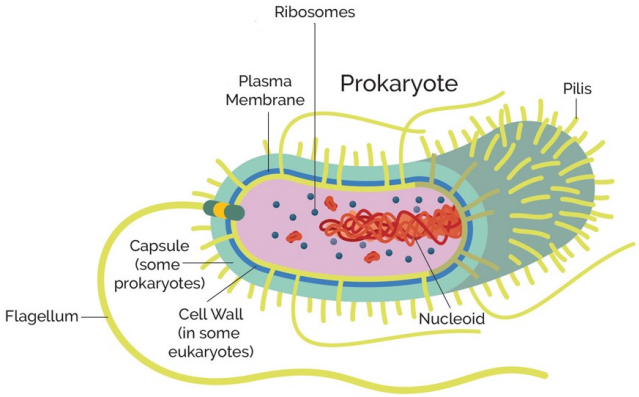
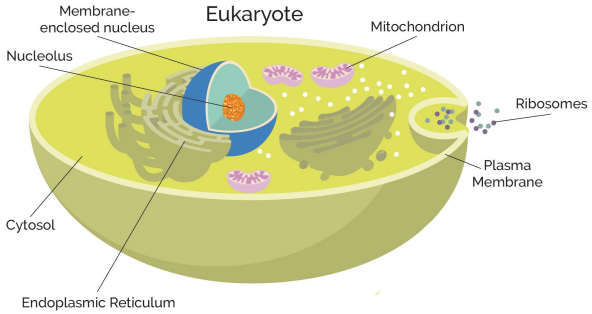
# Overview
# Parasites/Fungi/Bacteria/Viruses

# Key differences:

## Prokaryotes



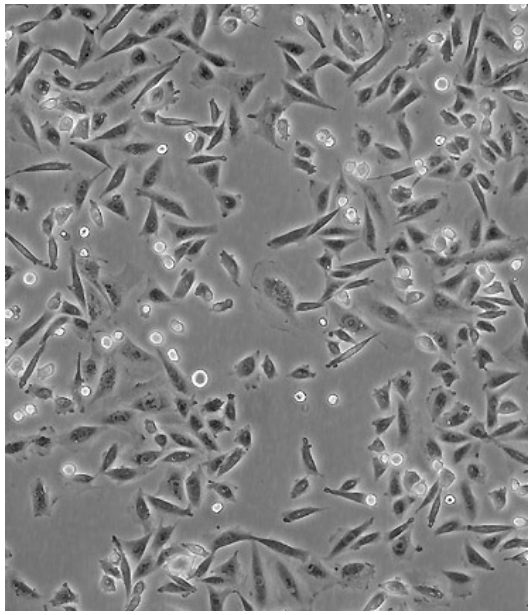

## Eukaryotes



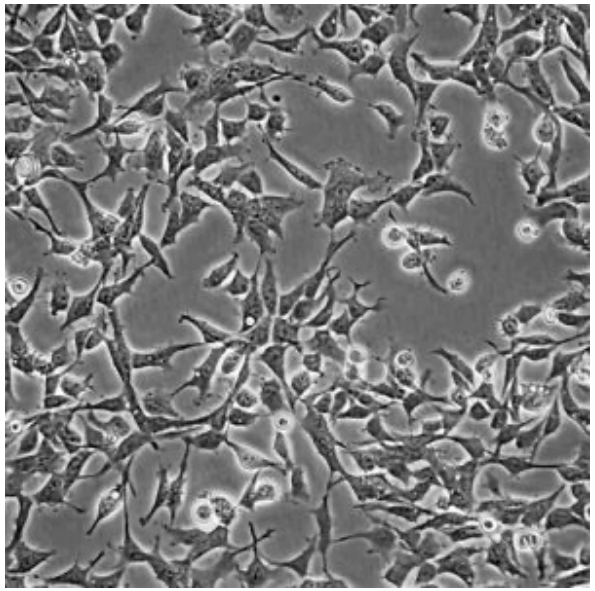

| | | |
|---|---|---|
| Nucleus: | Absent | Present |
| Membrane-enveloped organelles | Absent | Present |
| Cell structure | Unicellular | Mostly multicellular, a few unicellular |
| Cell size | 0.5-1 μm (diameter) | 5 – 100 μm (diameter) |

# CHO cells/HEK cells (Eukaryotes)

- Cell sizes: 10-15 μm in diameter



CHO cells



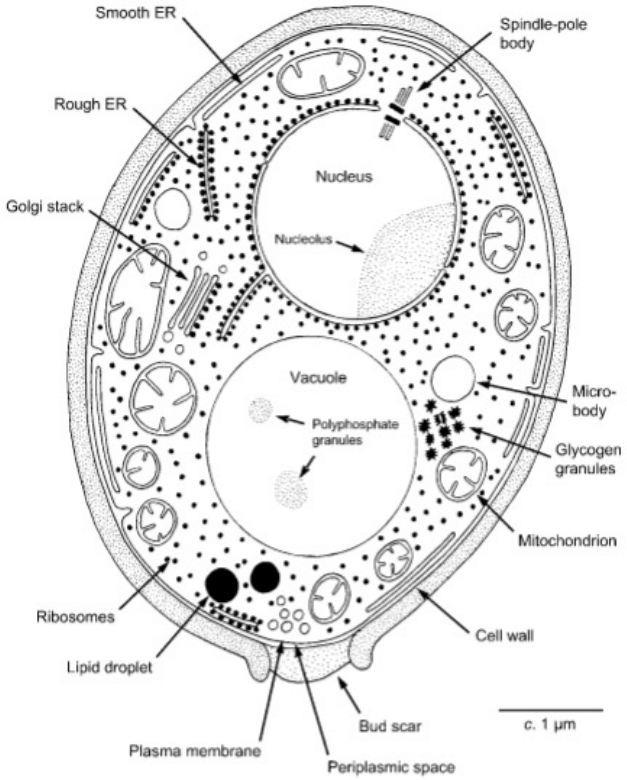
HEK 293 cells

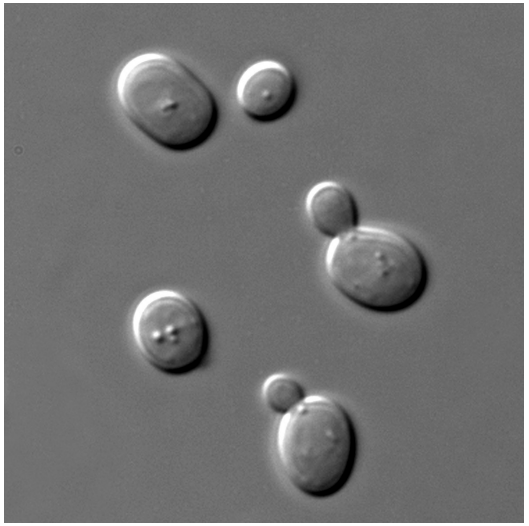
# Diseases caused by eukaryotic parasites

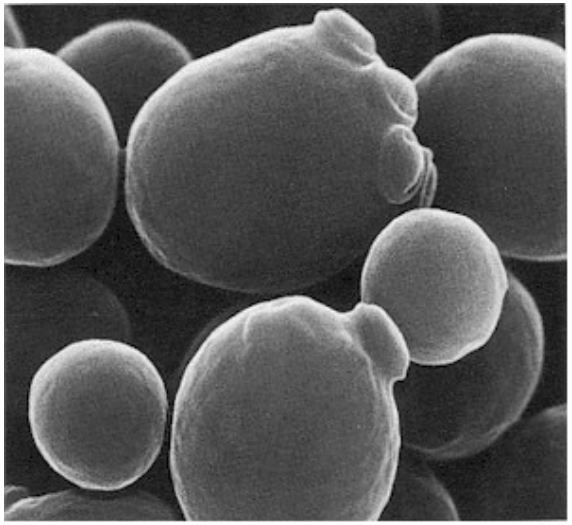
- ***Plasmodium***: Causes malaria, one of the world's most deadly parasitic infections, transmitted through mosquito bites.
- ***Toxoplasma gondii***: Responsible for toxoplasmosis (eye, lung, brain disease), which can be transmitted through cat feces or undercooked meat and is dangerous for pregnant women and immunocompromised individuals.

# Yeast: *Saccharomyces cerevisiae* (Eucaryotic cell)

Cell size: 5μm in diameter;
Cell wall containing chitin (structural polysaccharide)



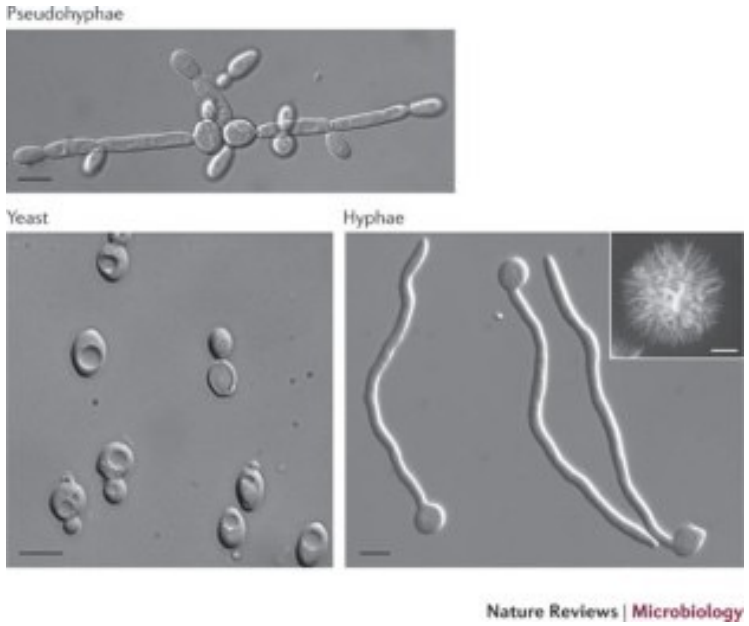





Microscopic images of the budding yeast: *S. cerevisiae*

# Major fungal diseases (Europe)

- Candidasis
- ***Candida albicans:*** For instance mouth infection with white patches on the tongue or other areas of the mouth and throat



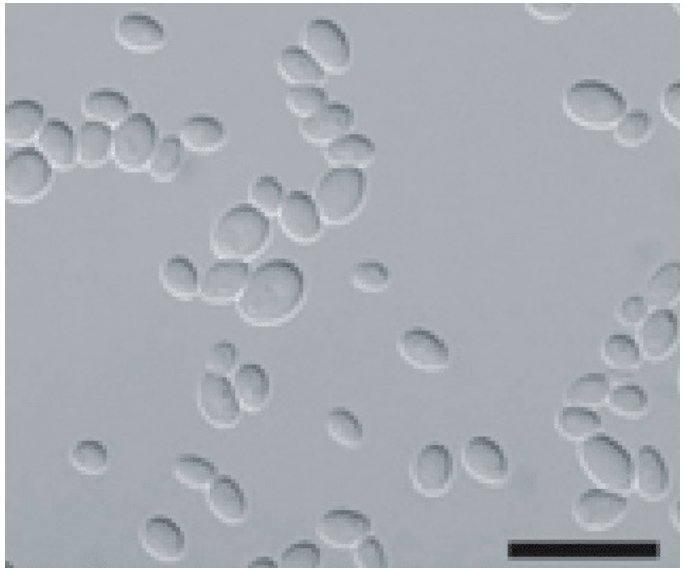

Sudbery, P. Growth of *Candida albicans* hyphae. *Nat Rev Microbiol* **9**, 737–748 (2011).

