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Computational Assessment of Sustained Off-Resonance Irradiation (SORI) in a Cubic FTICR Ion-Trap

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Trajectories of an ion undergoing sustained off-resonance irradiation (SORI) in Fourier transform ion cyclotron resonance mass spectrometry (FTICR MS) were examined by means of computer simulations, which take account of non-uniform excitation and trapping electric fields within a cubic FTICR ion-trap. The equation of motion used for the simulations also contains a friction term proportional to the ionic velocity, reflecting a collisional damping of the motion (viscous drag model). The relationship between the initial position of the excited ion and the translational energy was explored; to give a practical index of the collision energy in SORI-collisional activation. The translational energy appears to be independent of the initial *z*-displacement of the ion. In contrast, the initial magnetron radius represented by the initial *x*-displacement is a sensitive factor for the translational energy. It is suggested that a diffusion of a trapped ion cloud in the course of a trapping may affect the precision of the collision energy in a controlled SORI-collisional activation. This trajectory simulation can provide a better insight into the energetic property of SORI than a conventional theoretical approach based on a statistical kinetics and a uniform electric field, and may be an effective tool to estimate an availability of collision energy range unless scattering of activated ions becomes a dominant process in the SORI dynamics.

1. Introduction

Peptide and protein sequencing in tandem mass spectrometry (MS/MS) has increased its significance in the field of bioscience, particularly, since the combination of mass spectrometry with advanced ionization techniques, such as electrospray ionization (ESI) or matrix assisted laser desorption ionization (MALDI). Metastable decomposition (MD) and collisionally activated dissociation (CAD) or collision induced dissociation (CID), which are key techniques of the MS/MS, provide a peptide fragmentation pattern which is particularly valuable for the structural analysis when structural modifications render inapplicable classical sequencing techniques.

However, MD derived by fast atom bombardment (FAB) or MALDI and low-energy CAD carried out in the collision cell of a triple quadrupole or hybrid instrument often yield fragment spectra including prominent fragment peaks formed *via* a rearrangement process involving loss of the C-terminal amino acid residue. A spectral peak position of the C-terminal rearrangement product is shifted from that of the simple cleavage fragment due to the retention of one of the carboxyl oxygens in the C-terminal residue.¹⁾ Figure 1 shows an example of a triple-quadrupole CAD product spectrum containing the C-terminal rearrangement product. The fact can confuse the interpretation of fragment spectra at routine measurements. An improved understanding of the rearrangement mechanism, including energetics, is required to facilitate sequencing of protonated peptides using the MS/MS method.

Fourier transform ion cyclotron resonance mass spectrometry (FTICR MS) is known as its outstanding high performance in a higher *m/z* range; *e.g.*, high sensitivity, ultrahigh resolving power and multistage tandem mass spectrometry (MS^{*n*}) capability.²⁾ In addition, its static ion-trapping manner is suitable for analyzing extended time-scale, slow ionic processes in gas-phase, such as rearrangement reactions. These unique features of FTICR MS allow sophisticated low-energy CAD experiments for peptide and polypeptide ions.^{3)–5)}

Among the low-energy CAD techniques in FTICR MS, sustained off-resonance irradiation (SORI) is based

Fig. 1. Product ions derived by low-energy CAD of bradykinin $[M+H]^+$, recorded by a Quattro tandem quadrupole instrument (Micromass, Manchester, UK; equipped with an electrospray interface and upgraded to Quattro II specifications). A prominent peak of *m/z* 906 was caused by the C-terminal rearrangement process. Argon gas was used as collision target. Experimental conditions were; analyte concentration: 10 pmol/ μ L; ESI injection flow rate: 3 μ L/min; collision target pressure: 1 Torr; collision energy: 30 eV. The measurement was carried out by using the facilities of the Michael Barber Centre for Mass Spectrometry in UMIST.

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on a trajectory of ions undergoing alternate acceleration and deceleration caused by the dipolar ICR excitation electric field of an off-resonance frequency.⁶⁾ The SORI technique is thought to achieve so extremely low and finely controllable collision energy of precursor ions that the infrared radiative multiphoton dissociation (IRMPD) experiment can be emulated. SORI-CAD is expected to reveal the energetics of the C-terminal rearrangement process of peptide ions. However, the characteristics of SORI have not been clearly elucidated yet, in particular, concerning the effects of the spatial inhomogeneity of the SORI electric field, which may affect the precision and selectivity of SORI-CAD. This article reports a computational study aiming at the assessment of the capability of SORI-CAD for tracing potential surfaces of extremely low-energy collisional activation processes, such as the rearrangement process of protonated peptides.

