

Appendix A

Full Interview Protocol

Background

1. Tell me about your college experiences thus far. How is it going?
 - a. Major, future plans
 - b. Science courses in HS

Reflection on individual courses

To start out, we are going to talk about your chemistry and biology courses individually.

Thinking first about your general chemistry course, you were in CLUE last semester and this semester, correct? Let's talk about the course as a whole.

1. Tell me about your experience taking chemistry.
 - a. Enjoy it? Find it worthwhile? How does it compare to HS?
2. Why don't you take a few minutes and brainstorm a list of some of the things you learned in chemistry?
 - a. Could you briefly tell me about the things on your list?
 - i. Follow up on the very general or confusing
 - ii. Check that the list covers both semesters of general chemistry
 - b. Thinking about the course as a whole, what do you think some of the big ideas or take-home messages were?
 - c. Why would you call these big ideas?

Now let's talk about your cell and molecular biology class.

3. Tell me about your experience taking biology this semester?
 - a. Enjoy it? Find it worthwhile? How does it compare to HS?
4. Could you brainstorm a list of some of things you learned in this biology course?
 - a. Could you briefly tell me about the things on your list?
 - i. Follow up on the very general or confusing
 - b. Thinking about the course as a whole, what do you think some of the big ideas or take-home messages were?
 - c. Why would you call these big ideas?

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Connections and misconceptions between courses

Now let's talk about your experience taking both biology and chemistry.

5. What has that been like for you?
 - a. Did you find taking them at the same time beneficial in any way?
6. Can you describe the ways in which you see your chemistry and biology courses as being connected?
7. Were there any ideas or topics that you covered in your chemistry class that you found useful in thinking about biology?
 - a. How did you find that helpful?
 - b. When you are sitting in your biology course, how often would you say you think back to your chemistry?
8. How about ideas or topics that you covered in your biology class that you found useful in thinking about chemistry?
 - a. How did you find that helpful?
 - b. How often do you feel like you're in your chemistry course and you think back to your biology?
9. Many colleges require that students take some chemistry as a prerequisite for biology.
 - a. Why do you think this is the case?
 - b. In your opinion, should chemistry be a pre-req for biology?
 - i. Why do you say that?
 - c. Are there any chemistry ideas that you think are necessary to understand biology?
 - d. Why do you think those ideas are necessary?
10. Thinking again about your experience in chemistry and biology, have there been times where you felt confused about how a concept was discussed in one course compared to the other?
11. Are there places where you think that information from one course has conflicted or contradicted with something you learned in the other course?

Follow-ups for questions 10 and 11

- a. How did you come to notice that?
- b. How did that affect your experience?
- c. Do you feel that it was detrimental in anyway?
- d. How have you dealt with that?

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Crosscutting concepts - general

Sometimes we think about concepts or themes that span both chemistry and biology; ideas that connect them.

12. Do you have any ideas about what some of those themes might be?
 - a. Why would you consider that to be a theme?
 - b. Do you think that understanding that idea has helped you understand [chemistry/biology]?

Crosscutting concepts - energy

13. Many consider energy to be a theme that spans chemistry and biology.
 - a. Why do you think that is?
 - b. Tell me about some ways you talk about energy in chemistry?
 - c. How about way you talk about energy in biology?

Two concepts were discussed in more detail, energy transfer and the conservation of energy. Energy transfer was introduced first, unless discussion of conservation of energy was initiated by the student. The following questions were asked about both concepts.

- d. Let's discuss the concept of [energy transfer/conservation of energy].
 - i. What does that make you think of?
 - ii. How did that relate to the topics you discussed in [chemistry/biology]?
 - iii. Do you think that this concept was emphasized in either of your courses?
 1. (If only one course is mentioned) What about the other one?
 2. (if no for either course) Do you think that it should have been?
 - iv. Do you think that this concept is important for understanding other ideas in [chemistry/biology]?
- e. If students discussed energy transfer and conservation of energy together at any point:
 - i. How would you describe these two ideas as being related?

