Bacteriophages

Bacteria-infecting viruses. The lytic and lysogenic cycles.

Introduction

Even bacteria can get a virus! The viruses that infect bacteria are called bacteriophages, and certain bacteriophages have been studied in detail in the lab (making them some of the viruses we understand best).

In this articles, we'll take a look at two different cycles that bacteriophages may use to infect their bacterial hosts:

The lytic cycle: The phage infects a bacterium, hijacks the bacterium to make lots of phage’s, and then kills the cell by making it explode (lyse).
The lysogenic cycle: The phage infects a bacterium and inserts its DNA into the bacterial chromosome, allowing the phage DNA (now called a prophage) to be copied and passed on along with the cell's own DNA.

A bacteriophage is a virus that infects bacteria

A bacteriophage, or phage for short, is a virus that infects bacteria. Like other types of viruses, bacteriophages vary a lot in their shape and genetic material.

Phage genomes can consist of either DNA or RNA, and can contain as few as four genes or as many as several hundred.

The capsid of a bacteriophage can be icosahedral, filamentous, or head-tail in shape. The head-tail structure seems to be unique to phage’s and their close relatives (and is not found in eukaryotic viruses).

Bacteriophage infections

Bacteriophages, just like other viruses, must infect a host cell in order to reproduce. The steps that make up the infection process are collectively called the lifecycle of the phage.

Some phage’s can only reproduce via a lytic lifecycle, in which they burst and kill their host cells. Other

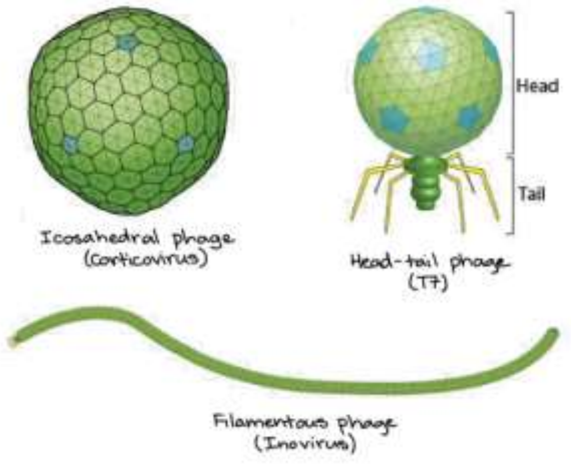

Image modified from "Corticovirus," "T7likevirus," and "Inovirus, by ViralZone/Swiss Institute of Bioinformatics, CC BY-NC 4.0.

Bacteriophage infections

Bacteriophages, just like other viruses, must infect a host cell in order to reproduce. The steps that make up the infection process are collectively called the lifecycle of the phage.

Some phage’s can only reproduce via a lytic lifecycle,

in which they burst and kill their host cells. Other phage’s can alternate between a lytic lifecycle and a lysogenic lifecycle, in which they don't kill the host cell (and are instead copied along with the host DNA each time the cell divides).

Let's take closer look at these two cycles. As an example, we'll use a phage called lambda (λ), which infects E. coli bacteria and can switch between the lytic and lysogenic cycles.

Lytic cycle

In the lytic cycle, a phage acts like a typical virus: it hijacks its host cell and uses the cell's resources to make lots of new phage’s, causing the cell to lyse (burst) and die in the process.

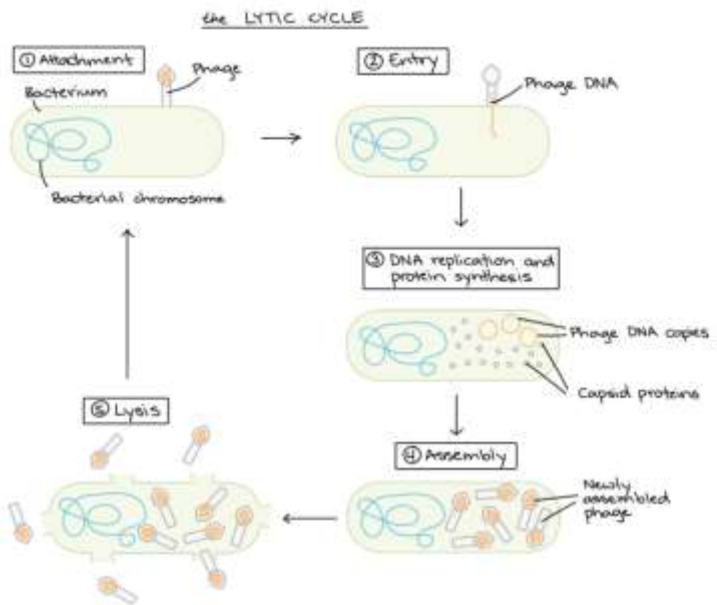

Image modified from "Conjugation," by Adenosine (CC BY-SA 3.0). The modified image is licensed under a CC BY-SA 3.0 license. Based on similar diagram in Alberts et al.[6]

The stages of the lytic cycle are:

1. Attachment: Proteins in the "tail" of the phage

bind to a specific receptor (in this case, a sugar transporter) on the surface of the bacterial cell.