2. Theory

2.1 General expression of motion of an ion undergoing numerous ion/neutral collisions

An ion motion in an FTICR ion-trap can be treated with the classical electromagnetic dynamics as far as collisions between ions and neutrals can be ignored. In contrast the case of SORI-CAD, in which the ion/neutral collisions play an important role, must be treated with the statistical kinetics to take account of the collision effect. We can apply the same procedure to this problem as the Beauchamp's theory of collision-broadened ICR spectral line shapes.⁷⁾ His theory was based on the Boltzmann transport equation and obtained the equation of the "average" motion of ions undergoing a time-varying electric field $E(t)$ and a static magnetic field B :

$$\frac{\partial \bar{v}}{\partial t} = \frac{qE(t)}{m} + \frac{q\bar{v} \times B}{m} - \bar{\nu}_c \cdot \bar{v} \quad (1)$$

where $\bar{v}$ is the average ion velocity and $\bar{\nu}_c$ is the velocity average of the elastic collision frequency between the ions and the neutrals (for derivation of Eq. (1) see Appendix A).

Equation (1) is a general expression of ion motion in which a great number of ion/neutral collisions take place. The Beauchamp's statistical theory does not figure out a large deviation from the average velocity, thus assumes a collisional friction to be dominating over other collisional effects, such as a scattering. This theoretical model is called "viscous drag", and is particularly applicable to the case of a large $\bar{\nu}_c$. The motion of an ion was analyzed by using Eq. (1) throughout the present study.

2.2 Characteristics of SORI-CAD in spatially uniform electric and magnetic fields

The equation of motion Eq. (1) does not yet give a general solution in the analytical form. The simplest approximate solution is obtained by assuming that the electric and magnetic fields are uniform and intersect perpendicularly to each other.

$$B = Bk \quad (2)$$

$$E(t) = E_0 \sin(\omega_e t) i \quad (3)$$

where i, j , and k are unit vectors parallel to x -, y -, and z -axes, respectively. The linearly polarized electric field $E(t)$ can be resolved into two circularly polarized com-

ponents rotating in the opposite directions:

$$\begin{aligned} E(t) &= E_1(t) + E_2(t) \\ \begin{cases} E_1(t) = \{E_0 \sin(\omega_e t) i + E_0 \cos(\omega_e t) j\} / 2 \\ E_2(t) = \{E_0 \sin(\omega_e t) i - E_0 \cos(\omega_e t) j\} / 2 \end{cases} \end{aligned} \quad (4)$$

Only the component rotating in the same direction as the ion, $E_1(t)$, can accelerate the ion. Hence the electric field acting on the ion can be approximated by ignoring $E_2(t)$ component. Then Eq. (1) is resolved into x - and y -components:

$$\begin{cases} \dot{v}_x = \frac{qE_0}{2m} \sin(\omega_e t) + \omega_c v_y - \bar{\nu}_c v_x \\ \dot{v}_y = \frac{qE_0}{2m} \cos(\omega_e t) - \omega_c v_x - \bar{\nu}_c v_y \end{cases} \quad (5)$$

where v_x and v_y are x - and y -component of the average ion velocity $\bar{v}$, and $\omega_c = qB/m$ is the cyclotron angular frequency of the ion. The general solution of Eq. (5) is given by

$$\begin{cases} v_x = \exp(-\bar{\nu}_c t) \{c_1 \sin(\omega_c t) + c_2 \cos(\omega_c t)\} \\ \quad + \frac{qE_0}{2m} \frac{\bar{\nu}_c \sin(\omega_e t) + (\omega_c - \omega_e) \cos(\omega_e t)}{(\omega_c - \omega_e)^2 + \bar{\nu}_c^2} \\ v_y = \exp(-\bar{\nu}_c t) \{c_1 \cos(\omega_c t) - c_2 \sin(\omega_c t)\} \\ \quad + \frac{qE_0}{2m} \frac{\bar{\nu}_c \cos(\omega_e t) - (\omega_c - \omega_e) \sin(\omega_e t)}{(\omega_c - \omega_e)^2 + \bar{\nu}_c^2} \end{cases} \quad (6)$$

The coefficients c_1 and c_2 are determined from the initial condition of the ion motion.

