

Biology 4, Exam 2

*In compliance with the Dartmouth honor principle, all the work you hand in on this exam is to be your own. Please remember to be **precise** in your wording – scientific descriptions rely on accurate use of specific terms. Also, try to keep your answers **concise**. If you can say something briefly there is no need to create a lengthy answer just to fill up space. Use the space provided and the point values for each question as indicators of the amount of detail your answer should contain. If you really need extra space for an answer, turn the page over and continue your answer on the back of the same piece of paper. To facilitate grading, we separate the exam by page; if your answer is on a different sheet of paper we will not see it. **Please put your name on each page now.***

If something is not clear to you, please ask me during the exam. That is why I stay in the room. Good luck. - Prof. Gross

1. In prokaryotes, positive control is mediated by activators, while negative control is mediated by repressors. The Lac operon uses both kinds of control. Explain how each kind of control works in the Lac operon and how this control allows the cell to respond specifically to glucose and/or lactose. You can use a labeled diagram. **6 points**

negative control: Lac repressor binds to DNA to prevent transcription. If lactose is present it binds to the repressor and causes it to not bind to the operator regions, thus allowing the synthesis of lactose metabolizing gene products. Therefore, the cell will only make lactose metabolizing enzymes when there is lactose present.

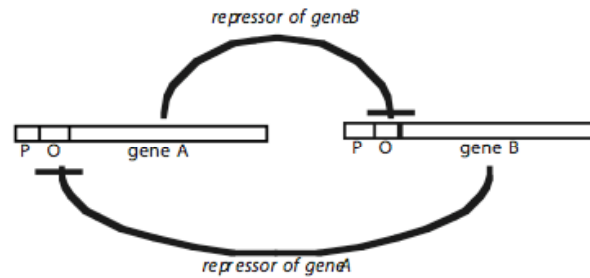
positive control: when the activator protein is complexed with cAMP (special small molecule in the book) it binds to an activator site near the lac promoter to stimulate transcription. If cAMP is not available, the activator protein cannot bind to the activation site, thereby only allowing a trickle of transcription to occur. The level of cAMP is inversely related to the level of glucose available (more glucose, less cAMP). This allows the cell to utilize its preferred carbon source, glucose, if both lactose and glucose are available.

2. Explain how T4 phage makes the switches from early to middle to late gene expression. You may use a labeled diagram. **4 points**

Early genes are transcribed using a promoter that is recognized by the bacterial holoenzyme (RNA polymerase core + host sigma factor). One of the products of the early genes is a middle specific sigma factor, while another product of the early genes is a protein that interferes with the host sigma factor. This serves to stop initiation at the early promoter (no host sigma is available) and start initiation at the middle promoter (core + middle sigma). Switching from middle to late works in a similar manner. One product of the middle genes is a late specific sigma; another product blocks the middle sigma. This causes a switch to late genes.

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3. Consider the situation in the figure.
There are two genes present that each synthesize a repressor to inhibit the other gene.



- a. Describe the state of balance of these two gene products in the cell. Is this a stable situation (can it become unbalanced easily)? **4 points**

Each gene will be transcribed at approximately the same rate since each gene synthesizes an inhibitor of the other. This situation is not very stable since any small change in the rate of synthesis of either gene A or gene B product will dramatically affect the balance.

- b. The cell comes in contact with a toxin that interacts with the product of gene A to render it unable to interact with the operator for gene B. Describe how this affects the state of balance of the gene products A and B. **2 points** Explain if this will be a stable state even if the toxin is removed. **2 points**

If the toxin is removed, gene A is still highly repressed and gene B is ON. Since there is no functional gene A product, gene B is not repressed. In this state, there is lots of gene B product and no gene A product being made. If the toxin is removed, there still won't be any gene A product being made because it is totally inhibited by the massive amount of gene B product around. Thus, the cell is now in a stable state with gene A off and gene B on.

4. How do transcription factors so precisely regulate the expression of different genes in different cells under different conditions? **5 points**

Different genes have specific collections of TF binding sites by which they are regulated. The level of activation of a gene will depend on which TFs are present in a cell (and on their concentrations) and on which specific sequences reside in front of a gene. If the gene has sites for binding many of the present TFs it will be transcribed at a high level. Fewer binding sites and TFs will lead to a lower level of transcription. As the conditions in (and around) a cell change, levels of different TFs change. This allows for very fine level of control of transcription for each gene.

