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

Golding Lab,
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McMaster University

April 4, 2019

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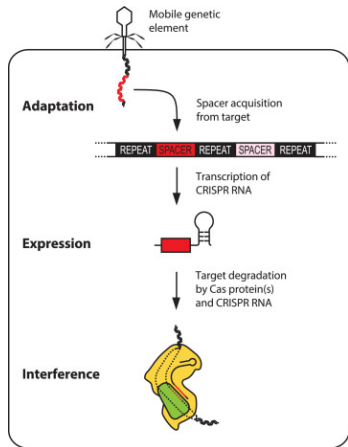
CRISPR-Cas systems

What Are They?

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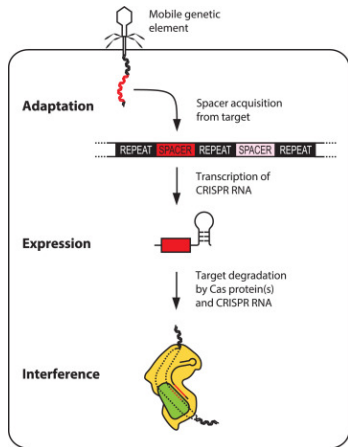
- Adaptive Bacterial Immune System

(Rath et al., 2015)

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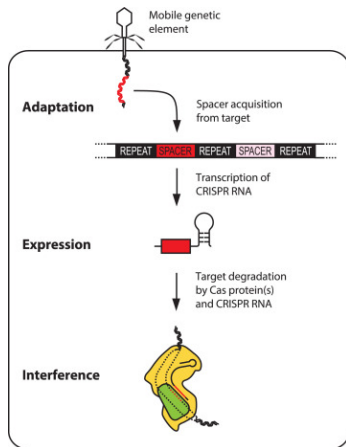- Adaptive Bacterial Immune System
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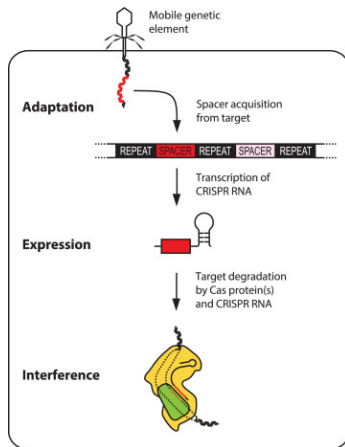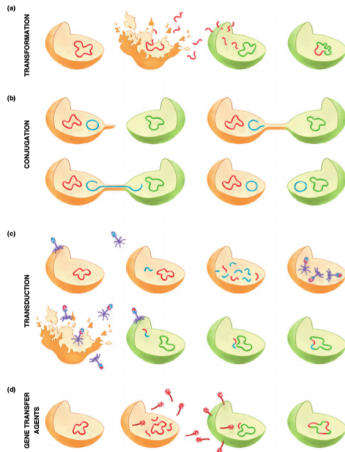

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- 45% of bacteria have CRISPR loci ($n = 6782$) (Grissa, I. and Drevet, C. and Couvin, D., 2017)
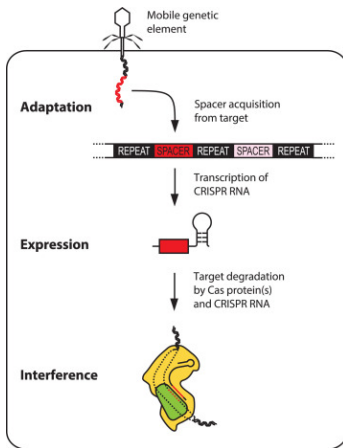
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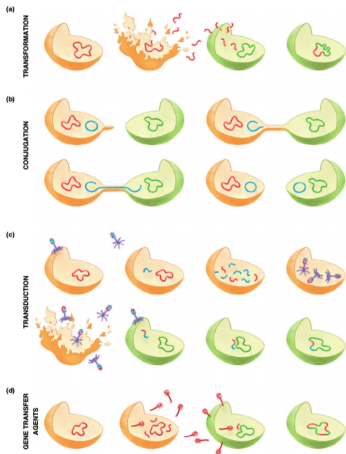# Horizontal Gene Transfer

