Elveflow User Guide

MFS

Microfluidic flow sensor

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SYMBOLS USED IN THIS DOCUMENT

IMPORTANT INFORMATION. Disregarding this information could increase the risk of damage to the equipment, the risk of personal injuries, and influence your user experience.

HELPFUL INFORMATION. This information facilitates the use of the instrument and contributes to its optimal performance.

ADDITIONAL INFORMATION is available on the internet or from your Elveflow representative.

PLEASE READ THE ENTIRE DOCUMENT CAREFULLY BEFORE STARTING ANY EXPERIMENT.

By disregarding the document, the user might be exposed to dangerous situations and the instrument can undergo permanent damage.

Elveflow cannot be held responsible for any damage related to the incorrect use of the instruments.

Material compatibility

Remember to always check your fluids for compatibility with the Elveflow equipment's wetted materials. Exposing Elveflow equipment to multiple chemicals and compounding application factors like temperature, pressure, concentration, etc... can result in significantly different performance. Specific material compound formulations can significantly alter generalized performance ratings.

Elveflow can not be held responsible for damage caused by a chemical. The user needs to determine the suitability of the chemicals prior to any experiment. Elveflow makes no warranty, expressed or implied on actual performance in specific end user applications. It's the user's responsibility to evaluate specific chemical compatibility of parts prior to use.

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1. Introduction

The Elveflow Microfluidic Flow Sensor (MFS) is an in-line sensor that enables fast measurements of liquid flow rates based on thermal time-of-flight technology. The flow sensors are designed to monitor different ranges of flow rates enabling numerous microfluidic applications.

The simple construction of the flow sensor, combined with the high grade materials used, ensures excellent chemical resistance and biocompatibility.

It can be either used for display with a sensor reader or for control combined with a pressure controller or a Cobalt device. In the latter cases, a feedback loop can be implemented. In both cases, the MFS is a great addition to your experiment.

This user guide will go through the steps to integrate MFS units (all ranges and either digital or analog units) in your experiment, physically and on the ESI software and then how to fine tune your experimental set-up and parameters in order to get a precise flow rate control.

2. Design and package content

Package content

Before using your MFS unit, please check the package contents to ensure you received all the items below.
Each package includes the following:

FOR MFS 1, 2 or 3:

Microfluidic flow sensor

M8 data cable (one or the other references is supplied)

Connectors 6-40 to 1/4-28

FOR MFS 4 or 5:

Microfluidic flow sensor

M8 data cable (one or the other references is supplied)

No Connectors needed

In addition to the above items, the user should have the necessary fluidic accessories (tubing, fittings) to connect the inlets / outlets of the MFS unit to the rest of the setup.

Defects or missing items:
Please report any defects or missing items **within one month** of your order receipt.

Design

The MFS has an aluminum casing, with In and Out flow ports, and a data connection slot for M8 cable (Fig 1).

Each MFS sensor has a label on which the following information can be found:

- the flow direction for positive flow rate values (arrows)
- the working flow rate range
- the sensor internal diameter that will depend on the model of the sensor
- the maximum operating pressure
- the serial number of the sensor
- the type of communication, either digital or analog
- Product Number (i.e. the sensor model type, a "D" stands for "digital")
- Production Date (wwyy format): 5020 would indicate a sensor made on week 50 of year 2020 (7-11th december 2020).

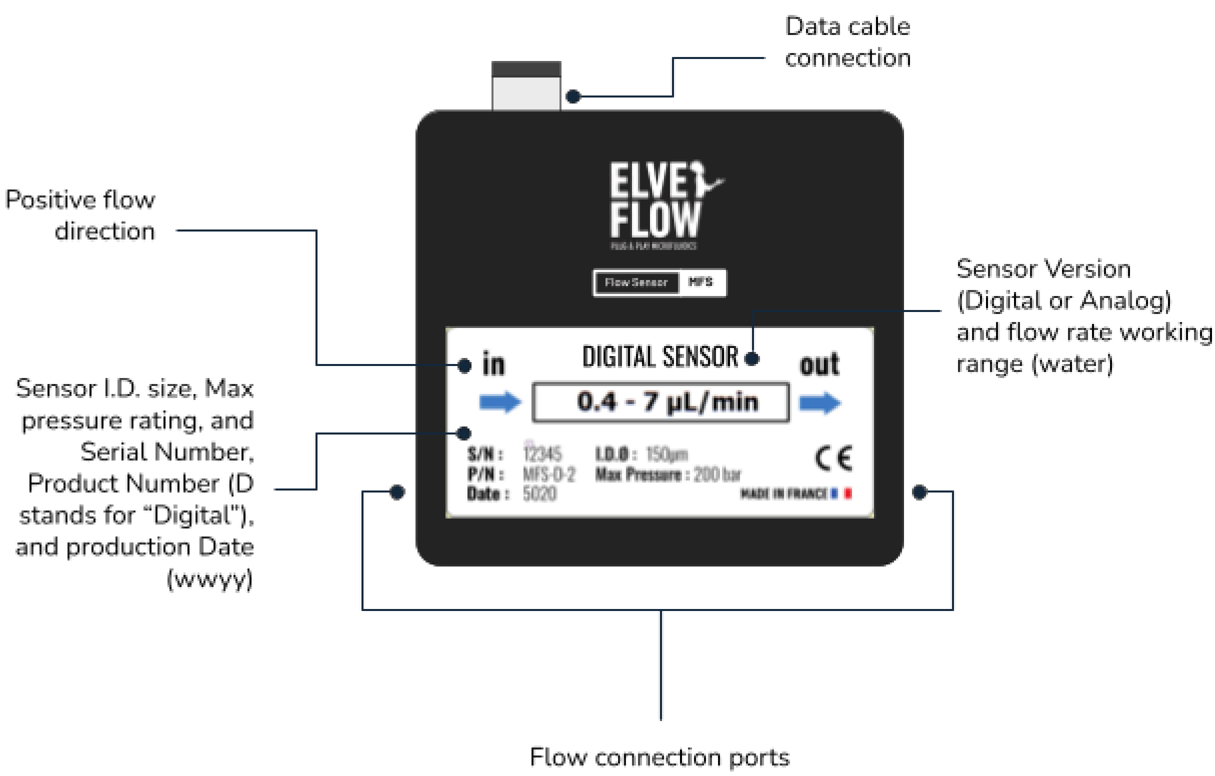


__Fig 1.__ Description of a digital Elveflow MFS flow sensor (MFS-D-2 type).

3. Set-up of the equipment

This section will guide you through the different steps required to install your flow sensor physically in your fluidic path and to understand how it works on the ESI software.

MFS Installation

The flow sensors have “in” and “out” markings which indicate the flow direction. The sensor can read flow in both directions. A positive value indicates that the fluid is flowing from “in” to “out”, and a negative value indicates a flow in the opposite direction, i.e. from “out” to “in”.

Microfluidic Connection

The MFS units should be connected to the flow path through the 1/4-28 receiving ports. In practice, place the tubing in a 1/4-28 flangeless nut, then position the ferrule on the tip of the tubing (Fig 2.a). Note that this last step may be difficult, since the ferrule is designed to achieve maximum sealing. Once inserted, the tubing must be at the same level as the flat face of the ferrule.

For MFS1, MFS2 and MFS3, screw the 6-40 to 1/4-28 PEEK adapter (Fig 2.b) to the sensor and then connect the 1/4-28 fitting (Fig 3).

For MFS4 and MFS5, the adapter is not required. Screw directly the 1/4-28 fitting to the MFS ports (Fig 3).

- When working with 6-40 connectors, first tighten them to the inlet and outlet of the sensor. Then **add the ¼-28 fittings while holding the 6-40 connector to prevent the lattest from turning and being over tight when you turn the ¼-28 connector.**

- **Do not overtighten the adapters and fittings:** be careful when you tighten the fluidic connectors. Too much tightening may cause damage to the connectors and sensors.
- **If you happen to break an adapter in the MFS port, do not try to remove the broken appendix.** You may damage the sensor even more. We advise you to contact the support team.

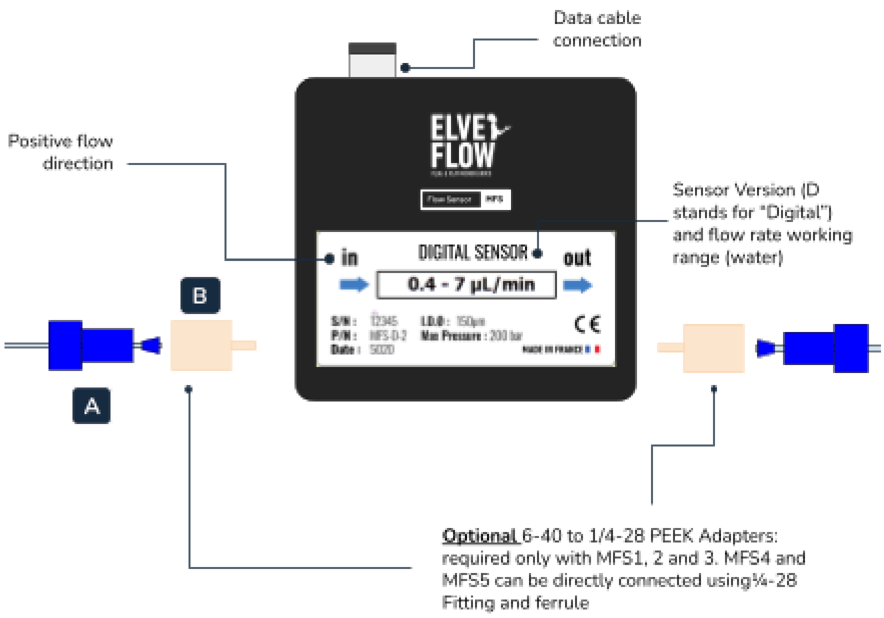


Fig 2. *Description of the Elveflow MFS flow sensor electrical and fluidic connection.*

