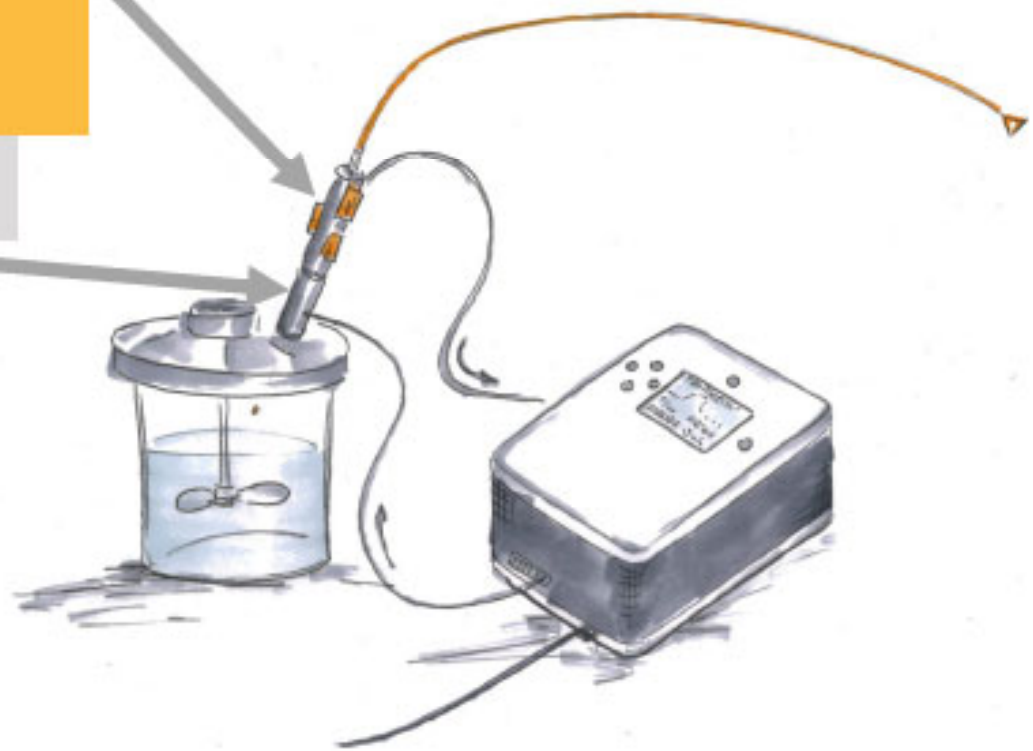
Herzlich Willkommen

Inline measurement of submicrolitre droplets using differential pressure flow sensors, Simon Zumbrunnen

2011 Micro dosing device for bioreactors

Idea: Inline droplet sensor
- Viscosity independent
- Double DP-Sensor

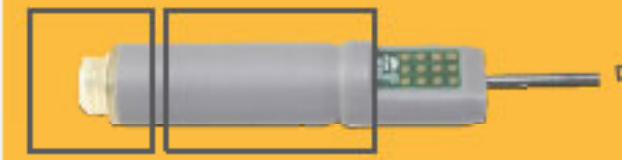
micro dosing valve:
- Viscosity dependent
- Pressure dependent
- Production variation



B-drop control 2016

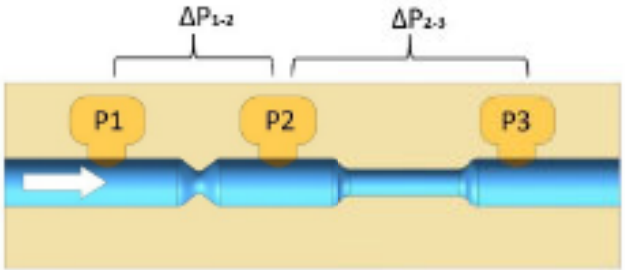
Highly sensitive, micro dosing device for fluid additions to bioreactors.

