

Laser Desorption of Large Molecules: Mechanisms and Models

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HOW CAN LARGE MOLECULES SURVIVE VOLATILIZATION?

It has always been a challenge for the practitioners of the different spectroscopic methods to volatilize large and thermally unstable molecules. Because of their thermal instability large classes of important materials, available only in solid state, were out of the scope of investigations. This was especially true in mass spectrometry, where the separation and identification of a species depended on the possibility to establish ion trajectories in vacuum.

To overcome this difficulty, several strategies were developed. Already in the seventies, fast heating was looked upon as a possible way to promote vaporization over decomposition [1,2]. Pyrolysis mass spectrometry was the first candidate to make use of this concept. This method, however, has never been able to provide heating rates high enough to avoid fragmentation completely. Other ways to energize solids with a high rate were sought intensively. Medium (keV) and high (MeV) energy ions or atoms impinging on a solid surface turned out to be capable of ejecting large organic ions into vacuum [3]. The corresponding fast atom bombardment, secondary ion and plasma desorption methods exhibited high mass limits in the 30.000–40.000 dalton region, making a vast number of biologically important compounds available for mass spectrometric investigation. Lasers, first regarded as fast heating tools, also proved to be useful in achieving volatilization of complex molecules [4–8].

Recently, further evidence has accumulated, showing that very large molecules (≥ 100.000 dalton) can be brought into gas phase by applying Q-switched laser pulses onto solid–vacuum interface [9–14]. Using matrix assisted laser desorption, even the possibility to volatilize and ionize molecules with masses as large as 250.000 dalton was demonstrated [15]. In this mass region electrospray ionization remained the only rival method [16] to transfer large molecules into gas phase.

Despite of the vigorous progress in methodology, the understanding of underlying processes is lagging behind. Indeed, even the dilemma: How can large molecules survive the energetic environment created by the laser pulse? – has not been addressed yet. In this communication we suggest a general scheme to answer this question on the basis of the energy deposition and redistribution concept [17].

One of the special features of laser light is, that it is able to excite a well defined degree of freedom of the material. In other words, the energy deposited into the sample creates a strongly non-equilibrium situation, where certain degrees of freedom are highly excited, while others retain their equilibrium population. The natural course of events, customary in low heating rate experiments, is to gradually approach equipartition of the excitation energy among the different degrees of freedom. Taken the large energy density achievable by the lasers, it inevitably would lead to the destruction of the large molecules, i.e. to extensive fragmentation.

The possibility to escape degradation arises with the appearance of a disintegration event preceding fragmentation. Let us examine a system which is composed of two subsystems coupled by weak interactions. Subsystem 1 is a good and Subsystem 2 is a weak absorber of the laser radiation. The coupling between the two subsystems can be Van der Waals interaction or cohesion or adsorption forces. We identify Subsystem 2 with the large molecule embedded in, or adsorbed to the other subsystem. Under the influence of a laser pulse, the energy deposited into certain degrees of freedom of Subsystem 1 starts to equilibrate immediately. During the equilibration process, energy has to be mediated by the cohesive and/or adhesive forces to the vibrational modes of the large molecules (Subsystem 2). If, by any means, the cohesive or adsorption bonds break before sufficient energy is transferred to heat up Subsystem 2, relatively cold large molecules can be liberated. A schematic representation of these processes is shown in Figure 1. Two characteristic arrangements are depicted: desorption from a substrate surface as a heterogeneous process (Fig. 1/a) and a homogeneous process leading to phase disintegration (Fig. 1/b). The most common laser desorption experiments are listed in Table 1, where the corresponding subsystems and the possibly involved disintegration processes are also indicated.

In the laser induced thermal desorption (LITD) experiment the large molecules are adsorbed on a metallic substrate or on fine metallic particles. Part of the laser energy is absorbed by the metal leading to extremely high surface heating rates ($\geq 10^8$ K/s) and consequently to desorption [5]. Matrix assisted laser desorption (MALD) is based on embedding the large molecules in ample excess of strongly absorbing, easily disintegrating matrix. Fast heating of the matrix may result in volatilization of the whole phase including the embedded molecules [7]. Laser induced explosive desorption is observed in low coverage adsorption situations above threshold UV excitation levels [18]. Sudden pumping of a system of anharmonic oscillators in external field is thought to lead to phonon avalanche and consequently to non-selective complete desorption. Mechanical stress and shock wave induced by uneven thermal response of the sample to laser pulses can also liberate molecules from the solid surface by mechanical disintegration [4,6]. Under short wavelength UV excitation conditions, certain materials show ablative photo-decomposition in marked contrast to thermal processes [19]. Coherent excitation of repulsive electronic states seems to be a likely explanation of the disintegration phenomenon.

