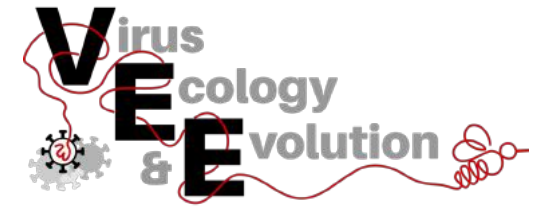




university of
 groningen

faculty of science
 and engineering

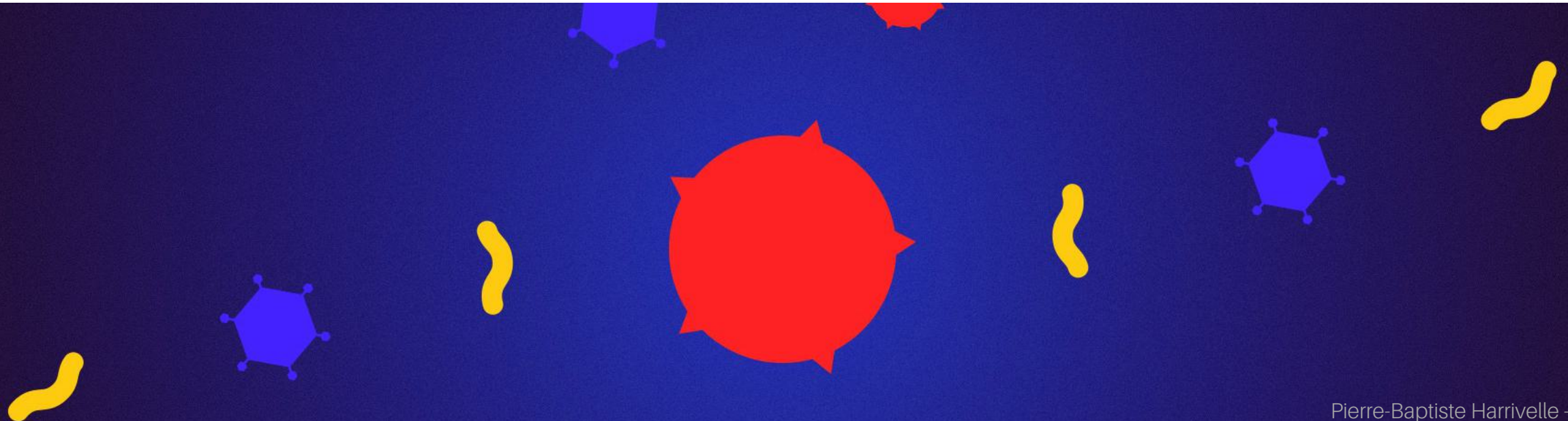
groningen institute for
 evolutionary life sciences



The constant change of viruses

– evolutionary biology in action

Sebastian Lequime (Assistant professor) s.j.j.lequime@rug.nl



Name viruses you know.

What do you associate with
viruses?



Contagion, 2011



Outbreak, 1995





Outline

1 What are viruses?

2 SARS-CoV-2

3 How do RNA viruses evolve?

4 Evolution and future of SARS-CoV-2

Outline

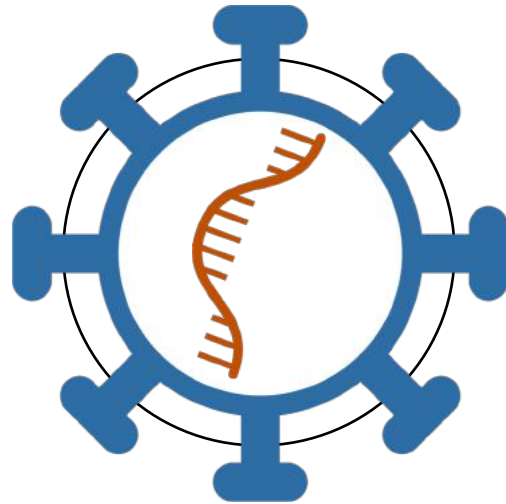
1 What are viruses?

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“A virus is a piece of (bad) news wrapped in protein”.
– Peter Medawar (Nobel Prize 1960)



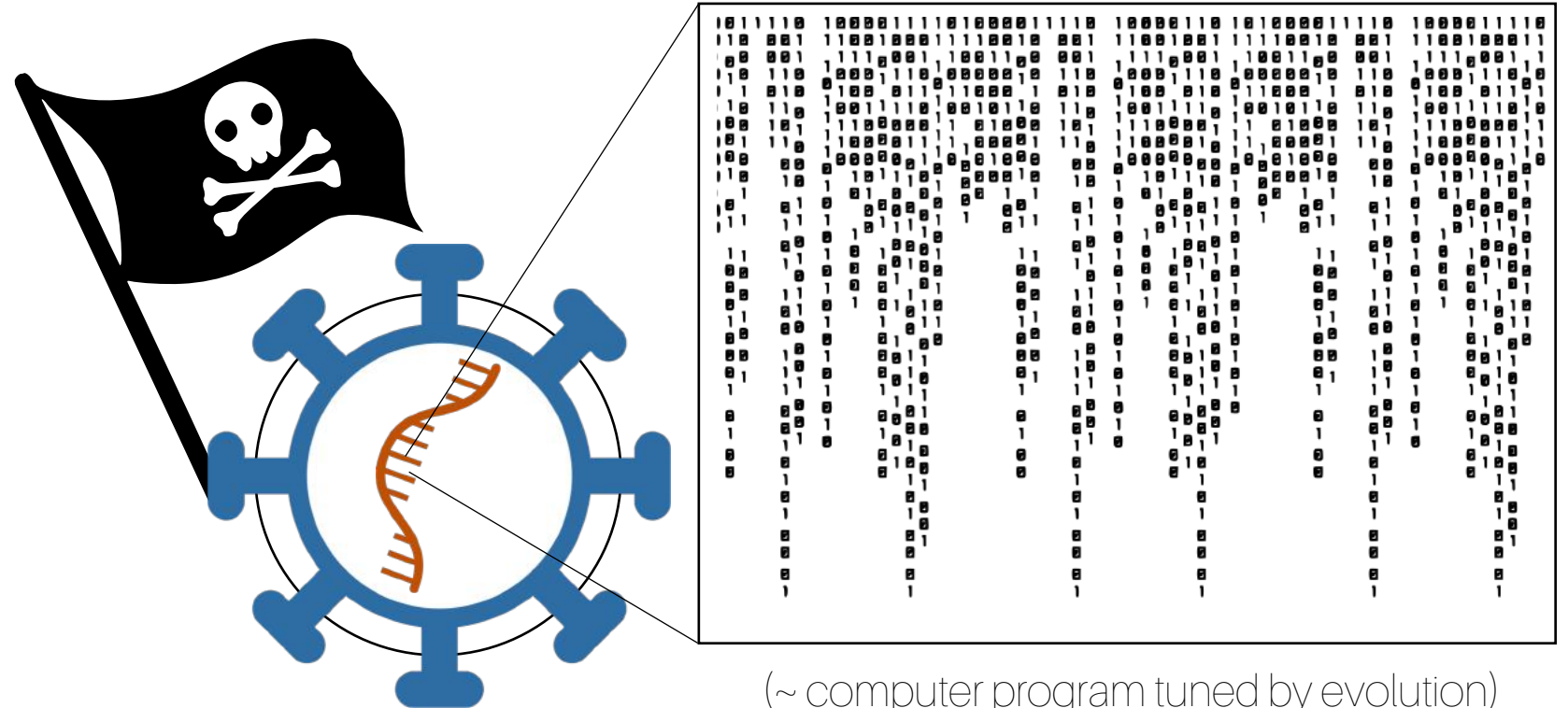
“Viruses appear to be **obligate parasites** in the sense that their reproduction is **dependent** on living cells”.

– Thomas Milton Rivers (1926)



Viruses are passive agents!

– Vincent Racaniello (at least 2012)



(~ computer program tuned by evolution)

Abundance

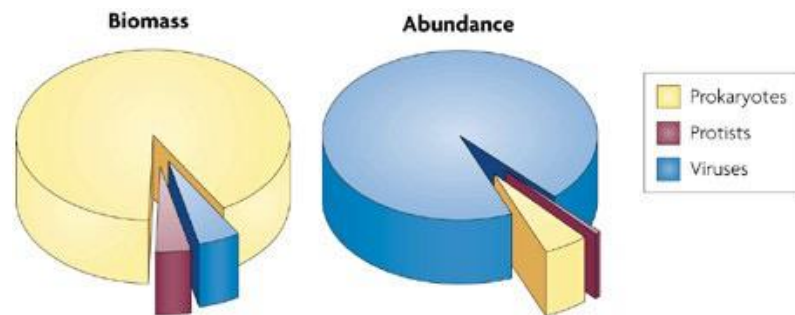
All three domains of life have been found infected by viruses

For example, marine viruses:

10^{30} viruses in the entire marine biota (estimate)

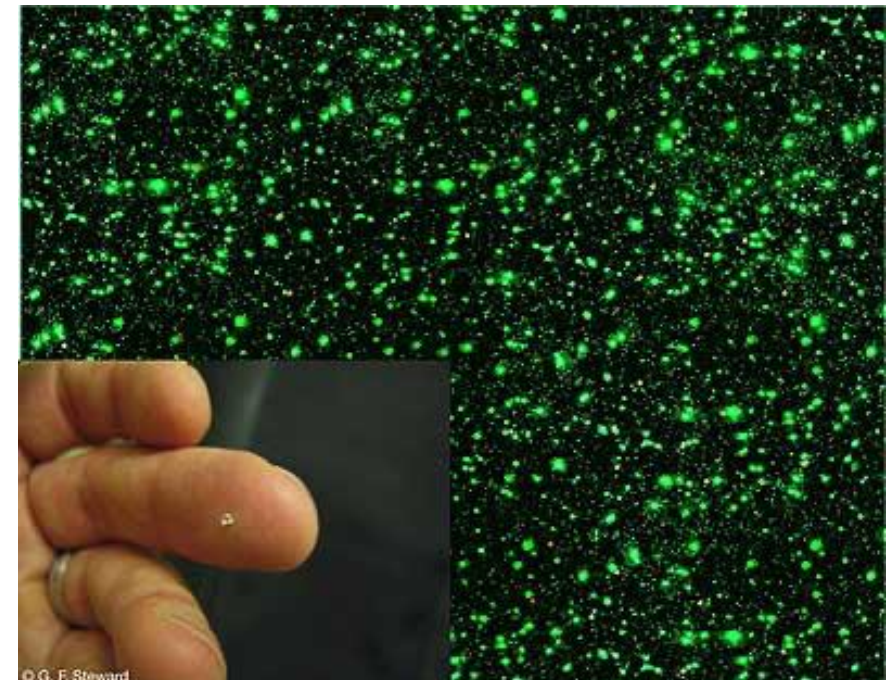
10^{23} viral infections every second (estimate)

Viruses kill about 20% of the total microbial biomass every day forcing a constant and large-scale turnover



