Fall 2003 Genomics Exam #3
Genomic Medicine and Sequencing Tools

There is no time limit on this test, though I don't want you to spend too much time on this. You know I work hard to design challenging tests, but not ones that are excessive. You do not need to read any additional papers other than the ones I send to you. There are three pages for this test, including this cover sheet. You are not allowed discuss the test with anyone until all exams are turned in at 2:00 pm on Friday December 18. **EXAMS ARE DUE AT 2 PM TIME ON FRIDAY DECEMBER 18**. You may use a calculator, a ruler, your notes, the book and the internet. You may take it in as many blocks of time as you need to. NOTE: I WILL BE OUT OF TOWN DEC. 12-16 SO DO NOT WAIT TO ASK ME QUESTIONS.

The **answers to the questions must be typed in a Word file and emailed to me as an attachment (redundancy for mission critical processes)**. Be sure to backup your test answers just in case. You will 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. Print this test but make sure the screen shots are big enough to be seen easily. Turn in the hard copy by the deadline to Mrs. Hartsell in the Biology Office or slide your test under my door.

-3 pts if you do not follow this direction.
Please do not write or type your name on any page other than this cover page.
Staple all your pages (INCLUDING THE TEST PAGES) together when finished with the exam.

Name (please print):

Write out the full pledge and sign:

How long did this exam take you to complete (excluding typing)?

20 pts.

1) In a recent paper, Jansen et al. (*Science* 302: 449. 17 Oct. 2003) working in Mark Gerstein's lab (a yeast lab) at Yale, designed a computer method to compile all known interactome and microarray data into a single set of protein-protein interactions. I am going to outline the main features that will allow you to use the database without having to read the paper. You should not have to read the paper to answer this question.

In their process, they measured the quality of the data suggesting two proteins interacted by comparing the data to known interactions (positive gold-standards) and proteins believed not to ever interact (negative gold-standards). MIPS was the source of their positive gold-standards because this database is curated by scientists who have personal experience with their proteins. Proteins localized to distinct compartments (Golgi vs. mitochondria) were used as the negative gold-standards.

They created three types of ineractomes from their work: PIP is predicted protein interactome; PIE is protein interactome based on experimental data; PIT is the union of PIP and PIE. The probability score (called L_{cut}) was determined to be 600 for interactions that had > 50% chance of really interacting for those in the PIP set.

Question Starts Here:

A. Go to <http://genecensus.org/intint>.
B. Click on the multicolor icon that is labeled "26S Proteosome".
C. You should see a short list of yeast ORFs.
D. Find an ORF to use as the central node that interacts with many other proteins most of which would have been included in the PIE. Grab a screen shot of this and insert it in your exam. Make sure it is big enough for me to read the labels.
E. Go to DIP and query the database with a node that indicates it has DIP verification. When you generate the display with your query ORF, grab a screen shot of this and insert it in your exam. Make sure it is big enough for me to read the labels.
F. Label the two nodes in the DIP image that were the two nodes in the Gerstein image (the original "bait" and the node you used to query DIP.
G. Comment on the degree of certainty DIP indicates for the interaction you have chosen.
H. Return to the node you identified in step D. Click on a couple gray nodes and grab one screen shot (your choice) of a new interactome. Do you see any results that suggest to you that these data should not be trusted? Based on what you see, what does the gray color indicate?

All the remaining questions are derived from a paper published in the 27 November, 2003 issue of *Nature* (Xiong and Ferrell). I have created two links for you to download the paper and a review article <www.bio.davidson.edu/courses/genomics/Exams/exams.html>. All of the information you need to answer the following questions can be found in the two papers plus a little background information I will provide below that will make sense once you read these two papers.

Background:

- When frog oocytes mature into eggs, the produce a small white spot that indicates they are mature eggs, but not fertilized.
- Germinal vesicles reside just under the plasma membrane of an oocyte and they decompose, or break down, to release their contents into the cytoplasm.
- Oestrogen (British spelling) is a hydrophobic hormone whose receptor has two cellular locations. The receptor is normally located in the cytoplasm, but when

oestrogen binds, the receptor relocates into the nucleus. Oestrodiol is a version of oestrogen that has no functional differences with oestrogen.

2 pts.
1) Use any database and determine the function of human Araf1. A simple sentence or two is sufficient. Include your source of information.

20 pts.
2) Using all the information in this paper, but only this paper, draw the circuit diagram (similar to figure 8.23 in style) described in this paper. The authors repeated refer to figure 1d, but this is a pathetic circuit diagram. Do a better job. In your diagram, be sure to include these components:
progesterone, Raf:ER, Cdc2, PD98059, Mos, cycloheximide, MEK, cyclin A, MAPK, Myt1, Cdc25, oestrodiol and Mos-AS. I do not want you spending your time searching for a website or book, etc that has many of these already diagramed. Please design your circuit diagram form information in these two papers only (primarily the research paper). Trust me, I have searched many databases to find a way to find this circuit and there is no place you can generate the right image except by doing it yourself. Besides, when you deduce this circuit, you will be in a much better position to answer the remaining questions. You may had draw this, or use a drawing program. Just make sure I can read it.

20 pts.
3) Explain the main concept and graphics (screen shots encouraged) in Box 1. Use a combination of your own words and the images in the box.

For questions 4 and 5: Be forewarned that one panel in a figure is less compelling than many panels so don't hold back on screen shots. However, you do not have to explain every single lane you show – just summarize the lessons learned from the panels you show.

15 pts.
4) Show data and explain them in your own words that reveal this system is a bistable toggle switch.

15 pts.
5) Show data and explain them in your own words that reveal this system requires positive feedback to sustain the signal that keeps eggs from reverting back to oocytes.

Short Answers:
8 pts.
6) A. Is this paper an example of genomic circuits that is biologically relevant? Explain your answer.
B. Do you think this is an example of systems biology as claimed by Jill Sible of VA Tech. who wrote the review article? Explain your answer. (As surprising as it may sound, VA Tech is one of the national leaders in proteomics.)