Chapter 8

Precisely Addressed (DNA Gene) Spray Microfluidic Chip Technology

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Additional information is available at the end of the chapter

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Abstract

This study is the subject of precisely addressed (DNA Gene) spray microfluidic chip. It is a special chip (ASIC) designed to spray liquid medical wisdom DNA gene sequencing system technology transfer fabric onto the glass slide. Thermal bubble liquid bead generation, it produces a very large thrust bubble in a short time to launch the liquid. It forms micro-droplets. It is in the biomedical micro-beads quantitative, it uses the address spray liquid crystal structure of the cavity. It uses the principle of ink-jet printer cloth DNA liquid onto glass slides. It does DNA sorting for each style. Bubble inkjet technology is in the inkjet head position on the wall with heating electrodes. It is by pulsing the selected heating element by electrical pulses. It produces ink droplets on the inkjet head. It is heated to a certain temperature after the electrode. It makes the droplet a tiny bubble and explodes. It is then discharged through the heating chamber through the inkjet head. It is attached to the substrate surface. It is printed on the amount of ink droplets depends on the temperature control of the heating device.

Keywords: DNA gene, microfluidic chip, addressed

1. Introduction

Introduction and application of inkjet technology, inkjet technology is involved in electronics, electrical, mechanical, materials, chemical, physics and other fields of expertise. It is highly integrated technology. Inkjet technology is in industrial applications with high-speed operation, quiet, non-contact and computer-controlled features. It does not require the use of photomask, process simplification, material utilization, low cost and more environmentally friendly. Jetting technology is a widely used technology [1–12]. The principle of ink-jet technology is mainly that the liquid in the chamber is squeezed by an Actuator

so that the liquid is squeezed by the pressure to be ejected through the spray hole. It is because each jetting hole in the ink jetting device has an independent jetting chamber, an actuator and a micron-sized jetting hole. Spray chamber can be filled with a certain amount of liquid [13–18]. When the actuator squeezes the liquid in the chamber and then passes through the micron-sized orifice, the fixed-size and uniform-size micrometer-sized liquid droplets can be jetted, as shown in **Figures 1** and **2**. This study has established a complete jet technology. For example, from the droplet nucleation and flow simulation, spray chip design, spray device package, corrosion head design, back pressure control technology, micro-droplet detection technology … and so on. It can be the most complete jet design for the technology, assembly and testing. It currently except in the relevant technology transfer to the industry outside. It also uses this technology in the display, power machinery, bio-chip, printed circuit board (PCB) and other industries in the development of new technologies.

It generates surface tension suction. It pulls the new liquid to replenish the liquid ejection area. Thermal bubble jet technology is constructed from such integrated cycle technology programs and materials.

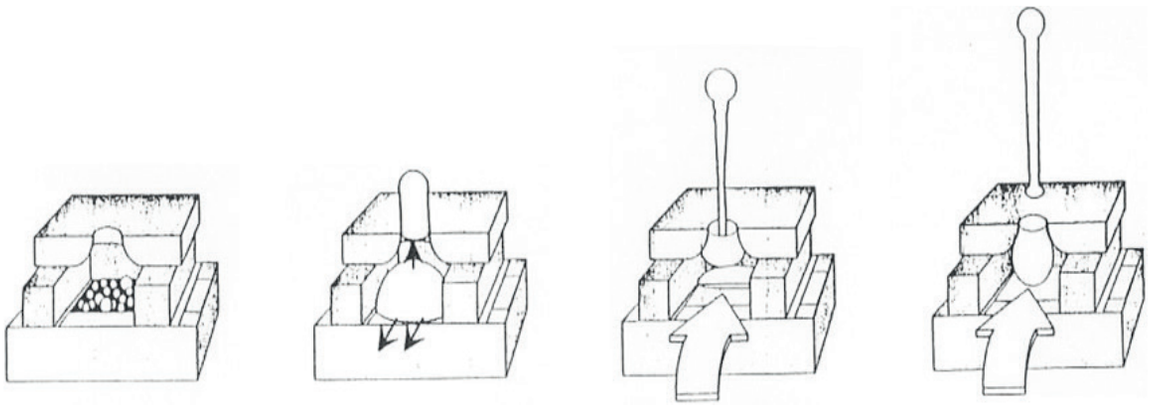

Figure 1. Spray device spray diagram (top jetting).

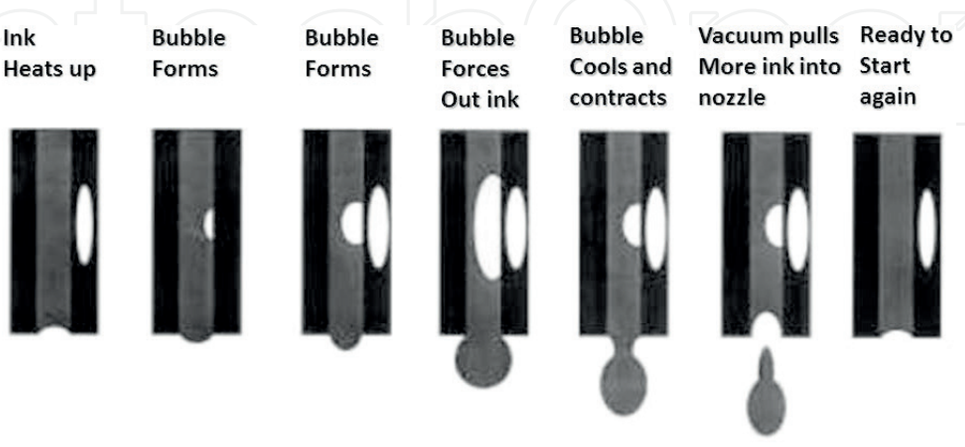

Figure 2. Spray device spray diagram (side jetting).

