Universität Rostock Traditio et Innovatio
HelmholtzZentrum münchen
Deutsches Forschungszentrum für Gesundheit und Umwelt
JOINT MASS SPECTROMETRY CENTRE

Detection of Security-Relevant Substances via Soft Ionization Mass Spectrometric Methods Using Ambient Pressure Laser Desorption

Kumulative Dissertation
zur Erlangung des akademischen Grades eines
doctor rerum naturalium (Dr. rer. nat.)
der Mathematisch-Naturwissenschaftlichen Fakultät
der Universität Rostock

vorgelegt von
Sven Ehlert
geb. am 20. August 1982 in Rostock

Rostock, April 2014

Die vorliegende Arbeit entstand in der Zeit von Oktober 2008 bis April 2014 in der Arbeitsgruppe Analytische Chemie des Instituts für Chemie an der Universität Rostock im gemeinsamen Massenspektrometrie-Zentrum der Universität Rostock und des Helmholtz Zentrums München.

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Datum der Verteidigung: 08.07.2014

Danksagung

An dieser Stelle möchte ich mich bei allen bedanken, die mich direkt oder indirekt bei der Anfertigung dieser Arbeit unterstützt haben.

Zunächst gilt mein Dank Prof. Dr. Ralf Zimmermann für das äußerst spannende und anwendungsnahe Thema, die Aufnahme in die Arbeitsgruppe und die freundschaftliche Betreuung.

Dr. Martin Sklorz möchte ich danken, der mir geholfen hat, mich in dem Thema trotz der recht kurzen Einarbeitungszeit zu Recht zu finden und auch für Fragen und Diskussionen immer zur Verfügung stand.

Darüber hinaus möchte ich mich natürlich auch für die gute Zusammenarbeit bei den aktiven und ehemaligen Kollegen der gesamten Arbeitsgruppe bedanken, namentlich herausgehoben Maren, Jasper, Christian, Christoph, Martin, Claudia, Sabine, Harald und all den anderen.

Dem BMBF (Bundesministerium für Bildung und Forschung) und dem VDI (Verein Deutscher Ingenieure) danke ich für die Finanzierung und Betreuung des „Safe Inside“ Projektes. Michael Pütz (BKA), Guido Törber (Schindler Endoskopie Technologie), Bert Ungethüm (Airsense Analytics GmbH) möchte ich für die gute Zusammenarbeit und die Möglichkeiten im Projekt danken.

Darüber hinaus gilt mein Dank auch Dr. Andreas Walte, der mir als Geschäftsführer der Photonion GmbH gerade in der finalen Phase der Arbeit Freiräume geschaffen hat, um diese fertig stellen zu können.

Ich danke meinen Freunden und Ehrenamtskollegen, die für den manchmal nötigen Abstand gesorgt haben.

Nicht zuletzt gilt mein ganz persönlicher Dank meiner Familie, meinen Eltern, meinem Bruder und natürlich dir Franzi, dass ihr für mich da seid und mich immer unterstützt habt, auch gerade die schweren und frustrierenden Phasen zu überstehen.

Herzlichen Dank!

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Abstract

Global terrorism, terroristic attack, organized crime, or clandestine drug laboratories are recent dangers in our globalized, fast, and connected world. Thus, it is even more important to develop a fast, secure, sensitive, selective, and—most importantly—reliable analytical method to detect these common threats. This work focuses on a steady sampling method used especially for substances having a low vapor pressure, partially combined with a thermal instability. In this classification, many of the common explosives need to be sorted, as well as some common narcotics appearing as salt compounds such as the cocaine hydrochloride. In addition, this study sheds light on selectivity enhancement to get reliable results and increase the confidence of an operator to the results.

First, the ambient pressure laser desorption (APLD) sampling is introduced. Using 4-ns short-pulsed laser radiation of 532-nm wavelength enables direct shockwave ablation of target molecules from an investigated surface. The desorbed analyte molecules can be analyzed with varying analytical instruments. However, for practical and security reasons the laser radiation was coupled with glassy fibers to reach hidden surfaces such as the inside of shipping containers, boxes, or pieces of luggage. In general, the transfer line transporting the analytes to the detector needs to be heated to avoid surface adsorption and a loss of substance inside the transfer line.

Second, soft ionization techniques such as single photon ionization (SPI) or chemical ionization (CI) in an ion trap mass spectrometer (IT-MS) are discussed. For a wide range of narcotics, SPI allows a very selective, fragment-free ionization with simultaneous suppression of matrix molecules such as nitrogen, oxygen, or gaseous water. Within the project measurements, SPI ionization energies (IE) and the respective appearance energies (AE) of fragments were performed using the BESSY II synchrotron (German translation: “**B**erliner **E**lektronen **S**peicherring Gesellschaft für **Sy**nchrotronstrahlung mbH”). In this way, the IEs and AEs of various compound classes such as drugs, narcotics, explosives, warfare agents, and many individual compounds were determined. Consequently, the resulting CI was chosen as the ionization method for the explosives. This decision was based on the relatively high IEs of many explosives, an AE that is in some cases below the IE, and a weak photon cross section of many explosives; thus, the needed sensitivity and limits of detection (LOD) for an effective application could not be reached using SPI.

Abstract

Additionally, to further enhance the selectivity and reliability of the substance identification, the MS^n capability of the IT-MS system was used. It allows a conscious fragmentation of an analyte mass getting an accessorily fragment fingerprint spectra to verify an identification.

In a semifield test the functionality of ambient pressure laser desorption (APLD) could be successfully shown in conjunction with a handheld IMS device and with the SPI-IT-MS and the CI-IT-MS. These tests were performed at and in cooperation with the Bundeskriminalamt (BKA) in Wiesbaden, Germany. Consequently, the investigated analytical method could be tested with real crime scene samples and specially prepared samples.

1. Introduction

In an increasingly globalized and interconnected world, the potential risks become more and more global, more diverse, and much more present. Major events and individual and goods traffic are only a few examples of potential threats and targets of terrorist attacks. In light of these increasingly present threats, there is a challenge in developing detection devices with enhanced selectivity and sensitivity with a simultaneous requirement of system mobility.

The common analytical pathway forms a sequence of sampling and sample preparation, and preseparation, separation, and detection with a subsequent data analysis. However, especially for security-related substances and applications, time is a major challenge in addition to the ones previously mentioned. In general, a balance among all of these parameters needs to be found to get an optimal result in relation to the respective analytical task and application.

According to the disproportionate time consumption of single elements of the whole detection sequence, namely processes like sampling, sample preparation, and preseparation, there is a huge optimization potential. Another important parameter that focuses primary on the correctness of a chemical analysis is the sampling step. [2] In light of this fact, ambient pressure laser desorption provides a fast, easy, and time-saving alternative method for surface sampling. Thus, there is an excellent suitability of APLD sampling for less volatile substances generally characterized as a result of the low vapor pressure. [3–5] In this context, the explosives are the most prominent class in the range of security-relevant substances. Additional problems arise typically as a result of the relatively low thermal-destruction threshold of explosives. In contrast to other sampling methods, the APLD reveals its specific strengths especially in this context.

After reducing the time and effort needed for the sampling and sample preparation using APLD, a selective and sensitive detection device is needed to avoid additional time and trouble caused by an interposed preseparation such as GCs, when coupled further with selective detectors like MS systems. In mass spectrometry, especially soft ionization techniques provide reliable results because of the reduced undesirable fragmentation and a clear signal to substance classification. Target specific fragmentation, namely MS^n, can additionally increase the information content and the reliability of an analysis.

2. Security-Relevant Substances

A wide range of chemical substances poses potential threats. The respective scenarios and appearances differ in the concerned target group, harm intensity, spatial limitation, and effects. Although chemical warfare agents (CWAs), explosives, or toxic industry chemicals (TICs) generally have an enormous hazard potential for commonality substances, drugs are primarily an individual hazard potential. Further threats occur for clandestine laboratories and respective fire or explosion sources. Naturally occurring substances that can be used for terroristic attacks such as explosives or substances that develop their harmful potential through accidental or conscious release are much more interesting regarding civil security. An overview of different categories within the chemical, biological, radiological, nuclear, and explosive (CBRNE) substance classes, and examples of respective security-relevant substances, are shown in Fig. 1.

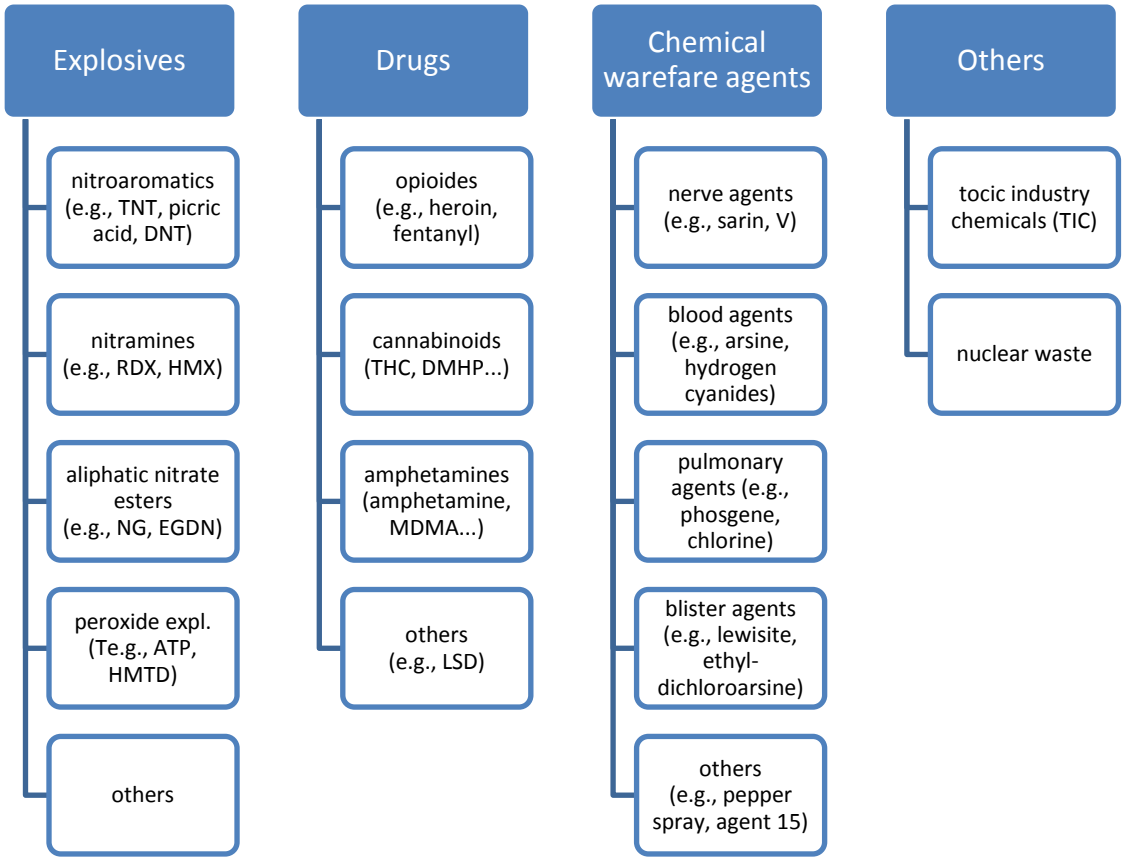

Fig. 1. Schematic overview of different groups, classes, and examples of security-relevant substances (composed according Schramm) [6]

In the current work the focus is primary set on explosives, drugs, and partially on TICs. The CWAs are highly volatile and extremely toxic in smallest concentrations; thus, the analytical challenge would be the sensitivity of detection and not the sampling strategy. APLD aims to trace detection on surfaces, such as detecting hidden explosives or finding clandestine laboratories.

2.1. Explosives

Gunpowder or black powder is considered to be the oldest explosive in the world. Although it first appeared in Europe in the 13th century, it was invented approximately 400 years earlier in China. However, it was the invention of Nobel's Dynamite, which introduced a more secure handling of explosives and enabled a variety of applications. In addition to Nobel's Dynamite, trinitrotoluene (TNT) is the most famous explosive in the world. It can be synthesized through nitration, starting with toluene over the precursor steps p-nitrotoluene (p-NT), the 2,4-initrotoluene (2,4-DNT). [7] The first documented synthesis of TNT was made by German Chemist Dr. J. Wilbrand in 1863. [8]

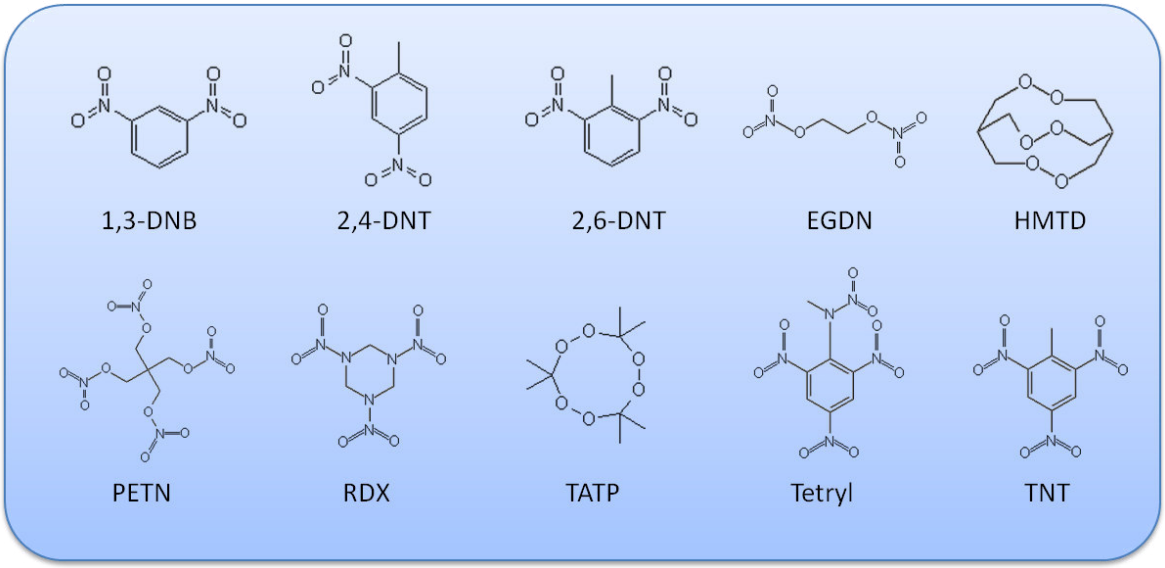

Fig. 2. Chemical structures of some common explosives (1,3-DNB: 1,3-dinitrobenzene; 2,4-DNT: 2,4-dinitrotoluene; 2,6-DNT: 2,6-dinitrotoluene; EGDN: ethyleneglycoldinitrate; HMTD: hexamethylenetriperoxidediamine; PETN: pentaerythritoltetranitrate; RDX: hexogen or cyclotrimethylenetrinitramine; TATP: triacetonetriperoxide; Tetryl: 2,4,6-trinitrophenyl-methylnitramine; TNT: trinitrotoluene)

Modern explosives can be found in many fields of civilian industry and applications such as mining, material science and engineering, demolition business, or in theater and movies. Of course, it is also used centrally for military purposes. Nevertheless, the focus of this work is especially on the illegal usage of explosives in, for example, terrorist attacks. Naturally, in this context there are nearly all kinds of explosives, such as industrial, military, and the homemade explosives. To enhance the security and facilitate a potentially necessary redetection, so-called taggents are used to label it during or after the production process. Normally, homemade explosives and explosives from illegal sources do not have this security feature, which complicates the detection of them

