

Bacteria utilize genomic reorganization, such as rearrangements and inversions, to create genetic diversity (Hughes et al. 2000; Belda et al. 2005) and assist in speciation and adaptation (Kresse et al. 2003). This reorganization can help with adaptation strategies (Rocha 2004; Hanage 2016) and gene conversion (Hanage 2016). Inversions are one particular type of genomic reorganization that can promote spontaneous genome rearrangements (Sun et al. 2012). There has been evidence that inversions are non-random and provide specific functions in bacterial genome evolution (Kresse et al. 2003). In some cases, inversions are the only source of rearrangement in bacteria.

Inversions can have a number of effects on a variety of molecular trends. For example, inversions can impact gene gain and loss (Furuta et al. 2011), outer membrane proteins (Furuta et al. 2011), gene orientation, and intracellular signalling (Sekulovic et al. 2018). These can all impact the conservation of a gene or how genes are co-regulated depending on their orientation (Huynen et al. 2001). Since inversions can promote recombination (Segall et al. 1988), there is a potential for inversions to promote the introduction of genes with novel function.

One interesting role that inversions can play is the role of a control switch. These, “switches” can impact, for example, antibiotic resistance and turn it “on/off” (Cui et al. 2012). Some inversions have the ability to revert or reverse (Hill and Gray 1988; Louarn et al. 1985; Cui et al. 2012). This switching appears to be random, but maintaining an inverted or reverted state is organized (Cui et al. 2012; Sekulovic et al. 2018). These inversions allow the bacteria to switch between various states (Borst and Greaves 1987) such as having a flagella or not (Li et al. 2019).

As mentioned previously, inversions provide a way for bacteria to epigenetically alter their gene expression (Zieg et al. 1978; Sekulovic et al. 2018; Li et al. 2019). In some cases inversions can bring a silent gene to the expression site, “turning on” expression for that gene (Cerdeño-Tárraga et al. 2005). Other times the gene expression alteration is non-specific and the inversions causes genes in areas close to the inversion to become differentially expressed (Cerdeño-Tárraga et al. 2005; Naseeb et al. 2016; Sekulovic et al. 2018). This again depends on the organism and inversions, as there have been cases where inversions do not alter expression of nearby genes, or the organism is so robust that inversions which should alter gene expression, have no impact (Alokam et al. 2002).

Previous studies investigating the impacts inversions have on bacterial gene expression have largely focused on a single inversion (Zieg et al. 1978; Sekulovic et al. 2018), or the impact inversions have on the expression of a few genes (Li et al. 2019). The few studies that have taken a more whole genome approach to analyzing inversions and their impact on gene expression, have concluded that there is differential gene expression between inverted and non-inverted segments (Alokam et al. 2002; Naseeb et al. 2016). Although, there appears to be no pattern of genes being completely up- or down- regulated in inverted or non-inverted segments (Alokam et al. 2002; Naseeb et al. 2016). Most of these whole genome analysis are focused on yeast (Naseeb et al. 2016), with only one looking at genome wide inversions in bacteria (Alokam et al. 2002). Alokam et al. (2002) focus on comparing inversions between the distantly related species *Salmonella* and *E. coli*. In this work, we aim to explore differences in gene expression due to inversions between closely related strains of *E. coli*. Although there has been work done to identify inversions between closely related strains (Sun et al. 2012), to our knowledge, an in-depth analysis of gene expression and inversions in the same strain of bacteria has not been investigated. Most inversions have an unknown function (Raeside et al. 2014), including how they impact gene expression.

