

## Teaching Summary

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This chapter introduces your students to key themes in physiology and physiological research. Emphasize to your students that learning basic patterns, themes, and the “big picture” will simplify learning the details of physiology. Here are some ideas for teaching this chapter:

- Throughout this text, the focus is on integration of physiological function. Look for links in the text and in the lecture outlines. These will key you into topics previously discussed that you may choose to integrate into a current lecture.
- If you are interested in comparative physiology, this is a good place to point out that humans are animals, with special physiological adaptations that allow us to survive in a terrestrial habitat.
- If you plan to emphasize problem-solving skills, talking about experimentation and experimental design at the beginning of a course shows students how important this skill is in real life.
- Almost all students have difficulty reading and constructing graphs. Teach them the basics in the first week of class.
- Many students lack the ability to handle large amounts of detailed information. Teaching them how to map and encouraging them to continue mapping throughout the class will provide them with a tool for organizing material.

## Student Learning Outcomes

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When students complete this chapter, they should be able to:

- LO 1.1 Define physiology.
- LO 1.2 List the levels of organization from atoms to the biosphere.
- LO 1.3 Name the 10 physiological organ systems of the body and give their functions.
- LO 1.4 Distinguish between mechanistic explanations and teleological explanations.
- LO 1.5 List and give examples of the four major themes in physiology.
- LO 1.6 Define homeostasis. What happens when homeostasis fails?
- LO 1.7 Name and describe the two major compartments of the human body.
- LO 1.8 Explain the law of mass balance and how it applies to the body’s load of a substance.
- LO 1.9 Define mass flow using mathematical units and explain how it relates to mass balance.

- LO 1.10 Define clearance and give an example.
- LO 1.11 Distinguish between equilibrium and steady state.
- LO 1.12 List the three components of a control system and give an example.
- LO 1.13 Explain the relationship between a regulated variable and its setpoint.
- LO 1.14 Compare local control, long-distance control, and reflex control.
- LO 1.15 Explain the relationship between a response loop and a feedback loop.
- LO 1.16 Compare negative feedback, positive feedback, and feedforward control. Give an example of each.
- LO 1.17 Explain what happens to setpoints in biological rhythms and give some examples.
- LO 1.18 Explain and give examples of the following components of scientific research: independent and dependent variables, experimental control, data, replication, variability.
- LO 1.19 Compare and contrast the following types of experimental study design: blind study, double-blind study, crossover study, prospective and retrospective studies, cross-sectional study, longitudinal study, meta-analysis.
- LO 1.20 Define placebo and nocebo effects and explain how they may influence the outcome of experimental studies.

## What's New?

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- Glossary: removed interactomics, lipidome
- Updated search numbers in Running Problem
- Added DOI numbers to literature citation information

## Teaching Outline

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### Physiology Is an Integrative Science

Figs. 1.1, 1.2, 1.3 (**Focus On: Mapping**)

Key Words: physiology, anatomy, integration of function, emergent properties, levels of organization, cell, cell membrane, tissue, organ, organ system, integumentary system, musculoskeletal system, digestive system, respiratory system, urinary system, reproductive system, immune system, nervous system, endocrine system

- ▶ With increasing complexity in design and organization comes increased integration.
- ▶ Boyd CAR and Noble D (Eds.). *The logic of life: The challenge of integrative physiology*. Oxford, UK: Oxford University Press, 1993.
- ▶ Another example of integration is the regulation of calcium concentrations in the body. The endocrine system acts on bones, kidneys, and intestines to ensure that plasma calcium concentrations remain within a certain range.
- ▶ A change in special cells that act as sensory receptors can trigger a cascade of neurally or endocrine-mediated responses that may affect many cells of the body.

**First day activity:** Begin the first day by asking students what they know rather than by telling them what they should know. Some topics to ask them about might include:

What is physiology? How is it different from anatomy?

Name the 10 physiological organ systems.

