

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,
Biology Department,
McMaster University

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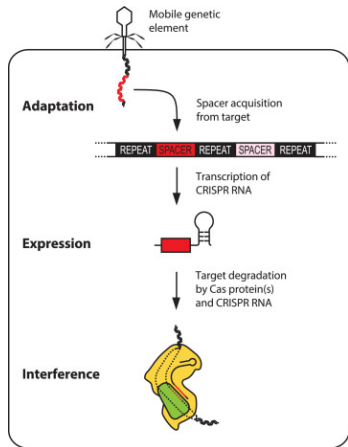
1. Background
2. My Project
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CRISPR-Cas systems

What Are They?

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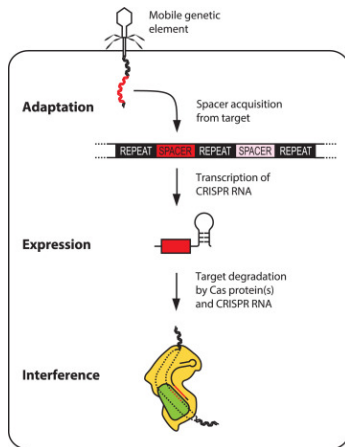
- Adaptive Bacterial Immune System



(Rath et al., 2015)

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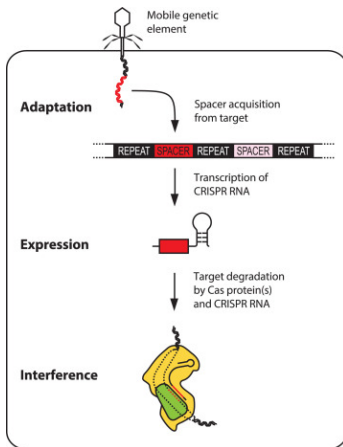
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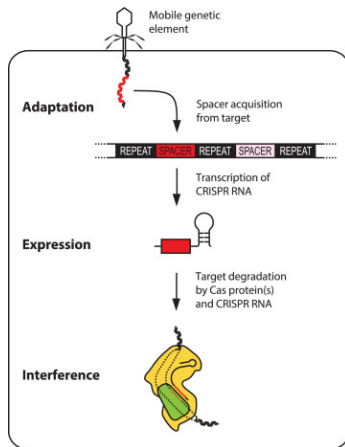
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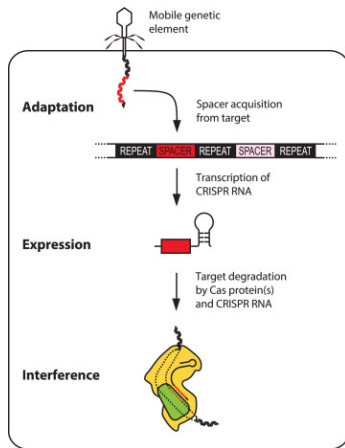
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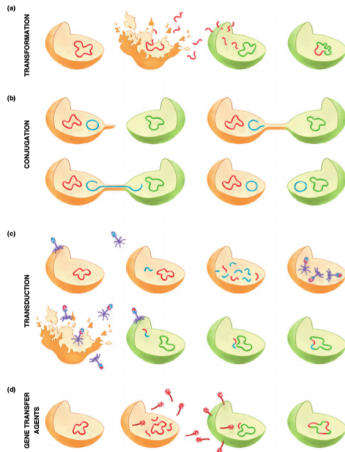
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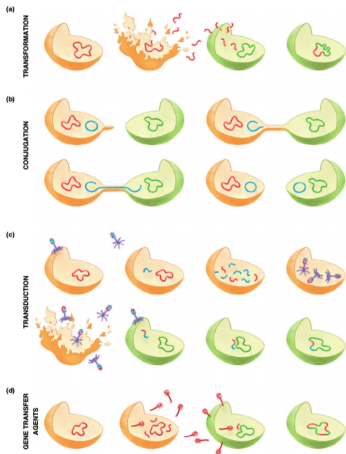
Horizontal Gene Transfer

Horizontal Gene Transfer Mechanisms



(Popa and Dagan, 2011)

