Marine Viruses –
There are good viruses!

Mom: Will I get infected by viruses if I swim in the ocean?

A hospital in Kansas during the flu epidemic in 1918. From the U.S. National Museum of Health and Medicine. https://en.wikipedia.org/wiki/Spanish_flu

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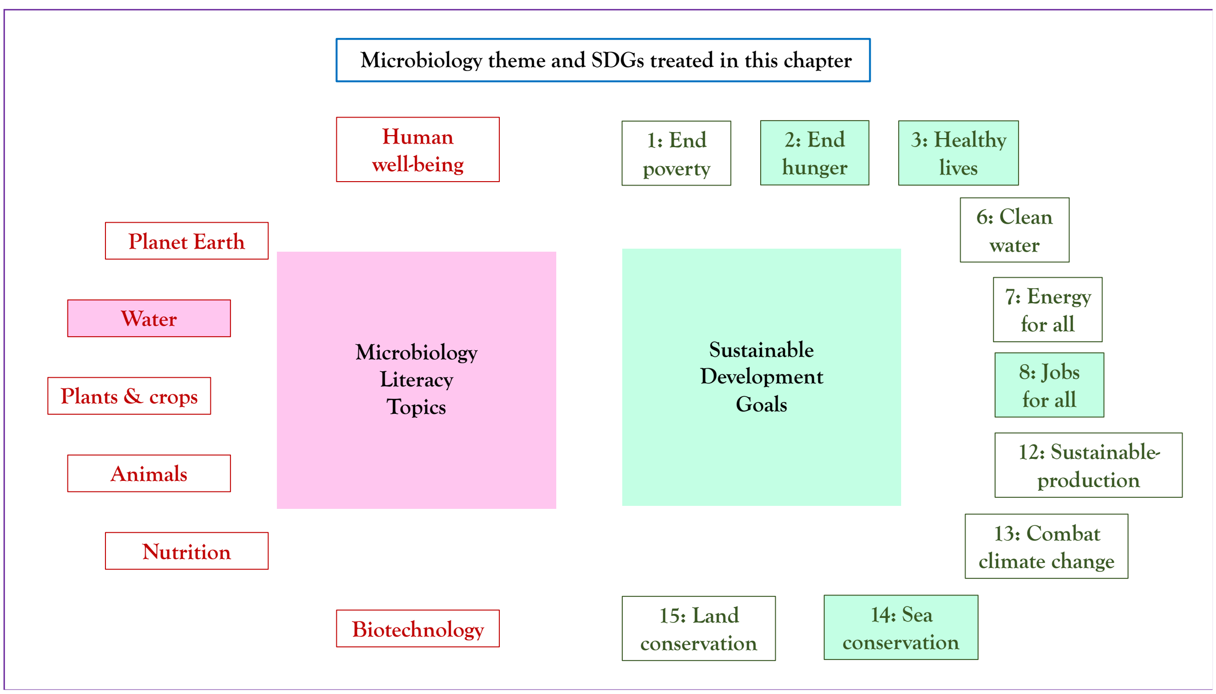
Marine Viruses

Storyline

Because of Covid-19, AIDS, influenza, and other diseases, we are all too familiar with viruses as pathogens. But most viruses are not human pathogens. Natural habitats are home to vast numbers of viruses that do not infect humans or the animals and plants we value. These viruses are a natural part of food webs and are important in nutrient cycling that supports all life on the planet. Here we'll focus on viruses in the oceans because we know more about marine viruses than viruses in other natural habitats. Viruses help the oceans provide fish and shellfish – protein-rich food – to billions of people around the world.

