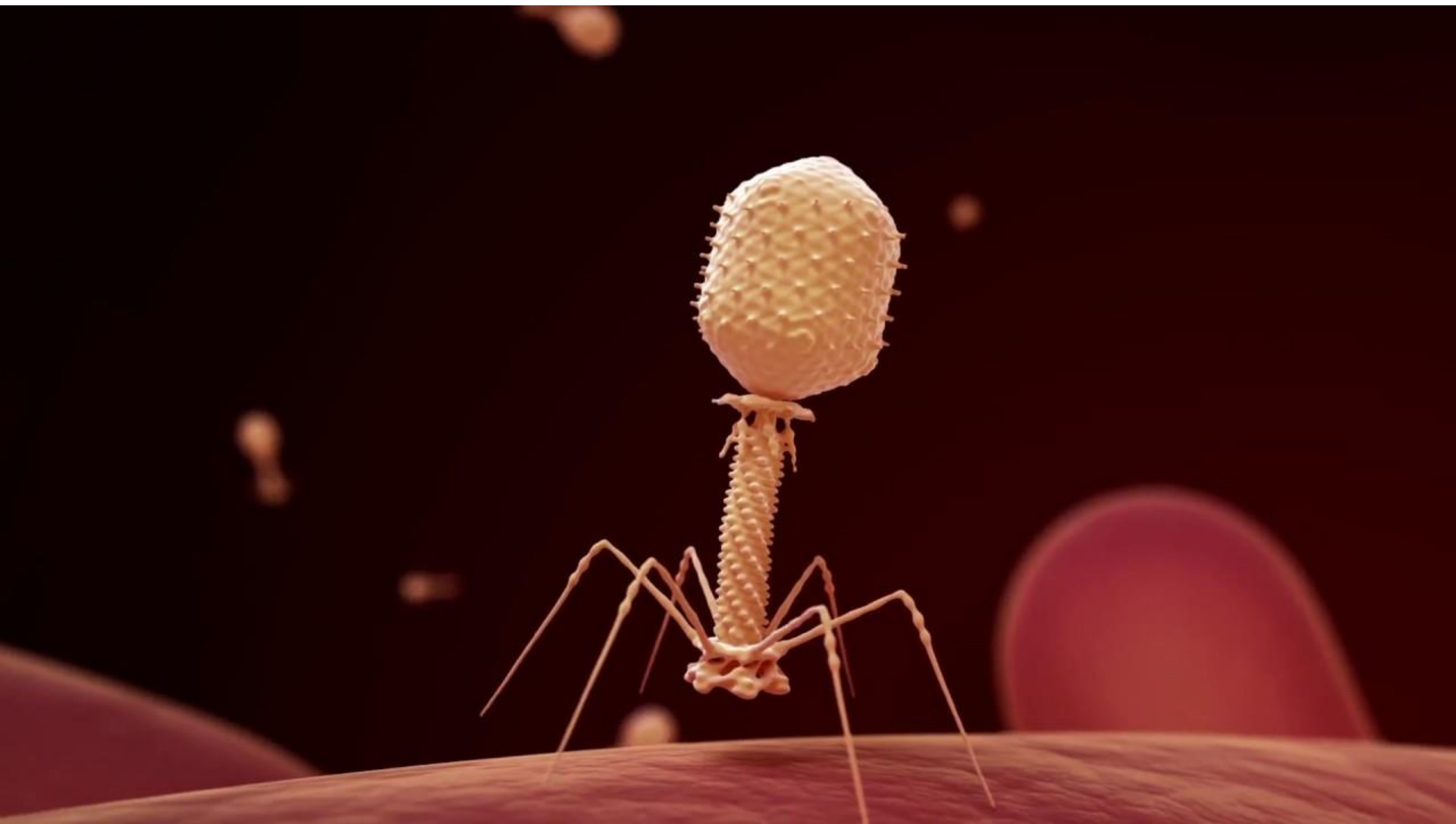


PHAGE THERAPY



COMPILED BY HOWIE BAUM

PHAGE THERAPY

AN ALTERNATIVE TO ANTIBIOTICS IN THE AGE OF MULTI DRUG RESISTANCE

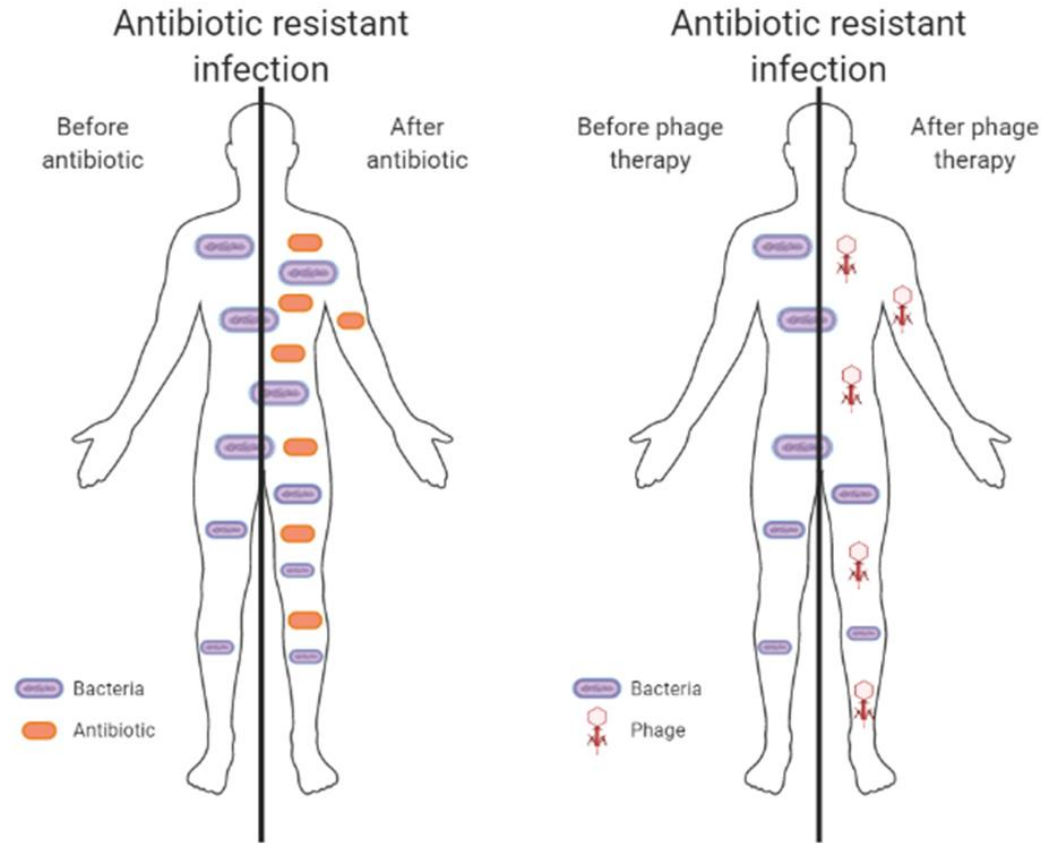
WHY DO WE NEED IT ?

- The ability of bacteria and other microorganisms to resist the effects of an antibiotic to which they were once sensitive.
- Antibiotics resistance is mostly developed due to the excessive use and misuse of it.
- Genetic variations and mutations happen in bacteria that can cause diseases so its important to kill them.



MULTI-DRUG RISTANCE

- **It is one of the biggest threats to global health, food security, and development today.**
- It can affect anyone, of any age, in any country.
- It occurs naturally, but misuse of antibiotics in humans and animals is accelerating the process.
- **A growing number of infections – such as pneumonia, tuberculosis, gonorrhea, and salmonellosis – are becoming harder to treat as the antibiotics used to treat them become less effective.**



How does antibiotic resistance occur?



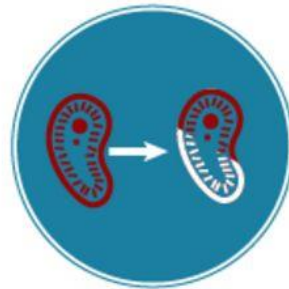
1 Some bacteria in the human body are drug resistant.



