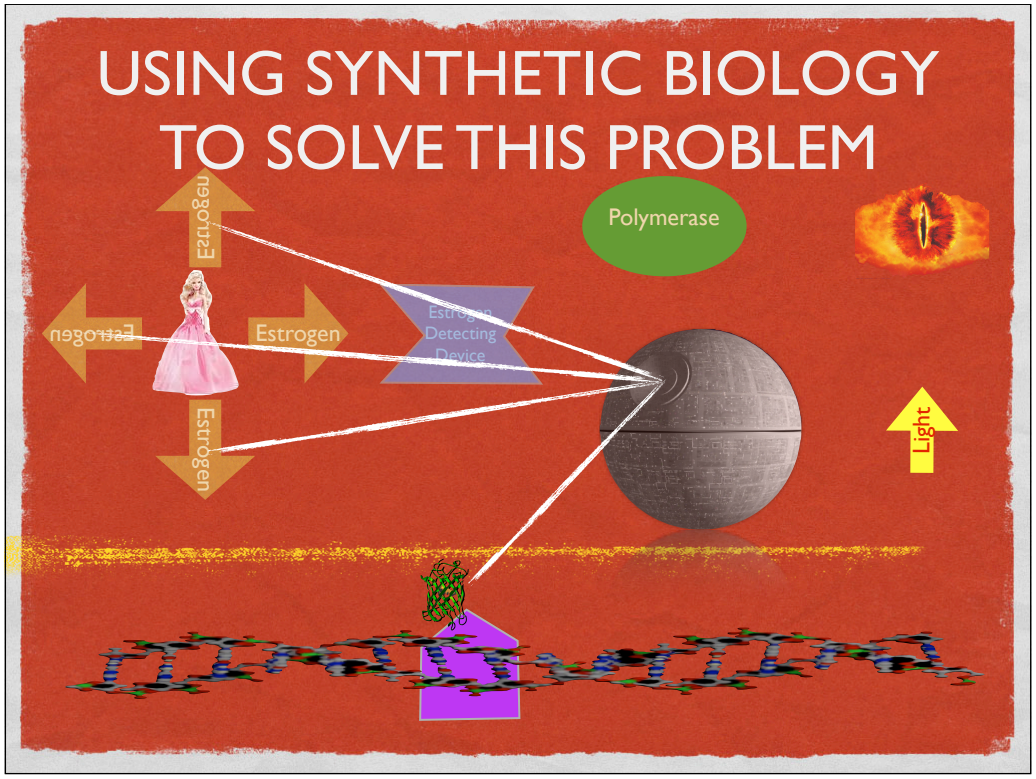
so for the first part of the three part series, build new e. coli; save the world, we will discuss the possibility of engineering e. coli which could be used to detect and degrade environmental estrogens.

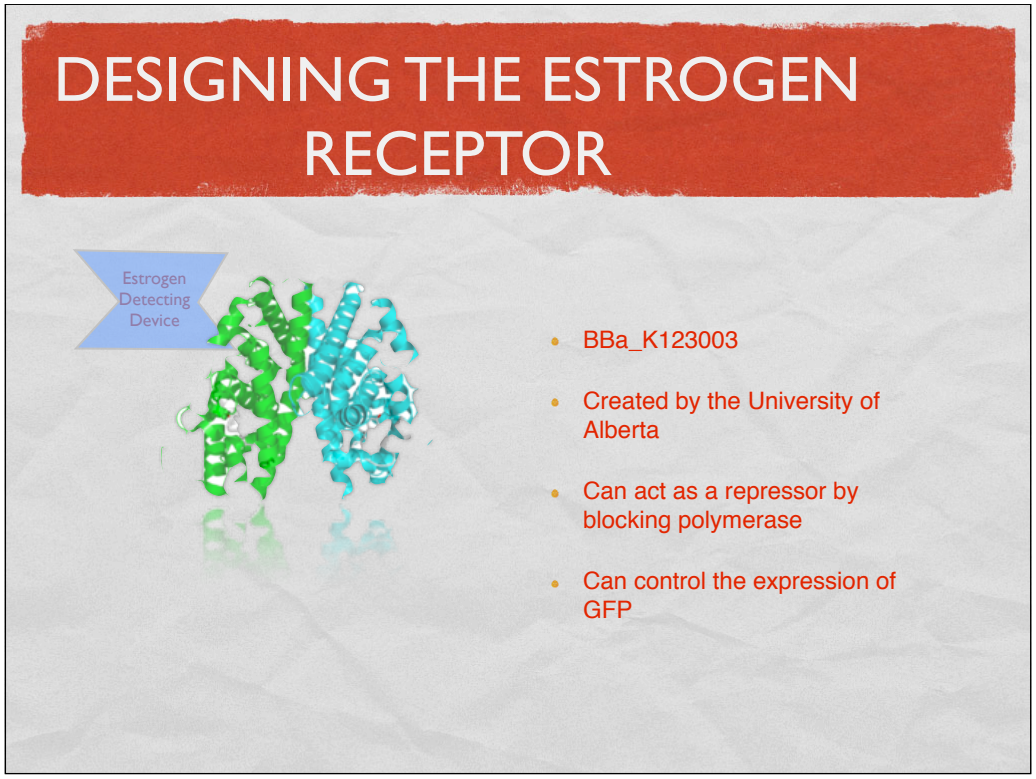
HOW PLAYING WITH BARBIE CAN LEAD TO INFERTILITY