Suttle 2005 Nature
<https://www.nature.com/articles/nature04160>

Wietz et al 2017 Nature
<https://www.nature.com/articles/nature23295>

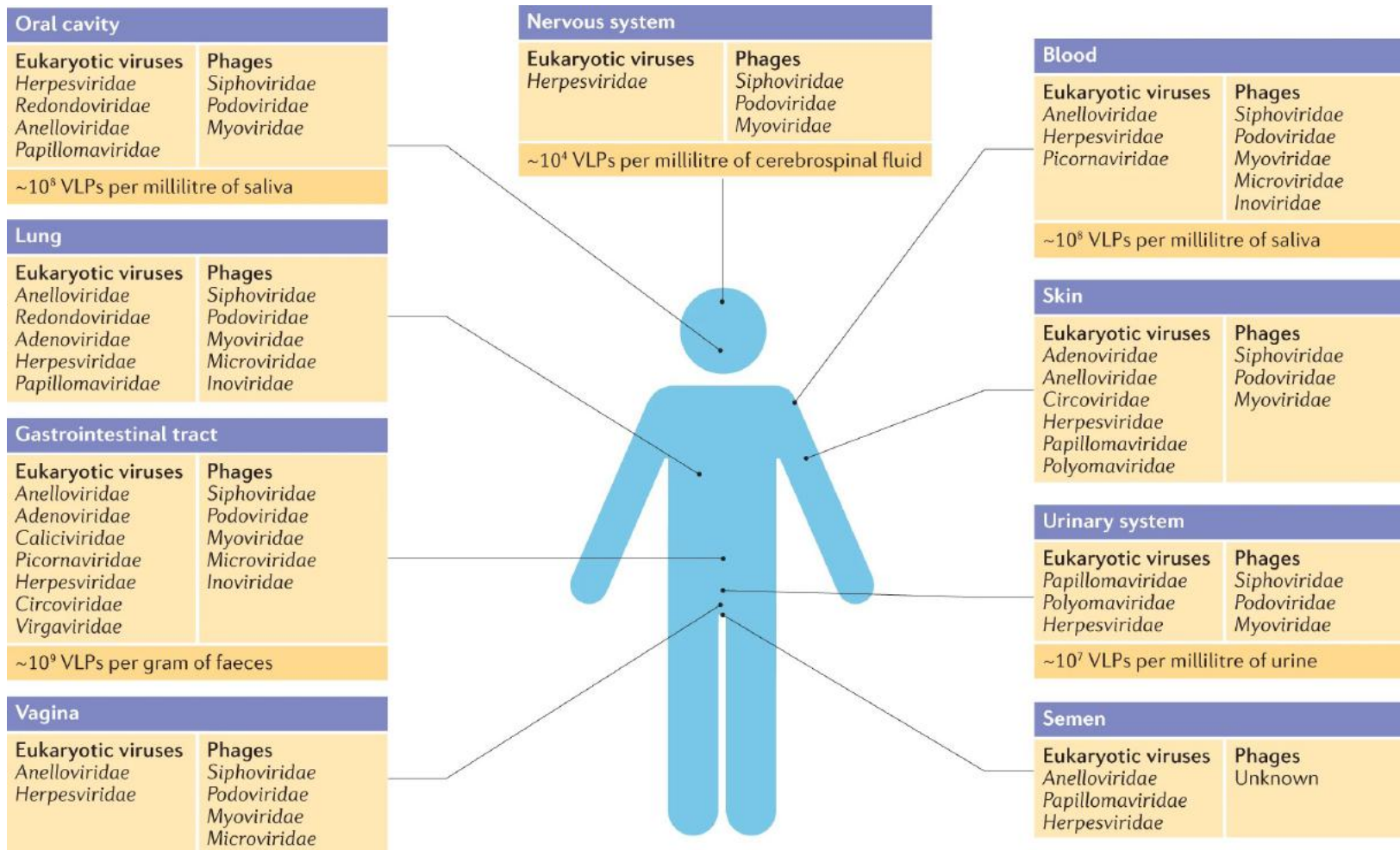


Abundance

Gray whale $\sim 10^6$ calicivirus per gram of feces

Excretes 10^{13} (10,000,000,000,000) viral particles every day

Abundance



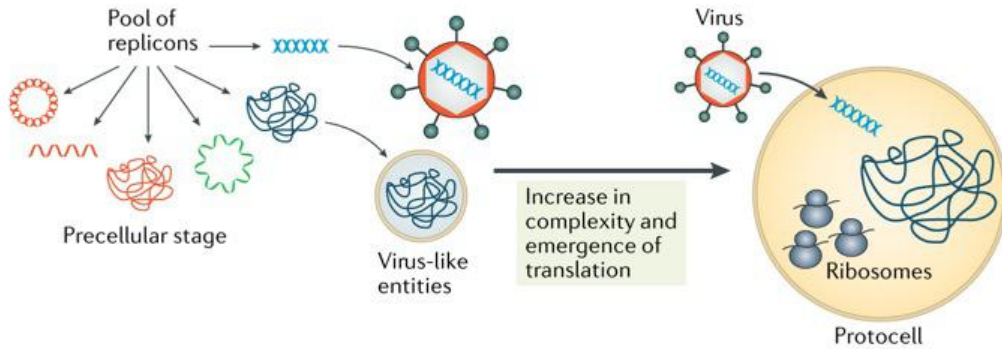
Viruses are part of all microbiomes

Infesting directly the host (e.g. Herpesviruses)

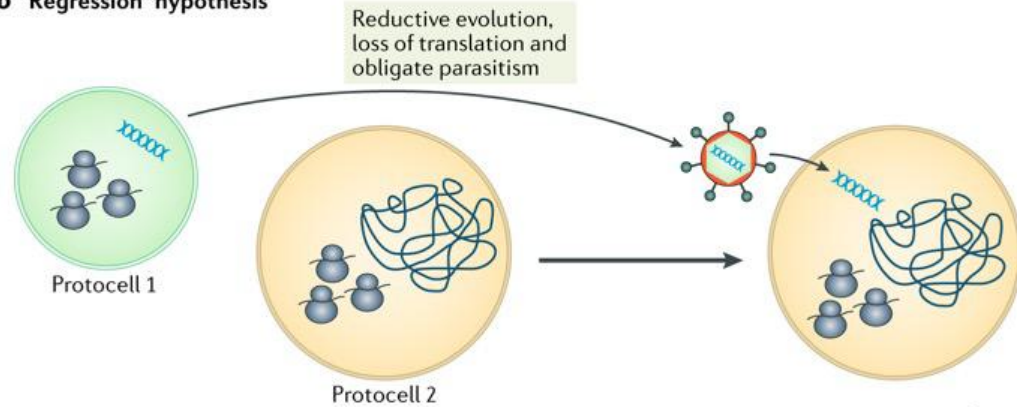
Infesting other members of the microbiome

Origin of viruses

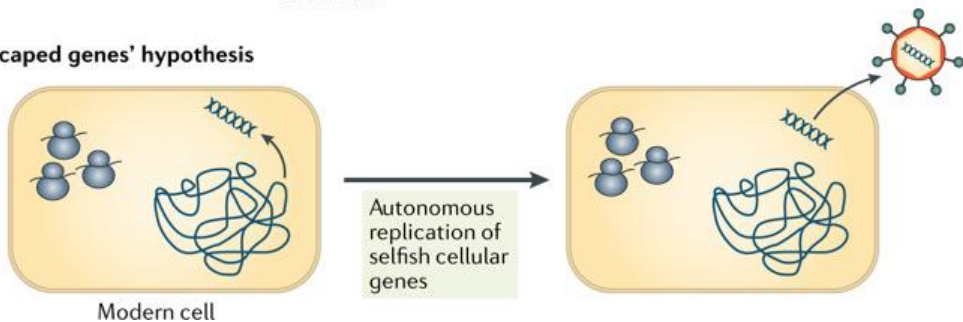
a 'Virus early' hypothesis



b 'Regression' hypothesis



c 'Escaped genes' hypothesis

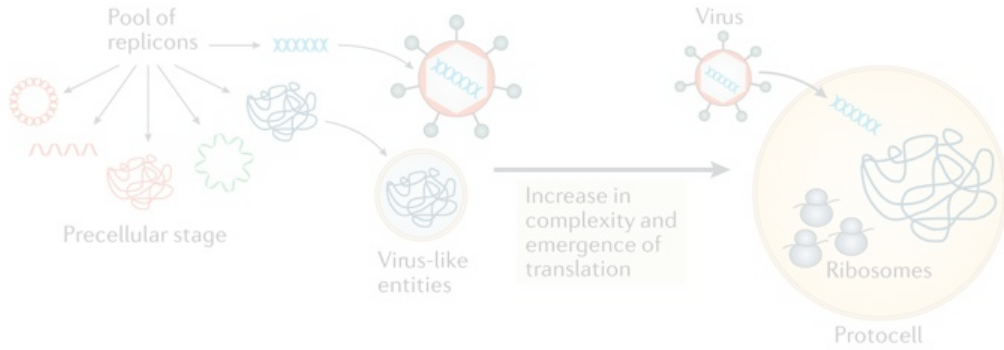


Theory 1: Viruses predate cells

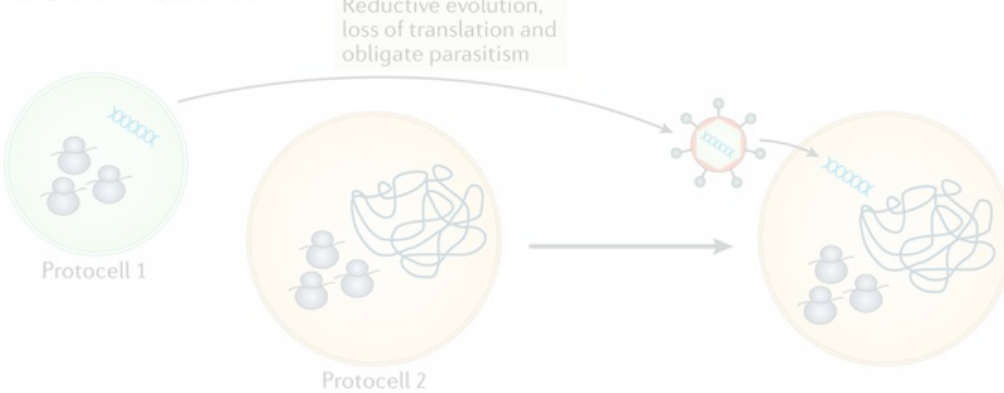
Theory 2: Viruses do not predate cells

Origin of viruses

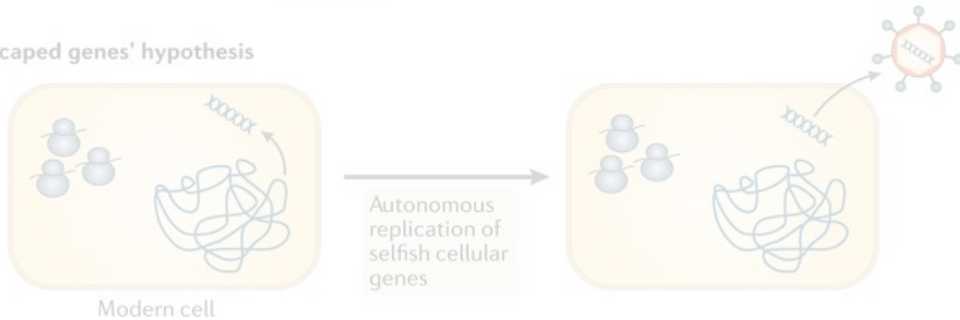
a 'Virus early' hypothesis



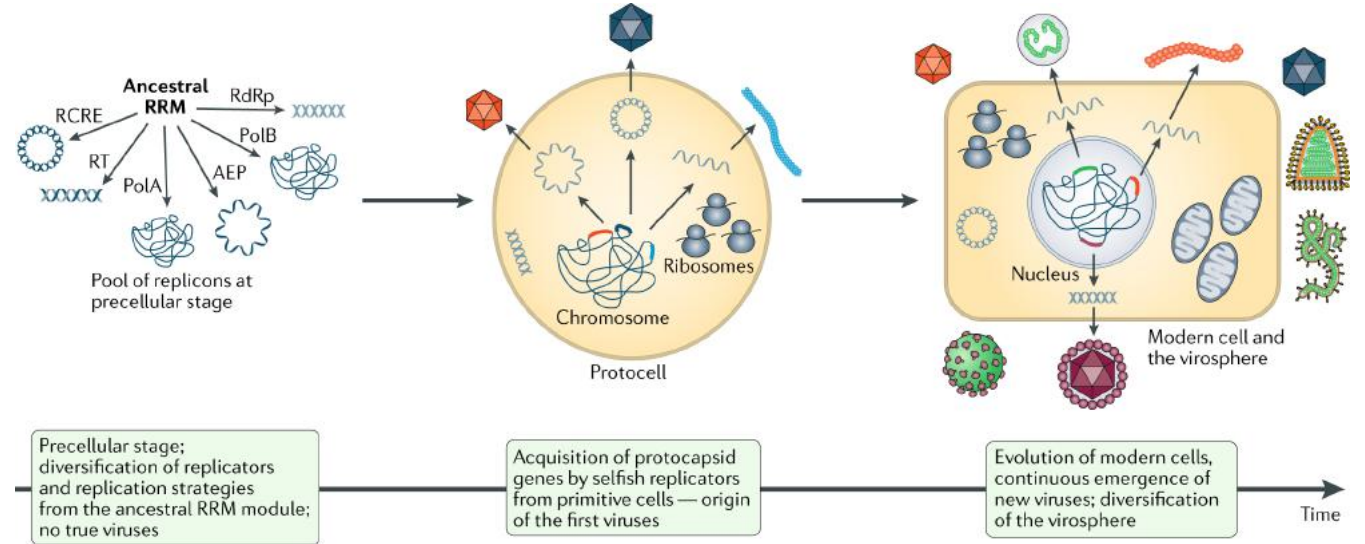
b 'Regression' hypothesis



c 'Escaped genes' hypothesis

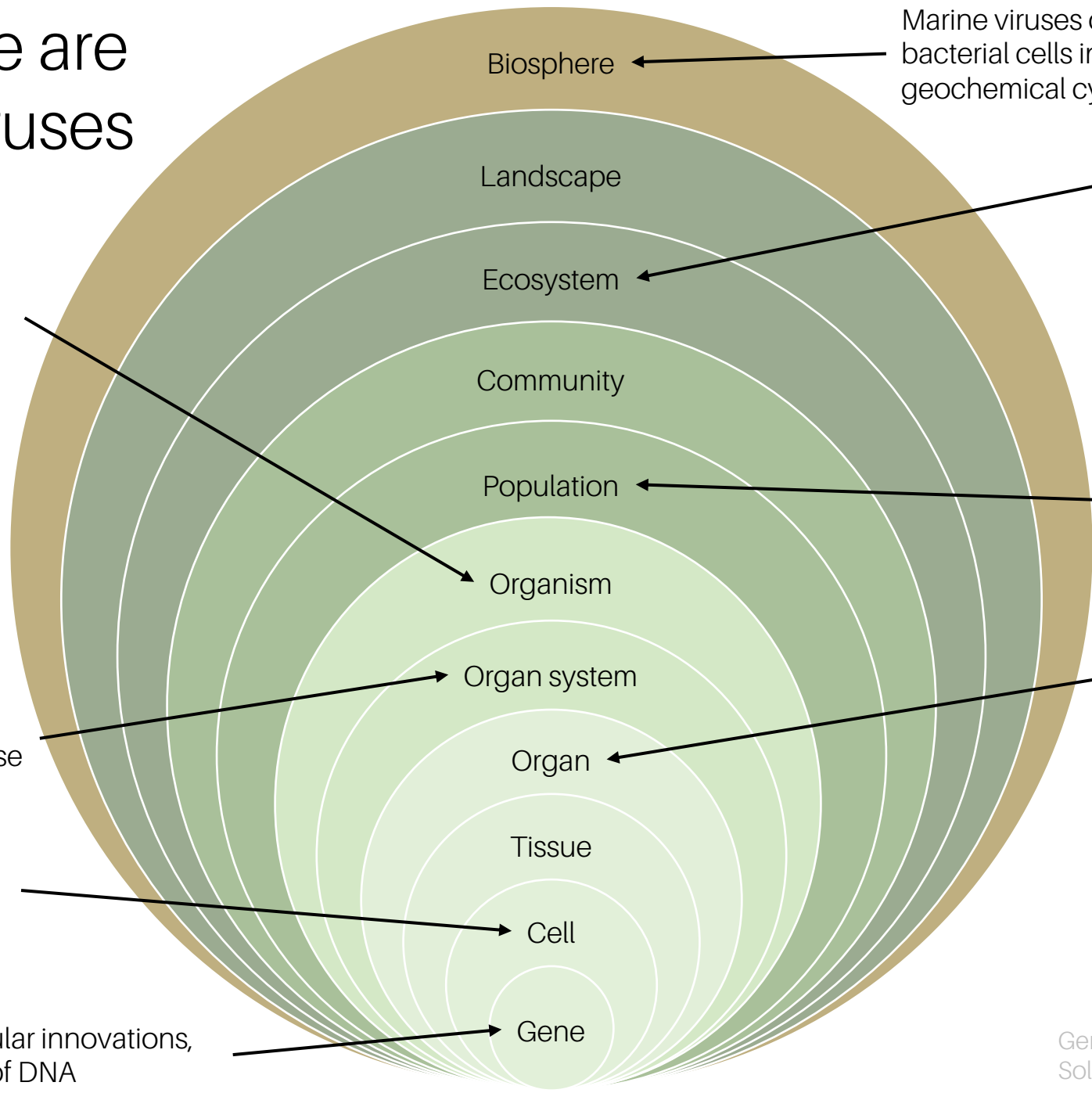


Chimeric hypothesis (co-evolution)



