The Effects Of CRISPR-Cas Systems On The Rate Of Horizontal Gene Transfer

A Network Theoretic Approach

Siddharth Reed
Undergraduate Thesis

Golding Lab,
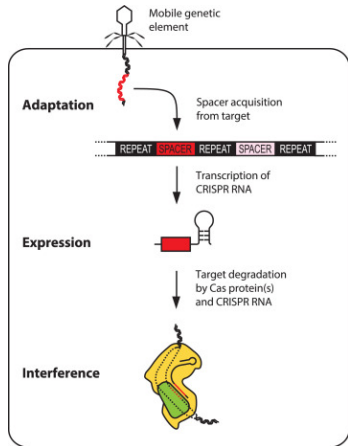Biology Department,
McMaster University

December 4, 2018

McMaster University
BIOLOGY

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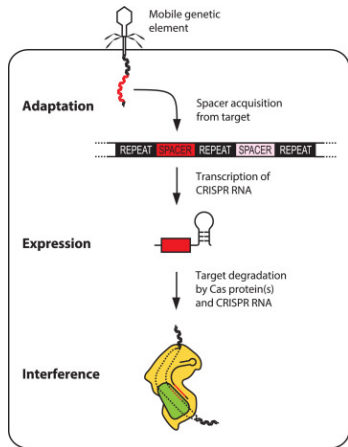# CRISPR-Cas systems

What Are They?

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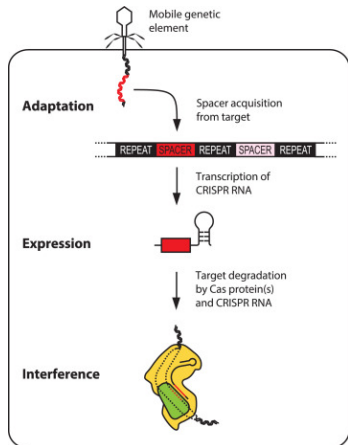
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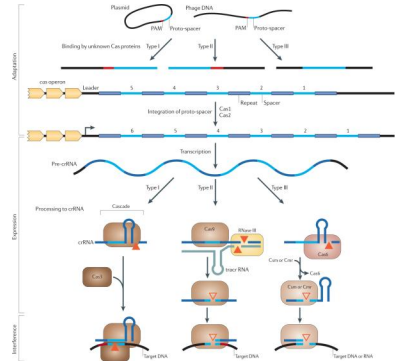- Protects against foreign DNA

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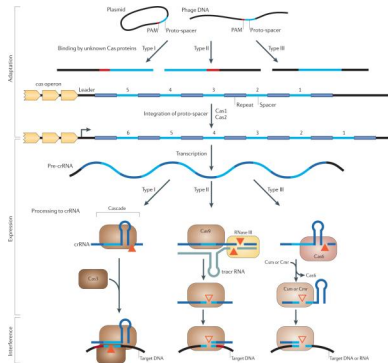- Requires Cas proteins and CRISPR loci

Diversity & Ubiquity

Diversity & Ubiquity

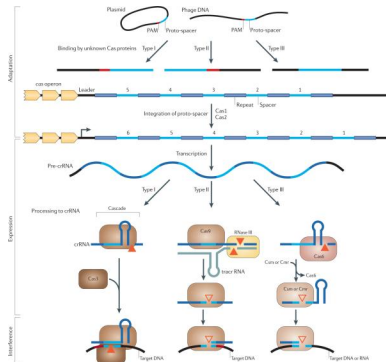- 45% of bacteria have CRISPR loci ($n = 6782$)[2]

Diversity & Ubiquity

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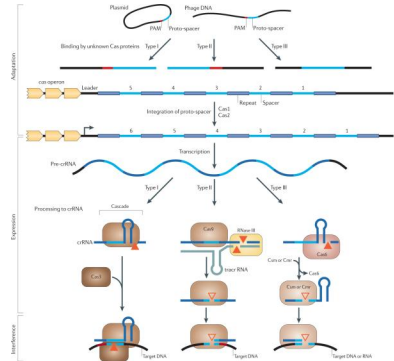## Diversity & Ubiquity

