

Hydrodynamic Model of Matrix-Assisted Laser Desorption Mass Spectrometry

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In this paper we present a model to explain matrix-assisted laser desorption (MALD) of intact large molecules. According to preliminary estimates of energy deposition it seems likely that laser heating of the matrix up to the phase transition temperature is one of the prerequisites to carry out successful MALD experiments. The generated plume is described in terms of hydrodynamics. The results reflect several important features of the measurements: the velocity of neutral particles and the power law of total desorbed flux versus laser irradiance. Furthermore, expansion cooling of the plume is reported, rationalizing the absence of thermal degradation processes.

INTRODUCTION

The development of biochemistry and polymer chemistry demanded the analysis of ever larger and more complex molecules. Gas-phase analysis of these molecules encountered significant difficulties with increasing molecular weight. Matrix-assisted laser desorption offered a viable solution for gas-phase ion generation from large and/or thermolabile molecules.¹⁻³ Among the first and—as of today—most important applications of this phenomenon is the mass spectrometric investigation of large molecules.⁴⁻¹¹ Relatively little attention has been paid, however, to answering basic questions concerning the mechanism of volatilization and ionization.

Some systematic measurements describing several details of the desorption process have been reported.¹² The most important findings included establishing accurate threshold irradiances and revealing that the underlying process is collective in nature. Experiments in alternative configurations showed that the presence of a solid substrate is not indispensable, opening the possibility of performing MALD experiments in transmission geometry.¹³ It also was shown that mass spectrometry is not the only method for detecting large molecules.¹⁴

Theoretical investigations date back to efforts devoted to the understanding of plasma desorption and other high energy particle induced desorption techniques.¹⁵ The intriguing similarity between MALD and other soft ionization methods is that they all start with sudden energy deposition and they all yield large molecules in the gas phase. Energy deposition and redistribution processes seemed to be a key factor in the description of MALD mechanisms.^{16,17} Attempts have also been made to account for the energy transfer to the large molecules during their volatilization.^{16,17} A possible reason for the lack of degradation of these molecules is the presence of an energy-transfer bottleneck due to frequency mismatch between lattice vibrations in the solid and intramolecular vibrations in the large molecules.^{18,19}

In the present paper we describe the fate of the deposited energy in terms of solid- and gas-phase processes as they are described by the laws of mass, momentum, and energy conservation.

THEORY AND CALCULATION

In our model the laser energy deposited in the solid matrix is assumed to lead to heating and phase transition. The generated plume, in turn, expands and exhibits cooling. First we estimate the threshold irradiance to achieve phase transition in the matrix. In the second part of this section we describe the hydrodynamic calculations for plume expansion.

Irradiance Threshold for Plume Formation. It is important to realize that there are several different regimes

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of laser–solid interaction, depending on laser irradiance and the nature of the sample and its absorption coefficient. We are going to exclude certain nonlinear effects from the present model. Thermal and optical runaway (nonlinear dependence of absorption coefficient on temperature and/or laser irradiance) are predominant in semiconductors. In transparent insulators avalanche breakdown may occur at high irradiance due to the oscillating electric component of the laser light.

The present model is most suitable for the description of laser–solid interaction in metals and opaque insulators. At moderate irradiances ($<1 \text{ GW/cm}^2$) the interaction may involve one or more of the following possibilities: surface heating with thermal desorption, surface melting with surface evaporation, volume evaporation, formation of an optically thick plume, and plasma absorption in the plume. There are three different thresholds, such as volatilization threshold, I_0^{volat} , plasma ignition threshold, I_0^{plasma} , and optical breakdown threshold, I_0^{break} , marking transitions between the different regimes. Although their values are well-defined, shifts can be expected in a given experiment according to the choice of laser or target material.

