Corso integrato Microbiologia e Virologia
Modulo di Virologia, AA 2025/2026

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Modulo di Virologia
Corso integrato Microbiologia e Virologia

Libro di testo:

Dimmock, A. J. Easton, K. N. Leppard
”Introduzione alla Virologia Moderna”
Casa Editrice Ambrosiana 2017

G. Dehò, E. Galli “Biologia dei microrganismi”
III Edizione Casa Editrice Ambrosiana 2019
Cap. 14.

Modalità esame del Modulo di Virologia

- L’esame è orale e sarà possibile sostenerlo nelle date di appello pubblicate su Infostud dai titolari del corso integrato Microbiologia e Virologia, prof Gianni Prosseda e prof.ssa Bianca Colonna

- Per chi desidera la modalità scritta sono previsti degli esoneri in data da stabilirsi

Per partecipare agli esoneri è necessaria la prenotazione su elearning2.uniroma1.it alla pagina relativa al modulo di Virologia del corso integrato Microbiologia e Virologia utilizzando l’applicativo specifico per ogni data.

Parti del testo “Introduzione alla Virologia Moderna” da consultare per questa lezione

- **Capitolo 1** (qui trovate anche illustrata la “Curva di crescita a ciclo unico” (par. 1.2)
- **Capitolo 2** fino a pg. 14 e paragrafi 2.4, 2.5, 2.6 e 2.7

We live and prosper in a cloud of viruses

- Viruses infect all living things
- We eat and breathe billions of virions regularly
- We carry viral genomes as part of our own genetic material

Why we study viruses?

- ✓Viruses Are Everywhere
- ✓Viruses Infect All Living Things
- ✓Viruses Can Cause Diseases
- ✓Viruses Can Cross Species Boundaries
- ✓Viruses Are Uniquely Valuable Tools to Study Biology
- ✓Viruses Can Be Used To Manipulate Biology
- ✓Virus ‘R’ Us (HERV endogenous viruses)

Viruses global health impact

The facts: viral diseases exert a shocking toll on global health.

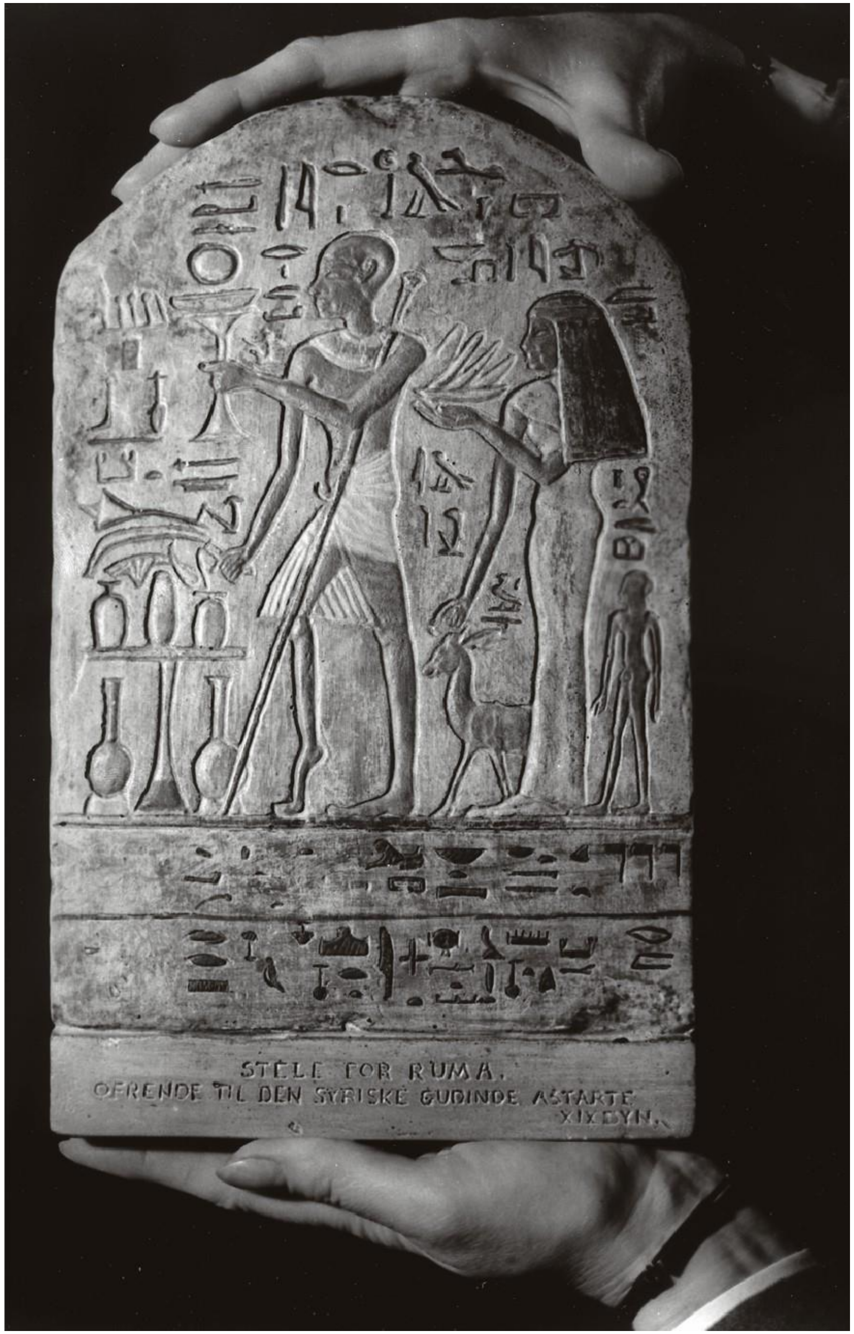
- ✓ Over 600 000 people died from AIDS-related illnesses in 2024.
- ✓ About half of the world's population is now at risk of dengue, with an estimated 100–400 million infections occurring each year.
- ✓ Rotavirus, a cause of common diarrhoea, kills an estimated 120,000 children each year.
- ✓ Around 50 million people, are chronically infected with hepatitis C.
- ✓ In West Africa alone, there are some 500,000 cases of Lassa fever every year.
- ✓ Furthermore many viruses are emerging

The (pre) history of Virology

Virus prehistory

Perhaps the first written record of a virus infection consists of a heiroglyph f rom Memphis, drawn in approximately **1400 BC**, which depicts a temple priest called, which depicts a temple priest called **Ruma** showing typical clinical signs of paralytic poliomyelitis.

B



The Pharaoh **Siptah** (ruled Egypt from 1200-1193 BC) died suddenly at the age of about 20. His mummified body laid undisturbed in his tomb in the Valley of the Kings until 1905 when the tomb was excavated. The mummy shows that his left leg was withered and his foot was rigidly extended like a horse's hoof – classic paralytic poliomyelitis

In addition, the Pharoh **Ramses V**, who died in **1196 BC**, is believed to have succumbed to smallpox.

Viral diseases were treated

- Smallpox, endemic in China by 1000 BC.
- Recognizing that survivors of smallpox outbreaks were protected from subsequent infection, the practice of **variolation** developed.
- Practiced since 11 th century survived until 20th century.

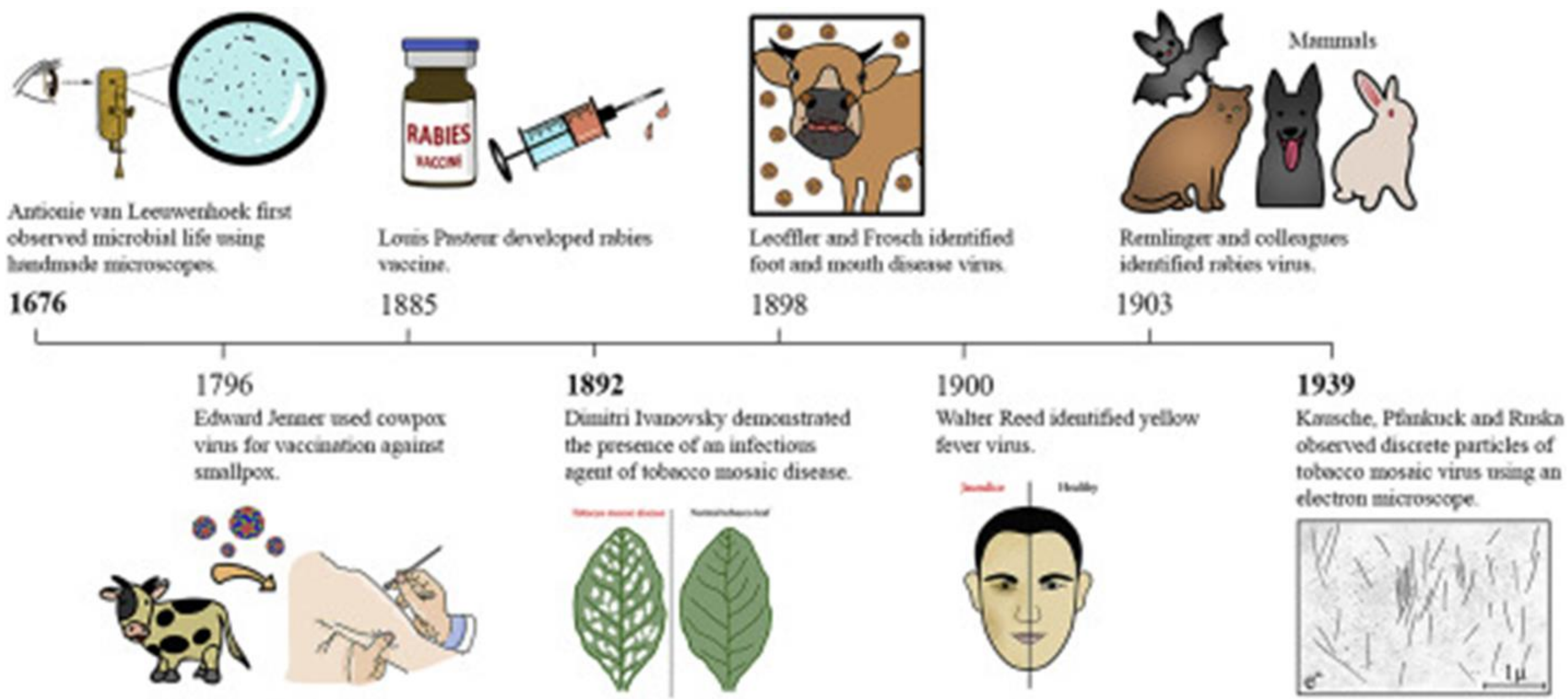
Historical illustration showing the transmission of rabies. Arabic painting by Abdallah ibn al-Fadl, Baghdad school, 1224.
Freer Gallery of Art, Washington, DC.

Humans manipulate viruses

A painting by N. Robert (1624-1685). Striping patterns (color breaking) in tulips were described in 1576 in western europe and were caused by a viral infection (tulip mosaic virus)

La storia della virologia

La storia della virologia



Prima descrizione di patologia di origine virale: Vaiolo in Cina nel X secolo a.C. ed alterazioni simil-vaiolose nella mummia del faraone Ramsete V (circa 2000a.C.)

Tentativi di prevenzione e cura di patologie di origine virale in atto prima della scoperta dei virus stessi: Jenner, vaccinazione antivaiolosa alla fine del ‘700 e Pasteur che lavorò sul vaccino per la rabbia alla fine del ‘800

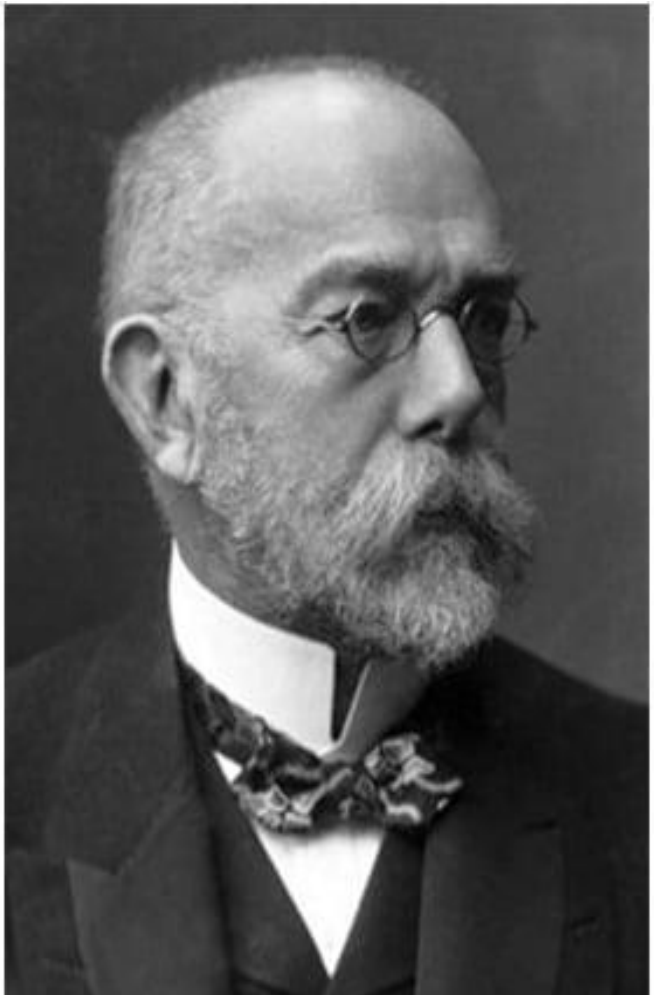
La storia della virologia

1882: Adolf Mayer osserva che la linfa di foglie di tabacco malate era in grado di determinare la patologia se inoculata in piante sane.

