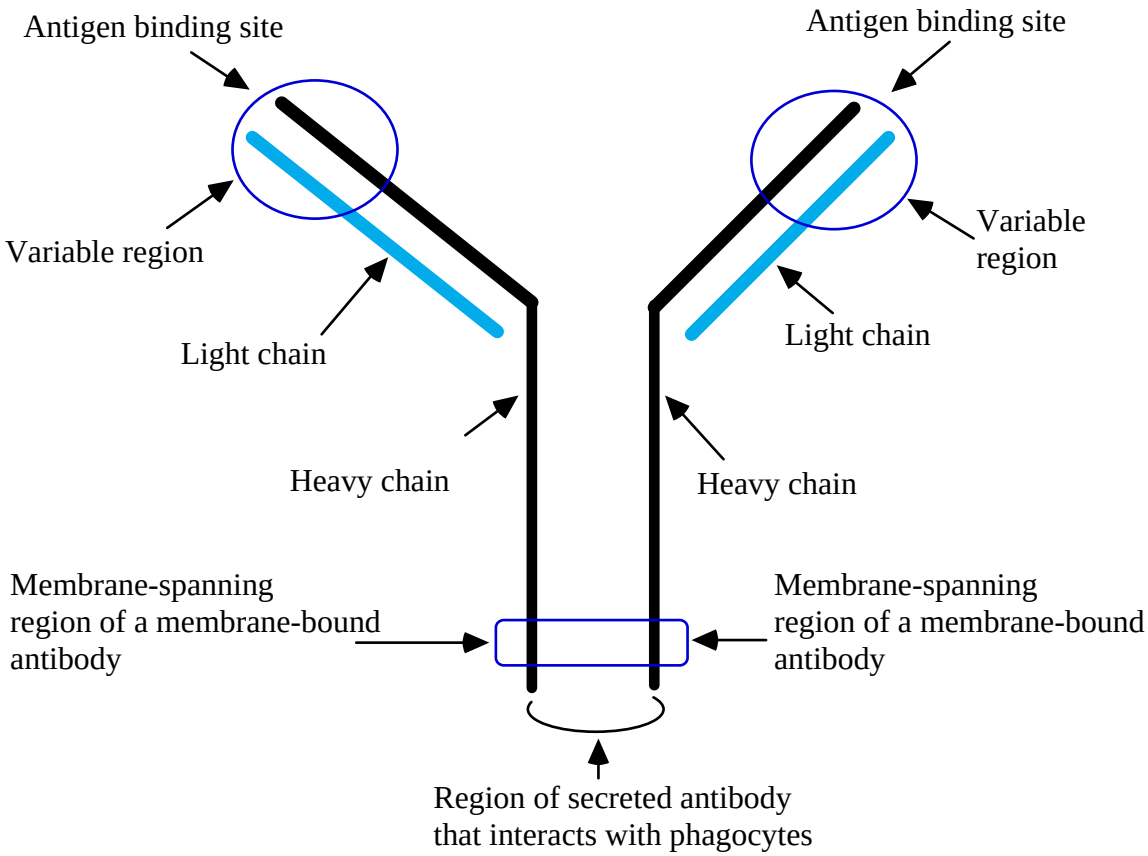
7.014 Problem Set 7 Solutions

Question 1

Part A



On the diagram label the following structures (a) – (d) on the antibody diagram.

a) the antigen binding sites

b) the heavy chains and the light chains

c) the variable regions

d) i) If this was a membrane-bound antibody, indicate the membrane-spanning region of the antibody

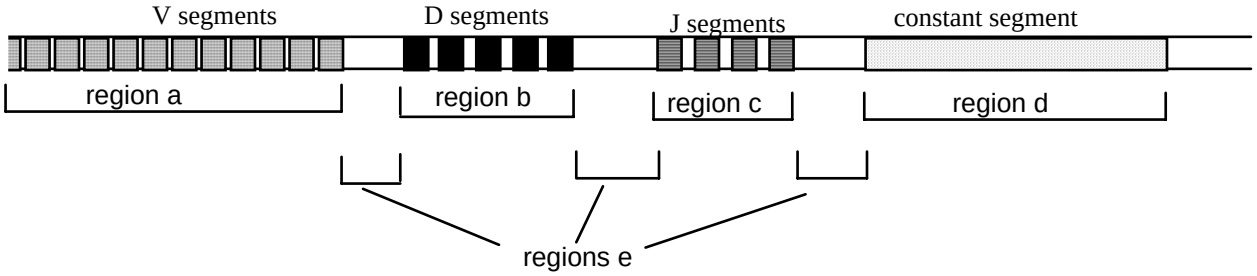
ii) If this was a secreted antibody, indicate the region of the antibody that would interact with phagocytic cells

e) List two ways that combinatorial joining generates antibody diversity.