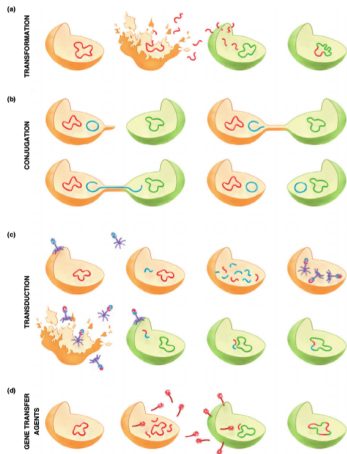
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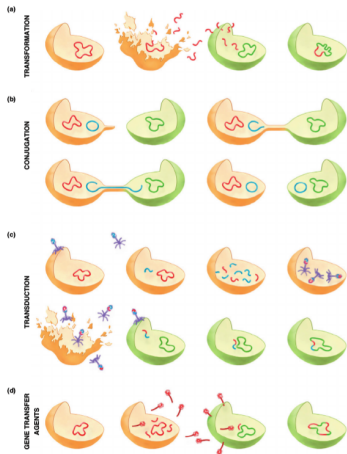
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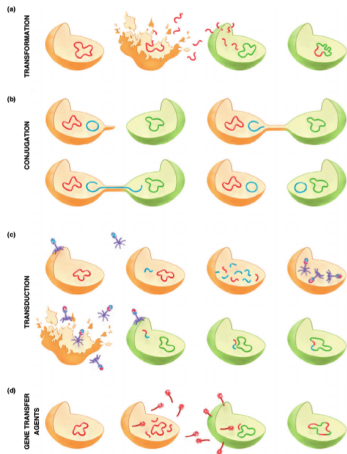
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- **CRISPR-Cas directly affects HGT** (Popa and Dagan, 2011)

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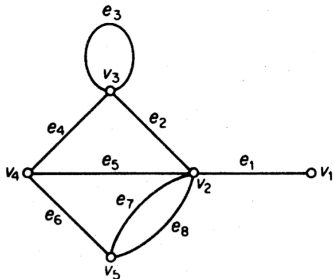
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Phylogenomic Networks

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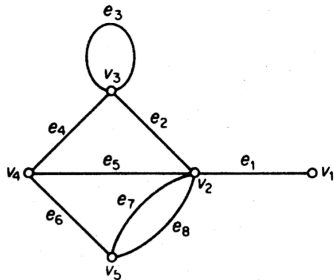
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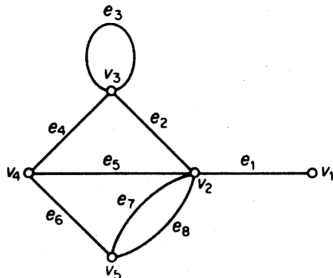
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Do CRISPR Systems Affect Horizontal Gene Transfer?

Yes

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

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 - 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 CRISPR containing OTUs to non-CRISPR containing OTUs.

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Gene Indel Rates vs. Network Statistics

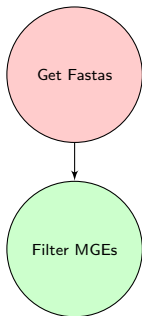
Compare gene Indel rates to node/network statistics for CRISPR containing and non-CRISPR containing OTUs

Workflow (Per Genus)

