Is Sharing Caring?

Elucidating the Effects of the Presence of CRISPR-Cas Systems on Rates of Horizontal Gene Transfer Using Network Analysis

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MolBiol 4C12 Thesis

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Biology Department,
McMaster University

April 1, 2019

Table of Contents

CRISPR-Cas systems

What Are They?

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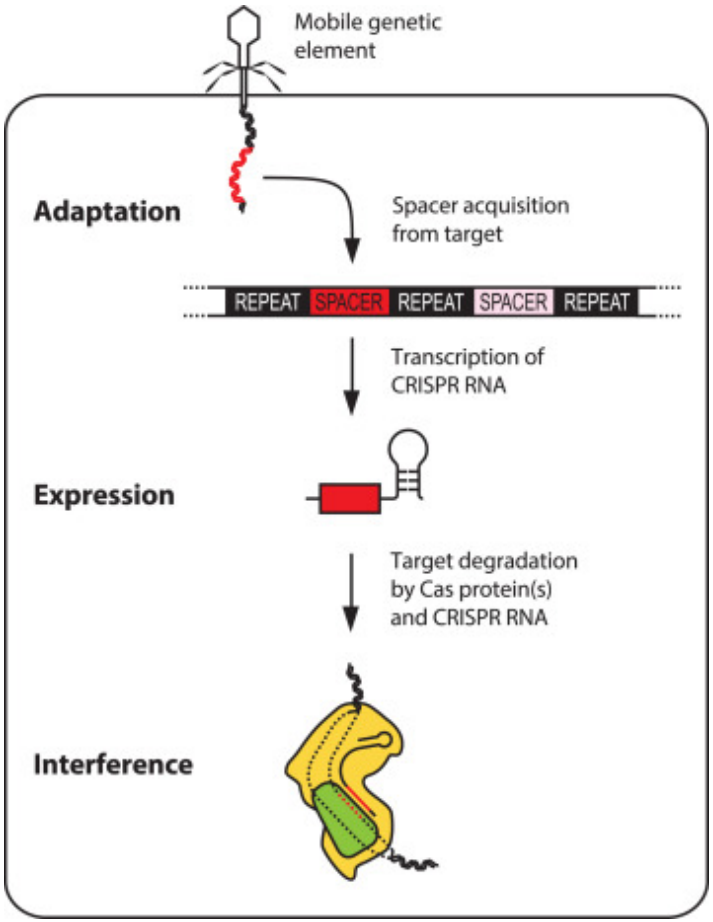
- Adaptive Bacterial Immune System



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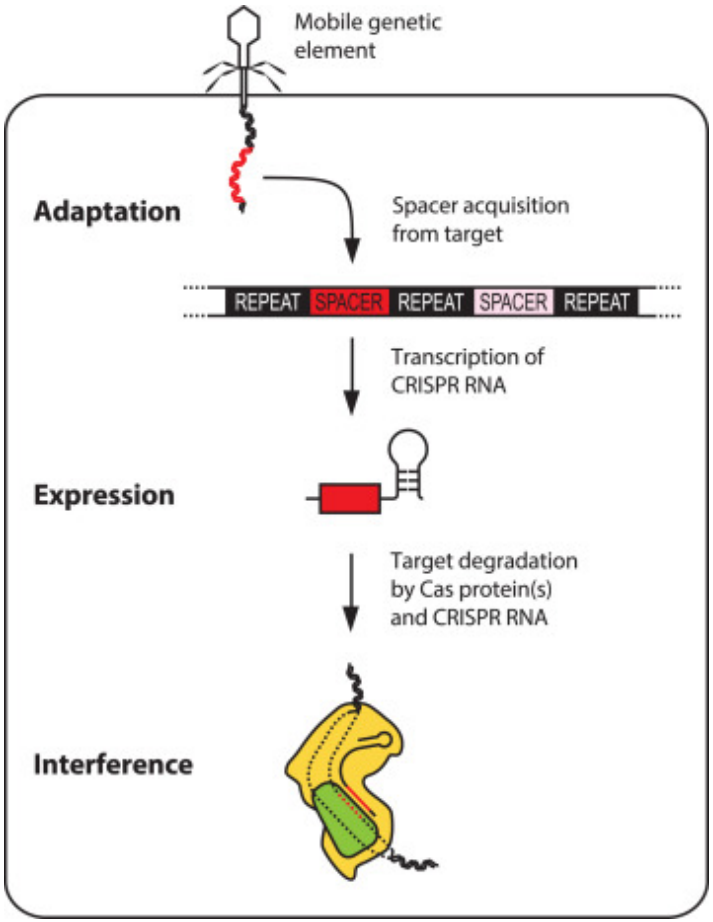

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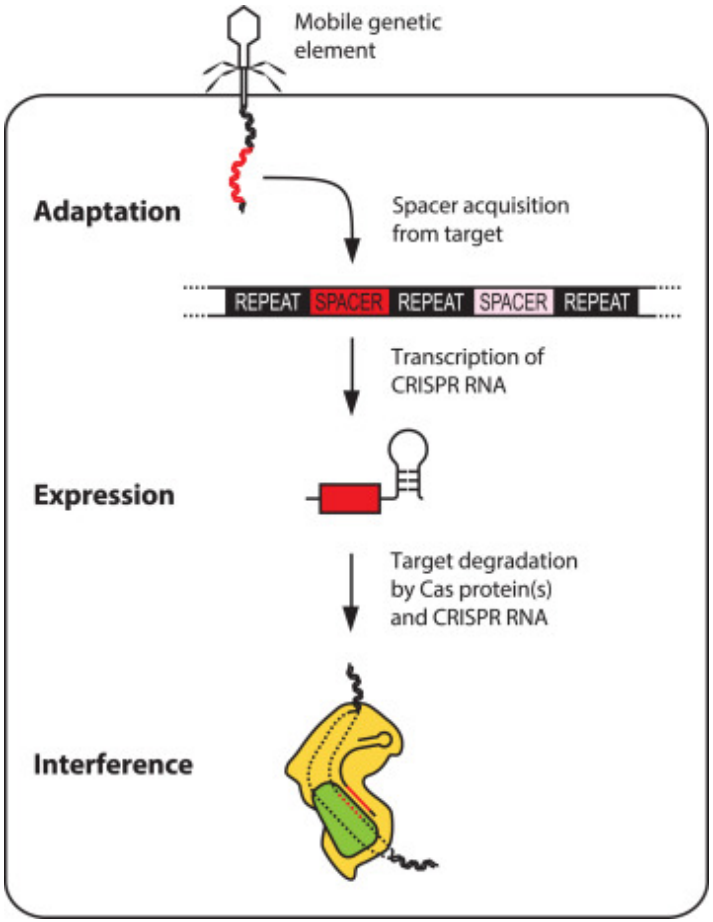

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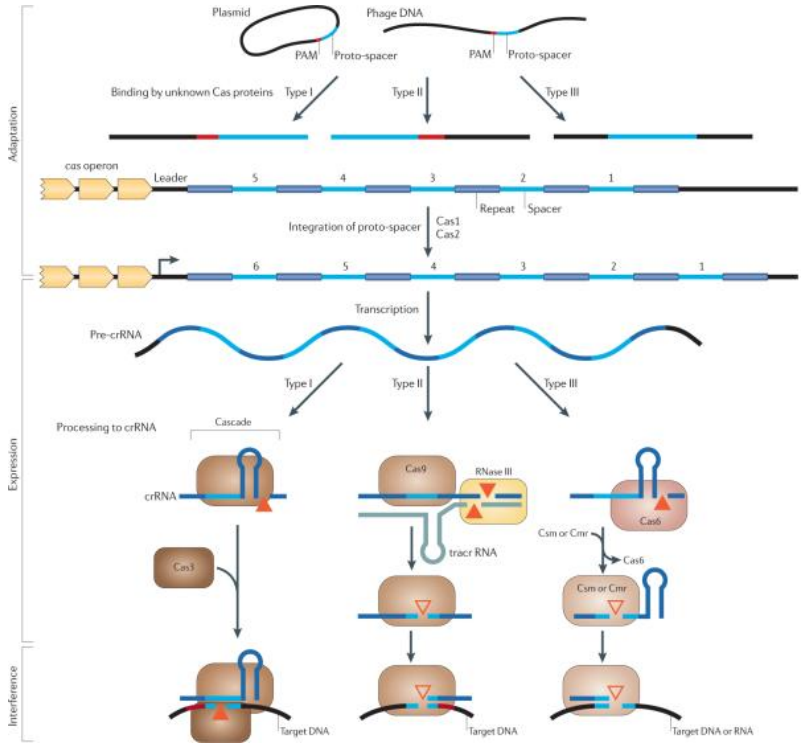

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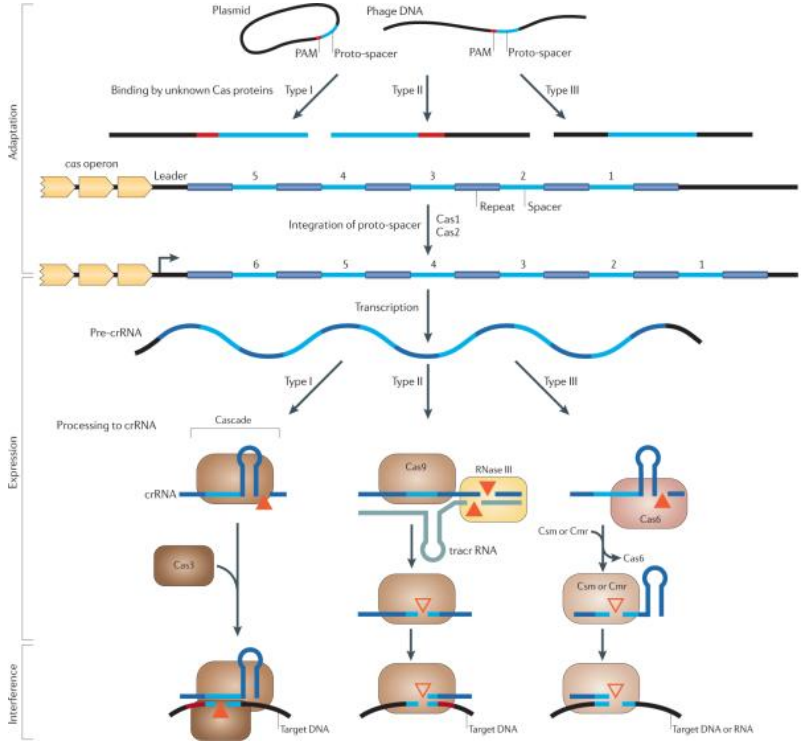

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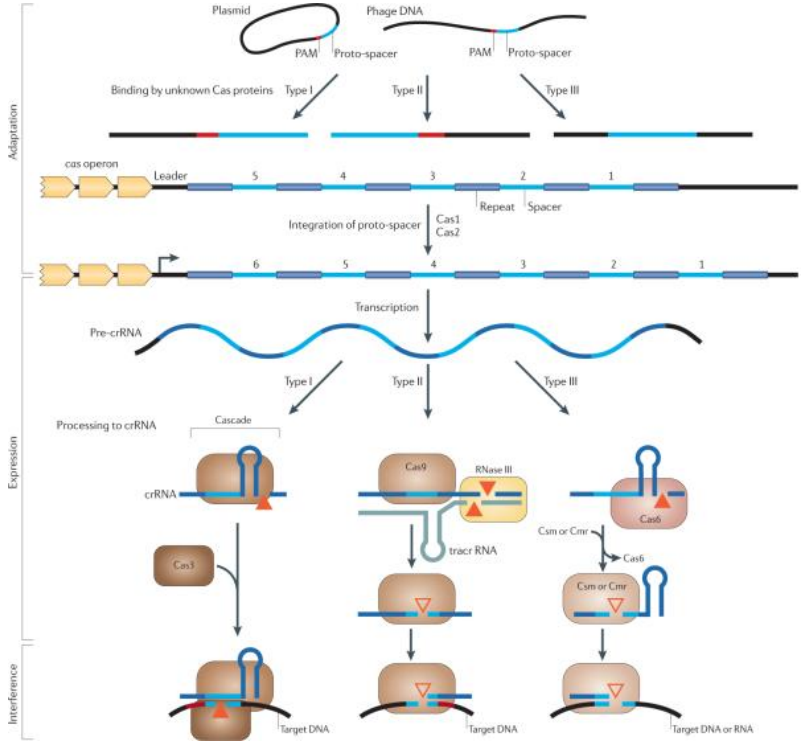

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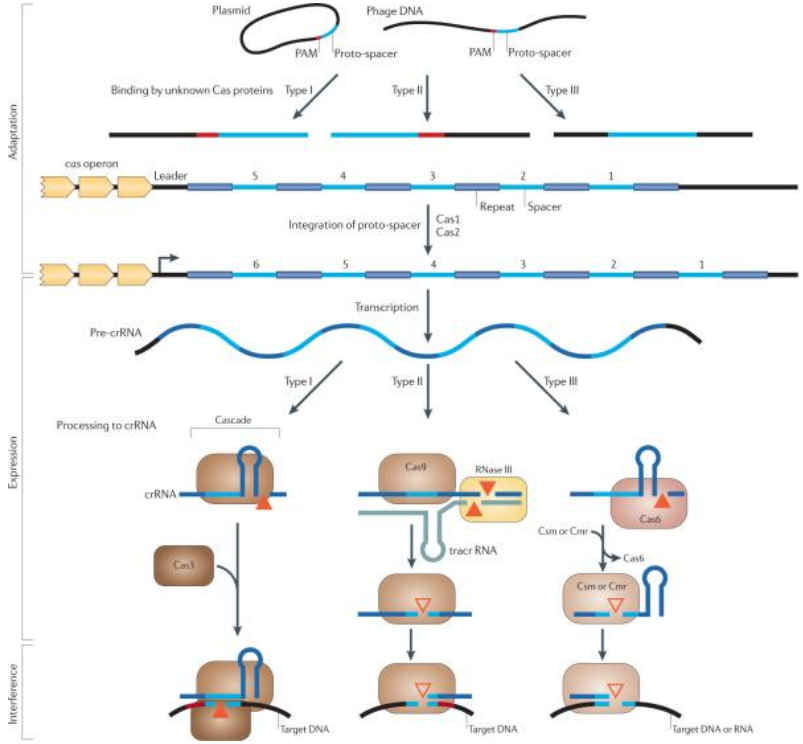
- $11\% - 28\%$ are false or orphaned CRISPR loci (Zhang and Ye, 2017)



