



人工智能时代的空间组学：技术，算法生态，生物学应用与大模型展望

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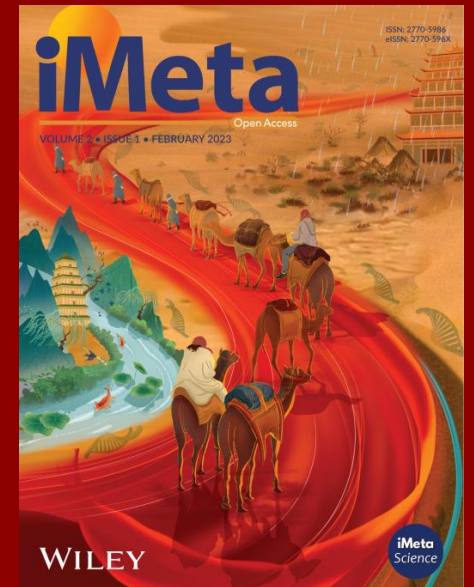
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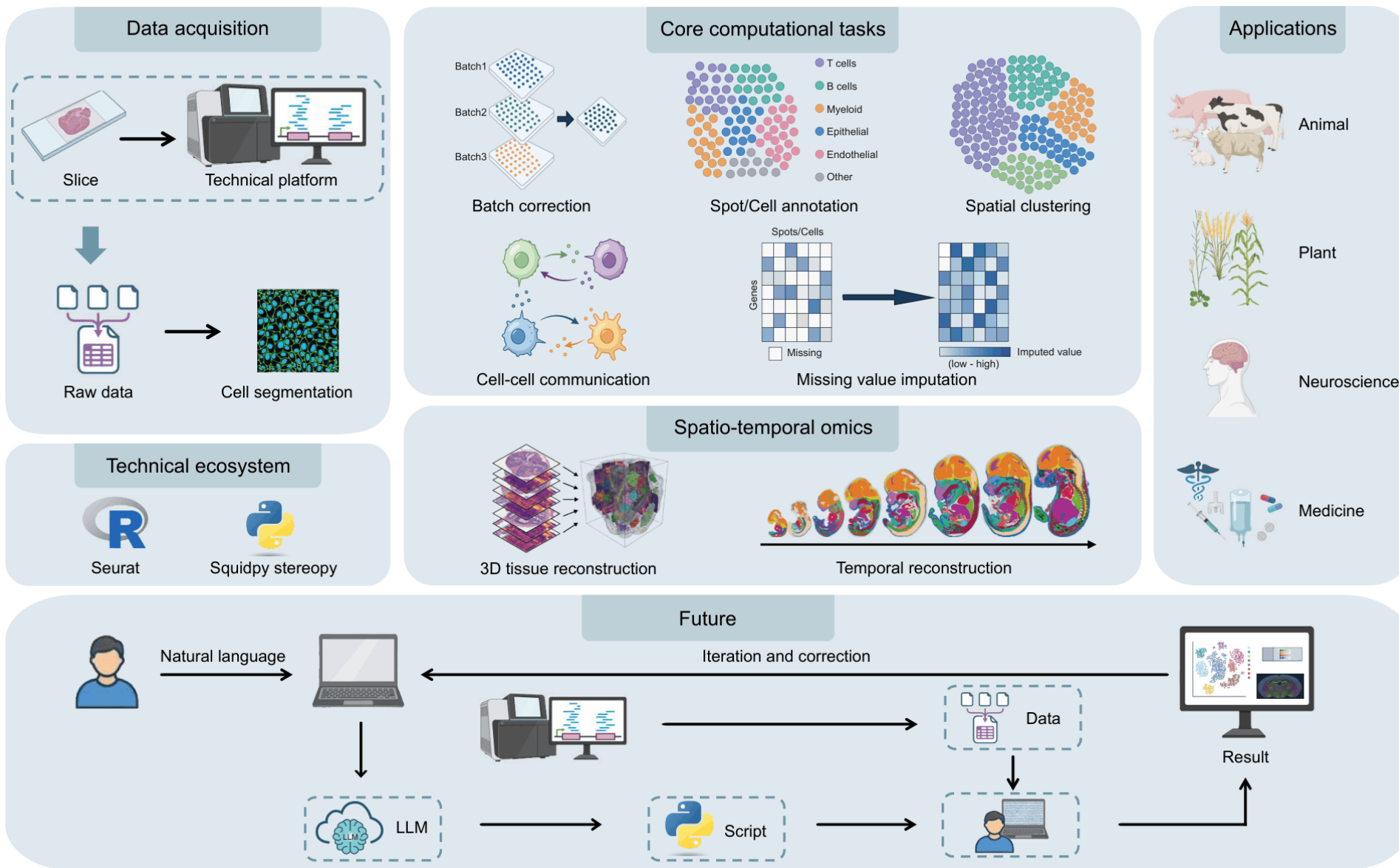
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简介



