# CASE TEACHING NOTES
# for


by
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## INTRODUCTION / BACKGROUND

This directed case is combined with an activity in which students use the knowledge gained from the directed portion of the case to produce a rational design for a drug to treat a case of neurotoxin poisoning.

The case is presented in three different editions. The General Biology Edition is designed for an introductory non-major or mixed major biology course. The basic story and core objectives of the General Biology Edition are carried over into a Human Anatomy and Physiology Edition and an introductory Cell and Molecular Biology Edition. These alternate editions use directed questions to take the students down variable knowledge paths appropriate to the content found in a typical human anatomy and physiology course or a cell biology course.

In discussions with students regarding the integration of the textbook into a biology course, it becomes clear that one of their major concerns is the application of material across several topics. From Day 1, we give our students the impression that biology is the "Study of Life," and then we show them that the way to understand life is to "chunk it up" into pieces and address one piece at a time. As instructors, we foster this view of biology when we present our course syllabus as a "list" or "schedule" of topics. This impression is an especially dangerous one for "non-majors." They need to feel that the topics are connected and that several concepts covered in the course can be applied in a single problem.

In a search for textbooks, it is important to find a book that addresses the connection of ideas. Textbooks can become a library of exploration for the student. If a student is provided with a knowledge base on some core issues in biology, a directed case study can tempt the student to use the book to apply this basic knowledge. This directed case study is an excellent example of this approach. The concepts of ions, membrane structure, and the role of voltage-gated ion channels in membrane transport are traditionally presented in the earliest chapters of a biology textbook. The neuron is an excellent example of a type of cell where all of these entities come together. Unfortunately, the structure and function of neurons and the nervous system are often presented as part of a much later chapter in a physiology unit. Just the physical distance alone can give the impression to a student that these topics are not connected.

One approach to solving this problem would be to add lecture material to the unit on chemistry and membrane structure to include the structure and function of neurons as an example. If this approach is used, then special attention must be given to the syllabus to include the chapter on the nervous system as part of the readings. This has the potential to add confusion and congestion to an already difficult subject. An alternative approach is the use of a directed case study. In this approach, the case study is introduced as part of the cell membrane structure and function section of the course. By this time, the student will already have studied the basic chemistry of cells and the important membrane transport

mechanisms that cells employ. The case study requires that the student then apply the material that has been covered in this portion of the course. In addition, it directs them through an independent study of the function of membranes, neurons, and the nervous system.

## Goals and Objectives

### Core Goals and Objectives (apply to all editions)

After working through the case, students will:

- Apply basic principles of organic and inorganic chemistry to answer questions related to the case.
- Apply the basic concepts of cell membrane structure and function to answer questions related to the case.
- Explore the distribution of ions and charged molecules in the cellular environment.
- Use knowledge of membranes and transport mechanisms to explore membrane potentials (resting and action potentials).
- Use knowledge of membrane potentials to explore the structure and function of a neuron.
- Be introduced to the concept of neurotoxins and their actions at the molecular level of cell function.
- Use rational design to describe the mechanism of action of a drug that students design to treat neurotoxin poisoning.
- Speculate on topics that are not covered in a course textbook, but have connections to the basic concepts that are applied within the case.
- Be engaged in a discussion of the case in an effort to understand how several course topics can be connected within a single problem.

### Human Anatomy & Physiology Edition Goals and Objectives

In addition to the core goals and objectives (see above), after working through the Human Anatomy and Physiology Edition of the case, students will:

- Understand physiological terms used to describe a person suffering from neurotoxin poisoning.
- Understand the difference between sensory and motor neurons.
- Understand the connection between motor neurons and muscle function.
- Explore the function of the autonomic nervous system.
- Understand the difference between the sympathetic and parasympathetic nervous systems.
- Use basic experimental observations to explain the mechanism of action of an unknown neurotoxin.

### Cell/Molecular Biology Edition Goals and Objectives

In addition to the core goals and objectives (see above), after working through the Cell and Molecular Biology Edition of the case, students will:

- Understand how molecules interact with each other to affect function.
- Explore the difference between reversible and irreversible binding of molecules.
- Understand the concept of the dissociation constant ($K_d$) and its use in understanding the strength of a molecular interaction.
- Use basic experimental observations to explain the mechanism of action of an unknown neurotoxin.
- Explore the difference between competitive and noncompetitive inhibition in molecular interactions.

