Bacterial genetics and viral

I. bacterial genetics

1. Reminder of anatomy of the Bacterium

- **The nuclear system of bacteria**

Like all prokaryotic protists, bacteria have a nuclear apparatus made up of deoxyribonucleic acid (DNA) which is the support for genetic information.

- **DNA chromosomal**

It consists of a double helix of circular DNA. Unfolded, the bacterial chromosome is nearly 1 mm long (1000 times the length of the bacterium) and 3 to 5 nanometres wide.

Chemical analysis of the nuclear apparatus shows that it is made up of 80% DNA (the chromosome), 10% ribonucleic acid or RNA (structuring role) and 10% proteins. The latter are represented in particular by DNA polymerases, which copy the double strands of DNA, topoisomerases, which unwind them to enable the action of the polymerases, and RNA polymerases, which synthesise the various RNAs.

- **DNA extra -chromosomal**

In addition to the chromosome, which is the basis of heredity, the bacterium may contain small genetic elements (DNA) (0.5 to 5% of the bacterial chromosome) that are extra-chromosomal. These elements, called plasmids, are not essential to the life of the bacteria under normal growth conditions.

They replicate independently and generally more rapidly than the bacterial chromosome. The plasmid genes are not necessary for the normal metabolism of the cell, but are advantageous for the bacteria:

-They mediate numerous properties that enable bacteria to adapt better

-They participate in horizontal gene transfer between bacterial populations.

Some plasmids are capable of integrating into chromosomes; these plasmids are called episomes.

The best known of these plasmids are the following:.

- **The sexual factor or F factor**

The sexual factor or F factor ensures the transfer of bacterial chromosome fragments by conjugation (pairing of two bacteria).

- **Antibiotic resistance plasmids (or R factors)**

These carry genes that give bacteria resistance to various antibiotics.

- **The other plasmids**

Some plasmids are responsible for virulence (e.g. toxin production), resistance to antiseptics, the metabolism of certain compounds (lactose, lysine, etc.) and the degradation of substances such as salicylic acid.

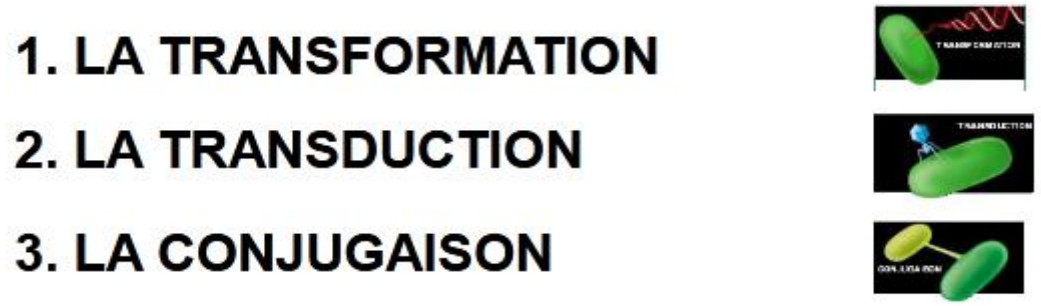
2. The bacterial recombinations

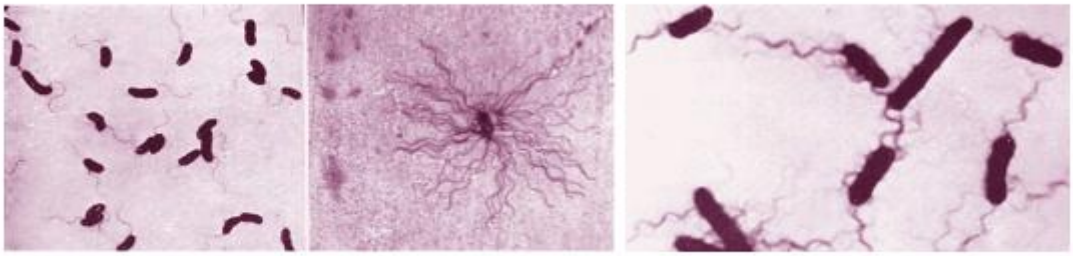
Bacteria multiply asexually by binary fission. A mother cell will give rise to two genetically identical daughter cells, so genetic mixing is virtually non-existent. To compensate for this, there are 3 major mechanisms for horizontal gene transfer:

1) **Transformation:** incorporation of naked DNA from the environment directly into the bacterium

2) **Transduction:** transfer of genetic material from one bacterium to another via a phage

3) **Conjugation:** transfer of DNA from one bacterium to another by direct contact.





Horizontal transfer plays a major role in bacterial diversity, but is also one of the causes of the increase of the resistances to antibiotics.

