Introduction and Diversity of bacteriophage
Paper: Virology
Unit=2

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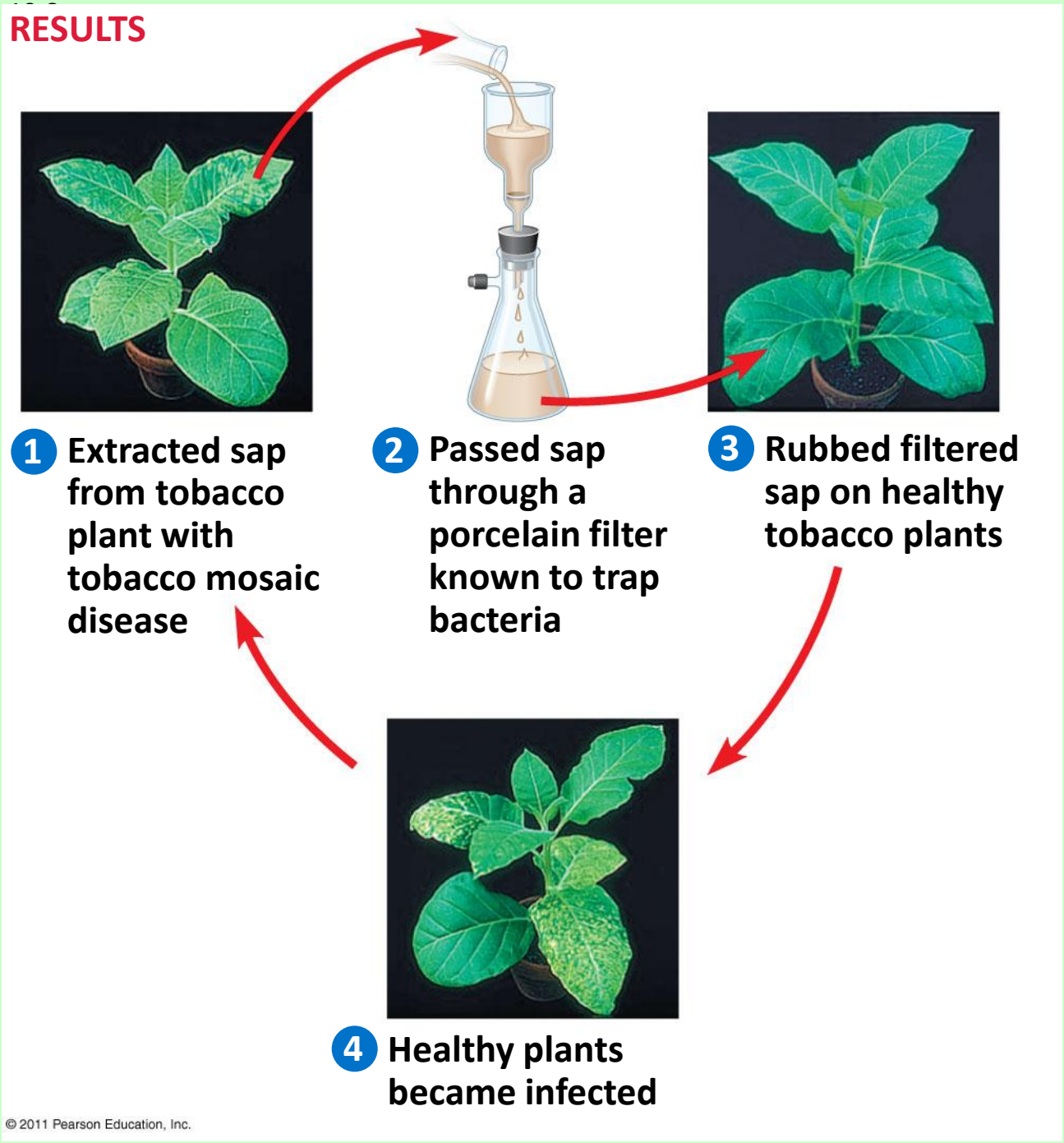
Outline

- **The Discovery of Viruses: *Scientific Inquiry***
- **History**
- **Why study the structure-function relationship of phages?**
- **Classification of Bacteriophage**

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)

Figure


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
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History

- Bacteriophages were discovered more than a century ago. **In 1896, Ernest Hanbury Hankin**, a British bacteriologist (1865 –1939), reported that something in the waters of rivers in India had unexpected antibacterial properties against cholera and this water could pass through a very fine porcelain filter and keep this distinctive feature (Hankin, 1896). However, Hankin did not pursue this finding.

