A Lab-on-Chip for Biological Fluids Analysis

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The same basic fabrication concepts and materials which have made microelectronics successful are now being adapted to making low-cost, small, high-performance biomedical based systems devices, e.g., a laboratory on chip for biochemical analysis. Microtechnology enables the fabrication of precise and small structures (such as microchannels, micromixers, microfilters, micropumps, microvalves, microchambers) in glass, quartz or silicon wafers. The lab-on-chip has the potential to highly automate the sample preparation procedures, drastically reduce costs associated with laboratory experiments and diagnostic testing. Moreover, the lab-on-chip can be used for different analysis; analytical testing costs can be extraordinarily reduced in several ways, since nanoliter quantities of reagents and samples are needed.

The biological fluids (such as blood, sweat, saliva and urine) have special interest for medical diagnostics and are potential candidates for the lab-on-chip. For example, a physician can perform sophisticated diagnostic testing at a patient's bedside in few minutes with minimal distress. The lab-on-chip also provides a significant improvement in lab safety. Spills, explosions, and other laboratory accidents that can occur with conventional sample preparation techniques are not a problem with lab-on-chip testing.

This abstract presents a microsystem for urine analysis, which includes: integrated photodiodes, optical filters, microelectronics and a lab-on-chip. The principle used to force fluids to move through the lab microchannels is Capillary Electrophoresis (CE). In CE application of a voltage gradient causes ions in the fluid to migrate toward an oppositely charged electrode.

The microfluidic device is fabricated in a glass wafer. Wet-etching techniques applied to the wafer glass allows the fabrication of microchannels, mixerchannel and detection chamber. Typical microchannel dimensions are 20-40 um deep and 100-200 um wide. The required microchannel length for CE operation is about 2 mm.

The silicon wafer has an integrated photodiode, an optical filter limiting the optical range of interest and readout electronics with a light-to-frequency converter. All these functions are done in CMOS technology in a standard process.

Both wafers (the glass wafer containing the microlaboratory and the silicon wafer including the optical detector and microelectronics) are thermally sealed with wafer-bonding techniques.

Proteins (e.g. albumin) in urine are the first target of the lab-on-chip. The protein detection system consists in color analysis based on optical absorption. A monochromatic light beam or white light must be directed into the detection chamber, where some spectral components are absorbed or reflected. The intensity of the transmitted light when measured by the photodetector can therefore give information about the proteins concentration. Experimental results (with test kits) show maximum absorption at 628 nm when a albumin sample reacts with bromcresol green (0.30 mmol/l, pH=4.2). Albumin is present in human urine in appreciable quantities (10-140 mg/l, normal values) that allows microliter manipulations.