

• A PARTNERSHIP BETWEEN •

W. H. FREEMAN

&

SCIENTIFIC AMERICAN



# biology

FOR A CHANGING WORLD

SECOND EDITION

MICHÈLE SHUSTER | JANET VIGNA  
MATTHEW TONTOZ | GUNJAN SINHA

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*Publisher* Susan Winslow  
*Acquisitions Editor* Beth Cole  
*Development Editor* Andrea Gawrylewski  
*Marketing Director* John Britch  
*Market Development Manager* Shannon Howard  
*Marketing Assistant* Tess Sanders  
*Manager of Digital Development* Amanda Dunning  
*Associate Media Editor* Betsye Mullaney  
*Assistant Editor* Jane Taylor  
*Project Editor* Liz Geller  
*Copyeditor* Nancy Brooks  
*Art Director* Diana Blume  
*Designer* Tom Carling  
*Art Manager* Matthew McAdams  
*Artwork* Precision Graphics  
*Photo Editor* Christine Buese  
*Photo Researchers* Jacqui Wong, Donna Ranieri, and Teri Stratford  
*Production Manager* Paul Rohloff  
*Composition* MPS Limited  
*Printing and Binding* RR Donnelley

Library of Congress Control Number: 2013956230

ISBN-13: 978-1-4641-2673-4

ISBN-10: 1-4641-2673-9

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Printed in the United States of America

First printing

W. H. Freeman and Company  
41 Madison Avenue  
New York, NY 10010  
Houndmills, Basingstoke RG21 6XS, England  
[www.whfreeman.com](http://www.whfreeman.com)

**TO OUR TEACHERS AND STUDENTS**

*You are our inspiration*

# About the Authors



*From left to right: Michèle Shuster, Matthew Tontonoz, Janet Vigna*

**Michèle Shuster, Ph.D.**, is an associate professor in the biology department at New Mexico State University in Las Cruces, New Mexico. She focuses on the scholarship of teaching and learning, studying introductory biology, microbiology, and cancer biology classes at the undergraduate level, as well as working on several K-12 science education programs. Michèle is an active participant in programs that provide mentoring in scientific teaching to postdoctoral fellows, preparing the next generation of undergraduate educators. She is the recipient of numerous teaching awards, including the Westhafer award for Teaching Excellence at NMSU. Michèle received her Ph.D. from the Sackler School of Graduate Biomedical Sciences at Tufts University School of Medicine, where she studied meiotic chromosome segregation in yeast.

**Janet Vigna, Ph.D.**, is an associate professor in the biology department at Grand Valley State University in Allendale, Michi-

gan. She is a science education specialist in the Integrated Science Program, training and mentoring K-12 science teachers. Janet has 18 years of undergraduate teaching experience, with a special interest in effectively teaching biology to nonmajors. She has recently been recognized with the GVSU Outstanding Teacher Award. Her scholarly interests include biology curriculum development, the effective use of digital media in science education, and research on the effects of biological pesticides on amphibian communities. She received her Ph.D. in microbiology from the University of Iowa.

**Matthew Tontonoz** has been a development editor for textbooks in introductory biology, cell biology, biochemistry, evolution, and environmental science. After a brief stint in medical school in California, he realized he was better suited to saving sentences than saving lives. Matt received his B.A. in biology from Wesleyan University and his M.A. in the history and sociology of science from the University of Pennsylvania. He is currently staff science writer at the Cancer Research Institute, where he covers advances in cancer immunology and blogs about the history of medicine. He lives in Brooklyn, New York.

**Gunjan Sinha** has been writing about science for over a decade. Her articles have been published in *Science*, *Nature Medicine*, *Nature Biotechnology*, *Scientific American*, and several other magazines and journals. She holds a graduate degree in molecular genetics from the University of Glasgow, Scotland, and a graduate degree in journalism from New York University. She currently works as a freelance science journalist and lives in Berlin, Germany.

## DEAR READER,

*Thank you for opening this book! We hope that your journey through it will be as rewarding for you as our journey in writing it has been. When we first came together to collaborate on the development of this text, our biggest goal was to get students interested in biology by showing its relevance to daily life. We wanted to create a textbook that students would actually want to read. Our model and partner in this process has been Scientific American, a visually stunning magazine that's been successfully bringing science to the public for more than 150 years. The result is a unique textbook that takes a novel approach to teaching biology, one that we think has the potential to greatly improve learning. We hope that this brief introduction will serve as a road map of the book, so that you can get the most out of your experience with it and be as captivated by the wonders of life as we are.*

*The main approach of each chapter is the presentation of key science concepts within the context of a relevant and engaging story—a story of discovery, of determination, of human interest, of adventure. From the search for life on Mars to the problem of antibiotic-resistant bacteria, we use stories to bring science to life and to show scientists in action. After all, science is not just a collection of facts, so why would we present it that way? We ask you, our students, to study biology so you can use knowledge to make choices in the real world. We value those stories that will lead you to ask questions about life and how it works and to see the relevance of biology to daily activity. We have seen how stories engage students in our classrooms, and we hope you will be similarly intrigued.*

*While gripped by a story, you may not even realize how much you are learning. To reinforce the basic learning process, we rely on several strategies:*

- ▶ *Each story is prefaced by a set of Driving Questions. By keeping these in mind as you navigate the story, you will have a good framework for learning the key science concepts.*
- ▶ *Eye-catching Infographics highlight and drill down into the science of each story. The set of Infographics in a chapter provides a science storyboard for that chapter, illustrating the key scientific concepts and linking them to the story.*
- ▶ *Key terms are defined in the margins, making it easy to check a definition without having to leave the story.*
- ▶ *Chapter summaries provide a concise set of bullet points that distill the key scientific concepts.*
- ▶ *Test Your Knowledge questions at the end of each chapter reinforce basic facts and also allow the facts to be applied through data interpretation and mini cases.*

*By taking full advantage of these resources, you will be better able to appreciate how biology affects each and every one of us as well as our close and distant relatives on this planet. We hope that you will talk about biology with your friends and family, and that what you learn here will be applicable to your life. We hope that you will think as critically about every decision you make in the future as we will ask you to do here in these pages.*

*Welcome to Biology for a Changing World. We hope that you enjoy your journey, and complete it more prepared for your life in a changing world.*

MICHÈLE SHUSTER

JANET VIGNA

MATTHEW TONONZOZ

GUNJAN SINHA

## Science taught through stories

*Current, engaging stories capture the imagination and inspire students to read*



*Real people, real voices, and real science bring the story to life*

# Modern magazine look and feel

Key Terms are easy to find

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UNIT 1 • WHAT IS LIFE MADE OF? CHEMISTRY, CELLS, ENERGY

**4**

**COFACTOR**  
An inorganic substance, such as a metal ion, required to activate an enzyme.

**COENZYME**  
A small organic molecule, such as a vitamin, required to activate an enzyme.

Vitamins and minerals play numerous roles in the body. Some play structural roles—the mineral calcium, for example, is a primary component of bones and teeth. Others play a functional role, helping other molecules to act. Perhaps their most critical role is serving as **cofactors** for enzymes.

Cofactors are accessory or “helper” chemicals that enable enzymes to function. Cofactors include inorganic metals such as zinc, copper, and iron. Cofactors can also be organic molecules, in which case they are called **coenzymes**. Most vitamins are important coenzymes. Without cofactors and coenzymes that bind to enzymes and enable them to bind to substrates, cell metabolism would grind to a halt (**INFOGRAPHIC 4.6**).

By adding extra vitamins and minerals to the milk that children were receiving in the hospital, Manary found that he could get the death rate to go way down, but the recovery rate still wouldn't budge. That's when he knew it was time for a new approach.

**INFOGRAPHIC 4.6 VITAMINS AND MINERALS HAVE ESSENTIAL FUNCTIONS**

Minerals are micronutrients, nutrients that are essential for health but required in far smaller amounts than macronutrients.

Some vitamins and minerals are structural elements.

The minerals calcium and phosphorus are important for building strong teeth and bones.

