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Dr. Abir Igamberdiev
Editor-in-Chief
BioSystems

Dear Dr. Igamberdiev,

I am pleased to submit “The Geometry of Biological Shadows: Quantifying Topological Aliasing in High-Dimensional Systems” for consideration in *BioSystems* as a computational companion to my recently published paper (Todd, 2025; vol. 258, 105608).

Context:

The earlier paper argued theoretically that Popperian falsifiability faces structural limits in high-dimensional biological systems. That work remained qualitative. This manuscript provides the computational framework to *measure* those limits.

The Central Contribution:

We introduce the “Topological Aliasing Rate”—the first standardized metric for quantifying how much 2D projections (t-SNE, UMAP) misrepresent high-dimensional neighborhood relationships. Our key empirical finding: across four standard single-cell benchmark datasets (90,300 cells total), **75.5% of apparent neighbors in 2D projections were NOT neighbors in the original high-dimensional space.**

This is not a property of any particular dataset. It is a geometric consequence of projecting $D_{sys} \approx 10\text{--}40$ dimensions into $D_{obs} = 2$.

The Deliverable:

The accompanying **falsifiability** Python library (pip-installable, archived on Zenodo: DOI 10.5281/zenodo.17791874) enables any researcher to compute aliasing rates on their own data. We provide practical calibration guidelines:

- Aliasing < 30%: Visual clusters likely reflect high-dimensional topology
- Aliasing 30–60%: Clusters should be interpreted with caution
- Aliasing > 60%: 2D is for visualization only; quantitative analysis must occur in high-dimensional space

Why BioSystems:

This work directly extends the epistemological framework of my earlier *BioSystems* paper, operationalizing philosophical arguments into measurable quantities. More specifically, it provides

computational tools to test ideas that have been developed theoretically in this journal over the past decade:

- The “internal measurement problem” (Igamberdiev & Brenner, 2021; Louie, 2020): We show that the aliasing rate *quantifies* the measurement gap that relational biology describes qualitatively.
- “Computational irreducibility” (Azadi, 2025): We demonstrate that irreducibility manifests empirically as >75% topological aliasing—the system cannot be reduced without losing most of its causal structure.

The **falsifiability** toolkit is not a bioinformatics utility; it is the experimental apparatus for testing *BioSystems*-style theory. The audience that engaged with these foundational papers is precisely the audience for this computational companion.

Thank you for your consideration.

Sincerely,

Ian Todd
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