



Molecular Evolution of Bacteriophage

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Outline of Content

Introduction

- What is Bacteriophage?
- Morphology of Bacteriophage
- Genome Structure
- Life Cycle
- HGT in Evolution
- Phages in Gut

Evolutionary Mode

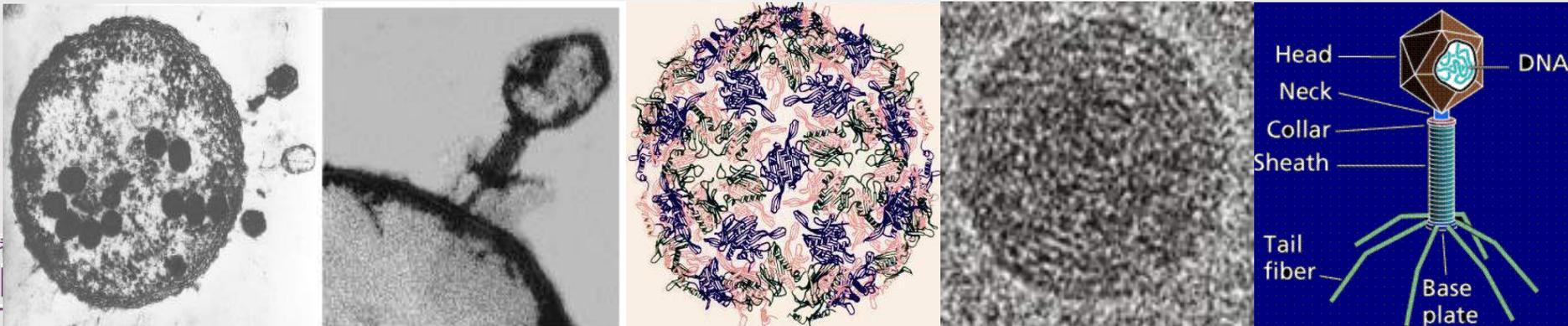
- Two Different Evolutionary Mode
- Different Host Phyla
- Rate of HGT
- Different Genome

Phage Therapy in Future

- Viral Fraction Transplantation

What is Bacteriophage (Phage)?

- Virus taking **prokaryotes** as host
- Double stranded DNA, single stranded DNA, RNA (**3k-500kbp**)
- lytic phage vs. temperate phage



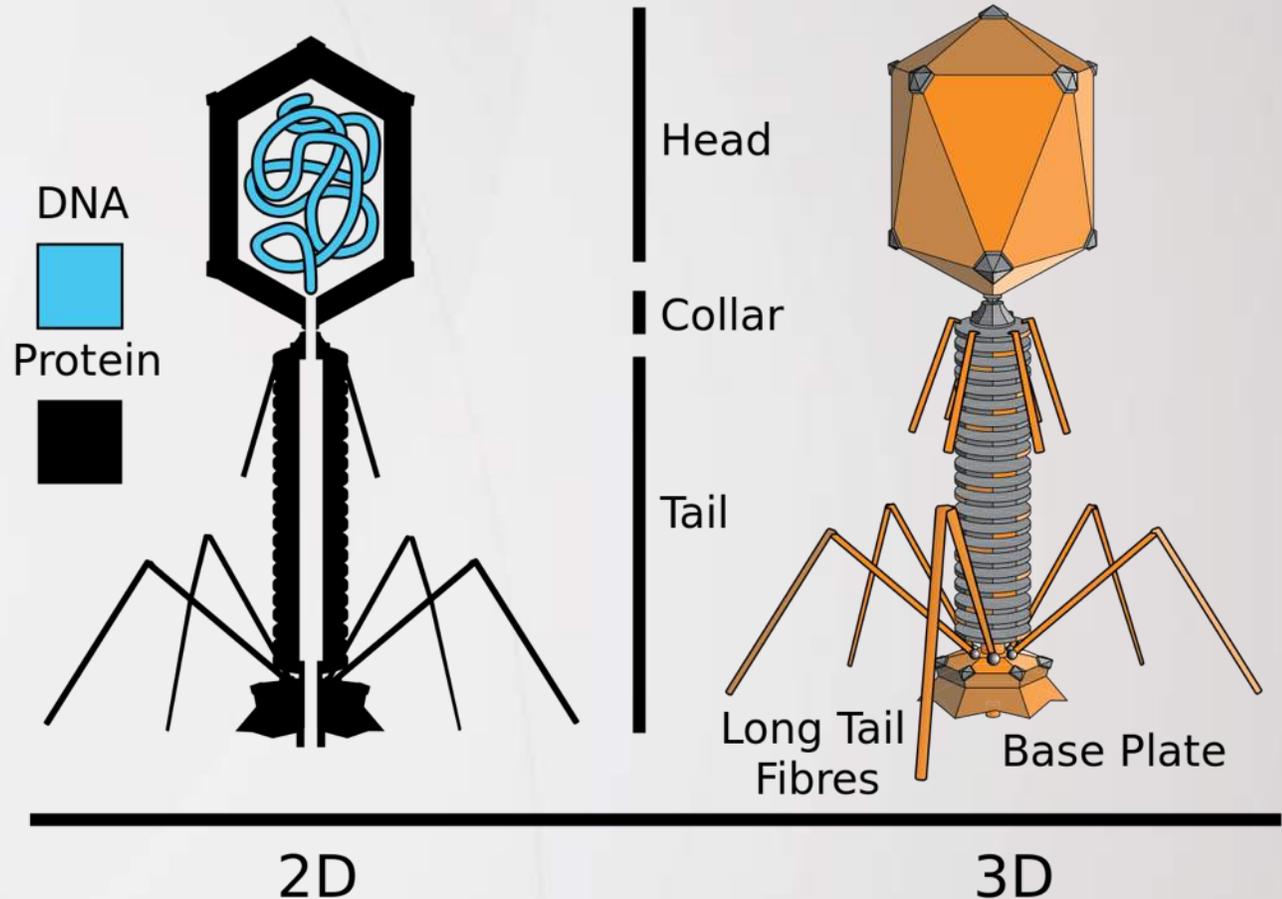
Morphology of Bacteriophage

Head

- Hexagonal protein
- **Nucleic acid** (DNA or RNA) cover by capsid

Tail

- Cylindrical
- **Hollow core** or tube (surround by sheath)
- **Short spike** & long tail fibre



