Bacteriophages (contd)

Attachment

- To enter a host cell, bacteriophages attach to **specific receptors** on the surface of bacteria, including lipopolysaccharides, teichoic acids, proteins, or even flagella.

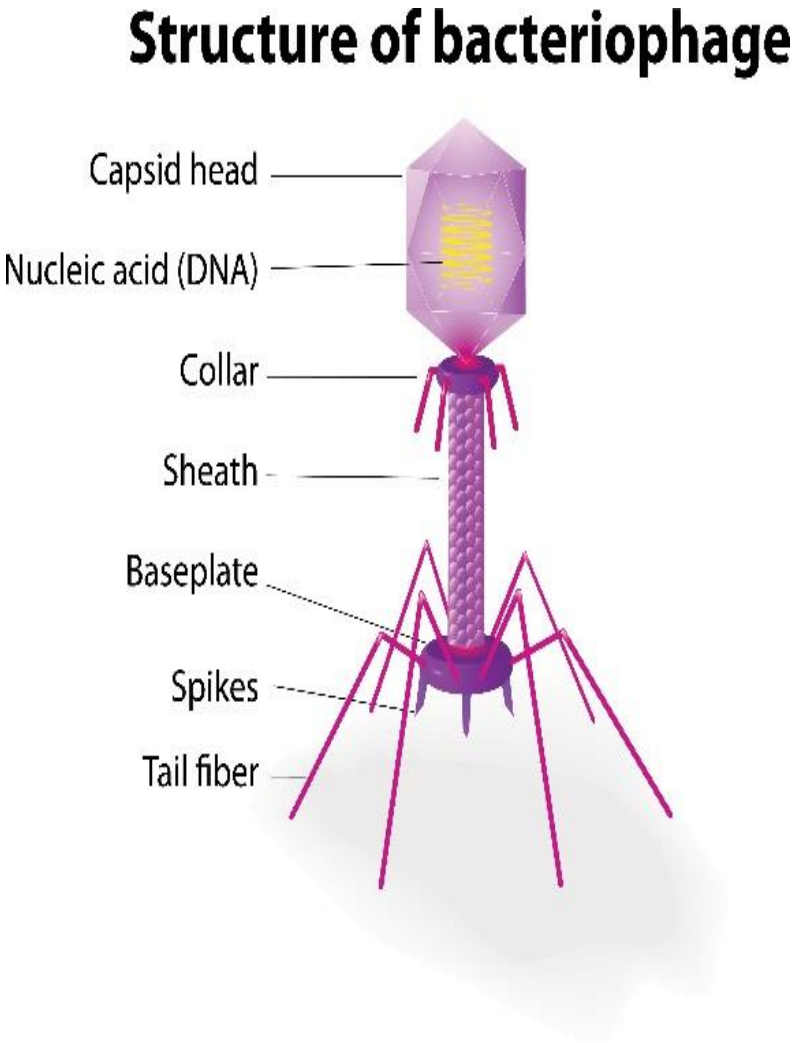
- This specificity means a bacteriophage can **infect only certain bacteria** bearing receptors to which they can bind, which in turn determines the **phage's host range**.

