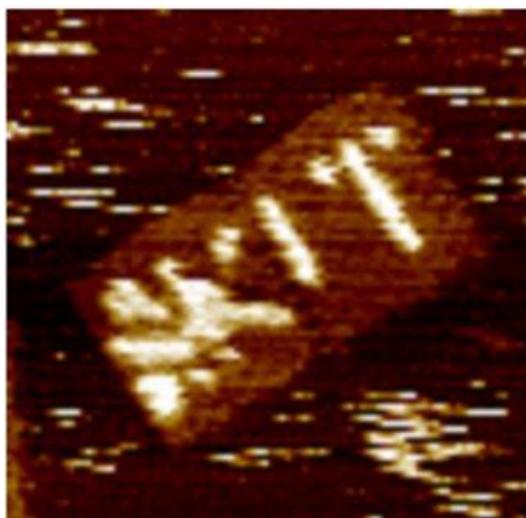


Unveiling the Grammar of Biological Cells

Chemists Develop MOSAIC Method to Decode not only Individual Cell Signals, but also Spatial Interactions of Various Signals



By means of the MOSAIC method, molecules can be arranged with high accuracy on a pegboard of 50 times 100 nm in size. (Photo: KIT)

Cells in the body exchange a number of signals with their surroundings. Deficient signal pathways may adversely affect the function of cells and cause diseases. However, we hardly know more than the vocabulary of cellular language. It is unknown how the “words” are combined in “sentences”. If cell grammar was known, complex processes in cells might be understood. Researchers of KIT have now presented a method to decode the grammar of cell signals in the journal *Angewandte Chemie (Applied Chemistry)*. DOI: 10.1002/anie.201509772

“Receptors on cell membranes react to a multitude of signal molecules. They represent the vocabulary of communication,” Christof Niemeyer of the Institute for Biological Interfaces of KIT explains. As a rule, several, spatially distributed receptors are addressed in parallel, just as in human language, where several words are combined in a sentence. The exact meaning of the individual words is determined by the context of all components of the sentence only. “With the help of our new MOSAIC method, we can now specifically decode not only vocabulary, but whole sentences of the cell language.”

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To address an individual cell with a defined sentence, Niemeyer and his team first fixed the desired signal molecules on a type of pegboard of about 100 nm in length with an accuracy of 5 nm. Then, dozens of these pegboards were applied to the cell carrier. In this way, many molecules can be arranged on a larger area with nanometer accuracy. "We succeeded in combining in the MOSAIC method both self-organization of molecules and a microscopic printing technology," Niemeyer says.

The pegboards are composed of long DNA molecules according to a precise blueprint. In a self-organized manner, the DNA molecule then folds to form a board of 100 nm in length and 50 nm in width, which can take up the desired signal molecules at defined places. The foundations of the pegboards are printed on the cell carrier from DNA fragments. These specific foundations are a few micrometers in diameter and can be printed on an area of up to 1 cm². By selecting appropriate DNA sequences, the pegboards adhere to the right foundation with the right orientation. To prove functioning of the MOSAIC (Multiscale Origami Structures as Interfaces for Cells) method, the researchers demonstrated by the first study that the model cell line MCF7 reacts differently to pegboards with variable arrangement densities.

"Many diseases, such as cancer or autoimmune disorders, can be attributed to the malfunction of receptors and signals in cells. Understanding complex signal pathways, hence, is the basis for future therapeutic approaches and drug development," Niemeyer emphasizes.

Multiscale Origami Structures as Interface for Cells (pages 15813–15817), Alessandro Angelin, Simone Weigel, Ruben Garrecht, Dr. Rebecca Meyer, Jens Bauer, Ravi Kapoor Kumar, Dr. Michael Hirtz, and Prof. Dr. Christof M. Niemeyer, DOI: 10.1002/anie.201509772, onlinelibrary.wiley.com/doi/10.1002/anie.201509772/abstract

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