Product Catalog

iFlow™

Cell Perfusion System

Organ-On-a-Chip (OOC) System

Doc: 01F08
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iFlow™ Perfusion Systems

PreciGenome

Key Benefits

- **High Performance & Reliability**
- **Flexible Control Modes**
- **Simple Setup**
- **Multi Perfusion Modes**
- **Cost Effective**
- **Custom design &OEM**

Applications

- Droplet cell culture on chip
- Cell response to medium change
- Live cell imaging
- 3D cell culture
- Stem cell assays
- Shear stress experiments
- Drug screening
- Toxicity tests
- Calcium imaging
- Bioreactor research
- Drug response studies
- Intracellular trafficking

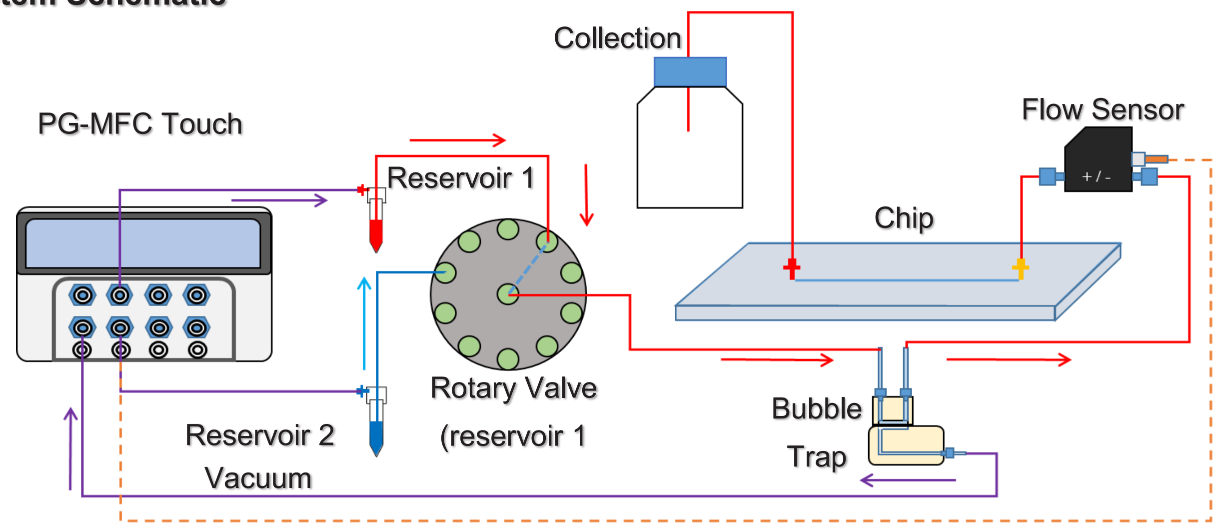
Multi-Reagent Perfusion System

When used with our **rotary selection valves**, **PreciGenome's PG-MFC pressure controller** can allow multiple reagent switching, which is perfect for organ-on-a-chip and cell culture.

Our rotary valves have a dead volume of only **4.5 µl.** Precise flow rate control can be achieved by an optional **liquid flow sensor**.

System Contents
iFlow controller PG-MFC-8CH
SwitchEZ rotary valve (6, 8, 10, 12, & 16 available)
2x reservoir kits (1.5, 15, or 50 ml)
PG-LFS flow sensor (assorted full scale, optional)
Tubings & fittings

System Schematic



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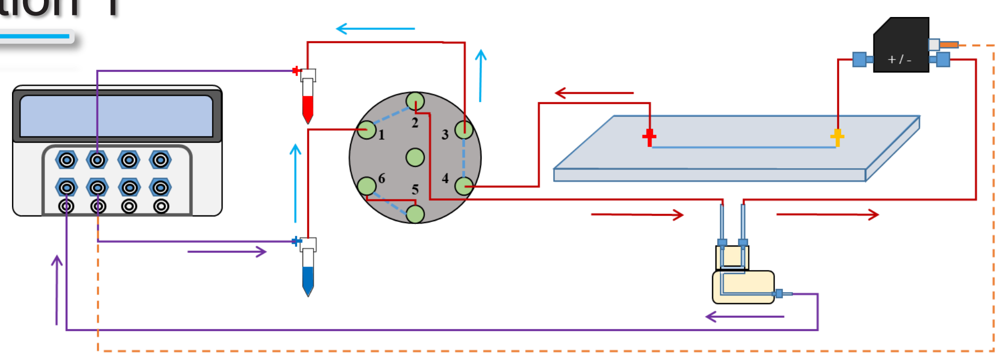
Recirculating Perfusion System

PreciGenome's PG-MFC pressure controller can allow a recirculating perfusion system when used with a **rotary switching valve**, which is perfect for shear force studies on cell culture.