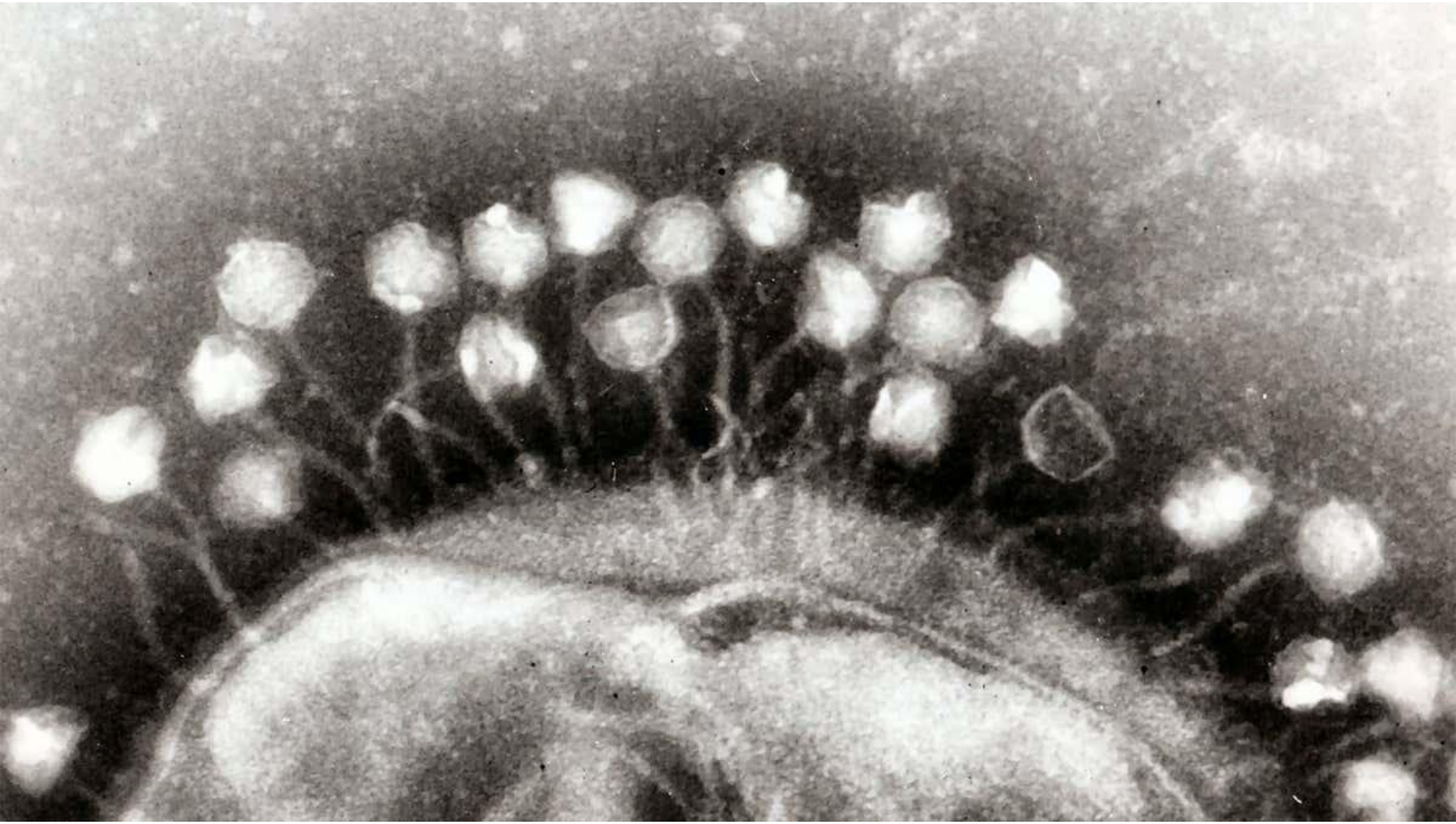
- **Host growth conditions** also influence the ability of the phage to attach and invade them.

- As phage virions **do not move independently**, they must rely on **random encounters** with the right receptors when in solution (blood, lymphatic circulation, irrigation, soil water, etc.).

- After making contact with the appropriate receptor, the **tail fibers flex** to bring the **base plate closer to the surface** of the cell.

- This is known as **reversible binding**.

