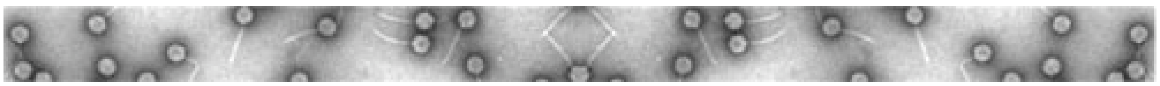
Background

The following is from the American Society of Microbiologists website on bacteriophages. Other reference articles are available on the server.

Division M: Bacteriophage



Division M is composed of researchers and teachers dedicated to the study of bacterial viruses. Current topics of interest are: assembly and structure, genome structure, initiation of infection, regulation of transcription and translation, replication, recombination, repair, virus-host interactions, new phage systems, molecular cloning technology, and bacteriophage evolution.

What is a bacteriophage, anyway?

Members of Division M certainly know what bacteriophages are, but other readers of this page may wonder what it is about these tiny microorganisms that would make so many scientists devote their professional lives to understanding how they work. This part of the site provides a brief primer for the uninitiated about what bacteriophages are, what they do, and what they do for us; and gives a quick refresher for those who once knew something about bacteriophages. Teachers who wish to include bacteriophages in their curricula will find some useful links in our "Resources for teachers", "Books", and "Links" pages.

- What is a bacteriophage—the basics
- Abundance & variety of bacteriophages
- History of bacteriophage research
- The practical phage— Human uses of bacteriophages

What is a bacteriophage?—the basics

Bacteriophages ("phages" for short) are viruses whose hosts are bacterial cells. Like all viruses, phages are metabolically inert in their extracellular form (the "virion"), and they reproduce by insinuating themselves into the metabolism of the host. The mechanisms by which phage virions infect their host cells—described in more detail below—vary among the different types of phages, but they all result in delivery of the phage genome into the cytoplasm of the bacterial host, where it interacts with the cellular machinery to carry the phage life cycle forward. The result of infection can be, and often is, total devastation for the cell. A good example of this is infection by the *E. coli* phage T4, the *Tyrannosaurus rex* of phages, which commandeers the material and energetic resources of the cell and turns them toward making more virions, after which it causes violent lysis of the cell and release of the progeny virions. At another extreme, the large group of phages known as temperate phages have the option when they infect of setting up a state of coexistence with the host ("lysogeny") in which the genes that would harm the host are prevented from being expressed, while a small set of genes that provide benefit to the host are expressed. Both scenarios result in replication and perpetuation of the bacteriophage.

Follow this link for guidance on pronouncing the words 'bacteriophage' and 'phage'.

Abundance and variety of bacteriophages

There are probably more individual bacteriophages in the biosphere than there are of any other group of organisms, including all the prokaryotes. Until recently nobody knew how to get even an approximate estimate of how many phages there are, but a little over ten years ago, it occurred to someone that at least for the best studied group of phages, the tailed phages, their shape is so distinctive that their numbers in aquatic environments could be estimated simply by centrifuging them onto an electron microscope sample grid and counting them. Astonishingly, in coastal sea water there are typically as many as 10^7 (ten million) tailed phages per milliliter. In some fresh water sources there are up to 10^9 (a billion) per milliliter. Although there is still little information about how uniform is the distribution of phages around the globe, these numbers give at least a rough basis for calculating the global population. The remarkable result of such a calculation is that there may be as many as 10^{30} tailed phage globally. For people who like their numbers written out, that's 1,000,000,000,000,000,000,000,000,000,000. If you were to gather them all up and weigh them, they would outweigh the world population of elephants by a thousand-fold or more.

The tailed phages are also known as the dsDNA tailed phages because their genomes are molecules of linear double-stranded DNA.

Their genomes are relatively large for viruses, with most of them in the vicinity of 50 kbp (50,000 base pairs). However, some are less than 20 kbp, the common and well studied 'T4-like' group is more like 160 kbp, and bacteriophage G is the largest virus on record, with a genome of nearly 500 kbp—bigger than the smallest bacterial genomes.

Although the dsDNA tailed phages account for about 95% of all phages reported in the scientific literature, and may in fact make up the majority of phages on the planet, there are other phages that occur abundantly in the Biosphere sporting very different virions, genomes, and lifestyles. These are listed in more detail in the "Phage Facts & Portraits" pages on this site, but they include phages with ssDNA, ssRNA, or segmented dsRNA genomes, virions with and those without membrane components, and many other differences. In fact, the diversity of phages is at least as great as the diversity of plant and animal viruses, in keeping with the probability that phages and viruses of eukaryotes share common ancestry.

History of bacteriophage research

Bacteriophages were discovered a little over 80 years ago—in 1915 by the Englishman Frederick Twort and independently in 1917 by the French Canadian Félix D'Herelle. Initial research on phage was concerned with defining the nature of the bacteriophage—the two leading theories being that it was a filterable virus, like the Tobacco Mosaic Virus that had been discovered some 20 years earlier, or a self-perpetuating enzyme whose expression caused destruction of the bacterial cell.