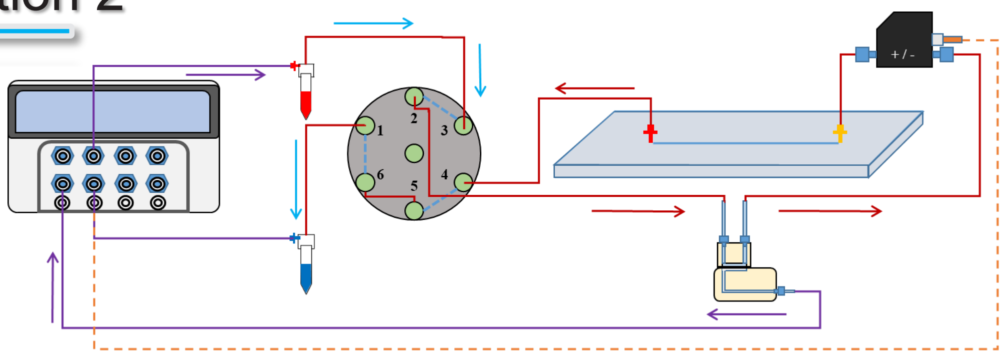
Such systems can be configured for **unidirectional/bidirectional flow**. Precise flow rate control can be achieved by an optional **liquid flow sensor.**

System Contents
iFlow controller PG-MFC-8CH
SwitchEZ bidirectional 3-way/2-position rotary valve
2x reservoir kits (15, 50, or 100 ml)
PG-LFS flow sensor (assorted full scale, optional)
Tubings & fittings

Position 1



Position 2



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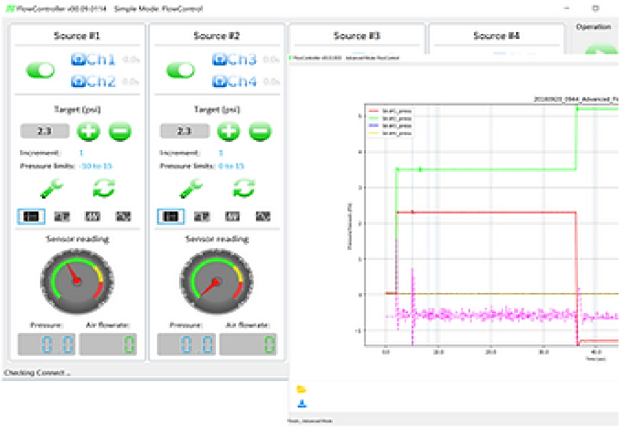
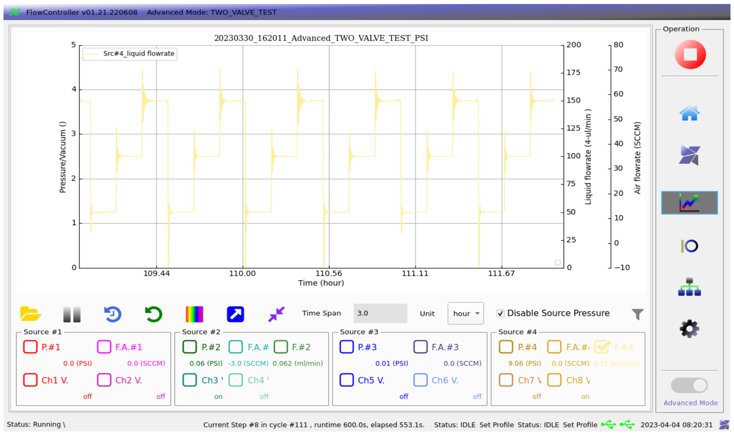
Perfusion System Extended Runtime



UI Software and API library for complex process control and real-time data monitoring

With the **iFlow software's advanced scripting**, users can create looping protocols that run for **over a week** with no drop in performance or accuracy. Nonrecirculating perfusion systems (not pictured) are also capable of these extended runtimes.