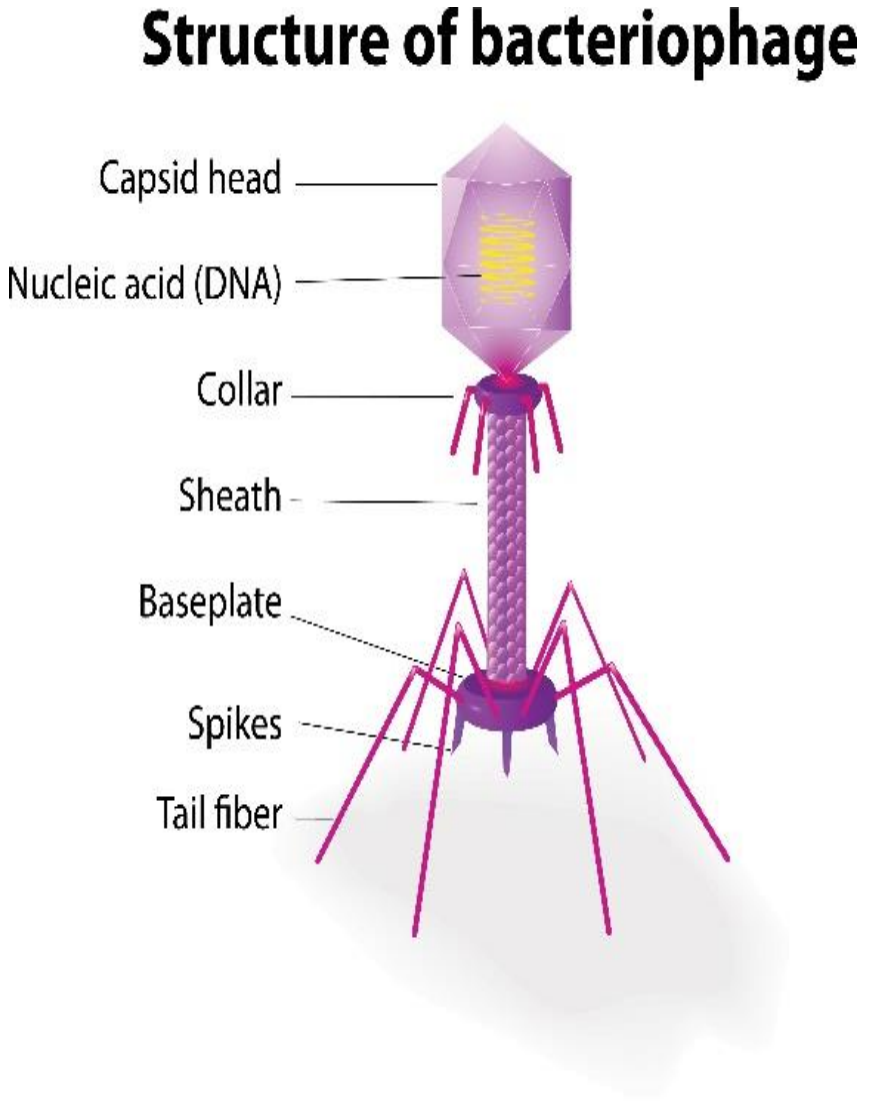


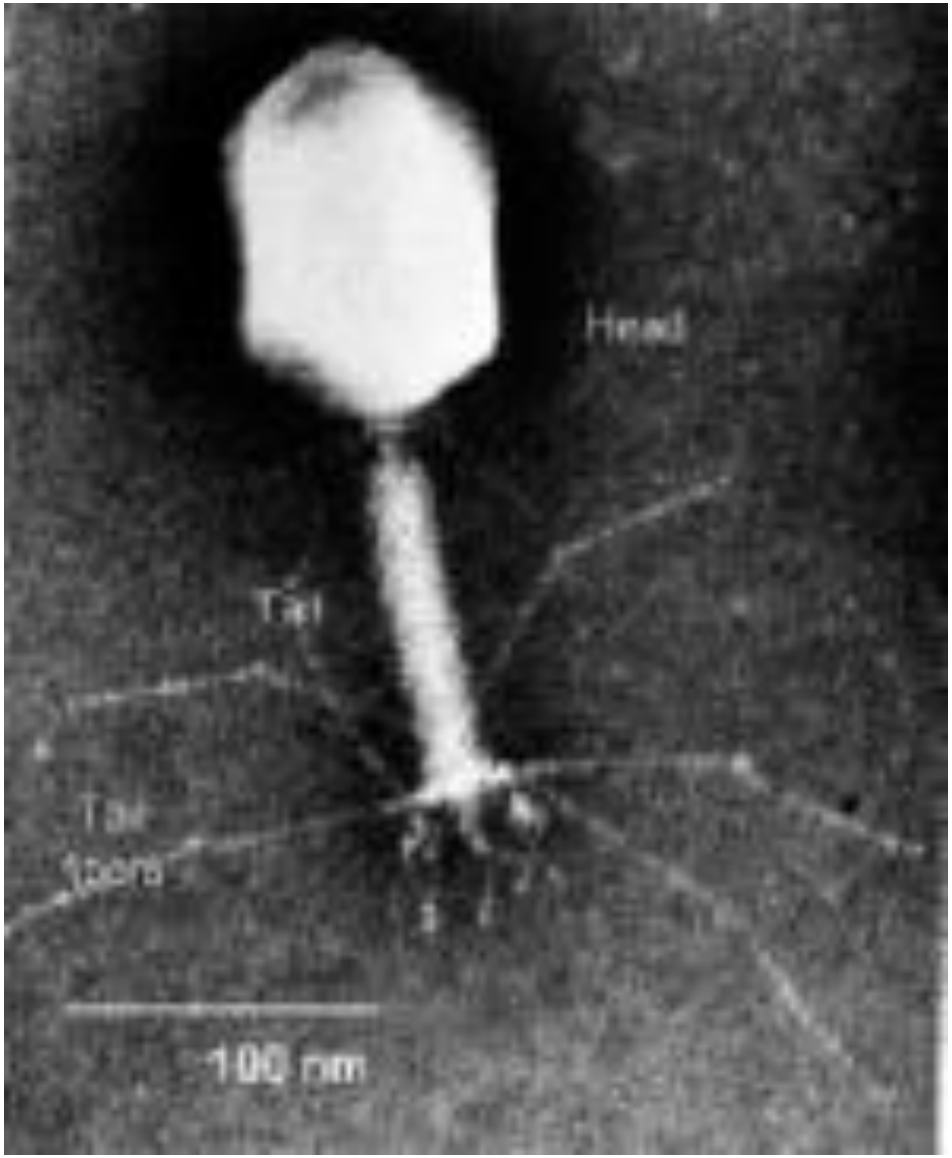


Penetration

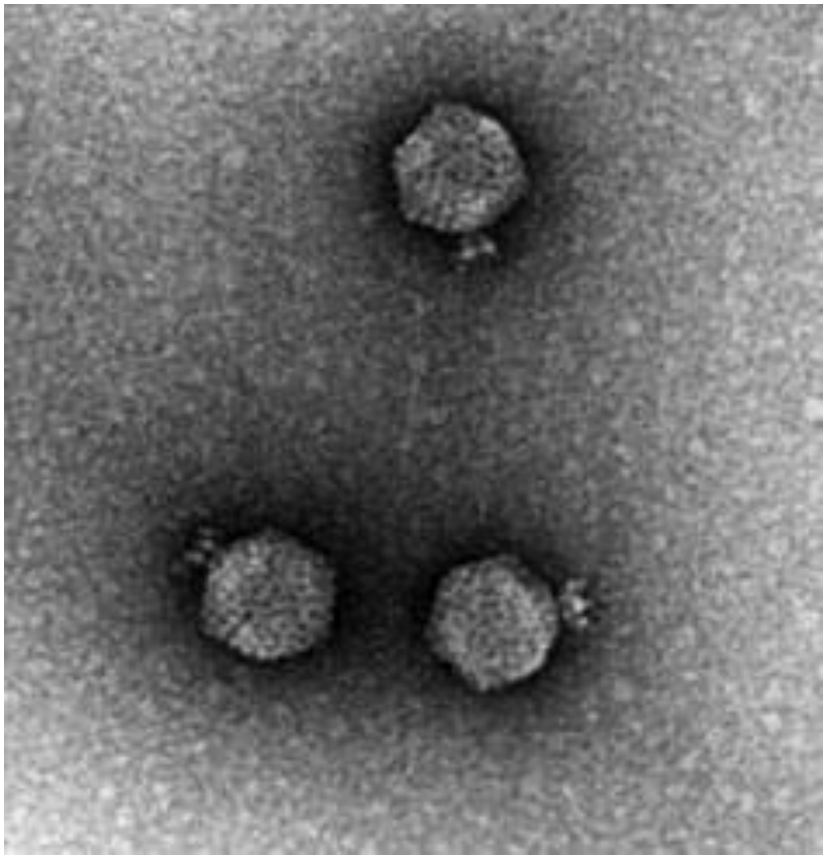
Myovirus bacteriophages use a **hypodermic syringe-like** motion to inject their genetic material into the cell.

