Unit 9
Biophysics

Introduction

There is still much lack of knowledge about this advanced level of organization of matter we call 'life', and its novel non-material consequences. However, at this stage, it is simply 'lack of knowledge', and not 'discrepancy' with the present concepts of physics
– Manfred Eigen, biophysicist and 1967 Nobel Laureate

Biologists operate in a very different domain than physicists—they study microscopic structures and particles, deep inside the body, buffeted by collisions with millions of other microscopic particles within the cellular soup. How can the ideas and approaches of physics be used in such a complex environment? This unit addresses how physicists have provided key insights and techniques in the world of biology, helping to push the frontiers of both science and medicine. Many of the concepts of *emergence*, introduced in Unit 8, apply to these topics in the biological realm.

What Will Participants Learn?

Participants will be able to:

1. Recognize how the tools of physics do and do not apply in biological systems and describe some of the limitations of these tools in biology.
2. Explain how protein folding is consistent with the physical principles of *entropy* and *energy landscapes*, and how these principles have been useful in explaining/describing these biological processes.
3. Describe the concept of a *fitness landscape* in evolution and use it to explain the evolution of one or two different *genotypes* (e.g., sickle cell anemia or beak size).
4. Describe how the brain is fundamentally different from a computer.

What's in this Unit?

Text: Unit 9: *Biophysics* covers four main areas where physics has informed the practices of biology, in increasing size scale: DNA, protein folding, evolution, and the mind and consciousness. DNA contains the genetic code, and contains a huge amount of information—more, in fact, than is needed to determine the structure of the organism. Quantifying the information in a strand of DNA is a topic of study within physics. DNA codes for the sequence of amino acids in a protein, but the actual folded structure of that protein depends on a wide array of variables. Physicists have contributed the concept of *free energy landscapes*, and *local minima*, to help understand how proteins choose from the many possible folded configurations. The diversity of the genetic code is closely tied to how particular genomes affect an organism's fitness level—i.e., the process of evolution. How organisms evolve in response to stress can be understood, in some part, with an application of physics principles. Finally, the study of computation has provided some insights into the mind and memory—though the limitations of this approach highlight how the mind and consciousness are fundamentally different from a computer, representing an emergent phenomenon.

Video: The program covers two medical treatments that have been inspired by research in physics. Vinothan Manoharan and a team at Harvard University study *self-assembly*—a topic of Unit 8. Since viruses appear to create their outer shell (called a *capsid*), the study of how this self-assembly occurs could be advantageous in fighting disease. Harald Paganetti, of Massachusetts General Hospital and Harvard Medical School, works on *proton therapy*, which uses radiation to destroy cancerous cells in a more targeted fashion than traditional radioactive treatments. Proton radiation research is directly borrowed from physicists' particle accelerators.

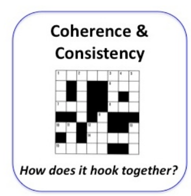
Interactive Lab: *Laser Cooling*. Learn the basics of how to manipulate atoms with light, and cool a hot atomic beam to a few millionths of a degree above absolute zero.

Activities:

- The Hook: Big Forces at Small Distances (15 minutes)
- Activity 1: Life and the Second Law (15 minutes)
- Activity 2: Breakfast Proteins (30 minutes)
- Activity 3: Fitness Landscape (15 minutes)
- Activity 4: Watch and Discuss the Video (50 minutes)
- Activity 5: Pulling it Together (15 minutes)
- Back to the Classroom (10 minutes)

(*Note:* The video for this unit is not closely tied to the content of the written text. Thus, you may choose to assign the video and discussion questions for homework. If you choose to show the video in class, you may wish to drop the second half of *Activity 1: Life and the Second Law* in the interest of time.)

Nature of Science Theme: *Coherence & Consistency*. You may wish to display the *Coherence & Consistency* icon during the session and remind participants of the central ideas of this theme. Science is not a set of independent facts and formulas (as often seen by students). Rather, scientific findings are accepted as true because they hold together with other ideas and findings. Conflicts between results or between experiment and theory reduce scientists' confidence in either the experiment or the theory.



Exploring the Unit

The Hook: Big Forces at Small Distances

Time: 15 Minutes.

Purpose: To introduce the idea that different forces (namely, *collisional* and *thermal forces*) dominate at the microscopic scale rather than at the familiar macroscopic scale.

Materials:

- A heavy ball and a light ball (e.g., steel ball and a ping pong ball)
- Digital projector
- PhET simulation "Gas Properties" http://phet.colorado.edu/simulations/sims.php?sim=Gas_Properties

(*Note*: You do not need to be connected to the internet to run these simulations. Choose “Download” to save to your computer.)

To Do and To Notice

Roll the light ball across the floor. What happens? What affects how far it rolls? What might stop it? Roll the heavy ball across the floor. Why does it roll further?

Project the PhET simulation “Gas Properties.” Select “Light Species” for the *Gas in Pump*. Pump the handle a small amount, so a few (5 or fewer) red balls enter the chamber. What do participants notice about their behavior? Does it look similar to the ball rolling across the floor?

