

Why Bacteriophage Encode Toxins & Other Virulence Factors

Stephen T. Abedon

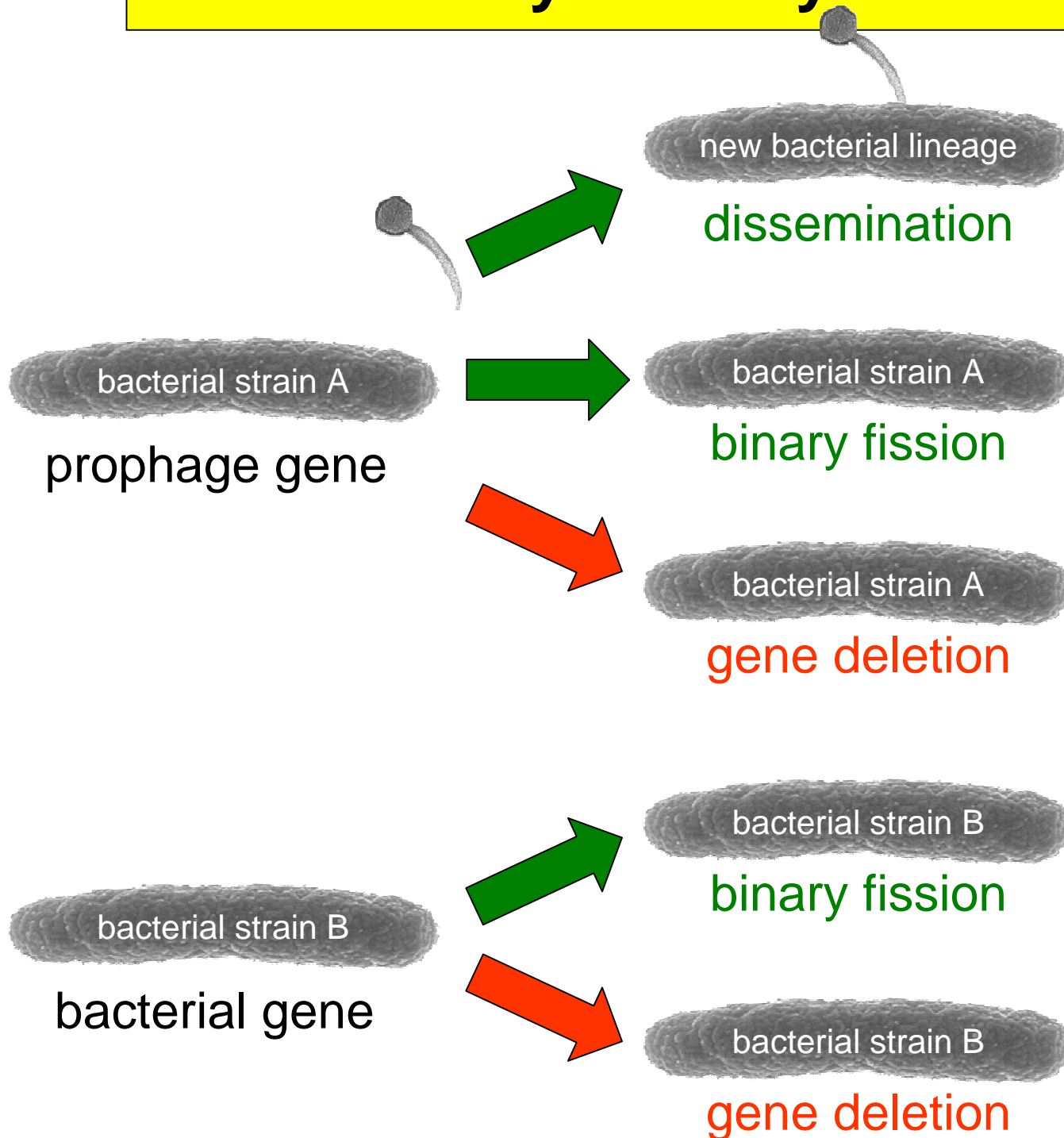
Department of Microbiology
The Ohio State University

www.phage.org

abedon.1@osu.edu

Abstract: Numerous bacterial virulence factors (VFs) are prophage encoded. As a consequence, both the emergence and progression of many diseases may be affected by temperate-phage movement between bacteria as well as prophage control of VF expression. Here I consider a more fundamental issue: **Why do prophage even encode VFs?** In principle there exist at least four entities that could benefit from this association: the VF gene, the bacterial host, bacterial populations, and the encoding prophage. **I present various scenarios whereby a VF gene-prophage association may be selectively maintained.**