What are the characteristics of living organisms?

Which organ systems carry out which functions of life?

If your students have had chemistry and introductory biology and you do not plan to teach Chs. 2–4 to your class, ask them some review questions, such as:

Where does energy for life processes come from? How is energy stored in animals?

List the four primary tissues of the body, their characteristics, and some examples.

Draw a cell, add as many organelles as you can, and give their functions.

List the steps of protein synthesis, including as many details as you can.

- ▶ Physiologists are interested in everything from the molecular level to how physiological adaptations affect an organism's ability to adapt to and survive in particular environments.
- ▶ Some students will separate muscular and skeletal systems. The question sometimes arises about whether the lymphatics are a system. They are an anatomical system, but physiologically, the lymphatics function as part of three systems: circulatory (returning excess fluid and escaped proteins from interstitial space to the plasma), digestive (transporting fats from the intestine to the circulation), and immune (lymph nodes contain clusters of immune cells).

## Function and Mechanism

Key Words: function, teleological approach, mechanistic approach, processes/mechanisms, translational research

- ▶ Discuss teleological vs. mechanistic approaches to science and life. *See Richardson DR. A survey of students' notions of body functions as teleologic or mechanistic. *Advances in Physiology Education* 258(6): S8, 1990.*
  1. Ask the students “Why does blood flow?” or “Why do we breathe?” Analyze responses and determine if they're teleological or mechanistic.
  2. Have students ask one of these questions to nonscience friends outside of class. Compile a list of teleological and mechanistic responses.
- ▶ Be careful not to write test questions that begin with “Why...” when you expect the students to answer with a mechanistic answer. Instead, ask “Explain the mechanism that is the basis for blood flow.”
- ▶ Not all structures or processes have an obvious or known function. Some may be remnants of organs that are no longer useful (the appendix, the hormone calcitonin in humans), or it may simply be that we do not yet understand what their function is.
- ▶ This is a good place to point out to students that we do not fully understand the mechanisms for all physiological processes. There are still a large number of “black boxes” where we do not know what is going on, and these are the areas of active research. You may also want to warn them that “facts” that they learn in this course will change in the future as we solve the mysteries of physiology. There is a tendency for students to learn facts and then feel that they are immutable, when this is not the case.

## Themes In Physiology

Table 1.1

- How many applicable examples can your students think of for these themes?

### Theme 1: Structure and Function Are Closely Related

#### ***Molecular Interactions***

Covered in Chapter 2.

#### ***Compartmentation***

Covered in Chapter 3.

### Theme 2: Living Organisms Need Energy

Covered in Chapter 4.

### Theme 3: Information Flow Coordinates Body Functions

The fundamentals are covered in detail in Chapters 5 (membranes and membrane functions) and 6 (chemical communication in the body).

### Theme 4: Homeostasis Maintains Internal Stability

Key Word: homeostasis

## Homeostasis

Fig. 1.4

Key Words: homeostasis, pathological, pathophysiology, diabetes mellitus

- Cannon WB. Organization for physiological homeostasis. *Physiological Reviews* 9(3): 399–431, 1929 July.

## What Is the Body's Internal Environment?

Fig. 1.5

Key Words: extracellular fluid (ECF), intracellular fluid (ICF)

## Homeostasis Depends on Mass Balance

Fig. 1.6

Key Words: law of mass balance, load, excretion, mass flow

## Excretion Clears Substances from the Body

Key Word: clearance

Clearance is described quantitatively in Chapter 19.