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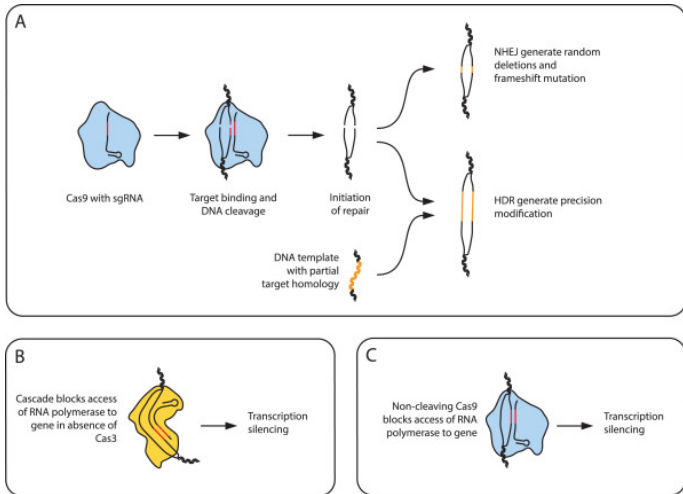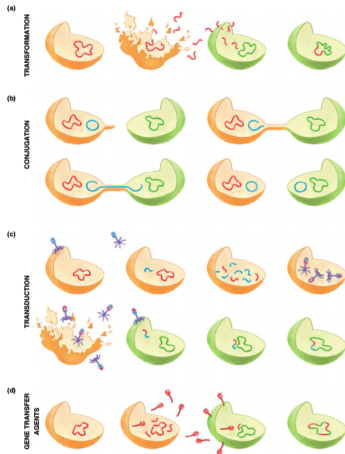- $11\% - 28\%$ are false or orphaned CRISPR loci[4]

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Biotech Application

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Horizontal Gene Transfer

Mechanisms

6

Mechanisms

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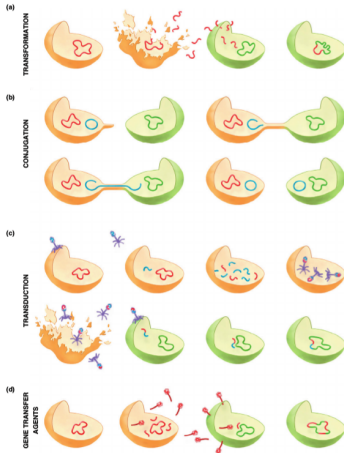
6

Mechanisms

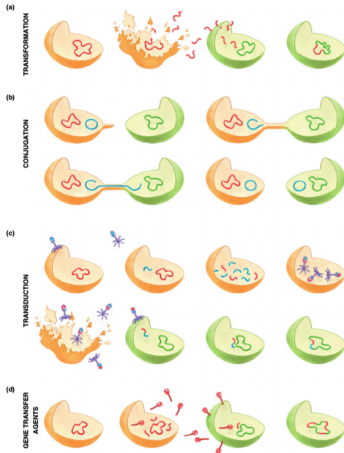- Conjugation: Transfer of DNA through cell-cell connections[6]
- Transformation: Incorporaion of free-floating DNA into the genome[6]
- Transduction: Transfer of DNA through phage[6]
- **CRISPR-Cas directly affects Transduction and Transformation**[6]

