ThermoFisher SCIENTIFIC

Design and evaluation of an automated low-flow ion source and replaceable-emitter cartridge platform for LC-MS

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Product Management



The world leader in serving science

Today we have sophisticated front and back ends



Accessibility

- ✓ Automated diagnostic routines
- ✓ System checks & calibrations





Standardization

- ✓ Software integration
- ✓ Method templates

…but the connection between the two remains a challenge

The weakest link is the interface between the LC and MS

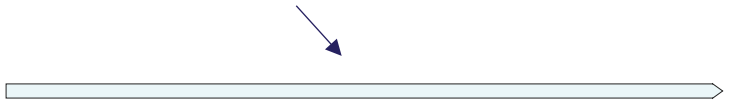


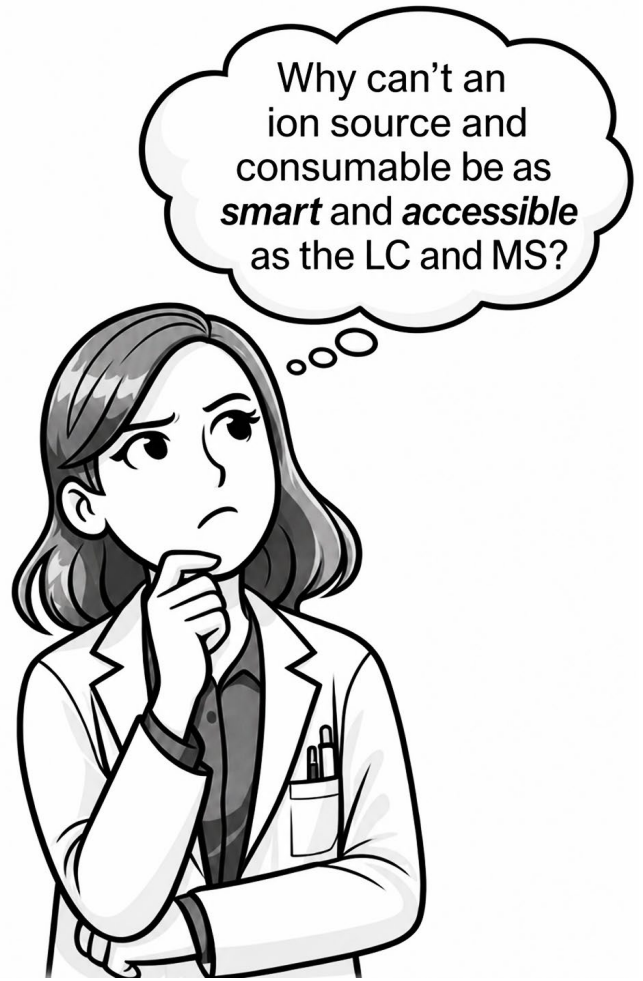






Your favorite homemade column and emitter!







Low accessibility & standardization

- Emitter positioning adds complexity and variability
- Spray stability over time may be variable
- Column lifetime is limited, particularly with an integrated emitter
- Manual fluidic connections impact data quality

Thermo Scientific™ OptiSpray™ Technology solves these four weaknesses

- Resolution 1: Automate emitter positioning
- Resolution 2: Monitor the spray
- Resolution 3: Improve the emitter and its lifetime
- Resolution 4: Integrate leading column technology



Multiview cameras & white and green LEDs

Plug-and-play cartridge installation

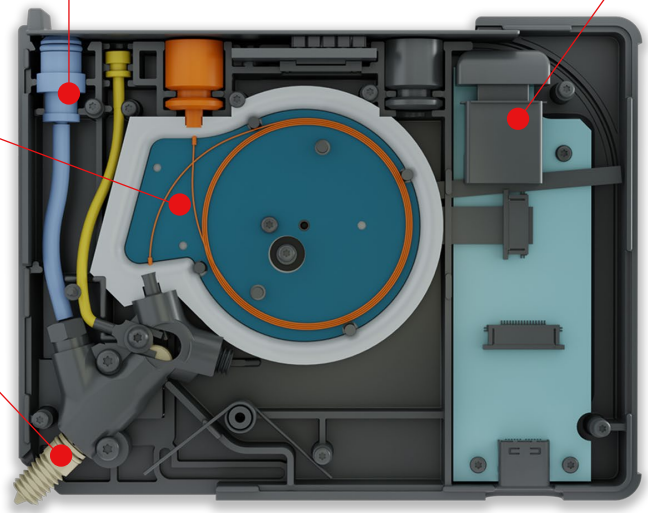
3-axis motors

Integrated sheath gas

On-board memory

Temperature-controlled column

Integrated exchangeable emitters



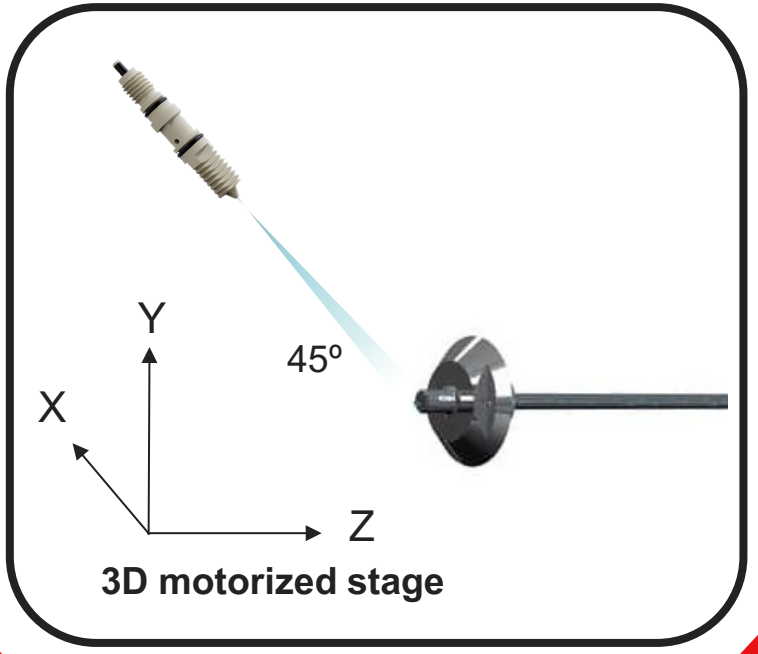






OptiSpray cartridge portfolio

Resolution 1: Automate emitter positioning



Algorithm 1

Emitter position optimization
at nano-flow (<1 µL/min)

