Spatial Transcriptome-Stereo-seq

Stereo-seq is a spatio-temporal omics technology that captures mRNA from tissue sections using stereo chips and restores the spatial context by utilizing spatial barcodes (coordinate IDs, or CIDs). This method establishes a solid foundation for further understanding the relationship between gene expression, cell morphology, and the local environment.

As a pioneering tool, Stereo-seq achieves nanoscale resolution and can theoretically achieve a 100% cell capture rate, resulting in more informative and accurate cell clustering results.

It provides a centimeter-scale panoramic field of view with a maximum size of 13 cm x 13 cm, enabling the creation of a panoramic molecular cell map of organs and tissues. By recognizing the location of the nucleus through fluorescent imaging and combining this with advanced algorithms, Stereo-seq can produce expression maps at an approximate single-cell level.

Project Workflow

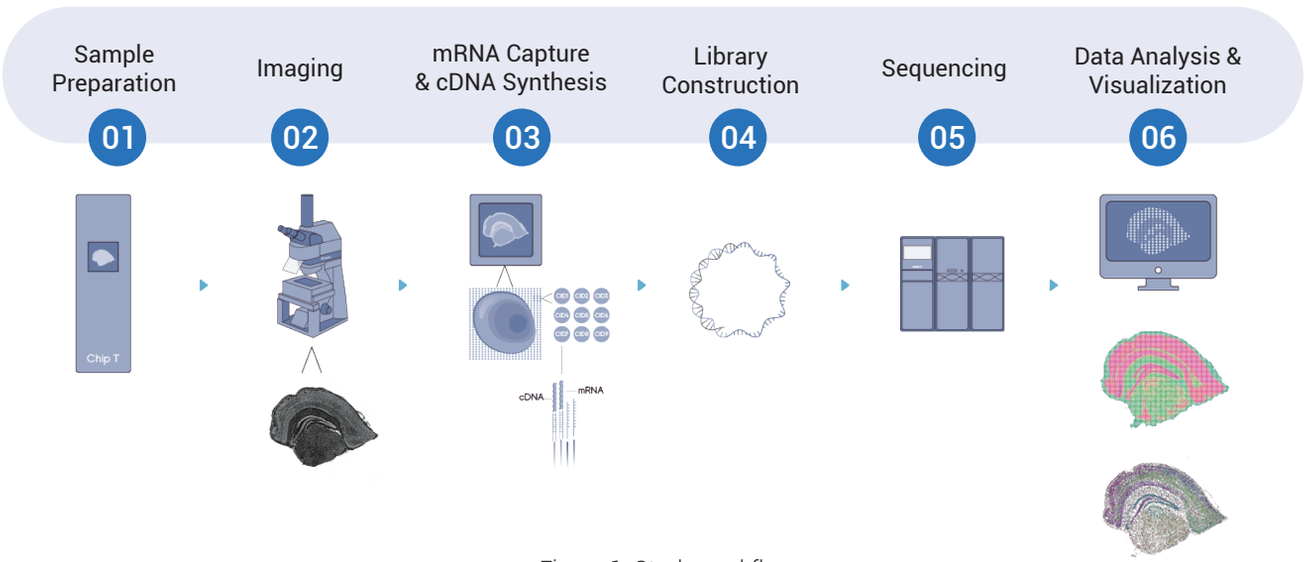
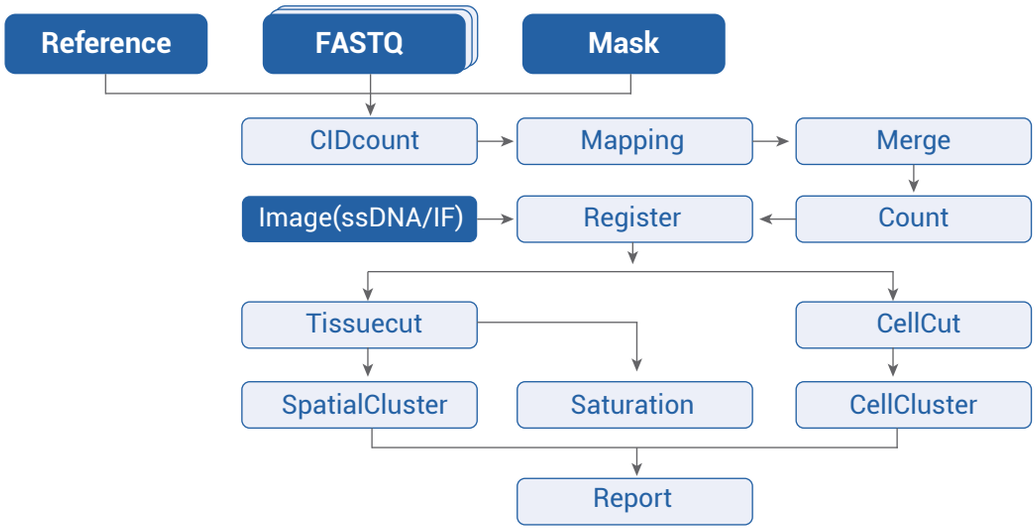