Image: Wikipedia

# Major fungal diseases (Europe)

- Candidiasis
- ***Candida auris***: multi-drug resistant yeast reproducing by budding
- Skin infections, invasive blood stream infections (risk of Sepsis) often in healthcare settings

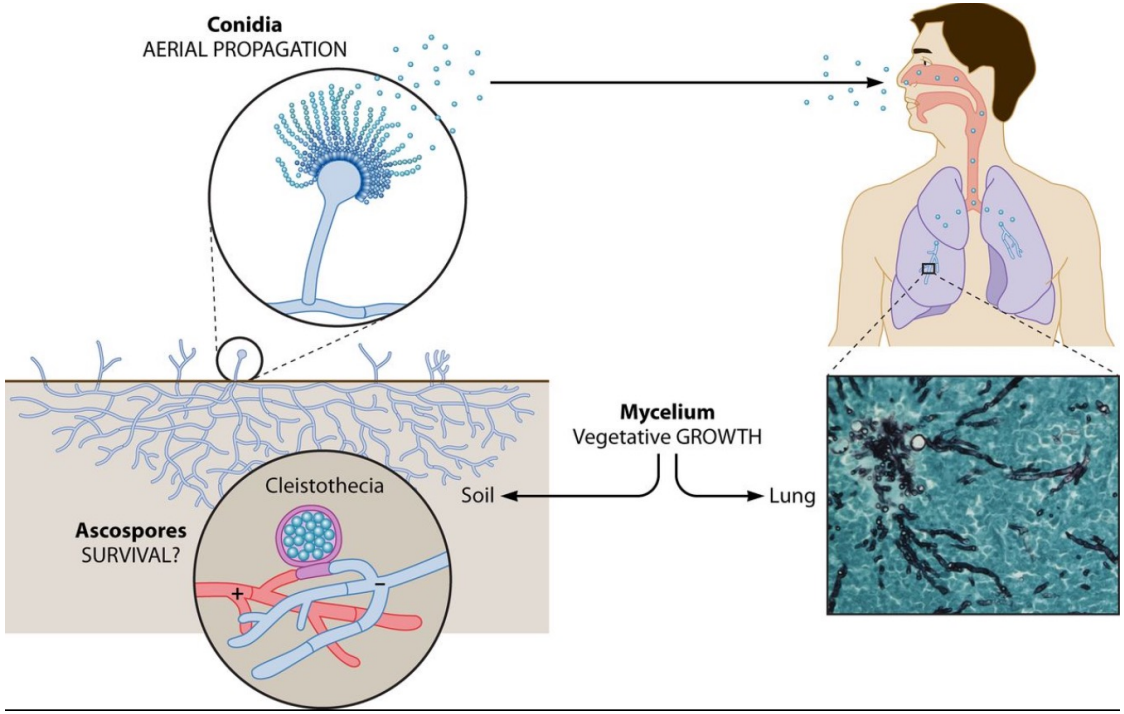
*Candida auris* skin infection



Microscopic image
*Candida auris*: Scale 10 μm

# Major fungal diseases (Europe)

- Aspergillosis

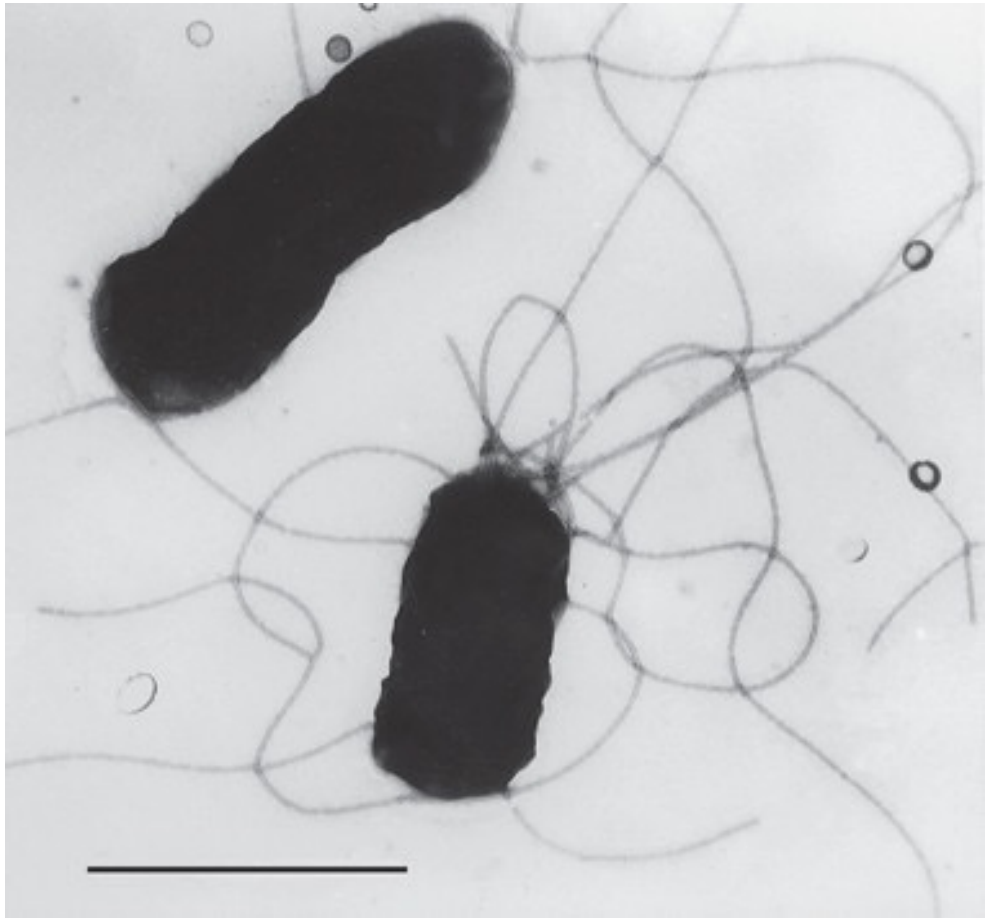



Aspergillus fumigatus, filamentous fungus with vegetative mycelium in nature and in patients.
Latgé J, Chamilos G. (2019) Aspergillus fumigatus and Aspergillosis in 2019.
*Clin Microbiol Rev* 33:10.1128/cmr.00140-18.

# Bacteria

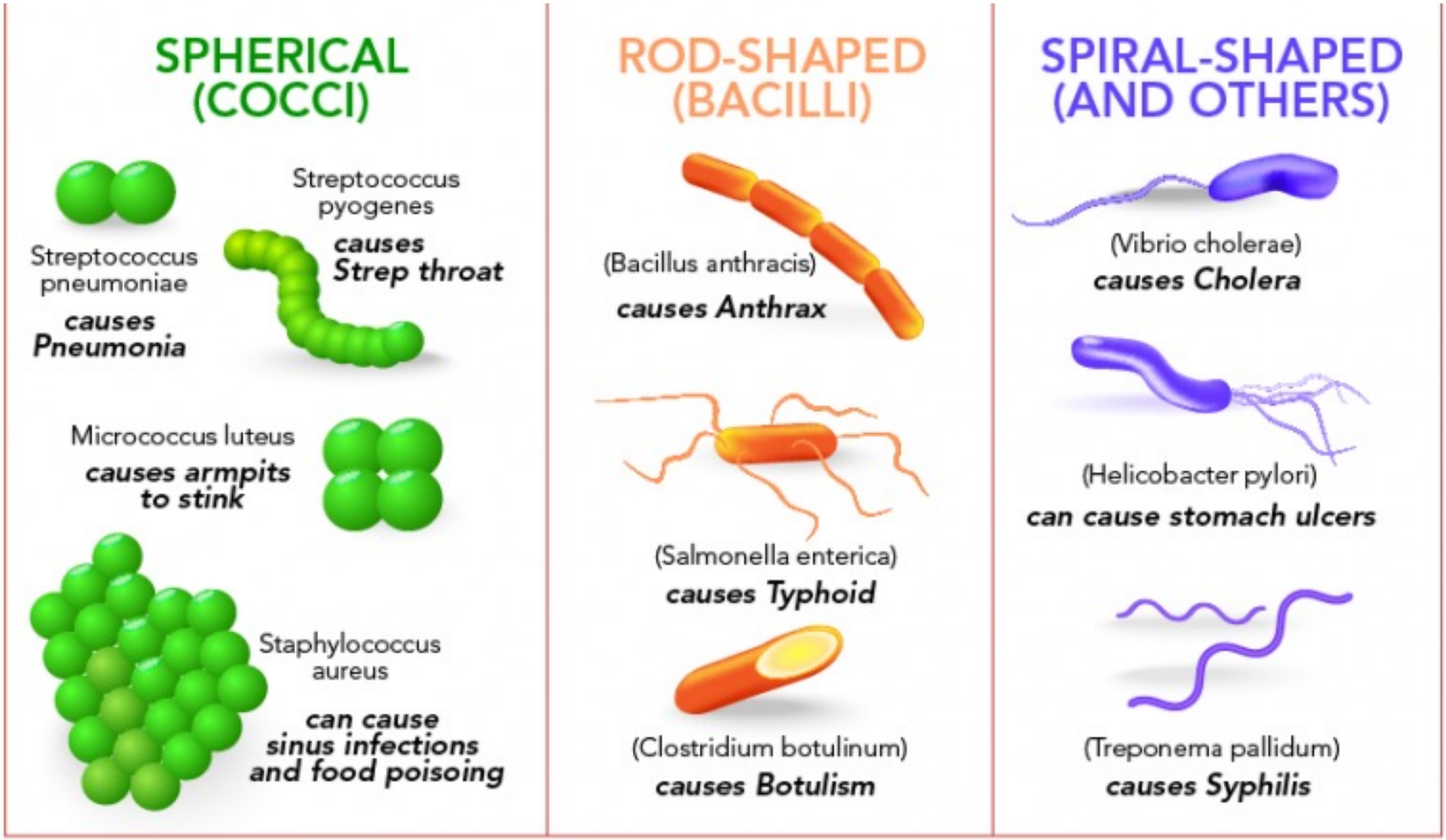
- Are classified as prokaryotes (no membrane enclosed nucleus)
- Small single-celled organisms (average size 0.5-1 μm in diameter)
- Can be found almost everywhere on earth
- Some species can live under extreme temperature and pressure conditions.

# E. coli



Flagella of E. coli observed in transmission electron microscope. Bar, 1 μm.
Eisenbach, Michael. (2001). Bacterial Chemotaxis. 10.1038/npg.els.0001251.

# Shapes of bacteria



# Bacterial diseases

Plague (bubonic/pneumonic)
Syphilis
Cholera
Diphtheria
Tuberculosis
Pertussis
Tetanus
Streptococcus
Staphylococcus

# Bacteria (Role of human microbiota)

Most bacteria in the body are harmless, and some are even helpful. A relatively small number of species can cause a disease.

**National Institute of Health (NIH) (Bethesda, Maryland, USA)**
**Human Microbiome Project (2007-2016)**

- Nearly everyone routinely carries pathogens, microorganisms known to cause illnesses. In healthy individuals, however, pathogens cause no disease; they simply co-exist with their host and the rest of the human microbiome
- HMP researchers now calculate that several thousand microbial species occupy the «human ecosystem».

