# Suppression of Variation in Cell-Size: A Control Theoretic Approach

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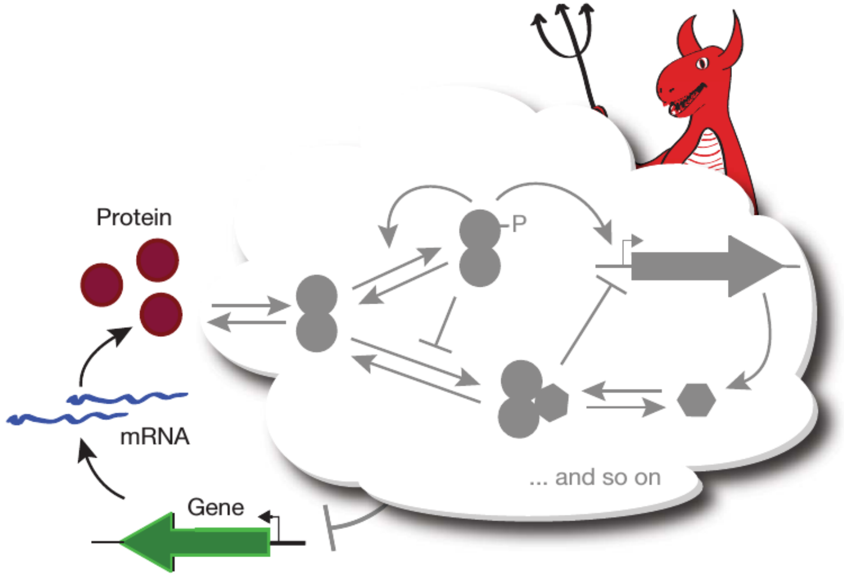
Building over a recent work [1], we explored the possibility of creating networks of small networks which can be utilized for controlling cell size. We explored few topologies in direction of finding a control network which can keep the size of the cell fixed and put an upper bound on the size of the Endosome. Some progress has been made on building a simulator for these topologies in an event-driven simulation environment (SystemC library of C++) [1].

[1] https://github.com/dilawar/FeedbackSimulator/

# Background

- Inside the cell, randomizing and correcting statistical forces battle it out and create fluctuations - noise. Many control circuits have evolved to eliminate or exploit the noise.
- In this rotation project, we used a recent result [1] which establishes limits on 'controllability' in a feedback network to build control networks for controlling cell-size.
- To explore such network construct, we started building a simulation environment using C++ and event-driven simulation library **SystemC**.

# A Feedback Network Studied in [1]



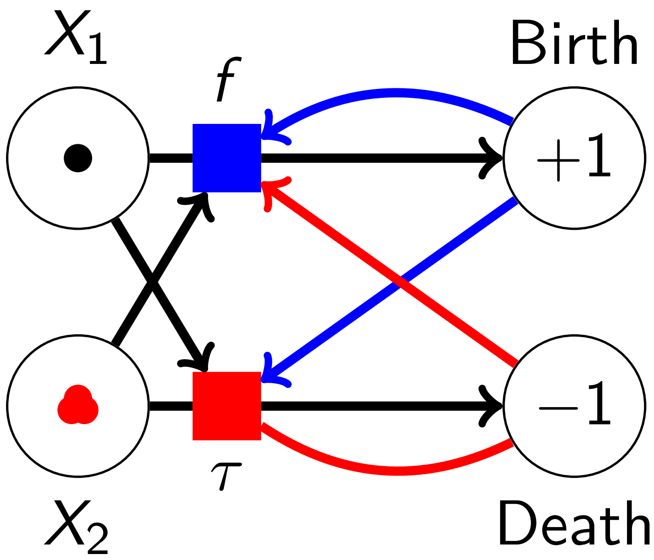




Figure : On left, mRNA/Protein network, from [1]. An equivalent description using Petri Nets on the right with $X_1$ as mRNA and $X_2$ as its protein. Signalling events are probabilistic.

