BE 159 Spring 2014

Talking points: Sprinzak, et al., "*Cis*-interactions between Notch and Delta generate mutually exclusive signalling states"

1. What does "lateral inhibition" mean?
2. What is "mutual inactivation"?
3. What do the authors mean by "signal amplification"? How is this amplificiation achieved in the Delta-Notch system?
4. How did the authors manage to separate the *cis* and *trans* Delta-Notch interactions experimentally?
5. Prior to this paper, common belief in the field was that Delta cis-inhibited activation of Notch, but Delta itself was not affected. What would the experimental results look like if cis inhibition were not mutual? How do the authors rule out this "enzymatic" model in favor of a mutual inactivation model?
6. Which interaction, the *cis* interaction or the *trans* interaction, do you think is more dominant in this system? What experimental observations support your opinion?
7. To demonstrate mutual inactivation, the authors must show that Notch receptors can inhibit ligands from sending signals. Do you see any possible issues with the experiment (referred to in Supplementary Figure 9) that is meant to demonstrate this effect?
8. A general theme of Notch-dependent patterning processes is that it is a "difference maker" between neighboring cells. Does the observed *trans* activation mechanism support this characterization? What about the observed *cis* interaction mechanism?
9. Based on the model in the paper, what would you expect to happen to the veins in a fly wing if we could gradually decrease or increase Notch levels (blue dotted line in Figure 4c) or the Delta profile (red dotted line in Figure 4c)?