These modes are unidirectional, affecting only one of the two organisms involved in the exchange of genetic material.

They are based on the existence of donor bacteria (the exogenote) and recipient bacteria (the endogenote).

There is not necessarily any contact between the exchanging organisms.

2.1. The transformation

This is a process whereby exogenous DNA naked to a bacterium is captured and transferred by diffusion and incorporated into the bacterial genome.

Transformation is widespread in both Gram-positive and Gram-negative bacteria.

The transforming DNA and the DNA of the recipient bacteria must be similar, and transformation is only possible between bacteria of the same species or between bacteria of neighbouring species.

Absorption takes place in single-stranded form, and by substitution rather than addition.

Not all cells can be transformed. Cells capable of receiving genetic information in the form of free DNA are said to be competent.

Natural competence: is a hereditary trait under the control of several genes.

These genes code for proteins responsible for absorbing the exogenous DNA molecule and protecting it from the nuclease action of the receiving cell.

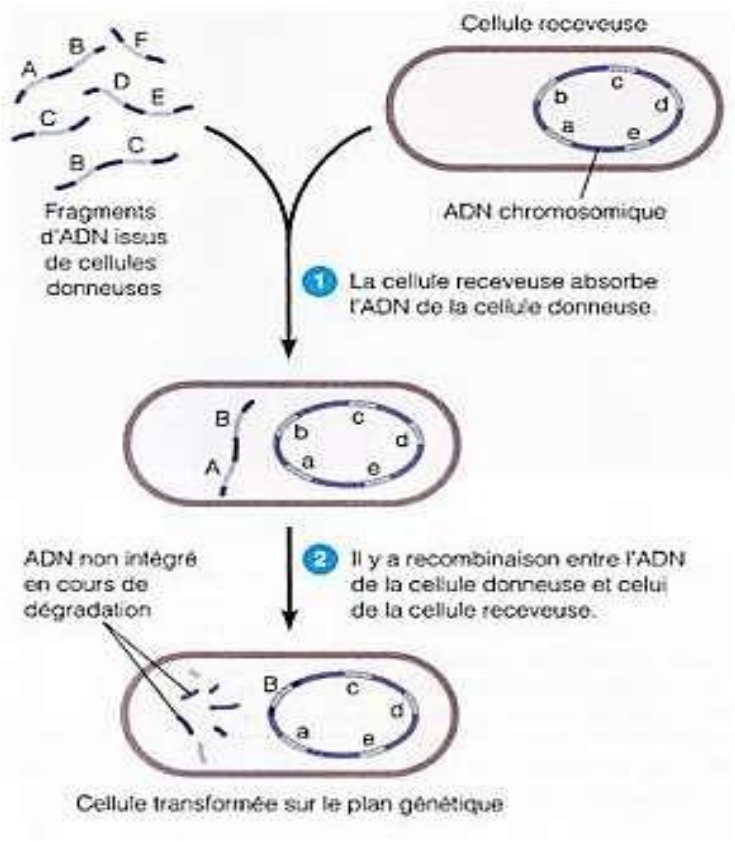


Figure : Bacterial transformation

Artificial competence : treatment of non-competent cells with calcium or rubidium chloride or with heat shock can cause alterations of the bacterial envelope, thereby increasing their capacity to absorb DNA, making them competent.

2.2. The conjugation

This method enables the unidirectional transfer of plasmid or chromosomal DNA between two bacteria. This process requires contact, via sexual pilus, between a donor bacterium (+ type bacterium) and a recipient bacterium (- type bacterium).

F factor

The fertility factor or F factor is the first conjugative plasmid found in bacteria. It carries a large number of genes, including the following:

- Genes for the synthesis of sexual pili, enabling an F+ donor bacterium (possessing the plasmid) to dock with an F- recipient bacterium (not possessing the plasmid).

- Genes enabling the synthesis and transfer of DNA from one bacterium to another.

The contact between the donor bacterium (F+) and the recipient bacterium (F-), achieved by the sexual pili, is followed by the formation of a cytoplasmic bridge allowing the transfer of DNA. Transfer begins at the site known as the "origin of transfer" (oriT) and proceeds in a rolling circle.

Bacterium Hfr

Since the F plasmid is capable of integrating onto the bacterial chromosome, a bacterium carrying the F factor on its own chromosome is called Hfr (high recombination frequency).

When an Hfr bacterium crosses an F- bacterium, the transfer and replication of (chromosomal) DNA begins at the origin of transfer (oriT). The various genes are transferred one after the other, and it is only when the whole chromosome is transferred (about 2 hours) that the F factor is also completely transferred.