What could be the impact(s) of viruses?
(some are evident, some are deep,
all are important)

All scales of life are **affected** by viruses



Marine viruses drive large-scale turnover of bacterial cells influencing indirectly climate & geochemical cycles

Host jumps linked to ecological disturbances



Epidemics

Endogenous retroviruses and placenta



Required for the life cycles of several insects (e.g. parasitoids)



Evolution of complex and hypervariable immune response

Evolution of cells

Molecular innovations, origin of DNA

General references:
Solé & Elena, 2019; Odum and Barrett, 2005



Lagoa da Pampulha, Belo Horizonte, Brazil

Case study in weirdness: Yaravirus

Collection of muddy water from creeks of an artificial urban lake in Belo Horizonte, Brazil

Inoculation of water samples on cultures of amoeba

New virus! **Yaravirus brasiliensis**

(Yara = the mother of water in Tupi-Guarani mythology)

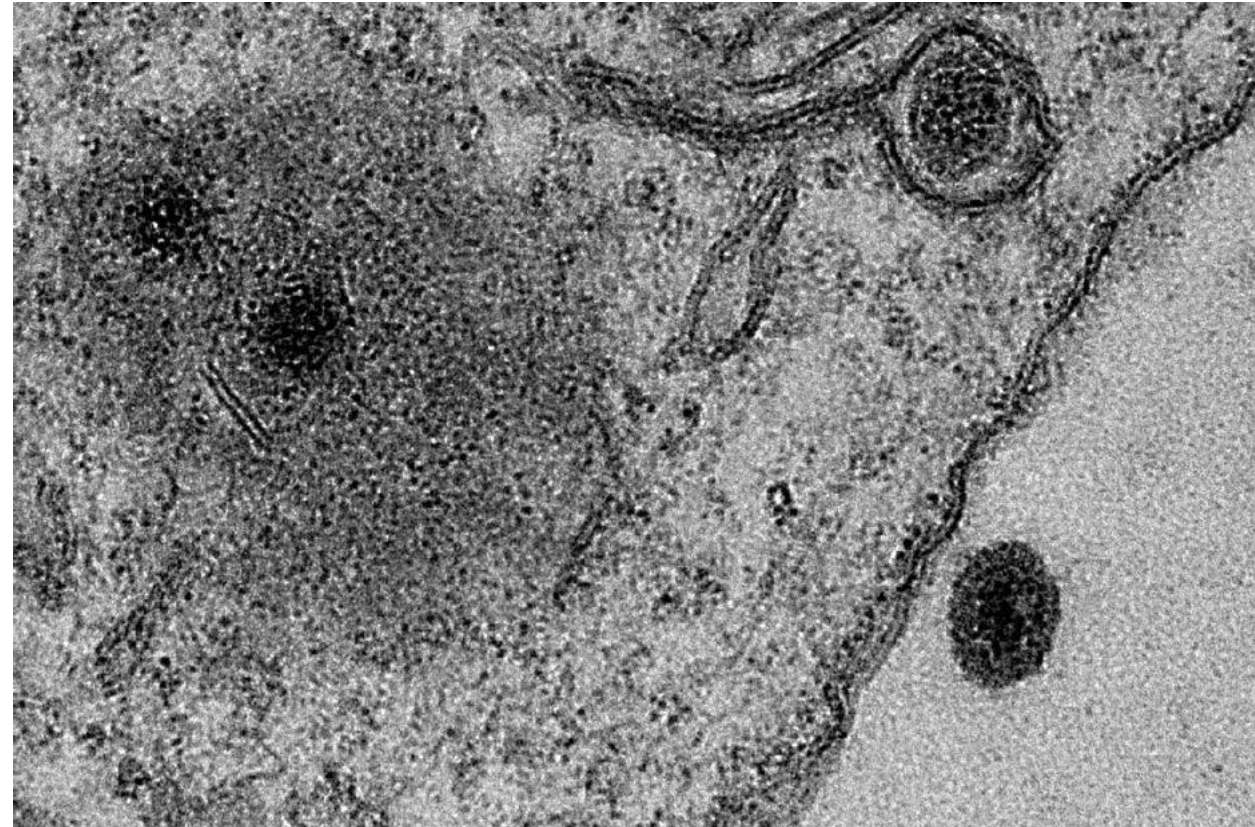
dsDNA

~45 kb

74 predicted proteins

Only six genes have distant homologs in public databases.

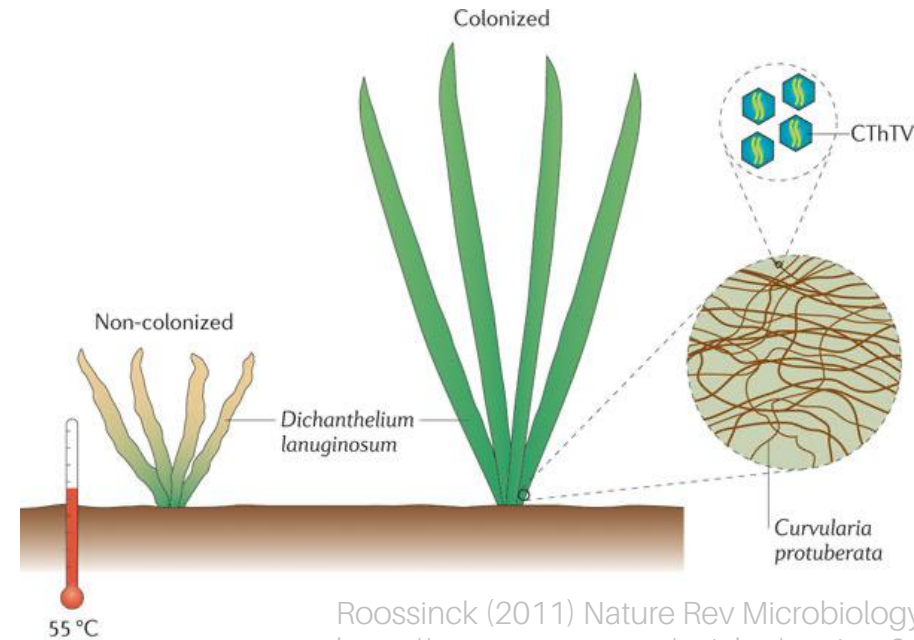
The rest is **unknown**.



Mutualists!

Yellowstone plant needs to be associated with a fungus itself infected with a virus to survive hot soils

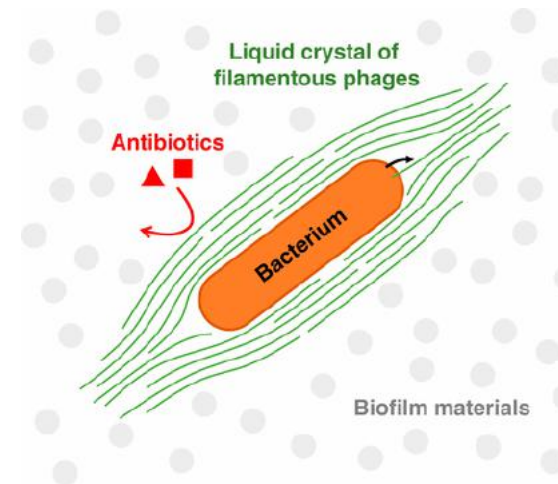
Marquez et al. (2007) Science



Roossinck (2011) Nature Rev Microbiology
<https://www.nature.com/articles/nrmicro2491>

Pf phages promote *P. aeruginosa* survival in harsh environments:

- decoy for the host immune system by triggering an antiviral response
- promotes antibiotic tolerance of *P. aeruginosa* by self-assembling into higher-order liquid crystalline structures



Tarafder et al. 2020 PNAS <https://doi.org/10.1073/pnas.1917726117>



Viruses...

...are everywhere...

