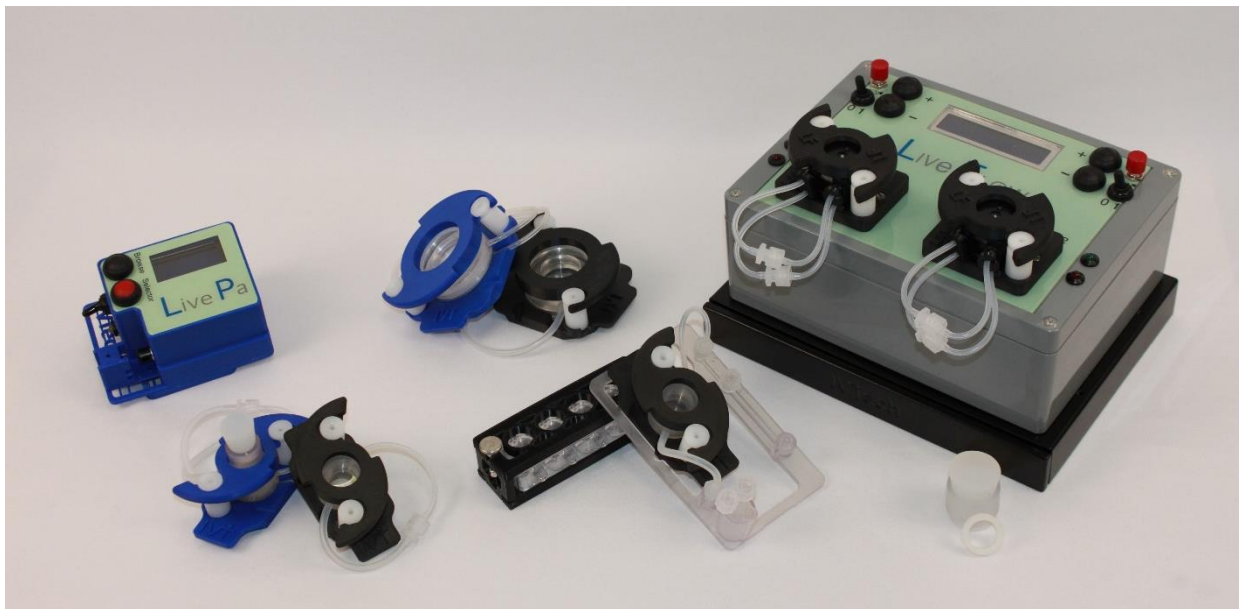




# IVTech:

A STEP CLOSER TO HUMANS



# Introduction

IVTech is an Italian biotech company, working in the Life Sciences field. Our mission is to provide a **versatile** and **user-friendly fluidic platform** to support our customers in the development of 5D in-vitro models. Moreover, our goal is to enable users to combine the advantages of fluidics with the possibility to maintain the standard cell culture and monitoring protocols.

With our technology, you can:

- ◆ Simulate a **dynamic environment**
- ◆ Develop a **multi-organ approach**
- ◆ Control the **environmental conditions** (e.g., pressure)

*Figure 1* represents some of the tissues that have been simulated based on our technology.



**Figure 1:** *Tissues that can be developed with our products*

## 5D in-vitro models

Our products portfolio is composed by different systems for the development of 5D in-vitro models. We provide:

- ◆ **Cell culture chambers**, suitable to house 3D biological structures – e.g., scaffolds, organoids, biopsies – in different conditions – e.g., attached cell culture, floating or circulating conditions
- ◆ Tools to simulate a **dynamic microenvironment**, where a medium flows, mimicking the action of the blood in human circulation
- ◆ Tools to induce **environmental stimulation** (e.g., the pressure), to study different pato-physiological scenarios

Here an overview of our products portfolio. (Figure 2)



Cell culture chambers



Tools for dynamicity



Environmental control tools

**Figure 2:** IVTech products portfolio

# LiveBox1

LiveBox1 (LB1) is a transparent bioreactor suitable to develop 2D or 3D dynamic in-vitro models in attached cell culture conditions. Recently, it has been used also with floating organoids (> 1 mm in diameter).

