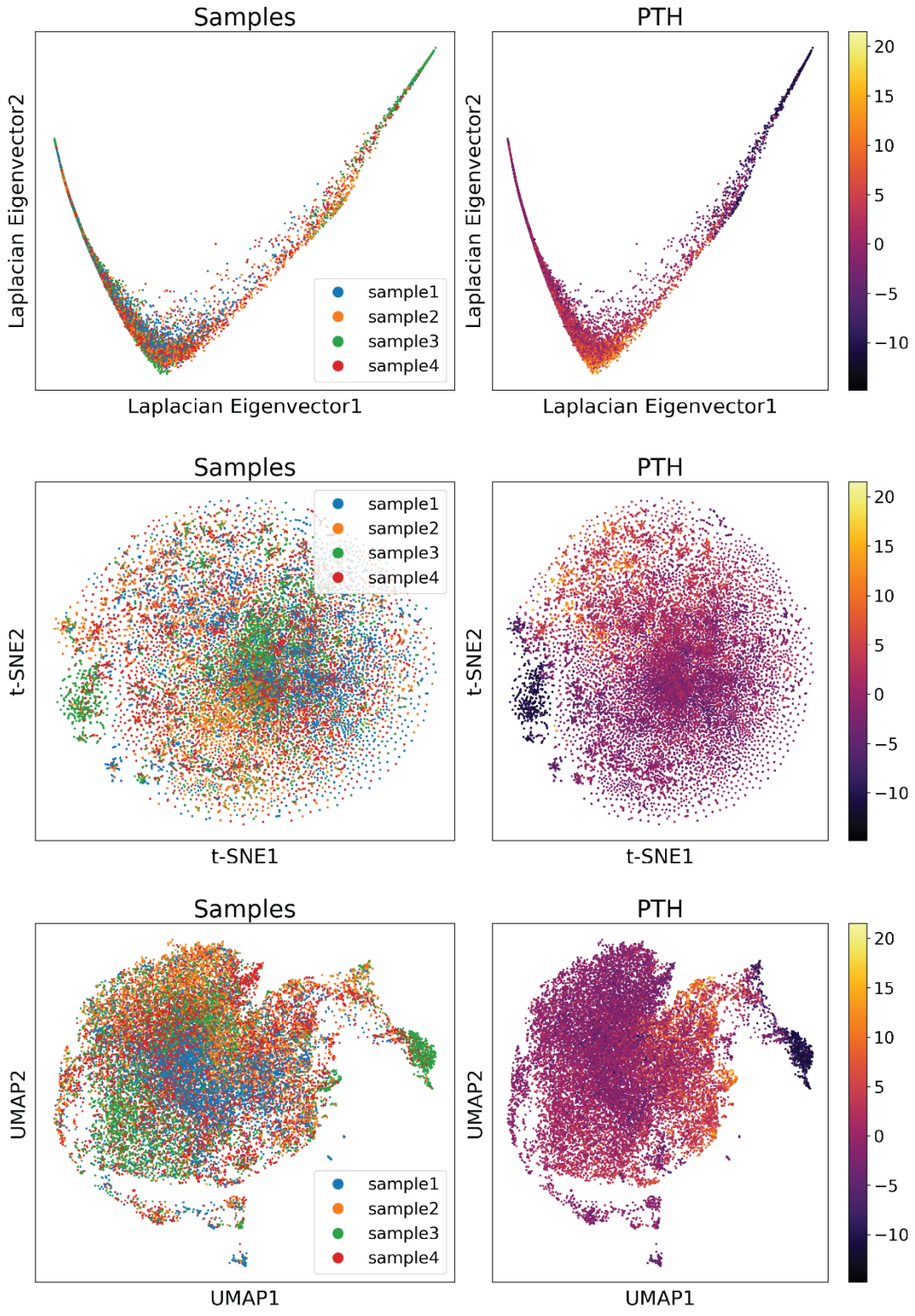
Supplemental Note S1. Preservation of diffusion distances reveals a single trajectory of parathyroid cells.

In single-cell transcriptomics, many analysis tools have been designed to embed individual cells into two-dimensions such that cells with similar expression are positioned close together [1-11]. PHATE [12] captures both local and global nonlinear structure using an information-geometric distance between data points. To do this, PHATE applies a diffusion framework popularized by diffusion maps [13]. Kobak and Linderman [14] have recently shown that difference in preservation of global structure between *t*-SNE and UMAP can be attributed to initialization with Laplacian eigenmaps [15], which are equivalent to diffusion maps for a symmetric normalized Markov matrix like in single-cell data.

To corroborate our findings in the paper, we show that visualization of the NHP parathyroid cells by the first two Laplacian eigenvectors captures the main axis of variation, which corresponds to a single trajectory. Visualization with UMAP and *t*-SNE using diffusion distances also identifies a single axis along which PTH changes nonlinearly.


Samples
PTH
Laplacian Eigenvector2
Laplacian Eigenvector1
sample1
sample2
sample3
sample4
20
15
10
5
0
−5
−10
t-SNE2
t-SNE1
UMAP2
UMAP1

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