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Improvement of MALDI-TOFMS Ion Source for Higher Resolving Power over Wider Mass Range

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1. Introduction

Delayed pulse extraction is commonly used as a method which compensates for the initial kinetic energy scattering to obtain higher resolving power of time of flight mass spectrometer (TOFMS) with matrix-assisted laser desorption/ionization (MALDI). However, the effective mass range of this method is limited and not wide enough. We have previously developed a new method which expands the effective range by dividing ions according to their masses before applying pulse voltage. In this study, we improved the method to further expand mass range by non-linear field.

2. Methods

2-1. Pre-extraction method

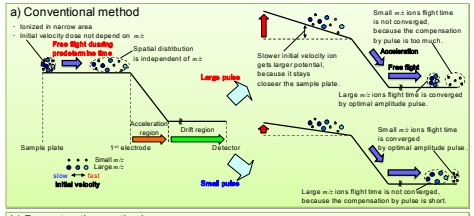

Figure 1 Extraction method

Figure 1 shows the schemes of a) conventional and that of b) pre-extraction delayed pulse method. The initial ion velocity is independent of the mass, which is a feature of MALDI. Therefore the spatial distribution during the delay time is also independent of the mass without the pre-extraction as in figure 1 a), and each mass needs to be supplied optimum energy by pulse field. That is, effective mass range by specific pulse is narrow. On the other hand, by the separation of pre-acceleration field, the effective mass range of pre-extraction method is wider (Figure 1 b).

2-2. Optimum potential distribution

Before the pulse voltage is applied, the electric field E_0 between sample plate and 1st electrode (extraction electrode) is constant. The potential $V_0(x)$ is expressed as

$$V_0(x) = V_s - E_0 x \quad (1)$$

where V_s is the initial sample voltage and x is the distance from sample plate surface. The flight time $t = 0$ is defined as the time when ions are generated on the sample plate surface. When the initial velocity is v_0, it may have a distribution from $v_0 - \Delta v_0$ to $v_0 + \Delta v_0$. Thus, the difference in kinetic energy ΔK between ions which have initial velocities $v_0 + \Delta v_0$ and $v_0 - \Delta v_0$ is

$$\Delta K = \frac{1}{2}m(v_0 + \Delta v_0)^2 - \frac{1}{2}m(v_0 - \Delta v_0)^2 = 2mv_0\Delta v_0 \quad (2)$$

where m is the ion mass.

When the pulse voltage is applied at $t = t_0$, ion's position and velocity are

$$x = v_0 t_0 + \frac{1}{2}\frac{qE_0}{m}t_0^2 \quad (3)$$

and

$$v = v_0 + \frac{qE_0}{m}t_0 \quad (4)$$

respectively, where q is the ion charge. Furthermore Eq. (3) gives mass-to-charge ratio m/q as

$$\frac{m}{q} = \frac{E_0 t_0^2}{2(x - v_0 t_0)}. \quad (5)$$

Here, the difference in distance $\pm\Delta x$ between the ions position of initial velocity v_0 and $v_0 \pm \Delta v_0$ is expressed as $\pm\Delta v_0 t_0$ from Eq. (3). In the case, the ion which has the initial velocity $v_0 \pm \Delta v_0$ obtains additional potential $V_p(x)$ at $t = t_0$, the difference in the potential ΔU is

$$\Delta U = -2\Delta x \times q\frac{d}{dx}V_p(x) = -2q\Delta v_0 t_0 \frac{d}{dx}V_p(x). \quad (6)$$

When ΔU compensates for ΔK, the equation would be

$$\frac{d}{dx}V_p(x) = -\frac{m}{q}\frac{v_0}{t_0} \quad (7)$$

from Eqs. (2) and (6), where $\Delta U = \Delta K$. And substituting Eq. (5) into Eq. (7) gives

$$\frac{d}{dx}V_p(x) = -\frac{E_0 v_0 t_0}{2}\frac{1}{x - v_0 t_0}. \quad (8)$$

So, after integrating Eq. (9), we have

$$V_p(x) = -\frac{E_0 v_0 t_0}{2}\ln(x - v_0 t_0) + V_c. \quad (9)$$

When the potential at $t = t_0$ defined $V_1(x)$, we can write it as

$$V_1(x) = V_0(x) + V_p(x) = V_s' - E_0\left\{x + \frac{v_0 t_0}{2}\ln(x - v_0 t_0)\right\} \quad (10)$$

from Eq. (9), where $V_s' = V_s + V_c$.

Eq. (10) does not include mass-to-charge ratio m/q. Consequently, by applying pulse voltage which satisfies Eq. (10), we can compensate any mass ion for initial kinetic energy difference. However it doesn't work for time focusing since ions fly at same velocity in the drift region. Though further compensation is required for the ideal time focusing, it is clear that the compensation is based on $V_1(x)$ and the form should be non-linear.

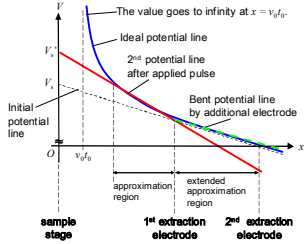

Figure 2 Ideal and approximate potential

For applying non-linear potential, we virtually added another extraction electrode (2nd extraction electrode).