In an earlier study we dealt with the transition from normal absorption of the laser-generated plume to plasma absorption characterized by 10^8 – 10^9 W/cm^2 threshold irradiances.²⁰ For the high-irradiance transitions, the threshold was established by investigating normal absorption versus plasma absorption. Matrix-assisted laser desorption is a much milder process typically requiring about 10^6 W/cm^2 irradiance and low melting point or low sublimation temperature materials. Recently, it has been shown by elaborate irradiance threshold measurements of ion generation that the underlying process is a collective effect, similar in principle to phase transitions.¹² Furthermore, threshold irradiance values change little by changing the mass of the guest molecules over 1 order of magnitude.²¹ In our analysis we assume that the phase transition and not the ionization process is the rate-limiting step in ion generation. To estimate the required irradiance we set the following condition: in order to reach volatilization by laser heating the elevated surface temperature must exceed the melting or sublimation temperature of the matrix:

$$T_{\text{surf}} \geq T_{\text{subl}} \quad (1)$$

The rise of surface temperature, $\Delta T_{\text{surf}}(t)$, at time t under the influence of a uniform penetrating light source with I_0 irradiance is²²

$$\Delta T_{\text{surf}}(t) = \frac{I_0}{K} \left[\frac{\delta}{\pi^{1/2}} - \frac{1}{\alpha} \left[1 - \exp\left(\frac{\alpha\delta}{2}\right)^2 \operatorname{erfc}\left(\frac{\alpha\delta}{2}\right) \right] \right] \quad (2)$$

where $\delta = 2(\kappa t)^{1/2}$ and the thermal diffusivity $\kappa = KV_M/c_p$. K , V_M , and c_p are the thermal conductivity, the molar volume, and the specific heat of the material, respectively. Although analytical formulas are shown to overestimate the temperature jump in pulsed surface heating at the irradiances of our concern ($<5 \times 10^7 \text{ W/cm}^2$), the error is negligible.²³

Substituting material parameter values for nicotinic acid ($\alpha_{265} = 4 \times 10^4 \text{ cm}^{-1}$; $c_p = 150 \text{ J/mol}\cdot\text{K}$; $V_M = 83.5 \text{ cm}^3/\text{mol}$; $K = 2 \times 10^{-3} \text{ W/cm}\cdot\text{K}$), by the end of a frequency-quadrupled Nd–YAG laser pulse ($t = 10 \text{ ns}$; $I_0 = 10^6 \text{ W/cm}^2$) the surface temperature rise is $\Delta T_{\text{surf}}(t) = 202 \text{ K}$. This value—if superimposed on the room temperature—compares extremely

well with the sublimation temperature of this matrix $T_{\text{subl}} = 236 \text{ }^\circ\text{C}$. Indeed, detailed investigations show the threshold irradiance of ion generation with MALD for both nicotinic acid²⁴ and sinapinic acid¹² matrix to be around 10^6 W/cm^2 . Other quantities influencing eq 2 (such as K , V_M , and c_p) show little variation for these materials. On the basis of these data and on the evaluation of eq 2, it seems understandable that several matrices have similar threshold irradiances. Thus, we may infer that the phase transition scenario we put forward in the Introduction does not contradict our energy deposition estimate.

In the next part of this section we describe the state of the plume, for it is most relevant in the fate of entrained large molecules.

Plume Hydrodynamics. The expansion of laser-generated plumes has been described for a variety of conditions earlier.^{26–28} We are interested in the density, temperature, and velocity distributions of these plumes as they develop in time. In contrast to laser plasma generation calculations we expect moderate temperatures during the volatilization of low sublimation point matrices.

During laser–solid interaction two distinct phases can be recognized. The *first phase* covers the period with T_{surf} of the solid does not reach the phase transition temperature. In this regime material transport can be neglected and the description only accounts for generating a hot spot on the solid surface. The temperature distribution is governed by the relation between the laser heating and cooling of the spot by heat conduction:

$$\frac{\partial(\rho e)}{\partial t} = -\frac{\partial}{\partial z} \left[\kappa \frac{\partial(\rho e)}{\partial z} \right] + \alpha_{\text{solid}} I \quad (3)$$

Here ρe and α_{solid} stand for the energy density and for the absorption coefficient of the solid material. We have seen already a special solution of this equation for the case of uniform penetrating source (eq 2). Because we allow both for phase transitions in the solid and for different laser pulse profiles, numerical solution of this equation shall be sought. This solution can be used afterward as boundary condition for the description of plume expansion.