Then pump the handle about twice, so that there are many light gas molecules in the chamber. It’s difficult to follow the motion of these molecules with the eye, so add 3 or 4 heavy gas molecules using the manual controls on the right. What do participants notice about the behavior of these blue molecules? Add more red molecules with the pump and increase the pressure, and notice how the behavior of the blue molecules becomes more erratic. How easy would it be to “throw” a blue molecule from one side of the chamber to the other?

What’s Going On?

The heavy ball rolls further than the light ball because of its greater mass. It is slowed, and eventually stopped, by friction—both with the table, and with the molecules of the air. Our intuition is useful in answering these questions.

Our intuition is less useful when we look at microscopic objects. The isolated red gas molecules in “Gas Properties” are mainly affected by their own momentum, as were the rolling balls. Once many molecules are added, however, they begin to show Brownian motion due to the multiple collisions. As the number density of the red gas molecules is increased, their behavior becomes increasingly erratic. This is the experience of microscopic sized objects, such as proteins and DNA, which exist in a sea of water molecules inside the human body. When a ball is thrown across the room, it collides with air molecules, but its motion is mostly dictated by its own weight and momentum. When a blue molecule is thrown across the chamber, however, its motion is mostly dictated by collisions with other molecules. Its momentum only affects its behavior for a fraction of a second. Thus, forces like *viscous drag* are very important for objects in the cell.

Below is a list and description of important forces at this size scale.

Force	**Sample calculation**[1]
Collisional and thermal	Collisions are equivalent to thermal energy. The force due to a collision is given by $F = \Delta p/\Delta t=\Delta(mv)/ \Delta t$. If struck by a water molecule (average v = 600 m/s, average m = $30\text{x}10^{-27}$ kg) once per second, $F=36\text{x}10^{-12}$ pico Newtons (pN). The effects of random collisions drives Brownian motion. Due to the large number of collisions, the overall force is relatively large (~500 pN on a typical protein). Similarly, if a protein were accelerated forward, it would only move forward under that force for a fraction of a second before hitting another object (or being slowed by drag, see below).
Viscous	Drag forces are also relatively larger on small objects, due to the greater ratio of drag to momentum as an object's mass decreases. DNA would come almost immediately to a stop. For a similar reason, it takes 10 hours for a protein to move a distance of 100 mm in a spinning centrifuge. Drag increases with the size and shape of the object; for a typical protein at typical speeds the viscous force is about 480 pN.
Electrostatic	A charged particle experiences a force $F=qE$ in an electric field. Due to the small electric charges of, for example, an ion, these forces are usually only a few pN. The atoms on a protein chain, however, experience high electric fields due to their proximity, resulting in forces up to 100 pN between atoms in a protein. This is important in protein folding, later in the session.
Elastic	Proteins and DNA both have stiffness; this stiffness may be demonstrated by grabbing and dragging the optical trap apparatus on the bottom of the screen. If "show DNA force" is checked, the restoring force will be shown. For a typical motor protein, this force might be about 1 pN for a stretch of 1 nanometer.
Gravity	Gravity is negligible for these small masses. A protein mass is about $166\text{x}\ 10^{-24}$ kg, giving a gravitational force of only $1.6\text{x}10^{-9}$ pN. This is 11 orders of magnitude smaller than viscous forces!

Take-home message: Biological molecules are suspended in liquid, and experience thousands of collisions each second. Because of their small mass, these collisions affect the momentum of the particle much more than most external forces (such as electricity, or mechanical forces).

Activity 1: Life and the Second Law

COMPUTER SIMULATION

Time: 15 Minutes.

Purpose: To explore how entropy relates to biological systems, both in terms of protein folding and the existence of life itself. Molecular collisions leading to Brownian motion explains why the DNA strand in the PhET simulation "Stretching DNA" moves erratically, and entropy explains why it folds when released from the trap. (*Note: Part 2* is self-contained and may be eliminated in the interested of time.)

[1] Sample calculations from J. Howard, "Mechanics of Motor Proteins and the Cytoskeleton" Sinauer Press, 2001.

Materials:

- Latex gloves (enough for every one or two participants)
- Digital projector
- PhET simulation "Stretching DNA"
  http://phet.colorado.edu/simulations/sims.php?sim=Stretching_DNA
  (*Note*: You do not need to be connected to the internet to run these simulations. Choose "Download" to save to your computer.)

1. Dancing DNA

To Do and To Notice

Project the PhET simulation "Stretching DNA." Explain that what is shown is a strand of DNA—a biological polymer. Proteins are also biological polymers, so similar behavior would be seen if this were a protein. The pushpin represents one end of the DNA molecule that is pinned in place. The yellow ball represents a dielectric bead, which is held in an optical trap just like the molecules of a Bose-Einstein condensate (BEC) in Unit 6 and 7. Demonstrate that the ball may be moved, stretching the DNA. What do participants notice about the behavior of the strand of DNA? What forces might be responsible for the behavior that they see? Discuss briefly before presenting the clicker question.

Clicker/Discussion Question:

What do you think are the three most important forces on the strand of DNA (not including the force from the optical trap)?

