Information transmission rate through the MAPK/ERK pathway

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***Short Abstract* — Many intracellular signaling pathways can transmit around 1 bit of information about the amplitude of a constant stimulus. However, much more information can be encoded in a dynamic input, and the cell should potentially be able to process it. Here, we evaluate the ability of the MAPK/ERK pathway to transmit a time-varying signal. We use MCF-10A cells expressing a light-activatable FGF receptor and an ERK activity reporter. By stimulating the cells with random trains of light pulses we demonstrate that the information transmission rate through the MAPK/ERK pathway, from FGF receptor to ERK, can exceed 6 bits per hour. This allows the MAPK/ERK pathway to coordinate multiple processes, including cell movement.**

***Keywords* — cell signaling, optogenetics, bitrate, channel capacity, temporal encoding**

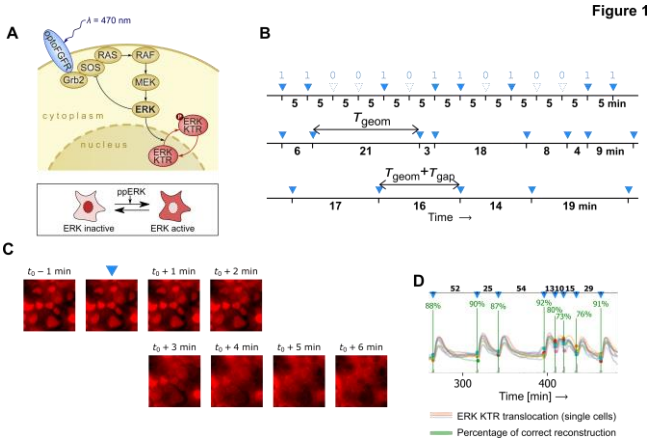
I. Background

At the single-cell level, intracellular signaling pathways typically respond to stimulation in an all-or-nothing manner. Thus, the amount of information about the (constant) ligand concentration available at the effector protein level hardly exceeds 1 bit [1]. This is sufficient to digitally switch on the expression of the pathway-specific genes, however, to control more complex processes and respond to a time-varying input, the cell should use some kind of temporal coding.

II. Results

In this work [2], we experimentally estimated the maximum transmission rate of information encoded in a sequence of pulses through the MAPK/ERK pathway, from receptor (FGFR) to effector (ERK). We stimulated the MCF-10A cells with short (100 ms) blue light pulses according to specific information encoding protocols to activate optoFGFR. The signal was then transmitted to ERK (Fig. 1A) and the fluorescent ERK kinase translocation reporter (ERK KTR) moving from the nucleus to the cytoplasm upon phosphorylation by ERK. The ERK KTR translocation was observed with one-minute resolution (Fig. 1C) and quantified (Fig. 1D).

Based on the quantified single-cell trajectories of nuclear ERK KTR, we reconstructed the input sequence of light pulses using a method based on the *k*-nearest neighbors algorithm and data within a 8-min window sliding over the ERK KTR translocation trajectory. We computed the mutual information between the reconstruction and the true stimulation sequence, and thus established how much information (at least) was transferred through the pathway within a given period of time.



To find the most efficient way of information transmission, we tested three kinds of protocols (Fig. 1B), and obtained the following lower bounds:

(1) 4.4 bit/h when information is sent as 0/1 digits at regular time intervals (optimally: 3–5 min apart),

(2) 5.6 bit/h when input pulses are sent according to a Poisson process (optimally: on average 30–40 min apart),

(3) 6.6 bit/h when input pulses are sent like in a Poisson process, but with a minimal inter-pulse interval (optimally: 23–30 min on average, but at least 8–10 min apart).

III. Conclusion

We explicitly estimated the information transmission rate from FGFR to an ERK activity reporter to find that the MAPK/ERK channel capacity exceeds 6 bit/h. This shows that the pathway is efficient in transferring information encoded in a train of input pulses, which suggests that the precise timing of ERK activity may play a significant role in processes, in which the pathway is involved.

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