The *second phase* starts when the solid surface is heated above phase transition temperature. At this stage the vapor pressure of the material becomes significant and the material transport across the surface cannot be neglected. In order to deal with the expansion problem we have to solve a simplified set of hydrodynamic equations expressing the conservation of mass, momentum, and energy:

$$\frac{\partial[\rho]}{\partial t} = -\frac{\partial[\rho v]}{\partial z} \quad (4)$$

$$\frac{\partial[\rho v]}{\partial t} = -\frac{\partial[p + \rho v^2]}{\partial z} \quad (5)$$

$$\frac{\partial[\rho(e + v^2/2)]}{\partial t} = -\frac{\partial[\rho v(e + p/\rho + v^2/2)]}{\partial z} + \alpha_{\text{plume}} I \quad (6)$$

where ρ , v , p , and α_{plume} denote the density, hydrodynamic velocity, pressure, and absorption coefficient of the plume, respectively. We shall note that all four transport equations (eqs 3–6) are written in one-dimensional form. Therefore, only processes along the z coordinate (perpendicular to the surface) are accounted for, and radial transport is neglected

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in the model. Considering Gaussian beam profile, this approximation is good in the middle of the beam where radial gradients are negligible. The relevance of our results, however, is not altered by this restriction because at the volatilization threshold (where most of the experimental work is done) only the center of the spot is hot enough to contribute substantially to volatilization.

Coupling between eqs 4–6 and eq 3 is provided by the Clausius–Clapeyron equation for vapor pressure. Under laser desorption conditions (i.e., near threshold irradiance) the plume remains optically thin, so the absorption term in eq 6 can be neglected.

Thus, the plume is heated only by the transfer of warm material across the interface and cooled by the expansion process. Due to the relatively low temperatures thermal ionization and radiative cooling are not significant factors either. Solutions of eqs 3–6 were found by a computer code developed and reported earlier.²⁶

RESULTS AND DISCUSSION

The nicotinic acid–vacuum interface was investigated under the influence of a 10-ns frequency-quadrupled Nd–YAG laser pulse. The temporal profile of the 10^7 W/cm² irradiance pulse was approximated by a square wave. At the beginning of the experiment the solid (matrix + biomolecule) is heated by the laser pulse, producing more and more vigorous evaporation through direct sublimation. By the end of the laser pulse, a certain amount of the solid is evaporated and the surface of the solid will be superheated (Figure 1a; 10-ns curve). After the laser pulse has ceased, the heat conduction and evaporation quenches the surface under the phase transition temperature (Figure 1a; 50-ns curve).

Spatial distribution of temperature, density, and velocity are shown near the surface in Figure 1a–c both in the solid and in the gas phase. Three different time stages are depicted in order to visualize postpulse behavior. The spatial density profile at the end of the laser pulse (10 ns) showed monotonous decay (Figure 1b). Subsequent cooling of the surface substantially lowered the rate of evaporation. Consequently, the density immediately above the target dropped quickly and the plume detached from the surface producing a drifting and expanding packet (50 ns, 100 ns).

We also were interested in the effect of the laser irradiance on desorption from the sinapinic acid target. The effect of six 308-nm laser shots covering the threshold irradiance region was investigated. Plume density distributions at the 40-ns time stage are depicted in Figure 2. Increasing the laser irradiance from 2×10^6 to 4×10^6 W/cm² showed dramatic enhancement both in plume size and in plume density (notice the logarithmic density scale).