Thinking more generally about energy as a theme that spans chemistry and biology

- f. Do you think that understanding energy was more important for one course over the other or equally important for both?
- g. Do you think that most of what you learned about energy came from one course or did they work together to improve your understanding?

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- h. Were you able to use what you learned about energy in one course to help understand the other?

Crosscutting concepts – the relationship between structure, properties, and function

14. Another theme consists of three ideas: structure, properties, and function.

(write the terms out on the Livescribe paper)

- a. What do you think of when I say structure?
 - i. Properties?
 - ii. Function?
- b. Can you describe how you see these ideas as being related?
- c. How do you think about these concepts with respect to [chemistry/biology]?
 - i. Do you use all three ideas in [chemistry/biology]?
 - ii. For [chemistry/biology], would you order these ideas into a progression of any sort?
- d. Why would do you think the relationship between these ideas would be considered a theme that spans chemistry and biology?
- e. Do you think that these ideas and their relationship were emphasized in either of your courses?
 - i. (if no) Do you think that it should have been?
 - ii. What about the other course?
(student directed which course was discussed first)
 - iii. Do you feel they were emphasized to an equal extent?
- f. Do you think that your understanding of the relationship between these ideas came more from one course over the other or did they work together to improve your understanding?
- g. Do you think that understanding of the relationship between these ideas was more important for one course over the other or equally important for both?
- h. Can you think of any times when you used a progression of these ideas in your chemistry/biology course?
- i. Were you able to use what you learned about this progression in one course to help understand the other?
 - i. What about the other direction?

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- j. Has anyone ever talked to you about this these ideas and their relationship before?
- k. Have you ever thought about it explicitly before?

Appendix B

A Third Approach: The Common Discussion of Potential and Kinetic Energy Transfer

The transfer of kinetic energy via collisions is an essential component to the initiation of energy transfer, providing the activation energy for reactions, and for controlling the formation of molecular complexes (e.g. the dissociation of an enzyme-product complex or the DNA-protein interactions involved in gene expression). However, it is insufficient to explain how energy is transferred from one reaction to another, either in chemical or biological systems. Disciplinary experts acknowledge the fundamental importance of reaction coupling, but it is uncommon for introductory science courses to provide an explanation of the underlying mechanism. This may be due to the difficulty in constructing an explanation that is both appropriate and satisfactory for students, and that is feasible for instructors to tackle given the constraints of their courses. The disconnect [between chemistry and biology](#) on the subjects of molecular collisions and reaction coupling undermines students' abilities to use these concepts to construct complementary explanations of biological systems.

Consider first the explanatory value of collisions to biological systems. Most instances of energy transfer originate with a collision. It is only through the direct interaction of molecules (perpetually in motion) that changes between or within systems can occur. Therefore, it is difficult to think critically about what is happening at the molecular level without understanding the stochastic nature of collisions. The cellular environment is incredibly crowded resulting in the frequent collisions of molecules; some of these collisions will lead to reactions, while others will not. It is difficult to reconcile this basic fact with how Clarice and Aaron described the metabolic cycles. To believe that energy flows "down the chain of events" implies a superficial understanding of systems that could provide little support for considering how changes in the concentrations of the various reactants involved may alter such processes. It certainly makes it difficult to understand how reaction systems can run in reverse (e.g. in the case of gradient driven ATP synthesis and ATP hydrolysis driven gradient formation), particularly in an age where new techniques are revealing the stochastic behaviors of single cell systems that are relevant to a range of biological processes (Symmons & Raj, 2016). For example, phenotype variation between genetically identical organisms arises through stochastic variation and impacts resistance to drugs and survival (ibid). By incorporating collisions into the descriptions of chemical and biological systems in our courses, we can provide a more realistic picture of what

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is occurring at the molecular level.

