BE 159: Signal Transduction and Mechanics in Morphogenesis

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Questions to consider: Goentoro and Kirschner, "Evidence that fold-change, and not absolute level, of β-catenin dictates Wnt signaling"

Following are some questions that it will be helpful to understand when reading the paper. They are definitely not exhaustive, but useful to help you understand the motivation of the work and the experimental protocols.

1. What is Weber's Law?
2. Why does robust fold change detection rely on an aggressive β-catenin destruction complex?
3. What is positive feedback?
4. Why is it important for a cell to be in the "insensitive region" with regards to Wnt-induced fold change of β-catenin?
5. How does β-catenin overexpression lead to more sensitivity?
6. What evidence do the authors provide that fold changes in β-catenin, and not absolute levels, dictate cell morphology?
7. In what way does the Wnt/β-catenin signaling system have error checking?
8. Mechanistically, how might fold change (as opposed to absolute level) be detected by the gene expression machinery of a cell?
9. The authors use steady state analysis to generate their plots regarding responses to Wnt levels. Is this valid? How might we check this? What are the time scales associated with approaching the steady state.
10. The authors talk about a separation of time scales. What time scales are they talking about?
11. What are the dominant terms in the temporal dynamics of β-catenin?
12. Why do they do the experiments with human RKO cells?
13. What is a coefficient of variation (CV)?

14. What is the dorsal-anterior index (DAI)?
15. Why do the authors normalize the blots with respect to actin?