tissue samples

from both affected and unaffected individuals;

• no other tissue samples contained viruses;

• there were more viruses in muscle of affected people

than in unaffected people; and

• the viruses appeared to be associated with actin

filaments in the muscle.

Ask students to consider these results as they develop their

Pages 87–88

plan to answer Questions 4 and 5 on the director’s memo. For

Step 2

instance,

• how do students interpret the presence of virus and the

absence of disease, and

• how might this relate to how the virus produces disease

in susceptible individuals?

Ask groups

Pages 88–89

• to form a hypothesis based on their assessment of the

Steps 3–4

data presented in Step 1, Part 2, and

• to formulate a plan to test their hypothesis.

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Student

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How Y

Using our

T Brain Understands

echnology to Study What Your

Cellular Ear

and Hears

Molecular Biology

Ask a group to present its hypothesis and research plan.

Page 89

Step 5

Ask if any groups have a different hypothesis or research plan.

Page 89

Step 6

Part 3, What Can We Do About It?

Inform the class that they must now think about developing a

Page 89

drug to treat the disease.

Step 1

On the basis of the hypotheses they developed in Part 2, how

Page 89

might students use a drug to treat the disease?

Step 2

Tell students that new data have been obtained. Give each

Page 89

group a copy of Master 3.7, *Muscle Protein Structures Deter-*

Step 3

mined by X-Ray Crystallography, or use a transparency for the

class.

Inform the class that they are to evaluate these structures and

Pages 89–90

answer a series of questions, which you write on the board.

Step 4

• How does the structure of the affected muscle protein

compare with the unaffected muscle protein?

• Do these results support a way that the virus could

cause the disease?

• What approach might be taken to develop a drug to

treat the disease?

• Using the technologies available, how could potential

drugs be tested for effectiveness before using them to

treat

humans?

Allow groups 10 to 15 minutes to work on their responses.

Page 90

Reconvene the class and ask each group to present their

Step 5

answers.

Part 4, This, Too, Is What Science Is All About

Remind students that reporting their results is also a part of

Page 91

doing science.

Step 1

Instruct students to prepare a report that summarizes the work

Page 91

done within their group.

Step 2

= Involves copying a master.

= Involves using a transparency.

Lesson 4

Evaluate

Technology: How Much Is Enough?

Overview

At a Glance

This lesson gives students an opportunity to pull information together and demonstrate an understanding of the basic concepts discovered in earlier lessons. In the first of two activities, students use the scenario from Lesson 3 to evaluate technology from a historical perspective. They first develop timelines for key developments in biology, medicine, and technology. They then are asked, If you were a scientist in the mid-1800s, how much progress would you make in solving the problems in Lesson 3? In the second activity, students consider whether our technology tool-box is complete. They choose one of three problems and propose a tech-nology or combination of technologies to solve it.

Major Concepts

New technologies are developed, and old technologies are improved and refined, continuously. This must be done to meet the demands created by new and existing problems.

Objectives

After completing this lesson, students will

• be able to describe the need for new or improved technologies;

• be able to explain the general process of developing technologies,

including the need to have input from multiple disciplines.

Teacher Background

See the following sections in Information about Using Technology to Study Cellular and Molecular Biology:

4 Major Techniques in the Study of Cellular and Molecular Biology *(pages 26–35)*

5 Technology and the Origins of Molecular Biology *(pages 35–38)*

In Advance

Web-Based Activities

Activity

Web Version

1

No

2

No

Photocopies

Activity 1

• Master 4.1, *Microscopes Across Time*, 1 transparency

• Master 4.2, *Some Key Developments in Biology, Medicine, and Technology*, 1 transparency

Activity 2

none required

Materials

Activity 1 • 24 sheets of white copying paper

• black marker

• blank transparency; or a string as long as the width of classroom, 29 paper clips, and 5 sheets of white copying paper

Activity 2

none required

Preparation

Activity 1

On each of 24 sheets of white paper, use the black marker to write one of the key developments listed on Master 4.2, *Some Key Developments in Biology, Medicine, and Technology* (eight developments are listed in each of three categories: biology, medicine, and technology). Do *not* provide the year of the development or the name(s) of the individual(s) involved. There are two options for this activity: use a blank transparency to record student responses as they construct the timeline for developments in biology, medicine, and technology, or stretch the string across the width of the classroom and affix it well at both ends. If you choose the second option, write *one* of the following on each of five sheets of white paper: 1600, 1700, 1800, 1900, or 2000. Use a paper clip to attach the sheet indicating 1600 at the near the left end of the string. Attach the sheet indicating 2000 near the right end of the string. Attach the remaining sheets with 1700, 1800, and 1900 in order between 1600 and 2000.