Vitamin A, also known as retinol, is important for eye photoreceptors for vision and for maintaining the health and growth of skin.

Some vitamins and minerals are cofactors that allow substrates to bind enzymes.

Vitamin B<sub>12</sub> or folic acid is an important coenzyme for an enzyme involved in DNA synthesis.

Substrate (e.g., a nucleotide precursor)

Inactive enzyme + Cofactor (e.g., vitamin B<sub>12</sub>) → Activated enzyme can now bind its substrate.

Enzyme activity leads to DNA synthesis, which is essential for cell division and inheritance.

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**4** NUTRITION, METABOLISM, ENZYMES



Before and After: For many children in Malawi, peanut butter RUTF has been a life-saver.

**EMPTYING THE WARDS**

By the time Manary began seriously thinking about home-based therapy, he had been working in Malawi for about 5 years, witnessing the failure of the standard WHO treatment, and he had spent time in villages. In his head, he'd been tossing around the idea of something new and different. Out of the blue, he got an e-mail from a doctor in France, André Briand, who was also thinking about home-based therapy as a treatment for malnutrition.

The two scientists corresponded for about a year by e-mail, weighing the pros and cons of various foods that could be eaten at home yet still pack a nutrient wallop. After considering various options—they considered biscuits, pancakes, even Nutella—the two researchers eventually decided on peanut butter as the best choice. In 2001, they decided to test the idea. Briand had some of the peanut butter RUTF made up in France and then sealed in foil packets and shipped to Malawi. They then used this product in a carefully designed scientific study. After a brief stabilization phase in the hospital (during which antibiotics were given, if necessary), the children were discharged and sent home on one of three different treatment regimens: (1) ample amounts of traditional food—corn flour and soy; (2) a small amount of peanut butter-based RUTF to be used as a supplement to the normal diet at home; and (3) the full dose of peanut butter-based RUTF, with sufficient nutrients to meet the total nutritional needs of the children. The regimen was most effective.

Within a few months, the results were astonishing: 98% of the children who received the full peanut butter-based RUTF recovered. Those who received traditional food also did pretty well—about 75% of them recovered, but still the peanut butter was better. And all the home-based treatments were significantly better than standard hospital-based milk therapy, which historically had a 25%–40% recovery rate.

The science is taught in context of the story

Shorter chapters hold student attention and make the science more manageable



## Driving Questions are the roadmap for each chapter

**1**

**THE PEANUT BUTTER PROJECT**  
A doctor's crusade to end malnutrition in Africa, a spoonful at a time

**DRIVING QUESTIONS**

1. What are the macronutrients and micronutrients provided by food?
2. What are essential nutrients?
3. What are enzymes, and how do they work?
4. What are the consequences of a diet lacking sufficient nutrients?

**DRIVING QUESTIONS**

1. What are the macronutrients and micronutrients provided by food?
2. What are essential nutrients?
3. What are enzymes, and how do they work?
4. What are the consequences of a diet lacking sufficient nutrients?

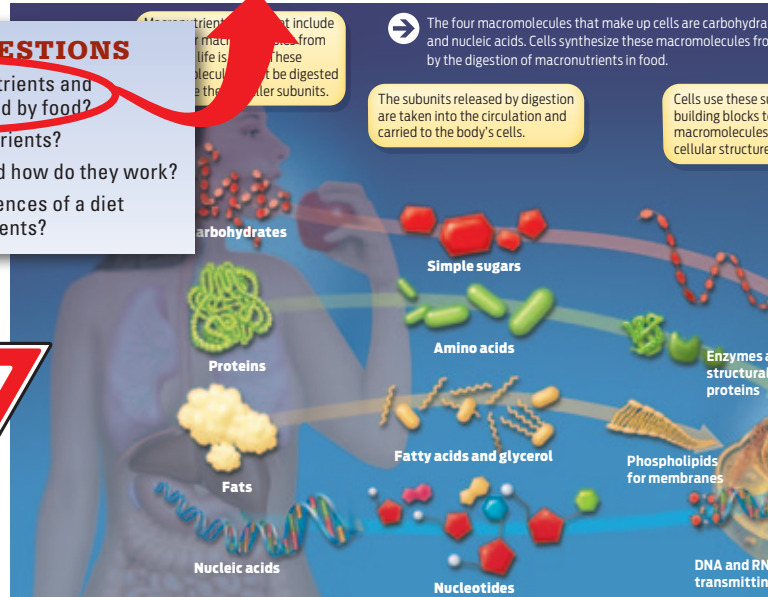
**4**  
NUTRITION, METABOLISM, ENZYMES

Colorful and engaging infographics teach the most important science

### INFOGRAPHIC 4.3 MACRONUTRIENTS BUILD AND

**DRIVING QUESTIONS**

1. What are the macronutrients and micronutrients provided by food?
2. What are essential nutrients?
3. What are enzymes, and how do they work?
4. What are the consequences of a diet lacking sufficient nutrients?



INFO + GRAPHIC = INFOGRAPHIC

UNIT 1 • WHAT IS LIFE MADE OF? CHEMISTRY, CELLS, ENERGY

4

3. A multivitamin supplement is a(n) \_\_\_\_\_ supplement.

a. macronutrient  
b. micronutrient  
c. mineral  
d. enzyme  
e. a and b

4. Which of the following foods is a rich source of protein?

a. lean meat, such as chicken breast  
b. whole grains (e.g., whole wheat bread)  
c. olive oil  
d. leafy greens  
e. berries (e.g., blueberries and raspberries)

**USE IT**

5. Explain the difference between macronutrients and micronutrients.

6. A typical multivitamin supplement contains vitamin A, vitamin C, vitamin D, vitamin E, vitamin K, vitamin B<sub>1</sub>, vitamin B<sub>2</sub>, vitamin B<sub>6</sub>, biotin, calcium, iron, magnesium, zinc, selenium, copper, manganese, and chromium. Explain your answers to the following questions.

a. Are all of these vitamins? If there are ingredients that are not vitamins, what are they?  
b. Are all of these micronutrients?

**DRIVING QUESTION 2**  
What are essential nutrients?

By answering the questions below and studying Infographics 4.3 and 4.5 and Table 4.1, you should be able to generate an answer for the broader Driving Question above.

10. Which component of essential amino acid \_\_\_\_\_

a. milk powder  
b. peanut butter  
c. sugar  
d. vegetable powder  
e. powdered vitamin  
f. a and c

11. Corn lacks the essential amino acids lysine and tryptophan and methionine. Beans lack the essential amino acids \_\_\_\_\_

a. Could someone survive on a diet with a corn-based protein alone? Why or why not?  
b. How many traditional diets combine corn (e.g., tortillas) with beans?  
c. Why did one of the home-based feeding therapies (e.g., Metamucil) combine soy flour with corn flour?

**DRIVING QUESTION 3**  
What are enzymes, and how do they work?

By answering the questions below and studying Infographics 4.4, 4.5, and 4.6, you should be able to generate an answer for the broader Driving Question above.

**KNOW IT**

12. The substrate of an enzyme is \_\_\_\_\_

a. an organic accessory molecule.

### DRIVING QUESTIONS

1. What are the macronutrients and micronutrients provided by food?
2. What are essential nutrients?
3. What are enzymes, and how do they work?
4. What are the consequences of a diet lacking sufficient nutrients?



Crucial practice built around the Driving Questions

## INFOGRAPHIC 4.4 ENZYMES FACILITATE CHEMICAL REACTIONS

Cells require enzymes to break down and build up macromolecules. Enzymes are proteins that speed up chemical reactions.