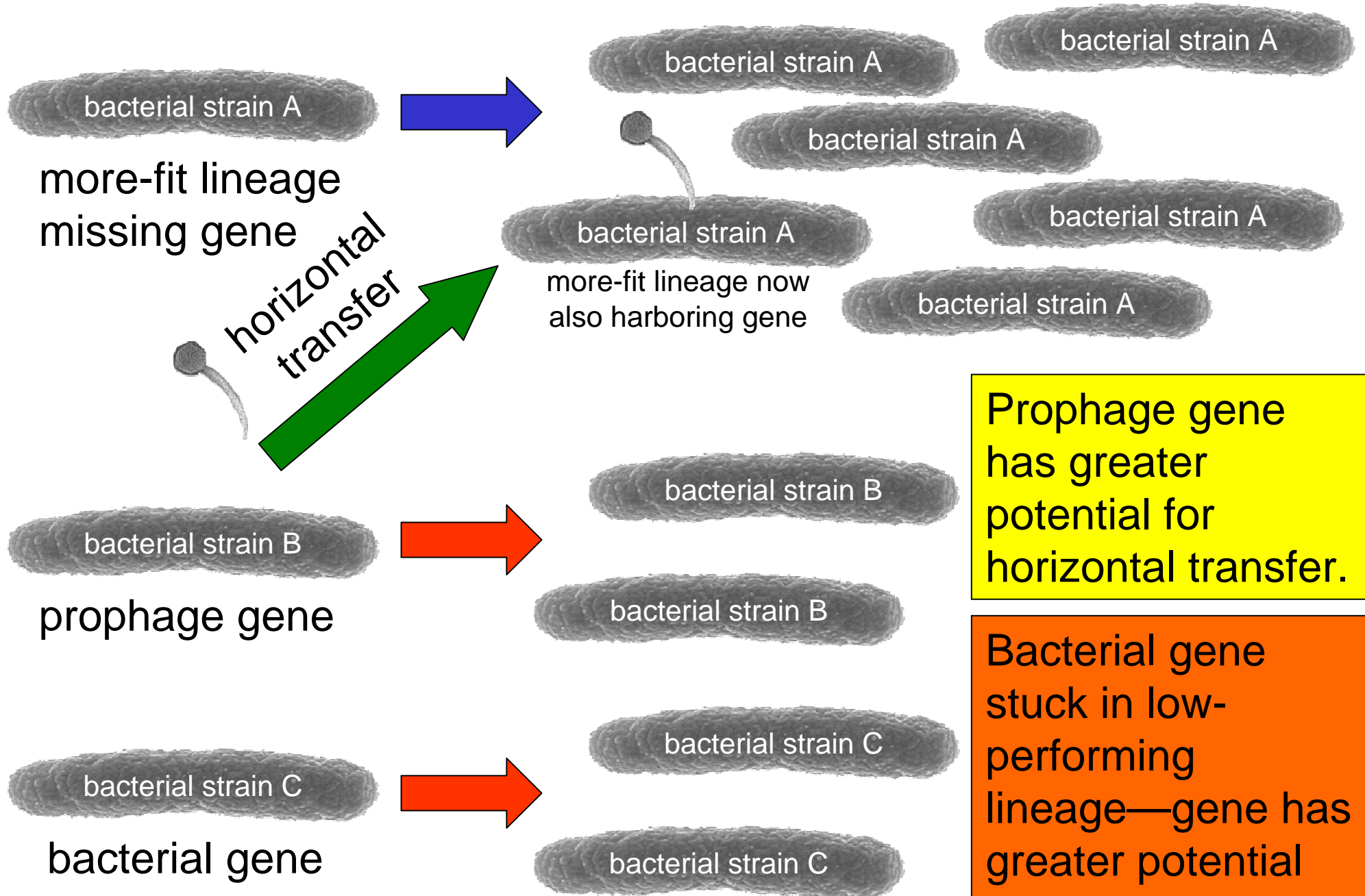
1. Rare-Utility Mobility Advantage to Gene



Gene potential for higher equilibrium density— particularly if gene bestows only rare utility—given propagation by phage-mediated dissemination in addition to binary fission.

Greater likelihood of deletion from population given only rare selection for bacterial gene maintenance.