History

- Bacteriophages were discovered twice at the beginning of the 20th century.
- In 1915, the English bacteriologist **FW Twort described a transmissible lysis in a "micrococcus"** and, in 1917, the Canadian **Felix d'Herelle** at the Pasteur Institute in Paris, described the **lysis of Shigella cultures**
- d'Herelle coined the term "bacteriophage", signifying an entity that eats bacteria.

History

- **In 1923**, the Eliava Institute was opened in Tbilisi, Georgia, to study bacteriophages and to develop phage therapy. Since then many scientists have been involved in developing techniques to study phages and using them for various purposes such as **use in treating bacterial infections a decade before the discovery of penicillin.** Unfortunately a lack of knowledge on basic phage biology and their molecular organization has led to some clinical failures.

Why study the structure-function relationship of phages?

- World War II or At the end of 1930s when antibiotics were discovered, this natural potential therapeutic agent got little attention or nearly wiped out and only considered as a research tool for many years
- However, a new problem of bacterial resistance to antibiotics has arisen after many years of using them.

- Bacteria adapted themselves to become resistant to the most potent drugs used in modern medicine. The emergence of modified pathogens such as *Mycobacterium tuberculosis, Enterococcus faecalis, Staphylococcus aureus, Acinetobacter baumannii* and *Pseudomonas aeruginosa, and* methicillin-resistant *S. aureus* (MRSA) has created massive problems in treating patients in hospitals (Coelho et al., 2004, Hanlon, 2007; Burrowes et al., 2011). The time required to produce new antibiotics is much longer than the time of bacterial adaptation.
- Modern studies on the phage life cycle have revealed a way for their penetration through membrane barriers of cells. These results are important in the development of methods for using bacteriophages as a therapeutic option in the treatment of bacterial infections (Brussow & Kutter, 2005).

Introduction

- Bacteriophages are the most abundant entities on earth. These bacterial viruses have genetic material in the form of **either DNA or RNA**, encapsidated by a protein coat
- Phages are obligate intracellular parasites, meaning that they are able to reproduce only while infecting bacteria. **A virus that specifically infects bacteria.**
- Their genomes may encode as few as four genes, and as many as hundreds of genes.

Introduction

- Bacteriophages occur in over **140 bacterial or archaeal** genera.
- Over **5500 bacteriophages** (Ackermann, 2007) have been examined in the electron microscope since 1959. Of these, at least **4950 phages (96%)** have tails. Of the tailed phages **61% have long, noncontractile tails (Siphoviridae).** Tailed phages appear to be the oldest known virus group.

