Supplemental Material

CBE—Life Sciences Education
Dulai *et al.*

Supplemental File S1: TBL Group/Team Formation Questions

Q1. Which year are you in?

Q2. What grade did you get in your last basic Science class?

Q3. Do you have real world work experience?

Q4. Have you studied overseas?

Q5. What is your gender?

Q6. Do you like to work with others?

Q7. In which direction does the Earth spin?

Supplemental File S2:

Legend: Typical set of questions utilized for the Readiness Assurance Test (RAT) set. First six questions form the iRAT. The additional four were added to comprise the tAMT. This question set was administered in lecture 16)

iRAT Questions

1. During depurination, a ------- or an -------- can be removed from DNA.
    a) Guanine, cytosine
    b) Guanine, thymine
    c) Guanine, adenine
    d) Adenine, cytosine
    e) None of these choices

2. The ---------- radiation in sunlight can cause the formation of ---------- dimers.
    a) gamma, adenine
    b) gamma, thymine
    c) ultraviolet radiation, adenine
    d) ultraviolet radiation, thymine

3. DNA ligase ___.
    a) doesn't use ATP since ligation is energetically favorable
    b) joins sections of DNA together
    c) chops linker DNA from between histones.
    d) cuts out damaged DNA
    e) is only used to repair broken DNA

4. Homologous recombination:
    a) uses an invading strand of undamaged DNA to repair existing damage
    b) will not make a perfect repair due to not having a reliable template to use
    c) is unique to prokaryotes (bacteria and archaea)
    d) repairs RNA only
    e) repairs both double-stranded DNA and double-stranded RNA

5. When is the base Uracil found in DNA?
    a) Never
    b) After a depurination reaction
    c) After a deamination reaction
    d) After a urination reaction
    e) None of these choices

6. Which of the following is not involved in DNA Replication?
    a) Initiator Proteins
    b) Helicase
    c) DNA Polymerase III
    d) DNA Polymerase II
    e) All of these are involved in DNA Replication

tAMT Questions (same six as above plus the following)

7. What are the 2 most frequent chemical reactions known to create serious DNA damage in cells?

a) Depurination and deamination
b) Depurination and hydrolysis of DNA
c) Deamination and hydrolysis of DNA
d) Depurination and DNA alkylation
e) None of these choices

8. The basic mechanism of DNA repair involves 3 steps: (order in the correct sequence)

A) Repair: DNA polymerase fills in the missing nucleotides
B) Excision of segment of damaged strand
C) DNA ligase seals the nick

Step 1 >
Step 2 >
Step 3 >

9. Which of the following DNA Polymerases is involved in DNA Replication?

a) DNA Polymerase I
b) DNA Polymerase II
c) DNA Polymerase III
d) DNA Polymerase I & DNA Polymerase II
e) DNA Polymerase I & DNA Polymerase II

10. Mistakes that escape the DNA replication proofreading and repair pathways most often lead to advantageous mutations for the cell.

a) True
b) False

Supplementary Table S1:

Legend: Standard COPUS Observation codes used in this study.

1. Students are Doing	
L	Listening to instructor/taking notes, etc.
Ind	Individual thinking/problem solving. Only mark when an instructor explicitly asks students to think about a clicker question or another question/problem on their own.
CG	Discuss clicker question in groups of 2 or more students
WG	Working in groups on worksheet activity
OG	Other assigned group activity, such as responding to instructor question
AnQ	Student answering a question posed by the instructor with rest of class listening
SQ	Student asks question
WC	Engaged in whole class discussion by offering explanations, opinion, judgment, etc. to whole class, often facilitated by instructor
Prd	Making a prediction about the outcome of demo or experiment
SP	Presentation by student(s)
TQ	Test or quiz
W	Waiting (instructor late, working on fixing AV problems, instructor otherwise occupied, etc.)
O	Other – explain in comments
2. Instructor is Doing	
Lec	Lecturing (presenting content, deriving mathematical results, presenting a problem solution, etc.)
RtW	Real-time writing on board, doc. projector, etc. (often checked off along with Lec)
FUp	Follow-up/feedback on clicker question or activity to entire class
PQ	Posing non-clicker question to students (non-rhetorical)
CQ	Asking a clicker question (mark the entire time the instructor is using a clicker question, not just when first asked)
AnQ	Listening to and answering student questions with entire class listening
MG	Moving through class guiding ongoing student work during active learning task
1o1	One-on-one extended discussion with one or a few individuals, not paying attention to the rest of the class (can be along with MG or AnQ)
D/V	Showing or conducting a demo, experiment, simulation, video, or animation
Adm	Administration (assign homework, return tests, etc.)
W	Waiting when there is an opportunity for an instructor to be interacting with or observing/listening to student or group activities and the instructor is not doing so
O	Other – explain in comments

Supplementary Table S2:

Legend: Description of the collapsed COPUS codes adopted by this study (adopted from Smith *et al.* 2013)

	Collapsed Codes	Individual Codes	Description
Instructors are:	Presenting (P)	Lec	Lecturing or presenting information
		RtW	Real-time writing
	Guiding (G)	FlUp	Follow-up/feedback on clicker question or activity
		PQ	Posing non-clicker question to students (nonrhetorical)
		CQ	Asking clicker question (entire time, not just when first asked)
		AnQ:	Listening to and answering student questions to entire class
		MG	Moving through class guiding ongoing student work
		1o1	One-on-one extended discussion with individual students
	Administration (A)	Adm	Administration (assign homework, return tests, etc.)
	Other (OI)	W	Waiting (instructor(s) late, working on fixing technical problems)
		O	Other
Students are:	Receiving (R)	L	Listening to instructor(s)
	Talking to class (STC)	AnQ	Student answering question posed by instructor
		SQ	Student asks question
		WC	Students engaged in whole-class discussion
		SP	Students presenting to entire class
	Working (SW)	Ind	Individual thinking/problem solving
		CG	Discussing clicker question in groups of students
		WG	Working in groups on worksheet activity
		OG	Other assigned group activity
		Prd	Making a prediction about a demo or experiment
	Assessment	TQ	Test or quiz
	Other (OS)	W	Waiting (instructor(s) late, working on fixing technical problems)
		O	Other

Supplemental Table S3

Description of the CDOP coding matrix and coding scheme adopted by this study (adopted from Kranzfelder *et al.* 2020)

