

DISCIPLINA: BMM 400 -MICROBIOLOGIA BÁSICA- ENFERMAGEM

Módulo de Virologia

Propriedades Gerais dos Vírus

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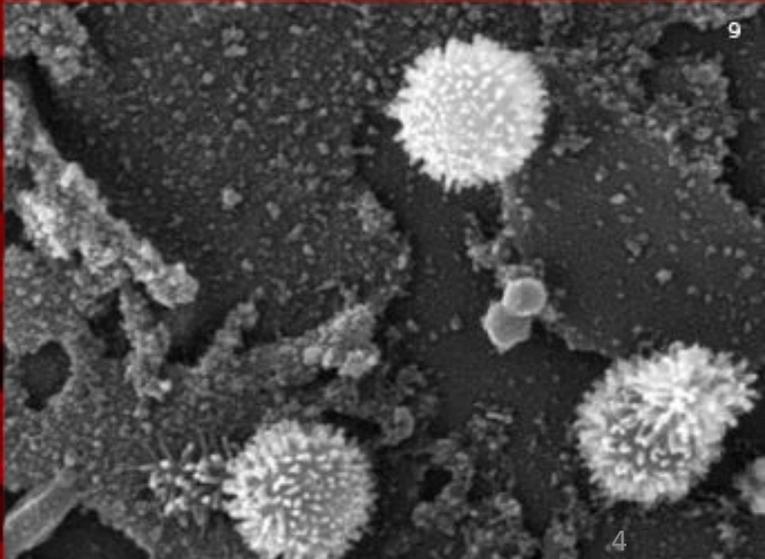
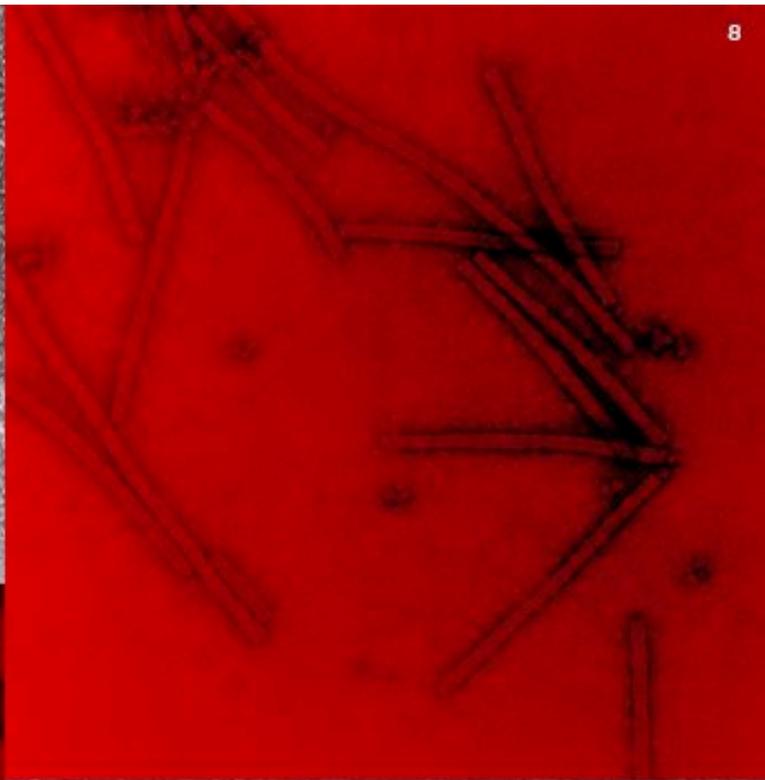
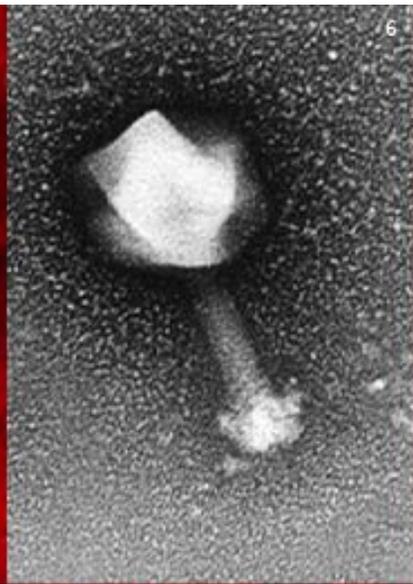
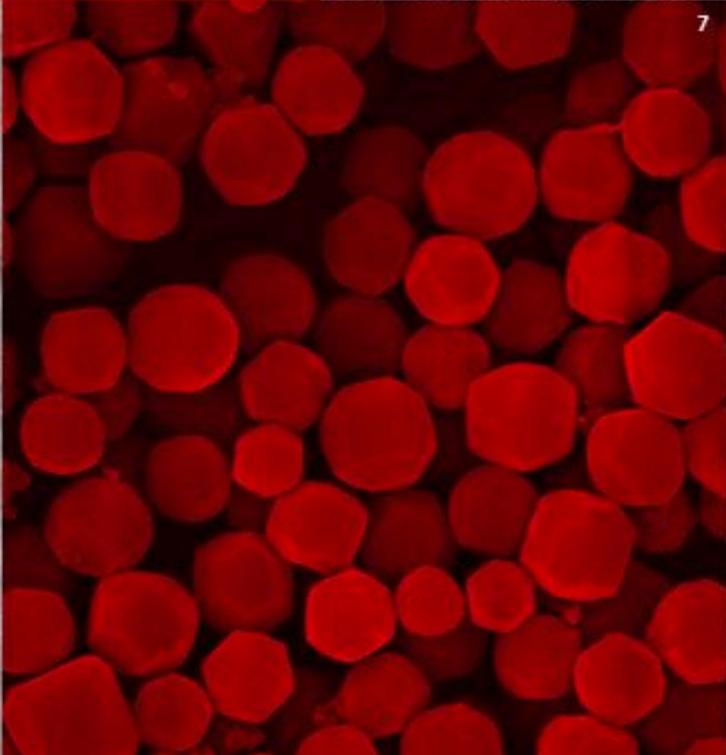
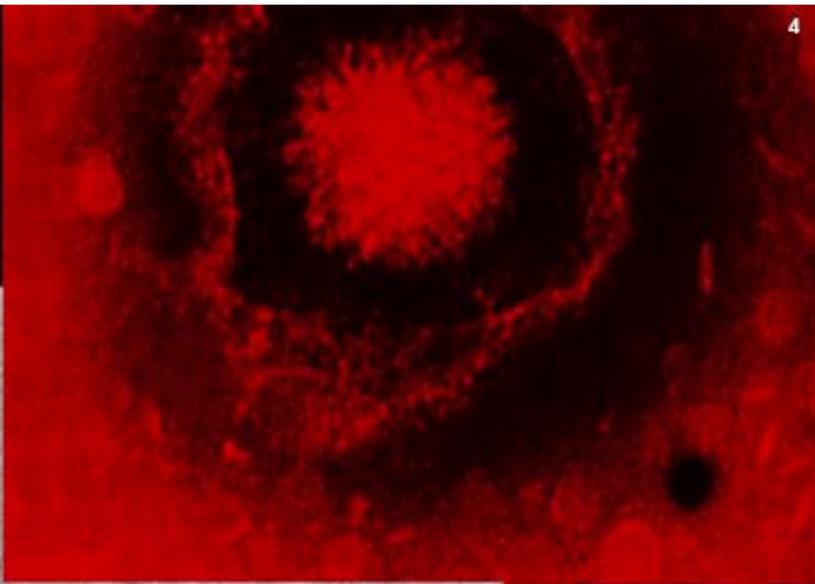
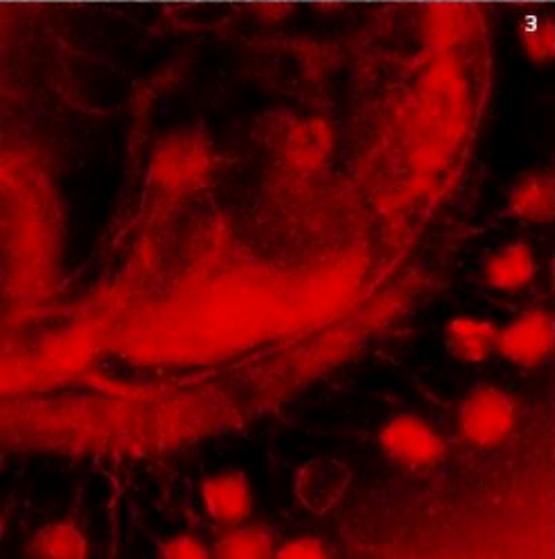
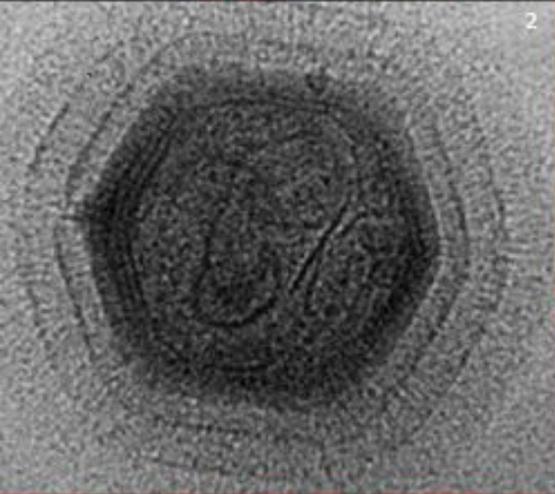
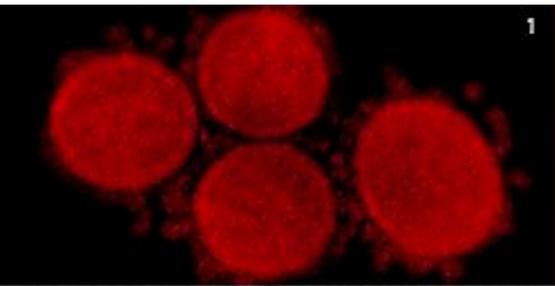
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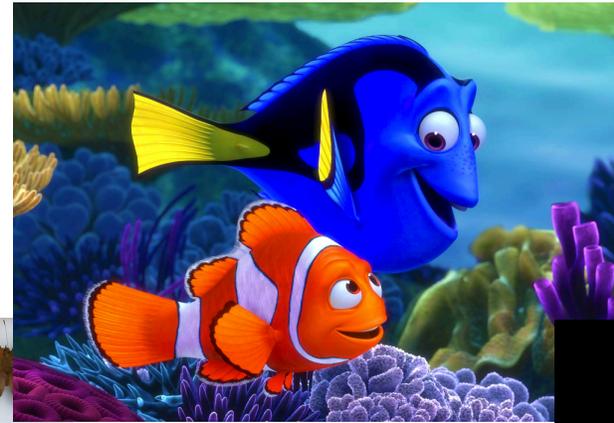
Introdução à Virologia

