# Supplemental Material

***CBE—Life Sciences Education***

**Klymkowsky *et al.***

**Learning goals for MCDB 1150-003: Biofundamentals**

- To bring a recognition of the (uninterrupted) continuity of life (at the cellular, structural, dynamical, informational levels) from the origin of life to all current organisms. Students are encouraged to consider this basic biological fact in their descriptions and models of biological behaviors, traits, and scenarios.

- To be able to apply appropriate evolutionary mechanisms (mutation and genome dynamics, selection at both the individual and social levels, sexual selection, and stochastic (non-adaptive) mechanisms, such as genetic drift and gene linkage) to a generate a plausible analysis of a particular behavior or trait. In particular we use social evolutionary concepts to consider (and interpret) the behavior of multicellular organisms.


- To generate plausible molecular level scenarios (molecular machines) to be applied to essentially all cellular behaviors (DNA regulation and repair, gene expression, polypeptide synthesis and protein assembly and turnover.

  - This requires that students develop and be able to accurately apply an understanding of the factors involved in molecular interactions (affinities, on-off rates, concentrations), knowledge upon which our analysis of membrane structure and properties is based, as well developing a working understanding of the features of the molecules and macromolecules from which molecular machines are built, and upon which these machines act to carry out specific functions, e.g. the repair of damaged DNA, the movement of molecules across membranes, the coupling of chemical reactions, etc.

  - Students need to develop the ability to use their biological knowledge to apply or (if necessary develop) plausible models for biological behaviors, such as quorum sensing, programmed cell death, and other social behaviors, the stochastic features of the lac operon and differentiation (e.g. in *Dictyostelium*). This year we hope to extend this emphasis to a consideration of a range of stochastic bioligical behaviors, including the bursting aspects of transcription and translation.

# Relatives & Ancestors

Homology versus analogy is a topic in evolutionary biology that can be confusing to students. Homologous structures are those adaptations which have arisen from the adaptation of a common ancestor and so have a shared evolutionary history. Analogous structures are those which have arisen independently but are similar in form and function. They have arisen from different ancestors and different genetic backgrounds to solve the same evolutionary problem.

In order to find out how well students understood the idea of homology, we asked:

"What type evidence would convince you that structures in two different organisms are homologous?"

Here, we are looking for two major points. One, does the student understand that the structure should be similar in for and function? Two, does the student require some type of evidence to convince them that the structures arose from a common ancestor?

Nearly all students (87/96) understood that the structure needed to be similar in form or function. Additionally, 46% (44/96) students realized that the structures needed to be related by descent to be truly homologous. In terms of actual evidence, only 16 (~17%) students noted that they would require either fossil record data or genetic data in order to determine common ancestry:

> "I would like to go back into the fossil record to see if these two organisms had an identifiable common ancestor, where perhaps these two similar structures came from."
>
> And
>
> "DNA evidence would convince me that structures in two different organisms are homologous. This is because with mere cosmetic data, it is difficult to determine unambiguously whether the traits are similar because of convergent evolution or because of common ancestry. If I had an unusual boney ridge serving some purpose in a bird which appeared similar to such a ridge in another bird, I would not know if they were homologous or analogous without DNA evidence."

We clearly need students to understand that simply mentioning that the organisms must share a common ancestor isn't evidence enough. They must invoke a method for discovering common ancestry (through the fossil record or genetic evidence, for example).

As a follow-up, we delved more deeply into the students' understanding of analogous structures:

"Why doesn't convergent evolution produce exactly the same solution in different organisms? Why is a bat's wing not exactly the same as a bird's wing?"

Here, we are looking for an explanation of convergent evolution that makes it clear the students understand that the same evolutionary challenge is being solved in different ways with different physical and genetic make-ups. Complete answers will primarily acknowledge that features (or mutations that cause those features) arise independently from each other, and thus are quite unlikely to be identical on the genetic or phenotypic level:

> "Convergent evolution does not produce exactly the same solution in different organisms for several reasons. First, the mutations from which these 'solutions' arise occur independently; it is unlikely that two different organisms will experience the exact same mutations. Additionally, the 'solution' will be a product of the environment (and the organism's role in the environment)."
>
> And
>
> "Because they are still different species and will evolve in varying ways. Convergent evolution happens when only certain solutions to survival / reproductive problems are available, but species evolve to fit those solutions differently. Bats and birds both met the need to fly, but they had dissimilar traits before having wings that the types of wings that were advantageous to bats were slightly unlike those that were good for birds".

Students generally failed to answer the question correctly when their answer lacked detail or contained misconceptions about the evolutionary process, as below:

> "This is because natural selection is random so traits appear differently in different organisms."
>
> And
>
> "Because one of the fundamental laws of evolution is that whatever works is passed on. Both of these structures serve the same function, which increases the chances of that organism's success."

The above students likely had a general idea of the correct answer, but failed to formulate a robust explanation. Out of 96 replies, 79 (~ 82%) students crafted an acceptable response to this question, using the guidelines listed above, leaving only 17 (~18%) students who failed to use enough detail or who misunderstood the evolutionary process. Overall, this question was answered quite successfully, with a majority of students answering in an acceptable fashion that demonstrated an understanding of the materials at hand.

**MCDB 1150-003 FINAL 2015 NAME:**_____

***Directions***: You must take the final. There are a total of 25 two-part questions. Each question is worth a maximum of 6 points, for 150 points total on the final.

**YOU HAVE THE OPTION OF TAKING** one, two, or all three "I know it now" (IKIN™) tests. **Each is worth 25 points** and consists of 5 questions, each worth 5 points each.

If you want to take these tests **you must check here or we will not grade it!**

**I am taking:**

- □ **IKIN exam 1 (for midterm 1)**
- □ **IKIN exam 2 (for midterm 2)**
- □ **IKIN exam 3 (for midterm 3)**

**FINAL COURSE GRADES:**

| | | | | |
|---|---|---|---|---|
| **midterm 1 exam** _____ | **+ IKIN1** _____ | **=** | _____ | **(max 100)** |
| **midterm 2 exam** _____ | **+ IKIN2** _____ | **=** | _____ | **(max 100)** |
| **midterm 3 exam** _____ | **+ IKIN3** _____ | **=** | _____ | **(max 100)** |
| **midterm 4 + final exam** | | | _____ | **(max 150)** |
| **extra credit** | | | _____ | **(5 points)** |
| **NB** ____ **+ beSocratic** ____ | | | _____ | **(max 50 points)** |

**500 total possible points** _____ **total**

_____ **percent** _____ **letter grade**

**GOOD LUCK!**

**1. You have isolated and characterized a new organism,** a type of fern; its genome is 20 times the size of the human genome. This means that each of its somatic cells ….

- ☐ A. has 20 times as many genes as a human somatic cell
- ☐ B. has 20 times as many different proteins as a human somatic cell
- ☐ C. has 20 times as much DNA as a human somatic cell ☐ no idea
- ☐ D. the answer would depend on how the genome is organized

**Explain** why genome size is not a good measure of an organism's genetic complexity.

Grading rubric: The amount of DNA not equal to number of genes; much DNA does not consist of genes (various repetitive elements)

**2. You compare two related species** whose common ancestor lived approximately 50 million years ago; one is an obligate parasite of a single kangaroo species while the other is free living and is found in a wide range of environments. You would be justified in concluding that …

- ☐ A. the obligate parasite had a smaller genome and few genes
- ☐ B. both organisms have similar numbers of genes ☐ no idea
- ☐ C. the free living species would have a smaller genome and fewer genes

**Explain** the logic of your answer.

Grading rubric: Because the functions of many genes are being carried out by the host, the corresponding genes in the parasite can be lost without negative effects; these genes are preserved by selection in the free-living form.

