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Noise and fidelity of information transmission through the Tumor Necrosis Factor signaling circuit

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Molecular noise restricts the ability of an individual cell to resolve input signals of different strengths and gather information about the external environment. We developed an integrative theoretical and experimental framework, based on the formalism of information theory, to quantitatively predict and measure the amount of information transduced by molecular and cellular networks. Analyzing tumor necrosis factor (TNF) signaling revealed that individual TNF signaling pathways transduce information sufficient for accurate binary decisions, and an upstream bottleneck limits the information gained via multiple integrated pathways. Negative feedback to this bottleneck could both alleviate and enhance its limiting effect, despite decreasing noise. Bottlenecks likewise constrain information attained by networks signaling through multiple genes or cells. We further use this new analysis formalism to "map" the noise amplitude across different parts of the network. Finally, we show that the redundancy in signaling due to the existence of parallel pathways is not absolute, and that parallel pathways can transmit different types of information about the input, i.e., the duration vs. amplitude.