Toward the ideal mass analyzer with data-independent acquisition and parallel accumulation – serial fragmentation (diaPASEF)

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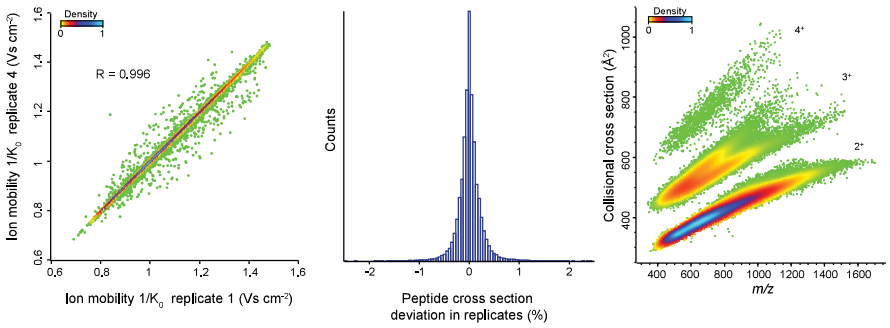
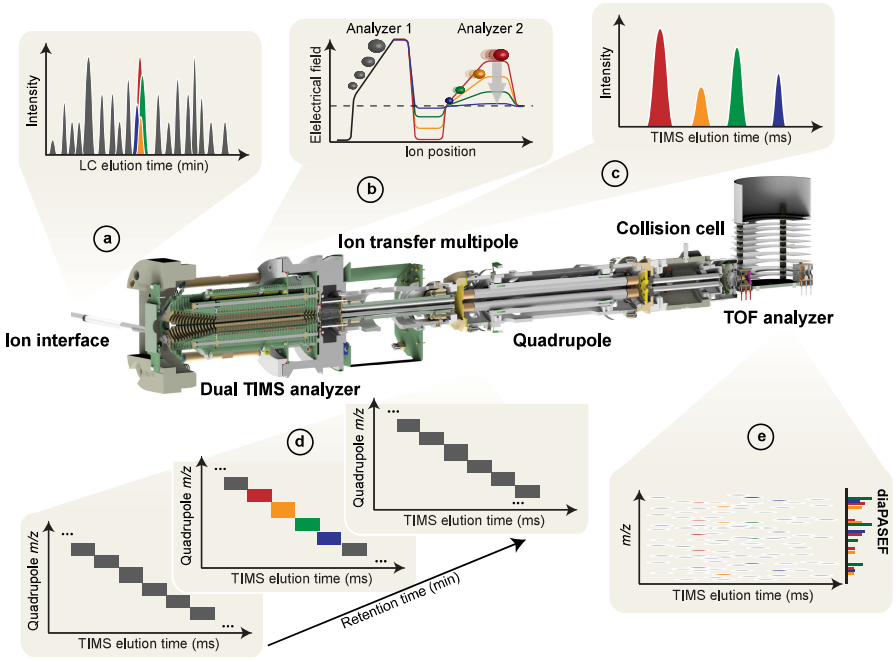
Introduction

In bottom up proteomics, state-of-the-art mass spectrometers efficiently transfer ions into the vacuum, but mass analyze only a small fraction of the ion beam. In principle, a 100% duty cycle could be achieved by parallel ion storage and sequential release from a trapped ion mobility (TIMS) [1] device into a quadrupole time-of-flight mass analyzer. Synchronizing the ion release from the TIMS device with the quadrupole (PASEF) increases the MS/MS sequencing speed by more than 10-fold without any loss in sensitivity in online DDA experiments [2,3]. Here, we asked if the PASEF principle can be transferred to DIA, combining the advantages of both. Data analysis has been integrated in the OpenSWATH pipeline [4].

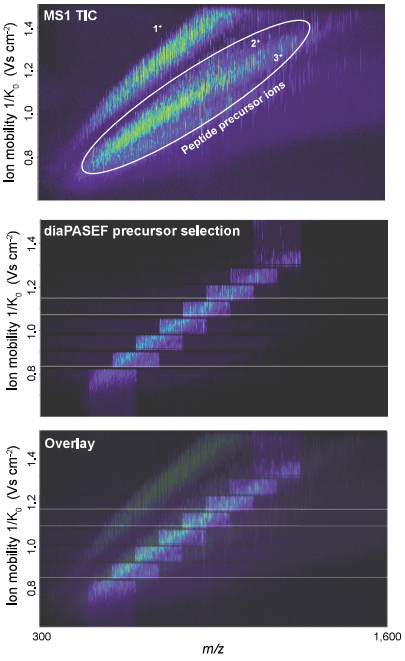
Adding a fourth dimension to proteomics



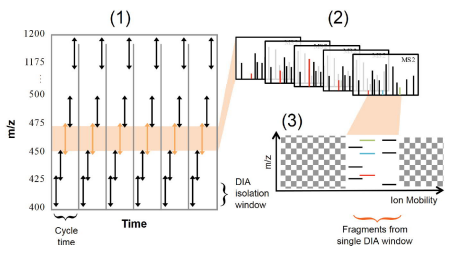
Implementation of diaPASEF on the timsTOF Pro

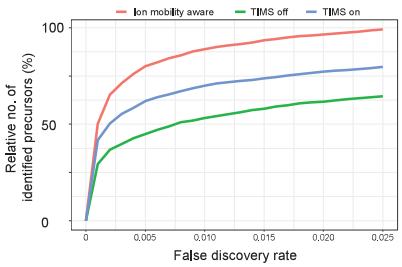


Analysing a HeLa digest with up to 100% duty cycle



OpenSWATH data analysis pipeline





Conclusions

PASEF on the timsTOF Pro is a valuable addition to the technological toolbox in proteomics, with a number of unique operating modes that are only beginning to be explored. The high reproducibility of peptide ion mobility values makes library-based approaches, such as data-independent acquisition, very attractive. Unlike conventional DIA methods, the diaPASEF method presented here captures and utilizes a very large proportion of the available ion current while still employing a quadrupole mass filter to isolate precursor mass ranges - going a long way towards the ideal of a mass analyzer.

[1] Ridgeway, ..., Park, *Int. J. Mass Spectr.* 2018
[2] Meier, ..., Mann, *J. Proteome Res.* 2015
[3] Meier, ..., Mann, *bioRxiv* 2018
[4] Roest, ..., Aebersold, *Nat. Biotechnology* 2014

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