Discourse approach	CDOP code	CDOP code description	Examples of classroom discourse
1. Authoritative, Non-Interactive	sharing	Teacher shares information, answers student question, or provides instructions for finding the solution	Teacher: *"Just think of, kind of, chromatid pairs, sister chromatid paired, it's a little easier to think of the numbers."*
	real-worlding	Teacher relates idea to conventional knowledge, broader perspective, and instructor's or student's personal experiences	Teacher: *"Successful genotypes-look around the room. Nothing but winner in this room, right? We have all made it to reproductive age."*
	linking	Teacher associates past topic to current topic	Student: *"You don't have a bigger potential as well because there's more connections, there's more access to the axon terminals?"* Teacher: *"Well, remember, we had that summation of action potentials. We had an action potential and we had the nodes and it could split off."*
	forecasting	Teacher associates current topic to future topic	Teacher: *"You're going to do something in lab actually focused on human population and population growth."*
2. Authoritative, Interactive	evaluating	Teacher repeats, accepts and/or rejects student's response, or acknowledges that they don't know the answer to a student's question	Student: "*And then in the first case, it would be one chance times one chance which is still one sixteenth."* Teacher: "*Right."*
	Generative	Teacher asks student to recall facts, and basic concepts, or related information	Teacher: "*Those come together in fertilization to make a zygote, right?"* Teacher: "*Yes."*
	Checking-in	Teacher asks student if they have a question or need clarification	Teacher: "*Does that make sense?; Do you have any questions?; How's it going?; Are we good?"*
3. Dialogic, Interactive	clarifying	Teacher asks student to elaborate on condensed, cryptic, or inexplicit statement	Teacher: "*Can you say more about that? What do you mean by that? Can you give an example?"*
	connecting	Teacher asks student to associate past topic to current topic	Teacher: "*Costs of sex that haven't been mentioned plus what we've been talking about for the last week."* Student: *"Is it overpopulation?"*
	contextualizing	Teacher asks students to relate idea to conventional knowledge, broader perspective, and their personal experiences	Teacher: *"Anyone have an example that they really want to hear about/talk about (referring to student responses to finding analogies between cell processes and common household items)?"*
	representing	Teacher asks student to create a visual or mathematical representation of content	Teacher: *"Think about how you could draw that out, too."*
	constructing	Teacher asks students to build knowledge by interpreting and/or making judgments based on evidence, data, and/or model	Teacher: *"In your own words, what is your conclusion when you look at those data?"*
	requesting	Teacher asks student to justify or explain their reasoning	Teacher: *"I'm liking what I see but explain it to me"* (referring to student whiteboard work calculating the number of fertilization events that produce a specific offspring).
	explaining	Teacher asks student to explain reasoning to other students	Teacher: "*Can you explain your work to everybody else at your table so that they can figure that out?"*
	challenging	Teacher asks student to evaluate another student's idea	Teacher: *"Cost of sex?"* Student: *"Pregnancy. Instructor: I acknowledge that it's a good point, and why is there a problem with calling pregnancy a cost evolutionarily?"*
4. Other	no content discourse	Teacher is not talking or asking students to talk about content (see examples of *Instructor Talk* in Seidel et al. (2015))	
	other	TDM not described by these codes	

Supplemental File S3:

Legend: Mid-Semester survey questions.

1. The simultaneous presence of multiple instructors during in-class time helps me to achieve the learning outcomes for the course.
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Please explain:

2. Having multiple office hour options increases the likelihood of my attending them.
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Please explain:

3. Being part of a learning team in-lecture encourages me to participate in class.
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Please explain:

4. The classroom learning environment gives me a sense of belonging to a team-learning community.
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Please explain:

5. The following pre-lecture materials prepared me for the in-class learning activities: - Top Hat textbook compendium, videos, pre-lecture reading assignments, traditional slides, readiness quiz.
   a. Top Hat textbook compendium
      Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   b. Videos
      Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   c. Pre-lecture reading assignments
      Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   d. Traditional slides
      Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree

   Please explain:

6. Do you have any suggestions for how this course could be improved?

Supplemental File S4:

Legend: End of the semester survey questions.

1. The simultaneous presence of multiple instructors during in-class time helps me to achieve the learning outcomes for the course.
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Please explain:

2. Having multiple office hour options increases the likelihood of my attending them.
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Please explain:

3. Being part of a learning team in-lecture encourages me to participate in class.
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Please explain:

4. The classroom learning environment gives me a sense of belonging to a team-learning community.
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Please explain:

5. The following pre-lecture materials prepared me for the in-class learning activities: Top Hat textbook compendium, videos, pre-lecture reading assignments, traditional slides, readiness quiz.
   Top Hat textbook compendium:
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Videos:
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Pre-lecture reading assignments:
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Traditional slides:
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Readiness Quiz:
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree
   Please explain:

6. Remote instruction has impacted my collaborative learning experience in this course.
   Strongly agree- Agree- Neither Agree nor Disagree- Disagree- Strongly Disagree-
   Please explain:

7. What worked well for you in this collaborative learning environment?

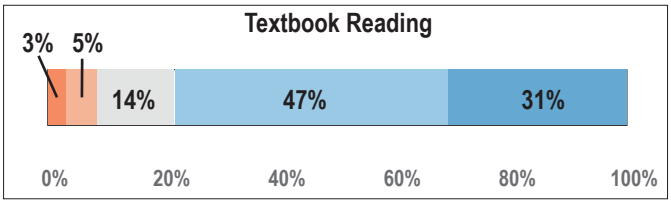
8. What did you find challenging in this collaborative learning environment?

9. What additional support would benefit your learning in this collaborative learning environment?

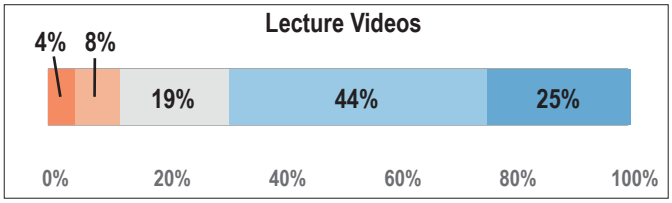
10. How would you improve this collaborative learning environment?

Dulai, *et. al.* Supplement Figure S1 - Mid-semester survey results and select student comments on pre-lecture material.

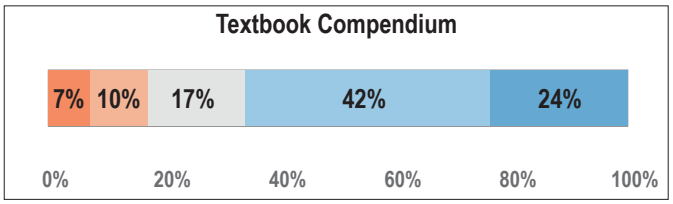
Mid-semester feedback results: Pre-lecture material (n=167)



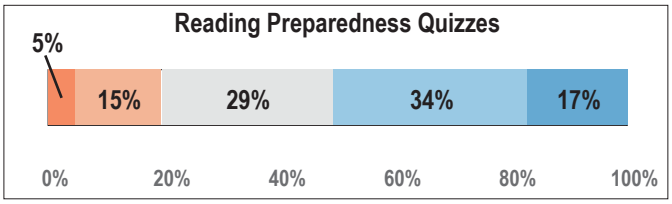
Ready available in-depth information
"The pre-readings have helped me since they give me the information I need right away."
Readings provide detailed information
"I highly rely on the readings because the compendium is too generalized on its own."



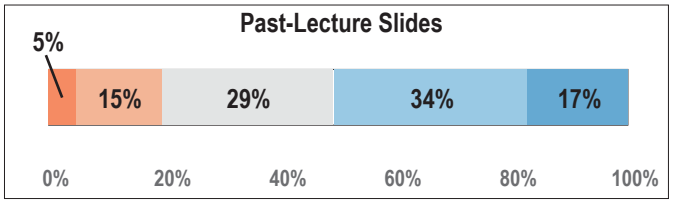
Material for reinforcement
"The videos are very lecture based and the images he draws for you are very useful in understanding the lecture."
Help break down information
"The videos actually do help break things down quite well, but it can occasionally be a bit surface level which is why I then refer to the textbook."



Easy and concise overall information
"The textbook by far is the most useful element in helping me comprehend the material as the information it contains is so in-depth that it covers the same, if not more, material we go through in class."
Isn't necessary since the same information is already provided through other resources
"TopHat at the beginning was very useful but it isn't something that should be relied on because the material in the books and videos is a lot more detailed."



Good motivation to read the textbook
"Requiring us to read the textbook by giving us quizzes helps motivate me and since I read the textbook I understand the material more."
Quizzes aren't helpful to my learning
"The quizzes don't help much with learning."

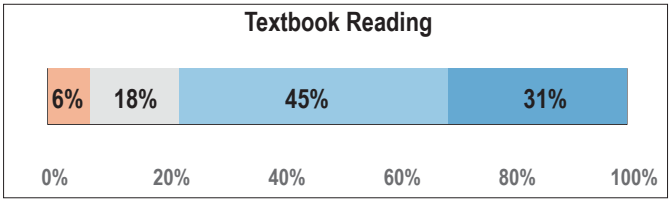


Other resources provided were more helpful
"I never used past lecture slides because it seems so insignificant and not essential compared to all the other resources."