1. Gravity
2. Elastic stretching
3. Thermal/collisions
4. Viscous drag
5. Electricity and magnetism

A. 1, 3, 4 (gravity, thermal, viscous drag)
B. 2, 3, 4 (elastic, thermal, viscous drag)
C. 1, 3, 5 (gravity, thermal, electricity and magnetism)
D. All of them are important
E. Something else

CLICKER/DISCUSSION QUESTION

How does the behavior of the DNA strand differ from, say, a string sitting in a glass of water?

What's Going On?

Because of its size, DNA is affected by very different physical forces than more familiar objects. The best answer to the clicker question is (B). Make sure that participants understand that (a) gravity is negligible and (b) thermal/collisional effects are important at this scale. This is why the DNA strand shows such erratic behavior whereas a string in a glass of water sits perfectly still, to our eye. The string's mass is much more significant with respect to the water molecules. The DNA's erratic behavior can also be explained in terms of entropy, as described below.

2. Entropy and Life

To Do and To Notice

Ask participants for a definition of the *second law of thermodynamics*, and write it on the board. Facilitate a Think-Pair-Share.

- What is *entropy*?
- Is life consistent with the second law of thermodynamics?

Ask participants to put on the latex glove and stretch the latex rapidly against their skin. What do they notice?

Clicker/Discussion Question:

If the latex glove gets warm as it is stretched, what must be true of the entropy of the glove as it is stretched?

A. It increases
B. It stays the same
C. It decreases
D. The heat of the glove isn't related to its entropy
E. Something else

Return to the PhET "Stretching DNA" simulation. Turn off the power on the optical trap, releasing the yellow molecule. What happens to the DNA strand?

Think-Pair-Share

- How can this be explained in terms of entropy?

What's Going On?

The second law of thermodynamics includes the following principles:

- Thermal energy flows from high temperature to low temperature
- The total entropy (or microscopic disorganization) of a system increases during an irreversible process

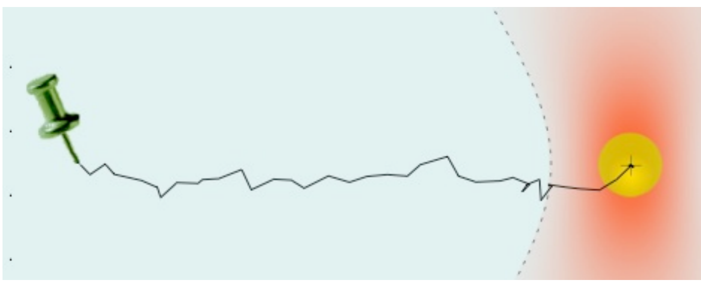
Life might appear to violate the second law because life is a highly ordered, low entropy state. But entropy only increases in isolated systems. Living things are not an isolated system; they exchange matter and energy with their environment. Living things spend a lot of energy to maintain a state of not being in equilibrium with their environment. If an organism is in thermal equilibrium with its environment, it is probably dead. In order to stay alive and maintain their high degree of order (and thus low entropy), life increases the overall entropy of the universe. Thus, the entropy of the universe (a closed system) does increase, and life does not violate the second law.

As the entropy of a system increases, its thermal energy increases, and less energy is available for doing work. This can be illustrated by considering an ice cube. As it melts, it absorbs heat from the environment. Melting represents an increase in entropy, as the highly-ordered crystal becomes a disordered liquid. Freezing represents a decrease in entropy, as the disordered liquid becomes an ordered crystal.

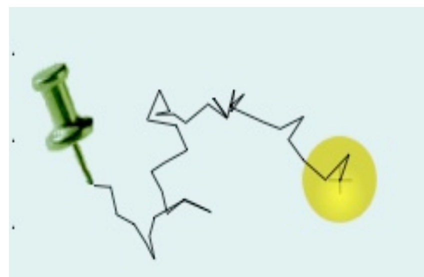
If the latex glove gets warm as it is stretched, then its entropy must be decreasing. Heat flows from the latex during this decrease in energy, like heat flows from water as it freezes into ice. This means that the stretched latex is more ordered than the unstretched latex. Latex is made of polymers, a type of molecular rubber band that is not unlike DNA or a protein. A coiled or folded polymer is less ordered (and thus has higher entropy) than a stretched polymer.

Because both DNA and proteins are polymers, the demonstrations with the PhET simulation on DNA would equally apply to proteins. Thus, the proteins fold because this is a more disordered, high entropy state. In this way, entropy explains why things happen—objects seek a high entropy state.

The different ways that a polymer can fold, or different configurations of the polymer, are called different states of the polymer. Statistically, high entropy means that there are more states. Liquid water has more states than solid ice because the molecules can rearrange themselves in many different ways (each rearrangement is one state). Thermal energy, or collisions with other molecules, "bumps" the polymer into different configurations. Similarly, collisions between water molecules "bump" them into different positions. This allows the polymer, or water, to explore many different states.[2]



Stretched DNA or protein
Low entropy; high order



Folded DNA or protein
High entropy; low order

Take-home message: Coiled or folded polymers are in high entropy, disordered states. Thus, a protein will fold, when left to its own devices, because systems tend towards high entropy. The way that it folds—the particular folding pattern that it chooses—is enabled in part by the thermal energy from collisions with surrounding molecules.

