

IM-MS Interest Group Workshop Report

Title: IM-MS technology in the industry – barriers and opportunities

Date: 03-06-2020

Organizers: Jakub Ujma, Ian Webb, Kelly Hines

Attendance: ~120

Workshop Goals

The availability of commercial instrumentation and continuous improvements in technology have led to the adoption of IM-MS in fields benefiting from complex samples and complex mixture analyses. The latter statement is particularly true for academic labs and discovery led R&D; in other words, promising proof-of-principle experiments have been demonstrated but not always followed by implementation of IM-MS as a routine technique in an industrial setting. In this year's workshop, we attempt to explore the origins of this situation. We invited colleagues from several industries to take part in the panel discussion and share their views on IM-MS technology in their companies.

Invited Panelists

Iain Campuzano

Dr. Iain Campuzano currently leads a multidisciplinary mass spectrometry and analytical team providing analytical support across multiple departments and projects within Amgen Research, Thousand Oaks, California, for multiple modalities including small molecules, peptides, proteins, antibodies, bispecific-bivalents and siRNA. Prior to joining Amgen, Iain worked within the application research department at the Waters Corporation (Manchester, UK) focusing on biological mass spectrometric applications, instrument developments and customer support. Iain has published 54 peer reviewed scientific manuscripts (21 of which are first and/or corresponding author). Iain is also listed as the main inventor/co-inventor of 6 mass spectrometric instrument design and application patents. Iain has given multiple oral presentations and organised interactive workshops and sessions at many international conferences such as the ASMS Annual Meeting, ASMS Sanibel, PITCON, FACS, PEGS, Discovery on Target and IMSC. Iain is currently a member of the JASMS Editorial Board and a Fellow of the Royal Society of Chemistry.

Cris Laphorn

Dr. Cris Laphorn is currently an Investigator at GSK using mass spectrometry to support drug development including impurities and degradants mostly working with small molecules. He previously held positions as Head of Mass Spectrometry Services at the University of Greenwich, Head of Open-Access Mass Spectrometry & NMR at Pfizer and as a mass spectrometry specialist at Novartis. He is the recipient of the 2014 British Mass Spectrometry Society (BMSS) Bordoli Prize. Research interests include using ion mobility with molecular modelling.

Christina Jones

Dr. Christina M. Jones is currently a Research Chemist in the Chemical Sciences Division of the National Institute of Standards and Technology (NIST) where she leads programmatic efforts focused on quality assurance and quality control for metabolomics, a tool for precision medicine. Dr. Jones joined NIST as a National Research Council Postdoctoral Associate in 2015 at the Hollings Marine Laboratory (HML) campus. While at HML, she helped establish a mass spectrometry-based environmental metabolomics program. Before joining NIST, Dr. Jones received her doctoral degree in Analytical Chemistry from the Georgia Institute of Technology. Under the advisement of Dr. Facundo M. Fernández, she developed an ambient mass spectrometry sampling and analysis method for metabolomics research in addition to using traditional chromatographic-based methods for onco- and ecometabolomics applications. Her work has been published numerous times and was featured on the cover of the Proceedings of the National Academy of Sciences.

John Stutzman

Dr. John Stutzman is a mass spectrometrists in the Dow Chemical Company located in Midland, Michigan. He resides in the Analytical Sciences department within Core R&D. John focuses on small molecule structural characterization utilizing HRAM instrumentation and tandem mass spectrometry. He collaborates with a variety of scientists to innovate new products, improve product performance, and resolve current product issues.

Ivana Blazenovic

Dr. Ivana Blazenovic is a senior metabolomics scientist at DiscernDx where she aims to integrate metabolomics into personalized medicine. Her research focuses on the advancement of structure elucidation tools as they represent a major bottleneck in metabolomics. As a former postdoctoral scholar in the Fiehn lab Ivana was involved in multiple projects related to compound identification, including the liquid chromatography ion mobility mass spectrometry technology. She has used the additional orthogonal parameter, collision cross section information of lipids, to annotate previously unknown milk lipids using various machine learning methods.

Workshop Discussion

Following the short introductory presentation from each panel members workshop became a panel discussion where attendees could ask questions via Q&A. Below, we provide a list of questions which were discussed together with the corresponding times in the workshop recording.

(47:20) How would you go about establishing CCS as a standard since CCS values right now are quite variable?

(51:20) What is the most challenging hurdle the IM-MS has to face for more routine use in the industry and how we as a community can help to address that? Automation, applications, training, issues related to regulated environment.

(54:40) What about education and training? Is it easy to recruit scientists with experience in IM-MS?

