What is a virus?

Lecture 1
Biology 3310/4310
Virology
Spring 2017

"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

Biology 3310/4310
Virology

- Prof. Vincent Racaniello, Ph.D.
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  - twitter.com/@profvrr
  - plus.google.com/+VincentRacaniello
  - facebook.com/thisweekinvirology
- TA: Amy Rosenfeld, Ph.D.
  - abr22@cumc.columbia.edu

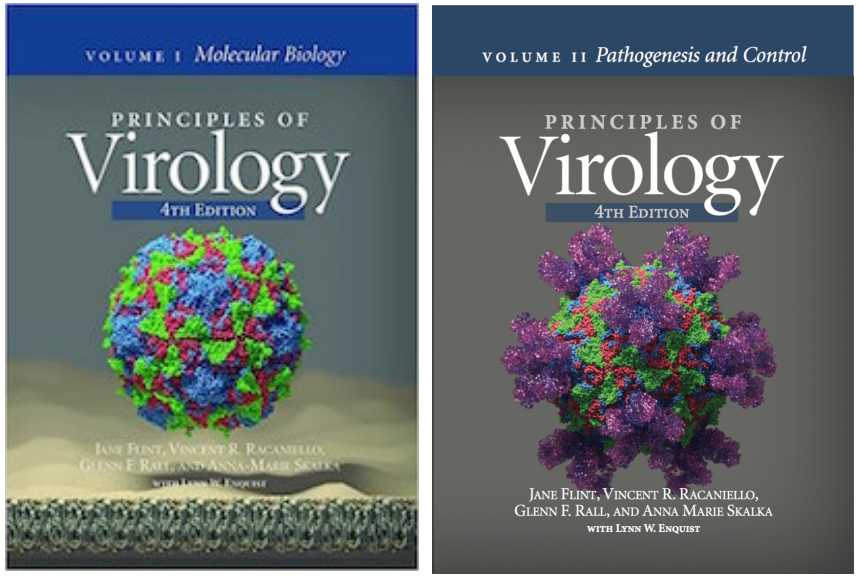
Biology 3310/4310
Virology

- courseworks.columbia.edu
  - Schedule, lecture slides, study questions, readings, video, quiz, grading
- virology.ws/course

Biology 3310/4310
Virology

RecommendedTextbook: *Principles of Virology*

Fourth Edition, ASM Press



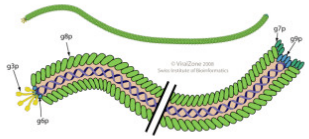
Sample chapter on Courseworks

Biology 3310/4310
Virology

virology blog
About viruses and viral disease

Viruses help form biofilms

17 DECEMBER 2015



Bacteria frequently grow in communities called biofilms, which are aggregates of cells and polymers. An example of a biofilm is the dental plaque on your teeth. Biofilms are medically important as they can allow bacteria to persist in host tissues and on catheters, and confer increased resistance to antibiotics and dessication. Therefore understanding how biofilms form is crucial for controlling microbial infections. An advance in our understanding of biofilms formation is the observation that filamentous phages help them assemble, and contribute to their fundamental properties.

Pseudomonas aeruginosa is an important human pathogen which is a particular problem in patients with cystic fibrosis. The ability of this bacterium to form biofilms in the lung is linked to its ability to cause chronic infections. *Pseudomonas aeruginosa* biofilms contain large numbers of filamentous Pf bacteriophages (pictured; image credit). These viruses lyse cells and release DNA, which becomes one component of the biofilm matrix.

Mixing supernatants of *P. aeruginosa* cultures with hyaluronan, which is present in airways of cystic fibrosis patients, resulted in the formation of a biofilm – in the absence of bacteria. A major component of *P. aeruginosa* biofilms was found to be Pf bacteriophages. When purifed Pf bacteriophages were mixed with hyaluronan, biofilms formed. Similar biofilms also formed when the filamentous bacteriophage fd of *E. coli* was mixed with hyaluronan. Mixtures of Pf bacteriophages and various polymers (alginate, DNA, hyaluronan, polyethylene glycol) formed liquid crystals (matter in a state between a liquid and a solid crystal).

Pf phages were detected in sputum from patients with cystic fibrosis, but not in uninfected patients. Addition of Pf phage to sputum from patients infected with *P. aeruginosa* made the samples more birefringent, a property of liquid crystals. Compared with a strain of
of virus-producing strains
Pf phage help organize the

BY VINCENT RACANIELLO

Earth's virology Professor
Questions? virology@virology.ws

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EARTH'S VIROLOGY COURSE

Columbia U
iTunes U
Coursera
Virologia en Español
Virology 101
Influenza 101
Virology Toolbox
Textbook: *Principles of Virology*

PODCASTS

This Week in Virology
This Week in Microbiology
This Week in Parasitism
Urban Agriculture
This Week in Evolution

OTHER CONTENT

Ebolavirus
ME/CFS
Inside a BSL-4
The Wall of Polio
Microbe Art

USEFUL RESOURCES

Lecturio Online Courses
HealthMap
mSphere
Polio eradication
Promed-Mail

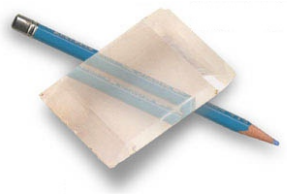
www.virology.ws

TWiV
THIS WEEK IN VIROLOGY

Shows Archive Letters Picks Guests Viral video Virology 101

TWiV 368: Infected, you will be

December 20, 2015



Hosts: Vincent Racaniello, Alan Dove, Rich Condit, and Kathy Spindler

A plaque of virologists explores the biology of Zika virus and recent outbreaks, and the contribution of a filamentous bacteriophage to the development of biofilms.

00:00 00:00

Click arrow to play

Download TWiV 368 (86 MB .mp3, 119 min)

Subscribe (free): iTunes, RSS, email

Links for this episode

- More cowbell (Wikipedia) 7:50
- Microcephaly in Brazil (Outbreak News) 18:40
- Non-vector borne Zika transmission (EID) 30:40
- Zika virus outside Africa (EID) 29:20
- Zika virus possible sexual transmission (EID) 32:50
- Zika virus in saliva (J Clin Virol) 32:10
- Dengue's cousin Zika (Micr Inf) 34:25
- Filamentous phage promote biofilm assembly (Cell Host Micr) 38:40
- Biofilm history (MSU) 41:10
- *Pseudomonas* phage Pf1 45:10
- Image credit
- Letters read on TWiV 368 11:10, 1:1
- This episode is sponsored by Clinica nnifer. Thanks!

Weekly Science Picks 1:44:00

Alan – Twelve days of norovirus

Vincent – This Week in Evolution

microbe.tv/twiv

Biology 3310/4310
Virology

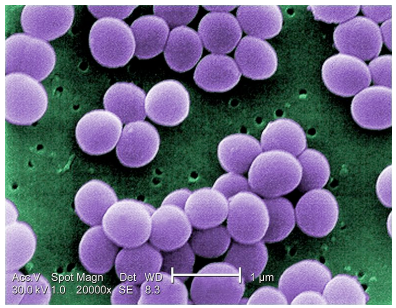
- Weekly quiz (Courseworks)
- 4 exams (2/8, 3/6, 4/5, final)
- Discussion sessions (4310 only)
- Reviews before exams (TA Amy)

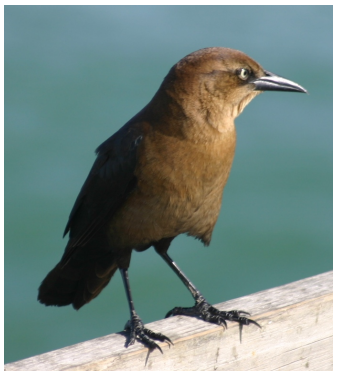
Biology 3310/4310
Virology

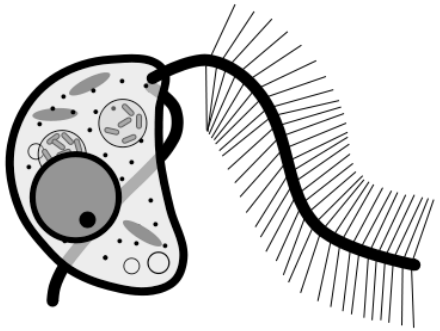
- Office hours: Thursdays 4-6 PM, HHSC 1310B, 701 W. 168th (Medical Center)
- Open format
- Appointments
- Questions during lecture
- https://piazza.com/columbia/spring2017/biol33104310/home

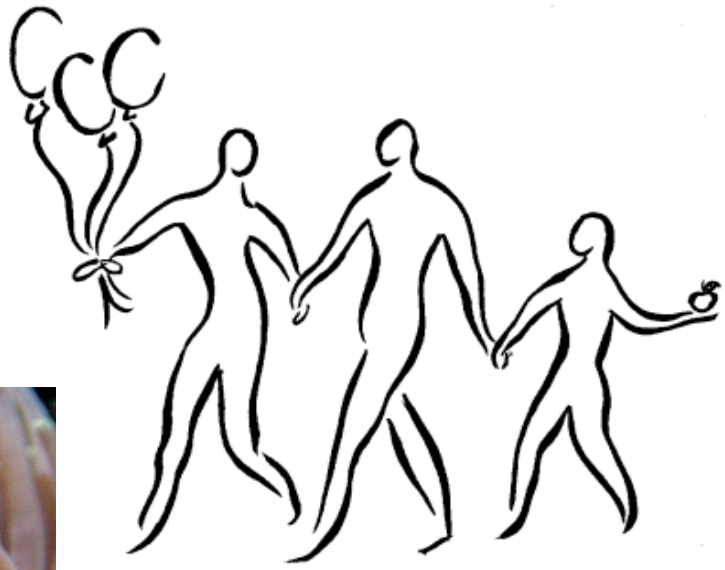
We live and prosper in a cloud of viruses

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

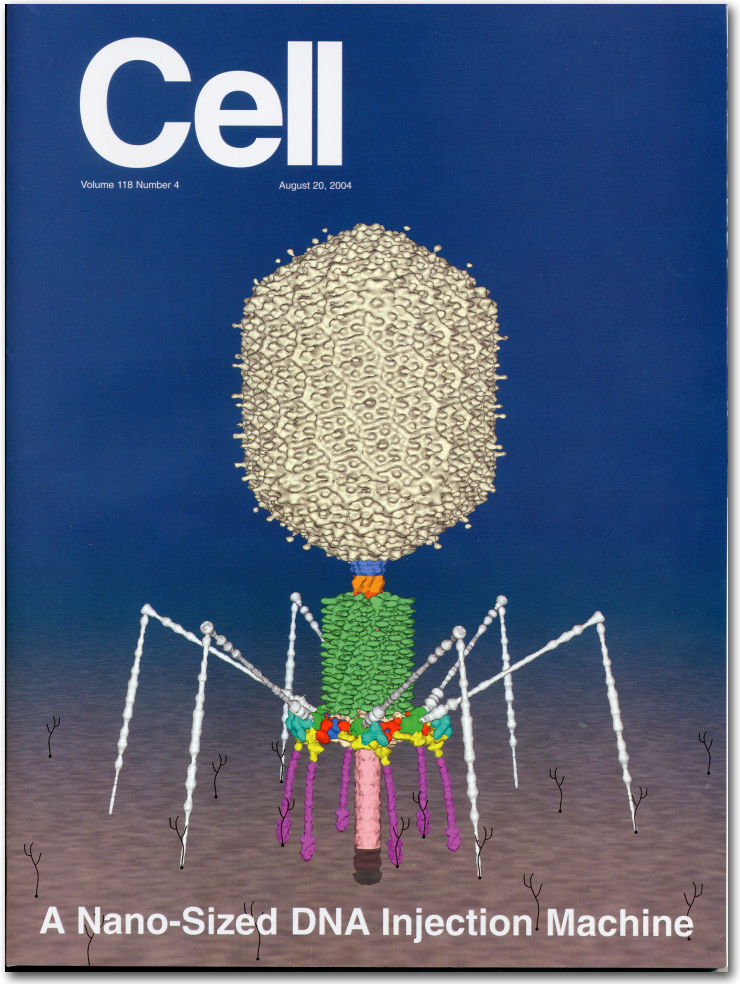








The number of viruses on Earth is staggering



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

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

  10^{30} X 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!

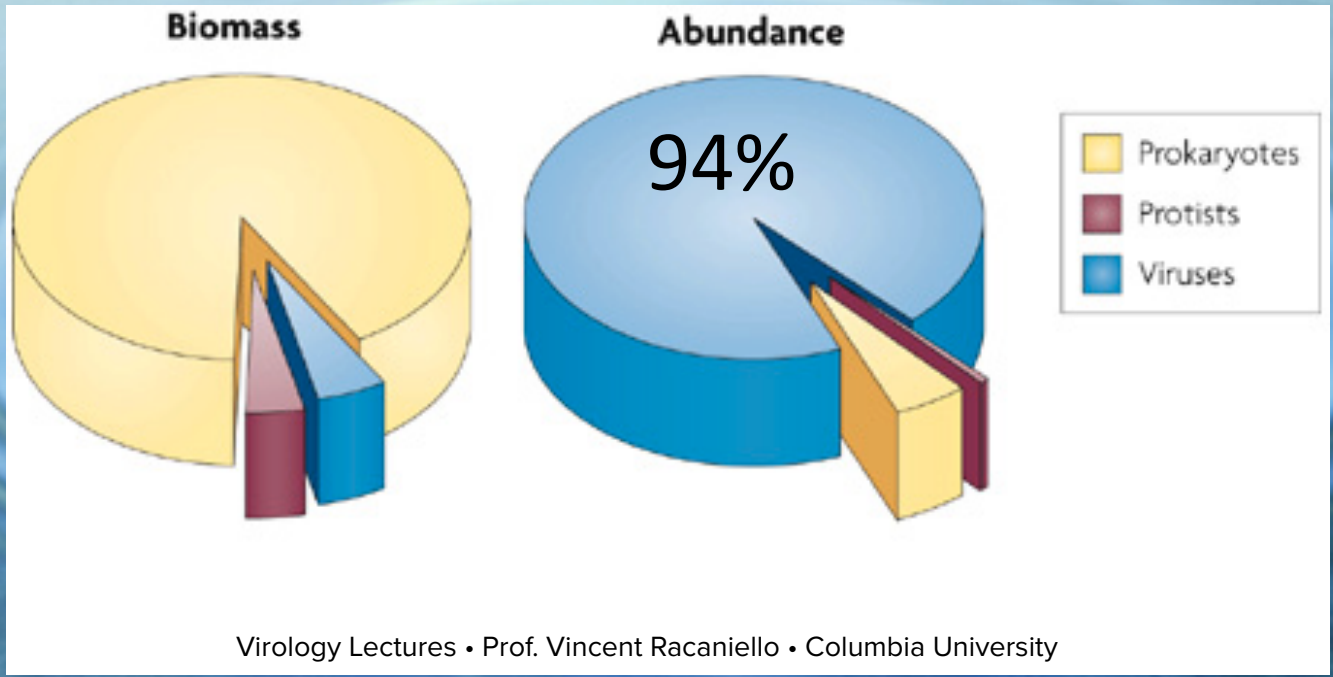
http://www.phagehunter.org/2008/09/how-far-do-those-phages-stretch.html