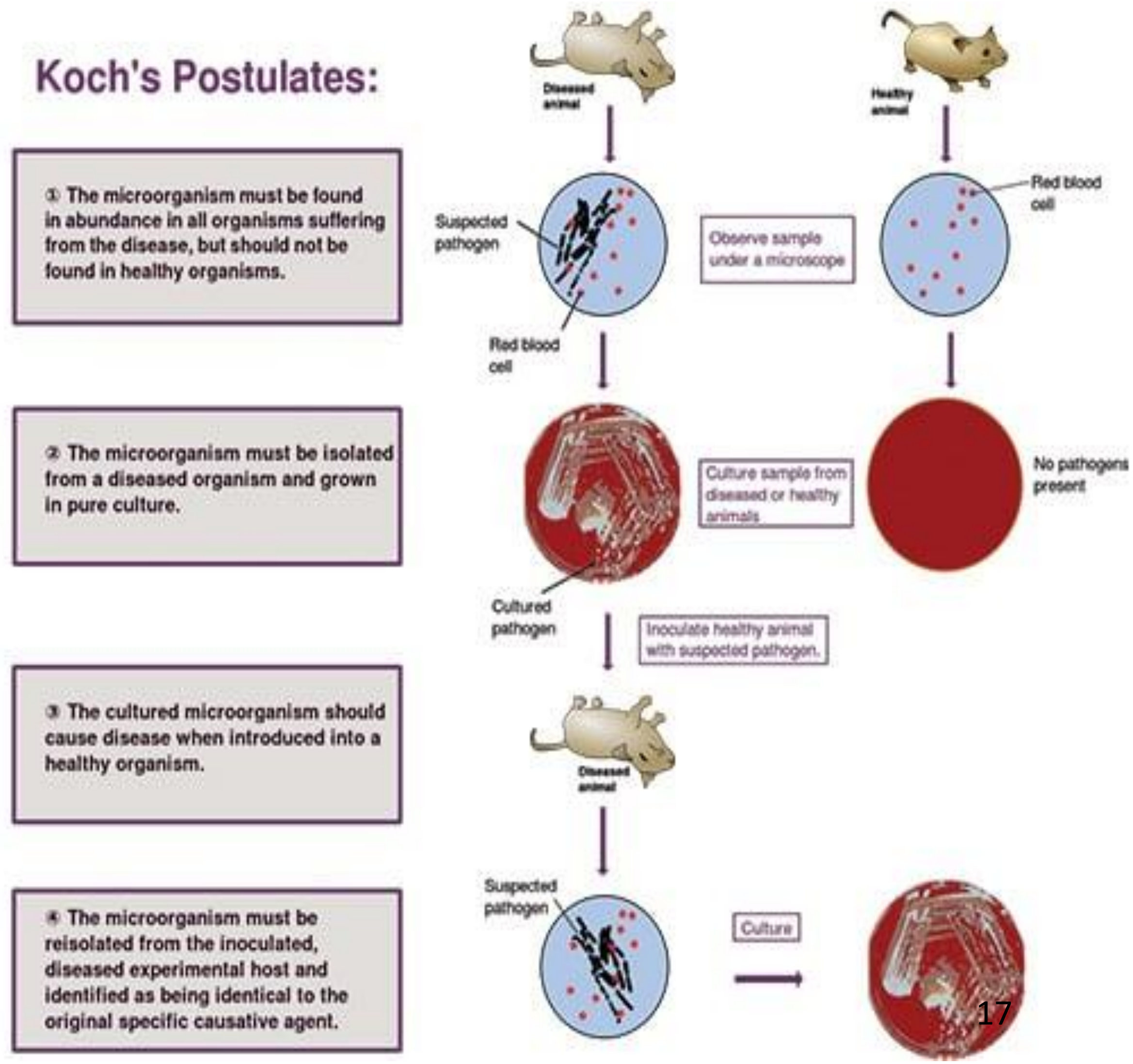
1892: Dimitri Iwanovski ripeté gli esperimenti di Mayer ma dimostrò che la causa della depigmentazione delle foglie di tabacco era dovuta ad un agente che passava la barriera dei filtri da batteriologia abbastanza selettivi da poter trattenere anche il più piccolo batterio.
Tuttavia, non essendo rispettati i postulati di Koch, pensò si potesse trattare di una tossina.

La storia della virologia

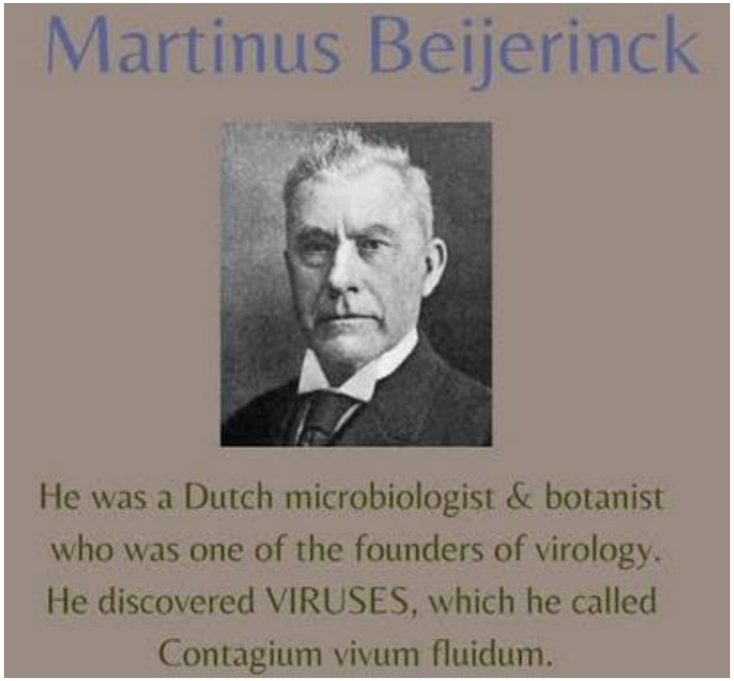
Koch's postulates were not satisfied by the «contagium» in pioneering observations



Robert Koch (1843 - 1910)



La storia della virologia



1898 Martinus Beijerinick confermò ed estese i risultati di Iwanovski sul *Tobacco mosaic virus* dimostrando che la linfa filtrata diluita era in grado di infettare (riprodursi) in tessuti vegetali vivi. Fu il primo a sviluppare il concetto di virus, a cui si riferì come "**contagium vivum fluidum**" (un agente vivente solubile).

Nella letteratura dei primi anni del 900 ci si riferisce ai **virus** come **agenti filtrabili**

DISCOVERY OF THE TOBACCO MOSAIC VIRUS

Adolf Mayer (1886)

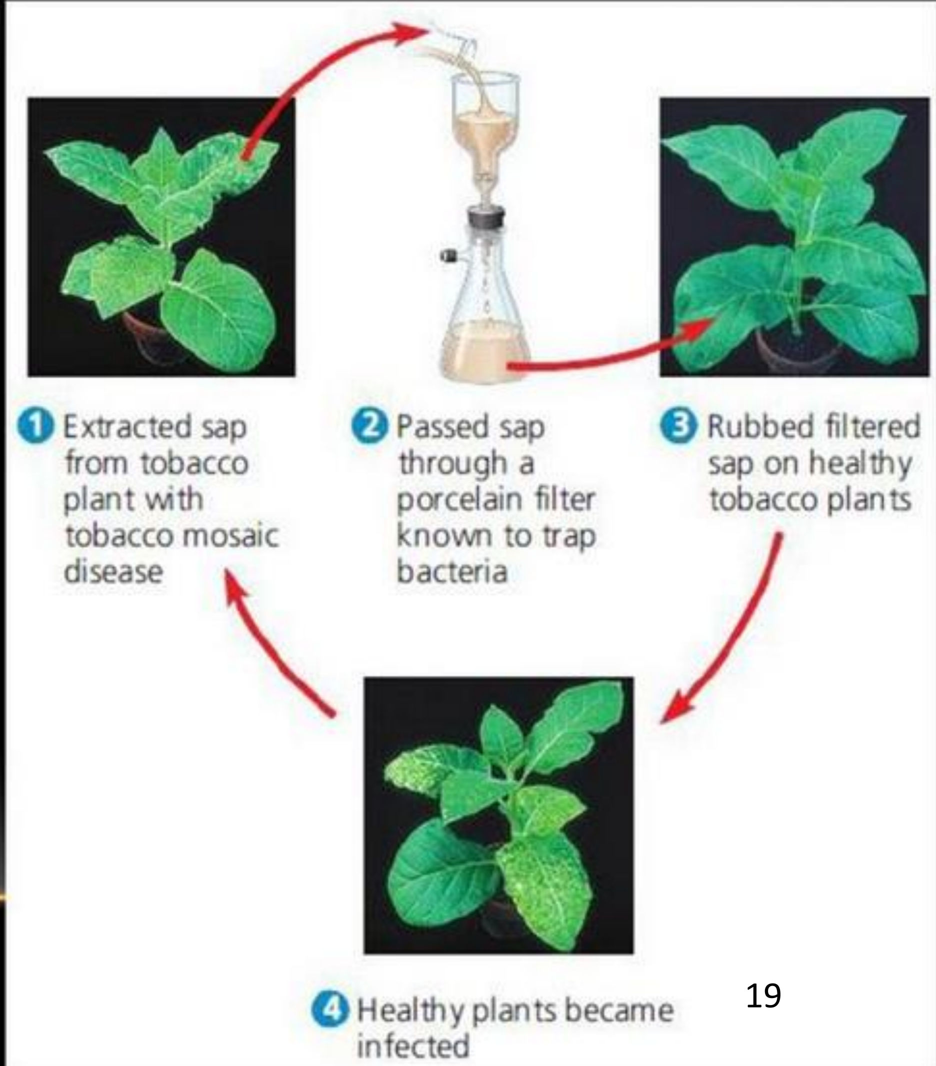
- Tobacco mosaic disease could be transferred between plants

Dmitri Ivanovsky (1892)

- Pathogen is non-bacterial and can pass through fine filters

Martinus Beijerinck (1898)

- Independently replicated Ivanovsky's experiments
- Agent was able to reproduce and multiply in host cells of tobacco plants
- Coined term "virus"



The history of Virology

So, viruses were initially identified in **negative terms**:

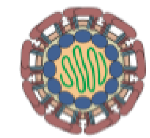
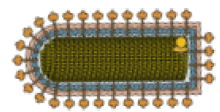
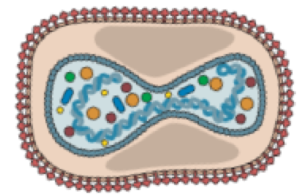
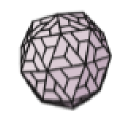
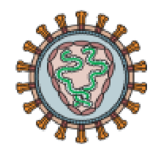
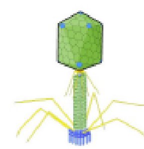
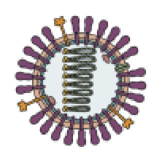
- They could not be visualized,
- They could not be cultured without living cells,
- They were not retained by filters.

La storia della virologia

1898: Freidrich Loeffler & Paul Frosch dimostrarono che un agente filtrabile era responsabile dell'afta epizootica nel bestiame (Foot and Mouth Disease virus).

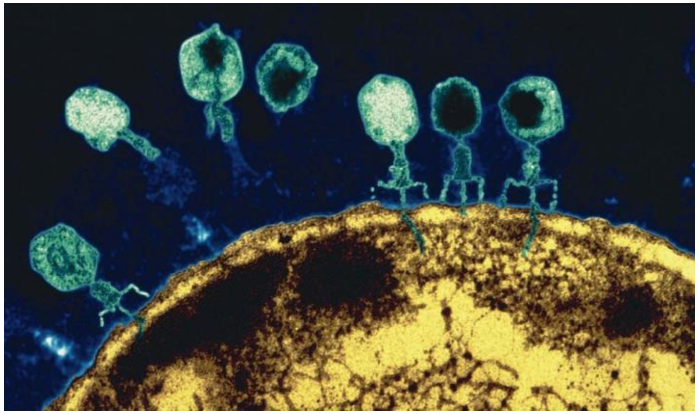
1901: viene identificato il primo virus umano da un team a Cuba guidato da Walter Reed, è il virus responsabile della febbre gialla (Yellow fever virus). Dimostrerà inoltre quanto postulato già tra il 1865 ed il 1881 da Carlos Juan Finlay: il virus è trasmesso dalle zanzare.

La storia della virologia

- 1901 - first human virus, yellow fever virus 
- 1903 - rabies virus 
- 1906 - variola virus 
- 1908 - chicken leukemia virus, poliovirus 
- 1911 - Rous sarcoma virus 
- 1915 - bacteriophages 
- 1933 - influenza virus 

Nei primi 30 anni del 900 si scoprono poi un numero sempre crescente di virus umani, si evidenziano inoltre importanti caratteristiche dei virus studiando i batteriofagi e i retrovirus

La scoperta dei batteriofagi



Frederick Twort (1915) & Felix d'Herelle (1917) sono stati i primi ad identificare i virus che infettano i batteri che d'Herelle chiamò batteriofagi (mangiatori di batteri)

Twort osservò come cambiavano morfologia le colonie di cocchi assumendo un aspetto trasparente. Una volta diventate trasparenti non erano più coltivabili e questa proprietà veniva trasmessa alle cellule con morfologia normale. Per spiegare questo fenomeno ipotizzò la presenza di virus batterici o di un enzima in grado di lisare le cellule produttrici.

d'Herelle utilizzo batteri che causavano dissenteria (Shigella) ed osservò che le feci dei pazienti una volta filtrate erano in grado di distruggere colture pure dei batteri precedentemente isolati. Nominò le aree trasparenti «*Taches vierges*» o Placche

The history of Virology

In the **1930s and the following decades**, **Salvador Luria**, **Max Delbrück**, and many others used these viruses as **model systems** to study various aspects of virology, including viral structure, genetics, replication, and more.

The **history of virology** is the history of the development of **experimental systems and tools** that made it possible to study viruses—opening up entirely new areas of biology.

A FEW DATES…

1798 : JENNER ➔ World's first vaccine : smallpox (variola) vaccine

1879-84 : PASTEUR ➔ Extension of the principle of vaccination + first preventive vaccines against different infectious agents (eg Rabies vaccine).

Microbes too small to be observed with light microscopy can cause diseases

1886 : MAYER : tobacco mosaic disease ➔ ***transmission from diseased plants to healthy plants***

1892 : IVANOVSKI ➔ tobacco mosaic disease transmitted by a substance that passed through a filter with pores small enough to retain most bacteria

1898 : BEIJERINCK ➔ tobacco mosaic disease infectious agent could reproduce and multiply in host cells of tobacco plants (➔ ***parasitism, no bacteria)***

Birth of a new life concept = the concept of virus : a novel organism smaller than bacteria and that could multiply only in living cells. (First exemple = **T**obacco **M**osaic **V**irus, **TMV**)

1901: Discovery of the first human virus ➔ **yellow fever virus**

1915-17 : TWORT & d'HERELLE ➔ Discovery of ***BACTERIOPHAGES*** (viruses of bacteria).

