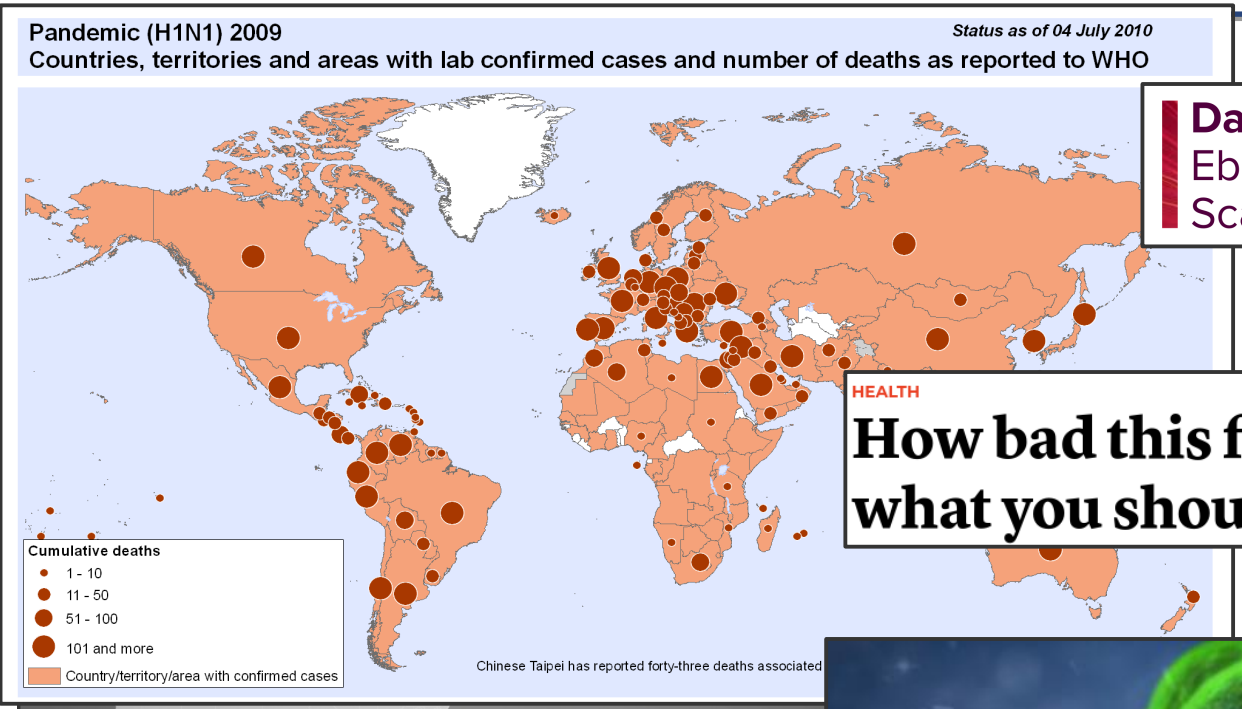
JGI JOINT GENOME INSTITUTE
A DOE OFFICE OF SCIENCE USER FACILITY

Establishing standards and best practices for describing genome sequences of uncultivated viruses (MIUViGs)

Simon Roux, DOE Joint Genome Institute, LBNL
GSC 20 – San Diego, May 4th 2018

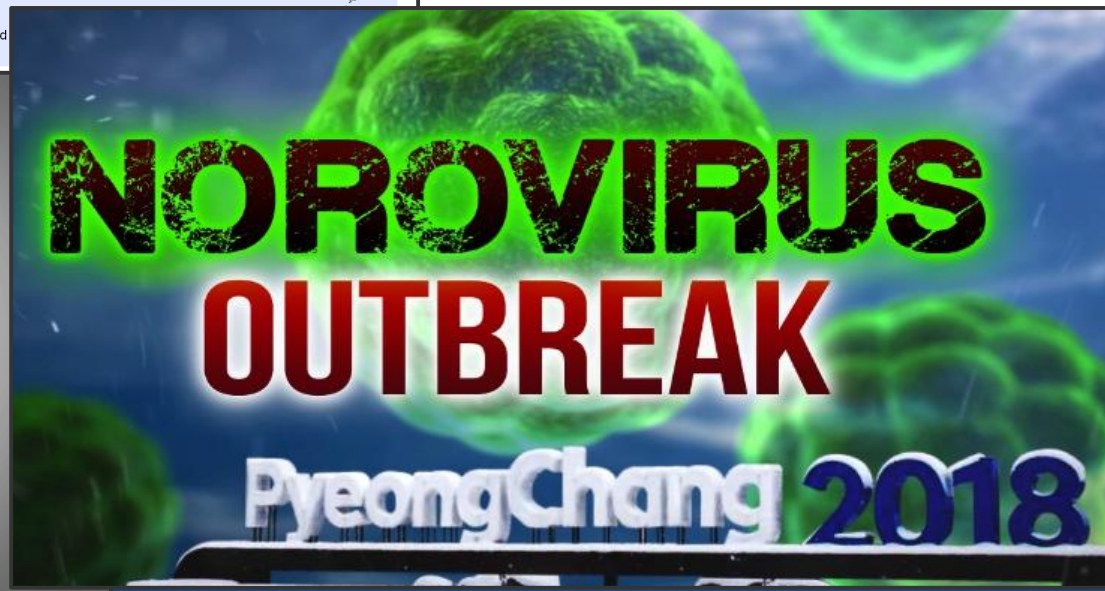
Viruses in the news



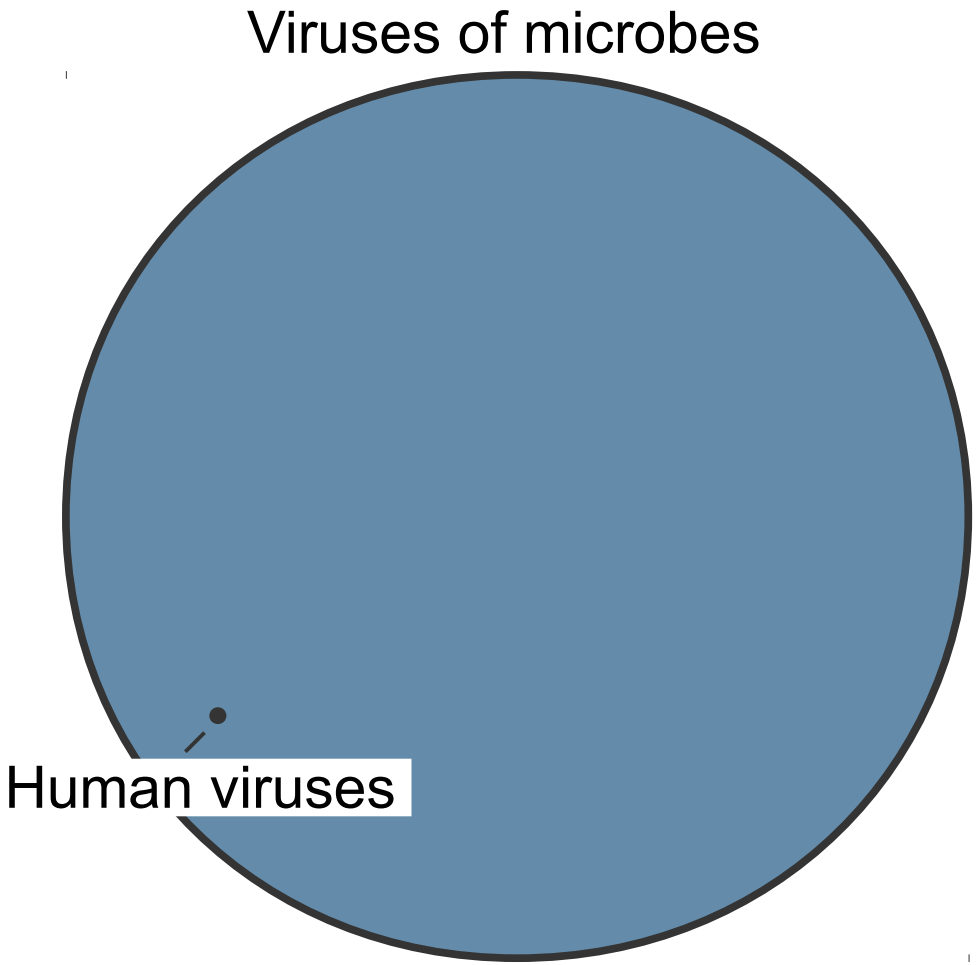
David Quammen:
Ebola to Zika and Beyond:
Scary Viruses in a Globalized World

HEALTH

How bad this flu season really is—and what you should do about it



Viruses of microbes are everywhere



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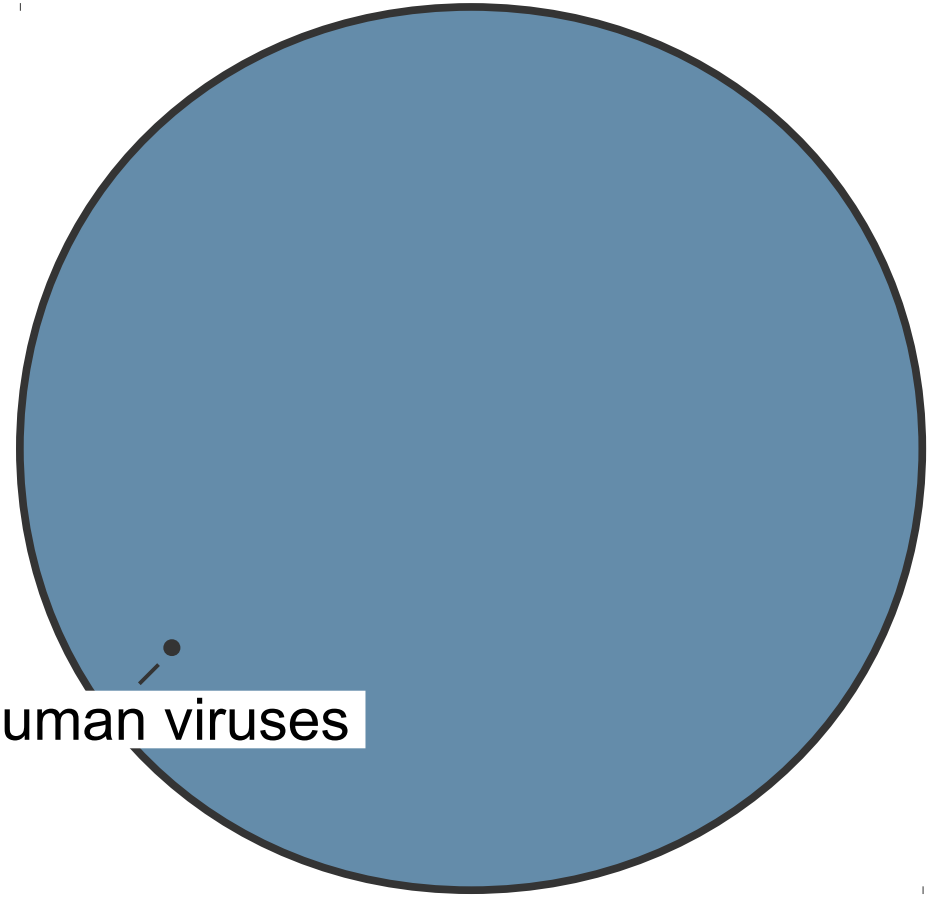
BioSciences



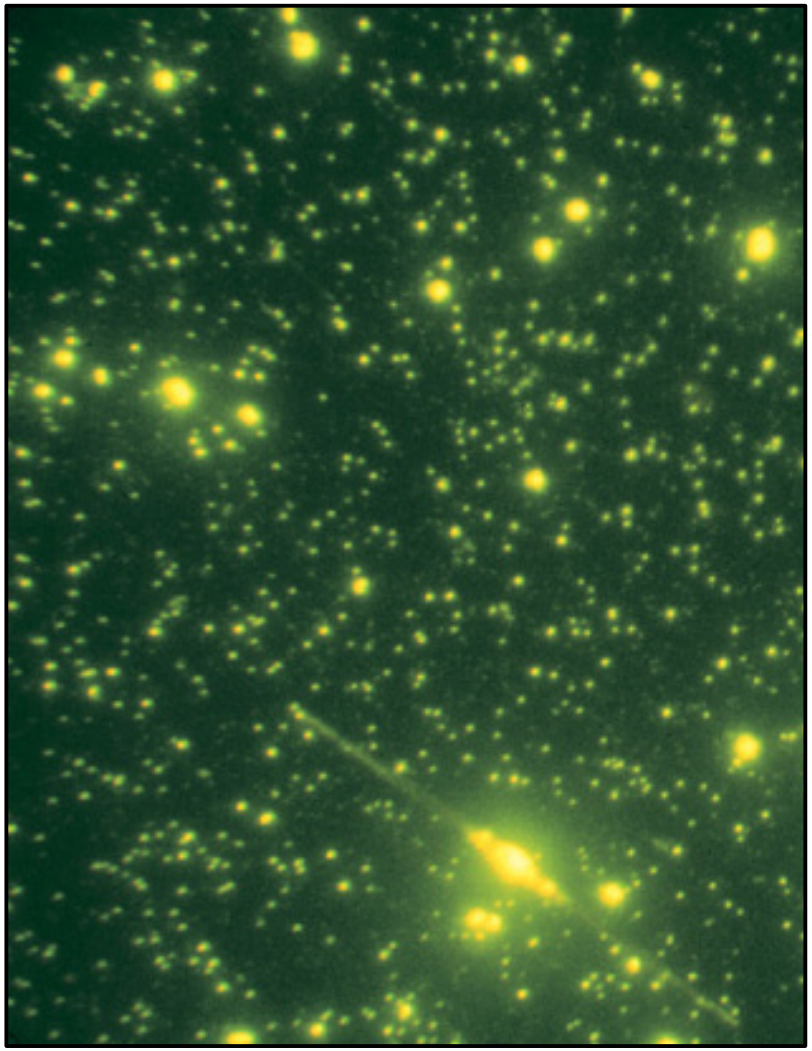


Image: Fuhrman Lab

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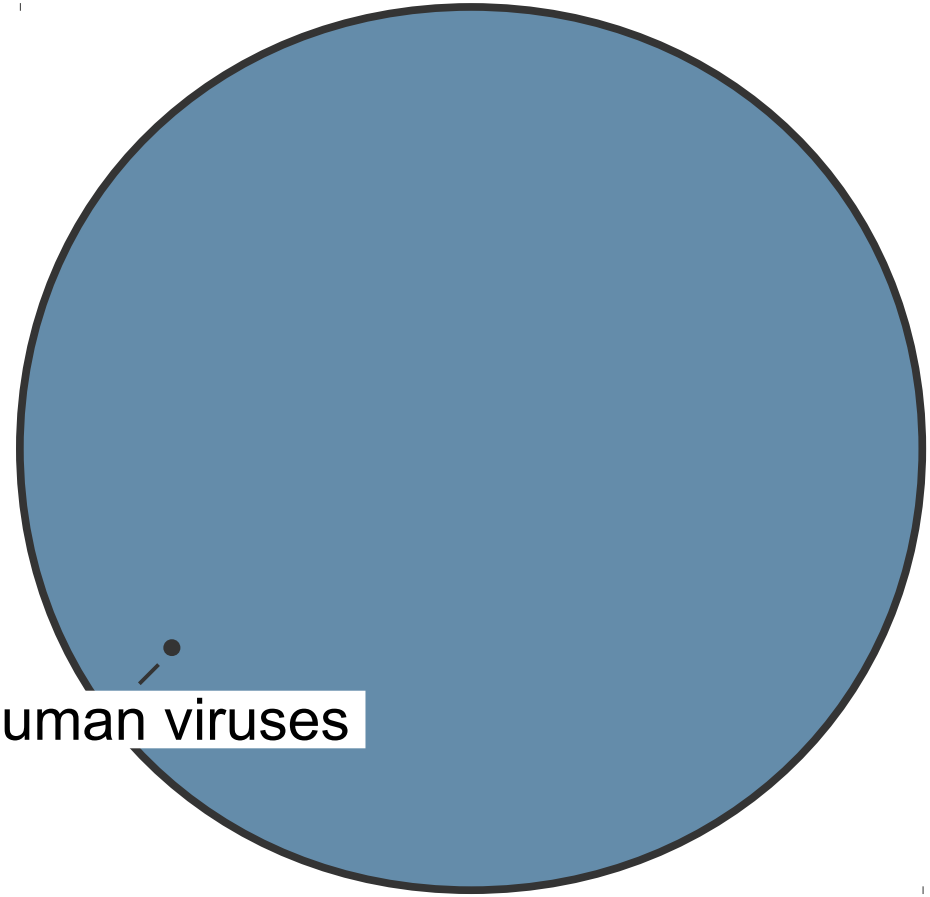