6

Pan-Genomes

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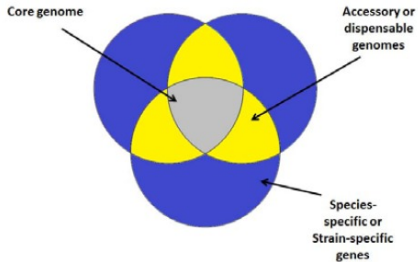
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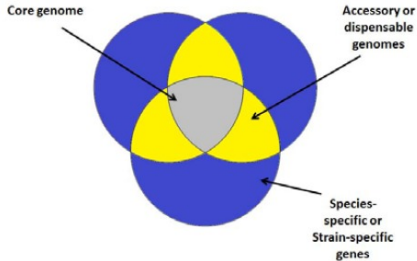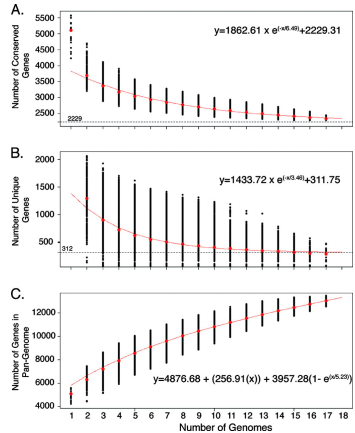
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- Sequence compatibility

Applications

Applications

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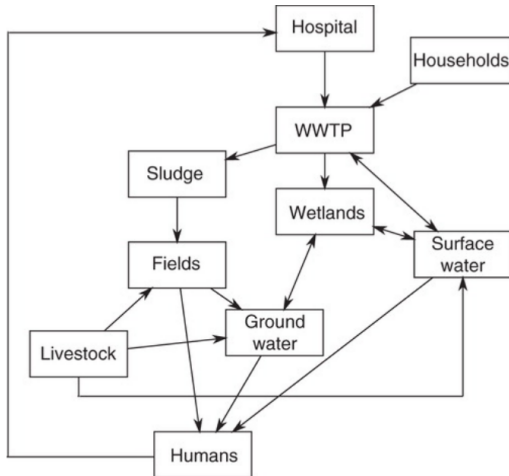
Phylogenomic Networks

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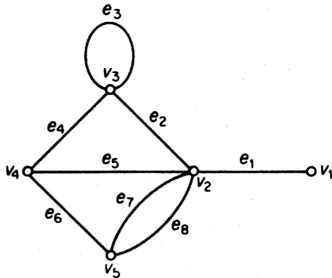
- Useful mathematical abstraction of real world system
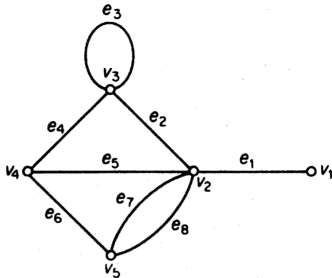
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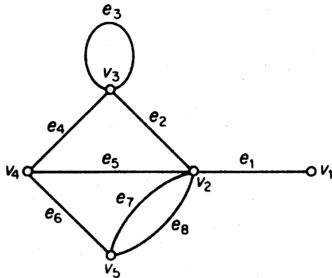
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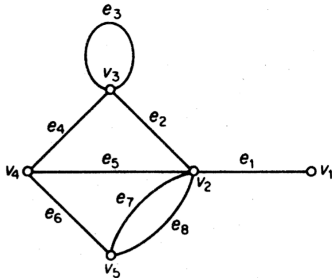
- Useful mathematical abstraction of real world system
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- Directed or Undirected Edges
- Weighted or Unweighted Edges

10

Prokaryotic "Net of Life"

