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**INSTRUCTOR:** So let's consider a reaction and consider the effect of temperature on this reaction on the thermodynamics of the reaction. So this is the decomposition of sodium bicarbonate. Does anyone know what another name for bicarbonate is? If you were going to send someone to the grocery store to buy some, what would you tell them to get?

**AUDIENCE:** Baking soda.

**INSTRUCTOR:** So you would probably say, look for baking soda. Does anyone know what this is used for or how it works?

**AUDIENCE:** Baking.

**INSTRUCTOR:** Baking, yes. So what is baking soda doing? What step of baking are you using it for?

**AUDIENCE:** [INAUDIBLE]

**INSTRUCTOR:** Yeah, bread rising. So in this reaction, you're forming gas, and that gas helps bread to rise. So this process happening while it's baking allows for bread rising and things like that. So baking soda-- you always want to make sure you add your baking soda.

So let's consider the thermodynamics of this reaction.  $\Delta H_0$  is a positive value, 135.6 kilojoules. And why don't you tell me which of these you think is going to be the  $\Delta S$  of these options?

**AUDIENCE:** [CHATTER]

**INSTRUCTOR:** Just 10 more seconds.

**AUDIENCE:** [CHATTER]

**INSTRUCTOR:** So the positive value-- that is a very good guess and that is correct. Because we're going from solids to gases, so you would predict that entropy would be increasing. Things are not moving very much with a solid. With a gas, they can. You have more disorder, more freedom.

So that is, in fact, the correct value for this  $\Delta S_0$  is plus 0.334 kilojoules. I already put it in kilojoules for you. And now we can calculate the  $\Delta G$  for this reaction. And let's first do it at room temperature.

So we have  $\Delta H$ , positive value and endothermic reaction. We're doing it at room temperature first, in Kelvin so we can cancel our units. And we put in our  $\Delta S$  value here. And then we can calculate it out.

And  $\Delta G_0$  is plus 36.1 kilojoules per mole. That is not a spontaneous reaction. So our bread is not going to rise, and our baking will be failed, except that we're probably not going to be baking it in the oven at room temperature. So this would be non-spontaneous but when we bake, we're going to heat the oven, and so usually 350 or something, which is 450 Kelvin.

So now we can do the equation again. We plug-in our  $\Delta H$ , our new temperature, and our  $\Delta S$ , and we get a negative value.  $\Delta G_0$  is minus 14.7 kilojoules per mole at 450 degrees Kelvin. So this would be spontaneous. So when you're baking, you want to remember to turn your oven on, heat it up, and put in your baking soda.

So let's think about now this type of reaction that has a positive  $\Delta H$  and a positive  $\Delta S$ . So these both have the same sign. And if both  $\Delta H$  and  $\Delta S$  have the same sign, temperature can be used to control spontaneity. It will be non-spontaneous at one temperature but spontaneous at another temperature. And if we assume  $\Delta H_0$  and  $\Delta S_0$  are independent of temperature, which is fine to do-- that's a good assumption-- then  $\Delta G_0$ , which is definitely dependent on temperature, is linear-- is a linear function with temperature.

So let's plot now those two values of  $\Delta G$  that we just calculated. So here is our plot. We have  $\Delta G_0$  kilojoules per mole on the y-axis and temperature on the x-axis. And let's put in the numbers that we had.

So we had calculated at room temperature, around 300 Kelvin, a value of about 26-- positive 26 kilojoules per mole. And we calculated then at about 450 Kelvin a value about minus 14.7, almost minus 15 kilojoules per mole. And when you have two points, you can draw a beautiful straight line. When you have more, sometimes it's more complicated. But it is linear.  $\Delta G_0$  is linear with temperature.

So now let's think about this is a straight line, and we can think about an equation for a straight line. So the equation that we know and love,  $\Delta G_0$  equals  $\Delta H$  minus  $T \Delta S$ , can be now rearranged. We have  $\Delta G$  on the y-axis here. We have temperature is our x-axis. So now we've just rearranged. We've pulled minus  $\Delta S_0$  over here, and  $\Delta H_0$  are over here.

