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Multidimensional Analytical Method Based on Binary Phase Shaping of Femtosecond Pulses

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Multidimensional chemical detection and identification based on phase shaped femtosecond laser pulses coupled to mass spectrometry is demonstrated. The method based on binary phase shaping (BPS) takes into account the accuracy and precision standards required by analytical chemistry. It couples multiphoton intrapulse interference of ultrashort laser pulses with time-of-flight mass spectrometry (TOF-MS). We demonstrate that BPS-MS provides a rigorous multidimensional technique for the detection and identification of analogues to chemical agents and mixtures in real time. Experimental results on dimethyl phosphite and pyridine illustrate the new approach toward the real-time accurate detection and identification of chemical compounds including isomers.

Real-time detection and identification of chemicals in the environment has become a necessity for reasons of safety and security. Modern analytical tools aimed at the identification of compounds in chemically complex mixtures depend on multidimensionality to sort out the different components. Current technologies, such as portable gas chromatography mass spectrometry (GC-MS), provide information about contaminants but suffer from several downfalls. Their detection and identification are on a time scale measured in minutes. Also, these instruments are not always accurate and usually are incapable of identifying molecular isomers. In principle, these limitations can be lifted by the use of more dimensions, such as the GC-MS-MS method, whereby the fragments produced by the first MS event are further fragmented in the second MS process.[1,2]

The identification method presented here is based on the observation that shaped laser pulses can influence the photofragmentation and ionization of molecules.[3,4] Until now, the goal for active laser control has been to devise electromagnetic fields to drive the outcome of a chemical reaction toward a desired set of products.[5−7] Here, laser control offers the possibility of achieving different dimensions of analysis, assuming that each laser pulse yields a different fragmentation and ionization pattern from a given molecule. These different patterns are analogous to different fingerprints, which can be used to identify the molecule uniquely.

For this method to meet the robustness (in terms of accuracy and precision) expected for analytical chemistry, the results need to be highly reproducible. To this end, we introduced the use of phase compensation using multiphoton intrapulse interference phase scan (MIIPS) to characterize the laser pulses and to correct unwanted phase distortions at the sample.[8,9] This step was critical because the highly nonlinear interaction between the laser pulse and the molecules, which leads to ionization and fragmentation, is highly sensitive to phase variations in the laser pulse.

Starting with reproducible transform-limited pulses, differently tailored phases are used in a search for different fragmentation patterns. The challenge was how to find the phases that cause maximal differences in the fragmentation patterns. Using a shaper with 128 pixels across the spectral bandwidth of the laser pulse and a phase that could be adjusted to at least 100 different values gave us a staggering 100^{128} ($=10^{256}$) different pulse shapes to explore. The more popular approach to this challenge is to use an evolutionary genetic algorithm (GA) to explore the search space.[10] Being limited to less than 10^8 experimental tests per day, we were aware that an exhaustive search would be impossible.

On the basis of our experience in controlling the multiphoton excitation of polyatomic molecules in condensed phases,[8,9,11−15] we assumed that, for intermediate intensity laser fields, control between different pathways depends on the relative phase between pairs of frequencies within the bandwidth of the laser pulse. On the basis of this assumption, we used only two phase settings (0 and π) in the design of the frequency-domain phase functions. By this observation alone, we reduced the search space to 2^{128} ($=10^{39}$). This reduction in the search space using binary phase shaping (BPS) and its effect on multiphoton intrapulse interference (MII) had been reported earlier.[14] The constructive or destructive (intrapulse) interference caused by the shaped laser pulse as it interacts with the molecule gives rise to the desired different fragmentation pathways, as described below.