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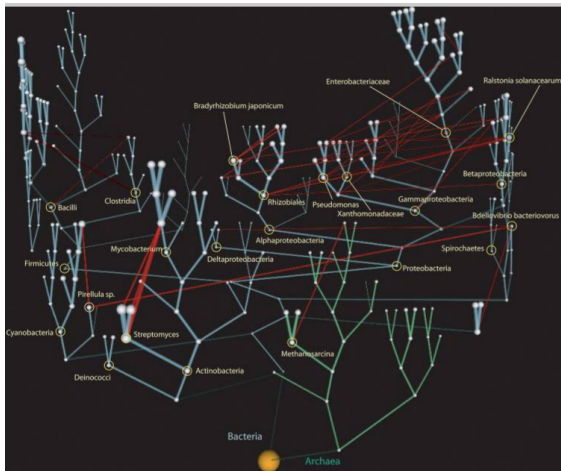
Construction
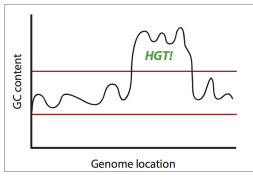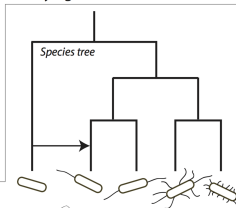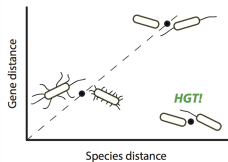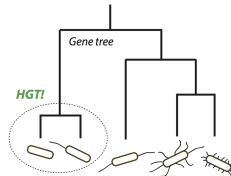
Do CRRISPR Systems Affect Horizontal Gene Transfer?

Yes

CRISPR Cost Complexity

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- Cost tradeoff factors:

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  - Anti-CRISPR systems[3]
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  - Prophage abundance[15]

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- Selective CRISPR inactivation[1]
- CRISPR can enhance transduction-mediated HGT[15]

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  - 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
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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
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For genera with no CRISPR conatining strains, compare the network statistics of mixed to non-CRISPR-containing networks.

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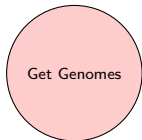
Between Network Comparisons

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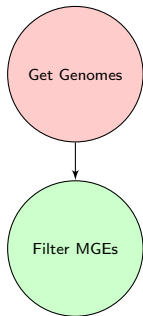
Gene Indel Rates vs. Network Statistics

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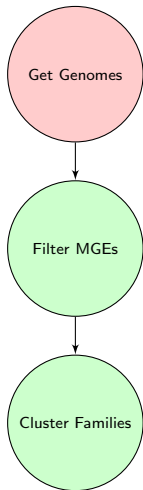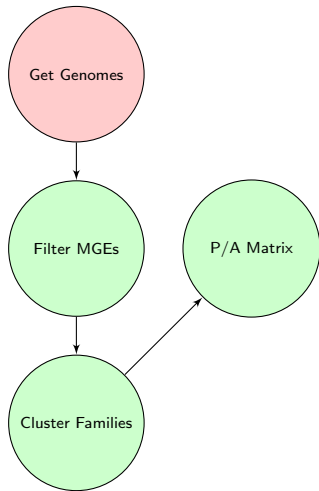
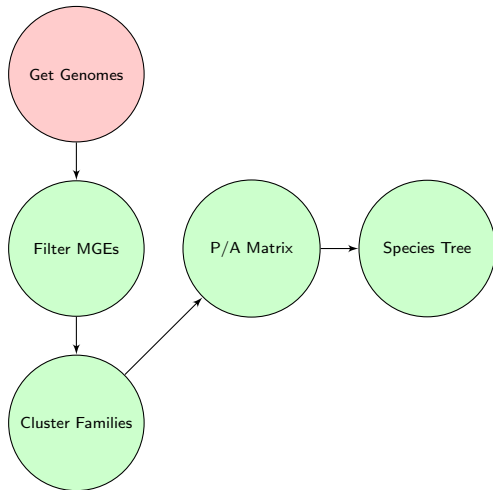# Workflow