Recirculation System Automation

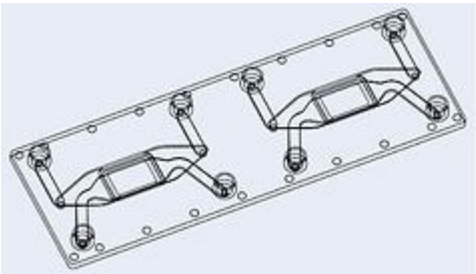
Catalog #	Name
PG-PF-LT2-A	Duplex Perfusion System Type-A
PG-PF-LT2-B	Duplex Perfusion System Type-B
PG-PF-8-MRD	Multi-Reagent Perfusion System w. iFlow Touch™ controller
PG-PF-LT2-MRD	Multi-Reagent Perfusion System w. iFlow Light™ controller
PG-PF-4-REC	Recirculating Perfusion System w. iFlow Touch™ controller (4 channel)
PG-PF-8-REC	Recirculating Perfusion System w. iFlow Touch™ controller (8 channel)
PG-PF-LT2-REC	Recirculating Perfusion System w. iFlow Light™ controller

Microfluidic Chips

Perfusions chambers are a critical aspect of cell perfusion, especially for live-cell imaging. They have to meet two important requirements: maintain cells in a healthy state and allow the living cells to be observed with the highest possible resolution.

A wide range of commercial perfusion and imaging chambers are now available. It includes conventional perfusion chambers, i.e. glass bottom Petri dishes, multi-well chambers mounted on microscope slides, heating stages with a variety of interchangeable perfusion adapters, or microfluidic chips. Depending on your experiment, some chambers will be more suited to your needs.

PreciGenome offers a variety of microfluidic chips in different materials to meet most of our customers' application requirements. Three types of materials, including polymers, glass and silicon, are commonly used to fabricate microfluidic chips. Material of the chip is selected depending on the application requirements, including chip design, types of solvent or reagent used for experiment, needs of the application, budget, and fabrication time, etc.



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Key Factors for Perfusion System Selection

Media Recirculating or Non-recirculating System

It depends on the whether the cell to cell chemical interaction is essential or not in your experiment.

Recirculation perfusion system uses a given volume of culture medium and recirculates the medium throughout the perfusion flow. By using the same culture medium, the molecules secreted by the cells are kept in the same culture flow.

Non-recirculating perfusion system can be used for experiments where cell-cell chemical communication is not important or these chemical cues should be ruled out. This perfusion system allows to remove secreted factors, waste products and thus wash cells through the media flow.

Shear Stress

In perfusion cell culture, hydrodynamic shear stress can be a limiting factor.

Lower shear stress is desired in order to eliminate its effects by different approaches. One way is to lower the perfusion flow rate. Another way to reduce shear stress is to use microfluidic chips with dedicated geometries. For example, microfluidic chips with a porous membrane can be used as a barrier for the medium flow to minimize the shear stress.

On the other hand, some experiments use high level of shear stress to investigate endothelial cell function with different shear stress conditions in in-vivo conditions.

Bubble Issue

Air bubbles have a significant detrimental effect on cell culture. First, the liquid flow can obstructed seriously by bubbles trapped inside tubing or microfluidic channels. Second, cells can be killed at their gas-liquid interface of the bubbles in the culture flow.

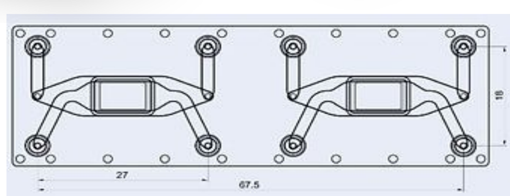
One way to eliminate bubbles is to flush the system by applying a high flow rate before the cells are seeded. Adding proper soft surfactant (i.e. SDS) is very effective way to release air bubble from perfusion chamber. Another way is to add an inline bubble trap in the perfusion flow to remove the bubble generated during the cell culture.

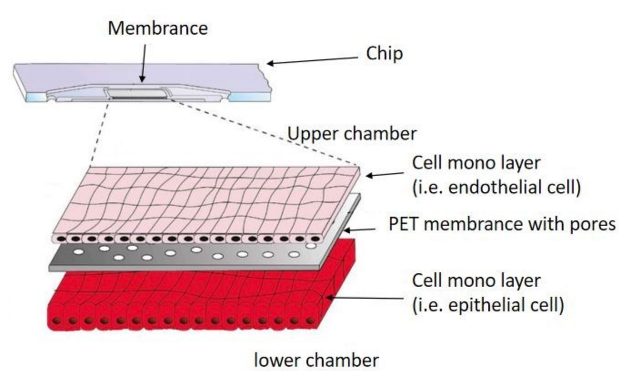
Temperature control

For long-term live cells studies, temperature is a critical parameter of the cell environment.
Keeping the cells at a proper temperature with temperature control system is required for the perfusion experiment. PreciGenome also offers temperature control solutions.

iFlow™

Organ-on-a-Chip System





PreciGenome

iFlow™ Organ-on-a-Chip Systems

Organ-on-a-Chip (OOC) technology provides a novel in vitro platform with a possibility of reproducing physiological functions of in vivo tissue, more accurately than conventional cell-based model systems.

