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A Research paper on Introduction to DNA Chips: Constructions, Types, and Applications

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Abstract: - DNA chips are tiny devices that work by allowing DNA to stick to its matching DNA in a very specific way. This process is called hybridization. Scientists use DNA chips in medical tests to help diagnose diseases and to figure out which drugs might be most effective for certain people. This research paper covers everything from the basics of DNA Chips to the different types and how they're made, as well as how they're used in different areas.

Keywords – Hybridization, Diagnose, Test, Washing, Performance, Framework, Nanogold

1. INTRODUCTION

DNA chips, also referred to as microarrays, are a potent tool utilized in molecular biology to explore gene expression, diagnose diseases, and identify genetic variations. They are composed of small glass slides or silicon wafers with thousands of probes, which are tiny wells or spots designed to specifically bind with complementary DNA sequences in a sample of DNA or RNA.

To employ a DNA chip, the DNA or RNA sample is first labelled with a fluorescent dye and then hybridized to the probes on the chip. Subsequently, the chip is scanned using a laser, and the fluorescent signal from each spot is measured. This signal intensity corresponds to the abundance of the corresponding DNA or RNA sequence in the sample. DNA chips have numerous applications, such as gene expression analysis, DNA sequencing, SNP genotyping, and the diagnosis of genetic disorders. They are particularly valuable for investigating complex biological processes like cancer development because they can measure the expression of thousands of genes in a single experiment.

The uses of DNA chip analysis are extensive and constantly expanding. They include fundamental research, human genetics, infectious disease diagnosis, genotyping, gene expression monitoring, pharmacogenomics, and environmental control. Recent studies have demonstrated the identification and detection of mutations in genes responsible for cancers and how DNA chip analysis of individual polymorphisms can aid clinicians in determining the most effective treatment for their patient's specific form of the disease.

DNA chips come in various dimensions, offering hybridization sites ranging from 50 to 200 microns, producing arrays of 100 to over 10,000, or even 400,000 different probes per square centimeter.[1][8]

2. LITERATURE SURVEY

2.1 HISTORY OF DNA CHIPS:

The origin of DNA chips, also referred to as microarrays, can be traced back to the early 1990s, when two independent research groups first proposed the idea of using small DNA fragments immobilized on a solid surface for gene expression analysis. In 1996, Pat Brown and colleagues at Stanford University created the first DNA microarray, which contained around 4,000 genes from the yeast genome and was used to measure gene expression changes under various growth conditions.

The first commercial DNA microarray was developed in 1994 by Affymetrix, which used photolithography to synthesize oligonucleotide probes directly on the chip's surface. In 1998, Agilent Technologies introduced its first DNA microarray, which used inkjet printing to deposit probes onto the chip's surface. Over time, DNA chip technology has advanced considerably, with the development of high-density microarrays containing hundreds of thousands of probes, and the utilization of next-generation sequencing technologies for whole genome sequencing.

Today, DNA chips have become an indispensable tool in molecular biology and are widely used for gene expression analysis, SNP genotyping, DNA sequencing, and disease diagnosis. They have facilitated the analysis of complex biological systems and generated large-scale datasets that have led to new insights into genes' role in human health and disease.[8]

2.2 WHY DNA CHIPS ARE REQUIRED:

DNA chips, also known as microarrays, have revolutionized the field of molecular biology by providing a highly efficient and accurate method for analyzing the expression of thousands of genes simultaneously. Before the development of DNA chips, analyzing gene expression required time-consuming and labor-intensive techniques such as Northern blotting and RT-PCR, which could only analyze a few genes at a time.

With DNA chips, researchers can easily and quickly measure the expression of thousands of genes in a single experiment, providing a comprehensive view of genetic activity in a sample. This enables the identification of gene expression patterns associated with specific diseases or conditions, as well as potential targets for drug development. In addition to gene expression analysis, DNA chips are also useful for genotyping, DNA sequencing, and disease diagnosis. For example, they can detect single nucleotide polymorphisms (SNPs) associated with disease susceptibility or mutations in specific genes linked to inherited disorders. Overall, DNA chips are a powerful and efficient tool that has transformed molecular biology research by enabling the study of gene expression, identification of genetic variations, and diagnosis of diseases in a comprehensive and accurate manner.[8]

2.3 FEATURES OF DNA CHIPS:

Some of the key features of DNA Chips include:

- **High-throughput Analysis:** By allowing for the analysis of numerous genetic variations or gene expression levels at the same time, DNA chips provide a comprehensive overview of genetic activity in a sample. This can encompass thousands, or even millions, of such variations, resulting in an unparalleled understanding of the genetic makeup of the sample.
- **Versatility**: The design of DNA chips can be adapted to suit a variety of applications, such as gene expression analysis, SNP genotyping, DNA sequencing, and the diagnosis of diseases. In other words, DNA chips have the flexibility to be tailored to meet the specific needs of various genetic research fields.
- **Speed**: By offering a fast and efficient means of analyzing significant amounts of genetic data, DNA chips significantly decrease the time required for data analysis, from potentially taking several months or years to just a few hours. In other words, the speed and efficiency of DNA chips allow for the analysis of vast amounts of genetic information in a short amount of time.
- **Accuracy:** DNA chips are capable of detecting even the slightest differences in gene expression or genetic variations, resulting in highly precise and accurate results. In other words, DNA chips are known for their ability to discern small changes in genetic activity with a high degree of accuracy.
- **Reproducibility:** DNA chips are capable of generating consistent and reproducible results, even when analyzing changes in gene expression or genetic variations across multiple experiments or samples. In other words, DNA chips provide reliable and consistent data, allowing researchers to draw meaningful conclusions from their analyses.
- **Customizability**: DNA chips can be customized and designed to fit the specific needs of a given research project, enabling the addition or removal of probes based on genes or genetic variations of interest. This feature allows researchers to tailor DNA chips to their specific research objectives, resulting in more targeted and effective analyses.[7]

3.1 CONSTRUCTION OF DNA CHIPS:

Patrick Brown and his colleagues at Stanford University created the initial DNA microarray, which they utilized to examine the intricate mechanisms by which yeast cells produce spores. This technology has been employed for numerous experiments since then. Recently, they have been utilizing DNA microarrays to identify genes associated with or responsible for causing cancer. Specifically, they aim to characterize gene expression patterns for melanoma and other types of malignancies in order to determine the presence and stage of a tumour.[6]

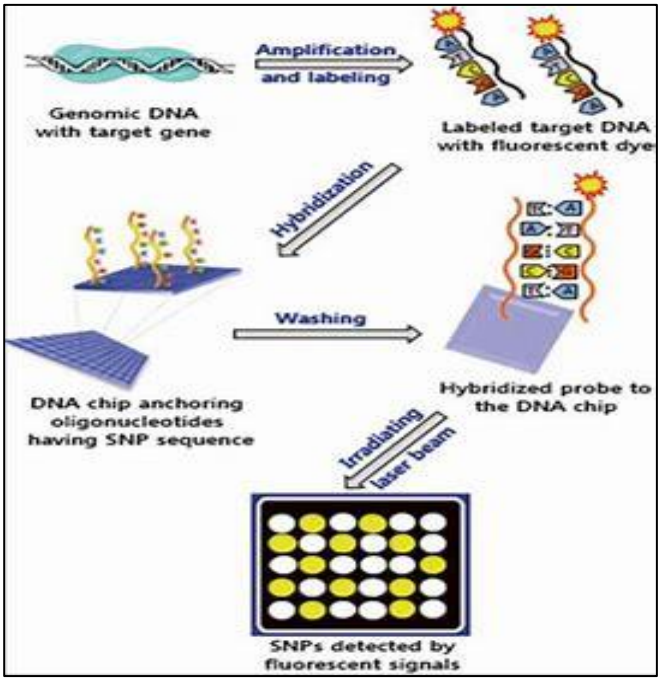

Fig no. 1 DNA Chips sequence

3.2 WORKING OF DNA CHIPS:

The process of constructing a DNA chip begins with probe design, which involves creating short, single-stranded DNA molecules that are designed to bind specifically to a target sequence. The probes are then synthesized using chemical or enzymatic methods, and purified and quality-checked to ensure their high quality.

Next, the probes are spotted on a solid surface, such as a glass slide or silicon wafer, using a microarray printer or robot. To prevent non-specific binding, the chip surface is blocked with a solution containing a mixture of proteins.

The sample of DNA or RNA to be analyzed is then labeled with a fluorescent dye and hybridized to the probes on the chip. The chip is incubated under specific conditions to allow the probes to hybridize with complementary target sequences in the sample.

The chip is then scanned using a fluorescence detection system to detect the fluorescent signal from each spot on the chip. The signal intensity is proportional to the abundance of the corresponding DNA or RNA sequence in the sample.

Finally, specialized software is used to analyze the data generated from the chip to determine gene expression levels or identify specific genetic variations or mutations.