## Homeostasis Does Not Mean Equilibrium

Fig. 1.7

Key Words: plasma, steady state, equilibrium, disequilibrium

## Control Systems and Homeostasis

Fig. 1.8

Key Words: regulated variables, setpoint, control systems, integrating center

### Local Control Is Restricted to a Tissue

Fig. 1.9

Key Word: local control

### Reflex Control Uses Long-Distance Signaling

Fig. 1.10

Key Words: reflex control, response loop, sensor

- ▶ Traditionally, reflexes were associated with the nervous system, for example, the knee jerk reflex. Then they were extended to include neuroendocrine reflexes, such as the hypothalamic-anterior pituitary-endocrine gland axis. This book expands the meaning one step further to include strict endocrine reflexes, such as the response of the pancreatic beta cells to blood glucose concentrations.
- ▶ The pattern shown in Fig. 1.10 is a key pattern for students to learn. In later chapters, when they are trying to remember the reflex responses, this pattern can help them remember all the steps of the reflex.
- ▶ The value of integrating centers becomes apparent when there are multiple signals coming into the center. The integrating center must evaluate the strength and importance of each signal and initiate an appropriate response. One example of reflex integration in physiology involves the secretion of aldosterone, a hormone that regulates sodium excretion by the kidney. When a person becomes dehydrated, the loss of body fluid causes a drop in blood pressure. This acts as a signal to secrete aldosterone. At the same time, however, dehydration increases body osmolarity. Increased osmolarity is a signal to inhibit aldosterone secretion. When these two conflicting signals are sent to the endocrine cells that secrete aldosterone, the endocrine cells must evaluate the information received and decide which stimulus is the most important. In this example, regulation of osmolarity is more important than blood pressure, so the integrating center (the adrenal cortex) does not secrete aldosterone.
- ▶ You might want to consider introducing the concept of learned reflexes. Many homeostatic reflexes are innate and present from birth but other reflexes are learned through experience. Pavlov's dogs learned to associate a bell with food and experienced reflex salivation at the sound of the bell. The startle reflex is innate, but a fight-or-flight response to the sound of screeching brakes behind you is a learned reflex.

### Response Loops Begin with a Stimulus

Key Words: setpoint, antagonistic control

- ▶ See how many different types of response loops students can think of in everyday life. One example is the automatic pet watering system that has a normal water level within which the water flow is shut off. If the water level drops below that range, the valve opens and water enters until the critical level is reached. A heating or air-conditioning system in a house might be another example. A "smart" system that turns on either heat

or air as needed might be correlated to a dual-control system, such as the autonomic control of heart rate.

## Feedback Loops Modulate the Response Loop

Key Word: feedback loop

## Negative Feedback Loops Are Homeostatic

Figs. 1.11, 1.12a

Key Words: negative feedback, oscillation around a setpoint

## Positive Feedback Loops Are Not Homeostatic

Figs. 1.12b, 1.13

Key Word: positive feedback loop

## Feedforward Control Allows the Body to Anticipate Change

Key Word: feedforward control

- ▶ You can use the aquarium example shown in Fig. 1.10 to illustrate feedforward control by adding a box (Box A) that sits in the air and is attached by a wire to the control box. Box A represents a sensor that is monitoring the air temperature. In this case, let's say that the air temperature has been stable at 30° C, the same as the setpoint for the water. If the air temperature suddenly falls to 25° C, the temperature of the water will be slow to equilibrate with that of the air because water has a tremendous capacity to hold heat. On the other hand, Box A senses the change in the air as soon as it occurs, long before the change affects the water temperature. Box A sends a message to the integrating center that the air temperature has fallen below the desired range. The integrating center evaluates this information: water temperature is still normal, but air temperature has fallen and therefore water temperature will soon decrease. The integrating center then turns on the heater in anticipation of a drop in temperature. This allows the aquarium to keep its temperature close to the setpoint, and stability is maintained.

## Biological Rhythms Result from Changes in a Setpoint

Fig. 1.14

Key Words: circadian rhythm, acclimatization, acclimation

- ▶ This is often an area of interest to students. Ask them if they think that computer programs that claim to plot a person's biorhythms are accurate, and why.
- ▶ How many examples of biorhythms in humans, animals, and plants can students think of?