# Human gut microbiota

- Gut microbiota ($10^{14}$ bacteria, 1 kg of bacteria) up to 1000 different species.
- Fermentation of non-digestible substrates (fibres) Bacteria help to digest foods and absorb nutrients that otherwise would be unavailable.
- Bacteria produce beneficial compounds: vitamins and anti-inflammatory compounds that our genome cannot produce
- Inhibition of growth of pathogenic bacteria (antimicrobial peptides)
- Strengthen intestinal barrier system (biofilms)

Reference: Manasa et al., (2015) World. J. Gastroenterol. 21(29): 8787–8803

# Human skin microbiota

- $10^{10}$ bacteria live on the skin (1000 different species)
- Protection against invading pathogens
- Boost our immune system  (communication between bacteria, skin and immune cells)
- Byrd A., et al., Nature Reviews Microbiology 16, pages143–155 (2018)

# Oral microbiota

- 700 species of bacteria
- Bacteria form of a biofilm. It plays a crucial role in protecting the oral cavity, and preventing disease development.

Reference: Kilian et al., (2016) British Dental Journal: 221, pages 657-666

# Bacterial diseases

Plague (bubonic/pneumonic)
Syphilis
Cholera
Diphtheria
Tuberculosis
Pertussis
Tetanus
Streptococcus
Staphylococcus

# Gram negative bacteria

For example:
**E. coli**
**Salmonella**
**Helicobacter**
**Spirochaeta**
**Bordetella pertussis**
**Pseudomonas**

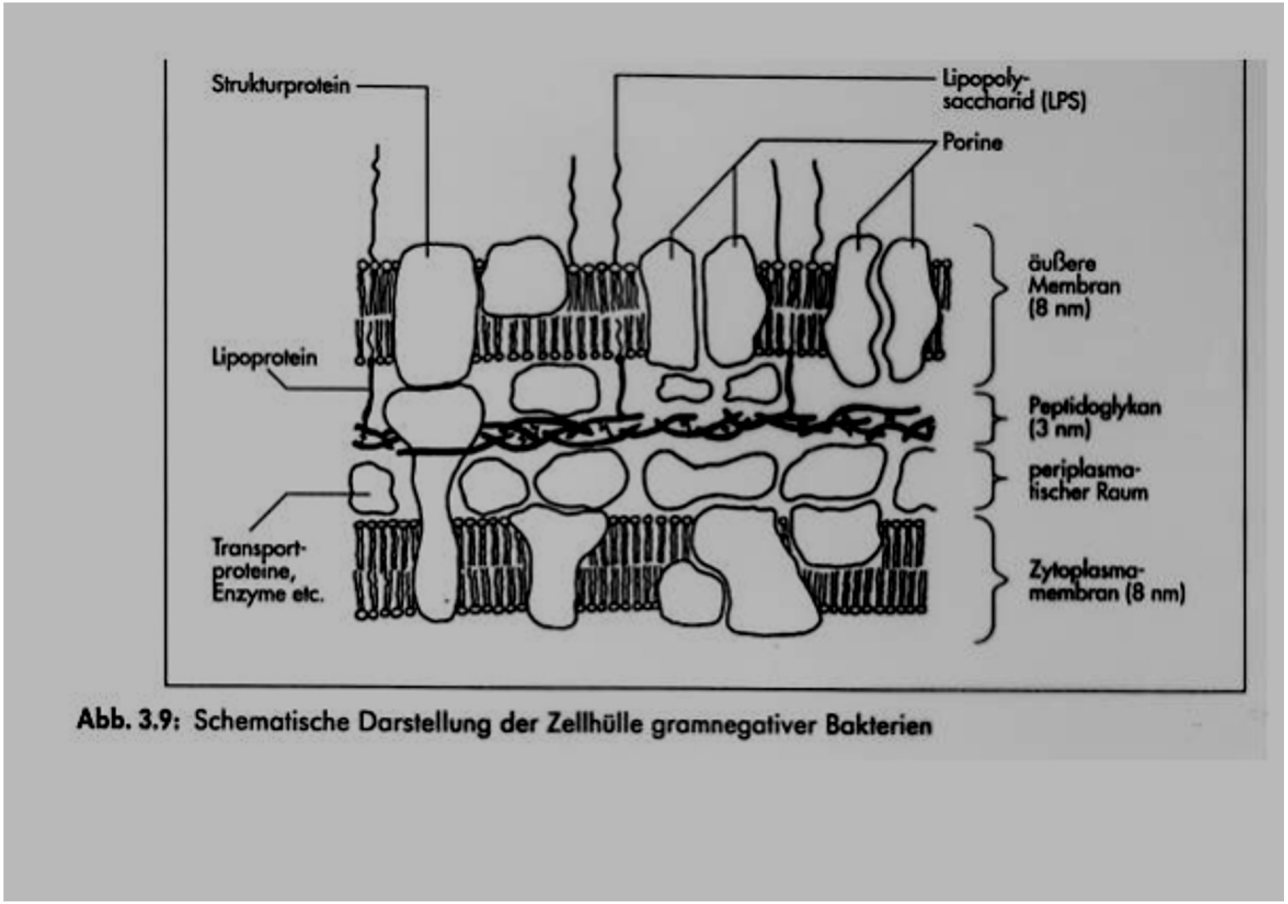



**Abb. 3.9:** Schematische Darstellung der Zellhülle gramnegativer Bakterien

# Gram positive bacteria

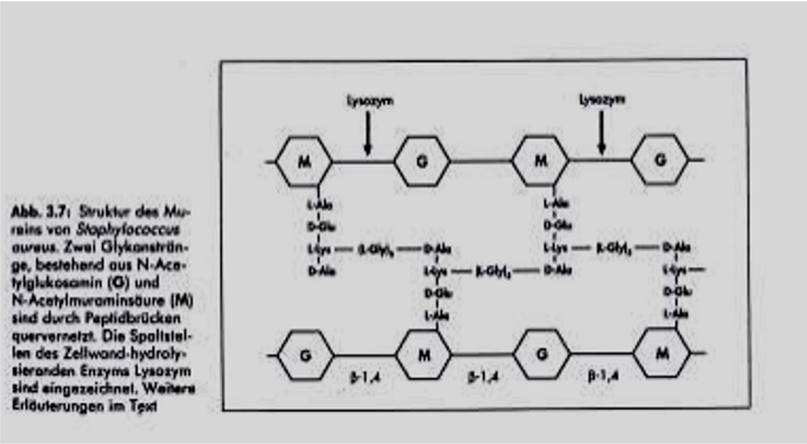



Abb. 3.7: Struktur des Murains von *Staphylococcus aureus*. Zwei Glykanstränge, bestehend aus N-Acetylglukosamin (G) und N-Acetylmuraminsäure (M) sind durch Peptidbrücken quervernetzt. Die Spaltstellen des Zellwand-hydrolysierenden Enzyms Lysozym sind eingezeichnet. Weitere Erläuterungen im Text

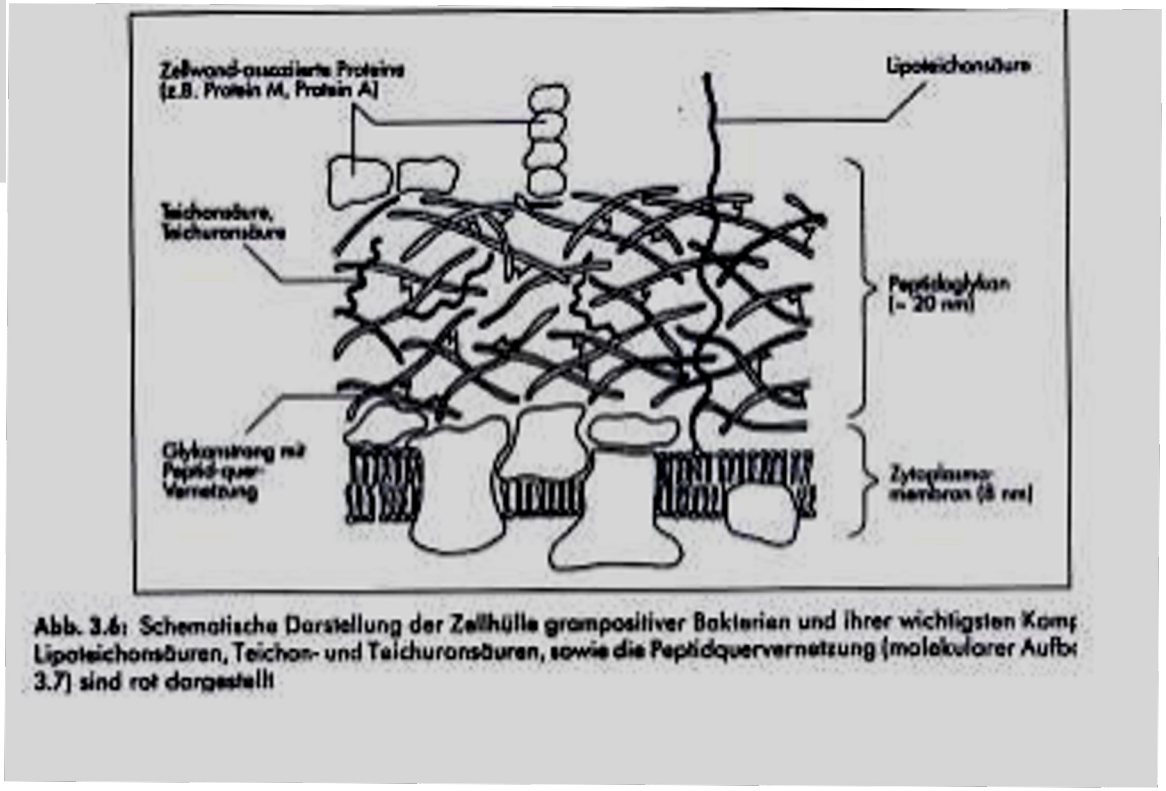
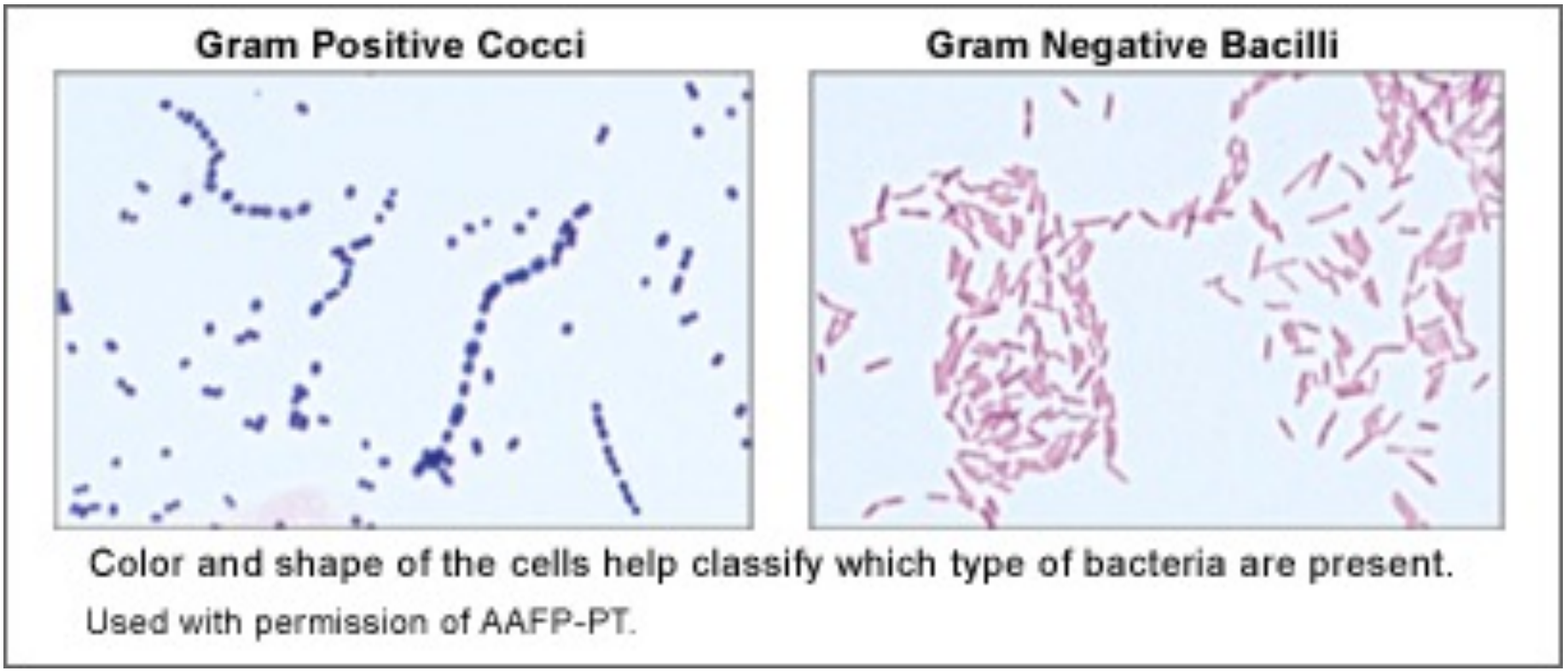