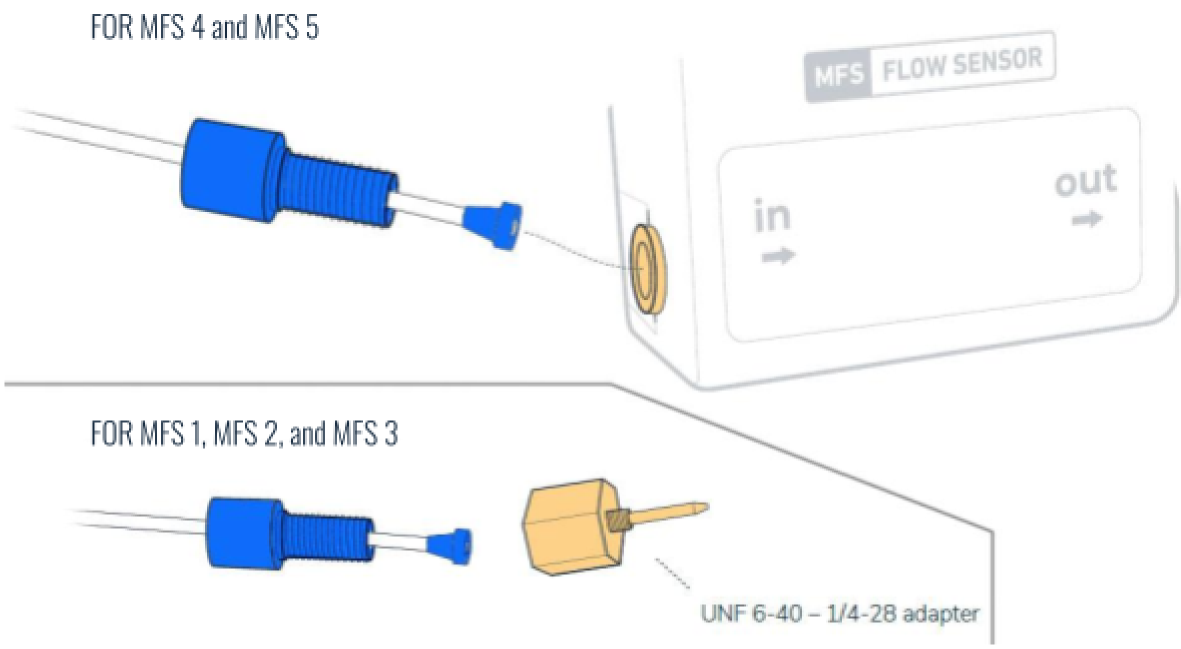


Fig 3. *Description of the two different types of microfluidic connections depending on the type of flow sensor.*

As a general rule, and unless otherwise specified, electronic devices should be kept in a dry environment. Do not use the Elveflow OB1 or a sensor inside a Cell Culture Incubator, or in any situation where relative humidity would be above 80%.

All kinds of tubing can be adapted to the MFS flow sensor.
Tubing 1/16" OD can be used directly with the ¼-28 fitting and ferrule. For 1/32" OD tubing, some microfluidic sleeves should be used in order to adapt the dimensions.

Connect the sensor to a controller using the data cable

Connect the female part of the M8 data cable provided to the male connector of the flow sensor. Then, connect the male part of the cable to the female connector on your controller device, either directly on a pressure controller or to a Cobalt device, or using a MSR Sensor Reader.

If you are interested in connecting the MFS unit with a custom electrical connection, please refer to Annex 6 for details.

Add your sensor to the ESI software

To install the software on your computer, you can download the ESI software through the Elveflow Website.
You will find the software description and operation details in the ESI guide under the .zip archive downloaded with the software or on the support portal.
Before adding the sensor to the ESI software, we recommend checking the compatibility of the sensor's version with the controller (see Annex 1).

To add a MFS to the ESI software, click on the ADD SENSOR button in the ESI main window (Fig 4.a). In the New Sensor window, choose the type of sensor (Fig 4.b), a flow sensor in this case, and choose the communication type, either digital or analog (Fig 4.c).
Then, give a name to the sensor, choose the instrument and the channel your sensor is connected to (if applicable) (Fig 4.e) and click on OK.

Check the type of sensor you are working with and strictly follow the information displayed on the sensor's sticker. **Do not add a digital sensor as an analog one and vice-versa.**

If connecting a digital sensor, the model of the sensor will be automatically recognized by the software when you click on OK.
However, if connecting an analog sensor, a selector will appear at the top right corner for you to choose the model of sensor you are using (Fig 4.d).

Most of the following explanations are related to the connection of a flow sensor to the OB1 pressure controller. If you are using a MFS with a MSR or a Cobalt, we recommend you to have a specific look at the dedicated user guides for more details.

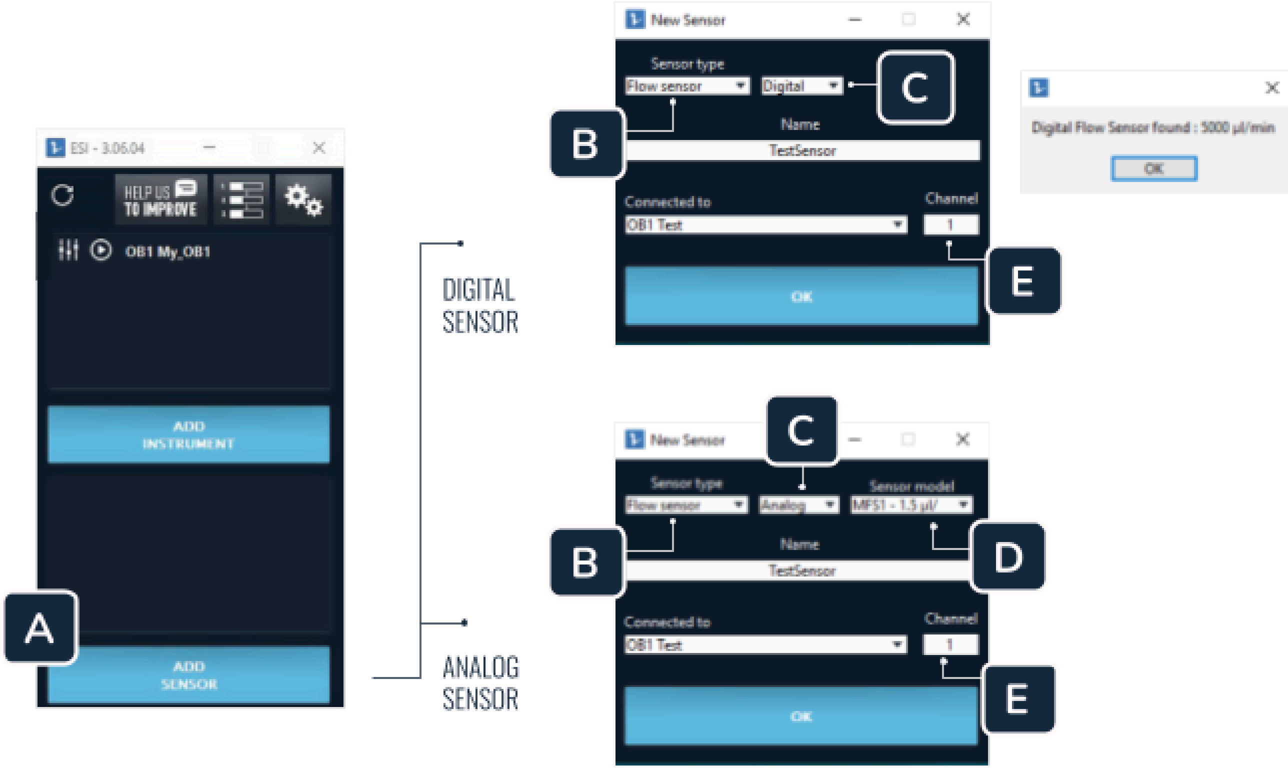


Fig 4. Adding a MFS unit to an OB1 pressure controller in the ESI software.

To view the flow values, open the OB1 window. They appear in the gray area next to the pressure values (Fig 5).

Fig 5. Visualization of the MFS values on the OB1 window.

If you want to remove your MFS from the sensor list, click the “delete” red button (Fig 5.b) in the ESI sensor settings tab (Fig 6.a).

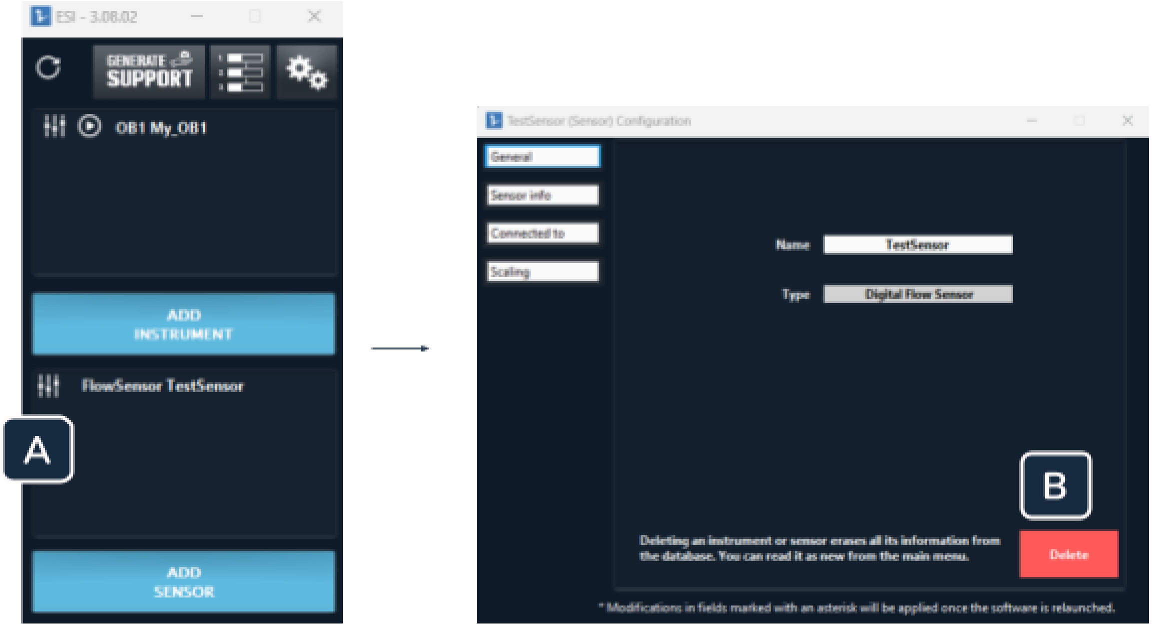


Fig 6. *Removing a sensor from the sensor list.*

We recommend **starting the installation of a flow sensor from a clean state.** Delete any MFS installed and not used in your set-up before adding a new sensor.

