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Dielectrophoresis spectroscopy for nucleotide identification in DNA

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ABSTRACT

DNA sequence with a known physical position on a chromosome is called a genetic marker, so the causal gene may identify with genetic markers in different kinds of hereditary diseases. DNA segments near one another on a chromosome often inherit the other concurrently; as a result, the inheritance of a neighboring gene that has not yet been discovered but whose general position is tracked by using genetic markers. So, Genetic markers can play a significant role in biological research because they can contribute to identifying many diseases. Single nucleotide polymorphism, or SNP (pronounced "snip"), is the variation of a single nucleotide in a DNA due to genetic disorders. For example, in a specific region of DNA, an SNP may displace the nucleotide cytosine (C) with the nucleotide thymine (T). SNPs, or single nucleotide polymorphisms, are one of the most common genetic variations that assist in detecting many human diseases such as Migraine, Cancer, Schizophrenia, Sickle Cell Anemia, Alzheimer's Disease, etc. Hyperchromicity, Short Oligonucleotide Analysis Program (SOAP), quantitative PCR techniques, Fluorescence Polarization Melting Curve Analysis, SNP Microarrays, Intercalating Dyes, and many other techniques are commonly used to identify SNPs nowadays. However, those methods are not much reliable, a bit costly, time-consuming, and difficult to use, whereas dielectrophoresis can be an excellent way to detect SNP easily. A non-uniform electric field generated by electrodes interacts with polarizable suspended particles to regulate and alter particle movement; this process is known as dielectrophoresis (DEP). Cell transfer, in vitro fertilization, and biological testing are a few uses for dielectrophoresis, particularly in the biomedical industry. Cell fusion using dielectrophoresis has also improved crossbreeding, cancer treatment, and scientific research. Most notably, dielectrophoresis is used to classify changes in the electrical characteristics of cells. In this phenomenon, when a dielectric particle is exposed to a non-uniform electric field, a force is produced on it, and this DEP force may be utilized to recognize the variations in a single location in a DNA sequence. DEP is less time-consuming, cheap, and reliable than other processes to detect SNPs easily.

1. Introduction

DNA is one of the most prevalent genetic components in all living creatures (Travers and Muskhelishvili, 2015). DNA's nucleotides are significant aspects of biological systems, as they are involved in cell signaling, metabolism control, expression of genetic information, the storage of cellular energy so on (Strezsak et al., 2022; Bowater and Gates, 2015). Genetic markers are widely applied in global and local aspects, for example, to estimate the inbreeding coefficient or the intensification of migration (Tereba and Konecka, 2021). Single nucleotide polymorphisms account for the vast majority of all variations in human DNA. (Hyman et al., 2022). The replacement of a single base at a particular location in a gene is known as a single nucleotide polymorphism (SNP). Since genotyping and SNP detection assist in determining genetic disorders, including disease risks and susceptibility to particular drugs, there is a significant demand for SNP detection and genotyping procedures (Takahashi et al., 2020). Genome-wide association study (GWAS), SNP-LAMP probs, and many other methods can be used to detect SNP (Hyman et al., 2022; Zhang et al., 2019a). On the other hand, dielectrophoresis is also a commonly used biological method in which a force is applied to a polarized particle suspended in a medium due to a non-uniform electric field [EF] to detect SNPs (Reynaud et al., 2021; Swami et al., 2021; Zhang et al., 2020; Cheng et al., 2010). Moreover, spectroscopy is the most commonly applied technique (Wang et al., 2021a), and many spectroscopic methods are used nowadays in the research fields, such as Laser-induced breakdown spectroscopy [LIBS]

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(Laserna et al., 2018), Quantum gravitational spectroscopy (Nesvizhevsky et al., 2015), Nuclear magnetic resonance (NMR) spectroscopy (Liu et al., 2019), Dielectrophoresis spectroscopy (Chung et al., 2018), etc. The precise identification of DNA sequences that may only vary by a single nucleotide polymorphism (SNP), which is a crucial factor in many genetic diseases, is one of the main aims of these DNA detection methods (Li, Li) (see Tables 1 and 2, Figs. 1–7).

1.1. Single nucleotide polymorphism (SNP)

The DNA sequence variation is known as a single nucleotide polymorphism (SNP), which is caused because of a single nucleotide [Adenine (A), Thymine (T), Cytosine (C), or Guanine (G)] alteration in the genomic sequence (Koopaee and Koshkoiyeh, 2014). This single nucleotide polymorphism (SNP) is a tool for marker-assisted selection used to identify alleles related to diseases. (Chen et al., 2009; Duran et al., 2009; Boccacci et al., 2020). SNPs are the most common, prominent, newest, and simplest sequence variation in the human genome, which are useful polymorphic genetic markers, too (Alam et al., 2021; Chaitanya et al., 2018; Aftabi et al., 2020; Fadason et al., 2022). SNPs are most frequently found between the nucleobases C and T because Cytosine GC-rich areas are generally methylated, and C changes to T due to spontaneous deamination (Yang et al., 2020). Gene-gene/SNP–SNP interactions or non-coding regions have been shown to have a more significant role in the causation of many complex diseases (Fadason et al., 2021; Lin et al., 2021), such as Cancer (Möhlendick et al., 2019), Autism (Génin, 2020), Alzheimer's Disease [AD] (van der Linden et al., 2021), Type 2 Diabetes Mellitus [T2] (Ban et al., 2010), Sickle Cell Disease [SCD] (Adekile et al., 2021), Autoimmune Diseases (Pellenz et al., 2021), Chronic Obstructive Pulmonary Disease [COPD] (Liu et al., 2020) so on (Guan et al., 2020). The global pandemic known as the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) killed a lot of people across the world (Marino et al., 2020; Grady et al., 2020). The COVID-19 outbreak began in China's Wuhan city at the end of December 2019 and quickly expanded to South Korea, Japan, Iran, Thailand, Singapore, and worldwide within a few months (Umakanthan et al., 2020). Using sequenced Severe acute respiratory syndrome coronavirus 2 [SARSCoV-2] data, scientists recently developed an SNP identification process to detect genetic variation (Harper et al., 2021; Yamayoshi et al., 2020; dos Santos et al., 2021). However, the development of on-site SNP detection faces many problems, such as costly equipment and labor-intensive procedures (Cao et al., 2019).

