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1.

From Genome to Drug Targets: A Computational Pipeline for *Setaria digitata*

Bará Adi, Stockholm University / SciLifeLab
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Identifying drug targets in parasitic nematodes remains a challenge in early-stage drug discovery. This ongoing study presents a computational pipeline to rank proteins in Setaria digitata, a model nematode for Wuchereria bancrofti, enabling translational insights into filarial parasites

The framework integrates protein essentiality, orthology-based annotation, and subcellular localisation into a unified scoring system. Proteins were prioritised using a weighted composite score. Structural analysis was subsequently applied to top candidates, including 3D structure prediction and binding pocket identification to assess druggability and ligand accessibility

Top-ranked proteins demonstrated strong biological plausibility and literature support, further reinforced by structural validation. This integrated pipeline provides a reproducible and biologically informed strategy for prioritising high-confidence drug targets in parasitic systems, with the aim of informing therapeutic development

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2.

Nanoscale kidney tissue imaging and AI assisted diagnostic support

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This poster will highlight our developments in high-resolution microscopy for nanoscale molecular tissue imaging across scales (< 20 nm to cellular resolution) for kidney science. AI assisted image analysis moreover allows automatic quantification and stratification of renal diseases.

3.

A Cross-Species Single-Cell Atlas of Brain Injury and Regeneration

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Recent advances in technology and biology have expanded evidence for adult neurogenesis across several vertebrate groups, including birds, fish, amphibians and mammals. The field has progressed from discovery and acceptance to detailed efforts to uncover the underlying mechanisms driving production and integration of nascent neurons. However, the field still lacks landmark datasets with sufficient breadth and single-cell resolution. Thus, understanding neurogenesis remains one of the major challenges in modern neuroscience.

Here, I present a cross-species and cross-injury atlas for the comparison of conserved and divergent cellular programs activated within different injury contexts. I will consolidate publicly available and in-lab-generated single-cell datasets from adult vertebrates and analyse them in a shared comparative and evolutionary framework. I will systematically evaluate foundation-model families, including scGPT, protein language models and Geneformer on their ability to embed species into biologically meaningful representations, bridging the challenges posed by gene vocabulary mismatch across species. I aim to benchmark cross-species cell-type alignment, construct trajectory inference across injury time course and disentangle species-specific from conserved programs that form the core of effective repair. Finally, learning from strong regenerators, I will identify candidate gene regulatory networks and test their roles using modern multi-species adult neural stem cell culture systems.
My preliminary analysis reveals that foundation model transfer is feasible and that paralog-aware gene mapping via protein language model embeddings holds great potential. Scaling up these aligned representations across species highlights not only the current limits of single-cell biology but also lays the groundwork for concrete strategies to promote brain repair.

4.

Scaling Cell Biology with Smart Microscopy: Adaptive Workflows as a Service

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Microscopy is moving beyond automated acquisition toward adaptive experimental systems, where image analysis, computational models, and AI-agents influence what, where, and how data are acquired. This Smart Microscopy framework opens exciting possibilities for cell biology at scale: experiments become more selective, quantitative, and responsive to biological variability. However, the field faces an important transition. Many adaptive workflows remain tied to individual microscopes, software environments, or laboratories, making them difficult to reproduce, transfer, and operate as shared services.

Here, I will discuss smart microscopy from the perspective of a research infrastructure (RI). Rather than focusing on specific workflows, I will address what is needed to make adaptive imaging broadly accessible: orchestration layers that connect microscopes, analysis pipelines, data management systems, and decision-making agents in a transparent manner. A key future direction is interoperability with commercial microscope ecosystems. RIs rely on stable, vendor-supported instruments, so the goal should not be to rebuild microscope control software, but to develop abstraction layers that communicate with vendor software through documented interfaces.

A second major challenge is data representation. Smart microscopy generates multiple views of the same specimen across scales, modalities, coordinate systems, and processing states. To scale these approaches, the community needs frameworks linking raw data, derived data, spatial transformations, metadata, and experimental decisions. Emerging standards such as OME-Zarr, combined with S3-compatible storage for cloud computing and web-based viewers for collaborative data exploration, provide important building blocks. RIs are well positioned to move smart microscopy from isolated solutions toward reusable, service-oriented platforms for data-driven biology.

5.

Agentic-J: An All-Round AI Agent for Cell Biologists Analyzing Microscopy Images from Exploration to Publications

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In this presentation, we want to introduce Agentic-J, an all-round AI agent working with cell biologists on their microscopy images from exploration to publications. The letter “J” is to recognise the legendary ImageJ in our community, but Agentic-J is far more than “ImageJ + LLM”. Agentic-J lets biologists focus on biology.

Agentic-J is not published yet, and this is the first-time we would like to show this agent to the public and could even in the form of a live software demonstration to get feedbacks and ignite future discussions. In the spirit of the CB@S meeting, the presentation will be discussion-oriented, with special focus on what could be the future for AI agents related to microscopy images for cell biologists.

In general, the cell biology community has witnessed the potentials of AI agents from pilot efforts, such as Biomni and ClawBio, which are primarily designed for bioinformatic analysis, not yet optimized for microscopy image analysis, no matter for one example image, a handful of images, or high-throughput imaging experiments. To this end, in this presentation, we will first present our experience in building Agentic-J. Users can provide microscopy images (samples or a full dataset) and explain the analysis goal, the agent can navigate through available tools (or build something new if necessary), planning a few candidate workflows to choose or try, help at each step until the analysis goal is achieved.

There are many great potentials we observed during the development: (1) AI agent redefines interoperability, which is now all orchestrated by an LLM. Agentic-J uses ImageJ as the base visualization platform, accesses the extensive collection of ImageJ plugins, but could also communicate with Napari when necessary and call Python / R into play when it is needed. (2) AI agent could redefine the dissemination of community standards. Agentic-J integrates community standards in its own knowledge database, and can guide you through the analysis and make sure, e.g. statistical analysis or reporting analysis steps or making figures, everything conforming to community and publication standards. (3) AI agent paves a new path for training the younger generation of bioimage analysts: For a student who wants to learn a specific part of bioimage analysis or explore a particular plugin, the agent can guide them click-by-click, while explaining the underlying information and why it matters, turning every analysis into a learning opportunity.

