CMACS
Computational Modeling and Analysis for Complex Systems

2009 CMACS Workshop on Modeling Biological Systems

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Workshop Objectives?

- Get students excited about the research problems and the use of our modeling techniques
- Find good prospects for REU and graduate programs
- Encourage under-represented minorities to enter STEM fields
- Encourage inter-disciplinary work
- ???

Challenges and Issues

- Developing problems that will be interesting and accessible to undergraduates
- Attracting the “right” kind of student
  - Minority?
  - Smart?
  - Excellent background?
  - Candidate for REU/grad school?
  - Not currently interested in science?
- Presentation of the material

I need your help…

- Planning
  - Subject Matter Resources
  - Problems
- Introductory/Summary Lectures
- Graduate students
  - Planning
  - Teaching

Workshop schedule

- Three weeks (most of January) each year
- Rotate challenge problems:

Challenge Problem	Year
1. **Signaling Pathways in Pancreatic Cancer**	Winter 2010 Faeder, Langmead
2. **Fibrillation Onset in Cardiac Tissue**	Winter 2011 Flavio Fenton
3. **Distributed Automotive Control**	Winter 2012?
4. **Aerospace Control Software**	Winter 2013?

Workshop Approach

- Your part:
  - Help with planning
  - Help develop presentation techniques
  - Visit or videoconference during workshop
- Pedagogy:
  - Problem-oriented
  - Interdisciplinary teams
  - Minimal lecture

Team- and problem-oriented

- Based on study of physics students
- Use of “context-rich” problems
  - Need to present clear methodology
  - Students work in small groups
- Group formation
  - Three to a group (tie-breaker)
  - Mixed abilities
- Prepare them to understand some open problem(s)

Winter 2010 Workshop:

Pancreatic Cancer

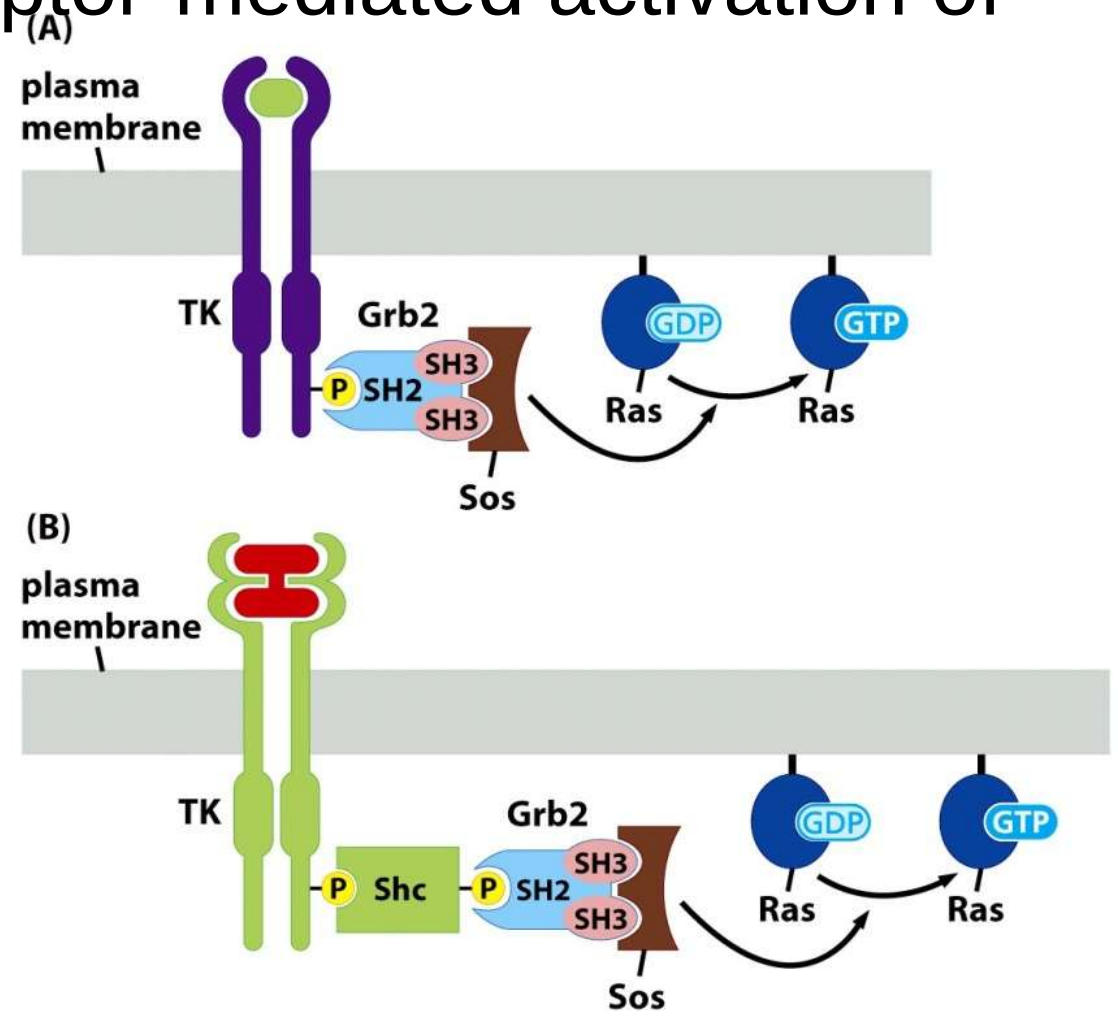
- Workshop planning: Jim Faeder, Chris Langmead, Nancy Griffeth
- Workshop staff: Nancy Griffeth, Ziping Liu (Baruch College), Loes Olde Loohuis (CUNY Graduate Center)
- Workshop activities
  - Model normal cell signaling pathway
  - Model cancer cell signaling pathway
  - Use BioNetGen

