>> Izzy: Dude, I like what you built there.

What's it do?

>> Dude: Oh...hi Iz.

This is a cool bug.

I made it using an electronics building kit that Sally got me.

She wanted to get me a genetics kit but nothing's available yet.

Eesh! I don't get it.

Why is it so easy to turn on and off the lights for this electronic bug but so hard to turn things on and off in biology?

>> Izzy: What do you mean Dude?

The arsenic sensor that we built in bacteria a few years ago works pretty well.

If there's arsenic in the water being tested the sensor turns on.

And when arsenic isn't in the water, the sensor is off.

And we built that sensor with natural biological parts!

>> Dude: So arsenic works like this switch?

How is that possible?

How does the cell know?

>> Izzy: We used parts from the ArsR operon to program arsenic-inducible expression.

>> Dude: Hold up!

Arsenic-inducible expression?

What's that mean??

All I know is that arsenic is toxic.

Don't the cells just die when you poison them?

>> Izzy: Cells have come up with a bunch of clever ways to survive.

In the case of arsenic, the cells make a pump to get the poison out as soon as any comes inside the cell.

>> Dude: That makes sense.

So ass-er is the pump?

And why did you call it inducible?

>> Izzy: Dude, be careful how you say it: the protein is called ArsR since it's the ARSenic Repressor protein.

And ArsR isn't the pump.

It just tells the cell when to make the pump.

The operon has promoter, which is where the cell's RNA polymerase binds.

And at least three genes: the ArsR gene, which encodes the repressor protein, the ArsB gene, which encodes the pump, and the ArsC gene, which encodes an enzyme that reduces arsenic in the cell so it can be pumped out.

Most of the time, the operon is turned "off" since the ArsR protein binds the DNA near the promoter to stop transcription.

But when arsenic comes into the cell, it binds the ArsR protein.

And when the repressor is bound to arsenic, it can't bind the DNA so RNA polymerase can.

That way the cell makes more of the repressor, the pump, and the enzyme only when there's arsenic around.

That's the inducible part.

>> Dude: So why did you include the whole operon in your arsenic sensor?

It seems like you could just include the ArsR gene and the promoter parts for your arsenic sensor device?

>> Izzy: Nice work.

That's actually exactly what we did.

We simplified the natural system to only use the parts we wanted.

So it looks like this...

>> Dude: So you're arsenic sensor works like this?

>> Izzy: Dude, that's great but I have two even simpler way to write it.

This is called a truth table and this is called a transfer curve.

Both tell you that when arsenic levels are low, the operon is mostly off and when arsenic levels are high, the operon turns on and starts cranking out proteins.

Earth to Dude...what are you doing?

>> Dude: Well here's the thing Iz.

I'm always looking for some way to get Buddy's gas-o-matic module to turn off before he gets too big.

I was hoping I could maybe switch this operon around to get the truth table working like this.

And get the transfer curve looking like this.

>> Izzy: No problem!

You're looking for a simple digital device called an inverter.

>> Dude: Oe-kaaay.

Can we turn this operon into an inverter or do I have to build something completely different?

>> Izzy: There are already a few transcription-based inverters in the registry, but I don't know if anyone's built one using the arsenic repressor.

Maybe you can be the first.

Do you want to try?

>> Dude: You bet!!

But how?? What about this idea: lets take this promoter that binds the "Ars R" protein and move it to the end of the operon.

This way if I put my gas-o-matic device after the promoter, then high production of the arsenic operon gives low production of the gas-o-matic device.

Input 1 Output 0...I think I nailed it!

>> Izzy: Nice thinking Dude.

Most of the Registry's transcriptional inverters are of that form: DNA that encodes the repressor and then a promoter that's repressed by it.

One thing to remember about transcriptional inverters is that they're pretty slow to switch.

It can take over an hour for the inverter to change its output signal after it receives a change in input signal.

>> Dude: Well that might be ok.

It's not like Buddy grows super fast.

>> Izzy: Well then maybe for your application a transcriptional inverter is just fine, or maybe the registry has one that will work better.

>> Dude: Registry.

Search Parts .Inverter.

I like this number: Q04401.

Hmm that's strange.

The Registry says that BBa_Q04401 works but the transfer curve doesn't look like what you've drawn.

>> Izzy: Well, the transfer curve that I drew is a perfect inverter transfer curve.

But when you actually build the devices, they aren't going to have perfect behavior.

And that's as true in electrical engineering and biological engineering.

Devices won't switch from high to low as sharply as what I've drawn.

>> Dude: I'd really like a sharper change than this though.

Maybe I should just build the ArsR inverter to try in Buddy?

>> Izzy: I think it would be worth a shot ...let's get the parts you'll need and we can start today...