2 Antibiotics kill bacteria, but not those resistant to drugs.



3 Resistant bacteria then have space to multiply.

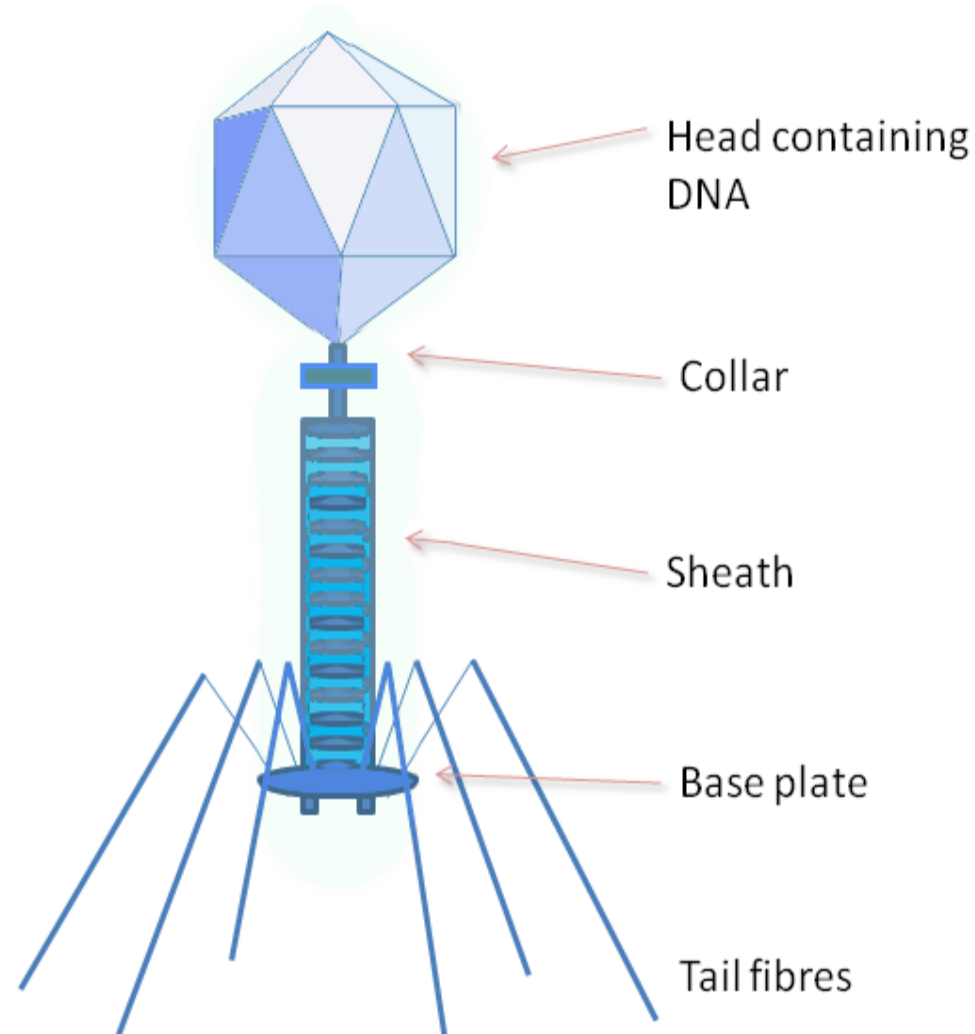


4 Bacteria can even transfer their drug resistance to other bacteria.

Enter the Phage

Bacteria's Natural Predator

- 900,000,000 virions/millimeter in the oceans.
- Virions are the active, infectious form of the **virus**
- **The most abundant life form on earth**
- Infects 70% of marine bacteria which helps to keep the water healthier.



BACTERIOPHAGE

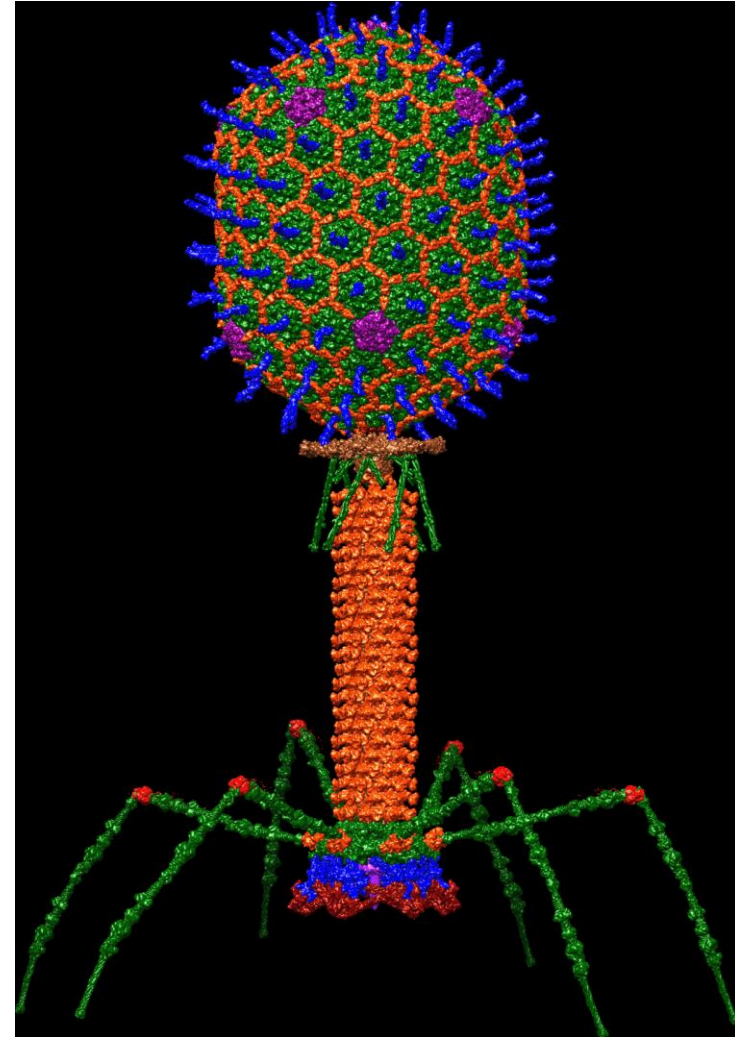
Their name is abbreviated as a Phage and were first discovered in 1915.

They are a virus that infects, replicates in bacteria, which then kills it.

They target the dangerous microbes without harming human cells, due to how specific they are.

The term was derived from "bacteria" and the Greek (phagein), meaning "to devour".

They are made of proteins that encapsulate a DNA or RNA genome with as few as 4 genes and as many as hundreds, in the top section.



https://www.youtube.com/watch?v=5AAR7bNSM_s

go to 40 seconds

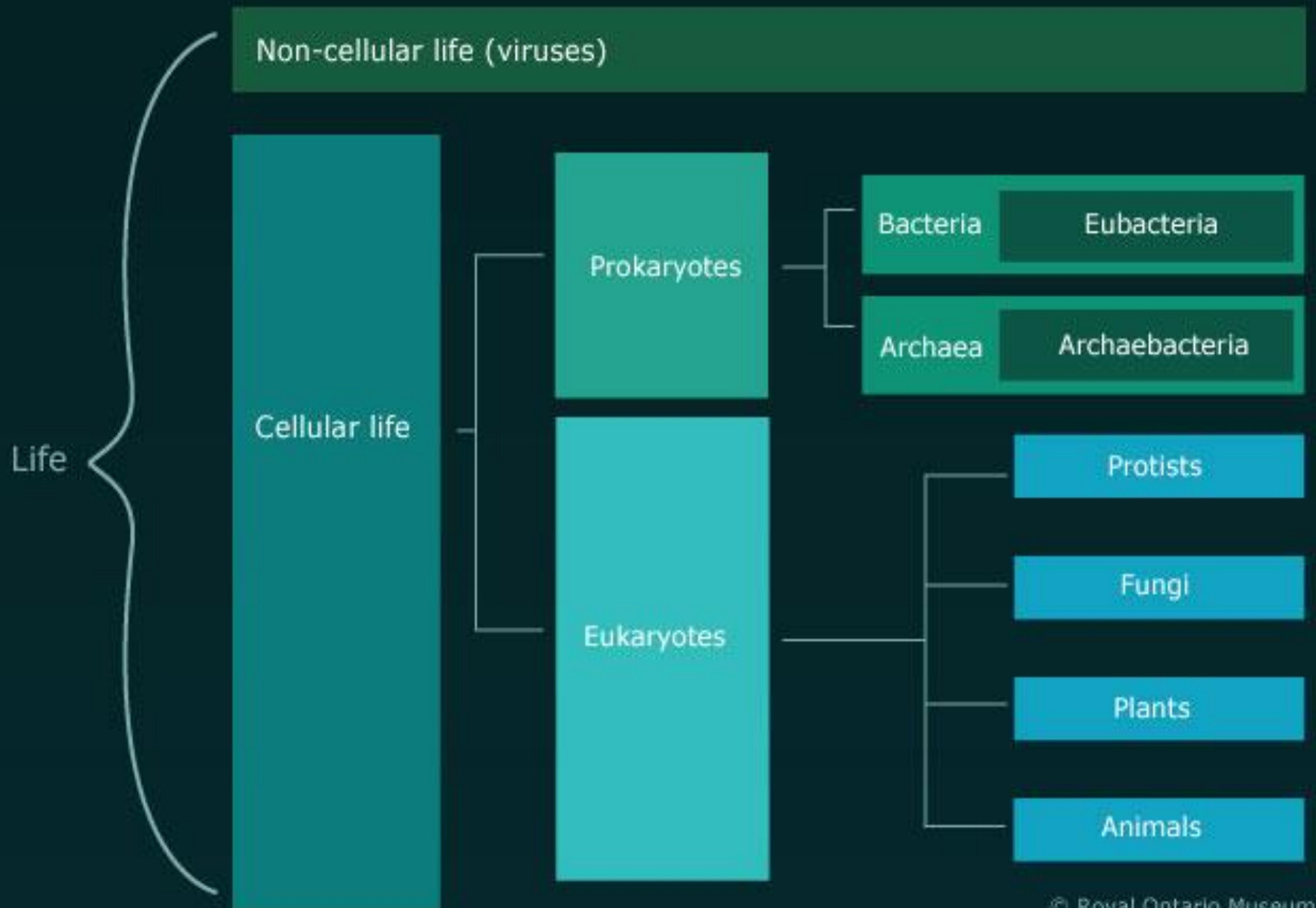
PHAGE THERAPY IS CURRENTLY BEING USED THERAPEUTICALLY IN

- **Russia**
- **Georgia** (a country located at the intersection of Eastern Europe and Western Asia
- A Phage Therapy unit in **Wrocław, Poland**, established in 2005 - the only such center in a European Union country.
- Phages are also the subject of renewed clinical attention in western countries, such as the **United States.**



In 2019, the United States Food and Drug Administration (FDA) approved the first US clinical trial for intravenous phage therapy.

