What about viruses?

Truth is nobody really knows! Fact — much of the Eukaryotic genome is viral derived. “Viruses have been found in all cellular forms of life, from bacteria to chordates. Pathogenic human and animal viruses are causative agents of serious diseases such as AIDS, encephalitis, hepatitis, influenza, SARS, etc. Plant viruses are responsible for many major agricultural problems. Therefore, studying various viruses and their interaction with hosts is a prerequisite for finding remedies against viral diseases and understanding the principles of the organization of life.”

But where did they come from?

- Viral origins are unknown —
- Did they come before, or after cells;
- If after, are they degenerate cells, or ‘escapees’ from cells; Or maybe . . .
- They coevolved right along with cells.
- Who knows, but some very interesting recent work is leveraging the virus early hypotheses. For a great 2006 review see:

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1779534/?tool=pubmed
"A possible iterative scenario for viral eukaryogenesis and nuclear virogenesis. (a) A primitive DNA virus (a bacteriophage ancestor) gets trapped within an RNA cell and becomes a primitive nucleus. (b) Cellular genes are progressively recruited to the enlarging nucleus because of the selective advantages of DNA biochemistry. (c) For a while this situation remains unstable and reversible, allowing new 'pre-eukaryotic viruses' to be created. These viruses reinfect other cells at various stages of this iterative process. (d) This hypothetical scheme provides a mechanism for the emergence of various overlapping but not monophyletic virus lineages as well as for the rapid reassortment of genes from the viral and cellular pools before they reach their 'Darwinian threshold' [29], that is, (e) the evolution of a stable eukaryotic cell with a fully DNA nuclear genome."  [Link](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1779534/?tool=pubmed)
Regardless, what is a virus?

“A virus is a small, infectious, obligate intracellular parasite, capable of replicating itself in a host cell. Virions are formed by de novo assembly from newly synthesized components: the genome and a number of copies of at least one viral protein (capsid, or coat protein). Then the virions exit the cell and enter new cells, thereby beginning a new infectious cycle.”

“A viral genome consists of either single-stranded or double-stranded DNA or RNA in either linear or circular form, and can comprise one or more segments.”

What is a virus?

- Viruses are NOT cellular
- Obligate parasites of cellular life

Virus encounters cell
Virus injects genetic material
Virus hijacks cell metabolism to copy itself
Virus offspring released

protein shell
genetic material:
dsDNA
ssDNA
ssRNA
dsRNA

OK, what’s that mean?
Therefore, to summarize...

- A virus is an infectious agent much smaller than cells.
- All viruses have:
  - Genetic information encoded as either...
  - DNA or RNA, and either...
  - Single- or double stranded. They also have a...
  - Protein coat (capsid) made of capsomeres, which can be...
    - Spherical, icosahedral, rod-shaped, or oval.
- Some also have envelopes derived from host cell membranes.
- And there are 2000 or so known species (probably way more, but the species concept doesn't work very well here)!
There are lots of great references out there in the same sources we’ve been using all semester:

* [http://tolweb.org/Viruses/5](http://tolweb.org/Viruses/5)
* [http://www.ucmp.berkeley.edu/alllife/virus.html](http://www.ucmp.berkeley.edu/alllife/virus.html)
* And currently there are over 4000 viral reference genomes at NCBI!
Here’s a survey table of some human pathogenic ones. Don’t worry about memorizing which are which of these.

<table>
<thead>
<tr>
<th>DNA—Single Stranded</th>
</tr>
</thead>
<tbody>
<tr>
<td>B19 virus (erythema infectiosum)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>DNA—Double Stranded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variola major (smallpox)</td>
</tr>
<tr>
<td>Herpesviruses (oral and genital herpes; chickenpox)</td>
</tr>
<tr>
<td>Epstein–Barr virus (mononucleosis, Burkitt lymphoma)</td>
</tr>
<tr>
<td>Papillomaviruses (warts, cervical cancer)</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RNA—Single Stranded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human immunodeficiency virus (AIDS)</td>
</tr>
<tr>
<td>Coronaviruses (e.g., SARS)</td>
</tr>
<tr>
<td>Poliovirus</td>
</tr>
<tr>
<td>Influenza viruses</td>
</tr>
<tr>
<td>Measles virus</td>
</tr>
<tr>
<td>Mumps virus</td>
</tr>
<tr>
<td>Rabies virus</td>
</tr>
<tr>
<td>Ebola virus</td>
</tr>
<tr>
<td>Rhinovirus (common cold)</td>
</tr>
<tr>
<td>West Nile virus</td>
</tr>
<tr>
<td>Hepatitis A and C viruses</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RNA—Double Stranded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotavirus (respiratory and gastrointestinal infections)</td>
</tr>
</tbody>
</table>
They come in lots of sizes (but mainly pretty darn tiny) and shapes.
Some more examples...  

