

# Viromics

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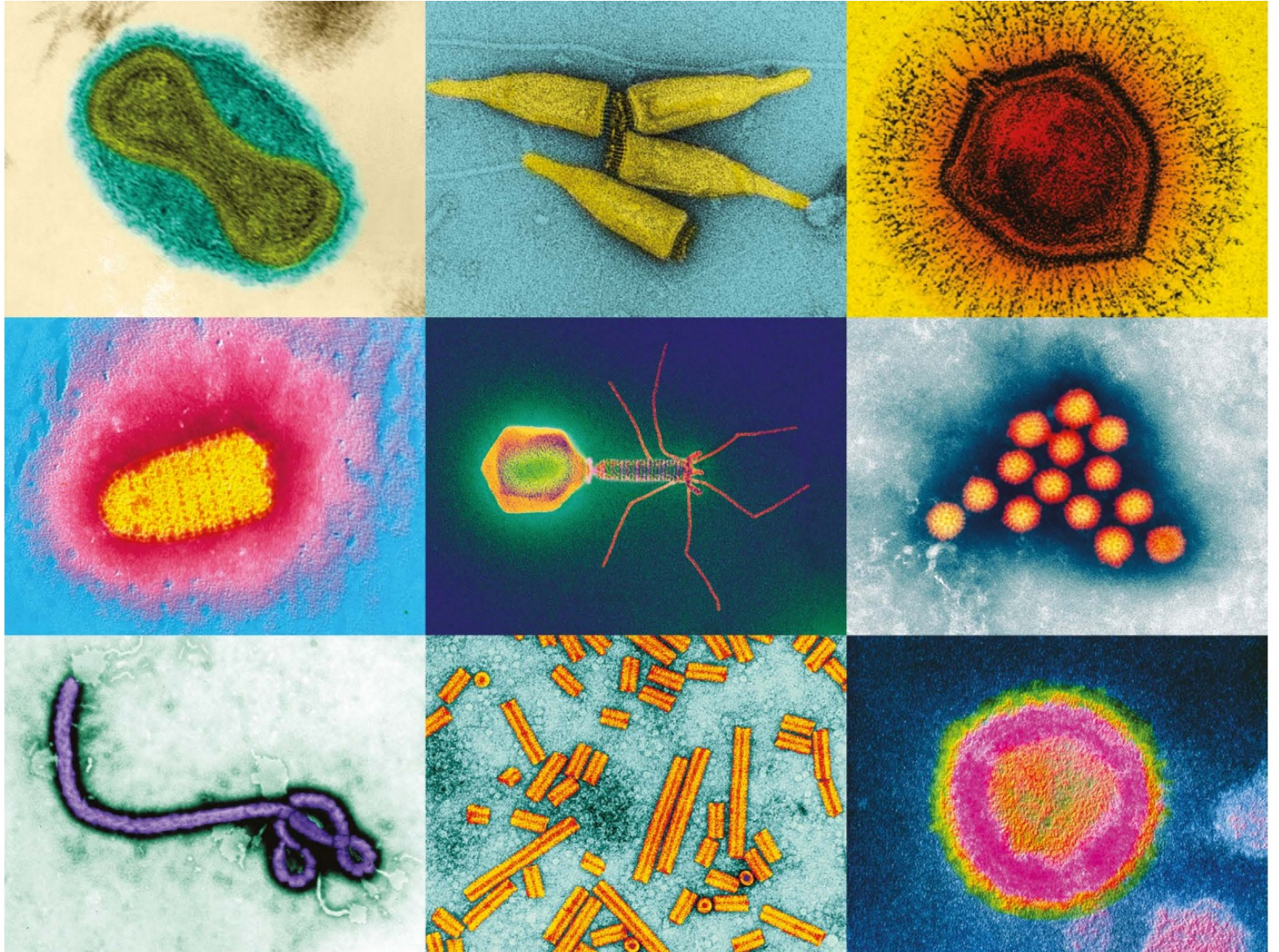
Arctic Microbial Ecology group

Faculty of Agriculture and Forestry

University of Helsinki

# Viruses

- Intracellular parasites
- Extremely abundant and diverse
- Different infection and replication strategies
- Huge impact on their hosts:
  - control abundance
  - modulate metabolism
  - mediate horizontal gene transfer
  - drive evolution



Viruses come in all shapes and sizes, such as the giant mimivirus (top right) and the lunar-lander-shaped bacteriophage (centre).

FALSE-COLOUR ELECTRON MICROGRAPHS (NOT TO SAME SCALE). TOP ROW L-R: SMALLPOX VIRUS; ACANTHAMOEBA POLYPHAGA MIMIVIRUS; CENTRE ROW L-R: RABIES VIRUS; T4 BACTERIOPHAGE; ROTAVIRUS. BOTTOM ROW L-R: EBOLA VIRUS; TOBACCO RATTLE VIRUS; HIV-2. SPL: M. HÄRING ET AL./J. VIROL.; E. GHIGO ET AL./PLOS PATHOG.; FREDERICK A. MURPHY/CDC GLOBAL



# Viruses

- Can be found in any environment where cells are present
- Infect all life forms
- Life cycle:
  - intra- and extracellular phases
  - lytic vs lysogenic

