

# BIOFLUX™

## Bringing Physiological Flow To Live Cell Assays

Many physiological processes take place under flow conditions: plaque forms on teeth in the presence of saliva flow, cancer cells circulating throughout the body and blood flowing through the vasculature. Many of these processes are still studied *in vitro* without the presence

of flow. BioFlux combines the **throughput and convenience of a well plate with the physiological relevance of controlled shear flow to emulate *in vivo* conditions.** The system comes complete with all the tools necessary to generate your data quickly and reliably.

### Microscope

- The system works with your existing inverted microscope or one of our automated microscopy stations
- Compatible with fluorescence, brightfield, phase and confocal imaging

### User friendly software

- Automation of experiments
- Powerful analysis package
  - Fluorescence intensity
  - Percent adhesion
  - Rolling velocity / particle tracking
  - Image stacking
  - And more

### Benchtop instrument

- Up to 24 assays in parallel
- Precise control of shear force (0,1 - 200dyne/cm<sup>2</sup>)
- Reduction of consumption of expensive reagents and valuable cells
- Quick and easy setup with no messy pumps or tubing



# Applications in Hematology

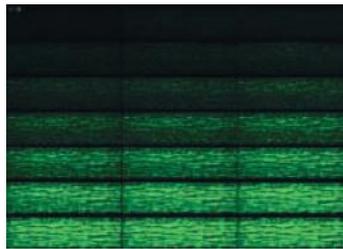
## Platelet Function

Platelet aggregation, or thrombosis, occurs in response to vascular injury where the extracellular matrix below the endothelium has been exposed. It can be triggered in the presence of shear flow and is dependent on many biochemical interactions present in whole blood. The BioFlux system enables simulation

of vasculature shear rates up to 200 dyne/cm<sup>2</sup> (5000 s<sup>-1</sup>) using whole blood, platelet-rich plasma or other cells of interest. Experiments can be run on purified matrix proteins (von Willebrand factor, collagen, etc.) or endothelial cell monolayers. The system uses as little as 20µL of reagents per experiment.

### Representative applications:

- Platelet aggregation and adhesion
- Thrombosis
- Atherosclerosis models



Thrombosis on vonWillebrand factor under high shear - 10 minute timelapse (going from right to left then down) with calcein AM labeled whole blood. Anti-thrombotic compounds can be screened and evaluated for dose-response using human cells and whole blood under physiological shear, a model which is impossible to replicate in a conventional well plate.

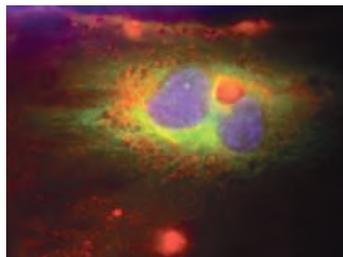
## Vascular Biology

The endothelium is a dynamic mediator of many physiological phenomena and the crossroads for immune system function, cancer metastasis and atherosclerosis among others. Endothelial cells have been shown to alter their morphology and gene expression in the

presence of the shear flow they routinely see in the vasculature. As such, the relevance of endothelial cell culture and downstream assays increases significantly with the presence of flow.

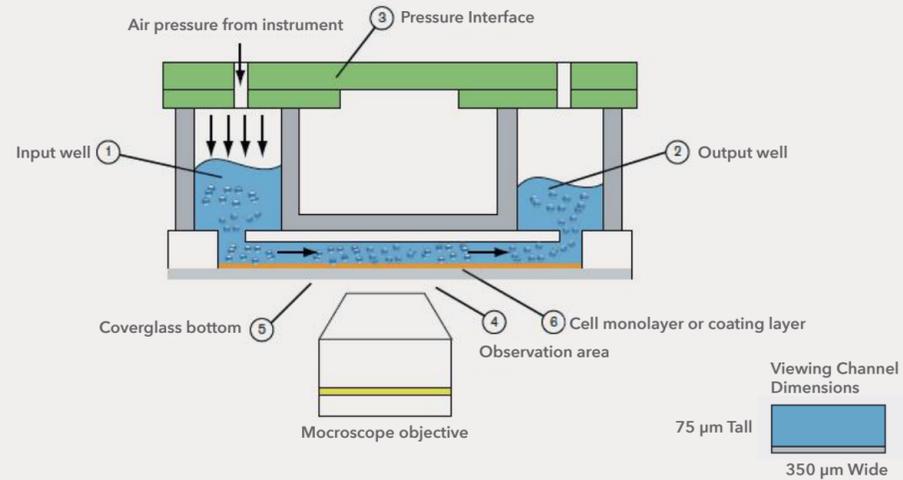
### Representative applications:

- Specialized cell culture
- Cell adhesion
- Atherosclerosis
- Mechanical loading
- Thrombosis
- Migration and invasion



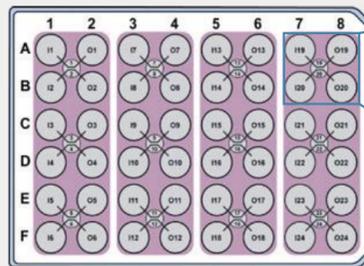
A primary peripheral blood monocyte (red) attached to endothelial cells. Post-fixation and permeabilization, cells were stained with anti-tubulin (green), wheat germ agglutinin (red) and Hoescht 33342 (blue). The BioFlux system enables a variety of assays which span the entire adhesion cascade from initial rolling adhesion to transmigration.

## Principles of Operation



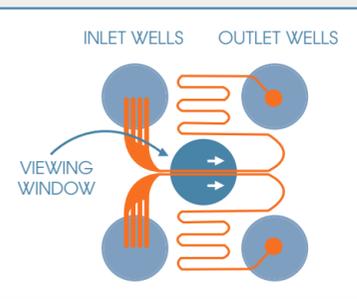
BioFlux plates contain an array of microfluidic flow channels arranged on a well plate format. Each flow channel connects to an **input well (1)** and an **output well (2)** on the plate. To begin an experiment, cells and other reagents are loaded into designated input wells using a standard pipettor or automated liquid handling robot. The BioFlux **Pressure Interface (3)** couples to the top of the well plate and applies a controlled pneumatic pressure from the control instrument to the top of the wells which drives the fluid through the channels at a user-defined flow rate. Reagents in the channel flow across an **observation area (4)** which is situated between the wells. High resolution imaging data is acquired at this location.

The bottom of the channels are comprised of **180 μm coverslip glass (5)** which make them compatible with brightfield, phase, fluorescence and confocal microscopy. After clearing the observation area, the fluidic reagents collect in the output well. The flow channels can be **coated with proteins, adhesion molecules and cellular monolayers (6)** to conduct a wide range of cell-cell and cell-ligand interaction assays. The flow profile in BioFlux Plates is extremely uniform and laminar. This ensures that each experiment is reliable, meaningful and reproducible. The micron-sized channel dimensions reduce the required reagent volumes to as little as 20 μL per well.



### 48-well Plate, High Shear, 200 dyne/cm<sup>2</sup>

This plate features 24 experimental channels, each with an input and output well. The channels have been designed to reach a maximum shear stress of 200 dyne/cm<sup>2</sup> making them suited for platelet adhesion and aggregation assays, as well as other high shear applications.



## BioFlux Plate Configurations

BioFlux Plates are consumable devices featuring Well plate Microfluidic™ technology. There are different plate designs to accommodate a wide range of applications.

### 48-well Plate

This plate features 24 experimental channels, each with an input and output well. The high number of experimental channels makes it ideally suited for testing larger sets of conditions, such as compound screening or genetic variants.

- Up to 24 assays
- Up to 1 mL per well
- Glass, PDMS or custom bottom 0 – 20 dyn/cm<sup>2</sup>
- Glass bottom 0 – 200 dyn/cm<sup>2</sup>

### 24-well Plate

This plate features 8 experimental channels, each with two input wells. It provides the ability to dynamically (<500msec) change between two input sources. The secondary input can be used to add compound, change media type, introduce a second cell type or exchange wash buffer. Ideally suited for overnight experiments, stem cell applications, drug screening, and high content analysis.