Dulai, *et. al.* Supplement Figure S2 - End-semester survey results and select student comments on pre-lecture material.

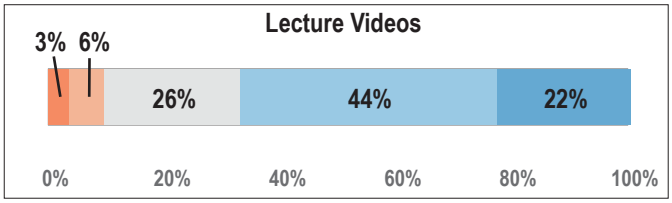
End-semester feedback results: Pre-lecture material (n=224)

Textbook Reading



Readings were quite challenging to understand.
"I thought that the readings were sometimes too complex and dry making it very difficult to understand the material."

Lecture Videos

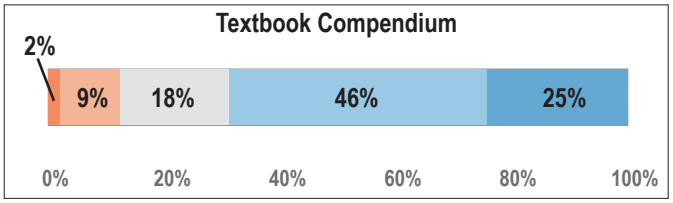


Video was helpful in preparing for learning activities.
"The top hat readings and prelecture videos were the best help in preparing for the learning activities."

There were no pre-lecture videos for some chapters.
"For some chapters there were no pre-lecture videos which I would have appreciated a lot."

Videos were too long to watch and stay engaged.
"I feel like the pre-lecture videos are too long. Students already have to read the topcoat compendium and read the textbook as well, so having a long video is not necessary. I am aware we are supposed to put more time into courses with many units, however, reading from both TopTat and the textbook already takes much of our time."

Textbook Compendium

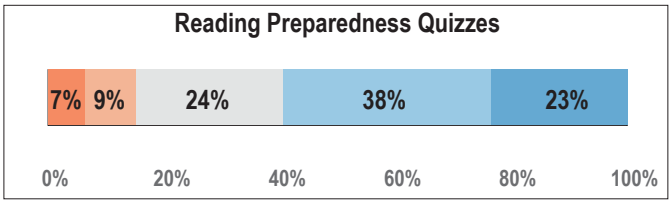


TopHat textbook compendium helped me feel better prepared for class.
"In my opinion, the textbook compendium was the most helpful as it gave me a basic understanding of what to expect in the chapter which prepared me for reading the textbook."

Did not feel prepared for class without reading the compendium.
"If I didn't read the compendium or do any of the above mentioned then I felt unprepared for class that day"

TopHat Textbook Compendium did not help me feel prepared for class because the material was not fully covered.
"Most of what was in the Top Hat compendium was not on the in-lecture quizzes. Some parts of the book were on there"

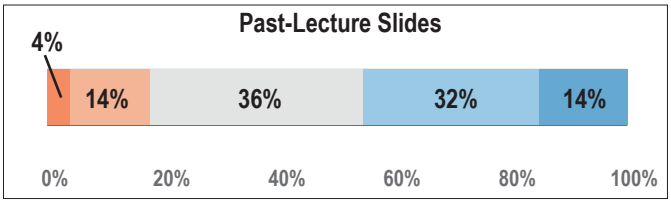
Reading Preparedness Quizzes



The quizzes are helpful in preparing for lecture.
"I helped it very helpful to read the pages assigned on the textbook before lecture as well as reading the top-hat"

Quizzes are not useful in feeling prepared for lecture.
"The Reading preparedness review on Top Hat is not as beneficial. The questions aren't on the same level."

Past-Lecture Slides



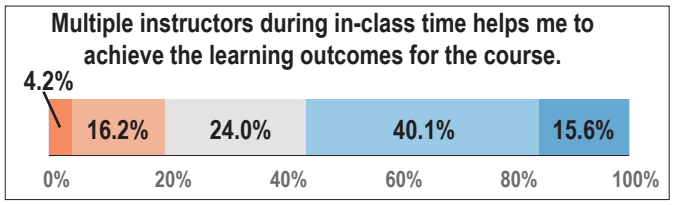
Slides helped me the best to prepare for this class.
"Personally, slides helped me best prepare for this class. I think that's the best way for me to clearly understand the material"

Did not use lecture slides.
"I used every resource except past lecture slides and I am doing well in course."

Past lecture slides were not helpful.
"The past lecture slides seem insignificant to focus on while the other resources provide more than enough help to prepare myself for in-class activities."

Dulai, *et. al.* Supplement Figure S3 - Mid-Semester Student Feedback Results and Comments: Questions 1-4

Mid-Semester Student Feedback Comments: Q1-Q4



Question 1

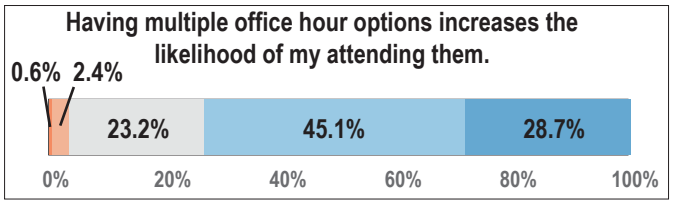
Multiple teaching and explanation styles (23/122)
"Each professor has different teaching styles. By having multiple professors there, they can help address student's different learning achievements."

Increase in professor availability (20/122)
"There were enough people to go around and answer questions and to help a large amount of students."

Multiple professors offer different viewpoints on the topics covered in class (17/122)
"I am able to understand different points of view from the professors and also I am able to get in-depth answers from the professor who studied that topic."

Having multiple instructors is confusing and makes it harder to learn because of all of the different teaching styles (18/122)
"It is more difficult to get used to and understand each professor's method of teaching. It is harder to adapt to the professor."

It can be distracting (4/122)
"Personally, I think it gets too distracting to have multiple instructors and only takes away time from learning when switching back and forth between instructors."

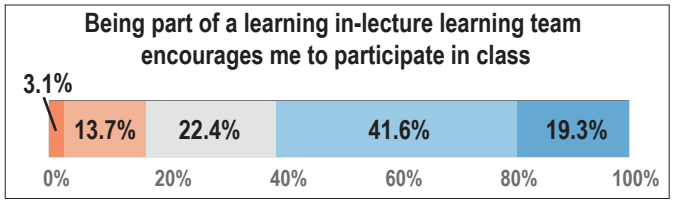


Question 2

Reduces scheduling problems (64/119)
"This year my schedule pretty much conflicted with the majority of all my professor's office hours so being able to be more flexible with more hours can help students who have conflicting schedules."

Having more time options available is helpful (16/119)
"Yes, more time, more options, more likely to attend."

They provide additional 1-on-1 help with the instructor (8/119)
"Many ways for the professors and the TA's to help us further understand the material."



Question 3

Sharing ideas with other students makes it easier to learn the material (15/118)
"Discussion helps me understand the topics more and explaining/asking my peers is also helpful."

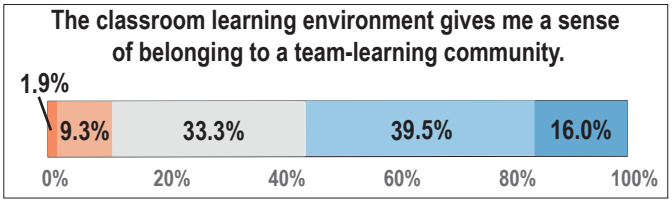
I am able to work with people that I am comfortable with (12/118)
"I get to know the group more and more and it gets to a point where we can comfortably share and discuss our opinions about the lecture without feeling embarrassed about what we say."

