BMM 0160 – Microbiologia Básica para Farmácia

Módulo de Virologia:

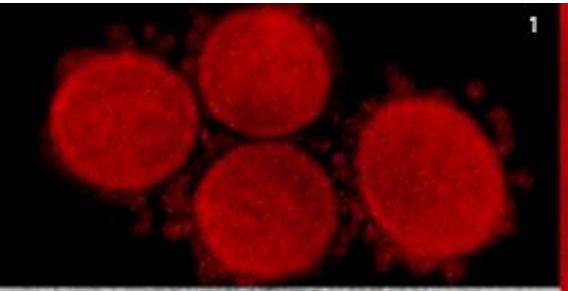
Profa. Patricia C. B. Beltrão Braga

Bibliografia

1. Trabulsi, L.R et al Microbiologia. 4a edição. 2004.
2. Brock, Madigan, Martinko, Parker. Biology of Microorganisms. 9a edição. 2000.
3. **Fields, B.N. Virology. 2a edição. 1990**
4. **Principles of Virology, Flint; Raccanielo; Rall; Skalka. 4th Edition, 2015.**

Introdução à Virologia

PROPRIEDADES GERAIS DOS VÍRUS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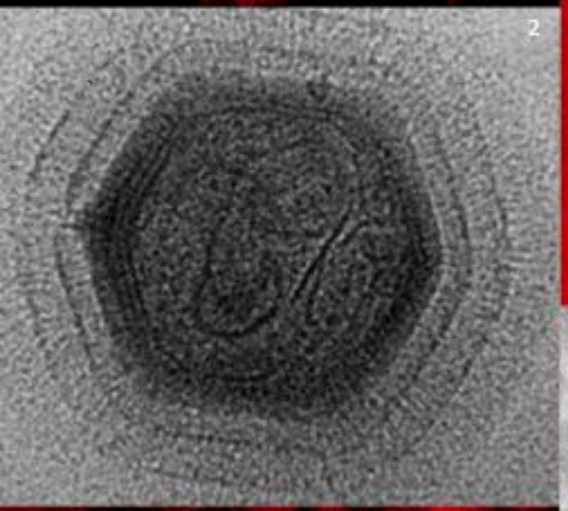
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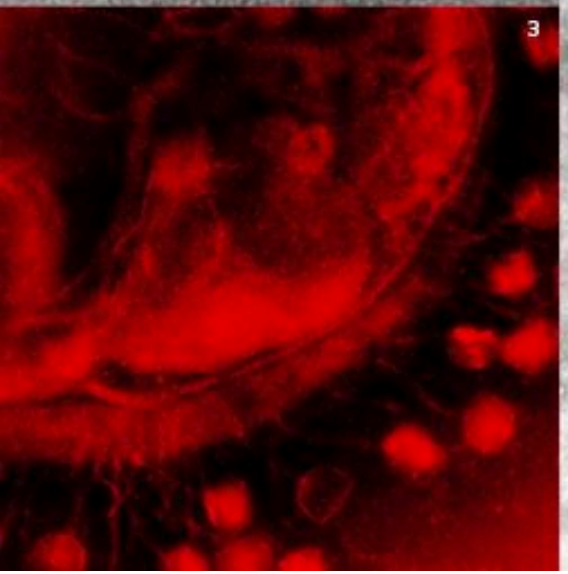