By the 2nd electrode, approximation region for the ideal potential was computationally extended, as shown in Figure 2. As the result, we obtain wide mass range of high resolving power on TOFMS.

3. Results

To demonstrate our postulate, we compared the effective mass range of three methods by computer simulation and experimental data obtained from linear MALDI-TOFMS whose length and accelerator voltage were 1.2 meter and 18 kV, respectively.

3-1. Simulation Results

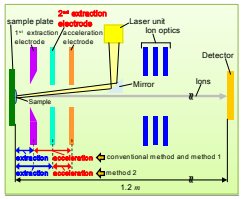

Figure 3 Schematic representation of linear TOF setup

Figure 3 shows the scheme of linear TOF ion source adopted non-linear field. By setting electrode parameters as in Table 1, the ion source can function as a) conventional method, b) pre-extraction method with linear potential distribution (method 1), and c) pre-extraction method with non-linear potential distribution (method 2).

Table 1 Parameters of each electrodes in simulations

	Sample plate			1st extraction electrode			2nd extraction electrode (kV)	acceleration electrode (V)
	Base (kV)	Pulse (V)	Delay (ns)	Base (kV)	Pulse (V)	Delay (ns)		
Conventional method	18.0	1200	600	18.66	-	-	5.0	0
Method 1	18.0	800	450	17.2	-	-	5.0	0
Method 2	18.0	1540	730	17.2	830	730	16.0	0

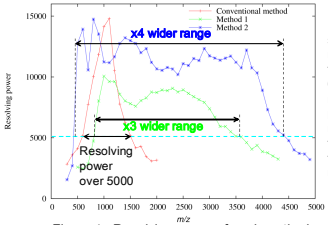

Figure 4 Resolving power of each method

Figure 4 shows simulation results of resolving power when the initial ion velocity is 600 ± 300 m/s. The mass ranges, resolving powers over 5000, of method 1 and 2 are 3 times and 4 times wider than conventional method, respectively.

3-2. Experimental Results

We measured MS spectra of 7-mix peptides and PMMA to evaluate these methods. Table 2 shows the parameters used in the measurements, mostly based on the simulation results from Table 1. Some of them were optimized by experiment.

Figure 5 shows an MS spectrum of 7-mix peptide and Figure 6 shows the peaks and resolving power of each method. It is clear that the effective mass ranges of method 1 and 2 are wider than the range of conventional method. ACTH7-38 isotopic peaks were separated when method 2 was used.

Figure 7 is an MS spectrum of PMMA peaks and Figure 8 shows the resolving power at each mass. In the case of method 2, the mass range over 3000 is 2.5 times wider than that of conventional method. This result proves that new method is effective to improve the mass range of higher resolving power.

Table 2 Parameters of each electrodes in experiments

	Sample plate			1st extraction electrode			2nd extraction electrode (kV)	acceleration electrode (V)
	Base (kV)	Pulse (V)	Delay (ns)	Base (kV)	Pulse (V)	Delay (ns)		
Conventional method	18.0	1430	730	18.66	-	-	4.7	0
Method 1	18.0	1050	400	17.5	-	-	6.0	0
Method 2	17.9	1750	790	17.0	1000	790	16.5	0

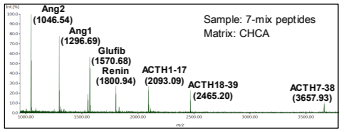

Figure 5 MS spectrum of 7-mix peptides

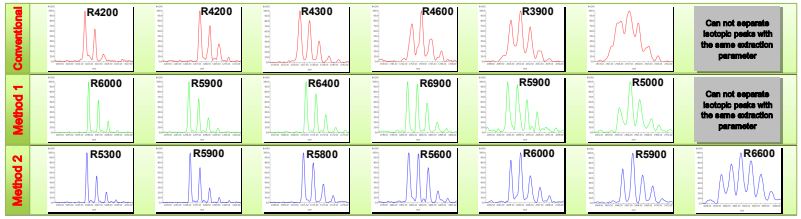

Figure 6 Peaks of each method

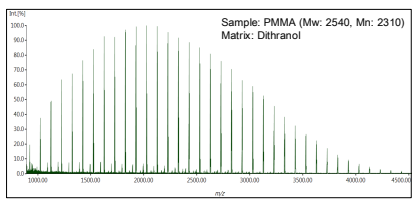

Figure 7 MS spectrum of Poly(methyl methacrylate) (PMMA)

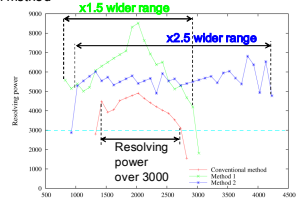

Figure 8 Resolving power of PMMA peaks with each method

4. Conclusions

- We developed a new ion source adopted non-linear field to improve the mass range of higher resolving power.
- In the simulation study, the mass range of new method is 4 times wider than that of conventional method.
- In the experimental study, the mass range of new method is 2.5 times wider than that of conventional method.

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