Figure 2 shows the time plots of the translational energy $K = m(\bar{v}_x^2 + \bar{v}_y^2)/2$ of a bradykinin $[M+H]^+$ ion (m/z 1060) during a SORI-CAD process calculated from Eq. (6) for several collision rates. In the zero-pressure limit (i.e., no ion/neutral collisions take place), K oscillates due to the acceleration-deceleration cycle of SORI. With increase of the collision rate $\bar{\nu}_c$, the oscillation of K damps quickly and converges into a smaller value.

Because the time constant for a decay of K is much smaller than a typical SORI-CAD period (> 100 ms), the oscillating first terms on the right-hand side of Eq. (6) can be neglected in a long-time limit.

$$\begin{cases} v_x = \frac{qE_0}{2m} \frac{\bar{\nu}_c \sin(\omega_e t) + (\omega_c - \omega_e) \cos(\omega_e t)}{(\omega_c - \omega_e)^2 + \bar{\nu}_c^2} \\ v_y = \frac{qE_0}{2m} \frac{\bar{\nu}_c \cos(\omega_e t) - (\omega_c - \omega_e) \sin(\omega_e t)}{(\omega_c - \omega_e)^2 + \bar{\nu}_c^2} \end{cases} \quad (7)$$

Hence the terminal translational energy of the ion is given by

Fig. 2. Time plots of the translational energy of a bradykinin $[M+H]^+$ ion (m/z 1060) as a precursor ion of SORI-CAD ($B = 5$ T, $E_0 = 19.7$ V/m, $\Delta\omega = 800$ rad/s), calculated from Eq. (6).

$$\tilde{K} = \frac{q^2 E_0^2}{8m \{(\omega_c - \omega_e)^2 + \bar{\nu}_c^2\}} \quad (8)$$

It should be noted that Eq. (8) in the limit of $\bar{\nu}_c \rightarrow 0$ is not equal to the average translational energy in the zero-pressure limit (see Appendix B).

Figure 3 shows the variation of $\tilde{K}$ as a function of the collision rate $\bar{\nu}_c$ and the excitation frequency offset $\Delta\omega = \omega_c - \omega_e$. The terminal translational energy can be decreased by increasing either $\bar{\nu}_c$ or $\Delta\omega$. To increase $\bar{\nu}_c$, however, we must introduce the collision gas of a higher pressure, which can reduce the FTICR MS performance such as the ultra-high resolving power. Thus increasing $\Delta\omega$ might be recommendable approach to a lower collision energy. Nevertheless, we will be faced on another problem in the case of a larger $\Delta\omega$. Figure 4 shows the selectivity of SORI-collisional activation as a function of $\bar{\nu}_c$ and $\Delta\omega$. The vertical axis represents an index of the selectivity which is evaluated by $1 - (\tilde{K} \text{ of } b_8 + \text{H}_2\text{O}) / (\tilde{K} \text{ of } [\text{M} + \text{H}]^+)$, where $[\text{M} + \text{H}]^+$ and $b_8 + \text{H}_2\text{O}$ denote the protonated molecule (m/z 1060) and the C-terminal rearrangement product ion (m/z 904) of bradykinin. A higher value of the index means a better selectivity for the activation of the precursor. At a larger $\Delta\omega$ the SORI electric field can activate not only the precursor but also the product ion $b_8 + \text{H}_2\text{O}$. To avoid an unexpected activation, the value of $\Delta\omega$ must be kept in $< 2 \times 10^4$ rad/s. Besides, a higher magnetic field strength should have an advantage in the selectivity of SORI-CAD.

ity of SORI-CAD.

