Project MFMET main achievements and impact

Elsa Batista, Portuguese Institute for Quality, Portugal
MFMET project Coordinator

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

EMPIR MFMET Overview

Call: 2020 Normative

JRP name: Establishing metrology standards in microfluidic devices

JRP refeence: 20NRM02 MFMET

Total budget: ~ 1 M€

Total labour: ~120 MM

Duration: 36 months

Start date: June 2021

Coordinating Organisation: IPQ

Partners - 9 NMIs/DIs, 4 research institutions/university, 4 companies (17). 12 countries

Collaborators/stakeholders: 37

Chief stakeholder: The Microfluidic association

https://mfmet.eu,
https://zenodo.org/communities/mfmet

MFMET Consortium

MFMET
Establishing Metrology Standards in Microfluidic Devices

RI. SE
Research Institutes of Sweden

Bronkhorst®
Flow Technology

enabling MNT
micro nano
technology

DANISH TECHNOLOGICAL INSTITUTE

Hahn Schickard

University of Glasgow

TÜV SÜD
National Engineering Laboratory

microfluidic ChipShop

leti
ceatech

CETIAT
ensemble, innover et valider

CZECH METROLOGY INSTITUTE

LABORATOIRE NATIONAL DE MÉTROLOGIE ET D'ESSAIS
LNE

IMT
PRECISION ON GLASS

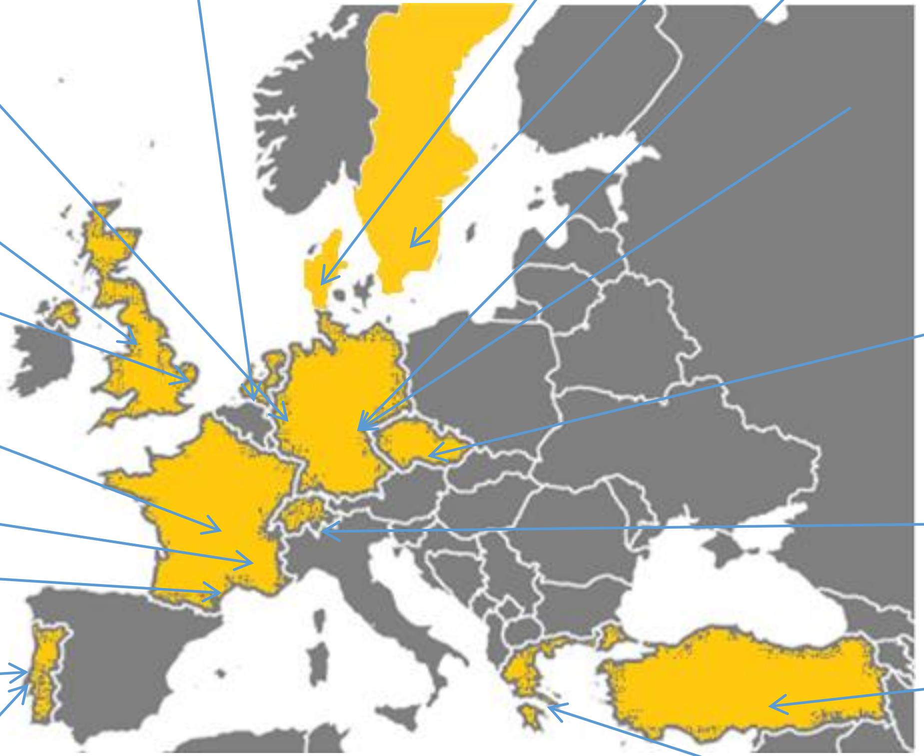
IPQ

inesc mn®
Microssistemas e Nanotecnologias

TÜBİTAK

ESYP

EIM



Overview

This project aims to contribute to the development of globally accepted standards for microfluidics and disseminate them to end users in industry (health and pharmaceutical sectors) and academia.

- ✓ by the development of **consensus-based measurement protocols & guidelines**

- ✓ By the **dissemination of metrology standards** towards normative committees (ISO TC48/WG3), industry and end users

Work Packages Summary

Project Coordinator – Elsa Batista

WP no.	WORK PACKAGE TITLE	WP LEADER	
WP1	Establishment of consensus-based flow control specifications for microfluidics	INESC MN	Vania Silverio
WP2	Development of measurement protocols for microfluidics	CETIAT	Kevin Romieu
WP3	Development of general standards and guidelines for interfaces and connectivity	IMT	Christina Pecnik
WP4	Development of guidelines for the standardisation of dimensions for modularity and sensor integration	microfluidics ChipShop	Elena Müller
WP5	Creating impact	DTI	Thomas Daugbjerg
WP6	Management and coordination	IPQ	Elsa Batista

Major achievements for each WP

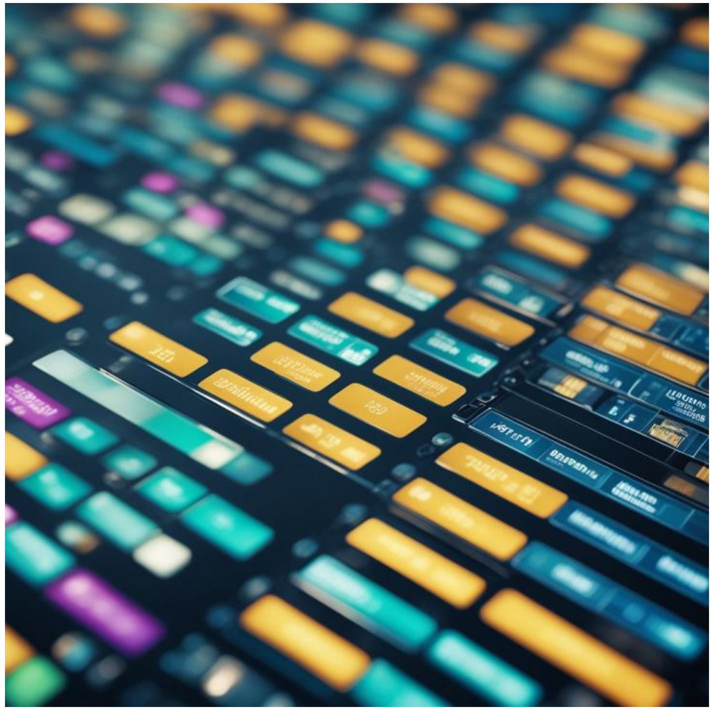
WP1 - Consensus-based flow control specifications for microfluidics

- 1 Deliverable finished, 1 deliverable ongoing
- Input to 2 Standards
- 1 video for MFMET Webinar
- 1 White Paper
- 8 Reports + 1 ongoing
- 1 Database Flow components
- 3 Protocols for leakage testing

WP1 - Consensus-based flow control specifications for microfluidics

MFMET
Establishing Metrology Standards in Microfluidic Devices

Database of microfluidics flow components, available online



MFMET

Overview Database input MFMET.eu

Choose class

Flow sensor | Export all data

Search:

Type	Flow range	Flow stability	Flow unit	Pressure range	Pressure unit	Connection size	Connection unit
Coriolis mass flow meter	0 to 30	0 to null	kg/h	0 to 200	Bar	6	mm
Coriolis mass flow meter	0 to 2	0 to null	kg/h	0 to 200	Bar	6	mm
Coriolis mass flow meter	0.05 to 200	0.4 to 0.4	g/h	0 to 0	bar		
Differential pressure flow sensor	60 to 12000	0.3 to 60	µL/h	0 to 0	bar		
Other technology for flow measurement in microfluidic	0 to 0	0 to 0	nL/h	6 to 89	bar		
Thermal sensor	0 to 3000	0 to null	µL/h	0 to 50	Bar	1/16	inch
Thermal sensor	0 to 99.6	0 to null	mL/h	0 to 0	bar		
Thermal sensor	90 to 300000	4.5 to 15000	µL/h	0 to 0	bar		
Thermal sensor	0.005 to 2	0.0001 to 0.0001	g/h	0 to 0	bar		
Thermal sensor	30 to 360	0.05 to 10.8	mL/h	0 to 0	bar		
Thermal sensor	0 to 0.09	0.001 to 0.001	mL/h	0 to 0	bar		

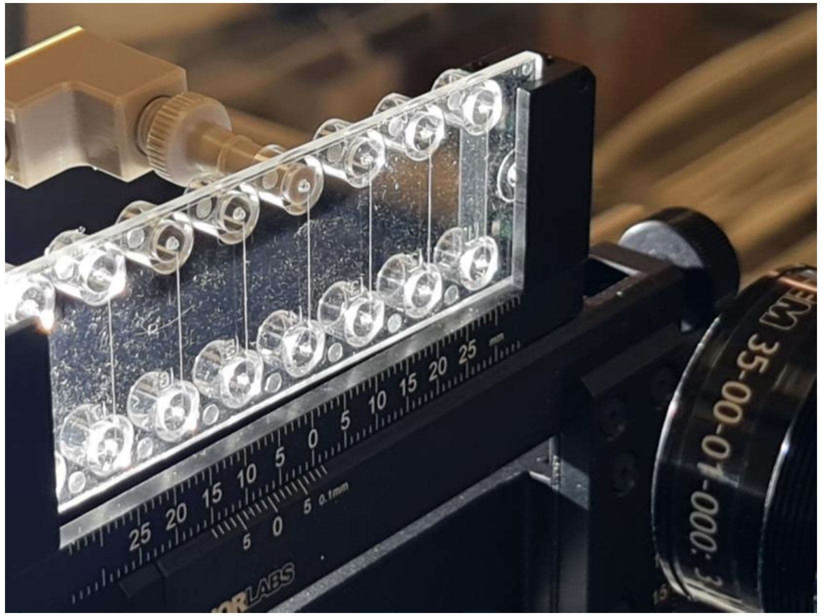
Showing 1 to 11 of 11 entries

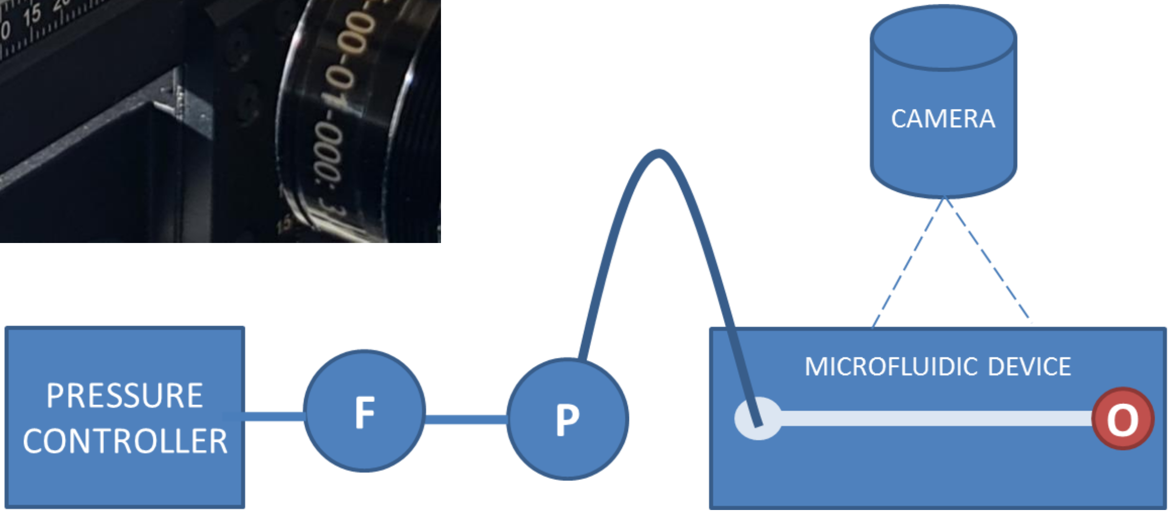
Overview - MFMET (teknologisk.dk)

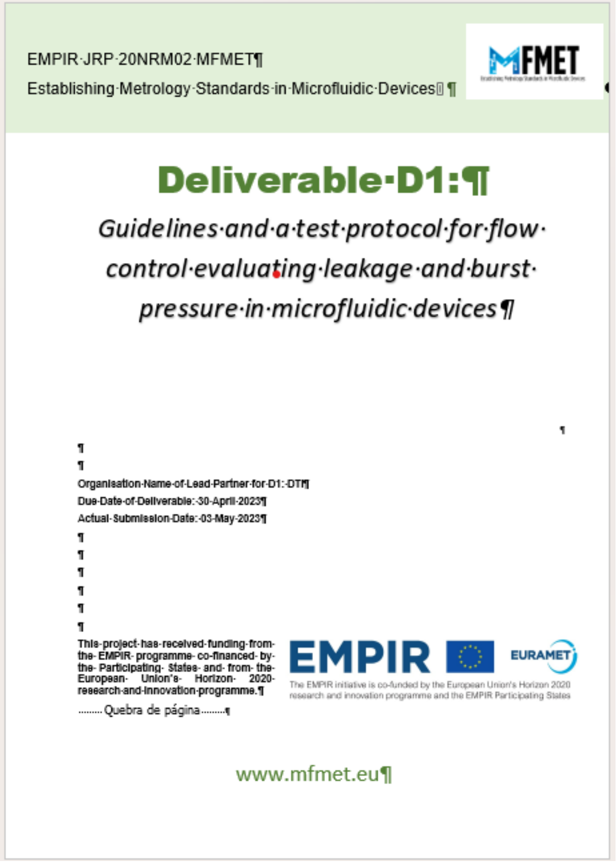
WP1 - Consensus-based flow control specifications for microfluidics

MFMET
Establishing Metrology Standards in Microfluidic Devices

Deliverable 1: Guidelines and a test protocol for flow control evaluating leakage and burst pressure in microfluidic devices







EMPIR JRP 20NRM02 MFMET
Establishing Metrology Standards in Microfluidic Devices

Deliverable D1:

Guidelines and a test protocol for flow control evaluating leakage and burst pressure in microfluidic devices

Organisation Name of Lead Partner for D1: DTI
Due Date of Deliverable: 30 April 2023
Actual Submission Date: 03 May 2023

This project has received funding from the EMPIR programme co-financed by the Participating States and from the European Union's Horizon 2020 research and innovation programme.

