INNOVATIONS IN MOLECULAR BIOTECHNOLOGY
2024, VOL. 2, pp. 16-18
https://doi.org/10.61577/imb.2024.100003

RESEAPRO JOURNALS

MINI REVIEW

OPEN ACCESS

Unravelling genomic mysteries: Advancements, applications, and future perspectives of next-generation sequencing (NGS)

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ABSTRACT

Next-Generation Sequencing (NGS) has revolutionized genomics by offering high- throughout, rapid, and cost-effective methods for decoding entire genomes with unknown accuracy. This transformative technology has surpassed traditional sequencing approaches, enabling large- scale studies in different fields similar as mortal health, agriculture, and environmental science. Over the once two decades, nonstop advancements in NGS platforms have bettered read length, accuracy, and speed while reducing costs, making sequencing accessible to a wider range of researchers. Major technological milestones include the development of Illumina sequencing, single- molecule real-time (SMRT) sequencing by PacBio, and nanopore sequencing by Oxford Nanopore Technologies, each with unique capabilities and operations. NGS has driven significant progress in individualized drug, especially in cancer genomics and rare disease diagnosis, by easing precise detection of inheritable variations and practicable mutations. Also, it has converted microbial genomics, enabling comprehensive metagenomic analyses and pathogen surveillance. Despite these advances, challenges remain in terms of data management, interpretation, and scalability for clinical use. Arising trends, similar asultra-fast movable sequencers and integration with artificial intelligence, pledge to further enhance the capabilities of NGS.

KEYWORDS

Next-generation sequencing; NGS technology; Genome sequencing; Cancer genomics; Metagenomics; CRISPER, Single-molecule sequencing

ARTICLE HISTORY

Received 16 August 2024; Revised 5 September 2024; Accepted 13 September 2024

Introduction

The ability to decode the inheritable design of organisms has transformed natural research and clinical practice. Since the first successful sequencing of DNA in the 1970s, sequencing technologies have evolved significantly, climaxing in the advent of Next- Generation Sequencing (NGS), a breakthrough that enables rapid-fire and large- scale genomic analysis. Unlike traditional Sanger sequencing, NGS offers largely resemblant sequencing of millions of DNA fragments, performing in lesser speed, accuracy, and reduced costs [1]. This paradigm shift has opened new avenues for scientific exploration, leading to unknown discoveries in genomics, transcriptomics, and epigenomics.

NGS has not only advanced abecedarian research but has also set up critical applications in different fields. In clinical settings, it plays a vital part in diagnosing inheritable disorders, guiding cancer treatment, and enabling individualized drug. In agriculture, it supports genomic selection, crop enhancement, and the identification of disease- resistant traits [2]. Also, NGS has propelled the study of microbial communities through metagenomics, slipping light on microbial ecosystems and their impact on mortal health and the terrain.

Despite its wide adoption, NGS faces challenges similar as handling large datasets, icing sequencing accuracy in complex genomic regions, and reducing costs further for routine clinical use [3]. Ongoing inventions, including third- generation sequencing and real- time nanopore sequencing, promise to overcome these hurdles, paving the way for briskly and more accurate genome analysis.

This provides an overview of the crucial advancements in NGS technology, explores its broad applications, discusses current limitations, and highlights arising trends that are likely to shape its unborn trajectory. By unraveling genomic mysteries, NGS continues to review our understanding of life at the molecular position.

Technological Advancements in Next-Generation Sequencing (NGS)

Since its inception, NGS has significantly advanced, transforming from first-generation methods like Sanger sequencing into powerful platforms that can sequence entire genomes rapidly and accurately. Key to this evolution has been innovative methodologies and diverse sequencing applications across genomics, transcriptomics, and epigenomics.

Second-generation sequencing (High-throughput platforms)

Platforms such as Illumina and Ion Torrent have revolutionized sequencing by enhancing throughput and reducing costs. Illumina utilizes sequencing-by-synthesis to achieve high accuracy in short reads, ideal for whole-genome sequencing (WGS) and targeted panels [4]. Conversely, Ion Torrent uses semiconductor sequencing, detecting hydrogen ions released during nucleotide incorporation for a fast and economical alternative.

Third-generation sequencing (Single-molecule approaches)

Technologies like PacBio and Oxford Nanopore have pioneered single-molecule sequencing, enabling longer read lengths.

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PacBio's SMRT captures real-time nucleotide addition, beneficial for complex genomic regions. Oxford Nanopore's method leverages nanopores to sequence by measuring electrical changes, enabling real-time and portable sequencing [5].

The integration of automation and bioinformatics has streamlined NGS workflows, enhancing efficiency and reducing costs, thus broadening access to genomic research. Ongoing advancements, like ultra-fast real-time sequencing and AI data integration, promise further breakthroughs in the field.