Table 1
A list of the methods which are commonly used in the identification of Single Nucleotide Polymorphisms (SNPs).

No	Methods	Procedure/Definition/Details	References
1.	Oligonucleotide Analysis Method	This method helps identify the variations of nucleotides.	(Iannone et al. et al.)
2.	PCR-based methods	PCR-based methods for SNP/mutation detection are broadly classified into two types: (Travers and Muskhelishvili, 2015) polymorphic or mutant allele-directed specific analysis, which employs primers matched with substituted nucleotides or oligonucleotides to block or clamp the nontargeted template, and (Strezsak et al., 2022) melting curve analysis, which applies hydrolysis probes, hybridization probes, or double-stranded DNA-binding fluorescent dyes in combination with real-time PCR techniques	Matsuda (2017)
3.	Mass Spectrometry	The detection of single-base extension products of a primer directly next to the SNP site is used for SNP genotyping by mass spectrometry.	Butler et al. (1999)
4.	Hybridization	The hybridization method comprises two allele-specific probes intended to hybridize to the target sequence only when they match entirely.	Kwok (2001a)
5.	Primer Extension	Primer extension is a particularly efficient allelic discrimination technique. It is highly adaptable and requires only a few primers/probes.	Kwok (2001a)
6.	Fluorescence Detection	For ultrasensitive detection of single-nucleotide polymorphism (SNP), a simple, label-free, and highly effective nucleic acid amplification approach is created called Fluorescence detection.	Ma and Gao (2018)
7.	Fluorescence Polarization	It has the capacity to establish an organism's mutational status or genotype swiftly and has several uses in molecular diagnostics, clinical genetic testing, population genetics, and agricultural biotechnology.	Kwok (2002)
8.	Molecular Beacon Genotyping	This is a common technique to detect SNPs.	Mhlanga and Malmberg (2023)

Table 2
The drawbacks of the other techniques in comparison with the Dielectrophoresis Spectroscopy method.

No	Methods	Drawbacks and Benefits	References
1.	Quantitative PCR Method	Since this method is challenging, has a low success rate, is time-consuming, and needs costly equipment, it impedes the research of the genetic association to identify many diseases.	Smith and Osborn (2009)
2.	SNP Genotyping Method	SNP genotyping instruments cannot retain all genomes perfectly.	Dvornyk et al. (2004)
3.	Oligonucleotide Analysis Method	This is a very complex method with experimental errors.	Wang et al. (2003)
4.	SNP Microarrays	The SNP Microarrays process is unable to detect the balanced genomic rearrangements, for example, translocations or inversions.	Balagué-dobón et al. (2022)
5.	Mass Spectrometry	Professionals are needed in MS detection, which has the fundamental drawback of requiring a very high-purity sample.	Kim et al. (2017)
6.	Next-Generation Sequencing (NGS) Technology	Not so popular, traditional sequencing technologies are widely established.	Alkan (2011)

1.2. Possible methods of identifying single nucleotide polymorphisms (SNPs)

1.2.1. Quantitative PCR method

One of the oldest techniques for SNP genotyping is the TaqMan method (Applied Biosystems, Foster City, CA), depending on fluorescently-tagged, allele-specific probes identified by real-time polymerase chain reaction (PCR)-based determination (Broccanello et al., 2018). At this time, it is hard to think about molecular biological research without PCR. Saiki et al. initially described this ground-breaking method in 1985, followed by Mullis and Faloona in 1987, who applied it to amplify the -globin genome sequence to diagnose sickle cell anemia (Matsuda, 2017). Real-time TaqMan PCR was first proposed in 1991 and subsequently developed for commercial use (Stucki et al., 2012). In