**3. PICK THE WRONG ANSWER:** Consider the movement of a transposon from one place in the genome to another. Its movement could lead to a mutation in a host gene by…

- ☐ A. disrupting the coding region of the gene in which it inserts ☐ no idea
- ☐ B. disrupting the regulatory region of the gene in which it inserts
- ☐ C. inactivating the enzymes required for transposon movement

**Explain** why the wrong choice is wrong

Grading rubric: Such a mutation would block transposon movement, it would not influence host gene function.

**4. Scientists estimate** that, in humans, less than less that 10% of genomic DNA encodes genes (both regulatory and transcribed regions). To be completely certain that a particular region of DNA is not part of a gene, you would need to …

☐ A. examine whether it contains an open-reading frame ☐ no idea

☐ B. determine whether there are variations of the sequence within the human population

☐ C. determine the effects of mutations in that region on the phenotype of the organisms

**Explain** the logic of your choice.

Grading rubric: Because such mutations would disrupt gene function, and presumably produce a phenotype, that is, an effect on transcription, translation, cellular or organismic behavior.

**5. A region of the genome that contains four genes** is duplicated and moves into a new position within the genome**.** These genes are now …

☐ A. orthologs of the original genes

☐ B. paralogs of the original genes

☐ C. alleles of the original ☐ no idea

**Explain** why the two wrong answers are wrong or irrelevant.

Grading rubric: Paralogs are related by a duplication event, orthologs are related by vertical inheritance (ancestry). Alleles are different versions of the same gene.

**6. After a gene has been duplicated …**

☐ A. one gene will inevitably be inactivated by mutation

☐ B. the two genes are subject to the same selective pressures ☐ no idea

☐ C. one gene can evolve independently and assume distinct functions

**Explain** the logic of your choice.

Grading rubric: Once duplicated the two genes can evolve independently. There is no inevitable inactivation of one, and mutations in regulatory and coding regions can lead to different functions.

**7. The ability to import DNA into a cell** and use it as genetic material, as opposed to food, is the basis of …

□ A. mutation

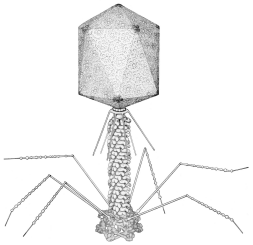
□ B. vertical inheritance

□ C. horizontal gene transfer □ no idea

**Explain** how this would look in an evolutionary context. Feel free to use a phylogeny to help explain your answer.

Grading rubric: A gene could appear in an organism that was not present in its immediate ancestor (parent).

8**. PICK THE WRONG ANSWER: Consider the process by a bacterial virus imports DNA into its head. Given what you know this is likely …**



□ A. to be a spontaneous, thermodynamically favorable process

□ B. to be a thermodynamically unfavorable process requiring coupling to an process such as ATP hydrolysis

□ C. to involve specific proteins, encoded by the virus □ no idea

**Explain why** the wrong answer is wrong.

Grading rubric: The movement of DNA (negatively charge) into a small space (the capsid head)would be an unfavorable event (-ΔG); it would be expected to coupled to a favorable reaction (NTP hydrolysis) likely to involve virally encoding proteins.

**9. A bacterial virus (a bacteriophage) can move DNA** from one cell to another. The amount of DNA such a virus can move is limited by the space within its capsid (head). We might predict that if a particular virus has lots of non-viral DNA in its head it would …

□ A. not be able to replicate when it infects another cell

□ B. be able to replicate perfectly well when if infects another cell

□ C. produce fewer viruses when it infects another cell □ no idea

**Explain** the logic of your answer …

Grading rubric: The normal viral genome, with genes essential for viral replication, will have been deleted to make room for the cellular DNA - this will result in the loss of viral genes, leading to a failure in replication.

**10. One response to viral (phage) infection** by a bacterium is that it will kill itself before the virus has a chance to reproduce. This also "kills" the virus. This type of behavior is an example of …

☐ A. natural selection
☐ B. social selection
☐ C. sexual selection ☐ no idea

**Explain** the evolutionary benefit of this type of behavior

Grading rubric: Neighboring bacterial likely to be related (relative), inclusive fitness applies.

**11. In Griffith's studies,** bacteria with the rough (R) non-virulent phenotype were transformed into bacteria with the smooth (S) virulent phenotype. What is going on?

☐ A. horizontal gene transfer of a wild type gene
☐ B. evolution of a new wild type gene
☐ C. a change in gene expression with the R type cells ☐ no idea

**Explain** the logic of your answer.

Grading rubric: The R-type cells picked up gene from dead S-cells encoding the gene responsible for virulence.

**12. In contrast to mitosis,** during meiosis new alleles can be generated when …

☐ A. DNA is replicated
☐ B. a cross-over event over occurs between genes
☐ C. a cross-over event occurs within a gene ☐ no idea

**Explain** why the wrong answers fail to generate a new allele.

Grading rubric: DNA replication occurs in both processes, crossing over between genes does not effect genes, no new allele generated.

**13. In contrast to mutations** that occur in somatic cells, mutations that occur in the cells of the germ line …

☐ A. can be passed to the next generation of organisms

☐ B. are efficiently repaired

☐ C. do not influence the phenotype of the organism ☐ no idea

**Explain** the logic of your answer.

Grading rubric: Mutations in the cells of the germ line can influence the next generation (passed to haploid cells - gametes) mutations in the somatic are not.

**14. Particularly in small populations,** the processes of meiosis and gamete fusion can influence the frequency of alleles in the next generation because …

☐ A. all alleles are passed from one generation to the next ☐ no idea

☐ B. which alleles are passed on is random, beneficial alleles can be lost

☐ C. these processes do not influence allele frequencies, only natural selection does that

**Explain** the logic of your answer.

Grading rubric: Since each gamete contains only one allele, and fusion is random, alleles can be lost, i.e. not passed to the next generation (resulting in genetic drift)

**15. Based on genomic sequence data,** you discover a gene present in barnacles and gorillas that is over 90% identical in encoded polypeptide sequence. These two genes are likely to …

☐ A. be the result of random genetic drift ☐ no idea

☐ B. reflect common ancestry and evolutionary conservation

☐ C. unrelated, with similarities due to analogous functions

☐ D. the same set of mutations occurred independently in the ancestors of the two species

**Explain** the logic of your answer.

Grading rubric: Because such similarity in sequence is unlikely to arise by convergent processes.

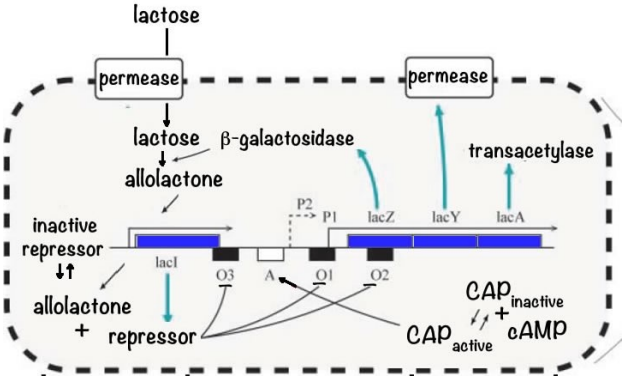
**16. Consider the lac operon,** its expression is regulated both positively and negatively. Its positive regulation (by CAP) insures that… ☐ no idea

☐ A. the operon is off when energy is abundant

☐ B. the operon turns on when lactose is present

☐ C. the operon is off if lactose is absent

**Explain** the logic of your answer.




Grading rubric: There is no need to expend energy to transcribe and translate the operon if another source of energy is available.

