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BIOSENSORS

Functional tattoos

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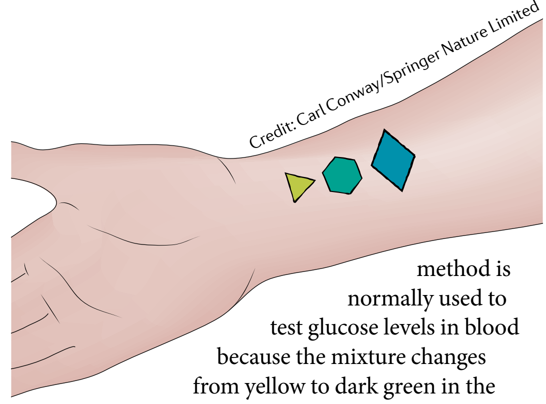
Metabolic disorders cause anomalous productions of chemicals in our bodies that lead to acid–base imbalance or serious diseases such as diabetes and hypoproteinaemia. People suffering from metabolic disorders need to constantly monitor the concentrations of specific metabolites in their bodies. Now, writing in *Angewandte Chemie International Edition*, Ali K. Yetisen and colleagues demonstrate the use of analyte-selective tattoo inks for colorimetric detection of metabolites.

Wearable sensors such as electrochemical on-skin patches or subcutaneous fluorescent fibres have been previously proposed. "Existing wearable devices are often bulky and have drawbacks, such as electrochemical signal drift, the time lag due to the indirect measurement, the required frequent calibration or photoinstability, that limit the continuous monitoring of biomarkers in the body," says Yetisen. "Tattoos are widely used as an artistic platform. This project aimed at replacing traditional non-functional tattoo inks with colorimetric biosensors to detect metabolites in the dermis."

The idea by Yetisen and co-workers is to quantify the biomarkers in the interstitial fluid surrounding the skin cells by injecting colorimetric biosensors directly into the skin. The chemical composition of the interstitial fluid closely mirrors that of the blood because of the constant exchange of metabolites, water and ions between the blood plasma and the interstitial fluid. Therefore, the group developed multiplexed colorimetric sensors that, once injected in ex vivo porcine skin tissue in the form of artistic tattoos, change colour in response to changes in the pH and concentrations of glucose and albumin. "Colorimetric sensors had previously been demonstrated in aqueous solutions and strip test format in vitro. These assays had been designed for one-off measurements. Our study explored the possibility of using these colorimetric sensors in a reversible manner for biomarker detection in vivo," explains Yetisen.



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The chromogenic dyes for the detection of pH include bromothymol blue, methyl red and phenolphthalein. These compounds are characterized by different pK_a values and are commonly used as indicators in different pH ranges. For example, bromothymol blue changes from yellow to blue as the surroundings transition from low (<6.0) to high (>7.6) pH values. Similarly, methyl red transitions from red (4.3) to yellow (6.2), and phenolphthalein from colourless (low pH) to green (neutral) to fuchsia (high pH).

In order to measure glucose concentration, Yetisen and colleagues chose a mixture of glucose oxidase (GOD), peroxidase (POD) and 3,3,5,5-tetramethylbenzidine. The GOD/POD enzymatic method is normally used to test glucose levels in blood because the mixture changes from yellow to dark green in the 2.0–50.0 mmol L^{-1} range.

Finally, dermal albumin sensing was achieved using 3′,3′′,5′,5′′-tetrachlorophenol-3,4,5,6-tetrabromosulfophthalein. This molecule forms a complex with albumin, and changes from yellow to green in response to increasing albumin concentrations.

The complex mixture of dyes was injected in ex vivo porcine skin tissues using a standard tattoo gun, and a smartphone camera was used to analyse the red, green and blue values for quantitative measurements.

"Our study demonstrates that colorimetric sensors can be injected into the dermis to form functional tattoos that change colour in the visible spectrum in a reversible and quantitative manner," remarks Yetisen. He concludes "the application of dermal sensors has implications in the continuous monitoring of biomarkers in interstitial fluid in point-of-care settings. However, future studies need to assess the immunogenicity and foreign body reaction to the colorimetric sensors for in vivo use."

Gabriella Graziano

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