The technology opens up great opportunities for next-generation experiments of mimicking human organ functionality, microphysiology and morphology in vitro, replacing traditional animal-based model systems.

By realizing different organ functions on a chip, Organ-on-a-Chip technology is potentially useful for building models of complex diseases. The technology can also be used to study pharmacokentic model when new drugs are being developed.

PreciGenome offers customizable Organ-on-Chips system, which is able to recreate the dynamic in-vivo conditions for modeling biochemical and biophysical features of cells' native environment. Combining the PG-MFC flow controller and microfluidic membrane chips, the system provides multi-channel perfusion or reagent recirculation capability to ensure cell nurturing over weeks.

System Benefits

High Performance & Reliability

Flexible Control Modes

Simple Setup

Cost Effective

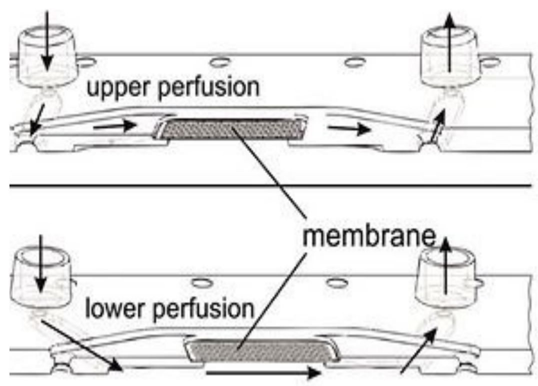
Custom Design & OEM

Catalog #	Name
PG-OOC-LT2-MRD	OOC system w. iFlow Light™ controller
PG-OOC-8-MRD	OOC system w. iFlow Touch™ (8CH) controller
PG-OOC-LT2-REC	OOC system w. iFlow Light™ Controller (recirculating)
PG-OOC-8-REC	OOC system w. iFlow Touch™ (8CH) controller (recirulating)

Organ-on-a-Chip Chips

The chips contain two cavities, each comprising an integrated membrane serving as cell culture area. Cells cultured on the membrane are perfusable independently from both the apical or basal side through upward directed (upper perfusion) and downward directed (lower perfusion) channels. The chips have two in- and outlet ports above and below the membrane.

The chip is made by injection molding from polystyrene (PS) or Topas. A 12 µm thick polyethylene terephthalate (PET) membrane (TRAKETCH) with a pore diameter of 8 µm or 0.2 um and a pore density of 1X10e5 pores/cm² was integrated in the upper and lower part of the chip by heat-sealing with the bulk material. This allows for organ-on-a-chip experiments such as small molecule transfer measurements, on-chip dialysis or cell culture experiments.



OOC membrane chip

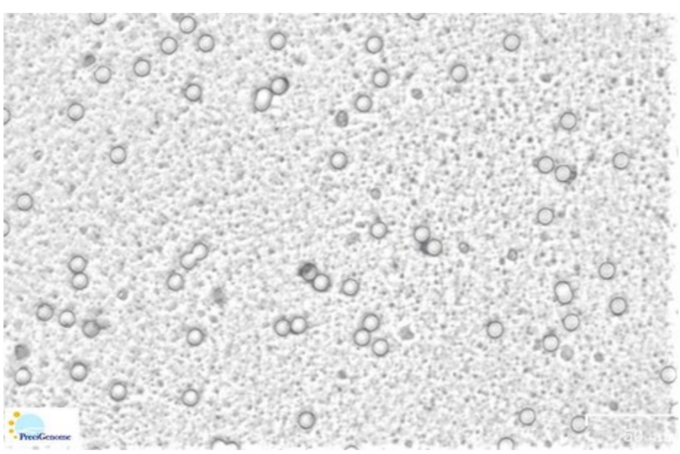
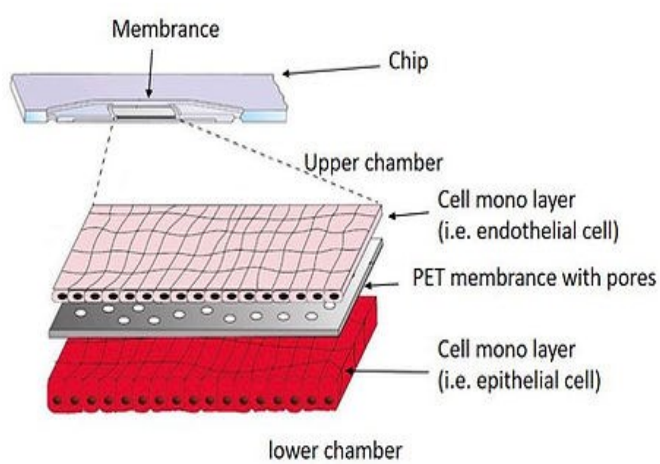
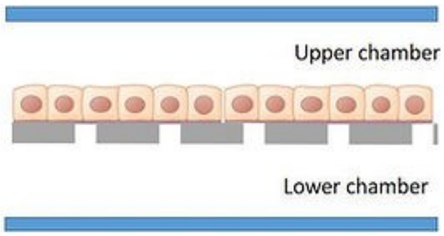