## Student Preparation

This case was designed as part of a series of case studies called *Connections: Case Studies in the Life Sciences*. "Connections" refers to the idea that students are given preparation in basic concepts related to a case story, and then they are directed to make connections to concepts that would traditionally be introduced much later in the sequence of topics of a traditional course in the life sciences. Although students are asked to explore topics that have not been covered in class, the preparation in the basic concepts is designed to give the foundation needed to explore those topics with confidence. The use of a directed method in the first part of the case helps ensure that the students have some direction as they embark on this journey. The prerequisites listed below for each edition of the case would be covered in the traditional lecture portion of the course. The "connections" are topics that will be explored by the students with the foundation supplied from that lecture material. The case would be introduced into the course after the prerequisite concepts had been covered in class.

| Edition | Prerequisite Concepts | Connections |
|---|---|---|
| GENERAL BIO | Inorganic and organic chemistry<br>Membrane structure<br>Membrane transport mechanisms | Membrane potentials<br>Nervous system function |
| ANAT & PHYS | Language of anatomy<br>Inorganic and organic chemistry<br>Membrane structure<br>Membrane transport mechanisms | Membrane potentials<br>Peripheral nervous system<br>Central nervous system |
| CELL / MOLECULAR | Inorganic and organic chemistry<br>Membrane structure<br>Membrane transport mechanisms<br>Membrane potentials | Ion channel structure<br>Ion channel function<br>Molecular interactions<br>Forms of binding inhibition |

## CLASSROOM MANAGEMENT

This case requires approximately 3 to 4 hours of class time to complete. This time could be spread out across two or three class periods. The estimate includes time for group and class discussion and assumes that all of the prerequisites have been covered before introducing the case to the class.

This case was originally designed as an in-class activity, although there are several places in the case where out-of-class assignments can be produced. When conducted in class, a small library of biology textbooks can be created for student use. In addition to the course text, it is often helpful to have several other references readily available for student use. It is also very helpful to have a classroom that is equipped with Internet access for the students to use websites as another source of reference material.

The case is presented in three parts. Part I contains the directed questions used to explore the content related to the story. In Part II, a continuation of the story is followed up by questions where students are asked to apply concepts explored in Part I. Part III is a design component where students use knowledge from Part I to design a drug to treat the neurotoxin poisoning described in the story.

**Part I**

The directed questions found in each edition of the case were designed in blocks. Small groups of three students are assigned the case in class, and then the blocks are described for them. The question blocks cover important content associated with the various courses.

| Case Edition | Block | Concept | Questions |
|---|---|---|---|
| GENERAL BIOLOGY | A<br>B<br>C<br>D | Chemistry<br>Membrane function<br>Membrane potentials<br>Nervous system function | 1 - 3<br>4 - 6<br>7 - 9<br>10 - 12 |
| ANAT & PHYS | A<br>B<br>C<br>D<br>E<br>F | Language of anatomy<br>Chemistry<br>Membrane function<br>Membrane potentials<br>Peripheral nervous system<br>Central nervous system | 1<br>2 - 4<br>5 - 7<br>8 - 10<br>11 - 13<br>14 - 16 |
| CELL / MOLECULAR | A<br>B<br>C<br>D | Membrane function<br>Membrane potentials<br>Ion channel structure / function<br>Molecular interactions | 1 - 3<br>4 - 6<br>7 - 9<br>10 - 12 |

When the small groups are assembled with three students, a jigsaw approach can be used to work through Part I. For each block, students within the group are assigned one of the three questions. After being given time to research the topic using the supplied classroom resources, the small group can reassemble to discuss their findings before moving on to the next block. The instructor can move through the room and sit with groups when they are assembling between blocks. This will provide opportunities for providing the groups direction and clearing up any misconceptions as the student groups work through Part I.