Before starting your experiments, we advise you to have a look at the rest of this user guide. Indeed, to properly size and use your sensor, additional steps may be necessary.

- Depending on the sensor model used, you may need to **adapt the tubing of your experiment to avoid turbulence in the capillary**.
- You need to ensure that the **microfluidic resistance of your set-up is correctly sized to facilitate control of your parameters**.
- If you are using a non-aqueous solution, **calibration may be necessary**.
- Adjust the offset to match the 0 flow to your system after calibration is done.

If these three items do not make sense at the moment, do not worry, we will guide you by exploring use case scenarios.

4. Use cases

Using an MFS coupled with an OB1 pressure controller or a Cobalt can lead to two main situations:

- pressure control and flow reading,
- flow control with a feedback loop to adjust the pressure according to the target flow.

This section will guide you through the different steps required to fine tune your experimental set-up in order to have a stable flow rate and a good control over it by introducing a really important concept in microfluidics: the **microfluidic resistance**.

Understanding this concept is crucial to achieving a stable flow rate and being able to control the flow rate precisely and with good responsiveness. The challenge is to set the feedback loop control of our ESI software in order to accurately monitor and control flow rates in your microfluidic setup.

This section includes how:

- to choose and adapt the microfluidic resistance of your set-up,

- to implement a feedback loop in order to control the flow rate precisely.

Experimental set-up

An experimental use case scenario is presented. The experimental setup comprises an OB1 (or any pressure controller), a reservoir, a MFS flow sensor and a waste tank (Fig 11). This flow experiment is only an example to give you installation advice.

We recommend **getting hands on flow rate control with a simple and easy experimental set-up to correctly understand all the concepts at stake.**
The setup can be incrementally complexified and adapted to your own application afterwards. You will have to repeat the various stages explained in this section on your final experimental system to assure correct operation.

For this experiment, you will need the following elements:
- 1 OB1 (or any pressure controller)
- 1 MFS flow sensor
- 1 reservoir filled with water
- Tubings (4 mm OD - 2.7 mm ID tubing for air pressure connections, and 1/16" OD tubing for liquids)
- Microfluidic resistance tubings and a cutting tool (to make clean cuts).
- A waste reservoir
- A computer equipped with the Elveflow Smart Interface (ESI).

The concept of adapting the microfluidic resistance (or resistance tuning) of your system will remain the same if the flow sensor is connected to a sensor reader or a Cobalt.

These elements should be connected like shown here. To help you set-up the OB1 pressure controller, please refer to the dedicated user guide.

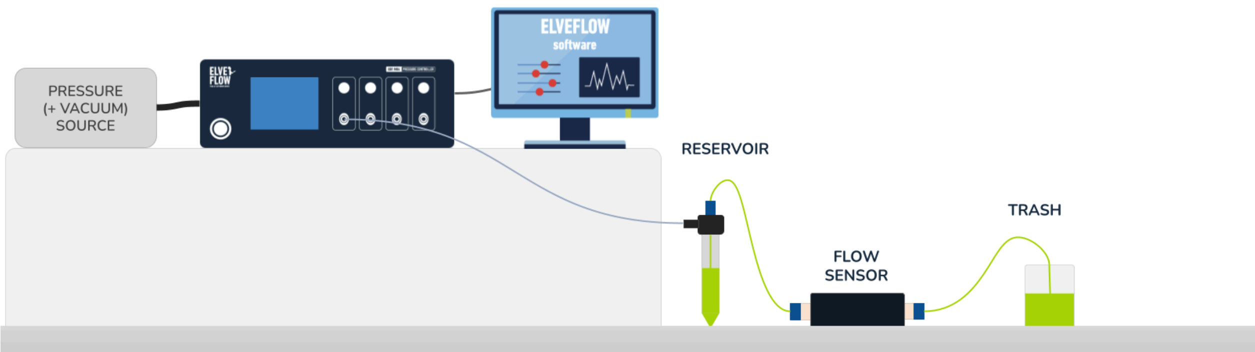


***Fig 11.** An example of a simple setup with which we advise to start.*

Installation tips:
- We recommend placing the OB1 higher or at least at the same level as the other elements.
- The tubing in the inlet reservoir must be immersed.
- We recommend immersing the tubing in the outlet reservoir in order to avoid drops dripping into the trash, as this may cause flow instability.

Adapt the microfluidic resistance of your fluidic experiment

A proper conditioning of the setup is needed in order to avoid poor setup performance. Without this tuning, your sensor values will most likely be not stable enough, making the flow control unstable, slow, or even over-reactive.

This tuning is done by adding microfluidic resistance to the fluidic path. To simplify this concept of microfluidic resistance, keep in mind that the **narrower the diameter and the longer the length of the tubing, the higher the pressure needed to push the liquid in** (see more details in Annex 3).

As a result, **the tuning consists in selecting a diameter and a length for the resistance tubing.**

Elveflow provides a set of standard resistances (Fig 13) that are designed to match most application cases.

***Fig 13.** Flow resistance kit*

If you are working with **aqueous solutions**, we share a table (Fig. 14) with indicative tubing's length and diameter, depending on the type of flow rate sensor and the pressure range used. You can use these values as a guide to determine the most suitable fluidic resistance for your system. Please note that the values in this table are estimated values and will need to be adapted depending on your experimental conditions.

	Pressure Channel	MFS version	Tubing I. D. (µm)	Tubing Length (cm)
Standard resistances table for water or equal viscosity η = 1mPa.s	0-2000	MFS-1	65	40
	0-2000	MFS-2	65	20
	0-2000	MFS-3	100	20
	0-2000	MFS-4	175	20
	0-2000	MFS-5	250	20

***Fig 14**. Standard resistances table when working with a 0-2 bar pressure channel.*

The fluidic resistance depends on the viscosity of the fluid. As a result, the resistance tubing will need to be checked each time you are using a solution with different properties.

The choice of a specific resistance tubing will **depend on the overall resistance of the system** (microfluidic chip, length of tubing....). If the fluidic path is modified (a change of the chip, the addition of a valve...), check the suitability of the resistance chosen.

Everytime the fluidic path of your system changes (addition of a component, change of microfluidic chip and tubing....), the resistance tubing needs to be adapted

Our online microfluidic calculator might help in designing the best experimental set-up (flow rate, pressure to apply, tubing resistance length, wall shear stress for biology applications, cell culture, and many more). However, you should regard the results provided by this tool as indications and not as absolute truths. Indeed, it is complicated to take into account the multitude of parameters present in an experiment in this simple calculator.

The adjustment of the diameter and length of the resistance tubing with the understanding of these parameters effects can provide the control needed for the user's application.

Flow Resistance tubing installation

Cut the resistance tubing selected to the right length using a microfluidic tubing cutter (Fig 15).

When cutting the resistance tubings, ensure to make clean cuts in order to avoid clogging the tubings. Elveflow strongly advises not to use office equipment such as scissors to cut your tubes.

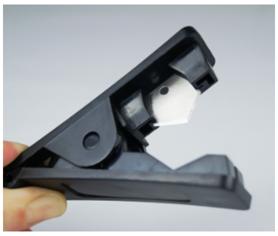


Fig 15. *Microfluidic tubing cutter*

The cutter gets “émoussé’ with time. We advise to replace it regularly.

Place ¼-28 fittings and ferrules to each side of the resistance tubing and connect this resistance to your flow path using a union (Fig. 16).

It is important that the **resistance should be placed after the flow sensor,** in order to keep the flow stable in the flow sensor.

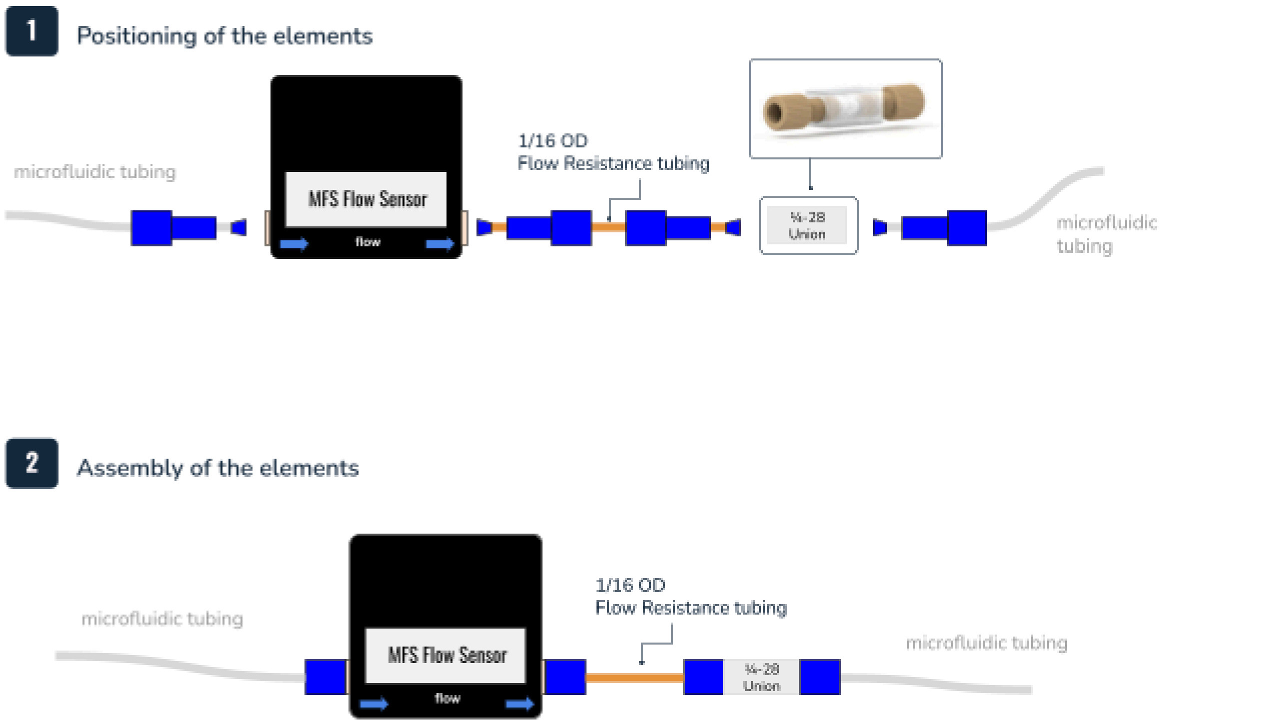


Fig 16. *Flow Resistance tubing installation, example for a MFS4 or MFS5. For MFS1, 2 and 3, add connectors 6-40 to 1/4-28 in between the flow sensor and the ¼-28 fitting.*

Do not tighten the connectors too much, as you risk breaking the capillary inside by exerting too much pressure.