VPg
38nm particle
10^{13}

Viruses are not just purveyors of bad news

More viruses in a liter of coastal seawater

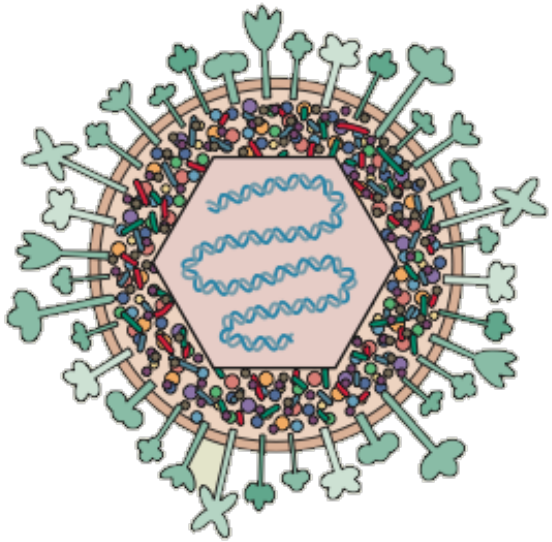
than people on Earth



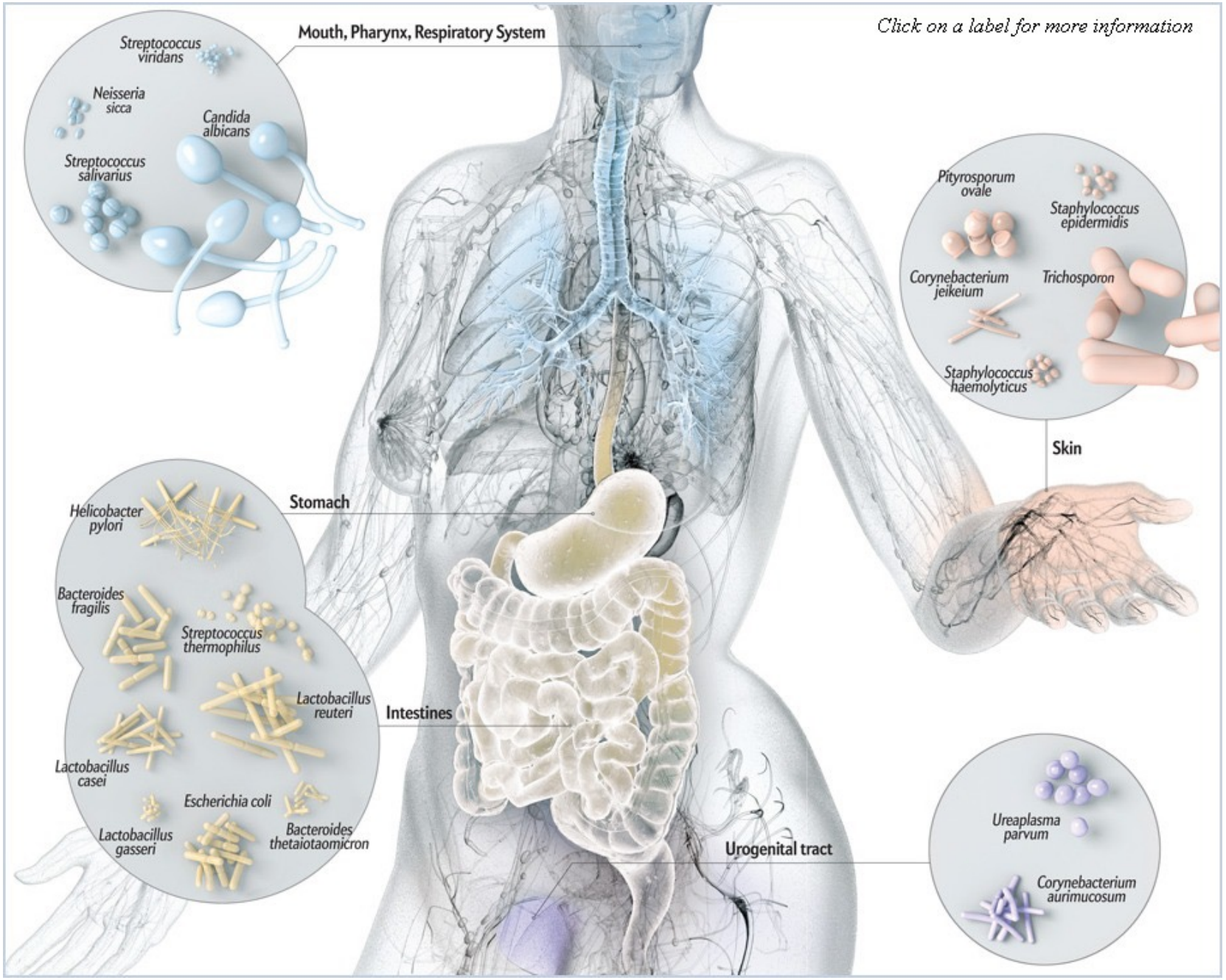
There are ~10^{16} HIV genomes on the planet today

How ‘infected’ are we?

