Review Aticle

Contemporary Genome Sequencing Technologies and Their Role in Three-Dimensional Genome Mapping: A Concise Narrative Review

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Abstract | Advances in DNA sequencing technologies have fundamentally transformed genomic research, clinical diagnostics, and molecular biology. The transition from first-generation Sanger sequencing to high-throughput next-generation sequencing (NGS), followed by the emergence of third-generation long-read platforms, has dramatically improved scalability, resolution, and cost-efficiency. These developments have also enabled comprehensive mapping of three-dimensional (3D) genome organization. This review aims to summarize the technological evolution of genome sequencing platforms, compare their methodological characteristics, and critically examine their role in enabling 3D genome mapping techniques. A narrative literature review was conducted using PubMed, Scopus, and Web of Science databases. Publications from 2000 to 2025 were screened using keywords including "Sanger sequencing," "next-generation sequencing," "long-read sequencing," "Hi-C," and "3D genome organization." Priority was given to foundational methodological papers, benchmarking studies, and high-impact review articles. NGS has replaced Sanger sequencing as the principal platform for large-scale genomic research due to its throughput and cost efficiency, while long-read technologies address structural complexity limitations. Together, these platforms underpin modern 3D genome mapping strategies and continue to reshape precision genomics.

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Introduction

Genome and transcriptome sequencing enable the diagnosis of genetic illnesses (Gorzynski *et al*., 2022; AlDubayan *et al*., 2020), facilitate research into gene-trait connections for pharmacological and agricultural applications, support reference genome development, provide genetic variant annotation resources, and inform imputation approaches (Manolio, 2010; Peloso *et al*., 2019; Snelling *et al*., 2020; Liao *et al*., 2023; Karczewski *et al*., 2020; Li *et al*., 2009). Primarily, attempts to evaluate sequencing accuracy relied on indirect criteria, such as the proportion of variant calls that were transitions rather than transversions, or whether the results were in accordance with Mendelian inheritance (Eberle *et al*., 2017). The genome revolutionised the capacity to evaluate precision in a Bottle standards, which

comprise a collection of seven human cell lines that underwent thorough genome characterisation using various technologies, analytical methodologies, and human curation (Wagner *et al*., 2022). The capacity to identify gains in accuracy beyond what existing individual approaches can achieve was enhanced by this resource, which, when coupled with community competitions and comparisons, sparked a surge of innovation in sequencing and analysis (Olson *et al*., 2022; Foox *et al*., 2021; Wenger *et al*., 2019; Tetikol *et al*., 2022; Scheffler *et al*., 2023) techniques that prove their inventions are valid. Tests have demonstrated that this innovation can detect disease-causing variations that were previously undetected, thereby improving diagnosis rates. A new approach to sequencing, developed by Element Biosciences, utilises avidity sequencing instead of synthesis sequencing. This method is reportedly superior to Illumina sequencing in terms of per-base accuracy. It can yield high-yield short-read sequencing, with over six 30× genomes in a single sequencing run (AlDubayan *et al*., 2020).

The purpose of this study is to provide a concise overview of nuclear genomes in three-dimensional structure from a broad perspective, encompassing progress in DNA sequencing applications and the development of new generations of sequencing technology.

Materials and Methods

This review follows a narrative synthesis approach. Literature searches were conducted in PubMed, Web of Science, and Scopus databases between January 2000 and March 2025. Search terms included combinations of:

- "Sanger sequencing"
- "next-generation sequencing"
- "third-generation sequencing"
- "long-read sequencing"
- "Hi-C"
- "chromatin conformation capture"
- "3D genome"
- "structural variation"

Inclusion criteria comprised primary methodological studies, platform validation reports, benchmarking analyses, and authoritative review articles published in peer-reviewed journals. Non-English articles, conference abstracts without full text, and non-peer-reviewed sources were excluded. Selected studies were analyzed for technical principles, read length, error profiles, throughput, sequencing depth requirements, and application domains.

An overarching perspective on nuclear genomes in three-dimensional structure

In the nuclei of eukaryotic cells, the genetic code is stored. It is encased in chromatin, dispersed across several chromosomes, and folded into intricate three-dimensional structures with protein factors and RNA molecules. Traditionally, microscopy-based approaches were used to study nuclear architecture and chromatin spatial organization within the nuclear space (Lowenstein *et al*., 2004). Amphibian and other animal oocytes display the earliest known chromatin loop structure, the "lampbrush chromosome" (Morgan, 2002). However, early imaging methods lacked the resolution necessary to comprehensively characterize genome-wide chromatin interactions.