Divisions of Life



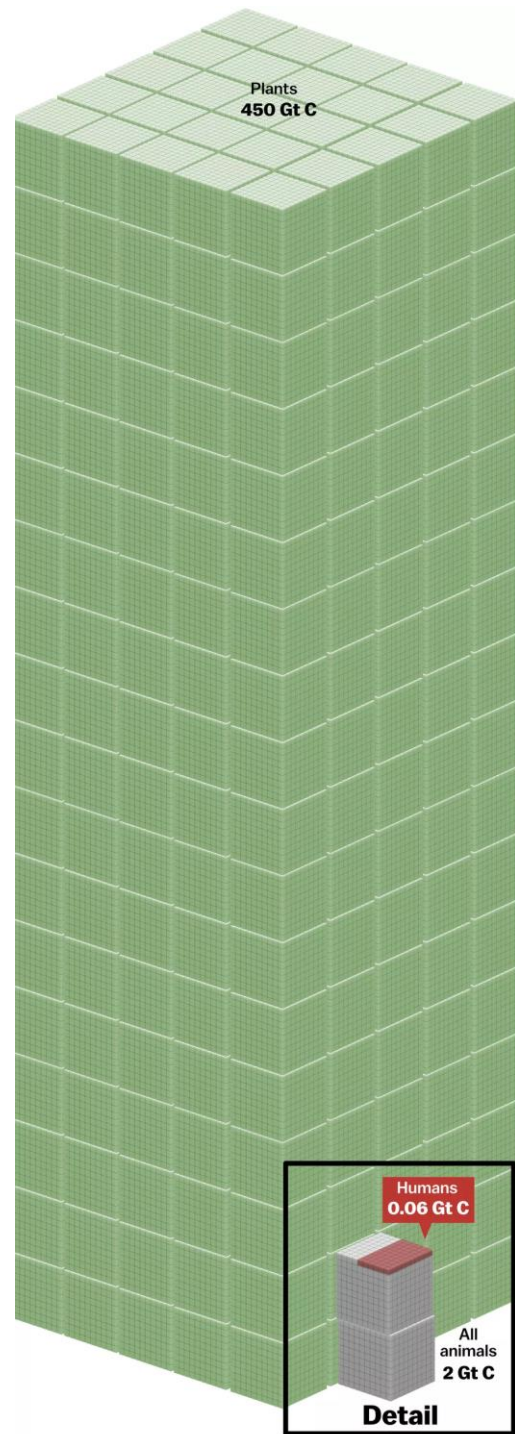
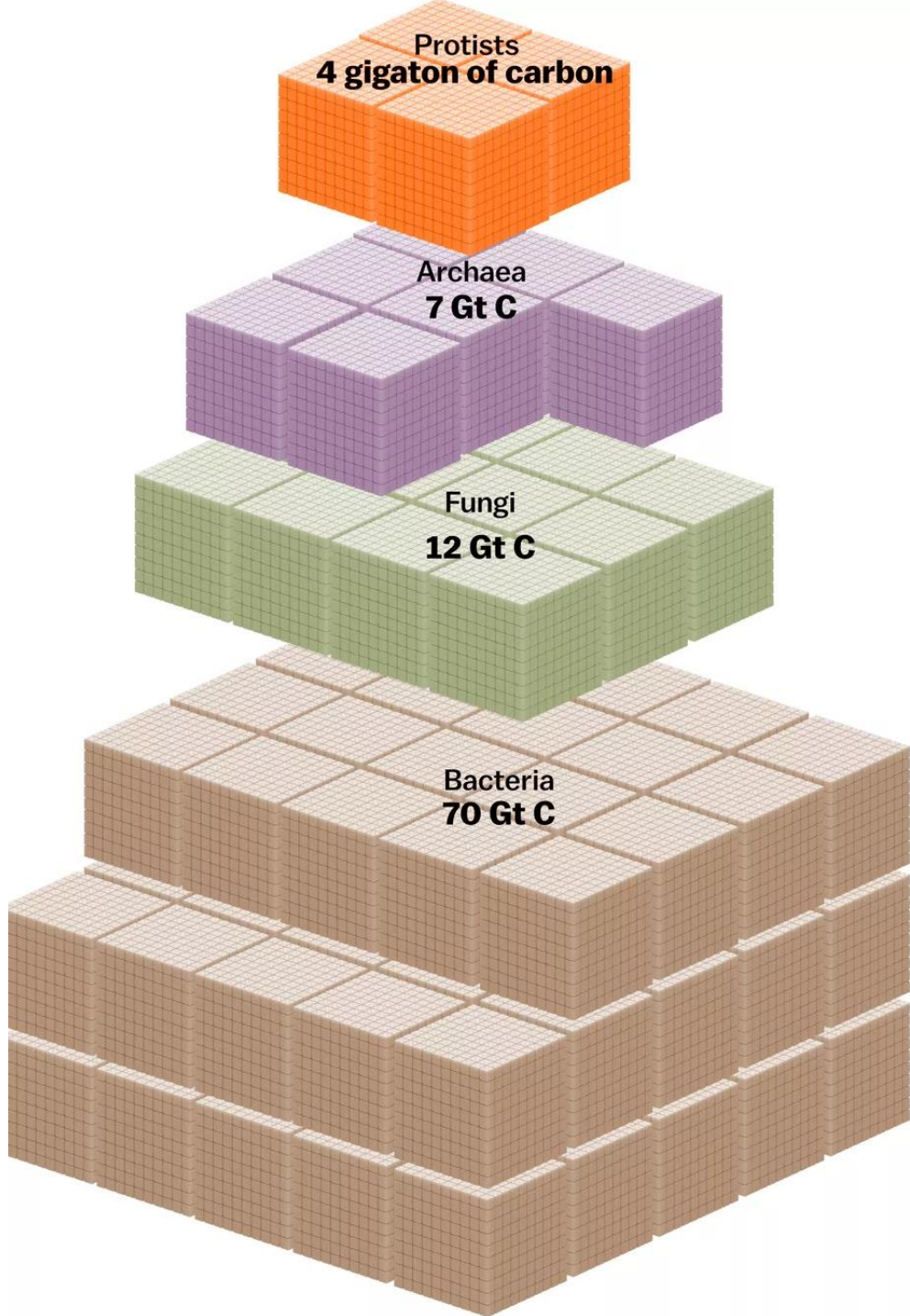
ALL LIFE ON EARTH, IN ONE STAGGERING CHART

To give a good comparison of how many bacteria there are, on the next 2 slides are 2 illustrations that represent the amount of the different types of Life on the Earth.

Each large block of this tower represents a gigaton of life, and the blocks are grouped into broad kingdoms.

A gigaton is equal to a billion metric tons. A metric ton is 1,000 kilograms, or about 2,200 pounds.

There are an estimated 550 gigatons of carbon of life in the world.



Humans
0.06 Gt C

All
animals
2 Gt C

Detail

From smallest to the largest, they are:

Humans – .01%

All animals, birds, fish, and insects - .04%

Protists (think microscopic life like amoebae) - .07%

Archaea (single-celled organisms similar to bacteria - 1.3%

Fungi (mushrooms and other types of fungus) – 2.2%

Bacteria – 12.7%

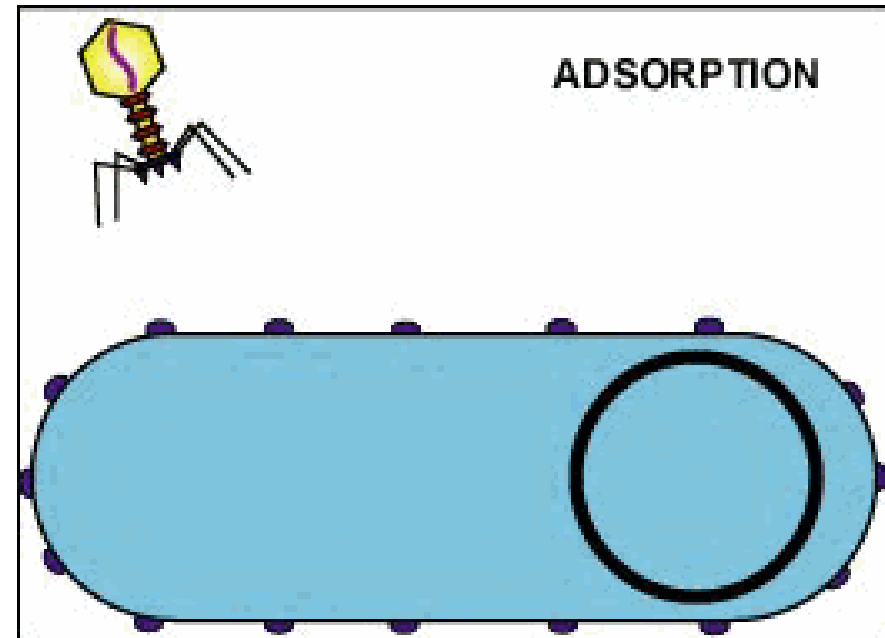
Plants (which dominate our world) – 81.8%

BACTERIOPHAGE

They are a virus that:

- 1) Parasitizes a bacterium by infecting it
- 2) Reproduce inside it
- 3) Makes multiple copies
- 4) The copies break out of it, so they can infect other bacteria or Archaea.