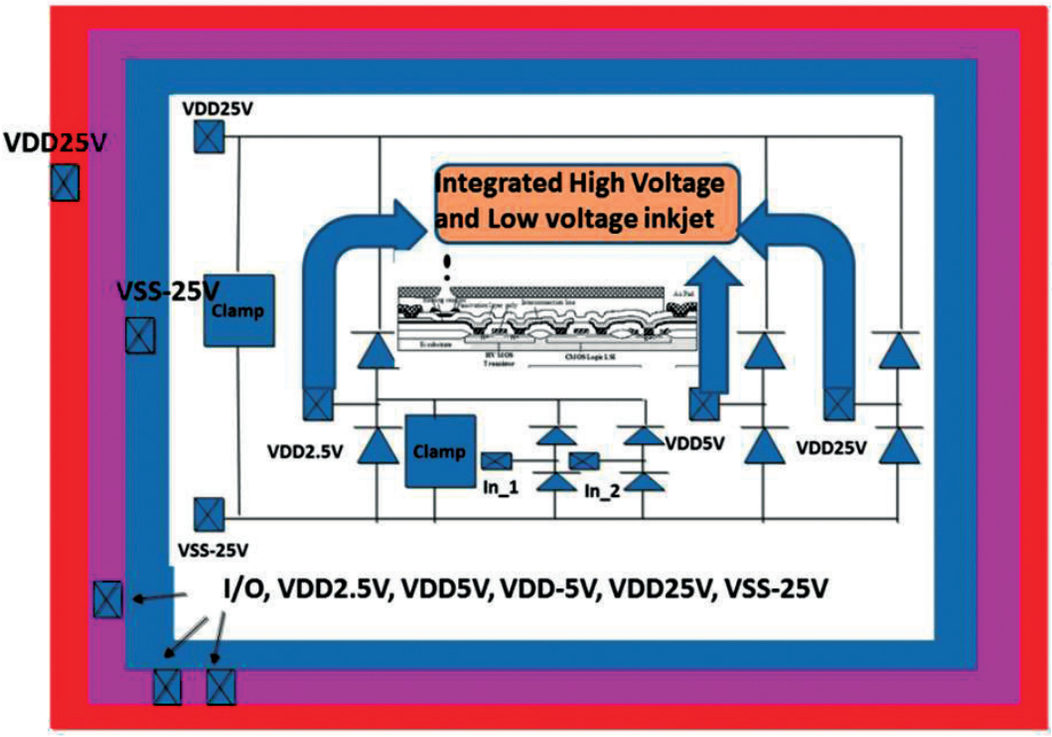

Figure 3. Monolithic DNA liquid jet integrated ESD multi-level output.

Jet dispensing wafer technology includes high-voltage drive, low-voltage logic signal processing, and micro-electromechanical structure array. As shown in **Figure 3**. It drops a small drop of liquid onto the paper. It combines imaging with very small droplets, only 50–60 μ (micron, one millionth of a meter). It is thinner than the human hair (70 μ). The position of the drip ink is precisely finely moved by the ink head. Each inch can be up to 1000 points or more. In this research, HV-ESD Clamp was integrated into the design and fabrication of monolithic inkjet chips for multi-level output integrated circuits. It contains a high-voltage drive power device array, low-voltage logic circuits, and micro-electromechanical components array structure integrated in a silicon substrate process. It is resistant to HBM (±4 kV), MM (±400 V) protection circuit testing.

2. DNA gene spray microfluidic chip technology

Biomedical wafers have many advantages such as trace detection, accurate quantification, automatic operation and rapid parallel processing. Compared with traditional biomedical testing, biomedicine wafers have great advantages and so far, many breakthroughs have been made Technological development. But it cannot be denied that biomedical chips are also facing many technical challenges that need to be overcome by scientists in different fields.

As the design and manufacture of biomedical wafers are cross-cutting projects that involve the operation of microfluidic systems, biomedical reactions and optical signal detection, they are quite different from the highly specialized professional division of labor in many traditional

engineering fields. In addition to professional requirements, biomedical wafer design and manufacturing, attaches great importance to cross-cutting technology and communication skills.

The design of the chip often starts from the system or encapsulation level and starts to reverse thinking. Whether the team has sufficient cross-communication between the fields except the experts in each field and jointly solve the problems derived from each other is often the relationship between chip design and The key to success or failure Therefore, different from the training requirements of traditional engineering technology, instead it is able to cross the field of micro-electromechanical systems, microfluidics systems, biomedical technology and optoelectronic technology and other fields, it is very important in the development of biomedical wafer.