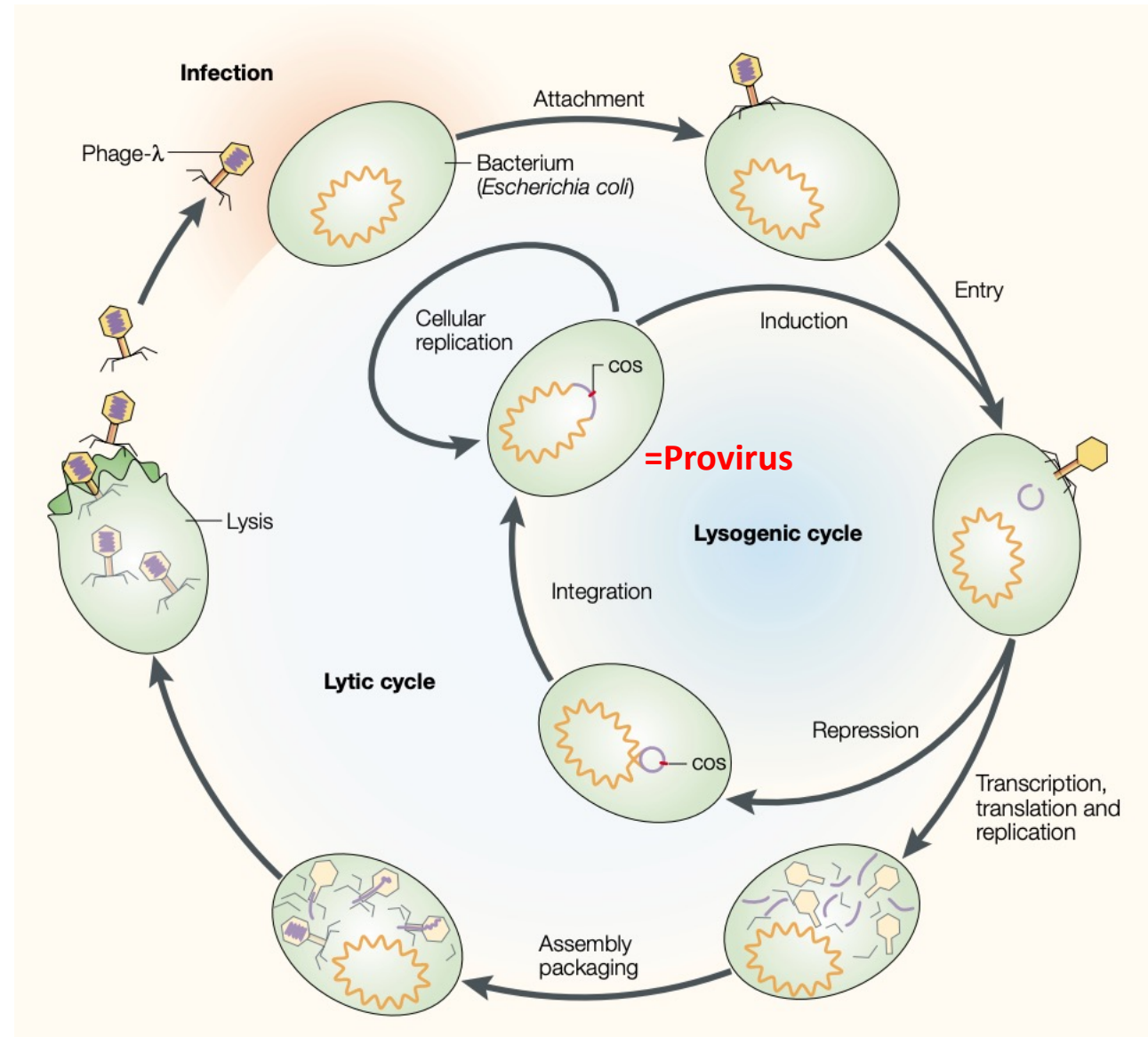


Figure credit: Campbell, Nature Reviews Genetics, 2003

# Viruses

- Virion:  
genome + protein shell  
(+ optionally envelope(s))
- Genome:
  - dsDNA
  - dsDNA (partial)
  - ssDNA
  - dsRNA
  - ssRNA(+)
  - ssRNA (-)