It helps me participate more in class (10/118)
"I feel more likely to participate in small groups."

It motivates me to do my work/engage with the material (9/118)
"I feel that by working in a team, rather than keeping the information within a notebook and opening it only before a midterm or final, the teamwork forces me to truly understand the subjects given."

Being part of a team doesn't play a role in my participation or how well I do in the course (10/118)
"I would engage in the same participation regardless."

It decreases productivity when no one knows the answer or isn't participating (7/118)
"Sometimes no one says anything so we just wait for an instructor to start talking."



Question 4

In-person interaction and approachable professors/TAs give students more opportunities to ask questions (41/137)
"I completely agree. I do like the way this class is set by multiple professors and TA in the same room. It helps in getting a quick response back on any area of confusion."

Collaborative teams make students not feel lost or confused during lecture (29/137)
Because the classroom is so big and can fit so many people, it reassures me that there are other people in the same position as me and that I can always ask for help.

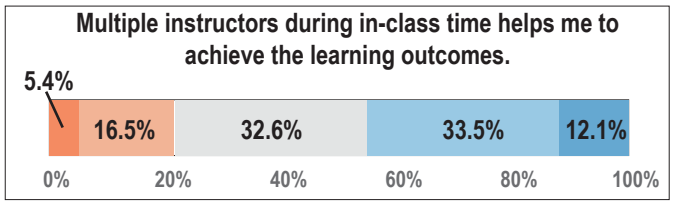
Team work implementation needs more organization (21/137)
"Sometimes I feel that teamwork holds people back if they are shy and don't want to give feedback, but for others it drags them out of their shell and helps them share their ideas more."

Students are indifferent towards the environment (11/137)
"I do not feel part of a team community because of my own choosing though I certainly do not feel left out."

Teams have a lack of participation (6/137)
"It's harder to speak when not everyone in your group wants to work together, are being forced to, or when the instructions aren't clear."

Dulai, *et. al.* Supplement Figure S4 - End-Semester Student Feedback Results and Comments: Questions 1-4

End-Semester Feedback Results: Q1-Q4



Question 1

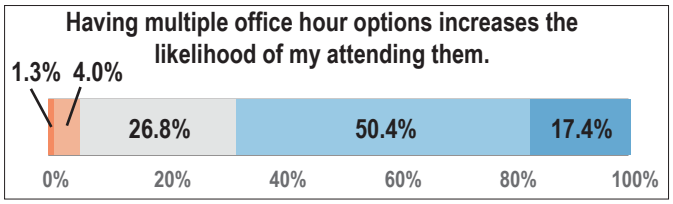
Multiple teaching and explanation styles (29/165)
"Multiple instructors correlates with multiple ways of learning content so instead of having to know only one way, I can ask the other instructors to help explain the content in a way that I can understand."

Increase in professor availability in class gives me more chances to ask for help (23/165)
"There are a lot of students during lecture so having many people walking around helps a lot because you can almost always have your questions answered."

Multiple professors offer different viewpoints on the topics covered in class (23/165)
"It's great to have multiple professors who share their distinct point of views and knowledge"

Having multiple instructors is confusing and makes it harder to learn because of all of the different teaching styles (19/165)
"The changing back and forth of instructors at times makes it difficult to understand a concept if a student has already gotten used to a certain way of instruction."

It can be distracting (6/165)
"Was distracting and the sudden change in instructors made me struggle when learning."

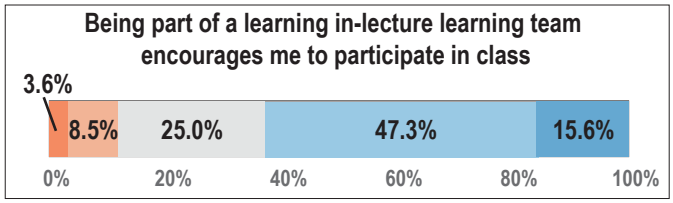


Question 2

Reduces scheduling problems (71/156)
"Everyone has a busy schedule and sometimes office hours don't always align with you schedule so now there are more opportunities to go."

Having more time options available is helpful (24/156)
"Having more available times allows for more opportunity to attend them."

They provide additional 1-on-1 help with the instructor (5/156)
"More opportunities to receive help from other faculty if necessary."



Question 3

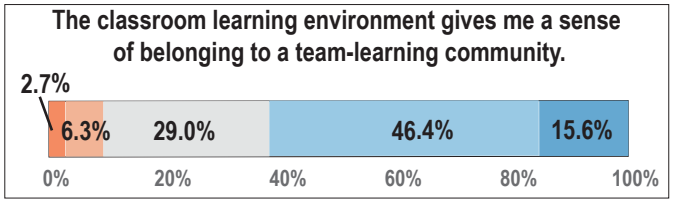
Sharing ideas with other students makes it easier to learn the material (26/152)
"Being in a group in class helped me learn the material more because I was able to talk with others over what I would learn and they would add to my learning or correct me in parts I didn't quite understand."

Understanding my peers points of view expands my learning (23/152)
"It is better learning and talking to others, it makes me understand the material from other perspectives."

I am able to work with people that I am comfortable with (16/152)
"I did enjoy being a part of a team because I had an assigned group of people to talk with so I wouldn't have to go through the whole process of talking to new people every week to discuss the topics. I was comfortable with my group so it was easy for me to talk to them more."

Teams are only helpful when everyone participates (25/152)
"This is only relevant if you are part of a group that you can bond with. My group never rarely communicated with each other, only when completely necessary (group project). It was basically doing this entire class solo but you were forced to be in the same room with other people. We might as well have done no groups at all and it would've been the same."

Being part of a team didn't contribute to my participation (7/152)
"I will participate with or without a group."



Question 4

Teams are friendly, which encourages students to help each other and ask partners questions (60/124)
"It helps give us a sense of belonging to a team-learning community because we are surrounded by people who have similar goals, so it makes it feel like we belong in a community where we are able to have the same thoughts or voice out opinions easily."

It is harder to learn the material through online lectures because the environment is different (24/124)
"It is much easier to learn inside of the classroom than it is inside of your actual room of your home."

