# Redefining the Search in Scientific Research: Organization through Cell Cycle Diagrams

Rachel King & Dr. Nicholaos Jones
University of Alabama in Huntsville

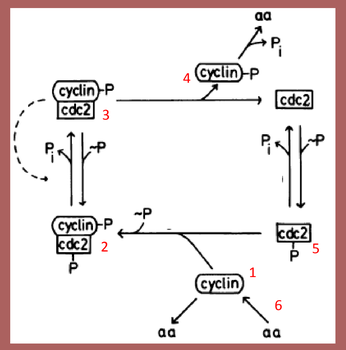
## Abstract

The diagrams of cell cycle modeling offers the scientific community a pictorial representation of developments in scientific knowledge over time. Typically cell cycle diagrams are presented in research documents as a tool to accurately portray the cycle mechanics described by the researcher. While most scientific documents are accessed and categorically organized by publication date and author, a closer analysis of the embedded cell cycle diagrams within these documents offers insight into an organization method that establishes cell cycle relation among the models in those documents. Through the implementation of Imre Lakatos' theory on the reconstruction of scientific history we will attempt to relay how our organization method reveals more dynamic and conclusive interdependent connections, as opposed to existing methods. In doing so, we will attempt to locate cell diagram "hard cores" and identify relations among them that supersede publication dates and citation notes.

## Organization Method

We employ Imre Laktatos' "hard core" concept of scientific reconstruction as the characteristic criterion to distinguish between various cell cycle diagram families. The "hard core" of a theory is the part that is methodologically protected from refutations. In this case, it is the component of a cell cycle diagram that is consistently recapitulated in various subsequent diagrams. We have identified two cores that provide two very distinct "hard cores" of cell cycle diagrams:

## Tyson "Hard Core"



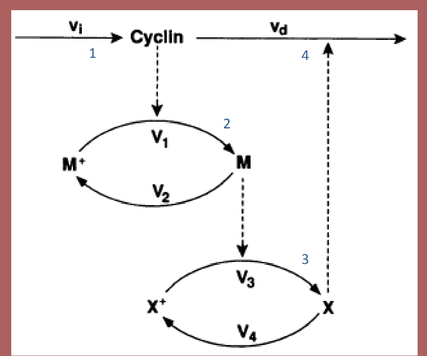

The basic Tyson "hard core" model relays the interactions of cyclin and CDC2 as a type of cell cycle control :

(1) Synthesis of cyclin protein
(2) Cyclin phosphorylation by attachment to CDC2-P
(3) Dephosphorylation of CDC2
(4) Release of phosphorylated cyclin
(5) Rephosphorylation of CDC2
(6) Repetition of cycle

## Goldbeter "Hard Core"

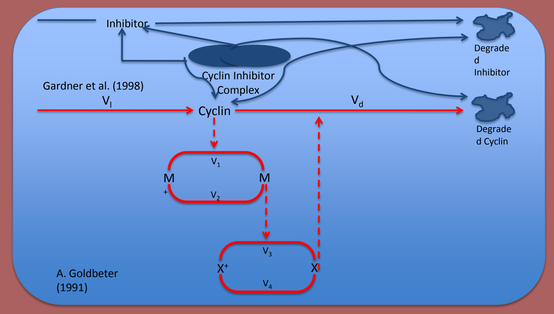
The Goldbeter hard core depicts the cyclin and CDC2 processes of the mitotic cell phase:

(1) Synthesis of cyclin protein
(2) Cyclin triggers inactive M (cdc2) to become active
(3) Active CDC2 triggers protease (X) to activity
(4) Active (X) degrades cyclin

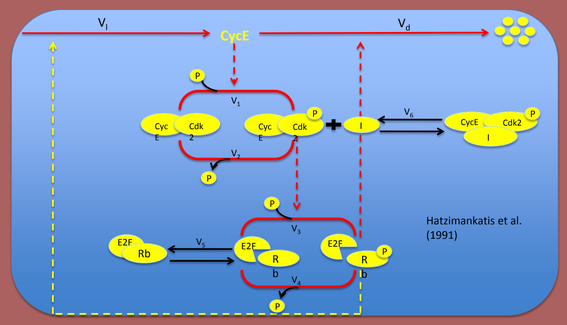



## Results - Auxiliary Tracking

Lakatos describes the auxiliary components of a theory as a "protective belt"; its purpose is to pose any hypotheses or examples of anomalies that may negatively affect the overall program or theory. The auxiliaries are more flexible and resilient than the hard core. Below are illustrations of the Goldbeter group auxiliaries; each picture represents the addition of a cell cycle inhibitor onto the original Goldbeter model.