When the amount of sample used to reduce, then faced with a sharp decline in signal detection problems. Increasing the signal strength or improving the sensitivity of the sensing device are two ways to solve the above problems. In terms of increasing signal intensity, there are currently artificial methods of replicating biomedical molecules to increase the weight of specimens, such as polymerization and per-chain reaction techniques; for those molecules that cannot be artificially increased, the number of markers for their markers or sensitivity, or to focus molecules in the detection area for detection. In enhancing the sensitivity of the sensing device, more sensitive new sensing technologies are also the focus of development besides reducing background noise.

In this project, the hot bubble liquid bead is generated by heating the liquid by using a micro-heating wire and generating bubbles of great thrust in a short time to push the liquid out to form micro-droplets, as shown in **Figures 3** and **4** below. In the quantification of biomedical microbeads, the integrity and cleanliness of the beaded pellets are often quantitatively

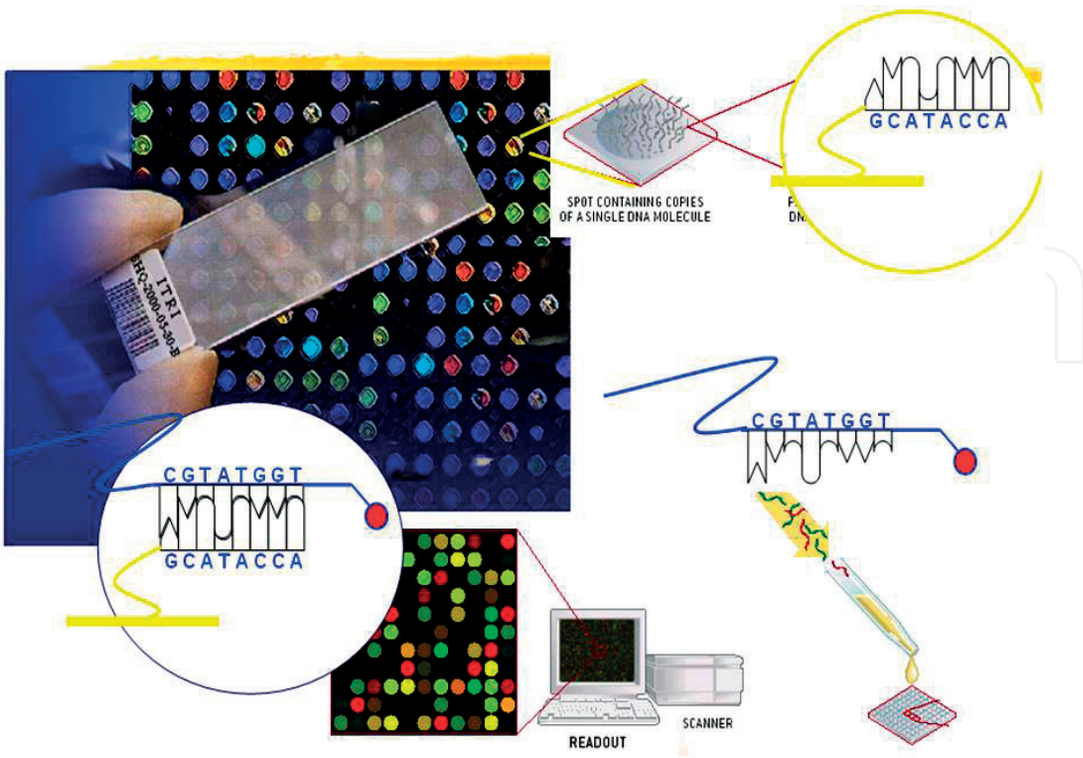

Figure 4. Gene microarray technology.

accurate or not. The way in which the foamed beads are produced will produce a series of beaded beads, that is, in addition to the main beaded beads, Subsequent satellite beads have a considerable degree of impact on accurate quantitation. The program has a complete set of main bead, quantitative determination of liquid beads, in line with biomedical specimens of liquid bead quantitative requirements, this study used to create disease detection and DNA sequencing of DNA microarray chip.

DNA micro-array, bio-chip or DNA chip combination of molecular, materials, motors and other fields of products. This system can be divided into DNA chip, protein chip, cell chip, tissue chip. However, only the first two are commonly used, in which a DNA chip can detect changes in the concentration of mRNA in a cell. The biggest advantage of gene microarrays is the ability to quickly and accurately provide a large number of genetic tests and to understand the performance of these genes. This is a considerable help in understanding the transmission of genes.

The main body of the chip is the use of glass, nylon, silicone, ceramic and other materials. Above there are probes made of oligonucleotides or proteins (DNA chip and protein chip, respectively). Its main principle is that these probes will adsorb their corresponding DNA or RNA species. People want to learn more about these genes or proteins. Currently there are three ways to probe the technology, one is the synthesis spotting method, the first synthesis of oligonucleotides or oligopeptides, and then the way the pressure on the board. The second is to take the light-guided approach, so that oligonucleotide or oligopeptide slowly in the main plate synthesis. The third is similar to the inkjet printer operating mechanism, the oligonucleotide or oligopeptide materials Yiyi sprayed on the board gradually formed.