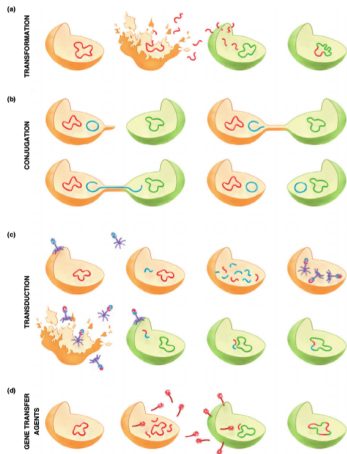# Horizontal Gene Transfer Mechanisms

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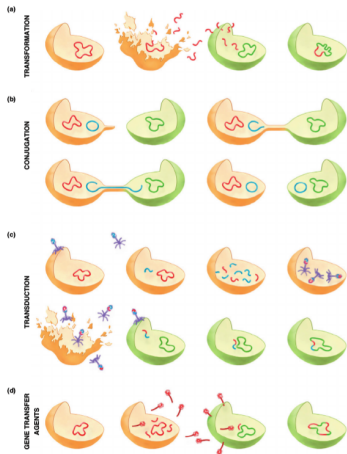
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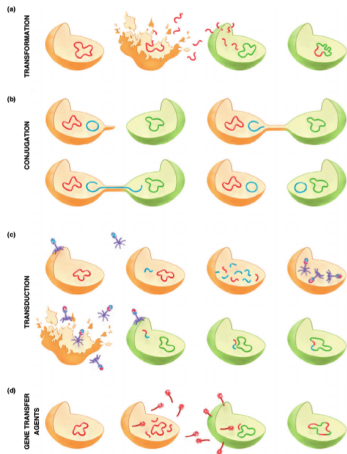- Transduction: Transfer of DNA through phage (Popa and Dagan, 2011)

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- Transduction: Transfer of DNA through phage (Popa and Dagan, 2011)
- **CRISPR-Cas directly affects HGT** (Popa and Dagan, 2011)

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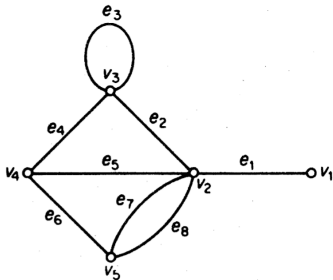- Selective pressures
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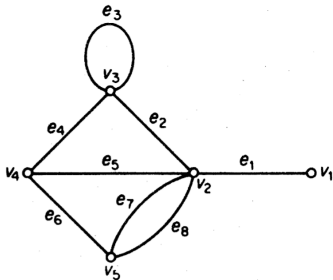# Phylogenomic Networks

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- Useful mathematical abstraction of real world system

(Bondy and Murty, 2002)
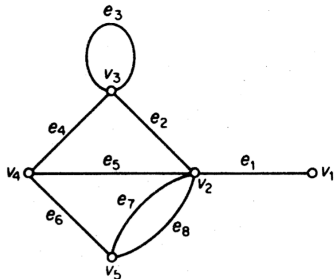
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Do CRISPR Systems Affect Horizontal Gene Transfer?

Yes

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  - Can see inhibitory effects of CRIPSR on HGT over short evolutionary time scales
  - Higher gene indel rates for CRISPR containing OTUs than non-CRISPR containing outgroups

My Project

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

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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 OTUs
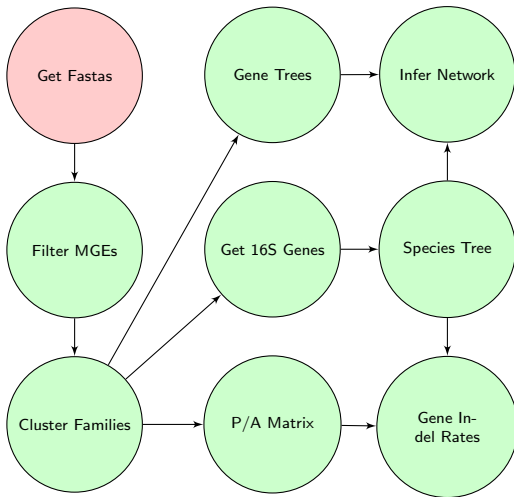
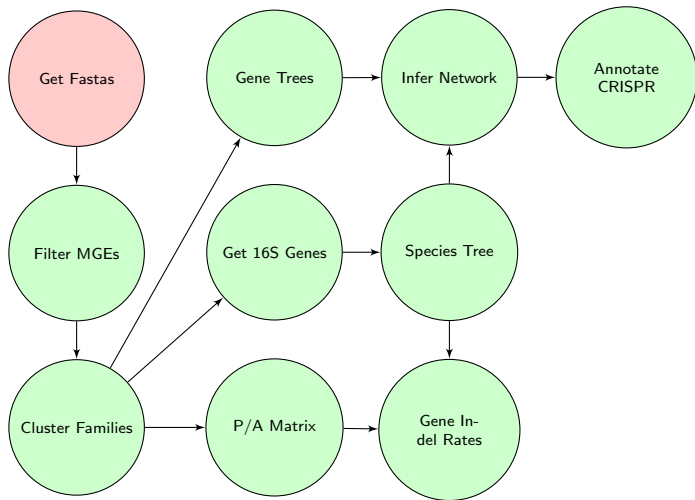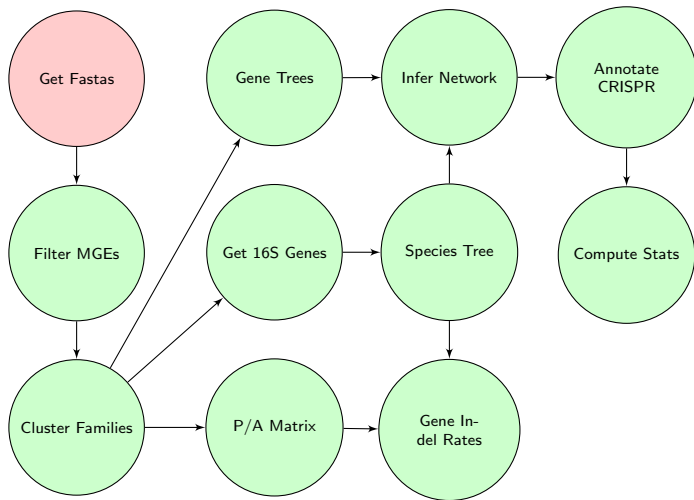# Workflow (Per Genus)