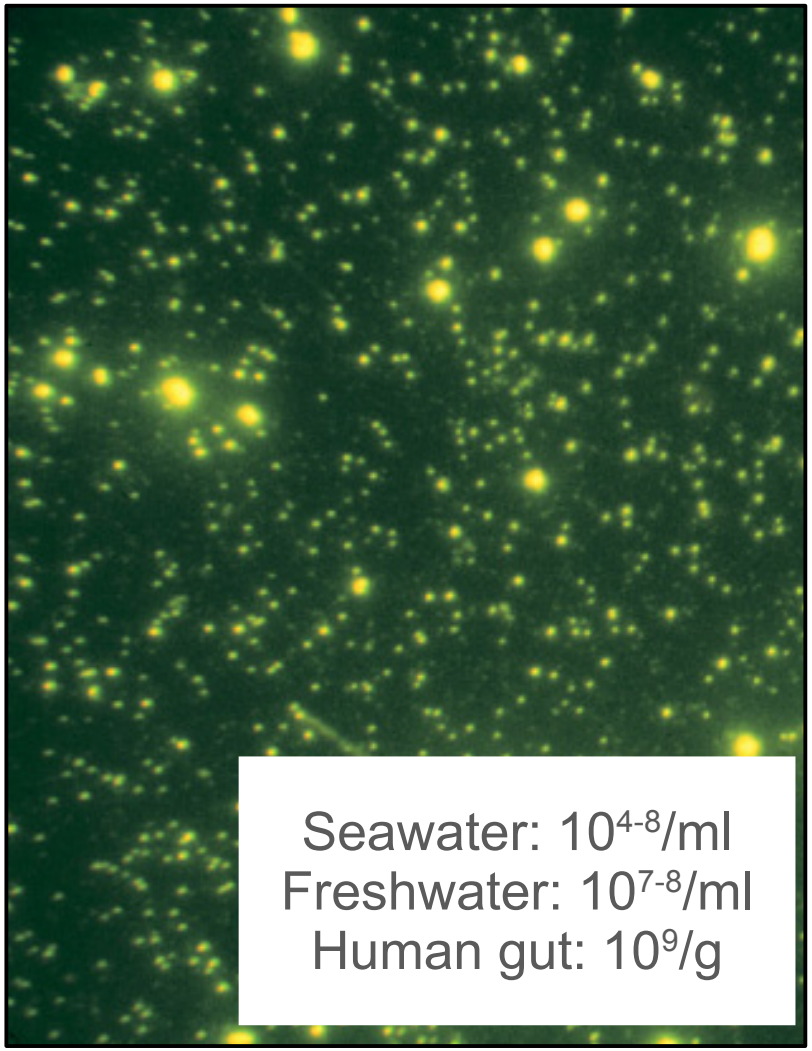

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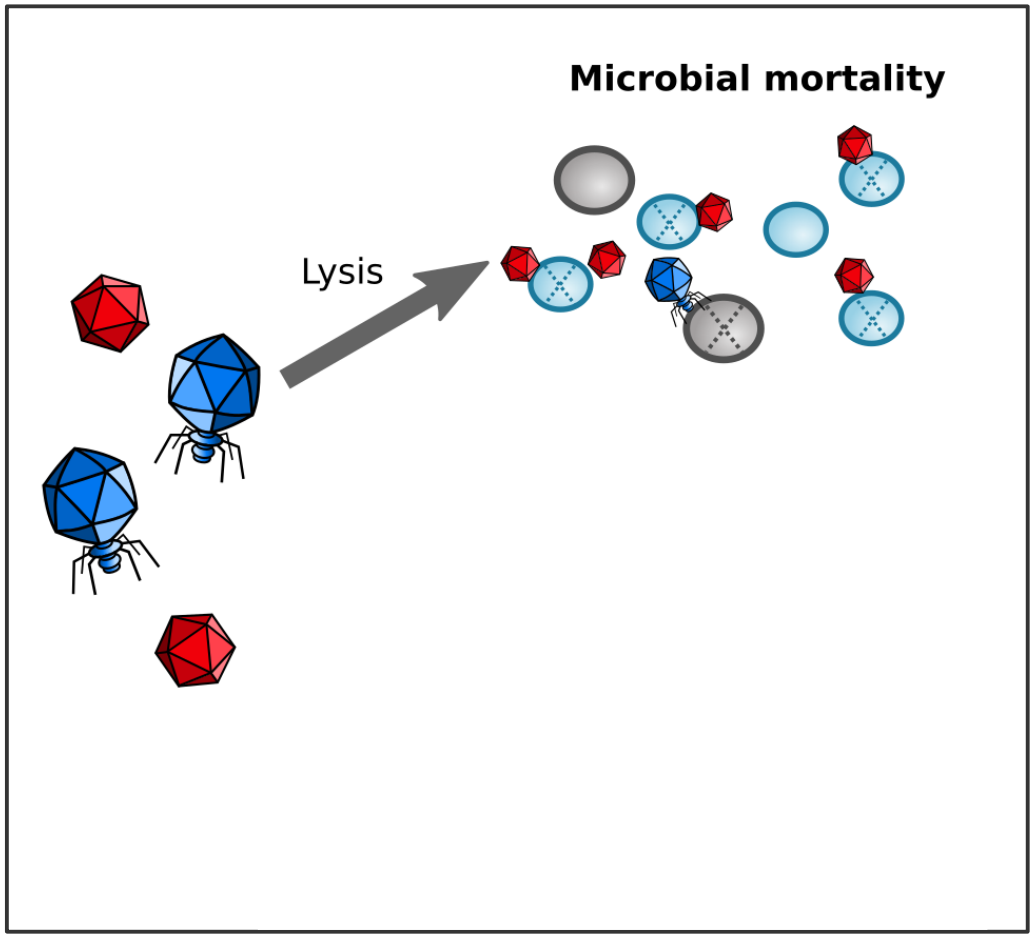

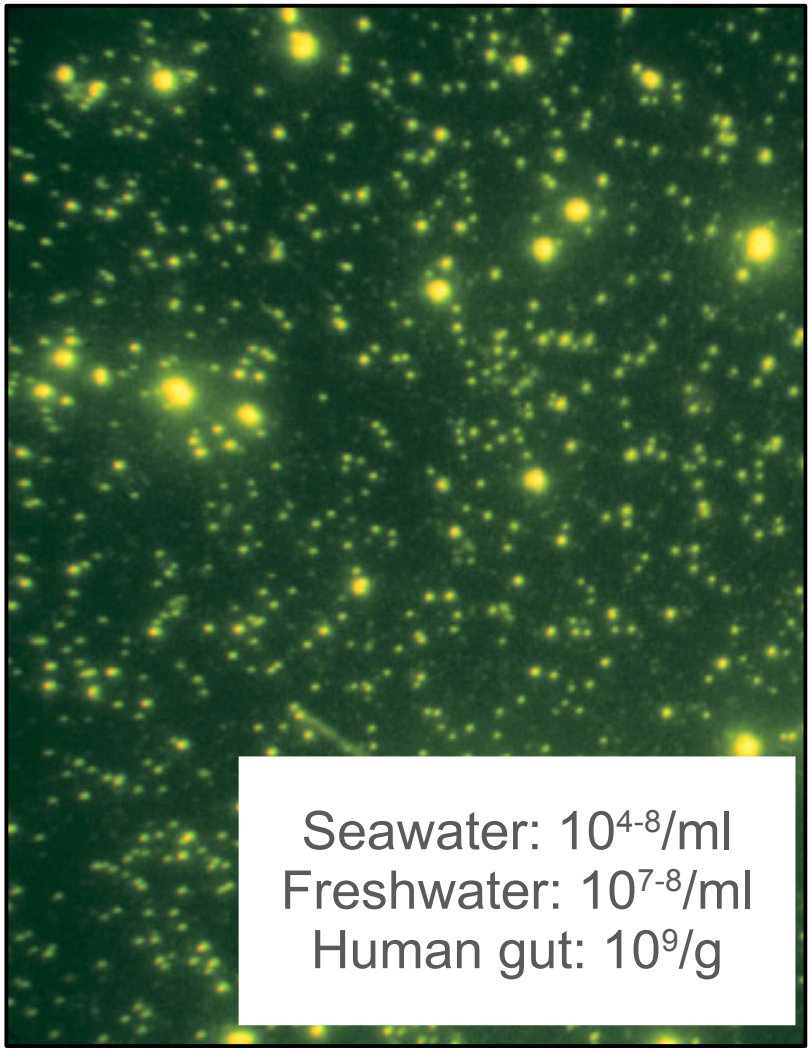

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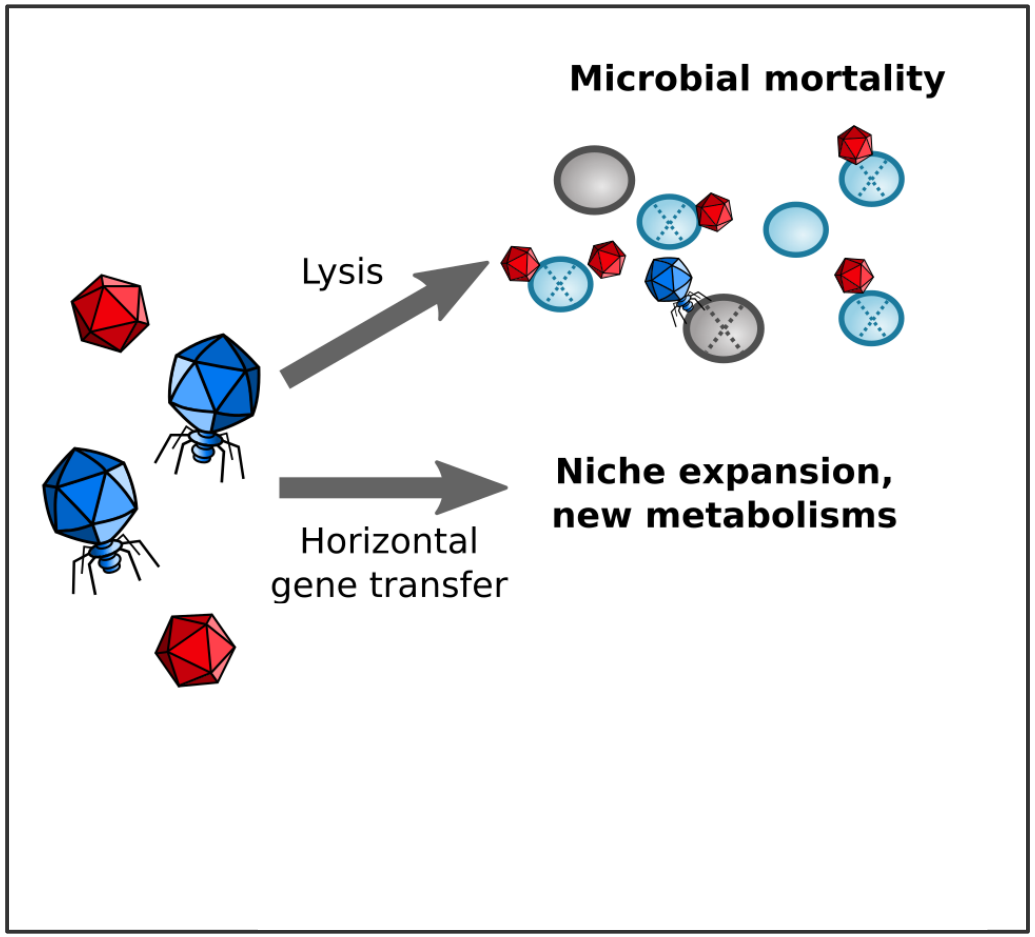

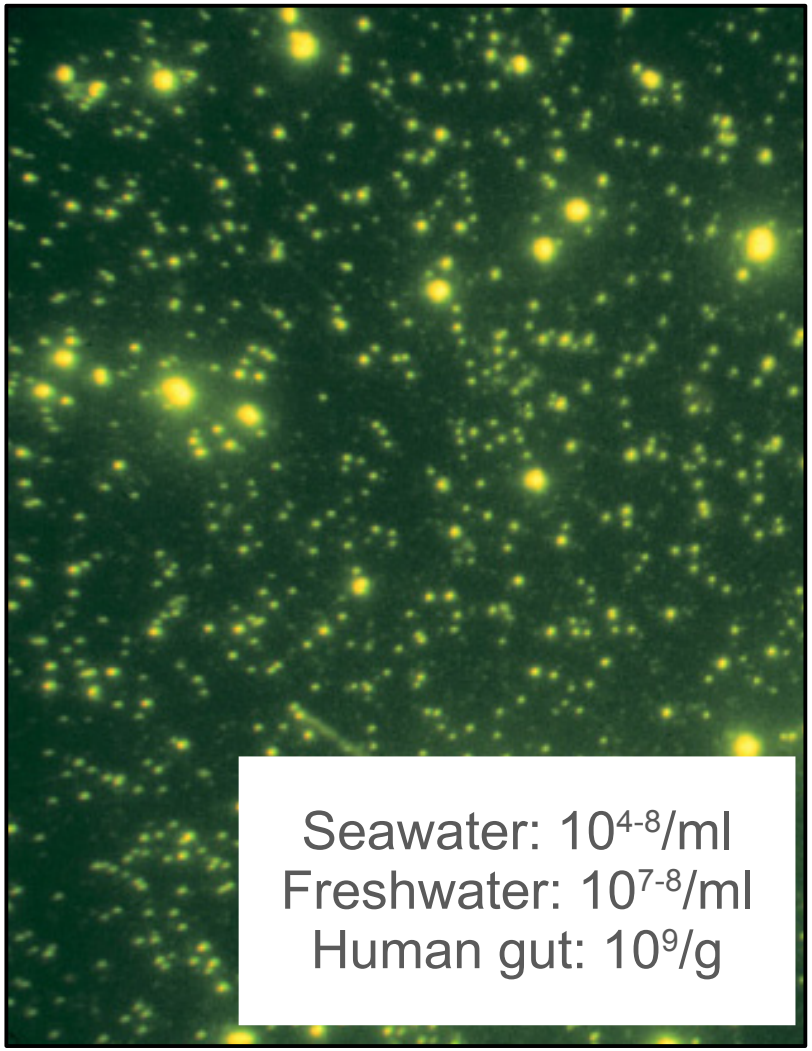

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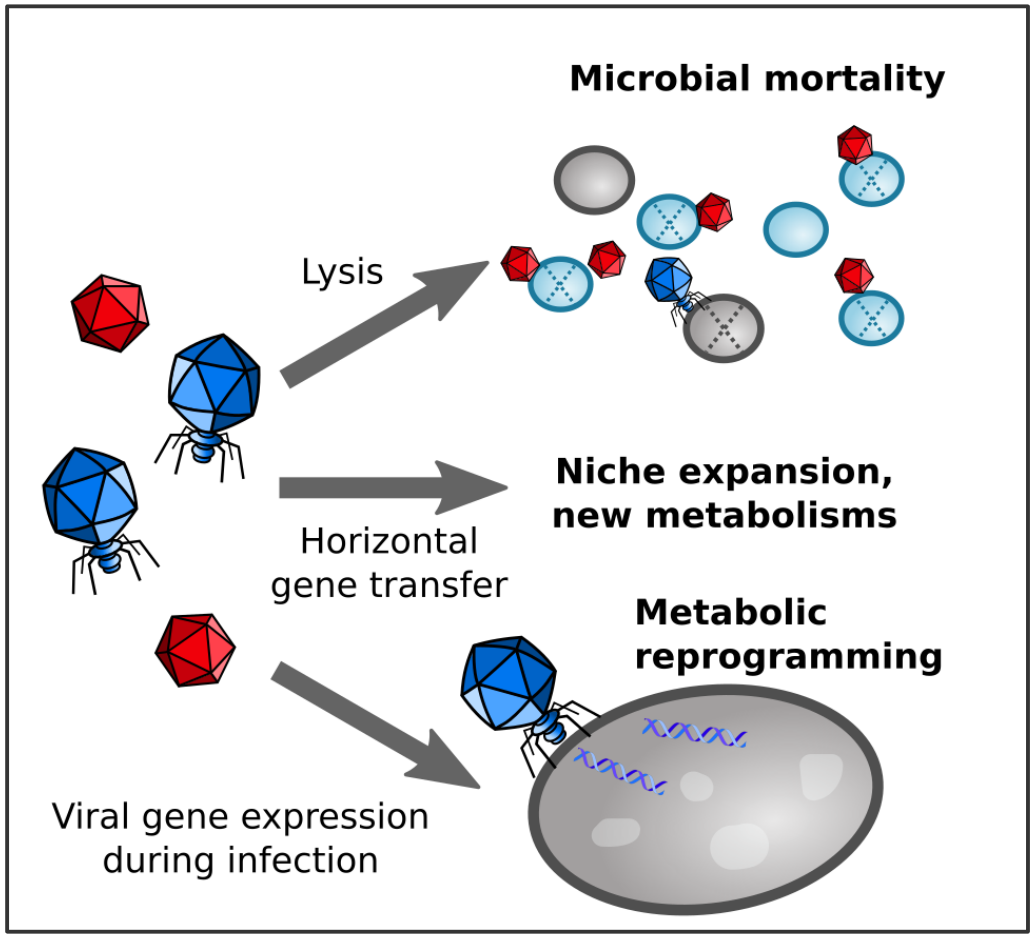