1) Association of different light chains and different heavy chains
2) Recombination of different V (D) and J segments on the immunoglobulin genes.
also: Imprecise joining of nucleotides at the joining sites.

Question 1, continued

Below is a schematic of the unrearranged immunoglobin heavy chain locus.



a) Indicate which region(s) contribute(s) to the formation of the antigen binding site of the antibody molecule.

Regions a, b, c

b) After rearrangement, which region(s) would be the same in different B cells?

Region d

c) Which region(s) would never appear in any mRNA transcribed from this locus in a population of mature B cells?

Regions e

d) Cindy wants to store cell samples from her chinchilla so that in the future she can produce a clone. She has isolated cell lines from the following four different cell types. However, freezer space in the lab is limited and she can keep only one. Which cell line should she keep?

Red blood cell (Gut cell) B cell T cell

Why keep this cell line rather than the others?

She should keep the gut cell line. Red blood cells do not have nuclei, and B and T cells have rearranged the DNA at the antibody and T cell receptor loci, respectively

Question 1, continued
Part B

The virus which causes AIDS (acquired immune deficiency syndrome) is called HIV (human immunodeficiency virus). HIV is a retrovirus, and its genome is a single RNA strand. Two copies of this RNA genome are packaged with two copies of the retroviral enzyme, reverse transcriptase, within a protein capsid.

a) For HIV infection to occur, a surface protein on the virus must interact with a surface protein on the cell. HIV specifically infects the helper T cells of the human immune system. Give one reason that HIV infection is specific for helper T cells.
A viral protein on the surface of the HIV particle binds to a protein that is only found on helper T cells.
b) Once infection has taken place, the RNA genome has to be made into double-stranded DNA. This process is mediated by reverse transcriptase. Once a double-stranded DNA copy of the HIV genome has been made, it is integrated into the host cell genome. The integration event is mediated by an enzyme, integrase.

i) What are the three steps required to produce double-stranded DNA from the single strand RNA genome?
1. *Synthesis of the complementary strand of DNA using the single strand RNA genome as the template.*
2. *Degradation of the single (+) strand RNA template.*
3. *Synthesis of the complementary strand of DNA using the single strand of DNA as the template to form double-stranded DNA.*

ii) The central dogma states that: 

Which one of the enzymatic activities possessed by reverse transcriptase goes against the central dogma? Explain your answer.
The RNA-directed DNA polymerase activity used to synthesize a single strand of DNA from a single strand RNA template. The central dogma states that only DNA can act as the template for DNA synthesis (in replication), and that only DNA acts as the template for RNA synthesis (in transcription).

The drug most widely used to combat AIDS is Azidothymidine (AZT). AZT is very similar to thymidine, except that the 3' hydroxyl (OH) group on the deoxyribose ring has been replaced by an azido (N_3) group.

c) Which process of the life cycle of the HIV do you think is inhibited by AZT?
As an analog of thymidine, AZT interferse with the synthesis of DNA. HIV reverse transcriptase incorporates AZT instead of thymidine into the growing DNA and it blocks further chain elongation because there is no 3' OH group.
d) What side effects, if any, do you expect from AZT treatment?
While AZT will inhibit DNA synthesis mediated by reverse transcriptase, it will also inhibit DNA synthesis in other cells and thus kill cells that are actively dividing (e.g. red blood cell precursors, skin cells, etc. However, HIV reverse transcriptase prefers to use AZT over thymidine while host cell DNA polymerase prefers thymidine over AZT. Therefore, AZT may be used at concentrations that inhibit HIV replication but are not yet toxic to host cell polymerases.
e) AZT-resistant forms of HIV have been isolated. These mutant viruses have mutations in one of the viral genes. In which viral gene do you think are the mutations most likely to be found? Why?
The mutations are most likely to be in the viral gene coding for reverse transcriptase (the pol gene) because mutations in this gene may directly cause the mutated reverse transcriptase not to prefer AZT during replication and thus become resistant to AZT.

