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The construction of biochemical models of cellular signaling networks requires the assimilation of a large number of kinetic constants from diverse sources. In this work, we present an experimental and modeling methodology that integrates novel, cell system-specific sensitivity measurements with published kinetic constants.

We have applied this methodology to quantify the interactions between receptors for the cytokines IL-2 and IL-7 in T lymphocytes. Using our method of heterogeneity analysis, we demonstrate that responsiveness to IL-7 is negatively correlated with expression of the IL-2 receptor α chain (IL-2R α) in T cells: cells with higher levels of IL-2R α have a 50-fold lower sensitivity compared to cells expressing lower levels.

We have constructed a computational model of the interactions in this biochemical system. To fit the model to our high-resolution data, we have employed a Bayesian framework that penalizes for deviation from both previously defined parameter values and the current data. Using this fitting algorithm, we identify the competition for the shared γ receptor as a mechanism for non-independence of IL-2 and IL-7 sensitivity. Implications for the differentiation memory T cells during an immune response are discussed. (Received January 30, 2012)