- Single use technology
- Sterile packaging
- Pre calibrated (ex works)
- Viscosity independent volume control
- Biocompatible materials



micro valve

flow sensor

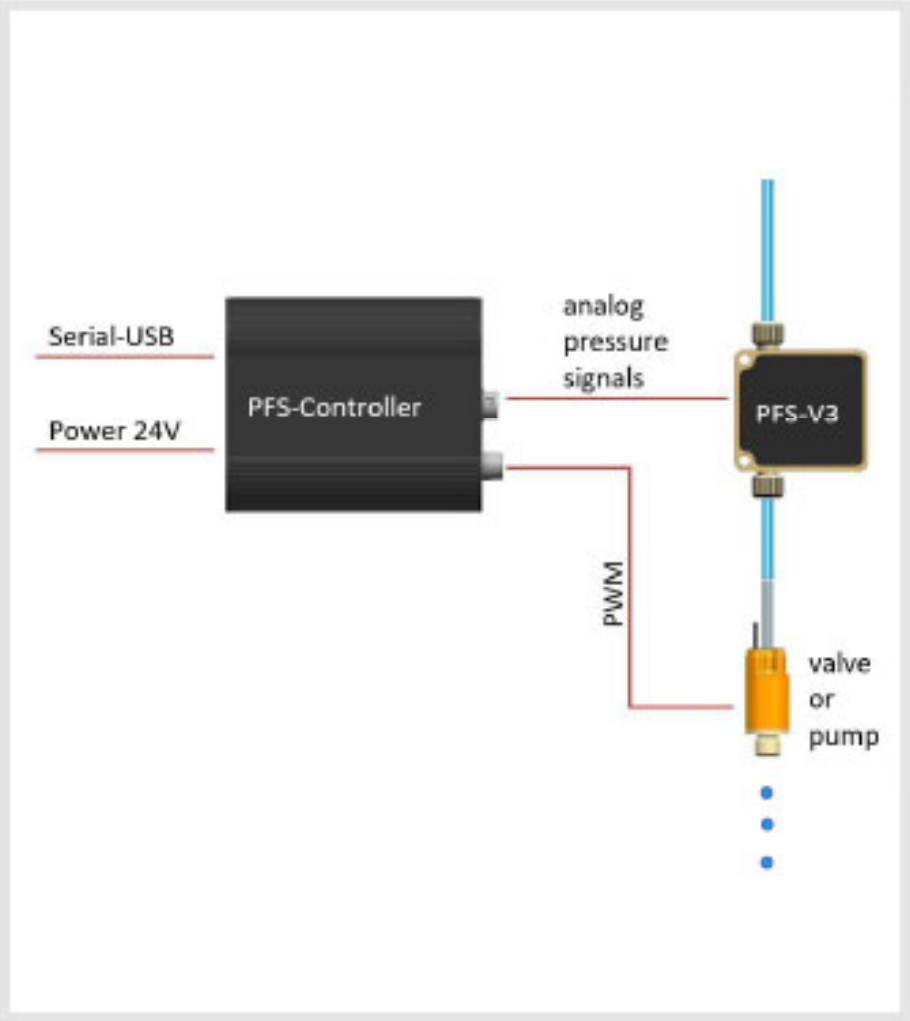


$$\left| \begin{array}{l} \dot{V} = f_1(\Delta P_{1\text{-}2}, \eta) \\ \dot{V} = f_2(\Delta P_{2\text{-}3}, \eta) \end{array} \right| \quad \Rightarrow \quad \dot{V} = f(\Delta P_{1\text{-}2}, \Delta P_{2\text{-}3})$$

viskositätsunabhängig

System: Applikon miniBio

Measurement Setup today



User interface:

Time-Pressure dispensing

PULSED FLOW SENSOR + MICRO VALVE

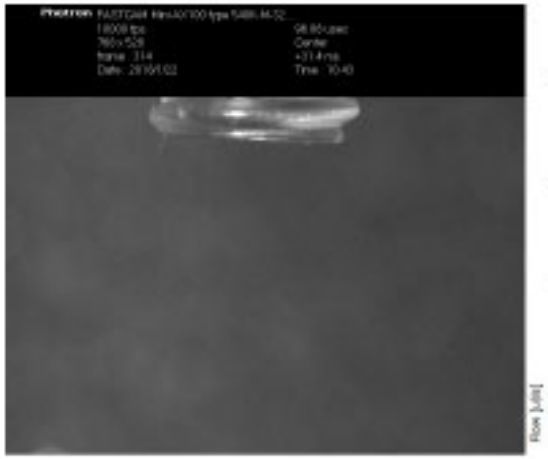
- Wetted materials: PEEK, FPM
- Response time < 1 ms

Version Nr.		PFS-V3-B1	PFS-V3-B2	
Parameters	Symbol			Unit
Calibrated flow rate	V'	3-30	10-100	ml/min
Operating pressure	pw	0-4	0-4	bar (absolute)
Smallest orifice diameter	Dmin	250	500	µm

Time-Pressure Dispensing

Droplet Event:

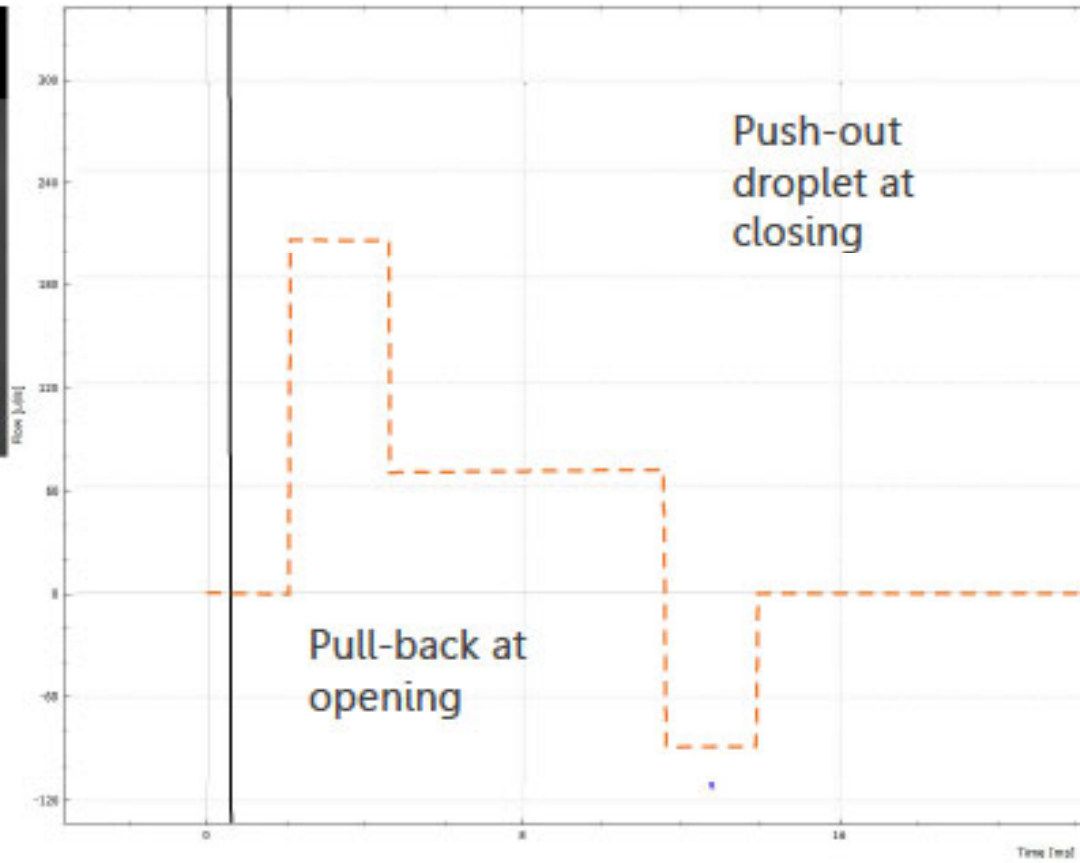
What does a microliter droplet look like?