Activity 2

No preparations needed.

Activity 1: *Time Travel*

Procedure

1.

Show students the transparency of Master 4.1, *Microscopes Across Time*. Ask them to look at the pictures of the microscopes and

describe the differences they observe.

Write student responses on the board. The pictures present microscopes developed over approximately 250 years. Students can respond to differences in design, such as the development of multiple objective lenses. Some students may respond with differences that are implied, such as better optics, electrical components, and computerized components. The objective of this question is to engage student thinking about the changing face of science and technology across time.

2.

Ask the class to imagine that they are scientists or physicians living in the mid-1800s. How much progress do they think they would make solving the problems in Lesson 3?

For example, could they have identified the infectious agent? Could they have determined how the disease was caused? Students will probably have little specific knowledge of when relevant discoveries were made or when relevant technologies were developed. Allow the students to wonder about the timeline of scientific discovery. Even though the problems in Lesson 3 are the same as in any time period, the technologies and knowledge available at a given time will determine the extent to which the problems can be solved.

3.

Divide the class into three groups.

One group will focus on biology, the second on medicine, and the

third on technology.

4.

Provide each student in the biology group with one sheet on which a biology development is written. Provide each member of the medicine and technology groups with one sheet on which a

Content Standard E:

development appropriate to their group is written.

Science often advances with new technologies.

In classes with fewer than 24 students, you can give students more than one sheet or you can give the group all eight sheets. In classes with more than 24 students, you can add the following developments:

• biology: covalent bond described (1916, Gilbert Lewis), gene-sequencing methods developed (1977, Walter Gilbert and Allan Maxam, and Fred Sanger and Alan Coulson);

• medicine: first vaccination (1796, Edward Jenner), aspirin introduced (1899, Felix Hoffmann);

• technology: protocol allowing different computer networks to interconnect and communicate with each other (1973, Vinton Cerf and Bob Kahn), automated

DNA sequencer introduced (1986, Leroy Hood and colleagues).

Other developments can be added at the teacher's discretion.

5.

Ask students to estimate the year the development on their sheet occurred.

6.

Ask students to consult with other group members to place all developments in their category in chronological order.

Allow only a few minutes for students to do this.

7.

Have students report their results.

This can be accomplished two ways. Students can call out their results to the teacher, who then records the information along a line drawn on a blank transparency projected for the class to see. Alternatively, students can clip their sheets to the string that spans the width of the room. Sheets should be placed at a location representing the approximate date of each development. For instance, a development occurring in 1850 would be placed midway between 1800 and 1900.

8.

Show students a transparency of Master 4.2, *Some Key Developments in Biology, Medicine, and Technology,* and quickly evaluate how students did at constructing their timeline.

9.

Looking at the timeline, ask students what progress they could have made in solving the problems in Lesson 3 if they were working in the mid-1800s.

Students see that technologies available in 1850 were not capable of providing the information required to solve the problems in Lesson 3. Students also develop a firmer understanding of the relationship between technology development and the advancement of knowledge.

Activity 2: *Is That All There Is?*

Teacher note: This activity should follow Activity 1 without a break in discussion.

1.

Ask students if our present technology toolbox is complete. With a show of hands, how many students believe we need new technologies?

You might ask students to suggest some new technologies and write these suggestions on the board. Student responses are less important than shifting the focus from existing technologies to new ones

Many scientific investi-

(or refinements of existing ones).

gations require contri-

butions from different

2.

Tell students that they will accelerate their journey through time.

disciplines, including

They are now scientists in the year 2052. Since students know

engineering.

that technologies are generally developed by teams whose mem-

bers have expertise in more than one discipline, they now will

Content Standard E:

work in teams.