Figure 1: Study workflow

1) Sample preparation: The OCT-embedded tissue was sliced, and RNA quality was assessed. The QCed sample slices were then affixed to the Stereo-seq chip.
2) Permeabilization: The tissue on the chip was sectioned for fixation and permeabilization. The Stereo-seq chip is equipped with capture probes that bind with mRNA molecules released by the tissue cells, capturing the mRNA of the target sample tissue cells on the chip and releasing cDNA.
3) Library preparation and sequencing: After cDNA synthesis, the library was constructed and sequenced on the DNBSEQ platform with a PE100 reading length.
4) Data analysis: Quality control was conducted on the sequencing data, followed by data analysis. This process ultimately provided spatially resolved transcriptome profiling of the same sample, enabling analysis across tissue, cell, and even sub-cell (molecular) levels.

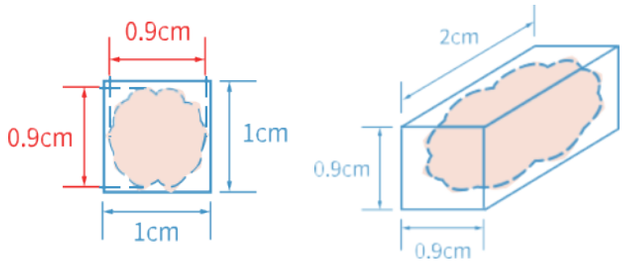
Data Analysis

The Stereo-seq Analysis Workflow (SAW) software suite is a set of pipelines designed to position sequenced reads to their spatial locations on the tissue section, quantify spatial gene expression, and visually present spatial expression distribution. SAW processes the sequencing data from Stereo-seq to generate spatial gene expression matrices. These files serve as the starting point for users to perform downstream analysis. SAW includes thirteen essential and recommended pipelines, along with auxiliary tools that support various additional functions.



Sample Requirements

For fresh frozen samples embedded in Tissue-Teck OCT, we recommend performing tissue embedding within 30 minutes after resection and wiping away excess fluid to avoid RNA degradation.



The tissue size should not exceed 0.9 cm x 0.9 cm x 2 cm, as the tissue section should cover not more than 80% of the chip area.

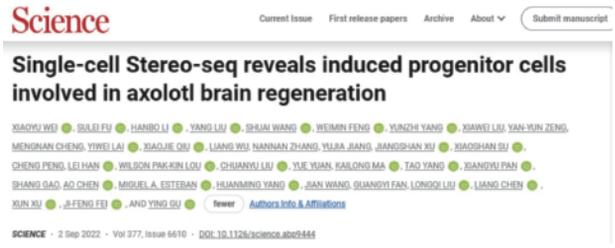
It is recommended to check the RNA quality (RIN value) of a tissue sample before proceeding with the Stereo-seq transcriptomics experiment. Total RNA can be extracted from 10 to 20 slices of 10 μm-thick tissue sections and stored at -20°C in a pre-cooled 1.5 mL EP tube. It is strongly recommended to use tissue samples with a RIN value >7.