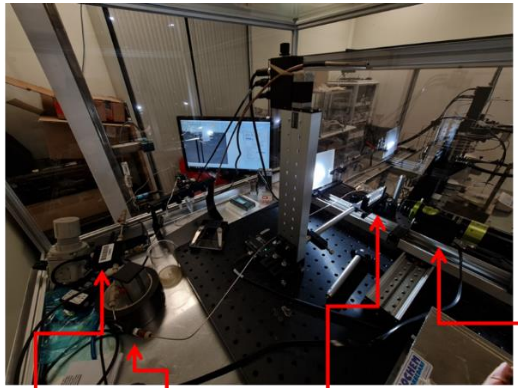
Quebra de página

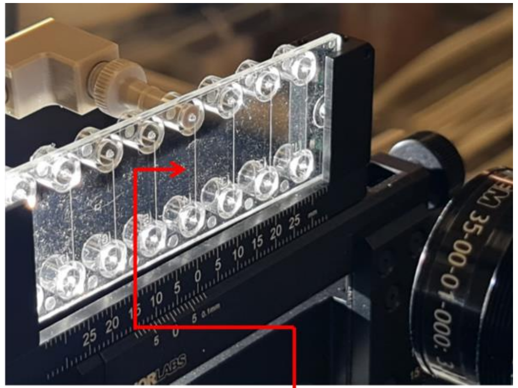
www.mfmet.eu

WP2 - Measurement protocols for different flow quantities and liquid properties

Establishing Metrology Standards in Microfluidic Devices

Deliverable 3: Calibration guide for the evaluation of **flow-related quantities** in microfluidic devices





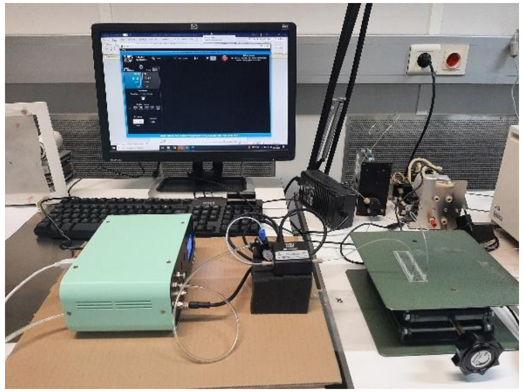
Thermal mass flow meter

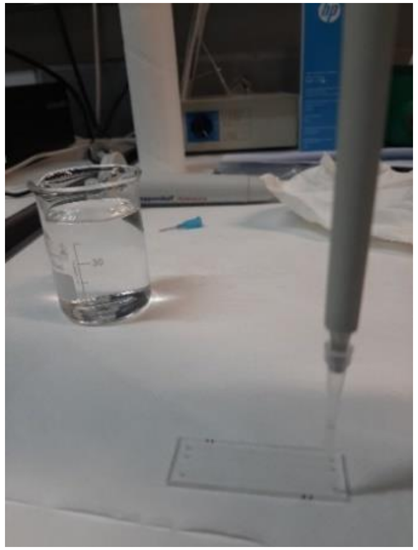
Pressure sensor

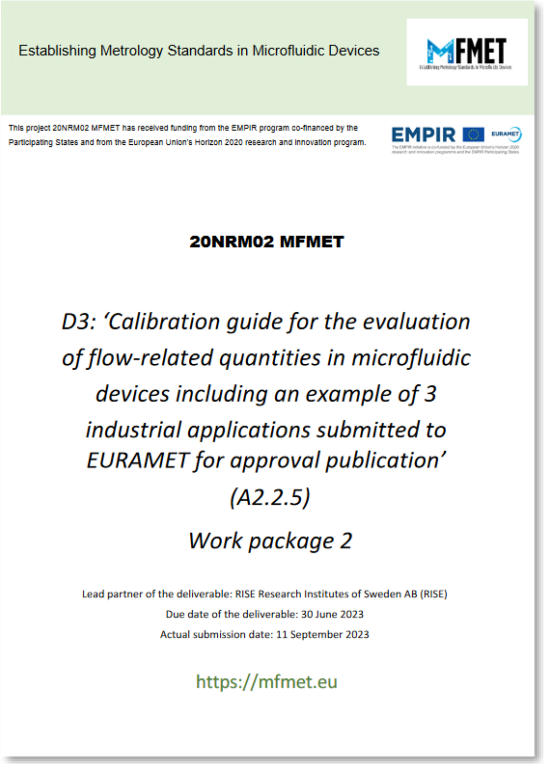
Chip under test

Camera for inline reference flow rate measurement

100x100 µm channel Outlet at atm. pressure







Establishing Metrology Standards in Microfluidic Devices

MFMET

This project 20NRM02 MFMET has received funding from the EMPIR program co-financed by the Participating States and from the European Union's Horizon 2020 research and innovation program.

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20NRM02 MFMET

D3: 'Calibration guide for the evaluation of flow-related quantities in microfluidic devices including an example of 3 industrial applications submitted to EURAMET for approval publication' (A2.2.5)

Work package 2

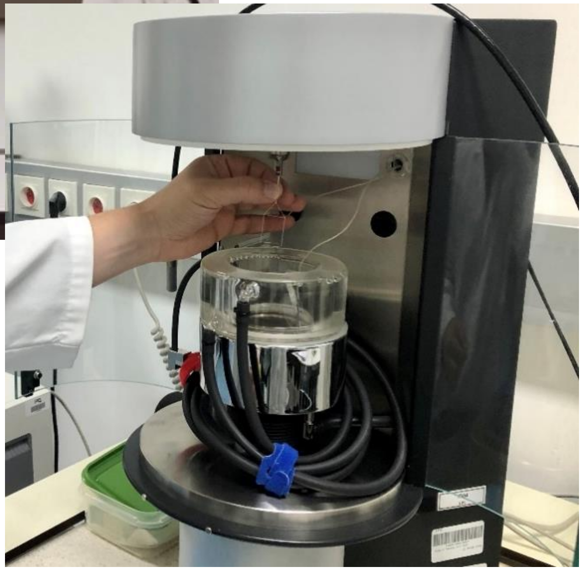
Lead partner of the deliverable: RISE Research Institutes of Sweden AB (RISE)
Due date of the deliverable: 30 June 2023
Actual submission date: 11 September 2023

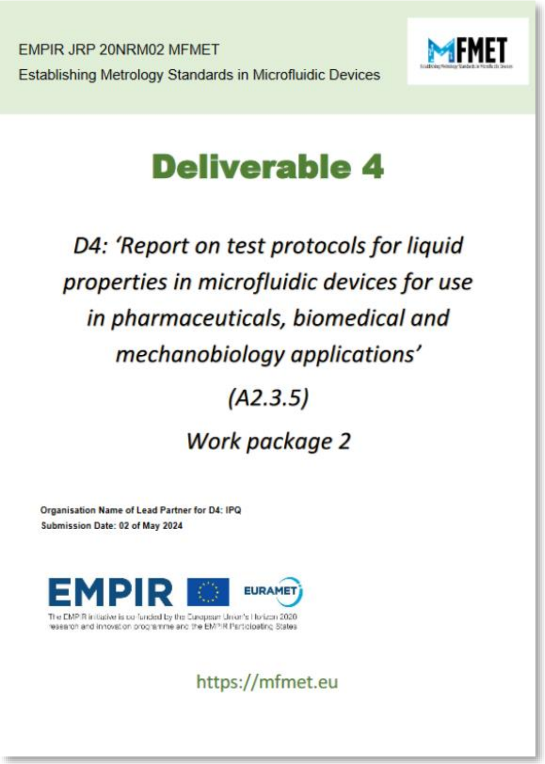
https://mfmet.eu

WP2 - Measurement protocols for different flow quantities and liquid properties

Establishing Metrology Standards in Microfluidic Devices

Deliverable 4: Report on test protocols for **liquid properties** in microfluidic devices for use in pharmaceuticals, biomedical and mechanobiology applications





