UNIT 5 MECHANISMS OF EVOLUTION

Contents

Learning Objectives

After reading this unit, you will be able to:

- appreciate the mechanisms of evolutionary forces and their importance;
- understand the different mechanisms of evolutionary forces; and
- learn about the example of natural selection, patterns of selection and types of genetic drift.

5.0 INTRODUCTION

The scope of evolution includes investigation of biological history of our planet, genetic diversity of populations, mechanisms of speciation and origin of living beings. Studies on evolution reveal how the different organisms originated during the course of time and what forces are responsible for their adaptation, survival and extinction. Population is the unit of evolution because sum of effect of all forces of evolution affects the entire population and causes

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changes from generation to generation. Evolution can be understood as changes taking place over time and include small or large, invisible or visible and non-adaptive and adaptive changes. Evolution is of two types. If changes occur overtime within the organism, it is called micro evolution and if it occurs from one being to another it is macroevolution. Microevolution cause changes in the allele frequency whereas macroevolution leads to speciation (production of new species from earlier species).

5.1 MECHANISMS OF EVOLUTION

There are four known forces of evolution, they are mutation, gene flow, natural selection and genetic drift. Mutation introduces new alleles into the population due to the occurrence of copying errors in DNA replication and transcription. Natural selection (due to the individual differences on the survival and reproductive success) and genetic drift (due to random sampling in small populations) differentially transmit alleles into the next generation. Gene flow, through migration, contributes alleles from one population to other (Vasulu, 2012). The interaction of the evolutionary forces is studied using genetic models to understand the distribution, turnover and diversity of alleles at the particular level. Evolutionary forces disturb the Hardy-Weinberg equilibrium and are responsible for the process of evolution. Interaction of evolutionary forces contributes to variation and spreading alleles within or between populations.

A detailed discussion on various evolutionary forces is given below.

5.1.1 Mutation

It is one of the evolutionary forces. It serves as a raw material of evolution. If evolution has to happen mutation should occur. Mutation occurs in every generation. Mutation is mostly random change in phenotype (colour, size and shape) or genotype forms. Genotype changes involve alteration in the sequence of DNA. Mutation introduces new alleles in the population and changes the allele frequencies. The survival of introduced allele depends on how it can affect the survival fitness of the population. If the introduced new allele is advantageous to the population it is supported by natural selection. Vernon Ingram was the first to identify change in the amino acid of valine in place of glutamic acid in the mutant haemoglobin of patients with sickle cell anaemia. The frequency of mutation in humans is one in 500 million nucleotides (Sudi and Ali– Dunkrah, 2005). Mutation includes all type of heritable changes. The process of introduction of mutation in a gene is called mutagenesis and resulting product is called mutant. The agent used to induce mutation is called a mutagen.

Depending on the frequency of mutant different terms are used. If frequency of genetic mutant is less than 1% it is called variant and if ≥1 it is termed as polymorphism. Mutations are known by different names depending on the number of bases, mechanism and region of localisation of variants as, single nucleotide polymorphisms, indels (insertion and deletion), short tandem and variable number of tandem repeats and copy number variations. Mutation rate is low and varies with the sites of the genome. In some sites its frequency is

higher than others and these are known as hot-spots of mutation. Higher rate of mutations occurs in intronic, repetitive sequences and non-coding regions of mitochondria (hypervariable regions 1 and 2, HV1 and HV2 respectively). Mutations in the HV1 and HV2 are useful to study the maternal history of population using haplo-group or population approaches. The rate of spontaneous mutations ranges from one in 10^4-10^8 gene per generation. Alu transposition element (short interspersed elements or repeats) events occur in every new birth.

Inborn errors of metabolism (IEM) are a group of genetic disorders that are caused by mutations. Their frequency is one in 2500 births across the globe (Jeanmonod et al., 2021) and in India it is one in 2497 births (Lodh and Kerketta, 2013). In the causation of IEM, autosomes, X, Y chromosome and mitochondria are involved. A total of 16000 genes' involvement in IEM has been observed. Information on the IEM is available in the database of "online inheritance in Man". Meta analysis (Waters et al., 2018) of global data showed aminoaciduria (abnormal level of amino acids in urine especially glutamate and aspartate) are highly prevalent IEM (14.7 per 100000 live births). Mutation in the solute carrier family1 member1 (SLC1A1) causes malfunction in the absorption of bicarboxylic amino acid reabsorption in the kidneys. In India, Glucose-6-phosphate dehydrogenase deficiency is one of the highly prevalent IEMs (Lodh and Kerketta, 2013) caused by mutation in G6PD gene. Carriers of G6PD deficiency are asymptomatic till exposed to antimalarial drugs.