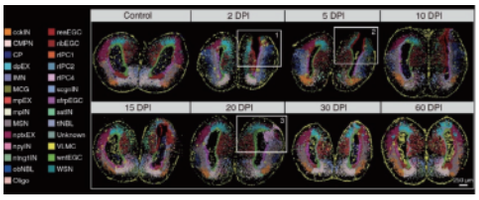
Sample Storage and Transportation

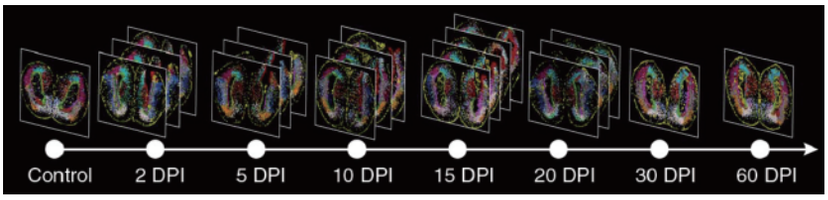
For storage, wrap the tissue block in aluminum foil and place it in a properly labeled, sealable plastic bag to prevent dehydration and damage. Then store it at -80°C. For transportation, ship samples on dry ice in accordance with local policies.

Case Study

Single-cell Stereo-seq reveals induced progenitor cells involved in axolotl brain regeneration.







Research summary:

Axolotl Regenerative Telencephalon Interpretation via Spatiotemporal Transcriptomic Atlas (ARTISTA) is a spatially resolved transcriptomic data resource that provides visualization of gene expression across the regeneration and development stages of axolotl telencephalon at single cell resolution, aiming to provide a systematic dissection of the molecular events underlying neural regeneration in the axolotl brain, laying the foundation for further mechanistic studies. To comprehensively understand cellular dynamics occurred during axolotl brain regeneration and development, here, we carried out a series of spatial transcriptome analyses on serial sections along the rostral-caudal axis of 2 (3 sections), 5 (3 sections), 10 (3 sections), 15 (4 sections), 20 (3 sections), 30- and 60-days post injury (DPI) brain tissues after removal of a reproducible portion of dorsal pallium in left telencephalic hemisphere of 11 cm length axolotl. We also collected sections from developmental (stage 44, 54, and 57), juvenile, adult, and metamorphosed axolotl telencephalons. Based on this dataset, researchers can quickly explore the gene expression profiles of their interested cell types in spatial map across different regeneration and development stages of axolotl telencephalon.

Species: *Ambystoma mexicanum*

Development stage:

Developmental stage 44, Developmental stage 54, Developmental stage 57, Juvenile, Adult, Metamorphosed animals, 2 days post injury, 5 days post injury, 10 days post injury, 15 days post injury, 20 days post injury, 30 days post injury, 60 days post injury.

Organ parts: Injured brain

Citation:

Wei, Xiaoyu et al. "Single-cell Stereo-seq reveals induced progenitor cells involved in axolotl brain regeneration." *Science* (New York, N.Y.) vol. 377,6610 (2022): eabp9444. doi:10.1126/science.abp9444

Publications

Title	Publication	IF	Year
A cellular hierarchy in melanoma uncouples growth and metastasis	*Nature*	69.504	2022
Spatiotemporal transcriptomic atlas of mouse organogenesis using DNA nanoball-patterned arrays	*Cell*	66.85	2022
Spatiotemporal insight into early pregnancy governed by immune featured stromal cells	*Cell*	64.5	2023
Single-cell spatial transcriptome reveals cell-type organization in the macaque cortex	*Cell*	64.5	2023
Single-cell Stereo-seq reveals induced progenitor cells involved in axolotl brain regeneration	*Science*	63.714	2022
Whole-brain spatial organization of hippocampal single-neuron projectomes	*Science*	56.9	2024
Identification of HSC/MPP expansion units in fetal liver by single-cell spatiotemporal transcriptomics	*Cell Research*	46.297	2022
An invasive zone in human liver cancer identified by Stereo-seq promotes hepatocyte-tumor cell crosstalk, local immunosuppression and tumor progression	*Cell Research*	44.1	2023
Clinical and translational values of spatial transcriptomics	*Signal and Transduction and Targeted Therapy*	38.104	2022
Single-cell multi-omics analysis of lineage development and spatial organization in the human fetal cerebellum	*Cell Discovery*	33.500	2024
A single-cell transcriptome atlas profiles early organogenesis in human embryos	*Nature Cell Biology*	21.3	2023

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