

# 1956 - 1965

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## The History of Phage Research

### Benzer's deletion map of rII

1955-1959 – Seymour Benzer

- First evidence that the gene is not an indivisible entity, as previously believed, and that genes are linear.
- Showed that recombination occurred within bacteriophage T4 using rII mutants, resulting in characterization of the rII region and the mapping of over 2400 mutations.
- Proved that mutations are distributed across a single gene and allowed for him to propose distinct classes of mutations.
- His work provided novel techniques and a model system for many molecular and phage biologist, such as Francis Crick and Alan Campbell.

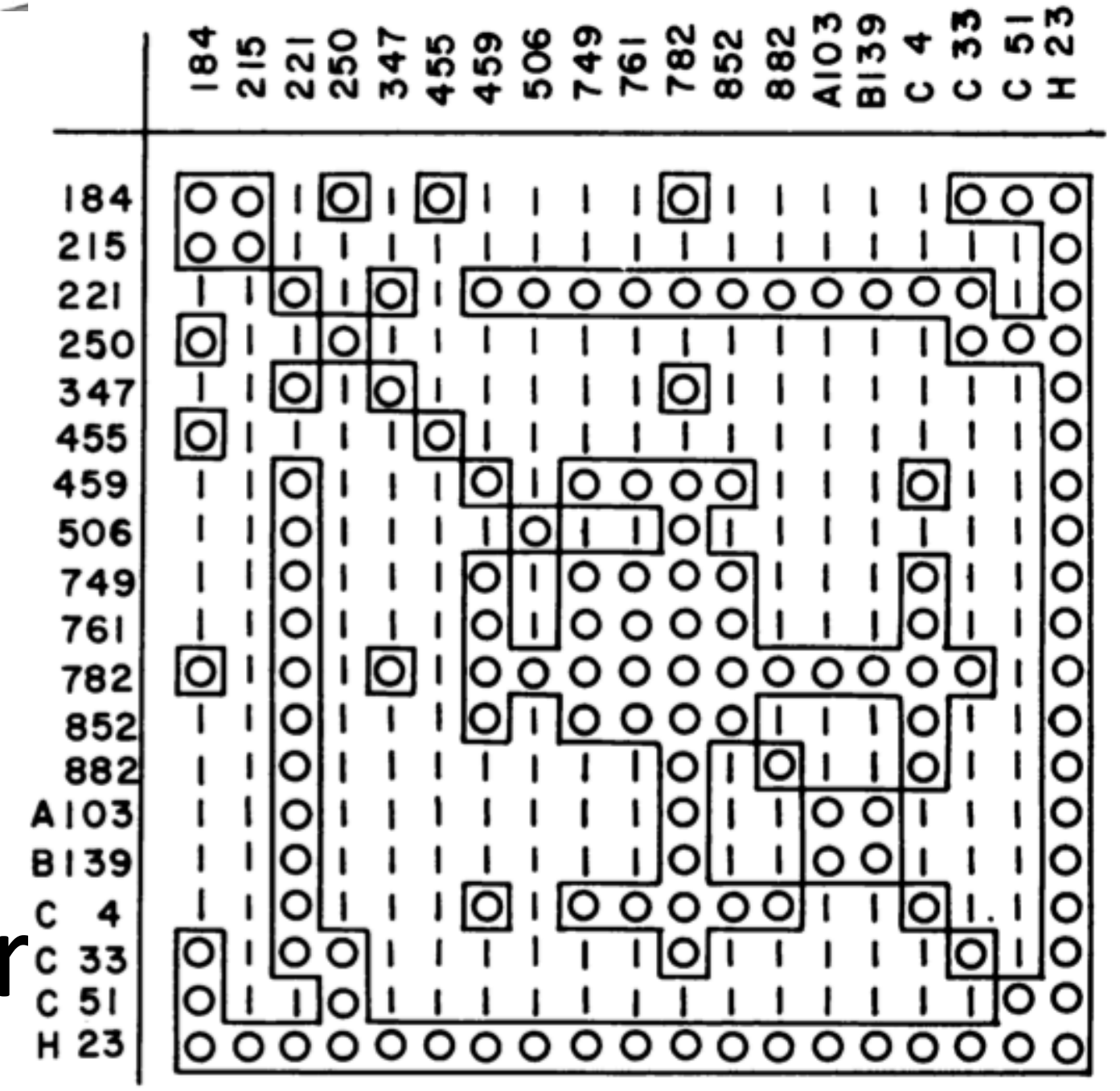
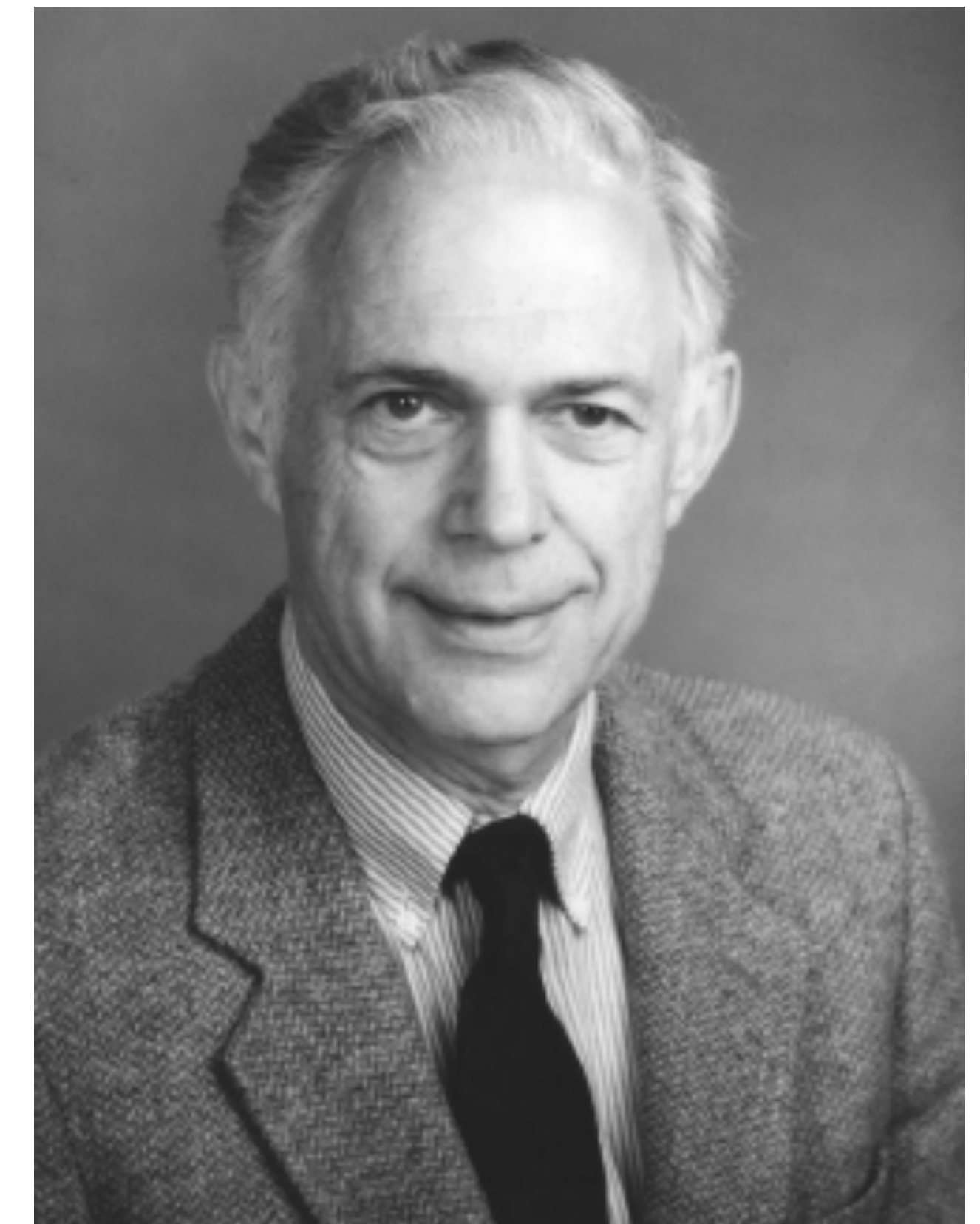