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

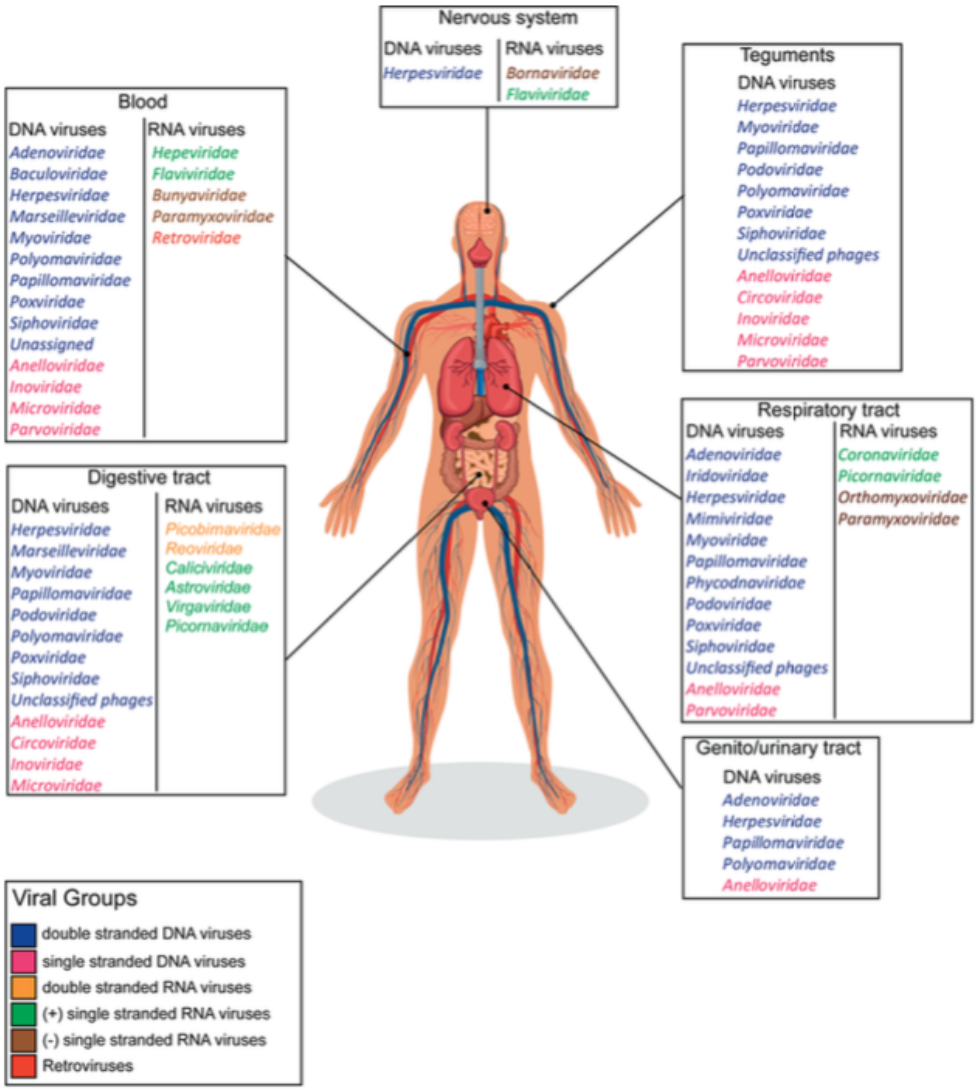


Microbiome

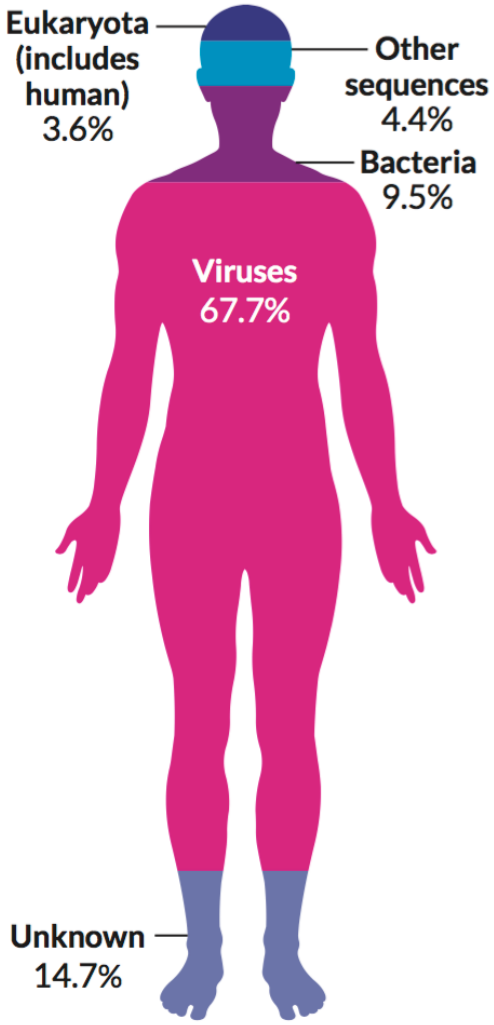


http://linxc10.wix.com/microbes#!the-microbiome/chht

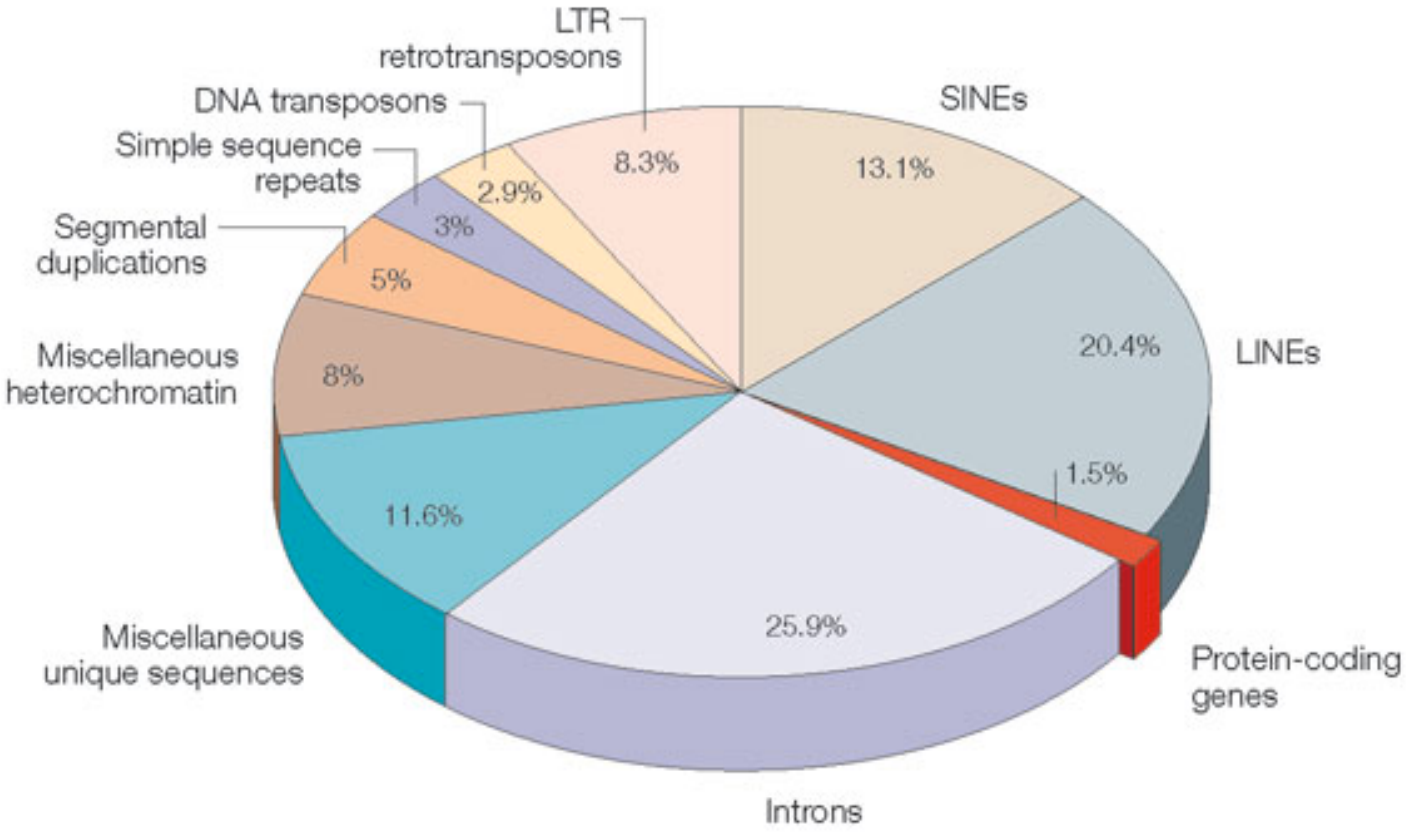
Virome



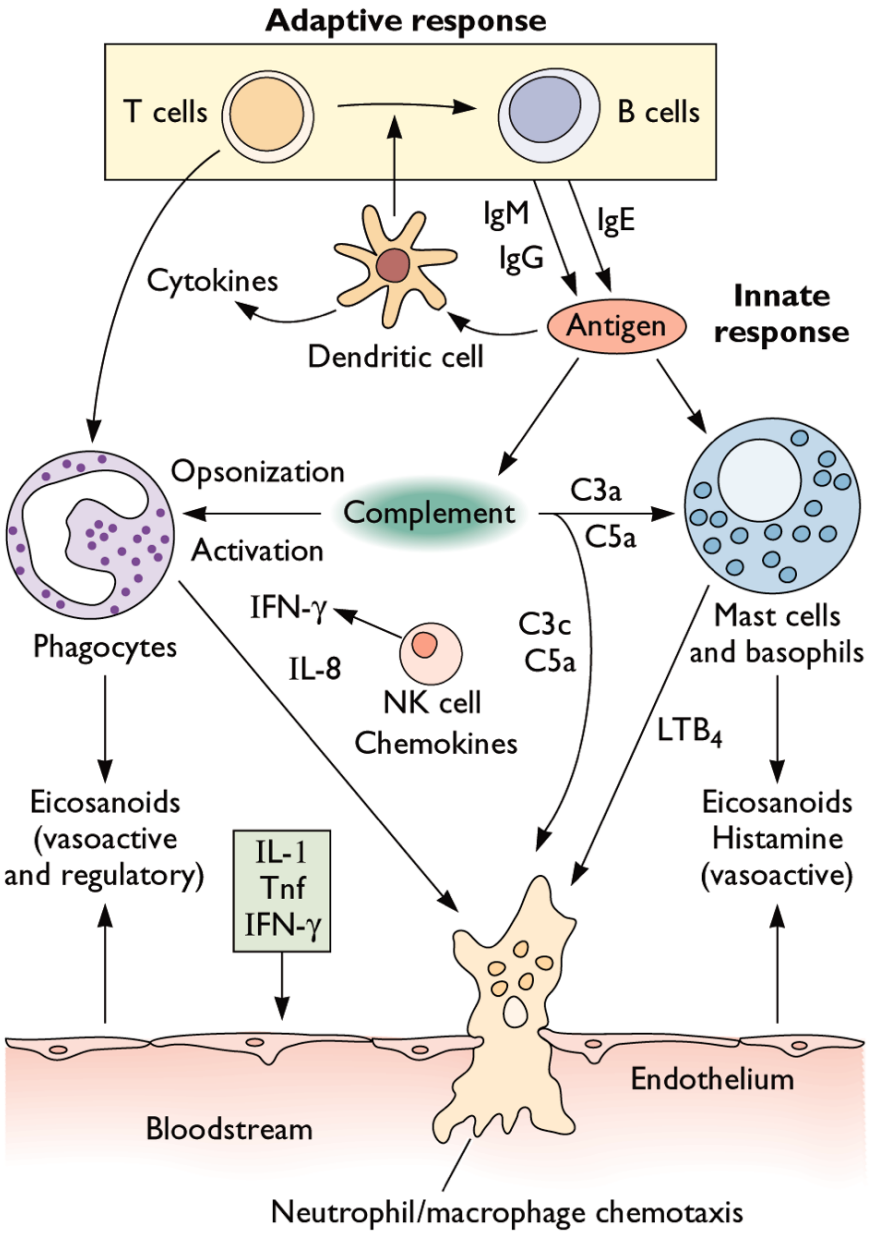
Intervirology 2013;56:395



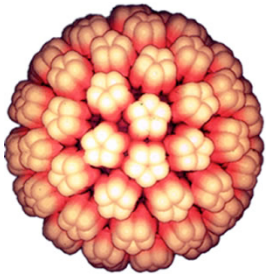
Science News 11 January 2014



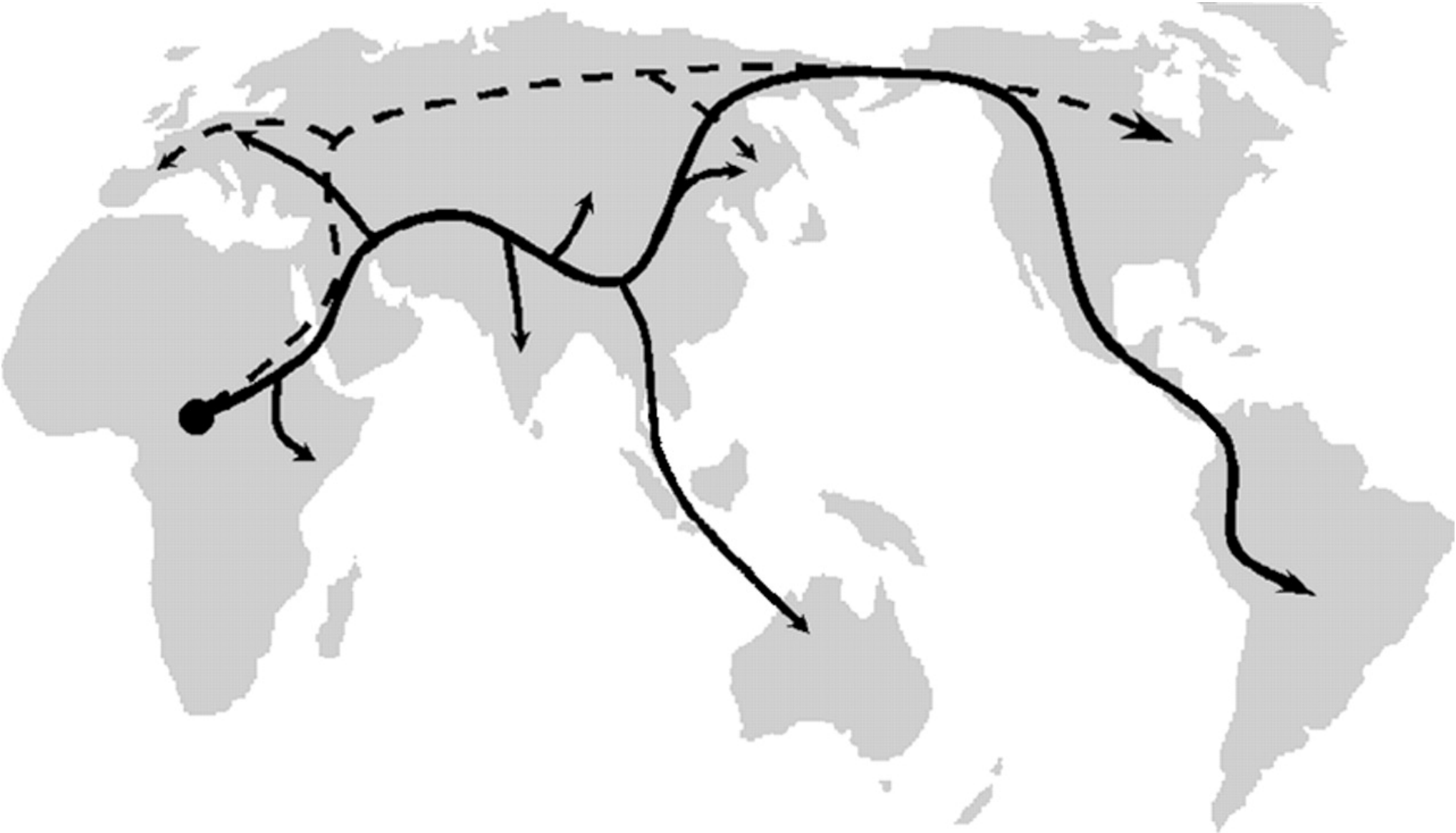
3.2 billion bases



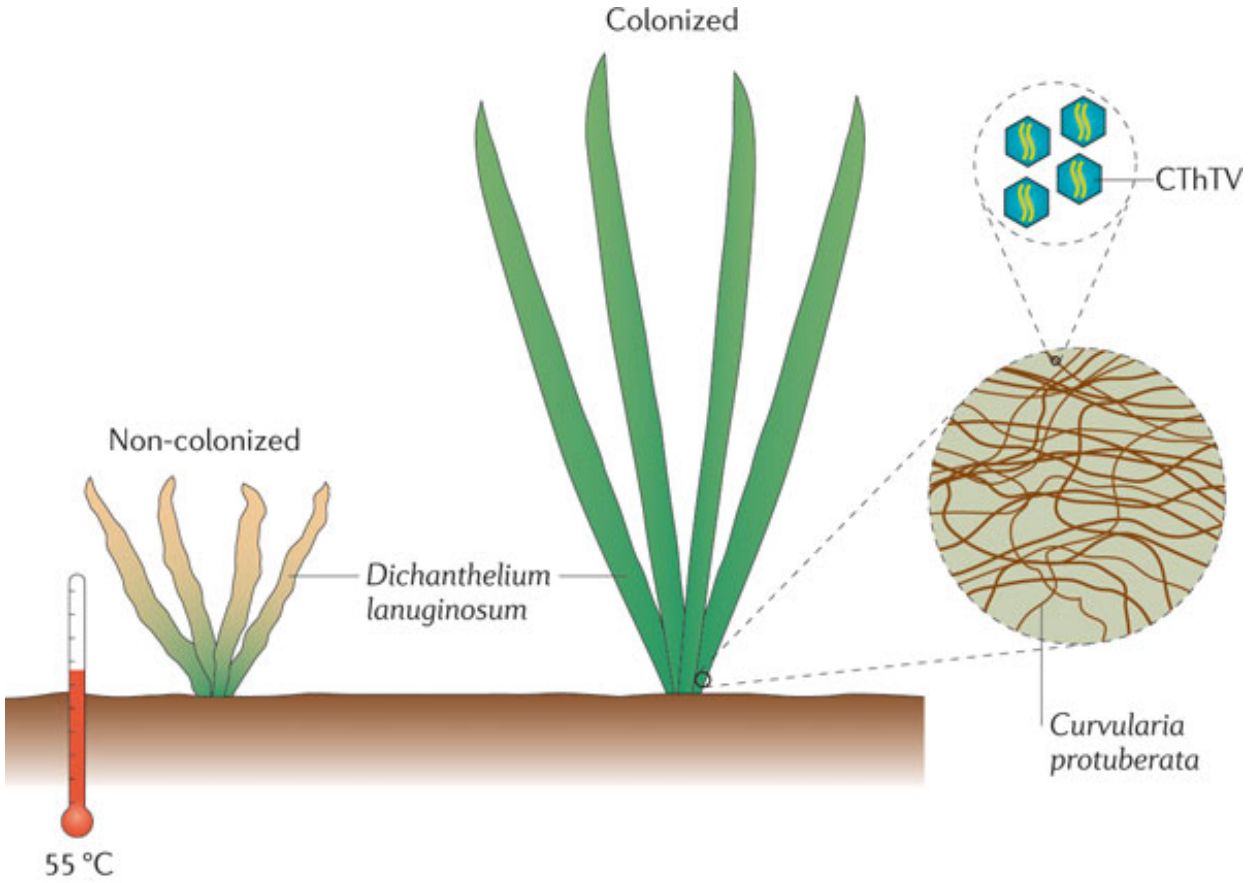
Amazingly, the vast majority of the viruses that infect us have little or no impact on our health or well being



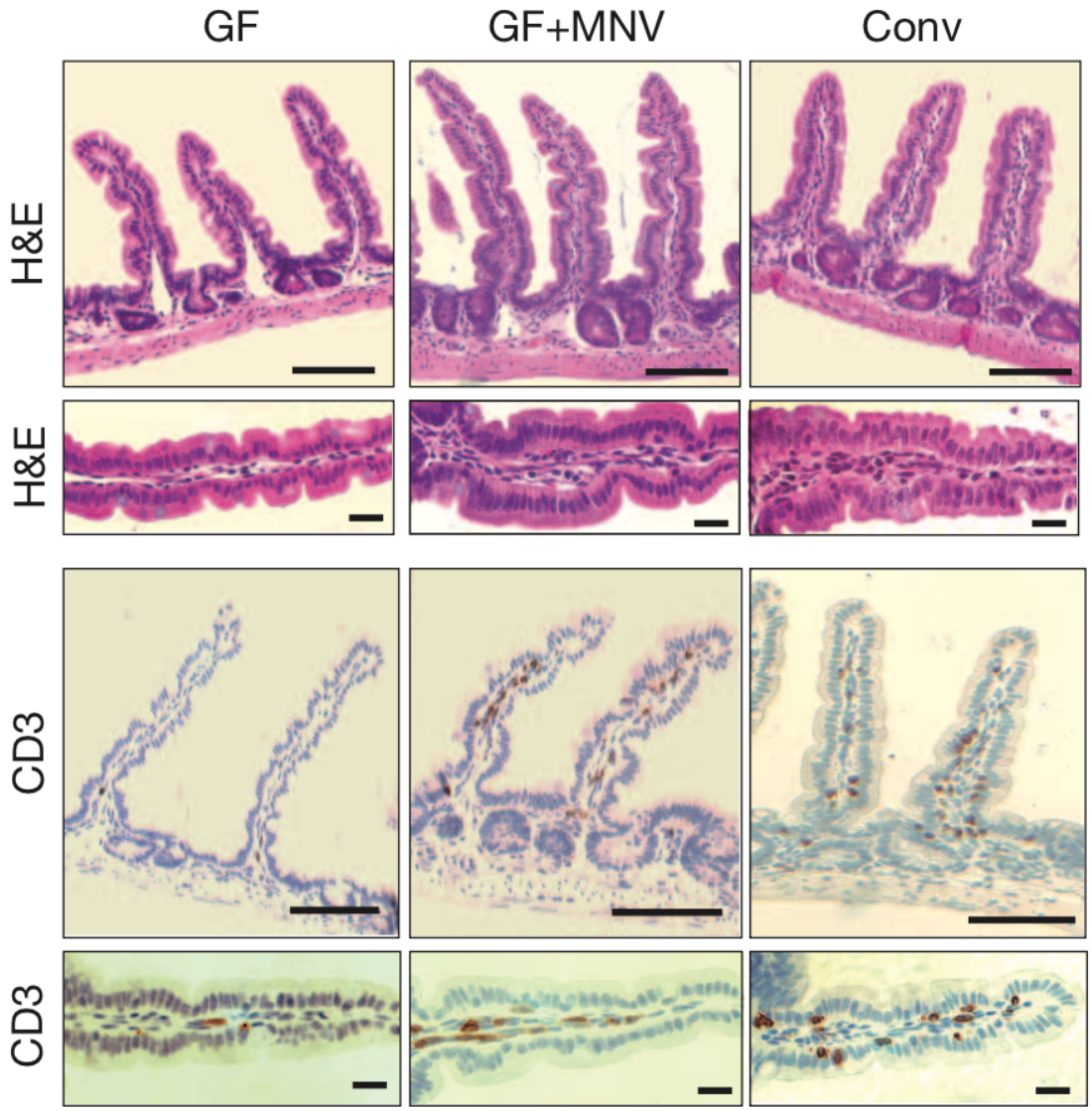
Not all viruses make you sick...