PROPRIEDADES GERAIS DOS VÍRUS



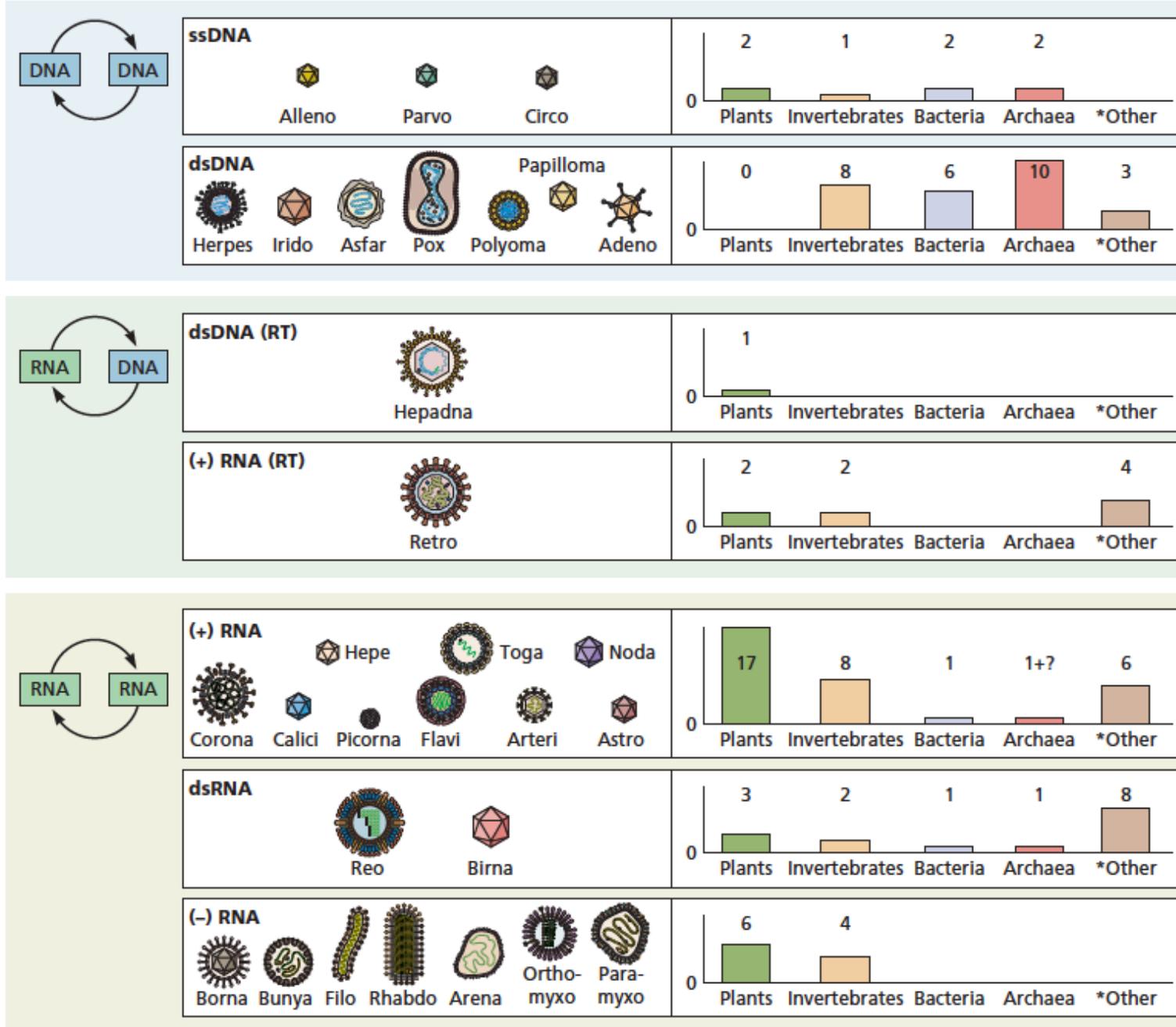
Vírus vivem no nosso organismo de maneira harmoniosa a milhares de anos

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



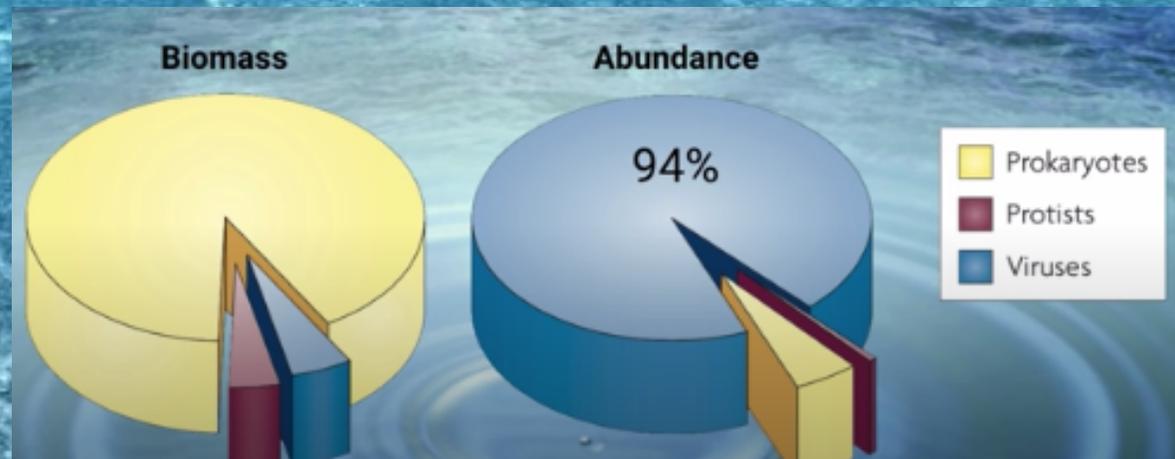
Families of viruses that infect vertebrates

