A Liquid-phase Ion Trap for Ion Trapping, Transfer and Sequential Ejection in Solutions

Supporting Information

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Ion motion simulation program

Due to the extremely small mass of an ion, the gravity is negligible. Therefore, only the electric field force caused by the charges q and the viscous drag force caused by the hydrodynamic radius R_h are taken into account. Based on the fact that these two forces can come into balance over a relatively short time $(< 1ns)$ in an aqueous environment, the steady-state velocity of an ion is directly calculated and utilized in simulation. In addition, the apparent velocity of an ion relative to the static tube is influenced by the flowing rate of the liquid injected into the pipeline. The velocity distribution of flowing liquid is subject to the Laminar flow due to the uneven temperature distribution and the boundary speed at the inner tube wall is zero. As a result, the apparent velocity of a specific ion at a certain time point t can be calculated according to its' position (x_t, y_t, z_t) in the pipeline.

To calculate and simulate the diffusion effect accurately, the axial length of the tube is divided evenly, so as to the radius. Then, each segment is ready to be estimated the degree and direction of the diffusion in the model. Finally, the exchange of ions is conducted in a random way. Hence, the diffusion effect is in all directions. Figure S1 shows the schematic flow chart of the program.

To obtain results of statistical significance, the total number of ions in simulation (6,000 for each type) is 12,000. The time step is 0.01 s. The inner diameter of each short tube is 75μm and its' axial length is 3.5cm. The axial length step is 0.07 cm and the radial length step is 6.25 μm. Moreover, considering the detection limit in the experiment is 3:1(the intensity of signal versus that of the noise), the threshold is set as 20 particles in simulation data processing, which is higher than practical condition. Meanwhile, the accuracy of time in statistics is 0.5 s, the same speed to get a mass spectrum.

Step 1.

- Liquid Environment:

1. The Velocity of liquid flow $v_{□□□□}$ is subject to Laminar flow.
2. Set the viscosity coefficient and temperature.

- Particles' quality:

1. The initial distribution of particles is subject to a uniform distribution in the radial circular face and along axial length respectively.
2. Set ion's charges q and hydrodynamic radius $R_□$.

- Electric field:

1. Set the unit length d of a single tube and the number of tubes n composed of the device.
2. Set voltage changes at the two ends of the device U.

Step 2.

- Calculate Relative velocity $v_{□□}$ between an ion and the surrounding aqueous environment according to the equation between the viscous drag force $f = 6\pi\eta R_□ v_{□□}$ and $F_{□□□□□□} = Uq/d$.
- Calculate the diffusion effect, in which the diffusion coefficient is $D = \frac{□□}{□□□□}$.

Step 3.

- Check radial and axial positions (x, y, z) of ions

1. If an ion is out of the device $(z \geq nd)$, then record the time at that moment.
2. If an ion is in the device $(z < nd)$, then go back to *Step 2*.

Figure S1. Flow chart of the ion motion simulation program

Parameter optimization

Parameters of the liquid-phase ion trap was first optimized for the enrichment of Ag II ions, including enrichment voltage, duration of enrichment and sample injection volume. 10 ng/mL of Ag II was selected as the analyte. Under the constant liquid driving force (buffer flow rate 0.15 μL/min), a voltage of 0, -1.0, -1.5, -2, -2.5 kV was applied on HV_1, respectively, with the rest of the electrodes grounded. The voltage was applied for 10 mins. Figure S2a showed the EIC spectra of m/z 523.77, and a narrower peak with higher intensity could be observed with a trapping voltage above -1.5 kV. -1.5 kV was then selected as the enrichment voltage of Ag II. Different sample injection durations were then tested. Samples were injected from the syringe with a pumping speed of 20 μL/h for different durations. With increased sample injection durations, stronger ion intensity could be observed, and a good linear correlation could be achieved as shown in the inset of Figure S2b.