The areas under the different density curves were integrated and the desorbed flux was compared with the experimental results of Ens et al.¹² Integrating the density distributions along the z axis provided a measure of the total desorbed amount from unit surface. The laser irradiance dependence of this quantity is depicted in Figure 3. Two interesting features of this figure are the existence of threshold irradiance and the power law relationship. Comparing Figure 3 of ref 12 and Figure 3 of this publication, a positive correlation can be established between the cool plume model and measurements. Measured laser irradiance thresholds for ion production are around 2×10^6 W/cm², whereas calculated plume formation thresholds are close to 2×10^5 W/cm². The difference in desorption thresholds may be attributed to uncertainties in the optical constants used in the calculations. Only solution-phase light absorption coefficients are available for sinapinic acid. Therefore, in the calculations the solid-phase value was substituted by extrapolated solution data.

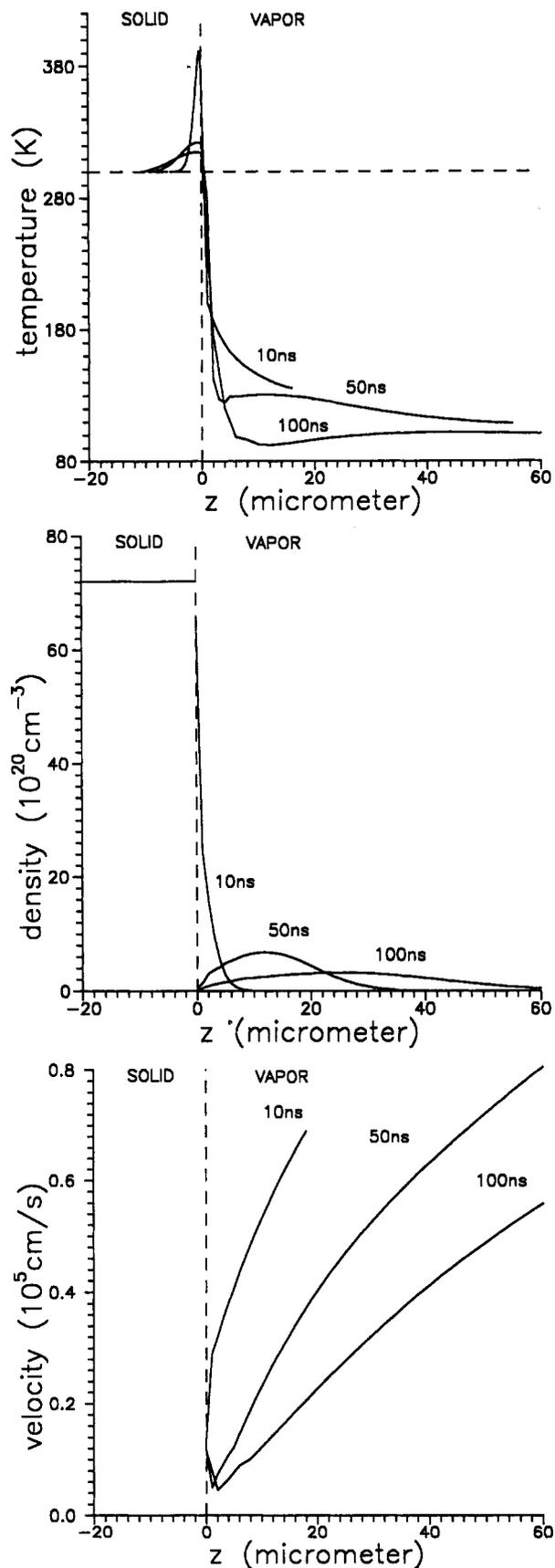


Figure 1. Effect of 10-ns frequency-quadrupled Nd–YAG laser pulse (10^7 W/cm²) on matrix–vacuum interface. Spatial temperature (a, top), density (b, middle), and velocity (c, bottom) distributions are shown at different times. Surface position is marked by vertical dashed line.