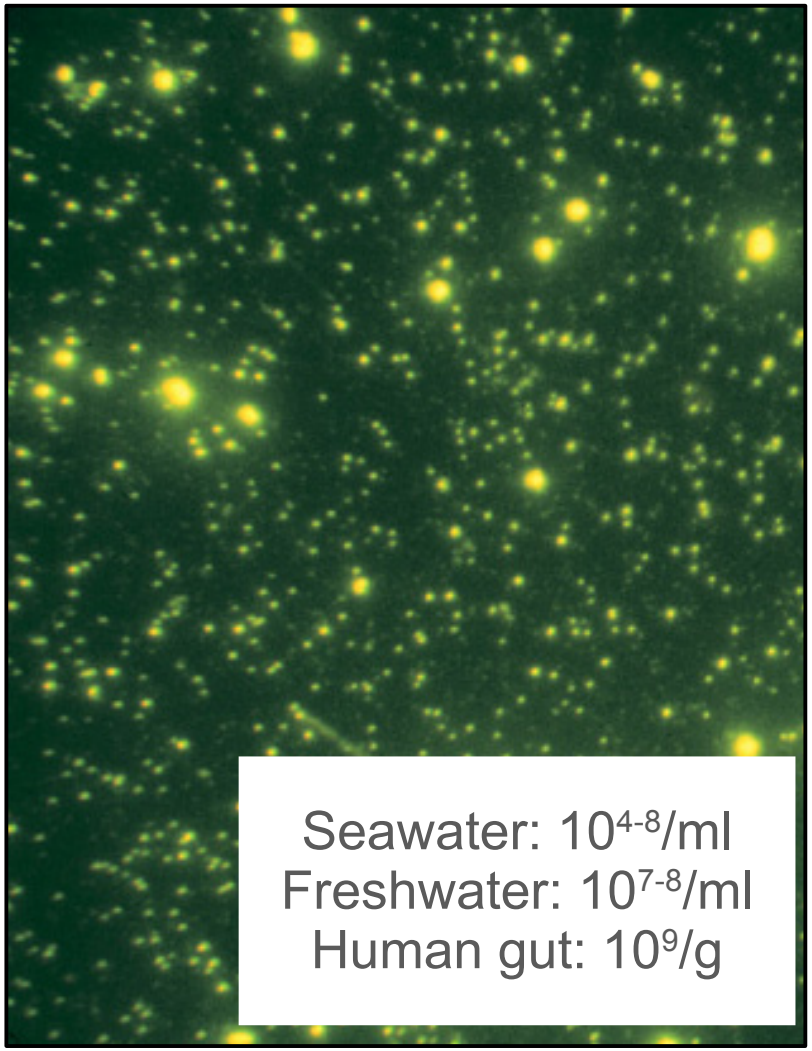

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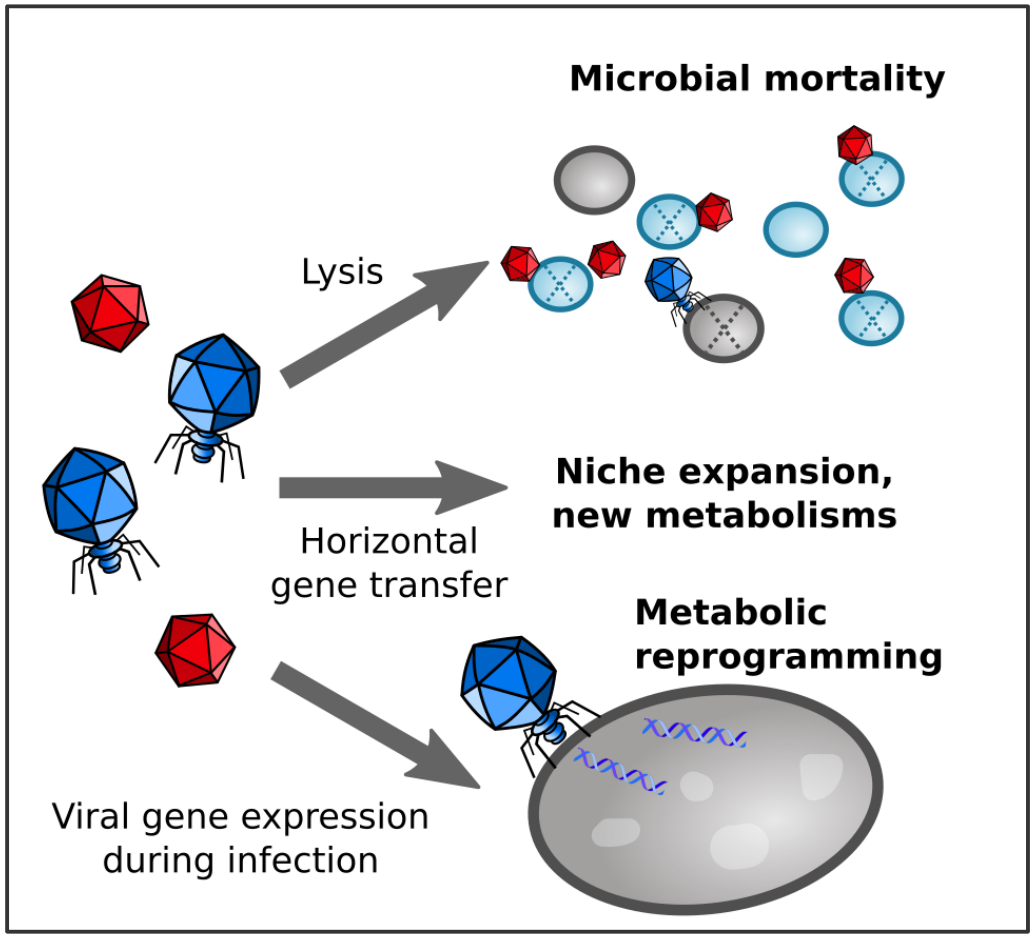
Challenges and unknowns



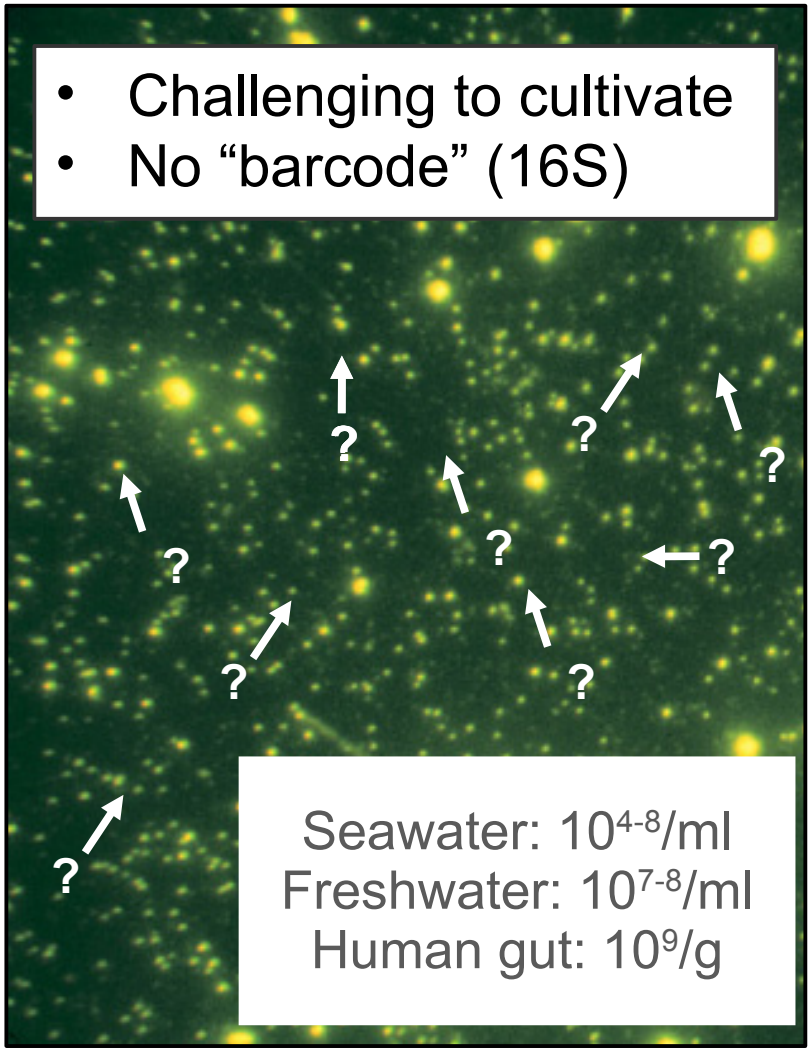
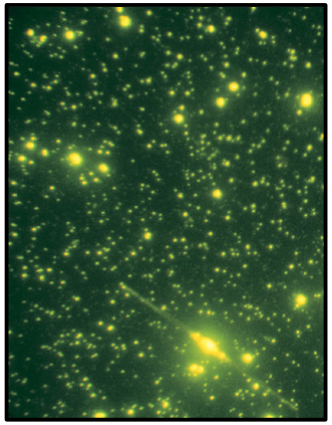
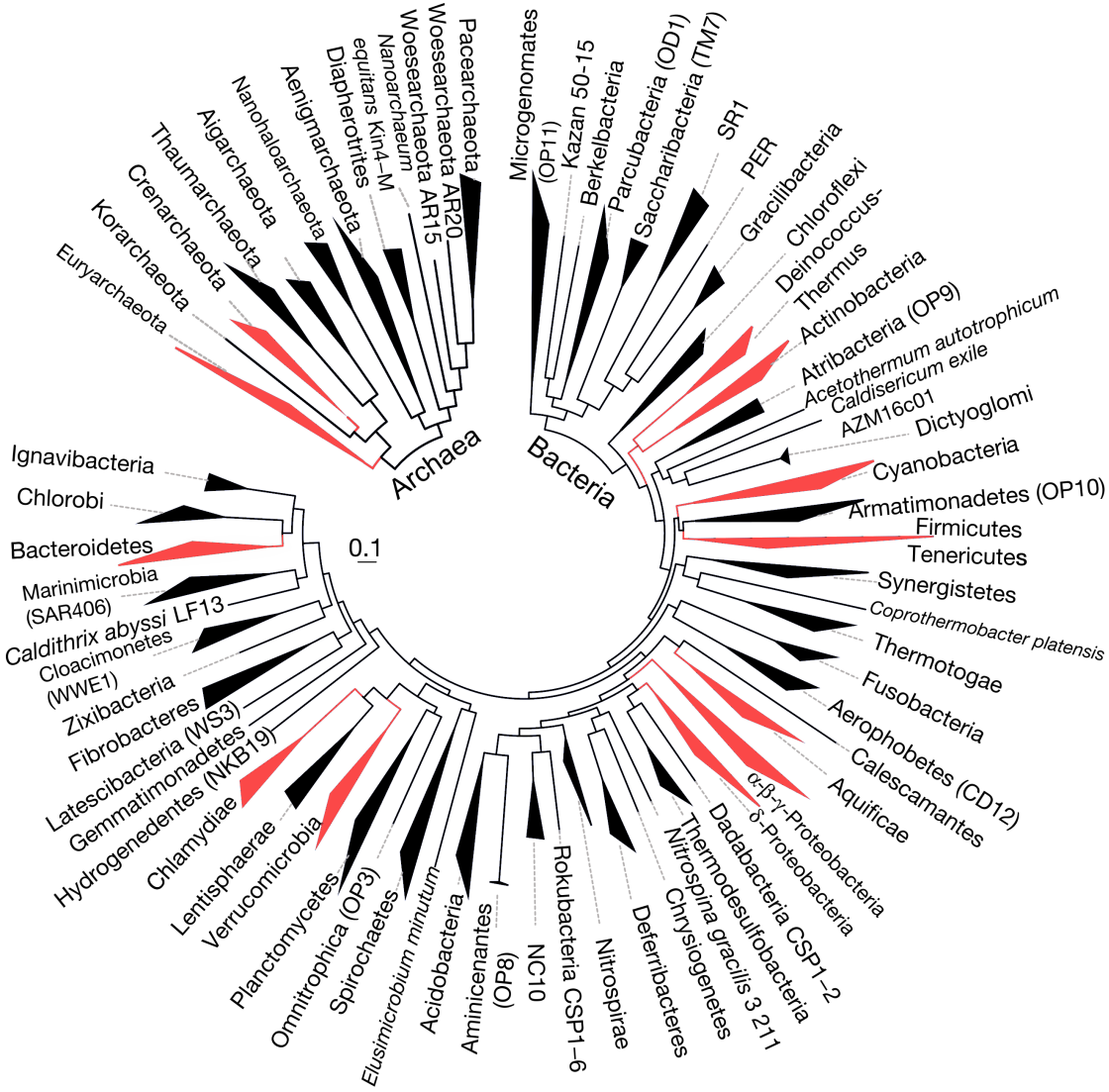


