Question 1 (20 points).

a) A pure-breeding, white-flowered pea is crossed to a pure-breeding, purple-flowered pea. All the F1 progeny have purple-flowers. What can you conclude?

(3 pts) Purple is dominant over white.

b) The F1 progeny are allowed to self-fertilize. What phenotypic ratios do you expect in the F2 progeny?

(3 pts) 3 Purple: 1 White  

“3:1” without specifying which (2 pts)

c) Around 1900, Bateson, Saunders and Punnet were working with two such varieties of pure-breeding, white-flowered sweet pea. When they crossed variety A to variety B, they were surprised to find that all the F1 progeny had purple flowers. Based on this result, what can you conclude?

(3 pts) Have mutations in two different genes (3 pts); “complement,” without further explanation (1 pt); vague “multiple factors,” “2 traits” (2 pts); -1 pt if listed additional erroneous possibilities.

d) Give the genotypes of the white-flowered parents and the purple-flowered F1 progeny in Bateson, Saunders and Punnet’s experiment. Define all symbols used.

A, B = dominant purple
a, b = recessive white

(5 pts) Designation indicates 2 genes (1 pt); parents = AAbb x aaBB (2 pts); F1 = AaBb (2 pts); no definition of symbols (-1 pt); inappropriate genetic notation (-1 or 2 pts); additional erroneous input (-1pt).

e) When Bateson, Saunders and Punnet allowed their F1 progeny to self-fertilize, 9/16 of the resulting F2 plants had purple flowers and 7/16 had white flowers. Explain these results.

Must be A_B_ to be purple. Being homozygous recessive at either loci results in white flowers.

\[
\begin{align*}
A_B_ &= 3/4 \times 3/4 = 9/16 = \text{purple} \\
aaB_ &= 1/4 \times 3/4 = 3/16 = \text{white} \\
A_bb &= 3/4 \times 1/4 = 3/16 = \text{white}  \\
aabb &= 1/4 \times 1/4 = 1/16 = \text{white} \\
\end{align*}
\]

7/16 total white

(6 pts) 9:3:3:1 (1 pt; -1 for “close to 1:1”). \( A_B_ = 9/16 \) (2 pts); white = 3/16 + 3/16 + 1/16 = 7/16 (1 pt).  \text{white} = \text{homozygous recessive at either locus (2 pts). Full credit for completely labelled (including phenotypes) Punnet square. Since explanation of mechanism was not required, no points deducted for erroneous explanations.}
Question 2 (20 points).
Imagine you are young Sturtevant sitting in your undergraduate dormitory late at night. You are attempting to figure out the first genetic map of an organism, gain scientific glory, and avoid returning to your busboy position in Prof. Morgan’s laboratory.

You are analyzing the relationship between four *Drosophila melanogaster* factors (genes): A, B, and D. You began your experiment by crossing females from one pure-breeding line with males from a different pure-breeding line. The F1 female progeny were then crossed with testcross males. Your inspection of 1000 F2 progeny yielded the following phenotypes:

<table>
<thead>
<tr>
<th></th>
<th>A-B</th>
<th>A-D</th>
<th>B-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>AbD</td>
<td>333</td>
<td></td>
<td></td>
</tr>
<tr>
<td>aBd</td>
<td>322</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABD</td>
<td>115</td>
<td>115</td>
<td>115</td>
</tr>
<tr>
<td>abd</td>
<td>130</td>
<td>130</td>
<td>130</td>
</tr>
<tr>
<td>ABd</td>
<td>44</td>
<td>44</td>
<td>44</td>
</tr>
<tr>
<td>abD</td>
<td>51</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>Abd</td>
<td>2</td>
<td>2*2 = 4</td>
<td>2</td>
</tr>
<tr>
<td>aBD</td>
<td>3</td>
<td>2*3 = 6</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1000</td>
<td>350</td>
<td>100</td>
</tr>
</tbody>
</table>

a) On the table above, CIRCLE the parental types.

(4 pts) *AbD and aBd* (2 pts each)

b) What is the map order? Explain your reasoning.

(4 pts) *A-D-B* (2 pts)

The rarest classes (*aBD and Abd*) represent double cross-overs. The allele that is different from the parental types is in the middle. Use of double cross-over class (2 pts) or mapping data (2 pts).

c) Using all of the relevant data, calculate each of the three two-factor recombination frequencies. Show your work below and on the table above. Express all frequencies as percentages.