The Microbiology and Societal Context

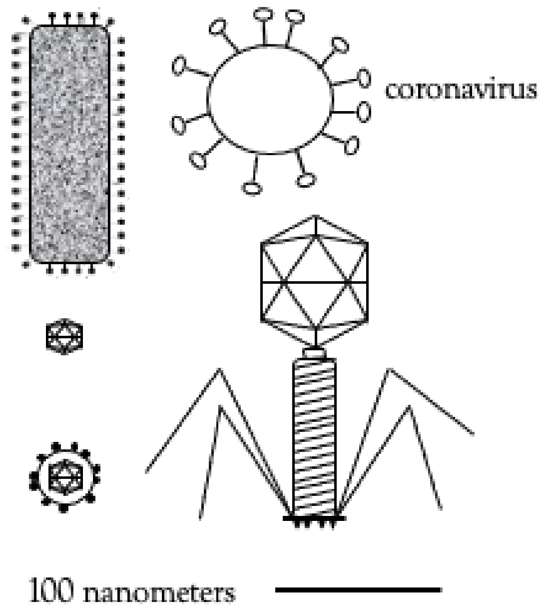
The Microbiology: virus abundance in natural environments; virus life cycle; control of microbial populations in the oceans; nutrient cycling; harmful algae control; transfer of genetic material. *Sustainability issues*: end hunger; healthy lives; employment for all; sea conservation.



Marine viruses: the Microbiology

1. ***What are viruses and what do they look like?*** Some viruses appear to be complicated, with shapes like a lunar landing module and outer surfaces studded with proteins, like the coronavirus causing Covid-19. But at heart, a virus is very simple. It consists of genetic material, either DNA or RNA, surrounded by a protein coat; some viruses have an additional protective layer of lipids. What they don't have are enzymes and all the other things cells need to gain

energy for survival and reproduction. For that reason, a virus is an obligate parasite. It must invade a cell and hijack its metabolism to make more viruses. When that cell is one of ours, the virus may cause a disease. But when that cell is a microbe living in a natural habitat, the virus contributes to many ecological processes maintaining the environmental health of a habitat. Regardless of the cell type, viruses are essential in the ecology and evolution of all organisms.