Once attached completely, **irreversible binding** is initiated and the tail **contracts**, possibly with the help of ATP present in the tail, **injecting genetic material** through the bacterial membrane.




Head
Tail
Tail
fibers
100 nm

Podoviruses **lack an elongated tail sheath** similar to that of a myovirus, so they instead use their **small, tooth-like tail fibers** enzymatically to degrade a portion of the cell membrane before inserting their genetic material.



Synthesis of proteins and nucleic acid

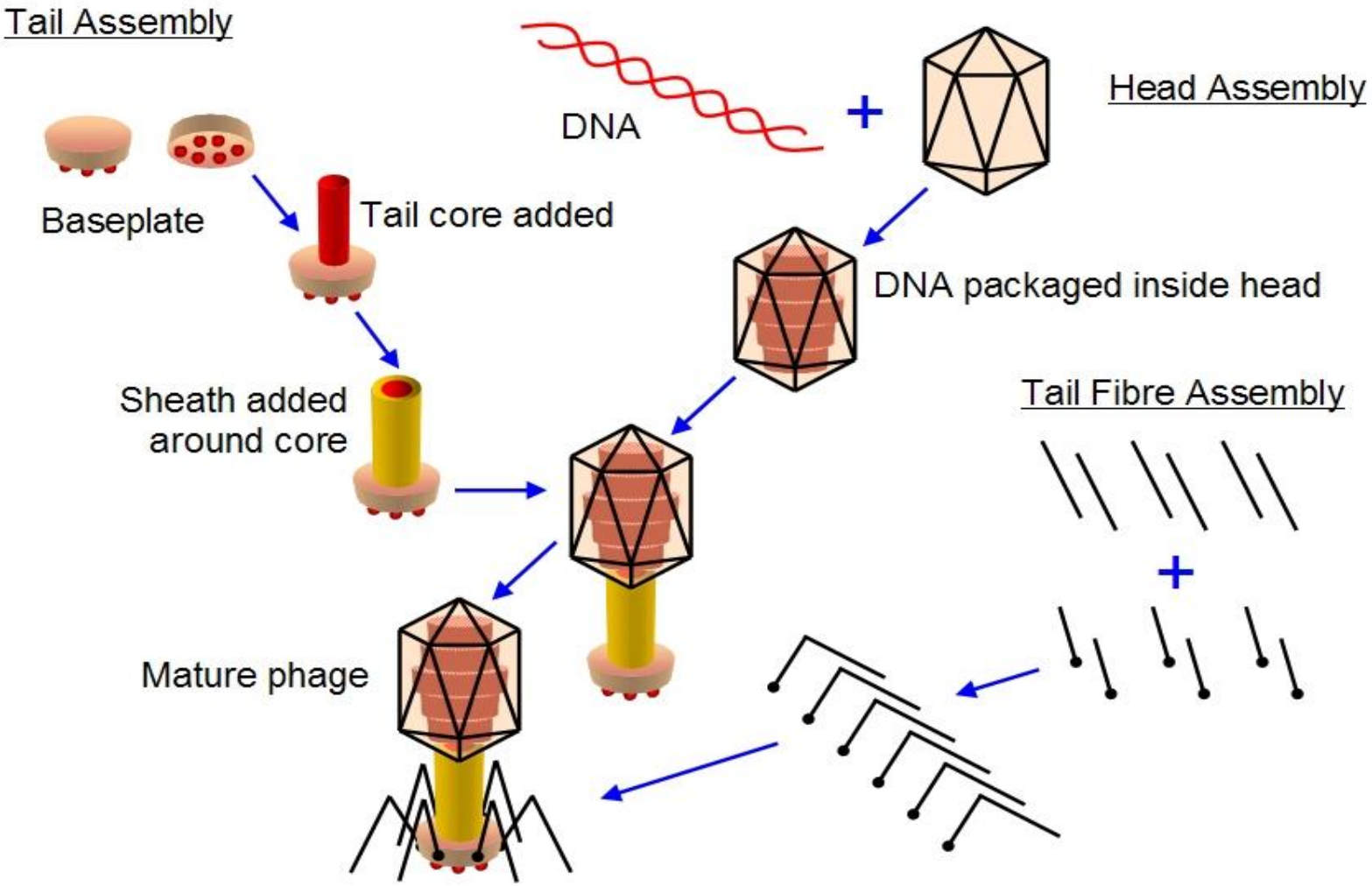
- **Within minutes**, bacterial ribosomes start translating viral mRNA into proteins.
- For RNA-based phages, **RNA replicase** is synthesized early in the process.
- Proteins **modify** the bacterial RNA polymerase so it **preferentially** transcribes viral mRNA.