Abb. 3.6: Schematische Darstellung der Zellhülle grampositiver Bakterien und ihrer wichtigsten Komp
Lipoteichonsäuren, Teichon- und Teichuronsäuren, sowie die Peptidquervernetzung (molekularer Aufb
3.7) sind rot dargestellt

- Staphylococcus aureus
- Streptococcus
- Clostridium tetani
- Bacillus anthracis
- Lactobacillus
- Corynebacterium diphtheria

# Gram staining

## 1884 Danish bacteriologist Hans Christian Gram




In gram-positive bacteria crystal violet stains the thick layer of peptidoglycan in their cell walls

# Viruses

## Categories – discuss

What are viruses?

Where do they come from?

What is their purpose?

How frequent are they?

# What are viruses?

- Viruses are **obligate intracellular parasites**
- They can **only replicate in a living host cell**
- Viruses do **not carry out metabolic processes** (they do not generate ATP)
- Viruses do not possess ribosomes (**cannot independently form proteins** from messenger RNA)

# Where do viruses come from?

## Progressive hypothesis

- Mobile genetic elements gained the ability to exit one cell and enter another.
- Retroviruses: encode a reverse transcriptase (RNA can be reverse transcribed into DNA) an integrase enzyme helps to integrate the DNA into a new location in the genome)

## Virus-First hypothesis

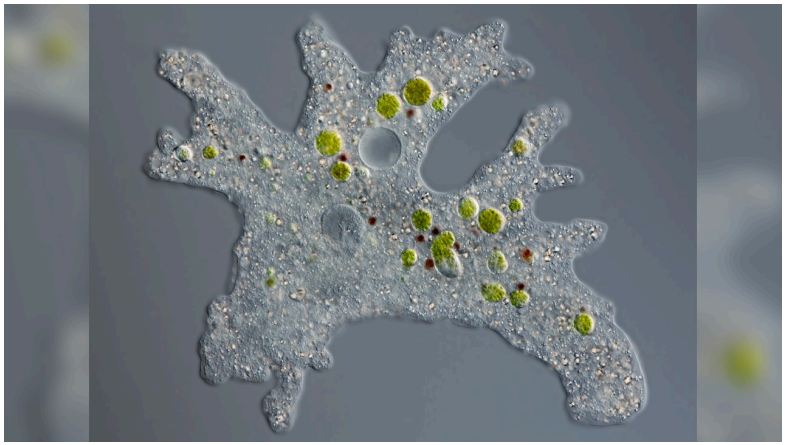
- Viruses as first replicating entities
- Over time viruses became more complex (presumably enzymes for membrane synthesis and cell walls evolved resulting in the formation of cells).
- Viruses may have existed before bacteria

## Regressive hypothesis

- Viruses have originated via a regressive or reductive process.
- Viruses may have evolved from more complex, possible free living organisms that lost genetic information over time and became adopted to a parasitic approach of replication.
- Mimivirus (diameter 750 nm much bigger than most viruses). Contains a repertoire of putative genes associated with “translation of DNA into RNA”.

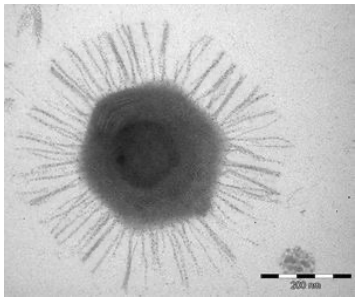
# Mimiviruses infect amoeba cells

- Amoeba

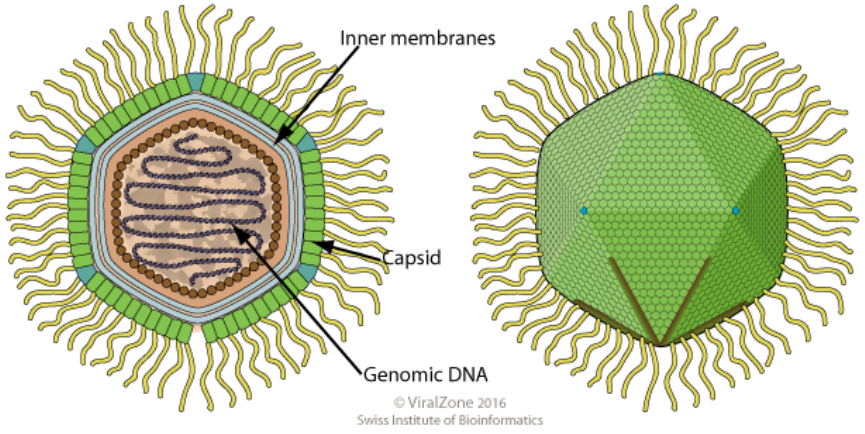


Unicellular eukaryotic organism that can alter its shape

Mimivirus



Microscopic image of a Mimivirus




Schematic view of a Mimi-Virion

# No single hypothesis may be correct

- Perhaps current viruses arose via multiple mechanisms
- Perhaps viruses arose via a mechanism yet to be uncovered.

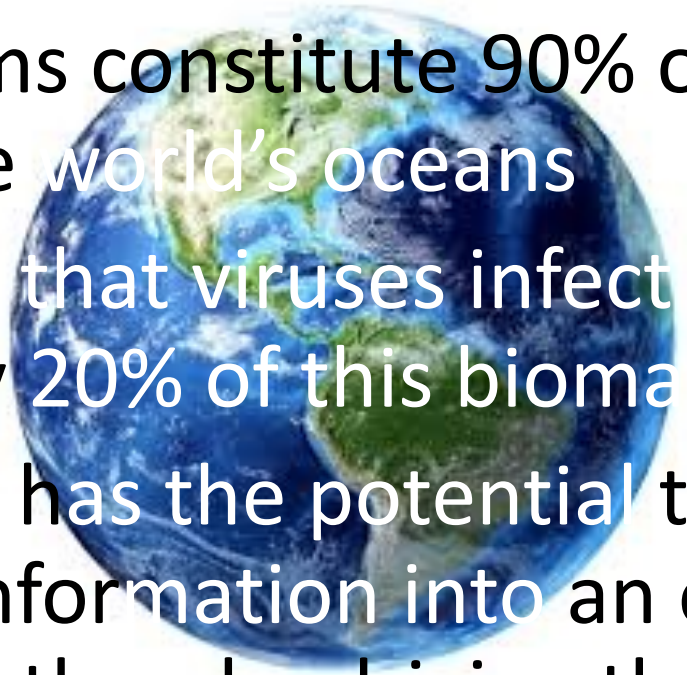
Reference: David Wessner et al., The Origin of Viruses (2010) Nature Education 3(9):37

# A few viruses for widely known human diseases

- Pox viruses
- Influenza viruses
- Hepatitis viruses (Hepatitis B)
- Herpes viruses (HSV, Cytomegalo virus)
- Retroviruses (HIV/SIV)
- Adenoviruses
- Polio virus
- Rabies
- Corona
- SARS
- Rhinoviruses
- Mumpsvirus
- Rotavirus

# What is the most abundant biological entity in the oceans?

- Estimated $10^{30}$ virions in the ocean
- Microorganisms constitute 90% of the living biomass in the world's oceans
- It is estimated that viruses infect approximately 20% of this biomass per day
- Each infection has the potential to introduce new genetic information into an organism or progeny virus, thereby driving the evolution of both host and viral assemblages

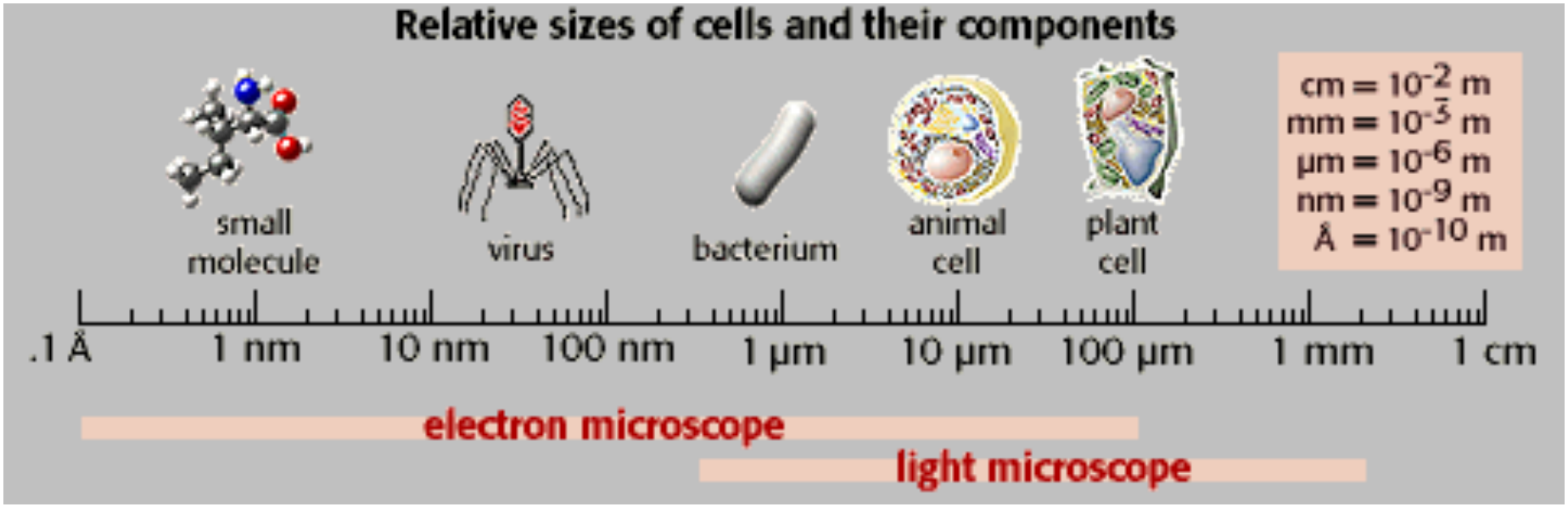


*Nature Reviews Microbiology* **5**, 801-812 (October 2007)