...and at the foundation of life

Outline

1 What are viruses?

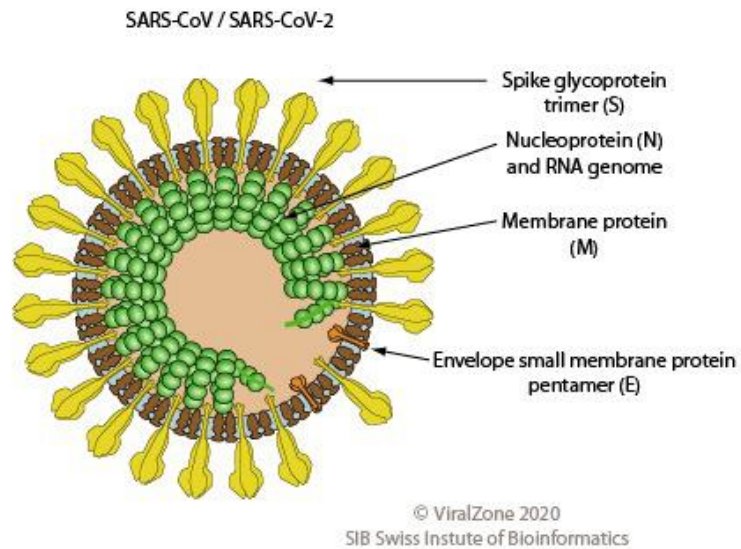
2 SARS-CoV-2

3 How do RNA viruses evolve?

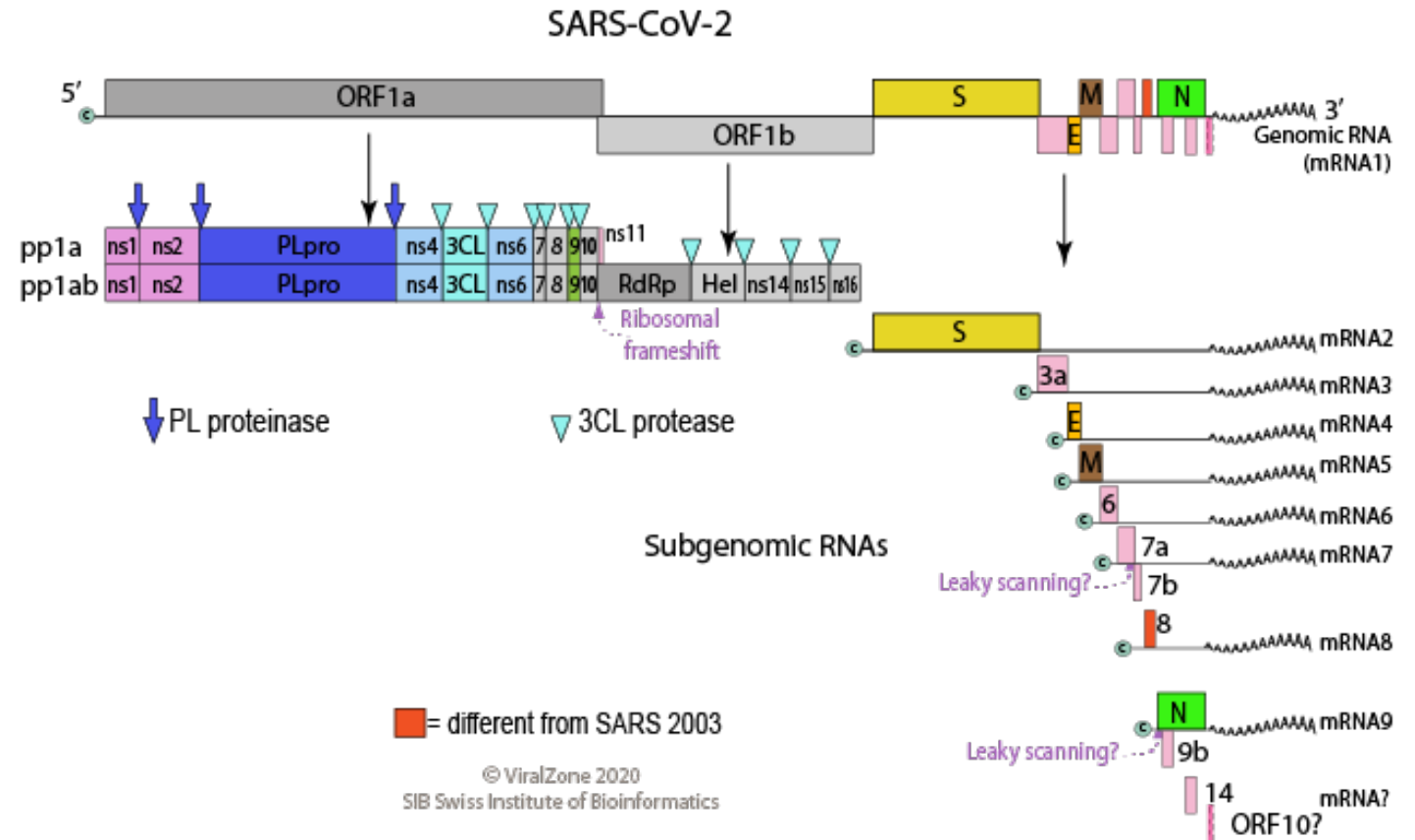
4 Evolution and future of SARS-CoV-2

SARS-CoV-2

Betacoronavirus

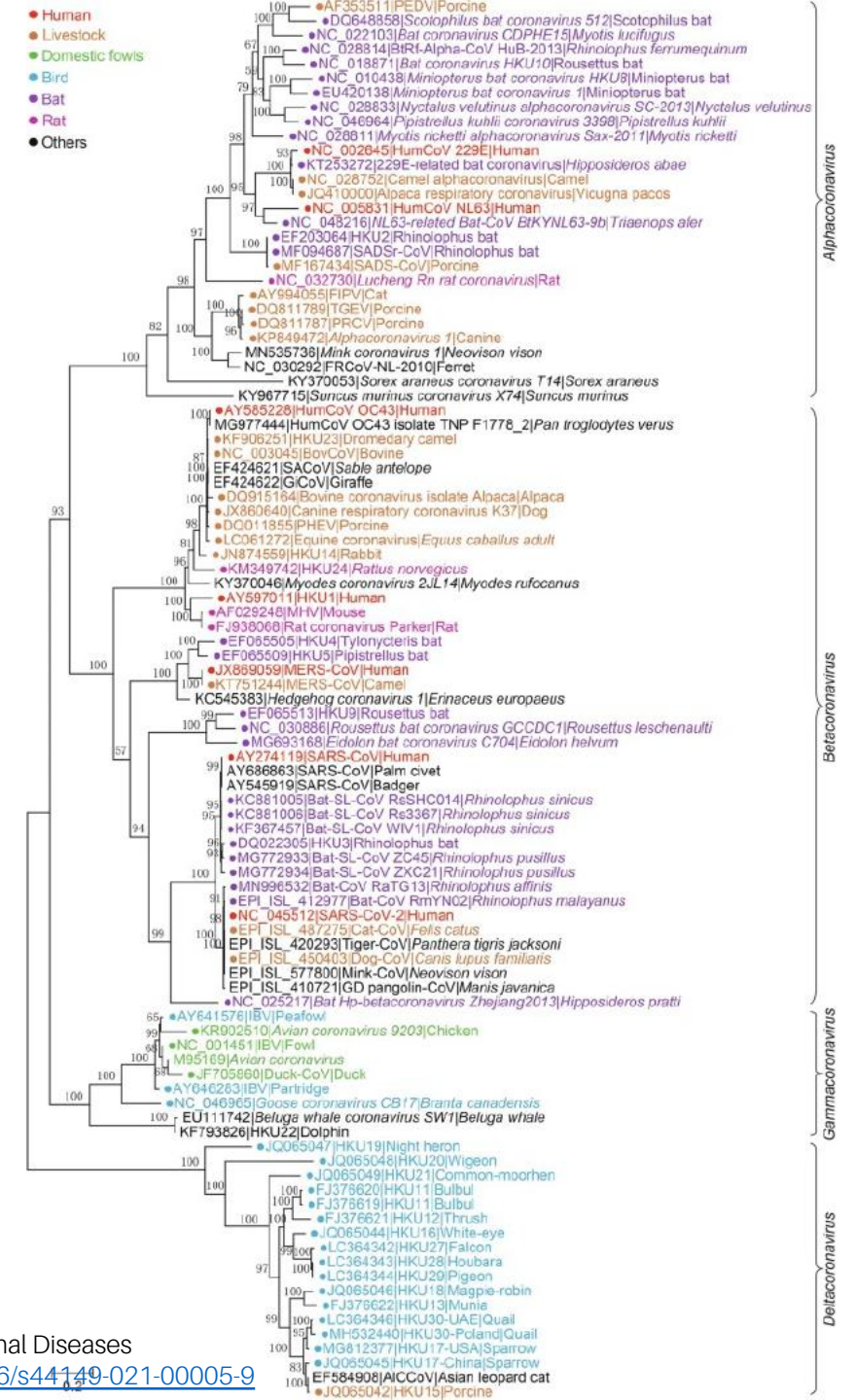
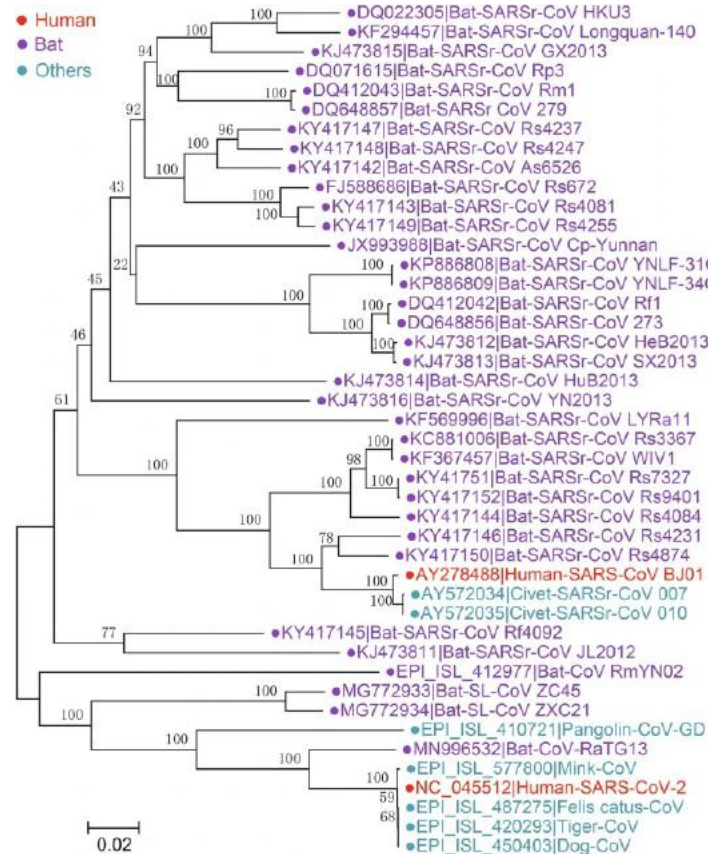


Monopartite
Linear ssRNA(+) genome
29.9 kb in size
13 Open reading frames



Betacoronavirus

Diverse sets of hosts (mammalians)



Outline

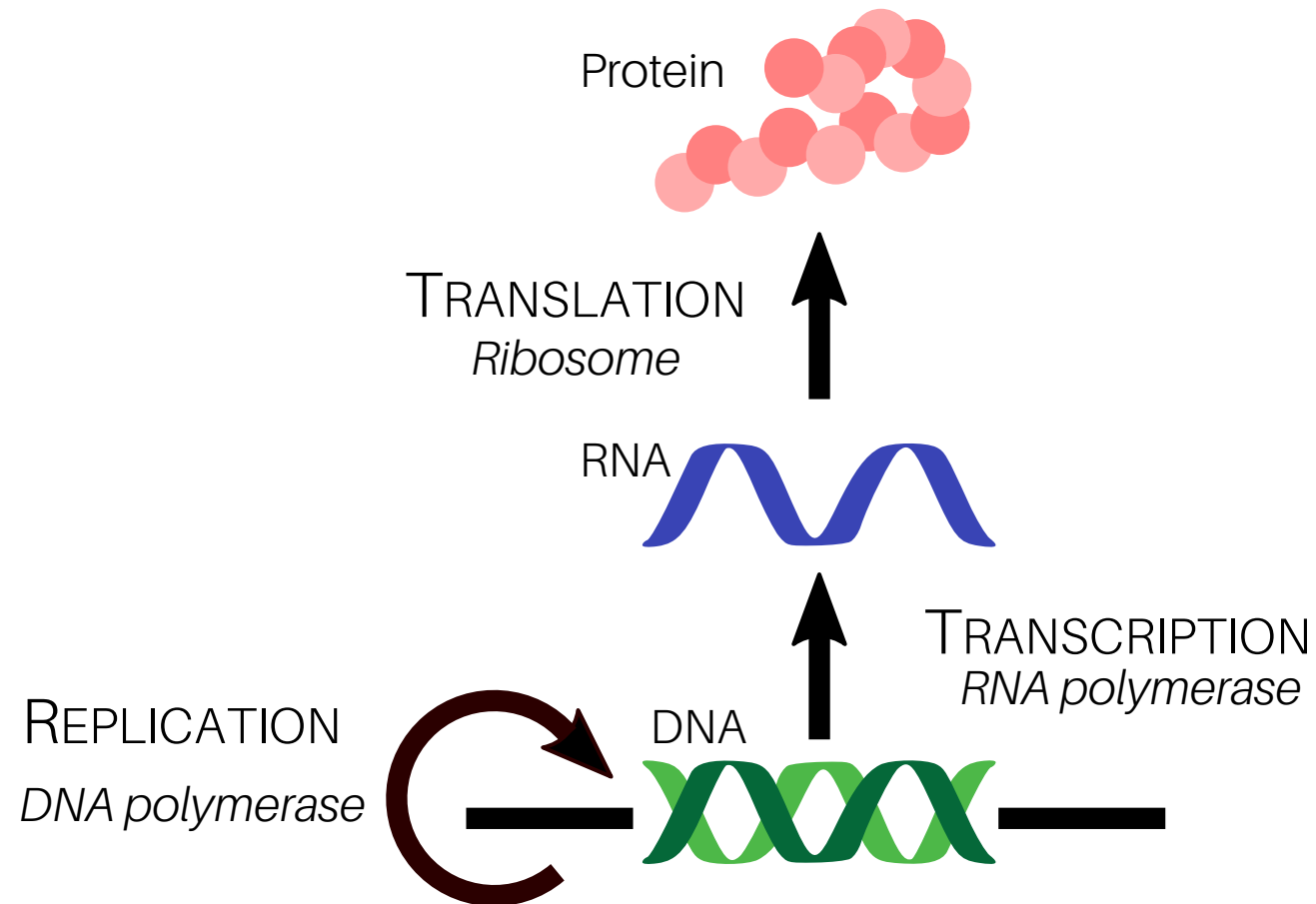
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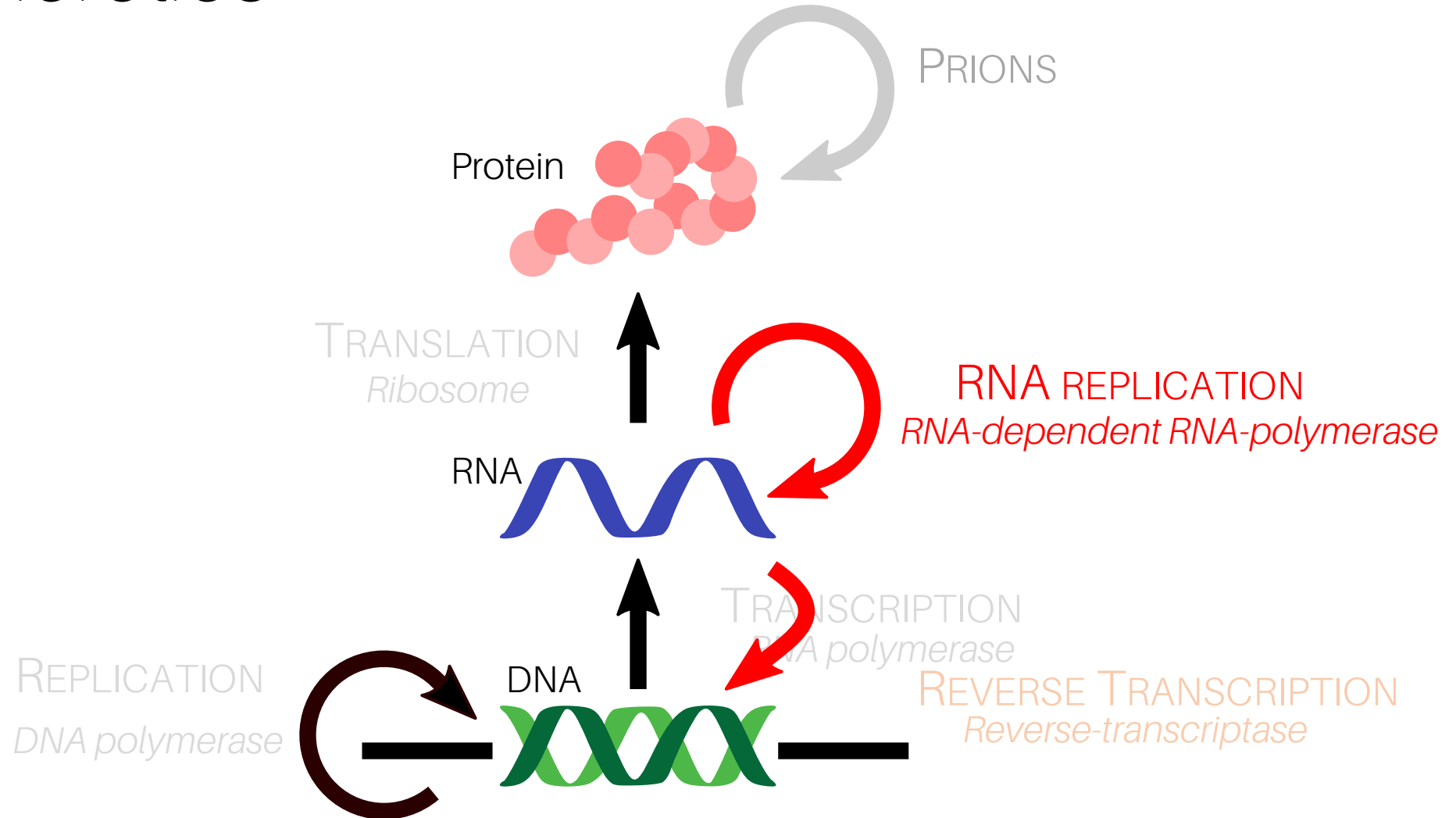
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Central dogma of molecular biology



