

文章编号 1004-924X(2009)09-2218-06

基于高场非对称波形离子迁移谱的生化传感器的设计

李 华, 王晓浩, 唐 飞, 林镇翔

(清华大学 精密仪器与机械学系 精密测试技术及仪器国家重点实验室, 北京 100084)

摘要: 基于高场非对称波形离子迁移谱原理设计了一种由离子源, 迁移区和检测器 3 部分组成的生化传感器。传感器采用真空紫外灯作离子源, 高纯氮(99.999%)为载气, 在常压下工作。加工了两种由两平行金属极板组成的迁移区, 一种由两平板铜块组成, 尺寸为 25 mm×10 mm×1 mm; 另外一种由微机电(MEMS)工艺加工, 尺寸为 20 mm×10 mm×1.5 mm。MEMS 工艺加工的迁移区间距为 1.5 mm, 电场强度 < 10 000 V/cm, 不能过滤丙酮离子; 铜块迁移区间距为 1 mm, 电场强度 > 10 000 V/cm。当方波非对称射频电压峰峰值为 1 600 V, 频率为 195.8 kHz, 占空比为 30%, 补偿电压为 -8.63 V 时, 采用平板铜块迁移区实现了丙酮离子的位移补偿, 实验结果验证了传感器的性能。

关键词: 高场非对称波形离子迁移谱; 生化传感器; 迁移区; 微机电系统

中图分类号: TP212.2 **文献标识码:** A

Design of biochemical sensor based on high-Field Asymmetric Ion Mobility Spectrometry

LI Hua, WANG Xiao-hao, TANG Fei, LIN Zhen-xiang

(Key State Laboratory of Precision Measurement and Instruments, Department of Precision Instruments and Mechanology, Tsinghua University, Beijing 100084, China)

Abstract: A novel biochemical sensor based on a high-Field Asymmetric Ion Mobility Spectrometry (FAIMS) theory is fabricated and characterized, which is mainly composed of an ionization source, a drift tube and a detector. By taking a VUV lamp as the ionization source and choosing an acetone with nitrogen (99.999%) as the carrier gas, the biochemical sensor works at ambient pressure. Moreover, two kinds of drift tubes consisting of two parallel plate electrodes are fabricated. One drift tube with the dimension of 25 mm×10 mm×1 mm is composed of two copper planar electrodes, the other with the dimension of 20 mm×10 mm×1.5 mm is fabricated by Micro Electro-Mechanical System(MEMS) technology. For the former, the gap between the two drift tubes is 1 mm and the electrical field is above 10 000 V/cm; but for the latter, the gap between MEMS drift tube is 1.5 mm and the electrical field is less than 10 000 V/cm, which can not separate the acetone. With a peak-peak of rectangular asymmetric waveform voltage up to 1 600 V, a frequency of 195.8 kHz, a duty cycle of 30% and a compensation voltage of -8.63 V, the acetone displacement is compensated and the sensor ability to separate ions is demonstrated by an experiment using the planar copper drift tube.

Key words: high-Field Asymmetric Ion Mobility Spectrometry(FAIMS); biochemical sensor; drift tube; MEMS

Received date: 2008-12-07; **Revised date:** 2009-04-30.

Foundation item: Supported by the National Natural Science Foundation of China (Grant No. 60706030, 20827007); the National High-Tech Research and Development Program of China(863 Program) (Grant No. 2007AA04Z337)

1 Introduction

The high-Field Asymmetric waveform Ion Mobility Spectrometry (FAIMS) for gas-phase ion separation is an advanced technology based on a chemical analysis technology, Ion Mobility Spectrometry (IMS), developed in 1970s, and it separates ions at ambient pressure based on the nonlinear dependence of the mobility coefficient on an applied electric field. Different chemical agents can be characterized by the drift velocities of the ionized sample molecules in a weak electric field at atmospheric pressure. In IMS, the electrical field in the drift tube is linear. IMS has many advantages, such as quick response, simple structures, and easy to combine with other chemical detectors^[1-3].

But the structure of the drift tube in IMS is complicated and is not feasible to be minimized. To overcome the shortcomings of the present test device, the research brings forward a biochemical sensor based on the FAIMS theory. It has many characteristics, such as miniature, high sensitivity, short test time, numerous test substances and low power. The sensor based on the FAIMS technology can be applied to quickly test the atmosphere, toxic gases, the organic pollutants in water, explosives, chemical warfare agents, the amino acid, etc, and it can be widely used in the fields of environmental monitoring, community safety, warfare biochemical threat, and so on.

