Reviewer’s Report for IEEE Milestone 2023-29

Dear Prof. Hase,

We have recently received a request for a peer review regarding IEEE Milestone. It was a great honor, and I examined carefully. In response to your question regarding "Milestone-Proposal: Laser Ionization Mass Spectrometer, 1988", I have the following comments to make.

Q1) Is the suggested wording of the Plaque Citation accurate?

Yes, I think the proposed Plaque Citation is appropriate. I am a researcher involved in mass spectrometry, especially in atmospheric environment field, and the MALDI-TOF type mass spectrometer (Matrix-Assisted Laser Desorption/Ionization-Mass Spectrometer, MALDI-TOFMS), which Shimadzu showed its prototype in 1988 as the LAMS-50K, has become a very important tool for us to understand the complex nature of various substances in the environment. The fact that mass spectrometry of macromolecules, such as biopolymers and artificial polymers, has become a fundamental tool for us humans to understand what is happening inside and outside the body (environment) at the molecular level, and as the Plaque Citation says, this has clearly contributed greatly to the development of molecular biology and medicine.

That's why Dr. Tanaka was awarded the Nobel Prize in Chemistry in 2002. The LAMS-50K is the first commercially produced MS equipment that can make use of the award-winning "soft desorption ionization method", so I think the Plaque Citation is appropriate.

Q2) Is the evidence presented in the proposal of sufficient substance and accuracy to support the Citation?

Yes, the evidence presented is sufficient and correctly cited.

The literature [3] shows that various technological developments were required to design MALDI-TOFMS product, which enables mass spectrometry of macromolecules, as well as the soft laser desorption/ionization technology that was the subject of the Nobel Prize. As shown in document [4], the LAMS-50K was released in 1988 and sold in 1990.
As one of its applications, Microorganism Identification is mentioned in the literature [7]. It is becoming more popular in various fields such as clinical, foods, beverages and pharmaceuticals. Mass spectra of bacteria are acquired by MALDI-TOFMS and compared with a database to identify their species. Compared to conventional methods, it is much faster, less expensive, and easier to execute. It could be said that it is the forefront of the dissemination and contribution of MALDI-TOFMS to medicine and pharmacy. Recently, a specially made microbial identification system using MALDI-TOFMS are produced through Shimadzu.

In addition, Mass Microscopy, which is shown in the literature [8], is also a field that is expected to develop in the future. Since the localization of the molecules of interest in tissue sample can be visualized according to their specific mass, in-depth understanding in molecular biology will be further developed, and contributions to medicine and pharmacy will be born.

The application of MALDI-TOFMS is not limited to those fields, but I believe that it will become an even more useful tool in wide range of science.

Q3) Does the proposed milestone represent a significant technical achievement?

Yes, I agree. Until then, there was no commercially available MALDI-TOMS equipment for measuring macromolecules, and as shown in the literature [3], it was the first device that could be created by combining various technologies other than Dr. Tanaka's "soft laser desorption/ionization technology". I think it can be said that it is a significant technical achievement. I think it is safe to say that the following MALDI-TOFMS products are almost the same in principle.

As mentioned above, the application fields of MALDI-TOFMS are expanding, and it is a significant technical achievement because it has greatly contributed to the development of molecular biology and medicine/pharmacology.

Q4) Were there similar or competing achievements? If so, have the proposers adequately described these and their relationship to the achievement being proposed?

As described on page 3865 in the literature [3], until Dr. Tanaka invented the "soft laser desorption/ionization technology", the molecular weight that could be ionized by the laser ionization method was up to about 1,000, and the molecular weight could only be detected by several thousand by other methods. With this invention, Dr. Tanaka measured ions with molecular weights of more than 35,000 in 1985 and more than 100,000 in 1987. The difference is close to two decades of magnitude, so it can be said that it is completely different from other methods. Referring to Dr. Tanaka's method, Dr. Karas and Dr. Hillenkamp published a paper in
1988 stating that they had succeeded in detecting a molecular weight of 10,000 (literature [16]). But since Shimadzu had already released the product LAMS-50K that year, it can be said that there is no other result that can be compared.

To discuss further, MALDI is a technology very similar to ESI (electrospray ionization) by Fenn et al. in that the target of interest is macromolecules. However, while MALDI targets solids, ESI targets liquids, which is a major difference, and therefore the application areas are also different. It can be said that there is no competition but is complemental relationship between MALDI and ESI.

I, the reviewer, conclude as follows. This proposal has the value of being certified as IEEE Milestone.

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If this is satisfactory, I would greatly appreciate it. Thank you.

Best regards,

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