Agentic-J is still far away from a mature product. We believe CB@S is a great opportunity to on one hand collect feedbacks from leaders in the cell biology community, and more importantly discuss what are the future directions for AI agent in the cell biology community. Some open questions we already have include, for example, how should we join the force in agent development to tackle multimodal multiscale cell biology research questions? What are best strategies for building AI agents that can take cell biologists’ domain knowledge into account? Should we already tell the agent a clear biomedical question or a clear analysis goal? Or should we also allow the agent to freely explore the multiscale multimodal data to discovery potential unknowns? There are alreayd some benchmarks for evaluating bioinformatic AI agents, but how can we fairly evaluate the pratical skills of microscopy image analysis AI agents? I believe there will be more questions from the meeting.

Link to Agentic-J: https://mmv-lab.github.io/Agentic-J/

6.

Exploring generative modeling for spatially resolved gene expression prediction

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Spatial transcriptomics offers a powerful opportunity to study how local tissue morphology relates to gene expression. We explore generative modeling approaches for predicting spot-level gene expression from hematoxylin and eosin image crops centered on spatial transcriptomics spots. Rather than treating this task purely as point-estimation regression, we investigate whether generative models can better represent uncertainty and biologically meaningful variation in morphology-conditioned expression profiles. Alongside model development, we examine how such predictions should be evaluated. Pearson correlation coefficient computed in log-transformed expression space is commonly used for this task, but prior work has raised concerns that high correlation does not necessarily imply faithful recovery of biological heterogeneity. We contribute to this discussion with quantified measurements of this behavior, including comparisons against mean-like prediction baselines, and use these observations to motivate discussion of alternative evaluation strategies for morphology-conditioned gene expression prediction.

7.

Interpreting Microscopy Images with Machine Learning

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8.

From Learning to Generating Representations: Constructing a Visual-based World Model for Virtual Cells at Meso-scale

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The construction of "virtual cells" is a frontier that spans all biological scales. However, at the cellular microscopy level, progress has lagged behind omics-driven approaches, primarily hampered by the high-dimensionality and low signal-to-noise ratio in optical imaging. Inspired by recent breakthroughs in vision-centric "World Models" in the general domain, we recognize a critical prerequisite for cellular simulation: robustly learning the underlying visual representation must precede pixel-level generation. Building upon our previous findings (NeurIPS 2025 spotlight), we demonstrate that task-driven visual representations—learned by explicitly overcoming complex physical degradations—exhibit generalization capabilities across diverse biomedical domains. Extending this philosophy, we propose the Cell World Model (CellWM). We curate Cell Mosaic, a methodology to aggregate different multiplexed fluorescence microscopy repositories into one large-scale dataset. Leveraging this, we train Cell JEPA (Joint-Embedding Predictive Architecture) via interleaved self-supervised tasks,

specifically focusing on multi-channel unmixing and modality restoration. By forcing the model to reconstruct the original multi-channel images, we wish to isolates the intrinsic spatial co-localization of organelles from stochastic sensor noise. Ultimately, these robust representation blueprints serve as priors for CellWM, which not only aims to predict the image after perturbations, but also remain functionality such as restoration, channel unmixing and mosaic integration/generation to support the reliability and practical usage of virtual perturbation.

9.

Morphological signatures of cancer dormancy revealed by single-cell imaging and machine learning

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Cancer dormancy is a critical yet poorly understood state that contributes to tumor recurrence and therapy resistance. However, identifying dormant cancer cells remains challenging due to the lack of robust, label-free approaches at single-cell resolution.
Here, we present an imaging-based computational framework to characterize and classify cellular states using quantitative morphological features. We first established and validated an in vitro breast cancer dormancy model. Leveraging single-cell imaging, we extracted high-dimensional morphological descriptors and applied dimensionality reduction techniques to visualize cellular heterogeneity. Dormant and proliferative cancer cells formed distinct clusters in low-dimensional space, indicating separable morphological signatures.
To systematically evaluate classification performance, we trained five machine learning models on extracted features, achieving over 90% accuracy on independent test datasets. Importantly, feature importance analysis revealed key morphological determinants associated with cellular dormancy, providing biological interpretability beyond black-box predictions.
Furthermore, we demonstrate the generalizability of our approach by distinguishing normal fibroblasts from cancer-associated fibroblasts (CAFs), as well as resolving cellular states under different culture conditions.
Together, our results establish a label-free, morphology-driven framework for identifying functional cellular states, offering a scalable strategy for studying cancer dormancy and microenvironmental heterogeneity.

10.

Integrating spatial multi-omics to reveal inflammatory and regulatory signalling niches in the lung

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Modern biology produces unprecedented multi-omic datasets: single-cell and spatial transcriptomics, epigenomics, proteomics, and lipidomics datasets are constantly released. Together these datasets can describe tissues at near-cellular, cellular and sub-cellular resolutions, and serve as well-annotated reference for functional studies. Today, most atlases focus on cell identities rather than how cells interact to maintain tissue homeostasis or drive pathology. Our study aims to integrate spatial transcriptomics and lipidomics to map and functionally decode intercellular communication in situ. Previously, we have created a human lung cell reference map based on three integrated spatial transcriptomics techniques. Current study provides additional spatial lipidomics layer to define and functionally characterise spatially organized signaling and inflammatory networks in healthy and diseased lungs. Distinct inflammatory and environmental niches, such as immune cell clusters in chronic obstructive pulmonary disease (COPD), and peri-epithelial parenchyma in asthma, locally reprogram neighbouring cells through altered signalling and metabolic pathways. These interactions can be quantitatively modelled using graph learning on multimodal spatial omics data, enabling prediction of signalling rewiring and identification of molecular drivers of tissue remodeling.

11.

Tunable Three-Photon-Activatable Cyclooctynes for Wavelength-Selective Labeling of Nascent RNA and Proteins in Cells

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Tunable fluorescent dyes have transformed the molecular life sciences by enabling multiplexed, wavelength-selective molecular readout across the visible spectrum, with applications spanning cellular imaging to high-throughput sequencing. Yet, analogous approaches for multiplexed optical writing in living cells remain limited. Here, we develop wavelength-selective photoactivatable cyclooctynes through dual tuning of the cyclooctyne scaffold. Methoxy substitution of the dibenzo backbone red-shifted absorption required for photocage decarbonylation, while backbone fusion modulated chemoselectivity, extending reactivity from azides to tetrazines. Coupling this chemistry with metabolic labeling enabled labeling of nascent RNA and proteins in cells. Proteins were labeled using spatially patterned one-photon UV activation with a digital micromirror device, whereas RNA labeling was achieved with micrometer-scale three-dimensional precision using three-photon excitation. Together, these results extend spectral multiplexing from molecular readout to molecular writing in living cells.