1935 : STANLEY ➔ Proteins purification and crystallization of TMV ➔ **TMV composed of proteins…**

1936-7 : BAWDEN et PIRIE ➔ TMV composed of nucleic acids (RNA)…

1939-60 : Electron microscopy, metal shadowing, negative staining… :

first observation of viral particles ➔ determination of the shape, morphology, structure…

etc.

La storia della virologia

1796–1930

- **1796:** Cowpox virus used to vaccinate against smallpox (Jenner)
- **1885:** Rabies vaccine (Pasteur)
- **1892:** Description of filterable infectious agent (TMV) (Ivanovsky)
- **1898:** Concept of the virus as a contagious element
  Plant virus (TMV) (Beijerinck)
  Animal virus (FMDV) (Loeffler, Frosch)
- **1901:** Human virus (yellow fever virus) (Reed et al.)
- **1903:** Rabies virus (Remlinger, Riffat-Bay)
- **1908:** Leukemia-causing virus (Ellerman, Bang)
- **1909:** Poliovirus (Landsteiner, Popper)
- **1911:** Solid tumor virus (RSV) (Rous)
- **1915–1917:** Bacterial viruses (bacteriophages) (Twort, d'Hérelle)

1930–1954

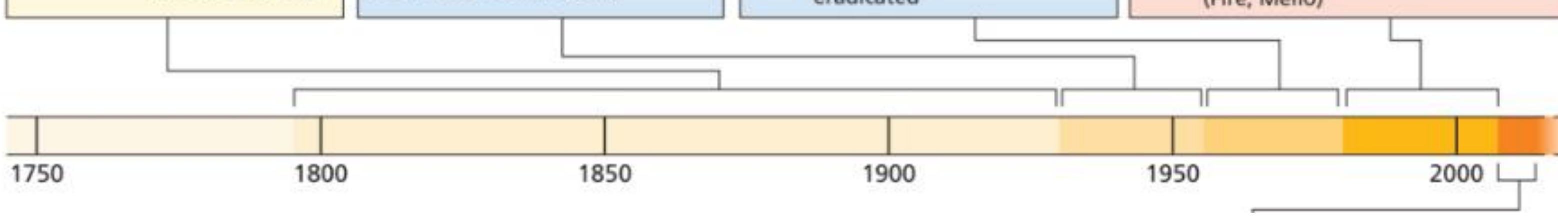
- **1931:** Virus propagation in embryonated chicken eggs (Woodruff, Goodpasture)
- **1933:** Human influenza virus (Smith et al.)
  Rabbit papillomavirus (Shope)
- **1935:** TMV crystallized (Stanley)
- **1938:** Yellow fever vaccine (Theiler)
- **1939:** One-step growth cycle for phages (Ellis, Delbrück)
- **1941:** Virus-associated enzymes (influenza virus) (Hirst)
- **1948** ↓ Poliovirus replication in nonneuronal cell cultures (Enders, Weller, Robbins)
- **1955:** Human single cell culture (HeLa) (Gey et al.)
  Optimization of cell growth medium (Eagle)
- **1952:** Poliovirus plaque assay (Dulbecco)
  Viral genome is nucleic acid (Hershey, Chase)
- **1954:** Polio vaccine (Salk)

1957–1980

- **1957:** In vitro assembly of virus (TMV) (Fraenkel-Conrat, Williams)
  Interferon (Isaacs, Lindemann)
- **1963:** Hepatitis B virus (Blumberg)
- **1967:** Phage λ repressor (Ptashne)
  Viroids discovery (Diener)
- **1970:** Retroviral reverse transcriptase (Temin, Baltimore)
- **1972:** Recombinant DNA (phage λ, SV40) (Berg)
- **1973:** MHC presents viral antigens to lymphocytes (Doherty, Zinkernagel)
- **1976:** Retroviral oncogenes are derived from cells (Bishop, Varmus)
- **1977:** RNA splicing discovered (adenovirus) (Roberts, Sharp)
  Tumor suppressor, p53 (SV40) (Levine, Crawford)
- **1978:** Viral genomes sequenced (Sanger)
  Virus crystal structure (TBSV) (Harrison)
  Recovery of virus from cloned DNA (Weissmann)
- **1979:** WHO declares smallpox eradicated

1980–2008

- **1983:** HPV causes cervical cancer (zur Hausen)
- **1983:** Discovery of the AIDS virus (HIV) (Barré-Sinoussi, Montagnier)
- **1983–1985:** Development of screen for HIV infection (Montagnier, Gallo)
- **1986:** Vaccine against hepatitis B virus (Merck), the first anti-cancer and the virus-like particle vaccine
- **1989:** Hepatitis C virus (Houghton et al.)
- **1994:** Kaposi's sarcoma virus (HHV-8) (Chang, Moore)
- **1997:** HAART treatment for AIDS
- **2003:** Severe acute respiratory syndrome (SARS) worldwide outbreak and containment
- **2003:** Discovery of Mimivirus (LoScola/Raoult)
- **2005:** Hepatitis C virus propagation in cultured cells (Chisari, Rice, Wakita)
  Reconstruction and sequencing of the 1918 influenza virus genome (Palese, Tumpey, Taubenberger)
- **2006:** Vaccine against human papillomavirus (Merck), the second anti-cancer vaccine
- **2006:** Gene silencing by double-stranded RNA, an antiviral response (Fire, Mello)

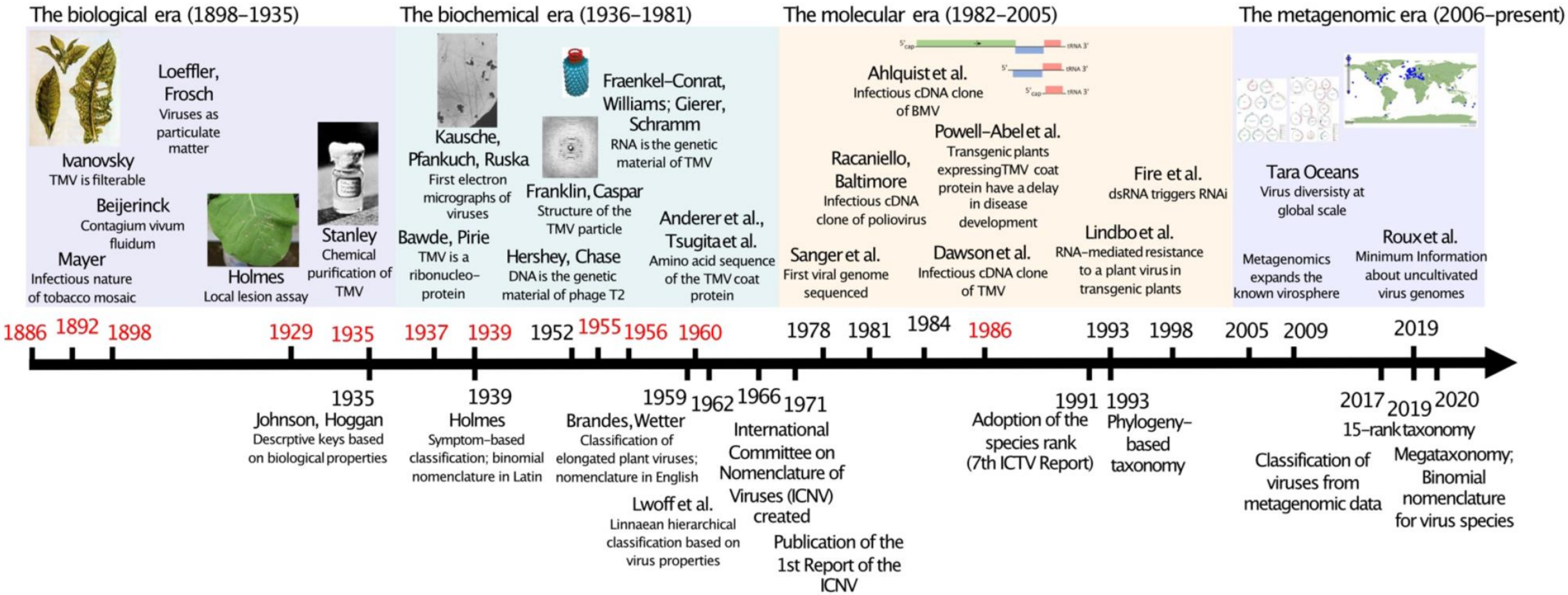


La storia della virologia

- Discoveries or advances recognized by a Nobel Prize
- Medical breakthrough
- Other important landmarks

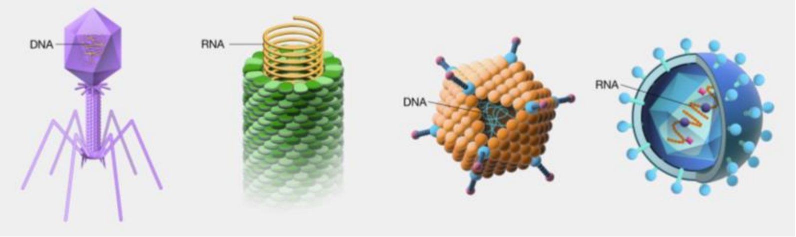
2008–2017	
2010:	Vertebrate genomes carry ancient non-retroviral genomes (Horie, Belyi, Katzourakis)
2011:	Rinderpest virus eradicated: first animal disease to be eradicated by mankind and the second after smallpox
2012:	CRISPR technology derived from bacterial antiviral immunity systems (Doudna, Charpentier, Zheng)
2013:	Discovery of *Pandoravirus salinus* with 2.5Mbp genome
	FDA approves Gilead drug (Sofosbuvir) to cure HCV
2015:	First approval for use on an oncolytic virus for cancer therapy (FDA)
2016:	Retrovirus mediated gene therapy approved for treatment of one form of severe combined immunodeficiency (EMA)
2017:	Nobel prize in chemistry for development of cryo-electron microscopy (Dubochet, Frank, Henderson)
2017:	Creation of CAR-T cells by retroviral gene transfer approved for cancer treatment by FDA
2017:	Adenovirus-associated virus based gene therapy approved for a rare form of congenital blindness

La storia della virologia



Proprietà generali dei virus

Proprietà generali dei virus



- Agenti patogeni in grado di infettare cellule animali, vegetali, fungine, batteriche...

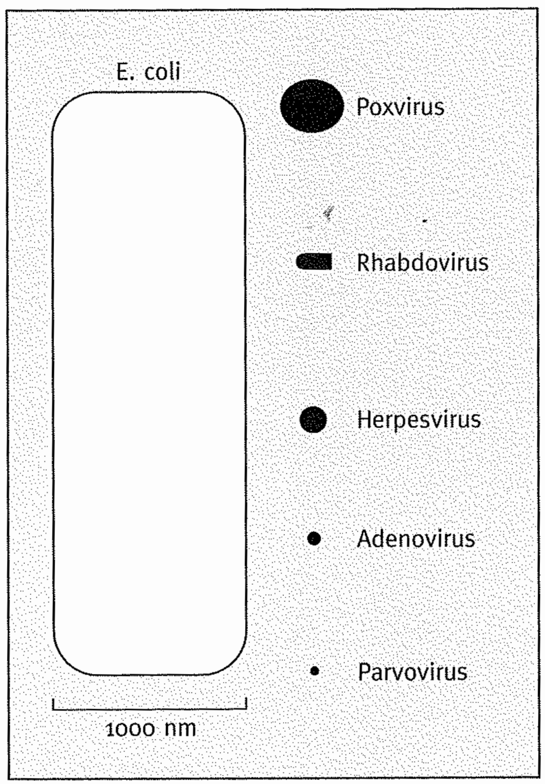
- Sono definiti **parassiti endocellulari obbligati** perché possono replicarsi soltanto all'interno di cellule viventi: essi non sono in grado di produrre e di immagazzinare energia né di provvedere autonomamente alla replicazione delle proprie unità costitutive

- Le particelle virali complete, virioni, sono caratterizzate da dimensioni estremamente modeste: 10-400 nm.

- Sono caratterizzati da una relativa semplicità di organizzazione strutturale.