Activity 2: Breakfast Proteins

Time: 30 Minutes.

Purpose: To create an analogy for how DNA codes for protein structure, including the role of RNA. Participants explore how the sequence of amino acids relates to the folded structure of the protein, and the huge array of folding possibilities.[3]

Materials:

- Fruit-flavored donut-shaped cereal (such as Froot Loops®)
- Chenille stems
- String
- Scissors
- Pencil
- Paper

[2] These are complicated ideas, and not every participant will understand the concept of states.
[3] Activity used with permission: "Breakfast Proteins," © Julie H. Yu, Exploratorium, 2010. http://exo.net/~jyu.

Before the session: Using letters to correspond to the different colors of the cereal (i.e., Y=yellow, R=red), write down a template for the cereal chain as follows: BRYBRYPRPYP. Tape this piece of paper in the corner of the room and section off this area with some string. Put some scrap paper and pencils next to this area.

To Do and To Notice

Tell people that the instructions to make their cereal chain are in the corner of the room. Since the instructions are taped down, they can use the scrap paper to help them remember them.

Place a cup of cereal and chenille stems in the main part of the room. People must construct their chains in this area.

In groups of 2–3:

- Compare the finished cereal chains. Is everyone's the same?
- Find the best folding pattern for the cereal chain assuming that "red wants to touch red." Is there only one folding pattern that accomplishes this?
- Going further: Which of these folding patterns is the lowest energy (and thus most likely)?

In the whole group:

- Field participants' questions and invite them to share their "gems" on the topics of the genome, proteins, free energy landscapes, and related topics from *Between Sessions* homework.

Clicker/Discussion Questions:

1. Imagine that a protein consists of ten segments. Each segment can fold in one of two ways. **How many different configurations are possible for the protein as a whole?**

   A. 2
   B. 12
   C. 20
   D. 200
   E. 1024
   F. Something else

2. The online text discussed the concept of *free energy landscapes*. **Which of the following have similar free energy landscapes?**

   A. An electron in empty space AND a ball rolling down a funnel
   B. An electron next to a proton AND a ball rolling down a funnel
   C. An electron in empty space AND a ball on the floor
   D. An electron next to a proton AND a ball on the floor
   E. More than one of these/Something else

CLICKER/DISCUSSION QUESTION

Discuss as a group.

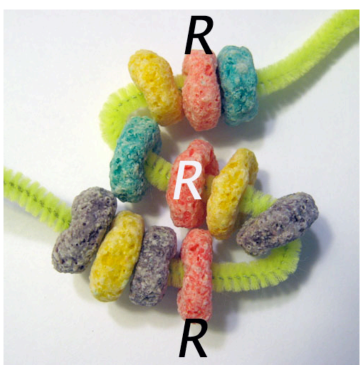
- How does the concept of free energy landscapes relate to protein folding?
- Where is the physics in this activity?

What's Going On?

Making the cereal chain is a model of protein synthesis from DNA. The initial template represents a portion of DNA (called a *gene*) that sits in the nucleus of the cell and gives instructions for how proteins are made. (Variations on each gene, such as a change in one letter, would be called an *allele* of that gene.) In order to get this information to an area where proteins can be made, it must be copied into RNA, which is very similar to DNA but has a different form. This is represented by the hand-written notes on the scrap pieces of paper. The copying process is called *transcription*. Just like in the cell, a single DNA template can give rise to many RNA transcripts. These transcripts move from the nucleus of the cell into the cytoplasm where ribosomes use the information to assemble proteins from amino acid subunits in a process called *translation*. In the cell, the genetic code dictates which amino acid residues correspond to a given DNA sequence, but in the cereal chain it is usually obvious that the letters in the instructions correspond to the color of the cereal. Each participant's cereal chain represents a protein.

The folding of a protein depends on the properties of the amino acids and sidechains (such as electric charge, hydrophobic or hydrophilic) that make it up. How a protein folds is important because this determines its function in the body. Alzheimer's and mad cow diseases are both caused by the misfolding of a single protein, as is sickle cell anemia.

The protein formed here can fold one of three main ways, given the rule that red must touch red.



Configuration #1: Line

Same as Configuration #1, but fold top part onto bottom part so that all three reds are touching

Configuration#2: Twisted line.

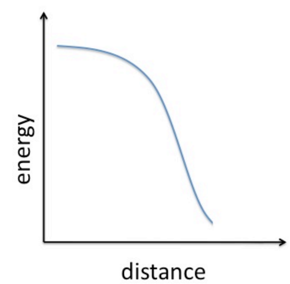
Configuration #3: Triangle

Configuration #2 is considered lower energy because (a) the three red pieces of cereal are all touching, unlike Configuration #1, and (b) there are no sharp kinks in the structure, as in Configuration #3. You can imagine why this would be lower energy if you consider the three red cheerios as connected by rubber bands. Configuration #1 stretches the rubber band and so would be at a higher potential energy than Configuration #2. Participants can experiment with protein chains and folding at The Molecular Literacy Project: http://molit.concord.org/database/activities/225.html.