Types of mutations, causes and examples are shown in Table 5.1. The effects of mutations include harmful, beneficial and neutral.

5.1.1.1 Harmful Effects

Mutations are responsible for genetic disorders and cancer. The genetic disorders involve single genes both autosomal (Sickle cell anaemia, Thalassemia, Cystic fibrosis, Huntington disease and Marfan syndrome) and sex linked genes (Haemophilia A and Vitamin-D resistant rickets) and also copy number variations or chromosomal abnormalities (Down syndrome, Jacob syndrome, Klinefelter syndrome, Turner syndrome, Super females, Patau syndrome and Edward syndrome). Mutations in BRCA1 and BRCA2 (tumour suppressor genes) cause breast, ovarian, pancreatic and prostate cancers.

5.1.1.2 Beneficial Effects

Carriers of sickle cell trait (HbAS) are known to be protected against *Plasmodium falciparum* malaria. Carriers of sickle cell anaemia with alpha thalassemia showed lower incidence of cardiac complications, jaundice, gall stone, pallor, splenectomy, acute splenic sequestration crises, stroke and avascular than those without alpha thalassemia (Ali Al-Barazanchi et al., 2021).

5.1.1.3 Neutral Effects

Mutations such as silent mutations do not any have effect either positive or negative effect on the organisms and do not change the amino acids they encode. Silent mutations have been shown to interfere in the splicing function of exon splicing enhancers in the desired place in nucleotide sequence (Dickson and Hyman, 2013).

Table 5.1: Type of Mutation, Causes and Example

Type of Mutation	Cause (s)	Example
Dominant	Mutation in single copy of gene.	Achondroplasia
Recessive	Mutation in both copies of gene.	Cystic fibrosis
Morphological	Affect the appearance of individual colour, shape, size	Albinism
Lethal	Cause death of the organism.	Cystic fibrosis, Sickle cell anaemia, achondroplasia
Biochemical	Recognised by the deficiency.	Galactosemia, Phenylketonuria
Resistant	Individual grow even in the presence of infection.	CCR5-delta32 in humans is resistant to HIV
Spontaneous	Errors in DNA replication, transcription, spontaneous lesions and transposition of transposable genetic elements.	Sickle cell anaemia
Induced	Structural changes caused by agents (mustard gas, ethyl urethane, phenol and formaldehyde), radiation, intercalating agents, oxidative agents, deamination, alkylating agents, 5-bromouracil.	Duchenne muscular dystrophy, Congenital myotonic dystrophy
Point (Figure 5.1)	Change of single base pair into another.	Sickle anaemia
(i) Silent or synonymous	Mutated triplet codon code for same amino acid.	In BRCA1, BRAC2 genes cause exon skipping and change protein structure either by creating or inactivating splicing site.
(ii) Missense or non-synonymous	Mutated triplet codon code for different amino acid.	Sickle cell anaemia
(iii) Nonsense	Mutated triplet codon is a premature stop codon,	Cystic fibrosis
Germline	Errors in DNA replication and oxidative damage,	*Familial adenomatous polyposis*
Somatic	Errors in DNA mechanisms or exposure to ultraviolet radiation chemicals and oxidative stress,	Cancer tumours
Copy number variation	Non-homologous end joining, errors in DNA replication and replication of non-contiguous DNA segments,	Huntington's disease

(i) Duplication	Duplication of the gene	Charcot-Marie-Tooth disease type 1 (CMT1
(ii) Deletion	Deletion of the gene	Prader-Willi syndrome
Frame shift	Insertion, deletion of one or more nucleotides leading to the change of reading frame of base sequence.	Cystic fibrosis, Tay-Sachs disease