By decomposing the electric field into the two counter-rotating components and discarding the one with a sense of rotation opposite to that of the ion, the analytical treatment of Eq. (1) becomes much easy. The quantitative aspect of this approximating approach, however, has not been discussed far enough. Hearn *et al.*⁸⁾ obtained the “exact” solution of the equation of motion of an ion in perpendicularly intersecting uniform electric and magnetic fields, by using the zero-pressure limit, but not applying the electric field decomposition. Their argument did not make clear the difference between the conventional and the exact solutions. Without the electric field decomposition approach, Eq. (5) can be rewritten as

$$\begin{cases} \dot{v}_x = \frac{qE_0}{m} \sin(\omega_e t) + \omega_c v_y - \bar{\nu}_c v_x \\ \dot{v}_y = -\omega_c v_x - \bar{\nu}_c v_y \end{cases} \quad (9)$$

This equation can be solved as

$$\begin{cases} v_x = \exp(-\bar{\nu}_c t) \{c_1 \sin(\omega_c t) + c_2 \cos(\omega_c t) \\ + \frac{qE_0}{m} \frac{(\omega_c^2 + \omega_e^2 + \bar{\nu}_c^2) \bar{\nu}_c \sin(\omega_c t) + (\omega_c^2 - \omega_e^2 - \bar{\nu}_c^2) \omega_e \cos(\omega_c t)}{\{(\omega_c - \omega_e)^2 + \bar{\nu}_c^2\} \{(\omega_c + \omega_e)^2 + \bar{\nu}_c^2\}} \\ v_y = \exp(-\bar{\nu}_c t) \{c_1 \cos(\omega_c t) - c_2 \sin(\omega_c t) \\ - \frac{qE_0}{m} \frac{2\omega_c \omega_e \bar{\nu}_c \cos(\omega_c t) - (\omega_c^2 - \omega_e^2 + \bar{\nu}_c^2) \omega_e \sin(\omega_c t)}{\{(\omega_c - \omega_e)^2 + \bar{\nu}_c^2\} \{(\omega_c + \omega_e)^2 + \bar{\nu}_c^2\}} \end{cases} \quad (10)$$

The above exact solution gives a damping translational energy, but which will not converge into a constant value at $t \rightarrow \infty$. The average translational energy in a long-time limit is given by

$$\bar{K} = \frac{q^2 E_0^2}{4m} \frac{\omega_c^2 + \omega_e^2 + \bar{\nu}_c^2}{\{(\omega_c - \omega_e)^2 + \bar{\nu}_c^2\} \{(\omega_c + \omega_e)^2 + \bar{\nu}_c^2\}} \quad (11)$$

A comparison between $\tilde{K}$ and the above $\bar{K}$ shows an excellent agreement. The deviation of $\tilde{K}$ from $\bar{K}$ (evaluated by $|1 - \tilde{K}/\bar{K}|$) is restrained less than 5% for the present system in a range of $\bar{\nu}_c$ and $\Delta\omega$ (see Fig. 5). It can be shown that Eq. (11) reduces to the identical form with Eq. (8) by assuming $\omega_c \approx \omega_e \gg \bar{\nu}_c$ and omitting the terms of $(\bar{\nu}_c/\omega_c)^2$ and $(\Delta\omega/\omega_c)^2$. The electric field decomposition approach might be a reasonable approximation for translational energies of SORI precursors. Although it is rarely demanded, translational energies of products in a SORI electric field can be estimated by Eq. (11) with a better accuracy than the electric field decomposition approach due to a larger $\Delta\omega$.

Fig. 3. The convergent value of $\tilde{K}$ (evaluated by Eq. (8)) of a bradykinin $[\text{M} + \text{H}]^+$ ion as a function of $\Delta\omega$ and $\bar{\nu}_c$ ($B = 5$ T, $E_0 = 19.7$ V/m).

Fig. 4. Variation of the selectivity of SORI-CAD for bradykinin $[\text{M} + \text{H}]^+$ and $b_8 + \text{H}_2\text{O}$ ions as a function of $\Delta\omega$ and $\bar{\nu}_c$ ($B = 5$ T, $E_0 = 19.7$ V/m), calculated from Eq. (8).

Fig. 5. Comparison between $\tilde{K}$ (evaluated by Eq. (8)) and $\bar{K}$ (evaluated by Eq. (11)) for a bradykinin $[\text{M} + \text{H}]^+$ ion as a function of $\Delta\omega$ and $\bar{\nu}_c$ ($B = 5$ T, $E_0 = 19.7$ V/m).

The present theoretical treatment ignores an effect of the resistive heating which occurs in an FTICR detection circuit. Comisarow⁹⁾ derived the time constant for a decay of cyclotron radius due to the resistive heating:

$$T_R = \frac{2Rmd^2(1/R^2 + \omega_c^2 C^2)}{Nq^2} \quad (12)$$

where R is the shunt resistance; C is the shunt capacitance; d is the detection plate spacing; and N is the number of ions. Applying a typical conditions ($R=1$ M Ω , $C=100$ pF, $d=5.08$ cm and $N=10^6$) for the present system, T_R can be evaluated as *ca.* 700 s, which is too long comparing with a timescale of SORI-CAD. So far as the present system, the resistive heating may not be effective. However, this may become more important in another case of, for example, a smaller m or a larger N .

