Conductivity Pulse Time-of-Flight Flow Sensor for Sub-Microliter/Minute Flow Rates

C. K. Harnett, B. P. Mosier, P. F. Caton, B. Wiedenman, and R. W. Crocker
Sandia National Laboratories, Livermore CA 94550

Sandia National Laboratories

Calibration was performed by pumping liquid into the chip and timing the outflow into a glass capillary of known volume. Calibration curves for the three ranges in 5 mM TRIS buffer are shown in Figures 9a (fast range), 9b (medium range) and 9c (slow range), with flow rate and flow rate error bars given by the capillary measurement method, and TOF error given by the standard deviation of 100 to 1000 flight time measurements. Flight time coefficients obtained by fitting a three-term polynomial to the data for each range are given in Table 1.

Introduction

A microfluidic flow sensor capable of measuring liquid flow rates ranging from 10-2000 nL/min was fabricated in a glass chip with integrated metal electrodes. Flow rate is determined by measuring the flight time of an ion pulse introduced by electrolysis at a pair of electrodes inside the channel. The resulting conductivity increase is detected downstream by another electrode pair. Flight times are advection dominated due to rapid mass transfer of ions from the electrode surface to the bulk flow.

Potential applications include microfluidic pump control for high-pressure liquid chromatography and other micro total analysis systems.

System Design and Operation

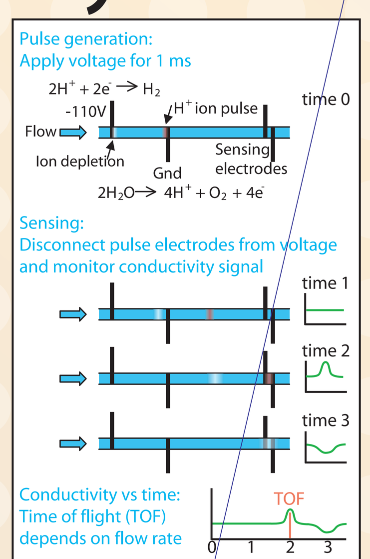


Figure 1: Ion pulse generation and flow rate sensing by monitoring arrival time of conductivity maximum

The CP-TOF sensor was implemented as an etched channel on a glass chip with embedded thin-film electrodes. These electrodes are used to generate an ion pulse in the fluid as well as to sense the arrival of the pulse at a location downstream. Figure 1 describes the ion generation and conductivity sensing functions.

During operation with aqueous acidic or neutral fluids, the high voltage electrode is pulsed at -110V for 1 ms. The adjacent downstream electrode is grounded. Ions generated by water oxidation at the ground electrode move downstream with the flow and are sensed as a conductivity increase at another pair of electrodes near the channel exit. Later, there is a conductivity decrease due to ion depletion at the -110 V electrode. Because of dispersion, the depletion peak amplitude is smaller than that of the ion peak. The TOF is defined as the time between the start of the high voltage pulse and the conductivity maximum.

By using different pairs of pulse electrodes for slow, medium, and fast flow rates, the flow rate can be measured over three orders of magnitude, with TOF measurements ranging from 20 ms to 200 ms.

Electronics/Software

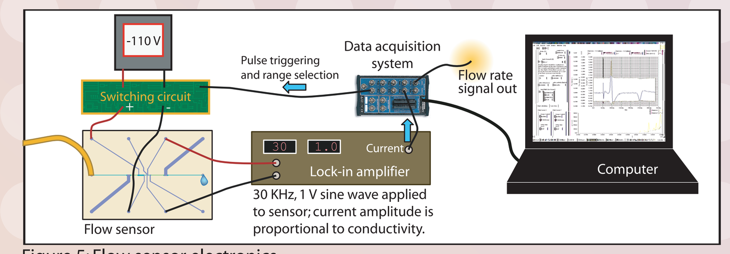


Figure 5: Flow sensor electronics.

A LabView application initiates the -110 V pulse from a small DC HV converter connected to the pulse electrode pair. It also controls switches to select "fast," "medium," or "slow" electrodes. The conductivity signal is acquired by a lock-in amplifier connected across the sensing electrodes as shown in Figure 5. After a TOF is acquired, the flow rate is computed and made available to other hardware as a 0-10V signal proportional to flow rate in nl/min.