1. Answer is (E); 1024. The number of possible folding configurations for any protein is huge. Scientists can't predict the folding of a protein from its amino acid sequence, in part, because there is a huge array of different folding possibilities. In this activity, if each protein segment can fold in one of two ways, then when two segments are strung together, the whole protein can fold in four ways ($4=2^2$). If three are strung together, the protein can fold in 8 ways ($8=2^3$). If ten are strung together, they can fold in 1024 ways ($1024 = 2^{10}$). Thus, the

number of combinations grows exponentially with the number of segments. In reality, each protein segment can fold in more than two ways, and the number of combinations is immense.

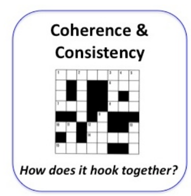
2. Answer is (E); More than one. Both (B) and (C) represent similar energy landscapes. Option (B) represents a flat landscape, and option (C) represents an energy minimum (see figure below). The ball seeks the lowest elevation by rolling down the funnel. This may not bring it to the lowest possible elevation—there may be a deeper funnel a few feet away. Similarly, biological structures try to minimize their potential energy, but not all states are accessible. Proteins find the best folding that they can by minimizing their energy within the local energy landscape. Thus, protein foldings represent *local minima*, or *metastable states* (recall the sand pile of Unit 8). Finding a local minima is more efficient than trying every possible folding configuration by trial and error, as in the Traveling Salesman problem (see *Activity 5*).



Rough energy vs distance diagram for a ball on a funnel or electron near a proton. "Distance" would be replaced with "folding configuration" for a protein energy landscape.

Physics comes into play in many areas of this activity, for example:

- Informatics of the genome
- Bonding between amino acid base pairs
- Intramolecular forces between different parts of the protein chain
- Entropy (See *Activity 1*)
- Energy landscapes



Thus, these biological systems are consistent with physical principles, even if physics is as yet insufficient to explain them in detail (see the quote for this chapter).

<u>Take-home message</u>: DNA codes for protein synthesis. The amino acid sequence of the protein dictates its folded structure. The protein folds to minimize its energy, but there are so many different possible folded structures (due to different combinations of the folding of the subunits of the proteins) that it's impossible for the protein to find the lowest-energy structure by trying all of them. The concept of energy landscapes, from physics, helps explain why proteins can find the lowest energy folded structure quite quickly. Thermal energy nudges a protein into different folded configurations, allowing it to explore the local energy landscape and find the local minimum. Folding is important because the protein function depends on its folded structure—an idea critical for evolution.

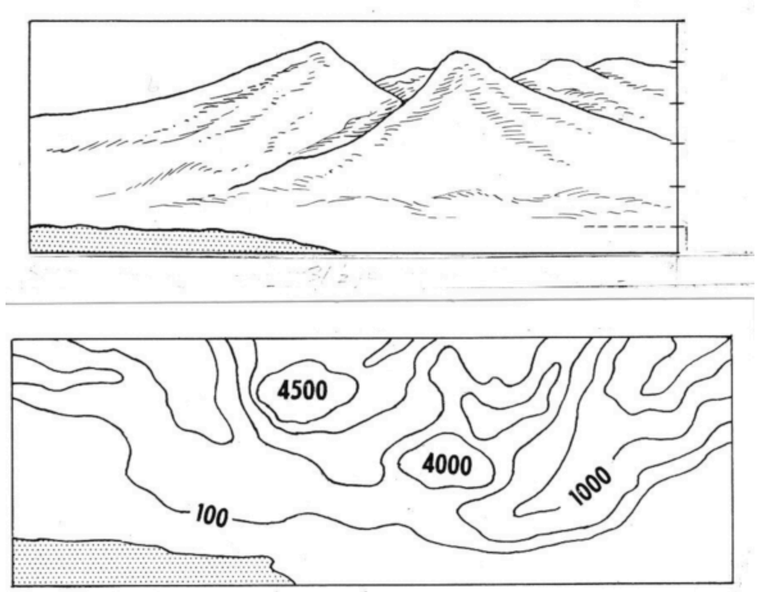
Activity 3: Fitness Landscape

Time: 15 Minutes.

Purpose: To explore the idea of fitness landscapes: How the evolution of a species is related to movement on that landscape, and how the landscape itself can depend on external factors.

To Do and To Notice

Show participants a copy of a topographic map, as below.



Topographic map as an analogy for a fitness landscape[4]
(Available in the online resource: *Facilitator's Guide High Resolution Graphics*)

This can be used as an analogy for a fitness landscape, in which the goal of species evolution is to seek a maximum of fitness. A finch with a long beak that can pick up smaller seeds is more fit (in terms of that particular trait) than its brother bird with a broader beak that has more trouble picking up seeds—that bird would be at a higher point on one of the mountains than its brother with the broader beak.

As a group, list the features of *free energy landscapes* and *fitness landscapes* in two columns on the board. What types of things does each landscape affect? Which is the best place for an object to be, a hill or a valley? What types of factors move an object up or down on the landscape?

Think-Pair-Share:

1. What are some other examples of processes that would push a species uphill?
2. What are some processes that would push a species downhill?

