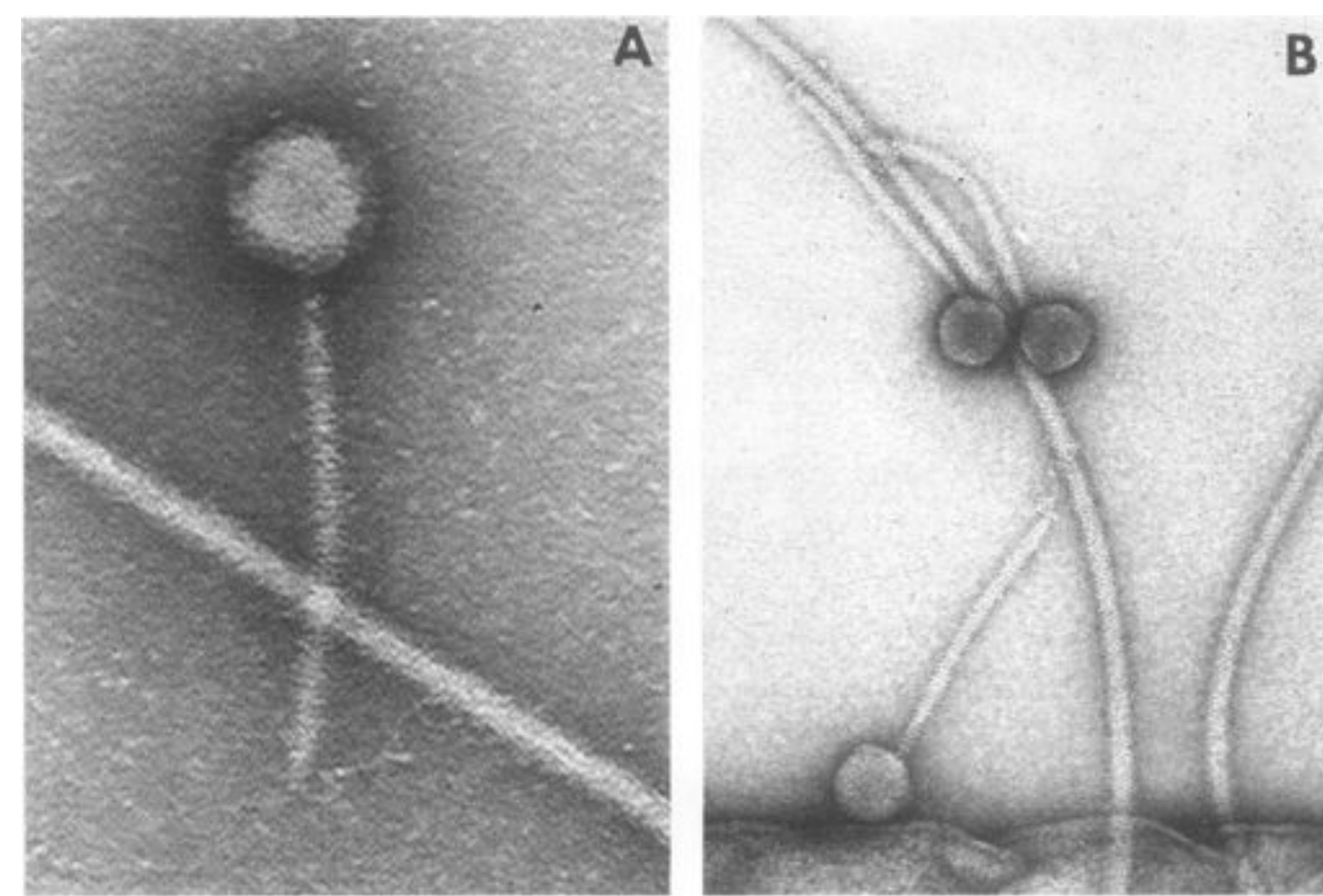


Improved Electron Microscopy Methods Shed Light on Phage Morphology & Assembly

1966-1967 – Edgar, Kellenburger, Anderson, Eiserling, Schade

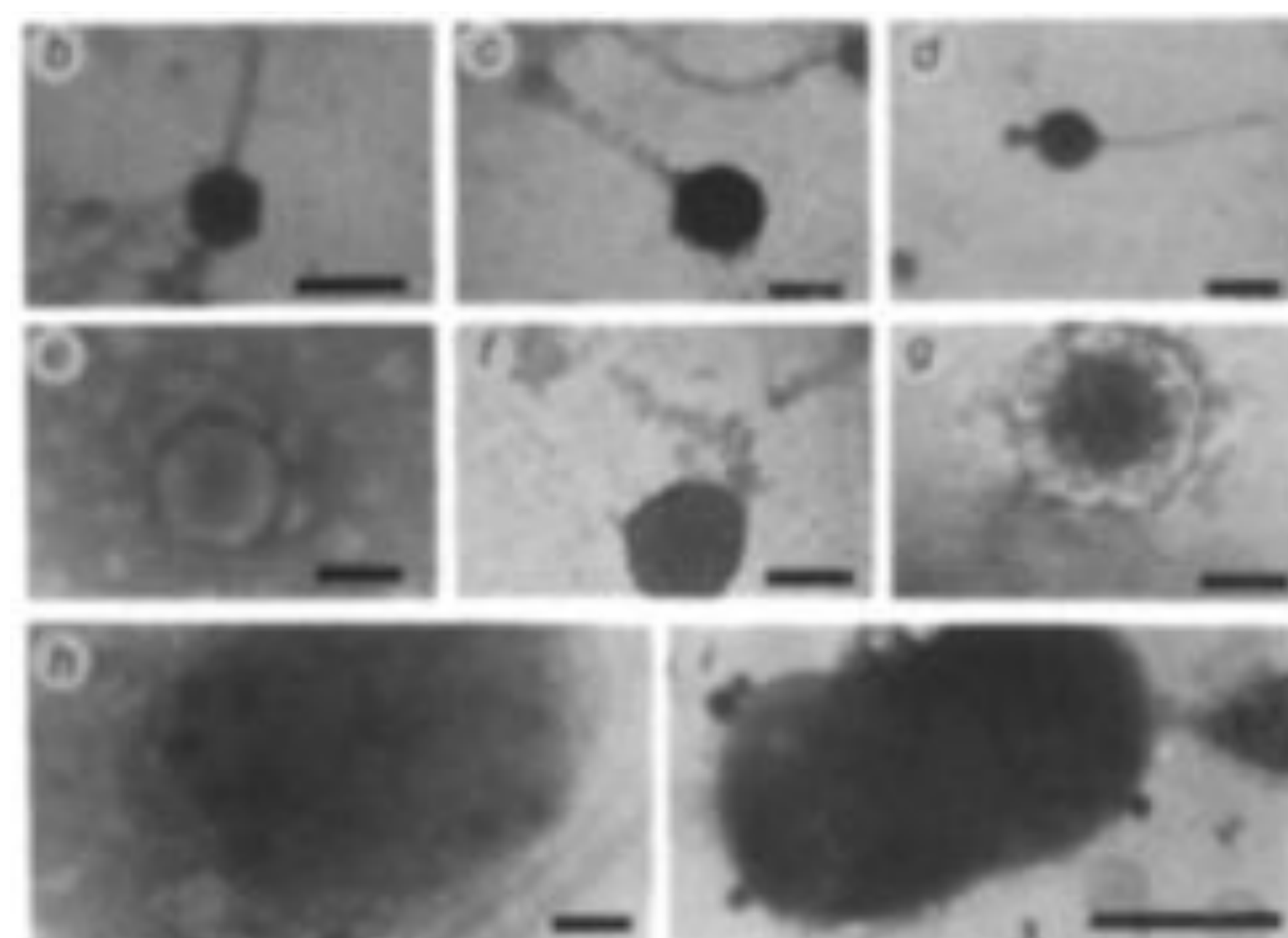
- At this point in time, physiological studies show that over 40 phage genes are involved with T4 morphogenesis. However, the mechanisms of phage assembly were unknown
- Exploitation of conditional lethal mutants of T4 ϕ
- Development of an *in vitro* system to demonstrate steps in phage morphogenesis
- Demonstration of how bacteriophage X attaches to motile bacteria via the flagella