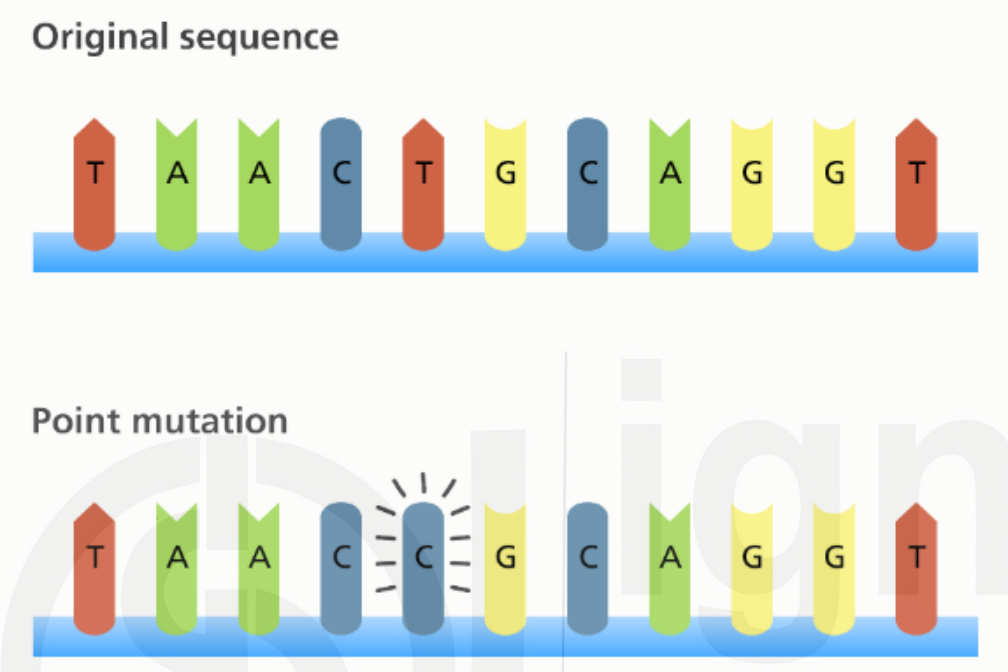

Fig. 5.1 : Mutation
(Source: https://www.yourgenome.org/facts/what-is-a-mutation)

5.1.2 Gene Flow

Diffusion of alleles across populations can be called gene flow. Human beings move from one population and join another population due to various socio-economic reasons, and choose mate and involve in interbreeding. This causes the gene flow or genetic admixture. As a result of gene flow, allele frequency changes in the population left and also the population in which they have joined. Examples of genetic admixture or gene flow (Figure 2) are the Anglo Indians, the American Blacks and the Siddis (Indo-African population). In Latin American countries, admixed populations are seen due to random mating among indigenous populations, Europeans and Africans. Another example is gradient distribution of the B blood group allele. B allele believed to have originated in Asia spread to western countries due to genetic admixture forced by invasions. The barriers to gene flow are geographical, cultural, linguistic, and political factors. For gene flow to occur, not only the large scale migrations and choosing of mates in the settled areas but also the mate selection in particular direction over a long span of time may be responsible. To explain the change in allele frequency contributed by gene flow, Sewall Wright proposed 'island' and 'isolation by distance' models whereas Kimura and Weiss contributed 'stepping stone model'. Stepping stone model assumes that a line or ring of populations exchange migrants with their immediate neighbours only whereas island model

allows exchange of migrants between populations. In contrast, 'isolation by distance model' proposes that gene flow decreases as the geographical distance increases.

