Bayesian inference of gene regulatory networks from factorial time-course experiments with applications to bone fracture healing

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Abstract

Bone fracture healing recapitulates many aspects of embryonic skeletal development. Besides age, metabolic conditions, and the presence of pharmacological agents, gender and genetic predisposition may affect the cellular environment and skeletal repair processes. Also, the fracture repair process takes place in stages over a long period of time with different networks of genes involved at different times. To improve the quality and speed of the repair process, it is important to understand how the genes involved behave under critical experimental conditions and longitudinally over time. As experimental designs become more complex such as in factorial time-course microarray studies, it becomes more challenging to answer questions of interest, such as how two experimental factors interact in their effects on gene expression over time. One may want to detect possible interactions between an experimental treatment and another factor while concurrently grouping genes showing similar effects into clusters. Only a few existing methods are able to simultaneously infer differential expression and take gene clustering into account. Motivated by the need to fully model a factorial time-course gene expression experiment, we propose a novel Bayesian statistical approach that can simultaneously estimate the longitudinal model signals under a factorial design and assign genes into biologically meaningful clusters, using fast hybrid MCMC algorithms. A unique feature of our framework is that all information about gene expression can be interpreted at all three levels– longitudinal, factorial, and transcriptional.