# Nanodiagnostics

*By Kaizan Kalyaniwalla*

What if there was a way doctors could determine your likelihood of contracting a disease without you actually acquiring the symptoms of that disease? Current diagnostic methods focus on technologies that detect the symptoms of disease. This may include the measurement of a particular antibody produced by the body in response to infection or the observation of a specific bacterium that is known to cause the disease. Methods such as these are slow and inefficient because they involve recognizing a disease based on the patient contracting the disease first. As KK Jain, author of Nanodiagnostics: applications of nanotechnology in molecular diagnostics, indicates, researchers within the field of nanodiagnostics are currently studying the ways nanotechnology will be able to extend the limits of current molecular diagnostic techniques (1). Nanotechnology implemented within current diagnostic equipment has the potential of analyzing entire genomes in minutes instead of hours. Based on which DNA sequences are deviated from the normal, doctors will be able to determine an individual's predisposition to either cancer or a specific disease. Current research into microfluidic technology is making it possible to integrate a number of complex diagnostic procedures into one simple device that will be able to give on the spot diagnosis.

## *Nanochips*

One of the most common techniques used today to analyze DNA sequences is hybridization, or the pairing of separated strands of DNA with complementary DNA strands of known sequence that act as probes (Campbell, 2). Currently, DNA chips called DNA micro array assays are used to analyze DNA. However, as Dr. Philip Chen, president of the Biotechnology company, Nanogen Inc., indicates, "Passive (non-electronic) technologies can be slow, tedious, and prone to errors because of non-specific hybridization of the DNA" (3). A company called Nanogen has developed a product called the "Nanochip" that employs the power of an electronic current that separates DNA probes to specific sites on the array based on charge and size (See Figure 1).

Once these probes are on specific sites of the nanochip, the test sample (blood) can then be analyzed for target DNA sequences by hybridization with these probes. The DNA molecules that hybridize with target DNA sequences fluoresce, which is detected and relayed back to an onboard system through platinum wiring that is present within the chip (Estes, 4). The secret behind this nano-chip is that each test site can be controlled electronically from the system's onboard computer. In other words, the chip can place different probes in different sites according to what DNA sequence is of interest. Therefore, if a mutation in the DNA sequence of a gene that causes a disease is known, doctors will be able to know

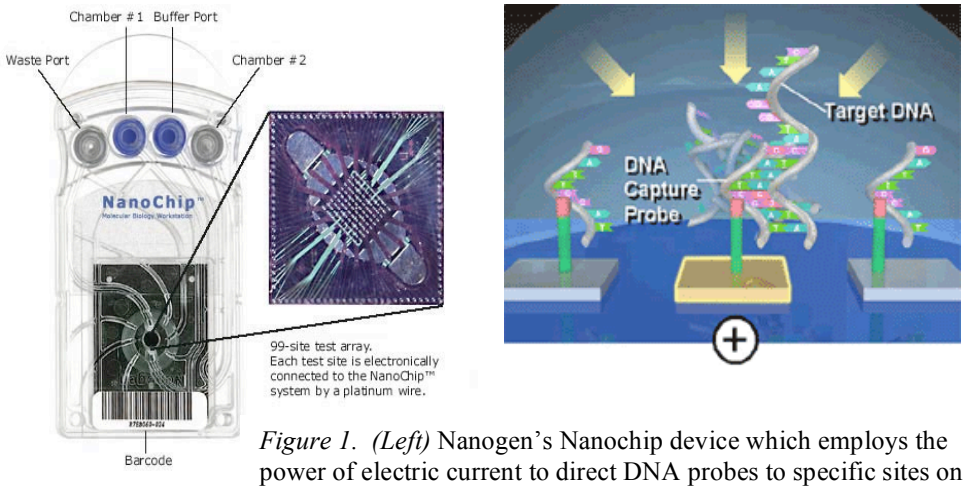


*Figure 1.* *(Left)* Nanogen's Nanochip device which employs the power of electric current to direct DNA probes to specific sites on the array. *(Right)* Close-up of DNA hybridization on three different sites. *Pictures are courtesy of Cognoscenti Health Institute (3)*

whether or not you're predisposed to that particular disease if hybridization with that probe occurs. The use of this electronic mediated hybridization accelerates detection of target DNA sequences to minutes instead of hours with conventional approaches.