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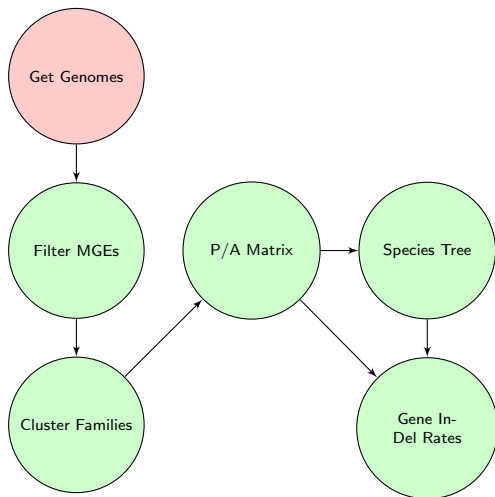
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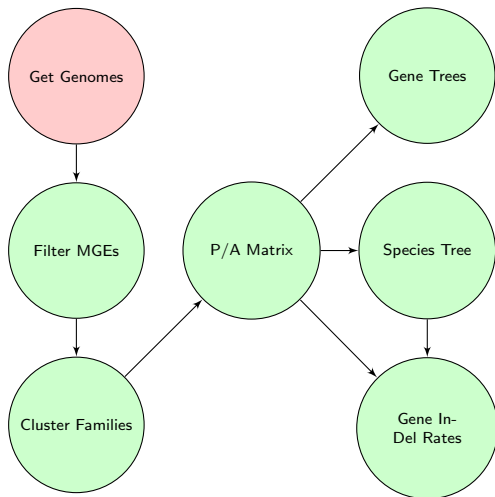
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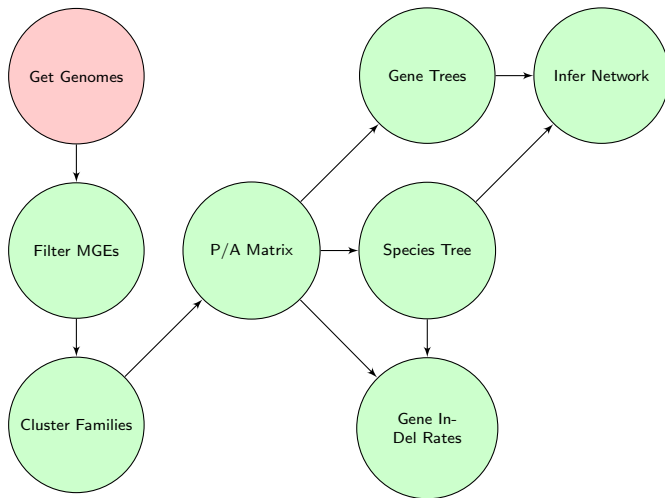
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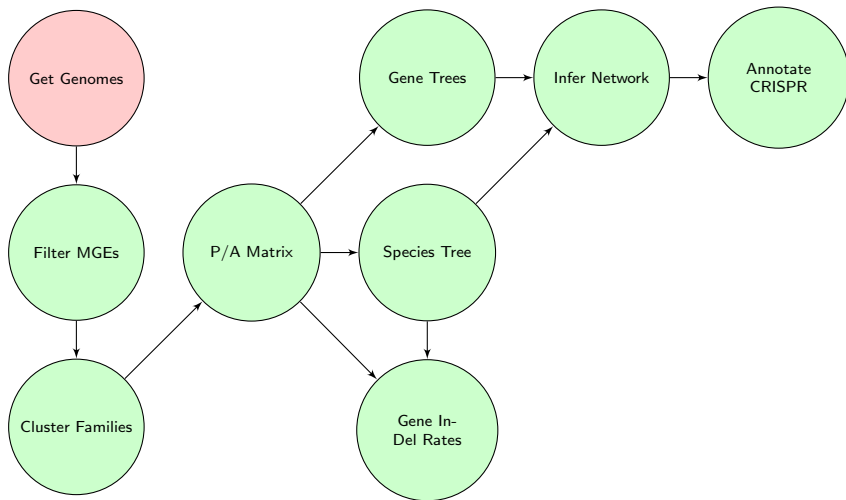
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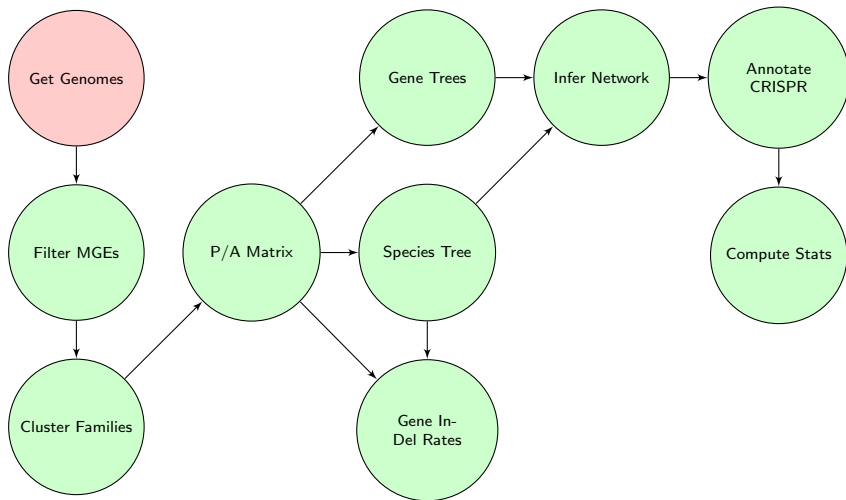
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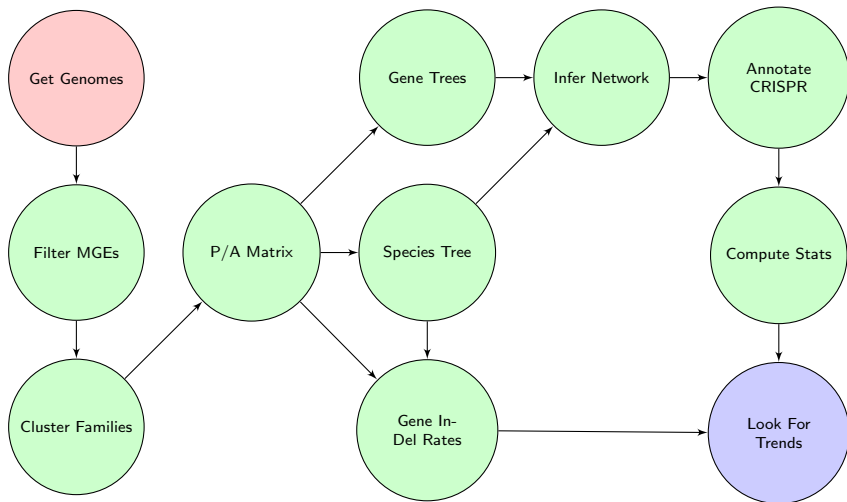
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- **Node Associativity**: $\frac{j(j+1)(\overline{k}-\mu_q)}{2E\sigma_q^2}$ where j is the excess degree of the node and $\overline{k}$ is the average excess degree of the node's neighbors and μ_q and σ_q are the mean and standard variation of the excess degree distribution.

Thanks

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

📄 Devashish Rath et al. "The CRISPR-Cas immune system: Biology, mechanisms and applications". In: *Biochimie* 117 (2015). Special Issue: Regulatory RNAs, pp. 119–128. ISSN: 0300-9084. DOI: https://doi.org/10.1016/j.biochi.2015.03.025. URL: http://www.sciencedirect.com/science/article/pii/S0300908415001042.

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Björn Berglund. "Environmental dissemination of antibiotic resistance genes and correlation to anthropogenic contamination with antibiotics". In: *Infection Ecology & Epidemiology* 5.1 (2015), p. 28564. DOI: 10.3402/iee.v5.28564. eprint: https://doi.org/10.3402/iee.v5.28564. URL: https://doi.org/10.3402/iee.v5.28564.

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James S. Godde and Amanda Bickerton. "The Repetitive DNA Elements Called CRISPRs and Their Associated Genes: Evidence of Horizontal Transfer Among Prokaryotes". In: *Journal of Molecular Evolution* 62.6 (June 2006), pp. 718–729. ISSN: 1432-1432. DOI: 10.1007/s00239-005-0223-z. URL: https://doi.org/10.1007/s00239-005-0223-z.

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