Number of virus families that infect other life forms



*Algae, fungi, yeasts, and protozoa

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





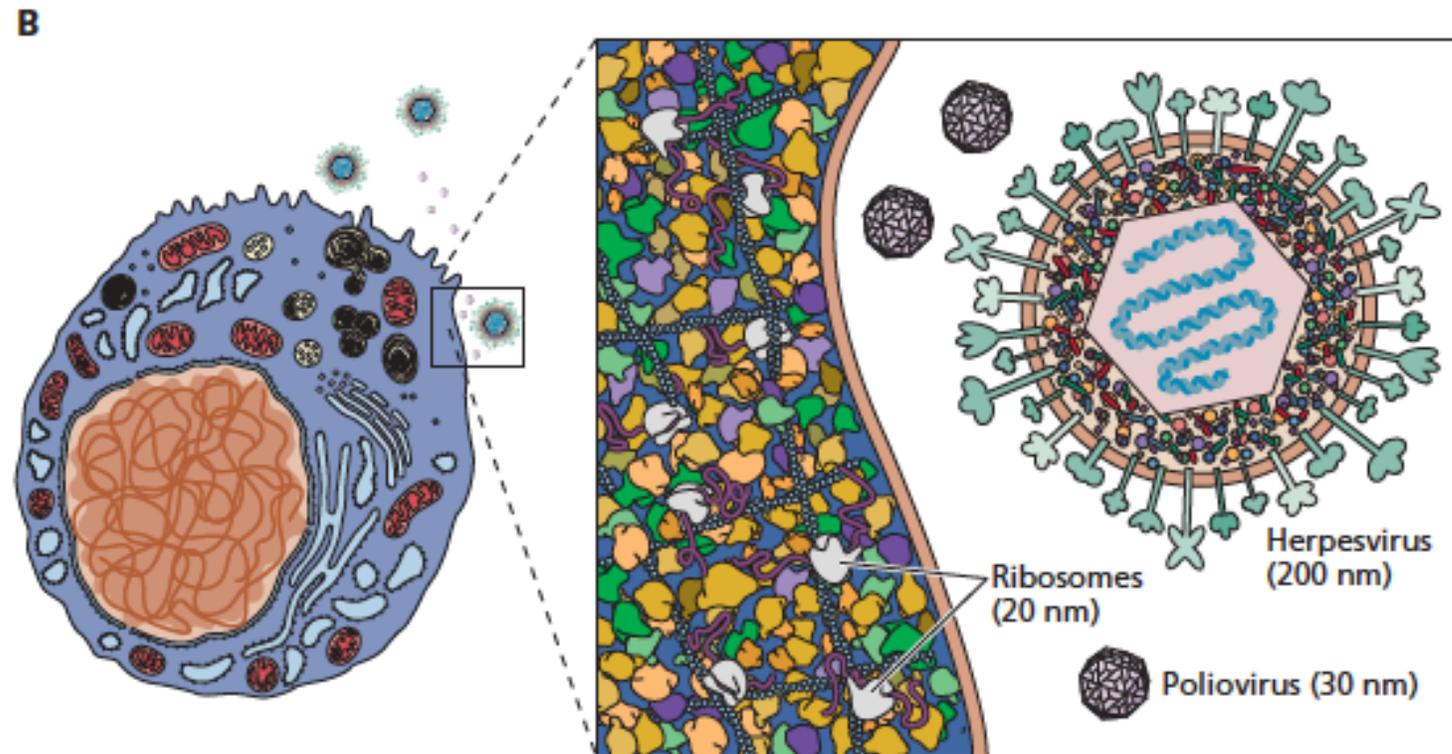
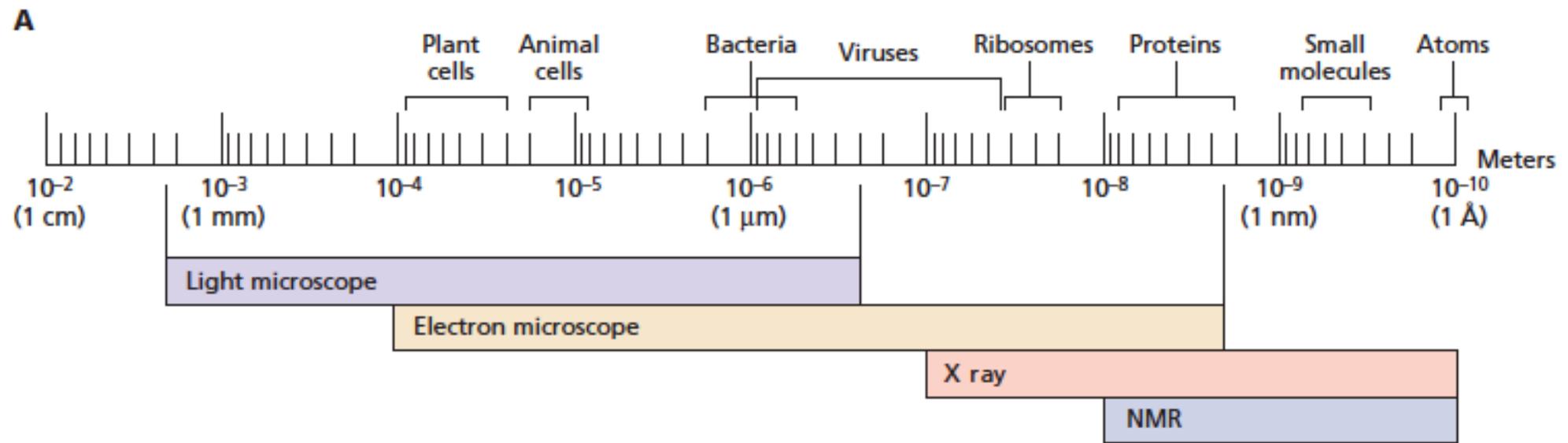
**Baleias: comumente infectadas por
Caliciviridae: 10^{13} partículas de vírus por dia**



**Corpo Humano
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



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.

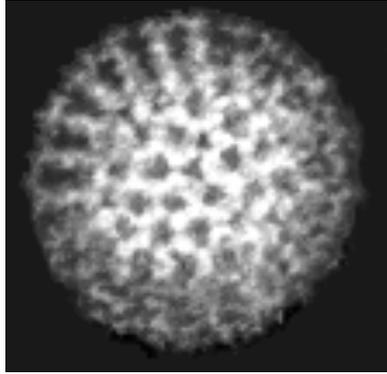
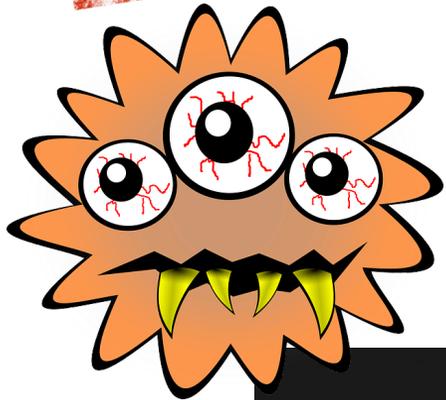
CONCEITO

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 virions serão liberados da célula hospedeira e irão infectar novas células, perpetuando a espécie.