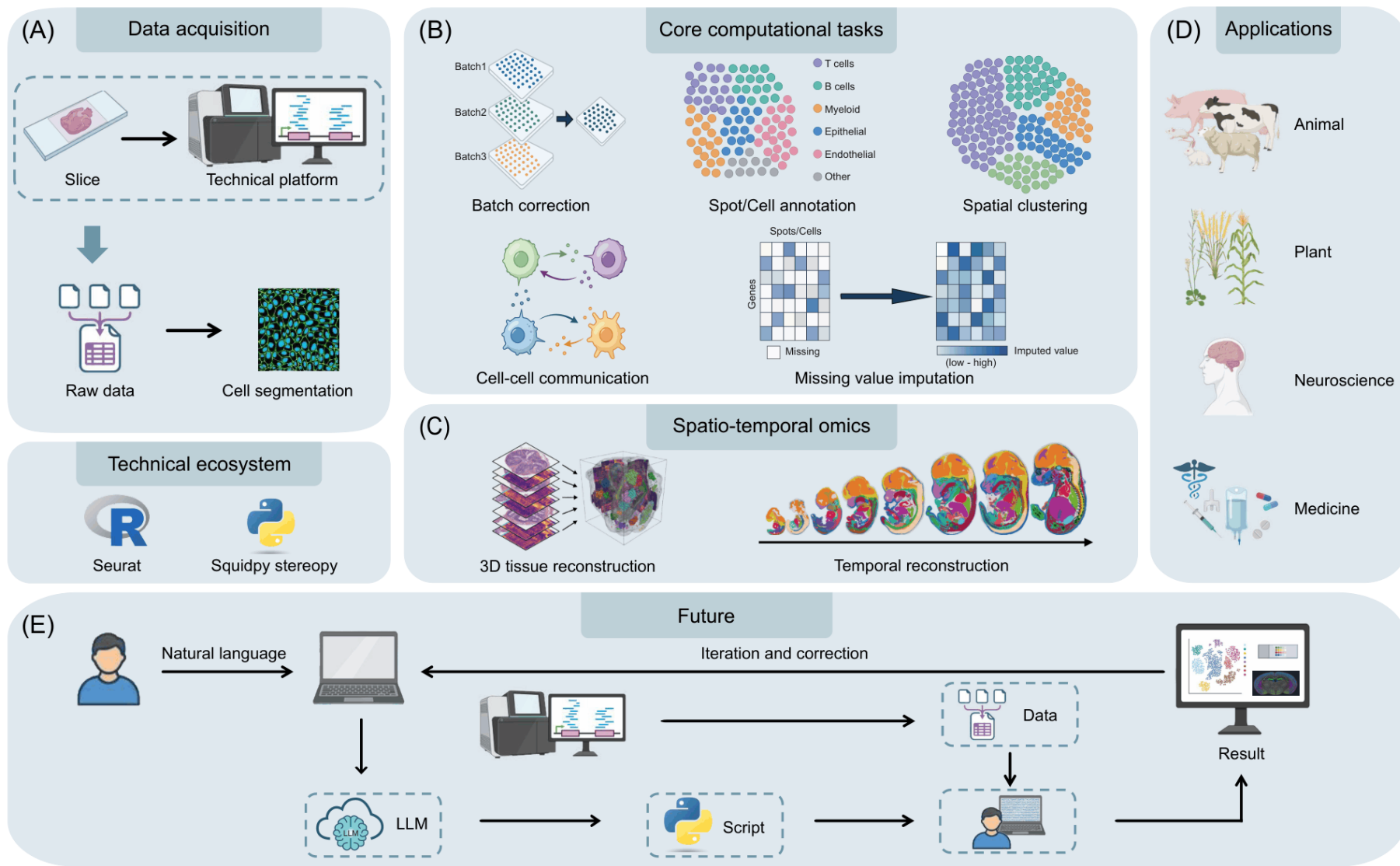


亮点

- 系统综述当下空间组学技术及其核心计算分析任务。
- 客观评析各类算法的适用场景、现存瓶颈及优选方案。
- 全面梳理空间组学在生物医学、神经科学与动植物科学领域的应用。
- 展望三维重构、虚拟细胞、时序建模与大语言模型的未来发展趋势。



文章介绍



本文综述按照空间组学研究的数据流转逻辑展开，依次介绍数据产出、数据分析与科学发现全流程。



空间组学技术

Table 1 Performance characteristics demonstration of a comprehensive spatial omics technology platforms.

Technology	Resolution	Core principle	Sample compatibility	Distinctive features
Sequencing-based spatial transcriptomics				
Visium	55 μm	Slide-based spatial transcriptomics for <i>in situ</i> mRNA capture and whole-transcriptome quantification	Human, mouse, rat; fresh, frozen, and FFPE tissues	Mature commercial workflow, high data reproducibility
Array-seq	30 μm	Modified oligonucleotide microarray for spatial transcriptomics with barcoded mRNA capture	Human, mouse; fresh, frozen, and FFPE tissues	Higher resolution, larger area, lower cost, comparable sensitivity vs Visium
DBiT-seq	10 μm	Orthogonal microfluidic barcoding for spatial co-mapping of transcriptome and proteome	Human, mouse; fresh, frozen, and FFPE tissues	Multi-omics integration (transcriptome and proteome)
HDST	2 μm	2 μm barcoded beads for high-definition spatial transcriptome sequencing	Human and mouse fresh-frozen tissues	Ultra-high-resolution
Nova-ST	10 μm	NovaSeq nanopattern-based HDMI barcoding for high-res spatial transcriptomics	Mouse fresh-frozen tissue samples	Enables large tissue section analysis & multi-chip spatial mapping

Spatial metabolomics				
LAESI-MSI	—	Atmospheric-pressure laser ablation ionization enables metabolite qualitative-quantitative and spatial imaging	IR Fresh plant samples	Mass Spectrometry-based Spatial Metabolomics
Spatial epigenomics				
Spatial-ATAC-seq	20 μm	Spatial chromatin accessibility sequencing at cellular level via <i>in situ</i> Tn5 and microfluidic barcoding	Fresh, frozen tissue sections, human and mouse samples	Similar principle to Spatial-CITE-seq; spatial information via microfluidics
Spatial-CUT&Tag	20 μm	Spatial histone modification profiling via <i>in situ</i> CUT&Tag, microfluidic barcoding and sequencing	Mainly human, mouse fresh and frozen tissue sections	Similar to Spatial-CITE-seq; spatial information via microfluidics

表格1：空间组学技术（空间转录组+蛋白组+代谢组+表观组）为例，展示跨平台的对比与介绍（全表覆盖30+技术）。本页仅选取部分展示。



商用空间组学平台对比

Table 2 Horizontal comparison of commercial spatial omics platforms.

Commercial Technology	Resolution	Number of genes profiled	Chip Size	Species	Advantages	Disadvantages	Cell Segmentation
Slide-seq V2	10 μm	Whole transcriptome	3 mm diameter	Any species	High sensitivity	Diffusion effect, small capture area	Normal
Stereo-seq	0.22 μm	Whole transcriptome	10 mm × 10 mm	Any species	Large chip, high-resolution, capable of simultaneous microbial detection	Diffusion effect, requires fresh-frozen tissue	Normal
Visium HD	2 μm	Whole transcriptome	11 mm × 11 mm	Human & mouse only	High detection sensitivity and specificity	Diffusion effect, relatively low sequencing saturation	Normal
Visium V1	55 μm	Whole transcriptome	6.5 mm × 6.5 mm	Any species	Mature protocol, widely applied	Diffusion effect, low resolution	NA
Xenium	Subcellular	5001	10.45 mm × 22.45 mm	Human & mouse only	Extremely low FDR, stable performance on archived FFPE tissues,	Relatively high operational barrier, relatively high cost	Best