Gene microarrays have several uses: piecing together an unknown DNA sequence and understanding the performance of a gene. Introduce a relatively simple application. Piece together the DNA sequence of the sample.

First, the DNA of the sample is shattered one by one, and the double-stranded DNA is heated to single-stranded helical DNA. It is a long piece of DNA into a small short DNA sequence. It is the only ATGC single-stranded sequence. It attaches a special sequence of DNA Xs to each small piece of DNA (for example, five A at the beginning). It has a small platform with short pins that correspond to the DNA sequence of the X sequence. To the above example, is to pick five T. In this way, these short DNA sequences are adsorbed onto these short needles.

The system begins to release the same nucleotide one by one and then the next step. For example, it frees C to see what needle DNA will react to it. This is a reaction to give a light. It can shine a bright needle. It can be learned that the first nucleotide of these DNA sequences on these needles is G. The system is constantly repeating this step (of course, to release different kinds of nucleotides) to know the DNA sequence on this needle. Then go through a jigsaw puzzle-like step (using a computer as an aid) to spell out an entire sequence of DNA.

3. Cell detection

In cancer cell detection, gene microarray technology also has an important place. It can be used to compare the difference between normal cells and cancer cells. It can further find out

which genes are more in cancer cells for further analysis. The method is to mark normal cells and cancer cells in different colors, then break them up and spread on the wafer because the DNA corresponding to the nucleotide probes on the wafer will remain on the plate. It looks like a colored plaid below.

Take the example on the right, red represents cancer cells and green represents normal cells. Next, quantify the color of the statistics and calculate the ratio between them. It will find that there is significantly more red in certain areas than in green, or significantly more in green than in red. So biologists can take this to know more or less cancer cells than the average number of genes. Suppose today we find that the X gene is much more numerous than normal cells tomorrow. Biologists speculate that the X gene may be a factor in cancer. To test this hypothesis, a biologist can make a cell that has an excess of the X gene and use it to produce the protein. It can see if he has any cancer cell features. With this method we can find out the genes associated with cancer cells. This treatment of cancer cells, whether there is much to be considered for help or prevention.

Gene microarray technology is a multi-field combination of technologies as shown in **Figure 4**. It helps us better understand or crack the genetic code. The combination of technologies in many areas may be more competitive than traditional single-area research. It can solve some difficult problems in a single area.

A biological genome refers to all genetic material on the biological chromosome. Its size is often expressed as the number of base pairs. A proteome refers to the entire protein product of a gene and its performance. Many genes produce more than one type of protein after transcription and translation. There are two main reasons for this: First, a single gene undergoes alternative splicing when it is transcribed into mRNA. It leads to different combinations of exons. It thus produces different proteins. The other is that the translated protein is modified so that the protein has more different structures and functions. Proteasomes are more complicated than the genomes. In addition, a mutation of a single nucleotide (A, T, C, G) may occur at about 100–300 bases per billion of the 3 billion bases in the human genome. It thus makes the DNA sequence change, known as single nucleotide polymorphism (single nucleotide polymorphism, SNP). Therefore, the structure of DNA between individuals is very similar. The difference is very large at the micro level. It leads to significant differences among individuals. After decoding the human genome, it was found that the sequences among different individuals were very similar. It is only 0.1% different. These slight differences determine each person's height, color, size and other aspects of the difference. It also determines the different characteristics of our body. It is easy to suffer certain diseases.

We use different restriction enzymes to process the DNA. It is unique because of each individual's DNA sequence. DNA is cut into fragments of varying lengths. It is different after electrophoresis analysis. This treatment with restriction enzymes gives rise to polymorphism in length of different DNA fragments. It is called restriction fragment length polymorphisms (RFLPs). It is different from everyone's RFLPs, just like our fingerprints. Therefore, RFLPs are also called DNA fingerprinting. RFLPs technology has been widely used in the identification of criminal cases and genetic diseases.

RFLPs technology can also be applied to genetic screening. Check if embryos, fetuses or newborns have a genetic disorder. It is for quick medication. The relatives have genetic disease, but their own asymptomatic people. It can also be used by gene scanning to determine if there is a mutant gene or is likely to develop the disease. In addition, DNA Test is the most accurate way to detect a gene. It directly analyzes DNA mutations. Due to PCR (polymerase chain reaction) technology matures. DNA testing requires only a few cells to complete. It applies to one or a few mutations caused by the disease. Gene scanning and DNA detection techniques are most commonly used to test for sickle-cell disease.

Sickle-shaped erythrocyte disease is a general term for a series of hereditary diseases caused by hemoglobin S (HbS). Sickle-anemia is just one of them. It arises from the point mutation in the beta-Hemoglobin gene. It causes heme β to be changed from normal glutamic acid to valine during translation. It is negatively charged by glutamic acid. Valine is electrically neutral. It makes the hemoglobin structure change. It leads to the formation of elongated needles in red blood cells. It causes red blood cells to deform, usually in severe cases. It is more minor growth and development.