Background

Micro-total analysis systems require flow sensors for several purposes, including precision reagent metering, providing closed-loop control to microfluidic pumps, and reproducible control of the flow conditions in reaction chambers, mixing chambers, and separation devices. The flow rates of interest are typically less than 100 microliters/min.

Recently, several types of flow sensors have been developed to provide feedback in microfluidic systems, including sensors that measure the pressure drop over a restriction and those based on the dispersion of a thermal pulse. We have developed a sensor based on the time ... an ion pulse generated by electroly...

The advantage of the condu... flight (CP-TOF) sensor over ... anemometers is that unlik... pulse cannot diffuse into ... Therefore, thermal isolat... walls with air gaps [1] ar... the sensor to be readily ... high-pressure systems.

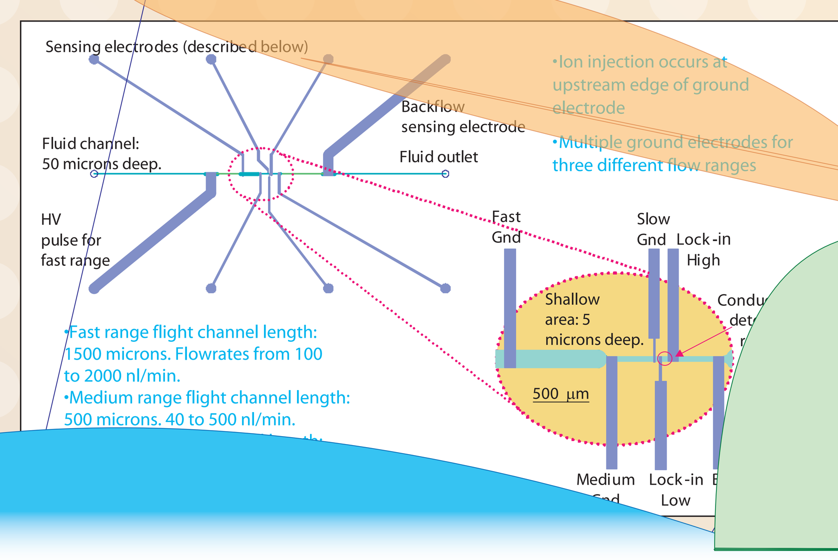
The CP-TOF sensor is als... viscosity variations, either fro... temperature fluctuations. In co... based on viscous drag, such as those ... pressure drop over a restriction [2], require flui... dependent calibrations.

However, the CP-TOF sensor requires fluids that support rapid electrolysis in response to a short, high-voltage electrical pulse. In addition, the ion pulse must persist long enough to reach the detector, as well as stand out above the conductivity background, which is not always the case in strongly-buffered solutions. Flow rates above 1 microliter/minute have previously been measured in strongly-buffered solutions using electrodes to detect the flight time of an oxygen pulse rather than an ion pulse [3].

Fluids of interest for chromatography that were used in the CP-TOF sensor include 5 mM aqueous tris(hydroxymethyl)aminomethane (TRIS) buffer, pH 8, and mixtures of water/acetonitrile containing 0.1% trifluoroacetic acid.

[1] Wu, S. Y., Lin, Q., Yuen, Y., and Tai, Y. C., "MEMS flow sensors for nano-fluidic applications," *Sens. Act. A* **89** (2001) 152-158.
[2] Oosterbroek, R. E., Lammerink, T. S. J., Berenschot, J. W., Krijnen, G. J. M., Elwenspoek, M., A. van den Berg, "A micromachined pressure/flow sensor," *Sens. Act. A* **77** (1999) 167-177.
[3] Wu, J. and Sansen, W., "Electrochemical time-of-flight flow sensor," *Sens. Act. A* **97-98** (2002) 68-74.

Chip Layout



...ers, ...bonding ...ds.

...reated by a 50 ...ntrated hydrofluoric ...ugh a lithographically ...terned silicon hardmask (Figure 3a).
- New areas are opened in the hardmask to define shallow channels for the pulse flight tube. These areas, and the previously etched channels, are etched 5 microns in the HF solution (Figure 3b).
- Thick photoresist (15 microns) is used to define the electrode pattern on top of the silicon. The silicon in the electrode areas is removed by plasma etching, then a 200 nm countersink is created for the electrodes by etching the glass in dilute HF (Figure 3c).
- A 20 nm titanium adhesion layer and a 180 nm thick platin... film are deposited by sputter coating (Figure 3d).
- Excess metal is removed by lifting off the photoresist in an ultrasonically agitated acetone bath (Figure 3e).
- Etched wafers and drilled cover plates are briefly dipped i... dilute HF to relieve stress caused by machining, then cleaned ... immersion in Piranha solution (4:1 H2SO4:H2O2) at 100 C. Wa... are further cleaned by immersion in concentrated sodium hydroxide, which also removes the silicon hardmask, then rin... with deionized water and dried in a spin-rinse dryer. Cleaned wafers are thermally bonded in a furnace at 610 C for 5 hours (Figure 3f).