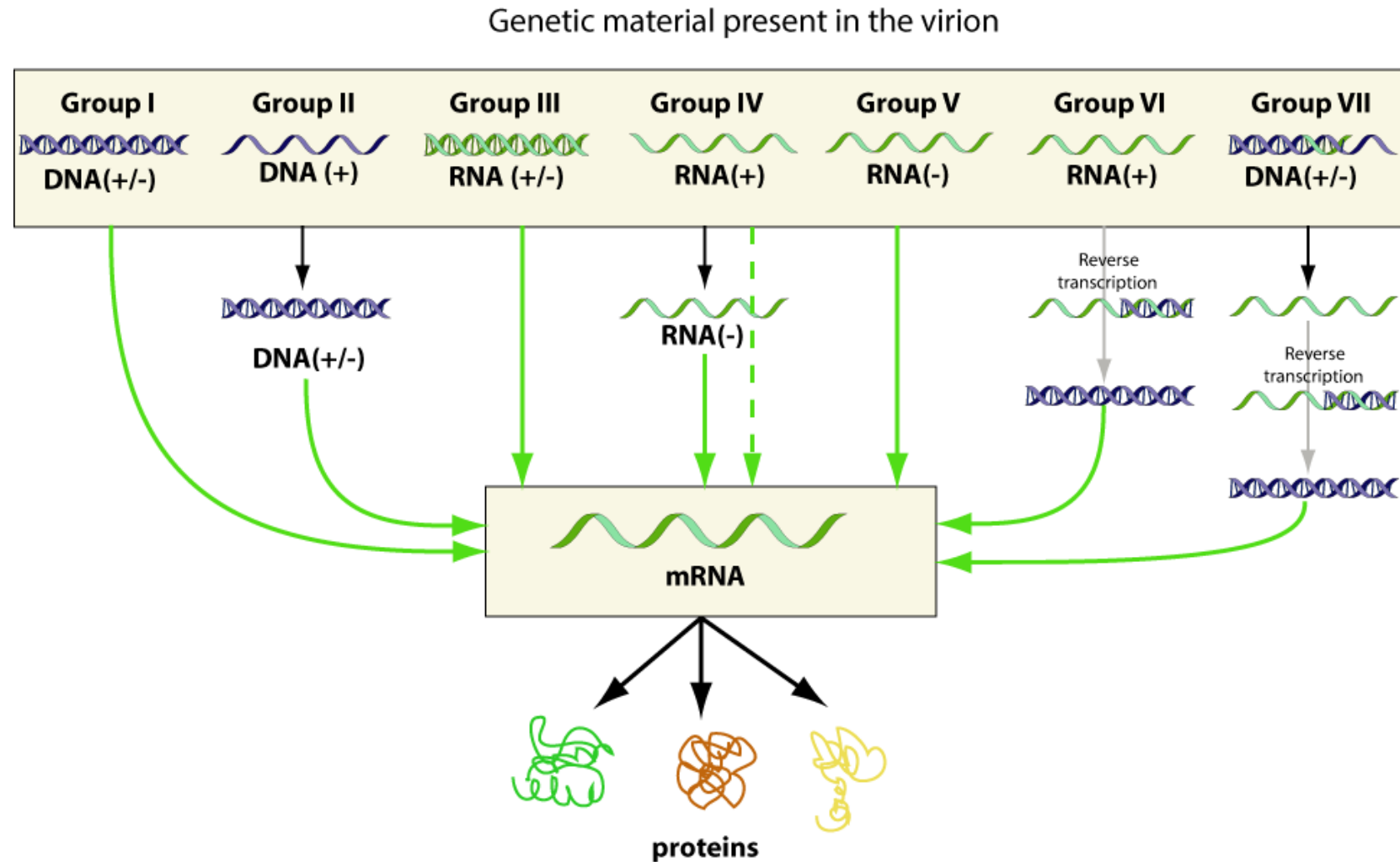


Figure credit: <https://viralzone.expasy.org/254>

# Methods to study viruses

## Culture-dependent

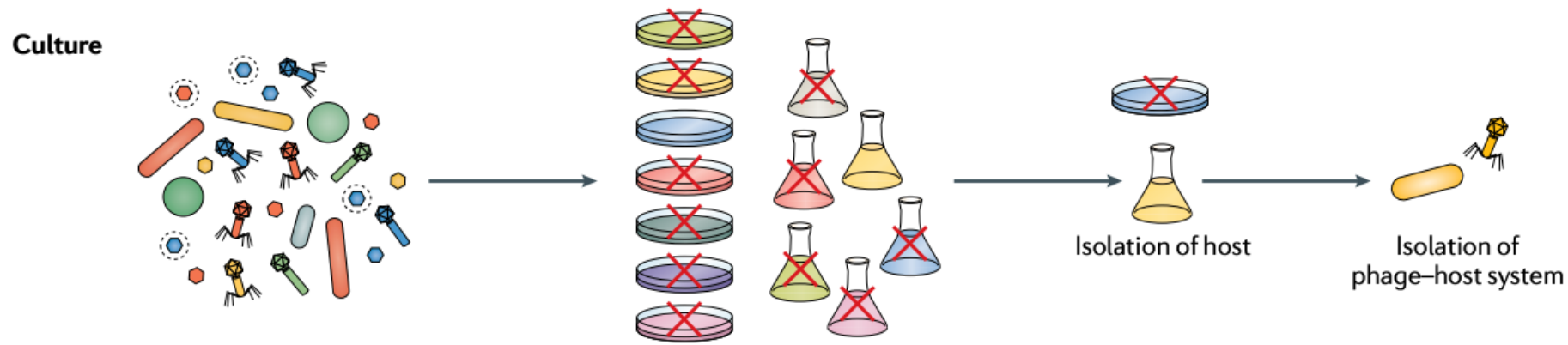


Figure credit: Martínez et al., Nat Rev Microbiol, 2020

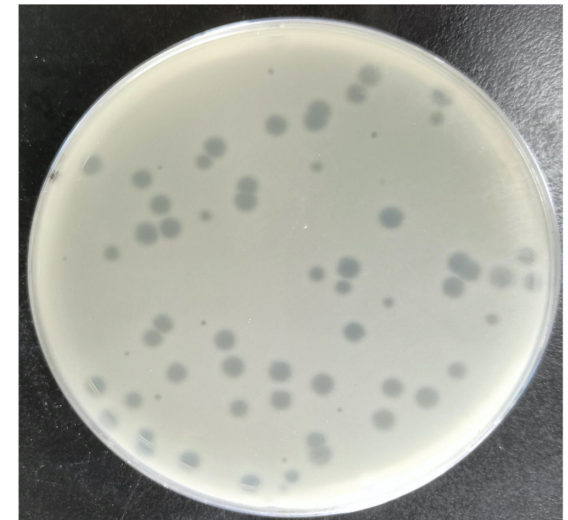


Figure credit:  
Khan et al, Front Microbiol, 2020

# Methods to study viruses

Culture-independent:

- EM of environmental samples
- Metagenomics
- Many more...

# Viromics = meta-omics of viruses

- Analysing of environmental DNA and/or RNA (sequencing techniques!)

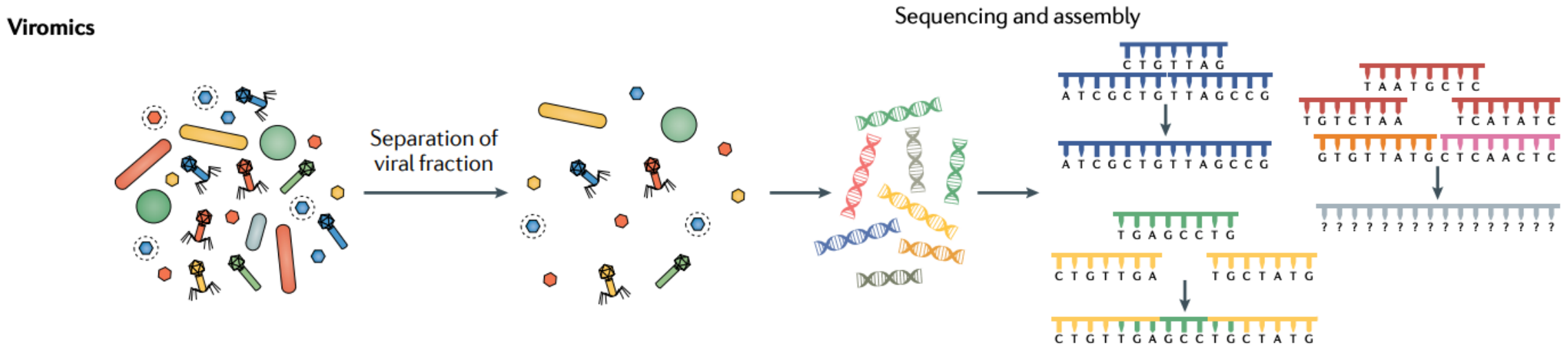


Figure credit: Martínez et al., Nat Rev Microbiol, 2020

- Pre-filtered samples:  
sample -> 220 nm filtering -> sequencing -> “only” viral sequences (=virome)

# Viromics = meta-omics of viruses

- Analysing of environmental DNA and/or RNA (sequencing techniques!)

