Intercellular Ca^{2+} Wave Propagation through Patterned HeLa Cx43 Cells

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Abstract

Molecular communication between cells can be exploited to expand the potential of synthetic biological systems [1]. For example, cell-cell signaling (e.g., intercellular Ca^{2+} signaling) may be used for distant cellular machines to communicate and coordinate to perform complex tasks. Here we report design and development of *cell wires* that can propagate Ca^{2+} waves through a line of patterned HeLa Cx43 cells, and that may be used as a means of communication in synthetic biological systems.

A platform for cell-patterning was established by utilizing surface chemistry. Glass (SiO_2) substrates were partly coated with gold (Au) layers, and SAMs (Self-assembled Monolayers) of polyethylene glycol (PEG) were formed on top of the gold layers. Our experimental results show that gold layers were effectively designated as cell-resistant areas while intact glass surfaces as cell-adhesive areas, so that a designed pattern of cells was formed. Then, either mechanical or chemical point stimulation was applied to a cell to initiate Ca^{2+} wave propagation (Figure 1). Adjacent HeLa Cx43 cells establish Cx43 gap junctional channels that are used to propagate Ca^{2+} waves intercellularly. Fluorescence microscopy was used to observe Ca^{2+} wave propagation, and communication related characteristics (e.g., speed of propagation) were obtained (Figure 2).

Reference

[1] T. Nakano, T. Suda, M. Moore, R. Egashira, A. Enomoto, and K. Arima, "Molecular Communication for Nanomachines Using Intercellular Calcium Signaling," IEEE NANO 2005 , June 2005.

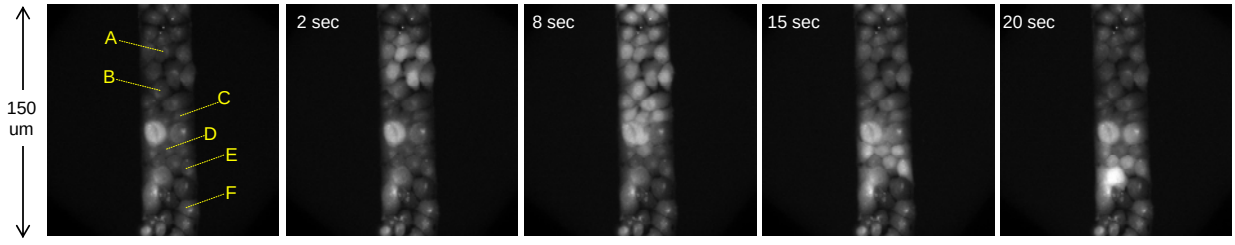

Figure 1: **(Prototype of cell wires)** HeLa cells expressing Cx43 were patterned into a straight line through cell patterning. The cells were cultured on the cell-patterning platform 1-2 days under standard cell culture conditions. Prior to imaging experiments, cells were loaded with a Ca^{2+} indicator (Fluo4); and were placed in buffer solution (HBSS-Hepes) containing caged-ATP. Flash photolysis of caged-ATP was used to initiate Ca^{2+} wave propagation. In the experiment, cell A was flashed, which increased its Ca^{2+} level as shown in Figure 2. The increased Ca^{2+} level propagated along the straight line about 5 um/sec, and reached the cell that was 10 cells away from the flashed cell. The Ca^{2+} wave propagation in this experimental setup is presumably facilitated by gapjunctional diffusion of messenger molecules (e.g., Ca^{2+} itself, IP_3) in addition to extracellular diffusion of photo-released ATP. In other experiments, alternative to flash-photolysis of caged-ATP, either flash-photolysis of caged-Ca^{2+}, flash-photolysis of caged-IP_3, or mechanical stimulation was used to initiate intercellular Ca^{2+} waves.

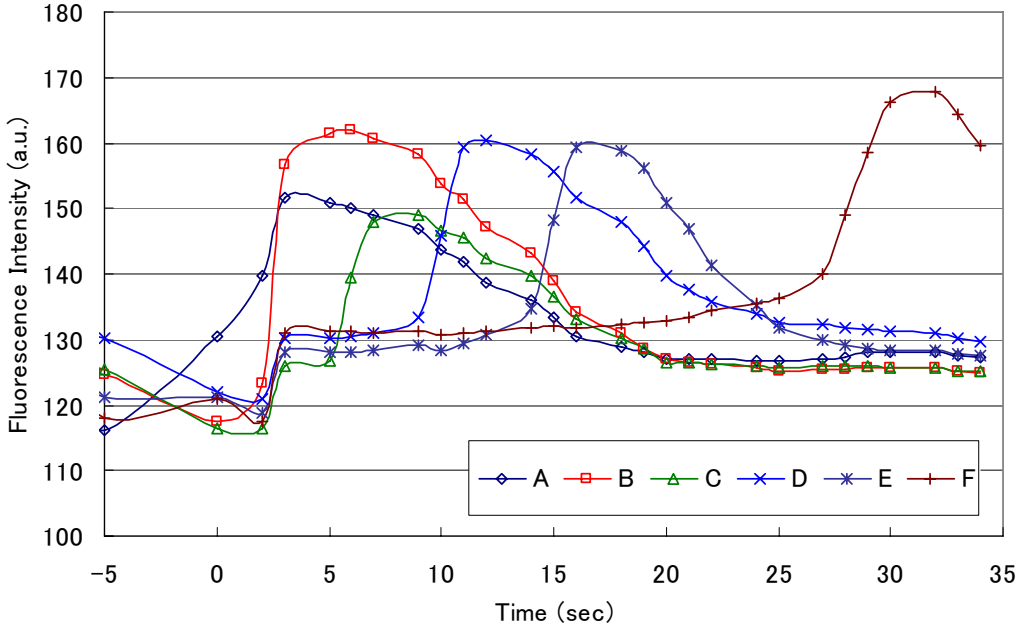

Figure 2: Fluorescence intensity of cells A, B, C, D, E and F
in response to stimulation at time 0.