The development of high-throughput sequencing technologies enabled a paradigm shift in studying genome architecture. Genome-wide chromatin conformation capture techniques, particularly Hi-C and ChIA-PET, have become central tools for interrogating three-dimensional genome organization (Lieberman-Aiden *et al*., 2009; Fullwood *et al*., 2009). These approaches combine proximity ligation with massively parallel sequencing to generate contact maps representing interaction frequencies between genomic loci across the entire genome.

Hi-C enables unbiased, genome-wide detection of chromatin interactions by crosslinking spatially proximal DNA fragments, digesting them with restriction enzymes, ligating interacting fragments, and subjecting the resulting chimeric products to deep sequencing (Lieberman-Aiden *et al*., 2009). The resolution of Hi-C interaction maps is strongly dependent on sequencing depth, with higher read counts allowing finer-scale detection of chromatin loops, topologically associating domains (TADs), and chromatin compartments (Dixon *et al*., 2012). Achieving kilobase-scale resolution requires extensive sequencing coverage, often reaching billions of read pairs, thereby underscoring the essential role of next-generation sequencing platforms in 3D genome research.

ChIA-PET integrates chromatin immunoprecipitation (ChIP) with proximity ligation and deep sequencing

to identify chromatin interactions mediated by specific DNA-binding proteins (Fullwood *et al.*, 2009). This method allows high-confidence mapping of regulatory loops associated with transcription factors such as CTCF or RNA polymerase II (Tang *et al.*, 2015). Compared to Hi-C, ChIA-PET provides protein-centric interaction maps but requires high-quality antibodies and substantial sequencing depth to achieve robust signal detection.

The hierarchical organization of the mammalian genome is now widely recognized, largely based on sequencing-driven discoveries over the past 15 years. Chromosome territories represent large-scale nuclear organization units, within which chromatin compartments segregate into transcriptionally active (A compartments) and inactive (B compartments) regions (Lieberman-Aiden *et al.*, 2009; Ouyang *et al.*, 2020). At a finer scale, TADs partition chromosomes into self-interacting domains (Dixon *et al.*, 2012), while chromatin loops often anchored by CTCF constitute the fundamental structural units of 3D genome architecture (Tang *et al.*, 2015).

Despite their transformative impact, sequencing-based chromatin conformation methods are subject to technical and analytical biases. Restriction enzyme selection, fragment length distribution, GC-content bias, PCR amplification efficiency, and ligation efficiency may influence interaction frequency measurements and coverage uniformity. Consequently, robust computational normalization methods are required to correct for systematic biases and ensure reproducibility of contact matrices (Lieberman-Aiden *et al.*, 2009). Sequencing depth, library complexity, duplicate read rates, and normalization algorithms critically determine the resolution, reproducibility, and interpretability of 3D genome datasets.

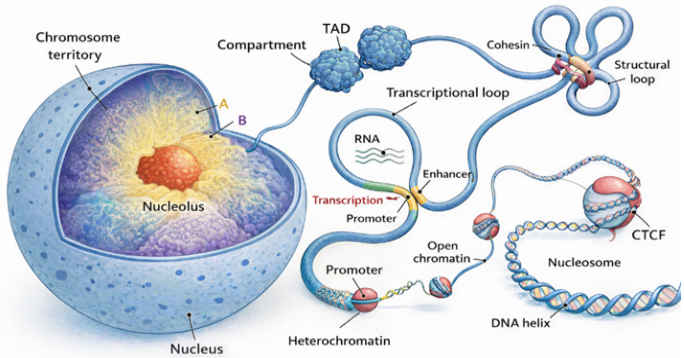

Figure 1: *An overview of the structure of the nuclear genome.*

Imaging-based approaches have further validated and complemented sequencing-based findings, strengthening our understanding of genome spatial organization (Wang *et al.*, 2016; Yang and Wang, 2024). Due to space limitations, the present review focuses primarily on sequencing-based technologies and their contribution to 3D genome biology.

Chromosome territories at the macro level, compartments at the micro level, topologically associated domains (TADs), and fine-scale loops comprise the genome›s hierarchical structure acronym: CCCTC-binding factor, or CTCF for short. Several short-read sequencing methods were detailed by Kumar *et al.* (2024), including nanoball sequencing, ion semiconductor sequencing, and sequencing by synthesis. Bypassing the shortcomings of short-read sequencing, third-generation long-read sequencing is expected to resolve repeat sequences and massive genomic rearrangements with greater reliability. Advancements in complementary techniques and massively parallel DNA sequencing have enabled a deeper understanding of the biological underpinnings of disease causes. Nanopore technology, in situ nucleic acid sequencing, and microscopy-based sequencing are just a few of the emerging approaches that will continue to drive the rapid evolution of this field. Precision and individualised medical treatment are the future promises of these cutting-edge technologies, which have several possible uses in the treatment of haematological illnesses (Kumar *et al.*, 2024). It was discovered by Akintunde *et al.* (2025) that there is a desire to clarify the precise sequencing and content of DNA molecules.

