

HYPERBOLIC REPRESENTATION LEARNING IN MULTI-LAYER TISSUE NETWORKS

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MOTIVATION

Predicting tissue-specific protein functions and interactions (PPI) is essential for understanding human biology and diseases. Yet, current solutions overlook the geometry of multi-layer PPI networks.

CONTRIBUTION

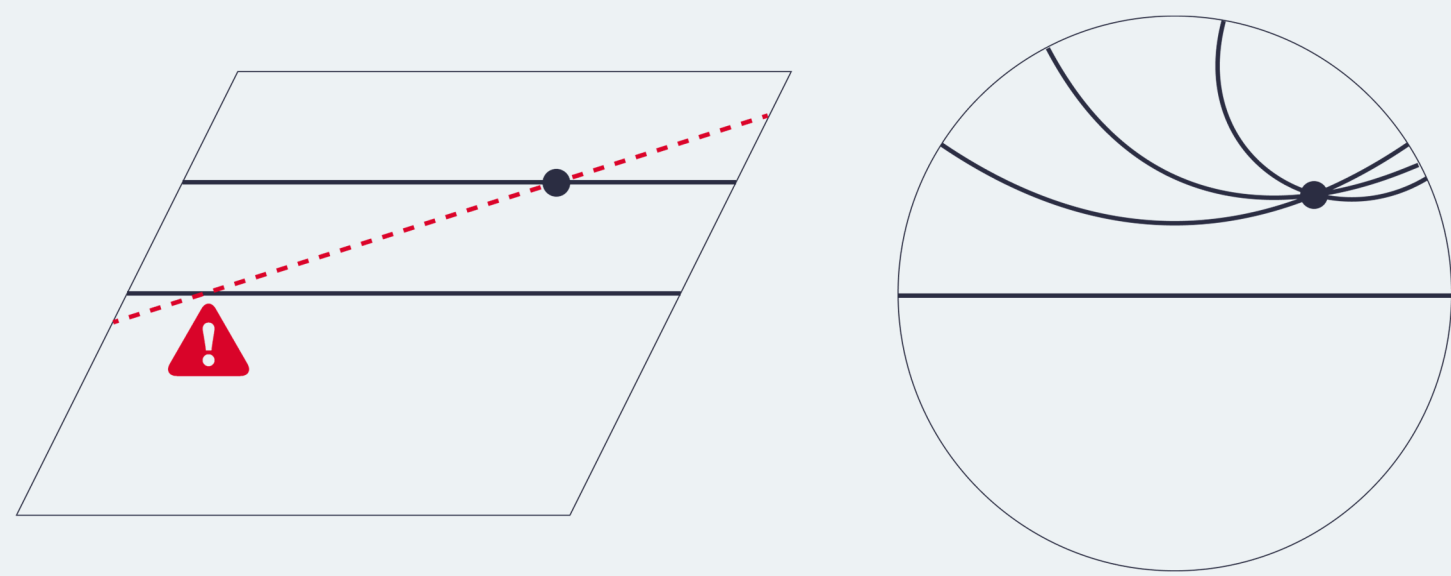
- Proposed a contextualized, tissue-specific representation learning method in non-Euclidean space.
- Compared Euclidean (\mathcal{E}) and hyperbolic (\mathcal{H}) embeddings.

