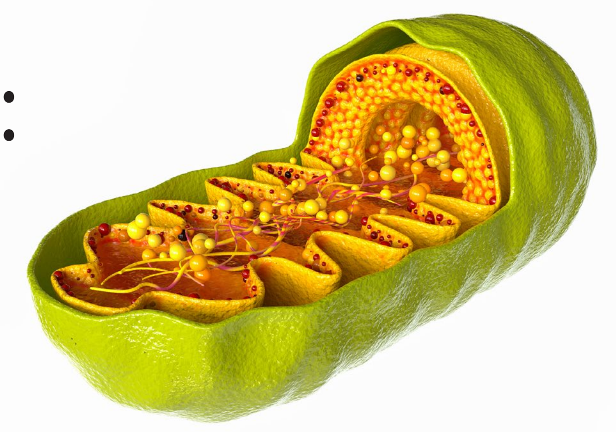
NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Mitochondrial Mysteries:

Cellular Respiration



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Before beginning this case study, list any information you know about the mitochondria.

Part I – Exam Preparation

Ivy was having a hard time keeping her eyes open, and not just because it was a rainy Sunday afternoon. The previous week, she had been diagnosed with Kearns-Sayre syndrome, a rare mitochondrial disease. Her doctor had explained that a deletion in her mitochondrial DNA meant her mitochondria lacked some important proteins, but she still didn't quite understand why that meant her cells had less energy available. She was very interested to learn more about exactly how mitochondria powered her cells, but it was hard to focus with her symptoms acting up. Luckily, she'd asked her classmate, Ali, to study together for their upcoming exam.

"Photosynthesis and cellular respiration are inverse processes," Ali pondered while looking at the equations on the whiteboard in their study room. "In photosynthesis, light energy and carbon dioxide produce glucose and oxygen. Then in cellular respiration, glucose is broken down to make carbon dioxide and energy in the form of ATP, and the process requires oxygen."

Photosynthesis

$$6CO_2 + 6H_2O + \text{Light} \longrightarrow C_6H_{12}O_6 + 6O_2$$

Carbon dioxide, Water, energy → glucose, oxygen

Cellular respiration

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O + ATP$$

Glucose, oxygen → Carbon dioxide, water, energy

Figure 1. Equations for photosynthesis and cellular respiration.

"I think Dr. Smith is going to ask us much more about cellular respiration than this equation describes," said Ivy. "There are a lot of processes that work together to make enough ATP for our bodies to function. I know you were in class and I saw you taking notes. What do you remember from that day?"

She notices when I'm in class… This thought made Ali grin. He'd better step it up so she'd keep meeting with him. "Hold on, let me take out my notebook and see what I've got for this lecture."

Cellular respiration November 11

4 processes

NADH and $FADH_2$ electron carriers

1. Glycolysis: glucose -> 2 pyruvate, 2 ATP, and 2 NADH. Occurs in cytoplasm. No O_2.
2. Pyruvate processing: 2 pyruvates -> CO_2, 2 acetyl CoA, and 2 NADH
3. Citric acid cycle: 2 acetyl CoA -> CO_2, 2 ATP, 6 NADH, and 2 $FADH_2$. Is a cycle.

ETC make proton gradient; OP makes ATP

4. Electron transport chain (ETC) and Oxidative Phosphorylation (OP)
   - NADH and $FADH_2$ are oxidized and their electrons go through the electron transport chain
   - Oxygen is required for this process
   - Energy released from redox rxn actively transports proteins across inner membrane – creates proton gradient H^+ H^+ H^+ H^+ H^+ H^+ H^+ H^+ H^+ H^+ H^+ H^+
   - Proton gradient established
   - ATP synthase (an enzyme, aka protein complex), makes ~25 ATP using proton gradient to drive the energy requiring process

- ❑ BEFORE STUDYING WITH IVY:
  - ❑ Draw out where processes occur in the eukaryotic cell (think mitochondria)
  - ❑ Think build-up of electron carriers, then energy production ramps up.
  - ❑ Know when oxygen is important

Questions

1. Using Ali's class notes (see previous page), complete Table 1.

   Table 1. Number of each molecule type produced per 1 glucose molecule.