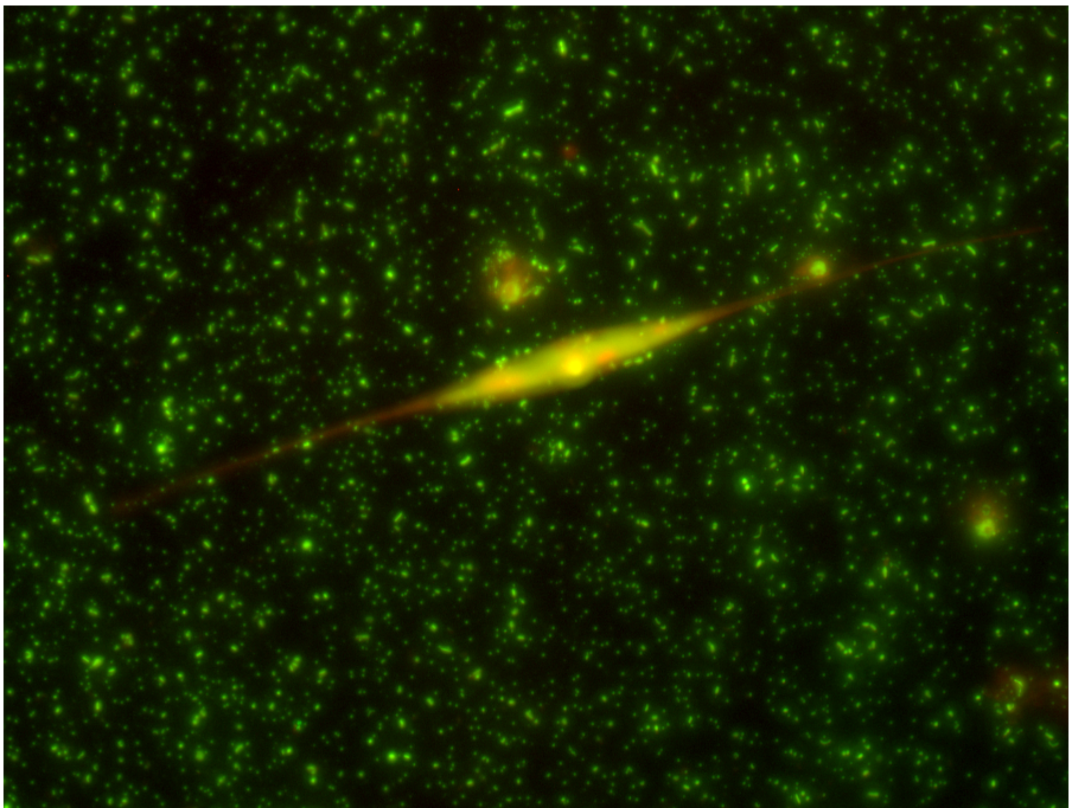


Some examples of viruses. The size of viruses varies greatly from a few nanometers to 1000 nanometers (1 micron), as big as some bacteria. A human blood is 100,000 nanometers (100 microns). A coronavirus causes Covid-19.

2. ***The bad reputation of viruses is undeserved.*** Viruses are all too familiar as pathogens that have killed uncountable numbers of people throughout history. Before being eradicated in the 1970s, the smallpox virus claimed hundreds of millions of victims over millennia, and between 1918 and 1920, the death toll of the Spanish influenza was as many as 100 million. More recently, the human immunodeficiency virus (HIV) that causes AIDS has killed over 30 million worldwide. Other viral diseases include Ebola, the common cold and seasonal influenza, herpes and cold sores, measles, mumps, chicken pox, and shingles. Then there is the SARS-CoV-2 virus and the Covid-19 pandemic.

There is another side to viruses that is less familiar to most people. More than just being pathogens, viruses are integral part of the evolution and the ecology of all organisms. Although too many viruses are "bad" and are deadly killers, by far most are important in natural environments and even in our own bodies.

3. ***Viruses are everywhere and are very abundant.*** There are many viruses in every habitat on Earth and in apparently healthy plants and animals, including humans. The human intestinal tract may harbor more than 1,000,000,000,000 viruses, or 10^{12} in scientific notation. (A thousand is 10^3, a million 10^6, and a billion 10^9.) More than just our gut, viruses are found in and on just about every part of the human body, from our skin and mouth to even our spinal fluid. Natural environments have even more viruses. One study estimated that the oceans, soils, and deep subterranean habitats each have roughly 10^{30} viruses. Altogether, Earth has about 10^{31} viruses, many more than sand grains on earth (10^{19}) or stars in the observable universe (5×10^{22}). One viral ecologist calculated that all viruses laid end to end would extend past the nearest 60 galaxies.



Viruses in the ocean. The smallest dots are viruses, which are about 10 times more abundant than the big dots, which are bacteria. The large oblong object is an alga. At this scale algae and other microbes are rarely visible. From Gunnar Bratbak, University of Bergen.

4. ***Most viruses are not human pathogens.*** Because they are everywhere, we breathe in hundreds of viruses every minute and ingest even more when we eat or drink. Viruses abound in lakes and oceans where we swim and fish, and in the soils where we garden, grow crops, raise livestock, or just walk. Despite being surrounded by these viruses, we don't get sick (except sometimes encountering a polluted habitat), because the vast majority of viruses are not human pathogens. A substantial number of viruses, over 250, are thought to be deleterious to us, but that's a tiny portion of the millions known or suspected viral types on the planet. Most viruses do not attack us nor the animals and plants we depend on or admire.

Most viruses infect the most abundant cellular organism on Earth, bacteria. These viruses are called "bacteriophages" or just "phages." ("Phage" is from the Greek for "to eat," so these viruses are "bacteria eaters.") There are many more bacteria in just a few liters of water or grams of soil than there are people on Earth. Each liter of water and gram of soil has about a billion bacteria, yet there are even more viruses in these natural habitats. There are roughly 10 viruses for each bacterium, although that ratio varies a lot for reasons not entirely understood by microbial ecologists. So, most viruses have specialized to attack the over 10^{30} bacteria on Earth rather than bothering with less numerous organisms, such as the 8 X 10^9 humans. Nearly all viruses in the human body are in the intestinal tract, which is where most of their victims, the bacteria, can be found.

