BE 159 Spring 2014
Talking points: Dubuis, et al., "Positional information, in bits"

1. Turing speculated on how concentrations of morphogens might be determinants of the fate of a given region of a developing organism. He quickly moved on to his study on how non-homogeneous concentration fields are set up, leaving the fate of regions of high and low morphogen concentration for future consideration. Similarly, the Dubuis, et al. paper also does not consider the "read out" of the morphogen concentrations. What considerations for read out of morphogen concentrations do you think are important?
2. In an interview published as a companion to this article in *PNAS*, Bill Bialek said, "Here we are fortunate that not only did we learn how to measure things that the theory suggested would be interesting, but there are aspects of the data that look the way the theory says they should look. Now, does that mean the theory is right? No, it means it's productive." What do you think about Bialek's comment in general? How about as it pertains to this article?
3. Turing also had many comments on using theory in biology. He said, in the opening of his famous paper on morphogenesis, "...a mathematical model of the growing embryo will be described. This model will be a simplification and an idealization, and consequently a falsification. It is to be hoped that the features retained for discussion are those of greatest importance in the present state of knowledge." What do you think about Turing's assertion about his theoretical model? In reference to Bialek's comments, in what ways is Turing's model "right" and/or "productive?"
4. What is entropy? (It is obnoxious to write the question this way, but it is important to think about. What does entropy mean, especially in the context of this paper?)
5. What does mutual information mean intuitively?
6. I think something is awry with equations 1 and 2. Do you? Are equations 3-6 ok? Does writing the mutual information as a difference of entropies provide insights about its meaning?
7. In equation 10, the authors take $P(x|\{g_i\})$ to be Gaussian. What are some potential issues with this?
8. The authors scale the morphogen profiles to be between zero and one. Why would they do this? What potential issues does this present?
9. What do the authors mean when they say there is "hidden" information? What does this hidden information have to do with signal transduction?
10. Why is uniformity in spacial uncertainty a signature of optimal information transmission?
11. Why is it advantageous to have gradients versus sharp boundaries?
12. How does having multiple morphogens result in more information?
13. The paper takes the morphogen profiles as given and investigates the information content. It does not comment on how the profiles themselves are set up. Do you have any speculation on how they are set up? Could expression of other genes by the cells in the embryo have an effect on the morphogen gradients?
14. In his book, *Biophysics: Searching for Principles*, Bill Bialek says, "...maximizing information transmission is much more than just minimizing noise." What did he mean by this? What significance does this statement have in the context of the Dubuis, et al. paper?

15. I often like to think about theory providing "sufficiency" in describing biological phenomena. In other words, a theory can often answer the question: "Say we have observed X about a biological system, and we know Y depends on X. Is X sufficient to explain how we get Y? Or, do we *need* something else to explain Y?". In this paper, the authors carefully analyzed observed morphogen profiles and then applied information theory. To what extent has this paper convinced you that setting up the morphogen profiles of the gap genes is sufficient to get one-cell specificity? What else would we need to know to complete the picture?