5. What are the three major steps in mRNA processing in eukaryotic cells? **3 points**
cap the 5' end, add poly(A) to 3' end, RNA splicing removes introns

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6. How was the ability to splice RNA (the appearance of introns) thought to have provided an evolutionary advantage to primitive eukaryotic organisms? **5 points**
Primitive organisms are thought to have had small genes, each with their own promoter. The termination of transcriptions was not that efficient. Sometimes transcripts started in one gene and ran into the next. If a cell developed a way to splice out the intervening RNA, it could create proteins with new capabilities combining the functionality of the two original genes. The new capability could provide the cell with an advantage. This would all be possible without deleting or rearranging any DNA - meaning that if it did not work out to be an advantage, there was no permanent loss to the cell. On the other hand, rearranging DNA to create the new protein would be an irreversible process since the cell would have lost some critical DNA.
7. You have developed a gene therapy approach to curing cystic fibrosis in mice. You can deliver the “correct” gene into all cells in the mouse, yet you find that the delivery of this gene has no effect on the mouse’s symptoms - there is no improvement. Give one explanation why this might be the case. **4 points**
A number of reasons are possible. Here are some of them: the gene is not transcribed, the bad gene product is still made and interferes with the good gene product, the gene is inserted into a heterochromatic region and is unavailable to be transcribed.
8. In one of the videos we saw, pre-implantation genetic screening was discussed in the case of Molly Nash, a young girl who was dying from a genetic disorder, but could be saved by a bone marrow transplant. There was no compatible donor, however, so the parents had another child that could serve as a donor for Molly. Is it ethical to select an embryo for implantation based on its ability to serve as a donor to save the life of an older sibling? Jodi Picoult then discussed another case in which the younger sibling had to continue to give blood, bone marrow, and even a kidney to save the older child. Does this continuing need on the part of the younger child change the ethical situation? Please explain your thinking. **14 points** (continue on other side if needed)

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9. A theme addressed by a number of our speakers was supporting people with disabilities. Given that the government has a limited budget and must make choices in what programs to support, how should choices be made among education, support for our elderly, support for people with disabilities, social security funding, and support for other endeavors (such as foreign policy and defense programs)? **10 points** (continue on other side if needed)

10. Explain how the switch from early to late operon is accomplished in T7 phage infection. **5 points**

The early operon is transcribed by the host RNA polymerase starting from the early promoter. One of the products of the early genes is a T7 specific RNA polymerase. The T7 RNA polymerase then recognizes the late promoter and transcribes the late operon.

11. The globin gene family contains a number of genes that are very similar. The subtle differences between family members are thought to have coincided with the development of placental mammals. Explain how this works. **4 points**

In placental mammals, the fetus needs to get oxygen from the mother's blood. In order to do this, the fetus uses versions of the globin genes that have a higher affinity for oxygen than the adult (mom's) globin genes. After birth, the fetal globin genes are turned off and the adult globin genes are turned on.

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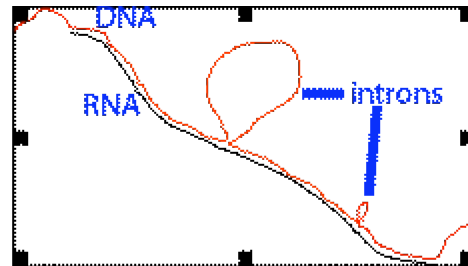
12. What are microRNAs and how do they work? **4 points**

MicroRNAs are small single stranded RNAs that bind to mature mRNAs in the cytoplasm. Their interaction serves to regulate translation of the mRNA.

13. tRNAs are interesting molecules. They all must be recognized (as generic tRNAs) by ribosomes during protein synthesis, yet they all must be recognized as specific versions (e.g. carrying a specific amino acid) within the cell. What features do they have that allow this apparent contradiction to work? **5 points**

tRNAs all share a cloverleaf structure that allows them to be recognized by ribosomes and other cellular structures. They all also share an anticodon at a specific location in the structure. Their specificity comes from the extra stem in the structure that has a different length for each tRNA and from the actual anticodon that specifies which codon the tRNA can bind to.

14. The figure at the right shows the result of a famous hybridization experiment between a globin mRNA and its corresponding genomic DNA. Label the DNA, the mRNA, and the intron(s). **4 points**



15. It is thought that humans have on the order of 20,000-25,000 genes yet can produce far more different proteins than that. How is this explained? **4 points**

This is due to the fact that many of the genes produce multiple different mRNAs through alternative RNA splicing in different tissues. This allows for more than one protein to be produced from the same gene under different conditions.

16. What is meant by the “RNA World” and what is its significance? **5 points**

It suggests that the first “living” things were actually RNA molecules. The original RNA molecule could replicate itself and not much more. Through errors, the RNAs developed additional abilities including protein synthesis. Eventually DNA evolved into the genetic material. Remnants of this world still exist as seen by the major role played by RNA in protein synthesis (rRNAs, mRNA), telomere maintenance (telomerase RNA), the use of RNA primers in DNA replication, finally miRNAs.

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17. What is a reporter gene and how is it used? **4 points**

A reporter gene is one that makes a product that is easily identified, such as a fluorescent protein. Reporter genes are typically placed downstream of a promoter to determine the conditions under which the promoter is active. Any tissue in which the promoter is active will be identifiable because it will be fluorescent.

18. What is an RFLP? Describe how RFLP patterns can be used in forensics. **6 points**

A restriction fragment length polymorphism is the result of small differences in the DNA sequences of different individuals in a population. Single base changes from one allele to another might cause the appearance of or the elimination of a restriction enzyme site or there could be different numbers of repeats between restriction sites. This would lead to different sized DNA restriction fragments corresponding to a particular location on the DNA from different individuals. These different patterns can be used to identify individuals. At crime scenes, trace amounts of DNA can be used to match with the RFLPs of suspects.