12.

SFUMATO — Bayesian probabilistic clustering for uncertainty-aware spatial transcriptomics

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In situ sequencing provides subcellular-resolution gene expression while preserving spatial context, enabling joint analysis of molecular profiles and tissue morphology. However, standard clustering partitions gene expression into discrete groups, imposing sharp boundaries that fail to capture biological continuity. We present a Bayesian probabilistic clustering framework for spatial transcriptomics that models continuous variation in either cell states or tissue organisation. The method operates directly at the transcript level, enabling segmentation-free cell typing and avoiding biases from nuclei detection.Uncertainty is encoded directly into color, with similarities in gene expression reflected by perceptual proximity, revealing gradual transitions and relationships between cell populations.Applied to Xenium data, our approach uncovers gradients and transitional zones that are obscured by hard clustering, providing an interpretable and flexible framework for spatial transcriptomics

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13.

Spatially Resolved Proteomics of Esophageal Tissue Heterogeneity

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Lifestyle exposures—such as alcohol, tobacco, and hot drinks— are known risk factors Esophageal Squamous Cell Carcinoma (ESCC), likely by driving the expansion of dormant mutant clones in normal tissue. However, the underlying mechanisms remain poorly understood.
We applied spatial proteomics on fresh-frozen samples to map epithelial, immune, and vascular features, focusing on markers of inflammation and fibrosis in non-cancerous esophageal tissues across populations with varying cancer incidence and exposure histories.
Our preliminary findings demonstrated a shift toward Keratin 16+ suprabasal phenotypes in high-risk tissues, indicating cellular stress. Furthermore, we observed localized niche changes, specifically an enrichment of CD8+ T cells and reduction in regulatory T cells in donors with tobacco and alcohol exposure.
Altogether, Spatial proteomics identifies distinct epithelial and immune signatures associated with ESCC risk factors. These findings could provide a molecular baseline for detecting early tissue remodeling and improving cancer prevention strategies.

14.

The Fourth Dimension: Probing Developmental and Evolutionary Time in Spatial Omics

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Cells exist not only in space, but also in time. While spatial omics technologies have revolutionized our ability to map molecular states within tissues, an equally important dimension remains harder to capture: the temporal history of cells. Development, differentiation, aging, regeneration, and evolution all unfold across multiple biological timescales, from minutes-long signaling events to developmental programs spanning entire lifetimes and evolutionary changes occurring over millions of years. Recent advances combining comparative spatial transcriptomics with cellular birthdating are beginning to bridge these scales, allowing researchers to reconstruct when cells are born, how they change, and how developmental trajectories evolve across species. Together, these approaches are transforming spatial biology into a truly four-dimensional view of life, where cellular identity is understood through its position, developmental history, and evolutionary context. As an example, we highlight recent technical innovations that enabled us to probe developmental time and infer evolutionary relationships between sensory neural circuits in vertebrates. Finally, we discuss the broader implications of time-resolved spatial analysis and argue for a new generation of spatial-omics approaches capable of integrating biological processes across temporal scales.

15.

Spatiotemporal proteomics for constructing virtual cell models

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The billion-year evolution of Earth’s first carbon-based cells contrasts sharply with the emerging prospect of engineering AI-driven virtual cells. I will talk about how to construct virtual cell models by learning the spatiotemporal dynamics of the proteome. Advances in mass spectrometry-based proteomics now enables high-throughput spatial mapping at subcellular resolution. Using tissue expansion, we preserve native architecture while achieving reproducible, quantitative protein profiling at the single-cell level. Perturbation proteomics further captures temporal dynamics by profiling proteome responses to genetic and chemical perturbations. Together, these spatiotemporal datasets, together with other multi-model and multi-omics data, allow AI models to predict previously unseen cellular states with high fidelity.

16.

Scaling up bioinformatics with Rust and hybrid-LLM-mediated refactoring

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Bioinformatics has progressed far over the past 20 years. From early days of scraping HTML using Perl, and writing aligners in pure C, there is now a broad ecosystem with easy-to-access tools. This rapid development has however come at a cost: It is increasingly difficult to manage compatibility between packages, and efforts like Conda struggle with the NP-complete nature of conflict resolution. Python and R are also dynamically typed, making the code slow, hard to validate, and are questionable choices for bringing bioinformatics to the clinic. They are also poorly designed in terms of multithreading, which is increasingly important for modern computing.

The emerging language Rust solves all these problems, removes need for Conda and containers, and also enables friction-free extension to web deployment. We show that static analysis combined with LLM enables easy translation of existing code, with potential of hundred-fold performance improvement for small file handling.

17.

An automated, live-cell, optical pooled screening platform

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18.

Methodology for Correlated Measurement of Hair Cell Calcium, Stereocilia Function, and Organelle Morphology in a Noise-Exposed Guinea Pig Model

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Acoustic overexposure causes hearing loss by damaging cochlear hair cells, but the underlying cellular mechanisms remain unclear. We focus on how overexposure affects intracellular calcium (Ca^{2+}) signalling, stereocilia function, and organelle structure. Hair cell Ca^{2+} dynamics and sound-evoked responses rely on stereocilia ion channels essential for mechanotransduction. We present a work-in-progress methodological pipeline for measurement of intracellular Ca^{2+}, stereocilia function, and organellar ultrastructure in cochlear hair cells from noise-exposed adult guinea pigs. The protocol begins with acoustic overexposure and functional assessment using auditory brainstem responses (ABR) and distortion product otoacoustic emissions (DPOAE). We then prepare a temporal bone preparation that preserves near in vivo conditions. Hair cells are loaded with Cal Red R525/650 to

image Ca^{2+} or ER-Tracker Green to visualize endoplasmic reticulum morphology. This setup enables simultaneous sound stimulation, cochlear microphonic recording, and live imaging. Stereocilia function is assessed via FM1-43 dye uptake, reflecting ion channel permeability. After imaging, samples are fixed and processed for expansion microscopy with pan-protein labelling to resolve organelles and stereocilia. This approach links single-cell physiology with ultrastructure, enabling investigation of early cellular changes driving noise-induced hearing loss.

