Spring 2014 Genomics Exam #3
Proteomics, Synthetic Biology & Systems Biology

There is no time limit on this test, though I don't want you to spend too much time on it. I have tried to design an exam that will take about the same amount of time as the first three exams this year. You do not need to read any additional papers. This exam consists of 12 questions and 1 paper. You are not allowed discuss the test with anyone until all exams are turned in no later than 9 am on Sunday May 11. **ELECTRONIC COPIES OF YOUR EXAM ANSWERS ARE DUE BY 9 AM ON Sunday MAY 11**. You may use a calculator, a ruler, your notes, the book, and the internet. You may print this test to work on your drafted answers, but make sure to dispose of your scrap paper so that no one will find it. You may take this exam in as many blocks of time as you want.

The answers to the questions must be typed in a Word file and emailed to me as an attachment. Be sure to backup your test answers just in case (I suggest a thumb drive or other removable medium). You may need to capture screen images as a part of your answers which you may do without seeking permission since your test answers will not be in the public domain. Remember to explain your thoughts in your own words and use screen shots to support your answers. Screen shots without ***your*** words are worth very few points. Support your answers with data using screen shots liberally (no permission required since your exam is a private document).

One characteristic of becoming educated is the ability to synthesize information so that you can distill the major points into a few key sentences. When your boss asks for a summary of the main points, he or she will not want a brain dump of all the information you have. For this reason, I am restricting your grammatical gymnastics and **limiting your answers by the number of words**. I will stop grading after the *n*th word as defined in each question.

-3 pts if you do not follow this direction.
Please do not type your name on any page other than this cover page.

Name (please type):

Write out the full pledge and sign (electronic signature is ideal):

How long did this exam take you to complete?

All the test questions are drawn from the attached systems biology paper by Garfield *et al*., 2013.

7 points

1) In 75 words or less, summarize the apparent contradiction under investigation in this paper. I other words, what two competing interests of the species are being studied by these researchers?

buffered development needs to be robust but flexible response to environmental changes and mutations

7 points

2) In 50 words or less, use Figure 1 to determine how the gene SM-30 is activated. Limit your answer to just the immediate cause, not all the way back to egg production. Describe SM-30 function using as many GO terms as you can find. (You may copy and paste as long as you provide the URL of your source.)

VEGFR + VegF ligand binding lead to the induction of SM30

- **Molecular Function**
  - binding (GO:0005488) — (IEA)
  - carbohydrate binding (GO:0030246)

http://www.spbase.org/SpBase/search/viewAnnoGeneInfo.php?spu_id=SPU_004867

20 points

3) Look at Figure 1 and find Notch in the endomesoderm integrated circuit of genes. Notice that it has only one arrow that winds its way upwards to point to a node. This node has a second arrow that also points to it.

3 points

a) In 40 words or less, what does this node represent?

Node = notch receptor binding to delta ligand.

2 pts

b) In 50 words or less, interpret the meaning of two arrows pointing to this single node.

Notch is translated from maternal mRNA in the egg as well as embryonically produced mRNA.

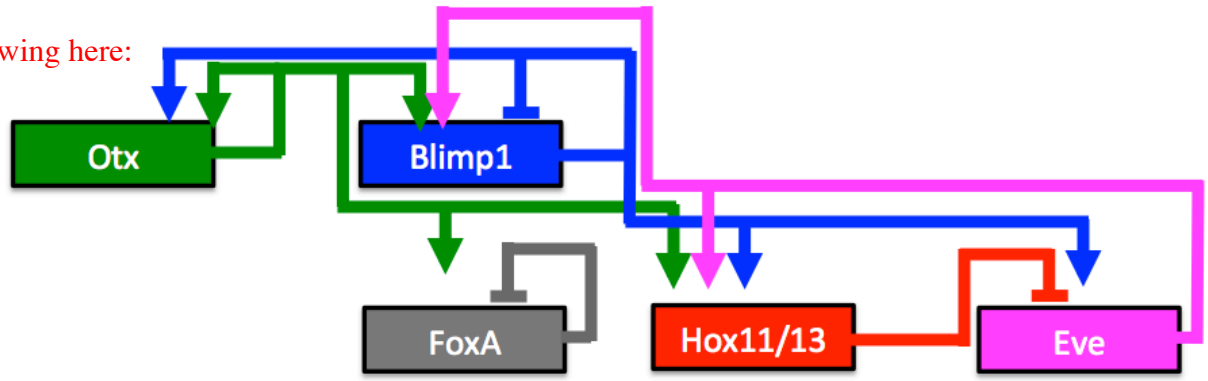
15 points

c) Find the maternal Otx and follow its arrow until it reaches Blimp1 in the endomesoderm integrated circuit of genes. Explain all the emergent properties exhibited by the subcircuit that contains these five genes: non-maternal Otx, Blimp1, FoxA, Hox11/13 and Eve. To answer this question, you must redraw (by hand and scan, or in a program and then insert screen shot) these 5 genes and their relevant edges. Then you need to use the numbered list below to analyze how each gene is regulated and any emergent properties exhibited by each of the five genes.