NADH	*$FADH_2$*	*ATP*

2. Draw a flow chart for the order of processes involved in getting energy from glucose. Indicate the inputs and outputs of each process.
   a. Put a circle around the processes that reduce electron carriers
   b. Put a square around the process that oxidizes the electron carriers.
   c. Place a star next to the processes that produces the most energy for the cell.

Part II – Where the Magic Happens

After finding the page in his notebook for this day, Ali regretted not looking at it sooner. "Ivy, I wrote down that we need to know where each of the four processes in the cell occur, but I didn't remember this until now."

"Can I see your notes?" Ivy asked. "I seem to have written down that oxidative phosphorylation is the payoff phase, but I don't know what's happening in that step. Can you figure that out, and I'll work on locations? I seem to have missed the point about knowing where each step happens, because I don't see it anywhere in my notes. I've been really interested in the mitochondria lately, so I do know something about their structure. Mitochondria have a typical **outer membrane** and then their **inner membrane** is large and folds in on itself a lot. These folds fill in the inside of the organelle with sac-like structures called **cristae**. The space between the inner and outer membranes is known as the **intermembrane space**. The area encapsulated by the inner membrane, where the cytoplasm is found inside a bacterium, is known as the **mitochondrial matrix**.

Questions

3. Using the information from the questions you answered in the previous section (Part I), explain why Ivy is calling oxidative phosphorylation the "payoff phase."

4. Critically read Ivy's description of mitochondrial structure and draw and label a mitochondrion in the space below. Include all of the bolded words from Ivy's description.

Part III – Putting It All Together

After 15 minutes of reading through the textbook, Ali and Ivy came back together to debrief.

"Here's what I read about the payoff phase," Ali began. "It appears to me that while some ATP is made during glycolysis and the citric acid cycle, the majority of the ATP energy is produced during oxidative phosphorylation. So, oxidative phosphorylation is the payoff phase because that's when most of the energy is actually being produced. The previous steps are really just setting up the cell and making the right molecules for this to happen. All of the electron carriers that are reduced during the first three processes are oxidized in the electron transport chain, which creates a **proton gradient**. This proton gradient then provides the large amount of energy needed to drive the production of ATP by ATP synthase. I guess it takes some effort to make energy. But what the heck is this proton gradient and where does it happen? What did you find out about the mitochondria?"

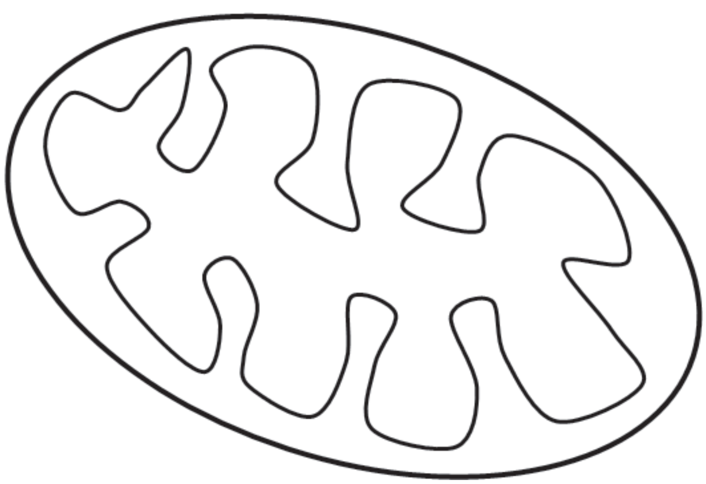
"Dividing to conquer these questions is making our study session quite efficient. We may be done in time for dinner," said Ivy with a smile. "Let me start from the beginning. I'm thinking about this as if our mitochondria are factories, producing ATP according to a defined plan. First, glucose enters the cell and glycolysis occurs in the cytoplasm. Then pyruvate, the product of glycolysis, is transported into the mitochondria through those porin proteins in their membranes. Pyruvate processing and the citric acid cycle occur in the mitochondrial matrix. Here's the tricky part: the electron transport chain involves a set of protein complexes that are located in the cristae of the mitochondrial inner membrane. Those protein complexes accept the electrons donated by NADH and $FADH_2$. This movement of electrons pumps protons (hydrogen ions, H^+) into the intermembrane space to create the proton gradient."