- The host's **normal synthesis** of proteins and nucleic acids is **disrupted**, and it is forced to manufacture **viral products instead**.

- These products go on to become part of **new virions** within the cell, **helper proteins** that help assemble the new virions, or **proteins involved in cell lysis.**

Virion assembly

- In the case of the **T4 phage**, the construction of new virus particles involves the assistance of **helper proteins**.
- The **base plates** are assembled **first**, with the **tails** being built upon them **afterward**.
- The **head capsids**, constructed **separately**, will **spontaneously** assemble with the tails.
- The DNA/RNA is **packed** efficiently within the **heads**.
- The whole process takes about **15 minutes**.



T4 Phage Assembly (simplified scheme)

Release of virions

- Phages may be released via **cell lysis**, by **extrusion**, or, in a few cases, by **budding**.

Cell lysis

- **Lysis**, by tailed phages, is achieved by an enzyme called **endolysin**, which attacks and breaks down the cell wall peptidoglycan.

- Released virions unless defective, are **capable of infecting** a new bacterium.

Extrusion:

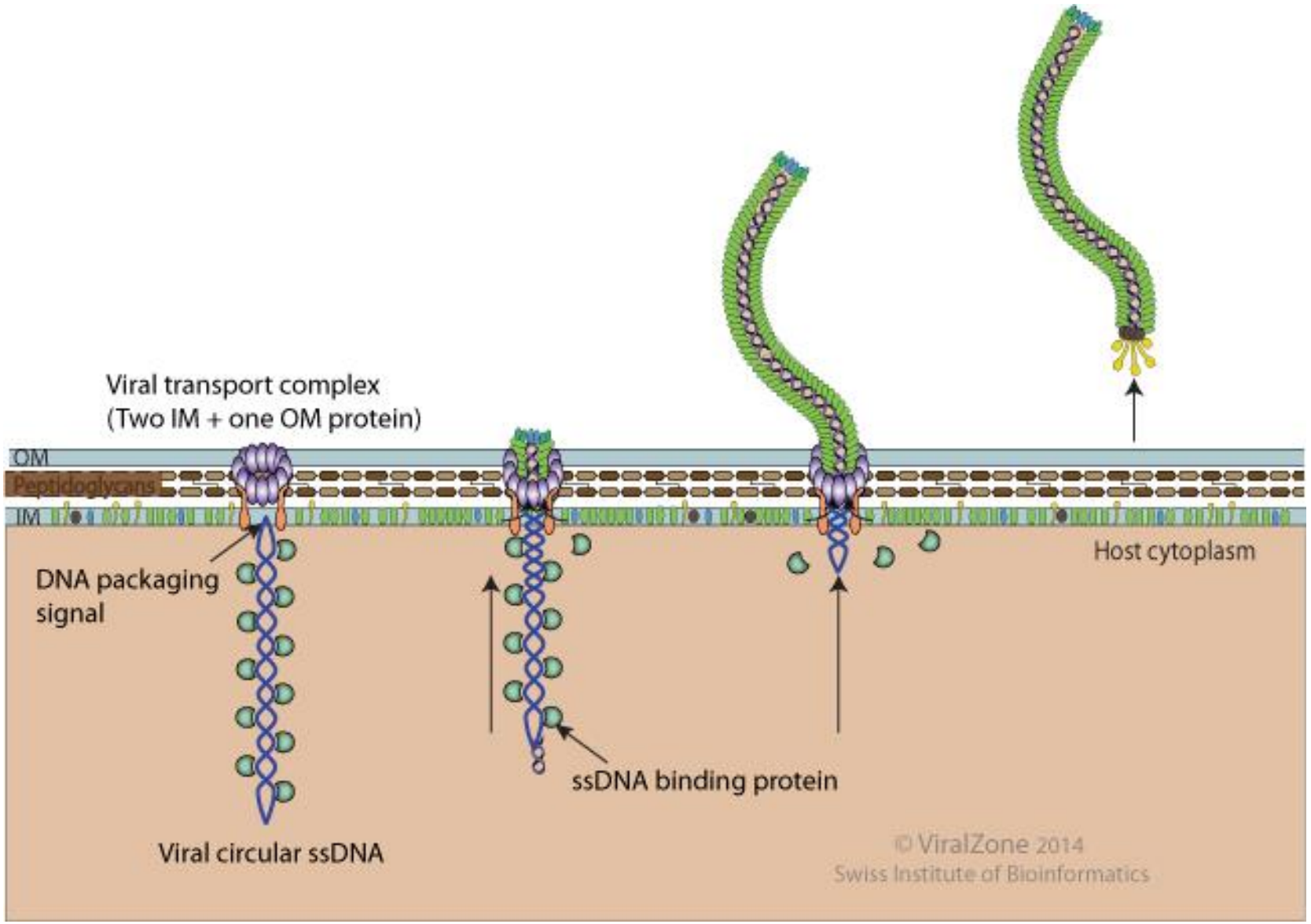
- **Filamentous phages** are released by a concerted mechanism of assembly and secretion called **extrusion**.