Schade S. Z., Adler J., Ris H., (1967) *J. Virol.* 1: 599-609

Isolation and Quantification of Aquatic Phages

1967 – Anderson



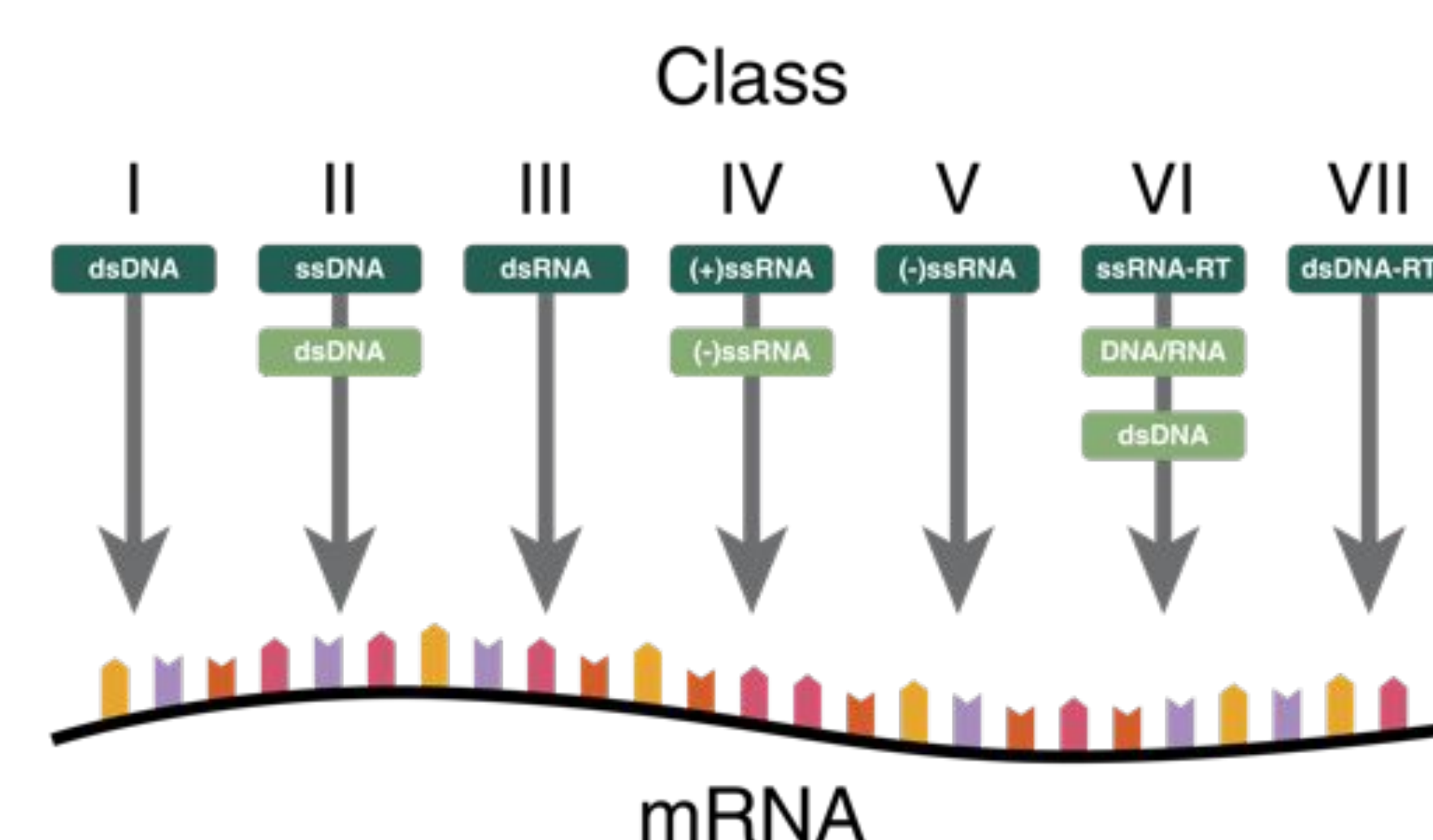
Bergh O, et al. (1989) *Nature* 340(6233): 467-68.

