The Big Debates from Eastbourne

Billions of dollars spent and proteomics has delivered nothing!

Tom Knapman (ABSciex) and Stephen Holman (University of Liverpool)

A highly emotive and controversial title set the scene for a lively discussion in the first of the panel discussions at BMSS 2013. Four expert panellists, Dr. John Griffiths (Cancer Research UK Manchester Institute), Dr. David Knight (University of Manchester), Professor Frank Pullen (University of Greenwich) and Professor Paul Thornalley (University of Warwick) answered a variety of questions from the floor focussing on all aspects of proteomics.

A particular topic that raised interest in an audience whose research is predominantly technology-focussed was whether there is simply too much methodological research in the field: several new papers appear in the published literature every month that report minor incremental advances over existing approaches. Should this work be eschewed in favour of more focussed biological studies where understanding of disease could be garnered? Or do we risk incorrect, and potentially dangerous, conclusions if such work is not built on solid analytical foundations? The responses from the panellists were mixed, but the overriding message was that the methods should always be fit for purpose and thoroughly evaluated before application to important biological questions.

Another interesting topic was that of biomarkers. Having been heralded as the approach to deliver clinically-relevant biomarkers for many diseases, proteomics has thus far failed in many people's eyes to fulfil this promise. The panellists felt that the one of the biggest impediments to delivering biomarkers was that of sufficient funding. Testing of a putative biomarker's ability to be diagnostic for a given condition requires large cohorts of patient samples (both diseased and healthy controls), which has an enormous attendant financial cost to sample and analyse, in addition to administrate. The panellists cited that the many academic groups engaged in biomarker discovery simply do not have the means to conduct such large-scale studies and translate their efforts into the clinic, and that for large companies the problem lies in deciding which potential biomarkers to pursue from the plethora reported in the literature; a problem akin to pharmaceutical companies deciding which candidates from discovery to progress to the development stage. A satisfactory solution is not obvious, but for proteomics to accomplish this long held goal significant financial risk needs to be taken, which is unlikely in the current economic climate.

An important point was made during the discussion and one that should not be forgotten: proteomics is a multi-disciplinary field encompassing not only mass spectrometry and analytical chemistry, but disciplines such as cell biology, clinical science and bioinformatics. For proteomics to truly deliver (some say that it already has, whilst others will disagree) then synergy between these different communities needs to be a priority. Spectacular advances in one will not address all of the biological questions that one may wish to answer, but will instead be hindered by the weakest link in the chain. It is up to the mass spectrometry community to ensure that they strive to provide the best possible analytical measurements for their colleagues in the field to further the science of proteomics.

Ambient ionisation workshop

Andy Ray and Dan Weston, AstraZeneca

The Ambient Ionisation Workshop 'Can we throw out all our LCs and GCs?' started with a review of the results from the Ambient Ionisation Survey. As expected the commercially available techniques dominated with an even split between DART, DESI and ASAP. The type of instruments used produced an even split between characterisation instruments (ToFs and Orbitraps) and more quantitative instruments (single and triple quadrupoles). The application areas showed a good distribution across the area with chemistry the largest area. No sample preparation and fast analysis were the most common reasons for wanting to adopt these techniques with the potential for imaging also of interest.

The Workshop then discussed whether ambient ionisation had delivered what was expected and if not what were the causes and potential solutions. The consensus was that ambient ionisation is more heavily used in a qualitative environment in a wide range of application areas (such as chemistry and forensics) but has perhaps not become a routine tool as may have been hoped. The large range of techniques available mean it is hard to know which technique is best for a particular application area. The discussion raised several possible reasons for this; a lack of understanding around the fundamentals of these techniques, limited automation, hard to demonstrate in new application areas, industry inertia and the acceptance barrier for new techniques (which is common for all new technologies not just ambient ionisation mass spectrometry). Some areas may not be suitable for ambient ionisation techniques currently, such as dried bloodspot analysis, although newer techniques such as Paperspray may offer a solution.

The general feeling was positive for the future of ambient ionisation as witnessed by ~100 people attending the workshop including several students actively working on ambient ionisation techniques. The solutions proposed to these issues include further work to understand the fundamentals, understanding the physico-chemical space that different techniques will ionise, continuing to develop new techniques but targeted at areas where current techniques are less successful and to allow more access to the techniques for new application areas. There was also interest in combined sources to maximise the range of compounds ionized.

Towards these solutions the Ambient Ionisation SIG will be holding a Round Robin to start understanding the physico-chemical space and we will be holding a meeting next year to report the results.