Ali jumped in, "So these protons are being actively put into the intermembrane space by the electron transport chain, meaning there are more protons in the intermembrane space than in the mitochondrial matrix. This seems like pushing water uphill – it's bound to want to come down."

"That's exactly how I thought of it! Now, oxidative phosphorylation is like the doors on a dam being opened so the turbines can create electricity from the flow of water back down the hill. There is another protein complex embedded in the inner membrane known as ATP synthase. This protein functions as the turbine. It has an area where protons can flow from the intermembrane space back into the mitochondrial matrix, and that flow of protons creates enough energy to catalyze ATP synthesis."

Questions

5. Using the drawing of a mitochondrion below, indicate where each of the four processes of cellular respiration occurs. Remember that the mitochondrion is surrounded by the cytoplasm of the cell! Your labels should include the parts of the cell and organelle, the names of the processes, and the molecules that are being shuttled.



6. What is a "proton gradient"? Explain why this is important for the production of ATP.

7. In your opinion, what are the three most important molecules needed for the production of ATP? Explain your reasoning.

8. Additional thought question: use the information in this part and previous information learned in the class to explain why aerobic organisms typically have a faster growth rate than anaerobic organisms.

Part IV – The Dinner

After studying, Ali and Ivy went out to a local sushi joint to relax and get away from campus for a bit. "I'm really glad you agreed to go to dinner with me! It's nice to spend time with someone who is as much of a science nerd as myself." Ali couldn't hold back his excitement, which was making him a little more awkward than he wished. He was always so cool and collected while studying.

"Can I ask you something?" said Ivy suddenly. "Have you noticed anything weird about my eyes?"

"Only that they are the color of Nutella," Ali replied.

"Well, I've started having trouble moving them around and it's becoming progressively harder to keep them open, even though I try to get enough rest. That day you found me in the coffee shop, I had just learned that I have a disease called Kearns-Sayre syndrome. It's caused by a deletion in my mitochondrial DNA. That's why I've been so obsessed with learning about this organelle."

This was a complete shock to Ali. He had thought she looked a little quirky, but had assumed that was just the way she was. "Oh my gosh, Ivy. I'm really sorry to hear that." He paused, wondering if it would be rude to ask more, but his curiosity got the better of him. "What is Kearns-Sayre syndrome? I've never heard of it before."

Fortunately, Ivy didn't seem to mind the question. "Well, do you remember when I said I'm thinking of mitochondria like ATP factories? I think of DNA as the instructions for how to make all of the machinery that the factory needs. While most of those instructions are encoded in the nucleus, a few are still encoded by mitochondrial DNA. Because of the deletion, my mitochondria don't have the blueprints for all of the proteins they need to efficiently make ATP."

"And the end result of too little ATP in your cells is trouble moving your eyes?"

"That's one of the main symptoms, yes. My doctor told me that eye muscles need a lot of energy from mitochondria, which is why they're most affected. But Kearns-Sayre syndrome is a rare disease. Scientists still don't completely understand how the deletion is linked to the specific effects." Ivy's frown grew deeper. "There's also no cure. I can manage the symptoms, but I'll always have trouble with my eyes."

Her voice had gone quiet, and Ali could tell she was feeling self-conscious. "Clearly it doesn't stop you from being a brilliant student," he said, grinning. "And hey, maybe we can both go into medicine and develop a cure someday, now that we're on our way to being experts on the mitochondria!"

Ivy laughed, feeling relieved. She had been worried he would just get up and leave. "Let's not get ahead of ourselves! I just wanted to get that off my chest. Why don't we eat our sushi and focus on the bio exam tomorrow? The rest can wait for another day."

Questions

9. Take five minutes and write down everything you now know about the mitochondria.

10. Compare the answer you gave for the first question in this case study (i.e., list any information you know about the mitochondria) and your response to Question 9 above. Describe three of the most interesting or exciting things you learned from this story.

Wrap Up

Watch the following videos to help you review what you have learned:

- *Cellular Respiration.* Running time: 2:47 min. Produced by RicochetScience, 2016. <https://youtu.be/eBl3U-T5Nvk>
- *Cellular Respiration and the Mighty Mitochondria.* Running time: 7:48 min. Produced by Amoeba Sisters, 2014. <https://youtu.be/4Eo7JtRA7lg>