

PRIMARY STANDARD FOR NANOFLOW RATES

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Abstract

In this paper is discussed a novel primary standard which is based on volumetric expansion due to a temporal temperature gradient. The principle, required corrections, traceability and preliminary results are discussed.

Introduction

Micro- and nanoflows are appearing more frequently in various applications, for example in life science and technology, automotive and lab-on-a-chip applications. Further, they are relevant for some medical applications, for example in (implanted) pain control pumps. For these applications, traceability is becoming more important for a safe and sound usage.

As of yet there does not exist a primary standard for flow rates lower than, say, 20 $\mu\text{l}/\text{min}$. Therefore, this research, which is part of [2], aims at developing a primary standard for liquid volume flows for flow rates from 1 up to 1000 nl/min .

The approach followed is a standard based on volumetric expansion (comparable to an old-fashioned thermometer). The upper limit of the given flow rate range could also be achieved with a 'conventional' standard based on the gravimetric standard (e.g. [3]). However, the uncertainty due to for example evaporation and buoyancy makes this principle not suited for the lower flow rates. Conventional syringe pumps are not feasible because the inner dimensions of the syringe cannot be determined with sufficient low uncertainty. A syringe pump based on a plunger rather than a piston, however, may be an interesting alternative.

Standard based on volume expansion

Principle

In Figure 1 a sketch of the standard is shown; the expanding liquid is contained in a reservoir that is placed inside a temperature controlled (water) bath. In Figure 2 the reservoir containing the expanding liquid is shown, whereas in Figure 3 the complete set up is shown.

The driving force for the volume is flow is the decrease in density over time. Hence, the flow rate follows from:

$$Q = -\frac{1}{\rho} \frac{dm}{dt}$$

where m is the mass of the expanding liquid and ρ is the density at the exit of the reservoir. Working out this equation gives the following main component:

$$Q = -\frac{Vk}{\rho_{MUT}} \left(\frac{\partial \rho}{\partial T} \right)$$

where V is the volume of the expanding liquid, k is the temperature gradient, ρ is the density and T is the temperature. Since the temperature is time controlled, one has a control over the time rate change of the density and thus also the volume flow rate.

Because the flow rate depends on the (actual) volume of the expanding liquid and the liquid properties, the flow rate will be inconstant for a constant temperature gradient. This is because over time the temperature increases which leads to a different mass and fluid properties. However, for sufficient small temperature gradients, say smaller than 0.02 K/s, the flow rate is fairly constant for at least 10 minutes.

Corrections

For the given flow rate a few corrections have to be made. For example, the reservoir holding the expanding liquid will also expand due to the temperature increase. In order to determine the flow rate through the meter under test (MUT), one has to correct for the following phenomena:

- expansion of the reservoir;
- inhomogeneous temperature gradient resulting in spatial variations in expansion rate;
- inhomogeneous temperature in the reservoir resulting in a spatial variation of the thermal expansion coefficient;
- cooling down of fluid elements after leaving the temperature controlled bath.

The first correction is by far the largest one; for a temperature of 20 degrees it is approximately 14% of the flow rate while for a temperature of 35 degrees it is approximately 8%. For a constant temperature increase over time the second correction is zero. This is because after a while all the liquid in the reservoir increases with the same temporal temperature gradient. The third and fourth correction are that small that they can be neglected.

Traceability

The flow rate can be made traceable directly to SI units. Therefore one needs to know the following parameters: volume (or mass) of the expanding liquid, temperature gradient and the liquid properties (density and expansion coefficient).

The volume of the expanding liquid follows from the mass difference between an empty and filled reservoir. The temperature gradient follows from temperature measurements inside the reservoir and just outside the reservoir (see Figure 2). Finally, the liquid properties follow from the Tanaka equation [4]. Therefore, ultra pure degassed water has to be used.

Uncertainty

The target uncertainty is 0.5%. Currently the uncertainty budget is being developed. The largest contributions are due to the expansion of the reservoir, the temperature gradient and the

spatial variation in the temperature gradient. Linear regression [1] is used to determine the uncertainty in the temperature gradient.