Breakthroughs in decoding the DNA sequence and the subsequent procedures have made new opportunities in research, biotech, and healthcare possible. Humanity and the global economy have benefited from, and will continue to benefit from, the use of high-throughput sequencing technologies in these sectors. A few hundred base pairs can be sequenced in days thanks to advancements such as the use of fluorescent dyes and the polymerase chain reaction (PCR) for amplification. Automation, on the other hand, made it possible to sequence thousands of base pairs in hours. There has been significant progress, but it could be even better. In this article, we will examine the background and current state of next-generation sequencing systems, as well as their potential applications in fields beyond biomedical

research (Akintunde *et al.*, 2025). According to Chai and Ruan (2025), chromatin consists of nuclear proteins and RNA. Its dynamic structure affects nuclear and genomic processes. High-throughput DNA sequencing technologies, such as Hi-C and ChIA-PET, have enabled the genome-wide mapping of chromatin folding structures, contributing to the development of 3D genome biology since 2009. This field has experienced rapid growth over the past 15 years of development. It›s improving our understanding of how genomic organisation influences nuclear functions in biological systems. In this study, we discuss the advances in sequencing-based technologies for mapping 3D genomic landscapes and the future of 3D genome biology (Chai and Ruan, 2025). According to Carroll *et al.* (2025), when comparing whole-genome sequencing of Element to Illumina sequencing at the same coverage, the former achieves better mapping and variant calling accuracy. However, at lower coverages (20-30x), there are bigger discrepancies. They are measuring the base error rates of element reads and have found that these regions, particularly those containing homopolymers and tandem repeats, have reduced error rates. As an alternative to the usual short-read sequencing, we leverage Element›s capability for paired-end sequencing with larger insert sizes. Long insert element sequencing provides more precise genome analysis across all coverages, and our results demonstrate that larger insert sizes lead to even greater accuracy (Carroll *et al.*, 2025).

Progress in DNA sequencing›s practical uses

DNA sequencing has numerous applications in science, healthcare, and agriculture, and it has significantly transformed the field of genetics. The potential uses of DNA sequencing technology have increased significantly over the years due to technological advancements and the development of new applications. The use of DNA sequencing has made great strides in personalised medicine, among other areas. The process of DNA sequencing enables the detection of genetic variants and mutations that may be associated with certain health issues. Medical practitioners can create individualised treatment programs by analysing a patient›s genome. The cancer diagnostic and therapeutic fields have benefited greatly from this strategy, as genetic testing has enabled the identification of tailored treatments and the prediction of treatment response (Gargis *et al.*, 2016). The investigation of microbiomes is another field that has benefited from DNA sequencing. To maintain our health, microbiomes—communities of microbes that inhabit our bodies—are essential. The genetic composition of these microbes and their interactions with humans can be studied by DNA sequencing. Novel approaches to treating inflammatory bowel disease and infectious disorders have resulted from this (Dethlefsen *et al.*, 2007). The agricultural sector is another field that has benefited from the application of DNA sequencing. Crops and cattle can benefit from genetic differences associated with desirable qualities, such as drought resilience or disease resistance, which can be discovered using DNA sequencing. New breeding strategies can be developed using this information to create crops and cattle with improved characteristics and better adaptation to certain conditions. As a result, environmental science found new uses for it. Soil and water microbe communities can be studied by DNA sequencing (Tanksley and McCouch, 1997).

Different sequencing technology generations

Reading technology DNA sequences have undergone fast evolution in the last 20 years (Sakamoto *et al.*, 2020; Goto *et al.*, 2020). This lightning-fast development has allowed for major advances in DNA sequencing, which in turn have given rise to three distinct generations of sequencing technology (**Figure 2**).

