

# VIROLOGY LIVE

WITH VINCENT RACANIELLO

## What is a virus?

Virology Live

Fall 2021

*"There is an intrinsic simplicity of nature and the ultimate contribution of science resides in the discovery of unifying and simplifying generalizations, rather than in the description of isolated situations - in the visualization of simple, overall patterns rather than in the analysis of patchworks"*

--SALVADOR LURIA

# Virology Live

- Prof. Vincent Racaniello, Ph.D.
  - [vincent@microbe.tv](mailto:vincent@microbe.tv)
  - twitter @profvrr
  - instagram @profvrr
  - [youtube.com/profvrr](https://youtube.com/profvrr)
  - [facebook.com/thisweekinvirology](https://facebook.com/thisweekinvirology)

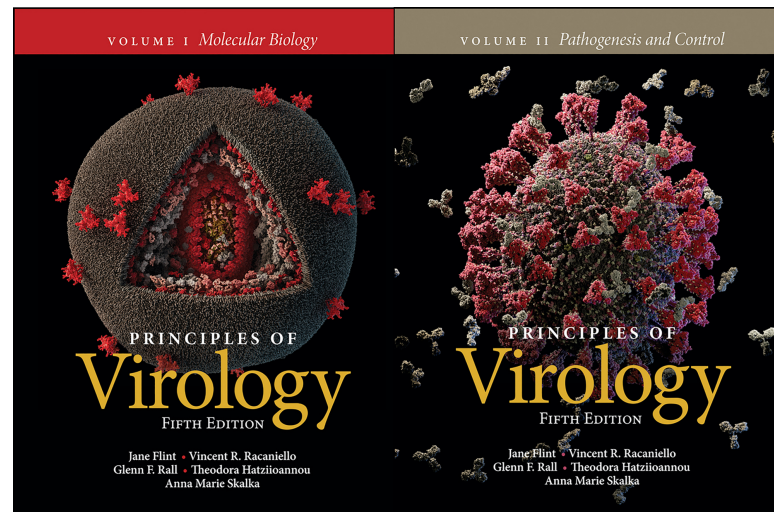
# Virology Live

- <https://www.virology.ws/virology-live-2021/>
- Schedule, lecture slides, study questions, readings, video, quiz

# Virology Live

Recommended Textbook: *Principles of Virology*

Fifth Edition, ASM Press



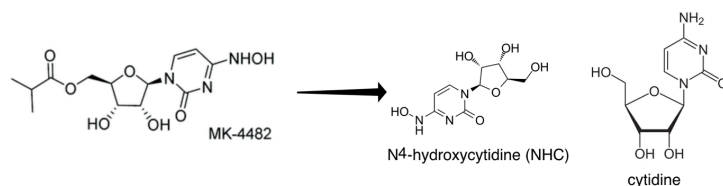
# Virology Live



## An antiviral compound that blocks SARS-CoV-2 transmission in ferrets

11 DECEMBER 2020

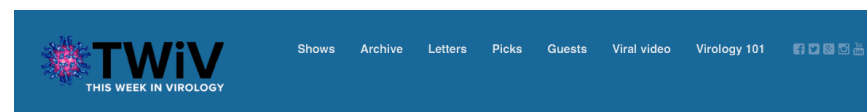
COVID-19 vaccine candidates are garnering all the news these days, which is appropriate as they are our key to ending this pandemic. Earlier in this outbreak antiviral drugs received a good deal of attention, but they have proven less useful in curtailing infection. Less discussed are the many antiviral drug candidates that are in testing, including one that appears to be effective in a ferret model of infection.



MK-4482 is an orally available pro-drug of the nucleoside analog N4-hydroxycytidine (NHC) (pictured above). The latter is a nucleoside analogue which is incorporated into RNA by the viral RNA-dependent RNA polymerase. Once incorporated into RNA, NHC is recognized as either C or U by the RNA polymerase. As a consequence, many mutations are introduced into the viral genome, causing lethal mutagenesis and inhibition of infectivity. NHC has been previously shown to have broad-spectrum anti-RNA virus activity and blocks transmission of influenza virus in a guinea pig model of infection.

[www.virology.ws](http://www.virology.ws)

Virology Live 2021 • Vincent Racaniello



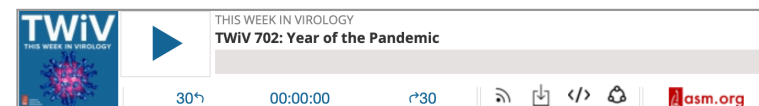
## TWiV 702: Year of the Pandemic

January 3, 2021

For this first episode of 2021, the complete TWiV team reviews compelling virology stories of 2020, and thanks the multitude of guests who have helped us to navigate the pandemic, and our many listeners who turn to us for scientific facts.



Hosts: [Vincent Racaniello](#), [Dickson Despommier](#), [Alan Dove](#), [Rich Condit](#), [Kathy Spindler](#), and [Brianne Barker](#)



[www.microbe.tv](http://www.microbe.tv)

# Virology Live

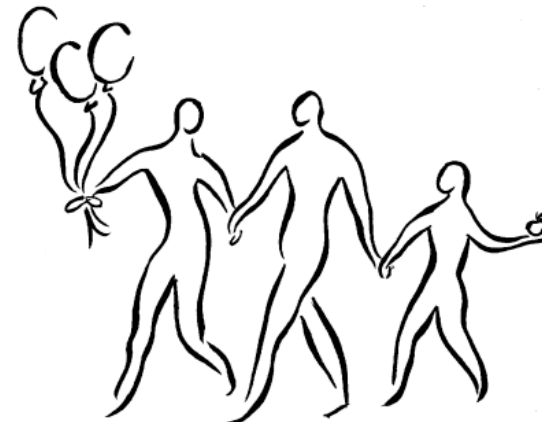
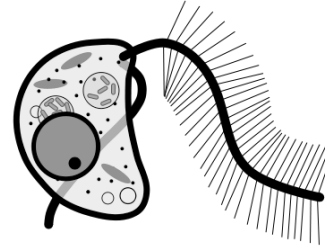
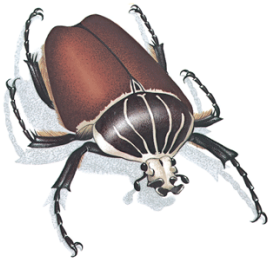
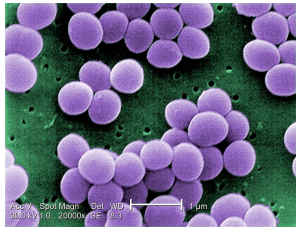
- Weekly quiz (website - up Thursdays for 1 week)
- 2 exams (Midterm, Final)

# Virology Live

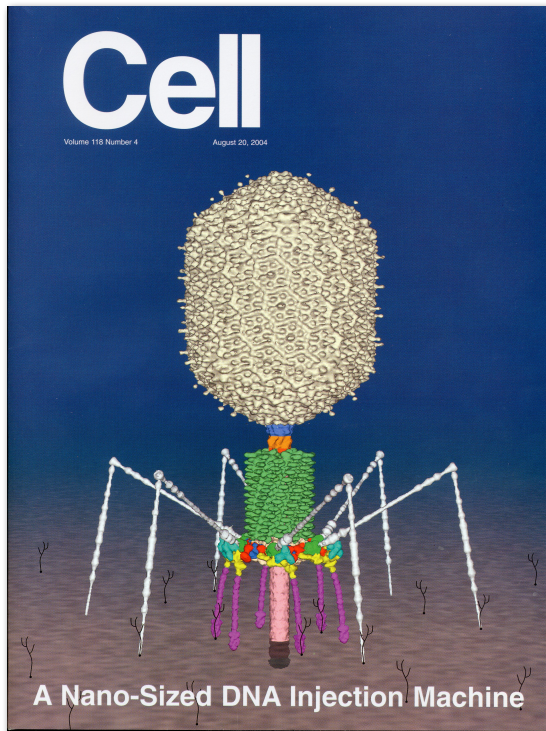
- Quizzes during sessions
- Ask questions relevant to the lecture during the live stream

# We live and prosper in a cloud of viruses

- Viruses infect all living things
- We regularly eat and breathe billions of virus particles
- We carry viral genomes as part of our own genetic material



# The number of viruses on Earth is staggering



More than  $10^{30}$  bacteriophage particles in the world's waters!



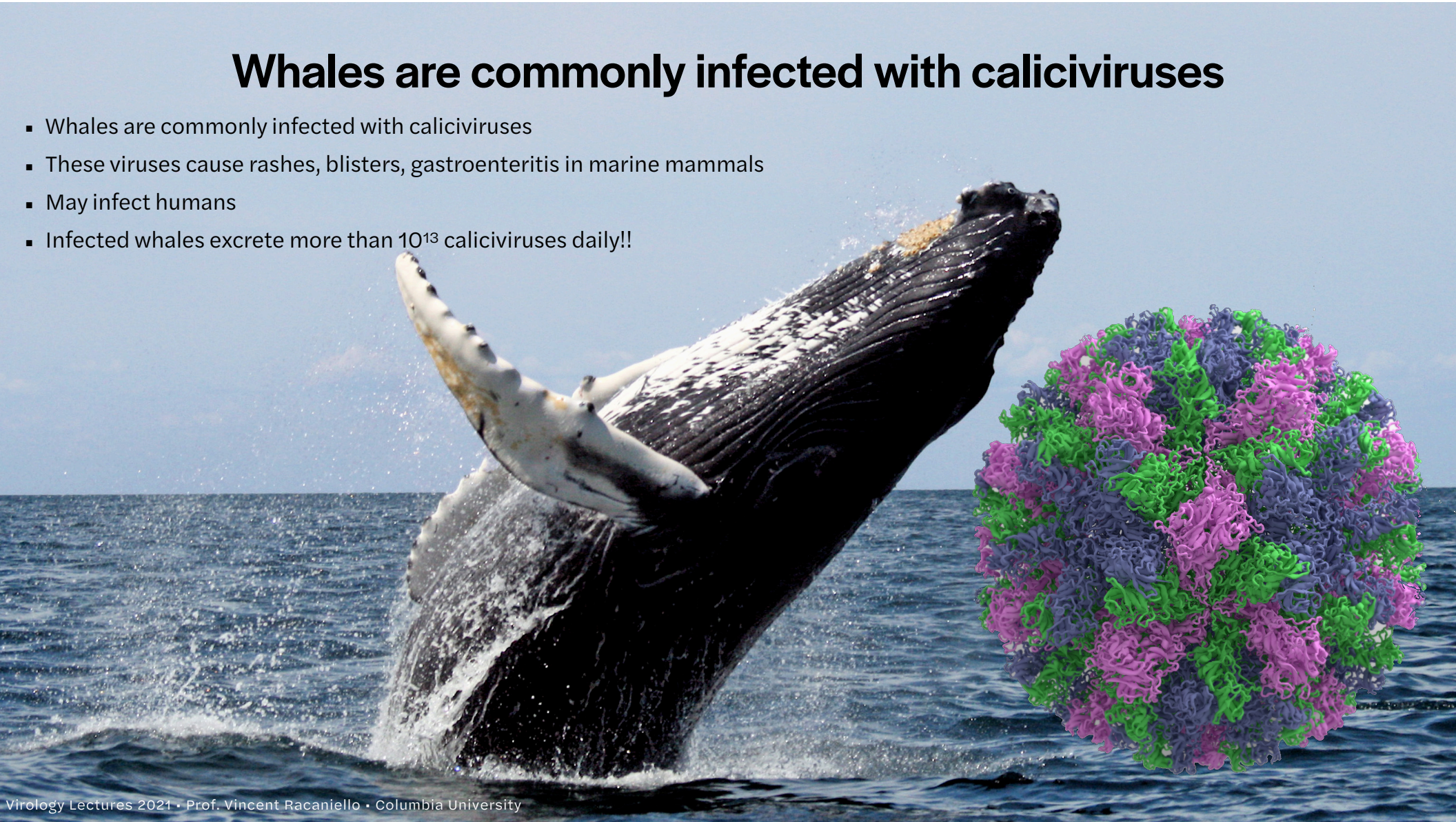
- A bacteriophage particle weighs about a femtogram ( $10^{-15}$  grams)

*$10^{30} \times 10^{-15}$  = the biomass on the planet of BACTERIAL VIRUSES ALONE exceeds the biomass of elephants by more than 1000-fold!*

- The length of a head to tail line of  $10^{30}$  phages is 100 million light years!

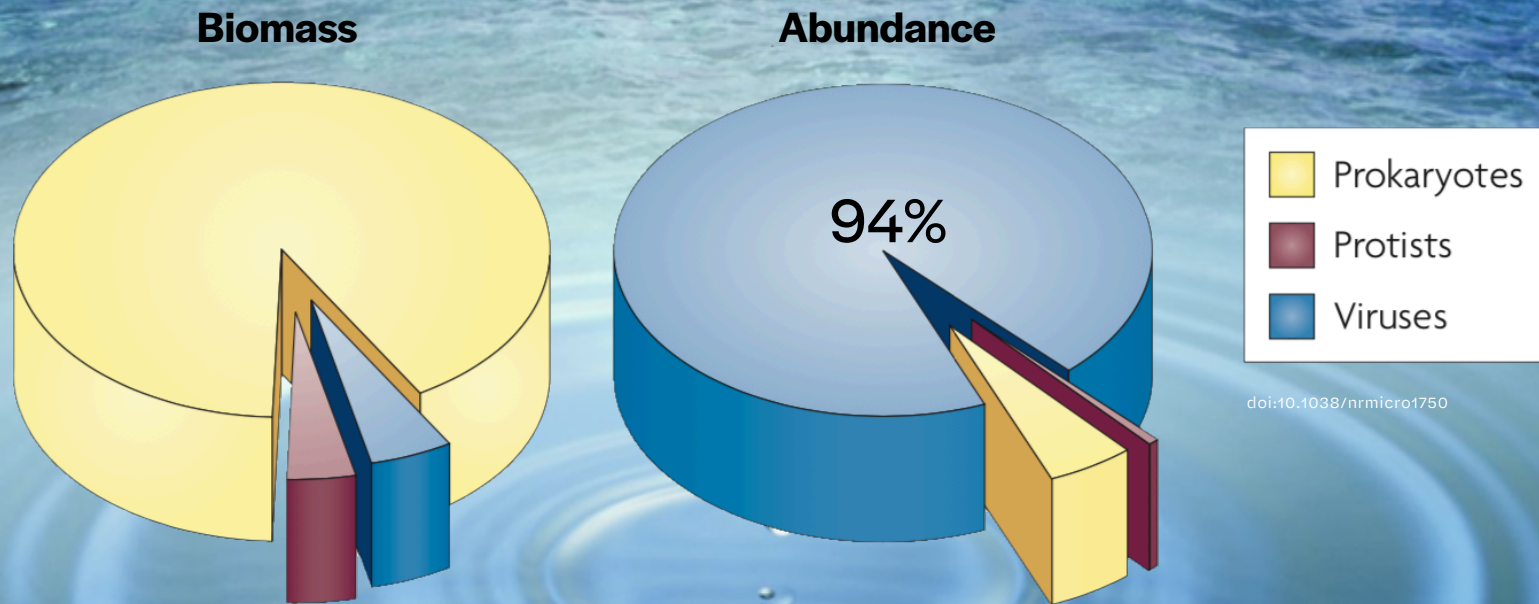
# Whales are commonly infected with caliciviruses

- Whales are commonly infected with caliciviruses
- These viruses cause rashes, blisters, gastroenteritis in marine mammals
- May infect humans
- Infected whales excrete more than  $10^{13}$  caliciviruses daily!!