From wikimedia

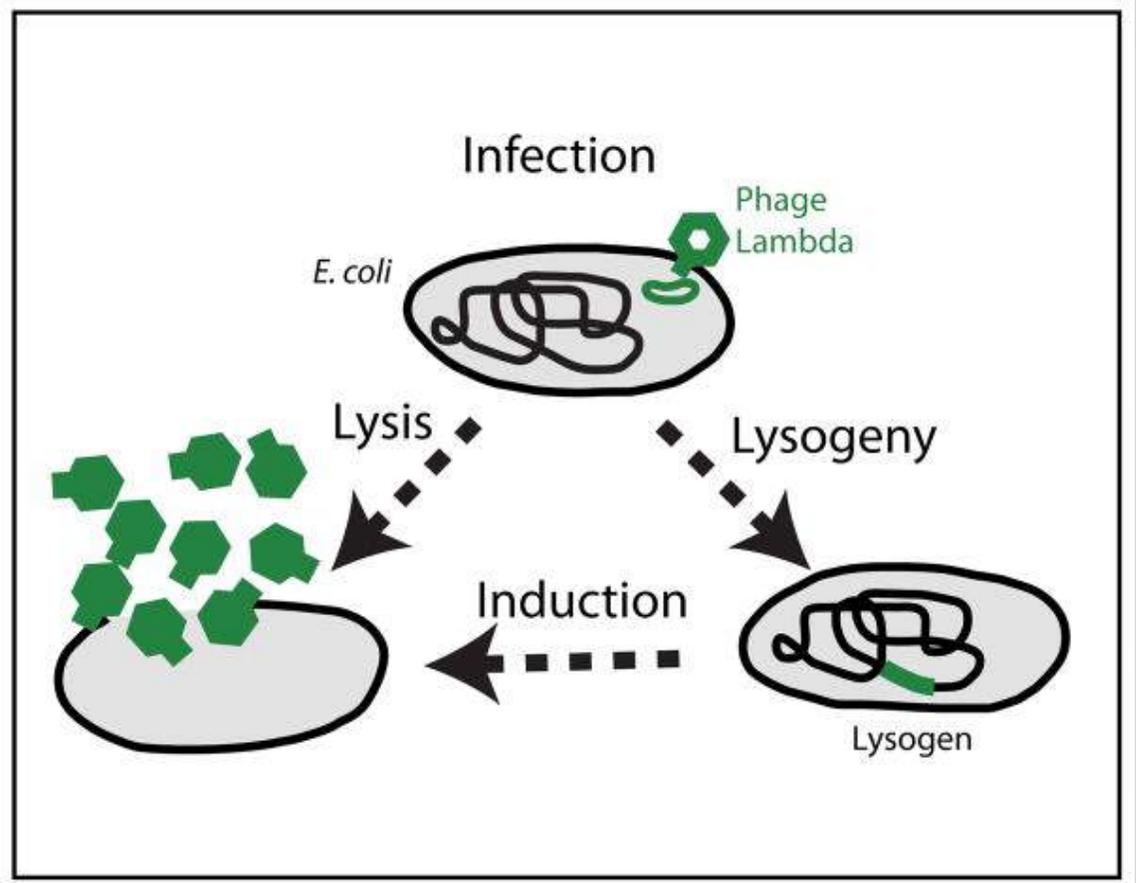
Life Cycle of Bacteriophage

Lytic Cycle

- Nucleic acid exists as **separate**
- Destruction of infected host
- Eg. Phage T4

Lysogenic Cycle

- Integration of nucleic acid into host's genome to generate prophages
- Lysogens
- Induction to **lytic growth**
- Eg. Phage Lambda



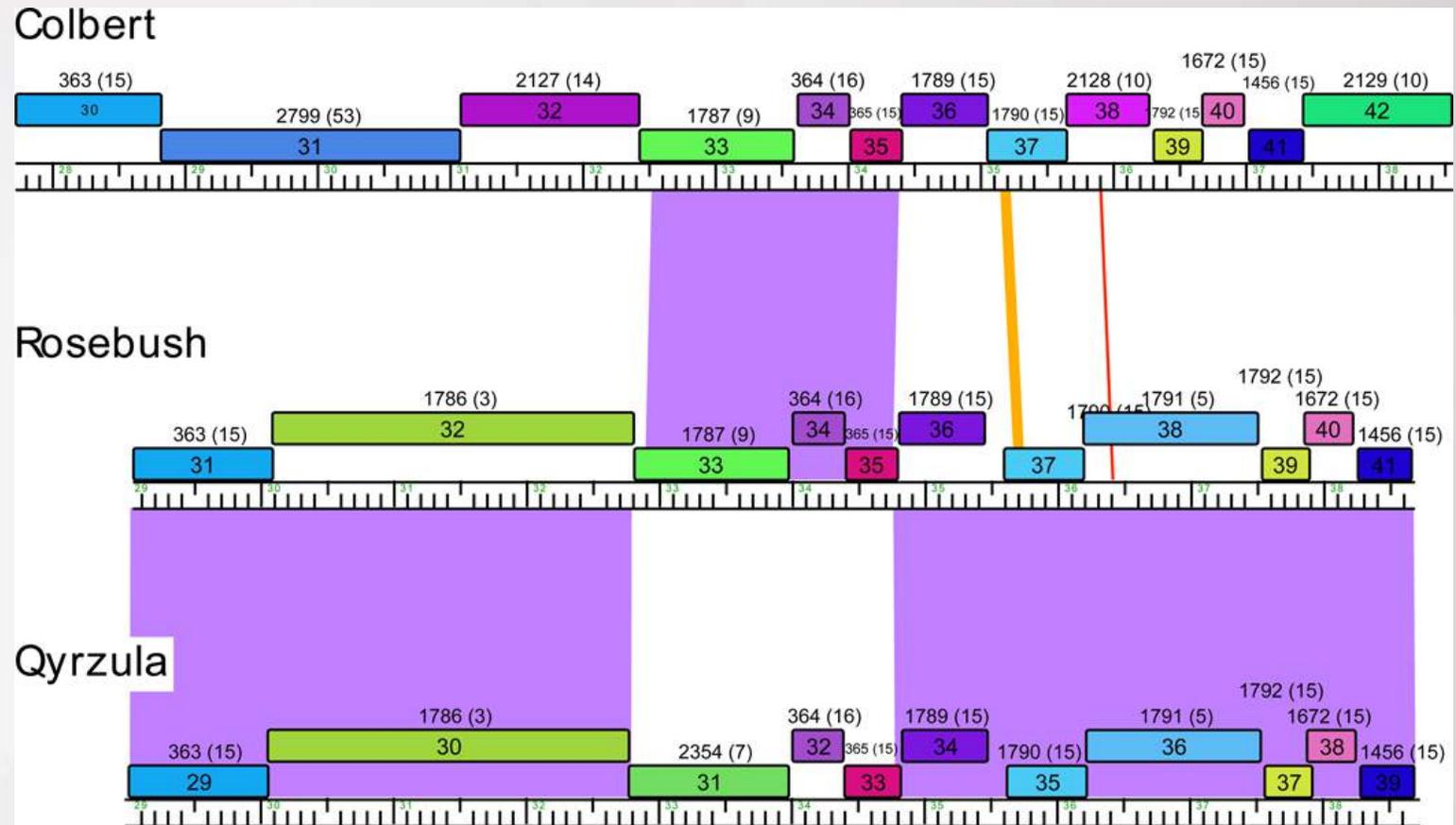
Golding, I., Decision making in living cells: lessons from a simple system. Annu Rev Biophys, 2011. 40: p. 63-80.

Genome Structure

Mosaicism

- Diversity
- Horizontal gene transfer (HGT)
- Occasionally occur
- Illegitimate recombination between short conserved sequences.