The cylinder and planar drift tubes have been developed in previous work. The cylinder drift tube has the ion focusing effect, but the drift tube is complicated and not feasible to be miniature^[4-5]. Comparably, the planar drift tube is easier to manufacture and offers reproducibility and cost benefits. G. A. Eiceman et al presented a MEMS (Micro Electro-Mechanical System) planar drift tube with a 0.5 mm gap^[6-8].

In the FAIMS system, the high-frequency

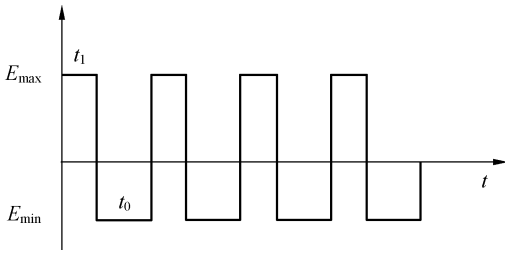
asymmetric waveform is a very important part. In the previous study, the bisinusoidal, the clipped displaced sinusoidal and the quasi-sinusoidal waveforms were employed for FAIMS^[9-13]. But in theory it shows that the rectangular waveform with a duty cycle of 1/3 is the optimum asymmetric waveform for FAIMS^[14]. The first attempt using a rectangular waveform was done by Roger Guevremont, which was impractical in reality for the low frequency (83 kHz) and the high power consumption^[15]. Recently, D. Papanastasiou et al adopted the rectangular asymmetric waveform with a voltage pulse amplitude up to 1 000 V and a frequency of 1 MHz for the drift tube with a 0.5 mm gap^[16].

In this paper, a new rectangular asymmetric power is designed for the FAIMS. Then, a FAIMS principle prototype is presented and its ability of separating ions is verified by experiments.

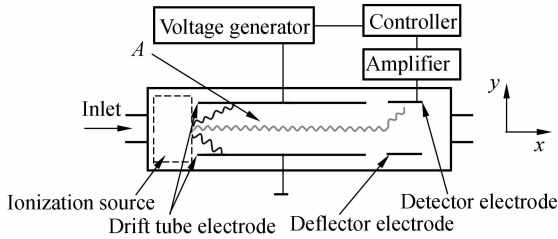
2 Principle

Unlike the IMS, the FAIMS works as an ion filter and transmits ions in a continuous fashion. The fundamental of FAIMS is shown in Fig. 1.

Just as shown in Fig. 1, FAIMS are mainly composed of three parts: an ionization source, a drift tube and a detector. Many kinds of ionization techniques can be used to form ions in a gas phase in atmosphere. For example, ⁶³Ni ionization, photoionization, corona ionization, etc, were used as the ionization sources in FAIMS^[4]. The drift tube is a most important part of the FAIMS, which consists of two parallel electrodes. The sample ions are formed in the ionization source with a stream of carrier gas. A high voltage RF (radio-frequency) waveform and a weak DC voltage are applied to the two parallel electrodes and verticle to the carrier gas flow. The asymmetric RF waveform voltage is de-



(a) Radio-frequency waveform voltage



(b) FAIMS operation principle

Fig. 1 Fundamental of FAIMS

signed and the time average electric field is zero in a period:

$$E_{\max} t_1 = E_{\min} t_0 = p, \quad (1)$$

Where p is a constant, E_{\max} is the electric field strength during t_1 time and E_{\min} is the electric field strength during t_0 time. When the ions carried by the carrier gas traverse the drift tube, the ions will follow trajectories perpendicularly to the gas flow under the action of electrical fields. For the RF waveform is asymmetric, the ion velocity toward to top electrode is different from that of the bottom electrode. This difference is due to the difference in the electrical field and the ion mobility dependence on the electrical field strength when the electrical field is greater than about 10 000 V/cm. So in every period of RF waveform, there is a net displacement for ions.

$$s = s_1 - s_2 = v_{\max} t_1 - v_{\min} t_0 = KE_{\max} t_1 - K_0 E_{\min} t_0 = (K - K_0) p, \quad (2)$$

Where v_{\max} is the ion velocity in the y direction during t_1 time; v_{\min} is the ion velocity in the y direction during t_0 time; K is the coefficient of mobility of the ion during t_1 time; K_0 is the coef-

ficient of mobility of the ion during t_0 time.