Sickle-shaped anemia test in two ways: First, amplified by PCR of DNA sequences, MstII restriction enzyme cutting. It is run by gel electrophoresis. Its normal sequence is cleaved by the restriction enzyme. The molecular weight is smaller and runs farther. Abnormal sequence cannot be cut by restriction enzyme, its molecular weight is larger, runs nearer. It can then check for mutations in the gene. The other is the use of artificial synthesis of two DNA test strips (one for the normal sequence "GGACTCCTC" and the other for the abnormal sequence "GGACACCTC"). It binds to normal or mutated DNA sequences amplified by PCR. Change in color to identify if there are mutations in the gene.

The human genome has about 3 billion nitrogenous bases. It contains only 5% of the DNA sequence. The rest of the sequence is mostly called junk DNA. There are more than 3 million repeats in the head. The number of these repetitive sequences varies from person to person. We call this variable number of tandem repeats (VNTRs). These repetitive sequences are ubiquitous in the genome. Its function is not yet fully understood. It is currently known to have more than ten diseases because of the excess number of repetitions in this area. For example, it is fragile X syndrome, Huntington syndrome, and the like. This area is also the main source of information for identifying paternity.

The genetic variation between people is only one ten thousandth. The main source of variation among individuals is the number of VNTR repeats. The number of repetitions per person varies with VNTR. When the restriction enzyme cuts the region, different individuals will produce fragments of varying lengths and numbers. We call this restriction fragment length polymorphism (RFLP). These cut-off fragments, it is different molecular weights. It has different mobility. It uses electrophoresis to separate DNA of different lengths. It goes through blotting, probe hybridization and other processes. It will show the thickness of the stripes. These stripes are called DNA fingerprinting. This was developed in 1984 by Dr. Alec Jeffreys in the United Kingdom.

It is passed on to offspring as VNTR follows Mendel's laws of inheritance. Every pair of homologous chromosomes is in each human body. It is one from the father, one from the

mother. Each person cut the fragment should be at least one of both parents the same. As long as it compares to the three-way RFLP, it can confirm the parent-child relationship.

In recent years, due to the development of polymerase chain reaction (PCR) technology. DNA identification technology uses PCR to amplify the sample DNA collected. It selects mini-satellites DNA with shorter repeat fragments in the VNTR as the target of the assay. Single-parent paternity tests can also be confirmed using maternally inherited mitochondrial DNA or paternally inherited Y chromosomes. Sperm contained in the mitochondria body is very small, most of the mitochondria within the fertilized egg from the egg. It compares the mitochondrial DNA in the offspring cells to determine if the relationship is mother-daughter, mother-daughter, or sibling. The male Y chromosome did not participate in synapsis or gene recombination during meiosis. It therefore determines the relatives of father, son, brother or paternal relative to the Y chromosome. These can be used as a paternity test to determine the relevant evidence.

4. Experiment and results

Micro-injection flow channel design parameters monomer, the impact of the ejection orifice thickness also caused performance is very important, its impact may be the effect of differences in both exit velocity of the droplets and flight direction. It is necessary to know the thickness of the sheet discharge orifice (nozzle plate thickness) affect the size ratio between the length of the two nozzle diameter caused respect. Through computer simulation can be obtained as shown in **Figure 5**. Simulation of DNA in the orifice thickness reduced from 50 to 25 μm single-aisle jet chamber. The results can be seen due to the reduced thickness of the orifice. Droplet flight directionality deteriorated. The reason is that the effect of the thickness of the orifice having rectified so that the flow field velocity with consistent directionality. But too thick so that it will produce additional drag exports slowed down. Orifice having a different orifice diameter should be of different sheet thicknesses. The calculation results are in 200 μs moment, obviously not yet fluid backfill is completed. It causes of reduced thickness orifice, causing the fluid velocity to large-amplitude reduction backfilling, because the droplet from the nozzle holes. Droplet tail flight directionality deteriorated. It has already begun to overflow orifice surface side. Resulting is in resistance, due to surface tension forces led by the great surface. Prevents fluid filled into the interior of the cavity injection phenomenon.

Single injection process in real time, and cannot ensure just above the orifice sheet ejection orifice center is located in the center of the cavity, it is necessary to simulate the effect of off-center position when the spray hole caused by the analysis. The results show that the ejected by the droplet and will not deviate from the center position of the nozzle holes, caused by large droplets tails flying directional radiation deteriorated. The results show the fluid actually increased after the injection backfilling operation speed, almost complete backfill to the surface of the nozzle holes, the reason may be because the orifice is placed away from the channel inlet of the injection cavity side wall surface side so that the fluid this reduces while reducing internal flow field reflux (circulation) from happening; directly back to fill in one