Winter 2010 Workshop
Educational Goals

- Introduce undergraduates to Systems Biology
  - Emphasizing the characterization of dynamic properties
- Hands on use of:
  - Modeling and Simulation software (BioNetGen)
  - Verification Tools (BioLab)

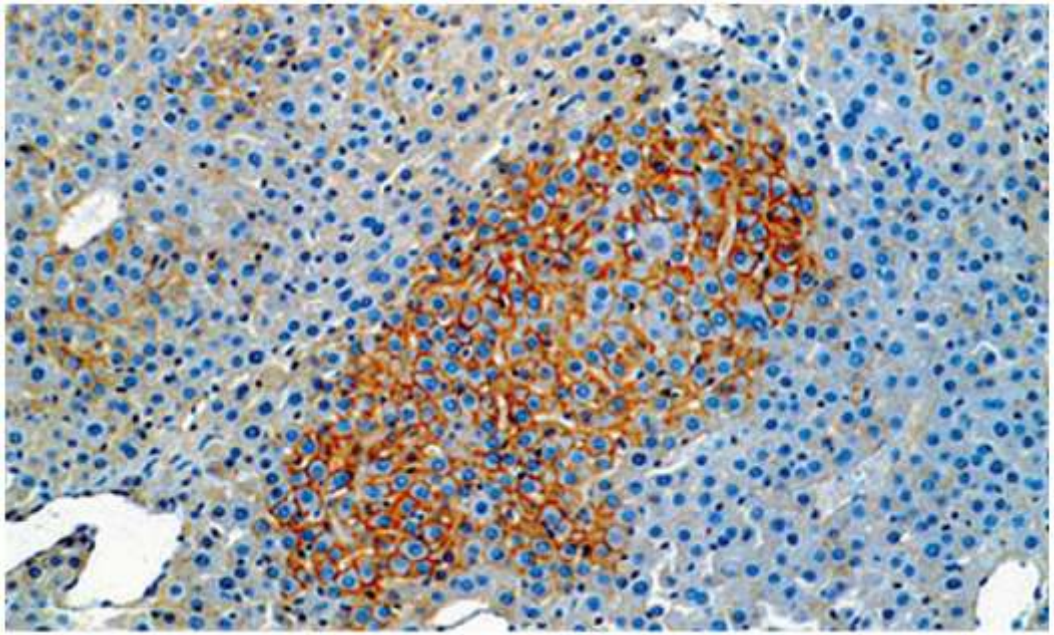
Development of BNG models

- Ex 1: Receptor-mediated activation of Ras

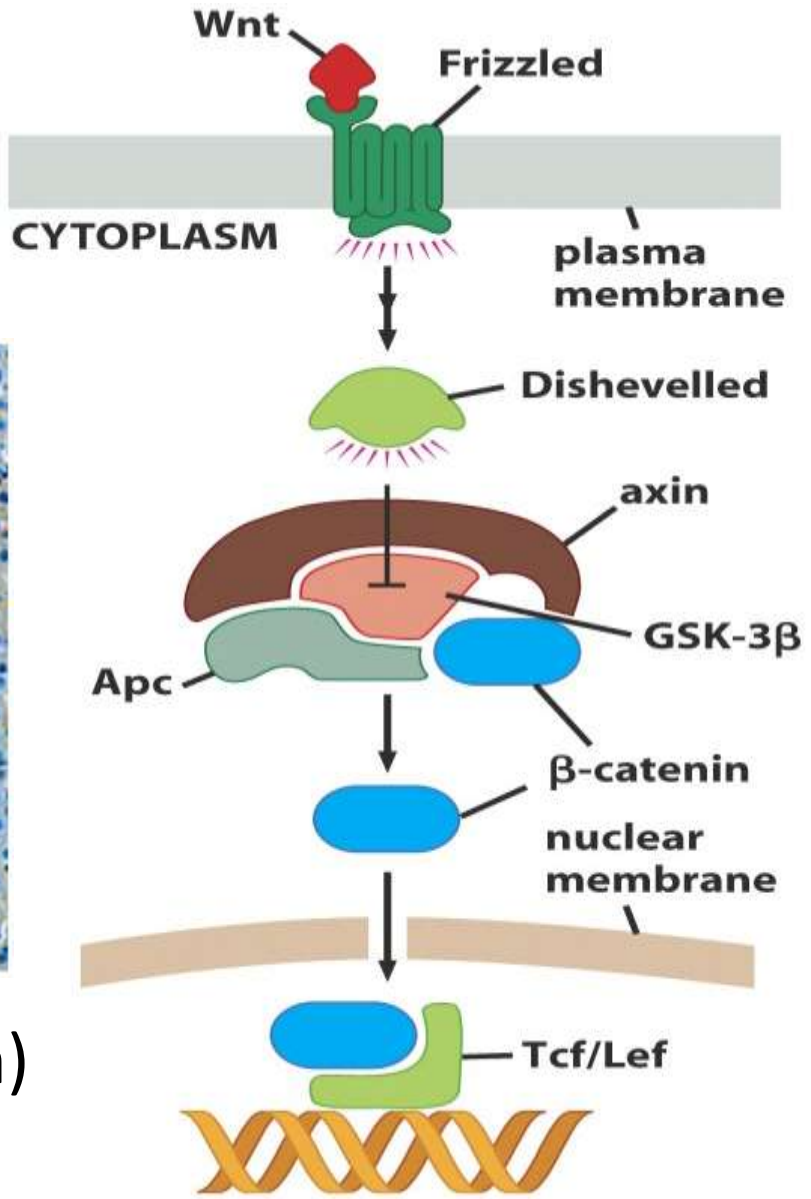


Development of BNG models

- Ex 2: Wnt ¯-catenin pathway



Accumulation of ¯ catenin (brown) in a pre-malignant hepatocyte.



Simulation

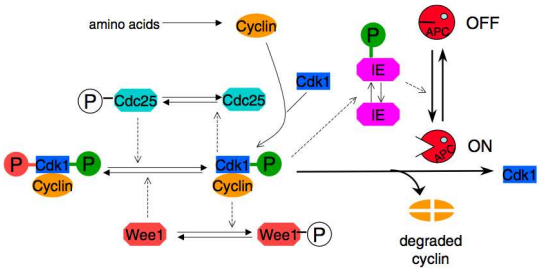
- Students will compare and contrast the results of simulating BNG models using stochastic simulation (SSA) and via ODEs
- The BioLab model checking tool will be used to verify properties of the models

Pedagogical Approach

- Start with verbal description
- Use diagrams to make verbal description more precise
- Develop mathematical model from diagrams
- Define computer model from the mathematical model
- Run simulation and experiment with the model

Pedagogical Approach

QuickTime™ and a decompressor are needed to see this picture.