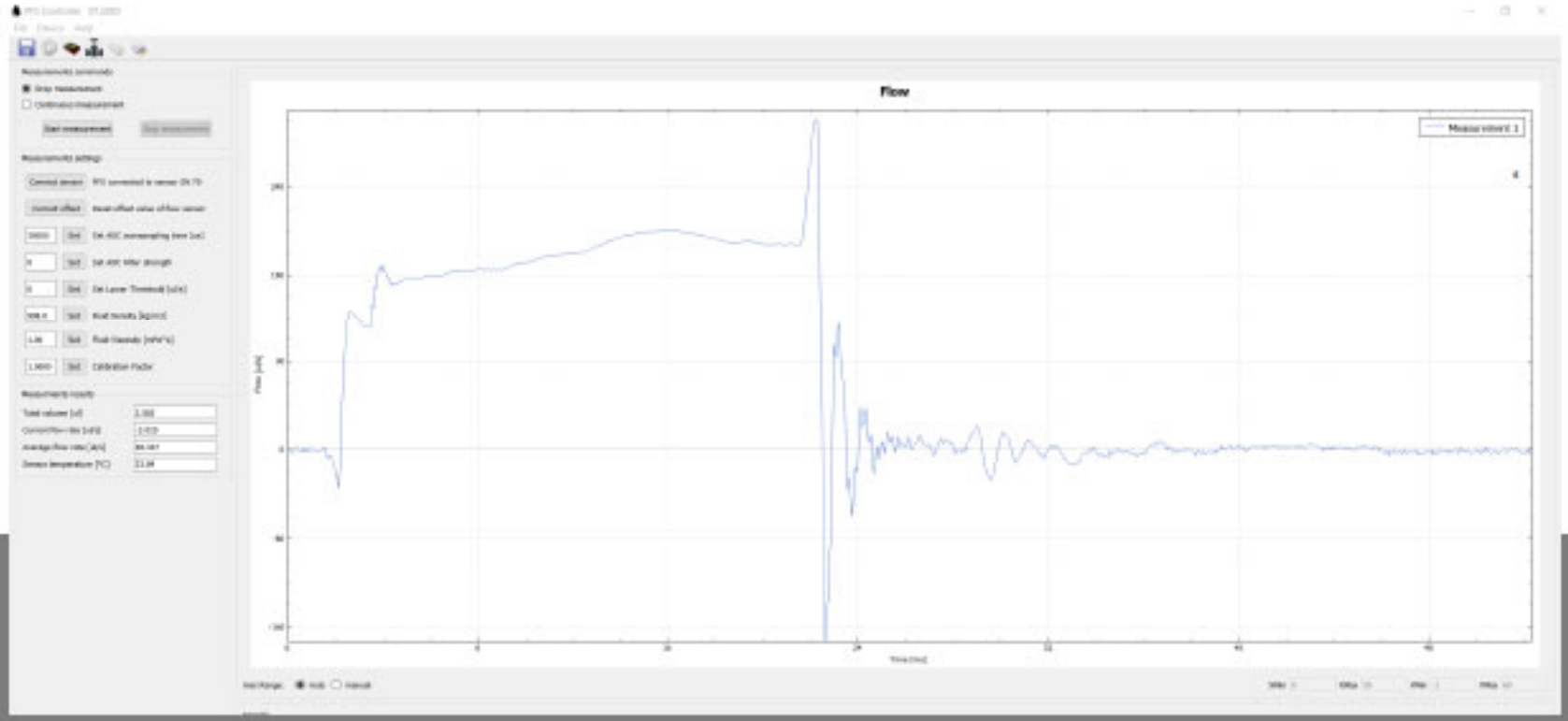
Parameters:

T_open = 10 ms

Volume = 1.7 µl



From «big» to small droplets



T_open: 16ms
Volume: 0.686 µl

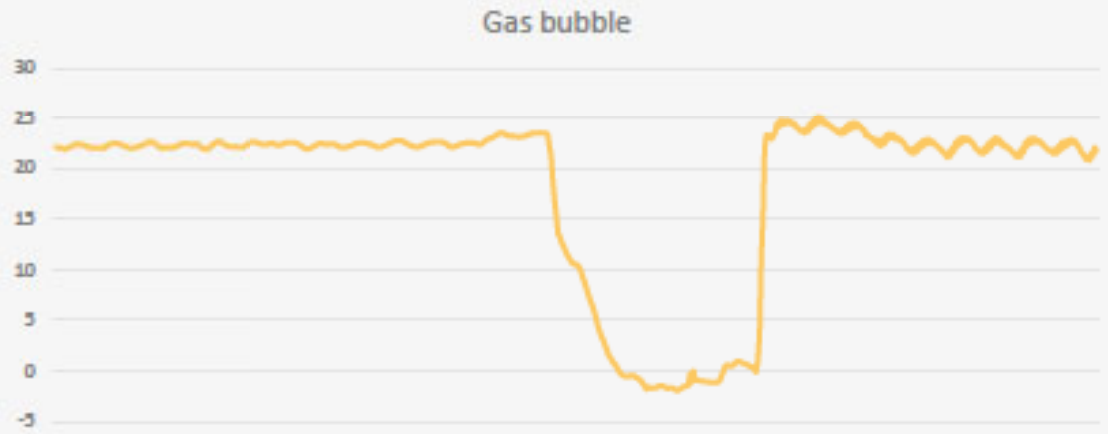
Filters and thresholds

- Minimal flow threshold
- Floating average filter
- Droplet end detection
- Trigger function for synchronization and high resolution

Measuring gas bubbles

Pulsed flow sensor V3-B1

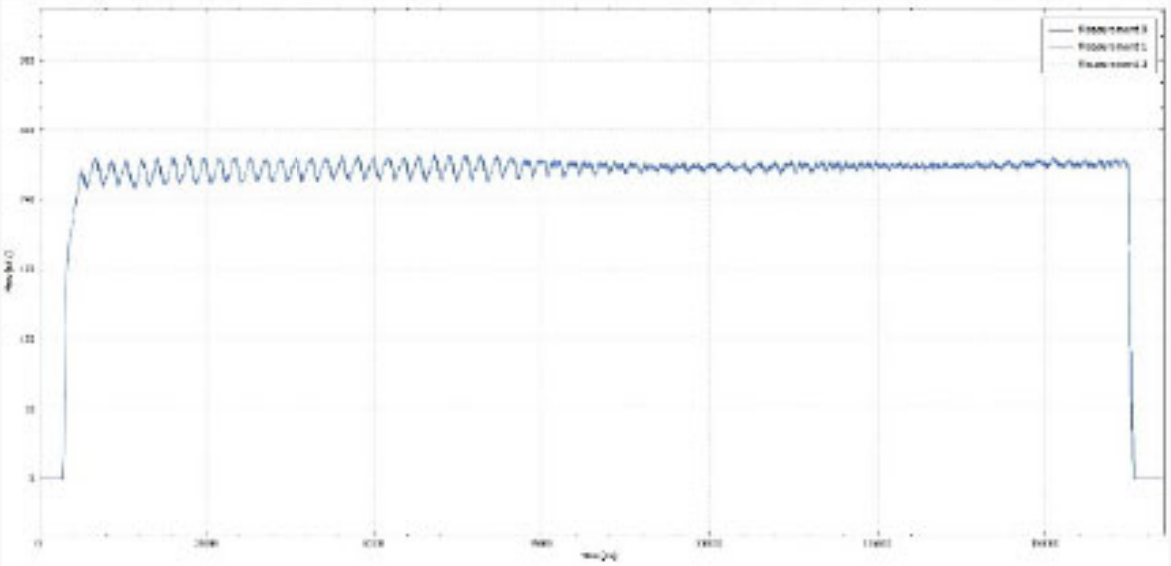
"A bubble is like an inverse dosing pulse"