Already at this point, we may anticipate the answer to the question exposed in the title of this section. *Large molecules can survive volatilization if their liberation by disintegration precedes their destruction by fragmentation.*

In the following section of this contribution we address several questions of energy deposition and redistribution. Furthermore, we will put special emphasis on the different disintegration mechanisms in a separate section, for their role has been almost completely neglected previously. Volatilization is not the last step in the laser-solid interaction. Especially not in the context of mass spectrometry, where ion formation leads to the particles finally detected. Therefore, in the closing section we will iterate on ion formation mechanisms potentially involved in laser desorption.

Table 1 Separation of the subsystems in laser desorption experiments and the corresponding disintegration mechanisms

Experiment	Subsystem 1	Subsystem 2	Disintegration
Laser Induced Thermal Desorption	Metal substrate Metal particles	Adsorbed molecule Surrounding mol.	Desorption Desorption
Matrix Assisted Laser Desorption	Absorbing Matrix	Guest molecule	Sublimation
Laser Induced Explosive Desorption	Absorbing molecule	Non-absorbing mol.	Phonon avalanche
Laser Induced Stress Desorption	Thermal Stress	Guest molecule	Crack formation
UV Laser Ablation	Electronic excitation	Vibrational excitat.	Repulsive state

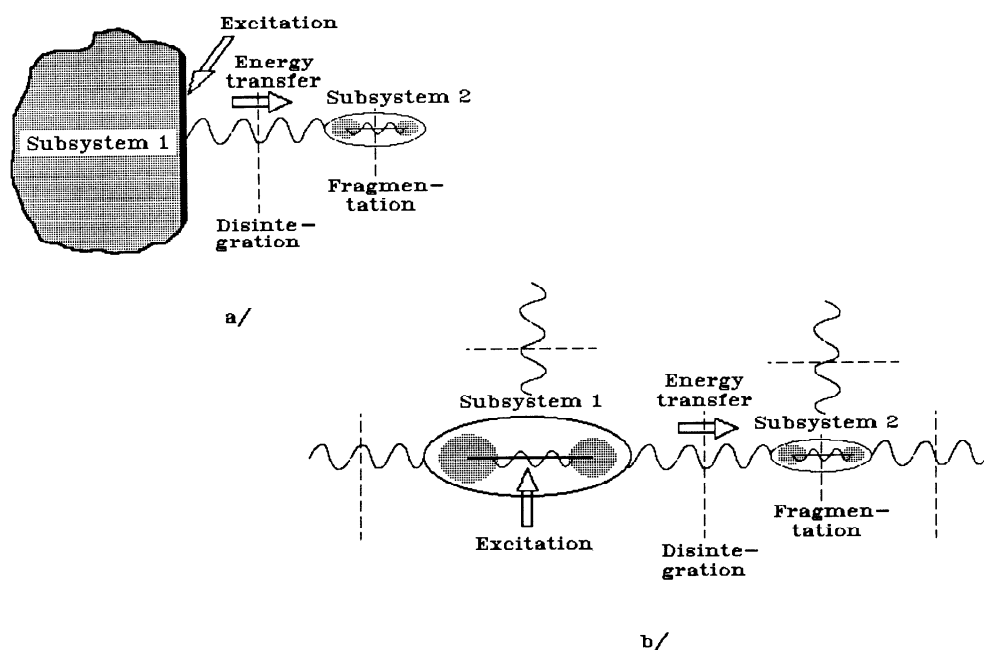


Figure 1. The general scheme of preserving non-equilibrium energy distributions by detachment of Subsystem 2 from Subsystem 1 (a/) or by the disintegration of the coupling of Subsystem 1 (b/). The energy is pumped into Subsystem 1 and transferred to Subsystem 2 by a consecutive process. In Fig. 1/a the two subsystems are detached before fragmentation could start in Subsystem 2 (see laser induced thermal desorption). In Fig. 1/b the coupling of Subsystem 1 disintegrates releasing Subsystem 2 before it can degrade. The springs represent particle interactions.

