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Technical Report

MALDI EasyCare: User-accessible source to maintain instrument performance for demanding applications

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Abstract:

The MALDI EasyCare systems have been designed to facilitate routine user maintenance to help retain optimal instrument performance for high-throughput or high-laser-shot-number MALDI-TOF-MS applications. All MALDI-TOF instruments are prone to fouling of the ion optics positioned close to the sample and this can lead to reduced instrument performance e.g., reduced sensitivity and resolution. With the MALDI EasyCare systems, end users can easily access, remove and clean the contaminated parts (i.e., extraction lens), thereby recovering instrument performance without the need for an expensive service engineer visit. A software wizard guides the user through the entire process including automated instrument conditioning and tuning. Here, we provide an example showing how the performance of a contaminated instrument was recovered by this simple user maintenance.

Keywords: contamination, source cleaning, MALDI EasyCare, MALDI-TOF, user maintenance

Introduction

Matrix assisted laser desorption ionization (MALDI) is a fast and highly sensitive ionization technique capable of generating ions from biological samples such as peptides, proteins, oligonucleotides, lipids and carbohydrates. Often coupled with a time-of-flight (TOF) analyser, MALDI-TOF is gaining increased attention for high-throughput biological screening applications due to its robustness and speed of analysis. In MALDI, the sample is mixed with a small organic compound (the 'matrix') and a small amount is deposited onto a target for analysis. Inside the instrument, a UV laser is used to irradiate the dried sample/matrix. The matrix absorbs the laser energy and is ablated from the target along with the sample ions of interest. During this process, some of the ablated material hits the extraction lens which is positioned close to the sample target, resulting in contamination of the lens (see Figure 1).

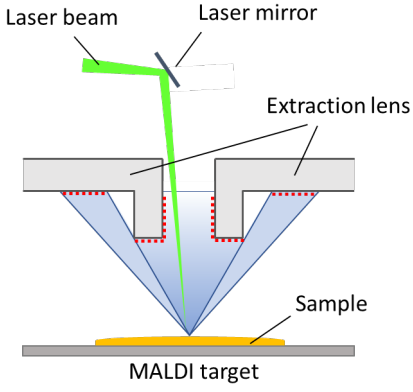

Figure 1: MALDI ion source showing extraction lens and regions prone to contamination/fouling (red dashed lines). During ionisation, the ions & neutrals generated by the incident laser beam expand towards the extraction lens, contaminating the exposed areas which eventually leads to reduced instrument performance.

The wide bore of the extraction lens on the Shimadzu MALDI-TOF instruments provides some protection against the effects of this contamination but heavy contamination ultimately results in a deterioration of instrument performance. In the majority of cases, the instrument performance can be recovered simply by cleaning the extraction lens, a job often reserved for trained service engineers. With the introduction of the MALDI EasyCare, this routine maintenance task can now be safely performed by instrument operators.

Loss of performance through extended use and source contamination

Figure 2 shows the effects of this type of source contamination. Figure 2(a) shows an example of the ion optics lens assembly and extraction lens following automated analysis of multiple sample plates for a high-throughput application. The contamination of the lens is clearly visible as a dark halo around the central bore. Figure 2(b) shows the ion optics and extraction lens after cleaning.

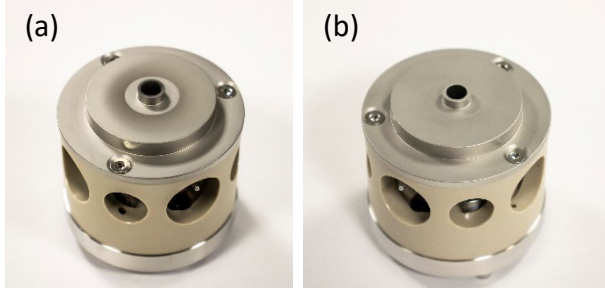

Figure 2: Photographs showing (a) contaminated and (b) cleaned extraction lens. In its normal configuration, the extended boss in the centre of the lens is pointing down towards the sample (see Figure 1). The 'clean' area immediately surrounding the boss in the image of the contaminated lens (Figure 2(a)) is a result of a shadow effect caused by the boss itself which protects this area from contamination (the white triangles either side of the extended boss in Figure 1).

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To demonstrate the effectiveness of the MALDI EasyCare functionality, urine was chosen as an example of a challenging biological matrix in which the high content of urea and salts is known to contaminate the ion optics leading to unavoidable loss in performance. The urine was diluted in water and spiked with a protein (bovine serum albumin (BSA)) to simulate pathological proteinuria scenarios and to monitor the drop in performance. The urine sample was premixed with sinapinic acid (SA) matrix before spotting onto FlexiMass-DS slides. Prior to running the urine samples, the instrument performance was checked (as per sensitivity test of the customer QC tests). Figure 3((a), red trace) shows the MS spectrum of the BSA in the diluted urine sample at the start of the contamination phase, while Figure 3((b), blue trace) shows the BSA profile where the poor signal and signal-to-noise clearly demonstrates a deterioration in performance. The loss in performance was also confirmed with the sensitivity test of the customer QC test.

