Lytic Cycle

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Introduction

- After DNA bacteriophages have reproduced within the host cell, many of them are released when the cell is destroyed by lysis.
- A phage life cycle that culminates with the host cell bursting and releasing virions is called a **lytic cycle.**

Lytic cycle: Adsorption to the Host Cell and Penetration

- Bacteriophages do not randomly attach to the surface of a host cell; rather, they fasten to specific surface structures called **receptor sites.**
- T-even phage adsorption involves several tail structures.
- Phage attachment begins when a tail fiber contacts the appropriate receptor site.
- As more tail fibers make contact, the baseplate settles down on the surface**.**
- Binding is probably due to electrostatic interactions and is influenced by pH and the presence of ions such as Mg2 and Ca2.
- After the baseplate is seated firmly on the cell surface, conformational changes occur in the baseplate and sheath, and the tail sheath reorganizes so that it shortens from a cylinder 24 rings long to one of 12 rings.
- That is, the sheath becomes shorter and wider, and the central tube or core is pushed through
- the bacterial wall. Finally, the DNA is extruded from the head, through the tail tube, and into the host cell.
- The tube may interact with the plasma membrane to form a pore through which DNA passes.

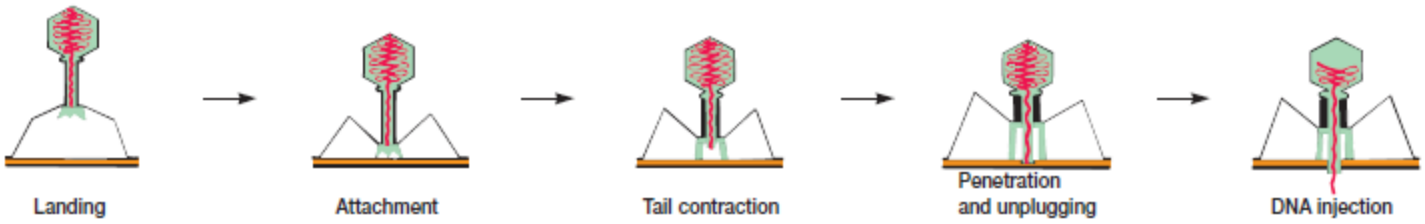


Figure 17.3 **T4 Phage Adsorption and DNA Injection.** See text for details.

Lytic Cycle: Synthesis of Phage Nucleic Acids and Proteins

- Soon after T4 phage DNA injection, the synthesis of host DNA, RNA, and protein is halted, and the cell is forced to make viral constituents.
- *E. coli* RNA polymerase starts synthesizing phage mRNA within 2 minutes.
- This mRNA and all other **early mRNA** (mRNA transcribed before phage DNA is made) direct the synthesis of the protein factors and enzymes required to take over the host cell and manufacture viral nucleic acids.
- Some early virus specific enzymes degrade host DNA to nucleotides, thereby simultaneously halting host gene expression and providing raw material for virus DNA synthesis.
- Within 5 minutes, virus DNA synthesis commences.

Lytic cycle: The Assembly of Phage Particles

- The assembly of the T4 phage is an exceptionally complex selfassembly process.
- **Late mRNA, or that produced after DNA replication,** directs the synthesis of three kinds of proteins: (1) phage structural proteins, (2) proteins that help with phage assembly without becoming part of the virion structure, and (3) proteins involved in cell lysis and phage release.
- Late mRNA transcription begins about 9 minutes after T4 DNA injection into *E. coli.*
- The baseplate is constructed of 15 gene products.
- After the baseplate is finished, the tail tube is built on it and the sheath is assembled around the tube.
- The phage prohead or procapsid is constructed separately of more than 10 proteins and then spontaneously combines with the tail assembly.
- Tail fibers attach to the baseplate after the head and tail have come together.
- Although many of these steps occur spontaneously, some require special virus proteins or host cell factors.