表格2： 横向对比主流商用空间组学技术平台， 评估指标包括分辨率、基因检测通量、芯片尺寸、适用物种、技术优势、局限性以及细胞分割效果。



空间组学的计算体系与分析流程

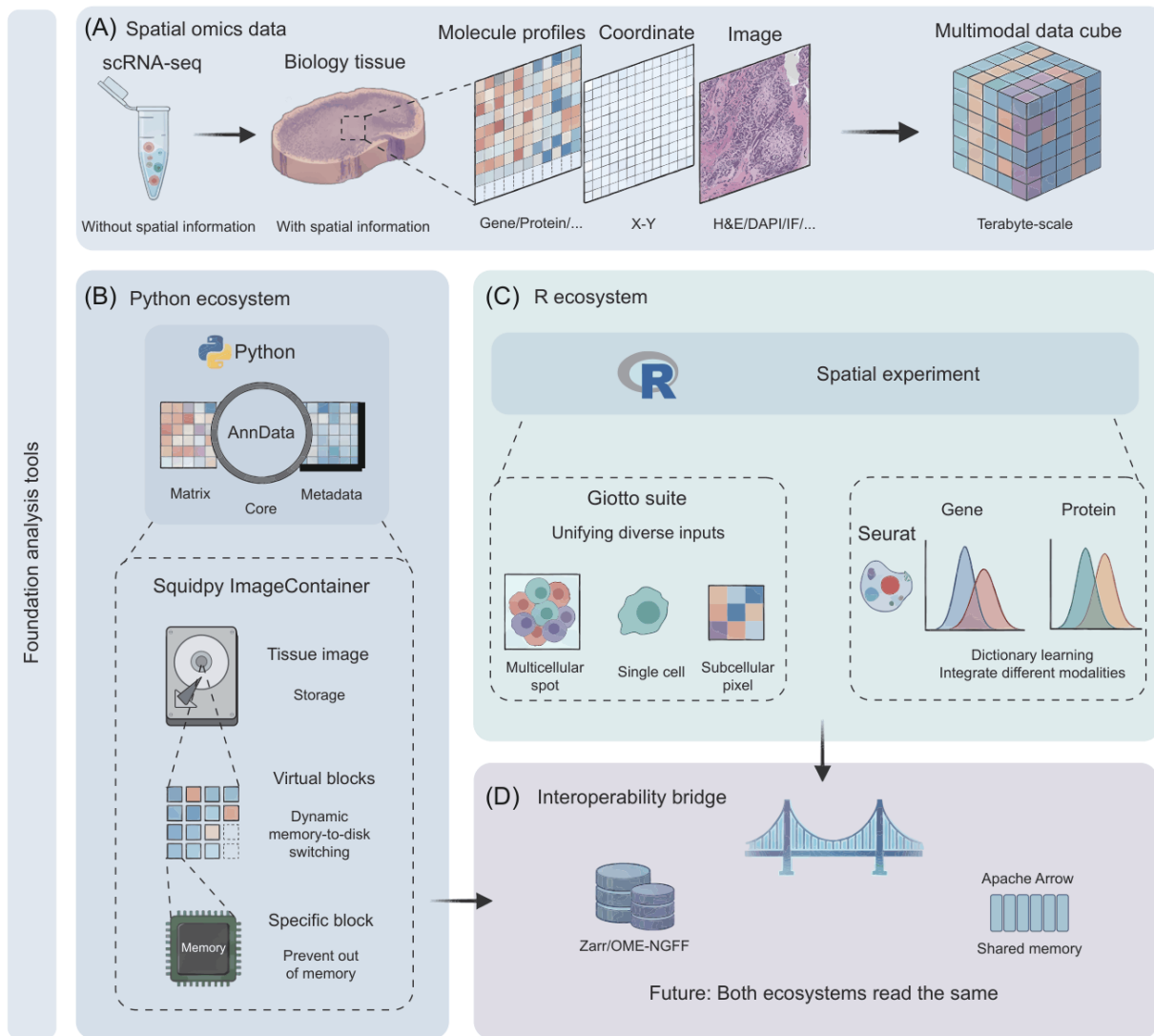


图2：空间组学的计算体系与分析流程

空间组学分别形成了以 AnnData、SpatialExperiment 为核心的 Python 和 R 计算体系，主流工具可完成数据整合、图像加载与多模态分析等工作。两类生态借助 Zarr、OME-NGFF、Apache Arrow 等通用格式，实现了跨语言的数据交互与兼容。