(58:10) Do you think that adding RF confining field to drift cells improve the resolution or only sensitivity?

(59:20) How would you decide whether to use Synapt G2 versus the Agilent 6560 since you have both instruments available?

(1:00:20) For dealing with identification of unknowns in complex mixtures, several computational methods have been used and proposed, notably the theoretical modelling and machine learning. Each of these comes with its trade-offs in terms of costs, low throughput or low accuracy. Where do you see the greatest advances to be made in those areas and which is more likely to allow for large scale predictive capabilities.

(1:04:50) Do you have example, where you solved a structural problem using CCS, without knowing the molecular structure in advance?

(1:06:45) Which ion mobility mass specs are used routinely at GSK?

(1:07:20) You mentioned use of ion mobility for analysis of impurities. Can you elaborate on that?

(1:08:10) Have you tried the new Agilent's multiplex and higher resolution de-multiplexing? Has this made any improvements in your workflow?

(1:09:00) Is the IM-MS most potentially used in structural characterisation/QC, release test or both?

(1:11:15) With the ever-increasing interest in IM-MS, would you consider a new inter-site comparison to establish the CCS as a molecular identifier or standard for the industrial side, or as a collaborative effort between academia and industry?

(1:16:20) Regarding determination of CCS from first principles. Does NIST have instrument making capabilities? Could this be used to build a drift tube instrument for reference CCS measurements?

(1:18:10) What biggest gaps would need to be filled for the IM-MS to be recommended for small molecule or higher order structural characterisation by regulatory agencies?

(1:20:20) Where do you see the technical developments in IMS going in the future? Is it the speed, higher resolution, cost, accuracy or something else?

(1:24:10) How is IM-MS software compliance ready? What kind of challenges doe open-source software packages present for compliance/industry applications?

Workshop Feedback

Following the workshop attendees have been asked to fill in two surveys. First one was to provide general feedback. The second one was aimed at the industrial scientists, where the goal was to identify barriers faced by industrial users.

General Feedback Survey

Responses:	13
Overall Experience (1-5):	4.0
Topic (1-5):	4.2
Format (1-5):	4.1

Comments:

"Thank you for dealing with audio issues right away! And doing the best possible job with the limitations of zoom."

"For next year I would really appreciate if we have a few Im-ms and machine learning talks. Thank you for all the talks this year."

"This was a really good session - actually something very similar next year would be great. It's good to hear how industry users view this relatively new technique and what can be done to broaden the scope and adoption of IM-MS."

"Hearing from industry professionals was a really unique perspective compared to previous years! Ideally I would have enjoyed more opportunity for audience participation in discussion beyond just questions, but realize the feasibility of that in a virtual format was low. Thank you for putting together such an informative and engaging workshop!"

"Thank you for organizing this meeting! I'd suggest inviting representatives from the IMS-MS companies (e.g. Kevin Giles from Waters) on the panel."

"Enjoyed the discussion as to the future of IM and where it needs to improve, especially to become routine for industry. I would have preferred more of a balance in the presentations on protein and protein assembly analysis by IM compared to small molecules, metabolomics and lipidomics analyses."

"The topic didnt seem particularly helpful. NIST calibrated standards on a drift tube would be nice, but there are downfalls to almost every low pressure commercially available system regarding accuracy vs. precision. Such work would almost have to be done on a home built drift tube, but the reference CCS/KO values would be immensely useful for TIMS/TWIMS people."

"Was expecting more concrete examples and data, though I understand that sharing industrial data is not easy. Also was hoping to see glycan work/research and the issues /barriers associated with glycan characterization in industry."

“This was a great workshop for a new grad student in an ion mobility applications lab. It was interesting to see how ion mobility is being used in industry but also where it falls short and things that we may need to work on to make it more widely applicable and worth the expense. I liked the format with short presentations and a longer Q&A discussion, but there was one panelist who spent a lot of time talking during the discussion and I would've liked to hear from the other panelists a little more. However, the moderator was great and gave plenty of time for others to chime in, so that panelist may have just given great answers that no one felt the need to add to.”

“There is a lot of work that must be done to make IMS-MS useful flexibly in industry. I must reference Viehland's book entitled "Gaseous Ion Mobility, Diffusion, and Reaction" where he claims more fundamental theoretical development in combination with molecular modeling is needed to unravel the issues. Viehland is a theorist and not an instrument developer. As an instrument developer, I always wanted speed of analysis and ease of interpretation that perhaps machine learning tools could provide (and I helped to implement them), but without fundamentals I realized there was no understanding of issues. I wish I could feel differently, but it has been a personal struggle for me after nearly 60 years of experience in this field to feel otherwise. Globularly shaped ion mobility peaks often produced by present day instruments exasperate me. In making these comments, I acknowledge that some really good work is going on and I greatly applaud those efforts. Unlike previous workshops, this workshop started to address the issues. Thanks so much!”

