IMPERIAL COLLEGE LONDON

B.Sc. Examination 2016

This paper is also taken for the relevant examination for the Associateship of the Royal College of Science

MOLECULAR BIOLOGY

Wednesday 15 June 2016 10.00 - 13.00

FOR FIRST YEAR STUDENTS IN BIOCHEMISTRY AND BIOTECHNOLOGY

Answer ALL questions in SECTION A using the answer sheet provided. Answer THREE questions from SECTION B, C & D using a SEPARATE answer book for each answer. You must choose ONE from SECTION B and ONE from SECTION C and ONE from SECTION D. Each question has equal weight to section A (i.e. 25 marks).

SECTION A

This section consists of 25 compulsory multiple choice questions. Using the answer sheet provided, mark the box or boxes to indicate your answer. Some questions in this section have more than one correct answer. Credit will be given for all correct answers but you will be penalised with a negative mark for incorrect choices. You will not be penalised if you do not select an answer.

1. Which of the following statements regarding Illumina Infinium II whole genome genotyping is/are TRUE?

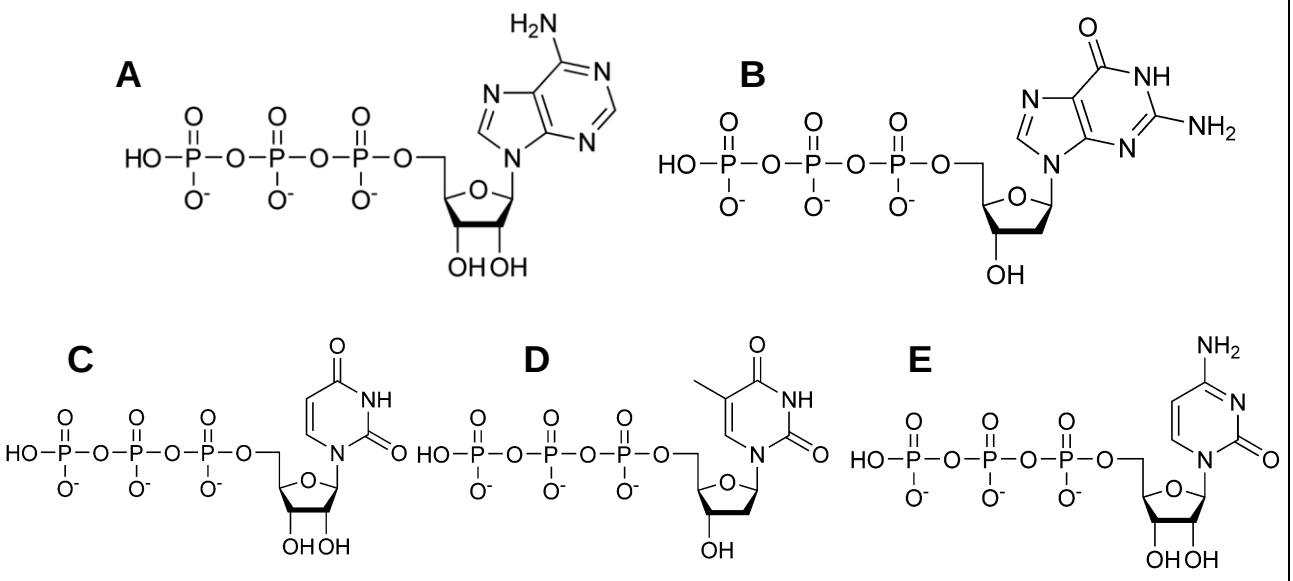
A The Infinium II protocol uses a single fluorescently labelled hapten.
B Oligonucleotide probes specific to a SNP locus are bound to very small beads.
C The Infinium II genotyping method involves a single base extension.
D Specific hybridization between the probe oligonucleotide and the genomic DNA determines which allele will be bound to the bead.
E The Illumina Infinium II assay tests SNP loci less than a 1kbp apart on average.

2. Which of the following statements regarding the Hardy Weinberg Equilibrium is/are TRUE?

A The genotype frequency of each homozygote is the square root of each allele frequency.
B The Hardy Weinberg Equilibrium applies in the case where there are multiple alleles of a locus.
C Hardy Weinberg Equilibrium does not apply in the case of sex linkage.
D The Hardy Weinberg Equilibrium does not allow for natural selection.
E The SNP in the HERC2 gene that gives blue eyes is not in Hardy Weinberg Equilibrium due to geographical isolation.

3. Which of the following statements regarding the effect of mutations on gene function is/are TRUE?

A Loss of function mutations will tend to be recessive.
B Mutations in the coding region of a gene will always have a phenotype.
C A leaky mutation is another word for a gain of function mutation.
D Mutations in introns can eliminate gene function.
E Dominant active mutations will usually lead to a loss of function.