19.

Electrical field stimulation modulates calcium oscillatory dynamics in pancreatic islets

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Pancreatic islets regulate blood glucose through a tightly coupled electro-metabolic cascade involving KATP channel closure, plasma membrane depolarisation, voltage-gated calcium influx, and insulin exocytosis. This intrinsic electrochemical activity makes islets compelling targets for both electrophysiological monitoring and electrical modulation. However, the mechanistic consequences of electrical field stimulation (EFS) on islet calcium dynamics remain poorly understood, and extracellular electrophysiology signals are difficult to interpret due to mixed contributions from different cell populations in intact islets.

We investigated the effect of EFS on pancreatic islets using fluorescence-based calcium monitoring via optical fiber with GCaMP3 and GCaMP6 mouse islets. EFS applied via non-contact chopstick electrodes resulted in dampened calcium oscillations during stimulation, followed by recovery at elevated peak amplitude post-EFS. This behaviour resembles the pharmacological effect of tolbutamide, a KATP channel blocker, suggesting EFS affects the depolarisation in insulin secretion pathway. In contrast, in-contact planar electrodes evoked fast oscillatory components during stimulation, followed by its elevated amplitude and frequency post-EFS, with recovery of synchronised fast calcium oscillations in older islets. To isolate beta cell-specific contributions, clonal MIN6m9 beta cells were cultured as 3D spheroids on poly-D-lysine/laminin-coated multielectrode array (MEA) and observed over one month. MEA recordings showed statistically significant increases in firing rate post-EFS at both Day 15 and Day 21, with gradual modulation across repeated stimulation cycles.

Taken together, the results demonstrate that EFS modulates islet activity in a geometry-dependent manner, producing distinct oscillatory responses. The observed transition between oscillation suppression, fast oscillatory component induction, and elevation of amplitude and frequency indicate that electrical stimulation in pancreatic islets and beta cells spheroid perturbs the underlying electro-metabolic dynamics. These highlight the need for interface designs optimised for slow, low-amplitude, and metabolically coupled signals from pancreatic microtissues or cells. Future work will focus on conformal bioelectronic interfaces with curved electrode geometries to improve cell-to-electrode coupling and enable cell-type-resolved functional interrogation toward in vivo translation.

20.

Morphological analysis of macrophage polarisation at single cell level

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21.

Same name, different cells: copy number drift as a hidden confounder in bulk multi-omics at scale

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Cell lines drift karyotypically across passages and laboratories, but bulk multi-omics studies of normal cells rarely check for it. We characterised Oli-neu, a mouse oligodendrocyte precursor used in 74+ publications over 30 years, and identified multi-Mb copy number amplifications on chromosomes 5 and 15, enriched for neuronal genes — the categories used to define this cell line's identity. Amplifications were confirmed by FISH and WGS and detected concordantly across Hi-C, RADICL-seq, ChIP-seq, ATAC-seq, and RNA-seq. Gene expression in amplified regions scales with copy number, indicating that apparent cell-type signatures are substantially dosage-driven. A second Oli-neu stock from an independent source lacks these amplifications, showing that cells distributed under the same name can differ between laboratories. We are developing CNATrace, a lightweight tool to detect CNAs from bulk DNA sequencing data, and invite discussion on how the field should audit karyotypic state at scale.

22.

Cells as Single-Molecule Protein Proximity Networks

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Cellular functions rely on dynamic protein interactions and spatial organization. Existing transcriptomic and proteomic single-cell profiling methods, based on abundance, lack the scale for high-resolution measurements of protein organization. We introduce the Proximity Network Assay (PNA), a DNA-based method for creating three-dimensional nanoscale maps of 155 plasma membrane proteins in single cells. PNA uses barcoded antibodies and in situ rolling circle amplification to generate >40,000 spatial nodes per cell, linked by gap-fill ligation and decoded via DNA sequencing, forming single-cell Proximity Networks. PNA measures abundance, self-clustering, and colocalization per single-cell, validating established interactions. This new modality offers a framework to discover novel spatial biomarkers, understand functional mechanisms, and advance translational studies in immunology, oncology, and cell therapy.

23.

Stitch-seq: A Facile and High-Throughput Perturbation Sequencing Method

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Large-scale pooled CRISPR screens are a powerful approach to identify genes that affect cell state and behavior. Viability and marker-based enrichment screens have already led to the discovery of countless genetic associations within cancer proliferation and drug resistance pathways. Incorporating high-complexity readouts, such as gene expression profiles, in pooled CRISPR screens will enable researchers to gain an even deeper understanding of cancer biology. However, the high cost of processing samples for single-cell transcriptome readout has hindered the applicability and scalability of such pooled gene expression screens. To address this limitation, we have developed Stitch-seq, a low-cost method for genome-wide screening of millions of cells with a gene expression and/or protein barcode readout. Our high-throughput droplet-based PCR method enables readout of the expression levels of 10-20 target mRNA transcripts or unlimited antibody oligo barcodes. Stitch-seq operates as a massively parallel single-cell emulsion RT-PCR that physically links CRISPR gRNA sequences to targeted sequences by overlap extension. The resulting library is sequenced, allowing Stitch-seq to detect expression effects in the mRNA/protein expression panel in the absence of a fitness effect or engineered activity reporter, making Stitch-seq generalizable to a wide range of biological systems.

24.

Building Foundational Subcellular Spatial Biology Data at Scale

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25.

From Sections to Structure: Contour-Based 3D Reconstruction of Clinical Spatial Transcriptomics

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Spatial transcriptomics has transformed our ability to map gene expression within tissue sections, yet the field remains fundamentally two-dimensional. Clinical specimens — particularly formalin-fixed paraffin-embedded (FFPE) blocks — are routinely sectioned serially, capturing rich molecular information across tissue depth that is currently discarded. We present a contour-based framework for reconstructing three-dimensional transcriptomic landscapes from serial spatial transcriptomics sections, with a specific focus on clinical compatibility.

