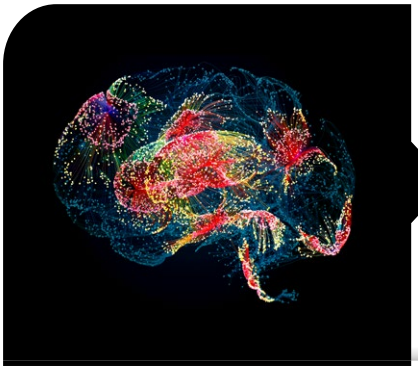
Introduction

The use of advanced technologies to study the brain at higher resolution—such as single-cell sequencing, optogenetics, and CRISPR-based genome-targeting tools—is a major trend in neuroscience research. These tools are enabling researchers to gain valuable molecular and functional insights. The high degree of complexity of the brain, interconnectedness of the nervous system, and limited access to brain tissue are some of the challenges faced by neuroscientists.

In particular, mature neurons and specific cell types like motor neurons and spinal cord cells are difficult to dissociate, prompting researchers to work with single-nuclei suspensions. Working with whole cells is still desirable, but sample quality, even for single-nuclei suspensions, depends heavily on a delicate balance between purity, speed, and gentleness, which is not easily achieved by most instruments.

The SH800 Cell Sorter strikes a perfect balance between the parameters that impact the quality of neural samples. As a result, the SH800 has been successfully used in many neuroscience studies for a variety of downstream applications including single-cell multiomic analysis, developmental trajectory studies, and disease model generation via gene-editing tools, among others. Some of the most recent and exciting discoveries enabled by the SH800 system are outlined in this publication.

Discoveries in Neuroscience Using the SH800 Cell Sorter



Source of neuronal cells

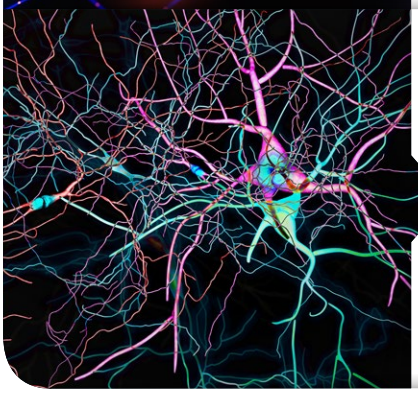
Fresh tissue	Hippocampi tissue[1,2,3]	Corpus callosum[4,10]
Frozen tissue	Frontal cortex[3,4]	Motor cortex[11]
	Prefrontal cortex[6,7,13]	Others[8,9,16,17,20]
Stem cells	Human iPSC[14]	
	Drosophila embryonic cells[5]	
Tumor tissue	H4 cells – human neuroglioma[15]	
	Medulloblastoma[19]	

Cell sorting benefits

Sample prep	Cell-type enrichment and debris removal[1,9,14]
High-throughput enrichment	Fast sorting of millions of cells for bulk analysis[19]
AAV and CRISPR-transfected cell enrichment	Viable cell recovery[14]
Sorting into 96- and 384-well plates	Single-cell and single-nuclei isolation[7,10,13]

Downstream applications

Transcriptome profiling	RNA sequencing via SMART-Seq2 and 10x Genomics platform[2,4,5,7,9,10,13,18]
DNA methylation	Bisulfite DNA sequencing[17]
Gene loci accessibility and protein-DNA binding analysis	ATAC-seq and CUT&RUN[1,3,6,8,11]
Tumor microenvironment analysis	Cytokine array panel[19]
Cell-cycle analysis	DNA staining[5]



Powerful insights

Neuronal diversity	Cell-type composition of various brain tissues[2,4,9]
Neural development	Gene activation and regulation during various stages of development[3,5,11,14]
Aging and neurodegenerative diseases	Role of immune cells in myelination and growth[2,20]
Memory	Transcriptional programs in remote memory[13]

How the SH800 enables neuroscience research

Research focus	Featured Publication	Experiment
Epigenomics of aging	Single-cell epigenome analysis reveals age-associated decay of heterochromatin domains in excitatory neurons in the mouse brain. *Cell Res.* 2022;32(11):1008-1021	Used the SH800 to isolate single nuclei from the hippocampus and frontal cortex of mice into 96-well plates. Combinatorial barcoded snATAC-seq was performed to study age-dependent changes in chromatin accessibility.
Tissue cell-type diversity	CD8+ T cells induce interferon-responsive oligodendrocytes and microglia in white matter aging. *Nat Neurosci.* 2022;25(11):1446-1457	Used the SH800 to enrich for viable oligodendrocytes and astrocytes from corpus callosum and optical tracts. Single cells were dispensed in 96-well plates. RNA sequencing with SMART-Seq2 was used to determine cell-type composition.
Cell-type diversity in development	Complex oscillatory waves emerging from cortical organoids model early human brain network development. *Cell Stem Cell.* 2019;25(4):558-569	Used the SH800 to sort cells from cortical organoids at various stages of development, based on size and viability. Single-cell RNA-seq analysis was performed using a 10x Genomics platform to determine cell-type composition.
Transcriptomics and phenotyping	Differential encoding in prefrontal cortex projection neuron classes across cognitive tasks. *Cell.* 2021;184(2):489-506	Used the SH800 with a 130-µm chip to sort healthy whole pyramidal cells from rodent prefrontal cortex into 96- or 384-well PCR plates. Transcriptome profiling was performed with SMART-Seq2 to correlate with corresponding projection type and encoding properties.
Genetics of development	SMARCB1 loss interacts with neuronal differentiation state to block maturation and impact cell stability. *Genes Dev.* 2020;34(19-20):1316-1329	Used the SH800 to perform FACS analysis of iPSCs subjected to neuronal differentiation. Neuronal maturation efficacy was determined via surface expression levels of NCAM1, a marker of mature neurons.
Epigenetics of development	Master regulators and cofactors of human neuronal cell fate specification identified by CRISPR gene activation screens. *Cell Rep.* 2020;33(9):108460	Used the SH800 to perform screens of iPSCs displaying high levels of CRISPR-activated transgene expression. Cells were isolated and replated in Matrigel-coated coverslips. Cells were harvested for various downstream assays including whole cell patch clamping.
Neural stem cell differentiation	Selective translation of epigenetic modifiers affects the temporal pattern and differentiation of neural stem cells. *Nat Commun.* 2022;13(1):470	Used the SH800 to sort GFP+ transfected *Drosophila* neural stem cells. Cell-cycle phase was determined based on DNA content using FACS analysis. Differentiated state was determined through RNA sequencing using a 10x Genomics platform.
Tumor microenvironment	Tumour-associated macrophages exhibit anti-tumoural properties in Sonic Hedgehog medulloblastoma. *Nat Commun.* 2019;10(1):2410	GFP+ tumor cells from murine medulloblastoma were sorted using the SH800 and lysed. A mouse cytokine array panel was used to measure cytokine levels of lysed cells.

Explore selected scientific discoveries enabled by the SH800

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