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Desorption Electrospray Ionization: Achieving Rapid Sampling Rates

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The sampling rate and imaging capabilities of desorption electrospray ionization (DESI) are examined using a rotating sample platform combined with Hadamard transform time-of-flight mass spectrometry (HTTOFMS), a multiplexed time-of-flight technique that allows for millisecond acquisition of full mass-to-charge ratio scans. DESI-compatible dyes are used to produce spatially defined sample patterns on poly(methyl methacrylate) discs. Control of disk rotation rate sets the residence time of the sample spots in the DESI plume, and thus the sampling rate. Surface patterns of alternating analytes are spectrally resolved up to 80 samples/s and single-analyte spots up to 50 samples/s. The rapid movement of the surface under the DESI plume allows for high DESI solution flow rates without blurring the chemical information on the surface. Data from multiple rotations can be additively combined, generating a chemical image of the surface with improved signal-to-noise characteristics. This multipass data enables analysis of the rising and falling edges of the analyte signal, placing a lower limit on both the temporal resolution of DESI and the maximum achievable sampling rate. Multipass analysis is proposed as a method for DESI surface imaging.

Mass spectrometry (MS) is a powerful analytical tool both for the quantity of chemical and structural information it yields and for the wide array of analytes amenable to analysis. However, like all analytical techniques, MS is not absolutely general. One requirement for MS analysis is that the analyte be converted into gas-phase ions without unpredictably changing its structure. Generation of gaseous analyte ions can be accomplished through a variety of methods, but if the analyte of interest cannot be ionized, another technique must be used for analysis. Thus, it is the invention of new ion sources that leads to the evolution of the field of MS by expanding the classes of analytes that can be analyzed or by decreasing the sample preparation needed to study a class of molecules. Electrospray ionization (ESI) and matrix-assisted laser desorption ionization (MALDI) were two such innovations: they enabled the study of large biomolecules that were previously very difficult to convert into gas-phase ions. The development of ESI and MALDI also changed the direction of instrumentation development, driving the improvements in resolution and mass accuracy that were required to carefully evaluate larger molecules. In addition, the development of MALDI caused resurgence in time-of-flight mass spectrometry (TOFMS), due to the shared pulsed nature and efficient coupling of both techniques. However, despite their enormous capabilities, ESI and MALDI still regularly require substantial effort in sample preparation, usually involving a chromatographic step to separate samples from their native matrixes.

Recently, many new atmospheric pressure ionization sources have been introduced which offer simple ways to ionize amenable analytes while substantially minimizing or eliminating sample preparation. Desorption electrospray ionization (DESI), introduced by Cooks' group,[1] and direct analysis in real time (DART), introduced by Cody et al.,[2] were two of the first of this new generation of atmospheric pressure ionization sources and have remained widely used. These ion sources share the motif of placing the analyte, either spotted on a plate or in its native state, in front of a stream of droplets or particles. Owing to its ease of implementation and applicability to a wide variety of molecules, DESI, in particular, has been widely adopted. In DESI, the spray from a capillary transporting solvent is oriented at an angle against a surface, onto which the analyte has been spotted. A high potential is applied to the solvent via a metallized tip or metal-T, generating an analyte-free electrospray plume. The spray is assisted by a nebulization gas, dry nitrogen, to enable higher solvent flow rates. The spray of charged solvent droplets strikes the surface and collects analyte, ultimately producing gas-phase analyte ions. It is hypothesized that stochastic momentum transfer lead to the desorption of the solvated analyte, which then ionizes through mechanisms similar to ESI.[3] To ensure complete droplet evaporation, droplets and DESI-generated ions are typically transported through a long heated capillary into the vacuum regions of a mass spectrometer.[1]

A partial list of applications of samples analyzed by DESI includes explosives,[4] illicit drugs,[5] and pharmaceuticals.[6,7] DESI has also been used to image surfaces,[8] bacteria,[9] and thin-layer chromatography plates.[10,11] DESI has also shown extremely high salt tolerance compared to ESI.[12] Sampling times for the above listed applications vary from subsecond to minutes. DESI is highly amenable to problems requiring rapid chemical screening and imaging. In one example of rapid screening, pharmaceutical pills

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(1) Takats, Z.; Wiseman, J. M.; Cologan, B.; Cooks, R. G. *Science* **2004**, *306*, 471–473.