## The Science of Physiology

Fig. 1.15 (Focus On: Graphs)

Key Words: hypothesis (-es), scientific inquiry, evidence-based medicine

## Good Scientific Experiments Must Be Carefully Designed

Key Words: independent variable, dependent variable, experimental control, data, replication, model, scientific theory

- ▶ Review the process of science with students and demonstrate the importance of good experimental design and good science.

This is a good place to point out the similarity between scientific research and what should take place in a classroom setting. Students are always asking, “Just tell me the right answer.” It’s important for them to learn that there may be no right answer, or several right answers. When faced with a problem, they should behave like scientists and generate several alternate hypotheses. They can then evaluate the validity of their hypotheses based on their understanding of physiology.

To promote this type of learning in the classroom, the faculty member must be supportive and make students comfortable with the notion that it’s OK to be wrong, as long as they can justify their reasoning. Collaborative groups in the classroom are very valuable in this regard, as students can learn from their peers that they were not the only person who doesn’t understand or have the correct answer.

- ▶ In more advanced classes that have studied statistics, this would be a good place to talk about which statistical tests could be used with each type of study. For example, crossover studies allow the use of a paired t-test.

## The Results of Human Experiments Can Be Difficult to Interpret

### **Variability**

Key Words: variability, crossover study, placebo

### **Psychological Factors**

Key Words: placebo effect, nocebo effect, blind study, double-blind studies, double-blind crossover studies

### **Ethical Considerations**

- ▶ Ask students to bring in articles about clinical research studies that are related to the use of human subjects.
- ▶ If you are comfortable, open the floor for ethical debates. See how your students feel about ethical considerations in science and scientific research. Should animals be used in research? What about in the college classroom? In the high school classroom? Are models and computer simulations an adequate substitute for working with living organisms?

To learn more about the use of animals in science, see the American Physiological Society website:

<http://www.the-aps.org/mm/SciencePolicy/About/Policy-Statements>

Or, search the topic “Animals in Research.” This site has many links to other resources.

- ▶ Zolman JF. Teaching experimental design to biologists. *Advances in Physiology Education* 277(6): S111, 1999 Dec.
- ▶ **Ethical Exercise:** You are the president of a pharmaceutical company that has just won approval from the Food and Drug Administration to sell a drug that can control a degenerative and potentially deadly disease that affects 200,000 people annually. However, half of those afflicted will not be able to afford this drug. Furthermore, your company has invested \$25 million in developing this new drug. Does your company have a moral obligation to administer this drug to people that cannot afford it?

- ▶ Rowan AN. The benefits and ethics of animal research. *Scientific American* 276(2): 79, 1997 Feb.
- ▶ Alberts B and Shine K. Scientists and the integrity of research. *Science* 266(5191): 1660–1661, 1994 Dec 9.

## Human Studies Can Take Many Forms

Key Words: longitudinal studies, prospective studies, cross-sectional studies, retrospective studies, meta-analysis

- ▶ The book mentions the variability of human subjects. If you decide to discuss the topic of animal research, you might point out how most animal research uses bred strains of animals (rats, mice, beagles, etc.) to minimize inter-individual variability.

- ▶ Have students compare the following two analyses:

McAlindon TE, *et al.* Glucosamine and chondroitin for treatment of osteoarthritis: A systematic quality assessment and meta-analysis. *Journal of the American Medical Association* 283(11): 1469–1475, 2000 Mar 15. doi: 10.1001/jama.283.11.1469.

Richy F, *et al.* Structural and symptomatic efficacy of glucosamine and chondroitin in knee osteoarthritis: A comprehensive meta-analysis. *Archives of Internal Medicine* 163(13): 1514–1522, 2003 July 14.

Note that the *Journal of the American Medical Association* article is an older meta-analysis of the use of glucosamine. You might also have students Google “NIH GAIT study” to read about the NIH-sponsored Glucosamine/Chondroitin Arthritis Intervention Trial.

