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Information Transmission and Crosstalk for Coupled Signaling Pathways

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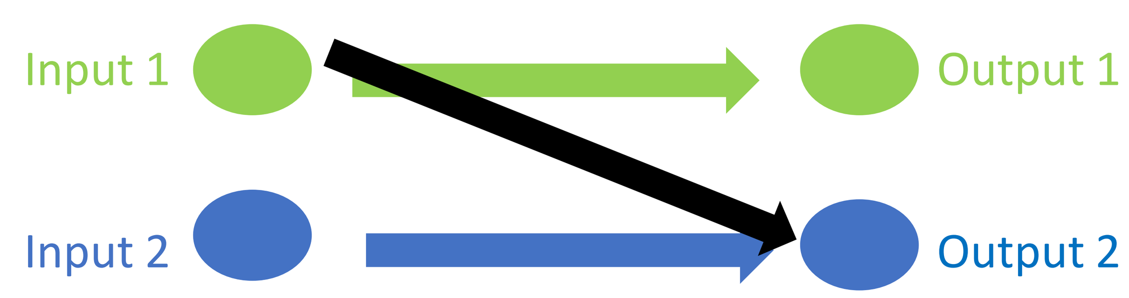
Introduction

Signaling pathways: chemical process in which the cell receives a signal from the outside environment conveying information (e.g., direction of nutrient concentration outside of the cell, chemical gradience for cell development)

Crosstalk: "The process inside a cell that occurs when the same signal is shared by two or more signaling pathways" (National Cancer Institute)

(1)



Question

How does crosstalk between signaling pathways affect mutual information between the input and output?

Mutual Information

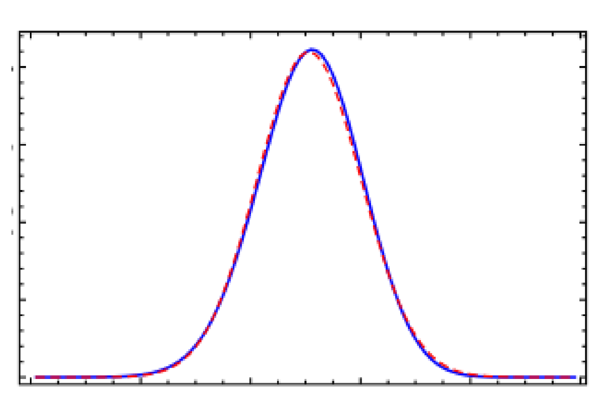
Based on Shannon's theorem, we use mutual information between the input and output as a measure of information transmission, which is given by:

$$MI(I\,;[O^*]) = \iint P(I\,,[O^*])\ \log\frac{P(I\,,[O^*])}{P(I)\ P([O^*])}\, dI\, d[O^*]$$

P(I): input probability distribution (we can assume is given)
P([O*]): activated output probability distribution (must be calculated)
P(I , [O*]): joint probability distribution of input and activated output (determined by finding conditional probability distribution P(I | [O*])

* Gaussian Distribution: $P(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{\frac{-(x-x_0)^2}{2\sigma^2}}$

Used to find P(I | [O*]) by calculating average and variance of probability distribution



(2)

Langevin Equation

A handy framework called the Langevin Equation helps describe the Brownian motion of particles by taking into account both the known forces (i.e., friction) and the random force (due to density fluctuations in the particle's surrounding environment). In our case, this equation is utilized to model information transmission.

Utilizing the Langevin Equation

The Langevin equation is used to find P(I | [O*]) which then let's us determine P(I , [O*])

deterministic (known) term; stochastic (random) term where ξ is white noise

$$\frac{d[O^*]}{dt} = A + B\xi(t)$$

The deterministic term is used to find a fixed-point value → The stochastic term is incorporated to find the variance of the conditional probability distribution → Gives us the joint probability distribution → Plugged in for the mutual information.

* To summarize: The Langevin equation is used to determine the conditional probabilities that are used to calculate mutual information.

Incorporating Crosstalk

To incorporate crosstalk for two coupled pathways with inputs I_1, I_2 and outputs O_1, O_2 (see Diagram 1), the Langevin equations become:

$$\frac{d[O^*]_1}{dt} = A_1 + B_1\xi(t) \quad \text{and} \quad \frac{d[O^*]_2}{dt} = A_2 + B_2\xi(t)$$

where A depends on direct rate constants (k_{11}, k_{22}), crossed rate constants (k_{12}, k_{21}) and the input and activated output concentrations at a fixed point while B also depends on noise strength (V). Through a similar process discussed above, a matrix of variances is determined through linearizing about the fixed points. These variances are then used for the mutual information calculations. This is a step towards answering our question on how crosstalk between signaling pathways affects mutual information between the input and output.

Ongoing Calculations

Current work involves plugging in certain values and analyzing how altering these values affects the mutual information between the input and output.