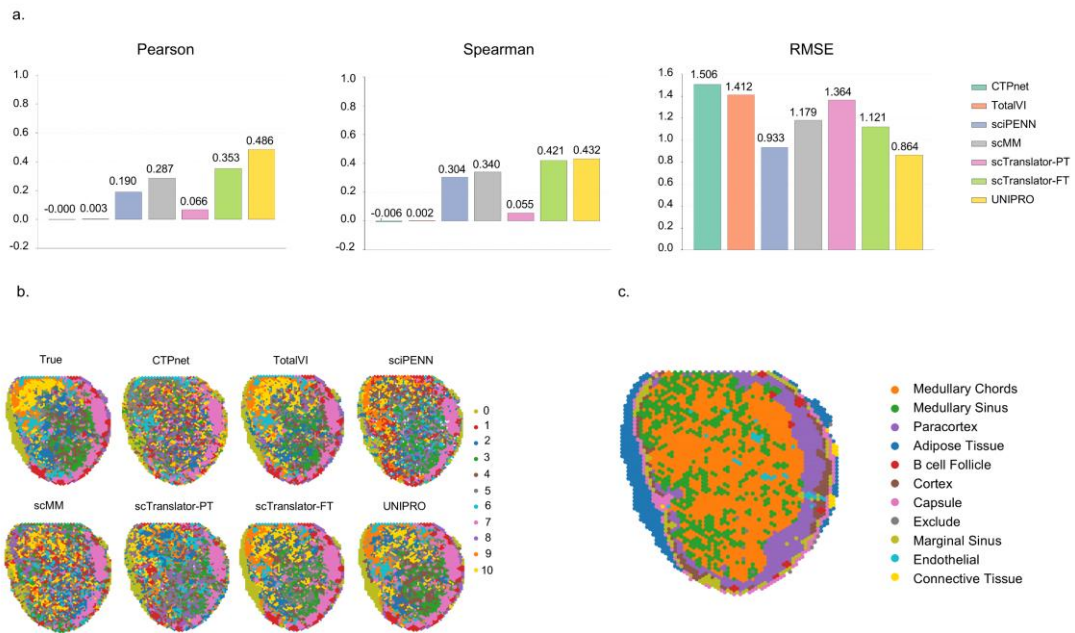


Details of comparison methods

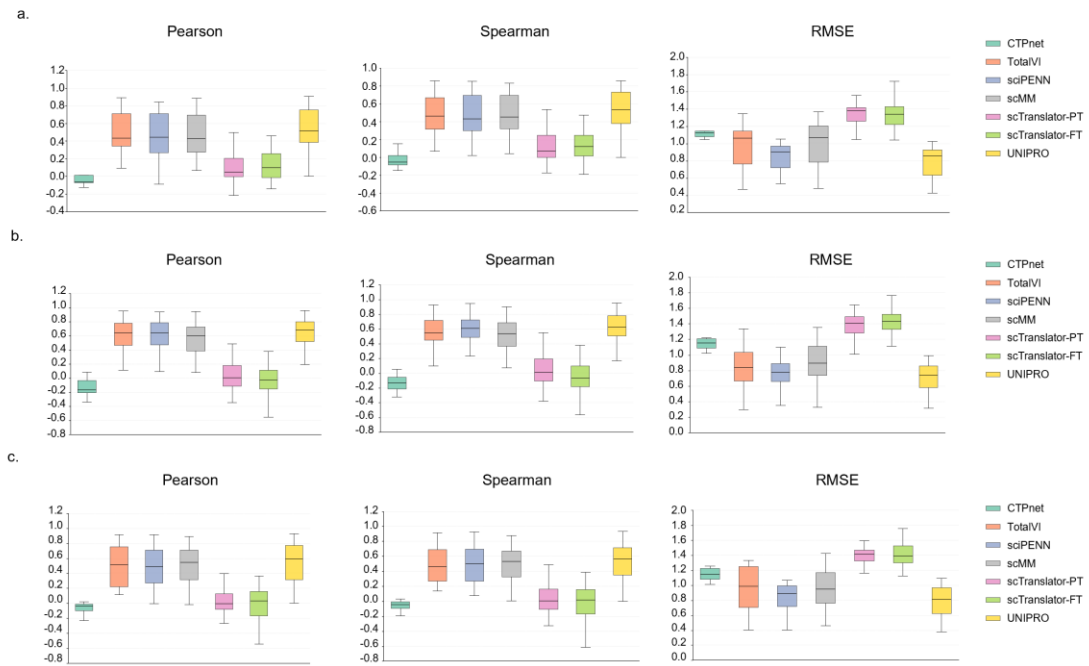
To evaluate the performance of UNIPRO, we compared it with six representative baseline methods: CTP-net, TotalVI, sciPENN, scMM, scTranslator, and scTranslator with fine-tuning. All baseline methods were implemented using their official codebases and original default settings, without additional hyperparameter tuning. For a fair comparison, baseline models requiring training were retrained on the same datasets used for UNIPRO, except for the original scTranslator model, which was evaluated following its official setting.

