Neutral Theory of Molecular Evolution

1) What is neutral theory of molecular evolution?
The evolution of traits with little or no effect on fitness is a random process involving mutation and genetic drift.
E = f(neutral mutation + random drift)

2) Who did put forward the neutral theory first?
M. Kimura put forward the Neutral Theory of molecular evolution first in 1968.

3) Explain the Neutral Theory of molecular evolution with two examples.
i) This theory focuses on neutral alleles resulted from neutral mutation which have no role on fitness. They do not affect morphology, physiology and behavior.
ii) Alleles are fixed in a population randomly by random genetic drift.
iii) The rate of random fixation of neutral mutation in evolution, per species per generation, is equal to the rate of occurrence of neutral mutation per species per generation and is independent of population size (Kimura, 1968).
iv) Evolutionary changes occur at molecular level and most of genetic variability within species includes protein and DNA polymorphism.
v) Many protein, chromosome and DNA variations are under selection but much molecular variations are nearly neutral.
vi) Nucleotide variation is the basis of protein polymorphism and this variation distinguishes two alleles within a species.
vii) Any gene with high mutation rate is deleterious and is eliminated or is maintained at very low frequency in the population.
viii) It includes two natural forces – mutation and genetic drift that cause molecular changes.
ix) Neutral mutations spread in a populations due to random genetic drift.
x) Molecular evolution involves insertion, deletion or substitution of molecules but the nucleotide evolution occurs majority by substitution at the rate of 5×10^{-9} per site per year maximally.
xi) Evolutionary rate per generation of a species is constant across lineage (Kimura,1968).
xii) Directional mutations give rise to many neutral mutations.

Example
Rising in number of amino acid in cytochrome c (cyt c) protein in different mammals follows a trend of evolution - 93 (Horse) → 95 (Pig and Dog) → 96 (Rabbit) → 104 (Rhesus monkey) →105 (Human and Chimpanzee) but the electron transport is not hampered.

The number of amino acids in α-globin changes in different vertebrates indicating a trend of molecular evolution - 62 (Shark) → 73 (Carp) → 79 (Newt) → 114 (Kangaroo) → 124 (Cow) → 141 (Human) over 440 million years of evolution. This change does not affect O_2 transport and H^+ regulation.

4) Mention the significance of Neutral Theory.
i) Many unimportant sites in DNA are predicted by the theory.
ii) Neutral theory is useful for thinking about the nature of evolutionary forces acting on variation at the DNA level.
iii) It has provided a set of testable predictions.
iv) This theory is a basic assumption of some methods of estimating phylogeny.
v) It affects molecular-clock hypothesis.
vi) It can predict evolutionary rate of a species.
vii) It states that there is an inverse relationship between importance of protein and its rate of evolution.

5) Drawbacks

i) Apparent disconnection between molecular and phenotypic changes.

ii) All tests of neutral theory have little statistical power i.e., indecisive.

iii)Testing of neutral theory is difficult because selection of genetic variation with no effect on fitness is difficult.

iv) It does not describe the adaptation of organism in environment.

v) It does not suggest that all morphological and genetic variations are neutral.

vi) It concludes that the natural selection is unimportant in shaping genome of a species. It is not true.

vii) This theory emphasizes on random process but the theory does admit a role of natural selection for selection of neutral allele as purifying agent.

6) Differentiate between Natural selection theory and Neutral theory in evolution.

Points	Natural Selection Theory	Neutral Theory
Change	Morphological, behavioural and ecological traits	Molecules of traits
Prime natural force	Mutation and natural selection	Genetic drift
Direction of evolution	Directional	Random
Selection of allele	It selects favourable alleles and deletes harmful alleles	Selects neutral alleles.
Focus	Adaptation	Random variation in composition of DNA
Variation and fitness	Variation affects fitness	Variation does not affect fitness