



## Biomedical Engineering Department Seminar

**Friday, October 19, 2007**

**Location: Cullimore Hall, Lecture Hall 3**

**Time: 11:30 AM – 12:30 PM**

### **Large Scale Cell-to-cell Variations in Gene Expression**

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Biologists usually grind up a tissue, extract its RNA and obtain its gene expression profile. These profiles represent the average number of mRNA molecules present in each cell. We have found that the numbers of mRNA molecules expressed by different cells of an identical genotype are so different from each other that very few cells correspond to the reported averages. Using an in situ hybridization procedure that has a single molecule resolution we were able to explicitly count the number of molecules of specific mRNAs produced in each cell in a population of cells. We found evidence for large-scale cell-to-cell variations. Akin to the gene expression "noise" previously reported in the prokaryotes and yeast, these variations stem from the nature of transcription in higher eukaryotes, which our results indicate, occurs in bursts. Randomness in the onset and dissipation of these bursts of mRNA synthesis, in combination with the short life-time of mRNA, results in these variations. The bursts of mRNA synthesis in different genes occur independently of each other. The origins of this stochastic mRNA synthesis may lie with the unique mechanisms that open up chromatin context of the gene and render it conducive for mRNA synthesis and later sequester the gene to turn off the synthesis.

If the magnitude of the observed variations is so large then how are cells able to maintain their relatively constant phenotypes? Part of the answer is that proteins generally stay around in the cell longer than the mRNAs do. The preexisting pools of proteins receive periodic inputs from the transient bursts of mRNA production. Since the size of the protein pools is relatively large it is buffered against the variations in mRNA levels. Thus the levels of proteins vary less than the levels of mRNAs between cells. However, the life-times of proteins vary a lot and the levels of short-lived proteins must be determined by the variations in the levels of their respective mRNAs. To cope with such variations organisms may have developed other yet unidentified mechanisms. In some situations these variations will even be beneficial, as they will serve as an extragenetic substrate for adaptation to the transient variations in the environment.

**Refreshments will be served.**