Within 1 hour more than 100 new phages are released from a single infected bacterium which makes the T4 phage one of the most efficient but also fascinating killing machines.



Phage therapy is an alternative to antibiotics in the age of multi-drug resistance

It relies on the use of naturally-occurring phages to infect and kill the bacteria at the site of infection.

A phage will kill a bacterium only if it matches the specific strain.

Phage mixtures ("cocktails") are often used to improve the chances of success.

Alternatively, samples taken from recovering patients sometimes contain appropriate phages that can be grown to cure other patients infected with the same strain



<https://www.youtube.com/watch?v=NWo4MwE3zfU&t=18s>
3 minutes

TEN MOST DANGEROUS ANTIBIOTIC RESISTANT BACTERIA



**NEISSERIA
GONORRHOEAE**



**ACINETOBACTER
BAUMANNII**



**STAPHYLOCOCCUS
AUREUS (MRSA)**



**BURKHOLDERIA
CEPACIA**



**PSEUDOMONAS
AERUGINOSA**



**CLOSTRIDIUM
DIFFICILE**



**ESCHERICHIA
COLI (E.COLI)**



**MYCOBACTERIUM
TUBERCULOSIS**



**KLEBSIELLA
PNEUMONIAE**



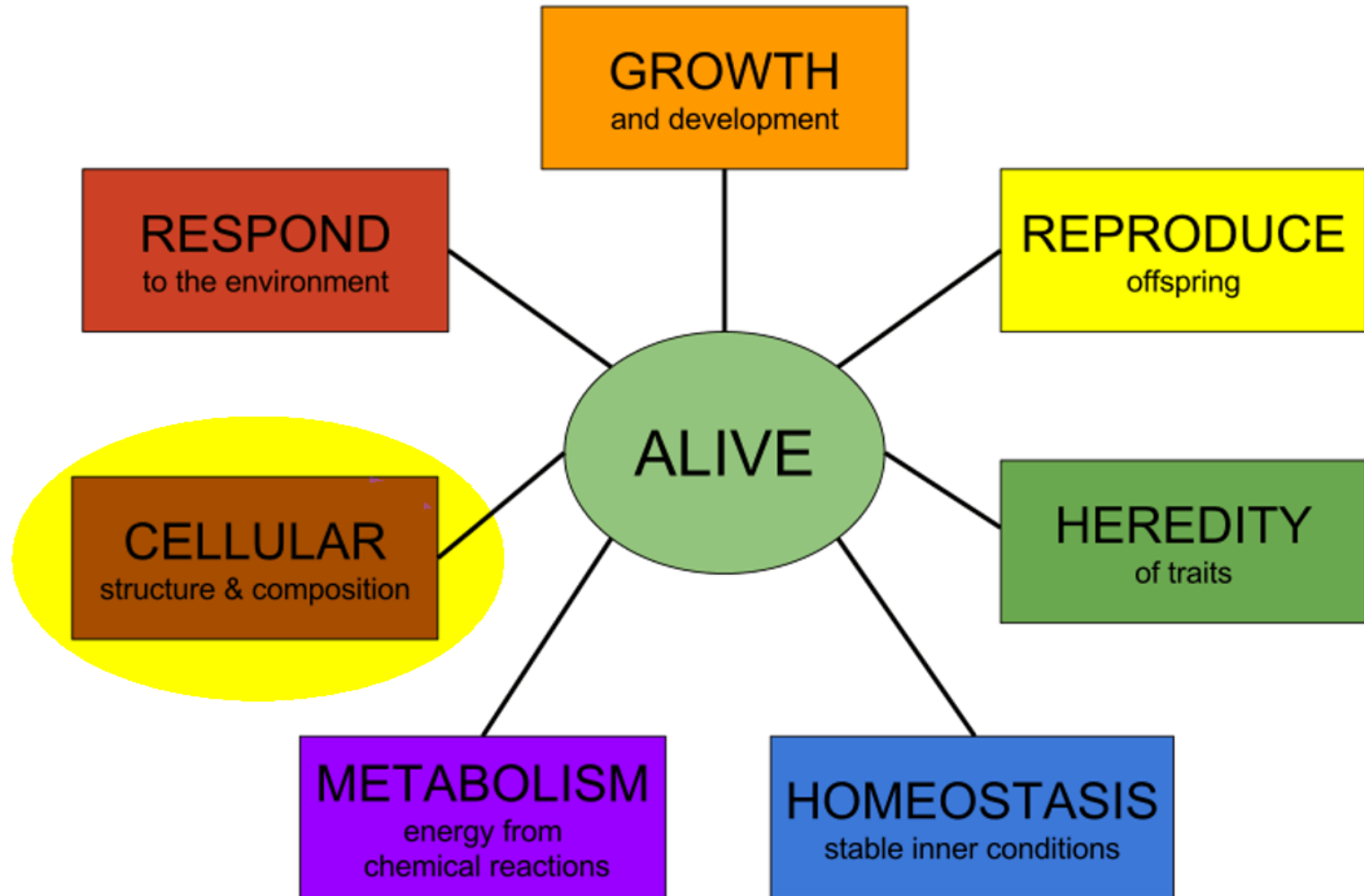
**STREPTOCOCCUS
PYOGENES**

Overview: A Borrowed Life

- Viruses called bacteriophages can infect and set in motion a genetic takeover of bacteria, such as *Escherichia coli*
- Viruses lead “a kind of borrowed life” between life-forms and chemicals
- The origins of molecular biology lie in early studies of viruses that infect bacteria

VIRUSES ARE NOT ALIVE !

Even though they can move towards a bacteria, they don't metabolize, grow, and aren't cellular.



A BACTERIA WITH PHAGES ALL AROUND IT



The Discovery of Viruses: *Scientific Inquiry*

- Tobacco mosaic disease stunts growth of tobacco plants and gives their leaves a mosaic coloration
- In the late 1800s, researchers hypothesized that a particle smaller than bacteria caused the disease
- In 1935, Wendell Stanley confirmed this hypothesis by crystallizing the infectious particle, now known as tobacco mosaic virus (TMV)

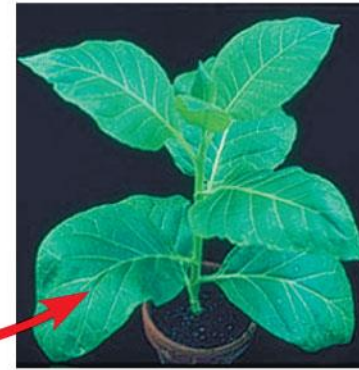
RESULTS



1 Extracted sap from tobacco plant with tobacco mosaic disease



2 Passed sap through a porcelain filter known to trap bacteria



3 Rubbed filtered sap on healthy tobacco plants



4 Healthy plants became infected

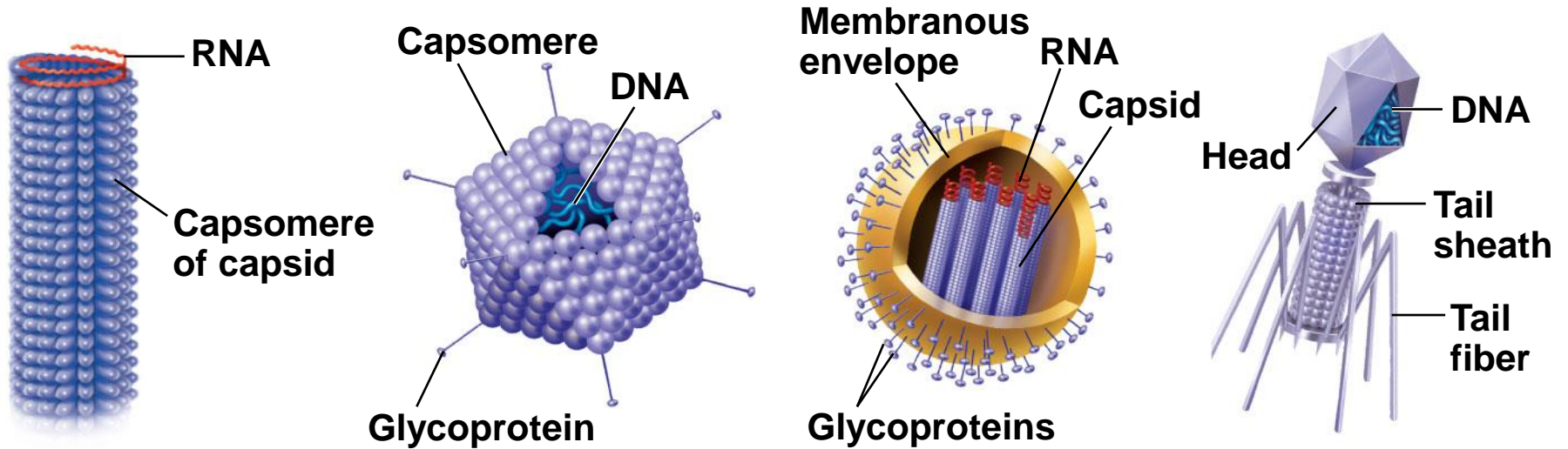
Structure of Viruses

- Viruses are not cells
- A **virus** is a very small infectious particle consisting of nucleic acid (DNA or RNA) enclosed in a protein coat and, in some cases, a membranous envelope
- Depending on its type of nucleic acid, a virus is called a DNA virus or an RNA virus