RESULTS

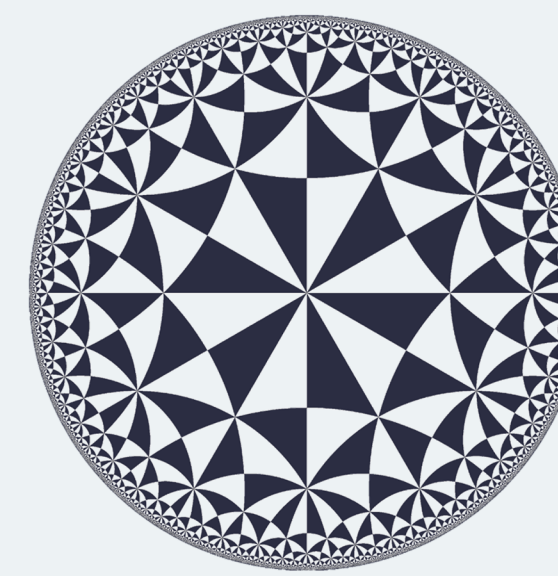
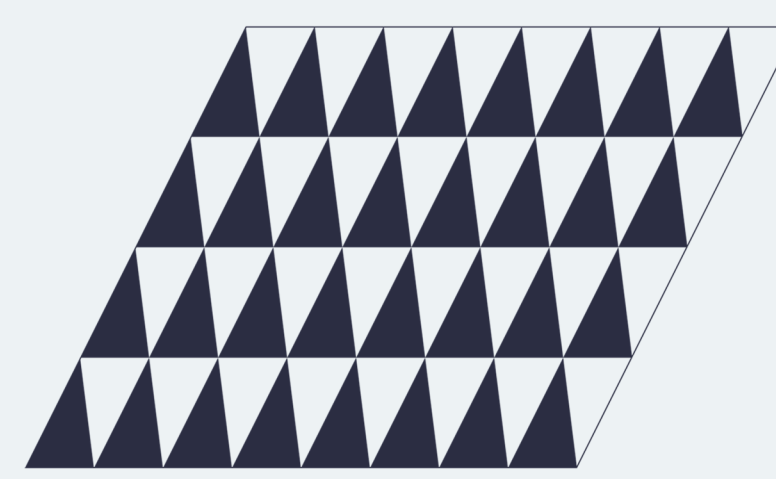
- Hyperbolic geometry captures the structure of multi-layer PPI networks with less distortion.
- Hyperbolic embeddings improve tissue-specific protein function prediction.

HYPERBOLIC GEOMETRY

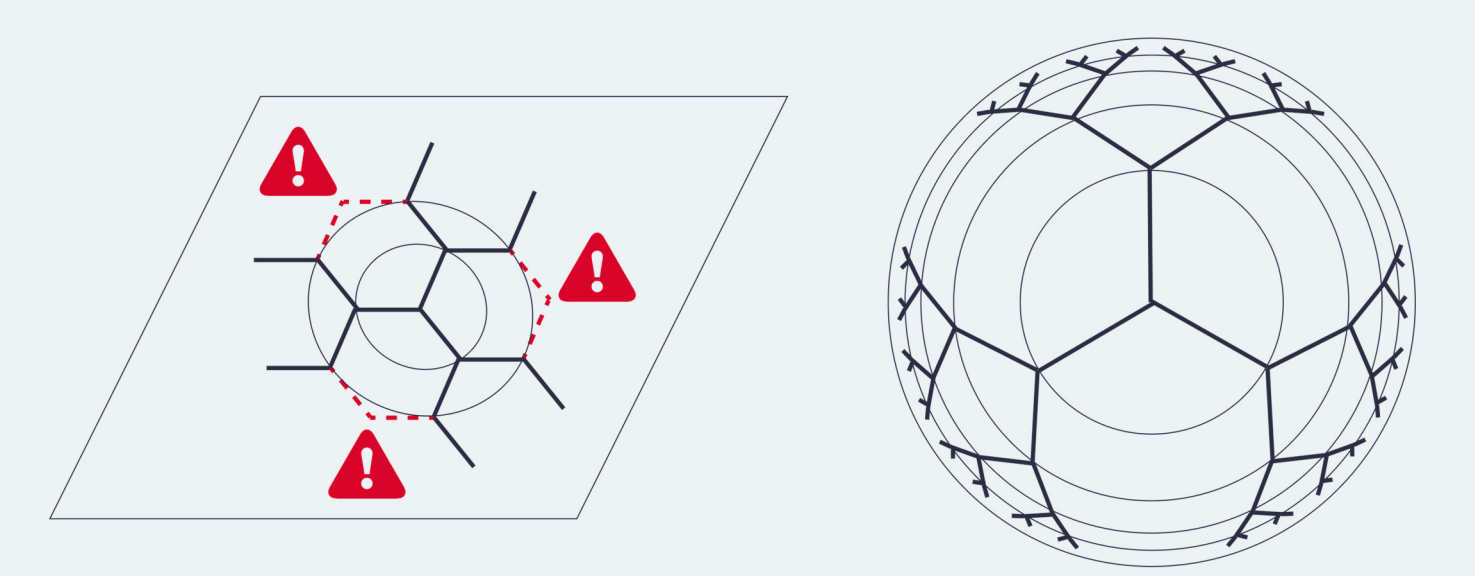
In \mathcal{E} , there is exactly one; in \mathcal{H} , there are at least two parallels through any external point to a given line.



In \mathcal{H} , the area grows exponentially; in \mathcal{E} , it grows only polynomially with respect to the radius.