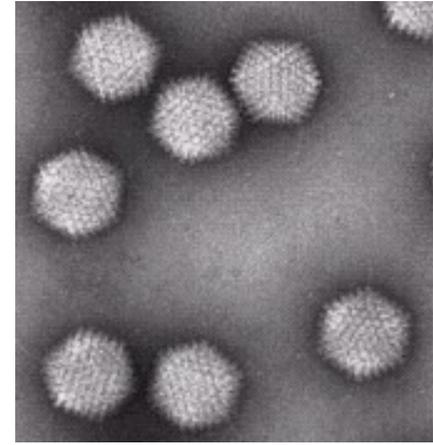
VIRUS



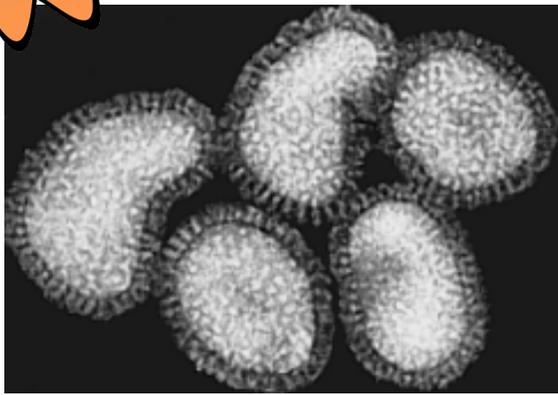
rotavírus



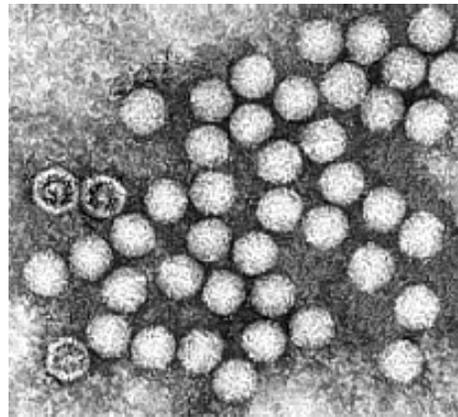
vírus Ebola



adenovírus



vírus influenza



poliovírus



vírus herpes

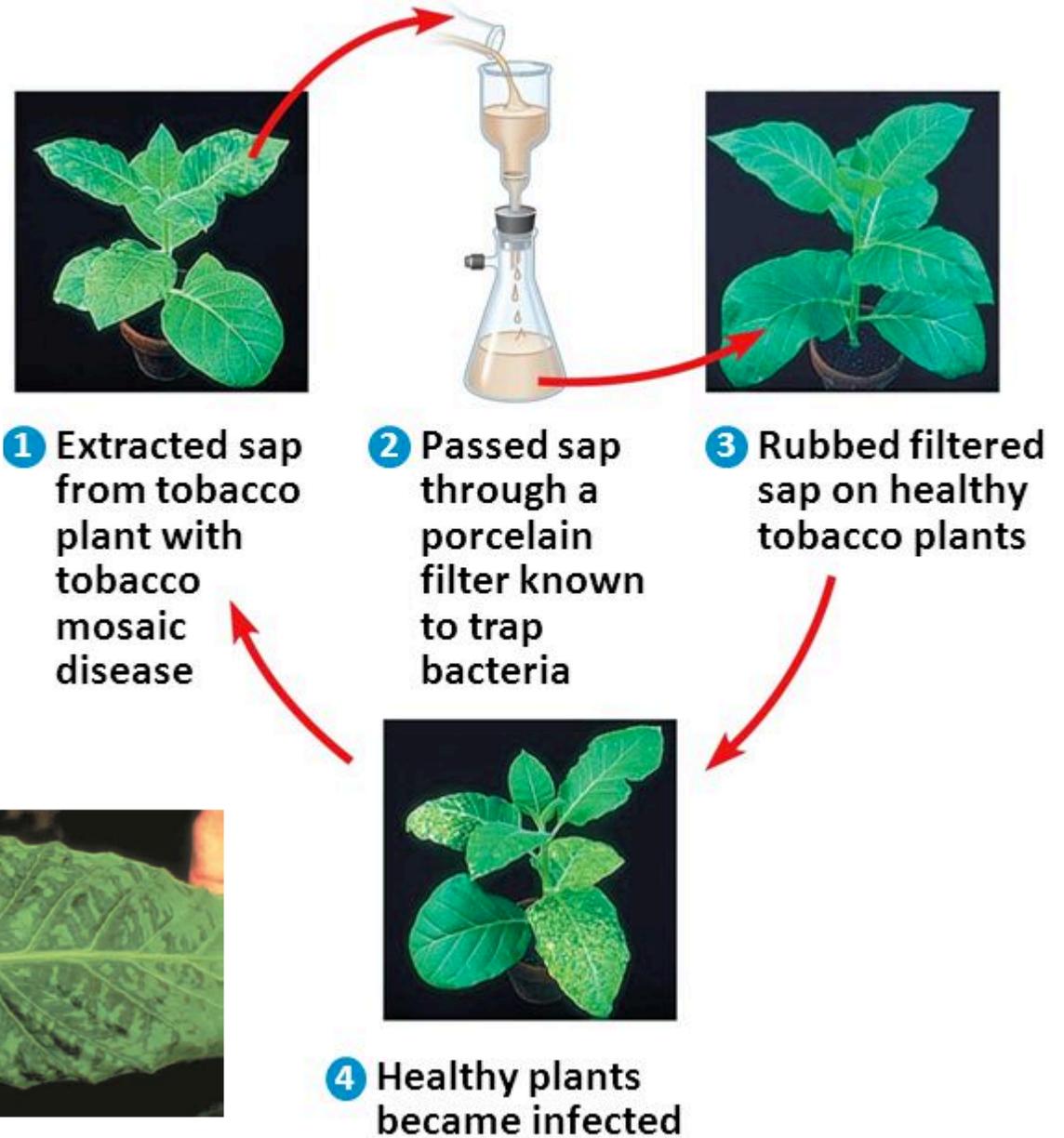
HISTÓRICO

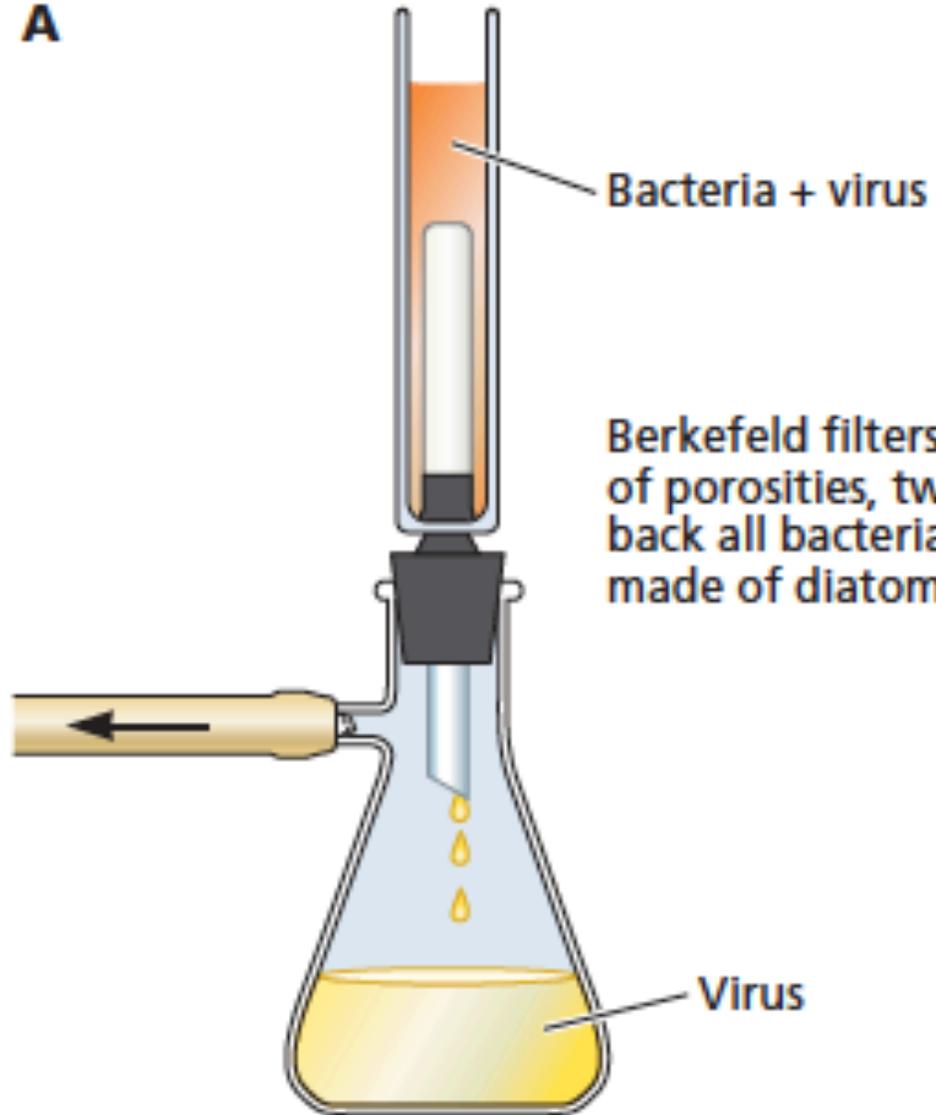


Dmitri Iwanowski
1864-1920

- 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 saudáveis 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

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

B

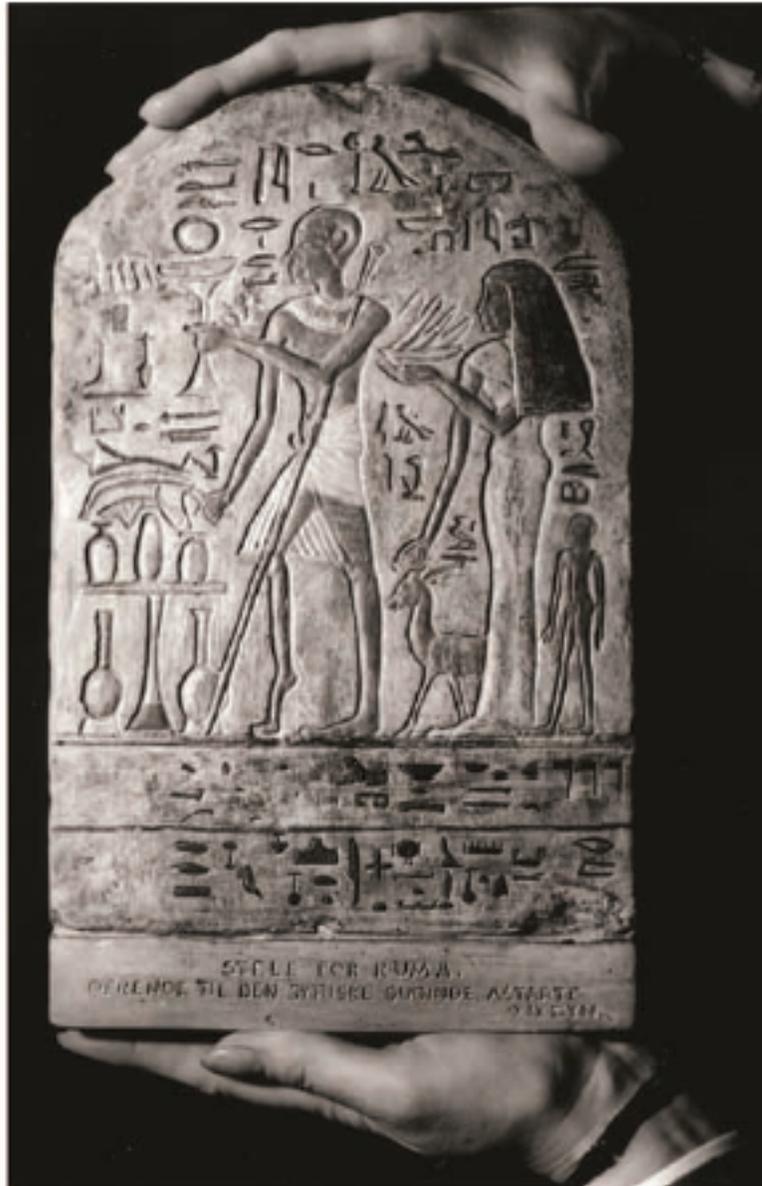
HISTÓRICO



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 saudias.
- 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).”