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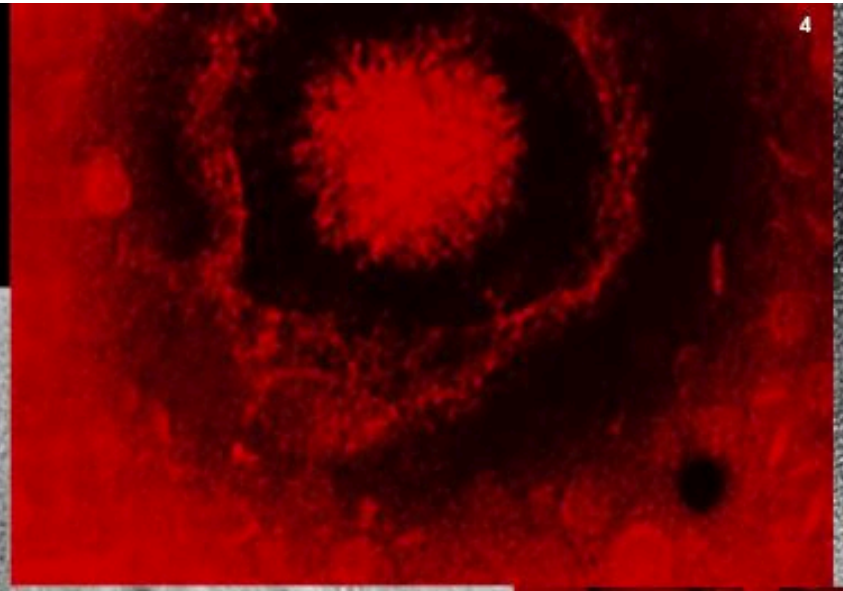
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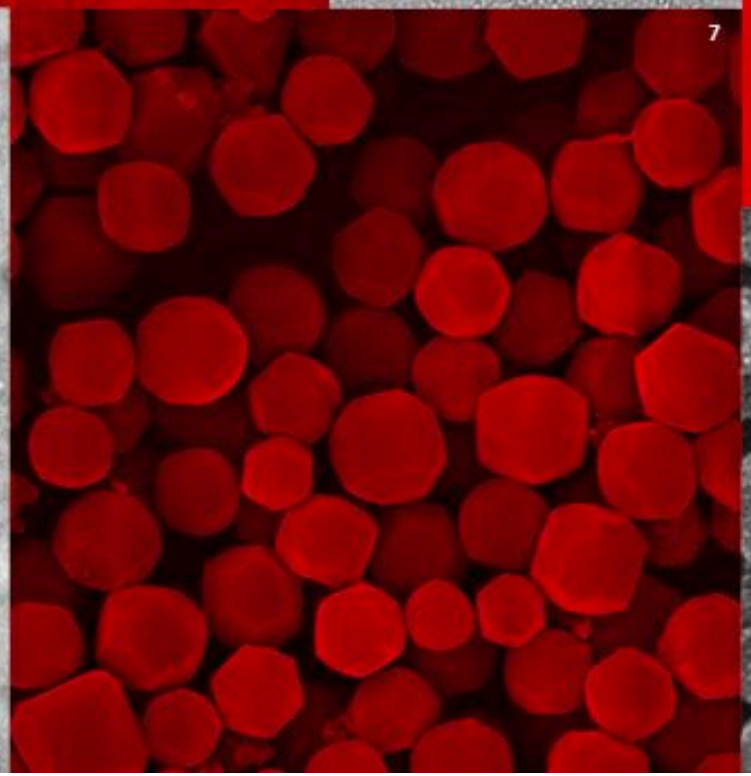
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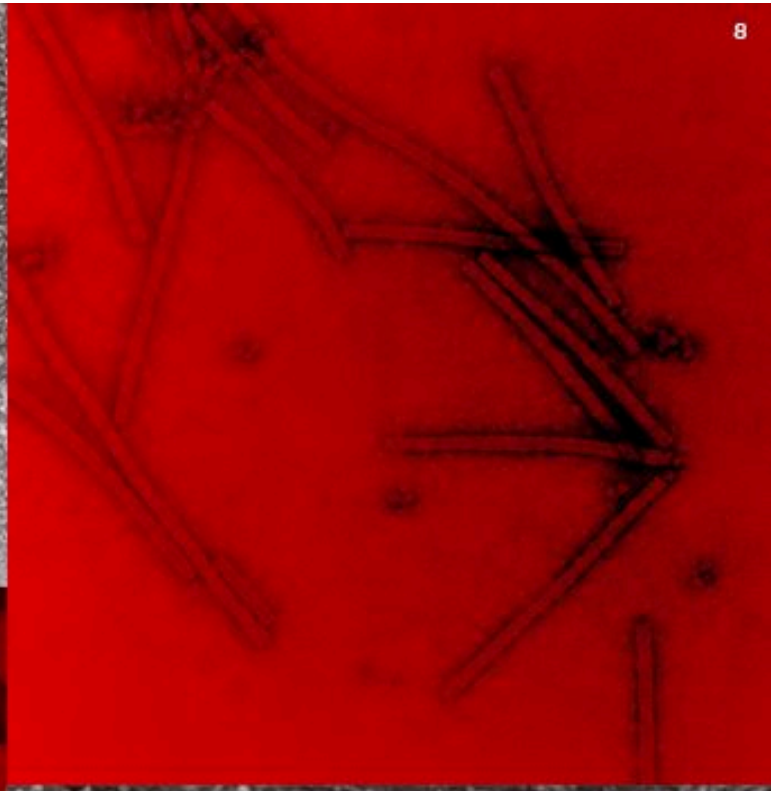
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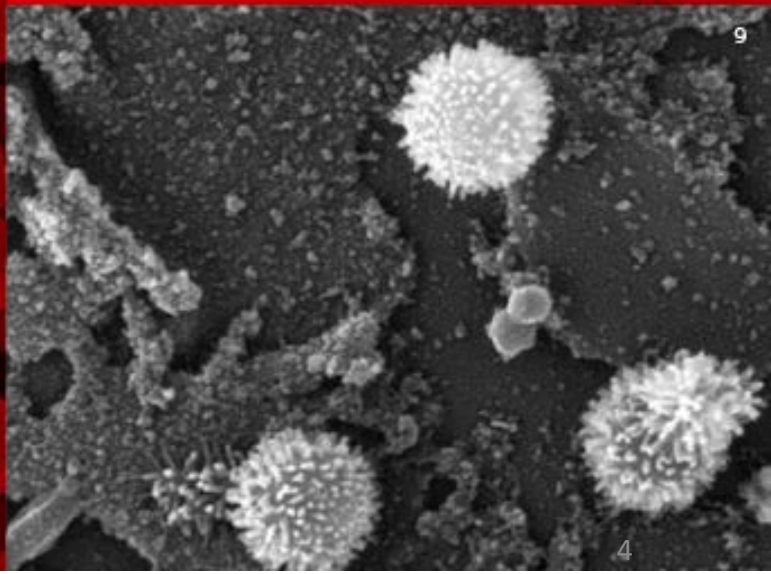
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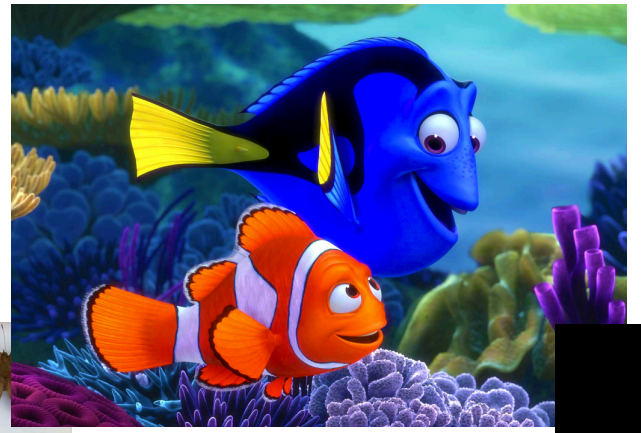
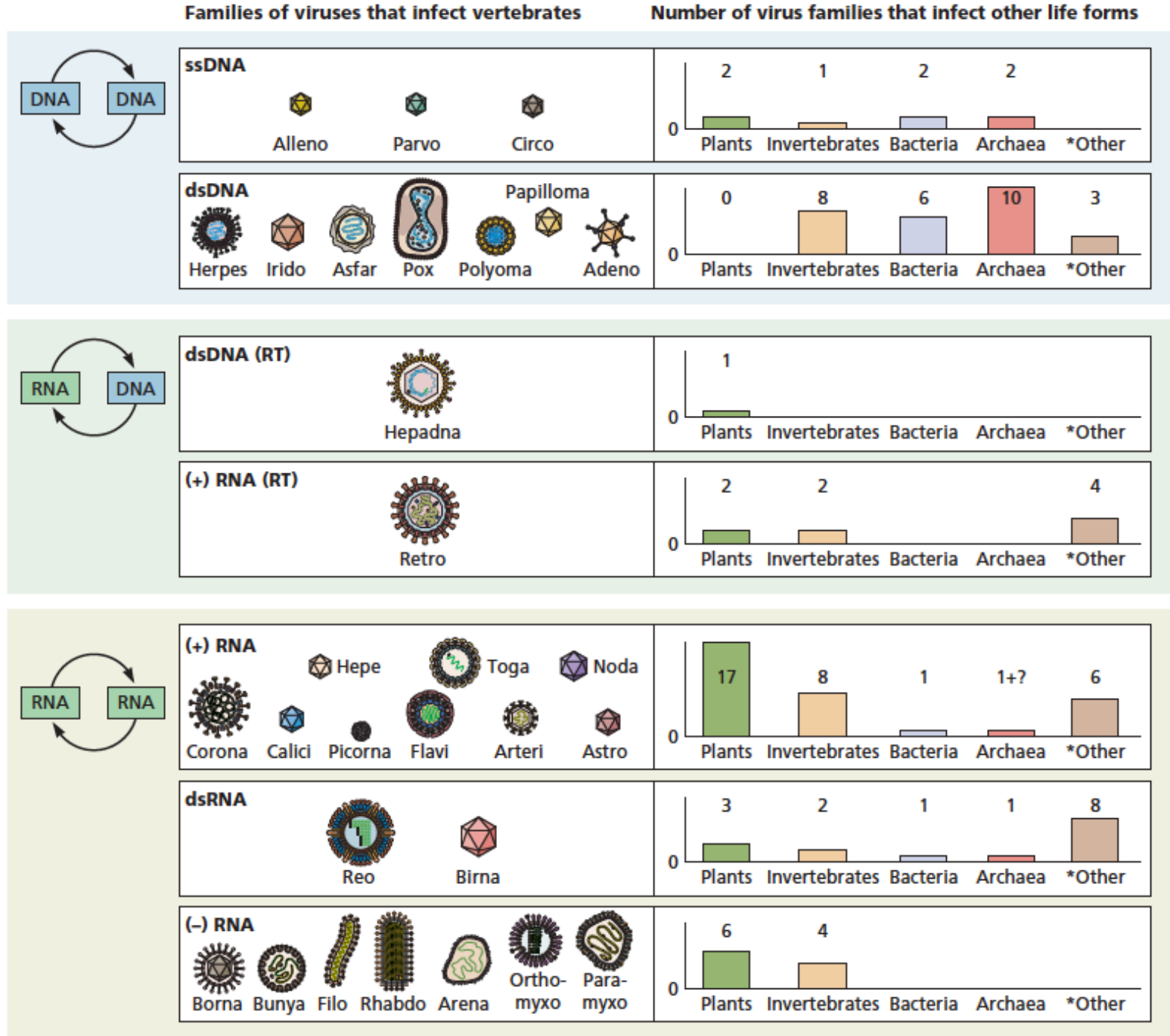
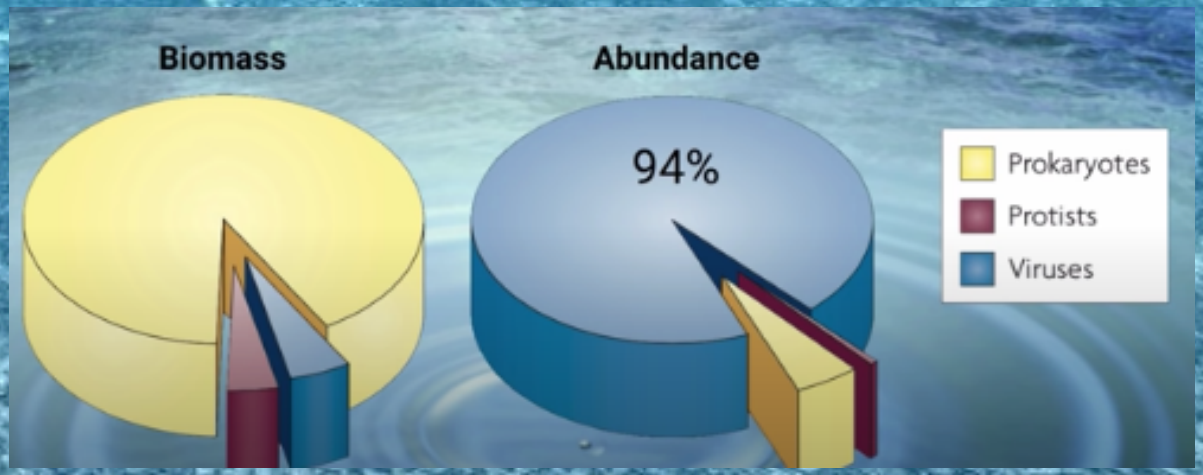
Vírus vivem no nosso organismo de maneira harmoniosa a milhares de anos

