FAST MOVING FRONTS - 2009

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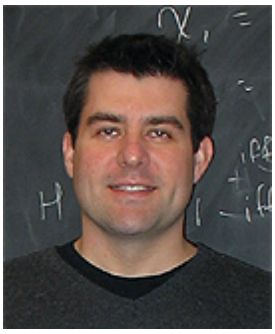
John D. Storey talks with *ScienceWatch.com* and answers a few questions about this month's Fast Moving Front in the field of Multidisciplinary.



Article: Significance analysis of time course microarray experiments
Authors: Storey, JD;Xiao, WZ;Leek, JT;Tompkins, RG;Davis, RW
Journal: PROC NAT ACAD SCI USA, 102 (36): 12837-12842 SEP 6 2005
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SW: Why do you think your paper is highly cited? Does it describe a new discovery, methodology, or synthesis of knowledge?

This paper provides a statistical approach for analyzing gene expression studies carried out over a time course. Gene expression is essentially a dynamic process, so characterizing gene expression variation over time is of fundamental importance. Besides the high interest in this question, the fact that the statistical approach can be applied to data through my lab's EDGE software package has probably contributed to the number of citations. The article represents a new set of statistical methodologies.

SW: Would you summarize the significance of your paper in layman's terms?

The article provides a set of methodologies to analyze the main types of study designs and statistical questions that one might ask in a time course gene expression study, where the levels at which genes are turned on are measured over a period of time.

The article provides a method that allows one to detect genes whose expression shows any change over time. For example, as a proof of concept in the paper, we identified genes whose expression changes in the human kidney as one ages.

It also provides a method to detect genes whose expression as it changes over time are different between two or more groups. In the paper, we identified genes whose expression changes over a 24-hour period in human blood were different between a group treated with endotoxin versus a control group.

SW: How did you become involved in this research and were any particular problems encountered along the way?

I initially became interested in this research because the decreasing cost of

microarrays was allowing researchers to make genome-wide measurements of gene expression levels on many more samples in a given study.

It was clear that this would lead to gene expression being measured over time rather than in "static" conditions where the passage of time is ignored. A statistical approach for this type of study would certainly be needed. The project took off when I joined a large-scale NIH project called "Inflammation and the Host Response to Injury," which is led by Dr. Ronald Tompkins of Massachusetts General Hospital.

This project involves measuring gene expression over the course of treatment for individuals who have been subjected to blunt force trauma, such as from an automobile accident. In collaboration with the Ron Davis lab of Stanford University, also participating in this NIH project, we began to develop the statistical approach.

The main challenge of this research was to provide a single framework that is applicable to the many different types of study designs and questions which might be considered. We also had to make the methods understandable to researchers across a wide range of areas of expertise.

"Specific to this paper, we have developed improved algorithms for carrying out the analysis of time-course gene expression studies."

SW: Where do you see your research leading in the future?

My research is aimed at developing and applying quantitative approaches in genomics to contribute to an understanding of the molecular biology of the cell and the causes of human disease.

As new genomics technologies continue to emerge and the costs of existing technologies decrease, we are faced with more and more data of an increasing complexity. My current and future research involves integrating multiple types of genomic data beyond the gene expression levels considered in the paper. These multiple data types may be measured at different points in time, in different conditions, and in different tissue types.

Specific to this paper, we have developed improved algorithms for carrying out the analysis of time-course gene expression studies. This includes speeding up the calculations as well as increasing the statistical power of the calculations by adapting our "optimal discovery procedure" approach to the time-course setting.

These new developments will be included in a forthcoming release of our EDGE software package. We have also applied these methodologies in the large-scale NIH project mentioned above, and we have made much progress in understanding how early gene expression changes relate to recovery from trauma.

SW: Do you foresee any social or political implications for your research?

No, this doesn't seem likely.

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PDF

back to top

2009 : November 2009 - Fast Moving Fronts : John D. Storey on Time Course Microarray Experiments

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