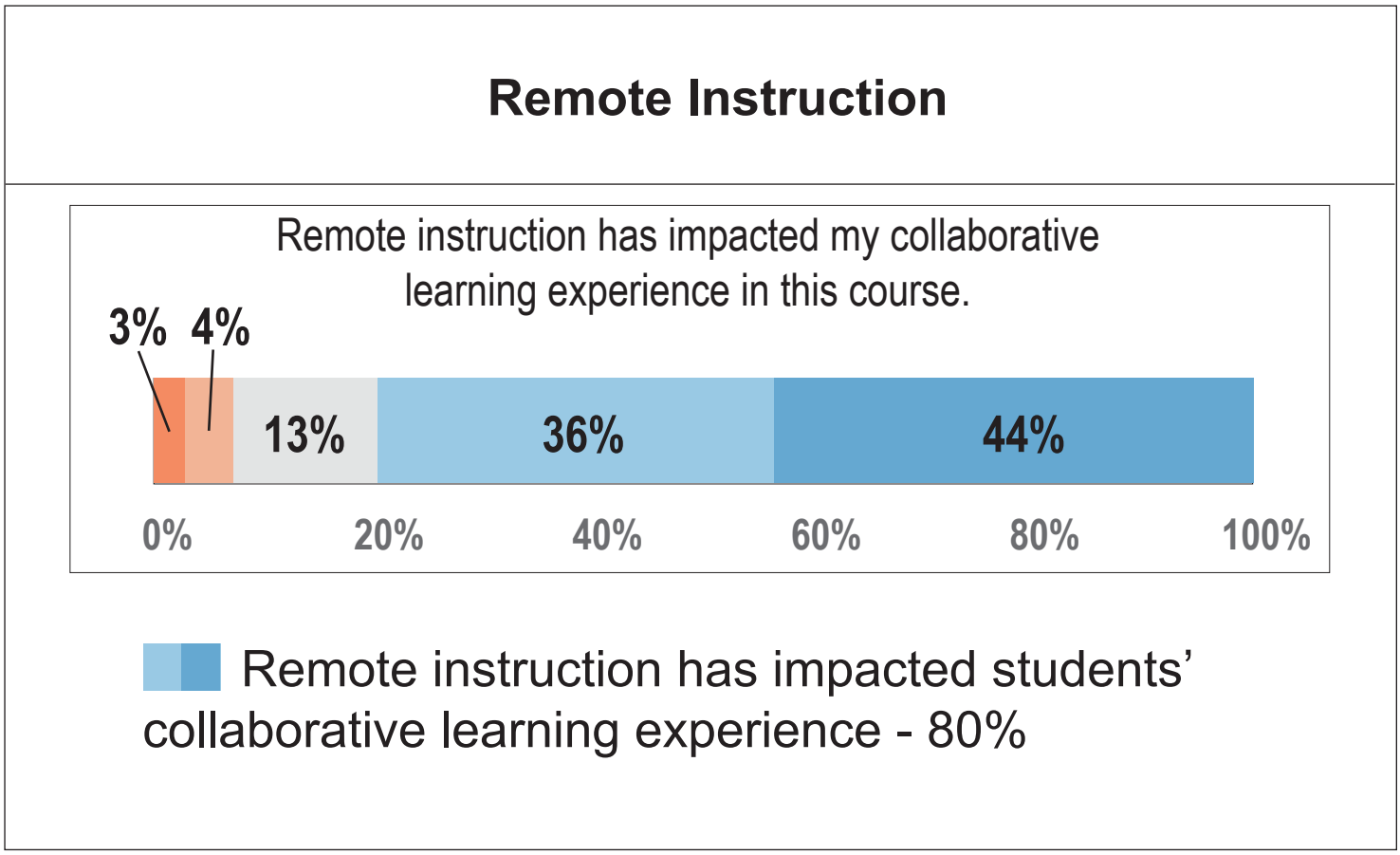
Students are indifferent towards the class (16/124)

Teams are not useful due to lack of participation (24/124)
"There were very few instances where the teams in the classroom collaborated with each other, therefore, I felt as though the environment didn't give me a sense of belonging to the classroom as a whole."

Students do not like that group work is forced on students (4/124)
"I do not like interactive lectures, they increase how much anxiety I get and actually make me question what I know more than I normally feel the need to."

I never bonded with my team so there was not a sense of belonging (3/124)
"Even though there is team collaborations there is never a sense of belonging and the class has increased my imposer syndrome feeling"

Dulai, *et. al.* Supplement Figure S5 - Impact of remote instruction on students



Supplemental Material

File S5

Example Chapter from Compendium

Chapter One: Life and Cells

Figure 1: Chemical Soup - Life can be found in the most inhospitable places.

Learning Goals

- **Define** life!
- **List** the properties exhibited by all living cells
- **Describe** five key aspects of a model organism
- **Compare** light and electron microscopes

Part 1: Defining Life

How is life defined? We all understand the definition of most things, including biology. This is the first section of your chapter and this is the introduction to the first section. Feel free to experiment with how you would start this section: a good quote, an attention-grabbing anecdote, an example of some type, or so on. You can even use videos and images!

Here is a simple to apply nemonic - **MR. GREy +**, where,

M = Metabolism

R = Respond

G = Grow

R = Reproduce

E = Evolve

[The 'y' has no association and is there to complete the word Grey]

The **+ sign** indicates that there are two more important criteria,

+ = Surrounded by a **membrane** forming a **cell**, and possesses **DNA** as its molecule of inheritance.

Each of the capital letters is there to remind you of one important aspect which any living object possess. For anything to be considered living **ALL** **seven** of the criteria, without exception, MUST apply!

Metabolism indicates that chemical reactions are taking place. Both **anabolic** reactions, which take simple chemistry and build it into more complex molecules, and **catabolic** reactions, which do the opposite, occur. Indeed every living cell is simultaneously performing millions of chemical reactions every second in a particularly highly organized set of spaces. These require energy and that energy is supplied by photosynthesis (if that cell is capable) and food.

Cells must ***respond*** if they are to continue to live. This includes responding to danger and to food. Immobile cells will attempt to prevent dangerous substance from entering their cytoplasm, but encourage the enter of food molecules. Motile cells will generally tend to move away from danger and towards food. Cells also respond to many chemical signals. One question to ask of students is how do cells know which is what? Do cells have 'eyes'? This is one of the bigger questions that shall be addressed in the coming chapters, along with many others. For now, it is enough to learn that some chemical signals are detected as beneficial whilst others are not, and some do not elicit a response at all!

Cells may grow in size by increasing their volume. This they do so by incorporating more chemistry. They may also grow in terms of numbers, via some type of cell division.

No cell is known to live forever! So all present day cells, including your own, must have come into existence from previous cells. Thus reproduction is the only way life has of continuing. There are a number of standard reproductive mechanisms employed by cells to produce offspring, including mitosis and meiosis, as part of the cell cycle.

Although an individual cell in itself does not evolve, over generations, through the accumulation of mutations in its DNA, its linage does. The present diversity of life (about 10 million species and counting) represents only a fraction of all life forms that have ever existed. The vast majority have gone extinct. Regardless, according to the most highly accepted scientific theories, life began on Earth about 3.5 billion years ago (bya), and we are all its descendants.

Progress Quiz A

Question 1 Show Correct Answer Show Responses

There are two letter 'R's in MR. GREy. What do they each represent?

A	Respond and Respire

B	Respire and Reproduce
C	Reproduce and Respire
D	Respond and Reproduce
E	None of the above answers

The Cell Theory

The observation that **exiting cells all come from previously existing cells** was made over a hundred years earlier. Combine this with two additional observations: **All living things are made of cells**, and **the cell is the smallest unit of life**, result in the formulation of the three tenets of the **CELL THEORY**.

Part 2: Classification of Life

We, humans, like to conquer concepts and ideas with assignment of material to groups. Cells are no different.

The clearest method of **differentiating** cells is based on a very simple criteria: ***the presence of a nucleus*** (a double-membranous compartment) inside the cell. Imagine you have discovered a new cell in the deep ocean. How would you classify it? Observing that cell under the microscope, look for a nucleus. If that cell has a nucleus, then it is classified as an **Eukaryote**. If it does not, then it is a **Prokaryote** (see Figure 2). That's it!

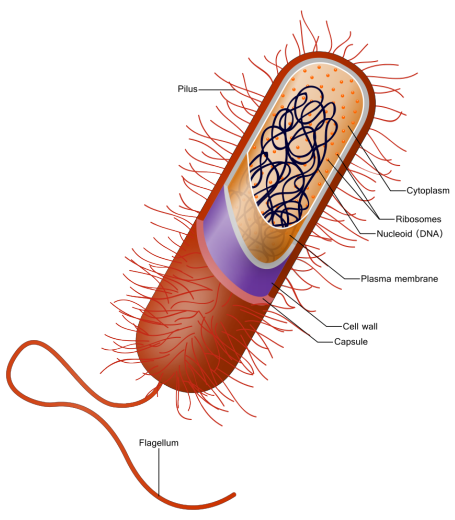


Figure 2 - Bacterial Cell - a nucleus is lacking!