Given that the goal here is to quickly and unequivocally alert to the presence of a chemical and not to find the absolute optimum pulse shape, we further reduced the search space by concentrating on the 100 central pixels in the shaper and by binning the pixels into groups of 10 superpixels. This finally

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reduces the search space to 1024. Because binary phases are insensitive to the addition of a factor of π, we obtain an additional factor of 2 reduction in the search space by fixing the first byte to 0; the resulting 512 binary phases (BPs) could be evaluated in minutes without the need of a search algorithm. They are referred to in the text as BP*X*, where *X* corresponds to the decimal value of the binary number; that is, the phase function 0000000011 corresponds to BP3 and 0111111111 corresponds to BP511. On the basis of differences arising from the molecular and electronic structure of the sample, different fragmentation pathways are accessed, forming a "library" of 512 mass spectra for a given compound. Therefore, the described approach gives a 512-dimensional analytical tool. Because not all different pulses lead to different outcomes, we searched for orthogonality in the results space. We selected several BP shapes for each compound, each corresponding to a different fragmentation "fingerprint" to be used in the identification of that compound.

The experiments were performed using a commercially available sub-50 fs (26 nm full width at half-maximum) 0.8 mJ/pulse laser system that was directed to a pulse shaper based on a two-layer 128 pixel spatial-light modulator. The pulse shaper was programmed for self-calibration and for MIIPS characterization and compensation.[9,14,15] The phase-only shaped pulses are focused by a 50 mm lens, where the sample (kept in the chamber at a pressure below 10^{-5} Torr) interacts with the laser field. For all samples, the laser was attenuated to 130 μJ/pulse at the sample. The molecular and fragment ions formed were detected by time-of-flight mass spectrometry (TOF-MS). Each mass spectrum was obtained after calibration of the arrival time at the detector and conversion of the arrival times to *m*/*z*. Each mass spectrum shown represents the signal average resulting from 128 laser shots. The MIIPS device has a dual purpose in the experiment. In the calibration mode, it accurately measures the pulses and compensates any spectral phase distortion, producing transform-limited pulses at the sample. In the discrimination mode, it sequentially introduces predetermined binary shaped pulses. Phase shaping causes no significant changes in the spectral profile of the excitation laser field throughout the experiment.

In Figure 1, we show BPS-MS results on dimethyl phosphite, an organophosphate chemical analogous to a number of nerve agents and insecticides. Note that we have been able to identify a number of binary phase shapes that result in statistically different fragmentation and ionization patterns. The standard mass spectrum[16] (Figure 1a) obtained by 70 eV electron impact shows that the peaks at 80 and 79 *m*/*z* are the strongest. The abundance of these masses in the electron-impact mass spectrum of dimethyl phosphite has been discussed elsewhere.[17] The BPS-MS data (Figure 1b−d) show control over the most prominent fragment, with *m*/*z* 80 2−3 times lower in intensity than *m*/*z* 79. Note the differences between the TL pulses (b) and the two binary phase functions (c and d). The data in Figure 1 show that some of the fragment ions are completely missing (molecular ion in part c, for example), indicating complete control over some fragmentation pathways. This finding is significant regarding ongoing efforts on bond selective chemistry.[3,4,18−22]

In Figure 2, we compare BPS-MS results on pyridine obtained for two relatively similar binary phases (BP173 and BP282). Note that the molecular ion (79 *m*/*z*) increases by a factor of 7, while the fragment ion (52 *m*/*z*) increases only by a factor of 2. BP173, therefore, enhances the fragmentation of pyridine to produce the butadiene fragment ion by a factor of 3.5. Given the relative low yields of these laser induced reactions (typically less than 1000 ions per laser pulse), their synthetic value may be limited. However, they are highly reproducible (tested several hundred times and on different days). Therefore, we are confident that any femtosecond laser system capable of 50 fs pulse duration and outfitted with a shaper with MIIPS and BPS could reproduce these results.

