The Untold Story of Lac Operon

Let’s define the characters in our story…

Imagine you turn 21 years old today and like most people at your age, you would like to test out your new ID to get into the hip new bar downtown—Bar Lac Operon. You are going to be the PROMOTER SITE in our story. Your two best friends, who are 21 already, are both at the bar and have been texting you for hours asking where you are. They are the Z and Y GENES, and their names are BETA GALACTOSIDASE and PERMEASE. Not only do your friends desperately want to celebrate your birthday with you, but also each of them has a special birthday cake recipe they want to give you. With these recipes you will finally be able to make the secret and world-renowned Beta and Permease Family Birthday Cakes. Finally, you just received your new ID card in the mail, and for our story, the ID card will represent LACTOSE.

Now, before we get too far along in the night we have to get some background information about the new bar. Like most bars on a busy weekend night, Bar Lac Operon has a BOUNCER that works at the front door. And what do bouncers do? You’re right, they check IDs. The bar also has a CHAIR for the bouncer to sit directly in front of the entrance. On normal nights, the bouncer arrives for work at 8pm and sits in his chair at the bar entrance. If you have your ID, he lets you into the bar. If you don’t have your ID you don’t get in.

There are just a few more details we need to discuss. First, the bouncer signed a contract with the bar that if he doesn’t have his CHAIR at the bar entrance he will not show up to work. He just simply refuses to work a 12-hour shift without being able to sit down. Second, if you get into the bar for any reason at all, you are going to get the recipes for the cakes from your friends (as long as they are in the bar as well) and YOU WILL MAKE THE CAKE FROM THE RECIPE. In other words, YOU INSIDE THE BAR + FRIENDS = CAKE 😊

OK, now that we have our story down we need to relate it to the lac operon. Let’s start with you. You are the PROMOTER SITE. This means that on normal days, if you are not sick, you can assemble your car and drive yourself to the bar door to meet your friends. This is the same as saying the promoter site is responsible for assembling the transcription machinery (transcription factors, polymerases, etc.) and initiating the transcription process which will transcribe the Z and Y genes in this system.

Your friends are simply the Z and Y genes that code for BETA GALACTOSIDASE and PERMEASE. Remember that the whole goal of the lac operon is to break down lactose into an energy source you can use… glucose! Both permease and beta galactosidase are responsible for helping to break down lactose.

The BOUNCER’S CHAIR is the OPERATOR SITE. This is the binding site for the repressor (THE BOUNCER IN OUR STORY). Just like a bouncer arrives at work and sits down on his chair to check IDs, the repressor travels (trans-acting) to the operator site in the operon and binds to the site, shutting down the lac operon.
Now, as far as you are concerned, you can either be P+ or P–:

- **P+** is when you are normal, feeling good, and capable of driving yourself to the bar, just like a normal promoter is capable of initiating transcription.
- **P–** is when you have caught bird flu and there is no way in the world you will make it out of the house to meet your friends, just like when the promoter region has been mutated and it no longer is recognized by the transcription machinery, and transcription never starts. And, if you NEVER LEAVE YOUR HOME, you will NEVER GET TO THE BAR DOOR. If you NEVER GET TO THE BAR DOOR, you will NEVER GET INSIDE to meet your friends and will NEVER GET TO MAKE THEIR BIRTHDAY CAKES.

As for the operator site, it can either be O+ or O–:

- **O+** just means that the bouncer’s chair is at the bar, right in front of the bar’s entrance. In other words, the binding site for the repressor is normal and the repressor can sit down on the sequence.
- **O–** means that someone came to the bar in the middle of the night and stole the bouncer’s chair. Keep in mind that having a chair is in the bouncer’s contract. If there is no chair at the bar, he WILL NEVER SHOW UP to check IDs. And if he NEVER SHOWS UP, THERE WILL NEVER BE A BOUNCER AT THE BAR. Now, we all know that if you get to a bar to meet your friends and there is no bouncer, surely you are not going to just wait outside. You will walk right in. So if the operator site is broken, the repressor will NEVER bind to the site, and it will therefore never stop the transcription machinery from following through with transcribing their target genes.