However, it is very rare for the whole chromosome to be transferred, so the recipient bacterium does not receive the F factor and therefore remains F-. It may, however, have

acquired some of the donor bacterium's genes through homologous **recombination.**

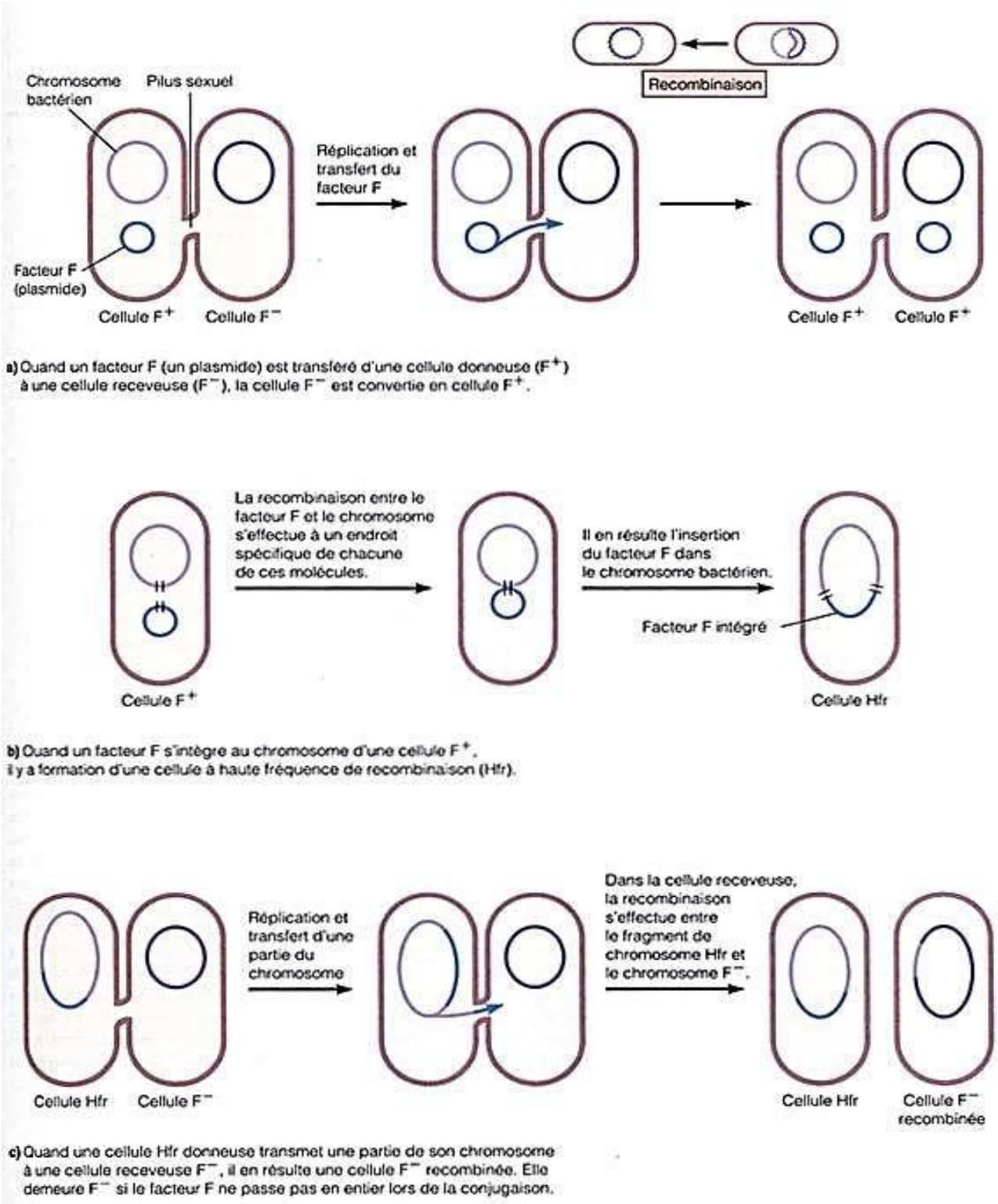


Figure: Bacterial conjugation

2.1. Transduction

An agent (bacteriophage) that carries genetic information from one bacterium to another. This is the transfer of genes from one bacterium to another by a phage.

There are 2 types of transduction: generalised = any gene in the donor bacterium can be transferred by the virus; and specialised = only certain genes can be transferred.