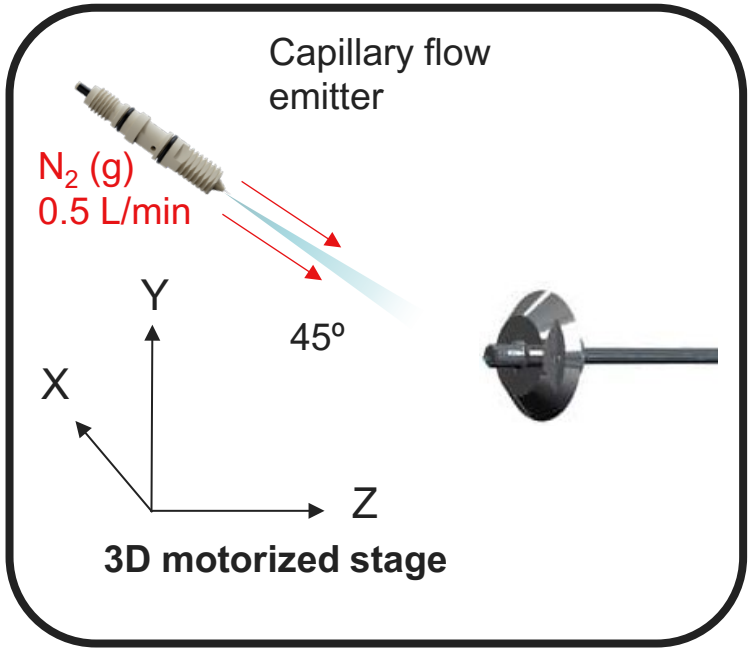
Algorithm 2

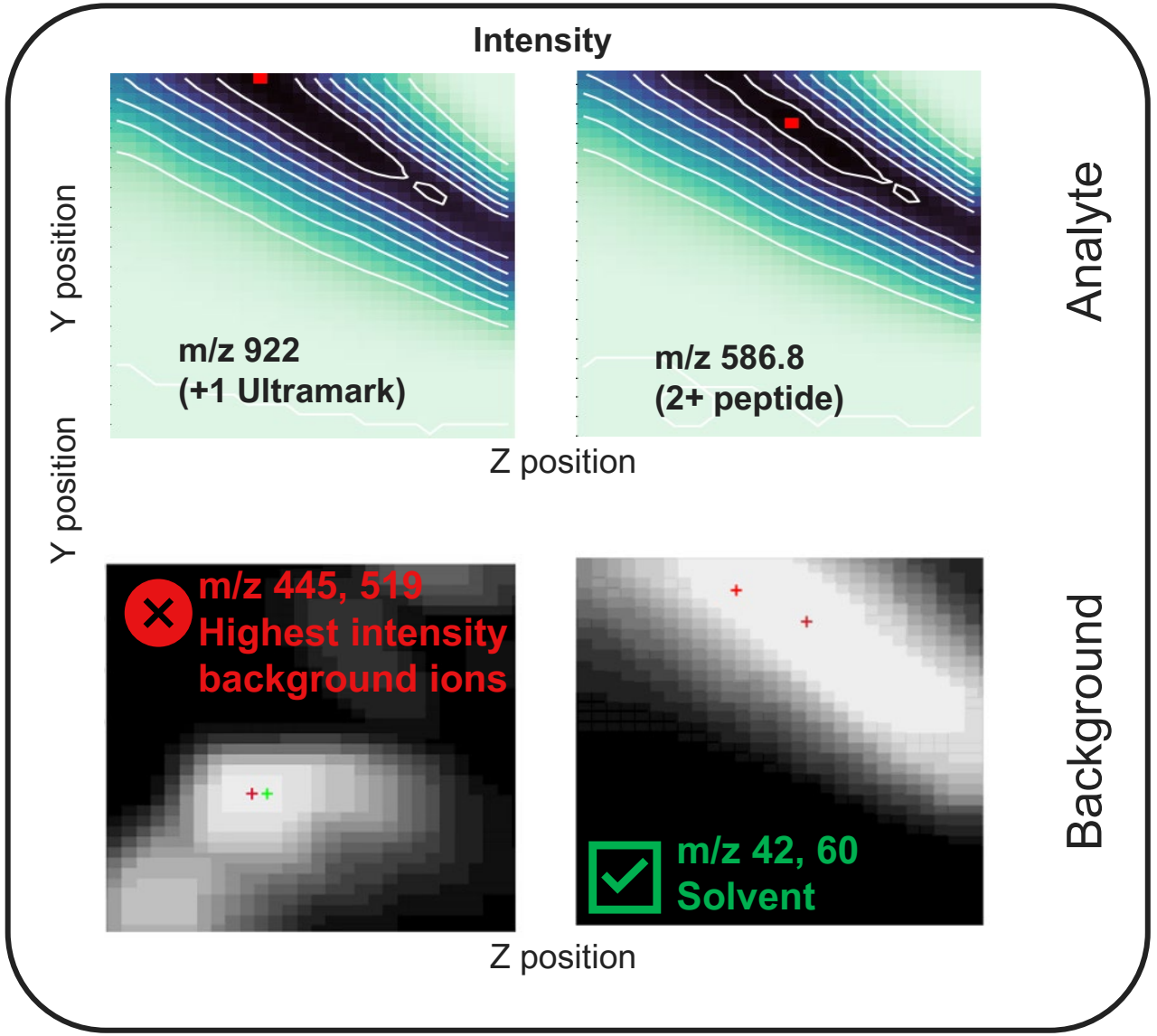
Emitter position optimization
at capillary flow(>1 µL/min)
with nebulization gas

…and don't forget positioning in front of different inlet types and with Thermo Scientific™ FAIMS Pro Interface!

Emitter optimization algorithm must use the right criteria

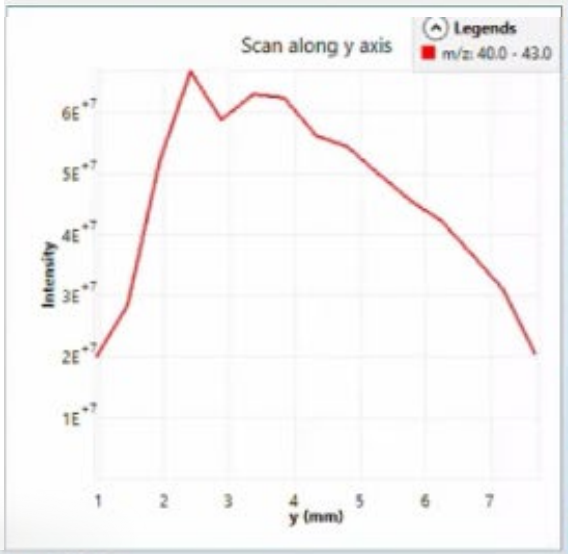
Goal: Match the analytical signal with target proxy ions