### MAINTAIN CELLS

es, proteins, lipids,  
in the subunits released

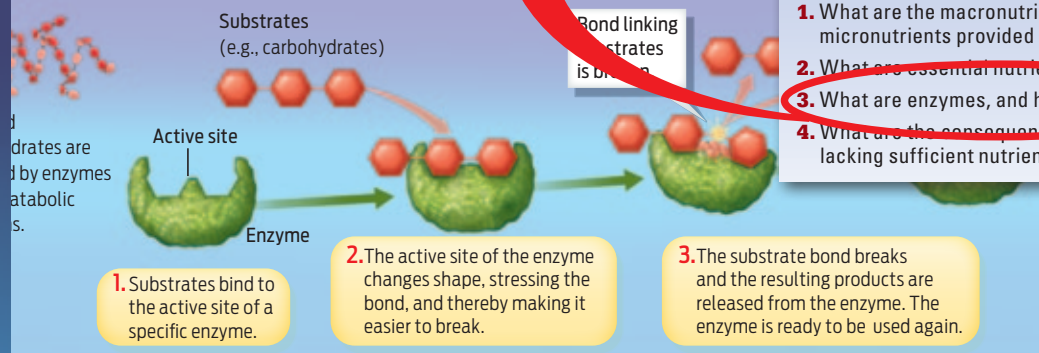
subunits as the  
assemble the  
necessary for  
and function.

Energy storage and  
cell-surface molecules

nd

A for storing and  
genetic instructions

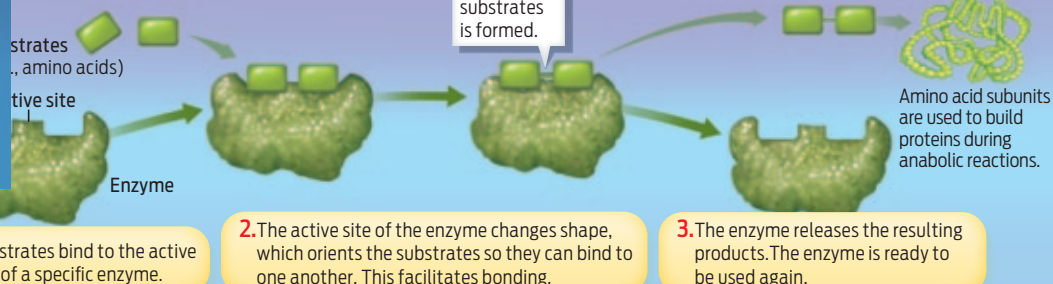
#### Catabolic Reaction: Bonds are broken



### DRIVING QUESTIONS

1. What are the macronutrients and micronutrients provided by food?
2. What are essential nutrients?
3. What are enzymes, and how do they work?
4. What are the consequences of a diet lacking sufficient nutrients?

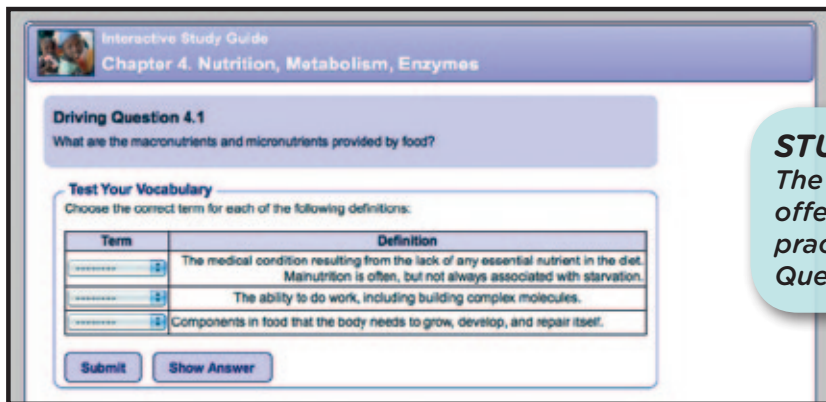
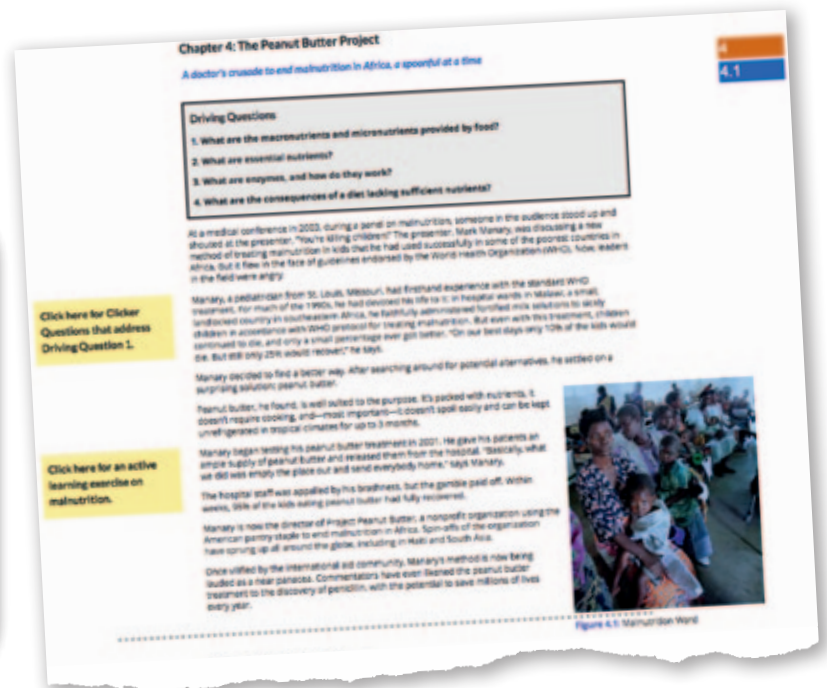
#### Anabolic Reaction: Bonds are created



## More ways to practice each Driving Question

### INSTRUCTOR'S GUIDE

The electronic Instructor's Guide is designed to help instructors make the most of our story-based text. Instructional tips from the book's author and other experienced non-majors instructors are integrated into the e-Book, a comprehensive resource for any instructor teaching with our text. Features include active learning exercises, misconception alerts, links to online resources, additional scientific detail, and more.



### STUDENT STUDY GUIDE

The Student Study Guide offers additional online practice with each Driving Question



### LEARNINGCURVE

LearningCurve is a set of formative assessment activities, built around the Driving Questions, that uses a gamelike interface to guide students through a series of questions tailored to their individual level of understanding. A personalized study plan is generated based upon their quiz results, and students can automatically link to the relevant passages in the e-Book for help.

# New data problems, case studies, and Bring it Home activities in each chapter

## INTERPRETING DATA

**26** The United States currently uses approximately 19 million barrels of oil per day. Of this, about half (9.67 million barrels per day) is imported, and the rest is from U.S. sources (offshore drilling or extraction from shale). The table shows production costs estimated for different oil sources. (The actual cost is driven by a variety of market and geopolitical factors, so we will use production costs as a substitute for actual cost.)

Source	Production Cost per Barrel (Range)	Production Cost per Barrel (Average)
U.S. (offshore)	\$70–\$80	\$75
U.S. (shale oil)	\$50–\$70	\$60
Canada (tar sands)	\$70–\$90	\$80
UAE	\$50–\$70	\$60
Brazil	\$60–\$80	\$70
Algal biofuel	\$140–\$900	\$520

SOURCE: <http://insideclimatenews.org/news/20101122/algae-fuel-indies-toward-price-parity-oil>; <http://www.odac-info.org/newsletter/2011.09.18>

- Using the data for cost per barrel of various oils, calculate the cost to produce oil to meet current U.S. daily use. Assume that approximately half the imports are from the United Arab Emirates (UAE), and the remainder is split equally between imports from Canada and from Brazil.
- Let's say that the United States replaces half of its current oil imports from the UAE with domestically produced algal biofuel. What will this do to the cost of producing our daily needs?

c. From what you've read in this chapter, how

## INTERPRETING DATA

**23** The table at right shows the frequencies for STR lengths (repeat number) in different U.S. populations. You can determine the probability of a particular combination of STRs by multiplying the frequencies: for example, the probability of a Hispanic person's having 14 D3S1358 repeats (0.079) and 18 TH01 repeats (0.125) is  $0.079 \times 0.125 = 0.009$

- What is the probability of a Caucasian American's having a 16, 17 combination for D3S1358?
- What is the probability of an African American's having a 16, 17 combination for D3S1358?
- What is the probability of a Hispanic American's having a 16, 17 combination for D3S1358?
- What is the probability of a Caucasian American's having a 16, 17 combination for D3S1358, and a 5, 9 combination for TH01?