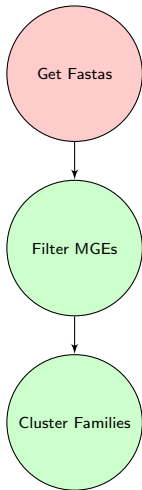


Get Fastas

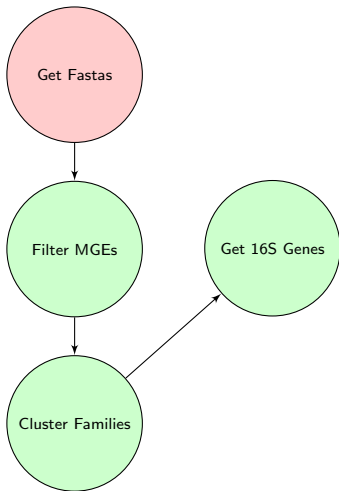
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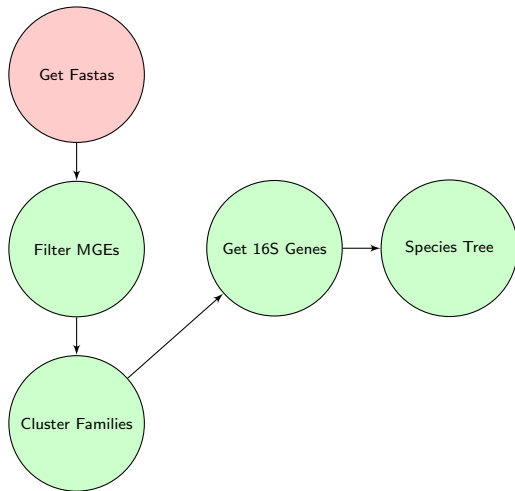
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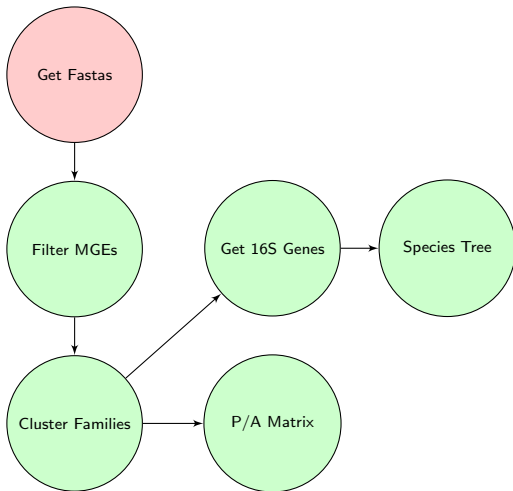
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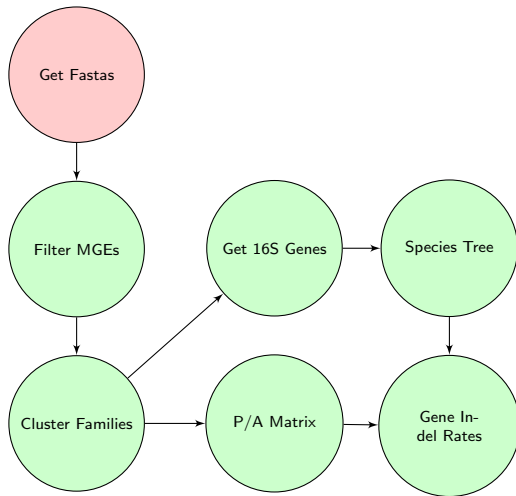
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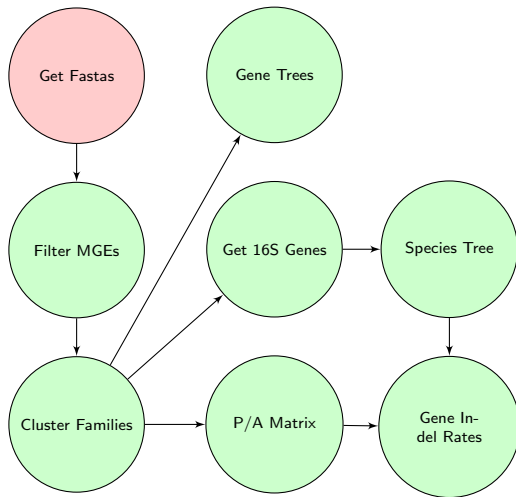