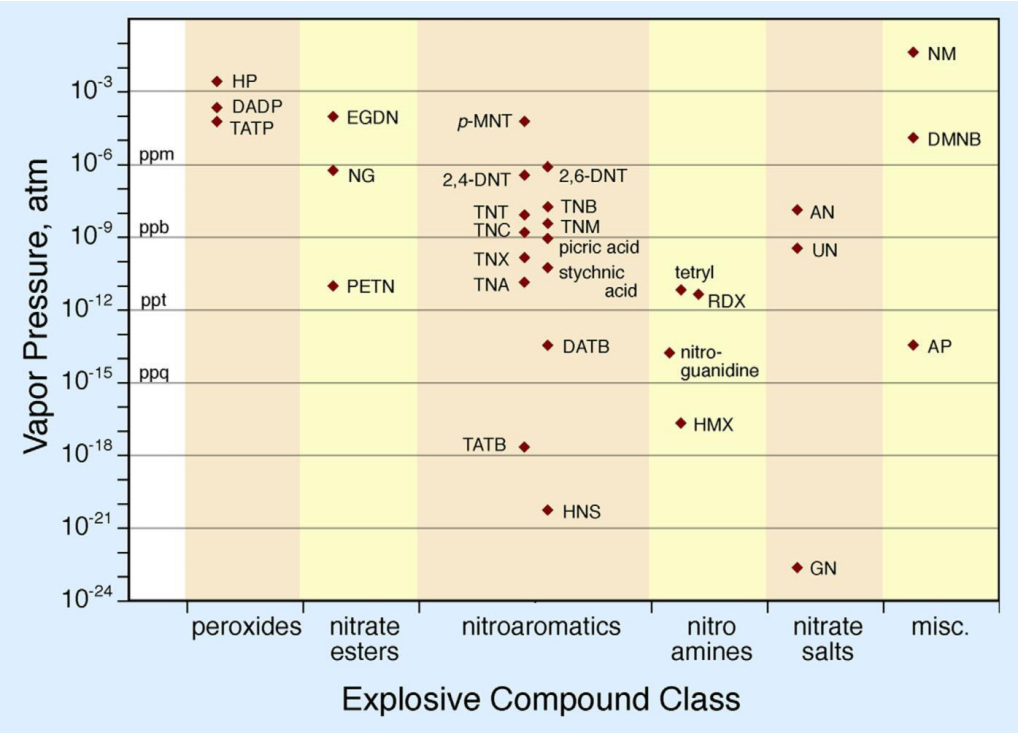

Fig. 3. "Plot of reviewed vapor pressures of explosives at 25°C respective the related explosive compound class" (directly copied from Ewing et al. [5])

In addition to the commonly practiced methods to detect explosives, as summarized in chapter 3, there are many scientific concepts to improve or replace these standards. [9] One of the major topics in recent years is the liquid homemade explosives such as triacetone peroxide (TATP), synthesized by using acetone and hydrogen peroxide. [10] However, other peroxide-based explosives are still the focus of scientific development and forensic investigation. [11–13] A commonly used technique for a fast detection of TATP is ion mobility spectrometry (IMS). [14] Furthermore, the sampling is one of the central issues in detecting security-relevant substances. The most prominent method is to use wipe pads for sampling, especially when trying new detection strategies for such explosives as PTR-MS. [15] However, there are alternative scientific sampling and detection concepts, such as desorption-electro-spray-ionization (DESI). [16] For surface sampling of explosives with very low vapor pressure, laser ablation IMS technology provides an effective solution. [17] Because one critical aspect in using IMS detection of

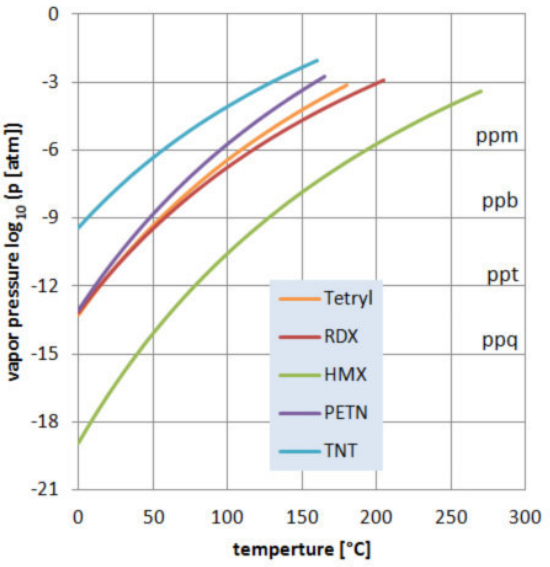

Fig. 4. Diagram of temperature dependency of vapor pressures for some explosives up to their specific thermal destruction threshold

security-relevant substances is the selectivity, it can be combined with other sensors to build sensor arrays or more selective techniques such as IMS-mass spectrometers. [18, 19] Generally, there are two main points of criticism to the actual use of IMS in routine controls, especially to the false alert causing subject's selectivity and sampling. [20]

Substance	MW [g/mol]	Lower VP limit [atm]	Upper VP limit [atm]
2,4-dinitrotoluene	182	$2.86 * 10^{-07}$	$8.84 * 10^{-06}$
2,6-dinitrotoluene	182	$7.46 * 10^{-07}$	$3.17 * 10^{-06}$
HMX (oktogen)	296	$3.94 * 10^{-18}$	$3.12 * 10^{-16}$
PA (picric acid)	229	$9.71 * 10^{-10}$	$9.71 * 10^{-10}$
PETN (nitropenta)	316	$7.00 * 10^{-12}$	$1.80 * 10^{-10}$
RDX (hexogen)	222	$3.14 * 10^{-12}$	$2.33 * 10^{-11}$
TATP (acetone peroxide)	222	$4.36 * 10^{-05}$	$2.44 * 10^{-04}$
Tetryl (nitramine)	287	$7.41 * 10^{-12}$	$7.41 * 10^{-12}$
TNT (trinitrotoluene)	227	$4.26 * 10^{-09}$	$6.80 * 10^{-07}$
Urea nitrate	123	$3.88 * 10^{-10}$	$3.88 * 10^{-10}$

Table 1. Literature-based summary of lower and upper vapor pressure limits of explosives at 25 °C [5]

A review of various ion-spectrometric methods for ultra-trace detection of explosives was made by Makinen *et al.* in 2011. [21] Nevertheless, the final detection is only the last step in the whole detection strategy.

Figure 3 summarizes the vapor pressures at 25°C of many explosives respective of the specific compound class and potentially needed gas phase detection limits. In summary, there are partially big variances in the documented vapor pressures as exemplarily shown in Table 1. However, because of the often very low vapor pressure, explosives are basically an interesting substance class for detection enhancement using APLD sampling. Figure 4 illustrates the vapor pressure dependency regarding a temperature increase. The displayed curves end at the thermal destruction threshold of the respective explosive. Even though the vapor pressure can be significantly increased by heating up the sample, the reached order of magnitude is still a problem for detection directly from the gas phase. In real sampling, further parameters as air flow and exchange also increase the difficulties. Furthermore, not all objects can be heated up easily.

2.2. Drugs and narcotics

The Betäubungsmittelgesetz (BtMG) is the general guideline for classification of narcotics in the range of common medical drugs. [22] Especially important are the Annexes I to III, because of the detailed listed substances, which are covered by the BtMG. The most restricted category is Annex I, which includes the "illegal drugs" such as LSD, heroin, cocaine, cannabis, and psilocybin. These substances need permission for use, trade or distribution, whereas this permission can only be issued exceptional for science or other use in public interest. Substances in Annex II can be traded, but not distributed, not even through prescriptions. Annex III substances are tradable and prescribable drugs such as morphine. Nevertheless, permission is needed for all listed substances. Moreover, an important factor especially for classification of new products like the upcoming herbal mixtures is that only specific substances can be classified and not substance classes or mixtures.

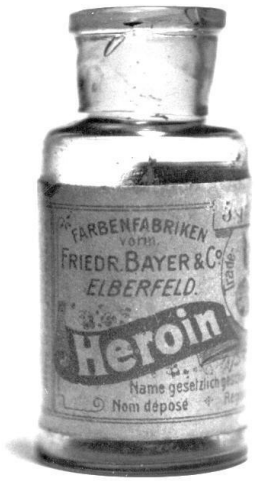

Fig. 5. Photo of a Bayer heroin bottle, produced before World War I by the Synthesis Pathway, developed by Felix Hoffmann in 1896 [1]

There are several substances that were developed or discovered for medical issues and later classified as illegal such as LSD, MDMA, or heroin. [23-26] In general, the classification of single drugs, narcotics, or other intoxicating substances is primarily driven by social norms and values, their temporal changes, as well as their negative effects on the society.

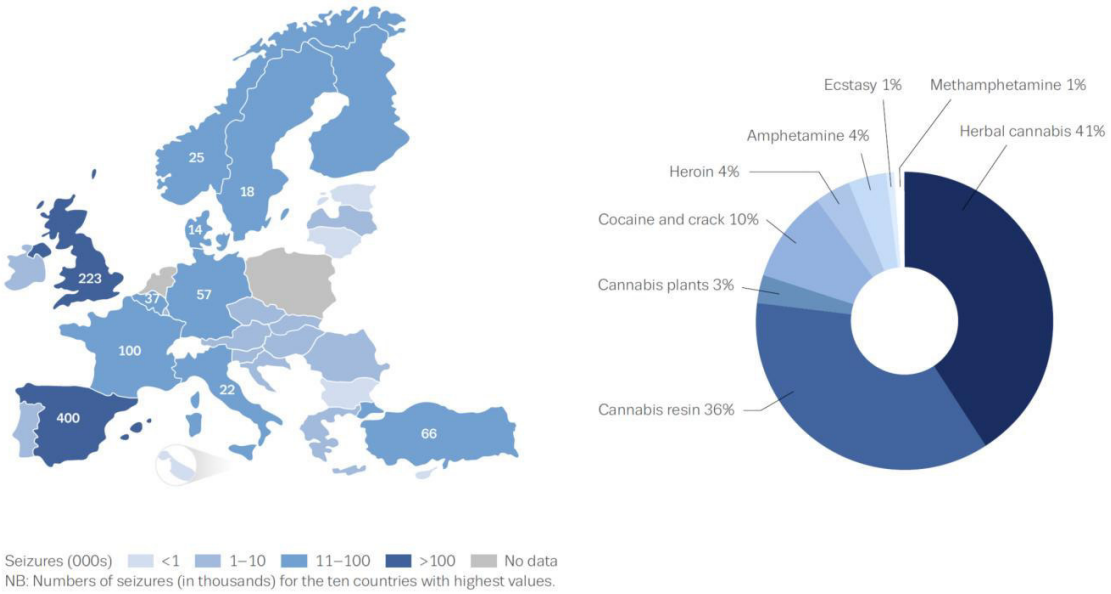

Fig. 6. (*left*) "Number of reported seizures by country (left) and proportion of seizures for the main drugs (right), 2011" (figure directly copied) [27]

In general, regarding Fig. 1, three main classes of illegal drugs can be differentiated. These are the opioids, containing such substances as heroin or fentanyl, the cannabinoids with the main representative tetrahydro-cannabinol (THC) and amphetamines, summarizing many “synthetic” drugs as MDMA (Ecstasy). Nevertheless, there are several illegal drugs that cannot be assigned to the mentioned classes, such as exemplarily lysergic acid diethylamide (LSD). Opioids, and especially heroin, had the development idea of a painkilling sedative and euphorigenic effect, which suppresses negative feelings like pain, fear, or emptiness and replaces it with happiness. [28] The amphetamines, with the most prominent being Ecstasy (MDMA), act in an increasing euphoriant and relaxing way by facilitating the communication and interaction with other people—on both a verbal and physically level. Thus, because it breaks down mental barriers and allows a deep exploration of one’s own feelings and thoughts, it is also used in psychotherapy. [29] The third class, and most widely spread, are the cannabinoids (Δ9-THC). In general, THC has a nausea suppressing, pain-relieving, anti-inflammatory, and relaxing effect. [30] Respective of the concentration of other recent cannabinoids in hemp plants, the effects differ among different types.

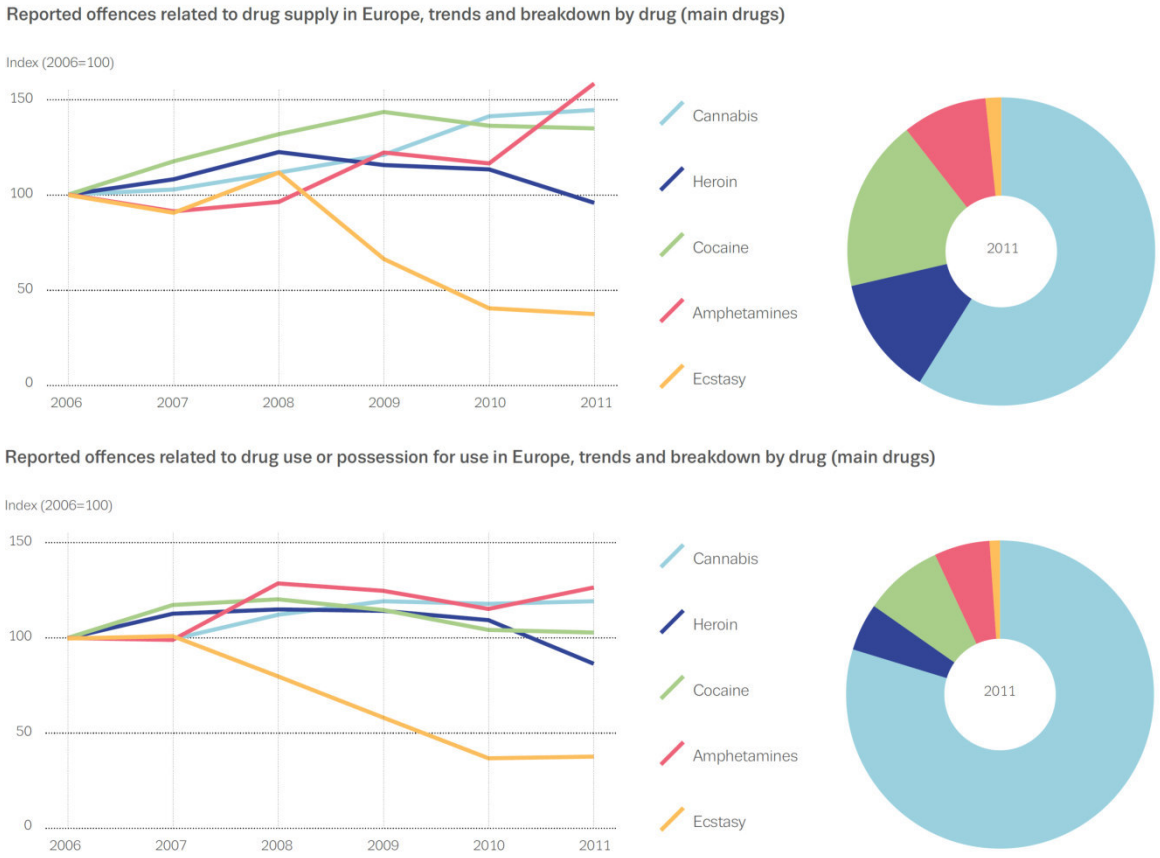

Fig. 7. Diagrams of the development of drug-related offences respective of the supply side (above) and the consumer side (below) since 2006 (figure directly copied) [27]

In connection with production, trading, and consumption, various criminal offences can be observed. Figure 7 illustrates the development of drug-related offences in Europe since 2006, separated for the most important illegal drugs. A clear decrease can be observed for Ecstasy on the consumer side as well as on the supplier side. Although the criminal offences on the consumer side have increased only slightly, on the supplier side a significant rise can be observed. Regarding civil security aspects, especially clandestine laboratories are of enormous interest. Figure 8 shows a professional clandestine laboratory producing MDMA for ecstasy tablets in the range of hundreds of thousands.

Fig. 8. Fully equipped clandestine MDMA (Ecstasy) laboratory near to the Dutch border; the picture was taken within a field test measurement campaign in collaboration with the BKA

Because of the demand on fast and reliable analytical tools for security-relevant applications, including forensic ones, the development is a scientific topic. Similar to the elaborations in chapter 2.1, the scientific challenge can be divided again into the sampling and the detection topics.