EMPIR JRP 20NRM02 MFMET

Establishing Metrology Standards in Microfluidic Devices

Deliverable 4

D4: 'Report on test protocols for liquid properties in microfluidic devices for use in pharmaceuticals, biomedical and mechanobiology applications'

(A2.3.5)

Work package 2

Organisation Name of Lead Partner for D4: IPQ

Submission Date: 02 of May 2024

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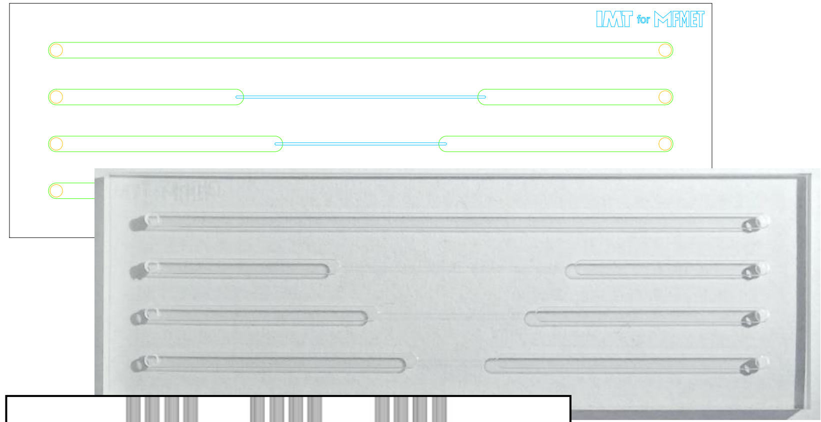
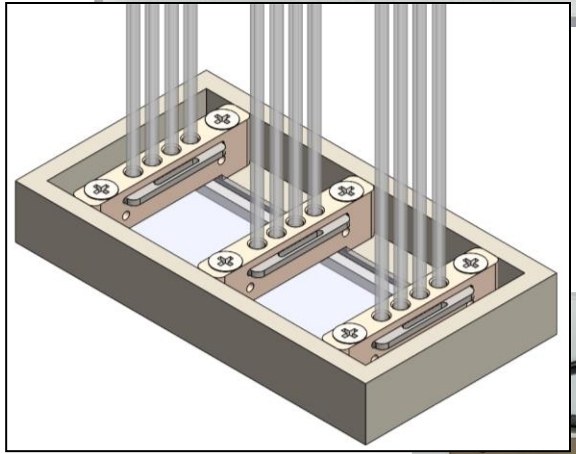
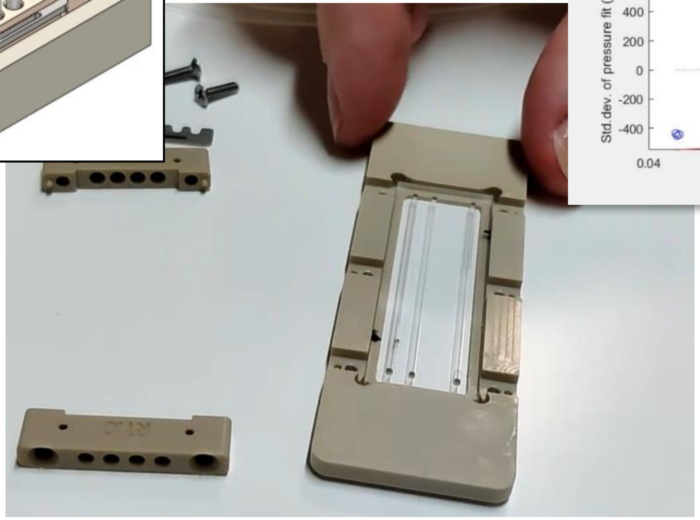
https://mfmet.eu

And… what about task 2.4? 😉

WP2: glass and polymer transfer standards



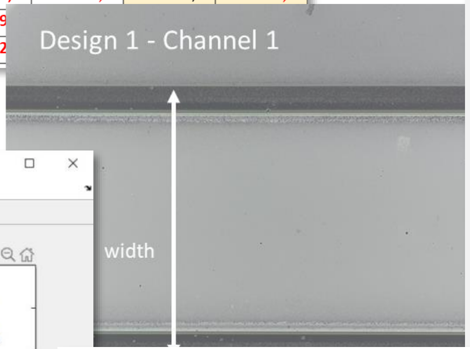




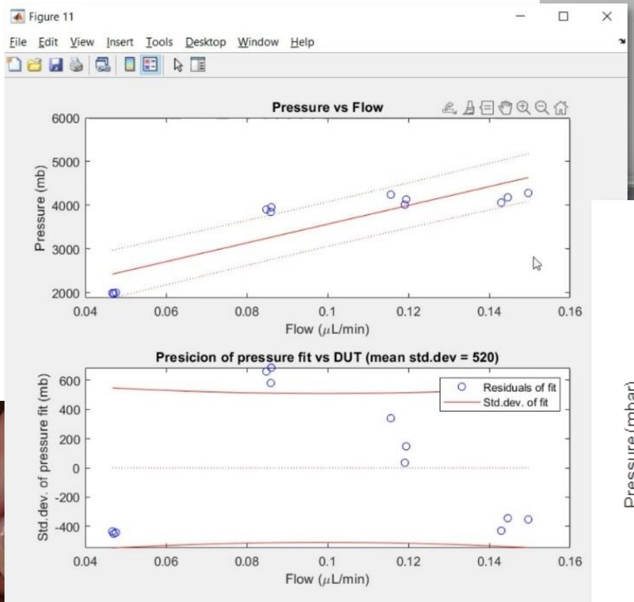
From design to actual chip…

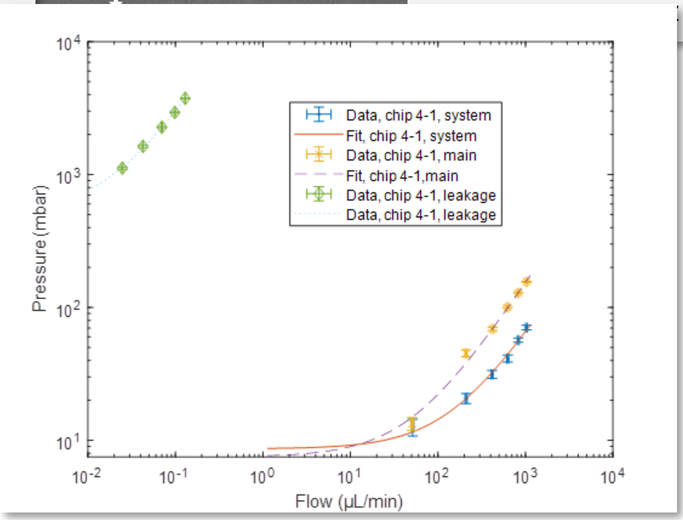
Serie 01

Design01	Hole 01		Hole 02		width		Length	
	Diam.	σ	Diam.	σ	Meas.	σ	Meas.	σ
Channel 01	813,14	11,37	829,02	1,61	998,10	1,78	40121,78	802,44
Channel 02	822,85	3,55	821,10	0,82	1001,59	2,93	40136,43	802,73
Channel 03	822,20	3,93	825,52	0,17	999			
Leakage Channel					152			