Regardless of the exact nature of the bacteriophage, it was quickly realized that bacteriophages had the potential to kill the bacteria that cause many infectious diseases in humans, as well as in agriculturally important plants and animals. This idea formed the basis for much research as well as for the Pulitzer Prize-winning 1924 novel Arrowsmith by Sinclair Lewis (still a good read). Félix D'Herelle in particular was a champion of the potential for therapeutic uses of phage, which he promoted vigorously. In 1933, D'Herelle co-founded an institute for phage research in the Soviet Republic of Georgia, together with Georgian microbiologist George Eliava. Although Eliava was killed in one of Stalin's purges in 1937, and D'Herelle never returned, the G. Eliava Institute of Bacteriophage survived and continued to supply phage for therapeutic uses to the entire Soviet Union until the recent breakup of the Soviet Union. In the West, research on such 'phage therapy' was dropped when penicillin and other chemical antibiotics were discovered starting in the 1940's, though there has been some renewed interest in phage therapy in recent years as antibiotic resistance of pathogenic bacteria has become a more prominent threat to public health.

Meanwhile, bacteriophage research continued. The viral nature of the bacteriophage was clearly established, the chemical composition of the virions (the extracellular virus particles) was measured and shown to be protein and DNA, new phages infecting a variety of bacterial hosts were isolated, and some rudimentary progress was made in understanding the virus life cycle. The first electron micrographs of phages, showing a tadpole-like shape, were obtained in 1942 by Tom Anderson.

The 'modern' era of bacteriophage research is usually dated from 1938 when the expatriate German physicist, Max Delbrück, began his work on phages at the California Institute of Technology. Salvadore Luria, an Italian expatriate at Indiana University (later at MIT) and Al Hershey, an American at Vanderbilt University (later at Cold Spring Harbor) soon joined Delbrück in pursuing bacteriophage research as a route to understanding the most fundamental features of biological life.

Phages soon became central players in the foundation of the discipline that later came to be known as molecular biology (the Journal of Molecular Biology started publication in 1959). Through the 1950's and 1960's, phage research had a dominant role in elucidating the most fundamental facts about what genes are and how the information in genes is read out to determine the properties of an organism. An underlying assumption (and justification) of the early phage molecular biologists was that the principles of life that could be learned from phages would also apply to other forms of life. As it has become clear in subsequent decades just how remarkably correct that assumption was, it has become similarly clear that the history of phage biology is a major and essential part of the modern history of biology as a whole.

The astonishing success of bacteriophage research over the 25-30 years prior to about 1970 in revealing the fundamental 'secrets of life' can be attributed largely to the fact that phages are so tractable as experimental systems. That is, they are genetically and structurally simple, they have a short life cycle that can be synchronized in a population, and genetic, biochemical, and structural approaches can be applied synergistically. The fact that phages interact intimately with their bacterial hosts means that virtually everything that is learned about phages is also informative about the bacterial cells they infect, and often about even broader biological questions.

Around 1970 the world of biological research began to be transformed by the ‘ recombinant DNA revolution’, with which it becomes possible to effectively change a gene from any organism—no matter how complex or how eukaryotic—into a phage gene. The suite of laboratory techniques that made this revolution possible was developed largely through research on phages (with, of course, major contributions from research directed at their bacterial hosts and their genetic cousins, the plasmids). The recombinant DNA revolution has produced some profound changes in bacteriophage research, as in all other areas of biological research. For one thing, the number of researchers working primarily on phages decreased precipitously as it became possible to study the genes of more complex—particularly eukaryotic—organisms with nearly the same ease as had been possible previously primarily with phages and bacteria. At the same time, the number of biological researchers using some form of phage in their research has increased substantially, since many of the tools of modern molecular biological research are phages or phage-derived (see The Practical Phage, below). And just as recombinant DNA and other ‘modern’ techniques have made it easier to study the molecular biology of fruit flies, elephants, and sea slugs, they have also greatly increased the sophistication of the experiments that can be done with phages. Thus for those scientific problems where phages provide advantageous experimental systems, bacteriophage research is still vigorous and in many cases leading the field .

The Practical Phage

Because phages attack bacteria, and bacteria are sometimes harmful to people, many phage biologists believe it is possible to use phage or phage products (such as phage-encoded enzymes) as disease therapy or in other ways to solve our bacterial problems. At this writing, with a few exceptions, these techniques are in research stages rather than in actual use. Examples include treatment of particular bacterial infections or infestations with specific phage, treatment of bacterial infections with phage products, and use of phage-encoded toxins to combat cancer. Among the issues that need resolution before application of these methods becomes practical are how the phage-based therapeutic agent is to be delivered to the patient, how to protect the phage-based agent from immune attack by the patient's body, and how to handle the expected development of phage-resistant pathogens.

On the other hand, phages are and have for decades been widely used as tools in recombinant DNA technology: important in applications and developing applications ranging from medical diagnostics and forensics to basic research. See above, History of bacteriophage research, and our page Major discoveries made with bacteriophages.

Messages from Division M Chairs:

"The Phage Manifesto", by Ry Young 2003(PDF file)
"Bacteriophage Annals", Fall 2002" by Mike Feiss (PDF file)

Officers of Division M

Meetings & events

Information about the ASM General Meeting, and other meetings of interest.

Resources for teachers

Instructions on assembling icosahedra, links to websites about teaching, books, and more.

Phage facts & portraits

Information about and micrographs, diagrams, or other images of specific phages.

Links

Links to other sites on the World Wide Web that are primarily about bacteriophages or generally about viruses.

Oddments

The hot topics of the day, and information about phage books, phage art, and phage history.