Modelling and analysis of G1-S cell cycle transition

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Description of cell cycle with special focus to G1-S transition

Description of the model published in Swat et al. 2004

It is a simplified model of transition between G1 to S phases of mammal cell division.

1th part is a core modul that is made of:
- pRB tumor suppressor
- E2F1 transcription factor targeting gene regulating cell life cycle
Double inibition-activ module showing bistability in core model, where E2F1 switches off pRB and thus increasing activity of itself.

2nd part is extension of core module.
In this extension there are added:
- AP-1 transcription factor for mitogenetic signals
- CycD which amount characterizes G1 to S phases transition a phosphorizates pRB
- pRB-p - phosphorizated pRB
This model module consider gradual phosphorization of pRB to pRB-p.
It is necessary to explain that pRB-p is less active when it comes to suppression of transcription factor E2F1 and so E2F1 is more active (also as transcription factor to itself which means that feedback loop is encouraged).

3rd part is extension of second module on top of core module. This adds:
- CycE as another complex of CDK
- pRB-pp - once more phosphorizated pRB-p
This module shows another level of progression in restriction of suppressor pRB by prolonging state of phosphorizated pRB.

In model can be seen several feed-back loop which lead to degradation of pRB suppressors activity on transcription factor E2F1.

Stochastic modelling

Stochastic modeling was done with CTMC model that was generated via CellDesigner's feature and edited as needed to match desired criteria for output.

Resulting model first tested with single runs to validate results.

Then with use of script for automated execution of PRISM CLI simulations of this model. Automation of CLI was used to run 150 simulations for each initial configuration (different model constants, specifically pRB protein degradation factor) from which last 100th iteration step was taken for each simulation and histogram was calculated and drawn.

For visible bifurcation on histograms it is necessary to choose parameter of pRB protein degradation carefully. Even though its value in article visibility was 0.005 noticeable change occurred much higher above value 0.01. This may be explained due not having enough simulation's iterations or 0.005 being lower limit.

Rule-based modelling

Boolean networks modelling