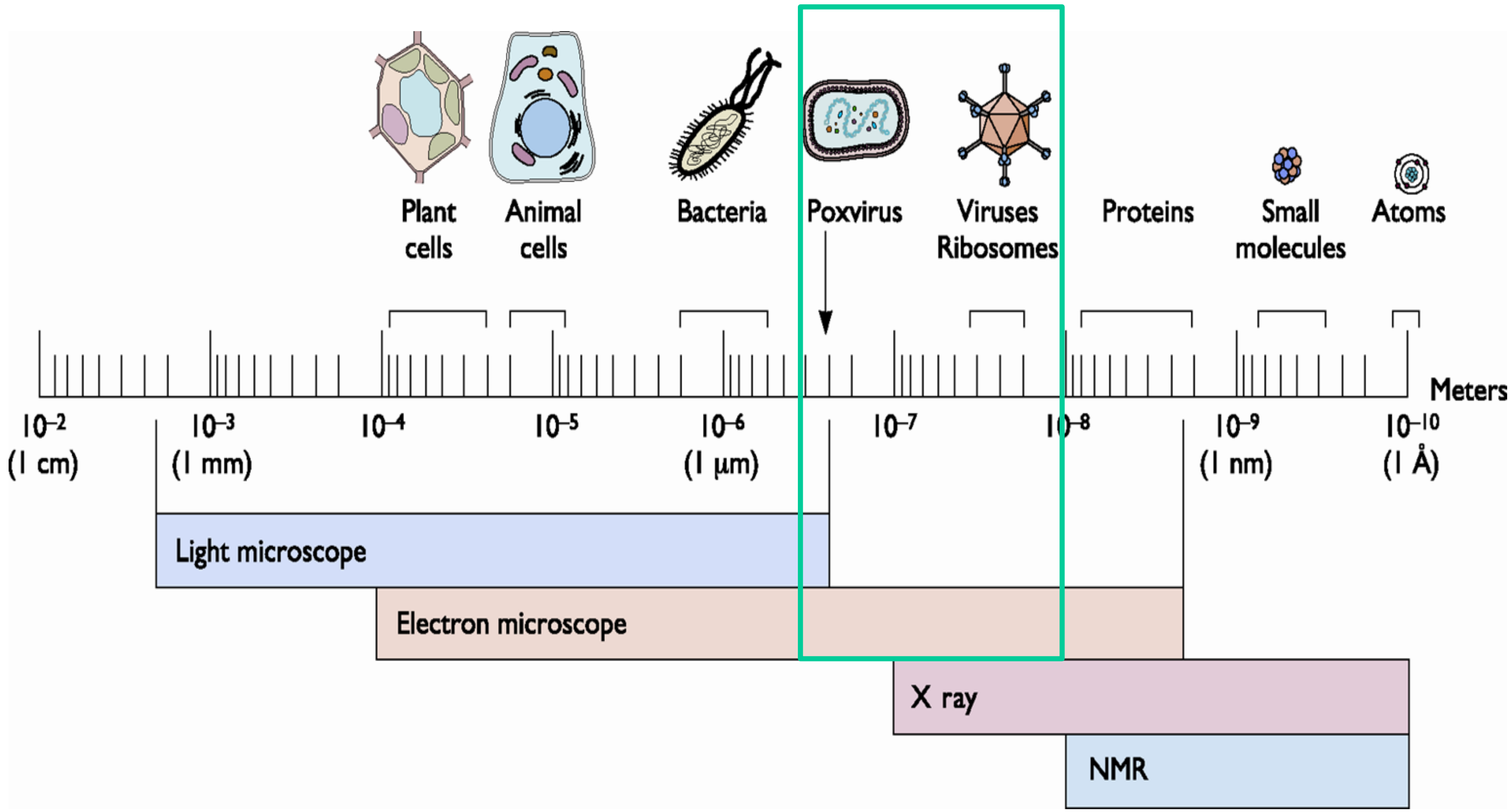
Viral particles → only observable by EM

	Size	Mean size
Viral particles	10 nm → 400 nm	100 nm
Bacteria (prokaryotic)	500 nm → 10 000 nm	2 000 nm (2 µm)
Animal cells	10 µm → 50 µm	20 µm
Plant cells	50 µm → 300 µm	100 µm



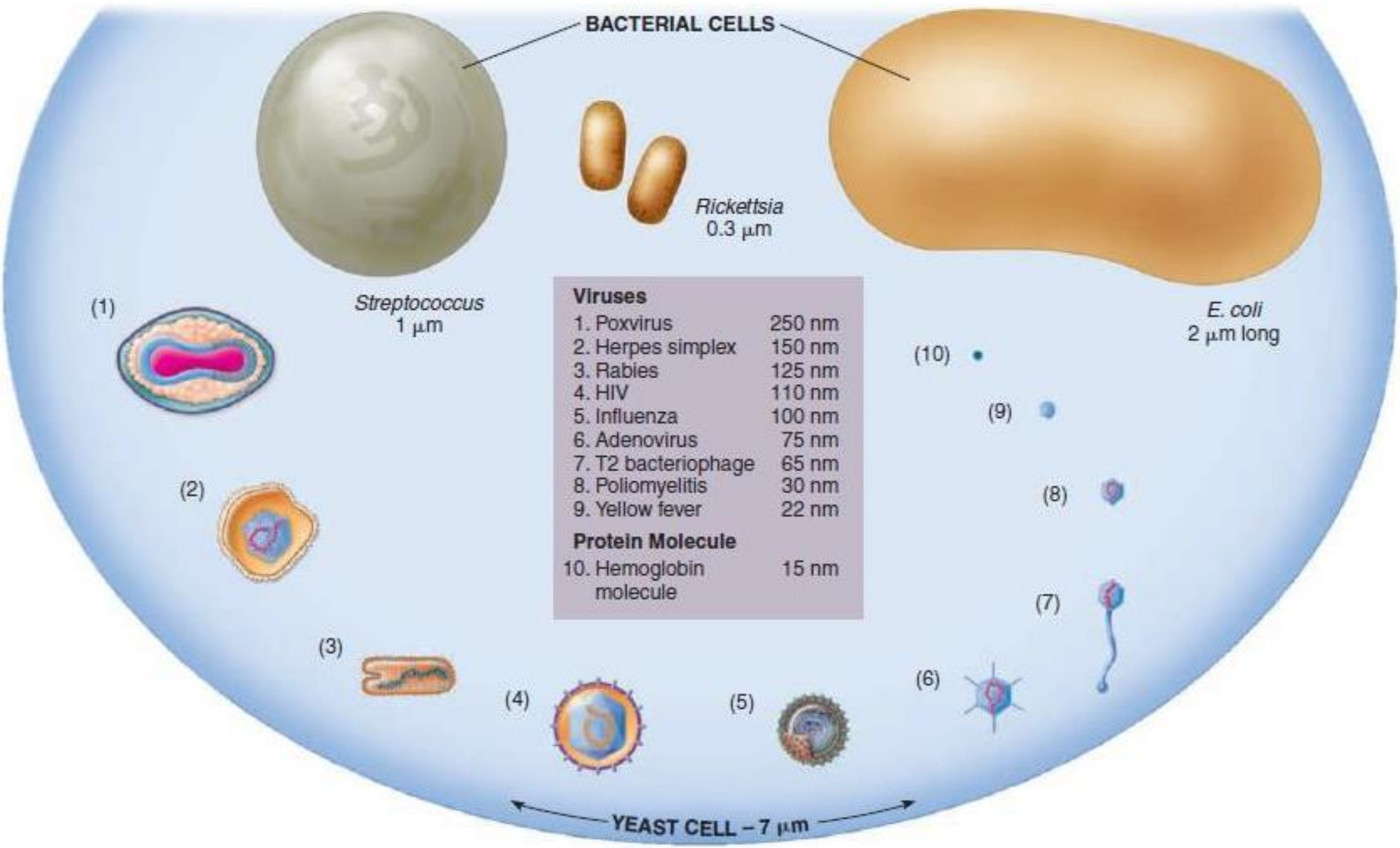
Dimensioni

- Dimensioni sub-microscopiche 10-400 nm



From Flint et al. *Principles of Virology* (2000), ASM Press

Dimensioni


BACTERIAL CELLS
Rickettsia
0.3 µm
Streptococcus
1 µm
E. coli
2 µm long
Viruses
1. Poxvirus 250 nm
2. Herpes simplex 150 nm
3. Rabies 125 nm
4. HIV 110 nm
5. Influenza 100 nm
6. Adenovirus 75 nm
7. T2 bacteriophage 65 nm
8. Poliomyelitis 30 nm
9. Yellow fever 22 nm
Protein Molecule
10. Hemoglobin molecule 15 nm
(1)
(2)
(3)
(4)
(5)
(6)
(7)
(8)
(9)
(10)
YEAST CELL – 7 µm

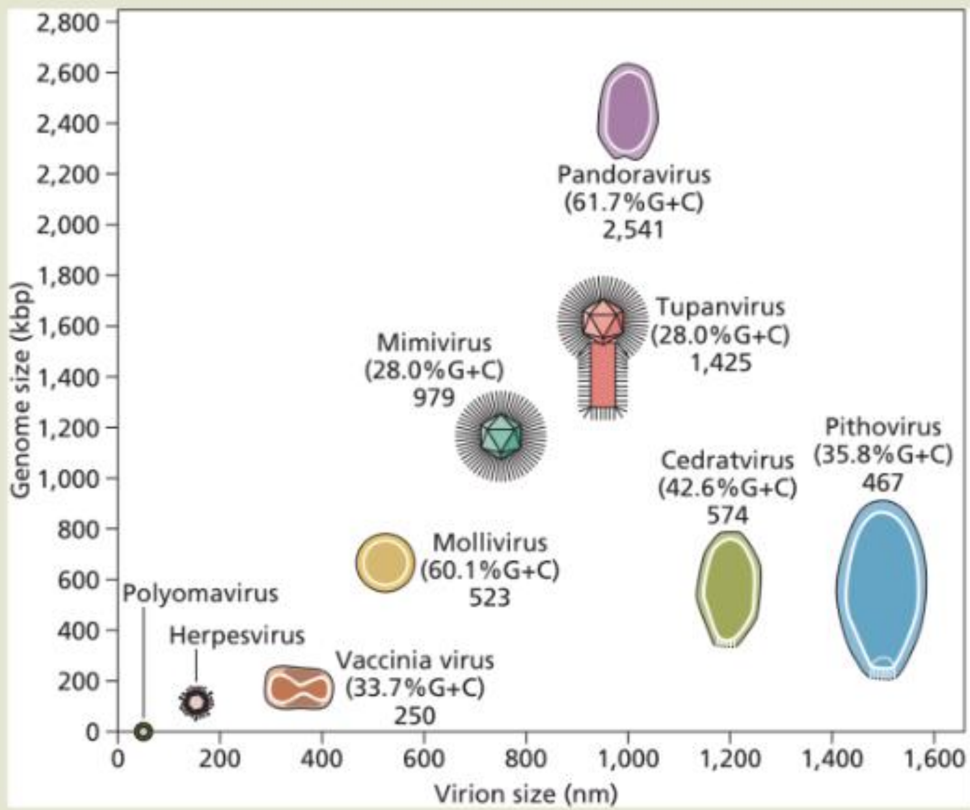
Dimensioni

DISCUSSION

Giant viruses discovered in amoebae

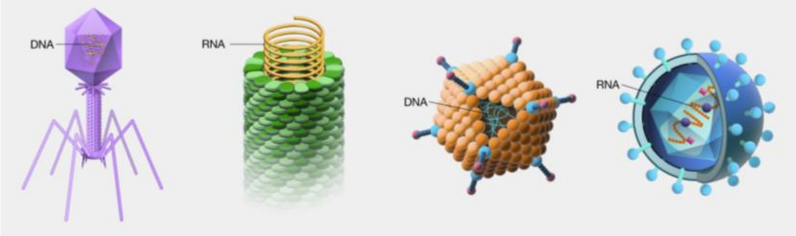
The mimivirus virion, the prototype member of the *Mimiviridae*, was the first giant virus of amoebae to be discovered. Isolated from water in a cooling tower in England in 1992, it is large enough to be visible in a light microscope and was initially thought to be an intracellular bacterium within its host. Not until publication of a brief note in 2003 did it become apparent that this giant was really a virus. The mimivirus genome of 1.2 Mbp was much larger than that of any known virus at the time, exceeding that of some bacteria. This giant encodes more than 900 proteins, many of which are components of the protein translational apparatus, a function for which other viruses rely entirely on the host.

Since reports of the first giant viruses, the use of different strains of amoebae to screen soil and water samples from diverse environments and geographic locations has yielded more than 50 isolates, assigned to nine distinct families. Among the most spectacular is a Pandoravirus isolate, discovered in saltwater off the coast of Chile in 2013. The genome of this giant is twice the size of the mimivirus genome, and contains ~2,500 putative protein-coding sequences, most of them never seen before. Furthermore, while mimivirus has a more or less familiar icosahedral capsid, the Pandoravirus has no regular capsid. Instead, the genomes of these viruses are surrounded by an ovoid envelope, with a pore at the apex that allows delivery of the internal compo-



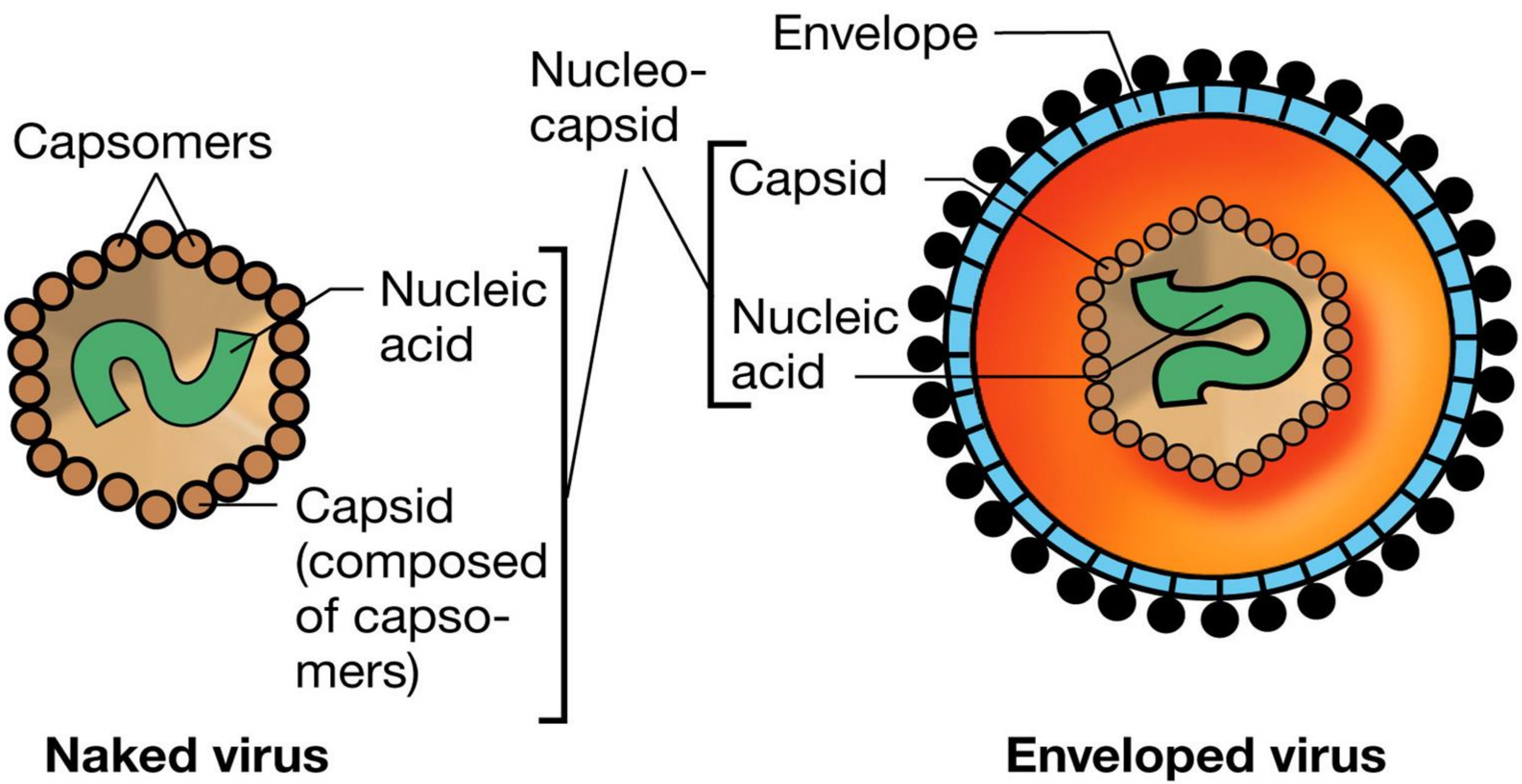
Properties of some of the largest currently known giants, all of which infect amoebae, with representative vertebrate-infecting DNA viruses, of which poxviruses are the largest. The broad range of nucleic acid composition among the amoeba viral genomes is illustrated by the substantial differences in their G+C content. The number of known or putative coding genes in each viral genome is listed. Examples of small, medium, and large mammalian viruses (poliovirus, herpesvirus, and vaccinia virus, respectively) are included for comparison.