## Talk the Talk

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adaptive significance	data (plural); datum (singular)	function
afferent pathway	dependent variable	genome
anatomy	diabetes mellitus	gradient resistance
antagonistic control	digestive system	histogram
average values	disequilibrium	homeodynamics
bar graphs	DOI number (Digital Object Identifier)	homeostasis
biological rhythms (biorhythms)	double-blind crossover study	hypothesis
blind study	double-blind studies	immune system
cell	ecosystems	independent variable
cell (or plasma) membrane	emergent properties	information flow
circadian rhythms	endocrine system	input signal
circulatory system	<i>et al.</i>	integrating center
clearance	equilibrium	integration
compartmentation	evidence-based medicine	integumentary system
control system	experimental control	interpolate
crossover study	extracellular fluid	intracellular fluid
cross-sectional studies	feedback loop	journals
	feedforward control	law of mass balance
		levels of organization

line graphs	output signal	review articles
load	pathological	scatter plots
local control	pathophysiology	scientific inquiry
longitudinal studies	peer-reviewed	scientific theory
mass balance	physiological control system	selectively permeable
mass flow	physiological processes or mechanisms	sensitivity
mechanistic approach	physiology	sensor
membranes	placebo	setpoint
meta-analysis	placebo effect	signal transduction
models	populations	steady state
molecular interactions	positive feedback loop	stimulus
musculoskeletal system	prospective study	systemic
negative feedback	reflex	target
nervous system	reflex control pathways	teleological approach
nocebo effect	regulated variables	themes
-omics (proteomics, genomics, etc.)	replication	tissues
organ systems	reproductive system	translational research
organelles	respiratory system	urinary system
organs	response loop	variability
oscillates	retrospective studies	variable(s)
		xenobiotic

## Running Problem: Searching the Literature

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Another activity you can do with your students involves asking them to evaluate web-based resources for aspartame's potential side effects.

Start here for a detailed description of the exercise:

<http://mediasmarts.ca/backgrounder/deconstructing-web-pages-teaching-backgrounder>

The following worksheet accompanies the deconstructing web pages exercise. Note that you will want to put the deconstructing web pages link on your course management resources to make it easier for students to access (or create a shortened URL through a site like [tinyurl.com](http://tinyurl.com)).

- Go to the following website: *www.medical-library.net*

1. Who is the sponsor of Doctors' Medical Library? \_\_\_\_\_
2. Scout around the site. Does this sponsor have any apparent biases that might influence what is posted on the site? Explain.

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- Use the site's SEARCH function to find an article on aspartame disease. Read the article.
3. Describe your initial reaction to the article.

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4. Who is the author of the aspartame page and what are her credentials? \_\_\_\_\_  
\_\_\_\_\_
5. What is the date of the aspartame article? \_\_\_\_\_
6. Now do a Google search to find out more about the author and her credentials. Summarize your findings below, citing the URLs where you found the information.

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- Now get to the following web page (link is in the online course resources). Read it to the end.

<http://mediasmarts.ca/backgrounders/deconstructing-web-pages-teaching-backgrounders>

7. Now what is your opinion now of the Doctors' Medical Library site article?

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## Supplemental Material

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### The Evolution of Physiological Systems

As organisms became larger and moved from seawater to fresh water and land, they had to alter their body systems to meet new challenges. The simplest life forms are single-celled marine organisms, separated from their environment by a single cell membrane. Most of their needs are the same as those of more complex organisms: the acquisition of oxygen and nutrients, energy production for synthesis and reproduction, and removal of wastes. However, since their internal environment is almost the same as that of the surrounding ocean, minimal energy is expended in maintenance of internal salt and water concentrations.