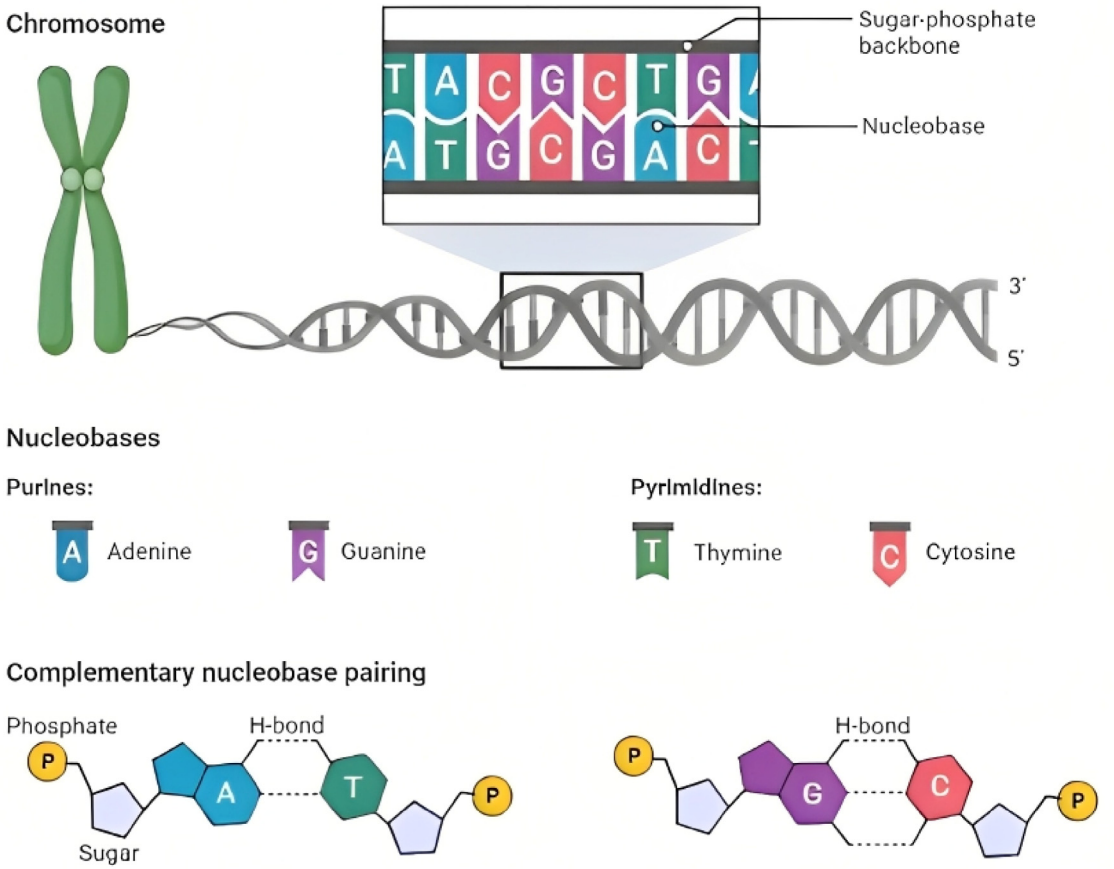

Fig. 1. Single-nucleotide polymorphisms (SNPs), the most prevalent kind of DNA variation, are single nucleotide alterations found in the genome sequence (Yoo et al., 2023). SNPs are places in a population wherein more than one nucleotide is detected. An SNP locus often has just two alleles, such as an A or a T. In humans, millions of SNP sites have been found (Daiger et al., 1016). SNPs are found more frequently in noncoding areas than in coding portions. SNPs mutate every 1000 nucleotides on average, assuming that around 5 million SNPs are associated with a person's genome (Youn et al., 2023).

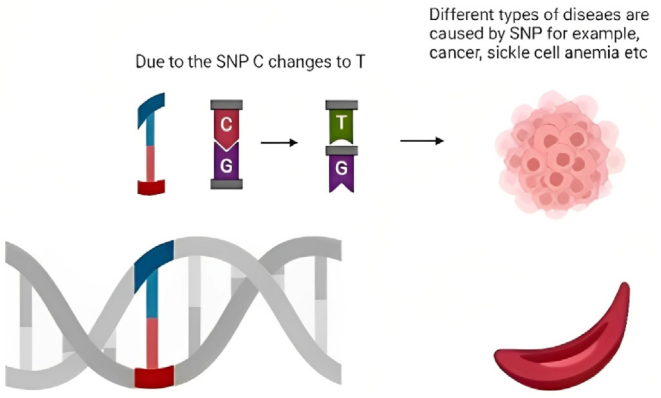

Fig. 2. A mutation is an alteration in the DNA sequence that affects at least 1% of the population and incorporates the replacement of one nucleotide (Youn et al., 2023). The SNP that causes the replacement of C with T is in the picture. Changing even one nucleotide in a DNA sequence may alter the protein's structure and function. Single nucleotide polymorphisms (SNPs) have been connected to a wide range of complicated disorders, including cardiovascular issues, diabetes, cancer, schizophrenia, high blood pressure, migraines, Alzheimer's, etc. (Yoo et al., 2023).

recent years, the real-time PCR platform has become commonly used in many global health and research laboratories (Price et al., 2010). Generally, a probe is used in the TaqMan-based real-time PCR to detect the specific DNA (Wang et al., 2021b). TaqMan probe-based real-time PCR detection can identify a single or small fraction of SNP sites (Zhao et al., 2021a). Besides, The TaqMan genotyper software is usually used to analyze the data, and this process needs an algorithm to assign a genotype to each sample (Bonelli et al., 2021). The TaqMan SNP Genotyping Assay is highly sensitive to detecting SNPs (Chen et al., 2019), and the sample detection time is much shorter (Zheng et al., 2020). Although TaqMan quantitative real-time PCR provides early detection, is accurate, and does not need gels, it does necessitate more costly equipment for the large-scale association studies, so it hampers the research of the genetic association in low-income countries to detect many diseases (Kovalchuk and Arkhipova, 2020; Yu et al., 2020; Pan et al., 2020; Sathirapatya et al., 2020; Islam et al., 2014; Shelton, 2006). Additionally, the TaqMan probe's design is challenging, and researchers had to attempt it so many times before finally succeeding (Xu et al., 2014). In addition to being time-consuming and labor-intensive, PCR processing may also bring contamination to a lab (Ert et al., 2004).