Get Fastas

Workflow (Per Genus)
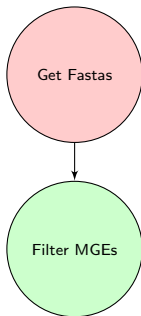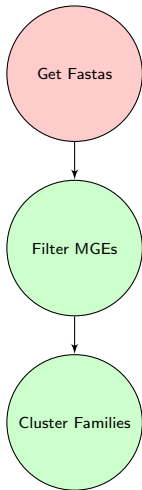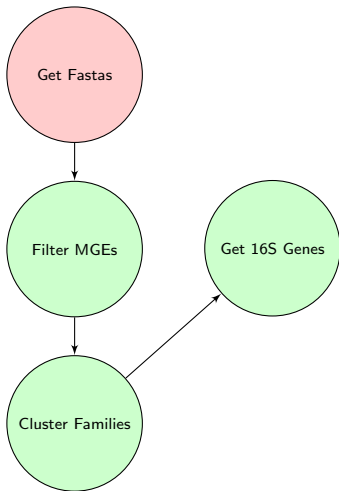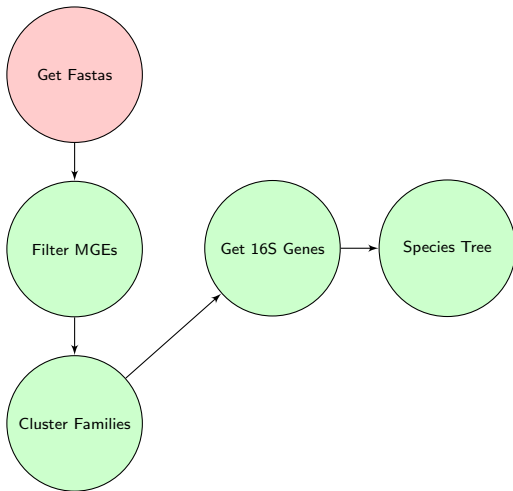
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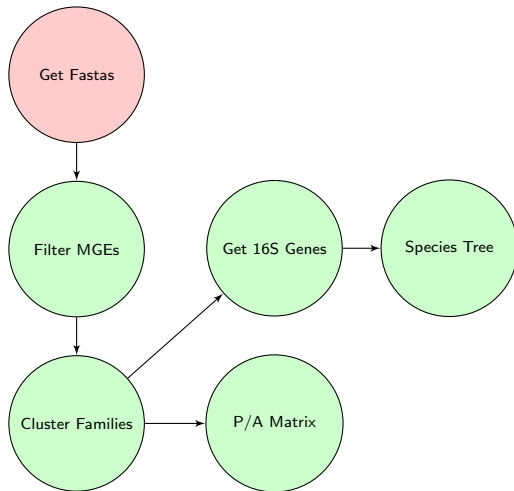
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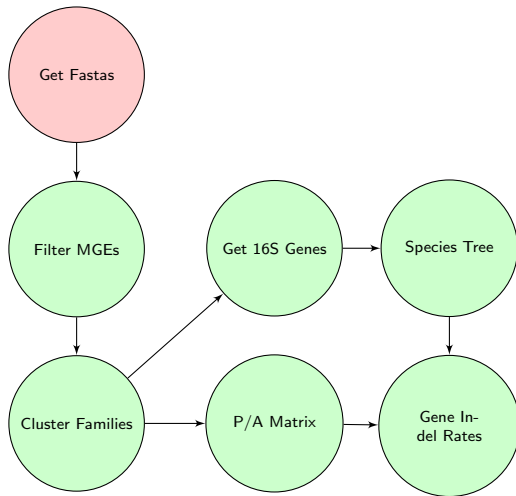
