Name_____ _____ _____
Last (as on TCard) First (as on TCard) Preferred First (optional)

Student #_____ Signature_____

UNIVERSITY OF TORONTO
Faculty of Arts and Science

APRIL 2011 EXAMINATIONS

HMB265H1S General and Human Genetics

Duration — 2 hours

Examinations Aids: Non-Programmable Calculator only

PLEASE HAND IN

This exam is out of 84 marks.

Instructions:

Write your full name and student number on every page of the exam.

Part 1- Multiple Choice (38 questions worth 2 marks each, total 76 marks)
1.1 Answer the multiple choice questions on the scantron.
1.2 Refer to the "MARKING INSTRUCTIONS" on the scantron for information on filling it out (*e.g.*, use HB pencil; no stray marks anywhere on the scantron).
1.3 In the "FORM" box on the scantron, indicate which "FORM" (A, B, C or D) is indicated on the top of your exam page.
1.4 Fill in SIGNATURE, SUBJECT and DATE on the scantron.
1.5 Correctly bubble in your STUDENT NUMBER, LAST NAME and INITIALS on the scantron.

Part 2- Short Answer (2 questions worth 8 marks total)
2.1 Answer all questions using complete, concise sentences and writing legibly using ink only in the lined space provided on this paper.

Good luck!

Invigilators are not permitted to interpret questions for individual students. If you think that a question is ambiguous, answer as you understand it, then make a note here. Please be specific.

HMB265H1S Final Exam 2010-11
FORM A
Name_____ Student #_____

Part 1--MULTIPLE CHOICE. Choose the one answer that best answers the question. 38 questions worth 2 marks each, total 76 marks.

1) What is the most likely outcome when a cell has one wild-type allele and one amorphic allele of the retinoblastoma (*RB*) gene?
   A) faster entrance into S phase
   B) more rapid completion of mitosis
   C) constitutive activation of Ras
   D) increased susceptibility to cancer formation

2) The *Igf2* gene was the first imprinted gene identified in mammals. What characterizes the regulation of gene expression of the *Igf2* gene?
   A) blocked by the regulatory protein CTCF on the maternal chromosome
   B) inactivated by methylation of the promoter on the paternal chromosome
   C) transcribed from both gene copies in most individuals
   D) under control of a downstream insulator region on the paternal chromosome

3) Which of the following terms does NOT refer to the genetics of more than one gene?
   A) pleiotropy
   B) independent assortment
   C) complementation
   D) epistasis

4) To date, several problems have been encountered with gene therapy. What has NOT been one of the problems encountered?
   A) pre-existing immunity to viral vectors causing death
   B) cannot limit expression of the introduced gene to a specific tissue
   C) introduced gene inserting into existing gene causing cancer
   D) lack of prolonged expression because of removal by the immune system

5) The chromosomes of a translocation heterozygote pairing during meiosis are shown in **Figure 4** at the end of the examination. Which of the following gametes would result from the adjacent-1 segregation pattern, and are the gametes viable?
   A) MNOJKL, MNOPQR; not viable
   B) GHIJKL, MNOJKL; viable
   C) GHIJKL, MNOJKL; not viable
   D) MNOJKL, MNOPQR; viable

6) The following three questions refer to the pedigree of the Barnes family shown in **Figure 1** at the end of the examination, where a very rare disease has been found in the family.

6) How is this disease most likely inherited?
A) autosomal dominant
B) X-linked recessive
C) X-linked dominant
D) autosomal recessive

7) What is the probability that individual II-3 is a carrier of the disease?
A) 3/4
B) 2/3
C) 1/4
D) 1/2

8) If individual III-3 had a child with individual III-4, what is the probability that the child has the disease?
A) 1/4
B) 1/2
C) 1/6
D) 1/12

9) Irina is conducting a mutagenesis screen in *Drosophila.* She isolates a number of mutations that affect anterioposterior patterning. If a *Drosophila* embryo has one mutant and one wild-type copy of the *bicoid* gene, and has a mother carrying two copies of the *bicoid* gene with a null mutation, what would be the predicted phenotype of the embryo?
A) missing the posterior region
B) missing both the anterior and posterior regions
C) missing the anterior region
D) wild-type