- The neosynthesized virions are co-ordinately exported as they are assembled at the cell surface in a secretory process that leaves the **host cell fully viable**.

- Extrusion requires **three non-capsid proteins:**

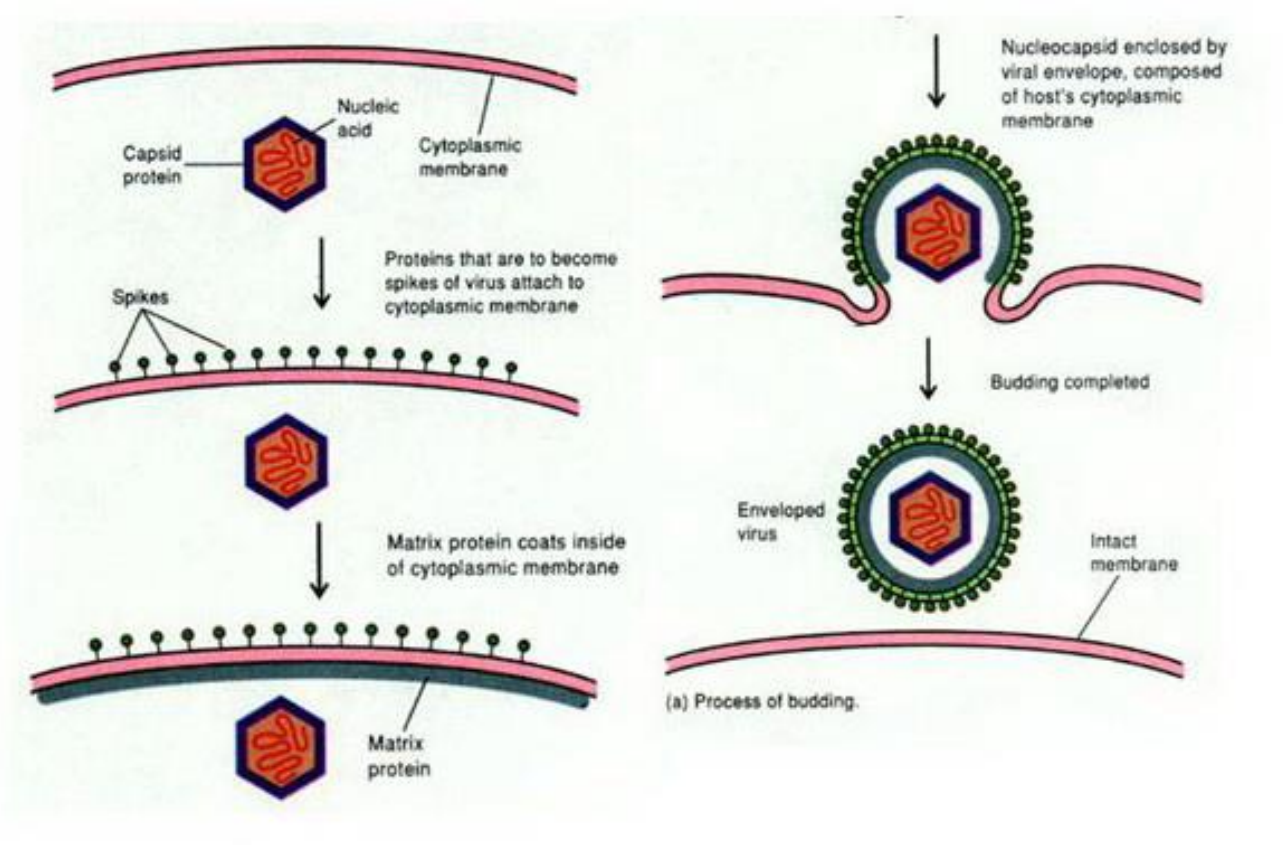
  Two of them allowing translocation through the **inner membrane (IM)**.