**17. Negative regulation of the operon** by the lactose repressor insures that …

☐ A. the operon is off when energy is abundant

☐ B. the operon turns on when lactose is present

☐ C. the operon is off if lactose is absent ☐ no idea

**Explain** the logic of your answer.

Grading rubric: There is no purpose to expend energy to transcribe and translate the operon if lactose is not present.

**18. The regulation of the activity** of both the lac repressor and the CAP proteins is an example of …

☐ A. post-translational modification

☐ B. proteolytic processing

☐ C. regulation of protein half-life

☐ D. allosteric regulation ☐ no idea

**Explain** the logic of your answer.

Grading rubric: cAMP acts as an allosteric regulator of CAP, while allolactone (lactose) acts as an allosteric regulator of the lac repressor.

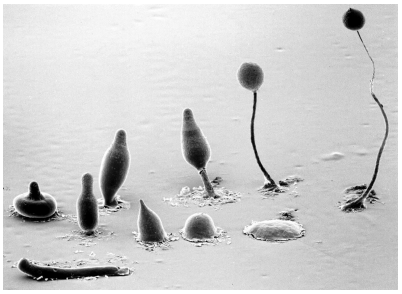
**19. A mutation occurs that disrupts** the ability of lac repressor to regulate the activity of the lac operon, the mutant cells would …

☐ A. always express the lac operon
☐ B. never express the lac operon
☐ C. express the lac operon whenever there were low energy levels in the cell
☐ D. lead to the death of the cell when lactose was present ☐ no idea

**Explain** the logic of your answer.

Grading rubric: Because without active lac repressor, as soon as the energy level drops, CAP would be active whether or not lactose was present.

**20. When starving**, cells of the cellular slime mold *Dictyostelium* aggregate to form a multicellular slug that can differentiates into stalk cells that die and spore cells that can reproduce. How might a mutation that creates a social cheater influence cellular behavior?



☐ A. Cheater cells would not form the stalk.
☐ B. Cheater cells would divide more frequently.
☐ C. Cheater cells would not form spores. ☐ no idea

**Explain** the logic of your choice.

Grading rubric: The cheater cells would avoid self-sacrifice for the good of the group, but insure they they became spore cells.

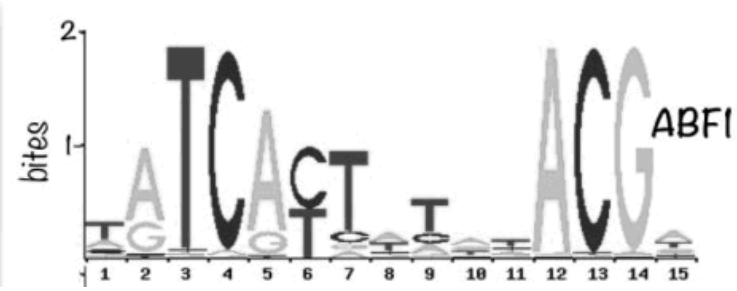
**21. PICK THE WRONG ANSWER: If individuals with "cheater" mutations** can avoid self-sacrifice and insure their survival and enhance their reproductive success, how is it possible that social processes can be maintained evolutionarily?

☐ A. Good behavior is its own reward. ☐ no idea
☐ B. A certain level of social interactions may be essential to reproductive success.
☐ C. Populations may be competing with one another and social interactions influence the outcome (that who wins) of this competition.
☐ D. Enhanced social interaction is a common outcome of random mutation and natural selection

**Explain** why the wrong choice is wrong.

Grading rubric: The social interaction trait does not emerge for non-evolutionary reasons. It must be selected for (or be link to a trait that is).

**22. Here is the binding motif for the positively acting ABF1 transcription factor** protein. A version of this motif is found in the regulatory region of the Xex gene, but it has Gs at positions 3, 5, and 10. A mutation occurs in a cell that leads to a dramatic increase in the expression of the Xex gene, it is most likely to be at which position?




☐ 3 ☐ 5 ☐ 10 ☐ can't be predicted, mutations are random ☐ no idea

**Which mutation** would produce the largest effect on Xex expression and explain why.

Grading rubric: The presence of Gs at sites 5 and 10 has little effect on TF binding, while the G at position 3 would likely abolish TF binding, a mutation at that site (from G to T) would generate a strong TF binding site leading to gene activation.

23. **PICK THE WRONG ANSWER:** Human female cells have two X-chromosomes while male cells have only one. Assume that in a particular population there are many different alleles for genes located on the X chromosome. The process of X-inactivation means that …

☐ different cells in a female that express a gene on the X chromosome will all express the same allele of a particular gene

☐ all cells in a male that express a gene on the X chromosome will express the same allele of that gene

☐ different cells in a female that express a gene on the X chromosome can express different alleles of that gene ☐ no idea

**Explain** why the wrong choice is wrong.

Grading rubric: Because expression is based on which X chromosome is active, and different X chromosomes are active in different cells, different cells will express different alleles.

**24. As a general rule you would predict** the greater the concentration of a specific transcription factor is present in a cell, the …

☐ the more noisy the target genes it regulates would be ☐ no idea

☐ the less noisy the target genes it regulates would be

☐ the noisiness of gene expression is not influenced by the concentration of regulatory factors

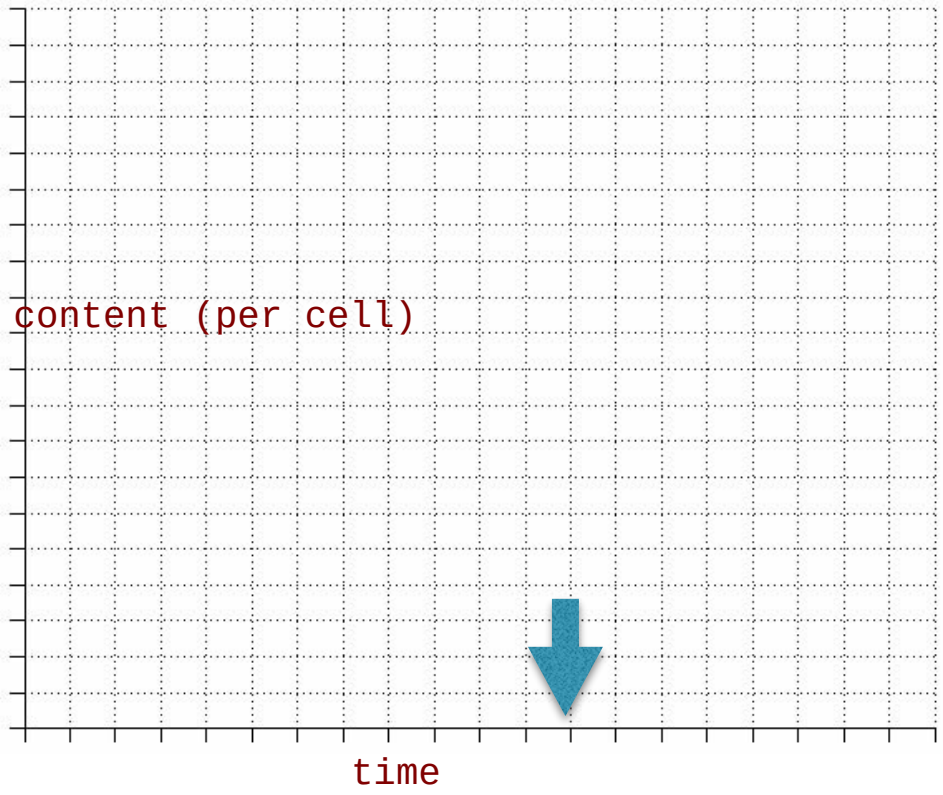
**Explain** the logic of your answer.