Image: Fuhrman Lab

Challenges of viral ecology

- **Low coverage of viral diversity**

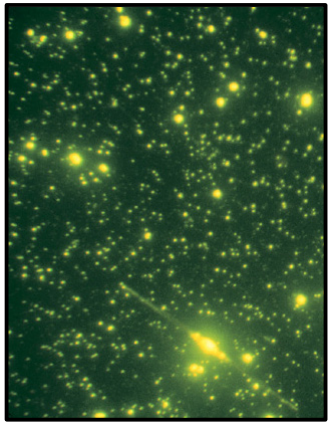


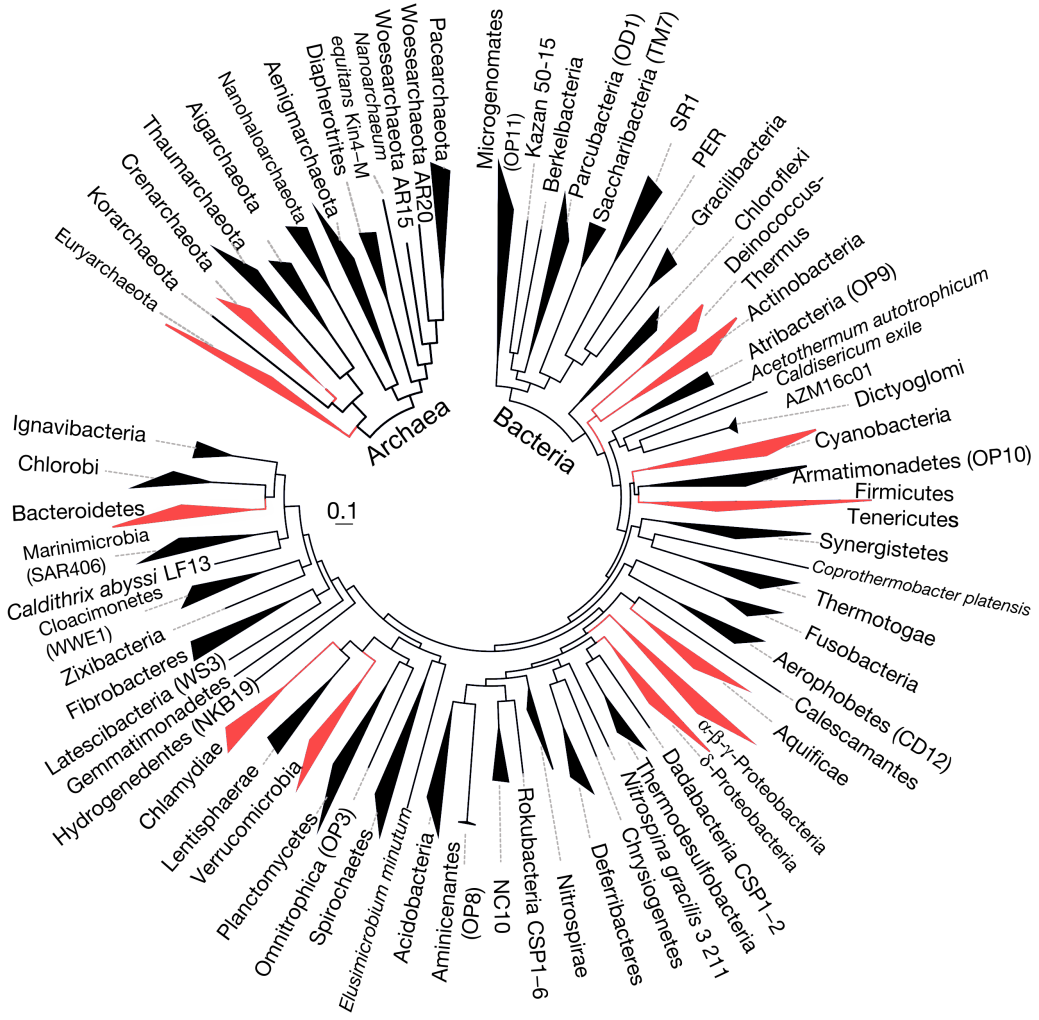


Adapted from
Paez-Espino *et al.*, 2016

Challenges of viral ecology

- Low coverage of viral diversity
- Genomes from uncultivated viruses





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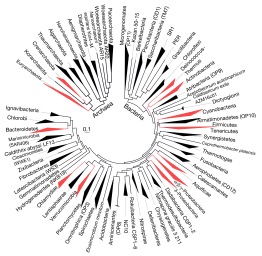
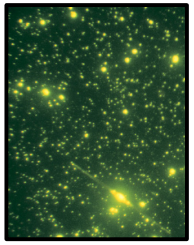
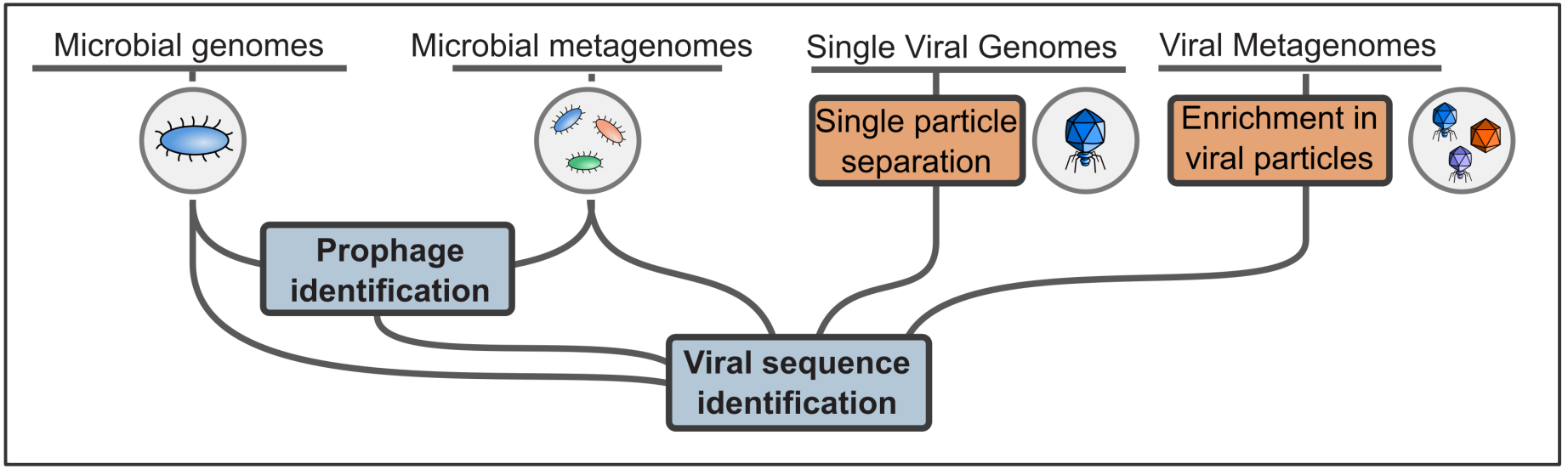
Mapping the viral sequence space

- **Low coverage of viral diversity**
- **Genomes from uncultivated viruses**
  - Leverage all types of datasets

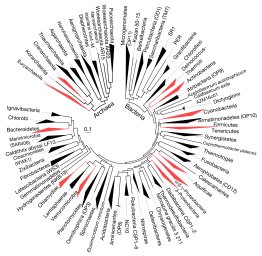


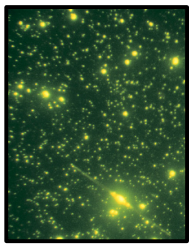


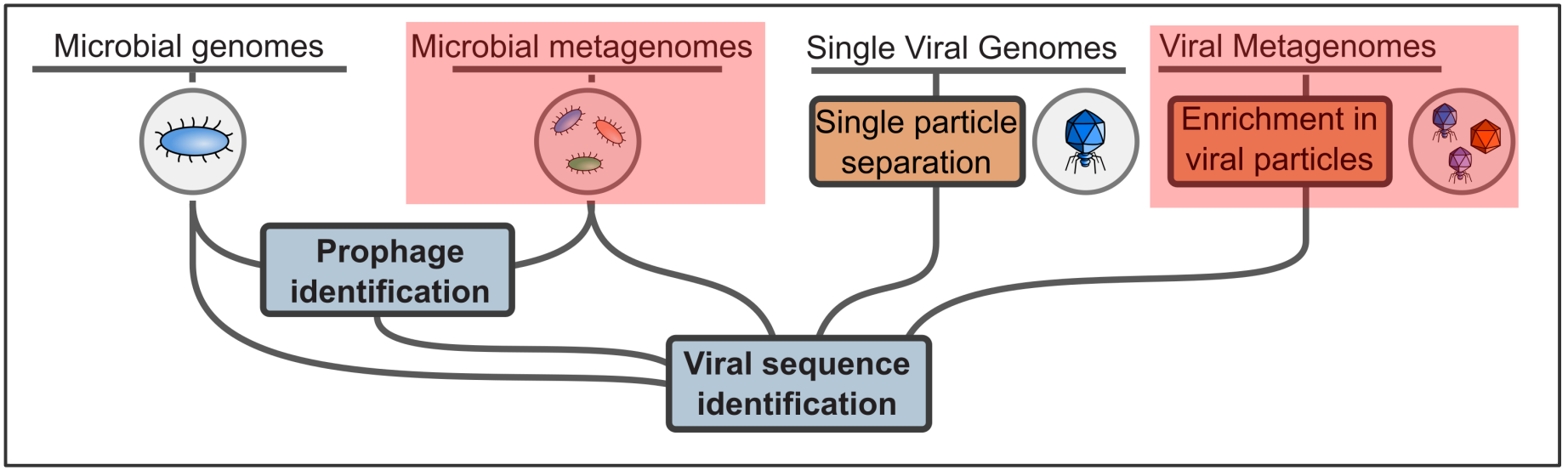


Mapping the viral sequence space

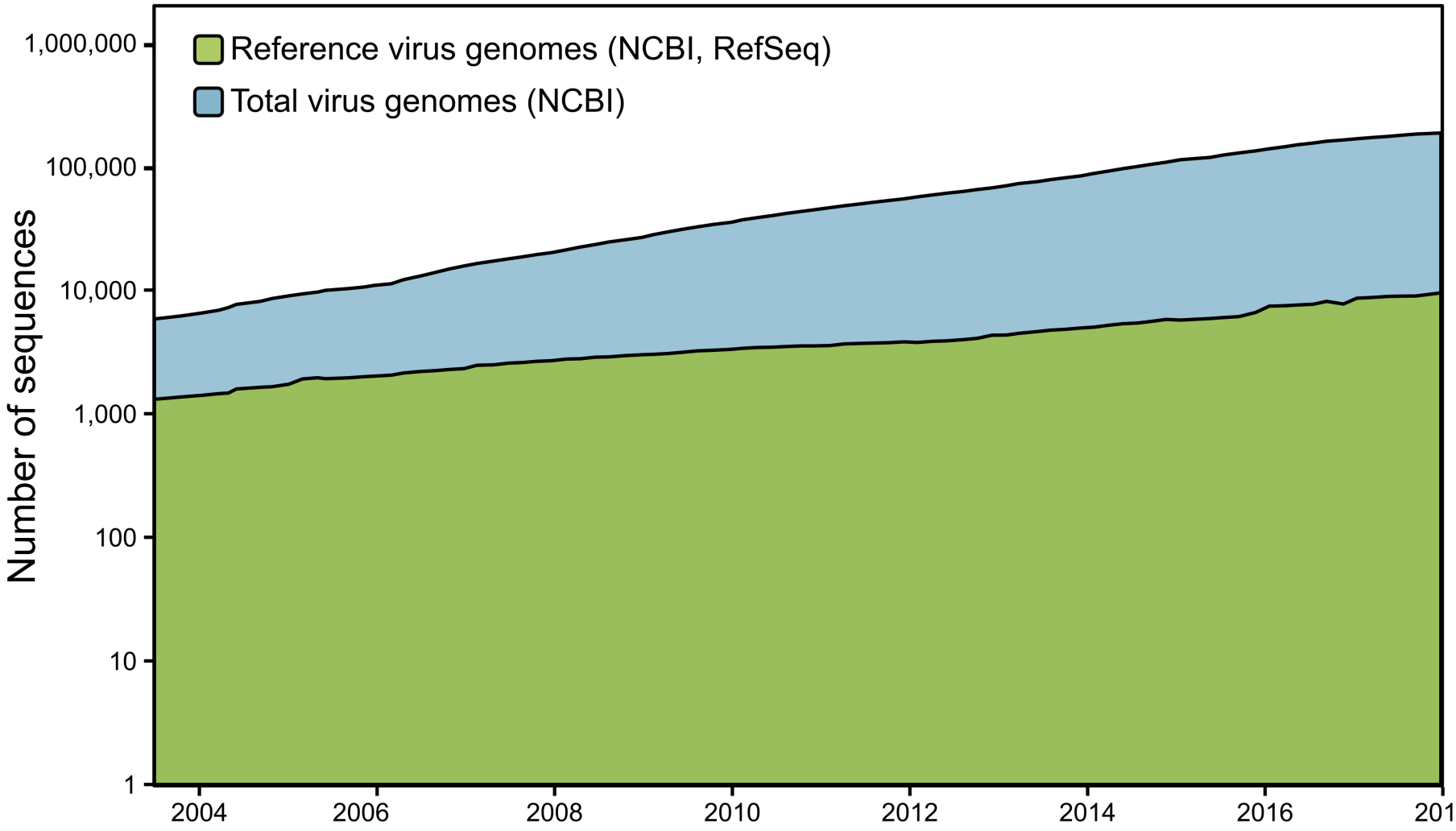
- **Low coverage of viral diversity**
- **Genomes from uncultivated viruses**
  - Leverage all types of datasets
  - Particularly useful: microbial and viral metagenomes

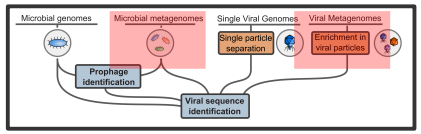






A frantic pace of viral discovery





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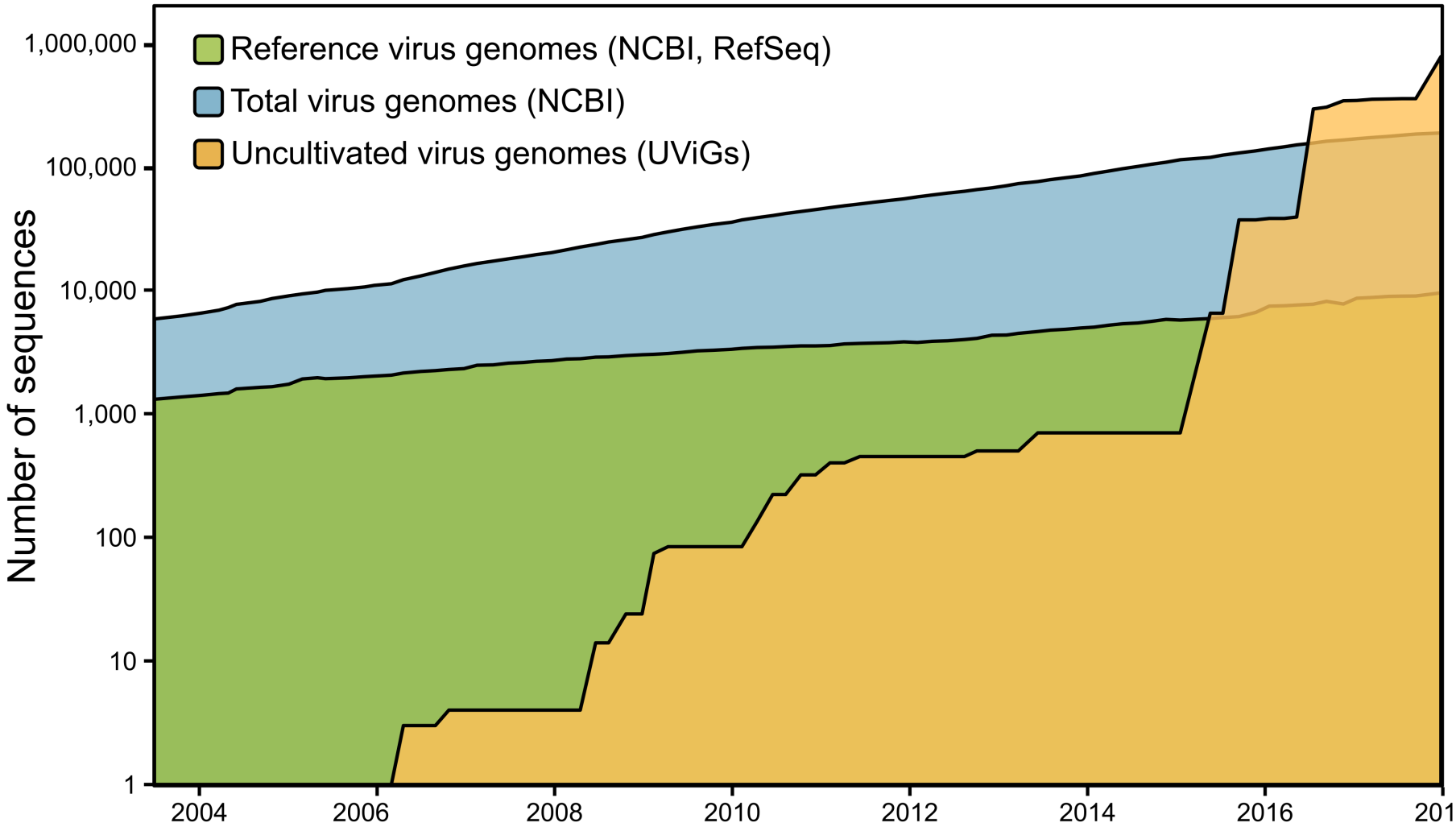