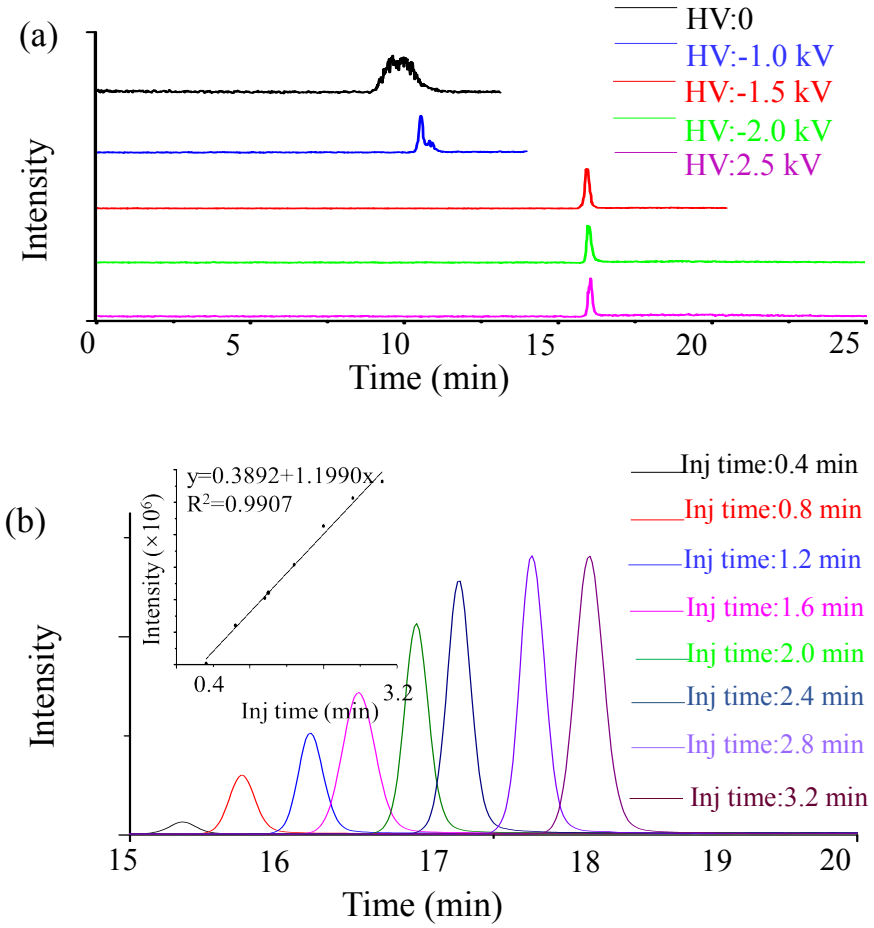

Figure S2. Parameters optimization for the liquid-phase ion trap. (a) enrichment voltage optimization, 10 ng/mL of Ag II was analyzed at a buffer flow rate of 0.15 μL/min. (b) optimization of injection volume, 10 ng/mL of Ag II were injected from the syringe with a pumping speed of 20 μL/h.

The enrichment of Ag II

The enrichment of 1 μg / mL Ag II was tested in non-trapping and trapping mode according to the 3.1 phenylalanine part. The EIC of Ag II showed a relatively low broad peak in the non-trapping mode (Figure S3a). After 10 minutes of continuous enrichment applied with -1.5 kV, the EIC of Ag II showed a peak with high intensity, high symmetry and good half width. In addition, the qualitative and quantitative analysis of 0.1-2000 ng/mL were compared in non-trapping and trapping. In the trapping mode, the signal to noise ratio of 0.1-100 ng/mL was listed in the Figure S3c. The results showed that the S/N of 5.2 could be achieved at 0.1 ng/mL, which reached the

qualitative limit, while that of 0.1 ng/mL and 1 ng/mL was not detected and S/N of 6.64 could be achieved at 100 ng/mL in the non-trapping mode, which only reached the qualitative limit. The detection limit of trapping mode was nearly 1000 times higher than that of non-trapping mode. The linear range of quantitation was obtained in the range of 0.1-100 ng/mL with a R^2 of 0.9994 (Figure S3d).

