The Inertial Microfluidics Engine Enabling Next-Generation Cell Processing Platforms

The rapid growth of cell therapy and automated diagnostics has outpaced the evolution of its core cell processing tools. Too often, the industry has been forced to fit modern applications onto legacy platforms like centrifugation, creating a bottleneck that hinders innovation. These older methods are difficult to automate, harsh on cells, and introduce process variability that is unacceptable for modern therapeutic and diagnostic systems.

BendBio provides the solution: a proven, purpose-built inertial microfluidics "engine" designed for OEM integration. Our core modules for cell sorting, washing, and concentration enable partners to build market-leading systems with superior cell yield, purity, and viability. Backed by a commercial-scale, automated manufacturing process, BendBio de-risks the supply chain and accelerates time-to-market for our partners. This white paper details our core technology, its seamless integration capabilities, and its proven performance in a demanding whole blood application.

Current Challenges

While downstream applications have advanced dramatically, many of the fundamental upstream unit operations—cell sorting, washing, and concentration—remain reliant on legacy, centrifugation-based methods. These manual, open-system processes are harsh on cells, leading to significant cell loss and functional impairment.

For developers of automated platforms, these legacy techniques present a major barrier. Their mechanical complexity makes them difficult to integrate, their batch-based nature breaks up continuous workflows, and their inherent variability undermines the goal of creating robust, walk-away systems that deliver the consistency and quality required by modern clinical and research operations.

BendBio's Approach: An Enabling Technology

BendBio is transforming cell processing by providing core technology modules based on inertial focusing, a technique that provides a simple, elegant, and high-throughput means of manipulating cells in microfluidic systems. Since its discovery at Massachusetts General Hospital, the founders of BendBio have refined, extended, and commercialized inertial focusing-based technologies to address critical challenges in medicine [1–5].

Our microfluidic platform sorts and concentrates cells by size with remarkable efficiency, all without centrifuges, reagents, membranes, or beads. The technology enables a closed, continuous flow process, which simplifies integration into automated fluidic pathways and minimizes the need for complex robotics. By providing the fundamental building blocks for cell processing, BendBio empowers its partners to develop systems that deliver exceptional consistency and reliability while improving critical performance parameters such as viable cell yield and purity.

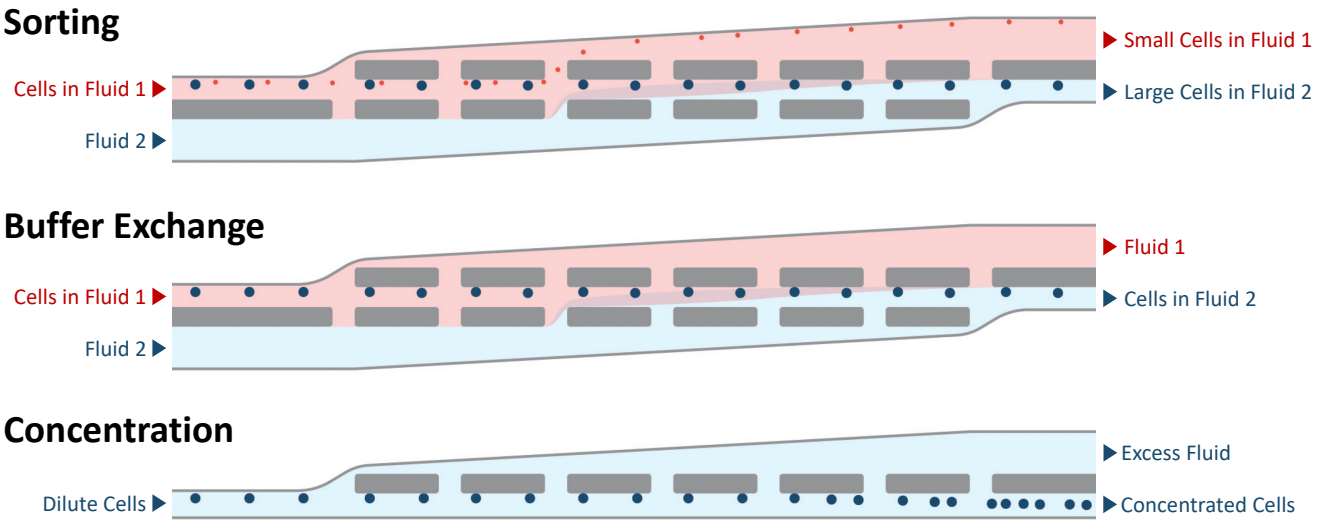

Figure 1: Schematic of Cell Processing Operations. *BendBio's cell processing technology leverages inertial lift to enable continuous flow cell sorting, washing, and concentration with exceptional yield, purity, and throughput.*

Technology Overview

Inertial focusing is a high-speed phenomenon in which particles align into a tight stream as they flow through a microchannel. BendBio harnesses this principle for three fundamental processes—cell sorting, fluid exchange (cell washing), and cell concentration—which can be used individually or combined into a single fluidic circuit (Figure 1).