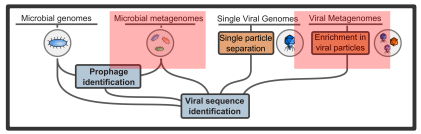

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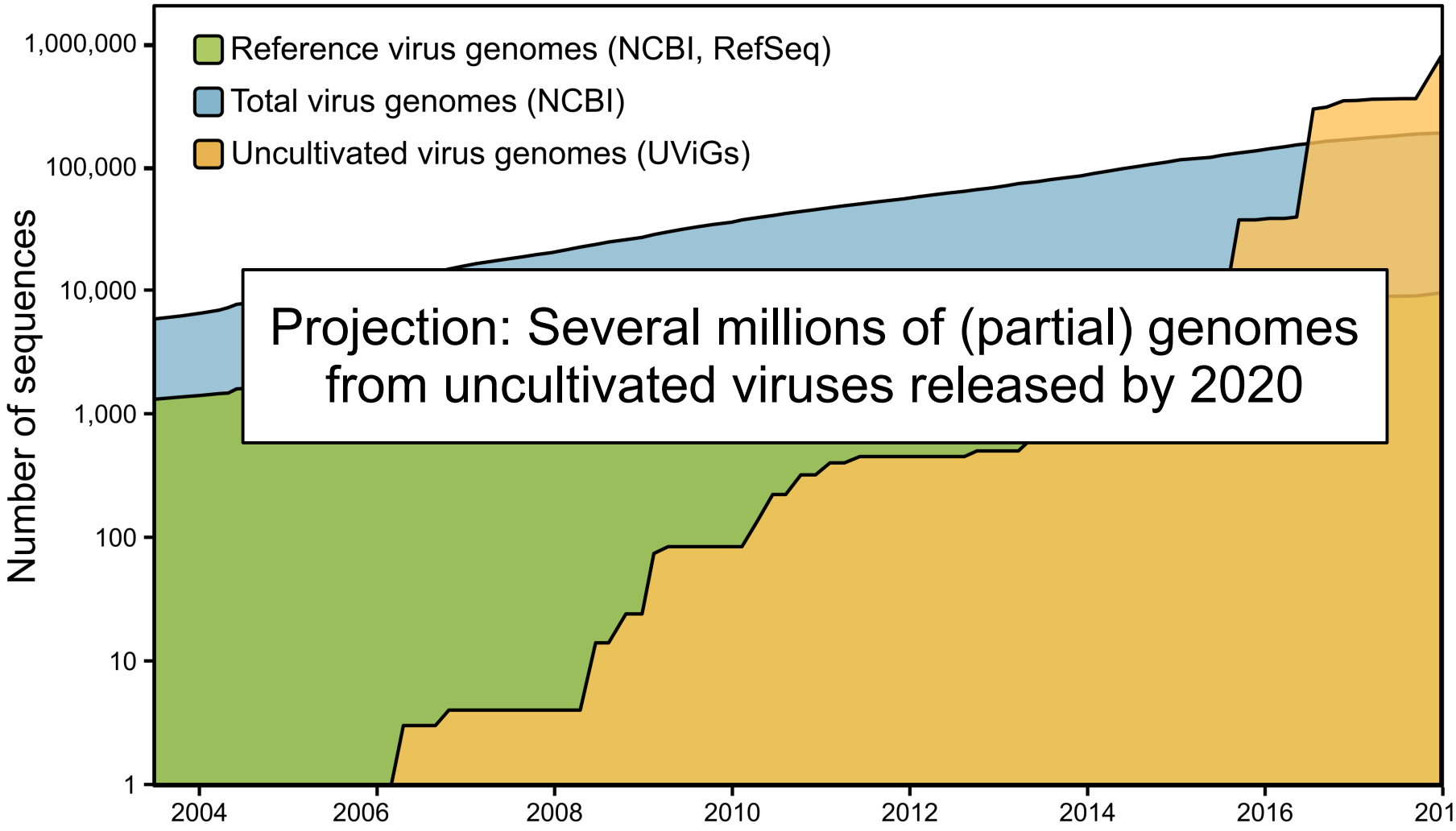

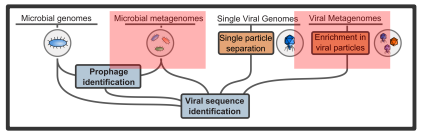

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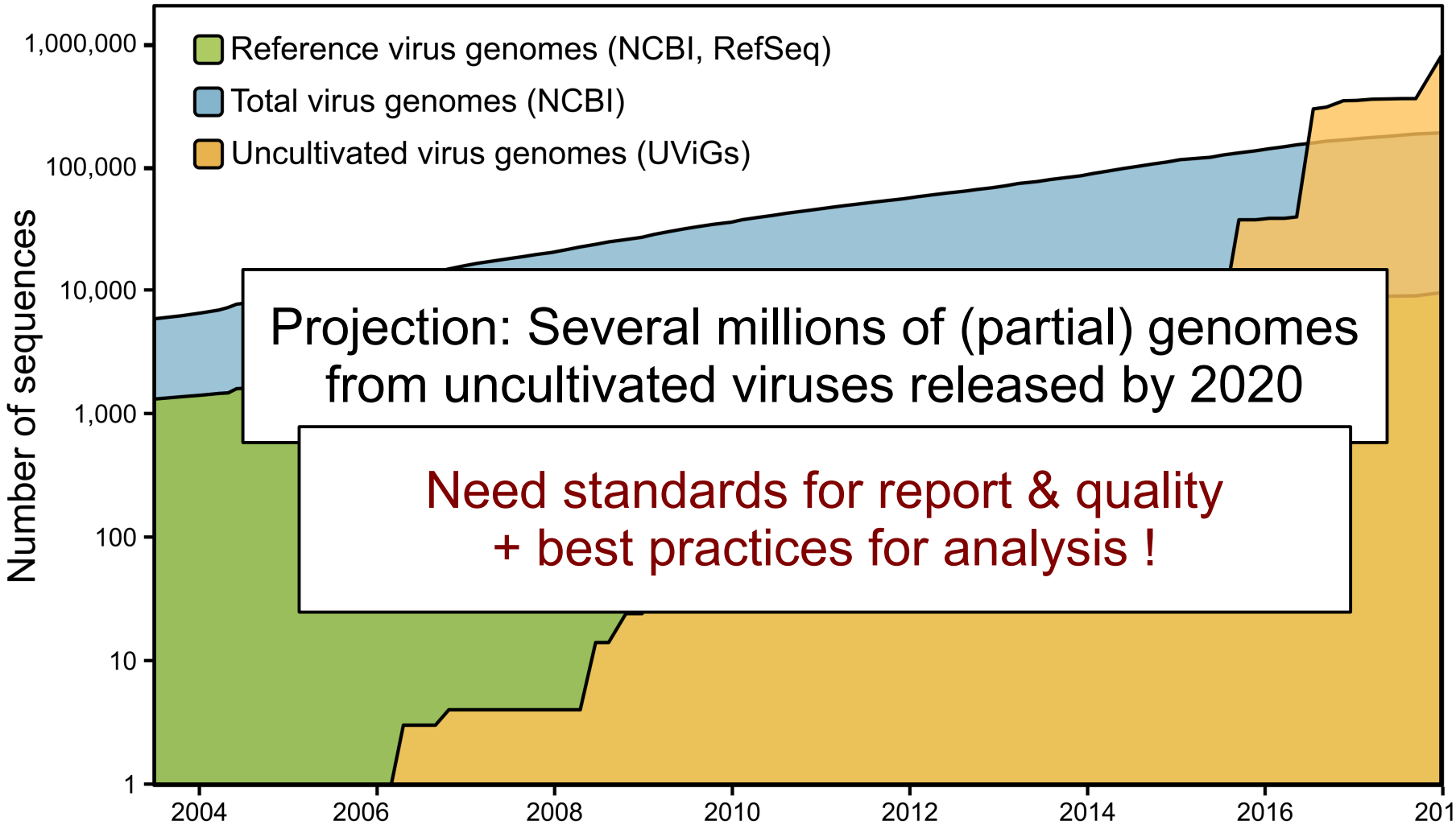

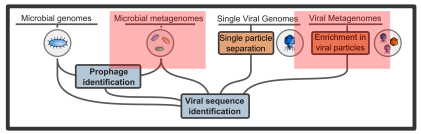

Built from MiMAGs & MiSAGs

nature biotechnology

PERSPECTIVE

Minimum information about a single amplified genome (MISAG) and a metagenome-assembled genome (MIMAG) of bacteria and archaea

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- **Similar framework:**
  - List approaches
  - Standard pipeline
  - Define quality tiers

Bowers et al., 2017

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- **Currently under review @ Nature Biotechnology**

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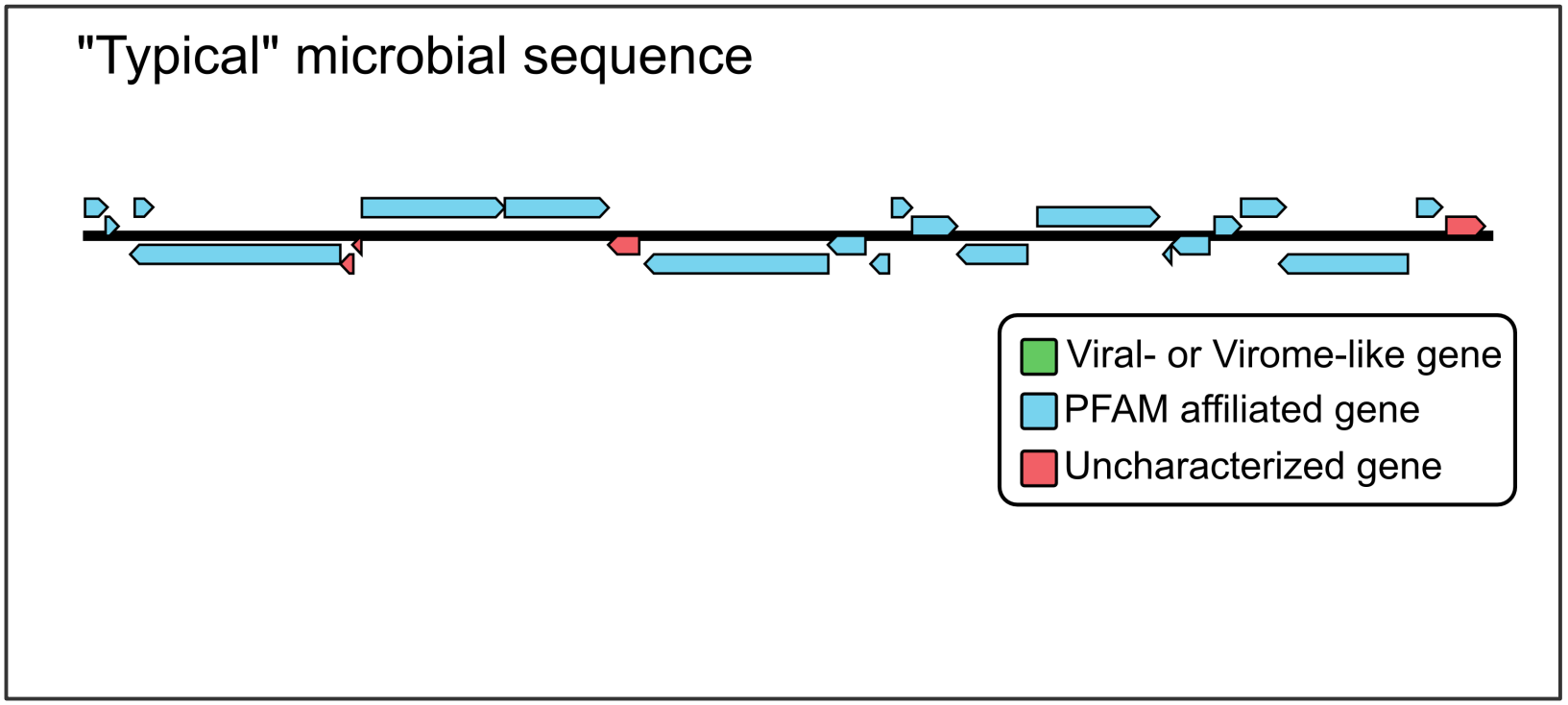

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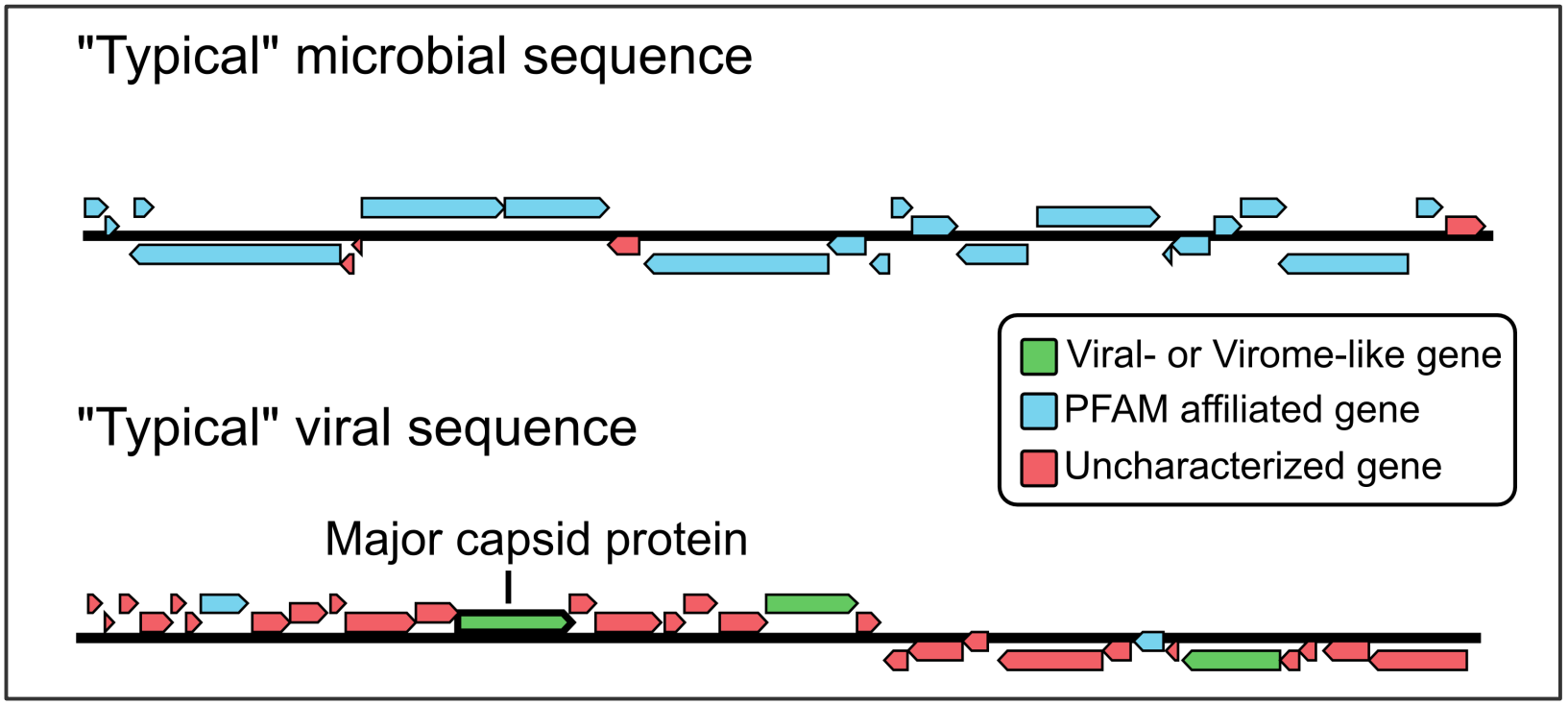

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  - Integrated viruses boundaries challenging to define:
    - flagged when releasing UViGs (i.e. "was part of a larger host contig")

Classification of novel UViGs

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Virus taxonomy: the database of the International Committee on Taxonomy of Viruses (ICTV)

Elliot J Lefkowitz ✉, Donald M Dempsey, Robert Curtis Hendrickson, Richard J Orton, Stuart G Siddell, Donald B Smith

Nucleic Acids Research, Volume 46, Issue D1, 4 January 2018, Pages D708–D717, https://doi.org/10.1093/nar/gkx932

Published: 13 October 2017 **Article history ▾**

Archives of Virology

April 2016, Volume 161, Issue 4, pp 1095–1099 | Cite as

Taxonomy of prokaryotic viruses: update from the ICTV bacterial and archaeal viruses subcommittee

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Virus group	Species demarcation criteria
Parvoviridae	Members of each species are antigenically distinct, as assessed by neutralization using polyclonal antisera, and natural infection is usually confined to a single host species. Generally, species are <95% related by non-structural gene DNA sequence.
P22-like viruses	Lack of DNA homology between species.
Coltivirus	RNA cross-hybridization assays: within a single species, RNA sequence that exhibit more than 74% similarity will hybridize at 36°C below the Tm of the fully base-paired duplex. Sequence analysis: Nucleotide identity of >89% in the conserved Seg12; amino acid identities of >55%, >57% and >60% respectively in VP6, VP7 and VP12 (the most variable proteins).