Measuring gas bubbles

Setup 1: only water

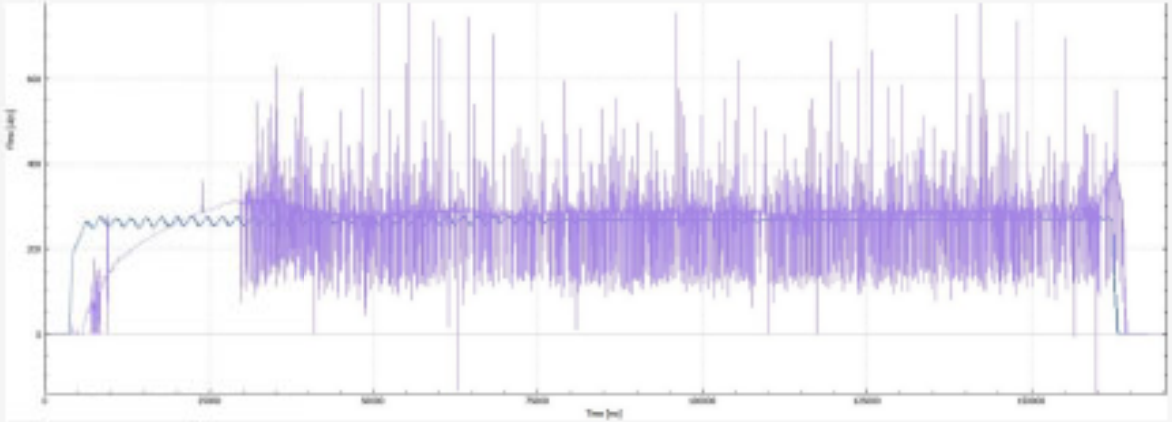
	only water
Run 1	40237 µl
Run 2	40302 µl



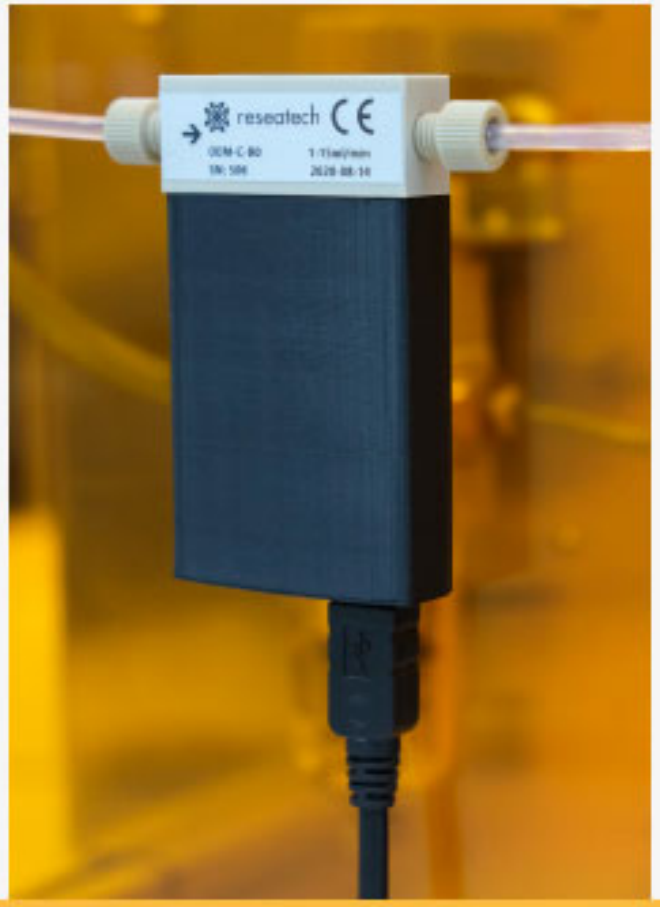
Measuring gas bubbles

Setup 2: 40 ml of water & 40 ml of air

	only water	water and air	difference
Run 1	40237 µl	40879 µl	+ 1.6 %
Run 2	40302 µl	40699 µl	+ 1.0 %



