Bioinformatics and Systems Biology: The *E.coli* Network of Transcriptional Regulation

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We are currenlty witnessing an explosion in mathematical studies of real networks. This explosion is part of what is currently called "systems biology" and complex systems. Our laboratory maintains the major international curation effort on transcriptional regulation, operon organization and expression of genes under different conditions in *Escherichia coli*. This literature compilation is reflected both in RegulonDB and EcoCyc, and is the basis for a collection of computational analyses and construction of prediction tools for promoters, regulatory sites, operons and microarray consistency analyses performed in our laboratory.

I will summarize the comparison between RegulonDB knowledge and microarray experiments (Gutiérrez-Ríos et al., 2003; *Genome Res.*). The observed consistency between experiments   and theoretical ratios is clearly higher than the one expected by chance, given the connectivity of the network and a set of complex interaction rules. Emerging general rules of the patterns of expression of E.coli will be presented. Furthermore, we have identified a set of converging criteria to define global regulators.

This work will show the use of bioinformatic more classic tools and methods, with those more theoretical on network analyses. The best known property of a network is its connectivity, that is, the number of regulated genes governed by each regulatory gene or protein.   It is known since the work by Michael Savageau, that the connectivity of the regulatory network in *E.coli* follows a power-law distribution. Additionally, Uri Alon has identified over-represented motifs when compared with a random network of similar connectivity. These motifs (bi-fan, feedfoward) with few genes, together with the organization of genes into transcription units, operons, and regulons, conform the essential building blocks of the topology of the network, and of its dynamics and local interactions. At a higher level of description, we searched two metrics to define modules, which were found to group genes that participate in similar physiological functions. The interconnectivity among these gene groups will be analyzed.