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- **Operational "species rank" grouping for ecological studies (vOTU)**
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- **Recommendations**
  - For ecological studies: vOTU from pairwise ANI/AF
  - For "true" taxonomic classification: group-by-group basis (not automated)

In silico host assignment

- **4 main types of approaches**

In silico host assignment

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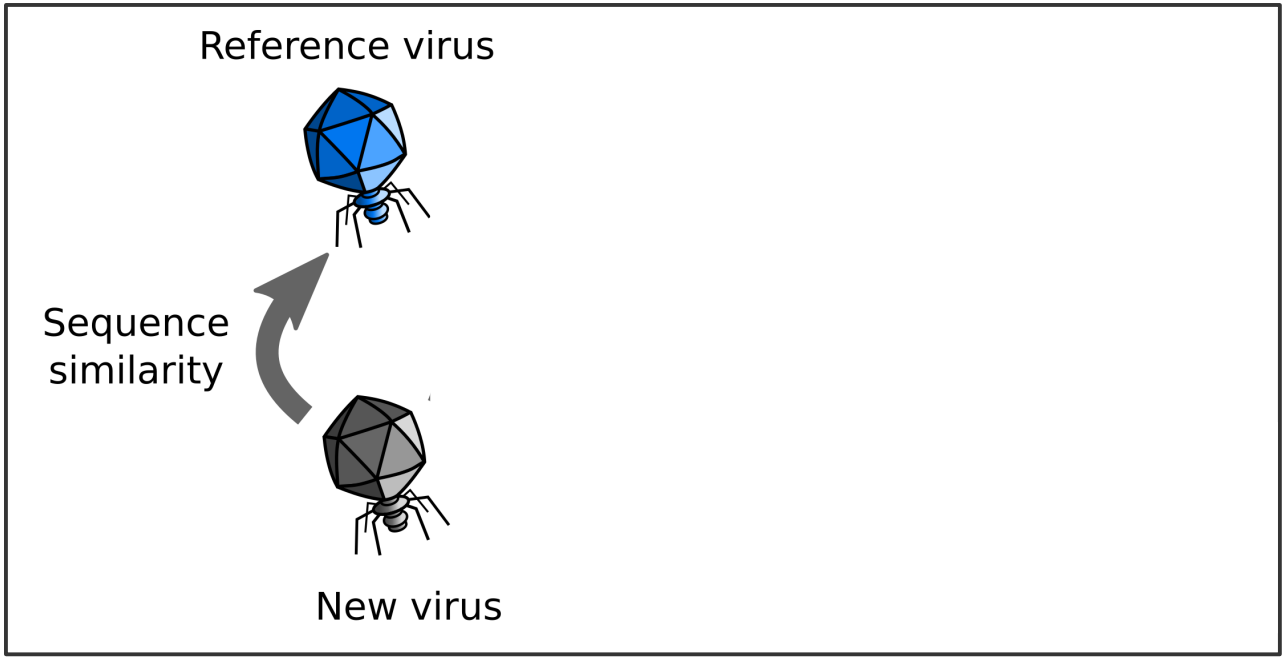
  - Sequence homology with isolate viruses



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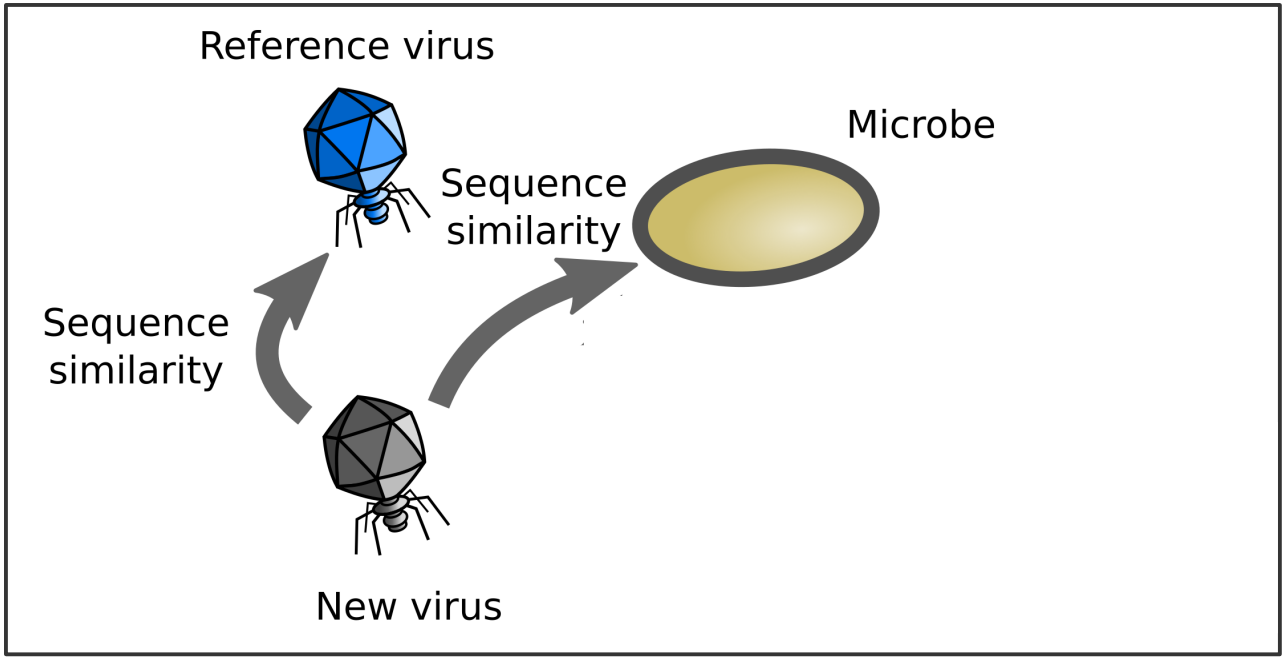

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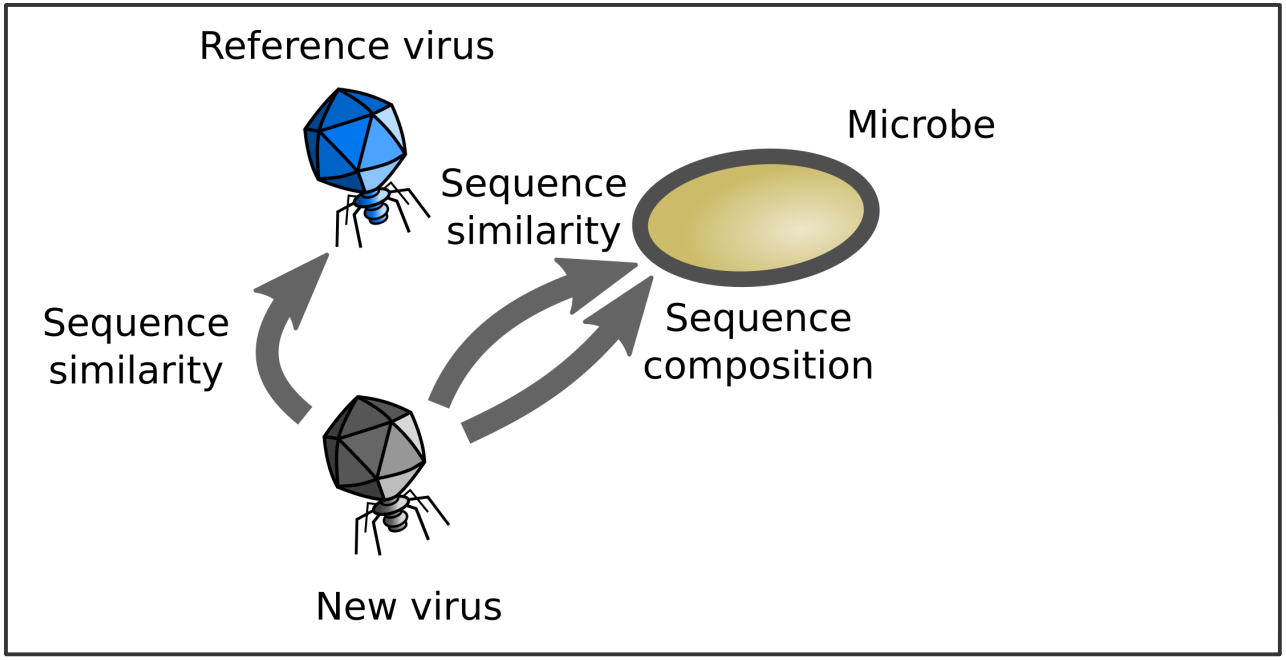

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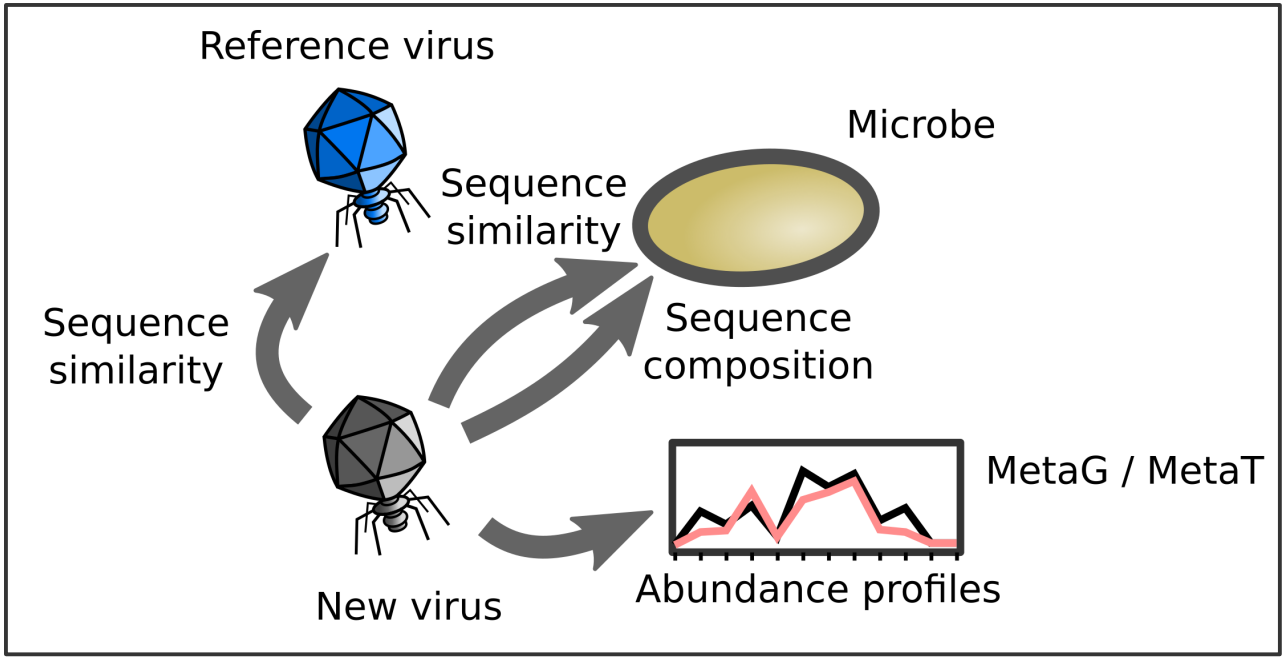

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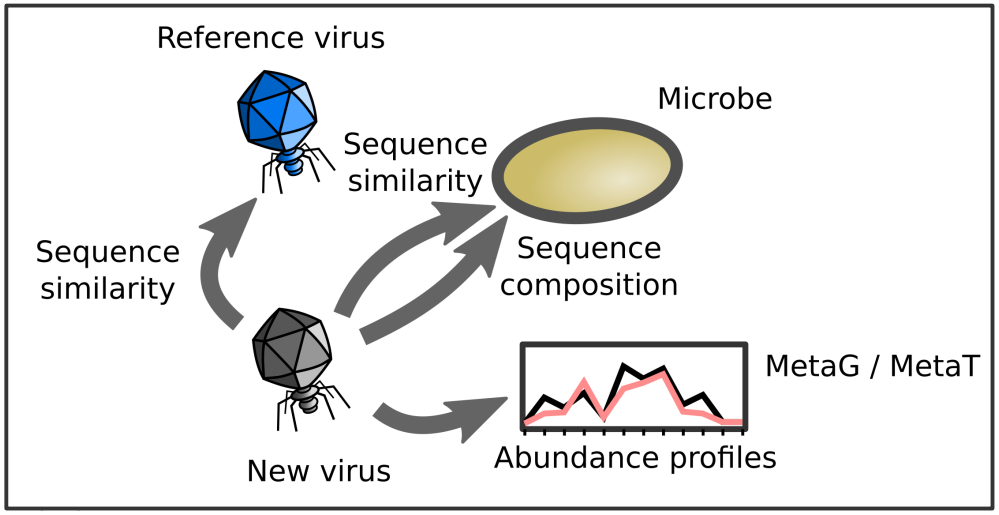
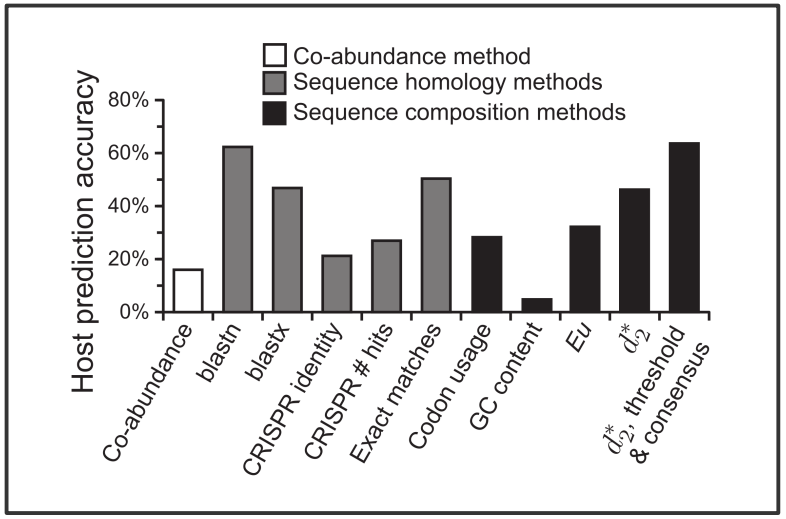
- **Challenges & limitations**
  - Limited accuracy and resolution (reviewed in Edwards et al., 2016)
  - No information on host range, infection rate and efficiency





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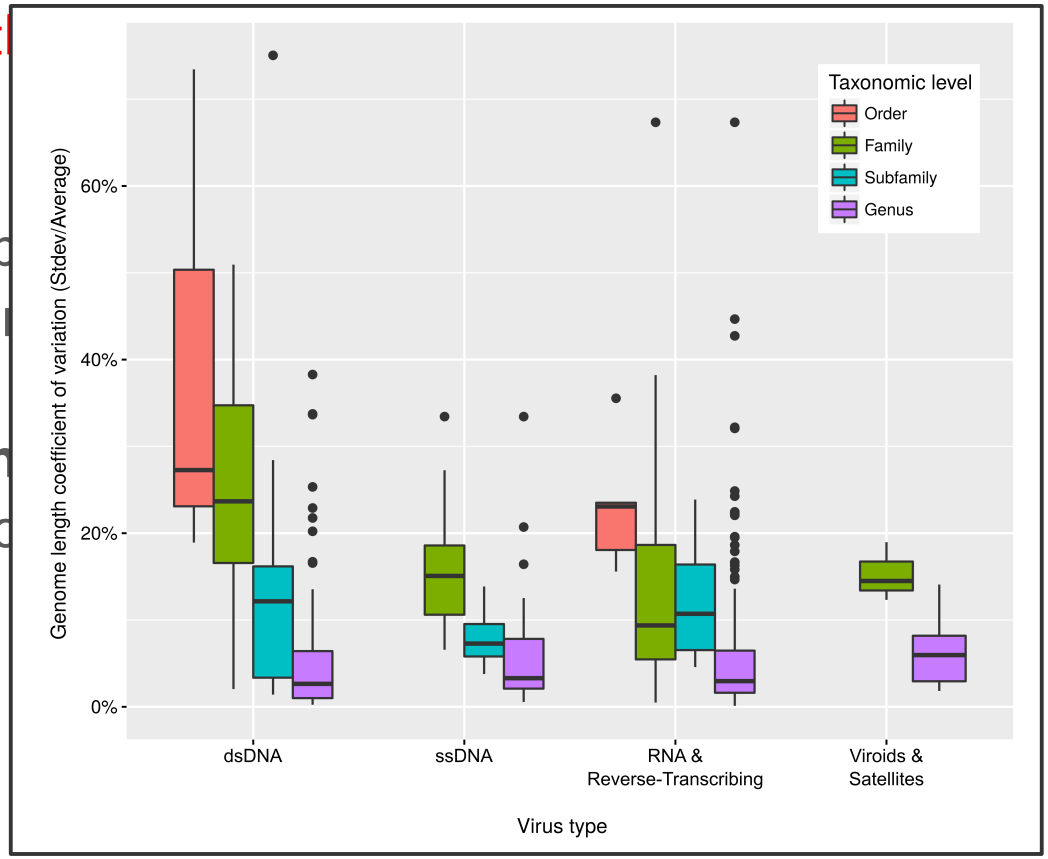