Because of their tiny size, these organisms needed no special structures to get sufficient oxygen and remove wastes, which simply passed through the cell membrane. In more complex organisms composed of single cells grouped into cooperative units or of multiple cells, interior cells have lost direct contact with the environment. Oxygen can no longer reach those internal cells by diffusing through the outer cells. Special body shapes met this challenge: thin-walled hollow bodies like the coelenterates, or flattened forms mean no cell is very far from the surface of the body. Other species have circulatory systems to move extracellular fluid, putting distant regions of the organism in contact with each other. As size and complexity increased, specialized respiratory surfaces increased surface area through various arrangements of folded membranes.

Because diffusion of gases is strictly limited by the size (and, to some extent, shape) of an organism, large bodies require some means of acquiring oxygen and nutrients and getting rid of wastes. Body shape moved from spherical or cylindrical to flattened dorsoventrally, to decrease distance between the body surface and the center of the body. Circulatory systems evolved with special molecules for gas transport and pumps to move the fluid throughout the body.

Motion and support evolved from soft bodies that moved at the mercy of wind and tide to rigid skeletons that move with the aid of muscles. In the absence of support from the buoyancy of water, terrestrial animals make use of structural frameworks: a chitinous exoskeleton in insects and other arthropods, a rigid internal skeleton powered by muscles in the vertebrates.

The transition from water to land presented the problem of dehydration. Mobile sperm require an aqueous environment, so terrestrial animals either return to water to mate or use internal fertilization. Gas exchange across respiratory epithelia requires a moist surface, so terrestrial animals have internalized exchange surfaces to minimize the problem of dehydration. Body surfaces are relatively impermeable to prevent evaporation, and kidneys are very efficient at conserving water and removing excess salts. Some animals, such as slugs, use a heavy mucus coat.

Behavioral adaptations to avoid overheating and dehydration also evolved. The desert comes alive at night, when the temperature drops. Slugs are also active at night, avoiding the dehydrating effects of the sun. The result of all these adaptations is an efficient organism that is suited for life in a hostile terrestrial world. In short, the human body is highly adapted to a mobile existence in a terrestrial environment.

## Focus On: Graphing

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### 1. Reading (and constructing) graphs:

- Find examples of good and bad graphs. *USA Today* is an excellent source of poorly designed graphs.
- Present graphs to students and ask them to write the legend and/or a short explanation of what the graph means.
- Give students graphs of something with which they are familiar (growth over time) and from which the axes have been removed. Ask them to place the labels on the appropriate axis.
- Give students small data sets and ask them to draw the appropriate graphs.

► Remind students that “data” is a plural noun and always takes the plural verb “are.”

### 2. The data points below represent the growth of fish between the ages of 3 months and 14 months.

<b>Age of fish (in months)</b>	3	6	7	9	12	13	14
<b>Length (cm) of males</b>	10	12	14	16	18	20	22
<b>Length (cm) of females</b>	8	12	12	14	16	16	18

What is the dependent variable? What is the independent variable? Draw and fully label a graph for this data.

You can also predict values from graphs by interpolation and extrapolation. Reading between the plotted points is called **interpolation**; extending the graph beyond the plotted points is called **extrapolation**. Which one is more likely to be inaccurate? *Extrapolation, because the trend indicated by the graph may suddenly change. For example, the correct shape of the oxyhemoglobin dissociation curve cannot be extrapolated from the shape of the curve between  $P_{O_2}$  values of 20 and 50 mm Hg.*

- ▶ Briscoe MH. *Preparing Scientific Illustrations: A Guide to Better Posters, Presentations, and Publications*. New York: Springer, 1996.
- ▶ Tufte ER. *The Visual Display of Quantitative Information*. Cheshire, CT Graphics Press, 1983.

## Focus On: Physiology

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1. How are the dependent and independent variables represented on a graph? What is the difference between a graph that shows the effect of breathing on blood oxygen level and a graph that shows the effect of blood oxygen level on breathing?