Elveflow strongly advises to use **filtered solutions to avoid clogging** of the microfluidic resistance tubing.

Your set-up is now ready for the experiments.

Flow rate display

Once your flow sensor is connected to the OB1 pressure controller and to the fluidic path, added to the ESI software and resistance in place, you can apply pressure and follow the evolution of the flow rate (Fig 15.b). It will take some time for the fluidic path to fill up, hence the flow rate display stays at 0 µL/min until the liquid arrives in the flow sensor.

By default, the control mode is in regulator control mode (Fig 17.a), meaning that the pressure regulates the entire system and the flow rate is displayed and not monitored (Fig 17.b).

Fig 17. *Flow Rate display in regulator mode*

In regulator mode, check that the resistance chosen fits the flow rate range you want to work with by setting the maximum pressure of your channel range. The general idea to keep in mind for successful operation is to match the pressure range with the flow rate range. By carrying out this check, you can ensure that you are using 100% of your system's performance.

For example, working with a 0-2 bar pressure channel and a MFS4, set the pressure at 2 bar and check that the flow range displayed is around 1000 µL/min (Fig 18). Of course, this example is the ideal situation, and the aim is to get as close to it as possible. However, in the vast majority of cases, an approximation will be sufficient to enable experiments to be carried out under good conditions. This tuning will also depend on your experiment and your expectations in terms of precision.

Tuning the resistance of your microfluidic set-up might take some time. Keep in mind that it is a **process of trial and error** and you will probably **need a few increments** before you get the result you want.

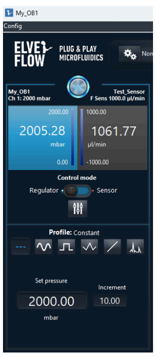


Fig 18. *Matching the range between pressure and flow*

- If the flow rate is below 1000 µL/min, your system is too resistive, you should either increase the inner diameter of the resistance or decrease the tubing length. In some cases, your system might not need any microfluidic resistance tubing or you might need to switch your entire microfluidic tubing. For example, switching a 1/16” OD (800 µm ID) tubing to a 1/8” OD (2.4 mm ID) tubing.
- If the flow rate is over 1000 µL/min, your system is not resistive enough and you should either decrease the inner diameter of the resistance or increase the resistance tubing length. You might also need to switch the entire microfluidic tubing to a smaller internal diameter one. For example, switching a 1/16” OD tubing (800 µm ID) to a 1/32” OD (300 µm) tubing.

Working flow rate range
Please note that beyond the working flow rate range of the sensor, the measured values are not accurate any more and may even decrease, while the actual flow rate value increases. If you're in this situation, get back to lower flow rates compatible with your sensor specifications. You may also need to increase the microfluidic resistance of your set-up.

Each MFS has a maximum operating pressure and burst pressure summarized here. As soon as you stay under this pressure you can push at a higher flow rate it won't damage the sensor. Just as explained before, the value read will have no sense. So for cleaning or filling purposes you can pass over the limit of the maximum work flow range.

	MFS 1	MFS 2	MFS 3	MFS 4	MFS 5
Operating pressure (bars)	200	200	100	15	15
Burst pressure (bars)	400	400	200	30	30

To refine your understanding of the system, you can carry out a second check by setting the pressure at the half range value (Fig 19). It should be especially helpful if the flow rate was above the maximum value of the range.

Fig 19. *Stability of the flow rate at mid pressure range*

- If your **flow rate is too reactive**, meaning that a small change of pressure leads to a wide change in the flow rate, you need to **increase the microfluidic resistance** of your system. In this case, you get to the maximum flow rate, using only a small part of the pressure range.
- If your **flow rate is not reactive enough**, meaning that a huge change of pressure leads to almost no change in flow rate, you need to **decrease the microfluidic resistance** of your system. In this case, you use the all range of pressure to get to only a tiny part of the flow rate range.

The tuning of the microfluidic resistance is an incremental procedure. You may need several iterations before finding the right match.

Feedback loop implementation

Once the microfluidic resistance of your system is well dimensioned and your flow rate stable in regulator mode, you can start working on the implementation of a feedback loop in order to do some flow control.
The objective is to regulate the flow rate of your system by adjusting automatically the pressure through PID regulation. Basically, a control loop is a system where a feedback mechanism is used to control a certain action. In many electronic devices, a software algorithm called PID is often used to control these systems. PID is an acronym that stands for Proportional, Integral, and Derivative. Its general principle is beyond the scope of this document.

The principle of this tuning is to adjust the PID parameters to end up with a system reaction type (fast reaction, stable reaction, etc...) that fits your needs. The software reads the flow rate value and adapts automatically the pressure to keep the flow rate following setpoints. Let's see how to set this PID regulation in Elveflow ESI software.

Flow Resistance tuning and PID parameters tuning are key pillars to a successful flow control. Please ensure you are tuning them before starting an experiment.

Tuning PID parameters in ESI

Tuning the Flow Rate Control feedback loop using a PID controller is the process of determining the ideal values for P, I, and D parameters, in order to achieve the desired response.

Two important checks before starting:

- Your flow path is connected (**no leak**)
- Your flow path is filled with liquid (**no air or bubbles**)

Before switching from “Regulator” to “Sensor” mode, you can **set the pressure close to the flow rate you want to work with** in order to help you.

Step 1:
Switch from a “Regulator” to a “Sensor” mode in order to set a flow rate as a target and not a pressure. Once the software is set on “Sensor” mode, a “Flow control configuration” appears, where the Flow Control regulation parameters can be reached (Fig 20).

Fig 20. Regulator and sensor regulation mode with the flow control configuration panel.

Several PID have been developed and can be selected from PID Type:

- **PI Basic (default and recommended)**: Generic PI regulator.
- PID Basic: Generic PID regulator that includes the D parameter.
- Large Reservoir: PI regulator more adapted for large volume (lot of air), since it takes time to fill the reservoir.

In general, we recommend using the PI Basic as it suits most of the applications.
As a precaution, default PID parameters are low (Default value: 0.001). Using the OB1 without adapting the default parameters will result in a non-reactive flow control.

In some experiments, you may want the controlled flow rate to reach the set point as quickly as possible even if it means overshooting the set point.

In other cases, overshooting the set point may be unacceptable (Fig 21).

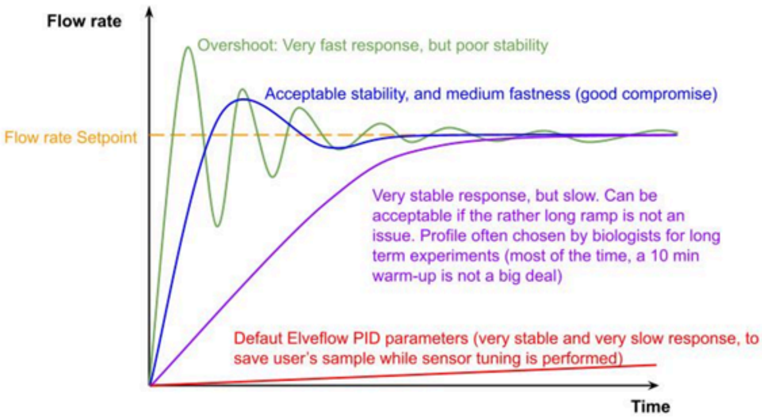


Fig 21. Overview of different flow rate behaviors

Step 2:
Set a constant flow rate and modify the values by clicking on the displayed ones and entering new values by hand to make a fine adjustment. Check the graph to see how the flow rate is responding.

Step 3:

To fine tune the P and I parameters, set a square flow rate profile. For the example in Fig 21, the flow rate goes from 0 to 500 µL/min every 10 seconds. Go to the “Flow control configuration “ panel and gradually increase the “P” and “I” parameters, check on the graph how the flow rate is responding to the changes.

- The parameter “I” is too high, resulting in oscillation, hence a decrease of the “I” parameter is necessary (Fig 21.a).
- The parameter “I” has been decreased, so the oscillations are gone. However, the system reacts too slowly now. Hence, one should increase the “P” and “I” parameters (Fig 21.b).
- The system is stable with no overshoot and a good responsiveness (Fig 21.c). Choosing P and I around 0.1 is a safe choice in most of the applications.

Make as many iterations as necessary to obtain the speed versus stability blend that suits you best. P and I parameters are for most applications between 0.1 and 1. However, it is only an indication and they need to be adapted to each configuration.