10) Ji-Yoo is using hydrogen peroxide to induce oxidative DNA damage in *Trypanosoma*, a unicellular parasite that normally swims by means of one flagellum. She screens the mutagenized population for members who lack a flagellum, and through this screen identifies a mutation in the gene encoding kinesin. What type of mutation has Ji-Yoo most likely introduced?
A) thymine dimer
B) deletion
C) transition
D) transversion

11) Beatrice has a male calico cat. Normally, the domestic cat has 19 pairs of chromosomes. How many chromosomes would you expect to see in the somatic karyotype of Beatrice's cat?
A) 19
B) 37
C) 39
D) 38

12) A corn cob is observed with many of its kernels colourless with purple spots. What most likely occurred to produce this phenotype?
A) wild-type *C* gene is present and *Ac* is absent
B) *Ac* has inserted into the *C* gene
C) *Ds* has inserted into the *Ac* gene
D) *Ds* has inserted into the *C* gene and *Ac* is absent

13) Gary is a graduate student investigating the causes of an autosomal dominant disease in humans. He performs linkage analysis in the Partridge family that has many members affected by the disease. The pedigree for this family is shown in **Figure 2** at the end of the examination. The father in the second generation is heterozygous for the dominant disease allele and for a molecular marker. For the third generation, 4 of the children are recombinant with respect to the father's contributing gamete. What is the LOD score for the third generation for the specific marker and disease gene?
A) -0.087
B) 3.10
C) 1.22
D) 0.087

14) A species of praying mantis in the Amazon rainforest is diploid, with a total number of 44 chromosomes in nerve cells. A researcher uses karyotype analysis to show that a member of this species he caught had nullisomy 2 and 5, trisomy 7 and 13, and tetrasomy 19; how many chromosomes would you expect to find in this praying mantis' nerve cells?
A) 45
B) 46
C) 44
D) 22

15) The normal sequence of 10 genes along a chromosome is ABC•DEFGHIJ (where • represents the centromere). A person is found to be an inversion heterozygote, with one normal copy of this chromosome, and another with the sequence ABC•DEIHGFJ. A single crossover event occurs during meiosis between two non-sister chromatids in the segment between the G and H genes. What products could result from this crossover event to produce gametes that were NOT viable?
A) ABC•DEFGGFJ•CBA and JIHHIED
B) ABC•DEFGHIED•CBA and JFGHIJ
C) ABC•DEFGGFJ and ABC•DEIHHIJ
D) ABC•DEFG•HIEDCBA and JFGHIJ

16) Human gene therapy trials for Leber's congenital amaurosis have been conducted with promising results. What characterized the trial presented in lecture?
A) A greater overall improvement in vision was observed in the older patients.
B) A complete reversal of blindness was observed in all of the patients.
C) The method was not safe and resulted in serious adverse events.
D) An adeno-associated virus (AAV) containing wild-type human RPE65 was used.

17) Suzanne's brother has an X-linked recessive disease, but no other family members have the disease. If Suzanne has three sons, what is the probability that none of the sons will have the disease?
A) 1/16
B) 1/2
C) 1/4
D) 1/8

18) While mapping a gene responsible for an autosomal recessive disorder, Tatiana identifies a molecular marker which seems to segregate with the disease phenotype. In order to determine the likelihood that the marker is actually linked to the disease locus, she performs LOD score analysis and finds a LOD score of 3 for this region. What can Tatiana conclude based on this information?
A) There is a 1/1000 chance that the marker and disease locus are not linked.
B) This region of the genome is highly polymorphic.
C) The marker is the gene which is causing the disease.
D) A larger sample size is required to determine if the marker and disease loci are linked.

19) Jasper is a summer student working in a lab that studies *E. coli*. He conducts a mutagenesis experiment which yields 5 mutant strains unable to synthesize a particular compound required for their growth. Each of these 5 strains contains a mutation in a different gene that blocks a different step in a particular biosynthetic pathway. In order to grow, these mutants require that a compound be supplied in the medium that a wild-type *E. coli* strain is able to synthesize for itself. **Table 1** at the end of the examination shows results from experiments in which the mutants were grown in media supplemented with the indicated compound. What is the order of the genes in this biosynthetic pathway, from earliest to latest?