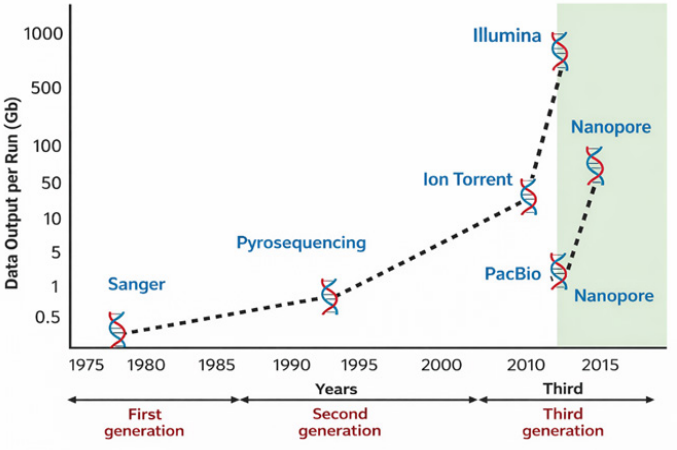

Figure 2: *Evolution of different sequencing technologies.*

There have been three distinct waves of advancement in sequencing technology throughout the last 40 years. Sanger sequencing, which laid the groundwork for DNA sequencing, represents the first generation of sequencing methods. Platforms like Illumina and Ion Torrent, which enabled massively parallel sequencing in the second generation, allowed for high-throughput

sequencing. Among the present third-generation options, we find PacBio and Nanopore, which provide the ability to sequence individual molecules as well as long reads (Satam *et al.*, 2023).

Technologies for first-generation sequencing

Initial efforts in DNA and RNA sequencing relied on chemical degradation or enzymatic cleavage to separate molecules into manageable pieces for individual analysis. In 1964, Robert Holley used ribonuclease from Saccharomyces cerevisiae to sequence Alanine tRNA, the first nucleic acid molecule to be sequenced (Holley *et al.*, 1965). The chemical degradation method that enabled the sequencing of whole bacteriophage PhiX174 was similarly created by Walter Gilbert and Allan Maxam (Heather and Chain, 2016). Nonetheless, Fredrick Sanger's creation of the chain termination-based sequencing approach was the true game-changer (Sanger *et al.*, 1977). This method enabled the generation of sequence readings that were several hundred nucleotides long by utilising dideoxynucleotides, which terminate the chain elongation of DNA strands during replication. Because it enabled the rapid sequencing of DNA and RNA, Sanger's approach was widely adopted and transformed molecular biology (Heather and Chain, 2016). Launched in 1987 in the US, the Applied Biosystems ABI 370 was the first commercial automated sequencing machine. Automating the Sanger sequencing process with fluorescently labelled dideoxynucleotides and capillary electrophoresis, this machine greatly improved the accuracy and speed of DNA sequencing (Schuster, 2008). The rapid adoption of the ABI 370 marked the beginning of a technological revolution that would eventually give rise to higher-throughput sequencers capable of generating longer reads. Although newer, higher-throughput sequencing technologies have largely replaced first-generation technologies, they remain a significant historical milestone in the evolution of sequencing methods. The capacity to sequence RNA and DNA has ushered in a new era of discovery and progress in the study of genetics and molecular biology, which, in turn, has transformed many branches of medicine and biology (Schuster, 2008; Hutchison, 2007).

Technologies for second-generation sequencing

Because second-generation sequencing technologies can sequence thousands to millions of DNA fragments simultaneously, they have revolutionised the DNA sequencing industry. When compared to conventional Sanger sequencing, these techniques stand out due to their parallel sequencing capabilities. One of the most popular second-generation sequencing platforms is Roche's 454, which utilises pyrosequencing a technique that enables the identification of sequences by detecting the release of pyrophosphate when nucleotides are added to a DNA template to determine the DNA copies. As an additional tool, Ion Torrent sequencing may identify the DNA sequence by monitoring the discharge of hydrogen ions as the manufacturing process progresses. Using reversible dye terminators, the Illumina sequencing platform enables sequencing by synthesis. This technology is widely employed in the field. The sequencing method known as SOLiD sequencing uses reversible terminators in a ligation-based approach to find the DNA sequence. Thanks to these second-generation sequencing methods, DNA sequencing is now significantly faster and has increased throughput, opening up numerous new possibilities in genomics and medical diagnostics. These systems have enabled targeted sequencing, transcriptome analysis, and whole-genome sequencing, which have enhanced our understanding of heritable diseases and facilitated more personalised medical care (Pervez *et al.*, 2022).