Fig. 4.—Recombination matrix for 19 rII mutants of phage T4, arranged in arbitrary order.

### The "Campbell Model" of virus insertion

1962 – Allan Campbell

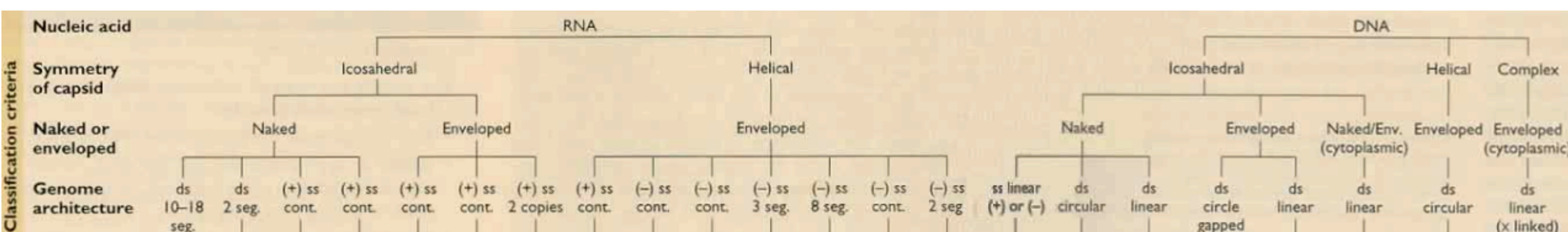
- Phage assume a circular intracellular form and become linearly integrated into the chromosomal DNA through a recombination event
- Provided conceptual basis for retroviral integration and lead to first detailed information on plasmid biology.
- Traditional view was that prophage were not incorporated into the bacterial chromosome but instead synapsed due to homology (Jacob & Wollman).



### The LHT classification of viruses

1962 – Lwoff, Horne, and Tournier

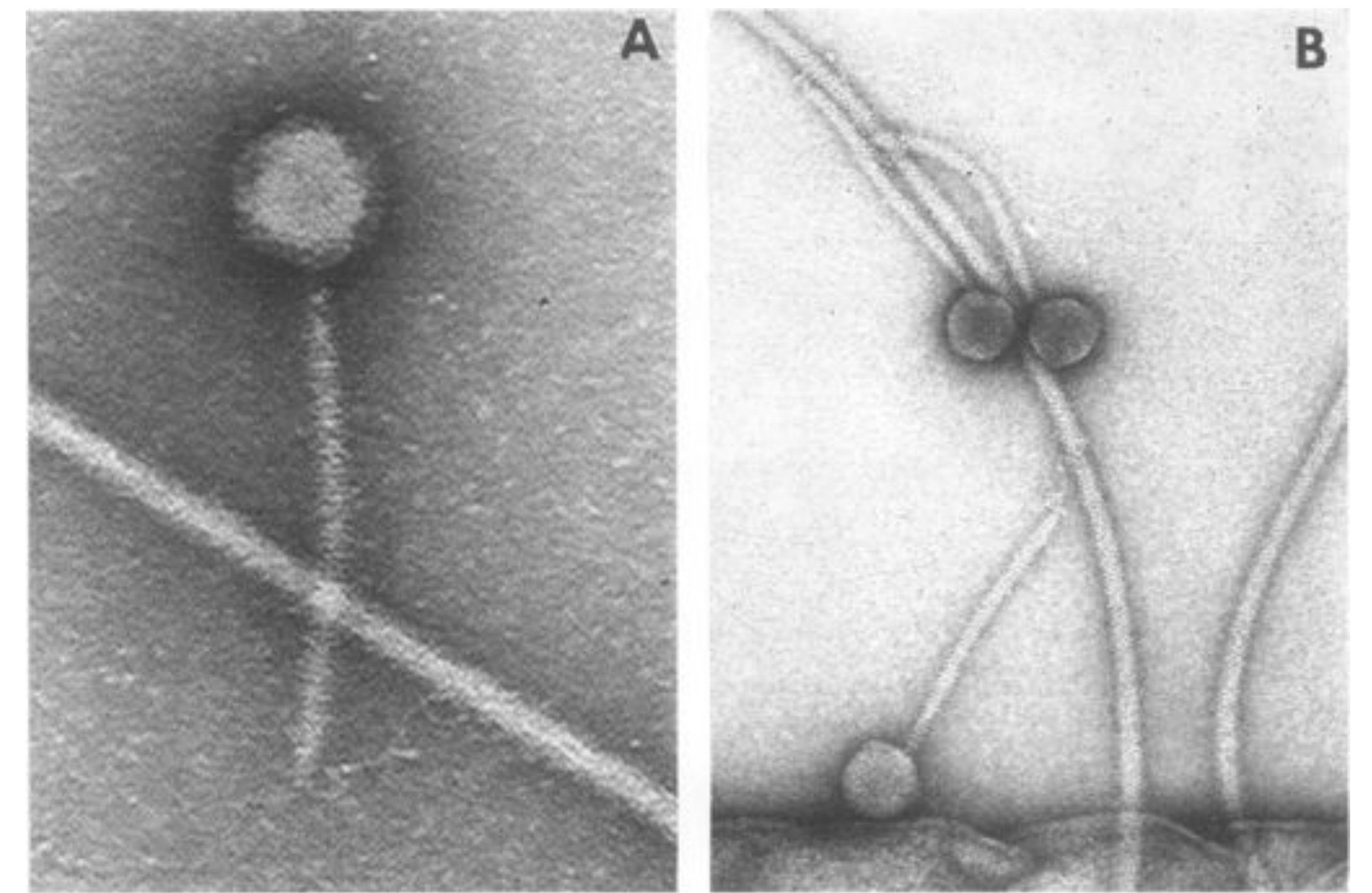
- Proposed the first virus classification scheme where viruses are grouped according to *their* properties, not the cells they infect.
- Four characteristics were to be used for the classification of all viruses: (1) Nature of the nucleic acid in the virion; (2) Symmetry of the protein shell; (3) Presence or absence of a lipid membrane; (4) Dimensions of the virion and capsid