Other sources mention the absence/presence of membrane-bound organelles, etc, but once the existence of the nucleus is established these other factors are moot! More recently biochemical and genetic analysis has provided additional criteria to apply to the relatedness of living things.

Three Domains of Life

At the next level of classification, known as the **domain**, each of the above cell categories is subdivided based on differences which attempt to reflect the true evolutionary lineage of living things. For prokaryotes, recent biochemical and genetic data easily suggest that they can be placed into two domains - **eubacteria** (true bacteria) and **archaea**.

Eubacteria include the typical forms of all bacteria, such as *Escherichia coli* (E. coli) which inhabit human intestines. The members of this domain possess characteristic components in their cell walls, compared to archaea. Archaea are most notable for their ability to reside in some of the most inhospitable places on Earth, such as the hot pools at Yellowstone National Park (Figure 1).

Eukaryotic cells are a domain to themselves - **eukaryota**. are divided into four kingdoms - animals, plants, fungi, and protists. Each kingdom employs a few key observations such as feeding mode, ability to move, and cell biochemistry as a means of differentiation - plants are autotrophs (self-feeding), lack the ability to move, and possess cell walls. Although the classification of animals, plants, and fungi are relatively clearcut, the kingdom protists is a catch-all. Any eukaryote not classified as one of the other three kingdoms is currently placed here.

The totality of this evidence is suggesting that life began just once and that current living organisms are its descendants, and that includes us. Additional finding support the fact that some features have really not changes much over the eons of time and these shared to a large degree, such as the way DNA is replicated. These **unite** living things. Other data show areas where there have been rapid changes, such as the development of sweat glands. These lead to the **diversity** amongst living things.

Progress Quiz B

Question 2 Show Correct Answer Show Responses

Which of the following combinations will apply to a prokaryotic cell?

A	Conforms to MR GRE only
B	Conforms to MR GRE +
C	Conforms to MR GRE only and has a nucleus
D	Conforms to MR GRE only and does not have a nucleus
E	None of the above answers

Progress Quiz C

Question of Animal Cells

VERSION A VERSION B

Use your existing knowledge to select which parameter below is NOT applicable to the kingdom animals.

A	Ability to move
B	Heterotrophic
C	Multicellular
D	Thin cell walls
E	All of the above
F	None of the above

Part 3: Cell Contents

Recall that **MR. GREy +** applies to **ALL** cells. Every cell has its DNA in the form of chromosomes. Some cells only have one chromosome, whilst others have many. The DNA of prokaryotic cells exists free in the cytoplasm - known as a **nucleiod**. The structure of this DNA is controlled to a fair degree. It can be supercoiled to save space, and then unwound when needed to activate regions. The majority of the DNA of eukaryotes, by contrast, is contained within the nuclear envelope, and not in the cytoplasm. It too is controlled (regulated) by being condensed and expanded as needed. It is complexed with extensive sets of proteins. One set is known as histones (Chapter 5) and the other are regulatory proteins, such as transcription factors. All cells have a plasma membrane (also known as the cell membrane). Bacterial cells (in the vast majority of cases) have no internal membranes. Whereas, all eukaryotic cells have many internal membranes (as we dicuss below). There are notable exceptions to this rule, namely red blood cells, which as they mature lose all their internal structures, including the nucleus and their DNA. This has evolved to make more space to carry their cargo!

Central Dogma of Biology

This is a pretty simple concept, in that it states a simple observation made of how information flows from DNA to other molecules within ALL living things. Genetic information, in the form of genes, is always first converted (transcribed) into RNA molecules. Some of these may further be converted (translated) into proteins (Figure 4). **But *never* directly from DNA to protein!**

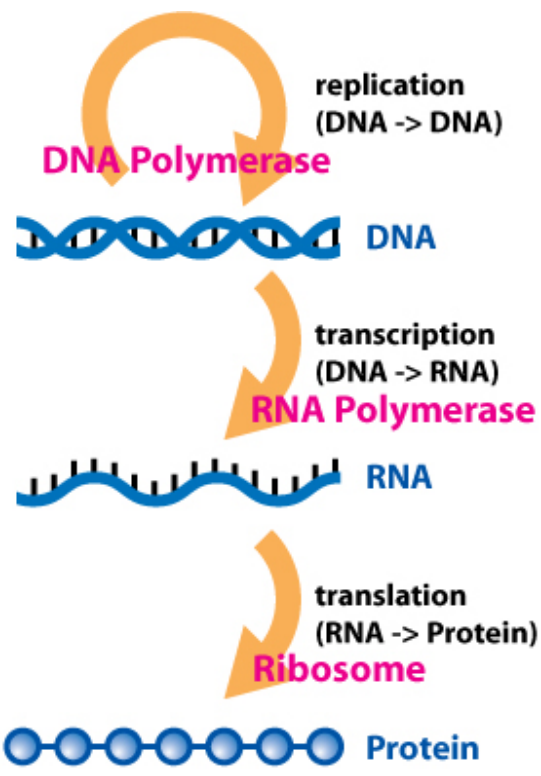


Figure 4 - Central Dogma of Biology

During DNA replication, the DNA is copied directly to make more DNA (Chapter 6). Nor can the system move backwards under natural circumstances, i.e., proteins make RNA. Some non-living things (i.e., some viruses) possess the ability to make DNA from RNA, but they are not living!!!

Learning Check List - Could you....?

1. **Compare, with examples, ways in which cells may vary in appearance and function.**
2. **Summarize how the relationship between DNA, RNA, and protein—as laid out in the central dogma—makes the self-replication of living cells possible.**
3. **Explain how the processes of mutation and selection promote the gradual evolution of individuals best suited for survival in a wide range of habitats.**
4. **Relate how differentiated cell types vary widely in form and function despite having the same genome sequence.**
5. **List the three tenets of cell theory and explain their ramification for the study of cell biology.**

Part 4: Tools for Studying Cells

Almost every cell is invisible to the human eye. Therefore, tools have been developed to elicit the finer details of cells. First came the magnifying glass, followed by various versions of the light microscope, and more recently powerful reiterations of the electron microscope.

Each of the above has contributed in various ways to our understanding of cells. Light microscopes offer a particular advantage in that for some procedures the specimen may be viewed still living. This is not possible with electron microscopy as a vacuum is necessary.

Light Microscopes - **Light microscopy** has transitioned into new arenas, with specialized tooling of microscopes for antibody detection, fluorescence emissions, phase contrast optics, etc. Specimens may be stained in a variety of ways to increase contrast and detection. Use of mineral oils improves resolution at higher magnifications so light may be refracted at a much greater angle. Structures as small as mitochondria can be seen at resolutions down to 0.25 micrometers. Light microscopes do have an upper limit on their functionality - that being the wavelength of light itself. The very best can magnify with good resolution to over 1250X.

Electron Microscopes - The perfection of the **electron microscope**, with its electron beams with wavelengths shorter than even protons has enabled greater magnification and resolution. It is possible to see actual molecules with certain instruments at this time. There are two main types of electron microscope in use

currently: the transmission electron microscope (**TEM**) and the scan electron microscope (**SEM**). With TEM the specimen is sliced into very thin sections before electron beams are passed through it. Certain heavy metal 'dyes', such as osmium, are used to bind to various regions of the specimen. Depending on the density of staining, electrons are absorbed and preventing from reaching a detector, where images are generated. Specimens prepped for SEM analysis are coated with a vaporized metal ion, usually gold. This results in the scattering of electron from the surface in various directions by reflection. The images generated are of the surface contours and produce stunning 3-D pictures, however they do not permit the interior of the specimen to be seen.

Video

Please visit the textbook on a web or mobile device to view video content.

Microscopy Show Correct Answer Show Responses

Multiple answers: Multiple answers are accepted for this question

Light microscopy may not offer the resolution of the electron microscopes, but it does provide some benefits. What are they?