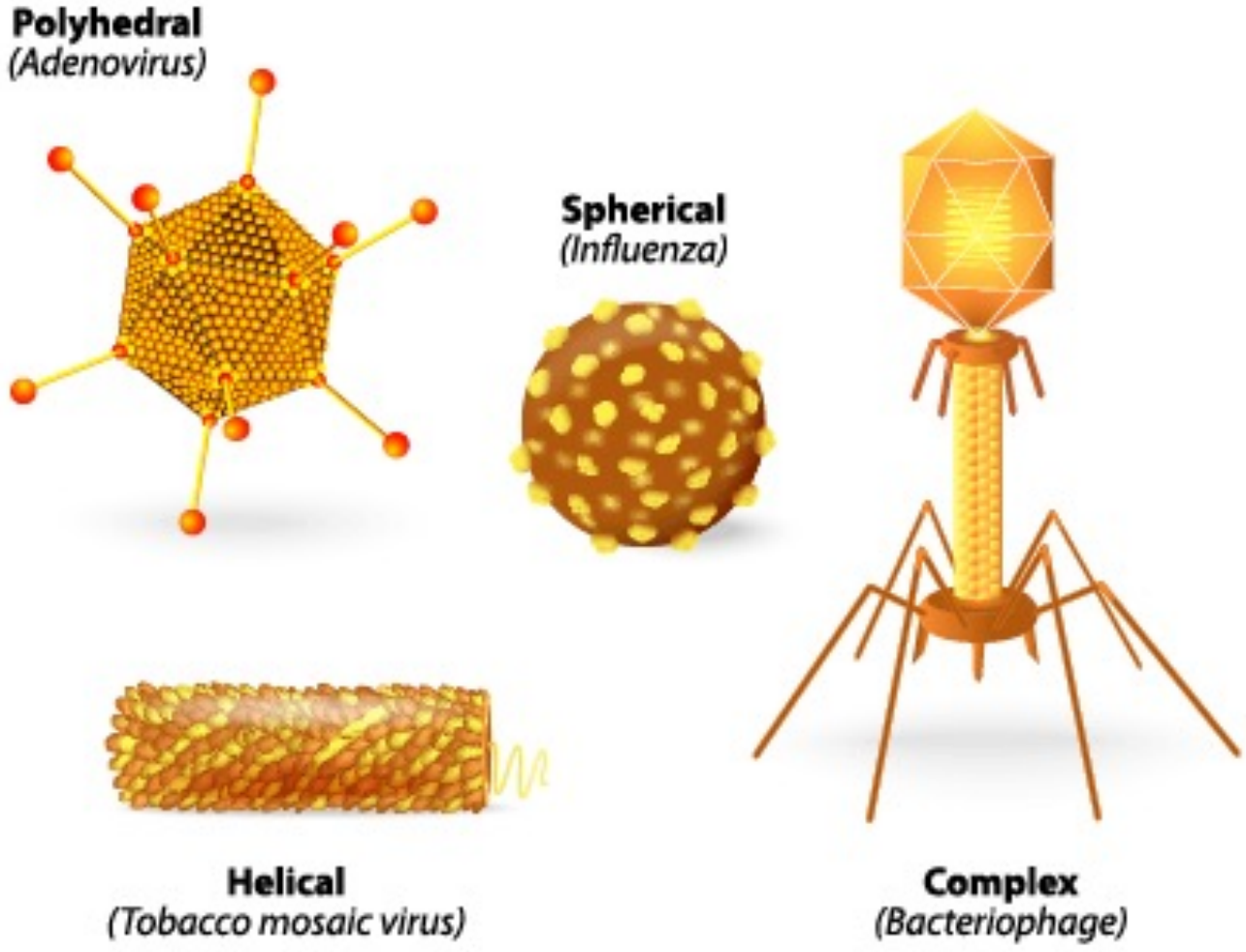
# Virus

- A virus is a small **infectious agent** that has **nucleic acid genome** that is transmitted in a **protein coat (capsid)**. The coat may or may not be covered with a **membrane (envelope)**. Viruses are very small ( generally 10 – 100 nm in diameter) and depend on other living organisms for their replication.

# Size distribution of viruses, bacteria and eukaryotic cells



# VIRAL SHAPES



# Genome sizes

- **Virus** 1700 nucleotides Hepatitis D virus – 1.2000 000 nucleotides Megavirus chilensis/ infects amoeba
- Influenza 8 genes,  14 000 nucleotides
- Herpes virus more than 80 genes

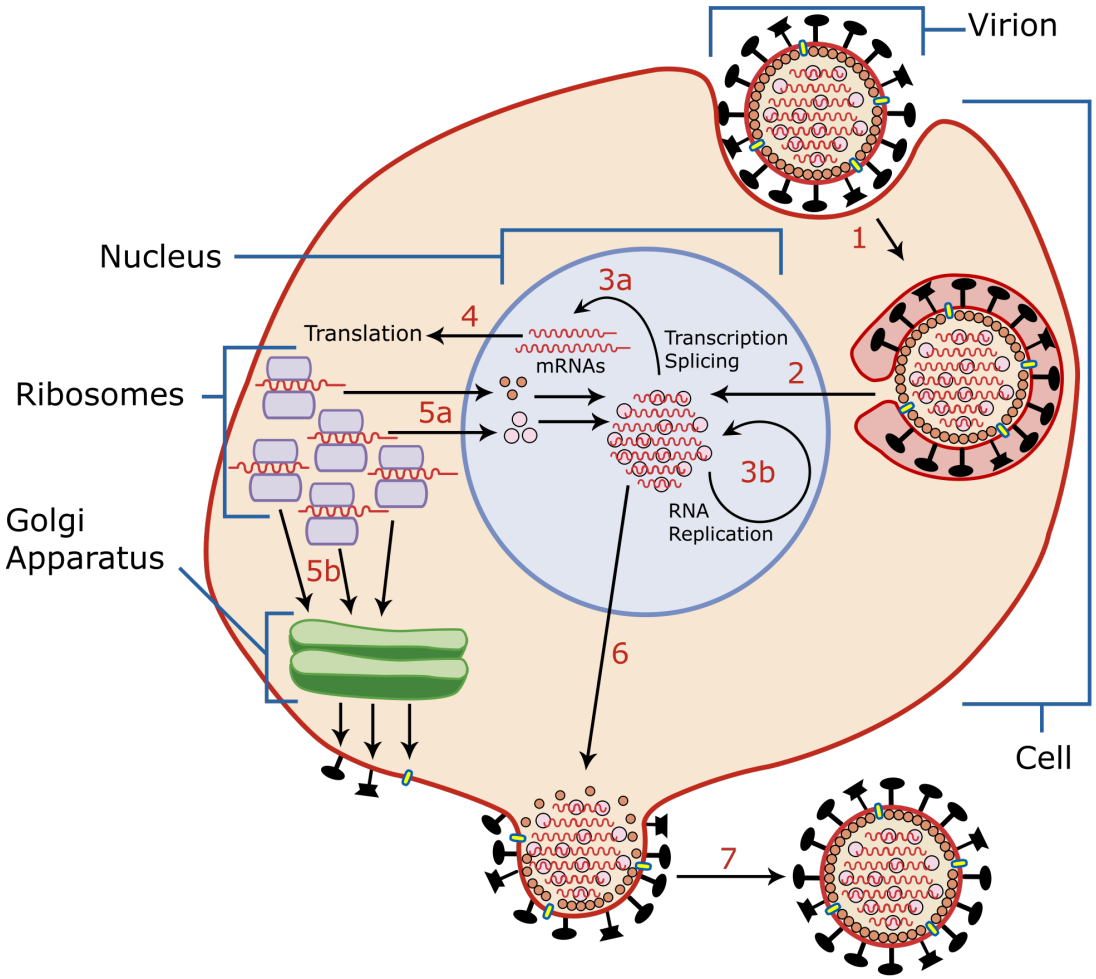
- **Bacteria**: E. coli
- $4.5 \times 10^6$ bp,  4300 genes

- **Human** genome
- $3 \times 10^9$ bp, 20 000 genes

# Genetic information in different forms

- Double stranded DNA
- Single stranded DNA
- Double stranded RNA
- RNA +
- RNA -

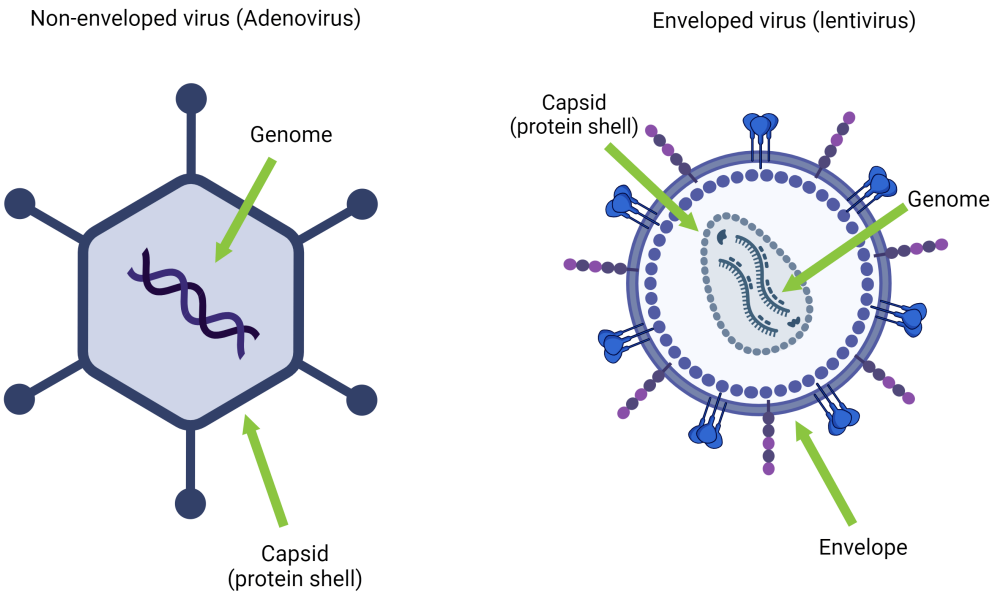
# Life cycle of a virus (Influenza)




(1) Attachment, (2) Penetration +Uncoating, (3) Gene transcription/replication (4) Protein synthesis (6) Secretion of proteins, (6) Virus assembly, (7) Release

# Virion

- the complete form of a virus outside a host cell:

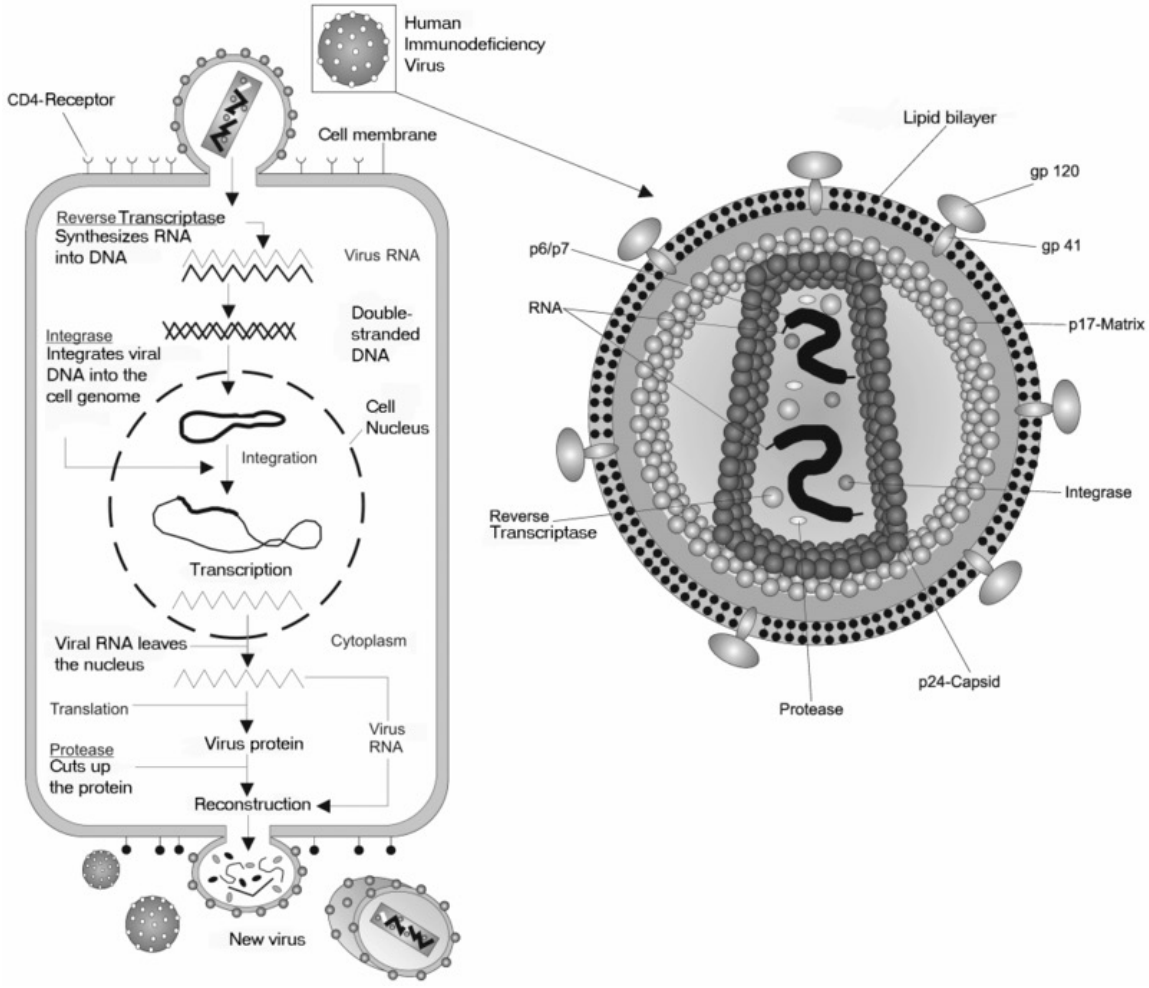



Comparison “non-enveloped” and “envelope” virions. The “envelope” is derived from the host cell.

# Retroviruses e.g. HIV

- *Retroviridae* : enveloped viruses that replicate in a host cell through a process of reverse transcription.
- Single stranded positive sense RNA virus
- Once inside the host cell the virus uses its own reverse transcriptase enzyme to produce DNA from its RNA genome.
- This DNA is then incorporated into the host cell genome by an integrase enzyme.

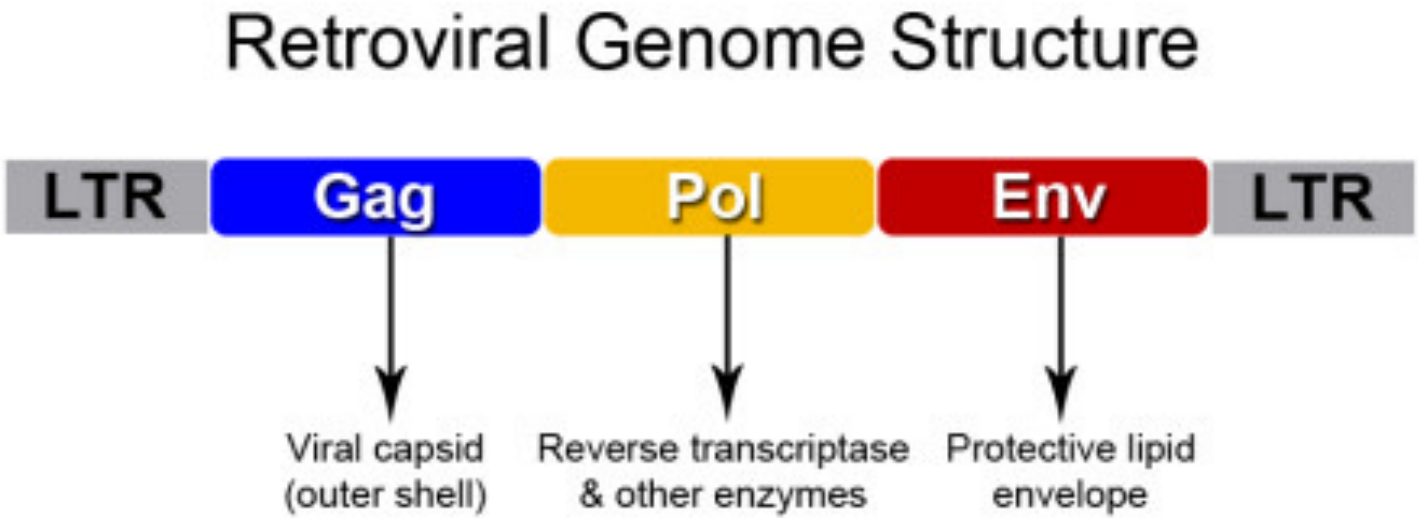
# Life cycle of a retrovirus




https://en.wikipedia.org/wiki/Retrovirus

# Retrovirus sequences in the human genome

- Around 8% of our genome is derived from sequences with similarity to infectious retroviruses



