What is the future of MS as a "Science"

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Alain Van Dorsselaer is Emeritus CNRS Research Director at the University of Strasbourg. His group has constantly developed new analytical methods and strategies based on mass spectrometry, first for large synthetic molecules and supramolecules, and then for peptide and protein characterization, including posttranslational modifications. He has developed new methods for the study of noncovalent interactions in chemistry for supramolecules and then in biology for protein/protein and protein/ligand interactions. His group is now focusing on structural mass spectrometry and on the development and the application of proteomic methodologies in a large variety of domains, including the characterization of biopharmaceuticals in collaboration with pharmaceutical companies.

Abstract:
This presentation is dedicated to young scientists interested in mass spectrometry. Some of them could fear that mass spectrometry will not allow any more basic research programs and will become a "service science for other disciplines". Indeed, after almost 30 years of constant efforts and progresses of the mass spectrometry community, it seems that it is now possible to identify and quantify rather accurately thousands of proteins from very low sample amounts. This can be achieved with instrumentation and software tools that are getting commonly available in core facilities of biology institutes, such as for genomics, transcriptomics, metabolomics, ...
However, proteomic analysis is far from producing a full description of proteomes since a full characterization of most proteins present is not yet possible. All proteoforms from one gene are usually detected and quantified under the same name and post translational modifications are rarely systematically detected. Almost nothing is known on their combination when they are multiple. While MS/MS fragmentation of digestion peptides may enable determining their full sequence, this is still hardly achievable for, as an example, multiply phosphorylated proteoforms using top down approaches. There is clearly a long way to go before this will be possible and a large room for the development of innovative approaches in separation sciences and mass spectrometry is open.
Besides proteomics, there are many other fields in which major developments will offer opportunities to extend the use of mass spectrometry-based structure determination methods both in biology and chemistry.
The main research fields our laboratory has contributed to over the past 30 years will be presented to illustrate the attractiveness of mass spectrometry and the importance of technical developments. For example: - From Hopane triterpenes as biomarkers in sediments and oils, to protein biomarkers for diagnostic of lymphopathies. - How the characterization of molecular self-assembled supramolecules led to the characterization of large multi-protein complexes. - How the determination of the assembly order of supramolecules subunits led to the elucidation of multiprotein complexes. - How, thanks to bioinformatics developments, proteomics analysis of organisms with unsequenced genomes was made possible for the study of new metabolic pathways in exotic animal models. - Performing differential display of peptides induced during the immune response from a single Drosophila. - How the use of proteomic analysis-derived

methods and Ion Mobility were used to guide the production of biologics, and in particular monoclonal antibodies, with high purity and batch-to-batch consistency.
This series of examples will illustrate that mass spectrometry remains a fascinating and attractive science for young scientists that are willing to evolve in highly stimulating multidisciplinary contexts.