### Improved Electron Microscopy Methods Shed Light on Phage Morphology & Assembly

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

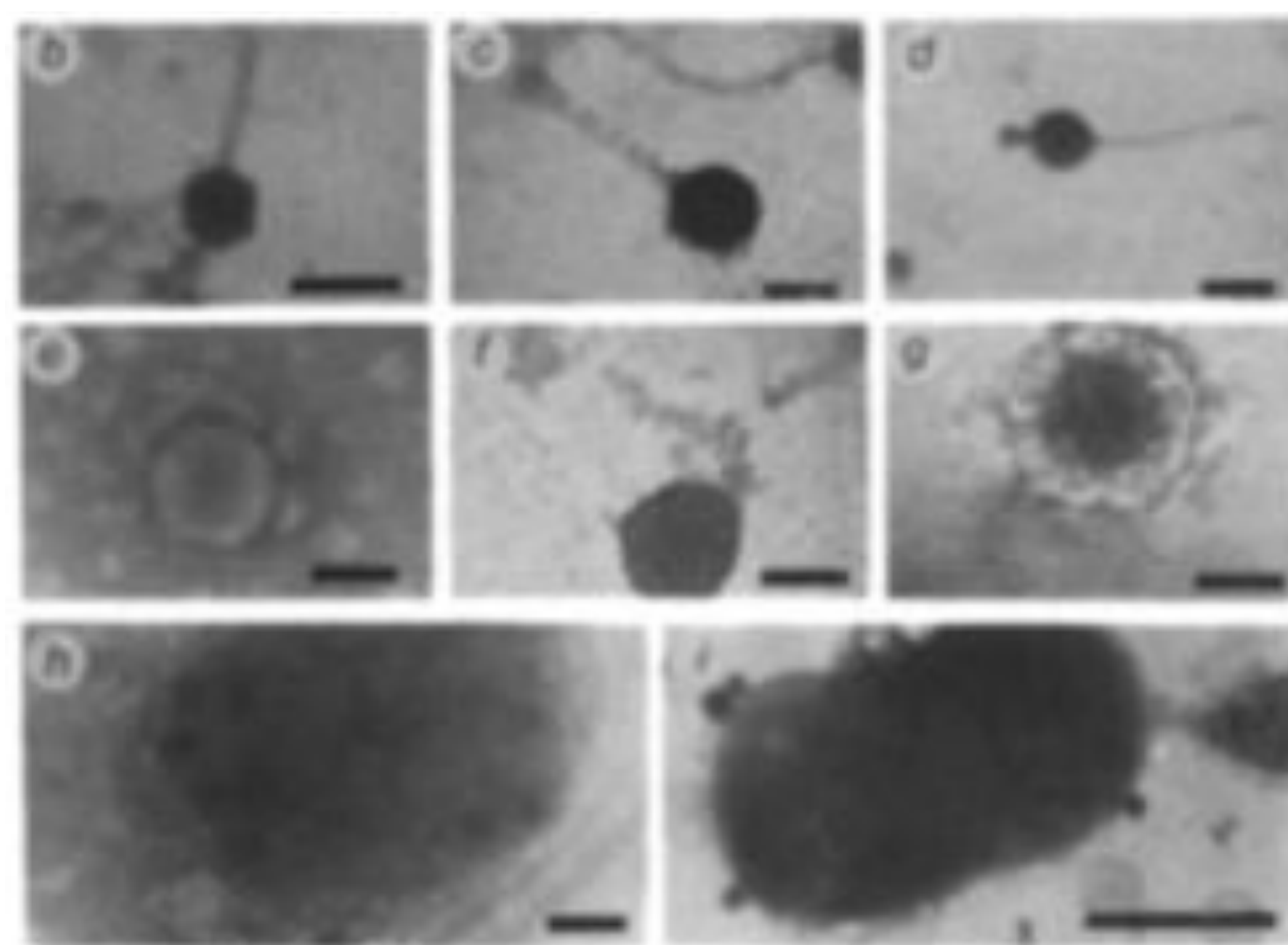
- At this point in time, physiological studies show that over 40 phage genes are involved with T4 morphogenesis. However, the mechanisms of phage assembly were unknown
- Exploitation of conditional lethal mutants of T4 $\phi$
- Development of an *in vitro* system to demonstrate steps in phage morphogenesis
- 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