Manual parameters adjustment

- **Do you have too much overshoot?** Decrease “P” parameter
- **Does the system react too slowly?** Increase “P” parameter
- **The system reacts quickly but slows down as it approaches the target?** Increase “I” parameter
- **Do you get some instabilities or too much oscillation?** Decrease “I” parameter

Fig 21. Overview of Flow Control tuning : setting a square profile and adjusting P and I parameters.

General recommendations:

- If your experiment requires rapid changes in flow rates, tuning the PI parameters is important in order to have a good balance between responsiveness and stability.
- If you plan on working at very stable flow rates, the PI values should be low.

Flow Sensor tuning is setup dependent. Therefore, the flow control feedback loop can not be factory pre-tuned.

Auto tune feature: PID regulation values can be roughly adjusted using the Auto-Tune feature available in the Flow control configuration panel (Fig 22). Note that this tool is a quick adjustment feature providing rough parameters.
Requirements:

- **Tuning the flow resistance first is mandatory** before using this feature or it will result in poorly chosen PID parameters.
- **Fill the fluidic path of your set-up before** launching the Auto-Tune feature. Avoid any air bubbles.
- Once the Auto-Tune feature has run, **manual adjustments** can provide the control you need for your application.

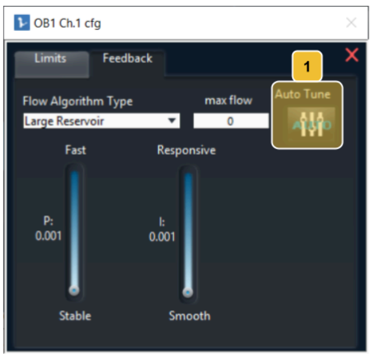


Fig 22. The "Auto-Tune" feature can be used to roughly adjust PID settings.

Everytime the fluidic path of your system changes (addition of a component, change of microfluidic chip or tubing....), the PID parameters needs to be adapted

Saving your Flow Control parameters for later use

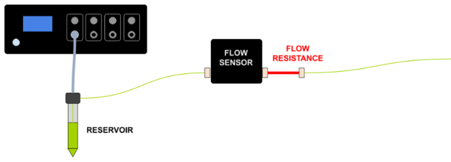
Once the correct PID parameters have been found you may want to save the configuration to keep the PID parameters, otherwise you will need to re-tune PID on the next ESI launch.
Go to the main OB1 window, in the Config section in order to save your current PID parameters (Fig 23).

To use previously saved PID parameters, load a configuration from the Config section.

Fig. 23. *You can save your flow control parameters, and load this configuration profile later anytime.*

General summary overview

1 We're assuming that **flow resistance is set correctly**



2 To proceed to **PID tuning**, please first check that:
- your flow path is connected (**no leak**)
- your flow path is filled with liquid (and **not air, or bubbles**)

3 Then **open the sensor PID parameters and choose a PID regulation type.** We recommend using PI Basic.

Adjust manually the parameters to get the best PID settings for your experiment (usually between 0.1 and 1)

<u>*Option*</u>: use the **Autotune feature** to get a rough estimation of the correct PI parameters. Manual adjustments are still necessary.

4 Set a **square flow rate profile** in order to precisely fine tune the PI parameters.

- **Do you have too much overshoot?** Decrease "P" parameter
- **Does the system react too slowly?** Increase "P" parameter
- **The system reacts quickly but slows down as it approaches the target?** Increase "I" parameter
- **Do you get some instabilities or too much oscillation?** Decrease "I" parameter

5 **Save the OB1 configuration to keep the PID parameters**, otherwise you will need to re-tune PID on next ESI launch. To use previously saved PID parameters, you need to **load a configuration.**

6 **Everytime the fluidic path of your system changes** (addition of a component, change of microfluidic chip or tubing....), **resistance tubing and PID parameters needs to be adapted.**

5. Preventive maintenance

Sensors cleaning general recommendations

As the flow sensor principle is temperature based, the measurement quality highly depends on the capillary surface cleanliness. Therefore, deposits on the capillary wall can reduce heat transfer for both heating and temperature measurements and lead to a measurement deviation and/or an offset.

Cleaning flow sensors after each use is necessary to ensure their longevity and measurement quality.

If possible, dedicate a discrete sensor for each different liquid to be measured. If this is not possible, plan a proper change of the media and include a cleaning step in-between.

Do not let the sensor dry out to avoid residue building in the sensor capillary over time. The more you space out cleaning, the more residues will accumulate, making cleaning increasingly complex and uncertain.
Once the sensor is clogged, it is inoperable. Sensor clogging often requires a replacement of the sensor and is **not covered by Elveflow guarantee.**

We recommend **cleaning the flow sensor after each use using DI water or solvents such as ethanol, methanol, IPA**... The choice of the cleaning procedure is left to the user as it highly depends on the specificities of each experiment performed. Ensure that you have found a good cleaning procedure before performing the first tests, and always clean immediately after emptying the sensor.

Once cleaning is complete, **blow clean air into the sensor to dry it**. A cleaning routine is the key to ensure a long life for your sensor.

Some solutions, as Hellmanex III, can be used to clean clogged sensors. However cleaning your sensor once it is clogged does not automatically imply unclogging success.

Resistance tubing is an expendable item that should be replaced after prolonged use.
With a small internal diameter, resistance tubings are more prone to clogging, and may need to be replaced over time, as part of your setup maintenance routine.

Serious Warnings and Precautions

Any cleaning by mechanical means should be avoided. Never enter the sensor's flow channel with rigid or sharp objects that could scratch the flow channel surface. Furthermore, no abrasives or liquids containing solids that can grind the flow channel surface should be used. Anything that affects the flow channel wall will cause deviations in the measurement performance, or permanently damage the flow meter.

Abrasive liquids are not to be used for cleaning! Strong acids and bases should also not be used to clean the flow meter.

Storing conditions

Store the sensor clean and dry.

Always drain the fluid, flush with a suitable cleaning agent and blow out with pressurized air.

Remove the microfluidic connectors and tubing and connect the yellow caps to prevent dirt and dust from entering the capillary (Fig 24).

Fig. 24. *Flow sensor storage conditions*

7. MFS troubleshooting guide

Connection issues

Prior to any diagnosis, please make sure that the instrument you are connecting the MFS to is powered (i.e : OB1, Sensor Reader, Cobalt) and the power button is pressed on (if applicable).

Please check the following:

- Check that the connection of the M8 data cable is secured
- Check that the instrument you are connecting the sensor to is correctly added to the ESI software
- When adding the sensor in the ESI, please make sure to declare the correct sensor type (digital or analog)
- Check the compatibility of your sensor model with your instrument (see Annex 1)
- Check that all sensors physically disconnected from the instruments are deleted from the ESI software. The sensors listed on your software must only be the one connected to your instruments.
- Check that the ESI version on your computer is the most recent one. You can download the most recent version of the ESI software on the Elveflow website.
- Start MFS addition from scratch. This procedure is recommended when connection problems persist. Find the ConfigESI.ini and .log files (Fig 22) and erase them. These files are located in C: \ Users \ Public \ Documents \ Elvesys \ ESI \ data. Once the files have been deleted, start the addition of the MFS to the software as explained in this user guide.

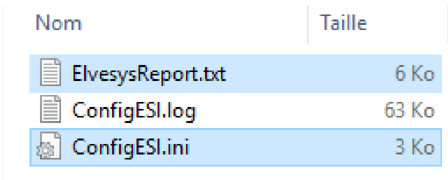


***Fig 22.** ConfigESI files*

Flow issues

No flow variation on the ESI software?

Check if you have any liquid coming out of the sensor outlet.

If liquid is flowing out of the flow sensor, check that the sensor is correctly installed on the ESi software (see section ”connections issues” above).

If no liquid is flowing out of the flow sensor, there is a clog somewhere and the flow path needs to be checked step by step. The idea is to start the inspection from the inlet tank and check at each connector that the liquid is flowing properly. When you come to a connector where no fluid is flowing, you can conclude that the plug is in this last section.

- If the clog is at the resistance tubing level, we recommend cutting off the end, referring to the appropriate section of the user guide, or replacing it.
- If the clog is at the MFS level, we recommend cleaning the flow sensor carefully following our cleaning recommendations. If the problem persists, contact the support team.

We also recommend using filtered solutions during your experiments as unfiltered solutions can cause sensor clogging.

Is your flow control unstable?

- Please check the tightening of all the connectors and tubings to avoid any leakages.
- If your problem is with flow regulation using the “Sensor” mode, check if by using the “Regulator” control mode and choosing any pressure value, the flow rate value is stable. If it is the case, you might want to adapt the total resistance of your microfluidic circuit and/or adjust your PID parameters (please check the sections above, to help you on that matter).
- Check if the tubing size is adapted to your sensor model.

Is your flow rate decreasing when the pressure increases?

In this case, you might be out of the operating range of your sensor (e.g: real flow rate is at 1000 µL/min and your MFS3 maximum is at 80µL/min).

We recommend decreasing the pressure in order to get the flow rate back in the operating range. You might need to adjust your microfluidic resistance in order to better size your experiment.

Is flow decreasing for a constant pressure?

During an experiment at a constant pressure, the flow rate may decrease with time, it’s similar for an experiment at constant flow rate the pressure increases to maintain the flow rate. This is rather common and due to an increase of the global fluidic resistance of the set-up. Indeed if a residue stays on the tube walls, or some particles get stuck in the set-up, these create some restriction in the flow that increases the global resistance. A good cleaning or some tube replacement may be needed to come back to the parameters found in the beginning of the experiment.

Difficulties to get no flow conditions?

Having perfect no flow conditions in a set-up is not easy as stopping the pressure, or setting the pressure at 0 mbar won’t stop the flow. Hydrostatic pressure will still rule the flow. No flow conditions can only be achieved by having no pressure difference between the inlet and outlet of the system.
There are two ways to do so:

- putting your inlet and outlet reservoir at the same pressure,
- adding valves (manual or automatic),

These zero flow conditions are the one to get to correct your offset (see annexe 6) in your ESI settings.