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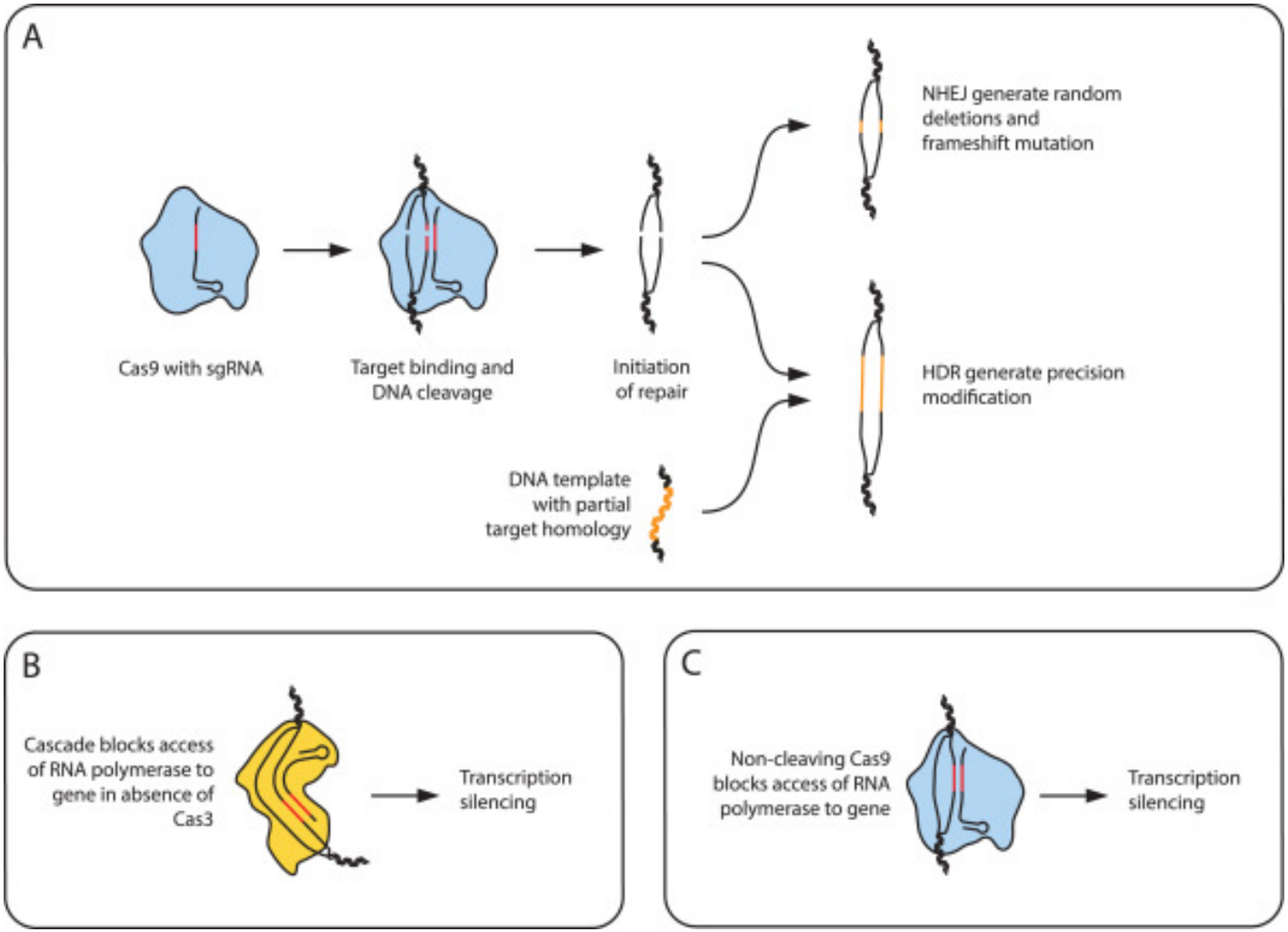

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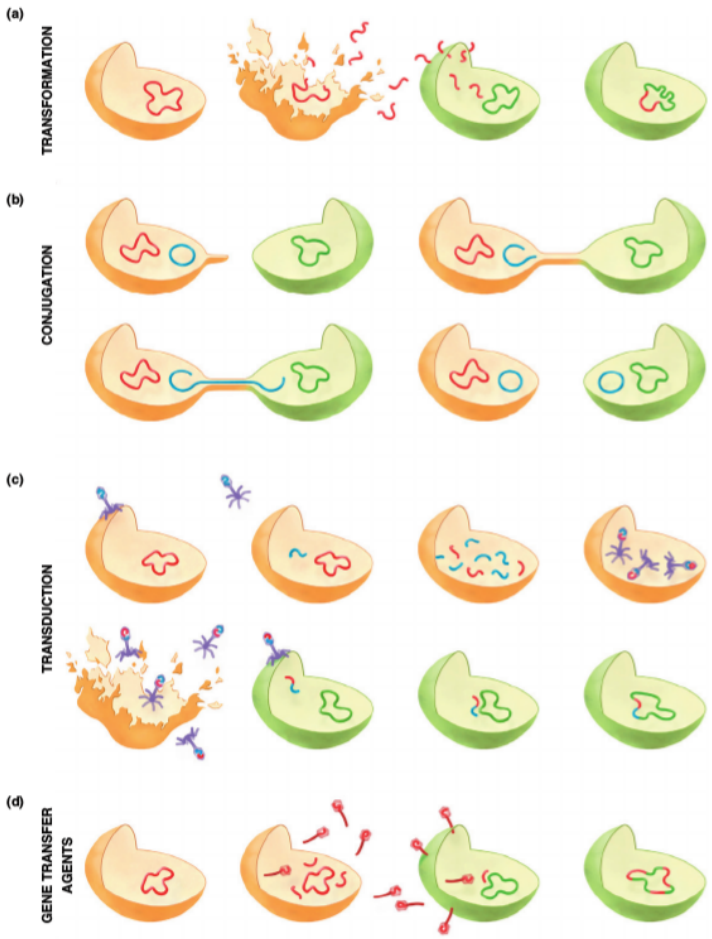
Horizontal Gene Transfer

Mechanisms



(Popa and Dagan, 2011)

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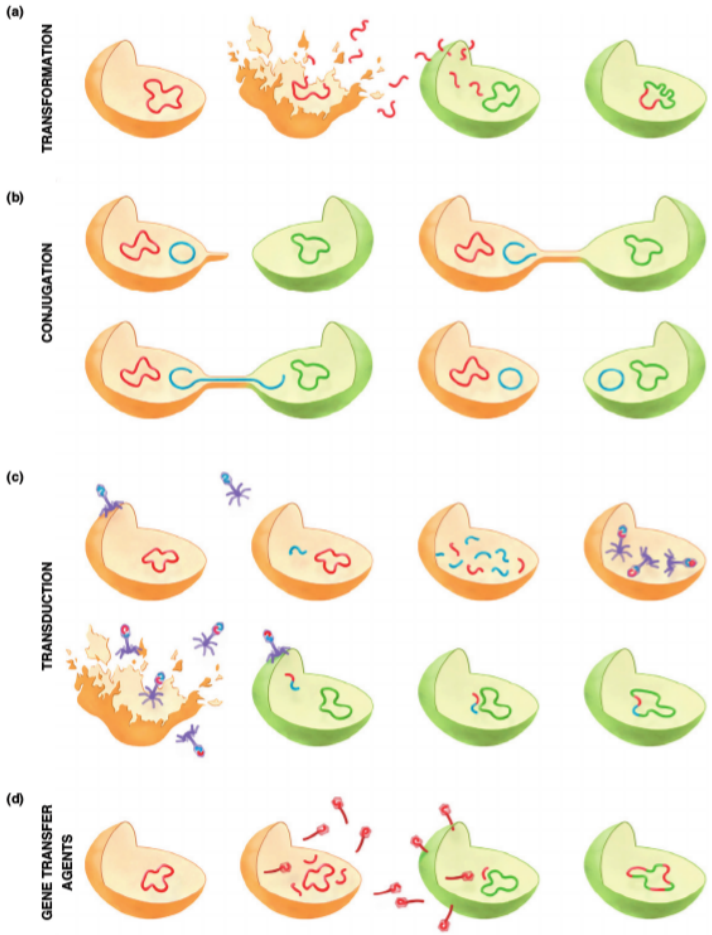

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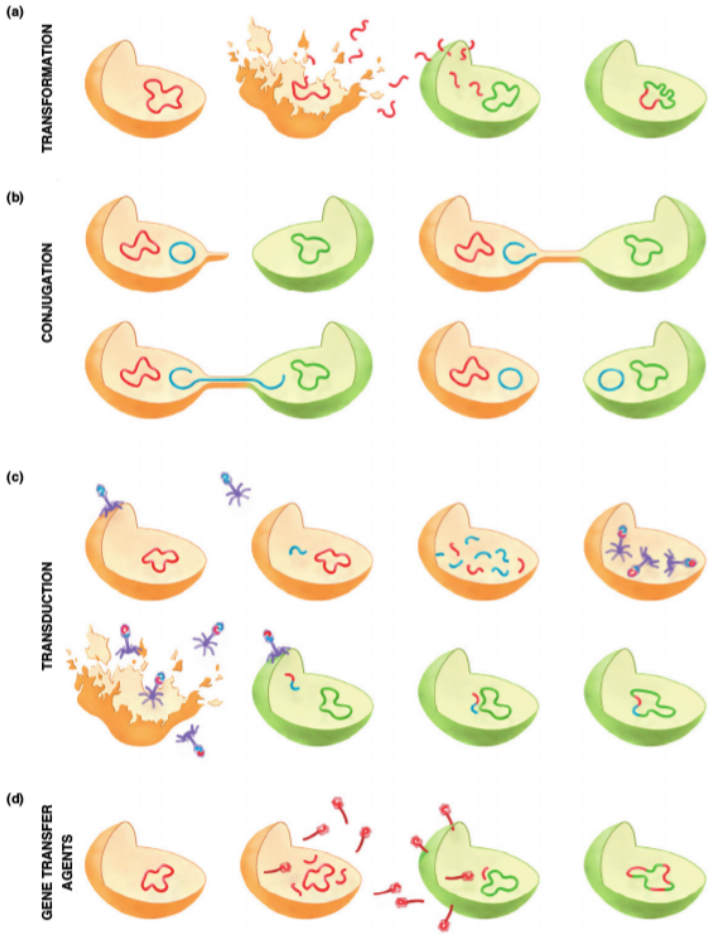

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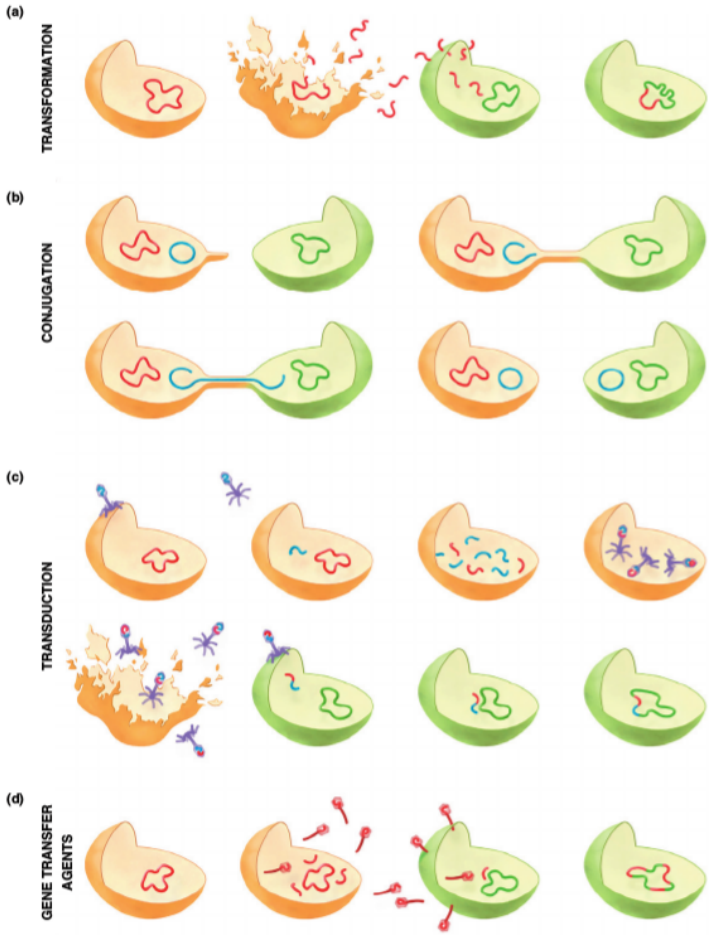

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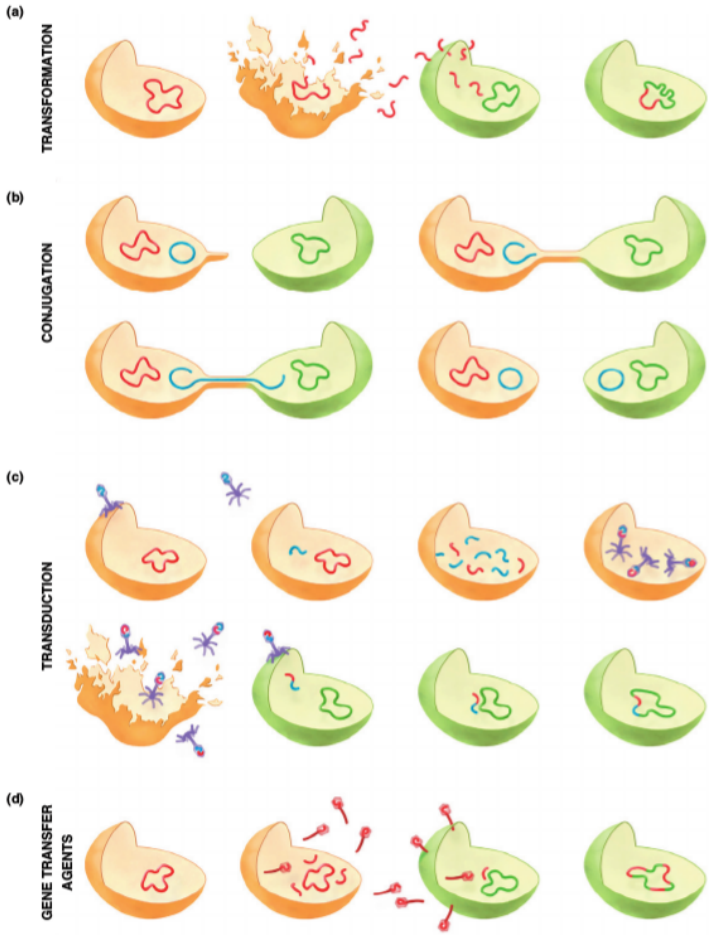