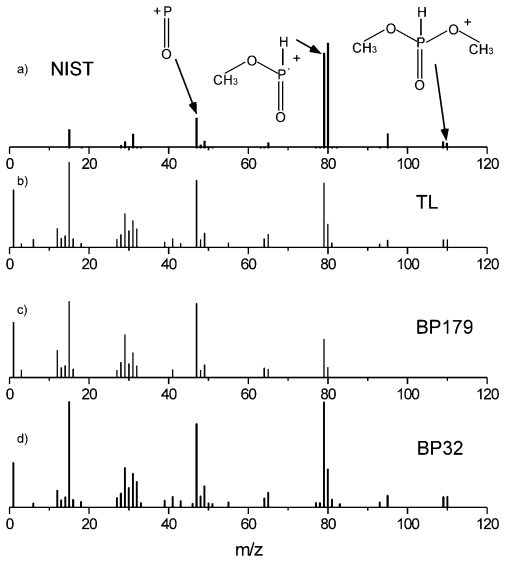

Figure 1. Electron-impact mass spectra (a)[16] and BPS-MS results obtained for dimethyl phosphite using TL pulses (b) and the following two other binary phase functions: BP179 (c) and BP32 (d). Notice the differences in fragmentation patterns induced by the different electric fields. Each mass spectrum constitutes a fingerprint that can be used to identify a particular molecule. The intensity of the data in (c) has been multiplied by a factor of 2. Throughout the text, *m*/*z* peaks at 47 and 79 are referred to as A and B, respectively. Comparing (c) and (d), we find different intensity ratios between fragments at *m*/*z* 47 and 79. For BP179, A/B is 1.93, while, for BP32, A/B is 0.79.

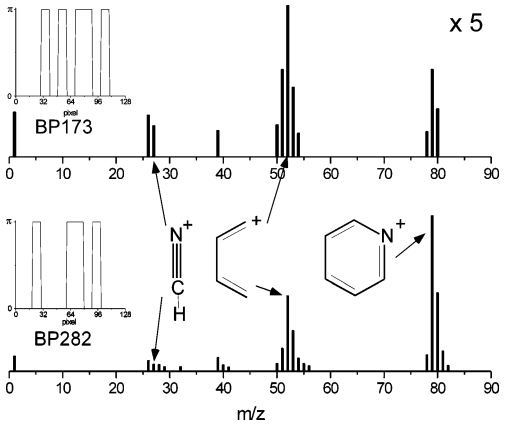

Figure 2. BPS-MS data for pyridine. The results demonstrate differences obtained between BP173 and BP282 (functions shown in the insets). These results illustrate how two uniquely identifying shaped pulses are selected on the basis of differences in the ratios for two or more peaks in their mass spectrum.

The BPS-MS results shown in Figures 1 and 2 indicate clear control in the photofragmentation and ionization patterns for two different chemicals. We have observed similar effects in 18 other chemical compounds. The scientific reason for the observed differences in our experiments has not been fully investigated. It is possible that the shaped pulse provides different pathways of resonance enhanced multiphoton ionization to the molecule. The principle would be similar to that used for controlling two-photon excitation of atoms,[23−27] or multiphoton excitation of molecular systems,[11−15] using MII. At the

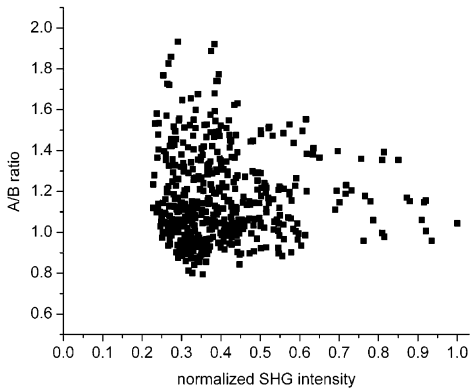

Figure 3. A/B ratio (47 and 79 *m*/*z*) for dimethyl phosphite. From the spread of the results, we conclude that the A/B ratio is not a simple function of peak intensity.

simplest level, one may speculate on the effect of laser pulse peak intensity. By introducing a binary phase, the duration of the laser pulses increases, and this leads to a concomitant reduction in peak intensity. Given that the second harmonic generation (SHG) of a laser pulse is inversely proportional to the peak intensity of the pulses, we plotted the ratio between two mass peaks A/B in the BPS-MS of dimethyl phosphite as a function of the second harmonic intensity (normalized such that TL pulses give unit intensity). A similar approach has been used by Gerber's group to demonstrate that pulse shaping is not just a matter of adjusting the peak intensity of a laser pulse.[28−30]

