How to Model Cell Decision Making Errors

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Short Abstract **— Due to signal transduction noise, cells respond differently to similar inputs, which may result in incorrect cell decisions. Here we present a method for modeling decision making processes in cells, and apply it to an important signaling pathway that is involved in cell survival. Our method reveals that cells can make two types of incorrect decisions. We compute the likelihood of these decisions using single cell experimental data, and demonstrate how these incorrect decisions are affected by the noise. We also study the connection between information transmission capacity of the pathway and decision making errors using experimental data.**

Keywords **— Cell decision making, noise, signaling errors, signaling networks, information capacity, TNF, NF-κB.**

I. INTRODUCTION

EACH cell continuously receives signals from its surrounding environment and is supposed to make correct decisions, i.e., respond properly to various signals and initiate certain cellular functions. In various organisms ranging from viruses to bacteria, yeast, lower metazoans and finally complex organisms such as mammals, various decisions are made in the presence of noise [1]. The noise, however, causes the cell to respond differently to the same input, which may result in incorrect (unexpected) cell responses [2]. Here we introduce a method for modeling and measurement of decision making processes in cells, using statistical signal processing and decision theory concepts. Given the importance of single cell modeling approaches to understand the biochemical processes in each individual cell [3], we use single cell experimental data [2].

II. THE METHOD AND THE RESULTS

Details of the method and mathematical formulation can be found in [4]. Analysis of the tumor necrosis factor (TNF) signaling pathway which regulates the transcription factor Nuclear Factor κB (NF-κB) using this method has identified two types of incorrect cell decisions called false alarm and miss. These two events represent, respectively, declaring a signal which is not present and missing a signal that does exist. Using single cell experimental data and the developed method, we have computed false alarm and miss error probabilities in wild-type cells and have investigated how they depend on the signal transduction noise level [4].

We also have shown that in the presence of abnormalities in a cell, decision making processes can be significantly affected, compared to a wild-type cell, and the method is able to model and measure such effects. In the TNF-NF-κB pathway, the method has revealed changes in false alarm and miss probabilities in A20-deficient cells, caused by cell's inability to inhibit TNF-induced NF-κB response [4]. In biological terms, a higher false alarm metric in this abnormal TNF signaling system indicates perceiving more cytokine signals which in fact do not exist at the system input, whereas a higher miss metric indicates that it is highly likely to miss signals that actually exist.

In addition to these findings, we have also studied how the developed cell decision making model relates to the information transmission capacity and dynamical modeling of the signaling pathway [4].

III. CONCLUSION

This study demonstrates the ability of a new method for computing cell decision making error probabilities under normal and abnormal conditions, and in the presence of transduction noise uncertainty. Using the method, decision making errors of molecular networks can be modeled. Such models are useful for understanding and developing treatments for pathological processes such as inflammation, various cancers and autoimmune diseases.

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