LB1 is compatible with the cell growth area of a single slot of a multiwell plate.

<i>Compatibility with the slot of</i>	6, 12, 24 plate
<i>Wet volume [mL]</i>	2.5
<i>Transparency</i>	✓



## Main features:

- ◆ **Dynamic environment:** the bioreactor is equipped with an inlet and an outlet to assure the flow of the culture medium
- ◆ **Real-time monitoring:** cells can be monitored in real-time due to the transparency of the chamber
- ◆ **Imaging platform compatibility:** LB1 is compatible with standard microscope stative, slide and plate readers
- ◆ **Recollection of biological material:** the glass disc can be easily removed to recollect the attached biological material
- ◆ **Multi-organ approach:** the LiveBox chambers can be interconnected, following a modular approach, to mimic the crosstalk between different tissues
- ◆ The product is **autoclavable** and **reusable**

## Available versions:

- ◆ LB1-6 → cell growth area of 9,6 cm<sup>2</sup>
- ◆ LB1-12 → cell growth area of 4,5 cm<sup>2</sup>
- ◆ LB1 → cell growth area of 1,8 cm<sup>2</sup>

## LiveBox2

LiveBox2 (LB2) is a transparent bioreactor designed to mimic patho-physiological barriers in dynamic conditions.

LB2 mimics a transwell system: a porous and removable membrane divides the chamber in an apical and a basal compartment.

Liquid-Liquid Interface (LLI) and Air-Liquid Interface (ALI) are implementable.



Compatibility with the transwell of	6, 12, 24 (*) plate
Interface	LLI, ALI
Transparency	✓

### Main features:

- ♥ **Dynamic environment:** the system is equipped with two inlets and two outlets to assure the flow of two different and independent media or one culture medium in a sigmoidal configuration
- ♥ **Real-time monitoring:** cells can be monitored in real-time due to the transparency of the chamber
- ♥ **Imaging platform compatibility:** LB2 is compatible with standard microscope stative, slide and plate readers
- ♥ **Recollection of biological material:** the membrane can be easily removed to recollect the biological material
- ♥ **Multi-organ approach:** the LiveBox chambers can be interconnected, following a modular approach, to mimic the crosstalk between different tissues
- ♥ The product is **autoclavable** and **reusable**

### Available versions:

- ♥ LB2-6t → cell growth area of 4,5 cm<sup>2</sup>
- ♥ LB2 → cell growth area of 1,8 cm<sup>2</sup>
- ♥ LB2-24isa → cell growth area of 0,6 cm<sup>2</sup>.

(\*) Compliance with the stand-alone commercial inserts (e.g., 9 mm i.d.)

# LiveFlow

LiveFlow (LF) is a compact and low weight peristaltic pump, compatible with the incubator environment.

LF mimics the interstitial flow of a real tissue. It permits the set-up of different flow rates.

Dimensions [w×l×h, cm]	21.5×16×14.5
Weight	1.5 Kg
Number of circuits	4



## Main features:

- ◆ **Reduced weight and compact dimensions** to assure an easy transfer from the laminar hood to the incubator
- ◆ **4 independent circuits:** possibility to implement up to 4 independent experiments (2 LF heads → 4 fluidic circuits)
- ◆ **2 dynamic conditions:** 2 motors drive the LF heads, thus it is possible to set-up 2 different flow rates in parallel
- ◆ **Fluidic circuits on board:** the pump is equipped with a drawer where the components of the fluidic circuits can be placed
- ◆ Each **LF head** is removable, **sterilizable** and **reusable**
- ◆ The **interface** is **user-friendly** and intuitive

## Available versions:

- ◆ **LiveFlow:** the direction and the flow rate remain constant during all the experiment
- ◆ **LiveFlow PRO:** it allows to divide the main period in three sub-periods and to set for each one the direction and the flow rate. Once programmed, the pump will adjust the working conditions autonomously
- ◆ **LiveFlow PLUS:** it is equipped with a powerful motor version and designed for specific applications, characterized by a relevant back pressure

## LivePa

LivePa allows to increase the hydrodynamic pressure in your dynamic in-vitro model.

