Tucker Ely review of Bradley Karas

Hey Bradley! Fascinating system. Don't forget to look at the edited copy of your paper which I returned with this. I took notes directly on it.

A quick note on your figures: Visually I really liked this paper. The diversity of figure types was nice, and Figures 2 and 3 are downright beautiful. The only thing I would change is the font size on your axes and tick marks, and you legends. Remember when you generate figures you have to already have in mind what size they will end up being in the final paper. When you scale them after they are already made, you wind up making the font on the axes to small to read.

Abstract: The abstract is definitely concise, as it should be. However, stylistically, it is very chopped up and does not flow well (too many consecutive sentences are too short). Also, if you have results beyond simply measuring TE and active information, you should include that here as well. Someone should be able to read your abstract and skip the paper if necessary. The paper should detail the work that the abstract summarizes.

Introduction: I really like your introduction. It could be slightly shorter as it feels a little repetitive, but overall it flows much better than the abstract. Also, it does a great job it given readers the background and purpose for the paper.

Model Description: This section is too short. Although what you do have conveys quite a bit of information, I found myself wondering things like "what do your time-steps represent? I know that I can guess at it and probably get it right, but being explicit about it would help. Maybe open this section with a couple sentences on how gene/protein networks communicate, and how this is displayed in FIG 1. I feel also that explanations of active information and transfers entropy belong here. It is my opinion that the following results section should be digestible by your readers without new model information.

Results: I had to re-read your results section a few times, but I feel like this would have been mitigated by a much more through and inclusive Model Description as described above.

Summary/Discussion: Reading through this and jumping between it and you results section, I found myself wishing you had put more direct figure references in this section of the text. Tell me where to look. You present a lot of data, and it is complex. Navigate your reader's attention as best you can to the right portions of the right figures as you describe what is going on in the data. Feel free to insert arrows into the figures to add in this.

At the end of your results section I found myself wanting to know what it all means. You have the very difficult task of explaining a narrative to your readers that includes two complex subjects (protein network signaling and information measures on network dynamics).

Walking away from this paper, what I got out of it is that a healthy vs. a damaged p53 regulatory network manifests as a point vs. a cyclic attractor for the same overall network topology. Not sure if that is correct, but that's what I took away. I also remember that the path length changes, which ends up shifting the TE over different history lengths. However, in both of these cases, I'm not sure what they mean. How does this information correspond to, or cause, misregulation of apoptosis and senescence?