Proprietà generali dei virus



- Le particelle virali (**virioni**) sono formate da acido nucleico rivestito da un involucro proteico (**capside**). In alcuni virus è presente una membrana pericapsidica contenente lipidi e glicoproteine (**envelope**)
- Il genoma virale consiste di **DNA** o **RNA**
- Il genoma virale guida la sintesi delle componenti virali all'interno di una cellula ospite appropriata.
- I vari componenti dei virioni sono «assemblati» pertanto i virioni non replicano per divisione.

The Virion = viral particle



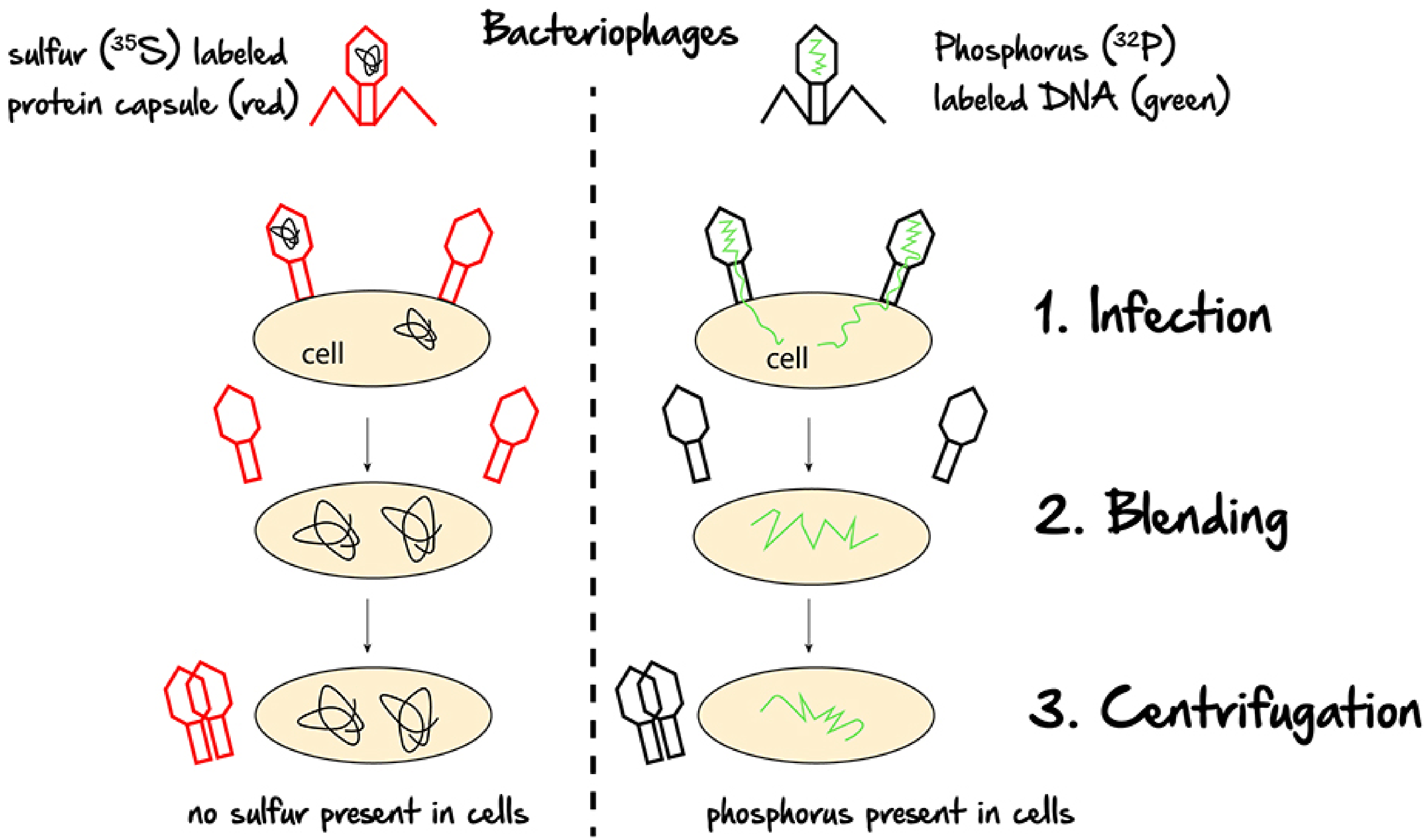
DNA or RNA contain the genetic information of viruses

Two seminal experiments:

Hershey And Chase with bacteriophages
Fraenkel-Conrat and Singer with TMV

The Hershey and Chase experiment

1952

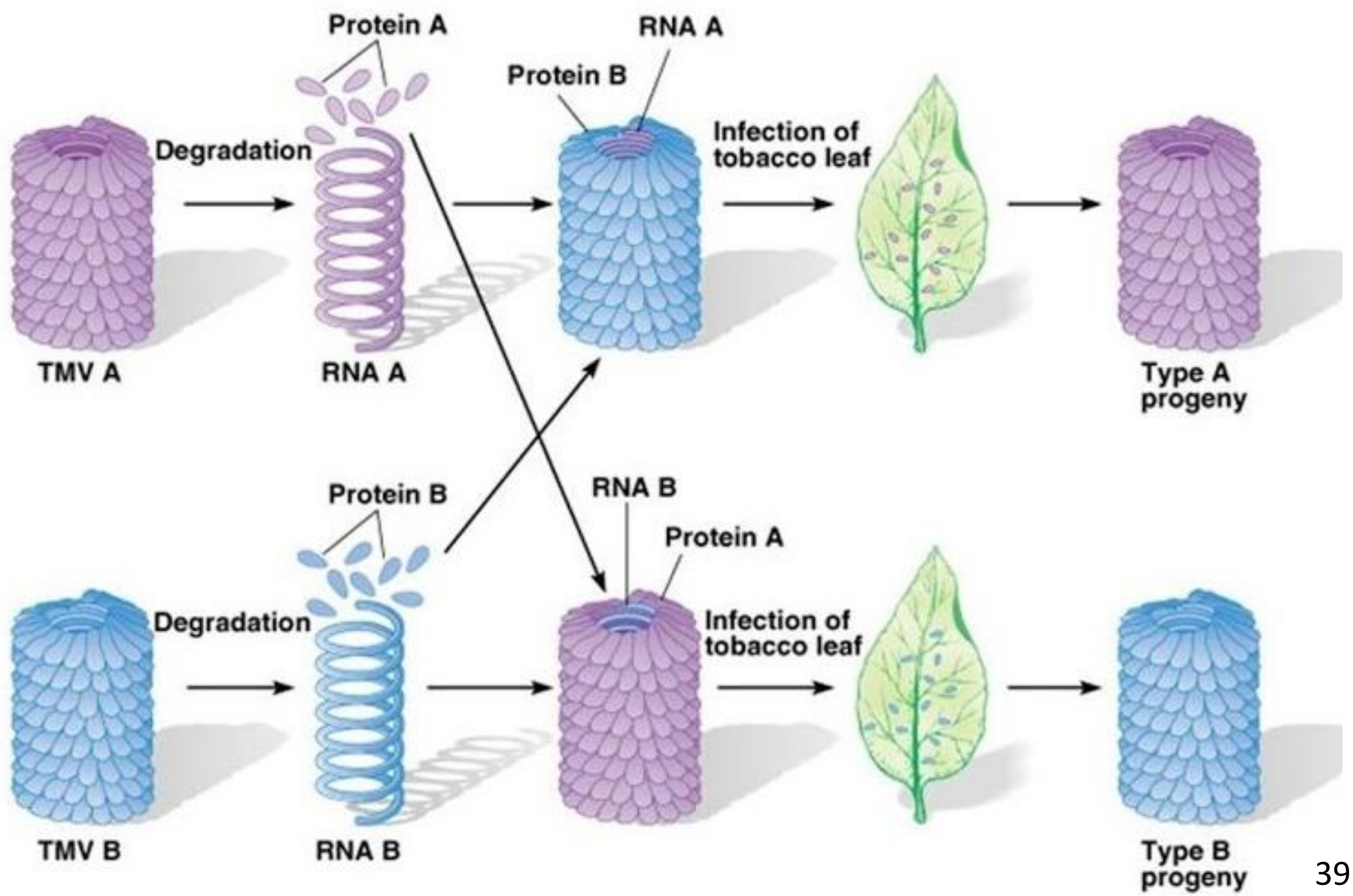


DNA (labelled with ^{32}P) is the genetic material of bacteriophage T2

The Fraenkel-Conrat and Singer experiment

1957

Demonstrated that RNA is the genetic material of TMV.



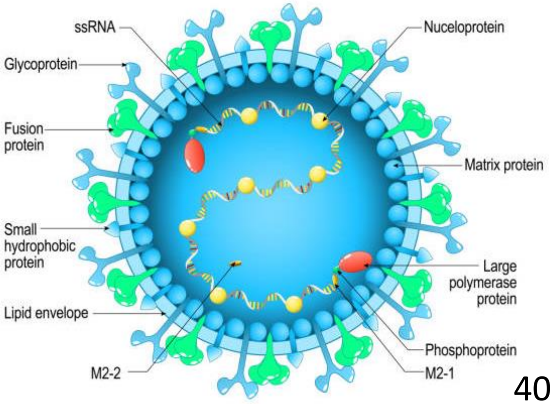
Viral proteins

Proteine strutturali: incorporate nelle nuove particelle virali come costituenti del capside o come strutture particolari presenti nell'envelope

Proteine strettamente associate agli acidi nucleici

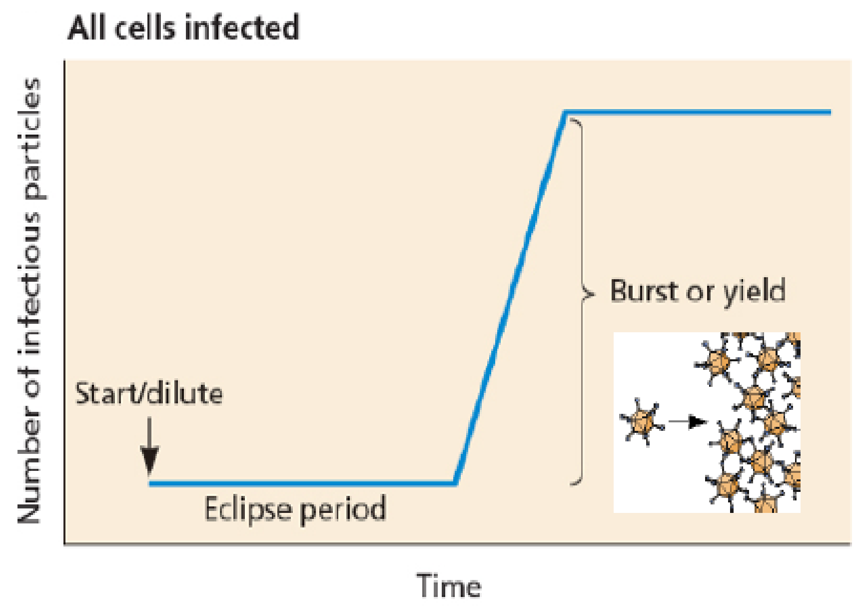
Proteine funzionali che permettono ad es. all'acido nucleico virale di replicarsi (DNA-o RNA-polimerasi)

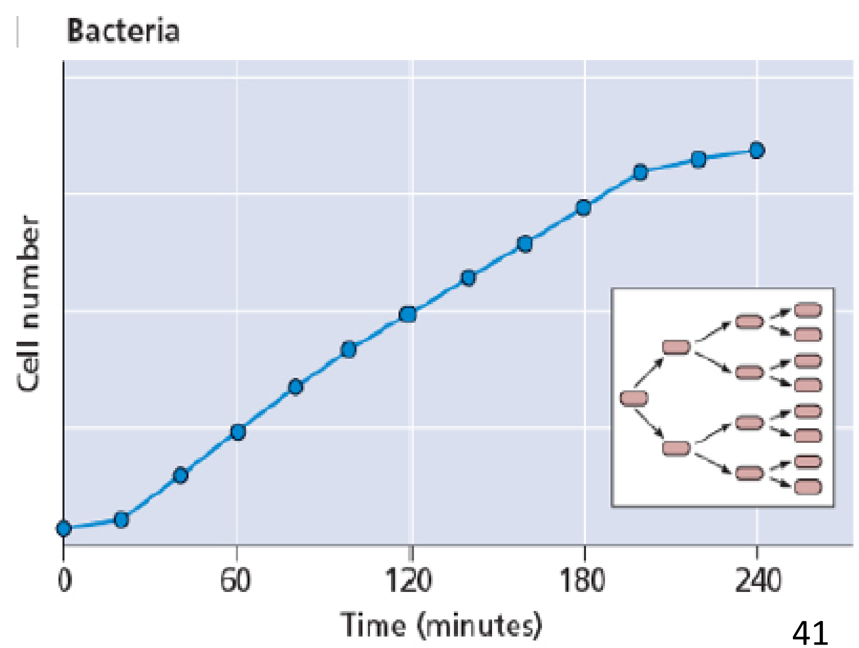
Proteine con funzione regolatoria che alterano alcune funzioni e strutture della cellula ospite



