Dynamic Modeling of Cell Signaling Cascades in Immune Response and Cancer

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Cell signaling networks are the pathways through which extracellular signals trigger cellular responses. Within these complex networks, biochemical cascades consist of building blocks (modules or sub-networks) that transform an input signal into an output which, in turn, acts as the input signal to the next module, eventually producing an overall cellular response. The temporal evolution of these processes can be modeled by nonlinear dynamical systems involving multiple time scales, which are determined by the biological parameters [6, 7].

Despite substantial progress in the study of specific biochemical circuits, a general framework describing how signals are transformed as they propagate across modules is still lacking. In particular, it remains unclear how network architecture and module dynamics jointly affect gain, sensitivity, saturation, and response times. In this work, we address these questions in the context of a signaling network associated with the immune response in triple-negative breast cancer (TNBC). More specifically, we consider the CD45–Csk–Lck signaling module involved in T-cell activation [1, 2]. Mathematically, we consider a class of biochemical cascades represented by a system of ordinary differential equations,

$$\dot{X}_i = k_i \frac{X_{i-1}}{K_i + X_{i-1}} (X_{i,T} - X_i) - d_i X_i, \qquad i = 1, \ldots, n,$$

where the saturating activation term is of Michaelis–Menten type [3].

The early output of the CD45–Csk–Lck module, represented by the phosphorylation level of the (ζ) chain is used as the input to a downstream cascade of the form

$$\zeta_p \longrightarrow \text{ZAP70} \longrightarrow \text{LAT} \longrightarrow \text{Ras/MAPK} \longrightarrow \text{ERK},$$

where each component represents a signaling protein or protein complex.

Motivated by recent research on immune signaling in TNBC [4, 5], we investigate how upstream perturbations, including the potential modulation of CD45 by galectin-3 and immunopeptides, are transmitted and transformed along the cascade.

More generally, we aim to identify the dynamical principles underlying signal processing in biochemical networks and to analyze how the structure of cascades shapes both signal propagation and the resulting response regimes. These principles are expected to be applicable to cell signaling networks associated with other pathologies.

Keywords: dynamical systems; biochemical cascades; signal processing; cell signaling.

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