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Uncertainty calculations in optical methods used for micro flow measurement

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ABSTRACT

This work aims to describe the uncertainty calculation methodologies associated with two optical methods used for micro flow measurements, both developed at the Portuguese Institute for Quality (IPQ) under the EMPIR project MeDD II – Metrology for Drug Delivery framework.
One of the methods is the front track which consists of tracking the meniscus of a liquid inside a capillary tube over time. The second method is the pending drop method that relies on measuring the volume growth of a drop over time. Both methods use a camera to capture images and convert them in volume or displacement length to determine flow rate.
The uncertainty calculations will be presented in detail. The values obtained for the front track method are much smaller than for the pending drop method, specially at very low flow rates.

1. Introduction

Optical metrology is the science and technology concerning measurement with light. Such measurements can either target properties of light and light sources or properties of objects such as dimensions, distances, and temperatures. There is no strict boundary between those fields, because often one uses measured properties of light not just to characterize a light source, but for other purposes – for example, optical distance measurements with lasers interferometers or the use of high resolution cameras to capture images that can be converted in other measuring quantities using the appropriated software. Depending on the quality of the optical source used, the accuracy of the measurements can be very high, down to 1%. Therefore, this technology can be applied in the calibration of flow measuring devices used in industrial, pharmaceutical and medical applications, in the nano and micro flow ranges.

Wider uptake of traceable calibrations of low and ultra-low flow infusion devices and improved knowledge of calibrating drug delivery devices in clinical environments, particularly in hospitals will lead, over time, to reduced errors in drug delivery, especially in devices that measure very small flow rates. Therefore, it is necessary to update flow facilities of the National Metrology Laboratories to enable the traceable determination of very small flow rates and volumes to offer characterization possibilities for insulin pumps or pain pumps (specifically intrathecal drug pumps) as these drug delivery devices administer very small volumes at a given time interval to the patients. This is one of the objectives of project MEDDII – Metrology for Drug Delivery [1] from EMPIR (European Metrology Programme for Innovation and Research), where IPQ is the coordinator.

IPQ-LVC, through a partnership with the Department of Mechanical and Industrial Engineering (DEMI) of the New University of Lisbon (FCT/UNL) has developed two optical methods, the front track method [2] and the pending drop method [3], with the purpose of measure flow rates down to 1 μL/h with 1% uncertainty.

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2. Methods

2.1. Front track method

The front tracking method is an optical method that consists of tracking the position of the meniscus of a liquid (liquid/air interface) inside a capillary tube over time. Knowing the displacement of the meniscus over time and the cross-section area of the capillary it is possible to calculate the flow rate. To track the meniscus, it is used a high-resolution camera of 12 Mpx of resolution (Alvium 1800 U-1240) and a telecentric zoom lens (Qioptic Optem 7:1 zoom) connected to a computer with an in-house image processing software that identifies the meniscus and calculates its position over time (Fig. 1). The software was developed in-house using the programming language Python and the open-source image processing library OpenCV.

The developed algorithm used in the software, captures the images from the camera, applies several segmentation techniques to identify the meniscus and determine its position and then calculates the average flow for a given time interval. The central point of the meniscus was taken as reference, corresponding to the position of the point on the capillary axis and coinciding with the meniscus (Fig. 2).

2.2. Pending drop method

The pending drop method relies on the measurement of the drop volume variation (ΔV) trough is radius (r) measurement using the pictures taken by the high resolution a camera, over a certain time interval (Δt) (Fig. 3), converting this value into the flow rate Q according to equation (1), and where the evaporation is also corrected (δ_{evap}).