It's designed to simulate phenomena characterized by an increase of pressure, like a disease scenario (e.g., hypertension, glaucoma) or a physiological evolution caused by a change of the environmental conditions (e.g., increase of pressure during the food ingestion).

<i>Dimensions [cm]</i>	8.5×2.8×1.9
<i>Compatibility with LF drawer</i>	✓



### Main features:

- 📍 **Pressure modulator:** LivePa is equipped with a motorized piston which allows to reduce the lumen of the outlet tube of a chamber, increasing the pressure
- 📍 **LF compliant:** LivePa is compatible with LF drawer

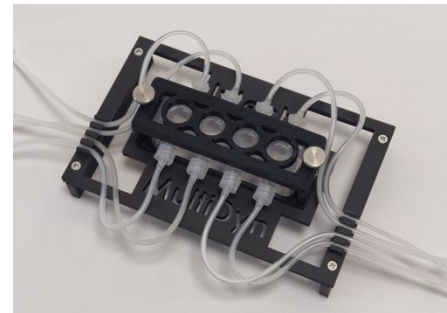
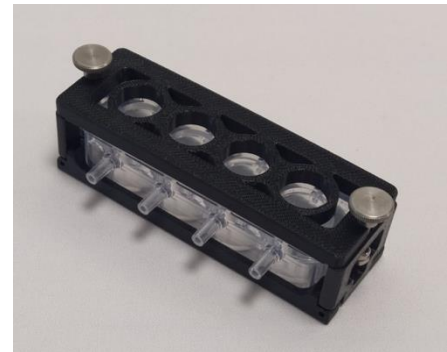
## MULTIDyn

MultiDyn (MD) is a compact multi-dynamic-chambers rack, based on the dimensions of a standard 24-well plate.

Each rack is transparent and equipped with 4 wells, each one compliant with the cell growth area of a 24-plate slot. Each chamber can be autonomously perfused, allowing for the development of 4 parallel and dynamic models. The volume of a single well is 2.5 mL.

MD is a semi-disposable product (reusable 3 times, sterilization with EtOH 70% + UV exposition).

<i>Dimensions/rack [w×l×h, cm]</i>	8.5×2.8×1.9
<i>Cell growth area/well [cm<sup>2</sup>]</i>	1.8
<i># Independent replicates/rack</i>	4
<i>Transparency</i>	✓



### Main features:

- ◆ **Standard monitoring and cell culture protocols:** MD is designed to reproduce the bulk dimension of a 24-well plate column. Each well is compliant with the cell growth area of the plate slot. Indeed, MD is compliant with automated plate readers as well as standard monitoring and cell culture protocols
- ◆ **Compatible with LiveBox1 protocols:** the protocols developed for a LiveBox1 (by IVTech srl) are compatible with MD
- ◆ **Real-time monitorable:** MD can be monitored in real-time, using an inverted microscope, due to its transparency
- ◆ **Multi-organ approach:** each rack is modular. Therefore, it is possible to join different MD to design, as in a Lego strategy approach, a customized fluidic platform, characterized by several chambers interconnected (multi-organ model), assuring 4 replicates. Each well mimics a different tissue, allowing for the cross-modulation between organs, due to the exchange of liquid