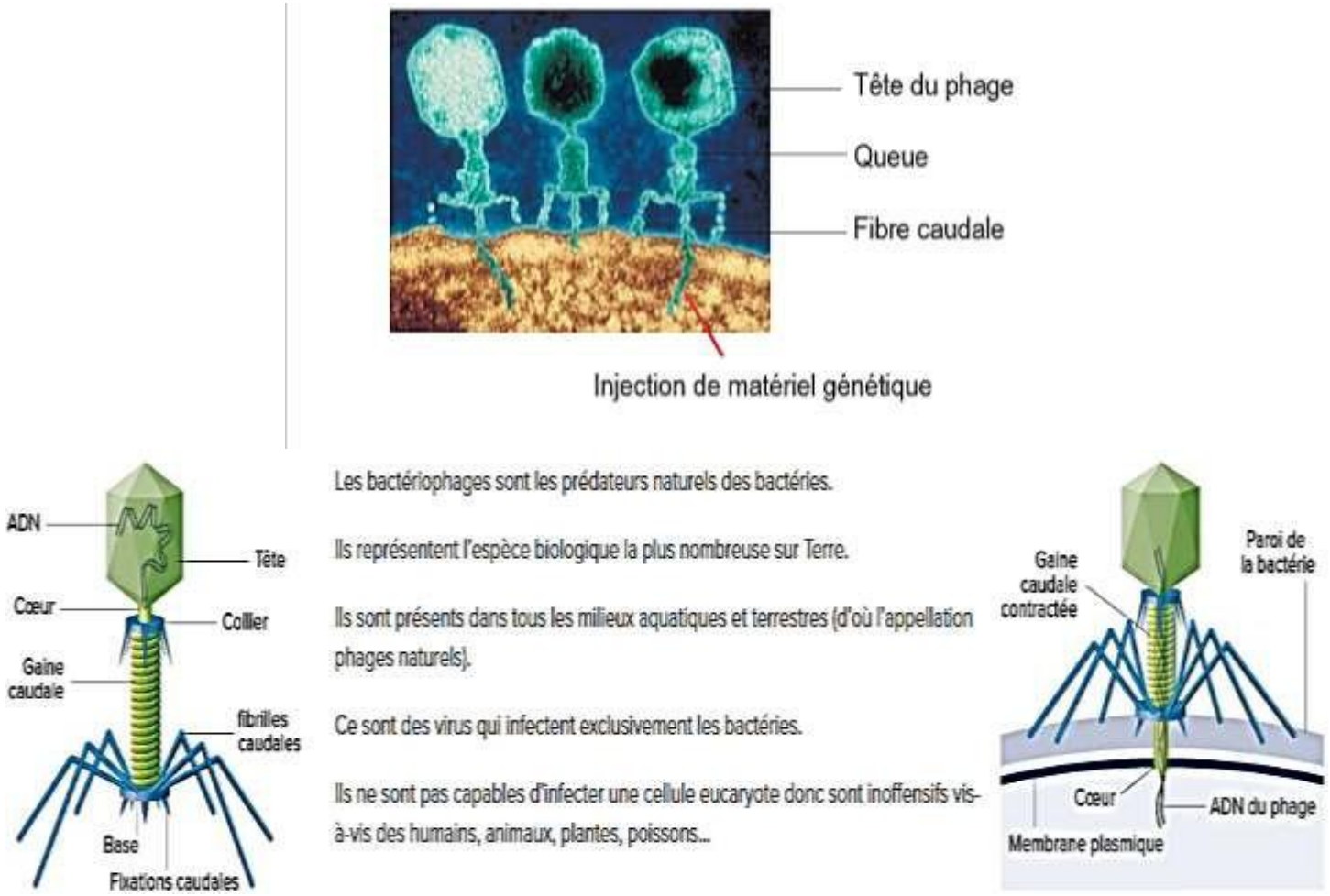
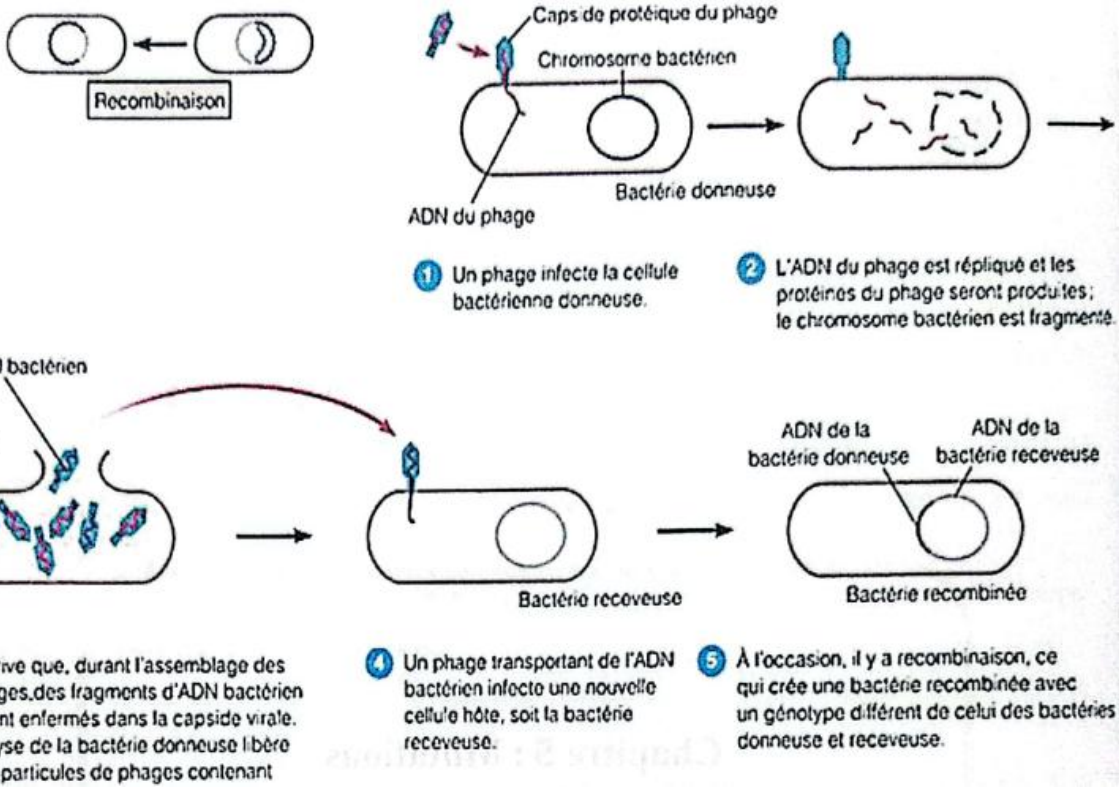


