Advocate’s Recommendation for the IEEE Milestone
#2023-29 “Laser Ionization Mass Spectrometer, 1988”

Date: February 9th, 2024.

Dear IEEE History Committee.


(1) Expert Reviewers:
I asked following three independent experts in the field of the proposal to conduct a detailed review from a technical point of view.

Dr. Yoshio Kodera:
Professor in the Department of Physics, School of Science, Kitasato University.
Director of the Proteomics Center for Disease, School of Science, Kitasato University.

Dr. Tohru Yamagaki:
Senior Researcher and Head of Division of Structural Biomolecular Science, Suntory.

Dr. Kanako Sekimoto:
Associate Professor, Graduate School of Nano-bioscience, Yokohama City University

(2) Expert Reviewer’s Reports:
I requested these expert reviewers feedback on four questions:
Q1) Is the suggested wording of the Plaque Citation accurate?
Q2) Is the evidence presented in the proposal of sufficient substance and accuracy to support the Citation?
Q3) Does the proposed milestone represent a significant technical achievement?
Q4) Were there similar or competing achievements? If so, have the proposers adequately described these and their relationship to the achievement being proposed?

Finally expert reviewer’s conclusions.
I will address each below.

Q1) Is the suggested wording of the Plaque Citation accurate?
Dr. Yoshio Kodera’s comment:
“Yes, the wording on the Plaque is written accurately and concisely. I specialize in disease proteomics,
and it is no exaggeration to say that the birth and great development of the field of proteomics since the late 1990s has been due to the development and spread of mass spectrometry that can be applied to macromolecules. The development of proteomics is directly linked to the development of molecular biology and medicine.

There are two main types of such mass spectrometers: Matrix-Assisted Laser Desorption/Ionization Mass Spectrometer (MALDI-MS) and Electrospray Ionization Mass Spectrometer (ESI-MS). The LAMS-50K is the prototype of MALDI-MS.

Dr. Koichi Tanaka, who invented the laser desorption ionization method that is the key to MALDI-MS, was awarded the Nobel Prize in Chemistry in 2002 together with Dr. John B. Fenn, the inventor of the ESI method. This is because these inventions have made an extremely significant contribution to molecular biology and medicine.

The year 1988, when the LAMS-50K was launched, was the year in which Dr. Tanaka (Shimadzu Corporation, Japan) and Dr. Hillenkamp and Dr. Karas (University of Munster, Germany) separately published papers on the fact that mass spectrometry of macromolecules could be realized by the MALDI method (Ref. [14] and [16]). At that time, there would have been equipment that could do this in the laboratory, but the LAMS-50K designed by Shimadzu was the first commercially available product. For this reason, this wording is appropriate. “

Dr. Tohru Yamagaki’s comment:
"Yes, the wording of the proposed Plaque Citation is accurate.

The 2002 Nobel Prize in Chemistry was awarded for the development of methods for identification and structure analyses of biological macromolecules. One half was devoted for the development of multidimensional NMR methods, and the other half was devoted to "the development of soft desorption ionization methods for mass spectrometric analyses of biological macromolecules". Half of them was for the Electrospray Ionization (ESI) developed by Dr. John B. Fenn in 1988, and the other half was for the "Soft Desorption Ionization Method" invented by Dr. Tanaka. As a result of these achievements, biomolecules can be analyzed precisely and accurately, and the analysis of biological phenomena has progressed dramatically, and it was recognized as worthy of the award.

The first instrument to realize this Nobel Prize achievement was the LAMS-50K, and it can be said that the prototype of the mass spectrometer popularized as MALDI-TOFMS was completed here. As the Nobel Prize in Chemistry suggests, MALDI-TOFMS has made a significant contribution to molecular biology and medicine.

Therefore, the wording of the Plaque Citation is appropriate."

Dr. Kanako Sekimoto’s comment:
"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?

Dr. Yoshio Kodera’s comment:
“...”

Dr. Tohru Yamagaki’s comment:
“Yes, the evidence presented is sufficient and correctly cited.
In the reference [4] it is indicated that in 1988 the LAMS-50K was launched, and in 1990 it was delivered to the City of Hope laboratory. In the literature [3](page 3868) also indicates that the product was installed at the City of Hope Institute.
By the same literature, it can be understood that various new technological developments and combinations were required for the development of the device. One notable example of MALDI-TOFMS continuing to develop and disseminate is the microorganism identification shown in the..."
literature [7], which is widely used in hospitals and medical institutes nowadays.

The application of MALDI-TOFMS, which I am currently paying a lot of attention to, is mass microscopy, which is mentioned in the literature [8]. Following the principle of MALDI-TOFMS, it is performed by mass mapping by laser irradiation scanning. In other words, we can know the localization of molecules. This technology is expected to become a very important tool for understanding life phenomena and the structure and dynamics of living organisms at the molecular level.