A) 2 → 5 → 1 → 3 → 4
B) 5 → 2 → 1 → 4 → 3
C) 4 → 3 → 1 → 5 → 2
D) 3 → 4 → 1 → 2 → 5

20) Javita is an undergraduate student working in an *Arabidopsis* lab. She identifies two independently-assorting genes, *A* and *B*, that contribute to the production of trichomes (fine hairs) on the leaves of a plant. The *A1* allele adds 7 trichomes, the *A2* allele adds 11 trichomes, the *B1* allele adds 5 trichomes, and the *B2* allele adds 8 trichomes. Javita crosses plants of genotype *A1/A1*; *B1/B2* with plants of genotype *A1/A2*; *B2/B2*. What trichome numbers would she expect to see in the progeny?

A) 27, 28, 30, 31, 32, 34
B) 27, 30, 31, 34
C) 24, 27, 28, 30, 31, 32, 34, 35, 38
D) 27, 34

21) Harvey is a summer research student working in a *Drosophila* lab interested in locomotory behaviour. He is using P elements to generate fruit flies with mutant locomotory phenotypes and obtains a fly with decreased locomotion. What characteristic of a P element could explain this result?

A) codes for a mutant locomotion gene
B) interrupted a gene important for locomotion
C) has altered DNA repair mechanisms
D) has caused activation of retrotransposons in the genome

22) Laryssa is a Master's student working in an agricultural lab. She is studying the heritability of height, a continuous trait, in sugarcane plants,. What could NOT describe the recombinant inbred lines (RILs) she creates?

A) produce "ladder-like mosaic" of maternal alleles
B) inbred for multiple generations
C) facilitate the fine mapping of traits
D) single line of descent generated from each F_2 individual

23) A species of plant found in Northern Ontario is normally diploid, with two sets of seven chromosomes. What would a variant with 13 chromosomes be called?
A) monoploid
B) trisomic
C) nullisomic
D) monosomic

24) Gene therapy trials that were performed in France to treat boys with X-linked Severe Combined Immunodeficiency Disease (SCID) illustrated one of the difficulties involved in gene therapy. What was the difficulty?
A) Exaggerated immune responses to viral vectors were observed in one of the boys and resulted in his death.
B) It was very difficult to get DNA into all of the cells in the body so gene therapy was not effective.
C) It was very difficult to get enough DNA into cells to correct the genetic defect and the boys had to be treated by other methods.
D) The transgene inserted into a proto-oncogene in some of the boys which led to leukemia.

25) Daniel inherits a loss-of-function mutant allele from his mother, and a wild-type allele from his father, of a gene that is paternally imprinted. Loss of function of the gene is associated with a particular disease. Will Daniel have the disease, and what percentage of his children (if any) will have the disease? (Assume that Daniel's partner is wild-type).
A) Yes; none of his children will have the disease.
B) No; none of his children will have the disease.
C) No; 50% of his children will have the disease.
D) Yes; 50% of his children will have the disease.

26) Neela is a fourth-year student studying transposition in bacteria. What type of transposition event in bacteria would be expected to increase the genome copy number of the transposon most rapidly?
A) conservative
B) replicative
C) target-site
D) "cut and paste"

27) Two genes, A and B, are linked with the map distance between the genes of 0.4 cM. A cross is made between AAbb and aaBB individuals, and an F1 individual is testcrossed to an individual that is aabb. What proportion of the progeny from the testcross will have the dominant phenotype at both A and B?
A) 0.1
B) 0.25
C) 0.2
D) 0.4

28) A woman with Turner syndrome is diagnosed with Duchenne muscular dystrophy, an X-linked recessive disorder. Neither her mother nor her father have the disorder. When would non-disjunction have occurred to best explain the simultaneous origin of Turner syndrome and Duchenne muscular dystrophy?
A) either the first OR second meiotic division in the mother
B) the first meiotic division in the mother
C) either the first OR second meiotic division in the father
D) the first meiotic division in the father

29) Hassan is performing a mutagenesis screen in *C. elegans*. He discovers a gene involved in gonadal development. The behaviour of a null allele of this gene in a heterozygous individual (wild-type/null) appears to be dominant. How can this gene be described?
A) epistatic
B) neomorphic
C) hypermorphic
D) haploinsufficient

30) Heidi is studying ear length in the beagle dog breed, which shows a phenotypic variation of 16 cm. The broad sense heritability of this trait is known to be 0.75. If the genetic variation due to dominance effects is 3 cm, and the genetic variation due to epistatic effects is 4 cm, what is the value for narrow sense heritability?
A) 0.31
B) 0.56
C) 0.25
D) 0.45