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- **CRISPR-Cas directly affects HGT** (Popa and Dagan, 2011)

Pan-Genomes

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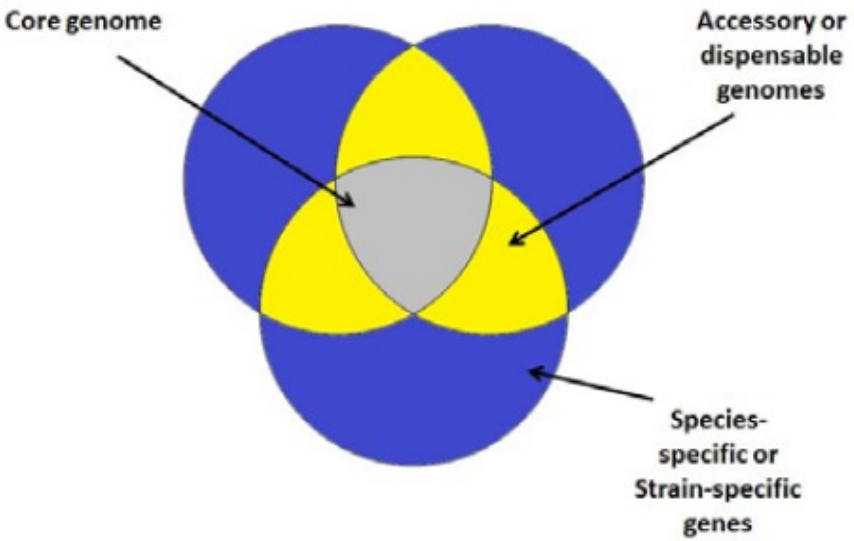

(Guimaraes et al., 2015)

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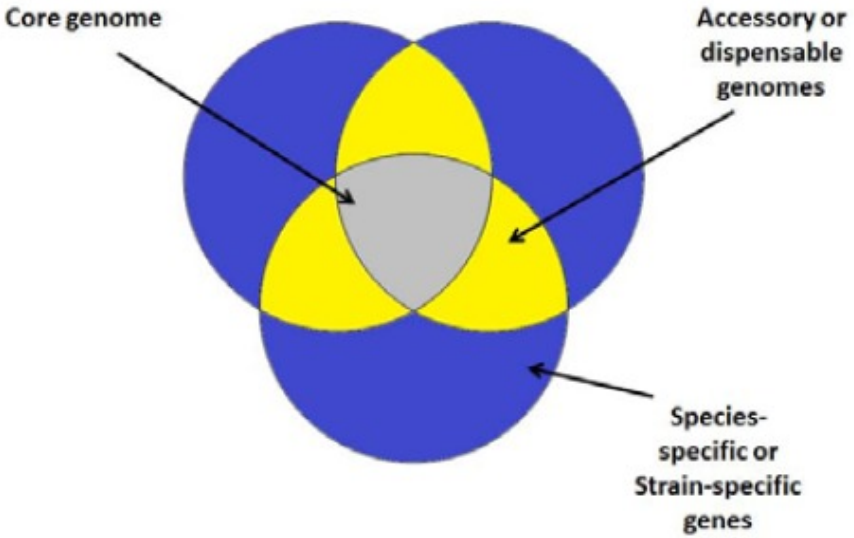

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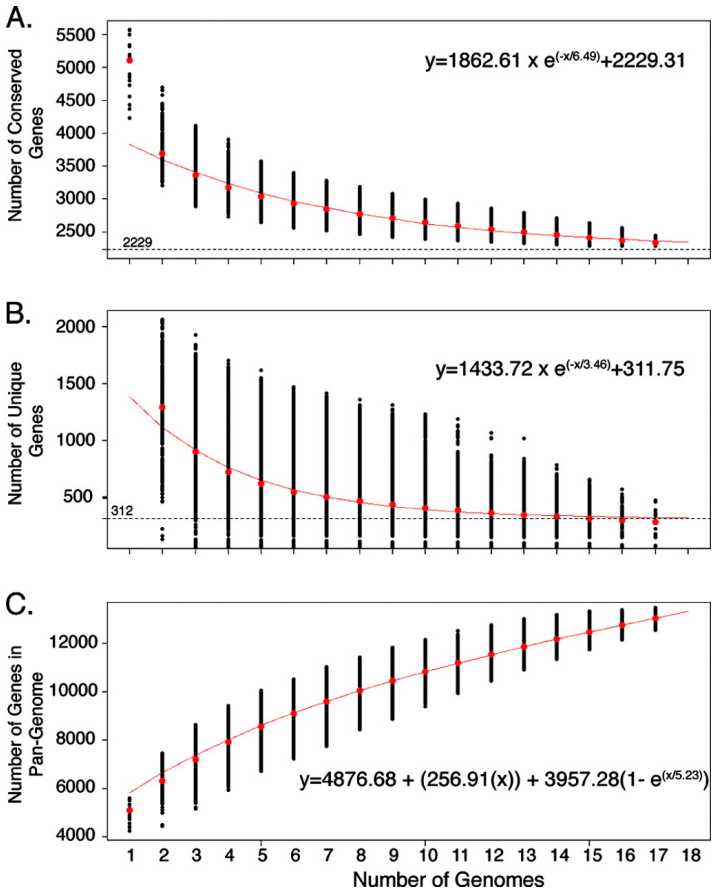

(Rasko et al., 2008)

Rate Influencing Factors

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- Amount of exogenous DNA/cell density/phage density

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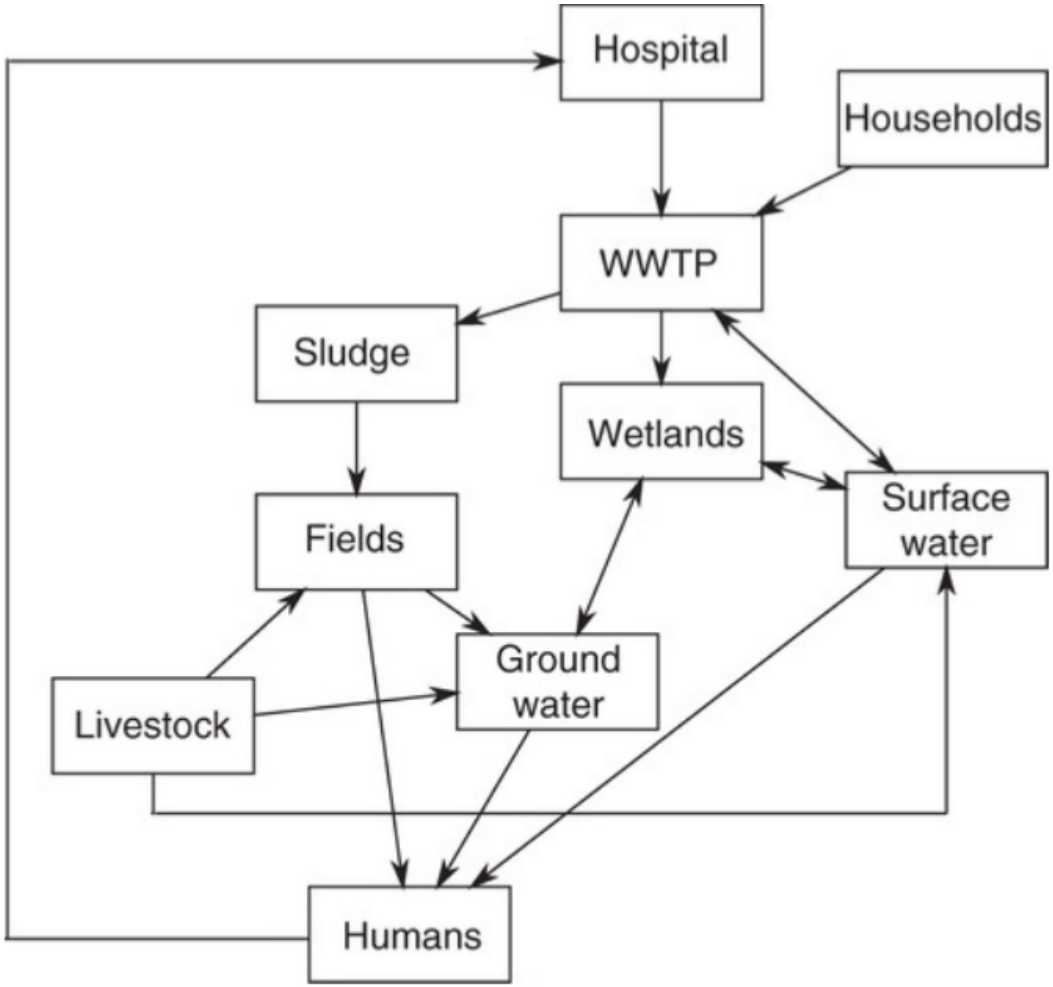

(Berglund, 2015)

Phylogenomic Networks

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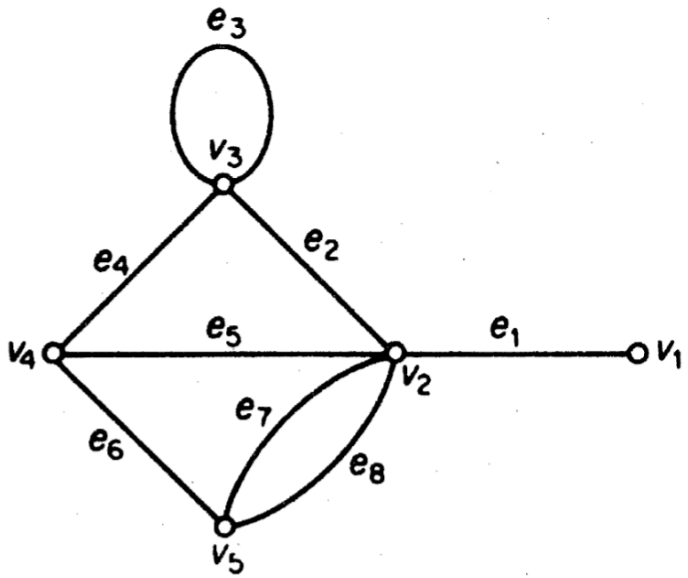

(Bondy and Murty, 2002)

- Useful mathematical abstraction of real world system

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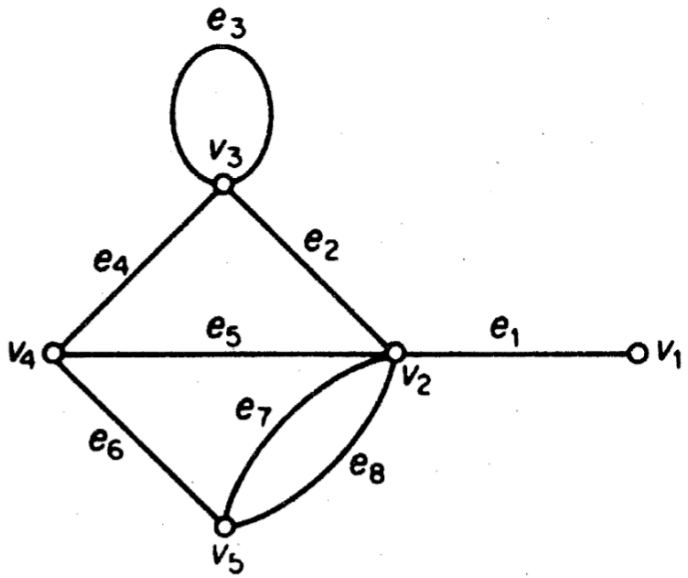

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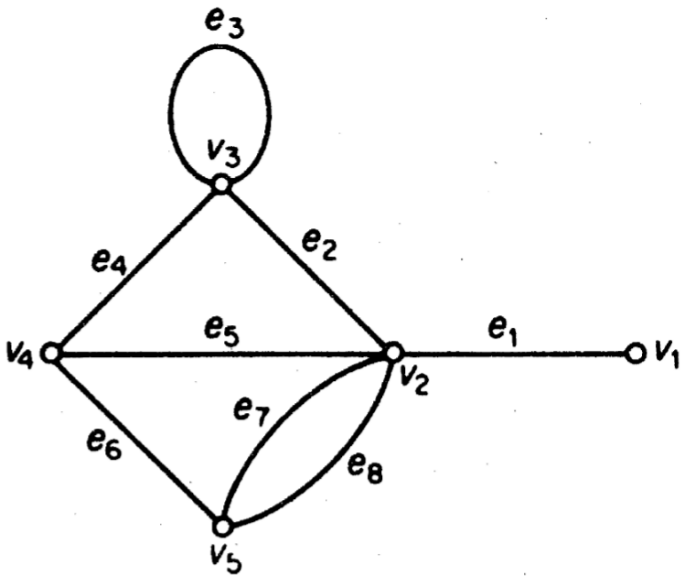

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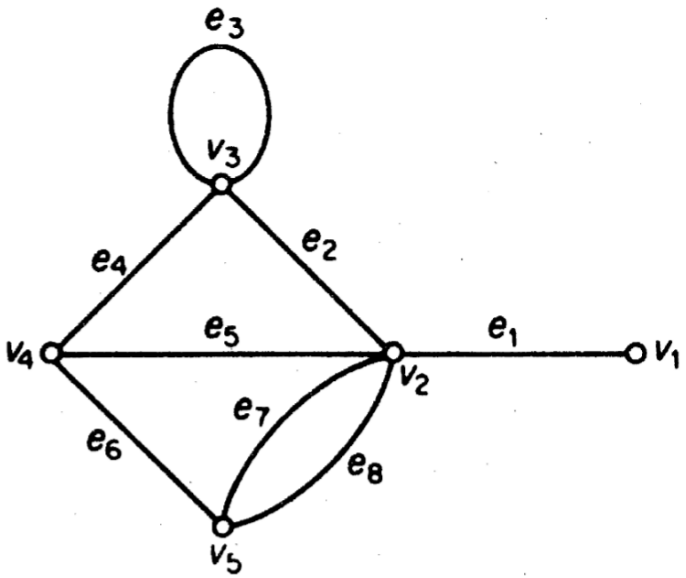

