

ENZYMATIC SIGNAL GENERATION AND DETECTION OF BINDING COMPLEXES IN STATIONARY FLUIDIC CHIP

RELATED APPLICATIONS

[0001] This application is related to "DEVICE AND METHOD FOR PARTICLE COMPLEX HANDLING" (07070-2011600), "METHOD AND DEVICE FOR BIOMOLECULE PREPARATION AND DETECTION USING MAGNETIC ARRAY" (07070-2005700), and "PROGRAMMABLE ELECTROMAGNETIC ARRAY FOR MOLECULE TRANSPORT" (07070-2011800), which are incorporated herein by reference.

FIELD OF INVENTION

[0002] The embodiments of the invention relate to devices for conducting biomedical assays, methods of making such devices, and methods of detecting the presence of an analyte using such devices. More specifically, the embodiments relate to devices and methods that combine fluidic devices and magnetic microarrays with an integrated circuitry element that perform versatile and/or convenient analysis of an analyte with design flexibility. The invention transcends several scientific disciplines such as nucleic acids chemistry, organic chemistry, surface chemistry, analytical chemistry, physics, engineering, microelectronics, and medical diagnostics.

BACKGROUND

[0003] Chemical analysis and medical diagnostics commonly use absorption, fluorescence, chemiluminescence, UV-Vis and Raman scattering to detect the presence of an analyte. For example, enzyme-linked immunosorbent assays (ELISA) are widely used to detect an analyte. ELISA assays are typically performed in microwell plates, and require multiple steps of adding reagents, washing the reactant plates, and applying a reaction substrate that is converted to provide a chromogenic or fluorescent signal. Furthermore, its detection limit ranges from the micromolar to picomolar. For markers with low copy numbers, more sensitive detection technology is needed.

[0004] The current methods and devices for detecting the presence of an analyte in a sample have multiple drawbacks. First, the sizes of the devices are too big to be used in field applications or at home environment, such as point-of-care (POC) environment. Second, the current devices require a large amount of sample, which not only is infeasible for certain applications, but also hinders activities such as mixing and heating of the sample required for many analyses. Third, the current devices have complex structures for fluidic control and are often not self-contained. Fourth, current devices are limited by their detection sensitivity. Fifth, the current devices are often designed for specialized applications, e.g. protein analysis only, or nucleic acid only. Thus, there is a need for miniaturized, integrated, and versatile devices for analysis of a sample suspected of containing an analyte that can perform on-site, flexible, rapid, sensitive, and/or efficient analysis.

BRIEF DESCRIPTION OF THE DRAWINGS

[0005] FIG. 1 illustrates an embodiment of the invention that comprises a fluidic network having a sample zone and other fluidic zones, associated with a magnetic microcoil

array, a detection element and an integrated circuitry component, linked to a circuit board.

[0006] FIG. 2 illustrates an exemplary top-down view of a magnetic microcoil array showing the movement of magnetic particles.

[0007] FIG. 3 illustrates a top-down view and cross-section view of the fluidic network.

[0008] FIG. 4 illustrates a more detailed top-down view and cross-section view of the fluidic network.

[0009] FIG. 5 illustrates a cross-section view of the fluidic network showing the movement of the binding complex to the detection zone.

[0010] FIG. 6A illustrates the use of the fluidic network in moving magnetic particles. FIG. 6B illustrates the fluorescence of a mixture of magnetic particles and Qdots, before and after washing. FIG. 6C quantifies the fluorescence of the samples in the tubes from FIG. 6B and samples taken from the fluidic network during FIG. 6A. FIG. 6D quantifies on-chip chemiluminescent detection of PSA.

[0011] FIG. 7 illustrates the formation of sandwich binding complexes ("sandwich binding" and "tandem binding") and a competitive binding complex.

[0012] FIG. 8 illustrates the use of codes with a magnetic affinity complex and a magnetic signal affinity complex.

[0013] FIG. 9 illustrates the general signal generation scheme for enzymatic signal amplification.

[0014] FIG. 10 illustrates the preparation of a signal particle.

[0015] FIG. 11 illustrates an example of optical signal generation and detection: chemiluminescence using AP.

[0016] FIG. 12 illustrates an example of optical signal generation and detection: chemiluminescence using HRP.

[0017] FIG. 13 illustrates an example of optical signal generation and detection: absorption using HRP.

[0018] FIG. 14 illustrates an example of optical signal generation and detection: fluorescence using HRP.

[0019] FIG. 15 illustrates an example of optical signal generation and detection: fluorescence using HRP & glucose oxidase.

[0020] FIG. 16 illustrates an embodiment of the particle (or molecule) transport device of the invention, showing major components which are (1) a fluidic network, e.g., a biochip, (2) an electromagnetic array, (3) a circuitry board; and (4) computer.

[0021] FIG. 17 illustrates electromagnetic coils of the array, showing reversible magnetic polarities, magnetic field gradients (flux) controlled by current flow directions and strength, and flux distributions that can be optimized by varying geometry (shapes) of the heads of the cores.

[0022] FIG. 18 illustrates a power delivery system, showing an example of ways to minimize the number of power switches.

[0023] FIG. 19 illustrates an experiment demonstrating magnetic particle concentrating, transporting by varying magnetic fields.

[0024] FIG. 20 illustrates a prototype system, showing the coil (inductor) array, switches and other electronic control elements, together with a prototype fluidic chip (biochip).