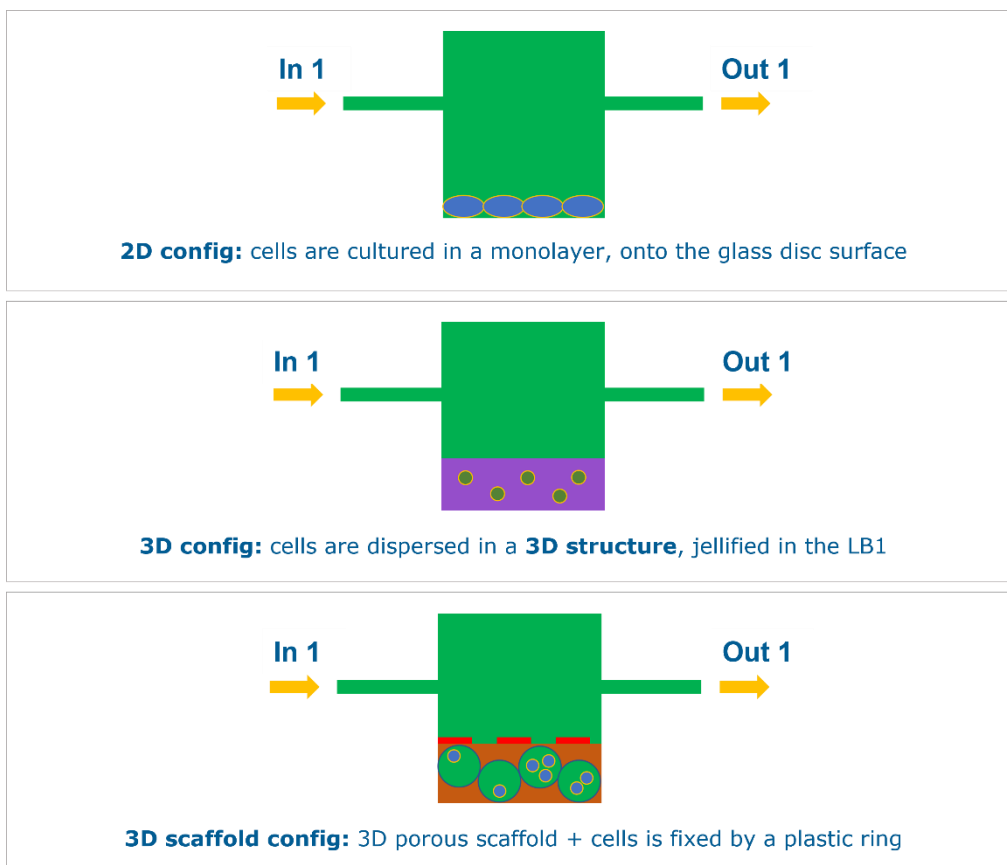
## Chambers | Configurations

LiveBox chambers and MultiDyn are versatile: you can set-up your desired in-vitro models, using different configurations of the products.

### LiveBox1 & MultiDyn

**LiveBox1** and **MultiDyn** allow to implement 2D or 3D models using a **single flow configuration**: the flow is tangential to the construct seeded onto the bottom part of the chamber. However, considering the type of the biological construct (*e.g.*, *cells monolayer*, *porous scaffold*, *hydrogel construct*), it is possible to design different experiments.

Figure 3 shows the designs that can be implemented using LB1 or MD.