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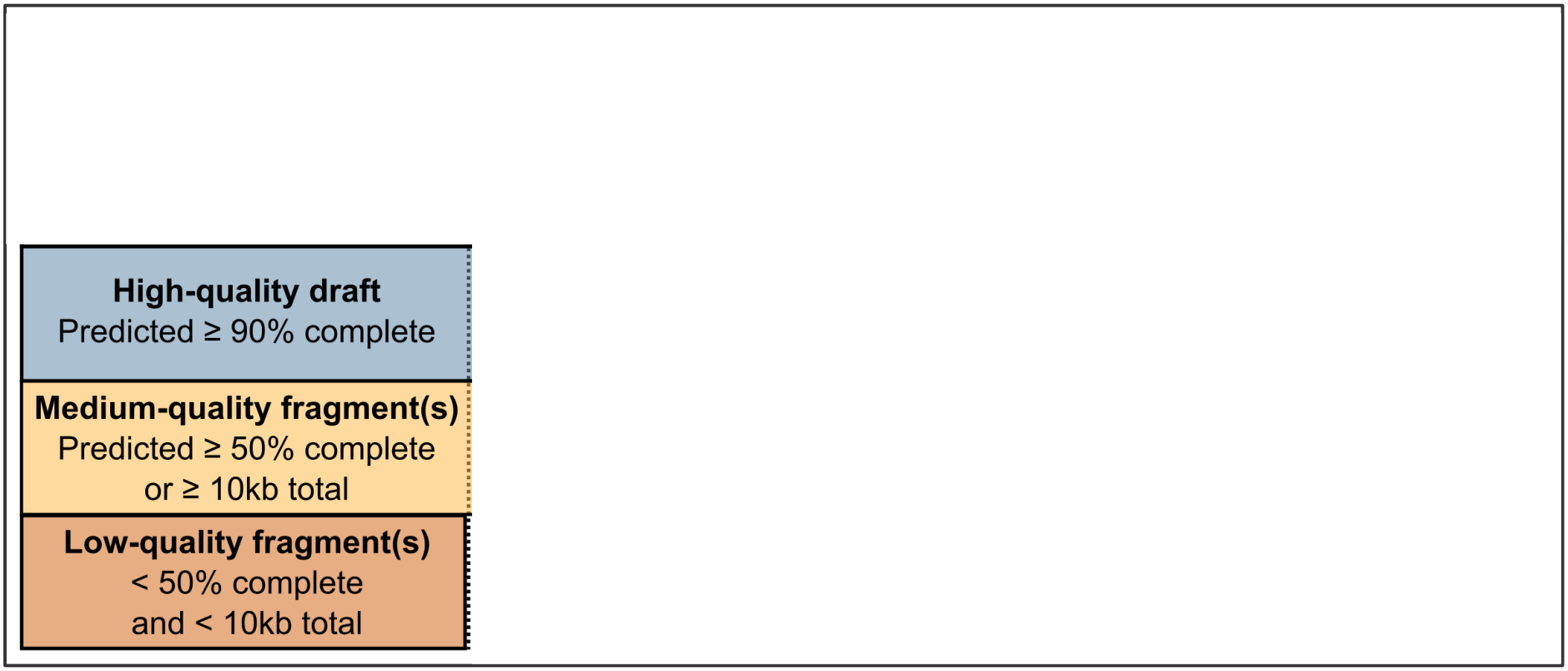

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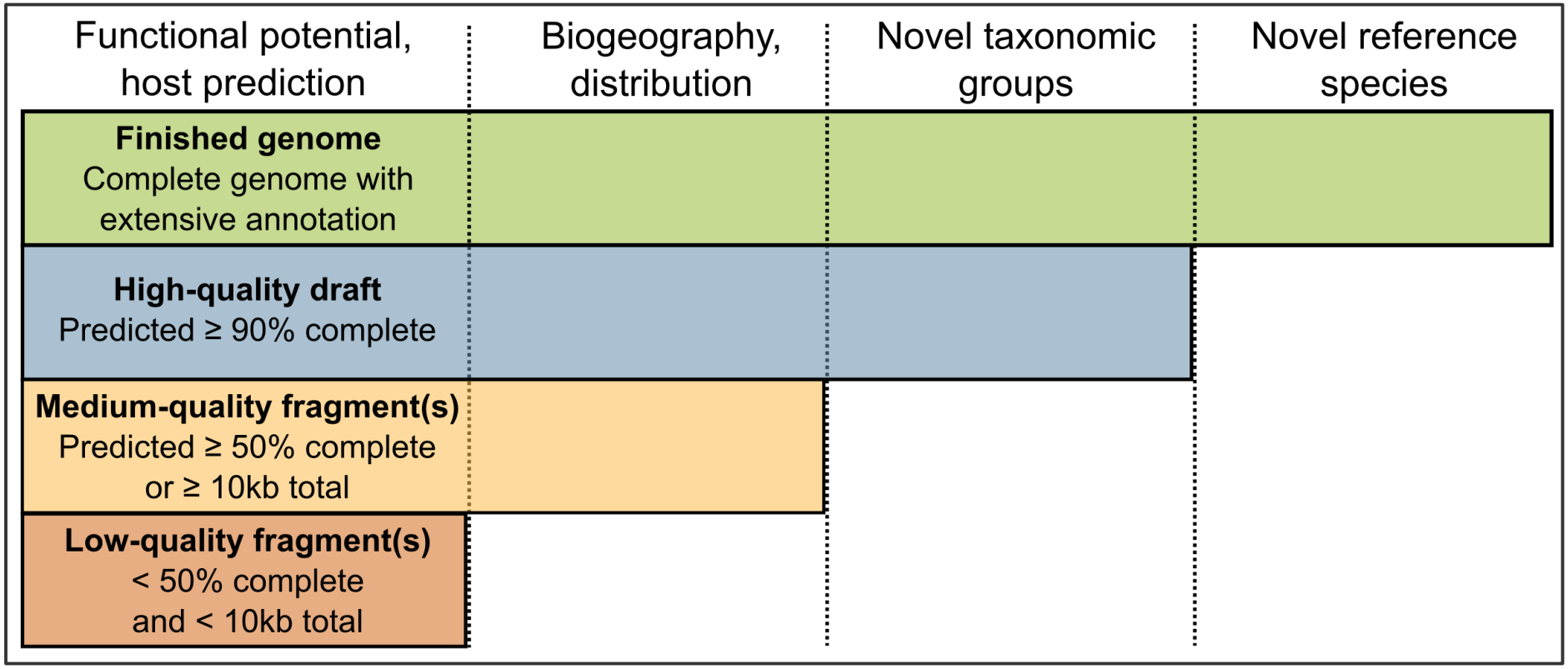
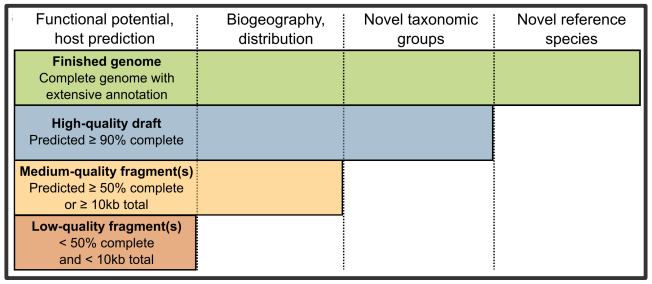


- **Classification in 4 categories**
  - Key information to guide genome analysis

UViG Quality estimation

- **Example Global Ocean Virome**
  - 15,222 contigs (≥ 10kb)



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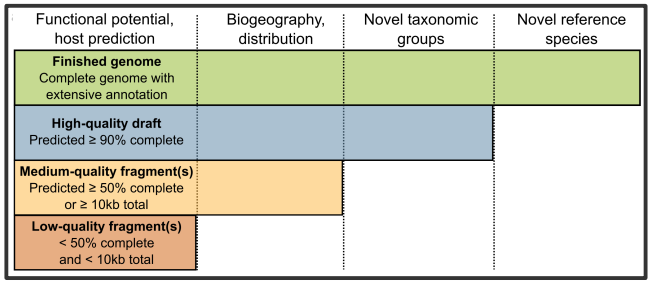

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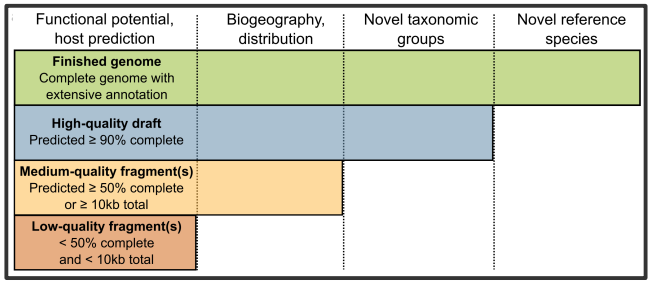

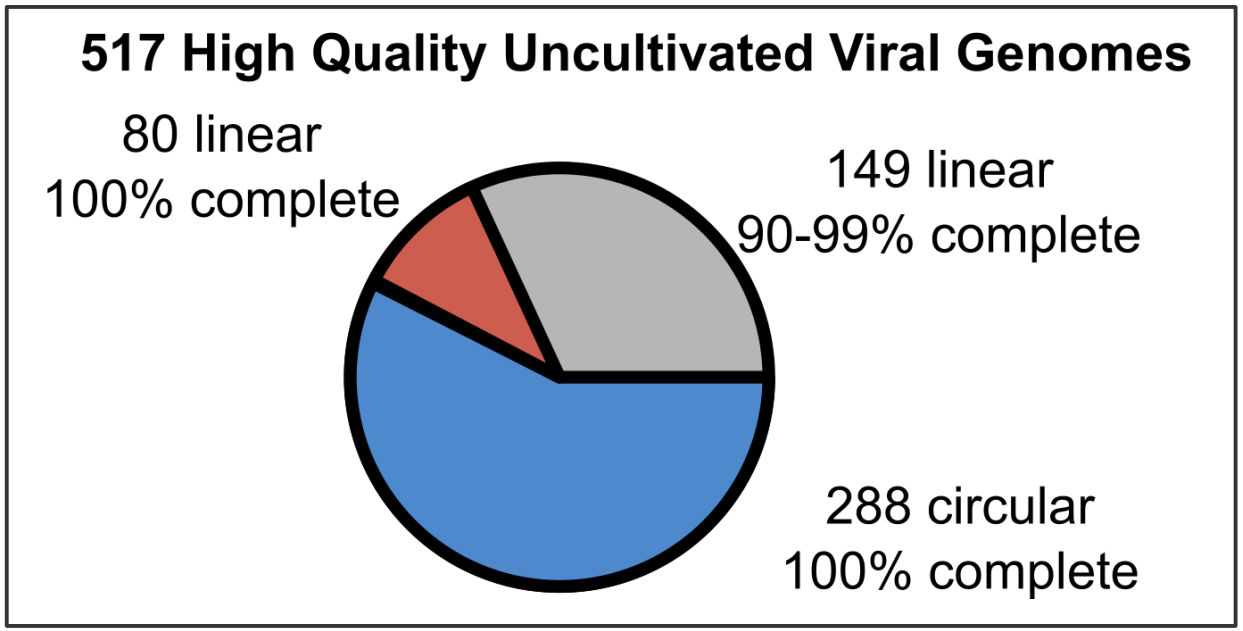

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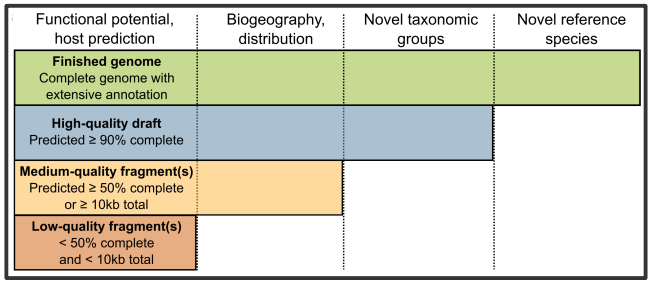

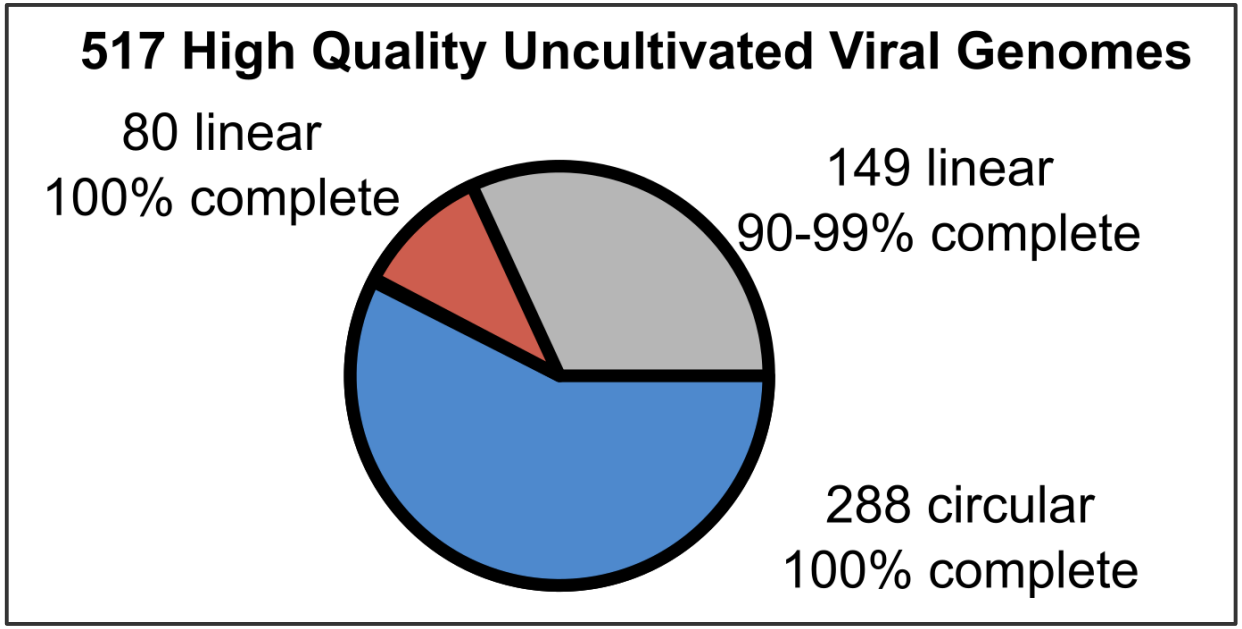

UViGs: data release

- **INSDC as central repository:**
  - Member databases: NCBI, EMBL-EBI, DDBJ
  - Submission using MIUViG checklist
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- **Active development areas**
  - "Universal" virus sequence detection tool
  - Robust genome-based taxonomy software
  - Unified, comprehensive, & annotated database of virus proteins

… All that for what ?

