

# True Flow Measurement for Capillary-LC

U. Kanne, Sensirion AG, Zurich, Switzerland

T. Preiswerk and G. Böhm, Flux Instruments AG, Basel, Switzerland.

**A new technology for the measurement of mass flow-rates has been developed: CMOSens - the combination of sensor and digital signal processing on a single CMOS microchip. Not only does this new technology raise performance limits in measurement technology, it also substantially reduces costs. This opens up entirely new perspectives for measurement and control of flow in liquid chromatography and gas chromatography systems.**

Measurement with this novel CMOSens technology offers very high sensitivity and speed thereby offering pioneering progress in the field of HPLC systems, not to mention remarkable emerging solutions for gas chromatography (GC). For more than 30 years, thermal mass flow measurements using coils around a steel capillary have been the norm in the precise measurement and dosing of mass flow-rates.

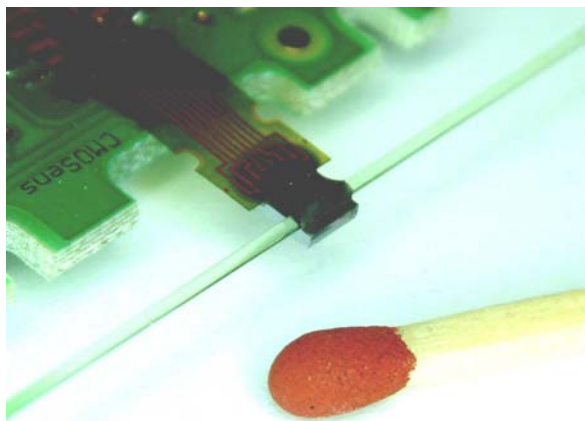
CMOSens technology, however, integrates this basic physical measuring principle in an extremely fast, miniaturized thermal sensor with all of the high-precision signal-conditioning circuitry on a single CMOS microchip. A heating element on the microchip adds a minimal amount of heat to the medium for the thermal flow measurement. Two temperature sensors, symmetrically positioned above and below the source of the heat, detect even the slightest temperature differences, thus providing basic information about the spread of the heat, which itself is directly related to the flow-rate. Integration on a single chip ensures that the sensitive analogue sensor

signals can be amplified with high precision, digitalized and processed further. Digital sensor processing and the stored calibration data together provide precision of <0.8% of the measurement value and allow for the output of a linear, completely calibrated flow measurement signal with speeds of up to 200 values per second. This is about 100 times faster than previous thermo pulse solutions and allows users to analyse even highly dynamic effects.

## **Just a Straight Capillary**

In addition to interesting solutions for GC applications, CMOSens technology enables mass flow measurements of even the smallest liquid flows. The sensor chip is completely isolated from the media without adding further dead volume. Sensors based on this new principle are extremely fast, small, lightweight and reliable. The accurate measurement of mass flow within the range of several millilitres per minute down to the sub nanolitre range poses no

problem. The highly sensitive microchips are mounted on PEEK, steel or fused silica capillaries completely isolated from the media. In other words: the flow meter for the fluid system is a simple, straight capillary without seals, dead volumes or restrictions.



*Fig. 1: A sensor mounted on a fused silica capillary*

A novel flow sensor with an inner volume  $<150$  nL has been designed based on a fused silica capillary with an i. d. of only 25 micrometres. One aspect is often viewed critically: as stated above, the functional principle of these sensors is based on a tried and tested thermal process whose advantages and drawbacks are well known. The amount of heat introduced into the medium is not a problem in practice with CMOSens, however, since the power supplied to the medium from the miniaturized system on the microchip is minimal at only a few milliwatts. One potential disadvantage is the dependence of the measurement on the physical properties of the medium (heat capacity, heat conductivity). In practice, this means the medium used must be known in order to achieve high absolute accuracy. Where reproducibility is concerned, as in chromatography, the new sensors have the advantage of a precision better than 0.6%. Developments at Sensirion AG have demonstrated how the variable mixing ratio of two media within a process can be managed. The special design of the CMOSens chip facilitated the development of a solution that allowed the mixed ratio and throughput of two gases to be accurately measured

simultaneously with up to 3% accuracy using the same sensor. Physical data are also established for the mixed ratio and the same sensor can determine the exact mass flow within the system.