1.2.2. Oligonucleotide analysis method

Oligonucleotides are a kind of short-chain nucleotides with a typical length of lower than 20 bases, along with short-chain single-strand DNA (ssDNA) and short-chain RNA (microRNA and siRNA), which are applied in a variety of analytical and diagnostic methods, and as therapeutic medicines (Enmark et al., 2021; Wang et al., 2019; Yesudas et al., 2015; Sahle and Lowe, 2020; Weidolf et al., 2021). Technology based on oligonucleotide arrays has been successfully used mostly for mapping genomic clones, identifying mutations and polymorphisms, tracking gene expression patterns, and discovering new genes. Oligonucleotide arrays,

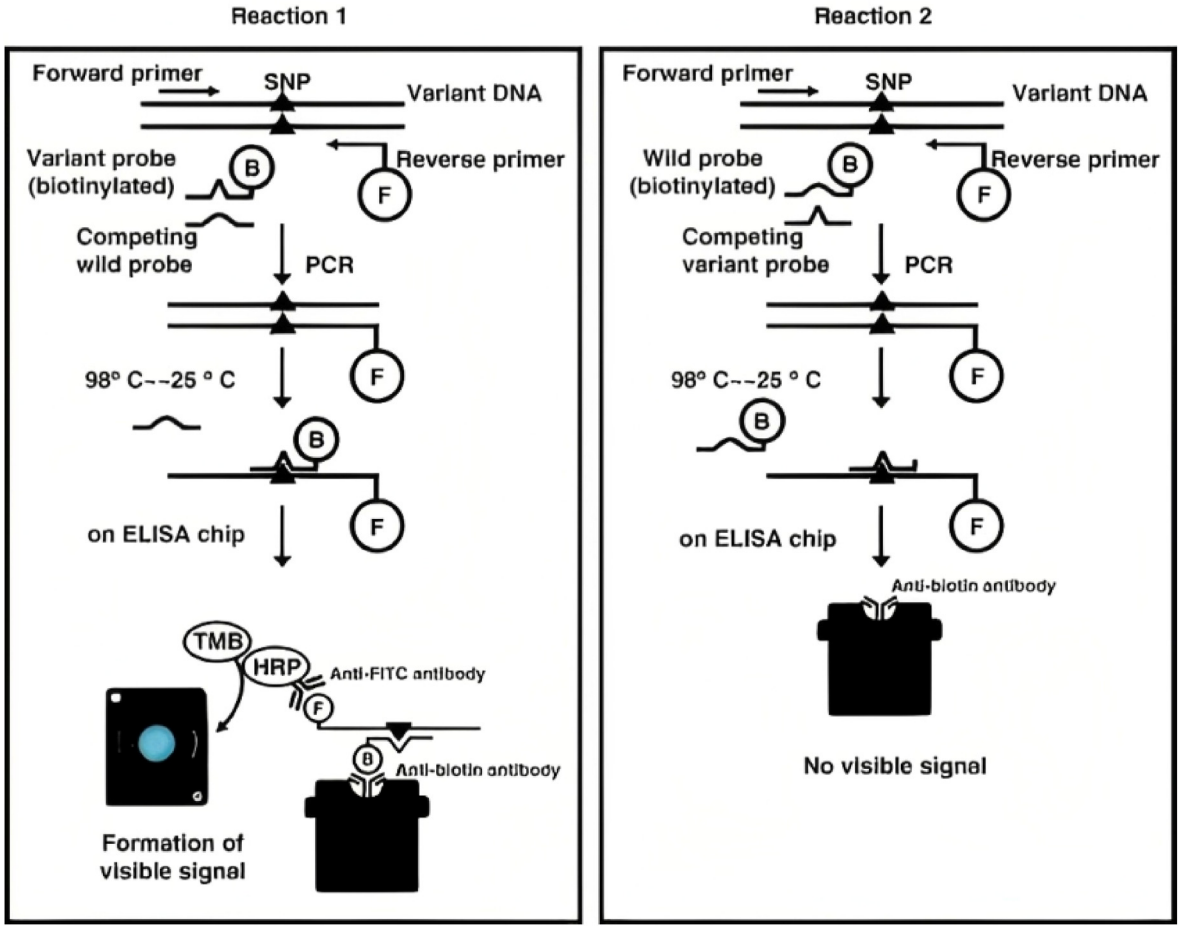

Fig. 3. Analyze variant DNA using reaction 1 (left) to identify a variant sequence and reaction 2 (right) to find a wild-type sequence. SNP sites are indicated by closed triangles. F is for fluorescein isothiocyanate (FITC) labeling; B stands for biotin labeling; HRP represents horseradish peroxidase; and TMB refers to 3,3V,5,5Vtetramethylbenzidine (Hiratsuka et al., 2006). [Figure is adopted from: Hiratsuka M, Ebisawa A, Sakuyama K. Competitive allele-specific short oligonucleotide hybridization (CASSOH) with enzyme-linked immunosorbent assay (ELISA) for the detection of pharmacogenetic single nucleotide polymorphisms (SNPs). 2006; 67:87–94. by taking permission from the authors].

therefore, provide a viable solution for high-throughput polymorphism analysis, with the capability to simultaneously identify thousands of SNPs (Guo et al., 2001). In addition, SOAP is software for efficiently aligning short oligonucleotides onto reference sequences, both for gapped and ungapped. SOAPsnp has gained popularity recently due to its close connection with SOAP aligner and other SOAP modules, which are regularly improved and offer a one-stop shop for the continuum of sequencing analysis (Kumar et al., 2012). The software is built to manage the massive quantities of short reads produced by parallel sequencing using the latest Illumina Solexa's sequencing technology (Li et al., 2008). Although SOAP has the quickest performance of all the tools (Bao et al., 2011), this is still a very complex method with experimental errors. High-density oligonucleotide arrays have been recommended in order to enhance the efficacy of SNP detection by covering all potential sequence permutations of the relevant genomic region and reducing experimental errors (Wang et al., 2003).

