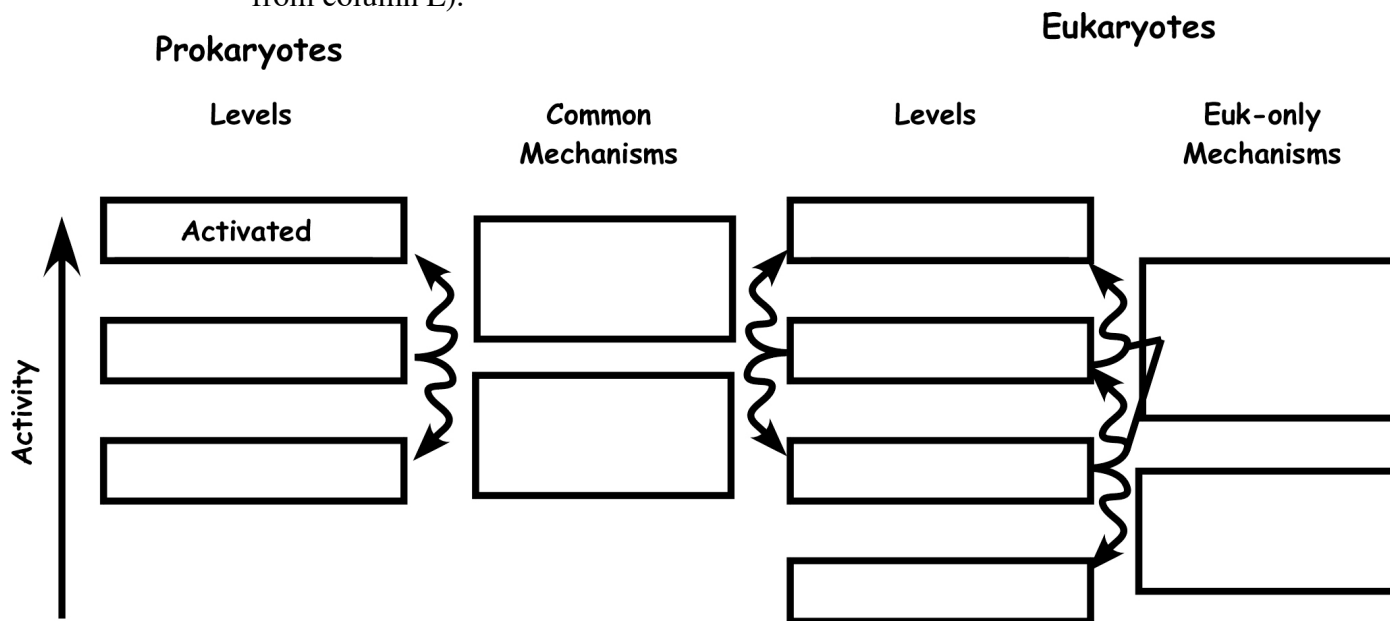


**1. (60 pts) Transcriptional Regulation**

(a; 14 pts) Fundamentally there are two different ways that prokaryotic transcriptional activators accelerate transcription initiation (the mechanisms are shared with eukaryotes). Name them and give a brief example for each.

(b; 25 pts) We discussed the idea that prokaryotes and eukaryotes are fundamentally different in terms of the levels of regulation of transcription.

- (i) Label the remaining two expression levels for prokaryotes and the four levels for eukaryotes.
- (ii) Specify how transitions are made between levels (fill in the boxes for mechanisms with partners like “transcriptional activators”).
- (iii) Indicate which is the baseline state for each kingdom (circle one from column P, one from column E).



(iv) Explain the heuristics of the baseline states -- why should it be this way?

(v) Explain how the different baseline state is enforced in eukaryotes.

(c; 11 pts) There are three fundamental mechanisms for chromatin remodeling. One is covalent modification of histones. Give a brief description of the histone code idea. Name one of the other fundamental mechanisms and briefly describe its function.

(d; 10 pts) In general, what do AAA+ proteins do? Name one and give its particular function.

## 2. (35 pts) Regulation by RNA

(a; 12 pts) We have described RNAi as likely descended from a sort of primordial immune system that defends against dangerous nucleic acids. What is the chemical nature of the dangerous nucleic acid \_\_\_\_\_? List two sources of this dangerous macromolecule. Describe one main advantage of using siRNA to knock down gene expression relative to a previously available method.

