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# For discrete-event architectures, modelling the cell cycle

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## Abstract

**The Computational modelling and the theory of nonlinear dynamical systems enable researchers to not only describe but also explain the events of the cell cycle, just like the theory of gravitation enables researchers to understand why cannonballs fly in parabolic arcs. The simplest forms of the eukaryotic cell cycle function as self-contained oscillators. The basic notion of oscillatory biochemical circuits is presented in this paper in the context of the Xenopus embryonic cell cycle. Boolean models, delay differential equation models, and, in particular, ordinary differential equation (ODE) models are investigated. We look at what it takes to produce oscillations out of two simple types of circuits using ODE models (negative feedback loops and coupled positive and negative feedback loops).**

***Keywords: Computational modeling; Xenopus embryonic cell cycle; Chemical method***

## Introduction

The cell cycle in many eukaryotic cells is a series of dependent events. A new cell must first grow to a certain size before it can be used. Before it can start replicating DNA. The cell must then finish DNA replication before moving on to mitosis. Last but not least, the cell before it can finish mitosis and restart the cycle, it must correctly organise a metaphase spindle. If a cell grows, DNA is produced when replication, or spindle assembly, slows, the cell cycle as a whole slows down. Although many biological processes appear to be nearly unfathomably intricate and incomprehensible, oscillators and clocks are the types of processes that we may have a fair chance of not only describing, but also comprehending. As a result, substantial work has gone into figuring out how simple cell cycles function in model organisms like Xenopus embryos and the fungus S. pombe and S. cerevisiae. This necessitates the discovery of the proteins and genes required for the embryonic cell cycle, as well as the understanding of the regulatory processes that link these proteins and genes. Huge strides have been achieved toward these goals during the last three decades. In each scenario, a protein circuit based on the cyclin-dependent protein kinase CDK1 and the anaphase-promoting complex drives the cell cycle

(APC). The activation of CDK1 causes the cell to enter mitosis, whereas the activation of APC, which is often delayed in comparison to CDK1, causes the cell to exit. However, a complete explanation of why the CDK1/APC system oscillates involves more than a description of components and connections; it necessitates a comprehension of why any regulatory circuit would oscillate rather than just settle into a stable steady state. What types of biochemical circuits can oscillate, and what are the requirements for particular circuit components to allow oscillations? The theory of nonlinear dynamics and computational modelling can yield such insights.

## Conclusion

A protein circuit that operates like an autonomous oscillator drives the Xenopus embryonic cell cycle. In this Primer, we'll look at how a protein circuit can cause oscillations. We looked at Boolean models, ordinary differential equation models, and delay differential equation models for simple oscillator circuits based on the CDK1/APC system. The discrete nature of Boolean models and the time lags imposed into delay differential equation models make it very easy to construct oscillations. Cell 144, March 18, 2011 a2011 Elsevier Inc. 883 Maintaining the model from settling into a stable steady state is more difficult with ODE models. Longer negative feedback loops are simpler to start oscillating than shorter ones, assuming all other factors are equal, and switch-like, ultrasensitive response functions inside the negative feedback loop also enhance oscillations.

When a negative feedback loop is combined with a positive feedback loop, oscillations are more likely to occur, and oscillators with this bistable trigger have unique properties that may make them particularly ideal for biological systems. Why does one ODE model oscillate while another does not is the subject of linear stability analysis. As a result, we've provided various stability analysis examples for simple oscillator circuits. Linear stability analysis is straightforward for one-ODE systems. However, when dealing with two or more ODEs, one must utilise matrix algebra techniques to calculate the system's eigenvalues at steady state (s). This requires some work, but it is worthwhile since it allows us to understand why a circuit oscillates or does not oscillate. The cell cycle in many eukaryotic cells is controlled by a CDK1/ APC circuit that acts more like a series of decisions or contingent events than an autonomous oscillator. Nonetheless, simple Xenopus oscillator models, such as the ones reviewed here, provide information that aids in the comprehension of more sophisticated cell-cycle circuits. Positive feedback loops can be used to produce a series of reliable switches, just like they can add resilience to an oscillator circuit. The link between clock-like cell cycles (like the Xenopus embryonic cycle) and domino-like cell cycles (like the somatic cell cycle) is likely due to the fact that they are both made up of bistable switches.

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