Capsids and Envelopes

- A **capsid** is the protein shell that encloses the viral genome, like the head of it.
- Capsids are built from protein subunits called *capsomeres*
- A capsid can have various structures

Figure 19.3

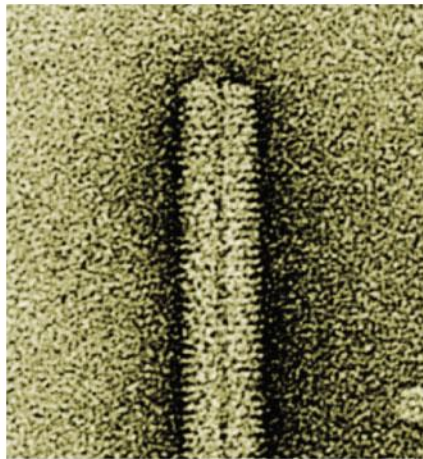


18 × 250 nm

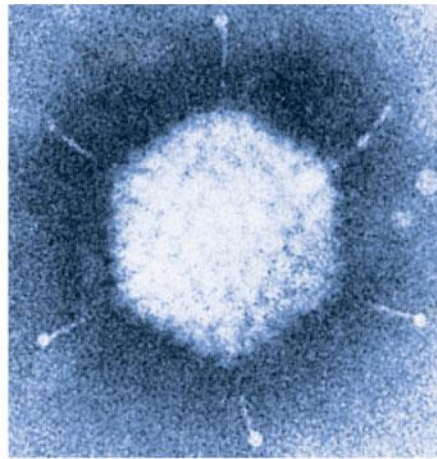
70–90 nm (diameter)

80–200 nm (diameter)

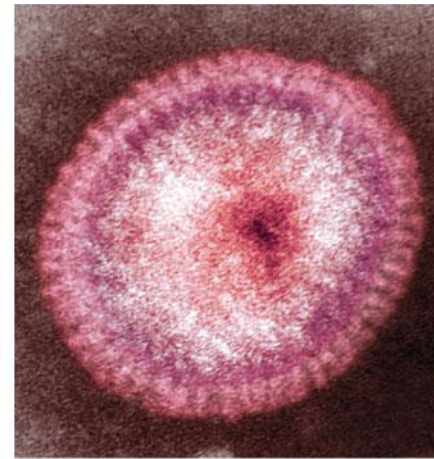
80 × 225 nm



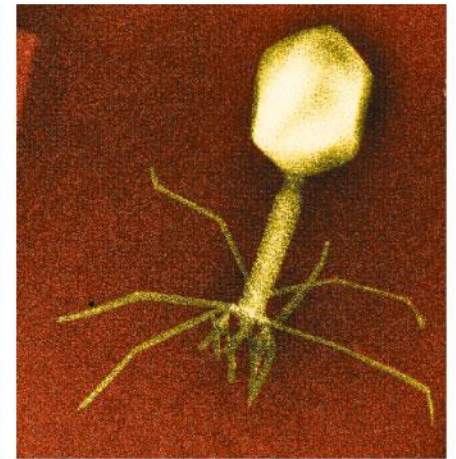
20 nm



50 nm



50 nm



50 nm

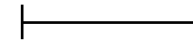
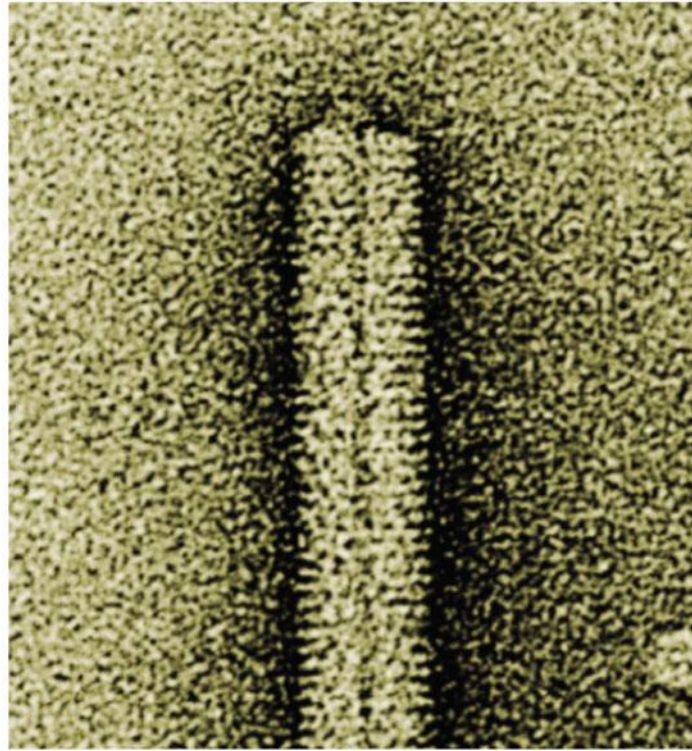
(a) Tobacco mosaic virus

(b) Adenoviruses

(c) Influenza viruses

(d) Bacteriophage T4

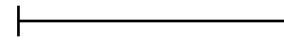
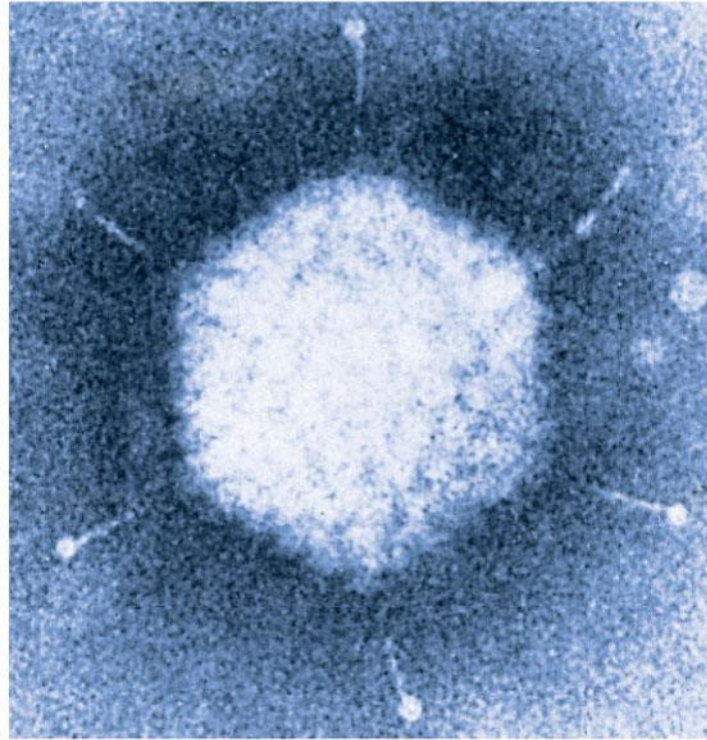
Figure 19.3a



20 nm

(a) Tobacco mosaic virus

Figure 19.3b

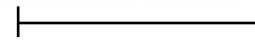
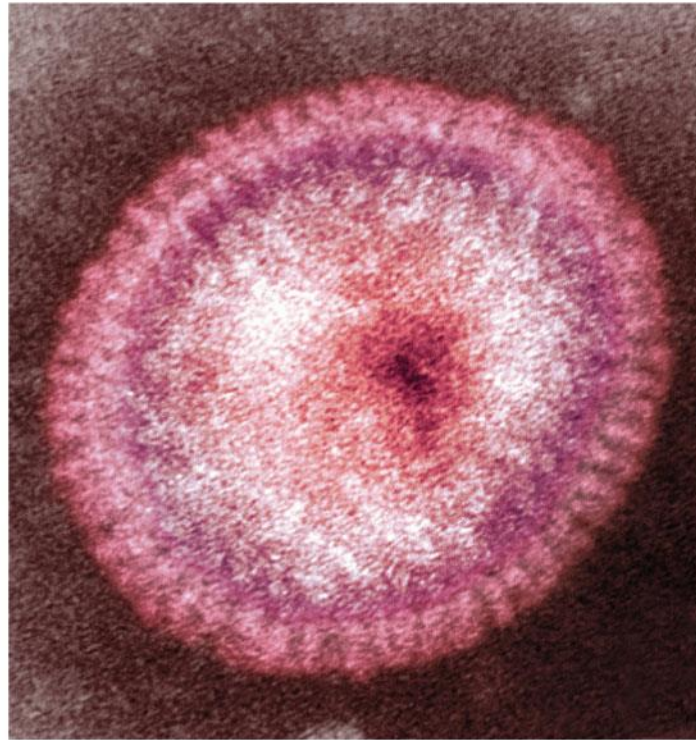