So  $\Delta H$  is our y-intercept. And for some reason, your notes just say "y dash i." I don't know what happened to "intercept" part. But anyway, that's the y-intercept is  $\Delta H_0$ . And what is the slope?

**AUDIENCE:** [INAUDIBLE]

**INSTRUCTOR:** Yeah. So the slope is negative  $\Delta S$ . So if you plotted  $\Delta G$ 's versus temperature, you could get out your  $\Delta H$ , or you could get out from the slope your  $\Delta S$ .

And let's think about these different parts of the plot. So over here  $\Delta G$  is greater than 0. It's of positive value. And what does that mean about the spontaneity of the reaction, if its  $\Delta G$  is positive?

**AUDIENCE:** Non-spontaneous.

**INSTRUCTOR:** Right, so that's non-spontaneous. Down here, we have  $\Delta G$  minus value less than zero, so there it's spontaneous. So at some temperatures, the reaction is non-spontaneous, and in other temperatures, the reaction is spontaneous.

And there is a certain value of  $T$ ,  $T^*$ , that is the temperature at which it switches from non-spontaneous to spontaneous, or if you're decreasing temperature, spontaneous to non-spontaneous. And for a particular reaction, you can calculate what that temperature value is, what  $T^*$  is. So let's do that.

So we can calculate  $T^*$ . And so again, this is the temperature at  $\Delta G$  equals 0 where you have that switch point between spontaneous and non-spontaneous. So we can set  $\Delta G_0$  equal to 0. And then we can solve for  $T^*$ . So  $T^*$  would just be  $\Delta H_0$  over  $\Delta S_0$ , because this is set to 0.

And we can plug these values in. So  $\Delta H$ , again, was plus 136 kilojoules per mole. And  $\Delta S_0$  was plus 0.334 kilojoules per Kelvin per mole. And we can calculate out a temperature of 406 Kelvin. So this is the temperature at which you have this switch from a

spontaneous to a non-spontaneous process.

So if you're cooking your bread below 406, you get something that looks like this. The first time-- my husband is the chef in our family. And the first time I was tasked with making cupcakes for my daughter's school, I forgot to put the baking soda in. But if you put enough frosting on it and the kids are four years old, it totally doesn't matter.

Anyway, if I had put in the baking soda and cooked it at temperatures above 406 Kelvin, I would have had something that looked a whole lot better, and I wouldn't have even had to put frosting on. But, no, I would have. Four years old, you have to put frosting-- never mind. It all worked out.

So there is this temperature at which you have a switch if the sign of  $\Delta H$  and the sign of  $\Delta S$  are the same. So now let's think about another case where you have  $\Delta H_0$  and  $\Delta S$  are both negative values. What would this plot look like? And here are some options for you.

**AUDIENCE:** [CHATTER]

**INSTRUCTOR:** Let's just do 10 more seconds.

**AUDIENCE:** [CHATTER]

**INSTRUCTOR:** 90%, excellent. So that is correct. So we can draw that now in your handout.

So here, if they're both negative, down here we have  $\Delta S$  is a negative value, spontaneous. You'll have a negative  $\Delta G$ . And here you have a negative  $\Delta H$  minus  $T$  times a negative  $\Delta S$ . So this will be a positive term and this will be a negative term. And to be spontaneous, you want a negative overall.

So at low temperatures, the unfavorable  $\Delta S$  is down-weighted. So at low temperatures, you're spontaneous. But as the temperature increases, you'll get to a magic temperature, a  $T^*$ , in which this  $\Delta S$  term now becomes greater than the  $\Delta H$  term. This will be a big positive value compared to a smaller one, and you'll switch to a positive  $\Delta G$  and a non-spontaneous process.

Let's consider all the options now. One more. 10 more seconds.

**AUDIENCE:** [CHATTER]

**INSTRUCTOR:** Great. Yeah, I knew those other clicker questions were going to be deciding the winners, I feel like.

So yes, this is always going to be spontaneous. So if we remember the equation-- and if you don't have it memorized yet, you will soon. Even though it will be on an equation sheet, most people don't need it. You use it so much. So when  $\Delta H$  is negative and this is positive,  $\Delta G$  is always going to be negative. So it'll always be spontaneous, and so when  $\Delta G$  will always be negative at every single temperature.