ENERGY DEPOSITION AND EQUILIBRATION

There are several features of Q-switched or mode locked lasers which can lead to special effects in laser – solid interaction. Most remarkable among them are the sharp temporal and spatial inhomogeneities (~ 10 ns; ~ 10 μm), the very broad range of irradiance values (10^5 – 10^{11} W/cm^2) and the extremely precisely defined wavelength of excitation (in the 118 nm $\leq \lambda \leq 10.6$ μm range). If laser energy is coupled to a solid target the induced processes reflect the peculiarities of the source. Due to the high irradiance, surface heating rates up to $\sim 10^{10}$ – 10^{11} K/s are easily attained. For the same reason, the excited populations in the target may reach saturation, giving rise to non-linearities in light absorption. High irradiance, in other words high photon flux, increases the possibility of multiphoton processes. The relation of laser wavelength to the favored transitions between energy levels in the solid determines the degree of freedom which is going to be excited.

If the sample is homogeneous in spatial and also in chemical sense, only *direct* light absorption is possible. The effectiveness of coupling is largely determined by the matching between photon energy and the energies of transitions in the solid. Different modes are accessible for infrared lasers (phonon structure: 0–50 meV; vibrational modes: 100–500 meV) and for ultraviolet lasers (electronic excitation: 1–5 eV). It has been quickly realized that direct excitation offers rather narrow possibilities to desorb intact large molecules. The reason seems to be that in the direct scheme laser energy has to be deposited into the molecules themselves.

A much more flexible arrangement is achieved by the *indirect* scheme. In these experiments the energy is deposited into a mediator, which in turn transfers it to the large molecules. This way a precise selection of the coupling mechanism and a fine tuning of the coupled amount of energy is practicable. The most common mediators are usually very good absorbers at the given wavelength. According to the geometry and to the number of phases involved, one can distinguish between three classes of mediators: solid surfaces, colloid particles and matrixes.

Energy levels and several favored pathways of energy redistribution are shown in Figures 2 and 3 for the two most successful laser desorption experiments. A typical matrix assisted laser desorption experiment involves frequency quadrupled Nd-YAG laser ($\lambda=266$ nm) excitation of nicotinic acid host molecules. The π electrons in the pyridine ring are excited to the π^* antibonding state. In Figure 2 the major redistribution processes due to this electronic excitation are visualized by arrows.

The electronic excitation is relaxed by fluorescence and by internal conversion which on the picosecond timescale leads to vibrational excitation of the ground level. An excited host molecule may transfer energy to neighboring host and guest molecules, to the lattice vibrations or, eventually, brake up and form fragments. The large molecules, embedded as guests, are acquiring energy either directly from the host or from the lattice and may also decay by fragmentation. If enough energy is transferred to lattice vibrations it can disintegrate by phase transition. It is the competition between the energy transfer directed towards guest fragmentation and towards lattice disintegration what determines the efficiency of releasing intact guest molecules.

The other typical example is laser desorption induced by infrared lasers. In this case the two main energy deposition mechanisms are substrate heating and direct multiphoton absorption by the adsorbate molecules (Figure 3). Anharmonicity of the vibrational modes makes the excited state spacing nonlinear, and therefore, direct multiphoton absorption increasingly difficult. Higher excited states can be reached more easily by intermolecular energy transfer. Excited molecules exchange energy also with the surface phonons. In the case of the indirect scheme, substrate heating is converted to surface phonon excitations. These excitations, in turn, can decay either by energy transfer to the vibrational modes of the adsorbate or by the detachment of the adsorbed molecules. Direct heating of insulating substrates is not very efficient. In this

