Micro-Manipulation and Micro-Robots


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Abstract: The author and Dr. Masayuki Nakao have been collaborating with clinicians from collegiate hospitals to develop a series of small three-dimensional structures to meet their special needs. So far, we have:
(1) Produced microchips for immunologic tests with 10 micron wide reaction grooves. The microchips reduced the testing time down to a hundredth of that of conventional tests.
(2) Developed a mechanical system for handling DNA.
(3) Built a multipoint electrode to embed in the brain for measuring acoustic potential.
(4) Developed an artificial voice generator and demonstrated that it can give vocal ability to speech-handicapped patients corpectomized by laryngeal cancer.
(5) Developed a micro-pump to aspirate pus from the middle ear, and applied it in surgery for patients with otitis media.
All these advances have demonstrated the benefits of collaboration between engineering and medical professionals.

Key words: Micro-manipulation; Micro-robot; Micro-chip; Micro-pump; Brain electrode; Artificial voice generator

Introduction

The author and Dr. Masayuki Nakao (Department of Engineering Synthesis at the University of Tokyo) have been pursuing studies in the fields of information communications, and important medical care/bioscience. The philosophy behind our studies is the concept that “micro-devices will make the largest contributions to the society in the future” (Fig. 1). At the same time, we fortunately became acquainted with many scientists including physicians, dentists, and genetic researchers to form teams for pursuing our cooperative studies. We strongly believed that good collaboration and team work between engineers and medical scientists could contribute greatly to society, and this belief led us to develop a number of “micro-devices”. Most of these devices were three-dimensionally structured and formed...
with precision in the order of microns. We also
developed methods for direct visual observation of these micro-devices during operations and handling, and achieved significant results.

Our major research contributions include
(1) developing immuno-chips, (2) mechanically manipulating DNA, (3) embedding electrodes in the brain, (4) developing an artificial voice generation system, and (5) developing a micro-pump for surgery.

Although we have conducted research in many other areas, this paper provides an overview of these five research themes.

Research Themes

1. Immuno-chip

An Immuno-chip is a plate of glass with small grooves for positioning the subject material of immune reaction testing. Its small flow
The reaction time to $1/100$ (Fig. 3).

The conventional practice of waiting several days after the test before beginning surgery has changed to running the test during surgery; a big change in the medical practice.

2. DNA research

Our research into DNA is quite unique compared to other research conducted around the world. Typical studies identify their base sequences by cutting the DNA into small pieces and multiplying them. Our method disentangles the chromosome using enzymes (Fig. 4) to extract a single thread of DNA (Fig. 5). The procedure then fixes the entire DNA strand to the reaction time to $1/100$ (Fig. 3).

(a) External view of reaction plate

(b) Structure of a micro-flow path

(a) Bulk

(b) On-chip lab.

Fig. 3  Comparison of reaction time of test with anti-CEA rabbit antibody

Fig. 2  On-chip laboratory for immunologic assays

Fig. 4  Schematic diagram of apparatus sending surface acoustic waves to chromosome

Fig. 5  Photomicrograph showing an extended chromosome
cut out the necessary part (Fig. 6) and reads the base sequence of the part cut out. This cutting requires special tools developed for this purpose. We are also building a near-field light microscope for direct observation of the DNA structure (Fig. 7).

3. Embedding electrodes

Production of micro-objects allows us to observe processes within the human body. For example, when sound enters the ear, we recognize it by an electrical signal that travels to the cerebrum. The motivation for our study was a desire to enrich the life of the hearing impaired by applying engineering means to directly repair the problem point, which may be anywhere along the external ear, internal ear, or path of the electrical signal to the brain, or within the brain itself.

Technology has already realized the wide availability of the artificial internal ear, which converts vibrations of the air into electrical signals for the hearing impaired. The next step, however, of revealing how the current is conveyed to the cerebrum, has not yet been adequately explored. We have developed an array of electrodes to embed in the brain (Fig. 8).

The embedding type electrode array has a number of small electrodes of sizes 20\(\mu\)m to 50\(\mu\)m. Embedding the electrode inside the cerebrum, the brainstem, or attaching it to the
cerebrum surface allows us to observe when and where the current runs and how the nerve system reacts upon hearing sound.

We are combining our research efforts with those of Dr. Tetsuo Ishii and Dr. Mikiko Taka-yama of the otologic department of Tokyo Women’s Medical University, and Dr. Kimitaka Kaga of the otologic department of the University of Tokyo, in an effort to realize this most desirable technology for medical doctors.

4. Artificial voice generation system

Devices currently in use, for people who have had their vocal cords removed due to laryngeal cancer or other reasons, add artificial vibrations from under the chin to generate vocal vibrations.

Our research has its basis in an entirely different principle. Our idea was that, if lack of vocal cords was causing loss of voice, we could place a vibrator inside a tooth so that the person with the implant could form the mouth into the proper shape for vocalization. This idea advanced into planting a vibrator in the mouth to amplify the vocal sound the person makes.

Our future plans involve storing the voice prior to cordectomy and producing the same voice by amplifying even the smallest enunciation after the surgery.

The study is making steady progress, however, we are troubled by the problem of the wire hanging out from the mouth.

5. Micro-pump

In treating otitis media with suppuration, myringotomy usually results in a large incision in the eardrum because viscous pus is difficult to extract from inside. This procedure causes thickening in the tympanic membrane where the cut was made and hardening of the entire membrane. This causes the patient to have hearing difficulty even after the cut is healed. There is a need to keep the extraction hole in the eardrum small while effectively pumping out the viscous pus inside.

Given these conditions, we developed a device that has a micro-spiral inside a 0.3 mm diameter injection needle which rotates at high speed to extract the viscous pus from inside.

The research continued for 7 to 8 years in pursuit of good results, and we are now working with researchers attached to a dental device manufacturer to commercialize the product for real use (Fig. 9).

Other Research Themes

Other research themes include, modifying an intravascular catheter to scratch out thrombus or embolus from blood vessels, and developing artificial insemination methods for inserting a sperm in the ovum with minimum disturbance. The latter involves microscopically holding down the ovum and inserting the sperm from a microscopically small opening. Another area of research involves measuring biting force using a sensor placed inside a molar.

Postscript

These researches require medical doctors and engineers to make joint efforts towards observing what many patients require, making suggestions, collaborating and merging the findings. Our research team at the engineering department of the University of Tokyo includes the author, who retired from the university in March of 2001, his successor Prof. Masayuki Nakao, and many other researchers who have been making cooperative efforts. These researches are, we feel, quite different from other
I believe the most important aspect of these researches has been to make steps within the world of medical science towards contributing to and improving the lives of ordinary people. We believe that micro-manipulation and micro-manufacturing to build and manipulate structures of 1 mm (1/1000 m), 1 μm, (1/1,000,000 m), and 1 nm (1/1,000,000,000 m) are crucial, and this belief has pushed our researches. “Micro” in general means small, but our word “micro-manipulation” signifies actual substances; the size of an atom is about 0.2 nm, and work in the nano-meter world is approaching the world of atoms.

We use the word “genome” when we think of DNA as a small unit of information. Objects composed of substances with the size of atoms determine the roots of people’s lives. I believe that directly working on the smallest substance clarifies the mechanisms of life and eventually will lead to happiness for humankind. It is my greatest pleasure to work with the people in these fields and make contributions to medical science and human life.