5. ***Viruses specialize in infecting one type of host.*** Viruses can only reproduce by infecting a living cell, what virologists call a "host." A virus has only genetic material, a nucleic acid, tucked away in a protein capsid, sometimes enveloped in a membrane stolen from a previous victim. A virus needs to invade a living cell with its genetic material, because it can't do anything on its own. It doesn't have the molecular machinery necessary to use or generate energy, to synthesize its own nucleic acids and proteins, or to do much of anything else. Away from cells, a virus is inert, without any sign of life, neither taking things in from the environment nor excreting waste products. There has been much debate about whether a virus can be considered a form of life or a lifeless chemical.

How a virus infects a host varies from virus to virus, but the overall strategy is roughly the same. Because a virus can't move on its own, it must rely on water, air, or an organism to carry it to an appropriate host cell. Once the virus bumps into its host, the virus then relies on stealth to get past the cell's membrane barrier, using proteins to attach to specific spots, or "receptors," on the host cell membrane. In the case of Covid-19, the spike protein of the coronavirus attaches, or binds to angiotensin-converting enzyme 2 (ACE2) located on the surface of epithelial cells in humans. This molecular match-up between virus protein and cell receptor then then triggers a process that ferries either the intact virus or its genetic material into the cell.

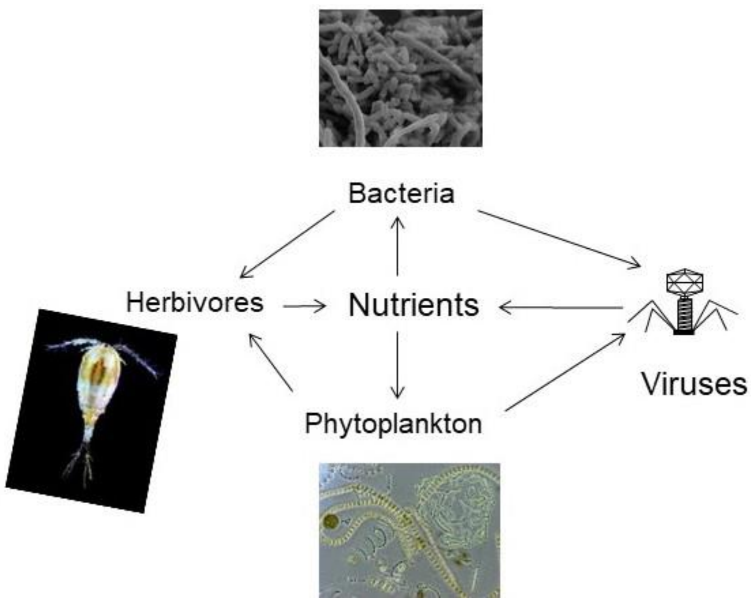
The molecular match-up is like inserting a key (the virus protein) into a lock (the receptor on the cell membrane of the host). If the key or the lock change, there is no match-up and no infection by the virus. For this reason, a virus usually can attack only one type of host. Phages cannot attack a human cell, and likewise bacteria have nothing to fear from the Covid-19 virus or other human pathogenic viruses. However, some viruses can infect closely related hosts, and microbial ecologists are trying to figure out the host range for the many viruses in natural habitats.

Moreover, mutations in the virus genetic information can change its receptor-binding protein, thereby enabling the virus to evolve and infect new hosts. For example, the original host for the Covid-19 virus was probably a type of bat before it "spilled over" to humans. Mutations also allow the virus to change its transmissibility in the same host, as we have seen in the COVID-19 pandemic.