One upcoming method for surface sampling is direct analysis in real time (DART), which can be used to sample a great variety of surface materials. This was especially shown for some common narcotics such as amphetamines, cocaine, heroin, fentanyl, and ketamin by Grange *et al.* [31] This technique was also tested for the detection of GHB (γ-Hydroxybutyric acid), also known as the “date rape drug” in liquids. [32] An increased

variety of the date rape drugs in four different drinks was investigated using PTR-MS with dynamic headspace sampling and direct liquid injection by Jürschik *et al.* in 2012. [33] Additionally, the PTR-MS technology could be successfully used for the detection of other common drugs using headspace sampling. [34]

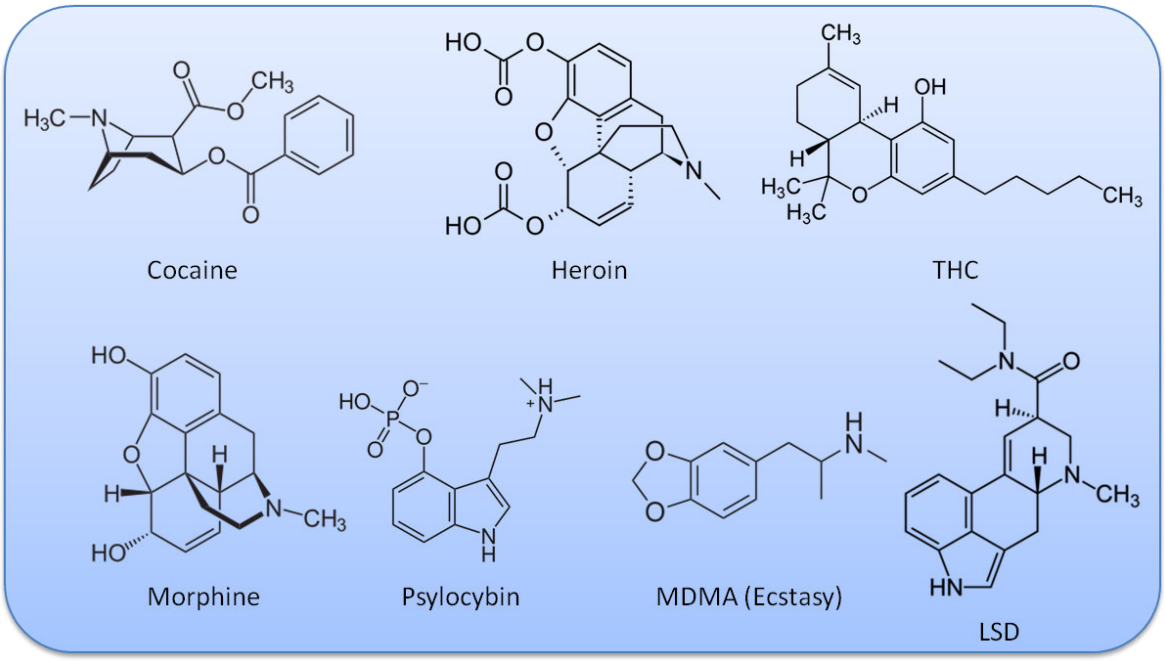

Fig. 9. Chemical structures of some common "illegal" narcotics

However, the most exciting and often investigated question of trace detection of illegal substances is the one for drug traces on the surfaces of banknotes and their distribution by counting machines. This question was investigated for several common drugs using different techniques like IMS, tandem MS, DART-ToF-MS, and DESI-MS, with the result being that cocaine contaminations are the most distributed on up to 75% of the banknotes with regard to the respective study and location. [35–38]

Concerning the actual work, the focus on detecting traces of illegal drugs and respective precursors is primarily to find clues about clandestine laboratories that represent potential security threats on the neighborhoods and populations.

2.3. Precursors, toxic industry chemicals, chemical warfare agents

Beyond explosives, drugs, and narcotics there is a wide range of other substances that need to be classified as security relevant. First, there are the precursors to explosives, drugs, and narcotics; and second, there are substance classes such as TICs and CWAs. Some examples of these groups are presented in Fig. 10. Thus, APLD is relevant only for some representatives of these classes in the following few special applications, and detection examples should be presented.

Sampling from contaminated surfaces is especially important to agrochemicals such as insecticides or pesticides. The determination can be performed using wipe pad IMS, LD IMS, or DESI techniques. [39–41] In contrast, CWAs are gaseous if released intentionally or by accident. Because of the high toxic potential and low effect-threshold level of chemical warfare agents, a sensitive detector such as an IMS is needed. [42]

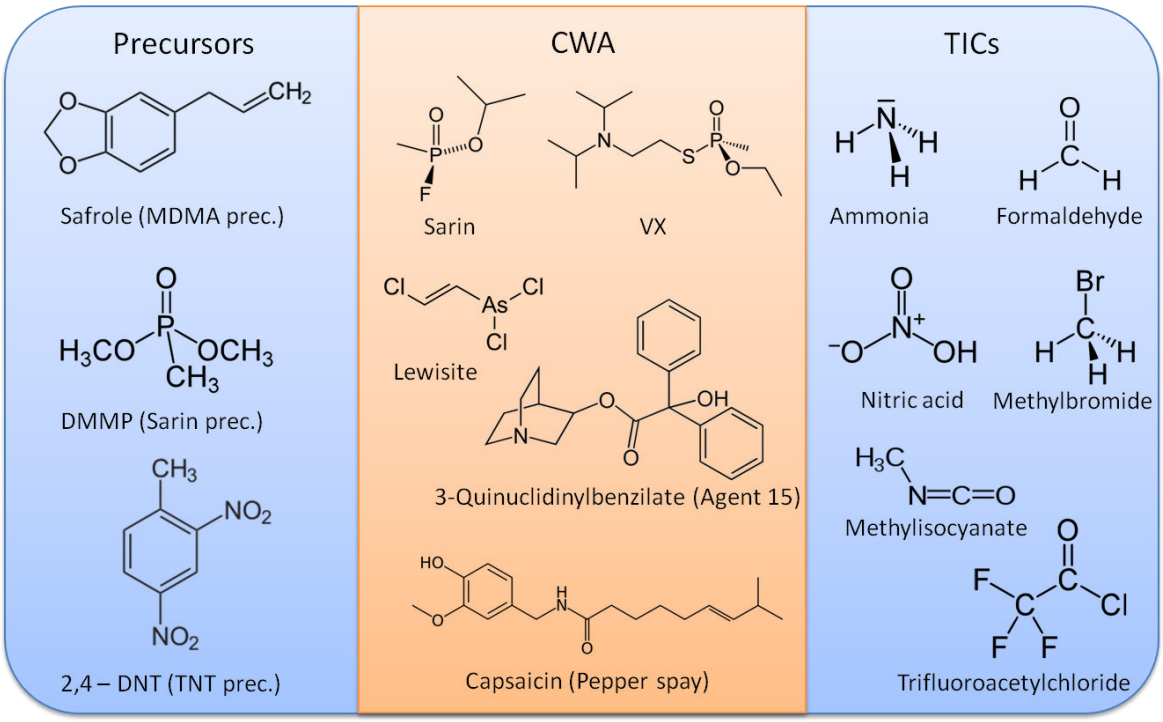

Fig. 10. Chemical structures of drugs, explosive and CWA precursors, a selection of some CWA structures, and a few representatives of the TIC class

Although the use of CWAs in weapons was outlawed internationally since 1997 by the Chemical Weapons Convention (CWC), from time to time respective reports of actual use by terrorist groups or governments appear in the media. Within this convention, the development, production, stockpiling, and use are prohibited. Responsible for the destruction control is the Organization for the Prohibition of Chemical Weapons (OPCW). Only six U.N. countries did not ratify the CWC: Angola, Burma, Egypt, Israel, North Korea, and South Sudan.

3. Commonly Used Detection Strategies for Explosives and Drugs

In actuality, many detection strategies for explosives and drugs are used simultaneously. The respective portfolio ranges from laboratory applications such as GC-MS, fast-detection IMS systems using wipe pad sampling, a wide range of animal-supported detection, down to unreliable rapid wipe tests.

The general question for the right detection system is often the challenge between animal and technically based methods. Figure 11 shows a schematic comparison of the fundamental advantages of animal use as detection systems versus a technically based solution. Although the discussion is much more versatile, it can be summarized as follows: Although offering the same sensitivity, the animal-based methods are faster and highly mobile, whereas technical devices score in selectivity, stamina, and reproducibility. The important aspect of cost is not answerable in general terms: expenses for the devices and maintenance costs versus expenses for training the animals and personnel. However, the decision for or against a certain strategy always depends on the specific case, situation, or environment.

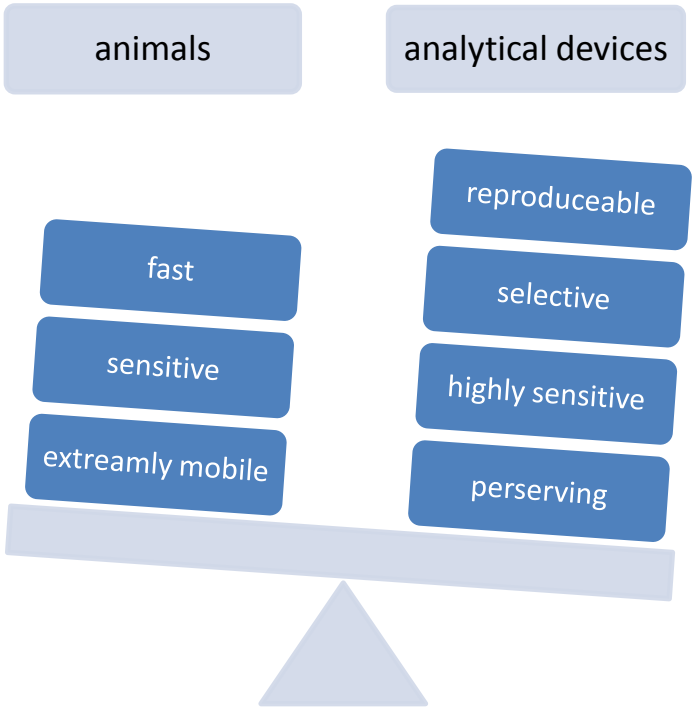

Fig. 11. Schematic comparison between advantages of animals in trace detection of explosives and drugs and respective technically based analytical devices

One of the most critical aspects in trace detection of many explosives is the relatively low vapor pressure. This leads to the requirement of an adequate sampling strategy and a sensitive detector. In daily use controls on traces of explosives as performed at airports, canines are used in addition to ion mobility spectrometers. Trained dogs have been used

for hundreds to thousands of years, for example, as hunting dogs. [43] Furthermore, in World War II dogs were used to locate explosives and bombs. [44] Since this time, the range of use has expanded to other fields such as the detection of pipeline leaks, melanomas, brown tree snakes, flammable or ignitable liquids, guns, drugs, or as rescue dogs searching for injured or dead people. [45–48] The detection of screwworms by dogs is also important. [49] A description of the general pathway of scent detection by a dog is provided by Furton *et al*. [44]

In cases of explosive detection by dogs there is a wide discussion about the effectiveness and reliability of these detections. The U.S. Department of Defense requires, for example, a detection rate of at least 95% for nine explosive standard odors, whereas the North American Police Work Dog Association defines a minimum demand of 91.6% detection rate of six explosives in four of five different environments. [50, 51] Concerning to the low vapor pressure problem of many explosives, the detection by dogs would be limited using pure explosives. The detection succeeds because of the side products, organic contaminations, or artificially added marker substances (taggant of explosives). The side products of exemplarily nitrocellulose production and its detection were characterized in an essay by Fetterolf. [52] In addition to the positive detection training of dogs, in contrast there is the negative training with blank samples and, more importantly, with substances that mask the smell of the target or distract it. Examples of such substances are aspirin, baby powder, breath mints, candy, coffee powder, pet food, shampoo, tobacco, and many others. [44] Alternatively, and especially for routine controls at airports or other places with increased security, technical scanning solutions have been developed. Figure 12 shows a variety of commercially available systems for luggage and goods control. All of these devices are based on IMS detectors. The inlet technologies range from the wipe pad in the IONSCAN devices and the direct gas inlet in the SABRE 5000 and GDA2. These techniques enable a very fast (less than 10 s) and sensitive detection of a manageable number of target substances (at least 40 substances for the IONSCAN 500DT of Smith Detection, U.K.). [53] There is a big challenge in increasing the selectivity to avoid commonly expensive and critical false alerts. Another critical aspect of these systems, especially in detecting substances with very low vapor pressure, is the sampling method. Gas phase sampling is unsuitable for these substances. Wipe pad sampling postulates that the substances can be transferred to the wipe pad, and more difficultly, that the substance can be desorbed thermally without destruction or significant loss. Furthermore, the wipe pad sampling is the most time-consuming step in this analysis.

Fig. 12. Commercially available IMS detectors for security application: (a) IONSCAN 500DT (Smith Detection, U.K.), the latest version of a wipe pad test device for explosives and narcotics [53]; (b) IONSCAN 400B (Smith Detection, U.K.), the previous version to the IONSCAN 500DT (most popular trace detector for explosives and narcotics) [54]; (c) SABRE 5000 (Smith Detection, U.K.), a handheld trace detector for explosives, chemical agents, and toxic industrial chemicals or narcotics [55]; (d) Gas Detector Array 2 (Airsense Analytics GmbH, Germany), a handheld trace detector for explosives, chemical agents, and toxic industrial chemicals or narcotics additionally equipped with GPS and WLAN [56]; (e) a mobilized version of the GDA2 device (Airsense Analytics GmbH, Germany)

A third on-site test strategy used especially for drug detection within human control is the rapid drug-wipe test. It uses the saliva, urine, or sweat of individuals in drug screenings for narcotics such as cannabis, amphetamines, cocaine, opiates, methadone, or benzodiazepine and the respective metabolites. The sample is applied to an immunoassay stripe containing specific antibodies that will react when the target substance is available. The reliability of these tests is controversial. In recent years, scientific studies report an enormous enhancement in the sensitivity, accuracy, and selectivity of these tests. The overall correctness of these tests is approximately 90%, although they do vary among the different sampling materials (urine, salvia, and sweat) and the respective narcotic and the test stripes. [57–59]

4. Concept of Laser Desorption

Laser desorption techniques are especially common for combined sampling/desorbing and ionization mechanisms in mass spectrometry such as laser desorption and ionization (LDI) or matrix-assisted laser desorption and ionization (MALDI). However, also for difficult sampling tasks, laser desorption provides variegated potentials especially without the direct ionization. Further developments are ambient pressure laser desorption (APLD) and ambient pressure laser-induced acoustic desorption (AP-LIAD). Because of the high-energy densities needed for desorption and the ionization process, pulsed laser sources are used. A very popular laser type for these applications is the solid state Nd:YAG laser, which can be adjusted in wavelength by frequency multiplication; thus, wavelengths of 1,064, 532, 355, 266, and 213 nm are possible.

$$\lambda = \frac{c}{f}$$

$$c = 299792458\ \frac{m}{s} \qquad \lambda_0 = 1064nm \qquad f_0 = 2{,}82 \cdot 10^{14} Hz$$

Multiplicator	Frequency [Hz]	Wavelength [nm]
1	2.82E+14	1064.0
2	5.64E+14	532.0
3	8.45E+14	354.7
4	1.13E+15	266.0
5	1.41E+15	212.8

The schematic working principle is shown in Fig. 13. The UV wavelength is especially important for the combined desorption/ionization techniques.