Matrix Assisted Laser Desorption in UV

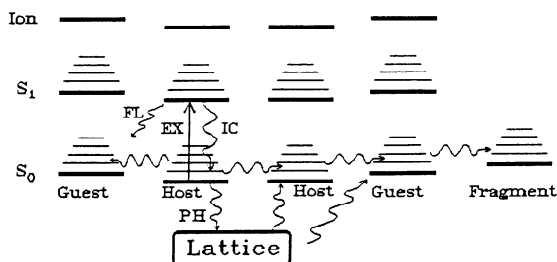


Figure 2. The energy levels and transitions involved in matrix assisted UV laser desorption. S_0 and S_1 are the ground and the electronically excited energy levels of the Host and the Guest molecules. EX, IC, FL and PH denote the laser excitation, internal conversion, fluorescence and phonon generation processes respectively. The large guest molecules can be pumped via direct Host - Guest interaction or by channelling energy through lattice vibrations. Fragmentation of the Guest molecules may occur from their highly excited vibrational states.

Laser Induced Desorption in IR

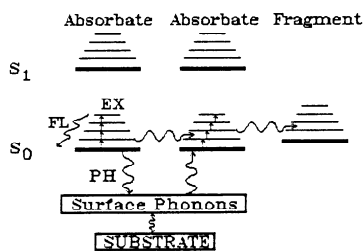


Figure 3. Energy levels and several transitions involved in infrared laser induced desorption. Direct excitation (EX), substrate heating, intermolecular energy transfer and energy gain from surface phonons are increasing whereas fluorescence (FL), fragmentation and phonon excitation (PH) are decreasing the energy content of the adsorbate.

case laser induced coherent surface phonon excitation may be involved in the desorption process [20]. Inter-adsorbate energy transfer, fluorescence and fragmentation have to be mentioned as major energy loss mechanisms.

Other forms of energy equilibration are also present. Spatial energy density inhomogeneities are smoothed by heat conduction [21]. These processes may become important on the nanosecond and on longer timescales. Gas phase processes have important effect on energy deposition if the vapor becomes optically thick. At elevated irradiances plasma absorption dominates over other forms of absorption [22] and hydrodynamics of the plume expansion has growing significance [23,24].

DISINTEGRATION

Disintegration is a crucial step in the volatilization of large molecules. If disintegration does not occur or it occurs too late, energy equilibration leads to high vibrational excitation and eventually to bond breaking in the large molecule. There is a large variety of disintegration mechanisms. Phase transition, phonon avalanche, crack formation, optical breakdown, photo ablation are just a few example from the list. Even desorption itself can be considered as disintegration, for breaking of the adsorption bond inhibits further energy transfer [25,26]. Here we describe several disintegration mechanisms which might play important role in successful volatilization of large molecules.

Disintegration via non-equilibrium phase transition

Sudden heating of the lattice of Subsystem 1 (Fig. 1/a) leads to disintegration in the form of phase explosion [27,28] if the lattice temperature exceeds $0.9 \times T_c$, where T_c is the critical temperature. This process, also described as homogeneous vapor nucleation, has been invoked earlier to explain fast atom bombardment ionization [27,28].

In laser induced explosive desorption [18] the phonon modes of the lattice are pumped by a system of excited anharmonic oscillators, i.e. by highly excited vibrational states of the molecules. Under the influence of an external force field this system can become unstable [29,30], give rise to a phonon avalanche and consequently to explosive desorption.

There is still another important question to answer. What prevents guest molecules from heating up in an environment where host molecules and lattice vibrations are both highly excited. The homogeneous bottleneck model (HBM), proposed for the description of matrix assisted laser desorption of large molecules, suggests that there is an obstacle in the energy transfer towards the embedded guest molecules. This, so called, energy transfer bottleneck is caused by the mismatch between the guest-host interaction frequency and the internal vibrational frequencies of the guest molecule. A simple kinetic model of the energy transfer processes shows that at an appropriately high sublimation rate the guest molecules will be liberated internally cold [31]. In Figure 4 the time development of host (H) and guest (G) internal temperatures are shown.

The laser power input, P_{in} , heats up the host molecules. The lattice temperature is proved to be identical with the host temperature. P_{out} shows the power drained from the system by phase transition, in this case by sublimation. Inspecting the figure it is clear that in the vicinity of maximum desorption rate the guest molecules are still close to their initial temperature. Thus, in this model, the possibility of volatilizing intact large molecules has been demonstrated. Recent experiments show, that the matrix assisted method is not bound to desorption from thin layers adsorbed on a substrate.

