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DNA NANOSENSORS

Lab in a particle

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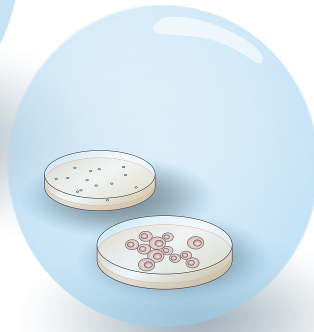

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Nanosensors allow us to probe otherwise inaccessible environments; however, existing technologies lack a data-storage mechanism and hence only permit on-line measurement. A smart nanomaterial that could both measure physicochemical properties and chemically store this information for readout at a later point in time would give us unprecedented access to complex systems (for example, biological processes within cells or underground water reservoirs). Wendelin Stark and co-workers at ETH, Zürich, have now created such a material, which they used as a nanospectrometer to measure the intensity of light exposure inside single cells.

A cornerstone of this work is DNA encapsulation technology developed at ETH by co-authors of the present study. Their stable DNA–silica hybrids can function as 'barcodes' — for example, to label industrial products or follow organisms within a food web — whereby the readout of the nucleic acid label can be easily performed by opening the silica in fluoride solution and transferring the DNA to a PCR machine. As Stark explains, "detection limits became lower and lower, and a few months ago, two of the co-authors managed to detect a single DNA–silica particle. In parallel, we were wondering: how small could we make a detecting unit?".

The key to imbuing this information-storage platform with the ability to respond to an environmental stimulus and record this data was to exploit established nucleic acid chemistry. First author of the paper, Gediminas Mikutis, explains: "We thought of designing a 'smart' material that allows the encapsulated DNA to perform something more than just carrying information. We came up with an idea to design DNA–silica particles in such a way that they respond to certain external physical or chemical stimuli." The researchers first realized this concept last year by creating a nanothermometer that operated on the basis of differences in the thermal stability of RNA and DNA. In their latest work, published in *Advanced Materials*, they used 'caged DNA' (DNA modifications that can be removed upon light irradiation) to create a nanosensor capable of recording cumulative light irradiation.

Their approach involves 'caging' three thymines with protecting groups, which is sufficient to prevent amplification using the PCR. If the DNA–silica probe is exposed to light, these nucleobases are deprotected and the DNA can then be amplified and quantitatively measured. Calibration of the sensors allows the cumulative light intensity in the microenvironment surrounding the sensors to be quantified. As a proof of concept, Stark's group successfully measured the light in single cells of the unicellular microorganism *Paramecium caudatum*. "The fact that we can measure a physical property inside individual cells and record the irradiation data as a DNA modification for later readout is the key concept of this work," says Mikutis.

Such caged-DNA nanosensors have great potential in various and otherwise inaccessible systems owing to their size, stability in harsh environments and very low cost, as Stark explains: "Think about following fish schools or underground water, or a microbial community — retrieving chemical and physical information on the nanoscale would give us a new way to look at ecological, biological, industrial or engineering questions." In addition, this new type of nanosensor may be used to simplify quality control processes, adds Mikutis, by "tracing raw and processed materials from the site of production across the supply chain to the final customer, describing what conditions they have 'seen' on their way to identify damage". Future work will probably see the integration of different caging groups responsive to different wavelengths to yield a 'nanospectrophotometer', as well as the development of multi-stimuli-responsive sensors that report on chemical (for example, pH and oxidation state) as well as physical properties.

Adam Brotchie

ORIGINAL ARTICLE Mikutis, G. *et al.* DNA-based sensor particles enable measuring light intensity in single cells. *Adv. Mater.* http://dx.doi.org/10.1002/adma.201504892 (2016)

FURTHER READING Paunescu, D., Fuhrer, R. & Grass, R. Protection and deprotection of DNA — high-temperature stability of nucleic acid barcodes for polymer labeling. *Angew. Chem. Int. Ed. Engl.* **52**, 4269–4272 (2013) | Puddu, M., Paunescu, D., Stark, W. J. & Grass, R. N. Magnetically recoverable, thermostable, hydrophobic DNA/silica encapsulates and their application as invisible oil tags. *ACS Nano* **8**, 2677–2685 (2014) | Puddu, M., Mikutis, G., Stark, W. J. & Grass, R. N. Submicrometer-sized thermometer particles exploiting selective nucleic acid stability. *Small* **12**, 452–456 (2016)