(2) Cody, R. B.; Laramee, J. A.; Durst, H. D. *Anal. Chem.* **2005**, *77*, 2297–2302.

(3) Costa, A. B.; Graham Cooks, R. *Chem. Phys. Lett.* **2008**, *464*, 1–8.

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have been analyzed at rates up to three pills per second.[6] In another application, DESI has been used to quantitatively measure each well in a 96 well plate in 3 min.[13]

In this study, we explore rapid sampling rates and probe the rise and fall times of ion signals using a DESI ion source coupled to a home-built Hadamard transform time-of-flight mass spectrometer (HTTOFMS). Briefly, HTTOFMS is a multiplexed TOF technique. It involves reproducibly deflecting a continuous ion beam on and off its initial flight axis according to a pseudorandom binary sequence on a megahertz time scale. To achieve deflection, an ion optic called a Bradbury−Nielsen gate (BNG) is used.[14] The positions and arrival times of deflected and undeflected ions are recorded using a microchannel plate detector coupled to a delay-line anode.[15] This x, y, t data enables visualization of both the deflected and undeflected ion beam signals and analysis of ion arrival events corresponding to both deflection states. This process of continuous deflection and imaging detection enables a 100% duty cycle measurement from a continuous ion beam. The continuous counting of ions allows HTTOFMS to be efficiently coupled to continuous ion sources without requiring a trapping stage, allowing it to maintain high temporal resolution for events occurring outside the mass spectrometer. Through multiplexing, HTTOFMS gains a peak height precision (PHP) advantage compared to traditional linear TOF instruments.[16] This advantage originates from counting more ions per unit of time. As a result, faster spectral acquisition rates can be achieved. The main drawback of the technique is that mass resolution is limited by the maximum achievable modulation frequency. The development of the HTTOFMS technique and associated theoretical calculations has been described in detail previously.[17−19]

In the following experiment, we utilize a disk spotted with analytes and spun at varying speeds to expose analytes to the DESI plume for short, controlled residence times, down to tens of milliseconds, giving a programmable sampling frequency. Additive combination of data from multiple passes of the disk is used to probe the rising and falling edges of the analyte signal. An upper bound for the maximum possible temporal resolution and sampling rate of DESI in the absence of sensitivity constraints is estimated and found to exceed previous DESI sampling rates.

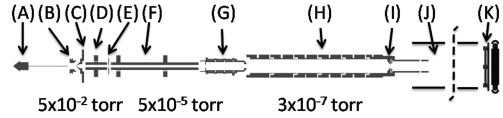

Figure 1. Schematic with associated pressures of each region of the instrument: (A) heated transfer capillary; (B) tube lens; (C) skimmer; (D) rf-only quadrupole ion guide; (E) lens; (F) rf-only quadrupole ion guide; (G) low-voltage lens stack; (H) high-voltage lens stack; (I) Bradbury−Nielsen gate; (J) drift tube; (K) position-sensitive ion detector.

