IMPERIAL COLLEGE LONDON

B.Sc. Examination 2018

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

MOLECULAR BIOLOGY

Thursday 21 June 2018 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 Single Nucleotide Polymorphisms (SNPs) is/are TRUE?

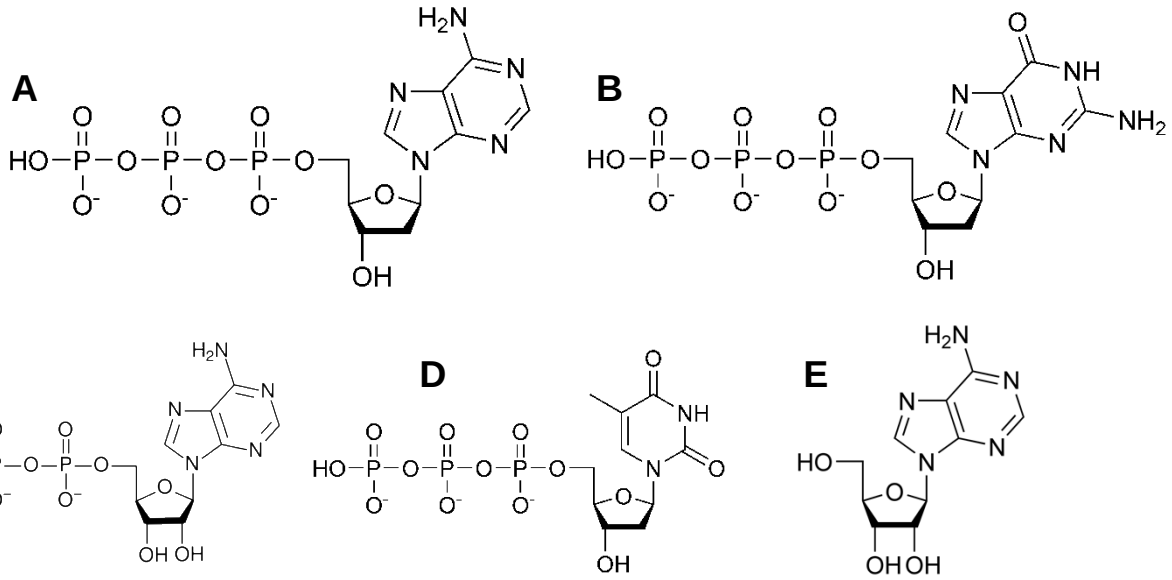
A SNPs are normally inherited in a non-Mendelian fashion.
B A-G changes (purine to purine) are more common than A-T changes (purine to pyrimidine).
C SNPs occur roughly every 100kbp in the human genome.
D SNPs in the mitochondrial DNA control region are more common than in the nuclear genome.
E The International HapMap Project focussed on common SNPs whereby more than 10% of the population show either allele.

2. What happens when double-stranded DNA is heated at 100°C?

A Digestion.
B Annealing.
C Denaturation.
D Hybridisation.
E Renaturation.

3. Which of the following statements about sequencing quality (Q) scores is/are TRUE?

A A score of 10 denotes 90% base call accuracy.
B A score of 40 presents 1 in 40 chance of incorrect base call.
C A score of 30 presents 1 in 1000 chance of incorrect base call.
D A score of 10 denotes 10% base call accuracy.
E A score of 30 presents 1 in 100 chance of incorrect base call.



Which of the above molecules:

4. Is a nucleoside?
5. Contains a purine base?
6. Is a precursor for DNA synthesis?
7. Lacks a gamma phosphate?

8. Which of the following is/are required in Sanger sequencing?

A 2'-Deoxycytosine triphosphate.
B 2'-Deoxycytosine diphosphate.
C 2', 3'-Dideoxycytosine triphosphate.
D 2', 3'-Dideoxycytosine diphosphate.
E 2', 3'-Dideoxyguanine triphosphate.

9. Which of the following statements regarding the Cystic Fibrosis gene is/are TRUE?

A The allele that leads to a deletion of the Phenylalanine residue in position 508 (F508) is the only known disease causing allele.
B Cystic Fibrosis is an example of a sex linked recessive condition.
C Most Cystic Fibrosis children are born from two unaffected parents.
D Random walking was used to clone the CF gene.
E The Cystic Fibrosis gene was identified by positional cloning.