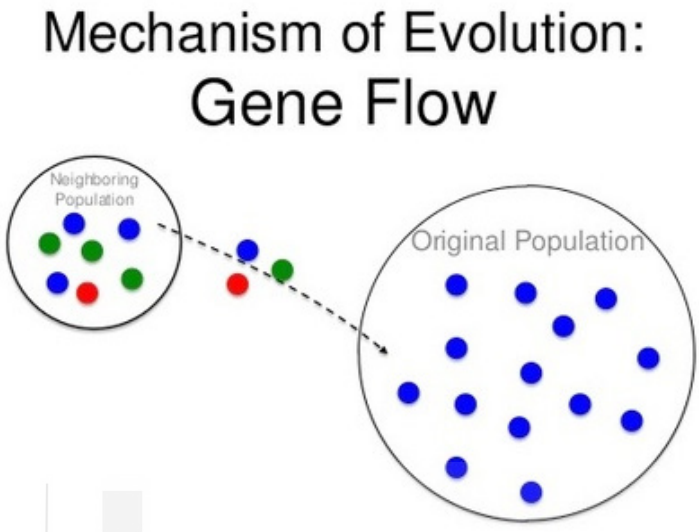

Fig. 5.2 : Gene Flow
(***Source:*** http://anthropologicalconcepts.weebly.com/blog/gene-flow)

5.1.3 Natural Selection

Natural selection is defined as differential survival and reproductive success. Mutation adds new alleles into the population. Natural selection determines the fate of newly added allele in the population. If it is not advantageous or not suitable to the environment, natural selection eliminates it by negative or purifying selection. The survival of allele in particular environment depends on its fitness/ adaptive value/ selective value. Various factors such as mate selection, female fecundity and survival in the reproductive age contribute to the fitness. Those who are fit to survive, have reproductive success and contribute more offspring than less fit people. This is also called adaptation. Natural selection facilitates the adaptation of the organism to the environment and the allelic composition carried by the fit individual is promoted that result in the change in allele frequency of the population due to the replacement of allele composition carried by the less fit individuals. In another words this is called positive selection or diversifying selection. When people of opposite sex carrying different genotypes marry, they pass on unequal alleles to their offspring as a result there may be a difference in the allele frequency of parents or progeny. An individual is the unit of natural selection.

Examples of natural selection are skin colour, physiological and genetic adaptation to high altitude, lactose persistence, sickle cell trait and Duffy blood group.

5.1.3.1 Skin Colour

It formed the basis to classify the humans into different races. Natural selection favoured light skin to those residing far from equator. The light skin allowed ultraviolet rays to enter and produce vitamin D to absorb calcium levels. For

those staying near equator natural selection favoured dark skin to prevent the loss of folic acid (vitamin B9) required for the development of healthy foetuses (Humanorigins.si.edu).

5.1.3.2 Physiological and Genetic Adaptations to High Altitude

Human beings living in plains when enter into the high altitudes, undergo hypoxic stress and develop adaptive responses like increase in the levels of red blood cells, greater lung volume and increased chest dimensions and respiration. These adaptations allow them to stay for short-term. It was observed that long-resident Andeans (altitude of 6961m) of South America have increased cardiac oxygen utilisation, larger lung volumes, less hypoxic pulmonary vasoconstrictor response, narrow alveolar to arterial oxygen gradients, greater uterine artery blood flow during pregnancy and mutations in the genes involved in the regulation of metabolic haemostasis, vascular control and erythropoiesis due to natural selection to support their survival at high altitude.

5.1.3.3 Lactase Persistence

Lactase is an enzyme that hydrolyses lactose, a carbohydrate present in milk, into glucose and galactose. The lactase activity decreases after weaning period in most mammals but some humans continue to produce this enzyme and digest the lactose in the milk. This trait is known as lactase persistence (LP) and has been observed in pastoralist populations. Correlation of estimates of mutation time with dairy practicing activities in Europe and Africa suggested LP trait coevolved with dairying by natural selection due to nutritional advantage associated with the consumption of milk.

5.1.3.4 Duffy Negative Phenotype and Resistance to Malaria

Duffy is one of the blood groups identified in humans. It has six antigens (Fya, Fyb, Fy3-Fy6) on red blood cells (RBC). The FY gene has two alleles FYA and FYB which code for antigens Fya, Fyb which differ by single amino acid. Homozygotes for single nucleotide polymorphism (-33T→C) in the erythroid promoter region of FYB allele have Duffy negative phenotype FY (-a-b) and lack antigens. RBCs lacking Duffy antigens are resistant to *Plasmodium vivax*. The malaria caused by *Plasmodium vivax* has been found to be absent in populations where 95% of them had Duffy negative antigens. Natural selection might have fixed Duffy negative antigens in adapting to *P. Vivax* endemic areas.