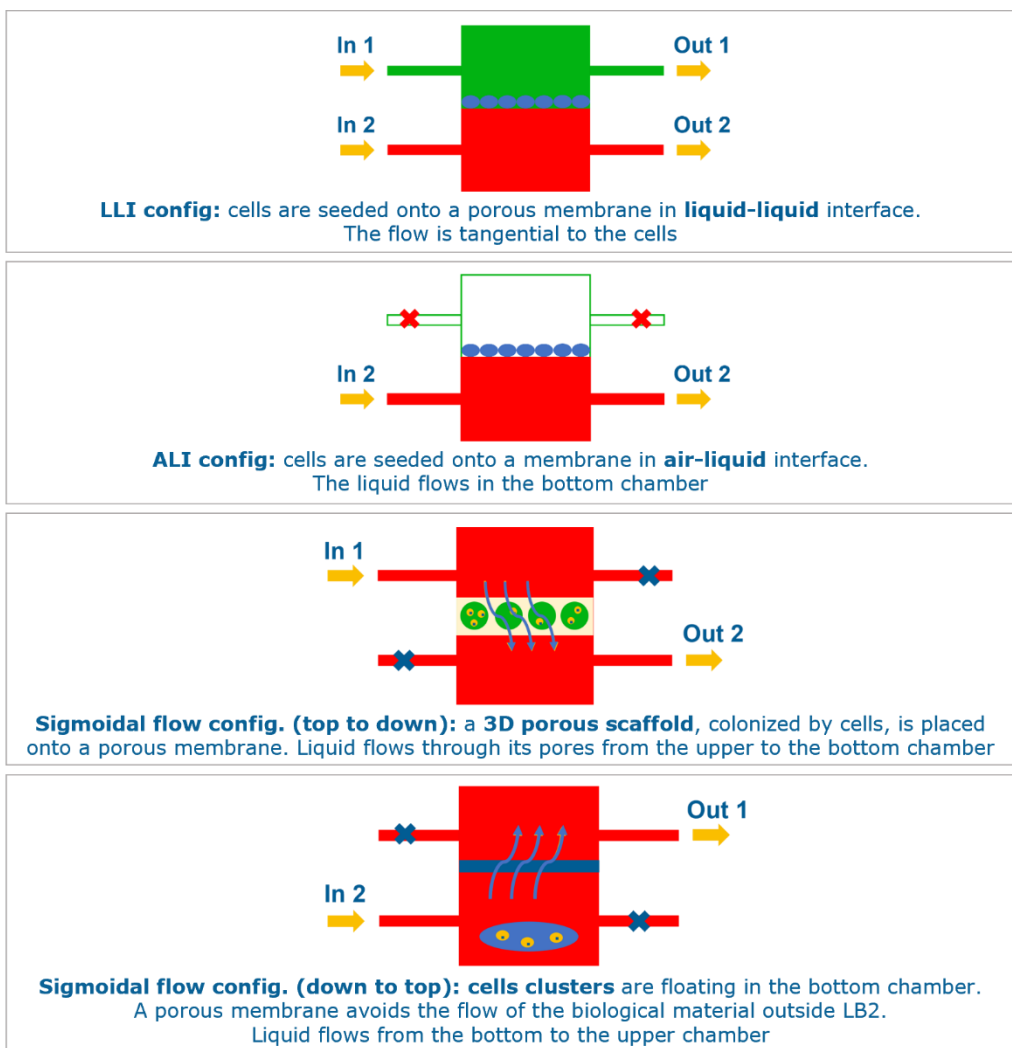


**Figure 3:** LiveBox1 and MultiDyn configurations

# LiveBox2

**LiveBox2** allows to implement dynamic models (*Figure 4*) based on:

- ◆ **Tangential flow configuration:** suitable for physiological barriers, both in Liquid-Liquid Interface (LLI) and Air-Liquid Interface (ALI). The *niche configuration* is a variant of the ALI: both the chambers are filled with the medium, but one of the compartments is not directly perfused by the flow (pseudo-static condition)
- ◆ **Sigmoidal flow configuration:** suitable to perfuse a 3D porous construct or to maintain spheroids and/or organoids in floating conditions