Our approach leverages contours — extracted from molecular information acquired by in situ platforms such as 10x Genomics Xenium — as registration anchors to align consecutive sections in three-dimensional space. By propagating cell segmentation contours across the z-axis and integrating transcript-level information volumetrically, we generate spatially coherent 3D cell atlases that preserve both molecular identity and anatomical context. Critically, the method is designed to work with irregularly spaced clinical sections, partial tissue coverage, and the geometric distortions inherent to routine histopathological processing.

26.

Targeting Mitochondrial Reprogramming as a New Vulnerability in Lethal Prostate Cancer

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Background
Prostate cancer (PCa) remains one of the most frequently diagnosed malignancies in men. While international consensus recommendations such as National Comprehensive Cancer Network (NCCN) provides frameworks for risk stratification based on clinicopathological features, there is a critical need for molecular biomarkers that reflect the underlying biology of disease progression. Recent evidence suggests that mitochondria serve as central regulators of cellular metabolism and inflammatory signaling, with mitochondrial dysfunction directly implicated in PCa aggressiveness.

Objective
The aim of this study was to characterize mitochondrial reprogramming as a prognostic indicator for progression of PCa by identifying a biomarker signature of mitochondrial dysfunction through an integrated multi-omics machine learning framework.

Methods
We utilized a multi-omics dataset (n = 420) incorporating RNA-seq, Copy Number Variation (CNV), and DNA methylation data. A transcriptomics-based signature was initially developed using an Elastic-Net Cox model with 200 bootstrap resampling iterations to ensure stability. To enhance prognostic accuracy, Multi-Omics Factor Analysis was employed to integrate diverse molecular layers and identify latent factors associated with clinical outcomes. The resulting biomarker, BC-MitoAct, was normalized against normal prostate tissue.

Results
The study successfully identified the BC-MitoAct signature, which showed a significant correlation with NCCN risk categories; patients classified as High/Very High risk exhibited significantly elevated BC-MitoAct scores. In the test set, the signature effectively stratified patients into high- and low-risk groups for PFS ($p = 0.0042$). Multivariable Cox regression analysis confirmed that BC-MitoAct is an independent prognostic biomarker after adjusting for standard clinical variables such as PSA levels and Gleason score. Furthermore, MOFA identified specific latent factors (Factors 2 and 9) that drove survival stratification and revealed that elevated mitochondrial dysfunction correlates with pro-inflammatory signaling pathways.

Conclusions
Mitochondrial reprogramming is a critical driver of aggressive prostate cancer phenotypes. The integration of multi-omics data via machine learning significantly enhances prognostic precision beyond traditional clinicopathological characteristics. These findings suggest that targeting mitochondrial metabolic failure and the associated tumor immune microenvironment may offer a novel therapeutic vulnerability in lethal PCa. Future work will focus on validating this signature in metastatic cohorts and elucidating the specific molecular mechanisms through in vitro and in vivo studies.

27.

SciLifeLab OMERO: A Collaborative HPC-Enabled Platform for Data-Driven Bioimaging Research

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The data revolution in the life sciences increasingly relies on close integration with artificial intelligence (AI) to transform raw data into biological insight—particularly for image data. Processing and analysis pipelines require high-performance computing (HPC) resources to handle today's large file sizes and complex datasets. At the same time, human-in-the-loop workflows continue to depend on intuitive visualization and annotation tools that can scale effectively to large datasets. To meet these competing requirements, collaborative access to image data sets located close to computing resources is needed for all actors in today's interdisciplinary research projects, from data producers to methods developers. Our future service, SciLifeLab OMERO, will provide exactly this. Built on the globally recognized, open-source data management solution OMERO for visualizing, managing, and sharing biological microscopy images, SciLifeLab OMERO offers active data storage connected to HPC resources for collaborative research projects using biological image data.

28.

Decode-im: A high-throughput image processing pipeline for Optical Pooled Screens

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Optical pooled screens are a high-throughput application of functional genomics that enable several experimental inquiries, in the form of genetic perturbations, to be carried out in a single vessel. Common applications leverage CRISPR technologies to modulate gene expression of a wide selection of targets coupled with a fluorescent visual phenotype. Identities of CRISPR perturbations are also elucidated visually using sequence-by-synthesis chemistry. To successfully decode and analyze this data, a workflow that performs CRISPR barcode detection, aligns cells across rounds, and generates accessible single-cell crops is necessary. We present decode-im, a front-to-back pipeline that seamlessly integrates repeated fundamental data processing steps and supports customizable analysis tools. Uniquely, decode-im is able to align and stitch microscope fields of view across any-sized single well in reasonable time, reducing cell dropout for analysis. It can also decode and assign multiple barcodes to a single cell, providing the opportunity to assess combinatorial genomic perturbations in pooled screens. The pipeline is tunable to different experimental configurations, such as multiple microscopes, cytoplasmic vs. nuclear puncta for in situ sequencing, and live vs. fixed cell experiments. Finally, decode-im is also able to rapidly access single cells in high-volume datasets through a lazy-loading technique that leverages decode's high-quality cell alignment and memory-efficient data formatting, providing single-cell crops matched to a decoded perturbation. All together, decode-im provides a comprehensive workflow for the span of optical pooled experiments that can be performed, elevating the analysis of high-throughput image-based genomic screens.

29.

Live-cell transcriptomics with engineered virus-like particles

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The dynamic regulation of gene expression is integral to the function of cells in development, homeostasis, stress response, and disease. Unbiased gene expression profiling via high-throughput RNA sequencing (RNA-seq) has become a cornerstone of modern biomedical science, yet existing approaches lyse cells and preclude direct analysis of transcriptional dynamics in the same sample over time. We addressed this limitation by engineering mammalian cells to “self-report” their transcriptional states via the export of cellular RNA molecules in virus-like particles (VLPs). Repeated sampling of culture media from VLP-producing cells faithfully captured evolving transcriptional states in complex biological settings, including acute inflammatory stimulation of primary cell spheroids and multi-day differentiation of pluripotent stem cells. VLP engineering with surface-displayed epitope tags enabled multiplexed transcriptional readouts from distinct cell-types in co-culture. Fusion of RNA binding domains to Gag tuned the repertoire of cellular RNAs packaged in VLPs or directed export of sgRNA transcripts for live-cell functional genomics screens. Finally, we demonstrated the unique utility of self-reporting for selective longitudinal tracking of endothelial cell dynamics within the enclosed architecture of a microphysiological co-culture system. Live-cell transcriptomics with self-reporting enabled a repeated-measures experimental design, which translated to enhanced statistical power to detect temporally dynamic genes and a significant reduction in resource requirements. We identified temporal gene programs underlying endothelial vasculogenesis, including divergent logic involving cellular metabolism and vascular maturation in response to different perivascular stroma. Altogether, this work establishes a broadly enabling technology for live-cell transcriptome-wide profiling to characterize cell state dynamics over time.

