AU-6999
Model Answer
B.A./B.Sc. (Fifth Semester) Examination, 2014
ANTHROPOLOGY
Paper: Second
(Fundamentals of Human Genetics)
Time Allowed: Three hours

Maximum Marks: 60 ***Pass Mark: 24***

Note: *Attempt questions of all* ***two*** *sections as directed.*
Distribution of marks is given with sections.

Section – 'A' **Marks 2X10=20**

1. Select one of the most appropriate answer from the following objective questions:

(i) The term "Meiosis" was coined by -
(a) Robert Brown (b) Farmer and Moore (c) Walter Flemming (d) Kolliker and Benda

(ii) Two different alleles at a particular locus is called _____ genotype.
(a) homozygous (b) compound (c) heterozygous (d) none of the above

(iii) _____ is the factory of the protein.
(a) Ribosome (b) Mitochondria (c) Nucleus (d) Lysosome

(iv) Identify the correct sequence -
(a) Diakinesis – Telophase I – Metaphase I – Anaphase I
(b) Anaphase I – Telophase I – Diakinesis – Metaphase I
(c) Diakinesis – Metaphase I – Anaphase I – Telophase I
(d) Metaphase I – Diakinesis – Anaphase I – Telophase I

(v) Phenylketonuria is due to deficiency of _____ enzyme.
(a) Phenylalanine hydroxylase (b) Glyoxalase
(c) Adenosine Deaminase (d) Glutamate Pyruvate

(vi) _____ is known as the building blocks for new DNA strand in PCR.
(a) Primer (b) Buffer (c) $MgCl_2$ (d) dNTPs

(vii) "Crossing Over" is observed during _____ cell division.
(a) Diplotene (b) Pachytene (c) Zygotene (d) Leptotene

(viii) Individual with 13 trisomy is called -
(a) Patau's syndrome (b) Klinefelter's syndrome
(c) Turner syndrome (d) Down's syndrome

(ix) Base substitution that leads to amino acid substitution is _____ mutation.
(a) silent (b) non-sense (c) missense (d) frame-shift

(x) STRP stands for -
(a) short term restricted length polymorphism
(b) smallest repeat polymorphism
(c) single time repeat polymorphism
(d) short tandem repeat polymorphism

Key Answers:

(i) b (ii) c (iii) a (iv) c (v) a (vi) d
(vii) a (viii) a (ix) c (x) d

Section – 'B' **Marks 4X10=40**

Note: *Write long answers of the following questions. Attempt any* ***four*** *questions. All questions carry 10 marks.*

2. Write short notes on:

(i) Klinefelter's Syndrome

Klinefelter's Syndrome was first reported by Jacob and Strong in 1959. Affected individuals posses an extra X chromosome. Therefore, produces more female hormone and hence balance is disturbed effecting the development and maturation of the normal male characters.

Important characteristic features of Klinefelter's Syndrome includes:

– It occurs 1 out of every 700 births of male children
– Occurs in males only
– Infants appears to be normal, but in course of maturity they develop certain phenotypic features
– Testes and penis are small
– Enlarge breasts (condition is called gynecomastia)
– Sparse body hair
– Longer limbs in proportion to the rest of the body
– Mentally retarded
– Usually always sterile
– Chromosomal karyotype is XXY
– Sex Chromatin Positive

(ii) Balance Polymorphism

Variant alleles are maintained in the population through various evolutionary forces like natural selection. The deleterious effects in a homozygous individual are balanced by its positive effects in a heterozygous person. One of the best examples of balance polymorphism is sickle cell trait. Sickle cell anaemia is caused by a mutation to a beta globin gene. Specifically, a single nucleic acid in this gene's DNA is altered, as a result of which the transcribed protein contains a valine where a glutamate should be. This resultant haemoglobin (sometimes called HbS, rather than the usual HbA) looks just like normal from a distance, but under low oxygen conditions, it has the unfortunate tendency to polymerise. These long chains of HbS stuck together form insoluble precipitates and distort the shape of the cell, causing it to sickle. The sickled cells aren't flexible enough to pass through our capillary beds, and so they lodge there, causing obstruction. The disease is often fatal. Sickle cell disease is an autosomal *recessive* trait, meaning that a person has to have *two* (out of two) copies of this bad allele before he shows symptoms.