- Anderson isolated and concentrated aquatic virions in waste water via ultracentrifugation and quantified the concentrates using transmission electron microscopy
- In pursuit to develop a robust method to determine viral abundances in the marine realm, Bergh *et al.* (1989) published what was thought to be a novel technique, however Anderson published the same method over two decades earlier

Classification and Nomenclature of Viruses

1967-1971 – Thomas, Abelson, Bradley, Wildy, Baltimore

- Isolation and characterization of DNA from phages enabled biologists to determine both genome size and type, complementing the morphological taxonomy of phages
- Creation of the first unified phage classification system based on morphology and nucleic acid content
- First report of the International Committee on Taxonomy of Viruses published



Molecular Advances in Phage Biology

1966-1975 – Sadowski, Hurwitz, Kutter, Wiberg, Streisinger, Tye

- *Restriction studies* – ϕ -encoded endonucleases cleave host DNA & T7 ϕ evades host restriction via the *Ocr* gene product
- *Transcription studies* – Phage transcribe own DNA via modification of the host RNA polymerase
- *Recombination studies* – P22 ϕ and λ recombination results in functional hybrids
- Demonstration that frameshift mutations in the *e* gene indeed shift the translation reading frame, resulting in the first *in vivo* coding assignments
- Characterization of P22 ϕ genome packaging system