空间组学关键计算任务

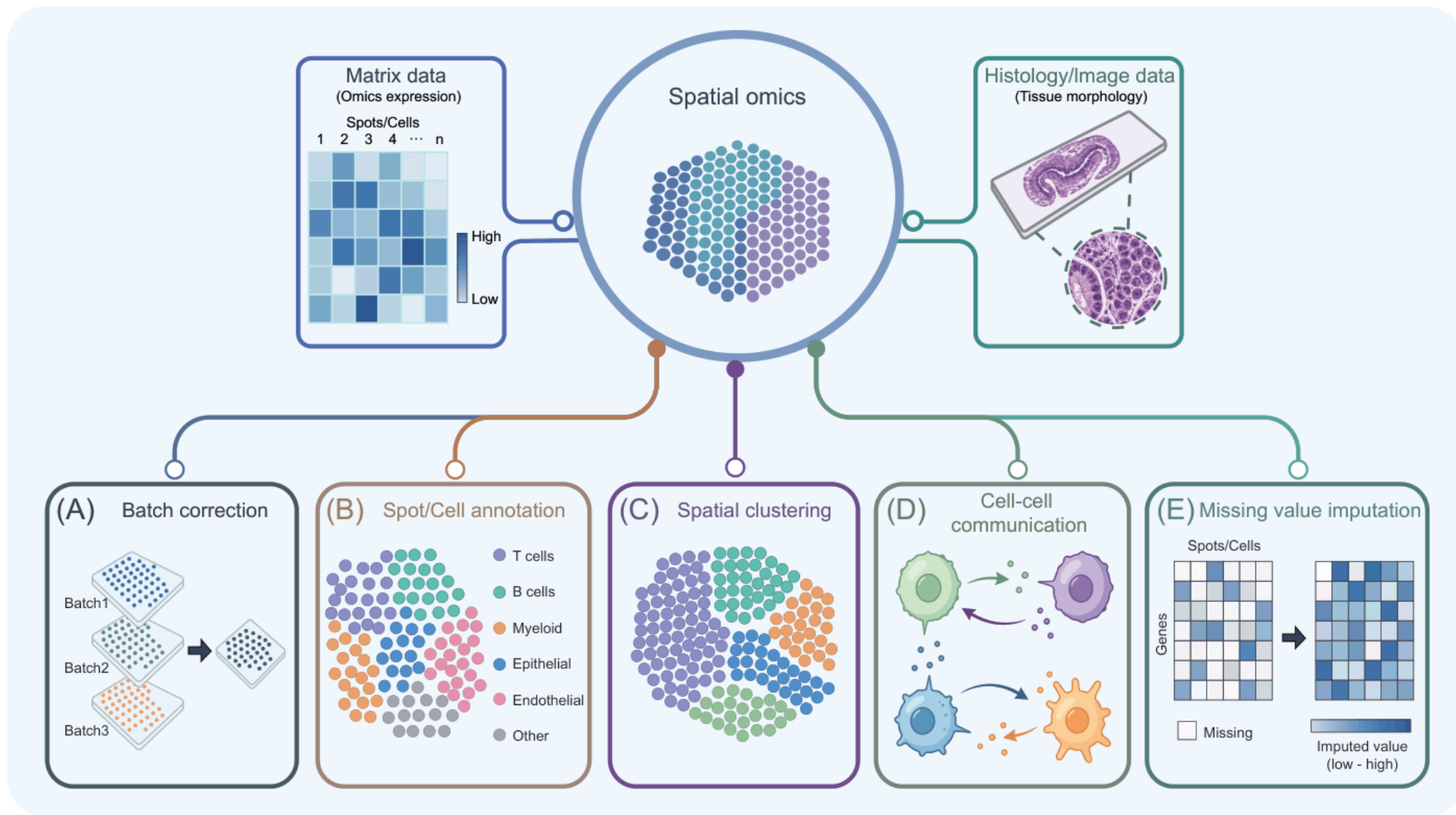


图3：空间组学领域的核心计算任务：(A) 批次校正 (B) 细胞注释（空间反卷积）(C) 聚类分析（空间区域识别）(D) 细胞间互作分析 (E) 空间组学数据插补



空间组学关键计算任务软件推荐

Table 3 Software recommendations for key computational tasks.

Task	Software	Language	Advantages
Clustering	BASS	R	Simultaneous clustering & spatial domain detection, adapts to high-sparsity data, reveals microenvironment-dependent states, strong versatility
	STAGATE	Python	Adaptive neighborhood similarity, balances denoising & spatial patterns, efficient computation, compatible with 10× Visium and large-scale data
	GraphST	Python	Superior boundary detection in brain/embryo tissues (top-ranked on 10× Visium). Unique batch effect correction. No predefined genes needed
Cell Annotation/Deconvolution	cell2location	Python	Integrates multi-batch/cross-platform data, accurately resolves cell composition in mixed spots
	RCTD	R	Multi-modes for high/low-resolution data, strong versatility
	Tangram	Python	Single-cell resolution reconstruction, compatible with multiple technologies, low memory, high speed
Batch correction	Harmony	R	Strong versatility, assists STAGATE/SEDR for batch calibration
	STAligner	Python	Same/cross-platform data integration, high alignment accuracy
	SpaCross	Python	Efficient multi-slice integration & batch correction
Cell communication	Cellchat	R	Fast speed, low memory, supports quantitative signal/pathway analysis, stable results
	stLearn	Python	Morphology-standardized expression data, identifies ligand-receptor interaction hotspots, excellent performance in brain/tumor data

表格3：空间组学领域的核心计算任务软件推荐。涵盖聚类，注释，批次矫正，细胞通讯，稀疏数据插补。本页仅展示部分推荐。



三维空间组学重构与虚拟细胞建模

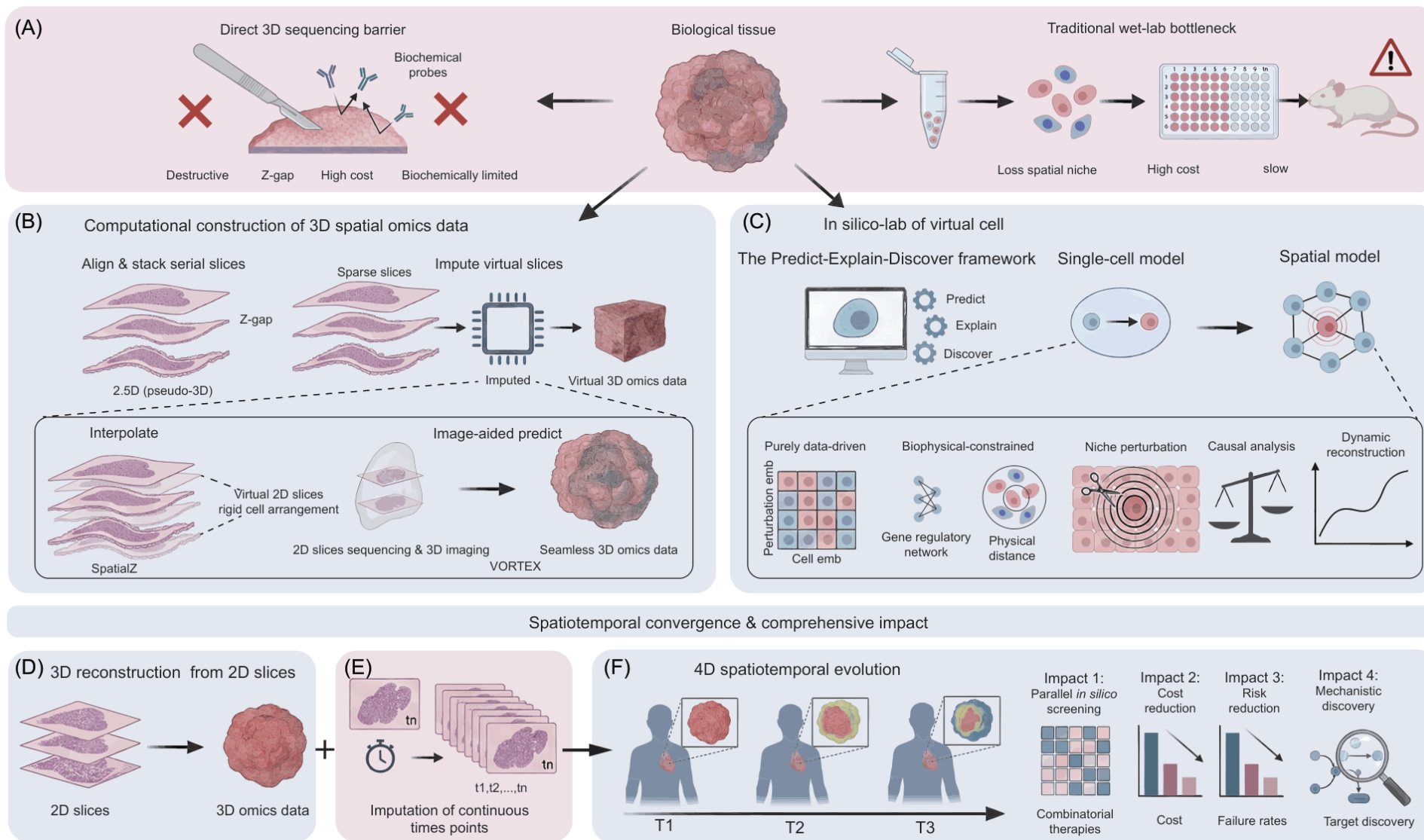
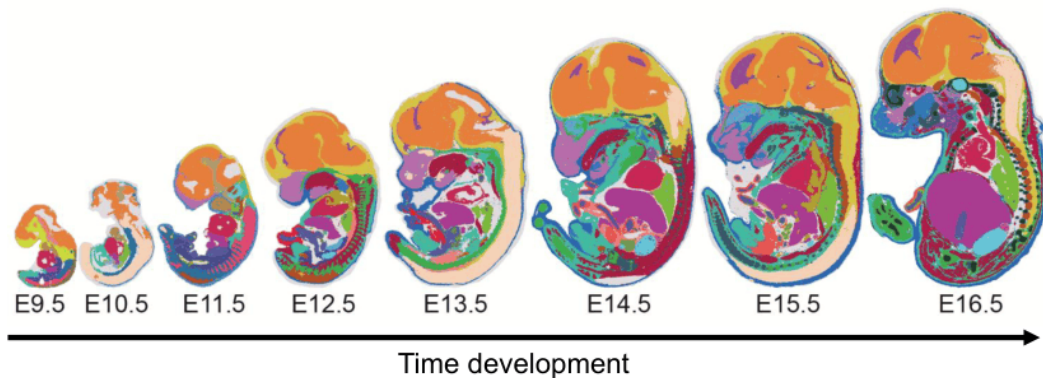