Figure: Bacteriophage natural

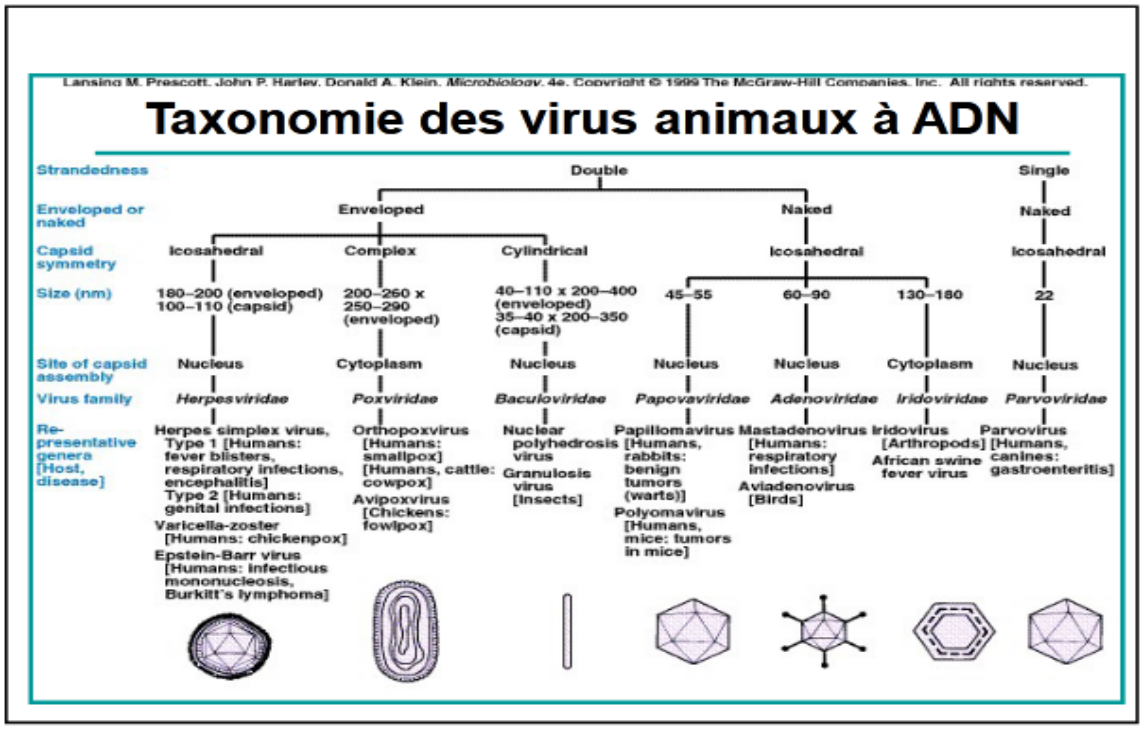
During infection by a phage, a bacterial DNA fragment or plasmid is incorporated into a viral particle. Then, when this particle infects another cell, this segment of bacterial DNA is exchanged with that of the infected cell (by recombination). So it is this particle that can transmit the information it carries to another bacterium.