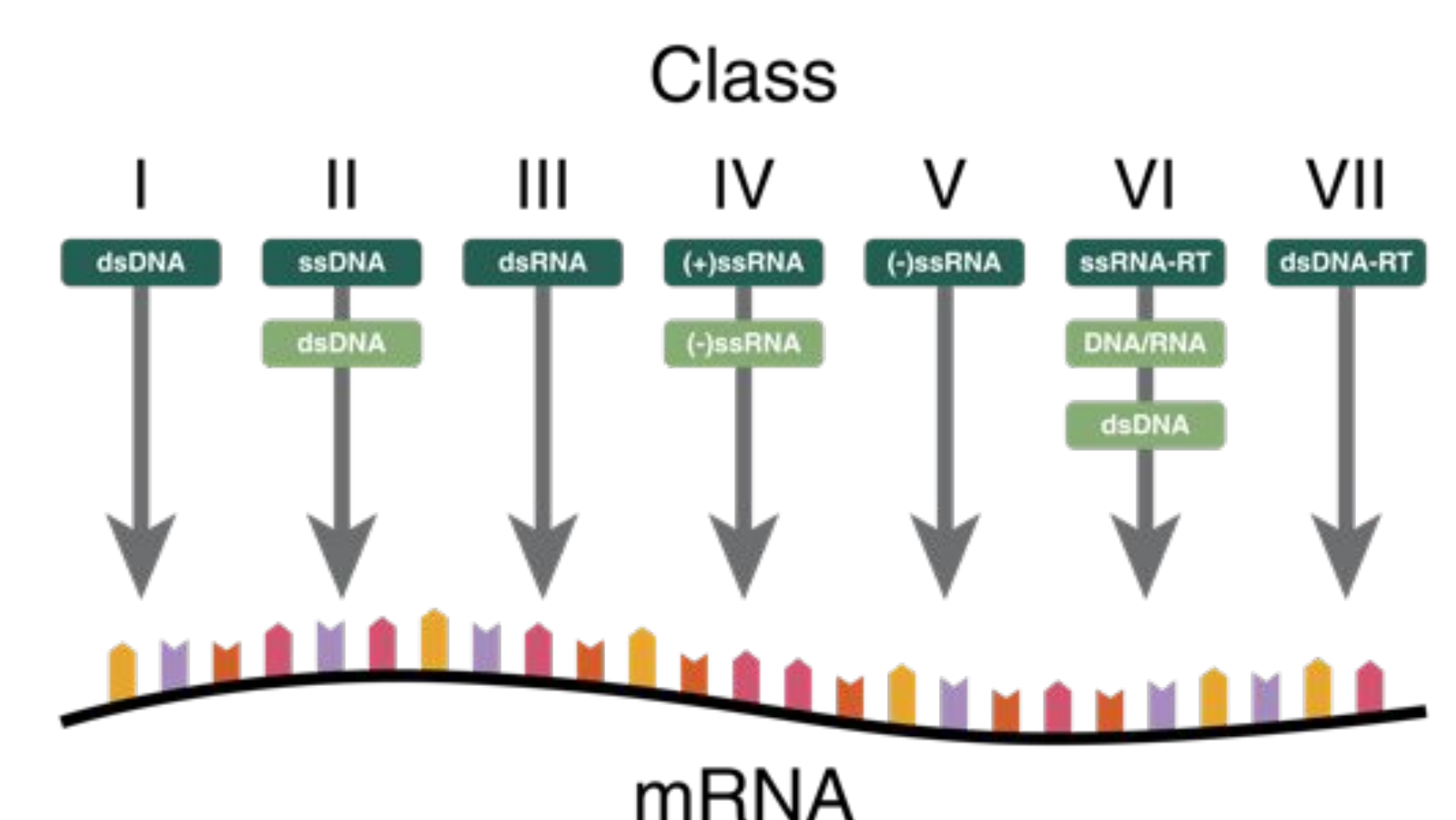
Bergh O, et al. (1989) *Nature* 340(6233): 467-68.

- 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* –  $\phi$ -encoded endonucleases cleave host DNA & T7 $\phi$  evades host restriction via the *Ocr* gene product
- *Transcription studies* – Phage transcribe own DNA via modification of the host RNA polymerase
- *Recombination studies* – P22 $\phi$  and  $\lambda$  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 $\phi$  genome packaging system