图4：三维空间组学重构与虚拟细胞建模

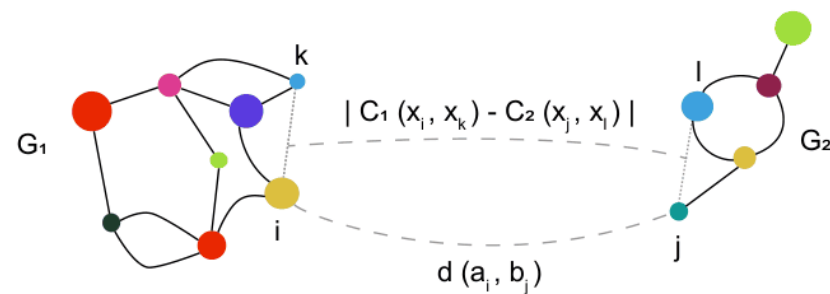


空间组学时序建模

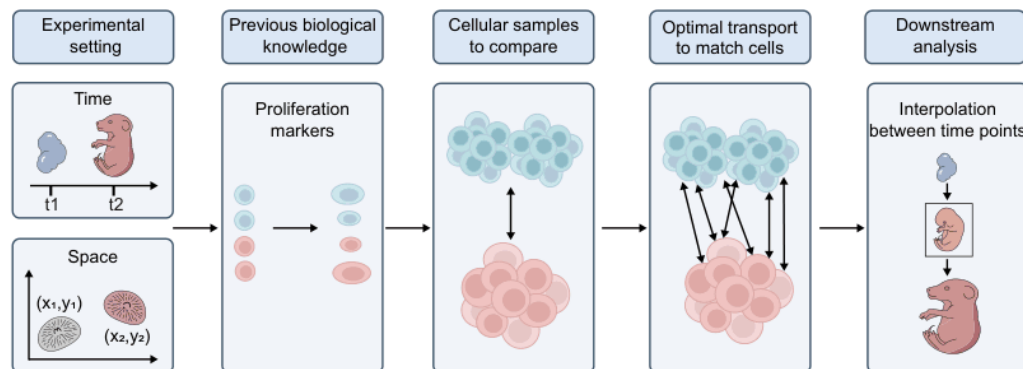
(A) The promise of temporal modeling



(B) Optimal transport



(C) Multi time point data modeling of growth and apoptosis phenomena (Moscot)



(D) Single spatial slice extrapolation of growth apoptosis dynamics (OSDR)

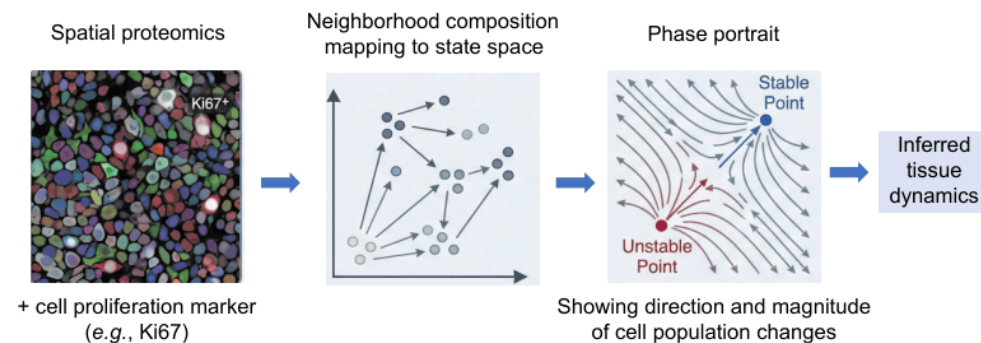


图5：空间组学时序建模前景与部分软件展示



多时间点空间组学数据比对核心算法横向对比

Table 4 Horizontal comparison of the core algorithms for multi-time-point spatial data alignment.

