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Detection of developmental stages from DNA microarray time series and robust modeling of gene expression evolution in *Drosophila*

Rooman Marianne

Université Libre de Bruxelles, Belgium

We analyze available DNA microarray time series that monitor gene expression along the developmental stages of multicellular eukaryotes or in unicellular organisms subject to external perturbations. Using a translation- and scale-invariant distance measure corresponding to least-rectangle regression to compare the gene expression profiles, we show that peaks in the average distance values are noticeable and are localized around specific time points. These points systematically coincide with the transition points between developmental phases or just follow perturbations. This approach can thus be used to identify automatically, from microarray time series alone, the presence of external perturbations or the transition between developmental stages in arbitrary cell systems. Moreover, our results show the existence of a striking similarity between the gene expression responses to these *a priori* very different phenomena. Based on these findings, we set up an adapted clustering method that uses the abovementioned distance measure and classifies the genes on the basis of their expression profiles within each developmental stage or between perturbation phases. This method was applied to the development of *Drosophila*. Average profiles representing each cluster were computed and their time evolution was analyzed using coupled linear and non-linear differential equations. Different model structures and parameter identification and reduction schemes were tested. The models so obtained were compared on the basis of their abilities to reproduce the data, to keep realistic gene expression levels when extrapolated in time, to show the biologically expected robustness with respect to parameter variations, and to contain as few parameters as possible. A family of non-linear models, constructed from the exponential of linear combinations of expression levels, reached all the objectives. It defined networks with a mean number of connections equal to two, when restricted to the embryonic time series, and equal to five for the full time series.

Biography

Marianne Rooman has completed her Ph.D in theoretical physics in 1984 and defended a thesis in structural bioinformatics in 1996 at the Université Libre de Bruxelles (Belgium). She is Research Director at the Belgian Fund for Scientific Research. She has published more than 80 papers in reputed journals in theoretical physics, structural bioinformatics and, more recently, in systems biology.