Grading rubric: As the concentration of the TF increases, the probability that it will occupy (bind to) its binding site increases (the level of noise) is reduced.

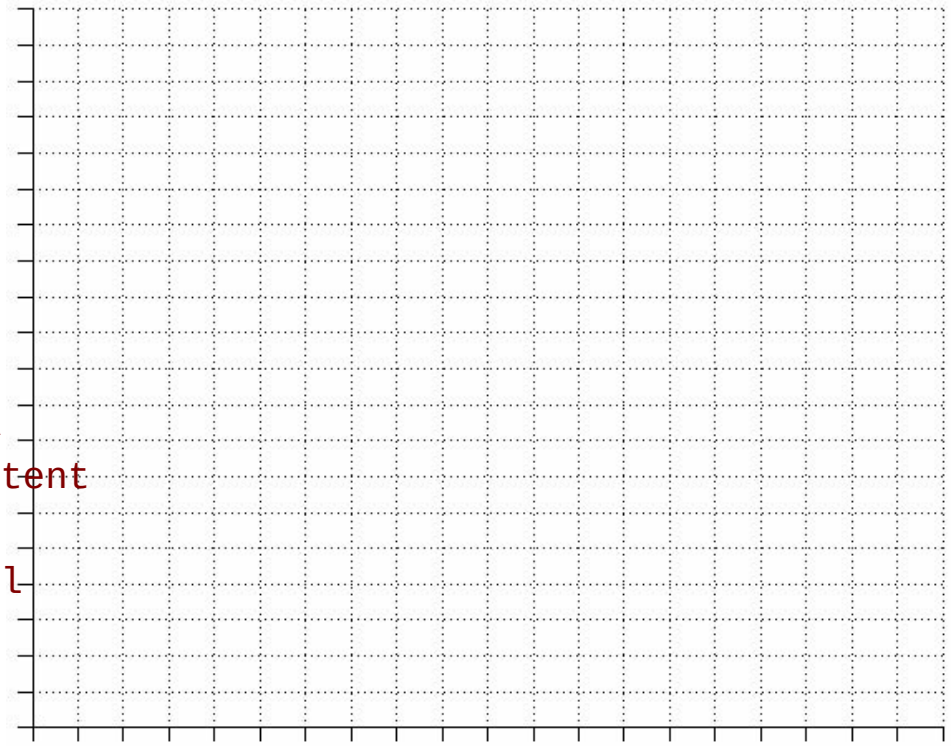
**25A. Consider a cell undergoing two rounds asexual reproduction (mitosis).** Take the time the two daughters separate from one another as time = 0. The cell will divide again at the point marked by the arrow.

Draw, as a function of time, the amount of DNA in an **individual** cell. On the graph indicate where DNA replication occurs. Make sure to mark your axes.

□ no idea




**25B. Now consider a cell involved in sexual reproduction.** Begin with final mitotic division that produces that meiotic cell, continue through the start of meiosis and end with fertilization, generate a similar graph of DNA content per cell.



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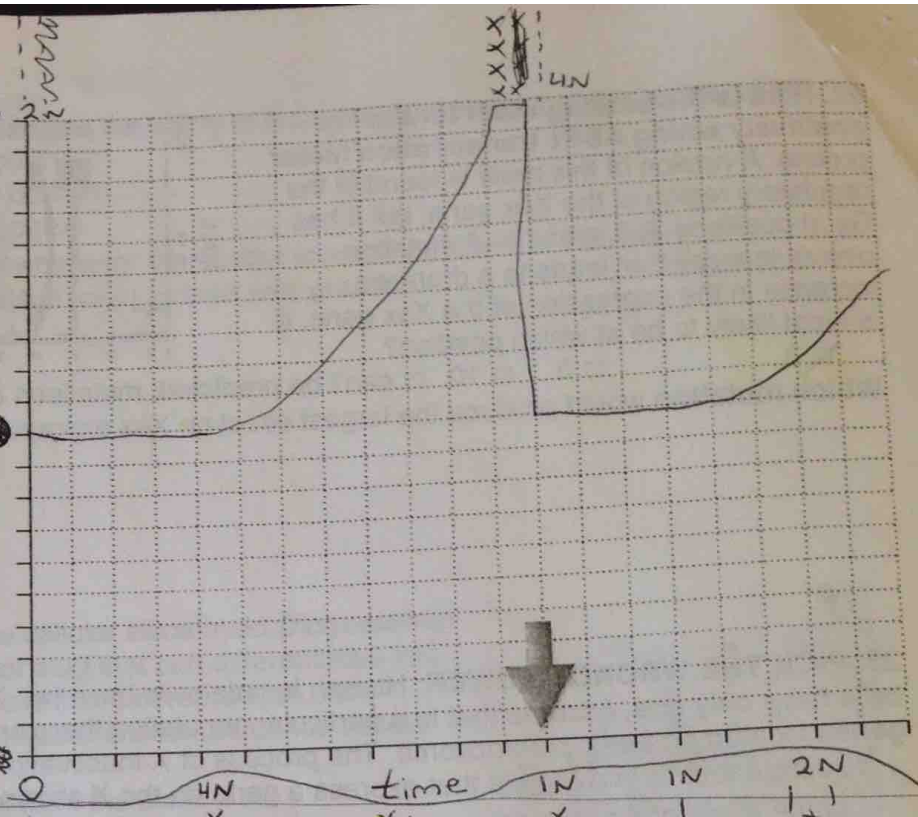
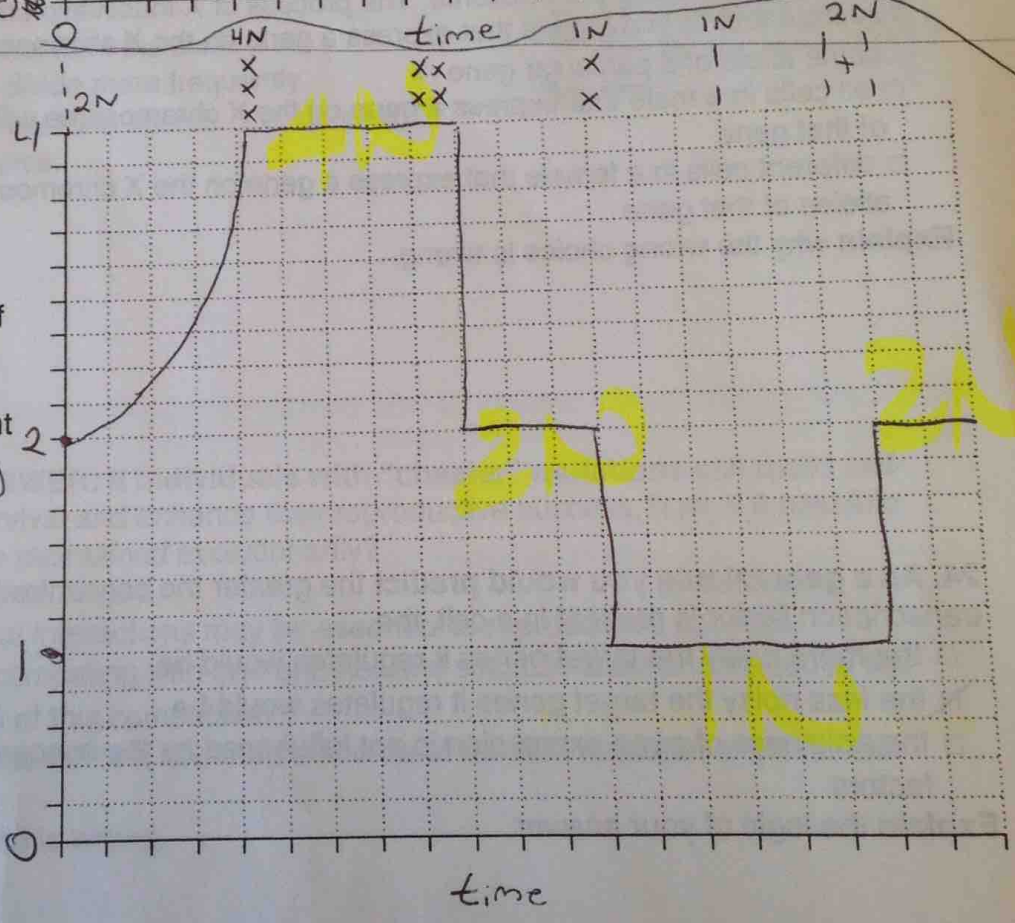
☐ no idea