Method	Key assumptions	Where the method breaks down
Balanced OT	Mass conservation; total cell abundance/transcript count is unchanged over time	Fails when cell death, proliferation, or regional cell loss/gain occurs; cannot handle unbalanced tissues
Unbalanced OT	Allows mass creation/destruction; weak cost consistency; no strict mass balance	May over-interpret noise as true cell movement; unstable under extremely sparse/low-quality data
Registration-based alignment	Spatial structure continuity; smooth deformation field; no drastic tissue reshaping	Breaks under large morphological changes, tissue folding, cutting artifacts, or rapid structural remodeling
Trajectory-aware alignment	Temporal smoothness; cells follow continuous differentiation/transition paths	Fails for discontinuous cell state transitions, non-sequential time points, or non-directional spatial remodeling

表格4：多时间点空间组学数据比对核心算法横向对比

空间组学在医学研究的应用

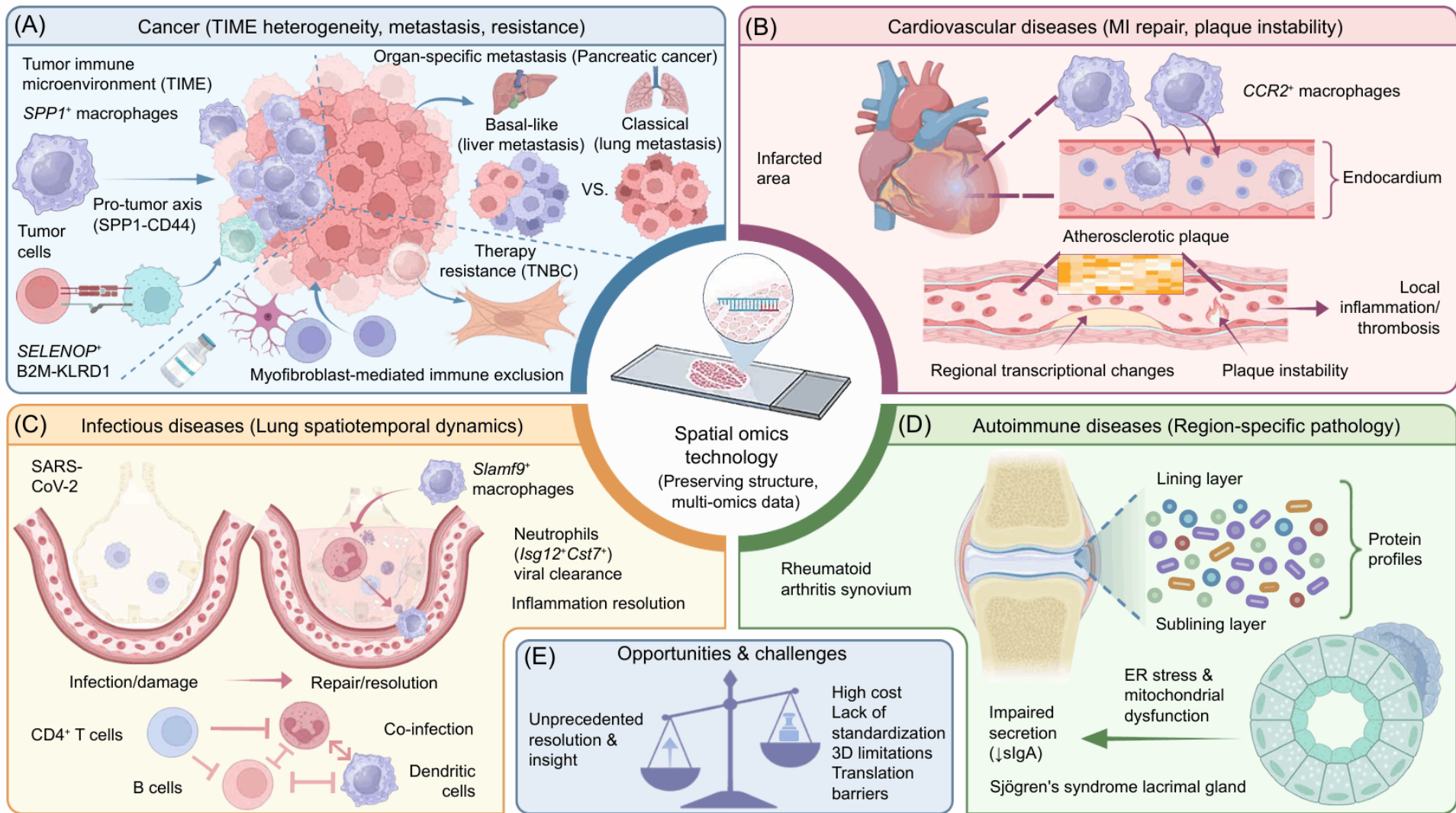
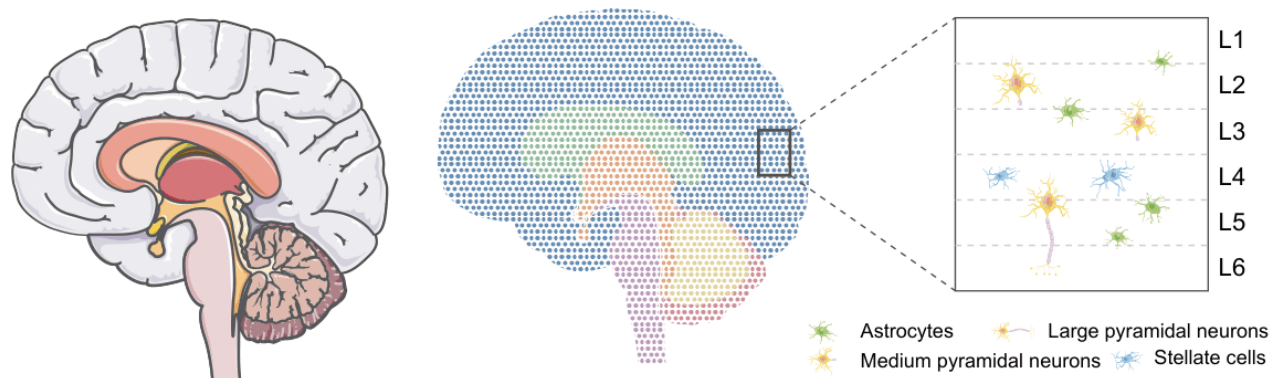