2.3 Simulation of SORI-CAD in a cubic ion-trap

In order to take account of non-uniform electric fields in a cubic ion-trap,¹⁰⁻¹³⁾ Eq. (1) was treated with a numerical integration.

The average elastic collision frequency $\bar{\nu}_c$ might be inversely proportional to the mean free time of the ions. Hence

$$\bar{\nu}_c = \bar{v}/\lambda \quad (13)$$

where λ denotes the mean free path of the ions and is estimated from

$$\lambda = (\pi\sigma^2 N)^{-1} \quad (14)$$

where σ is the effective collision diameter between the ions and the neutral targets, and N is the neutral target density. In the case of a slow collision (≤ 5 eV) between a protonated alkylamine (m/z 102) and helium, σ is estimated as $\sim 10^{-9}$ m.¹⁴⁾ Assuming σ between a protonated bradykinin and argon to be ten times larger than the case of alkylamine and helium, $\bar{\nu}_c \approx 10^4$ s⁻¹ was estimated for an argon pressure of $\sim 10^{-6}$ Torr. This value of $\bar{\nu}_c$ was applied to Eq. (1) throughout the present study.

Using a Cartesian coordinate system whose origin is laid on the center of a cubic trap, the boundary conditions for a SORI event may be expressed as

$$\begin{aligned} \phi(a/2, y, z) &= \phi(-a/2, y, z) = 0 \\ \phi(x, a/2, z) &= -\phi(x, -a/2, z) = (V_{e0}/2) \sin \omega_e t \\ \phi(x, y, a/2) &= \phi(x, y, -a/2) = V_i \end{aligned} \quad (15)$$

where a denotes the edge length of the cubic trap. V_i and V_{e0} indicate the trapping potential and the peak-to-peak amplitude of the excitation voltage, respectively. Under the boundary conditions of Eq. (15), the SORI electric field acting on an ion can be evaluated from the following equations¹⁵⁾:

$$\begin{aligned} E_x &= \frac{16}{\pi a} \sum_{n=0}^{\infty} \sum_{m=0}^{\infty} \frac{\sin \{(2n+1)\pi x/a\}}{(2m+1) \sinh \{\pi \sqrt{(2n+1)^2 + (2m+1)^2}\}} \\ &\times \left(V_i \cos \{(2m+1)\pi y/a\} \right. \\ &\times \left[\sinh \left\{ \left(\frac{z}{a} - 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right. \\ &\left. \left. - \sinh \left\{ \left(\frac{z}{a} + 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right] \right. \\ &+ V_{e0} \sin \omega_e t \cos \{(2m+1)\pi z/a\} \\ &\times \left[\sinh \left\{ \left(\frac{y}{a} + 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right. \\ &\left. \left. + \sinh \left\{ \left(\frac{y}{a} - 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right] \right) \end{aligned} \quad (16)$$

$$\begin{aligned} E_y &= \frac{16}{\pi a} \sum_{n=0}^{\infty} \sum_{m=0}^{\infty} \frac{\cos \{(2n+1)\pi x/a\}}{(2n+1) \sinh \{\pi \sqrt{(2n+1)^2 + (2m+1)^2}\}} \\ &\times \left(V_i \sin \{(2m+1)\pi y/a\} \right. \\ &\times \left[\sinh \left\{ \left(\frac{z}{a} + 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right. \\ &\left. \left. - \sinh \left\{ \left(\frac{z}{a} - 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right] \right. \\ &- \frac{\sqrt{(2n+1)^2 + (2m+1)^2}}{2m+1} V_{e0} \sin \omega_e t \cos \{(2m+1)\pi z/a\} \\ &\times \left[\cosh \left\{ \left(\frac{y}{a} - 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right. \\ &\left. \left. + \cosh \left\{ \left(\frac{y}{a} + 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right] \right) \end{aligned} \quad (17)$$