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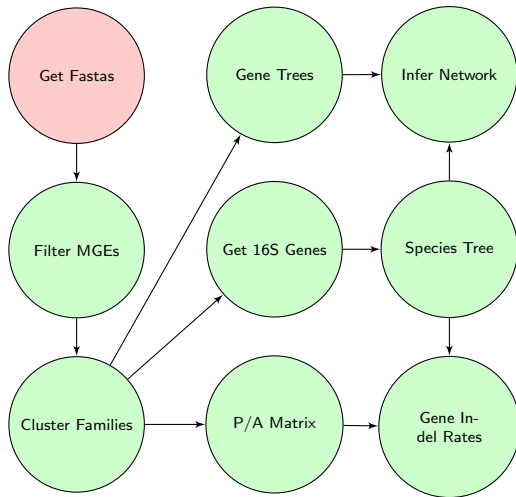
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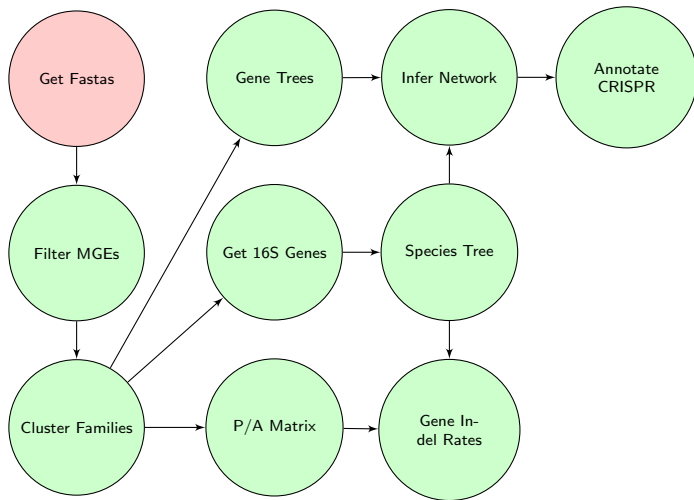
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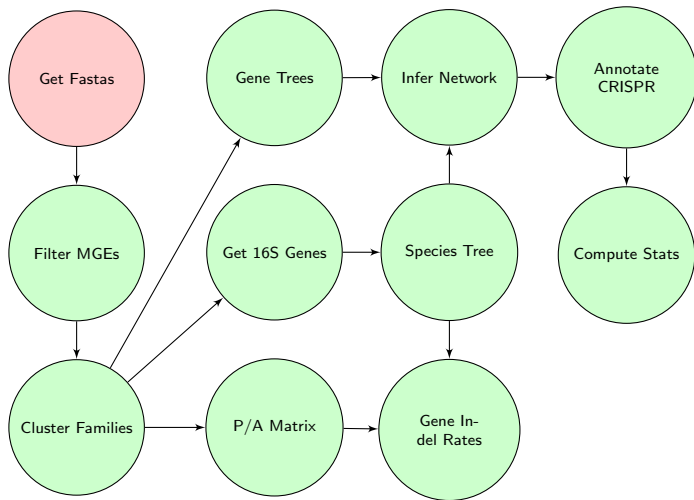
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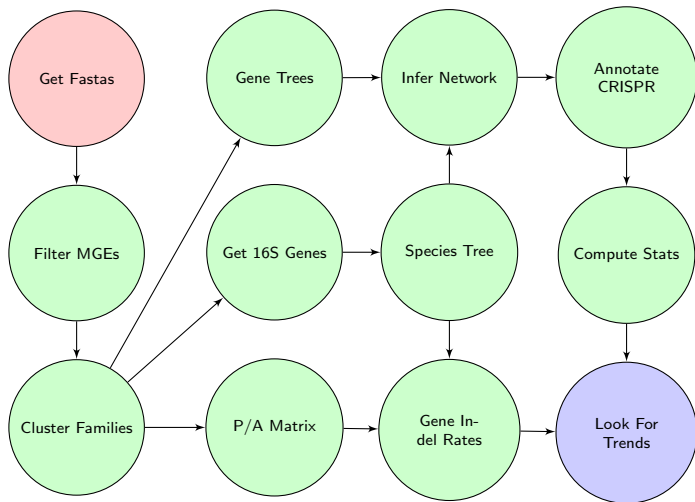
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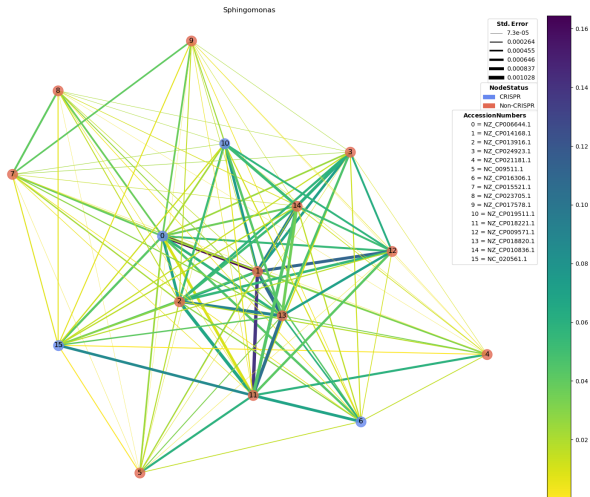