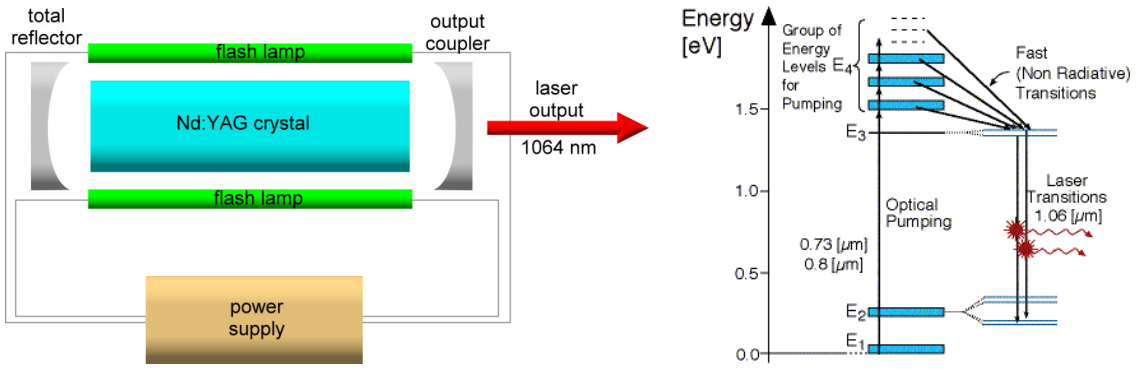

Fig. 13. (*left*) Working scheme of flash lamp pumped Nd:YAG laser; and (*right*) energy-level diagram of a Nd:YAG laser (directly copied) [60]

4.1. Matrix-assisted laser desorption/ionization (MALDI)

"MALDI, matrix-assisted laser desorption/ionization has been a success, no doubt. … Yes, MALDI has come of age!" [61] With these convincing words, the MALDI inventors Franz Hillenkamp and Michael Karas abstract their own review in the year 2000 on their experiences using the MALDI technique, approximately 15 years after their first publication describing a kind of LDI supported by a matrix substance. [62]

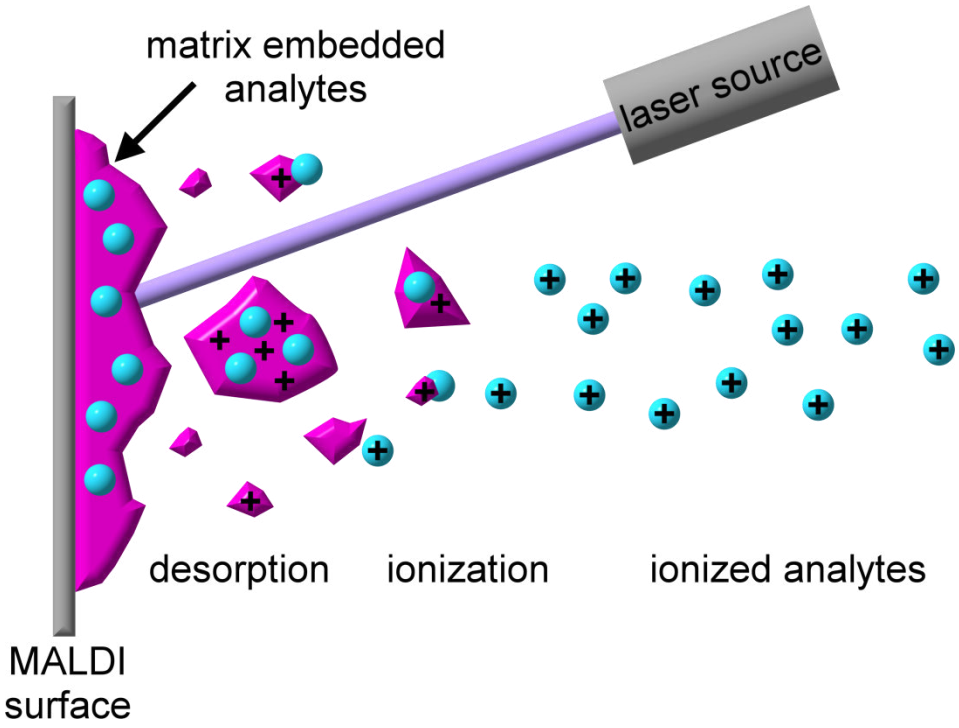

Fig. 14. Scheme of the general working principle of the MALDI technique; the laser pulse primarily couples with the matrix, thus it will be desorbed and ionized; in a second step the entrained analyte molecules will be ionized by the matrix ions through proton or charge transfer reactions

The MALDI process is a combination of a laser-based desorption step of matrix molecules and analyte, and a simultaneous laser ionization of matrix molecules. In a second step the analyte molecules become ionized by the matrix molecules. Thus, the MALDI fundamentals were developed primarily in an experimental way, so there is a wide range of tested lasers and matrix materials. [63] Common matrices are sinapinic acid, DHB (dihydroxybenzoic acid), ferulic acid, CHCA (cyano-hydroxycinnamic acid), picolinic acid, or hydroxypicolinic acid. [64–69] Systematic investigations on laser radiation parameters such as wavelengths, durations, or beam profiles as well as studies on material parameters, matrices, and plume dynamics with a focus on the desorption process in MALDI technology was made by Dreisewerd *et al.* [70] Further investigations on the special and temporal behavior of the desorption plume (formation, expansion, and scattering) was made in 2005 by Leisner *et al*. [71]

Concept of Laser Desorption

The second aspect of focus in the MALDI process is the ionization mechanism and ion formation. Respective of the various experimental parameters, Zenobi and Knochenmuss addressed this topic in an article published in 1998. [72] In general, the analyte ionization can be divided into two phases: the primary and the secondary ion formation. Some possible reaction pathways for primary ion formation are shown in the following equations:

$M \xrightarrow{n(hv)} M^{+\cdot} + e^-$	multiphoton ionization [72, 73]
$MM \xrightarrow{2hv} M^*M^* \rightarrow M + M^{+\cdot} + e^-$	energy pooling [72, 74]
$M^*M^* + A \rightarrow MM + A^{+\cdot} + e^-$	alternative pathway for energy pooling
$M + hv \rightarrow M^*$	excited-state proton transfer
$M^* + M \rightarrow MH^+ + (M-H)^-$	[72, 75]
$M^* + A \rightarrow AH^+ + (M-H)^-$	direct reaction with the analyte
$2M \xrightarrow{n(hv)} (MM)^* \rightarrow M^+ + M^-$	disproportionation reactions [72]

Further ionization principles are based, for example, on thermal ionization effects, pressure pulses, spallation, or desorption of preformed ions. The secondary ionization reactions are quite as diverse as the primary ones. The assumed reaction pathways are, for example, proton transfers (protonation or deprotonation), cationization, or electron transfer reactions.

MALDI as an ion source for mass spectrometric investigations is typically used for bigger molecules like peptides, proteins, or polymers. [76–78]

However, tendencies using MALDI technology under atmospheric pressure can also be observed in other ionization techniques. [79–81] Because of the relatively high signal background on lower masses caused by the MALDI reagents, this technique cannot be used for a reliable detection of smaller molecules. An application of using the porous silicon (pSi) sample layers without matrix coverage is called desorption/ionization on silicon (DIOS). [82–85] It could also be used for drug detection. [82] This method is an intermediate stage to the common LDI technique.

4.2. Laser desorption/ionization (LDI)

The most prominent difference between published MALDI and many reported LDI techniques is the type of matrix used. Although MALDI uses normally, organic matrix molecules, LDI uses various inorganic substances or special enhancing surface modifications. One respective example is surface-enhanced laser desorption/ionization (SELDI), which uses special or modified sample surfaces to support the LDI process, with inter alia hydrophobic, ionic, metal affine properties or biochemical-modified surfaces. [86] Gold and silver nano-particles or colloids are examples of inorganic matrices used in various LDI applications. [87–90] The graphite-assisted laser desorption/ionization (GALDI) graphite has an enormous effect on the LDI analysis, assisted by the inorganic matrices of high molecular mass target analytes such as proteins and low molecular weight polymers. [91–96]

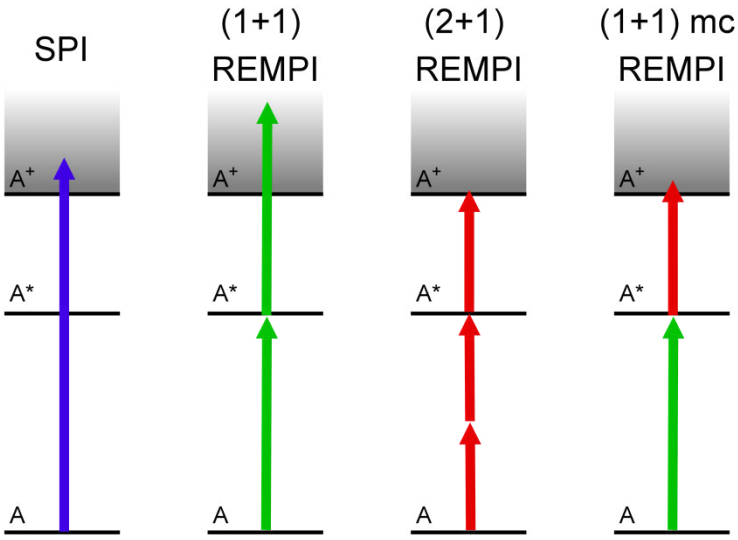

Fig. 15. Schematic comparison of single photon ionization (SPI) and resonance-enhanced multi-photon ionization (REMPI) mechanism [A: electronic ground state; A*: excited intermediate state; A^+: ionization continuum; mc-REMPI: multi-color REMPI (here, two color)]

Nevertheless, direct LDI can be performed if the irradiated analytes are exceeded by directly absorbing the laser energy to produce ions. In general, the resulting ionization processes are often (1+1) resonance-enhanced multi-photon ionization (REMPI) if UV laser radiation in a range between 200 and 300 nm is used for LDI. [97–99] Because of the aromatic structures, asphaltenes are perfectly suited to direct LDI and the respective (1+1) REMPI process, as shown in addition to the others in Fig. 15. They are often used with 266 nm generated by quadrupled Nd:YAG fundamental radiation or 248 nm generated by KrF laser. [100–105]

However, direct LDI is in opposition to the matrix-assisted varieties, which are primarily used for large molecules such as proteins, peptides, and enzymes, and normally used for smaller compounds in a mass range up to 1,000 m/z, such as cell metabolites, with the advantage of doing imaging without special sample preparation. [106]

As another application, electrospray-assisted LDI (ELDI) can be located in the transitional area to the APLD. [107] It is assumed that the laser radiation primarily volatizes the analytical target from the surface. The ionization is later performed by an ESI spray that collects the volatized molecules.

4.3. Ambient pressure laser desorption (APLD)

Within the APLD technique, the sampling is separated from the ionization. This scientific approach enables a higher flexibility in sampling and an increased variability in the ionization method. [108] Furthermore, respective studies have shown that using the optimal energy density, many more neutrals than analyte ions will be formed. [109] General aspects to the desorption mechanism of analyte molecules, surface parameters, and potential coupling methods are provided by Sundqvist, Zenobi, or Cotter. [110–112] Although the combined desorption and ionization regarding LDI and MALDI, as well as other methods such as DART or DESI, are generally well-suited for electropositive analytes like drugs such as cocaine, it is less effective for primarily electronegative substances such as many explosives. [31, 113] Additionally, the spatial separation allows increased distances between sampling and detection; thus, the sampling unit can be brought to the surface and not vice versa, which is important for big objects or those that are difficult to handle.

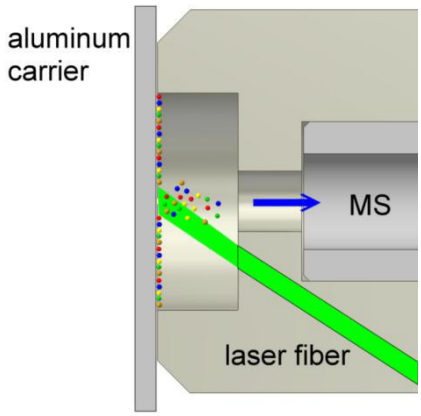

Fig. 16. Scheme of an in-use APLD interface during a laser pulse. The surface-adsorbed molecules of the sample layer are volatized by a 4–10-ns short laser pulse. Finally, the analyte can be sucked into a detection device such as MS or IMS systems

Common laser desorption is either in a vacuum or at ambient pressure if using an inert flow gas. [114–118] In contrast to these LD techniques, APLD is performed not only under ambient pressure but also under environmental conditions as temperature or gas matrix without using an inert gas. In contrast to thermal desorption, by which the sample must be evaporated and may be destroyed by the thermal intake, the laser desorption disperses the sample molecules in a very fast heating process, almost like a shockwave from the surface. [119] Because of the short duration of the single laser pulse in a nanosecond scale, the thermal strain of the desorbed target molecule can be minimized.

Figure 16 shows the scheme of the developed APLD unit and the principle functionality. The short laser pulse volatizes the analyte molecules from the sample surface; thus, it can be aspirated by a detector device such as MS or IMS systems.

4.4. Ambient pressure–laser induced acoustic desorption (AP-LIAD)

Another very gentle sampling technique is laser-induced acoustic desorption (LIAD). The left side of Fig. 17 shows the general working principal. A clear explanation of LIAD fundamentals is given by Golovlev et al. [120] Although the surface is hit by the laser beam, it results in a thermally caused, locally restricted expansion of the material. Because of the linked mechanical tensions, an acoustic wave is released in the material that moves to the opposite surface. Because of the wave reflection at the opposite surface, vibrations are caused that displace the surface-adsorbed analytes and surface particles. For very thin foils or high laser energies, the excitation can also lead to ionization. The right side of Fig. 17 shows the laser-faced front side and the black-ink-covered backside, as well as the effect of the LIAD. The ink is removed completely from the desorbed spots.

However, the mechanism was used previously, without using the LIAD term, to desorb nonvolatile organic molecules directly into the vacuum of a time of flight mass spectrometer. [121] Within this example, the ionization was combined with the desorption using a matrix of potassium iodide and sodium iodide on the metal surface layer of copper or gold. A significant reduction of fragmentation could be shown as compared with direct LD using an UV laser.

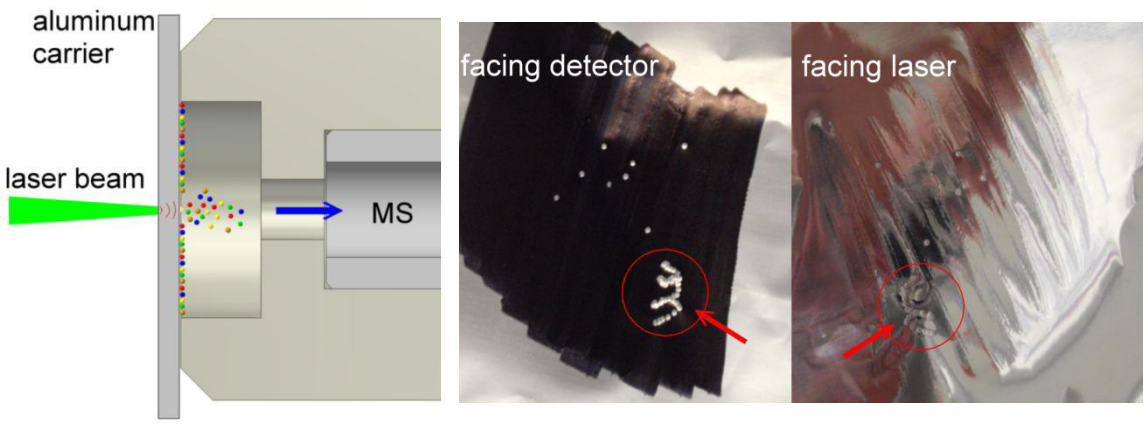

Fig. 17. (*left*) Scheme of an in-use AP-LIAD interface; and (*right*) photos of the black-ink-covered backside facing the detector and the laser facing the front side (desorbed areas are marked in the red circles)

Nevertheless, many parameters influence the LIAD process that can be classified as laser parameters, LIAD foil parameters, and sample parameters. [122] For example, the perfect LIAD sample carrier foil has a high thermal expansion coefficient, low thermal conductivity, and low reflectivity. [123, 124] In summary, metal foils seems to be the most effective LIAD sample carrier. [125]

Alternatively, in many applications the ionizing aspect of LIAD is neglected, whereas the focus is on the production of neutrals and a subsequent selective soft ionization—especially electro-spray ionization (ESI), SPI, chemical ionization (CI), or APCI. [126-130] It could be shown that the main fraction in LIAD are neutrals, whereas only a very small amount are ions. [131–133] Although LIAD was initially developed as a combined desorption and ionization principle, in praxis it is ultimately used as an effective sampling method, coupled with various ion sources.