EXPERIMENTAL SECTION

Hadamard Transform Time-of-Flight Mass Spectrometer. Figure 1 shows a schematic representation of the home-built HTTOFMS. This new HTTOFMS represents an improvement from the previous linear instrument[20] and a miniature and linear variation to the reflectron instrument reported by our group.[21] The ion source was made from portions of a ThermoFinnigan LTQ (San Jose, CA) instrument and contains a heated transfer capillary (A), tube lens (B), skimmer (C), and an rf-only quadrupole ion guide (D). The heated capillary was held at 250 °C for all experiments. The source mounts to a custom-built aluminum vacuum chamber. Following the source, there is a low-voltage lens (E), and a second rf-only quadrupole ion guide (F). Both quadrupole ion guides are powered by a PSRF-100 resonant power supply (Ardara Technologies, North Huntingdon, PA) operating at 1.46 MHz. The second quadrupole ion guide (F) is followed by four low-voltage ion optics (G). A stack of five high-voltage lenses (H) follows the low-voltage lens stack. The first lens serves to accelerate ions to high potential. The second lens is split to allow steering of the ion beam. The third through fifth lenses act as an Einzel lens to focus the beam on the active area of the Bradbury−Nielsen gate (BNG) (I). The drift region of the HTTOFMS instrument is labeled J and is approximately 0.9 m long. All lenses, quadrupoles, and the drift region tubing are constructed of stainless steel. All voltages, excluding the peak-to-peak rf voltage, are controlled with analog voltages generated with various National Instruments products (Austin, Texas). An in-house programmed LABVIEW instrument control panel provides the user interface (National Instruments). The Bradbury−Nielsen gate used in this instrument was fabricated from a silicon-on-insulator wafer using deep reactive ion etching. The construction and figures of merit of the microfabricated BNG were described in a previous publication.[22] A high-speed digital waveform I/O card (NI PCI-6551, National Instruments) is used to deliver the pseudorandom binary sequences to the BNG driver board. The BNG driver board is based on an H-bridge using DEIC

(4) Cotte-Rodriguez, I.; Takats, Z.; Talaty, N.; Chen, H.; Cooks, R. G. *Anal. Chem.* **2005**, *77*, 6755–6764.
(5) Leythold, L. A. *Rapid Commun. Mass Spectrom.* **2006**, *20*, 103–110.
(6) Chen, H.; Talaty, N. N.; Takats, Z.; Cooks, R. G. *Anal. Chem.* **2005**, *77*, 6915–6927.
(7) Williams, J. P.; Scrivens, J. H. *Rapid Commun. Mass Spectrom.* **2005**, *19*, 3643–3650.
(8) Ifa, D. R.; Wiseman, J. M.; Song, Q.; Cooks, R. G. *Int. J. Mass Spectrom.* **2007**, *259*, 8–15.
(9) Meetani, M. A.; Shin, Y.-S.; Zhang, S.; Mayer, R.; Basile, F. *J. Mass Spectrom.* **2007**, *42*, 1186–1193.
(10) Van Berkel, G. J.; Kertesz, V. *Anal. Chem.* **2006**, *78*, 4938–4944.
(11) Van Berkel, G. J.; Ford, M. J.; Deibel, M. A. *Anal. Chem.* **2005**, *77*, 1207–1215.
(12) Jackson, A. U.; Talaty, N.; Cooks, R. G.; Van Berkel, G. J. *J. Am. Soc. Mass Spectrom.* **2007**, *18*, 2218–2225.
(13) Manicke, N. E.; Kistler, T.; Ifa, D. R.; Cooks, R. G.; Ouyang, Z. *J. Am. Soc. Mass Spectrom.* **2009**, *20*, 321–325.
(14) Bradbury, N. E.; Nielsen, R. A. *Phys. Rev.* **1936**, *49*, 388–393.
(15) Jagutzki, O.; Lapington, J. S.; Worth, L. B. C.; Spillman, U.; Mergel, V.; Schmidt-Böcking, H. *Nucl. Instrum. Methods Phys. Res., Sect. A* **2002**, *477*, 256–261.
(16) Kimmel, J. R.; Yoon, O. K.; Zuleta, I. A.; Trapp, O.; Zare, R. N. *J. Am. Soc. Mass Spectrom.* **2005**, *16*, 1117–1130.
(17) Brock, A.; Rodriguez, N.; Zare, R. N. *Anal. Chem.* **1998**, *70*, 3735–3741.
(18) Yoon, O. K.; Zuleta, I. A.; Kimmel, J. R.; Robbins, M. D.; Zare, R. N. *J. Am. Soc. Mass Spectrom.* **2005**, *16*, 1888–1901.
(19) Fernández, F. M.; Vadillo, J. M.; Engelke, F.; Kimmel, J. R.; Zare, R. N.; Rodriguez, N.; Wetterhall, M.; Markides, K. *J. Am. Soc. Mass Spectrom.* **2001**, *12*, 1302–1311.
(20) Trapp, O.; Kimmel, J. R.; Yoon, O. K.; Zuleta, I. A.; Fernandez, F. M.; Zare, R. N. *Angew. Chem., Int. Ed.* **2004**, *43*, 6541–6544.
(21) Yoon, O. K.; Robbins, M. D.; Zuleta, I. A.; Barbula, G. K.; Zare, R. N. *Anal. Chem.* **2008**, *80*, 8299–8307.
(22) Zuleta, I. A.; Barbula, G. K.; Robbins, M. D.; Oh Kyu, Y.; Zare, R. N. *Anal. Chem.* **2007**, *79*, 9160–9165.