Viruses replicate by assembly of pre-formed components into many particles

Make the parts, assemble the final product





Not binary fission like cells

One-step growth curve

THE GROWTH OF BACTERIOPHAGE

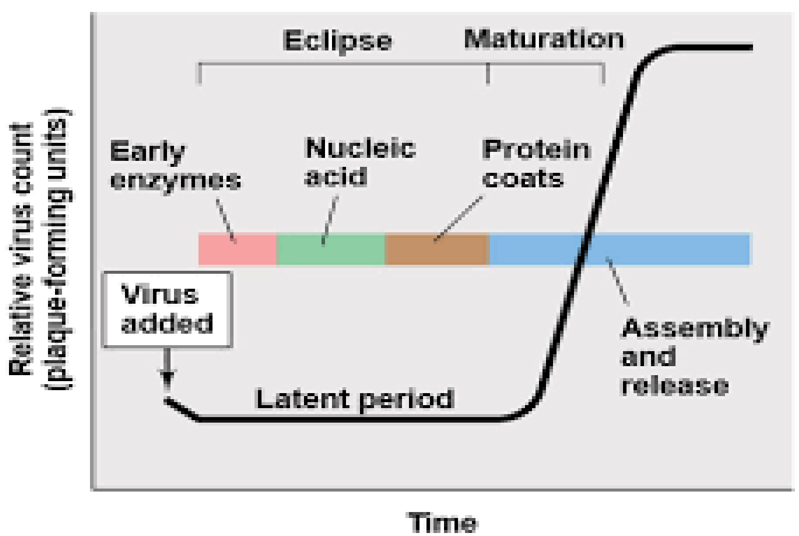
By EMORY L. ELLIS and MAX DELBRÜCK*

(*From the William G. Kerckhoff Laboratories of the Biological Sciences, California Institute of Technology, Pasadena*)

(Accepted for publication, September 7, 1938)

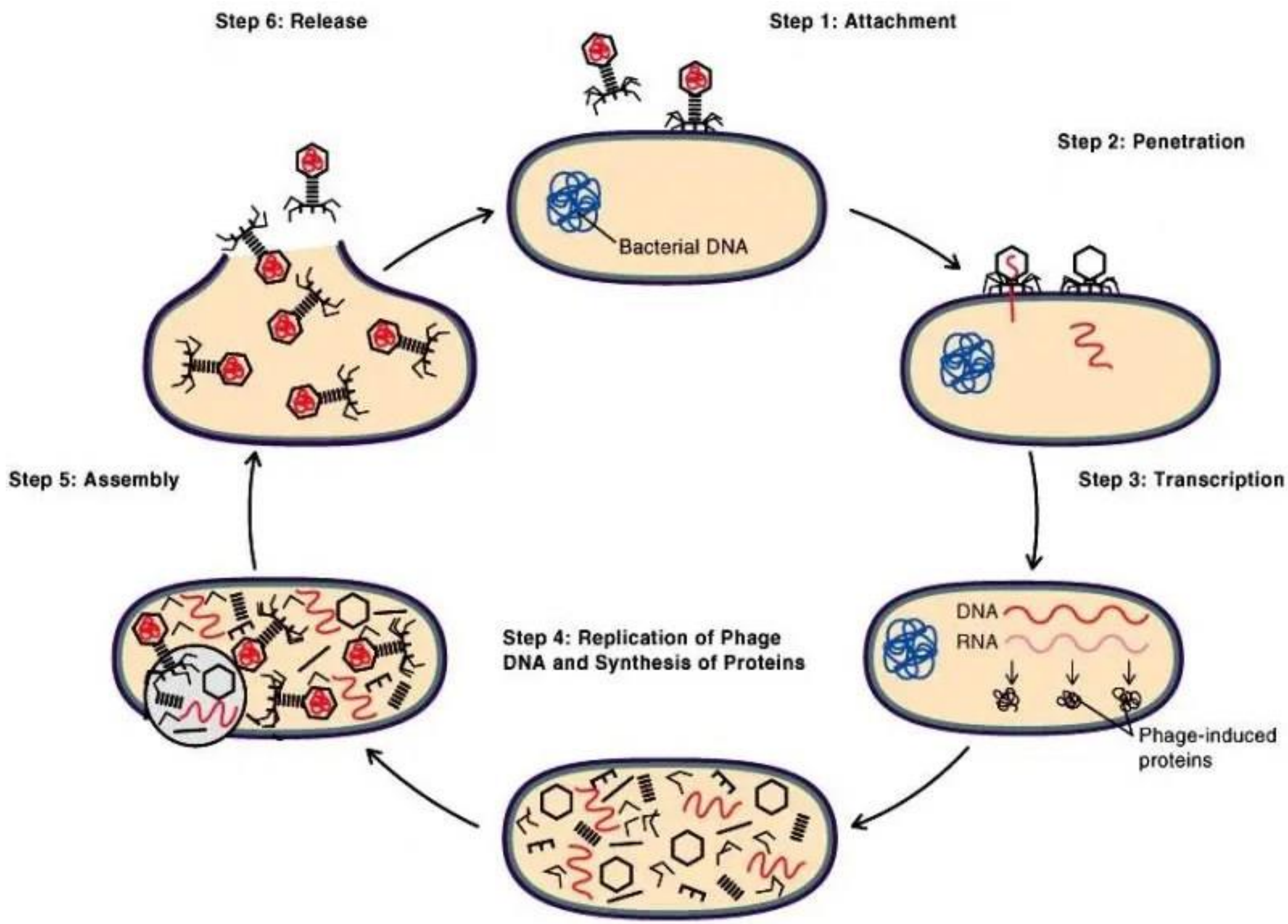
INTRODUCTION

Certain large protein molecules (viruses) possess the property of multiplying within living organisms. This process, which is at once so foreign to chemistry and so fundamental to biology, is exemplified in the multiplication of bacteriophage in the presence of susceptible bacteria.

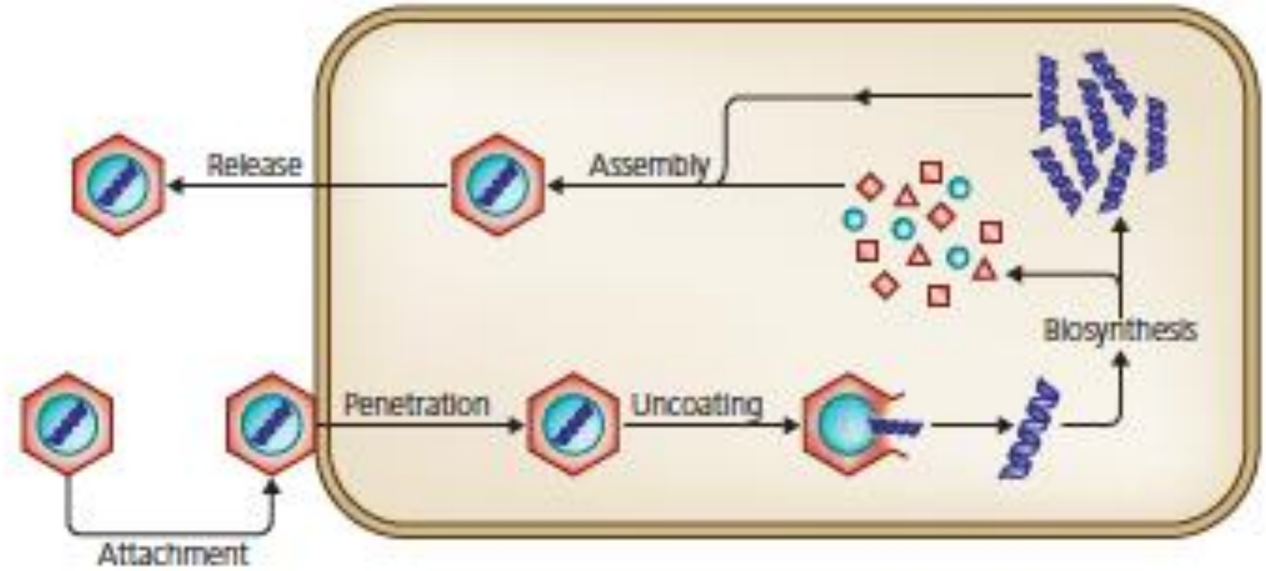


- A phage preparation is mixed with bacteria at a multiplicity of infection (m.o.i) of 10 infectious phages per cells, ensuring that all the cells are infected.
- At regular intervals cells and medium are separated and tested for infectious phages
- During the eclipse phase no infectious particles (the virus is uncoating)
- During the maturation the virus is assembled inside the cells
- The virus is then released (burst)

Replicative Cycle: bacteriophages

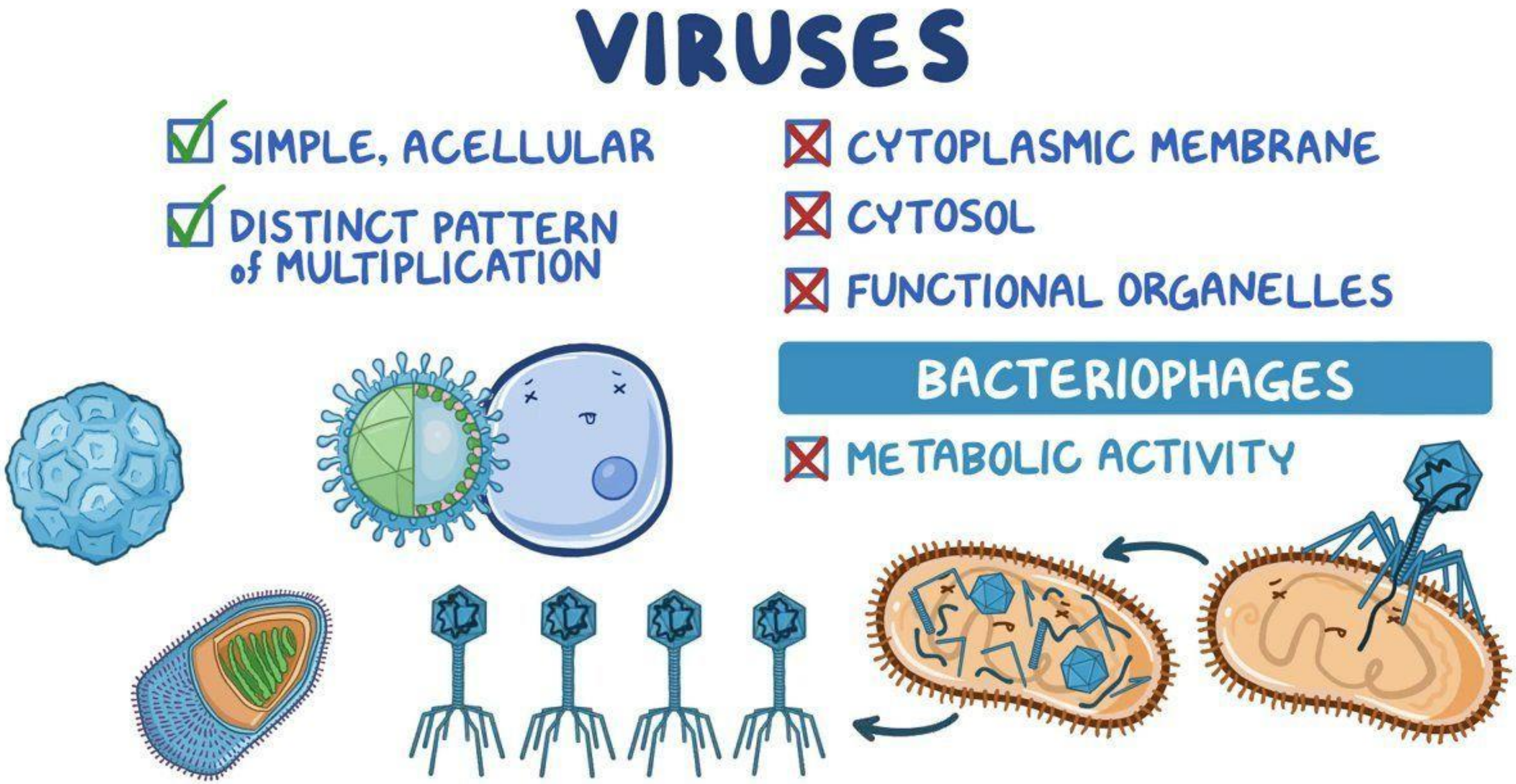


Replicative Cycle: animal viruses



Virus: proprietà distintive

Distinctive Properties of Viruses

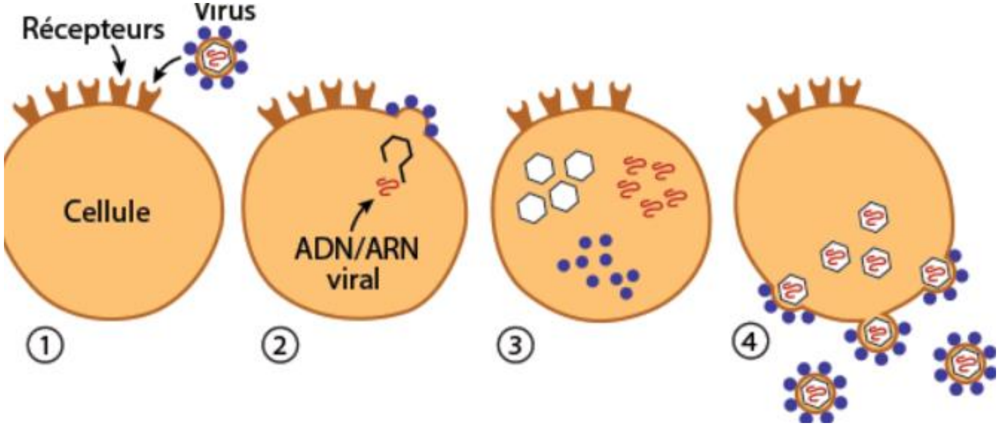


Viruses are insensitive to antibiotics.

Viruses are obligate intracellular parasites

Viruses can multiply only inside living cells:

- **hijack the machinery and metabolism of the host cell** for the synthesis of viral components
- need cellular enzymes to replicate their genome (DNA polymerase, RNA polymerase)
- use the cellular translation machinery to translate viral mRNA (cellular ribosomes, protease…)
- use energy produced by the host cell



Distinctive Properties of Viruses

- Viruses are **absolutely incapable of autonomous replication**—they cannot replicate outside of host cells.