Heterozygotes generally don't show symptoms of sickle cell disease, but they do display a marked resistance to malaria. These individuals are more likely to survive their initial acute malarial attacks than are people with two genes for normal hemoglobin. Also, they suffer none of the morbidity and mortality of sickle cell disease. Natural selection plays its parts in two important ways. First, many of the homozygous sicklers (HbS/HbS) die of anemia before attaining the age of reproduction. Secondly, many of the homozygous normal (HbA/HbA) die of malaria, as they have less resistance power to fight malaria. By the process of selection both types of homozygous persons are eliminated leaving the heterozygous and thereby a balance between the normal allele (HbA) and HbS allele is maintained.

3. Briefly describe principles of autosomal dominant inheritance with a suitable example.

The inheritance pattern of any particular trait could be studied under two broad categories such as autosomal inheritance and sex-linked inheritance. Further, autosomal inheritance could be divided into autosomal recessive and autosomal dominant, whereas, sex linked inheritance as X-linked (dominant or recessive) and Y-linked inheritance.

Pattern of Inheritance can be studied through Pedigree analysis. A pedigree shows the inheritance of a trait in a family through multiple generations. It can also be used to deduce genotypes of family members. By analysing a pedigree the nature of inheritance of a particular trait like autosomal dominant inheritance, recessive inheritance, X-linked inheritance, Y-linked inheritance could be ascertained.

Silent characteristic features of autosomal dominant inheritance –

(i) Every affected individual has at least one affected parent
(ii) an affected person has transmitted the trait to almost half of his or her offspring
(iii) Affected males and females appear in each generation
(iv) Affected mothers or father transmit the phenotype to both sons and daughters
(v) Both males and females are affected
(vi) No skipping of generations

Examples: Brachydactyly, Wooly Hair, Huntington Disease are good examples of recessive trait

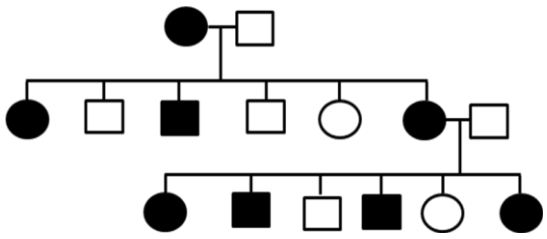

Figure: Pedigree showing diagrammatic representation of autosomal dominant inheritance

4. Explain electrophoresis and genotyping technique used in genetic studies.

Electrophoresis Techniques: It is the term used to describe the movement of ions in a solution under the influence of an electric field. This electrokinetic phenomenon was observed for the first time in 1807 by Ferdinand Frederic Reuss. This is caused by the presence of a charged interface between the particle surface and the surrounding fluid. It is the basis for a number of analytical techniques used in biochemistry for separating molecules by size, charge, or binding affinity. Electrophoresis is carried out in a buffer system whereby the solution containing the ions to be separated is supported in a more or less inert material such as paper, starch or agarose. The main apparatus / chemicals required for carrying out electrophoresis are: (i) Electric Power Supply (ii) Electrophoresis Tank (iii) Gel – starch, agarose, cellulose acetate, acrylamide (iv) Buffer solution.

The tanks are impregnated with buffer solution and the gel is suspended between the two buffer components. Electrophoresis of positively charged particles (cations) is called cataphoresis, while electrophoresis of negatively charged particles (anions) is called anaphoresis. Electrophoresis has been used as an analytical tool in clinical and research laboratories. One of the most widespread applications of this technique lies in the field of protein separations. Electrophoresis is carried out with the gel in either the vertical or

horizontal position. Based on the position, methods of electrophoresis are of two kinds i.e. Vertical Electrophoresis and Horizontal Electrophoresis.

Genotyping Technique: It is a technique use for identification of genotype. PCR products are used for understanding the genotype of the individual. Digested products obtained after PCR and restriction digestion were genotyped using agarose or polyacrylamide gel electrophoresis technique based on the desired band size. Gel electrophoresis allows the separation and identification of DNA fragments of various sizes. Polyacrylamide gels have a small range of separation, but very high resolving power. So, it can separate the smaller band sizes. While agarose gels have a large range of separation, but relatively low resolving power and are good for separating larger band sizes. So, the gel was chosen based on the expected band size. The digested product was mixed with loading dye and loaded into the wells in a supporting matrix of agarose or polyacrylamide and then exposed to an electrical field.
Loading dye acts as both coloring substance for naked eye visualization and also adds weight to the product into the well in order to prevent from floating out as submarine gels are used. The negatively charged DNA molecules migrate through the pores in the agarose or polyacrylamide matrix to the positive anode, their velocity decreases as their fragment size increases. The location of the DNA within the gel was determined by staining with a fluorescent intercalating dye such as ethidium bromide (EtBr) and viewed under a UV light source. In case of agarose gel, EtBr was added in making the gel but in case of polyacrylamide, the staining process was done after the electrophoresis run was completed. The gel was dipped in the solution of EtBr for 10 minutes.

