

### S3e<sup>™</sup> Cell Sorter

A stress free path to higher data quality.



# How Do You Get Your Cells?

New, powerful techniques like CRISPR and single-cell analysis are enhanced by the isolation of specific cells. But isolating cell populations of the right quality and quantity is both challenging and time consuming. This is especially true when working with rare and sensitive cell types. There's more than one way to isolate the cells you need. Methods using positive-negative selection columns or fluorescence, or even relying on a biobank are common.

### But, what are the differences?

#### Positive-Negative Selection

Facilitates sorting by incubating cells with magnetic nanoparticles coated with antibodies to target specific markers on the cells.

- Fast and easy
- Requires antibody for your marker
  Not suitable for CRISPR applications
  Not compatible with fluorescence
  Challenging to select for multiple markers
  Lack of purity

#### Biobank/Cell Provider

Off-site or third-party source provides a selection of cells.

- No expertise needed
- High cost per sample
  No guarantee of cell viability
  Variable cell quality
  Lack of available samples of interest

### Fluorescence-Activated Cell Sorting

This focused flow cytometry method rapidly sorts cells, one at a time, based on light scattering and fluorescent signatures from dyes and proteins.

Can be used for a wide range of applications
Compatible with internal and external fluorescence

Provides quantitative data

Delivers speed and flexibility
Improves sample purity

# Move Cell Sorting to Your Lab

On the path to your breakthroughs, there is little room for core facility wait times, low-quality samples, sample degradation during transport, or results you can't trust. Incorporating fluorescence-based cell sorting into your lab grants you powerful access to new research areas and rarer cell types without sacrificing efficiency or results.

But, bringing fluorescence-based sorting to your benchtop should address all of your needs. You need to consider who can use it, how adaptable it is, and whether it is capable of producing great data.

#### All Users Welcome

One of the most tedious things about introducing new methods into your lab is navigating the learning curve. To help inspire confidence in data from downstream applications, you need technology that can be used by anyone no matter their skill level. But that technology also needs to be sophisticated enough to account for user-to-user variability. You need a cell sorter that is simple enough to learn in half a day to help expand your lab's capabilities.

#### Time for More

High-speed cell sorters require dedicated operators to navigate instrument setup processes and monitor sorting performance. When bringing a cell sorter into your lab, the ideal system should be ready when you are, automate your set up and sorting processes, let you walk away to focus on other important tasks, and send you a message to let you know when your sort is done.

#### **Peak Performance**

Imagine a cell sorting system that can differentiate external and internal markers and sort 10,000 cells (with a 0.1% population frequency) in less than 20 minutes, all while ensuring healthy cells and quality data. Cell sorting systems improve data quality by increasing sample purity as much as 25% over other methods. A system designed to preserve cellular integrity, yet remain powerful and effective, keeps you assured in the sorting you do.



# Meet the S3e Cell Sorter



### Flexible Function for Your Lab

Groundbreaking science can come from your lab. Scientists like you are accomplishing more with the S3e Cell Sorter — to date, over 100 papers in the areas of stem cells, CRISPR, and single-cell analysis using it have already been published. Here are a few key papers demonstrating the importance of sorting pure, healthy cells.

Cancer

Jin HJ et al. (2016). **Identification and validation** of regulatory SNPs that modulate transcription factor chromatin binding and gene expression in prostate cancer. Oncotarget.

Duhachek-Muggy S et al. (2017). **Metalloproteasedisintegrin ADAM12 actively promotes the stem cell-like phenotype in claudin-low breast cancer.** Molecular Cancer.

Frame FM et al. (2016). Harvesting human prostate tissue material and culturing primary prostate epithelial cells. Methods in Molecular Biology.

CRISPR

Lander N et al. (2015). CRISPR/Cas9-induced disruption of paraflagellar rod protein 1 and 2 genes in *Trypanosoma cruzi* reveals their role in flagellar attachment. mBio.

Matabaro E et al. (2017). Molecular switching system using glycosylphosphatidylinositol to select cells highly expressing recombinant proteins. Scientific Reports.