Technologies for third-generation sequencing

The most recent developments in DNA sequencing, known as third-generation sequencing technologies, offer novel methods that overcome the drawbacks of earlier generations. These innovations enable long-read sequencing, which, compared to older techniques, allows for the reading of substantially larger DNA fragments. For instance, PacBio Sequencing allows for long-read sequencing of DNA fragments as long as tens of kilobases in length by employing a single-molecule, real-time (SMRT) method with fluorescently labelled nucleotides. Oxford Nanopore sequencing is another method that utilises nanopore technology to detect DNA sequences. This method involves passing a single-stranded DNA molecule through a nanopore and measuring the changes in electrical current. The sequencing technology offered by Oxford Nanopore enables large read lengths, high mobility, and real-time analysis (Jain *et al.*, 2016; Roberts *et al.*, 2013).

Conclusion

Significant progress has been made in DNA sequencing in the last several years. Researchers and

physicians now have easier and more inexpensive access to DNA sequencing as a result of the significant decrease in cost and time required for the process brought about by high-throughput sequencing technology. Researchers are facing new challenges in data analysis and interpretation due to the rapid increase in sequencing data resulting from the decline in sequencing costs. The development of increasingly precise DNA sequencing technologies has opened up a wealth of new possibilities in fields as diverse as infectious disease tracking, understanding the hereditary basis of traits and behaviours, and detecting mutations that cause disease. As a result, genetics, medicine, and biology have all made significant strides forward. In addition, DNA sequencing has numerous potential applications in fields such as environmental microbiology, personalised medicine, metagenomics, and many more. The further expansion of DNA sequencing and analysis of previously inaccessible genomic regions has been made possible by the development of new sequencing techniques, such as third-generation sequencing and nanopore sequencing.

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Novelty Statement

This review provides a concise yet integrated synthesis of the evolutionary trajectory of DNA sequencing technologies—from first-generation Sanger sequencing to third-generation long-read platforms—with a specific focus on their enabling role in three-dimensional genome mapping. Unlike broader sequencing reviews, this work explicitly links technological capabilities (e.g., read length, throughput, error profiles) to methodological requirements of chromatin conformation capture techniques such as Hi-C and ChIA-PET. It highlights recent advances including avidity sequencing and emerging long-read applications, offering a timely perspective on how sequencing innovations continue to shape 3D genomics and precision medicine.

Author's Contribution

Bahaa Burhanuldeen Kargule: Writing original draft. Zain Ulabdeen Naser Hussein: Literature search, data extraction. Qays Qays Qandeel and Fahad Bahaa Aljanabi: Review & editing

Generative AI and AI assisted technology statement

The authors declare that no generative AI and AI assisted technology was used in the creation of this manuscript.

Conflict of interest

The authors have declared no conflict of interest.

References

Akintunde, O., Tucker, T., Carabetta, V.J., 2025. The evolution of next-generation sequencing technologies. In: Carabetta, V.J., Akintunde, O. (Eds.), High Throughput Gene Screening. Methods in Molecular Biology, vol 2866. Humana, New York, NY, pp. 1–12. https://doi.org/10.1007/978-1-0716-4192-7_1

AlDubayan, S.H., Conway, J.R., Camp, S.Y., Witkowski, L., Kofman, E., Reardon, B., Han, S., Moore, N., Elmarakeby, H., Salari, K., Choudhry, H., Al-Rubaish, A.M., Al-Sulaiman, A.A., Al-Ali, A.K., Taylor-Weiner, A. and Van Allen, E.M. 2020. Detection of pathogenic variants with germline genetic testing using deep learning vs standard methods in patients with prostate cancer and melanoma. JAMA, 324(19): 1957–1969. https://doi.org/10.1001/jama.2020.20457

Carroll, A., Kolesnikov, A., Cook, D.E., Brambrink, L., Wiseman, K.N., Billings, S.M., Kruglyak, S., Lajoie, B.R., Zhao, J., Levy, S.E., McLean, C.Y., Shafin, K., Nattestad, M. and Chang, P.C. 2025. Accurate human genome analysis with element avidity sequencing. BMC Bioinf., 26: 194. https://doi.org/10.1186/s12859-025-06191-4

Chai, H., Ruan, Y., 2025. 3D genome sequencing technology in its mid-teens: Past, present, and future. Trends Genet., 41(8): 701–715.

Dethlefsen, L., McFall-Ngai, M., Relman, D.A., 2007. An ecological and evolutionary perspective on human–microbe mutualism and disease. Nature, 449(7164): 811–818. https://doi.org/10.1038/nature06245

Dixon, J.R., Selvaraj, S., Yue, F., Kim, A., Li, Y., Shen, Y., Hu, M., Liu, J.S. and Ren, B. 2012. Topological domains in mammalian genomes identified by analysis of chromatin interactions.

