# A Study of Cell Cycle Control Modeling in Eukaryotic Cell

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## 1 Purpose

Cell behavior is governed by thousands of biochemical interaction of genes and proteins. While the each molecular interaction has fairly simple mechanism, networks of the biochemical interactions regulate cell activities precisely. One of such biochemical interactions is a cell cycle, which is a reproduction by duplicating their contents and dividing themselves in two. We focus on the cell cycle, because the cell cycle is the fundamental means by which all living things are propagated. The cell cycle is caused by some protein synthesis, coupled with intermittent proteolysis. In this paper, We try to describe mathematical forms as an intracellular molecular event, and depict cell cycle control with differential equations and simulate this molecular event.

## 2 Background

The Cell division results in the production of two daughter cells containing identical genetic complements. Achieving this requires a carefully orchestrated series of nuclear and cytoplasmic events leading to the accurate replication and segregation of the chromosomes. In unicellular species, such as bacteria and yeast, each cell division produces an additional

organism. In multicellular species many rounds of cell division are required to make a new individual, and cell division is also needed in the adult body, to replace cells that are lost by wear and tear or by programmed cell death. Thus an adult human must manufacture millions of new cells each second simply to maintain, and if all cell division is halted – for example, by a large dose of ionizing radiation – the individual will die within a few days.

A powerful combination of molecular genetics, cell biology, and biochemistry has led to the isolation of key structural, enzymatic, and regulatory components governing these events. One of the most gratifying aspects of this research has been the realization that many of these components are highly conserved throughout the phyla. Therefore much of the knowledge learned from one system will probably applied to others.

The detail of the cell cycle may vary, but certain required are universal. First and foremost, to produce a pair of genetically identical daughter cells, the DNA must be faithfully replicated, and the replicated chromosomes must be segregated into two separate cells. The cell cycle comprises, at a minimum, the set of processes that a cell must perform to accomplish these tasks. The vast majority of cells also double their mass and duplicates all their cytoplasmic organelles in each cell cycle. Thus a complex set of cytoplasmic and nuclear processes have to be coordinated with one another during the cell cycle.

The major transitions in the cell cycle are driven by the successive activation of a family of cyclin-dependent kinase (CDKs). The CDKs are structurally related and their activity requires a physical association with cyclin. Regulation of CDK activity occurs through post-translational modifications and through associations with a conserved family of activating cyclins and a family of CDK inhibitors. Entry into mitosis occurs through the activation of a universal mitotic CDK. Activation occurs in a stepwise fashion: first by its association with cyclin and then through the progressive alteration of the phosphorylation states of key residues. The activated mitotic CDK initiates a diverse array of cytoplasmic and nuclear events driving the cell into mitosis. The mitotic CDK also activates the anaphase-promoting complex, a ubiquitin ligase responsible for the degradation of cyclin and other inhibitors of anaphase. This allows the cell to progress through anaphase, forming two daughter cells. Now, the trend of cell cycle studies has two directions, tumor suppressor gene and ubiquitin-proteasome system.

Uncontrolled cell proliferation is the hallmark of cancer, and tumor cells have typically acquired damage to genes that directly regulate their cell cycles. Genetic alterations affecting p16 (INK4a), CDK inhibitor, and cyclin D1, proteins that govern phosphorylation of the retinoblastoma protein (RB) and control exit from the pre DNA synthesis phase of the cell cycle, are so frequent in human cancers that inactivation of this pathway may well be

necessary for tumor development. Like the tumor suppressor protein p53, components of this "RB pathway," although not essential for the cell cycle, may participate in checkpoint functions that regulate homeostatic tissue renewal throughout life.
(retinoblastoma: an inherited predisposition to a rare cancer that occurs in the eyes of children)

Ubiquitin is a small and covalent modifier that forms a poly-ubiquitin chain on protein, which becomes a degradation signal attacked by a cascade reaction involving three enzymes, E1 (ubiquitin-activating enzyme), E2 (ubiquitin-conjugating enzyme) and E3 (ubiquitin-ligating enzyme), acting as a substrate-recognition molecule. A link between Parkinson disease and the ubiquitin system has been suggested in pathological studies and analyses of two gene products, UCHL-1 (ubiquitin carboxyl-terminal hydrolase) and alpha-synuclein, whose mutations cause autosomal dominant familial Parkinson disease. UCHL-1 is thought to produce ubiquitin by both cleaving polymeric ubiquitin and releasing ubiquitin from small adducts such as glutathione and cellular amines. Alpha-synuclein, one of the major components of Lewy bodies, is degraded by the 26S proteasome, indicating that it is modified by ubiquitin, and iths mutation is known to extend the half-life of the protein. And recently, *perkin*, mutations of which cause juvenile parkinsonism, is involved in protein degradation as a ubiquitin-protein ligase collaborating with the ubiquitin-conjugating enzyme.

# 3 Methods and Results

All biochemists are familiar with Michaelis-Menten theory, where a simple mechanism of enzyme catalysis is described by differential equations whose solution gives the time-course of the reaction. We translated the mechanism into rate equations (a set of differential equations - one for each time-dependent chemical concentration) and solved these equations to reveal the expected behavior of the mechanism. In this here, we converted the mechanism of cell division cycle into a set of differential equations describing how the concentrations of the major control variables change with time.

# 4 Discussion

To develop a precise mathematical model of protein interaction, we had made many specific assumptions, some of which were crucial to the model and others inconsequential. In this section, we report the two points of view to accomplish for making the more realistic modeled cell. One of the points is how to construct the mathematical model. And another is

how to deal with experimental raw data.

The process of model building and analysis is not itself an hypothesis subject to falsification, but rather a tool for exploring molecular mechanisms. Constructing the correct mechanism for a complex biochemical control system like the cell cycle is akin to assembling a jigsaw puzzle. We have used the computer as a table to layout all the pieces we know of the start puzzle in eukaryotic cell. Obviously, some pieces are missing and we have had to fill in the gaps with hypothetical interactions. But we believe the basic features of the overall picture are becoming clear. Future work will probably show that we have some of the pieces in upside-down, but, in the meantime, we hope this proposed solution will serve as a serious working hypothesis for cell cycle control in eukaryotic cell.