999-92-36 **Samuel Bernard**, **Branka Čajavec**, **Laurent Pujo-Menjouet**, **Hanspeter Herzel** and **Michael C. Mackey***, Department of Physiology, 3655 Drummond, Room 1124, Montreal, Quebec H4X 2C1, Canada. *Modeling transcriptional feedback loops: The role of Gro/TLE1 in Hes1 oscillations.* Preliminary report.

The transcriptional repressor Hes1 periodically changes its expression in the presomitic mesoderm. Drosophila Groucho (Gro) and its vertebrate counterpart, the transducine-like enhancer of split/Groucho-related gene product 1 (TLE1) protein, is a corepressor required by a number of transcriptional repressors, including Hes1. We propose three models for the regulation of observed Hes1 oscillatory expression, and search for common parameter value requirements. We introduce a model for Hes1 oscillatory expression that includes regulation of Hes1 transcription by Gro/TLE1. From detailed linear stability analysis, numerical bifurcation analysis and simulations, we conclude that the cooperativity coefficient (h) for Hes1 self-repression should be large (i.e., $h \geq 4$). The characteristic turnaround duration of the repression loop is between 40 min and 60 min. Depending on the model, explicit delays range from 10 to 40 min. Models of direct repression via Hes1 typically show an expression overshoot after transcription initiation in contrast to experimental data. Numerical simulation and theoretical predictions show that the cofactor Gro/TLE1 reduces the overshoot and is thus necessary for a rapid and finely tuned response of Hes1 to activation signals. (Received July 19, 2004)

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