CODIS* STR	NO. OF REPEATS	FREQUENCY (CAUCASIAN)	FREQUENCY (AFRICAN AMERICAN)	FREQUENCY (HISPANIC)
D3S1358	14	0.094	0.089	0.079
	15	0.111	0.186	0.293
	16	0.200	0.248	0.286
	17	0.281	0.242	0.204
	18	0.200	0.155	0.125
TH01	5	0.002	0.004	0
	6	0.232	0.124	0.214
	7	0.190	0.421	0.096
	8	0.084	0.194	0.096
	9	0.114	0.151	0.150
D18S51	10	0.008	0.006	0.004
	11	0.017	0.002	0.011
	12	0.127	0.078	0.118
	13	0.132	0.053	0.111
	14	0.137	0.072	0.139

probability of a Caucasian American's having a 16, 17 combination for D3S1358 and a 5, 9 combination for TH01 and an African American's having a 16, 17 combination for D3S1358 and a 5, 9 combination for TH01 and an African American's having a 16, 17 combination for D3S1358 and a 5, 9 combination for TH01 and an African American's having a 16, 17 combination for D3S1358 and a 5, 9 combination for TH01?

\* 15 autosomal STR loci on U.S. Caucasian, African American and Hispanic populations. Journal of Forensic Sciences 48(4): 906–910. A government database of DNA profiles from offenders, crime scenes, and missing persons.

## MINI CASE

**21** A college student returns home at the end of the school year. His mother is shocked by the large number of unhealed scrapes and sores on his knees and arms. She also notices that he has put on a few pounds. The student tells his mother that the scrapes are just left over from a skateboarding mishap a few weeks ago and that he guesses he could cut back on some of his snacks. A week after coming home, he goes to the dentist for his yearly checkup. The dentist is alarmed by his bleeding and swollen gums. When asked about his diet, the student notes that he and some of his friends challenged one another to see who could go the longest eating nothing but eggs, mac 'n' cheese, and toast with butter. He proudly announces that he had stayed on this diet for 6 months.

- Could this student be suffering from malnutrition? Explain your answer.
- What mineral(s) or vitamin(s) (or both) are you most concerned about, given the symptoms noted by the dentist?
- What dietary recommendations would you make for this student?

## BRING IT HOME

**23** A number of concerns have been expressed about GMOs. Search the internet for reliable sources about a particular GMO that you have heard of or in which you are interested (e.g., Golden Rice or genetically modified salmon). List what you consider to be the pros and cons of at least two GMOs. Has what you have read about other genetically modified organisms and the transgenic goats in this chapter changed your opinions about GMOs? What restrictions (if any) would you place on GMOs?

## Digital Resources Complete the Package

A robust suite of digital materials provides the tools that instructors and students need to teach and learn with *Biology for a Changing World*. Organized by each chapter's Driving Questions, our instructor and student resources will help ensure that students learn the science behind the stories.

### Instructor Resources



The new standard in online course management, LaunchPad makes it easier than ever to create interactive assignments, track online homework, and access a wealth of extraordinary teaching and learning tools. Fully loaded with our **customizable e-Book** and all **student** and **instructor resources**, the LaunchPad is organized around a series of prebuilt LaunchPad Units—carefully curated, ready-to-use collections of material for each chapter of *Biology for a Changing World*.

#### Instructor's Guide

The electronic Instructor's Guide is designed to help instructors make the most of our story-based text. With instructional tips from the book's authors and others who have taught using the text, the Instructor's Guide is a comprehensive resource for any instructor teaching with our text. Features include active learning exercises, misconception alerts, links to online resources, additional scientific detail, and more.

#### Lecture Tools

##### Optimized Art

Infographics are optimized for projection in large lecture halls and split apart for effective presentation.

##### Interactive Animated Infographics

Every piece of art in the text is interactive. All animations are embedded in the text of the LaunchPad e-Book.

##### PowerPoint Slides

Prebuilt lecture slides provide a great starting point for your lecture and help with the transition to a new textbook.

#### Clicker Questions

Designed as interactive in-class exercises, these questions reinforce core concepts and uncover misconceptions.

#### Story Summaries

The story summaries offer a brief synopsis of a chapter's main story, providing interesting details relevant to content found in the book and in online resources.

#### Activities from the Yale Center for Scientific Teaching



Teaching tidbits created by the Yale Center for Scientific Teaching provide new active learning exercises for the classroom. Each activity is created specifically for *Biology for a Changing World* as a part of Yale's "Theory and Practice of Scientific Teaching" course for graduate science students, and incorporates important tenets of the Scientific Teaching method. Tidbits include PPT slides for class, instructions for teachers, and any additional content needed to implement the activity in your own course. To learn more about Yale's Center for Scientific Teaching, visit <http://cst.yale.edu>.

#### Assessment

##### **LEARNING**Curve

LearningCurve is a set of formative assessment activities that uses a gamelike interface to guide students through a series of questions tailored to their individual level of understanding. A personalized study plan is generated based upon their quiz results, and students can automatically link to the relevant passages in the e-Book for help.

**Test Bank**

A collection of more than a thousand questions organized by chapter and Driving Question and presented in a sortable, searchable environment. The Test Bank includes multiple-choice, short-answer, and matching questions. Questions can also be sorted by type, difficulty level, and important word or concept.

**Instructor's Resource Flash Drive**

Combines a variety of instructor resources, including art, PowerPoint slides, Clicker Questions, and the Test Bank in one convenient package.

**Course Management System**

e-Packs are available for Blackboard, Canvas, Desire2Learn, and other course management platforms.

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## Student Resources

Student Resources reinforce chapter concepts and give students the tools they need to succeed in the course. All student resources are organized by Driving Questions and can be found in the LaunchPad.



Students have access to a variety of study tools in the LaunchPad along with a complete online version of the textbook. Carefully curated LaunchPad Units provide suggested learning paths for each chapter in the text.

**Student Study Guide**

Organized by Driving Question, the newly revised electronic Student Study Guide deepens students' understanding of chapter content. The Student Study Guide digs in to each Infographic and develops students' knowledge through a variety of open-ended and multiple-choice self-study questions.

**Interactive Animated Infographics**

Every piece of art in the text has been animated. All animations are embedded in the text of the LaunchPad e-Book.

**LEARNINGCurve**

LearningCurve is a set of formative assessment activities that uses a gamelike interface to guide students through a series of questions tailored to their individual level of understanding. A personalized study plan is generated based upon their quiz results, and students can automatically link to the relevant passages in the e-Book for help.

**Pre-Quiz Study Questions with Feedback**

Quiz questions with response-specific feedback help explain concepts and correct student misunderstandings.

**Art Notebook**

The art in each chapter is available in PDF form for students to download and print before lectures or for individual study.

**Key Term Flashcards**

Students can drill and learn the most important terms in each chapter using interactive flashcards.

# Acknowledgments

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We are thrilled to introduce the second edition of *Scientific American Biology for a Changing World*. We have replaced six stories and added two new Milestones to keep this book at the forefront of current issues in biology. New Driving Questions target students' reading, and new mini cases and data questions test their knowledge. A fresh, updated design showcases our unparalleled Infographics, and compelling narratives continue to reveal how biology is relevant to daily life.

As with the first edition, we could not have completed this project without the help of a great team at W. H. Freeman. The authors would like to thank Elizabeth Widdicombe, Susan Winslow, and the folks at W. H. Freeman and Company and *Scientific American* for continuing to support this vision for biology education. They recognized our diverse strengths and brought us together to make this vision a reality. We continue to learn so much from one another on this challenging and rewarding professional journey, and none of us has likely worked so hard and so passionately on a project as we all have on this one.

We would like to thank all those who were interviewed and who generously contributed information for the chapters in this edition. Their stories are central to the impact that this book will have on the students we teach. They are authentic examples of biology in a changing world, and they bring this book to life.