  One secretin-like protein forming the transmembrane channel in the **outer membrane (OM).**


Viral transport complex
(Two IM + one OM protein)
OM
Peptidoglycans
IM
DNA packaging
signal
Host cytoplasm
ssDNA binding protein
Viral circular ssDNA
© ViralZone 2014
Swiss Institute of Bioinformatics

Budding:

It is associated with certain **Mycoplasma** phages. It is similar to budding in animal viruses.



Genome structure

- Given the **millions of different phages** in the environment, phages' genomes come in a variety of forms and sizes.
- RNA phage such as **MS2** have the **smallest** genomes of only a **few kilobases**.
- However, some **DNA phages** such as **T4** may have large genomes with **hundreds of genes**.
- The size and shape of the capsid **varies** along with the size of the genome.

Effect of bacteriophage infection on host

- Phages often have **dramatic** effects on their hosts.
- As a consequence, the **transcription pattern** of the infected bacterium may change considerably.
- For instance, infection of *Pseudomonas aeruginosa* by the **temperate phage PaP3** changed the **expression of 38% (2160/5633)** of its host's genes.

Uses

Phage therapy

- Phages were discovered to be **antibacterial agents** and were used in the former Soviet Republic of Georgia during the **1920s and 1930s** for treating bacterial infections.

- The first regulated, randomized, double-blind **clinical trial** was reported in the Journal of Wound Care in **June 2009**, which evaluated the safety and efficacy of a **bacteriophage cocktail** to treat **infected venous ulcers** of the leg in human patients.

Dairy industry

- Bacteriophages present in the environment can cause fermentation failures of cheese starter cultures.

- In order to avoid this, **mixed-strain** starter cultures and culture rotation regimes can be used.

Food industry

- Since **2006**, the FDA and USDA have approved several bacteriophage products.
- **LMP-102 (Intralytix)** was approved for treating **ready-to-eat (RTE) poultry and meat products.**
- In the same year, the FDA approved **LISTEX** using bacteriophages on cheese **to kill *Listeria monocytogenes* bacteria**, giving them generally recognized as safe (GRAS) status.
- In July 2007, the same bacteriophages were approved for use on **all food products**.

Diagnostics

- In **2011**, the FDA cleared the first bacteriophage-based product for **in vitro diagnostic** use.

- The **KeyPath MRSA/MSSA Blood Culture Test** uses a cocktail of bacteriophage to detect ***Staphylococcus aureus*** in positive blood cultures and determine **methicillin resistance or susceptibility**.

- Results are available in about **5 hours**, compared to **2–3 days** for standard methods.


Thank You!