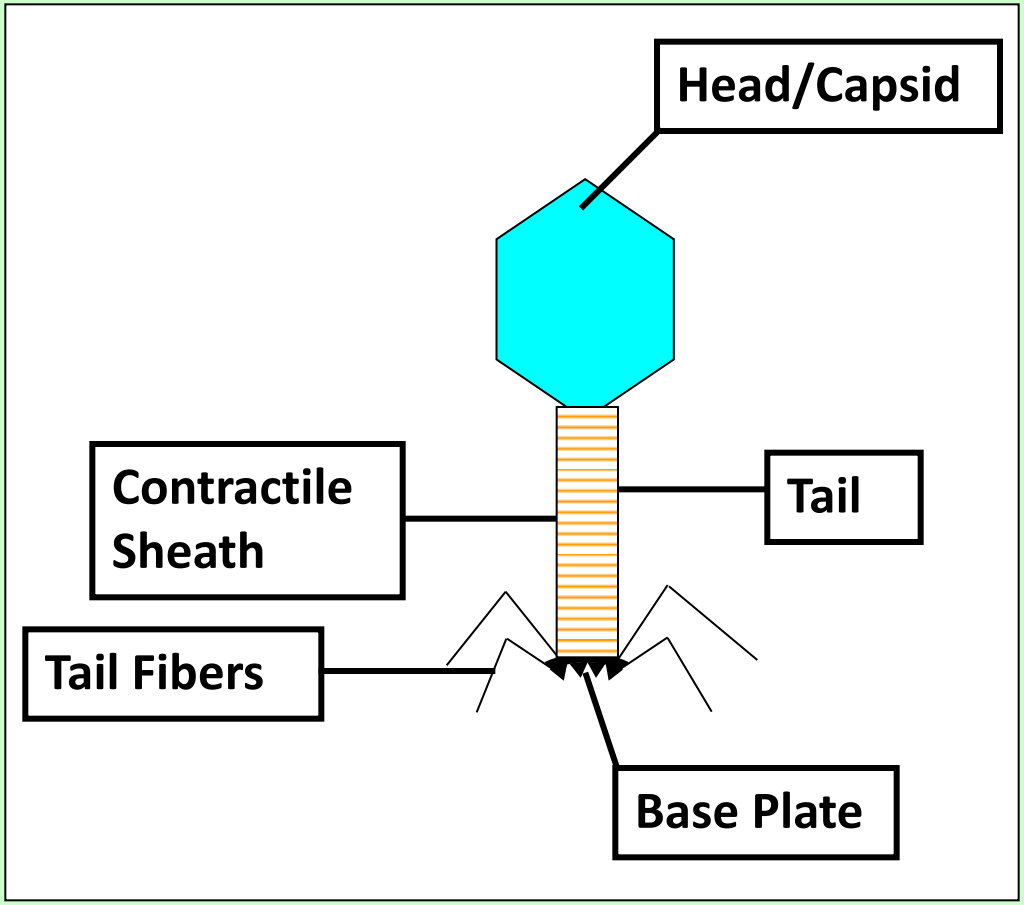
Distribution of Phages

- Phages are widely distributed in locations populated by bacterial hosts, such as soil or the intestines of animals.
- One of the densest natural sources for phages and other viruses is sea water, where up to 9×10^{8} virions per milliliter have been found in microbial mats at the surface.
- Up to 70% of marine bacteria may be infected by phages

Composition and Structure

- Composition
  - Nucleic acid
    - Genome size
    - Modified bases
  - Protein
    - Protection
    - Infection

- Structure (T_4)
  - Size
  - Head or capsid
  - Tail



Classification of Bacteriophage

Classification of viruses is based on several factors such as their host preference, viral morphology, genome type and auxiliary structures such as tails or envelopes. **The most upto-date classification of bacteriophages is given by Ackermann (2006).** The key classification factors are phage morphology and nucleic acid properties

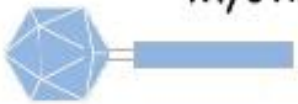
- **Phages are classified by the International Committee on Taxonomy of Viruses (ICTV) according to morphology and nucleic acid.**
- **Nineteen families** are currently recognised that infect bacteria and archaea. Of these, only **two families have RNA genomes** and only **five families are enveloped**. Of the viral families with DNA genomes, only **two have single-stranded genomes**. **Eight** of the viral families with **DNA** genomes have **circular genomes**, while nine have linear genomes.
- Nine families infect bacteria only, nine infect archaea only, and one **(Tectiviridae)** infects both bacteria and archaea.

13 Bacteriophage families

Double stranded DNA, Non-enveloped

P2

Myoviridae



T2

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Siphoviridae

P22

Podoviridae

SIRV 1, 2

Rudiviridae

Fuselloviridae SSV1

Tectiviridae PRD1

Corticoviridae PM2

Double stranded DNA, Enveloped

Plasmaviridae

TTV1

Lipothrixviridae

Single-stranded DNA

M13 & fd

Inoviridae

Microviridae ΦX174

Single stranded RNA

MS2

Leviviridae

Double stranded RNA

phi6[66]

Cystoviridae

RNA Bacteriophages

- Two families have RNA genomes:
  - **Cystoviridae (segmented dsRNA);** protein and **lipid outer layer**. Most identified cystoviruses infect Pseudomonas species. The type species is *Pseudomonas phage Φ6*, but there are many other members of this family: Φ7, Φ8, Φ9, Φ10, Φ11, Φ12, and Φ13 have been identified and named, but other cystoviruses have also been isolated.
  - **Leviviridae (linear ssRNA)**
    - Include the genera Allolevivirus (type species: *Enterobacteria phage Qβ*)
    - Levivirus (type species: *Enterobacteria phage MS2*).