Which of the above molecules:

4. Contains a purine base?
5. Contains an amino base?
6. Is a precursor to RNA?
7. Is needed in the Polymerase Chain Reaction?

8. Which of the following statements regarding Mendel's experiments is/are TRUE?

A Mendel allowed wind or insect born cross pollination between different pea plants.
B Mendel found that each of the traits that he studied consisted of two alternative forms, one of which was dominant and the other recessive.
C Mendel called the progeny from his original crosses the first filial generation or F1.
D The principle of segregation states that two genes sort independently of each other at meiosis.
E 9:3:3:1 is an example of a monohybrid Mendelian ratio.

9. Which of the following statements regarding chromosomal linkage is/are TRUE?

A Curt Stern's experiment looking at recombination between *Bar* and *carnation* showed that physical exchange accompanies genetic exchange.
B The closer together two genes are on the same chromosome, the smaller will be the interference between two crossovers between them.
C Double crossover progeny are always the smallest class in a tri-hybrid testcross.
D Linkage in corn is easy to measure because the genome is hexaploid.
E The unit of genetic distance is the milli-Morgan.

10. Which of the following statements regarding nucleic acid purification is/are TRUE?

A RNA is less susceptible to changes of pH than DNA.
B Differential centrifugation can be used to purify rRNAs from other types of RNA.
C Nucleases require sodium ions for activity.
D Hydrodynamic forces can cause shearing of large nucleic acid molecules.
E Qiagen plasmid purification relies on cation exchange chromatography.

11. Which of the following statements concerning the termination of transcription in *E.coli* is/are TRUE?

A The Rho protein factor is a dimeric DNA helicase.
B Rho dependent termination leads to unwinding of the DNA/RNA helix.
C Rho dependent termination requires GTP.
D Rho independent termination occurs at CA rich sequences in the RNA.
E Rho independent termination is caused by hairpin structures in the RNA.

12. Which of the following statements regarding the charging of tRNAs is/are TRUE?

A Amino-acyl tRNA synthetases can recognize the variable loop region of tRNAs.
B Threonyl tRNA synthetase is unable to hydrolyse serine bound to tRNA threonine.
C Some amino acyl tRNA synthetases are dimeric.
D The charging reaction involves a dAMP-intermediate.
E The end product of the charging reaction is an amino acid covalently bound to the 2'-OH group of the ribose at the 3' end of the tRNA.

13. Which of the following statements regarding the properties of the DNA Polymerase I is/are TRUE?

A DNA Polymerase I is highly processive.
B DNA Polymerase I is composed of a single subunit.
C DNA Polymerase I uses single-stranded DNA as a template.
D DNA Polymerase I has a 3'-5' exonuclease activity.
E DNA Polymerase I has no proof reading activity.

14. Which of the following statements regarding gene identification by computers is/are TRUE?

A Long open reading frames are statistically extremely unlikely.
B Any DNA sequence has three potential reading frames.
C Promoter sequences are found downstream of the translation initiation site.
D Degenerate codons for a particular amino acid are equally likely in an open reading frame.
E ESTs provide verification for predicted gene sequences.

15. Which of the following statements regarding RNA capping is/are TRUE?

A Capping is only carried out when the C-terminal domain of the RNA polymerase is phosphorylated.
B Capping modifies the 3' end of the mRNA by the addition of a 7-methylguanosine.
C mRNA guanylyl transferase removes the β- and γ- phosphates of GTP.
D Methylation occurs at the nitrogen 7 of the pyrimidine ring.
E RNA capping can be found in primary transcripts.

16. Which of the following statements regarding RNA Polymerase II is/are TRUE?

A It does not share any subunits with any other RNA Polymerase.
B It is responsible for the transcription of tRNAs.
C It requires many additional transcription factors for initiation.
D It recognizes the -35 and -10 sequences for DNA binding.
E It is responsible for the transcription of mRNA, most snRNAs and miRNAs.

17. Which of the following regulate the *trp* operon in *E.coli*?

A The Trp Repressor protein.
B Autoregulation.
C Attenuation.
D Negative Regulation.
E Positive Regulation.

18. Which of the following is/are TRUE about bacterial transposons?

A They only carry genes required for their own mobilisation and insertion.
B They always replicate themselves during transposition.
C They can move from chromosome to plasmid DNA and vice versa.
D They create inverted repeats in the flanking host DNA during transposition.
E Transposase expression is required for mobilisation and insertion into a new site.

19. Which of the following factors affect the efficiency of DNA hybridisation?

A GC content.
B Length of the hybrid.
C Na^+ concentration.
D Temperature.
E Bovine Serum Albumin (BSA) concentration.