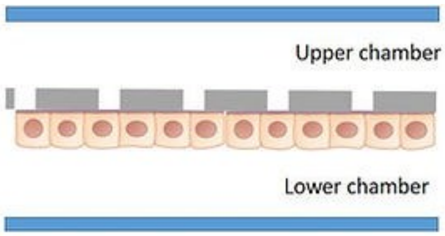
Image of porous PET membrane layer of the chip



Culture Modes and Applications

Mode #1: Single-sided Culture





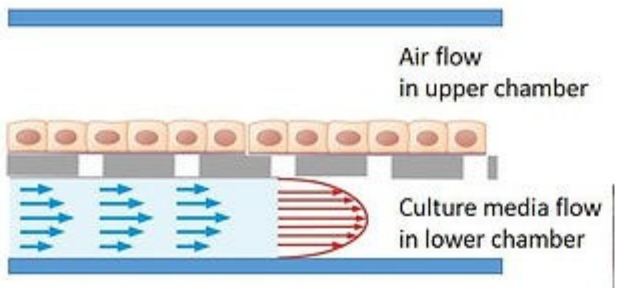
A cell monolayer is cultivated on one side of the membrane in the chip.

Application Examples of Single-sided Culture

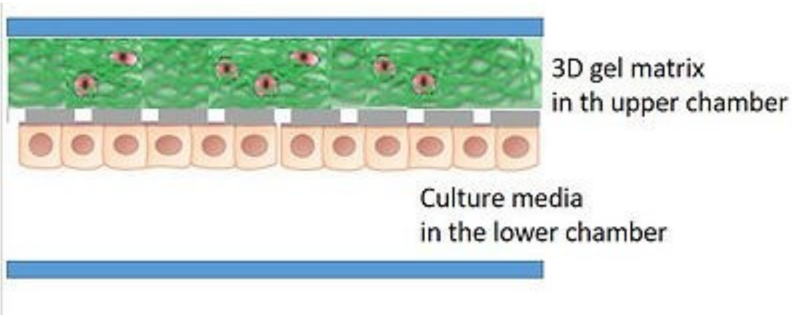
Skin-on-a-Chip Model

Skin Models with air-liquid interface are a good fit for this culture mode. Skin-on-a-chip (SoC) are used for testing of topical pharmaceuticals and cosmetics, studying the pathology of skin diseases and inflammation. Also it is to test for the presence of antigens or antibodies which could denote the presence of a pathogen.

The model in the figure shows a polarized skin cell monolayer is cultured on one side of the membrane with cells exposed to air in the upper chamber. The flow of culture medium goes through the lower chamber..

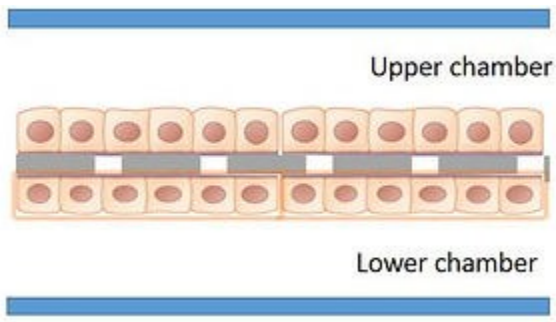


Apical-Basal Cell Polarity Assay Model



A cell monolayer is cultivated at one side of the membrane. On the other side, a 3D gel matrix fills the chamber. In some applications cells are embedded in the 3D gel matrix. Chemical factors inside the 3D gel matrix lead to the polarization of a cell monolayer at the opposite side of the 3D gel matrix.

Mode #2: Double-sided Culture

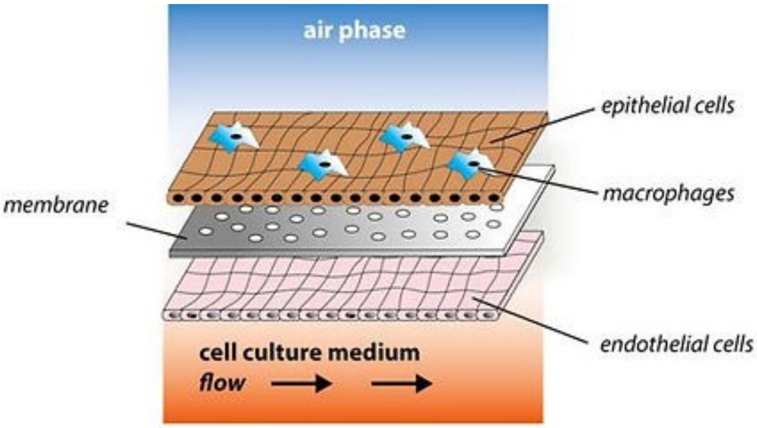


Two cell monolayers, one layer on the top of membrane and another layer beneath the membrane, are cultivated simultaneously in the chip. Molecules are transferable through the pores on the membrane. Thus, this culture mode is fit for cell studies such as signaling, co-culture, and transport studies.

