

Information Transmission by Heterogeneous Cell Populations

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The channel capacities of several mammalian signaling networks have been found to be much lower than what is observed. To address this discrepancy, we develop a new theoretical framework that explicitly accounts for intrinsic stochastic noise in signaling networks and extrinsic cell-to-cell variability when quantifying channel capacity. Using this framework, we estimate the channel capacity of two important mammalian pathways, the epidermal growth factor pathway, and the insulin-like growth factor pathway. Ultimately, our method leads to conceptually clearer and significantly higher estimates of channel capacities. We discuss the consequences for downstream cellular decision making.

Information, Extrinsic Variability, Stochastic Chemical Reaction Network, Maximum Entropy, Heterogeneity

I. BACKGROUND

CELLS employ signaling networks as a means to acquire information from their surroundings. As shown by Levchenko et al. [1], the performance of these networks can be described using information theory. While this has been a step forward in quantitatively assessing cell signaling performance, there has been a significant conceptual issue facing the study from its inception. Cells seem to be able to acquire more information from their surroundings than what is predicted by the mutual information of inputs and the population level response for optimal input distributions (channel capacity).

There are many explanations for this discrepancy, with Levchenko et al. proposing that cells leverage multiple pathways to gain sufficient information from their surroundings. Other methods focus on a cell's ability to process signals [2] or show how a system of cells can resolve signals when individual cells cannot [3]. While cells likely employ these approaches to improve their performance, single cells seem more capable of resolving individual signals than what was once thought [4], which motivates our study. Past applications of information theory have not handled variations in response from noise in single cell signaling networks (intrinsic noise) differently from variations in response due to cell-to-cell differences (extrinsic variability). However, the extrinsic variation does

not inherently corrupt individual cell signals in the way intrinsic noise does. By looking at the information throughput of cells conditioned on the extrinsic variability we isolate intrinsic noise as the only true source of cell signal corruption.

II. SUMMARY OF RESULTS AND CONCLUSIONS

We obtain the mutual information of the population response and the conditional mutual information for cells in-silico and in-vitro (example in-vitro results provided in fig. 1). In both cases we find the conditional mutual information describes a cell which can detect a wider range of signal inputs than what is indicated by the mutual information obtained at the population level. The conditional mutual information workflow also allows for insight into which components of a signaling network have the greatest impact on signaling performance. This analysis will be included for in-vitro cell signaling networks.

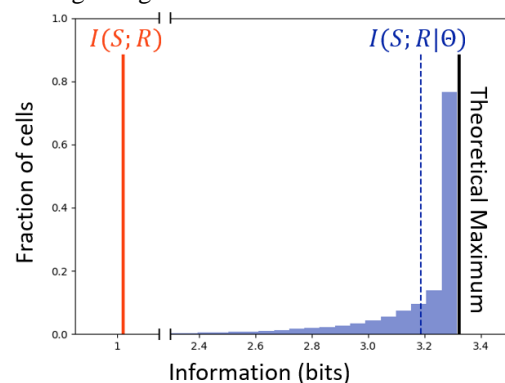


Fig. 1: Conditional mutual information vs mutual information of the population response at the channel capacity for both methods. Data obtained on the EGF pathway with MCF10a cells.

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