**25B. Now consider a cell involved in sexual reproduction.** Begin with final mitotic division that produces that meiotic cell, continue through the start of meiosis and end with fertilization, generate a similar graph of DNA content per cell.



**"I KNOW IT NOW!" EXAM #1 (5 questions for a total of 25 possible points)**

**IKIN 1.1: Consider Sewall Wright's equation** r times b > c, where c equals a trait's cost in terms of reproductive fitness, b equals the benefits in terms of reproductive fitness of other organisms, and r equals the relatedness between the organism that pays the price and the organism that reaps the benefit. Now consider a small population, derived from a larger population, generated by a founder effect, which is likely to be true (assume that this is a sexually reproducing population)?

☐ A. r will be lower in founder population

☐ B. r grow larger as the founder population increases

☐ C. r will be independent of population size in both the original and founder populations

Assuming that you could measure the **exact** value of r for all pairs of organisms, what would a value of r = 0 imply?

Grading rubric: the individuals are not related at all, so there is no inclusive fitness effect (but all individuals are related, albeit often distantly).

**IKIN 1.2: PICK THE WRONG ANSWER: Models of evolutionary relationships** are generally based on ….

☐ A. Differences between organisms

☐ B. Similarities between organisms

☐ C. Similarities because they are more easily quantified that differences

**Explain** the logic of your answer.

Grading rubric: Trait similarities (including DNA sequences) are used to establish relationships; differences are not informative (at least with regards to relationships).

**IKIN 1.3: PICK A WRONG ANSWER (there may be more than one): While common patterns of evolutionary adaptation,** such as the multiple independent appearance of flight, occur, their details are not predictable because of ….,

☐ A. the common occurrence of non-adaptive small population effects

☐ B. internal processes that force organisms to specific ends

☐ C. the random nature of mutations and genome dynamics

**Explain** why the wrong answer is wrong (scientifically).

Grading rubric: The overall direction of evolution is driven by selection, rather than internal forces.

**IKIN 1.4: An aspect of the evolution of social organisms**, such as humans, involves mechanisms that encourage socially beneficial behaviors (such as a willingness to sacrifice for others, group loyalty and coordination, and feelings of guilt associated with social behavior. At the same time, there are processes that guard against the proliferation of social cheaters. A social cheater is ….

- □ an individual lives as a hermit, disconnected from others
- □ an individual benefits from, but does not reciprocate social interactions
- □ an individual who takes part in social interactions, but does not benefit from them.

**Explain** why your answer is the best answer and the reasoning behind it.

Grading rubric: Cheating presumes an individual taking part in a non-reciprocal efforts social efforts, gaining the benefit and avoiding the cost.

**IKIN 1.5: A: Draw a simple circular tree** (include a few species such as members of the bacteria, archaea, plants, fungi, animals) for the relationship between known organisms.

B: On your tree include and mark the process involved in the evolutionary origin of the eukaryotes.

C: Indicate below how would your drawing would change if current organisms were derived from two ancestors that themselves were derived from independent origins of life?

**"I KNOW IT NOW!" EXAM #2 5 questions (for a total of 25 possible points)**

**IKIN 2.1: For reactions to be coupled,** which is necessarily true?

- □ A. They must both be thermodynamically favorable
- □ B. They must occur in the absence of catalysts
- □ C. They must share a common reaction component
- □ D. Their reaction rates must be independent of temperature

**Explain** the logic of your answer.

Grading rubric: The shared common intermediate couples the reactions (Le Châtelier's principle)

**IKIN 2.2: PICK THE WRONG ANSWER: The cell theory states** that cells come only from pre-existing cells. What is passed from mother to daughter cells?

- □ A. an active system of coupled reactions
- □ B. a distinct type of chemical energy unique to biological systems.
- □ C. already synthesized transcription factors and RNA polymerases
- □ D. ribosomes and the factors required for polypeptide synthesis
- □ E. chaperone proteins required for protein assembly

**Explain** the logic of your answer.

Grading rubric: there is no biologically-specific type of energy, only chemical energy associated with bonds and entropic effects.

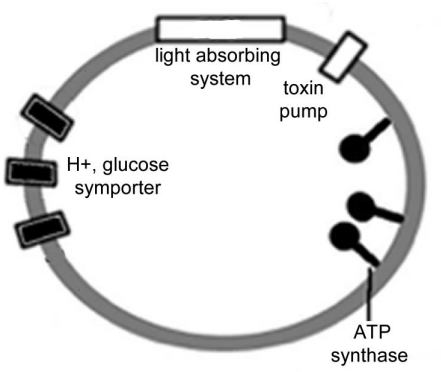
**IKIN 2.3: You are studying an obligate aerobic bacterium** that contains genes that are involved in the synthesis of a potent and secreted antibiotic that acts as an $H^+$ channel. How could it survive the presence of this antibiotic?

- □ Its membrane is completely different from the membranes of other organisms
- □ It does not use H+ gradients to generate energy or transport molecules across its membrane
- □ It also expresses an gene-encoded inhibitor the antibiotic H+ channel

**Explain** the logic of your answer.

Grading rubric: Such cells do not use an membrane-associated H+ gradient system to generate ATP synthesis

**IKIN 2.4: This is a simple photosynthetic organism.** It can actively pump out various toxin molecules, secreted by neighboring cells, that inhibit its ATP synthase.