Creativity, imagination,

and a good knowledge

3.

Divide the class into groups of four or five. Ask each group to

base are all required

choose one of the following problems:

in the work of science

• development of a technology to detect and measure concen-

and engineering.

trations of the abnormal protein in affected people from Les-

son 3 (that is, a *biosensor*),

• development of a technology to determine the structure of a

protein molecule without having to prepare a crystal of the

protein, or

• development of a technology that allows molecules of a drug to be delivered specifically to the protein of affected people from Lesson 3 in a way that allows the physician or scientist to know how much drug is delivered.

4.

Instruct students to work with their group members to outline the requirements of their technology.

This is a challenging activity for students. However, the key issue is the rationale students provide for their technology. Students should consider at least the following:

Content Standard G:

• What disciplines are involved in developing the technology?

Scientific explanations

• Is it a new technology or a refinement of an existing technology?

must meet certain

• What is the level of resolution required?

criteria such as consis-

• How are the issues of scale and probe size dealt with?

tency and accuracy.

• In general terms, how does the technology work?

5.

Reconvene the class. Each group in turn should present its technology.

Use class discussion to discover problems and weaknesses and to

help group members refine their ideas.

101

Student Lesson 4

Using Technology to Study Cellular and Molecular Biology

6.

As a final means of assessment, ask each student to prepare a written report describing his or her technology.

Technologies should be described in sufficient detail to indicate the student's understanding of the concepts presented in this module.

102

Activity

Lesson 4 Organizer

Activity 1: *Time Travel*

What the Teacher Does

Procedure Reference

Show students a transparency of Master 4.1, *Microscopes Across* Page 99

Time. Ask them to look at the microscopes and describe the dif-

Step 1

ferences they observe.

Ask the class to imagine that they are scientists or physicians

Page 99

living in the mid-1800s. How much progress do they think they

Step 2

would make solving the problems in Lesson 3?

Divide the class into three groups.

Pages 99–100

• One group will focus on biology, the second on medi-

Steps 3–7

cine, and the third on technology.

• Provide each student with a sheet of paper on which is

written one development in his or her focus area.

• Ask students to estimate the year the development on

their sheet occurred.

• Ask students to consult with other group members to

place all developments in their focus area in chronologi-

cal order.

• Have students report their results.

Show students a transparency of Master 4.2, S *ome Key Develop*- Page 100

ments in Biology.

Steps 8–9

• Evaluate how students did at constructing their timeline.

• Ask students what progress they could have made in

solving the problems in Lesson 3 if they were working in

the mid-1800s.

Activity 2: *Is That All There Is?*

Ask students,

Page 101

• “Is our present technology toolbox complete?”

Step 1

• “How many students believe we need new technologies?”

Divide the class into groups of four or five.

Page 101

• Tell students they are scientists in the year 2052.

Steps 2–4

• Ask each group to choose one of the following prob-

lems:

o development of a technology to detect and mea-

sure concentrations of the abnormal protein in

affected people from Lesson 3;

o development of a technology to determine the

structure of a protein molecule without having to

prepare a crystal of the protein; or

o development of a technology that allows mol-

ecules of a drug to be delivered specifically to

the protein of affected people from Lesson 3 in a

way that allows the physician or scientist to know

how much drug is delivered.

• Instruct students to work with their group members to

outline the requirements of their technology, focusing on

concepts learned in earlier lessons.

Reconvene the class and allow each group to present its

Page 101

technology.

Step 5

As a final assessment, ask each student to prepare a written

Page 102

report describing his or her technology.

Step 6

= Involves using a transparency.

