Review

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Archaeal viruses and bacteriophages: comparisons and contrasts

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Isolated archaeal viruses comprise only a few percent of all known prokaryotic viruses. Thus, the study of viruses infecting archaea is still in its early stages. Here we summarize the most recent discoveries of archaeal viruses utilizing a virion-centered view. We describe the known archaeal virion morphotypes and compare them to the bacterial counterparts, if such exist. Viruses infecting archaea are morphologically diverse and present some unique morphotypes. Although limited in isolate number, archaeal viruses reveal new insights into the viral world, such as deep evolutionary relationships between viruses that infect hosts from all three domains of life.

Discovery of archaeal viruses

All cellular organisms are susceptible to viral infections, which makes viruses a major evolutionary force shaping cellular life. Furthermore, it has been estimated that there are more than 10^{31} viruses on Earth [1,2]. Because prokaryotes, comprising archaea and bacteria, outnumber eukaryotes, their viruses are thus the most abundant biological entities in the biosphere. The first bacterial viruses, that is, bacteriophages, were described in the 1910s, and since then, thousands have been discovered [3]. However, the first archaeal virus to be described was isolated decades later, in the 1970s, even before the formal establishment of Archaea as the third domain of life [4,5]. Viruses infecting archaeal hosts have gained wider attention during recent years, and the number of studied archaeal viruses is now about 100 [6,7]. However, this is only a few percent of all known prokaryotic viruses because over 6000 bacterial viruses have been studied to date [8]. The aim of this review is to define the present knowledge of archaeal viruses and compare them to bacteriophages.

The domain Archaea has traditionally been divided into two major phyla, Crenarchaeota and Euryarchaeaota, including extremophiles (see Glossary) from habitats such as hot springs and salt lakes. Thermophiles and hyperthermophiles are found in both phyla whereas halophilic and methanogenic archaea are so far classified only into Euryarchaeaota [9,10]. Archaea have also been cultivated from moderate environments such as seawater and soil. Consequently, an additional phylum, Thaumarchaeota, has been formed to contain mesophilic and thermophilic ammonia-oxidizing archaea [11]. However, all known archaeal viruses infect extremophiles – mainly hyperthermophiles belonging to the crenarchaeal genera *Sulfolobus* and *Acidianus* or halophiles of the euryarchaeal genera *Haloarcula*, *Halorubrum*, and *Halobacterium* [6,7]. Even though bacteria are also found in diverse extreme habitats such as hypersaline lakes, archaea typically dominate at extreme salinities, based on both cultivation-dependent and -independent studies [6,12–15]. Consequently, archaeal viruses do the same in hypersaline environments. About 50 prokaryotic haloviruses were recently isolated from nine globally distant locations, and only four of them infected bacteria [6,16]. In contrast to archaeal isolates, bacterial viruses have been isolated for both non-extremophiles and extremophiles, and the majority of the studied bacteriophages infect the former [8,17]. Although no archaeal viruses have yet been isolated from non-extreme niches, a putative provirus was recently recognized in the genome of a thaumarchaeon and virus-like particles (VLPs) resembling archaea-specific viruses have been detected in freshwater sediments [18,19]. To date, the isolated bacterial viruses infect hosts belonging to almost 200 different genera, whereas archaeal hosts belong to less than 20 genera [8].

In addition to virus isolates, several proviruses have been detected in archaeal genomes. These proviruses show similarity to head-tailed, tailless icosahedral, spindle-shaped, and ovoid-shaped archaeal viruses [20–23]. In this review, we take a virion-centered view (Box 1) and focus on cultivated viruses (Figure 1). Taken together, archaeal viruses are morphologically more diverse than bacterial

Glossary

Alkaliphile: an organism that requires a high pH to grow, usually above 9.
Extremophile: an organism that is dependent on extreme habitats such as hypersaline or hyperthermic.
Halophile: an organism that requires at least 0.17 M [1% (w/v)] NaCl for optimal growth.
Head-tailed virus: a virus with an icosahedral capsid and a helical tail.
Hyperthermophile: an organism that grows optimally above 80°C.
Mesophile: an organism that grows optimally at 15–60°C.
Methanogen: an anaerobic organism that produces methane by reduction of carbon dioxide, acetic acid, or other, often simple, carbon compounds.
Neutrophile: an organism that grows optimally at a pH around 7.
Thermophile: an organism that grows optimally above 60°C and up to 80°C.

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Box 1. What is a virus?

Viruses are self-replicating obligatory parasites without inherent metabolism. When they exist in extracellular environment, viruses are usually biochemically inert. In addition, viruses are traditionally considered to be very small filterable agents. However, this view has been challenged after the discovery of an archaeal virus developing its tails *ex vivo* [59] and after realizing that viruses such as Mimivirus and Pandoravirus can be even larger than the smallest cells [114,115].

Viruses consist of particles containing a nucleic acid (either DNA or RNA), which encodes the information necessary for their replication. Furthermore, viral genomes are either circular or linear, single- or double-stranded (ss or ds), and as one molecule or segmented. In the Baltimore system, viruses are divided into seven classes of DNA, RNA, and reverse-transcribing viruses [116].

When the genetic information includes a gene (or genes) encoding a capsid protein (or capsid proteins), which is capable of forming a capsid shell, then a virus particle can be formed. The capsid-encoding gene found in the viruses distinguishes them from other self-replicating entities such as plasmids. A virion is defined as an infectious virus particle, which functions as both a protective shell for the genome and a vehicle for nucleic acid delivery to an appropriate cell to initiate a new reproduction cycle.