It lays a foundation for frequent evolution!!

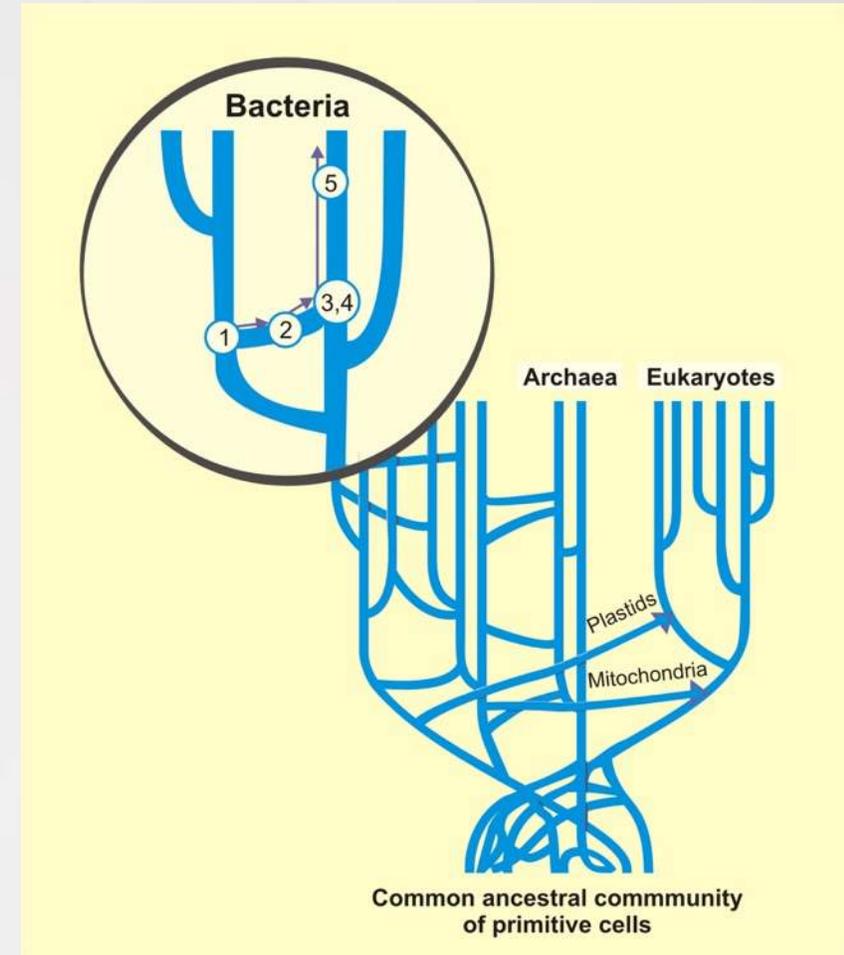


Hatfull, G.F. and R.W. Hendrix, *Bacteriophages and their genomes*. Curr Opin Virol, 2011. 1(4): p. 298-303.

Horizontal Gene Transfer (HGT) in Evolution

HGT is the movement of genetic material between multicellular organisms, and it is an important factor in the evolution of many organisms.

- Organelle to nuclear genome
 - Bacteria to fungi
 - Endosymbiont to insects
 - Organelle to organelle
 - Virus to plant
 - Virus to bacteria
- so on...



From Barth F. Smets.

Bacteria–Phage Antagonistic Coevolution (AC)

Gut bacteria:

- 90% are members of the Firmicutes and Bacteroidetes phyla
- Remaining members belong to Proteobacteria, Actinobacteria, Fusobacteria and Verrucomicrobia phyla

Gut phages:

- Mostly double-stranded and single-stranded DNA phages
- *Myoviridae*, *Podoviridae*, *Siphoviridae* and *Microviridae*
- Infect members of the Firmicutes, Bacteroidetes, Proteobacteria and Actinobacteria
- Mostly integrated as prophages

Positive impact of within-host AC

- Higher microbial diversity
- Niche exclusion
- Bacterial Attenuation
- Adaptive immunity
- Enhanced metabolic function

Negative impact of within-host AC

- Altered microbiota
- Altered bacterial metabolic function
- Increased virulence
- Inflammation
- Intestinal disease

Scanlan, P. D. Bacteria-Bacteriophage Coevolution in the Human Gut: Implications for Microbial Diversity and Functionality. *Trends Microbiol* **25**, 614-623, doi:10.1016/j.tim.2017.02.012 (2017).

Gut Phages and Intestinal Diseases

The potential role of phages in gut

Regulation of the bacterial population

Anti-inflammatory action

Regulation of local immunity (immunomodulation)

Probiotic activities

- Bacteriophages control the bacteria population in the human gut and influence the bacterial diversity and metabolism, which may cause some diseases.

- Increase in the richness of *Caudovirales* phages is related to **IBD** and **Crohn's disease**.
- Lysis of bacteria leads the release of proteins, lipids, which induce **intestinal inflammation**.

Lusiak-Szelachowska, M., Weber-Dabrowska, B., Jonczyk-Matysiak, E., Woiciechowska, R. & Gorski, A. Bacteriophages in the gastrointestinal tract and their implications. *Gut Pathog* 9, 44, doi:10.1186/s13099-017-0196-7 (2017)

EVOLUTION!!!

nature
microbiology

LETTERS

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Bacteriophage evolution differs by host, lifestyle and genome

Travis N. Mavrich and Graham F. Hatfull*

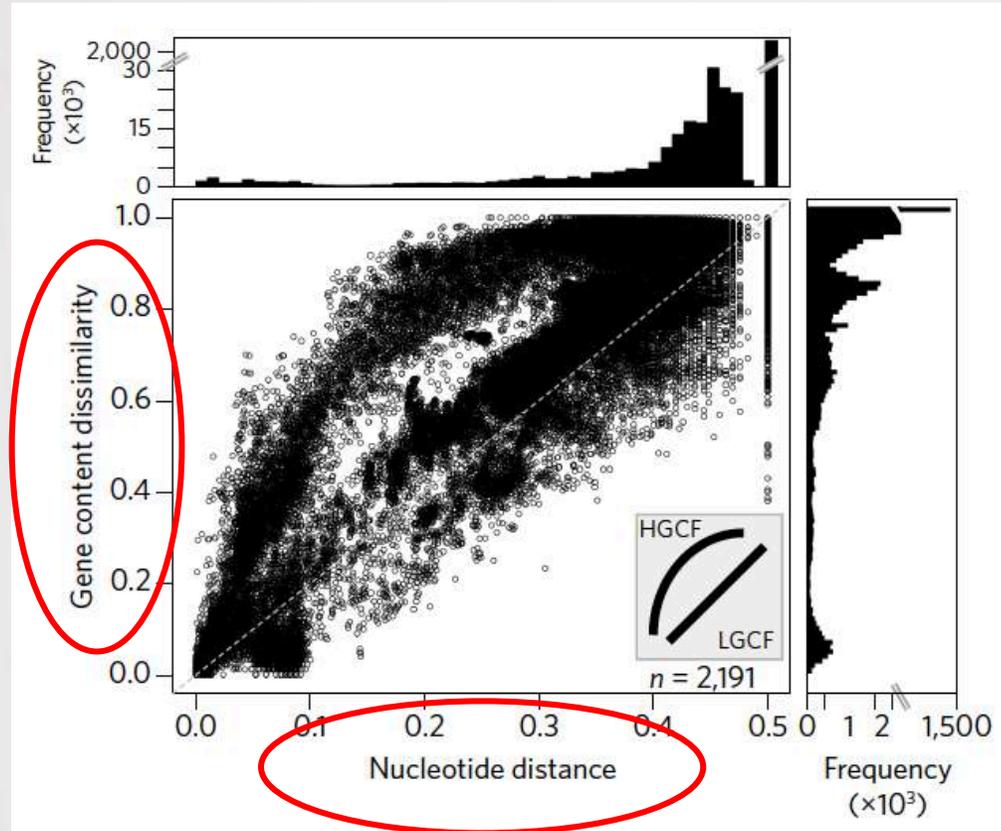
NO universal genetic marker for identifying phages, which makes the issue complicated !!

