Role of noise in gene expression in the multiple antibiotic resistance (*mar*) network of *Escherichia coli*

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Resistance to antibiotics has become a major public-health problem in the last three decades. Bacteria can become resistant to antibiotics via inherited genetic changes or through transient non-genetic mechanisms. Transient mechanisms allow cells to temporarily increase their tolerance of antimicrobial agents by inducing expression of resistance genes without requiring those genes to be expressed all the time. These strategies increase efficiency by requiring the induction of resources only when they are necessary. In cases where the tolerance mechanism is burdensome (slowing growth or utilizing resources), the population can rely on phenotypic variability or "noise" in gene expression to relegate the task to a small subset of the population; this allows for near optimal growth under non-stressed conditions and survival in the presence of antibiotics. While resistance due to inherited genetic changes has been extensively studied, transient resistance has been challenging to study with traditional methods due to its asynchronous and temporary nature. In some circumstances transient resistance can extend antibiotic treatment times and in cases it can cause the treatment to fail.

We focus on a specific multidrug resistance pathway, the multiple antibiotic resistance (*mar*) network of *Escherichia coli* that regulates more than 60 genes, many of which are implicated in resistance to antibiotics. We are interested in understanding the role of phenotypic variability in this system and hypothesize that the noise properties of the network are due to a set of nested feedback loops that control the expression of the *mar* operon. Our initial experiments quantify noise in the *mar* network using flow cytometry to obtain single-cell resolution measurements and explore the implications that different levels of *mar* expression have in resistance to antibiotics.