Viromics



Sequencing and assembly

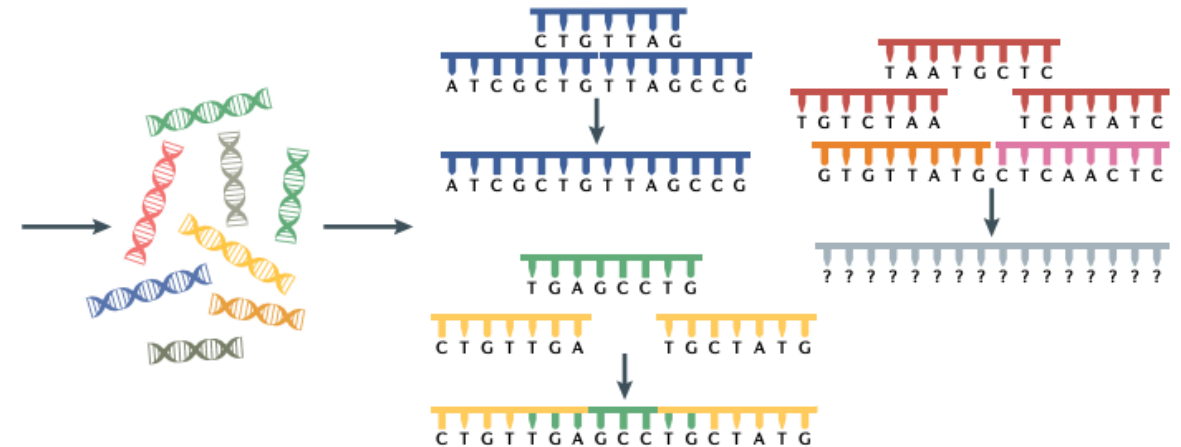


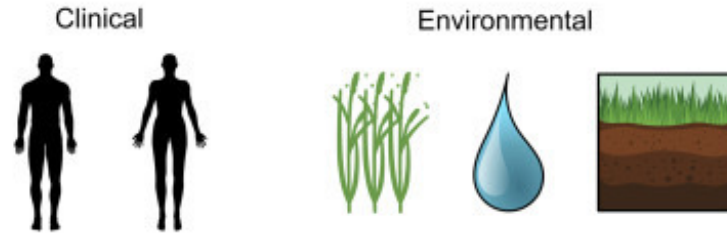
Figure credit: Martínez et al., Nat Rev Microbiol, 2020

- Extracting viral sequences from **bulk metagenomes**:  
sample -> sequencing -> metagenome -> selecting viral sequences