1. Un phage infecte la cellule bactérienne donneuse.
2. L'ADN du phage est répliqué et les protéines du phage seront produites; le chromosome bactérien est fragmenté.
3. Il arrive que, durant l'assemblage des phages, des fragments d'ADN bactérien soient enfermés dans la capside virale. La lyse de la bactérie donneuse libère des particules de phages contenant
4. Un phage transportant de l'ADN bactérien infecte une nouvelle cellule hôte, soit la bactérie receveuse.
5. À l'occasion, il y a recombinaison, ce qui crée une bactérie recombinée avec un génotype différent de celui des bactéries donneuse et receveuse.

II . Viral Genetics

Viral genetics studies the mechanisms by which viruses store, replicate, and transmit their genetic material. Unlike cells, viruses are infectious agents that can reproduce only within a host cell, using the host cell's cellular mechanisms to produce new viral particles (virions).



Taxonomie des virus animaux à ARN

Strandedness	Double	Single				
Single-strand sense		Positive				DNA intermediate during replication
Enveloped or naked	Naked	Enveloped	Enveloped	Naked	Naked	Enveloped
Capsid symmetry	Icosahedral	Icosahedral	Helical	Icosahedral	Icosahedral	Icosahedral
Size (nm)	75–80	40–75 (enveloped) 25–35 (capsid)	80–160 (enveloped) 14–16 (capsid diameter)	22–30	35–40	80–100 (enveloped)
Site of capsid assembly	Cytoplasm	Cytoplasm	Cytoplasm	Cytoplasm	Cytoplasm	Cytoplasm
Virus family	*Reoviridae*	*Togaviridae*	*Coronaviridae*	*Picornaviridae*	*Calciviridae*	*Retroviridae*
Representative genera and groups [Host, disease]	Orbivirus [Humans: encephalitis] Rotavirus [Humans: diarrhea] Cypovirus [Insects: cytoplasmic polyhedrosis virus	Alphavirus [Humans: encephalitis] Flavivirus [Humans: yellow fever, dengue] Rubivirus [Humans: rubella] Pestivirus [Pigs: hog cholera]	Infectious bronchitis virus [Humans: upper respiratory infection]	Enterovirus [Humans: polio] Rhinovirus [Humans: common cold] Hepatovirus [Humans: hepatitis A]	Vesicular exanthema of swine Norwalk virus Hepatitis E virus	Oncornavirus C [Birds, mice: sarcomas, leukemias] Human T-cell leukemia virus Human immunodeficiency virus

Taxonomie des virus animaux à ARN

Strandedness	Single				
Single-strand sense	Negative				
Enveloped or naked	Enveloped	Enveloped	Enveloped	Enveloped	Enveloped
Capsid symmetry	Helical	Helical	Helical	?	Helical
Size (nm)	80–120 (enveloped) 9 (capsid diam.)	70–80 x 130–240 (bullet-shaped)	90–100 (enveloped)	50–300	125–250 (enveloped) 18 (capsid diam.)
Site of capsid assembly	Cytoplasm	Cytoplasm	Cytoplasm	Cytoplasm	Cytoplasm
Virus family	*Orthomyxoviridae*	*Rhabdoviridae*	*Bunyaviridae*	*Arenaviridae*	*Paramyxoviridae*
Representative genera and groups [Host, disease]	Influenza virus [Humans, swine]	Lyssavirus [Warm-blooded animals: rabies]	California encephalitis virus [Humans]	Lassa virus [Humans: hemorrhagic fever]	Paramyxovirus [Humans: colds, respiratory infections, mumps] Pneumovirus [Humans: pneumonia, common cold] Morbillivirus [Humans: measles]