# Viruses are not just purveyors of bad news

*More viruses in a liter of coastal seawater than people on Earth*



doi:10.1038/nrmicro1750

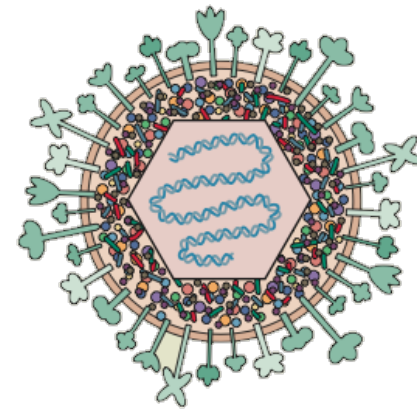
*Viruses are catalysts for biogeochemical cycling*

**There are  $\sim 10^{16}$  HIV genomes on the planet today**

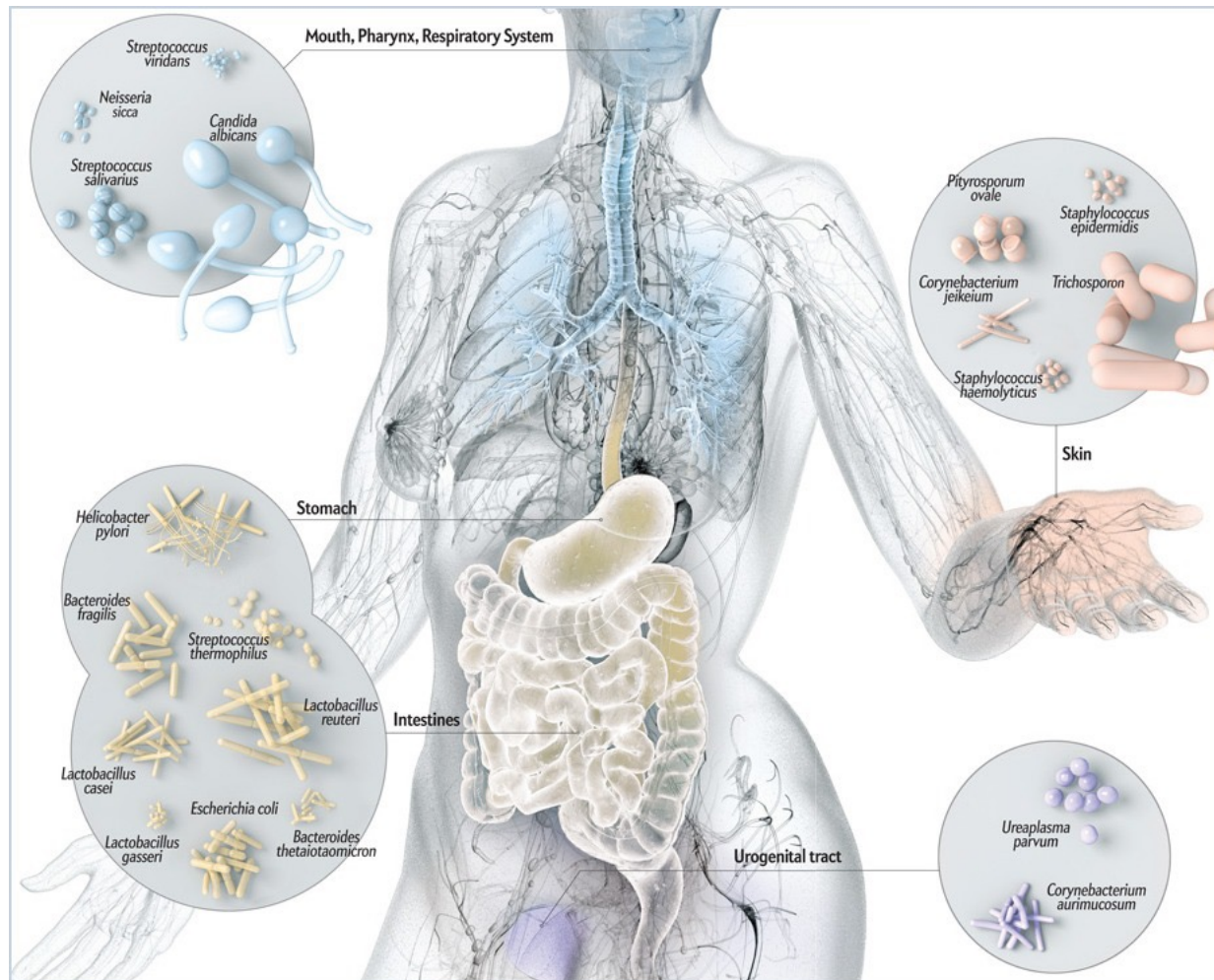


## How 'infected' are we?

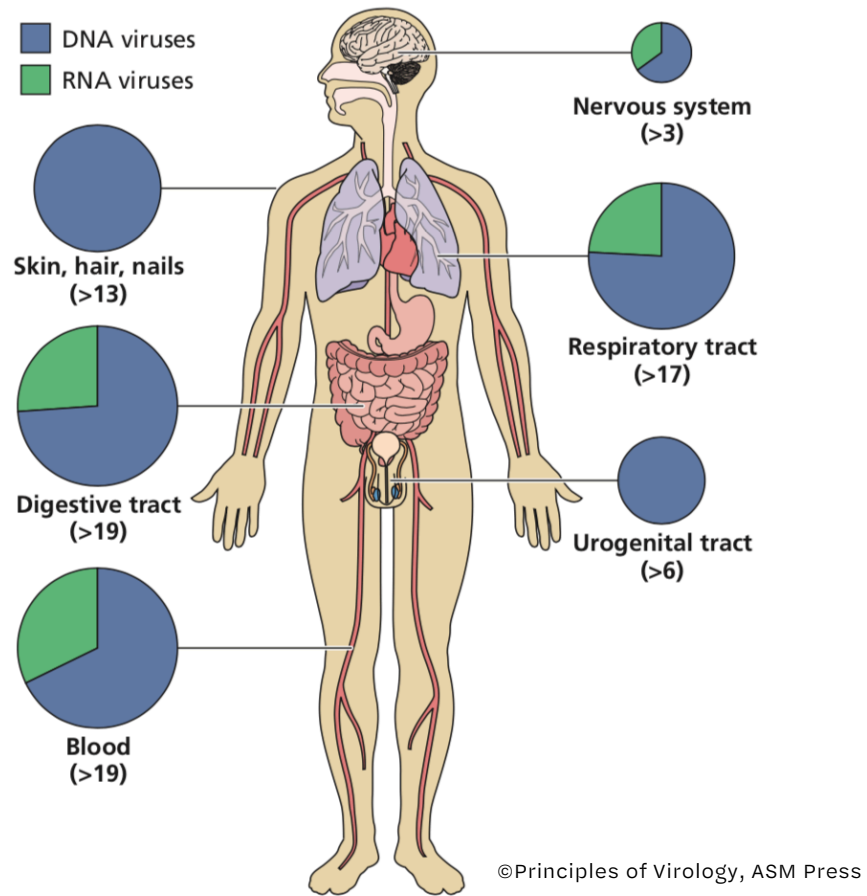
- HSV-1, HSV-2, VZV, HCMV  
EBV, HHV-6, HHV-7, HHV-8
- Once infected, it is for life