Lung-on-a-Chip Model

The lung-on-a-chip is a complex, three-dimensional model of a living, breathing human lung on a microchip. The device is made using human lung and blood vessel cells and it can predict absorption of airborne nanoparticles and mimic the inflammatory response triggered by microbial pathogens. Lung-on-a-chips are being designed in an effort to improve the physiological relevance of existing in vitro alveolar-capillary interface models. Such a multifunctional microdevice can reproduce key structural, functional and mechanical properties of the human alveolar-capillary interface.

In this example (reference [2]), a lung-on-a-chip model establishes a human in vitro alveolus model system, consisting of vascular and epithelial cell structures with cocultured macrophages. The infection of epithelial cells induced a high inflammatory response that spread to the endothelium. The system demonstrated significant endothelial cell damage associated with loss of barrier function. It can be used as an immune-responsive model reflecting the complex crosstalk between pathogens and host. This is a powerful system for mechanistic studies of host-pathogen interactions and the identification of molecular and cellular targets of novel treatment strategies in pneumonia.



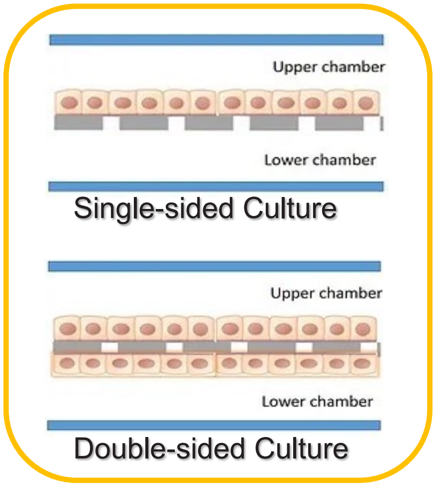
Example of Lung on a Chip model with alveolar epithelial cells in air phase in the upper chamber and endothelial cells cocultured with perfusion medium in the lower chamber. Figure is from reference [2].

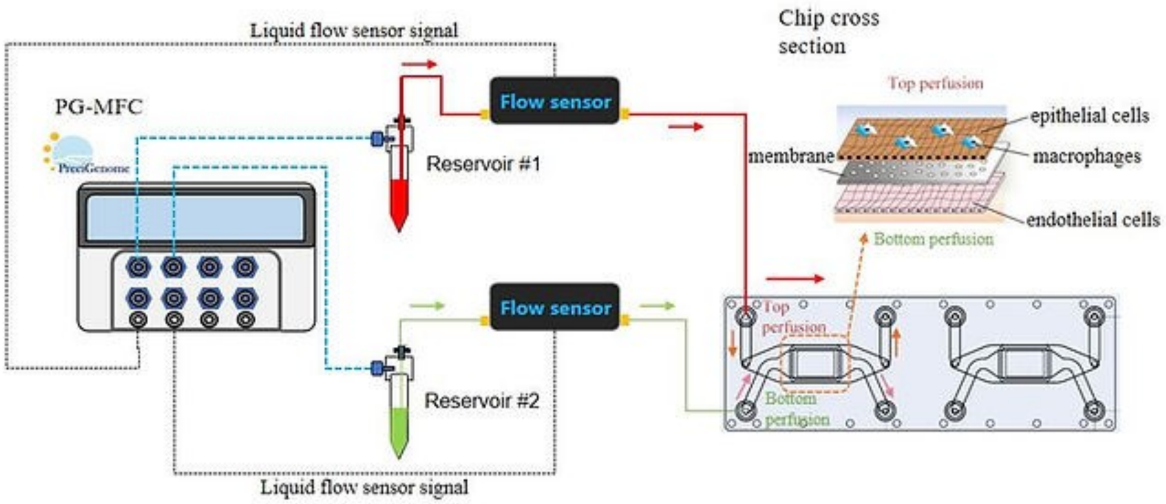
References
1. Raasch, M.; Rennert, K.; Jahn, T.; Peters, S.; Henkel, T.; Huber, O.; Schulz, I.; Becker, H.; Lorkowski, S.; Funke, H. Microfluidically supported biochip design for culture of endothelial cell layers with improved perfusion conditions. Biofabrication 2015
2. Deinhardt-Emmer S, Rennert K, Schicke E, Cseresnyes Z, Windolph M, Nietzsche S, Heller R, Swiczak F, Haupt KF, Carlstedt S, Schacke M, Figge MT, Ehrhardt C, Löffler B, Mosig AS; Co-infection with Staphylococcus aureus after primary influenza virus infection leads to damage of the endothelium in a human alveolus-on-a-chip model., Biofabrication, 2020