The scope of application of MALDI-TOFMS is not limited to these, but in order to understand its widespread use and development, it is sufficient to check the above current situation in conjunction with market research reports such as reference [6].”

Dr. Kanako Sekimoto’s comment:

“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-deep 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?

Dr. Yoshio Kodera’s comment:

“Yes, I think so. First of all, in order to perform mass spectrometry, it is necessary to ionize molecules without decomposing them, and Dr. Tanaka was the first in the world to achieve this, which earned him the Nobel Prize. However, mass spectrometry cannot be performed simply by ionization. Mass
spectrometry can be performed and made into a product only by achieving all of the things that were not possible with conventional equipment, such as separating macromolecule-ions according to their mass without scattering them, converting them into electrical signals at high speed with a detector that receives ions, minimizing the loss of ions in the device as much as possible, and maintaining their performance for a long time. The above document [3] shows that various technological developments have been made for this purpose. The fact that this has been achieved as a product makes the LAMS-50K a breakthrough.

Dr. Tohru Yamagaki’s comment:
“Yes, I agree. Dr. Tanaka’s "soft desorption ionization technology" was so groundbreaking that he was awarded the Nobel Prize. As described in the literature [3], the instrumental configuration for realizing mass spectrometry of macromolecules required various new technologies and their combinations in order to take advantage of the revolutionary ionization technology. Since it has come to fruition as a product, it can be said that it is an epoch-making technical achievement.”

Dr. Kanako Sekimoto’s comment:
“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?
Dr. Yoshio Kodera’s comment:
“Prior to the invention of soft laser desorption/ionization technology by Mr. Tanaka and others, as a method of ionizing polymers, Field Desorption (FD) [9], Fast Atom Bombardment (FAB) [10] and others were known, but the molecular weight that could be practically ionized by these methods was up to about 5,000. The laser ionization method was also known, but it could only ionize up to about 1,000 molecular weights.
As shown in the literature [14], Dr. Tanaka et al. achieved the measurement of a molecular weight of 100,000 in 1988, and the advantage is obvious. The LAMS-50K was commercialized in 1988, and there was no competing product at the time.”
Dr. Tohru Yamagaki's comment:
"As detailed in the document [3], page 3865, Section 6 "Ionization Technology", before Dr. Tanaka and colleagues invented soft laser desorption/ionization technology, the molecular weight that could be ionized was limited to several thousand, and Mr. Tanaka's invention increased it to 100,000. The fact that was truly groundbreaking. The MALDI method itself first became known to the world in 1988, when a paper by Dr. Tanaka et al. [14] and an article by Karas et al. [16] were published. At that point, the LAMS-50K was commercialized, so it can be said that there are no achievements such as competing products. Similarly configured "Laser Ionization Mass Spectrometers" were tried [17] and commercialized before, but they are not in the same category with LAMS-50K for they focused to small molecules and were not applicable to macromolecules."

Dr. Kanako Sekimoto's comment:
"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, 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 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 complementary relationship between MALDI and ESI"  

Expert Reviewer's Conclusions:
Dr. Yoshio Kodera's comment:
"Based on the above facts, the reviewer makes the following judgment. This proposal is valid without any objection and should be certified as an IEEE Milestone."

Dr. Tohru Yamagaki's comment:
"The reviewer considers this proposal to be of great value and strongly recommend that 'Laser Ionization Mass Spectrometer' be certified as IEEE Milestone."
Dr. Kanako Sekimoto’s comment:
“I, the reviewer, conclude as follows. This proposal has the value of being certified as IEEE Milestone.”

(3) Advocate’s Comment and Conclusion:
I received the above satisfactory peer review results from three experts in the field of proposals.

Citation:
Three expert reviewers responded that citation is accurate, judging by the answers to question Q1. They also reported that they confirmed that the contents of the citation are supported by evidences, judging by the answers to question Q2.
As an advocate, I have the same judgment as reviewers, too.
One thing I would like to point out is that Koichi Tanaka’s name is in citation. He was awarded the Nobel Prize in Chemistry in 2002 for the technology used in the proposed device. His achievement is significant in the world, and I strongly support his name-in-citation as an advocate.
I hope that this matter will be approved by the Sub-committee in History Committee discussions.

Technical significance and historical value:
Three reviewers gave me detailed answers to question Q3 and Q4.
They explained the technical significance of the Mass Spectrometer with this Laser Ionization technology, and the historical value was explained, too. This can be seen easily from the fact that Koichi Tanaka was awarded the Nobel Prize in Chemistry in 2002.

Advocate’s Conclusion:
All three expert reviewers gave the proposal strong recognition and support that it deserves the IEEE Milestone certification.
I have considered carefully both the proposal and the expert reviewer’s reports and have the same thought as reviewers.
In conclusion, I strongly recommend this proposal to the IEEE Milestone as an advocate.

Best regards,

Tomohiro Hase

Dr. Tomohiro Hase, IEEE Fellow.
Advocate #2023-29, IEEE History Committee.