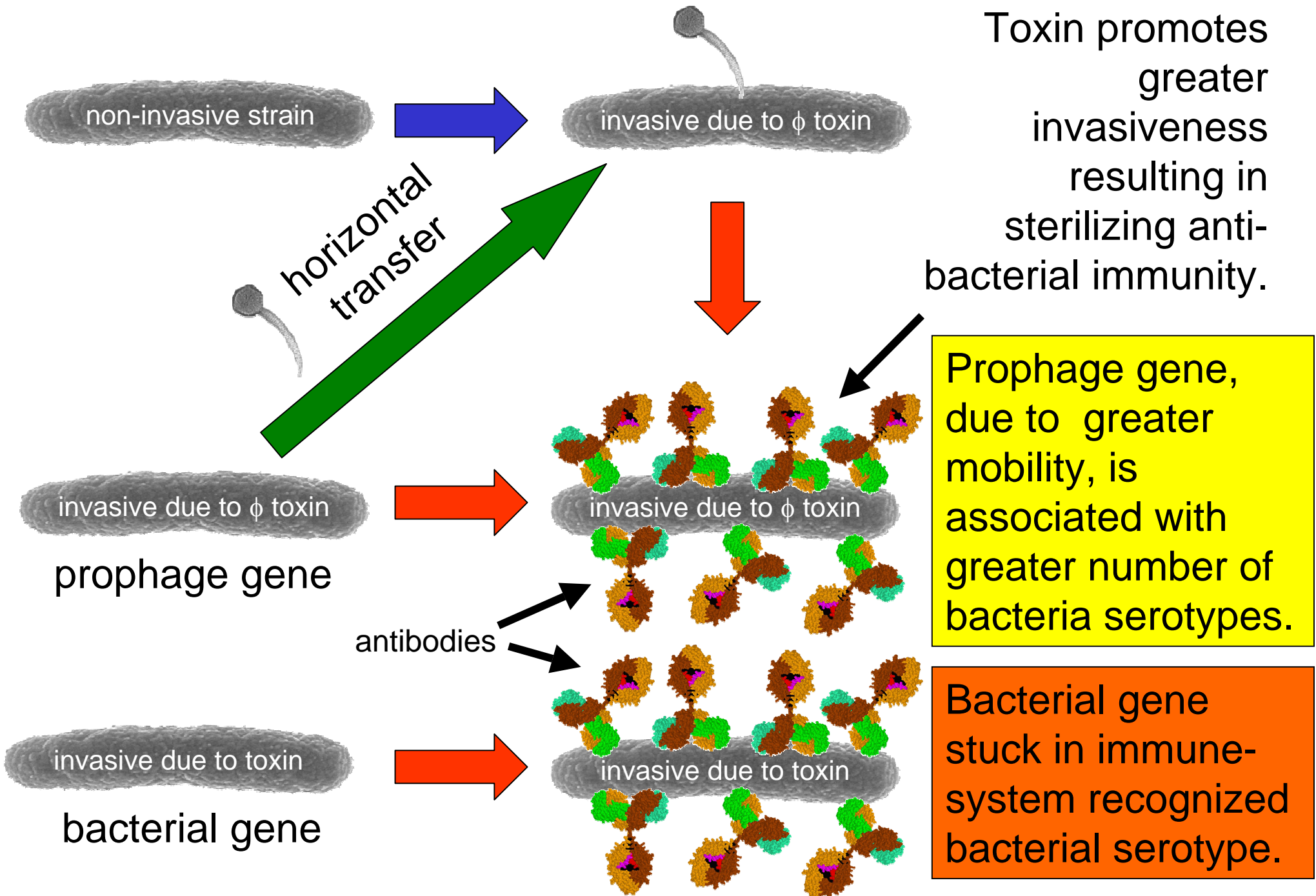
2. Gene Hitchhiking on More-Fit Bacterial Lineage



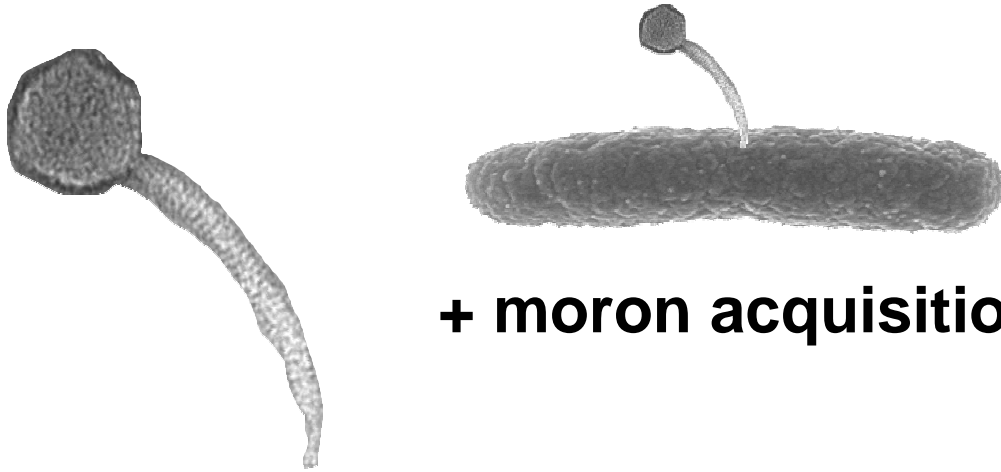
Prophage gene has greater potential for horizontal transfer.