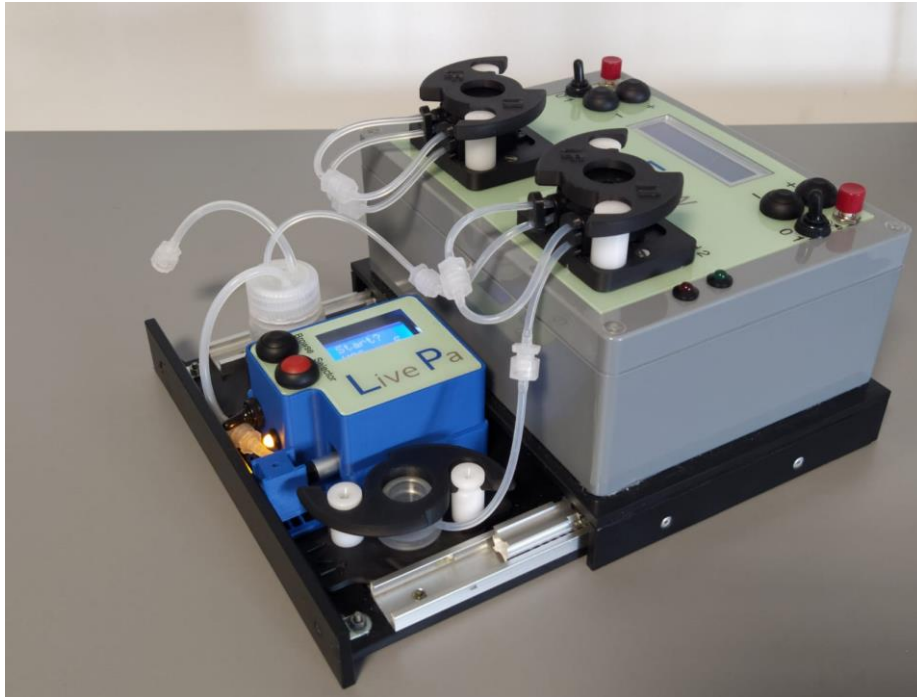
**Figure 4:** LiveBox2 configurations

## Fluidic circuit | The set-up

In *Figure 5*, a typical fluidic is represented. It is composed by:

- ◆ At least one **LiveBox chamber**
- ◆ At least one **mixing chamber** to contain the culture medium
- ◆ **Tubes** (optional) to join the different fluidic modules
- ◆ The **LiveFlow pump** to assure the circulation of the culture medium
- ◆ The **LivePa pressure modulator** to increase the pressure inside the LiveBox chamber

The whole platform is compatible with the incubator environment and easily movable between the cabinet and the incubator.



**Figure 5:** A fluidic circuit composed by a LiveBox1, the LiveFlow, a mixing chamber and the LivePa

# Overview | The applications

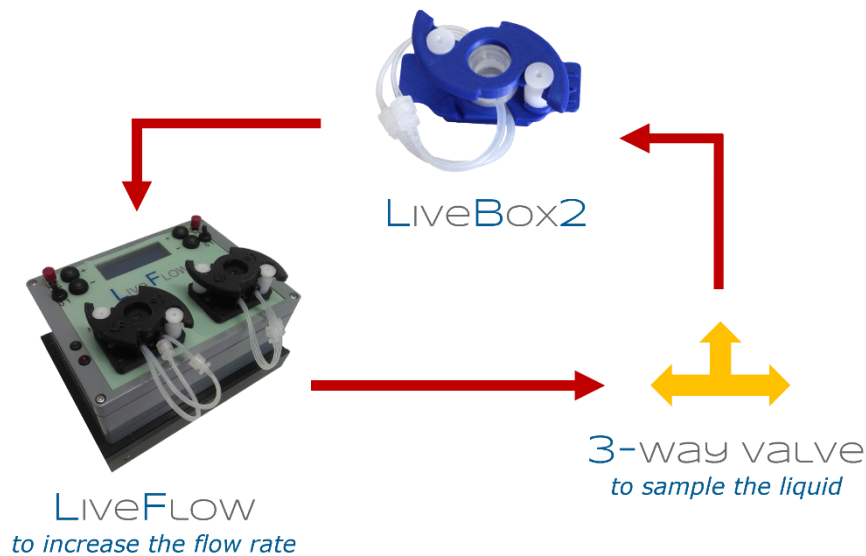
Our products are currently used in a wide range of applications. *Table 1* recapitulates some models that have been implemented by our customers, clustered in the field of applications.

