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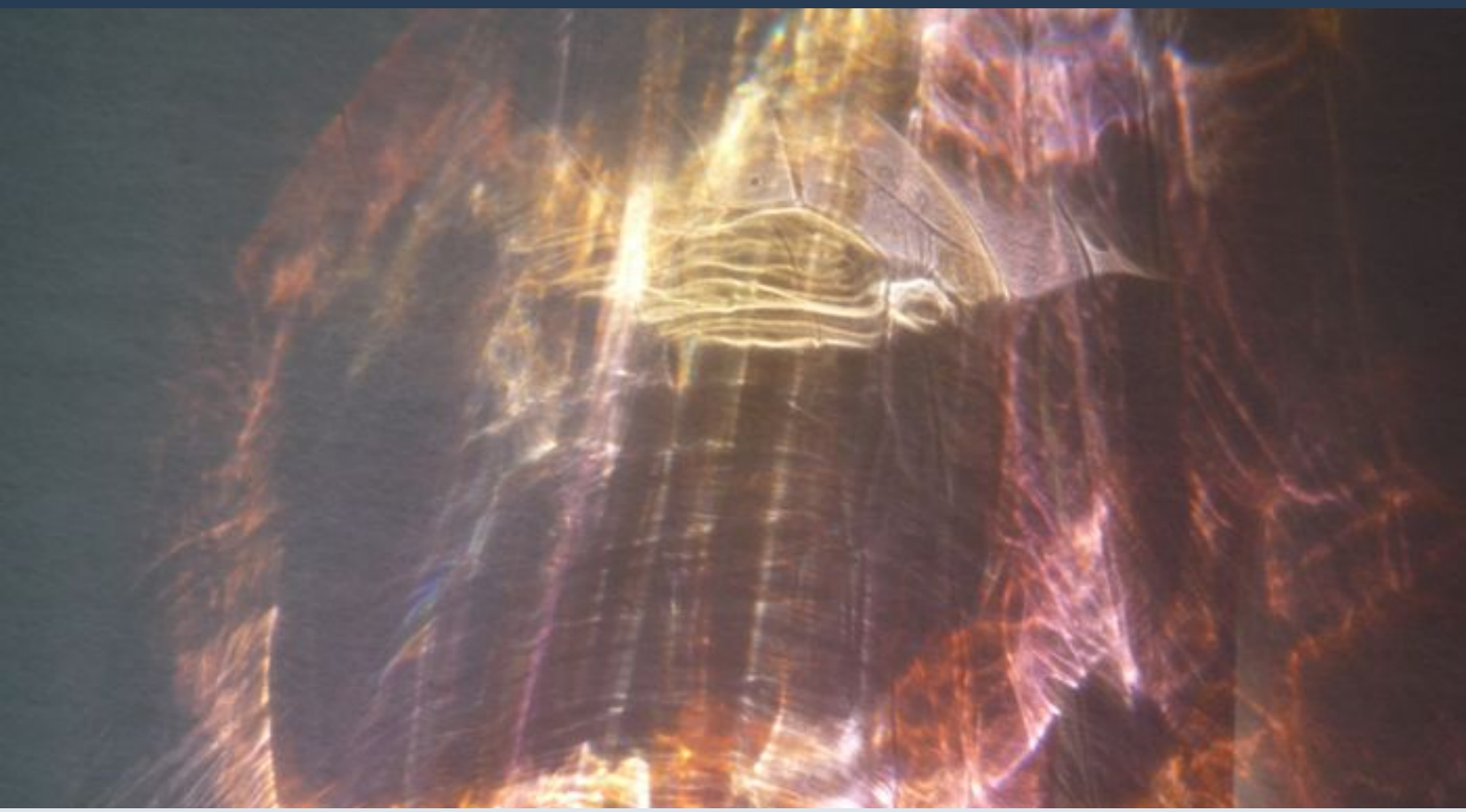
Surface Enhanced Raman Scattering (SERS) Molecule Detection: Novel Substrate Material and Manufacturing Process

Highly reproducible and tuneable manufacturing process for the generation of a novel substrate material for SERS.



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Seeking

Licensing

About **University of Birmingham**

At the University of Birmingham our research leads to new inventions and fuels innovation and business growth.

Background

The urgent need for rapid, early-stage detection of pathogens or disease-indicative biomarkers poses many challenges to the development of rapid and reliable tests or point-of-care (PoC)-diagnostics for human and animal health, food and water safety, and homeland security. Markers released in miniscule amounts (or at early stages of a disease) are undetectable with available biochemical techniques. Currently, no technology exists to measure these compounds with sufficient sensitivity and timeliness at PoC.

In terms of PoC-diagnostics, the golden standard technologies are ELISA, PCR and mass-spectrometry. However, these technologies are limited to laboratory use because they rely on sample purification and sophisticated instruments, are time and labour intensive, expensive and require highly-trained operators. In addition, the sensitivity of these technologies is unsatisfactory for detecting trace levels of biomarkers.