Bacterial gene stuck in low-performing lineage—gene has greater potential for extinction.

3. Gene Escape from Immune Surveillance



4. Random Acquisition and Retention by Phage



+ moron acquisition +



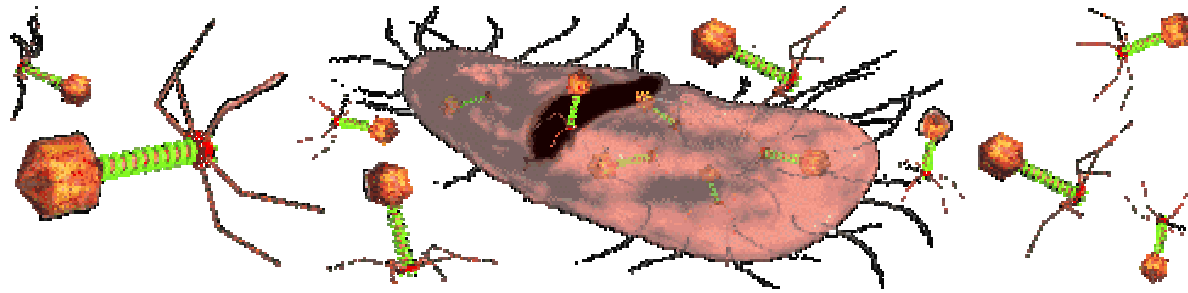
phage/bacteria sequencing

= phage-associated gene

(no matter how recent phage acquisition)

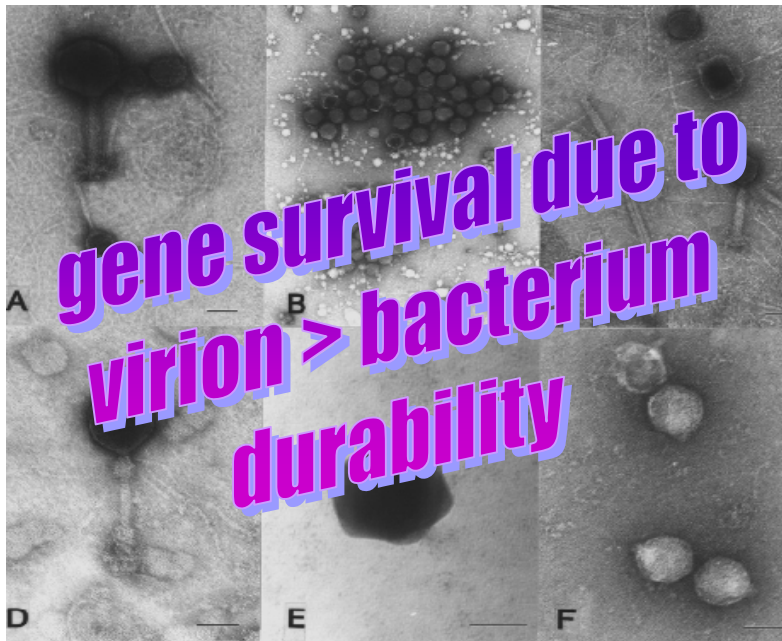
Caveat: Make sure that a phage-encoded gene is associated with at least more than one independently isolated phage lineage before declaring that it is *generally* phage encoded.

5. Benefits of Gene Linkage to Other Phage Genes



Selection for close proximity (linkage) between toxin gene and efficacy-enhancing phage gene(s).

Release of toxin via phage-mediated bacterial lysis (e.g., Shiga toxin)