In Figure 3, we show the ratio (A/B) of peaks at 47 and 79 *m*/*z* as a function of laser peak intensity (integrated SHG intensity) for the 512 different BP shapes. From these results, we can conclude that selectivity, demonstrated by the results presented in Figures 1 and 2, is not a simple function of peak intensity. For TL pulses (SHG intensity of 1), one obtains an A/B ratio of ∼1. More interestingly, we see that a number of phases are highly selective. The different A/B values may be a consequence of nonadiabatic multielectron (NME) dynamics.[31] Briefly, the electronic response of polyatomic molecules to intense nonresonant (infrared) laser pulses results in multielectron excitation−ionization mechanisms.[31] Pulse shaping influences the NME excitation−ionization process and the subsequent fragmentation occurring in the picosecond time scale. The NME interpretation is consistent with the fact that the A/B ratio for a fixed phase was found to be relatively insensitive for up to a factor of 2 decrease in the laser pulse intensity (data not shown). Our results are consistent with the findings of Bañares et al.[32] who studied the intensity dependence of femtosecond laser pulse induced ionization and fragmentation of $Fe(CO)_5$. From their data, one can see that for intermediate intensities a factor of 2 change in laser intensity had little or no effect on the fragment distribution. We found that, as the laser intensity was increased above 150 μJ per pulse, the selectivity of our method, as discussed below, was greatly reduced.

For BPS-MS to succeed as an analytical method, it is important to demonstrate that each shaped pulse in the library can be considered as an independent dimension of analysis. For every pair of shaped pulses (for example, pulse *i* and pulse *j*), we must demonstrate that they have an orthogonal component by showing that they produce different fingerprints, as measured by the ratio between two peaks *a* and *b* according to

$$O_{ij} = \left(\frac{a_i}{b_i}\right)\left(\frac{b_j}{a_j}\right) \geq 1 + \sigma_i + \sigma_j \qquad (1)$$

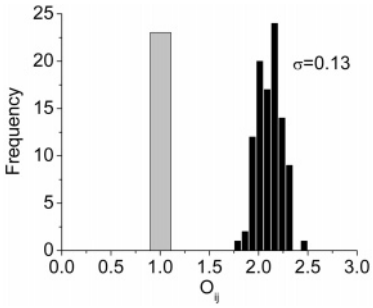

Figure 4. Standard deviation histogram indicating the degree of orthogonality O_{ij} between two binary phase functions. The histogram summarizes 100 measurements for each of the two BPs applied (BP179 and BP32). The mean O_{ij} value was 2.11 with a standard deviation of 0.13. Notice that the values are well outside the gray region near $O_{ij} = 1 \pm \sigma$, indicating that the two phase functions represent two distinguishable fingerprints.

where σ_i and σ_j are the experimental standard deviations for each of the ratios being measured.

In Figure 4, we show the distribution of O_{ij} values obtained from peaks at 47 and 79 *m*/*z* (see Figure 1), obtained from 100 measurements each for two selected functions that yielded the largest A/B and B/A ratios. The product, calculated as prescribed by eq 1, above, is 2.11. Given that the experimental error, σ_i and σ_j, is 5%, the two pulse shapes show a clear statistically determined orthogonal value that can be used in the identification of this compound because $O_{ij} > 1.1$. In most cases, the O_{ij} values range from 2 to several hundred. The results from our method are good enough to allow us the possibility to distinguish between isomers,[33] something that cannot be done using conventional GC-mass spectrometry because of the physical and chemical similarities. The selectivity of BPS-MS arises from the fact that the fragmentation and ionization processes depend on the nonlinear quantum mechanical interaction between the shaped laser field and the molecular and electronic structure of the chemical compound.

In conclusion, we have demonstrated this method is capable of identifying chemical agents (20 tested so far) in pure form or in mixtures with other compounds. We have taken the concept of laser control of chemical reactions and used it for the unequivocal identification of chemical compounds. To meet the strict requirements of standard analytical chemistry methods, it was important to ensure that the phase introduced in the pulses was highly reproducible. This was facilitated by the MIIPS method. We then used binary phase shaping, which decreased the search space by hundreds of orders of magnitude. Finally, we identified a number of phase functions that can be used for multidimensional chemical identification. We have already constructed libraries for six-dimensional analysis; however, in most cases, two or three dimensions are sufficient. A detailed presentation of the methodology and a more complete analysis of the data will be published elsewhere.

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