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BIOCHIPS IN FOOD TECHNOLOGIES

One of the modern technology development trends is the biochips' elaboration and introduction. In this article characteristics and the biochip industry development stages are given, also the principle schemes are considered. It is shown, that due to the biochips' advantage, they are expedient to use for the food products' analysis realization to determine their high quality.
Keywords: *biochip, biosensors, microarray.*

БИОЧИПЫ В ПИЩЕВЫХ ТЕХНОЛОГИЯХ

Одним из современных направлений развития технологий является разработка и внедрение биочипов. В статье дана характеристика и приведены этапы становления индустрии биочипов, рассмотрены их принципиальные схемы. Показано, что благодаря преимуществам биочипов их целесообразно использовать для проведения анализов пищевых продуктов на доброкачественность.
Ключевые слова: *биочип, биосенсоры, матрица.*

БІОЧИПИ В ХАРЧОВИХ ТЕХНОЛОГІЯХ

Одним із сучасних напрямків розвитку технологій є розробка та впровадження біочипів. У статті надана характеристика та наведені етапи становлення індустрії біочипів, розглянуті їх принципові схеми. Показано, що завдяки перевагам біочипів їх доцільно використовувати для проведення аналізів харчових продуктів на доброякісність.
Ключові слова: *біочип, біосенсори, матриця.*

I. INTRODUCTION

Contaminated food has been in the news a great deal lately. These incidents expose the obvious need for testing food samples for the presence of many different, harmful substances in a single, fast, affordable test.

In molecular biology, biochips are essentially miniaturized laboratories that can perform hundreds or thousands of simultaneous biochemical reactions. Biochips enable researchers to quickly screen large numbers of biological analytes for a variety of purposes, from disease diagnosis to detection of bioterrorism agents.

II. MAIN PART

One of the first portable, chemistry-based sensors was the glass pH electrode, invented in 1922 by Hughes. Measurement of pH was accomplished by detecting the potential difference developed across a thin glass membrane selective to the permeation of hydrogen ions; this selectivity was achieved by exchanges between H+ and SiO sites in the glass. The basic concept of using exchange sites to create permselective membranes was used to develop other ion sensors in subsequent years. For example, a K+ sensor was produced by incorporating valinomycin into a thin membrane. Over thirty years elapsed before the first true biosensor (i.e. a sensor utilizing biological molecules) emerged. In 1956, Leland Clark published a paper on an oxygen sensing electrode. This device became the basis for a glucose sensor developed in 1962 by Clark and colleague Lyons which utilized glucose oxidase molecules embedded in a dialysis membrane. The enzyme functioned in the presence of glucose to decrease the amount of oxygen available to the oxygen electrode, thereby relating oxygen levels to glucose concentration. This and similar biosensors became known as enzyme electrodes, and are still in use today.

In 1953, Watson and Crick announced their discovery of the now familiar double helix structure of DNA molecules and set the stage for genetics research that continues to the present day. The development of sequencing techniques in 1977 by Gilbert and Sanger (working separately) enabled researchers to directly read the genetic codes that provide instructions for protein synthesis. This research showed how hybridization of complementary single oligonucleotide strands could be used as a basis for DNA sensing. Two additional developments enabled the technology used in modern DNA-based biosensors. First, in 1983 Kary Mullis invented the polymerase chain reaction (PCR) technique, a method for amplifying DNA concentrations. This discovery made possible the detection of extremely small quantities of DNA in samples. Second, in 1986 Hood and co-workers devised a method to label DNA molecules with fluorescent tags instead of radiolabels, thus enabling hybridization experiments to be observed optically.

The rapid technological advances of the biochemistry and semiconductor fields in the 1980s led to the large-scale development of biochips in the 1990s. At this time, it became clear that biochips were largely a "platform" technology which consisted of several separate, yet integrated components. The actual sensing component (or "chip") is just one piece of a complete analysis system. Transduction must be done to translate the actual sensing event (DNA binding, oxidation/reduction, etc.) into a format understandable by a computer (voltage, light intensity, mass, etc.), which then enables additional analysis and processing to produce a final, human-readable output. The multiple technologies needed to make a successful biochip — from sensing chemistry, to microarraying, to signal processing — require a true multidisciplinary approach, making the barrier to entry steep. One of the first commercial biochips was introduced by Affymetrix. Their "GeneChip" products contain thousands of individual DNA sensors for use in sensing defects, or single nucleotide polymorphisms (SNPs), in genes such as p53 (a tumor suppressor) and BRCA1 and BRCA2 (related to breast cancer). The chips are produced using microlithography techniques traditionally used to fabricate integrated circuits.