Hole01_Channel01.Diamètre	0.8049
Hole01_Channel02.Diamètre	0.8048
Hole01_Channel03.Diamètre	0.8286
Hole02_Channel01.Diamètre	0.8089
Hole02_Channel02.Diamètre	0.8423
Hole02_Channel03.Diamètre	0.8055
Width_Channel01.Largeur	0.9914
Width_Channel02.Largeur	0.9919
Width_Channel03.Largeur	0.9923
Width_LeakageChannel.Largeur	0.1430
Length_Channel01.DXY	39.8079
Length_Channel02.DXY	39.8262
Length_Channel03.DXY	39.8191
Length_LeakageChannel.DXY	5.9988
Height_Channel01.DZ	0.6945
Height_Channel02.DZ	0.6922
	0.6909

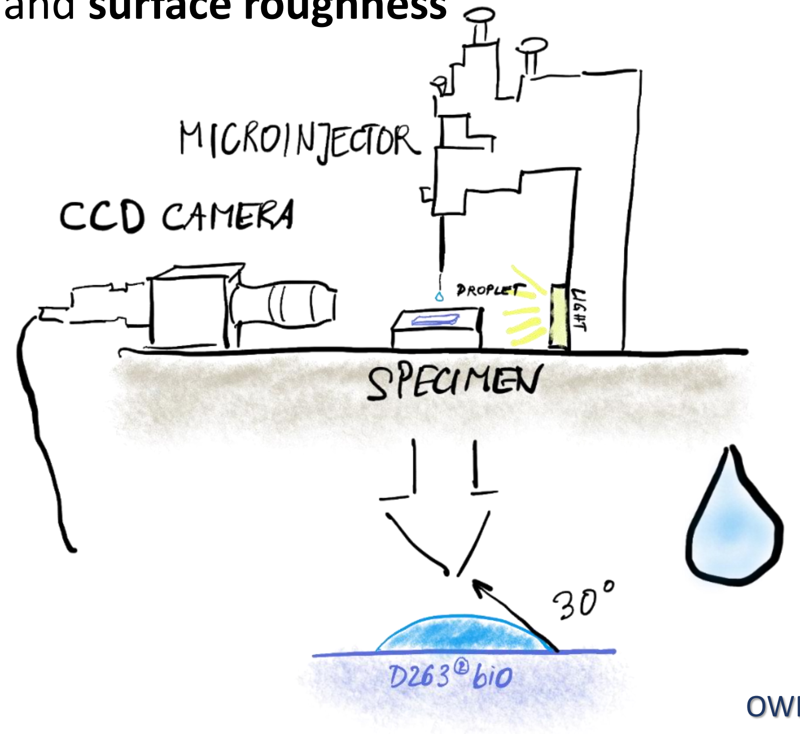




Travelling through 8 international laboratories for the measurement of dimensions, flow rates, flow resistivity, leakage!

WP3 - General standards and guidelines for interfaces and connectivity

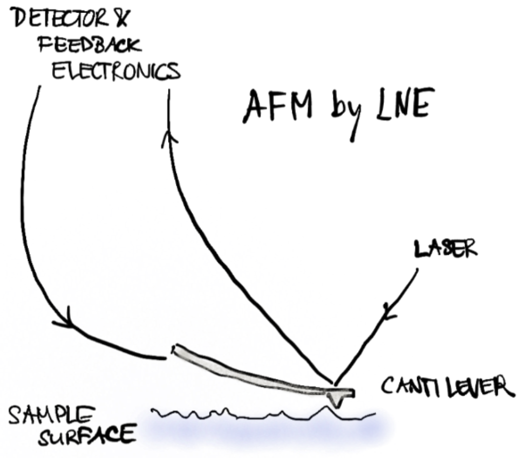
- Development and application of **contact angle** test protocol and calculation of surface energy (quantifying wettability) and **surface roughness**

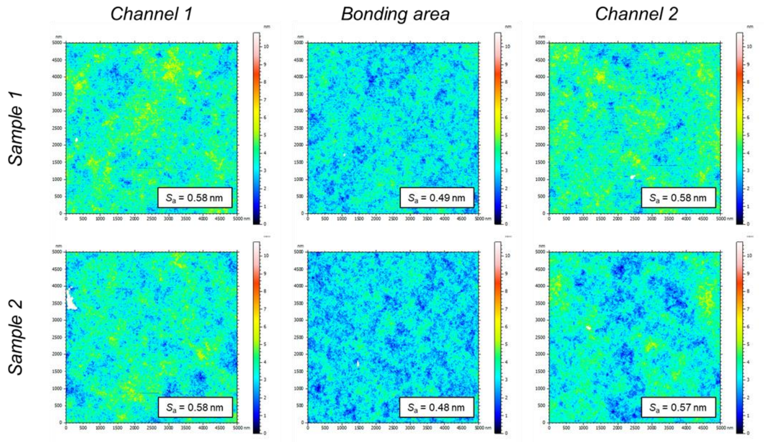


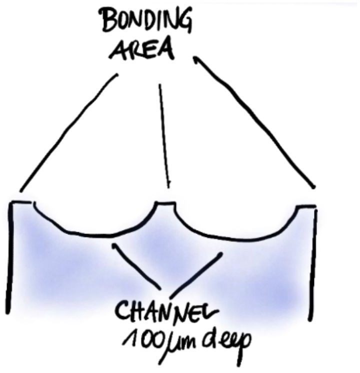
Ultra pure H_2O
Di-iodomethane
Ethylene glycol

OWRK model
From contact angle [°]
to surface energy [mN/m]

σ ≈ 62 mN/m
(D263® bio)



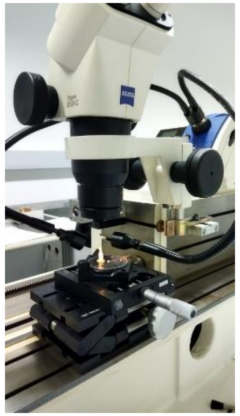


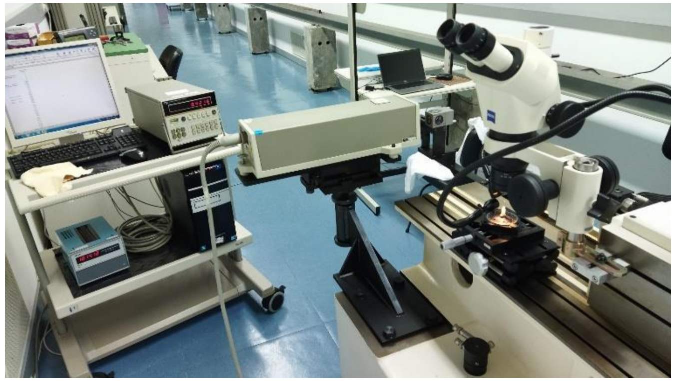


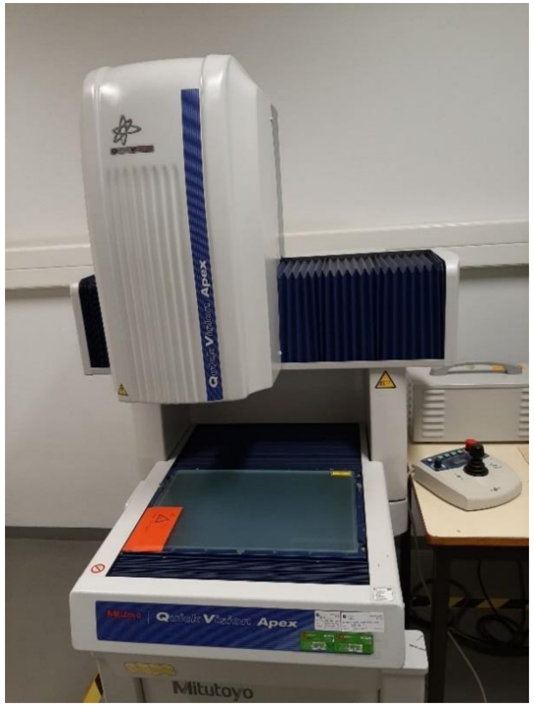
Deliverable 5 – Guidelines for the measurement of key performance parameters of microfluidic connections including the identification of key properties in an interface.