10. Which of the following statements regarding chromatin is/are TRUE?

A DNA is wrapped around nucleosomes.
B A nucleosome is an octamer of histones H1, H2A, H2B and H4.
C Histones are not highly conserved.
D The histone octamer interacts with 146 bp of DNA.
E Histone H1 locks the octameric complex.

11. 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.

12. If a genome is sequenced to a depth of coverage of 12x, which of the following statements is/are TRUE?

A Each sequence read is present in 12 copies.
B Every nucleotide is present in 12 sequence reads on average.
C Each chromosome was sequenced 12 times.
D Every nucleotide is present in exactly 12 sequence reads.
E Every nucleotide is present in at least 12 sequence reads.

13. Which of the following statements regarding Type II restriction enzymes is/are TRUE?

A They have exonuclease activity.
B They have endonuclease activity.
C They require ATP for cleavage.
D They recognize specific sequences.
E They exist in the cytosol of eukaryotic cells.

14. Which of the following statements regarding Taq polymerase is/are TRUE?

A It uses RNA as a template.
B It adds an adenosine residue to the 3' end of the amplified product.
C It can act as a polymerase at 72°C.
D It has exonuclease activity.
E It has endonuclease activity.

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

A Loss of function mutations tend to be dominant.
B Partial function mutations are also called hypomorphs.
C A dominant negative form of a gene results from a silent or neutral mutation.
D Most changes in DNA result in silent or neutral mutations.
E A gene which does not have enough function in a heterozygote to be functionally wild type is called haplosufficient.

16. Which of the following statements concerning horizontal gene transfer in bacteria is/are TRUE?

A During transformation, uptake of DNA is initiated by the recipient.
B Transformation requires the donor to synthesize a competence pilus.
C In conjugation, the donor initiates DNA transfer.
D Transduction requires cell-cell contact.
E Transduction is mediated by bacteriophages.

17. Which of the following is/are palindromes?

A GCGCGCGC.
B GGGGCCCC.
C GGGGAAAA.
D CGGGGGGC.
E GGCCGGCC.

18. Which of the following statements regarding bacterial conjugation is/are TRUE?

A The F pilus is synthesized by the donor cell and assembled by the type IV secretion machinery.
B The transfer of bacterial plasmid is bidirectional.
C Strains lacking the F factor are recipients and designated F^-.
D A complex between relaxase and ssDNA migrates through the Tra pore.
E The RP4 plasmid has a narrow host range.

19. Which of the following statements regarding sex linked inheritance and chromosomal inheritance is/are TRUE?

A Bridges' exceptional progeny from the cross white eyed females x red eyed males were XXY and XO individuals.
B The Y chromosome is inherited in a strictly maternal pattern of inheritance.
C Non-disjunction arises when each chromosome separates to opposite poles during meiosis I.
D The X and Y chromosomes are an example of a heteromorphic pair of chromosomes.
E Non-sex chromosomes are called karyosomes.

20. Which of the following statements regarding the Hardy-Weinberg equilibrium is/are TRUE?

A It does not apply to a gene where there are more than two alleles present in a population.
B Mating is not assortative with regards to MHC alleles in humans.
C The genotype frequencies of heterozygotes will be $2pq$ where p is the frequency of one allele and q the frequency of the other.
D It only applies where there is no migration of alleles into or out of the population.
E It does not apply to VNTR alleles and genotypes.

21. Which of the following statements regarding bacterial transformation is/are TRUE?

A The process is solely encoded by the recipient bacteria.
B The Com pilus is related to another structure found on bacteria - the F pilus.
C Transformation is a conserved process in Gram (-) and Gram (+) bacteria.
D E coli was the first species to be discovered as transformable.
E The RecA protein polymerises on ssDNA and promotes a homology search along chromosomal DNA.

22. Which of the following statements is/are TRUE for both transcription and DNA replication?

A Both require a primer.
B Both require a DNA template.
C Both require the addition of nucleotides to the 3' end of the growing chain.
D Both require RNA polymerase.
E Both comprise of initiation, elongation and termination phases.