For CTP-net, protein abundances were estimated from gene expression matrices by running the official training script with default parameters (<https://github.com/zhoulilu/ctpnetpy>). For TotalVI, the model was trained using the official implementation and default configuration provided in the TotalVI reproducibility repository (https://github.com/YosefLab/totalVI_reproducibility). For sciPENN, protein prediction was performed using the official sciPENN codebase with its default training and inference settings (<https://github.com/jlakkis/sciPENN>). For scMM, we used the official implementation and default model settings to learn multimodal representations and generate protein profiles from transcriptomic inputs (<https://github.com/kodaim1115/scMM>). For scTranslator, we followed the official implementation and evaluation protocol provided by the authors without modifying the default settings (<https://github.com/TencentAILabHealthcare/scTranslator>). For scTranslator with fine-tuning, we further fine-tuned the official scTranslator model on the same training data used for UNIPRO, while keeping the original fine-tuning procedure.

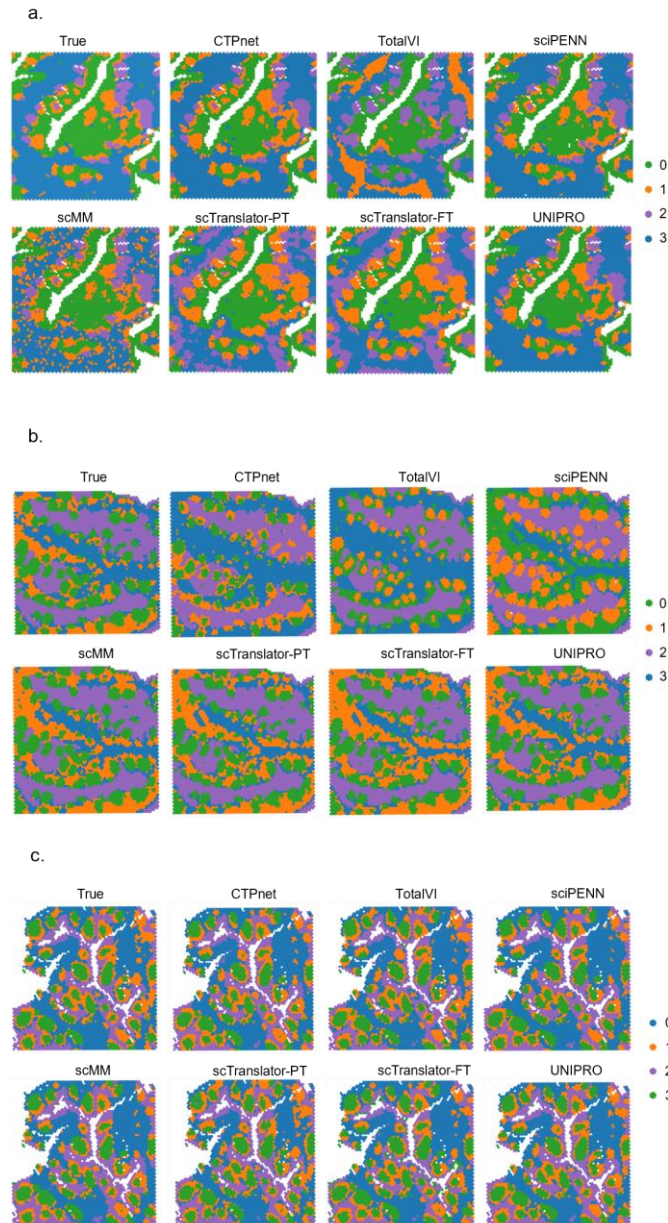
Supplementary Figures



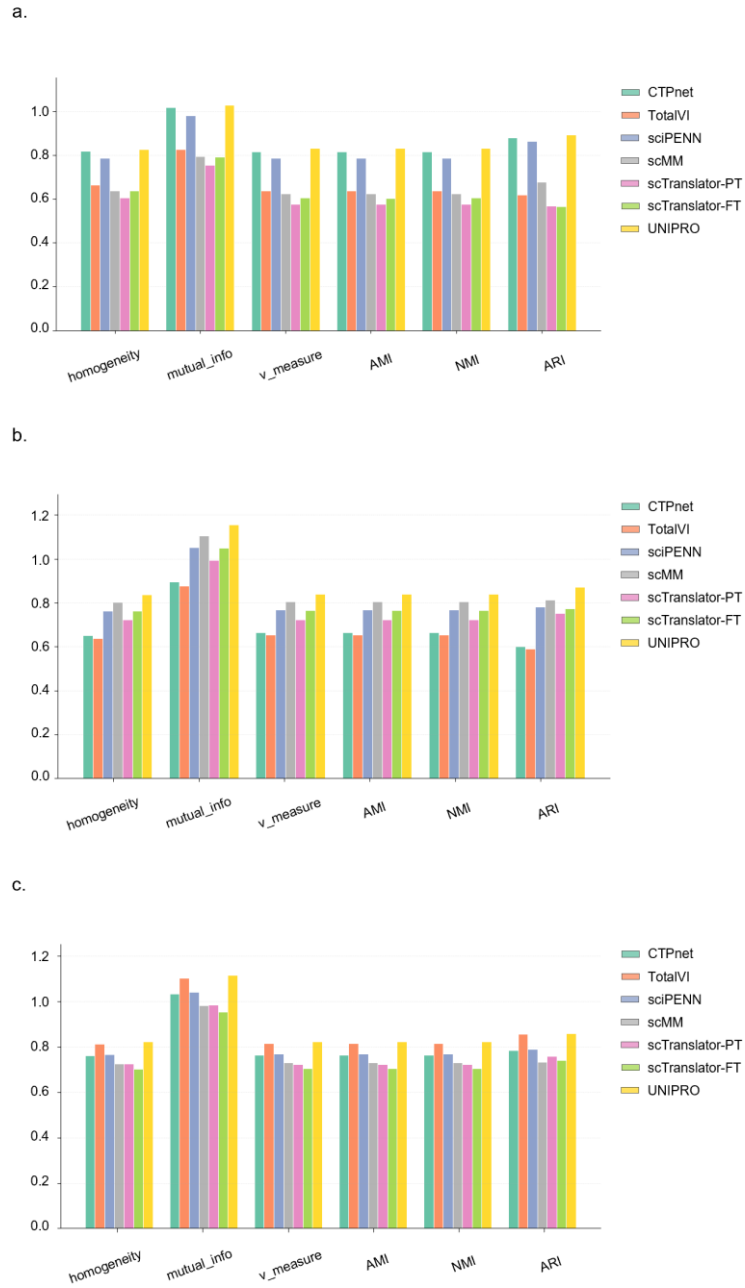
Supplementary Fig. 1 Additional results on spatial human lymph nodes. **a.** Average protein inference performance across all proteins. **b.** Spatial plots of human lymph node sample, clustering of integrating RNA and true or inferred protein of each method with SpatialGlue. Note that the colors of clusters do not directly correspond to the same captured structures across different methods. **c.** Manual histological annotation of the human lymph node section.