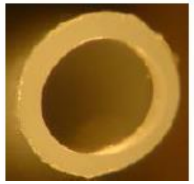
WP3 - General standards and guidelines for interfaces and connectivity

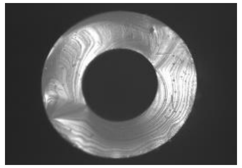
- Development and application of **dimensions** measurements test protocol for microfluidic components

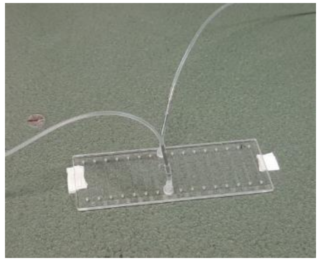












Deliverable 6 - Guidelines for the implementation of standardized methods of microfluidic components focusing on port connection from microscale fluidic channels to the macroscale world and associated changes in flow and pressure

WP3 - General standards and guidelines for interfaces and connectivity

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Paper submitted

International Journal of Metrology and Quality Engineering

Measurement of wettability and surface roughness for metrology and quality control in microfluidics

--Manuscript Draft--

Manuscript Number:	
Article Type:	Research article
Full Title:	Measurement of wettability and surface roughness for metrology and quality control in microfluidics
Short Title:	
Section/Category:	Testing and Validation Method
Order of Authors:	Thomas Schrøder Daugbjerg, Ph.D.
	Loïc Crouzier
	Alexandra Delvallée
	Florestan Ogheard
	Christina Pecnik
	Kevin Romieu
	Fernanda Saraiva
	Elsa Batista

Paper accepted

metrology
MDPI

Communication

The Importance of Dimensional Traceability in Microfluidic Systems

Elsa Batista [1,*], João Alves e Sousa [1], Fernanda Saraiva [1], André Lopes [2], Vania Silverio [3,4], Rui F. Martins [2] and Luis Martins [5]

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3 INESC Microsistemas e Nanotecnologias, INESC MN, 1000-029 Lisboa, Portugal; vania.silverio@tecnico.ulisboa.pt
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5 LNEC—Laboratório Nacional de Engenharia Civil, 1700-066 Lisboa, Portugal; lfmartins@lnec.pt
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WP4 - Development of guidelines for the standardization of dimensions and accuracy for modularity and sensor integration

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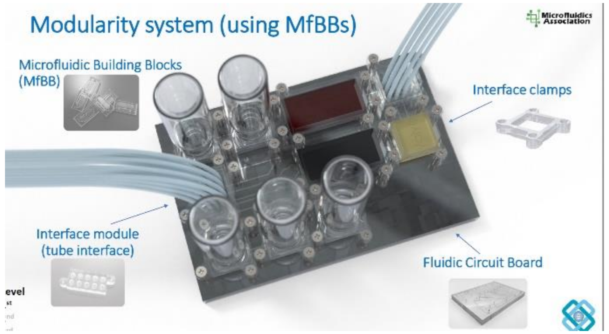

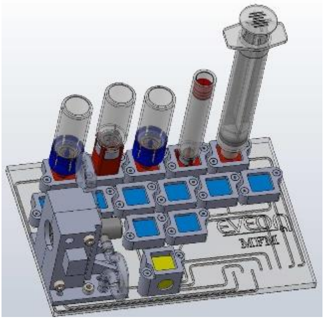

From the design point of view, standardization is important, when devices and systems need to be combined, e.g.:

1. Existing equipment from e.g. laboratory automation, liquid handling, inspection or fabrication aspects.
2. Existing components that must interface from the use-case requirements: e.g. syringes, swabs, pipettes, electronic contacts etc.
3. When it’s necessary to use components from external suppliers, in a development or commercial phase.

Metrology protocols need to be developed (or existing protocols adapted) to ensure compatibility and proper functioning:

- Flow control related issues (Dead volume, internal volume, flow resistivity etc.).
- Material related issues (Cytotoxicity, biocompatibility etc.).
- Reliability related issues (Leak tightness, accelerated tests etc.).

Deliverable 7 – Landscape document identifying standardization requirements for microfluidic component design and manufacturing with respect to modularity and heterogenous integration.

WP4 - Development of guidelines for the standardization of dimensions and accuracy for modularity and sensor integration

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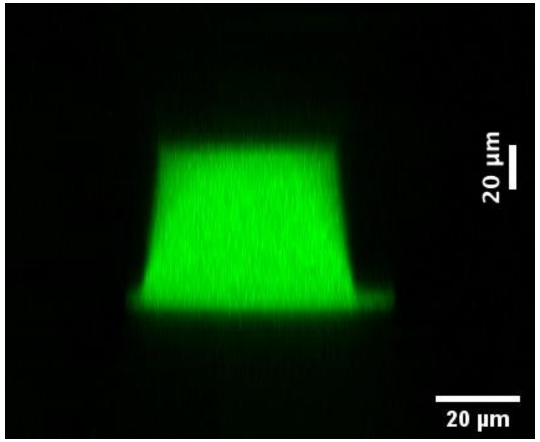
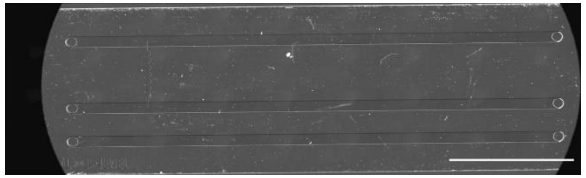
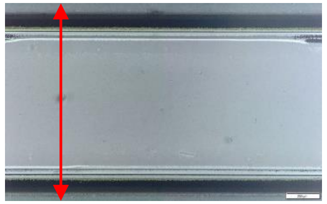
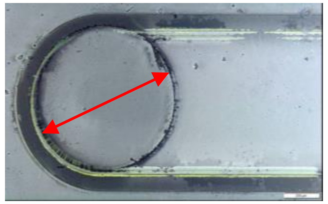
- Optical microscopy
- White light interferometer
- Confocal laser (scanning) microscopy
- Profilometer
- Atomic force microscopy (AFM)









Deliverable 8 – Measurement protocols for dimensional characterization of microfluidic components

Dissimination

- 4 peer review **Papers** published
- 5 **Whitepapers** published in collaboration with The MFA
- 25 **presentations in international conferences**

Flomeko 2022 *(China)*, INO4VAC 2023 meeting *(online)*, RIQUAL 2023 *(Portugal)*, microTAS 2023 *(Poland)*, VI Congreso de Microfluidica Argentina 2023 *(Argentina)*, CIM 2021 and 2023 *(France)*, EUROOCs 2022 *(France)*, MPS Berlin 2023 *(Germany)*, **EC Workshop on the Future of Metrology *(Belgium)* *2023***, Conference Polymer Replication Nanoscale 2022 *(Ireland)*, LABSUMMIT 2024 (Portugal) and many more…