Verbal description

Wiring diagram

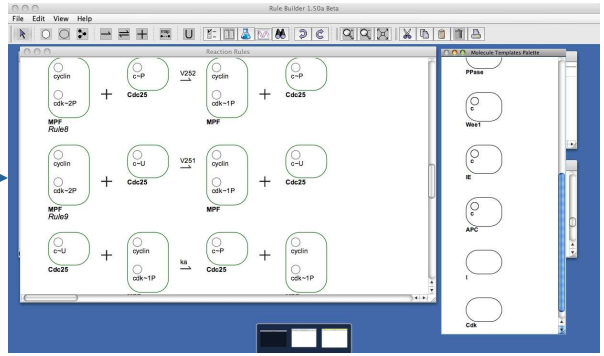
1. $\frac{d}{dt}[\text{Cyclin}] = k_1 - k_2[\text{Cyclin}] - k_3[\text{Cyclin}][\text{Cdk}]$

2. $\frac{d}{dt}[\text{MPF}] = k_3[\text{Cyclin}][\text{Cdk}] - k_2[\text{MPF}] - k_{wee}[\text{MPF}] + k_{25}[\text{preMPF}]$

3. $\frac{d}{dt}[\text{preMPF}] = -k_2[\text{preMPF}] + k_{wee}[\text{MPF}] - k_{25}[\text{preMPF}]$

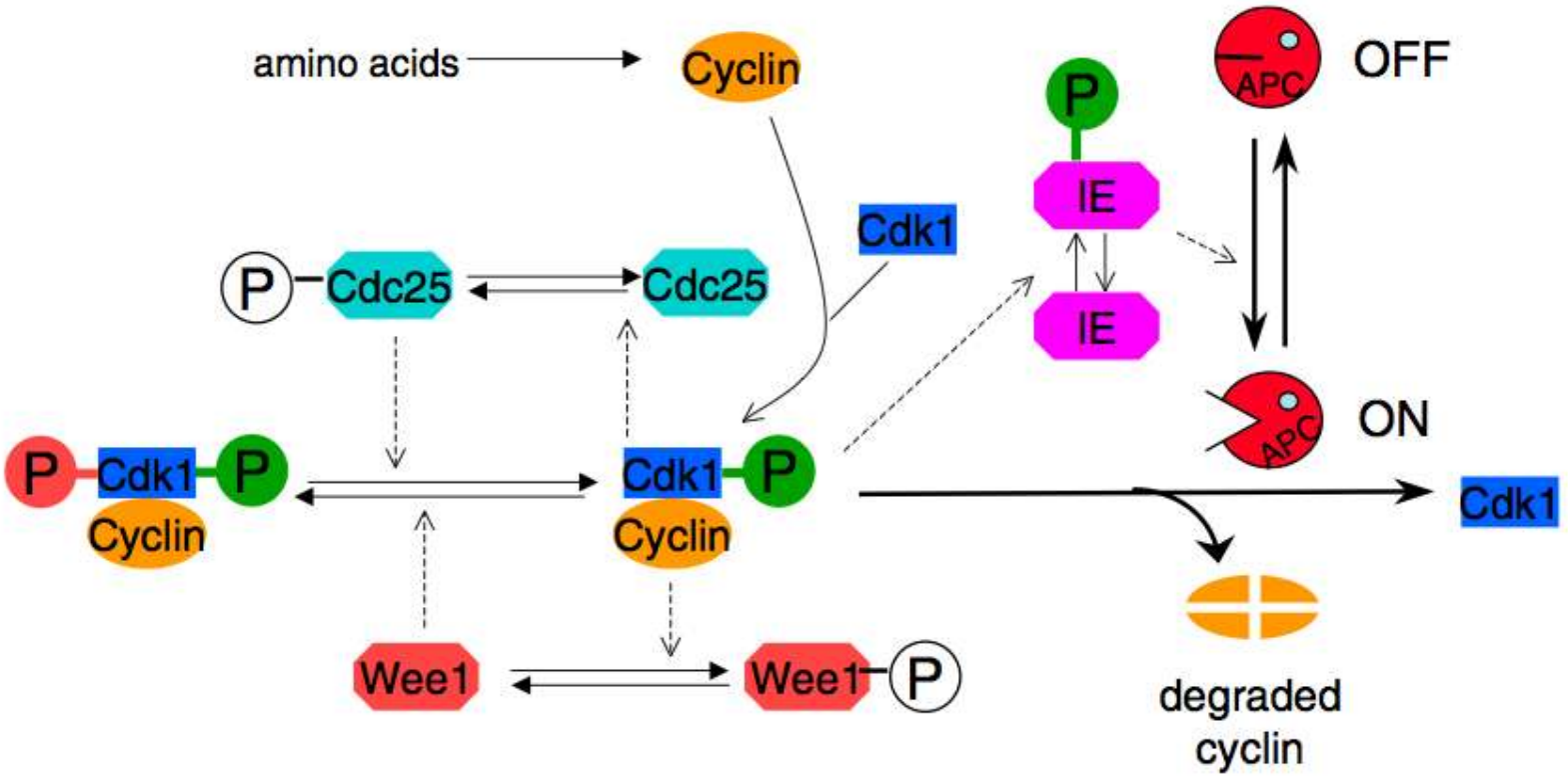
4. $\frac{d}{dt}[\text{Cdc25P}] = \frac{k_a[\text{MPF}]([\text{total Cdc25}] - [\text{Cdc25P}])}{K_a + [\text{total Cdc25}] - [\text{Cdc25P}]} - \frac{k_b[\text{PPase}][\text{Cdc25P}]}{K_b + [\text{Cdc25P}]}$