104

Lesson 1

Engage

title

Masters

Lesson 1, *What Is Technology?*

At a Glance

Master 1.1, *Searching for Scale*

1

copy

per

student

Lesson 2, *Resolving Issues*

Master 2.1, *Probing for Answers Score Sheet*

1

copy

per

2

students,

1

transparency

Master 2.2, *Probes*

1

copy

per

12

students

Masters 2.3 to 2.8, *Probing for Answers—Levels 1–6*

1 copy of each per 12

or

fewer

students;

2

copies

of

each

for

13–24

students;

3

copies

of

each

for

25–36

students

Master 2.9, *Solution to Probing for Answers*

1

transparency

(*print version* only)

Lesson 3, *Putting Technology to Work*

Master 3.1, *Memo from the Director, Global Science*

and Health Organization

1

copy

per

group

Master 3.2, *Research Plan*

1

copy

per

student,

1

transparency

Master 3.3, *Example of* a *Research Plan* 1

transparency

Master 3.4, *Drug Discovery Evaluation Form*

1

copy

per

student

(*Web version* only)

Master 3.5, *Available Technologies*

1

transparency

(*print version* only)

Master 3.6, *Science Reference Manual*

1

copy

per

group

(*print version* only)

Master 3.7, *Muscle Protein Structures Determined by*

X-Ray Crystallography

1

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per

group

or

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transparency

(*print version* only)

Lesson 4, *Technology: How Much Is Enough?*

Master 4.1, *Microscopes Across Time*

1

transparency

Master 4.2, *Some Key Developments in Biology, Medicine, and Technology*

1

transparency

105

Searching for Scale

Name:

Date:

Biological Structure	Actual Diameter	Size Relative to Cell	Object Used to Measured	Size Relative to Model Cell	Size of Model Biological structure	Model Object (the Room)

Cell

1 × 10–5

1 × 10–5

Room

10 meters

10

= 1

= 1

1 × 10–5

10

Bacterium

1 × 10–6

1 × 10–6

Desk

1 meter

= 1

1 = 1

1 × 10–5 10

10 10

Mitochondrion

5 × 10–7

5 × 10–7 = 1

1 × 10–5 20

Virus

1 × 10–7

Ribosome

1 × 10–8

Protein

5 × 10–9

Glucose

1 × 10–9

molecule

H2O molecule

1 × 10–10

Master 1.1

Probing for Answers Score Sheet

A

B

C

D

E

F

G

H

I

1

2

3

4

5

6

7

8

9

Master 2.1

Probes

Master 2.2

Probing for Answers—Level 1

A

B

C

D

E

F

G

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I

1

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9

Level 1

Master 2.3

Probing for Answers—Level 2

A

B

C

D

E

F

G

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1

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Level 2

Master 2.4

Probing for Answers—Level 3

A

B

C

D

E

F

G

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Level 3

Master 2.5

Probing for Answers—Level 4

A

B

C

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Level 4

Master 2.6

Probing for Answers—Level 5

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Level 5

Master 2.7

Probing for Answers—Level 6

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C

D

E

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G

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Level 6

Master 2.8

Solution to Probing for Answers

Master 2.9

Memo from the Director, Global Science and

Health Organization

Global Science and

Health Organization

Memo

TO:

Members, Scientific and Health Evaluation Teams

FROM:

Director, Global Science and Health Organization

RE:

New disease

Our Division of Disease Surveillance recently reported a new disease affecting approximately 30% of the persons living in a small rural area of the United States. Affected individuals have a lack of energy and demonstrate a progressive loss of muscle function. Although we have no information yet, we believe the disease is caused by an infectious agent. Consequently, to limit the spread of this disease, immediate intervention is critical.

We need your expertise to answer these questions:

1.

Is there evidence of disease at the cellular level? If so,

2.

Is the disease caused by an infectious agent? If it is,

3.

What is the infectious agent?

4.

Does the infectious agent attack muscle tissue?

5.

How might the infectious agent cause the disease?

6.

Is there a drug to treat or prevent the disease?

Blood and muscle tissue samples from unaffected and affected individuals are waiting for you. The microscopy and X-ray crystallography facilities at GSHO are being readied for your arrival. In order to gain information as quickly as possible, please develop a solid research plan before beginning your investigations.

Good luck!

Master 3.1

Research Plan

Name:

Date:

1.

To answer the question,

2.

I will use this technology:

3.

I chose this technology because

4.

My hypothesis is

5.

I expect one of the following two results:

6.

Observations (actual results) and interpretation:

Master 3.2

Example of a Research Plan

1.

To answer the question, Is there evidence of disease at the cellular level (in

muscle cells)?