So now let's think about this one. Positive  $\Delta H$ , negative  $\Delta S$ -- what will this be? You can just yell it out.

**AUDIENCE:** Never.

**AUDIENCE:** Never spontaneous, right. So positive, and then here with another positive, a minus, a minus, another positive-- it'll never be spontaneous. How sad for it. So  $\Delta G$  will always be positive at all temperatures. So here are cases where  $\Delta H$  and  $\Delta S$  have different signs.

But now we have cases where they're both positive or they're both negative. So for the both positive case, this will be sometimes spontaneous. It will depend on  $T$ . So when will  $\Delta G$  be negative and, therefore, the reaction be spontaneous, when  $T$  is greater or smaller than  $T^*$ ?

**AUDIENCE:** Greater.

**INSTRUCTOR:** Greater, right. So here, we have a positive  $\Delta H$  endothermic reaction. We have a positive  $\Delta S$ . And so when  $T$  is big here, this term will dominate. And you can still get a negative  $\Delta G$ , so when temperatures are above that magic temperature.

And then our last case, when we have a negative  $\Delta H$ , an exothermic reaction, and a negative  $\Delta S$ -- and again, that will depend on temperature. So when they have the same signs, temperature makes a difference. And here, you will have a negative  $\Delta G$  when you have a smaller temperature, because here you want the  $\Delta H$  term. That's a negative term. And you want that to be the bigger term, and so you want to have smaller temperatures that will down-weight the negative  $\Delta S$  over here.

So these are our four possibilities-- always spontaneous; never spontaneous; and then

sometimes spontaneous, and it depends on the temperature compared to  $T^*$ . And  $T^*$ , again, is the temperature at which you switch between spontaneous and non-spontaneous.

So temperature is important. Temperature is important to thermodynamics, and temperature is also important to kinetics. Most of the time, you can speed up a reaction, or at least an elementary reaction, when you increase the temperature.

So now, let's think about thermodynamics in biological systems, and think about a very important interaction in biological systems which is hydrogen bonding. So this is also great review for the exam on Monday. So hydrogen bonding are interactions between hydrogen bond donors.

So what is a hydrogen bond donor? A hydrogen bond donor is a hydrogen in a polar bond. So this is why it's good review for exam 2 because for exam 2 you should be able to identify polar and non-polar bonds.

So a hydrogen bond donor is a hydrogen in a polar bond, and a hydrogen bond acceptor is an electronegative atom with a lone pair. And electronegativity is also a topic on exam 2, so might as well learn it for Monday and then continue to learn it, because you'll also need it for thermodynamics and later on as well.

So here we have a bond between something X and a hydrogen, and here we have Y that's an electronegative atom with a lone pair. And this little, squiggly plus thing here indicates that it has a partial positive charge. And here you have a negative charge, and that's going to make for a nice favorable interaction, this hydrogen bond.

So X is something that will lead to a polar bond, such as nitrogen, oxygen or fluorine, nitrogen and oxygen being the most relevant to biological systems. So if you have N or O here, that's a polar bond. And so that will then form a hydrogen bond with an electronegative atom that has a lone pair. And examples of that are also nitrogen, oxygen, fluorine, and nitrogen and oxygen, again, being the most relevant for biological systems. So we have this interaction because these sort of partial charges here that form this nice hydrogen bonding interaction.

So if we look at one of the most important molecules that hydrogen bonds which is water, we see that water has polar bonds between the oxygen and the hydrogen, because those have electronegativity difference of greater than 0.4, and it has two lone pairs. So water is capable of being a hydrogen bond donor with its hydrogen and also a hydrogen bond acceptor.

And so if we draw the hydrogen bonds as dotted lines here, we see this OH polar bond is a hydrogen bond donor, and this oxygen here with its lone pair is the hydrogen bond acceptor. So here we have this network of hydrogen bonding interactions, both on the board and on my t-shirt. I also have water-hydrogen bonding on my t-shirt today.

So these hydrogen bonds in water are really important for life. This is a very, very important property. Now just for exam review, what is the shape of that molecule?