Finally we get to the bouncer (or repressor). The BOUNCER can be I+, I–, or I+:

- **I+** bouncers are perfectly healthy. They show up for work, sit in their chairs and check IDs.
- **I–** bouncers have caught the same bird flu as you have if you are P–. They never leave their house to go to work. This is just like saying the repressor gene (I) is broken and no longer makes repressors. If no repressors are made, there will NEVER be any binding to the operator and you can walk right into the bar.
- **I+** means that it is the super repressor. It binds to the operator and stays! No amount of IDs will ever get that repressor to move. This is the same as imagining a bouncer that decided to take a bunch of “anger” medication for breakfast. The bouncer then shows up to work so angry that they decide to turn EVERYONE AWAY FROM THE DOOR. It doesn’t matter whether you have an ID or not, if there is a “SUPER BOUNCER” sitting in his chair, you will NEVER GET INTO THE BAR.

Now that we have exhaustively defined all of our characters, we get to the magical three questions. These questions are to be asked in a specific order and only this order. You also **ONLY GET TO ASK THE NEXT QUESTION IF YOU PASS YOUR FIRST QUESTION.** And you pass the questions only if that site is NORMAL or has a + sign.
OK, let’s get started. The questions are:

1. What am I doing on Friday night? Can I physically get into my car and drive to Bar Lac Operon to meet my friends? This is asking if the P site is normal?
   a. Only if the P site is normal do you get to ask question 2.
   b. If the P site is P–, you are done, the promoter site is broken and transcription will never take place, and so you will never make beta galactosidase or permease.

Assuming the P site is normal (P+) you will then ask:

2. Is the bouncer’s chair in front of the entrance to the bar? Meaning, is the operator site functional and can it accept a repressor?
   a. Only if the O site is normal do you get to ask question 3.
   b. If the O site is Oc, you are done and you know that since there is no chair EVER in front of the door, the bouncer will NEVER show up to the bar, and you will ALWAYS be able to walk right into the bar and make beta galactosidase and permease.

Assuming the O site is normal (O+) you will then ask:

3. Is the bouncer even at work? And if so, which bouncer is it?
   a. Remember, if the bouncer is normal (I+), he will be checking IDs.
   b. If the bouncer is sick (I–) he will NEVER BE SITTING AT THE BAR DOOR, and you will ALWAYS be able to walk right into the bar and make beta galactosidase and permease.
   c. If the bouncer is SUPER ANGRY (Is) he will be sitting at the bar door and NEVER LET YOU INTO THE BAR and you will NEVER MAKE beta galactosidase and permease.
Now we can begin to do some practice trials:

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If you saw this you would ask:
1. Will I be able to get to the bar? (Answer = Yes, so you go to Question 2)
2. Is the bouncer’s chair at the bar door? (Answer = Yes, so you go to Question 3)
3. Is the bouncer in his chair checking IDs (Answer = Yes)

At this point you know that you are at the bar door, ready to meet your friends and make their birthday cakes, the bouncer’s chair is there and the bouncer is in his chair, NOT SUPER ANGRY, and checking IDs. This is now the situation where you either have or don’t have your ID. Remember, your ID is lactose. IF lactose is present, it will bind the repressor, and the repressor will no longer be bound to the operator. Transcription of the Z and Y gene will then take place. This is the same as saying, if you HAVE YOUR ID YOU WILL GET INTO THE BAR AND MEET YOUR FRIENDS.

As you can see, the answer shows you that when the INDUCER (LACTOSE) IS ABSENT you do not make either gene product. IF the inducer is PRESENT, you will make the product.

Let’s do a few more examples:

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If you saw this you would ask:
1. Will I be able to get to the bar? (Answer = Yes, so you go to Question 2)
2. Is the bouncer’s chair at the bar door? (Answer = NO, so you are done with questions)

At this point you now know that you are at the bar door, ready to meet your friends and make their birthday cakes, AND the bouncer’s chair is NOT there, so the bouncer will NEVER BE CHECKING IDs. If they never check IDs, you will ALWAYS get into the bar regardless of whether lactose is present. Transcription of the Z and Y gene will ALWAYS take place.