420 driver chips (Directed Energy Incorporated, Ft. Collins, CO) and described elsewhere.[23]

Detection and Data Acquisition. Following the drift region, a detector consisting of a microchannel plate (MCP) pair and a delay-line anode is mounted on a custom flange (K). The MCPs are imaging grade (model APD 2 40/6/5/8 I 60:1 MP EDR, Burle Industries, Lancaster, PA) and are arranged in a chevron configuration. The front MCP plate was held at −2090 V, and the rear plate was grounded. The delay-line anode (DLD-40, RoentDek Handels GmbH, Germany) allows for $x-y$ position information to be recorded for each ion arrival event in addition to timing information. The use of a delay-line anode in an HTTOFMS instrument has been previously described.[21] Briefly, electrons emitted by the MCP stack strike two wire pairs. Current pulses from the electron burst travel across the each wire set. By measuring the difference in the arrival times of the current pulses at each end of a wire, the position of the electron burst related to the event is determined. Each dimension has two wires to allow for differential reading of the electron burst currents. The signals are fed into constant-fraction discriminators (ATR-19, RoentDek Handel GmbH, Germany) which output NIM logic pulses. The NIM pulses are sent to a time-to-digital converter (TDC) (TDC8HP, Cronologic OHG, Germany). Raw timing data is used to construct ion events containing position and arrival time information which are saved as binary numbers to be post processed in MATLAB (Natick, MA). Ion event construction and data saving is carried out by an in-house written dynamic-link library (DLL) written in C++, allowing for LABVIEW to access the TDC.

Chemicals. HPLC grade methanol, ultrafiltered water, and glacial acetic acid were used as received from Fischer Scientific (Pittsburgh, PA).

Discs and Rotation. Discs were designed and machined out of poly(methyl methacrylate) (PMMA) with dimensions matching miniature compact discs, 8 cm in diameter with a 1.48 cm hole in the center. Red and blue Sharpie markers (Sanford Corporation, Oak Brook, IL) were used to draw the imaged pattern and sample spots. The detected components of the red and blue markers were rhodamine 6G and basic blue 7, respectively.[8] The patterns were drawn by hand with the aid of a ruler and were imaged on the same day. A stepper motor with an integrated controller (23MD, Anaheim Automation, Anaheim, CA) was used to rotate the disk. The motor was driven by TTL pulses from a DS345 function generator (SRS, Sunnyvale, CA). The stepper motor was operated at 1600 steps per revolution producing nearly continuous rotation on the time scale of most experiments. The apparatus was capable of controlling speeds of rotation up to 20 Hz. The discs and stepper motor were interfaced using a mount made of anodized aluminum that held the discs through their center holes.

DESI Source. The DESI source was constructed from the electrospray head of a ThermoFinnigan LTQ (San Jose, CA) ESI source. With the use of a custom-made mount, the head was interfaced to an x, y, z manipulator and a ball and socket pivot joint, allowing for easy linear and rotational translation. The stepper motor holding the disk was mounted on a separate x, y, z manipulator. The emitter was held at a potential of +5 kV. Dry nitrogen (Praxair, Danbury, CT) was used as a nebulizing gas. The spray solvent was a mixture of water and methanol (1:1 v/v) with 0.1−1.0% glacial acetic acid (Sigma-Aldrich, St. Louis, MO). Spectra were collected with flow rates ranging from 5−50 μL/min controlled via a syringe pump (Harvard Apparatus, Holliston, MA). Figure 2 illustrates the DESI and disk setup.