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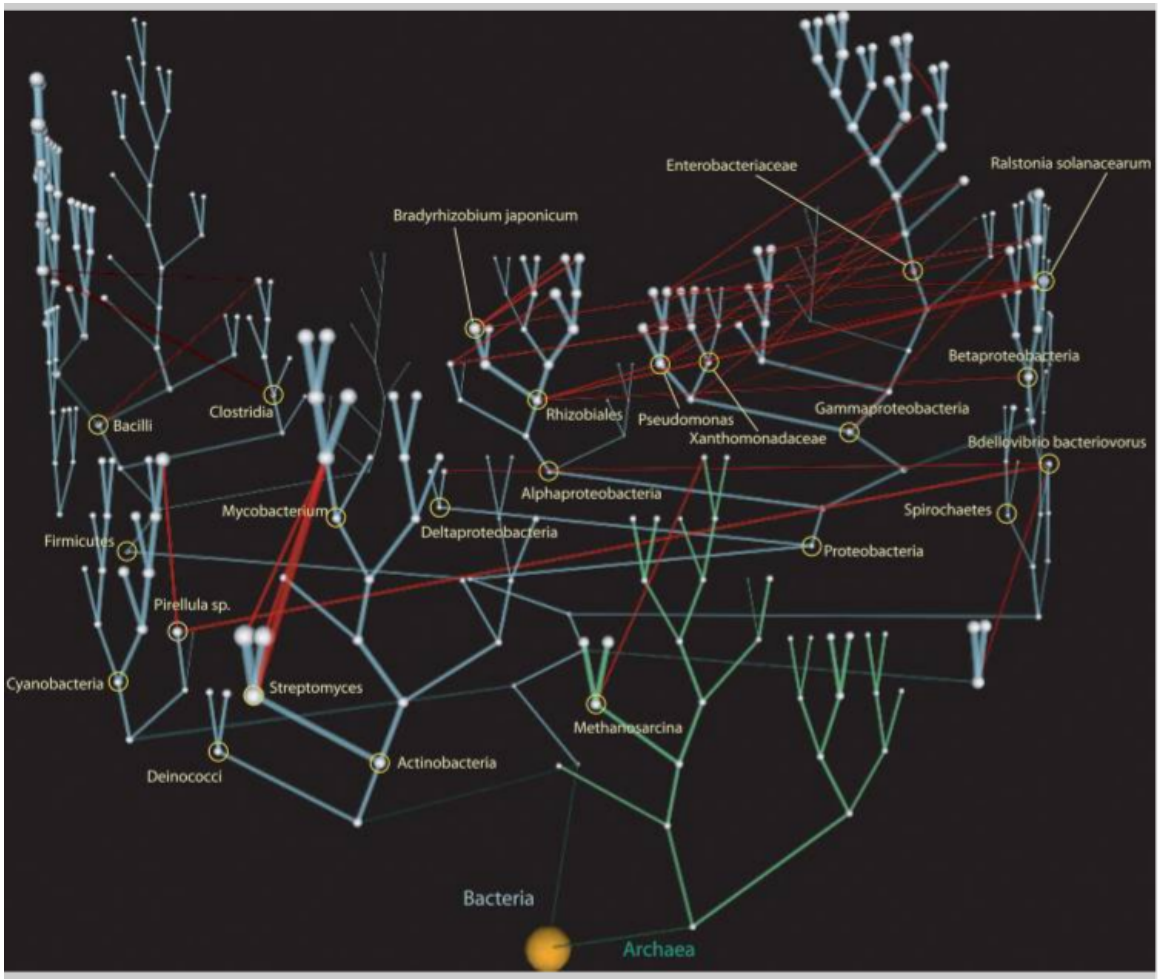
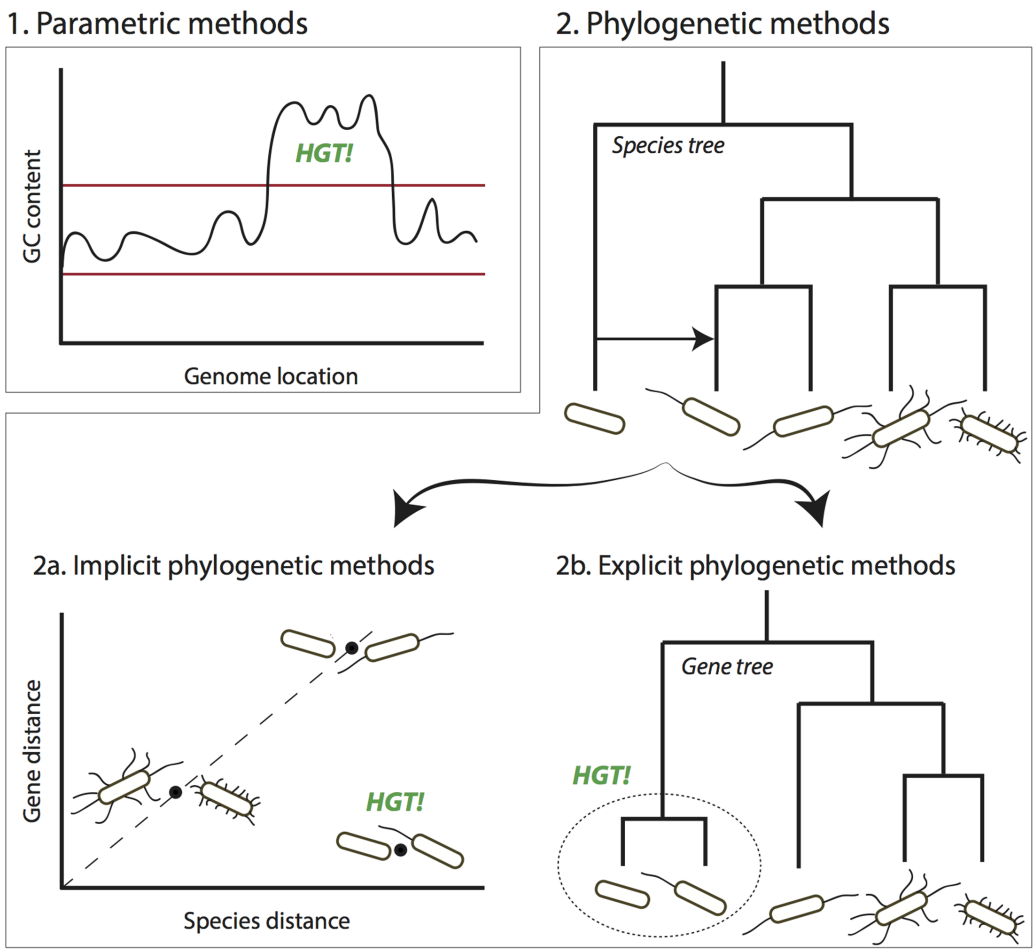


(Kunin et al., 2005)

Construction



(Ravenhall et al., 2015)

Do CRRISPR Systems Affect Horizontal Gene Transfer?

Yes

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  - Prophage abundance (Watson, Staals, and Fineran, 2018)

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- CRISPR can enhance transduction-mediated HGT (Watson, Staals, and Fineran, 2018)

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- Contradicted by a former underdraduate thesis student
  - Can see inhibitory effects of CRIPSR on HGT over short evolutionary time scales
  - Higher gene indel rates for CRISPR containg genera than non-CRISPR containing outgroups

My Project

Hypothesis

Null Hypothesis

Bacterial strains or genera with known CRISPR systems will show no significant differences in network statistics compared to those strains or genera without known CRISPR systems.

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Alternative Hypothesis

Bacterial strains or genera with known CRISPR systems will show a significant difference in at least 1 network statistic compared to those strains or genera without known CRISPR systems.

Objectives

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Within Network Comparisons

For genera with CRISPR conatining strains, compare the node statistics of CRIPSR-containing strain to non-CRISPR-containing strains.

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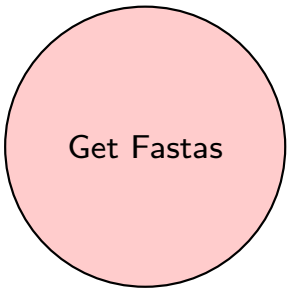
Gene Indel Rates vs. Network Statistics

Compare gene InDel rates to node/network statistics for CRISPR-containing and non-CRISPR-containing strains/genera.

Workflow



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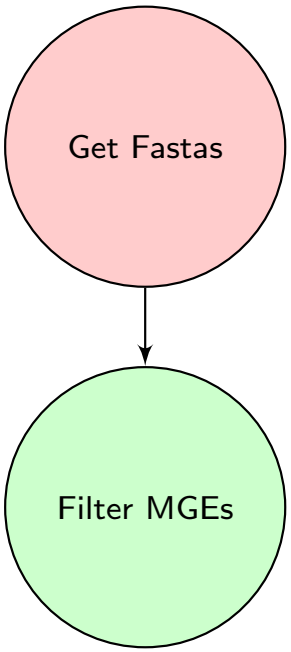

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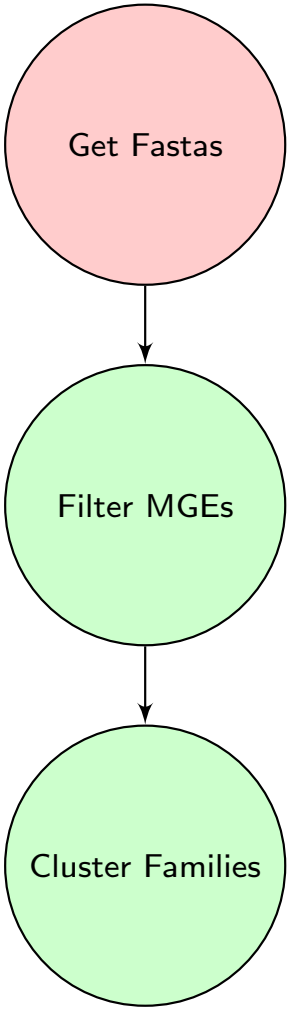

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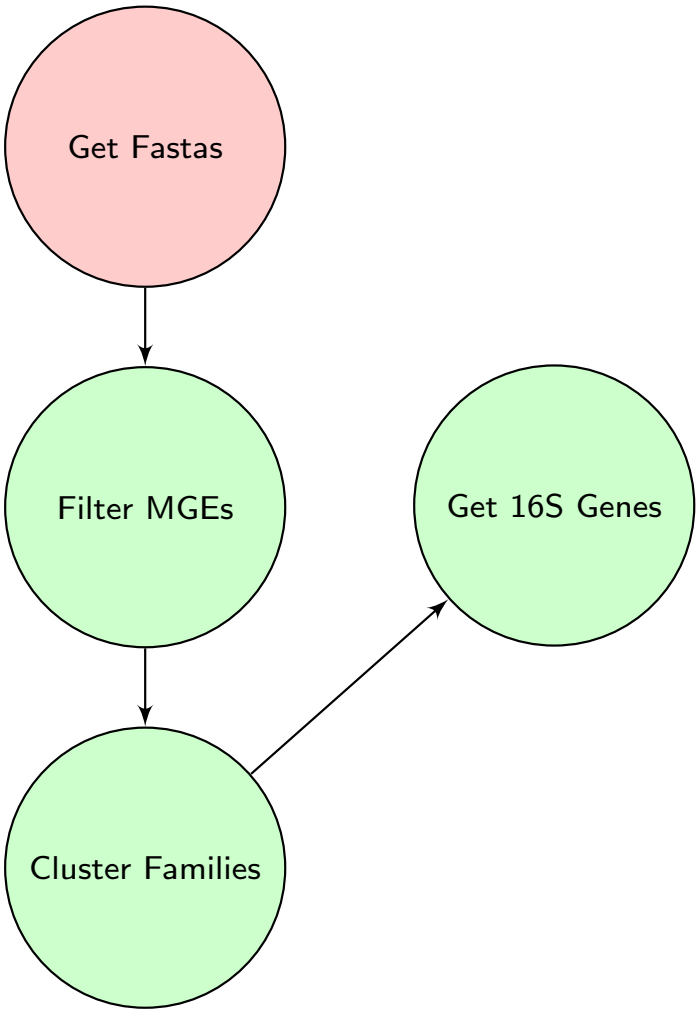

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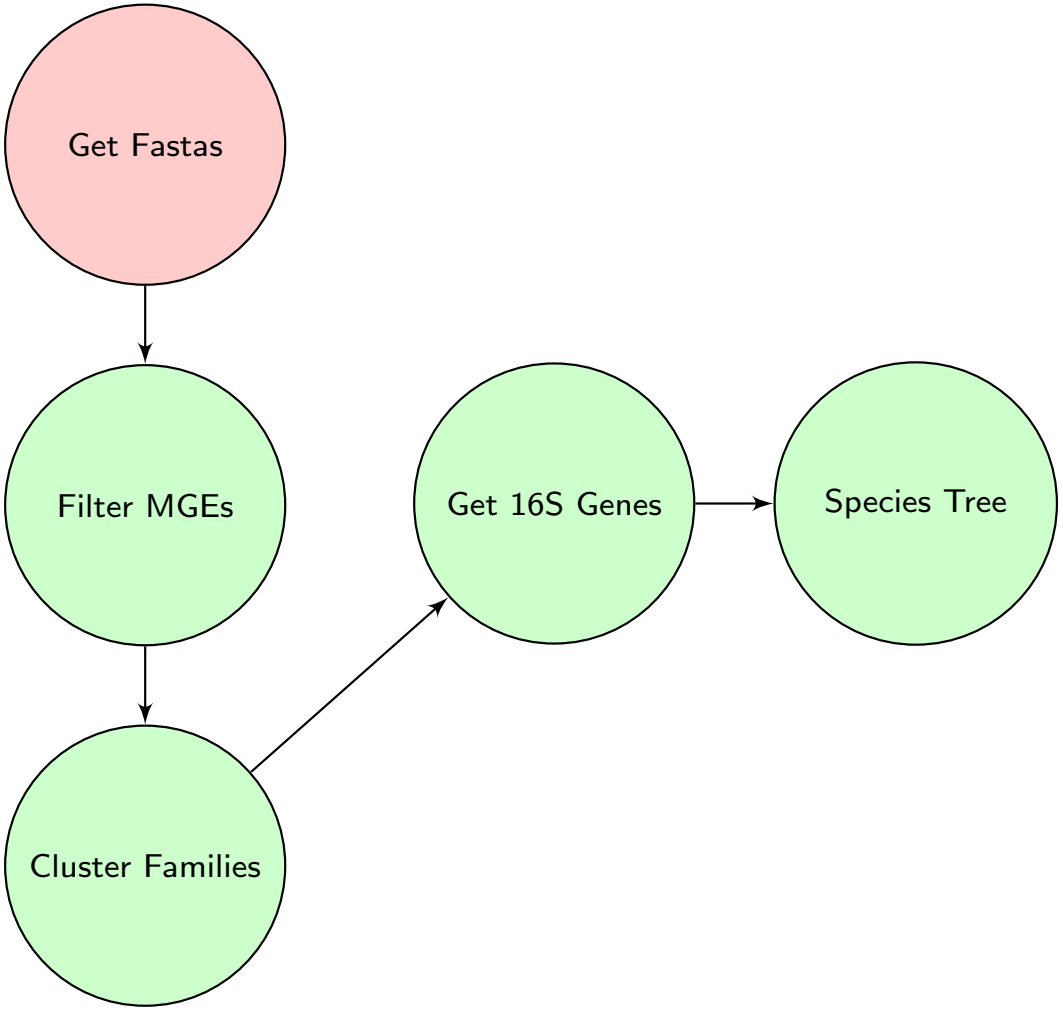
Get Fastas
Filter MGEs
Cluster Families
Get 16S Genes
Species Tree