31) A researcher is studying the heritability of coat length in llamas, a trait that shows continuous variation. In one family, broad sense heritability for an F_2 group of siblings was calculated as 0.40, while different variances were calculated as follows: For V_G: V_D=45, V_I=25, and V_A=150. For this trait, what is the environmental variance?
A) 330
B) 375
C) 220
D) 550

32) Certain mutations in the *BRCA1* gene confer a higher risk of getting breast cancer, but not all individuals with those mutations will get the disease. What does this illustrate?
A) codominance
B) incomplete penetrance
C) pleiotropy
D) expressivity

33) Farooq is studying the Her2 receptor tyrosine kinase. He creates a mouse strain with a missense mutation that causes receptor dimerization. What result would you NOT predict?
A) constitutive activation of the mutated receptor
B) increased stimulation by epidermal growth factor (EGF)
C) expression of the neu oncogene
D) increased breast cancer risk

34) The frequency of a recessive disease is known to be 9% in the population. Assuming random mating, what fraction of the population is expected to be heterozygous carriers?
A) 0.18
B) 0.35
C) 0.42
D) 0.81

35) Victor is studying a gene encoding a protein that promotes apoptosis when a cell is damaged. How would this gene be classified and what type of mutation in the gene would cause cancer?
A) proto-oncogene; gain-of-function
B) proto-oncogene; loss-of-function
C) tumour-suppressor gene; loss-of-function
D) oncogene; gain-of-function

36) A female guinea pig with genotype Aa;bb;Cc is crossed with a male guinea pig with genotype aa;Bb;Cc. What proportion of the offspring will be homozygous recessive for all genes?
A) 1/4
B) 1/8
C) 1/2
D) 1/16

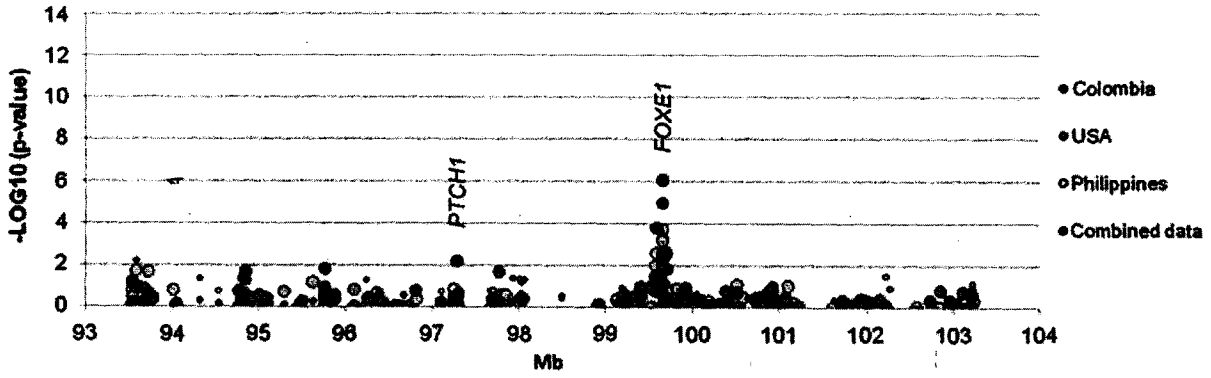
37) In deletion mapping experiments, fruit flies homozygous for different deletions in a chromosomal region were generated and crossed with fruit flies that were homozygous for mutations in specific genes within the region. The regions deleted (represented by the lines in Panel A) and the results of the crosses (Panel B) are shown in **Figure 3** at the end of the examination booklet. What is the order of genes *a* to *g* that are located in positions 1 to 7 on the chromosome?
A) *a-d-g-b-e-f-c*
B) *g-a-d-e-b-c-f*
C) *d-a-g-b-e-c-f*
D) *f-e-c-g-b-d-a*

38) A cross is performed between an inbred white-flowered, short-stemmed plant and an inbred blue-flowered, long-stemmed plant. The progeny are all blue flowered with short stems. If the genes are completely linked, and F1 individuals are crossed with each other, what proportion of the F2 generation will have blue flowers and long stems?
A) 1/16
B) 1/8
C) 1/4
D) 1/2

Name_____ Student #_____

Part 2- Short Answer (2 questions worth 8 marks total) Answer all questions using complete, concise sentences and writing legibly using ink only in the lined space provided on this paper.