[4] Source: © Wikimedia Commons, License: None. Author: Pearson Scott Foresman. http://commons.wikimedia.org/wiki/File:Contour_map_%28PSF%29.png.

3. Sickle cell anemia is caused by a genetic mutation that causes a single protein to misfold, making blood cells sickle-shaped. Sickle cell anemia reduces life expectancy. People with sickle cell anemia are less likely to get malaria. How might the fitness landscape for the sickle cell mutation depend on geographic location?
4. Going Further: People who survived the plague called the "Black Death" had a particular genetic mutation that protected them from getting the disease. Before the Black Death, this mutation had no effect on their fitness. Explain this using the concept of fitness landscapes.

Field participants' questions and invite them to share their "gems" on the topics of evolution and fitness landscapes from *Between Sessions* homework.

What's Going On?

Free energy landscapes and fitness landscapes are similar concepts, with key differences:

	Free energy landscape	**Fitness landscape**
Things affected by the landscape	Proteins and molecules	Generations of organisms, or genomes
It's best for those things to move to…	Valleys	Peaks
The factors affecting movement on the landscape	Charge, hydrophobicity, etc.	Finding things to eat, reproducing, resistance to disease, etc.

1. Species can be pushed uphill by a variety of factors. The introduction of antibiotics both puts *selection pressure* on bacteria which are immune to the antibiotic, and *mutation pressure* on bacterial populations to develop immunity to the antibiotic.

2. Species can be pushed downhill by genetic mutations that are maladaptive. Possible discussion point: What type of role do rare mutations from, say, radiation, play in these landscapes (imagine Godzilla as a fictional example). Lack of genetic diversity can also lead to a downhill movement, as the species does not have enough diversity to adapt to its environment.

3. In Africa, sickle cell anemia protects against malaria, so it is adaptive. That genotype will be a peak on the fitness landscape. In Europe, sickle cell anemia is, instead, a valley, representing its maladaptivity.

4. Before the Black Death, the landscape for that particular gene was flat. With the arrival of the Black Death, which killed a large percentage of Europe's population, a sharp peak in the fitness landscape appeared, showing the strong selection pressure for people with this genotype.

Coherence & Consistency

How does it hook together?

<u>Take-home message</u>: One can consider a species to be under the effects of a variety of forces, or stresses, or pressures, similar to a physical object. The opposing forces of mutation, selection, inbreeding, and crossbreeding must balance in order for an organism to be static in terms of its evolution. Thus, the concepts of (a) equilibrium, (b) opposing forces or pressures, and (c) locally stable but non-optimized states, are useful concepts from physics that apply to biology, further demonstrating the coherence of scientific disciplines.

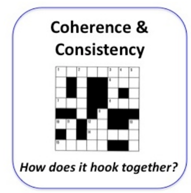
Activity 4: Watch and Discuss the Video

Time: 50 Minutes.

If participants are watching the video in class, have them view it now. Remind them of the guiding questions listed in *Between Sessions* from the previous unit.

- As you watch, mark things that you've seen or heard about before. Why are they showing up here in biology?
- What are some other examples of the results of one field informing another field?
- What are some things that one has to consider when working with biological systems that one doesn't have to worry about in non-biological systems

Discuss the video with participants, focusing on the discussion questions.



The perspectives of physics relate to questions of biology in a wide variety of ways. If you examine the table of contents of an introductory Biophysics textbook, you will see many familiar concepts from introductory physics (e.g., energy, forces, bonding, heat and energy transfer), chemical physics (e.g., reaction rates, diffusion) as well as from more advanced or modern physics (e.g., neural networks) and physical techniques (e.g. x-ray, nuclear magnetic resonance, optical tweezers, atomic force microscopy).

String theory is another example of one field informing another, as the mathematics developed for this physical theory has proven useful for various branches of mathematics. The physics of superconductors has been important for developing the branch of medical imaging called *magnetic resonance imaging*, or MRI.

Biological systems are, in many ways, messier than physical systems. One has to consider the rather complicated chemical and physical environment of most biological processes. As discussed in *The Hook* activity, the energy scale of interactions in biological systems is quite different from that in many physical systems. As seen in the video, for medical research one also has to be aware of side effects of treatments. This is not a concern in physics (except when considering the safety of technicians and scientists).

Activity 5: Pulling it Together

Time: 15 Minutes.

Purpose: To see how the different aspects of this unit relate to one another, and discuss the highest level of organization—consciousness and the brain.

Materials:
- *Find the Highest Note* http://www.exploratorium.edu/exhibits/highest_note/
- Related files at http://asa.aip.org/demo27.html)
- *Optional*: Traveling salesman route through Germany from online resource: *Facilitator's Guide High Resolution Graphics*

1. Consciousness and the Mind

To Do and To Notice

Use the auditory illusion *Find the Highest Note*. (Let the cursor hover over each key to play the sound. This can be slow to load—be patient or use the non-interactive "Shepard Scale" version at http://asa.aip.org/demo27.html). Be sure to play the "continuous" version at that website as well—it's quite striking. Ask participants, "What do you notice?" Use this activity, and the online text, to discuss the question:

- How is the brain different from (and similar to) a computer?