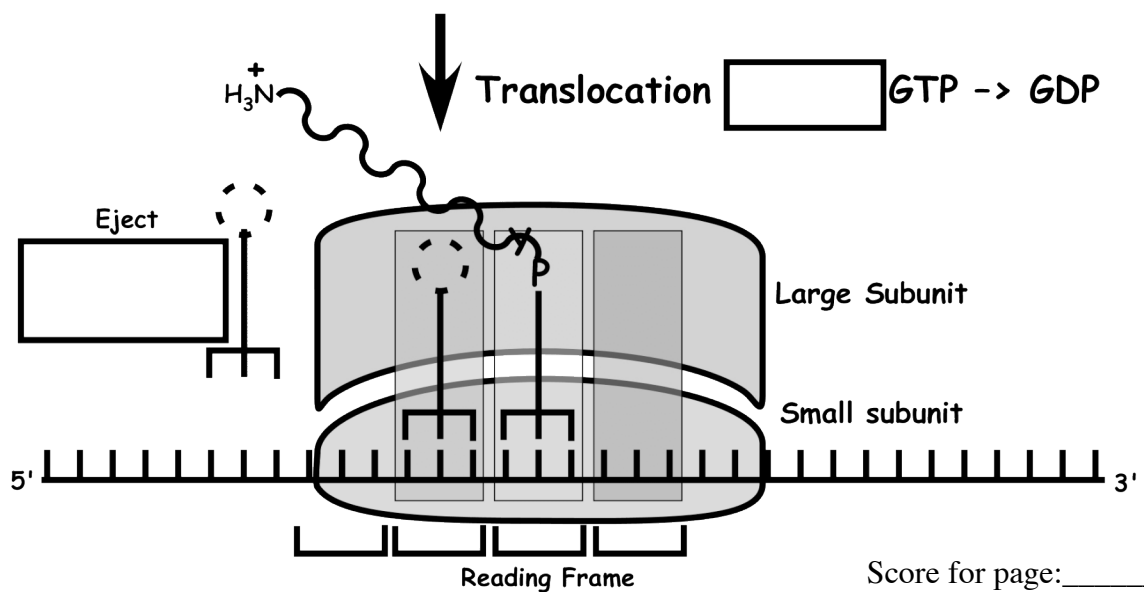
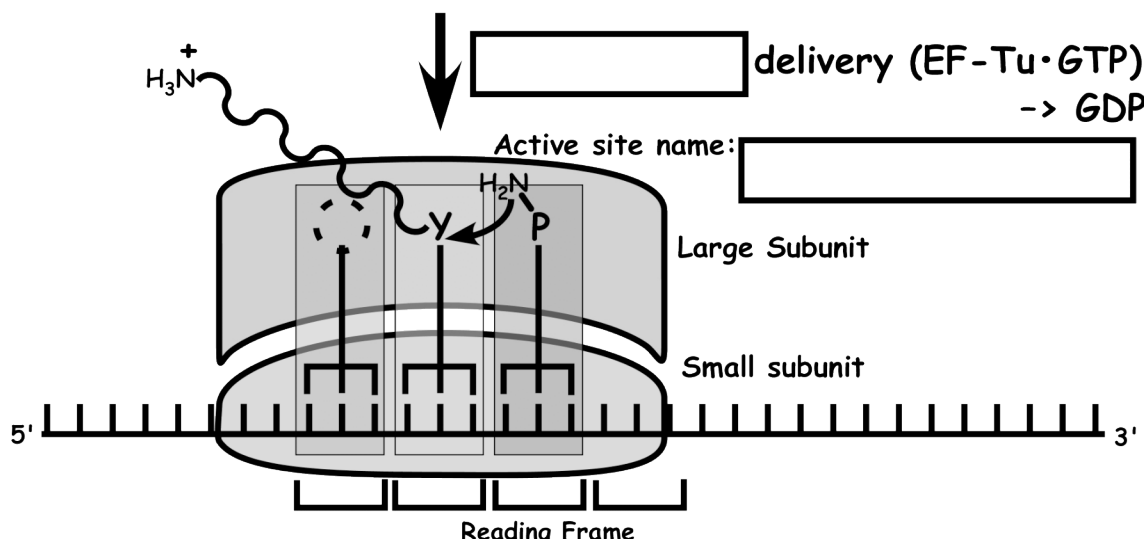
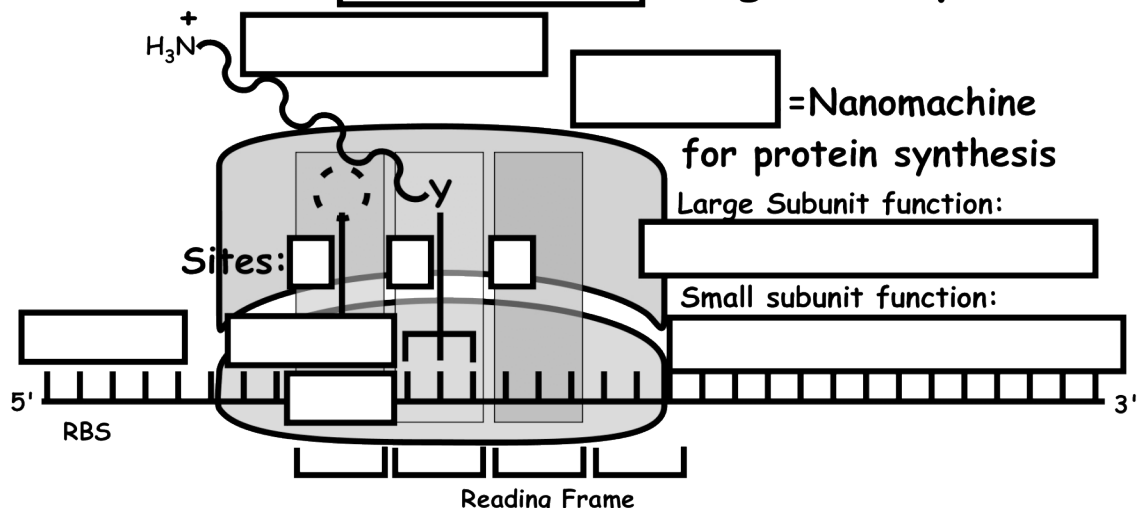
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(b; 7 pts) Micro RNAs (miRNAs) are processed similarly to siRNAs, although they often cause translation inhibition rather than mRNA cleavage. Give a plausible scenario for the evolution and the benefits of miRNA regulation.