In summary, because of the very gentle desorption mechanism, LIAD is not only perfectly suited for huge organic molecules like proteins or peptides, but also for sampling labile substances like explosives. [17]

5. Soft Ionization in Mass Spectrometry

For specific analytical problems involved in complex systems, forensic or security-related analyses with a high requirement for accuracy and reliability are key issues for soft ionization techniques in mass spectrometry. There is a big variety of different soft ionization methods, depending on the kind and aggregate state of the respective sample, such as LDI for solid ones, ESI for liquids, or CI for gaseous samples. For APLD investigations in the current work, EI, SPI, and positive/negative CI were used. Figure 18 shows the resulting mass spectra for these different ionization techniques for APLD of 2,6-DNT in reference to the standard NIST spectra produced by using 70 eV EI MS.

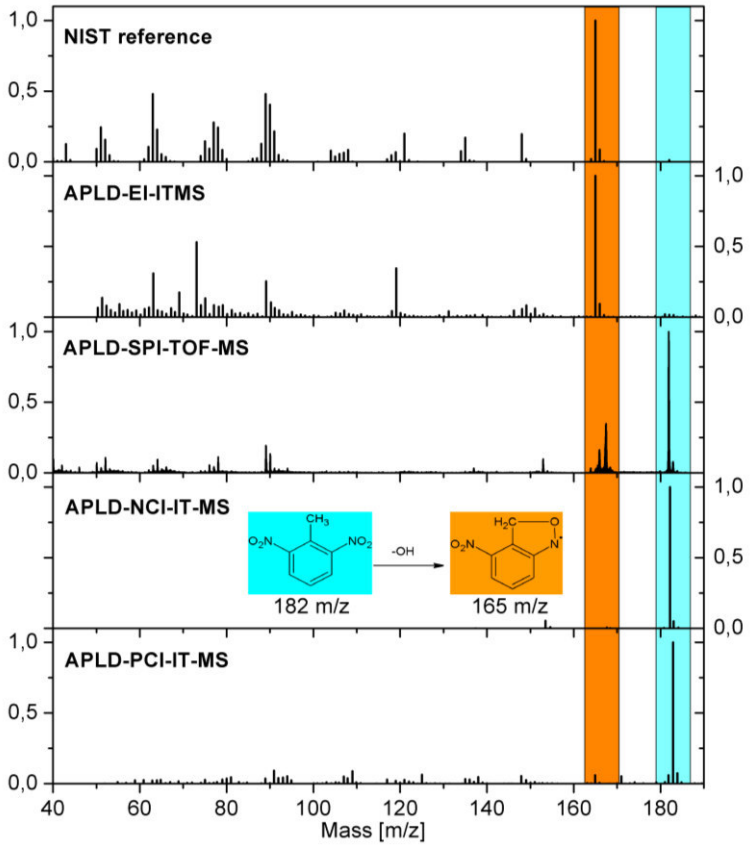

Fig. 18. Comparison of different ionization techniques using APLD of 2,6-DNT (2,6-dinirtotoluene) with the parent molecular signal at 182 m/z and the first fragment at 165 m/z. [134] The differences in the fragment pattern—especially that of smaller fragments in the APLD-EI-ITMS spectra compared with the NIST reference—is caused by additional collision processes in the ion trap using buffer gas and higher pressures (normalized signal intensities)

Using EI MS, the main peak is a fragment signal on mass 165 m/z. The difference in the fragment pattern between the NIST reference and the APLD-EI-ITMS is based on a higher pressure in the IT, resulting in additional collision and reaction processes. However, the main peaks in measurements using soft ionization is the parent molecular peak M^+ on mass 182 for SPI, and negative CI or the $[MH]^+$ on mass 183 for positive CI. Although

fragments do not appear in either positive CI or in negative CI, in SPI the 165 m/z signal as well as signals of smaller fragments can be observed. The reason can be assumed to be two independent processes. First, the fragment appearance energy (AE) of 2,6-DNT can be exceeded with the VUV light source. A further description of this phenomenon is integrated in the following chapter. Second, the appearance of photoelectrons may be produced by photons that hit metal surfaces. These photoelectrons lead to a fragmentation of the target molecules and the appearance of especially smaller fragments. Thus, this measurement was performed in a high-vacuum time-of-flight mass spectrometer; the fragment pattern of the small fragments is comparable with the NIST reference spectrum.

5.1. Single photon ionization (SPI)

Because of the high selectivity, single photon ionization (SPI) as a soft ionization technique can be used especially for analysis of complex chemical systems and mixtures such as combustion and pyrolysis products, smoke compound, polymers, analysis of aerosol particles, or monitoring of roasting processes. [135–142] A second approach is to use SPI for specific matrix suppression in critical or forensic analysis. [143, 144]

Single photon ionization provides analyte ions for mass spectrometric detection by molecular absorption of single photons by analyte molecules. The molecular excitation of the underlying reaction depends on the energy of the photons and can be generally described by the following equation:

$$M + hv \rightarrow M^* \rightarrow M^{+\cdot} + e^-$$

Furthermore, the respective energy, which is needed to ionize a specific substance molecule, is a substance characteristic value called ionization energy (IE). Although too-low energy results only in an excitation of the molecule, a too-high one leads to fragmentation or dissociation. This energetic border is called AE for appearance energy of fragments. A more detailed explanation of the processes is captured by Hatano. [145, 146] Figure 19 illustrates the IE and AE for 2,4-DNT, TNT as representatives from the class of explosives and their precursors, and psilocybin as a representative from the class of illegal drugs and hallucinogens.

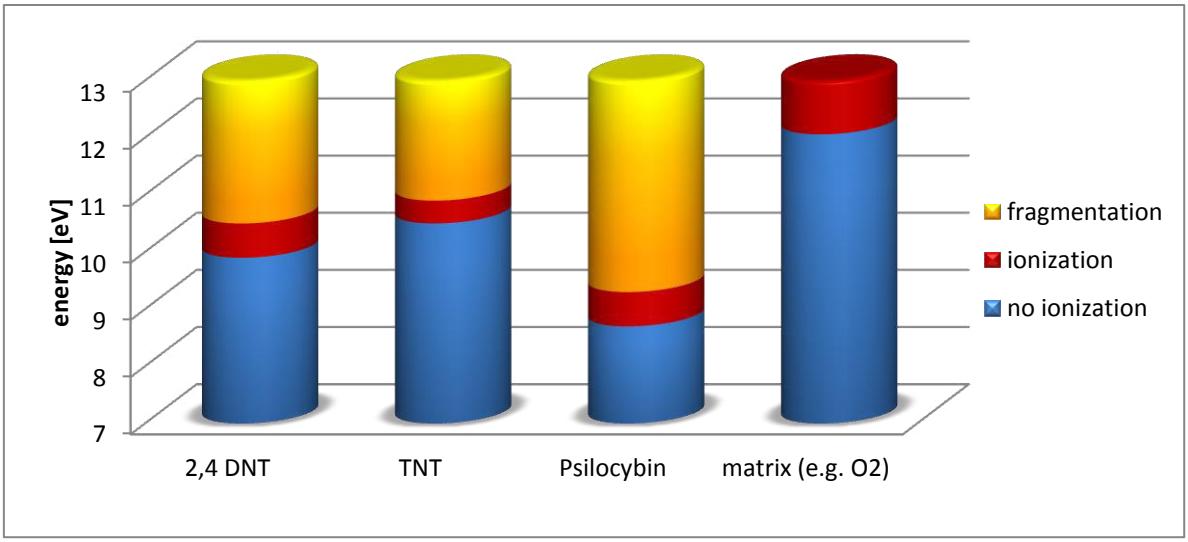

Fig. 19. Diagram of IEs and AEs of 2,4 DNT, TNT, psilocybin, and oxygen as a matrix compound to illustrate different borders in the photoionization process

The most prominent advantage of single-photon ionization is also clarified in Fig. 19. Using common SPI light sources enables the suppression of disturbing matrices such as oxygen (IE = 12.06 eV), nitrogen (IE = 15.58 eV), carbon dioxide (IE = 13.77 eV), and especially water vapor (IE = 12.62 eV) from the gas phase. [147] In addition, this advantage can be used in the analysis of liquid phase mixtures, choosing a solvent that will not be ionized with common SPI light sources. The main idea is to choose a vacuum ultraviolet light (VUV) having an energy that is high enough to ionize all target molecules, but that is low enough that the ionization of matrix molecules is simultaneously suppressed and the appearance of fragments can be avoided or at least reduced.

Because of the complexity involved in the technical aspects of selecting adequate VUV light sources, it is very important to know the specific IEs and AEs of the investigated substances. Common VUV light sources are Kr Excimer lamps (8.4 eV), Ar Excimer lamps (9.8eV), Kr/Ar mixed Excimer lamps (10.7 eV), or laser-pumped Xe-cells (10.5 eV).

In addition to the ionization energy, the ionization cross section has an enormous influence on the suitability of SPI ionization to a given analytical problem. The ionization cross section is a value that characterizes the effective area that an electron needs to pass in order to interact with a neutral molecule. [148, 149] Although the IE of a target substance is low enough that the molecules can be ionized by the chosen VUV wavelength, it is possible that the cross section is that low, in which case the limit of detection is in a nonapplicable range for practical trace detection.

SPI is a powerful tool in mass spectrometry to achieve a selective and sensitive detection and investigation method. [150]

However, one effective and tunable scientific photon source to provide adjustable radiation for IE and AE determination experiments is synchrotron radiation, as it is readily available at the BESSY II synchrotron (German translation: "**B**erliner **E**lektronen **S**peicherring **G**esellschaft für **Sy**nchrotronstrahlung mbH"). Preaccelerated electron packages are stored in a 240-m-diameter circular storage accelerator ring. While passing undulators (structures of alternating dipole electromagnets), the electron packages are forced to oscillate and emit radiation. This undulator-produced radiation can be used for experiments at the various beamlines. Using monochromators (diffraction grids and apertures), the radiation can be separated into user-defined bands of wavelengths. Within the SPI required energy range, the 10-m normal incidence monochromator (NIM) at the quasi-periodic undulator U125-2 can produce photons in a continuum up to energies of 40 eV, whereas the actual mass spectrometric setup is limited by a LiF window at 12 eV. [151] A respective overview of the accelerator and storage rings and the beamlines is shown in Fig. 20.

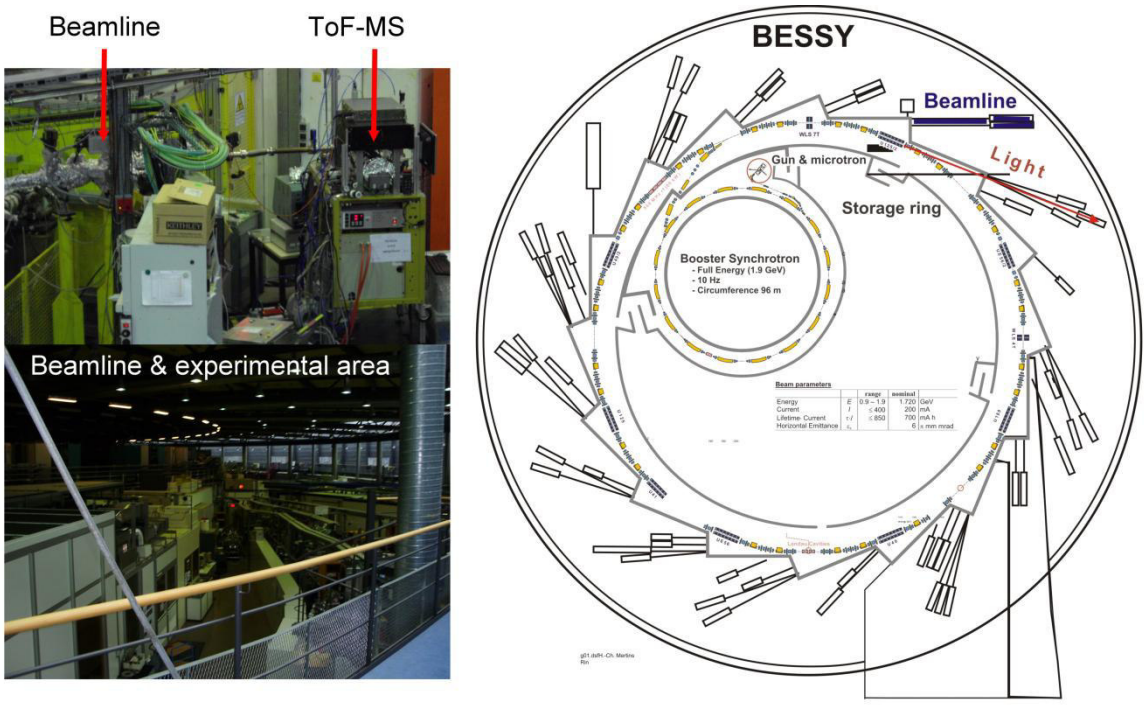

Fig. 20. (*left)* Pictures of the setup (beamline–ToF MS coupling) and the beamline/experimental hall; and (*right)* schematic of the BESSY II synchrotron and respective beamlines [152]

5.2. Chemical ionization (CI)

In the soft ionization techniques, the chemical ionization is one of the most famous and most varied ones. The most common reactant gases for CI source are methane, isobutene, ammonia, or acetonitrile. An exceptional case is the PTR-MS (proton transfer reaction-MS) technique, which uses water as the reagent compound in a drift tube. The chemical ionization technique in mass spectrometry was introduced in the 1960s as an alternative to electron impact ionization (EI), producing manageable and more convincing spectra. [153]

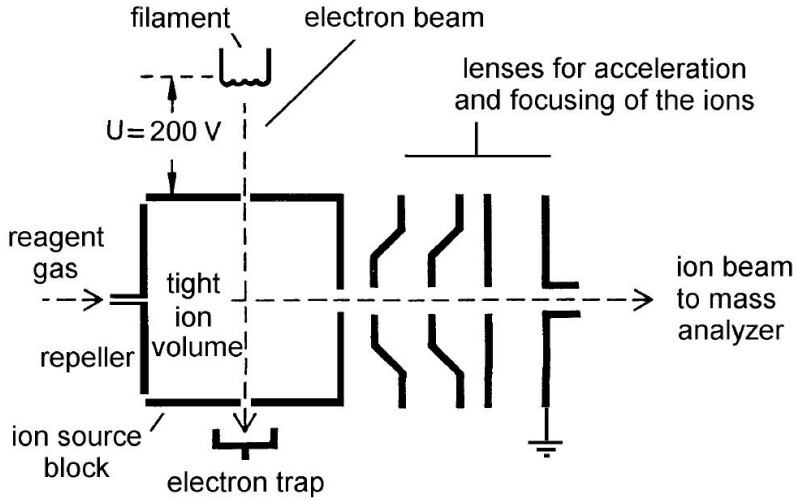

Fig. 21 Schematic layout of a chemical ionization source [taken directly from Gross [148] English version]

The following equations provide the general ionization mechanism using methane as the reactant gas in positive CI mode. In a first step, the reactant ions are produced. The methane molecules are activated with accelerated electrons. Thus, there is a wide range of resulting reactive species. An excerpt of three important pathways of reactant ion formation is shown as follows:

$$CH_4 + e^- \rightarrow \cdot CH_4^+ + 2e^- \rightarrow CH_3^+ + H\cdot$$

$$\cdot CH_4^+ + CH_4 \rightarrow CH_5^+ + \cdot CH_3$$

$$\cdot CH_4^+ + CH_4 \rightarrow C_2H_5^+ + H_2 + \mathrm{H}\cdot$$

The relative abundance of the different reactant ions changes enormously in relation to the partial pressure of the reactant gas. In the rise of the methane partial pressure from 10^{-4} Pa to 10^{2} Pa, the bigger species becomes more significant. [154] Additionally, a reactant gas partial pressure of 10^{2} Pa causes an effective shielding of the analyte molecules against the primary electrons.