Viral heretics



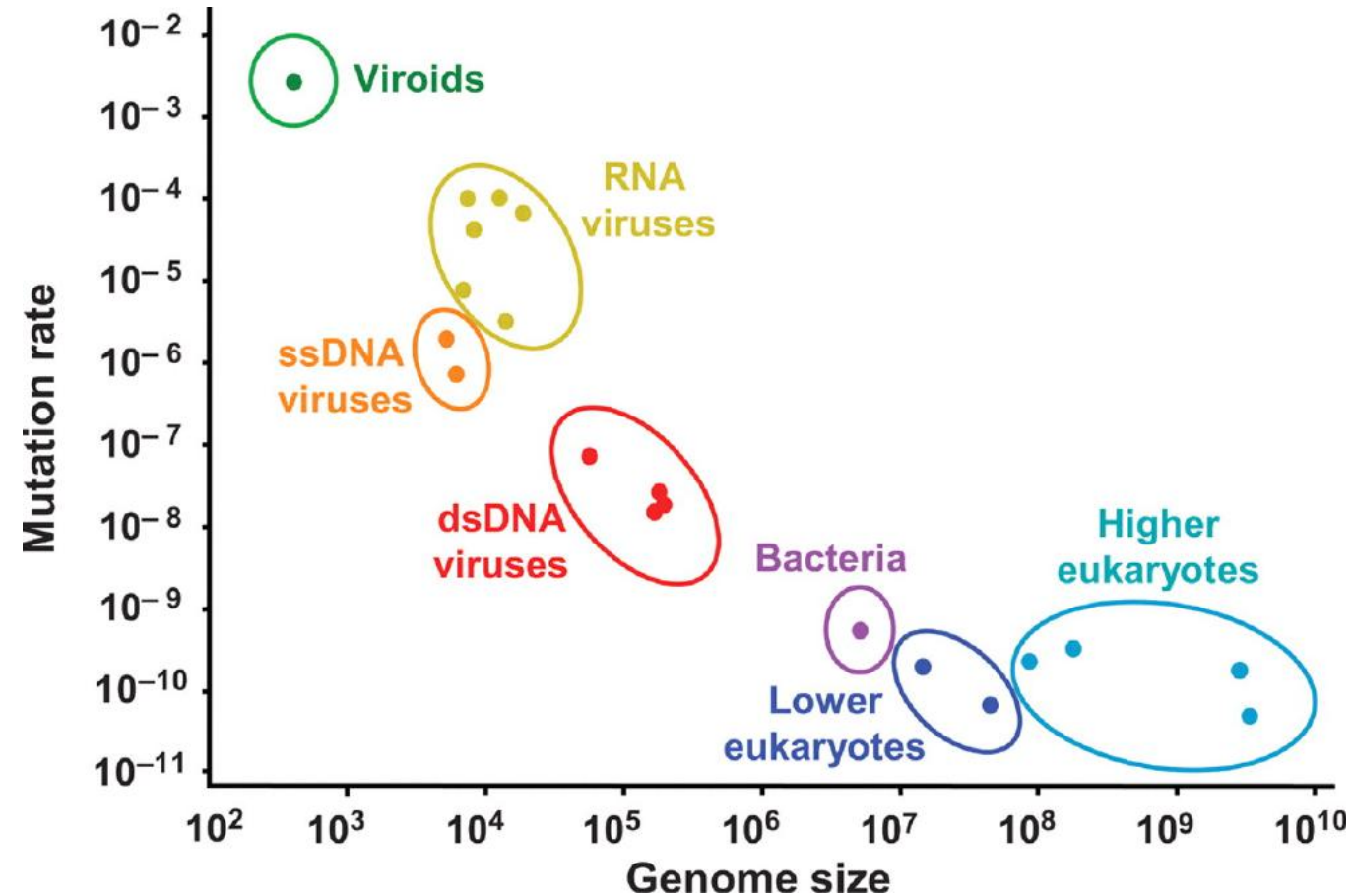
RdRP is error-prone

DNA polymerase: 10^{-7} to 10^{-9} error/nt replicated

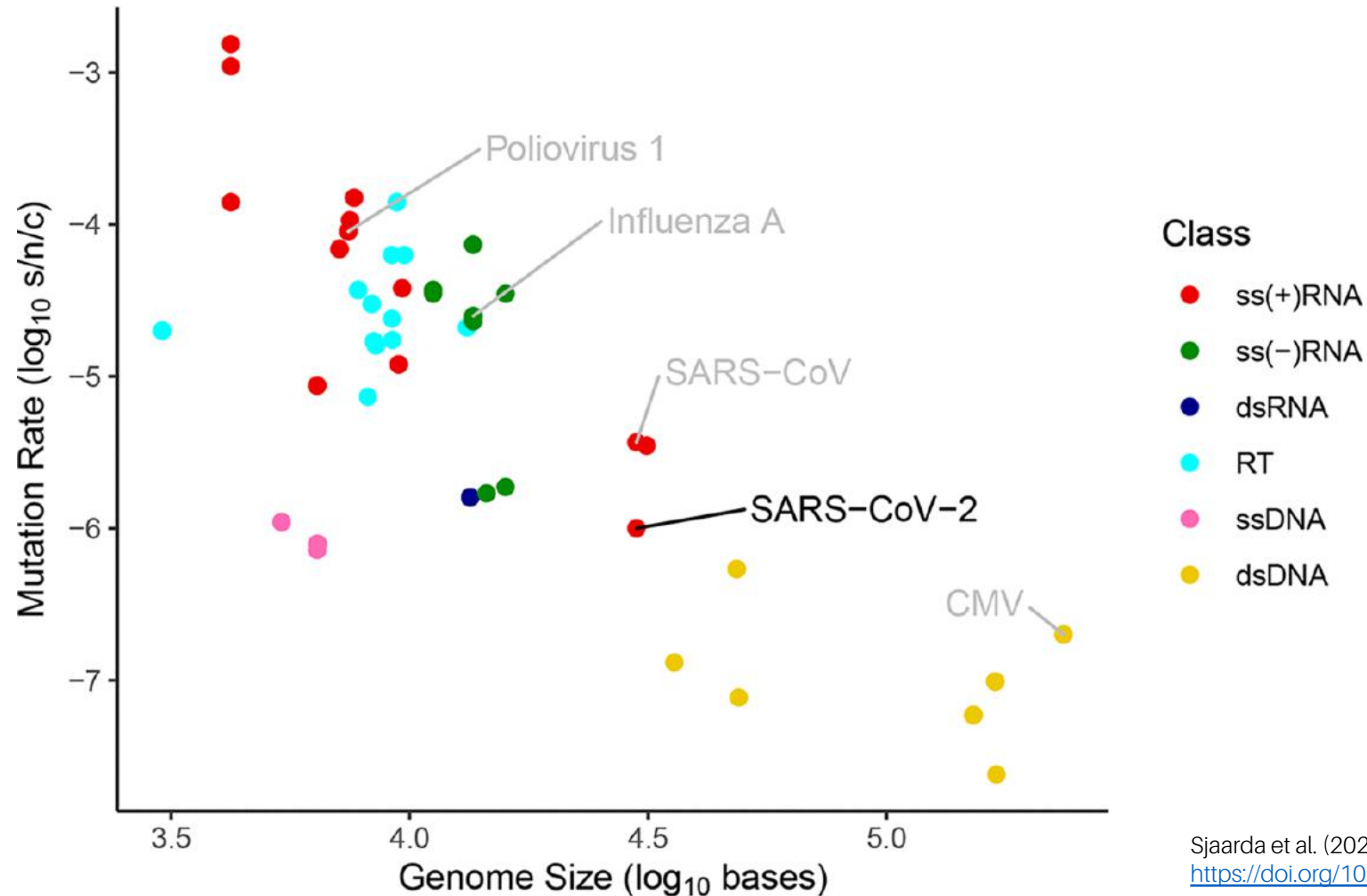
RNA-dependent-RNA-Polymerase: 10^{-3} to 10^{-5} error/nt replicated

lack of proofreading ability in RNA polymerases

Virus mutation rate



SARS-CoV-2's RdRP is slightly less error-prone



Proof reading activity!

Between-host evolution

Viral population is shaped by:

Bottleneck,

Immune response,

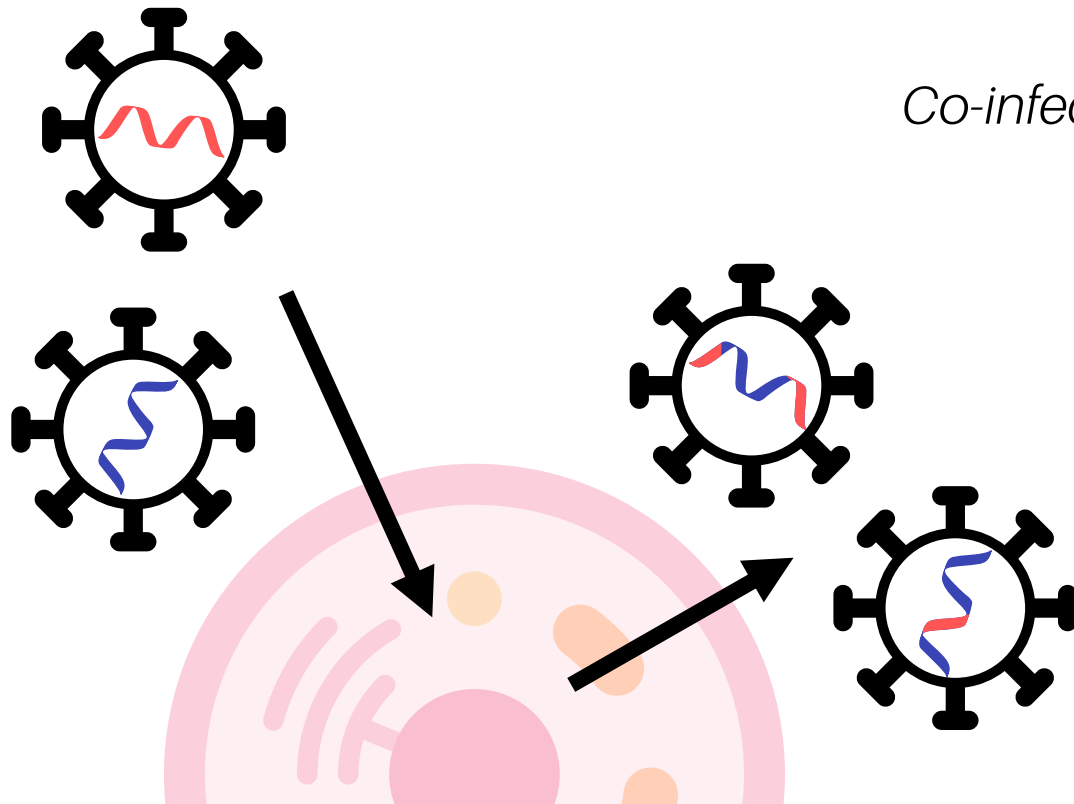
Host genetic background & physiology,

Environment...

~ It's a complex mess.