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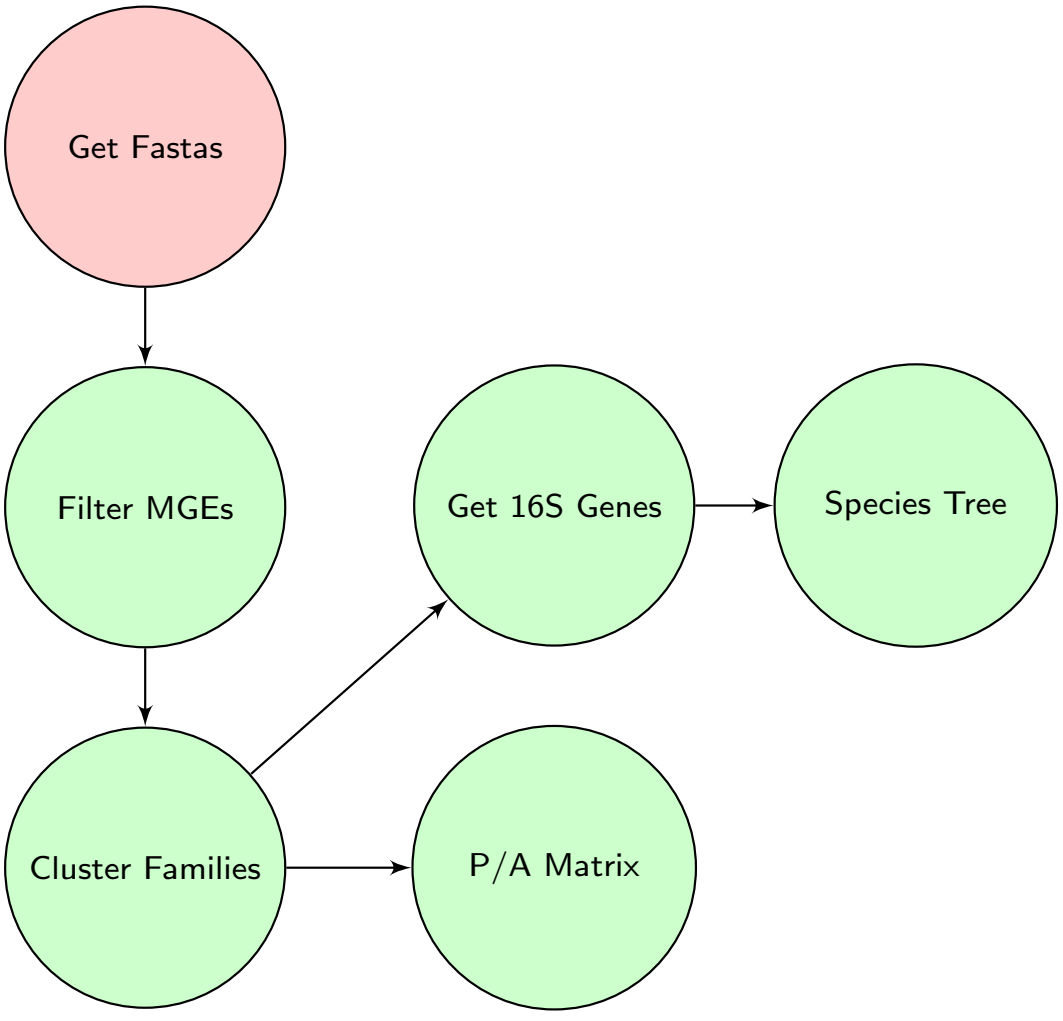
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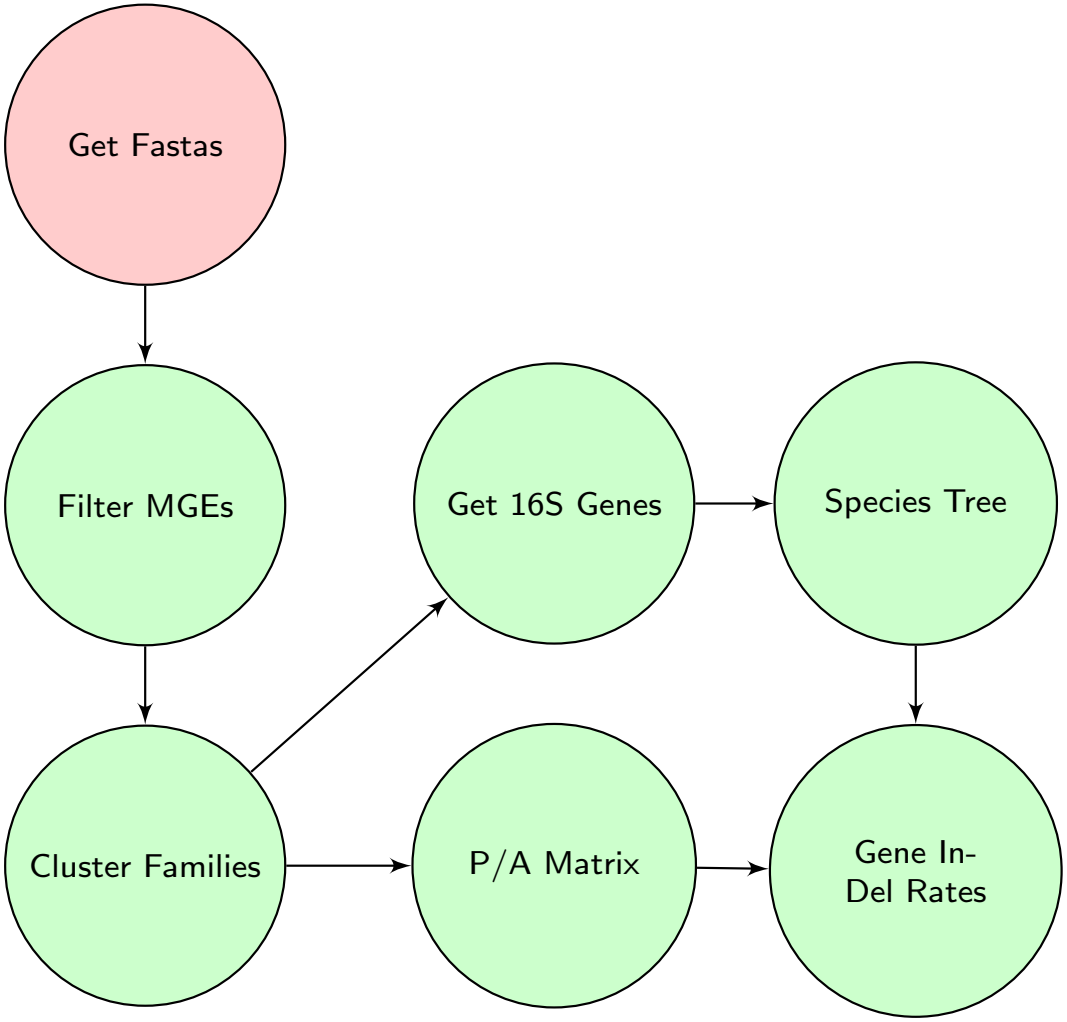
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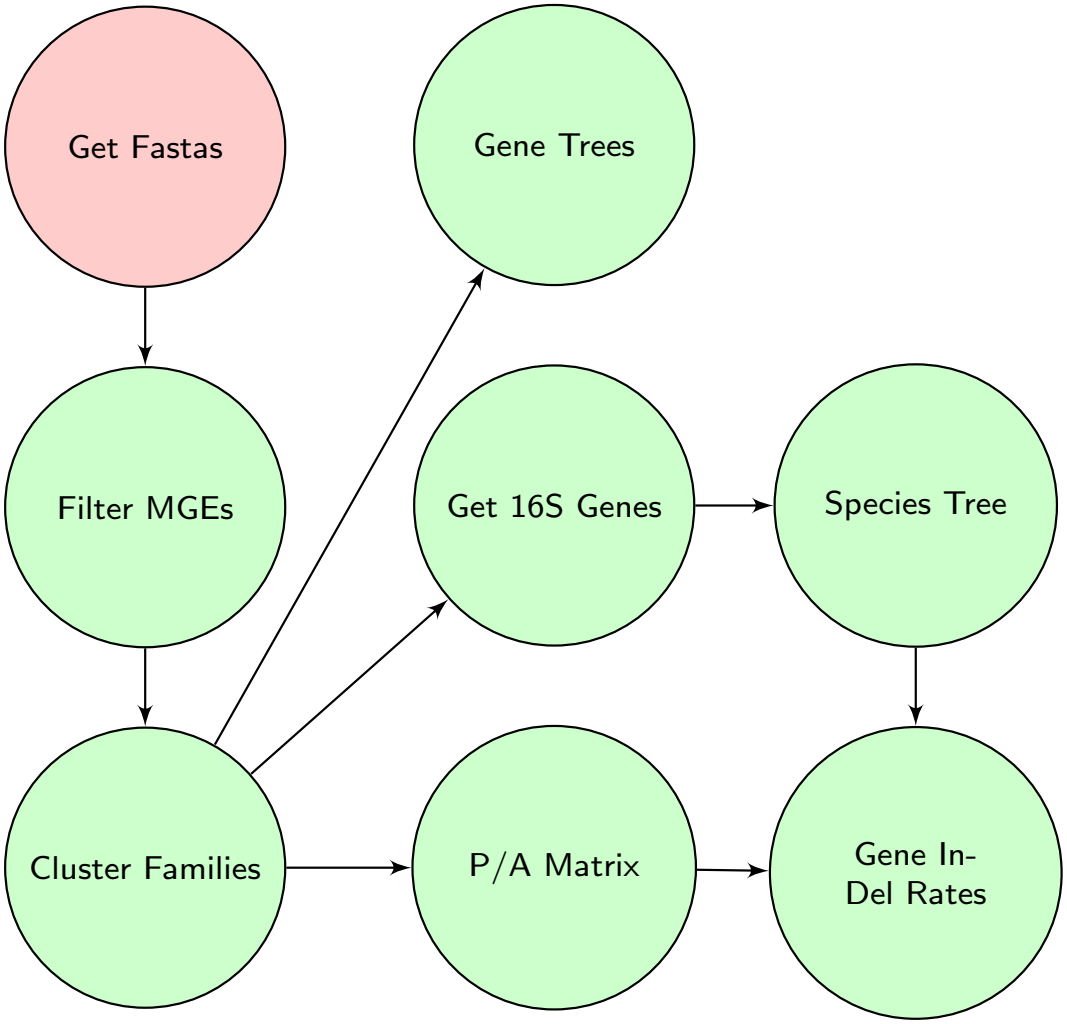
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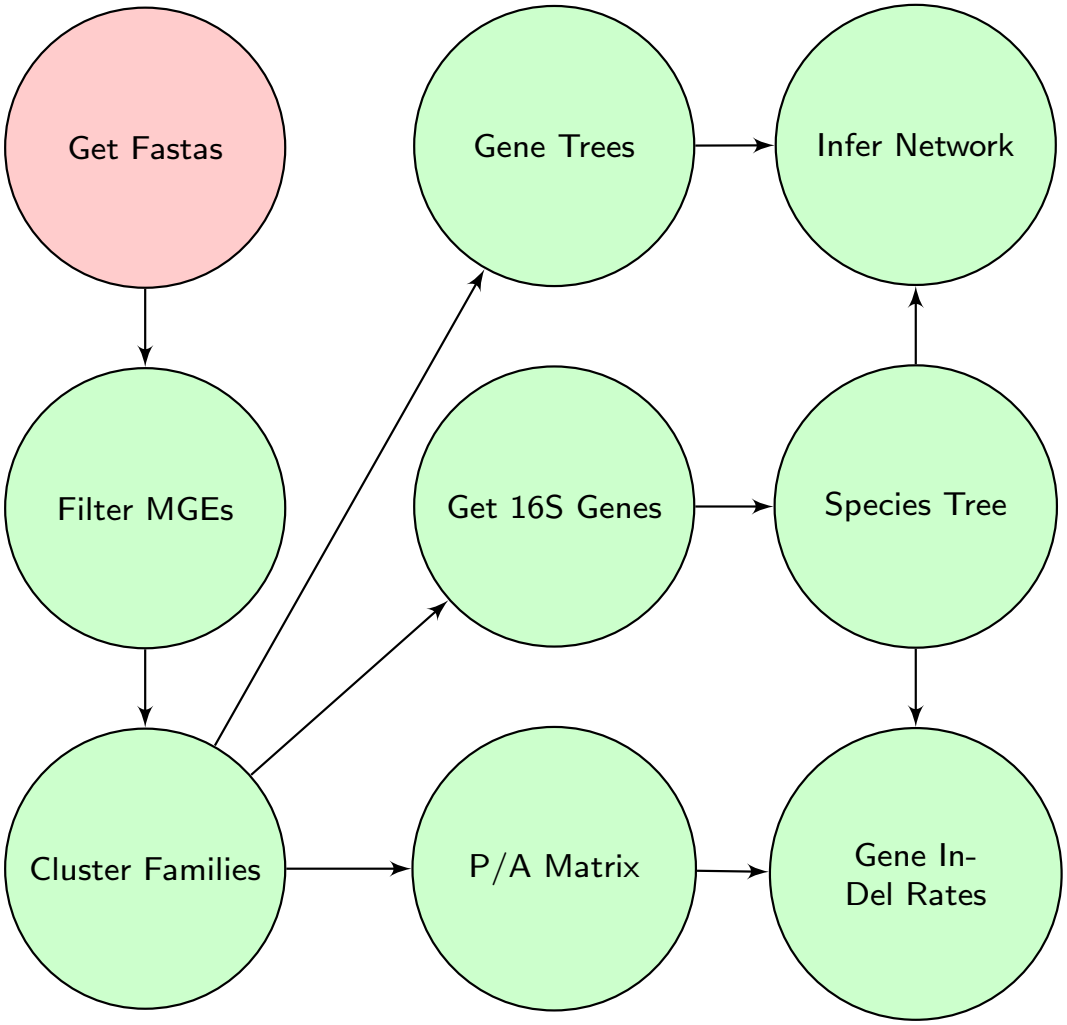