A	Magnification
B	Speed
C	Examine living specimens
D	Cost
E	All of the above
F	None of the above

Learning Check List - Could you....?

1. **Contrast light microscopy, high-resolution fluorescence light microscopy, and electron microscopy in terms of how the samples are prepared or treated for each**
2. **Detail whether they can be used to view living cells**
3. **Compare their approximate limits of resolution, and which cell components can generally be distinguished using each approach.**

Part 5 - Model Organisms

The area of model organisms is beginning to blur! Why? Compared to the past when the tools available to scientists were fewer and equipment was more specific to experimentation, today it is much easier to explore the biology of almost any creature, using the wealth of technology available, and thus one is not as restricted to what is researched.

If you take yourself back to the dawn of molecular biology at the end of the 17th century with the first notion of cells, only very crude microscopes were available, and specimens which were readily available were favorites for analysis. Then in the mid-20th century an explosion of research into living cells tool place. At that time researchers decided that it would be more resourceful to concentrate their efforts of a select group of organisms so that techniques and knowledge could be shared. They chose representative species from most of the branches of life. These were named **model organisms**!

There are an estimated 10 million species of organisms alive on the Earth presently. Scientists have come to an informal agreement to select certain representative species from various groups for the purposes of research and study. This broad agreement to use the same set of organisms permits research finding to be directly correlated and conclusions to be drawn.

The mounting evidence clearly points to life originating once about 3.5 BYA on this planet. Although we are not sure whether it came on a meteor from space, evolved in deep oceanic depths, or in primordial pools, the fact is that life has flourished to fill many habitats. Strong evidence also tells us of at least five mass extinctions which killed off over half the species each time. Regardless, many of the fundamental biological processes are shared by organisms, as well as many that have diverged. In our quest to learn, scientists have chosen certain non-human organisms to study in a laboratory setting, so as to gain a better understanding of biological processes. Some of the criteria employed to study model organisms are common considerations, such as ease of manipulation, reproductive rate, generation times, cost to breed and/or maintain, and size. For instance, elephants may be prohibitive to use as model organisms due mainly to their size and costs. The number of model organisms utilized continues to grow, but a number of them still represent the main focus of research attention, as outlined below.

The main representative of the prokaryotes is *Escherichia coli* (*E. coli*). Much of our discoveries of cell replication mechanisms, including the processes of DNA replication, as well as how cells make proteins from instructions contained in genes, have all come from this tiny rod shaped cell, usually a beneficial inhabitant of our digestive system.

The fungi are represented by the unicellular baker's yeast, *Saccharomyces cerevisiae*. It represents the simplest eukaryotes, and its study lead to the determination of the Central Dogma of Biology, in that genes code for proteins. Further, an understanding of the organization of our chromosomes, as well as their regulation during the cell cycle has emerged from studies on *S. cerevisiae*. A fair number of genes (about 20%) are shared with humans, mainly connected to the cell cycle and metabolism. Important findings about cell cycle disruption have revealed some secrets of cancer cells.

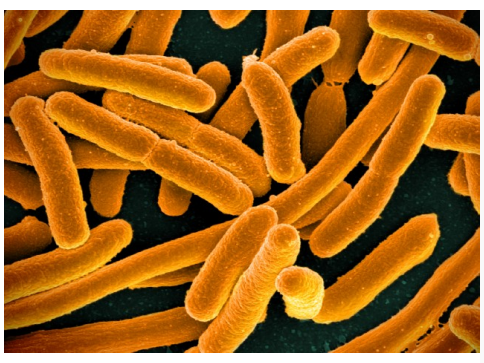


Figure 3. E. coli cells

Plants are commonly represented by a small weed, *Arabidopsis thaliana*. It was the very first plant to have its entire genome sequenced. It has been useful in eliciting the biology of many plant traits, such as hormones plants use to detect light, danger, water, as well as flower development. It has proven its worth in plant evolution, population genetics, and general molecular biology of plants.

The invertebrate animal world is represented by both the fruit fly *(Drosophila melanogaster)* and a nematode worm (*Caenorhabditis eleganes). Drosophila* has been used as a model organism since the earliest days of research. It has about 77% of the same genes as humans, and its genetics has much overlap too. There are important differences too, such as the formation of polytene chromosomes in salivary gland cells. *C. elegans* has proven to be a developmental goldmine! Normal adult worms have exactly 959 cells. The fate of each cell is known. Being transparent has aided us in visualizing developmental pathways and mutations therein. The impressive reproductive rate, cost effectiveness, combined with the ability to freeze cultures has been a boon to research.

Fish and mice are also valuable model organisms. The zebrafish, *Danio rerio*, has provided very valuable data on human genetics and disease. This 1" long, highly reproductive, fast growing fish offers us an ample supply of embryos for research. Many current human diseases have been modeled in this fish, such as muscular dystrophy. The mouse, *Mus musculus*, has been the mammalian model for genetic research. This animal permits testing of new therapies before clinical trials on humans. Immune therapies have been trialled in immunodeficient mice, with encouraging results.

The video below attempts to explain some of the characteristics used to select model organisms.

Video

Please visit the textbook on a web or mobile device to view video content.

Model Organisms Show Correct Answer Show Responses

Multiple answers: Multiple answers are accepted for this question

Which of the following parameters is an important consideration when selecting model organisms?

A	Generation time
B	Space to grow
C	Cost
D	Likability
E	All of the above
F	None of the above

As we have learned earlier in this chapter, there are certain features shared by living organisms, while others have changed - **the unity and diversity of life!** This observation allows us to apply knowledge across organisms if appropriate. This is where model organisms aid us in our research.

The criteria for the selection of model organisms was not set in stone, but consideration was given to time, space, and money. Some of the main criteria would include:

- **Time to reproduce** - How long between generations - the gestation period of a mouse is far shorter than that of an elephant.
- **Space** - lager organisms require more space than smaller ones - think rats verses mice.
- **Cost to maintain** - bacteria can be grown on cheap culture plates with minimal cost of food - compare this that of maintaining a colony of rats.
- **Shared knowledge** - for some organisms a wealth of knowledge has already been accumulated and that can be used to extend our understanding.
- **Biology** - obviously if one is researching the biology of flowering plants it would be impracticable to use a non-flowering fern. Also, cell cycle understanding has benefited from studies on yeast (fungus) since it shares a lot of biology with most eukaryotes, including humans.

- **Transparency** - sone see through spices exist - i.e. the nematode worm, *C. elegans*, is both transparent and has an exact number of cells (959) in a normal adult. It is great to study if one is looking to see where the individual cells develop.
- **Exceptions** - sometimes you have to study a particular organism as a substitute will not do. For instance research on how females think should be untimely performed on female human subjects.

There are many others, some particular to certain restraints and parameters, but the above list gives a good idea of why model organisms exist, and the list below presents the most common ones.

- Bacteria = *Escherichia coli* - common human gut microbe
- Yeast = *Saccharomyces cerevisiae* - brewers yeast used in bread making and brewing.
- Plant = *Arabidopsis thaliana* - a common flowing weed.
- Invertebrate animal = *Drosophila melanogaster* - the common fruit fly
- Invertebrate worm = *Caenorhabditis elegans* - a small nematode worm found in soil
- Vertebrate animal = *Danio rerio* - the zebrafish, an inch long fish.
- Vertebrate animal = *Mus musculus* - the common house mouse
- Vertebrate animal = *Homo sapiens* - human

Learning Check List - Could you....?

Define life as a checklist.

How does the cell theory compare to a three legged stool.

Diagram the division of life, with respect to classes, domains, and kingdoms.

List the structural differences between prokaryotes and eukaryotes.

Explain, using current day evidence, the theory of endosymbiosis.