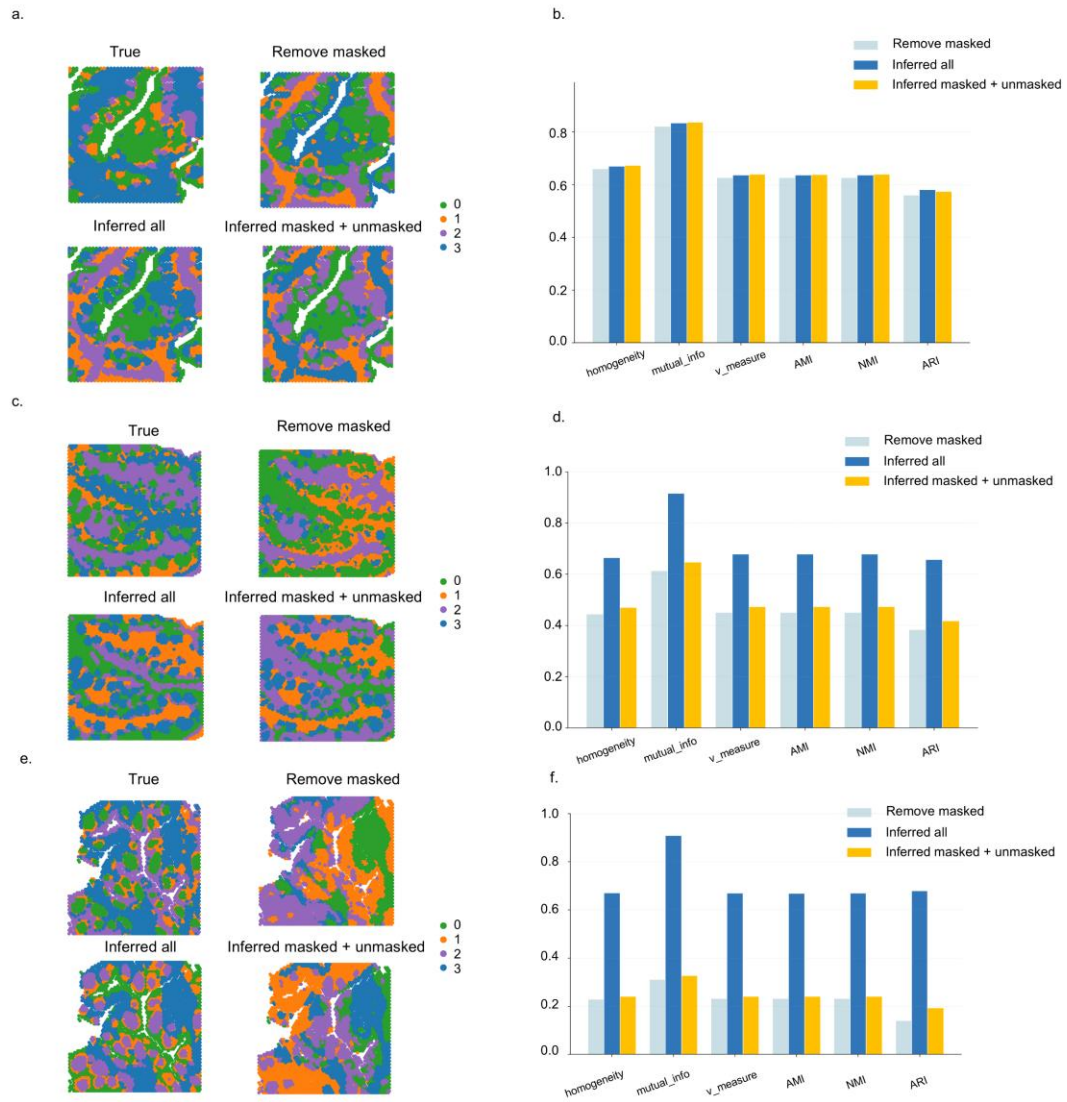
Supplementary Fig. 2 Cross-section protein inference in the remaining held-out human tonsil sections. a. Box plots showing the Pearson correlation, Spearman correlation and the RMSE between the second human tonsil's predicted and true values for each method. b. Box plots showing the Pearson correlation, Spearman correlation and the RMSE between the third human tonsil's predicted and true values for each method. c. Box plots showing the Pearson correlation, Spearman correlation and the RMSE between the fourth human tonsil's predicted and true values for each method.



Supplementary Fig. 3 Spatial analysis based on the inferred protein in the remaining held-out human tonsil sections. a. Spatial plots of the second held-out human tonsil sections, clustering of integrating RNA and true or inferred protein of each method with SpatialGlue. b. Spatial plots of the third held-out human tonsil sections, clustering of integrating RNA and true or inferred protein of each method with SpatialGlue. d. Spatial plots of the fourth held-out human tonsil sections, clustering of integrating RNA and true or inferred protein of each method with SpatialGlue.



Supplementary Fig. 4 The Homogeneity, Mutual Information, V-measure, AMI, NMI, and ARI of the resulting spatial domains. a. Bar chart of six supervised metrics with scores of clustering results about the second held-out human tonsil section. b. Bar chart of six supervised metrics with scores of clustering results about the third held-out human tonsil section. c. Bar chart of six supervised metrics with scores of clustering results about the fourth held-out human tonsil section.



Supplementary Fig. 5 Cross-section protein imputation and spatial domain analysis in the remaining held-out human tonsil sections. a-b. Protein expression imputation and spatial domain analyses in the second held-out human tonsil section. c-d. Protein expression imputation and spatial domain analyses in the third held-out human tonsil section. e-f. Protein expression imputation and spatial domain analyses in the fourth held-out human tonsil section.

