What is a virus?

Lecture 1
Biology 3310/4310
Spring 2019

“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

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Biology 3310/4310 - Virology

- courseworks2.columbia.edu
  - Schedule, lecture slides, study questions, readings, video, quiz, grading

- virology.ws/course

Course Syllabus

Lecture 1 - What is a virus?
Wednesday, 23 January 2019

Readings:
- Flint, Vol. I, Chapter 1
- The virus and the virion
- Cell size and scale
- Pandoravirus, bigger and unlike anything seen before

Files:
- Lecture 1 slides (pdf)
- Lecture 1 study questions (Word)
- Lecture 1 video - YouTube

Lecture 2 - The infectious cycle
Monday, 28 January 2019
Biology 3310/4310
Virology

Recommended Textbook: *Principles of Virology*

Sample chapter on Courseworks
RNA in circles

17 January 2019

The diversity of cellular RNA structure and function has progressed from the early days of molecular biology, when we thought only about mRNA, tRNA and ribosomal RNAs. Then RNA splicing was discovered along with the many small nuclear RNAs that mediate that process. Next came small interfering RNAs and microRNAs and long noncoding RNAs, master regulators of cell processes. The latest addition to the RNA toolbox are circular RNAs (circRNA), first found in viroids, then cells, and now encoded in the genomes of two herpesviruses.

Circular RNAs were first found to constitute the genetic information of viroids, unusual pathogens of plants that encode no protein. Later circular RNAs were found in uninfected cells, where they are produced by backsplicing: a downstream 5’-splice donor joins an upstream 3’-splice acceptor (illustrated). They have a number of diverse functions in cells, including acting as miRNA sponges, sequestering miRNAs

www.virology.ws

Virology Lectures 2019 • Prof. Vincent Racaniello • Columbia University

TWiV 531: Circ du RNA

January 20, 2019

Patrick Moore returns to TWiV to discuss the discovery from the Chang-Moore laboratory of circular RNAs in cells infected with herpesviruses.

Hosts: Vincent Racaniello, Dickson Despommier, Alan Dove, and Kathy Spindler

Guest: Patrick Moore

Click arrow to play
Download TWiV 530 (65 MB .mp3, 107 min)
Subscribe (free): iTunes, Google Podcasts, RSS, email

microbe.tv/twiv
Biology 3310/4310
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- Weekly quiz (Courseworks - up Sundays for 1 week)
- 4 exams (2/13, 3/6, 4/10, final)
- Discussion sessions (4310 only, TBA)
Biology 3310/4310
Virology

- Office hours: Thursdays 4–6 PM, HHSC 1310B, 701 W. 168th (Medical Center)
- Open format
- Appointments
- Questions during lecture
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)

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

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

Viruses are not just purveyors of bad news

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

DNA viruses
RNA viruses

Nervous system (>3)
Respiratory tract (>17)
Urogenital tract (>6)
Skin, hair, nails (>13)
Digestive tract (>19)
Blood (>19)
The Human Genome

- Protein-coding genes: 25.9%
- SINEs: 13.1%
- LINEs: 20.4%
- Miscellaneous unique sequences: 11.6%
- Miscellaneous heterochromatin: 8%
- Simple sequence repeats: 3%
- Segmental duplications: 5%
- DNA transposons: 2.9%
- LTR retrotransposons: 8.3%

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

Why not?
Most viruses just pass through us

We ingest many non-animal viruses regularly with foods

...in one study it was found that cabbage purchased from 5 different supermarkets in the Washington D.C. area were all contaminated with baculoviruses to such an extent that each serving (about 100 cm\(^2\) of leaf material) would contain up to \(10^8\) particles of a virus pathogenic for the cabbage looper

- Metagenomic analysis of RNA viruses in human feces reveal that most viral sequences are similar to plant viruses
- Of 36,769 sequences obtained, 25,040 (91\%) resembled plant viruses
- Most abundant human fecal virus: pepper mild mottle virus, \(10^9\) virions per gram of dry fecal matter.
The good 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 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
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
An infectious, obligate intracellular parasite comprising genetic material (DNA or RNA) 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?

Pick one:

Yes - (1967 votes)

No - (2170 votes)

They are something in between - (2020 votes)

I don't know - (301 votes)

Total Answers 6556

Total Votes 6555

http://www.virology.ws/are-viruses-alive/
The virus and the virion

*A virus is an organism with two phases*

**virion (infectious particle)**

**infected cell**
Be careful: Avoid anthropomorphistic 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

E. coli 100,000x

1,000,000x
How many viruses can fit on the head of a pin?

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

2 mm = 2000 microns
Not as small as we once thought!
Pandoravirus
Viruses replicate by assembly of pre-formed components into many particles

Make the parts, assemble the final product

*Not binary fission like cells*
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?

- 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
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:
\[ \text{C}_{332,652} \text{H}_{492,388} \text{N}_{98,245} \text{O}_{131,196} \text{P}_{7,501} \text{S}_{2,340} \]
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 - Once driven only by disease

Analyzed RNA from 220 invertebrate 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
Next time: The Infectious Cycle