The measured ion yield, Y_i , shows a power law dependence on the laser irradiance: $Y_i \propto I^6$. Integrated plume density distributions, Y_n , from the model exhibit power law depen-

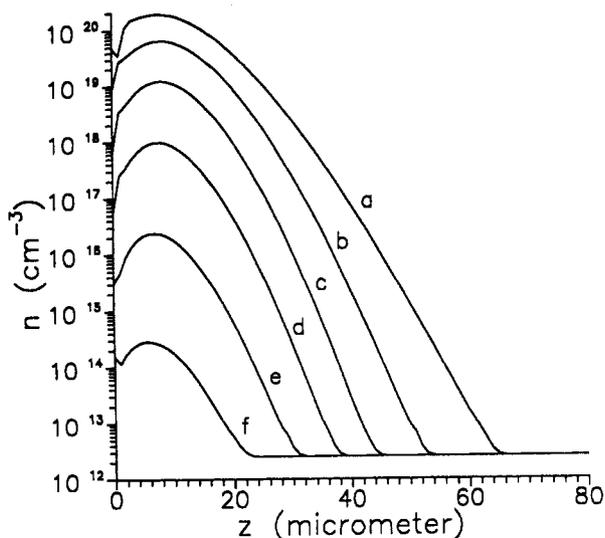


Figure 2. Plume density profiles of sinapinic acid at 40 ns after the 10-ns, 308-nm laser pulse using different irradiances. (See explanation in text.)

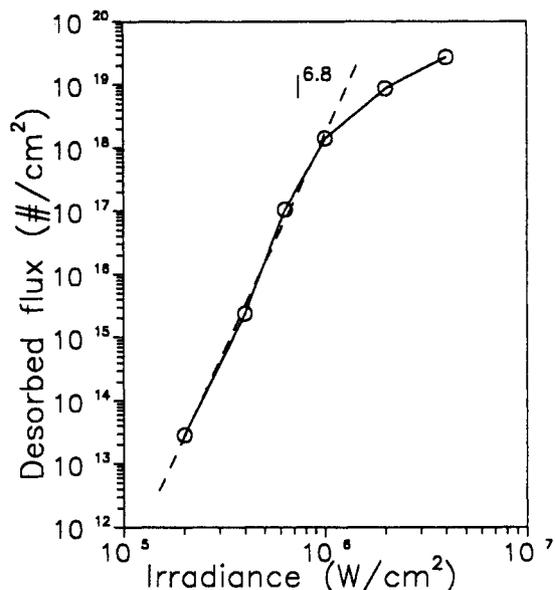


Figure 3. Calculated desorbed flux of matrix molecules as a function of laser irradiance (sinapinic acid matrix; 308-nm laser). Hydrodynamic model predicts power law with 6.8 exponent.

dence on laser irradiance, as well, but the exponent is somewhat higher $Y_n \propto I^{6.8}$. One can only speculate concerning the origin of this difference. First there is an uncertainty in the fitted exponent due to the statistical error of the experimental data. Furthermore, one may argue that the measured ion yield and the calculated desorbed flux are not directly proportional. The departure from power law at high irradiances shows saturation-like behavior both in the experiments and in the calculations. Another self-consistent explanation of ion yield-laser fluence data was based on Gaussian fluence distribution on the sample surface.²⁵ Clearly, more detailed experiments are needed to verify any of the suggested explanations.

We also estimated the plume velocity stemming from translation. Measured velocity distributions are available for the sinapinic acid matrix using the frequency-tripled Nd-YAG laser (10 ns, 10^6 W/cm² pulses)³⁴ and for a ferulic acid matrix using the frequency-quadrupled Nd-YAG laser (5 ns,

10^7 W/cm² pulses).²⁹ Calculations were carried out for similar targets and irradiation conditions. The calculated drift velocity of the plume center of mass for ferulic acid neutrals, $v_{\text{drift}} = 250$ m/s at 40 ns, compares quite well with the maxima ($300 \text{ m/s} < v_{\text{max}} < 400 \text{ m/s}$) of measured neutral particle velocity in the MALD of the ferulic acid matrix.²⁹ The calculated drift velocity for sinapinic acid neutrals, $v_{\text{drift}} = 250$ m/s at 40 ns, is substantially lower than the measured 1140 m/s ion velocities.³⁴ This difference may be attributed to the presence of a large extraction field in this experiment. One has to distinguish between these velocities evaluated from the displacement rate of the plume center and the local velocities of individual volume elements shown in Figure 1c.

