DOI 10.5162/sensor2013/P1.5

A standard to measure flow rates between 1 and 50 nl/min

M. Ahrens[1], St. Klein[1, 2], Chr. Damiani[1], B. Nestler[1, 2]
[1] Medical Sensors and Devices Laboratory, Lübeck University of Applied Sciences, Lübeck, Germany
[2] Centre of Excellence for Technology and Engineering in Medicine (TANDEM), Lübeck
martin.ahrens@fh-luebeck.de

Keywords: Nanoflow Measurement, Primary Standard, Front Tracking, Drug Delivery, Flow Characterization

Introduction

The performance of medical devices for transfusion, infusion and injection of fluids must be checked using flow standards before they can be placed on the market. In the near future, however, medical devices should deliver and measure even variable flow profiles down to 1 nl/min (e.g. programmable implantable medicament pumps). Current standards for extremely low flow rates are based on gravimetric measurements and are only reliable for constant or slowly changing flow profiles down to 300 nl/min [1], the uncertainty increases with shorter measurement times. Thermal flow sensors are calibrated to a minimum flow of 50nl/min, but have a relatively high flow resistance [2]. To characterize the fluid flow characteristics in the low range, a minimum fluid resistance of the sensor is necessary [3]. This work presents a highly sensitive front tracking system which can now be used to measure fast changing flows down to 1 nl/min within minutes over a period of hours.

Methods and Materials

The experimental setup is shown in Figure 1. It comprises a fire-wire camera (B) with a zoom lens (C), attached to a precision linear stage (D) directly above a high precision glass capillary (A). Two different capillaries with inner diameters of 150 µm and 300 µm were used for the measurements; both capillaries were 250 mm long. Back-light illumination of the capillary was provided by a focused white LED (F). A custom made image processing software running on a standard PC (E) was used for the image acquisition and edge detection as well as to control the linear stage. The fluidic devices to be tested were attached to one end of the glass capillary using PEEK/ETFE tubing and connectors (G1, 2). The other end of the capillary remained open and exposed to atmospheric pressure. The linear stage was used to track the motion of the meniscus along the capillary for long measurements. This was done by feeding the current position of the liquid front into a PID algorithm which controlled the motion of the stage. All fluidic components of the system were held at 37 ± 0.05 °C (body temperature) in a temperature regulated chamber (I). The temperature was continuously monitored using four type-K thermocouples (T1 – T4). The whole setup was placed on an air-damped table to reduce the effects of vibrations from the environment.

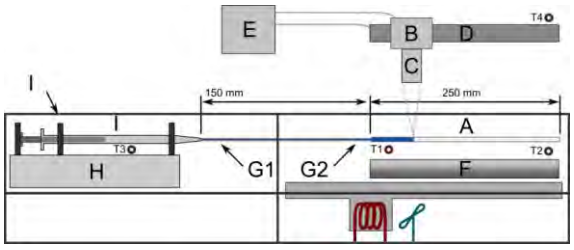

Figure 1: Experimental setup: (A) capillary, (B) camera, (C) objective lens, (D) linear motion stage, (E) Control-PC, (F) LED, (G1,2) tubing and connectors, (H) syringe pump, (I) measurement box (temperature regulated), (T1 - 4) thermo couples.

Results

The flow measurement based on an absolute measurement method. Provided that all errors are known, a calibration would not be necessary, however, any error influences must be considered in a maximum error estimate. The volume flow $\dot{V}$ can be expressed as the front velocity multiplied by the cross sectional area of the capillary:

$$\dot{V} = \frac{dV}{dt} = v \cdot A = \frac{x_2 - x_1}{t_2 - t_1} \cdot \pi \cdot R^2$$

where A is the cross sectional area of the capillary, v the average speed of the front

between positions 1 and 2, (x_2 - x_1) is the displacement of the front during the time interval (t_2 - t_1), and R the radius of the capillary. The error can be expressed as x = |Δx, systematic| + |Δx, random|.
If the systematic errors are larger than the random error, a linear error analysis was carried out (maximum error estimate), in the opposite case, a square error analysis (Gaussian error analysis) was performed [5, 6]. A detailed error analysis was performed, in case of the position and the time errors, the random uncertainties dominates, in case of the capillary uncertainty, the systematic error dominates. Overall the random errors dominate. We have now taken different scenarios (flow rates, durations and capillary diameter were varied) to calculate the corresponding error of various flows, measurement times and capillary diameters, see Table 1.

Table 1: Calculated errors for different measurement configurations.

duration / sec	60			
diameter / µm	300		150	
	error		error	
flow / nl/min	nl/min	%	nl/min	%
1	n.a.	n.a.	0,28	31,6
5	n.a.	n.a.	0,29	5,83
10	1.08	10.78	0.34	3.39
20	1.09	5.45	0.47	2.36
50	1.17	2.35	0.99	1.98

duration / sec	300			
diameter / µm	300		150	
	error		error	
flow / nl/min	nl/min	%	nl/min	%
1	n.a.	n.a.	0,06	6,03
5	n.a.	n.a.	0,11	2,20
10	0.23	2.35	0.20	1.97
20	0.29	1.43	0.38	1.91
50	0.52	1.04	0.95	1.90

Conclusion

The presented front tracking system is capable of measuring flow rates down to 1 nl/min; the aimed accuracy of 10% was reached. The capillary should be adapted to the flow rate. The reason for larger deviations than predicted could be identified as the influence of contamination of the capillary inner surface and the volume changes due to temperature fluctuation. The method proved to be suitable for direct flow measurements down to 1 nl/min, flow changes within 1 minute could be detected. The influence of temperature fluctuations of 0.1°C or even less could be characterized. Coated capillaries minimized significantly the stick slip effect.

Acknowledgement

The authors want to thank the state of Schleswig-Holstein, the German Federal Ministry of Education and Research (BMBF), and the company Tricumed/Kiel for partly funding this project.

References

[1] EMRP Call 2011 - Health, SI Broader Scope & New Technologies, JRP HLT07 MeDD - Metrology for drug delivery, URL http://www.emrponline.eu/call2011/SRTs2011/SRT-h18.pdf
[2] Sensirion AG: 'SLG1430 SLG1430 - Liquid Mass Flow Meter'. Laubisruetistrasse 50. CH-8712. Staefa ZH. Switzerland. rev. 1. December 08. http://www.sensirion.com/images/getFile?id=35
[3] Tricumed (2007), 'IP 2000V - Technische Daten', technical information, Röntgenstrasse 7a, 24143 Kiel. Germany
[4] Seed, B., Current Protocols in Immunology, Silanizing Glassware, John Wiley & Sons, Ltd, 2001, URL http://dx.doi.org/10.1002/0471142735.ima03ks21
[5] International Organization for Standardization (Geneva), Guide to the Expression of Uncertainty in Measurement, ENV 13005:1999
[6] International Organization for Standardization (Geneva), Measurement of fluid flow -- Procedures for the evaluation of uncertainties, ISO 5168:2005RSS