1.2.3. SNP microarrays

In 1998, the technique of using SNP arrays for genotyping was established. There have been significant advancements in the method since then, making it one of the most productive instruments for genetic analysis (Mao et al., 2007). The SNP microarrays are a helpful ancillary tool for developing SNP genotyping because this SNP-based microarray may reliably identify specific genetic changes (Cho et al., 2020; Hedayat et al., 2017; Utine et al., 2014; Hamilton et al., 2015; Berry et al., 2019). According to the research, over half of the DNA samples examined using SNP microarrays had SNP call rates above 95% (de Vries et al., 2022). By improving the ability to identify genetic variation, SNP microarrays have significantly assisted disease research and diagnosis (Baugher et al., 2013). Besides, SNP array analysis is a very demanding method in the area of cancer research because of the diversity of genetic variations in cancer cells (Mao et al., 2007). A specific category of cancers that affect the bone marrow, blood, and lymphatic systems is referred to as "haematological malignancies." SNP microarrays especially provide lots of benefits when identifying various haematological malignancies, for example, Hodgkin lymphoma, non-Hodgkin lymphomas, myeloproliferative neoplasms, leukaemia, multiple myelomas, myelodysplastic syndromes, etc. (Berry et al., 2019; Papakonstantinou et al., 2021). Although microarrays to detect single nucleotide polymorphisms (SNPs) provide a cost-effective, robust, reliable, and fast (within 24 h) method, research showed that SNP-microarrays have a disadvantage in detecting the genes also (Gardner et al., 2013; Berry et al., 2020; Docherty et al., 2007; Kurokawa et al., 2016). In addition, SNP arrays are able to identify genomic abnormalities, but it is failed to detect the balanced genomic rearrangements like translocations or inversions (Steventon-jones et al., 2022).

1.2.4. Mass spectrometry

There are several applications for the genotyping of single nucleotide polymorphisms (SNPs) that can be utilized for the identification of complex diseases, and one of the most promising methods for SNP analysis is called mass spectrometry, which is efficient for large-scale

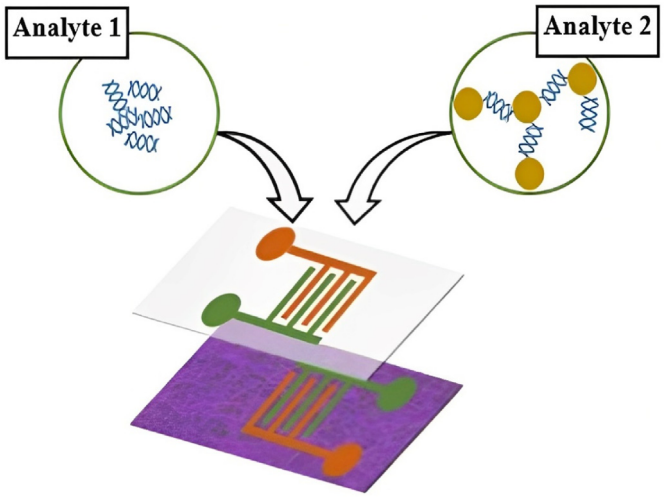

Fig. 4. DEP is extensively employed in biological applications such as drug administration, cell manipulation, and particle separation, among others. DEP may be performed using a variety of electrodes, including metal electrodes, insulator electrodes, light induced electrodes, and carbon electrodes. The most prevalent kind of DEP is metal electrode-based DEP, which is carried out using different structures composed of conducting metal, the most often utilized of which are IDEs (Bhatt et al., 2019). [Figure is adopted form: Bhatt G, Mishra K, Ramanathan G, Bhattacharya S. Dielectrophoresis assisted impedance spectroscopy to detect gold-conjugated amplified DNA samples. Sensors Actuators B Chem [Internet]. 2019; 288(March):442–53. Available from: https://doi.org/10.1016/j.snb.2019.02.081 by taking permission from the authors]. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

genome variation assessment (Hou et al., 2006; Sauer et al., 2003). The mass spectrometry-based identification technique has shown to be an effective research instrument that provides the possibility of assessing forensic DNA samples and simply identifying SNP variations (Zhang et al., 2019b). Mass spectrometric SNP genotyping can identify the single-base extension products of a primer that is located very next to the SNP site (Butler et al., 1999). It is also a very precise technique for determining the mass-to-charge ratio of analyte ions in either positive-ion mode or negative-ion mode (Sauer et al., 2006). Since mass spectrometry-based analysis allows for quick and reliable repeated assessments of a sample in a broad detection range, it has been commonly used to accomplish label-free multiplex genotyping (Jung et al., 2016). Genome variation analysis can be significantly benefited from the implementation of several Mass spectrometry methods, including matrix-assisted laser desorption/ionization (MALDI) and electrospray ionization (ESI) (Sauer, 2006). Mass spectrometry's signal accuracy and fast analysis allow it to stand out from other DNA characterization methods in clinical studies (Interference) but MS detection has the fundamental drawback of requiring the sample with a very high purity. This limitation may be overcome with improved product purification methods (Kwok, 2001b).

1.2.5. Next-generation sequencing (NGS) technology

A new era of commercially accessible sequencing technology, commonly referred to as next-generation sequencing (also known as high-throughput sequencing - HTS), was launched in 2004 with the Roche 454 FLX Pyrosequencer (NGS). The “next” in NGS indicates the ground-breaking scientific advances that enable the vast parallelization of the DNA fragment sequencing method, comparable to millions of individual Sanger sequencing experiments performed simultaneously (Larson et al., 2022; Khan et al., 2023). It is a revolutionary method that allows for the rapid sequencing of all nucleic acids (RNA and DNA) in a sample without previous knowledge of the target sequence (Khan et al., 2023). Thus, NGS methods can generate sequences of all nucleic acids present in a sample, allowing them to identify both known and unknown sequences (Khan et al., 2023). The deployment of NGS technologies has increased significantly over the last several years, including the Solexa/Illumina sequencer, 454/Roche system, and SOLiD/ABI system. An NGS platform may produce data at the gigabase-pair scale, which often includes millions or even hundreds of millions of sequencing read from a single sequencing run; as a result, NGS technologies are more suitable instead of other identification technologies (Yu and Sun, 2013). Besides the Metagenomic next-generation sequencing (mNGS) is also a new method that is being applied more frequently in the clinical diagnosis of infectious diseases, uncommon infections, difficult-to-detect infections, novel infections, complex infections, and severe infections nowadays.