1976 - 1985

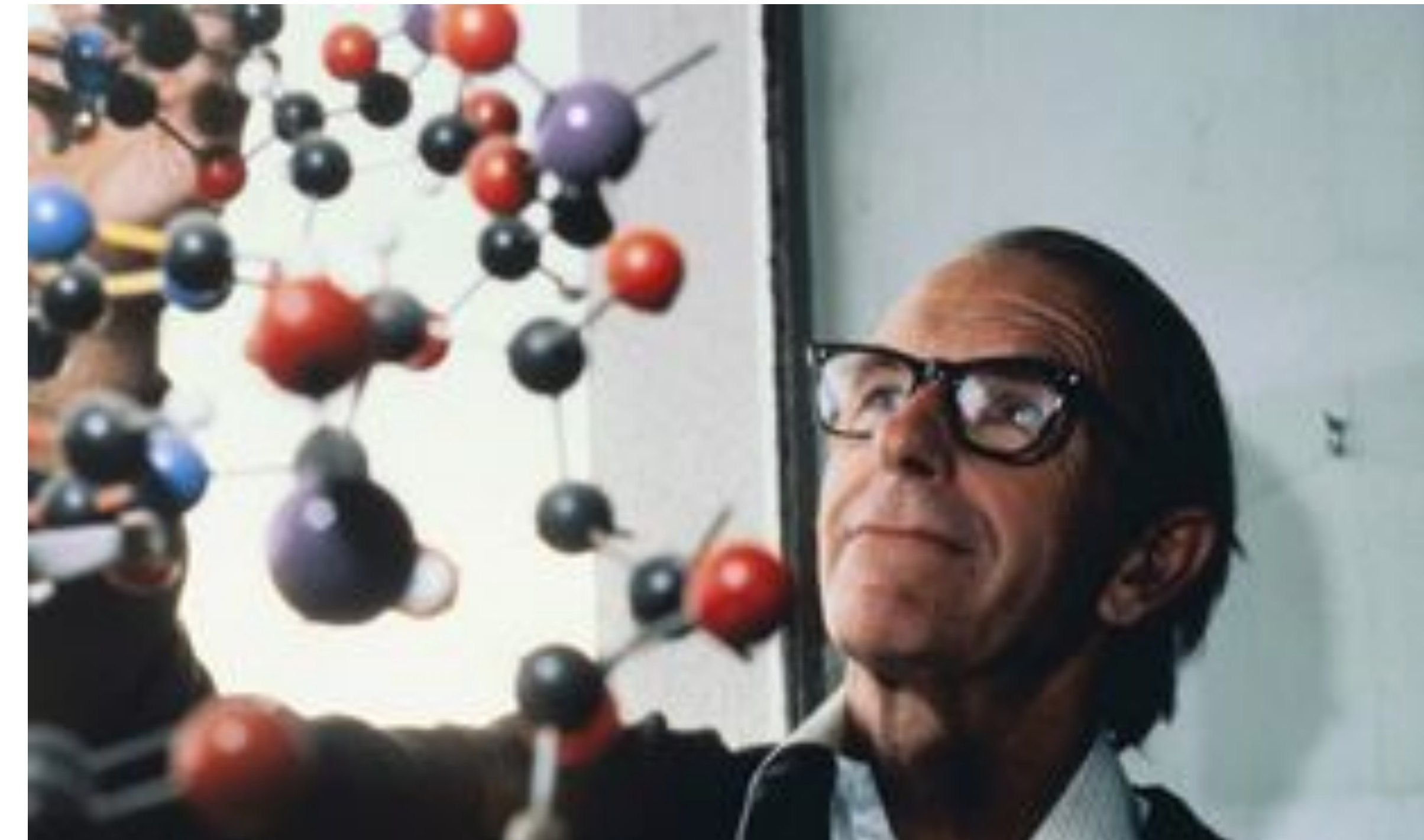
Cynthia Silveira &
Aaron Hartmann

The History of Phage Research

First phage genome sequenced

1977 – FREDERICK SANGER

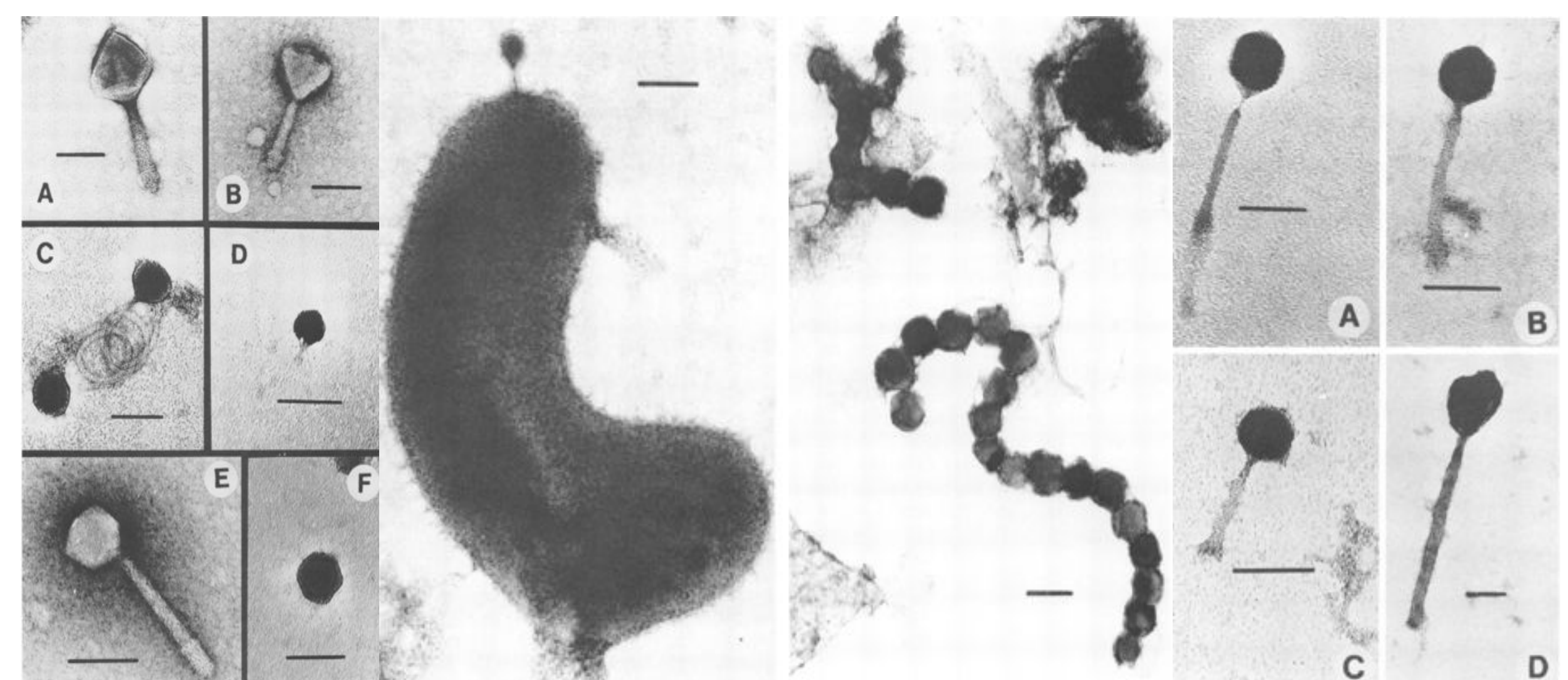
- Helped develop chain-terminating inhibitor technique for DNA sequencing
- Technique allowed Sanger *et al.* to sequence of the first phage genome: phi X 174 - encoding 11 proteins
- Later sequenced lambda phage (1982)