The good viruses

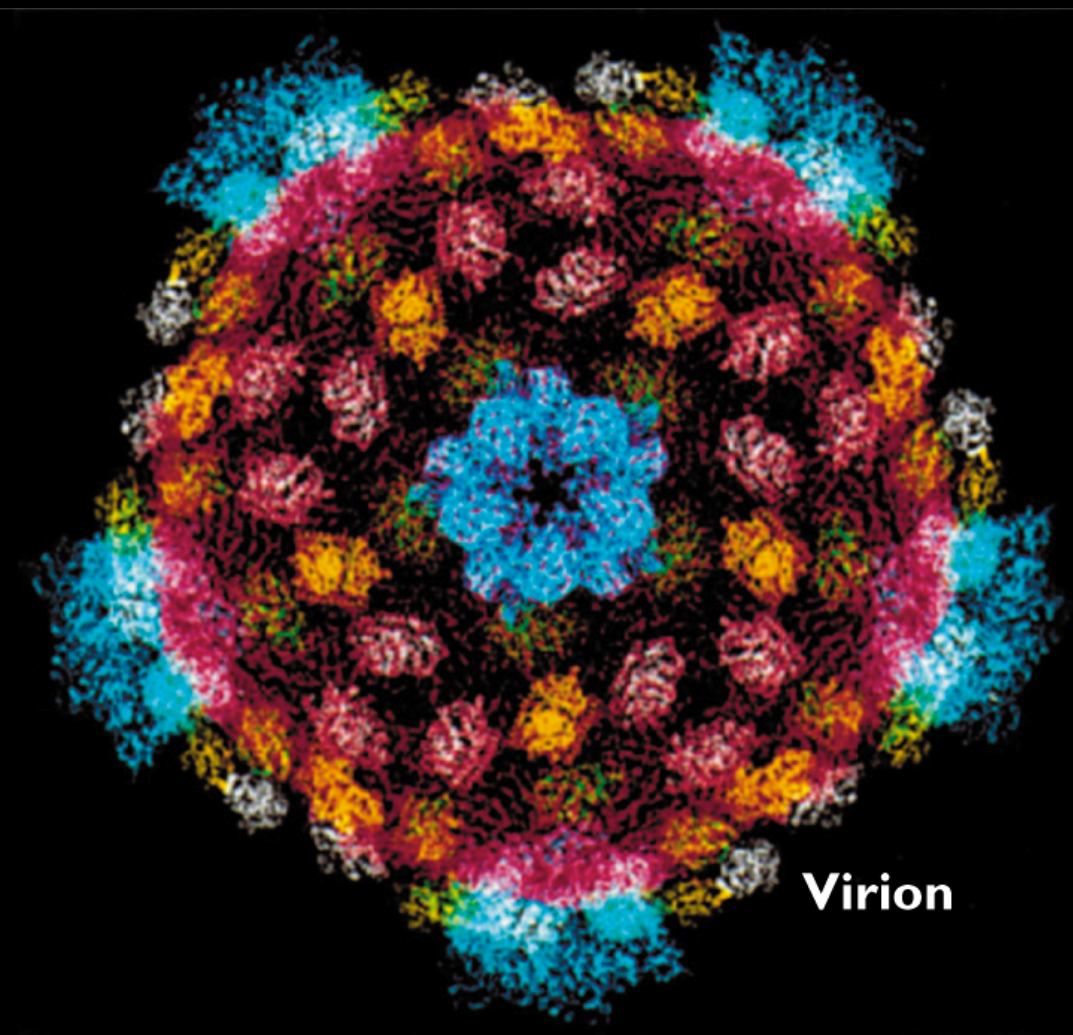


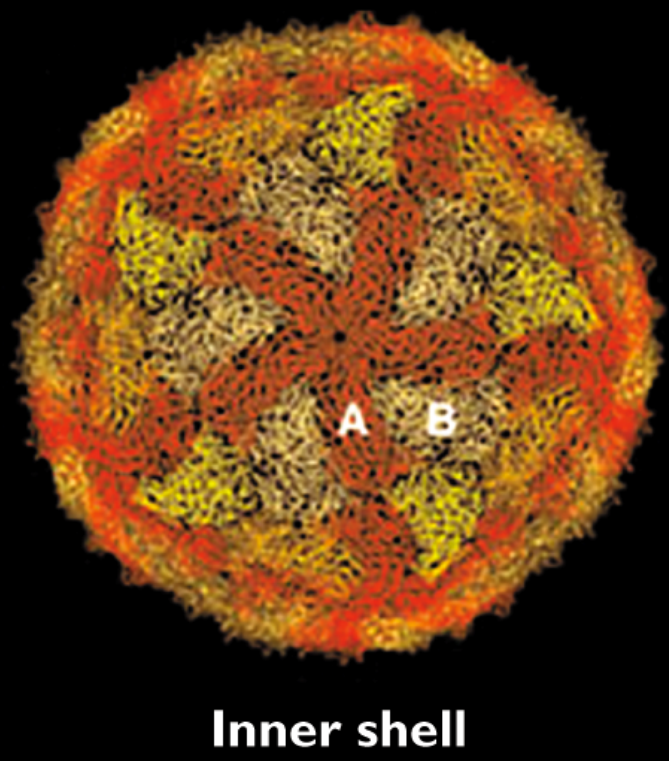
An enteric virus can replace the beneficial function of commensal bacteria



doi: 10.1038/nature13960

Viruses are amazing





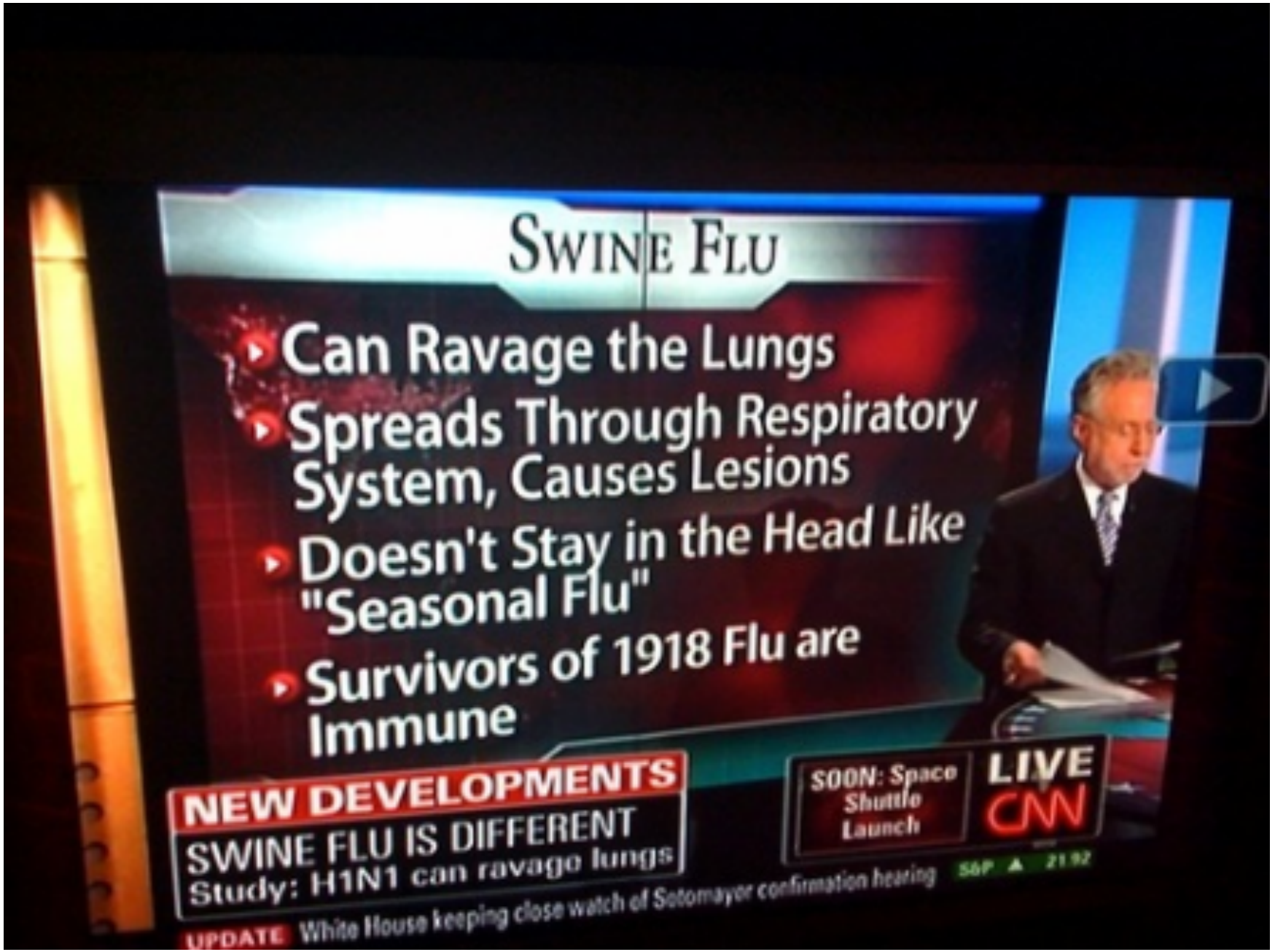
Virology is an integrative science

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*


SWINE FLU
Can Ravage the Lungs
Spreads Through Respiratory System, Causes Lesions
Doesn't Stay in the Head Like "Seasonal Flu"
Survivors of 1918 Flu are Immune
NEW DEVELOPMENTS
SWINE FLU IS DIFFERENT
Study: H1N1 can ravage lungs
SOON: Space Shuttle Launch
LIVE
CNN
UPDATE White House keeping close watch of Sotomayer confirmation hearing
S&P ▲ 2192

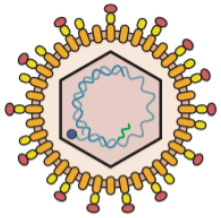
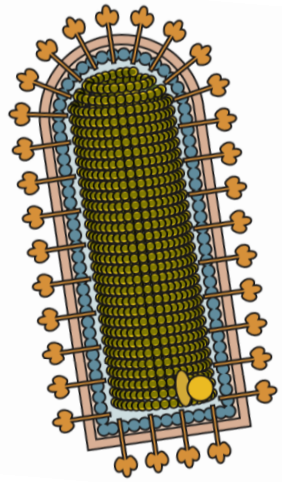
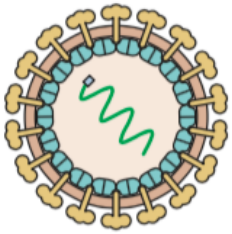
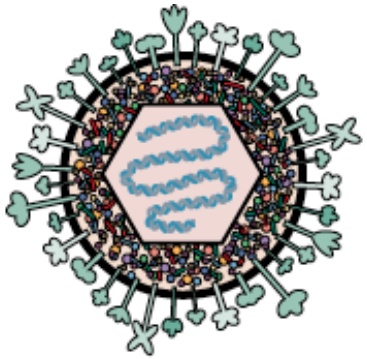
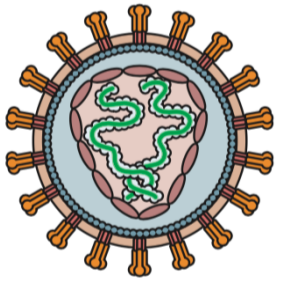
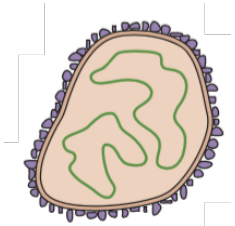
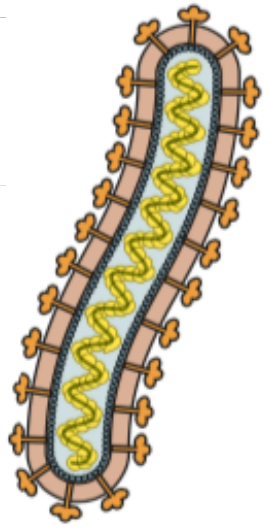
I will use Socrative
to deliver quizzes during lectures

Go to:
b.socrative.com/login/student
room number: virus

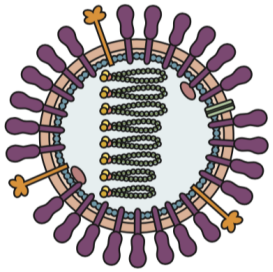
Which statement is true?

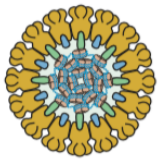
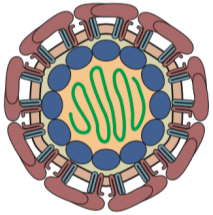
1. All viruses make us sick and can be lethal
2. Our immune system can manage most viral infections
3. Humans are usually infected with one virus at a time
4. The press is usually correct in their virology reporting
5. Our immune system cannot handle most viral infections

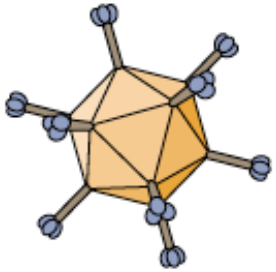
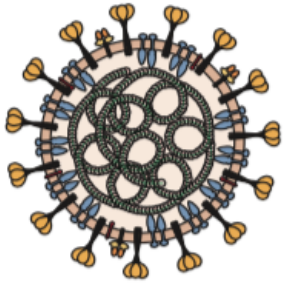
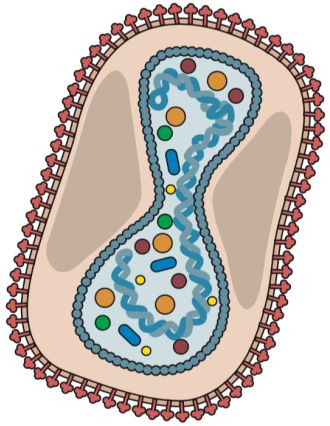
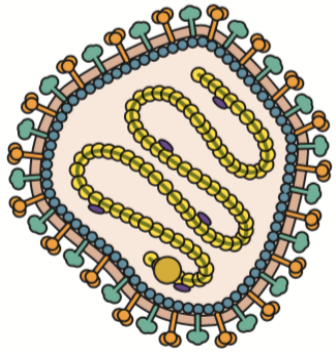
What is a virus?