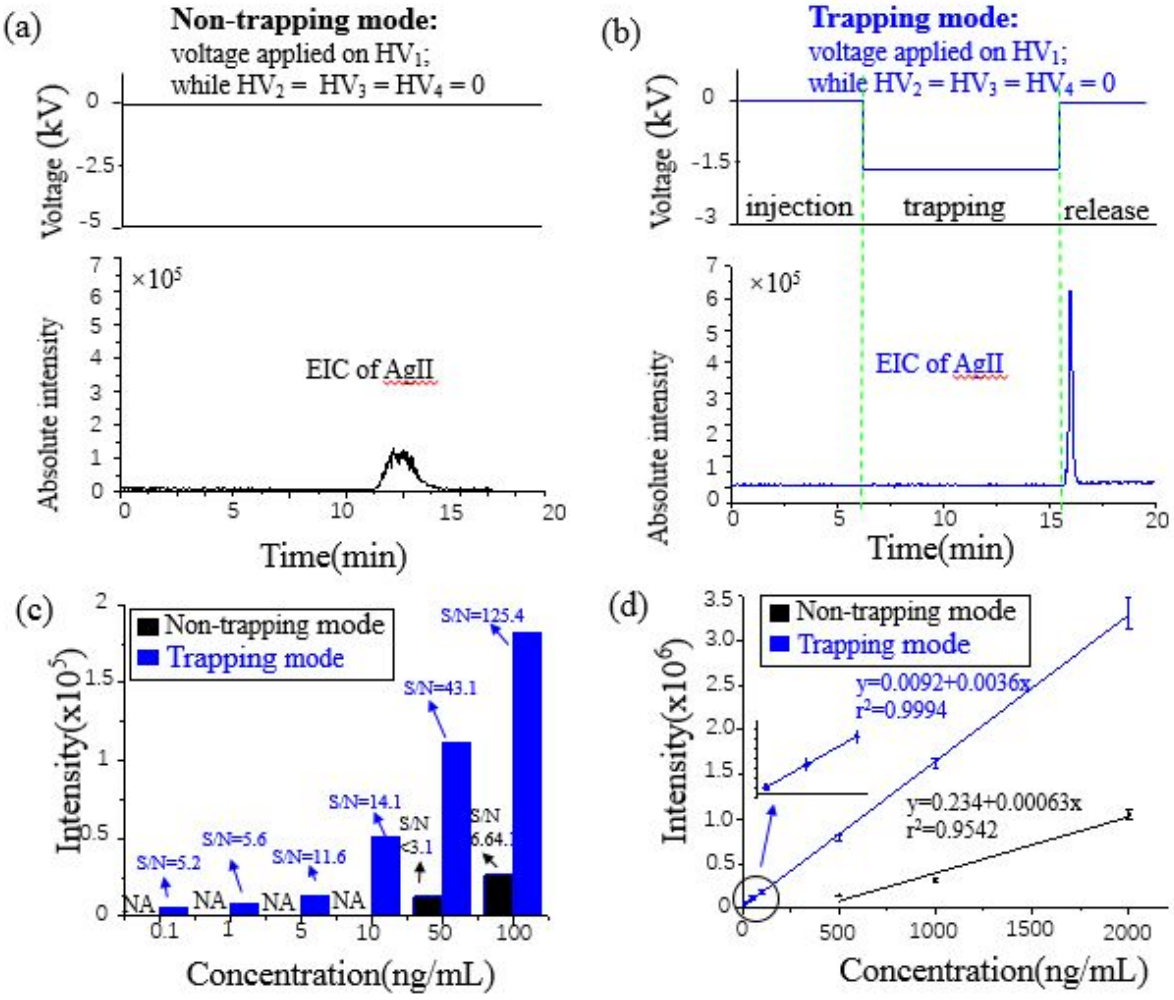

Figure S3. Trapping and accumulation feature of the liquid-phase ion trap. (a) EIC of 1 μg / mL Ag II in the non-trapping mode. (b) EIC of 1 μg / mL Ag II in the trapping mode. (c) S/N ratios of Ag II at different concentrations. (d) The linear of quantitation curves of Ag II using the trapping and non-trapping modes.

Ion loss rate characterization

Phenylalanine (500 ng/mL) sample was injected and trapped in the liquid-phase ion trap for different durations to test the ion loss rate. The EIC peak areas of

phenylalanine were calculated to calculate this ion loss rate. Ions might lose on the surface of the electrode, as well as the liquid channel cell wall due to the electroplating effect.

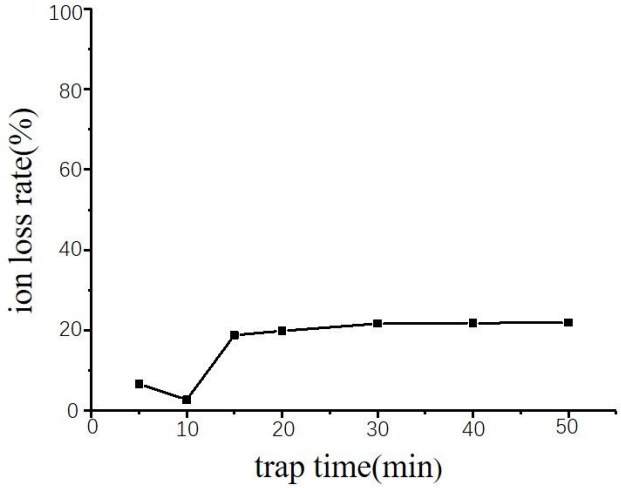

Figure S4. Ion loss rate of phenylalanine (500 ng/mL) with different ion trapping time.