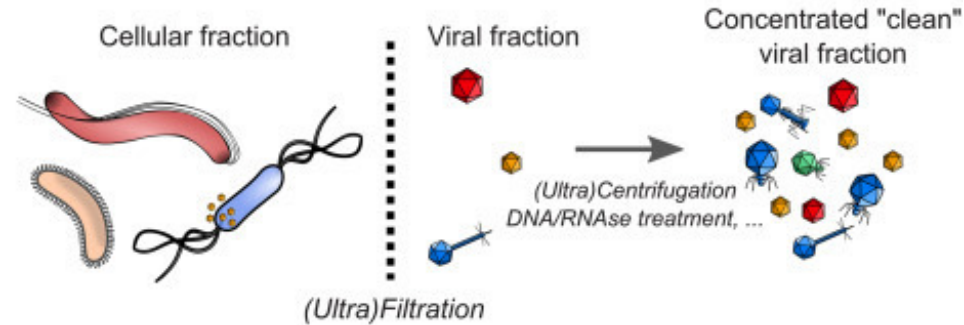


# Workflow steps

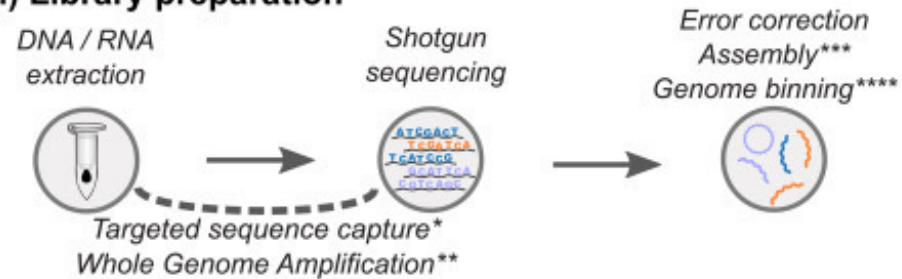
## (i) Sample collection



## (ii) Sample preparation



## (iii) Library preparation



## (iv) Sequence analysis



Figure credit:  
Roux et al., Encyclopedia of Virology, 2021

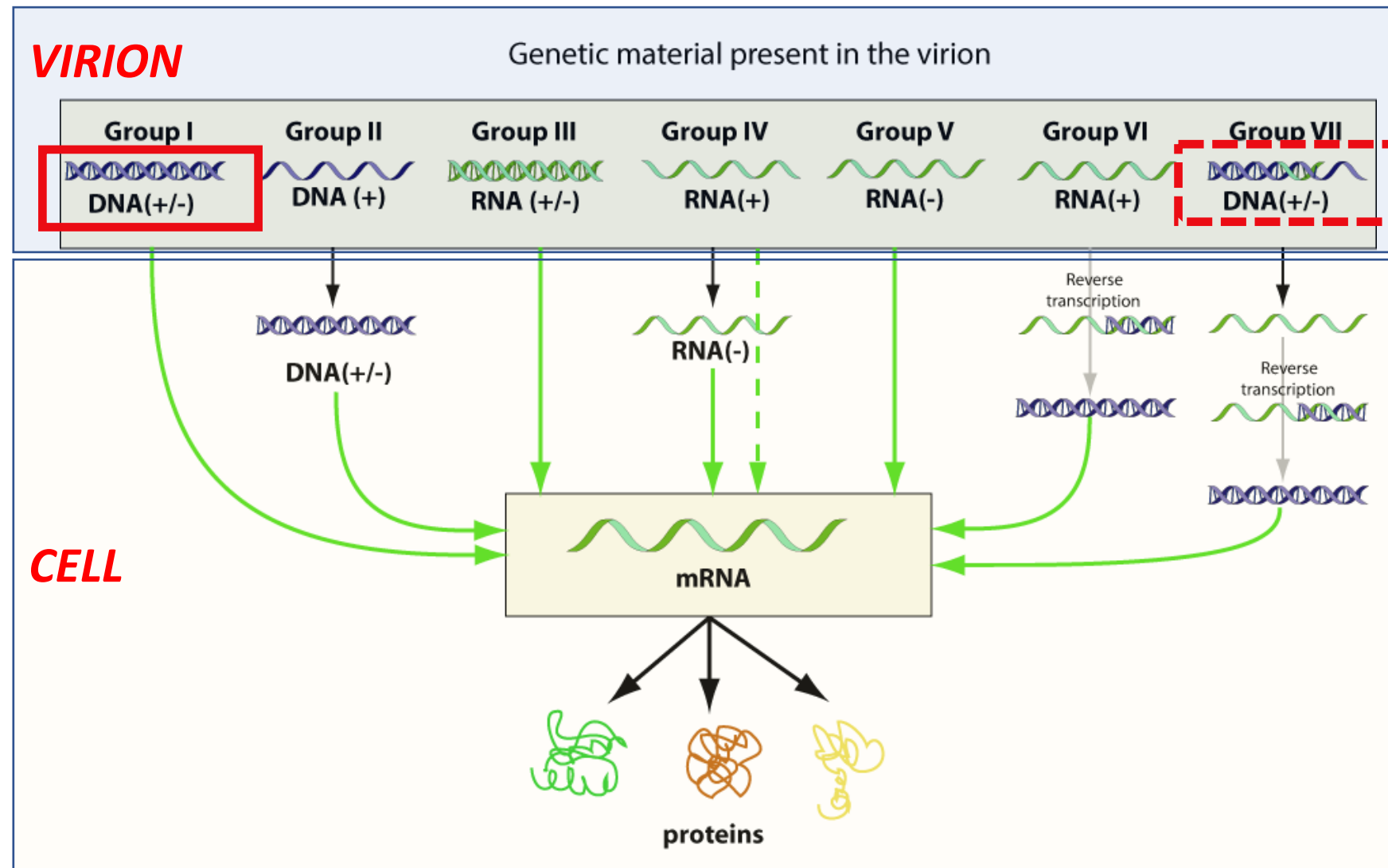
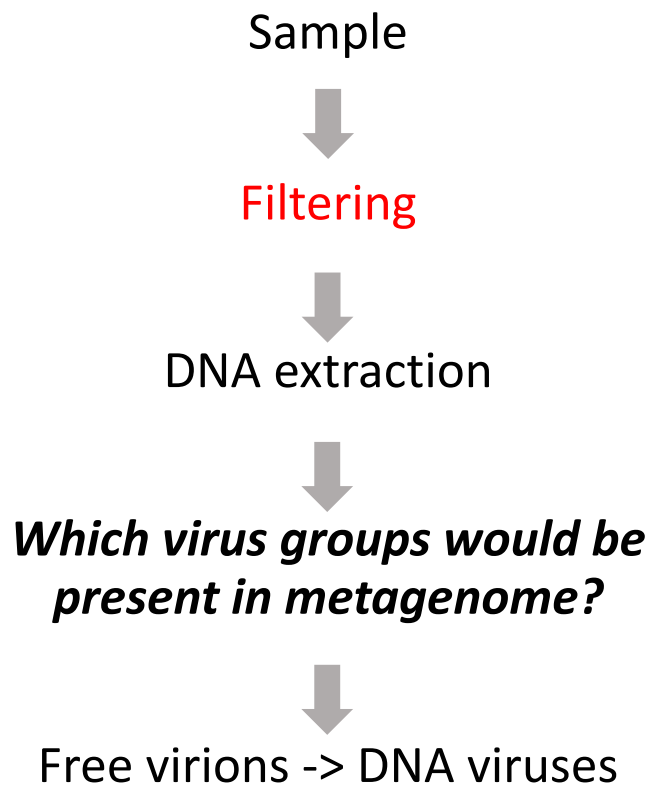