23. Which are the following statements regarding chromosome organisation is/are FALSE?

A Chromosomal chromatids may consist of helically packed loops of 30 mm fibres.
B Interphase chromatin is equally condensed.
C Euchromatin is not transcriptionally active.
D The telomeres and the centromere are important for the manoeuvring of chromosomes in cell division and protection of DNA ends.
E Heterochromatin contains large proportions of repetitive sequences.

24. Which of the following are properties of miRNAs?

A They block replication.
B They block translation.
C They promote messenger degradation.
D They are active in the cytoplasm.
E They are present in prokaryotes and eukaryotes.

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

A Epistasis is an example of gene interaction.
B Recessive epistasis occurs when one allele of one gene masks the expression of all other genotypes of another gene.
C The *B* and *E* genes in labradors which affect coat colour provide an example of dominant epistasis.
D The 9:3:3:1 Mendelian dihybrid ratio is an example of recessive epistasis.
E The *yellow* and *white* genes on the *Drosophila* X chromosome provide an example of recessive epistasis.

SECTION B

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

26. You created a cDNA library using rat brain mRNA and oligo dT primer, with a *Not*I sequence contained at the primer's 5' end. An *Eco*RI adaptor (cohesive end) has been added to the cDNA and *Not*I digestion was performed. This cDNA library was then cloned into plasmid A at *Eco*RI (5' side of cDNA) and *Not*I (3' side of cDNA) sites. This library cloned into plasmid A was transformed into *E.coli*, and the bacteria cells were grown on an agar plate. Colonies were transferred to a nitrocellulose membrane, and colony hybridisation was performed using radio-labelled DNA fragment of gene B as a probe. X-ray autoradiograph was performed, and you identified two colonies as positive. The two original colonies on the agar plate were isolated and cultured overnight in LB medium. The plasmid DNA was purified from these two colonies, and named as plasmid C and plasmid D. The fragment sizes from the restriction enzyme digest patterns of plasmid A, C, D are shown in Tables 1-3.

Table 1: The digest patterns of plasmid A

*Eco*RI + *Not*I	2.5 kb
*Kpn*I	2.5 kb
*Kpn*I + *Eco*RI	1.5 kb, 1.0 kb
*Hind*III	2.5 kb
*Hind*III + *Eco*RI	2.0 kb, 0.5 kb

Table 2: The digest patterns of plasmid C

*Eco*RI + *Not*I	3.0 kb, 2.5 kb, 1.5 kb
*Kpn*I	4.7 kb, 2.3 kb
*Kpn*I + *Eco*RI	2.5 kb, 2.2 kb, 1.5 kb, 0.8 kb
*Hind*III	4.7 kb, 2.3 kb
*Hind*III + *Eco*RI	3.0 kb, 2.3 kb, 1.2 kb, 0.5 kb

Table 3: The digest patterns of plasmid D

*Eco*RI + *Not*I	2.5 kb, 1.5 kb
*Kpn*I	4.0 kb
*Kpn*I + *Eco*RI	2.5 kb, 1.5 kb
*Hind*III	2.3 kb, 1.7 kb
*Hind*III + *Eco*RI	2.3 kb, 1.2 kb, 0.5 kb

(a) Construct maps of plasmid A. The distances (in kb) between each restriction sites should be indicated. (20%)

(b) Construct maps of plasmid C. The distances (in kb) between each restriction sites should be indicated. (20%)

(c) Construct maps of plasmid D. The distances (in kb) between each restriction sites should be indicated. (20%)

(d) What are the fragment sizes for a *Eco*RI + *Not*I + *Kpn*I + *Hind*III digest of plasmid C? (20%)