It is worthwhile mentioning that the calculated plume density was relatively high; at the 50-ns time stage its maximum density still exceeded $1/10$ th of the solid density. With further expansion of the vapor cloud, the density dropped quickly. The high initial plume density has important repercussions regarding the possibility of gas-phase processes. It seems possible that certain fast reactions are induced in this dense cloud of particles. The most important among them can be the protonation, alkalination, and adduct ion formation of the guest molecules.

Another interesting feature of the plume was the spatial and temporal variation of temperature. The surface of the nicotinic acid was heated up near to the phase transition temperature, but quick decay of plume temperature was observed with increasing distance from the surface (Figure 1a). The actual value of the temperature in this calculation drops well below room temperature due to expansion cooling. Comparing density and temperature distributions at 100 ns provided an estimate of 110 K at the center of mass of the plume. The obvious consequence of such cooling would be the stabilizing effect for embedded large molecules. Some experimental verification of low plume temperatures by using thermally labile molecules as molecular thermometers had been reported earlier.³⁰ Other results, however, indicate elevated internal temperatures after MALD.³¹ More detailed analysis of our model shows that the actual internal temperature of an embedded molecule depends on the rate of energy transfer between internal degrees of freedom and translation and the time available for energy exchange. These processes may vary depending on the nature of the guest-host interaction and the initial conditions provided by the energy deposition into different degrees of freedom.

We have to note that simple heating of the matrix lattice by the laser pulse gives no satisfactory explanation of all the findings of UV MALD experiments. In contrast to the presence of intact guest molecules in the plume, host fragments can be abundant in the mass spectrum. This observation points to the importance of exploring the possible energy-transfer pathways in the system.¹⁷ In the UV experiments primary energy deposition leads to electronic excitation of the host molecules ($\pi \rightarrow \pi^*$, or $n \rightarrow \pi^*$ transition in case of a nicotinic acid matrix).³²

Part of the deposited energy is reemitted through fluorescence.³³ Another portion is channeled via fast internal conversion and/or intersystem crossing processes and leads to vibrationally highly excited states. Some host molecules will decompose from these vibrational states; others will transfer their energy to the lattice. Thus, the lattice is heated up and the phase transition temperature can be reached

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occasionally. At this stage the question arises as to what prevents energy transfer to the guest molecules. According to our calculations of energy-transfer rates in this system, there is a bottleneck hindering the heating of internal vibrational degrees of freedom of the guest molecules.^{18,19} This bottleneck is related to weak coupling between the lattice vibrations and the intramolecular vibrations of large molecules.

Another important question is the origin of ions in the system.³⁵ It is clear from postionization experiments that the degree of ionization in the plume is very low. In the light of the calculated temperature values, it is also obvious that thermal ionization is not a feasible ion production mechanism in these experiments. Rather, protonation and other adduct ion formation mechanisms shall be regarded as the primary

source of ions. These processes can be discussed in terms of preformed ion volatilization or ion-molecule reactions in the gas phase. Guest particles that are in their ionized form already in the solid state (preformed ions) can give rise to gas-phase ions extremely easily. Molecular ions of these substances in MALD experiments could be produced even without ion production from the matrix.³⁰ These findings support the idea that the role of the matrix is to embed and separate the guest particles in the solid phase and to entrain them during volatilization.

ACKNOWLEDGMENT

A.V. was supported by the National Science Foundation (Grant CTS-9212389) and by the George Washington University Facilitating Fund during part of this project.

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RECEIVED for review February 4, 1993. Accepted May 19, 1993.