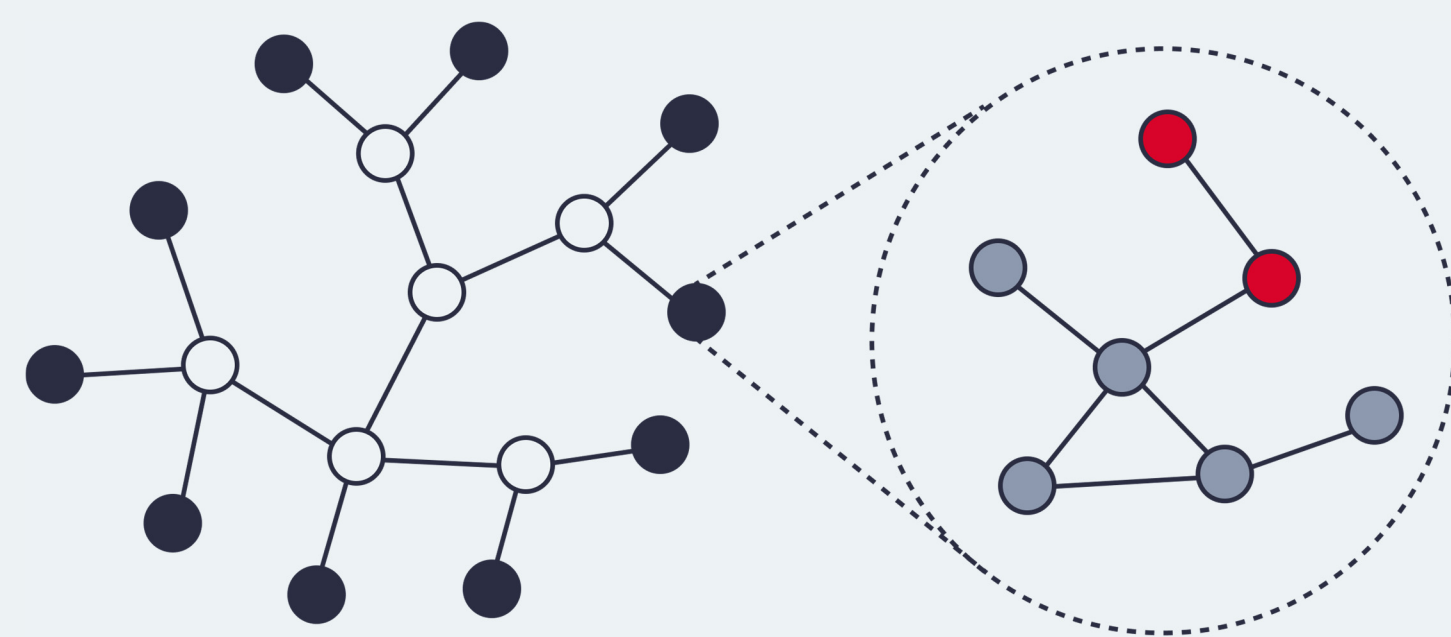


\mathcal{H} is, therefore, suitable for embedding trees / scale-free networks with many leaves / small degree nodes [1].