Field participants' questions and invite them to share their "gems" on the topics of consciousness and the mind from *Between Sessions* homework.

What's Going On?

In *Find the Highest Note*, each key is actually a collective of notes spaced by an octave. The volume of the different notes in the chords changes as you go around the keyboard, creating the illusion of a never-ending staircase of sound.[5] This, and any other illusion, can show how our perception of the world is different from what is actually there. See also *The Hook* activity from the Introductory Unit. Thus, our mind is different from a computer in that it does not simply process what is there. The complex interactions of many neurons give rise to surprising behaviors, like reasoning or consciousness.

2. What's Complexity?

To Do and To Notice

Think-Pair-Share:

- Where would you place each of the topics from this unit (DNA, protein folding, evolution, and the mind) on your concept map from Unit 1? Do they belong here? Do they need a new concept map?
- Describe the complexity in each of these areas. That is, what are the basic building blocks in each system, and what are the interaction forces or pressures that are resulting in complex behavior?
- How does the Traveling Salesman problem relate in each case?
- How do these types of complexity, or emergence, differ from the types of emergence we saw in Unit 8? Is there something qualitatively different about them, or not?

What's Going On?

In many ways, these ideas require their own **concept map,** and one could organize them hierarchically. However, all the things listed in this unit are made of the "matter particles" identified on the concept map, and they interact through the "force particles" or *bosons*. Thus, one could argue that, for example, protein is made of "matter particles" which interact using the "force particles" but in a very complex manner giving rise to new behavior.

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[5] More on this activity here: http://www.exo.net/~pauld/summer_institute/summer_day1perception/find_the_highest_note.html.

We can identify the individual constituent pieces, and their interactions, for each of the topics in this unit:

Topic or Phenomenon	Individual piece	Multiple possibilities for individual pieces	Interactions
DNA/Genome	Amino acids	Sequence of amino acids	Mutations
Protein folding	Amino acids	Many folded structures	Between amino acids and between amino acids and environment
Evolution	Genes and alleles of genes	Many different genotypes	Between organism and environment (fitness)
The mind	Neurons	Many different network structures	Connections between neurons

The "Traveling Salesman" problem is a famous optimization problem. Given a list of cities and the distances between each of them, how can a salesman find the optimal route that minimizes the total distance but visits each city only once?

An optimal tour through Germany's 15 largest cities – the shortest out of exactly 43,589,145,600 (14!/2) possibilities[6]
See the online resource: *Facilitator's Guide High Resolution Graphics*

Solving this problem by trial and error requires a huge amount of time (and hundreds of cities can take years to solve computationally). When there are multiple possibilities for any outcome (such as the number of ways that a protein can fold, the different genotypes that might be adaptive in an environment, or the different paths through which neurons could connect together in a network), nature cannot use trial and error to find the optimal solution. Instead, it finds a good solution based on local variables (See energy or fitness landscapes).

These examples of emergence, or complexity, are similar to those in Unit 8 in that the interaction of many small parts gives rise to new behavior. However, in the previous chapter, one could argue that if we knew a little bit more, we could indeed predict that behavior. We know something about the mechanistic interactions between those parts, we just don't know how to solve a problem with that many pieces. In this unit, we have much less understanding of the fundamental processes and interactions that are giving rise to that emergent behavior.

[6] Public domain image: http://en.wikipedia.org/wiki/File:TSP_Deutschland_3.png.

Back to the Classroom

Time: 10 Minutes.

Following is a list of high school topics and standards that are relevant to this material. See http://strandmaps.nsdl.org/ for a visual representation of science standards and benchmarks.

- **Where might this unit fit into your curriculum?** Brainstorm a list of topics with participants. You may share additional items from the list below, as you see fit.
- **What do your students know about this topic?** Brainstorm with participants.
- Optionally, you may ask participants to **find one or more of the relevant topics on the Science Literacy Maps**, and explore related ideas and misconceptions.

Topics and Standards

(*Note:* See "The Living Environment" at http://strandmaps.nsdl.org/ to explore standards and benchmarks, and common misconceptions, related to biology.)

Forces and Motion. The change in motion of an object is proportional to the applied force and inversely proportional to the mass ($F=ma$). An unbalanced force acting on an object changes its speed or direction of motion or both. Any object maintains a constant speed and direction unless an unbalanced force acts on it.

Energy. Energy appears in many forms (such as kinetic and potential). Thermal energy in a system is associated with the disordered motions of its atoms or molecules. Chemical energy is associated with the configuration of atoms in molecules that make up a substance. Some changes of configuration require a net input of energy whereas others cause a net release. In any system of atoms or molecules, the statistical odds are that the atoms or molecules will end up with less order than they originally had and that the thermal energy will be spread out more evenly. The amount of order in a system may stay the same or increase, but only if the surrounding environment becomes less ordered. The total amount of order in the universe always tends to decrease.

Electricity and Magnetism. Electric forces acting within and between atoms are vastly stronger than the gravitational forces acting within and between atoms.

Size and Scale. Natural phenomena often involve sizes, durations, or speeds that are extremely small or extremely large.