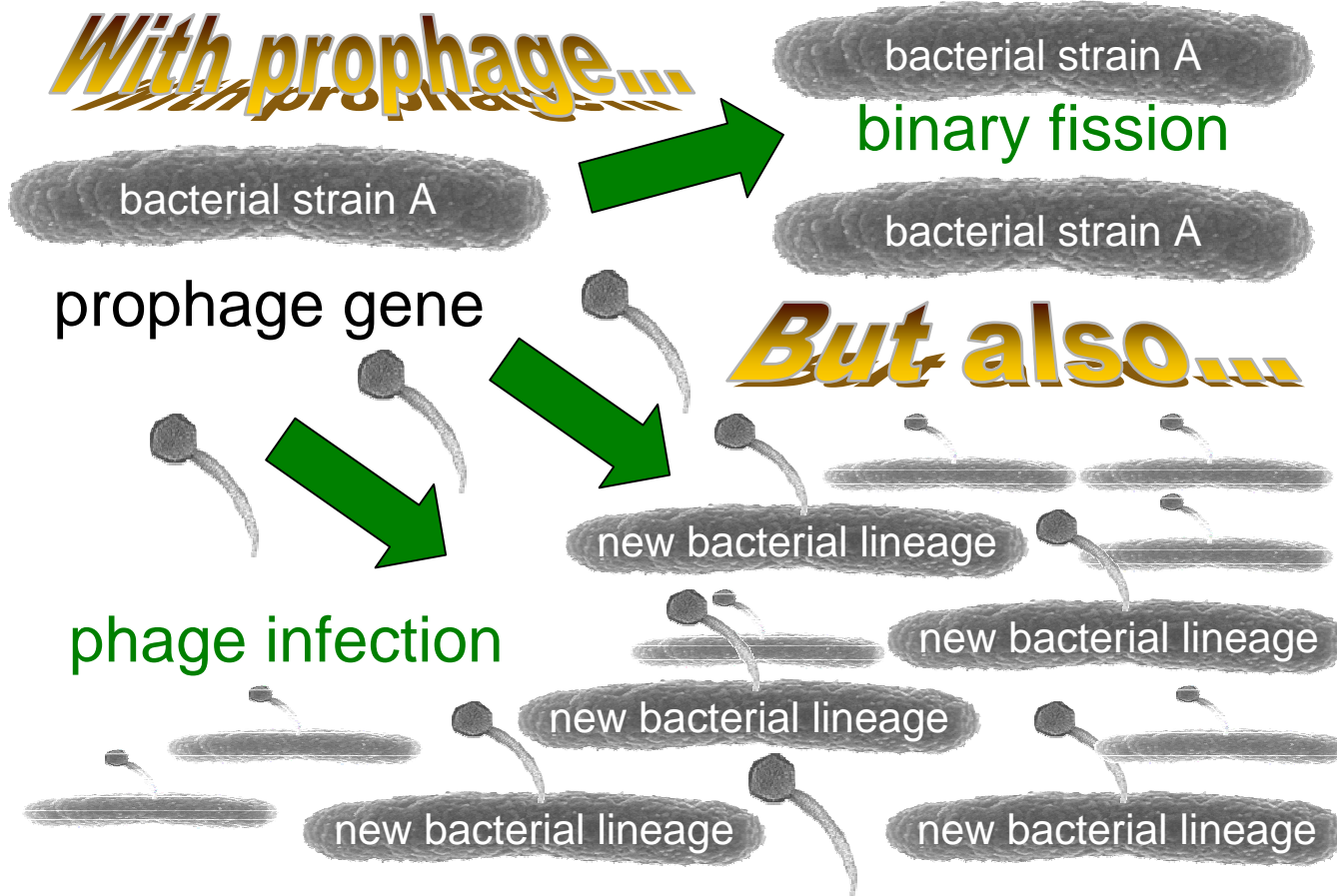


But what mechanisms make virion survival more relevant to one class of bacterial gene relative to the rest of a bacterium's genome? Could it be rare or modular gene utility?

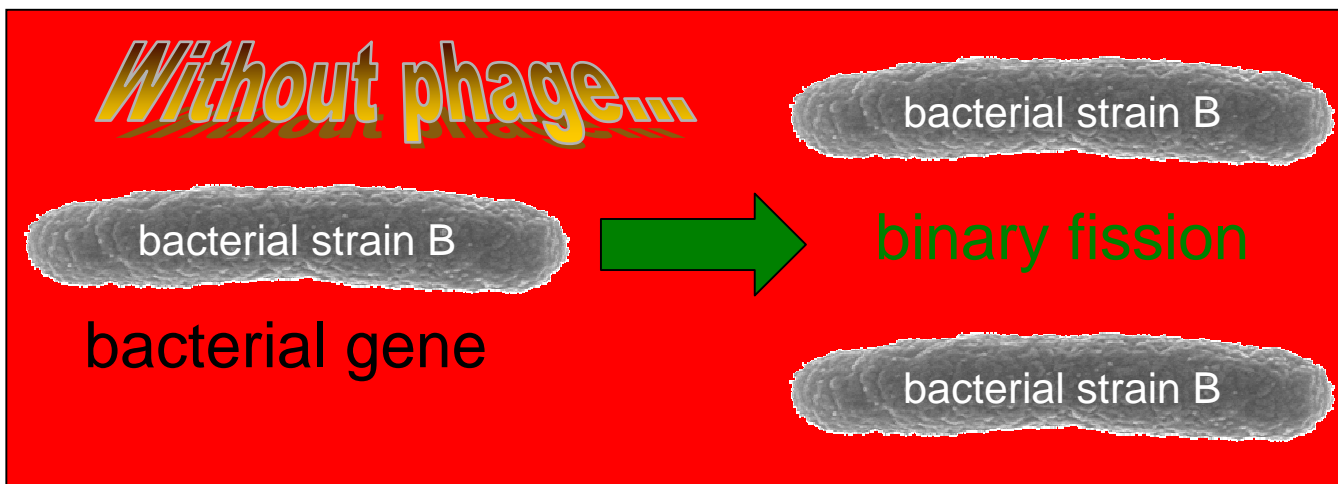
6. Faster Gene Exploration of Sequence Space