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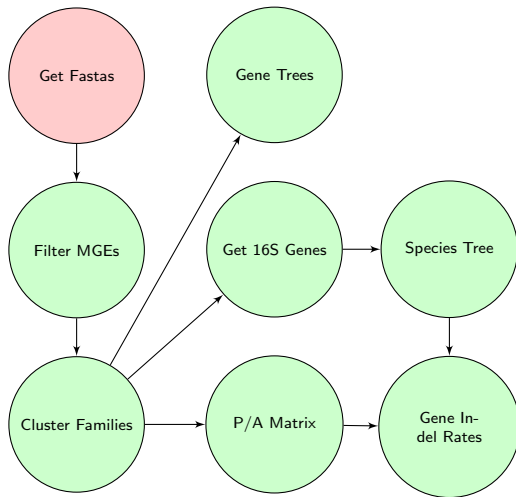
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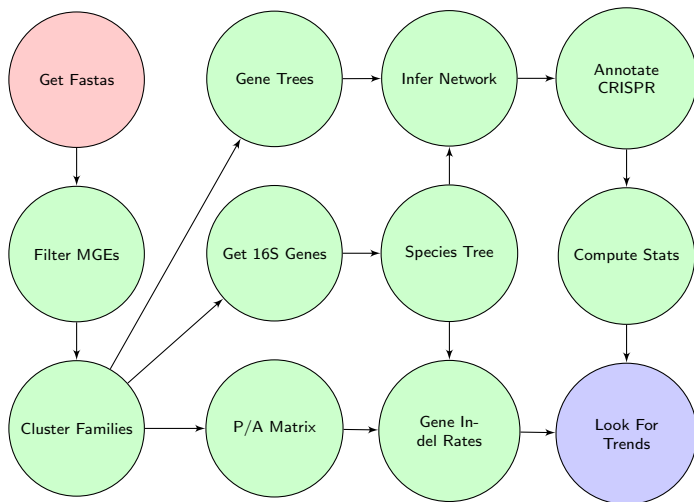
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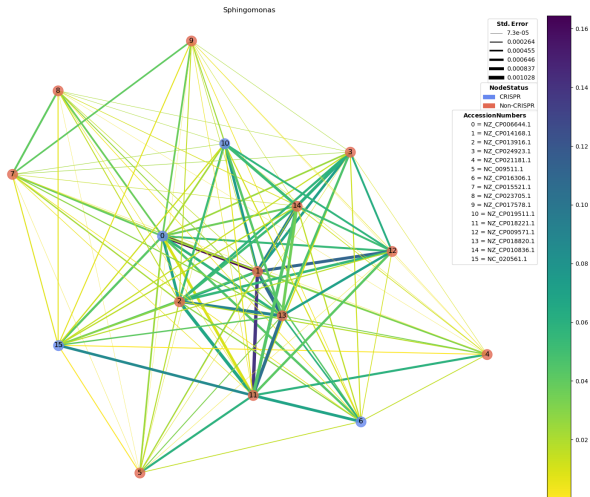
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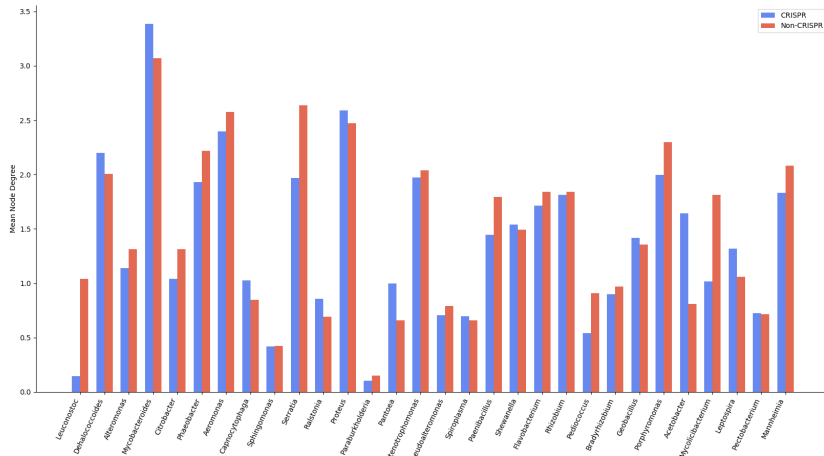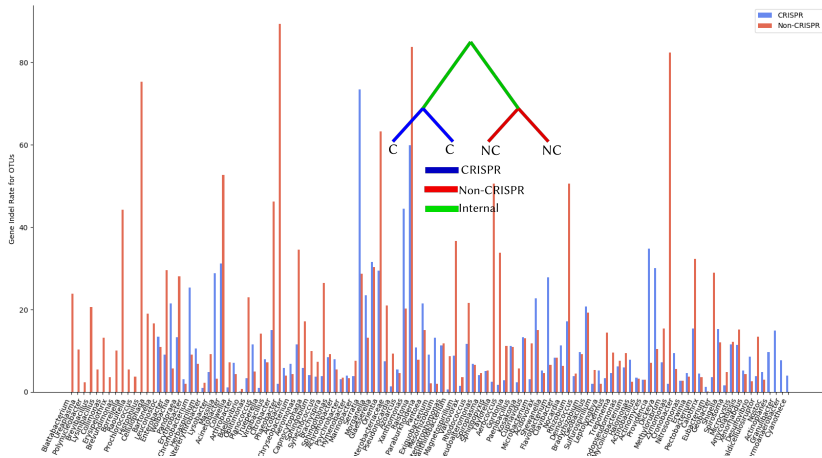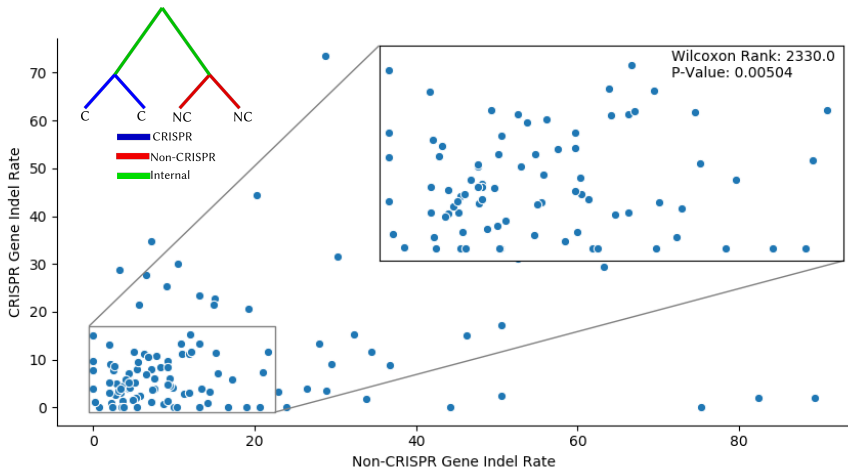
Results