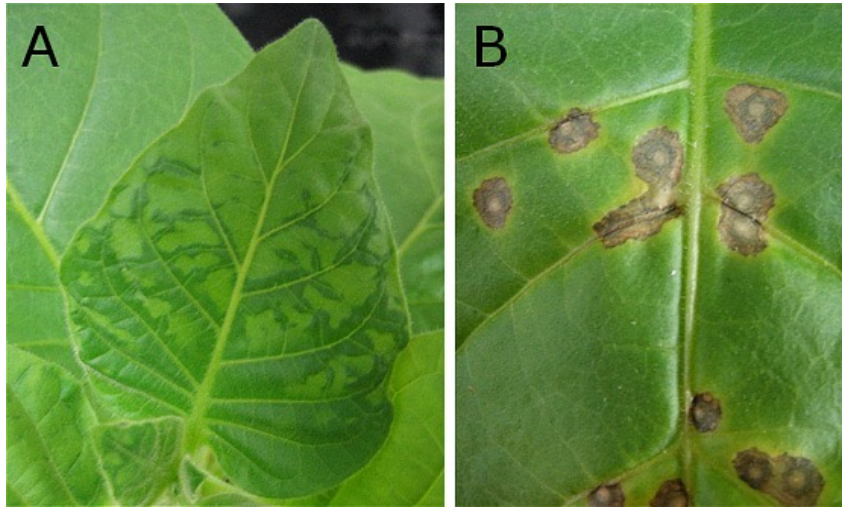

Genome Biology, 2012 (2) reviews1017.1-1017.5

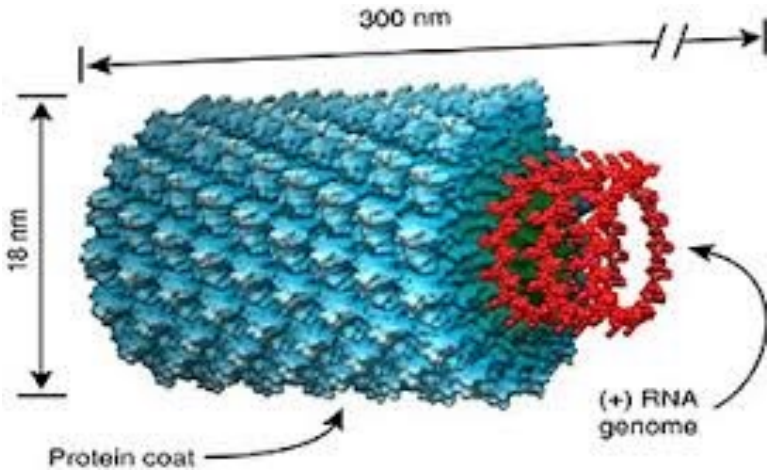
# Viruses affect

- Bacteria
- Archaea
- Fungi
- Parasites
- Animals
- Plants

# Dimitri Ivanovsky 1892 founder of virology

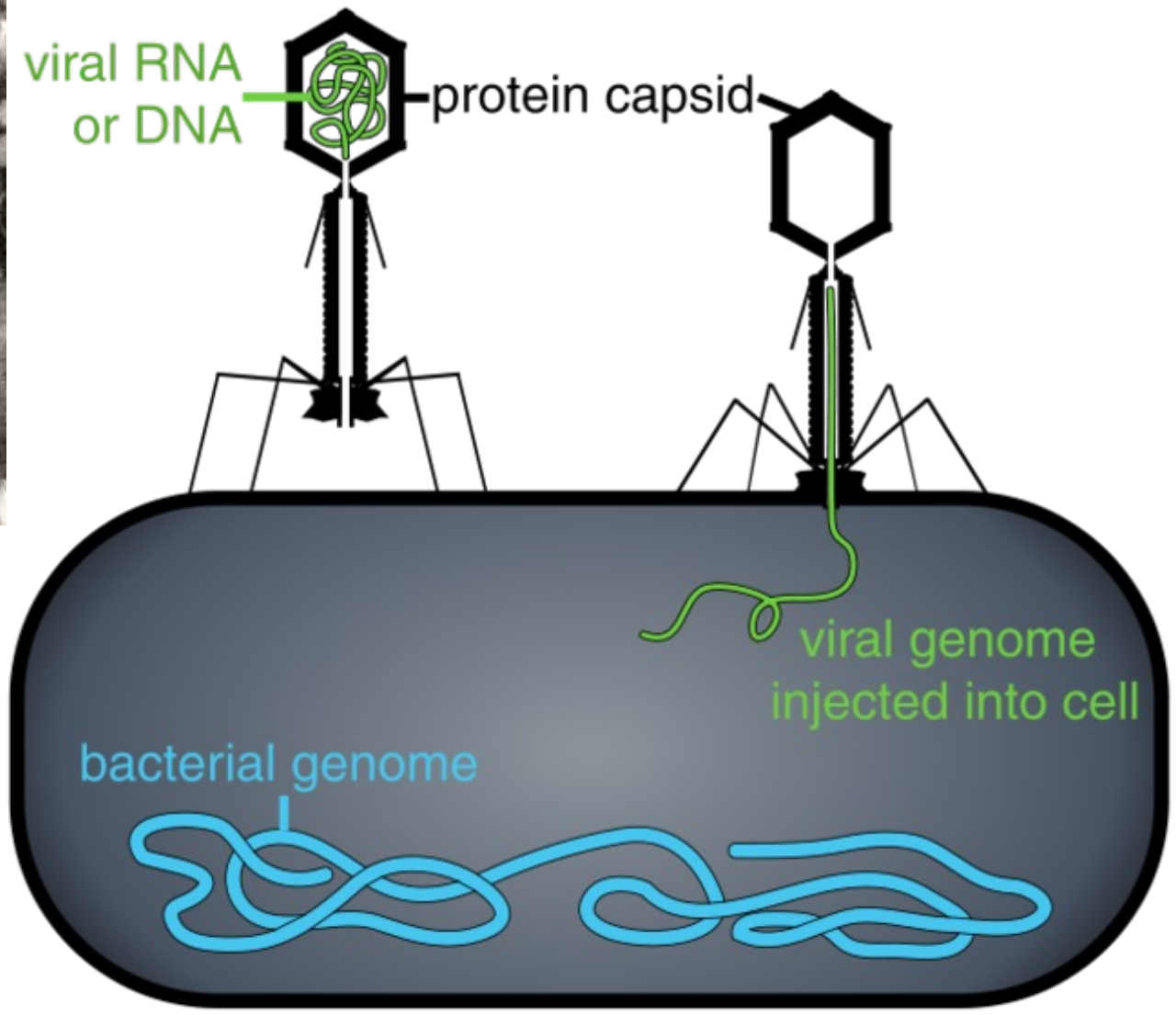
- Tobacco Mosaic Virus



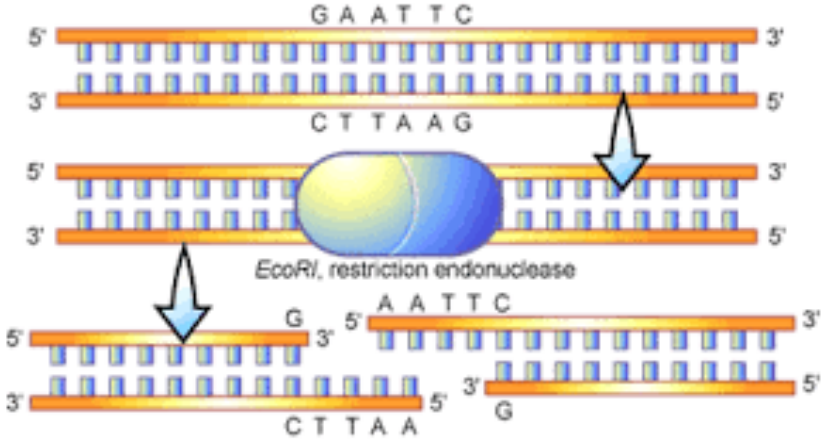

# Viruses of bacteria (phages)

Electron micrograph bacteriophages/ Wikipedia.



# Werner Arber Nobel Prize 1978

- Restriction enzymes



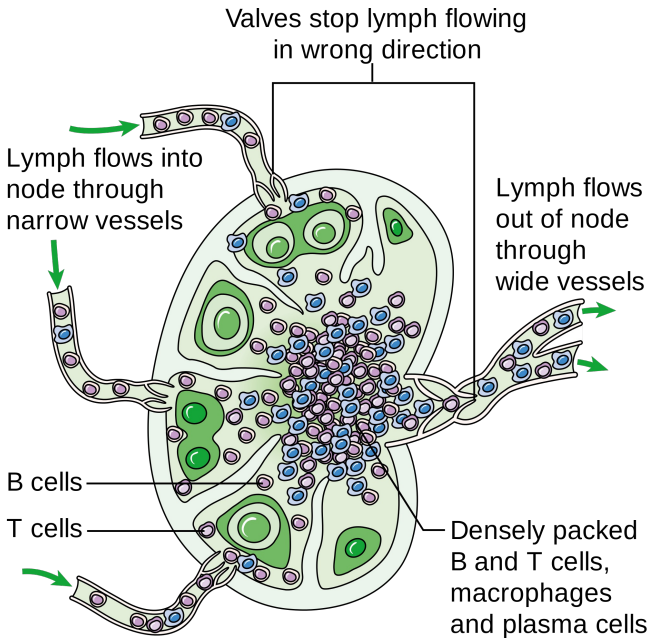

Basel Biozentrum

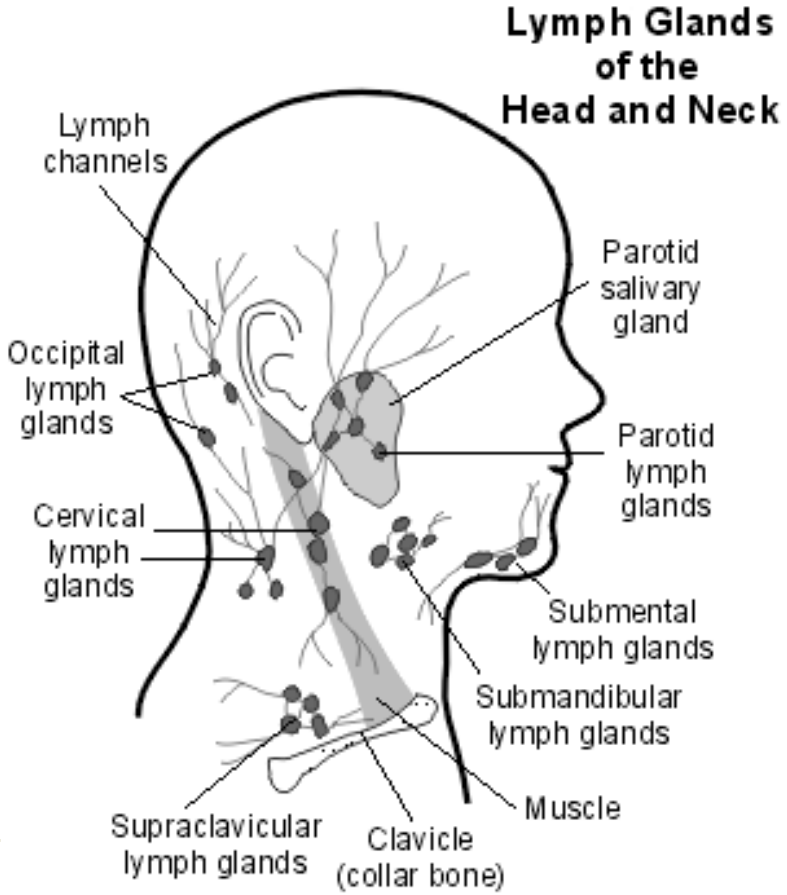
# Viruses capable of causing human cancers

- **Epstein-Barr** virus, **human papilloma virus**, **hepatitis B virus**, and **human herpes virus-8** are the four DNA viruses that are capable of causing the development of human cancers.

# Viruses that can cause cancers

- (1) **Epstein Barr virus**/ Burkitt's lymphoma



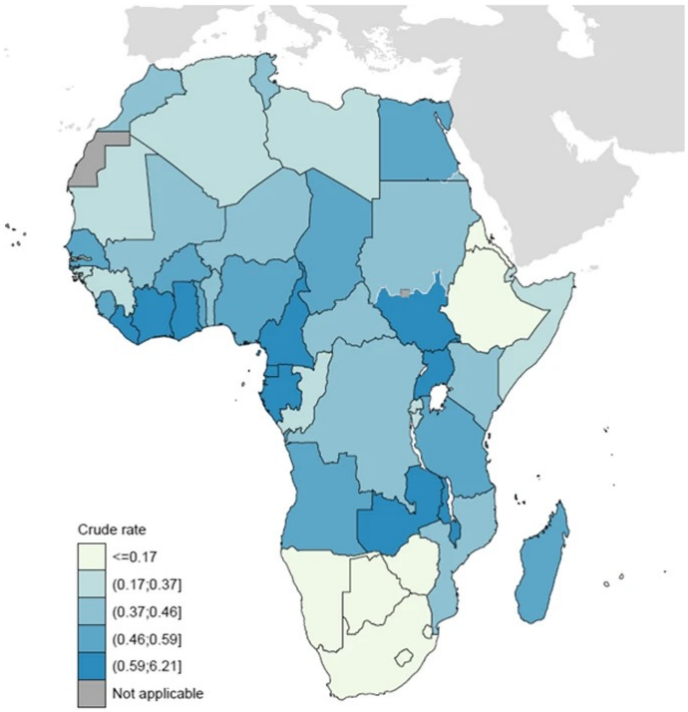



# Burkitt's Lymphoma

- High proliferation rate of B-cells due to de-regulation of c-myc

# The burden of Burkitt lymphoma in Africa

- Hämmerl et al., *Infectious Agents and Cancer. vol.14*. Article number: 17 (2019)




Burkitt lymphoma, patient age 0–14 years – both sexes (estimated incidence per 100,000 in 2018)

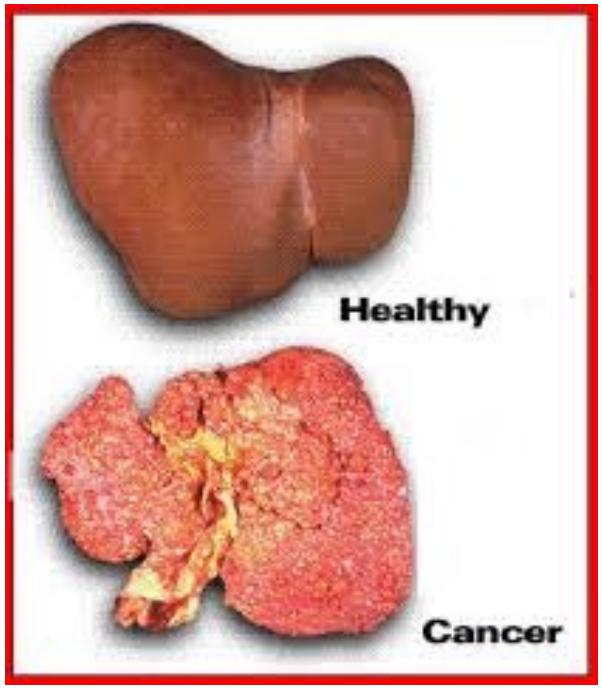
# Endemic disease

- A disease regularly occurring in a specific area or population.