Sensor for outgassing media



OEM-C flow sensor

Specific sensor for outgassing media

- Continuous sampling rate of 100Hz
- Readout interval 0.01 – 100 s (average)
- Serial readout (RS232)

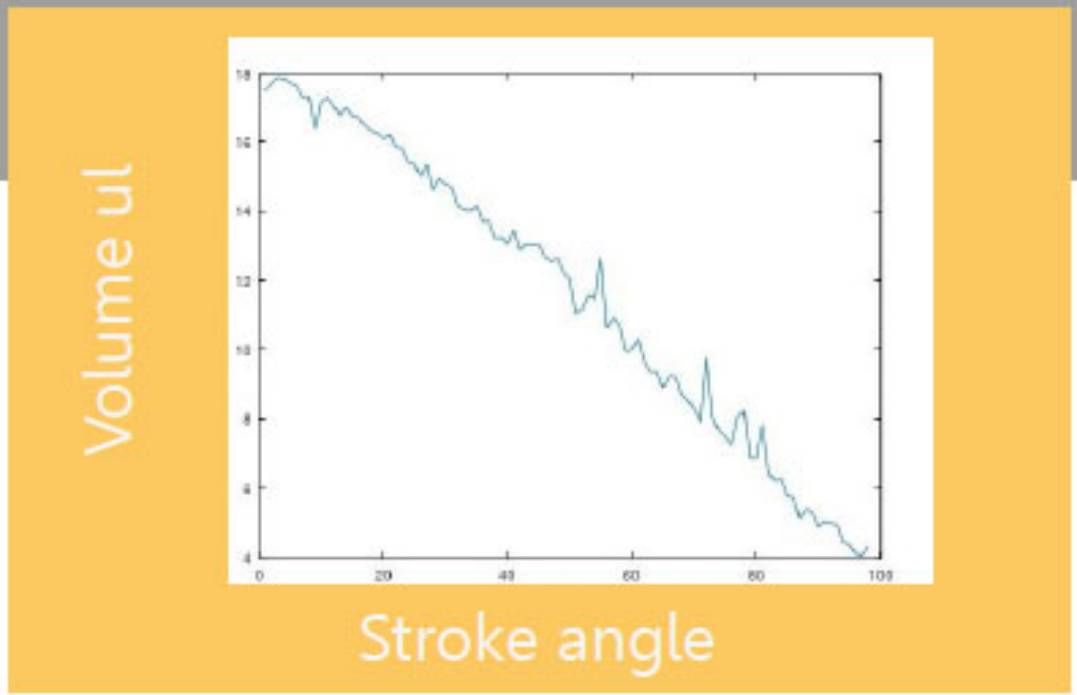
Version		OEM-C B0	OEM-C-B1	OEM-C-B2	
Parameters	Symbol				Unit
Calibrated flow rate	V'	1 - 15	3 - 30	10 – 100	ml/min
Restrictor orifice diameter	Dmin	200	300	500	µm

Controlling a micro dosing pump

Pulsed Flow Sensor

In this project a KNF **FMM-20 dosing pump** was used to dispense droplets with a size of 4 to 18 microliters. Its stroke was adjusted by a servo motor to variate the volume. For a control loop the Pulsed Flow Sensor (PFS-V3) was used as a reference.

www.knf-flodos.ch



System: Applikon miniBio

Controlling a micro dosing pump

Measurements:
For 35 different plunger strokes, the droplet volumes were recorded by the Pulsed Flow Sensor at a sampling rate of 20 kHz. The data shows:

- Small plunger strokes show an earlier raise in flow than big plunger strokes
- Big plunger strokes show a plateau and an acceleration before closing
- The closing event at 50 ms and the post-pulse oscillation is very reproducible.

Figure 2: Volume flows produced by continuously increased plunger stroke.

Controlling a micro dosing pump

Implementing a control circuit

With a PID control loop the droplet volume was guided to follow a Target volume of 9, 12 and 7 microliters per shot. The flow sensor signal was used as the control variable. As a second reference, a balance measured the droplet volumes.

