Trends in biosensors and bioelectronics

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Recent developments in biotechnology have been remarkable. This paper describes the trends in research on biosensors and biochips, the field in which we have been studying. First, the processing technology for semiconductors that has been used for the fabrication of biosensors is described; then, our attempts to commercialize the biosensors we have developed will be explained. Thirdly, research and development of biosensors for environmental analysis will be introduced, and, finally, DNA chips and protein chips, which are called biochips and are attracting a great deal of attention, will be presented.

1. Application of semiconductor processing technology

We have developed microelectrodes and micro oxygen electrodes, which are used for the measurement of hydrogen peroxide, by making use of the semiconductor processing technology. Furthermore, we have been conducting basic studies on biochips.

In the fabrication of microelectrodes used for measuring the concentration of hydrogen peroxide, three gold electrodes were formed on a sapphire substrate by the vacuum deposition method, and enzyme was fixed on them using photoresist. In this way, glucose sensors and other sensors were produced. This technology will be used in biosensors for the measurement of glucose in urine from now.

In the initial stage of the development of microelectrodes for the measurement of oxygen concentration, the oxygen electrodes were formed on silicon substrates utilizing microfabrication technology. Futhermore, we succeeded in large-scale production by applying micromachine technology, and, as a result, micro oxygen sensors are now being placed on the market.

To make microbiosensors, enzymes or microorganisms are fixed on these oxygen-sensing chips by the use of photoresists. Such amperometric biosensors and micro-biosensors made by the use of semiconductor processing technology are currently produced only in Japan. Japan can apply its semiconductor processing technology, to the production of biosensors since it has special techniques.

2. Examples of commercialization research

The following are examples of attempts to transfer and commercialize technologies that have been developed by universities to private companies. All of these technologies have been or are being transfe red at present.

The first example is the development of immunochips, which are small chips used to measure infectious diseases. The second example is the glucose sensor used for the diagnosis of diabetes.

Immunochips used to check for infectious diseases utilize the phenomenon in which latex beads agglomerate within a short time by the antigen-antibody reaction when certain pulses are applied and, then, measure for infectious diseases rapidly with high sensitivity. Compared to the conventional immunoassay method, the sensitivity is increased by a factor of 100 to 1000. This breakthrough technology reduces the very high analysis cost of the conventional method to a level of 1/100 to 1/1000. Three companies are now applying for the license of this technology with the intention to complete new type immunochips.

Next, I introduce glucose chips that can hypoglycemia. While the detection of hypoglycemia plays a very important role when administering insulin, conventional glucose chips cannot be used for detecting hypoglycemia. Solving this problem, we have succeeded in developing glucose chips that can apply to the fields where conventional glucose chips cannot use. The technology to produce these chips has already been transferred to a company and commercial products are scheduled for introduction into the market by this autumn.

Toilets equipped with glucose sensors for the measurement of glucose in urine have also been developed. These toilets have been developed for the treatment of diabetics. When a diabetic patient sits on this type of a toilet, the concentration of glucose in urine is measured and that of blood sugar is predicted. Ten years ago, I proposed the development of biosensors for toilets and have been giving lectures on this subject all over the world. Thus, my dream has been finally realized and will now be commercialized. The data obtained when use the toilet are sent to doctors in hospitals by the internet to diagnose. My idea has led to a dream come true where a toilet is transformed into a clinical laboratory for a life-style linked ailment.

3. Research and development of biosensors used for environmental analysis

The BOD (Biochemical Oxygen Demand) sensor is a device that enables easy measurement of how river water or industrial wastewater is polluted with organic materials. Because river water contains such materials as cellulose, lignin and humic acid that are difficult to decompose, conventional BOD sensors cannot be used for the measurement of river water. We applied pseudomonas sp., to a BOD sensor and succeeded in measuring BOD values of river water containing above organic materials.

This BOD sensor is much more sensitive than conventional BOD sensors, making it possible to monitor the quality of river water. The technology used in this sensor has just been transferred to a manufacturer, and the prototype sensors are fabricated. After practical studies, these sensors will be commercialized in the future.

4. Research and development of biochips

DNA chips enable easy determination of whether a person is susceptible to a certain disease, because it is possible to elucidate SNP (single nucleotide morphorism)—the difference of single DNA base—using DNA chips. For example, it appears there is a difference in the level of sensitivity to diseases between Asians and Westerners due to the difference in SNP.

Plasma polymerized films are formed on a glass substrate using microfabrication technology, and a compound called streptavidin is embedded in the films. By forming plasma polymerized films of just about 30 angstroms, streptavidin is embedded appropriately. Then, DNA modified with biotin is combined with the streptavidin. In this way, DNA chips are produced by embedding protein in the plasma polymerized films formed by using microfabrication technology. This method can be used for not only fixing DNA, but also for fabricating protein arrays by embedding antibodies after streptavidin is embedded. By utilizing semiconductor technology in such a way, DNA arrays and protein arrays can be produced on a massive scale. Since it is expected that medical services tend to lean towards so-called tailor-made services, the measurements of DNA and proteins using such chips will become indispensable for medical care.

We will be starting a new project from this April. This project, "Focus 21," is being sponsored by the Ministry of Economy, Trade and Industry of Japan and it aims at the research and development of "protein system chips" (or may be called "system biology on silicon chips"). The idea of this project is to detect proteins that cause diseases by separating proteins on a small chip and labeling them with fluorescence, etc., so that they can be detected using a highly sensitive detector and displayed on a screen. The plan is to spend US$4,000 per year on research for three years from this April, with the total amount reaching about ¥1200 million. As an objective of this project, we plan to make possible diagnoses of diseases by comparing proteins of normal tissues with those of tissues in disease tissue to identify proteins that appear or disappear in particular disease states. Furthermore, we think these chips will play an important role in the development of new medicines by the use of genomics.

Details of the mechanism cannot be described here as the project has yet to begin, but we expect such chips will be used for medical care in three years from now making it possible to diagnose diseases based on proteins.

5. Research on bionics

Finally, I would like to introduce our Bionics Department of which I will be taking the position of a dean this coming April. This department's research building has an area of about 15,000 tsubo (one tsubo equals 3.3 square meters) and has a laboratory for business-academia collaboration. Last April, 18 staff members transferred over from Tokyo University where I used to work.

The term "bionics" originated from the term mechatronics in the U.S. in the 1950s and is not a new word. It is now used as a short form of bioelectronics or biorobotics. However, we are now proposing a new concept that "bionics" is a technology to improve the quality of human life. And we intend to proceed with our research based on the new concept that bioelectronics and biorobotics will support technologies required for the improvement of the quality of human life (called humanics) including medical services, biotechnology, and environmentology.

The research on bionics is an attempt to apply the superior functions of living organisms to a wide range of areas including electronics, robotics and environmentology, and biotechnology is now being applied to various fields of engineering. Of course, nanotechnology is included. Living organisms are typical examples that work on the nanoscale and they are models of nanotechnology. We believe that the trends described above show one direction of development in science and technology in the 21st century.