1 Otx: Induces itself (positive feedback loop) and also induces Blimp1, FoxA and Hox11/13.

2 Blimp1: represses itself (negative feedback loop) but induces Otx, Hox11/13 and Eve. By inducing Otx, Blimp1 is in an positive feedback loop as well. This creates a competition between positive and negative feedback loop.
3 FoxA: FoxA is induced by Otx and represses its own activity in a negative feedback loop. It has other edges outside this subcircuit.
4 Hox11/13: Is activated by Otx, Blimp1 and Eve. Hox11/13's only activity shown is repression of Eve which produces a negative feedback look for Eve.
5 Eve: Induced by Blimp1, repressed by Hox11/13 which sets up a competition to regulate Eve's activity. Eve activates Hox11/13 which produces a negative feedback loop. Eve activates Blimp1 which produces a positive feedback loop for Eve.

Drawing here:



7 points

4) What is the significance of Figure 2C in the context of this paper? Integrate Figure 2C with Figure 1 for this answer. Limit your answer 120 words or less.

3: Pmar is strongly transcribed in progeny from one female (light blue) while barely transcribed from the other larva in the population.
4: Pmar's only shown function is to repress HesC which represses 8 other genes. By having high levels early, these individuals would not express as much of the 8 genes as other larva. This early genetic variance indicates the pathway must be robust to withstand genetic variation in early signaling genes.

5 points

5) Interpret the biological relevance of the data in Figure 3. Limit your answer 100 words or less.

2 = At the earliest time points and stages of development, the maternal mRNAs and proteins have a greater effect. 3 = Later, the parental genotype has very little influence which means environmental factors have more over time.

7 points

6) Figure 4A has a profound impact on the take home message for this paper. Use Figure 4A to support the claims of the authors from this research. Limit your answer 120 words or less.

As time progresses, paired genes have higher correlation showing that as you get closer to the end of development, later events are more closely linked (environmental response = 1 pt) than the less flexible beginning of development.

15 points

7) Explain the inherent complexity of embryogenesis as exhibited by these three panels. Limit your answer 100 words or less for each panel. (5 pts each)

Figure 5A: consistant correlation throughout dev.

Figure 5B: toggle switch from off to on with consistent level once on

Figure 5C: different slopes as development progresses (steep followed by shallow)

7 points

8) The authors invented several complex visualization systems for this paper. Explain the meaning of the diagram in Figure 6C. Add to your explanation any apparent contradictions or aspects of the data that don't make sense. Limit your answer 150 words or less.

- shape of boxes matches circuit diagram
- yellow are regulatory and purple are structural
- early time points (red) correlated with structural changes in morphology higher in circuit
- number of inputs to a structural gene indicates its degree of importance for control of expression
- contradiction – early ones are buffered!
- some blue ones high up circuit
- FoxO (lowest blue box in regulatory area) has no known target

7 points

9) A reviewer of this paper claimed the authors have shown that early gene expression does not correlate with a morphological trait that would be subject to natural selection. Support or refute (your choice) this claim using data from this paper. Limit your answer 120 words or less.

various correct answers as long as supported with cited data

7 points

10) Which category of genes are the most sensitive to mutations that would lead to a phenotype change that could be acted upon by natural selection? List three genes as examples of the gene category you identified. Limit your answer 100 words or less (not counting list of 3 gene names).

C-lectin = no inputs or outputs and yet authors show importance (Fig. 6C, D and E)
FoxO = pioneer TF that affects chromatin instead of single genes (Fig. 6C, D and E)
SM30-E = terminal gene and direct impact on morphology (Fig. 6C, D and E)

3 points

11) What is a pioneer transcription factor? Explain how it differs from a regular transcription factor. Limit your answer 50 words or less.

affects chromatin broadly rather than single gene

8 points

12) In your spare time, you co-authored a grant proposal to the National Science Foundation to collaborate with this research group from Duke University. Describe in general terms the most important set of experiments you would perform next to push this research forward. Limit your answer 120 words or less.

proteomics experiments would be best answer
alter env. and see what changes