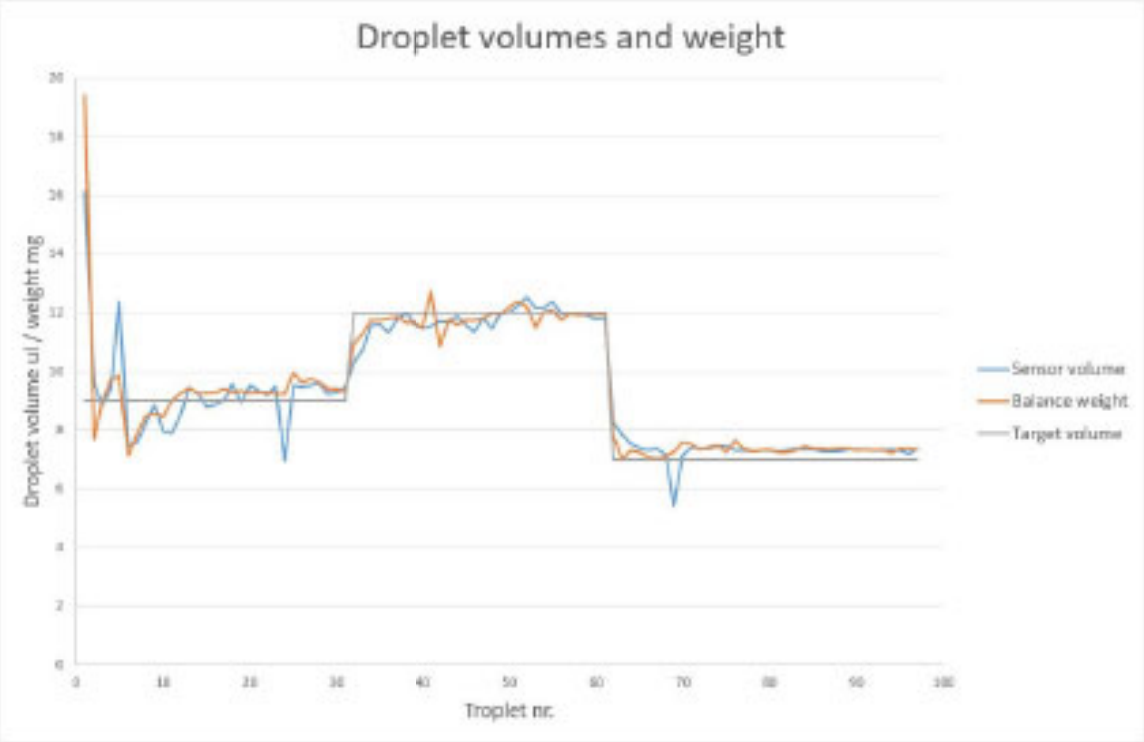
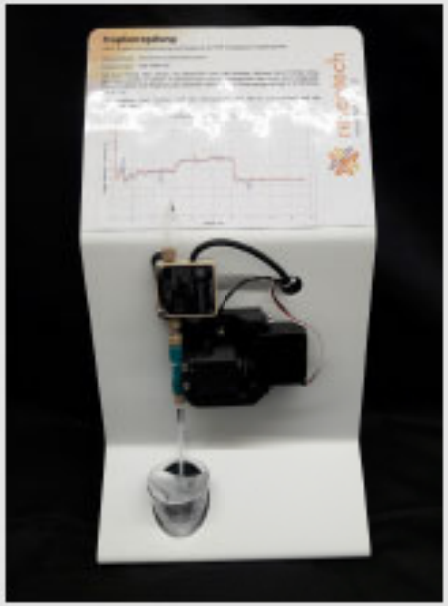


Figure 3: a control loop adjusts the plunger stroke to follow the targeted volumes.

Tabletop exibition

Time-pressure dispensing



Membrane pump Control-loop

Droplet measurements

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