**Part II**

In Part II, Dr. Westwood is exposed to a new neurotoxin that has similar effects to the toxin contained in the pufferfish. In this continuation of the story, the new toxin is presented with an unknown mechanism. Students are then presented with summaries of experiments that were run to try and determine the mechanism of action of this new toxin. Knowledge gained in Part I of the case can be used to answer the questions, which reinforce important concepts introduced in Part I. Although Part I was designed as a jigsaw activity, the small student groups should be encouraged to work on Part II problems as part of a small group discussion.

The overall objective of Part II is to have students begin to feel comfortable applying their new knowledge. The concepts that are reinforced in this section are listed below.

| Edition | Part II Concepts |
|---|---|
| GENERAL BIOLOGY | • The changes in membrane potential that occur during an action potential.<br>• The action of a voltage-gated ion channel. |
| ANATOMY & PHYSIOLOGY | • The changes in membrane potential that occur during an action potential.<br>• The action of a voltage-gated ion channel. |
| CELL/MOLECULAR BIOLOGY | • The changes in membrane potential that occur during an action potential.<br>• The action of a voltage-gated ion channel.<br>• The dissociation constant.<br>• Competitive vs. non-competitive inhibition. |

After the small groups have had some time to discuss Part II, the class can come together for a large group discussion. This becomes important, because Part III will require that students have a solid understanding of the principles introduced in Parts I and II. This large group discussion will provide opportunities to ensure that there are no major misconceptions. It will also provide opportunities for the instructor to add depth to some of the material in places where students may have only explored on a superficial level.

**Part III**

Part III should be completed as a small group discussion. In an advanced course, this section could also be assigned as an out-of-class assignment that students turn in for an assessment. In either case, it is important that the instructor provides a detailed description of the expectations of the students for this open-ended design portion. If done as a small group discussion, a report on the drug that the group designs could be an oral report to a large group, or a written report prepared by the group and turned in for assessment.

The primary issue that needs to be addressed is the level of depth that should be provided in the report from the group (or individual). Many students will have the tendency to provide very superficial descriptions of how their drug will work. For example, one of the most common answers is to suggest that the drug acts like an enzyme to break up the TTX molecule so that it cannot bind to the channels and have its effect. Directing the students to provide more detail on the "break up" portion of their description forces them to think about how enzymes work. If hydrolytic enzymes had been discussed as part of the course, students could be directed to think about the action of these enzymes.

This open-ended section is designed to have students suggest the mechanism of action of their drug. There are several possible answers here. Although many of the answers will be highly unlikely, it is important to discuss answers that address the basic biology of the case. Examples of answers that students have come up with when this case has been run in the classroom are described in the Answer Key.

At some point, a large group discussion can be conducted where the instructor lists all of the companies, their drug names, and their mechanisms of action for the entire class to see. Individual mechanisms can be highlighted, and then the entire class can suggest further possibilities during the discussion.

## ANSWER KEY

Answers to the questions posed in the case study are provided in a separate answer key to the case. Those answers are password-protected. To access the answers for this case, go to the key. You will be prompted for a username and password. For the username and password, contact the National Center for Case Study Teaching in Science administrator at answerkey@sciencecases.org.

## REFERENCES

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### Internet


- Toxicity, Tetrodotoxin
  http://www.emedicine.com/emerg/topic576.htm
  *Article on tetrodotoxin poisoning by Theodore Benzer, MD, PhD, Chief of Toxicology, Instructor, Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School.*
- Tetrodotoxin...an ancient alkaloid from the sea...
  http://www.chm.bris.ac.uk/motm/ttx/ttx.htm
  *Article by Jim Johnson, Alumnus of the Department of Molecular Biophysics & Biochemistry at Florida State University.*
- Eye of NEWT, Skin of TOAD, Bile of PUFFERFISH
  http://www.calacademy.org/calwild/sum98/eye.htm
  *Article by William Haugen Light in the summer 1998 on-line version of California Wild, a quarterly publication produced by the California Academy of Sciences.*
- Tetrodotoxin: Mode of Action
  http://www.life.umd.edu/grad/mlfsc/zctsim/ionchannel.html
  *Information on the mechanism of action of TTX from the University of Maryland's LFSC 680, Chemical Ecology Course.*


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