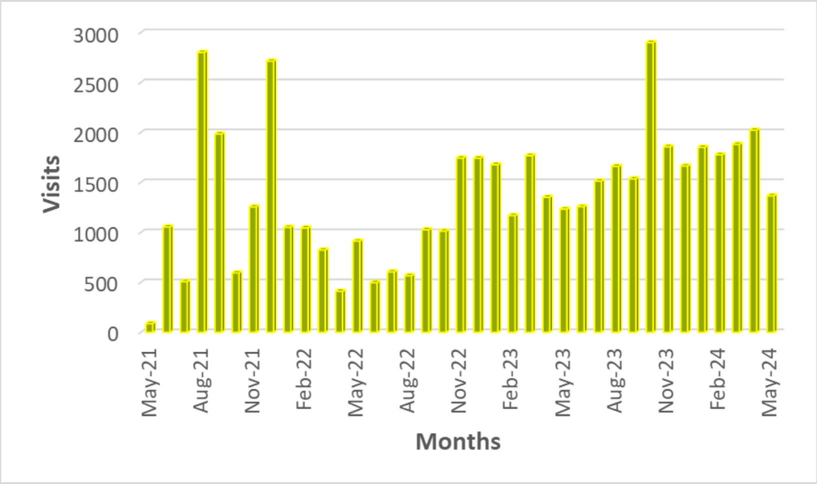
- 3 **Articles** published in trade/professional press
- 21 **technical reports/protocols** available on the MFMET webpage
- 3 **news stories** published by EURAMET
- 5 **Newsletters**
- MFMET **Database** for Flow Control Components
- 2 **Surveys**

MFMET website statistics

https://mfmet.eu

https://zenodo.org/communities/mfmet

Total of 52448 views
Average of 1413 visits per month
Zenodo: Views 2913, Downloads 2219



zenodo

MFMET A2.1.1: Metrology Methodology
Florestan Ogheard; Elsa Batista; Zoe Metaxiotou — 296 views, 186 downloads

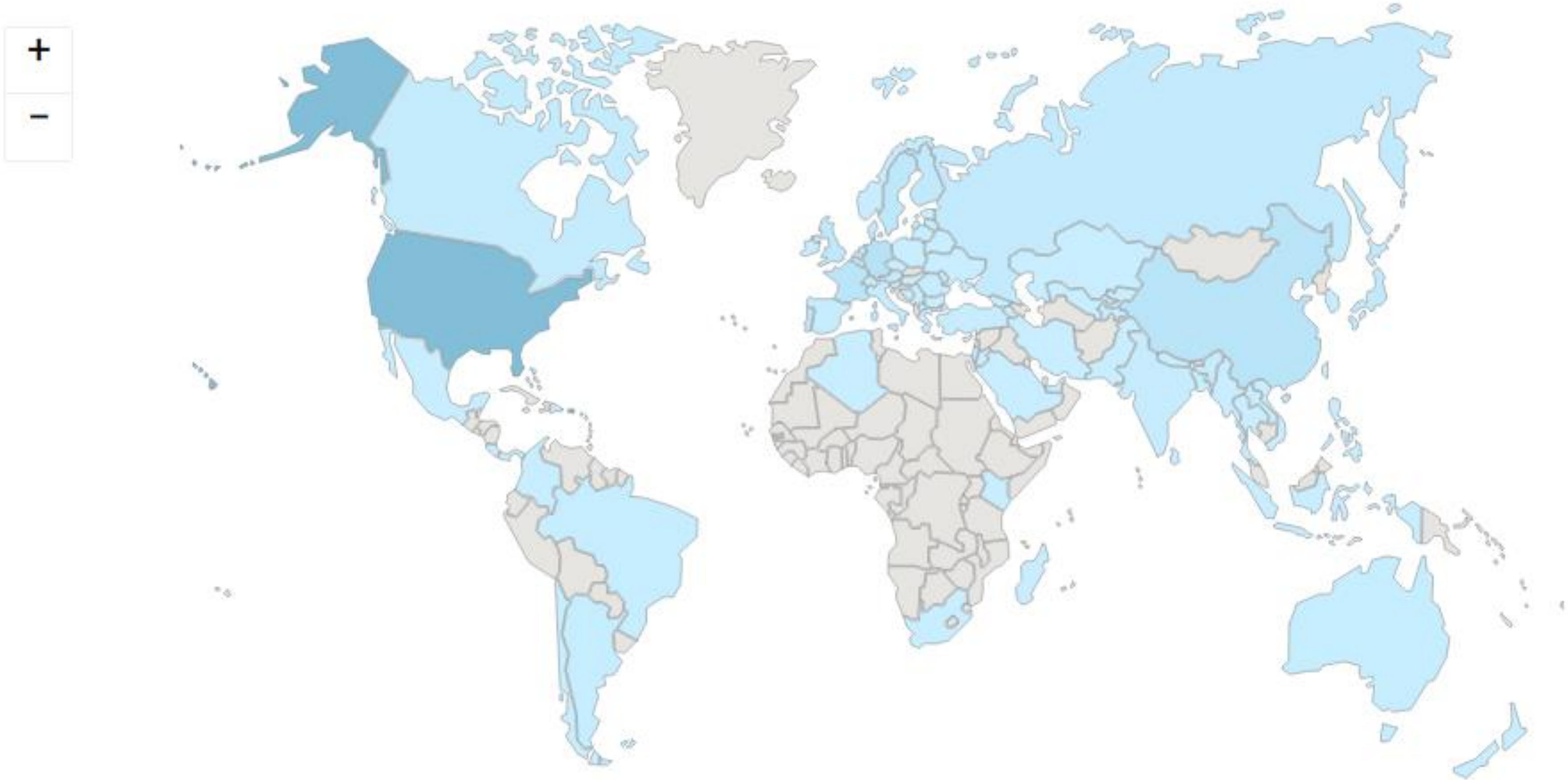
MFMET A2.2.2: Development of test protocols for microfluidic devices
Mikkel Copeland; Florestan Ogheard; Elsa Batista; and 1 other — 230 views, 144 downloads

MFMET A2.2.1 - Literature review of existing metrology and normative standards related to the flow properties and microfluidic devices
Akselli, Başak; Ogheard, Florestan; Batista, Elsa — 228 views, 142 downloads

MFMET A1.1.2 - Definitions Symbols and Vocabulary of Flow Control
Silverio, Vania; Metaxiotou, Zoe; Batista, Elsa; and 3 others — 209 views, 148 downloads

Global Visitor Distribution ⓘ

Reload ▲



1 Jun 2021 - 20 May 2024 ▼

Impact

End user's workshops

The workshop “**On the road to standardization in Microfluidics and Organ-on-Chip**” hosted by CETIAT, the in France in November 2023, attended by 45 participants from 10 countries and 3 continents (Europe, North America and Asia).

Workshop on “**Challenges and opportunities around the integration of sensors and electronics in microfluidics**” organized by MFA with support from MFMET at IMEC on March 2024 with over 100 attendees.

Microfluidic ChipShop organized a one-day workshop on **standardization in Microfluidics** in Jena, Germany on May 16th. The event aimed to address the importance of standardization in microfluidics and had the participation from MFMET, UNLOOC, and AGRARSENSE partners.