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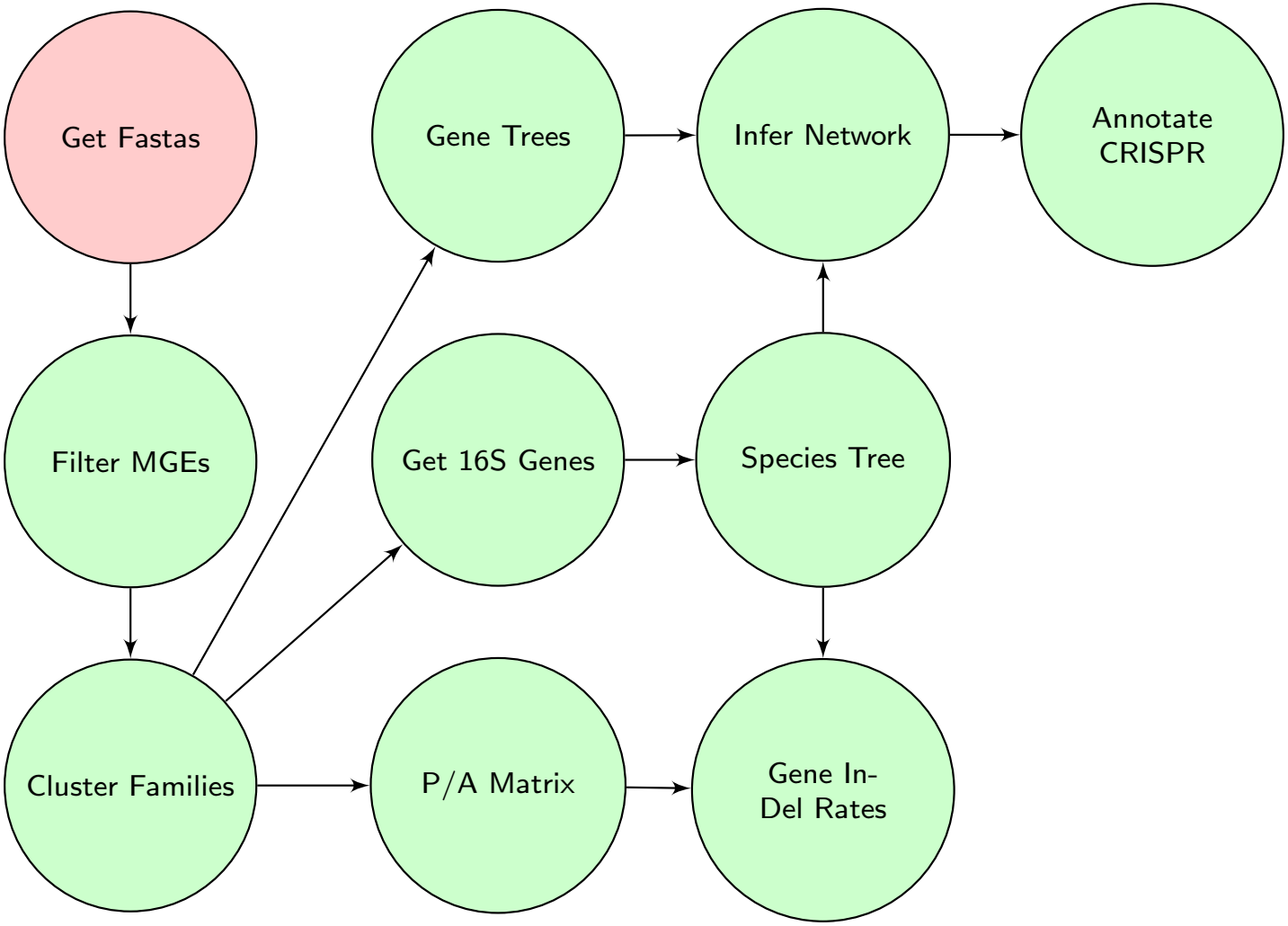
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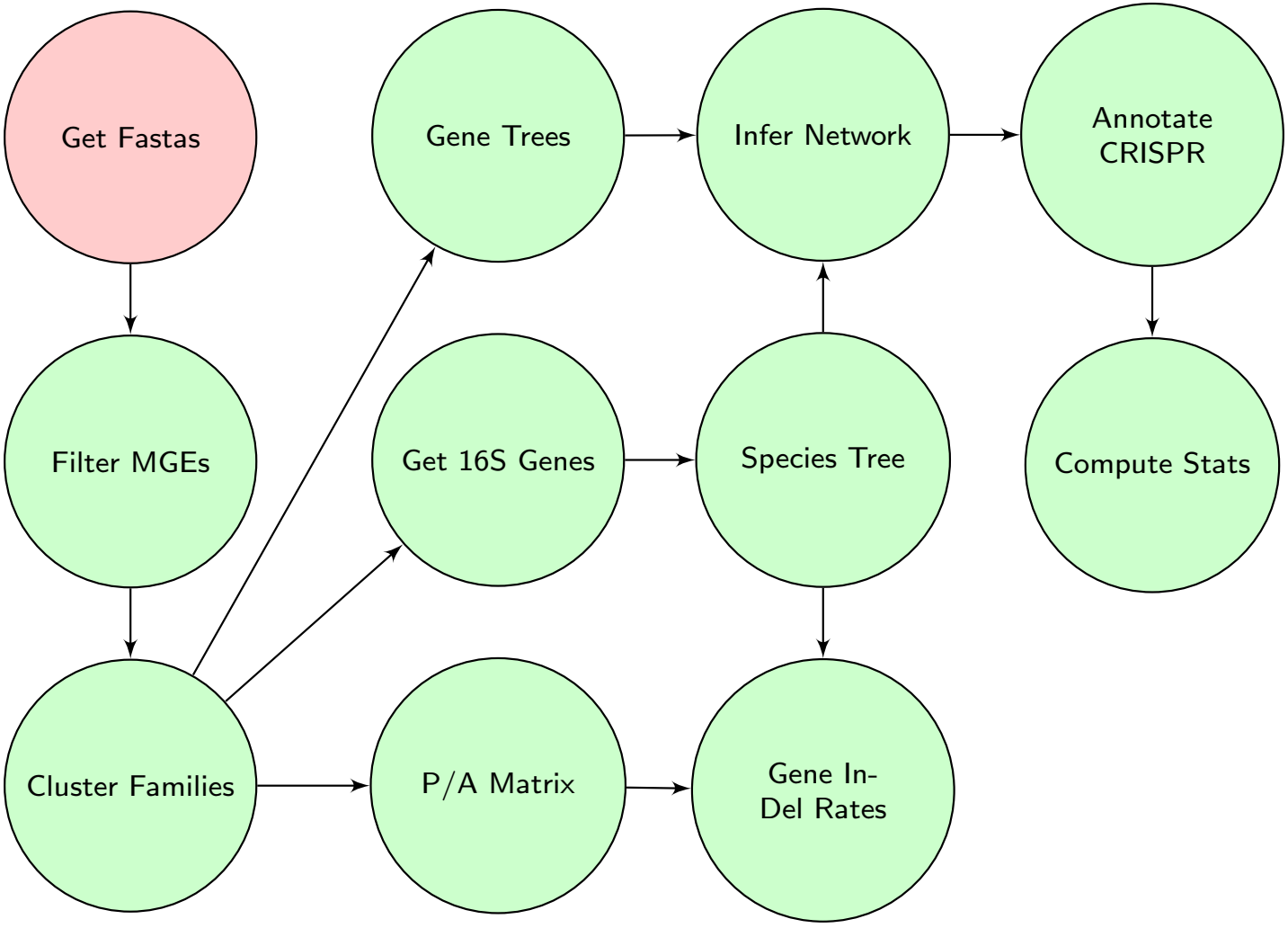
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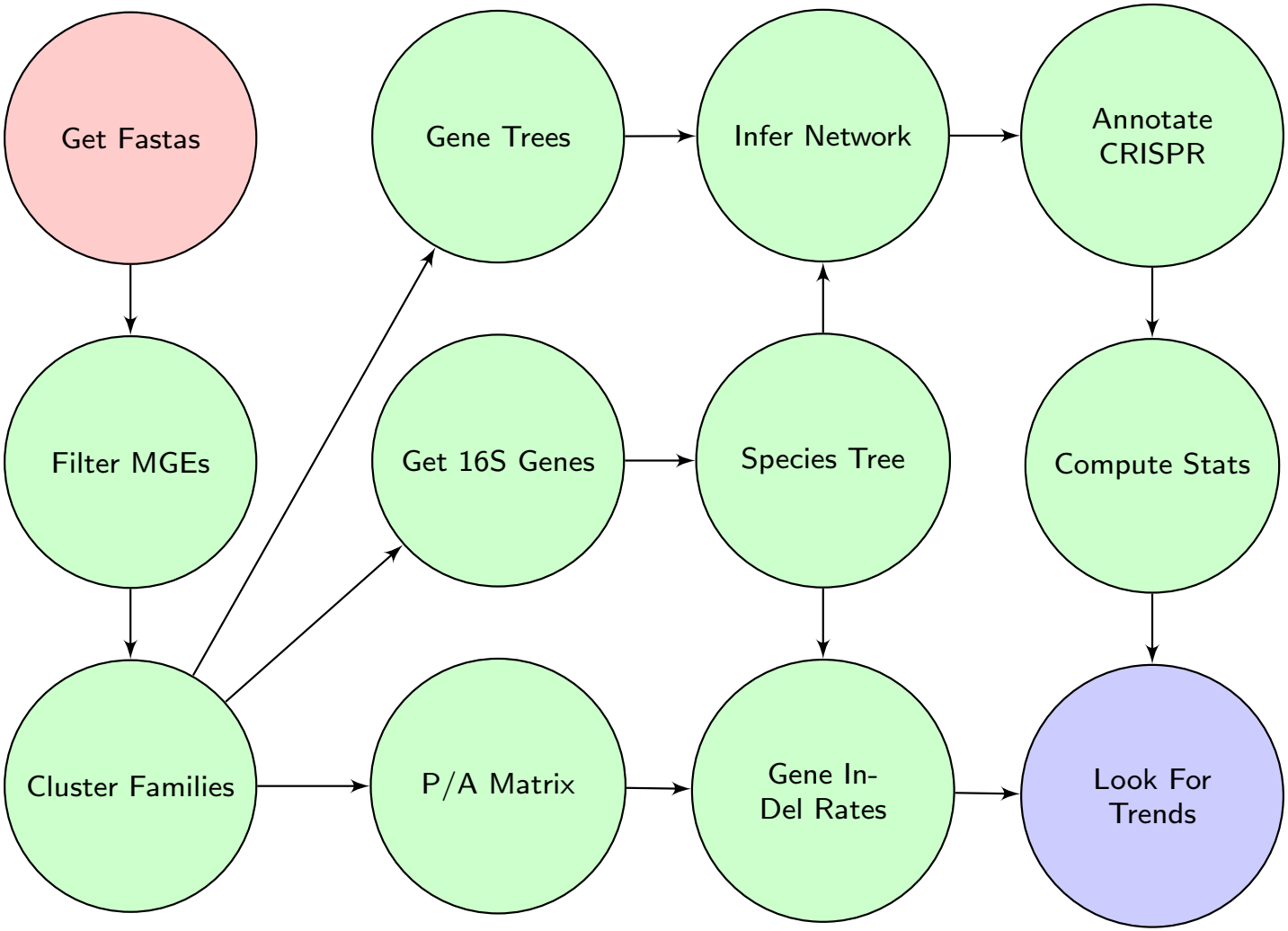
Gene In-Del Rates