Mathematical Model



Computer model

Example Diagram



Example Mathematical Model

1. $\frac{d}{dt}[\text{Cyclin}] = k_1 - k_2[\text{Cyclin}] - k_3[\text{Cyclin}][\text{Cdk}]$

2. $\frac{d}{dt}[\text{MPF}] = k_3[\text{Cyclin}][\text{Cdk}] - k_2[\text{MPF}] - k_{wee}[\text{MPF}] + k_{25}[\text{preMPF}]$

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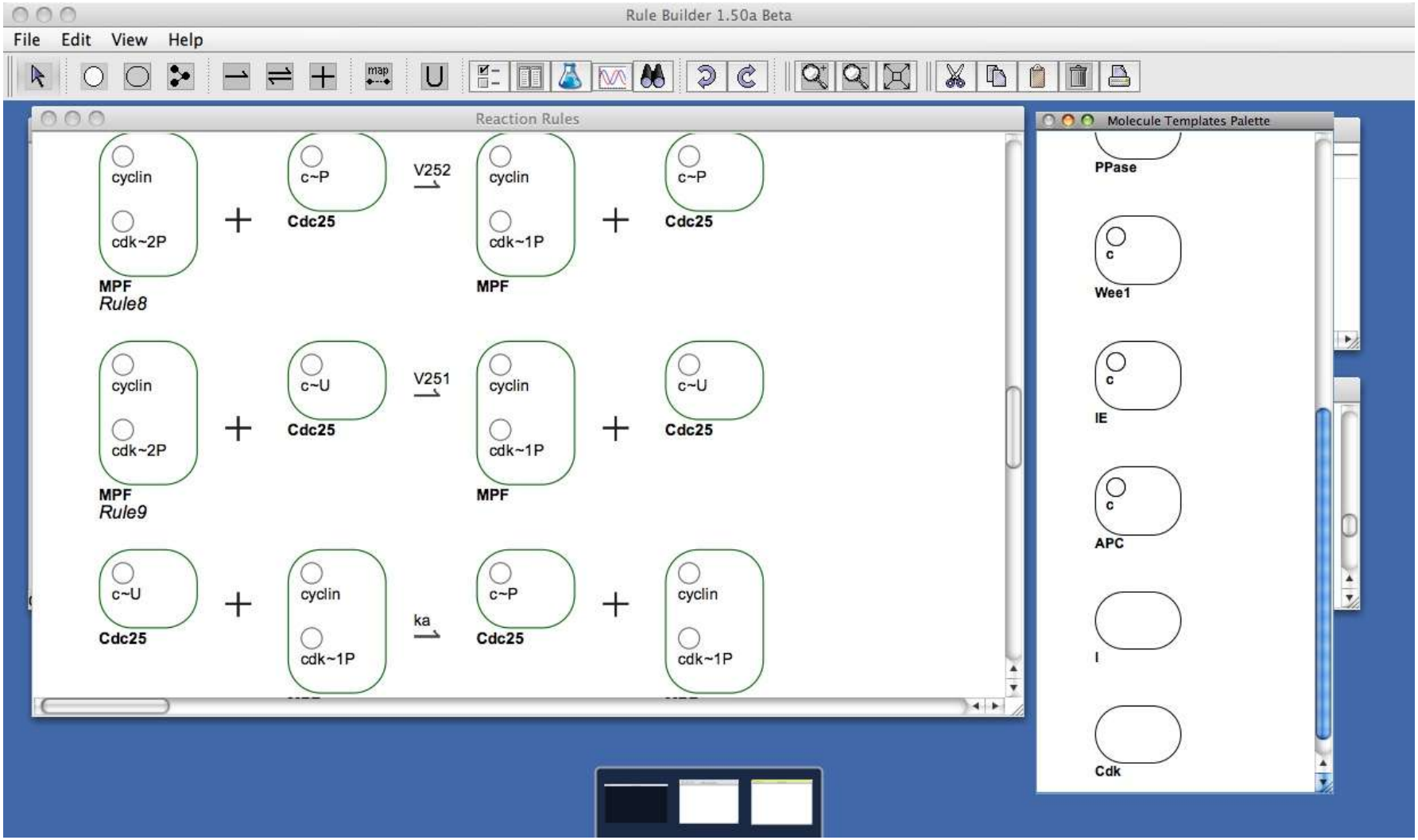
Example Computer Model



