

## IMS Workshop Report: When Chromatography Just Won't Do.

### ASMS 2019 Atlanta

This year's workshop focused on ion mobility spectrometry in applications requiring fast separations or when a particular gas-phase experiment was not compatible with traditional chromatographic methods. Keeping with this theme, we invited young scientists to share their experiences with ion mobility technologies used to solve their research problems. The goal of these talks was to generate discussion in the workshop regarding the variety of solutions enabled by IMS coupled in tandem with MS and also to highlight the range of challenges facing the integration of chromatographic techniques with high resolution and new IMS approaches.

### Workshop Presentations

Representing the workshop organizers, **Brian Clowers** gave a short introduction to the session in which he introduced invited speakers and honoured the foundational work performed in Atlanta (Georgia Tech) by Earl McDaniel and Edward Mason. In addition, possible topics for the next year's workshop were suggested along with community driven initiatives, such as standardized IM instrument ("NIST-Tube").

**Klaudia Kocurek** from Texas A&M shared her work on liquid surface extraction analysis (LESA) coupled with MS. LESA workflow allowed for rapid sampling of minute amounts of biological material, directly from bacterial colonies. Mass spectral data yielding from such samples is often very complex; moreover, the signals originating from molecules of interest (in this case proteins) may be heavily suppressed. To alleviate this issue, Klaudia implemented a field asymmetric ion mobility separator (FAIMS) between LESA interface and MS inlet. FAIMS enabled the effective filtering of molecules originating from different molecular classes and reduced ion suppression. Thus, Klaudia was able to detect many intact proteins, including some which have not been previously characterized.

**Kyana Garza** from the University of Texas at Austin presented her work on desorption electrospray ionization (DESI) imaging. DESI imaging is a technique that can be performed at atmospheric pressure with minimal sample preparation, which is appealing to histopathology and clinical applications. A key requirement in any imaging-MS technique used in the clinical setting is the speed of analysis. In her research, Kyana encountered similar problems to those of Klaudia, including the presence of a high amount of the "chemical noise" which interfered with the identification of the ions of interest. Following the incorporation of a FAIMS module between the DESI imaging stage and her mass spectrometer, Kyana was able to "filter-out" the interfering background ions and interest and enhance the detection of intact proteins directly from the brain tissue. Thus, FAIMS proved very efficient in improving the DESI-MS imaging of proteins from brain tissue sections.

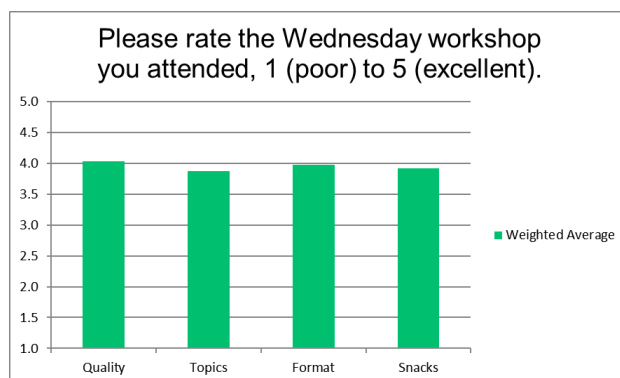
**Cara D'Amico** from the University of Michigan is working on the project bridging capillary electrophoresis (CE) with structural characterization approaches offered by IM-MS instrumentation. In her research, she uses the technique of collisional induced unfolding (CIU) where IM separation is used to monitor changes in the protein structure due to collisional activation. The so-called "CIU fingerprints" offer highly specific information about protein structure, stability, and ligand binding. However, the traditional CIU implementation was too slow for Cara's needs, especially in the context of coupling with CE upfront. Thus, an automated control software was implemented to enable "fast

CIU” experiments, requiring 15x less analysis time. Cara’s results highlighted the potential of “fast CIU” in drug discovery applications, such as high-throughput screening of enzyme and protein-protein interaction inhibitors.

**Ansgar Kirk** from Leibniz University Hannover gave a very entertaining talk showcasing his recent development of linear drift tube IM coupled with ToF-MS. The designs featured relatively short (~15 cm) drift cells, operating at atmospheric pressure under a strong electric field (~1.7 kV/cm). Together with the specially designed ion shutters, Ansgars’ setup allowed for mobility separations at resolving powers in excess of 200 at very short time scales. Interestingly, his IM separations were so fast that ToF-MS sampling of arrival time distribution was insufficient. Thus, he highlighted the fact that the novel, rapid IM separators may soon become too fast for the current MS detection systems. Additional information was also provided regarding efforts to couple such high resolution IMS systems with fast GC for a variety of applications.