Today, a large variety of biochip technologies are either in development or being commercialized. Numerous advancements continue to be made in sensing research that enable new platforms to be developed for new applications. Cancer diagnosis through DNA typing is just one market opportunity. A variety of industries currently desire the ability to simultaneously screen for a wide range of chemical and biological agents, with purposes ranging from testing public water systems for disease agents to screening airline cargo for explosives. Pharmaceutical companies wish to combinatorially screen drug candidates against target enzymes. To achieve these ends, DNA, RNA, proteins, and even living cells are being employed as sensing mediators on biochips. Numerous transduction methods can be employed including surface plasmon resonance, fluorescence, and chemiluminescence. The particular sensing and transduction techniques chosen depend on factors such as price, sensitivity, and reusability.

The microarray — the dense, two-dimensional grid of biosensors — is the critical component of a biochip platform. Typically, the sensors are deposited on a flat substrate, which may either be passive (e.g. silicon or glass) or active, the latter consisting of integrated electronics or micromechanical devices that perform or assist signal transduction. Surface chemistry is used to covalently bind the sensor molecules to the substrate medium. The fabrication of microarrays is non-trivial and is a major economic and technological hurdle that may ultimately decide the success of future biochip platforms. The primary manufacturing challenge is the process of placing each sensor at a specific position (typically on a Cartesian grid) on the substrate. Various means exist to achieve the placement, but typically robotic micro-pipetting or micro-printing systems are used to place tiny spots of sensor material on the chip surface. Because each sensor is unique, only a few spots can be placed at a time. The low-throughput nature of this process results in high manufacturing costs.

Fodor and colleagues developed a unique fabrication process (later used by Affymetrix) in which a series of microlithography steps is used to combinatorially synthesize hundreds of thousands of unique, single-stranded DNA sensors on a substrate one nucleotide at a time. One lithography step is needed per base type; thus, a total of four steps is required per nucleotide level. Although this technique is very powerful in that many sensors can be created simultaneously, it is currently only feasible for creating short DNA strands (15…25 nucleotides). Reliability and cost factors limit the number of photolithography steps that can be done. Furthermore, light-directed combinatorial synthesis techniques are not currently possible for proteins or other sensing molecules.

As noted above, most microarrays consist of a Cartesian grid of sensors. This approach is used chiefly to map or "encode" the coordinate of each sensor to its function. Sensors in these arrays typically use a universal signalling technique (e.g. fluorescence), thus making coordinates their only identifying feature. These arrays must be made using a serial process (i.e. requiring multiple, sequential steps) to ensure that each sensor is placed at the correct position.

"Random" fabrication, in which the sensors are placed at arbitrary positions on the chip, is an alternative to the serial method. The tedious and expensive positioning process is not required, enabling the use of parallelized self-assembly techniques. In this approach, large batches of identical sensors can be produced; sensors from each batch are then combined and assembled into an array. A non-coordinate based encoding scheme must be used to identify each sensor.

The most common biochip scheme is shown on figure 1.