Preliminary results

Based on actual temperature measurements the flow rate is given in Figure 4. One can clearly see that a steady state flow rate is achieved after the initial start up. As of yet no cross checks are performed. However, there are the following options:

- Comparison against a gravimetric primary standard (upper limit nano flow rate standard against lower limit gravimetric standard).
- Comparison against a flow meter where the calibration curve is obtained by means of extrapolation.

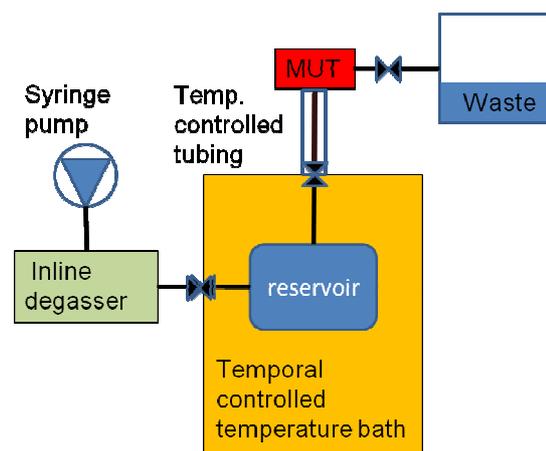


Figure 1 Sketch principle standard.

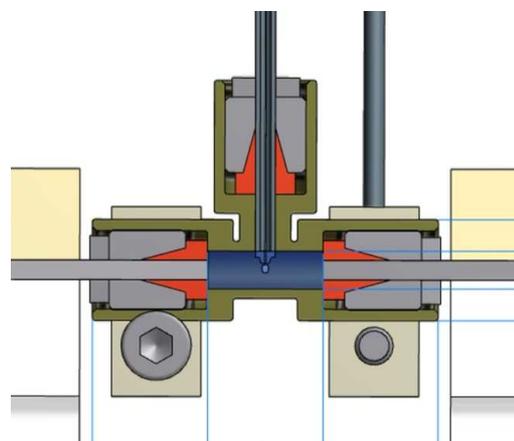


Figure 2 Close up reservoir holding the expanding liquid. The temperature is measured in the center of the reservoir

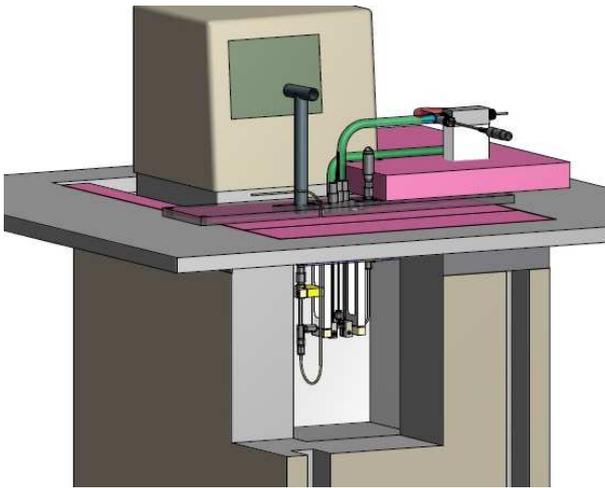


Figure 3 Set up primary standard for nano flow rates. The MUT is shown on the right (in white). The pink material is insulation, whereas the lever shown is to open and close one of the valves.

[1] Cox, M.G., Harris, P.M., Software support for metrology best practice guide no. 6 – uncertainty evaluation, NPL technical report, 2006.