### Workshop Feedback

The workshop was very well attended with many participants standing due to lack of seating. The survey response was overall positive. Survey responders (n=91) considered the workshop to be of good quality (4.0/5.0). The workshop format and this years' theme did appeal to most of the responders (4.0/5.0 and 3.9/5.0 respectively).



The survey comments are listed below:

*“This session is great! People presented their innovations in the IMS technology and methodology. Some presentations are even better than those in the IMS oral sessions.”*

*“I was interested in learning IMS basics and fundamentals, but this seemed targeted towards those with more experience.”*

*“Difficult to hear the speakers at times. Microphones were not working properly at the beginning of the session.”*

*“It didn't feel as much like a workshop in terms of explaining how the coupling of chromatography to IMS was achieved, and focused more on results of the research. Last year's workshop did a better job of explaining how to build your own build your own IMS. The last speaker this year was amazing though.”*

*"Also, that room was absolutely packed, and a bigger room needs to be allotted to this workshop next year."*

*"The IM workshop basically was 3 presenters, who gave fine presentation. But essentially there was no time for discussion, so it was just 3 more IM talks. Not super useful. I know that previous IM workshops were kind of a PI yelling match (entertaining), and this setup is probably designed to mitigate that. But ultimately it just became 3 additional oral talks on IM that I attended. I know the yelling matches can be rough, but at the end of the day there are a lot of challenges in our field that need discussion. Even if it is tough, to move the field forward these topics need to be addressed (like accepting single field IM CCS values), should computational CCS be acceptable in databases, and other topics."*

*"Again, presentations were too long and not open for discussions."*

*"This workshop had longer presentations (10 mins) than others I attended, and seemed to have much less discussion as a result. The 5 min presentation format seems to work well in promoting discussion compared to 10 min presentations."*

*"Too much of 'oral presentation', not enough discussion."*

*"Too much time spent on FAIMS that did not work. Fundamentals of IMS analyzer operation missing."*

*"Should have just been called FAIMS appreciation session."*

*"The talks were all very good; however, there is some overlap between ion mobility and structure elucidation, and both of these workshops were held on the same night."*

*"This was excellent!!!! very good selection of talks, mostly young and smart women, even better than talks I have seen in oral session!"*

*"Well organized. Looking forward to next year!"*

*"there were no snacks on my level of the building, beer and chips is fine, but for those of us who are dry..."*

*"It would be more interesting if there were more speakers focused on IMS for not only imaging and FAIMS."*

*"Not what I was expecting given the title. As someone just trying to get into IMS I was hoping for a more general presentation and discussion. It seemed more geared towards established IMS users. Which is fine, but the description and title made it sound more beginner friendly."*

*"Long talks feel like an extension of afternoon orals. Interest groups should be a little meta, discussing trends or the topics within a broader framework."*

*"Was more focused on FAIMS than I expected."*

*"This workshop needs to be held in a bigger room."*

*"I attended your Wednesday ASMS workshop. I found the talks very interesting and diverse for a workshop. The speakers were well chosen and its nice to see the young students presenting too."*

*However, I think they may have been a little too focused and heavily academic biased."*

*I can't remember what the topic was last year, however, the format in 2017 worked well when there was a discussion about standardization, and from that can Valerie's recent manuscript. It was certainly a well-timed discussion.*

*As a suggestion for next year I think you need to address why IM is not really being used and applied in pharma and other industries. I would recommend having half your presenters from industry explaining why they do or do not use IM or why they think its more niche to solve specific problems. You may want to consider a slightly controversial presentation to stimulate a bit of discussion.*

*I worry that the IM workshop remains too academic and too fundamentals focused. I have been trying to understand over the past number of year why we in pharma just don't use IM, and I have not yet come to a conclusion. I may have some nice pharma related examples for ASMS next year, where IM makes a difference and complements other analytical techniques.*

*What I do know is that there are many other, more well established techniques such as DSC, DSF (for protein unfolding) and SFC-MS for molecule separation. Maybe contrasting these techniques with IM would make a useful workshop discussion?"*

*"Well done!!"*

*"Would've liked to see more of an interactive tips&tricks format, rather than just shorter conference talks."*

*"I would like the workshop to be more discussion-based. Maybe half talks/lectures and the other half structured discussion."*

Workshop organizers would like to thank for all the comments and the constructive feedback. Next year we will do our best to facilitate open discussion and involve the audience. We also appreciate the suggestion for the requirement of the fundamentals "refreshers" which we will try to accommodate together with the main topic of the workshop.

With very best regards,

Jakub, Brian and Ian.