- Presentes em todas as formas de vida
- Nós comemos e bebemos bilhões de partículas virais
- Vírus são partes do nosso material genético




Families of viruses that infect vertebrates
Number of virus families that infect other life forms
DNA
DNA
ssDNA
Alleno
Parvo
Circo
2
1
2
2
0
Plants
Invertebrates
Bacteria
Archaea
*Other
dsDNA
Papilloma
Herpes
Irido
Asfar
Pox
Polyoma
Adeno
0
8
6
10
3
RNA
DNA
dsDNA (RT)
Hepadna
1
(+) RNA (RT)
Retro
2
2
4
RNA
RNA
(+) RNA
Hepe
Toga
Noda
Corona
Calici
Picorna
Flavi
Arteri
Astro
17
8
1
1+?
6
dsRNA
Reo
Birna
3
2
1
1
8
(–) RNA
Borna
Bunya
Filo
Rhabdo
Arena
Ortho-myxo
Para-myxo
6
4
*Algae, fungi, yeasts, and protozoa

Existem mais vírus em um litro de água do mar do que pessoas no mundo!

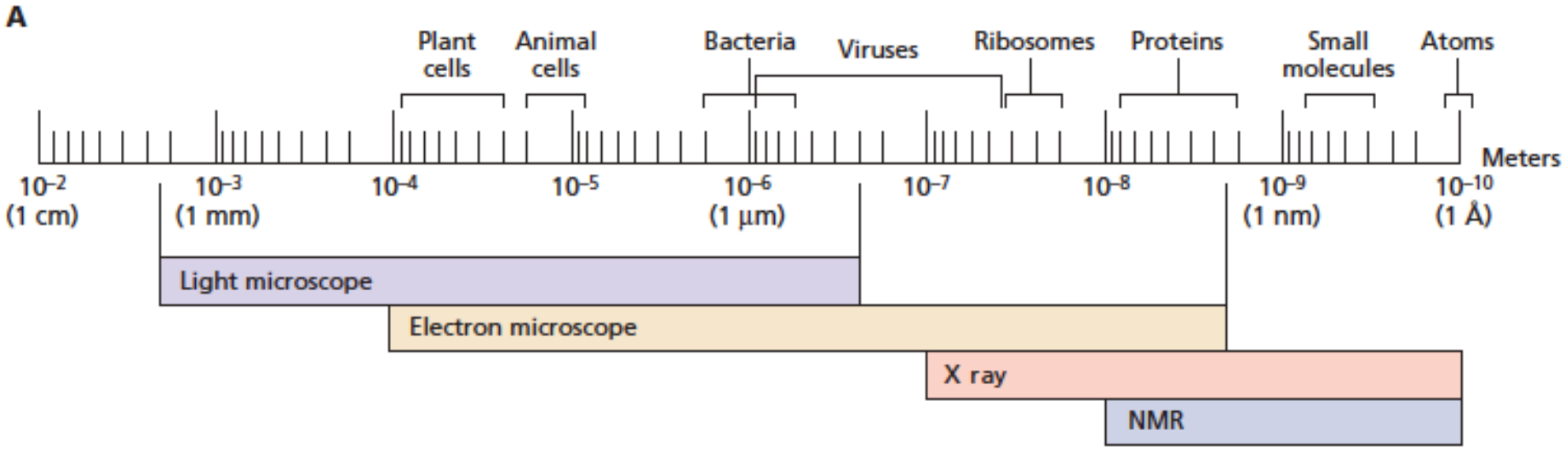


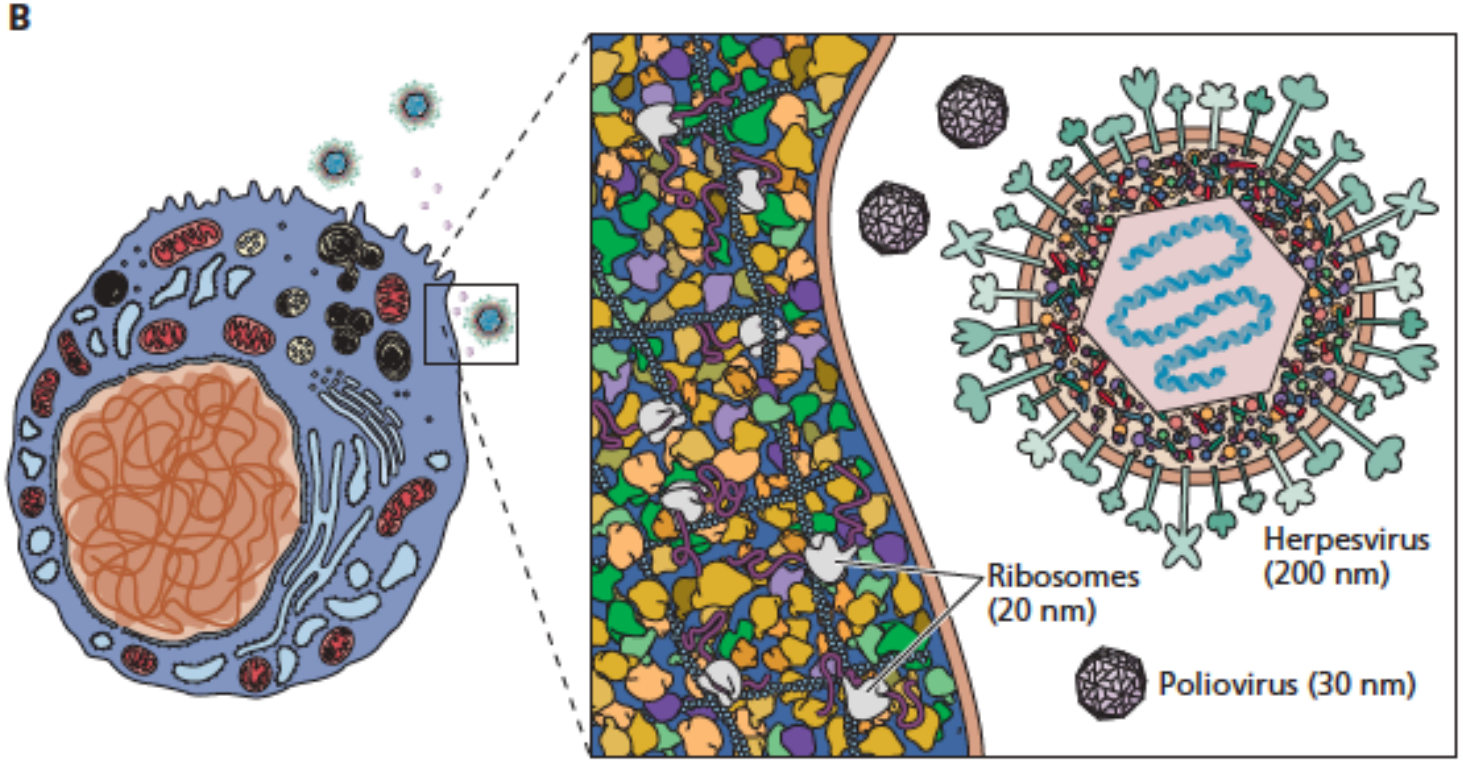
Baleias: comumente infectadas por Caliciviridae: 10^{13} partículas de vírus por dia

<u>Corpo Humano</u>
Células: 10^{13}
Bactérias: 10^{14} (10x)
Vírus: 10^{15} (100x)

CONCEITO: o que são os vírus?

- Os vírus são microrganismos de grande simplicidade:
  - pequenos, de 20 a 300 nm de diâmetro


A
Plant cells
Animal cells
Bacteria
Viruses
Ribosomes
Proteins
Small molecules
Atoms
Meters
10–2 (1 cm)
10–3 (1 mm)
10–4
10–5
10–6 (1 µm)
10–7
10–8
10–9 (1 nm)
10–10 (1 Å)
Light microscope
Electron microscope
X ray
NMR


B
Herpesvirus (200 nm)
Ribosomes (20 nm)
Poliovirus (30 nm)

CONCEITO: o que são os vírus?

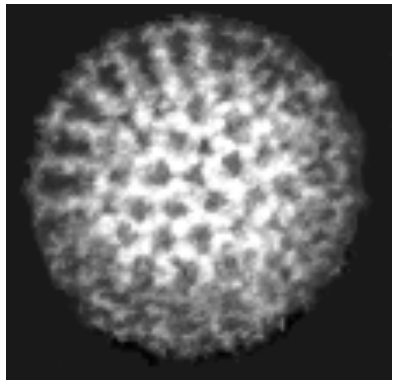
- Os vírus são microrganismos de grande simplicidade:
  - pequenos, de 20 a 300 nm de diâmetro
  - possuem apenas um tipo de ácido nucléico (RNA ou DNA)
  - desprovidos de estrutura celular
  - não crescem, não metabolizam
  - não sofrem divisão
  - inertes fora de células vivas
  - são parasitas intracelulares obrigatórios.

CONCEITO

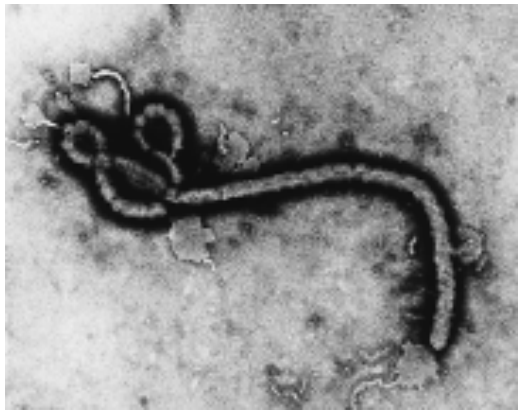
Os vírus podem ser definidos como organismos acelulares, cujos genomas são replicados, obrigatoriamente, no interior de uma célula hospedeira.

Com base no seu código genético e utilizando parte do maquinário metabólico celular, sintetizam os seus componentes (proteínas e ác. nucléico) que se agrupam formando novas partículas (virions).

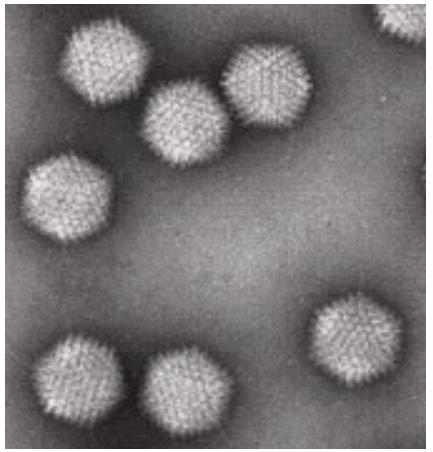
Os novos vírions serão liberados da célula hospedeira e irão infectar novas células, perpetuando a espécie.