- They **survive for a limited time** (from minutes to a few days depending on the virus type) in the extracellular environment, but **never replicate outside cells**.

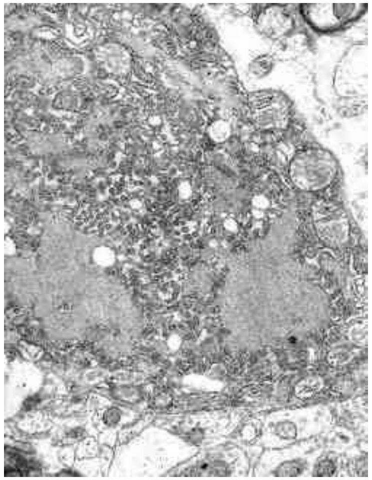
- As **obligate intracellular parasites**, viruses require not only nutrients produced by host cells, but especially the **transcription and translation systems** of those cells.

- They contain **essential enzymes** for their replication cycle (e.g., **polymerases**, **proteases**, etc.), while all other enzymes are provided by the host cell.

Virus: proprietà distintive

I virus attraversano i comuni filtri, sono invisibili al microscopio ottico (con l'eccezione di alcuni virus particolarmente grandi), ma visibili al microscopio elettronico.

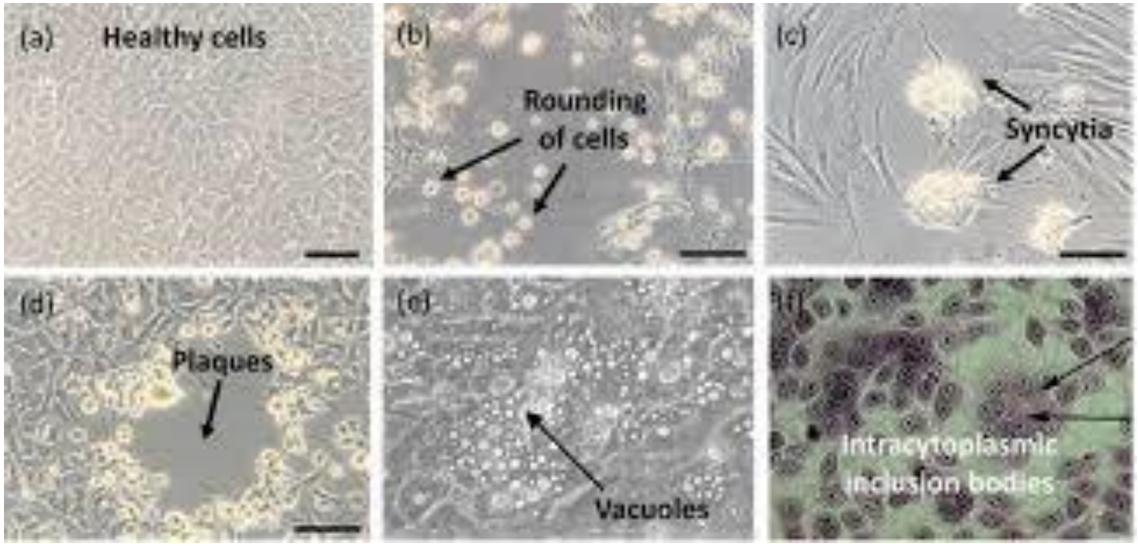
Determinano spesso, nelle cellule infettate, la presenza di corpi inclusi intranucleari o citoplasmatici.



Fotografia al M.E. con numerosi virus della rabbia ed i corpi di Negri, più grandi inclusioni cellulari tipiche dell'infezione di rabbia.

Distinctive Properties of Viruses

•They can be **cultured in vitro** using isolated eukaryotik cells or bacteria, depending on the virus type.



•Their **resistance to pH varies**, influencing their **pathogenicity**:

For example, **rhinoviruses** are destroyed at pH 3 (gastric pH ≈ 1), making them **non-pathogenic for the gastrointestinal tract**.

Other **picornaviruses** are resistant to gastric pH and thus **pathogenic in the gastrointestinal system** (e.g., **enteroviruses**).

Virus: proprietà distintive

I virus rappresentano un sistema altamente sofisticato di trasferimento genetico da cellula a cellula.

Tramite i virus, e' possibile modificare il corredo genetico (e quindi fenotipico) di una cellula, favorendone, quindi, l'acquisizione di nuovi caratteri.

Data questa loro caratteristica naturale, sono usati, nella manipolazione genetica, come vettori finalizzati al trasferimento di nuovi caratteri a cellule infettabili da un determinato virus.

Are viruses living organisms?

Se la vita è:
«la condizione di esseri che, caratterizzati da una forma precisa e da una struttura chimica particolare, hanno la capacità di conservare, sviluppare e trasmettere forma e costituzione chimica ad altri organismi.»

I virus rappresentano la forma vivente più semplice. Non hanno una compartimentazione di tipo cellulare.

BOX 1.8

DISCUSSION

Are viruses living entities? What can/can't they do?

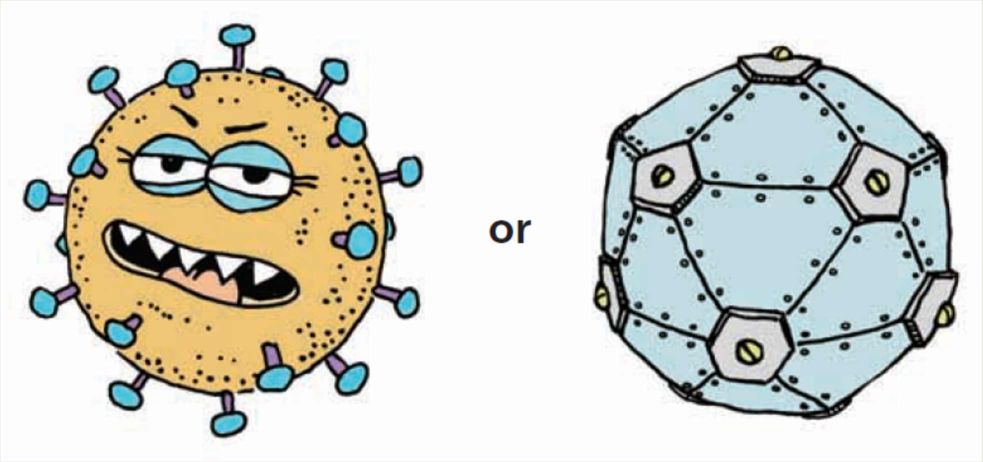
Viruses can be viewed as microbes that exist in two phases: an inanimate phase, the virion; and a multiplying phase in an infected cell. Some researchers have promoted the idea that viruses are organisms and that the inanimate virions may be viewed as "spores" that come "alive" in cells, or in factories within cells. This has long been a topic of intense discussion, stimulated most recently by the discovery of giant viruses such as the mimiviruses and pandoraviruses. Check out what the contemporary general public feels about this topic (http://www.virology.ws/are-viruses-alive/).

Apart from attributing "life" to viruses, many scientists have succumbed to the temptation of ascribing various **actions** and **motives** when discussing them. While remarkably effective in enlivening a lecture or an article, anthropomorphic characterizations are inaccurate and also quite misleading. Infected cells and hosts respond in many ways after infection, but viruses are **passive** agents, totally at the mercy of their environments. Therefore viruses cannot employ, ensure, synthesize, exhibit, display, destroy, deploy, depend, reprogram, avoid, retain, evade, exploit, generate, etc.

As virologists can be very passionate about their subject, it is exceedingly difficult to purge such anthropomorphic terms from virology communications. Indeed, hours were spent doing so in the preparation of this textbook, though undoubtedly there remain examples in which actions are attributed to viruses. Should you find them, let us know!

Bândea Cl. 1983. A new theory on the origin and the nature of viruses. *J Theor Biol* **105:**591–602.

Claverie JM, Abergel C. 2013. Open questions about giant viruses. *Adv Virus Res* **85:**25-56.

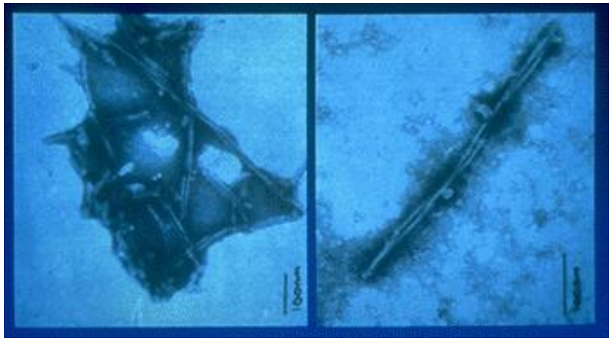


From Flint Principles of Virology

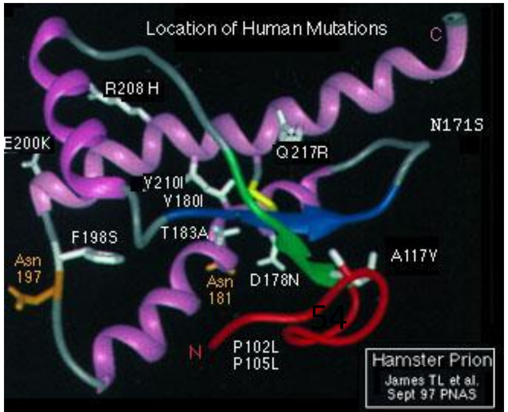
I virus sono, a tutti gli effetti, dei semplici aggregati macromolecolari forniti di, ed in grado di trasferire, informazioni genetiche.

Alcuni agenti infettanti subvirali (**viroidi**) sono costituiti da solo materiale genetico (RNA) senza guscio proteico. Altri (**satelliti**) hanno bisogno di un altro virus (helper) per replicare

Infine, i **prioni**, anche questi agenti infettanti di ancora più piccole dimensioni, sarebbero costituiti da soli frammenti glicoproteici autoreplicanti, senza acido nucleico. Alcuni di essi colpiscono il sistema nervoso, determinando malattie mortali tuttoggi incurabili (kuru, scrapie, malattia di Creutzfeld-Jacob). Sono al limite tra forma vivente e non vivente.



Electron micrograph of **PRION PROTEIN** (scrapie associated fibrils) Bar=100*nm*
(Coutesy of Dr. A.C. Scott of Central Veterinary Laboratory, UK)



Origine dei virus

Origine dei virus

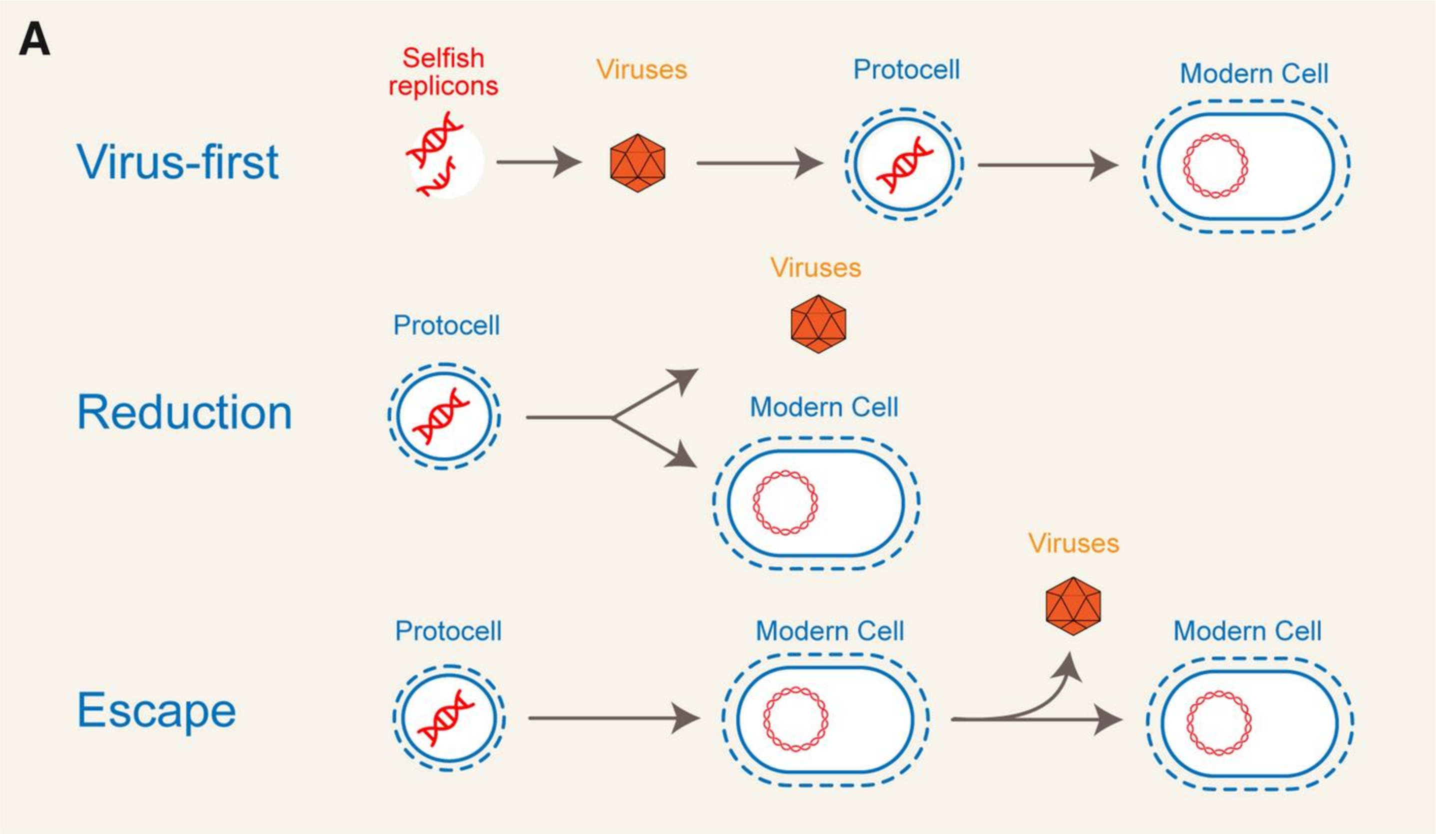
Three main theories on RNA and DNA viruses' origin (which are not mutually exclusive):