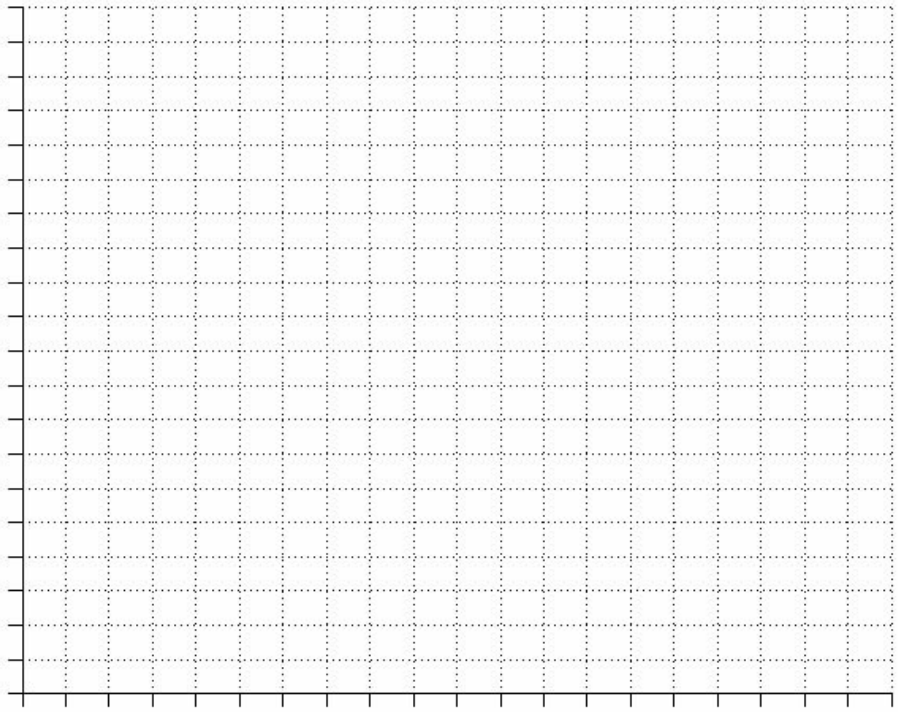

1) Indicate on the diagram which direction $H^+$s move in response to light.

2) Indicate where ATP is synthesized.

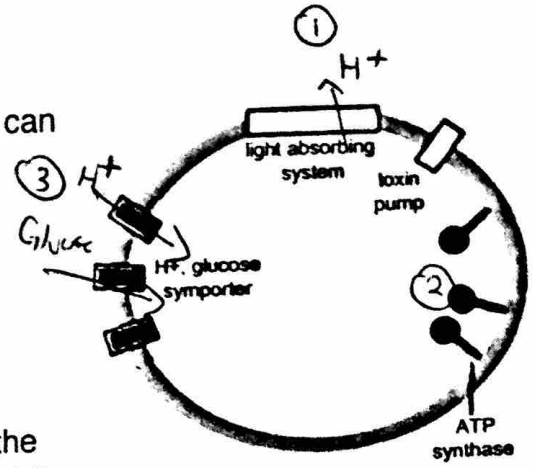
3) Assuming glucose is present at low concentrations in the environment, indicate which direction glucose will move while the cell is in the light.

PART B: NOW, assume that toxin begins to appear in the environment around time = 4 and that the gene that encodes the toxin pump is active **only** when the cell starts to experience low ATP levels.

Use the graph to indicate how the levels of ATP levels change over the course of a day.



**IKIN 2.4: This is a simple photosynthetic organism.** It can actively pump out various toxin molecules, secreted by neighboring cells, that inhibit its ATP synthase.



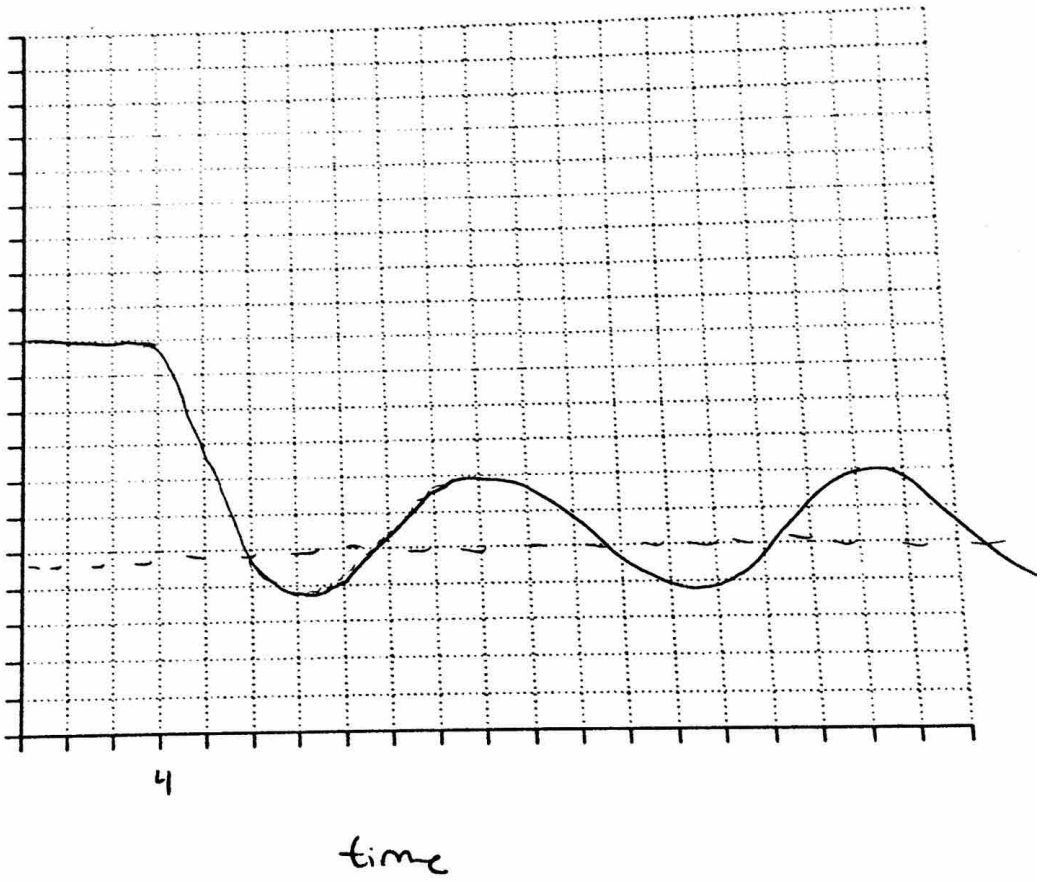

1) Indicate on the diagram which direction H+s move in response to light.

2) Indicate where ATP is synthesized.

3) Assuming glucose is present at low concentrations in the environment, indicate which direction glucose will move while the cell is in the light.

PART B: NOW, assume that toxin begins to appear in the environment around time = 4 and that the gene that encodes the toxin pump is active **only** when the cell starts to experience low ATP levels.

Use the graph to indicate how the levels of ATP levels change over the course of a day.




Toxin lowers ATP levels?