Performance recovery using MALDI EasyCare

Using the software wizard, the operator was guided through the process of safely venting and powering down the instrument before removing and cleaning the contaminated lens. Figure 2(b) shows the ion optics lens assembly after manual cleaning. After reinstalling the cleaned ion optics assembly using the simple twist-lock design, the software performs unattended vacuum recovery, high voltage conditioning (necessary after venting the system to atmospheric pressure) and tuning of the instrument parameters to ensure optimum ion transmission. After tuning, the instrument performance recovery was confirmed with the sensitivity test of the customer QC test. Figure 3((c), green trace) shows the MS spectrum of the BSA in the urine sample after manual source cleaning and automated instrument tuning. As it can be observed, the sensitivity and signal-to-noise were fully recovered.

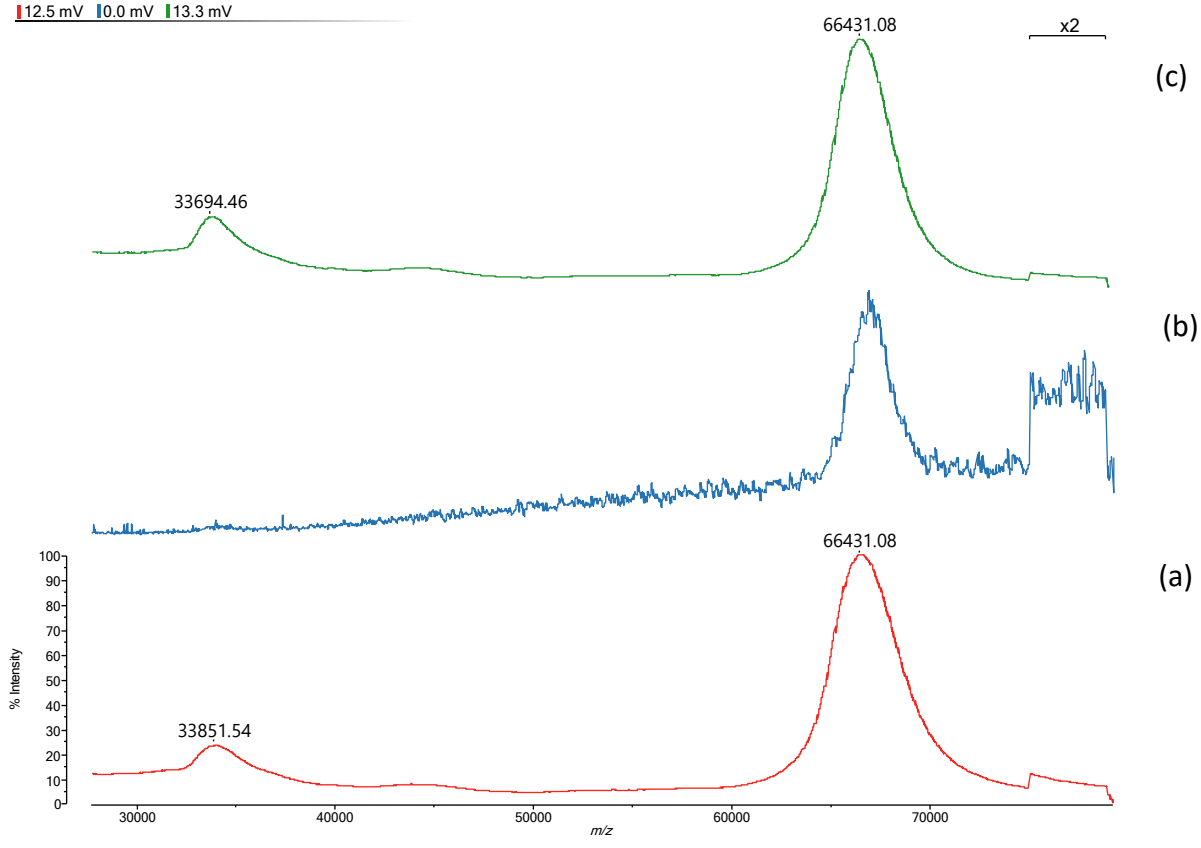

Figure 3: MS spectrum of the BSA in the diluted urine sample (a) at the start of the contamination phase, (b) at the point where the performance was deemed lost due to poor signal and signal-to-noise (region of magnified noise: 75000-80000 Da), and (c) after manual cleaning of the extraction lens and automated instrument optimisation, demonstrating full sensitivity recovery.

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