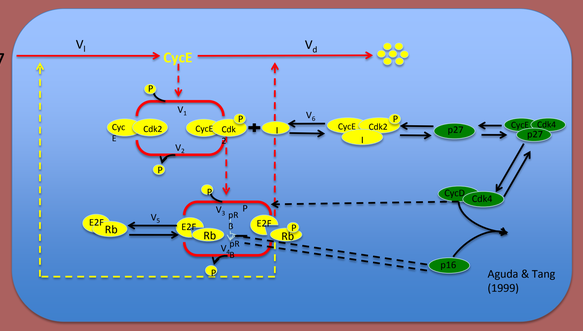



•The Cyclin Inhbitor Complx acts as a reversible binding reaction
•Acts upon "free floating" cyclin
•Inhibits synthesized cyclin from continuing phase processes

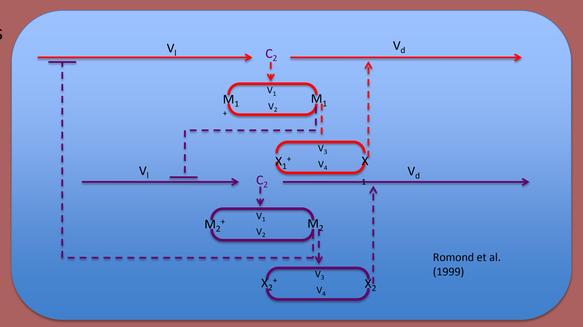



•The Cyclin Inhbitor Complx seen above is transposed to reflect a reversible binding reaction with the CycE and Cdk2 complex
•Inhibition takes place at a later point in the phase
•Free E2F's promote G1/S transition

•The Cyclin-Cdk2 inhibitor is formally identified as p27
•Continuation of above inhibitor complex
•Shows another reversible binding reaction with p27- leading to CycD:Cdk4:p27 inhibitor complex
•Second inhibitor complex directly affects E2F concentration

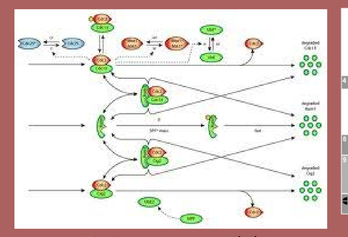



•In this model, Cdk1 ($M_2$) is the inhibitor that affects cyclin synthesis in preceding and subsequent phases
•Suggests inhibitions naturally arise and are naturally controlled
•Balanced inhibitor strength allows for aperiodic oscillations

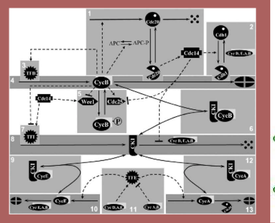



## Significance of Results

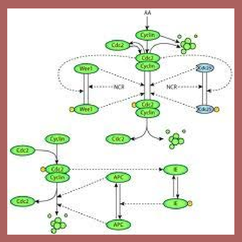
•Formation of cell cycle groups revealed correlations among research papers without citation references
  •Among outlined Goldbeter group only one paper lists Goldbeter as a reference: Gardner, Dolkin, Collins (1998). "A Theory For Controlling cell cycle dynamics using a reversibly binding inhibitor" (1st illustration)
•Diagrams useful for overall group classifications and identification of cores used by same author
•Research papers with shared scientific authors, in-text references and citation references prove not to be directly related following analysis of corresponding cell cycle diagrams
  •Ex. The diagrams below each represent a different cell cycle group under the authorship of Tyson



Fission yeast model



Eukaryotic cell model



Sea Urchin embryo diagram

## Future Applications

Continuation of this research could supply sufficient criterion for distinguishing among various cell cycle diagrams which could lead to the development of online scientific databases with search queries designed to correlate research papers by diagrammatical reference.

## Conclusion

By examining cell cycle diagrams through the lens of Imre Lakatos' "hard core " theory we were able to make connections among seemingly unrelated research papers as well as pin-point divisions among citation related research. The relations we found within the Goldbeter and Tyson "hard core" groups provide a glimpse of the search efficiency and effectiveness of research organization through cell cycle diagrams. Such organization could aide in the productivity of scientific studies and research.

## Selected References

• Hacking, Ian (1981). "Lakatos's Philosophy of Science." Oxford Readings in Philosophy: *Scientific Revolution*
•Salmon et al. (1992). Research Programs and Progress. *Introduction To The Philosophy of Science*. Indianapolis: Hackett Publishing Company
• Tyson (1991). Modeling the Cell Division Cycle: cdc2 and Cyclin Interactions. *Proc. Nati. Acad. Sci.* 88: 7328-7332.
• A. Goldbeter (1991). A minimal cascade model for the mitotic oscillator involving cyclin and cdc2 kinase. *Proc. Natl Acad. Sci.* 88: 9107-9111.

## Acknowledgments

This research was funded by the RCEU program with funds provided the the Presidents/Provosts office, funds provided by the Vice President for Research, funds provided by the Chemistry Department through their patent account, and external funding from the Alabama Space Grant Consortium.