**IKIN 2.5**: Consider the reactions: reaction 1: $A + B \leftrightarrows 2D + C$

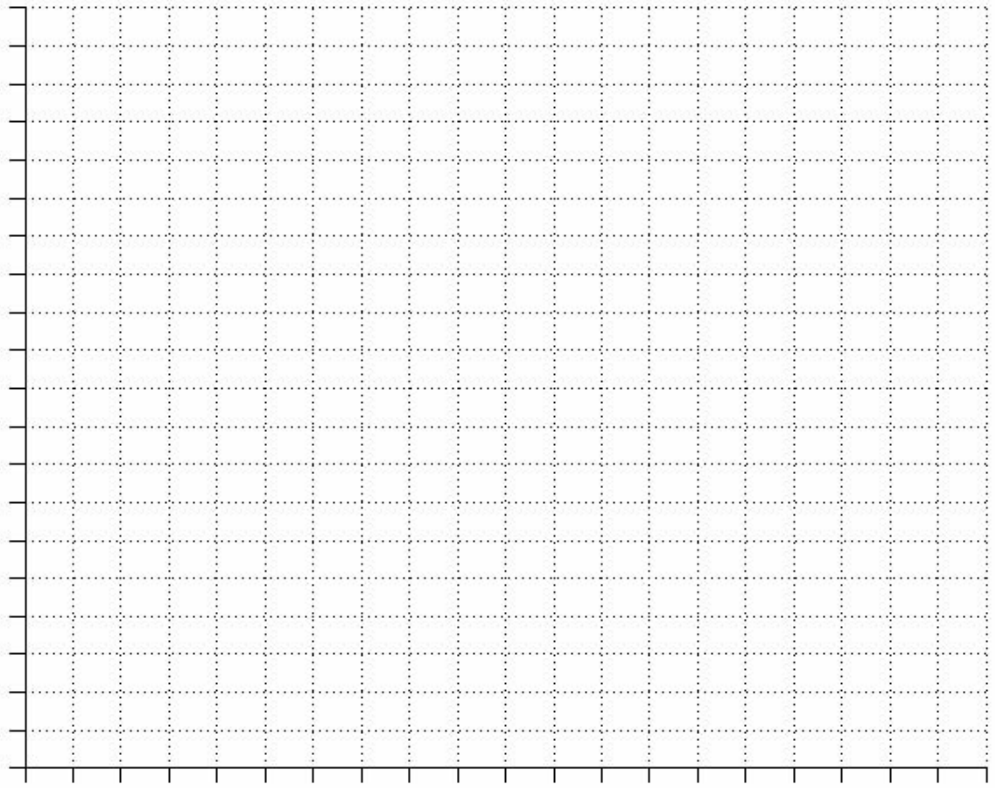
reaction 2: $C \leftrightarrows 2E$

Reaction 1 reaches equilibrium rapidly without any catalyst but it is highly thermodynamically unfavorable. Reaction 2 is very favorable but it requires a catalyst to occur to any significant extent.

You mix together solutions so as to end up with equal concentrations of A and B. After 15 minutes you add the catalyst for reaction 2; reaction 2 reaches equilibrium within 10 seconds. When you compare the concentration of D in the system before and after you added the catalyst, you will find that it has...

- ❏ increased
- ❏ decreased
- ❏ remained unaltered

**Generate a graph that describes the behavior of the system, and indicate the logic of your answer.**



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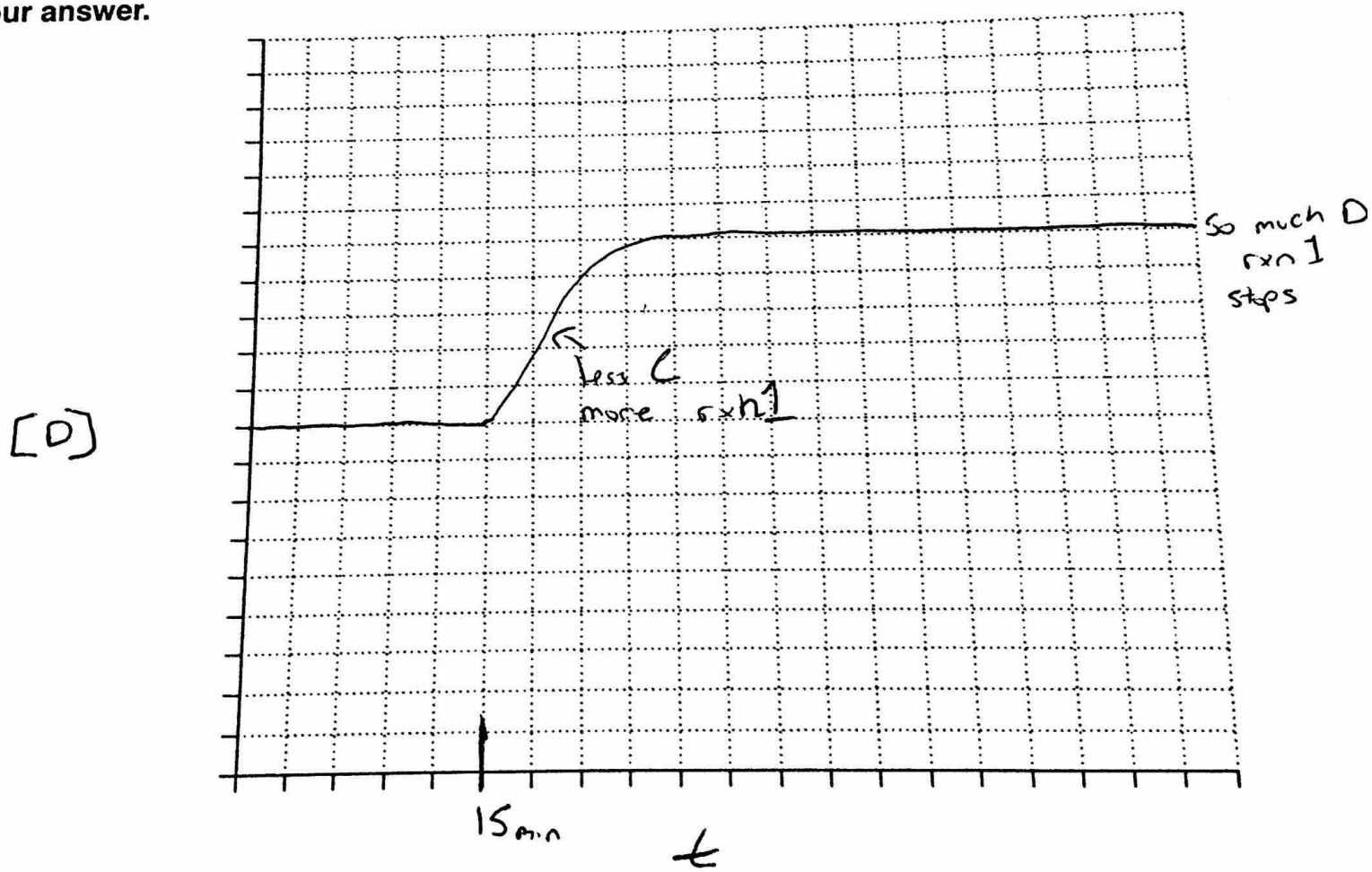


**"I KNOW IT NOW!" EXAM #3  5 questions for a total of 25 possible points)**

**IKIN 3.1: A protein is composed of 8 different polypeptides**; each is the product of a different gene. Disrupting the function of the protein would require …

□ a genomic rearrangement that disrupted the relative positions of the genes
□ a mutation in a single gene could disrupt the protein's function
□ mutations in at least half of the genes
□ mutations in all 8 gene.

**Explain** how these polypeptide can come to be assembled into a functional protein.

Grading rubric: They are generated through independent translation event; must assemble together (likely in the cytoplasm) that may involve a chaperone.

**IKIN 3.2: There are two different ways that abnormal folding of the PrPc protein** can lead to brain disease. One involves the transfer of the misfolded protein through cannibalism or surgery while the other involves a mutation in the gene that encodes PrPc. What does this mutation do?

□ decreases the half-life of the PrPc protein, thereby increasing its concentration in the brain
□ increases the probability that the PrPc protein will be misfolded
□ increases the rate of PrPc gene expression, thereby altering its concentration in the brain
□ alters the location of the PrPc in the cell

**Explain** the logic of your answer

Grading rubric: The mutation influences how the protein folds, favoring the pathogenic form.

**IKIN 3.3. Consider a human gene** that encodes a 380 amino acid-long polypeptide. You are studying the effects of two mutations. The first has a change in the amino acid normally found at position 65, while the second has a change in the amino acid normally found at position 360.