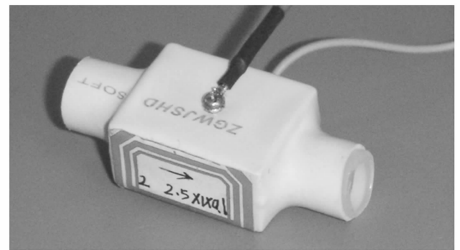
If a certain DC compensation potential is added to the electrode, the ions whose displacement in a period is zero can pass through the drift tube and register at the detector, just as A shown in Fig. 1. Other ions will strike the electrode, then, they are neutralized and removed from the FAIMS by the carrier gas flow.

Different ions correspond to different DC compensation voltages, so the samples can be identified by the DC compensation voltages.

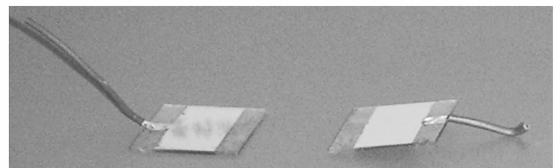
3 Experiments

3.1 Fabricated ionization source and drift tube

The biochemical sensor consists of an ionization source, a drift tube, a signal detector and so on, as shown in Fig. 1. The ionization source adopts a VUV lamp ion source. The sample ions are created in air at ambient pressure by the VUV lamp ion source with a 10.6 eV photo discharge lamp ($\lambda=116.5$ nm). Two kinds of drift tubes composed of two parallel plate electrodes are fabricated as shown in Fig. 2. One drift tube is composed of two copper planar electrodes and the dimension is 25 mm \times 10 mm \times 1 mm and the other is fabricated by MEMS technology and the



(a) Copper planar electrodes



(b) Electrodes fabricated by MEMS technology

Fig. 2 Two kinds of drift tube electrodes

dimension is 20 mm × 10 mm × 1.5 mm. The MEMS fabrication process includes lithography, sputtering, wire bonding, and so on. The MEMS drift tube is fabricated from two Pyrex wafers. The metal Ti/Pt/Au electrodes are fashioned on the Pyrex wafers using a sputter deposition. Then, the Pyrex wafers are diced into rectangular pieces.

3.2 Preparation of sample and carrier gas

Chemical used in the experiment is acetone. The carrier gas is pure nitrogen (99.99%), which is purchased from Beijing Hua Yuan Gas Chemical Industry Corporation.

3.3 Experimental instrument

The acetone is adopted to characterize the biochemical sensor. In the experimental system (Fig. 3), a rotameter is chosen as the flow meter and the detector instrument is a JMS-T100GC time-of-flight Mass Spectrometer (MS) made in Japan. The mass spectrometer works on the positive ion mode and the ratio of charge to mass is 20~200 amu.

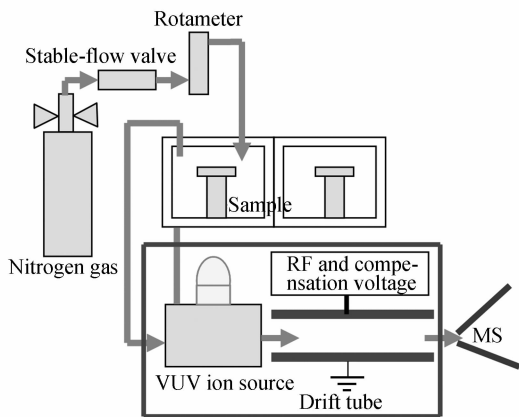


Fig. 3 Schematic of FAIMS experimental system

The photograph of experimental system is shown in Fig. 4. In the experiment, the acetone is carried by nitrogen gas (99.999%) into the VUV lamp ion source at a gas flow of 200 l/h. The Radio-Frequency (RF) voltage is a periodic signal of high-field asymmetric positive and negative pulses (peak-peak voltage about +1 600 V) at a frequency of 195.8 kHz and a duty cycle