20. Which of the following statements regarding T4 bacteriophage is/are TRUE?

A T4 phages always kill their host.
B 1 in 10^4 T4 phage particles will incorporate host DNA.
C T4 phages only transfer specific regions of host DNA.
D A T4 replication cycle can be completed in approximately 20 min.
E A T4 replication cycle produces 10-100 viral particles.

21. Which of the following statements regarding nucleic acid labelling is/are TRUE?

A Polynucleotide kinase can be used for END labelling.
B α^{32}PATP can be used to replace the phosphate at the 5' end of DNA fragment.
C ^{32}PdATP can be used for fill-in reaction by Klenow fragment, but not ^{32}PdCTP.
D Fluorescein label can be introduced onto bases.
E Digoxigenin label can be introduced onto sugars.

22. Genetic linkage maps in *E.coli* were initially created using which of the following factors?

A Temperate phages for fine mapping.
B Hfr strains for time of entry mapping.
C Auxotrophic strains.
D Naturally transformable bacteria.
E Genome sequencing.

23. Which of the following statements regarding Type II restriction endonucleases is/are TRUE?

A They require ATP for cleavage.
B They always create sticky ends.
C They can recognise inverted repeat palindromes.
D They cannot be used to cut mammalian DNA.
E The reaction they catalyse is hydrolysis.

24. Which of the following statements regarding DNA agarose gel electrophoresis is/are TRUE?

A Agarose is a linear polymer extracted from seaweed.
B Larger DNA fragments move faster than smaller fragments.
C The higher the voltage applied, the slower the DNA fragments move.
D Electrophoretic mobility decreases with increasing gel concentration.
E Unlike circular DNA, linear DNA separation is not due to the molecular sieving effect.

25. Which of the following statements is/are TRUE?

A Oswald Avery identified DNA as the carrier of genetic material.
B Linus Pauling solved the structure of DNA.
C Rosalind Franklin isolated the first type II restriction enzyme.
D Kary Mullis developed the polymerase chain reaction.
E Arthur Kornberg isolated DNA polymerase I.

SECTION B

Answer ONE question from this section, in a SEPARATE answer book

26. Fat mice can be produced by two independently assorting genes. The homozygous genotype *ob*/*ob* produces a fat mouse called "obese" whilst its dominant allele *Ob* produces normal growth. *ad* when homozygous also produces a fat mouse called "adipose", and its dominant allele, *Ad*, produces normal growth. A completely homozygous strain of fat mice is crossed to a normal strain. The F_1 are normal and on backcrossing to the fat strain, litters containing 40 fat and 20 normal pups are produced. When normal backcross progeny (i.e., the 20 above) were inbred 70 normal and 42 fat progeny were produced.

    (a) Construct a genetic scheme that accounts for these data. Diagram the crosses using Punnett squares. (50%)

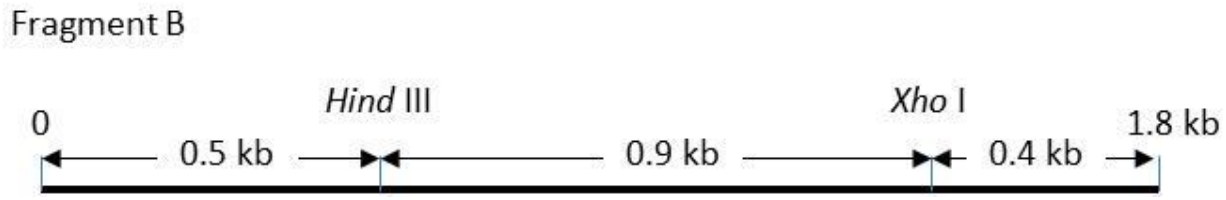
    (b) Compare the data from both crosses with expectations based on your model using Chi-square (see table at end of paper); departures should not be significant. (20%)

    A random pair of fat mice from the backcross progeny are mated (one male, one female).

    (c) What is the probability that they will produce at least some fat pups (at least in theory)? (30%)

Explain your reasoning throughout.

27. You have amplified a 1.8 kbp PCR product of gene A using *Taq* DNA polymerase and a cDNA library as template. This PCR product was named fragment B. You then cloned fragment B into plasmid C by TA cloning, and this newly created plasmid is called plasmid D. The TA cloning site in plasmid C is located in the middle of *LacZ* gene, and there is a *Hind*III site just upstream of the TA cloning site, a *Bam*HI site just downstream of the other side of the cloning site, and an *Eco*RI site 2.0 kb upstream of the cloning site. There is only one site for *Hind*III, *Bam*HI, and *Eco*RI in plasmid C. The size of plasmid C is 4.3 kbp. Following ligation and bacterial transformation, positive clones were identified by blue/white selection. The restriction map of fragment B is shown below. There are no restriction sites for *Eco*RI and *Bam*HI in fragment B.



    a) In the blue/white selection, which colonies are likely to have the fragment B insert? Explain why. (20%)

    b) Construct two possible restriction maps of plasmid D. The distances (in kbp) between each restriction sites should be indicated. Mirror images are not counted as separate maps. (40%)

Question continues on next page

c) What are the fragment sizes for a *Hind*III + *Eco*RI digest of plasmid D? There are two possible combinations. (20%)

d) If you perform Southern blotting for *Hind*III + *Bam*HI digested plasmid D using the 1.8kb fragment B as a probe, what is the expected size of bands? (20%)

Explain your reasoning throughout.