Cell Sorting & Fluid Exchange. The cell sorting process is designed to isolate target cells from a complex biological sample with exceptional yield and purity [3]. It efficiently removes smaller, contaminating cells, such as red blood cells and platelets, while simultaneously transferring the larger target cells into a clean buffer (Figure 2). This gentle process happens in a fraction of a second, preserving cell health and function. The robustness of the sorting mechanism ensures a consistent, purified input is provided to sensitive downstream processes, regardless of variability in the starting sample. This integrated fluid exchange is simple, high-yield, and complete. As a fundamental unit operation, it is ideal for everything from initial sample purification to gentle buffer exchange for final product formulation.

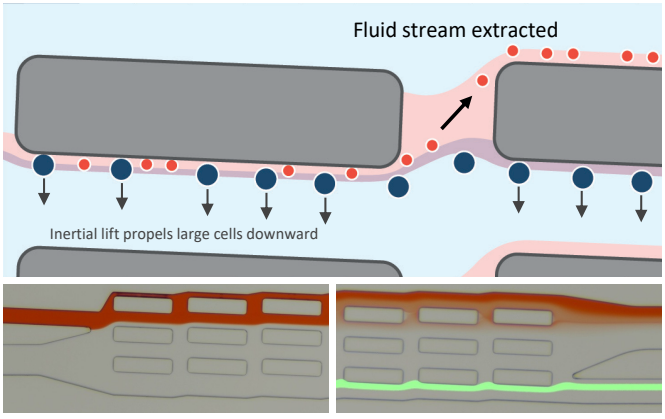

Figure 2: Inertial Sorting & Fluid Exchange. *The microfluidic array creates flow patterns that cause inertial lift to propel large, nucleated cells across the array, leaving the source fluid and small contaminant cells (red blood cells and platelets) behind. The target cells pass into a destination fluid; hence, the cells are both sorted and washed.*

Cell Concentration. The cell concentration process rapidly reduces the volume of a dilute cell suspension to enrich the target cell population [4] (Figure 3). Like sorting, this process occurs in a fraction of a second, ensuring minimal cell stress.

Up to a 400-fold reduction in volume has been demonstrated. The concentration process is high yield and deterministic. It provides a simple means of tuning cell concentration to meet the requirements of downstream processes, such as preparing cells for downstream analysis, transfection, cryopreservation, or formulating a therapeutic dose.

Cell Filtration. Beyond cell sorting and concentration, BendBio has developed microfluidic filtration modules that are highly effective in capturing cellular debris (e.g., nucleic acids) that interfere with downstream processes and assays. The filters have minimal dead-volume and trap debris without affecting cells.

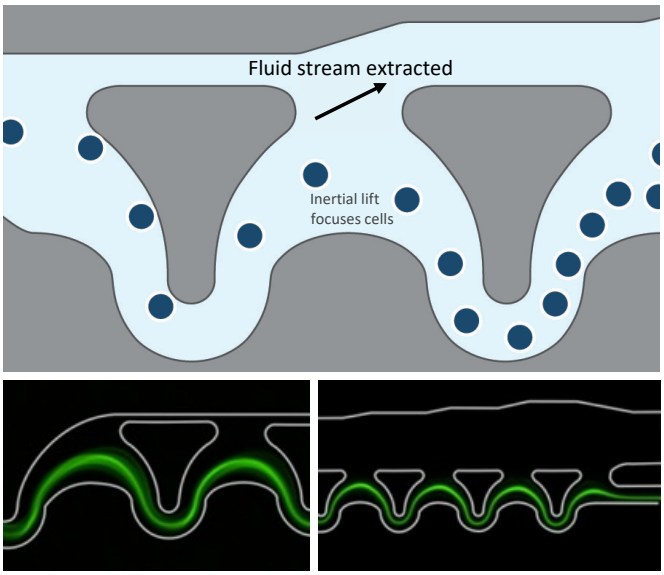

Figure 3: Inertial Concentration. *The microfluidic array is designed so that inertial lift focuses cells in the curving channel as excess, cell-free fluid is repeatedly extracted into the adjacent waste channel. The cell concentration in the curving channel gradually increases, with a 50-fold increase achievable in a single stage and more in a multi-stage device or process.*