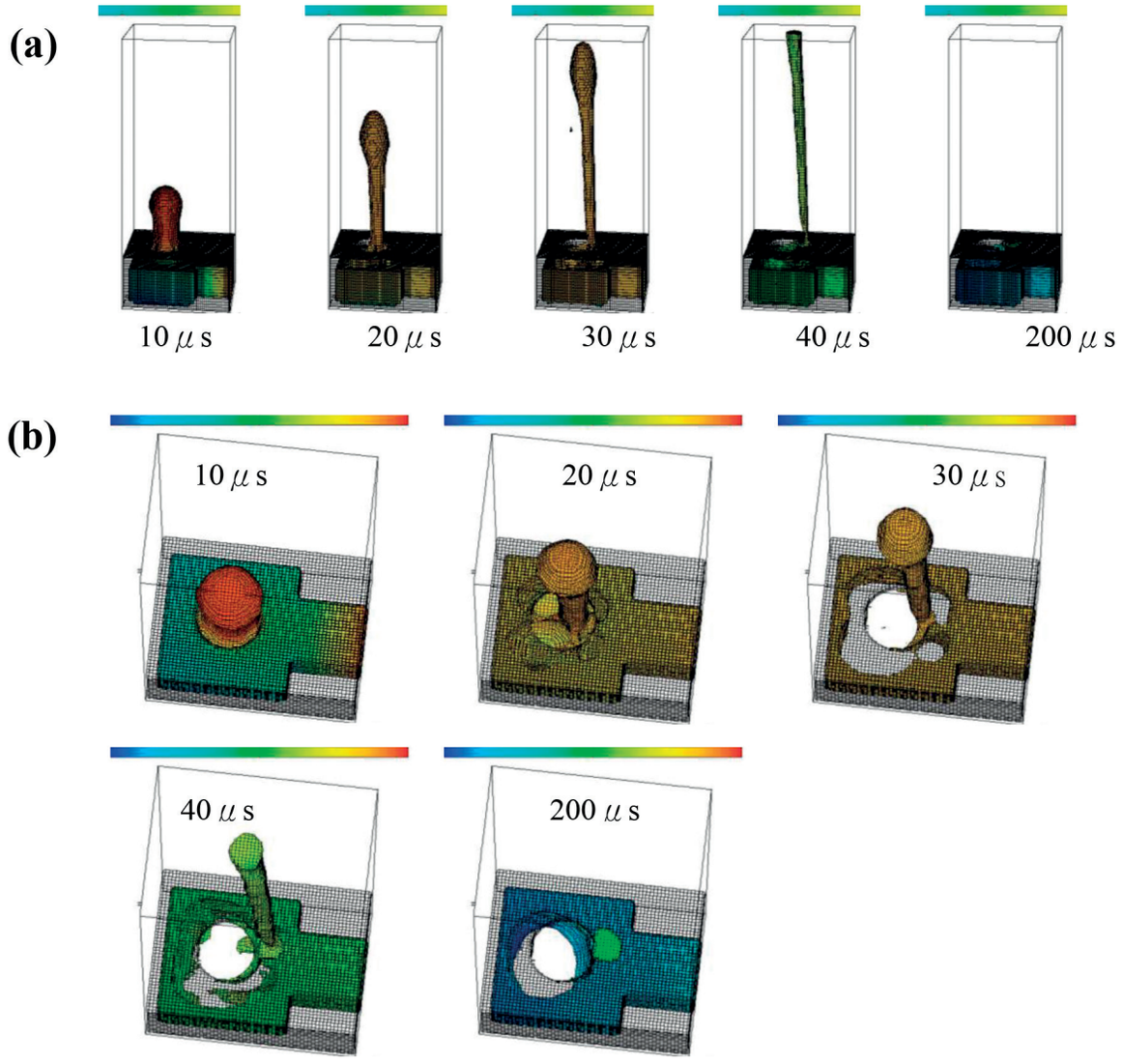

Figure 5. The simulation of DNA was calculated on a three-dimensional top view of (a) a three-dimensional side view (b) at 10, 20, 30, 40 and 200 μs at a single channel ejection cavity with a hole diameter of 60 μm and a thickness of 25 μm at an operating frequency of 5 KHz spray situation.

direction from the channel inlet cavity injection, such as speed XY sectional flow field in an instant 200 μs shown can clearly see resistance to the flow field, it is resulting in increased velocity of the fluid backfill. **Figure 6** is shown Droplet generation control simulation.

Figure 7 is a schematic diagram of a cross-sectional view of a precise overall DNA jet multi-dimensional drive addressing chip. The amount of each single point DNA sequencing (spray volume) is determined by the magnitude of the amplitude power. DNA trace differences can be adjusted. Heater also increases the number of pads as the number of thermal resistance components increases. DNA jetting system costs also increase proportionally. Therefore, Heater thermal resistance components must increase the number of logic multiplexed control circuit. It integrates the related process technology. Making the appropriate driver circuit and selective switching circuit can dramatically reduce the required number of external Pads and reduce manufacturing costs.