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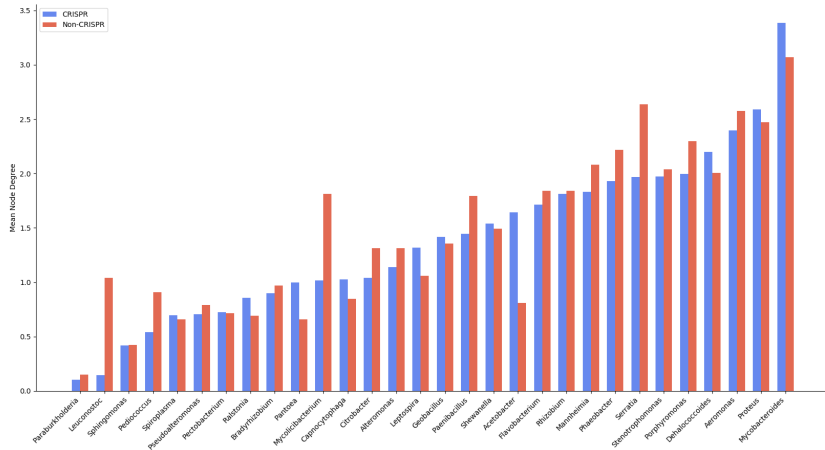