[2] Lucas, P., *Metrology for drug delivery*, 2012 - 2015, partners VSL, Cetiati, CMI, DTI, EJPD, IPQ, Tubitak, project summary at http://www.euramet.org/index.php?id=emrp_call_2011

[3] Melvad, C et al, “Design considerations and initial validation of a liquid micro flow calibration setup using parallel operated syringe pumps”, *Meas. Sci. Technol.*, 21, 2010

[4] Tanaka, M., et. al; Recommended table for the density of water between 0 °C and 40 °C based on recent experimental reports, *Metrologia*, 38, 301-309, 2001

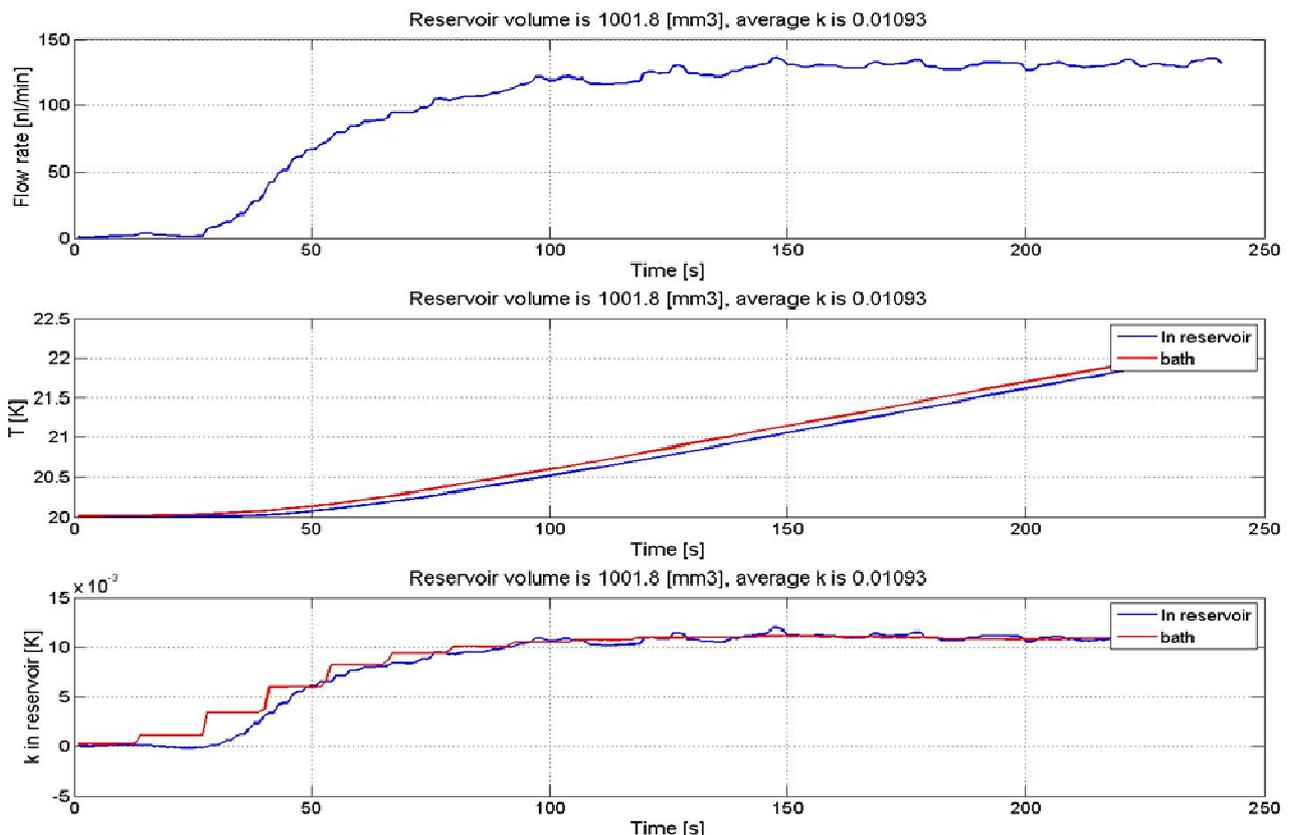


Figure 4 Flow rate [nl/min], temperature [K] (measured) and temperature gradient [K/s] as function of time (reservoir volume 1000 mm³, temperature gradient 0.01 K/s). After roughly 100 seconds a steady flow rate is obtained. Steady state is not reached immediately because it takes some time because the whole reservoir starts warming up. The oscillations shown are due to irregularities in the temperature gradient. Potentially this is just noise of the measurements and not a physical phenomenon.