(23) Bolton, C. *Electronics Design News* **2002** (October 3), p 88.

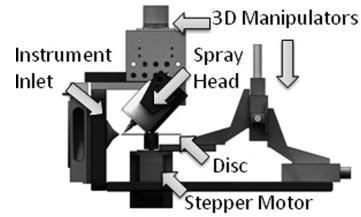

Figure 2. Disc platform for rapid DESI analysis.

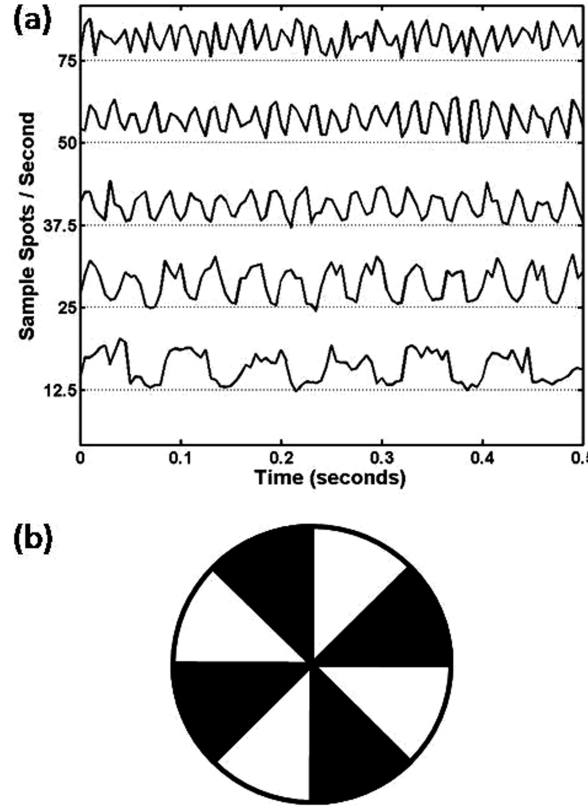

Figure 3. (a) Ion intensity of the basic blue 7 peak plotted vs time for various sampling rates and (b) cartoon of the analyzed disk surface with black sectors representing analyte-painted region.

RESULTS AND DISCUSSION

Rapid Sampling. One potential application of DESI with great promise is online or process monitoring. Chen et al. have suggested the evaluation of pharmaceutical products using pill-by-pill analysis on a moving assembly line.[6] We have developed a system to evaluate the fundamental limits of such a protocol where each analyte undergoes a single pass through the analysis window. By patterning a disk with alternating blank and chemically labeled regions, a pill-by-pill system can be modeled as shown in Figure 3b. Pills are three-dimensional objects and thus are less ideal surfaces for a DESI experiments. We divided the disk into eight sectors, where each sector was approximately 3.1 cm in length at the edge where the disk was analyzed. Sample spots were drawn using a marker containing basic blue 7. The stepper motor was programmed to produce rotation rates equivalent to different

numbers of sample spots per second. Figure 3a shows the ion intensity from the basic blue 7 peak taken from a series of spectra collected at varying rates of rotation. The 0.5 s time window shown corresponds to multiple rotations of the disk.

The HTTOFMS data collection scheme allows the determination of the spectral acquisition rate after the analysis has been completed and can be matched to provide appropriate time resolution for different sample rates. The data presented in Figure 3a is shown at 200 spectra/s. The rate of 200 spectra/s is limited by the average count rate collected by our HTTOFMS. For a typical count rate of 100 000 ions/s, the 200 spectra/s rate corresponds to spectra representing 500 ion arrival events within the 5 ms time bin. The use of the 5 ms time bins allows for analysis at rates up to 80 samples/s by defining a peak by using two to three points. Defining a peak using one point is difficult because the spectral averaging time and residence time of the analyte would need to be synchronized to see ion signals return to a baseline value, making every measurement a changing average value of analyte and blank disk. The use of two to three points is insufficient to provide a chemical image of the surface and peak height stability but allows for determination of presence or absence because some fraction of the peaks are solely analyte.