1. **Pre-cellular or virus-first:** viruses originated in the primordial RNA world
2. **Regressive or reduction:** viruses are regressed copies of cellular species that have shed those genes whose functions are provided by the host
3. **Progressive or Escape:** viruses evolved after the first cellular organisms as escaped genes that aquired capsid proteins and the ability to replicate

Evidences are present supporting the different theories, different viruses could have originated according to different theories or yet to be identified mechanisms

https://www.nature.com/scitable/topicpage/the-origins-of-viruses-14398218/#

Origine dei virus



Models of viral evolution. (A) Classic frameworks of viral evolution associate virus origins to the origin of the virion or its components. The *virus-first* hypothesis postulates ancient origins of viruses that preceded cellular life. The *reduction* hypothesis suggests that the origin of cells preceded that of viruses, with DNA viruses evolving via reduction in their genomes. The *escape* hypothesis deems viruses as selfish genetic elements that escaped control of cellular machinery and 'pickpocketed' genes via Horizontal Gene Transfer

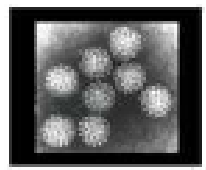
Mughal, F., Nasir, A. & Caetano-Anollés, G. The origin and evolution of viruses inferred from fold family structure. *Arch Virol* **165**, 2177–2191 (2020)

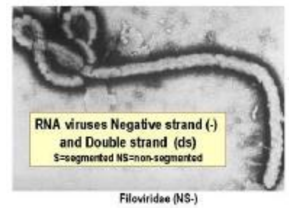
Viral Structure

virus

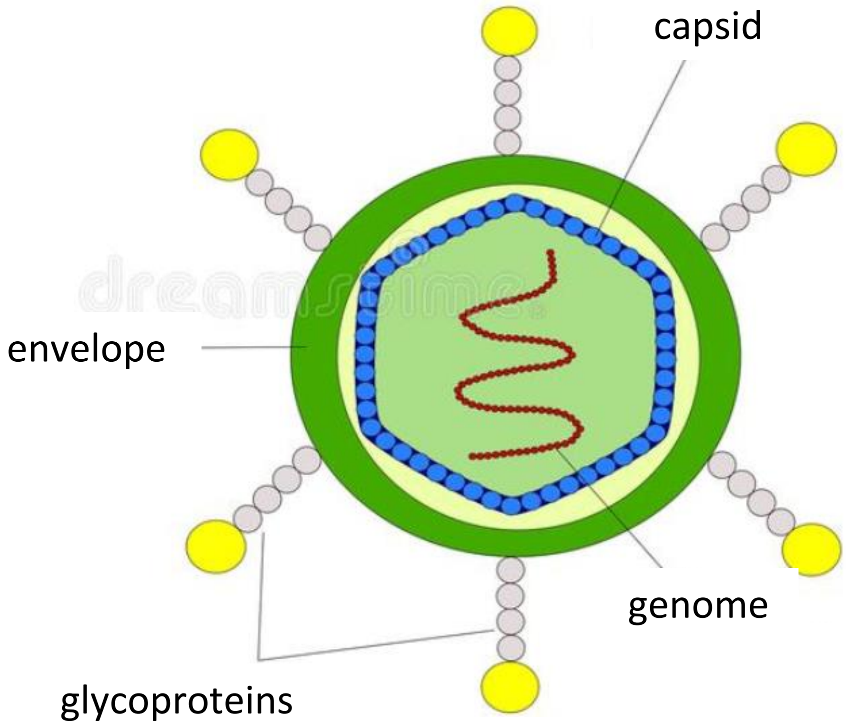
- **An extracellular dissemination form** : free, inert, distinctive structure

  = **viral particle or virion**





- **An intracellular parasite form**: lost of the distinctive structure
  > allowing the virus multiplication and/or persistance



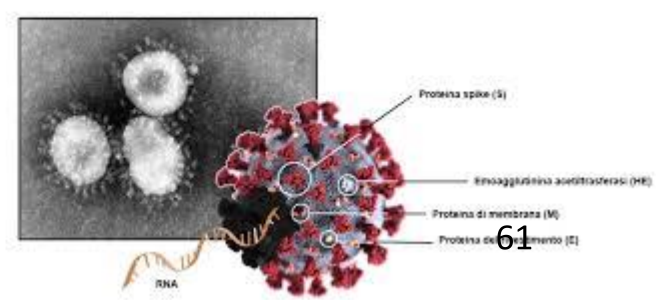
Viral particles
Virion's architecture

= extracellular dissemination of the virus

- not cells ➔ **acellular structure**
- genetic material : 1 or several nucleic acid molecules (DNA or RNA) ➔ **viral genome**
- a protective protein coat ➔ **viral capsid**
- genome + capsid = **nucleocapsid**
- some viruses : nucleocapsid surrounded by an envelope (+/- protein matrix) ➔ **enveloped virus**
- viruses without envelope ➔ **non-enveloped virus = naked virus**

Viral components

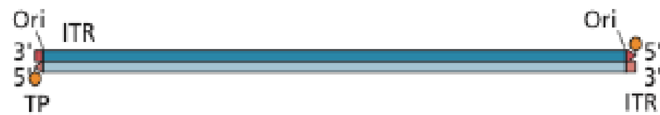
- **Viral genome**: RNA or DNA
- **Capsid**: a protein coat that surrounds and protects the nucleic acid. It's made up of smaller protein subunits called **capsomers**.
- **Envelope**: an outer layer, present in some viruses, that is derived from the host cell's membrane. It often contains glycoproteins that help the virus attach to and enter new host cells.
- **Nucleocapsid:** consisting of the nucleic acid and capsid
- **Virion:** viral particle



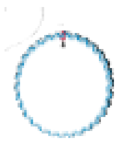
Viral genome

Viral DNA or RNA genomes are structurally diverse

- Linear

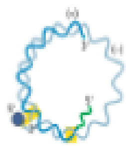


- Circular

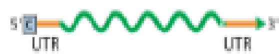


- Segmented

- Gapped



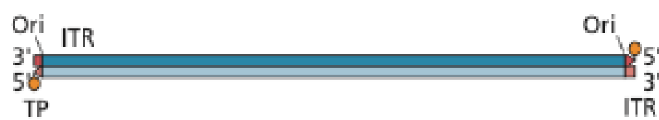
- Single-stranded (+) strand



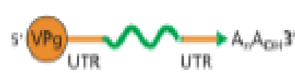
- Single-stranded (-) strand

- Single stranded, ambisense

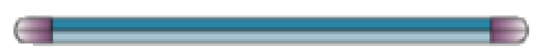
- Double-stranded



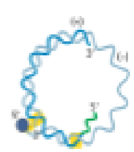
- Covalently attached proteins



- Cross-linked ends of double-stranded DNA



- DNA with covalently attached RNA



Genoma dei virus

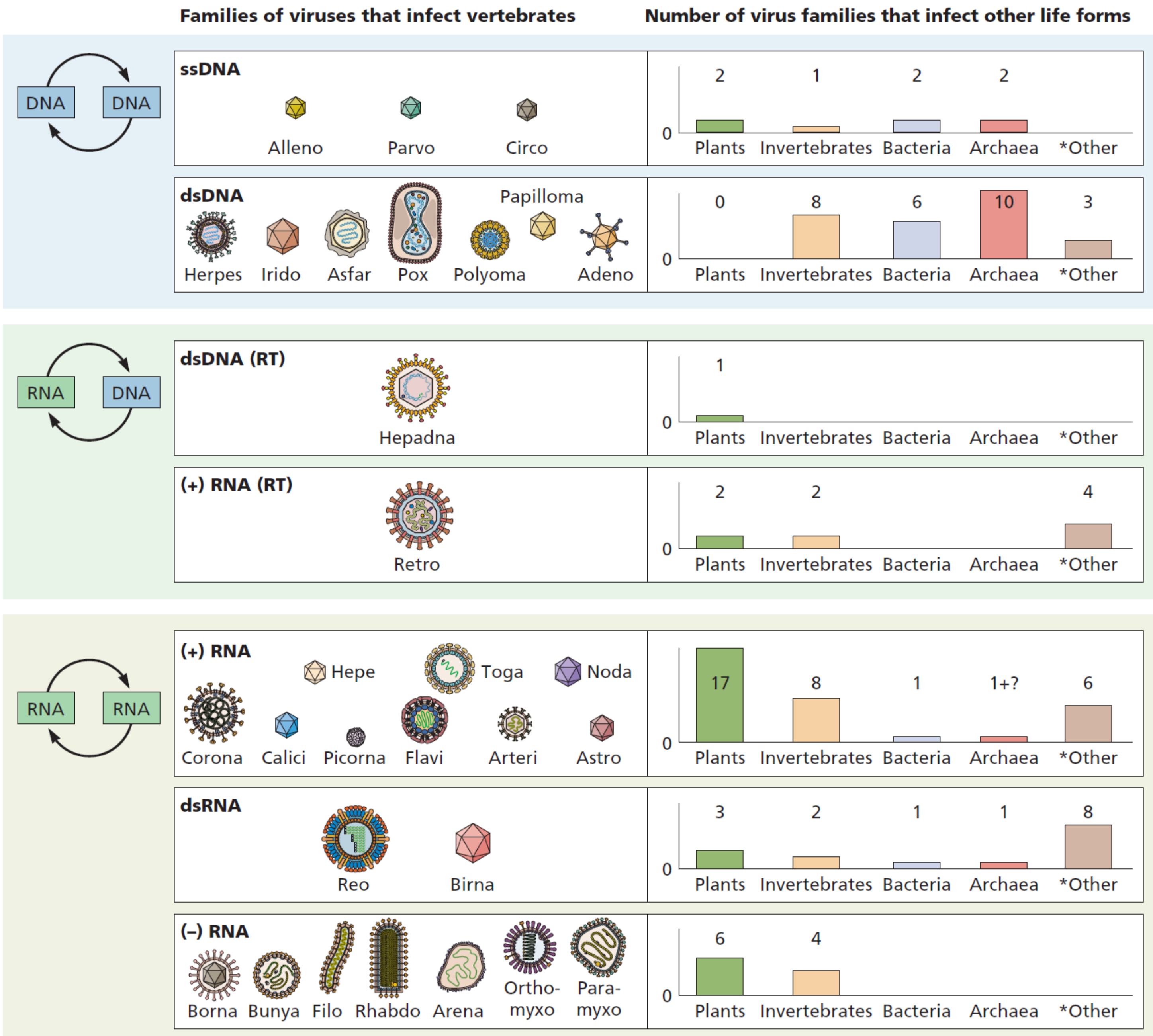
Virus a DNA: tra questi, quasi tutti i virus animali contengono DNA a doppio filamento, con l'eccezione di *Parvoviridae* (virus adeno-associati), *Circoviridae ed Anelloviridae*.

Genoma dei virus

Virus a RNA: quasi tutti i virus a RNA contengono RNA a singolo filamento, con l'eccezione dei *Reoviridae* (p.e. *rotavirus*) che contengono RNA a doppio filamento.

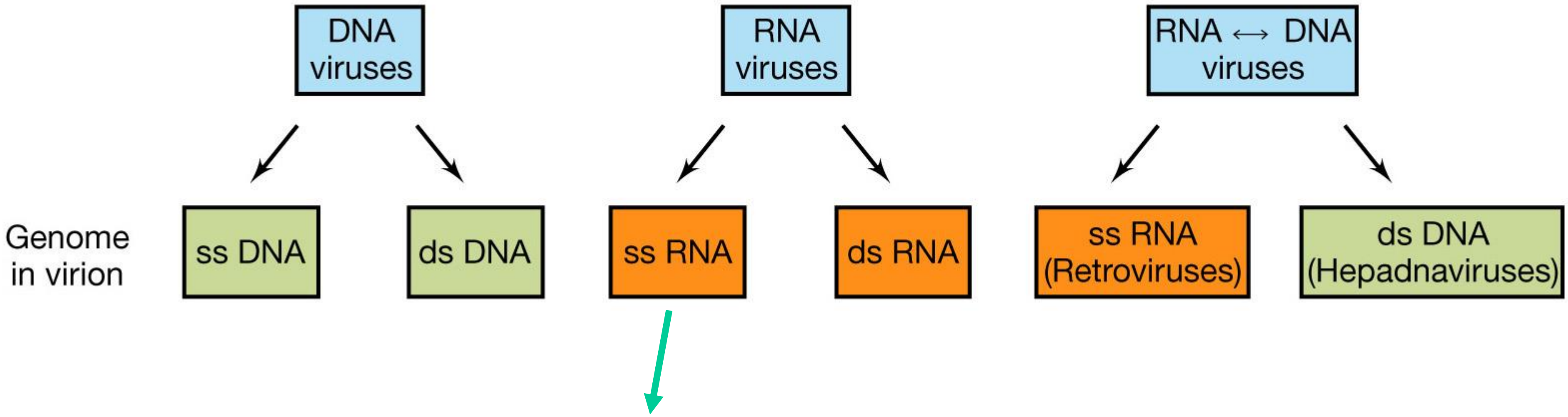
Cellular and Viral Polymerases

Type	Template → Product	Function
DNA-dependent DNA-Polymerase	DNA → DNA	Replication
DNA-dependent RNA-Polymerase	DNA → RNA	Transcription
RNA-dependent RNA-Polymerase	RNA → RNA	Replication and transcription of RNA-viruses
RNA-dependent DNA-Polymerase	RNA → DNA	Reverse transcription



*Algae, fungi, yeasts, and protozoa

Genome architecture



Virus con RNA a **polarità positiva (+)** che può fungere nella cellula direttamente da RNA messaggero.

Virus con RNA a **polarità negativa (-)** che funge da stampo per la sintesi dell’RNA messaggero- questi virus <u>hanno l’enzima RNA polimerasi RNA dipendente associato al virione</u>.

I retrovirus hanno due molecole di RNA (+): sono diploidi

Genome architecture

Virus con genoma ad RNA a filamento negativo: cioè genomi con polarità opposta a quella dell’RNA messaggero.

Alcune famiglie hanno genoma monopartito, ordine dei *Mononegavirales*; altre hanno un genoma segmentato (*orthomyxoviridae* con 8 o 7 segmenti, *arenaviridae* con 2 segmenti e *bunyaviridae* con 3 segmenti).

Queste ultime due famiglie sono uniche in quanto possiedono un genoma definito **ambisenso** (cioè un genoma contenente RNA a polarità sia + che -)