5. Writ short note on DNA polymorphism and its importance in anthropological studies.

The term DNA polymorphism refers to a wide range of variations in nucleotide repeats, or single nucleotide variants and they provide the basis for direct physical analysis of genotype using molecular methods. DNA polymorphisms that have no known function are called anonymous loci. Genetic polymorphism is the existence of variants with respect to a gene locus (alleles), a chromosome structure (size of centromeric heterochomatin), a gene product (variants in enzymatic activity or binding affinity), or a phenotype. Coding Region SNPs includes: *Synonymous* (the substitution causes no amino acid change to the protein it produces) and *Non-Synonymous* (the substitution results in an alteration of the encoded amino acid).
Types of DNA polymorphism: (i) Single nucleotide polymorphism (SNPs) (ii) Restriction fragment length polymorphism (RFLPs) (iii) Amplified Fragment Length Polymorphisms (AFLPs) (iv) Short tandem repeat polymorphism (STRPs) (v) Variable number of tandem repeat polymorphism (VNTR) (vi) Interspersed Repetitive DNA Polymorphism (vii) Randomly amplified polymorphic DNAs (RAPDs).
Some important applications of DNA Polymorphism in anthropological studies are: (i) used in genetic mapping studies to identify DNA markers that are genetically linked to disease genes in the chromosomes in order to pinpoint their location, (ii) used in DNA typing for identifying individuals (iii) tracking the course of virus and bacterial epidemics (iv) studying human population history, (v) improving cultivated plants and domesticated animals, (vi) genetic monitoring of endangered species and for many other purposes.

6. Draw the structure of DNA and write its properties and functions.

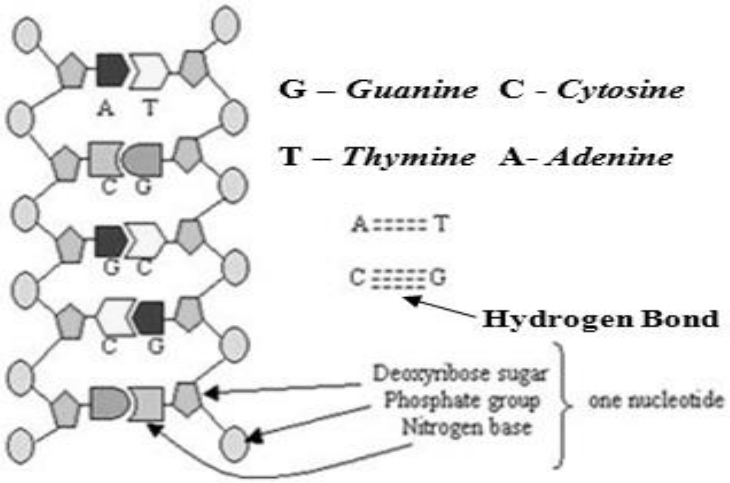

Figure: Diagrammatic representation of DNA Structure

Properties: DNA is a long polymer made from repeating units called nucleotides. The structure of DNA of all species comprises two helical chains each coiled round the same axis. DNA has a number of special physical and chemical properties that are important to its structure and functioning.

(a) Physical Properties: In living organisms such as humans, DNA exists as a pair of molecules rather than a single molecule. These strands are entwined in the shape of a double helix and the helix is kept stable by hydrogen bonds, which can be found between the bases attached to the two strands. DNA is made up of smaller units called nucleotides. Each nucleotide consists of a phosphate group, a sugar and a nitrogenous base. *(b) Base Pairing:* In DNA, bases are specific in that an adenine base only pairs with a thymine base. Cytosine base will only bond to a guanine base. This base pairing is known as complementary base pairing.