50 nm

(b) Adenoviruses

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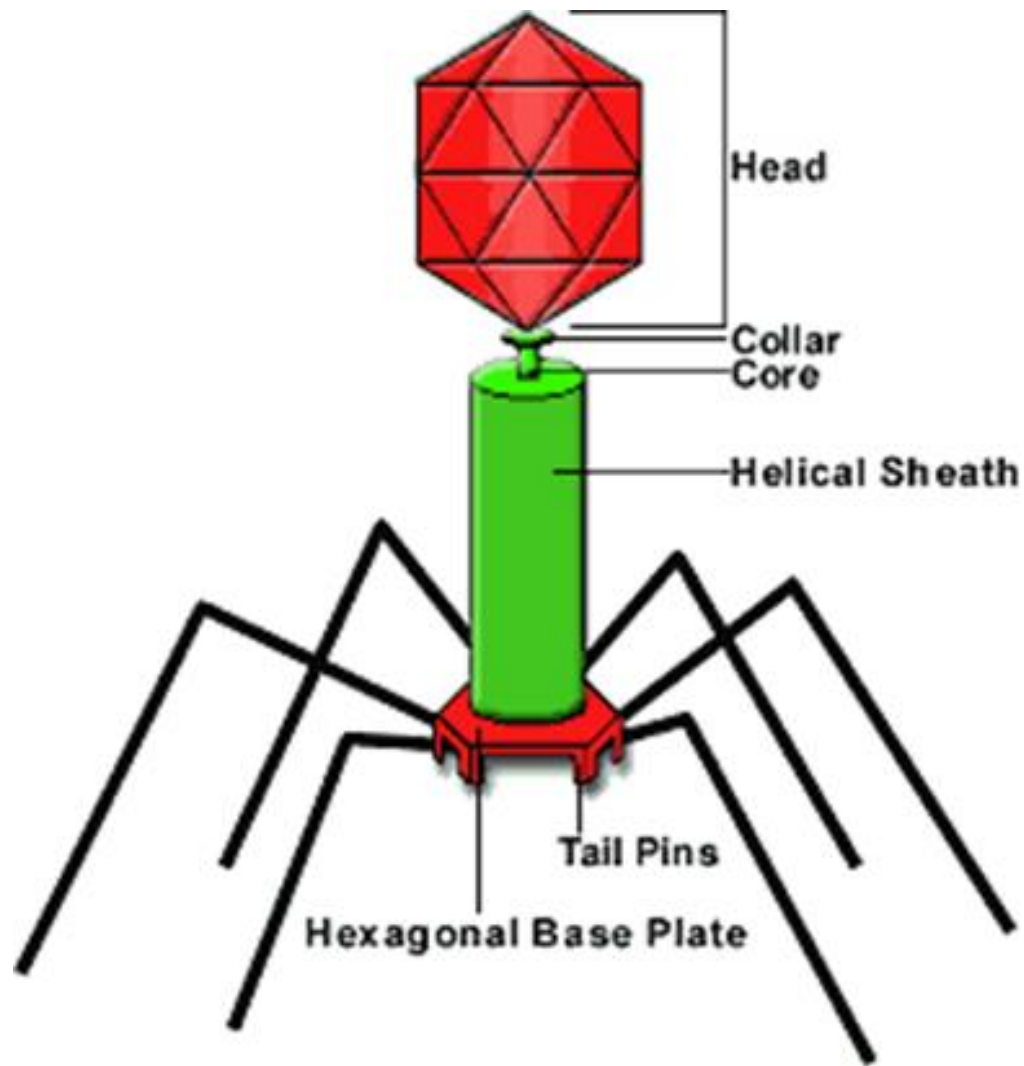
Figure 19.3c



50 nm

(c) Influenza viruses

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(d) Bacteriophage T4

They attack E Coli bacteria

VIRUSES REPLICATE ONLY IN HOST CELLS

- Viruses are intracellular parasites, which means they can replicate only within a host cell.
- Each virus has a **host range**, a limited number of host cells that it can infect.
- **This infection is specific to a specific species of bacteria.**
- **A phage that infects E. coli for instance, will not infect anthrax bacteria.**

General Features of Viral Replicative Cycles

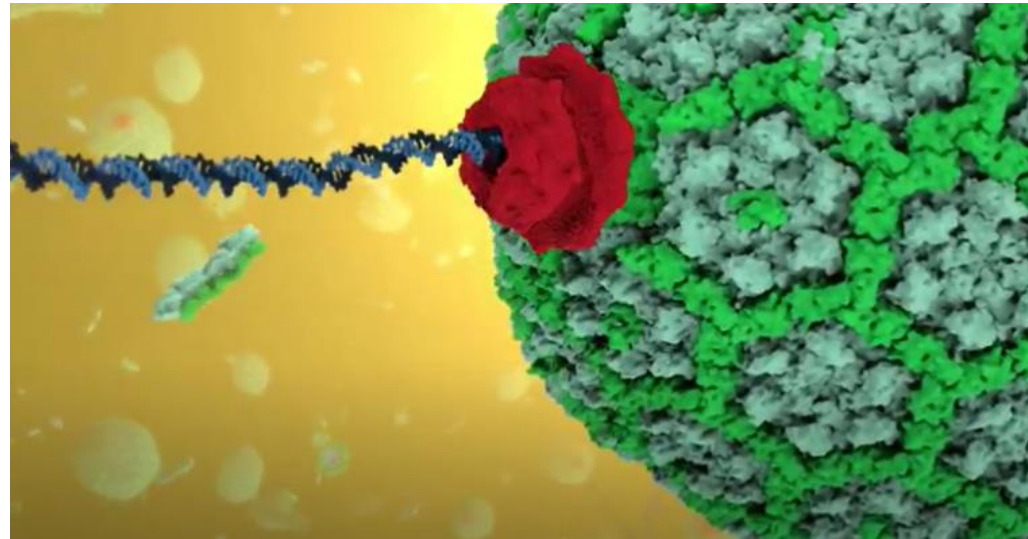
- Once a viral genome has entered a cell, the cell begins to manufacture viral proteins
- The virus makes use of host enzymes, ribosomes, tRNAs, amino acids, ATP, and other molecules
- Viral nucleic acid molecules and capsomeres spontaneously self-assemble into new viruses

HOW DOES THE DNA OR RNA GET INTO THE VIRUS ?

Once the DNA strand is available , a molecular packaging motor and pro-head interact and the DNA is rapidly threaded through a pore in the circular motor at the speed of 2,000 base pairs a second.

Once the head is full, the packaging motor cuts the DNA and the complex falls off.

The shaft and long tail fibers are attached to complete the infectious particle.



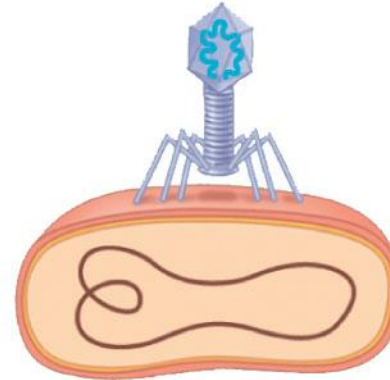
<https://www.youtube.com/watch?reload=9&v=RbL3BZCGPA4>

Replicative Cycles of Phages

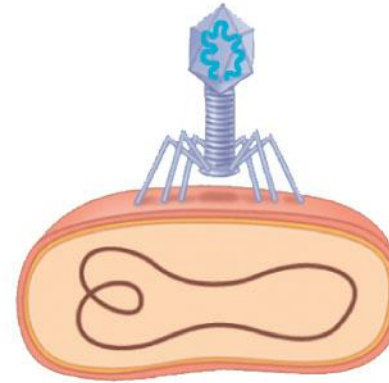
- Phages are the best understood of all viruses
- Phages have two reproductive mechanisms:
- The lytic cycle
- The lysogenic cycle

THE LYTIC CYCLE

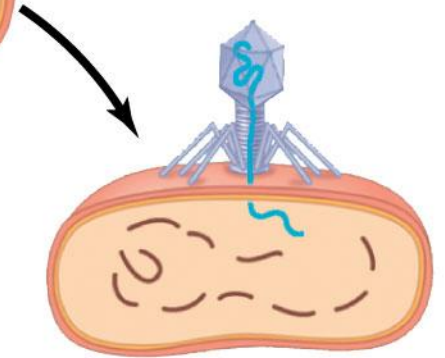
1 Attachment



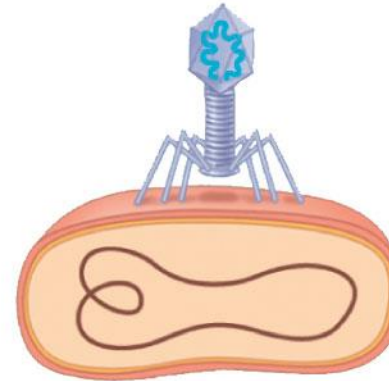
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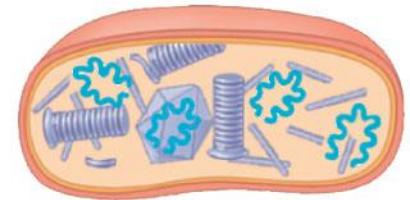
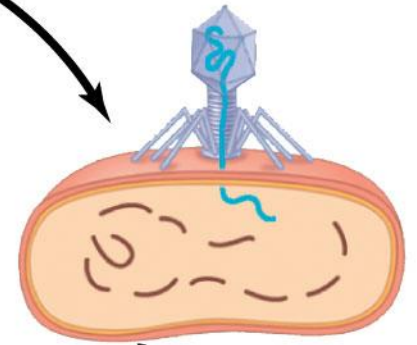
2 Entry of phage DNA and degradation of host DNA