**AUDIENCE:** Bent.

**INSTRUCTOR:** What angle do we expect between the hydrogen, oxygen, and the nitrogen?

**AUDIENCE:** [INAUDIBLE]

**INSTRUCTOR:** Less than 109.5. That's right. What would be the SN number?

**AUDIENCE:** 4.

**INSTRUCTOR:** 4, Yes. Good! If those answers seem like "I have no idea what everyone's talking about," you know what your weekend is going to involve. Those are things that are going to be on the exam. VSEPR, yes.

So let's compare now hydrogen bonds with covalent bonds. So here we have a hydrogen bond donor and acceptor versus a covalent interaction. So a covalent interaction where you have a bond, where you have bonding electrons are being shared between the two. So covalent bonds are stronger than hydrogen bonds, for sure. And let's look at some examples.

So if we consider this X as an oxygen here, in a oxygen hydrogen polar bond interacting with another oxygen, the value for that hydrogen bond would be about 20 kilojoules per mole as opposed to the covalent bond, here just the hydrogen and oxygen, has 463 kilojoules per mole. So the hydrogen bond is considerably weaker than a covalent bond, but it's still-- weak bonds turn out to be really important in biological systems.

Now let's consider a case where we have nitrogen as the acceptor. So we're going to have a nitrogen acceptor here. So if this is OH donating to N, then we have 29 kilojoules per mole. NH interacting with N14, compare to a covalent bond between H and N of 388. So when you compare to covalent bonds, hydrogen bonds are much less, but they are still super important.

So for bonds that are made up between molecules here-- intermolecular, between molecules--

hydrogen bonds are the strongest kind of interactions that are between molecules here. So hydrogen bonds can be between molecules. They can also be made within a molecule. So this just shows hydrogen bonding in a protein structure between these are called beta strands here. And hydrogen bonding is incredibly important in forming protein structure-- really, really important.

So hydrogen bonds are responsible for protein folding-- very important in proteins. Hydrogen bonds are also really important for DNA. So all of the main in RNA, all of our macromolecular molecules of life, hydrogen bonding is really important.

So let's look at a GC base pair that forms in DNA. And we can think about the hydrogen bonds here. So here are three of them.

So we have this polar bond between N and H. And it's the hydrogen bond donor, and we have the lone pair on oxygen accepting that hydrogen bond. Here we have a polar bond between nitrogen and hydrogen donating over here to a nitrogen lone pair. And here we have an NH polar bond as a hydrogen bond donor to the lone pair on this oxygen. And this hydrogen bonding pattern is what allows DNA to have its beautiful double helix, and is very, very important.

So why don't you give it a try and tell me how many hydrogen bonds you would get between these guys here. And I'll leave this structure up so you can see what it looks like. 10 seconds.

**AUDIENCE:** [CHATTER]

**INSTRUCTOR:** The answer is 2. Let's take a look at that over here.

So you have a nitrogen polar bond over here making an interaction with this lone pair. You have a polar NH bond here, hydrogen donor to this lone pair. Why is that not a hydrogen bond? Because it is carbon hydrogen.

So carbon hydrogen, the electronegativity difference is not greater than 0.4, so carbon hydrogen is not a polar bond. So you need to have both a polar bond, and you need to have an electronegative atom that has lone pairs to be the hydrogen bond acceptor. So here you have a hydrogen bond acceptor, but you don't have a hydrogen bond donor.

And so this actually turns out to be important because you want to specifically recognize one base with another base, and so the hydrogen bonding pattern is essential for that working out.



So here, these are hydrogen bonds. I said they're weaker than covalent bonds, but they're strong enough to help stabilize the structure of DNA. But they're not so strong that DNA cannot unzip.

And you need to unzip DNA to read it, and by reading, that's essential to make another copy, to have cell division, or to translate your genetic code. So that's, I think, why hydrogen bonds are so important in biology, because you don't want a lot of super strong bonds. You want weaker interactions because in biology things are moving around.

So let's talk about the importance of hydrogen bonding. And for this we have another *In Their Own Words* segment.

[VIDEO PLAYBACK]

- My name is Lourdes Aleman, and my research is on RNA interference or RNAi. RNA interference is simply a silencing mechanism the cells use to turn down the expression of a gene.