A comparison of the orthologs of the gene in other species indicates that the region between amino acids 20-80 is highly conserved, while the region between 320 and 380 is highly variable. You would be justified in predicating that …

□ A. the two mutations will have similar effects on the function(s) of the gene
□ B. the first mutation will have a greater effect on gene function than the second
□ C. the rate of the gene's transcription will be influenced to a greater extent by first mutation

**Explain the logic of your choice.**

Grading rubric: Because the mutation occurs in the conserved (functional) region of the polypeptide

**IKIN 3.4: PICK THE WRONG ANSWER: A mutation occurs that inactivates the nuclear localization sequence of a transcription factor protein.** You would expect to find …

□ A. effects on protein half life

□ B. effects on the intracellular localization of the protein

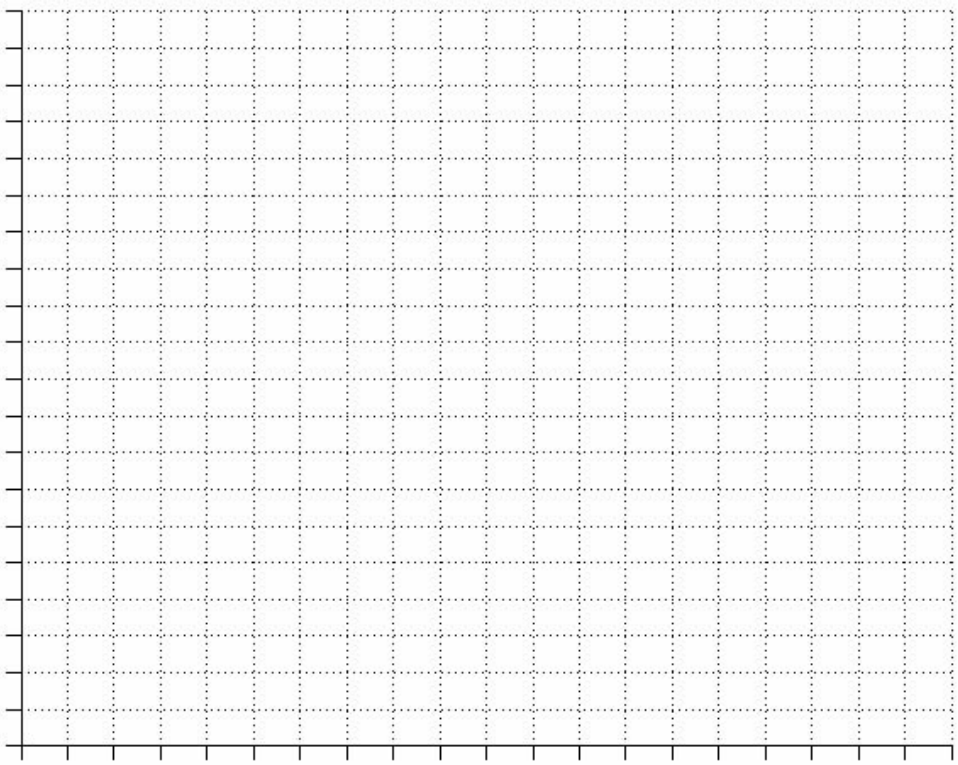
□ C. effects on gene expression

**Indicate** the most obvious direct and indirect effects of the mutation described above.

Grading rubric: while the mutation will effect polypeptide location (since it is in the NLS) and function (transcriptional regulation) these are correct, while there is no a priori reason to believe that it will influence half-life.

**IKIN 3.5: The GOO protein** contains distinct nuclear localization (NLS) and nuclear exclusion sequences (NES). When phosphorylated the GOO protein's NLS is activated and its NES is inactivated. Phosphorylation of the GOO protein increases the rate at which the cytoplasmic GOO protein is degraded but has no effect on the stability of nuclear GOO. The activity of this protein kinase is positively regulated by a small molecule, S.

Assuming that the rate of GOO protein synthesis is constant and that sufficient S is added at time 0 to activate the kinase throughout the course of your study, indicate on the graph how the amount of GOO protein present in the cytoplasm compares with the amount of GOO protein in the nucleus as a function of time (remember, label your axes).



Make a diagram to indicate what happens what S is added to the system.

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- ☒ A. effects on protein half life
- ☐ B. effects on the intracellular localization of the protein
- ☐ C. effects on gene expression

**Indicate** the most obvious direct and indirect effects of the mutation described above.

Direct:

Less transcription with the factor out of the nucleus

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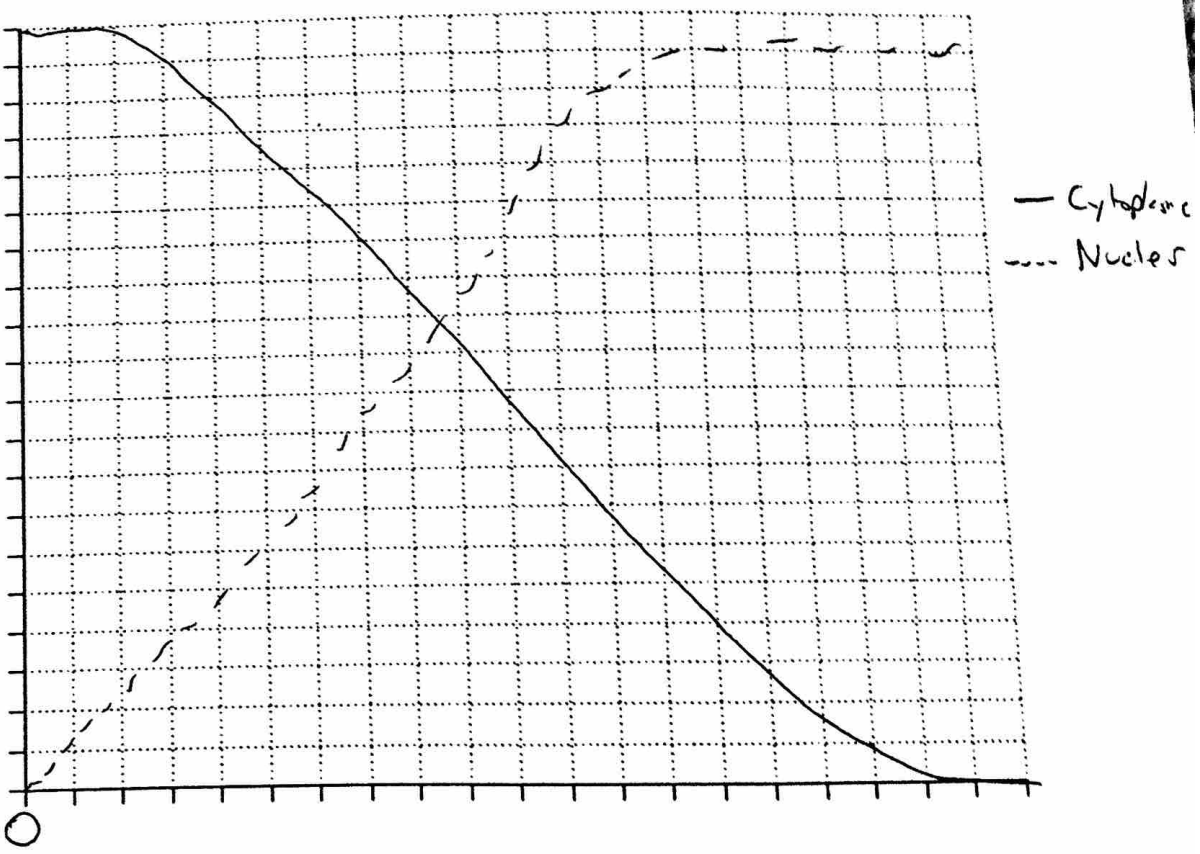


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