Check Your Progress

1) What is the importance of Duffy blood group in Malaria?

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5.1.3.5 Sickle Cell Trait and Resistance to *Plasmodium Falciparum* Malaria

Presence of sickling Hb (HbSS) in homozygous state is called sickle cell anaemia and in heterozygote state (HbAS) is termed as sickle cell trait. Sickle

cell anaemia results from point mutation in the beta globin gene at codon 6th position which results in replacing amino acid glutamic acid with valine. Heterozygous carriers of haemoglobin (HbAS) (A=adult and S=Sickling) in malaria endemic areas have shown protection against *Plasmodium falciparum* induced malaria than homozygous carriers of sickling Hb (HbSS). Heterozygotes (HbAS) carrying one sickling allele don't show any symptoms and survive on par with normal individuals. Natural selection favoured heterozygotes carrying genotype (HbAS) in areas endemic to *P. Falciparum* malaria. This is an example of balanced polymorphism. HbAS individuals have been found to have higher fitness than either AA or SS.

Selection is of five types. They are of the following:

1) Selection for the heterozygotes (heterozygotes have higher fitness than homozygote) (Example Sickle cell trait explained under 5.1.3.5).

2) Selection against heterozygotes or under dominance (lower fitness assigned to heterozygotes against two homozygotes). The example cited for this type of selection by Magori and Gould (2006) is described here. Homozygous individuals containing alternate forms of a chromosomal translocation marry, heterozygotes are fit because they have single copy of all genes from both parents and when these heterozygotes marry each other they give birth children among them a fraction of them lack important trans locational segment and not viable. If we observe this fitness phenomenon over generations this can be called as underdominance or selection against heterozygotes.

3) Selection with the co-dominant allele (alleles are co-dominant and one allele (heterozygotes) is favoured). Example for this type of selection is ABO blood group. Co-dominance means no allele can mask the expression of other allele. If an individual inherits B allele from mother and A allele from father both are expressed, he/she has AB blood group. In AB blood group both are co-dominant alleles and in heterozygous state which favoured

4) Selection against dominant allele (expressed as heterozygote). Achondroplasia is an example for this type of selection. This is an abnormality of bone growth occur in 1 in 20-30,000 live births. This abnormality is caused by mutation in fibroblast growth factor receptor 3 (FGFR3) gene. It is inherited as autosomal dominant pattern. The patients of Achondroplasia are characterized by short stature, short arms and legs, fingers during extension appear as trident, unusual large head with a prominent forehead, flat nasal bridge and prominent abdomen and buttocks.

5) Selection against recessive homozygotes (harmful allele is favoured). Example for this type of selection is Tay Sachs disease. Its incidence is 1 in 250-350 people. Most commonly observed in Ashkenazi Jews, South eastern Quebec and among Cajun of Louisiana. It is an autosomal recessive disorder (inheritance of two copies of abnormal gene from both

parents). Homozygotes are characterized by deficiency of hexosaminidase, An enzyme which leads to failure of breakdown of GM2-ganglioside (glycosphingolipids), accumulation of GM2-ganglioside and progressive deterioration of central nervous system. The disease is due to mutation in hexosaminidase subunit alpha gene (HEXA) and 80 mutations are observed in this gene. Cherry red spot in the macula of eye is characteristic symptom of this disease. Eye, ear, brain and cognitive abnormalities are observed in these patients and life threatening complications develop by the age of 15 years. Individuals receiving abnormal gene from one parent is called carrier who don't develop the disease.

5.1.3.6 Modes or Patterns of Selection

Patterns or modes of natural selection are of four types. 1. Stabilising selection 2. Directional selection 3. Disruptive/ diversifying selection. 4. Balanced Selection.

5.1.3.6.1 Stabilising Selection

This type of selection takes place when both the environment and the genetic composition of population are stable. Intermediate or heterozygote phenotype or allele is favoured and two extreme phenotypes or alleles are eliminated. Examples of stabilising selection are 1. height distribution in a population. 2. Based on birth weight new born are categorised into low birth weight (<2500g), high birth weight (>4500g) and average birth weight (2500-4500g). Two extreme birth weight newborns have less fitness, high morbidity and mortality and therefore natural selection favours average birth weight babies.