Double-stranded RNA pieces have some sort of complementarity to a sequence within the genome. That double-stranded RNA piece binds to a big large protein complex, it unwinds the double stranded piece, takes one of those strands only, and finds the gene that it complements with. And once it does, it binds to that particular RNA from that gene and it destroys it and not allowing protein to be made from that RNA.

DNA and RNA both can form base pairs by hydrogen bonding. The short piece of RNA that is found in this protein complex guides that RNA and basically finds its match by hydrogen bonding. So if it forms a hydrogen bond along the whole entire sequence, it knows it has found a match somewhere in the sequence. And that's how it recognizes the gene that it's targeting.

Macular degeneration is a disease of the retina. There are too many blood vessels in the retina, and they can bleed and scar over time, and eventually these patients can become blind. Some patients with this disease, one of the reasons they have an outgrowth in the retina is because there is a gene called the VEGF that there's too much of. And VEGF tells cells, "Make blood vessels."

RNA interference is being used to silence the expression of this gene so that in patients with

macular degeneration, you don't get further growth of more blood vessels and more bleeding and scarring as a consequence. My dream for RNAi would be that as a patient you will go into the doctor if you were diagnosed with some sort of disease. The doctor would go into the computer, order you a some double-stranded RNA for the particular gene that has been mutated or is malfunctioning in your disease, and you would then come back, and they would put that double-stranded RNA into you, and you will get better. That would be my dream, that it could be applicable to pretty much any disease or viral infection that you can think of.

How many of you have heard of like RNAi or treatments and things and sort of-- a number of people-- like customized medicine. I mean, I think that that would be such an incredible thing if this works out, to really be able to treat every individual based on their DNA. So we're not there yet, but there's a lot of people who are working on this. And there's a lot being done at MIT research in RNA, and that particular work was in Phil Sharp laboratory. Phil Sharp is one of our Nobel laureates here at MIT.

So that's why hydrogen bonding is important. So let's just do one more example of thermodynamics in biological systems. And we're back to thinking about ATP, which we talked about already, and the hydrolysis of ATP. So we saw that this is a spontaneous reaction before, and this can be what's called "coupled" to a spontaneous process to drive that non-spontaneous reaction.

So the total change in free energy of a coupled reaction is the sum of the individual delta G's. So if you have one that is unfavorable and one that's favorable, one that's positive and one that's negative, you sum that up and if it's overall negative, then it will become a spontaneous coupled reaction.

So let's look at this example again. So we have delta G 0 for ATP at 310 Kelvin. Why do you think I'm using 310? What do you think that temperature is?

**AUDIENCE:** Body temperature.

**INSTRUCTOR:** Body temperature. So we have ATP, so you have triphosphates-- that's the TP-- and hydrolysis. You're losing one of the phosphates. You're going to a diphosphate. And hydrolysis means a cleavage reaction that involves water.

So we saw before that the delta H0 for this is negative. It's an exothermic reaction minus 24 kilojoules per mole. Delta S0 is plus 22 joules per Kelvin per mole. And so if we plug this into

our delta G equation, we have  $\Delta H - T \Delta S$ . At body temperature, this is a negative value, negative 31 kilojoules per mole.

So this is spontaneous. The hydrolysis of ATP is spontaneous. Now we want to couple this to something that's non-spontaneous. And the reaction we're going to couple to that's non-spontaneous is the addition of a phosphate group to glucose. And this keeps the glucose in the cell, because things that have charge can't come and leave the cell as readily. So nature often does this, its way of holding the things that it wants inside the cell inside the cell.

But this is a non-spontaneous process. The  $\Delta G_0$  is plus 17 kilojoules per mole, but if we couple that to the hydrolysis of ATP, which is minus 31 kilojoules per mole, and we can add those together, so 17 minus 31, gives us minus 14 kilojoules per mole. And now this non-spontaneous reaction is driven forward.

So we've taken something that wasn't favorable and made it favorable by coupling it to ATP hydrolysis. So if ATP hydrolysis is so favorable and it's spontaneous, why isn't it happening all the time, which would be really bad for us because we store our energy in the form of ATP, so we want to keep it in its good form? And the answer again is kinetics. It's a slow process. So ATP is inert enough that we can use it as an energy storage.