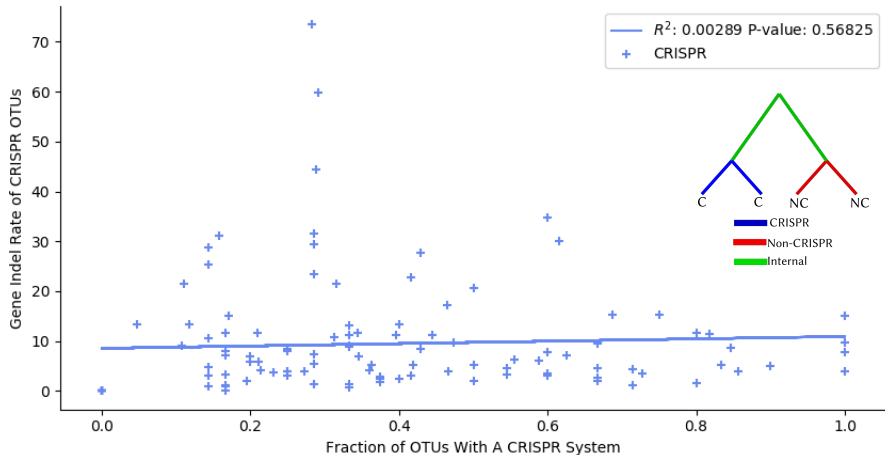# Example "Consensus" Network

Mean Node Degree

Gene Indel Rates

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Gene Indel Rate Vs. Fraction of CRISPR OTUs
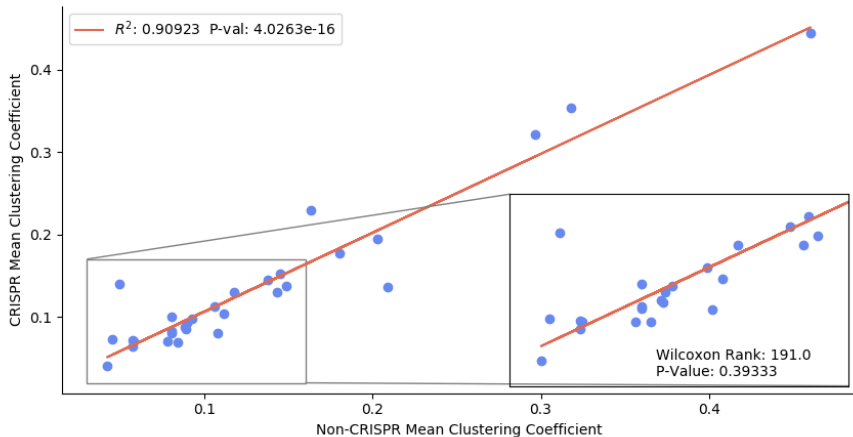
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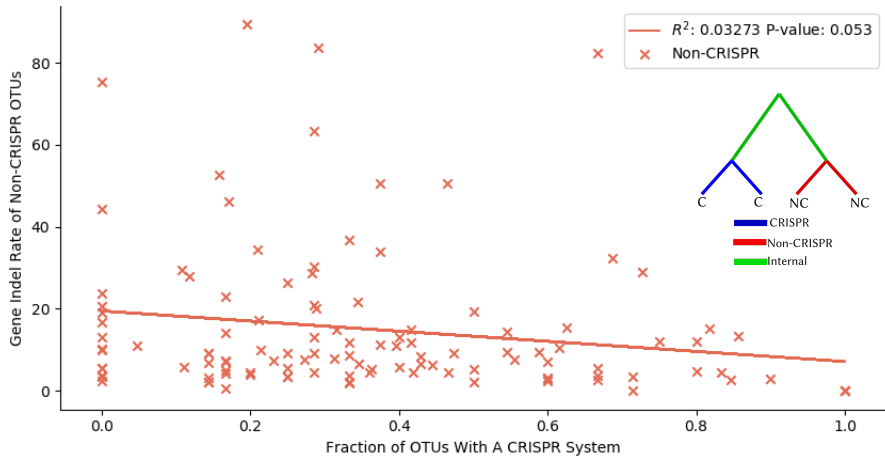
Mean Node Weighted Clustering Coefficient

Modularity Distributions
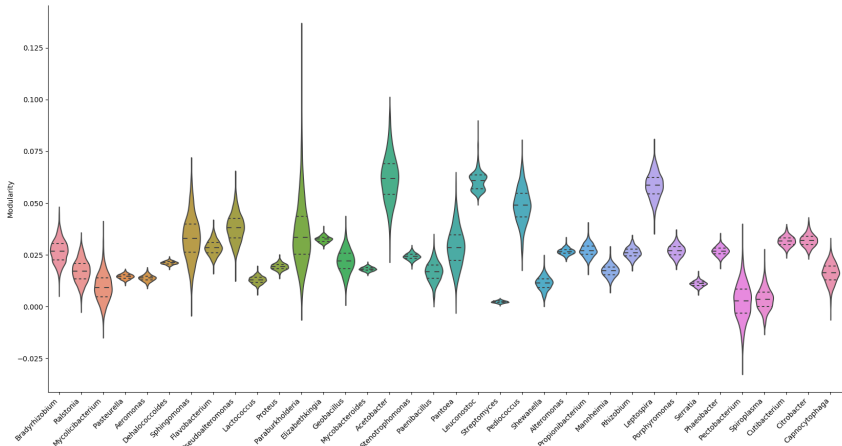
Assortativity Distributions
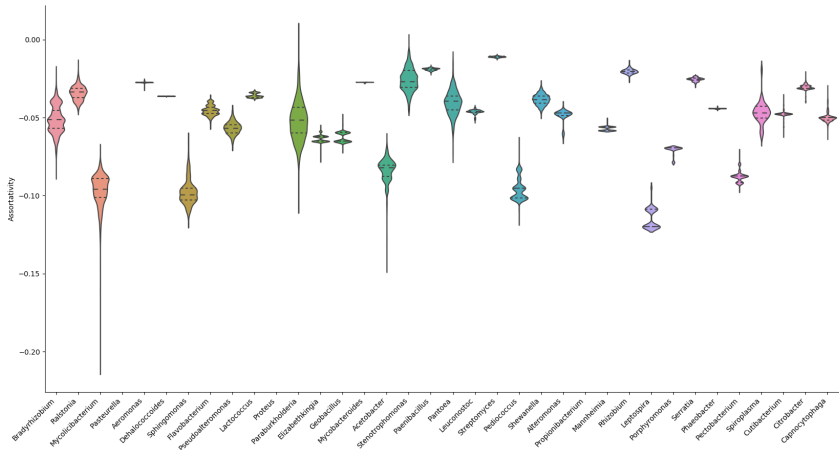
Conclusion

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- Large variation in HGT rate between genera.
- CRISPR-Cas systems broadly associated with lower HGT rates, with prominent exceptions
- Population level effects of CRISPR-Cas systems may decrease HGT rates
- Interplay of CRISPR-Cas systems and HGT is complex and warrants further study

Possible Future Directions

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- **Intergenic comparisons**: Combine any set of fasta files from OTUs for analyzing transfer dynamics
- **Considering bacterial ecology and environments**: Consider geographically close OTUs or differences between networks due to environmental factors

Is Sharing Caring?