These modules are the fundamental building blocks for automated cell processing. They can be integrated in series for a single, continuous flow process or incorporated into independently addressable devices for use at multiple steps in a complex workflow—for example, an upfront sort followed by a series of buffer exchanges and a final concentration step. This flexibility allows our partners to automate virtually any cell handling protocol.

A key advantage of our platform is its inherent scalability. Throughput can be precisely tuned by multiplexing—running multiple microfluidic channels in parallel—to meet the needs of a wide range of applications, from low-volume diagnostics to large-scale cell manufacturing. Furthermore, the design minimizes dead volume, which is critical when working with precious or limited patient samples.

Designed for Integration

BendBio's technology is a partnership-ready platform. Our core technology is embodied in robust, compact sorter and concentrator modules that have been reduced to practice. These modules serve as the foundational building blocks for integration, featuring standard Luer-lock ports for simple fluidic connection and a stackable, compact design to minimize disposable size (Figure 4).

We work with our OEM partners to deliver a customized microfluidic engine that meets the specific needs of their system.

Benefits of Partnering with BendBio

- **Accelerate Time-to-Market:** Leverage a proven, de-risked core technology to shorten R&D cycles.
- **Differentiate Your Platform:** Integrate a superior cell processing engine for a competitive advantage.
- **Focus on Your Core Competency:** We deliver a complete, validated microfluidic subsystem, freeing your team to innovate on instrument design, software, and workflow integration.
- **Customizable & Flexible:** We partner with you to optimize device characteristics, fluidic interfaces, and form factor to meet your specific application performance and instrument requirements.

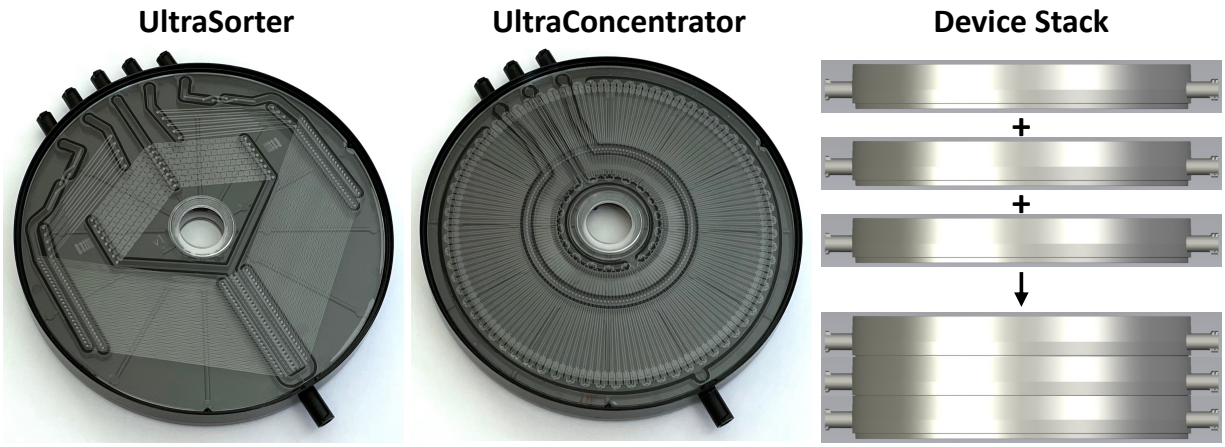

Figure 4: High-throughput Cell Processing Devices. *Devices feature luer-lock ports and are available in simplex (interface with a fluidic disc on one side) and duplex (interface with fluidic discs on both sides) configurations for even higher throughput. The devices are designed to stack, providing a clean and compact cell processing package for integration.*

Our integration support includes:

- **Compact Form Factor:** The small footprint of our devices allows for easy integration within existing or new instrument designs.
- **Standardized Interfaces:** Devices are designed with standard fluidic ports for simple, robust connection to existing pump and tubing systems.
- **Material Biocompatibility:** Chips are constructed from biocompatible polymers (e.g., cyclic olefin copolymer) suitable for sterile, single-use clinical and research applications.
- **Throughput Scalability:** We collaborate with partners to configure multiplexed arrays that achieve the precise throughput required for their application, from milliliters to liters per hour.