5.1.3.6.2 Directional Selection

This type of selection occurs when there is change in the environment in a particular direction and shift takes place in mean of the character of a distribution. Extreme phenotype or allele that has higher fitness and ability to produce more offspring is favoured and fixed while eliminating the less fit phenotype or allele. Examples are increased body size in response to cold environment, antibiotic resistance in microbes due to the development of new mutant and change of Biston betularia (peppered moth) from light colour in pre-industrial era to black colour in post industrial era to protect from predators.

5.1.3.6.3 Disruptive/ Diversifying Selection

Disruptive selection happens when homogenous populations are separated into different adaptive groups. Extreme phenotypes or alleles are favoured and average phenotype or allele is eliminated. Fifteen species of Passeriforms (order of birds) or Darwin's finches (Figure 5.3) (song birds) found on the Galapagos archipelago and Cocos Island of Pacific Ocean under administrative control of Ecuador are closely related but differ in the size or shapes of their beaks due to adaptation to consuming different food sources.

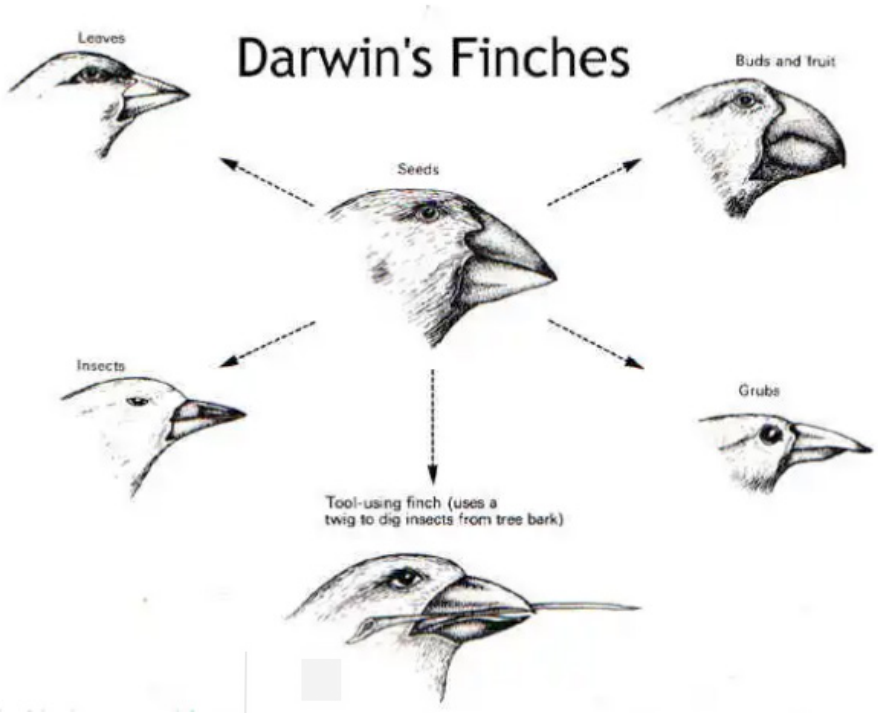

Fig. 5.3 : Darwin's Finches

(***Source:*** https://shrabontibhowmik.wordpress.com/2016/10/02/darwins-theory-of-natural-selection-and-how-did-it-start/)

5.1.3.6.4 Balanced Selection

Heterozygotes than homozygotes of either spectrum have higher fitness, are favoured and contribute more offspring to the next generation. This type of selection is also called heterozygote advantage or over-dominance. The best example for this type of selection is advantage of sickle cell trait in areas endemic to *Plasmodium falciparum* malaria. The details of sickle cell trait have been discussed under the example of natural selection in this unit.

To investigate the selection in human populations, Crow formulated an index. This index has mortality and fertility components. These are influenced by several factors such as variation in fertility, age at marriage, menarche, age of death and survival to reach to fertility age. To account for fertility and mortality during conception, Johnston and Kensinger (1971) have proposed modified Crow index to measure selection in the population. Studies conducted on selection intensity among tribes of India showed higher index of mortality compared to fertility and in urban populations due to public health facilities and higher socio-economic conditions decreased index of mortality and fertility was observed.