$$\begin{aligned} E_z &= \frac{16}{\pi a} \sum_{n=0}^{\infty} \sum_{m=0}^{\infty} \frac{\cos \{(2n+1)\pi x/a\}}{(2n+1) \sinh \{\pi \sqrt{(2n+1)^2 + (2m+1)^2}\}} \\ &\times \left(\frac{\sqrt{(2n+1)^2 + (2m+1)^2}}{2m+1} V_i \cos \{(2m+1)\pi y/a\} \right. \\ &\times \left[\cosh \left\{ \left(\frac{z}{a} - 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right. \\ &\left. \left. - \cosh \left\{ \left(\frac{z}{a} + 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right] \right. \\ &+ V_{e0} \sin \omega_e t \sin \{(2m+1)\pi z/a\} \\ &\times \left[\sinh \left\{ \left(\frac{y}{a} + 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right. \\ &\left. \left. + \sinh \left\{ \left(\frac{y}{a} - 0.5 \right) \pi \sqrt{(2n+1)^2 + (2m+1)^2} \right\} \right] \right) \end{aligned} \quad (18)$$

The sums of the infinite series were truncated at the term which was less than 1×10^3 V/m for the practical computation. An evaluated instantaneous value of the SORI electric field was substituted into Eq. (1), then the equation of motion was integrated by using fourth order Runge-Kutta-Gill method. The computational time increment of the integration was determined as 5×10^{-9} s from the balance between the accuracy and the calculation time.

Other parameters used for the simulations are: $B=5$ T; $a=5.08$ cm; $\omega_e=4.5 \times 10^5$ rad/s ($\Delta\omega \approx 900$ rad/s). Bradykinin $[M+H]^+$ and b_8+H_2O were used as model ions. The initial velocity of the ions is (70, 70, 0) m/s, whose magnitude corresponds to the thermal velocity of these ions at *ca.* 400 K.

3. Results and Discussion

It is clear from Eqs. (16)–(18) that the electric field in the ion-trap depends on a position. Ions with a large initial displacement from the center of the ion-trap may experience a serious inhomogeneity of the excitation electric field. Xiang and Marshall reported a simulation study which illustrates the effect of ion initial z -position on the ion coherence, the induced signal and the radial or z -ejection.¹⁶⁾ Similarly, the initial position (x_0, y_0, z_0) of the activated ion may be the primary “unpredictable” factor for SORI-CAD events. In the present study trajectory simulations were carried out for several sets of the initial ion position ($x_0, 0, z_0$) and the excitation voltage V_{e0} . The following two types of K values were monitored as the collision energy during a SORI-CAD process: the maximum value $K_{\max}$ and the final value K_{fin} after 20 ms of SORI-CAD. The later may roughly reflect the equilibrium condition of SORI-CAD; however, the internal energy deposition will occur also

Fig. 6. (a) The final value and (b) the maximum value of translational energy K of a bradykinin $[M+H]^+$ ion undergoing a SORI-CAD process ($\bar{\nu}_c = 1 \times 10^4 \text{ s}^{-1}$, $\omega_c = 4.5 \times 10^7 \text{ rad/s}$) in 20 ms, for various sets of excitation voltage V_{e0} and initial ion location z_0 ($x_0 = 0.01 \text{ mm}$).

Fig. 7. (a) The final value and (b) the maximum value of translational energy K of a bradykinin $[M+H]^+$ ion undergoing the same SORI-CAD process as Fig. 6, for various sets of V_{e0} and x_0 ($z_0 = 0.01 \text{ mm}$).

during the pre-equilibrium period in which the oscillation of K is damping toward the final value. Therefore K_{max} will be informative to estimate the maximum internal energy deposit in SORI-CAD.

Figure 6(a) shows K_{max} of the $[M+H]^+$ ion as a function of V_{e0} and z_0 for a constant trapping potential; $V_t = 4 \text{ V}$. Despite the inhomogeneous electric field in the ion-trap, K_{max} appears not to be sensitive to z_0 . Besides, we found a rather better linearity between V_{e0} and K_{max} than that of an equivalent simulation for an on-resonance excitation without collisions (result not shown). The appearance of K_{fin} , shown in Fig. 6(b) is almost the same as that of K_{max} . This simulation result suggests that the collision energy could be well-defined by SORI, even if the precursor ions initially distributed over an extended region along the z -axis of the ion-trap.