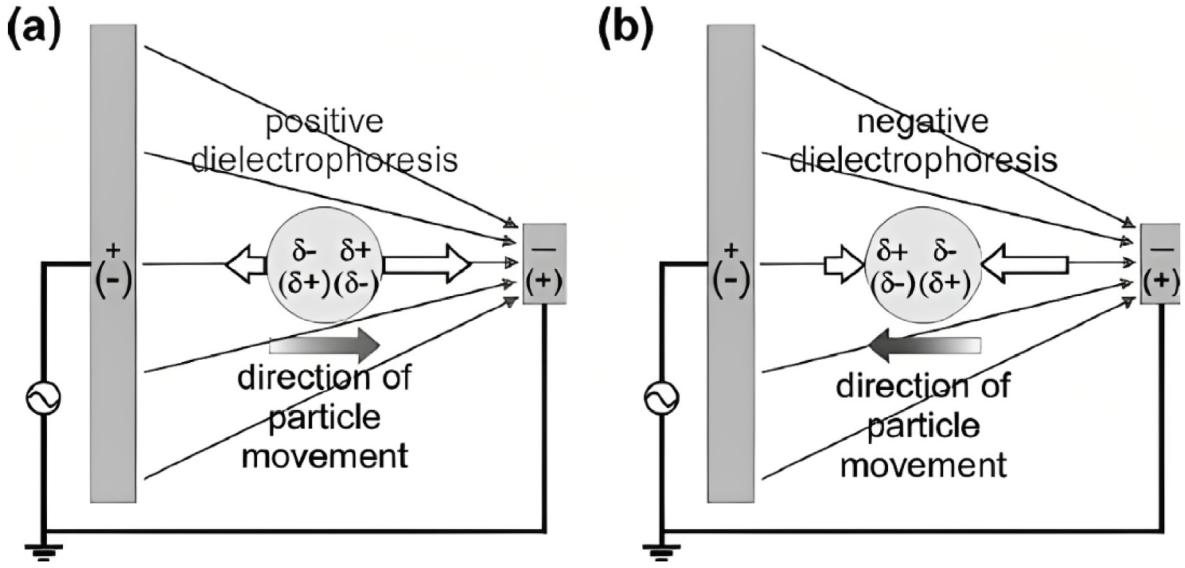

Fig. 5. When a particle or cell is exposed to an electric field, it gets polarized. If the electric field is inhomogeneous, the electrostatic forces at the dipole's two ends are not equal, and movement is triggered. (a) Positive DEP arises when the particle's polarisability exceeds that of the surrounding medium. Positive DEP is attracted to the greater electric field. (a) If the particle is less polarizable than the surrounding buffer medium, adverse DEP outcomes. Negative DEP drives the particle away from high-field-intensity locations and toward low-field-intensity ones (Pamme, 2007). [Figure is adopted from: Pamme N. Continuous flow separations in microfluidic devices. 2007 by taking permission from the authors].