39. (4 marks) Karina is a graduate student working in a human genetics lab. She wants to determine the genes responsible for a common complex birth defect, cleft lip. The results of her experiments are shown in the figure below (adapted from Moreno *et al.*, Hum. Mol. Genet. 18:4879 (2009)).



39.a) Briefly describe the experiment she performed to get the results shown? (2 sentences maximum)

_____

_____

_____

_____

39.b) Describe what the results mean. (2 sentences maximum)

_____

_____

_____

_____

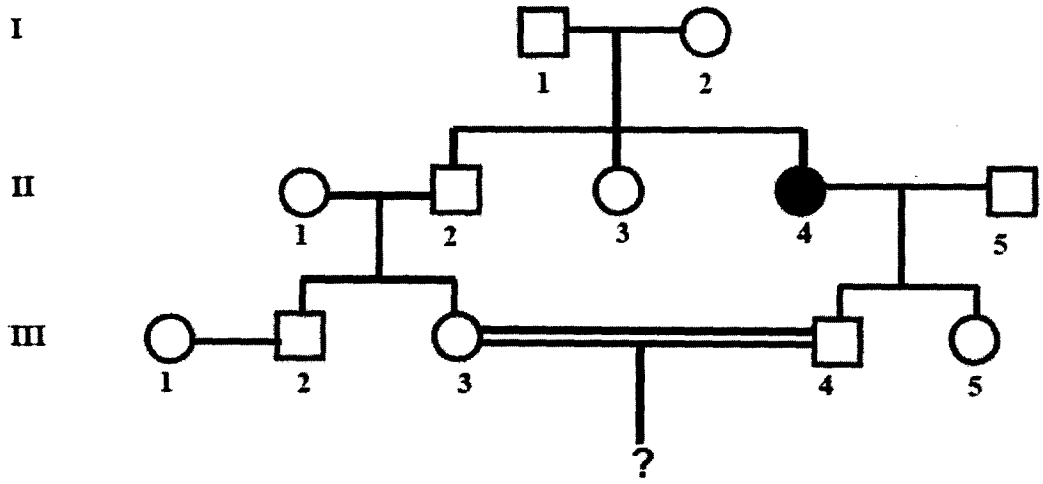
Name_____ Student #_____

40. (4 marks) Drew is a graduate student studying anterioposterior patterning in *Drosophila*. Describe the four experimental steps that Drew would perform to determine which regions of a pair-rule gene are responsible for the striped pattern of expression of the gene in the *Drosophila* embryo. (4 sentences maximum)