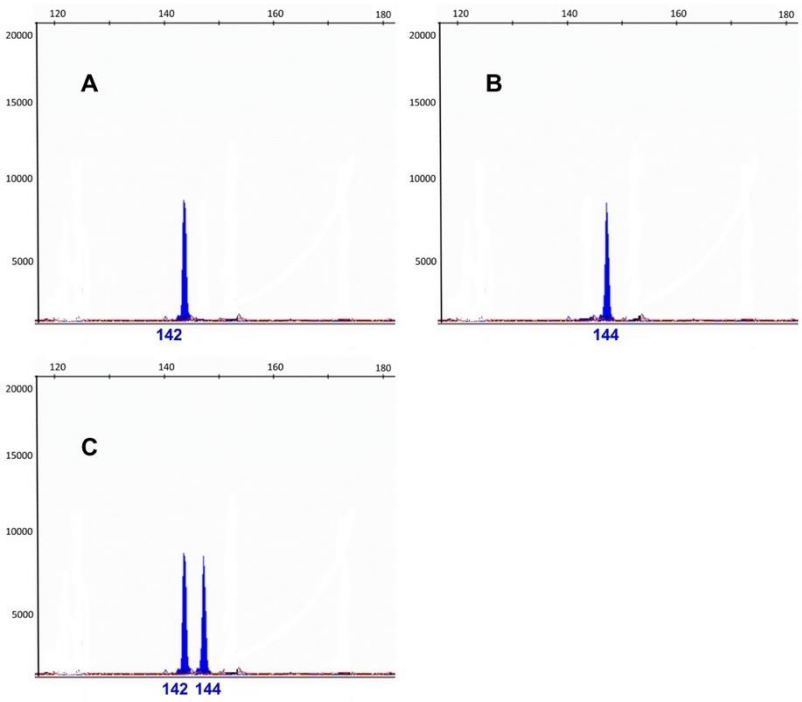
(e) Indicate which 2 fragments in part (d) most likely contain the hybridisation site for the gene B probe. State the restriction sites for both ends of the fragments with the fragment sizes. (20%)

Explain your reasoning throughout.

27. The *Drosophila* gene *easily shocked* has a recessive mutant “bang sensitive” mutant phenotype whereby mutants become paralysed with seizure when the vial is banged on the bench. When mutant males from a pure breeding stock are crossed to pure breeding wild type females, all of the F1 are wild type. When the F1 are allowed to interbreed, half of the F2 male offspring exhibit the mutant, bang sensitive phenotype whereas the other half are wild type. All of the F2 females are wild type.

(a) From the information given so far, what can you deduce about the chromosomal location of the *easily shocked* gene? (15%)

The parental flies are genotyped using capillary gel electrophoresis for a microsatellite locus whose location is unknown. The male parents exhibit a band pattern shown in the diagram on the next page as panel A. The female parents exhibit a band pattern corresponding to panel B.



(b) Giving reasoning for your answer, what would you predict the band pattern of the F1 females to be? (10%)

When the F2 progeny are genotyped, the following microsatellite band patterns are observed amongst the different phenotypic classes:

	Electrophoretic band pattern	Number of F2
Wild type F2 females	C	252
Wild type F2 females	B	246
Wild type F2 males	A	26
Wild type F2 males	B	223
Bang sensitive F2 males	A	227
Bang sensitive F2 males	B	24

(c) What chromosome must the microsatellite locus be on? (15%)

(d) The map position of the *easily shocked* gene is 53. What are the possible map positions of the microsatellite locus? (35%)

(e) Describe how you would distinguish the possible map positions of the microsatellite locus. (25%)

Explain your reasoning throughout.

SECTION C

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

28. Explain how TA cloning works, highlighting its advantages and disadvantages compared to other cloning strategies.

29. Explain the reasons why replication is “semi-discontinuous”, describing the process happening at the replication fork. Use labelled diagrams to illustrate your answer.

30. What are the essential features required of a plasmid vector for growth, selection and expression in bacteria?

31. With reference to the structure of DNA, define the terms primary, secondary and tertiary structure.

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. Describe how pedigree analysis and gene association methods can lead to the identification of disease loci in the human genome.

34. Discuss the methods used by ab initio gene prediction programs to predict gene structures in prokaryotes and eukaryotes. Your answer should include the genomic features used by these programs to make their predictions.

35. Explain how two genes within the same genome can be inherited in relation to each other (70%). Describe how linkage relationships can be used to construct genetic maps of the genome (30%).

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