- i. More rounds of replication (as phage gene) results in greater mutation rates (than seen with bacterial genes).
- ii. Lower-fidelity phage replication also results in greater mutation rates.
- iii. Higher likelihood of recombination with divergent DNA than available to purely bacterial genes.
- iv. Greater diversity of genetic backgrounds (e.g., greater variation in encoding phage genomes as well as harboring host genomes).
- v. For greater variation to bestow greater fitness, organism must inhabit fluctuating environment.

7. Dissemination of Effective Toxin Dose



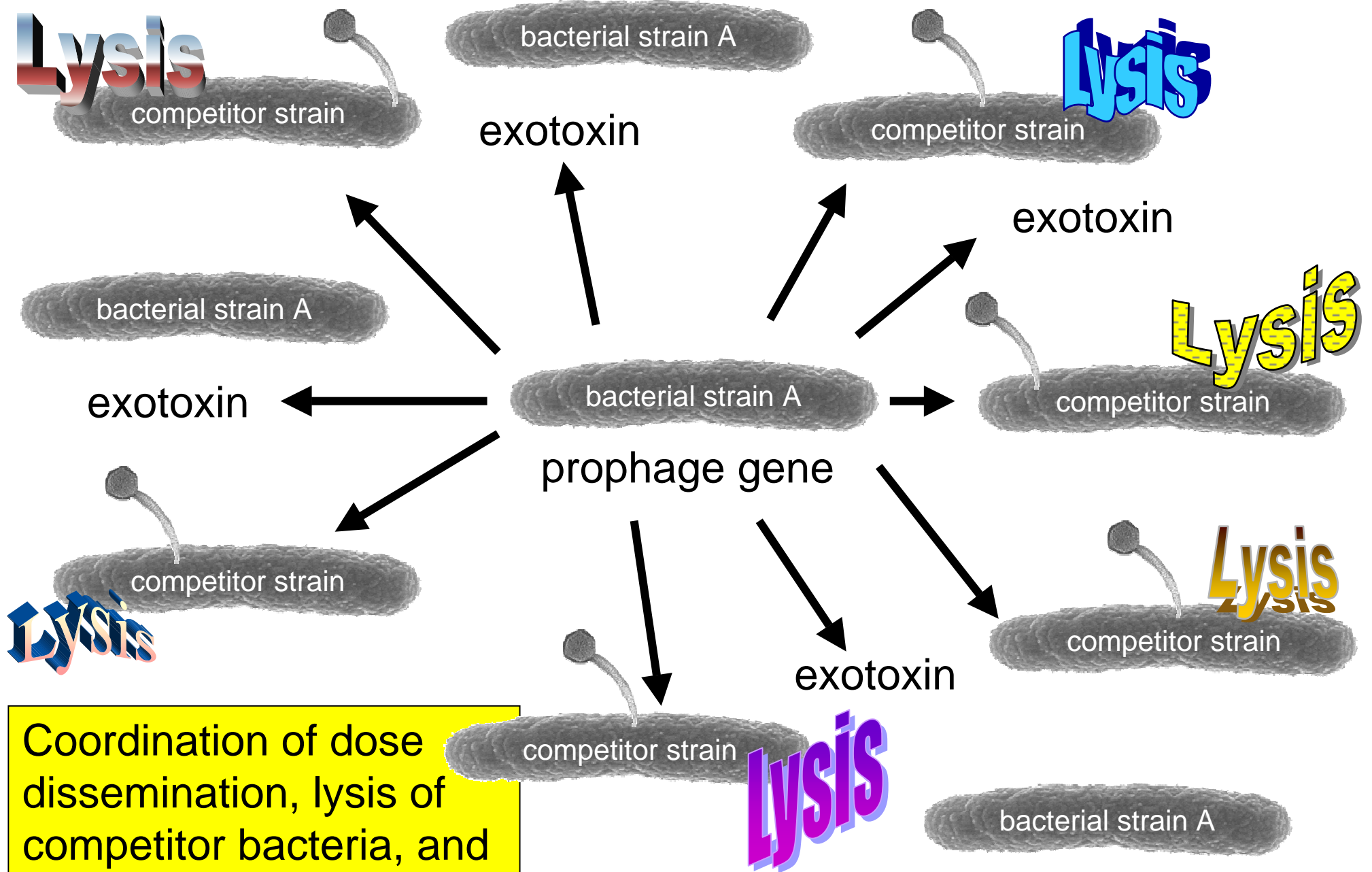
If more VF is better, then a prophage-encoded VF may increase in density due to phage-mediated gene dissemination to other bacteria. Particularly effective if VF is produced during lytic infection.