1 Attachment

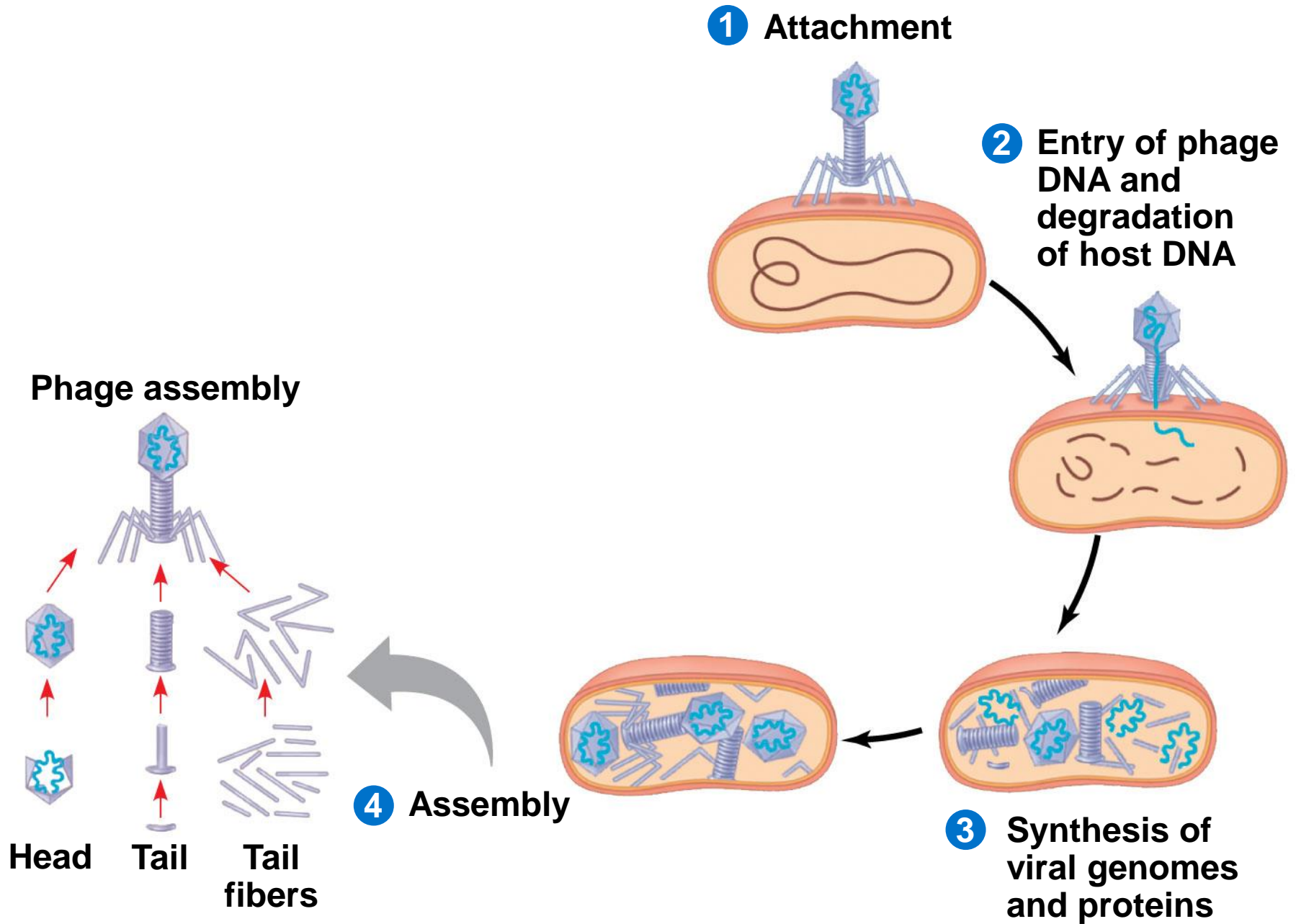


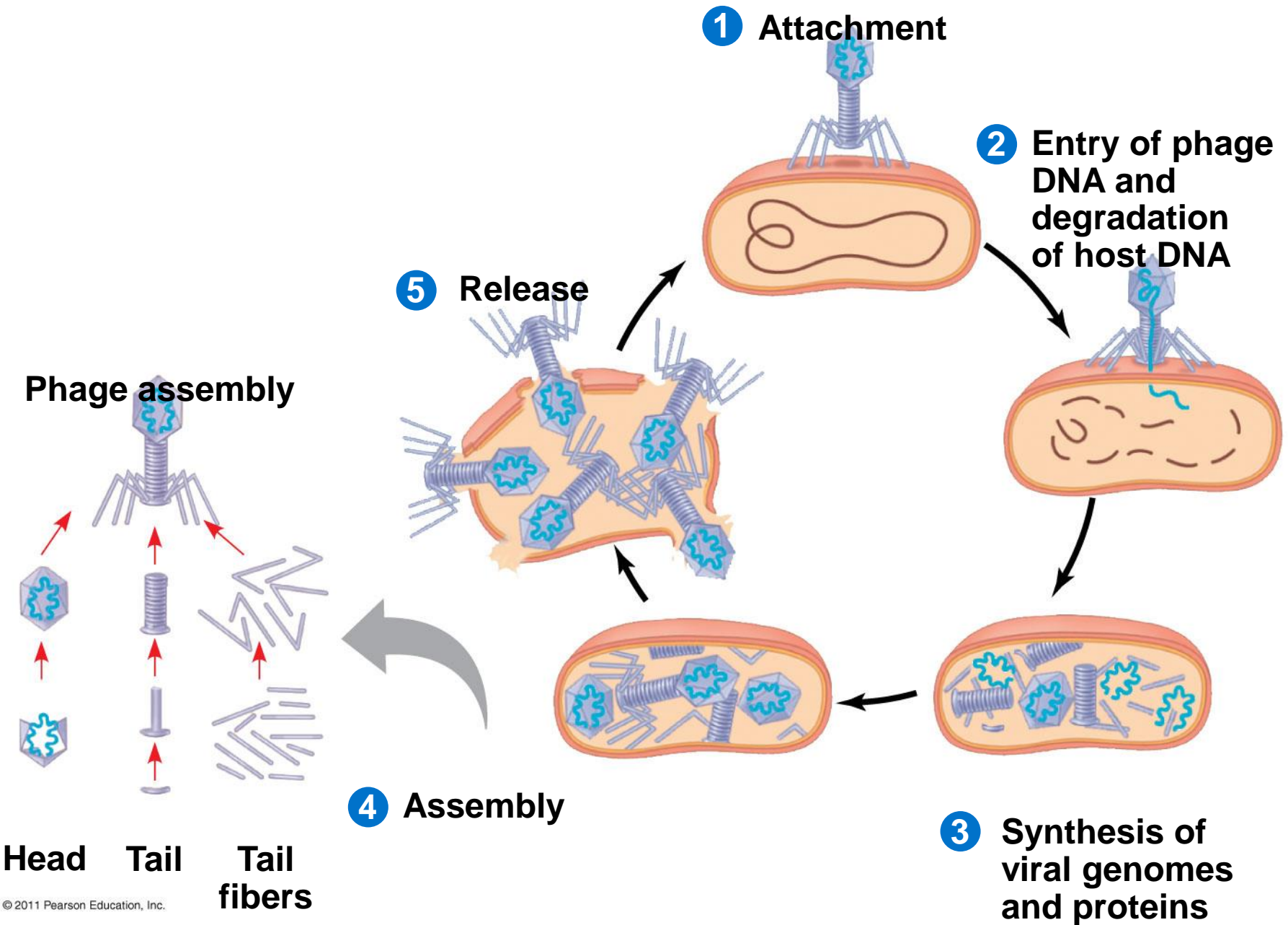
2 Entry of phage DNA and degradation of host DNA



3 Synthesis of viral genomes and proteins

Figure 19.5-4





<https://www.youtube.com/watch?v=uFXuxGuT7H8>

1.3 minutes

The Lysogenic Cycle

- The **lysogenic cycle** replicates the phage genome without destroying the host
- The viral DNA molecule is incorporated into the host cell's chromosome
- This integrated viral DNA is known as a **prophage**
- Every time the host divides, it copies the phage DNA and passes the copies to daughter cells

- An environmental signal can trigger the virus genome to exit the bacterial chromosome and switch to the lytic mode
- Phages that use both the lytic and lysogenic cycles are called **temperate phages**
- <https://www.youtube.com/watch?v= J9-xKitsd0> 1.3 minutes

Bacteriophages: Classification



- At present, over 5,000 bacteriophages have been studied by electron microscopy.
- They can be divided into 13 virus families.