8. Customer Support

You are welcome to browse through our online Elveflow Support Portal. You will find extensive information and guidance regarding all our product lines. It is very likely that the answers you are looking for can be found there. In case you have further questions or need clarification, please contact the support at customer@elveflow.com.

With the critical information readily available, the Elveflow Support team will be better able to help you.

The essential troubleshooting elements are:

1. The serial number of the Elveflow device(s) (Sensors, Instrument).
2. Screenshots of the error messages received, if applicable.

3. Pictures or movies of your setup and your issue. You can [use WeTransfer to send us a big folder and files up to 2GB](). Make sure to add the download link to your reply.

9. Annex

Annex 1: Sensors compatibility chart with Elveflow instruments

Elveflow updates regularly its instruments' range to integrate technological advances. As a result, some sensor versions are not compatible anymore with a type of instrument. To have a general overview of the sensor compatibility with our instruments, please refer to the following table (Fig 25). If you would like to update your analog sensors to digital ones, feel free to contact our sales team at contact@elveflow.com.

		MFS	
		Analog	Digital
OB1	Mk2	✔	✘
	Mk3	✔	✘
	Mk3+	✔	✔
	MK4 OEM	✔	✔
	Mk4	✔	✔
Cobalt	Pressure	✘	✔
	Dual	✘	✔
MSR	V2	✔	✔
	V3	✔	✔

✔ compatible
✘ not compatible

Fig. 25. *Sensors compatibility depending on the type of instrument*

Adapt the tubing to your sensor model

The measurement quality highly depends on the laminarity of the flow inside the capillary due to the very working principle of the sensor (see Annex 2 for some explanations on the working principle). If not laminar, measurements deviation and/or an offset might be observed.

It is then necessary to avoid any turbulence inside the capillary of the sensor.

To do so, we recommend the inner diameter of the tubing before the sensor being of the same size or larger than the sensor's capillary. The idea is to be in a situation where the MFS acts as a flow resistor.

We must avoid that a small ID tubing connected to a large ID sensor's capillary forms a jet, leading to a highly distorted flow profile inside the sensor and hence erroneous results, especially at high flow rates.

Meeting this recommendation is particularly critical for the MFS 5 (ID=1.8 mm).

Here is the list of tubing recommendations depending on the inner diameter of the sensor's models.

- MFS1: 25 µm or larger connection tubing ID
- MFS2: 150 µm or larger connection tubing ID
- MFS3: 430 µm or larger connection tubing ID
- MFS4: 1 mm or larger connection tubing ID
- MFS5: 2 mm or larger connection tubing ID. See an example of fitting connections for a MFS5 in Fig 12.

Due to a 25µm ID sensor capillary size, we advise using the MFS1 under clean room conditions.
We advise cleaning all flow sensors regularly following our cleaning procedures as deposits could impair its operation and falsify the data. Moreover, **sensor clogging is not covered by warranty.**

Fig 12. *Recommended mounting for MFS5*

Annex 2: MFS flow sensor working principle

The flow sensor working principle is based on locally slightly heating the fluid passing through a capillary inside the sensor and measuring the temperature on both sides of the heater (Fig 26). The difference of temperature between the two sides allows the sensor to deduce the flow rate. The measurement quality highly depends on the cleanliness and the laminarity of the flow inside the capillary.

If the inner surface of the capillary is not clean due to biofilm deposition or any kind of particle deposit, measurement deviation and/or an offset might be observed. It is then necessary to clean the flow sensor after each experiment, following the cleaning recommendations, and to store it in good conditions.

Measurement deviation and/or offset might also be observed when the flow inside the capillary is not laminar. It is then necessary to avoid any turbulence inside the capillary of the sensor. To do so, it is recommended to adapt the diameter of the microfluidic tubing to the inner diameter of the flow sensor.

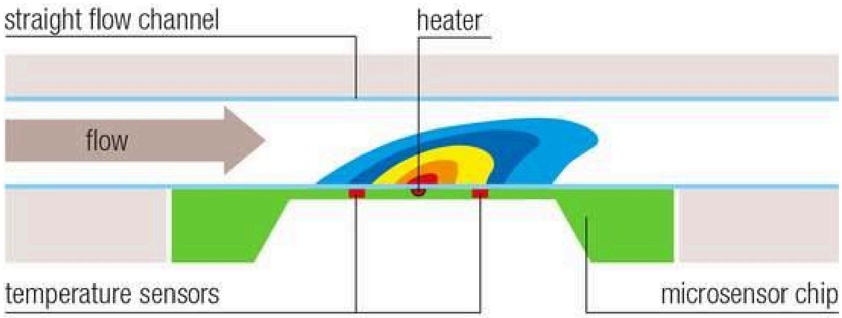


Fig 26. *MFS flow sensor working principle*

Annex 3: Flow resistance formulas

One can describe a relative relationship between microfluidic flow, the pressure difference and microfluidic resistance as:

$$Q = \Delta P/R$$

Where Q is the flow rate (volume / time), ΔP is the pressure difference and R is the resistance to flow due to friction between moving fluid and the stationary channel and tubing walls.

The resistance to flow through a cylindrical microfluidic channel depends on several factors (described by Poiseuille) as follows:

$$R=(8\ L\ \eta)/(\pi\ r^4)$$

Where r is the channel internal radius, L the channel length, and η the viscosity.

It is important to note that a **small change in microfluidic channel radius** will have a **very large influence** (4th power) on the flow resistance. A small decrease of channel internal radius can significantly increase the resistance to flow

The idea here is to have an appropriate flow resistance to avoid extreme situations such as :
- The resistance is too low, and a small working pressure (ΔP) results in high and unstable flow rates,
- The resistance is too high, and the friction developed between moving fluid and the stationary channels and tubing makes it difficult for the flow to move into the circuit.

Annex 4: MFS settings

Set flow rate units

Go to the ESI general settings (Fig 7.a) and set the system flow rate units to the desired unit (Fig 7.b). You can change the unit at any time.

When the flow rate unit is updated, restart the ESI for the change to be taken into account.

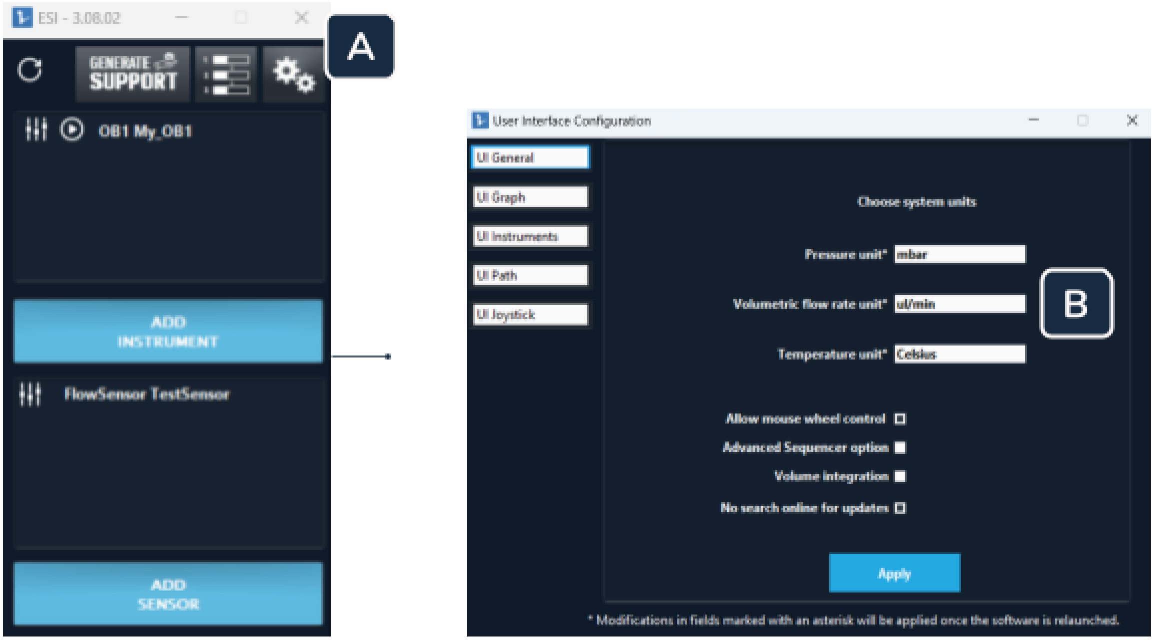


Fig 7. *Set flow rate units in the ESI software*

Set connection and visualization settings

For some applications, it might be convenient to visualize the MFS on more than one channel.

If you want to visualize your MFS onto two different pressure channels, go to the flow sensor settings tab in the main ESI window (Fig 8.a), then to the “Connected to” tab (Fig 8.b) and click on the “Edit sensor visualized in” button (Fig 8.c). A new window opens (Fig 8.d).

You may need to click on the “+” button to scroll through the different channels available on the OB1 (Fig 8.e).
The channel where the MFS is already connected to and then already in use is grayed out. You can not select it.

Select the available channel you want to visualize your flow sensor to (for example the channel 2, Fig 8.f). Then click on the arrow to transfer the channel to the selected channel section (Fig 8.g). Then click on “Edit Channel” to confirm the change (Fig 8.h)

The sensor is now visualized in channel 1 and 2 (Fig 8.i) and you can read the flow rate on channel 1 and 2 on the OB1 window (Fig 8.j).