Chen Y et al. (2017). Gene editing in rat embryonic stem cells to produce in vitro models and in vivo reporters. Stem Cell Reports.

Genomics

Tang WWC et al. (2015). A unique gene regulatory network resets the human germline epigenome for development. Cell.

Furuta A and Nakamura T (2017). **DNA** hypomethylation circuit of mouse rDNA repeats in the germ cell lineage. Biochemical and Biophysical Research Communications.

Alexandrov A et al. (2017). Fluorescence amplification method for forward genetic discovery of factors in human mRNA degradation. Molecular Cell.



Gil-Cruz C et al. (2016). Fibroblastic reticular cells regulate intestinal inflammation via IL-15-mediated control of group 1 ILCs. Nature Immunology.

Imhof BA et al. (2016). CCN1/CYR61-mediated meticulous patrolling by Ly6C low monocytes fuels vascular inflammation. Proceedings of the National Academy of Science of the United States of America.

Goossens S et al. (2017). Oncogenic ZEB2 activation drives sensitivity toward KDM1A inhibition in T-cell acute lymphoblastic leukemia. Blood.



Bidlingmaier S et al. (2016). Proteome-wide identification of novel ceramide-binding proteins by yeast surface cDNA display and deep sequencing. Molecular and Cellular Proteomics.

Winer BY et al. (2017). Long-term hepatitis B infection in a scalable hepatic co-culture system. Nature Communications.

Vilchèze C et al. (2017). Enhanced respiration prevents drug tolerance and drug resistance in *Mycobacterium tuberculosis*. Proceedings of the National Academy of Science of the United States of America.



Chal J et al. (2015). Differentiation of pluripotent stem cells to muscle fiber to model Duchenne muscular dystrophy. Nature Biotechnology.

Murakami K et al. (2016). NANOG alone induces germ cells in primed epiblast in vitro by activation of enhancers. Nature.

Chen YW et al. (2017). A three-dimensional model of human lung development and disease from pluripotent stem cells. Nature Cell Biology.

### Increased Lab Efficiency and Productivity

Your time for a project is often limited, yet the demands on your time can feel limitless. It's not enough to employ a cell sorting method that just sorts. Once incorporated into your workflow, the S3e Cell Sorter grants you access to unique, innovative features designed to streamline your genomics and proteomics research.

"Now that we have it here I can sort cells every day. So that's 10 experiments every week that I can get done. It definitely sped things up. Now my problem is trying to manage all my data."

### **Email and Text Message Alerts**



S3e sort status updates can be sent to your smart devices. You don't have to sit, watch, or wait on an instrument. Instead focus on other tasks during sorting runs.

#### Scheduled Startup



Starting up an instrument and setting up experiments shouldn't be complicated. The S3e can be scheduled to be ready when you are.

#### Fluidics Monitoring



Onboard the S3e, ProSort™ Software continually monitors sheath, DI water, and waste fluidics so you'll know exactly when to replace fluids.

#### Hot Swap



Sort for up to 50 hours before exchanging fluids, thanks to the onboard dilution system for concentrated 8x sheath fluid. And you can swap containers mid-sort with no need to recalibrate or repressurize.

### Volume Tracking



The S3e is the only benchtop system that lets you set volume limits. With volume tracking enabled, the S3e automatically stops sorting when a collection vessel is full.

#### **Bubble Detector**



The S3e is equipped with an inline bubble detector that alerts ProSort Software to pause sorting when a sample tube has run dry.

## Stress-Free Cell Sorting

Taking steps to ensure excellent results you can trust is an integral component to stressfree sorting. So we made sure it would be a defining characteristic of the S3e Cell Sorter.

#### **Intuitive Interface**

Designed with novice users in mind, ProSort Software lets firsttime users effortlessly find their way around instrument controls to help make cell sorting a less stressful experience. With onscreen prompts, tool tips, and guided processes, ProSort instructs the researcher through the entire sorting process for a better user experience and easier experimental setup.