For the highest sample rate, 75 samples/s, insufficient ion intensity to allow for finer time binning led to poor resolution of individual sample spots. The individual spots are better resolved at 50 samples/s. At this sampling rate, the residence time of each spot is 10 ms, because half the disk is blank, and the linear velocity of the disk at the point of measurement is approximately 3.1 m/s. The rate of 50 samples/s presents a maximum sampling rate 18.7 times greater than the result by Chen et al. of 2.67 samples/s.[6] To contrast our result, the work by Chen et al. was completed using a linear ion trap mass spectrometer. The conditions for their result may represent more realistic analytical conditions and may better present an upper limit to practical analysis. However, we believe that our result shows the potential of this method to achieve a higher sampling rate where the analysis conditions are highly controlled. In our system, the analysis of samples by DESI at 50 samples/s is limited by experimental conditions. However, the analyte signal decay is not instantaneous. This is manifested in Figure 3a by intensities being at their baseline value for less than half the time. The time scale on which the signal decays for an analyte spot will place a limit on the maximum achievable sample analysis rate.

Application to Chemical Imaging of Surfaces. Another promising direction in the applications of DESI is to image surfaces. Chemical imaging is often difficult with spectroscopic methods because there is often not a clear mapping between spectroscopic features and unique chemical identifications for complex and unknown systems. In contrast, MS generally offers unique chemical identities for any ionizable molecule. Various non-mass-spectrometric chemical imaging techniques are available, including but not limited to scanning probe microscopy techniques like near-field scanning optical microscopy, Raman, fluorescence, infrared spectroscopy, surface plasma resonance, and scanning Auger microscopy. Mass spectrometric techniques include secondary ion MS, laser desorption ionization, and two-step laser MS. DESI imaging is highly generalizeable to an array of analytes, but it does not have the spatial resolution of some of the spectroscopic techniques; there is a loose trade-off between quantity of generic chemical information and spatial resolution. DESI imaging has achieved spatial resolutions below 500 μm.[8] Through controlling the alignment of the system, the produced images can accurately reflect the surface's chemical contents.[24] In both studies, imaging speeds varied from 100 to 500 μm/s.

To offer insight into potential limits of DESI imaging on faster time scales, we studied the maximum sampling rates of adjacent patterned samples. Figure 4 shows the data from a different eight sector discs on which alternating red and blue strips were drawn, as shown in Figure 3b with the blank sections representing rhodamine 6g. The linear velocity at the edge of the disk was 2.5 m/s, corresponding to a 12.5 ms sample residence time. In Figure

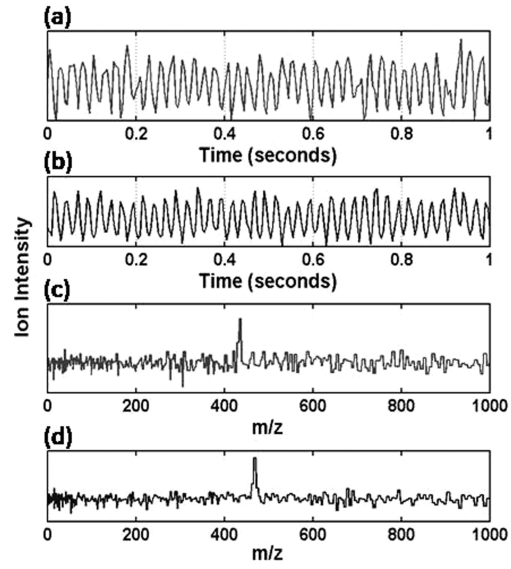

Figure 4. Ion intensity time courses for (a) rhodamine 6G and (b) basic blue 7 as well as representative spectra from single-analyte sectors recorded over 5 ms (c and d), respectively.