In general, there are five mechanisms of ion formation in positive CI, clearly illustrated with different methane-based reactant ions:

$$M + CH_5^+ \rightarrow CH_4 + [M+H]^+ \qquad \text{protonation}$$

$$AH + CH_3^+ \rightarrow CH_4 + A^+ \qquad \text{deprotonation}$$

$$M + CH_3^+ \rightarrow [M-A]^+ + [A+CH_3] \qquad \text{anion abstraction}$$

$$M + CH_5^+ \rightarrow [M+CH_5]^+ \qquad \text{electrophilic adduct formation}$$

$$M + CH_4^+ \rightarrow CH_4 + M^+ \qquad \text{charge transfer}$$

The deprotonation is a special case of the illustrated anion abstraction. In this case, a hydride ion is transferred. A respective behavior can be observed for aliphatic alcohols. [155, 156]

Simultaneously to the positive ion formation, negative ions are also produced. Using a polarity switch for acceleration voltage, it can be decided whether positive or negative ions will be extracted. [148] Possible reactions for negative chemical ionization (NCI) are dissociations, nucleophilic additions, resonance capture, or ion pair production. [157–160]

$$M \rightarrow [M-H]^- + H^+ \qquad \text{dissociation of acids}$$

$$M + A^- \rightarrow [M+A]^- \qquad \text{nucleophilic addition}$$

$$M + e^- \rightarrow M\cdot^- \qquad \text{resonance capture}$$

$$M + e^- \rightarrow [M-B]^- + B^+ + e^- \qquad \text{ion pair production}$$

Because of the electrophilic character of NCI reactions, it is especially interesting for detecting many explosives containing nitro groups such as TNT, RDX, or Tetryl. [161–164] Additionally, many organic matrix molecules will not be ionized in NCI; thus, the resulting spectra become clearer with a better response from the respective targets. As a consequence, a higher sensitivity and enhanced LODs can be achieved.

6. Results and Discussion

6.1. Determination of ionization energies (Publ. 2 and 4)

Within the scientific approach of using soft ionization techniques there is a requirement of knowing some basic fundamental parameters of the defined target substance range, like security-relevant substances. In the specific case of SPI, these parameters are photon ionization energy, fragment appearance energy, and the respective cross sections. Neglecting the quantitative aspect of an analytical measurement, qualitative conclusions to cross sections are sufficient to estimate the suitability of a method to a given task or substance.

Fig. 22. Pictures of the BESSY measurement campaign in October 2010. *(top left)* Building of BESSY II; (*top right*) sample preparation; (*bottom left*) model of BESSY II storage ring, accelerators, and beamlines in the lobby of BESSY; (*bottom right*) ionization chamber of TOF MS with U125/2-NIM fundamental beam; and (*center*) transport box of the explosives samples

However, at BESSY, various substances and many more than the security-relevant ones could be investigated with respect to its individual IEs and AEs. This includes, among others and in addition to the explosives and illegal drugs, growing alkene chains (C16-C31), pharmaceuticals and legal narcotics, flavors, pyrolysis products from wood combustion as levoglycosan, or tobacco compounds. Furthermore, the used energy spectrum ranges from 7.1 to 11.9 eV, extracted from the basic beam using diffraction grids and the maxima of first order to separate the ionization wavelengths/energies. The lower limit is a defined value that should include all target substances, and the upper one is limited by the installed LiF window and the respective spectral cutoff. The separation

window is needed to separate the vacuum in the ion chamber of the MS from the enhanced vacuum in the BESSY beamline. The detailed setup and parameters are described in publication 2. [165]

Figure 22 illustrates some impressions of the measurement campaign in October 2010 (the BESSY II location, the model of the electron accelerator and storage rings, the improvised sample preparation lab corner, and the view through the ionization chamber of the mass spectrometer into the fundamental beam of the U125/2-NIM line).

In addition to an earlier campaign of the working group in 2008, IEs and AEs of an enlarged substance range could be determined. [166] The results of the actual campaign regarding the substance class of explosives are summarized in Table 2.

No.	Substance	Mass [m/z]	IE [eV]	AP [eV] & fragment
1	1,3-dinitrobenzene	168	10.5	>11.8
2	2,4-dinitrotoluene	182	10.0	10.5 [165 m/z]
3	2,6-dinitrotoluene	182	10.0	10.3 [165 m/z]
4	3,4-dinitrotoluene	182	10.0	11.3 [94 m/z]
5	Urea nitrate	123		10.1 [60 m/z]
6	TATP	222	9.1	9.4 [58 m/z]
7	HMTA	140	9.3	
8	HMTD	208	8.7	10.1 [89 m/z]
9	PETN	316		8.3 [45 m/z]
10	Picric acid	229	10.2	10.3 [30 m/z]
11	RDX	222		10.3 [128 m/z]
12	Tetryl	287	10.1	10.3 [241 m/z]
13	TNT	227	10.5	10.8 [210 m/z]

Table 2. Summary of the determined ionization energies of investigated explosives as well as appearance energies of the fragment and the respective nominal mass of the most prominent fragment

Figure 23 shows the IE and AE determination results of 2,6-DNT, an explosives or precursor for TNT synthesis, from the BESSY campaign. The IE value can be specified as 10.0 eV and the AE as 10.3 eV. When comparing the EI spectrum with the huge variety of fragment signals, the SPI spectra shows primarily the response signal of the molecular ion with a nominal mass of 182 m/z or at higher energies, in addition to the fragment formed

by losing OH with a nominal mass at 165 m/z. The respective reaction is further demonstrated in Fig. 23.

Within the example of hexamethylene-triperoxide-diamine (HMTD), which is summarized in Fig. 24, the general idea of a mass spectrometric detection using a SPI source can be explained. Although the ionization of HMTD molecules starts at 8.5 EV photon energy and later fits to the photon flux current, the appearance of fragments is at approximately 9.8 eV; thus, there is a well-usable ionization energy window. Because of the weak signal response, it must be assumed that the HMTD molecules have bad photon cross sections, so an analytical use respective of LOD values is severely limited.

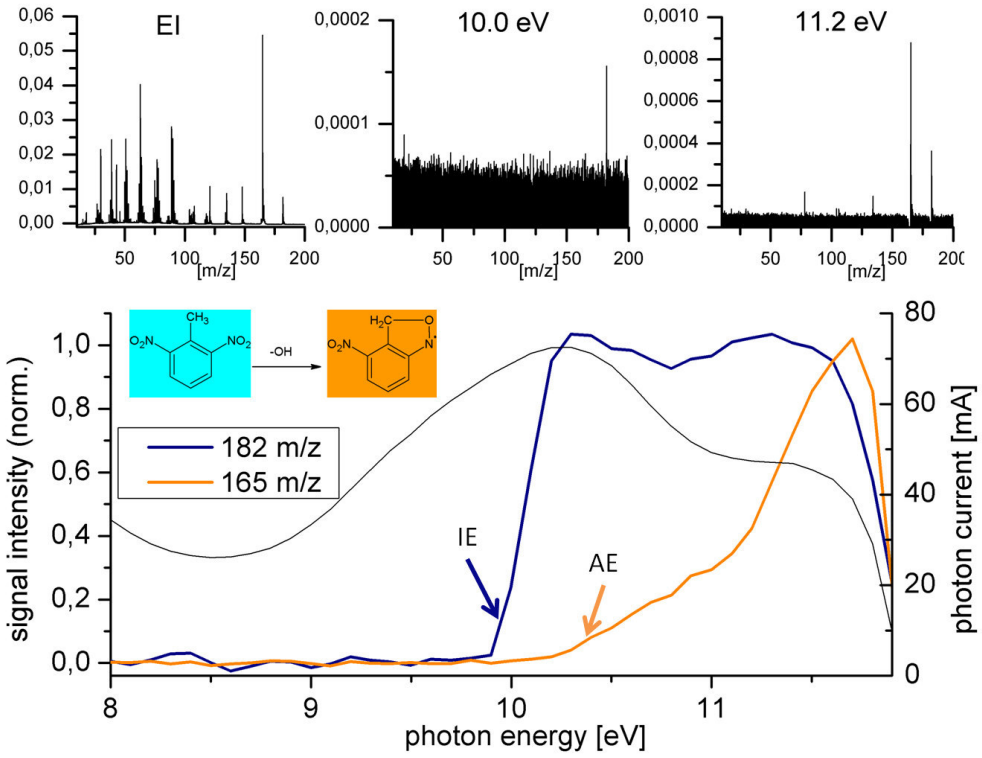

Fig. 23. IE and AE determination results of 2,6-DNT. In the 10.0 eV SPI spectrum, the first appearance of the 182-m/z molecular ion can be observed. Within the 11.2-eV spectrum, some other fragments—especially the 165 m/z fragment—are present. In contrast, the EI spectrum shows a great variety of fragments

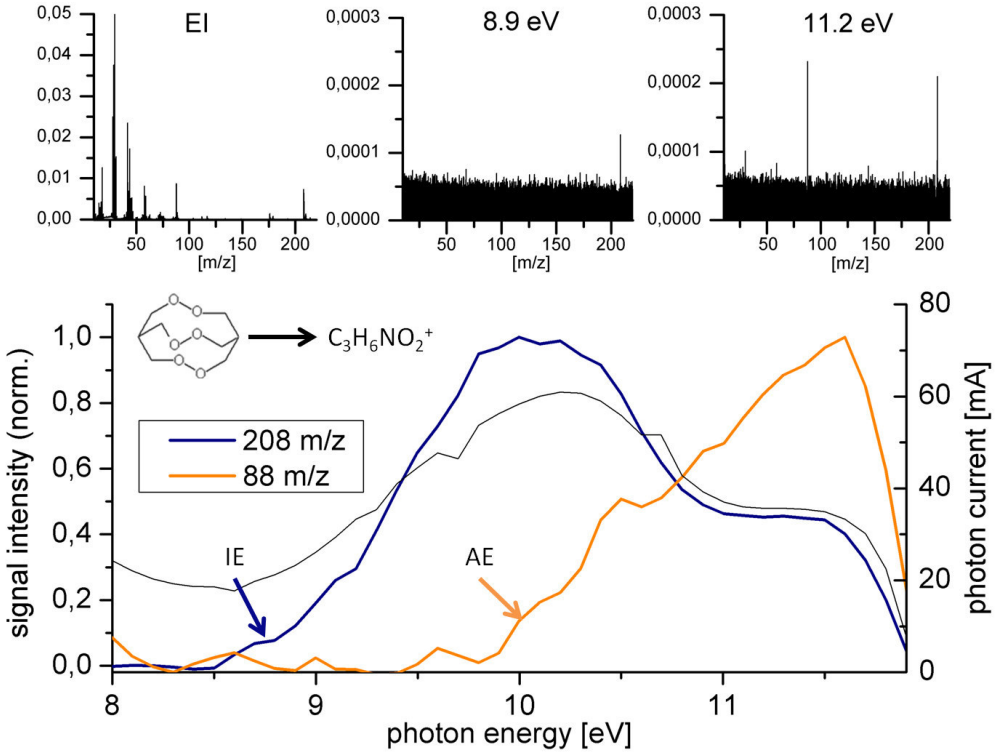

Fig. 24. IE and AE determination results of HMTD. In the 8.9 eV SPI spectrum, the first appearance of the 208-m/z molecular ion can be observed. Within the 11.2 eV spectrum, one additional signal—the 88 m/z ($C_3H_6NO_2^+$) fragment—is present. In contrast, the EI spectrum shows a variety of smaller fragments again

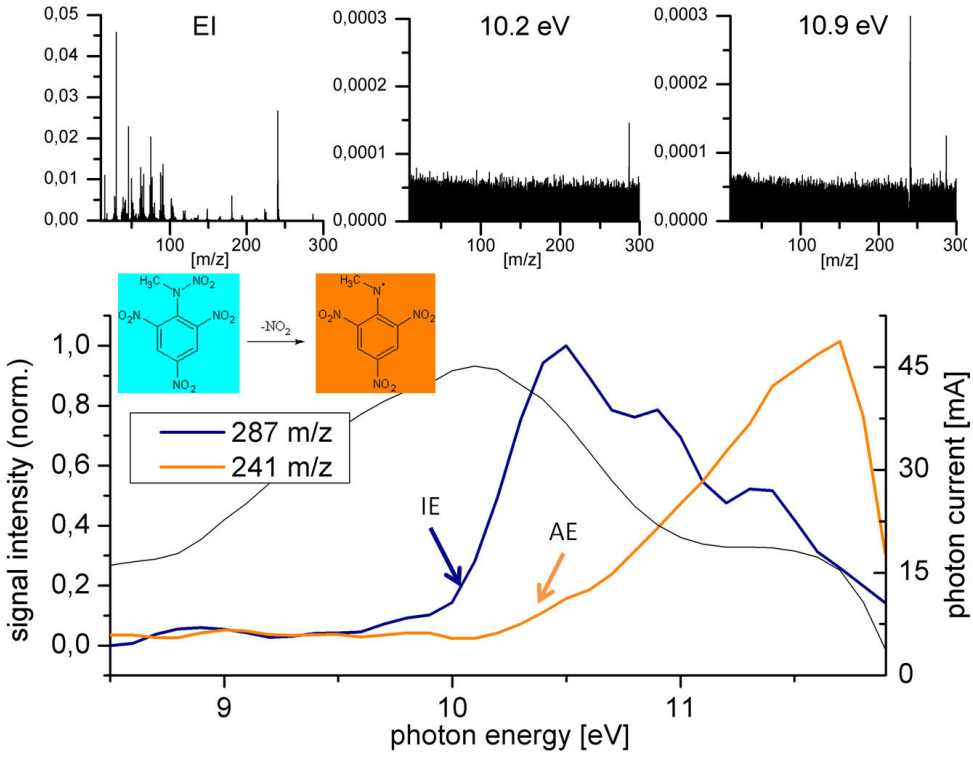

Fig. 25. IE and AE determination results of Tetryl. In the 10.2 eV SPI spectrum, the first appearance of the 287-m/z molecular ion can be observed. Within the 10.9 eV spectrum, one additional signal—the 241 m/z [M^+-NO_2] fragment—is present. In the EI spectrum, the molecular signal is nearly not present

In the case of Tetryl, as illustrated in Fig. 25, two aspects become clear. First, the IE is only slightly below the AE; and second, Tetryl has a very bad photon cross section. Moreover, the cross section of the first fragment, with a nominal mass of 241 m/z, is higher. Although the SPI has big strength, the enormous reduction of unwanted fragmentation, which is primarily important for complex mixtures, can be illustrated especially when comparing the SPI spectra to the EI spectra; the disadvantage of a bad cross section makes SPI unsuitable for practical use in an analytical method concerning Tetryl.

In summary, SPI is a useful ionization method for many substances and classes, including the security-relevant one. Unfortunately, many of the interesting explosives appear to be exceptions, either because they have a too high IE, an IE near or even below the AE, or the cross section is too low to reach the significant LOD ranges.

6.2. APLD and AP-LIAD of explosives using handheld IMS (Publ. 3)

The physical dimension of a mobile detection system is especially relevant and needs to be considered during development. Ion mobility spectrometers can cover this and are distinguished by a high sensitivity, flexibility, and variability in use. [167–172] Figure 26 shows the working scheme of an IMS working with a membrane inlet and a radioactive Ni63 ionization source.

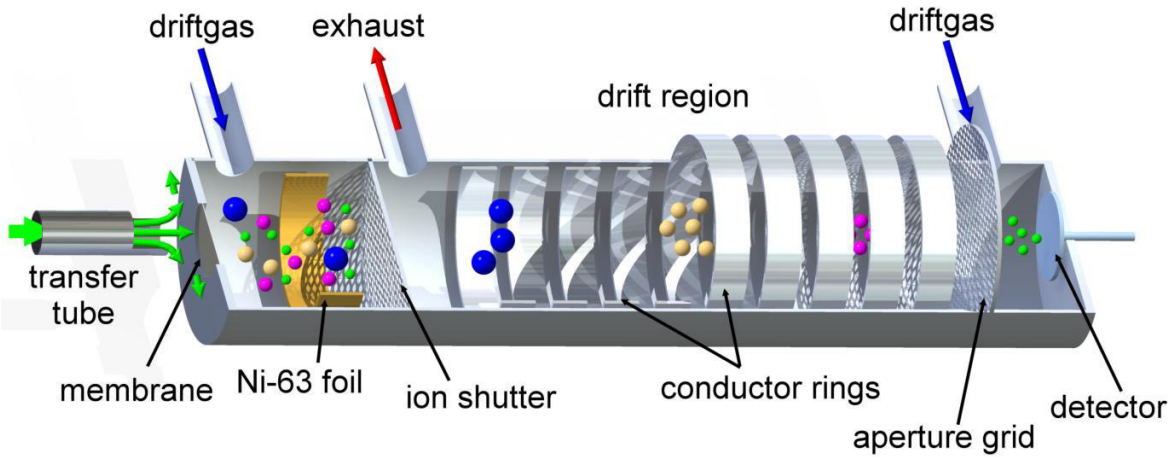

Fig. 26. Working scheme of an IMS drift tube with membrane inlet as it is used in the handheld IMS systems

Furthermore, many different inlet systems and ionization sources such as UV light or corona discharge sources are used for various applications [173–177]. For the current work, a handheld system as described in the upper figure was used. The laser desorption interface as described in Fig. 16 and the one for the laser-induced acoustic desorption

described in Fig. 17 were directly attached to the inlet system of the IMS. A schematic overview is shown in Fig. 27.