#### Lossless Cell Sorting

Another way we enable stress-free sorting is through Lossless Cell Sorting — the sorting mode that sets the S3e Sorter apart. Other benchtop cell sorters limit you to sorting either in Purity Mode (which increases unwanted loss of target cells) or Enrichment Mode (which reduces sample purity). But, with the S3e Cell Sorter, you can sort in both modes at the same time, which means more of the cells you want, with fewer sample manipulations and better cell health.

#### Be Gentle on Cells

Achieving stress-free cell sorting isn't just about the user. It's about the cells, too. Stressed cells die or change their gene expression patterns, affecting your results. To maintain healthy cells, you need to keep them at the right temperature, prevent sample-to-sample contamination, and keep them in suspension. The S3e Cell Sorter is designed exactly to address these issues.



#### **Onboard Temperature Controls**

Sample loading stage and sort collection area can be maintained at 4-37°C to preserve cell viability using Peltier solid-state technology.



#### Automatic Sample Line Flushing

Thorough backflushing of the sample line between runs reduces cross-contamination risk.



#### Magnetic Agitator

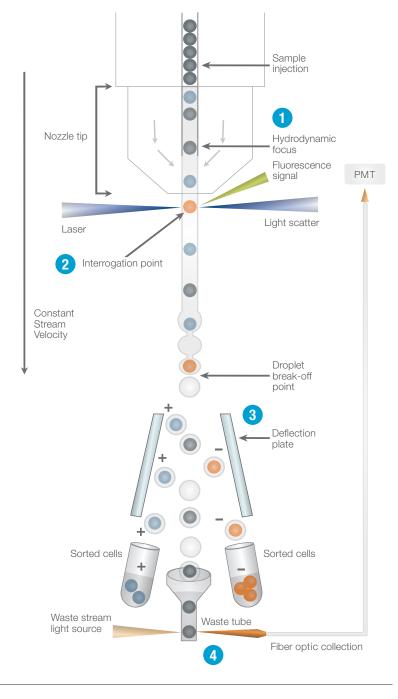
Continuous sample vortexing while sorting prevents cell clumping, reduces sample loss, and reduces clogging.

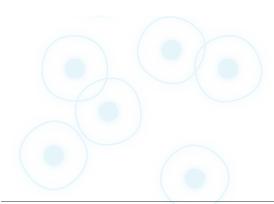
# High Performance with Jet-in-Air Sorting

With the S3e Cell Sorter, you'll benefit from a sorting system that maintains a constant stream velocity during runs, which means cells are sorted gently and accurately, even at high speeds. In many systems, cell health is compromised by shear forces that result from rapid pressure changes within fluid streams. But, the S3e Cell Sorter uses jet-in-air sorting to avoid these instabilities and preserve cell health.

#### How It Works

- A sample (cells and debris) is ordered into a stream of single particles as it enters the nozzle by hydrodynamic focusing.
- The stream carries each cell from the nozzle through the laser interrogation point. Light scattering and fluorescence data from the interrogation point are immediately collected and cross-referenced against user criteria.
- 3 As a target cell reaches the break-off point, the stream is charged so that as the cell is captured in a droplet it retains the charge and is deflected and sorted into a designated collection vessel.
- Droplets filled with debris or absent of target cells are directed to the waste tube to prevent sample contamination. Because the interrogation point focuses on a stream of single cells, one-at-a-time, jet-in-air sorting delivers the sample purity and cell recovery you need.





## Rare Cell Recovery with ProDrop™ Technology

Engineered by experts with over 30 years of cell sorting experience, ProDrop technology complements the jet-in-air setup of the S3e Cell Sorter to ensure sorting precision and maximize rare cell recovery.

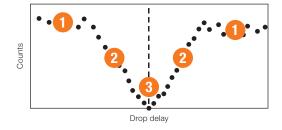
#### **Automated Drop Delay Calculation**

Calculating the time it takes a cell to travel from the interrogation point to the droplet break-off point — also known as the drop delay — is critical to maximizing recovery of your cells. Imprecise determination of drop delay leads to inaccurate deflection of cells and results in poor yields and low sample purity. Traditional systems force you to calculate drop delay manually. ProDrop technology automatically calculates and fine tunes the drop delay through direct counting of ProLine™ Universal Calibration Beads in the waste stream during the QC process.

