Artificial gene transfer and the Dynamics of Gene Expression

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Abstract:

The transfer of foreign DNA into eucaryotic cells requires artificial vectors as physical carriers. Such nanoparticles are subject to general transport phenomena in soft matter, such as diffusion in polymer networks, particle membrane interaction and directed transport towards the nucleus using microtubular trackage. Using enhanced green fluorescence protein (EGFP) as a reporter, gene expression in a large number of individual cells in culture was monitored by semi-automated time-lapse fluorescence microscopy. The time courses are described by a linear gene expression model that includes the maturation kinetic of EGFP into its fluorescent state. The analysis captures the stochasticity in the gene expression kinetics within a cell culture populations. The distributions of expression onset times, expression rates at half maximum intensity, and steady state EGFP fluorescence intensities were determined for two synthetic gene delivery systems, linear polyethyleneimine (PEI) and lipofectamine. It is proposed that the variance in single cell GFP expression reflects the distribution of size of the DNA delivery complexes along with a Poisson like distribution of nuclear entry events. The statistical analysis of single cell gene delivery indicate that gene transfer - although dependent on many factors - bears generic features of a stochastic birth process.