Single-Stranded DNA Bacteriophages

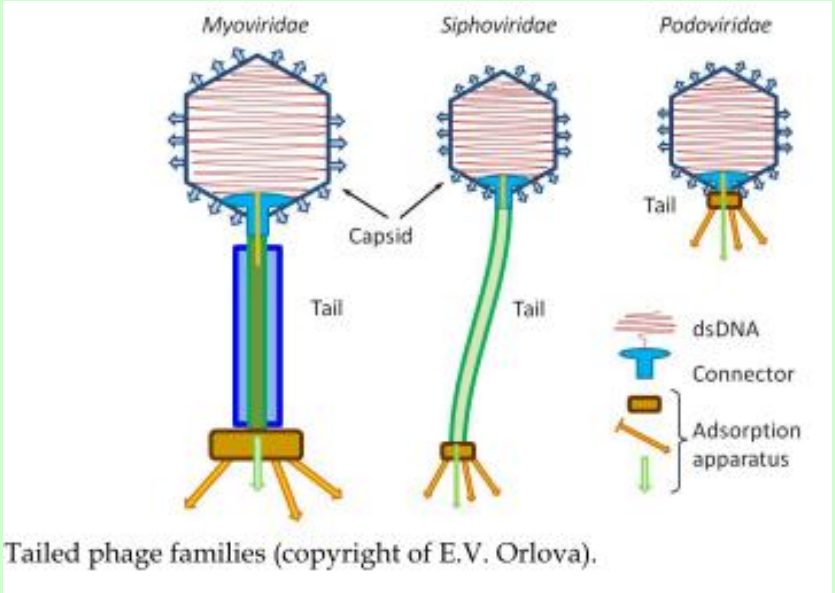
- Of the viral families with DNA genomes, only two have single-stranded genomes.
  - **Inoviridae** (filamentous bacteriophages)

  Two genera in this family: Inovirus and Plectrovirus
  - **Microviridae (**phiX174)

Double-Stranded DNA Bacteriophages

- 15 families

- The most studied group of phages is the tailed phages **(order *Caudovirales*)** which are classified by the type of tail;
  - *Siphoviridae* have a long non-contractile tail,
  - *Podoviridae* have a short non-contractile tail
  - *Myoviridae* have a complex contractile tail



Tailed phage families (copyright of E.V. Orlova).

Morphological Groups of Bacteriophages:

On the basis of EM studies, Bradley (1967) has described the six morphological types of bacteriophages

- virus with hexagonal head, a rigid tail with contractile sheath and tail fibers dsRNA, T-even (T2, T4, T6) phages.
- phage contains a hexagonal head but lacks contractile sheath. Its tail is flexible and may or may have tail fiber, for example dsDNA phages, e.g., Lembda phage.

- hexagonal head and a short without contractile sheath and may or may not have tail fiber, for example dsDNA phages, e.g., T3, T7.
- head which is made up of capsomers but lacks tail, for example ssDNA phages (e.g., ϕX174).
- head made up of small capsomers but contains no tail, for example ssRNA phages (e.g., F2, MS2).
- filamentous phage, for example ssDNA phages (e.g., fd, f1).

Strategies for virus survival

- **Finding and getting into a host cell.**
- **Making virus protein.**
- **Making viral genomes.**
- **Forming progeny virions.**
- **Spread within and between hosts.**
- **Overcoming host defences.**

Three problems every virus must solve

- How to reproduce during its “visit” inside the cell. How to
  - copy its genetic information and
  - produce mRNA for protein production
- How to spread from one individual to another
- How to evade the host defenses. This need not be complete.