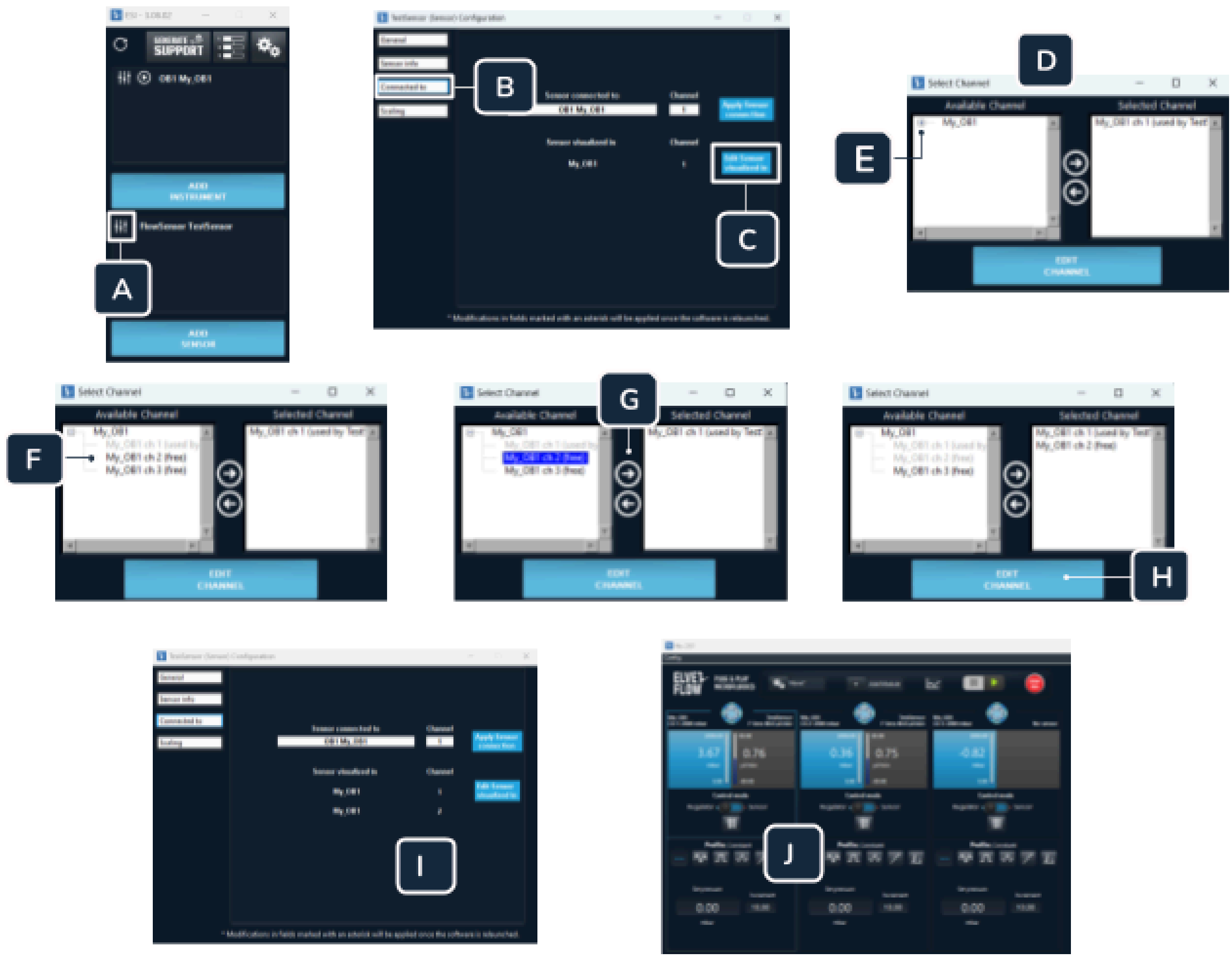


Fig 8. *Visualization of the MFS on multiple OB1 channels*

If you want to reverse this action, repeat the same steps the other way around.

MFS scaling

On the “Scaling” tab in the ESI sensor settings window (Fig 10.a), you can change the sensor's parameters.

You can change the **resolution** of your sensor (Fig 10.b) and choose between 8 different values, from 16 bits to 9 bits (Fig 10.c). The higher the bit value, the more the flow rate is averaged out. At 9 bits, you have low resolution and fast acquisition time. The relationship between resolution and acquisition time is exponential (Fig 9).

Resolution [bit]	Processing Time [ms]		
	Min.	Typ.	Max.
9	0.5	0.8	0.9
10	1.0	1.3	1.5
11	2.0	2.4	2.6
12	4.1	4.6	4.9
13	8.2	8.9	9.4
14	16.4	17.5	18.5
15	32.8	34.8	36.7
16	65.5	69.3	73.2

Fig 9. *Relationship between resolution and processing time.*

By default, the **calibration** of the flow sensor is set to the calibration with H_2O. If you want to change the pre-configured calibration and use the Isopropyl one, go to the scaling tab in the ESI sensor settings window and choose between the two saved calibrations (Fig 10.d).

If you perform a calibration of the sensor with a specific liquid, you need to change the **scale factor** (Fig 10.e) and the **offset** (Fig 10.f) accordingly.
To know more about calibration and how to perform one, please go to Annex 5.

Finally, the list “Parameter to measure” shows everything that our range of sensors is capable of measuring (Fig 10.g). Depending on the type of sensor chosen, only compatible measurements are left active.

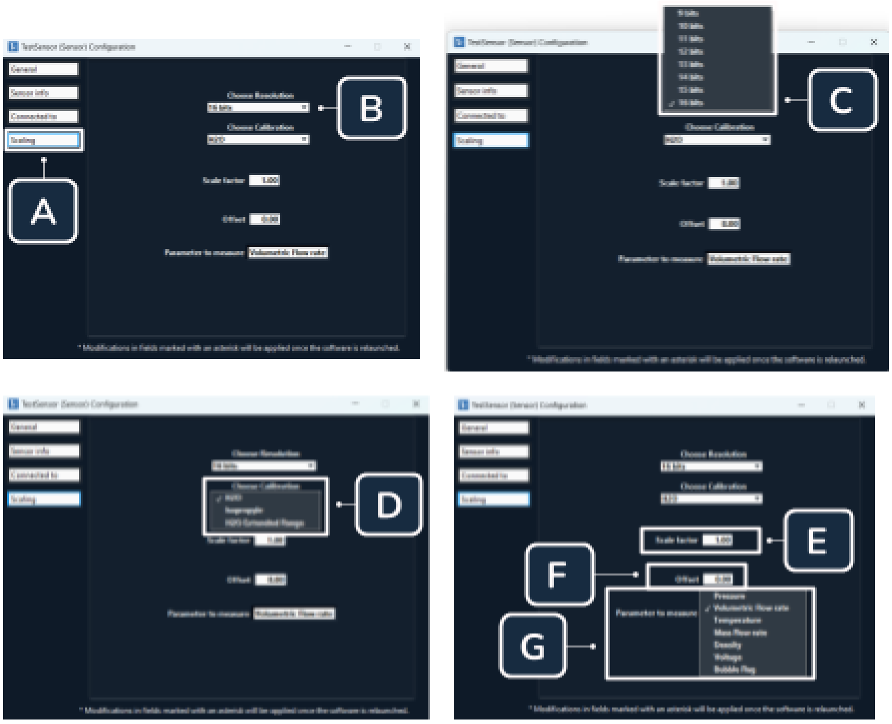


Fig 10. *MFS scaling*

Annex 5: MFS Calibration

Elveflow MFS flow meters have preset calibration for specific types of liquids. If a different liquid needs to be measured, the sensor performance with that liquid should be verified and it may be necessary to apply a correction to the sensor output. This correction is often referred to as “sensor calibration”.

Why is it necessary to calibrate the MFS?

As the MFS flow sensors are thermal flow sensors, the relation between the temperature difference and the flow rate depends on the properties of the liquid passing through (thermal conduction, thermal capacity, etc...). Thus the sensor must be calibrated depending on the liquid flowing in, in order to deliver a relevant flow rate output value.

The digital MFS (2, 3 and 4) have two different available preset calibrations : H_2O and Isopropyl Alcohol (IPA).

When working with solutions other than aqueous solutions or IPA, manual calibration is highly recommended, because the flow rate measured by the MFS often does not match the real flow rate inside the system.

To allow the use of MFS with other solutions, one should choose the preset calibration that best matches the fluid, and then set a scale factor.

The scale factor, as well as the preset calibrations, can be changed in the configuration window of the MFS in the ESI software (Fig 27).

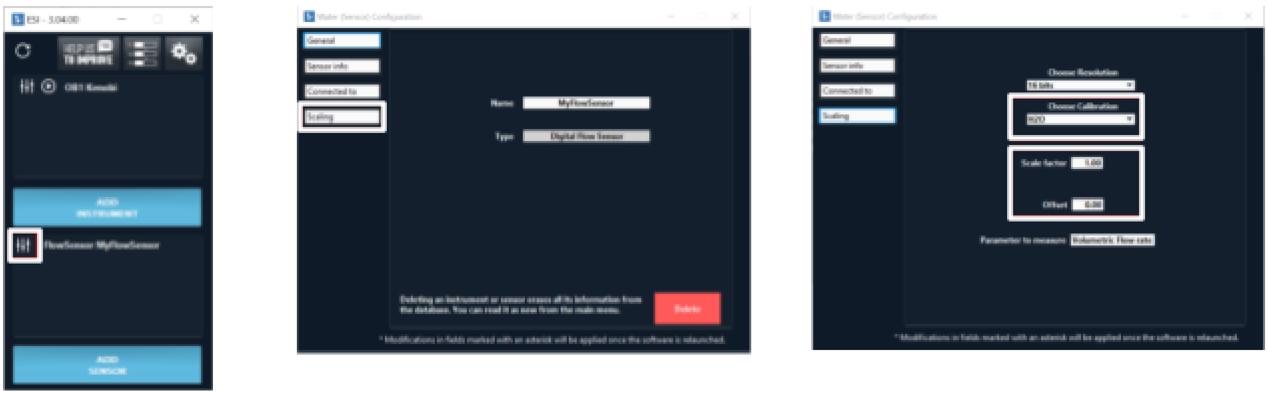


***Fig 27.** MFS flow sensor working principle*

Elveflow recommends **using the calibration H_2O when working with aqueous solutions**, and to **use the calibration Isopropyl when working with oils and carbon chains**.

When do you need to calibrate?

It is recommended to calibrate a MFS when working with a liquid for the first time. Scale factors and offsets slightly vary from one MFS to another of the same range. However, scale factor and offset could significantly vary from one MFS to another with a different working range (for example, a MFS2 and a MFS3 could not have the same calibration parameters).