Earliest counts of marine phage abundance

1979 – FRANCISCO TORRELLA & RICHARD MORITA

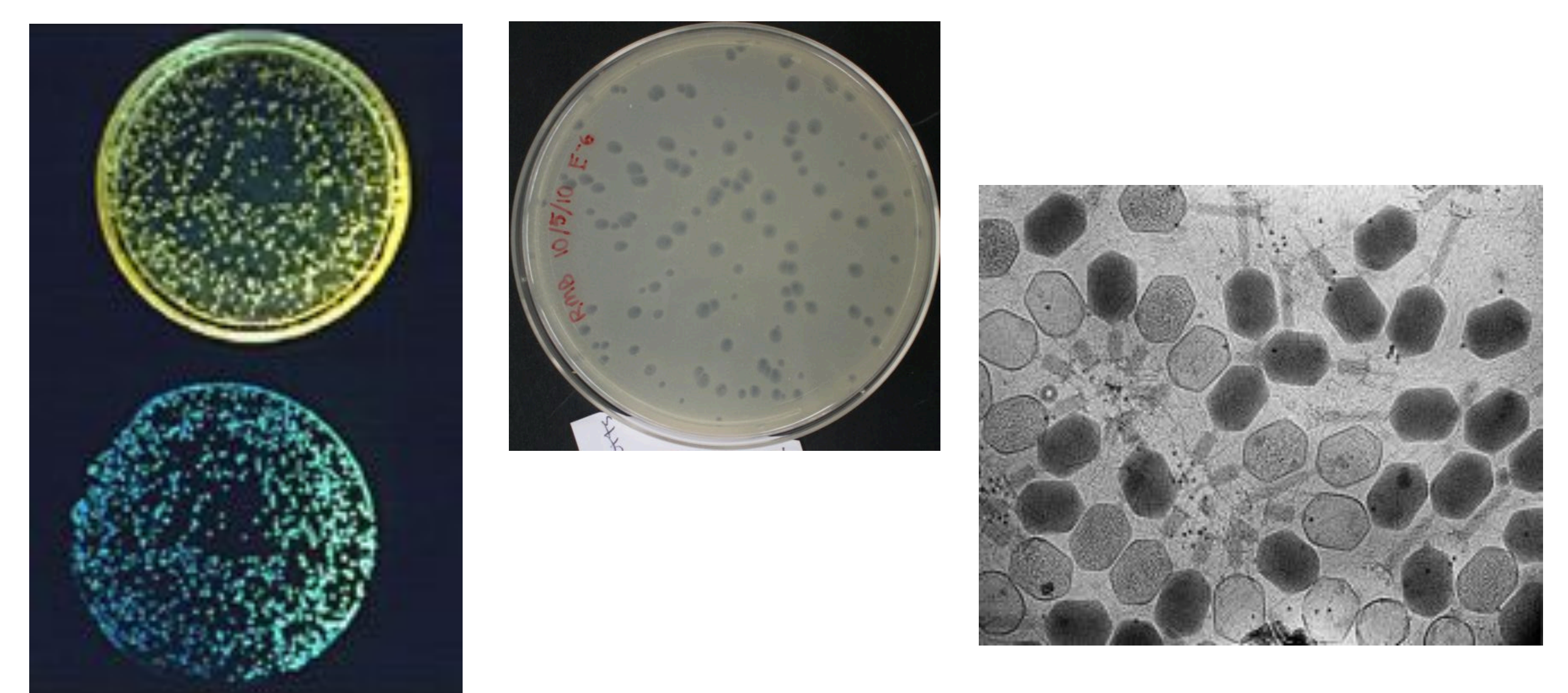
- Applied transmission electron microscopy to the counting of marine phage
- Estimated there were 10^4 phage/ml of seawater
- Estimates for marine bacteria at that time were 10^5 cells/ml of seawater



Complex interaction networks between phage and bacteria identified in the marine environment

1980-1983 – FRANCISCO TORRELLA & RICHARD MORITA

- Performed hundreds of cross-inoculation experiments of phage isolates and bacterial cultures from the marine environment
- Raised new ideas about complex interaction networks between bacteria and phage



Development of human phage therapy in Poland

1983-1986 – STEFAN SLOPEK



- Phage were used to treat septicemia caused by multiple bacterial agents, including those with antibiotic resistance
- The series of papers produced by this group are considered some of the most detailed English language reports on phage therapy in humans