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Multicoloured microcosm: 124 colours thanks to RGB technology

Red, green and blue: normally, no more than three different colours can be detected simultaneously in fluorescence microscopy. Thanks to recent RGB nanotechnology, similar to that used in computer monitors, it is now possible to generate 124 virtual colours under the microscope. The three primary colours are arranged in various mixing ratios on a special DNA lattice. This creates individual colour pixels under the microscope. The new method was developed by scientists at the Max Planck Institute of Biochemistry, Ludwig Maximilian University of Munich, Germany, and the Wyss Institute for Biologically Inspired Engineering at Harvard University in the US. The team's work was published in the journal *Science Advances*.

Biomedical research has made tremendous strides in recent decades. Using the latest microscopes, scientists are analyzing the function and interactions of molecules in cells with ever greater detail. Now, researchers are looking for methods to image multiple molecules simultaneously.

RGB nanotechnology

A team of scientists from Germany and the US headed by Ralf Jungmann and Peng Yin has now developed substances known as metafluorophors. "The technology can be compared to that of an RGB monitor," explains Jungmann, Leader of the Molecular Imaging and Bionanotechnology Research Group. To display a wide range of colours on a screen, each colour is mixed from the three primary colours: red, green and blue. "We've transferred this approach to the nanometre scale. Instead of a single fluorescence dye molecule, multiple fluorescent molecules are applied to a carrier material, which serves as a kind of experimental board. Depending on the proportion of the three primary colours, they appear in different colours under the microscope, comparable to nanometre-scale colour pixels on a computer screen. "

DNA origami

The team uses what is known as DNA origami for the lattice. These are self-organizing nanometre-scale DNA structures consisting of a long framework strand. The strand folds into a two- or three-dimensional shape in a predetermined manner. This strand is stabilized by around 200 short binding strands that bridge various parts of the framework. The researchers integrate small colour probes (normally red, green, or blue fluorescent probes) into the self-folding DNA structures. Depending on the colours to be generated, the number of required colour probes is calculated in advance. “If you compare the size of the lattice, which only measures 60 x 90 nanometres, with a pixel on a full-HD television, the entire screen would measure only around 0.2 x 0.1 mm,” Jungmann explains.

124 virtual colours
This nanotechnology approach currently offers a range of 124 virtual colours. “This figure can be adjusted in the future,” says Yin, a faculty member at the Wyss Institute and professor of system biology at Harvard Medical School. “Our study allows researchers to construct a large collection of metafluorophores with finely tuned optical properties. Those, in turn, can be used to image a variety of molecules in a sample, such as specific DNA or RNA sequences,” Yin says.

“At the moment, the DNA origami structures are still too bulky to diffuse into the interior of a cell. We’re looking for ways to allow flexible, short DNA molecules to cross cellular membranes and to take on their three-dimensional form only after binding to their target. We’ve outlined the first steps in this direction in the publication,” Jungmann says in anticipation of future research.

About Ralf Jungmann
Ralf Jungmann studied physics at Saarland University in Saarbrucken from 2001 to 2006. After graduating from the University of California Santa Barbara, USA, he earned a doctorate from the Technical University of Munich in 2010. This was followed by a postdoctoral fellowship at the Wyss Institute for Biologically Inspired Engineering at Harvard University. Since 2014, he has been head of the independent Molecular Imaging and Bionanotechnology Research Group at the Max Planck Institute for Biochemistry in Martinsried and Ludwig Maximillian University (LMU) in Munich. He has held a professorship in experimental physics at LMU since 2016. In 2016 Jungmann was awarded the ERC Starting Grant of the European Research Council.

About the Max Planck Institute of Biochemistry
The Max Planck Institute of Biochemistry (MPIB) belongs to the Max Planck Society, an independent, non-profit research organization dedicated to top level basic research. As one of the largest Institutes of the Max Planck Society, 850 employees from 45 nations work here in the field of life sciences. In currently eight departments and about 25 research groups, the scientists contribute to the newest findings in the areas of biochemistry, cell biology, structural biology, biophysics and molecular science. The MPIB in Munich-Martinsried is part of the local life-science-campus where two Max Planck Institutes, a Helmholtz Center, the Gene-Center, several bio-medical faculties of two Munich universities and several biotech-companies are located in close proximity. (http://biochem.mpg.de)

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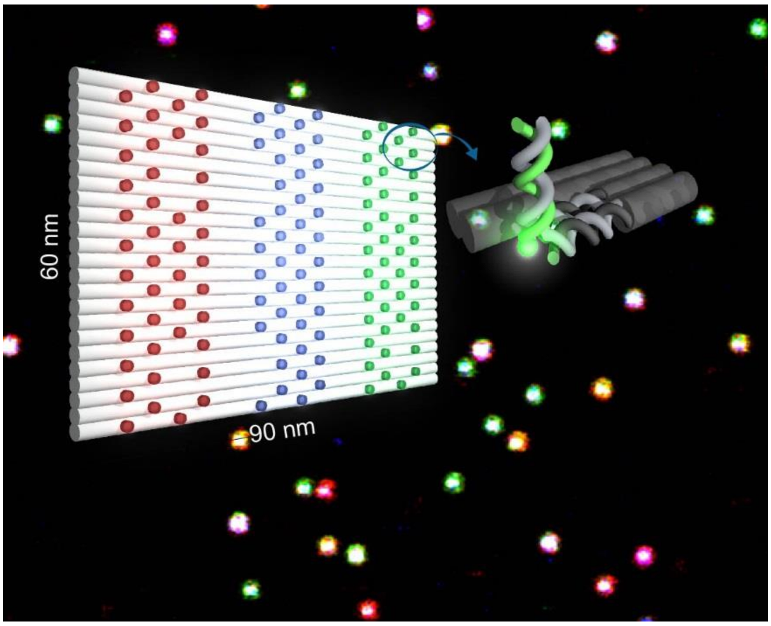
About The Wyss Institute for Biologically Inspired Engineering at Harvard University

The Wyss Institute for Biologically Inspired Engineering at Harvard University uses Nature's design principles to develop bioinspired materials and devices that will transform medicine and create a more sustainable world. Wyss researchers are developing innovative new engineering solutions for healthcare, energy, architecture, robotics, and manufacturing that are translated into commercial products and therapies through collaborations with clinical investigators, corporate alliances, and formation of new startups. The Wyss Institute creates transformative technological breakthroughs by engaging in high risk research, and crosses disciplinary and institutional barriers, working as an alliance that includes Harvard's Schools of Medicine, Engineering, Arts & Sciences and Design, and in partnership with Beth Israel Deaconess Medical Center, Brigham and Women's Hospital, Boston Children's Hospital, Dana–Farber Cancer Institute, Massachusetts General Hospital, the University of Massachusetts Medical School, Spaulding Rehabilitation Hospital, Boston University, Tufts University, Charité – Universitätsmedizin Berlin, University of Zurich and Massachusetts Institute of Technology. (http://wyss.harvard.edu)



Caption

Thanks to RGB nanotechnology it is now possible to generate 124 virtual colours under the microscope. The three primary colours are arranged in various mixing ratios on a special DNA lattice. This creates individual colour pixels under the microscope (background).

Original publication:

J.B. Woehrstein, M.T. Strauss, L.L. Ong, B. Wei, D. Y. Zang, R. Jungmann & Peng Ying "Sub-100-nm metafluorophores with digitally tunable optical properties self-assembled from DNA". *Science Advances*, June 2017
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