6. ***Marine viruses keep microbial numbers in check and contribute to nutrient cycling.*** After the virus gets past the host cell membrane, it may hide out within the cell before doing anything else. Eventually, however, in order to reproduce, the virus must hijack the host cell's metabolism and command the cell to make more viruses. For some types of viruses, newly formed

viruses can escape the host cell without disrupting the cell, but for many marine phages, the virus escapes by breaking the bacterium open, spewing out tens to hundreds of new viruses into the surrounding environment. The host cell is killed, or "lysed" during the virus's escape. Viral lysis is thought to account for roughly half of bacterial mortality in the oceans. (The other half is due to predation by protozoa.) In short, phages help to keep bacteria from overrunning the oceans.

Other viruses also infect phytoplankton, the plant-like microbes at the base of aquatic food chains. A phytoplankton cell lysed by a virus takes away food for the next trophic level, the herbivores, which has negative consequences for the entire food chain. Some phytoplankton, however, are toxic and form harmful algal blooms that can cause fish kills and sicken even animals on land, including humans. Most such coastal blooms are caused by nitrogen and phosphorus fertilizer run-off from agricultural land into surface waters, many of which drain into the sea, and can severely impact commercial finfish and shellfish operations, as well as tourist activities like swimming and snorkeling. Viruses are known to curtail these blooms and prevent them from further damaging coastal habitats.



Release of nutrients by viruses. When viruses lyse a cell, it releases nutrients that can be used by phytoplankton and bacteria.

The impact of viruses on the bacteria or phytoplankton they infect isn't "good" (they die), but the other, uninfected organisms can greatly benefit. Viral lysis releases not only new viruses but also the cellular contents of the doomed cell. These contents contain valuable nutrients needed to sustain bacterial and phytoplankton growth and to keep marine food chains running.

7. ***Marine viruses are a way for bacteria and other organisms to have sex.*** The standard way in which genetic information is exchanged and passed down from one generation to another, that is to say, sex, is through the mating of male and female from the same species. The offspring from sexual reproduction have a mix of genes from their male and female parents. Bacteria and

several other microbes are incapable of sexual reproduction and reproduce only when one cell divides into two; this is asexual reproduction. Unlike sexual reproduction, offspring from asexual reproduction have the same genes as the original parent cell (assuming no mutations have occurred).

Viruses can be a form of sex for bacteria and other microbes. Viruses can be the vessels by which genes are exchanged sometimes even between unrelated organisms. Viruses can pick up some of their host's genetic material (DNA) during the synthesis of new viruses, which then ferry genes from the old host to new ones. Virologists call this form of genetic transfer "transduction." If the genes from the old host are not present in the new one, transduction gives the new host novel metabolic capabilities. A virus can also have its own version of a gene already present in a host. For example, a virus that infects a type of phytoplankton (cyanobacteria) carries its own version of a gene involved in photosynthesis and primary production. It has been estimated that this viral photosynthesis gene accounts for roughly 10 percent of primary production in the ocean.

8. ***Viruses profoundly affect evolution.*** Scientists see the impact of transduction in the genomes of bacteria and other organisms. Many genes are similar to those in an organism's ancestors, and the familial relationships between these organisms can be presented in a tree, such as the one Darwin first sketched out while writing *On the Origin of Species*. These genes are said to be vertically transmitted. However, the genes introduced by transduction stand out as being different and are more similar to those in a distantly related organism than to a close relative's genes. These genes are said to have undergone "horizontal gene transfer," also called "lateral gene transfer." Because of horizontal gene transfer, a simple tree doesn't adequately depict the taxonomic and evolutionary relationships among organisms. The tree is at least tangled, or perhaps a bush is a better model. Transduction is one mechanism effecting this form of gene transfer and mode of evolution.

The fingerprints of viruses are found not only in the genomes of bacteria, but also in all organisms, including humans. It has been estimated that maybe as much as eight percent of the human genome is from viruses. One current hypothesis is that viruses enabled the evolution of the human placenta. Viruses house a huge amount of genetic diversity that is the raw material for evolution.