## Birth and Death in Network

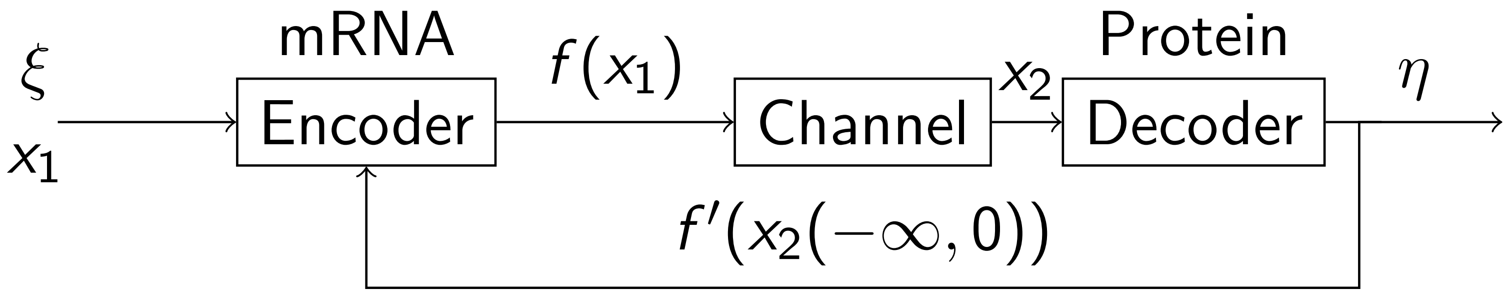
$$X_1 \xrightarrow{f'(x_2(-\infty,t))} X_1 + 1 \qquad X_1 \xrightarrow{\tau_{x_1}} X_1 - 1 \tag{1}$$

$$X_2 \xrightarrow{f(x_1)} X_2 + 1 \qquad X_2 \xrightarrow{\tau_{x_2}} X_2 - 1 \tag{2}$$

# Information theoretic modelling

*How much we can infer about $X_1$ by knowing the time-series of $X_2$?*
The following stochastic equation describes $x_1$.

$$dx_1 = \frac{f' - x_1}{\tau_1} dt + \sqrt{\frac{2\langle x_1 \rangle}{\tau_1}} dw \tag{3}$$




## Channel Capacity

$$C = \langle f \rangle \log(1 + \frac{\sigma_f^2}{\langle f \rangle^2}) \tag{4}$$

# Information theoretical modelling

## The bounds

1. There is bound on variance in $x_1$ whenever there is a bound on error with which $x_1$ can be measured.
2. To measure $x_1$ with small estimation error, a minimal capacity is required for channel $x_1 \rightarrow$.
3. To achieve a certain capacity, a minimal variance in the $f$ is required.
4. If $f$ depends on $x_1$, then high variance in $x_1$ is needed to increase the channel capacity $C$.

*Reducing the variance reduces the channel capacity which in turn makes is harder to further reduce the variance.*

$$\frac{\sigma_{x_1}^2}{\langle x_1 \rangle^2} \geq \frac{1}{\langle x_1 \rangle} \times \frac{2}{1 + \sqrt{1 + 4N_2/N_1}} \tag{5}$$

$$N_1 = \langle x_1 \rangle, N_2 = \langle f \rangle \tau_1 \tag{6}$$

# Network of networks

## Cascade of network

Put a figure here.

A linear cascade of networks causes information loss like the game of broken-telephone.

$$\frac{1}{N_{eff}} = \sum_{j=2}^{n+1} {N_j}^{-1} \tag{7}$$

# Cell-Size control: endocytosis and exocytosis

- Size of cell: $X_1$. Size of the endosome: $X_2$.
- $U$ is a controller which controls $X1$.

- **Endocytosis** $X_1 \xrightarrow{\tau_{x_1}} X_1 - 1$, and $X_2 \xrightarrow{f(x_1)} X_2 + 1$
- **Exocytosis** $X_1 \xrightarrow{U(x_2(-\infty, t))} X_1 + 1$, and $X_2 \xrightarrow{\tau_{x_2}} X_2 - 1$.

## Questions considered

1. Assume $U$ is most the optimum, what is the variance in $X_2$ when $X_1$ is kept at $S_0$?
2. Assume $U$ is the most optimum, how well network controls $X_1$ under random fluctuations (simulation)?
3. For given benchmarks (fixed $S_0$ and variance in $X_2$), can $U$ be designed?

# References & Acknowledgements

Ioannin Lestas., Glenn Vinnicombe, Johan Paulsson
Fundamental limits on the suppression of molecular fluctuations
Nature, Vol 467, Sep 09, 2010

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