By integrating BendBio's technology, you can deliver significant performance and workflow advantages to your customers.

Benefits for Your Customers

- **Exceptional Cell Quality:** The gentle, reagent-free process preserves cell viability and function, delivering the highest quality starting material for downstream applications.
- **Standardized Performance:** Automation removes manual variability, providing highly reproducible results from donor-to-donor and run-to-run.
- **Simplified & Automated Workflow:** A "load-and-go" process eliminates complex manual steps and the risk of operator error, ensuring consistency across all users and sites.
- **Enhanced Sample Integrity:** The sterile, fully closed, single-use fluid path protects precious samples by eliminating the risk of microbial and cross-contamination.

A Proven Path to Scale: Commercial-Ready Manufacturing

A key challenge in commercializing microfluidic technologies is the transition from prototype to high-volume manufacturing. BendBio has solved this challenge. We have established a robust manufacturing process with our partner, Stratec, a global leader in high-precision polymer consumables (formerly Sony DADC).

Figure 5: Automated Manufacturing Line. *Parts are injection molded and assembled using a high-precision, automated line capable of commercial-scale production.*

Our devices are produced on a fully automated, high-precision injection molding line, ensuring quality and scalability from day one (Figure 5). This established process provides our OEM partners with critical advantages:

- **Quality & Consistency:** Our ISO 13485-certified manufacturing process minimizes lot-to-lot variability, ensuring reliable and reproducible performance of every chip—a critical requirement for diagnostic and clinical-grade products.
- **Supply Chain Security:** Our partnership provides proven capacity for high-volume production, securing the supply chain for your instrument launch and growth.
- **Commercial Viability:** Injection molding provides a clear path to a cost-of-goods that supports commercially successful products.
- **De-risked Partnership:** By leveraging a proven manufacturing process, you can focus on your core system development, confident in the quality and scalability of the core processing module.

Application Example: High-Performance WBC Isolation and Concentration from Whole Blood

To demonstrate the power and versatility of our platform when its modules are combined, BendBio developed a reference design for a whole blood processing module. This example showcases how sorting and concentration functions can be combined into a single, compact cartridge to deliver exceptional performance, transforming a multi-step manual process into a rapid, automated procedure.

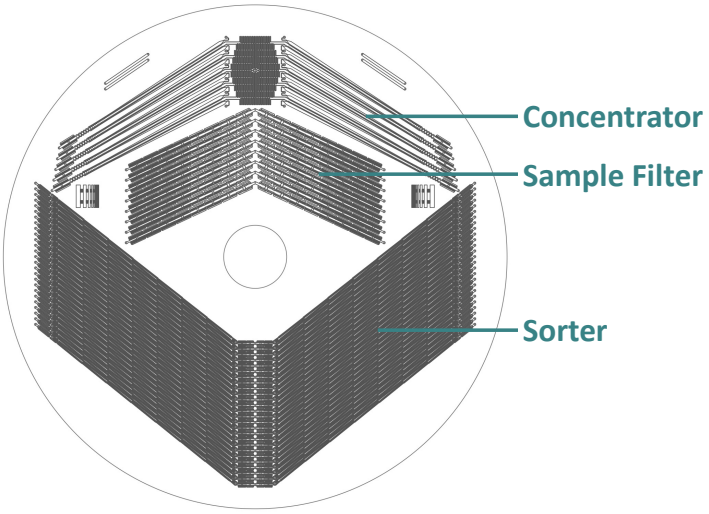

Figure 6: Whole Blood Processing Chip. *This reference design features three integrated modules: sample filter, sorter, and concentrator. Blood is processed at a rate of 150 mL/hour, with each individual cells spending just a fraction of a second in the chip. The white blood cell product is highly enriched and concentrated 10-fold relative to the input sample.*

In this reference design, a single-use cartridge incorporates three modules—a filter, a cell sorter, and a cell concentrator—to enrich nucleated cells from anticoagulated whole blood (Figure 6). The sample first passes through an in-line filter to remove debris. It then sequentially flows through the cell sorting and concentration modules, which use high-

speed inertial focusing to remove contaminating red blood cells and platelets and concentrate the target white blood cells.

