Dissecting the Functional Importance of Gene Circuit Architecture

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CELLULAR processes are typically controlled by gene regulatory circuits that are comprised of interactions among genes and proteins. However, the functional importance of a particular pattern of interactions (architecture) that constitutes a genetic circuit remains poorly understood. To investigate this problem, we compared the circuit that controls differentiation of *Bacillus subtilis* cells into the state of competence to a seemingly equivalent engineered counterpart with an alternative architecture. The architectures of the native and synthetic circuits differed primarily in the order of successive activation and repression reactions, but retained the same overall feedback structure. Comparative analysis showed that the reversed order of positive and negative reactions between natural and synthetic circuits give rise to distinct levels of temporal variability in single cell dynamics (noise). This noise difference in turn controlled the physiological response range of competence to varying extracellular DNA concentrations. These results demonstrate a noise-mediated tradeoff between temporal precision and physiological reliability that is encoded into the architecture of a cellular differentiation circuit.