In accordance with the predictions of the HBM theory, it can be carried out without substrate, from suspended crystals [32].

The criterion to liberate internally cold molecules from a strongly absorbing matrix can be expressed in a very general form:

$$\tau(T_L = T_{subl}) \ll \tau(T_G \approx T_H) \quad (1)$$

where $\tau(T_L = T_{subl})$ is the time required to reach sublimation temperature, T_{subl} by the lattice temperature, T_L , and $\tau(T_G \approx T_H)$ is the approximate time to reach the equality of T_H and T_G , the host and the guest temperature.

The key material factors in the model appear to be the low heat of sublimation, subcritical concentration of the guest molecules and the high irradiance input in a short time compared to the sublimation induction period [31]. The model is homogeneous in that the energy density is taken to be uniform within the 'hot region' of the matrix. The two competing effects are the rates of energy transfer from the matrix to the guest molecules and the desorption by sublimation. It is the bottleneck for energy transfer to the embedded guest molecules that makes their energy content lag behind that of the matrix. This is particularly the case for an initially cold sample. When a sufficiently high rate of sublimation can be achieved (e.g., using a high power laser), the guest molecules (or adduct ions) will desorb internally cold and will thus not fragment.

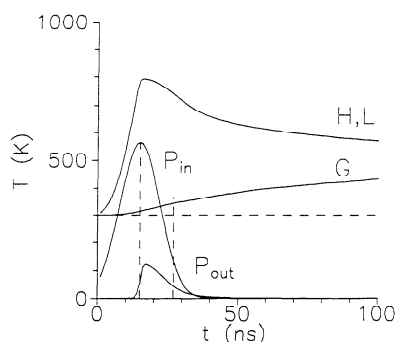


Figure 4. Energy pathways for UV laser irradiation of nicotinic acid matrix containing 10^{-4} volume fraction of a $M_G = 10^5$ protein. P_{in} and P_{out} are the laser power input and the power output carried by sublimation per unit matrix area, respectively. See text for further details [31].

Disintegration via mechanical stress and shock

Another way of disintegration is the result of thermally induced mechanical stress [6] and shock [4]. The energy absorbed from the laser pulse causes inhomogeneous heating of the sample. Thermal expansion of the illuminated region produces mechanical stress. Already at moderate laser irradiances the thermally induced stress, σ , may

exceed the critical stress value, σ^* , where cracks are formed and mechanical fragmentation occurs. In principle, crack formation can be observed if the strain energy exceeds the energy of new surfaces created by the cracks. It is also possible to prove that upon mechanical fragmentation a large number of quite small fragments are formed [33], therefore, many of the embedded guest molecules are released into the gas phase.

The condition to release intact large molecules by thermally induced stress and crack formation is:

$$\tau(\sigma = \sigma^*) \ll \tau(T_G \gg T_0) \quad (2)$$

where $\tau(T_G \gg T_0)$ is the time needed for the guest temperature to depart substantially from the initial temperature of the system, T_0 .

In Figure 5 the time history of crack formation is shown for a sample where large molecules are embedded in an alkali halide matrix. Because of the much longer pulse duration of the applied CO_2 laser, energy exchange becomes complete between host and guest molecules already from the beginning of the excitation. The energy deposition by the laser pulse, P_{in} , generates rapidly rising thermal stress which reaches the critical value before the overall temperature can rise excessively.