A special thank you is required for our Acquisitions Editor, Beth Cole, for her unwavering encouragement and ability to bring stable direction and support to the project. Development Editor Andrea Gawrylewski has spent many hours in the pages of this book, editing the details, managing our chaos, and smoothing our rough edges. Sara Blake and Jane Taylor were invaluable in the scheduling, reviewing, and managing of this edition. We thank them for their dedication, patience, experience, and expertise. Thanks go to Betsy Mullaney and Amanda Dunning for their tireless work on our media and assessment program.

Many thanks to Liz Geller, Nancy Brooks, Diana Blume, Matthew McAdams, Christine Buese, Paul Rohloff, and all the people behind the scenes at W. H. Freeman for translating our ideas into a beautiful, cohesive product. We would like to thank Rachel Rogge and Jan Troutt at Precision Graphics for their outstanding work on the Infographics. We appreciate their patience with the many edits and quick timelines throughout the project. They do amazing work.

We'd like to thank John Britch and Shannon Howard for their enthusiasm and hard work in promoting this book in the biology education community. We thank the enthusiastic group of salespeople who connect with biology educators across the country and do a wonderful job representing this book.

We would like to thank our families and friends who have been close to us during this process. They have been our consultants, served as sounding boards about challenges, celebrated our successes, shared our passions, and supported the extended time and energy we often diverted away from them to this project. We are grateful for their patience and unending support.

And finally, a sincere thank you to our many teachers, mentors, and students over the years who have shaped our views of biology and the world, and how best to teach about one in the context of the other. You are our inspiration.

## Media and Assessment Authors

John Harley, Eastern Kentucky University, *Learning Curve Activities*  
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 Carolyn Wetzel, Holyoke Community College, *Test Bank*  
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 Jodi DenUyl, Grand Valley State University, *Pre-Quiz Study Questions*  
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 Julie Glenn, Gainesville State College  
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We would like to extend our deepest thanks to the following instructors who reviewed, tested, and advised on the book manuscript at its various stages of development.

Stephanie Aamodt, <i>Louisiana State University-Shreveport</i>	Judith Carey, <i>Springfield Technical Community College</i>
Marilyn Abbott, <i>Lindenwood University</i>	Jennifer Carney, <i>Finger Lakes Community College</i>
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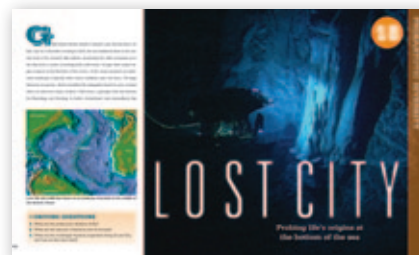
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– GRETCHEN FRÜH-GREEN, CHAPTER 18



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*“In its simplest sense, sustainability is just doing things today to ensure a vibrant successful future for others.”*

— STACEY SWEARINGEN WHITE, CHAPTER 24

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# JAVVA REPORT

Making sense of the latest buzz  
in health-related news



## ►► DRIVING QUESTIONS

1. How is the scientific method used to test hypotheses?
2. What factors influence the strength of scientific studies and whether the results of any given study are applicable to a particular population?
3. How can you evaluate the evidence in media reports of scientific studies?
4. How does the scientific method apply in clinical trials designed to investigate important issues in human health?



**I**N 1981, A STUDY IN THE PROMINENT *New England Journal of Medicine* made headlines when it reported that drinking two cups of coffee a day doubled a person's risk of getting pancreatic cancer. Drinking five cups a day supposedly tripled the risk. "Study Links Coffee Use to Pancreas Cancer," trumpeted the *New York Times*. "Is there cancer in the cup?" asked *Time* magazine. The lead author of the study, Brian MacMahon of the Harvard School of Public Health, appeared on the *Today* show to warn of the dangers of coffee.

"I will tell you that I myself have stopped drinking coffee," said MacMahon, who had previously drunk three cups a day.

Just 5 years later, MacMahon's research group was back in the news, reporting in the same journal that a second study had found *no* link between coffee and pancreatic cancer. Subsequent studies by other researchers also failed to reproduce the original findings.



**A global affair: Customers in the Yunnan province in China line up for their morning coffee fix at a Starbucks.**

Today, more than 30 years later, coffee is once again making headlines. Recent studies have suggested that, far from causing disease, coffee may actually help *prevent* a number of conditions—everything from Parkinson disease and diabetes to cancer and tooth decay. “Java Junkies Less Likely to Get Tumors,” announced a 2010 CBS News headline. “Morning Joe Fights Prostate Cancer,” proclaimed a blog. The September 2010 issue of *Prevention* magazine ran an article titled “Four Ways Coffee Cures,” itemizing supposed health benefits for each additional cup consumed.

Not everyone is buying the coffee cure, however. Public health advocates are increasingly alarmed by our love affair with—some might say, addiction to—caffeine. Emergency rooms are reporting more caffeine-related admissions, and poison control centers are receiving more calls related to caffeine “overdoses.” In response, politicians are pressuring the Food and Drug Administration (FDA) to force manufacturers to place warning labels

on energy drinks. Nevertheless, caffeine’s “energizing” effect is advertised on nearly every street corner, where, increasingly, you’re also likely to find a coffee shop. As of 2012, according to Foodio54.com, there were 231 Starbucks within a 5-mile radius of a Manhattan zip code; nationally, the average within the same radius is 10.

Why the mixed messages about caffeine? Are researchers making mistakes? Are journalists getting their facts wrong? While both of these possibilities may be true at times, the bigger problem is widespread confusion over the nature of science and the meaning of scientific evidence.

“Consumers are flooded with a firehose of health information every day from various media sources,” says Gary Schwitzer, publisher of the consumer watchdog site HealthNewsReview.org and former director of health journalism at the University of Minnesota. “It can be—and often is—an ugly picture: a bazaar of disinformation.” Too often, he says, the results of studies are reported in incomplete or misleading ways.

Why might consuming coffee or caffeine be associated with such dramatically different results? The risks or benefits of a caffeinated beverage may depend on the amount a person drinks—one cup versus a whole pot. Or maybe it matters *who* is drinking the beverage. The *New England Journal of Medicine* study, for example, looked at hospitalized patients only. Would the same results have been seen in people who weren’t already sick? Sometimes, to properly evaluate a scientific claim, we need to look more closely at how the science was done (**INFOGRAPHIC 1.1**).

## SCIENCE IS A PROCESS

When many people think about science, they think of a body of facts to be memorized: water boils at 100°C; the nucleus is a part of a cell. But that’s not the whole story. **Science** is a *way* of knowing, a *method* of seeking answers to questions on the basis of observation and experiment. Scientists draw conclusions from the best evidence they have at any one

### ► SCIENCE

The process of using observations and experiments to draw conclusions based on evidence.

time, and the process is not always easy or straightforward. Conclusions based on today's evidence may be modified in the future as other scientists ask different—and sometimes better—questions. Moreover, with improved technology, researchers may uncover better data; new information can cast a new light on old conclusions. Science is a never-ending process.

Perhaps the best way to understand science is to do it. Let's say you want to determine scientifically if coffee has energizing effects. How might you go about investigating this question? A logical place to start would be your own experience. You may notice that you feel more awake when you drink coffee or that coffee helps you concentrate. Such informal personal observations are called **anecdotal evidence**. This is a type of evidence that may be interesting but is often unreliable, since it isn't based on systematic study. A poll of your classmates to find out how they experience coffee would also be anecdotal evidence.

Nevertheless, this anecdotal evidence might lead you to formulate a question: Does coffee improve mental performance? Will it help me study or do better on a test? To

find out what information currently exists on the subject, you could read relevant studies that have already been conducted, available in online databases of journal articles or in university libraries. Generally, you can trust the information in scientific journals because it has been subject to **peer review**. The aim of peer review—the review of an article by experts before publication—is to weed out sloppy research as well as overstated claims, and thus ensure the integrity of the journal and its scientific findings. To further reduce the chance of bias, authors must declare any possible conflicts of interest and name all funding sources (for example, pharmaceutical or biotechnology companies). With this information, reviewers and readers can view the study with a more critical eye.