Name_____ Student #_____

Figures and Tables

Figure 1 – Pedigree for the Barnes family



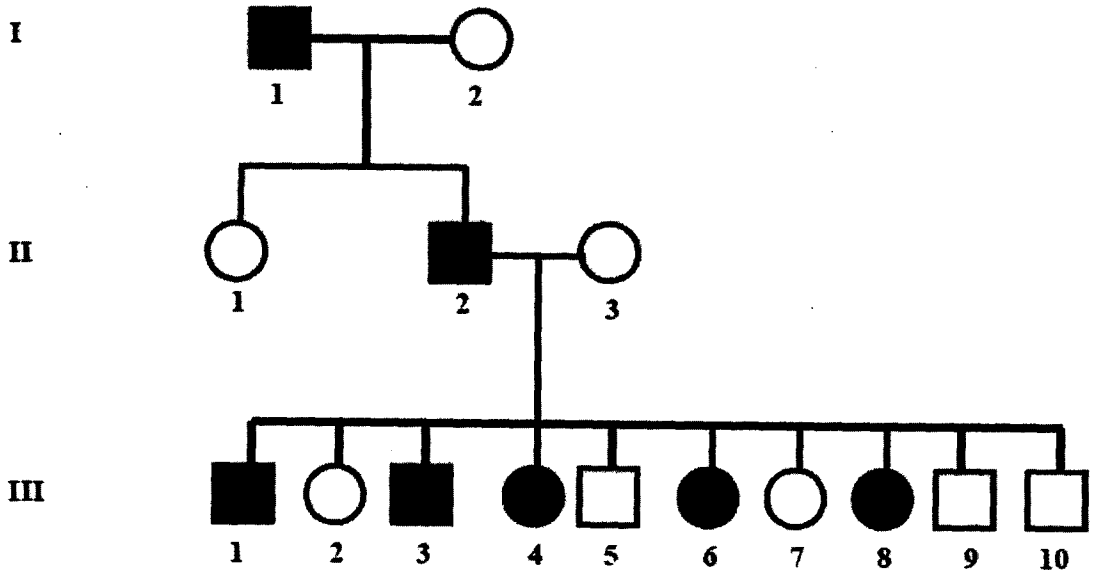
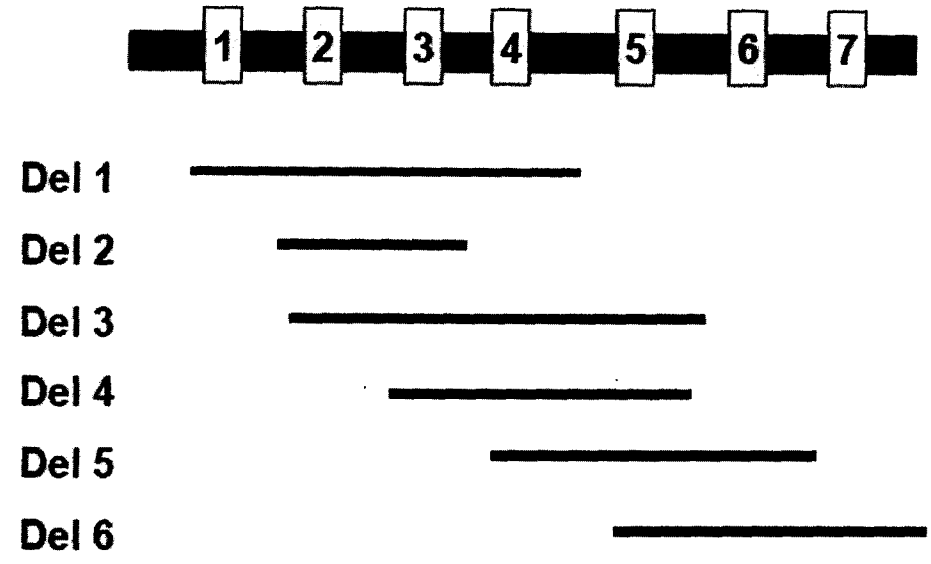


Figure 2: Partridge family pedigree

Name_____ Student #_____

Panel A



Panel B

	a	*b*	*c*	*d*	*e*	*f*	*g*
Del 1	-	-	+	-	+	+	-
Del 2	-	+	+	+	+	+	-
Del 3	-	-	+	+	-	+	-
Del 4	+	-	+	+	-	+	-
Del 5	+	-	-	+	-	+	+
Del 6	+	+	-	+	-	-	+

Figure 3: Deletion mapping experiment. Panel A: Chromosome and regions that are deleted in the deletion mutants. Panel B: Results from the cross described in the question. (+) indicates the phenotype is wild-type and (-) indicates the deletion uncovers a recessive mutant allele.

Name_____ Student #_____

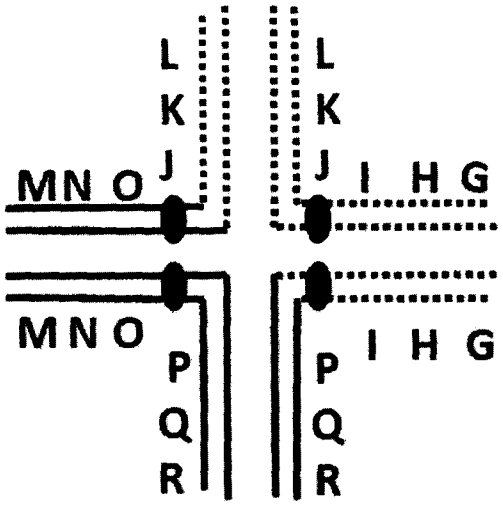


Figure 4: Chromosomes of a translocation heterozygote pairing during meiosis.

Table 1: Growth in media with the supplemental compound is indicated by (+), no growth is shown by (-).

	Compound added					
Mutant	**A**	**B**	**C**	**D**	**E**	**G**
1	-	-	+	+	-	+
2	-	-	-	+	-	-
3	-	+	+	+	-	+
4	+	+	+	+	-	+
5	-	-	-	+	-	+

Total Pages = 14
Total Marks = 84