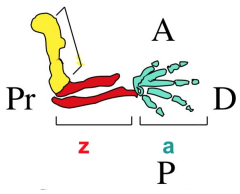
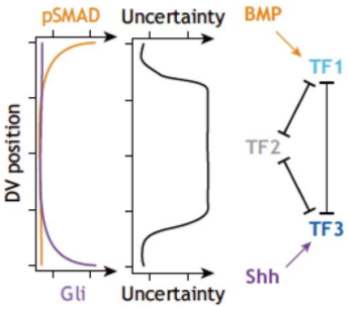
A guide to studying. Look over the slides and your notes, consider the questions asked in beSocratic - can you answer them clearly? Reflect on the following points.

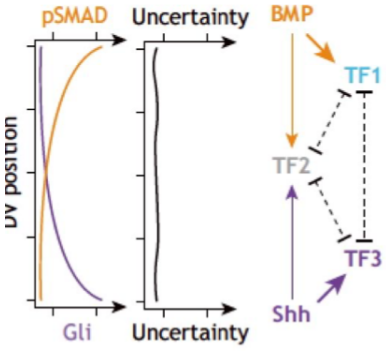
DEVO 2023 Course review - part 3

1. **Overall Goal**: to apply our knowledge of cellular and gene network (molecular) interactions to explain how perturbations influence the behavior of a morphogenic system.
2. In a signaling gradient, which factors influence the concentrations at which the system response initiates and saturates. What is involved in system responses? How does a system change over time, after an initial exposure to a signaling system (or altered gene expression, as in the case of somatic cell reprogramming?
3. Consider a regulatory loop, be able to describe how changes in rate and timing of synthesis and degradation can influence outcomes (the Hes7 system is a good model).
4. Describe how the establishment of the embryonic axis in the mouse (human) distinct from the process in Xenopus, fruit fly, or nematode.
5. Describe how, in Xenopus and other organisms, the process of gastrulation leads to changes in the interactions between cell types (be able to make a drawing, what important structures form during gastrulation?)
6. Consider general patterns of interactions (clock and wavefront) for the formation of the somites.
7. Consider the sources of asymmetry in the developing neural tube, and the specification of various neuronal cell types. How do HOX gene expression influence the neural tube?



8. In general terms, what are the basic processes associated with limb formation and patterning (axis formation)? What processes mediate the patterning of the digits? Indicate the position of Shh and FGF signaling centers in the developing limb. Predicate phenotypes associated with their loss or ectopic expression.
9. How can a single nucleotide change specifically effect Shh's role in limb but not the notochord/ neural tube? How do distant regulatory elements can influence gene expression.
10. What type of experiment can be used to demonstrate that gene organization (e.g. in the HOX cluster) matters?
11. Consider the problem a cell in a gradient (or between opposing gradients; how does it make decision early, when positional uncertainty is low versus later, when positional uncertainty is much higher.
12. Based on models of signaling pathways, how can signal timing influence the outcome (genes expressed, etc).
13. How can different cellular responses arise from the same set of signaling events.
14. Consider the expression of HOX genes in the limb, neural tube/somites, and neural crest?



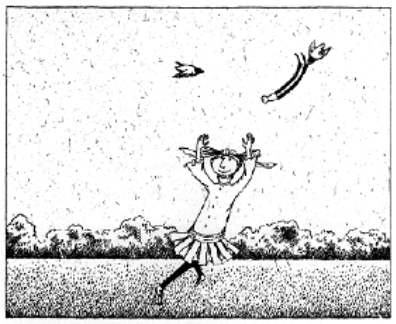


15. What factors the differentiation of neural crest cells (in general).
16. Explain why various "insults" (e.g. cyclopamine, ethanol, viral infection) often have greater impacts on the developing fetus compared to the adult.
17. Cyclopamine inhibits smoothened activation of the transcription factor GLI; why does this mimick the absence of Shh? You can use the Shh pathway from your notes.
18. Describe the differences between ES and IPS cells, explain the original of the variations seen when cells are examined by single cell RNA sequence during a developmental process.
19. You compare outcomes from the transgene approach to reprogramming versus the use of retroviral vectors that encode the Yamanaki factors, what are the drawbacks and benefits of each?

