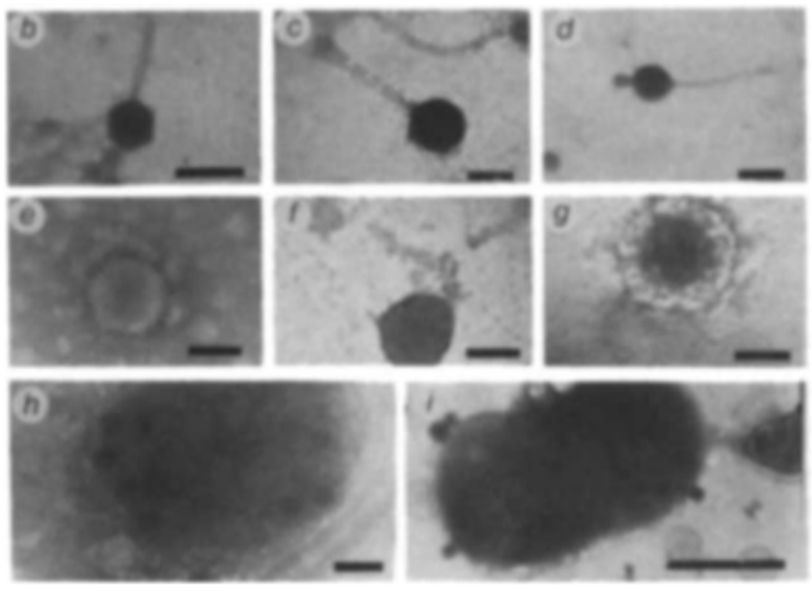
Ben Knowles &
Steven Quistad

1986 - 1995

The History of Phage Research

High Abundance of Phage in the Environment

1989 – Bergh et al



- Previously, viruses were thought to be rare in the ocean
- Using Transmission Electron Microscopy (TEM), Bergh et al found 100,000,000 phage per milliliter of seawater in 1989 (ie highly abundant)
- Today we know there are about 10,000,000 phage per milliliter throughout the global ocean

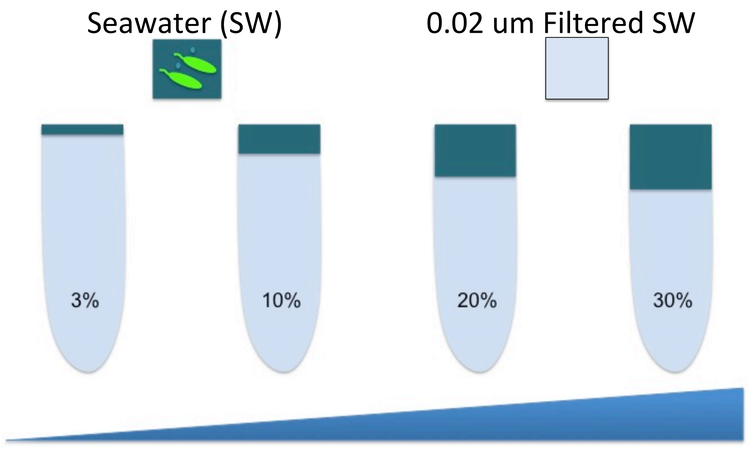
The Unknown Predator is Revealed…

1990 – Bratbak et al, Proctor and Fuhrman, Suttle et al

- Throughout the 1970s and 1980s, researchers were unable to balance environmental Carbon budgets; unknown predators were killing a high proportion of microbes
- One year after viruses were shown to be abundant, radiotracer studies researchers knew revealed that phage kill up to 50% of microbes in an environment daily, with up to 70% of microbes infected at any given time

The Fundamental Experiment (Wilcox and Fuhrman 1994)

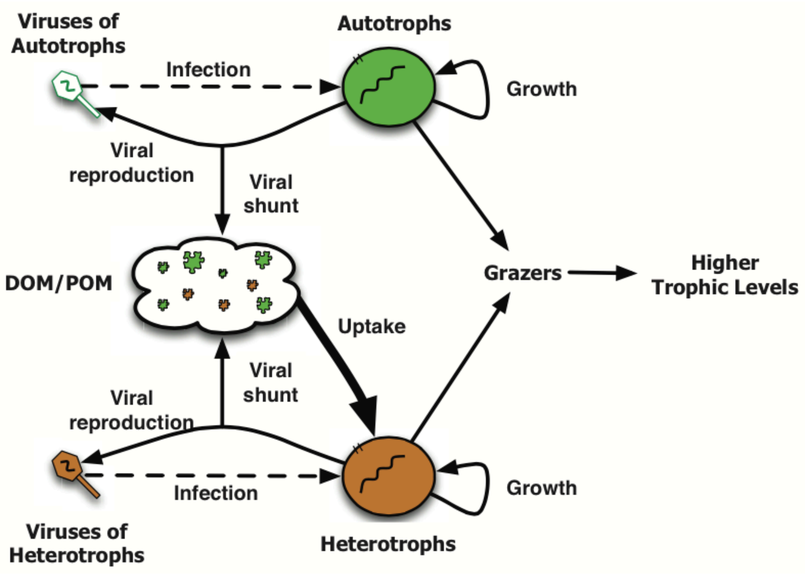
- By diluting microbial and viral communitties with filtered seawater, and thus reducing the encounter rate between phage and their hosts, Wilcox and Fuhrman showed that lysis does not occur when viral and host densities are low
- This suggested that lytic dynamics are density dependent, and that this viral lifestyle is dominant in the ocean