As you can see, the answer shows you that regardless of whether the INDUCER (LACTOSE) IS PRESENT OR NOT you will make the product.
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If you saw this you would ask:

1. Will I be able to get to the bar? (Answer = NO, so you are done with questions)

At this point you now know that you are sick and you never leave the house to even go to the bar. And if you never even go to the bar you will NEVER MAKE THE GENE PRODUCTS. If the promoter site is broken, transcription will never be initiated!

You might be saying, “Wait, the bouncer’s chair is missing, I can always get into the bar.” But remember, there is an order to our questions. Since you didn’t pass the first question, it doesn’t even matter if the bouncer’s chair is present or not, the Promoter site is broken and so the lac operon is broken.

As you can see, the answer shows you that regardless of whether the bouncer’s chair is present or absent, and regardless of whether INDUCER (LACTOSE) IS PRESENT OR NOT you will NEVER make any gene product.

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If you saw this you would ask:

1. Will I be able to get to the bar? (Answer = Yes, so you go to Question 2)
2. Is the bouncer’s chair at the bar door? (Answer = Yes, so you go to Question 3)
3. Is the bouncer in his chair checking IDs (Answer = Yes)
   a. BUT**** REMEMBER, this is “SUPER ANGRY” bouncer!

At this point you now know that you are at the bar door, ready to meet your friends and make their birthday cakes, the bouncer’s chair is there and the “SUPER ANGRY” bouncer is in his chair. He is so angry that you will NEVER GET INTO THE BAR. And if you never get into the bar, you will never transcribe the Z and Y genes.

As you can see, the answer shows you that regardless of whether INDUCER (LACTOSE) IS PRESENT OR NOT you will NEVER make any gene product.
If you saw this you would ask:

1. Will I be able to get to the bar? (Answer = Yes, so you go to Question 2)
2. Is the bouncer’s chair at the bar door? (Answer = NO, so you are done with questions)

At this point you now know that you are at the bar door, ready to meet your friends and make their birthday cakes, AND the bouncer’s chair is NOT there, so the bouncer will NEVER BE CHECKING IDs. I know, I know, there is “SUPER ANGRY” bouncer. But remember, even the super angry bouncer will ONLY WORK IF HE CAN SIT DOWN. Since he has no chair, even the angriest of bouncers will never be checking IDs, and so you will ALWAYS get into the bar regardless of whether lactose is present. Transcription of the Z and Y gene will ALWAYS take place.

As you can see, the answer shows you that regardless of whether the INDUCER (LACTOSE) IS PRESENT OR NOT you will make the product.

Sometimes there are situations where there is a second copy of the lac operon inserted to study the way certain mutations interact and whether they are cis-acting or trans-acting. For two-operon situations, you will go through the problems the same way and answer each side separately. The catch is that after you do this, you will have one more question to ask:

4. How do the bouncers affect the other bar?

**Bouncers, or repressors, are trans-acting.** That means they can “tra-vel” around town and work multiple jobs or at multiple bars. Repressors from one operon can bind to the operators of a different bar as well as their own. Let’s work through an example on the next page.
An example might be:

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**INITIAL ANALYSIS**

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**AFTER TRANS AFFECTS**

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**OVERALL AFFECT:**

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For the **left side**, your initial round of questions will tell you that there is NO bouncer and so you will ALWAYS make the gene products regardless of whether the inducer (lactose) is present.

On the **right side**, you will reach the same conclusion but this time because there is NO bouncer’s chair…so the bouncer never shows up to work to check IDs.

However, when you look at how the bouncer’s affect the other bar, the RIGHT side’s repressor changes the left side to be inducible. The left side does not affect the right side solution at all.

Finally, the overall affect is that there is at least one + in each of the four columns and so the products will be made regardless of whether inducer is present or not.