A range of Surface Enhanced Raman Scattering (SERS) diagnostic platforms have been also developed to address the above issues but key limitations exist. Current lithographic and nano-particle techniques are not cost effective and are unable to manufacture reproducible SERS active nano-features thereby limiting test specificity and sensitivity. SERS specificity and sensitivity is strongly correlated to size, shape and composition of the nano-metal features. Additionally, specific capture tags must be used for each target molecule, thereby significantly increasing test costs for each additional molecule considered, hence limiting the inherent SERS benefit of multiplexing.

Development and adoption of SERS has been hampered by the lack of a fabrication process that can repeatedly form nanostructured materials with a consistent signal enhancement, something which can only be obtained by a high level of substrate reproducibility. This challenge distils to a clear statement of the required level of reproducibility.

Tech Overview

Academics at the University of Birmingham, by an unprecedented combination of methods, have successfully developed lithographically defined, optimised hierarchical electrohydrodynamic (EHD)-SERS-substrates which are considerably more stable than nanoparticle-based systems, offering more degrees of freedom in the design and tuning of structural parameters, to enable reproducible, multiplex, high-SERS-enhancements. The developed novel EHD lithography uses electric field induced instabilities to generate advanced reproducible and tuneable SERS-substrates. Each of the resulting EHD-based SERS-active platforms demonstrated significant signal enhancement (>108), thus acting as an ideal detection platform. Importantly, each of the EHD-patterned individual structural units yielded a considerable SERS-enhancement enabling each structure to function as an isolated sensor, indispensable for multiplex detection.

This technology uses a highly reproducible and tuneable manufacturing process for the generation of a novel substrate material for SERS characterised by micro- and nano-scale features with:

- Signal Enhancement >10^8
- High degrees of design freedom;
- High accuracy (size, shape, structure, distribution);
- High reproducibility of measurement;
- Cost efficiency.

Further Details:

SERS is a highly sensitive spectroscopic technique enabling detection down to single molecule levels via enhancement of localized optical-fields on metallic sub-microstructures. It offers distinct advantages over other spectroscopic methods for sensing, including immediate detection of molecules without complex sample-preparation and undergoes no bleaching. SERS is the only detection technique that can be deployed out of a laboratory setting without a significant loss in performance and is capable of rapid sensing with considerably lower detection limits than high-performance liquid-chromatography. This unique set of attributes dramatically extends the range of available applications as wide as, for example, homeland security, chemical and biological detection, forensics, analytical chemistry, and pharmaceutical drug development. Additionally, it is well suited to address the challenges associated with PoC-diagnostics.

Intelligent engineering of carefully designed and optimised SERS-based devices enables the next-generation sensing technologies fulfilling multitude criteria with the substrate on which SERS is performed often being the critical component for successful detection.

A complementary portable technology is also under development. This is based on these controllable EHD sub-microstructures engineered for multiplexed-SERS detection and complemented with miniaturised optofluidic platforms for rapid detection of molecules down to picomolar concentrations from fluids or solid matter to enable real-time detection or diagnostics.

Stage of Development:

Highly reproducible substrates for SERS applications demonstrated significant signal enhancement (>10^8). Manufacturing rig and protocol established. Detection of TBI-biomarkers in blood successfully achieved. Integration of lab-on-chip surfaces into the optofluidic microchip and combination with portable Raman system for PoC testing currently under development.

Benefits

SERS substrate material offers enhanced specificity, sensitivity and multiplexing at low cost:

- Design freedom in tuning the size, shape, structure and composition (multi-layer materials) of the nano-scale columns
- Accuracy in terms of the pillar size, shape and structure at the micro- and nano-scale

- Consistency/Reproducibility – ensuring repeatability in manufacture across substrate surfaces and between substrate batches; hence, reproducibility of measurement;
- Low Cost – a simple manufacturing process enables high volumes of substrate material to be manufactured quickly

Elimination of expensive capture tags (e.g. antibodies) on the substrate surface:

- Accurate and reproducible substrate nano-features enable direct analysis of SERS spectra; thereby eliminating the need for expensive molecule capture tags

Rapid screening for a wide range of target molecules:

- Computational software enables rapid screening of SERS spectra for many target molecules stored on a database – 'Massive Multiplexing' within a single test

High signal enhancement (>108) for single molecule detection.

Applications

This is a platform technology.Current Application:

- Detection of biomarkers in Traumatic Brain Injury (TBI) for discriminating mild and severe TBI.

Potential Applications:

- Diagnostic PoC testing for detection of an ample spectrum of biomarkers. Indications we are currently focusing include stroke and sepsis.
- Pathogen detection
- Animal Health (diagnostics)
- Food and water safety (detection of pathogens, toxins etc.)
- Homeland security (chemical and biological agents etc.)
- Forensics
- Pharmaceutical Drug Development

Opportunity

This technology is available for licensing. The researchers are seeking partnerships for scale-up of SERS substrate manufacturing and co-development of portable handheld Raman Spectrometers enabling rapid screening of SERS spectra.

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Patents

- Patent application on manufacturing process and portable system being filed soon.