According to Leo O'Connor, author of Nanotechnology Advances, the electric current within the Nanogen nanochip can also be used to separate different cell types within the sample of blood. For example, "Escherichia coli cells can be isolated from a whole blood sample in about four minutes" (O'Connor, 5). This process involves electrophoretic separation of these cells, electronic lysis of the isolated E.Coli, and then digestion of the bacterium's leftover proteins. All three steps are performed on one chip contained in a flow chamber. Nanogen is currently working on continuing development of miniaturized electronic devices for isolating and detecting biological warfare and infectious disease agents from human blood samples.

## *Microfluidics (Lab-on-a Chip)*

The newest technologies within nanodiagnostics involve microfluidic or "lab on a chip" systems, in which the DNA sample is completely unknown. The idea behind this kind of chip is simple: the combination of numerous processes of DNA analysis are combined on a single chip composed of a single glass and silicon substrate. The device itself is composed of microfabricated fluidic channels, heaters, temperature sensors, electrophoretic chambers, and fluorescence detectors to analyze nanoliter-size DNA samples (See Figure 2).

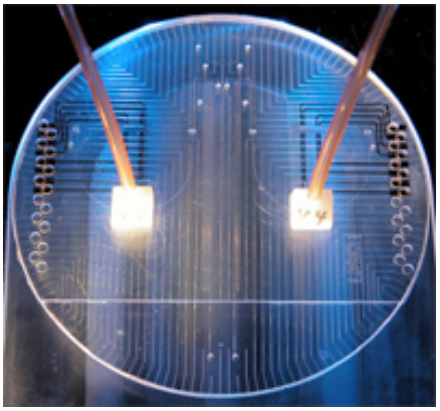

*Figure 2.* A top view of a lab on a chip system that is structured on a glass-silicon substrate. *Picture courtesy of National Caner Institute (6)*

In an article in Science Magazine, An Integrated Nano-liter DNA Analysis Device, this device is described as capable of measuring aqueous reagent and DNA-containing solutions, mixing the solutions together, amplifying or digesting the DNA to form discrete products, and then separating and detecting those products (Burns, 7). Using a pipette, a sample of DNA-containing solution is placed on one fluid-entry port and a reagent-containing solution on the other port. Capillary action draws both solutions into the device, but hydrophobic patches positioned just beyond the vent line in each injection channel stop the samples (O'Connor, 5). Air pressure lines placed throughout the device are critical for measuring correct amounts of reagent/DNA and moving the fragments of DNA from one process to the next. By the pressurization of air vents, DNA pieces for

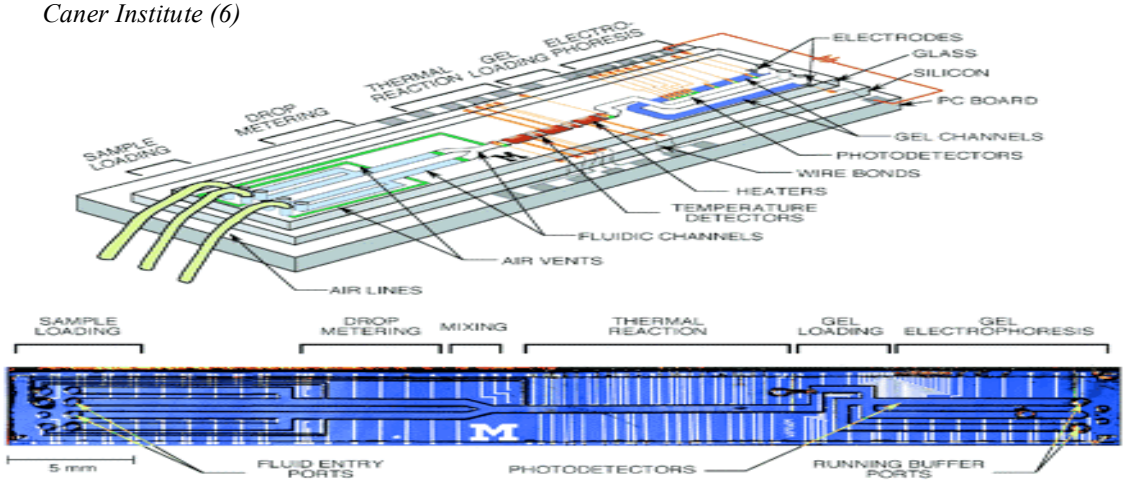


*Figure 3.* An example of an integrated nano-liter device. The fluid substrate moves from one chamber to the next for processing by delicate air pressure controls. *Pictures are courtesy of Science Magazine (7)*