20. What exactly is an organoid? What types of factors determine (or influence) the types of cells / tissues formed? How (and why) does the species origin of the cells influence organoid formation?
21. How can neural (cerebral) organoids be used to study the effects of developmental perturbations (e.g. Zika infection)? What are the limitations of this approach?
22. How is metastatic cancer similar to neural crest, how is it different?
23. What are the general properties of a morphogen? Use an image (drawing/graph) to clarify your answer.
24. How can you best determine the expression domain of a particular gene. Why is RT-PCR not (generally) a good answer?
25. Under what conditions should genetic engineering of an embryo be allowed or banned? What are the social dangers of genetic engineering in humans?
26. Suppose you could generate a clone of yourself without a brain (for organ transplantation); would that be ethical or not?

MCDB 4650 DEVO – Course Review Questions (looking back and forward)

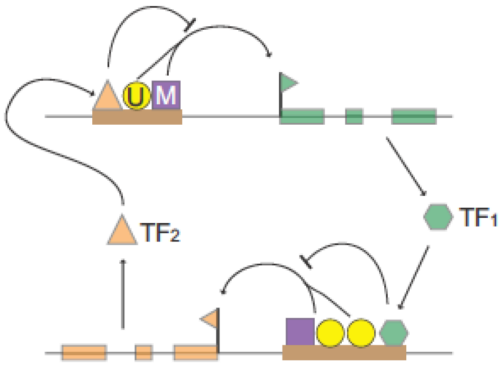
1. How would you define an animal?
2. How is quorum sensing in bacteria similar to and different from a morphogenic gradient in a metazoan?
3. When thinking about cellular signaling processes, what are the implications of the cell theory?
4. Under what conditions is it possible for social cheaters to arise?
   4b. Provide an example of a social cheating behavior in a multicellular eukaryotic organism and explain why, exactly, it is cheating?
   4c. Provide an example of a social cheating behavior in human society and explain why, exactly, it is cheating?
   4d. What processes can be used to limit / control / remove social cheaters? how do cooperative populations and organisms defend themselves against cheaters?



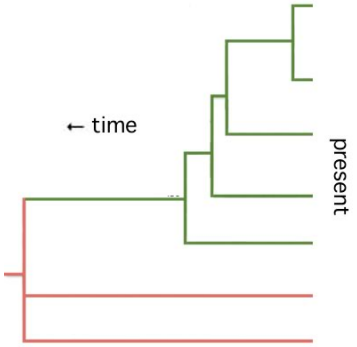
They enjoyed themselves very much until it was nearly evening;

5. How are cells inherently asymmetric?
   5b. Describe the differences between inherent molecular asymmetries and overall cellular asymmetries and consider their implications in the context of embryonic development.
   5c. Over and above internal asymmetries, how can cellular asymmetries be generated?
6. How are early asymmetries generated in *Drosophila*, *C. elegans*, Xenopus, and mouse (and presumably human) embryos?
7. What features are present (and essential) in all molecular machines?
8. Contrast the half-life of a radioactive isotope (atom) and the half-life of a molecule within a cell. How are they the same, how are they different?
   8b. What can lead to a change in the half-life of an isotope atom versus a biological molecule?
   8c. What factors influence the concentration of a biological molecule in a cell?
9. How is a polypeptide different from a protein?
10. What factors would you consider to decide whether a particular sequence of DNA was a gene?
    10b. How would you use mutations to test your prediction?
    10c. How might gene organization be used to control gene expression?
    10d. What factors would you consider to decide whether an RNA encodes a polypeptide? How would you test your prediction?
    10e. How can different, but related polypeptides be produced from the same gene?
11. What is meant by evolutionary "costs and benefits"? Why aren't organisms perfect?
12. What types of bacterial processes can benefit from quorum sensing control and why?
    12b. How can cells control who is included in their quorum group?
    12c. What, if anything, are the benefits of stochastic decision making? What features of the system insure that the process is stochastic. Consider a specific case, such as the lac operon, or make up your own.
    12d. Under what condition does "altruistic self-sacrifice" make biological (evolutionary) sense?