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Two Different Evolutionary Patterns



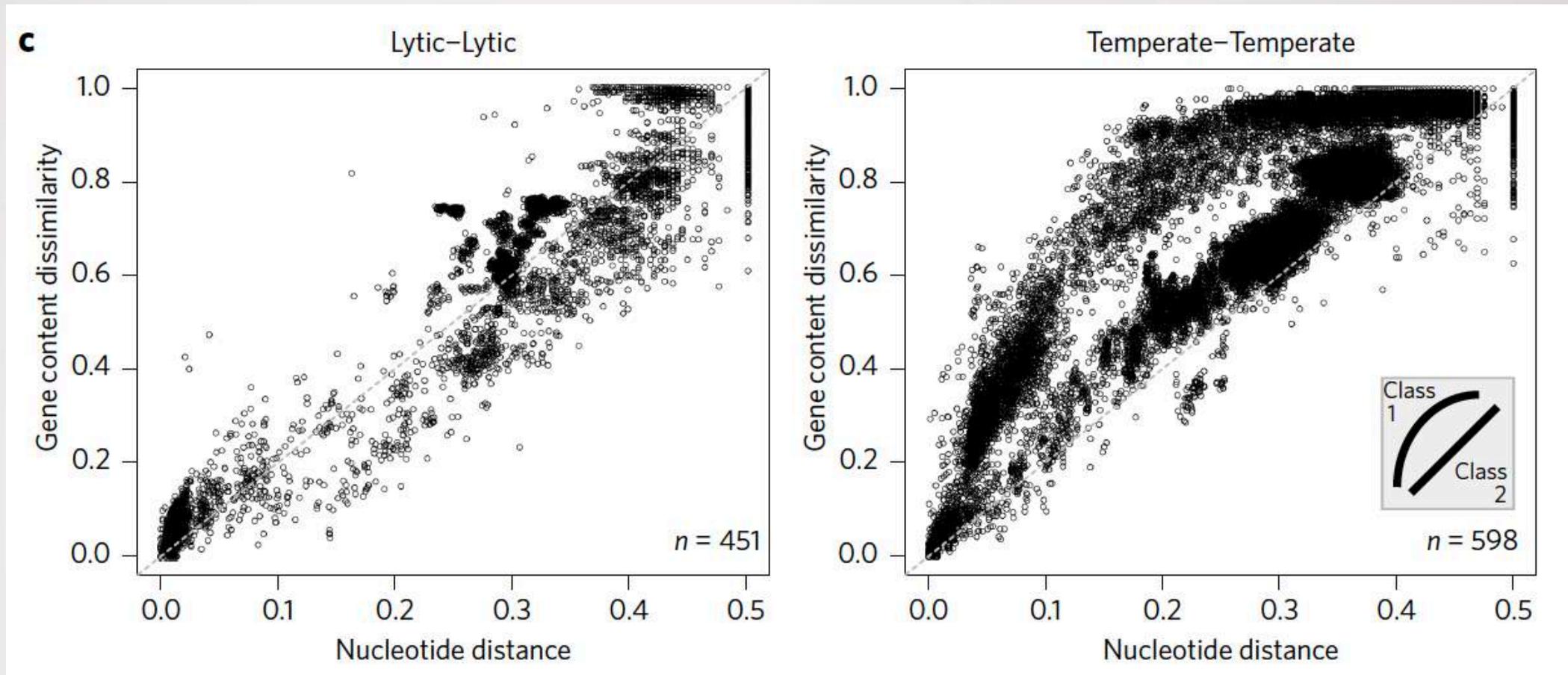
Comparisons between genomes reveal two distinct evolutionary patterns.

- Gene content dissimilarity **increases more quickly** as nucleotide distance grows
- Gene content dissimilarity is **proportional** to nucleotide distance