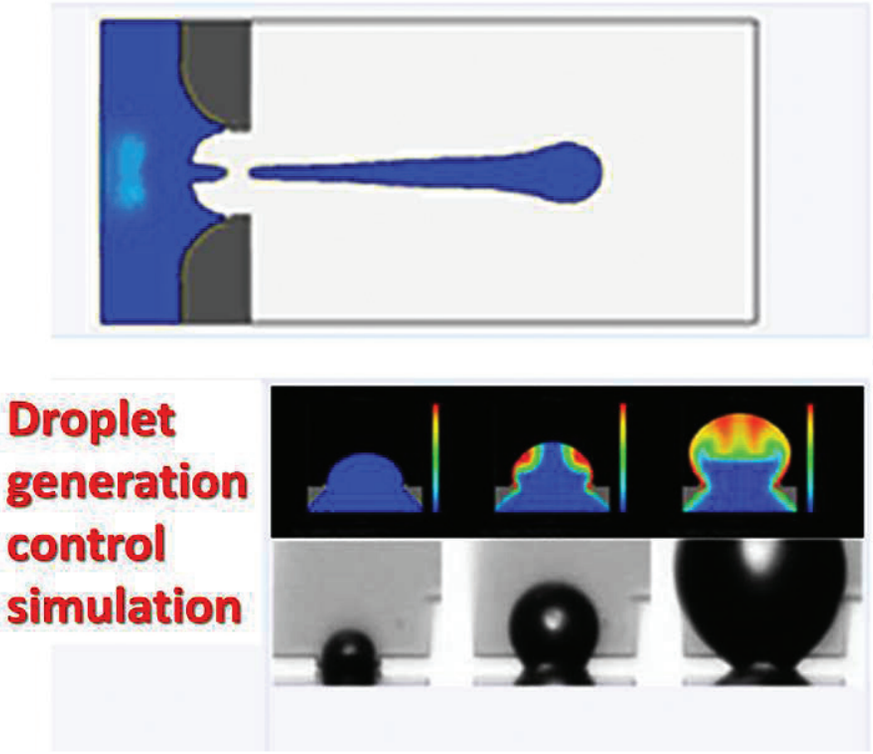

Figure 6. Droplet generation control simulation.

The original voltage source is a group of DC voltage drop. The voltage divider is divided into eight groups by nine resistors, and one group of voltages is selected by three pairs of eight decoders. This circuit architecture can convert the original 5 V logic pulse into the voltage required by the circuit system, and output the required voltage through the PN transistor, Smooth error compensation process, to achieve the amount of liquid DNA is determined by the size

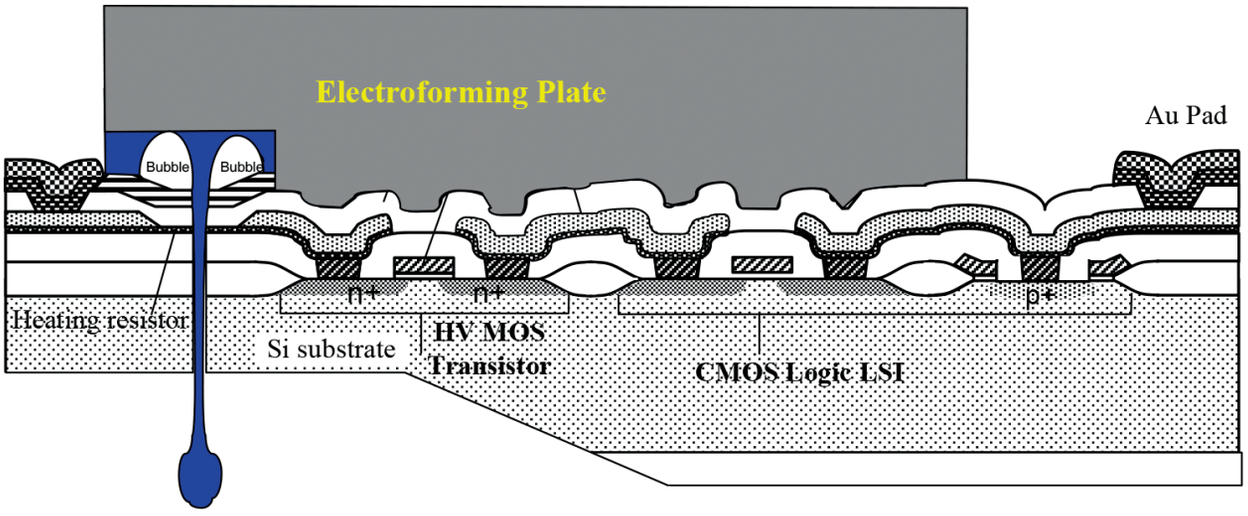

Figure 7. A schematic diagram of a cross-sectional view of a precise overall DNA jet (the merging of multi-dimensional data registration circuit and DNA jet technologies).

