News

Bruker Announces Major Advances in CCS-Enabled 4D Proteomics at ASMS

- ***Bruker PaSER™ software now incorporates transformative CCS-enabled DIA-NN deep neural network learning with breakthrough dia-PASEF capabilities to identify:***
  - >8000 quantified cell lysate proteins with 40-minute gradients
  - >5000 quantified cell lysate proteins with 4.8-minute separations on Evosep One
  - >5000 quantified proteins in just 10 ng of cell lysate digest with 95-minute gradients
- ***Work-in-progress CCS-enabled 'prm Live' on timsTOF Pro enables low-cost, targeted proteomics with >1800 peptides quantified with highest sensitivity and excellent CVs***
- ***Advances in CCS-enabled TIMScore™ algorithm yield significantly greater phosphopeptide and protein coverage with more confident peptide identifications***
- ***Novel OligoQuest™ software and workflow for high confidence sequence verification in support of RNA and modified oligonucleotide therapeutics development***
- ***SCiLS™ autopilot software for automated Mass Spectrometry Imaging (MSI) acquisition on the timsTOF fleX and rapifleX® MALDI platforms using Bruker IntelliSlides™***
- **Showcasing two novel systems launched already in June 2021:**
  - *timsTOF SCP* for unbiased single cell proteomics (SCP), e.g., to study cell-type specific proteomes in spatial cancer biology and correlate them with sc-RNA-seq transcriptomes
  - next-generation *timsTOF Pro 2* with unprecedented proteomic depth and throughput

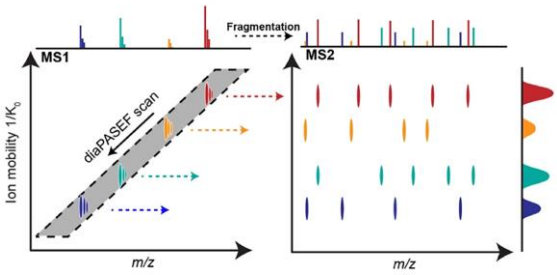
PHILADELPHIA, Pennsylvania – November 2nd, 2021 – At the 69th ASMS meeting in Philadelphia, Bruker Corporation (Nasdaq: BRKR) announced novel CCS-enabled 4D proteomics for major capability enhancements for *timsTOF Pro 2, timsTOF fleX* and *timsTOF SCP* mass spectrometers.

Dr. Rohan Thakur, Bruker's EVP for Life Sciences Mass Spectrometry explained: "*TIMScore* developed by the Yates Lab at Scripps reduces peptide candidate ambiguity by evaluating predicted against experimental CCS, for forward and decoy/reverse peptides. The utility of CCS values augments DIA-NN in our collaboration with the Ralser Lab at Charité, and it also enhances the detection of PhoX™ crosslinked peptides in our collaboration with the Scheltema Lab at Utrecht University. Finally, the Marto Lab at Dana Farber Cancer Institute just published CCS-enabled *prm Live* with real-time retention time corrections for parallel targeted high-sensitivity, low CV quantitation of over 1800 peptides."

A. *PaSER* powered by CCS-enabled *DIA-NN* for dia-PASEF workflows

Translational proteomics, requiring high-throughput, short gradients and uncompromised proteome depth is achieved using dia-PASEF, published in *Nature Methods* [Mann, Nat Meth 2020], and supported by various proteomics software packages including DIA-NN, Spectronaut, MaxQuant and PEAKS Online. The DIA-NN software [Demichev, Nat Methods. 2020] version 1.8 incorporates a novel CCS module for deep neural network learning to score peptide spectrum matches [Demichev, bioRxiv 2021] in dia-PASEF.

In collaboration with Drs. Vadim Demichev and Markus Ralser at the Charité – Universitätsmedizin Berlin, Bruker is now integrating CCS-enabled DIA-NN into PaSER GPU-powered proteomics software for the timsTOF platform for enhanced identification and quantification. Professor Ralser and co-workers work accelerates translational proteomics in large sample cohorts and is transformative by identifying >5000 quantified proteins in 5-minute acquisition times with dia-PASEF.



Graphical representation of dia-PASEF scan function

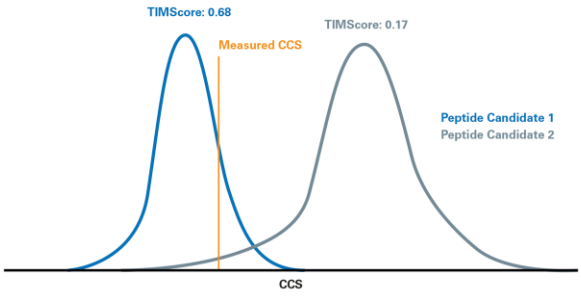
Dr. Markus Ralser, Einstein Professor of Biochemistry at Charité, commented: "We've been very impressed with the performance of the timsTOF Pro in our laboratories. We're also pleased to see Bruker incorporating the open-source version of Vadim Demichev's DIA-NN in its PaSER real-time proteomics workflows and look forward to working with Bruker to further improve 4D-Proteomics workflows."