$$Q = \frac{4\pi \times r^3}{3\Delta t} + \delta_{evap}. \quad (1)$$

The camera is connected to a computer with an image processing

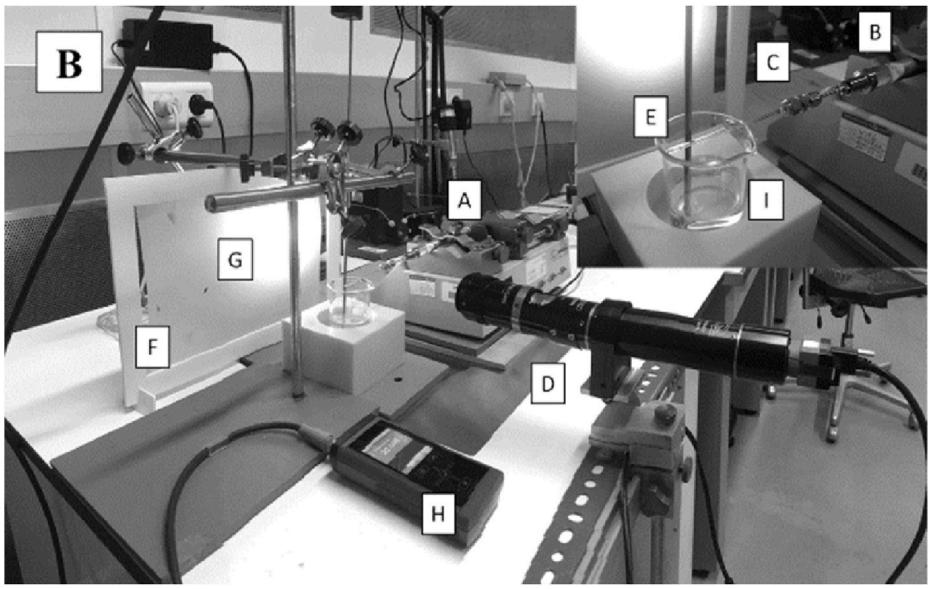

Fig. 1. Front track experimental setup, where A is the Nexus pump, B is the glass syringe, C is the connection line, D is the camera, E is the capillary tube, F is the translucent paper and G is the LED light.

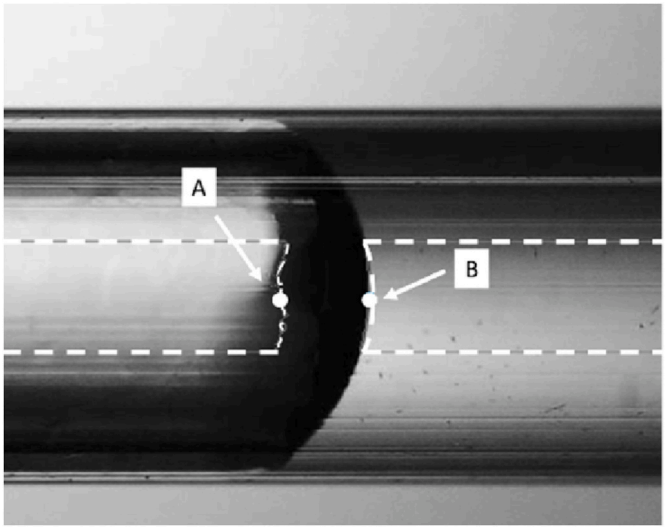

Fig. 2. Two points identified by *findContours* function library, where B is the reference point.

software developed in the language Python. The open-source image processing library OpenCV that enables to the scale definition, image segmentation, determines the contour of the drop and performs the volume calculation (Fig. 4). The image segmentation is performed by the image decomposition into simpler segments to simplify the analysis. The thresholding method was used to segment the section of the tube used in the scale definition, and to segment the image of the droplet to determine its contour [4].

The choice of the threshold value used is a critical point in this method, since this value depends on the lighting conditions of the experimental setup, and for different values the binary image may not correspond to the real image [5].

3. Theoretical model and calculation of uncertainty

The uncertainties for microflow determination were estimated according to the Guide to the expression of Uncertainty in Measurement (GUM) [6].

3.1. Front track method

This method relies on determining the mass of the liquid inside a specific section of the capillary and converting this value to volume, [7]. For the presented setup, the instantaneous flow (Q) can be calculated through the equation (2).

$$Q = \frac{x_2 - x_1}{\Delta t} \times \pi \times r^2 \times [1 - \gamma(T_w - 20)] \tag{2}$$

where, x_1 and x_2 are the meniscus positions, t is the time, r is the inner radius of the capillary, γ is the capillary material coefficient of expansion and T_w is the calibration liquid temperature (in °C).