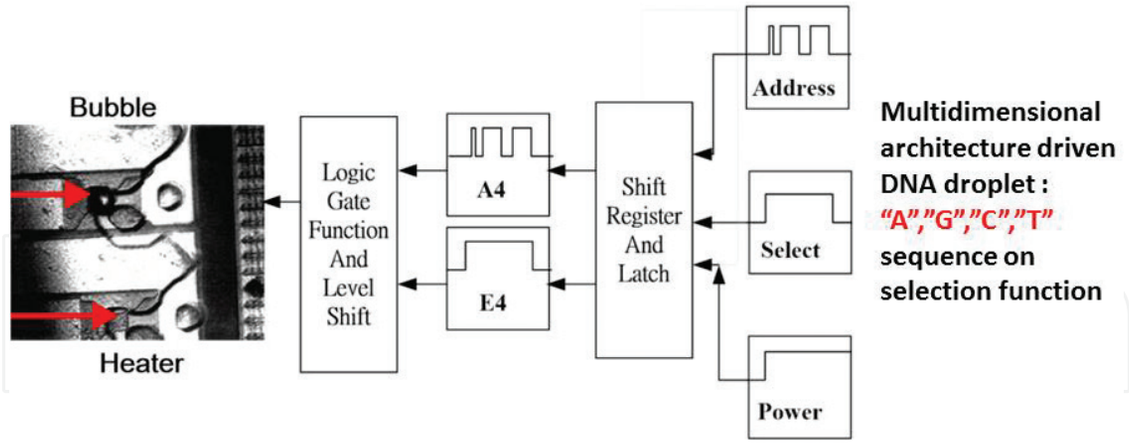

Figure 8. Open pool printhead chip.

of the amplitude and power, DNA trace differences can be adjusted action. For the same DNA sequence of the password, to be able to get different lengths of continuous fragments, and know the end of these fragments corresponding to the A, T, C, G base. Thus, as long as the length of these fragments ordered, the original DNA sequence of the complete base to know. As for the method of obtaining a large number of fragments; after a large amount of DNA to be sequenced is copied first, the DNA is cut at different bases. For example, the restriction will cut off double helical DNA at specific base alignments. The effect of cleaving DNA at specific bases can also be achieved by chemical reactions that remove bases. Also, copy the DNA that used to contain the complete passcode as a template. It is randomly interrupted to interrupt without growth. It produces a variety of pieces of different lengths. It sorts DNA fragments of different lengths. It is a technique called gel electrophoresis. Gel electrophoresis can distinguish small differences in DNA fragments that have been cut off. The rationale is that the flow rate of a molecule fragment in the gel is inversely proportional to the logarithm of the number of base pairs. The shorter the molecular fragment, the faster it will drift in the colloid. Gel electrophoresis on the length of fragment resolution is very high. It is for two DNA fragments that themselves are hundreds of units long. The difference between the length of only one nucleotide can be distinguished.

This systematic phase verification follows the DNA droplet addressing requirements. It is the first plan to send signals to the output thermal resistance module, as shown in **Figure 8**. Each thermal resistance has a corresponding signal and open pool measurement. It allows this signal is generated after the designated system contains quantitative circuits. It can adjust the voltage level of the output circuit to accurately quantify DNA. Adjustable jet emits DNA flow through the system wafer. DNA jetting system wafer characteristics measurement, pulse width modulation (PWM) power corresponding quantitative DNA gene-matching parameters, high voltage power transistor driver design compensation. It optimizes the parameters of power components to observe the changes of DNA beads under different operating conditions. The DNA liquid tube array and droplets on the carrier is shown in **Figure 9**.

In the biomedical micro-liquid bead quantitative, the integrity and cleanliness of the liquid bead is often about the accuracy of quantitative or not. Hot bubble bead generation, will produce a series of beads. It is in addition to the main liquid beads, there are satellite beads

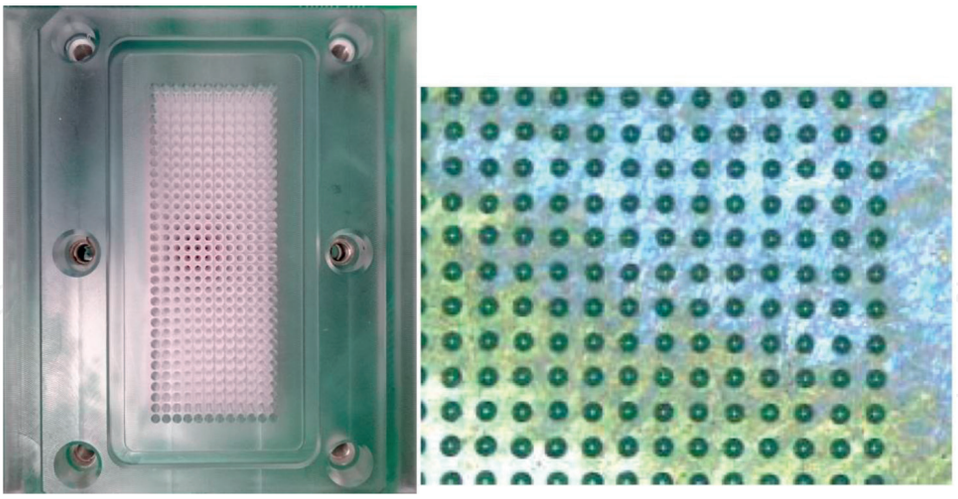

Figure 9. Multiplexer DNA solution jet part.

followed. It has a considerable degree of impact on accurate quantitation. In this study, a complete master bead was used and the beads were quantitatively accurate. It meets the biomedical specimen liquid bead quantitative requirements. The study was used to create DNA microarray chips for disease detection and gene sequencing.

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