2.

I will use this technology: Light Microscope

3.

I chose this technology because its resolution level allows me to see muscle cells.

4.

My hypothesis is There is evidence of disease in muscle cells.

5.

I expect one of the following two results: I will see abnormal muscle cells in affected individuals OR I will see NO abnormal muscle cells in affected individuals.

6.

Observations (actual results) and interpretation:

Result 1—Muscle cells from affected individuals are different from normal muscle cells and those from unaffected individuals; interpreted as evidence of disease in muscle of affected individuals. Proceed to next question.

1.

To answer the question, Is the disease caused by an infectious agent (bacteria)?

2.

I will use this technology: Light Microscope

3.

I chose this technology because its resolution level allows me to see bacteria.

4.

My hypothesis is (continue as above).

OR

6.

Observations (actual results) and interpretation:

Result 2—Muscle cel s from affected individuals appear the same as normal muscle cel s and muscle cel s from unaffected individuals. Interpreted as lack of evidence of disease in muscle cel s of affected individuals. Look for evidence of disease in other tissues.

1.

To answer the question, Is there evidence of disease at the cellular level (blood)?

2.

I will use this technology: Light Microscope

3.

I chose this technology because its resolution level allows me to see blood cells.

4.

My hypothesis is (continue as above).

Master 3.3

Drug Discovery Evaluation Form

Name:

Date:

Molecule 1: Evaluation of X-ray crystallography, protein structure data:

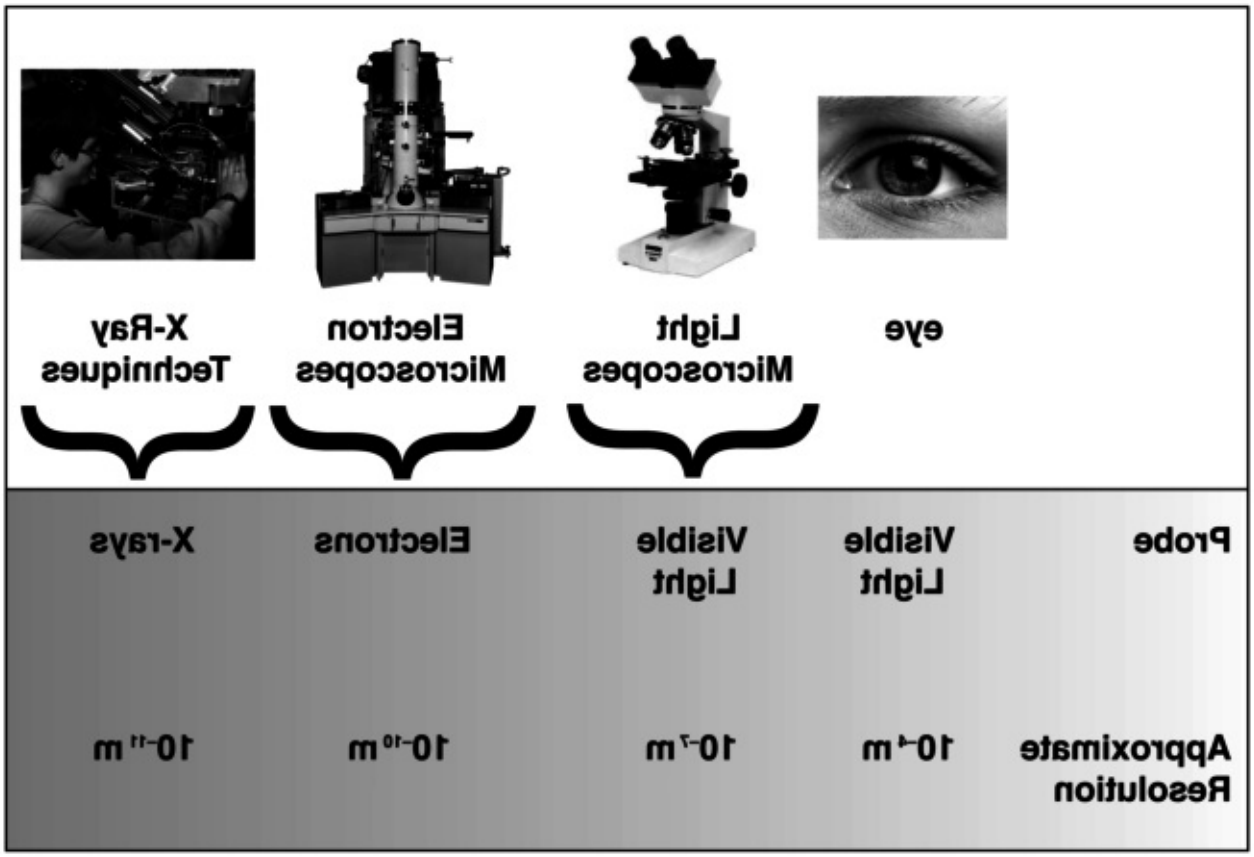
Molecule 2: Evaluation of X-ray crystallography, protein structure data:

Molecule 3: Evaluation of X-ray crystallography, protein structure data:

Molecule 4: Evaluation of X-ray crystallography, protein structure data:

Overall evaluation: Is there a drug you would recommend to treat the disease? Justify your response.

Master 3.4



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Master 3.5

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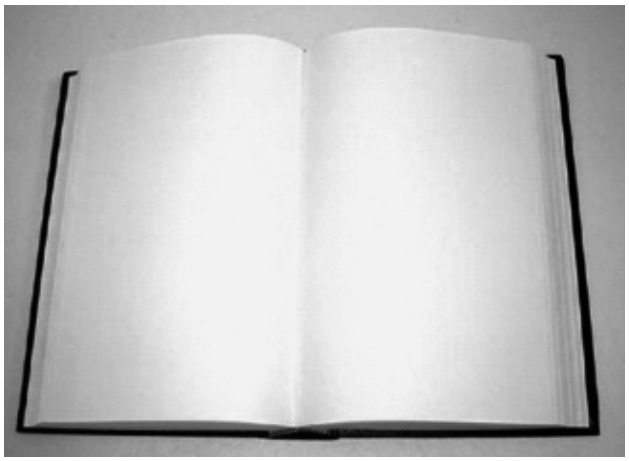

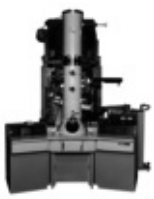

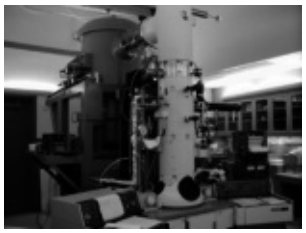

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discoveries wer

In the late 1600s, Antonio van Leeuwenhoek

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Section 3: Blood

Section 4: Muscle

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Section 5: Drug Discovery

Rational Basis for New

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Section 2: Infectious

Disease Causative Agents

Infectious Disease

Bacteria

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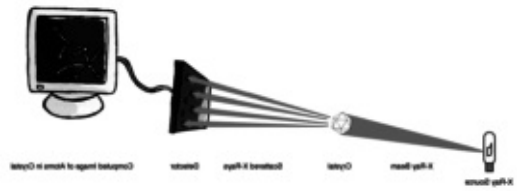

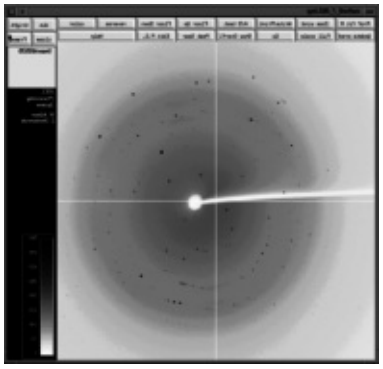

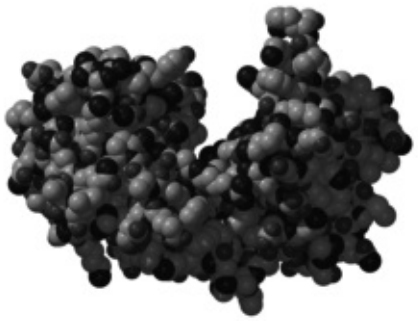

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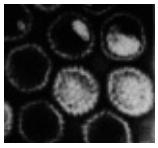