The average flow rate is the mean value of the sum of the calculated instant flows for the duration of the test.

The main standard uncertainties considered are: meniscus displacement, $u(\Delta x)$; time interval between frames, $u(t)$; capillary radius, $u(r)$; water temperature, $u(T_w)$; material expansion, $u(\gamma)$; stability, $u(\delta Qsta)$; standard deviation of the measurements $u(\delta Qrep)$.

For the calculation of the standard uncertainty associated with the displacement determination $u(\Delta x)$ and the standard uncertainty of the calliper used for the measurement of the external diameter of the tube, according to the following equation:

$$u(\Delta x) = \sqrt{\left(\frac{scale/2}{\sqrt{3}}\right)^2 + \left(\frac{0.03}{2}\right)^2} \tag{3}$$

To calculate the uncertainty associated with the time, two components are considered:

- Chronometer standard uncertainty (u_{crono}), with the value of 0.0014s.
- The standard uncertainty associated with time delay (u_{delay}), with the value of 0.01s.

$$u_t = \sqrt{\left(\frac{u_{crono}}{2}\right)^2 + \left(\frac{u_{delay}}{\sqrt{3}}\right)^2} \tag{4}$$

The standard uncertainty associated with the internal radius of the capillary tube was determined by gravimetry.

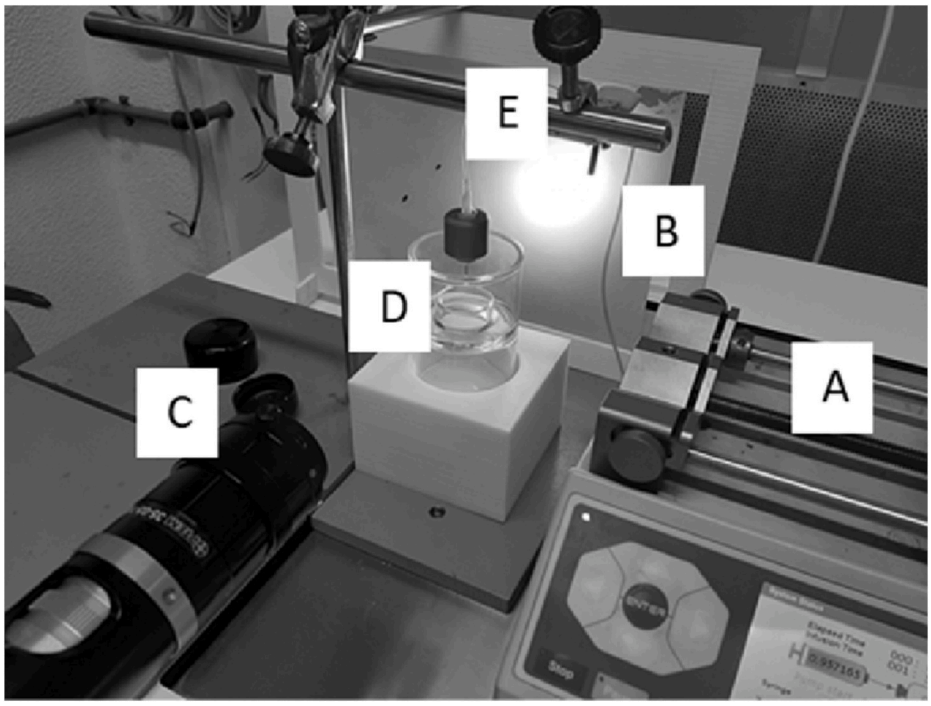

Fig. 3. Pending drop experimental setup where A is a flow generator, B is the connection line, C is the high-resolution camera, D is the evaporation trap, E the LED light.