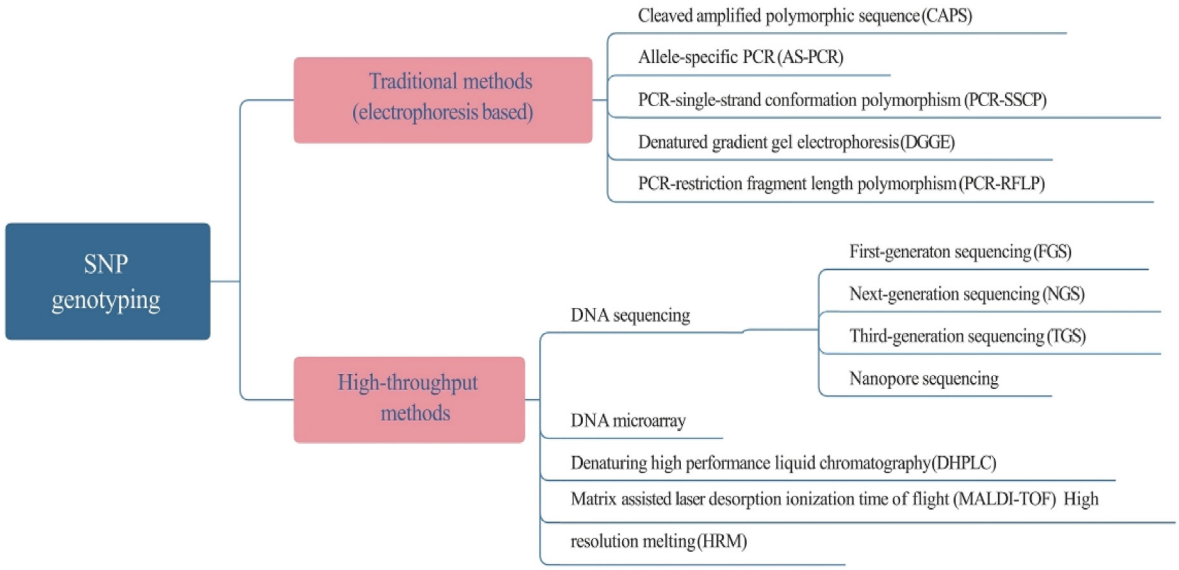

Fig. 6. Two different types of SNP methods can be found: (a)Traditional methods for SNP genotyping include cleaved amplified polymorphic sequence (CAPS), allele-specific PCR (AS-PCR), PCR-single-strand conformation polymorphism (PCR-SSCP), denatured gradient gel electrophoresis (DGGE), and PCR-restriction fragment length polymorphism (PCR-RFLP). (b) High-throughput technologies include DNA sequencing, DNA Microarray, denaturing high-performance liquid chromatography, matrix-aided laser desorption ionization-time of flight (MALDI-TOF), and high-resolution melting (HRM). First-generation sequencing (FGS), next-generation sequencing (NGS), third-generation sequencing (TGS), and nanopore sequencing are the four types of DNA sequencing (Yang et al., 2020). [Figure is adopted from: Yang S, Gill RA, Zaman QU, Ulhassan Z, Zhou W. Insights on SNP types, detection methods and their utilization in Brassica species: Recent progress and future perspectives. J Biotechnol [Internet]. 2020; 324(September):11–20. Available from: https://doi.org/10.1016/j.jbiotec.2020.09.018 by taking permission from the authors].

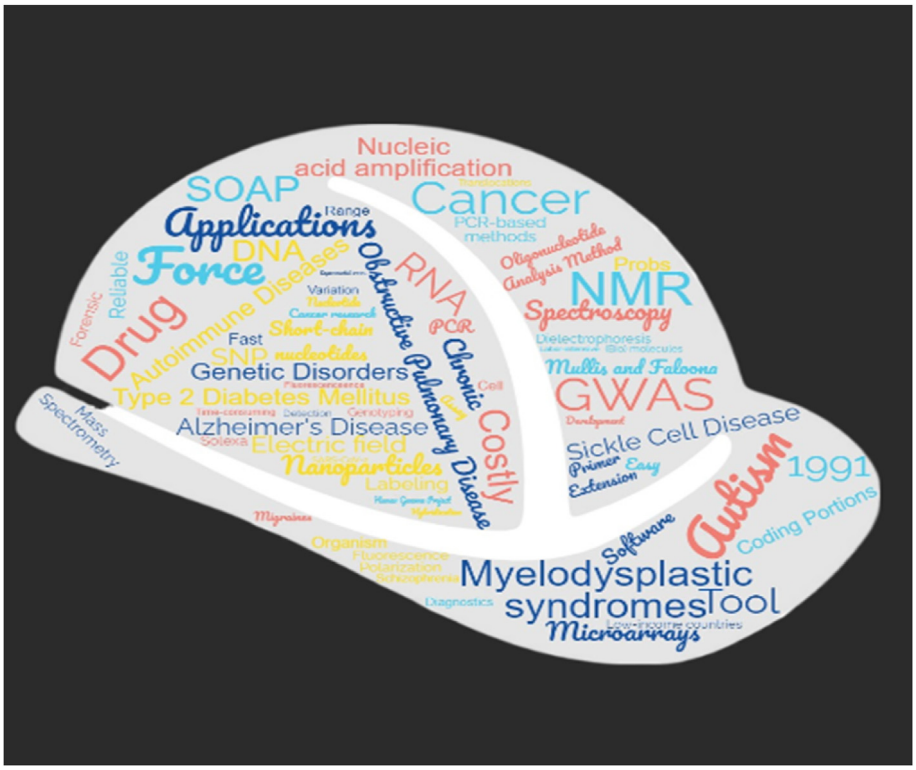

Fig. 7. Word cloud(https://www.wordclouds.com) represents the primary keywords of this manuscript.

This high throughput technology, may identify all infections in a clinical sample in a single sequencing run, giving additional information to guide treatment options and improve antibiotic stewardship. mNGS has been effectively used in a variety of infectious disorders, according to published case reports and clinical research (Lin et al., 2022). It can instantly sequence the nucleic acids in clinical samples and then compare the findings to the database so that it is easy to identify harmful objects in clinical samples rapidly (Gao et al., 2023). Although by using the next-generation sequencing technology, the identification of single nucleotide polymorphisms (SNPs) has become quicker and more

affordable, new SNP detection techniques for NGS technologies are still limited by a lot of challenges, including systematic and random errors, despite the fact that SNP detection techniques for traditional sequencing technologies are widely established (Yu and Sun, 2013; Xu et al., 2012; Souaiaia et al., 2011).

1.2.6. Dielectrophoresis spectroscopy method

Since the early 1990s, Dielectrophoresis (DEP) has been considered a valuable and widely used technology for collecting living cell information (Turcan et al., 2021; Ji et al., 2021). Dielectrophoresis comprises two words: dielectro, which refers to how motion is affected by dielectric characteristics, and phoresis, which relates to motion (Bakewell et al., 2013). In other words, Dielectrophoresis (DEP) is an analytical and manipulation technique that is a force produced by electrically polarizable particles because of the interaction between their induced dipole and non-uniform electric fields (Soffer et al., 2020; Kim et al., 2019; Yoshioka et al., 2016). This is a convenient method for the selective manipulation of (bio) molecules as it is a non-invasive procedure (Viefhues and Eichhorn, 2017). It is a noninvasive, nondestructive, and rapid technology that provides enormous benefits for the controlled manipulation, separation, and analysis of biological materials, so it plays an essential role in life science applications (Viefhues and Eichhorn, 2017). Dielectric techniques, such as dielectric spectroscopy and AC electrokinetic procedures (dielectrophoresis, electrorotation, and electro-orientation), illustrate useful information regarding cells (Patel and Markx, 2008; Abdulhameed et al., 2021).