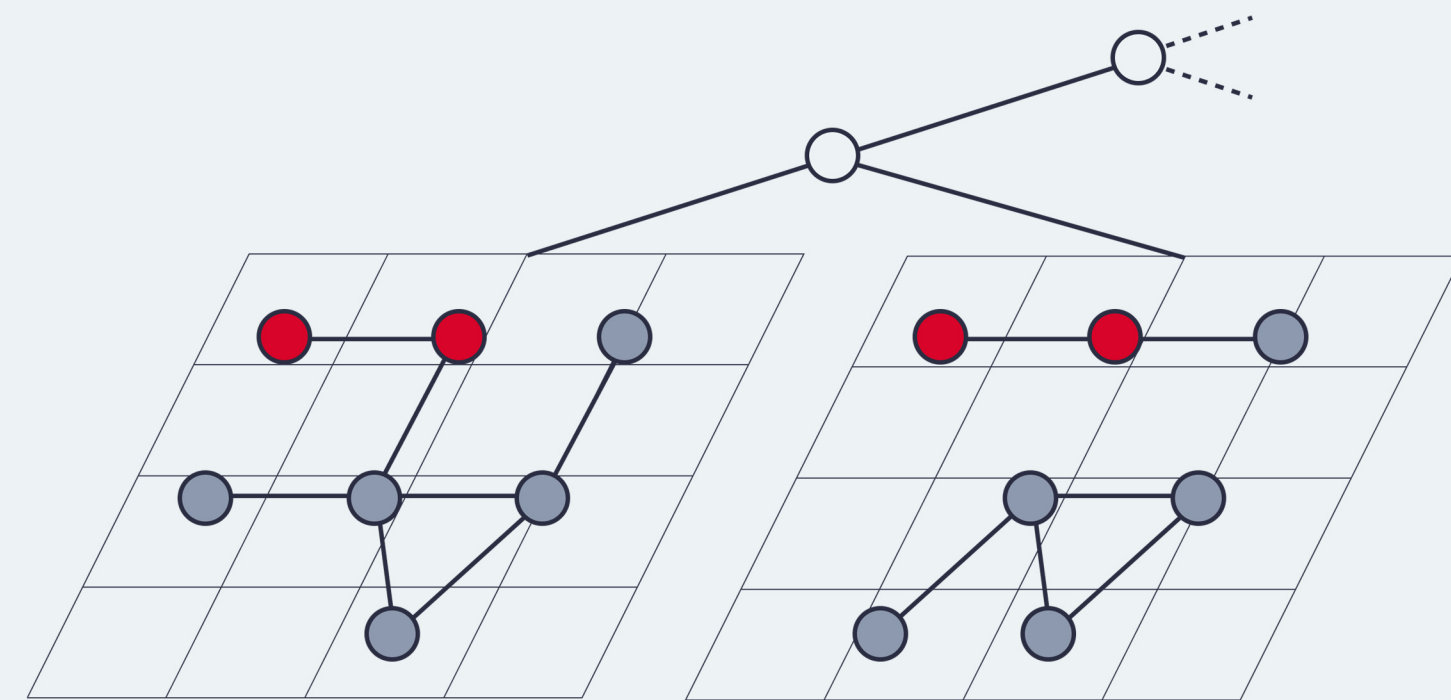


METHODS

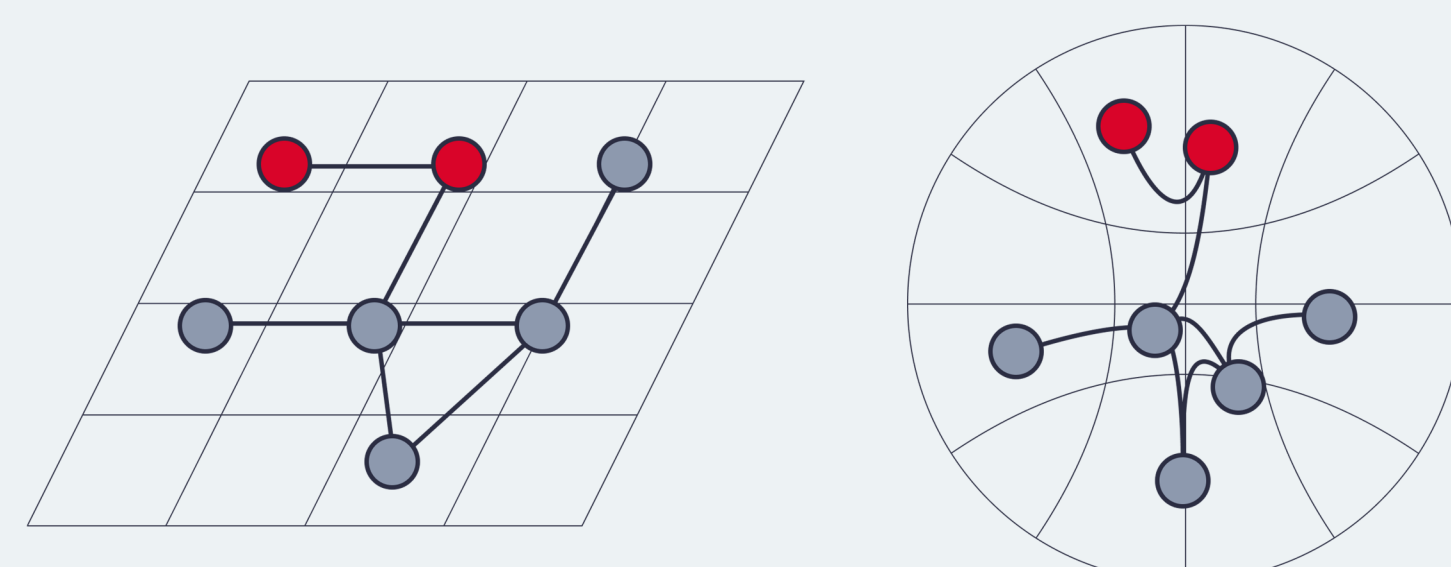
Tissue hierarchy with 112 internal and 107 leaf nodes containing **tissue-specific PPI networks** and binary-labeled **protein functions**.