Virus Biodiversity

1 micrometer = $1/1000^{th}$ of a millimeter

(a) Vaccinia virus  
(b) Paramyxovirus (mumps)  
(c) Herpesvirus  
(d) Orf virus  
(e) Rhabdovirus  
(f) T-even coliphage  
(g) Flexuous-tailed phage  
(h) Adenovirus  
(i) Influenza virus  
(j) Polyomavirus  
(k) Picornavirus  
(l) φX174 phage  
(m) Tubulovirus
The viral “host range” is the type of organism a particular virus can infect.

- It requires very specific, membrane-bound receptor/attachment molecules. These...
- May be specific cells in several related organisms, or only in a specific organism.
- Animals, fungi, plants, protists, bacteria, archaea, all life forms, get viral infections!
- Reservoirs – carry a virus without symptoms while spreading the virus to other host species.
Most viruses are quite specific, but overall, all of life is susceptible.

Who do viruses attack?

- ALL cellular life

Eukaryotes

Eubacteria

Archaea
What is their habitat . . .

Where do viruses exist?

- Everywhere
- AND tend to outnumber other organisms at least 10-fold
Viruses

THerefore, viruses most numerous of Earth’s denizens

Human global population \( \approx 6,762,258,500 \) (as of July 29, 2009)

Viruses \( \approx 10^{31} \) \( (10,000,000,000,000,000,000,000,000,000) \) particles !!!

250 million light years of viral genes laid end to end
But are they alive?

- Most biologists do not consider viruses to be alive, because they . . .
- Do not metabolize, respond to stimuli, or reproduce on their own. However, they . . .
- Do have features in common with life:
  - They have genetic material, and . . .
  - They evolve (very quickly)!
- The extreme genetic diversity of viruses suggests they do not have a single common ancestor. But, who knows.
- They are not a part of any domain or kingdom.
- Viruses are assigned species, genera, and families, but no taxonomy higher than order (what does that mean?).
Viral replication  They must replicate inside living cells. (In labs, viruses are grown in host cells.)

There are five stages to most virus life cycles:

1. Attachment:
   * Attach to host cell by adhering to specific surface molecules.

2. Penetration:
   * Different methods exist – enzymes create holes, endocytosis, etc.

3. Synthesis:
   * The host cell provides all the resources such that the ...  
   * Viral genome is transcribed and translated.

4. Assembly:
   * The capsid subunits join, and the genetic information is packaged.

5. Release:
   * They may burst the cell, or enveloped viruses bud from the cell over time.
   * All together, this damages or destroys the host cell resulting in disease.
   * The time between infection and cell death varies greatly.
Here's the picture.

1 Attachment:
Virus binds cell surface receptor.

2 Penetration:
Viral nucleic acid is released inside host cell.

3 Synthesis:
Host cell manufactures viral nucleic acids and proteins.

4 Assembly:
New viruses are assembled from newly synthesized coat proteins, enzymes, and nucleic acids.

5 Release:
New viruses leave the host cell.
Bacteriophage T2 does it that way.

http://www.bio.fsu.edu/~stevet/VSU/animations/Chapter17/lifecycle_t2_phage.swf
So does T4 . . .

http://www.bio.fsu.edu/~stevet/VSU/animations/Chapter17/steps_in_replication_of_T4_phage_in_E_coli.swf
But not all of them – lytic or lysogenic?

* **Lytic infection:**
  * The virus enters the cell, and immediately replicates, which causes the cell to lyse releasing lots of new virus particles.

* **Lysogenic:**
  * The virus enters the cell. And...
  * Inserts its DNA (or RNA) into the host as a prophage (or provirus).
  * It can remain latent without causing symptoms.
  * And is copied along with host the DNA into new cells as the host cell replicates.
  * But eventually some signal causes the prophage (or provirus) to emerge and become lytic.
Which route to go?

Lysis occurs; new viruses released from host cell.

Viral DNA released in host cell.

Host cell produces viral proteins and viral DNA.

Viral proteins

Viral DNA incorporated in host chromosome as prophage.

Host chromosome replicates as cell divides.

(A) LYTIC PATHWAY

Host DNA

Virus infects new host cell.

Daughter cells carry integrated viral DNA.

(B) LYSOGENIC PATHWAY

Wednesday, March 14, 2012
And here’s the process in bacteriophage Lambda; it can go either way.

When phage Lambda infects E. coli, either the lytic or the lysogenic cycle may be followed. In both cases, the first step involves the phage attaching to the host cell and injecting its DNA into the host cell.

http://www.bio.fsu.edu/~stevet/VSU/animations/Chapter17/Lambda_phage_replication_cycle.swf
Some animal viruses can remain latent for years.

- And then emerge when possible or necessary to replicate. Examples include the . . .
- Herpesvirus, cold and/or genital sores; and . . .
- HIV, which is a retrovirus with an RNA genome.
- It penetrates helper T cells, and . . .
- Uses reverse transcriptase to make DNA.
- A persistent latent HIV infection may last years until some trigger causes a fully productive stage that can then destroy the immune system.
Other examples of human latent viruses include...