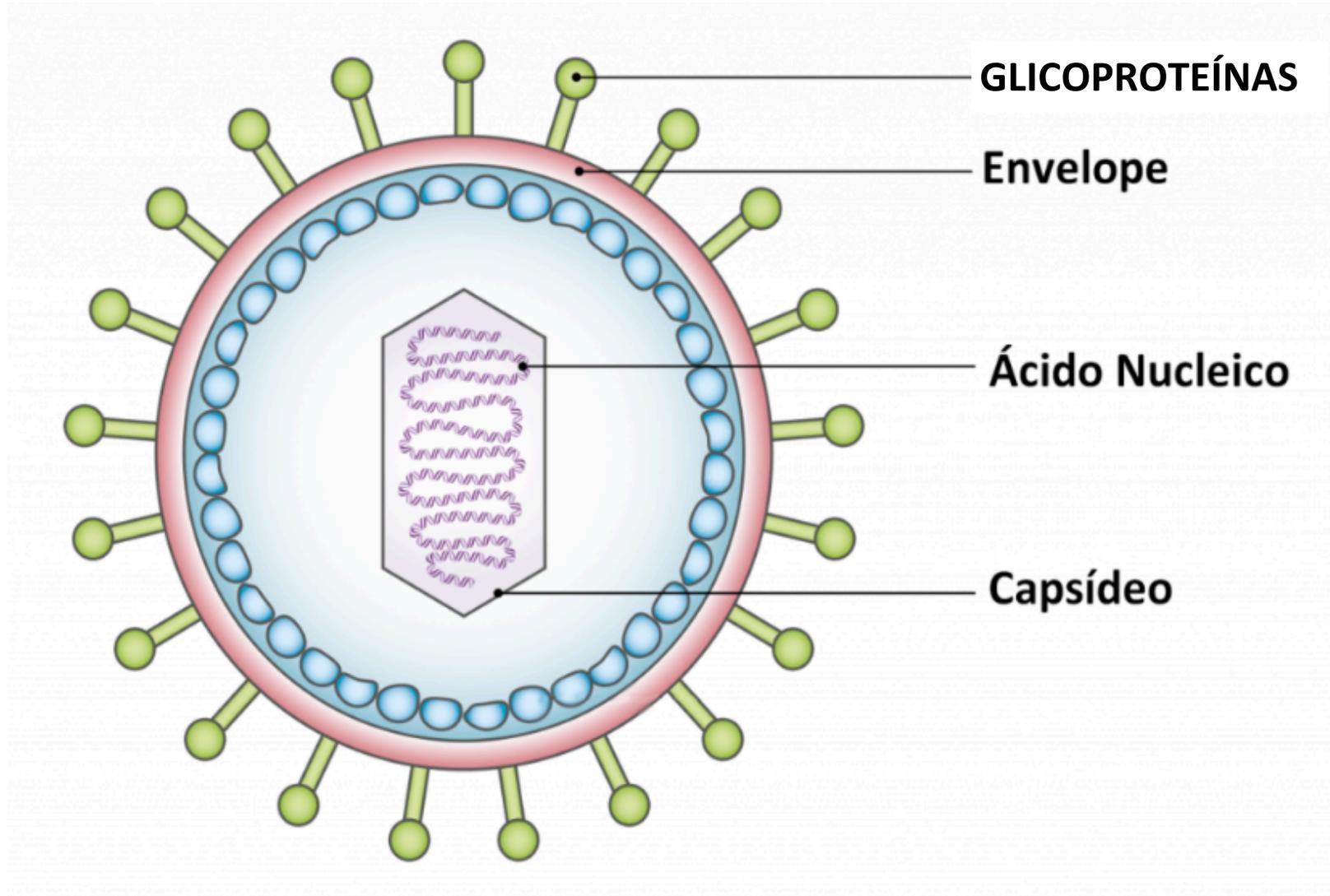
Ser vivo

- ✓ 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.

Nucleocapsídeo:

Ácido nucleico com o envoltório

protéico

Proteínas :

- protômeros
- capsômeros
- capsídeo

Envoltório:

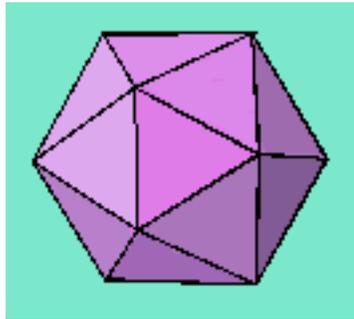
membrana lipo-protéica:

lipídeos - da célula

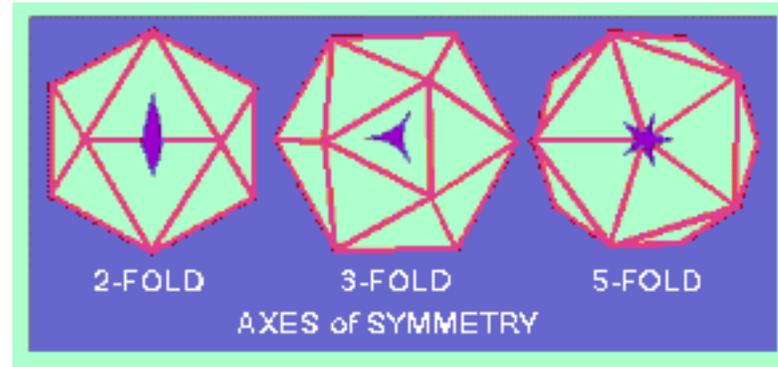
proteínas - virais

ESTRUTURA

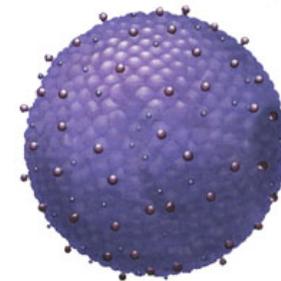
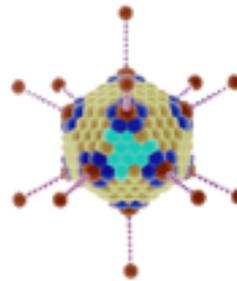
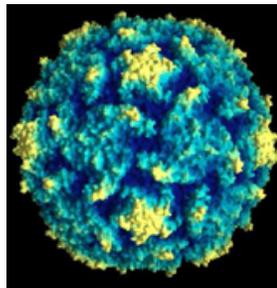
- A simetria icosaédrica