While reaction coupling is more commonly referenced than collisions in introductory biology courses, it is difficult to provide a coherent explanation of the process that is accessible to both students and instructors. While there are approaches being developed that do emphasize reaction coupling, there are currently no assessment data to show how students respond to this approach (Klymkowsky, 2010; Klymkowsky, Rentsch, Begovic, & Cooper, 2016). Typically, little more than a definition is provided in biology courses. And in chemistry courses, reaction coupling is usually discussed (if at all) in the context of Hess's Law - typically shown as a simple algebraic addition of two (often seemingly unrelated) reactions rather than a mechanistic explanation. Though some may argue that this is sufficient for chemistry, our work shows that this has left some students feeling dissatisfied with their understanding. If we want students to understand how reactions can be coupled to drive thermodynamically unfavorable processes, we need to negotiate what an appropriate explanation in both disciplines would look like, what it contains and explicitly acknowledges.

Ideally, we might want students to explain that energy transfer mediated by ATP actually involves the transfer of a phosphate group from ATP to the reactant. This results in a 'common intermediate' which is more reactive than the unphosphorylated reactant. Therefore, less energy must be supplied by collisions for the next step, in which *the intermediate* undergoes the following reaction. These ideas quickly become complicated when put in the context of a complex series of reactions such as those in glycolysis. And so, if we want students to develop a foundational understanding of the molecular level mechanism upon which to build, it is necessary to begin with a simple example (Appendix C). It is not our intention to suggest that biology majors should be required to develop expertise in the field of chemistry or even that all biology majors require the same understanding of chemistry. However, given the numerous education reform efforts that highlight the importance of energy in both chemistry and biology (American Association for the Advancement of Science, 2011; College Board, 2014, 2015; National Research Council, 2012; Tansey et al., 2013), we would argue that this is a topic that should be given particular attention.

Whatever the approach used to improve the ways that students can connect energy ideas across disciplines, the question is, how much of this can we expect students in introductory courses to understand and whose responsibility is it to address this material? Can we expect

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biology faculty who teach an already crowded curriculum (at least as delineated in common textbooks) to make room for a complex molecular explanation of reaction coupling? Conversely, do chemistry faculty make room in their courses for an explanation of reaction coupling that goes beyond a simple use of Hess's Law? To provide a foundation on which to build their understanding, we would propose using a collisions-based Le Chatelier explanation of reaction coupling from an equilibrium perspective (Appendix C). Our work shows that it is currently difficult for students to reconcile what they are presented with in introductory chemistry and biology course in a way that leads them to a coherent (trans-disciplinary) understanding of why and how reactions are coupled. Simply implying that ATP 'is' energy leads to the erroneous idea that energy is released when the 'high energy' bonds of ATP are broken.

Appendix C

An Explanation of Reaction Coupling

The question of how energy is transferred through biological systems is fraught with problems. In biology courses, ATP is often referred to (at least implicitly) as some kind of energy currency – which is not incorrect – the more ATP units produced, the more energy is eventually available to drive unfavorable processes. However, as discussed in the main body of the paper, this idea can lead students to believe that ATP is energy, or that it contains energy in its bonds that is released when the bonds are broken. The question then, is how can we help students understand energy transfer in biological systems without need for a Ph.D. in physics or chemistry?

If we want to help students understand the mechanism by which ATP can drive unfavorable reactions, we have to get across to students how these reactions are coupled by common intermediates. Often this fact is obscured by the presentation of energy transfer in both chemistry and biology. For example, in chemistry rather than emphasizing coupled reactions, most students are drilled in the use of Hess's law, where they are taught to add, multiply or subtract chemical equations as if they were algebraic equations to determine the overall energy change for a multistep reaction¹. In biology, coupling is usually presented as the reaction of interest driven in some mysterious way by ATP hydrolysis, which is often represented as a separate reaction, rather than providing the common intermediate by which the reactions are linked.