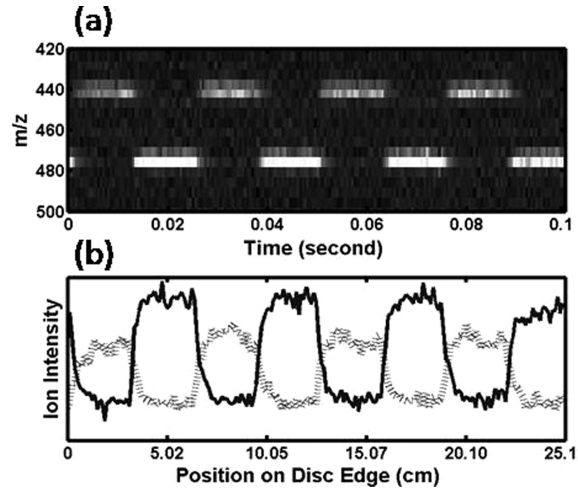

Figure 5. Average of 50 passes of the disk used to make Figure 4 showing (a) the mass spectra vs time and (b) the signal intensity of each analyte as a function of position on the disk's edge. Note that the drawn pattern is reproduced when ion intensities are sufficient to allow for fine time binning (0.5 ms).

(24) Kertesz, V.; Van Berkel, G. J. *Anal. Chem.* **2008**, *80*, 1027–1032.

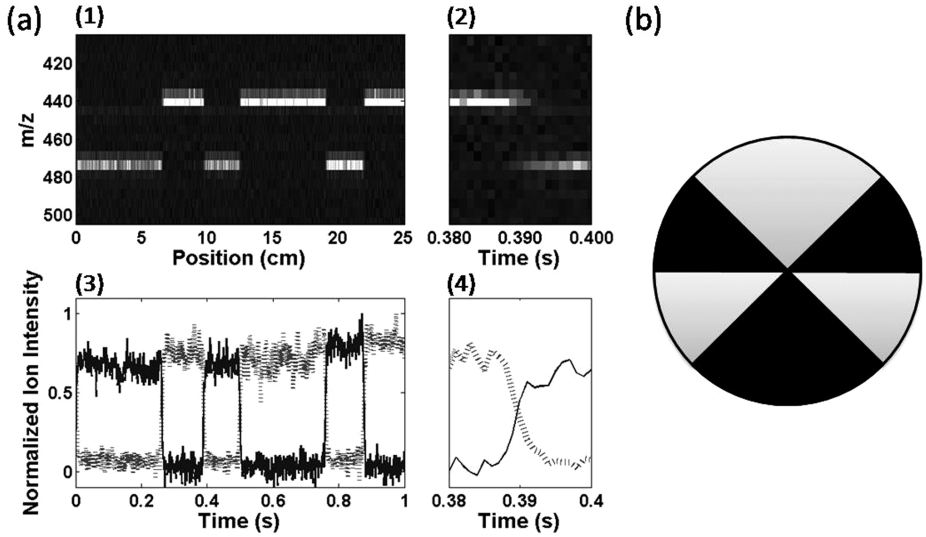

Figure 6. (a) Average of 40 passes of the disk shown in panel b which contains alternating basic blue 7 and rhodamine 6G with unequal sector sizes. The transition region between different analytes is shown in (2) and (4), whereas (1) and (3) are the mass spectra vs time and the resulting analyte signal intensities vs time, respectively.

4, plots a and b show the ion intensities for rhodamine 6G and basic blue 7, respectively, where the total sampling rate was 80 samples/s, counting both analytes. This is a higher rate than shown in Figure 3a, but had blanks been counted, there is no observed improvement in achievable sampling rate by having adjacent analyte spots.