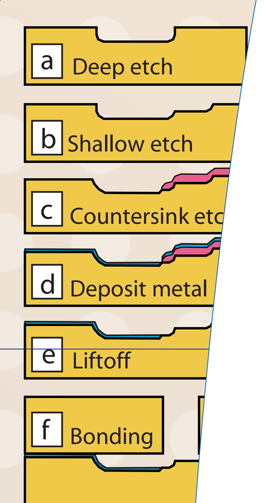


Figure 3: Proces...

Packaging

- Wafers are diced into chips containing two sensors each. Fluid connectors are bonded over via holes with epoxy, and devices are attached to chip carriers for electrical connections. Figure 4 is a photo of a finished two-sensor device.

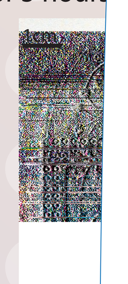


Figure 4: Tw... ...ow sensors on chi... ...arrier.

Conductivity Traces

Figure 6 shows conductivity data for four different concentrations of TRIS buffer. The raw conductivity data is then filtered as described in Figure 7. The filtered signal in 5 mM, pH 8 TRIS buffer is plotted for several flow rates in fast range (Figure 8a), medium range (Figures 8b and 8c) and slow range (Figures 8d and 8e.)

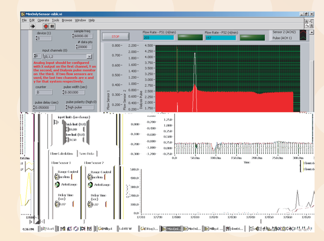


Figure 7: Flow sensor screenshot showing raw signal (red) and differentiated, amplified conductivity signal (white). This filtering process removes DC electronic drift.

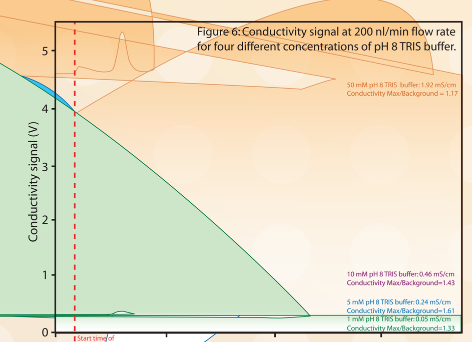


Figure 6: Conductivity signal at 200 nl/min flow rate for four different concentrations of pH 8 TRIS buffer.