Nature, 485(7398): 376–380. https://doi.org/10.1038/nature11082

Eberle, M.A., Fritzilas, E., Krusche, P., Källberg, M., Moore, B.L., Bekritsky, M.A., Iqbal, Z., Chuang, H.Y., Humphray, S.J., Halpern, A.L., Kruglyak, S., Margulies, E.H., McVean, G. and Bentley, D.R. 2017. A reference data set of 5.4 million phased human variants validated by genetic inheritance from sequencing a three-generation 17-member pedigree. Genome Res., 27(1): 157–164. https://doi.org/10.1101/gr.210500.116

Foox, J., Tighe, S.W., Nicolet, C.M., Zook, J.M., Byrska-Bishop, M., Clarke, W.E., Khayat, M.M., Mahmoud, M., Laaguiby, P.K., Herbert, Z.T., Warner, D., Grills, G.S., Jen, J., Levy, S., Xiang, J., Alonso, A., Zhao, X., Zhang, W., Teng, F. 2021. Performance assessment of DNA sequencing platforms in the ABRF next-generation sequencing study. Nat. Biotechnol., 39(9): 1129–1140. https://doi.org/10.1038/s41587-021-01049-5

Fullwood, M.J., Liu, M.H., Pan, Y.F., Liu, J., Xu, H., Mohamed, Y.B., Orlov, Y.L., Velkov, S., Ho, A., Mei, P.H., Chew, E.G., Huang, P.Y., Welboren, W.J., Han, Y., Ooi, H.S., Ariyaratne, P.N., Vega, V.B., Luo, Y., Tan, P.Y. 2009. An oestrogen-receptor-α-bound human chromatin interactome. Nature, 462(7269): 58–64. https://doi.org/10.1038/nature08497

Gargis, A.S., Kalman, L., Lubin, I.M., Assimes, T.L., 2016. High-throughput sequencing for the diagnosis of inherited disease. Expert Rev. Mol. Diagn., 16(7): 735–748.

Gorzynski, J.E., Goenka, S.D., Shafin, K., Jensen, T.D., Fisk, D.G., Grove, M.E., Spiteri, E., Pesout, T., Monlong, J., Baid, G., Bernstein, J.A., Ceresnak, S., Chang, P., Christle, J.W., Chubb, H., Dalton, K.P., Dunn, K., Garalde, D.R., Guillory, J. 2022. Ultrarapid nanopore genome sequencing in a critical care setting. N. Engl. J. Med., 386(7): 700–702. https://doi.org/10.1056/NEJMc2112090

Goto, Y., Akahori, R., Yanagi, I. and Takeda, K.I., 2020. Solid-state nanopores towards single-molecule DNA sequencing. J. Hum. Genet., 65(1): 69–77. https://doi.org/10.1038/s10038-019-0655-8

Heather, J.M., Chain, B., 2016. The sequence of sequencers: The history of sequencing DNA. Genomics, 107(1): 1–8. https://doi.org/10.1016/j.ygeno.2015.11.003

Holley, R.W., Apgar, J., Everett, G.A., Madison, J.T., Marquisee, M., Merrill, S.H., Penswick, J.R. and Zamir, A. 1965. Structure of a Ribonucleic Acid. Science, 147(3664): 1462–1465. https://doi.org/10.1126/science.147.3664.1462

Hutchison, C.A., 2007. DNA sequencing: Bench to bedside and beyond. Nucl. Acids Res., 35(18): 6227–6237. https://doi.org/10.1093/nar/gkm688

Jain, M., Olsen, H.E., Paten, B. and Akeson, M., 2016. The Oxford nanopore MinION: Delivery of nanopore sequencing to the genomics community. Genome Biol., 17(1): 239. https://doi.org/10.1186/s13059-016-1103-0

Karczewski, K.J., Francioli, L.C., Tiao, G., Cummings, B.B., Alföldi, J., Wang, Q., Collins, R.L., Laricchia, K.M., Ganna, A., Birnbaum, D.P., Gauthier, L.D., Brand, H., Solomonson, M., Watts, N.A., Rhodes, D., Singer-Berk, M., England, E.M., Seaby, E.G., Kosmicki, J.A. 2020. The mutational constraint spectrum quantified from variation in 141,456 humans. Nature, 581(7809): 434–443. https://doi.org/10.1038/s41586-020-2308-7

Kumar, K.R., Cowley, M.J. and Davis, R.L., 2024. Next-generation sequencing and emerging technologies. Semin. Thromb. Hemost., 50(7): 1026–1038. https://doi.org/10.1055/s-0044-1786397

Li, Y., Willer, C., Sanna, S., Abecasis, G., 2009. Genotype imputation. Annu. Rev. Genomics Hum. Genet., 10: 387–406. https://doi.org/10.1146/annurev.genom.9.081307.164242