Results

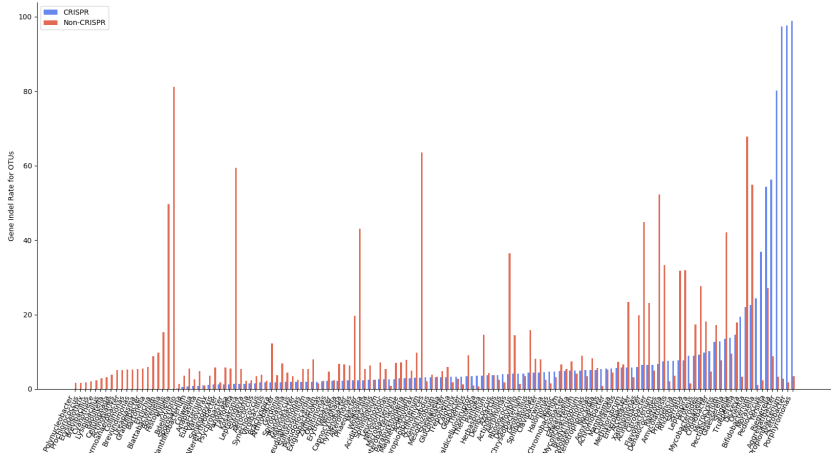
Example "Consensus" Network



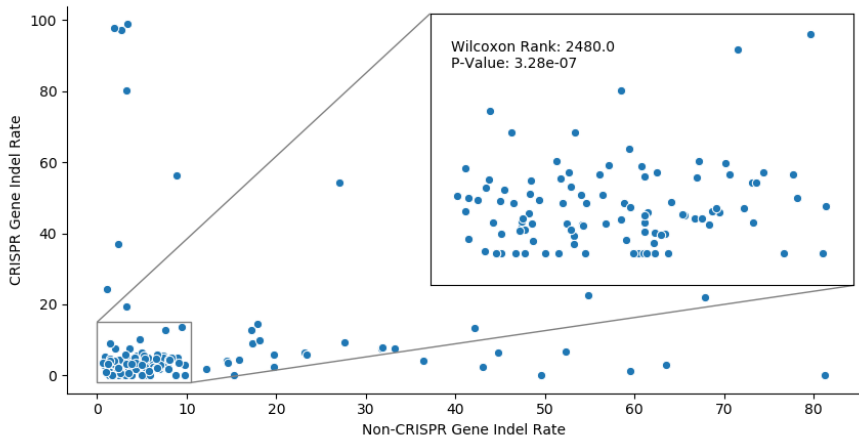
Mean Node Degree



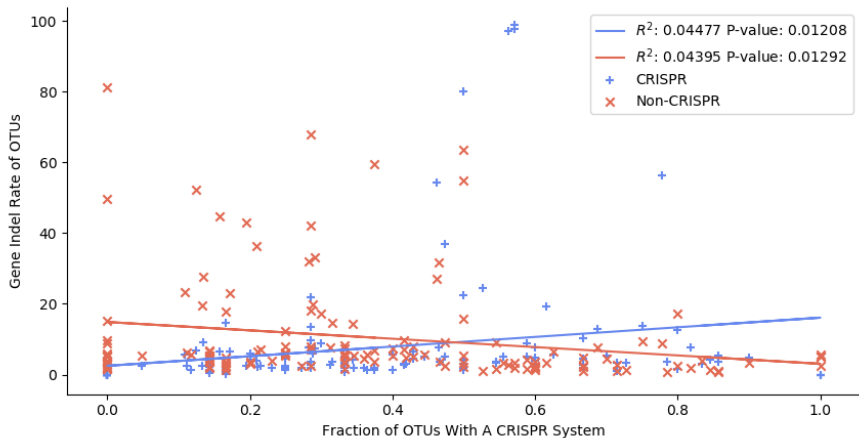
Gene Indel Rates



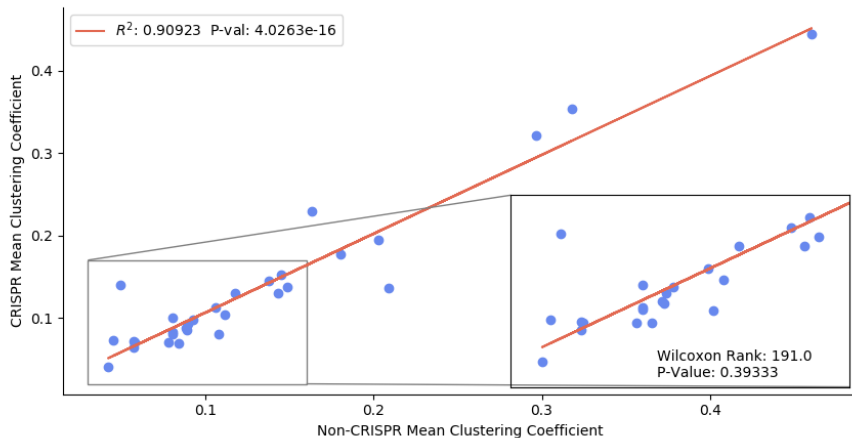
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Gene Indel Rate Vs. Fraction of CRISPR OTUs



Mean Node Weighted Clustering Coefficient



Conclusion

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- 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

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- **Considering bacterial ecology and environments:** Consider geographically close OTUs or differences between networks due to environmental factors

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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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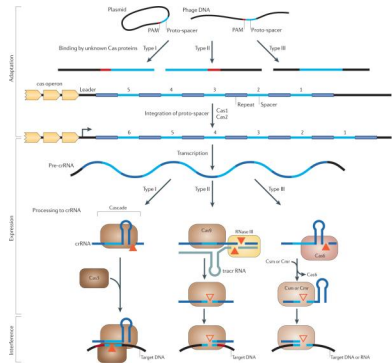


