Single Use Cartridge: Passive Whole Blood Processing + Sensor integration

Objectives: A disposable system for collecting a sample of 2-10uL of whole blood, diluting 20-40x, mixing and delivery to a sensor mounted on a circuit board.

Challenges: (i) The sample must be mixed completely without active pumping. (ii) The sensor is wire bonded and mounted on a circuit board, creating an irregular surface around the perimeter of the sensing surface.

Solutions: (i) A blood metering device draws sample with +/- 2% variability, which is then diluted with buffer and delivered to the cartridge. (ii) A three component cartridge, about the size of a USB stick was developed which included a leak-proof seal to enclose the sensing surface, and provide for air-bubble trapping and sample overflow.

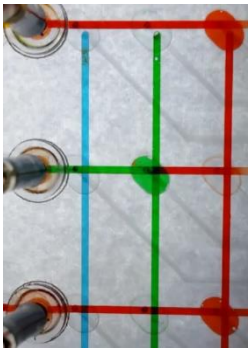
Single-Use Cartridge: Water Quality Test + Active Fluid Control

Objective: A disposable system which manages the downstream metering mixing and delivery to the sensor from a concentrated water sample.

Challenges: Integrate multi-step workflow into a disposable suitable for use with a backpack-based instrument system.

Solution: Develop a cartridge that performs binding assays using on board, pneumatically controlled valves with a rugged instrument interface. Semi-automated control is used to perform all steps required for the assay (volume metering, mixing, capture, washing, detection).

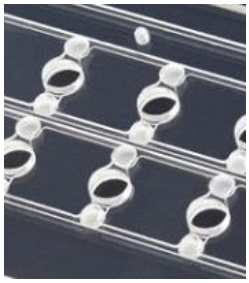
Highly Multiplexed Fluid-Handling Manifolds



Objective: Highly multiplexed valve manifolds for programmable fluid delivery from multiple inlets to multiple output ports.

Challenges: Minimize dead volume and separate the electromechanical controls from the fluids.

Solution: A manifold with on-board pneumatic valves, actuated by external electro-mechanical controls. 32 fluid streams can be managed and combined by addressing different sets of on board pneumatically controlled valves and delivered to multiple output ports.



Cell Culture & Organ-on-Chip

Objective: Multi-chamber flow-cells for parallelized study of cell culture and interaction.

Challenges: Use a single inlet and outlet to provide equal flow rate to each chamber while preventing direct interaction between different compartments.

Solution: Integration of custom membranes at the inlets and outlets of each chamber to control fluidic resistance and providing cell confinement. Applications include liver co-cultures, and lung co-culture.

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Scientific Expertise & Analytical Objective

The Analytical Objective

Microfluidics provides a means for miniaturizing an assay workflow and porting it into a small total analytical system that is portable and rugged.

The Analytical Objective means the product achieves the sensitivity, dynamic range and limit of detection required for diagnostic application.

Scientific expertise in the physics and chemistry of microfluidics, and an in depth knowledge in bioanalytical systems are required to integrate the materials, biology, and engineering.

While many developers can mold and machine channels with great sophistication, few understand the underlying science which controls the analytical performance.

ALine brings years of experience in scientific disciplines including physics, bio-chemistry, microfluidics, materials science and various engineering disciplines to address all aspects of the microfluidic system.

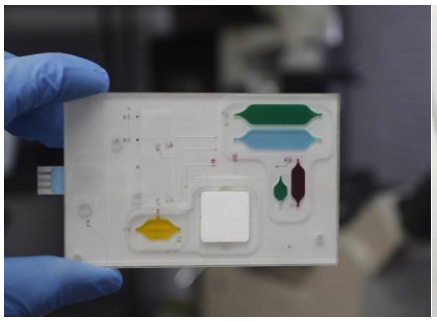
We deliver not just a device, but industry know-how in product development.

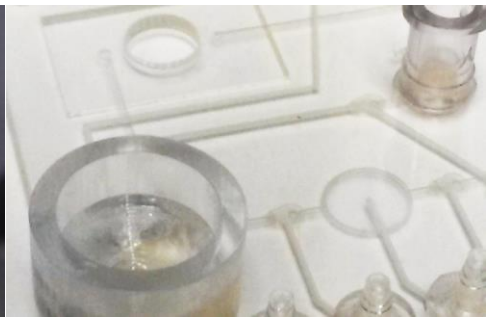
Performance Engineering - Design Rules & Toolbox of Functions

ALine has established a set of design rules and geometries that demonstrate:

- Metering of volumes between 5 and 25 uL with < 5% variability
- De-bubbling of rigorously mixed solutions
- Mixing to increase kinetics of binding
- On-board valve integration with well-characterized performance
- On-board peristaltic pumping, with variable pump volumes per cycle

Performance characteristics are supported by a series of technical publications, available through confidential disclosure. Contact info@alineinc.com to get access to these articles.





Integrated Functional Solutions

- Incorporate electrodes, membranes, on-board valves & pumps
- Integrate optical and electro-active sensors; PCBs, silicon and glass
- Integrate injection molded components and blister packs
- Reagent deposition
- Pop-on fluidic components that interface to a fluidic 'motherboard'

Selected Scientific Publications Using Custom ALine Devices

Live Mammalian Cell Arrays
Kristina Woodruff, Luis M Fidalgo, Samy Gobaa, Matthias P Lutolf, Sebastian J Maerkl, **Nature Methods** 10, 550–552 (2013)

Automated Reagent-Dispensing System for Microfluidic Cell Biology Assays
Jimmy Ly, Michael Masterman-Smith, Ravichandran Ramakrishnan, Jing Sun, Brent Kokubun, R. Michael van Dam. **Journal of Laboratory Automation**, 2013, 18,6, 530-541.

Microfluidic Device for Mechanical Dissociation of Cancer Cell Aggregates into Single Cells. Xiaolong Qiu, Janice De Jesus, Marissa Pennell, Marco Troiani and Jered B. Haun **Lab Chip**, 2015,15, 339-350

A Microfluidic Device for Dry Sample Preservation in Remote Settings
Stefano Begolo, Feng Shen and Rustem F. Ismagilov
Lab Chip, 2013,13, 4331-4342

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