Fig. 4 Photograph of experimental system

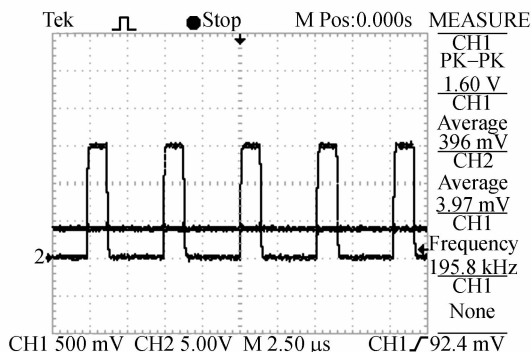


Fig. 5 Radio-frequency (RF) voltage

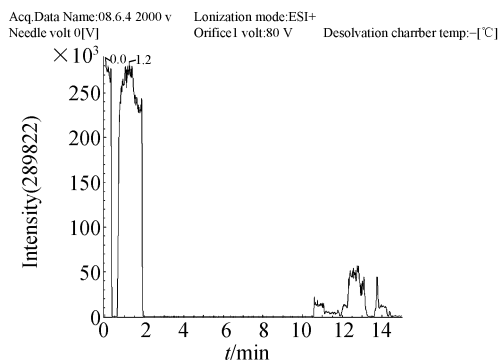
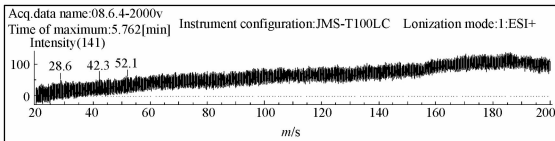


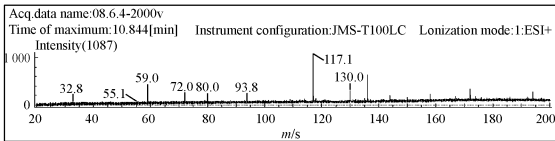
Fig. 6 Ion strength in 15 min

of 30%, as shown in Fig. 5. As the gap between the two MEMS drift tubes is 1.5 mm and the electrical field is less than 10 000 V/cm, the MEMS drift tube can't separate the acetone ions. For the copper drift tube, the gap is 1 mm and the electrical field is above 10 000 V/cm. As shown in the Fig. 6 and Fig. 7, firstly, there are many ion peaks in mass spectrometer file when no RF waveform and compensation voltage are applied to the drift tube, which shows that the sample are ionized by the ionization source and

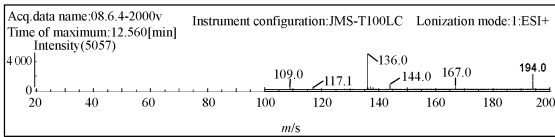
pass through the drift tube without the RF waveform and the compensation voltage. Next, there are no ion peaks in the mass spectrometer file when the RF waveform is on and the compensation voltage is off (Fig. 7(a)). In the third experiment the RF field is on and the compensation voltage sweeps.



(a) $V_{p-p} = 1\ 600\ \text{V}$ and $V_{dc} = 0\ \text{V}$



(b) $V_{p-p} = 1\ 600\ \text{V}$ and $V_{dc} = -8.63\ \text{V}$



(c) $V_{p-p} = 1\ 600\ \text{V}$ and $V_{dc} = -12.41\ \text{V}$

Fig. 7 Mass spectra of ions in different conditions

When the compensation voltage sweeps to $-8.63\ \text{V}$, acetone ion peaks ($m/z=59$) appear in the mass spectrometer file (Fig. 7(b)). When the compensation voltage sweeps to $-12.41\ \text{V}$, acetone ion peak ($m/z=59$) disappear, which shows that the voltage of $-8.63\ \text{V}$ is the compensation voltage of the acetone (Fig. 7(c)).

4 Conclusions

With the peak-peak voltage up to $1\ 600\ \text{V}$, the frequency of $195.8\ \text{kHz}$ and the duty cycle of 30% , a rectangular asymmetric waveform power is successfully designed and tested, which brings a prior choice for FAIMS as compared with bisinusoidal, clipped displaced sinusoidal and quasi-sinusoidal waveforms. At atmosphere pressure, the VUV ion source is a viable alternative to ^{63}Ni ionization and corona ionization. The performance of the biochemical sensor based on FAIMS theory that adopts the rectangular asymmetric waveform and VUV ion source is verified by the FAIMS-MS experiment, which shows that ions can be separated and filtrated by the novel biochemical sensor. It also shows that the smaller drift tube gap is, the more likely FAIMS separates ions. And the miniaturized drift tube is the development tendency for FAIMS.