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Diversity & Ubiquity

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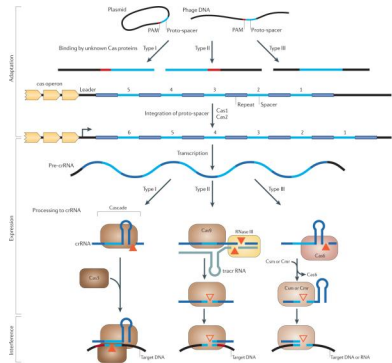
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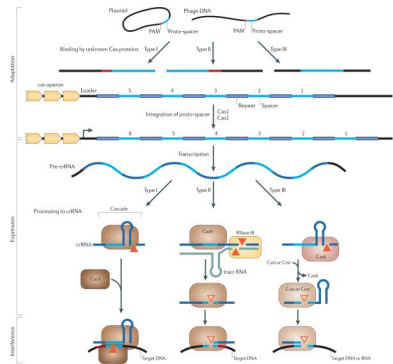
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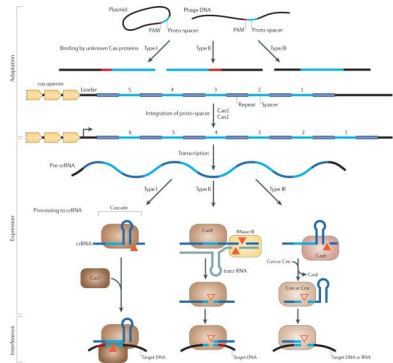
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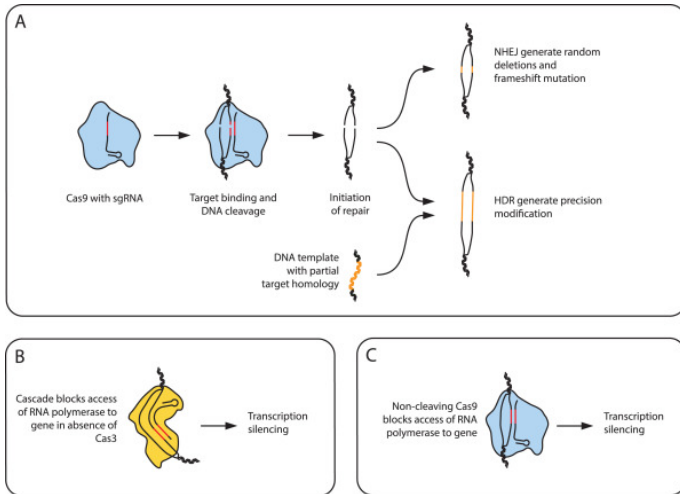
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CRISPR Biotech Application

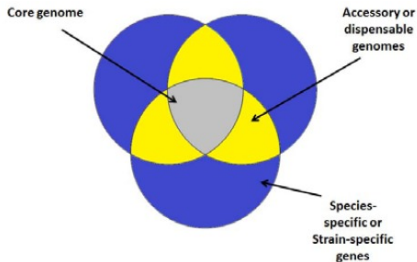
CRISPR Biotech Application



(Rath et al., 2015)

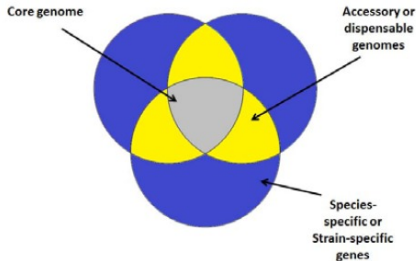
Pan-Genomes

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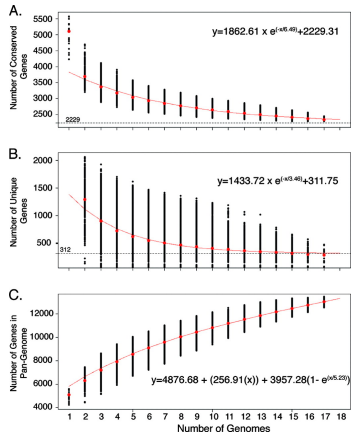


(Guimaraes et al., 2015)