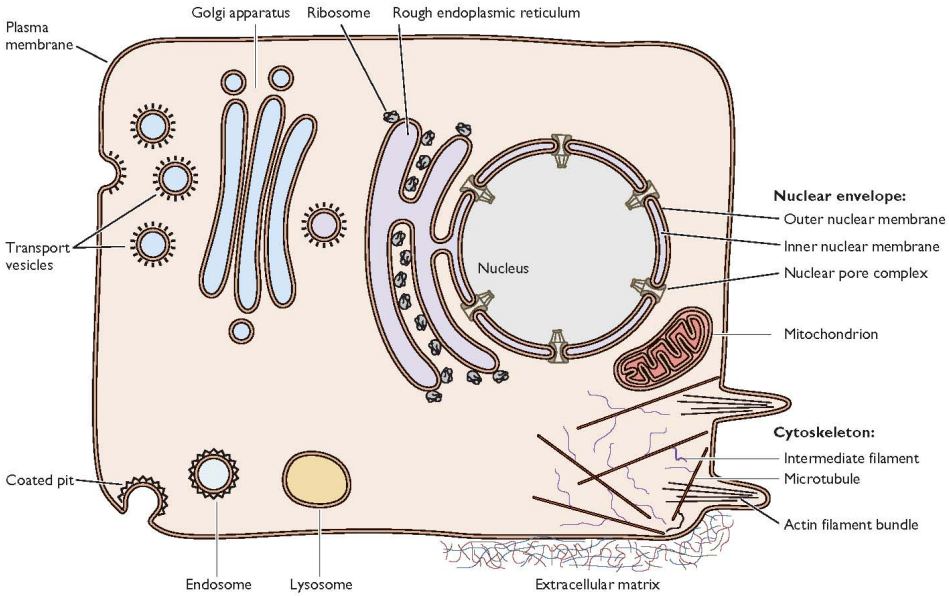









An *infectious, obligate intracellular parasite comprising genetic material* (DNA or RNA) surrounded by a protein coat and/or a membrane

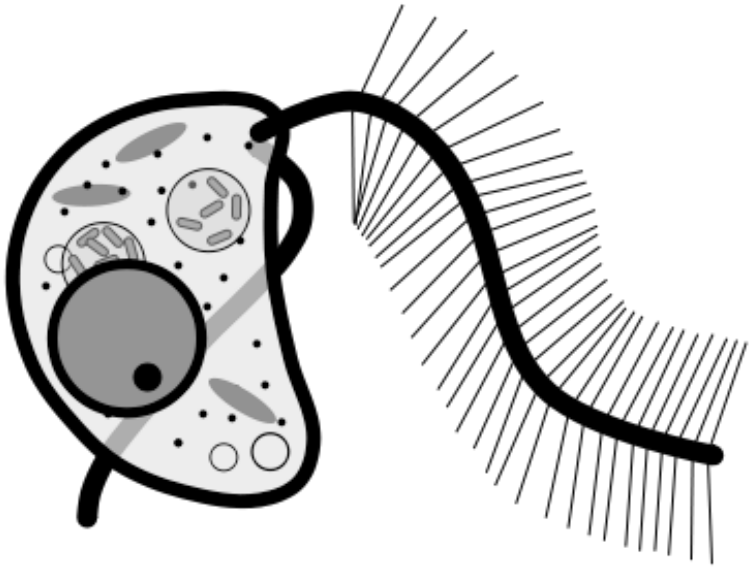


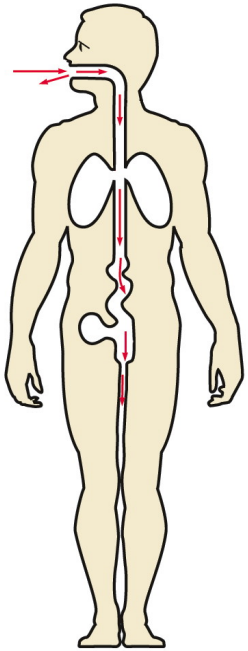



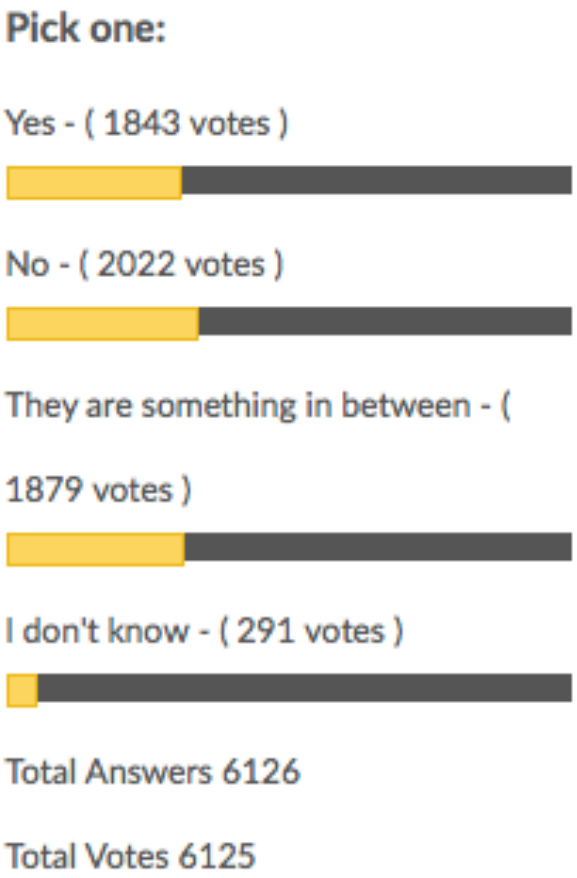


As virions are obligate molecular parasites, every solution must reveal something about the host as well as the virus





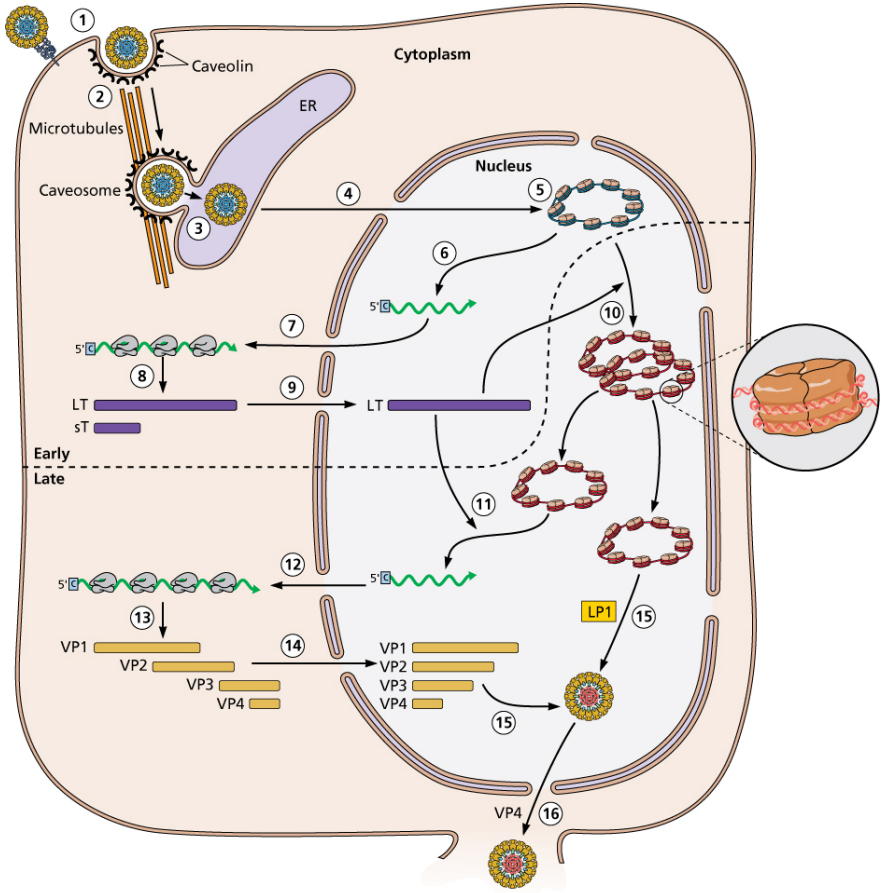
Are viruses alive?



http://www.virology.ws/are-viruses-alive/

The virus and the virion

A virus is an organism with two phases



virion

infected cell

Be careful: Avoid anthropomorphic analyses

Viruses do NOT think!

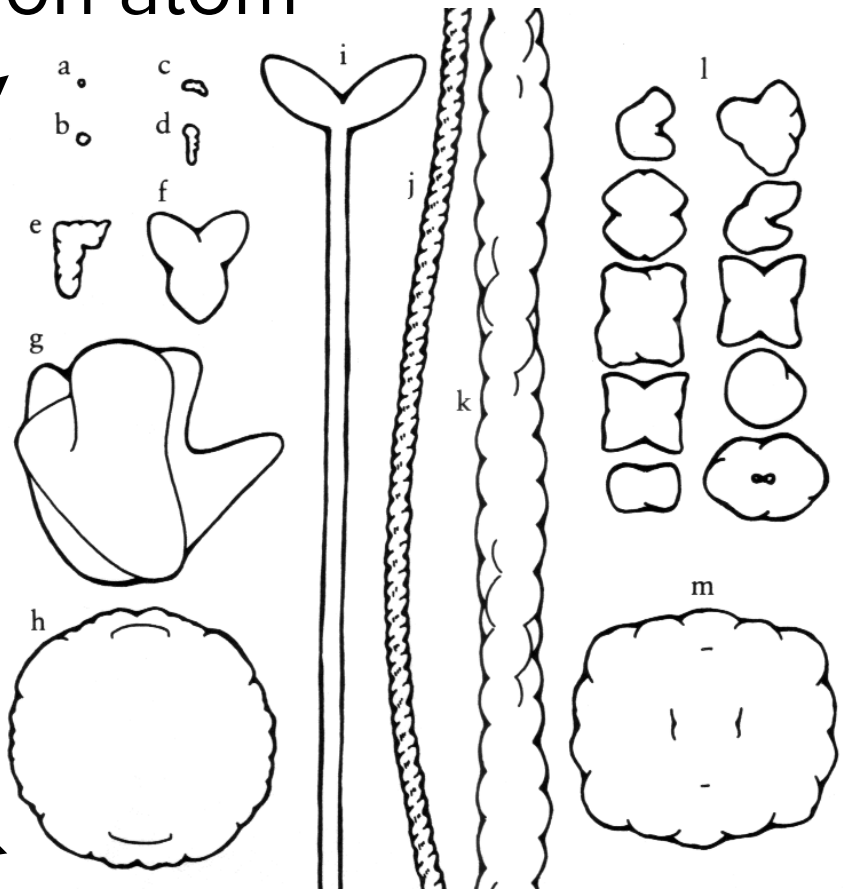
(or employ, ensure, exhibit, display, etc...)

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

Viruses are passive agents!