HGCF=high gene content flux

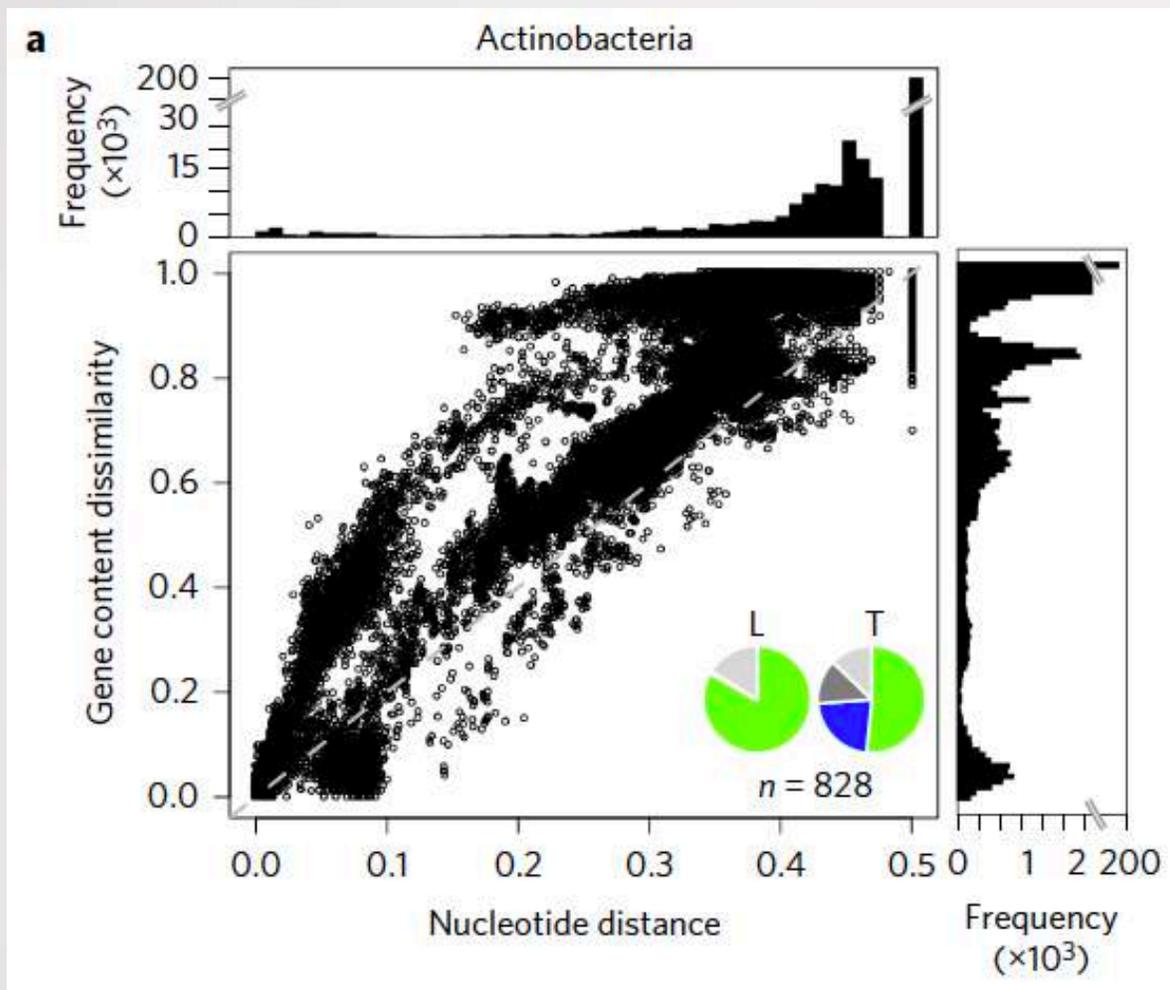
LGCF=low gene content flux

Life Style Determines the Evolution Mode



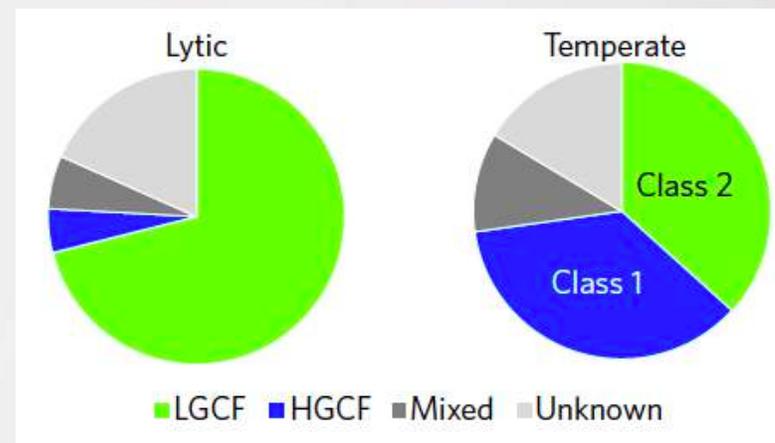
- Lytic phages lie within **the LGCF mode (94%)**
- Temperate phages segregate into both the **HGCF (43%)** and **LGCF (57%)**

Host Phyla Influence the Evolutionary Distribution



