Animal viruses

In humans and other animals, viruses cause many diseases (see p 141). Animal viruses are also transmitted by direct contact or via insects. They apparently gain entry into the host cell by phagocytosis or pinocytosis. The genetic material of animal viruses can be either DNA or RNA. Whilst DNA is usually present as a double stranded helix, RNA is found as a single stranded polynucleotide chain.

Bacterial viruses

Viruses that use bacterial cells as hosts are called bacteriophages. The presence of bacteriophages is recognised by the appearance of **plaques** or lytic holes in a continuous bacterial lawn. Phage nucleic acid occurs either as double or single stranded DNA or as single stranded RNA. The phages of *Escherichia coli*

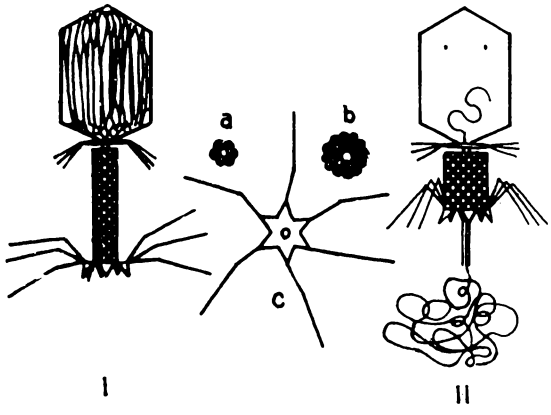

Fig. 6.4 Model of a T_2 phage.
i. Phage with stretched sheath before adsorption
ii. Phage with contracted sheath after adsorption
a) Transverse section through stretched tail; 6 sheatned protein unit in one plane
b) Transverse section through the contracted tail; 12 - sheathed protein unit in one plane
c) view of the basal plate of phage, ready for adsorption.

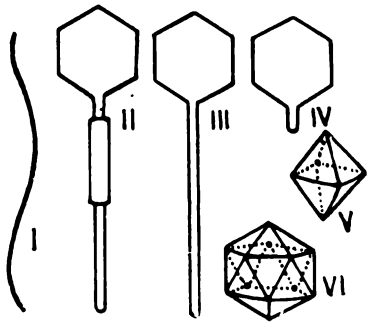

Fig. 6.5 Various shapes of bacteriophages (i-iv) and geometrical shapes of phage heads (v-vi).
i. Thread-like form of coliphage fd.
ii. Hexagonal head with contractile sheaths (eg; T_2, T_4, T_6)
iii. Head with long flexible non-contractile tail (eg; T_1, T_5)
iv. Head with short tail (eg; T_3, T_7)
v. Octahedron vi. Icosahedron.

The shapes and forms of bacteriophages have been elucidated mainly for T-series of *E. coli* phages. The coliphage T_2 consists of a polyhedral head, about 100 nm in length and a tail (Fig. 6.4). It is called a composite virus. The head comprises capsomere and contains DNA; protein and DNA each comprises about 50 % of the head. The tail has a rather complicated structure consisting of three parts. A hollow **stylus** is surrounded by a contractile sheath which bears on its distal end a base plate covered with claw like tail fibre and host specific adsorption spikes. According to their form and structure the T-series bacteriophages of *E. coli* have been numbered as T_1, T_2. . .T_7 etc. The morphology of these bacteriophages ar presented in fig. 6.5.

Algal viruses

Many of the blue-green algae are attacked by viruses that are known as cyanophages. They were first discovered in 1963 by Safferman and Morris. These groups are usually designated by the initials of the generic names of the corresponding hosts to which arabic numerals are added for designating the serological sub-groups. In morphology they resemble the bacteriophage. Grouping of cyanophages is done on the basis of their host specificity, morphological and serological properties (Table-6.2).