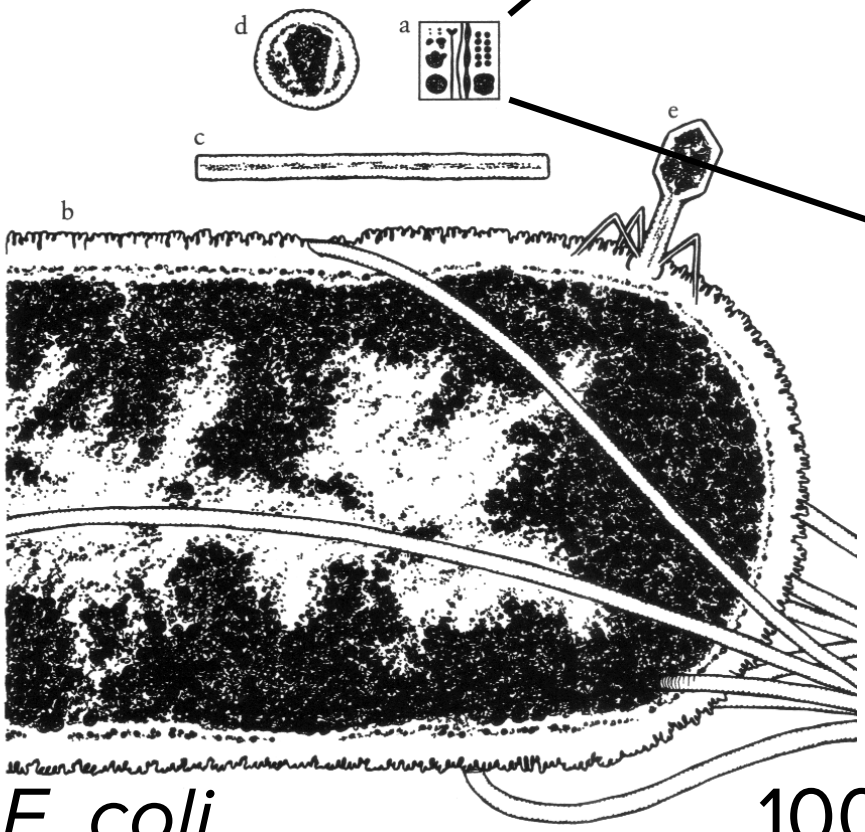
Viruses are very small

Carbon atom



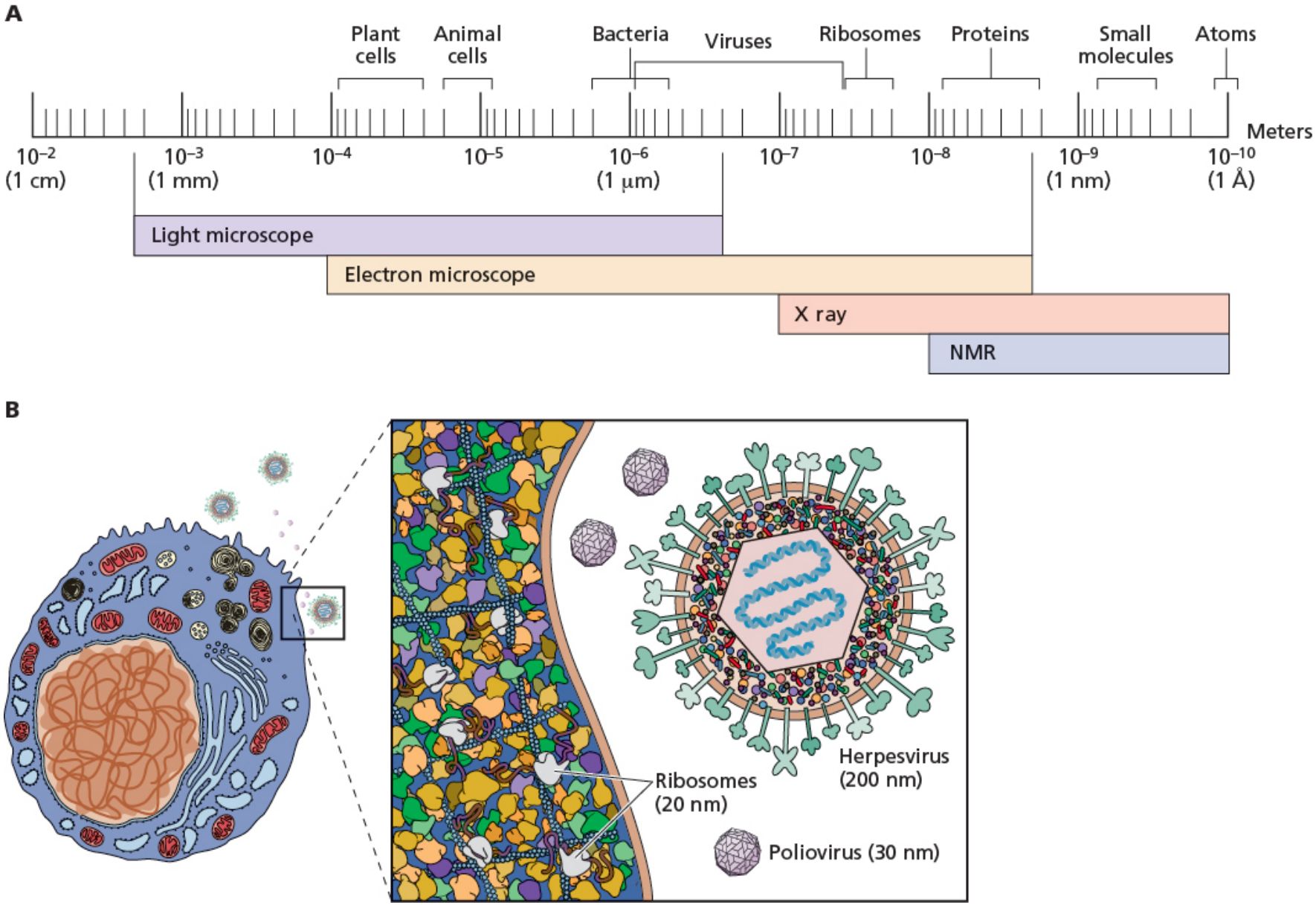
myosin actin

1,000,000x

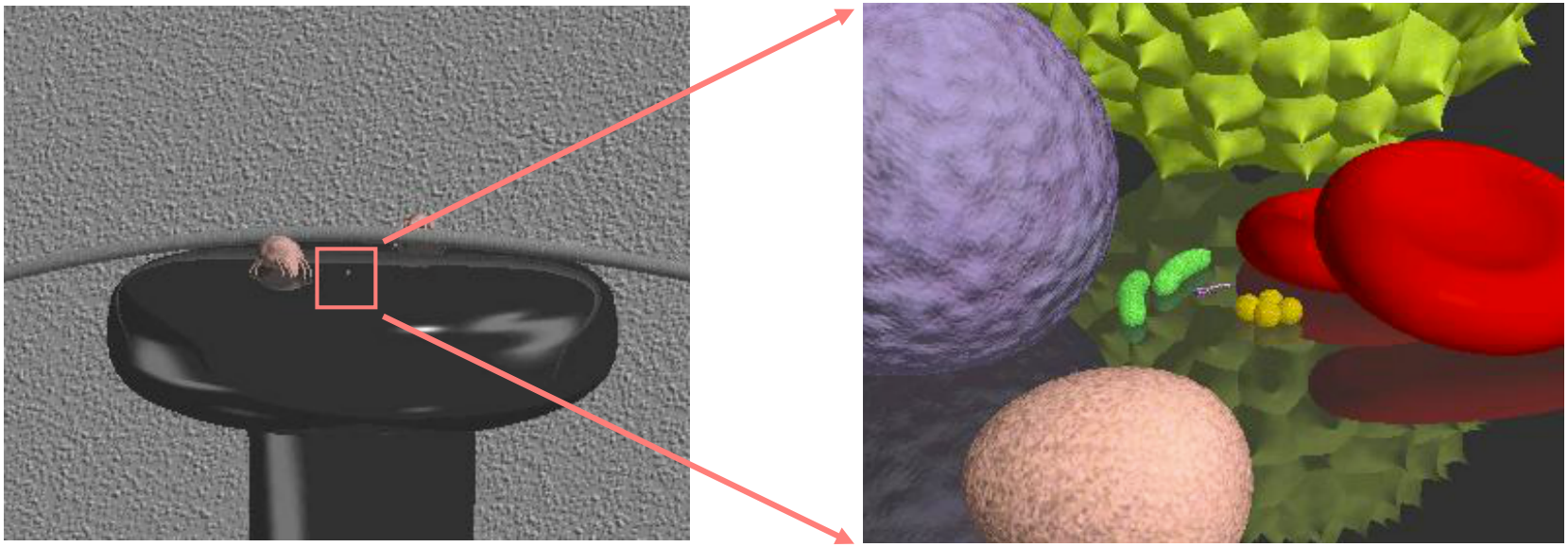


E. coli

100,000x



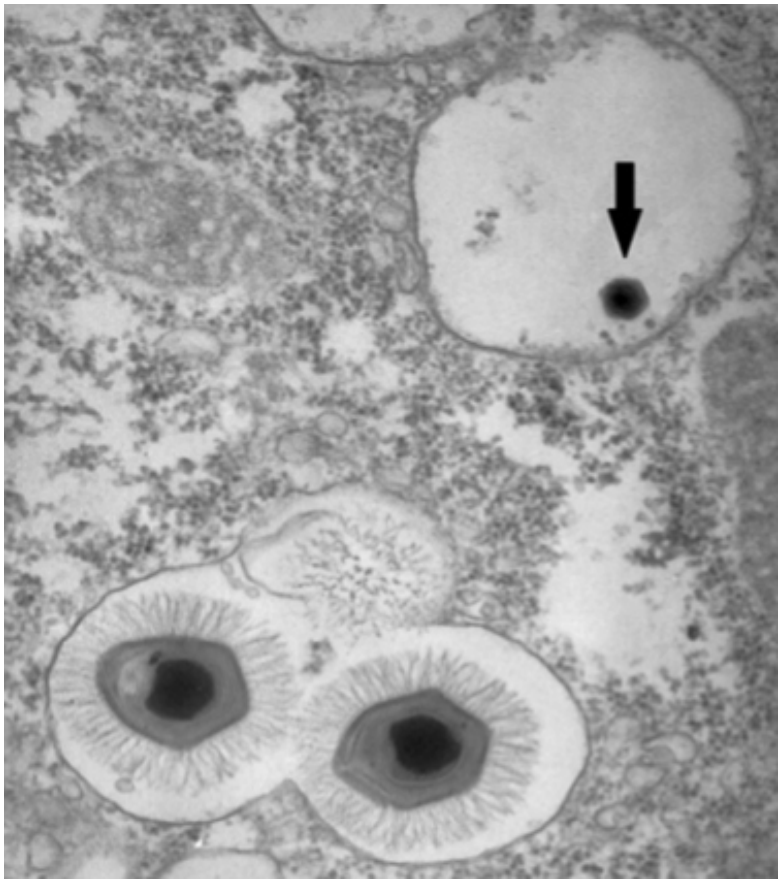
How many viruses can fit on the head of a pin?



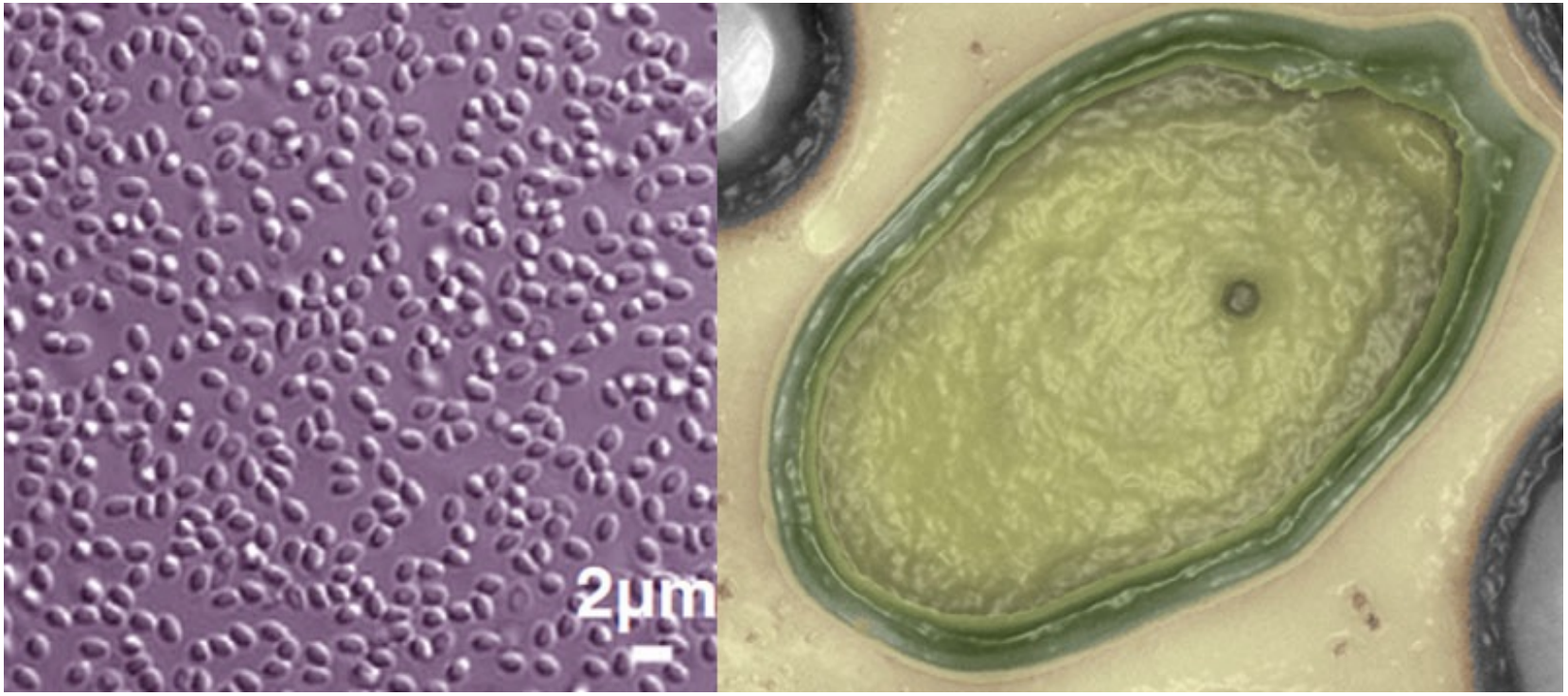
2 mm = 2000 microns

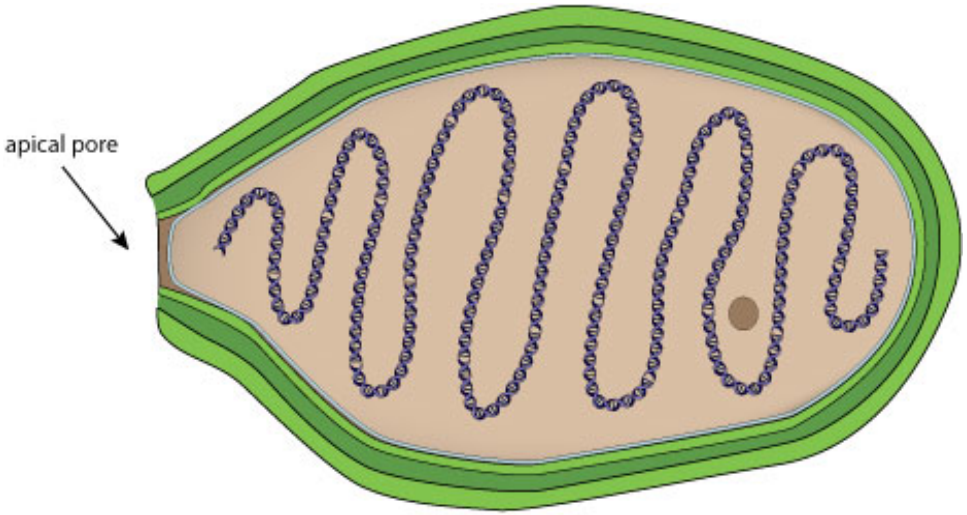
- 500 million rhinoviruses
- When you sneeze, you fire an aerosol that contains enough viruses to infect thousands

Not as small as we once thought!



Pandoravirus



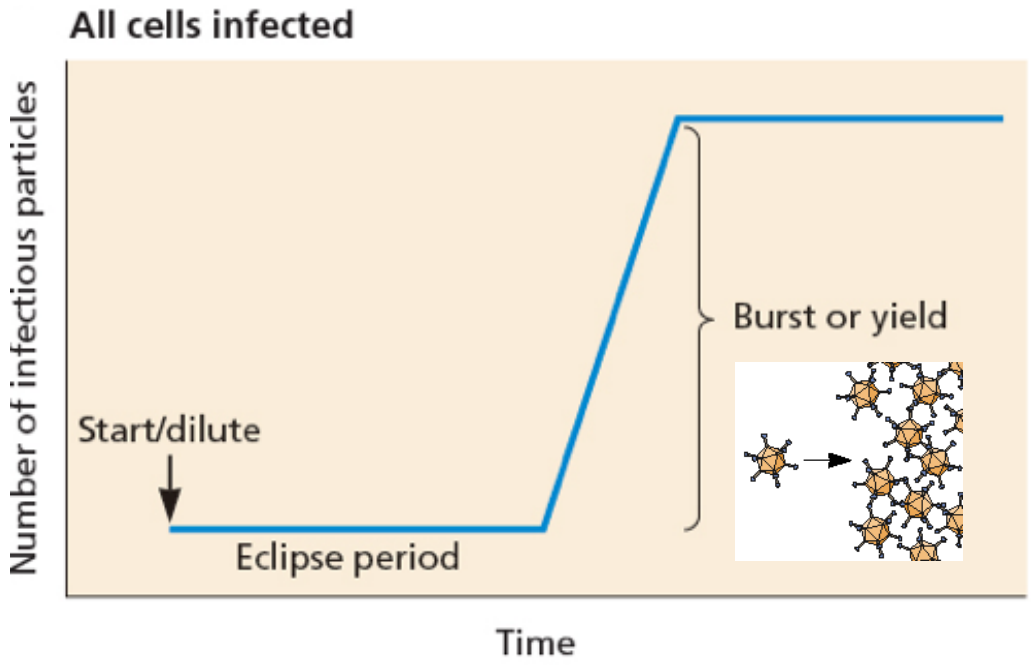


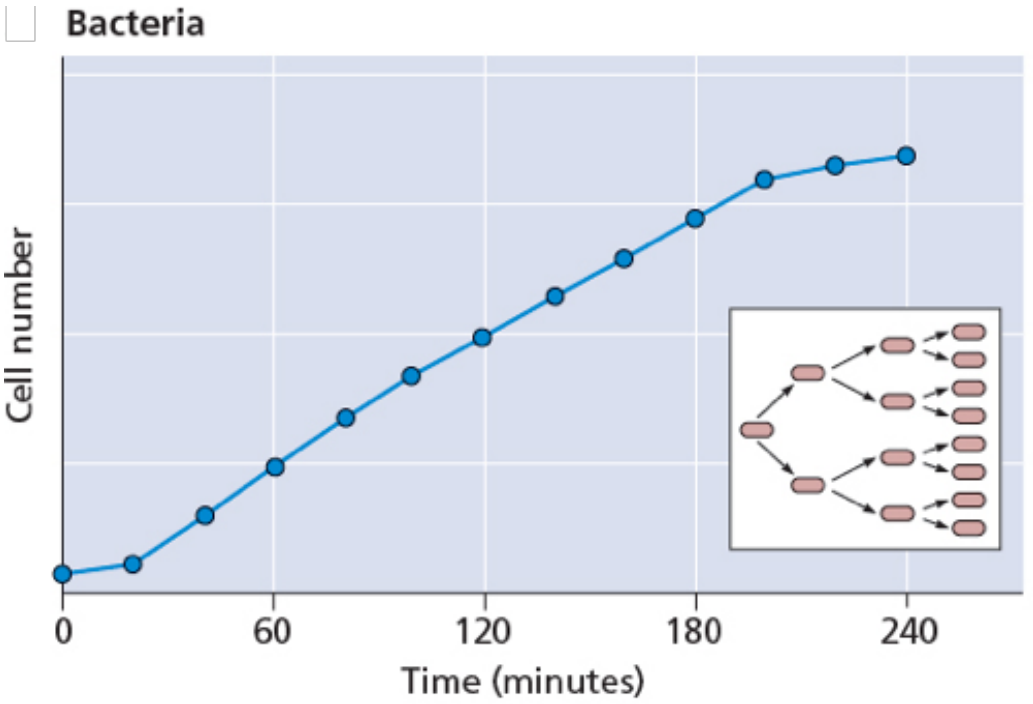
DOI: 10.1126/science.1239181

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

Make the parts, assemble the final product

Not binary fission like cells





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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?