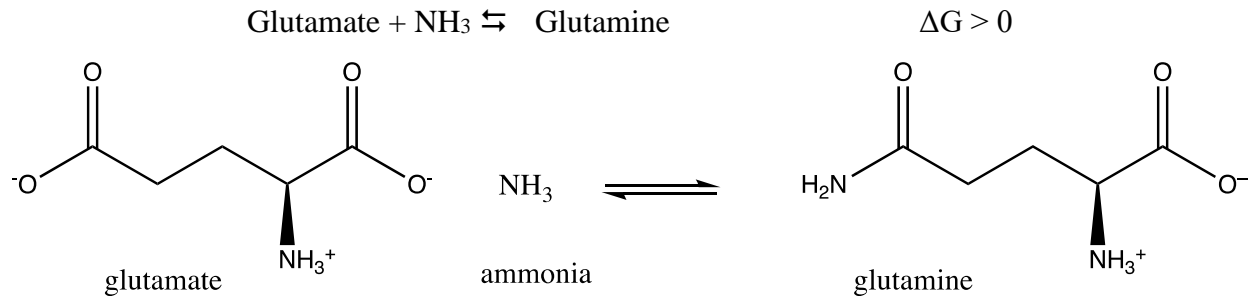
In fact, ATP is NOT hydrolysed during any coupled reaction (hydrolysis literally means reaction with water). ATP reacts with one component of the reaction to form an intermediate, which then reacts with the other component to form the product. The important point is that there is a common intermediate (the phosphorylated reactant). While it is true that the overall effect is that ATP is hydrolysed ($\text{ATP} + \text{H}_2\text{O} \rightarrow \text{ADP} + \text{Pi}$), this is not the mechanism by which ATP coupled reactions occur.

Since this idea is so difficult and so fraught with problematic understandings, we recommend that a relatively simple model system be used. A possible example (simplified here for clarity) is the reaction of glutamate acid to form glutamine (a model for any peptide bond formation) which is a thermodynamically unfavorable reaction $\Delta G > 0$. The equilibrium position

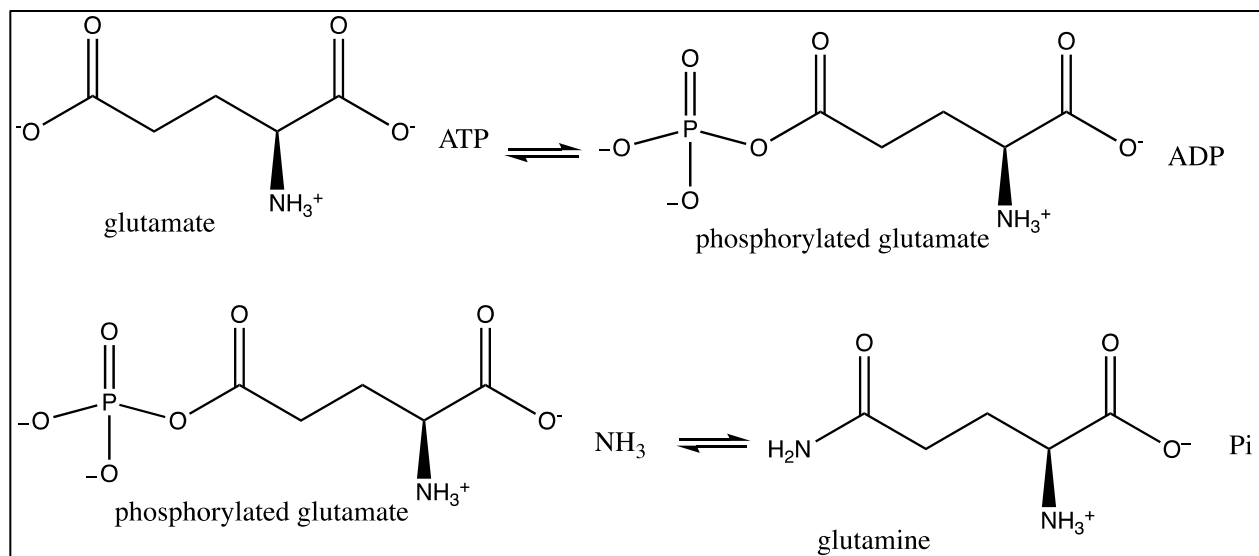
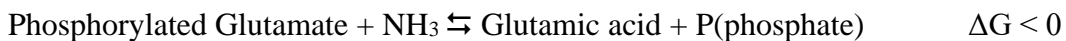
¹ A particularly pernicious example: https://en.wikipedia.org/wiki/Hess%27s_law