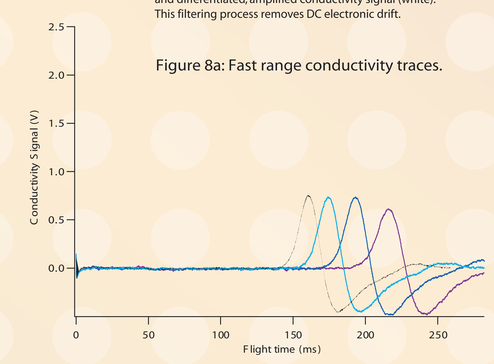
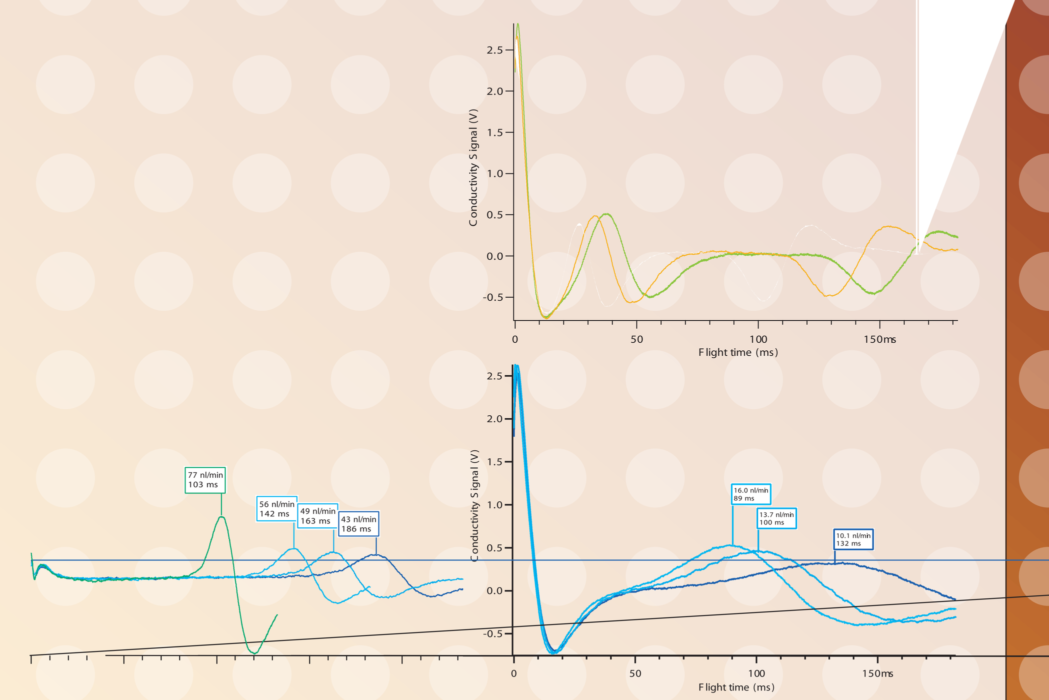
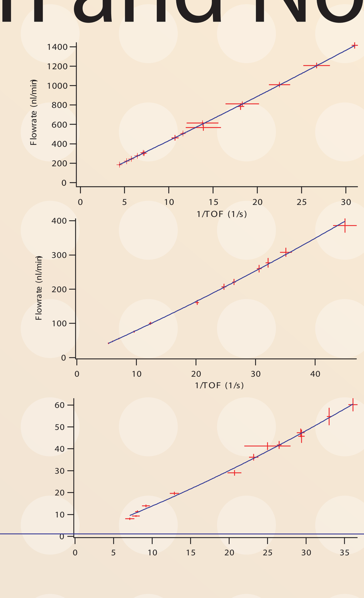


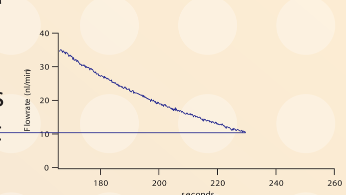
Figure 8a: Fast range conductivity traces.



Calibration and Noise Analysis



Noise was analyzed by pressurizing the sensor, measuring the flow rate while the pressure was allowed to decrease to atmosphere, then fitting the flow rate data to a decaying exponential. These curves appear in Figure 10a (fast range), 10b (medium range) and 10c (slow range.) Subtracting the exponential from the measured flow rate at each point gives an estimate of the noise. These residuals appear in Figure 11a (fast range), 11b (medium range) and 11c (slow range.) For 5 mM pH 8 TRIS buffer, the CP-TOF flow rate measurement error is typically 1% of the flow rate. At the lowest flow rate of 10 nL/min, the error is ~5% of the measured flow rate.



Conclusions

The CP-TOF sensor is well suited to aqueous solutions with low buffer concentrations (<50 mM). It is easily integrated into the microfluidic fabrication process, and has been operated at fluid pressures up to 1200 psi. Electrolysis from the brief voltage pulse does not produce bubbles or bulk pH changes. Because the sensor detects particles and bubbles, it should be used with filtered solutions. To eliminate bubbles, solutions may be degassed or the system may simply be operated at high pressure. With the triple-range system, flow rate measurements from 10 to 2000 nl/min can be acquired at a minimum rate of 5 Hz. For these reasons, the CP-TOF sensor is suited to providing flow rate feedback in microscale systems where high-purity reagents are dispensed at high pressures.

Acknowledgements

We wish to acknowledge financial support from Waters Corporation and technical discussions with Keith Fadgen at Waters, advice on integrating the flow sensor with pumping systems from Ken Patel, the microfluidic packaging contributions of Ron Renzi and Judy Rognlien, and the microfabrication expertise of Bill Kleist, Sue Jamison, and George Sartor.

Waters

Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AI85000.