494a A Mathematical Programming Network Model for Gene Pathway Analysis

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The human genome project was completed in the year 2003; however there are still many genes in the genome whose functions are not known. A method for identifying the possible functions of these uncharacterized genes is by comparing their expression patterns (for example through DNA microarray technology) with known genes. DNA microarray technology has the ability to measure the expression levels of thousands of genes in a single experiment. In addition to gene function, for a known bio-molecular system it is interesting to investigate the possible effects of perturbing various components, which define the cellular mechanism. This leads to many potential applications in medicine and molecular biology especially in the identification of metabolic pathways, complex genetic diseases, drug discovery and toxicology analysis. In this work we propose a procedure for predicting gene expression from a single microarray experiment using a network model that takes into account the inherent reaction engineering and time delay factor. Next we embed the network model in a linear programming framework in order to simulate a genetic network. This helps in correctly identifying the group of genes that effect each other's expression and regulate genetic pathways. We note that most network models (Spellman, 1998; Akutsu, et al., 2000; Dasika et al., 2004, D'haeseleer, 2000; D'haeseleer, 1999, Marnellos and Mjolsness, 1998; Marnellos et al. 2000) provide insights to the regulatory and other biological behavior but they do not take into account the inherent reaction engineering and time delay factor. The proposed linear programming model employs a clustering algorithm (Garg et al., 2002). The idea is primarily based on a modified form of the Boolean network and Pearson's correlation. The pair wise correlation obtained for the set of gene clusters yields the initial set of connection strength (weight matrix) among the clusters. The complete model contains linear ordinary differential equations, which represent the kinetics. We investigated the differentiation of gene expression of early bone cell using data from the University of Connecticut Medical School. The study investigated the time evolution of gene and preliminary results show that the experimental results from the network model compare very well with the data obtained from microarray analysis. From the preliminary results, we have shown and expect that this model would be appropriate in situations where either there is a paucity of experimental data or experiments cannot be performed.

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