(4pts)

\[ R_{ab} = \frac{350}{1000} = 35\% \] (2 pts)
\[ R_{ad} = \frac{100}{1000} = 10\% \] (1 pt)
\[ R_{bd} = \frac{250}{1000} = 25 \% \] (1 pt)

\[ R(ab) = 34\% \text{ (omitted DCO's)} \] (1 pt); if used \( R(ab) = R(ad) + R(bd) \) 2 pts for \( R(ab) \) even if \( R(ad) \) or \( R(bd) \) incorrect.

d) What is the frequency of double recombination? Show your work.

(4 pts) Double recombinants are:
- \( Abd \quad 2 \)
- \( ABD \quad 3 \)

Frequency = \( \frac{2+3}{1000} = \frac{5}{1000} = 0.5\% \) (4 pts); -2 pts for decimal place error

e) What frequency of double recombination would you calculate if the data contained no evidence of interference? Show your work.

(4 pts) \( R_{ad} \times R_{bd} = 10\% \times 25\% = 2.5\% \) (4 pts)
-2 pts if “25” (number instead of freq); -2 pts if “0.025%”; -3 pts if “25%” (should realize that this is far too high).

Question 3 (20 points).
A benign ovarian teratoma is a mass of differentiated tissues which occasionally develops in the ovary without fertilization. Such a teratoma develops in a patient who is heterozygous \( Aa \) for a locus closely linked to the centromere of a chromosome and heterozygous \( Bb \) for another locus weakly linked to the centromere of the same chromosome.

It is found that cells of the teratoma have the normal human female karyotype (XX; 22AA) and are homozygous \( A/A \) and heterozygous \( B/b \). Which of the following suggested origins for the teratoma can simply account for the above findings and which cannot? Explain your reasoning in each case.

a) proliferation of a cell that completed the first division of meiosis normally, but failed to undergo the second division.

(8 pts) Yes (2 pts); after meiosis I, cells are 2n [demonstration of understanding of meiosis I] (2 pts); in order to obtain \( AB/Ab \) (or \( B/b \)), recombination between \( A \) and \( B \) loci must have occurred (4 pts). Indication only that recombination necessary (2 pts); if indicated or diagrammed as 2 chromosomes (-1 pt); if indicated that without recombination cells would be \( AaBb \) (-4 pts).

b) proliferation of a cell derived from a normal ovum in which the chromosomes duplicated without nuclear division, a process known as diploidization.

(6 pts) No (2 pts). All loci would be homozygous (4 pts), thus could not produce \( B/b \).

c) proliferation of a cell formed by fusion of two normal ova.

(6 pts) Yes (2 pts). Fusion of \( AB \) ovum with \( Ab \) ovum (4 pts). If stated only that this would result in diploid (without reference to genotype) (2 pts).
Question 4 (16 points).
You are studying an inversion heterozygote.

The order of genes along one homolog is
centromere – A – B – D – E – F

The order of genes along the other homolog is
centromere – A – E – D – B – F

a) Assuming that the first homolog is the normal chromosome, draw an arrow(s) at that
breakpoint(s) that gave rise to the abnormal chromosome
   (2 pts) See above. If shown on inverted chromosome (1 pt).

b) The homologs undergo recombination between genes B and D. Draw a clear sketch depicting
the chromosomes of this inversion heterozygote as they align at pachytene. In your sketch, only
include the chromatids undergoing recombination.

   (5 pts) [see figure] No centromeres indicated (-1 pt); no cross-over indicated (-1 pt);
   error in placement of gene (-1 pt); attempted loop – but didn’t quite get it (3 pts).

c) Draw a clear sketch of the recombinant products from such as cross-over event.

   (4 pts) [see figure] 2 pts for each chromosome. No centromeres indicated (-1 pt). No
deduction if non-recombinant chromosomes shown and ABDEA indicated as bridge
between.

d) Will the recombinant chromatids segregate normally during cell division? Explain.
   (5 pts) No (1 pt); decentric will be pulled to opposite sites during anaphase, resulting in
chromosome breakage (2 pts); acentric cannot attach to spindle OR may be lost (2 pts).
Question 5 (20 points).
The following *E. coli* strains were grown under the conditions noted. Indicate with a "+" each case in which beta-galactocidase is produced at HIGH LEVELS.