Separation of a peptide mixture

The separation of a peptide mixture (Ag II and bradykinin) was performed in both simulation and experiments. In the ion motion simulation, different liquid flow rates and different voltage drop rates were tested. As shown in Figure S5, slower voltage drop could improve the ion separation, but induce broadened peaks. This is due to the stronger ion dispersion effects at slower voltage drops. While keeping the same voltage drop rate, slower liquid flow rate could help reduce the ion dispersion effect.

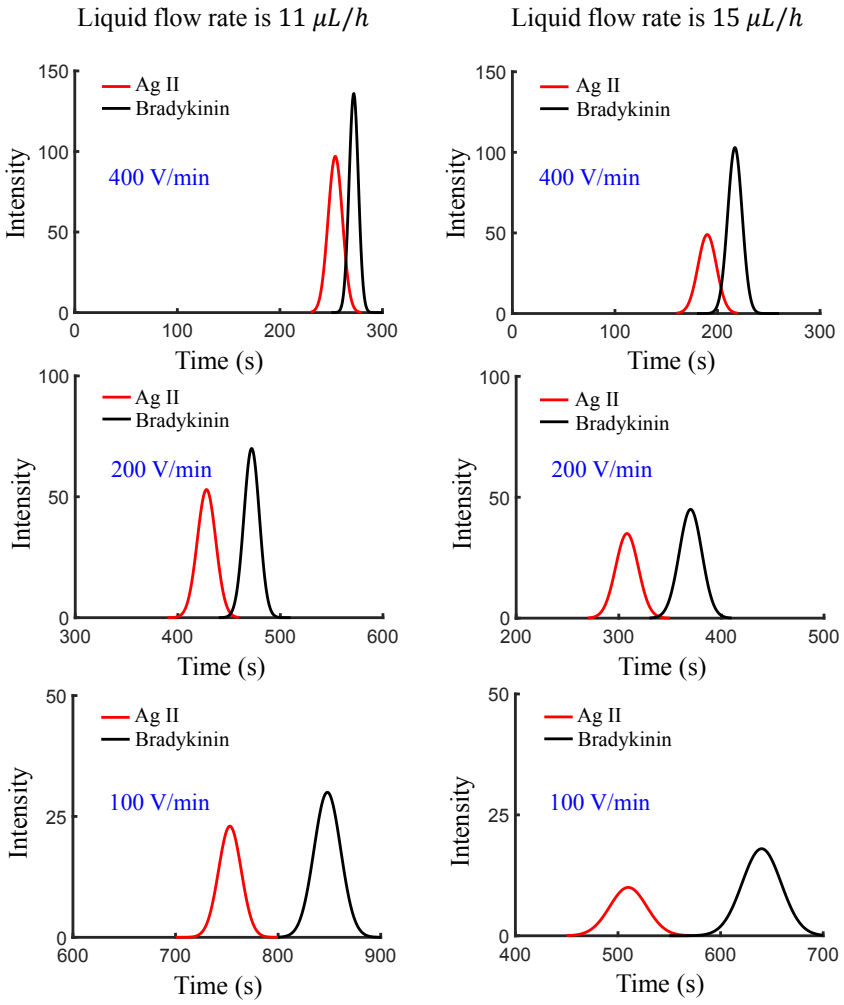

Figure S5. Simulated separation results of a mixture of Ag II and bradykinin at different buffer flow rates and voltage drop rates.

A mixture of Ag II (1 μg/mL) and bradykinin (1 μg/mL) were analyzed, and the flow rate of the buffer was set as 0.15 μL/min. A negative high voltage, -1.5 kV was applied on HV_1, with the rest electrodes grounded. After 10 minutes of continuous enrichment, the voltage applied on HV_1 was linearly decreased. Different voltage drops rates including 300 V/min, 150 V/min, 100 V/min were tested. As plotted in Figure S6, improved ion separation could be achieved with slower voltage drop. However, decreased ion intensity and broadened peaks were also observed, which are the results of increased ion dispersion within the Laminar flow.