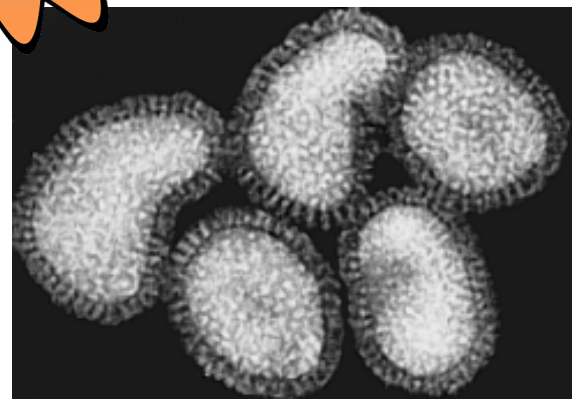
rotavírus



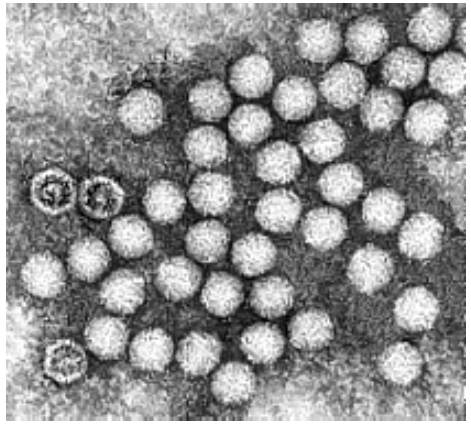
vírus Ebola



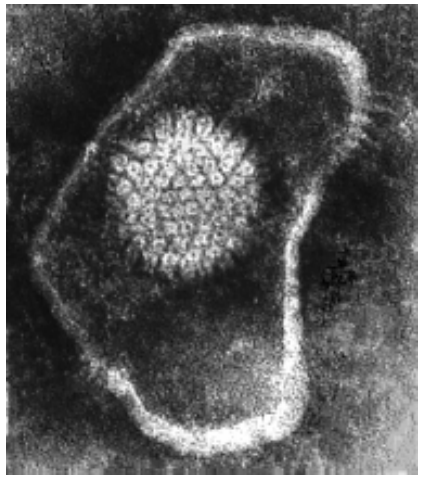
adenovírus



vírus influenza



poliovírus



vírus herpes

HISTÓRICO

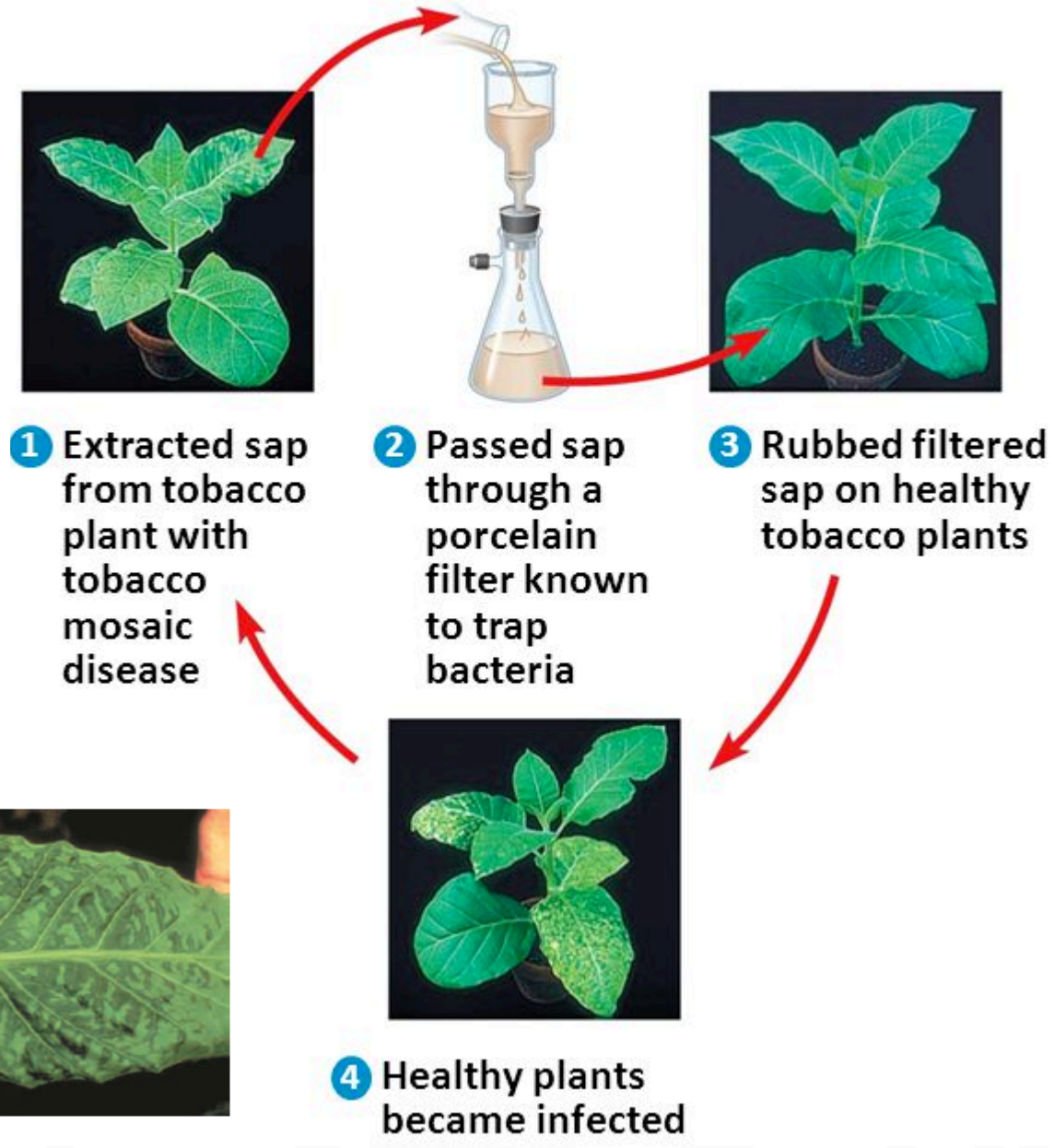
Dmitri Iwanowski
1864-1920

- A virologia teve seu início no final do século XIX, com o reconhecimento da existência de agentes infecciosos capazes de passar através de filtros que retinham bactérias.

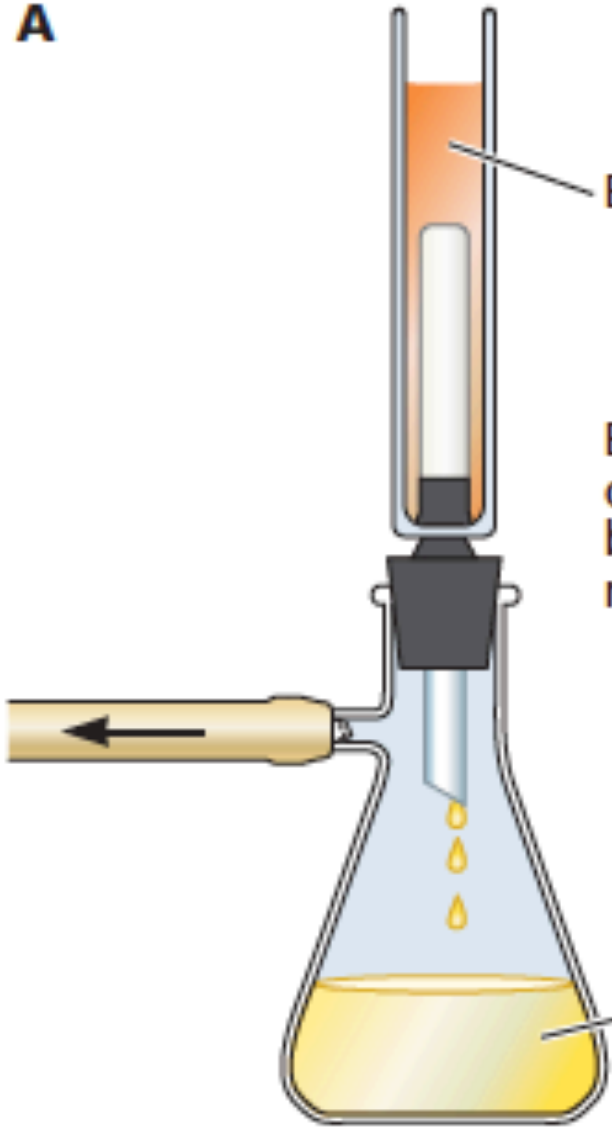
- A primeira descrição do vírus foi feita por Dmitri Iwanowski que, em 1892, referiu que o agente da doença do “mosaico do tabaco”, poderia passar livremente através dos filtros: definição de vírus como “agentes filtráveis”

- Ao utilizar filtrados de plantas doentes como inóculo em plantas sadias e susceptíveis, houve o surgimento da doença

Filtração de extrato de plantas contaminadas com a doença do mosaico do tabaco utilizando filtros bacteriológicos (vermelho), os vírus passam junto com o filtrado para o frasco.



A



Bacteria + virus

Berkefeld filters have three grades of porosities, two of which hold back all bacteria. These filters are made of diatomaceous earth.

Virus

B

HISTÓRICO

Wendell Meredith Stanley
The Nobel Prize in Chemistry 1946

Prize motivation: "for their preparation of enzymes and virus proteins in a pure form."

- Marco fundamental: Wendell Stanley (1940) descobriu que o vírus do mosaico do tabaco podia ser cristalizado (assim como os sais inorgânicos e proteínas moleculares) e que os cristais inanimados, podiam produzir doença em plantas sadias.

- A controvérsia: organismos vivos ou não?

An Egyptian stele, or stone tablet, from the 18th dynasty (1580–1350 b.c.) depicting a man with a withered leg and the “drop foot” syndrome characteristic
of polio.

Livro: Flint, 2015

O vírus é um ser vivo?

Organismo acelular

- ✓ “ Um organismo é uma unidade elementar de uma linhagem com uma história evolutiva individual.” (Luria, 1978)
- ✓ “acelular = sem estrutura de célula (protoplasma circundado por membrana).”

Ser vivo

- ✓ Apresenta capacidade de: nutrição, respiração, excreção, irritabilidade, movimento,crescimento e reprodução.
- ✓ Apresenta capacidade de: estocar e replicar informações genéticas e potencial de atividade enzimática.
- ✓ Vida pode ser um fenômeno associado com a replicação de sistemas de informação auto-codificados.

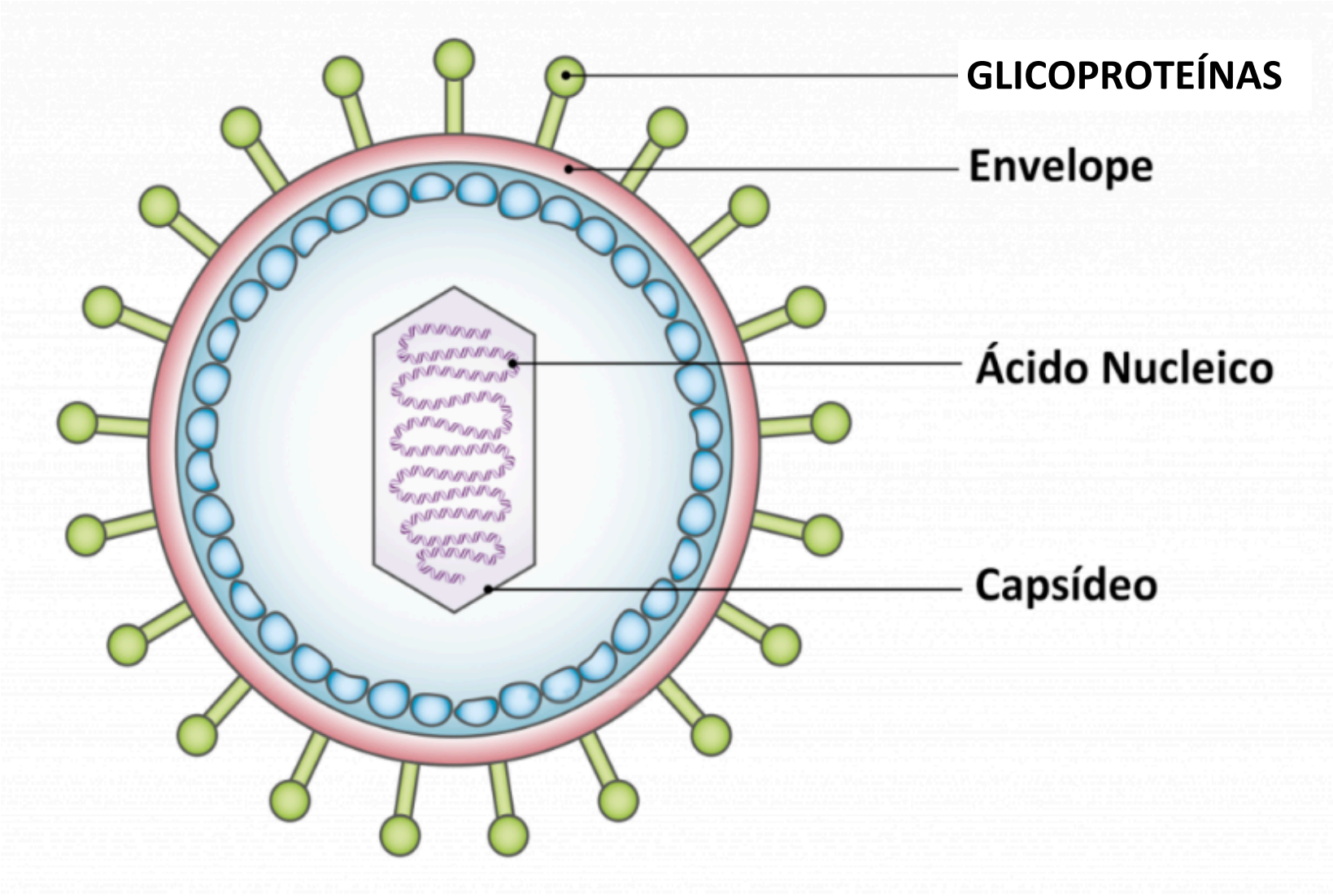
ORIGEM

- Seriam componentes celulares que adquiriram um invólucro proteico e tornaram-se autônomos (involução)?