icosaedro

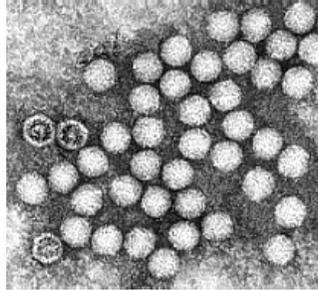


Eixos de simetria

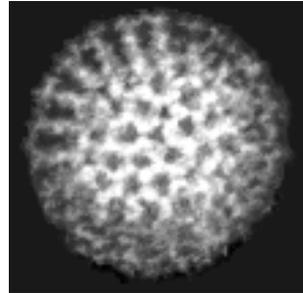


Modelos de vírus icosaédricos

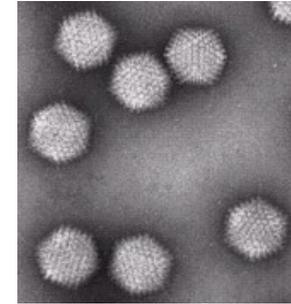
Vírus com simetria icosaédrica



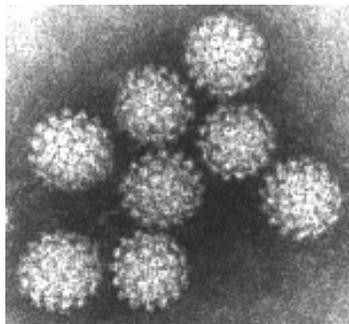
poliovírus



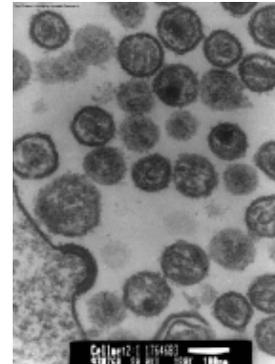
rotavírus



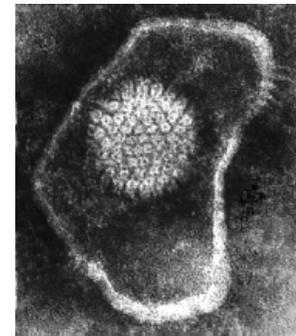
adenovírus



papilomavírus



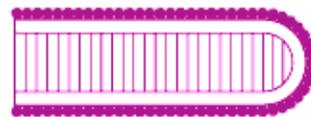
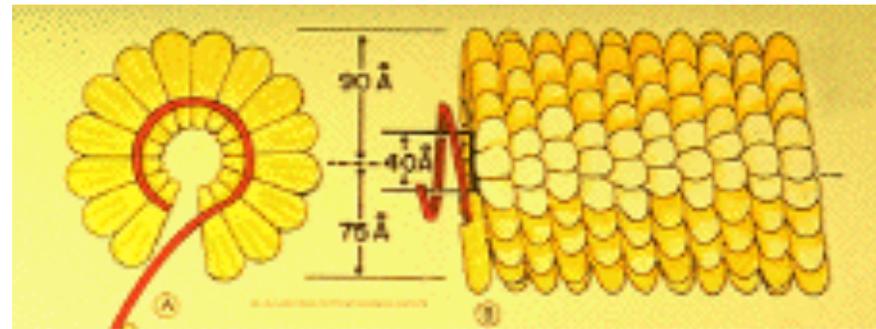
vírus HIV



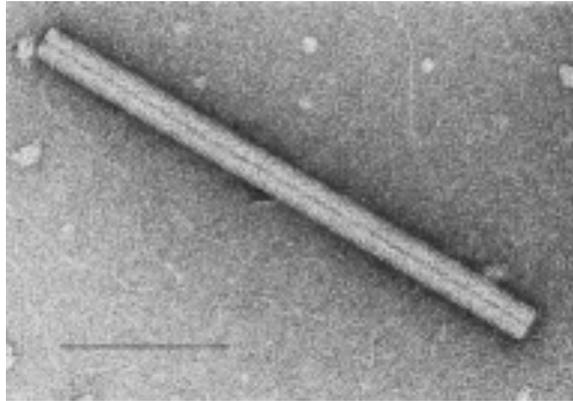
vírus herpes

ESTRUTURA

- A simetria helicoidal



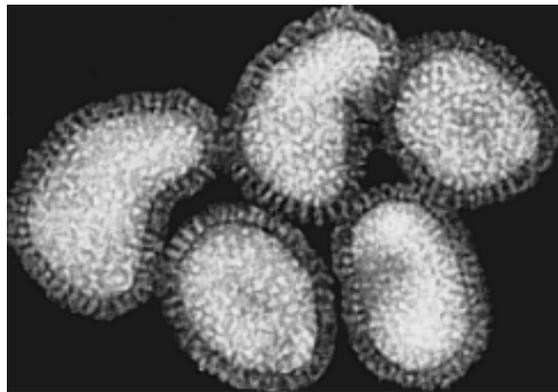
Vírus com simetria helicoidal



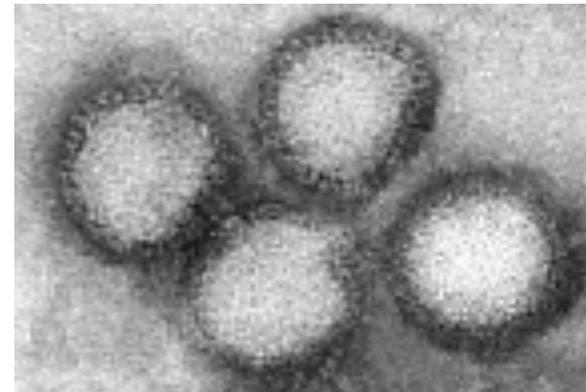
vírus do mosaico do tabaco



vírus Ebola



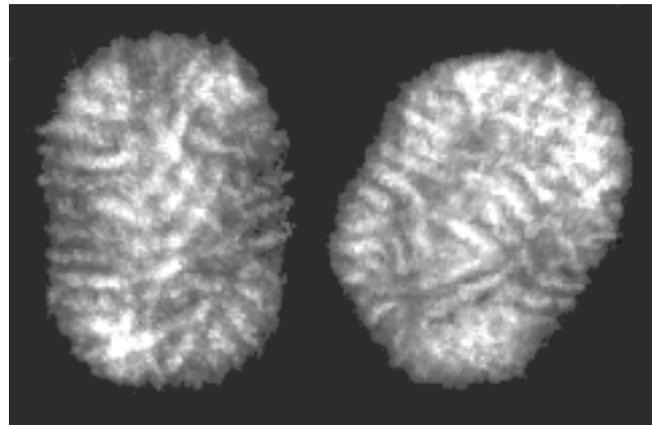
vírus influenza



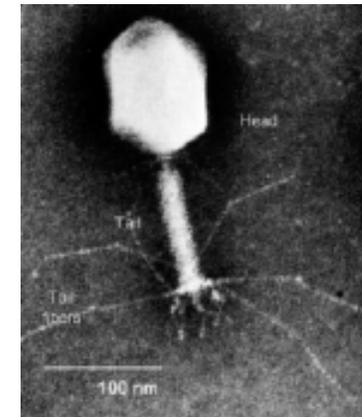
hantavírus

ESTRUTURA

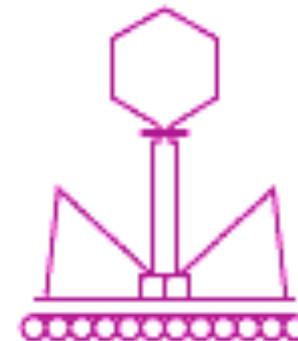
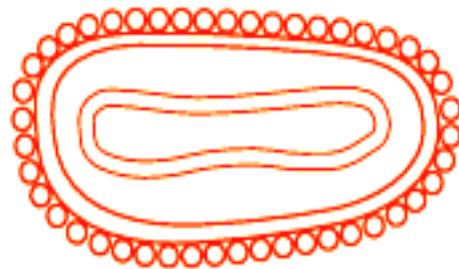
■ Vírus de simetria complexa



Poxvirus

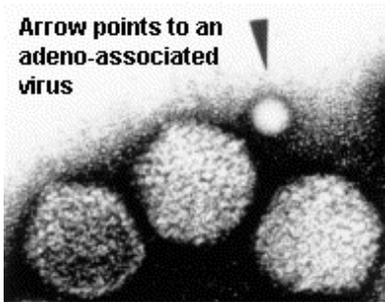


Bacteriófago T4



São os vírus os menores agentes infecciosos?

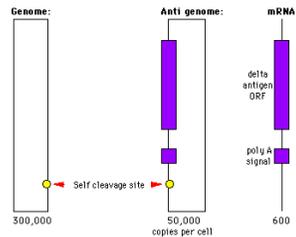
Partículas subvirais:



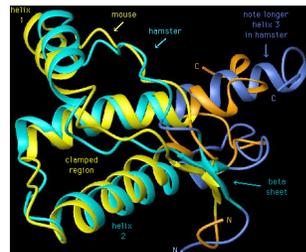
- **vírus satélite**

- ✓ 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 nucleicos - 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