13 Bacteriophage families

Corticoviridae	icosahedral capsid with lipid layer, circular supercoiled dsDNA
Cystoviridae	enveloped, icosahedral capsid, lipids, three molecules of linear dsRNA
Fuselloviridae	pleomorphic, envelope, lipids, no capsid, circular supercoiled dsDNA
Inoviridae genus (Inovirus/Plectrovirus)	long filaments/short rods with helical symmetry, circular ssDNA
Leviviridae	quasi-icosahedral capsid, one molecule of linear ssRNA
Lipothrixviridae	enveloped filaments, lipids, linear dsDNA
Microviridae	icosahedral capsid, circular ssDNA
Myoviridae (A-1,2,3)	tail contractile, head isometric
Plasmaviridae	pleomorphic, envelope, lipids, no capsid, circular supercoiled dsDNA
Podoviridae (C-1,2,3)	tail short and noncontractile, head isometric
Rudiviridae	helical rods, linear dsDNA
Siphoviridae (B-1,2,3)	tail long and noncontractile, head isometric
Tectiviridae	icosahedral capsid with, linear dsDNA, "tail" produced for DNA injection

Replicative Cycles of Animal Viruses

- There are two key variables used to classify viruses that infect animals
- DNA or RNA?
 - Single-stranded or double-stranded?

Viruses, viroids, and prions are formidable pathogens in animals and plants

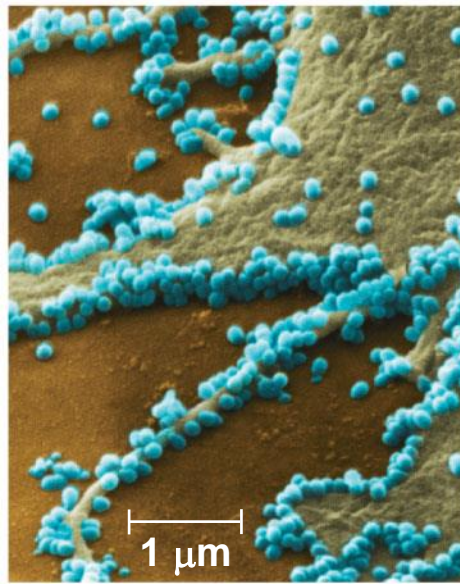
- Diseases caused by viral infections affect humans, agricultural crops, and livestock worldwide
- Smaller, less complex entities called viroids and prions also cause disease in plants and animals, respectively

Emerging Viruses

- Emerging viruses are those that suddenly become apparent
- A general outbreak (**epidemic**) of a flu-like illness appeared in Mexico and the United States, caused by an influenza virus named H1N1
- Flu epidemics are caused by new strains of influenza virus to which people have little immunity

- Viral diseases in a small isolated population can emerge and become global
- New viral diseases can emerge when viruses spread from animals to humans
- Viral strains that jump species can exchange genetic information with other viruses to which humans have no immunity

- These strains can cause **pandemics**, global epidemics like the Covid-19 pandemic we are experiencing now.
- The 2009 flu pandemic was likely passed to humans from pigs; for this reason it was originally called the “swine flu”



(a) 2009 pandemic H1N1 influenza A virus

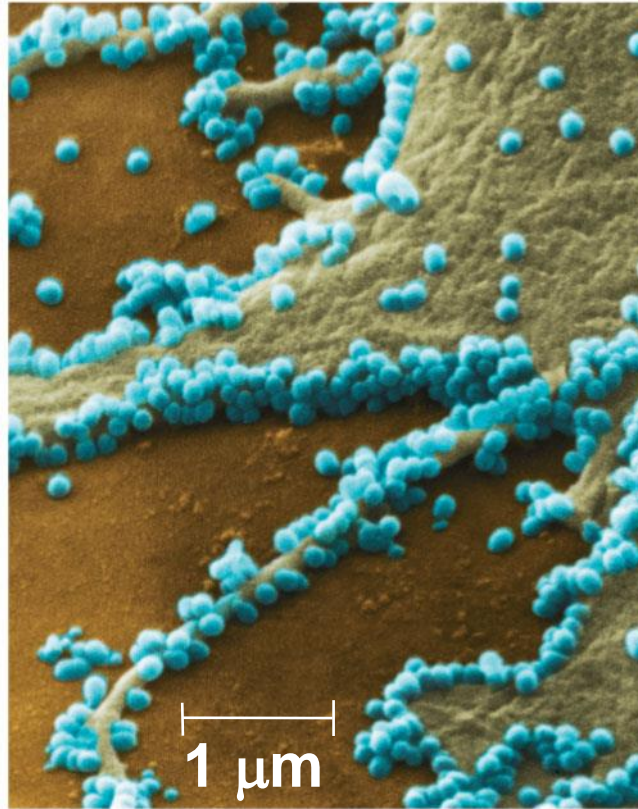


(b) 2009 pandemic screening



(c) 1918 flu pandemic

Figure 19.9a



**(a) 2009 pandemic H1N1
influenza A virus**

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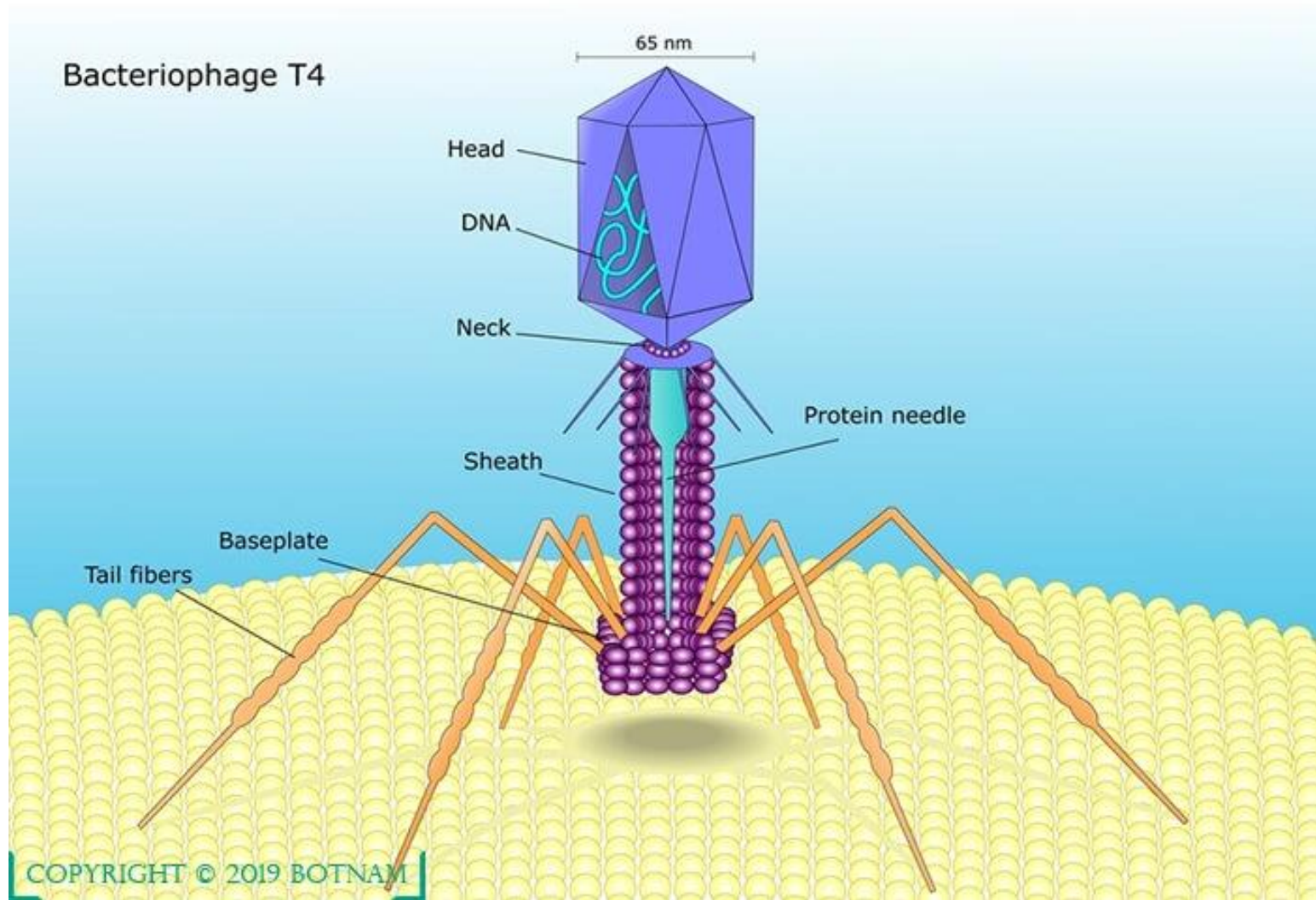
Figure 19.9c



(c) 1918 flu pandemic

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BACTERIOPHAGE STRUCTURE



https://www.youtube.com/watch?v=Ofd_IgEymto&t=6s

5.5 minutes

gp stands for glycoprotein

The image features a vibrant, golden-yellow background with a radial, starburst-like pattern. The lines radiate from a central black point, creating a sense of motion and energy. The text "THE END" is centered in a bold, white, sans-serif font.

**THE
END**