Researchers simulate information signaling between cells

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(Phys.org)—Many natural systems are described by dynamics of traveling wavefronts. Sharp traveling fronts are employed in countless phenomena, including fluid convection, chemical reactions, and cellular phenomena. Living systems use front propagation encoded in biochemical reactions to communicate and perform computations, but these dynamics are difficult to study in three dimensions (i.e., in vivo). Thus, to understand how propagating gene expression fronts work in complex living systems, it is important to study how they work in minimal systems.

A group of researchers in Israel and the United States report in *Nature Physics* the results of a study of a one-dimensional array of artificial cells in a silicon chip—in essence, a system of coupled cells in which the researchers could implement reaction-diffusion effects and study how they propagate among cells.

Artificial cells?

Artificial cells are engineered systems of various kinds that simulate a number of functions of biological cells. In this case, the array of cells consists of 15 compartments inside which the researchers patterned gene circuits. The compartments simulate the microencapsulation of the biological membranes of cells, separating the internal cellular mechanisms from other "cells" while allowing the exchange of small molecules.

Carved into a silicon substrate, the compartments were fed by a main flow channel and interconnected by fork-shaped capillaries. Cell extract from Escherichia coli was fed continuously through the main channel. The researchers were interested in how biological multicellular systems use traveling wavefronts to communicate. Signals dissipate over short distances within a medium, so cells accomplish long-range transmission of information by consecutive local cell-to-cell interactions. In living systems, the transmission models are too complex to study, but this isolated array of artificial cells revealed interesting dynamics likely applicable to the study of actual multicellular systems.

Though front propagation has been studied in the past, yielding results that have applications in science and industry, the authors note that this is the first time anyone has created a synthetic, spatially coupled cellular system capable of long-range cell-to-cell communication. The first compartment was patterned with a small amount of starter protein construct, and as the medium flowed through the channels, the researchers found that the DNA starter initiated diffusion of the activator to the neighboring compartment. This created an autocatalytic reaction in which the neighboring compartment created a new source of activator.

The researchers characterized expression-diffusion dynamics by measuring the timescales between the diffusion of proteins along the capillaries, which occurred over minutes, and the gene expression dynamics in the compartments, which changed over hours. In essence, the researchers created a system of autocatalyzing protein synthesis in which the activator signal cascaded through the compartments, which amplified it and diffused it to neighboring compartments.

The authors write, "The spatial organization of DNA circuits together with short interaction length, set by the array geometry, will allow integrating long-range signaling with local information processing

reactions based on gene expression, in analogy to multicellular systems, electronic circuits, and neural networks."

More information: "Propagating gene expression fronts in a one-dimensional coupled system of artificial cells." *Nature Physics* (2015) DOI: 10.1038/nphys3469

Abstract

Living systems employ front propagation and spatiotemporal patterns encoded in biochemical reactions for communication, self-organization and computation. Emulating such dynamics in minimal systems is important for understanding physical principles in living cells and in vitro. Here, we report a one-dimensional array of DNA compartments in a silicon chip as a coupled system of artificial cells, offering the means to implement reaction–diffusion dynamics by integrated genetic circuits and chip geometry. Using a bistable circuit we programmed a front of protein synthesis propagating in the array as a cascade of signal amplification and short-range diffusion. The front velocity is maximal at a saddle-node bifurcation from a bistable regime with travelling fronts to a monostable regime that is spatially homogeneous. Near the bifurcation the system exhibits large variability between compartments, providing a possible mechanism for population diversity. This demonstrates that on-chip integrated gene circuits are dynamical systems driving spatiotemporal patterns, cellular variability and symmetry breaking.