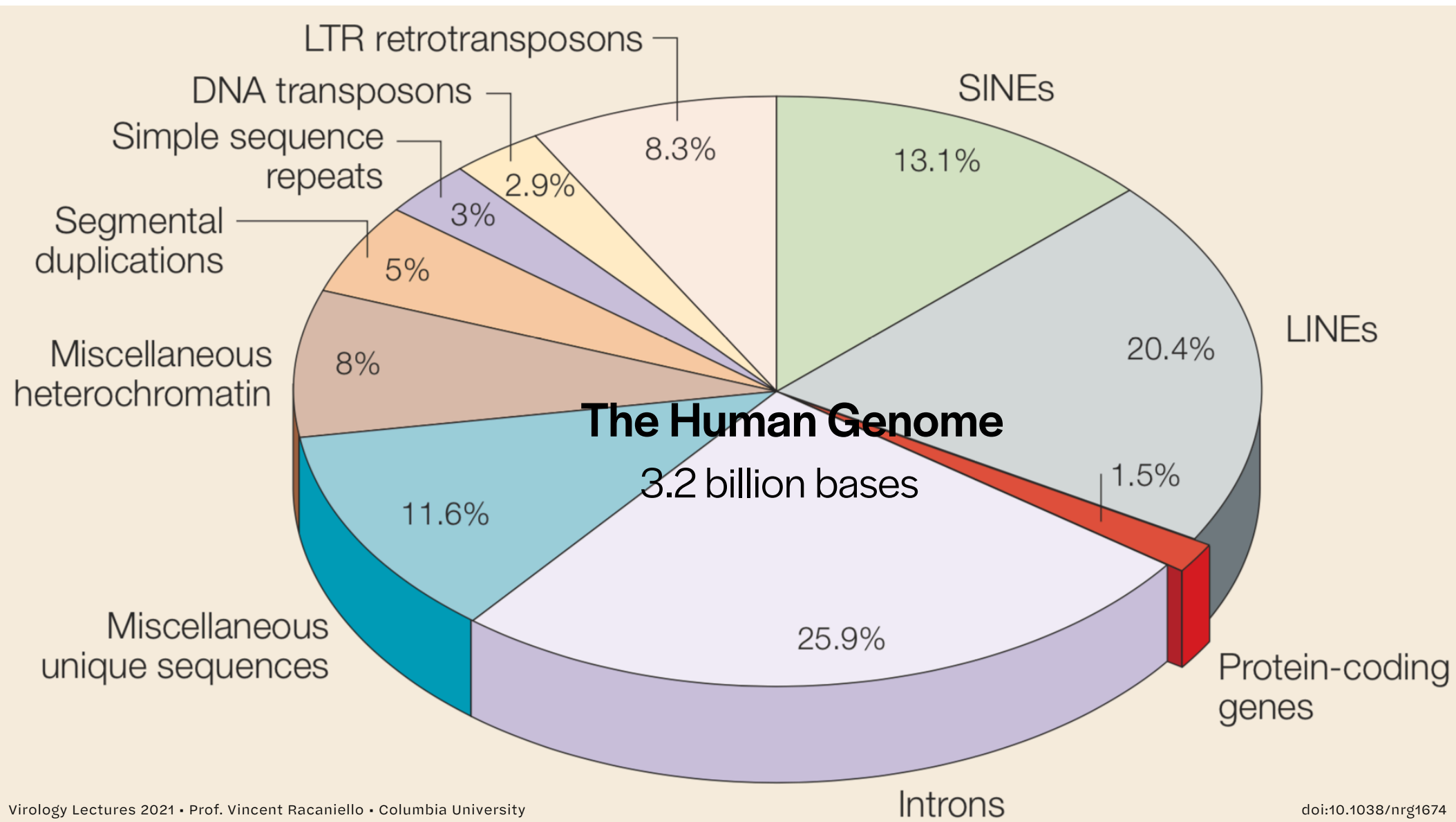
# Microbiome



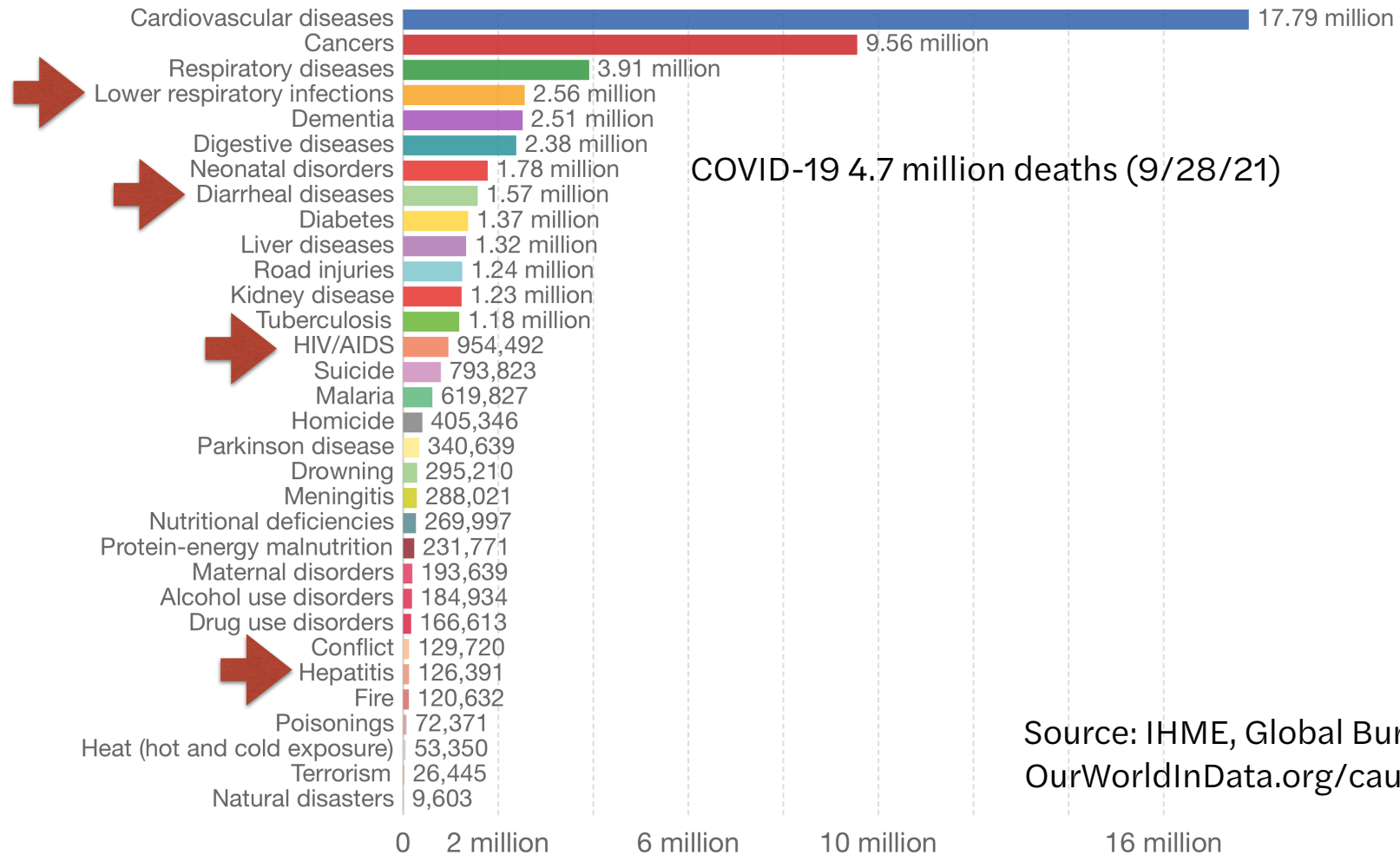
# Virome



DOI: 10.3390/v10060300



# Causes of 2017 global deaths



Source: IHME, Global Burden of Disease  
OurWorldInData.org/causes-of-death

Last Updated at (M/D/YYYY)  
9/28/2021, 9:21 PM

Total Cases  
**232,702,991**

Total Deaths  
**4,763,415**

Total Vaccine Doses Administered  
**6,147,373,041**

**Cases | Deaths by**  
Country/Region/Sovereignty

**US**  
28-Day: **3,965,198** | 50,617  
Totals: **43,221,483** | 692,511

**United Kingdom**  
28-Day: **948,752** | 3,761  
Totals: **7,772,615** | 136,736

**India**  
28-Day: **928,701** | 8,813  
Totals: **33,697,581** | 447,373

**Turkey**  
28-Day: **700,250** | 6,914  
Totals: **7,066,658** | 63,372

**Brazil**  
28-Day: **614,114** | 15,079  
Totals: **21,381,790** | 595,446

**Iran**  
28-Day: **587,246** | 12,498  
Totals: **5,559,691** | 119,888

**Russia**  
28-Day: **531,520** | 21,782  
Totals: **7,355,883** | 201,854

**Philippines**  
28-Day: **514,656** | 4,075  
Totals: **3,500,157** | 127,507

28-Day Cases  
**15,128,916**

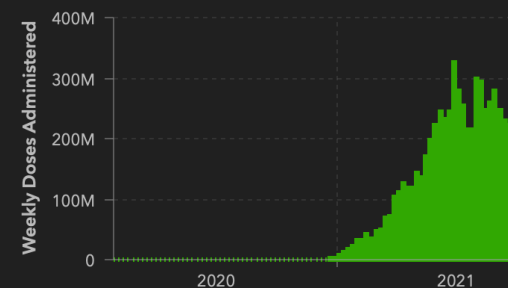
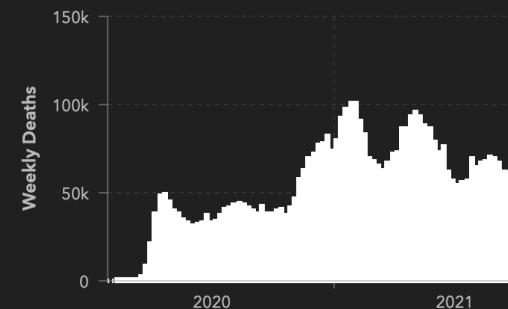
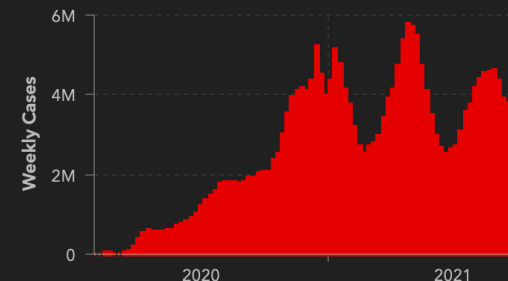
28-Day Deaths  
**245,088**

28-Day Vaccine Doses Administered  
**837,293,947**



Esri, FAO, NOAA

Powered by Esri



Admin0

28-Day

Totals

Incidence

Case-Fatality Ratio

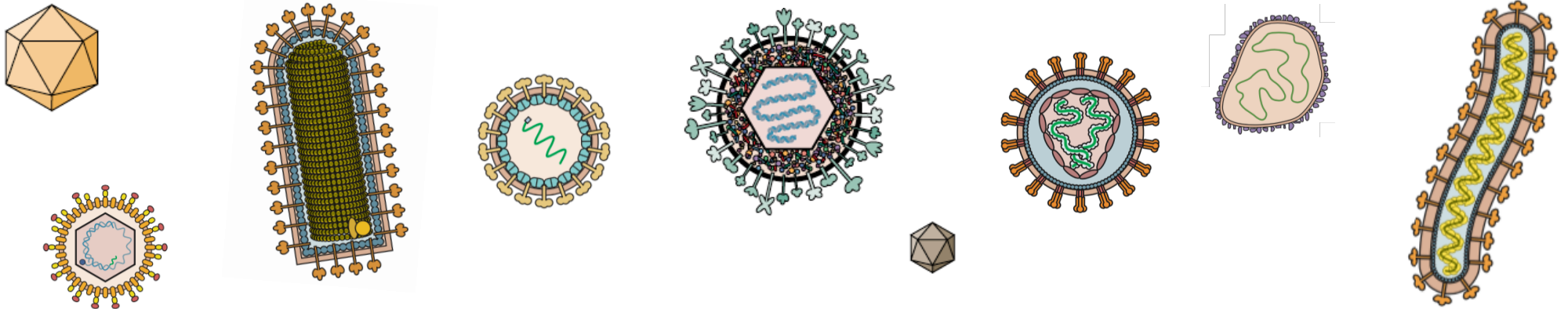
Global Vaccinations

US Vaccinations

Terms of Use

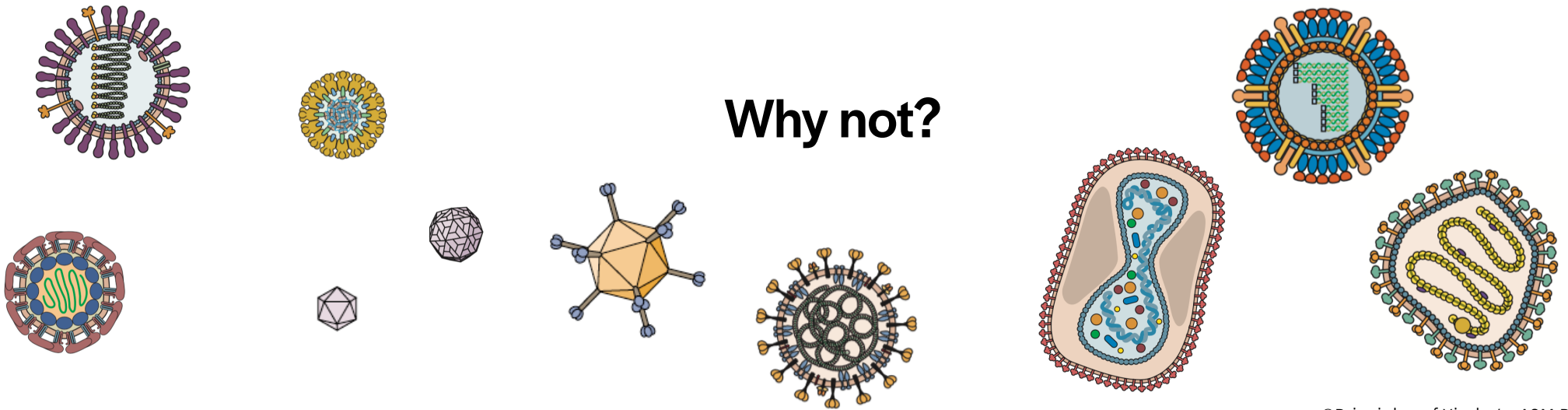
Weekly

Daily



**Amazingly, the vast majority of the viruses that infect us have little or no impact on our health or well being**

**Why not?**

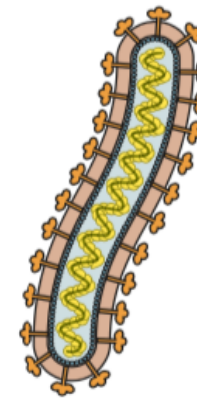


# Most viruses just pass through us

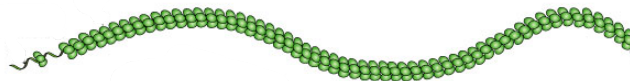
*We ingest many non-animal viruses regularly with foods*



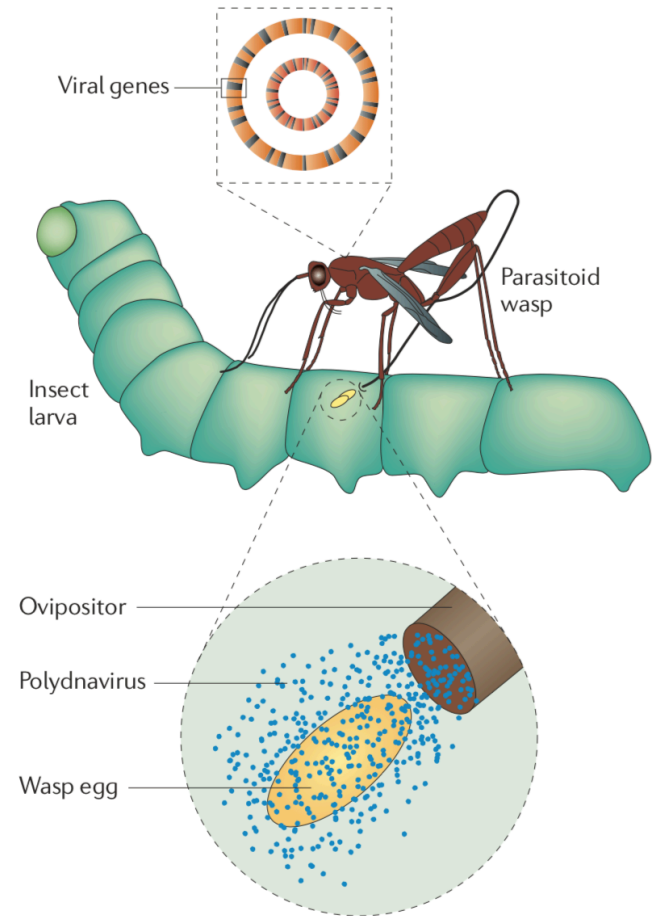
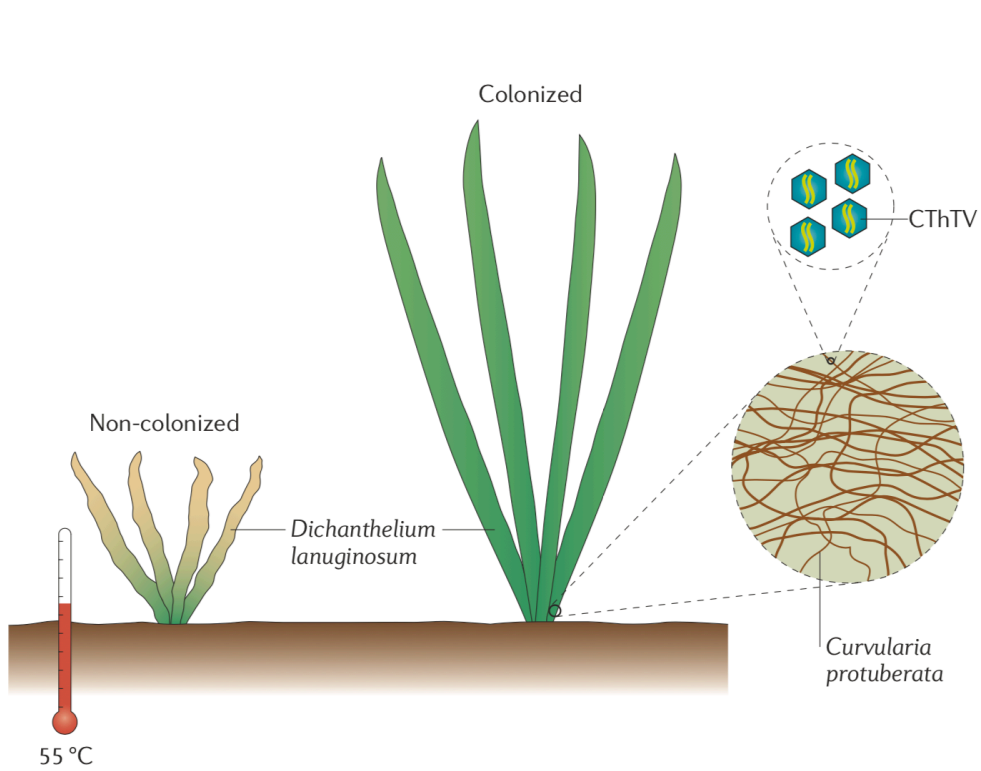
- Cabbage from 5 different supermarkets in Washington D.C.
- Each serving (~100 cm<sup>2</sup> of leaf material) would contain up to 10<sup>8</sup> particles of a virus pathogenic for the cabbage looper



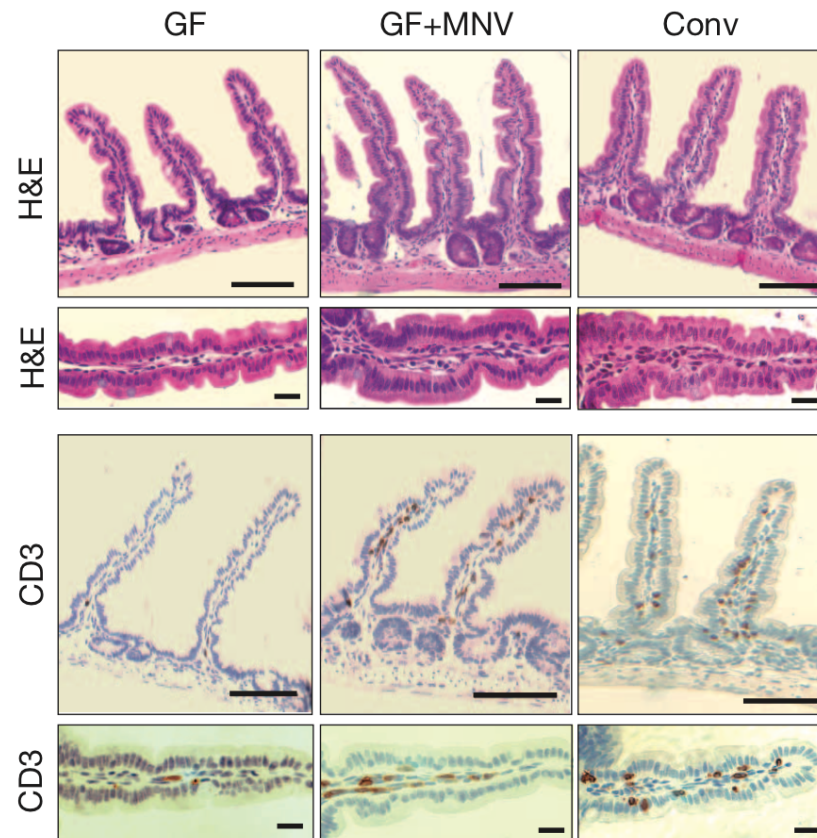
- Most RNA virus sequences (91%) in human feces are similar to plant viruses
- Most abundant human fecal virus: pepper mild mottle virus, 10<sup>9</sup> virus particles per gram of dry feces