Relevance of effect may be limited to virulence factors that may be shared among bacteria, e.g., exotoxins.

Thanks go to Jeff Smith whose work on E.T.D. provided the catalyst for this entire project.

8. Gene Association with “Lysogen Allelopathy”



Coordination of dose dissemination, lysis of competitor bacteria, and exotoxin release/utility.

9. Gene Enhancement of Phage Replication

- i. Dual use as virulence factor and phage protein, e.g., phage-encoded hyaluronidase or *Streptococcus pyogenes* phage (spd1)-encoded DNase.
- ii. Expression resulting in increase in phage burst, decrease in phage latent period, etc.
- iii. Modification of bacterial environment to increase nutrients available to bacteria: **Phage-Encoded Exotoxins as Environment Modifiers that Enhance Phage Population Growth!**

With more nutrients available:

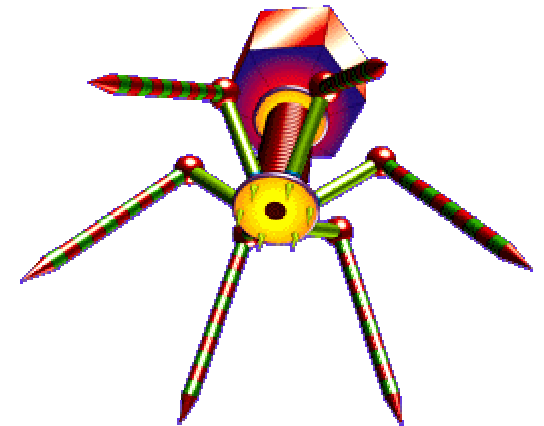
- Lysogens may replicate faster.
- Induced prophage may produce more progeny.
- Released virions may find more bacteria to infect.
- Infections may produce more phage progeny.

10. Gene Enhancement of Phage Dissemination



If bacteria can induce diarrhea to aid their dissemination to new animal hosts, then why can't phage express exotoxins to facilitate the transmission of phage progeny?

Note that stool loosing may also break up spatial structure within the intestinal lumen, thereby aiding phage dissemination within intestines to find new bacteria.



www.phage.org — The Bacteriophage Ecology Group Home of Phage Ecology and Evolutionary Biology

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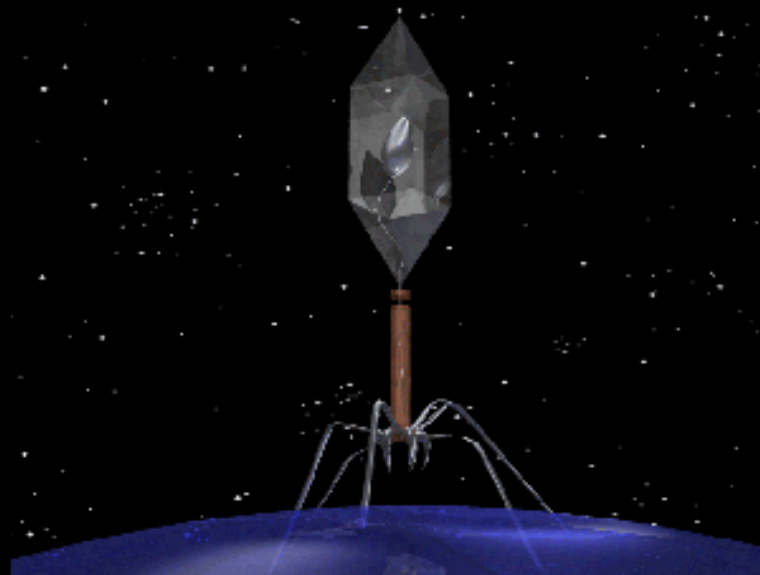
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 - Early Development of Mol. Bio. <
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 - Packaging of dsDNA <
 - General Aspects of Lysogeny <
 - Regulatory Circuitry of Phage λ <
 - Regulation of λ Transcription <
 - Phage Lysis <
- Cubic & Filamentous Phages III.
 - ϕ X60 et al., the *Microviridae* <
 - Filamentous Phage <
 - PRD1 Genome, Structure, Entry <
 - Lipid-Containing phage PM2 <
 - Single-Stranded RNA Phages <
 - Segmented dsRNA Genomes <
- Individual Tailed Phages IV.
 - The T1-like Bacteriophages <
 - T4 and Related Phages <
 - Bacteriophage T5 <
 - The T7 Group <
 - Bacteriophage N4 <
 - Phage ϕ 29 and Its Relatives <