- Environmental estrogens mimic human estrogen
- Found in plastics, pesticide, lotion, and many other synthetic chemical products
- Can cause cancer, infertility, defective genitalia, and early puberty

so what are environmental estrogens? how do they work and why are they a problem? essentially, environmental estrogens are synthetic compounds which mimic estrogens, to the extent that they can trick the natural estrogen receptors within your body.|
-they come from a variety of ever increasing synthetic compounds. each year about 1000 new chemical compounds are formulated. little are known about the chronic effects of many of these chemicals. for instance, in 1999, it was found that 95 percent of baby bottles were potential emitters of environmental estrogen because of the polycarbonate used in them. specifically, bisphenol-A, or BPA was released when these bottles were heated of scratched.
-these estrogens have a profound effect on animals, such as causing some species of fish to change genders. their influence of humans is also quite dangerous. for example, from 1979 to 1991, the rate of testicular cancer increased by 55% from previous rates in england and wales and 300 percent in denmark. accidental contamination of cattle feed with PCBs in 1973 lead to strange breast milk in women who ate this beef. subsequently, their sons exhibited defective genitalia. finally, 50 years ago, 1 in 20 women developed breast cancer. the rate now is 1 in 8. so are environmental estrogens becoming a real problem?



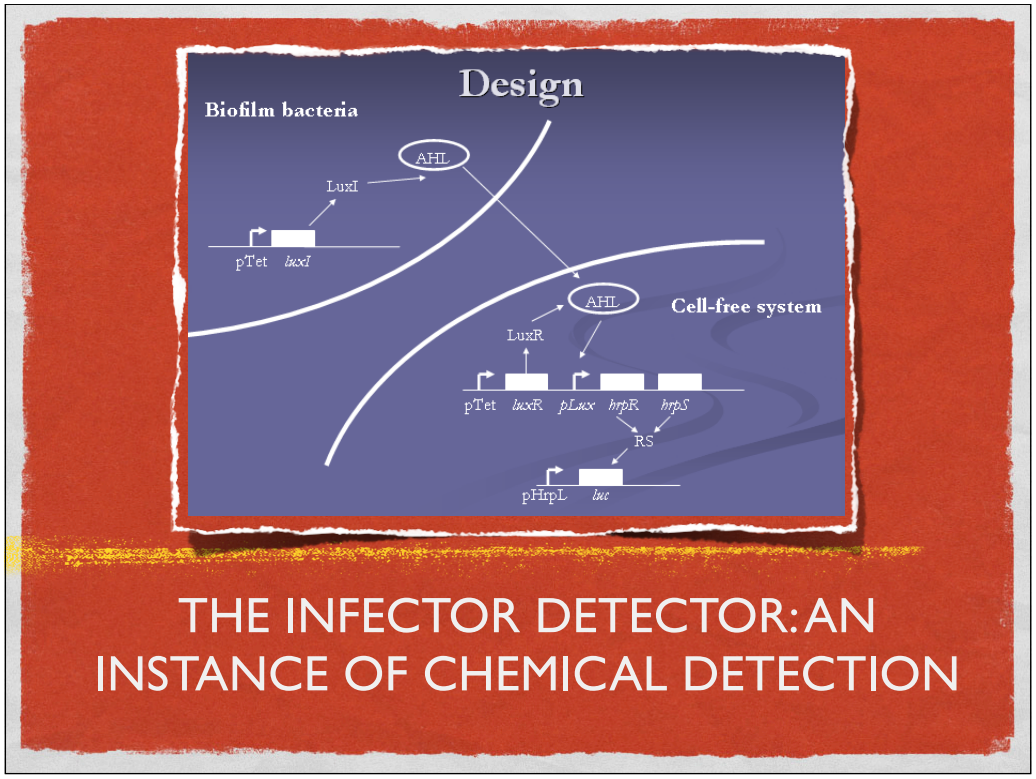
-so i've decided to use a bit of abstraction similar to the type we have been learning about in class. i think one of the advantages of this project is that it can be put together in parts. this will allow us to envision this project in parts. it will also allow us to work on this device component by component and give us something to present even if the entire thing can't be completed. you first have a barbie as described in the previous slide
-she's releasing estrogen which of course is bad
-so what we would need to detect this estrogen, and so the first component we would need to detect is a estrogen detecting device
-this estrogen receptor can then bind to estrogen to form an estrogen, receptor complex
-afterwards, we want a way of enacting some kind of transformation in our biological system once the device has bound its ligand. one could imagine, for instance, the bound complex acting as a transcription factor, not any different from the normal estrogen receptors in your body.
-the receptor, estrogen complex can then act as a promoter for GFP, which would then send off a signal to the eye so that you would be warned about the dangers of this plastic.
-of course, we also want a means of degrading the estrogen afterwards. so another component we would want to design would be an estrogen degrading cell.