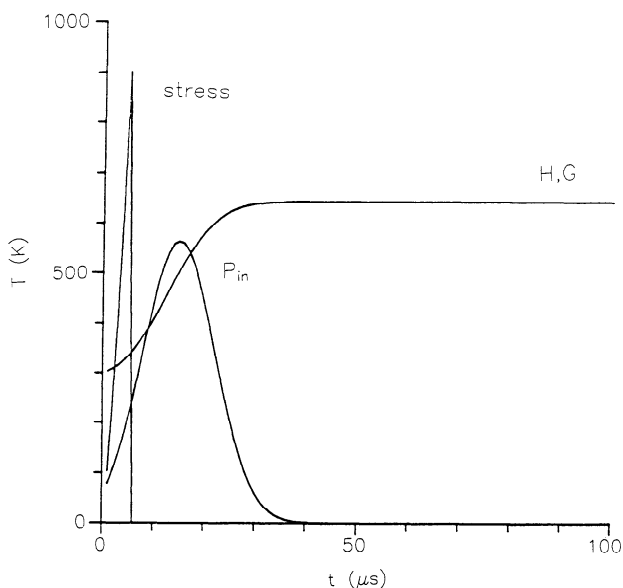


Figure 5. Temporal evolution of host (H) and guest (G) temperature and thermally induced stress for a CO_2 laser pulse. The pulse profile vs. time is labelled as P_{in} . The stress curve is $1000(\sigma/\sigma^*)$ where σ^* is the critical stress. At $\sigma = \sigma^*$ the matrix fragments releasing some part of the guest molecules [33].

The material parameters which determine the instance of crack formation are the light absorption coefficient, the volume thermal expansion coefficient, the bulk modulus and the critical stress value. In order to reach earlier crack formation and guest molecules liberated with lower internal energy content, modifications are to be sought to increase the volume thermal expansion coefficient and/or the bulk modulus of the sample or to decrease the critical stress value. In terms of this model it is possible to explain the observation that the introduction of fine metal powder into the sample improves the efficiency of volatilization [6].

Another mechanism of releasing large molecules by mechanical effects is shock wave induced desorption. It is proved that laser pulses at elevated irradiances generate shock waves in the ablated plume and compression waves in the solid target [17,24]. If a slab-like sample is thick enough not to be perforated by the laser pulse, but thin enough to experience the effect of the compression wave at the back surface in a short time, intact large molecules can be detached from the sample [4]. The description of this phenomenon is complex and out of the scope of the present discussion. The only remark we make here is that in order to be able to desorb cold molecules the compression wave propagation velocity has to exceed the heat conduction velocity in the sample.

Disintegration via repulsive states

Investigation of desorption processes induced by low energy electron impact has already led to the idea of repulsive state participation in the mechanism of detachment [34,35]. If by electron impact or by the absorption of UV photons an adsorbed molecule is excited electronically, the resulting state can be an antibonding state, a higher lying excited state or an ionized state. Because of the Franck–Condon principle these excited states are not in their equilibrium geometry. The adsorbates in these configurations are frequently in the repulsive range of the interaction potential.

In Figure 6 we outline schematically how the system will behave in the case of electronic excitation. If the antibonding state is reached the adsorbed particle will experience a monotonous repulsive field and leave the surface with $(E_{ex} - E_a)$ kinetic energy, where E_{ex} and E_a are the excitation and the adsorption energies respectively. If the antibonding potential surface is intersected by the potential surface of a bonding excited state, intersystem crossing may occur and the adsorbate can be retarded. Ion desorption is observed in the case of excitation to even higher electronic states, generally attained by multiphoton processes.

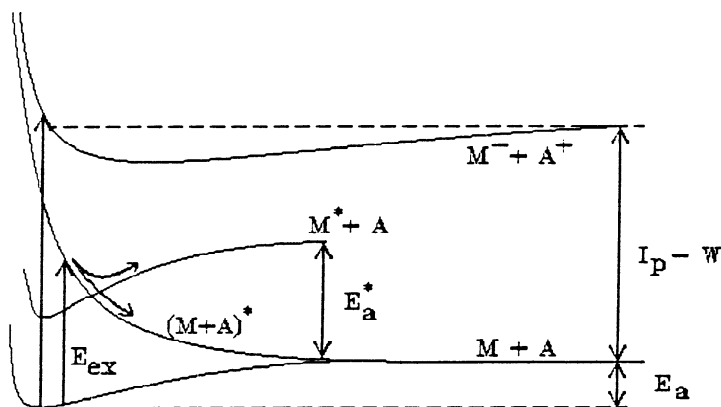


Figure 6. Development of laser induced desorption from a metallic surface (M) via repulsive states. The adsorbate (A) – surface interaction can be electronically excited to a repulsive state. Decay to M + A desorbed state or intersystem crossing to the hypersurface of the M* + A system can be observed. Higher excitation energy or two photon presses may provide enough energy to ion desorption: M⁻ + A⁺.