Actinobacteriophage

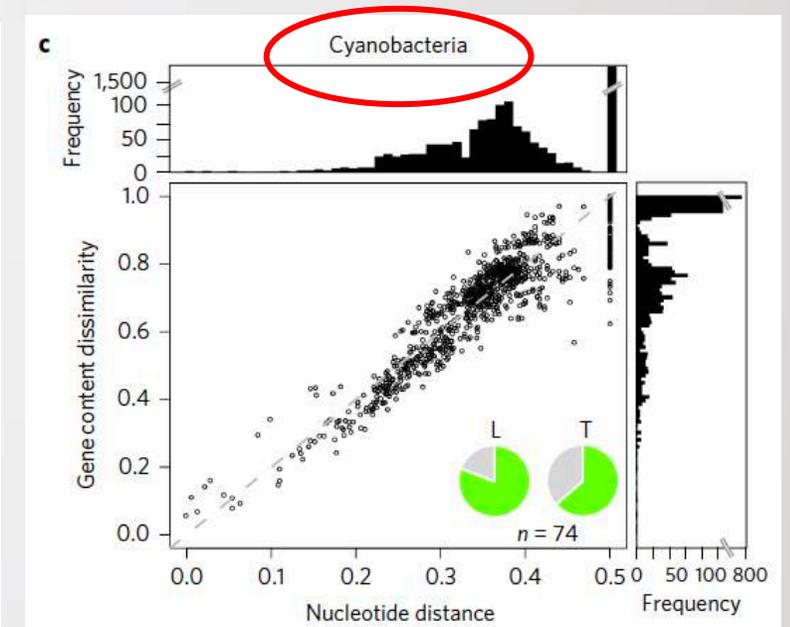
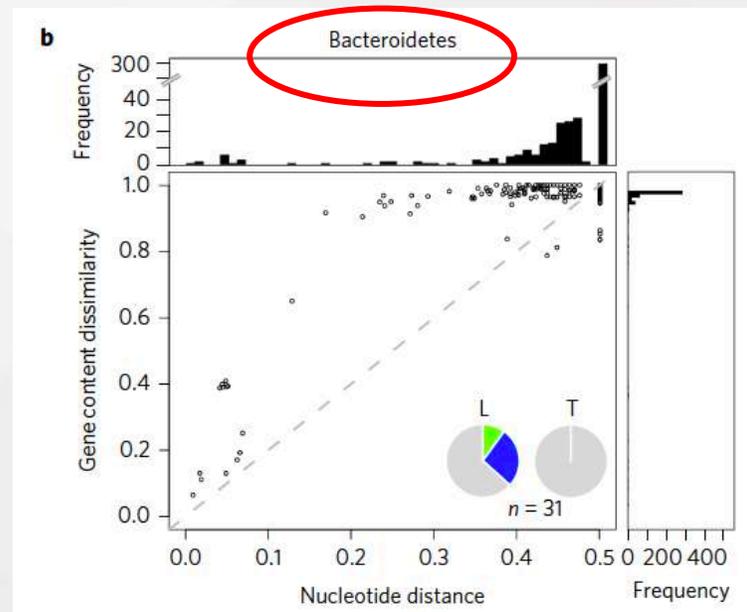
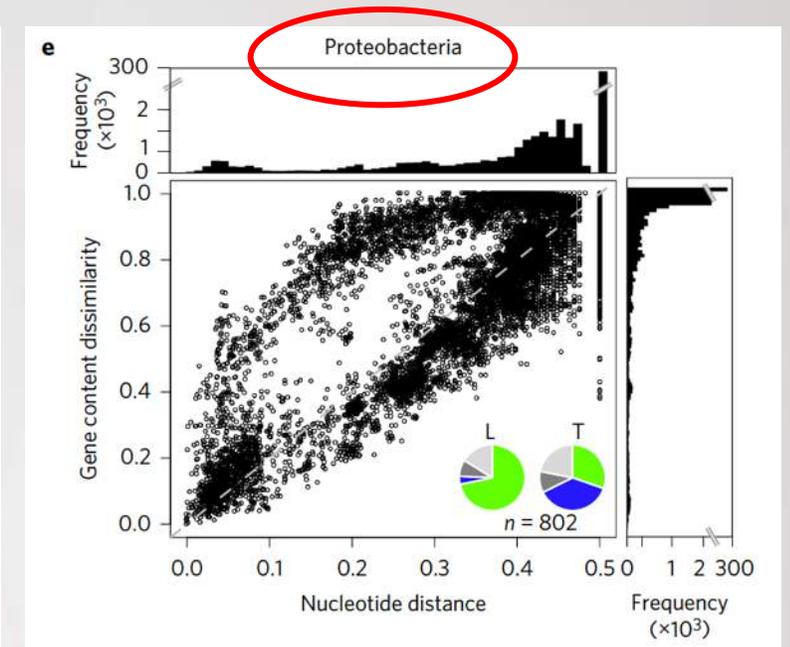
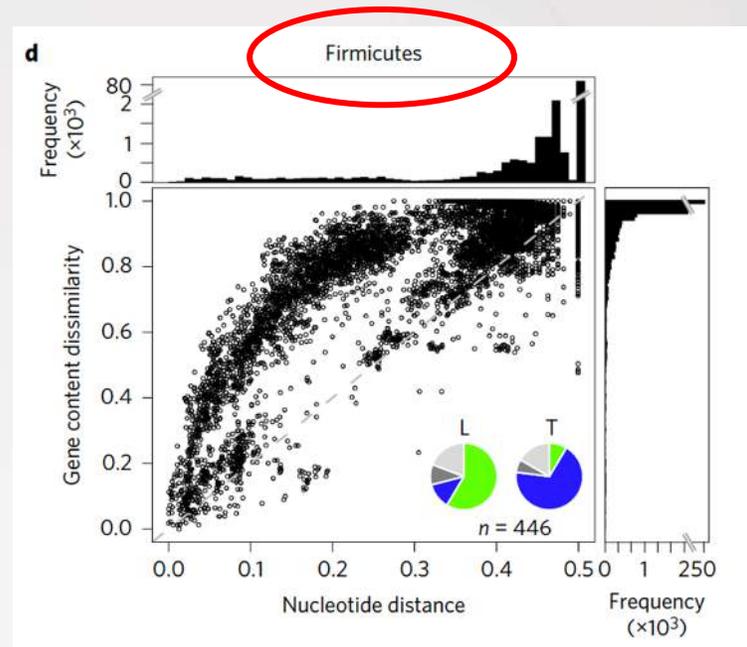
- **Both lytic phages and temperate phages** infect the actinobacteria
- Phages infecting actinobacteria lie within both **HGCF** and **LGCF**