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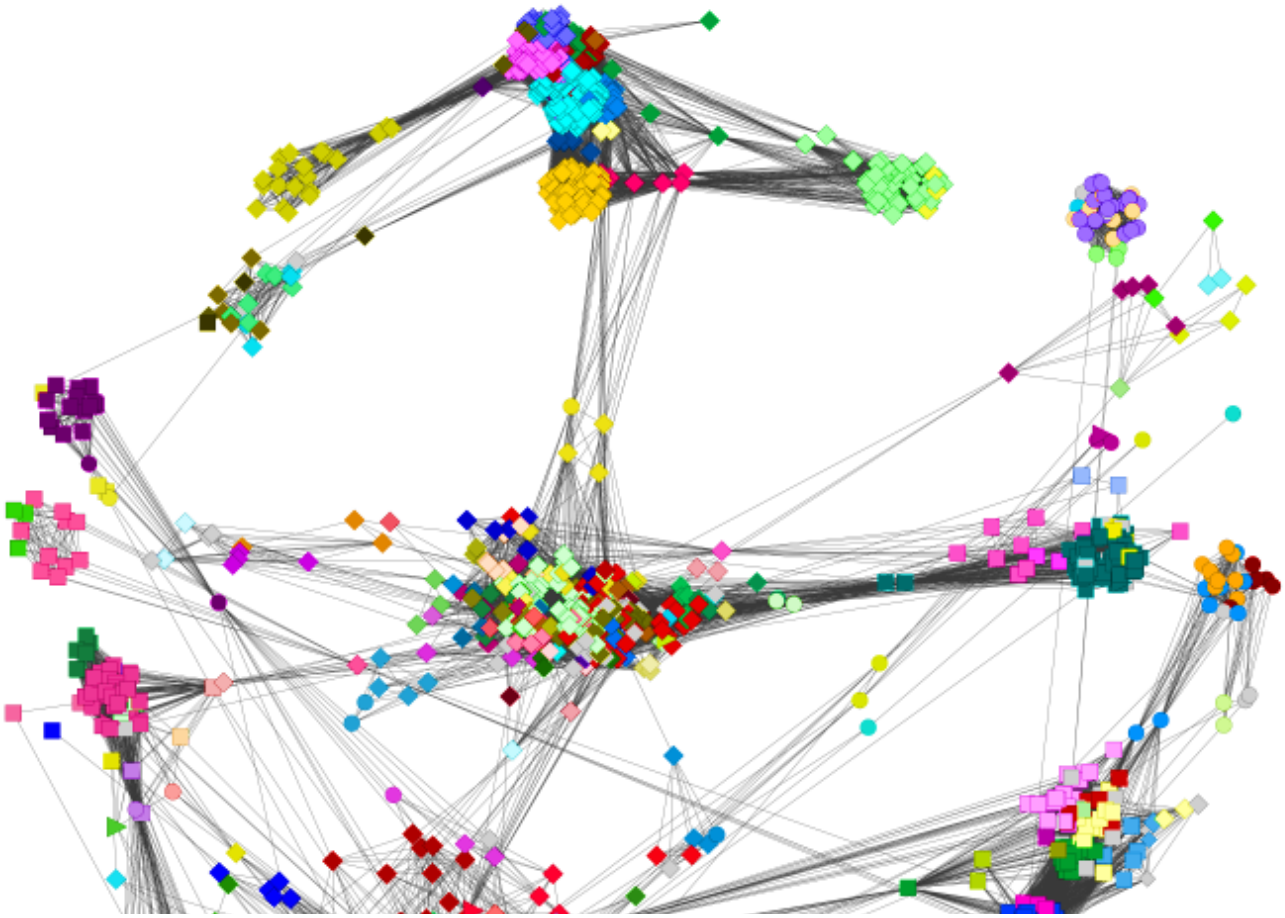
End goal: comprehensive (host-resolved) mapping of the virosphere



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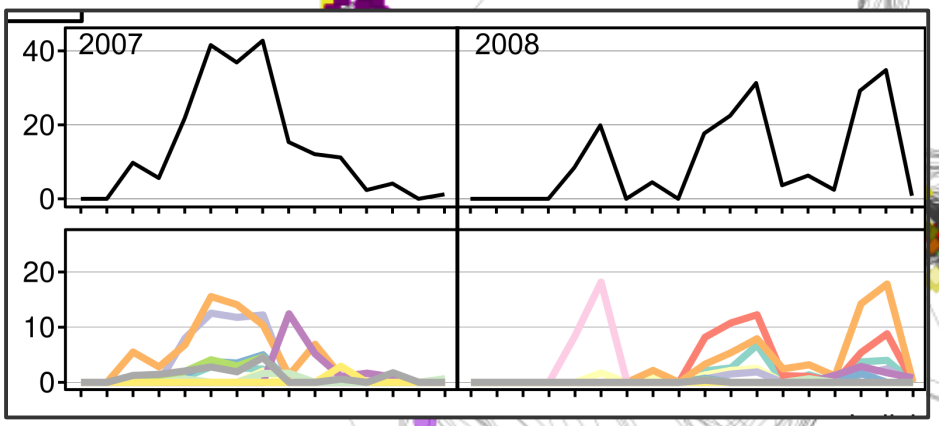
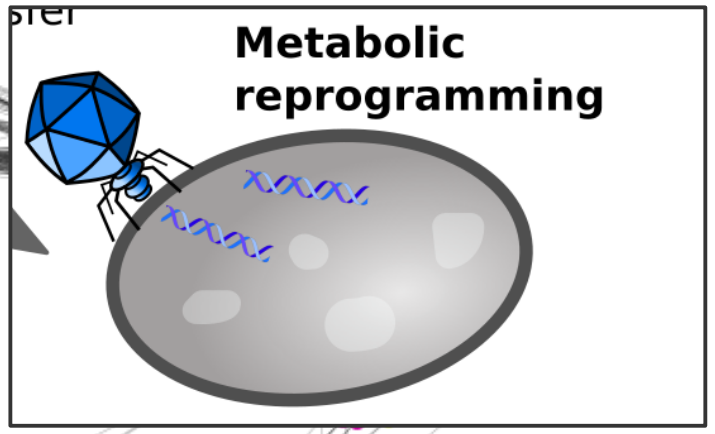
  - infection dynamics in nature
  - virus-aware ecosystem models





- **Microbial manipulation**
  - host cell takeover mechanisms
  - biotechnological applications

Thanks

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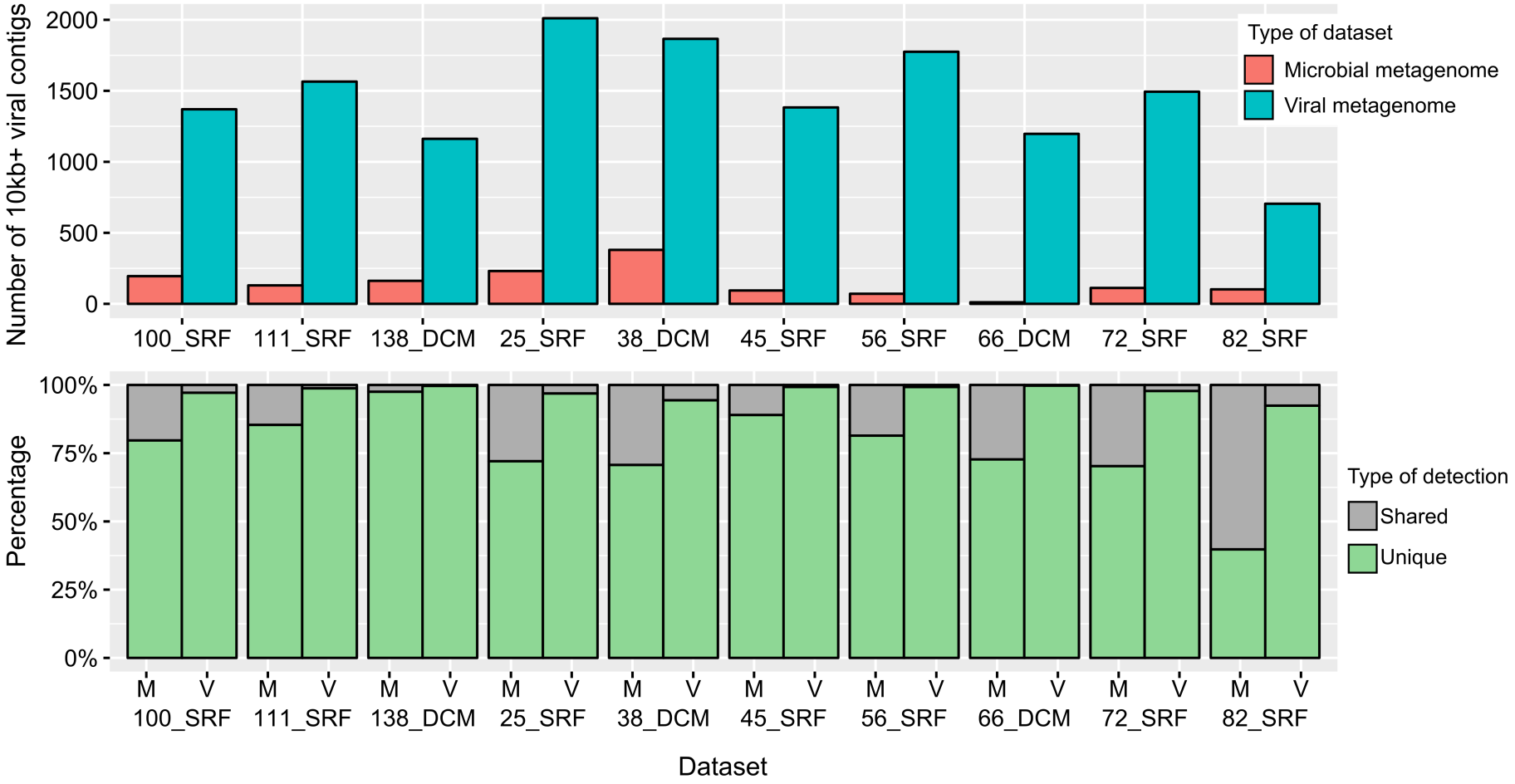
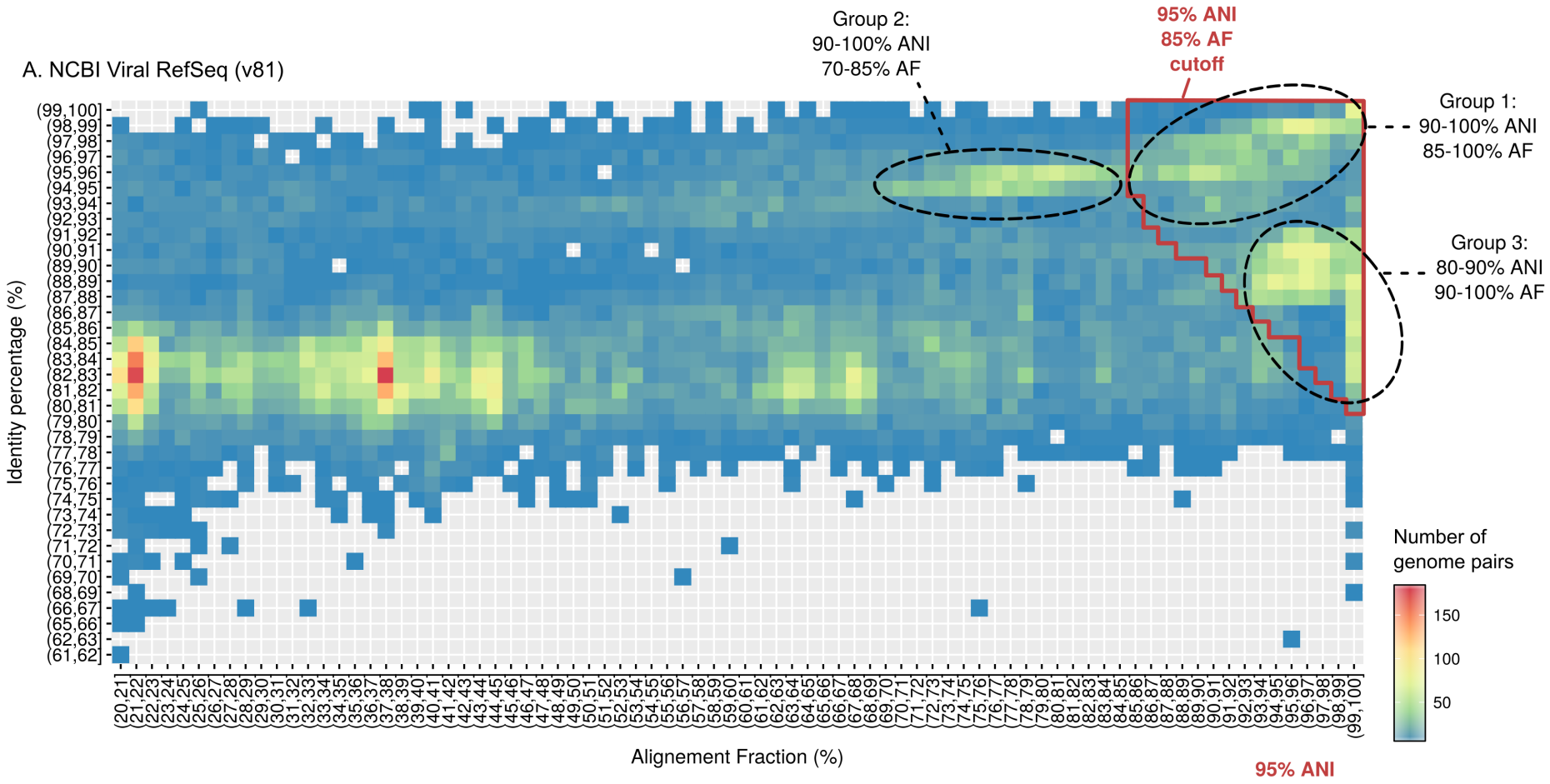
> 50 contributing labs !

Targeted vs untargeted



vOTU threshold



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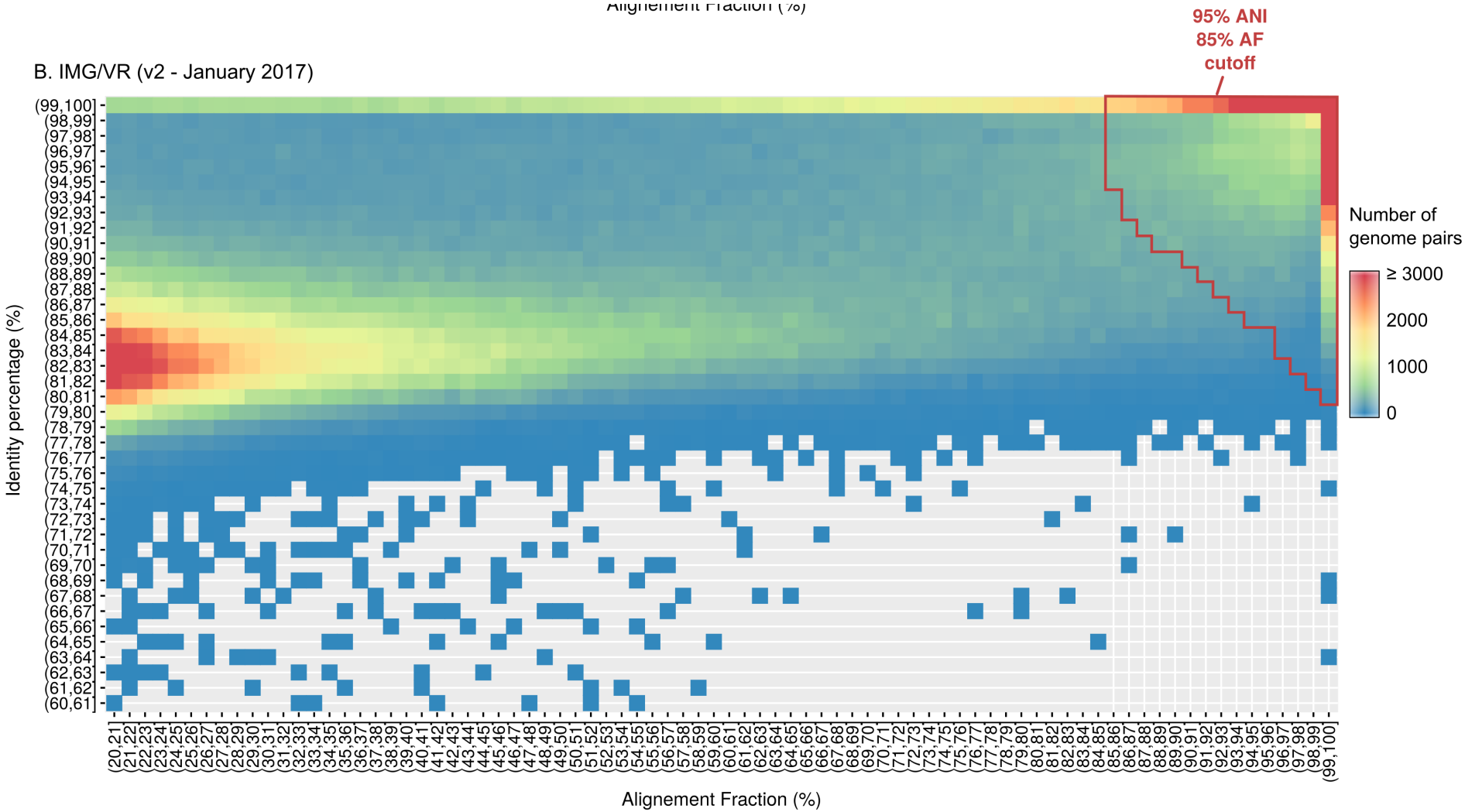

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