-so luckily, if we search through the registry of standard biological pars, we notice that there are a few estrogen receptors. one i would like to talk about in particular is known as BBa_K123003. the part was devised by the university of alberta for their 2007 igem project.

-This basic part is derived from the Human Estrogen Receptor Alpha and optimized for activity in E. coli. When estrogen or an estrogen like compound is present the receptor binds to it and forms a homodimer. This homodimer is then able to bind to an Estrogen Responsive Element. We have therefore designed this part to act as a repressor when bound to the ERE by physically blocking the polymerase.

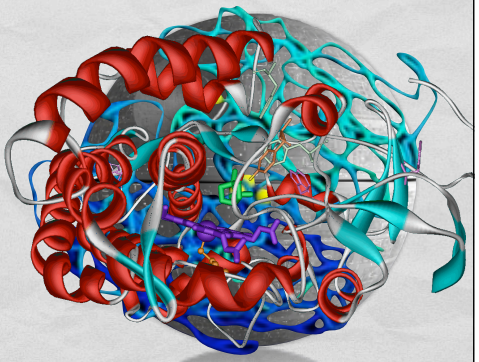
-so one way we can imagine this system working is by having GFP turned on constantly.



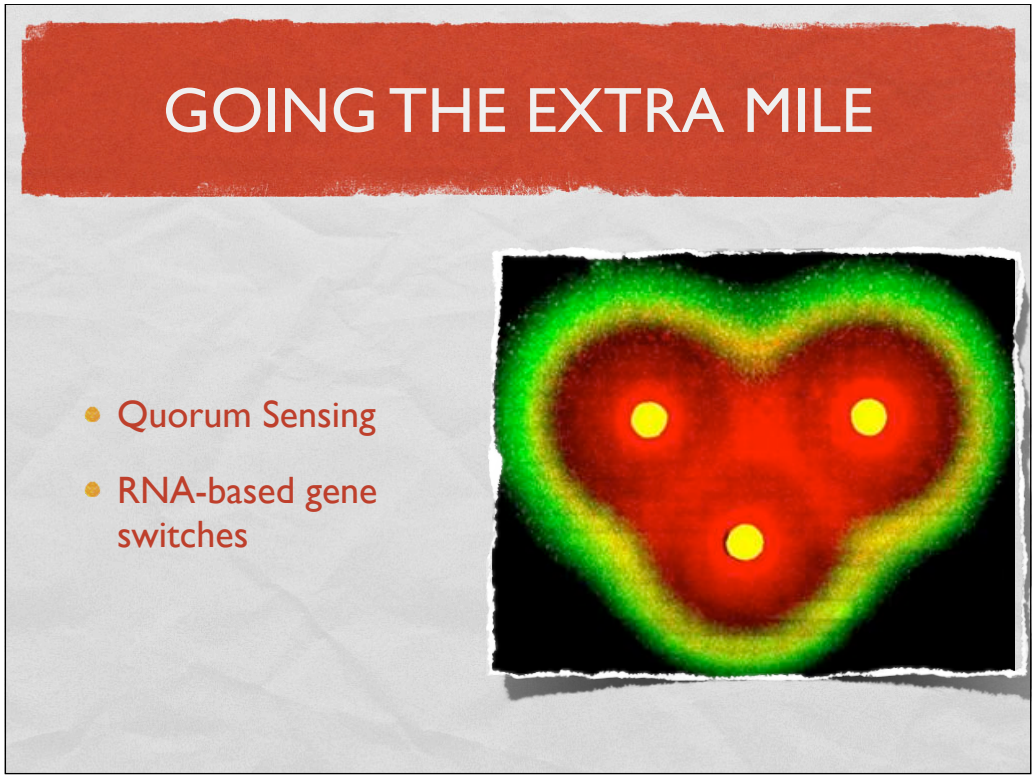
here is an example of a similar project by the imperial college in england. for their 2007 presentation, they used cells to detect the presence of harmful biofilm on the end of catheters. one thing that was immediately clear to me was the complexity of this system for performing a relatively straight forward task. one of course, they amplified their results and everything. this also illustrates the importance of compartmentalization.

