Function-based discovery of characteristic temporal expression profiles in endothelial cells stimulated with insulin

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A main objective of microarray studies is the evaluation of gene interactions from high-throughput time-series expression data. To this purpose, it is important to detect the main temporal patterns characterizing the data, and associate them with information on gene function and topological architecture of biological networks.
We recently developed a method (Di Camillo et al., 2007) that searches the main temporal patterns in sets of biologically relevant genes, such as genes annotated with the same Gene Ontology (GO) term, chromosomal location or transcription factor binding motifs. In particular, a computational framework has been developed which allows associating the main temporal patterns with every kind of annotation, possibly organized as a hierarchical data structure. The output of the method is a list of functional groups; each group is characterized by a set of characteristics temporal patterns.
The method has been applied to study insulin regulation in endothelial cells, in order to identify transcripts and dynamic expression profiles characterizing insulin action. The experimental protocol has been designed to distinguish insulin effect from other processes, which take place simultaneously in cells by monitoring both insulin-treated and control cultures. A first gene selection procedure, based on a confidence threshold that controls false discovery rate, has been employed in order to identify statistically significant changes in gene expression. Many functional groups associated with dynamic patterns are highly correlated with a-priori knowledge on endothelial cells physiological response, such as ”positive regulation of angiogenesis”, ”elevation of cytosolic calcium ion concentration”, ”activation of MAPK activity”. These profiles can be used to reverse engineer the network of interactions between genes belonging to the same GO or to analyze temporal relationships between different GO terms.