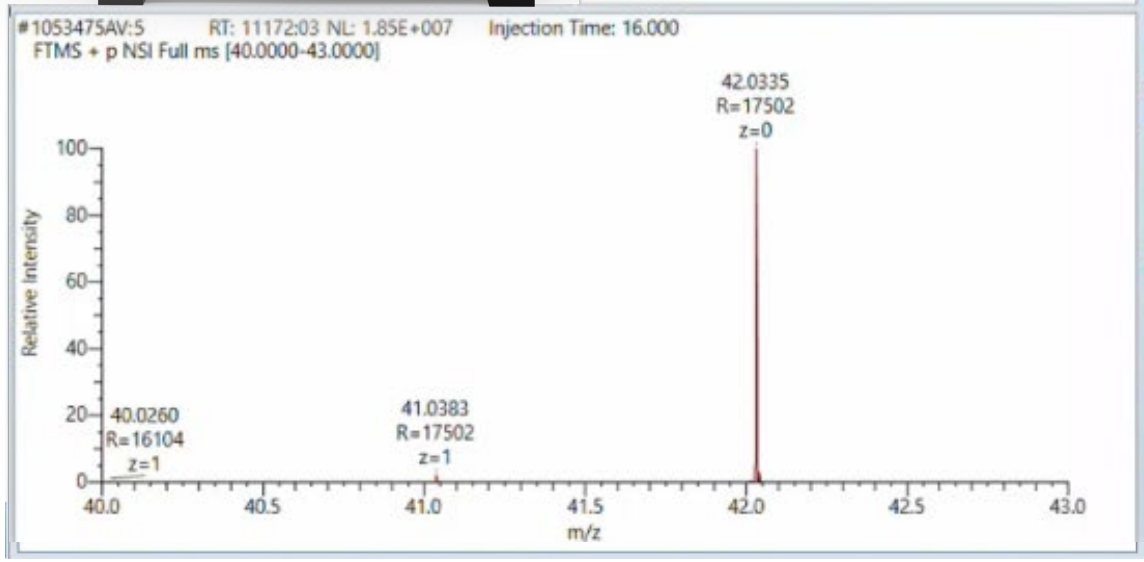


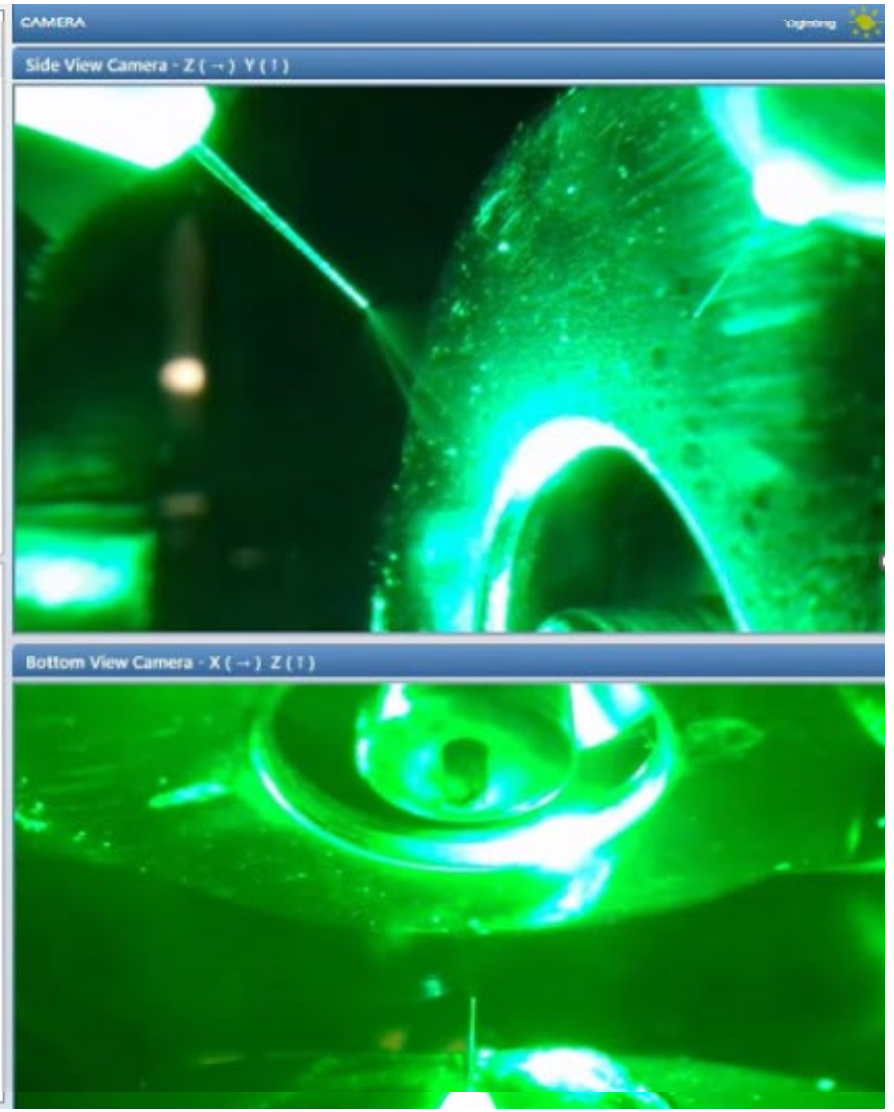


Emitter optimization routine in action





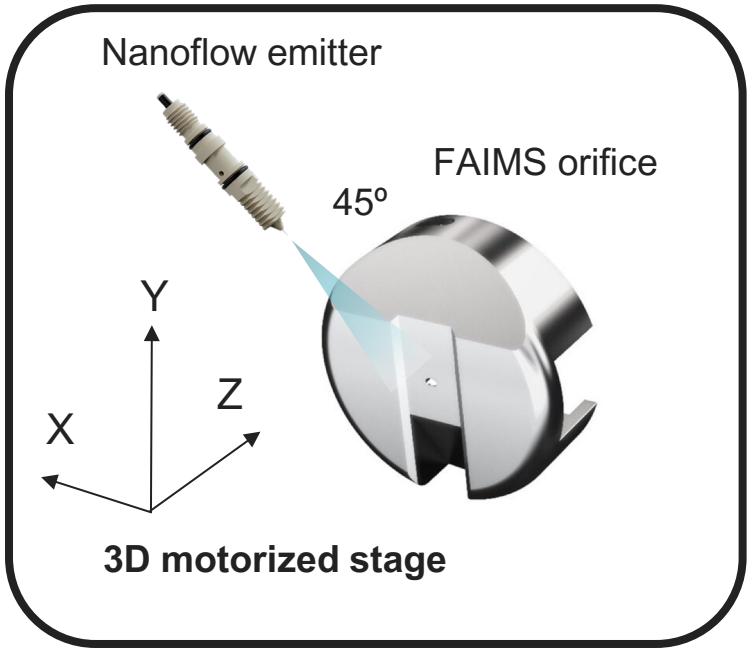


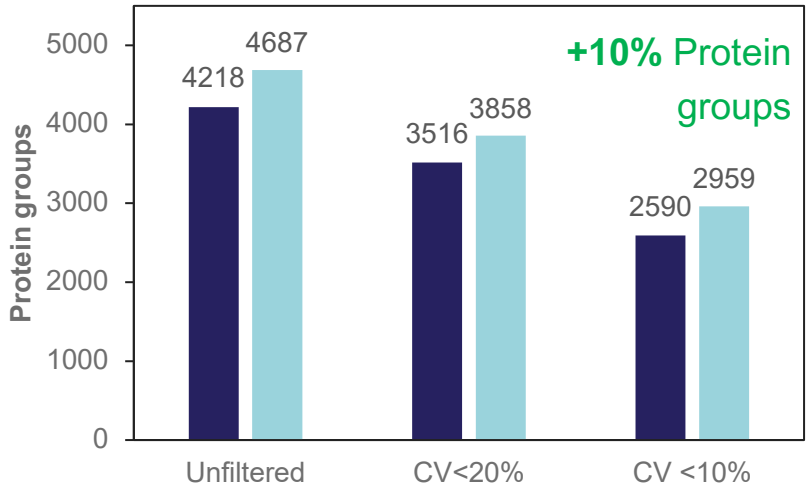


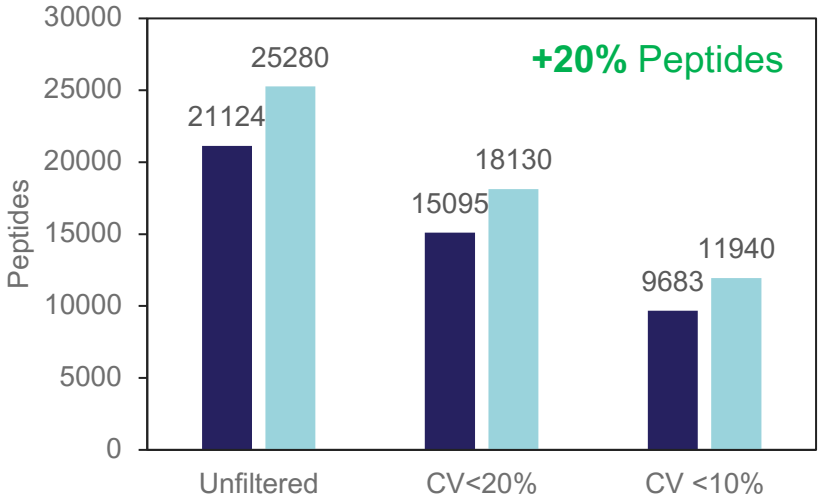
Side view

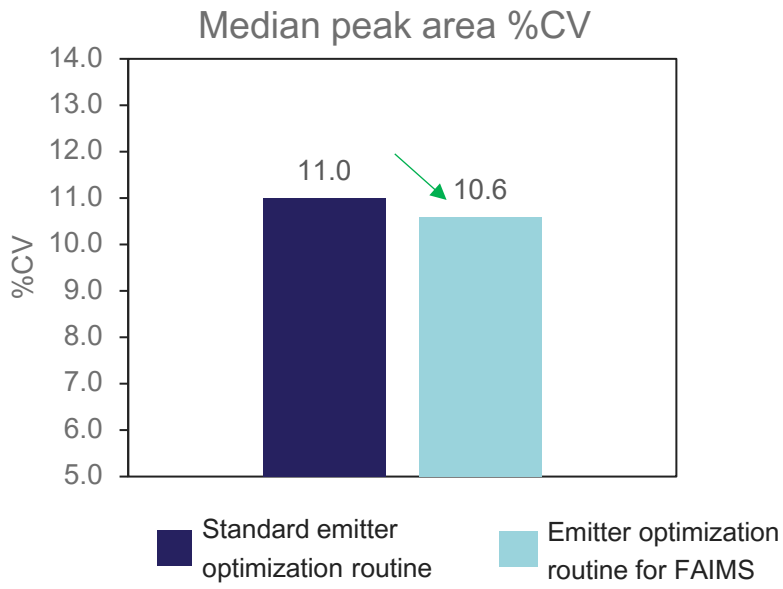
Bottom view

Automated positioning is designed for FAIMS



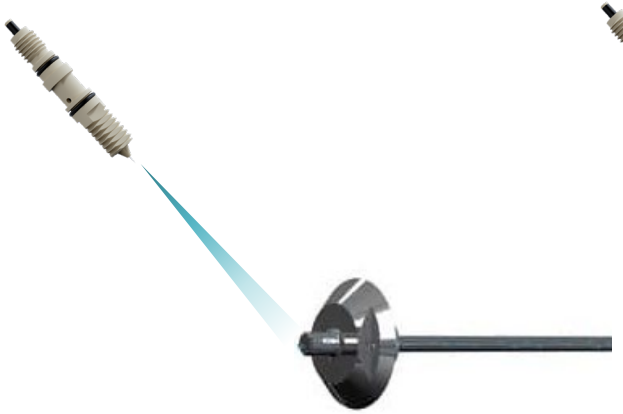




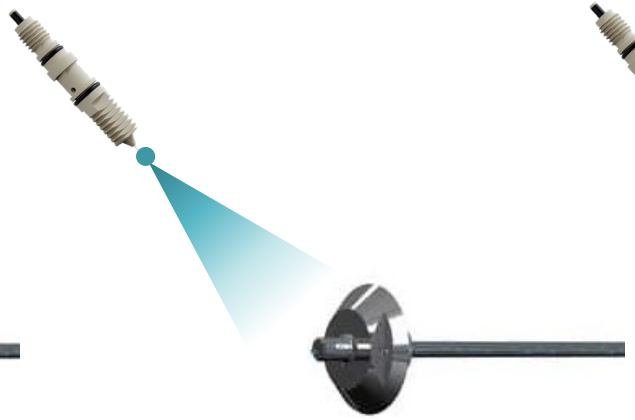


1 ng HeLa with a 0.3 uL/min 20 min gradient DIA method on a Thermo Scientific™ Orbitrap Lumos™ MS with Thermo Scientific™ FAIMS Pro Duo Interface.
Analyzed in Spectronaut 19