METHODS OF DEGRADING ENVIRONMENTAL ESTROGENS

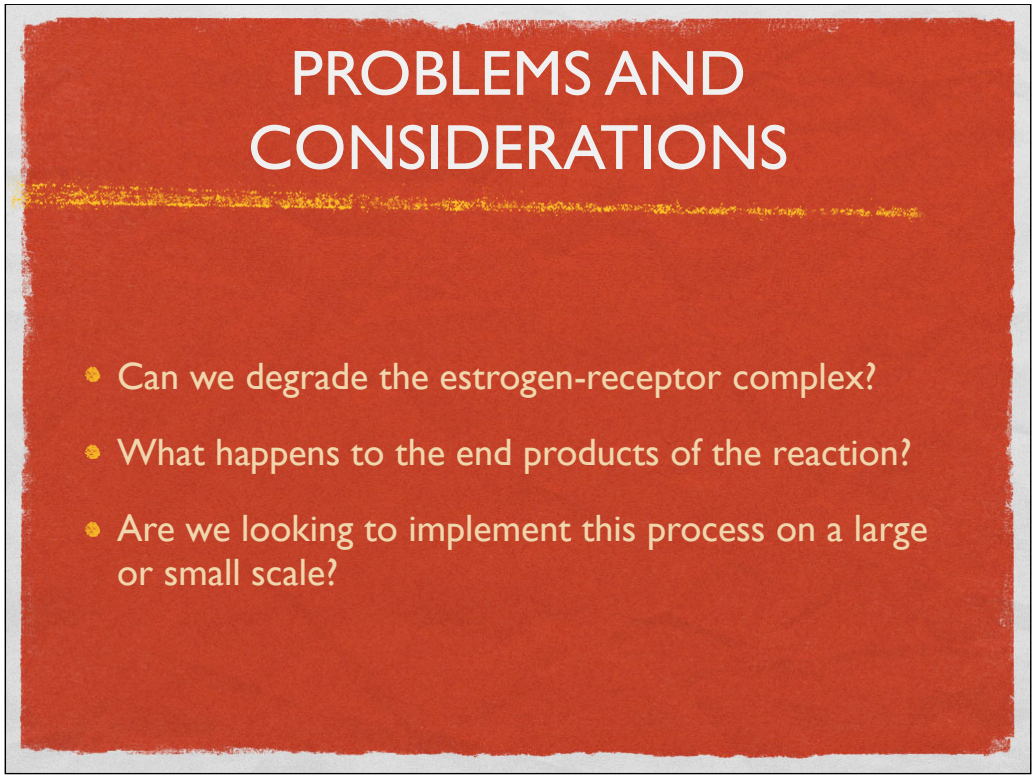
- Failures of current methods of degradation
- Cytochrome P450
- Laccase



activated carbons as a BPA absorbent. works for drinking water but not for wastewater, natural water, or polluted soil because the compounds in such solutions interfere with carbon absorption. some enzymes and microorganisms have been tested but there have been some problems. one is that the end products tend to polymerize rather than decompose. sometimes the end products are no less toxic than the beginning.
so far, scientists have classified some known components which contribute to the degradation of BPA, an environmental estrogen. one example is cytochrome p450, which was isolated from strain AO1 of Sphingomonas. In the tests, the organisms were found to be able to degrade 115 micrograms per a ml of BPA in under 6 hours with no side toxins.
laccase is an enzyme which catalyzes oxidation or reduction to enact chemical change upon the various estrogens.
i think degradation of the estrogens would be a much more challenging task because that are could potentially be a lot of metabolic steps which we would have to figure out and a lot of potential problematic byproducts we would need to consider. the chemistry might get a little hairy as well. the above things i have listed are just components of the entire metabolic process. in order to truly consider this project, we should ensure that characterizing the entire metabolic process of a plastic degrading organism is within our capabilities.



so we want the cells to cover a large area so that they can detect estrogen if present, but once that estrogen has been detected, we want them to gather together. gathering together will produce a more noticeable light and lead to faster degradation.
of course i'm not going to leave this out of my presentation. making a switch which could turn on and off various components of the system would be extremely useful. unfortunately, we don't have an aptamer for estrogen.



so one problem that we run into is that because estrogen is a steroid, it binds to receptors which are in the cytoplasm of the cell. as a result, the estrogen which we are hoping to degrade is bound to the receptors. while there have been mechanisms to degrade estrogen, can we upgrade this procedure to degrade estrogen bounded to the receptor?
after the estrogen has been degraded, what do we do with the end products? do we just have the humans consume the end products along with the bacteria or do we have the bacteria self-destruct? are there any dangers to having the live bacteria in our system? (such as destroying our natural estrogen hormones?)
do we want to do this on a large scale like at water purification labs or on a smaller scale like in our nalgene bottles? a lot of things need to be considered when answering such a question, like do we even need a detection system if we are looking to implement this on a large scale?