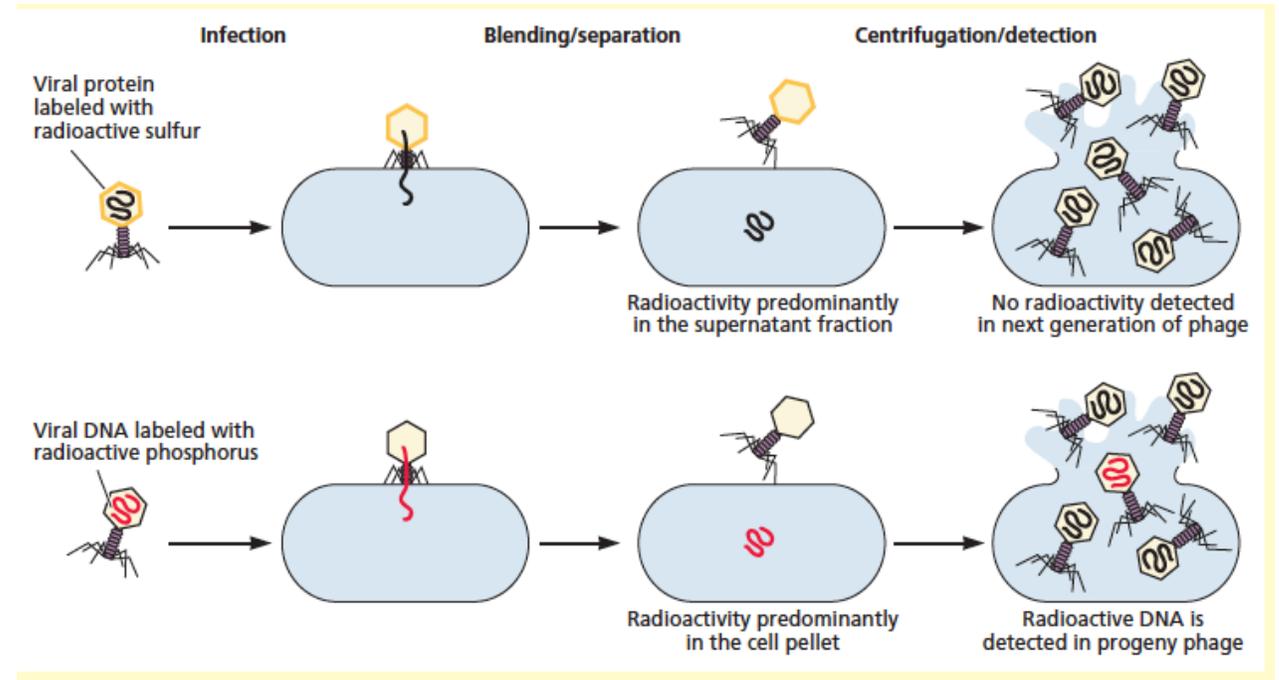
Estruturais

- proteção do genoma
- reconhecimento da célula
- atividade biológica

Não estruturais

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

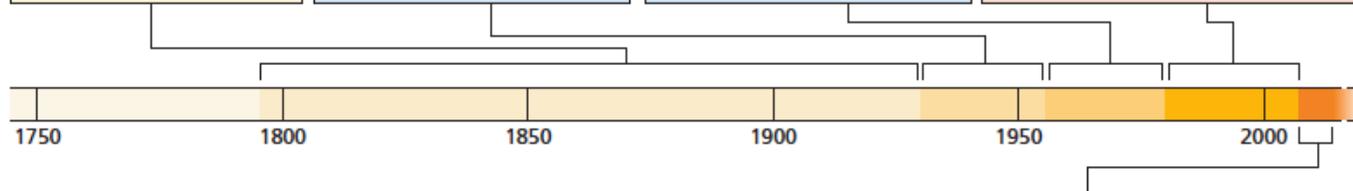
- **The Hershey-Chase experiment**



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)	Middle (1930–1954)	Late (1957–1980)	Recent (1980–2008)
1796: Cowpox virus used to vaccinate against smallpox (Jenner)	1931: Virus propagation in embryonated chicken eggs (Woodruff, Goodpasture)	1957: In vitro assembly of virus (TMV) (Fraenkel-Conrat, Williams)	1983: HPV causes cervical cancer (zur Hausen)
1885: Rabies vaccine (Pasteur)	1933: Human influenza virus (Smith et al.) Rabbit papillomavirus (Shope)	Interferon (Isaacs, Lindemann)	1983: Discovery of the AIDS virus (HIV) (Barré-Sinoussi, Montagnier)
1892: Description of filterable infectious agent (TMV) (Ivanovsky)	1935: TMV crystallized (Stanley)	1963: Hepatitis B virus (Blumberg)	1983–1985: Development of screen for HIV infection (Montagnier, Gallo)
1898: Concept of the virus as a contagious element Plant virus (TMV) (Beijerinck) Animal virus (FMDV) (Loeffler, Frosch)	1938: Yellow fever vaccine (Theiler)	1967: Phage λ repressor (Ptashne) Viroids (Diener)	1989: Hepatitis C virus (Houghton et al.)
1901: Human virus (yellow fever virus) (Reed et al.)	1939: One-step growth cycle for phages (Ellis, Delbrück)	1970: Retroviral reverse transcriptase (Temin, Baltimore)	1994: Kaposi's sarcoma virus (HHV-8) (Chang, Moore)
1903: Rabies virus (Remlinger, Riffat-Bay)	1941: Virus-associated enzymes (influenza virus) (Hirst)	1972: Recombinant DNA (phage λ, SV40) (Berg)	1997: HAART treatment for AIDS
1908: Leukemia-causing virus (Ellerman, Bang)	1948: Poliovirus reproduction in nonneuronal cell cultures (Enders, Weller, Robbins) ↓	1973: MHC presents viral antigens to lymphocytes (Doherty, Zinkernagel)	2003: Severe acute respiratory syndrome (SARS) worldwide outbreak and containment
1909: Poliovirus (Landsteiner, Popper)	1955: Human single cell culture (HeLa) (Gey et al.) Optimization of cell growth medium (Eagle)	1976: Retroviral oncogenes are derived from cells (Bishop, Varmus)	2005: Hepatitis C virus propagation in cultured cells (Chisari, Rice, Wakita) Reconstruction and sequencing of the 1918 influenza virus genome (Palese, Tumpey, Taubenberger)
1911: Solid tumor virus (RSV) (Rous)	1952: Poliovirus plaque assay (Dulbecco) Viral genome is nucleic acid (Hershey, Chase)	1977: RNA splicing discovered (adenovirus) (Roberts, Sharp) Tumor suppressor, p53 (SV40) (Levine, Crawford)	2006: Vaccine against human papillomavirus (Merck), the second anticancer vaccine after the hepatitis B vaccine
1915–1917: Bacterial viruses (bacteriophages) (Twort, d'Hérelle)	1954: Polio vaccine (Salk)	1978: Viral genomes sequenced (Sanger) Virus crystal structure (TBSV) (Harrison)	2006: Gene silencing by double-stranded RNA, an antiviral response (Fire, Mello)
		1979: WHO declares smallpox eradicated	



- 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/viophage 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 <i>Pandoravirus salinus</i> ; 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

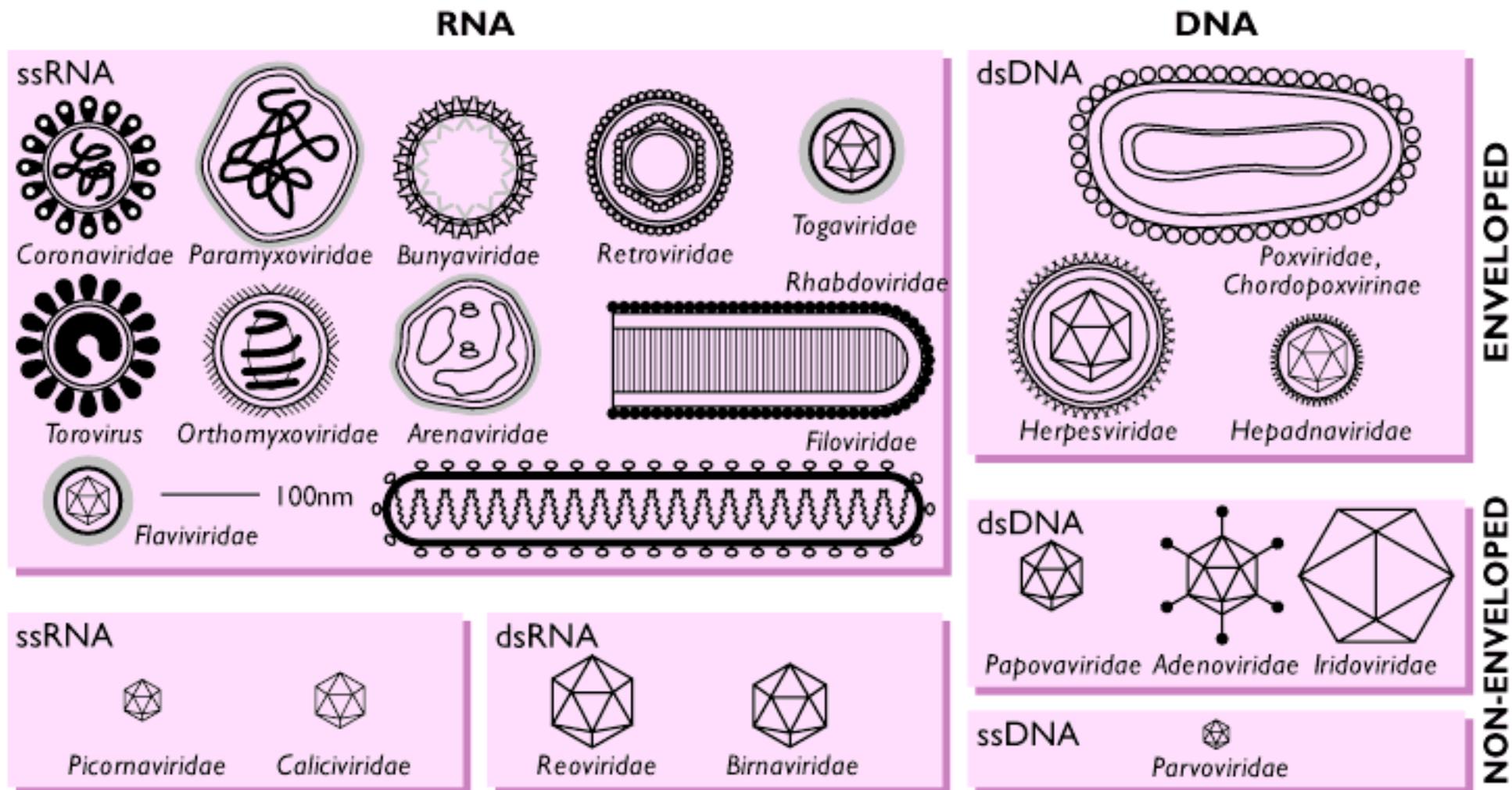


Fig. 5 Diagrammatic representation of the families of viruses infecting vertebrates, grouped according to the nature and strandedness of their genome and the presence or absence of an envelope. Reproduced with permission from Springer-Verlag.