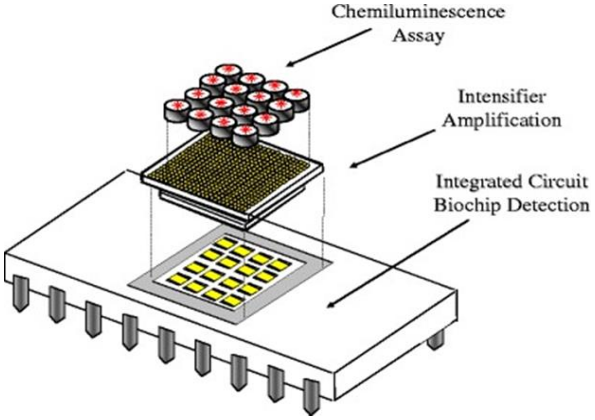

Figure 1 *– The most common biochip scheme*

University of Rhode Island researchers have invented a technology that uses inexpensive fiber-optic biochips (probes) to detect pathological bacteria in foods in real-time. Currently, food samples must be sent to a lab for testing, and obtaining results takes several days. A fiber-optic probe, however, can be inserted into foodstuffs at the processing plant to test levels of bacteria in about an hour.Unlike other efforts, such as one at Purdue University, the Rhode Island approach couples biosensor techniques with fiber-optic technology. By dipping the end of an optical fiber into the food to be tested, the new system can accurately detect and quantify the levels of pathogen present.First, microscopic beads called microspheres are prepared by coating them with antibodies that bind to the pathogen cells to be tested. The microspheres are then mixed into a sample of the food, and pathogens begin immediately to bind to the spheres.

After about an hour, a fiber-optic probe can be inserted into the food to measure its pathogen levels. Each microsphere is labeled with a fluorescent dye so that it can be easily counted with software that reads the fiber-optic probe signal. Different pathogens can be tested simultaneously by mixing in different microsphere beads.The beads are magnetic, simplifying the process of focusing them in front of the optical fiber. A laser-based measurement algorithm running on data from the optical fiber enables the biosensor to measure the levels of each selected pathogen for which a microsphere bead was previously mixed. The measurement process takes only 60 to 90 seconds (after the beads have been mixed in for an hour).For the long term, the researchers are planning a handheld surface-scanning system, similar to a laser scanner, that can be held over any food to detect pathogens without touching it.

The global value of the overall biochips market, by end use was $3.5 billion in the year 2010. The size of the biochips market will increase from $3.9 billion in 2011 to nearly $9.6 billion by 2016, a compound annual growth rate (CAGR) of 19.5%. Tools markets for biochips will experience slowing growth due to maturation of some market segments-including gene expression analysis and single nucleotide polymorphism (SNP) genotyping. This market will grow at a CAGR of 8.4% from 2011 to 2016 and will reach to $2.7 billion. The diagnostics market segment is set for high growth. This market was around $1.05 billion in 2010 and is expected to reach $2 billion by 2011. The diagnostics market is forecasted to grow at a CAGR of 28.2% and to reach $4.1 billion by 2016.Global value of biochip products is shown on figure 2.

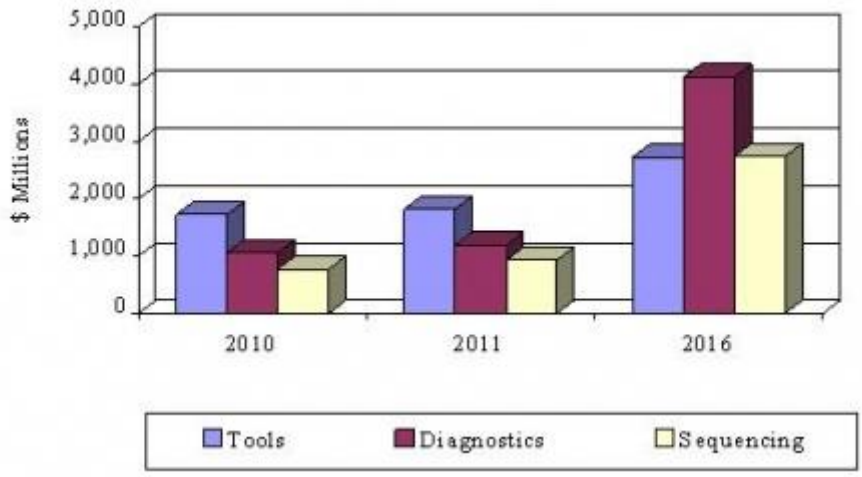

Figure 2 *– Global value of biochip products, 2010-2016 ($ MILLIONS)*

III. CONCLUSIONS

Biochip Array Technology (BAT) is an innovative assay technology for multi-analyte screening of biological samples in a rapid, accurate and easy to use format. The future aim is to develop biochips capable of detecting genetically modified organisms (gmo's) and other harmful substances in food.

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