#### How ProDrop Fine Tunes Drop Delay

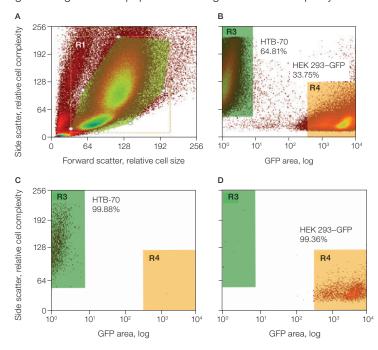
ProLine Universal Calibration Beads are sorted at increasing or decreasing drop delay values.

- If the drop delay is incorrect, the beads are not sorted and travel through the waste tubing, then get excited by the waste bead laser and are counted.
- The closer the drop delay is to the correct value, the greater the chance a bead will be deflected and not counted by the waste bead system.
- At the correct drop delay, no beads should be detected by the waste bead system because all beads should be properly deflected.



#### What about Purity While Sorting?

ProDrop technology not only calculates drop delay without user intervention, it also maintains purity while sorting. During a sort, ProDrop technology continually monitors drop formation and adjusts drop delay values to accommodate any changes. With ProDrop, you get homogenous cell populations with greater than 99% purity.



High precision sorting. HEK 293-GFP or HTB-70 cells were sorted by forward scatter (relative cell size) against side scatter (relative cell complexity) on the y-axis. A region was drawn and applied to subsequent plot. A-B, presort analysis of positive cells; C-D, postsort analysis revealed HTB-70 cells at 99.88% purity and HEK 293-GFP cells were sorted to 99.36% purity.

## Superior Customer Care

Although the S3e Cell Sorter makes cell sorting in your lab easy, you may still have questions or just need help troubleshooting. And when you do, we're here to help. We offer reliable and flexible assistance and we can help you solve problems right on your instrument, even remotely.

#### Bio-Rad's Expert Care Service

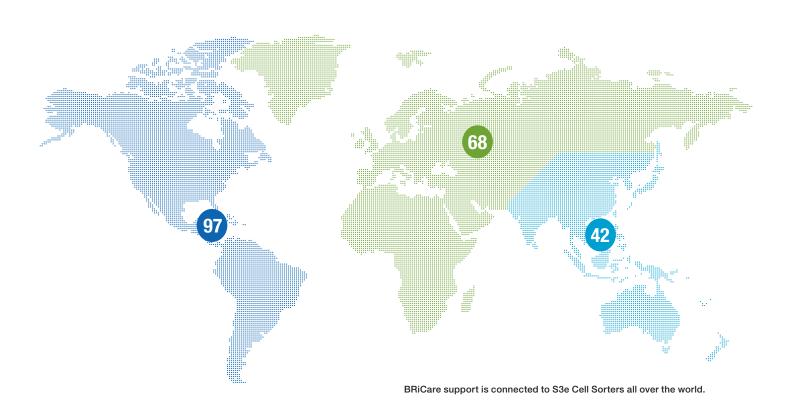
Whether you need routine maintenance or you just need immediate guidance, you can always put your trust in Bio-Rad.

Bio-Rad retains a team of dedicated specialists with direct access to the latest procedures, parts, tools, and industry knowledge. And they're always only a phone call or email away.

#### BRiCare<sup>™</sup> Remote Support

When you need help diagnosing a problem, sending your instrument away is a hassle. So we put BRiCare onboard the S3e.

BRiCare is Bio-Rad's exclusive remote monitoring system. It allows us to troubleshoot or solve problems from anywhere in the world without having you ship back the instrument. That means your instrument can stay at home in your lab, right where it belongs.



