Editorial Review: Fisher

Thanks for your submission, which presents some intriguing original results for the mammalian cell cycle network that warrant further investigation. It was enthusiastically received. Before proceeding with publication, please address comments by the two reviewers, as well as the editorial feedback below (which does not address typesetting due to the article not being complete for submission).

* Please clarify why you say with confidence that the “overall dynamics of the system was preserved regardless of updating rules”. This seems inconsistent with the discussion just prior on the differences between the models – do you intend to mean that the key features are retained? If so, what are they?
* In what sense are you using ‘control kernel’ in the discussion after Fig. 3. Typically a kernel is a set of nodes but you appear to refer to control kernels in the plural. What do you mean by ‘knocking out’, be specific – do your remove the edges associated with the node? In general this part of the discussion needs to be clarified to be more precise for interpretation by your reader.
* Fig. 3 you may want to highlight your attractors.
* What is meant by “transfer entropy per node” since TE is measured between *pairs* of nodes? You note in particular the TE value of p27 – is that summed over all its pairs? What is meant by this statement? Other nodes are mentioned as having specific values that need to be clarified as well.
* Also, why do you say the distributions in Fig. 3 are scale-free? They do not appear as though they could be fit to a power-law distribution with any kind of efficacy – did you try and get a good fit? If so you should include the fit? I am also unsure of why you say the result of the TE scaling being scale-free is unsurprising. You should explicit state why a scale-free degree distribution (which you state you are unsure you have?) should yield a scale-free TE distribution, if that is the connection you intend to make and can find motivation for it.
* Fig. 3 has very intriguing trends. Where do your control nodes fall within this distribution (perhaps related to the question above about the values for pairs of nodes). You could perhaps expand on the discussion immediately following the figure.
* Fig. 4 – the curves fit to your AI distributions are misleading (the blue in particular has AI values above 1 which are not possible). I would recommend removing the fits and just plotting the values obtained. Can you rank order by either the wildtype or knockout to see a clearer transition in the trends?
* The discussion above Fig. 4 is interesting, but please explain more the significance of the differences observed.
* Ref Kim et al?