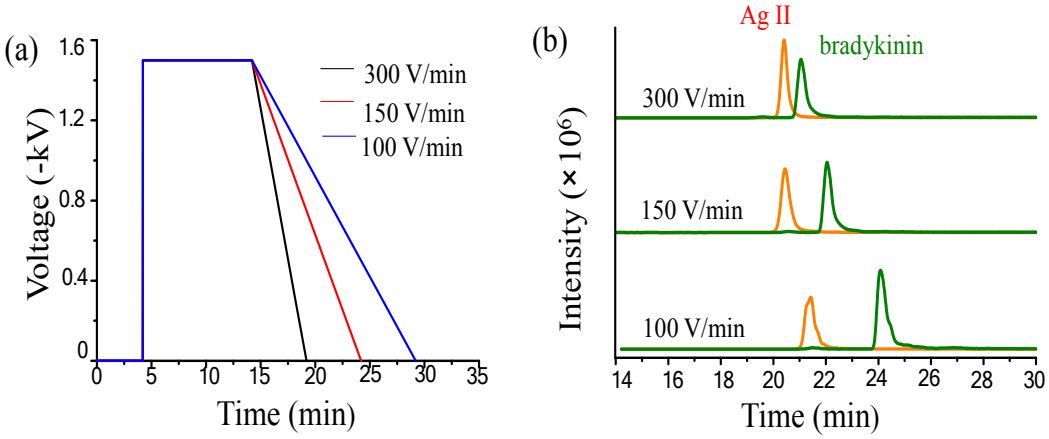

Figure S6. Peptide separation using the liquid-phase ion trap with linearly decreased separation voltage. (a) Different voltage waveforms of HV_1. (b) The corresponding peptide separation at different HV_1 gradients.

Isomeric peptide separation

The separation and sequential release of a pair of isomeric peptides were also demonstrated in this device. A micro valve (DIKMA. Beijing, China) was used as injection valve, a 20 μL quantitative loop was used in this experiment. A capillary with an inner diameter of 250 μm and an outer diameter (o.d.) of 1/16 inch was used as the liquid channel. The liquid channel from the six-way valve to the first micro T-connector was 20 cm long. The four micro T-connectors were connected by 5 cm capillaries. The front end of the capillary was grounded (close to the u-ESI side). Analytes were ionized by the u-ESI source directly and analyzed by the consequent mass spectrometer. A negative high voltage from 4000V was applied on the MS inlet, which provides the ionization voltage for the u-ESI source. The following MS parameters were used in the experiments: gas temperature 300 °C, gas flow rate 8.0 L/min, fragmentor: 80, mass scan range: 100−1000 m/z.

Then, the mixture of GRGDS (1 μg/mL) and GDSRG (1 μg/mL) was analyzed, and the flow rate of the buffer was set at 0.38 mL/h. HV_1 was set at –3.5kV, and the rest electrodes were grounded. HV_1 was tuned linearly from -3.5 kV to 0 V at a step of 50 V/12 s. The same method was applied to test unmixed peptide samples. Figure S7

showed the EIC spectra of m/z 491.22 for a mixture sample and for unmixed pure peptide samples. With the liquid-phase ion trap, the peptide isomers could be well separated. The retention time of GRGDS peak was earlier than that of GDSRG peak.

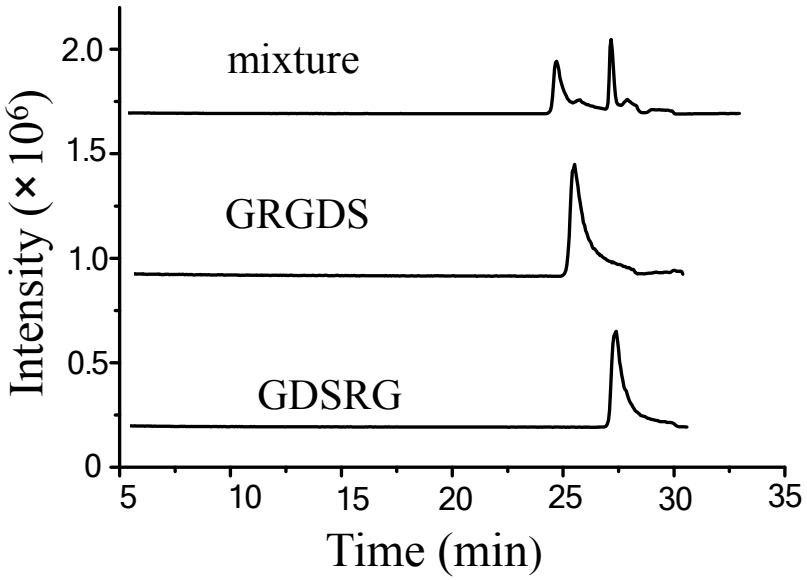

Figure S7. Separation of isomeric peptides by the liquid-phase ion trap.