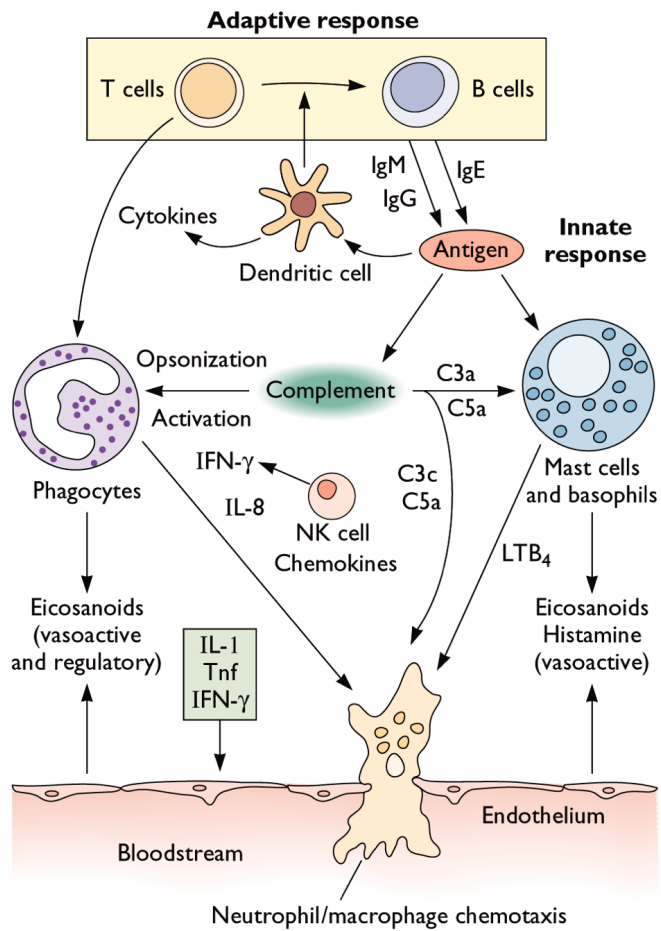


# Beneficial viruses



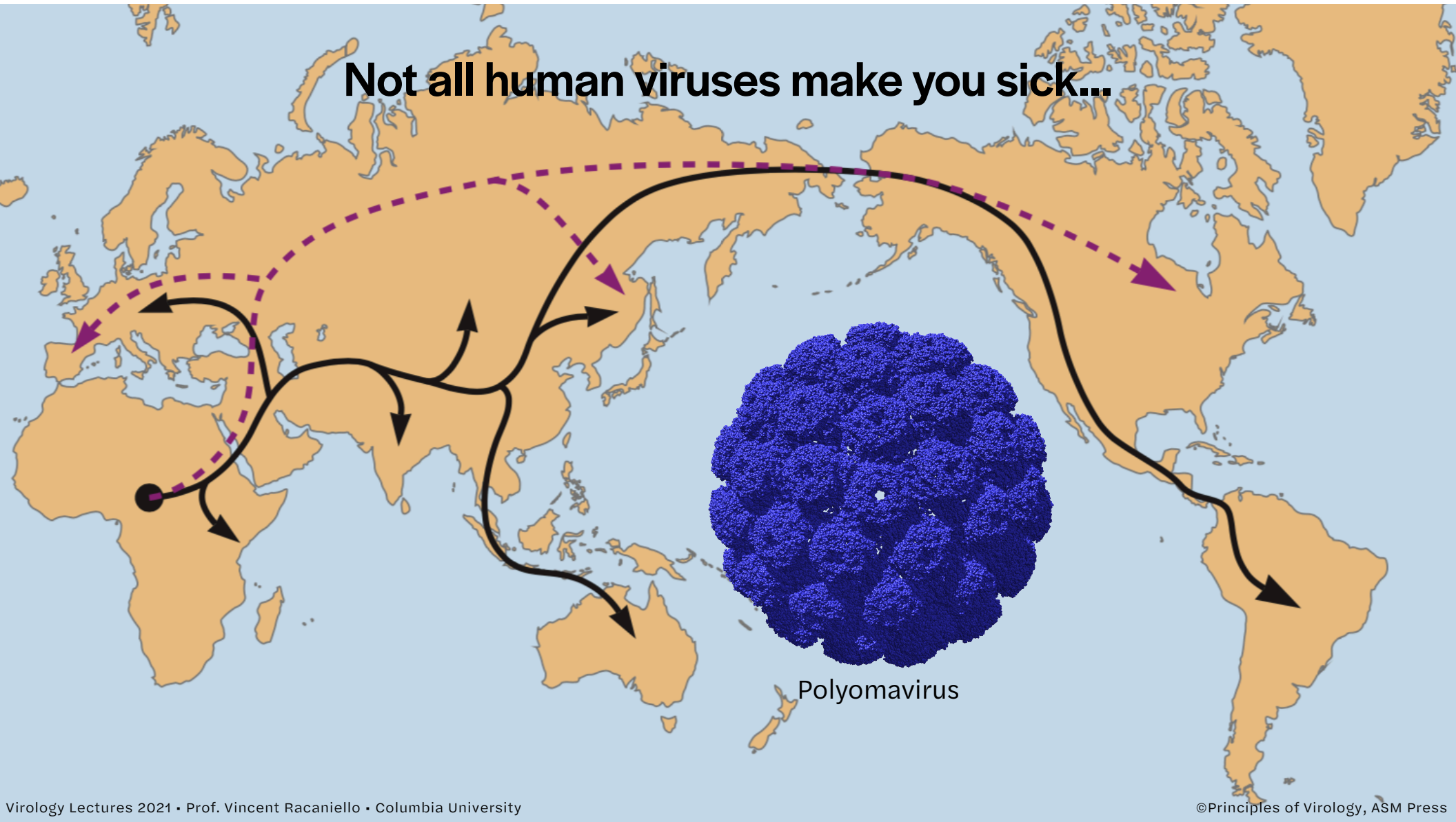
# An enteric virus can replace the beneficial function of commensal bacteria





**We have an amazing immune system**

**Not all human viruses make you sick...**

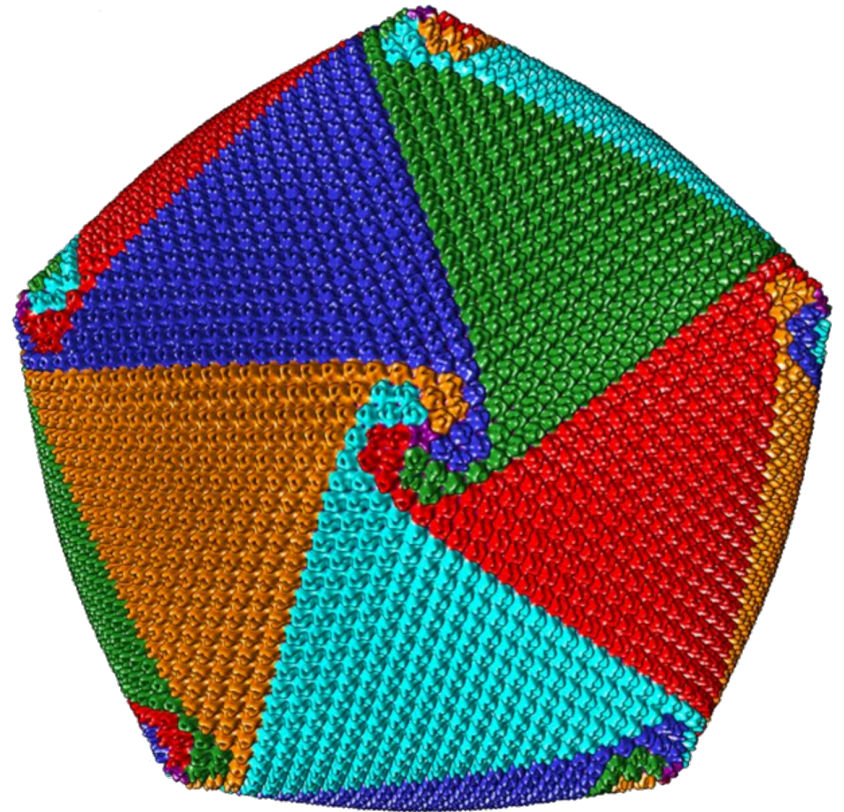
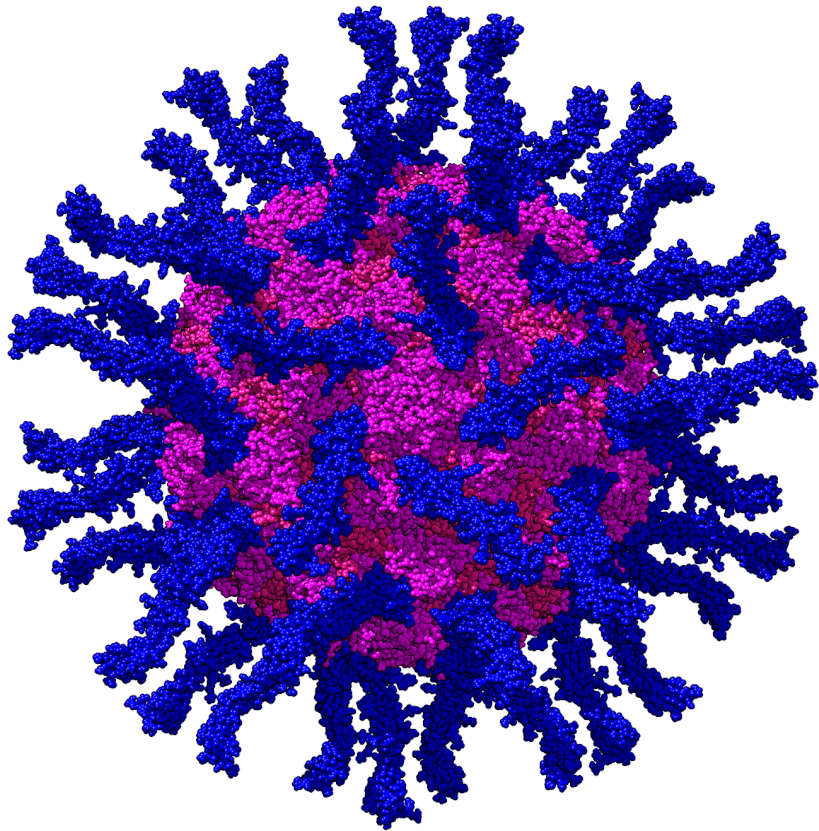


# Viruses shape host populations and vice-versa

*Some ocean viruses infect eukaryotic phytoplankton and can collapse large blooms*



**Viruses are amazing**



*Virology is an integrative science*

## Course goals

- This course is designed to help you see the ‘big picture’ of virology
- I’ll show you how to think about virology as an integrative discipline, not an isolated collection of viruses, diseases, or genes
- You will learn the fundamentals about these molecular wizards that amaze the informed and frighten the uninformed

# ‘Don’t go to Wuhan, don’t leave Wuhan’: Coronavirus could mutate and spread further, China officials warn

Some 440 cases confirmed so far as disease reported in Thailand, Japan, South Korea and United States

## China warns virus could mutate and spread as death toll rises

Updated / Wednesday, 22 Jan 2020 11:45



*“Evidence has shown that the disease has been transmitted through the respiratory tract and there is the possibility of viral mutation”* — National Health Commission Vice Minister Li Bin

Opinion

## The Coronavirus Is Mutating, and America’s Leaders Are Flying Blind

Travel restrictions might make sense, but what this country really needs is better disease surveillance.

**By The Editorial Board**

The editorial board is a group of opinion journalists whose views are informed by expertise, research, debate and certain longstanding values. It is separate from the newsroom.

Dec. 22, 2020

# **I will use Socrative to deliver quizzes during lectures**

**Go to:**

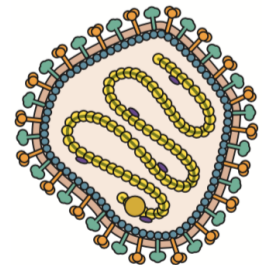
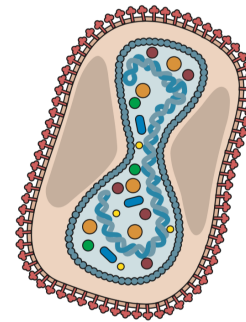
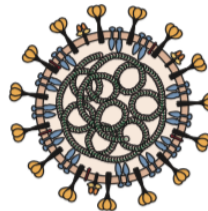
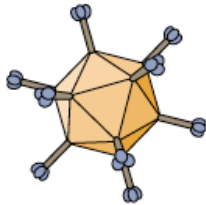
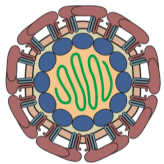
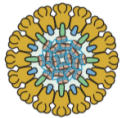
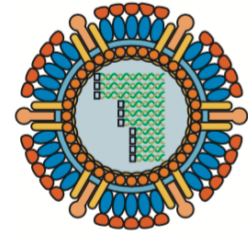
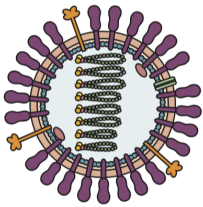
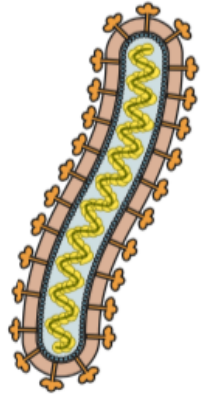
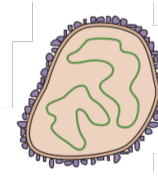
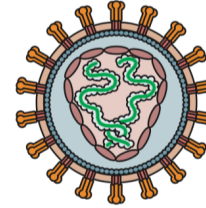
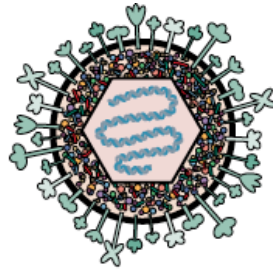
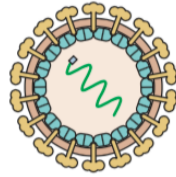
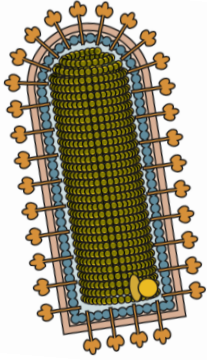
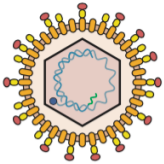
**b.socrative.com/login/student/  
room number: virus**

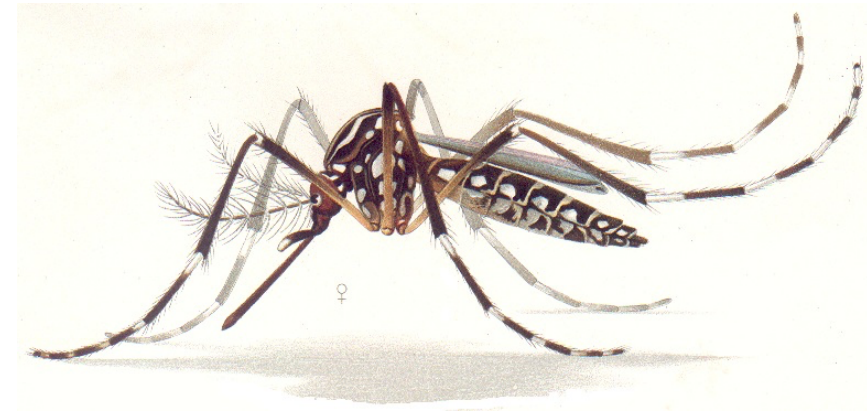
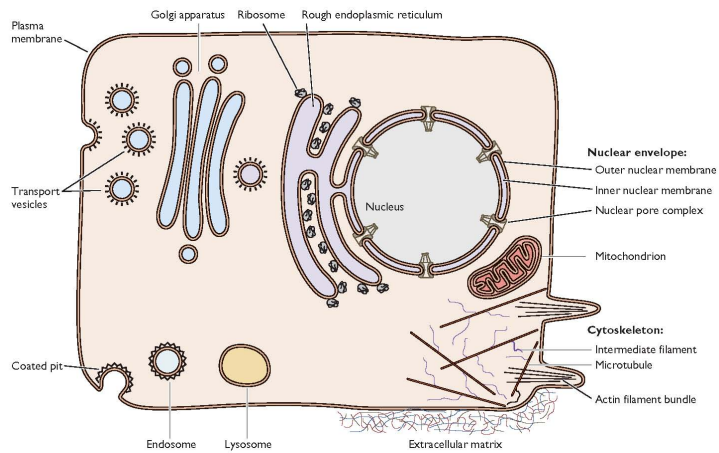
Which statement is true?