13. What kind of behavior(s) emerged in *Chlorella vulgaris* in response to the predator *Ochromonas vallescia*? (Borass et al paper)
14. What is meant by the terms homolog, ortholog, paralog, and convergence?
15. How do new genes arise? What is the role of gene duplication?
    What are the possible fates of a newly generated gene?
16. What is a null mutation? how can a null mutation have a genetically dominant effect?
    16b. Under what conditions can a mutation generate a dominant negative (anti-morphic) effect?
    16c. Describe a plausible mechanism by which a point mutation could lead to a change in the timing or pattern of gene expression. Given what you (now) know about embryonic development, how can such a mutation influence the formation of an embryonic tissue (e.g. the limb).
17. Sperm entry in Xenopus leads to a new, microtubule-based asymmetry; what is it about microtubules that allows for that asymmetry to develop?
18. What exactly is meant by ectopic expression and how is it done?
19. How, basically, could the expression of Myo1D lead to a change in left right asymmetry in an embryo?
20. What is meant by the term "chimera" in relation to a polypeptide or a gene? How is it possible that a chimeric polypeptide retains "wild type" functions?
21. How can a morpholino influence gene expression?
    21b. What determines the specificity of a morpholino? How is this similar or different from the mechanism that determines the specificity of CRISPR CAS9 mutagenesis.
22. What is going on (what is described) in this picture (→). What would you need to know in order to be able to predict the behavior of the system? Which genes are not shown in this figure? What proteins are implicitly assumed to be present, but are not shown?
    22b Which interactions might be cooperative?
    22c. How would a null mutation in the gene encoding TF1 influence the synthesis of TF2?

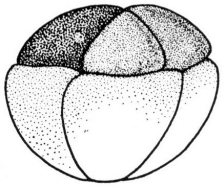


23. How would you go about determining how many enhancers a particular gene has?
24. Besides differences in the rate of mRNA synthesis, what other ways might you get a protein gradient?
25. We give you a TF sequence logo, how would you the rank binding affinities of various sequences?
    25b. In a similar way, we show you the sequence conservation of homeobox proteins, how would you predict, from the sequence of a particular protein's homeobox region, whether it will bind specifically to a DNA sequence?
26. What factors might influence the behavior (response) of cells at various positions along a morphogen gradient?
27. What characteristics of an organism would you use as a reasonable measure of complexity?
    27b. Does complexity always increased with evolutionary time? Are modern organisms necessarily more complex than long extinct organisms? Explain your reasoning.

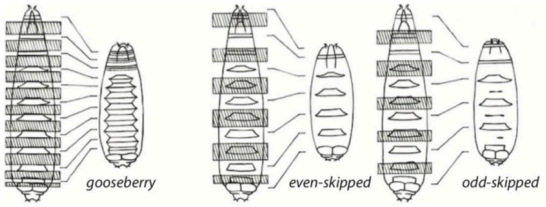


28. You are told that a gene is "essential"; what is the effect of a null mutation in that gene? Does the phenotype become visible before or after reproduction?
29. How might you prove that genes are not lost during embryonic development in most organisms? Why are genetic markers necessary for such an experiment?
30. Why are genetic markers needed to characterize the ability of a nucleus from a differentiated cell to generate a normal embryo (adult)?
31. How are the early blastomeres of a Xenopus (or *Drosophila* or *C. elegans*) embryo different from those of an early mouse (human) embryo.
    31b. How might you demonstrate that the blastomeres of an 8 cell mouse embryo are totipotent.

32. In broad terms, how are early embryonic axes determined in *Xenopus* (*Drosophila, C. elegans*) compared to mouse and other placental mammals.



33. How would you determine whether blastomeres in Xenopus or mouse are uniquely determined as the are in *C. elegans*.
34. How could a gene have more than one activity? Provide an explanation for how different mutations in the same gene could produce different phenotypes.
35. If the Drosophila embryo developed as does the mouse embryo, predict whether Wieschaus and Nusslein-Volhard's screen would have produce similar or different phenotypes - what types of phenotypes would you predict and why?



36. Is it possible for a maternal effect gene to be genetically dominant? explain how.
37. Using a graph of total mutations isolated and the number of genes identified, explain how you would decide whether a mutational screen had reached saturation.
38. What is the "simplest" type of homeotic mutation you could imagine in a mammal, what would be the phenotype and the molecular basis of the effect.
39. Explain what it is about the *C. elegans* embryo that makes identifying mutations involved in apoptosis easy to identify.
40. How does the process of compaction and subsequent cell division influence the differentiation and totipotency of cells in the mouse embryo?
    40b. Assume you identify a mutation that blocks cell-cell adhesion (e.g. a mutation in a cadherin or beta-catenin); predict its possible effects on compaction and subsequent development.
41. How is the migration and differentiation of neural crest cells influenced by factors involved in the patterning of the anterior-posterior and dorsal ventral axes of the embryo?

41b. How would you expect neural crest cells arising at different anterior-posterior levels of the embryo to vary molecularly.
    41c. What possible roles might the rest of the developing embryo play in the migration and differentiation of neural crest cells?
42. What systems are active in neural tube specification and patterning.