Oscillating gene expression from delayed effects in gene regulatory networks

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Oscillations in gene expression stem from two often ignored facts: feedback loops and delayed effects in gene networks. Most gene networks incorporate feedback loops and are almost never acyclic tree-like structures. But most network inference algorithms assume the acyclic property or perform badly in the presence of these feedback loops. Additionally, effects are delayed because of cellular processes that are not happening instantly, that is transport, translation, modification and transcription of involved molecules. Together, delayed effects and feedback loops can give rise to stable oscillations in gene networks, one prominent example being the circadian gene network. A system of delayed differential equations (DDEs) is the best way to approach this kind of network. Two different approaches were used to infer the underlying network structure while a particle swarm optimization finds suitable parameter configurations for the real parameters of the DDE systems. The network structure was either coded with binary values as a whole and evolved with a genetic algorithm or each gene's parental candidates were evaluated separately and combined in a combinatorical procedure. In either case the parameters of the DDEs were found with particle swarm optimization. Given time series data of gene expression, these procedures find candidates for network models that enable oscillations.