Relevance for Sustainable Development Goals and Grand Challenges

- **Goal 2. End hunger, achieve food security and improved nutrition and promote sustainable agriculture**. Viruses play a key role in biomass turnover and nutrient recycling in the oceans and hence in marine food webs and, as such, contribute significantly to providing food, in particular finfish and shellfish, for humans and for farm animals.
- **Goal 3. Ensure healthy lives and promote well-being for all at all ages.** Viruses help to maintain the balance in coastal waters that are threatened by nitrogen and phosphorus fertilizer used in agriculture. These fertilizers run off into surface waters that ultimately drain into the sea, where they cause blooms of algae and cyanobacteria, some of which produce nasty toxins. Fish and other animals, including us, get sick when we swim in water containing toxic microbes. Moreover, filter-feeding shellfish can take in and accumulate these toxic microbes and

subsequently pass them on to organisms higher in the food chain, some of which we eat. Thus, not only does marine wildlife get ill from toxic microbes, but land organisms like us that eat seafood can too. By infecting toxic algae and cyanobacteria, viruses curtail toxic blooms and reduce health risks for us.

- **Goal 8. Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all**. With help from viruses, microbes are not only major contributors to marine food resources, and hence to the industries and sources of employment based upon fishing, but they are also essential for maintaining marine water quality. By degrading pollutants such sewage, petroleum, and industrial chemicals, microbes help to keep marine ecosystems healthy. And viruses help keep microbial communities healthy. A healthy coastal marine ecosystem is essential for tourism, which is a major employer and a large source of financial support for some countries.
- **Goal 14. Conserve and sustainably use the oceans, seas and marine resources for sustainable development**. The metabolic activities of microbes, modulated by viruses, are responsible for maintaining the water quality of marine systems and are crucial for the removal of pollutants originating in agriculture and industry. Viruses play a key role in biomass turnover and cycling in the oceans and hence in maintaining a healthy marine ecosystem.

Exercises

1. Using the information presented above, calculate the number of viruses in a liter of seawater and in a gram of soil.
2. A virus varies greatly in size from 20 nanometers (a nanometer is 10^{-6} meters) to giants about 1000 nanometers long. Assuming a virus is 200 nanometers, how many would be needed to make a pile as tall as the Eiffel Tower (324 meters)?
3. One virus-caused disease, hepatitis, can be contracted by eating raw shellfish, especially oysters, which feed on microbes and other particles in seawater. However, hepatitis is only a problem if the oysters live in water contaminated by human waste. Why is raw shellfish from pristine habitats safe to eat even though it contains a lot of viruses?

The Evidence Base, Further Reading and Teaching Aids

Lecture on viral ecology: https://www.youtube.com/watch?v=8jDqUcnBotk
Popular science article about marine viruses: https://theconversation.com/marine-viruses-the-tiny-microbes-that-orchestrate-life-in-the-ocean-153311
Popular science book about viruses: https://carlzimmer.com/books/a-planet-of-viruses/
Review of marine viruses, written for scientists: https://www.nature.com/articles/nrmicro1750
https://www.cshl.edu/the-non-human-living-inside-of-you/
https://www.nytimes.com/2017/10/04/science/ancient-viruses-dna-genome.html
https://whyy.org/segments/the-placenta-went-viral-and-protomammals-were-born/

Glossary

Bacteriophage, or phage: a virus that infects bacteria
capsid: the protein coat used by viruses to protect its genetic material, which also contains proteins to gain entry into its host
harmful algal blooms: large accumulation of algae that is deleterious to other organisms and the habitat
host: the cell invaded by a virus, which is hijacked to make more viruses
horizontal gene transfer: the exchange of a gene between distantly related organisms, such as mediated by transduction
lysis: the breaking of a cell when a virus needs to escape into the surrounding environment
microbial ecology: the study of microbes, including viruses in natural environments
phytoplankton: free-floating algae or plant-like microbes that carry out photosynthesis in aquatic habitats
protozoa: a type of microbe with a metabolism similar to an animal's
transduction: the transfer of an old host gene to a new host effected by a virus
virology: the study of viruses