1. All viruses make us sick and can be lethal
2. Our immune system can manage most viral infections
3. Humans are usually infected with one virus at a time
4. The press is usually correct in their virology reporting
5. Our immune system cannot handle most viral infections

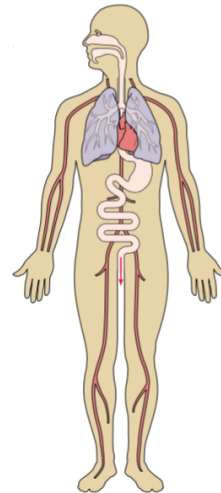
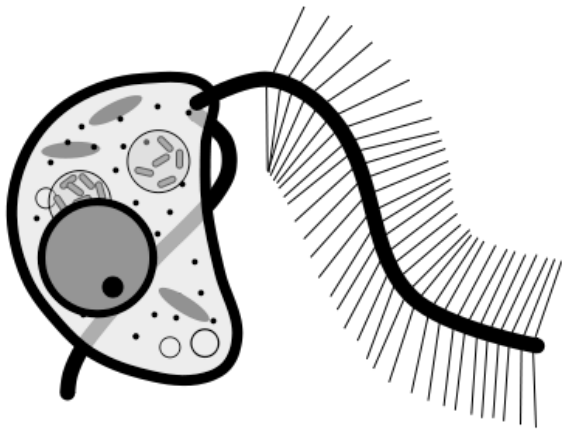
# What is a virus?

*An infectious, obligate intracellular parasite comprising genetic material (DNA or RNA), often surrounded by a protein coat, sometimes a membrane*





*As viruses are obligate molecular parasites, every solution must reveal something about the host as well as the virus*



# Are viruses alive?

Yes - ( 2045 votes )



No - ( 2258 votes )



They are something in between - ( 2112 votes )



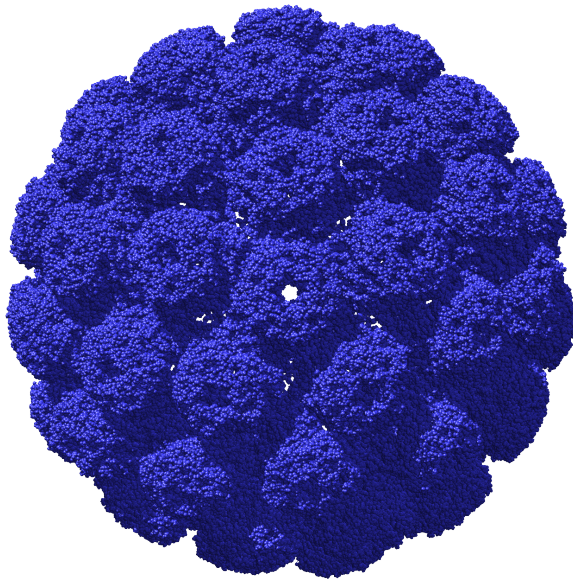
I don't know - ( 307 votes )



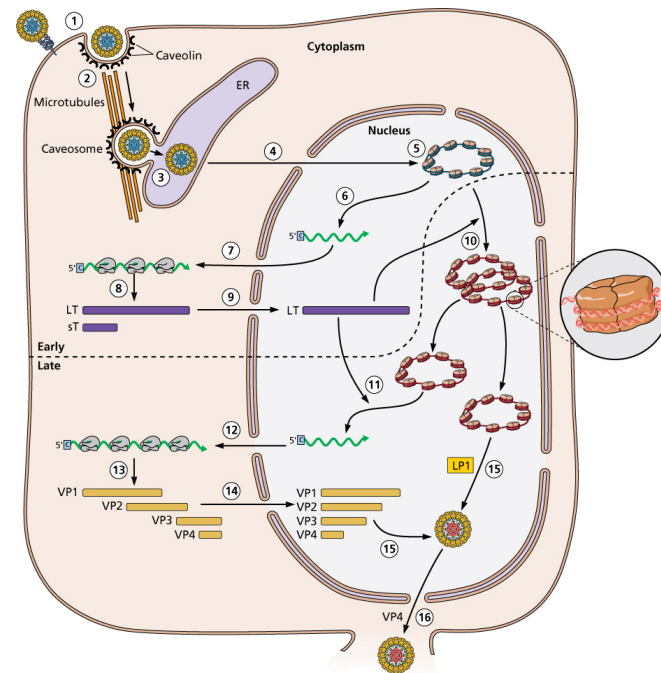
Total Answers 6827

Total Votes 6826

# A virus is an organism with two phases

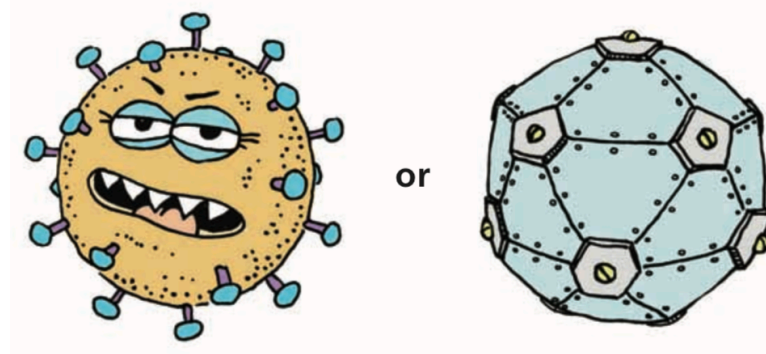


virion (infectious particle)



infected cell

## Be careful: Avoid anthropomorphic analyses



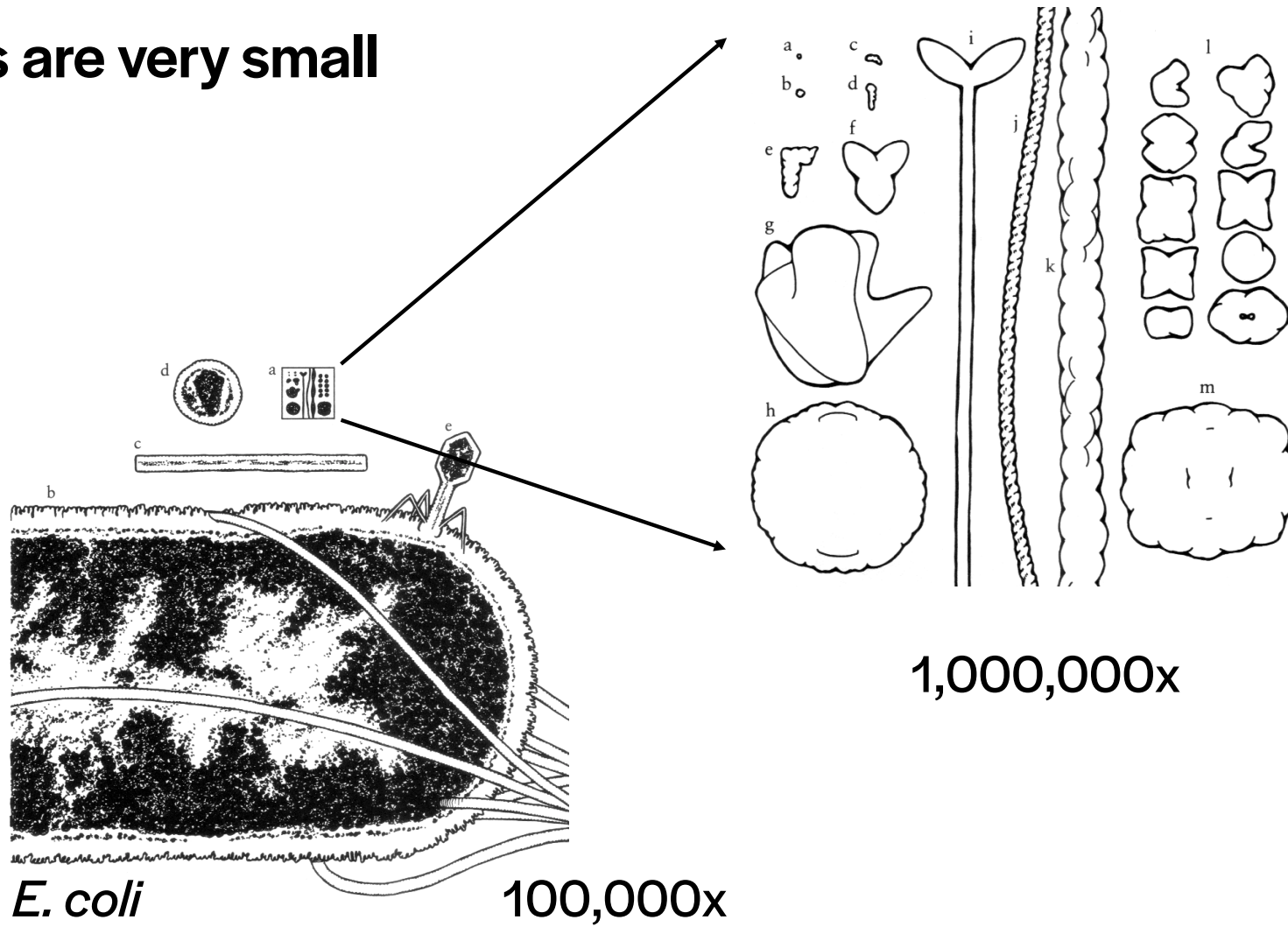
Viruses do NOT think!

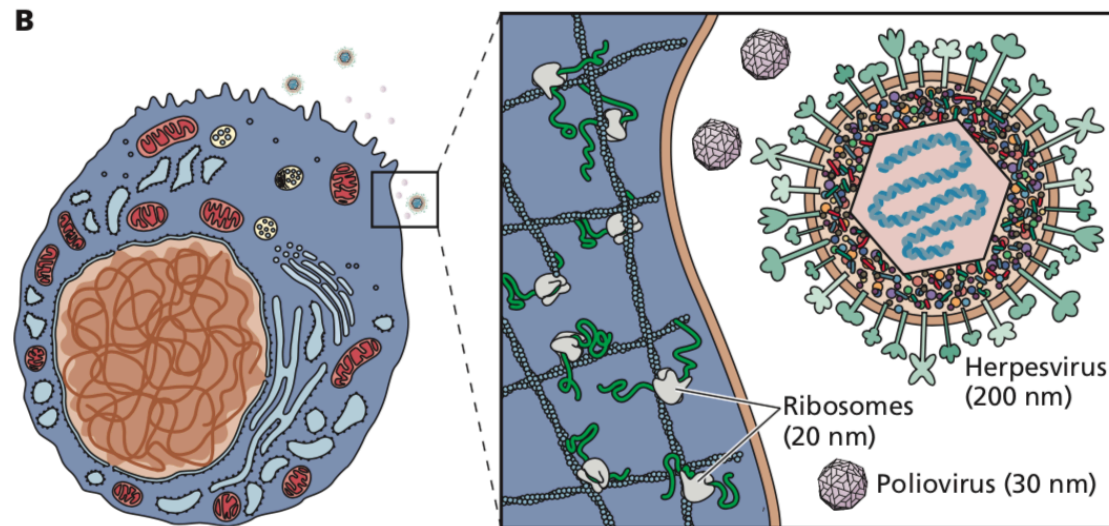
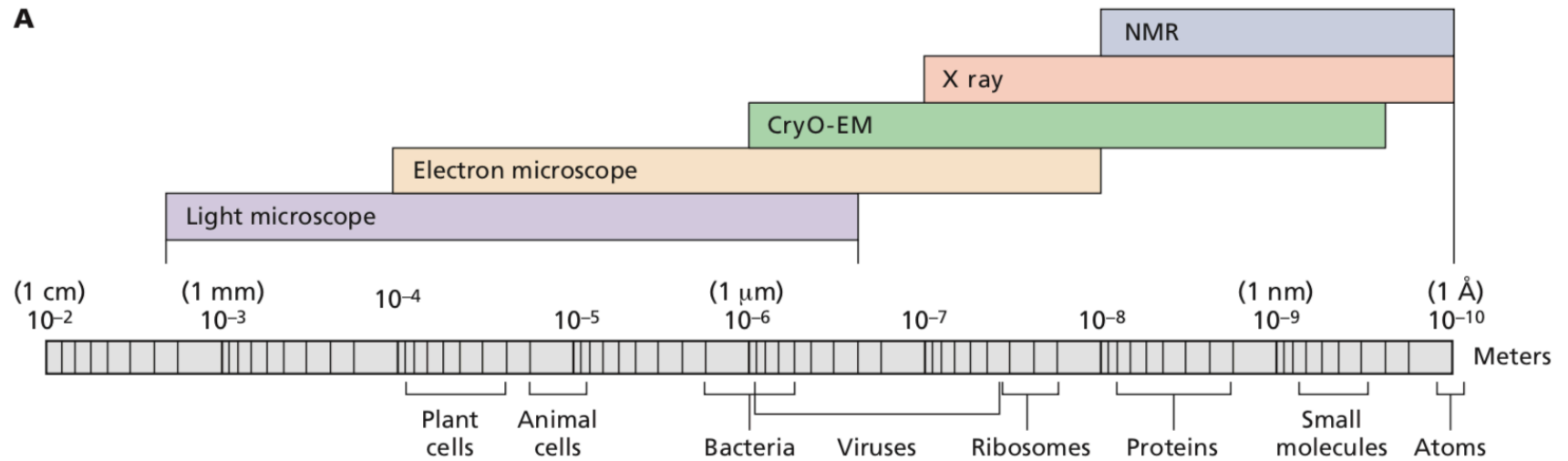
(or employ, ensure, exhibit, display, etc...)

They do not achieve their goals in a human-centered manner

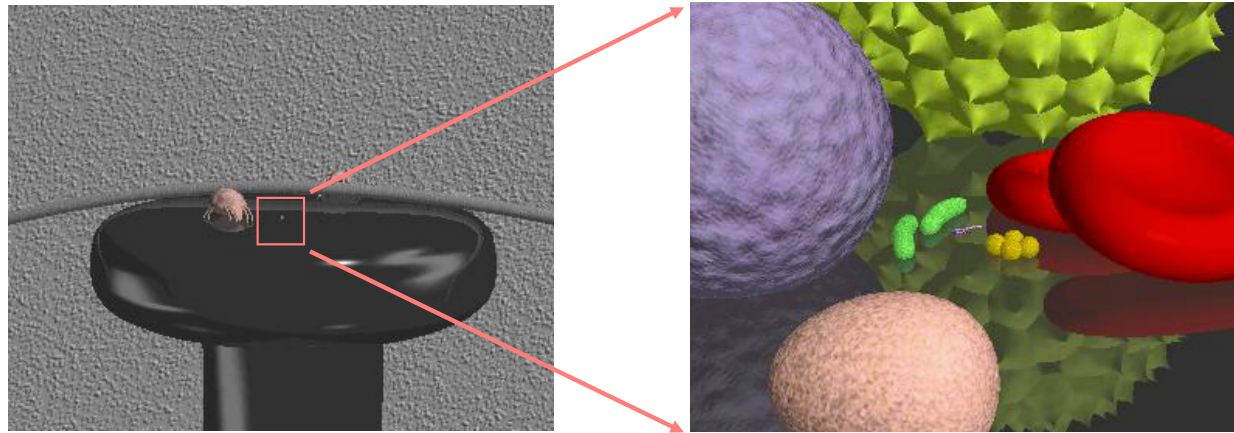
Viruses are passive agents!