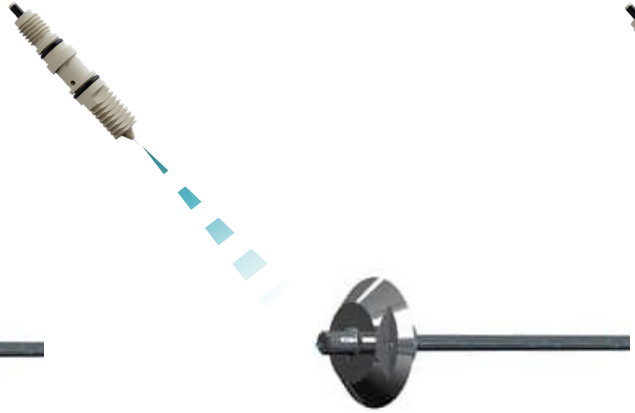
Resolution 2: Monitor the spray



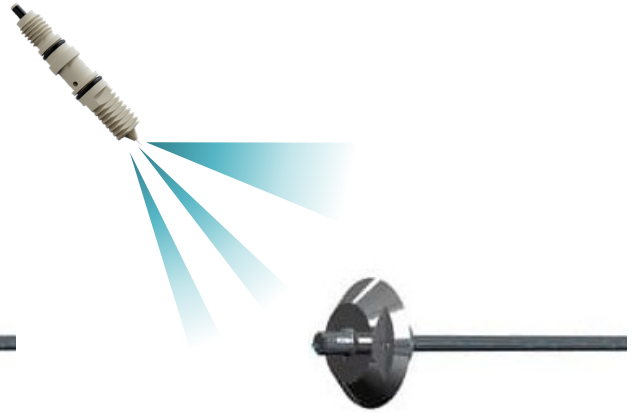
Good spray



Spray off a droplet

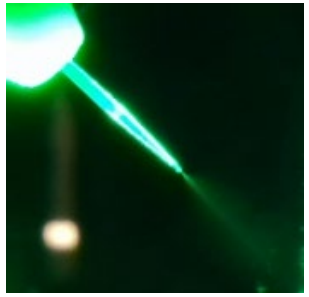


Sputtering spray



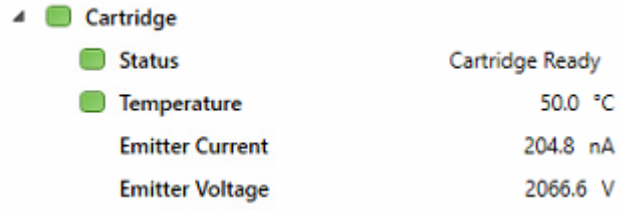
Unstable spray

Two ways to monitor the spray



Your eyes

Measuring the emitter current



Resolution 3: Improve the emitter and its lifetime

Prevent failure of the consumable from a clogged emitter → **Replaceable** emitter



Reduce post-column volume → **Replaceable *integrated*** emitter



Support both nanoflow and capillary flow →

Two replaceable *integrated* emitters:

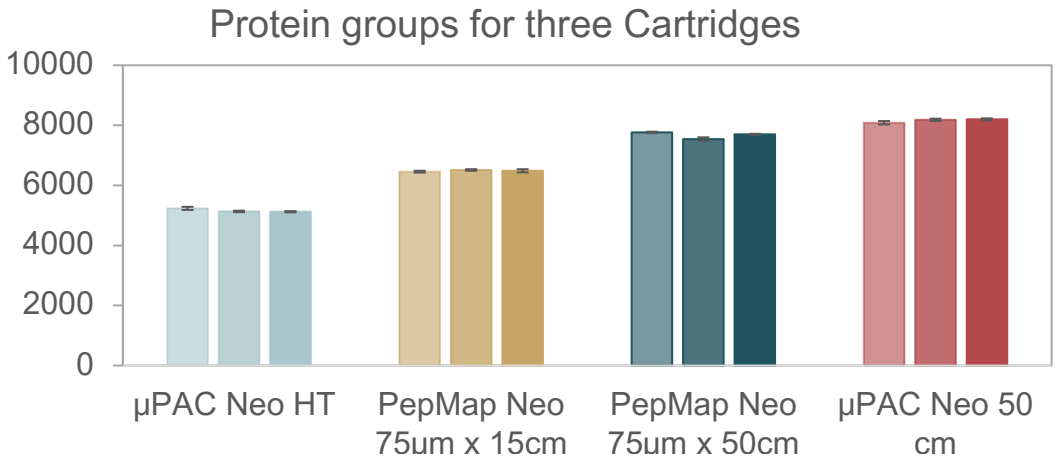
Nano emitter for <1 µL/min

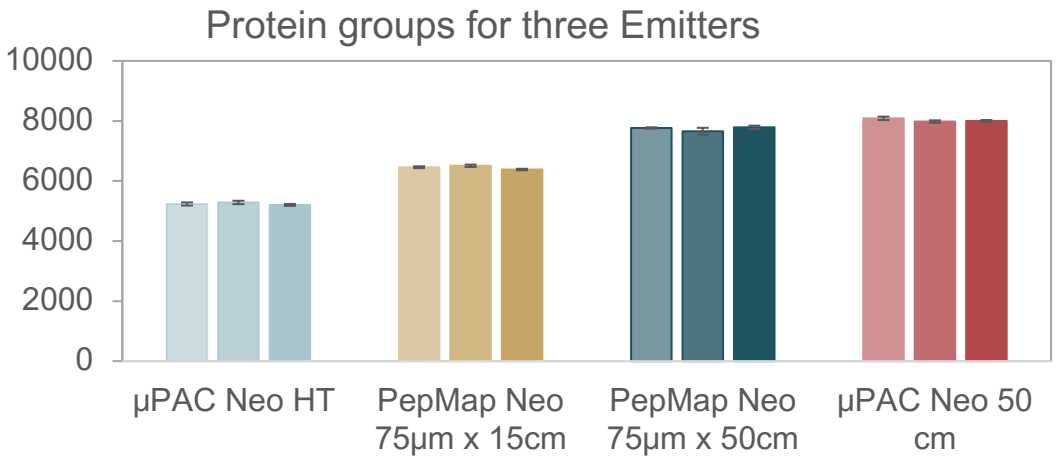
Capillary emitter for >1 µL/min

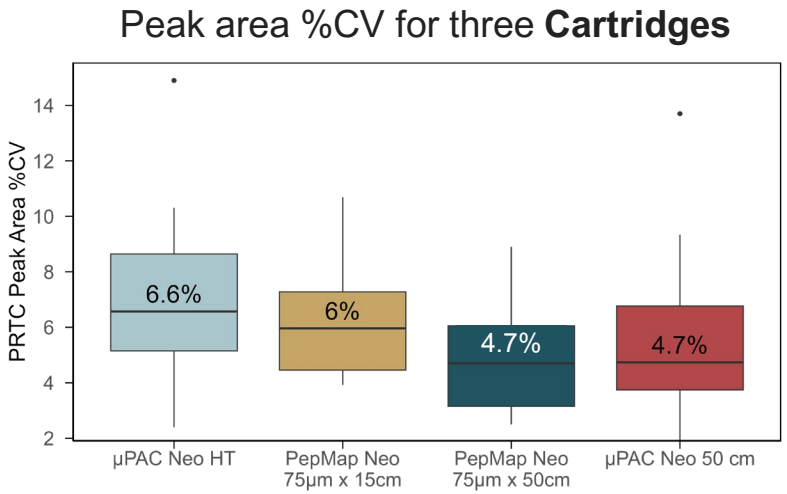


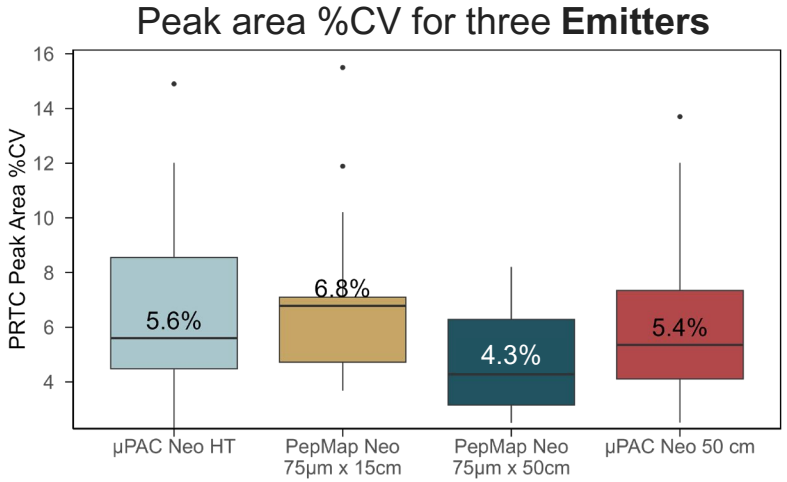


OptiSpray technology delivers optimal performance across emitter replacement









Low inter-cartridge and inter-emitter variability in both protein identifications and peak areas

200 ng HeLa and 50 fmol PRTC peptides with a 15-90 min gradient DDA method (n=5 injections) on a Thermo Scientific™ Orbitrap Ascend™ MS with FAIMS Pro Duo interface.
Analyzed in Thermo Scientific™ Proteome Discoverer™ Software with CHIMERYS and Skyline

Resolution 4: Integrate leading column technology with different strengths

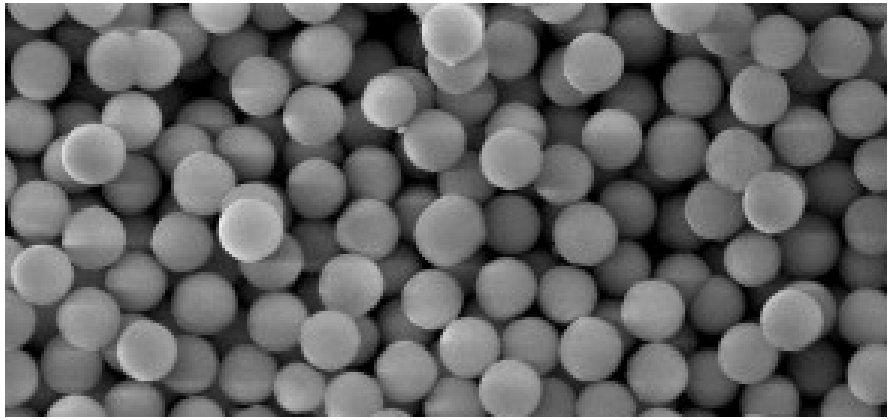
Thermo Scientific PepMap™ Neo Columns
for high pressure tolerance and wide range of sample types



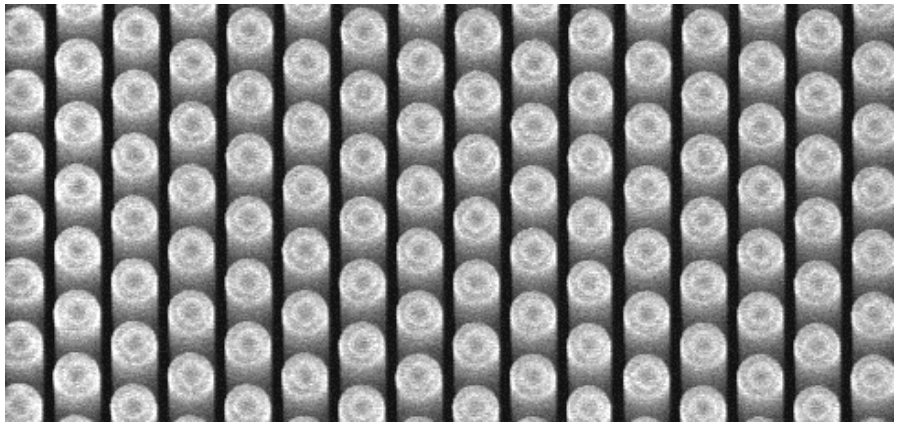




Thermo Scientific™ µPAC™ Neo Columns
for ultimate reproducibility/longevity and large-scale deep dive proteomics



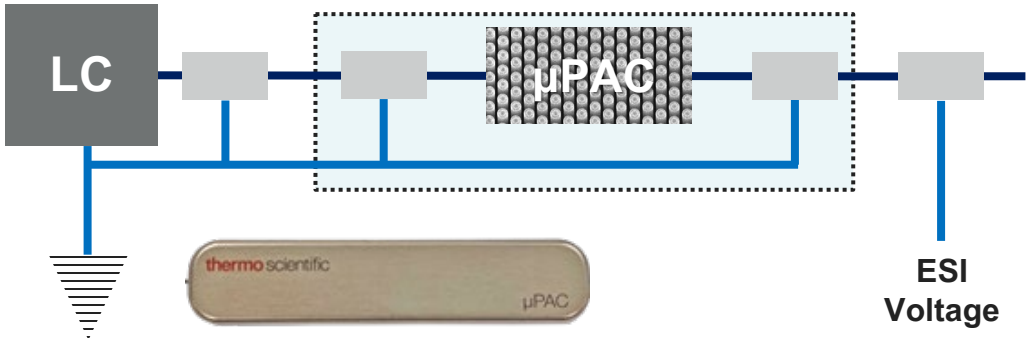




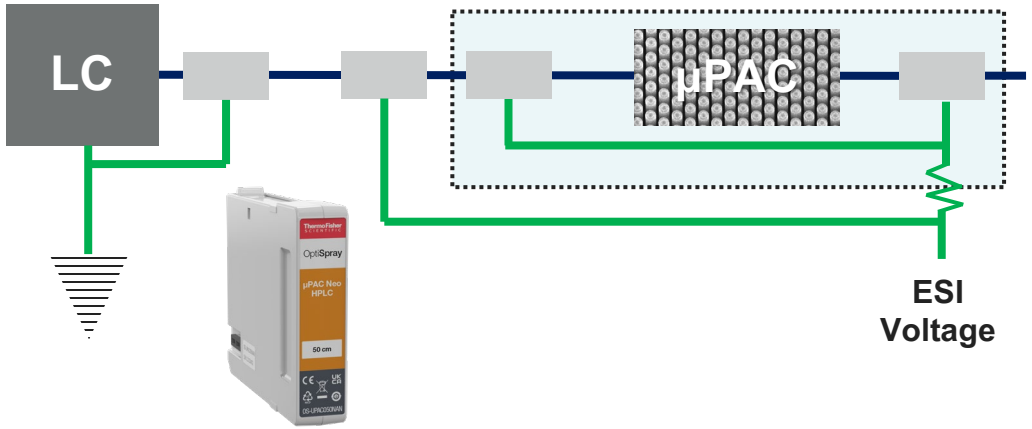


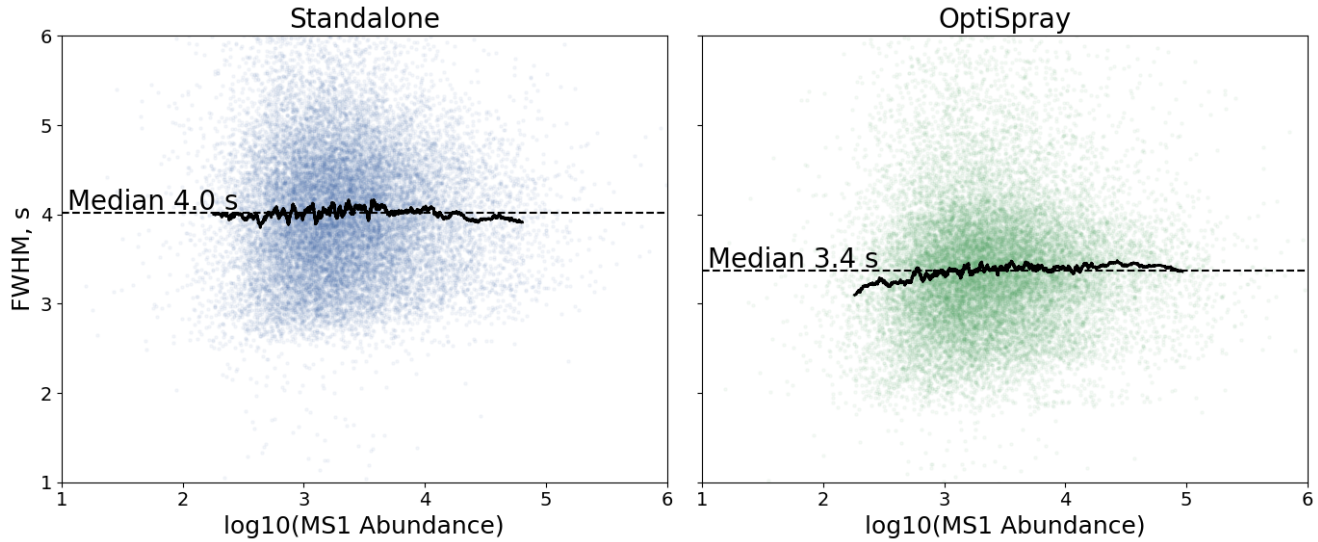
Cartridge design for µPAC improves chromatography and proteome coverage

