1、Micro-electro-mechanical (MEMS) sensor device

Quote Ref: KT050804

Keywords: Micro-Electro-Mechanical System (MEMS) sensor device, cyclically symmetrical microfabricated resonator, self-compensating, biosensor.

Of Interest To: Companies needing an accurate diagnostic platform within the Medical Diagnostics, Drug Discovery, Environmental, Food Safety, Bio-processing, Defence and Homeland Security sectors.

The Problem: The fundamental problem with conventional mass detection technologies, such as cantilevers, surface acoustic wave devices and quartz crystal microbalances are that they are not intrinsically self-compensating systems (i.e. they require stringent environmental control or external electrical compensation). For example, non-specific effects such as non-specific bio-molecular interactions and changes in temperature can drastically affect the achievable mass sensitivity of such resonant sensors.

The Solution: Scientists based at the Newcastle University have developed a novel resonant mass sensor detector that measures the frequency split produced in the vibration modes of a circular disc resonator. Specific recognition components are immobilized onto selected regions of the disc and the spatial distribution of added mass due to binding of analyte is designed to disrupt the axisymmetric mass distribution of the basic resonator. It is known that the modes of an axisymmetric disc occur in pairs and that each pair shares a common natural frequency, a property called 'modal degeneracy'. When additional mass is non-uniformly deposited (i.e. when analyte is bound to a recognition component immobilized on a region governed by one of the modes of vibration), the modal pairs no longer share this common frequency and the resonant frequencies of the modes split by an amount proportional to the amount of added mass (i.e. bound analyte). Although resonant mass sensors have been previously described using Rayleigh and Lamb waves and thickness shear vibrations in piezoelectric plates, they rely on determining an absolute change in the frequency of the resonator. Such devices operate in the MHz range and look to measure a

10~100Hz change in frequency. To achieve this, the resonator frequency must be stable and its change with physical parameters such as temperature and pressure and with non-specific biological binding events must be characterized. Normally, compensation for such effects is attempted by the use of parallel measurements with 'identical' resonators. This is notoriously difficult to achieve. The MEMS resonant mass sensor does not require this stability since it operates in a differential manner. In addition, the added sensitivity obtained in comparison with single frequency resonator devices is at least two orders of magnitude better. Advantages of this technology include: a) inherent design and performance characteristics which imply a two-order of magnitude increase in sensitivity, compared with existing mass sensors based on resonant structures, b) an in-built compensation mechanism for all non-specific interactions, c) dimensions and geometry which are particularly suited to the development of multi-sensor, multi-analyte arrays.

Position: National stage patents have been granted in Europe and the USA, with patent pending in Canada and Japan.

Opportunity: The technology is available for co-development and licensing.

2、Nanoscale sensors for in vivo genomic and proteomic analysis

Quote Ref: KT063552

Keywords: Quantum dot, probe, microscopy, imaging

Of Interest To: Biotechnology and life science companies with an interest in developing and commercialising innovative biological probes.

The Problem: Although a vast amount of information relating to gene/protein expression is now being produced, the analytical and molecular biology techniques employed to generate this data have a number of serious drawbacks. Techniques such as microarrays and 2D electrophoresis/MALDI-TOF fail to provide any direct information on the dynamic biochemical

processes occurring within cells and require cell lysis or disruption. Current labelling technology is largely based upon luminescent probes, (e.g., organic dyes and fluorescent proteins) whose limitations include susceptibility to photobleaching, high levels of background luminescence, pH dependent variations in the luminescence and difficulties in quantitation due to self-quenching effects. In addition, all luminescence probes suffer from limitations arising from the broad and relatively featureless nature of luminescence spectra and requirement for individual dyes to be excited using different wavelengths of light which makes it difficult to image different biological molecules simultaneously. Increasingly, quantum dots are being used in place of fluorescent dyes/proteins or as complementary tools for bioimaging applications in order to overcome many of these problems. However, luminescence spectra whether obtained using quantum dots or traditional fluorescent dyes/stains are only useful for determining spatial distribution and do not provide biochemical information on their own. In view of this there is a need to develop probes that not only allow determination of distribution in real time but also permit identification of unknown analytes and provide more detailed chemical/biochemical information from the medium in which the probes are deployed.