2. Entry: The phage injects its double-stranded DNA genome into the cytoplasm of the bacterium.

3. DNA copying and protein synthesis: Phage DNA is copied, and phage genes are expressed to make proteins, such as capsid proteins.

4. Assembly of new phage: Capsids assemble from the capsid proteins and are stuffed with DNA to make lots of new phage particles.

5. Lysis: Late in the lytic cycle, the phage expresses genes for proteins that poke holes in the plasma membrane and cell wall. The holes let water flow in, making the cell expand and burst like an overfilled water balloon.

Cell bursting, or lysis, releases hundreds of new phage's, which can find and infect other host cells nearby. In this way, a few cycles of lytic infection can let the phage spread like wildfire through a bacterial population.

Lysogenic cycle

The lysogenic cycle allows a phage to reproduce without killing its host. Some phage's can only use the lytic cycle, but the phage we are following, lambda (λ), can switch between the two cycles.

In the lysogenic cycle, the first two steps (attachment and DNA injection) occur just as they do for the lytic cycle. However, once the phage DNA is inside the cell, it is not immediately copied or expressed to make proteins. Instead, it recombines with a particular region of the bacterial chromosome. This causes the phage DNA to be integrated into the chromosome.

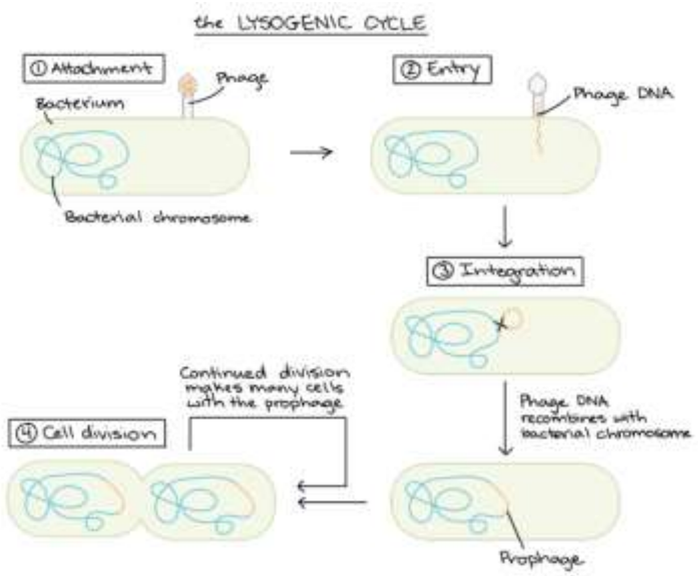

Image modified from "Conjugation," by Adenosine (CC BY-SA 3.0). The modified image is licensed under a CC BY-SA 3.0 license. Based on similar diagram in Alberts et al.[6]

The integrated phage DNA, called a prophage, is not active: its genes aren't expressed, and it doesn't drive production of new phage's. However, each time a host cell divides, the prophage is copied along with the host DNA, getting a free ride. The lysogenic cycle is less flashy (and less gory) than the lytic cycle, but at the end of the day, it's just another way for the phage to reproduce.

Under the right conditions, the prophage can become active and come back out of the bacterial chromosome, triggering the remaining steps of the lytic cycle (DNA copying and protein synthesis, phage assembly, and lysis).

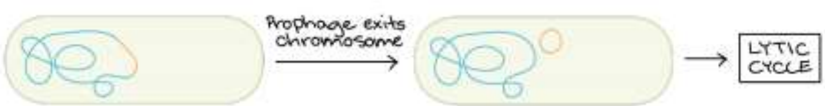

Image modified from "Conjugation," by Adenosine (CC BY-SA 3.0). The modified image is licensed under a CC BY-SA 3.0 license.

To lyse or not to lyse?

How does a phage "decide" whether to enter the lytic or lysogenic cycle when it infects a bacterium? One important factor is the number of phage’s infecting the cell at once. Larger numbers of co-infecting phage’s make it more likely that the infection will use the lysogenic cycle. This strategy may help prevent the phage’s from wiping out their bacterial hosts (by toning down the attack if the phage-to-host ratio gets too high).

What triggers a prophage to pop back out of the chromosome and enter the lytic cycle? At least in the laboratory, DNA-damaging agents (like UV radiation and chemicals) will trigger most prophages in a population to re-activate. However, a small fraction of the prophages in a population spontaneously "go lytic" even without these external cues.

Bacteriophage vs. antibiotics

Before antibiotics were discovered, there was considerable research on bacteriophages as a treatment for human bacterial diseases. Bacteriophages attack only their host bacteria, not human cells, so they are potentially good candidates to treat bacterial diseases in humans.

After antibiotics were discovered, the phage approach was largely abandoned in many parts of the world (particularly English-speaking countries). However, phage’s continued to be used for medical purposes in a number of countries, including Russia, Georgia, and Poland, where they remain in use today.

There is increasing interest in bringing back the "phage approach" elsewhere, as antibiotic-resistant bacteria become more and more of a problem. Research is still needed to see how safe and effective phage’s are, but who knows? One day, your doctor might write you a prescription for phage’s instead of penicillin!