Vírus de bactérias

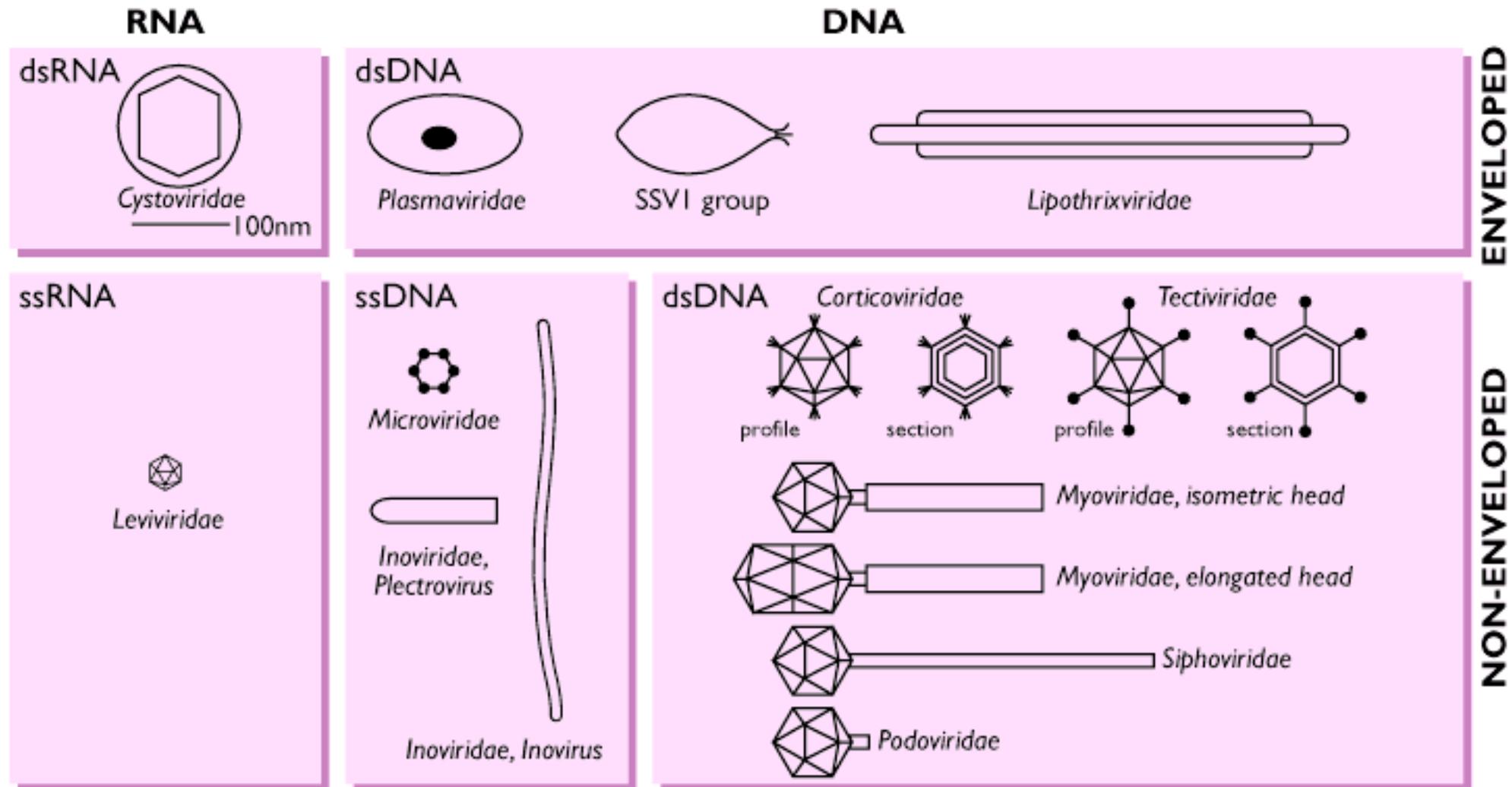


Fig. 1 Diagrammatic representation of the families of viruses infecting bacteria, group according to the nature and strandedness of their genome and the presence or absence of an envelope. Reproduced with permission from Springer-Verlag.

TABLE 2.1 Summary Characteristics of Vertebrate Virus Families

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

CLASSIFICAÇÃO

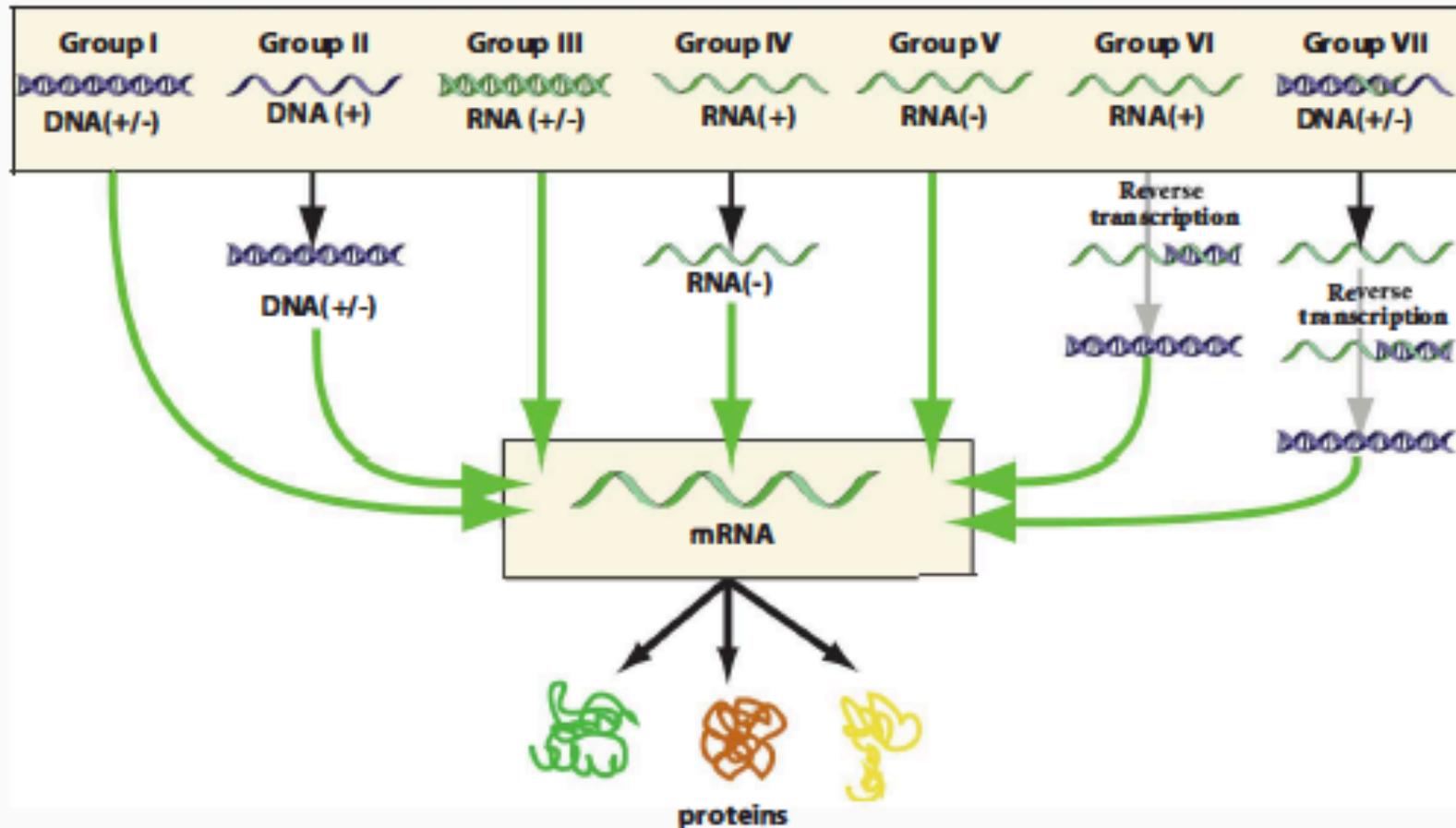


FIGURE 2.1. The Baltimore classification, a virus classification scheme based on the form of nucleic acid present in virion particles and the pathway for expression of the genetic material as messenger RNA.¹

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.)