# Fluorophore Compatibility with the S3e Cell Sorter

	Laser	Excitation Maximum, nm	Emission Maximum, nm	Fluorescence Emission Color					
Fluorophore or Dye				405/488/561	405/488/640	488/561/640	488/561	488/640	488
DyLight 405	405	400	420	FL1	FL1				
Alexa Fluor 405	405	401	421	FL1	FL1				
Brilliant Violet 421	405	407	421	FL1	FL1				
BD Horizon V450	405	404	448	FL1	FL1				
Pacific Blue	405	401	452	FL1	FL1				
DAPI	405	359	461	FL1	FL1				
ECFP	405	434	477	FL1	FL1				
EGFP	488	488	507	FL2	FL2	FL1	FL1	FL1	FL1
CFDA-SE (1351201)*	488	492	517	FL2	FL2	FL1	FL1	FL1	FL1
DyLight 488	488	493	518	FL2	FL2	FL1	FL1	FL1	FL1
FITC	488	495	519	FL2	FL2	FL1	FL1	FL1	FL1
Alexa Fluor 488	488	499	519	FL2	FL2	FL1	FL1	FL1	FL1
EYFP	488	514	527	FL2	FL2	FL1	FL1	FL1	FL1
DyLight 550	561	562	576	FL3		FL2	FL2		
PE	488, 561	496, 565	578	FL3	FL3	FL2	FL2	FL2	FL2
tdTomato	561	554	581	FL3		FL2	FL2		
RFP (tag)	561	554	584	FL3		FL2	FL2		
DsRed	488, 561	554	586	FL3	FL3	FL2	FL2	FL2	FL2
mCherry	561	587	610	FL4		FL3	FL3		
PE-Texas Red	488, 561	496, 565	613	FL4	FL3	FL3	FL3	FL2	FL2
Propidium Iodide (1351101)*	488, 561	538	617	FL4	FL3	FL3	FL3	FL2	FL2
7-AAD (1351102)*	488, 561	548	648	FL4	FL4	FL4	FL4	FL3	FL2
APC	640	650	660		FL4	FL4		FL3	
Cy5	640	649	666		FL4	FL4		FL3	
PE-Alexa Fluor 647	488, 561	496, 565	668	FL4	FL4	FL4	FL4	FL3	FL2
Alexa Fluor 647	640	650	668		FL4	FL4		FL3	
PE-Cy5	488, 561	496, 565	670	FL4	FL4	FL4	FL4	FL3	FL2
DyLight 650	640	652	672		FL4	FL4		FL3	
PerCP	488	482	676	FL4	FL4	FL4	FL4	FL3	FL2
PerCP-Cy5.5	488	482	690	FL4	FL4	FL4	FL4	FL3	FL2
PE-Cy5.5	488, 561	496, 565	690	FL4	FL4	FL4	FL4	FL3	FL2
APC-Cy5.5	640	650	694		FL4	FL4	· • • · ·	FL3	
Alexa Fluor 680	640	679	702		FL4	FL4		FL4	
DyLight 680	640	692	712		FL4	FL4		FL4	
Alexa Fluor 700	640	696	719		FL4	FL4		FL4	
APC-Cy7	640	650	785		FL4	FL4		FL4	
PE-Cy7	488, 561	496, 565	785	FL4	FL4	FL4	FL4	FL4	FL2

<sup>\*</sup> Indicates Bio-Rad catalog number. 7-AAD, 7-aminoactinomycin D; APC, allophycocyanin; CFDA-SE, 5(6)-carboxyfluorescein diacetate succinimidyl ester; DAPI, 4',6-diamidino-2-phenylindole dihydrochloride; ECFP, enhanced cyan fluorescent protein; EGFP, enhanced green fluorescent protein; EYFP, enhanced yellow fluorescent protein; FITC, fluorescein isothiocyanate; PE, phycoerythrin; PerCP, peridinin chlorophyll protein; RFP, red fluorescent protein.

		Filter Set					
Instrument Filter Configuration	Catalog Number	FL1	FL2	FL3	FL4		
S3e Cell Sorter (488 nm)	1451005	525/30 (510–540)	540 LP				
S3e Cell Sorter (488/561 nm)	1451006	525/30 (510-540)	586/25 (573-598)	615/25 (602-627)	655LP		
S3e Cell Sorter (488/640 nm)	1451008	526/48 (502-550)	593/40 (573-613)	670/30 (655-685)	700LP		
S3e Cell Sorter (405/488/561 nm)	12007058	447/60 (417-477)	525/30 (510-540)	586/25 (573-598)	600LP		
S3e Cell Sorter (405/488/640 nm)	12007059	447/60 (417-477)	526/48 (502-550)	593/40 (573-613)	650LP		
S3e Cell Sorter (488/561/640 nm)	12007052	525/30 (510-540)	586/25 (573-598)	615/25 (602–627)	655LP		