(c) DNA Grooves: DNA has two kinds of grooves that play important roles in its functioning. Major and minor grooves are structures to allow for necessary proteins in your body to make contact with bases. DNA grooves seen in the structure of DNA facilitate the binding of proteins like transcription factors, which then serves to keep the cellular processes occurring effectively within our body. *(d) DNA Supercoiling:* Supercoiling is a central property of DNA. DNA can be in a relaxed or coiled state and it is this coiling that allows extremely long strands of DNA to fit or 'pack' into the comparatively much smaller cells in our bodies. This supercoiling property makes DNA more efficient by allowing it to make better use of space and fit neatly into a significantly smaller space relative to its relaxed, longer size. *(e) DNA Conformations:* DNA can exist in different conformations and these conformations interact with enzymes and they are also involved in aspects such as DNA repair. *(f) DNA Sense and Antisense:* DNA holds the genetic 'codes' to make RNA. In turn, RNA is needed in body because it holds the codes for the amino acids that make proteins. The antisense strand is the DNA strand that carries important information to make proteins by binding to the RNA. This antisense strand is the key for making proteins. In comparison, the sense strand is the one that does not code for RNA.

Biological Functions: DNA usually occurs as linear chromosomes in eukaryotes, and circular chromosomes in prokaryotes. The set of chromosomes in a cell makes up its genome; the human genome has approximately 3 billion base pairs of DNA arranged into 46 chromosomes. The information carried by DNA is held in the sequence of pieces of DNA called genes. Transmission of genetic information in genes is achieved via complementary base pairing.

7. Define biochemical genetics with a suitable example.

Biochemical Genetics is the branch of biology that deals with the formation, structure, and function of macromolecules essential to life, such as nucleic acids and proteins, and especially with their role in cell replication and the transmission of genetic information. It is the study of genes governing the biochemical process. The processes can be explained and exemplified by various serious afflictions such as inborn errors of metabolism, the haemoglobinopathies and immunoglobinopathies.

Biochemical Genetics involves the diagnosis and management of inborn errors of metabolism in which patients have enzymatic deficiencies that perturb biochemical pathways involved in metabolism of carbohydrates, amino acids, and lipids. Examples of metabolic disorders include galactosemia, glycogen storage disease, lysosomal storage disorders, metabolic acidosis, peroxisomal disorders, phenylketonuria, and urea cycle disorders.

Pharmacogenetics – is a special branch of biochemical genetics deals with the drug responses and their genetic modifications. These genetically determined variations in drug responses are known through the well known drugs like hydrogen peroxide, succinylcholyne, isoniazid, primaquine and their hypothesis.

Example: Phenylketonuria (PKU) is an autosomal recessive metabolic genetic disorder characterized by a mutation in the gene for the hepatic enzyme phenylalanine hydroxylase (PAH), rendering it non-functional. The PAH gene is located on chromosome 12 (q22-24.1). It helps/necessary in conversion/metabolism of amino acid phenylalanine to the amino acid tyrosine. Mutation in PAH gene reduced the activity/production of enzyme causing accumulation of phenylalanine and converted into phenylpyruvate (also known as phenylketone) instead of tyrosine. This phenylketone can be detected in the urine.

8. Define DNA fingerprinting and write its significance in Forensic Anthropological studies.

DNA fingerprinting was developed in 1984 by Alec. J. Jeffrey at the University of Leicester.

An actual human fingerprint is a series of ridges on the tip of each finger. The pattern of these ridges varies from person to person and is so distinctive that each person can be identified by their fingerprint. DNA fingerprinting uses the pattern of DNA fragments caused by specific enzymes to identify individual organisms: humans, other animals, plants, or any other organism with DNA.

DNA fingerprinting is a technique that analyzes the pattern of DNA fragments generated when a DNA genome is cleaved using enzymes that recognize and cut at specific sequences in the DNA. The enzymes that are used were selected so that the pattern of DNA fragments for an individual will be unique, just as our physical fingerprints are. No DNA fingerprint test can prove defendant's guilt, but a match can establish probability. A fingerprint begins with a biological sample of tissue such as blood, skin, or semen followed by isolation of DNA from the available sample. Amplification of the target region in the DNA sequence is done using Polymerase Chain Reaction and restriction enzyme digestion break DNA into more manageable sizes for fingerprinting. Gel electrophoresis separates the DNA fragments by size of the base pairs, as the smaller base pairs move faster through the gel. This technique is use to determine whether a blood sample from an individual matches a crime scene blood, semen or tissue sample. It is also used in paternity analysis, identification of victims of disasters or war and many studies of ecology and evolution.