Viral Predation Enhances Productivity

1990, 1994 – Bratbak et al

- Viral predation can lead to elevated microbial productivity through the recycling of cellular lysates
- This phenomenon was ultimately labeled the Viral Shunt in 1998 by Wilhelm and Suttle
- Scientists now know that viruses modulate global-scale biogeochemical cycles through the activity of the Viral Shunt; viruses control the world through predation



Lysogeny is Highly Prevalent in the Ocean

1994, 1996 – Jiang and Paul

- In contrast to this lytic-centric research, Jiang and Paul showed that lysogeny can account for ~50% of daily microbial mortality, similar to lytic effects
- Lysogeny was shown to be more prevalent in oligotrophic conditions while lysis was dominant in eutrophic areas

1996 - 2005

The History of Phage Research

Ana Cobian &
Sandi Calhoun

Structure of filamentous phage determined

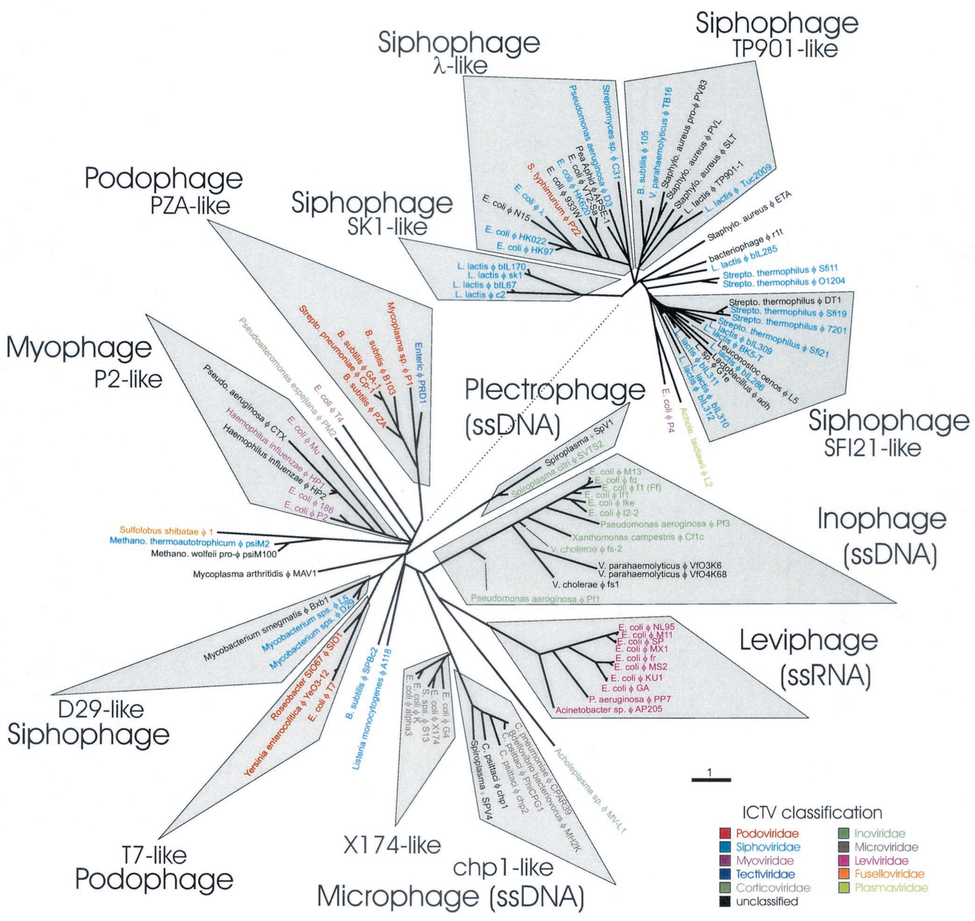
1998 – D.A. Marvin

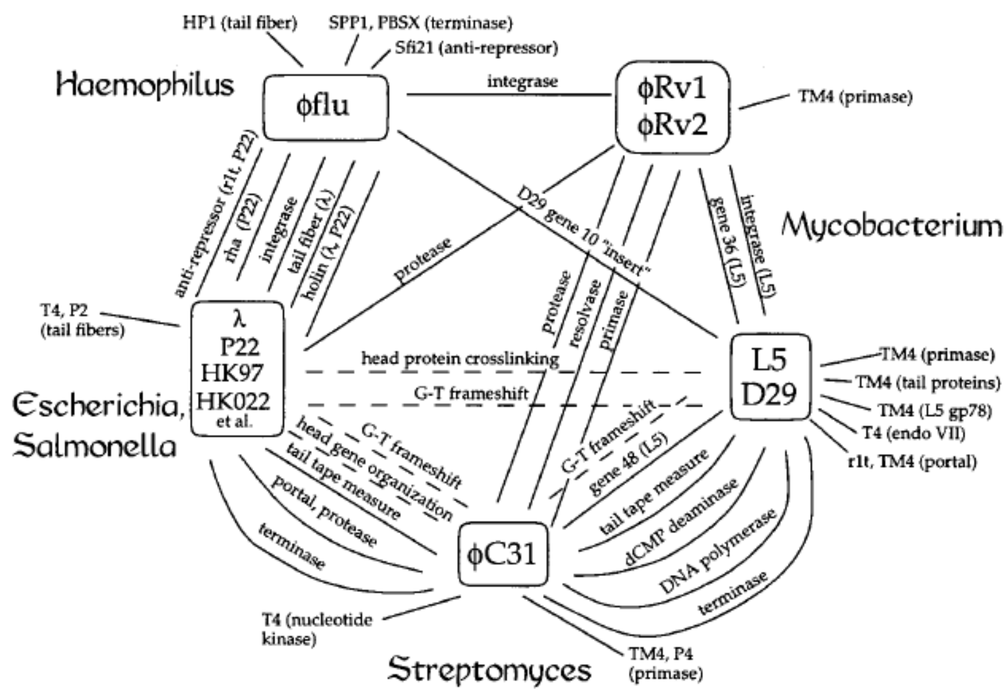
- High resolution X-ray crystallography data combined with previous genetic and molecular data to reveal the structure, infection and assembly of F1 phage

All the world's a phage

1999 – Roger W. Hendrix *et al.*

