

# Control of Cell-Size and Suppression of Variance in Endosome-Size in a Feedback Network

Dilawar Singh, Madan Rao

Building over a recent work [1], we explored the possibility of creating networks of small networks which can be utilized for controlling the cell size . We explore possible topologies which can keep the size of the cell "fixed" and put an upper bound on the variance of the size of the Endosome. Only endocytosis and exocytosis events affect the cell- and endosome-size in this treatment. A simulator for exploring these topologies in an event-driven simulation environment (SystemC library of C++) has been written <sup>1</sup>.

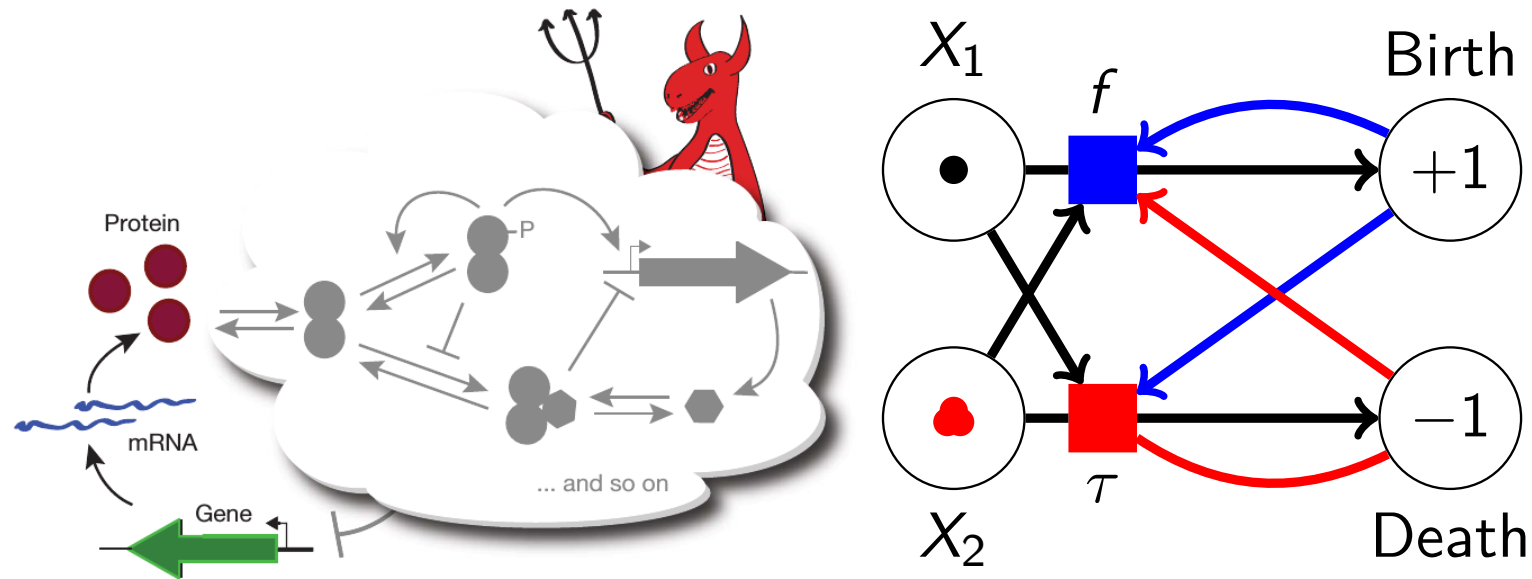
---

<sup>1</sup><https://github.com/dilawar/FeedbackSimulator/>

# Introduction

- ▶ Inside the cell, randomizing and correcting statistical forces create fluctuations - noise. Many control circuits are found in cell which eliminates, tolerates, or exploits the noise.
- ▶ In this rotation project, a recent result [1] which establishes fundamental bounds using information theory on noise-suppression in a feedback network is used to explore control networks for controlling cell-size.
- ▶ To analyze such possible networks, we have been 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

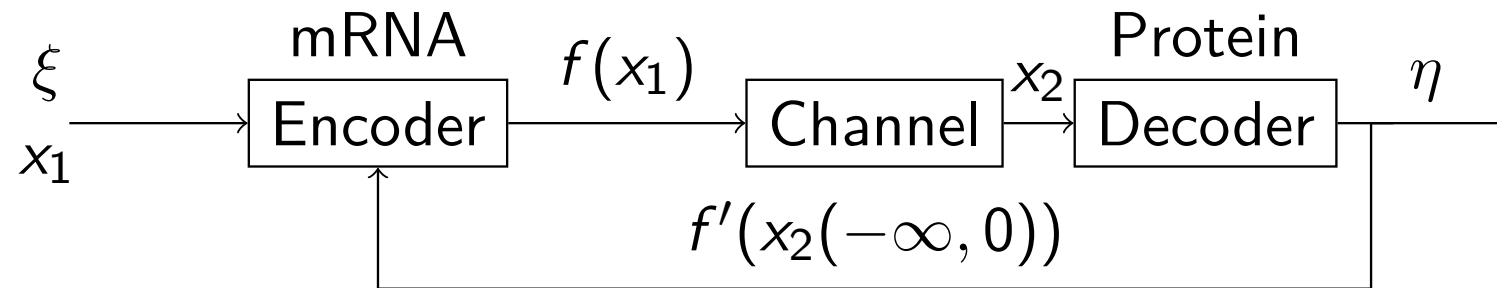
$$X_1 \xrightarrow{f'(x_2(-\infty, t))} X_1 + 1 \quad X_1 \xrightarrow{\tau_{x_1}} X_1 - 1 \quad (1)$$

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

# Information theoretic modelling

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

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



## Channel Capacity

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

# 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 it harder to further reduce the variance.*

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

$$N_1 = \langle x_1 \rangle, N_2 = \langle f \rangle \tau_1 \quad (6)$$

# Network of networks

## Cascade of network

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

$$x_2 \xrightarrow{\lambda} x_2 + 1$$

$$x_n \xrightarrow{\alpha_{n-1}x_{n-1}} x_n + 1$$

$$x_{n+1} \xrightarrow{\alpha_n x_n} x_{n+1} + 1$$

$$x_2 \xrightarrow{x_2/\tau_2} x_2 - 1$$

$$x_n \xrightarrow{x_n/\tau_n} x_n - 1$$

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

# Cell-Size control: endocytosis and exocytosis

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

I'd like to thank Dr. Madan Rao for advice and discussions during the rotation; and Amit for walking me through the needed theory. And various Open Source Softwares especially L<sup>A</sup>T<sub>E</sub>X.



# Simulation Flow

