Neuroscience 586 (2025) 152–153

Contents lists available at ScienceDirect

Neuroscience

journal homepage: www.elsevier.com/locate/nsc

Letter to the Editor

Reassessing PCA-based characterization of spiral ganglion neuron cell lines

ARTICLE INFO

Keywords:
Spiral ganglion neuron
Cell line
Principal component analysis
Limitations of linear methods
Statistical validation

Letter to the Editor

Wang et al. (2025) have made a valuable contribution to auditory neuroscience by establishing the immortalized cochlear spiral ganglion neuron cell line, SIO-SGN1, as a promising tool for hearing loss research. To support its utility, they demonstrate a key finding: its transcriptomic profile is remarkably similar to that of primary spiral ganglion neurons (SGNs). This similarity is most pronounced when compared to SGNs from the critical developmental stages of embryonic day 15.5 and postnatal day 1, and the profile remains clearly distinct from other inner ear cell types. While this finding is compelling, the visualization of its global transcriptomic similarity relies heavily on Principal Component Analysis (PCA). While the authors also present functional analyses and specific gene comparisons, this central reliance on a linear technique for visualizing the overall landscape warrants further discussion.

PCA, the primary tool used to visualize transcriptomic similarity in their study, is a linear dimensionality reduction technique. Although PCA is widely used for interpreting high-dimensional datasets, its effectiveness depends on the assumption that the underlying data structure is linear (Mohseni & Elhaik, 2024; Yao & Ochoa, 2023; Elhaik, 2022; Dey & Lee, 2019; Lenz et al., 2016). However, this assumption may fail in biological systems, such as gene regulatory networks and cellular state transitions, which often follow non-linear patterns. As a result, linear methods like PCA may overlook biologically meaningful heterogeneity, potentially leading to an oversimplified interpretation of transcriptomic similarity. While Wang et al.'s analysis distinguishes major cell types, their dimensionality reduction approach does not fully account for the non-linear structure of transcriptomic dynamics. Combined with bulk RNA sequencing, this may have limited their ability to detect subpopulations at different differentiation stages or reveal more complex relationships with primary cells.

To address these limitations, future characterization should adopt a comprehensive framework that includes rigorous alternatives to established dimensionality reduction and statistical modeling techniques. For biologically meaningful feature selection, unsupervised, non-linear, and non-parametric methods such as Feature Agglomeration and Highly Variable Gene Selection offer more powerful alternatives to linear and parametric PCA (Zhang et al., 2020; Xie et al., 2025). Their value lies in the fact that they do not assume simple linear relationships between genes and can flexibly model the true distribution of complex biological data, making them well-suited for capturing subtle heterogeneity and dynamic gene expression patterns. Furthermore, non-parametric correlation measures such as Spearman's rho and Kendall's tau are effective tools for detecting complex, non-linear associations, offering additional flexibility in transcriptomic analysis (Okoye & Hosseini, 2024; Yu & Hutson, 2024).

In conclusion, fully characterizing the SIO-SGN1 cell line requires approaches that move beyond linear assumptions. By integrating non-linear methods for feature selection and correlation analysis, researchers can more rigorously assess cellular homogeneity and uncover subtle transcriptomic dynamics. While the current study provides a strong foundation, incorporating complementary strategies could further refine the resolution and interpretability of the data. These suggestions aim to extend the impact of Wang et al.'s work and support the confident application of SIO-SGN1 in future hearing loss research.

Funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability

No new data was generated or analyzed in support of this research.

CRediT authorship contribution statement

Souichi Oka: Conceptualization, Writing – original draft. **Ryota Ono:** Investigation. **Yoshiyasu Takefuji:** Project administration, Supervision, Writing – review & editing.

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.

https://doi.org/10.1016/j.neuroscience.2025.09.036
Received 22 September 2025; Accepted 22 September 2025
Available online 23 September 2025

References

Dey, R., Lee, S., 2019. Asymptotic properties of principal component analysis and shrinkage-bias adjustment under the generalized spiked population model. J. Multivar. Anal. 173, 145–164. https://doi.org/10.1016/j.jmva.2019.02.007.

Elhaik, E., 2022. Principal component analyses (PCA)-based findings in population genetic studies are highly biased and must be reevaluated. Sci. Rep. 12, 14683. https://doi.org/10.1038/s41598-022-14395-4.

Lenz, M., Müller, F.J., Zenke, M., Schuppert, A., 2016. Principal components analysis and the reported low intrinsic dimensionality of gene expression microarray data. Sci. Rep. 6, 25696. https://doi.org/10.1038/srep25696.

Mohseni, N., Elhaik, E., 2024. Biases of principal component analysis (PCA) in physical anthropology studies require a reevaluation of evolutionary insights. eLife 13, RP94685. https://doi.org/10.7554/eLife.94685.2.

Okoye, K., Hosseini, S., 2024. Correlation tests in R: Pearson Cor, Kendall's Tau, and Spearman's Rho. In: Okoye, K., Hosseini, S. (Eds.), R Programming: Statistical Data Analysis in Research. Springer Nature, pp. 247–277. https://doi.org/10.1007/978-981-97-3385-9_12.

Wang, X., Zhang, M., Meng, Y., An, W., Wang, M., Chen, F., Chen, L., Suo, A., Xing, Y., Kong, L., Wang, H., Liu, W., Xu, L., 2025. An immortalized cochlear spiral ganglion neuronal cell line: a promising tool for hearing loss study. Neuroscience 581, 256–268. https://doi.org/10.1016/j.neuroscience.2025.07.017.

Xie, Y., Jing, Z., Pan, H., Xu, X., Fang, Q., 2025. Redefining the high variable genes by optimized LOESS regression with positive ratio. BMC Bioinf. 26, 104. https://doi.org/10.1186/s12859-025-06112-5.

Yao, Y., Ochoa, A., 2023. Limitations of principal components in quantitative genetic association models for human studies. eLife 12, e79238. https://doi.org/10.7554/eLife.79238.

Yu, H., Hutson, A.D., 2024. A robust Spearman correlation coefficient permutation test. Commun. Stat.- Theory Methods 53, 2141–2153. https://doi.org/10.1080/03610926.2022.2121144.

Zhang, J., Wu, X., Hoi, S.C.H., Zhu, J., 2020. Feature agglomeration networks for single stage face detection. Neurocomputing 380, 180–189. https://doi.org/10.1016/j.neucom.2019.10.087.

Souichi Oka*, Ryota Ono

Science Park Corporation, 3-24-9 Iriya-Nishi Zama-shi, Kanagawa 252-0029, Japan

Yoshiyasu Takefuji

Faculty of Data Science, Musashino University, 3-3-3 Ariake Koto-ku, Tokyo 135-8181, Japan

E-mail address: takefuji@keio.jp.

* Corresponding author.

E-mail addresses: souichi.oka@sciencepark.co.jp (S. Oka), rono@sciencepark.co.jp (R. Ono).