Review of eukaryotic cell cycle (see any molecular biology textbook)
Cell cycle phases: G₁, S, G₂, and M; first three comprise interphase.
Checkpoints: G₁ checkpoint, G₂ checkpoint, metaphase arrest.
Cell cycle control is based on Cdns and cyclins; complexed together they form “start
kinase” or M-phase promoting factor, which is MPF.
In Xenopus (frog) life cycle, oocyte stops at metaphase arrest until fertilization, then
rapidly divides without growth many times during early embryo stage, then
transitions to growth-limited cell divisions.
During the early embryo stage, cyclin rises throughout interphase as MPF levels are
low, then MPF spikes briefly, cyclin drops, and cell enters mitosis. Cycle repeats.

Tyson’s 1991 cell cycle model
This was the first cell cycle model that was pretty good.

\[
\text{cdc2} = \text{cyclin-dependent kinase, aa = amino acids.}
\]

This model includes core cdc2-cyclin interactions. It ignores lots of things, including:
cdc2 activation by phosphorylation, likely targeting of cyclin for degradation by
ubiquitin rather than phosphate as shown here, MPF enhancement of cyclin
degradation, effects of wee1 and cdc25, and downstream effects. Additional
assumptions include: total concentration of cdc2 is fixed and phosphorylation in
reaction 3 is much faster than dimerization.
Parameters include: initial concentrations (not given in Tyson’s paper) and reaction
rate constants. Several methods allowed simplification of rate constants,
including: several values could be set to either 0 or “very large” without further
details, some collections of unknowns could be grouped together to create single
unknowns, and some parameters were varied during model exploration.
Mass action kinetics were used to convert the model reactions to differential
equations. The sole exception was that reaction 4 required a special rate equation
to represent positive feedback.
Because of positive feedback, MPF levels rise slowly at first, and then rise faster and faster. MPF growth stops when inactive MPF (P-cdc2-cyclin-P) runs out.

Considering only reactions 4 and 5, the system is at a fixed point if active MPF production (reaction 4) is at the same rate as active MPF loss (reaction 5).

Positive feedback can cause bistability. If MPF production is faster than MPF loss, then MPF increases, and vice versa. Looking at the rates of production and loss (figure, below), the system naturally tends towards either of the two stable fixed points (filled dots) and away from an unstable fixed point (open circle).

Simulating a model
Tools include: Excel, MatLab, Mathematica, Copasi, SBW, and many others. Helpful databases include: Cell cycle database and BioModels. SBML is a widely supported computer readable language for describing cell models.

Results of Tyson’s model
By varying $k_4$ and $k_6$, it can represent all three phases of Xenopus development, including metaphase arrest, rapid early embryo oscillations, and excitable oscillations that may represent growth-limited cell cycles. Time-dependent MPF and cyclin levels agree qualitatively with experiment. Model leaves many open questions, such as roles of wee1 and cdc25, exact nature of reaction 4 positive feedback, and mechanisms for growth-limited cell cycling.

A deeper understanding of the cell cycle
The core cell cycle system is technically a “substrate-depletion” oscillator, as discussed in Tyson et al. Current Opinions in Cell Biology 15:221, 2003. This combines substrate (cyclin) supply and depletion with a positive feedback that causes substrate to be depleted in bursts.

The core cell cycle dynamics are identical to those of a “rocking water fountain.” Water represents cyclin and the rocker state represents the cdc2 state, as shown with the diagrams below. The fountain can exhibit all of the same dynamics.