Nature of Science. There are different traditions in science about what is investigated and how, but they all have in common certain basic beliefs about the value of evidence, logic, and sound arguments.

Classroom Resources

Configuration Space. Learn the meaning of configuration space and how to model it as a surface with the Robot interactive. The accompanying text chapter provides background on this topic.
http://www.learner.org/courses/mathilluminated/interactives.

Foldit protein folding game. Solve protein folding puzzles along with other online players. Players' results actually contribute to biological science by providing researchers with algorithms and recipes for protein folding. http://fold.it/portal/.

Folding@home. A distributed computing project from Stanford University, where you can donate your computer cycles to solving protein folding problems. Includes some general information about protein folding. http://folding.stanford.edu/English/Science.

myDNA. DNA teaching activities, including scavenger hunt, the DNA code, and the genome. http://www.dnai.org/teacherguide/guide.html.

WNYC Radio Lab: Emergence. A charming and provocative radio episode on emergent phenomena, including a piece on the emergence of consciousness. Definitely worth a listen. http://www.wnyc.org/shows/radiolab/episodes/2005/02/18.

Self-assembly with nanomanufacturing. Scaffolded interactive java simulation activity using models of biological self-assembly.
http://molit.concord.org/database/activities/231.html.

DNA to Protein Synthesis interactive java simulation activity, using a model of gene transcription and translation through protein folding.
http://molit.concord.org/database/activities/245.html.

PhET Stretching DNA simulation.
http://phet.colorado.edu/simulations/sims.php?sim=Stretching_DNA.

Chaos and complexity. Resources for students and teachers. A series of tutorials (mostly concise summaries of the science) regarding different aspects of chaos and complexity in a variety of fields, including psychology, economics, and biology. http://www.societyforchaostheory.org/tutorials/.

Mathematics Iluminated. Video program and online text chapter devoted to this topic. http://www.learner.org/courses/mathilluminated/interactives.

Emergent Universe. A project of the Institute for Complex Adaptive Matter, this beautiful interactive website explores many aspects of emergent phenomena with compelling visual examples. Click on "The Fibril Connection" for an exploration of protein folding and Alzheimer's disease and how amyloid structures (a self-organization of individual proteins) relates to emergence. See especially "Explore Renegade Proteins".
http://emergentuniverse.org.

Bioquest. Community resources for problem solving in biology. A resource-rich website with curricular material on biology, with modules, case studies, and other hands-on learning. See in particular their "resource" section. Helpful for teachers looking for in-depth resources on biological applications. http://bioquest.org/.

Biocomplexity centers and organizations. The "Resources & Links" section includes a list of many centers engaging in biocomplexity research. Most do not have specific educational materials, but if one of these organizations is nearby, they may serve as a useful resource. http://biocomplexity.indiana.edu.

Materials for teaching biocomplexity from the Science Education Resource Center (SERC). A set of (rather old) documents related to biology, geology and complexity that could be useful in designing curricula or assessments.
http://serc.carleton.edu/NAGTWorkshops/biocomplexity/teaching.html.

Two great books on these topics: S. B. Johnson, *Emergence: The Connected Lives of Ants, Brains, Cities, and Software* (Scribner, NY, 2001); and S. H. Strogatz, *Sync: The Emerging Science of Spontaneous Order* (Hyperion, NY, 2004).

Between Sessions

Facilitator

Give participants one of the following values of an orbital radius to be used in the following simulation. They will find the velocity required to make a circular orbit for this radius. Not every value of radius needs to be assigned to a participant—if you have fewer participants than radii, select a well-spaced subset of the following values to assign: 30 – 50 – 90 – 115 – 120 – 140 – 150 – 167 – 175 – 200.

Participants

Text: Read Unit 10: *Dark Matter.* Make notes of any questions that occur as you read. You may wish to reconsider changing your concept map from Unit 1 to account for dark matter (and, optionally, dark energy).

Preparatory Assignment:
Download the PhET "My Solar System" simulation at
http://phet.colorado.edu/simulations/sims.php?sim=My_Solar_System.
Use the sun and one planet pre-set.

1. **Make the planet orbit the sun in a circular orbit.** Write down the settings you used.
2. **What happens when you reduce the velocity of the orbiting planet?** If you increase it? Write a few sentences describing what you see and the underlying physical principle. In particular, how does the magnitude of an object's velocity affect its orbit?
3. **Find a velocity that makes the object escape into outer space.** Now, try to find a way to keep it in orbit, *without changing its velocity or radius.* How did you do it?
4. **Explore the relationship between orbital velocity and radius.** How must you change the speed of an object to keep it in orbit when you reduce its orbital radius? Why?
5. **Find the velocity required to make a circular orbit for the value of orbital radius the instructor assigned to you.** Use the following values: M1=200, M2 = 1. Bring your results to the next session.

Video: As you watch the video for Unit 10, keep the following questions in mind. You may want to make some notes to aid you in discussion during the session.

1. What is the evidence for the existence of dark matter that is observed or would be observed in each experiment? Since we can't see dark matter, what observables would provide a clue to their existence?
2. What do we know about the nature of dark matter or about what makes up dark matter?