Generally speaking, aqueous solutions with low concentration of other molecules will need only little or no correction. However, carbon chain liquids other than IPA could sometimes require significant corrections (such as a scale factor near 10 for example).

Calibration protocol

In order to find the real flow rate value, you can use several techniques. Here, we suggest a simple protocol that relies on a common precision weighing scale.

To perform a calibration, you need:

- a pressure source
- an OB1 pressure controller
- a precision weighing scale
- two reservoirs
- a clean MFS (check the cleaning section of this user guide if necessary)
- a timer

The aim of this calibration protocol is to **find the match between the measured flow rates and the corresponding real flow rate**, deduced from the weight of the fluid obtained after a certain amount of time.

Generally speaking, in order to know what is the real flow rate Y inside the system when your MFS measures a given flow rate X, here is the way to proceed:

- Step 1 : Set up the following system : Pressure source -> Reservoir filled with the tested solution -> MFS -> Microfluidic resistance -> Outlet reservoir
- Step 2 : Fill the system with your solution. Here you can either set a pressure or set a flow rate using the sensor mode.
- Step 3 : Carefully weigh the output reservoir with a precise scale (let's note the mass m_1), and set the reservoir back in the system. Be careful of evaporation that may occur in the outlet reservoir so prevent the effect by closing it if needed.
- Step 4 : Open the module "flow injection" . It will integrate in real time the amount of volume measured by the flow sensor during the time of the experiment, then push your solution, launch the module and a timer at the same time.
- Step 5 : Once you think enough liquid has been moved (it depends on the precision of your scale and the precision you want to reach), stop the flow, the flow integration module (note the volume V) and the timer (note the time Δt). Weigh again the output reservoir with the precise scale. Let's note the second mass m_2.
- Step 6 : With the knowledge of the volumetric mass of the liquid (noted ρ), the duration of the experiment Δt and the moved mass of the liquid (m_2 - m_1), you can deduce the real flow rate Y that took place in the system.

The formula is the following one :

$$\boxed{Y = (m_2 - m_1)/(\rho \times \Delta t)}$$

With m_1 and m_2 in kg, ρ in kg/m^3, Δt in s, this formula gives Y in m^3/s.

1 m^3/s is equivalent to $6*10^{10}$µL/min.

You can also calculate the measured flow rate which is:

$$\boxed{X = V / \Delta t}$$

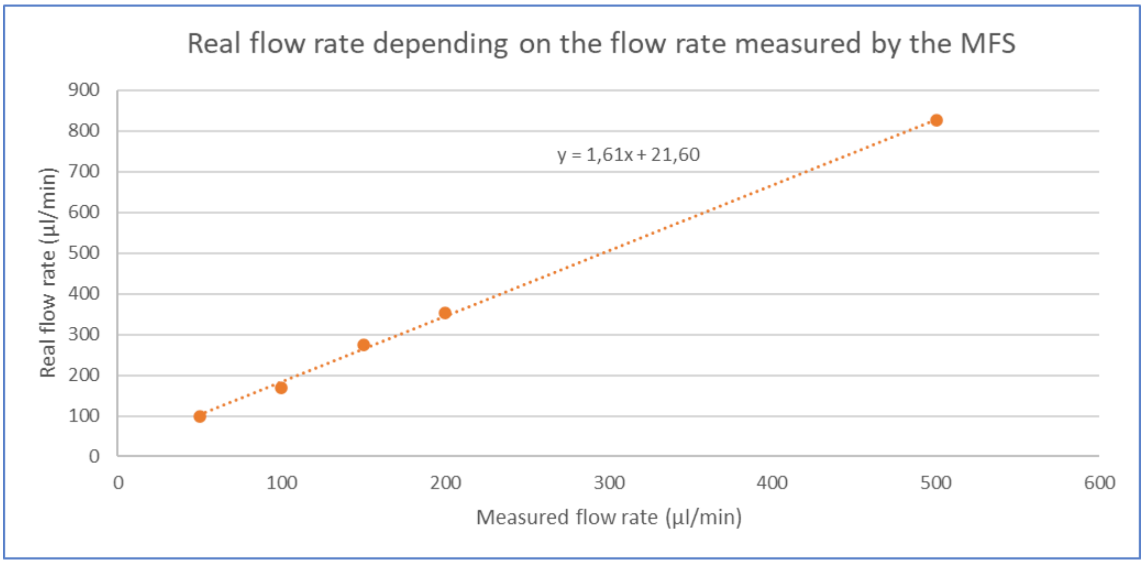
- Step 7 : Repeat step 6 with a different measured flow rate until you have at least two experimental relations between the measured flow rate and the real flow rate.

How to choose the measured flow rate? It is useful to choose the measured flow rates X near the limits of the working range of your MFS. Keep in mind that depending on the preset calibration you choose (Water or Isopropyl), the working range isn't the same. If possible, perform more than 2 measurements (4 or 5 would be the best, distributed along the range). If you know that you will use only a small part of the working range, you could do all your measurements in your working range of interest for a more precise calibration.

- Step 8 : To finish the experiment, draw the graphic of the real flow rate depending on the measured flow rate, and do a linear regression. You will deduce from this regression the values of scale factor which will be the coefficient of the slope.

Putting that concept into practice

For example, if I obtain this graphic :



I can found my scale factor: 1.61

Important Tips about MFS Flow Rate Correction

- **Evaporation may occur**, so be sure to collect and keep all the volume measured.
- **Choose the duration Δt long enough** to minimize your incertitude about the calibration. The higher the Δt, the higher the difference of mass m_2 - m_1, and the lower the relative errors will be.
- Fill the fluidic path before weighing the reservoir and actually performing the calibration.
- It is important to **have adequate resistance in the system**.

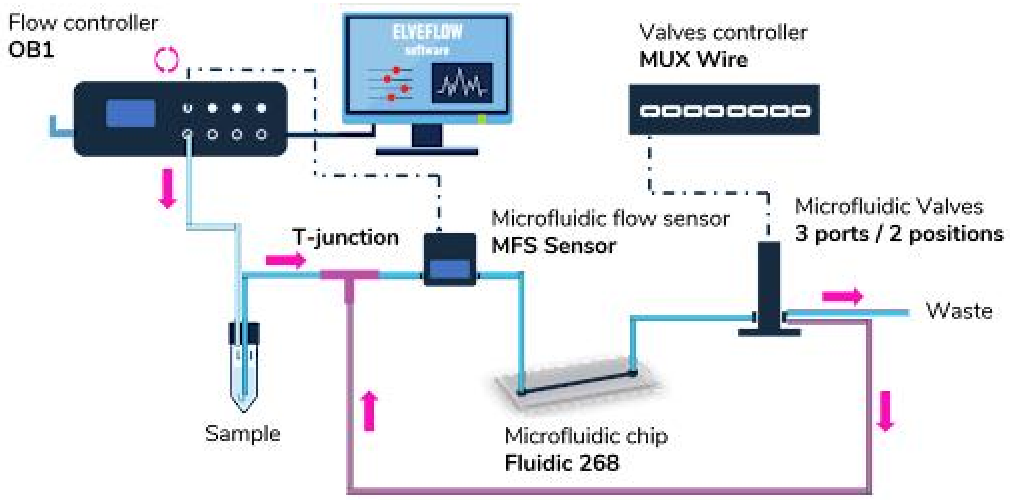
Annex 6: Offset correction

For several reasons even when there is no flow the sensor may still measure a value. This offset needs to be corrected in the settings of the flow sensor in the ESI software (Fig 27).

If you need to adjust the scale factor, the scale factor needs to be entered before correcting the offset.

To know the offset you need no flow, no flow conditions can only be achieved by having no pressure difference between the inlet and outlet of the system.
There are two ways to do so:

- putting your inlet and outlet reservoir at the same pressure, meaning having both at the atmospheric pressure and the liquids for inlet and outlet at the same level or using a specific pressure for the inlet and outlet. Here an example of a no flow set-up. (Fig 28)



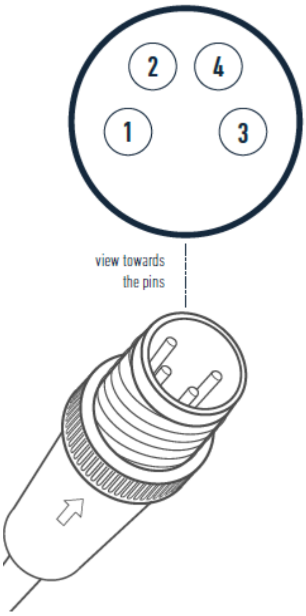
- adding 2/2 valves (manual or automatic) before the flow sensor, indeed mechanically stopping the flow will also put the rest of your fluidic path at atmospheric pressure.

Annex 7: Custom Connection

The MFS flow sensor signal can also be read through custom wiring, without requiring Elveflow equipment. The pin out diagram and the specifications are listed in detail below.

Any damage resulting from a miswiring or any other type of misuse is not covered by warranty. This information is for understanding purposes only. Sensor modification is not covered under warranty.

Sensor Pins Diagram



MFS flow sensor (Analog) Pinout

1. Vcc 6-12 V, 7 mA (typical current consumption)
2. Not in use
3. Ground
4. Signal - see below:

Model	Zero Flux Voltage [V]	Sensitivity [Ml/V]
1.5 µl/min	2.5	0.6795
7 µl/min	2.5	3.171
50 µl/min	2.5	22.65
80 µl/min	2.5	36.24
1000 µl/min	2.5	453
5000 µl/min	2.5	2.265

MFS- D Flow Sensor (Digital) Pinout

1. Vcc 4-12 V, 7 mA (typical current consumption)
2. SCL (clock line)
3. Ground
4. SDA (data line)

Digital communication between a master and the flow sensor runs via the standard I2C- interface. The physical interface consists of two bus lines, a data line (SDA) and a clock line (SCL) which need to be connected via pull-up resistors to the bus voltage of the system.

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