To date, all known archaeal viruses have DNA genomes, whereas the known bacterial viruses have either DNA or RNA genomes including circular ssDNA, circular dsDNA, linear dsDNA, linear ssRNA, or segmented dsRNA [17]. Bacteriophages with linear dsDNA genomes form the largest group. Most archaeal viruses also have dsDNA genomes, either linear or circular, and only a few viruses with circular ssDNA have been isolated [55,78,79]. Although no RNA viruses infecting archaea have been discovered, metagenomic analyses of viral sequences in archaea-dominated hot springs indicate that they might be there waiting to be discovered [117].

ones, although they are fundamentally underrepresented among the prokaryotic virus isolates [7,8]. So far, 16 different morphotypes have been described for archaeal viruses and many of these are unique (Figure 1 and Table 1). For bacteriophages, only nine morphotypes are known (Figure 1 and Table 1). Furthermore, no new bacterial virion morphotypes have been discovered since the 1970s even though thousands of isolates have been examined [8]. According to the International Committee on Taxonomy of Viruses (ICTV), archaeal viruses are classified into 15 families or corresponding groups, while bacterial ones belong to ten families [8,17]. In addition to virion morphotypes, one more peculiar feature of archaeal viruses is their genomes. Although morphologically diverse, all

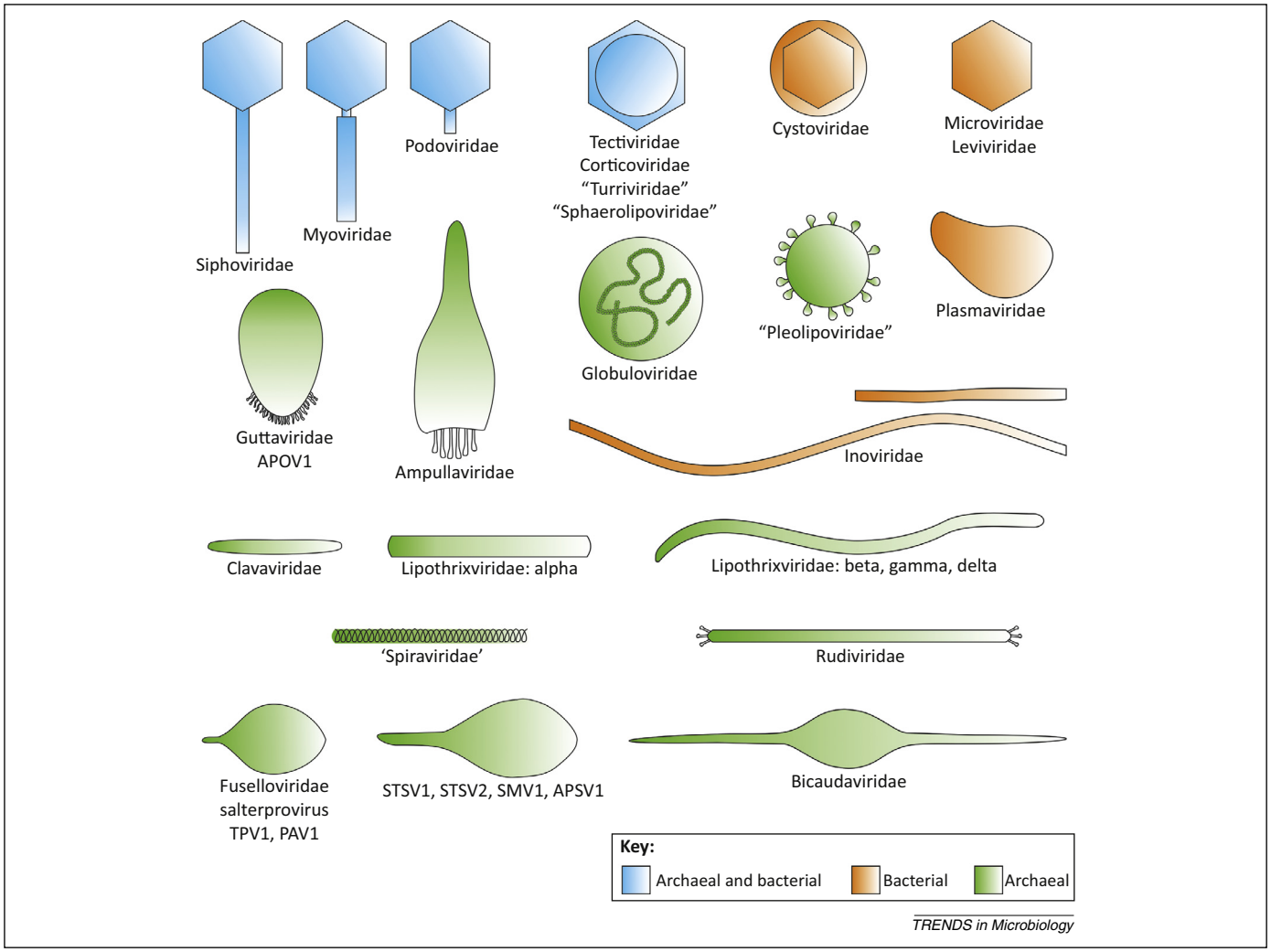

Figure 1. Virion morphotypes of prokaryotic viruses. Names of viral genera or families based on International Committee on Taxonomy of Viruses (ICTV) are indicated below the schematic virus particles. If an archaeal virus has not been assigned to any genus or family, individual virus names are given. The virions are not drawn to scale. Abbreviations: APOV1, *Aeropyrum pernix* ovoid virus 1; APSV1, *Aeropyrum pernix* spindle-shaped virus 1; PAV1, *Pyrococcus abyssi* virus 1; SMV1, *Sulfolobus* monocaudavirus 1; *Sulfolobus tengchongensis* spindle-shaped virus 1 (STSV1); STSV2, *Sulfolobus tengchongensis* spindle-shaped virus 2; TPV1, *Thermococcus prieurii* virus 1.