OhmNet model [2]: Leaf nodes: **Node2Vec** embeddings on PPI networks with **hierarchy regularization** to align proteins across tissues. Internal nodes: **Average** of the child and parent embeddings.

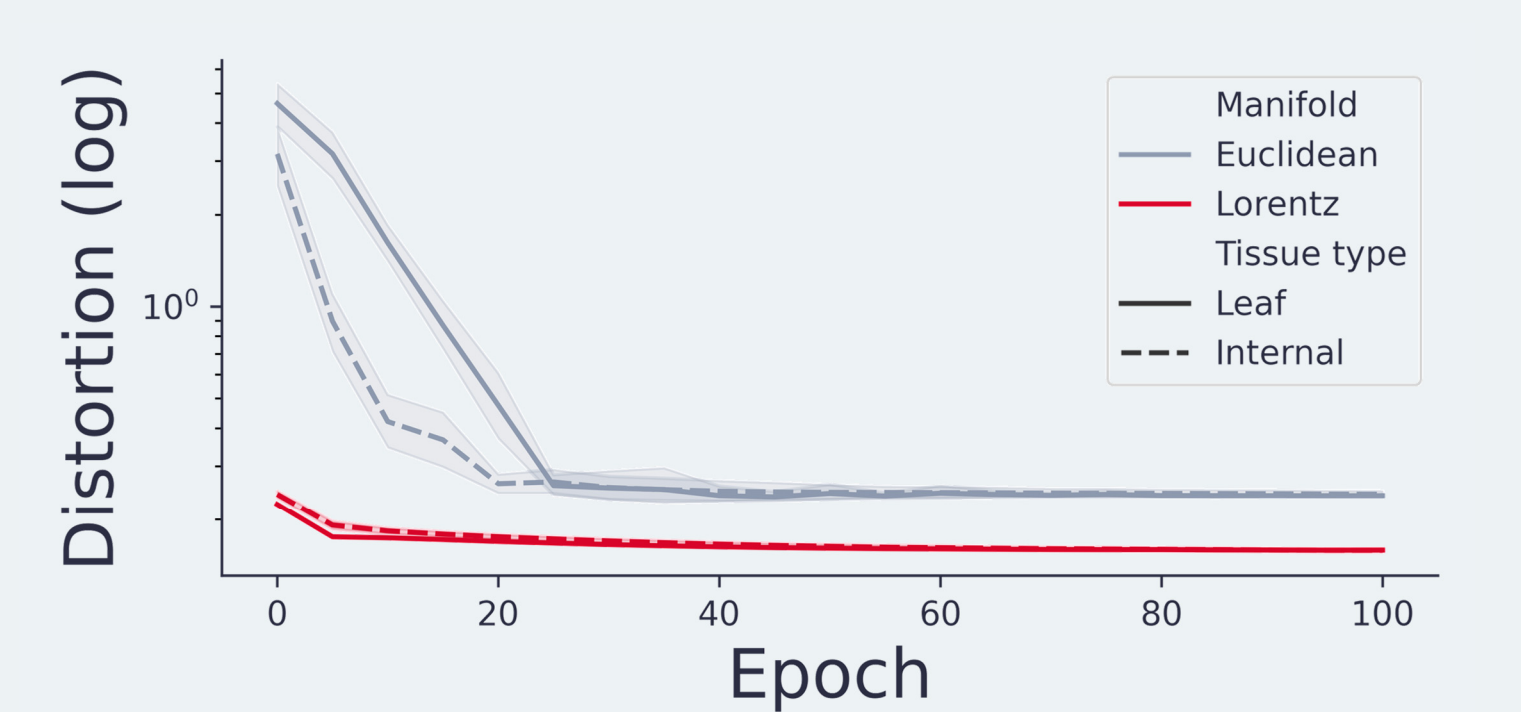


The hyperbolic version utilizes the **Lorentz manifold and distance** for the Node2Vec and hierarchy regularization, and it applies the Lorentz centroid for the internal representations.