Figure credit: <https://viralzone.expasy.org/254>

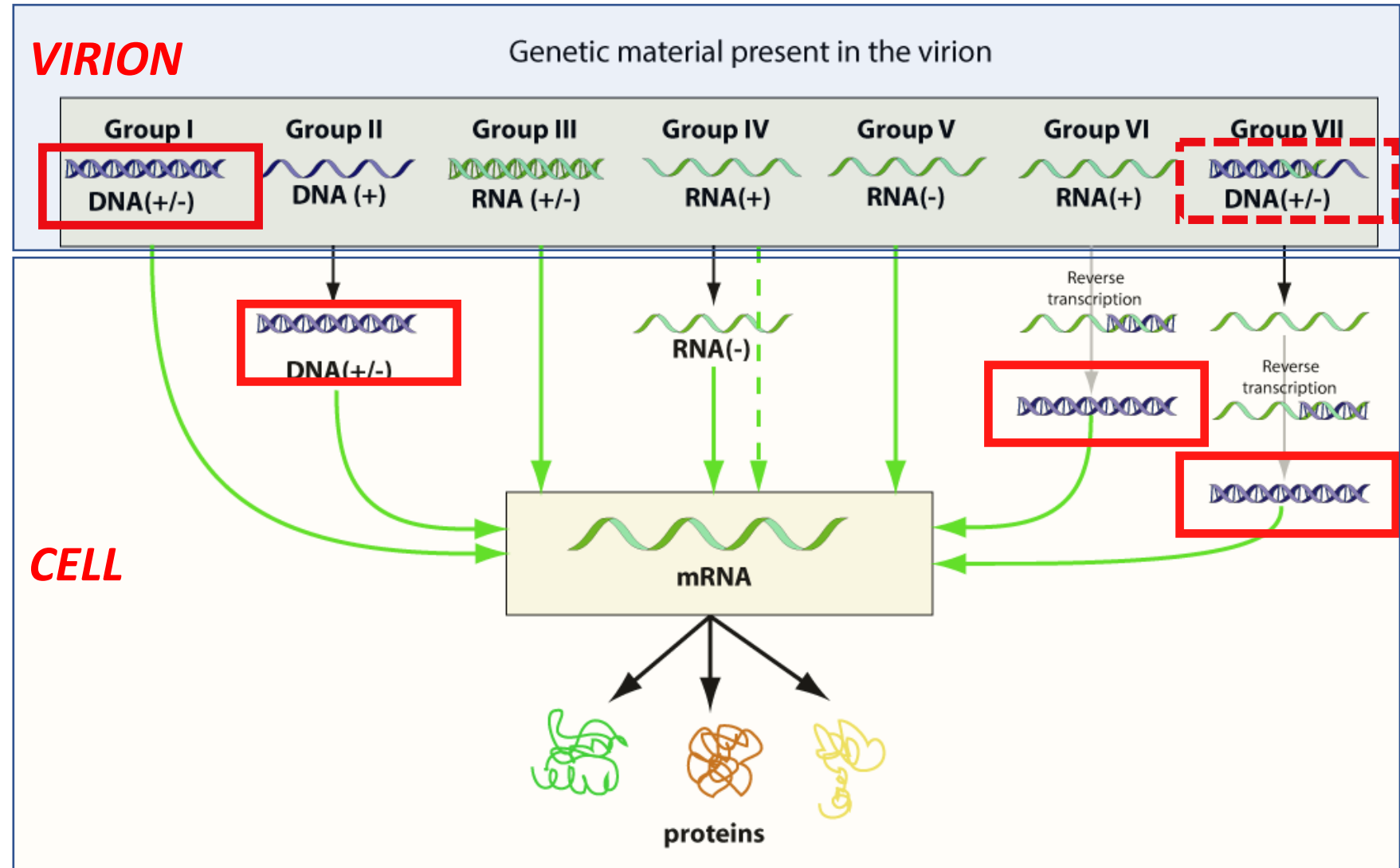
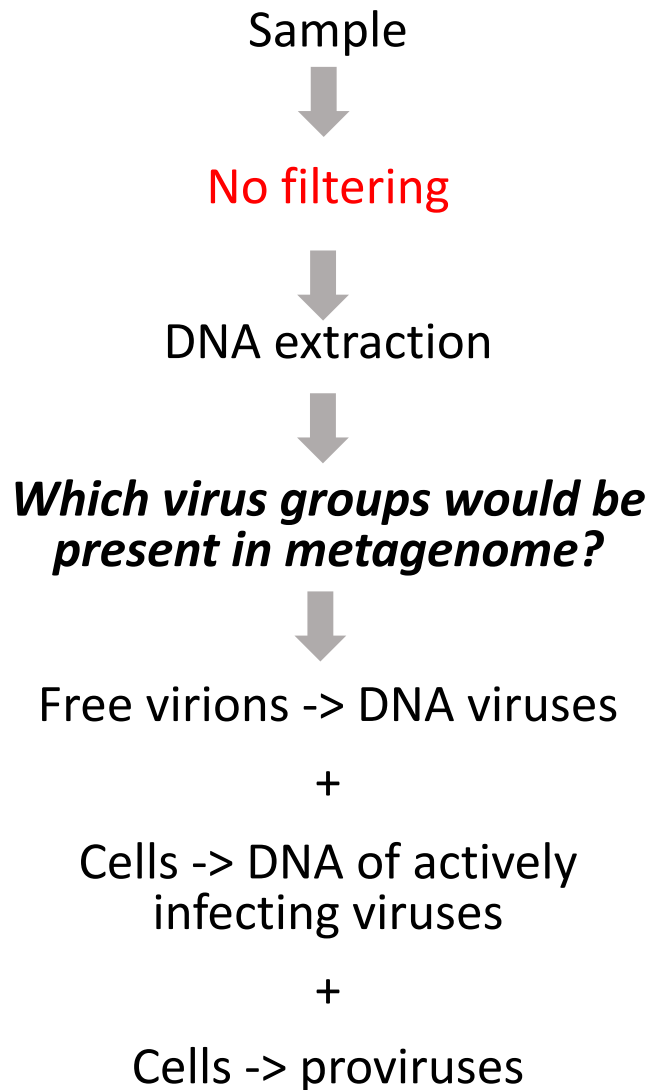


