Lighting the path for cells

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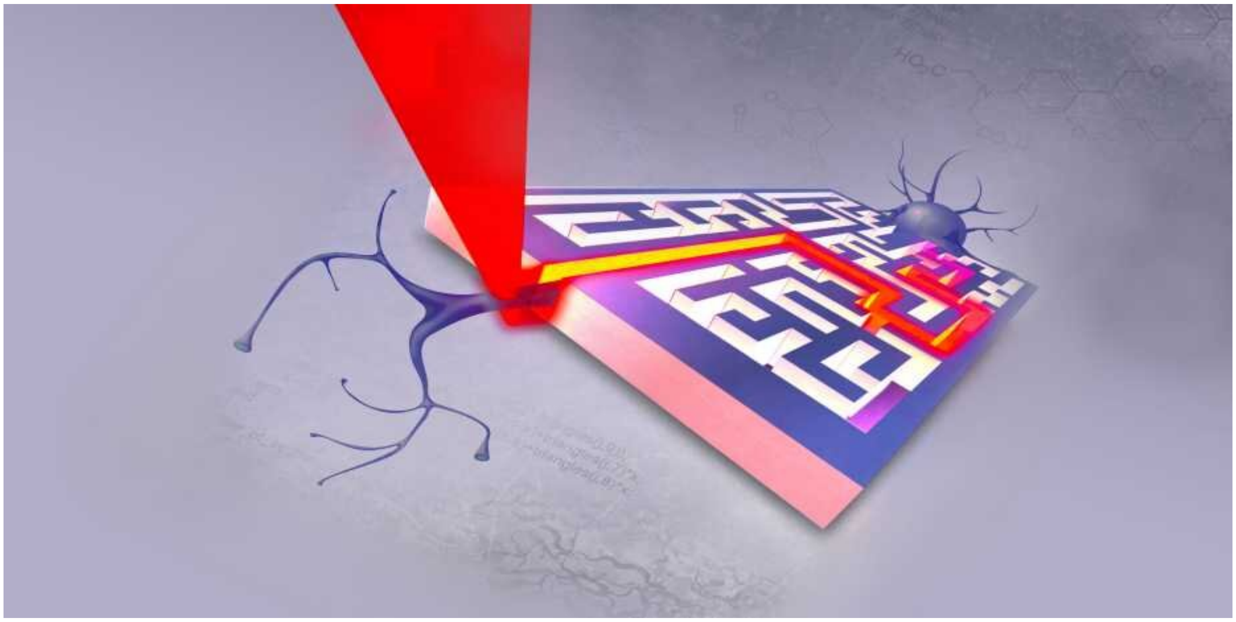

Neurons follow the mapped-out pattern in a hydrogel. Credit: ETH Zurich

ETH researchers have developed a new method in which they use light to draw patterns of molecules that guide living cells. The approach allows for a closer look at the development of multicellular organisms—and in the future may even play a part in novel therapies.

Highly complex organisms can arise from a single cell, which is one of the true miracles of nature. Substances known as morphogens have an important role in this development, namely by signalling to cells where they should go and what they should do. These signal molecules guide biological processes such as the formation of body axes or the wiring of the brain. To investigate such processes in more detail, researchers have to be able to position the signal molecules among living cells in three-dimensional space. This was made possible by a new method developed by Nicolas Broguiere and his colleagues in the research group headed by Marcy Zenobi-Wong. Their work is being published today in the journal *Advanced Materials*.

Drawing with light

"Our approach makes it possible to distribute bioactive molecules in a hydrogel with a high degree of precision," says Zenobi-Wong, Professor of Tissue Engineering and Biofabrication in the Department of Health Sciences and Technology at ETH Zürich. When living cells are encapsulated in the hydrogel, they can detect these biochemical signals. One such signal, nerve growth factor, determines the direction in which nerve fibres grow. In a method called two-photon patterning, the researchers used a laser to draw a 3-D pattern of this molecule in the hydrogel.

"Wherever the light is focused in the material, it triggers a chemical reaction that anchors the nerve growth factor to the hydrogel," Broguiere explains. "We carefully optimised the design of the photosensitive hydrogel so that the signal molecules attach only in the areas exposed to the laser—and nowhere else." Their new approach can create "paintings" of morphogens with details one thousand times smaller than a millimetre—the size of a single nerve fibre. The researchers could then observe through a microscope how the neurons follow the mapped-out pattern. "With this new method, we can now guide neurons effectively in 3-D, using their own biochemical language," Broguiere says.

When nerve fibres tear

Many biologists have long dreamt of instructing cells to grow in a particular direction. The new approach developed by the ETH research group brings them one step closer to fulfilling that dream. Zenobi-Wong and Broguiere believe their innovation also offers potential benefits for medicine—for example, if a nerve is severed during an accident, the reconnection happens haphazardly and full function is not restored. "I don't want to give the impression that we're ready to start treating patients with this method," Zenobi-Wong says, "but in the future, a refined version of our approach could help show neurons the right path directly in the body, thereby improving recovery from neural injuries."

More information: Nicolas Broguiere et al. Morphogenesis Guided by 3D Patterning of Growth Factors in Biological Matrices, *Advanced Materials* (2020). DOI: 10.1002/adma.201908299

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