B. *prm-PASEF Live* increases number of targeted peptides for high-sensitivity quantification

prm-PASEF workflows for parallelization of targeted compound acquisition maintains very high sensitivity while targeting more compounds than traditional PRM approaches. A new prm-PASEF editor can now be used independently or when Skyline™ is used to create prm methods. A recent paper by Professor Jarrod Marto et al. "PRM-LIVE with Trapped Ion Mobility Spectrometry and Its Application in Selectivity Profiling of Kinase Inhibitors" dynamically adjusts retention time windows for reproducible target scheduling using iRT peptides as retention time standards to quantify 1857 tryptic peptides from cell lysate in a 60 min acquisition. This innovative *prm-PASEF Live* concept overcomes chromatographic drift in retention time and improves quantitative precision and reproducibility of multiplexing targets. Dr. Marto will present at the Bruker Press Conference at ASMS on November 2nd at 11 am EDT.

C. *TIMScore* for CCS-enabled database search engines

CCS values in 4D-Proteomics applications are used in post processing for 'match between runs' for label-free quantitation [Cox, MCP 2020]. TIMScore now harnesses machine learning for a CCS-enabled algorithm enabling search engines to provide greater peptide and protein identification while retaining stringent false discovery rates (FDR). Hundreds of thousands of experimental data points were used to train a ML algorithm that can accurately predict CCS value of tryptic and phosphorylated peptides. Phosphorylation plays a critical role in cell signaling and biology, but phosphorylated peptides are more difficult to identify. TIMScore increased the number of phosphorylated peptides by >10% in unenriched leukemia cell line samples provided by Professor Eric Fischer at the Dana Farber Cancer Institute.



TIMScore, machine learning powered CCS prediction for reduced peptide ambiguity and increased confidence

Professor Stanley Stevens at the University of South Florida added: “TIMScore increased the identification of phosphorylated peptides enriched from mouse microglia cell line by 11%. CCS values and 4D-Proteomics have become indispensable in our application of mass spectrometry-based proteomics. TIMScore shows promise to transform how DDA searches are performed, identifying many more meaningful peptides and proteins allowing us to go deeper into the proteome using CCS.”

D. Launch of *OligoQuest*™

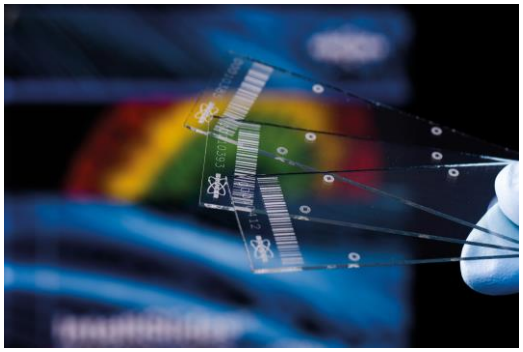
Bruker’s new OligoQuest software in the GLP-ready *BioPharma Compass* suite offers enhanced RNA and oligonucleotide characterization. *OligoQuest* leverages high isotopic fidelity from *maXis II* and *timsTOF Pro* to characterize nucleic acid macromolecules, such as single-guide RNA as well as their impurities. Furthermore, fast PASEF acquisition maps complex mixtures derived from digested mRNA samples.

Co-developed with RiboDynamics, LLC, *OligoQuest* offers algorithms and workflows to annotate tandem MS data from oligonucleotide sequences >100 nucleotides. Dan Fabris, CEO of RiboDynamics and Harold S. Schwenk Sr. Professor at the University of Connecticut, explained: “Isotopic fidelity combined with ultra-high resolution mass spectrometry has shown tremendous promise for the analysis of highly modified RNA, but commercial software tools have been unavailable. Simplifying this analysis with OligoQuest will dramatically accelerate research and development in the RNA space.”

OligoQuest interface displays 3’- and 5’-terminal and internal fragment matches for sequence confirmation

E. *SCiLS autopilot* for automating MALDI Mass Spectrometry Imaging (MSI)

Bruker introduces the automated setup of MALDI Imaging with *SCiLS*™ *autopilot* enabled by IntelliSlides™. *SCiLS autopilot* automatically conducts six key performance optimizations to quickly move from a prepared slide to acquisition of data. The scanned sample image is registered with on the barcode on the IntelliSlide, tissue margins are automatically detected, followed by automated multi-step optimization to decrease the time and expertise needed for MALDI Imaging, and to ensure reproducibility and image quality. Through SCiLS autopilot automation, MALDI Imaging can be easily integrated by non-expert users to add physiological tissue context to their 4D-Omics studies.



Enabling fast and precise automated setup of MALDI Imaging measurements

Dr. Michael Easterling, Bruker Director of MALDI Imaging, stated: “With market adoption of MALDI Imaging in biopharma, intelligent automation is important to ensure seamless integration of imaging and a driver of robust results. Deep platform integration of acquisition and processing software with imaging-optimized platforms, such as the timsTOF fleX, provides spatial physiological context to multiomics.”

References:

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[Demichev, bioRxiv 2021]: https://doi.org/10.1101/2021.03.08.434385

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[Marto, Anal. Chem. 2021]: https://doi.org/10.1021/acs.analchem.1c02349

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