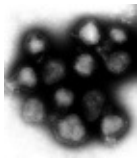

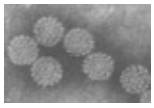

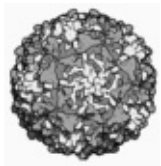

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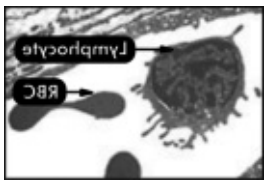

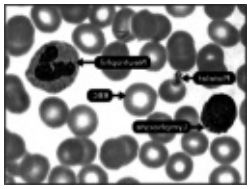

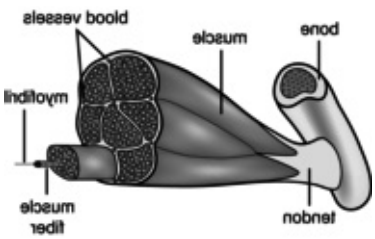

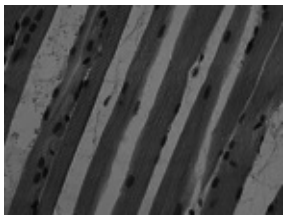

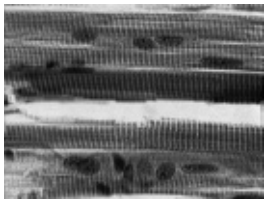

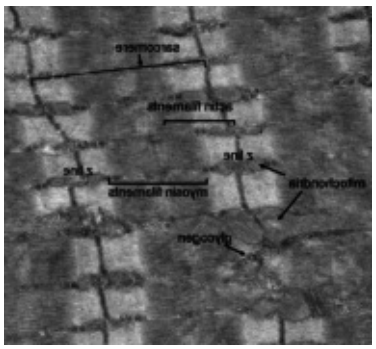

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the smallest units that can

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, and a membrane called the

. Each fiber contains multiple nuclei and

Muscle Structure

e arranged parallel to one another

ograph of human skeletal muscle.

ous mitochondria, because each muscle fiber develops fr

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colemma bundles them together

Skeletal muscle, also known as striated muscle, is made of many muscle

fibers, each of which extends the length of the muscle (up to 2.5 feet long).

Muscle fibers ar

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many cells called myofibrils that extend the length of the fiber

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Master 3.6(d)

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Blood smear viewed at 400

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Light micr

appearance of normal muscle fiber

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emainder of blood is composed of various cell types, as seen above.

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Red blood cells ar

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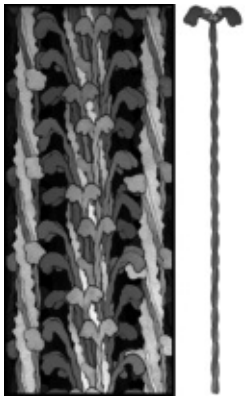

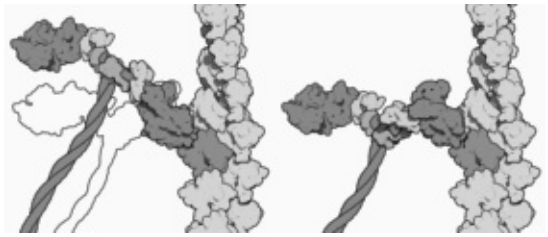

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Rational Basis for New Drug Development

e extensive and random testing.

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Myosin makes up about 45 to 50 per

muscle contractile pr

pr

Myosin uses chemical ener

motion. The myosin molecule looks some-

what like two golf clubs with their shafts

wrapped ar

Several other pr

structur

Cr

(left) and a thick myosin filament in between

two thin actin filaments (right).

The key to rational drug design is understanding the structur

biological molecules involved in disease development. T

disease, scientists sear

and molecular factors that play a r

drug design, including micr

analyses, and simulations.

The aim of rational drug design is to pr

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Science Reference Manual

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Muscle Proteins

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Muscle Contraction

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otein in muscle cells is actin, which forms the

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e twisted into a double helix to form an actin filament.