5.1.4 Genetic Drift

The National Human Genome Research Institute, Maryland, United States of America, defined genetic drift as random fluctuations in the frequencies of alleles from generation to generation due to chance events. Genetic drift is of two types and they are Bottle neck effect and Founder effect.

2) What is Genetic Drift?

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5.1.4.1 Bottleneck Effect

Pandemic like flu, severe acute respiratory syndromes, human immunodeficiency virus, COVID-19, natural calamities like tsunami, earthquakes and droughts and man- made events like exploding of nuclear and hydrogen bombs reduce to the effective size of the population and change genetic diversity. Effective size of a population refers to those interbreeding individuals who by mating contribute offspring to next generation. As a result of reduction in effective size of population the allele frequency will be different before the action of genetic drift which resembles the neck of the bottle restricting the flow of genes. Therefore, this is called bottle neck effect (Figure 5.4). Bottle neck effect reduces the genetic diversity and change the allele frequency. The example for bottle neck effect is Greenlandic Inuit. Analysing exome data of 18 individuals it was proposed that population reduction has been affecting the Inuit over the 15,000 years. Alleles that are rare (variant in TBC1D4 associated with type 2 diabetes and indel in SEMA4C linked to sucrose isomaltose) in East Asian or European population were found to be common in Inuit (Prohaska et al., 2019).

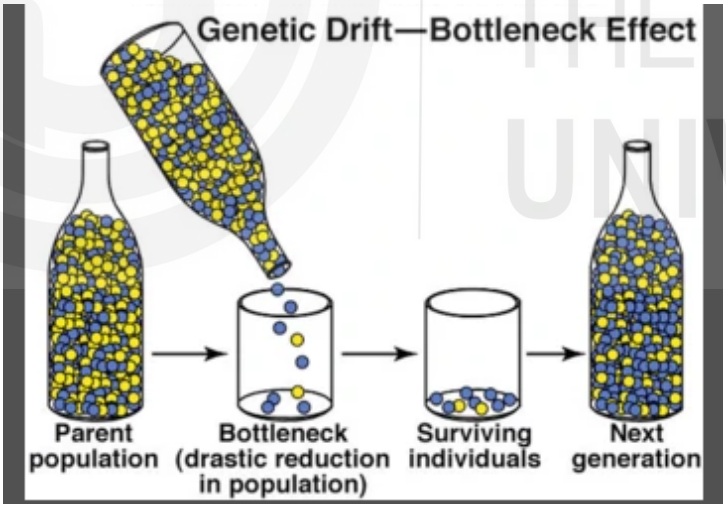

Fig. 5.4 : Bottleneck Effect

Source: https://dragonflyissuesinevolution13.wikia.org/wiki/Bottleneck_Effect)

5.1.4.2 Founder Effect

Founders are early settlers or ancestors who established new colony or population in foreign lands. The founding of new colony or subpopulation may also take place due to exploration of island or new area, warfare, survival from ship wreck, repeated migration over time or waves of migration from their lands to new landscapes. The founders of subpopulation carry random sample of genes. The new subpopulation after a few generations may be characterised

by the absence of alleles or higher prevalence of rare alleles against the larger population (Figure 5.5). Repeated migrations of humans during different time periods establish new subpopulation whose genetic composition will be different from the original population. This is called serial founder effect. Examples of founder effect are continental distribution of Y chromosome and mitochondrial haplo groups and tracing of genetic signature of African people in the population of America, Europe and South Asia, support evidence on out of Africa origin of human beings. Unusual frequency of morphological and genetic traits in north Indian population such as higher frequency of lactose malabsorption, lack of isoenzyme ALDH-1, AK2, pc, K, cde and A2 genes; high frequency of G6PD deficiency in Naga and Gd variant in Bodos and absence of Gd- variant in Adi and Hmar populations are some of the examples of founder effect in India (Vasulu, 2012).