At the spectral acquisition rate necessary to study this sample rate, the ion flux is not sufficient to produce high-fidelity chemical images of the disk from a single pass, but the chemical identities of the deposited analytes and their separation in time is recorded. Figure 4 plots c and d show a representative spectrum for each molecule, rhodamine 6g and basic blue 7, respectively. All data was parsed to 200 spectra/s. In order to test our hypothesis that ion flux represents the main limitation on sampling rate and imaging reproduction, we simulated a higher ion count rate by coadding the data that results from multiple rotations. In contrast to pill-by-pill single-pass analysis, this multipass analysis would be amenable to imaging static systems. Figure 5 shows 50 rotations, over the course of 5 s, of the disk patterned used for Figure 4 averaged together. It shows clearly that had ion intensities been higher to allow for finer time binning, the pattern on the disk would have been recovered. The effective linear imaging rate in Figure 5 is 50 mm/s.

Figure 6a shows the results from multipass averaging of 40 rotations, over the course of 40 s, of a disk with six sectors of two different sizes, alternating between two analytes. This pattern is shown schematically in Figure 6b. The disk was rotating at 25.1 cm/s with 1 ms time bins used in the figure corresponding to 250 μm on the disk. Plot 1 shows the reproduction of the pattern drawn on the disk with stable ion intensity for each peak achieved through averaging. The stability of the peak heights suggests that quantitative information is likely extractable if that were the experimental aim. Plot 2 magnifies one of the regions where the sample switches. The rise/fall times are on the order of 5 ms, which is equivalent to 1.25 mm of translation corresponding to the best approximation of spatial resolution of the experiment for this rotation rate. Physically, this value is only slightly larger than the size of the DESI spray plume on the surface, but the resolution is worse than others have demonstrated. The effective linear imaging rate for this experiment was 6 mm/s.

The present method represents an alternative to rastering a surface to image it and can provide rapid linear imagining rates at a cost to spatial resolution. One advantage of such an imaging process is that it allows for solvent flow rates much higher than those typically used, up to 50 μL/min in these experiments, without blurring the image on the surface. A regularly refreshed surface does not exhibit the same ion current saturation with increased flow rates as seen in previous work on stationary or slow surfaces.[25] Another advantage stems from reducing the effects of surface capacitance. Previously, different surfaces have been shown to have different effective capacitances.[26] Volný et al. showed surfaces initially exhibit high ion intensity which decays rapidly and to different degrees depending on the surface. Surfaces widely used for DESI suffered less than those generally avoided. They found PTFE to be the best of the tested surfaces, which was explained by its hydrophobicity. In our experiment, the constant rotation of the disk through the DESI plume exploits this period of high ion intensity, providing images more rapidly through higher ion count rates and the coaddition of multiple passes. This finding suggests surfaces not highly amenable to DESI might be better analyzed if repeated measurements are made followed by averaging them together as opposed to one slow scan.

CONCLUSIONS

We have applied a new HTTOFMS instrument and a novel disk-based sampling system to study the limits of rapid sampling with DESI-MS and the rising and falling edges of analyte signals. We have demonstrated sampling rates of 50 samples/s for a single analyte and 80 samples/s for alternating analytes using a disk-based platform. Averaging multiple rotations of the disk shows rising and falling edges of ion signals are on the order of milliseconds in duration for our experiment. This risetime suggests that with proper source conditions and instrument

(25) Venter, A.; Sojka, P. E.; Cooks, R. G. *Anal. Chem.* **2006**, *78*, 8549–8555.
(26) Volný, M.; Venter, A.; Smith, S. A.; Pazzi, M.; Cooks, R. G. *Analyst* **2008**, *133*, 525–531.

sensitivity, DESI could resolve more than 100 samples/s. Multipass averaged data yields chemical images of the surface at still relatively fast linear imaging rate with moderate spatial resolution. Further, a rapid passing surface allows for flow rates well above those typically used without blurring chemical information. Multipass averaging can also negate some of the deleterious effects of surface capacitance on ion intensity. Overall it is reaffirmed that DESI could be an effective tool for problems requiring both high throughput and chemical identification and possible quantitation.

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