# Viruses are very small





# How many viruses can fit on the head of a pin?

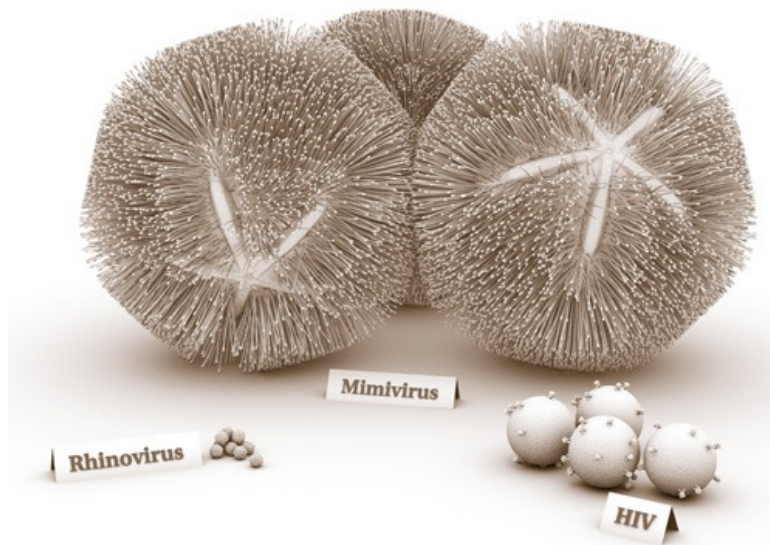


2 mm = 2000 microns

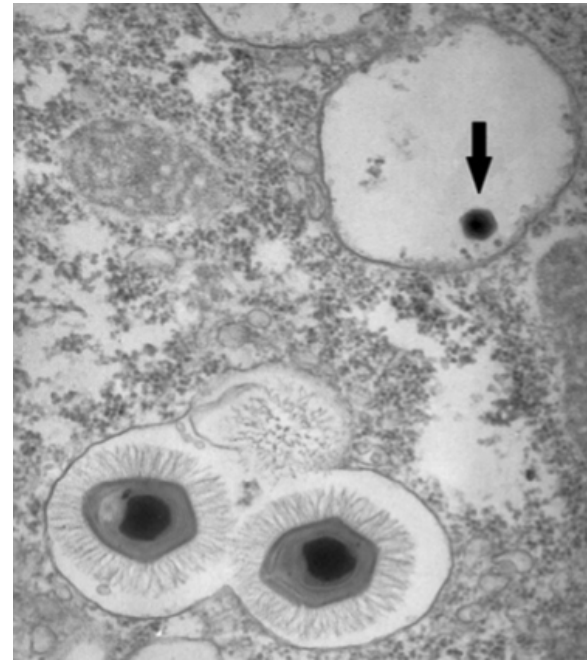
- 500 million rhinoviruses
- When you sneeze, you fire an aerosol that contains enough viruses to infect thousands

# Not as small as we once thought!

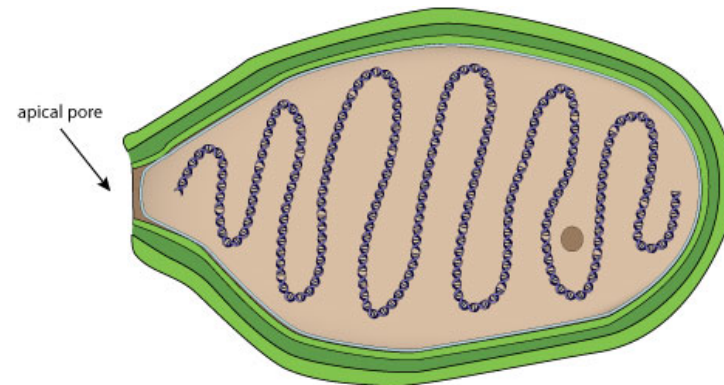
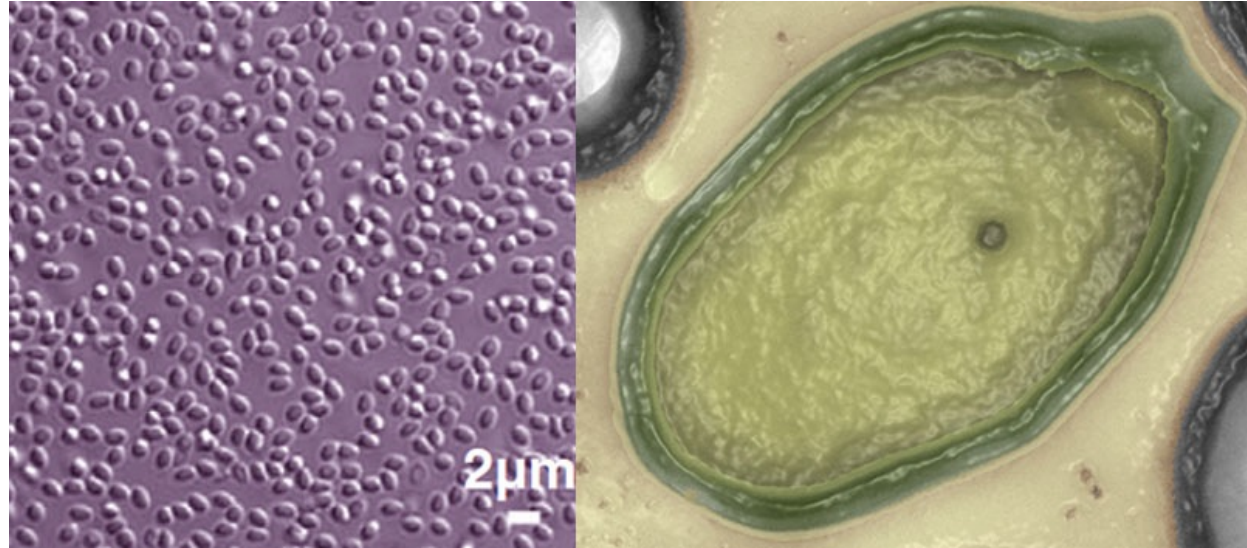
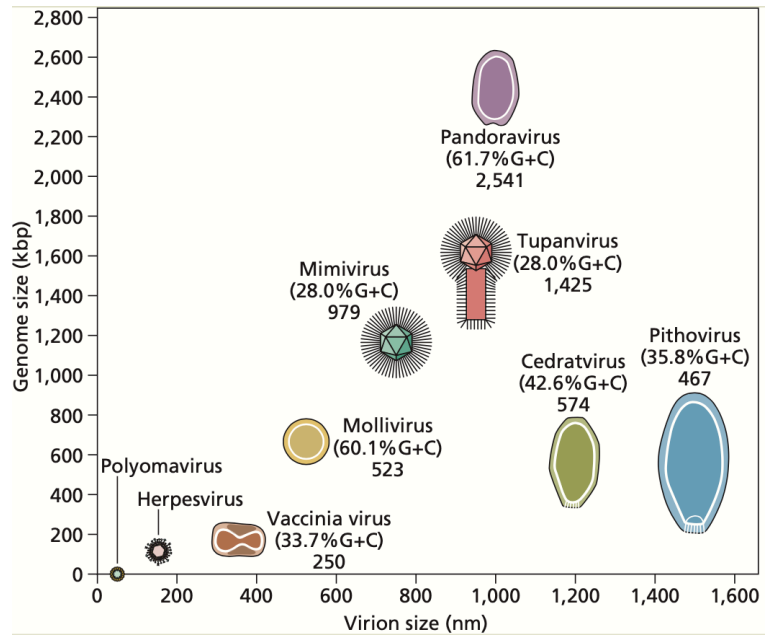
AMERICAN  
**Scientist**  
July–August 2011 [www.americanscientist.org](http://www.americanscientist.org)



**SIGMA XI**  
THE SCIENTIFIC RESEARCH SOCIETY



# *Pandoravirus*



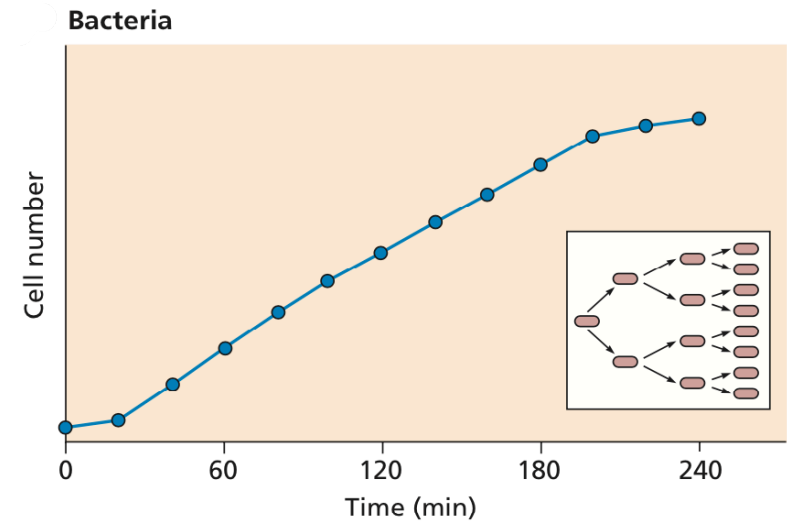
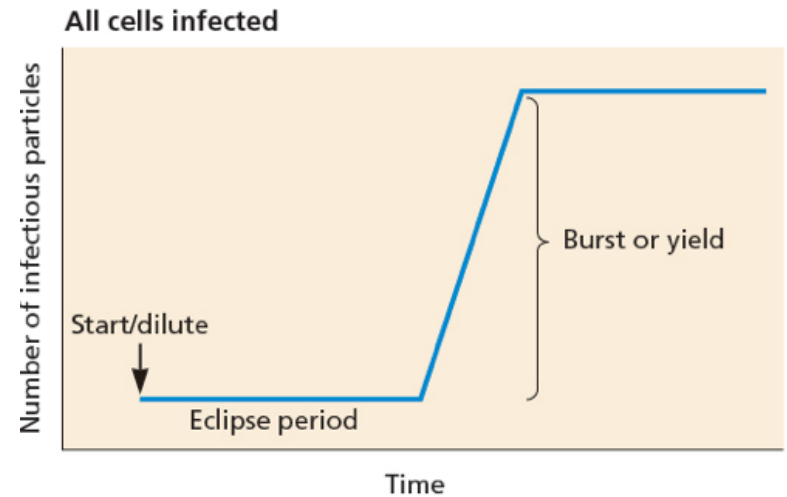
© ViralZone 2014  
SIB Swiss Institute of Bioinformatics

DOI: 10.1126/science.1239181

# Viruses replicate by assembly of pre-formed components into many particles

Make the parts,  
assemble the final product

*Not binary fission like cells*



**Go to:**

**[b.socrative.com/login/student](https://b.socrative.com/login/student)  
room number: virus**

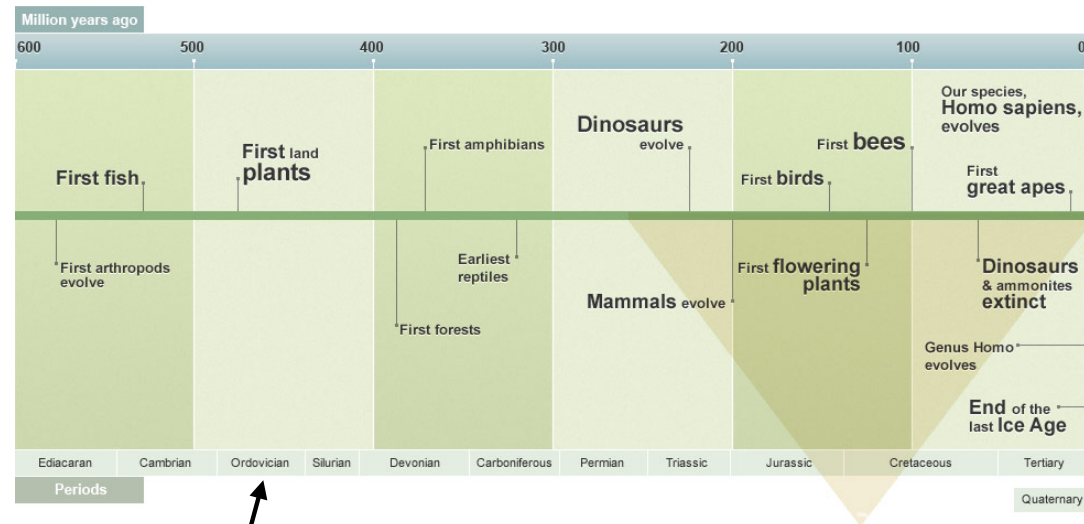
Which of the following is true concerning bacterial vs. viral replication?

1. Viruses must assemble using pre-formed components
2. Bacteria do not replicate via binary fission as viruses do
3. Bacteria must assemble using pre-formed components
4. Viruses do not have an "eclipse" period
5. Viruses replicate by binary fission

# How old are viruses?

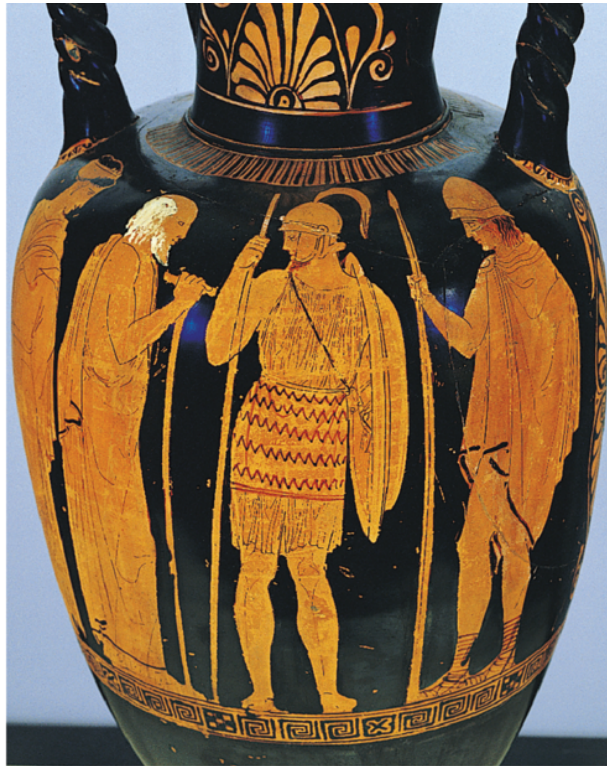


Nobu Tamura (<http://spinops.blogspot.com>)



- Estimates of molecular evolution suggest marine origin of some retroviruses >450 Ma, Ordovician period
- Likely originated billions of years ago - before cells?