Pan-Genomes



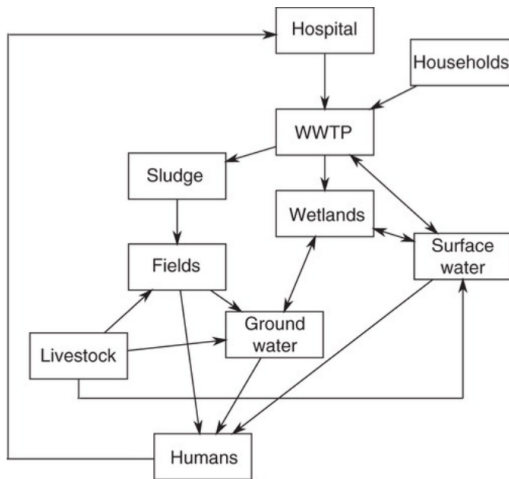
(Guimaraes et al., 2015)



(Rasko et al., 2008)

HGT Applications

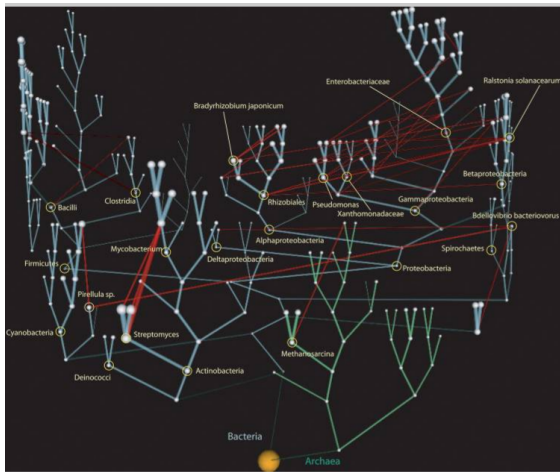
HGT Applications



(Berglund, 2015)

Prokaryotic “Net of Life”

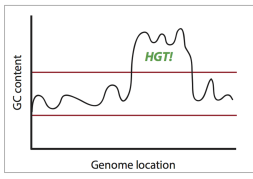
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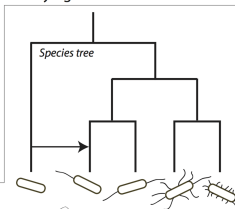
(Kunin et al., 2005)

Phylogenomic Network Construction

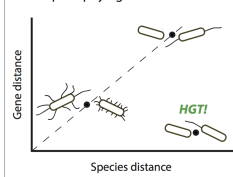
1. Parametric methods



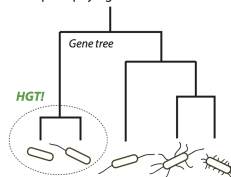
2. Phylogenetic methods



2a. Implicit phylogenetic methods



2b. Explicit phylogenetic methods



(Ravenhall et al., 2015)

Network Statistics

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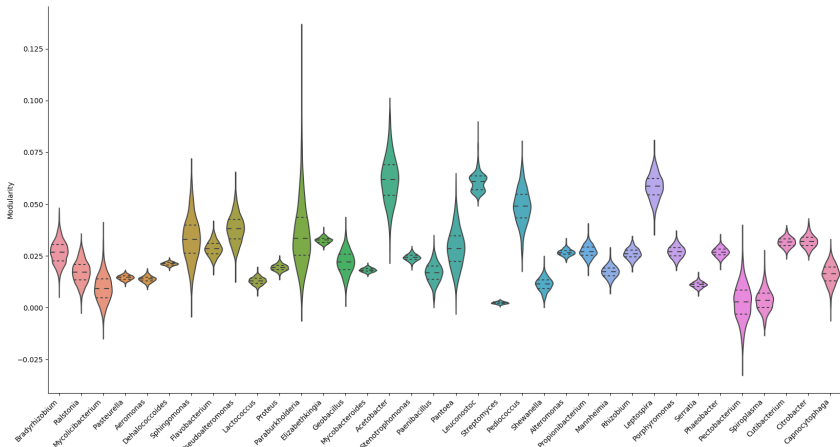
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- **Network Modularity:** $Q = \frac{1}{2m} \sum_{uv} [W_{uv} - \frac{k_u k_v}{2m}] \delta(u, v)$ where m is the total weight of all edges, k_u is the degree of u and $\delta(u, v)$ is 1 if u and v both have or do not have CRISPR systems and 0 otherwise.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

Modularity Distributions



Assortativity Distributions