Orthoceras, a nautiloid cephalopod, 488 Ma

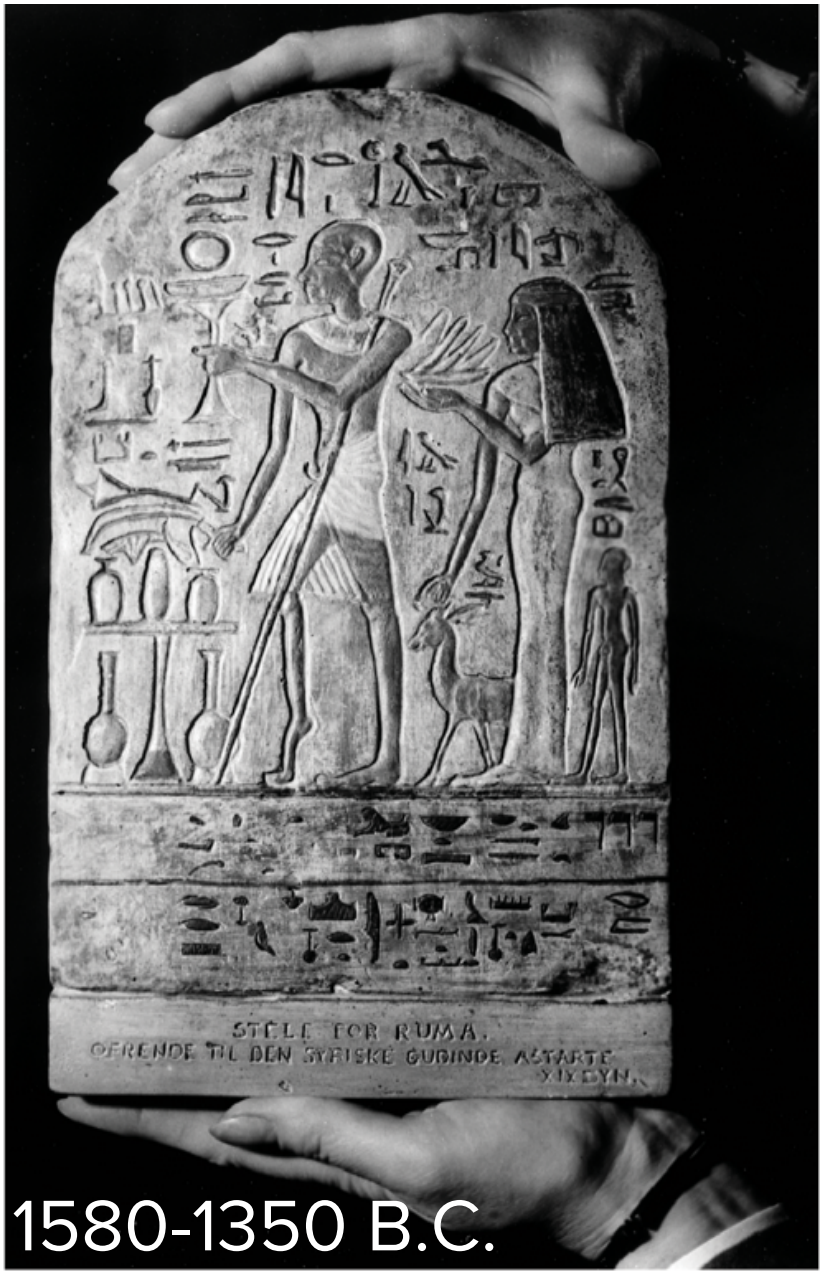
Nobu Tamura (http://spinops.blogspot.com)

- 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.

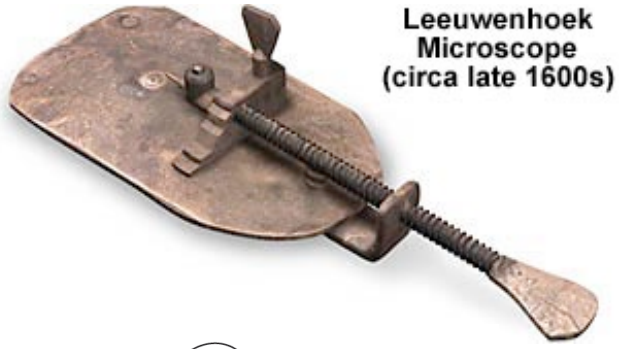


1580-1350 B.C.

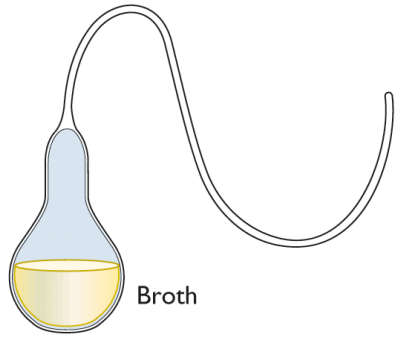
Immunization

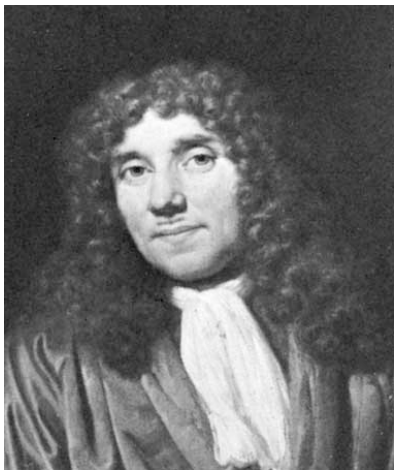
- Variolation - China (11th century), Lady Montagu (1700s)
- No knowledge of agent
- Survivors of smallpox protected against disease
- 1790s - experiments by Edward Jenner in England establish vaccination

Concept of microorganisms



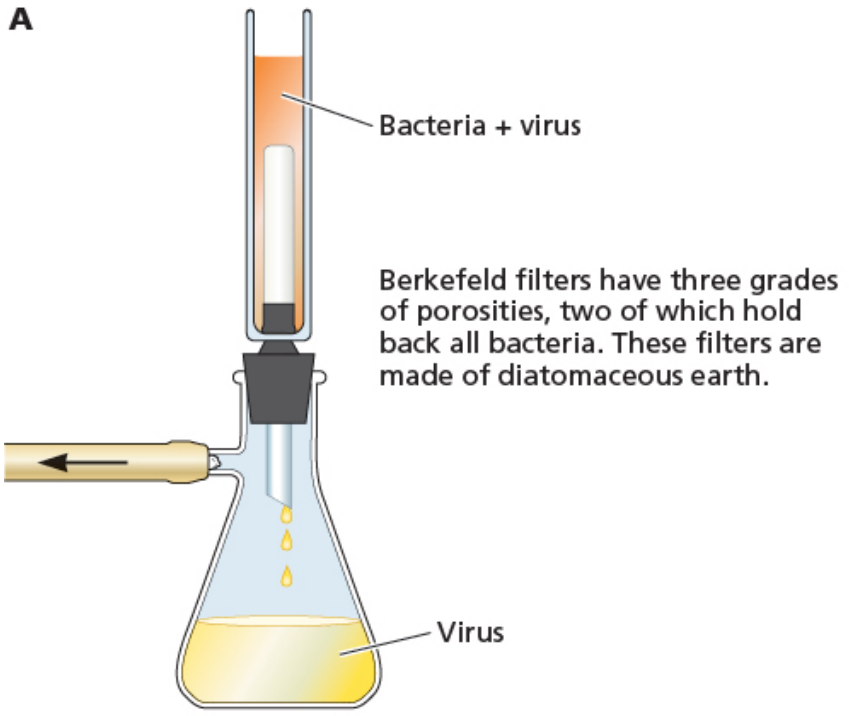
- Leeuwenhoek (1632 - 1723)
- Pasteur (1822 - 1895)
- Koch (1843-1910)





Virus discovery - filterable agents

- 1892 - Ivanovsky
- 1898 - Beijerinck: *contagium vivum fluidum*
- Virus: slimy liquid, poison

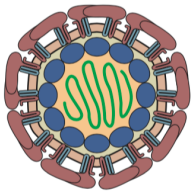


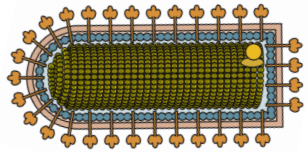
Virus discovery

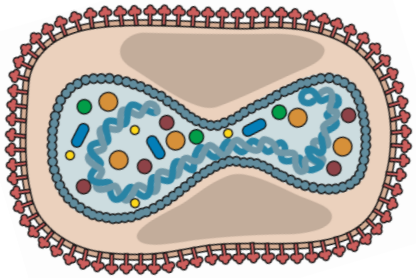
- 1898 - Loeffler & Frosch - agent of foot & mouth disease is filterable
- Key concept: agents not only small, but replicate only in the host, not in broth
- 0.2 micron filters (μm, one millionth of a meter)

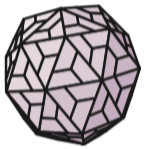
Virus discovery

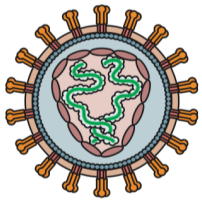
- 1901 - first human virus, yellow fever virus
- 1903 - rabies virus
- 1906 - variola virus
- 1908 - chicken leukemia virus, poliovirus
- 1911 - Rous sarcoma virus
- 1915 - bacteriophages
- 1933 - influenza virus