30.

Mechanistic AI models of cancer cells predict transcriptional effects of genetic alterations

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Cancer arises from complex interactions between mutations, copy number alterations, the cell type of origin, and the micro-environmental context, complicating causal inference and prediction of therapeutic responses. We address this using mechanistic AI: deep learning models constrained by molecular interaction networks.

We present a framework modeling how genetic alterations shape cancer cell states. It integrates ~60,000 interactions across ~15,000 biomolecules, capturing feedback within and between signaling and gene regulation. Perturbations are mapped to molecular targets, and their effects propagate through the network to predict transcriptomic responses. The system is implemented as a recurrent neural network that iteratively updates molecular states until stable attractors emerge.
The framework predicts gene expression in unseen cell lines, infers unmeasured molecules across time, and generates hypotheses on non-canonical signaling pathways.

31.

From State to Function: Dynamic Cell Biology in Physiological Context

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Cell biology is entering a predictive era, where large-scale molecular profiling and machine learning aim to infer cellular behavior across biological contexts. Efforts such as SciLifeLab's Alpha Cell are at the forefront of developing integrative models of cellular function and increasingly emphasize the need for experimental frameworks that connect molecular state to functional behavior in living systems. Often, cells are described through snapshot-based representations, while the underlying molecular interactions are dynamic and continuously changing; this dynamic activity contributes to function across molecular, cellular, and physiological scales.
From an experimental perspective, this reveals a structural gap between scalable molecular measurements and cellular behavior in living systems. Addressing this gap requires experimental modalities that directly capture molecular interactions and dynamic cellular behavior in vivo. At the Intravital Microscopy Facility at Stockholm University (IVMSU), fluorescence lifetime imaging microscopy (FLIM), including FRET- and environment-sensitive approaches, enables quantitative and functional readouts of protein interactions, signaling activity, and metabolic states in space and time. A key strength of this approach is its ability to span experimental systems across a continuum of physiological relevance, from in vitro and organotypic models to ex vivo human material and in vivo or humanized models, enabling functional interrogation under controlled perturbation and longitudinal observation. In this context, dynamic, in vivo readouts provide a functional layer needed to ground and validate predictive models of cell biology.

32.

Developmental regulation of alternative splicing across human and non-human primate tissues

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Alternative splicing is a major driver of transcriptomic diversity and is dynamically regulated across tissues and developmental stages. While adult splicing landscapes have been extensively characterized, the developmental trajectory of splicing regulation in humans and its evolutionary conservation across primates remains incompletely understood. Moreover, adult-derived transcript metrics such as proportion expressed across transcripts (pext), widely used for clinical variant interpretation, are limited in their ability to capture early developmental isoform usage.

Here, we leveraged the developmental Genotype-Tissue Expression (dGTEx) resource together with age-matched macaque and marmoset datasets (NHP-dGTEx), including prenatal stages, to characterize developmental splicing programs across humans and non-human primates.

Using splice junction-based cluster modeling across human tissues, we identified hundreds of age-differentially spliced genes (DSGs) per tissue, with the most striking changes observed in testis and muscle. While some of the apparent splicing events can be explained by alternative transcription start site usage, many lead to differences in the expressed coding DNA sequence of protein-coding genes. DSGs are enriched in tissue-relevant biological pathways, such as muscle contraction-related pathways in muscle and small intestine, and are generally overrepresented among genetically

constrained genes, highlighting the functional and evolutionary importance of developmental splicing programs.

Orthogonal analyses of transcript isoform usage revealed coordinated isoform redistribution across developmental timepoints. These changes are concordant with shifts in exon-level expression (pext). Analysis of millions of clinically relevant sites (ClinVar variants) using pext revealed significant differences between dGTEx-derived and adult GTEx pext values, underscoring the importance of developmental context for variant interpretation. Cross-species comparisons further demonstrated that many developmental splicing patterns identified in humans are conserved in macaques and marmosets, while also revealing lineage-specific regulatory events.

Together, these results establish a cross-species framework for understanding developmental isoform regulation and its evolutionary dynamics across humans and non-human primates.

33.

Nervoid: A Cell-Agnostic AI Platform for Inferring Functional Cellular States from Microscopy Images at Scale

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Advances in high-content imaging and automated microscopy have enabled large-scale generation of cellular images across diverse perturbations, cell types, and experimental conditions. However, extracting biologically meaningful functional insights from these datasets remains a major bottleneck, often requiring costly multi-omics assays, extensive labeling strategies, or cell-type-specific model development. Here, we present Nervoid, a cell-agnostic AI platform that directly infers cellular state, gene expression programs, signaling pathway activity, and toxicity-associated phenotypes from microscopy images at scale.
Nervoid integrates deep learning–based feature extraction, morphological embedding generation, and latent-space mapping to connect image-derived cellular phenotypes with curated multimodal biological datasets. The platform is designed to operate across diverse imaging modalities, including fluorescence and brightfield microscopy, and across multiple cellular systems including 2D cultures, primary cells, and 3D organoids. By training on large-scale perturbation datasets spanning CRISPR knockouts, drug libraries, and gene overexpression experiments, Nervoid learns generalized morphology-to-function relationships that enable prediction on previously unseen perturbations and cell states.
We demonstrate the ability of Nervoid to distinguish chemical exposure signatures, infer pathway-level perturbations directly from morphology, and identify functionally related cellular neighborhoods in latent space. In addition, the platform enables scalable analysis of heterogeneous organoid systems by identifying distinct cell populations and predicting associated biological programs from label-free imaging data.
By transforming microscopy images into functional biological insight without requiring destructive downstream assays, Nervoid provides a scalable framework for accelerating drug discovery, toxicity screening, and automated cell culture workflows. This work highlights the potential of foundation AI models trained on cellular morphology to serve as a universal interface between imaging and systems-level cell biology.