System Option #1: Multi-Channel Culture System

PreciGenome's iFlow pressure controllers can be purchased with bundles for **organ-on-a-chip** applications. The iFlow controller's **combined vacuum/pressure functionality** make it perfect for culture media recirculation.

Bundles come in both multi-channel and recirculating configurations. Chips may be used in single or multi-sided applications.





System Contents
iFlow controller PG-MFC-8CH
2x reservoir kits (1.5, 15, or 50 ml)
OOC membrane chip (optional)
PG-LFS flow sensor (assorted full scale, optional)
SwitchEZ rotary valve (PG-OOC-X-REC only)
2x SwitchEZ 3-way valves (PG-OOC-LT2-REC only)
Tubings & fittings

System Setup Example
Lung-on-a-Chip

In this lung-on-a-chip case, two pressure and one vacuum sources are used which connect to different inlets of a chip with our PG-MFC controller. PG-MFC controller has multiple sources of vacuum and pressure. It meets most requirements of organ-on-a-chip applications.

Two pressure lines push different culture media to deliver into the chip to mimic blood flow into lung and exchange chemicals through cell channel bilayer. The vacuum line connects to the side chamber to simulate the breathing process in a lung.

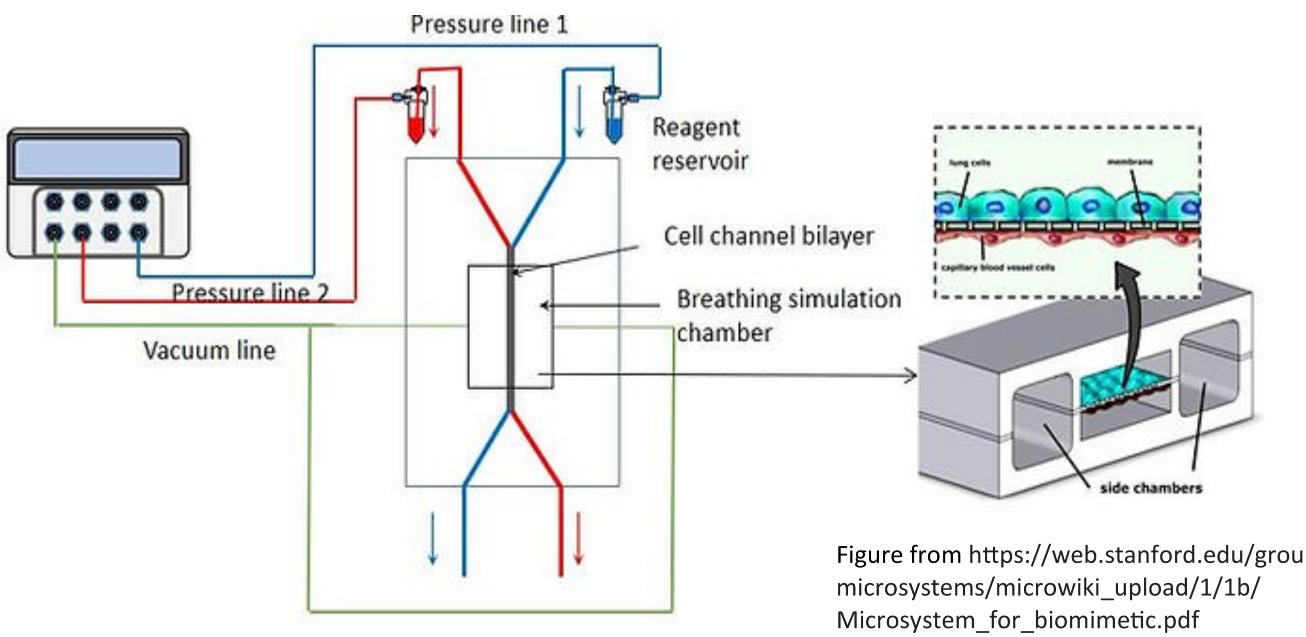
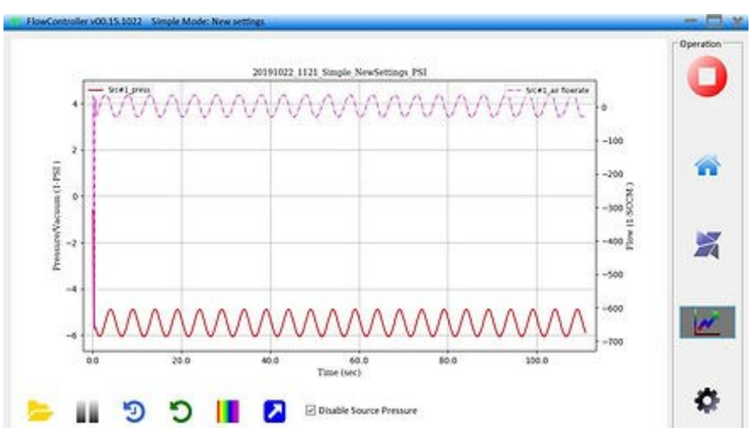