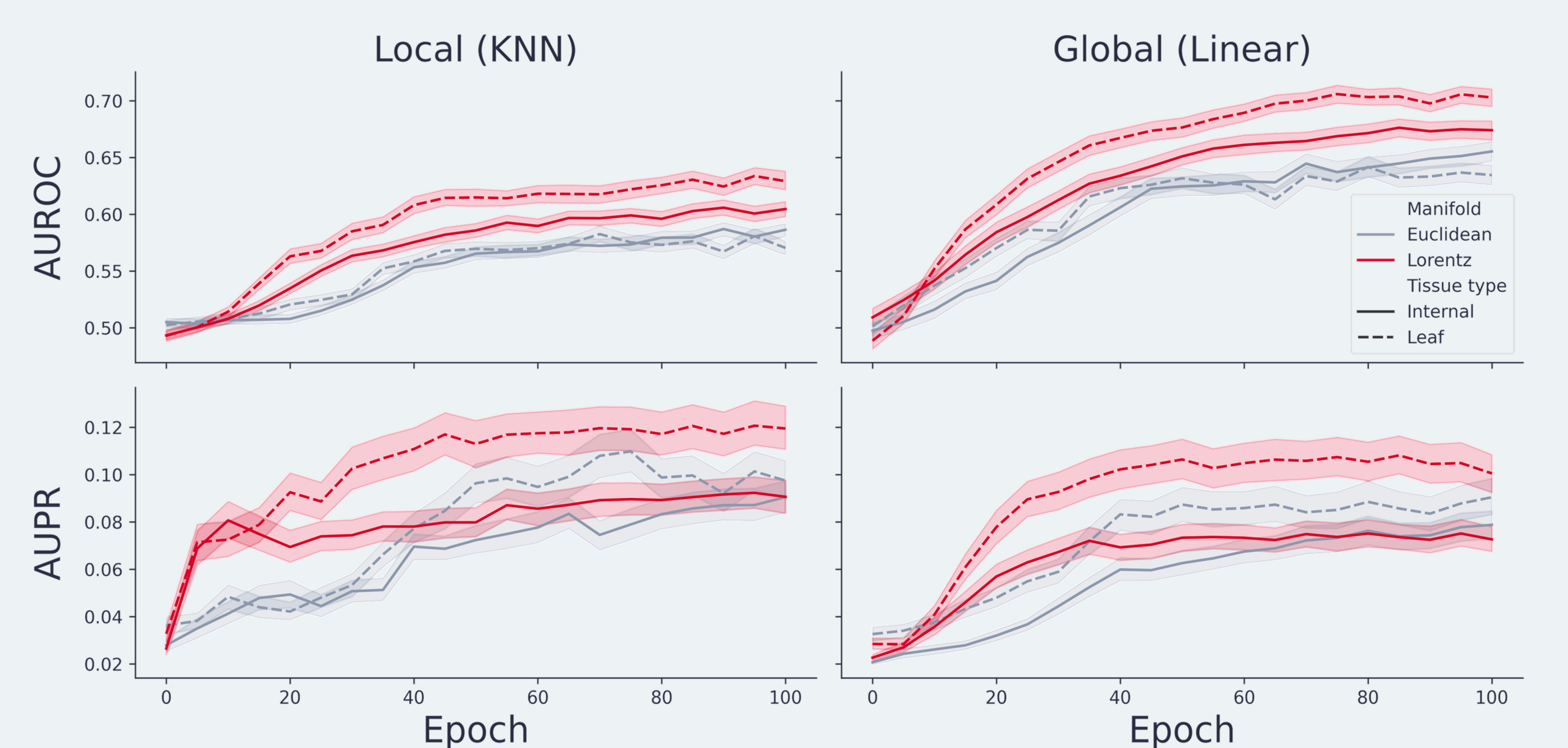


RESULTS

Distortion between manifold distances in the embedding space and shortest-path distances in the PPI networks **is lower in \mathcal{H}** .



Embeddings in \mathcal{H} achieve superior performance in tissue-specific protein function prediction. Both linear classifiers (relying on a single global separating hyperplane) and K-Nearest Neighbors classifiers (capturing the local structure) perform better in hyperbolic space.



- [1] Krioukov, D., Papadopoulos, F., Kitsak, M., Vahdat, A., & Boguná, M. (2010). Hyperbolic geometry of complex networks. *Physical Review E—Statistical, Nonlinear, and Soft Matter Physics*, 82(3), 036106.
[2] Zitnik, M., & Leskovec, J. (2017). Predicting multicellular function through multi-layer tissue networks. *Bioinformatics*, 33(14), i190-i198.



Scan for more details!
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