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Information processing and signal integration in bacterial quorum sensing

PANKAJ MEHTA, Princeton University

Bacteria communicate with each other using secreted chemical signaling molecules called autoinducers (AIs) in a process known as quorum sensing. Quorum sensing enables bacteria to collectively regulate their behavior depending on the number and/or species of bacteria present. The quorum-sensing network of the marine-bacteria *Vibrio harveyi* consists of three AIs encoding distinct ecological information, each detected by its own histidine-kinase sensor protein. The sensor proteins all phosphorylate a common response regulator and transmit sensory information through a shared phosphorelay that regulates expression of downstream quorum-sensing genes. Despite detailed knowledge of the *Vibrio* quorum-sensing circuit, it is still unclear how and why bacteria integrate information from multiple input signals to coordinate collective behaviors. Here we develop a mathematical framework for analyzing signal integration based on Information Theory and use it to show that bacteria must tune the kinase activities of sensor proteins in order to transmit information from multiple inputs. This is demonstrated within a quantitative model that allows us to quantify how much *Vibrio*'s learn about individual inputs and explains experimentally measured input-output relations. Furthermore, we predicted and experimentally verified that bacteria manipulate the production rates of AIs in order to increase information transmission and argue that the quorum-sensing circuit is designed to coordinate a multi-cellular developmental program. Our results show that bacteria can successfully learn about multiple signals even when they are transmitted through a shared pathway and suggest that Information Theory may be a powerful tool for analyzing biological signaling networks.