The Solution: Scientists based at the University of Newcastle have overcome the well documented technical difficulties in this field to develop nanoscale probes capable of generating luminescence and Raman 'fingerprint' spectra simultaneously. Due to their amenable surface chemistry these probes can be linked to a range of biorecognition molecules (e.g. nucleic acids and peptides) to enable specific targeting within the cell. The major advantage of this approach is that it not only permits spatial localisation of the target within the cell, but also allows collection of chemical information relating to the target and other cellular components in the vicinity by Raman spectroscopy. This information allows researchers to identify unknown analytes in real time based upon their unique chemical signatures, without the need for cell lysis and complex molecular biology techniques. The real time in-vivo detection of the biochemical interactions occurring within living cells will prove invaluable in the elucidation of intracellular processes. In addition, these probes retain their photoluminescence for prolonged periods, are highly resistant to photobleaching, stable in aqueous/biological media and non-toxic.

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Position: A PCT and UK patent application has been filed.

Opportunity: The technology is available for co-development and licensing.

3、Technology to pattern biological molecules to substrates in their active state

Quote Ref: KT063528

Keywords: Three-dimensional capture, biomolecule immobilisation and active state capture.

Of Interest To: Companies wanting to improve the sensitivity of existing biosensors and/or monitoring devices.

The Problem: One of the major limitations in the development of any biologically integrated device, such as a biosensor, is the ability to immobilise biomolecules (such as antibodies, nucleic acid sequences, enzymes etc.) in a highly accurate, site-specific way onto a defined target surface such that the biological species is immobilised at high density and with a high degree of biological activity. Existing technologies including; protein micro-contact printing, imprint and dip-pen lithography have been used to lay down specific biomolecules with high resolution, although these methods are only able to immobilise biomolecules within a few monolayers. Similarly, conventional lift-off techniques have been shown to be efficient in patterning chemically active groups onto solid substrates that subsequently react with biomolecules, however these techniques are also only capable of capturing biomolecules within a few monolayers. For biosensor applications, the underlying consequence of this type of immobilisation can result in limited sensitivity and dynamic range. Furthermore, since the surface background and the chemical pattern share a common planar dimension the control of non-specific adsorption of biomolecules becomes an issue. This limitation has partially been solved by the development of sol-gel bioencapsulation techniques in which the biomolecule is permanently encapsulated as an integral component of a covalently formed framework. This three-dimensional approach leads to higher density of biomolecules

although this is not entirely compatible with standard lift-off techniques since organic solvents often affect biological function irreversibly.

The Solution: Scientists based at the Newcastle University have developed a completely new patterning methodology to overcome these limitations. The process technology employs a three-dimensional polymer that is able to capture biomolecules at a high concentration whilst retaining their biological activity. The technique also has the advantage of being able to use conventional e-beam/UV lithography techniques for high resolution definition. The major advantage of this technology is the ability to generate a three-dimensional matrix in situ on solid substrates (e.g. silicon, gold) using the reactivity of a bifunctional silane (e.g. aminopropyltriethoxysilane) in a highly alkaline and non-nucleophilic medium (e.g. triethylamine). This technique is fully compatible with standard lithographic processes, leading to high resolution patterning at the micro- and nanoscale, with polymer thicknesses ranging from 50 nm to a few microns. Moreover, the 3-D porous structure gives the polymer a 'sponge-like' quality that captures biomolecules (e.g. antibodies, enzymes, nucleic acids, etc) via a simple incubation step. With this technique, biomolecules are patterned in an active state with optimal biological activity without the need for subsequent chemical manipulation. Once functionalised with the recognition biomolecule of interest, the sponge-like polymer is able to trap significant amounts of the target analyte with high specificity (high activity, low non-specific adsorption) and with a dynamic range extending over orders of magnitude.

Position: National stage patents have been filed in the following territories: Europe, USA, Canada and Japan.

Opportunity: The technology is available for co-development and licensing.

4、Thermostable DNA polymerase

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Keywords: PCR, Thermostable, Polmerase, Taq, dUTP, DNA, amplification

Of Interest To: Suitable for use in dUTP /Uracil glycosylase PCR product containment protocols. Increased efficiency for the improved amplification of long sequences and for the improved amplification of sequences rich in GC content.

The Solution: A novel thermostable DNA polymerase possessing enhanced performance characteristics when used in the PCR. The genetically engineered archaeal polymerase has found to have inherent benefits of improved thermostability and fidelity over Taq polymerase. The engineered polymerase has been designed to efficiently amplify DNA regardless of dUTP, while still retaining the fidelity and thermostability characteristics of the native enzyme.

Position: We are pursuing protection based on our PCT/GB03/001623 filing in the following territories: Germany, Netherlands, France, Denmark, Switzerland, Belgium, UK, Japan, Austalia, Canada and the USA.

Opportunity: The technology is available for exclusive licence in the food testing, forensics and veterinary fields and non-exclusively in the diagnostics field.

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