- > Bacteriophage SPP1
- > Bacteriophage P1
- > The P2-like Bacteriophages
- > The Satellite Phage P4
- > λ Genetic Neighborhood
- > N15 Linear Plasmid Prophage
- > Phage P22
- > Bacteriophage Mu
- V. Phages by Host or Habitat
 - > Viruses of Archaea
 - > Phages of Cyanobacteria
 - > Marine Phages
 - > *Yersinia* Phages
 - > *B. subtilis* Temperate Phage
 - > Phages of *Lactococcus lactis*
 - > The *Listeria* Bacteriophages
 - > Mycobacteriophages
 - > *Streptomyces* Phages
 - > Mycoplasma Phages
 - > *Lactobacillus* Phages
- VI. Applications
 - > Control of Bacteriophage in... Fermentation Facilities
 - > Phage... Expression Systems
 - > ...in Display
 - > ...as Pollution Indicators
 - > ...as Diagnostic Systems
 - > ...in Bacterial Pathogenesis
 - > Phage Therapy

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- 1. **Phage and the Early Development of Molecular Biology**, William C. Summers
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- 14. **Lipid-Containing Bacteriophage PM2, The Type-Organism of *Corticoviridae***, Dannis H. Bamford and Jaana K. H. Bamford
- 15. **Single-Stranded RNA Phages**, Jan Van Duin and Nina Tsareva
- 16. **Phages with Segmented Doubled-Stranded RNA Genomes**, Leonard Mindich
- 17. **The T1-like Bacteriophages**, Gregory T. German, Raseev Misra, and Andrew M. Kropinski
- 18. **T4 and Related Phages: Structure and Development**, Gisela Mosig and Fred Eiserling
- 19. **Bacteriophage T5**, Jon R. Sayers
- 20. **The T7 Group**, Ian Molineux
- 21. **Bacteriophage N4**, Krystina M. Kazmierczak and Lucia B. Rothman-Denes
- 22. **Phage ϕ 29 and Its Relatives**, Margarita Salas
- 23. **Bacteriophage SPP1**, Juan C. Alonso, Paulo Tavares, Rudi Lurz, and Thomas A. Trautner

- 24. **Bacteriophage P1**, Hansjörg Lehnerr
- 25. **The P2-like Bacteriophages**, Anders S. Nilsson and Elisabeth Haggård-Ljungquist
- 26. **The Satellite Phage P4**, Gianni Dehò and Daniela Ghisotti
- 27. **Phage Lambda and its Genetic Neighborhood**, Roger Hendrix and Sherwood Casjens
- 28. **N15: The Linear Plasmid Prophage**, Nikolai V. Ravin
- 29. **Phage P22**, Peter E. Prevelige
- 30. **The Bacteriophage Mu**, Luciano Paolozzi and Patrizia Ghelardini
- 31. **Viruses of Archaea**, Kenneth M. Stedman, David Prangishvili, and Wolfram Zillig
- 32. **Phages of Cyanobacteria**, Nicholas H. Mann
- 33. **Marine Phages**, Robert V. Miller
- 34. **Yersinia Phages**, Stefan Hertwig, Mikael Skurnik, and Bernd Appel
- 35. **Temperate Bacteriophages of *Bacillus subtilis***, Pamela S. Fink and Stanley A. Zahler
- 36. **Phages of *Lactococcus lactis***, Lone Brøndsted and Karin Hammer
- 37. **The *Listeria* Bacteriophages**, Martin J. Loessner and Richard Calendar
- 38. **Mycobacteriophages**, Graham F. Hatfull
- 39. **Molecular Genetics of *Streptomyces* Phages**, Margaret C. M. Smith
- 40. **Mycoplasma Phages**, Jack Maniloff and Kevin Dybvig
- 41. ***Lactobacillus* Phages**, Harald Brüssow and Juan E. Suárez
- 42. **Control of Bacteriophage in Commercial Microbiology and Fermentation Facilities**, Gregg Bogosian
- 43. **Phage-Based Expression Systems**, Noreen E. Murray
- 44. **Phage in Display**, Björn H. Lindqvist
- 45. **Bacteriophage as Pollution Indicators**, Charles P. Gerba
- 46. **The Use of Phage as Diagnostic Systems**, Cath Rees
- 47. **Bacteriophages in Bacterial Pathogenesis**, Patrick L. Wagner and Matthew K. Waldor
- 48. **Phage Therapy**, Carl R. Merrill, Dean Scholl, and Sankar Adhya