From your perusal of the scientific literature, you would soon discover (if you didn't know it already) that coffee contains caffeine, and that caffeine is a chemical known to stimulate the brain. Brain regions controlling sleep, mood, memory, and concentration are especially sensitive to this chemical, and some researchers believe that caffeine accounts for the general feeling of alertness that many coffee drinkers experience.

#### ▶ ANECDOTAL EVIDENCE

An informal observation that has not been systematically tested.

#### ▶ PEER REVIEW

A process in which independent scientific experts read scientific studies before they are published to ensure that the authors have appropriately designed and interpreted the study.

## INFOGRAPHIC 1.1 CONFLICTING CONCLUSIONS

➔ A variety of studies published in peer-reviewed scientific journals report different conclusions about the risks and benefits of coffee. In order for the public to understand and use these outcomes to its advantage, a closer look at the scientific process and the factors that surround coffee drinking is necessary.

### Scientific Studies Report That Drinking Coffee...

- May cause pancreatic cancer
- Is linked to infertility and low infant birth weight
- Lowers the risk of Parkinson disease
- Does not cause pancreatic cancer
- Reduces risk of ovarian cancer



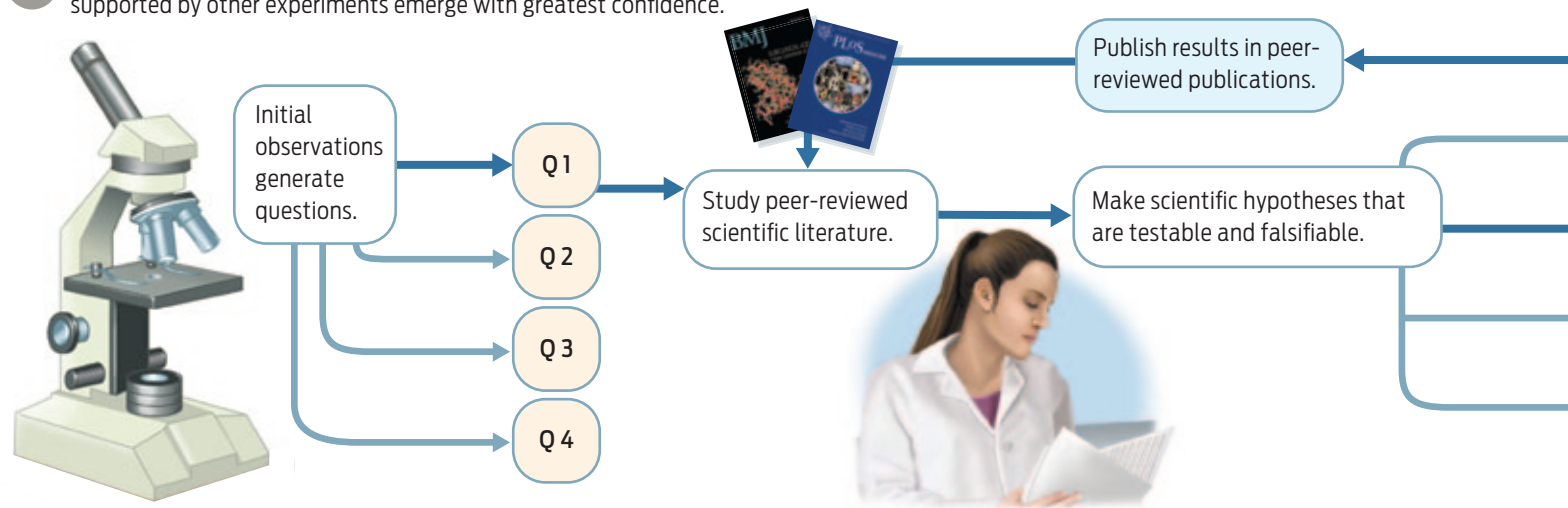
### Factors That May Influence These Results:

- Chemicals naturally present in coffee, including caffeine
- The climate and soil in which different coffee plants are grown (which in turn influences the chemicals in coffee)
- How the beans are roasted and processed
- How much coffee a person drinks
- The gender, age, and general health of a coffee drinker
- Other social factors, such as whether coffee is consumed with a meal or with a cigarette
- Other unknown factors that just happen to correlate with coffee drinking



## INFOGRAPHIC 1.2 SCIENCE IS A PROCESS: NARROWING DOWN THE POSSIBILITIES

Multiple scientists doing multiple experiments narrow down the pool of possible hypotheses. Those that are rigorously tested and supported by other experiments emerge with greatest confidence.



Armed with this information, you could go one step further and formulate a specific **hypothesis** about how coffee affects mental performance. A hypothesis is a possible answer to the question under investigation. For example, one hypothesis about coffee might be that consuming the caffeine in coffee improves memory. Another might be that high levels of caffeine increase concentration. Not all possible explanations will be *scientific* hypotheses, though. A scientific hypothesis must be **testable** and **falsifiable**—that is, it can be established or rejected by experiment; and if it is false, it can be proved wrong. Statements of opinion and hypotheses that depend on supernatural or mystical explanations that cannot be tested or refuted fall outside the realm of scientific explanation. (Some call such explanations “pseudoscience”; astrology is a good example.)

With a clear scientific hypothesis in hand—“caffeinated coffee improves memory”—the next step is to test it, generating evidence for or against the idea. If a hypothesis is shown to be false—if the finding is “caffeinated coffee does not improve memory”—the hypothesis can be rejected and removed from the list of possible answers to the origi-

nal question. You, the scientist, are then forced to consider other hypotheses. On the other hand, if data support the hypothesis, then it will be accepted, at least until further testing and data show otherwise. Because it is impossible to test whether a hypothesis is true in every possible situation, a hypothesis can never be proved true once and for all. The best we can do is support the hypothesis with an exhaustive amount of evidence (**INFOGRAPHIC 1.2**).

There are a number of ways in which a hypothesis can be tested. One is to design a controlled **experiment**. In this case, you might measure the effects of coffee drinking on a group of participants. In 2002, Lee Ryan, a psychologist at the University of Arizona, decided to do just that. Ryan noticed that memory is often optimal early in the morning in adults over age 65 but tends to decline as the day goes on. She also noticed that many adults report feeling more alert after drinking caffeinated coffee. She therefore hypothesized that drinking coffee might prevent this decline in memory, and devised an experiment to test her hypothesis.

First she collected a group of participants—40 men and women over age 65,

### ► HYPOTHESIS

A tentative explanation for a scientific observation or question.

### ► TESTABLE

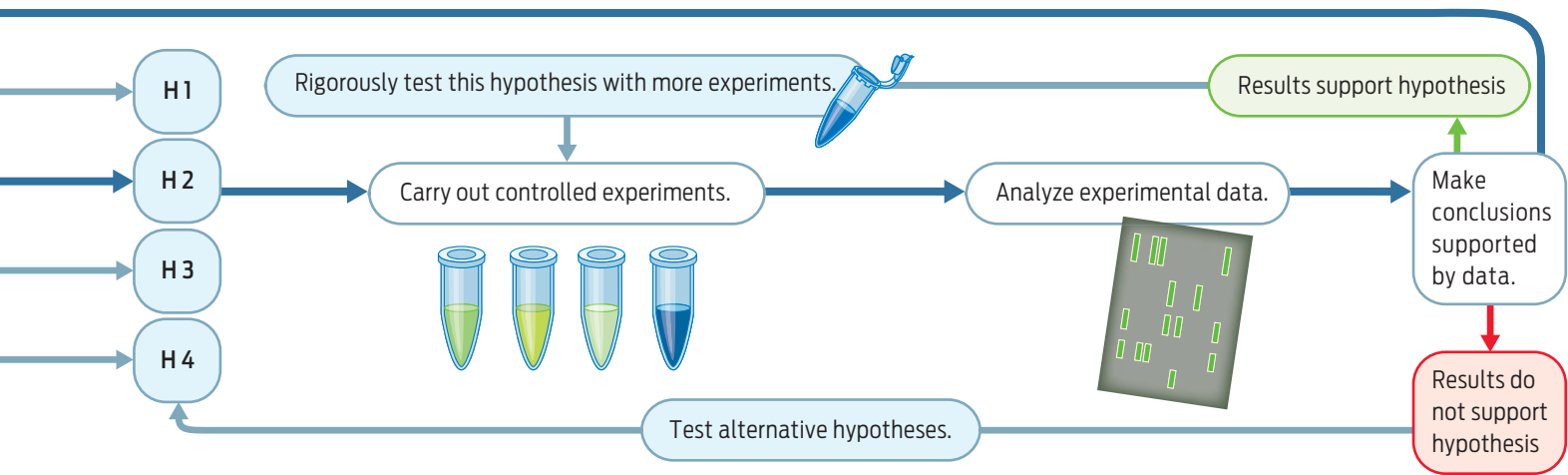
A hypothesis is testable if it can be supported or rejected by carefully designed experiments or observational studies.