- Confirmed the mosaic nature of phage genomes
- Showed common ancestry of all dsDNA tailed phages
- First time a phage phylogenetic tree was proposed





Phage proteomic tree assembled

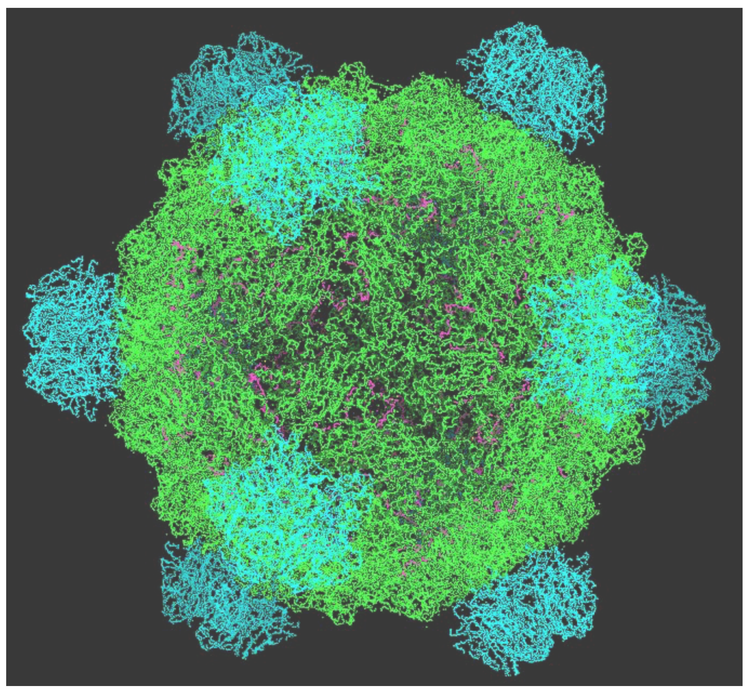
2002 – Forest Rohwer and Rob Edwards

- Proposed taxonomic classification of phages based on genetic sequences of proteins
- Used 105 completely sequenced phage genomes
- Showed that genome-based taxonomy recapitulates much of previous morphology-based taxonomy, and even resolves morphology-based discrepancies

The first synthetic genome: φx174

2003 – Craig Venter

- Assembled 5,386 bp of synthetic DNA to form a complete genome based on the ϕx174 genome sequence
- Completed in 14 days
- The synthetic virons were able to infect *E. coli* and replicate normally



Viral metagenomics shows high abundance of unknown sequences

2005 – Forest Rohwer and Rob Edwards

- Advances in sequencing technology allow for large numbers of short-read DNA sequences to be assembled into metagenomes
- An analysis of 5 viral metagenomes reveals that they contain mostly novel sequences
- The undiscovered nature of viral sequences and overall viral community structures fuels large scale sequencing efforts