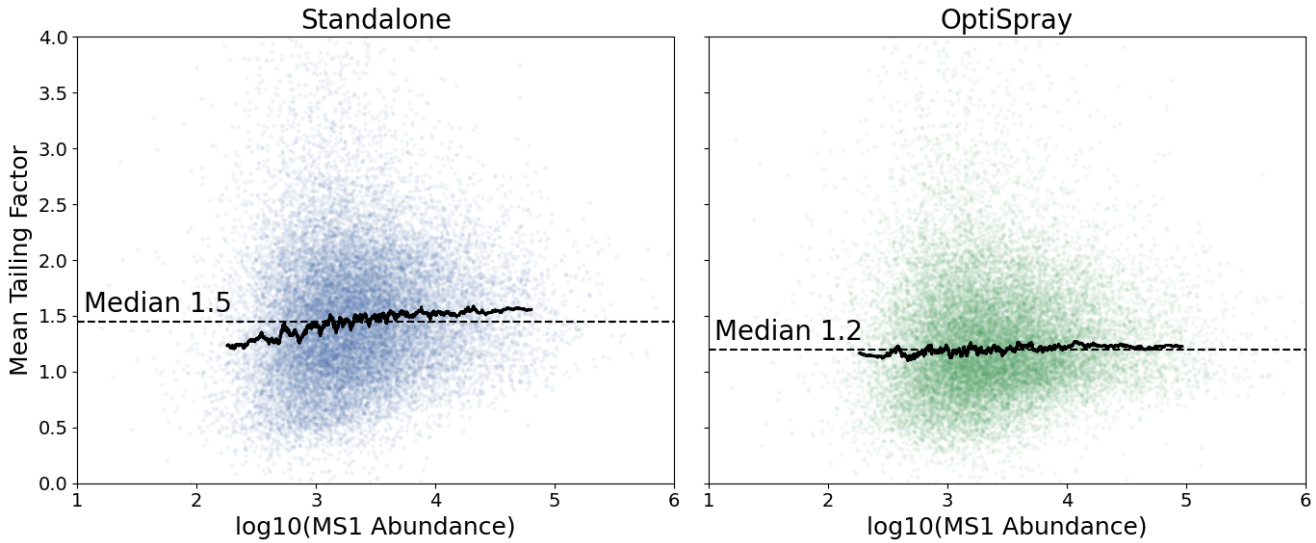
Standalone µPAC Column Electrical Scheme – “Ground”



µPAC **Cartridge** Electrical Scheme – “Float”



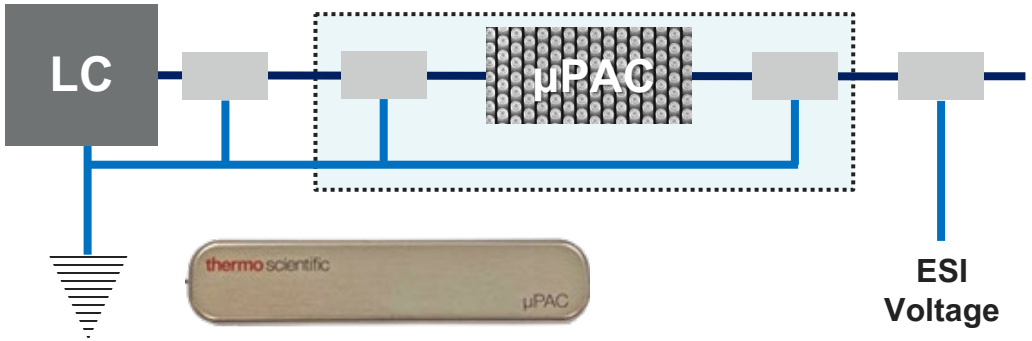




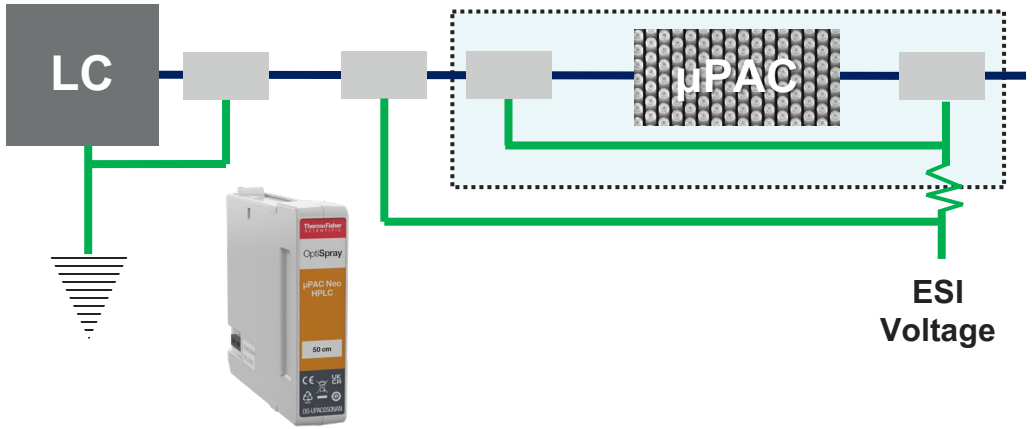
1 ng HeLa with a 0.3 uL/min 20 min gradient DIA method on a Thermo Scientific™ Orbitrap Lumos™ MS with FAIMS Pro Duo Interface. Analyzed in Spectronaut 19

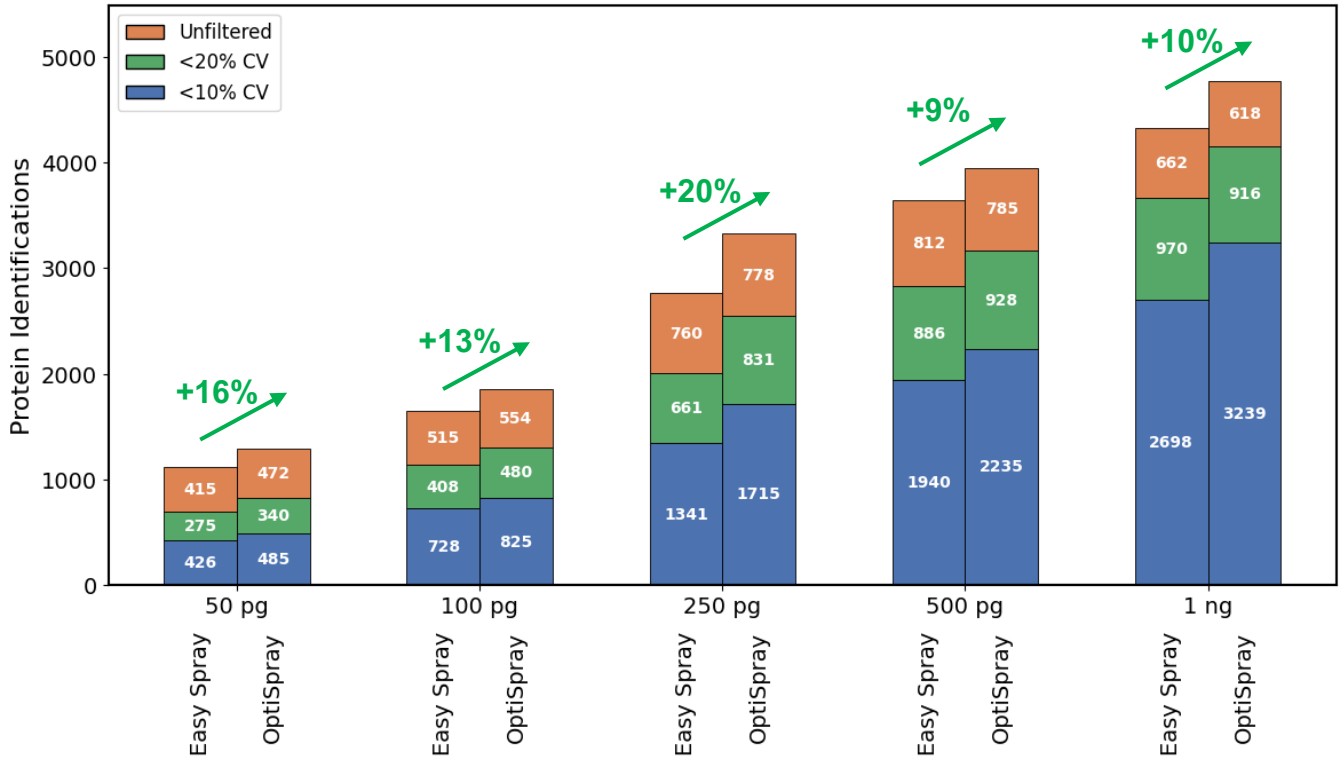
Cartridge design for µPAC improves chromatography and proteome coverage