SECTION C

Answer ONE question from this section, in a SEPARATE answer book

28. Describe what the nucleosome is in terms of both its composition and its function.

29. Describe the steps involved for mRNA processing into miRNAs and describe how they act as gene regulatory components. In particular describe the key role they play in *C.elegans* early stage larval development.

30. Describe how you would go about purifying nucleic acids from cells (prokaryotic or eukaryotic) and what chemical and physical properties you would exploit to do so.

31. Compare and contrast the relative roles of RNA and protein in the process of bacterial translation when proteins are synthesized.

SECTION D

Answer ONE question from this section, in a SEPARATE answer book

32. Conjugation and transformation can both aid in the acquisition of genetic material and hence bacterial evolution and diversity. Compare and contrast how these two processes occur highlighting how they can be differentiated *in vitro*.

33. Give an example of the application of gene cloning in agriculture.

34. With reference to the structure of eukaryotic genes, indicate how genes are identified from genome sequence using bioinformatic tools.

35. Describe how Mendel's principle of Independent Assortment explains the dihybrid ratios he observed and explain why these ratios do not always apply at the genetic and chromosomal level.

End of paper

Percentage Points of the Chi-Square Distribution

Degrees of Freedom	Probability of a larger value of x^2								
	0.99	0.95	0.90	0.75	0.50	0.25	0.10	0.05	0.01
1	0.000	0.004	0.016	0.102	0.455	1.32	2.71	3.84	6.63
2	0.020	0.103	0.211	0.575	1.386	2.77	4.61	5.99	9.21
3	0.115	0.352	0.584	1.212	2.366	4.11	6.25	7.81	11.34
4	0.297	0.711	1.064	1.923	3.357	5.39	7.78	9.49	13.28
5	0.554	1.145	1.610	2.675	4.351	6.63	9.24	11.07	15.09
6	0.872	1.635	2.204	3.455	5.348	7.84	10.64	12.59	16.81
7	1.239	2.167	2.833	4.255	6.346	9.04	12.02	14.07	18.48
8	1.647	2.733	3.490	5.071	7.344	10.22	13.36	15.51	20.09
9	2.088	3.325	4.168	5.899	8.343	11.39	14.68	16.92	21.67
10	2.558	3.940	4.865	6.737	9.342	12.55	15.99	18.31	23.21
11	3.053	4.575	5.578	7.584	10.341	13.70	17.28	19.68	24.72
12	3.571	5.226	6.304	8.438	11.340	14.85	18.55	21.03	26.22
13	4.107	5.892	7.042	9.299	12.340	15.98	19.81	22.36	27.69
14	4.660	6.571	7.790	10.165	13.339	17.12	21.06	23.68	29.14
15	5.229	7.261	8.547	11.037	14.339	18.25	22.31	25.00	30.58
16	5.812	7.962	9.312	11.912	15.338	19.37	23.54	26.30	32.00
17	6.408	8.672	10.085	12.792	16.338	20.49	24.77	27.59	33.41
18	7.015	9.390	10.865	13.675	17.338	21.60	25.99	28.87	34.80
19	7.633	10.117	11.651	14.562	18.338	22.72	27.20	30.14	36.19
20	8.260	10.851	12.443	15.452	19.337	23.83	28.41	31.41	37.57
22	9.542	12.338	14.041	17.240	21.337	26.04	30.81	33.92	40.29
24	10.856	13.848	15.659	19.037	23.337	28.24	33.20	36.42	42.98
26	12.198	15.379	17.292	20.843	25.336	30.43	35.56	38.89	45.64
28	13.565	16.928	18.939	22.657	27.336	32.62	37.92	41.34	48.28
30	14.953	18.493	20.599	24.478	29.336	34.80	40.26	43.77	50.89
40	22.164	26.509	29.051	33.660	39.335	45.62	51.80	55.76	63.69
50	27.707	34.764	37.689	42.942	49.335	56.33	63.17	67.50	76.15
60	37.485	43.188	46.459	52.294	59.335	66.98	74.40	79.08	88.38