- Up to 8 assays
- Up to 3 mL per well
- Glass or PDMS bottom 0 – 20 dyn/cm<sup>2</sup>

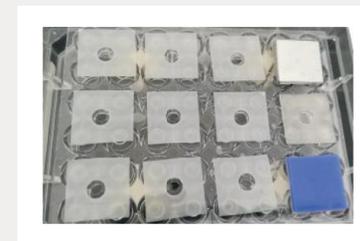
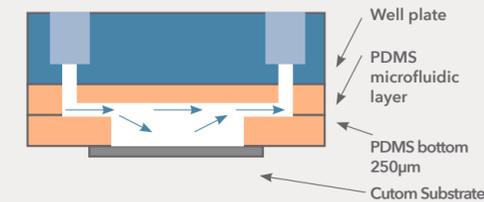
### 6-well Plates for Long Term Culture

- Up to 3 assays
- Up to 16 mL per well
- Glass bottom 0 – 50 dyn/cm<sup>2</sup>

NEW

## Custom substrate plate for testing novel materials

These plates allow users to control physiological parameters and observe bacterial attachment and biofilm growth over a variety of substrates. In particular infections of dental implants, orthopedic implants and in-dwelling device surfaces and environmental biofilms in industrial settings.



Generation of physiologically relevant gas gradients

A variety of materials and coatings can be used as long as a low roughness surface of at least 15x15mm (25x25mm shown) is available. Once stuck, the coupon can be recovered for further analysis by cutting it with a scalpel.



## A system that meets YOUR needs

The BioFlux System was designed with a keen understanding that every lab has its own unique needs. That's why the BioFlux can be configured in a variety of ways to meet your specific requirements for automation, analysis and budget.

### BioFlux EZ



### BioFlux 200



### BioFlux DCIS



### BioFlux 1000Z



Overview	The most cost-effective BioFlux system	The solution for labs with a microscope	The fully integrated, easy-to-use solution	The fully customized solution
<b>Configuration</b>	Standard	Standard	Standard	Fully customized
<b>Applications supported</b>	All but Chemotaxis, Wound Healing and Angiogenesis	All	All	All
<b>Throughput</b>	8 flow assays	24 flow assays (96 with Quattro)	24 flow assays (96 with Quattro)	24 flow assays (96 with Quattro)
<b>Temperature control</b>	Optional	Yes	Yes	Yes
<b>Pulsatile flow option</b>	No	Yes	Yes	Yes
<b>Gas or Dual gas option</b>	No	Yes	Yes	Yes
<b>Plate formats</b>	6-well 48-well	6-well 48-well 24-well (2 inlet)	6-well 48-well 24-well (2 inlet)	6-well 48-well 24-well (2 inlet)
<b>Microscope</b>	Use existing	Use existing	Standard configuration	Fully customizable
<b>Autofocus</b>			Yes	Yes
<b>Camera</b>			2 included: Monochrome for fluorescence plus color camera	Yes, user defined
<b>Epifluorescence</b>			Yes	Optional
<b>Filter cubes</b>			DAPI, GFP, RFP	User selected
<b>Motorized Stage</b>			Yes	Yes
<b>Onstage incubator</b>			Optional	Optional enclosure
<b>Fluorescence channels</b>			4	6
<b>Objectives included</b>			10X and 20X included, 5 positions total	10X and 20X included, 6 positions total
<b>Endpoint and live cell imaging</b>			Yes	Yes
<b>Fits in hood</b>	Yes	Yes	Yes	No
<b>Automated plate screening</b>			Yes Basic cell analysis	Yes
<b>Image analysis software</b>	Basic cell analysis	Basic cell analysis standard; optional advanced cell analysis software	Basic cell analysis standard; optional advanced cell analysis software	User selected, wide range of analysis modules for advanced users

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