图6：空间组学在医学研究中的应用

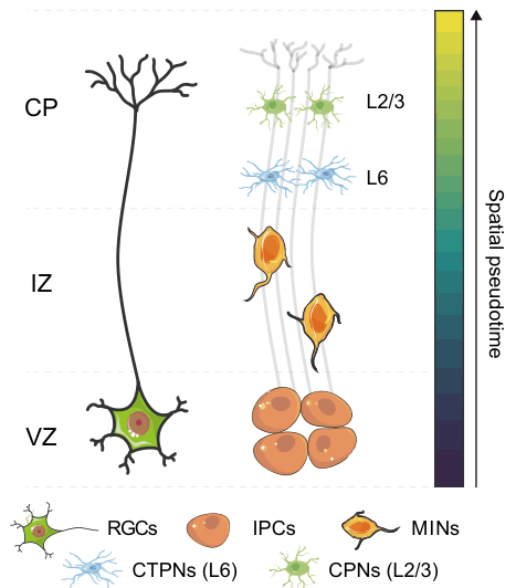


空间组学在神经科学领域的应用

(A) Molecular spatial architecture



(B) Spatiotemporal developmental trajectory



(C) Spatial motifs of pathological microenvironments

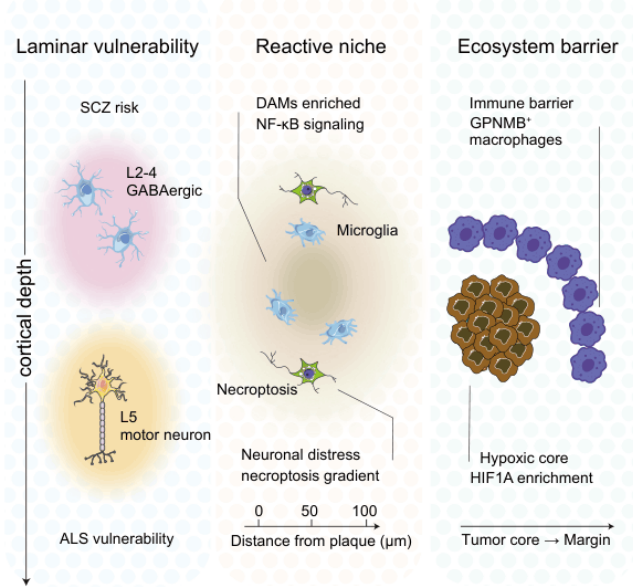


图7：空间组学在神经科学领域的应用展示与归纳



空间组学在动植物领域的应用

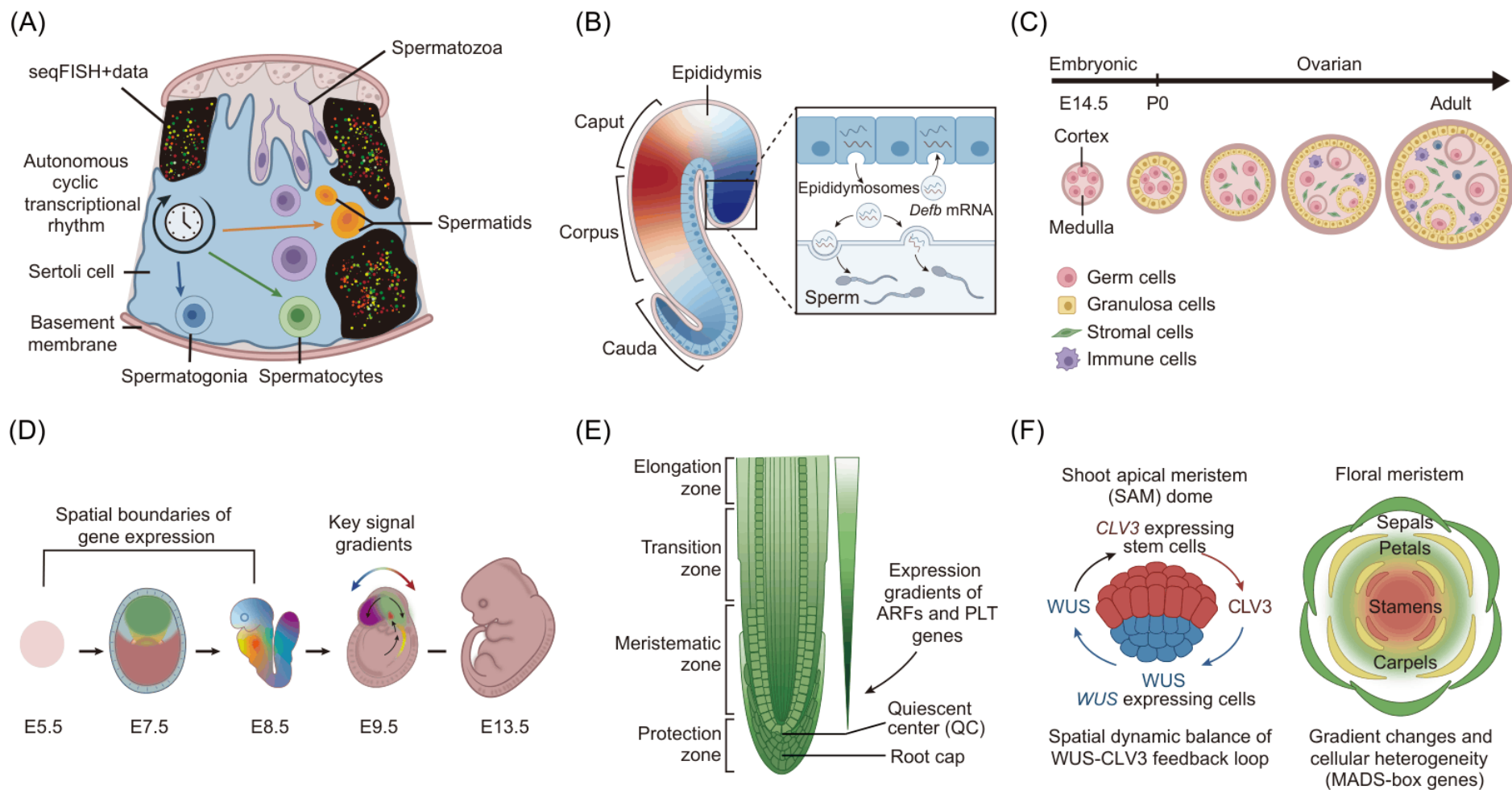


图8. 空间组学在动植物领域的部分应用展示



空间组学大型模型前瞻介绍

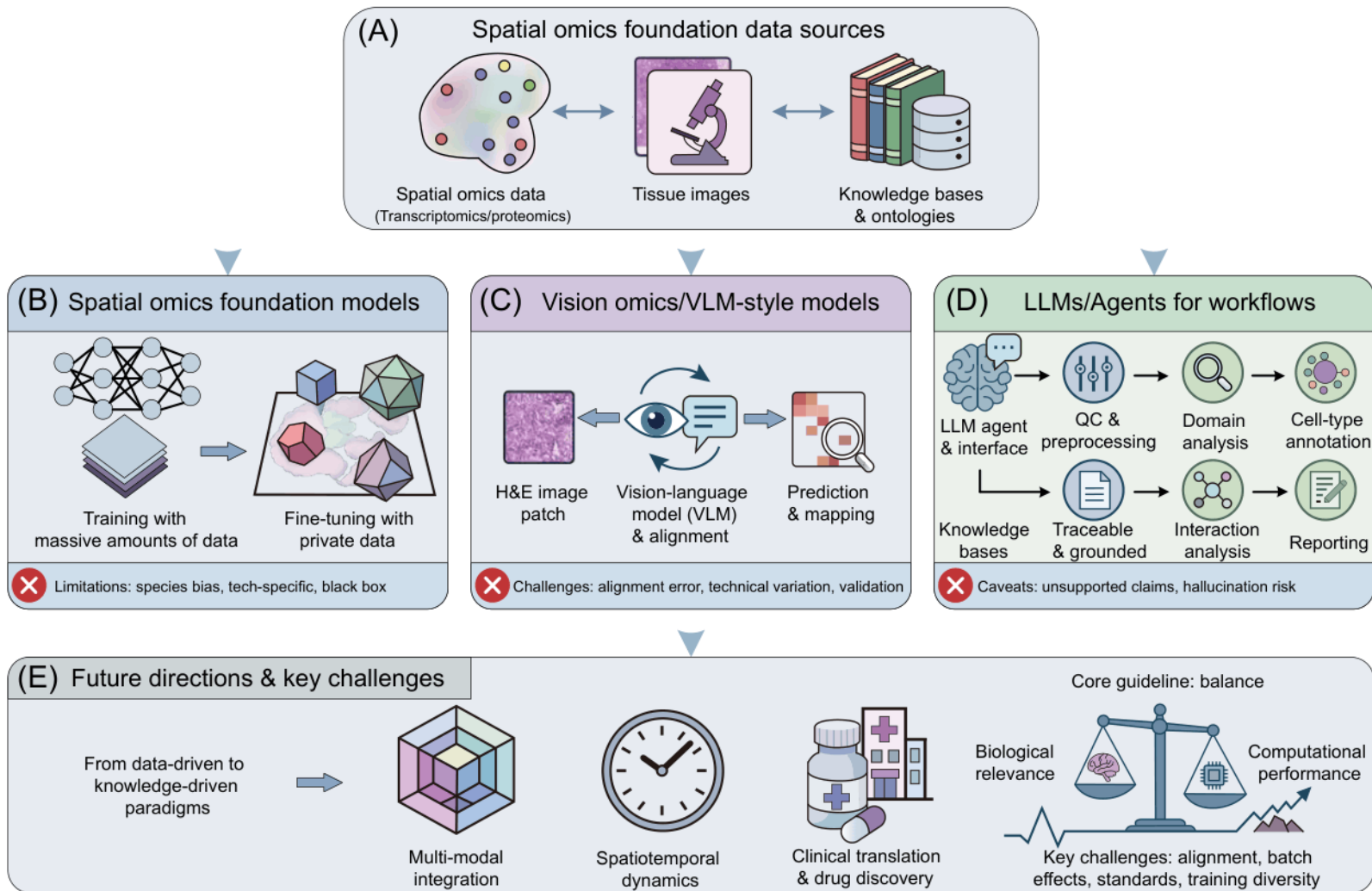


图9. 空间组学在大型模型领域的介绍与挑战



前沿方向软件推荐

Table 5 Software recommendations for cutting-edge research directions.

Task	Software	Language	Advantages
3D reconstruction	Spateo	Python	Embryo 3D molecular hologram, reveals multi-scale spatial biology, links morphogenesis & molecular dynamics, supports spatiotemporal quantification
	SpatialZ	Python	Supports virtual slicing/3D rendering/spatial query, cross-platform compatible, extensible to multi-omics
Temporal alignment	moscot	Python	Aligns multi-time-point spatial omics, supports > 500k cell datasets, incorporates growth/apoptosis gene prior knowledge
	DeST-OT	Python	Validated on axolotl data, models growth/apoptosis with triplet loss (no growth/apoptosis gene prior knowledge)
Dynamics reconstruction	OSDR	Python	Estimates division/clearance rates, maps neighborhood to state space, constructs phase portraits to identify stable/unstable points
	StVCR	Python	Addresses cross-time-point alignment difficulty/cell population imbalance, end-to-end reconstructs differentiation/migration/proliferation/apoptosis dynamics
