

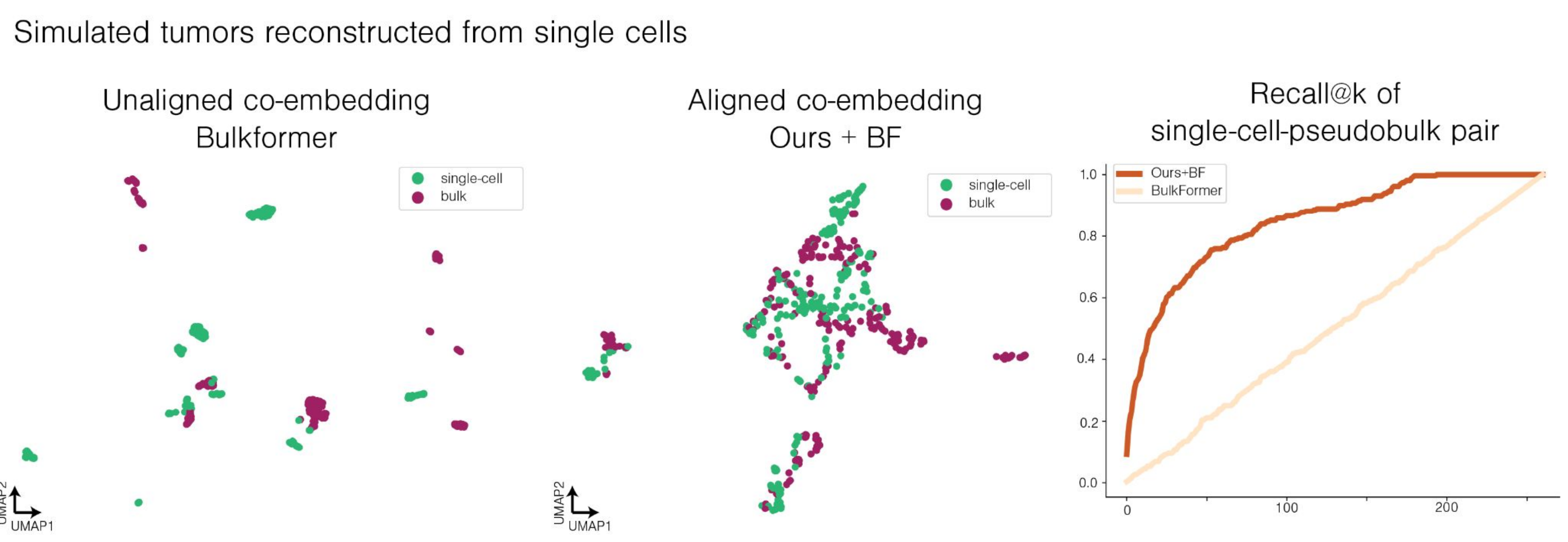
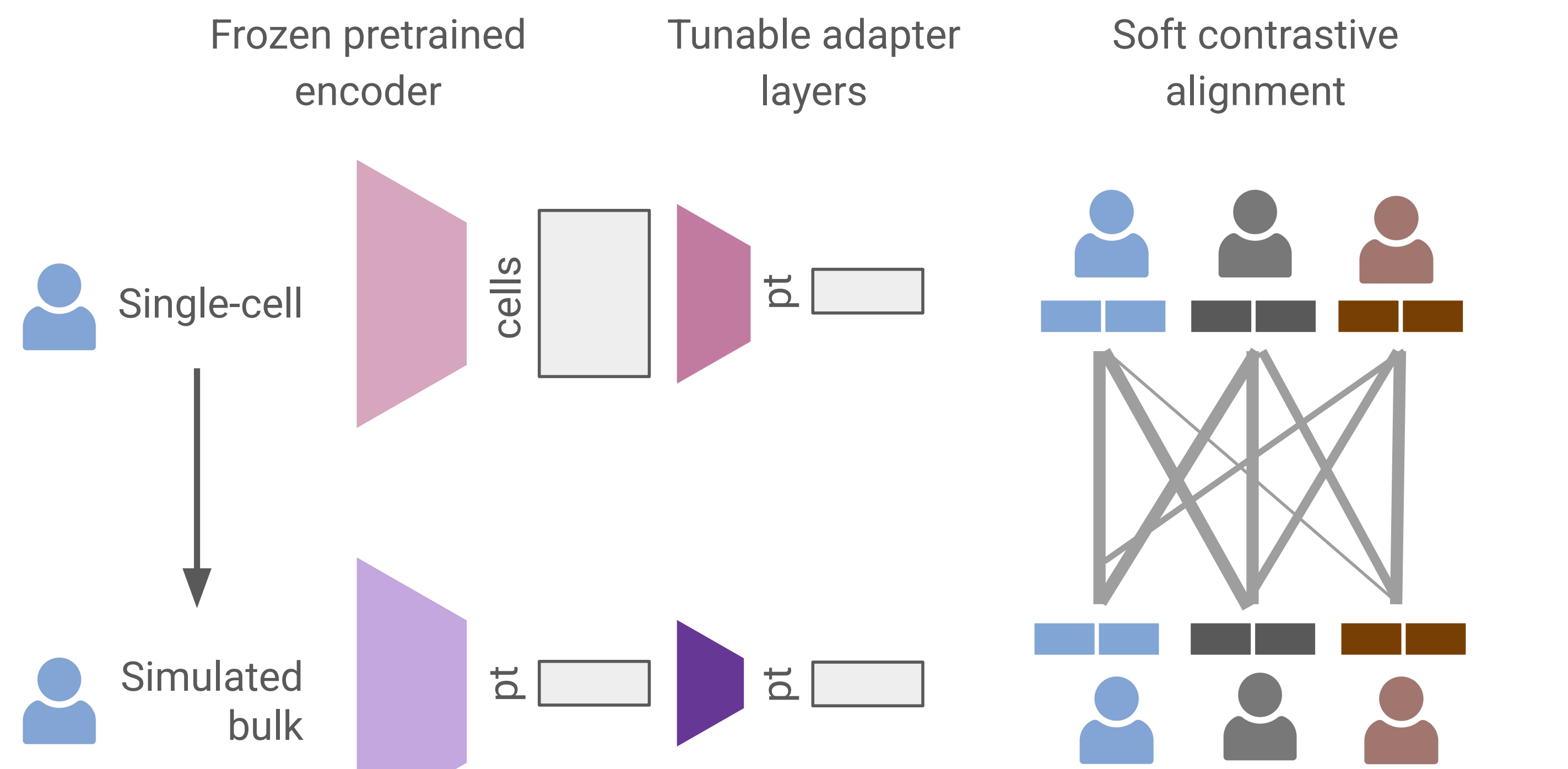
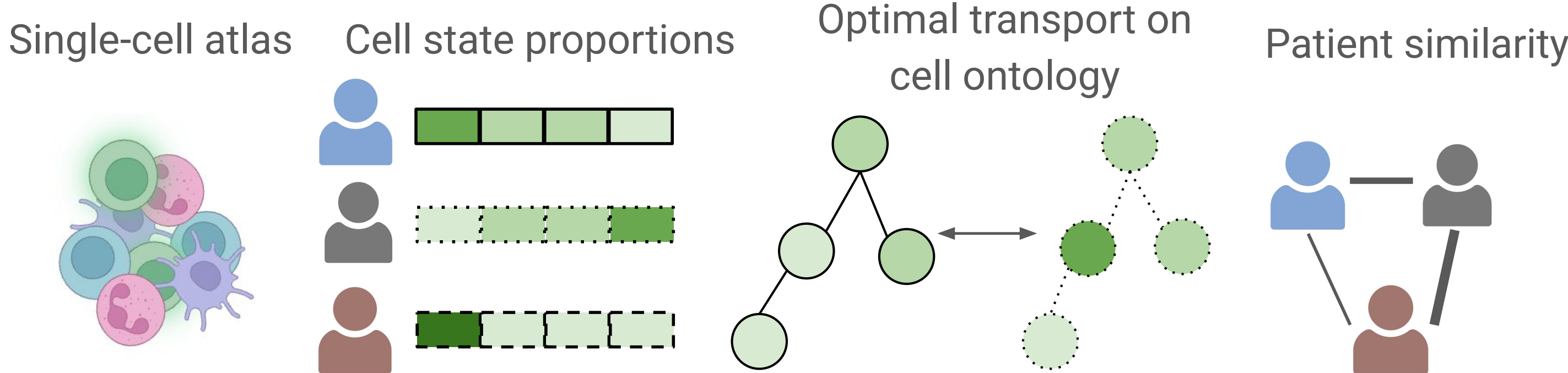
Cross-modal transfer learning for mapping bulk transcriptomes at the cellular level