Figure from https://web.stanford.edu/group/microsystems/microwiki_upload/1/1b/Microsystem_for_biomimetic.pdf

Note: Chip is NOT included.



Example of sine output on vacuum Line, which is used to actuate the membrane between the top and bottom chambers.

Meanwhile, the airflow rate is also monitored in real-time to indicate the leakage in the flow.

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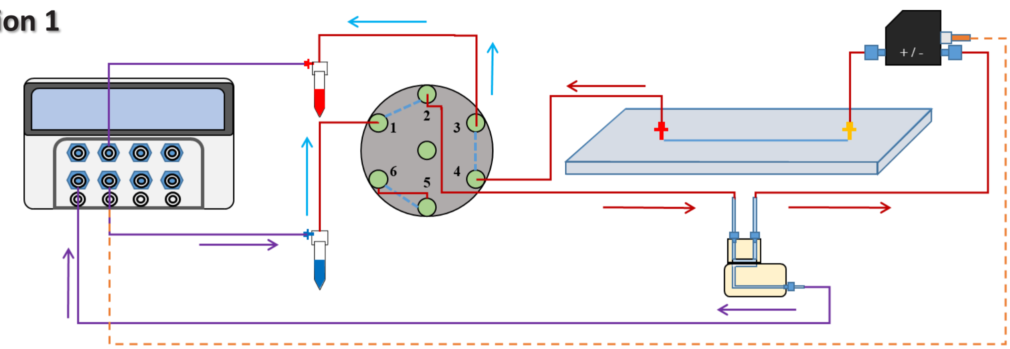
System Option #2: Culture Media Recirculation System

PreciGenome's PG-MFC pressure controller can allow a controlled recirculating perfusion system when used with a rotary switching valve, which is perfect for shear force studies on cell culture.

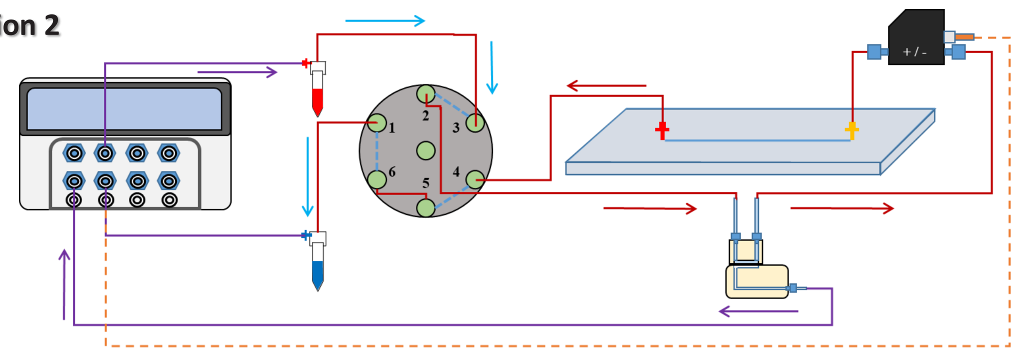
Such systems can be configured for unidirectional/bidirectional flow. Precise flow rate control can be achieved by an optional liquid flow sensor.

System Contents
iFlow controller PG-MFC-8CH
SwitchEZ bidirectional 3-way/2-position rotary valve
2x reservoir kits (15, 50, or 100 ml)
PG-LFS flow sensor (assorted full scale, optional)
Tubings & fittings

Position 1



Position 2



Notes

Some of Our Customers

PreciGenome is located in the heart of Silicon Valley, San Jose, California, USA. We have been focusing on developing nanoparticle synthesis systems and solutions for our customers since we started our business. Our technology enables rapid prototyping with high quality and reliable performance for lipid nanoparticles, liposomes, PLGA, etc.

HEADQUARTER

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