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| Journal Name: | [**Asian Journal of Biochemistry, Genetics and Molecular Biology**](https://journalajbgmb.com/index.php/AJBGMB) |
| Manuscript Number: | **Ms\_AJBGMB\_134760** |
| Title of the Manuscript: | **The Intimate Read: Nanopore Sequencing and the Philosophical Recalibration of Life's Code** |
| Type of the Article | **Minireview Article** |

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| PART 1: Comments | | |
|  | Reviewer’s comment **Artificial Intelligence (AI) generated or assisted review comments are strictly prohibited during peer review.** | Author’s Feedback  The following disclaimer has been added in Competing interests section -The authors affirm that no generative artificial intelligence tools—including but not limited to large language models (e.g., ChatGPT, Gemini, Copilot) or text-to-image systems—were employed in the drafting, revision, or conceptual development of this manuscript. All content reflects original human intellectual work- |
| **Please write a few sentences regarding the importance of this manuscript for the scientific community. A minimum of 3-4 sentences may be required for this part.** | The article goes beyond a technical review and combines molecular biology with philosophical and ethical reflections, making it unique and interdisciplinary. | I completely agree. From my perspective, the article’s true strength lies in its ability to weave the technical sophistication of nanopore sequencing with philosophical and ethical reflection. This is not merely an addition of disciplines, but an invitation to rethink molecular biology through broader and more critical epistemic lenses. |
| **Is the title of the article suitable?**  **(If not please suggest an alternative title)** | It is suitable | ok |
| Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here. | I don't have a comment about the abstract | ok |
| Is the manuscript scientifically, correct? Please write here. | Yes, i don't find errors | ok |
| **Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.** | Most of the references cited are from 2018–2021, and do not include the latest studies on Oxford Nanopore Technologies (ONT) and long-read sequencing. It would be beneficial to incorporate more recent publications, particularly those covering the latest ONT chemistries, basecalling models, and advances in the detection of DNA and RNA modifications. For example: <https://www.nature.com/articles/s41592-024-02492-3>, <https://pubmed.ncbi.nlm.nih.gov/39846015/>, <https://pubmed.ncbi.nlm.nih.gov/39846015/>, <https://pubmed.ncbi.nlm.nih.gov/38003667/>, <https://pubmed.ncbi.nlm.nih.gov/39438075/> etc | A new section was added The 2025 Nanopore Landscape: Pushing Towards Temporal Omics and Macromolecule Sequencing   1. A last sentence in section of conclusions was added |
| Is the language/English quality of the article suitable for scholarly communications? | The style of the article requires a high level of preparation. The density of philosophical terms and metaphors may make it difficult for readers without the appropriate background to understand. | We appreciate the reviewer's concern about readability. Our goal is to make complex ideas about nanopore sequencing accessible while maintaining depth. The philosophical perspective helps researchers think critically about how they use this powerful technology. But we agree it should never come at the cost of clarity. |
| Optional/General comments | I would like to thank the authors for this thoughtful and philosophically rich manuscript. The article successfully explores important questions that have been debated for years in the context of sequencing technologies, especially those related to Illumina. It is refreshing to see an interdisciplinary approach that links molecular biology with epistemological, ontological, and ethical considerations.  That said, I believe the manuscript would benefit from a broader and more critical engagement with the technical and practical limitations of Oxford Nanopore Technologies (ONT), in addition to the ethical and philosophical discussions already provided.  While the authors mention certain challenges, the manuscript does not sufficiently highlight that ONT still exhibits relatively high error rates, especially in the context of single-nucleotide polymorphism (SNP) detection. This is a significant omission, as SNPs are critical for identifying disease-associated variants and personalized medicine applications. Until basecalling accuracy further improves, ONT remains limited in these clinically relevant areas.  The discussion on epigenetics may come across as overly optimistic. Although ONT can detect various epigenetic modifications, the biological interpretation of these marks remains immature, and their reliability in reflecting complex traits (e.g., stress levels, lifestyle, or socio-economic status) is still under debate. It may be premature to suggest that epigenetic data can meaningfully inform such assessments at this stage.  One of the most intriguing issues raised in the article is the question of data ownership. Yet, the manuscript only hints at this point without developing it further. I would be interested in the authors’ perspective on this issue — especially in decentralized or field-based sequencing scenarios. Who owns the data produced in such contexts? How should consent and data governance be handled? A deeper exploration would strengthen the ethical section.  I would also like to see more illustrative material - graphs, diagrams, comparisons. For example, on the volume of data generated by short and long read technologies.  And also - does the volume of data produced by ONT really continue to grow, or do Illumina and its analogues still dominate the industry? It would be useful to receive comments from the authors on this matter.  By the way, is the section "Ontological Reconfigurations: The Fluidity and Annotation of the Living Code" a new conceptual part?  While the philosophical nature of the article is appreciated, it sometimes leans too heavily into abstraction without offering actionable conclusions. In my opinion, this article would be even more impactful if the authors took clearer positions on some of the core questions they raise. | Thank you for your thoughtful engagement with our manuscript and for recognizing the value of its interdisciplinary approach. We greatly appreciate your suggestion to strengthen the discussion of ONT's technical and practical limitations  We sincerely appreciate the reviewer’s thoughtful engagement with our manuscript. While we acknowledge the value of technical and actionable recommendations, we respectfully argue that the primary contribution of this work lies in its critical reflection—not in prescribing specific technical solutions or governance policies. Here’s why this approach is deliberate and necessary:  1. Purpose: Provoking Reflection, Not Prescribing Practice  Our goal is to interrogate assumptions and frame new questions about nanopore sequencing’s societal and philosophical implications—not to optimize its technical implementation. For example:  Ethics: We highlight tensions in data ownership (e.g., Who "owns" a microbiome sample sequenced in the field?) to expose gaps in current paradigms, not to propose a one-size-fits-all solution.  Epistemology: We question how real-time sequencing reshapes what counts as "knowledge" (e.g., Can we trust dynamic genomic annotations?), not how to improve basecalling accuracy.  This is analogous to philosophy of science works (e.g., Kuhn’s Structure of Scientific Revolutions) that critique scientific paradigms without offering lab protocols. |

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| **PART 2:** | | |
|  | Reviewer’s comment | Author’s comment *(if agreed with the reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)* |
| **Are there ethical issues in this manuscript?** |  | Original Manuscript has been highlighted on the modified parts |