example, move from the reaction zone of the device to the electrophoretic chamber (Burns, 7). A recent article in Science magazine called Miniature Analytical Methods for Medical Diagnostics states that microfluidic systems have also been crafted to analyze cell composition. As long as the starting material has some fluidity to it, the device can be specifically designed to separate cell contents and analyze the products that were present within this fluid. Many of these systems are still rudimentary and remain more complicated and bulkier than a simple integrated miniature device (Walt, 8).

## *MEMS*

Related to microfluidic systems are microelectromechanical systems or MEMS. The difference between MEMS and microfluidic systems are that MEMS do not require reagents or a fluidity based substrate to react upon. Although MEMS are primarily used in drug-delivery systems, one primary application of MEMS in diagnostics are the swallowed capsule technology pills that allow doctors to visualize GI bleeding (See Figure 4).


*Figure 4.* A camera the size of a pill that contains metal-oxide semiconductor particles. *Picture courtesy of Science magazine (8)*

According to Walt, "The patient swallows a capsule containing a light-emitting diode for illumination, a CMOS (complementary metal-oxide semiconductor) video camera and optics for taking images, a battery, and a transmitter" (8). The images are then transmitted to a receiver worn on the patient's belt and the doctor is then able to diagnose the cause of the ailment.

## *Applications/Current Research*

The field of nanodiagnostics is currently seeing a trend towards hand-held devices that are easy to use and are marketable to customers. One company has created a product called "Gluco-watch" which permeates your skin with fluidic nanochip biosensors that sense the level of blood sugar and then relate this read out to a wrist-watch. Nanodiagnostic technology such as this have the potential to free up large proportions of the health care industry that are devoted to monitoring patients' (especially the elderly) blood composition. Routine appointments with the hospital for blood tests would no longer be needed if such devices became available to the public. However, there should be concern with making nanodiagnostic techniques available to the public, since the lack of patients coming in to hospitals to get routine blood tests, could cause the health-care industry to lose money. Nanodiagnostic devices would also make the job of a physician easier. As of now, doctors order tests to confirm their hypotheses on what they think a particular disease may be. With the use of nanodevices, doctors could order large scale tests that are able to differentiate between diseases based on mutated DNA sequences.

The field of nano diagnostics raises certain ethical concerns related with the testing of blood. For example, if a nanochip were to be able to analyze our entire DNA sequence from a drop of blood, would it be morally correct for hospitals to know an individual's entire genetic makeup? Shouldn't individuals have some say in whether or not hospitals have access to these records? Another area of concern is with the use of MEMS devices within the body. If the capsule device breaks down in one's stomach, harmful metal oxide particles could cause the introduction of free radicals that are harmful to cells. Researchers still do not know if the introduction of these devices within one's body would leave residual nanoparticles that would be harmful to the digestive system (Walt, 8).

It is clear that the field of nanodiagnostics still has a long way to go before diagnostic equipment will be available to consumers. Companies such as Nanogen have not yet perfected their methods of analyzing DNA sequences through the use of probes and they are no where near making

this as easy as one-touch operating. Other companies are still in the process of making microfluidic chips which can analyze your whole DNA sequence without the use of any probes and/or hybridization techniques. Even if nanodiagnostic devices become mass-produced, it is hard to say whether these instruments will ultimately benefit or hurt the health-care industry.

This student-produced report is part of a larger pamphlet on nanotechnologies circa 2005, the partial output of a course on "Nanotechnology and Society" (Science and Technology Studies, Section 84405, by C. Tahan) which was taught in the spring semester of 2005 at the University of Wisconsin-Madison. Visit http://tahan.com/charlie/nanosociety/course201/ for the other reports and more information.

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