Foundation models	Novae	Python	Removes batch effects, identifies spatial domains, supports multi-downstream analyses & multi-modal integration
	ScGPT-spatial	Python	Adapts to multi-downstream tasks: cell annotation, multi-batch/multi-omics integration, perturbation prediction, gene network inference, etc.
Vision-omics model	OmiCLIP	Python	Tissue registration/region annotation/cell deconvolution, retrieves transcriptomic data & predicts spatial expression profiles using only H&E sections
Expert agent	SpatialAgent	Python	An autonomous AI agent for spatial biology
	CellAgent	Python	LLM-driven multi-agent framework for automated scRNA-seq data analysis

表格5. 空间组学前沿方向软件推荐。

涵盖3D重建，时序建模，动力学分析，大模型，视觉组织模型，智能体多个方向



总结

- 本文我们基于空间组学全流程进行了系统性总结，便于入门者快速建立宏观认知。
- 与大多数空间组学综述论文不同，我们引入了3D重构，虚拟细胞，时序建模等前沿新颖领域，并展示了部分软件。
- 本文基于基准测试，算法原理出发，为不同计算任务提供了工具推荐，便于使用者选择合适方法。
- 从生物学应用出发，涵盖医学，神经科学，动植物领域展示了目前空间组学的应用案例。
- 基于目前的人工智能浪潮，我们系统性地针对空间组学大型模型作了归纳与总结

Haoxiu Wang, Xinwang Yang, Siheng Wang, Zhe Yang, Xiuhui Yang, Yutong Yang, Zirong Li, et al. 2026. Spatial omics in the AI era: Technologies, algorithmic ecosystems, biological applications, and large model perspectives. *iMeta* 5: e70146. <https://doi.org/10.1002/imt2.70146>

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iMetaOmics (宏组学)，定位IF>15对标**NC/SA**的生物/医学综合期刊，已被**ESCI**、**PubMed**等收录。

iMetaMed (宏医学)定位IF>15的医学综合期刊，欢迎投稿！



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