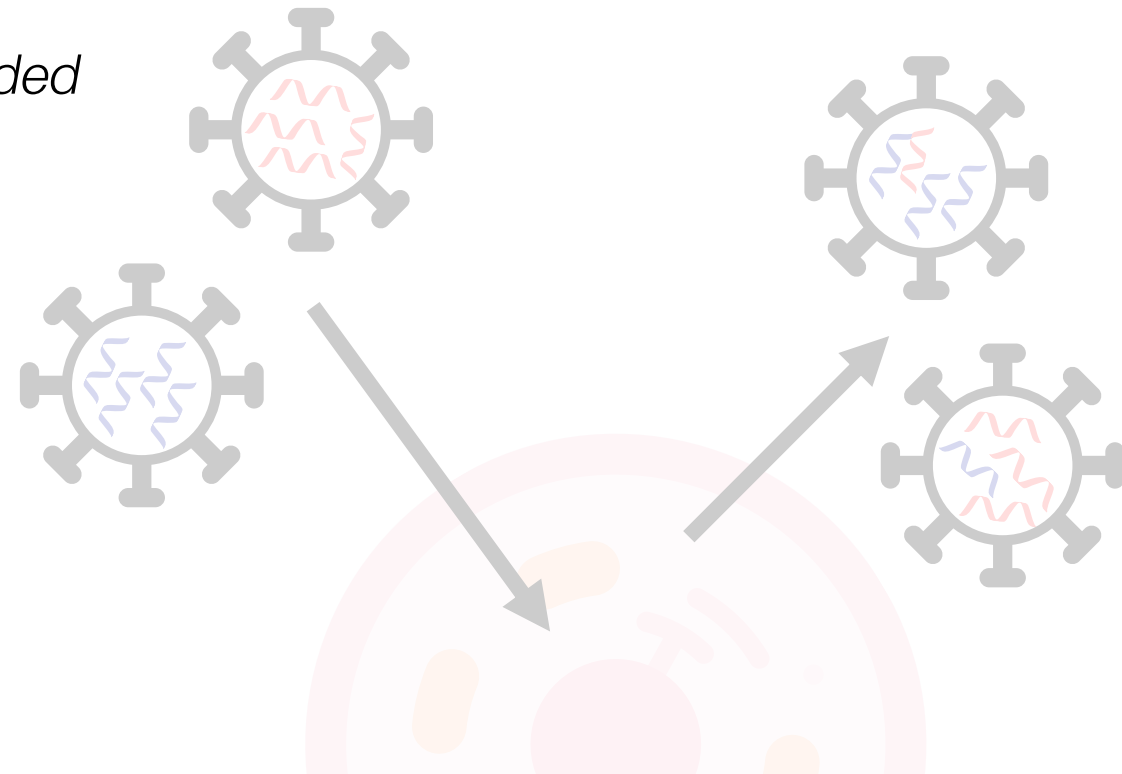
Other mechanisms of virus evolution

Recombination

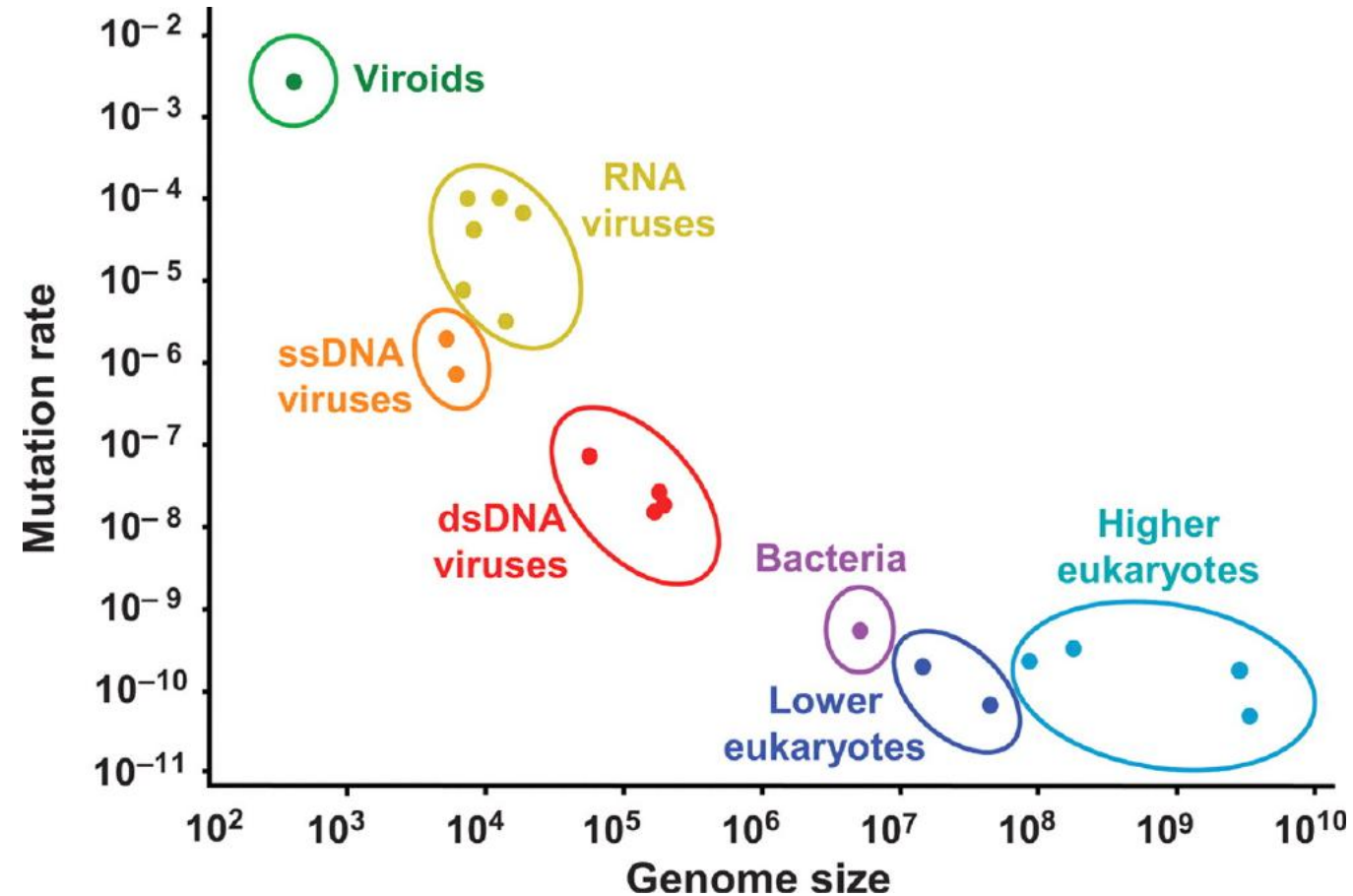


Co-infection is needed

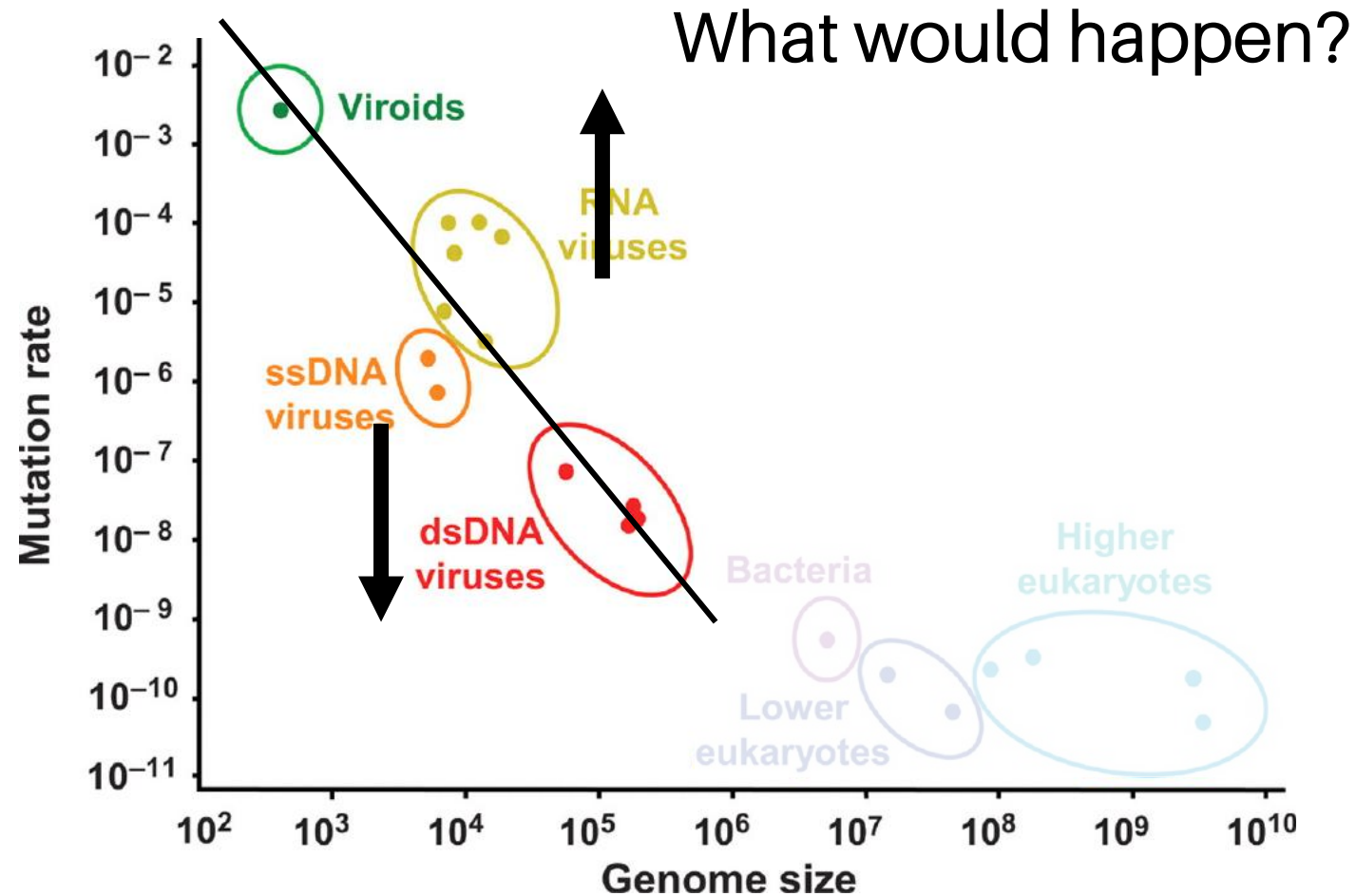
Reassortment



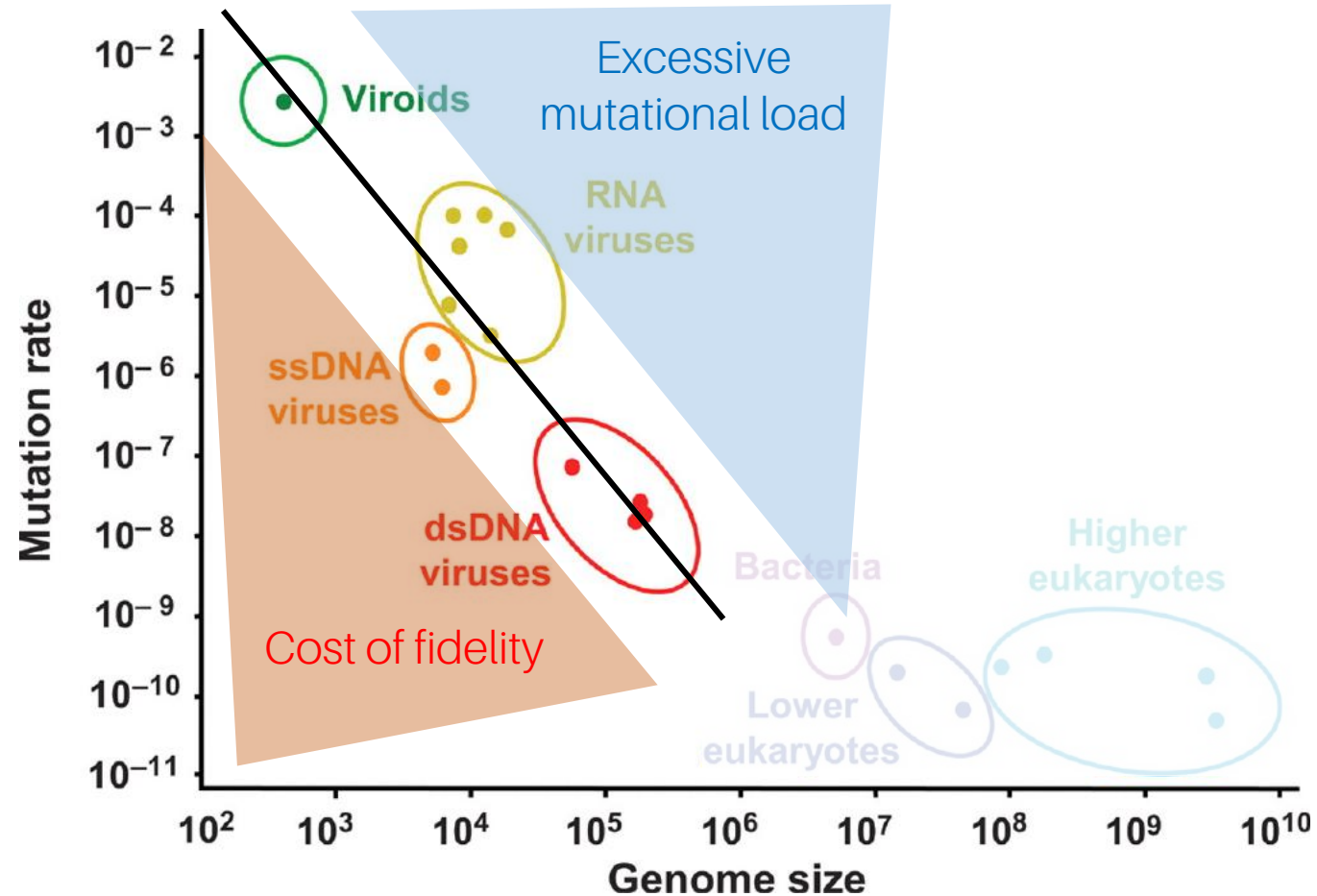
Virus mutation rate



Constraints on virus evolution



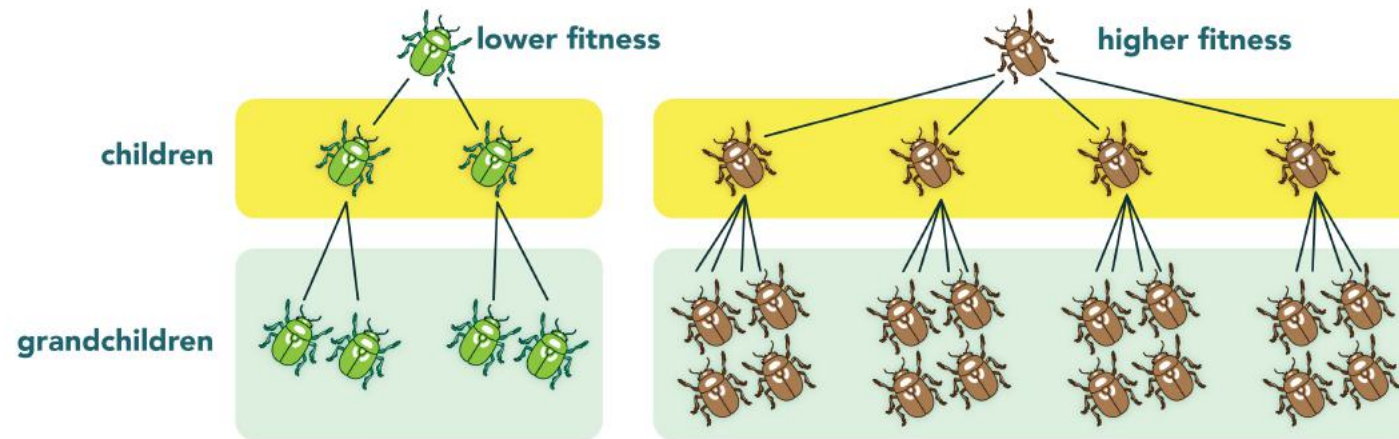
Constraints on virus evolution



Fitness?