### ► FALSIFIABLE

Describes a hypothesis that can be ruled out by data that show that the hypothesis does not explain the observation.

### ► EXPERIMENT

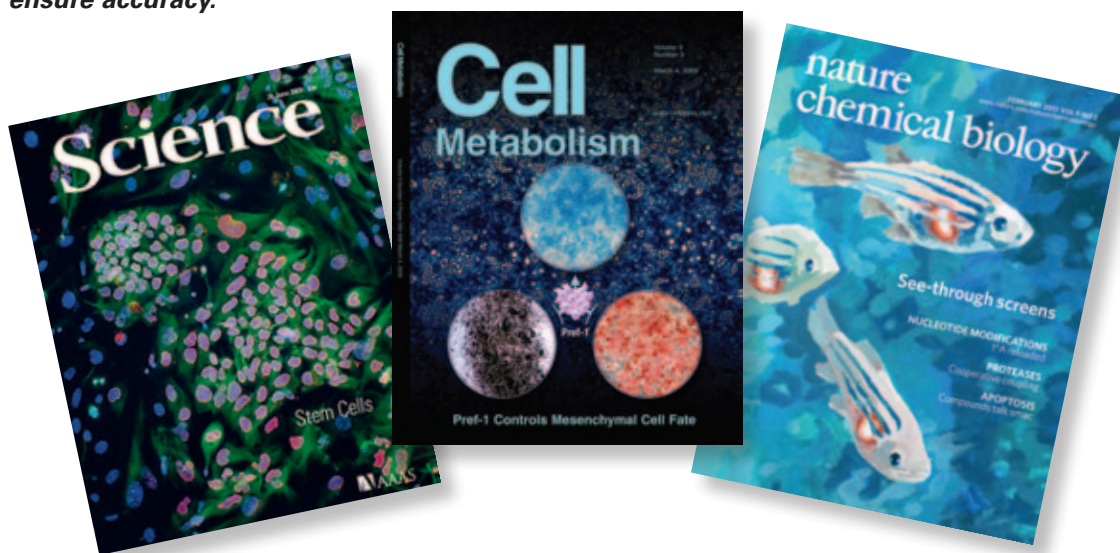
A carefully designed test, the results of which will either support or rule out a hypothesis.



who were active, healthy, and who reported consuming some form of caffeine daily. She then randomly divided these people into two groups: one that would get caffeinated coffee, and one that would receive decaf. The caffeine group is known as the **experimental group**, since these participants are receiving the factor being tested—in this case, caffeine. The decaf group is the **control group**, which serves as

the basis of comparison. Both groups were given memory tests at 8 A.M. and again at 4 P.M. on two nonconsecutive days. The experimental group received a 12-ounce cup of regular coffee containing approximately 220-270 mg of caffeine 30 minutes before each test. The control group received a **placebo**: a 12-ounce cup of decaffeinated coffee containing no more than 5-10 mg of caffeine per serving. No participants knew

*The studies reported in scientific journals are reviewed by experts before publication to ensure accuracy.*



#### ▶ EXPERIMENTAL GROUP

The group in an experiment that experiences the experimental intervention or manipulation.

#### ▶ CONTROL GROUP

The group in an experiment that experiences no experimental intervention or manipulation.

#### ▶ PLACEBO

A fake treatment given to control groups to mimic the experience of the experimental groups.



## INFOGRAPHIC 1.3 ANATOMY OF AN EXPERIMENT



There are many ways to approach a scientific problem. Controlled experiments are one way. As illustrated here, controlled experiments have two groups—the control group and the experimental group—that differ only in the independent variable.

**Hypothesis: Drinking caffeinated coffee prevents daily memory decline.**



Population of 40 men and women over age 65

	Control Group	Experimental Group
<b>Random placement into equivalent groups</b> (with respect to age, gender, health, activity level, etc.)		
<b>Independent variable</b> (the variable that is changed in a systematic way)	<b>Placebo Treatment</b> 12 oz. <b>decaffeinated</b> coffee (30 minutes prior to test)	<b>Test Treatment</b> 12 oz. <b>caffeinated</b> coffee (30 minutes prior to test)
<b>Dependent variable</b> (the variable that is measured in the experiment)	<b>Memory Test</b> given morning and afternoon on different days	<b>Memory Test</b> given morning and afternoon on different days
<b>Results from data</b>	<b>Memory Test Scores</b> Afternoon scores were <u>worse</u> than morning scores	<b>Memory Test Scores</b> Afternoon scores were <u>the same</u> as morning scores
<b>Evidence-based conclusion</b>	<b>Caffeinated coffee prevents memory decline in this population.</b>	

### ▶ INDEPENDENT VARIABLE

The variable, or factor, being deliberately changed in the experimental group.

### ▶ DEPENDENT VARIABLE

The measured result of an experiment, analyzed in both the experimental and control groups

to which group they were assigned—in other words, the study was “blind.” (In a “double-blind” study, neither the investigator nor the participants know who is getting what treatment.)

By administering a placebo, Ryan could ensure that any change observed in the experimental group was a result of consuming caffeine and not just any hot beverage. In addition, all participants were forbidden to eat or drink any caffeine-containing foods or drinks—like chocolate, soda, or coffee—for at least 4 hours before each test. Thus, the con-

trol group was identical to the experimental group in every way except for the consumption of caffeine.

In this experiment, caffeine consumption was the **independent variable**—the factor that is being changed in a deliberate way. The tests of memory are the **dependent variable**—the outcome that may “depend” on caffeine consumption.

Ryan found that participants who drank decaffeinated coffee did worse on tests of memory function in the afternoon compared to the morning. By contrast, the experimen-

tal group who drank caffeinated coffee performed equally well on morning and afternoon memory tests. The results, which were reported in the journal *Psychological Science*, support the hypothesis that caffeine, delivered in the form of coffee, prevents the decline of memory—at least in certain people (**INFOGRAPHIC 1.3**).

Because other factors might possibly explain the link between coffee and mental performance (perhaps coffee drinkers are more active, and their physical activity rather than their coffee consumption explains their mental performance), it's too soon to see these results as proof of coffee's memory-boosting powers. To win our confidence, the experiment must be repeated by other scientists and, if possible, the methodology refined.

## SIZE MATTERS

Consider the size of Ryan's experiment—40 people, tested on two different days. That's not a very big study. Could the results have simply been due to chance? What if the 20 people who drank caffeinated coffee just happened to have better memory?

One thing that can strengthen our confidence in the results of a scientific study is **sample size**. Sample size is the number of individuals participating in a study, or the number of times an experiment or set of observations is repeated. The larger the sample size, the more likely the results will have **statistical significance**—that is, they will not be due to chance (**INFOGRAPHIC 1.4**).

News reports are full of statistics. On any given day, you might hear that 75% of the

### ▶ SAMPLE SIZE

The number of experimental subjects or the number of times an experiment is repeated. In human studies, sample size is the number of participants.