## Ancient references to viral diseases



*Here this firebrand, rabid Hector, leads the charge.*

Homer, *The Iliad*,  
translated by Robert Fagels  
(Viking Penguin)

**700 B.C.**



**1580-1350 B.C.**

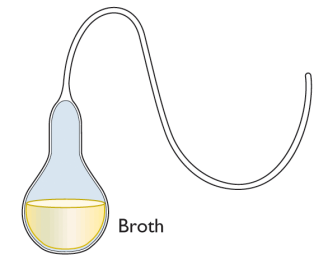
# Vaccination to prevent viral disease

- Variolation - China (11th century), Lady Montagu (1700s)
- No knowledge of agent
- Survivors of smallpox protected against disease
- 1790s - experiments by Edward Jenner in England establish vaccination



# Concept of microorganisms

- Leeuwenhoek (1632 - 1723)
- Pasteur (1822 - 1895)
- Koch (1843-1910)



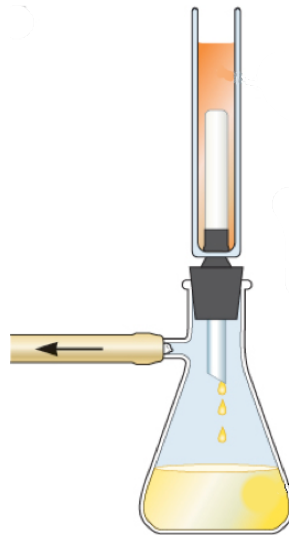
# The evolving concept of virus

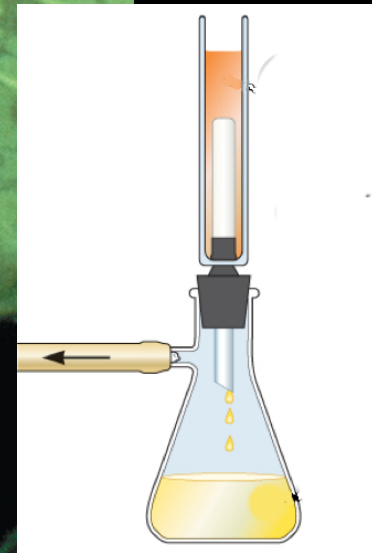
- As early as 1728, 'virus' was used to describe an agent that causes infectious disease
- Virus = Latin, poison; so thought to be liquids
- Pasteur (1822 - 1895): “Every virus is a microbe”



## Key event: Chamberland filter

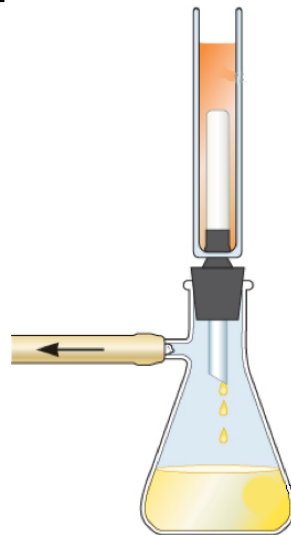
- Developed a porcelain filter to remove bacteria from drinking water
- Pasteur found that rabies agent passed through it, thought it was a small bacterium





## Virus discovery - filterable viruses

- 1892 - Ivanovsky
- 1898 - Beijerinck: *contagium vivum fluidum*
- Agent of tobacco mosaic disease passed through filters that retain bacteria



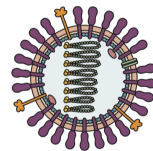
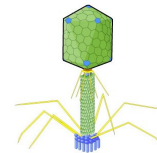
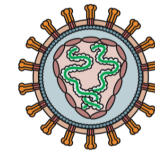
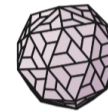
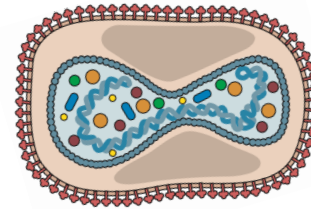
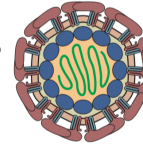
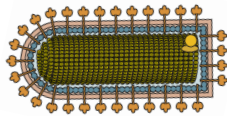
## Filterable viruses

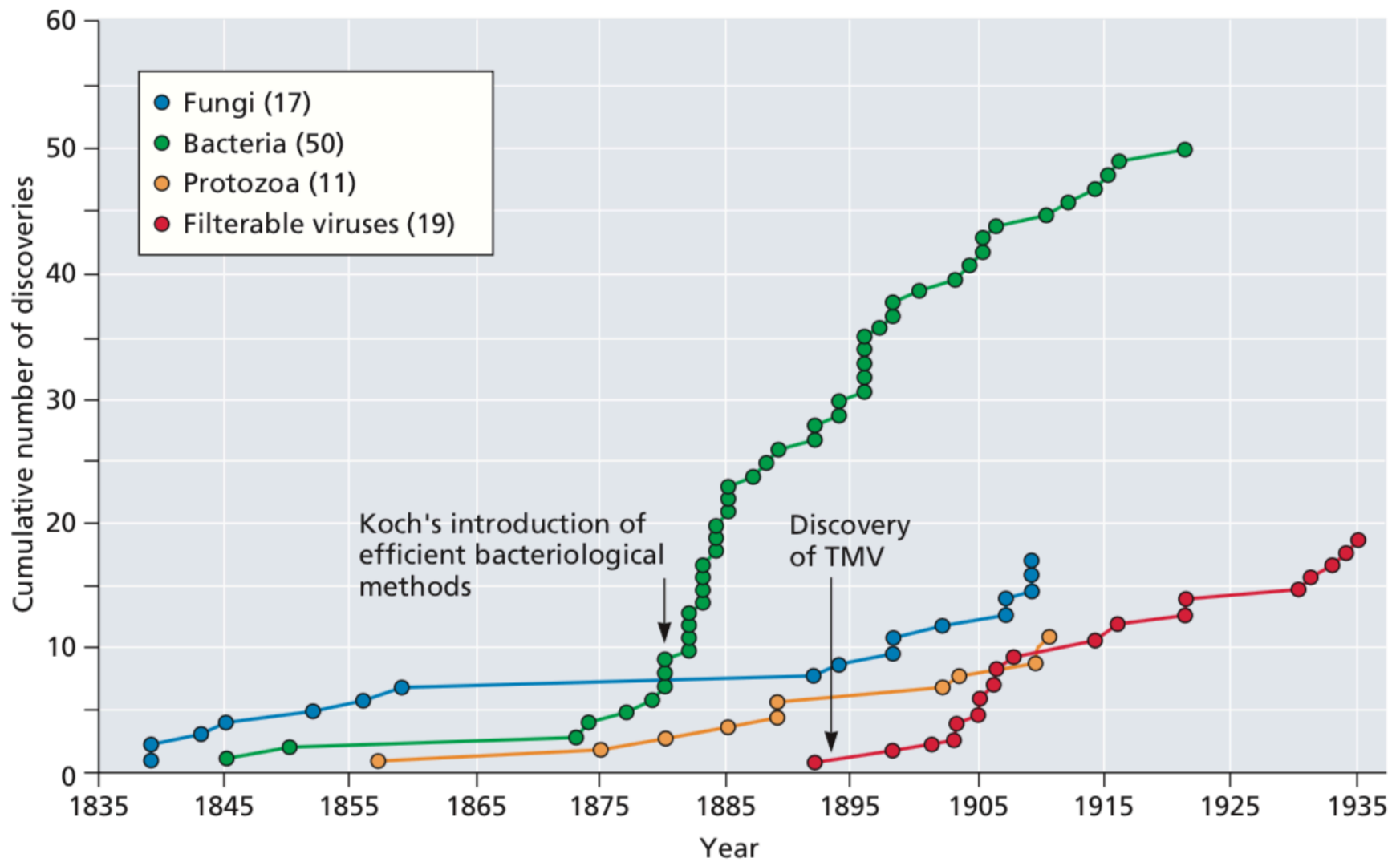
- 1898 - Loeffler & Frosch - agent of foot & mouth disease is filterable
- Key concept: agents not only small, but replicate only in the host, not in broth
- 0.2 micron filters ( $\mu\text{m}$ , one millionth of a meter)
- Still thought to be *liquids*



## Filterable virus discovery

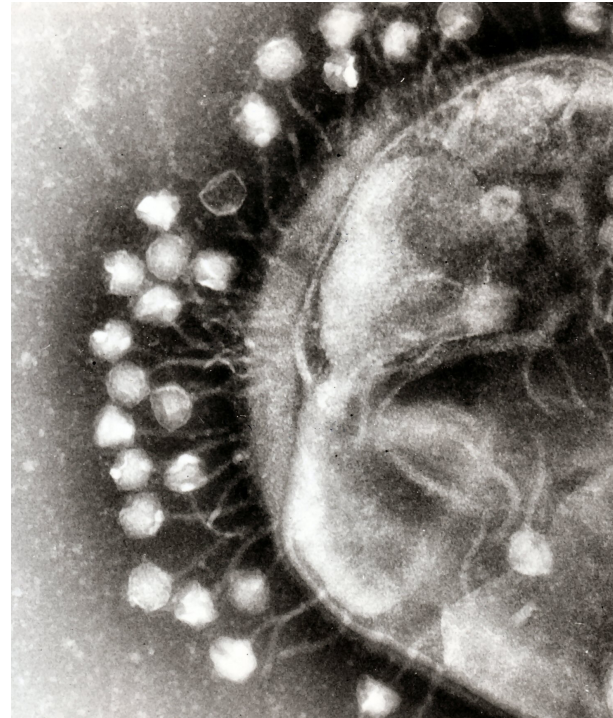
- 1901 - first human virus, yellow fever virus
- 1903 - rabies virus
- 1906 - variola virus
- 1908 - chicken leukemia virus, poliovirus
- 1911 - Rous sarcoma virus
- 1915 - bacteriophages
- 1933 - influenza virus





## 1939 - Viruses are not liquids!

- Helmut Ruska built first electron microscope 1933
- First EM of bacteriophage, 1939



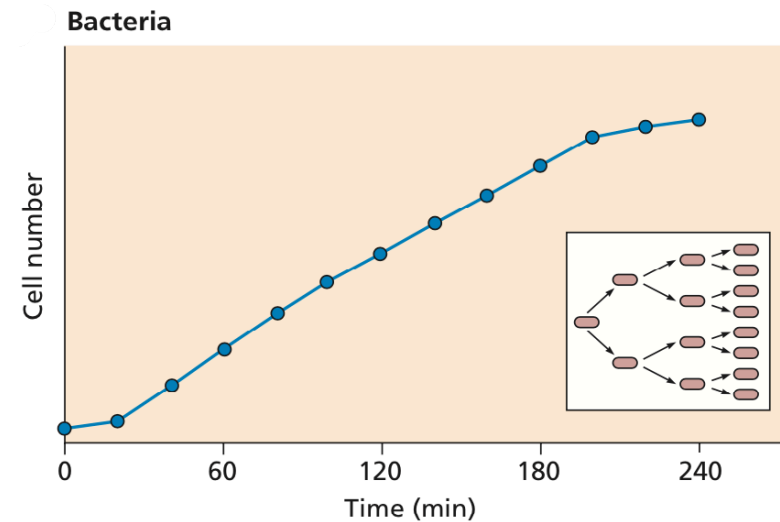
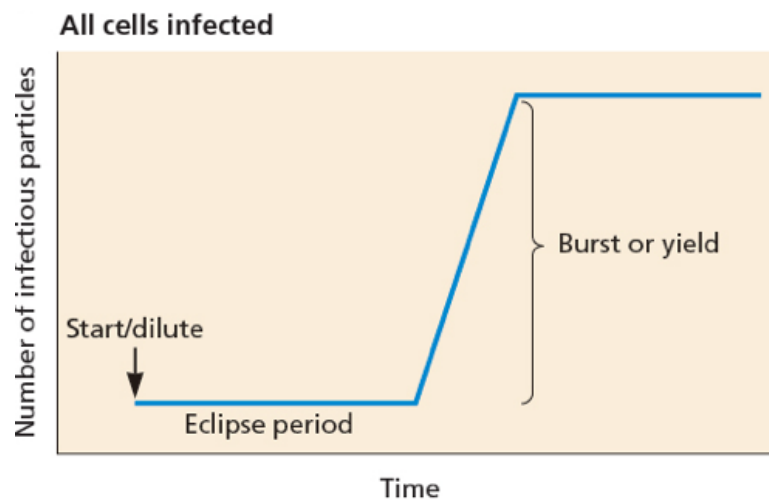
**Go to:**

**[b.socrative.com/login/student](https://b.socrative.com/login/student)  
room number: virus**

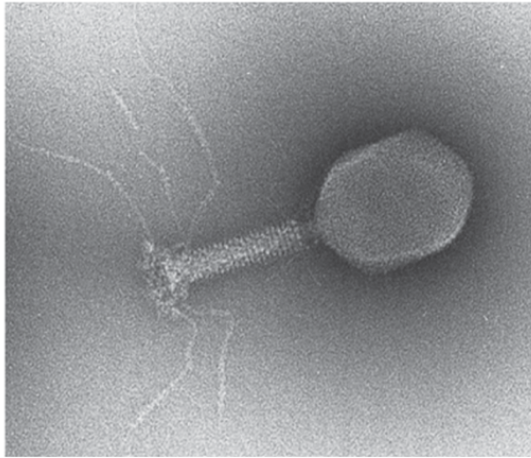
Which is a key concept first discovered about viruses that distinguished them from other microorganisms?