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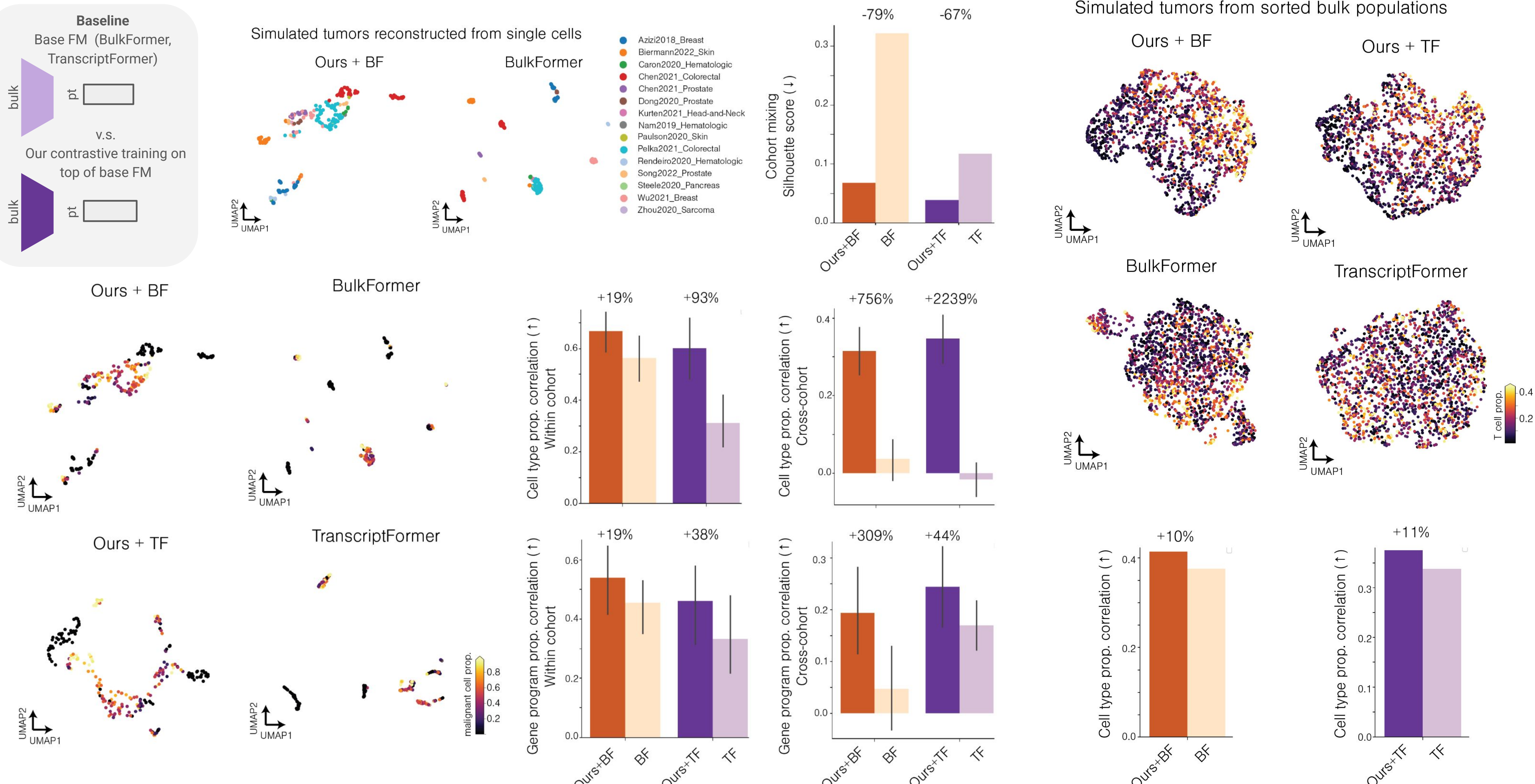
Work in progress – please do not share!