Other Host Phyla

- **More than 80%** of firmucutes phages are temperate phages.
- **Less than 50%** of temperate phages infecting Proteobacteria.

- Phages infecting Bacteroidetes and Cyanobacteria distribute almost exclusively to HGCF and LGCF respectively.

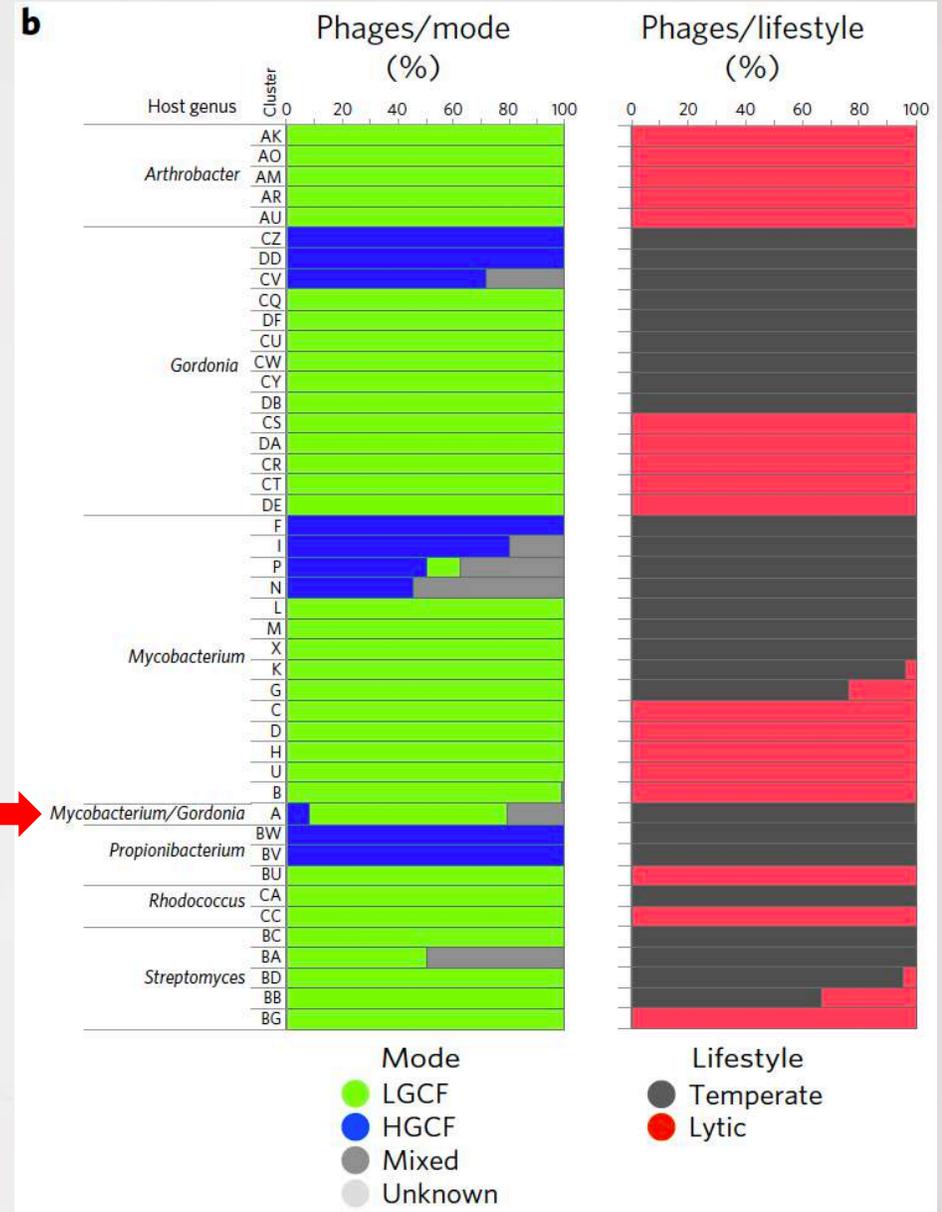


Clusters in Actinobacteria Phylum Differ in Evolution Mode

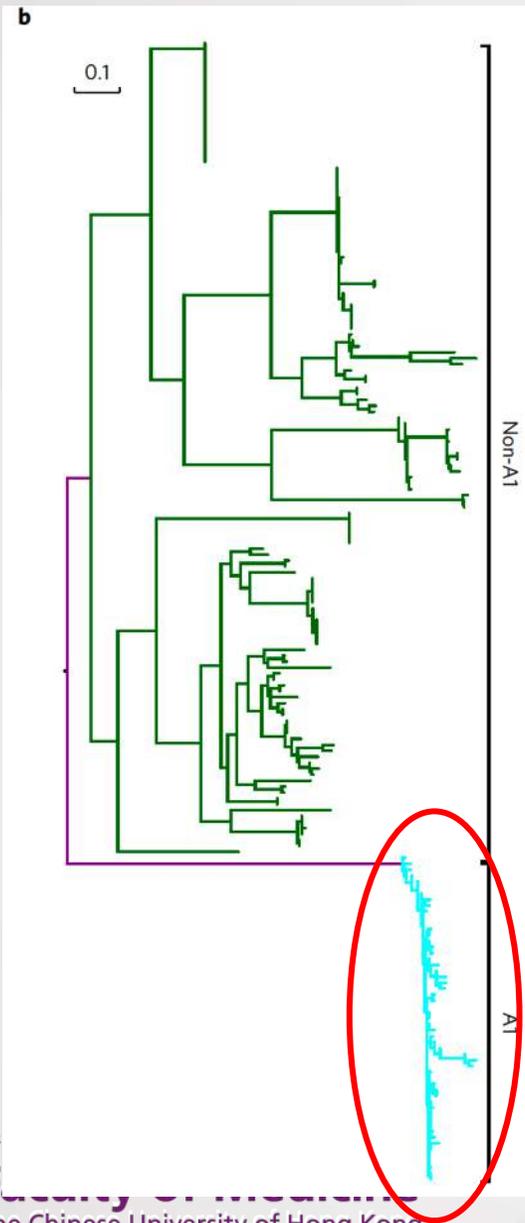
- ◆ The correlation between genome type and evolutionary mode extends to most of the clusters, and the genome contribute to the phages lifestyle.



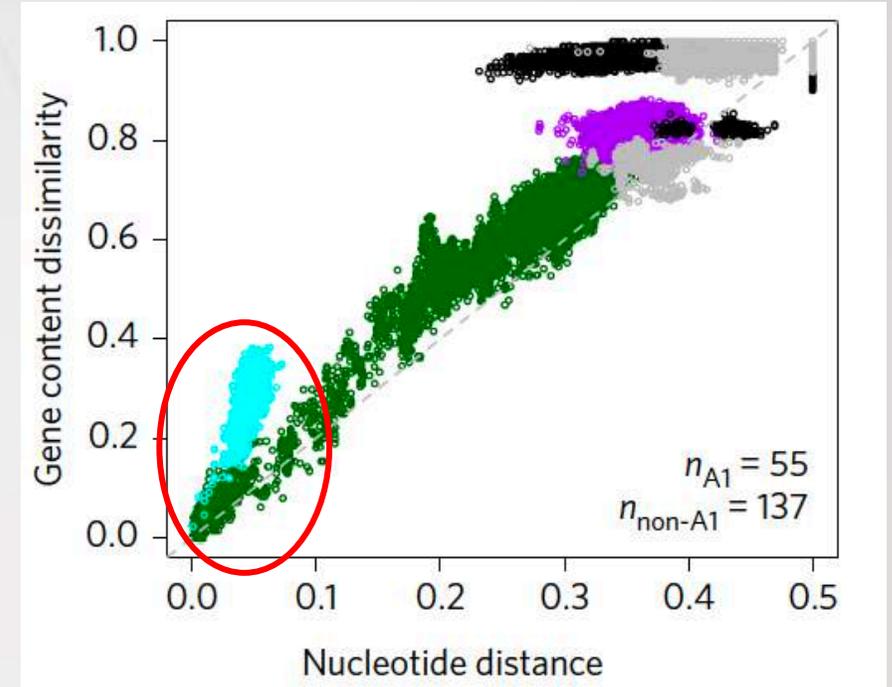
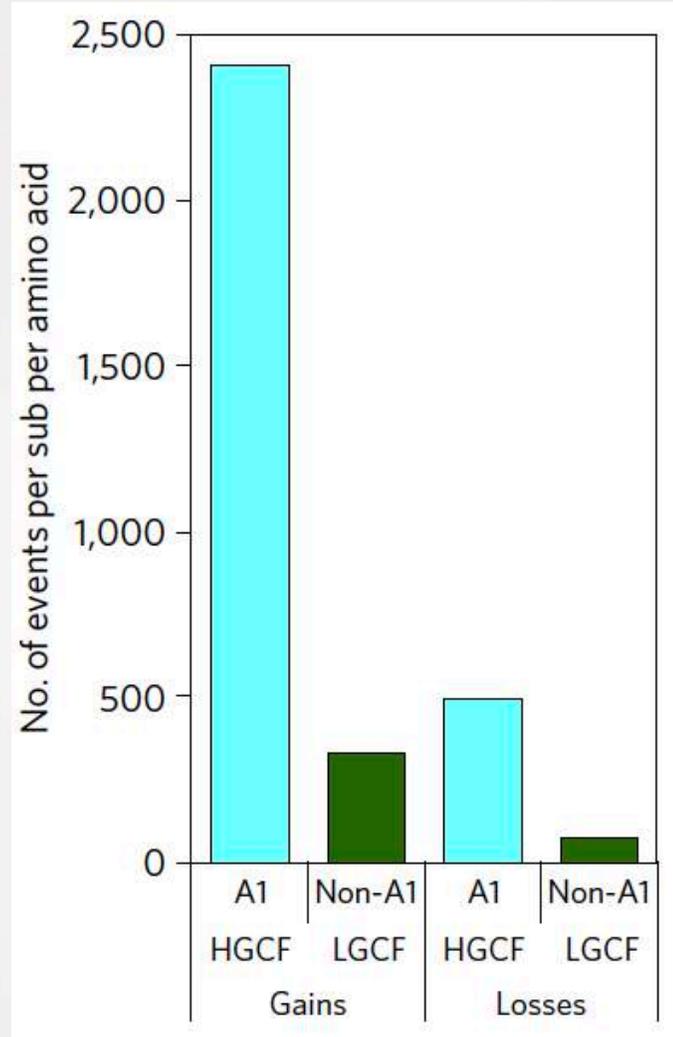
Actinobacteria