It is the peculiarity of this completely non-thermal mechanism that in the case of coherent electronic excitation the energy conversion leads to coherent translational motion of the desorbed particles. As a result, melting of the surface layer is avoided and in the case of a volume process extremely well defined pits are produced. The removed particles exhibit velocity distributions oriented strongly towards the surface normal [19].

Microscopic modeling of laser ablation by molecular dynamic simulation supports the feasibility of this mechanism, especially for far-UV radiation [19,36]. Ab initio density functional calculations and effective medium theory reveal finer details of the adsorbate – surface interaction and its perturbation by electronic excitation [37]. It is shown that the desorption of ions from metal surfaces is largely enhanced by the screening of the image charge in the metal. In the framework of this model, multicharged ions remain strongly bound to the surface, a prediction not supported by experiments with large adsorbed molecules [38].

Energy distribution measurements of desorbed ions and neutrals show marked difference in the translational energy of the two species [39]. Neutrals have kinetic energies in the order of 0.1 eV, whereas the ions exhibit about ten times higher values. If the desorption is attributed to electronic transitions, it is straightforward to rationalize this difference. The neutrals can be desorbed by single photon excitation to a repulsive state, whereas the ions are the result of a two photon process leading to the ionic state (Fig. 6). The amount of the kinetic energy of desorbing particles is a function of the potential surface shape and of the excitation energy. Excitation to the steep repulsing part of the ionic state interaction potential may result in departing energetic ions.

ION FORMATION

Ion formation mechanisms can be classified according to the ion formation site and according to the process involved. Certain molecular solids are built up of ion associates. For example, nicotinic acid – an often used matrix in MALD experiments – is built up of molecular dimers, held together by charge disproportionation. Defects and impurities are also sources of ionized particles. Surface states and adsorption itself are frequently promoting ion formation by preforming the gas phase ion. However, gas phase processes are the most effective in producing the ionized species. Electron impact ionization and ion-molecule reactions have high cross sections and the ions generated in the gas phase are directly collected by the electric field of the spectrometer.

Thermal ion formation is not likely in the case of large molecules because the required temperatures would certainly destruct the molecules. Photo-processes are very inefficient for IR radiation but deserve some interest in UV experiments. Indeed, two photons of the most often used frequency quadrupled Nd-YAG laser provides enough energy to ionize many organic molecules.

Inspecting laser desorption mass spectra still tells us: the most favored channel of molecular ion formation is cationization. Protonated and/or alkalinated molecular ions are usually abundant in positive ion spectra. Not too much is known about the formation of these ions. It seems likely that protonated ions are formed already on the surface or even in the solid phase by proton hopping and alkalinated ions are mostly the products of gas phase ion-molecule reactions [40].

In the case of negligible dipole moments ion-molecule reactions are described by the Gioumousis–Stevenson theory [41]. A simple rate constant expression can be derived for the case of the cationization of a very large molecule by a relatively light ion ($M_2 \ll M_1$):

$$k = 2\pi\epsilon\alpha^{1/2}/M_2^{1/2} \quad (3)$$

where α and M_2 are the polarizability of the large molecule and the mass of the light

ion. It is easy to estimate that protonation is six times faster than the reaction with K^+ if the concentrations are similar. Calculations of the desorption profiles and ion-molecule reaction rates show feasible ion production rates also for small molecules [42,43]. However, Eq. (3) predicts moderate deterioration of gas phase cationization with increasing ion mass.

There are other types of ions abundant in the high mass region. Adduct ions are formed by the combination of the high mass molecules with fragment ions of the matrix. Their origin is probably also a gas phase ion-molecule process. Multiply charged species are easy to form from large molecules as it is learned in electrospray ionization experiments. Because of the possibility of independent ionization at different sites of the molecule and because of distant charge locations the increasing size is accompanied by increasing number of charges. Ionized clusters appear quite often in the spectra. It is unlikely that these clusters are formed in the gas phase, for guest molecule concentration is very low already in the matrix. Most experiments are performed on peptides and on proteins. These compounds have amphoteric character and readily associate in solution. In principle the associates can survive sample preparation and desorb as a single particle.

Because only a small fraction of the desorbed species is ionized, increasing ionization efficiency could mean significant improvement in detection limits and an even broader range of applications. Clearly, more work is needed to understand laser induced ion formation from large molecules.

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