<table>
<thead>
<tr>
<th>Lactose Absent</th>
<th>Lactose Present</th>
<th>Lactose + Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>$I^+ O^+ Z^+ \text{ CAP}^+$</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>$I^- O^+ Z^+ \text{ CAP}^+$</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>$I^+ O^+ Z^+ \text{ CAP}^+$</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>$I^+ O^C Z^+ \text{ CAP}^+$</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>$I^- O^C Z^+ \text{ CAP}^-$</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

1 pt for each of the 18 correct; +2 pts if first two correct (wild type with and without lactose) [to penalize random guessing].

Question 6 (12 points).
A mutant screen resulted in large numbers of yeast mutants that are auxotrophic for the amino acid histidine. These mutants were then grown on minimal media plates supplemented with chemicals structurally related to histidine. It was found that the mutants could be grouped into four classes, 1-4.
Supplemented with His (histidine), all strains will grow
Supplemented with LHP (L-histidinol phosphate), only class 2 and 3 strains will grow
Supplemented with IP (Imidzolacetol phosphate), only class 3 strains will grow
Supplemented with L-His (L-Histonol), only class 2, 3, 4 strains will grow
(a) Propose a biochemical pathway for the synthesis of histidine.

```
precursor \rightarrow \text{IP} \rightarrow \text{LHP} \rightarrow L\text{-His} \rightarrow \text{His}
```

(4 pts) 1 pt for each pair correct; explicit indication of “precursor” not required.

(b) Show the relationship between the steps in the pathway above and the genes in the four classes of mutants.

```
precursor \rightarrow \text{IP} \rightarrow \text{LHP} \rightarrow L\text{-His} \rightarrow \text{His}
```

(8 pts) 2 pts for each class indicated correctly; -2 pts if class indicated over substrate, rather than over arrows. If pathway is incorrect: +1 pt for each class “pointing to” correct substrate. If otherwise 0 pts: +2 pts for correct order (3,2,4,1); +1 pt for 3 in order (3,2,4). Compensatory: +1 pt if explain that each class represents a gene that encodes an enzyme for a biochemical step in the pathway.
Question 7 (22 points).
You are studying a gene in *E. coli* that specifies a protein enzyme. Part of the wild-type sequence is given below. You recover a series of mutants for this gene that show no enzyme activity. Isolating and sequencing the mutant products, you find the following protein sequences (assume each mutant is the result of a single nucleotide change):
- **Wild-type:** - Met - Cys – Ala - Gln - Ile – Tyr –
- **Mutant 1:** - Met - Cys – Ala - Gln - Thr – Tyr –
- **Mutant 2:** - Met - Cys – Ala
- **Mutant 3:** - Met - Val – Pro – Arg – Phe – Thr

a) How may different mRNA sequences could code for this portion of the wild-type protein? Show your work.

<table>
<thead>
<tr>
<th>amino acid</th>
<th>Met</th>
<th>Cys</th>
<th>Ala</th>
<th>Gln</th>
<th>Ile</th>
<th>Tyr</th>
</tr>
</thead>
<tbody>
<tr>
<td># codons</td>
<td>1 x</td>
<td>2 x</td>
<td>4 x</td>
<td>2 x</td>
<td>3 x</td>
<td>2 x</td>
</tr>
</tbody>
</table>

\[ 1 \times 2 \times 4 \times 2 \times 3 \times 2 = 96 \text{ mRNA sequences} \]

(4 pts) 96 possible (4 pts); -1 pt for each component incorrect; -1 for math error.

b) For the FIRST amino acid affected by each mutation, give the original codon(s) and the mutant codon(s) as specifically as possible. Use all the data and show your work. Clearly indicate the type of mutation that has occurred.

(18 pts; 6 pts for each mutant)

- **Mutant 1 =** Ile  ->  Thr
  \[ \text{AUU} \rightarrow \text{ACU} \]
  \[ C \rightarrow C \]
  \[ A \rightarrow A \]
  must include some indication of location or amino acids affected; any one of: missense/T (or U) to C substitution/transition (2 pts); “point mutation” (1 pt). Failure to resolve ambiguity (-1 pt); incorrectly resolved ambiguity (-2 pts).