- Seriam formas primitivas de vida ou moléculas primitivas auto-replicativas?

- Não possuem origem única, provavelmente evoluíram com seus hospedeiros.

ESTRUTURA DA PARTÍCULA VIRAL



ESTRUTURA

ácido nucléico protegido pelo capsídeo viral.

Nucleocapsideo:

Ácido nucleico com o envoltório protéico

Proteínas :

- protômeros
- capsômeros
- capsídeo

Envoltório:

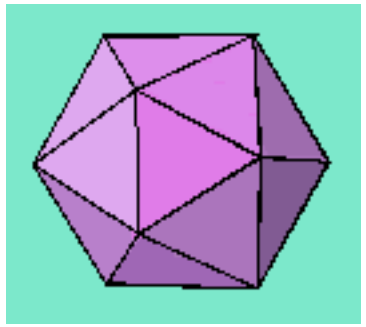
membrana lipo-protéica:

lipídeos - da célula

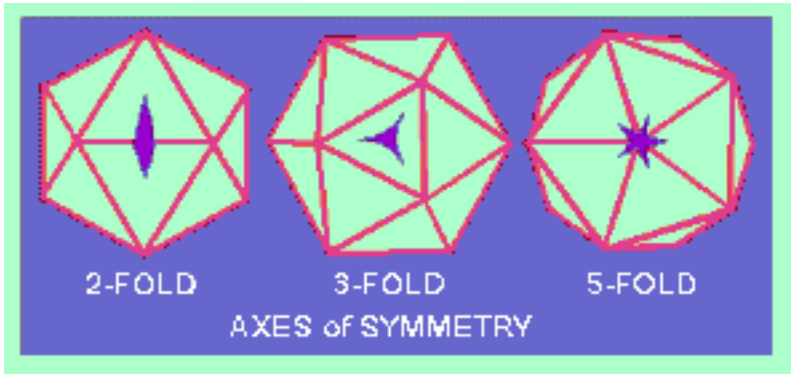
proteínas - virais

ESTRUTURA

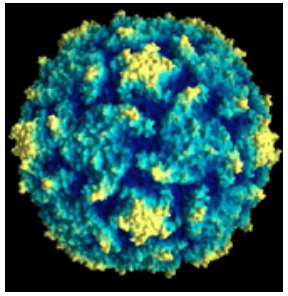
- A simetria icosaédrica

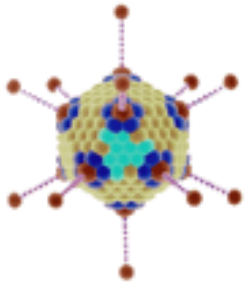


icosaedro



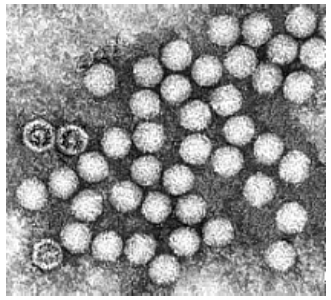
Eixos de simetria



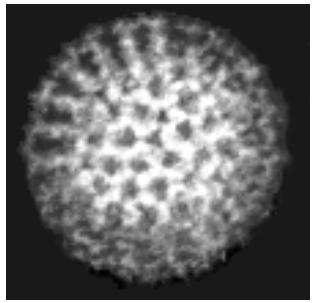


Modelos de vírus icosaédricos

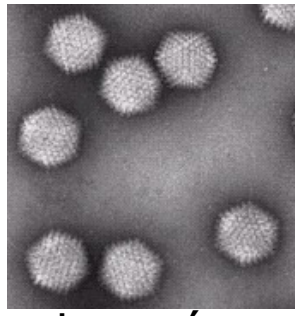
Vírus com simetria icosaédrica



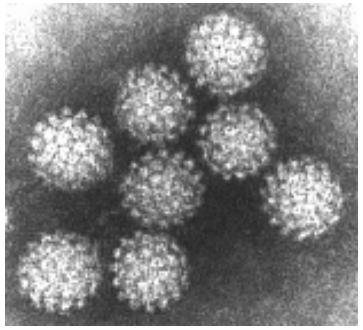
poliovírus



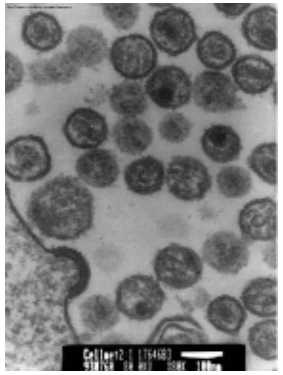
rotavírus



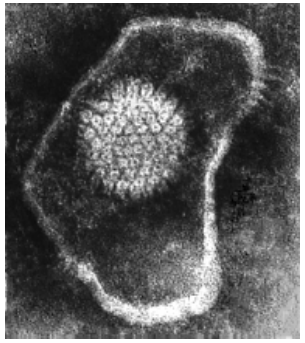
adenovírus



papilomavírus



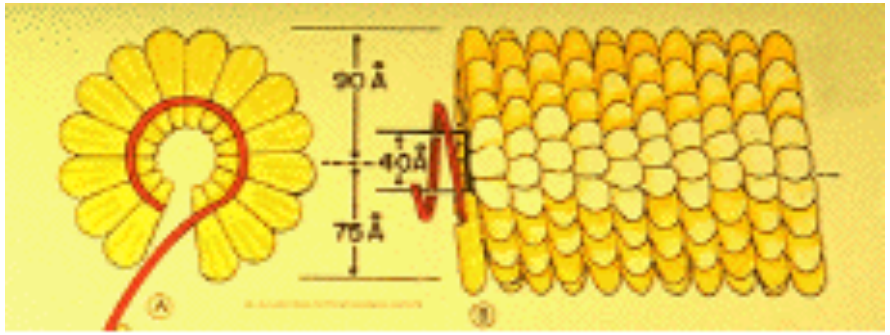
vírus HIV

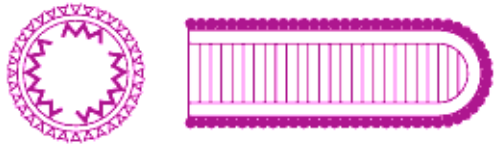


vírus herpes

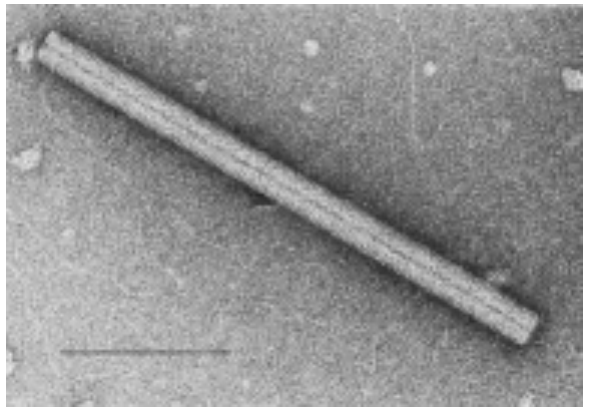
ESTRUTURA

- A simetria helicoidal

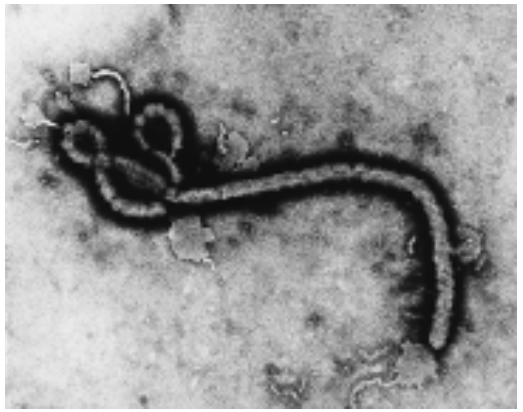




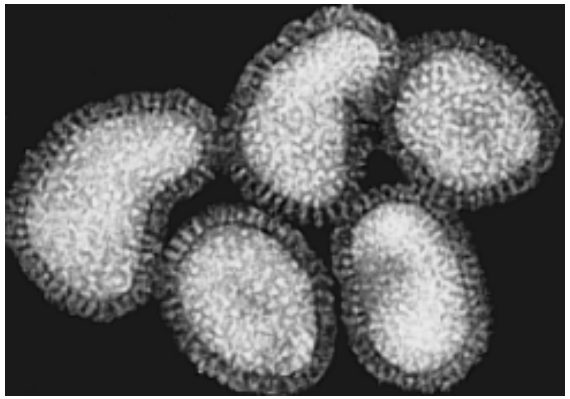
Vírus com simetria helicoidal



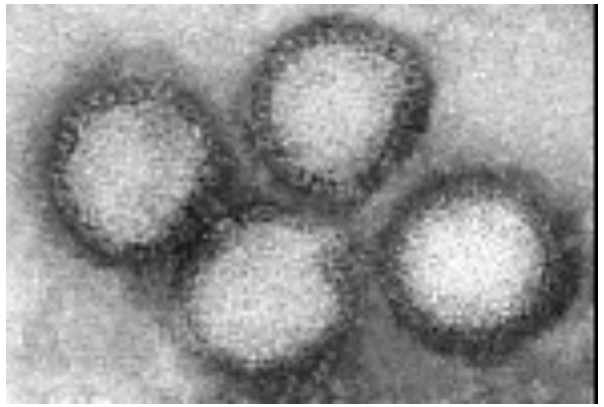
vírus do mosaico do tabaco



vírus Ebola



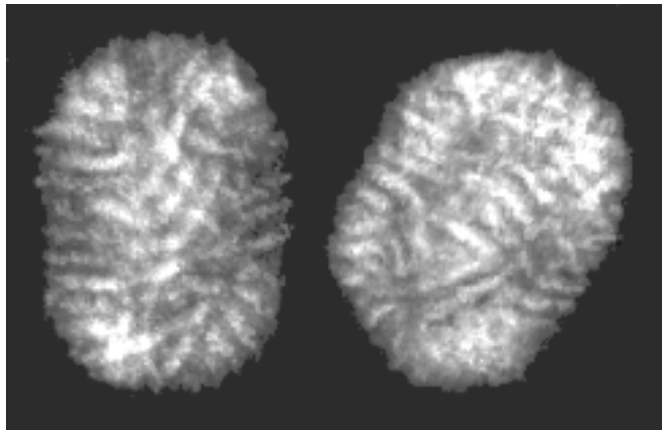
vírus influenza