References

- Alokam S, Liu S.-L, Said K, and Sanderson K E (2002). Inversions over the terminus region in *Salmonella* and *Escherichia coli*: IS200s as the sites of homologous recombination inverting the chromosome of *Salmonella enterica* serovar typhi. *J Bacteriol* 184(22), 6190–6197.
- Belda E, Moya A, and Silva F J (2005). Genome rearrangement distances and gene order phylogeny in gamma-proteobacteria. *Mol Bio Evol* 22(6), 1456–1467.
- Borst P and Greaves D R (1987). Programmed gene rearrangements altering gene expression. *Science* 235(4789), 658–667.
- Cerdeño-Tárraga A M, Patrick S, Crossman L C, Blakely G, Abratt V, Lennard N, Poxton I, Duerden B, Harris B, and Quail M A (2005). Extensive DNA inversions in the *B. fragilis* genome control variable gene expression. *Science* 307(5714), 1463–1465.
- Cui L, Neoh H, Iwamoto A, and Hiramatsu K (2012). Coordinated phenotype switching with large-scale chromosome flip-flop inversion observed in bacteria. *Proc Natl Acad Sci* 109(25), E1647–E1656.
- Furuta Y, Kawai M, Yahara K, Takahashi N, Handa N, Tsuru T, Oshima K, Yoshida M, Azuma T, and Hattori M (2011). Birth and death of genes linked to chromosomal inversion. *Proc of Natl Acad Sci* 108(4), 1501–1506.
- Hanage W P (2016). Not so simple after all: bacteria, their population genetics, and recombination. *Cold Spring Harbor perspectives in biology*, a018069.
- Hill C W and Gray J A (1988). Effects of chromosomal inversion on cell fitness in *Escherichia coli* K-12. *Genetics* 119(4), 771–778.
- Hughes T R, Marton M J, Jones A R, Roberts C J, Stoughton R, Armour C D, Bennett H A, Coffey E, Dai H, He Y D, et al. (2000). Functional discovery via a compendium of expression profiles. *Cell* 102(1), 109–126.
- Huynen M A, Snel B, and Bork P (2001). Inversions and the dynamics of eukaryotic gene order. *Trends Genet* 17, 304–306.
- Kresse A U, Dinesh S D, Larbig K, and Römling U (2003). Impact of large chromosomal inversions on the adaptation and evolution of *Pseudomonas aeruginosa* chronically colonizing cystic fibrosis lungs. *Mol Microbiol* 47(1), 145–158.
- Li J W, Li J, Wang J, Li C, and Zhang J R (2019). Molecular Mechanisms of hsdS Inversions in the cod Locus of *Streptococcus pneumoniae*. *J Bacteriol* 201.
- Louarn J M, Bouche J P, Legendre F, Louarn J, and Patte J (1985). Characterization and properties of very large inversions of the *E. coli* chromosome along the origin-to-terminus axis. *Mol Gen Genet* MGG 201(3), 467–476.
- Naseeb S, Carter Z, Minnis D, Donaldson I, Zeef L, and Delneri D (2016). Widespread impact of chromosomal inversions on gene expression uncovers robustness via phenotypic buffering. *Mol Biol Evol* 33(7), 1679–1696.
- Raeseide C, Gaffé J, Deatherage D E, Tenaillon O, Briska M, Ptashkin R N, Cruveiller S, Médigue C, Lenski R E, and Barrick J E (2014). Large chromosomal rearrangements during a long-term evolution experiment with *Escherichia coli*. *MBio* 5(5), e01377–14.
- Rocha E P C (2004). Order and disorder in bacterial genomes. *Curr Opin Microbiol* 7(5), 519–527.
- Segall A, Mahan M J, and Roth J R (1988). Rearrangement of the bacterial chromosome: forbidden inversions. *Science* 241(4871), 1314–1318.
- Sekulovic O, Garrett E M, Bourgeois J, Tamayo R, Shen A, and Camilli A (2018). Genome-wide detection of conservative site-specific recombination in bacteria. *PLoS Genet* 14(4), e1007332.

- Sun S, Ke R, Hughes D, Nilsson M, and Andersson D I (2012). Genome-wide detection of spontaneous chromosomal rearrangements in bacteria. *PloS one* 7(8), e42639.
- Zieg J, Hilmen M, and Simon M (1978). Regulation of gene expression by site-specific inversion. *Cell* 15(1), 237–244.