Question 2

a) Below is a Cohort Life Table for a population of gray squirrels. Fill in the remaining spaces:

Gray Squirrel Cohort Life Table

x	n_x	l_x	d_x	m_x	L_x	T_x	e_x	b_x	l_xb_x
0	500	1	0.7	0.7	325	794	1.588	0	0
1	***150**	0.3	0.06	0.2	135	469	3.127	0.5	0.15
2	120	***0.24**	0.048	0.2	108	334	2.783	2	***0.48**
3	96	0.192	0.038	0.2	***86.5**	***226**	***2.354**	2	0.348
4	77	***0.154**	***0.03**	***0.2**	69.5	139.5	1.811	2	0.308
5	62	0.124	***0.062**	***0.5**	46.5	70	1.129	***1**	0.124
6	31	0.062	0.046	0.75	***19.5**	***23.5**	***0.758**	0	0
7	8	0.016	0.016	1	4	4	0.5	0	0
8	0	0	0	0	0	0	0	0	0

b) When the table was made, some of the values were measured and others were calculated from those values. Which three values in the table must be measured in order to construct the rest of the table?

x, n_x, b_x

The gray squirrels have a high infant mortality rate (m_x), but those that survive tend to not die of natural causes until age five to seven. In the meanwhile, those that die do so because of a natural predator of the gray squirrel, the Sports Utility Vehicle (SUV).

c) Given the table above, what is the replacement rate (R_o) of the population? Is this population increasing, decreasing or staying the same?

R_o = 1.41. Because R_o is greater than one, the population is increasing.

d) A migration of SUVs into the area has increased the mortality rate (m_x) of all squirrels between the ages of one and four years by 0.2.

i) Calculate the number of animals (n_x) and the proportion of the original cohort surviving to each age (l_x) for the years one through five given this new mortality rate. For any fractional values of n_x, round to the nearest whole number.

$n_{1\text{-}5}$ = 150, 90, 54, 32, 19

$l_{1\text{-}5}$ = 0.3, 0.18, 0.108, 0.064, 0.038

ii) What is the new replacement rate for the population? Is this population increasing, decreasing or staying the same?

R_o= 0.892. Therefore, the population is now decreasing.

Question 2, continued

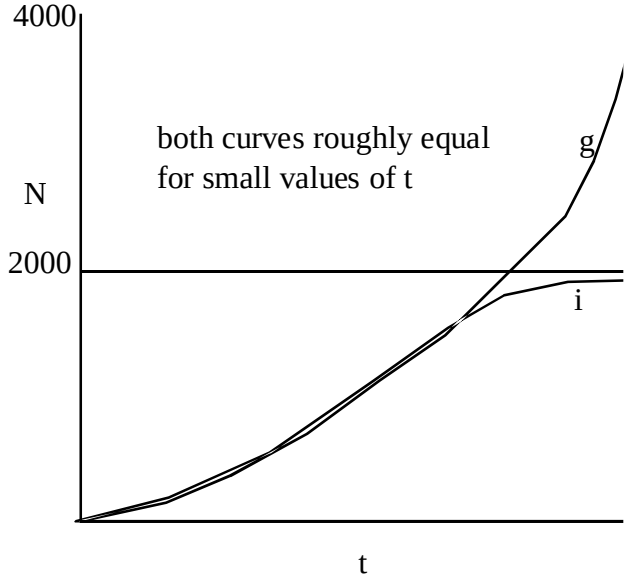
e) Given the original conditions, what is the generation time (G) of the gray squirrels? *(Hint: $G = (\Sigma l_x b_x x) / R_o$)*

$G = (\Sigma l_x b_x x) / R_o$ Therefore G = 4 years

f) What is the intrinsic rate of increase (r) of the gray squirrels? (*Hint: $r = lnR_o / G$)*

$r = lnR_o / G$ Therefore r = 0.086 per year

g) In the space below, draw a graph showing the growth of the cohort and its offspring as a function of time. Recall that $N_t = N_o e^{rt}$. Let your time axis go from 0 to 25 years.



h) How many gray squirrels are present after 25 years? Is this realistic? If so, explain why. If not, explain what we have not taken into account.