Figure credit: <https://viralzone.expasy.org/254>

Same pre-cautions  
when working with  
RNA samples

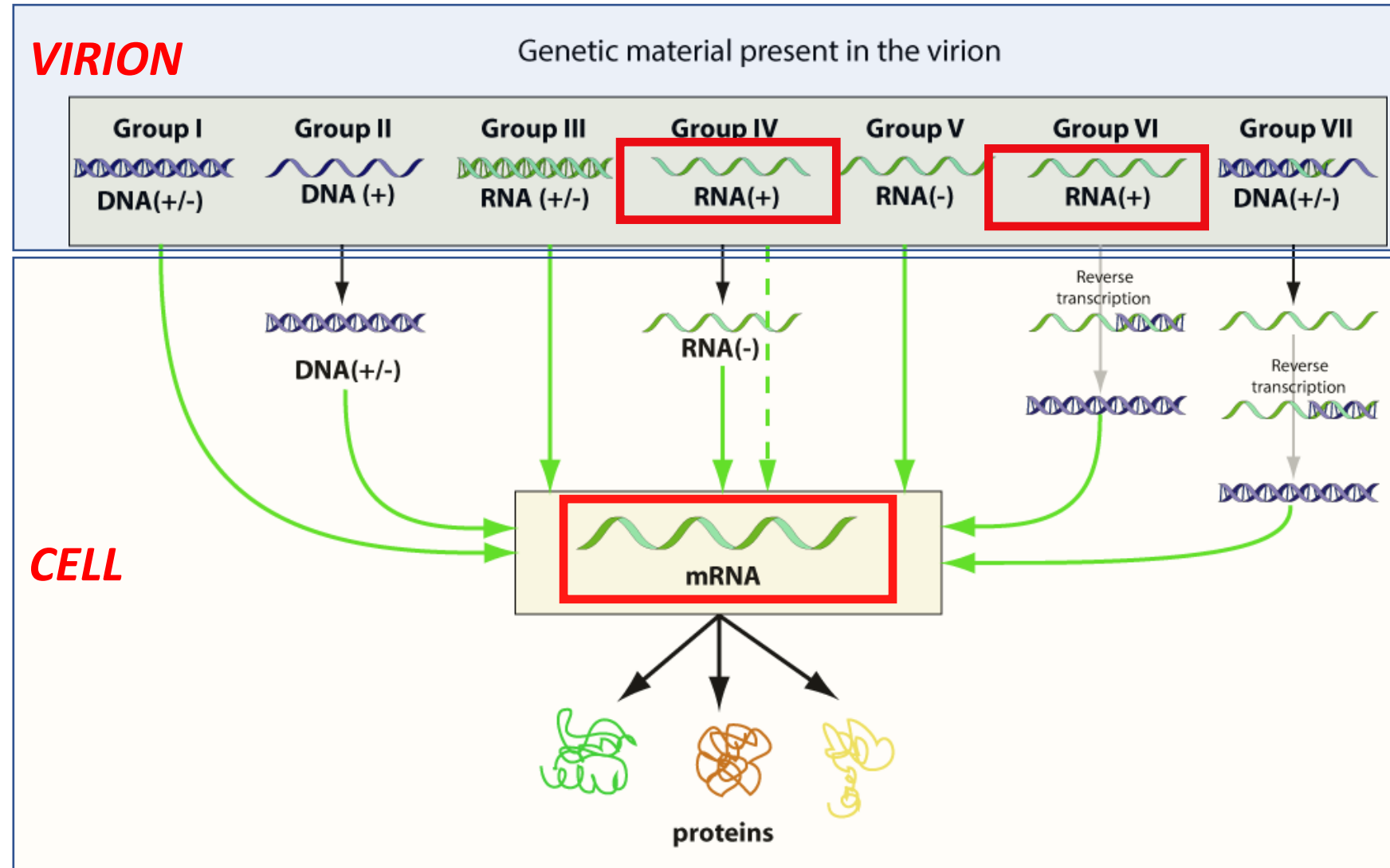


Figure credit: <https://viralzone.expasy.org/254>

# Viromes and bulk metagenomes biases

- Bulk metagenomes: viral sequences are only a minor fraction
- Viromes: size selection exclude larger virus particles
- Both under-represent rare and hypervariable viruses