SINGLE-CELL AND BULK CONTRASTIVE ALIGNMENT

One underappreciated capability of single-cell foundation models (FMs) is the potential for cross-modality transfer learning through constructing a shared space across experimental techniques. Here, we design a framework to transfer information from single-cell data from the Curated Cancer Cell Atlas (3CA) to tumor bulk transcriptomes in zero-shot and few-shot settings. We propose an ontology-aware contrastive learning objective that first models cell type proportions as signals on the Cell Ontology graph, then aligns single-cell and pseudobulk samples to preserve pairwise similarities defined by graph-based optimal transport. We further propose a cohort-aware hard negative sampling strategy to improve cross-cohort generalization. In a zero-shot manner, our approach improves cohort integration and preservation of cell type proportion similarity in simulated bulk tumors from single-cell and sorted bulk data compared to the base FM applied to bulk tumors. We additionally fine-tune a cross-attention module that predicts immunotherapy response in bulk melanoma samples using a large-scale single-cell melanoma atlas, identifying cell populations enriched in bulk responders.



OUR CONTRASTIVE ALIGNMENT ENABLES BETTER PRESERVATION OF CELL TYPE PROPORTION OVER BASE BULK FMS IN SIMULATED TUMORS FROM SINGLE-CELL AND SORTED BULK DATA



RESPONSE PREDICTION IMPROVES WITH OUR SINGLE-CELL REPRESENTATIONS V.S. BASELINE FM