34.

Beyond Dropout/Enrichment: Unlocking Advanced Phenotypic Profiling in Pooled CRISPR Screens

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Traditional pooled CRISPR screens are based on guide dropout/guide enrichment in selected cell populations and are thus limited to simple, sortable phenotypes. Single-cell approaches such as Perturb-Seq and CROP-Seq link CRISPR perturbations to transcriptional profiling, capturing complex cellular states, but are expensive, poorly scalable and do not preserve spatial context. Optical Pooled Screening (OPS) and Spatial Omics Pooled Screening (SOPS) combine pooled CRISPR perturbations with high-content imaging, spatial transcriptomics or proteomics. These methods map genetic perturbations to complex morphological phenotypes, preserve spatial information, and enable functional studies. OPS and SOPS bridge the gap between genetic perturbation and rich, spatially resolved phenotypic readouts, to greatly expand the scope of functional genomic discovery. The SciLifeLab CRISPR Functional Genomic- and In Situ Sequencing units are currently establishing these methods and expect to role those out as a service during 2027.

35.

How to achieve high throughput and correlative biophysical, physiological and multiomic data

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We see a boom of omics tools, however correlative physiological measurements at scale are still missing. We develop technologies for high throughput and correlative measurements of physiological, biophysical and multiomic data in spatial and temporal manner.

36.

BioImage Informatics at SciLifeLab Sweden: Enabling life science discovery through advanced image analysis

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The BioImage Informatics unit (BIIF) develops new computational technologies and provides access to expertise and state-of-the art software for processing and quantitative analysis of all kinds of microscopy image data, primarily for applications in the life sciences. BIIF is a SciLifelab unit, and part of the National Bioinformatics Infrastructure Sweden NBIS. We are active within the GloBIAS and EuroBioImaging networks. We offer - i) advice on best-practice and guidance on overall experimental design for research involving microscopy imaging and quantitative data analysis, ii) guidance on image analysis assay development, including image processing algorithm development and software

engineering to address challenging project goal, iii) advice on best-practice and guidance on high throughput/large-scale image processing using computing clusters, including data transfer and storage during the activity of the project, iv) guidance on large-scale data analysis and visualization and dissemination of bioimage analysis knowledge in courses and workshops.

As a part of the image analysis unit, few of our current projects are in the lines of,
Integration of multimodal data from spatial proteomics, metabolomics (mass spectrometry imaging) and spatial transcriptomics (xenium, visium)
Development of AI-based computational pipeline for segmenting an ecotoxicological test species to understand the toxicological effects of the tested environmental samples or industrial chemicals
Implementation of LLM- accelerated automated text extraction from handwritten microscopy slides
High content screening of chromatin organization in live cells
Development of a scalable 3D screening platform using volumetric U-Nets for analysing human motor neuron disease (MND) models using high-content microscopy

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37.

Dynamics of molecules at nanoscale

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Monitoring the proteins and lipids that orchestrate cellular processes demands imaging approaches with both high spatial precision and rapid temporal responsiveness. Reversibly switchable fluorescence nanoscopy, including STED and RESOLFT microscopy, offers high-resolution imaging in living systems but remains constrained by trade-offs between speed, phototoxicity, and field of view. Here, we introduce an event-driven, intelligent imaging framework that integrates biosensor feedback with deep learning–based detection to adaptively control multiscale acquisition. Upon identifying cellular events—such as protein recruitment, vesicle trafficking, or second messenger activity—our system autonomously triggers targeted 2D and 3D STED imaging in regions of interest. Capturing the dynamics of neuronal proteins with smart nanoscopy
This strategy maximizes temporal resolution while minimizing light exposure, enabling sustained nanoscale imaging in live cells. We capture synaptic vesicle dynamics, membrane trafficking events, and organelle interactions with sub-diffraction spatial resolution and millisecond-scale responsiveness following event onset.
Event-driven STED and RESOLFT microscopy, augmented by deep learning, extends the capabilities of smart imaging systems by coupling measurement to biological context in real time. This approach opens new avenues for observing transient nanoscale phenomena and supports the development of autonomous microscopes for discovery-driven cell biology.

38.

Functional PD-1/PD-L1 engagement defines a spatial biomarker of immunotherapy response

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Predictive biomarkers for immune checkpoint inhibitor (ICI) therapy remain a major unmet need across solid tumors. Here, we present an integrated spatial proteomics workflow that combines in situ proximity ligation assay with multiplex immunofluorescence to directly detect PD-1/PD-L1 signaling events within defined cellular phenotypes and their spatial context in intact tumor tissue. In a proof-of-concept study of metastatic urothelial carcinoma treated with pembrolizumab, PD-1/PD-L1 interactions involving cytotoxic $CD8^+$ T cells were enriched in complete responders but rare in progressive disease. This interaction-defined T-cell subset outperformed PD-L1 expression and immune cell abundance alone in discriminating clinical response. The workflow provides a spatially resolved, mechanistically informed biomarker framework with potential to support immunotherapy prediction across tumor types.

39.

MINFLUX – SRS – TPE FLIM imaging of bacteria and their targeted host cells

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Since its inception, MINFLUX has rapidly delivered unprecedented tracking and imaging capabilities with nanometre precision. It has been employed to visualize the motion of kinesin in live cells, monitor protein transport through nuclear pore complexes, and resolve the protein distributions at the nanoscale. While imaging individual protein distributions provides essential molecular context, integrating additional imaging modalities enables more holistic insights into cellular environments and metabolic activity.
In this work, we integrated a MINFLUX prototype with a novel Stimulated Raman Scattering (SRS) laser capable of switching between femtosecond (fs) and picosecond (ps) operation within minutes. This flexibility enabled SRS imaging alongside autofluorescence imaging of metabolic cofactors such as NADH and FAD via two-photon excitation (TPE). Furthermore, a time-correlated single-photon counting (TCSPC) system was incorporated to facilitate fluorescence lifetime imaging microscopy (FLIM) under TPE conditions. Using this multimodal setup, we acquired SRS and TPE-FLIM images of both bacterial and host cells, complemented by high-precision MINFLUX imaging within selected regions of interest. These proof-of-concept measurements lay the groundwork for future studies on bacterial infection and host-cell interactions.