Overall, the construction of DNA chips is a multi-step process that requires careful design, synthesis, and quality control to ensure the probes are specific and of high quality. However, once constructed, DNA chips provide a powerful tool for high-throughput analysis of gene expression and genetic variation.[6]

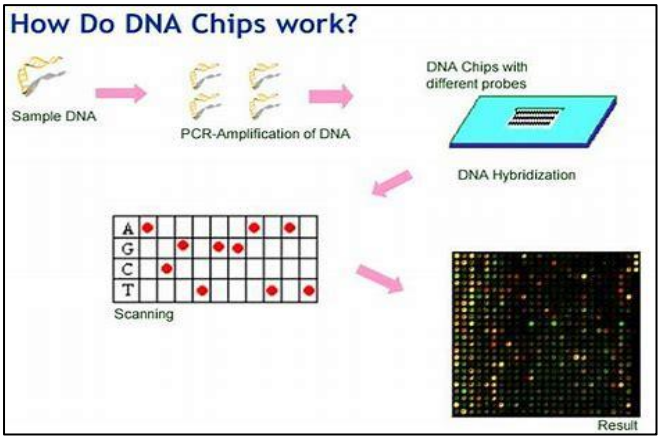

Fig no. 2 Working of DNA Chip

4. TYPES OF DNA CHIPS

There are two types of DNA Chips

1. cDNA

2. oDNA

1. cDNA:

One type of microarray is the cDNA-based microarray, which involves the following steps:

• The first step is to prepare the chip using cDNA, which can also be referred to as cDNA chips, cDNA microarrays, or probe DNA.

• The cDNAs are amplified using PCR.

• The amplified cDNAs are then immobilized on a solid support made of either a nylon filter or a glass slide (typically 1 x 3 inches) and loaded into a spotting spin through capillary action.

• A small volume of the DNA preparation is then spotted onto the solid surface, creating physical contact between the cDNAs and the solid support.

• The DNA is delivered mechanically or robotically.

2. oDNA:

- Oligonucleotide microarrays utilize short DNA
- oligonucleotides that are spotted onto the array, typically 20-25mers per gene.
- One of the primary advantages of this technology is that each gene is typically represented by multiple probes.
- These microarrays are made possible through the use of photolithography, a process borrowed from the computer industry, and are available as off-the-shelf products.

5. APPLICATIONS OF DNA CHIPS;

5.1 HEALTH CARE INDUSTRY:

The integration of DNA chips into healthcare systems has the potential to revolutionize the healthcare sector, but there are several technical limitations and privacy issues that must be addressed before widespread adoption. The incorporation of DNA chips into healthcare information systems will change the relationship between healthcare organizations and information systems. Previously, healthcare information systems only stored and processed data generated by healthcare organizations, but with the integration of DNA chips, a new relationship will form in which healthcare organizations purchase information from the chips. This will clarify and streamline the complexity of the healthcare supply chain, resulting in a better structure.

Additionally, the healthcare information supply chain can be connected with other systems through an open network

that allows for the integration of internal and external networks, as shown in the healthcare information supply chain diagram. Although the technology for an open network supply chain information system is available, privacy issues are preventing the widespread adoption of DNA chips in open network information systems.

The commercialization of DNA chips can significantly improve the quality of healthcare services. People can use DNA chips to test themselves for diseases regularly, and healthcare providers can assess the health status of patients more accurately through the healthcare information system connected to the chip. Healthcare organizations can also benefit from the commercialization of DNA chips by reducing the burden on medical personnel. Patients can use DNA chips to test for diseases at home, and only visit healthcare organizations for more precise secondary tests, leading to a reduction in the need for medical staff.

In developing countries where access to medical care is limited, DNA chips can be a game-changer. Patients can use DNA chips to test themselves at home and seek medical care only when necessary, reducing the burden on healthcare organizations and medical personnel. Overall, DNA chips have the potential to significantly impact the healthcare sector and improve the quality of healthcare services.