# Case studies

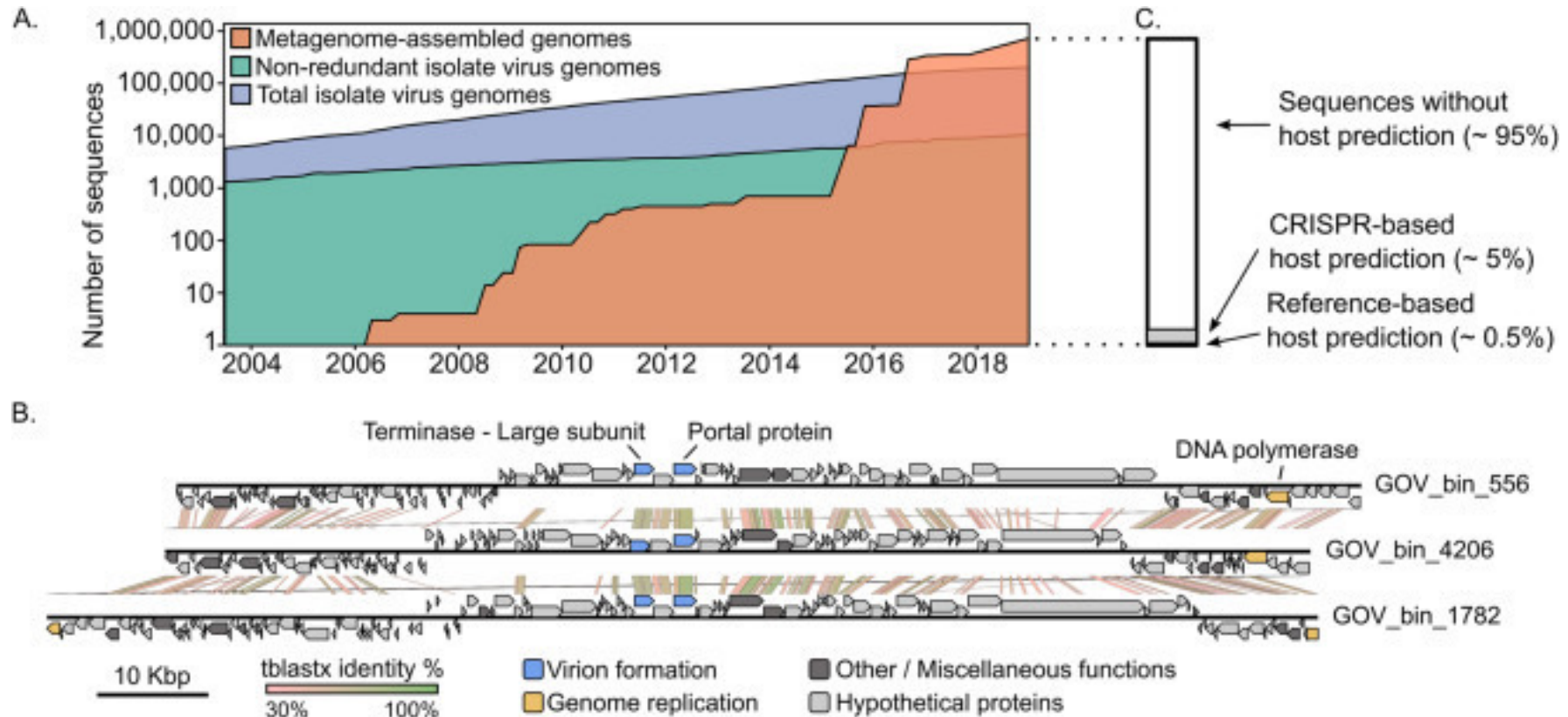


Figure credit:  
Roux et al., Encyclopedia of Virology, 2021

# Case studies

## Tara oceans

Review Article | [Published: 12 May 2020](#)

### ***Tara Oceans: towards global ocean ecosystems biology***

[Shinichi Sunagawa](#) , [Silvia G. Acinas](#), [Peer Bork](#), [Chris Bowler](#), [Tara Oceans Coordinators](#), [Damien Eveillard](#), [Gabriel Gorsky](#), [Lionel Guidi](#), [Daniele Iudicone](#), [Eric Karsenti](#), [Fabien Lombard](#), [Hiroyuki Ogata](#), [Stephane Pesant](#), [Matthew B. Sullivan](#), [Patrick Wincker](#) & [Colomban de Vargas](#) 

[Nature Reviews Microbiology](#) **18**, 428–445 (2020) | [Cite this article](#)


**12k** Accesses | **91** Citations | **154** Altmetric | [Metrics](#)

# Case studies

## crAssphage

Open Access | [Published: 24 July 2014](#)

### **A highly abundant bacteriophage discovered in the unknown sequences of human faecal metagenomes**

[Bas E. Dutilh](#) , [Noriko Cassman](#), [Katelyn McNair](#), [Savannah E. Sanchez](#), [Genivaldo G. Z. Silva](#), [Lance Boling](#), [Jeremy J. Barr](#), [Daan R. Speth](#), [Victor Seguritan](#), [Ramy K. Aziz](#), [Ben Felts](#), [Elizabeth A. Dinsdale](#), [John L. Mokili](#) & [Robert A. Edwards](#)


[Nature Communications](#) **5**, Article number: 4498 (2014) | [Cite this article](#)

# Programs we use during this course

- Virsorter2 (+CheckV)
- Lazypipe
- What-the-Phage (output provided)

## JOURNAL ARTICLE

### Novel NGS pipeline for virus discovery from a wide spectrum of hosts and sample types


Ilya Plyusnin , Ravi Kant, Anne J Jääskeläinen, Tarja Sironen, Liisa Holm, Olli Vapalahti, Teemu Smura [Author Notes](#)

*Virus Evolution*, Volume 6, Issue 2, July 2020, veaa091,  
<https://doi.org/10.1093/ve/veaa091>

**Published:** 02 December 2020

Software article | [Open Access](#) | [Published: 01 February 2021](#)

### VirSorter2: a multi-classifier, expert-guided approach to detect diverse DNA and RNA viruses

Jiarong Guo, Ben Bolduc, Ahmed A. Zayed, Arvind Varsani, Guillermo Dominguez-Huerta, Tom O. Delmont, Akbar Adjie Pratama, M. Consuelo Gazitúa, Dean Vik, Matthew B. Sullivan  & Simon Roux 

*Microbiome* **9**, Article number: 37 (2021) | [Cite this article](#)

Article | [Open Access](#) | [Published: 21 December 2020](#)

### CheckV assesses the quality and completeness of metagenome-assembled viral genomes

Stephen Nayfach , Antonio Pedro Camargo, Frederik Schulz, Emiley Eloie-Fadrosh, Simon Roux & Nikos C. Kyrpides 

*Nature Biotechnology* **39**, 578–585 (2021) | [Cite this article](#)

### What the Phage: A scalable workflow for the identification and analysis of phage sequences

 Mike Marquet,  Martin Hölzer, Mathias W. Pletz,  Adrian Viehweger, Oliwia Makarewicz, Ralf Ehricht, Christian Brandt

**doi:** <https://doi.org/10.1101/2020.07.24.219899>

If interested to try later other tools for extracting viral sequences from metagenomes (+ some analyses):

Tool	Reference
viralFlye	<a href="https://genomebiology.biomedcentral.com/articles/10.1186/s13059-021-02566-x">https://genomebiology.biomedcentral.com/articles/10.1186/s13059-021-02566-x</a> <a href="https://github.com/Dmitry-Antipov/viralFlye">https://github.com/Dmitry-Antipov/viralFlye</a>
MetaPop	<a href="https://microbiomejournal.biomedcentral.com/articles/10.1186/s40168-022-01231-0">https://microbiomejournal.biomedcentral.com/articles/10.1186/s40168-022-01231-0</a> <a href="https://github.com/metaGmetapop/metapop">https://github.com/metaGmetapop/metapop</a>
Multi-Domain Genome Recovery (MuDoGeR)	<a href="https://www.biorxiv.org/content/10.1101/2022.06.21.496983v3.full">https://www.biorxiv.org/content/10.1101/2022.06.21.496983v3.full</a> <a href="https://github.com/mdsufz/MuDoGeR">https://github.com/mdsufz/MuDoGeR</a>