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Promoter methylation in a mixed feedback loop circadian clock model

The circadian (about a day) clock strikes a balance between robust intrinsic rhythmicity and plasticity to environmental cues. At a cellular level, interconnected transcription-translation feedback loops produce reliable limit cycle oscillations in core clock proteins. Although there has been extensive mathematical modelling, important questions remain about the effects of environmental signals on the molecular circadian clock. For instance, recent experiments suggest that epigenetic factors play a role in stably altering the circadian period. Briefly, epigenetic factors encompass a variety of molecular modifications that convey heritable information without altering the DNA sequence. In this poster, we present and analyze a novel, minimal model of the circadian clock. By including an additional degree of freedom in the classical mixed feedback loop model of Francois and Hakim, we analyze how epigenetic regulation alters the dynamics of the clock. We obtain conditions for equilibrium uniqueness and an asymptotic approximation to the clock's period, which allow us to bound the influence of epigenetic factors in our model. We then use another set of approximations to connect our model to a modified version of the Goodwin oscillator, previously studied in this context by Kim and Forger. Analysis of this reduced model reveals that although epigenetic factors can alter the period, they may also result in a loss in rhythmicity. Our analysis adds a quantitative perspective to an active area of biological research and offers several avenues for future work.