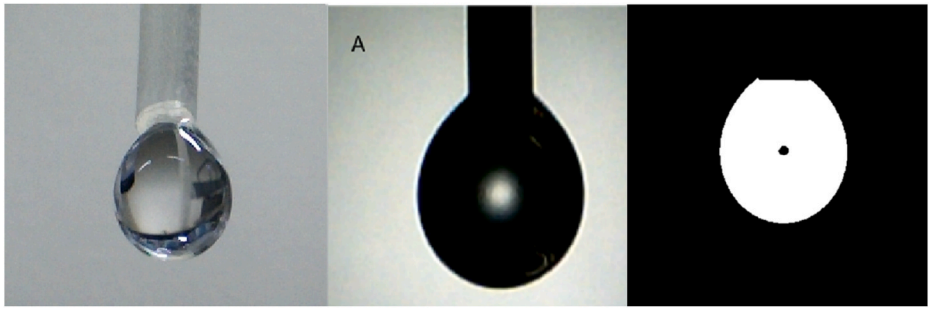

Fig. 4. From the left: image of a drop in a magnified view (400 x), phyton software drop picture and thresholding image.

$$u(r) = \frac{U(r)}{2} \ (\text{mm}) \tag{5}$$

The standard uncertainty of the expansion coefficient of the capillary is 5% of the tabled value [8]:

$$u(\gamma) = \frac{5\%\gamma}{\sqrt{3}} \ (^{\circ}\text{C}^{-1}) \tag{6}$$

The standard uncertainty of the temperature of the water $u(T_W)$ is dependent on the calibration of the thermometer u(therm), the drift of the results over time δT and the temperature gradients during the measurements ΔT.

$$u(T_W) = \left[\left(\frac{u(therm)}{2}\right)^2 + \left(\frac{\delta T_W}{\sqrt{3}}\right)^2 + \left(\frac{\Delta T_W}{\sqrt{3}}\right)^2\right]^{1/2} (^{\circ}\text{C}) \tag{7}$$

To calculate the standard uncertainty of stability $\boldsymbol{u}(\boldsymbol{\delta Q}\text{stab})$, associated with random effects such as liquid evaporation and pump vibrations, several tests were performed that consisted of acquiring data on the meniscus position with the flow generator on, without imposing flow.

The uncertainty related with repeatability $\boldsymbol{u}(\boldsymbol{\delta Q}\text{rep})$ is determined by the standard deviation of the measurements (STDm) and the number of measurements n.

$$u(\delta Q\text{rep}) = \frac{STDm}{\sqrt{n}} \ (\mu\text{L/s}) \tag{8}$$

The combined uncertainty associated with flow determination $u(Q)$, is calculated by the equation:

$$u(Q) = \sqrt{\begin{array}{l}\left(\frac{\partial Q}{\partial \Delta x}\right)^2 u^2(\Delta x)\left(\frac{\partial Q}{\partial t}\right)^2 u^2(t) + \left(\frac{\partial Q}{\partial r}\right)^2 u^2(r) \\ \left(\frac{\partial Q}{\partial T_W}\right)^2 u^2(T_W) + \left(\frac{\partial Q}{\partial \gamma}\right)^2 u^2(\gamma) + u^2(\delta Q stab) + u^2(\delta Q rep)\end{array}} \tag{9}$$

3.2. Pending drop method

Assuming that the drop is a sphere [7], Eq. (10) can be used to determine the volume from the sphere radius (r):

$$\boldsymbol{V} = \frac{4\boldsymbol{\pi}}{3} \times \boldsymbol{r}^3 \tag{10}$$

To determine flow rate (Q), Eq. (11) can be used:

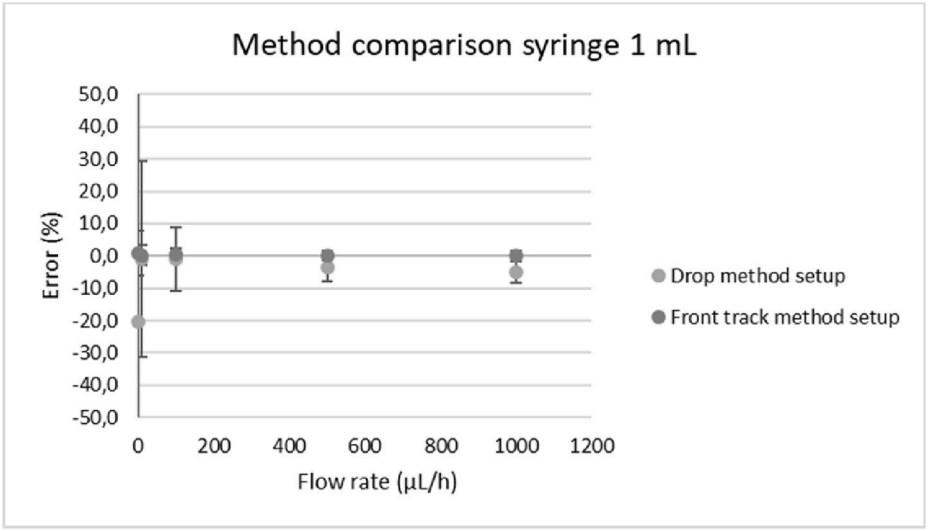

Fig. 5. Nexus pump calibration using the Front track and the pending drop method.

$$Q = \frac{4\pi \times r^3}{3\Delta t} + \delta_{evap} \tag{11}$$

The main standard uncertainties considered are: volume determination by the drop method $u(V)$ that includes the inaccuracy of the contour of the drop and the pixels determination, water evaporation $u(\delta Qevap)$, stability $u(\delta Qsta)$, time $u(t)$ and repeatability of the measurements $u(\delta Qrep)$.

To calculate the uncertainty associated with the volume determination of the drop $u(V)$, four major components are considered:

- Uncertainty associated with the scale calibration (u_{scale}). The experimental test consisted of measuring the difference in volume of two drops, through the program written in Python, considering the scale uncertainty equal to 0.01 mm/px. The difference in volume between the two drops was 0.00000023%.
- Uncertainty associated with focus (u_{focus}), with the value of 0.01%, several pictures were taken in different microscope alignment positions (where it was possible to observe clearly the drop) before the picture was taken, the standard deviation of this tests resulted in the described value.
- Uncertainty associated with the contour determination method ($u_{contour}$), with the value of 0.005%, this value being the error obtained in determining the volume when using the value of 43 for the Threshold.
- Uncertainty associated with distortion of the capture image caused by the glass of the evaporation trap (u_{amp}), was access and the obtained value was 0.008%.

Table 1
Uncertainty estimation for the front track method.

Uncertainty components	Estimation	$u(x_i)$	c_i	$(c_i \times x_i)^2$
Volume (mm^3)	15.054	9.72×10^{-04}	0.0194	1.89×10^{-05}
Time (s)	51.524	5.05×10^{-03}	−0.0057	8.20×10^{-10}
Evaporation (µL/s)	6.34×10^{-06}	3.66×10^{-06}	1	1.34×10^{-11}
Repeatability (µL/s)	1.70×10^{-03}	1.70×10^{-03}	1	2.89×10^{-06}
Flow rate (µL/h)	1052	u_{comb} (µL/h)	17	
ν_{eff}	2089.2	k	2.0	
U_{exp} (µL/h)	34	U (%)	3.4	

The uncertainty associated with the volume is calculated with the equation:

$$u(V) = \sqrt{\left(\frac{u_{scale\times V}}{2}\right)^2 + \left(\frac{u_{focus} \times V}{\sqrt{3}}\right)^2 + \left(\frac{u_{contour} \times V}{\sqrt{3}}\right)^2 + \left(\frac{u_{amp} \times V}{\sqrt{3}}\right)^2} \tag{12}$$

To calculate the uncertainty associated with the determination of time intervals between droplets photos, two components are considered:

- Chronometer uncertainty (u_{crono}), with the value of 0.0014s.
- Uncertainty associated with time delay (u_{delay}), with the value of 0.01s.

$$u_t = \sqrt{\left(\frac{u_{crono}}{2}\right)^2 + \left(\frac{u_{delay}}{\sqrt{3}}\right)^2} \text{ (s)} \tag{13}$$

The uncertainty of the evaporation of each drop size is obtained by the standard deviation of each drop size evaporation rate measurements performed in the same conditions as the test; 10 repetitions are performed in each flow rate tested.