As regards x_0 , which was employed to represent the initial magnetron radius, both K_{max} and K_{fin} are sensitive to the initial displacement (see Figs. 7(a) and (b)). The relationship between V_{e0} and K_{fin} can not be assumed to be linear any more, and becomes significantly complicated in a region of large x_0 . It is suggested that a collision energy of a precursor ion in a SORI event will vary with its magnetron radius. Hence the collision energy may not be controlled precisely if the ion cloud is not axialized before the SORI event. Previous theoretical studies pointed out that a shape of a trapped ion cloud may evolve from an initial “rod” form parallel to the cell axis into an ellipsoid form with the course of the trapping period, due to the effects of

Coulomb repulsion and ion/neutral momentum-transfer collisions.¹⁷⁾ A consequential broaden distribution of magnetron radii may affect a precise adjustment of collision energy in a SORI-collisional activation event, especially for an extremely low energy activation process. Although a spatial distribution of trapped ions can be controlled by the quadrupolar axialization,^{18–20)} other non-collisional cooling methods^{21), 22)} will be favorable treatments prior to SORI-CAD, because they can avoid an unnecessary collisional activation which accompanies the quadrupolar axialization.^{23), 24)}

It is found that the K_{max} values are one or two order of magnitude larger than the K_{fin} values. The internal energy deposition into the precursor ion per collision will be, however, much smaller than the K_{max} values. Previous works have shown that a higher energy collision renders a lower rate of the internal energy deposition.²⁵⁾ In the limit of an infinite number of collisions, which is thought to be an adequate approximation of SORI-CAD processes,⁶⁾ the internal energy deposition might be dominated by the terminal K value. The mechanism of internal depositing is an elusive problem of CAD, and may depend on molecular structures of individual ions. Further quantitative discussion will exceed the scope of this article, and may require another computational approach, such as a Monte Carlo simulation.

Figure 8 shows K_{max} of the $b_8 + \text{H}_2\text{O}$ ion during the SORI-CAD for $[M+H]^+$. The SORI-CAD can accelerate also the product ion up to a non-negligible translational energy. Because magnetron radii of CAD products are generally larger than that of the precursor,²⁶⁾ the

Fig. 8. The maximum K value of a bradykinin b_8 -H₂O ion undergoing the same SORI-CAD process as Fig. 6, for various sets of (a) V_{e0} and z_0 ($x_0 = 0.01$ mm) and of (b) V_{e0} and x_0 ($z_0 = 0.01$ mm).

x_0 -dependency of $K_{\max}$ of b_8 -H₂O may severely affect the selectivity of SORI-CAD in the case of a higher magnitude of the SORI electric field is applied for trapped ions.

4. Conclusion

The present simulation results illustrated the capability and potential problems of an energetics-oriented SORI-CAD experiment. Although SORI can achieve sub-electronvolt collision energies which are necessary to investigate the C-terminal rearrangement of protonated peptides, precise collision energy adjustment may be hampered by large magnetron radii of precursor ions. The following precautions may be useful to those who make use of SORI-CAD for obtaining breakdown onsets precisely; i) minimizing the post-transfer “cooling” period followed by the SORI-CAD event to prevent a magnetron expansion of the trapped ion cloud. If this is not amenable, then ii) axializing the SORI precursor ions by preferably using non-collisional axialization methods. Tandem MS incorporating low-energy collisional activation techniques is being proved to be promising tool to discover non-covalent interactions determining molecular conformation and supra-molecular architecture in biological systems. This situation will be accelerated by extended uses of SORI-CAD.

Finally, the proposed simulation program code can provide a better insight into the energetic property of SORI by comparison with a conventional approach based on a statistical kinetics and a uniform electric field, and may be useful to estimate an available colli-

sion energy unless scattering of activated ions becomes dominant. Because the majority of lost ions in SORI-CAD experiments is attributable to scattering, the simulation must be much improved by taking the scattering effect account in. A Monte Carlo simulation code is a possible solution for this purpose, and the preliminary work is being undertaken.²⁷⁾

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Appendix A. Derivation of the Equation of the Ion Motion

In 1967, Beauchamp developed a theory of collision-broadened spectral line shapes for CW-ICR mass spectrometry.⁷⁾ Although there was no concept directly connecting with SORI in these days, his theory can be adapted to express the SORI ion dynamics.