40.

Coordinated multi-cellular responses to Alzheimer's disease pathology

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Alzheimer’s disease (AD) involves multifaceted cellular changes that vary across cell types, though these changes are often considered independently from one another. Here, we consider the interaction of these cell-type effects in AD.
We analysed single-nuclei transcriptomics from dorsolateral prefrontal cortex (427 donors, ROSMAP). Cells were aggregated into metacells and genes into cell-type-specific modules. Linear mixed-effects models were applied across training and validation datasets to identify modules reproducibly associated with AD-related neuropathological phenotypes, resulting in 24 robust AD-associated gene modules (AGMs) in inhibitory, excitatory neurons and glial cells such as astrocytes, microglia, and OPCs. These AGMs were then analysed using partial least squares regression (PLS), pseudoprogression analysis, cell-cell communication (CCC) inference, and external replication in the SEA-AD cohort. We also systematically examined preprocessing parameter combinations that enhance models generalizability.
The PLS model identified two major axes of transcriptomic variation. The first axis was strongly associated with global AD pathology, while the second captured sex-associated variation in AGM expression. Pseudoprogression modeling revealed two broad trajectories of coordinated transcriptional change, suggesting simultaneous upregulation and downregulation of gene modules across multiple different brain cell types. CCC analysis further implicated AGMs in intercellular signalling networks between aforementioned cell types. Additional replication of the findings in the external SEA-AD cohort revealed that the PLS model signals were replicable and consistent across both datasets.
These findings suggest that AD does not act on isolated cell types, rather cellular responses to AD occur in concert rather than independently. Additionally, several AD-associated cellular responses showed clear sex differences.

41.

Cell Niche discovery via taxonomy-aware spatial association rule mining

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Understanding the spatial organisation of cells within tissues is fundamental for cell niches discovery. Advances in spatial omics technologies now yield high-resolution maps of cell populations across tissue sections, yet computational methods for systematically discovering recurrent, interpretable multi-cell assemblies remain limited, particularly when cell type annotations are organised in hierarchical taxonomies.

Cell type ontologies in modern atlases naturally form hierarchies, ignoring this structure leads to either redundant or missed niche patterns. We present our on-going work for cell niche discovery based on spatial association rule mining that is explicitly aware of these hierarchical relationships. By propagating colocation evidence through the taxonomy, we are able to identify multi-cell-type assemblies that co-occur significantly across tissue regions at both fine-grained and coarser levels of cell-type resolution, reducing redundancy while improving interpretability.

42.

Mapping drug-induced spatial reorganization in cancer-fibroblast co-cultures using cell-cell interaction graphs

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High-content imaging has become a powerful approach for profiling drug-induced phenotypic changes, yet conventional single-cell morphological profiling often treats cells as isolated units. In multicellular co-culture systems, this can overlook an important dimension of drug response like the reorganization of spatial relationships between interacting cell populations. Here, we construct Voronoi/Delaunay-based cell-cell interaction graphs from nuclei coordinates extracted from CellProfiler outputs to capture multicellular organization in cancer and fibroblast co-cultures across multiple drug classes tested at five different concentrations. We use these graph representations to evaluate whether local interaction patterns can recover broad phenotypic responses to drug perturbation. Treated wells are assigned to nine phenotypic categories describing cancer and fibroblast drug responses, including cell killing, morphological change, and unaffected conditions, based on CellProfiler-derived morphology and viability measurements. For each category, we generate representative interaction networks and extract network-level features describing viability, cell-type interaction composition, spatial organization, and community structure. We then compare network features from treated wells with control baselines to quantify how each perturbation alters multicellular organization. In parallel, we examine the distribution of feature changes across control and treated wells to determine whether phenotypic categories show reproducible spatial signatures. Preliminary results indicate that Voronoi-based interaction networks capture consistent patterns associated with broad drug-response classes. These findings suggest that cell–cell interaction graphs could help provide better understanding of how drug perturbations reshape tumor-microenvironment organization, revealing multicellular response patterns and interaction-driven effects that may improve the interpretation of drug mechanisms and support future cancer drug discovery efforts.

43.

AgentLens: An Agent-Mediated Operating Layer for Adaptive Microscopy Experiments

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Cell biology is increasingly limited not by image acquisition itself, but by fragmentation across planning, instrument control, analysis, and decision-making. We are developing AgentLens, an agent-mediated smart microscopy framework in which a general-purpose coding agent serves as a natural-language operating layer for end-to-end experiments. AgentLens supports closed-loop workflows linking experimental intent to hardware control, adaptive imaging, analysis, and reporting. In U2OS FUCCI demonstrations, the system supported adaptive plate-state triage, scheduled live-cell drug-response imaging, critical-path prioritization under live-cell constraints, and agent-guided choice of the most informative readout, using literature-informed reasoning with user approval to choose between fluorescence and morphology analysis. We are now extending the framework toward observe-decide-execute perturbation loops and more adaptive cell biology, including iterative experiments for reversible arrest.

44.

Embryonic cell state transitions define cell plasticity in paraganglioma and neuroblastoma

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Intratumor heterogeneity and cellular plasticity contribute to therapy resistance in neuroblastoma. Here, we show that combined loss of KIF1Bβ and NF1 in the mouse sympatho-adrenal lineage drives the formation of pheochromocytoma, neuroblastoma, and composite tumors. Using single-cell RNA sequencing, immunofluorescence, and RNAscope, we identify chromaffin-to-neuroblast cell state transitions during embryonic and postnatal stages that underlie tumor plasticity and invasion. Spatial transcriptomics and in situ sequencing reveal tumor heterogeneity and localize transitional regions. Integration with human PPGL datasets shows embryonic-like states enriched in metastatic tumors, highlighting clinically relevant lineage transitions.

45.

Facilitating community contributions to visualizing spatial biology

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TissUUmaps is an open-source, interactive web application for visualizing large multi-modal spatial omics datasets, including point clouds, vector geometries, and tiled image pyramids. Known for its GPU-enabled rendering of millions of points and static exports for publication, the TissUUmaps project is currently undergoing a major architectural modernization. This poster highlights the core features of TissUUmaps 4, its alignment with modern community standards such as OME-Zarr, and its new architecture designed to facilitate community contributions and long-term maintenance.