- Some strains of human papillomavirus (HPV), which cause genital warts, and can cause cervical cancer.
- New vaccines (Gardasil and Cervarix) can now protect us from them. See a great review at: http://caonline.amcancersoc.org/cgi/reprint/57/1/7.
- Epstein-Barr is another.
  - More than 80% of humans carry it, yet initial infections can cause mononucleosis, and sometimes eventually Burkitt lymphoma.
- Hepatitis C virus can also act that way, eventually causing liver cancer.
Here’s a diagram of HIV’s life cycle.

1. Virus binds receptors on cell membrane and enters cell. Enzymes remove viral protein coat.
2. RT catalyzes formation of DNA complementary to viral RNA.
3. New DNA strand serves as a template for complementary DNA strand.
4. Double-stranded DNA is incorporated into host cell's genome.
5. Viral genes transcribed to RNA. Some RNA will be packaged into new viruses.
6. Viral mRNA translated into HIV proteins at ribosomes in cytoplasm.
7. Protein coats surround viral RNA and enzymes.
8. New viruses bud from host cell.
And a nice animation of the same thing.

http://www.bio.fsu.edu/~stevet/VSU/animations/Chapter17/HIV_replication.swf
Effects of infection can be mild or so severe they are lethal.

* Different viruses have many different points of entry into a host’s body.
* They can be inhaled or ingested; they can be transferred by blood transfusion, sexual contact, birth, or insect vector; etc.
* The death of infected cells produces symptoms based on the kind and number of host cells that are destroyed.
* The host’s immune response to the infection can also cause symptoms – fever, aches, pains, etc.
Drugs and vaccines

* Antibiotics do not work against viruses!
* It is difficult to develop drugs against viruses, but a few exist, e.g. Tamiflu (http://en.wikipedia.org/wiki/Antiviral_drug).
* It’s complicated by the huge genetic variability and ultra-fast evolution of viruses.
* Vaccination is by far our most potent weapon!
* It ‘teaches’ the immune system to recognize components of the invader.
* Smallpox and polio vaccinations are highly effective. But we are . . .
* Unable to develop vaccinations against all viruses, because so many of them evolve so quickly.
Plant viruses

- Most use plant-eating insects to enter the host.
- They spread through plasmodesmata and vascular tissues.
- Symptoms may include blotchy leaves and/or abnormal growth.
- Plants don’t have an immune system like ours, but can fight viral infections with . . .
- Posttranscriptional gene silencing, which prevents the expression of viral genomes.
Viriods are a... Highly wound circle of naked RNA that lacks a protein coat.

- The coil double-strands with itself to help prevent the host cell from degrading it.
- Even though they don’t code for any proteins, they...
- Can cause severe disease in plants and ruin crops.
Prions are the strangest.

- They are not a virus or viroid. They are a protein.
- The prion molecule is responsible for a debilitating disease in animals, and yet is encoded by the organism’s own DNA; it may be involved in cell-cell communication in the brain. The gene is expressed in both normal and afflicted cells. Prion stands for . . .
- Proteinaceous infectious particle or PrP. The . . .
- Protein can exist in several conformations.
- The normal structural conformation is in animals’ brains and spinal cords all the time. But . . .
- Others are infectious because they can convert the normal conformation into the infectious one.
- It becomes a chain reaction in which abnormal PrP molecules trigger the normal PrPs to change.
Abnormal prions cause disease.

* It can occur in more than 80 types of mammals.
* Large amounts of proteinaceous plaques aggregate and are deposited in the brains of afflicted animals, and the brain becomes riddled with holes like a sponge.
* In humans it’s a rare condition called:
  * Kuru, which is associated with cannibalism, or
  * Creutzfeldt-Jakob disease (CJD), or
  * Gerstmann-Straussler Syndrome. It is also involved in . . .
  * Fatal Familial Insomnia (Seventeen inheritable pathologic allelic variants are listed in OMIM).
* Mad cow disease is bovine spongiform encephalopathy (BSE), which humans can get from infected beef.
* And in sheep it’s called scrapie (that’s where PrPSc comes from).
A ‘mad’ dead cow and the typical plagues and holes of afflicted animal’s brains.
Prions are so very weird.

There is evidence that the infectious agent associated with certain brain diseases such as Creutzfeldt-Jakob disease in humans and mad cow disease in animals may be caused by a protein.

http://www.bio.fsu.edu/~stevet/VSU/animations/Chapter17/prions.swf
What can we do?

* It is acquired by ingesting or receiving a transplant of infected material (abnormal prion molecules). No nucleic acid is associated with the infectivity!

* Heat, radiation, and chemical treatments to destroy viruses and bacteria do not affect prions at all!

* Therefore, many precautions have been implemented to keep animal brains and spinal cords out of both human and other animal food.

* Stanley Prusiner won the Nobel Prize for his work on this system in 1997. See his article for more:

http://www.sciencemag.org/feature/data/prusiner/245.dtl
OK, next time . . .

* We’ll review all this Eukaryotic diversity in preparation for Exam IV.

* Remember — it’s the major concepts that matter, not all the technical Latin names.

* Yes, know what critters are in what groups, with what characteristics, but I’ll provide ‘hints’ regarding the group names.

* And it’s all easier, if you can keep track of them on the Tree of Life!