Standalone µPAC Column Electrical Scheme – “Ground”



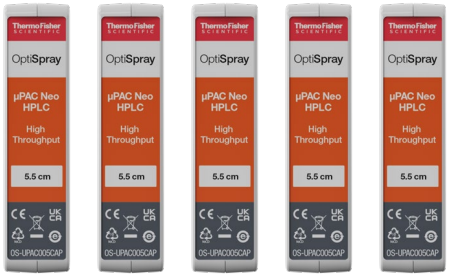
µPAC **Cartridge** Electrical Scheme – “Float”





1 ng HeLa with a 0.3 uL/min 20 min gradient DIA method on a Thermo Scientific™ Orbitrap Lumos™ MS with FAIMS Pro Duo interface. Analyzed in Spectronaut 19

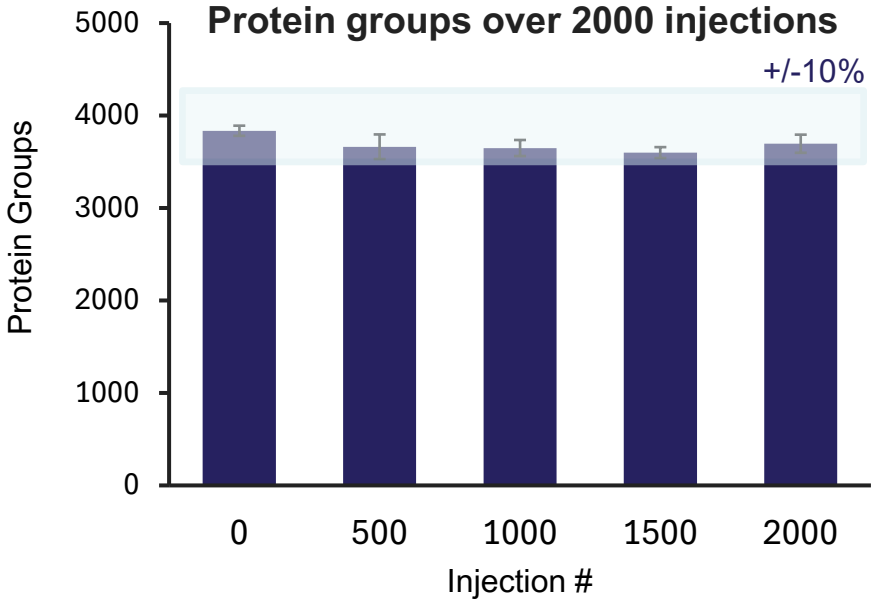
OptiSpray provides high reproducibility for large cohorts

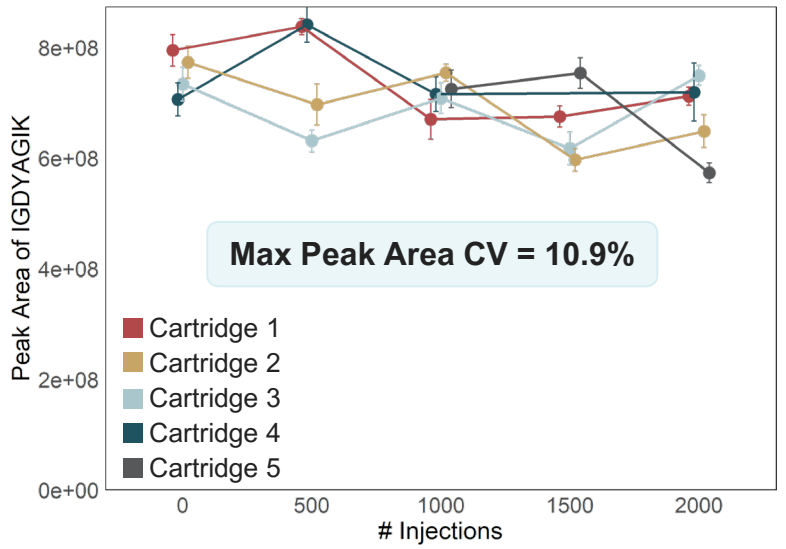


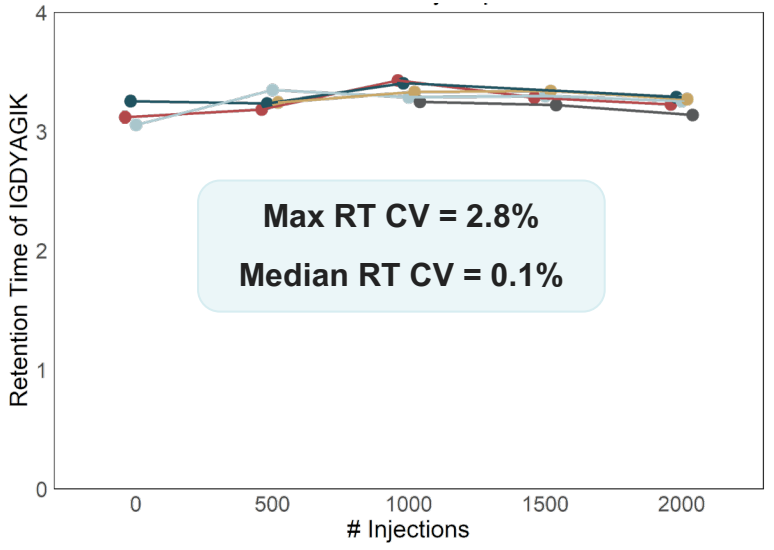


Thermo Scientific™ Orbitrap Exploris™ 480 MS
with Thermo Scientific™ Vanquish™ Neo UHPLC

2000 injections
= 500 hr = 45 mL solvent







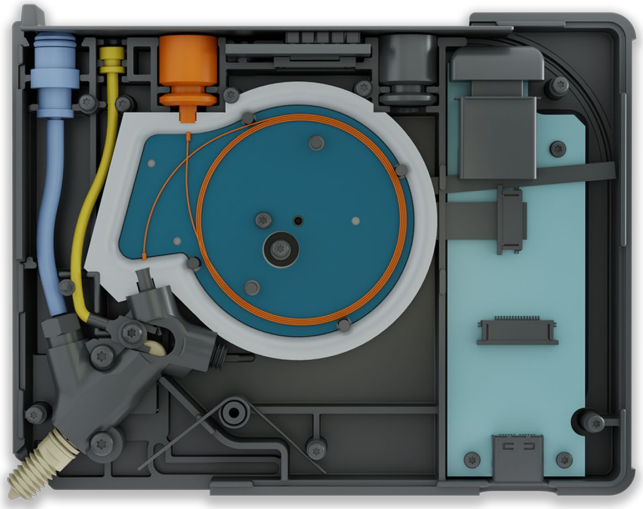
Consistent performance across 2000 injections on 5 cartridges demonstrates robustness and reliability of OptiSpray for large proteomics studies

200 ng HeLa with a 110 SPD 1.5 µL/min DDA method (n=5 rep inj). Analyzed in Proteome Discoverer software with CHIMERYS

OptiSpray technology solves these four weaknesses

- ✓ Resolution 1: Automate emitter positioning
- ✓ Resolution 2: Monitor the spray
- ✓ Resolution 3: Improve the emitter and its lifetime
- ✓ Resolution 4: Integrate leading column technology