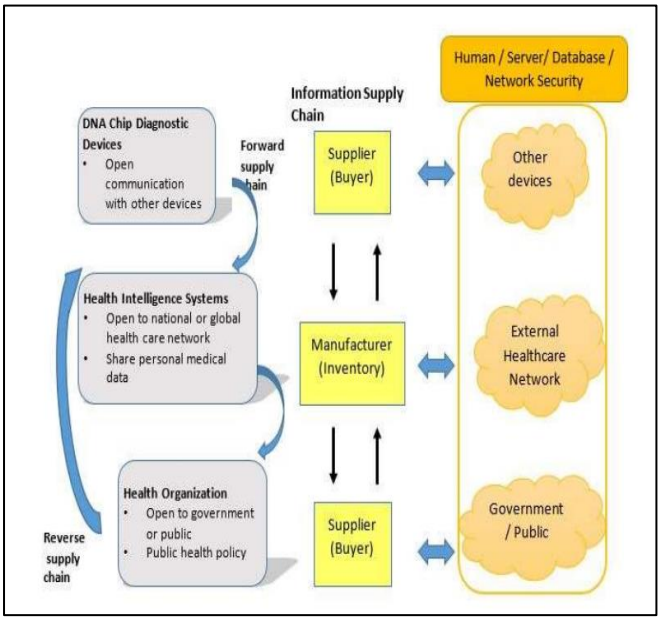

Fig no. 3 Healthcare information supply chain in Open Network

❖ **Miniaturization of DNA Diagnostic Chip:** The recent advancements in DNA chip technology have led to an increase in research utilizing these chips, as many technical limitations have been resolved or are near resolution. In the past, genetic disorders such as cancer were studied in laboratory settings, and significant progress was made in disease diagnosis. From the late 1990s, scientists attempted to develop new drugs using DNA chips, and in the early 2000s, DNA chips were used to predict the prognosis of breast cancer for the first time. Since then, researchers have utilized gene expression data obtained from DNA chips to diagnose various types of cancer, including brain cancer, with positive outcomes. Even today, investigations examining the link between DNA and disease continue.[4]

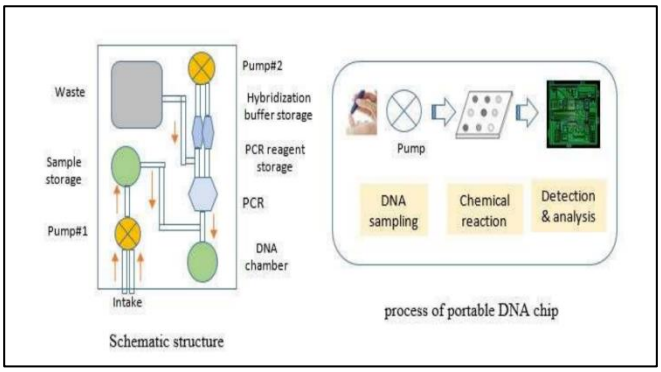

Fig no. 4 Prototype of portable DNA Chip

❖ **Performance measures of DNA Chips:**
- **Performance measures of DNA Chips**
- **Customer satisfaction based on market issues**
- **Security based on social issues**

Fig no. 5 Performance measure framework of DNA chip technology

5.2 NANOGOLD STAINING:

DNA microarray hybridization has become a crucial tool for biomedical research since the development of microarray technology by Schena and colleagues in 1995. DNA probes, such as oligonucleotide or complementary DNA (cDNA), are immobilized on solid phases, such as modified glass or membrane surfaces, for various applications including gene expression, pathogen detection, genotyping, resequencing, drug discovery, pharmacogenomic research, cancer diagnostics, and protein-DNA interactions. Due to the large number of genes to be probed, the quality of the array is of critical importance, and a reliable characterization of each chip before use can significantly increase the confidence of the data obtained. However, DNA microarray chips are still very expensive, and therefore, the methods described in this article to ensure the quality of a chip can save both money and time.

Fluorescence is the most popular technique to identify hybridization, but it usually requires a laser scanner with a confocal microscope device to achieve sensitive detection, which is very expensive. Recently, nanoparticles were introduced for the detection of DNA microarray hybridization. DNA probes were synthesized on gold nanoparticles and hybridized with DNA on the glass surface. The sensitivity of the gold labelling method is equivalent to that of fluorescent labelling. Silver enhancement is often used to further amplify the signal, but careful handling is essential to prevent overstaining by silver.

Several microarray quality control methods for spots have been used, but the characterization of microarray spots for each chip is critical before the hybridization. Wang and coworkers used third-dye array visualization (TDAV) technology to quantitatively evaluate and control every area. However, labelling DNA probes with fluorescence dyes was an expensive and tedious process, and the method of detection also required an expensive confocal laser scanner to reduce the background. Furthermore, the overlap in the emission wavelengths of Cy3 and Cy5 was a disadvantage.

To address these issues, the authors developed a method to assess the quality of DNA microarray spots and hybridize the target DNA on the same microarray using commercially available positively charged gold nanoparticles coated with amino groups on the surface. These gold nanoparticles were reported to be dissolved in a bromine-bromide solution. The same array could be subsequently used to perform hybridization. Cationic gold particles attract anionic DNA molecules, resulting in the deposition of gold particles on the surface, which is visible and can be scanned directly by a simple and inexpensive flatbed scanner[5]

6. CONCLUSION:

In summary, the advent of DNA chips has brought about a ground-breaking transformation in the realm of molecular biology, with a powerful and efficient method for the study of gene expression, identification of genetic variations, and diagnosis of diseases. These chips offer numerous benefits such as high-throughput analysis, speed, precision, sensitivity, reproducibility, and customizability. However, they also have drawbacks, including cost, complexity, sensitivity to experimental conditions, limited coverage, bias, and the need for validation. In general, DNA chips are a valuable instrument for genetic research and clinical purposes, but their application demands careful deliberation of experimental design, data interpretation, and potential limitations. With ongoing technological advancements, DNA chips are likely to grow even more powerful and versatile in their applications, thereby enhancing our understanding of genetics and human health.

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