# Viruses that can cause cancers

## (2) Hepatitis B (DNA-virus) + Hepatitis C (single-stranded RNA virus)

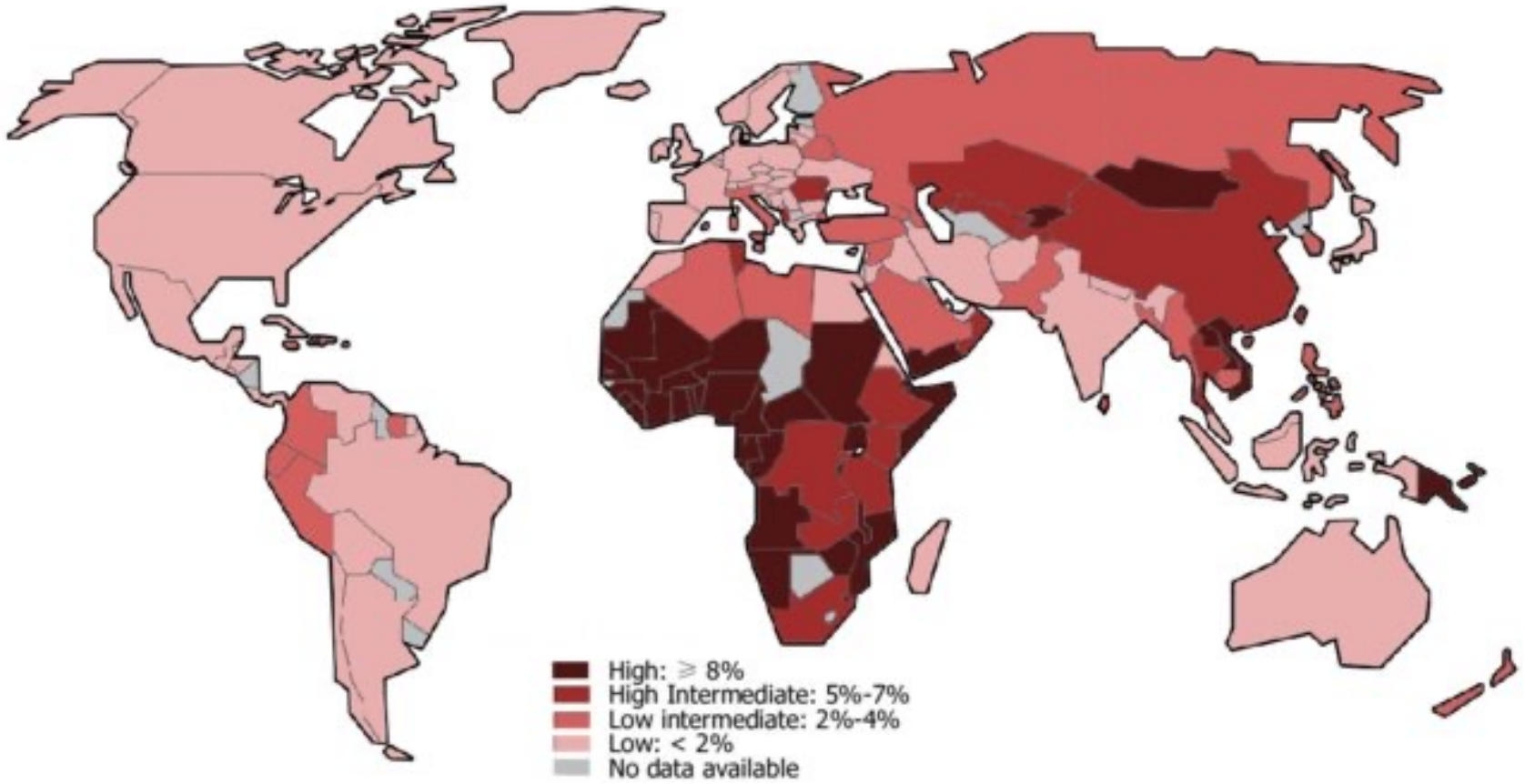
- 200 x higher risk of people having infection with Hepatitis B or C to develop liver cancer



# Vaccines against Hepatitis A/B available

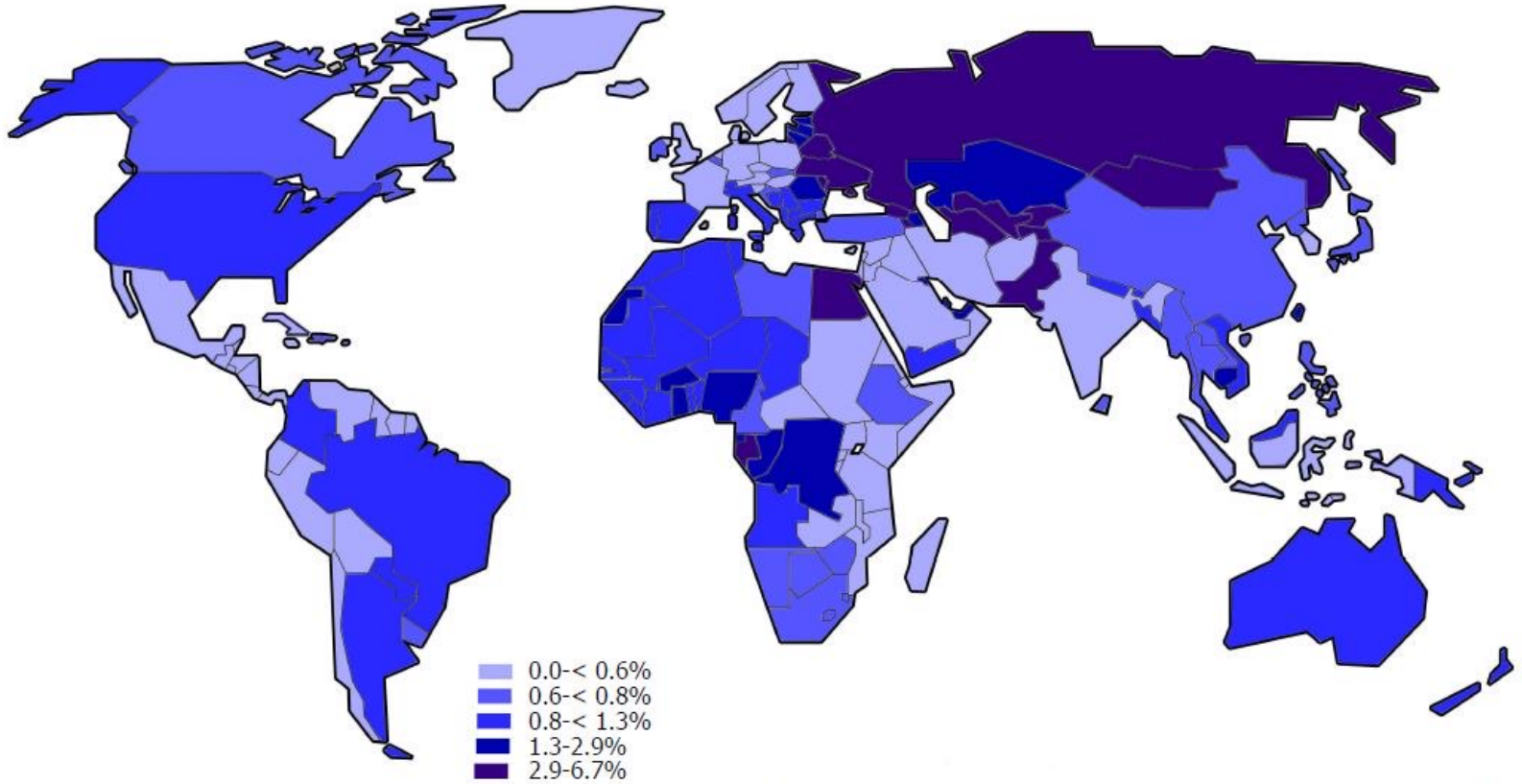
- Hepatitis B vaccine: Recombivax HB  (MERCK)
- Hepatitis B vaccine: ENGERIX-B (GlaxoSmithKline)

# Global distribution of Hepatitis B




Jefferies et al., (2018) World Journal of Clinical Cases 6(13):589-599

# Global distribution of Hepatitis C




Source: Gower *et al*. Global epidemiology and genotype distribution of the hepatitis C virus infection. J Hepatol. 2014 Nov; 61(1 Suppl): S45-57. DOI: 10.1016/j.jhep.2014.07.027. Epub 2014 Jul 30

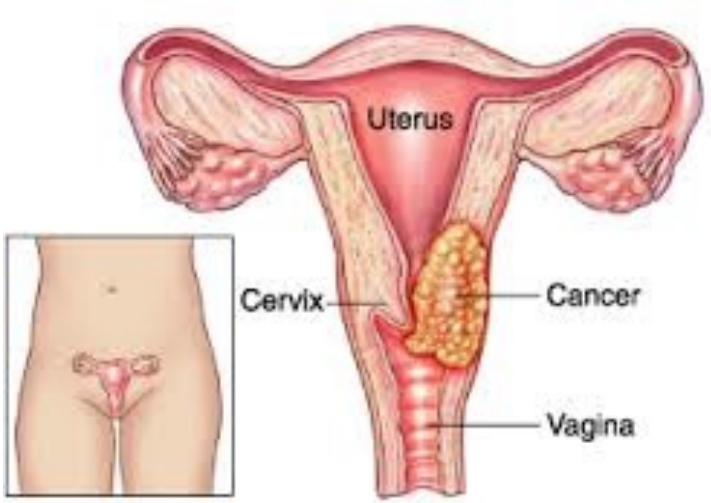
Hepatitis C prevalence (percent of population)

Jefferies et al., (2018) World Journal of Clinical Cases 6(13):589-599

# Viruses that can cause cancers

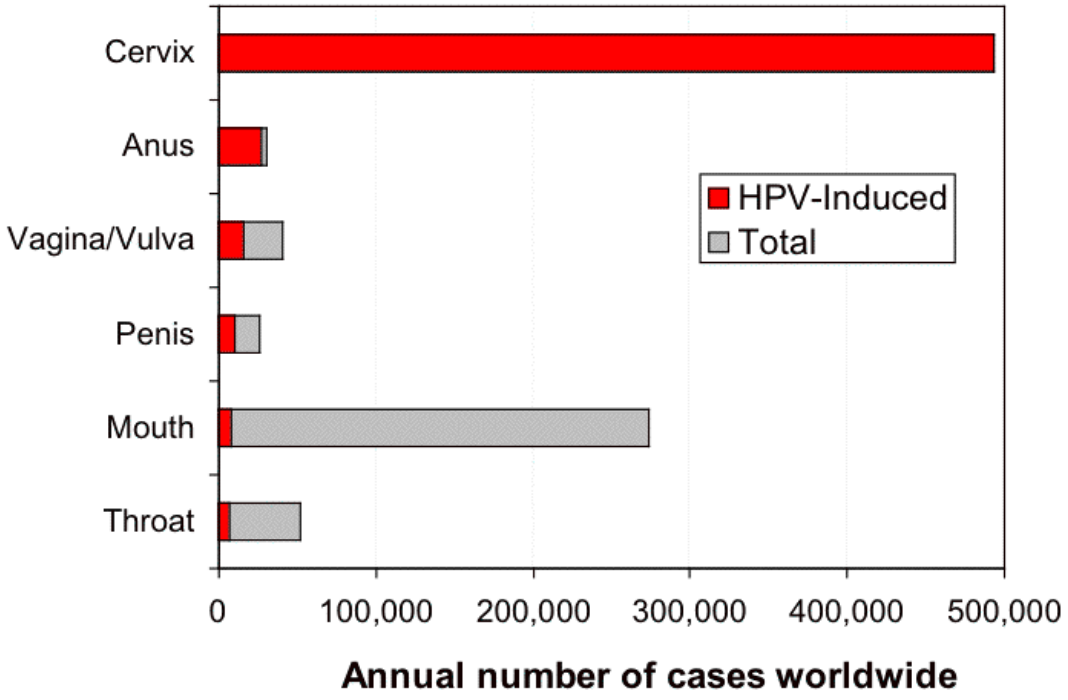
- <u>(3) Human papilloma virus</u>

Warts




Cervical Cancer

# Annual cases of human papilloma-caused cancers




Parkin DM (June 2006). *International Journal of Cancer*. **118** (12): 3030–44

# Vaccine against human papillomavirus

- HPV (Human Papillomavirus) Gardasil® Vaccine, **HPV** types (6, 11, 16, and 18)

- **Cervical cancer** in females,
- **Vaginal cancers** in females, and **anal cancer** in females and males.

# Sanofi Pasteur/France

Sanofi S.A. is a French multinational pharmaceutical company headquartered in Paris, France, as of 2013 the world's fifth-largest by prescription sales.

# Viruses that can cause cancers

- Human Herpesvirus-8
- Transmitted through saliva exchange
- Infects B cells and endothelial cells lining blood vessels
- Kaposi's sarcoma is a cancer that causes patches of abnormal tissue to grow under the skin. The patches are usually red or purple and are made of cancer cells and blood cells