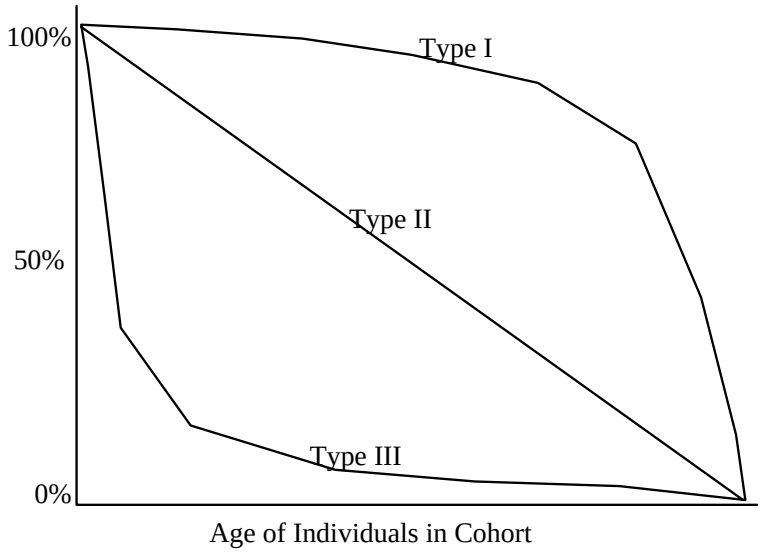
There are about 4,300 squirrels present after 25 years. This is not realistic because we have not taken into account any density dependent restrictions on the squirrels' growth such as limited space or resources.

i) If the carrying capacity (K) equals 2,000, make a very rough sketch of the growth of the cohort and its offspring on the graph that you have made above. Be sure to indicate which curve belongs to part g and which belongs to part i. Assume instantaneous feedback.

Question 2, continued

Survivorship curves reveal information about survival strategies of species. They are plots of the survival over time of individuals in a cohort (group of individuals in same population, born in same time period).

j) Draw three different types of survivorship curves (label your axes).



k) Use your drawing above to indicate which type of survivorship curve best applies to the cohorts given below.

i) Cohort of 20 sugar maple seedlings growing in the shadow of the parent, a tall sugar maple in mature forest.
Type III curve best applies, since the parent has generated many offspring but will invest no extra energy in caring for these offspring. In fact, in this case the parent is successfully out competing its offspring for the limited resource, light. When the tall sugar maple eventually dies, one or two of its offspring may grow tall to fill the gap created in the canopy. The other seedlings will remain small and will presumably die at a young age.

ii) Cohort of 100 babies born at Mass General Hospital.
Type I curve best applies, since human infant mortality is relatively low (when high quality health care is accessible) and since humans invest a tremendous amount of energy in caring for their offspring.

iii) Cohort of 1000 zooplankton in a lake containing a stable fish population which preys on zooplankton.
Type II curve best applies. Parental zooplankton don't invest energy in caring for their offspring. In this case, survivorship will mainly be determined by the rate at which the fish preys on the zooplankton. Presumably zooplankton don't acquire skill at avoiding predation as they age, so each zooplankton should be at an equal risk of predation throughout its life.

iv) Cohort of 100 corn plants planted and cultivated on a farm.
Type I. Plants will be protected from disease and predation and will live until they are harvested.

Question 4

Researchers isolated the XYZ protein from 12 different organisms (some extinct and some present now) and determined the amino acid sequences of a particular region from each. The sequences are listed below:

Organism	Sequence of XYZ
1	KSTSTDIKSREV
2	KTTATEIKSREV
3	KTTATDIKSKEV
4	KSTAVEIKSKLF
5	KTTATEIKSKLV
6	KTLATDIKSREV
7	KSTATDIKSREV
8	KSTATEIKSKLV
9	KTTATEIKSKEV
10	KSTATDVKSREV
11	KSTAVEIKSKLV
12	KTTATDIKSREV

a) Which amino acid(s) are invariant throughout this evolutionary tree? Why might have these amino acids been conserved in an actual organism?
The conserved sequence is K - - - - - - KS - - -
If these amino acids were important for maintaining the structure or the function of the protein in which they are found, they might be conserved in evolution.

b) Complementation across species.

i) Would you expect this protein from organism 1 to complement a deficiency in organism 11? Why or why not?
It is unclear from the data, but it is not very likely. The entire XYZ protein is only 12 amino acids long, and the difference between XYZ proteins from species 1 and 11 is 5 amino acids. Moreover, most of these substitutions are not conservative. However, if all that matters for function are the three conserved residues, complementation might still take place.

ii) Would you expect one of the glycolysis enzymes from organism 1 to complement a deficiency in organism 11? Why or why not?
Because glycolysis enzymes are highly conserved in evolution due to their essential nature, we would expect glycolysis enzymes from organism 1 to complement a corresponding deficiency in organism 11.

c) Suppose you were able to get the DNA sequences of this protein from the twelve species. Would you expect the tree constructed using the DNA sequences to be more or less accurate than the tree constructed using the protein sequences? Why or why not?
We would expect the DNA tree to be more accurate than the protein tree because we would be able to follow the evolution of the actual gene sequence, and not just the protein sequence that results from it. Following gene sequences would allow us to track silent mutations, as well as missense mutations, and would result in a more accurate tree.