. Their arrangement and individual pr

oteins stabilize the filament.

ectly involved in muscle contraction and r

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Muscle fibers ar

a specific way

muscle to function. Some pr

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Up to one-fifth of the pr

thin filaments of the cells.

About 360 actin molecules combine to form a long chain. T

these chains ar

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At the tip of the myosin molecule is a cleft that binds to the actin filament. The

lever arm of the myosin pushes the myosin molecule along the actin filament.

Muscle contraction r

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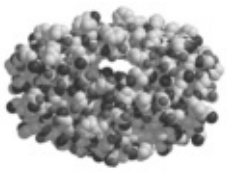

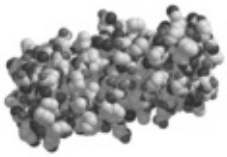

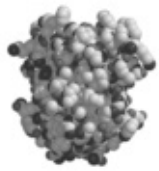

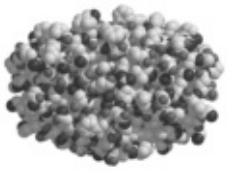

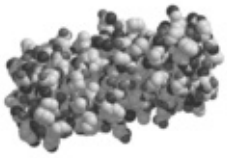

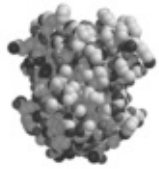

Muscle Protein Structures Determined by

X-Ray Crystallography

Muscle protein from affected people

Along z-axis

Along x-axis

Along y-axis

Muscle protein from unaffected people

Along z-axis

Along x-axis

Along y-axis

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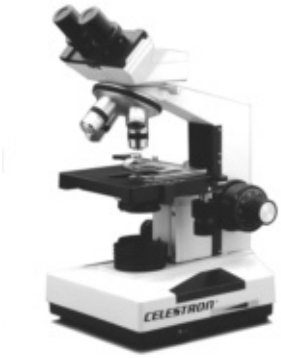

Microscopes Across Time

1754

1850

1909

Culpepper microscope

Ross microscope

Leitz Wetzler microscope

1948

2004

Spencer microscope

Modern research microscope

Master

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Some Key Developments in Biology,

Medicine, and Technology, by Year

BIOLOGY

1665

Cells first described (Robert Hooke).

1839

Proposal made that animal tissues are composed of cells (Theodor Schwann).

1869

DNA discovered (Friedrich Miescher).

1911

Structure of the atom discovered (Ernest Rutherford).

1942

Myosin *and* actin reported to be the main structural proteins of muscle (Albert Szent-Gyorgi and colleagues).

1953

Double helix model of DNA proposed (James Watson and Francis Crick; their model was supported by X-ray crystallography done by Maurice Wilkins and Rosalind Franklin).

1953

Structure of hemoglobin determined using X-ray crystallography (Max Perutz and John Kendrew).

2000

Atomic structure of the large subunit of a bacterial ribosome resolved using X-ray crystallography (Thomas Steitz and colleagues).

MEDICINE

1862

Germ theory published: infection is caused by bacteria (Louis Pasteur).

1868

First diagnosis made of a complex disease, multiple sclerosis (Jean Martin Charcot).

1892

Viruses discovered (Dimitri Ivanovsky).

1892

White blood cells identified (Elie Metchnikoff).

1893

First modern American medical school opens (Johns Hopkins University, Baltimore, Md.).

1895

First pharmaceutical research laboratory founded (Parke-Davis Company, Detroit, Mich.).

1928

Penicillin discovered (Alexander Fleming).

1959

First major drug to treat leukemia invented (Gertrude Elion).

TECHNOLOGY

1593

Thermometer invented (Galileo).

1883

First induction motor constructed, the basis of generating electricity (Nicola Tesla).

1895

X-rays discovered (Wilhelm Conrad Roentgen).

1912

X-ray crystallography invented (William Bragg).

1923

First electric refrigerator produced (Electrolux, Old Greenwich, Conn.).

1927

First working model of television (Philo Farnsworth).

1932

Electron microscope invented (Max Knoll and Ernst Ruska).

1969

First microprocessor designed, the basis for computer development (Marcian Hoff).

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