Liao, W.-W., Asri, M., Ebler, J., Doerr, D., Haukness, M., Hickey, G., Lu, S., Lucas, J.K., Monlong, J., Abel, H.J., Buonaiuto, S., Chang, X.H., Cheng, H., Chu, J., Colonna, V., Eizenga, J.M., Feng, X., Fischer, C., Fulton, R.S. 2023. A draft human pangenome reference. Nature, 617(7960): 312–324. https://doi.org/10.1038/s41586-023-05896-x

Lieberman-Aiden, E., van Berkum, N.L., Williams, L., Imakaev, M., Ragoczy, T., Telling, A., Amit, I., Lajoie, B.R., Sabo, P.J., Dorschner, M.O., Sandstrom, R., Bernstein, B., Bender, M.A., Groudine, M., Gnirke, A., Stamatoyannopoulos, J., Mirny, L.A., Lander, E.S. and Dekker, J. 2009. Comprehensive mapping of long-range interactions reveals folding principles of the human genome. Science, 326(5950): 289–293.

https://doi.org/10.1126/science.1181369

Lowenstein, M.G., Goddard, C. and Orr-Weaver, T.L., 2004. Long-range interphase chromosome organisation in Drosophila: a study using color barcoded fluorescence in situ hybridisation and structural clustering analysis. Mol. Biol. Cell, 15(12): 5678–5692. https://doi.org/10.1091/mbc.e04-04-0289

Manolio, T.A., 2010. Genomewide association studies and assessment of the risk of disease. N. Engl. J. Med., 363(2): 166–176. https://doi.org/10.1056/NEJMra0905980

Morgan, G.T., 2002. Lampbrush chromosomes and associated bodies: new insights into principles of nuclear structure and function. Chromosome Res., 10(3): 177–200. https://doi.org/10.1023/A:1015227020652

Olson, N.D., Wagner, J., McDaniel, J., Stephens, S.H., Westreich, S.T., Prasanna, A.G., Johanson, E., Boja, E., Maier, E.J., Serang, O., Jáspez, D., Lorenzo-Salazar, J.M., Muñoz-Barrera, A., Rubio-Rodríguez, L.A., Flores, C. and Kyriakidis, K. 2022. precisionFDA Truth Challenge V2: Calling variants from short and long reads in difficult-to-map regions. Cell Genom., 2(5): 100129. https://doi.org/10.1016/j.xgen.2022.100129

Ouyang, W., Xiong, D., Li, G., Li, X., 2020. Unraveling the 3D genome architecture in plants: present and future. Mol. Plant, 13(12): 1676–1693. https://doi.org/10.1016/j.molp.2020.10.002

Peloso, G.M., Nomura, A., Khera, A.V., Chaffin, M., Won, H.H., Ardissino, D., Danesh, J., Schunkert, H., Wilson, J.G., Samani, N., Erdmann, J., McPherson, R., Watkins, H., Saleheen, D., McCarthy, S., Teslovich, T.M., Leader, J.B., Kirchner, H.L., Marrugat, J., Nohara, A. 2019. Rare protein-truncating variants in APOB, lower low-density lipoprotein cholesterol, and protection against coronary heart disease. Circ. Genom. Precis. Med., 12(5): e002376. https://doi.org/10.1161/CIRCGEN.118.002376

Pervez, M.T., Hasnain, M.J.U., Abbas, S.H., Aslam, N. and Shah, S.S.M. 2022. A Comprehensive Review of Performance of Next-Generation Sequencing Platforms. BioMed. Res. Int., 2022: 3457806. https://doi.org/10.1155/2022/3457806

Roberts, R.J., Carneiro, M.O., Schatz, M.C., 2013. The advantages of SMRT sequencing. Genome Biol., 14(6): 405. https://doi.org/10.1186/gb-2013-14-6-405

Sakamoto, Y., Sereewattanawoot, S. and Suzuki, A., 2020. A new era of long-read sequencing for cancer genomics. J. Hum. Genet., 65(1): 3–10. https://doi.org/10.1038/s10038-019-0658-5

Sanger, F., Nicklen, S. and Coulson, A.R., 1977. DNA sequencing with chain-terminating inhibitors. Proc. Natl. Acad. Sci. USA, 74(12): 5463–5467. https://doi.org/10.1073/pnas.74.12.5463