1. Types of Viral Genomes

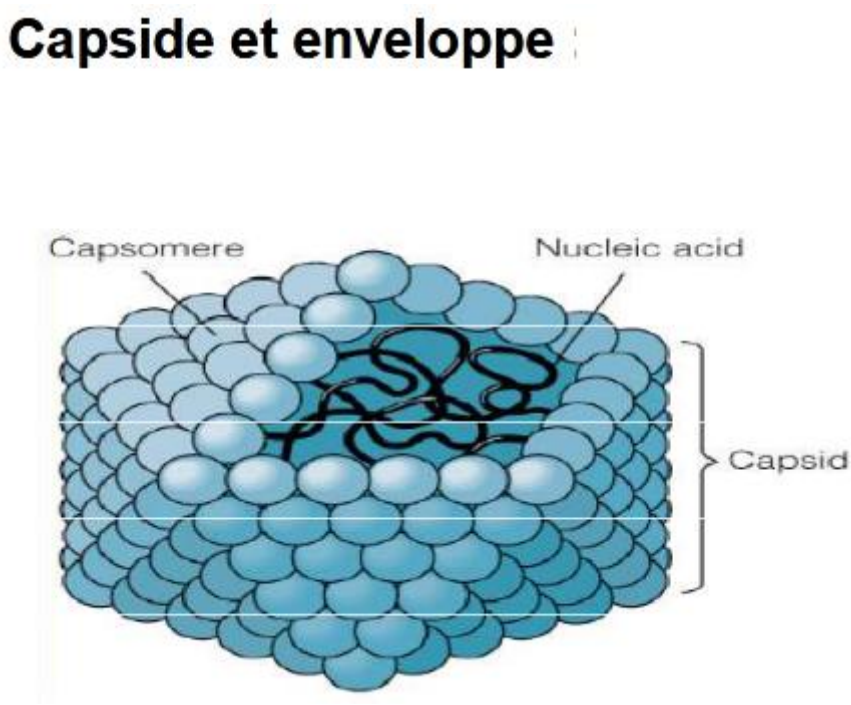
Viruses have a great diversity in their genetic material, which can be classified into several categories:

- **DNA or RNA** : Viruses can have a genome made up of DNA (single or double stranded) or RNA (single or double stranded).
- **Linear or circular form** : Some viruses have linear genomes (like the herpes virus) while others have circular genomes (like the human papillomavirus).
- **RNA Polarity** : RNA viruses can be classified according to the polarity of their RNA. Positive RNA viruses (e.g. poliovirus) have a genome that can be directly translated into proteins, while negative RNA viruses (e.g. influenza virus) must first transcribe their RNA into a positive sequence.
- **Segmented or non-segmented** : Some viruses have a segmented genome, made up of several fragments of DNA or RNA, such as the influenza virus, while others have a single genome.

2. Genetic Organization of Viruses

The viral genome is often organized very compactly, without introns, and each segment of DNA or RNA often contains several genes. These genes typically encode proteins needed for viral infection and replication, such as:

- **Capsid proteins** : These are the structural proteins that form the protein shell protecting the genetic material of the virus. This capsid is made up of the assembly of repetitive protein subunits sometimes called capsomeres. The assembly formed by the capsid and the viral nucleic acid is called nucleocapsid. In addition to the capsid and the viral nucleic acid, certain viruses are surrounded by a lipid envelope (coat): we then speak of "enveloped" viruses . On the other hand, in the absence of an envelope we speak of "naked" viruses.



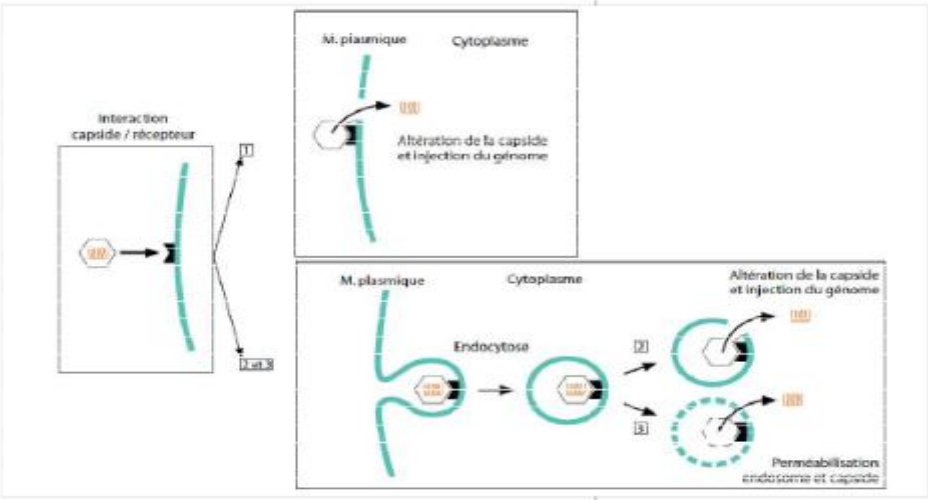
- **Viral enzymes** : Viruses often encode enzymes necessary for their replication cycle, such as polymerases for transcription and replication of viral DNA or RNA.
- **Adhesion proteins** : Certain proteins allow viruses to recognize and attach to specific receptors on host cells.