Applications of Next-Generation Sequencing (NGS)

The versatility and high throughput of NGS have transformed a broad range of fields, from clinical diagnostics to agriculture and environmental sciences. Its ability to generate massive amounts of data in a relatively short time has enabled breakthroughs in understanding genetic information at an unprecedented scale.

Clinical applications

NGS has become an essential tool in clinical settings, particularly in genetic testing and personalized medicine.

- **Genetic diagnosis:** NGS allows for comprehensive screening of genetic disorders by sequencing entire genomes or exomes, facilitating the identification of disease-causing mutations [6].
- **Cancer genomics:** NGS is widely used for detecting somatic mutations, copy number variations, and gene fusions in tumors, enabling personalized cancer treatment through targeted therapies.
- **Infectious disease genomics:** NGS enables rapid and accurate identification of pathogens, including bacteria and viruses, aiding in outbreak investigation and surveillance [7].

Agricultural biotechnology

NGS is extensively applied in agriculture to enhance crop yield, disease resistance, and environmental resilience.

- **Genomic selection:** By sequencing the genomes of plants and animals, breeders can identify favorable traits and accelerate the development of improved varieties.
- **Pathogen detection:** NGS-based metagenomic approaches are used to identify plant pathogens and understand microbial communities associated with crops, helping to develop effective disease management strategies [8].
- **Gene editing support:** NGS plays a crucial role in validating gene edits made using tools like CRISPR, ensuring the precision of modifications and absence of off-target effects.

Microbial genomics and metagenomics

NGS has revolutionized microbial genomics by providing insights into the diversity, function, and evolution of microbial communities in various environments.

- **Microbiome analysis:** NGS is key to studying complex microbial ecosystems, such as the human gut microbiome, which has implications for health and disease.
- **Bioremediation:** Environmental studies use NGS to assess microbial communities involved in breaking down pollutants, aiding in bioremediation efforts [9].

NGS continues to drive innovation in diverse fields, making it an indispensable technology for both fundamental research and applied science.

Challenges and Limitations

NGS has significantly advanced genomics; however, several challenges limit its adoption in clinical and industrial settings. High costs remain a primary concern, despite reduced expenses per base. Sample preparation, library construction, and bioinformatics analysis can still be quite expensive. Additionally, the complexity and volume of data produced by NGS necessitate sophisticated bioinformatics tools for accurate interpretation, but the absence of standardized processes and high computational demands hinder smaller laboratories [10,11]. Another key limitation is interpreting results from non-coding regions and complex structural variations due to insufficient genome annotations. Accuracy issues, particularly in repetitive and GC-rich areas, also persist, with long-read technologies showing higher error rates [12]. Furthermore, ethical issues around privacy and genetic information misuse demand robust regulation. Overcoming these challenges is essential for leveraging NGS's full potential, especially in precision medicine and genomic surveillance [13].

Future Perspectives

The future of Next-Generation Sequencing (NGS) is poised for significant advancements in both research and clinical applications. Key trends include the creation of ultra-fast, portable sequencers like handheld nanopore devices, enabling real-time sequencing in remote areas, thereby enhancing infectious disease surveillance, precision agriculture, and environmental monitoring [14,15]. Additionally, integrating NGS with artificial intelligence and machine learning will improve genomic data interpretation and facilitate personalized treatment strategies. As single-cell and spatial transcriptomics evolve, they will offer deeper insights into cellular diversity and disease mechanisms. Efforts to lower sequencing costs and simplify data analysis are making whole-genome and whole-exome sequencing more accessible in clinical settings [16]. Ethical concerns regarding privacy and equitable access will be vital as NGS technologies expand, ultimately empowering solutions for healthcare, food security, and biodiversity challenges.

Conclusions

Next-Generation Sequencing (NGS) has revolutionized genomics, facilitating significant advancements in both research and clinical applications. Transitioning from traditional Sanger sequencing to high-throughput platforms, NGS allows for an unprecedented exploration of genomes with enhanced depth, speed, and precision. This technology has propelled breakthroughs in human genetics and personalized medicine, while also promoting developments in diverse fields such as agriculture, microbiology, and environmental science. However, challenges like high costs, complex data analysis, and difficulties in sequencing repetitive regions still limit its widespread clinical use. Future innovations in sequencing—focused on improving

https://doi.org/10.61577/imb.2024.100003

read accuracy, extending read lengths, and creating portable devices—aim to overcome these hurdles. The combination of NGS with artificial intelligence and machine learning is expected to refine data interpretation and expand applications in precision medicine and synthetic biology. As these advancements progress, NGS is poised to play a crucial role in addressing global challenges, ranging from infectious diseases to food security, highlighting its immense potential for scientific breakthroughs and societal impact.

Disclosure Statement

No potential conflict of interest was reported by the authors.

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https://doi.org/10.61577/imb.2024.100003