### Capillary LC Application

A similar solution is possible for the gradient mode of HPLC systems. Pressure resistant (up to 200 bar/2900 psi), highly sensitive CMOSens liquid flow meters based on a fused silica capillary have recently become available and are becoming integral parts of LC pumps and systems. Monitoring the flow with these novel devices can ensure excellent reproducibility for analyses.

For capillary column applications in conjunction with a flow split, it is usually not possible to follow the actual through column flow. With high split ratios in particular, the through column flow represents only a tiny proportion of the master flow. The flow in the system is traditionally determined indirectly by measurements of the pressure or laborious offline measurements. Thus a blocked column often goes undetected leading to the loss of precious samples. Another application is the reproducible tuning of the electrospray source where the flow is an important parameter.

One of the first HPLC suppliers offering a system solution using CMOSens technology is Flux Instruments AG in Basel, Switzerland. They developed the AFM (Accurate Flow Monitor) software, enabling on-line gradient flow measurement together with the Rheos 2000 HPLC pump. The system permits on-line liquid flow measurement in isocratic and gradient capillary LC and LC/MS applications. Each AFM is individually calibrated for use with water, methanol and acetonitrile, allowing the sensor to measure the correct flow-rate at any time of a gradient run. This new AFM software enables instrument control, on-line monitoring and flow data logging for every run. It is designed for the use under ThermoFinnigan's Xcalibur© Shell software. A user-defined threshold value can be set to abort a sequence in the instance of a clogged or leaking column preventing the loss of precious samples. The dead volume free device accommodates flow-rates from 10 to 5000 nL/min, at a resolution of 10 nL. The

lowest detectable flow-rate is 10 nL/min, accuracy is 5%, repeatability is 0.6% (under reference conditions). A second device designed for low nL/min flow-rates is currently under development.

### Example Application:

Chromatographic Conditions

Column: Sisheido CAPCELL PAK C18 MGS-5  $\mu\text{m}$ , 0.3 mm i.d. x 150 mm

Solvent A:  $\text{KH}_2\text{PO}_4$  0.05 mol/L B: Methanol

Detection: Linear 200, UV 254 nm, UZ-Li-Cap illuminated volume 35 nL

Pressure: 100 bar

Split-ratio: 1:60, 300  $\mu\text{L}/\text{min}$  master flow

Gradient:

0 min 35% A, 1 min 35% A, 2 min 30% A, 3.9 min 30% A, 4 min 25% A, 5.9 min 25% A, 6 min 20% A, 7.9 min 20% A, 8 min 10% A, 13.5 min 10% A

Sensirion AG  
Eggbuehlstr.14,  
CH-8052 Zurich,  
Switzerland.

Tel +41 (0) 1306 4000

Fax +41 (0) 1306 4030

E-mail: [info@sensirion.com](mailto:info@sensirion.com)

Website: [www.sensirion.com](http://www.sensirion.com)

Flux Instruments AG

Hochstrasse 48,

CH-4002 Basel,

Switzerland.

Tel. +41 (0) 61366 9988

Fax +44 (0) 61366 9989

E-mail: [info@flux.ch](mailto:info@flux.ch)

Website: [www.flux.ch](http://www.flux.ch)

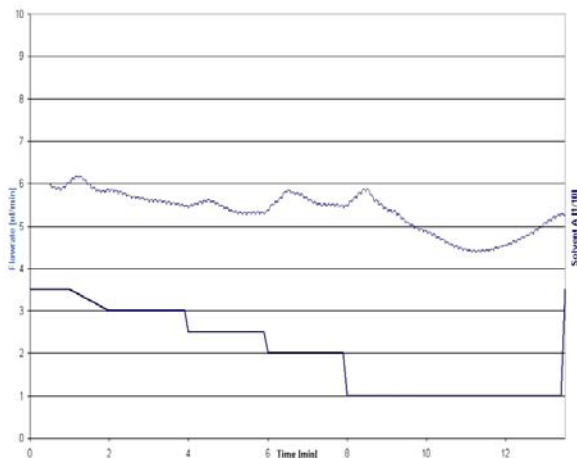


Fig.2: Gradient conditions see above measured flow rate (dotted line) corresponds to the expected profile showing column equilibration phenomena combined with a flow splitter

### Conclusion

The sensitivity and speed of CMOSens flow measurements offer totally new possibilities for LC systems. These features allow the sensors to be used in systems that were once clearly limited in terms of their performance because of a lack of or poor measuring technology. The increased reliability of capillary column applications with true flow measurement will save time and money.