*In the graph showing the effect of breathing on oxygen level, breathing is the independent variable and blood oxygen is the dependent variable. In the experiment, you would change breathing and measure the oxygen level that resulted. The second experiment is the reverse: you would change blood oxygen and see what effect that had on breathing.*

2. You are doing an experiment about how caffeine consumption affects reaction time. Which of the following would be a testable hypothesis?
  - a. The more coffee a person drinks, the more their reaction time is affected.
  - b. The higher the caffeine consumption, the faster a person reacts to a given stimulus.
  - c. The more caffeine consumed by a student, the higher the urine output is.
  - d. Coffee drinkers make better lovers.

In studying the relationship between caffeine consumption and reaction time, which would be the dependent variable? Which would be the independent variable? Briefly describe some ways you might manipulate the independent variable.

You compute the following average values from your experiment: Caffeine consumers' reaction time = 400 ms; Nonconsumers' reaction time = 650 ms. What would be a logical conclusion from these data?

Sketch a simple graph that would be an appropriate way to convey these results to your classmates or lab partners. What kind of graph did you choose? Why? Which variable did you plot on the x-axis? Which one did you plot on the y-axis? Why?

## Maps

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### Exercise for Beginning Students

Construct a concept map of “Sandwich Ingredients.” Before you begin, take a moment to think about all the types of sandwiches there are (hot, cold, open-faced, etc.) Can a hamburger be considered a sandwich? How about a taco? What is a minimalist definition of a sandwich? What about options (cheese or onion or lettuce or tomato) and condiment(s)? Decide on the main categories to go under the main topic of “sandwich” and construct a map.

### Exercise for Students with Background in Biology

Map the steps of following the scientific method. For a problem to solve, let’s say you have walked into your house and flipped on the light switch, and nothing happens. What do you do and/or think of and/or check on to conclude what the problem is?

Map a biological control system that maintains homeostasis. Assume that blood sugar level is directly related to hunger and appetite. What happens as your blood sugar level raises and lowers? What monitors are there for measuring the level? Where might these structures be located? What happens when these structures are stimulated?

Make a concept map to compare and contrast the definitions and relationships of cells, tissues, organs, and systems. Give some specific examples in the map.

## Additional Resources

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Baptista V. Starting physiology: Understanding homeostasis. *Advances in Physiology Education* 30(4): 263–264, 2006 Dec. doi: 10.1152/advan.00075.2006.

Carpenter RHS. Homeostasis: A plea for a unified approach. *Advances in Physiology Education* 28(4): 180–187, 2004 Dec 1. doi: 10.1152/advan.00012.2004. (Free access at <http://advan.physiology.org>)

Clarke GM. *Statistics and Experimental Design: An Introduction for Biologists and Biochemists*. 3rd ed. New York: Halsted Press, 1994.

Fye WB. *The Development of American Physiology: Scientific Medicine in the Nineteenth Century*. Baltimore: Johns Hopkins University Press, 1987.

Goldstein M and Goldstein IF. *How We Know: An Exploration of the Scientific Process*. New York: Plenum Press, 1978.

Goodfield J. *The Growth of Scientific Physiology; Physiological Method and the Mechanist-vitalist Controversy, Illustrated by the Problems of Respiration and Animal Heat*. London: Hutchinson, 1960.

Hall TS. *Ideas of Life and Matter; Studies in the History of General Physiology, 600 B.C.–1900 A.D.* Chicago: University of Chicago Press, 1969. (Published in 1975 under the title: *History of General Physiology, 600 B.C. to A.D. 1900.*)

Hodgkin L (Ed.). *The Pursuit of Nature: Informal Essays on the History of Physiology*. New York: Cambridge University Press, 1977. (These essays were written as part of the celebrations of the centenary of the Physiological Society in 1976.)

Pease CM and Bull JJ. Is science logical? *Bioscience* 42(4): 293–298, 1992. doi: 10.2307/1311678.

Rothschuh KE (Ed. and Trans. by Guenter B. Risse). *History of Physiology*. Huntington, NY: R. E. Krieger Pub. Co., 1973.