1. They were too large to pass through a 0.2 micron filter
2. They could replicate only in broth
3. They made tobacco plants sick
4. They were small enough to pass through a 0.2 micron filter
5. None of the above

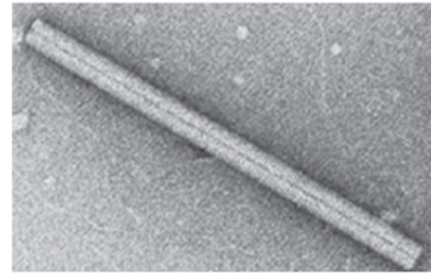
# Key 1939 experiment proved that viruses were not simply small bacteria



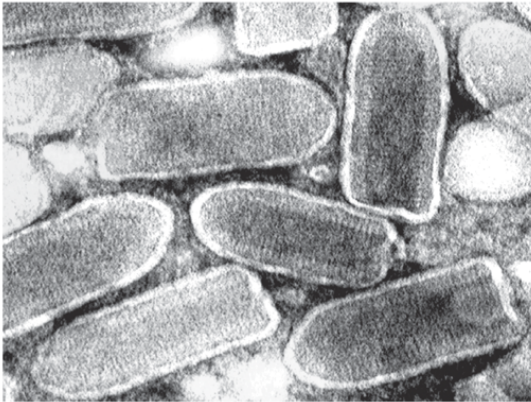
**A**



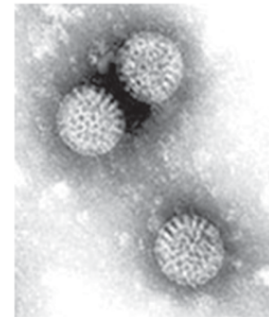
**B**



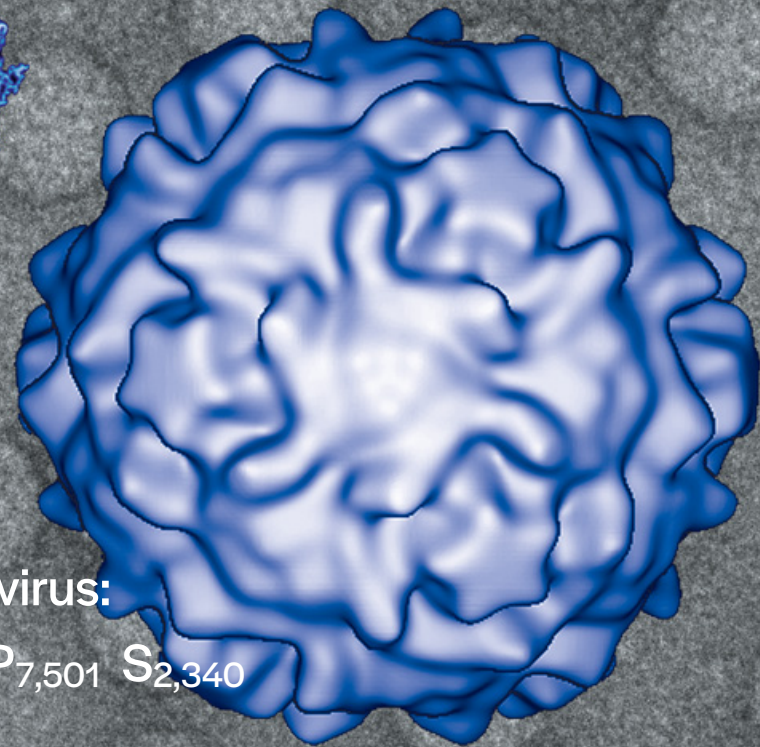
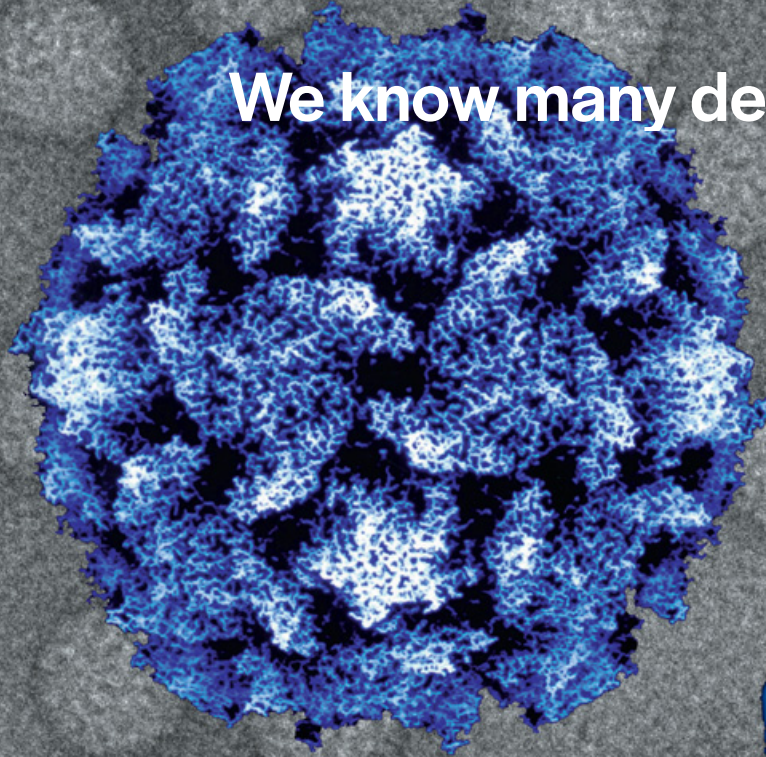
**C**



**D**



We know many details about viruses

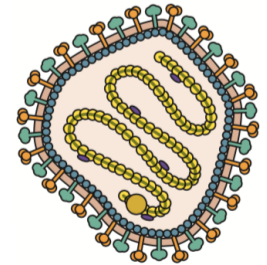
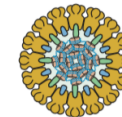
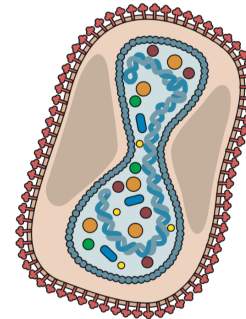
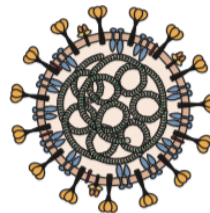
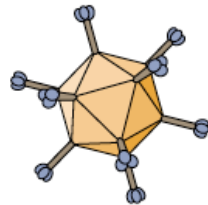
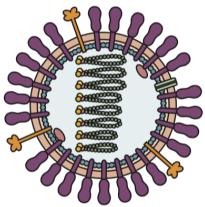
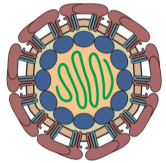
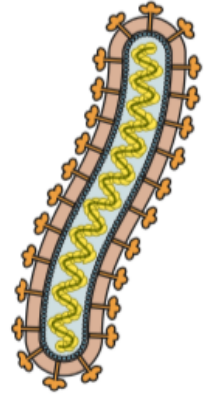
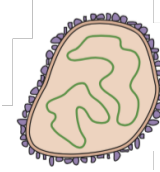
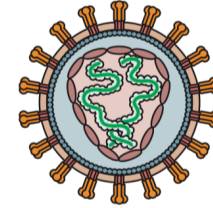
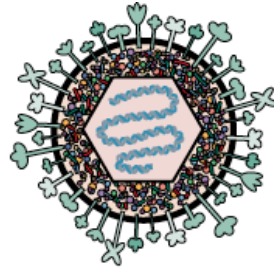
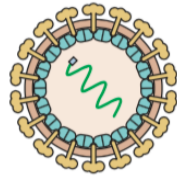
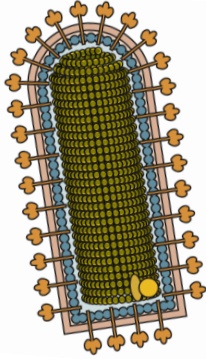
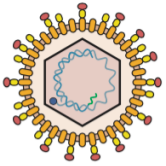


Chemical formula for poliovirus:

$C_{332,652} H_{492,388} N_{98,245} O_{131,196} P_{7,501} S_{2,340}$

# Virus classification

- Nature and sequence of nucleic acid in virus particle
- Symmetry of protein shell (capsid)
- Presence or absence of lipid membrane (envelope)
- Dimensions of virus particle



# Virus classification

<http://ictvonline.org/>

Classical hierarchical system:

Kingdom

Phylum

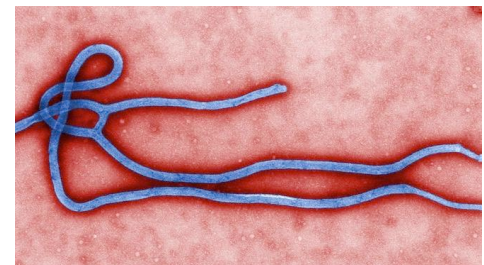
Class

Order (-*virales*)

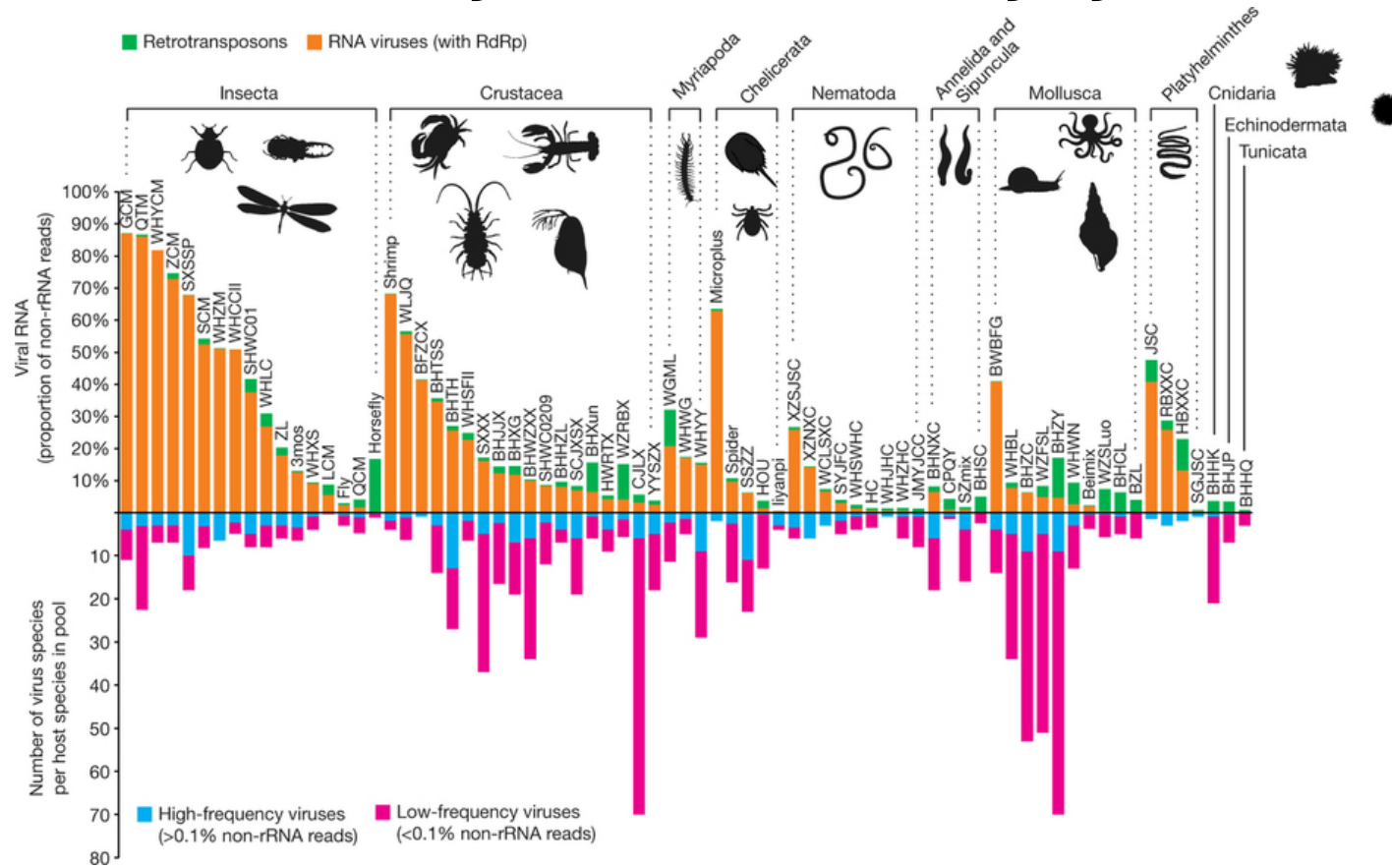
Family (-*viridae*) *Filoviridae* (filovirus family)

Genus (-*virus*) *Ebolavirus*

Species\* *Zaire ebolavirus*



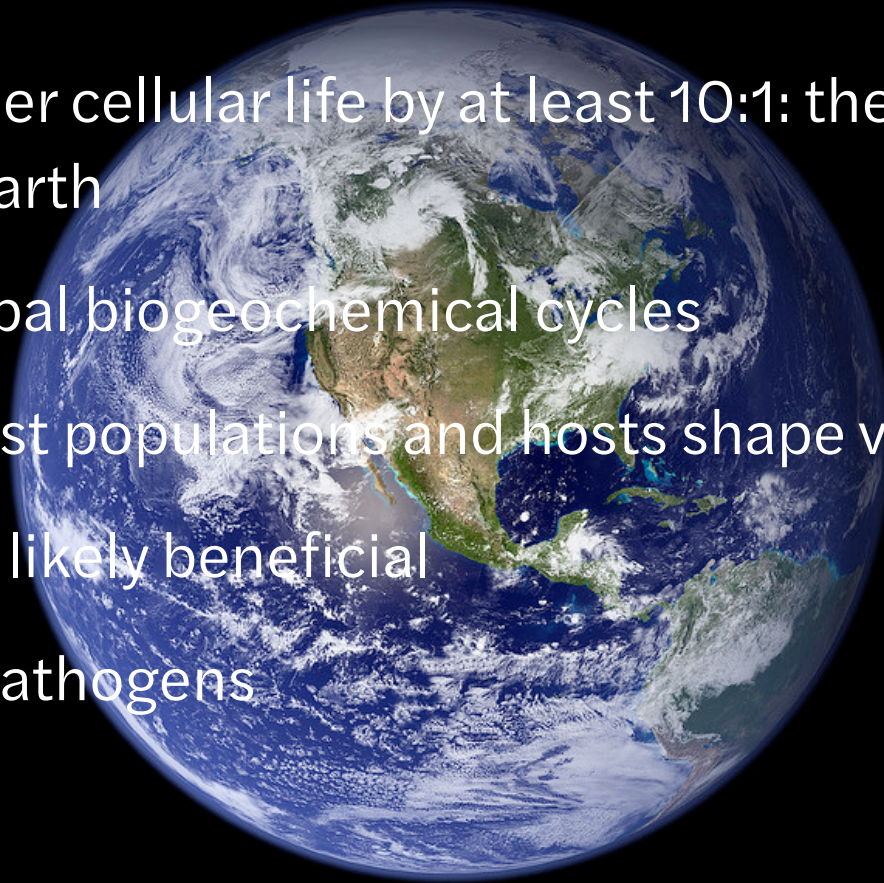
# Virus discovery - Once driven only by disease



Analyzed RNA from 220 invertebrate species, found 1,445 new viruses

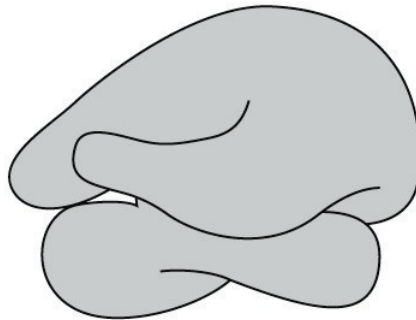
## Why do we care?

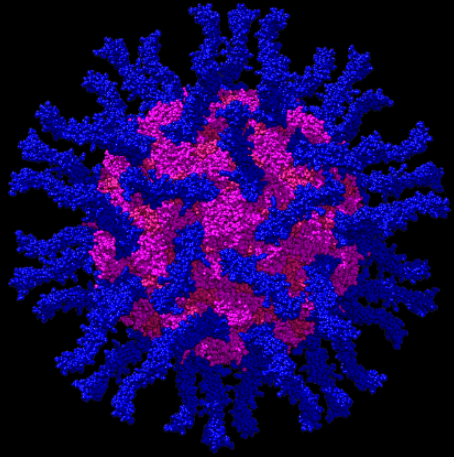
- Viruses outnumber cellular life by at least 10:1: the greatest biodiversity on Earth
- Viruses drive global biogeochemical cycles
- Viruses shape host populations and hosts shape virus populations
- Many viruses are likely beneficial
- Sources of new pathogens



## **There is an underlying simplicity and order to viruses because of two simple facts**

- All viral genomes are obligate molecular parasites that can only function after they replicate in a cell
- All viruses must make mRNA that can be translated by host ribosomes: they are all parasites of the host protein synthesis machinery





# **VIROLOGY LIVE**

**WITH VINCENT RACANIELLO**

**Next time: The Infectious Cycle**