- **Mutant 2 =** Gln  ->  STOP
  \[ \text{CAA} \rightarrow \text{UAA} \]
  \[ C \rightarrow U \]
  \[ AG \rightarrow AC \] (4 pts)
  must include some indication of location or amino acids affected; nonsense mutation (2 pts) OR stop codon (1 pt) due to transition (1 pt) OR stop codon (1 pt) due to C --> T (U) substitution (1 pt). Failure to resolve ambiguity (-1 pt); incorrectly resolved ambiguity (-2 pts).

- **Mutant 3 =**
  first codon affected  Cys  ->  Val
  \[ \text{UGU} \rightarrow \text{GUG} \]
  \[ C \rightarrow G \]
  \[ U \rightarrow G \] (4 pts)
  must include some indication of location or amino acids affected; frameshift (1 pt) due to deletion of 1 bp or indel (1 pt). Failure to resolve ambiguity (-1 pt); incorrectly resolved ambiguity (-3 pts). If otherwise 0 pts and indicate possible codons for amino acids involved (1 pt).
**Question 8 (16 points).**

The cell cycle diagram below shows the cyclin-cdk complexes that are essential for progression through various stages of the cell cycle.

Using the information in the diagram, predict what would happen to a cell containing the following mutations. Show your reasoning.
a) A homozygous loss-of-function mutation in cyclin D
(5 pts) No or reduced cyclin D (1 pt) [credit if not explicitly stated, but clear from context]; does not progress from G0/G1 (2 pts); cell cannot divide or does not proliferate (2 pts).

b) An inversion on one chromosome that places the wild-type coding region for cyclin B downstream of the promoter for a highly expressed tubulin gene.
(5 pts) Cyclin B overexpressed or constitutive (2 pts); premature transition from S phase to G2/M (3 pts; 2 pts if mention only rapid G2 to M or accelerated mitosis) cell will divide more rapidly (1 pt).

c) One of the mutations above can lead to additional mutations in other genes. Which mutation is it (mutation a or b) and how does it lead to additional mutations?
(6 pts) “b” (2 pts) Cell enters mitosis before DNA synthesis complete, resulting in gene loss (4 pts). Since mutation caused by inversion, could have resulted in mutations to other genes at the inversion breakpoints (4 pts). Since mutation caused by inversion, results in other problems (2-3 pts). Cell cycle checkpoints disrupted (3 pts). Cell cycle checkpoint effected by p53 disrupted (2 pts).

Question 9 (18 points).
The pedigree below shows the inheritance of a rare X-linked recessive disorder. The accompanying Southern blot shows inheritance of an RFLP that is 20 map units from the disease gene. Show your work and define any symbols used.

a) Using the above pedigree and ignoring the RFLP data, what is the probability that individual E will have an affected child?

“A” = wild-type disease gene (dominant)  “a” = mutant disease gene (recessive)  “Y” = Y chromosome
Individual C is Aa
(6 pts) E has 1/2 chance of being Aa (2 pts), 1/2 change of passing on “a” (2 pts), 1/2 chance of having son (2 pts)
1/2 x 1/2 x 1/2 = 1/8

b) Considering all the data, give the genotypes of the following individuals as COMPLETELY AS POSSIBLE.
(6 pts)
Individual B  \[
\begin{array}{c}
    a \ 1 \\
    Y
\end{array}
\]
Individual C  \[
\begin{array}{c}
    a \ 1 \\
    A \ 3 \\
\end{array}
\]
“1,” “2,” and “3” are the RFLP alleles
Individual D  \[
\begin{array}{c}
    A \ 3 \\
    Y
\end{array}
\]
2 pts each; -1 for any incorrect component. Must indicate linkage in genotype; linkage described, but not included in genotype (3 pts total). Notation or description indicate that disease gene and RFLP site are same locus (2 pts total). Only disease alleles or only RFLP alleles shown (1 pt total).

c) Considering all of the data, what is the probability the individual E will have an affected child?
Individual E inherited “1” from her mother, who is “a 1/A 3.” Chance of inheriting “a 1” chromosome is 80%. Chance of passing on “a” is 50%. Chance of having a son is 50%.

80% x 50% x 50% = 20%

20% (6 pts) 80% chance that E is Aa (3 pts); -2 pts for omission or error in either of the other factors: ½ chance passing on a; ½ chance child will be a son (-1 if error propagated from part a).