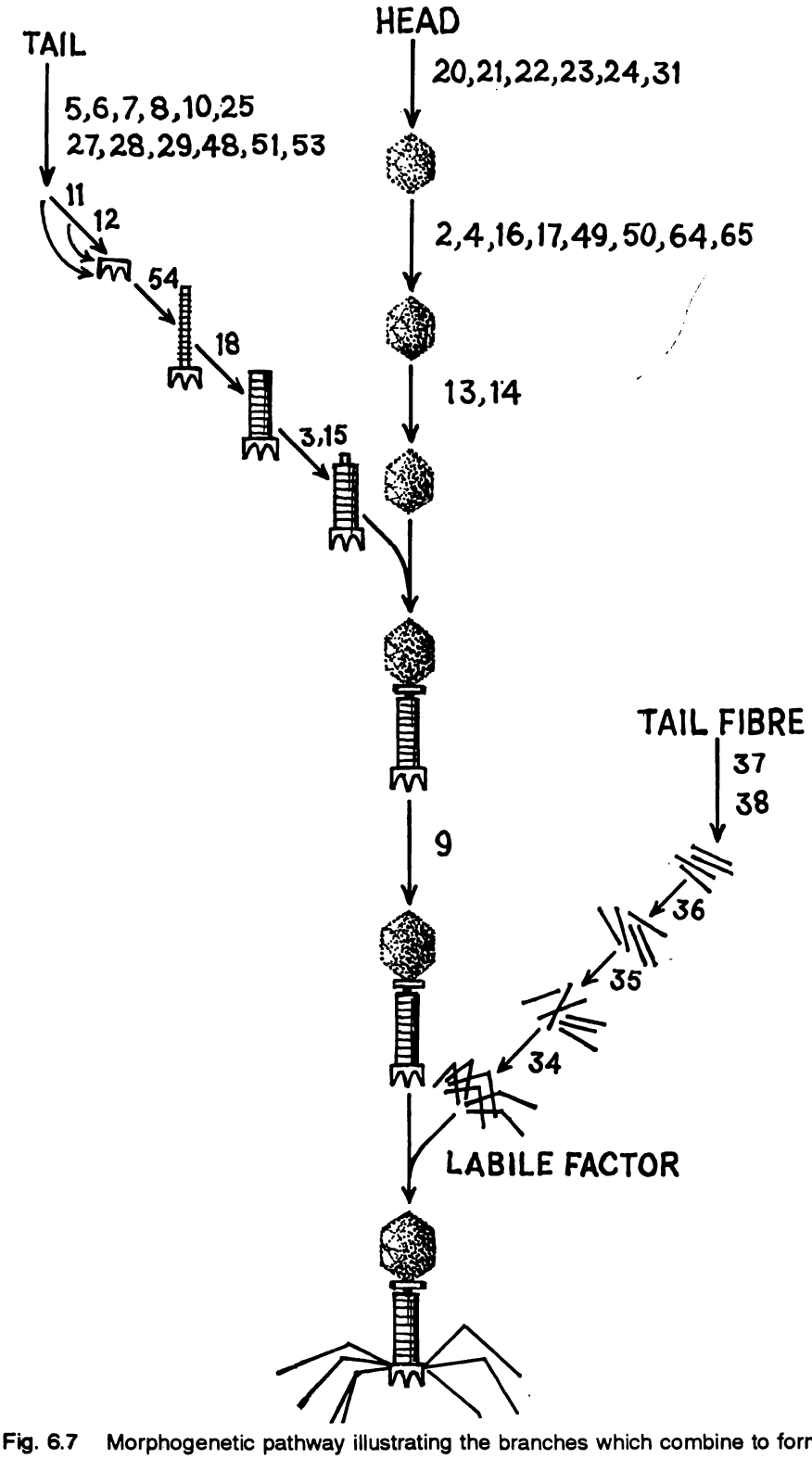

Fig. 6.7 Morphogenetic pathway illustrating the branches which combine to form complete virus particles.

7

GENETICS OF MICROBES

An organism resembles to its ancestors in most of its characters. The constancy of characters over the generation is called heredity. The distribution of characters in the progenies follows the **law of heredity** (first proposed by Johann Gregor Mendel) and the science dealing with the transfer of characters and variations among organisms is known as **Mendelian Genetics**. This classical genetics has undergone a radical change since the development of the concept of chemical structure of DNA, proposed by Watson and Crick in 1953 and during the last twenty five years it has flourished as a new branch of molecular biology on the pedastal of microbial genetics.

According to classical genetics the genes situated in the cell nucleus are arranged in linearly order. For a long time it was believed that genetic information was associated with the protein component of the nucleoplasm. However, the successful transfer of genetic information (transformation) by DNA revealed that this must be the material equivalent to hereditary characters. It was further demonstrated that the expression of genetic character is due to the action of enzymes. The **one-gene, one-enzyme** hypothesis proposed by Beadle and Tatum states that one gene contains the information necessary for one specific enzyme. Today this has been described more accurately - each **structural gene** codes for a specific polypeptide chain. A sudden change in, or of, a gene (mutation) leads to a loss of the enzyme or alteration of enzyme that ultimately results in the changes in hereditary characters. Thus the gene is recognised by its mutation and the genetic investigations are the studies of mutants. In eukoryotic system such mutation study is comparatively difficult and complicated as the number of genes in some cases may go to the extents of hundreds of thousand. Bacteria have been identified as ideal tool for the genetic research because :

(i) they can be propagated rapidly in short duration,

(ii) genetic homogeneity is maintained in the culture,

(iii) they are genetically simple organisms having single chromosome,

(iv) genetic material is easily transferred from one bacterial cell to another that enables to investigate the gene mechanism,

(v) they require less place and simpler cultural conditions.