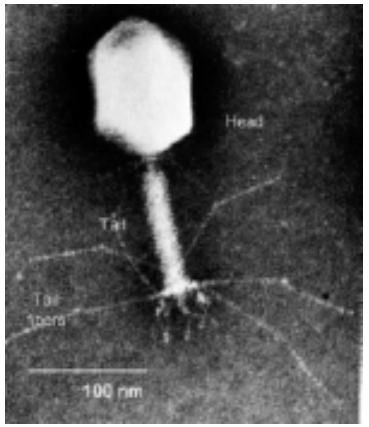
hantavírus

ESTRUTURA

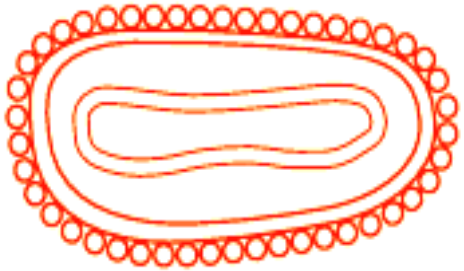
- Vírus de simetria complexa

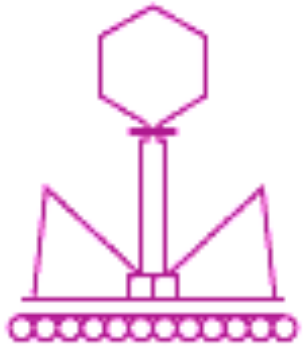


Poxvirus



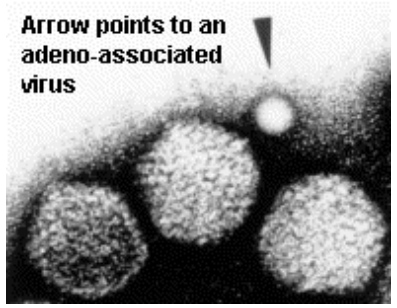
Bacteriófago T4





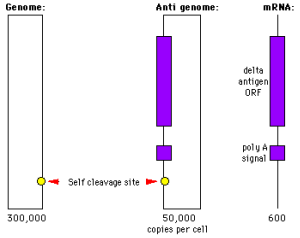
São os vírus os menores agentes infecciosos?

Partículas subvirais:

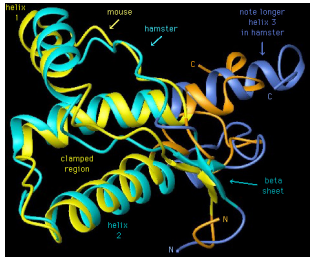


- **vírus satélite**
  - ✓ Vírus pequeno, defectivo,
  - ✓ Depende de outro vírus para se multiplicar
  - ✓ Ex: dependovírus

- **viróides**



  - ✓ Ácido nucleico (ssRNA circular)
  - ✓ capaz de se replicar quando infecta uma célula
  - ✓ codifica ou não uma proteína
  - ✓ pode ou não causar doença



- **prions**
  - ✓ Proteína (desprovida de ácido nucleico)
  - ✓ capaz de infectar células e causar doença

COMPOSIÇÃO QUÍMICA DOS VÍRUS

- Ácidos nucléicos - genoma

DNA

- fita dupla (ds)
- fita simples (ss)
- linear
- circular

RNA

- fita dupla (ds)
- fita simples (ss)
- linear
- circular
- fita única
- segmentado

COMPOSIÇÃO QUÍMICA

Proteínas

Codificadas pelo genoma viral

Estruturais

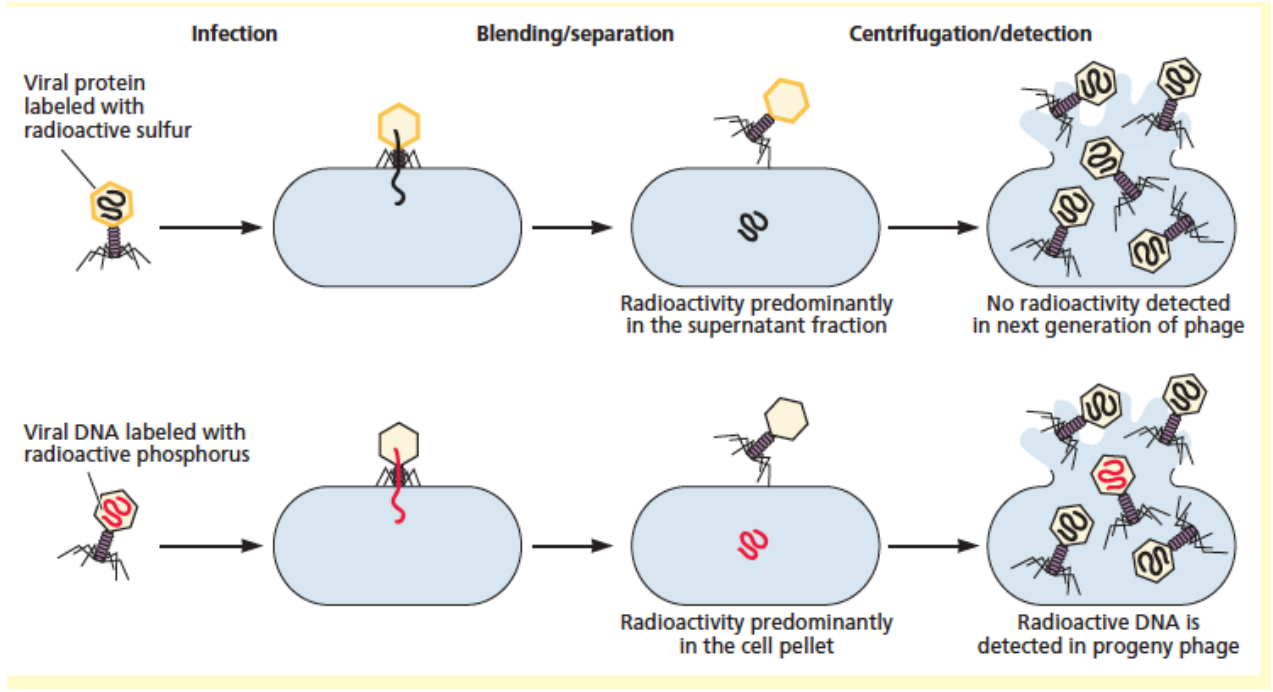
- proteção do genoma
- reconhecimento da célula
- atividade biológica

Não estruturais

- atividade enzimática:
  - replicação do ác. nucléico
  - proteólise
  - modificações

- regulação gênica

- **The Hershey-Chase experiment**



COMPOSIÇÃO QUÍMICA

- **Lipídeos**

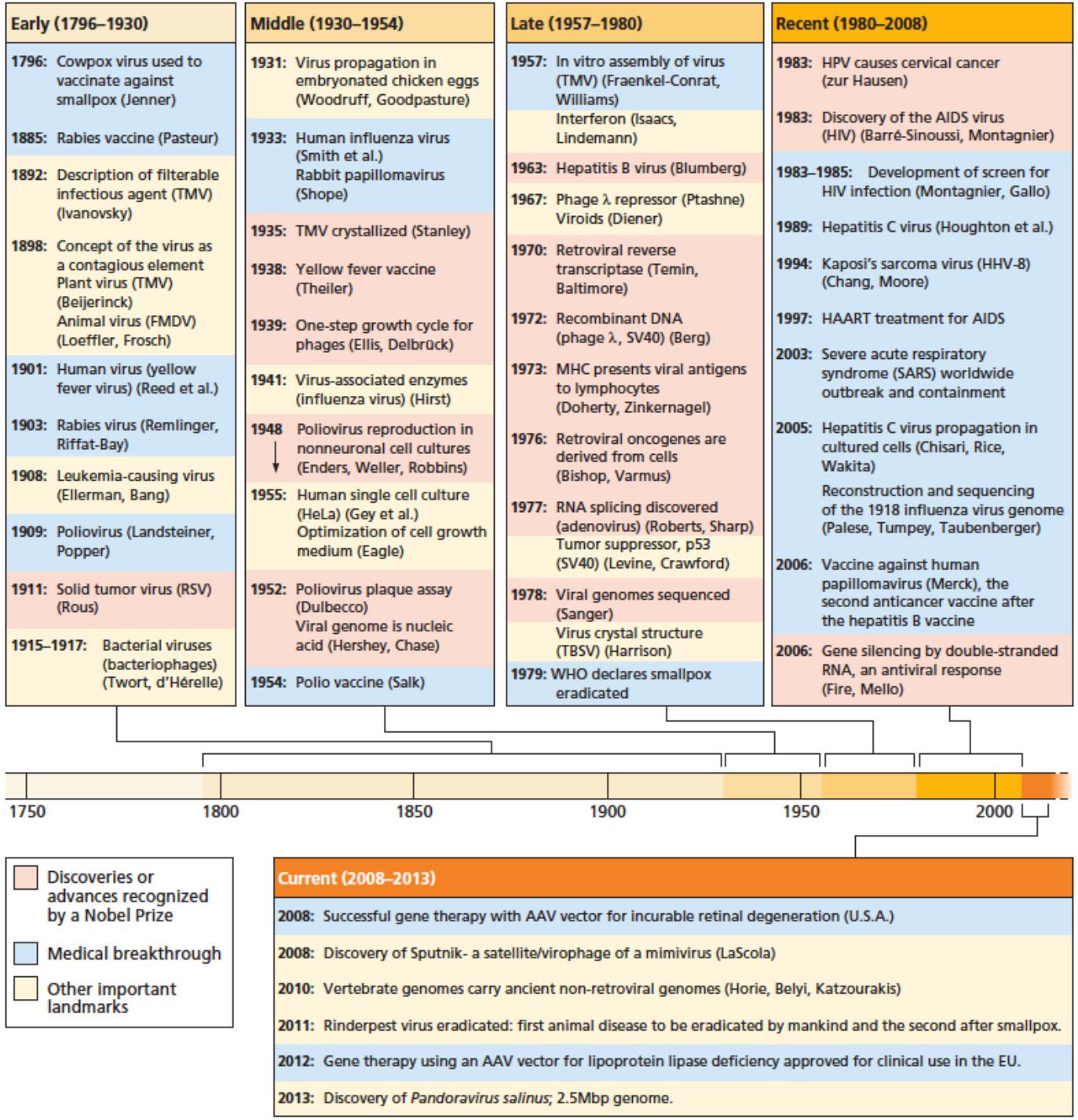
  - provenientes das membranas celulares