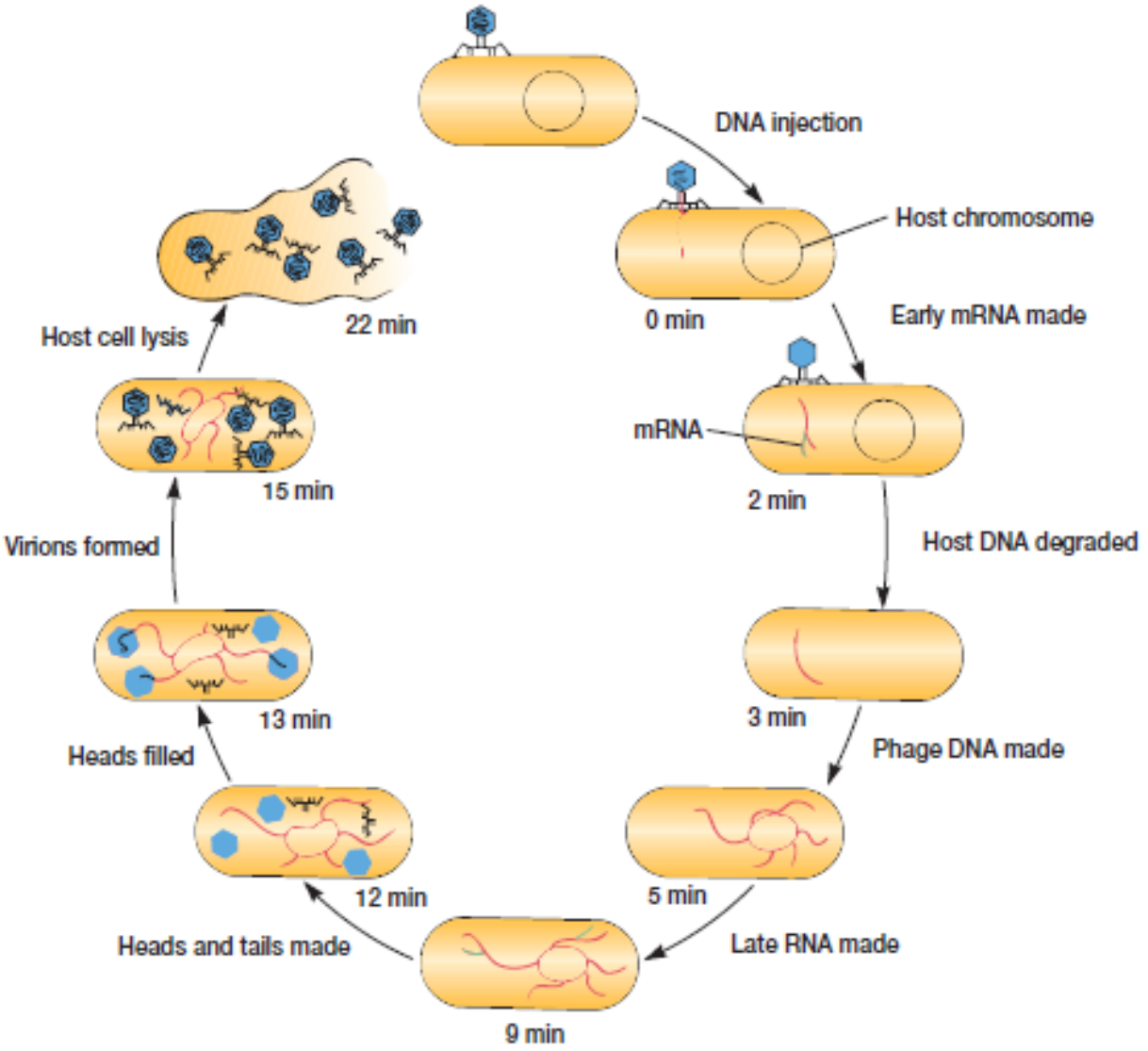
… Lytic cycle: The Assembly of Phage Particles

- DNA packaging within the T4 head is still a somewhat mysterious process.
- In some way the DNA is drawn into the completed shell so efficiently that about 500 μm of DNA are packed into a cavity less than 0.1 μm across!
- The first complete T4 particles appear in *E. coli* at 37°C about 15 minutes after infection.

Lytic cycle: Release of Phage Particles

- Many phages lyse their host cells at the end of the intracellular phase.
- The lysis of *E. coli* takes place after about 22 minutes at 37°C, and approximately 300 T4 particles are released.
- Several T4 genes are involved in this process.
- One directs the synthesis of an endolysin that attacks the cell wall peptidoglycan.
- Another phage protein called a holin produces a plasma membrane lesion that stops respiration and allows the endolysin to attack the peptidoglycan.
- Presumably it forms holes in the membrane.

The Life Cycle of Bacteriophage T4



One Step Multiplication Curve

- In a **one-step growth experiment, the** reproduction of a large phage population is synchronized so that the molecular events occurring during reproduction can be followed.
- A culture of susceptible bacteria such as *E. coli is mixed* with bacteriophage particles, and the phages are allowed a short interval to attach to their host cells.
- The culture is then greatly diluted so that any virus particles released upon host cell lysis will not immediately infect new cells.
- This strategy works because phages lack a means of seeking out host cells and must contact them during random movement through the solution.
- Thus phages are less likely to contact host cells in a dilute mixture.
- The number of infective phage particles released from bacteria is subsequently determined at various intervals by a plaque count.

...One Step Multiplication Curve

- A plot of the bacteriophages released from host cells versus time shows several distinct phases (**figure 17.2).**
- **During the latent period, which immediately follows phage addition, there is** no release of virions.
- This is followed by the **rise period or burst,** when the host cells rapidly lyse and release infective phages.
- Finally, a plateau is reached and no more viruses are liberated.
- The total number of phages released can be used to calculate the **burst size, the number of viruses produced per infected cell.**

… One Step Multiplication Curve

- The latent period is the shortest time required for virus reproduction and release.
- During the first part of this phase, host bacteria do not contain any complete, infective virions.
- This can be shown by lysing them with chloroform.
- This initial segment of the latent period is called the **eclipse period because the virions** were detectable before infection but are now concealed or eclipsed.
- The number of completed, infective phages within the host increases after the end of the eclipse period, and the host cell is prepared for lysis.

The One-Step Growth Curve. In the initial part of the latent period, the eclipse period, the host cells do not contain any complete, infective virions.
During the remainder of the latent period, an increasing number of infective virions are present, but none are released.
The latent period ends with host cell lysis and rapid release of virions during the rise period or burst.
In this figure the blue line represents the total number of complete virions.
The red line is the number of free viruses (the unadsorbed virions plus those released from host cells).
When *E. coli is infected with T2 phage at 37°C, the growth* plateau is reached in about 30 minutes and the burst size is approximately 100 or more virions per cell. The eclipse period is 11–12 minutes, and the latent period is around 21–22 minutes in length.