This gentle, yet efficient, procedure provides unmatched whole blood processing performance, delivering high cell viability with extremely low red blood cell and platelet carryover, as shown in the performance data (Figure 7). The process facilitates high levels of consistency while reducing the risk of cell loss, contamination, and sample mix-up inherent in manual methods.

Whole Blood Processing Performance

- 99% cell viability
- 99.99% red blood cell removal (<0.01% carryover)
- 99.99% platelet removal (<0.01% carryover)
- 10x volume reduction
- 150 mL/hour (200 million cells/second)

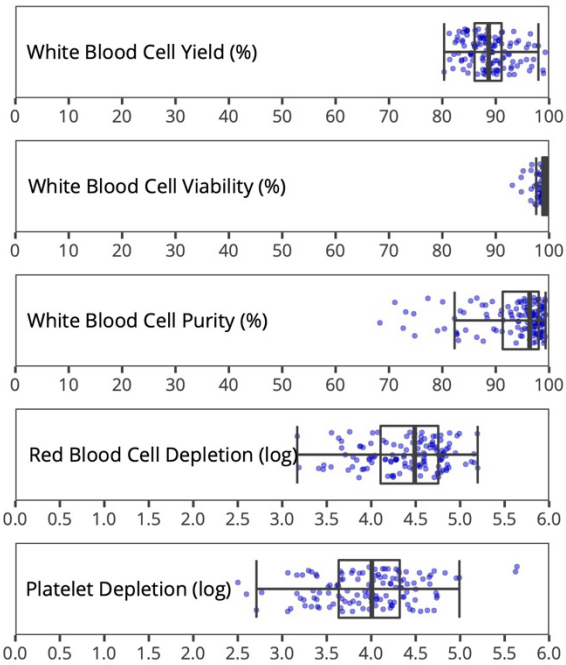

Figure 7: Whole Blood Processing Performance. *Across 127 donor samples, the device consistently isolated white blood cells with high yield, viability, and purity. The process is so efficient that it retains just 1 in 30,000 red blood cells and 1 in 10,000 platelets from the original sample.*

Conclusions

Conventional methods for cell processing fail to meet the consistency, yield, and automation requirements of today's sophisticated life science landscape. Instrument developers need a modern, integratable solution to stay competitive.

BendBio's inertial-focusing-based platform technology provides the core engine for next-generation automated systems. Our superior, partnership-focused approach provides significant advantages over centrifuge-based methods, enabling you to confidently develop and launch market-leading instruments for research and clinical applications.

About BendBio

BendBio is a life sciences technology company that develops and manufactures core microfluidic "engines" for cell processing. Our team comprises experts in microfluidic design, computational fluid dynamics, and scalable manufacturing. We partner with instrument manufacturers and life science companies to integrate our patented inertial focusing technology into their next-generation platforms for research, diagnostics, and therapeutics. Our mission is to enable our partners to deliver superior, automated solutions to the scientific and clinical communities.

To discuss a partnership, please visit **bendbio.com** or contact us directly at **partners@bendbio.com**.

bendbio.com

References

[1] D. Di Carlo, D. Irimia, R. G. Tompkins, and M. Toner, “Continuous inertial focusing, ordering, and separation of particles in microchannels.,” Proc. Natl. Acad. Sci. U.S.A., vol. 104, no. 48, pp. 18892–18897, Nov. 2007, doi: 10.1073/pnas.0704958104.

[2] E. Ozkumur et al., “Inertial focusing for tumor antigen-dependent and -independent sorting of rare circulating tumor cells.,” Sci Transl Med, vol. 5, no. 179, p. 179ra47, Apr. 2013, doi: 10.1126/scitranslmed.3005616.

[3] B. R. Mutlu et al., “Non-equilibrium Inertial Separation Array for High-throughput, Large-volume Blood Fractionation.,” Sci. Rep., vol. 7, no. 1, p. 9915, Aug. 2017, doi: 10.1038/s41598-017-10295-0.

[4] J. M. Martel et al., “Continuous Flow Microfluidic Bioparticle Concentrator.,” Sci. Rep., vol. 5, p. 11300, June 2015, doi: 10.1038/srep11300.

[5] J. F. Edd et al., “Isolation of circulating tumor cells,” iScience, vol. 25, no. 8, p. 104696, Aug. 2022, doi: 10.1016/j.isci.2022.104696.