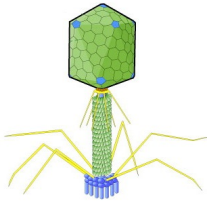


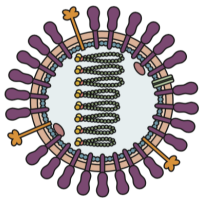












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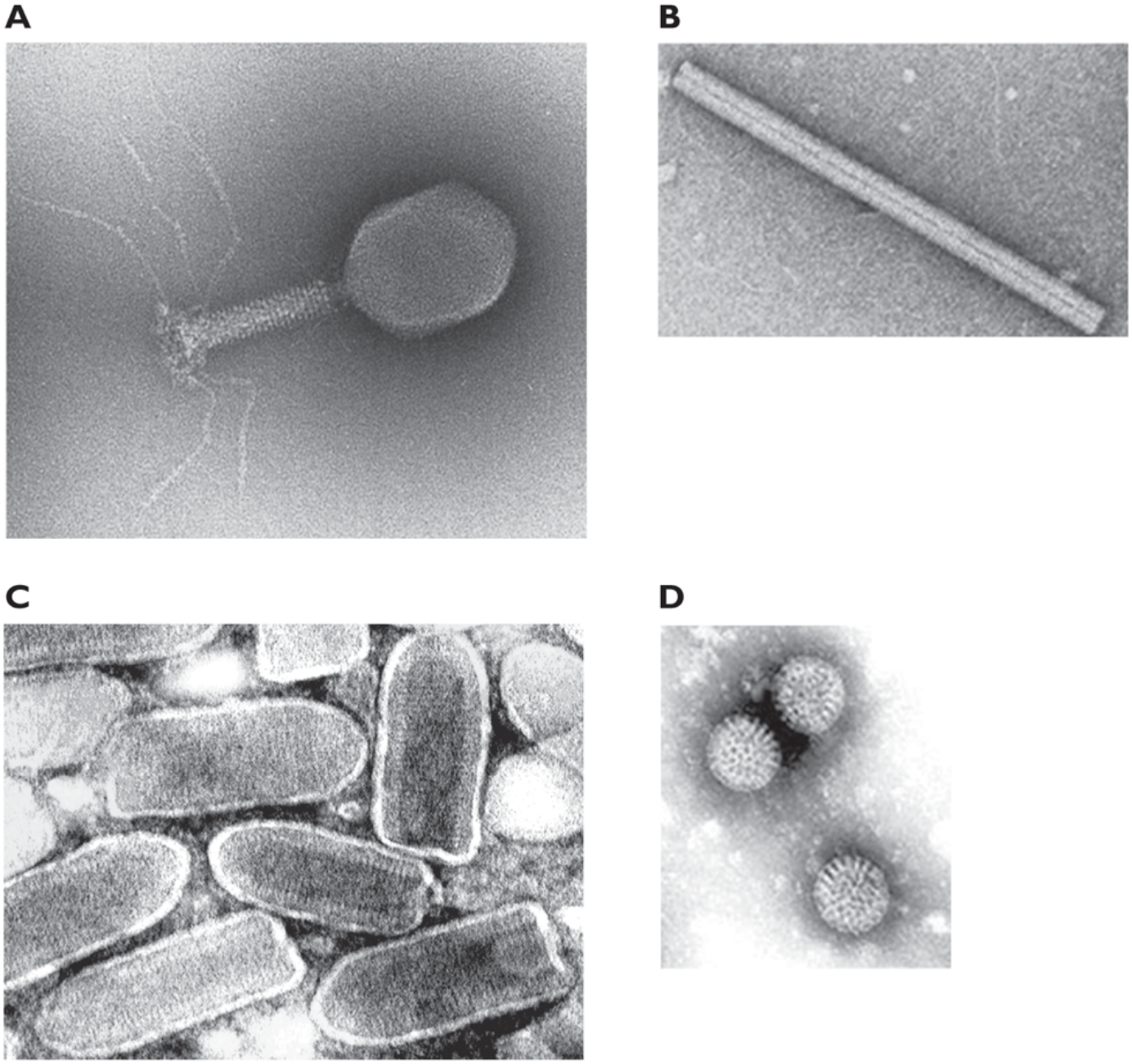
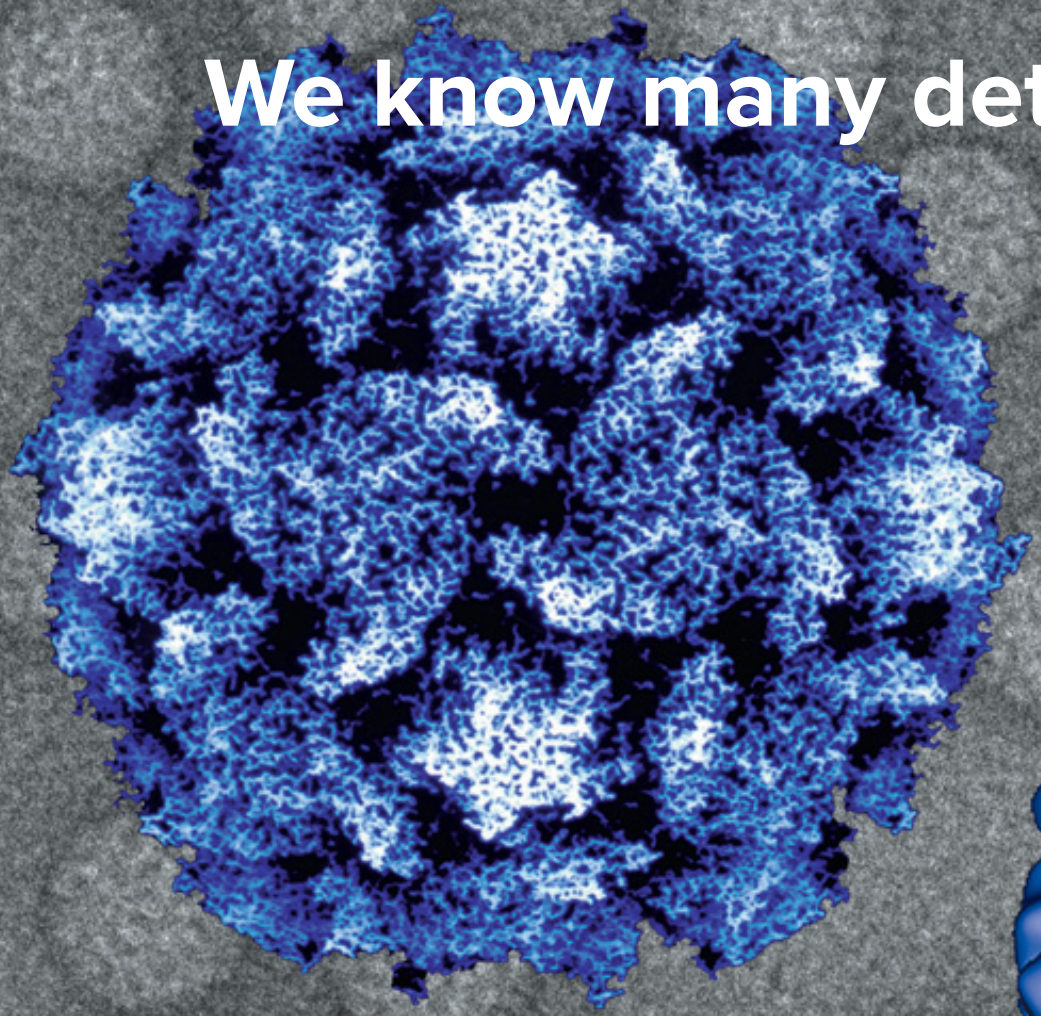
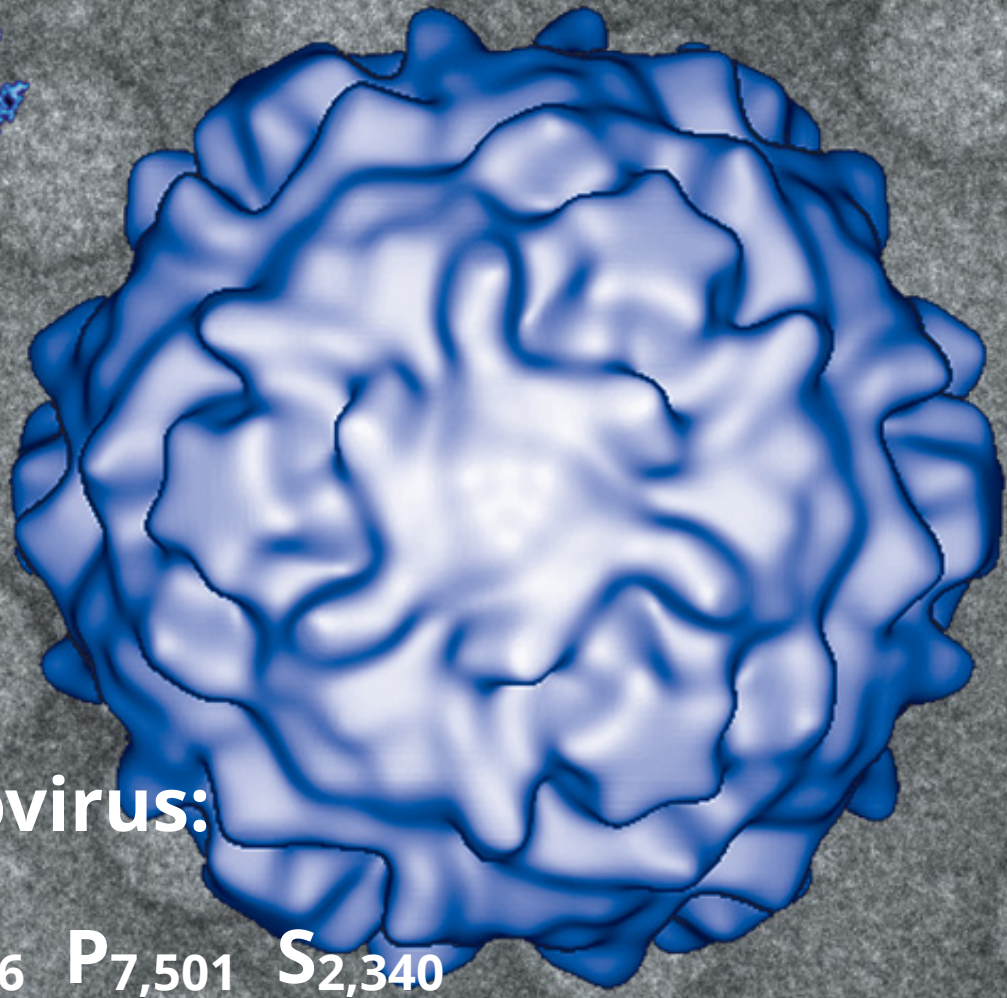
Which is a key concept first discovered about viruses that distinguished them from other microorganisms?

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



We know many details about viruses

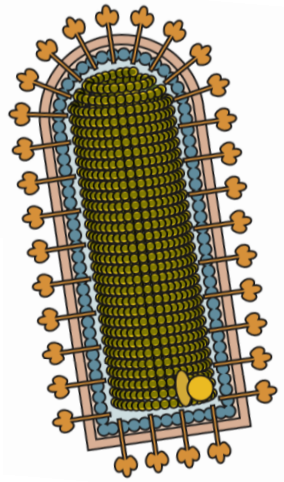
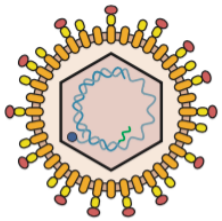
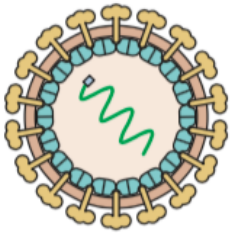
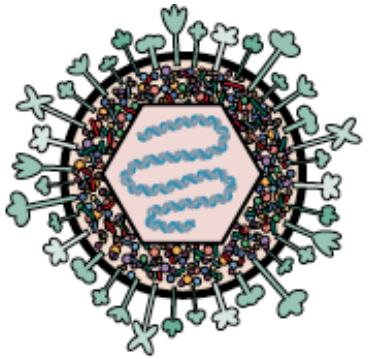
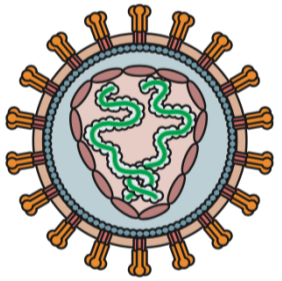
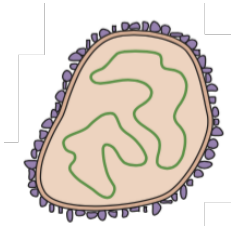
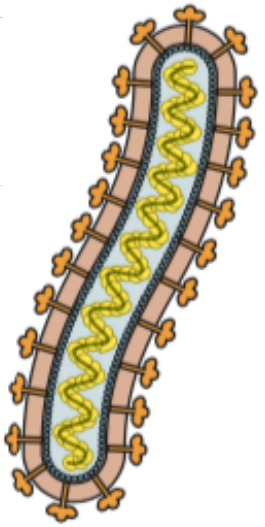




Chemical formula for poliovirus:

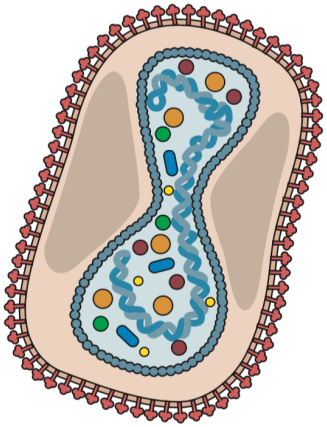
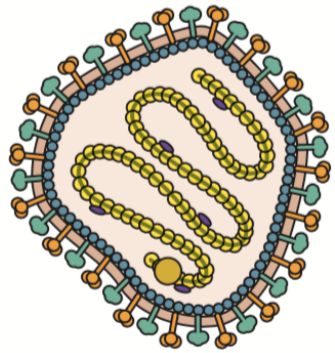
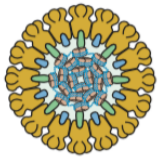
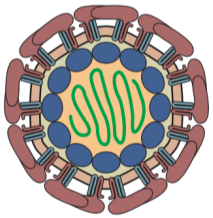
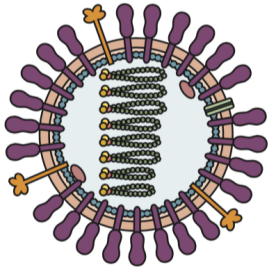
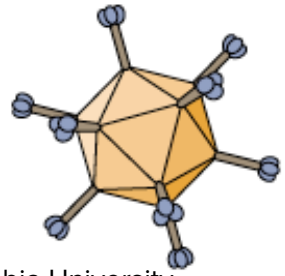
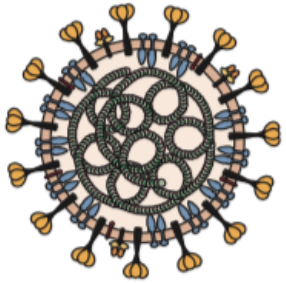
$C_{332,652}\ H_{492,388}\ N_{98,245}\ O_{131,196}\ P_{7,501}\ S_{2,340}$

Virus classification


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



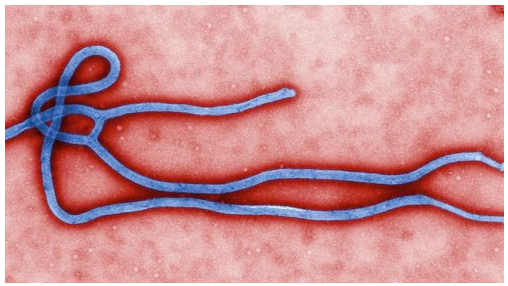








Virus classification

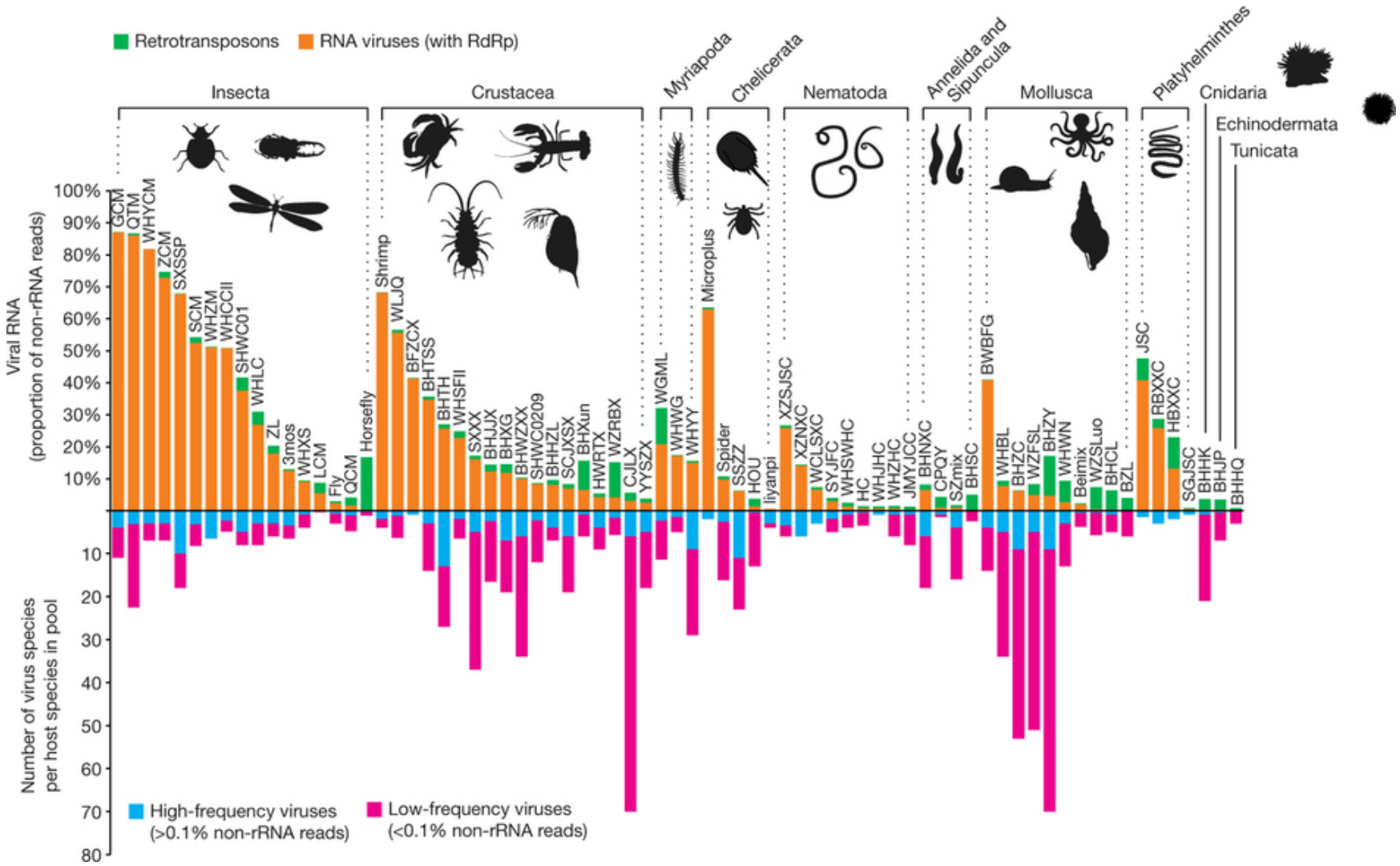
http://ictvonline.org/

Classical hierarchical system:

- Kingdom
- Phylum
- Class
- Order (-*virales*)
- Family (-*viridae*) — *Filoviridae* (filovirus family)
- Genus (-*virus*) — *Ebolavirus*
- Species — *Zaire ebolavirus*



Virus discovery



Analyzed RNA from 220 vertebrates species, found 1,445 new viruses.

http://www.nature.com/nature/journal/v540/n7634/full/nature20167.html

Why do we care?

- Viruses outnumber cellular life by at least 10:1: the greatest biodiversity on Earth
- Viruses drive global cycles
- 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