The theory treated the ion dynamics as the Boltzmann transport equation:

$$\frac{\partial}{\partial t} [n \langle \chi(v) \rangle_{AV}] = \frac{qn}{m} \left\langle [E(t) + v \times B] \frac{\partial \chi(v)}{\partial v} \right\rangle_{AV} - \int [\chi(v') - \chi(v)] f(v) F(V) |v - V| b db d\epsilon d\epsilon dV \quad (19)$$

where n , v , q , m , and $f(v)$ denote the number density, velocity, charge, mass, and velocity distribution function of the ions, respectively. The neutrals have the velocity V and the velocity distribution function $F(V)$. A time-varying electric field $E(t)$ and a static magnetic field B act on the ions. The scattering parameters are b , the initial impact parameter and ϵ , the scattering azimuth. Elastic collisions may change the ion velocity from v to v' . Equation (19) shows the rate of change of $\chi(v)$ which is an arbitrary function of the ion velocity. The equation of the ion motion involving ion/neutral collisions can be derived from Eq. (19) by setting $\chi(v) = v$.

$$\frac{\partial \bar{v}}{\partial t} = \frac{qE(t)}{m} + \frac{q\bar{v} \times B}{m} + \left(\frac{\partial v}{\partial t} \right)_{\text{coll}} \quad (20)$$

where $\bar{v}$ is the average ion velocity. The last term on the right hand side of Eq. (20) gives the collision effect.

$$\begin{aligned} \left(\frac{\partial v}{\partial t} \right)_{\text{coll}} &= \frac{1}{n} \int (v' - v) f(v) F(V) |v - V| b db d\epsilon d\epsilon dV \\ &= - \frac{2\pi N M}{n(m+M)} \int f(v) F(V) v (1 - \cos \theta) |v - V| b db d\epsilon dV \end{aligned} \quad (21)$$

where M is the neutral mass and θ is the scattering angle. The elastic collision frequency ν_c can be written by

$$\nu_c = \frac{2\pi N M}{m+M} \int (1 - \cos \theta) b db \quad (22)$$

where N is the number density of the neutrals. Hence Eq. (21) becomes

$$\begin{aligned}\left(\frac{\partial v}{\partial t}\right)_{\text{coll}} &= -\frac{1}{nN} \int v_c v f(v) F(V) dv dV \\ &= -\bar{v}_c \bar{v} \\ &\approx -\bar{v}_c \cdot \bar{v}\end{aligned}\quad (23)$$

where $\bar{v}_c$ is the velocity average of v_c . The last approximation can be applied unless v_c is strongly dependent on the velocity v and V . Then Eq. (20) is rewritten as the accessible form:

$$\frac{\partial \bar{v}}{\partial t} = \frac{qE(t)}{m} + \frac{q\bar{v} \times B}{m} - \bar{v}_c \cdot \bar{v} \quad (1)$$

Appendix B. The Average Translational Energy in the Zero-Pressure Limit

The average translational energy of an ion undergoing a SORI electric field in the zero-pressure limit, $\bar{K}_0$, has been expressed in several articles.^{4), 6), 28)} Although $\bar{K}_0$ is the simplest approximation of a SORI activation energy, we found an inconsistency and some errata among these expressions. Therefore it would be useful for readers to indicate the correct form with its derivation.

Substituting $\bar{v}_c = 0$ and assuming the initial velocity of the ion to be negligible, Eq. (6) reduces to

$$\begin{cases} v_x = -\frac{qE_0 \sin\{(\omega_c - \omega_e)t/2\} \cos\{(\omega_c + \omega_e)t/2\}}{m(\omega_c - \omega_e)} \\ v_y = \frac{qE_0 \sin\{(\omega_c - \omega_e)t/2\} \sin\{(\omega_c + \omega_e)t/2\}}{m(\omega_c - \omega_e)} \end{cases} \quad (24)$$

Hence the time-varying translational energy in the zero-pressure limit becomes

$$K_0 = \frac{q^2 E_0^2 \sin^2\{(\omega_c - \omega_e)t/2\}}{2m(\omega_c - \omega_e)^2} \quad (25)$$

Averaging over one period gives

$$\begin{aligned}\bar{K}_0 &= \frac{\omega_c - \omega_e}{2\pi} \int_0^{2\pi/(\omega_c - \omega_e)} K dt \\ &= \frac{q^2 E_0^2}{4m(\omega_c - \omega_e)^2}\end{aligned}\quad (26)$$

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