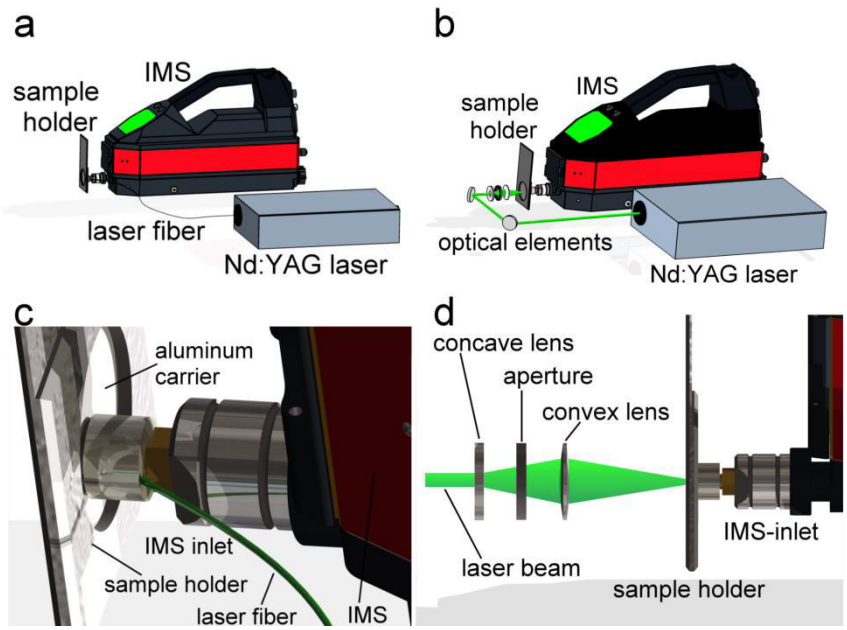

Fig. 27. Schematic overview of the fiber-coupled APLD setup (a & c) and AP-LIAD setup (b & d)

The samples were prepared on a thin aluminum foil carrier using respective dilutions of explosive stock solution. Further details are explained in the respective publication 3. [17] Within the measurements, ethylene glycol dinitrate (EGDN), urea nitrate, pentaerythritol tetranitrate (PETN), hexamethylene triperoxide diamine, hexogen (RDX), tetryl (2,4,6-trinitrophenylmethylnitramine), and trinitrotoluene were investigated using APLD-IMS as well as AP-LIAD-IMS. The determined range of detection limits for the specified substances begins with 0.5–1 ng for TNT and up to 50–100 ng for urea nitrate on a surface of approximately 1 cm^2. In general, the detection limit of AP-LIAD is by a factor of 2 to 4 lower than the one of the APLD. The reason for the higher sensitivity of AP-LIAD can be explained by the different desorption mechanism, as discussed previously. However, in the case of TNT, the laser desorption only assists in the detection process. TNT can already be detected by its own vapor pressure using a handheld IMS system.

Overall, the APLD and AP-LIAD sampling technique, coupled with a fast and handheld IMS device, can be considered a very effective analytical tool for detecting traces of explosives and the respective precursors in a very low nanogram range. In general, there is room for improvement first in the selectivity of the IMS technology by itself, and second, on the transfer tube and membrane inlet, to increase the already excellent sensitivity to explosives.

6.3. Online detection of explosives via SPI/CI-IT-MS (Publ. 1)

The general aim of this work was to develop the APLD into a working prototype for detecting security-relevant substances, especially with a focus on later use as a standardized trace detection device for responsible governmental authorities. Figure 28 shows the evolutionary steps from the first laboratory tests to the APLD desorption unit used in the prototype.

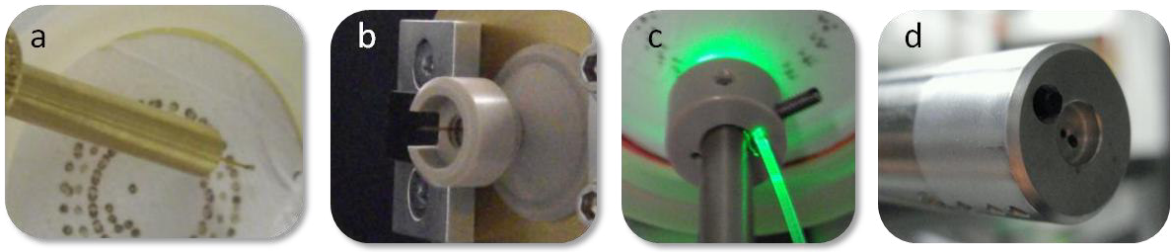

Fig. 28. Evolutionary steps of the LD unit, starting with experiments with open laser beam and sampling capillary. (*a*) The increasing encapsulation enhances sensitivity and LOD values. In the version shown in (*b*), the laser beam is led on the surface using a mirror. To realize a total encapsulation of the desorption volume, the laser light fiber is used. (*c*) The site effect of this construction is an improved laser security. (*d*) The laser desorption unit at the top of an endoscope as it is used in the prototype. A complete capillary heating is guaranteed.

The increasing encapsulation of the desorption unit first enhances the sensitivity of the device and, second, allows greater security in handling the laser radiation. The light is led through a glassy fiber (OPTRAN® WF 600/660T, Ceram Optec®). For technical and security reasons, a laser light wavelength of 532 nm is used, generated by the doubled fundamental radiation of a Nd:YAG laser with a pulse width of 4 to a maximum of 10 ns. For eye safety, the desorption unit is equipped with a surface contact interlock to prevent free radiation.

Figure 29 shows the general concept of the modular-designed prototype. The central issue is the sampling; thus, the system enables the sequential use of APLD, solid phase micro-extraction (SPME), wipe pad, or direct gas phase sampling. Using SPME-fiber gas samples can be collected especially in cavities that are difficult to access. Simultaneously, substance enrichment is accomplished on the SPME surface. Nevertheless, the system is designed for trace detection and the direct gas phase sampling provides highly valuable information, especially to first responders and potential appearing dangers such as explosive gas mixtures.

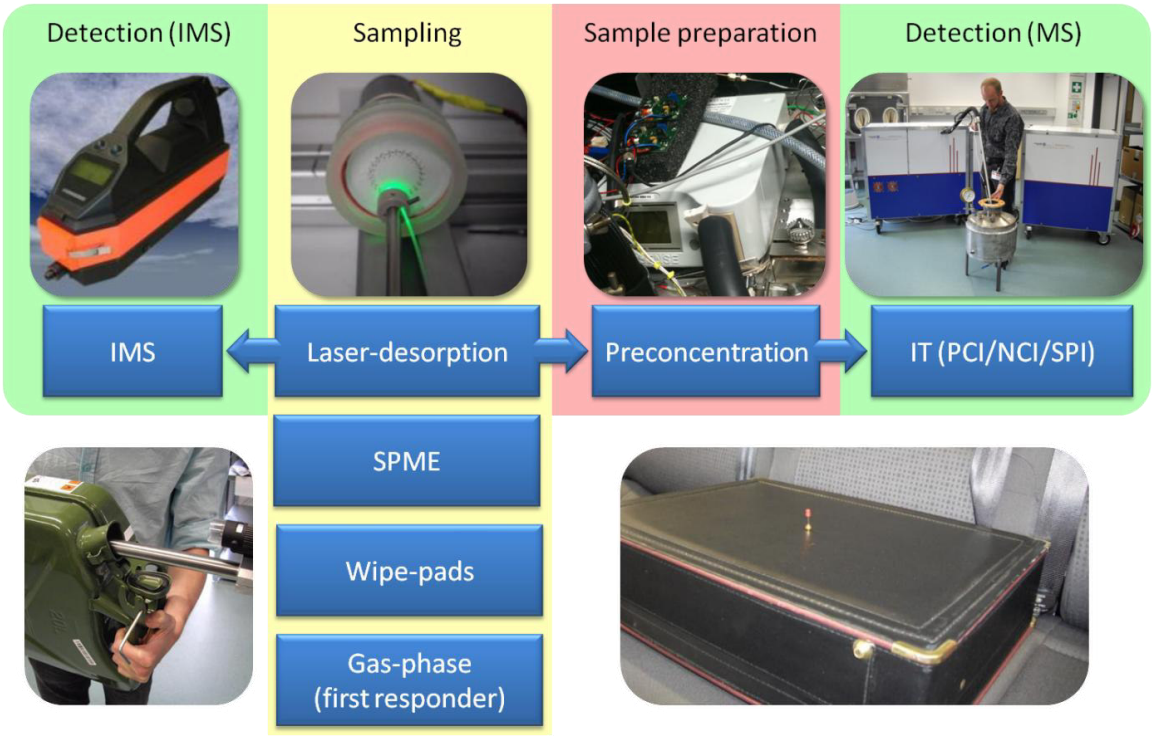

Fig. 29. Workflow and option scheme of prototype used at the Federal Criminal Police Office (Bundeskriminalamt, BKA, Wiesbaden, Germany) with real crime scene samples and simulated samples

Within fast and routine controls, an IMS is available to be coupled modularly to the respective sampling unit. Moreover, to receive a more selective analysis and a more reliable substance identification, the sampling unit can be coupled with a positive and negative Clequipped ion trap mass spectrometer (IT-MS) or with the SPI IT-MS. The MS^n capability of the IT-MS can also improve the selectivity and substance identification.

Furthermore, an optional preconcentration step can be implemented to increase the overall sensitivity. The substrate for enrichment can be adjusted to the respective analytical task or situation.

The prototype was finally tested in the Federal Criminal Police Office (Bundeskriminalamt, BKA, Wiesbaden, Germany) with real crime scene samples and simulated samples. In addition to the explosive samples already published, many narcotic-related court exhibits could be investigated. [178] Figure 30 shows the sampling on a leather jacket used for smuggling cocaine. It was impregnated with a cocaine solution and subsequently dried. In this case, APLD sampling, combined with positive-CI-IT-MS, was used. The spectrum on the left clearly shows the mass signal of the cocaine molecule in addition to many other signals. In comparison with the standard NIST spectrum (displayed on the left), it appears that the signals are related fragments of the cocaine parent molecule. Although the capillary is heated up to 250°C, a delay between desorption and the appearance of the

cocaine signal and a significant signal tailing can be observed. Consequently, it can be assumed that thermally driven adsorption and desorption processes are decisive for this behavior.

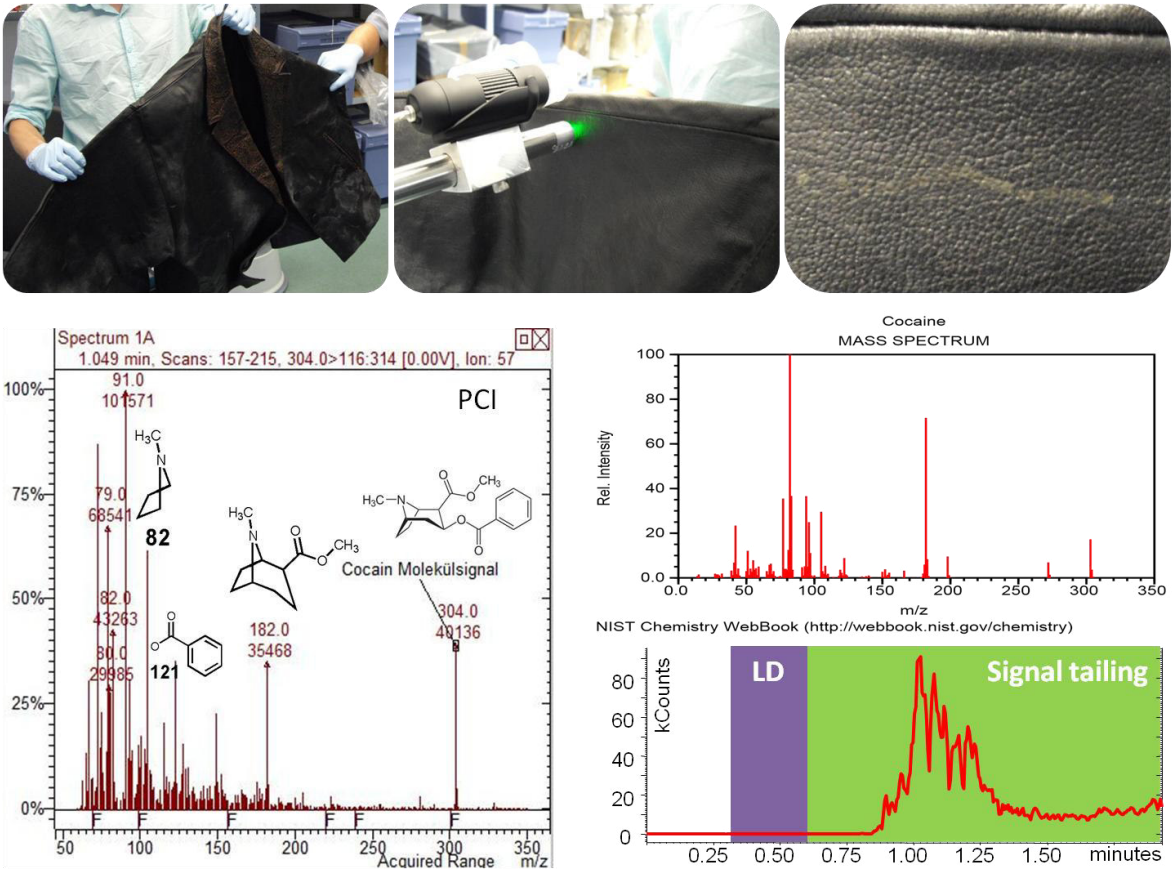

Fig. 30. Investigation of a leather jacket used for smuggling cocaine. (*top*) Photos of the sample and the APLD sampling; (*left*) positive CI-IT-MS spectrum of APLD sampled jacket; and (*right*) NIST reference spectrum and extracted ion signal of cocaine molecule

Nevertheless, the example illustrated in Fig. 31 is not an example to justify the use of APLD, but it is a good one to show the strength on the MS/MS capability. The resulting fragment pattern shows a clear separation and identification compared with other molecules with a m/z ratio of 135, such as benzothiazole, which is used for inks or in the rubber industry, and shows a clearly different fragment pattern.