  - compõem o envoltório ou envelope

- **Glicídeos**

  - presentes nas proteínas de envoltório

  - glicosilação é feita na célula hospedeira


Early (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)
Middle (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 reproduction 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)
Late (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 (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)
1979: WHO declares smallpox eradicated
Recent (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)
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
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 anticancer vaccine after the hepatitis B vaccine
2006: Gene silencing by double-stranded RNA, an antiviral response (Fire, Mello)
1750
1800
1850
1900
1950
2000
Discoveries or advances recognized by a Nobel Prize
Medical breakthrough
Other important landmarks
Current (2008–2013)
2008: Successful gene therapy with AAV vector for incurable retinal degeneration (U.S.A.)
2008: Discovery of Sputnik- a satellite/virophage of a mimivirus (LaScola)
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: Gene therapy using an AAV vector for lipoprotein lipase deficiency approved for clinical use in the EU.
2013: Discovery of *Pandoravirus salinus*; 2.5Mbp genome.

CLASSIFICAÇÃO/Taxonomia

- Segundo o hospedeiro
  - Vírus de vertebrados
  - Vírus de invertebrados
  - Vírus de plantas
  - Vírus de bactérias (Bacteriófagos)
  - Vírus de fungos (Micovírus)

- Segundo o tipo de ácido nucleico
  - vírus de DNA
  - Virus de RNA

The International Committee on Taxonomy of Viruses Universal System of Virus Taxonomy = ICTV
(Committee of the Virology Division of the International Union of Microbiological Societies)

Genera: -virus
Subfamilies: -virinae
Families: -viridae
Order: -virales

CLASSIFICAÇÃO/Taxonomia

- Presença ou ausência de envoltório:
  - envelopados
  - não envelopados

- Estrutura e simetria do capsídeo

- Composição química

- Homologia nucleotídica

Vírus de vertebrados

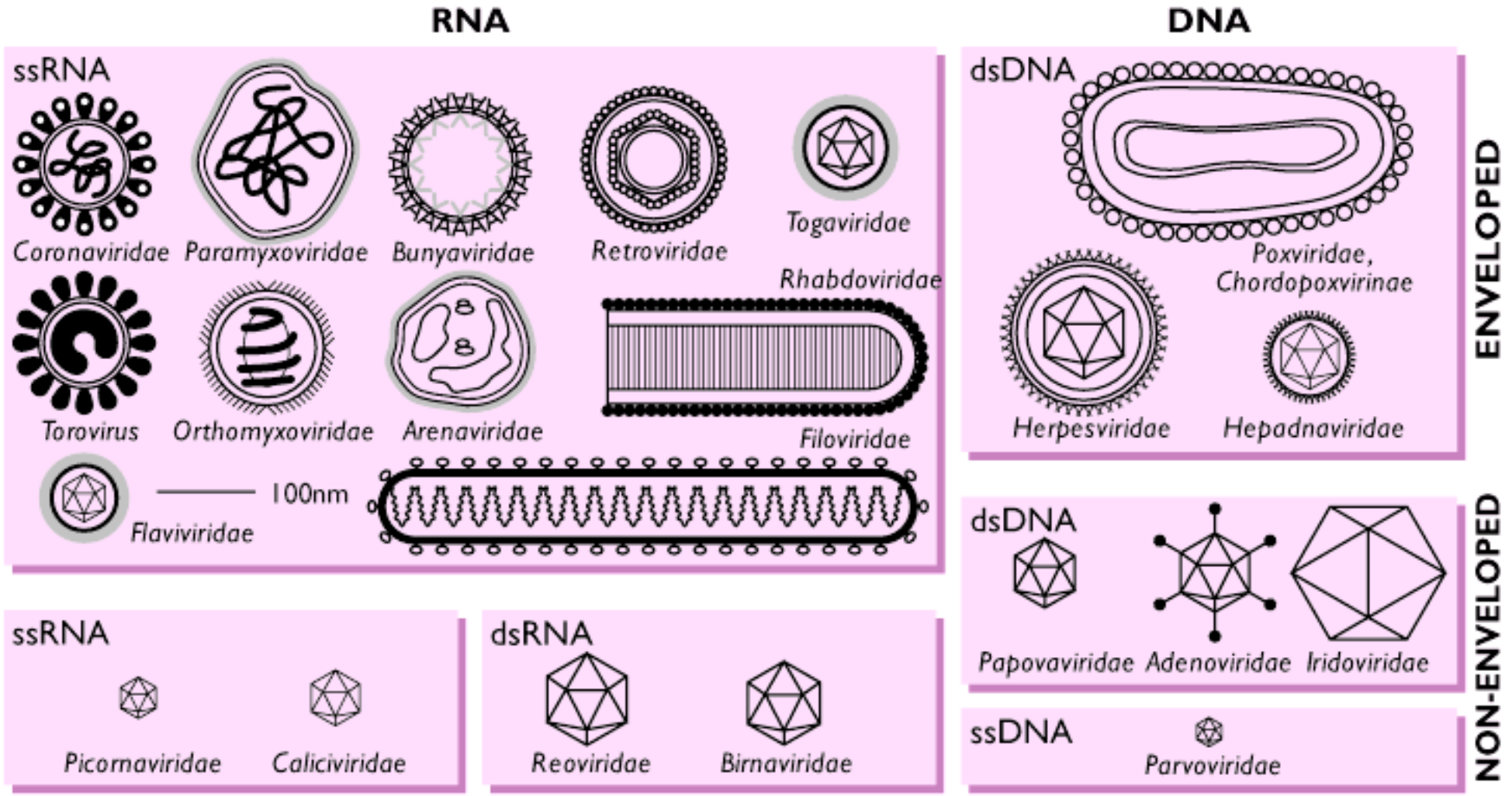


Fig. 5 Diagrammatic representation of the families of viruses infecting vertebrates, grouped according to the nature and strandedness of their genome and the presence or absence of an envelope. Reproduced with permission from Springer-Verlag.

Vírus de bactérias

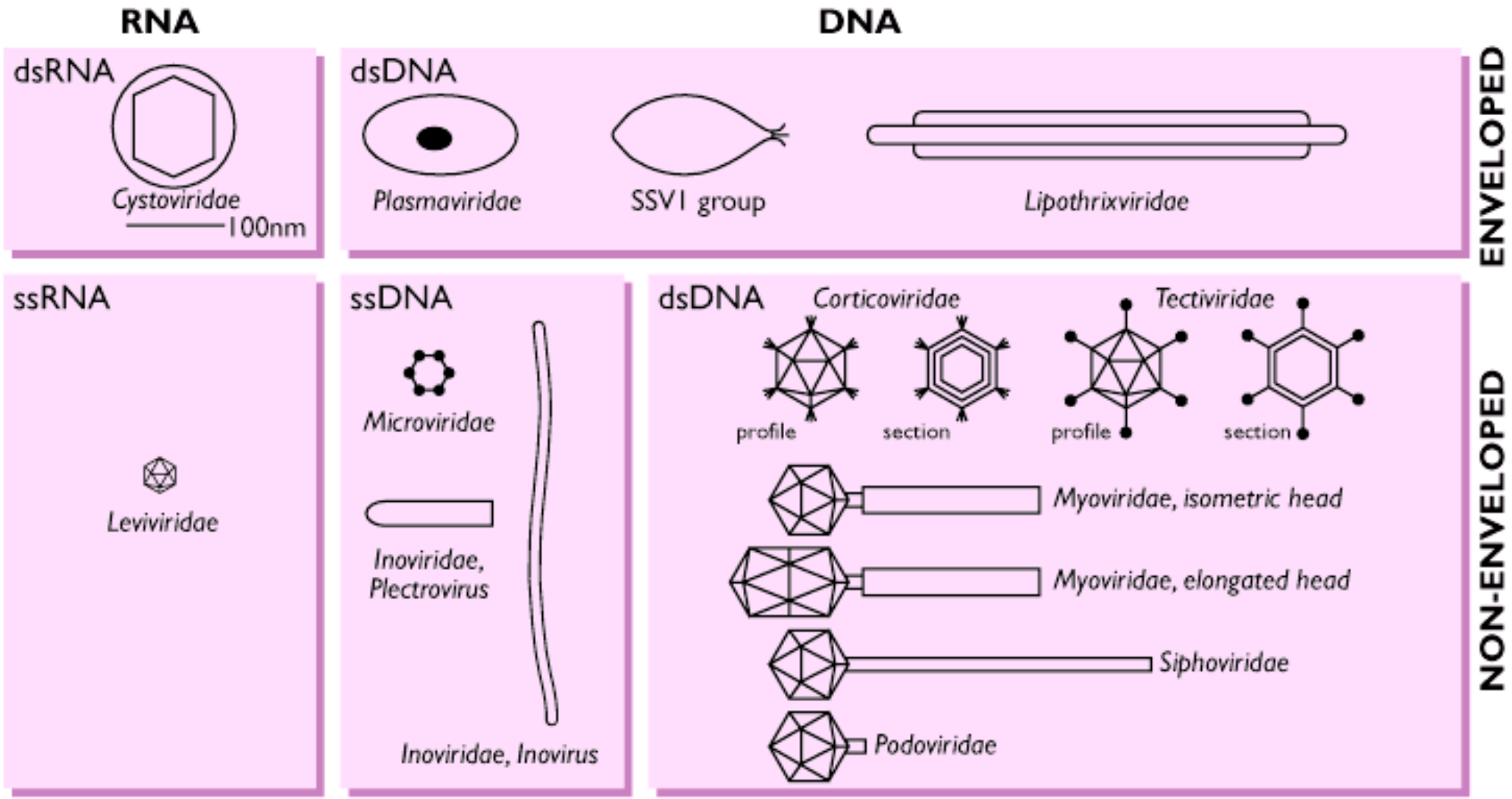


Fig. 1 Diagrammatic representation of the families of viruses infecting bacteria, group according to the nature and strandedness of their genome and the presence or absence of an envelope. Reproduced with permission from Springer-Verlag.