List the features possessed by model organisms which determine their fit for use as such.

Compare and contract cell organelles.

Label a typical animal and plant cell.

Compare and contrast light microscopes to electron microscopes.

Describe the term resolution.

*In **summary**, life is difficult to classify. Living things have been around since the early history of planet Earth. Since that time life has flourished into a myriad of different forms, which still share some features, as well as having evolved many differences. Most cells are at an order of a few micrometers (10^{-6} m) across, requiring the use of magnification tools to visualize. Some organisms are commonly used by scientists to study living processes, these are known as model organisms.*

Image Credits

Figure 1. Image courtesy of beachmobjellies under CC BY-SA 2.0 via Flickr

Figure 2. Image courtesy of Ali Zifan under CC BY-SA 4.0 via Wikimedia Commons

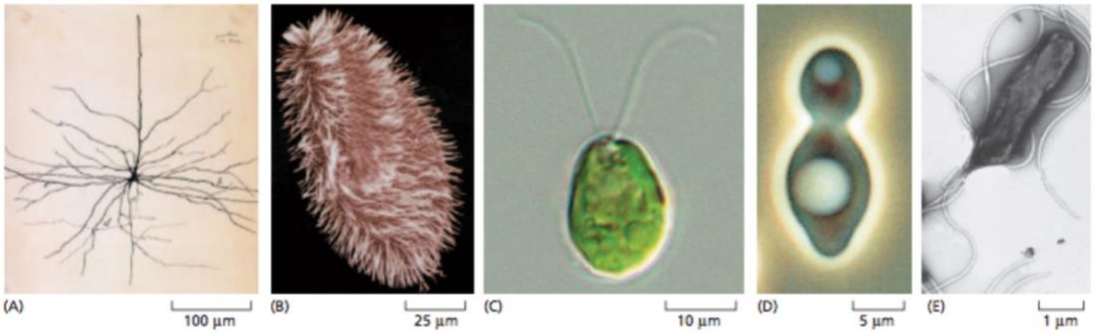
Figure 3. Image courtesy of NIAID under CC BY 2.0 via Flickr

Figure 4. Image courtesy of Dhorspool under CC BY 3.0 via Wikimedia Commons

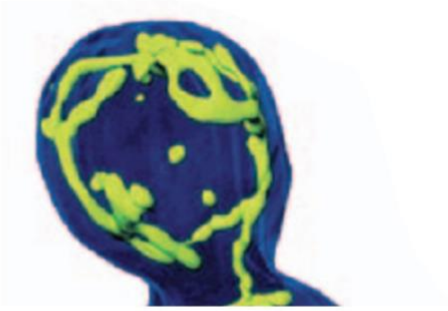
Supplemental File S6

Example Reading Preparedness Quiz (RPQ). These eight questions were offered to students to check their understanding once they had engaged with the pre-lecture resources, for Lecture 2.

HOW WELL DID YOU PAY ATTENTION TO THE FIGURES?
From Figure 1-1, which of the objects shown are Eukaryotic?
(A is mammalian nerve, B is Paramecium, C is Chlamydomonas, D is Saccharomyces cerevisiae, E is Helicobacter pylori.



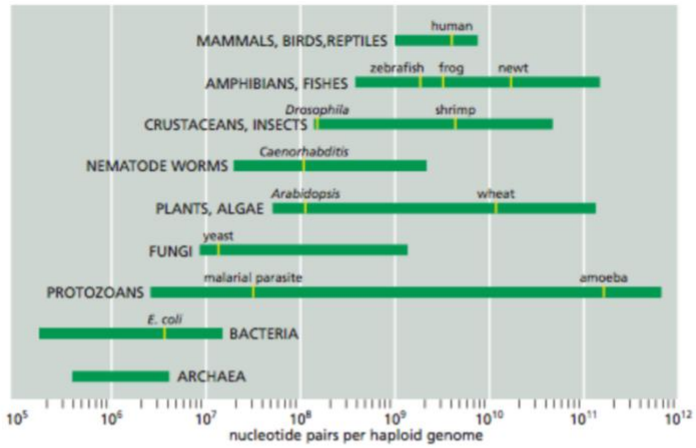
A	A only		0
B	A and B Only		0
C	A B and C		0
D	A B C and D		0
E	All of the above are Eukaryotes		0



DEEP READING: ATTENTION TO ALL INFORMATION IN REQUIRED READING.
The following image uses a green fluorescent protein to highlight what organelle(s)?

A	Nucleus		0
B	Cell membrane		0
C	Mitochondria		0
D	Endoplasmic reticulum		0
E	Golgi		0

DRAWING INFERENCES:
The take home message from the image shown (Figure 1-40) is: [Correlation if the data - Look at where things are positioned.]



A	Genome size is directly related to organism size		0
B	The genome of a bacteria is always smaller than any other type of organism		0
C	Animals have the most complex genomes		0
D	The size of an organism does not correlate directly to the size of its genome		0
E	None of the above		0

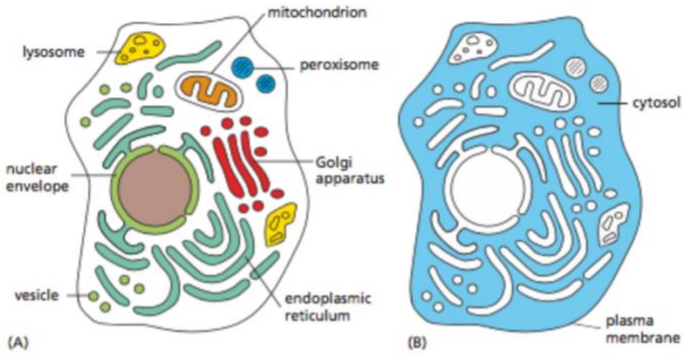
REVISION MATERIAL. THINKING BEYOND.
Which structures contain DNA in eukaryotic cells?

A	nucleus		0
B	mitochondria		0
C	chloroplasts		0
D	nucleus and mitochondria		0
E	nucleus, mitochondria, and chloroplasts		0

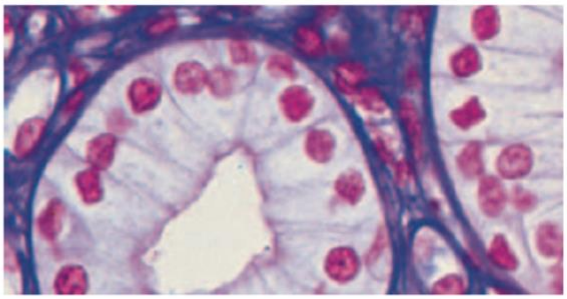
COMPREHENSION.
Which of the following is not an organelle with a membrane?

A	endoplasmic reticulum		0
B	peroxisome		0
C	chloroplast		0
D	Golgi apparatus		0
E	None of the above		0

OBSERVATION AND APPLICATION.
The cell pictured below (from Figure 1-23) may be a ----------, but certainly is not a ----.----------



A	Plant cell, animal cell		0
B	Bacterial cell, plant cell		0
C	Archaeal cell, bacterial cell		0
D	Bacterial cell, Archaeal cell		0
E	Animal cell, bacterial cell		0



DEEP READING: ATTENTION TO DETAIL.
What type of cells are represented in the following image? [Don't panic! Look at the arrangement of cells and remove those tissues that would not have this.]

A	Liver cells		0
B	Brain cellls		0
C	Kidney cells		0
D	Bacterial cells		0
E	Blood cells		0

KEY CONCEPTS.
The Central Dogma refers to

A	The flow of information from RNA to DNA to protein		0
B	The flow of information from protein to DNA to RNA		0
C	The flow of information from DNA to protein to RNA		0
D	All of the above are possible		0
E	None of the above		0