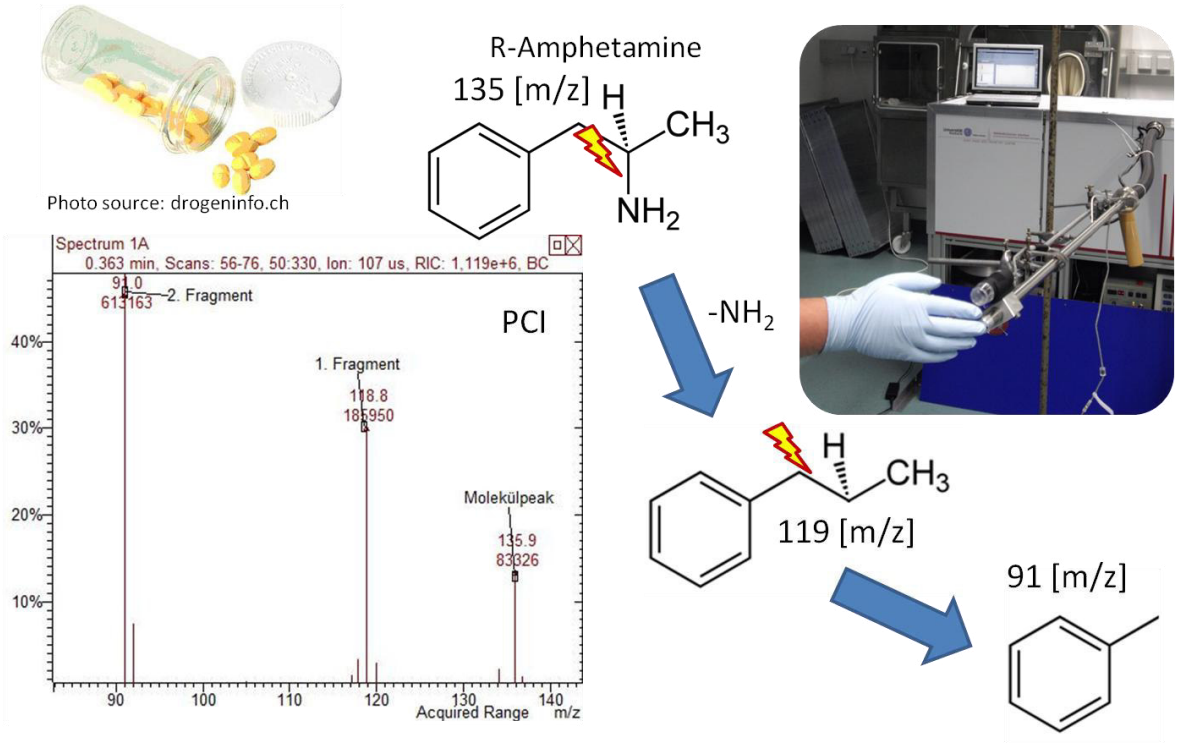

Fig. 31. Determination and identification of amphetamine on a laboratory glove using MS/MS PCI-ITMS. The glove was contaminated by opening an amphetamine vessel

To summarize, in analytical applications the reachable limit of detection (LOD) is always a central issue. In the laboratory-based studies with the prototype, the absolute LOD of a low nanogram range could be achieved, e.g., at 3 ng for TNT. For these measurements, APLD-NCI-ITMS was used. Because there is a general lack of information on the responsible security authorities about surface concentrations of respective substances that can be taken as valid detection threshold levels, a special sensitivity test for the prototype was set up. A total of 500 g of TNT was twice packed into resealable freezer bags. This package was stored in a common briefcase for 1 h under constant room temperature. After removing the TNT package, the leather parts inside the briefcase were sampled as shown in Fig. 32. The TNT traces were clearly measured and identified using MS/MS. This test illustrates that the system reaches the practical, relevant LOD levels for a successful positive detection. Within this test setup, a SPME test was also performed as shown in the lower-right corner of Fig. 29.

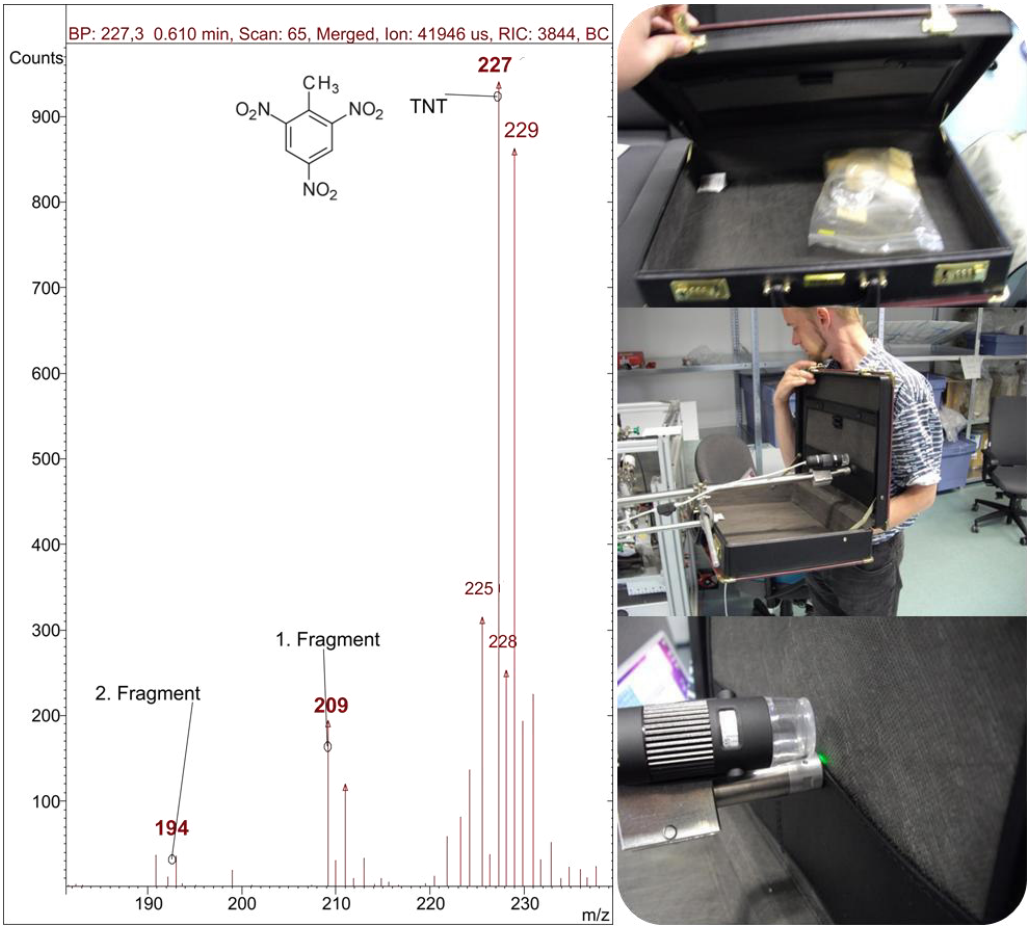

Fig. 32. TNT identification in a common briefcase using the test setup for determination of minimal significant surface concentration levels

To summarize, the developed prototype could be successfully tested with standards, artificially prepared objects, and real crime scene samples. Other real samples are shown in Fig. 33, such as a fuel tank cap used to smuggle heroin, an ammunition box, or a gas can used to transport precursor substances for illegal drug synthesis.

Fig. 33. Photos of other crime scene samples investigated within the measurement campaign at BKA (Wiesbaden, Germany)

7. Summary and Outlook

Ambient pressure laser desorption is a fantastic tool for providing an efficient sampling strategy for security-relevant substances, especially for those with a low or very low vapor pressure. Furthermore, the thermal stress to samples is much less, compared with classical thermal desorption methods, leading to increased fragmentation. In several tests the coupling opportunities of APLD to various detection systems could be shown. The selection of appropriate detection devices, ion sources, and methods in practical use can be done almost without restrictions. An easy, fast, and nearly universal applicable sampling strategy is presented with APLD.

In the presented work, the APLD coupling with a soft ionization ion trap mass spectrometry and the coupling with a handheld IMS system result in effective strategies for the detection of security-relevant substances. Although the selection of handheld IMS systems is not very extensive, especially regarding selectivity, the flexibility and mobility of the device compensates for its disadvantages by focusing on its use by first responders—especially in non-laboratory use—to scan for potential threats. From a forensic point of view, however, the selectivity of such a system is much more important. An explicit and reliable proof of substance identification can be provided using soft ionization with the MS/MS capability of ion trap mass spectrometers.

As it is typically the case for analytical method development, one general aspect for future work is the sensitivity enhancement of the system and the method. Because the current investigation focuses on shipping containers, cargo goods, forensic relevant objects, and similar applications, an extensive overview of the destruction thresholds of the surface materials is not necessary; however, it may be necessary, for example, for routine luggage checks. The laser energy must be high enough to vaporize the target analytes without any visible destruction of the surface. Especially for routine controls, an exceptional potential exists in the use of APLD as a handheld device with fast and small IMS detectors.

In addition to the security-related applications, other potential assignments for the APLD can be identified. It is usable for many kinds of direct sampling on surfaces as a direct alternative for methods such as desorption electro-spray ionization (DESI), direct analysis in real time (DART), and comparable techniques.

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9. Annex

I. List of Figures

II. List of Abbreviations

AE	**a**ppearance **e**nergy
AP-LIAD	**a**mbient **p**ressure **l**aser **i**nduced **a**coustic **d**esorption
APLD	**a**mbient **p**ressure **l**aser **d**esorption
Ar	argon
BESSY	German: "**B**erliner **E**lektronen-**S**peicherring Gesellschaft für **Sy**nchrotronstrahlung mbH"
BKA	**B**undes**k**riminal**a**mt
BtMG	**Bt**äubungs**m**ittel**g**esetz
CI	**c**hemical **i**onization
CWA	**c**hemical **w**arfare **a**gents
CWC	**C**hemical **W**eapons **C**onvention
DART	**d**irect **a**nalysis in **r**eal **t**ime
DESI	**d**esoption **e**lectro **s**pray **i**onzation
DIOS	**d**esorption/**i**onization **o**n **s**ilicon
DMHP	**d**i**m**ethyl**h**eptyl**p**yranande
DMMP	**d**i**m**ethyl-**m**ethyl**p**hosphonat
DNT	**d**i**n**itro**t**oluene
EGDN	**e**thylene **g**lycol **d**i**n**itrate
EI	**e**lectron **i**mpact ionization
ELDI	**e**lectro spray assisted **l**aser **d**esorption/**i**onization
ESI	**e**lectro **s**pray **i**onization
GALDI	**g**raphite **a**ssisted **l**aser **d**esorption/**i**onization
GC	**g**as **c**hromatography
GC-MS	**g**as **c**hromatographic **m**ass **s**pectrometry
GHB	**γ**-**H**ydroxy**b**utyric acid
GPS	**g**lobal **p**ositioning **s**ystem
HMTD	**h**exa**m**ethylene **t**riperoxide **d**iamine
HMX	octogen
IE	**i**onization **e**nergy
IMS	**i**on **m**obility **s**pectrometry/spectrometer
IT-MS	**i**on **t**rap **m**ass **s**pectrometer
KrF	**kr**yton**f**loride
LD	**l**aser **d**esorption

LDI	**l**aser **d**esorption/**i**onization
LIAD	**l**aser **i**nduced **a**coustic **d**esorption
LiF	**li**thium **f**loride
LOD	**l**imit **o**f **d**etection
LSD	lysergic acid diethylamide (German: **L**ysergs**s**äure**d**iethylamid)
MALDI	**m**atrix **a**ssisted **l**aser **d**esorption/**i**onization
MDMA	3,4-**m**ethylene **d**ioxy**m**eth**a**mphetamine
MS	**m**ass **s**pectrometry/spectrometer
MS^n	multiple tandem **m**ass **s**pectrometry
MS/MS	tandem mass spectrometry
NCI	**n**egative **c**hemical **i**onization
Nd:YAG	**N**eodymium-**d**oped **Y**ttrium **A**luminum **G**arnet ($Nd:Y_3Al_5O_{12}$)
NG	**n**itro**g**lycerine
NIM	**n**ormal **i**ncidence **m**onochromator
NIST	**N**ational **I**nstitute of **S**tandards and **T**echnology
NT	**n**itro**t**oluene
OPCW	**O**rganisation for the **P**rohibition of **C**hemical **W**eapons
PCI	**p**ositive **c**hemical **i**onization
PTR-MS	**p**roton **t**ransfer **r**eaction **m**ass **s**pectrometer
REMPI	**r**esonance **e**nhanced **m**ulti **p**hoton **i**onization
RDX	hexogen
SELDI	**s**urface **e**nhanced **l**aser **d**esorption/**i**onization
SPME	**s**olid **p**hase **m**icro-**e**xtraction
SPI	**s**ingle **p**hoton **i**onization
TATP	**t**ri **a**cetone **t**ri **p**eroxide
THC	**t**etra**h**ydro**c**annabinol
TIC	**t**oxic **i**ndustry **c**hemical
ToF	**t**ime **o**f **f**light
TNT	**t**ri**n**itro**t**oluene
U.S.	**U**nited **S**tates of America
UV	**u**ltra **v**iolet
VUV	**v**acuum **u**ltra **v**iolet
VX	O-ethyl S-[2-(diisopropylamino)ethyl] methylphosphonothioate
WLAN	**w**ireless **l**ocal **a**rea **n**etwork
Xe	**xe**non

III. List of Publications for Doctoral Thesis

1. Ehlert S, Hölzer J, Rittgen J, Pütz M, Schulte-Ladbeck, Zimmermann R: Rapid on-site detection of explosives on surfaces by ambient pressure laser desorption and direct inlet single photon ionization or chemical ionization mass spectrometry. Analytical and Bioanalytical Chemistry, 2013. 405(22): p. 6979-6993.

2. Kleeblatt J, Ehlert S, Hölzer J, Sklorz M, Rittgen J, Baumgärtel P, Schubert J K, Zimmermann R: Investigation of the Photoionization Properties of Pharmaceutically Relevant Substances by Resonance-Enhanced Multiphoton Ionization Spectroscopy and Single-Photon Ionization Spectroscopy Using Synchrotron Radiation. Applied Spectroscopy, 2013. 67(8): p. 860-872.

3. Ehlert S, Walte A, Zimmermann R: Ambient Pressure Laser Desorption and Laser-Induced Acoustic Desorption Ion Mobility Spectrometry Detection of Explosives. Analytical Chemistry, 2013. 85(22): p. 11047-11053.

IV. List of Further Publications

4. Ehlert S, Hölzer J, Baumgärtel P, Rittgen J., Sklorz M., Oster M., Zimmermann R. Determination of ionization and appearance energies of explosives and precursors using synchrotron radiation, (in preparation for publication)

5. Hertz-Schünemann R, Streibel T, Ehlert S, Zimmermann R, Looking into individual coffee beans during the roasting process: Direct micro-probe sampling on-line photo-ionisation mass spectrometric analysis of coffee roasting gases. Analytical and Bioanalytical Chemistry, 2013. 405(22): p. 7083-7096.

Annex

Publication	Personal contribution
1.	Design and construction of the modular prototype device, planning and performing the measurements, data analysis, manuscript preparation (text & figures)
2.	Realization measuring setup (preparation of MS device and coupling time of flight MS system to BESSY beamline), planning and performing the measurements at BESSY, supporting data analysis, delivery of text elements
3.	Design and Realization of APLD and LIAD-IMS coupling, planning and performing the measurements, data analysis, manuscript preparation (text & figures)
4.	Realization measuring setup (preparation of MS device and coupling time of flight MS system to BESSY beamline), planning and performing the measurements at BESSY, data analysis and manuscript preparation in progress
5.	Support data analysis, support visualization (figure creation)

VI. Publications

Publication 1

Ehlert S, Hölzer J, Rittgen J, Pütz M, Schulte-Ladbeck, Zimmermann R: Rapid on-site detection of explosives on surfaces by ambient pressure laser desorption and direct inlet single photon ionization or chemical ionization mass spectrometry. Analytical and Bioanalytical Chemistry, 2013. 405(22): p. 6979-6993.

(DOI: http://dx.doi.org/10.1007/s00216-013-6839-8)

Publication 2

Kleeblatt J, Ehlert S, Hölzer J, Sklorz M, Rittgen J, Baumgärtel P, Schubert J K, Zimmermann R: Investigation of the Photoionization Properties of Pharmaceutically Relevant Substances by Resonance-Enhanced Multiphoton Ionization Spectroscopy and Single-Photon Ionization Spectroscopy Using Synchrotron Radiation. Applied Spectroscopy, 2013. 67(8): p. 860-872.

(DOI: http://dx.doi.org/10.1366/13-06988)

Publication 3

Ehlert S, Walte A, Zimmermann R: Ambient Pressure Laser Desorption and Laser-Induced Acoustic Desorption Ion Mobility Spectrometry Detection of Explosives. Analytical Chemistry, 2013. 85(22): p. 11047-11053.

(DOI: http://dx.doi.org/10.1021/ac402704c)