### ▶ STATISTICAL SIGNIFICANCE

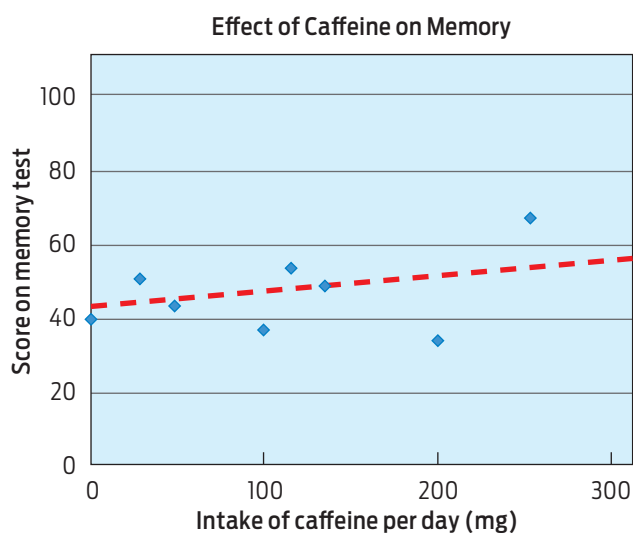
A measure of confidence that the results obtained are "real" and not due to chance.

## INFOGRAPHIC 1.4 SAMPLE SIZE MATTERS



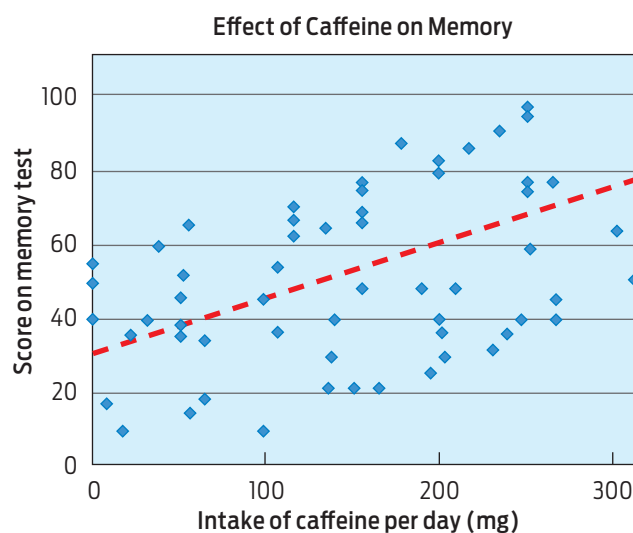
The more data collected in an experiment, the more you can trust the conclusions.

### Data from a few participants:



Conclusions drawn from these data might suggest that caffeine has only a slight positive influence on memory, a 15% average increase, but are not definitive because of the small sample size.

### Data from dozens of participants:



These data show a more convincing positive effect of caffeine on memory, a 45% average increase, because the observed effect is supported by more data. A statistical analysis would show that this positive influence is **significant** — in other words, it is not due to chance.

American public opposes a piece of legislation. Or that 15% of a group of people taking a medication experienced a certain unpleasant side effect—like nausea or suicidal thoughts—compared to, say, 8% of people taking a placebo. Are these differences significant, or important? Whenever you hear such numbers being tossed around, it's important to keep in mind the sample size. In the case of the side effects, was this a group of 20 patients (15% of 20 patients is 3 people), or was it 2,000 (15% of 2,000 is 300)? Only with a large enough sample size can we be confident that the results of a given study are statistically significant and represent something other than chance. Moreover, it's important to consider

the population being studied. For example, do the people reporting their views on a piece of legislation represent a broad cross section of the public, or are most of them watchers of the same television network, whose views lie at one extreme? Likewise, in Ryan's study, are the 65-year-old self-described "morning people" who regularly consume coffee representative of the wider population?

If you search for "caffeine and memory" on PubMed.gov (a database of medical research papers), you'll see that the memory-enhancing properties of caffeine is a well-researched topic. Many studies have been conducted, at least some of which tend to support Ryan's results. Generally, the more

## INFOGRAPHIC 1.5 EVERYDAY THEORY VS. SCIENTIFIC THEORY



In everyday life, people use the word "theory" to refer to an idea that they would like to follow up. In science, a theory is a hypothesis that has never been disproved, even after many years of rigorous testing.

### Everyday theory

An idea based on personal experience and knowledge

If you carry an umbrella with you, it won't rain.

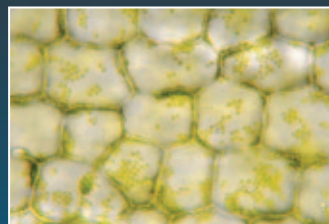


The freezer is the safest place to keep valuables.

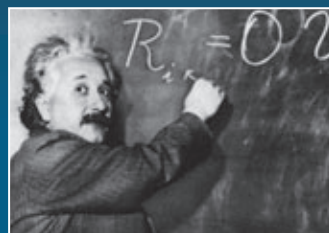
You feel more cheerful when you wear bright clothing.

### Scientific theory

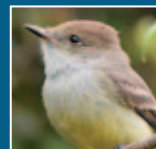
Important hypothesis supported by thousands of scientific experiments



**Cell Theory**  
All living things are made of cells.



**Theory of General Relativity**  
Gravity influences time and space.



**Theory of Evolution by Natural Selection**  
Populations of organisms change over time, adapting to their environment.

Science is a way of knowing, a method of seeking answers to questions on the basis of observation and experiment.

experiments that support a hypothesis, the more confident we can be that it is true.

Truth in science is never final, however. What is accepted as fact today may tomorrow need to be modified or even rejected, when more evidence comes to light. Nevertheless, scientific knowledge does progress. The highest point of scientific knowledge is what's called a **scientific theory**. The word "theory" in science means something very different from its colloquial meaning. In casual conversation we may say something is "just a theory," meaning it isn't proved. But in science, a theory is an explanation of the natural world that is supported by a large body of evidence compiled over time by numerous researchers. Far from being a fuzzy or unsubstantiated claim, a theory is a scientific explanation that has been extensively tested and has never been disproved (**INFOGRAPHIC 1.5**).

## THIS IS YOUR BRAIN ON CAFFEINE

Caffeine is a stimulant. It is in the same class of psychoactive drugs as cocaine, amphetamines, and heroin (although less potent than these, and acting through different mechanisms). Caffeine boosts not just memory and mental performance but physical performance as well. Sports physiologists agree that consuming caffeine before a workout can boost stamina—a fact that is no secret among athletes. A 2004 study found that 33% of 193 track and field athletes and 60% of 287 cyclists said they consumed caffeine to enhance their performance. Recognizing that caffeine is a performance-enhancing drug, the Interna-

tional Olympic Committee prohibited athletes from using it until 2004 (when the committee decided to allow it, presumably because it had become too common a substance to regulate).

While the exact mechanisms are not fully understood, scientists think that caffeine exerts its energizing effect primarily by counteracting the actions of a chemical in the brain called adenosine, which is a type of neurotransmitter. Adenosine is the body's natural sleeping pill—its concentration increases in the brain while we are awake and by the end of the day promotes drowsiness. Caffeine blocks the effect of adenosine in the brain, thereby delaying fatigue and keeping us more alert.

Consumption of caffeinated beverages has skyrocketed in the past 25 years, especially among young people. A 2009 study in the journal *Pediatrics* found that teenagers in a Philadelphia suburb consume anywhere from 23 mg to 1,458 mg of caffeine a day—the equivalent of nearly 10 cups of coffee, and more than three times the recommended safe dose for an adult of 400 mg/day or less. In excess, caffeine can cause anxiety, jitters, heart palpitations, trouble sleeping, dehydration, and more serious symptoms as well—especially in people who are sensitive to it. Of the 4,852 caffeine overdoses reported to poison control centers in the United States in 2008, 49% occurred in those younger than 19, according to a 2011 study in *Pediatrics*. In 2012, a 14-year-old Maryland girl died of cardiac arrhythmia after drinking two 24-ounce Monster Energy drinks (240 mg of caffeine each) in a 24-hour

### ► SCIENTIFIC THEORY

An explanation of the natural world that is supported by a large body of evidence and has never been disproved.