論文の内容の要旨

Single-cell information analysis reveals small intracellular and large intercellular variations increase cellular information capacity

(1 細胞情報量解析による小さな細胞内変動と大きな細胞間変動を介した正確な細胞情報伝達の解明)

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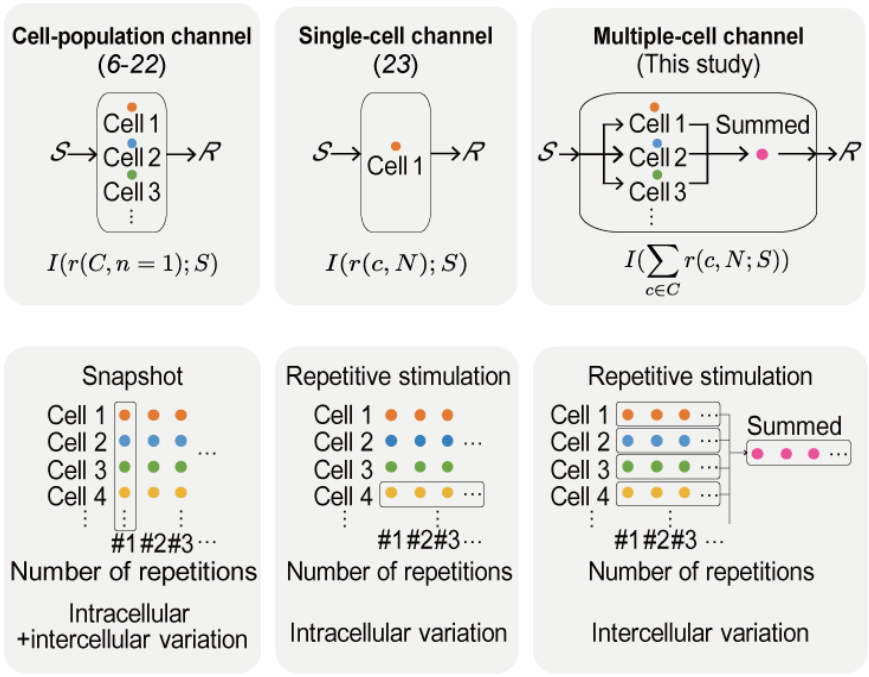
In biology, signaling pathways must reliably convert stimulation intensity into signaling activity in the presence of two sources of variability: Intracellular variation arising from within a cell (also referred to as intrinsic noise) and intercellular variation arising from cell-to-cell variability (also referred to as extrinsic noise). An example of intracellular variation is the stochastic fluctuation of a biochemical reaction; examples of intercellular variation, are the differences in gene expression and protein abundance among cells. In most models of biological systems, cell-to-cell variability causing different cellular responses between cells have thus far been considered “noise” that reduces the ability of the system to distinguish between different stimuli. Previous studies applying information theory to signaling pathways have examined the information transmission capacity at the cell-population level in which intercellular variation contributes to uncertainty and is noise, or at the single-cell level in which intercellular variation

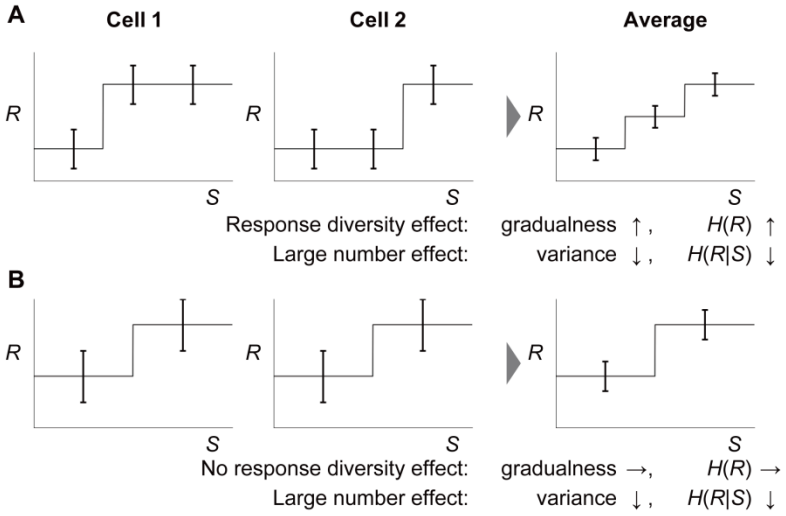
is absent (Summary Fig. 1). However, intercellular variation has the potential to enable individual cells to encode different information. Here, I hypothesized that some physiological systems, such as skeletal muscle, are better represented by a multiple-cell channel (Summary Fig. 1), which is a communication channel composed of a sum of single-cell channels and showed that intercellular variation increases information transmission of skeletal muscle with C2C12 differentiated myotubes, isolated single-fibers of mice skeletal muscle.

With intercellular variation, average dose-response of multiple-cells becomes graded, and I called this effect “response diversity effect” (Summary Fig. 2). I found that intercellular variation can serve as information rather than noise through response diversity effect, resulting more gradual dose-response of multiple-cell channel than that of a single-cell channel.

In both C2C12 myotubes and isolated single-fibers, the intracellular variation was small and intercellular variation was large, which means that each cell responds accurately and reproducibly to a particular stimulus, but their responses differ from each other. It means that not only each cell can control its response accurately, but also the accuracy of the response of a tissue is enhanced by response diversity effect, in which incorporated intercellular variation as information not noise In addition, I quantified the information transmission of human facial muscle contraction during intraoperative neurophysiological monitoring and found that information transmission of muscle contraction is comparable to that of a multiple-cell channel. Thus, the data in this study indicated that intercellular variation can increase information capacity of tissues.



Summary Fig. 1. Schematic overview of cell-population, single-cell, and multiple-cell channel.



Summary Fig. 2. the effect on the dose-response of multiple-cell channel with (A) and without intercellular variation (B).