SOLUTION-BASED ANALYSIS OF MULTIPLE ANALYTES BY A SENSOR ARRAY: TOWARDS THE DEVELOPMENT OF "ELECTRONIC TASTE CHIPS"

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The development of a chip-based sensor array composed of individually addressable polystyrene - polyethylene glycol and agarose microspheres has been demonstrated. With the appropriate choice of a microporous bead, these structures can be combined with micromachined silicon wafers to generate novel micro-bead array sensors. These derivatized microspheres can be prepared in a highly parallel manner (10^6 beads/gram) using standard solid-state synthetic methods. This feature combined with the use of standard lithographic procedures capable of fabricating a large number of micro-arrays suggest that this sensor methodology may find utility for a number of interesting applications wherein inexpensive/disposable sensor elements are needed.

The microspheres are selectively arranged in micromachined cavities localized on silicon wafers. These cavities are created with an anisotropic etch and serve as miniaturized reaction vessels and analysis chambers. A single drop of fluid provides sufficient analysis media to complete ~100 assays in these microetch pits. The cavities posses pyramidal pit shapes with trans-wafer openings that allows for both fluid flow through the microreactors / analysis chambers as well optical access to the chemically sensitive microspheres. Identification and quantitation of analytes occurs via colorimetric and fluorescence changes to receptor and indicator molecules that are covalently attached to termination sites on the polymeric microspheres. Spectral data is extracted from the array efficiently using a charge-coupled device (CCD) allowing for the near-real-time digital analysis of complex fluids. The power and utility of this new mircobead array detection methodology is demonstrated here for the analysis of complex fluids containing a variety of important classes of analytes including acids, bases, metal cations, sugars and antibody reagents.

From a careful inspection of the component features of the taste chip system along with those associated with the mature, macroscopic methods, some of the advantages of the taste chip approach become apparent. The important considerations here are as follows. First, current generation of taste chips employ ~280 μm diameter beads which possess internal volumes of ~10 nl and these spheres reside in containers (i.e. etched wells) with volumes of ~30 nl. These low volume elements combined with fluidic channels capable of providing flow of 2 ml/min with passage of reagents through "drains" at the bottom of each well, lead to a very efficient delivery of reagents and washes. In a typical experiment, >50,000 well-dead volumes are used to rinse away excess reagents as compared to the 2-3 washes for commonly exploited enzyme-linked immunosorbent assay (ELISA) methods. Significant reduction in the taste chip background signal is obtained with the fluidic channels and drain features. Second, in contrast to ELISA in which antigen-antibody interactions are built up from and limited by a single layer on the bottom surface of the well, the taste chip total analysis system benefits from the use of porous beads. This feature allows for the use of significantly higher relative amounts of capture agents. Moreover, the signal is localized in a confined volume allowing for the production of larger signals. Third, fluids are transported rapidly into the analysis chamber using a pressure driven flow or capillary forces. The active transport of reagents and small effective feature sizes of the components used here allow for the more rapid delivery of the reagents and washes. Slow steps associated with diffusion of reagents over macroscopic distances, which is prevalent with the majority of the system. Finally, the ability to complete a full assay at each bead site allows for the simultaneous execution of multiple trials. This capacity provides more accurate results through signal averaging and allows for multiplexed testing to occur as demonstrated here for the initial established methods, are minimized with taste chip cardiac theme chip.

The taste chip adaptation of immunological assays described here has yielded a functional miniaturized platform that exhibits assay characteristics (analytical range, detection threshold and coefficient of variance) superior, in many respects, to the mature macroscopic analogs. Adaptations of the taste chip methodology to important multianalyte immunoassay systems for the areas of human health, veterinary sciences, environmental testing, drug monitoring, toxin detection, military and food / beverage processing are currently in progress.

References

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