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Yes, for researchers

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Jury's still out for bacteria

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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Diversity & Ubiquity

- 45% of bacteria have CRISPR loci ($n = 6782$) (Grissa, I. and Drevet, C. and Couvin, D., 2017)
- 3 Main Types, multiple sub types (Bondy-Denomy and Davidson, 2014)
- CRISPR arrays represent unique life history of an organism
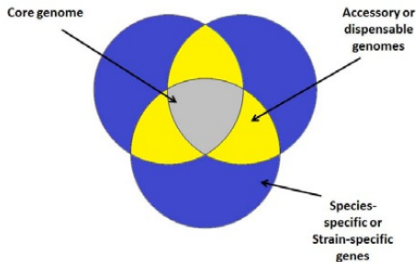- $11\% - 28\%$ are false or orphaned CRISPR loci (Zhang and Ye, 2017)
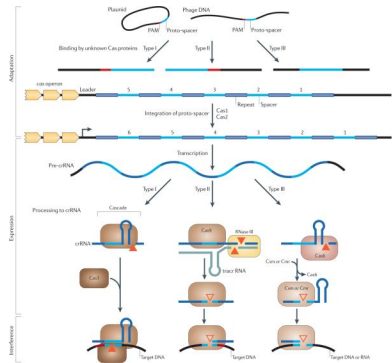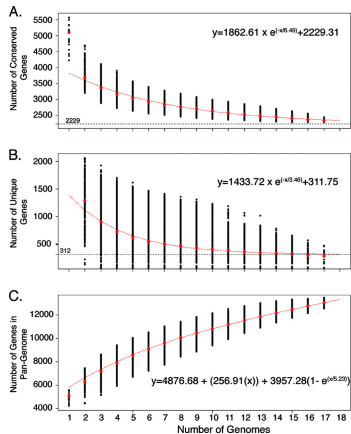

(Makarova et al., 2011)

CRISPR Biotech Application
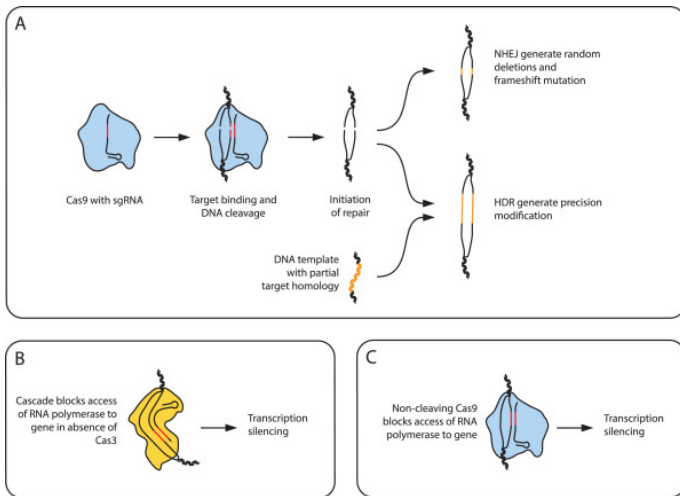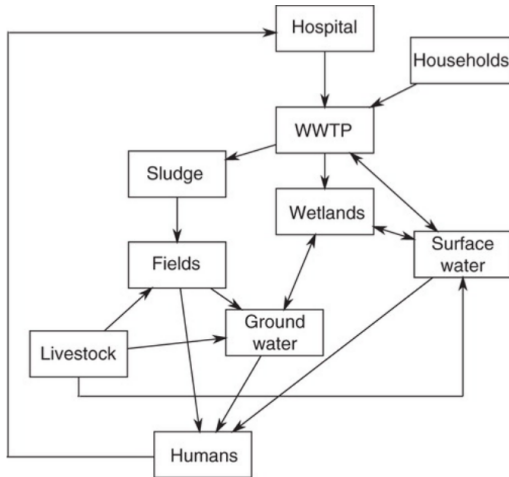

(Rath et al., 2015)

Pan-Genomes

(Guimaraes et al., 2015)

(Rasko et al., 2008)

HGT Applications

(Berglund, 2015)

Prokaryotic "Net of Life"
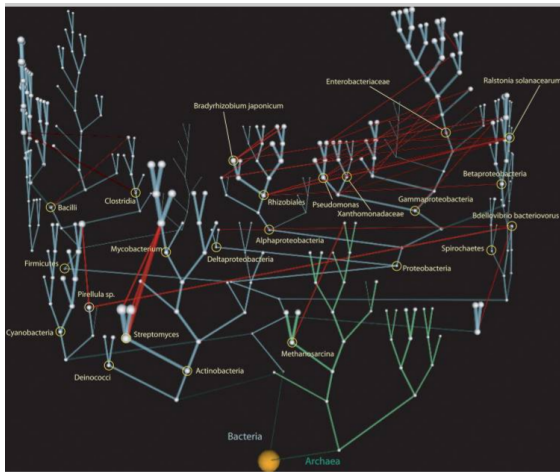
(Kunin et al., 2005)