$$u(\delta Qevap) = \frac{\Delta evap}{\sqrt{3}} \text{ (µL/s)} \tag{14}$$

The uncertainty related to the repeatability $u(\delta Qrep)$ is determined by the standard deviation of the measurements (STDm) and n the number of measurements.

$$u(\delta Qrep) = \frac{STDm}{\sqrt{n}} \text{ (µL/s)} \tag{15}$$

The combined uncertainty associated to the flow determination $u(Q)$, is calculated with the equation:

$$u(Q) = \sqrt{\left(\frac{\partial Q}{\partial V}\right)^2 u^2(V) + \left(\frac{\partial Q}{\partial t}\right)^2 u^2(t) + u^2(\delta Qevap) + u^2(\delta Qrep)} \tag{16}$$

4. Numerical example

For testing the two methods, a Nexus Pump, with a 1 mL glass syringe was calibrated at 5 different flow rates: 1000 µL/h, 500 µL/h, 100 µL/h, 10 µL/h, and 1 µL/h. Tests were performed in controlled conditions (temperature = (20 ± 3) °C and humidity >50%). Ultra-pure water was used as the calibration liquid. Both front track and pending drop method were used with an Alvium 1800 U-1240 high resolution camera. The

Table 2
Uncertainty estimation for the pending drop method.

Uncertainty components	Estimation	$u(x_i)$	c_i	$(c_i \times x_i)^2$
Meniscus displacement (mm)	11.76	1.50×10^{-02}	2.35×10^{-02}	1.25×10^{-07}
Radius (mm)	0.575	1.47×10^{-03}	9.63×10^{-01}	2.01×10^{-06}
Time (s)	44.107	2.97×10^{-03}	-6.28×10^{-03}	3.48×10^{-10}
Repeatability (μL/s)	0.0013	0.0013	1	1.80×10^{-06}
Stability (μL/s)	1.37×10^{-04}	1.37×10^{-04}	1	1.88×10^{-08}
Expansion coefficient (/°C)	0.00024	6.92×10^{-06}	-8.14×10^{-01}	3.18×10^{-11}
Temperature (°C)	22.94	0.005	-2.77×10^{-06}	1.92×10^{-16}
Flow rate (μL/h)	997.1	u_{comb} (μL/h)	7.2	
ν_{eff}	100.15	k	2.02	
U_{exp} (μL/h)	15	U (%)	1.5	

results are presented in Fig. 5.

From the results showed above it can be verified that the relative error and uncertainty with the front track method are significantly lower than that for the drop method. This situation was also observed in previous work of Batista et al. [9].

An example of uncertainty calculation for the front track method is presented in Table 1 and for the drop method is described in Table 2.

From the tables above it can be seen that the largest source of uncertainty for the front track method is the radius and for the drop method is the volume calculation.

5. Conclusions

Two optical methods for measuring microflow rates were developed, the front track method and the drop method. From the results obtained by the calibration of a Nexus pump in was verified that the front track method is much more accurate and reliable than the drop method but there is still some room for improvement in the latest, namely more evaporation control and new test stability. Also, for the front track method is possible to reduce the uncertainty, specially at low flow rates if a smaller diameter capillary is used, this method can be a good replacement for gravimetry specially at low flow rates, where the gravimetric method has some technical limitations.

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Elsa Batista*, Andreia Furtado, Maria do Céu Ferreira, Isabel Godinho
Portuguese Institute for Quality, Caparica, Portugal

Miguel Álvares, Joana Afonso, Rui F. Martins
UNIDEMI, NOVA School of Science and Technology, The New University of Lisbon, Caparica, Portugal

E-mail addresses: m.alvares@campus.fct.unl.pt (M. Álvares), jav.afonso@campus.fct.unl.pt (J. Afonso), rfspm@fct.unl.pt (R.F. Martins).

* Corresponding author.
E-mail addresses: ebatista@ipq.pt (E. Batista), afurtado@ipq.pt (A. Furtado), mcferreira@ipq.pt (M.C. Ferreira), igodinho@ipq.pt (I. Godinho).