Applicants (as of Oct 30)

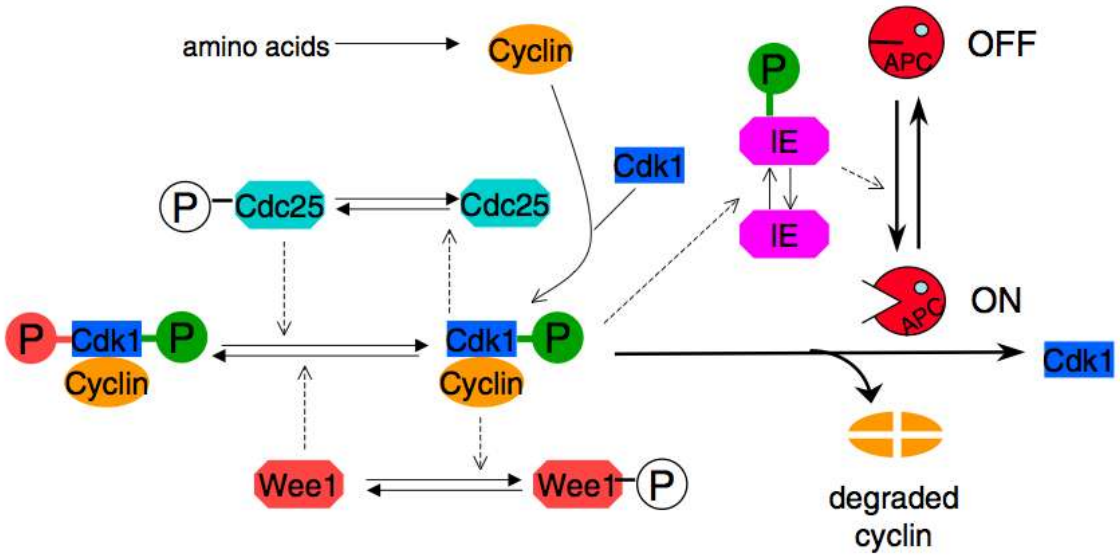
- **Colleges**: Hunter (8), Brooklyn (4), Lehman (5), Stony Brook (1)
- **Median GPA**: 3.77
- **Majors**: CS (6), Bio (4), Math (3), Chem (2)
- **Team Composition Goal**: 1 Bio or Chem, 1 CS, 1 Math
- **Minority**: 3/9 admitted, 6/15 applicants

Winter 2010 Workshop
Daily Activities

- Day 1:
  - Opening: Distinguished Visitor Lecture (Jim Faeder)
  - Introduction to Linux
  - Introduction to BioNetGen
  - Introduction to the cell cycle
- Day 2:
  - Opening: Distinguished Visitor Lecture (Chris Langmead)
  - Team Formation
  - The frog cell: Modeling the (normal) cell cycle replication network in a frog

Winter 2010 Workshop
Daily Activities

- Week 1, Days 3 to 5: Developing and studying the model



- Weeks 2 and 3: Modeling cancer cell replication
  - Last day: Awards and lectures from other PIs

Possible Daily Agenda

- 10 am - 11 am (in full group):
  - Discussion of previous day / brainstorming
  - Lecture on new material
- 11 am - noon (in teams):
  - Discuss and plan work for day
- Lunch
- 1 pm - 3 pm (in teams):
  - Execute work plan
- 3 pm - 4 pm (in full group)
  - Discussion of problems and possible solutions

Future Workshops

- Volunteer now, before all the slots are taken!!
- Comments and suggestions