Phylogenomic Network Construction
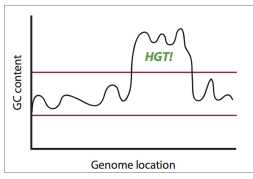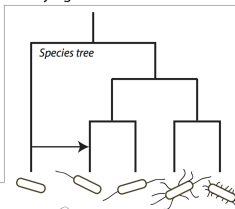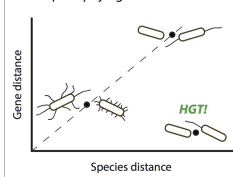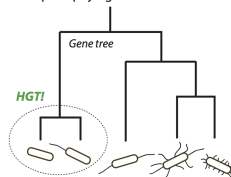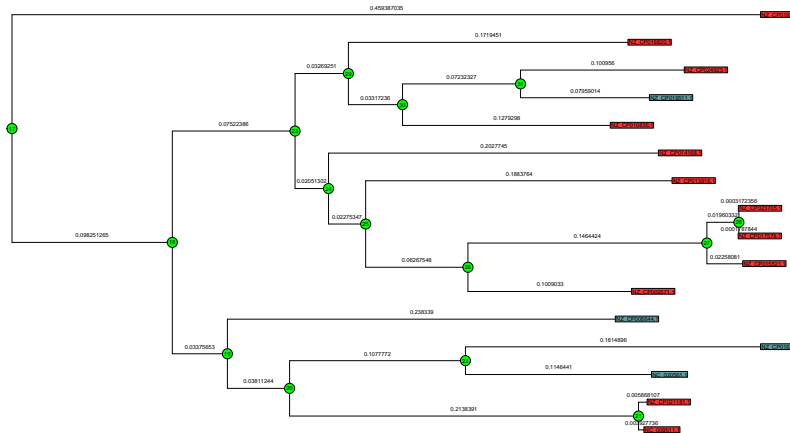

(Ravenhall et al., 2015)
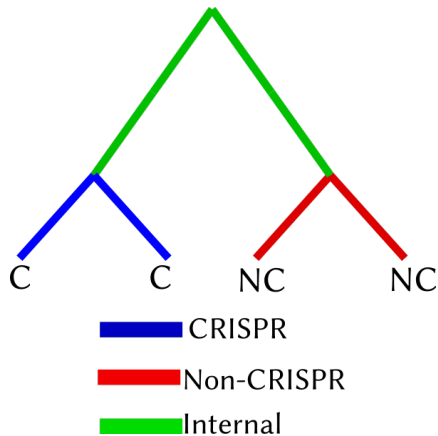
Sphingomonas Species Tree

Network Statistics

- **Average Node Degree**: $\frac{1}{|N_u|} \sum_{uv}^{N_u} w_{uv}$ where N_u is the set of nodes incident to u
- **Node Clustering Coefficient**: $\frac{1}{k_u(k_u-1)} \sum_{vw}^{T(u)} (\hat{w}_{uw} \hat{w}_{vw} \hat{w}_{uv})^{\frac{1}{3}}$ where $T(u)$ is the set of triangles containing u (Onnela et al., 2005)
- **Node Assortativity**: $A = \frac{Tr(M) - ||M^2||}{1 - ||M^2||}$ Where M is the mixing matrix of a given attribute and $||M||$ is the sum of all elements of M. $A \in [-1, 1]$. (Newman, 2002)
- **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 all edges, 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)

Genus Size Distribution
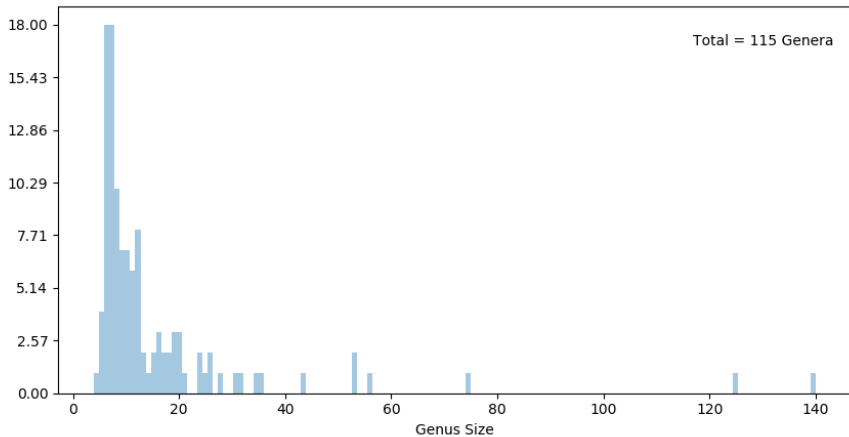
Branch Partition Example

Indel Rate Pair Plot