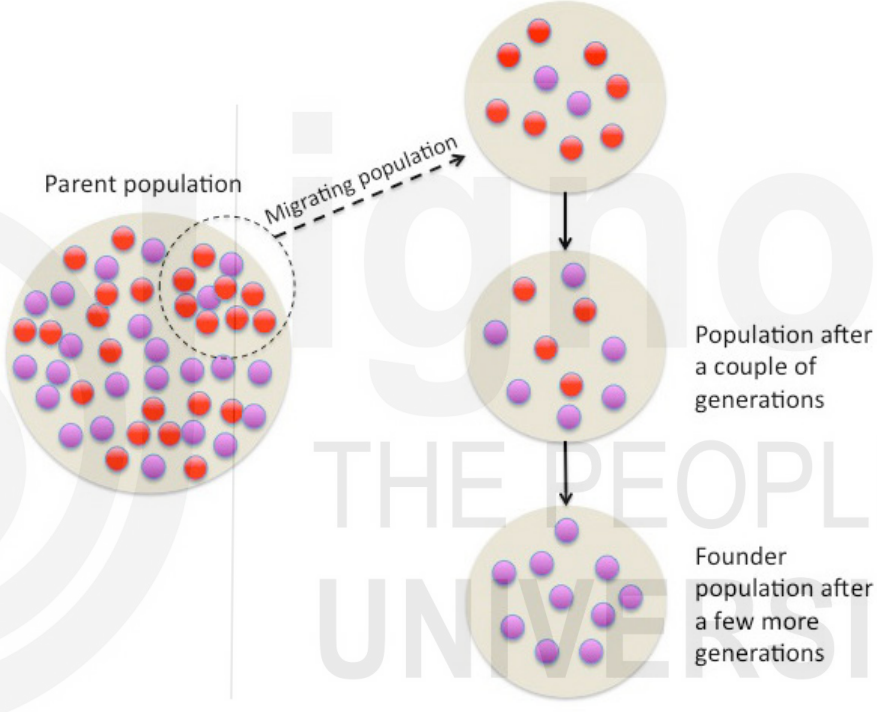

Fig. 5.5 : Founder Effect

(***Source:*** https://commons.wikimedia.org/w/index.php?curid=47951519)

5.2 SUMMARY

Evolution can be understood as changes taking place over time and include small or large, invisible or visible and non-adaptive and adaptive changes. The four forces of evolution are known and they are mutation, gene flow, natural selection and genetic drift. Mutation introduces new alleles into the population due to the occurrence of copying errors in DNA replication and transcription. Natural selection (due to the individual differences on the survival and reproductive success) and genetic drift (due to random sampling in small populations) differentially transmit alleles into the next generation. Mutations may cause harmful, beneficial and neutral effects. To explain the change in allele frequency contributed by gene flow, Sewall Wright proposed 'island' and 'isolation by distance' models whereas Kimura and Weiss contributed

'stepping stone model'. Natural selection is defined as differential survival and reproductive success. Natural selection determines the fate of newly added allele in the population. If it is not advantageous or not suitable to the environment, natural selection eliminates it by negative or purifying selection. Selection is of five types and they are (1) Selection for the heterozygotes (heterozygotes have higher fitness than homozygote) (2) Selection for against heterozygotes (lower fitness assigned to heterozygotes against two homozygotes) (3) Selection against codominant alleles (alleles should be codominant and one allele (heterozygotes) is favoured) (4) Selection against dominant alleles (expressed as heterozygote) and (5) Selection against recessive homozygotes (harmful allele is favoured). Patterns or modes of natural selection are (1) Stabilising selection (2) Directional selection (3) Disruptive/ diversifying selection. (4) Balanced Selection. Genetic drift is a random fluctuation in the frequencies of alleles from generation to generation due to chance events. Genetic drift is of two types and they are (1) Bottle neck effect and (2) Founder effect.

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5.4 ANSWERS TO CHECK YOUR PROGRESS

1) Duffy blood group is one of the 45 blood groups identified in human beings. Duffy blood group individuals lacking Duffy antigens are resistant to *Plasmodium vivax* induced malaria. Refer to sub-section 5.1.3.4.

2) It is a random fluctuation in the frequencies of alleles from generation to generation due to chance events. Refer to sub-section 5.1.4.