A biological cell's dielectrophoretic behavior is usually dependent on frequency, and a similar cell may exhibit both positive and negative dielectrophoresis in various frequency ranges. Dielectrophoretic behavior switches from positive to negative dielectrophoresis at a frequency known as the crossover frequency (Patel et al., 2008; Wei et al., 2009). Positive (pDEP) and negative (nDEP) DEP may be seen migrating particles toward high and low-intensity electric fields, respectively (Nejad et al., 2013). The response is called positive DEP when the nanomaterial travels with an attractive force (Okayama et al., 2019) towards the high electric field region (Liu et al., 2019; Chen et al., 2014; Hamada et al., 2013). In contrast, Negative DEP is the force exerted on dielectric particles away from the high-field areas by an electric field gradient in the opposite direction of the electric field gradient (Gudagunti et al., 2018; Suzuki et al., 2016). Positive dielectrophoresis usually has a greater dielectrophoretic force than negative ones (Suzuki et al., 2012). In DEP, the particles possess the electrical potential and conduct themselves differently to various frequencies. The particle size, density, molecular weight, and purity, on the other hand, govern particle manipulation in the electrophoresis procedure. Cataphoresis refers to the electrophoresis of positively charged particles (cations), while anaphoresis refers to the electrophoresis of negatively charged particles (anions). Another distinction between the two techniques is that DEP can build a particle trap using electromagnetic fields, while electrophoresis cannot generate stable non-contact particle traps (Rahman et al., 2017). DNA detection, cell sorting, positioning, and patterning have all been done using negative DEP (Piao et al., 2021). Dielectric spectroscopy (DS) is a potential way of detecting the dielectric characteristics of living cells in real-time that is non-invasive, label-free, and very quick (Mansoorifar et al., 2017). This (DEP) is a technology that is both accurate and, at a time, cost-effective (Leiterer et al., 2016).

1.3. The relationship between the SNP-dielectrophoresis process and a brief comparison with other standard methods

SNPs are genetic polymorphisms from single base-pair positioning changes in DNA sequences across individuals of similar species or between different species (Amiteye, 2021). According to estimates, there are around 10 million SNPs in the human genome (Chen et al., 2011). SNP markers can be used in genetic association studies to identify genetic factors responsible for complex phenotypes in various types of chronic diseases that are caused by a bit of change in the expression of genes, for example, cancer, cardiovascular disease (CVD), gout disease, etc., so it is essential to detect SNP (Lee, 2007; Zhao et al., 2021b; Verbeek et al., 2019; Gene et al., 2021; Bush and Moore, 2012). Nowadays, there are various ways of identifying SNPs (Shen et al., 2010), such as TaqMan probes (Cózar Guerrero et al., 2021), SNP microarrays (Vona et al., 2018), SNP MassARRAY system (Kulasinghe et al., 2021), next-generation sequencing (Sabiha et al., 2021), PCR-based allele amplification (Qu et al., 2019), electrochemical primer extension (Chahin et al., 2018), fluorescent nanosphere technique (Chen et al., 2018), etc. Besides, genetic mapping of quantitative trait loci (QTL), phylogenetic analysis, bulked segregant analysis, marker-assisted selection, DArTag™ panel (Arbon et al., 2021), genome-wide association studies (GWAS), and genome selection studies are a few of the SNP uses (Kumar et al., 2012; Guo et al., 2021). In dielectrophoresis (DEP), a non-uniform alternating current (AC) or direct current (DC) electric field polarises and moves suspended dielectric particles relative to the medium (Lu et al., 2020). Since the theoretical studies started on dielectrophoresis, several types of research have been conducted on implementing DEP in the biomedical area (Zhong and Kang, 2016). In recent years, dielectrophoresis has become a powerful tool that is cheap, non-invasive, non-destructive, easy to use, and quick (Srivastava et al., 2011; Páez-Avilés, Juanola-Feliu, Punter-Villagrasa). It is also easy to manipulate the motion of micro-and nanoparticles like DNA molecules by utilizing this technology (Shi et al., 2010). But a few problems can occur in dielectrophoresis; for example, electrode fouling and electrolysis are two significant difficulties encountered with DEP (Hanson and Vargis, 2017).

2. Discussion

SNP identification techniques are costly, but they may provide insight into the relationship between single-nucleotide polymorphism (SNP) frequency and other forms of genetic variants with specific characteristics in order to detect many prevalent disorders (Marczyk et al., 2021; Bastien, Boudhrioua, Fortin). Moreover, after the finalization of the Human Genome Project, one of the most challenging tasks in genome research is the analysis of DNA variation. Among the many uses are genotyping single nucleotide polymorphisms (SNPs) for disease dissection, pharmacogenetics, marker-assisted plant or animal breeding, and traceability (Sauer et al., 2003). The ideal genotyping method must have the following characteristics: (a) the assay should be rapidly and easily developed from sequence data; (b) the expense of assay development must be affordable in terms of marker-specific reagents and expert personnel time spent on optimization; (c) the reaction must be robust, such that even suboptimal DNA samples yield reliable results; (d) the assay should be done automatically and must need little hands-on operation; and (e) the assay must be easily automated and must require minimal hands (Kwok, 2001b). SNP markers are a significant advancement in molecular systematics since they give a quick and reliable technique of identification without the need for time-consuming morphological or biochemical examination(Yoo et al., 2023). However, when it comes to the detection of SNPs, it still has limitations because of its relatively expensive prices, complexity in data administration, and drawbacks when used in large-scale commercial breeding (Zhang et al., 2023). The dielectric properties of the bio-particle represent many structural, morphological, and chemical characteristics, allowing dielectrophoresis to be used for more selective and sensitive analysis of biological samples, as well as controllable, demanding, and accurate manipulation of target bioparticles (Khoshmanesh et al., 2011).

3. Conclusion

Because the dielectrophoresis technique is simple, convenient, inexpensive, and reliable, developing and underdeveloped countries may introduce this process in their healthcare systems. DEP is also used in medical diagnostics, drug development, cell therapies, and particle filtration.

Data availability statement

Not Applicable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amolm.2023.100009.

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