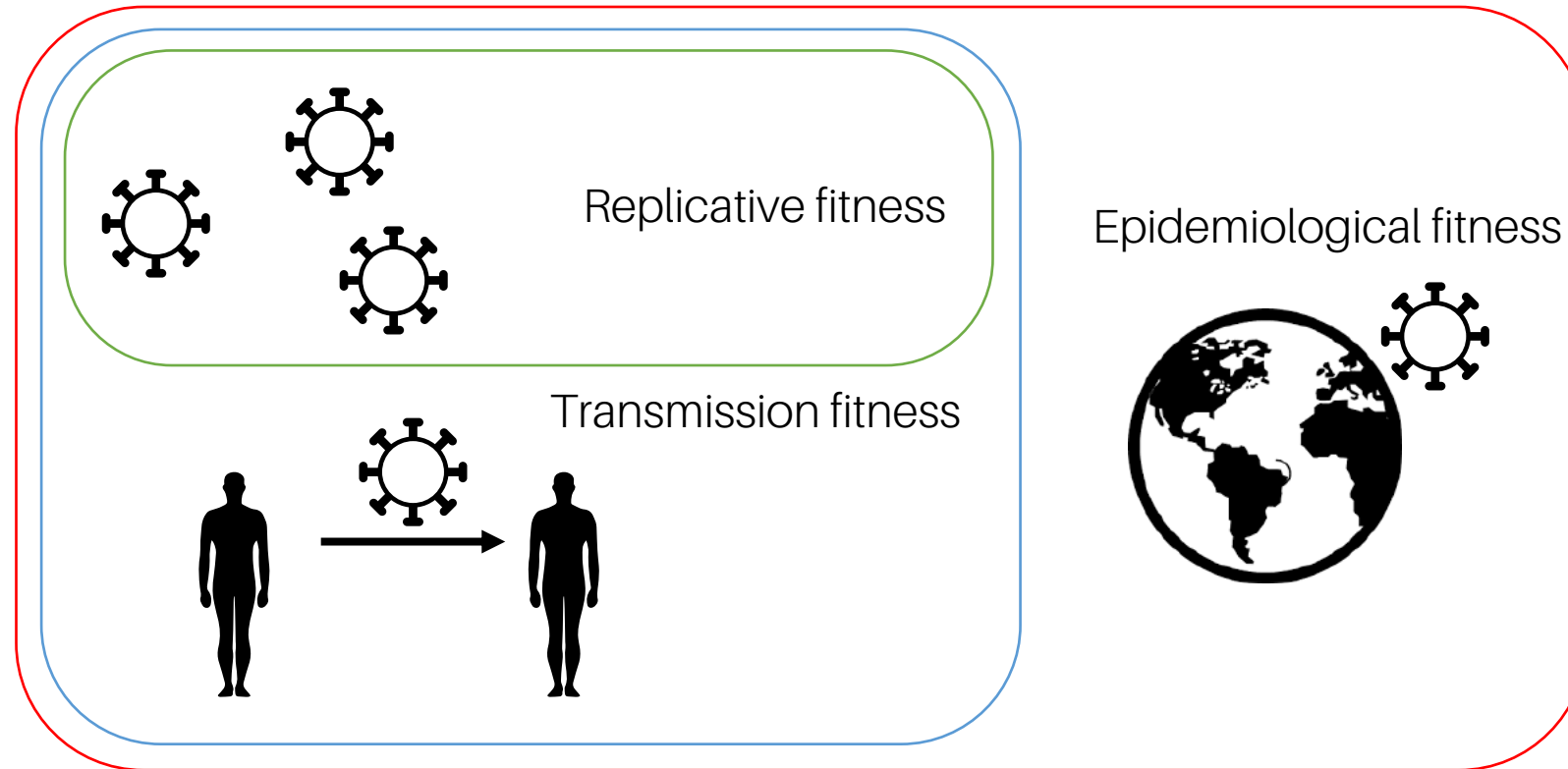
Evolutionary biologists use the word fitness to describe how good a particular genotype is at leaving offspring in the next generation relative to other genotypes

Of course, fitness is a relative thing.



What would be fitness for viruses?

Fitness of viruses



Outline

1 What are viruses?

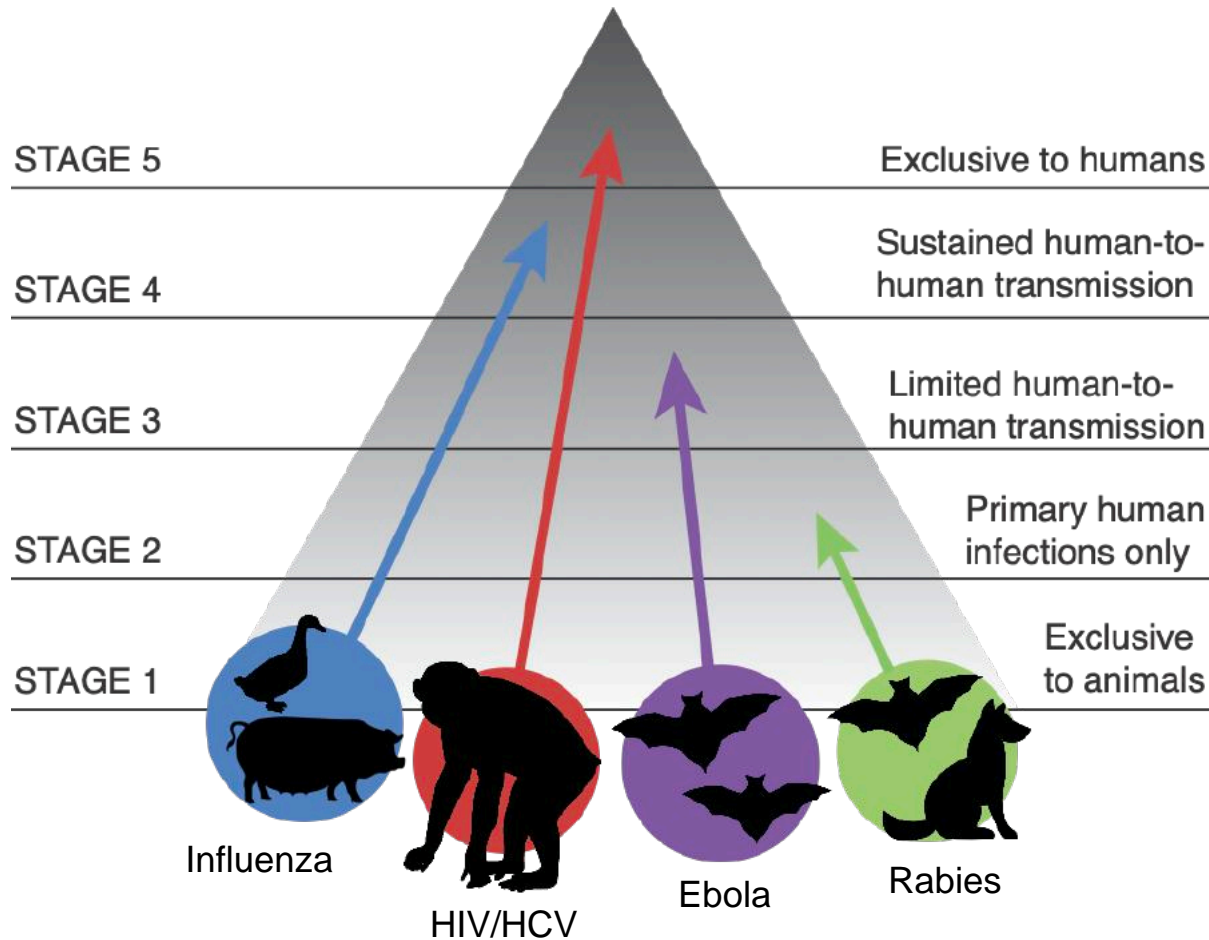
2 SARS-CoV-2

3 How do RNA viruses evolve?

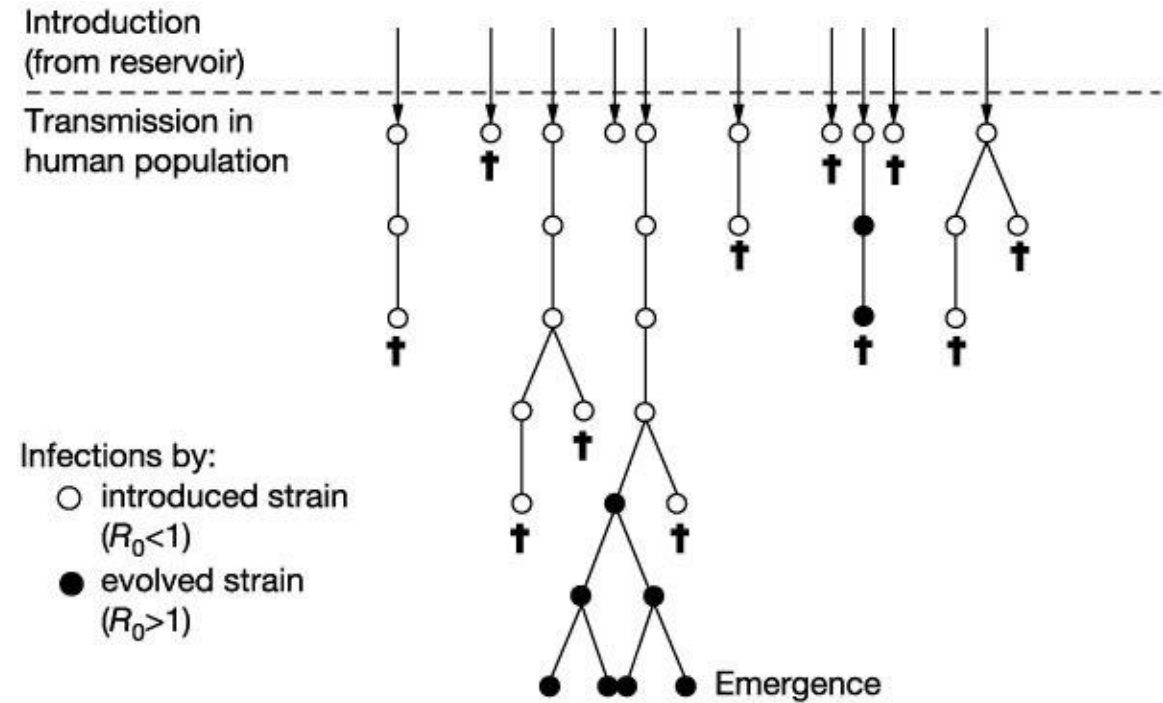
4 Evolution and future of SARS-CoV-2

Understanding the trajectory of SARS-CoV-2

Genetic changes (can) trigger/follow epidemiological change

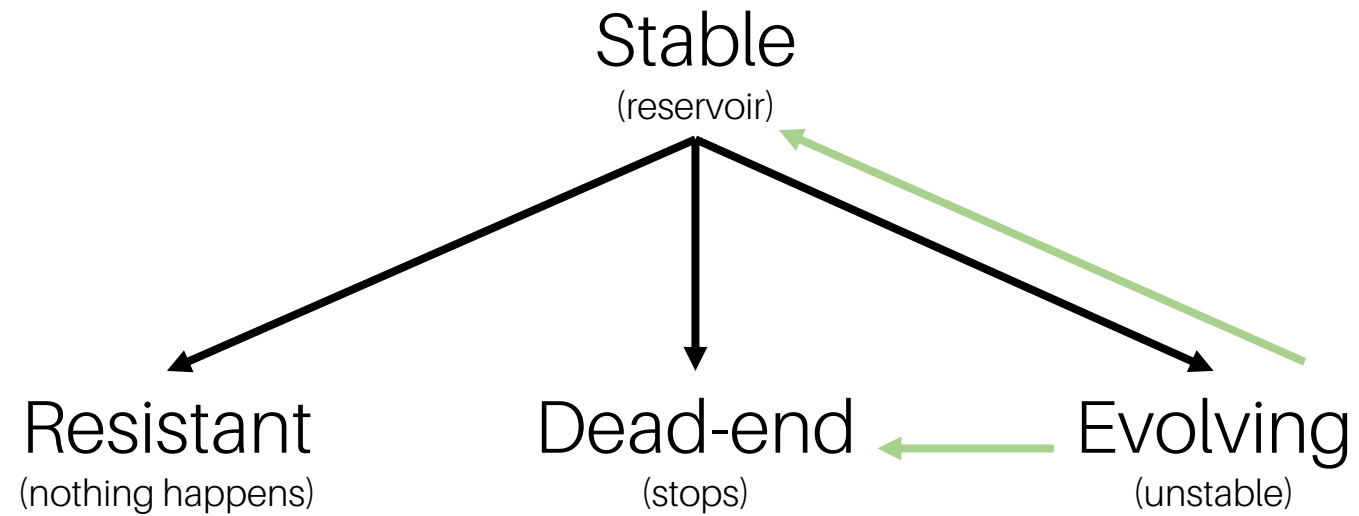


Wolfe et al. Nature 2007 <https://doi.org/10.1038/nature05775>
 Pike et al. CID 2010 <https://doi.org/10.1086/652860>



Antia et al. 2003 Nature
<https://doi.org/10.1038/nature02104>

Virus-host interaction



May take some time!