<p><u>Metabolism:</u></p> <ul style="list-style-type: none"> <li>✓ Stomach</li> <li>✓ Liver</li> <li>✓ Fat tissue</li> </ul>	<p><u>Permeability studies:</u></p> <ul style="list-style-type: none"> <li>❖ Lung</li> <li>✓ Intestine</li> <li>✓ Skin</li> </ul>	<p><u>Test of new materials:</u></p> <ul style="list-style-type: none"> <li>✓ Drug release</li> <li>✓ Mech. Prop. of scaffold</li> <li>✓ Surface treatments</li> </ul>
<p><u>Spheroids &amp; Organoids:</u></p> <ul style="list-style-type: none"> <li>✓ Ovarian tissue</li> <li>✓ Liver</li> <li>✓ Neural tissue</li> </ul>	<p><u>Tissue explant:</u></p> <ul style="list-style-type: none"> <li>✓ Nail</li> <li>✓ Muscle</li> <li>✓ Skin</li> </ul>	<p><u>Disease models:</u></p> <ul style="list-style-type: none"> <li>❖ Leukaemia</li> <li>✓ Glaucoma</li> <li>✓ Obesity</li> <li>✓ Parkinson's</li> <li>✓ Breast cancer</li> <li>✓ Kidney disease</li> <li>❖ Bone cancer</li> </ul>

**Table 1:** Models realized using the IVTech technology  
 ✓ → available scientific publications ❖ → on-going projects

## Case studies | Permeability

Permeability studies can be performed using a **LiveBox2** chamber, as it allows to mimic physiological barriers, connected to the **LiveFlow** pump. Moreover, as shown in *Figure 6*, a **3-way valve** can be used to sample the medium for further analysis of the drug or metabolites concentration.



**Figure 6:** A fluidic circuit to perform permeability studies

Using this set-up, you can evaluate:

- ◆ The **bioavailability** of a compound (e.g., a drug)
- ◆ The **toxicity** of a substance (e.g., a drug, a nutraceutical)
- ◆ The **efficacy** of a drug delivery system that has to cross a biological barrier

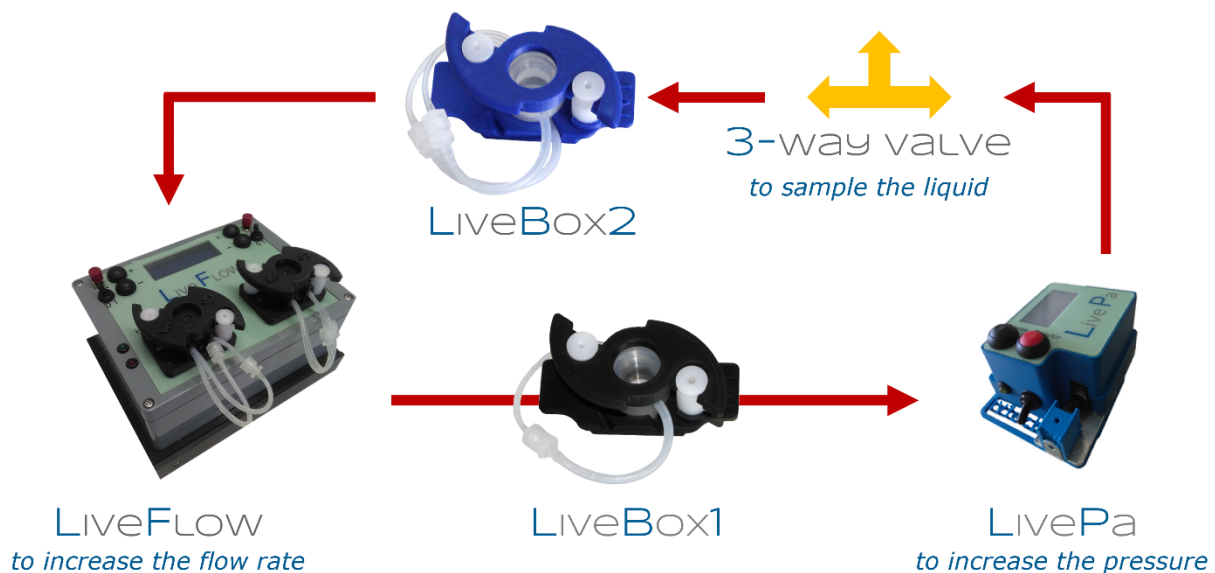
## Case studies | Multi-organ approach

Metabolism studies and disease models often require the development of a **multi-organ approach**, to evaluate the cross-modulation between different tissues, in mutual communication due to the exchange of liquid.