References:

- [1] STEINER W E, HARDEN C S. Detection of aqueous phase chemical warfare agent degradation products by negative mode ion mobility time-of-flight mass spectrometry [J]. *J. Am. Soc. Mass. Spectrom.*, 2006, 17(2): 241-245.
- [2] MYLESA L, MEYERSA T P, ROBINSONB L. Atmospheric ammonia measurement with an ion mobility spectrometer [J]. *Atmos. Environ.*, 2006, 40(30): 5745-5752.
- [3] ERICKSON R P, TRIPATHI A, MASWADEH W M. Closed tube sample introduction for gas chromatography-ion mobility spectrometry analysis of wa-
- [4] GUEVREMONT R, PURVES R. Comparison of experimental and calculated peak shapes for three cylindrical geometry FAIMS prototypes of differing [J]. *J. Am. Soc. Mass Spectrom.*, 2005, 16(3): 349-362.
- [5] GUEVREMONT R. High-field asymmetric waveform ion mobility spectrometry: a new tool for mass spectrometry [J]. *J. Chromatogr. A*, 2004, 1058(1-2): 3-19.
- [6] EICEMAN G A, NAZAROV E G, MILLER R A. A micro-machined ion mobility spectrometer-mass

ter contaminated with a chemical warfare agent surrogate compound [J]. *Anal. Chim. Acta.*, 2006, 556(2): 455-461.

spectrometer [J]. *IJIMS*, 2000, 1(3):15-27.

- [7] EICEMAN G A, KRYLOV E V, TADJIKOV B, *et al.*. Differential mobility spectrometry of chlorocarbons with a micro-fabricated drift tube [J]. *Analyt*, 2004, 129:297-304.
- [8] EICEMAN G A, TADJIKOV B, *et al.*. Miniature radio-frequency mobility analyzer as a gas chromatographic detector for oxygen-containing volatile organic compounds, pheromones and other insect attractants [J]. *J. Chromatogr. A* 2001, 917:205-217.
- [9] KRYLOV E V. A method of reducing diffusion losses in a drift spectrometer [J]. *Tech. Phys.*, 1999, 44(1):113-116.
- [10] GUEVREMONT R, BARNETT D A, PURVES R W, *et al.*. Calculation of ion mobilities from electrospray ionization high-field asymmetric waveform ion mobility mass spectrometry data [J]. *J. Chem. Phys.*, 2001, 114 (23): 10270-10277.
- [11] BURYAKOV I A, KOLOMIETS Y N, LUPPU B V. Detection of explosive vapors in the air using an ion drift nonlinearity spectrometer [J]. *J. Anal. Chem.*, 2001, 56(4):336-340.
- [12] BURYAKOV I A. Qualitative analysis of trace constituents by ion mobility increment spectrometer [J]. *Talanta*, 2003, 61(33):369-375.
- [13] KRYLOV E V, NAZAROV EG, MILLER R A, *et al.*. Field dependence of mobilities for gas-phase-protonated monomers and proton-bound dimers of ketones by planar field asymmetric waveform ion mobility spectrometer (PFAIMS) [J]. *J. Phys. Chem. A*, 2002, 106(22):5437-5444.
- [14] KRYLOV EV. Pulses of special shapes formed on a capacitive load [J]. *Instrum Exp. Tech.*, 1997, 40:628-631.
- [15] GUEVREMONT R, PURVES R W. Atmospheric pressure ion focusing in a high-field asymmetric waveform ion mobility spectrometer [J]. *Rev. Sci. Instrum.*, 1999, 70(2):1370-1383.
- [16] PAPANASTASIOU D, WOLLNIK H, RICO G. Differential mobility separation of Ions using a rectangular asymmetric waveform [J]. *J. Phys. Chem. A*, 2008, 112(16):3638-3645.

Authors' biographies:



LI Hua(1978—), male, post-doctor of the Department of Precision Instruments, Tsinghua University, his research interests are MEMS-based chemical and biological sensors, micro elastic elements, MEMS safety and arming device in fuze, *etc.* **E-mail:** huali@mail.tsinghua.edu.cn



WANG Xiao-hao (1971 —), male, Ph. D., Associate Professor of the Department of Precision Instruments, Tsinghua University, his research interests are scientific instruments, MEMS and micro aerial vehicles. **E-mail:** xh-wang@mail.tsinghua.edu.cn



TANG Fei (1973 —), male, received his B. S. and M. S. from Harbin Institute of Technology in 1995, and 1997, respectively, and Ph. D. from Tsinghua University in 2003. Now he is an Assistant Professor in Tsinghua University. He is mainly engaged in the research on precision measurement and control, microsystem design and technology.



LIN Zhen-xiang (1984 —), male, M. S. of Department of Precision Instruments, Tsinghua University, his research interests are scientific instruments, high voltage and radio frequency (RF) power.