GENE : Gene carries character. In both the eukaryotic and prokaryotic cells the molecule that serves as the ultimate agent of chemical control is deoxyribonucleic acid (DNA). A gene is the fraction of DNA molecule that codes for the production of a specific protein or RNA molecule or serves as an operator in controlling the transcription of RNA within an operon unit. An organism's DNA constitutes a catalog of genes known as the **genotype** of the organism. The expression of these genes is referred to as the **phenotype**.

A bacterium will 'breed true' from generation to generation so long the base sequence of its DNA does not change. Any change in base sequence will alter the informational content of the DNA and this in turn is likely to produce heritable changes in the structure.

Mutations in DNA base sequence may be of different kinds. Changes in the nature of a single base are called **point mutation**, removal of sections of the DNA are known as **deletions** and the removal of a piece of DNA from one position to another position on the same replicon or to a position on another replicon in the same cell is known as **translocation**. Sometimes the sequence of the DNA is altered either by adding or removing a single base pair. This is known as **frame-shift mutation**. Point mutations themselves are of two types : **transitions** and **transversions**. In the former a pyrimidine is replaced by a pyrimidine or a purine by a purine, while in the later pyrimidines are replaced by purines or vice-versa (Fig.7.3).

Point mutation is caused by a variety of agents known as **mutagens**. Many of these agents are chemical compounds which produce a direct change in the chemical nature of the DNA (e.g., nitrous acid, ethyl-methane sulphonate, mycotoxins etc.). Some ionising radiations are also potent mutagens. They bring about chemical changes in DNA sequence indirectly interacting either with a component of DNA itself or with other molecules in the immediate environment. One of the characteristics of point mutation is that they can revert by a further change in base sequence. Sometimes the DNA returns to its original structure and this is referred to as **back mutation**. The process leads to the production of the original protein and the back mutated cells are indistinguishable from the original parent. A more complex step is the generation of a further **forward mutation** that leads to the appearance of properties similar to but not identical with the original parent. Such a change is called a reversion to the **pseudo-wild-type**. In this case the activity can be reduced or destroyed by the first mutation and then partially restored by the second one.

Bacterial cells are subject to mutations occurring at certain rates without any outside intervention. These are called **spontaneous mutations**. They probably represent accidental error in the assembly of nucleotides during DNA replication. These errors are produced by tautomeric transposition (re-arrangement) of electrons in a base. For example, thymine is normally present in the *oxo* state forming a hydrogen bridge with adenine. However, if thymine were to change to the *enol* form during base pairing that takes place in DNA replication, it would pair with guanine. The new DNA would then contain a GC pair in the position where it would normally have an AT pair.

Usually a mutation is recognised as a sudden phenotypic change in the organism. However, at the molecular level every change may not be expressed phenotypically. In many triplet codons, for example, a change in the third base is without phenotypic consequences. Even a replacement of the first or second base of a triplet does not necessarily have the drastic consequences. Such change is known as **silent mutation**. The frequency of such mutational events can be increased by treating cells with mutagenic agents. This is called **induced mutations** and the resulting mutant cells are called induced mutants.

DNA DAMAGE AND REPAIR

Throughout the course of evolution DNA has been subjected to wear and tear both by endogenous causes (e.g., errors during replication) and exogenous mutagens. This natural burden of mutagens has been increased considerably by the activities of men themselves by polluting the environment with continuous discharge of chemicals and by military and civil use of nuclear fission. Such mutagenic activities lead to various forms of DNA damage. Some major forms of DNA damage are :

Hydrolytic damage (Reaction with water) : This includes loss of bases (depurination/depyrimidination) and deamination of exocyclic amino groups.

Adduct formation : Covalent binding of chemicals to DNA with the formation of chemically stable adducts plays a major role in the mode of actions of chemical mutagens. Adducts range in size and complexity from simple alkyl groups (e.g., methyl, ethyl) to aromatic hydrocarbons, aromatic amines, aflatoxins etc.