Satam, H., Joshi, K., Mangrolia, U., Waghoo, S., Zaidi, G., Rawool, S., Thakare, R.P., Banday, S., Mishra, A.K., Das, G. and Malonia, S.K. 2023. Next-generation sequencing technology: Current trends and advancements. Biology, 12(7): 997. https://doi.org/10.3390/biology12070997

Scheffler, K., Catreux, S., O'Connell, T., Jo, H., Jain, V., Heyns, T., Yuan, J., Murray, L., Han, J. and Mehio, R. 2023. Somatic small-variant calling methods in Illumina DRAGENTM secondary analysis. bioRxiv, 2023.03.23.534015. https://doi.org/10.1101/2023.03.23.534011

Schuster, S.C., 2008. Next-generation sequencing transforms today's biology. Nat. Methods, 5(1): 16–18. https://doi.org/10.1038/nmeth1156

Snelling, W.M., Hoff, J.L., Harhay, G.P., Kuehn, L.A., Keel, B.N., Lindholm-Perry, A.K. and Pickrell, J.K. 2020. Assessment of imputation from low-pass sequencing to predict merit of beef steers. Genes, 11(11): 1312. https://doi.org/10.3390/genes11111312

Tang, Z., Luo, O.J., Li, X., Zheng, M., Zhu, J.J., Szalaj, P., Trzaskoma, P., Magalska, A., Wlodarczyk, J., Ruszczycki, B., Michalski, P., Piecuch, E., Wang, P., Wang, D., Tian, S.Z., Penrad-Mobayed, M., Sachs, L.M., Ruan, X., Wei, C.L., Liu, E.T., Wilczynski, G.M., Plewczynski, D., Li, G. and Ruan, Y. 2015. CTCF-mediated human 3D genome architecture reveals chromatin topology for transcription. Cell, 163(7): 1611–1627. https://doi.org/10.1016/j.cell.2015.11.024

Tanksley, S.D., McCouch, S.R., 1997. Seed banks and molecular maps: unlocking genetic potential from the wild. Science, 277(5329): 1063–1066. https://doi.org/10.1126/science.277.5329.1063

Tetikol, H.S., Turgut, D., Narci, K., Budak, G., Kalay, O., Arslan, E., Demirkaya-Budak, S., Dolgoborodov, A., Kabakci-Zorlu, D.,

Semenyuk, V., Jain, A. and Davis-Dusenbery, B.N. 2022. Pan-African genome demonstrates how population-specific genome graphs improve high-throughput sequencing data analysis. Nat. Commun., 13(1): 4384. https://doi.org/10.1038/s41467-022-31724-3

Wagner, J., Olson, N.D., Harris, L., Khan, Z., Farek, J., Mahmoud, M., Stankovic, A., Kovacevic, V., Yoo, B., Miller, N., Rosenfeld, J.A., Ni, B., Zarate, S., Kirsche, M., Aganezov, S., Schatz, M.C., Narzisi, G., Byrska-Bishop, M., Clarke, W., Evani, U.S., Markello, C., Shafin, K., Zhou, X., Sidow, A., Bansal, V., Ebert, P., Marschall, T., Lansdorp, P., Hanlon, V., Mattsson, C.-A., Martinez Barrio, A., Fiddes, I.T., Xiao, C., Fungtammasan, A., Chin, C.-S., Wenger, A.M., Rowell, W.J., Sedlazeck, F.J., Carroll, A., Salit, M. and Zook, J.M. 2022. Benchmarking challenging small variants with linked and long reads. Cell Genom., 2(5): 100128. https://doi.org/10.1016/j.xgen.2022.100128

Wang, S., Su, J.H., Beliveau, B.J., Bintu, B., Moffitt, J.R., Wu, C.T. and Zhuang, X 2016. Spatial organisation of chromatin domains and compartments in single chromosomes. Science, 353(6299): 598–602. https://doi.org/10.1126/science.aaf8084

Wenger, A.M., Peluso, P., Rowell, W.J., Chang, P.C., Hall, R.J., Concepcion, G.T., Ebler, J., Fungtammasan, A., Kolesnikov, A., Olson, N.D., Töpfer, A., Alonge, M., Mahmoud, M., Qian, Y., Chin, C.S., Phillippy, A.M., Schatz, M.C., Myers, G., DePristo, M.A. 2019. Accurate circular consensus long-read sequencing improves variant detection and assembly of a human genome. Nature Biotechnol., 37(10): 1155–1162. https://doi.org/10.1038/s41587-019-0217-9

Yang, T., Wang, S., 2024. Image-based 3D genomics through chromatin tracing. Nat. Rev. Methods Primers, 4: 76. https://doi.org/10.1038/s43586-024-00354-y