### Biosafety

While the S3e Cell Sorter has an interlocked sort chamber door to protect from aerosols formed by the sort stream in the collection area, safety is always a key concern. Adhering to National Institutes of Health (NIH) biosafety standards, a biosafety cabinet is the primary containment system recommended. The S3e Cell Sorter fits seamlessly in the custom-designed S3e Biosafety System Class I. Fully integrated with ProSort Software, the system airflow is controlled and the HEPA filter is monitored in real time. The S3e Biosafety System Class I is uniquely designed with four magnetically attached vinyl walls, which allows easy access to the instrument inside for service or routine maintenance. This option is available to help labs comply with NIH standards. Feel confident in protecting both the user and the surrounding environment when performing sort experiments in an S3e Biosafety System Class I.



#### **Specifications**

Droplet frequency	37–43 kHz
Sorting type	True jet-in-air for high-performance sorting
Sorting rate	No hardware limitations for sort rate; limited only by droplet frequency and application
Sorting purity	>99% pure
Nozzle size	100 μm
Sorting direction	2-way sorting
Sorting collection	Up to 5 x 5 ml sample tubes each direction Up to 5 x 1.5 ml tubes each direction Microscope slides 8-well flat bottom strip each direction 8-well low-profile PCR strip each direction
Lasers	Single laser: 488 nm 100 mW Dual laser: 488 and 561 nm 100 mW; 488 and 640 nm 100 mW Tri laser: 488, 561, and 640 nm 100 mW; 405, 488, and 561 nm 100 mW; 405, 488, and 640 nm 100 mW
Detection	Forward scatter (FSC) with PMT Side scatter (SSC) with PMT Up to four fluorescence detectors with PMT Minimum resolution: 0.5 µm
Sensitivity	<125 MESF for FITC and PE
Temperature range	Sample and collection temperature control system: 4–37°C Peltier solid-state system
Fluidics	Onboard fluidics and dilution of ProFlow™ Sort Grade 8x Sheath Fluid with deionized water
Data format	FCS 3.1
Dimensions (W x D x H)	70 x 65 x 65 cm (2.3 x 2.1 x 2.1 ft)

#### **Ordering Information**

Catalog #	Description
Instrumentation	1
1451005	S3e Cell Sorter (488 nm), with two fluorescence detectors
	and ProSort Software
1451006	S3e Cell Sorter (488/561 nm), with four fluorescence detectors
	and ProSort Software
1451008	S3e Cell Sorter (488/640 nm), with four fluorescence detectors
	and ProSort Software
12007052	S3e Cell Sorter (488/561/640 nm), with four fluorescence
	detectors and ProSort Software
12007058	S3e Cell Sorter (405/488/561 nm), with four fluorescence
	detectors and ProSort Software
12007059	S3e Cell Sorter (405/488/640 nm), with four fluorescence
	detectors and ProSort Software
1451078	S3e Biosafety System Class I
Consumables	
1451086	ProLine Universal Calibration Beads, 3 x 5 ml bottles
1451082	ProFlow Sort Grade 8x Sheath Fluid, 5 x 4 L containers,
	preservative free
1451083	ProFlow Sort Grade Water, 5 x 4 L containers, sterile-filtered,
	endotoxin-tested water
1451085	ProLine Rainbow Beads, 1 x 5 ml bottle, mixture of 3.0–3.4 μm
	beads dyed with 8 different fluorescence intensities
Accessories	
1451065	S3e Accessory Kit, includes 100 µm nozzle tip, 2 nozzle O-rings,
	2 nozzle alignment disks, 1 ml syringe, 2 neutral density filters (1.0),
1451004	2 mm hex driver, spanner wrench
1451084	S3e Fluidic Container, 3 x 4 L containers, gamma-irradiated, sterile

Visit bio-rad.com/S3e for more information.

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