Frequent HGT Gives the HGCF Bias



25%

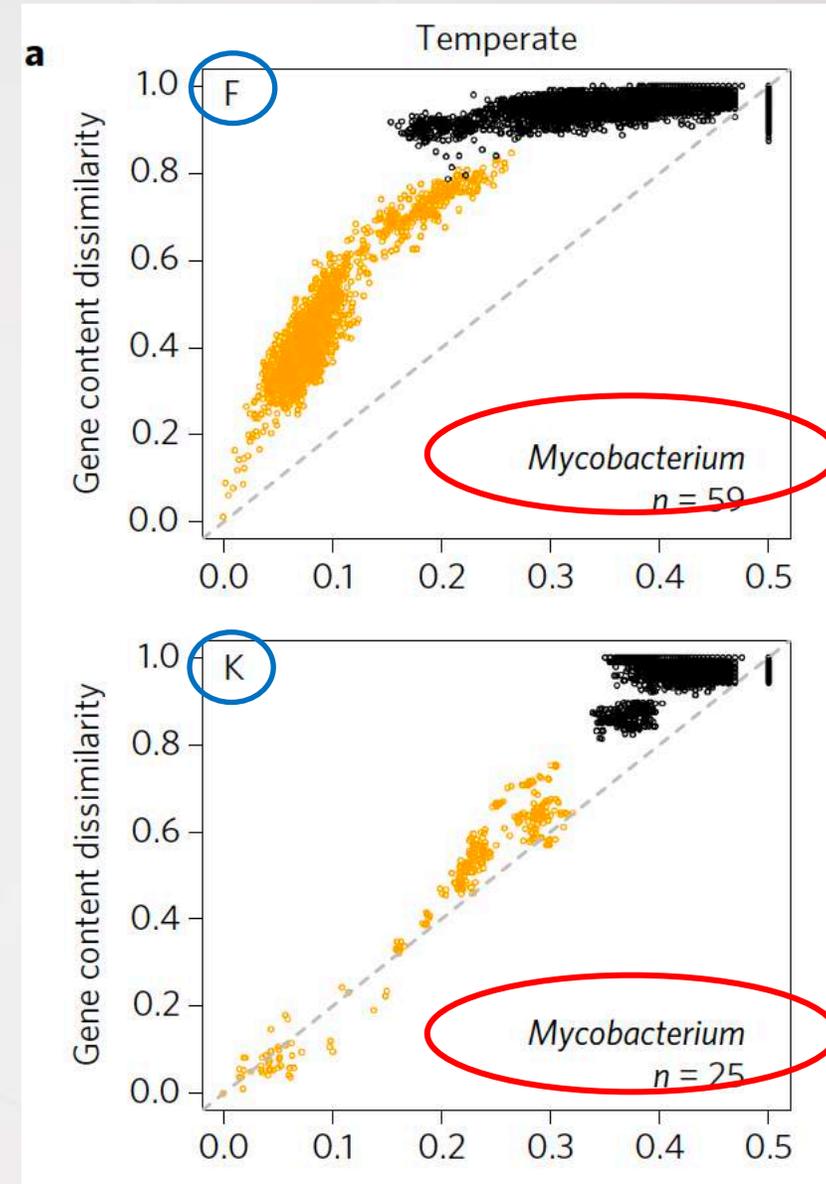


- Mycobacteriophage Cluster A
- Gene gains and losses 10 times over others
- Subcluster A1 distribute in HGCF

Genome Determines the Evolution Mode

The evolution of phages depends on the cluster classification.

Eg. temperate *Mycobacterium* Cluster F phages evolve exclusively in HGCF mode, whereas temperate *Mycobacterium* Cluster K exclusively evolve in the LGCF mode.

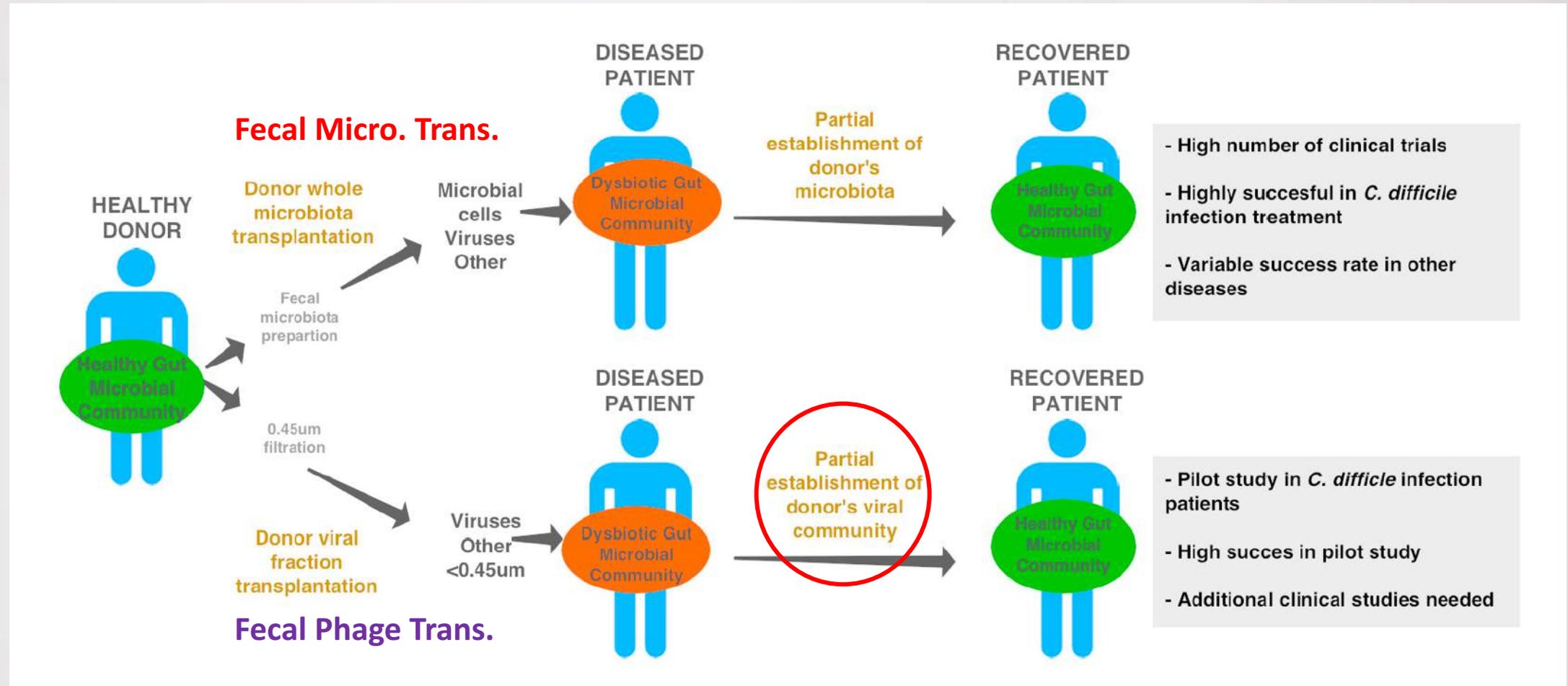


Summary

Although the biological mechanisms that cause the two evolutionary mode are unclear, the two mode have important biological implications.

- The bifurcation of evolutionary modes by host, environment, lifestyle and genome account for phage **genome mosaicism and evolution**.
- The traits of many **temperate phages** that contribute to host physiology, virulence and viral defence may **fuel the HGCF mode**.
- Some other factors, eg. **Variations in host evolution**, differential access to the common gene pool in **different environments**, and the roles of temperate phages at **different microbial densities**, are expected to contribute to these evolutionary mode.

Our Future – Phage therapy





Thanks for attention

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