TEAM: ROCKET (SHRED)
Tech Spec: Strengths/Weaknesses/Opportunities
Grade for Presentation: 97

Each project idea must have

+ A description of your system's design in terms of **devices**
+ A description of your system's design in terms of **parts**
+ A **timing diagram** to show anticipated system operation
+ A plan for **testing and debugging** your first generation system
+ A description of the **impact** you envision for your system
+ A description of any concerns raised and **open issues** within your team
+ A **"GO/NO GO"** decision
+ elaborate Tinkercell model!

You've designed an elegant and thoughtful way to try to control the activity of this cell death device. I like the thresholding effect that you've implemented (it will be helpful next time to describe just why tuning and timing are difficult with simpler setups). And your efforts to make this as generalizable as possible are not only in keeping with the heart of your team as a foundational advancing group, but also shows a bravery in your approach to this problem since it's a lot easier to design a widget that does one thing vs. a widget with many uses. So congratulations on working through a lot of difficult challenges to find an architecture you like. The next stage will be finding the right details to make your ideas play out, or perhaps modifying your network some to enable the building of it. Can't wait to see how it goes!

1. Strengths
    - *Great approach to make this a platform technology, e.g. "input" is black-boxed*
    - *Clever "thresholding" approach*
    - *Very thoughtful study of which DNase to use*
    - *Nice timing diagram and reduction of busy graph to build scenarios*

2. Weaknesses
    - *Currently undefined inhibitor and DNAse concentration sensor are integral to success of this architecture*
    - *May be sensitive to subtle fluctuations in "input" that lead to untimely demise of cell*
    - *Will need to consider points of failure from mutations in each component or failsafes will no longer operate*
    - *Testing for DNase "on"state will give rise to dead cells, I think.*

Some outstanding issues/questions…

- *Review which aspects of your system should be more digital in their transfer curves and which would benefit from some analog behavior*
- *Consider how tight promoters need to be if they are "on" and "off," or if you can live with/benefit from those that are "leaky"*

3. Opportunities

I think you have an opportunity here to really hit it out of the park. There will be some needed biology work to look at now that you have your framework in place. Don't be shy about enlisting your mentors to help with this part of the work. This project is clearly yours as a team and they can be helpful now (+ you'll be helping them remember this material too) if you drill into the details of what's possible together. It would be nice to consider in the next few weeks where your "proof of concept" application would be, since you've done a great job of making a platform technology but you'll need some instance proof to show it works.

Next steps
1. Perhaps look at recombination to flip promoters to get truly digital behavior
2. Define inhibitor and how tight the inhibition must be to keep cell protected from destruction
3. Define "DNase concentration sensor"—here is where a fusion protein to DNAse might be helpful. If you can fuse it to an integrase of some sort then will only make Inhibitor B when promoter flipped.
4. Think about where you'd like to see this applied first and how

Candidate consultants:

Drew Endy related to integrase/excisionase work,
Ron Weiss for gating of behaviors,
Chris Voigt for orthogonal promoters,
DNase enzymology (NEB?)

Other notes:
- Great connection of your project to what others had described in the afternoon
- Great connection to CCC hearings
- Loved the handout to help everyone keep the device in mind
- Good clarification of what will be physically linked DNA pieces vs device boundaries