(c; 16 pts) Sketch a mechanism of repression by a riboswitch in response to a small molecule ligand. This is an example of a (fill in)\_\_\_\_\_feedback loop. Consider the Trp repressor, which binds the promoter for Trp biosynthetic genes only when tryptophan is bound to the repressor, and the Lac repressor, which is induced by its ligand allolactose. Which one is part of the same kind of feedback loop:\_\_\_\_\_ (fill in).

3. (72 pts) A process that is part of the central dogma  
 (a; 20 pts) In the sketch below, fill in labels in all of the blanks.

### Essentials of Elongation Cycle



Score for page: \_\_\_\_\_

(b; 10 pts) What are the functions of burning each of the two GTPs in the process above?  
How was GTP hydrolysis represented in the movie shown in class?

(c; 12) What is the evidence that the ribosome is a ribozyme? Why has RNA catalysis by the ribosome been preserved when so many other presumed primordial catalysts have been replaced by protein? Why has RNA catalysis by the spliceosome been preserved?  
(Different answers)

(c; 15 pts) Aminoacyl tRNA synthetases are the guardians of the genetic code. They catalyze two sequential reactions. Write them out (names, not structures) and give the overall reaction. Fundamentally, why must they use ATP hydrolysis (why must the chemical step of protein synthesis be coupled to an exergonic reaction)? What sort of enzyme catalyzes the reverse of the protein biosynthesis reaction?

(d; 15 pts) What difficult and interesting problem do aminoacyl tRNA synthetases face in maintaining the genetic code? List three ways in which correct instructions in DNA could give rise to a protein with an incorrect amino acid (or stretch of amino acids).

**4. (33 pts) RNA Splicing and Processing**

(a; 16 pts) Sketch the chemical steps for either Group I intron self-splicing or pre-mRNA splicing. Why do we believe that RNA splicing is descended from self-splicing group II introns?



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(b; 5 pts) We have described the evidence for a primordial RNA world. What complicated enzyme was needed for the transition to a DNA world? Why is DNA preferable as the genomic nucleic acid?

(c; 12 pts) Sketch a generic example of alternative RNA splicing and explain why it is a relief to the human ego that alternative splicing is much more common in humans than in lower eukaryotes.

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