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for this reaction normally lies to the left. The question then is how and why does this reaction occur in biological systems?



The answer to this can be understood in several ways: the first is the application of Le Chatelier's principle. Rather than directly reacting glutamate and ammonia, glutamate instead reacts with ATP. This reaction is exergonic (ATP is very reactive – it has high potential energy) and produces the phosphorylated glutamate – which is also very reactive. To describe this, we say that the glutamate is 'activated' through an ATP-based phosphorylation reaction to give phosphorylated glutamate. Now the reaction between glutamate phosphate and ammonia (producing glutamic acid) is thermodynamically favorable.

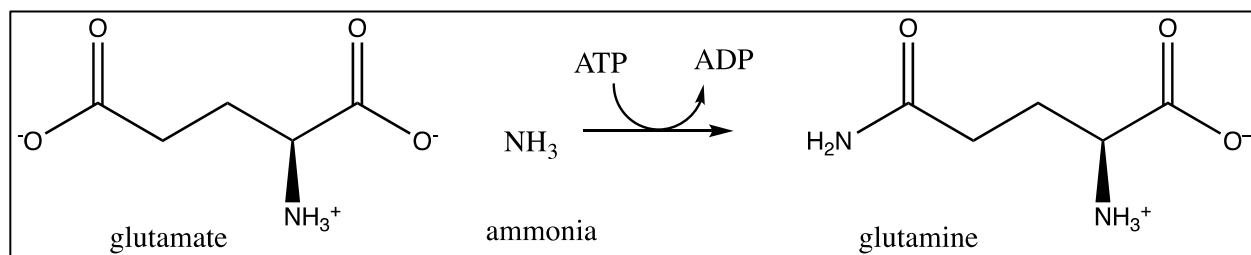


These two reactions are linked by a common intermediate, the phosphorylated glutamate, which

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as soon as it is formed is used up in the next reaction which disturbs the equilibrium from the first reaction and causes more phosphorylated glutamate to be formed. Recall, Le Chatelier's principle states that when a stress is applied to any reaction at equilibrium, the position of equilibrium shifts to counteract the stress.

During the reaction ATP does end up as ADP (+ phosphate), but it is an integral part of the reaction mechanism. As noted, in biology texts the reaction might be shown like this:



While this is a perfectly reasonable shortcut, once students understand the coupling mechanism, it does give the impression that it is the separate hydrolysis (bond breaking) of the ATP that is driving the reaction.

Energy transfer mediated by ATP typically involves the transfer of a phosphate group from ATP to the reactant. This results in a 'common intermediate' which is more reactive than the unphosphorylated reactant, and which reacts to produce the final product. Note, at no time is ATP hydrolyzed by water. This example provides a simple model for presenting the role of ATP coupled reactions: by splitting the reaction into two parts (both of which are thermodynamically favorable), coupled by a common intermediate, such that the overall reaction becomes favorable.

A second way to consider this coupled reaction is without thinking about the mechanism. However, in this case, it is important to emphasize that it is the production of stronger (lower potential energy) bonds in ADP + Pi that releases energy, rather than breaking a bond in the ATP. After all, bond formation releases energy while bond breaking absorbs energy. The overall energy change depends on the difference in bonding energy between the reactants and products. It is the production of more stable (lower potential energy) products that releases energy.

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