Transmission and emergence

R_0

“R nought” or “R zero”

Reproduction number
(in an idealized, naïve population)

R_t

Effective reproduction number
(takes into account immunity, etc)

average number of people who will contract the disease from one infected person

$R_0 < 1$

Decline, eventually dies out

$R_0 = 1$

Maintenance, endemicity

$R_0 > 1$

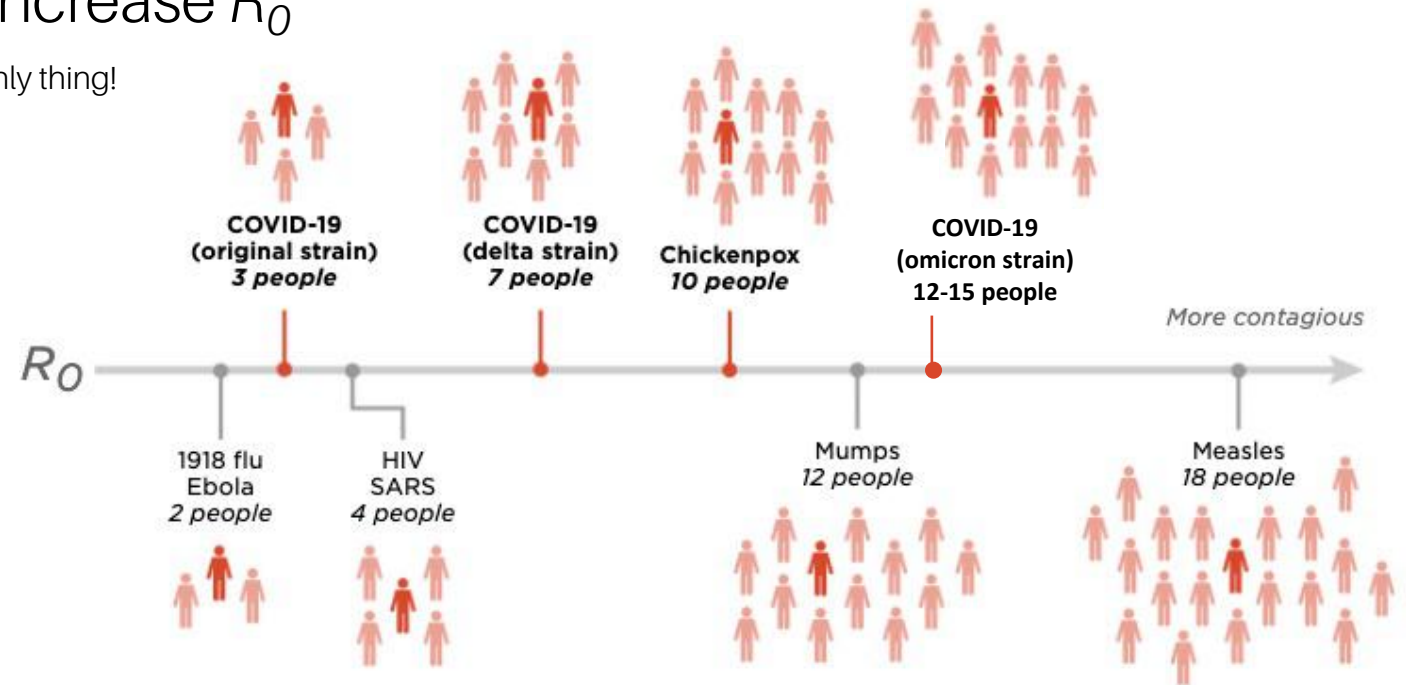
Epidemic

Do you know which pathogen has (usually)
the highest R_0 ?

Transmission and emergence

Increasing transmission can increase R_0

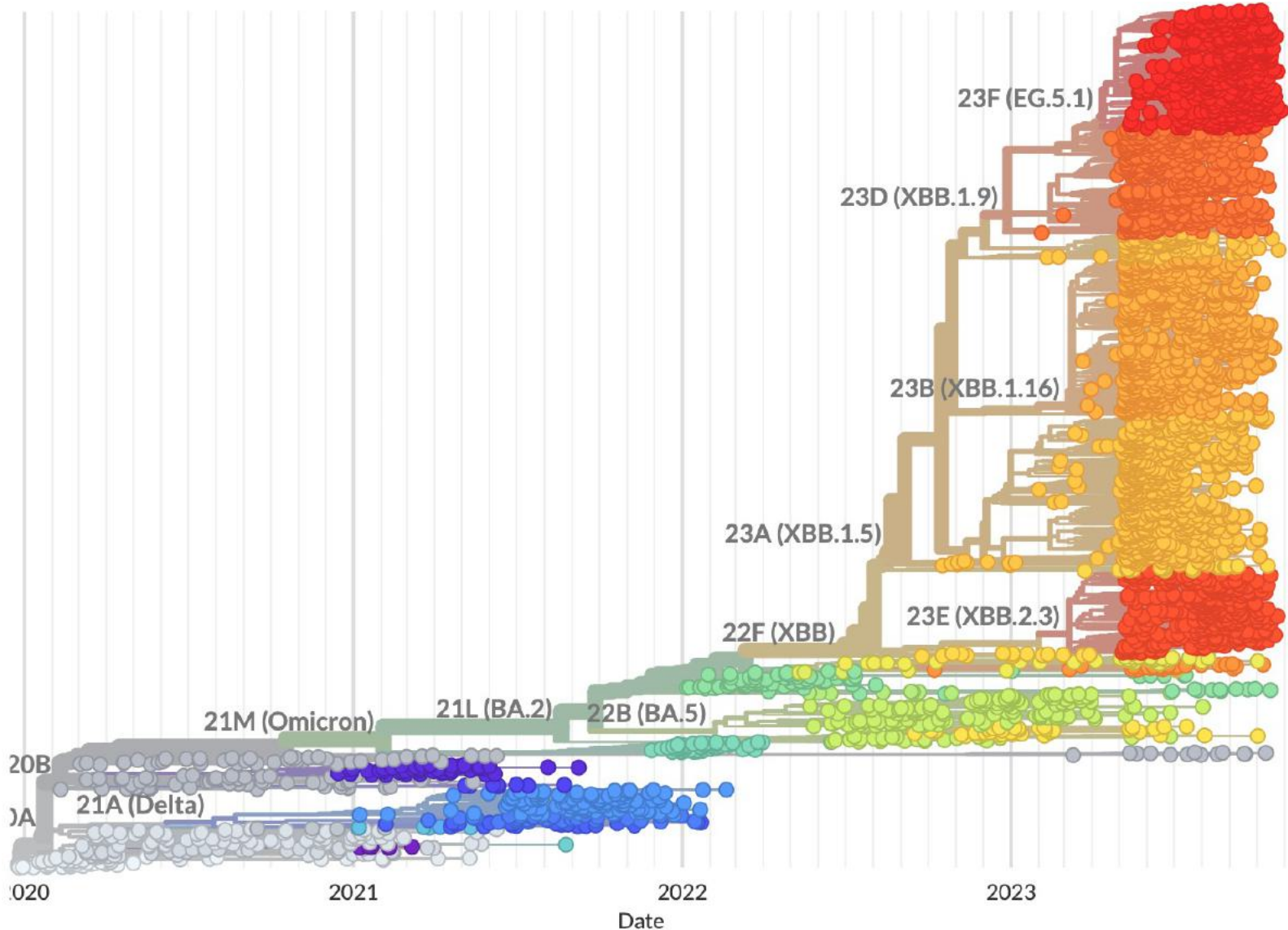
BUT it's not the only thing!



Michaeleen Doucleff, Alyson Hurt and Adam Cole/NPR, [link](#)

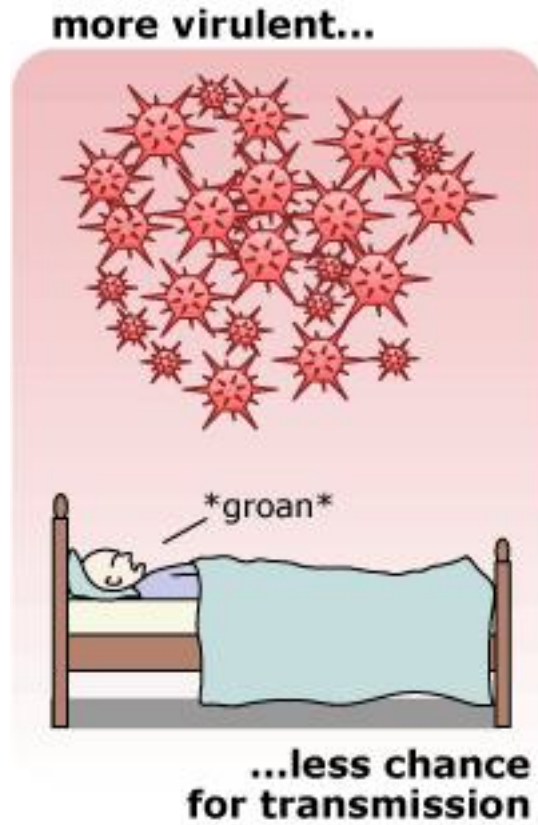
It is also dynamics; changes in the virus or else can change R_0

SARS-CoV-2 variants



It's just a mild flu...

Future of COVID

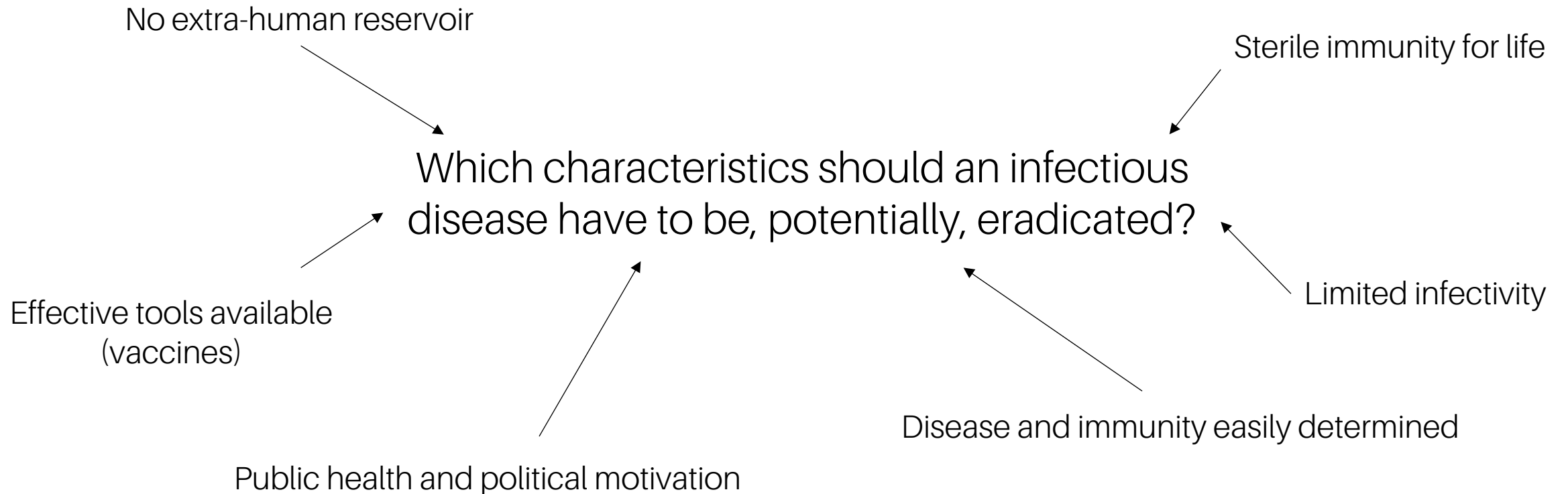


Eradicating SARS-CoV-2

Eradication of infectious diseases

Which characteristics should an infectious disease have to be, potentially, eradicated?

Eradication of infectious diseases





Virevo

tinyurl.com/virevo