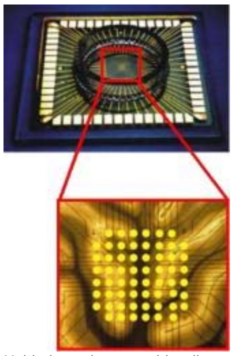
How chemists direct nerve cells

One of mankind's biggest dreams is being able to understand how the human brain works. As part of a cooperative project, Freiburg researchers are working to move a step closer to this dream. The chemists in the Freiburg team have already succeeded in chemically manipulating the surface of a specific chip, a multi-electrode array (MEA), in order to make neurones attach only at defined sites.

As part of this cooperative project, scientists from the Department of Chemistry and Physics of Interfaces at the Institute of Microsystems Technology (IMTEK) are working together with neurobiologists from the Bernstein Centre for Computational Neuroscience in Freiburg.



Multi-electrode array with cell culture dish. The section shows the electron array. (Illustration: Rühe group)

The targeted attachment of neurones on the chip leads to the connection of synapses – the contact sites between the neurones – in an ordered manner, which then forms a specific network. The project partners have already carried out the first measurements and hope that this will provide them with new information on the processing of brain activities.

Chemical tricks are not enough – understanding is a must

Prof. Jürgen Rühe's work group at the IMTEK has been analysing surface characteristics for more than 10 years. The researchers have found which surface characteristics are attractive to cells and which are not. "We performed some chemical tricks to make the cells attach to the sites we wanted them to," said Dr. Oswald Prucker, a scientist in Rühe's work group. However, the researchers did not know why the cells did this, and wanted to find out why some cells attached to specific surfaces, whereas others did not.

The members of Rühe's group are polymer scientists focusing on manipulating surfaces by coating them with thin and ultra thin plastic layers. For example, the Freiburg scientists were able to show that the attractiveness of a particular surface for cells did not only – as had long been assumed– depend on the degree of hydrophilicity. Hydrophilic substances repel proteins, and a surface without a protein layer repels cells," said Prucker. In consequence, the chemists are now coating the surface sections where no cells tend to grow with polymers that swell easily and that are interconnected by illumination. The scientists are also able to influence the attractiveness of surfaces by using charged polymers.

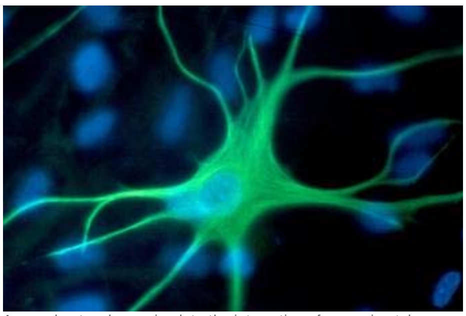
Nerve cells grow as desired

"We have not yet understood all the details of the interaction, but we have obtained some information as to how surfaces behave vis-à-vis cells and can make predictions on the attachment behaviour of the cells," said Prucker. In addition, the chemists are also able to deposit polymer layers on the chips in such a way as to make them stable throughout the whole experiment.

In cooperation with neurobiologists from the Bernstein Centre led by Dr. Ulrich Egert, the IMTEK scientists have used their experience and knowledge to coat commercially available MEAs so as to make the neurones form a square grid structure on the chip. The scientists' aim was to form a network that was complex at the same time as being clear and comprehensible.

Seeing what the entire network does

In the intact brain, each neurone is part of a network. The neurones alter according to processes in the brain and simultaneously manipulate the network through their actual presence. The researchers will now investigate these complex interactions using the networks on MEAs and the neurobiologists hope that the MEA measurements will provide them with results that come closer to the real situation in the brain than investigations using tissue samples. "The removal of a piece of brain impedes the function of this structure," explained Egert. Investigations involving such samples do not therefore exactly represent the interaction between the different neurones.



A neural network can simulate the interaction of approximately 100,000 neurones. (Photo: BCCN)

MEAs are coated in such a way as to make one cell attach to each of the electrodes on the chip. The electrodes are used to stimulate cells with electrical signals and record the electrical impulses that the cells receive. "We can determine the structure of the neural network and the probability of individual cells connecting with each other by way of the surface coating used. In the long term we hope to create stable structures that mature and eventually correspond to neurones in the adult state," said Egert. When activating a nerve cell through an electrode, the researchers are able to follow what the entire network does.

A large number of experiments is required to reach a stable network

Despite the experience of Rühe and his team, they still had to deal with some major challenges: “Neurones have different qualities to connective tissue cells or endothelial cells that cover the blood vessels,” said Prucker. It is impossible to culture neurones; instead, primary cells have to be used in the MEA experiments. “We had to carry out a large number of experiments before we were happy with the stability. We are now able to direct the neurones to the surfaces and keep them alive,” said Prucker. Egert has already conducted the first electrical measurements.

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