Impact

Online webinars

- MFMET webinar – 01. The role of Metrology and Standardization in microfluidic technology development
- MFMET webinar – 02. Flow in microfluidics
- MFMET webinar – 03. Wettability and surface roughness
- MFMET webinar – 04. Leakage in Microfluidic Devices – detection and quantification
- MFMET webinar – 05. Interfacing of microfluidic devices
- MFMET webinar – 06. Measuring the dimensions of microfluidic devices using optical methods

Impact

Deliverables

- **Deliverable 1** – Guidelines and a test protocol for flow control evaluating leakage and burst pressure in microfluidic devices.
- **Deliverable 3** – Calibration guide for the evaluation of flow-related quantities in microfluidic devices.
- **Deliverable 4** – Report on test protocols for liquid properties in microfluidic devices for use in pharmaceuticals, biomedical and mechanobiology applications.
- **Deliverable 5** – Guidelines for the measurement of key performance parameters of microfluidic connections including the identification of key properties in an interface.
- **Deliverable 6** – Guidelines for the implementation of standardized methods of microfluidic components focusing on port connection from microscale fluidic channels to the macroscale world and associated changes in flow and pressure.
- **Deliverable 7** – Landscape document identifying standardization requirements for microfluidic component design and manufacturing with respect to modularity and heterogenous integration.
- **Deliverable 8** – Measurement protocols for dimensional characterization of microfluidic components.

Impact at Standardization level

- Cooperation with MFA and ISO/TC/WG3 in **the microfluidics roadmap development**
- Active participation in **CEN-CENELEC Focus Group Standards for Organ-on-Chip**
- Active participation in **ISO/TC48/WG5**-Liquid handling devices- automatic
  - ISO/TR 6037 - Automated liquid handling systems – Uncertainty of the measurement procedures (waiting publication)
- Active participation in **ISO/TC48/WG3** - Microfluidic devices
  - ISO 22916:2022 - Microfluidic devices — Interoperability requirements for dimensions, connections and initial device classification
  - ISO 10991:2023 - Microfluidics — Vocabulary
  - ISO/TR 6417 - Microfluidic pumps — Symbols and performance communication (waiting publication)
  - New convenor, Vania Silverio INESC MN with Portuguese Secreatariat (Apormed)
- Cooperation with **EURAMET TC Flow, CCM-WGFF, IMEKO TC7** Measurement Science **and IMEKO TC9** Flow

Still missing

MFMET
Establishing Metrology Standards in Microfluidic Devices

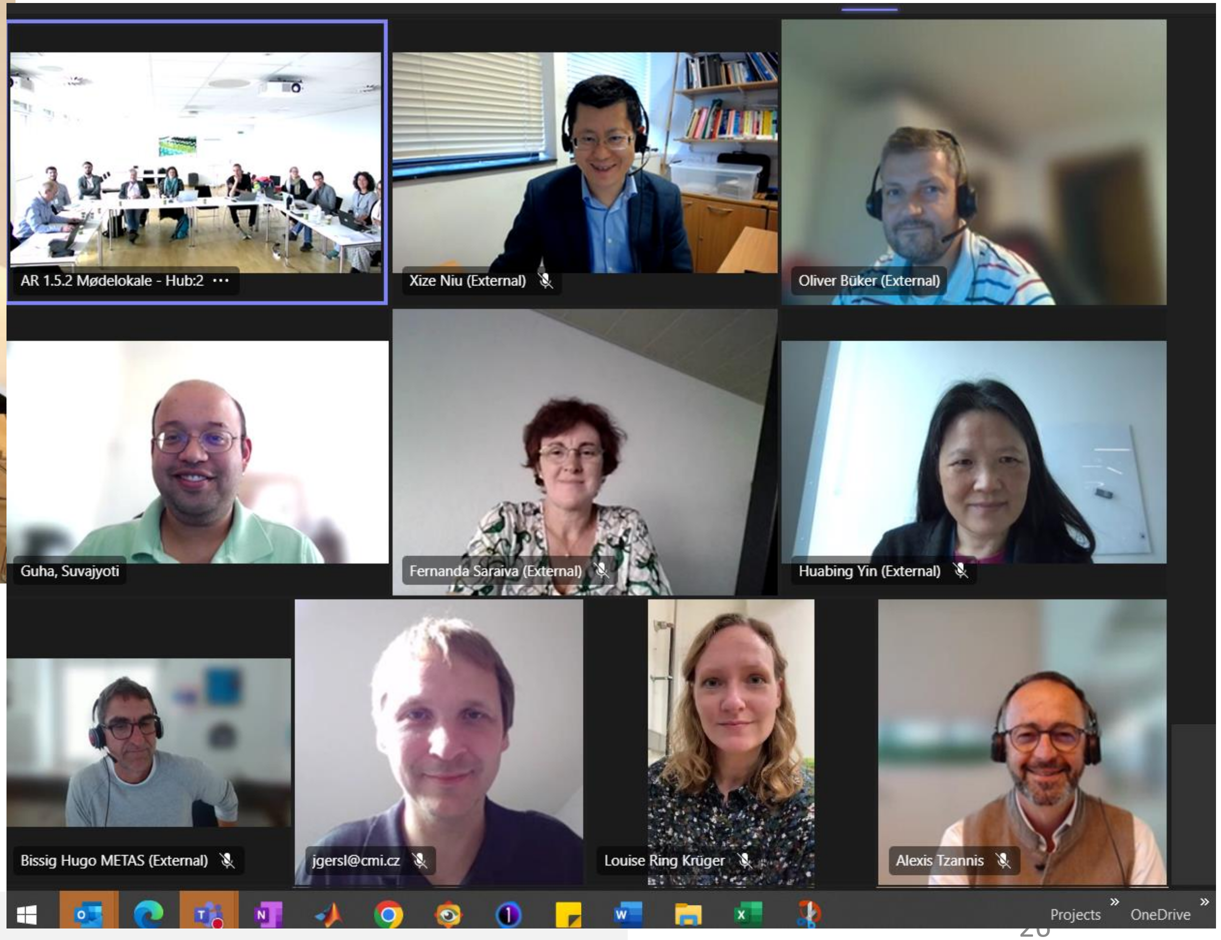
- **Deliverable 2-** Guidelines for the implementation of consensus-based flow control specifications in the microfluidics industry supply chain
- **A1.1.5 -** Report on the definition of flow control concepts, terms and components used in microfluidics and related database
- **A2.4.4 -** Technical report describing the design, fabrication, and calibration process of the transfer standards
- **A5.1.7 -** Report on reasons for failure of microfluidic devices
- **Deliverable 9** - Evidence of contributions to or influence on new or improved international guides, recommendations and standards with a specific focus on the following committees: ISO/TC48/WG3 and WG5, ISO/TC69/SC6, ISO/TC229, ISO/TC276, IMEKO TC7, CCM-WGFF, CEN/TC332/WG7 and EURAMET TC-Flow. Examples of early uptake of project outputs by end users

Follow up

- New EURAMET research project in Microfluidic and Orgon on Chip standardization, MFMET II proposed in February 2024

  1. Establish standard procedures to **metrologically assess and characterize** particle-laden flows (e.g., presence of droplets, bubbles, particles, cells), shear stress, pressure drop, flow resistivity, dead volume and total volume in microfluidic devices, including organ-on-chip.
  2. Investigate and develop protocols for the **integration** of sensors, actuators and fluidic components in microfluidics using scalable, cost-effective and sustainable manufacturing strategies (e.g., biodegradable materials). Study the integration of different materials and how that integration changes material shape.
  3. Define general standards and guidelines for **quality control, validation and characterization** regarding microfluidic system reliability/failure
  4. Design (simulate, fabricate and mount) and characterize a setup of an **integrated microfluidic system** with several sensors and actuators to access the influence of different quantities in the system performance in order to qualify and validate a microfluidic system. This setup will act as a metrological transfer standard.

The Team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THANK YOU

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