You can decide to join different chambers, thus different tissues, designing your own pathway. Each tissue has to be characterized in dynamic conditions (e.g., preliminary tests). Once this step has been completed, you can set-up your multi-organ model, imposing the suitable working conditions (e.g., flow rate) for all the tissues involved in the pathway.

Once the **physiological scenario** is assessed, you can **induce a pathological condition**, injecting a chemical substance or inducing a shift in the environmental stimuli (e.g., pathological condition related with an increase of pressure).

Figure 7 shows a typical fluidic circuit, suitable to evaluate pato-physiological scenarios.



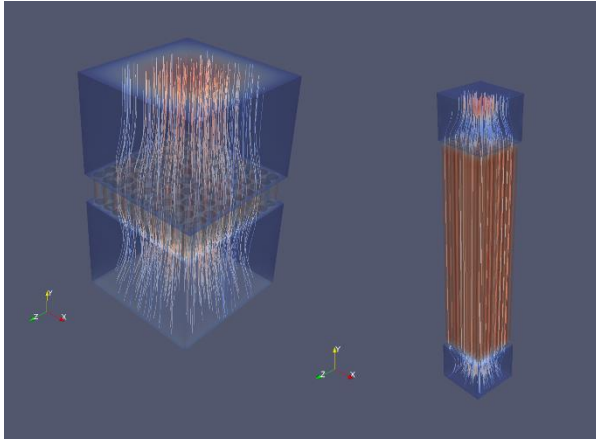
**Figure 7:** Dynamic set-up for the study of pato-physiological scenarios

Using this set-up, you can:

- ◆ Evaluate the **bioavailability** of a compound (e.g., a drug, a nutraceutical) and its effect on a target tissue
- ◆ Evaluate the **signal** exchanged between different tissues
- ◆ Investigate the **onset** of a **disease**
- ◆ Test the **efficacy** of drug treatments and investigate the **side effects** on the other tissues involved in the pathway

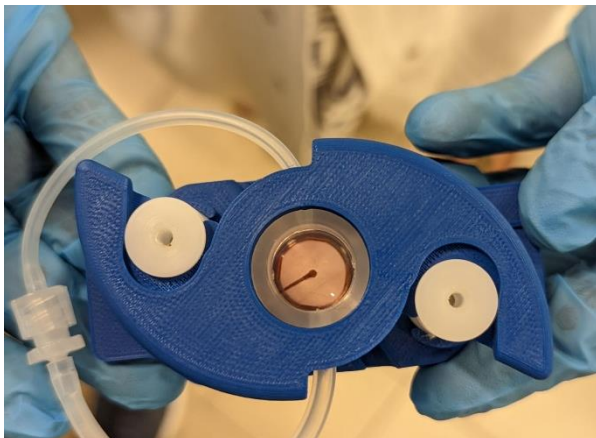
# Our services

We support our customers in the development of 5D in-vitro models, providing:



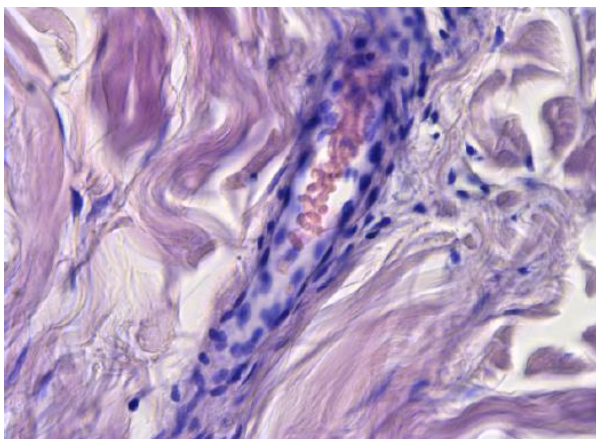
## Engineering services

Fluid dynamic studies and down scaling approach to set-up the main experimental parameters



## Customization

Development of customized technologies



## Biological models

Development of biological models (e.g., to test drugs as a service) in collaboration with our partners



## Our platform for 5D in-vitro models



info@ivtech.it  
www.ivtech.it

LinkedIn



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