3. Viral Replication Cycle

The virus replication cycle is a complex process that depends on the type of virus. However, most viruses follow the following general steps:

- **Adsorption and entry** : Viruses attach to specific receptors on the surface of host cells and enter the cell by membrane fusion or endocytosis.
- **Uncoating** : Once inside the cell, the viral capsid disintegrates, releasing the viral genetic material into the cytoplasm or nucleus of the cell.
- **Genome replication** : DNA viruses replicate their genome in the host cell nucleus using the cell's enzymes, while RNA viruses replicate their genome in the cytoplasm using their own viral RNA polymerase.
- **Transcription and translation** : The viral genome is transcribed into messenger RNA (mRNA) which is then translated into viral proteins by the host cell's ribosomes.
- **Assembly** : Viral proteins and genetic material are assembled to form new virions.

- **Release** : New virions are released from the host cell by cell lysis or by budding through the plasma membrane.



4. Mechanisms of Genetic Variability

Viruses have several ways of generating genetic variability, which allows them to adapt rapidly to new environmental conditions, such as host immunity or antiviral treatments.

- **Mutations** : Replication errors can introduce mutations into the viral genome, particularly in RNA viruses, which lack error correction mechanisms. These mutations can affect virulence, transmissibility, or resistance to antiviral drugs.
- **Recombination** : Some viruses, especially DNA viruses, can exchange DNA segments with other viruses infecting the same cell, generating new genetic combinations.
- **Genetic reassortment** : In viruses with segmented genomes, such as influenza virus, genome segments can mix during simultaneous infection by multiple viral strains, creating virions with a hybrid genome.
- **Lysogenic conversion** : In bacteriophage viruses, viral DNA can integrate into the genome of the host bacterium and be transmitted during cell division. This process can sometimes confer new properties to the bacterium, such as the production of toxins.

5. Genetic Transmission in Viruses

Transmission of viral genetic material occurs in several ways:

- **Vertical transmission** : Some viruses, such as retroviruses, can integrate their genome into that of the host cell, and this will be transmitted to the progeny of the infected cell. In multicellular organisms, some viruses can be transmitted from mother to offspring via the placenta or breast milk.
- **Horizontal transmission** : Horizontal transmission is the most common and includes transmission by direct contact (e.g. HIV), airborne (e.g. influenza virus), contact with bodily fluids (e.g. hepatitis B), or via vectors such as mosquitoes (e.g. Zika virus).

6. Mixed infection in viruses

Mixed infection, or coinfection , occurs when a host is simultaneously infected with several different viral species or strains. This phenomenon can have significant effects on the pathogenesis, transmission, and evolution of viruses.

6.1 Mixed infection types

1. **Co-infection with strains of the same virus**
   Example: Co-infection with several strains of influenza virus.
2. **Co-infection with different viruses**
   Example: Co-infection with HIV and hepatitis C virus.
3. **Superinfection**
   The host is first infected by one virus, then a second virus infects the host while the initial infection is still in progress.

6.2 Mixed infection mechanisms

1. **Genetic recombination**
   When two viruses infect the same cell, exchanges of genetic material can occur, creating hybrid viruses. This can lead to new viral strains with unique characteristics.
2. **Reassortment**
   This occurs when segments of RNA or DNA from different viruses are mixed, as seen in viruses with multiple segments (e.g., influenza virus).
3. **Complementation**
   In a co-infection , a defective virus can use proteins or enzymes from another virus to complete its replication cycle.

4. **Viral interference**
   A virus can inhibit or modulate the replication of another co -infecting virus, creating competition for cellular resources.

6.3 Examples of significant mixed infections

1. **Influenza and SARS-CoV-2 Significant respiratory**
   co-infection that can worsen symptoms and mortality rates.
2. **HIV and Hepatitis B or C**
   These co-infections are common in HIV patients due to similar transmission routes (blood, sexual practices).
3. **Dengue virus and Zika**
   These two viruses belong to the same family (Flaviviridae) and can circulate simultaneously in endemic regions, leading to co-infections .

6.4 Consequences of mixed infections

1. **Increased disease severity**
   Co -infections can lead to increased severity of clinical symptoms, making management and treatment more complicated.
2. **Resistance to treatments**
   Infection with multiple viral strains can complicate the effectiveness of antivirals, favoring the selection of resistant viruses.
3. **Accelerated viral evolution**
   Mixed infections allow for recombination and reassortment events, creating variants more rapidly than with a single virus infection.
4. **Impact on vaccination**
   Vaccines may be less effective against viruses that have evolved following mixed infections.