Low-Cost Calibration / Verification Tool for Pipetting Systems

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The exact volume dispensed by a pipetting system is typically verified today using expensive calibration equipment such as high precision balances or photometers. In the first case volume is calculated by measuring the weight of a nominal volume of a liquid with known density. In the latter case a light interaction property is measured of a sample into which a nominal volume of a standard is added. The calibration plate presented here can be manufactured by microinjection molding, i.e. is low-cost, and measures the volume directly. A patent is pending.

The calibration plate (in microtiter plate format) for pipetting systems developed at CSEM can be used to calibrate pipettes or any dispensing systems in general, by measuring the extension by which the channels of defined capacity are filled by a given dispensed volume. The calibration plate can be manufactured relatively inexpensively (e.g. injection-molding) and does not require any additional expensive calibration equipment, such as a precision balance or a photometer, in order to calibrate pipettes. In addition, as opposed to the gravimetric calibration method, dispensed volumes of liquids with unknown density can be measured, because the calibration plate can measure volume directly. The calibration tool can be read by a user directly or by a vision- or a capacitive -based system automatically.

Design: The hydrophilic micro-channels meander across the transparent substrate (100 mm from turn to turn) and in this example have a total length of up to 1.7 m (Figure 1). If the channel cross-section is known, the distance traveled by the liquid front in the channel after adding a certain volume enables one to exactly determine the amount of this volume. Scales added to the substrate enable the user to easily measure the distance traveled by the liquid column within a capillary.

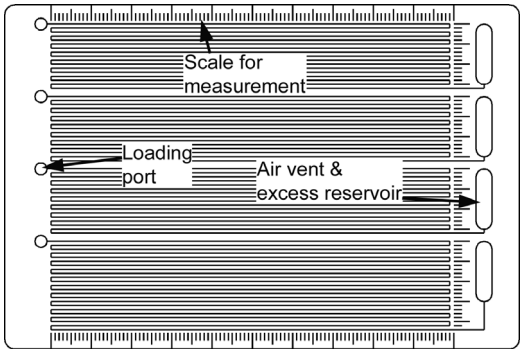

Figure 1: This example of a calibration plate has the same dimension as a SBS standard titer plate (85.48 mm x 127.75 mm). This example has 4 individual channels to be used to calibrate dispensed volumes. The bottom channel has a total length of 1.7 m.

The precision can be increased by using a nonius type slider (not shown). The volume is dispensed directly into ports connected to the start of a microchannel and will be drawn into the microchannels by capillary forces. Because exact measurement of a dispensed volume is only possible if all of the liquid is drawn into the microchannel, the wetting properties of the channels must be chosen accordingly. For aqueous solutions, often used in life-sciences applications, this requires hydrophilic channels.

The channel size is determined according to the volumes to be calibrated. As shown in Table 1, channels can be manufactured in different sizes for different volume ranges.

Table 1: Dependency between channel size and channel capacity.

Channel size:			Capacity / resolution
0.05 mm	x	0.05 mm	2.5 nl/mm
0.1 mm	x	0.1 mm	10 nl/mm
0.2236 mm	x	0.22236 mm	50 nl/mm
0.3162 mm	x	0.3162 mm	100 nl/mm
0.25 mm	x	1 mm	250 nl/mm

Function: Liquid is added to one of the loading ports, and due to the hydrophilic properties of the channel, the loading port empties completely (Figure 2 top). Subsequently, the volume of liquid to be calibrated (in this case 4 µl) is added to the same loading port and the difference of liquid front position is measured (Figure 2 bottom). This difference multiplied by the cross-section of the channel is equal to the volume dispensed. Here: (97 mm) * 0.21 * 0.2 mm^2 = 4.07 µl. Accordingly, in this example, the deviation of the pipette from the standard is 0.07 µl or 1.75%. This procedure is repeatable until liquid fills up the entire channel.

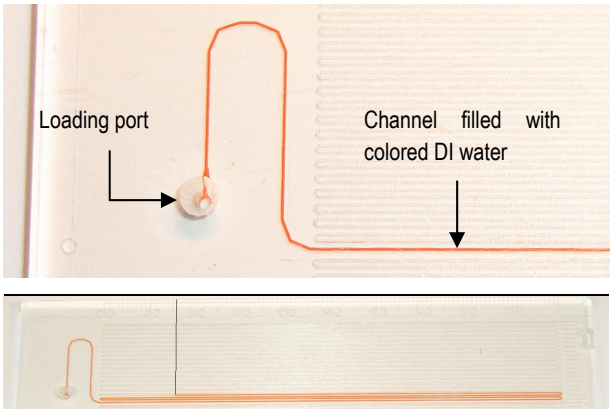

Figure 2: Top: calibration plate prototype with milled channels in PMMA with a size of 0.21 mm x 0.2 mm and a laminated lid. Bottom: the same plate with a position measurement at the liquid front.

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