CLASSIFICAÇÃO

TABLE 2.1 Summary Characteristics of Vertebrate Virus Families

Family	Nucleocapsid morphology	Envelope	Virion morphology	Genome[a]	Host[b]
dsDNA viruses					
Adenoviridae	Icosahedral	No	Icosahedral	1 ds linear, 26–48 kb	V
Alloherpesviridae	Icosahedral	Yes	Spherical, tegument	2 ds linear, 135–294 kb	V
Asfaviridae	Icosahedral	Yes[c]	Icosahedral	1 ds linear, 165–190 kb	V, I
Herpesviridae	Icosahedral	Yes	Spherical, tegument	1 ds linear, 125–240 kb	V
Iridoviridae	Icosahedral	No[d]	Icosahedral	1 ds linear, 140–303	V, I
Papillomaviridae	Icosahedral	No	Icosahedral	1 ds circular, 7–8 kb	V
Polyomaviridae	Icosahedral	No	Icosahedral	1 ds circular, 5 kb	V
Poxviridae	Ovoid	Yes	Ovoid	1 ds linear, 130–375 kb	V, I
ssDNA viruses					
Anellovirus	Icosahedral	No	Icosahedral	1 – circular, 2–4 kb	V
Circoviridae	Icosahedral	No	Icosahedral	1 – or ± circular, 2 kb	V
Parvoviridae	Icosahedral	No	Icosahedral	1 +, – or ± linear, 4–6 kb	V, I
dsDNA reverse transcribing viruses					
Hepadnaviridae	Icosahedral	Yes	Spherical	1 ds circular, 3–4 kb	V
ssRNA reverse transcribing viruses					
Metaviridae	Spherical	Yes	Spherical	1 + linear, 4–10 kb	F, I, P, V
Retroviridae	Spherical, rod or cone shaped	Yes	Spherical	1 + linear dimer, 7–13 kb	V
dsRNA viruses					
Birnaviridae	Icosahedral	No	Icosahedral	2 ds linear, 5–6 kb	V, I
Picobirnaviridae	Icosahedral	No	Icosahedral	3 ds linear, 4 kb	V
Reoviridae	Icosahedral	No	Icosahedral, layered	10–12 ds linear, 19–32 kb	V, I, P, F
Negative sense ssRNA viruses					
Bornaviridae	ND[e]	Yes	Spherical	1 – linear, 9 kb	V
Deltavirus[f]	Isometric	Yes	Spherical	1 – circular, 2 kb	V
Filoviridae	Helical filaments	Yes	Bacilliform, filamentous	1 – linear, 19 kb	V
Orthomyxoviridae	Helical filaments	Yes	Pleomorphic, spherical	6–8 – linear, 10–15 kb	V
Paramyxoviridae	Helical filaments	Yes	Pleomorphic, spherical, filamentous	1 – linear, 13–18 kb	V
Rhabdoviridae	Coiled helical filaments	Yes	Bullet shaped	1 – linear, 11–15 kb	V, I, P
Positive sense ssRNA viruses					
Arteriviridae	Linear, asymmetric	Yes	Spherical	1 + linear, 13–16 kb	V
Astroviridae	Icosahedral	No	Icosahedral	1 + linear, 6–8 kb	V
Caliciviridae	Icosahedral	No	Icosahedral	1 + linear, 7–8 kb	V
Coronaviridae	Helical	Yes	Spherical	1 + linear, 26–32 kb	V
Flaviviridae	Spherical	Yes	Spherical	1 + linear, 9–13 kb	V, I
Hepevirus[g]	Icosahedral	No	Icosahedral	1 + linear, 7 kb	V
Nodaviridae	Icosahedral	No	Icosahedral	2 + linear, 4–5 kb	V, I
Picornaviridae	Icosahedral	No	Icosahedral	1 + linear, 7–9 kb	V
Togaviridae	Icosahedral	Yes	Spherical	1 + linear, 10–12 kb	V, I
Ambisense ssRNA viruses					
Arenaviridae	Filamentous	Yes	Spherical	2 ± linear, 11 kb	V
Bunyaviridae	Filamentous	Yes	Spherical	3 – or ± linear, 11–19 kb	V, I, P
Subviral agents: prions					
Prions	—	—	—	—	V, F

CLASSIFICAÇÃO

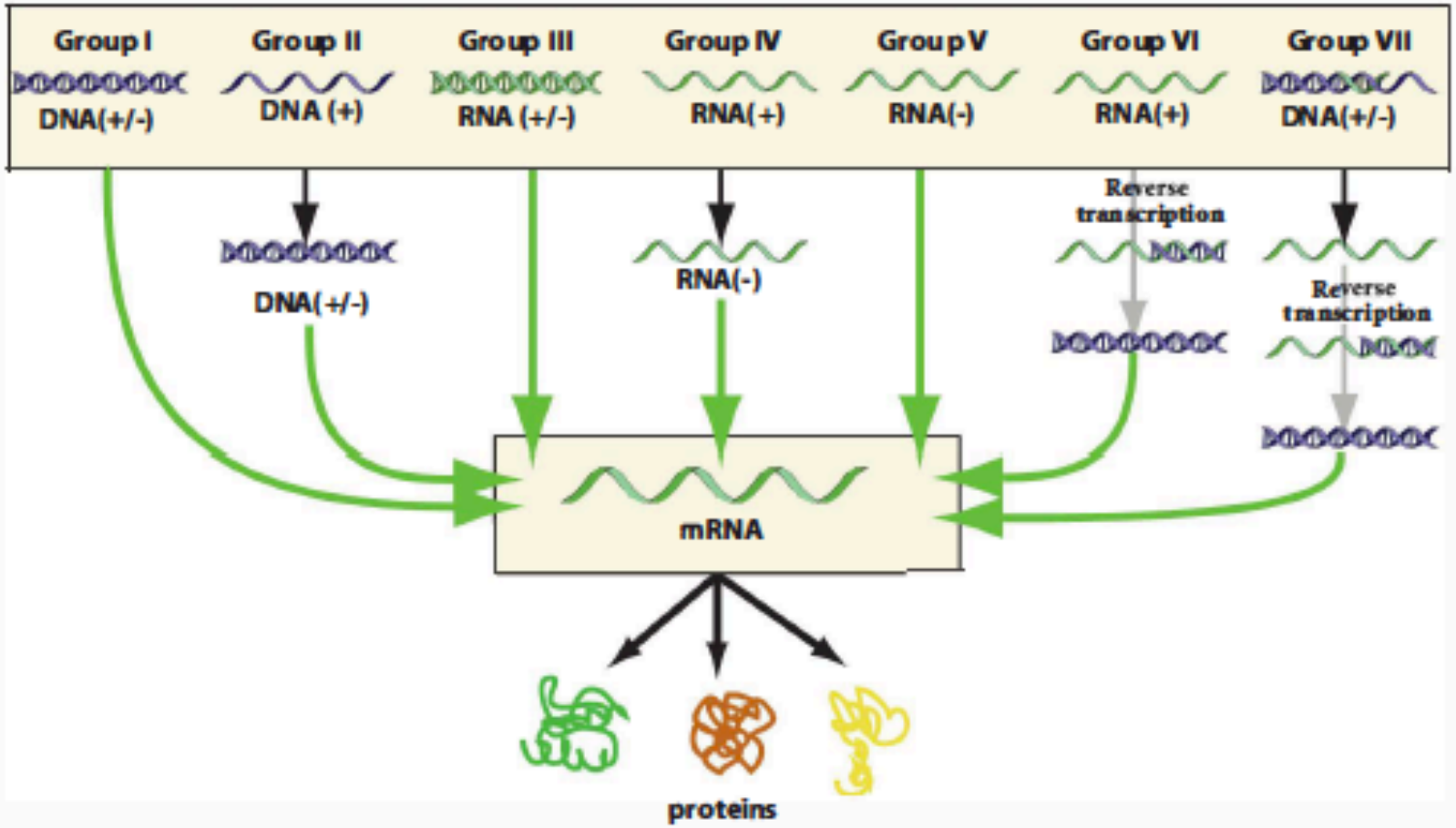


FIGURE 2.1. The Baltimore classification, a virus classification scheme based on the form of nucleic acid present in virion particles and the pathway for expression of the genetic material as messenger RNA.[1]
The original scheme contained groups I through VI and has been expanded to accommodate DNA-containing, reverse transcribing viruses. Viruses containing ambisense single-stranded RNA genomes are grouped under negative sense single-stranded RNA viruses. (Reprinted from Hulo C, de Castro E, Masson P, et al. ViralZone: a knowledge resource to understand virus diversity. *Nucleic Acids Res* 2011;39 (Database issue):D576–D582; ViralZone, Swiss Institute of Bioinformatics, http://www.expasy.ch/viralzone/, with permission.)