**A Dynamic *E. coli* Genome Architecture Uncovered by Monitoring Mu Transposition**

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**Abstract**

The problem of compacting genomes while still performing cellular processes is common to all life forms. The current view for *E. coli* is a compacted genome with well-organized domains where replication initiates and terminates. Some studies have suggested that these and other regions are sequestered or compartmentalized such that there is little to no interaction between them. In this work, we have exploited the high efficiency and promiscuity of phage Mu transposition to directly measure the *in vivo* rates of interactions between genomic loci, and have developed new tools for analyzing the proximity of loci across the genome. We observe widespread contacts between all regions of the *E. coli* chromosome, revealing a dynamic, effectively un-compartmentalized genome. We detect long-range interactions between several genes in different gene families such as *dna* and *rrna*, implicating spatial proximity of many distantly co-regulated genes for the first time in a prokaryote. We also see a higher interaction between the two halves of the chromosome during replication, consistent with the deduced proximity and higher mobility of the chromosomal arms as they segregate during replication. Our work advances a new view of genome organization in *E. coli*.