

# Chain-reaction, a model of gene expression dynamics

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One of the fundamental studies of transcription response to stimuli is to model the activation, repression of hundreds of genes, and their regulations. To further complicate the scenario, genes are regulated by multiple transcription factors, operating through different modes (earlier activation or secondary response). Thus, to fully understand the transcription response, a static analysis indicating which genes are induced at one given time point is not sufficient. Therefore, it is crucial to analyze the transcriptional dynamics in a systemic manner.

One of the common approaches to study transcription dynamics is to collect measurement of gene expression in a predefined time points following a treatment. In this issue of *Translational Cancer Research*, the paper by Cheng, *et al.* presents a close examination of gene-nutrient interaction, specifically in the form of estrogen synthesis pathway, an important pathway for converting substrate cholesterol to the progestogens, androgens, and estrogens. While understanding the mechanisms of estrogen-stimulated proliferation, for example, may provide a route to design estrogen-independent therapies that would be effective in cancer patients, the paper (1) presented in this issue, instead, puts the pathway under the microscope by studying the response of genes within the estrogen synthesis pathway after treated cells with various dietary supplement polyphenols (EGCG, genistein, and resveratrol) during puberty. In this paper, these antioxidants diet supplements showed altered gene expression in the estrogen synthesis pathway.

Different from other time-course data analysis methods, such as traditional clustering algorithms (2,3), Fourier Transform methods (4), pre-selected temporal profiles (5-7), impulse-response models (8,9), and regression (10-12), ordinary differential equations (13-15), Cheng, *et al.* proposed an interesting alternative to study the change during the time-

course by simulating the estrogen synthesis pathway as a chain reaction model, where genes are treated as a set of chemical species and changes are modeled as a conversion process through a reaction channel, or a chain reaction model (1). A set of ordinary differential equations were employed to represent reaction channels, and the reaction rates derived from these differential equations are used to describe interactions between genes in the pathway. The paper also presented a mathematical solution to address the issue of numerical error, stability and accuracy. The analytic results of the chain-reaction model demonstrated the capability of predicting gene expression changes and the effect of nutrient-containing diets on gene expression changes in the pathway.

Pathway modeling and inference is still a developing research area since the inception of microarray technology in 1995 (16), mostly because current gene expression data is inadequate for most types of cell dynamic studies. In addition, most inference methods apply to the simplest models (such as Boolean networks), and even in those overly simplified model in biology, the algorithms quickly become computationally intractable. While better data integration and inference algorithms may bring the quantitative and predictive analyses to a testable stage, we expect a chain of actions in cell dynamics modeling in the era of single cell genomics (17-19).

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