Workflow


Get Fastas
Gene Trees
Infer Network
Annotate CRISPR
Filter MGEs
Get 16S Genes
Species Tree
Compute Stats
Cluster Families
P/A Matrix
Gene In-Del Rates
Look For Trends

Network Statistics

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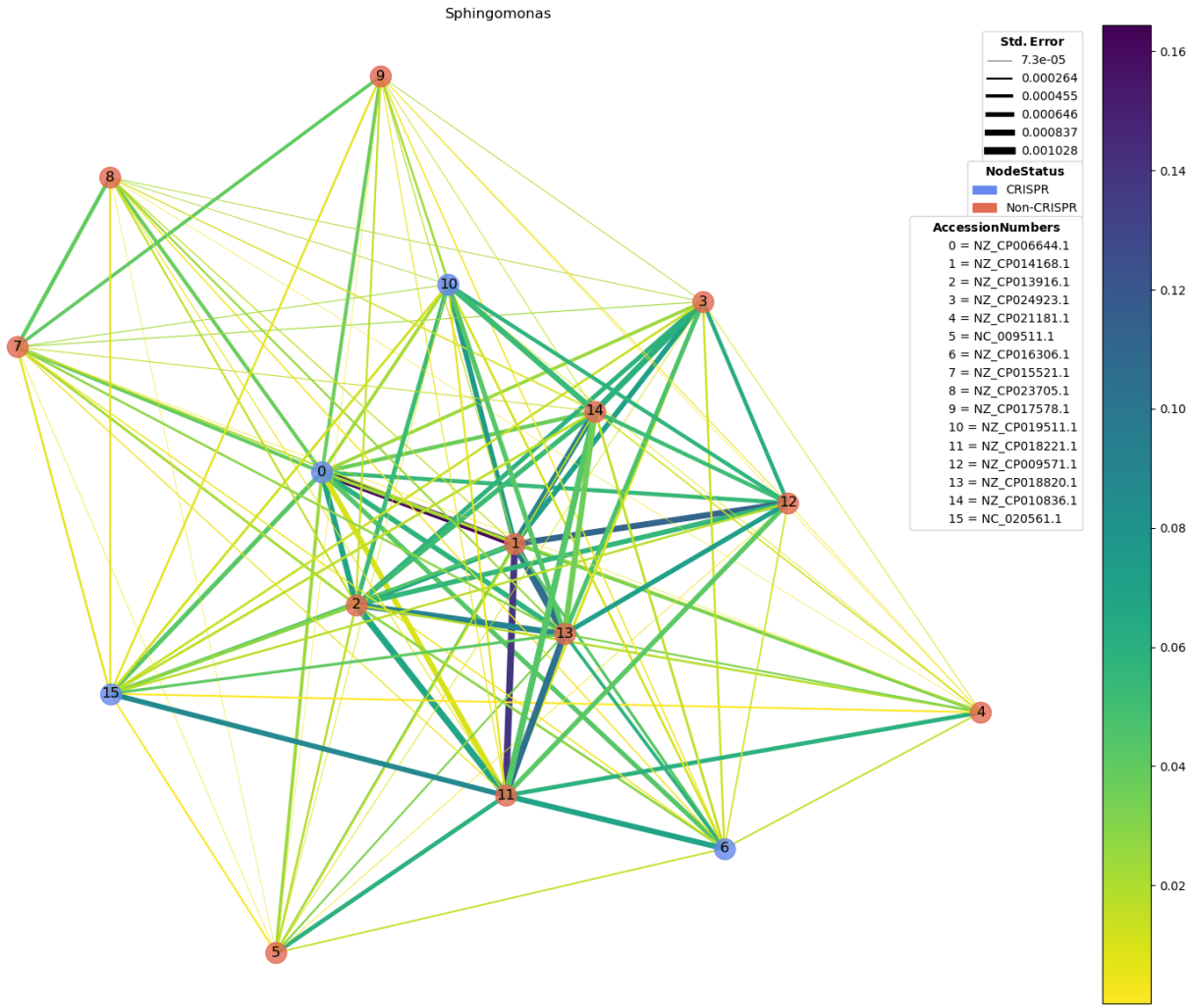
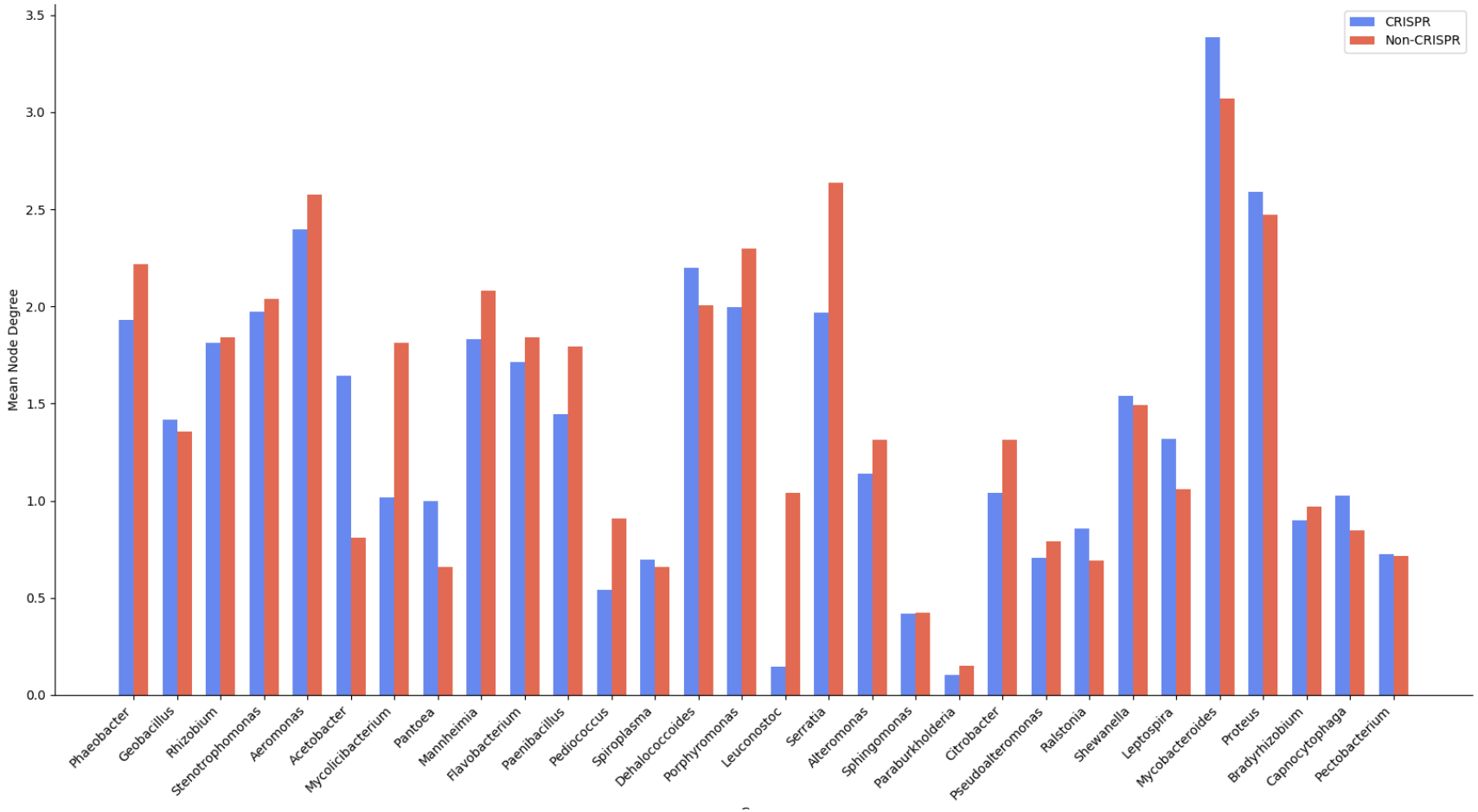
- **Network Modularity**: $Q = \frac{1}{2m}\sum_{uv}^{W}[W_{uv} - \frac{k_u k_v}{2m}]\delta(u, v)$ where m is the total weight of alledges, k_u is the degree of u and $\delta(u, v)$ is 1 if u and v both have or do not have CRISPR systems and 0 otherwise. $Q \in [-1, 1]$ (Newman, 2004)