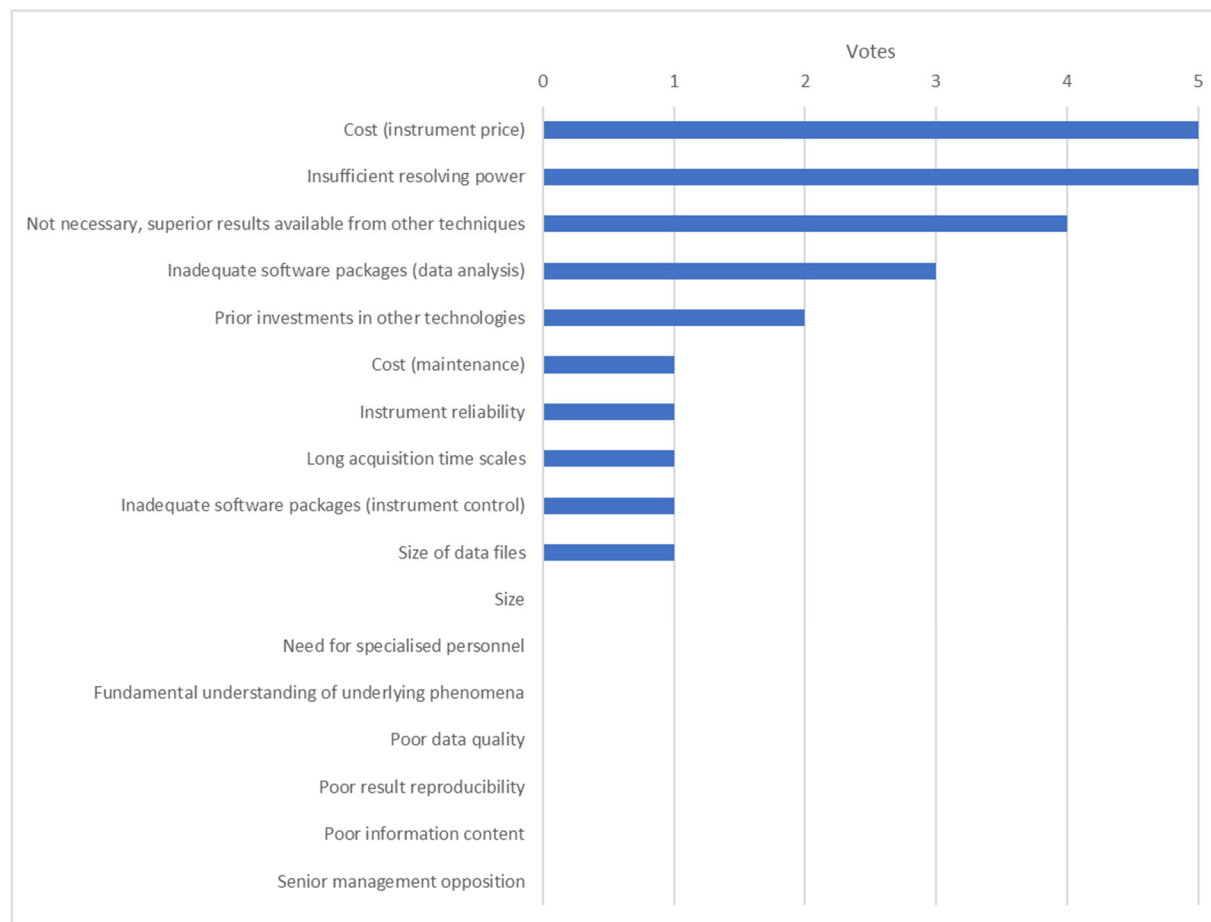
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“The industry based IM discussion worked very well. For next year, maybe consider a discussion on alignment on theoretical ccs algorithms. There are so many and all give slightly different values, which one is the most accurate? May also consider future hardware developments. Maybe Waters AGILENT, Bruker and PNNL would be willing to discuss what they think are the next phases of instrument evolution.”

Industrial Scientist Survey

Unfortunately, we only received five responses; thus, it is difficult to draw conclusions from this survey. Nevertheless, we provide a summary of replies below.



Comments:

"There is no need to complement NMR or choral chromatography when it is used in house and operated by led chemists. IM more of a MS person's toy than a tool for new chemists."