Question 10 (20 points).
Caenorhabditis elegans develops as either a self-fertilizing hermaphrodite or a male depending on its X to autosome (X:A) ratio. Diploid individuals with 2X chromosomes develop as hermaphrodites, and those with one X chromosome develop as males. There is no "Y" chromosome. Normally, hermaphrodites are XX and males are XO.

The table below describes recessive (loss-of-function) mutations in genes that affect sex determination in this species:

<table>
<thead>
<tr>
<th></th>
<th>XX</th>
<th>XO</th>
</tr>
</thead>
<tbody>
<tr>
<td>wild type</td>
<td>hermaphrodite</td>
<td>male</td>
</tr>
<tr>
<td>tra–</td>
<td>male</td>
<td>male</td>
</tr>
<tr>
<td>her–</td>
<td>hermaphrodite</td>
<td>hermaphrodite</td>
</tr>
<tr>
<td>xol–</td>
<td>hermaphrodite</td>
<td>hermaphrodite</td>
</tr>
<tr>
<td>sdc–</td>
<td>male</td>
<td>male</td>
</tr>
</tbody>
</table>
a) Based on the above data, what can you say about the normal function of each gene?

(8 pts) 2 pts each

To determine the regulatory pathway, of these genes, doubly mutant strains were constructed and their phenotypes scored.

<table>
<thead>
<tr>
<th>double mutants</th>
<th>XX</th>
<th>XO</th>
</tr>
</thead>
<tbody>
<tr>
<td>tra− ; her−</td>
<td>male</td>
<td>male</td>
</tr>
<tr>
<td>tra− ; xol−</td>
<td>male</td>
<td>male</td>
</tr>
<tr>
<td>her− ; sdc−</td>
<td>hermaphrodite</td>
<td>hermaphrodite</td>
</tr>
<tr>
<td>sdc− ; xol−</td>
<td>male</td>
<td>male</td>
</tr>
</tbody>
</table>

b) Based on the above data, what is the normal regulatory cascade of these gene products? Be sure to indicate whether an upstream gene negatively or positively regulates a downstream gene.

(8 pts)

(tra -> hermaphrodite and ---| male not required). If incorrect: 1 pt for every epistatic relationship correctly explained; 1 pt for every negative or positive regulation correct. Minimum of 1 pt for effort.

(c) It has been shown that the activity of xol is controlled by the X:A ratio. Does an X:A = 1 normally activate or repress xol activity? (Hint: What does the phenotype of xol mutants tell you?)

A loss-of-function mutation in xol leads to hermaphroditic development in both XX and XO animals. XO animals are normally males, so xol is required to inhibit hermaphrodite development. An X:A=1 occurs in normal hermaphrodites, where xol-1 is not required and thus repressed.

(4 pts) Represses xol activity (4 pts). If incorrect because state that X:A=1 is the case for males (1 pt). If correctly state that X:A=1 occurs in hermaphrodites, but otherwise incorrect (1 pt). Correct answer for the wrong reasons (2 pts).
Question 11 (16 points).
Which of the following statements about embryonic pattern formation in Drosophila are true and which are false? Briefly justify each answer. (Assume all mutations are null mutations.)

(4 pts each part) No credit for any section for which T/F incorrect.

a) One quarter of the embryos produced by parents heterozygous for a null bicoid mutation will exhibit abnormal patterns of gap gene expression.

False (1 pt). Bicoid mRNA transcribed from the maternal genome (maternal effect gene) (1 pt). Since mother has one good copy, all embryos will develop normally (2 pts).

b) An embryo homozygous for a pair-rule mutation exhibits abnormal patterns of segment polarity gene expression.

True (1 pt). Pair-rule genes are upstream of (epistatic to) segment polarity genes (3 pts).

c) One quarter of the embryos produced by parents heterozygous for a null HB-Z mutation will exhibit abnormal patterns of pair-rule gene expression.

True (1 pt). HB-Z is a gap gene (1 pt) OR HB-Z transcribed from the embryonic genome (zygotic) (1 pt). Gap genes are upstream of (epistatic to) pair-rule genes (2 pts).

d) Deletion of the 3’ untranslated region of bicoid can affect embryonic patterning.

True (1 pt). The 3’ UTR of bicoid required for proper localization of the bicoid mRNA (1 pt). Any 2 of the following: Localized to the anterior end (1 pt); site in the 3’ UTR bound to microtubules (1 pt); results in a gradient of bicoid protein (1 pt).