Results

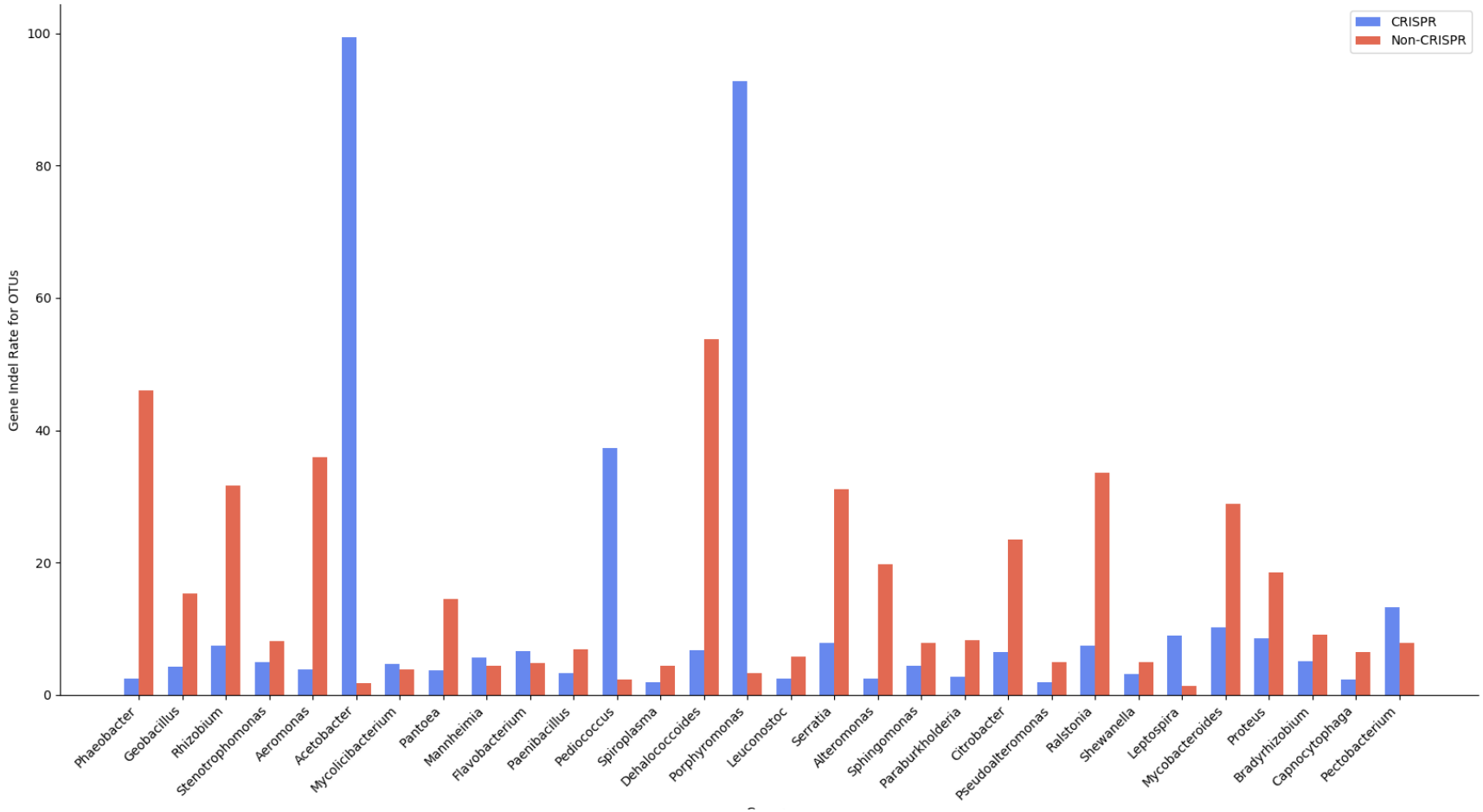
Example "Consensus" Network



Mean Node Degree



Gene Indel Rates



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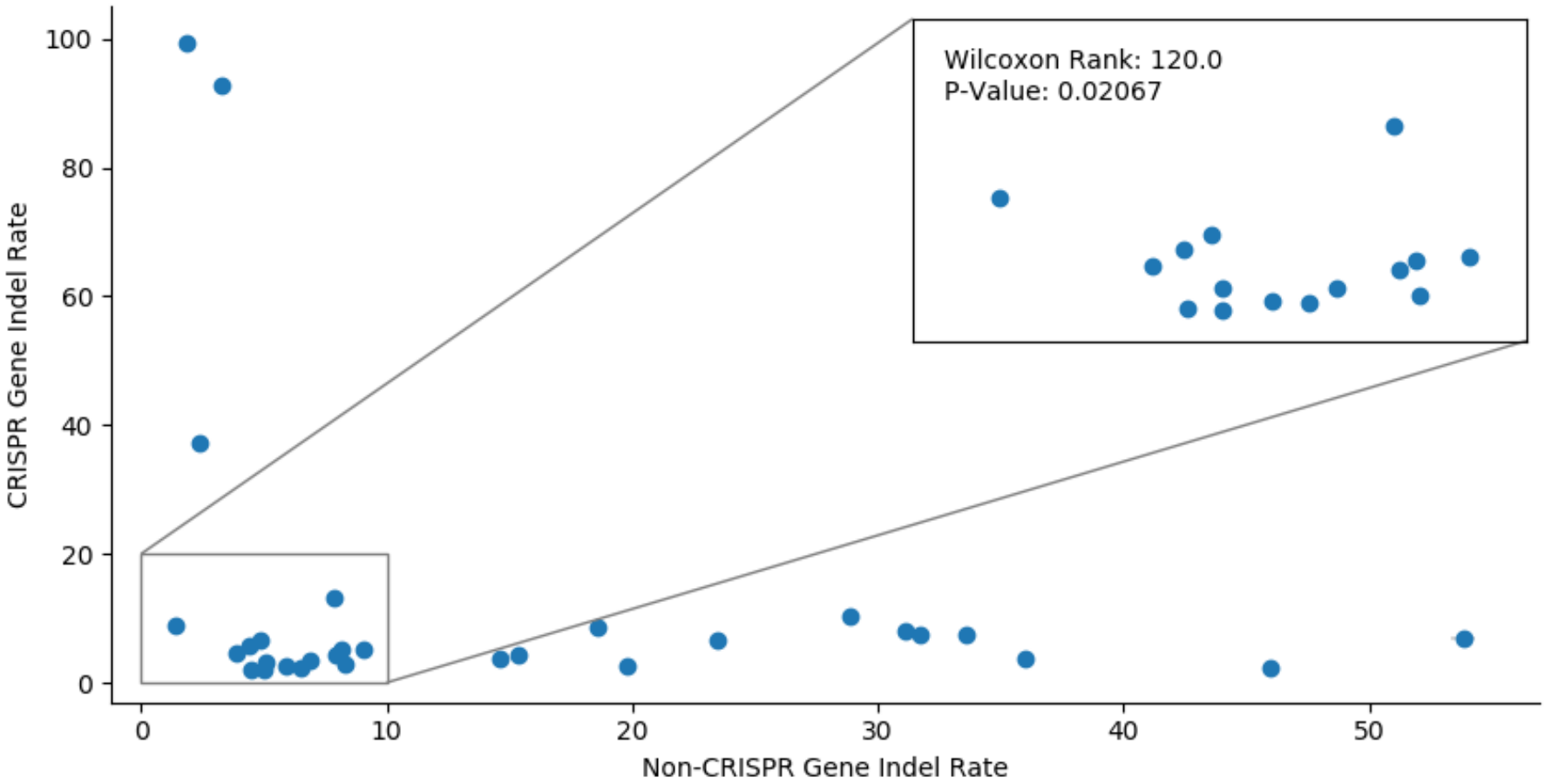
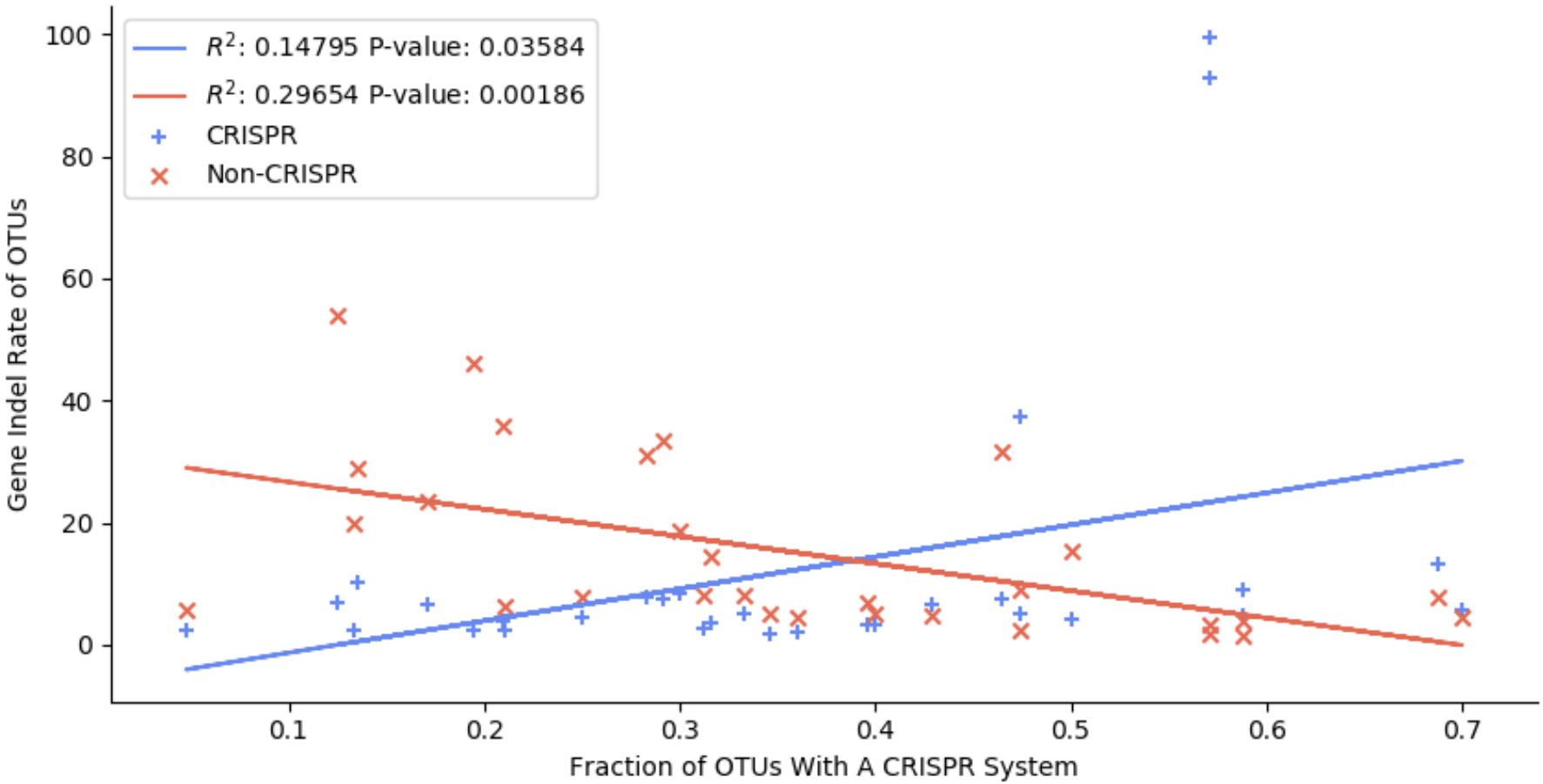
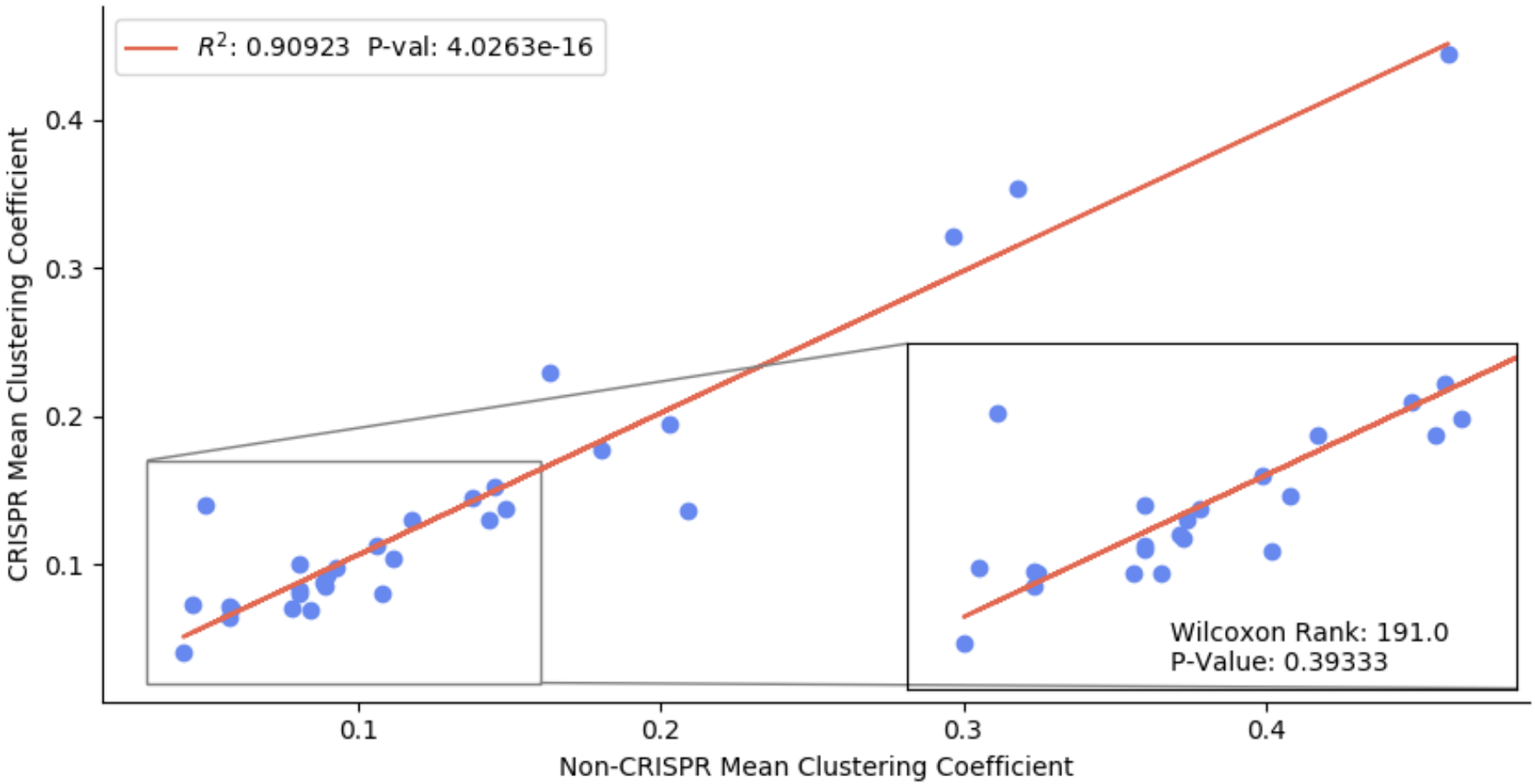


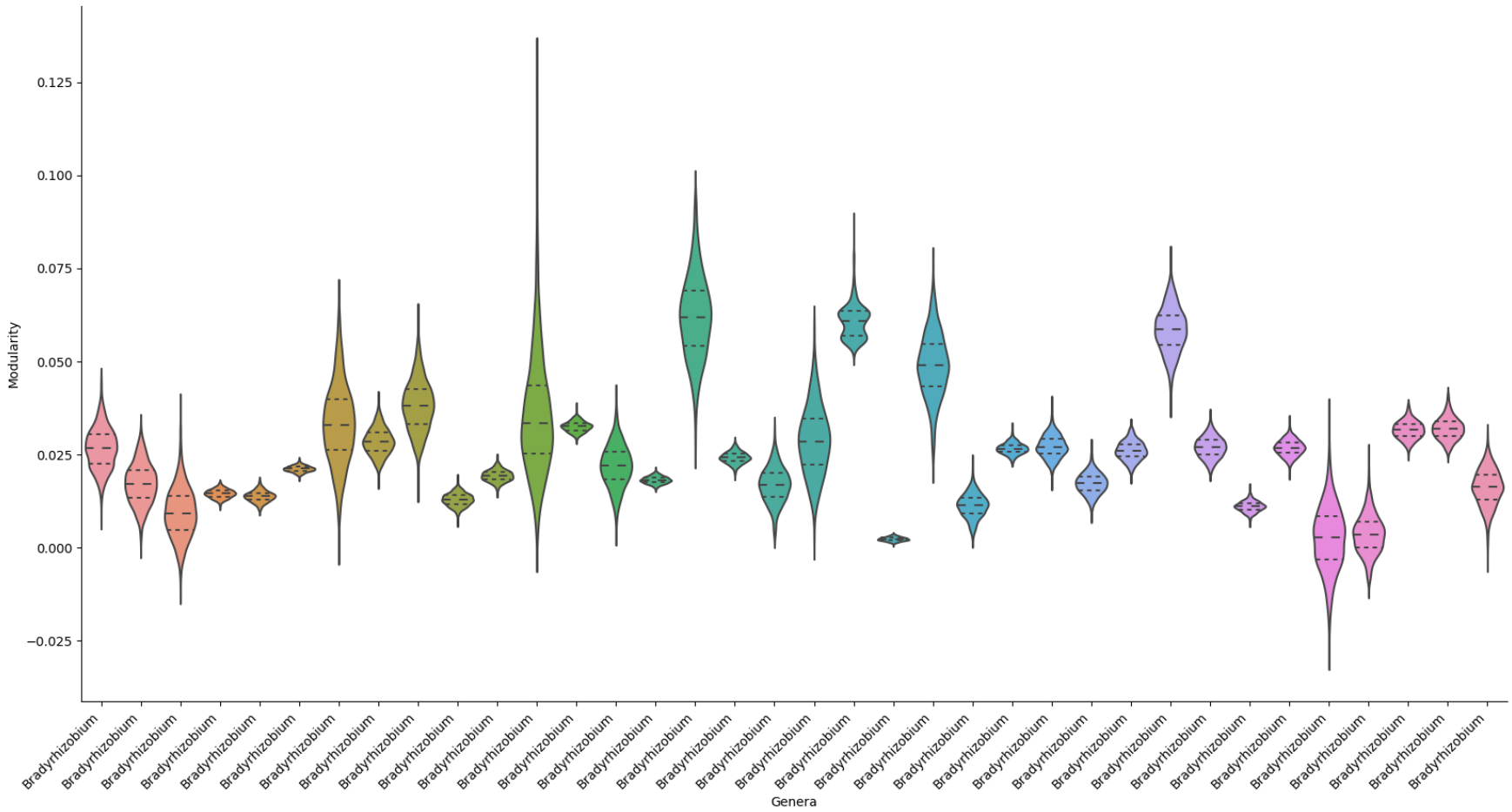
Gene Indel Rate Difference Vs. Fraction CRISPR Species



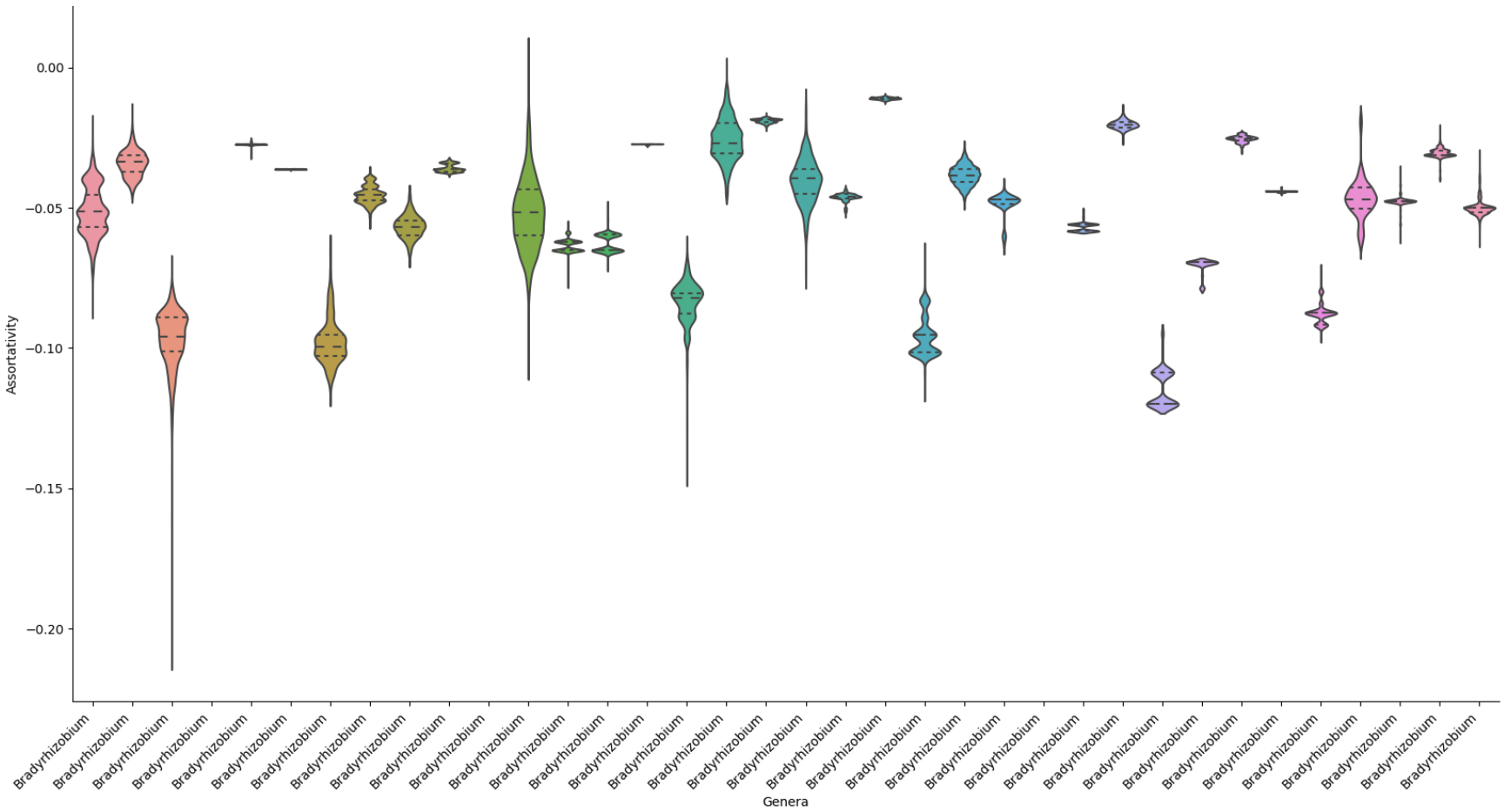
Mean Node Weighted Clustering Coefficient



Modularity Distributions



Assortativity Distributions



Conclusion

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- **Multifurcation Error**: Some species trees contained multifurcations, which were resolved randomly to generate a bifurcating tree. Estimating this error by examining variance over different resolutions is possible.

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- **Continuous CRISPR activity**: Labelling nodes by estimated CRISPR activity (array length, transciptomic data, etc.)
- **Considering bacterial ecology and environments**: Consider geographically close OTUs or differences between networks due to environmental factors

Thanks

Thank you to

- Dr. G. Brian Golding
- Dr. Ben Evans
- The Golding lab
  - Caitlin Simopoulos
  - Daniella Lato
  - Zachery Dickson
  - Sam Long
  - Geoge Long
  - Lucy Zhang
  - Brianne Laverty
  - Nicole Zhang
- Everyone here for listening

All code used for this project is available at https://github.com/DJSiddharthVader/thesis_SidReed

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