OptiSpray in the hands of expert mass spectrometrists





Dr. Brian Hood **Dr. Thomas Conrads**
Inova Health

Thermo Scientific™ OptiSpray™
PepMap™ Neo 75 um x 15 cm



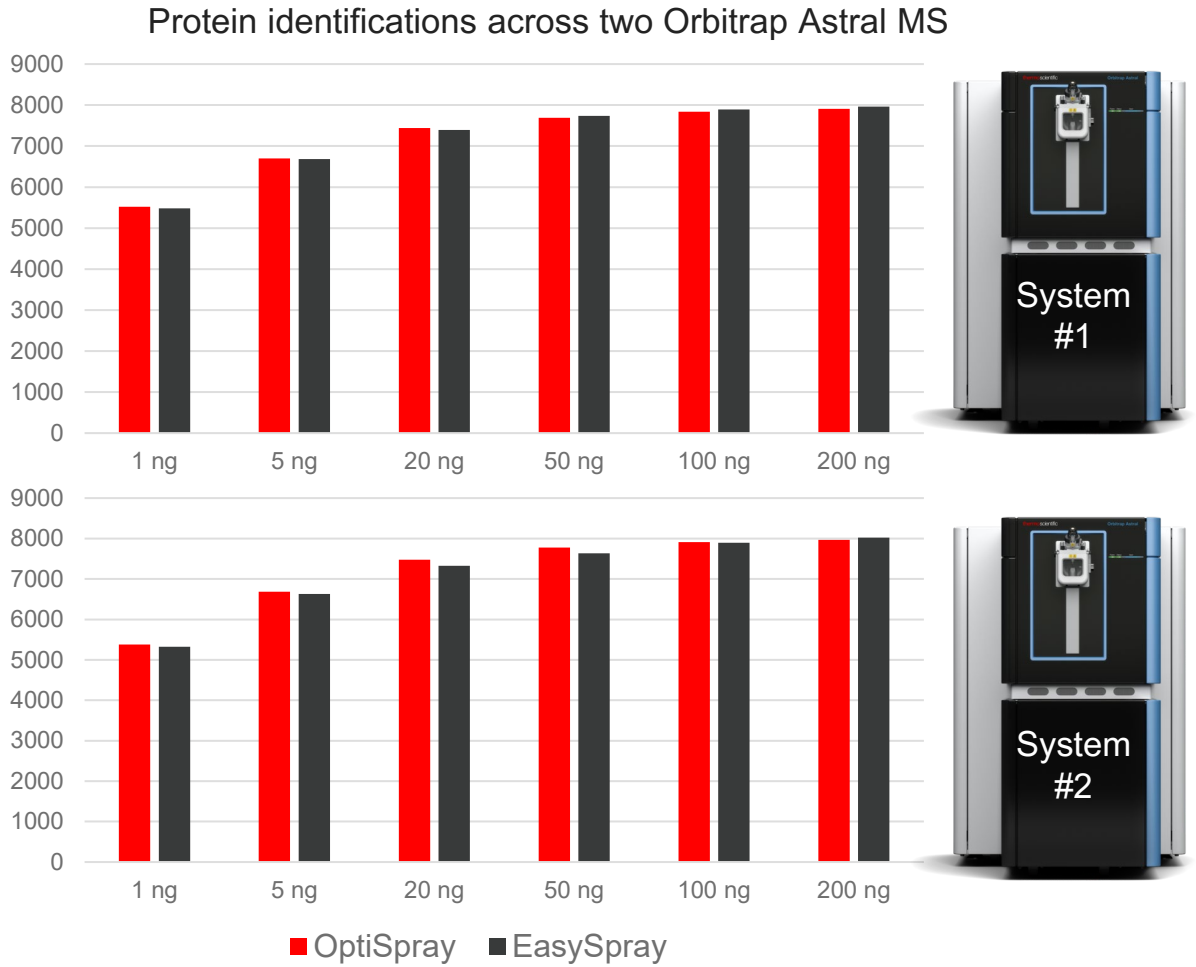
Positioned with nano-flow quick optimization emitter routine

Thermo Scientific™ EASY-Spray™
PepMap™ Neo 75 um x 15 cm



Manually positioned by expert mass spectrometrist

Same LCMS method originally optimized for EasySpray column



MSPE-prepared cell digest with a 12.8 min gradient (24 SPD) 0.35 uL/min DDA method (n=2 rep inj) on a Thermo Scientific™ Orbitrap™ Astral™ MS with Vanquish Neo UHPLC. Analyzed in DIA-NN 2.1

OptiSpray & Orbitrap Astral enable deep proteomic profiling

A comparative proteomic analysis of cross-pandemic viral complications

Study

COVID-19 SARS-CoV-1 Measles 1918 Spanish Flu

95 high-value biospecimens:

Brain, heart, and lung FFPE samples from autopsies across four pandemics

Large cohort high-sensitivity DIA LC-MS/MS Workflow



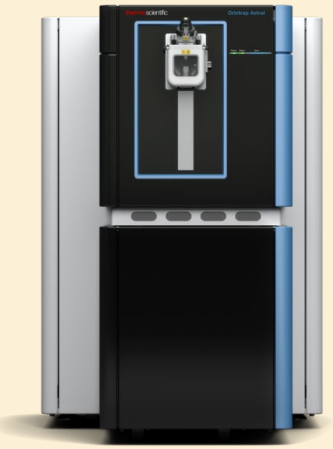
Vanquish Neo UHPLC



OptiSpray Ion Source



µPAC Neo 50 cm



Orbitrap Astral MS

9,034 Proteins identified

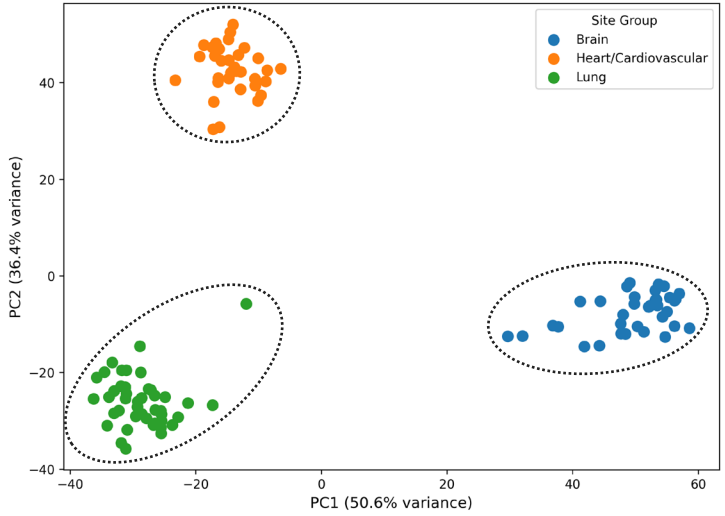
200 ng tissue digest with a 40 SPD 0.30 uL/min method (195 single injections) on an Orbitrap Astral with Vanquish Neo UHPLC. Analyzed in DIA-NN 2.1

Dr. Thomas Conrads
Dr. Brian Hood
Inova Health

Distinct proteomic signatures separate pandemics and reveal virus-specific molecular markers

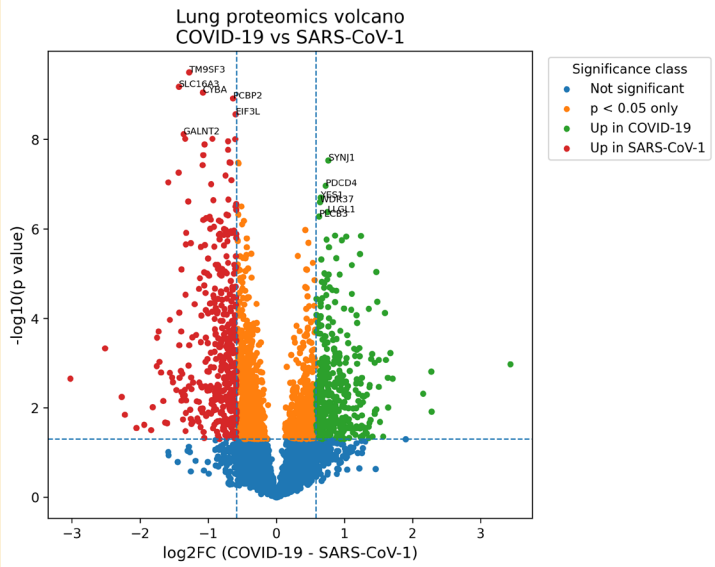
ThermoFisher SCIENTIFIC

Proteome clustering is driven by tissue type



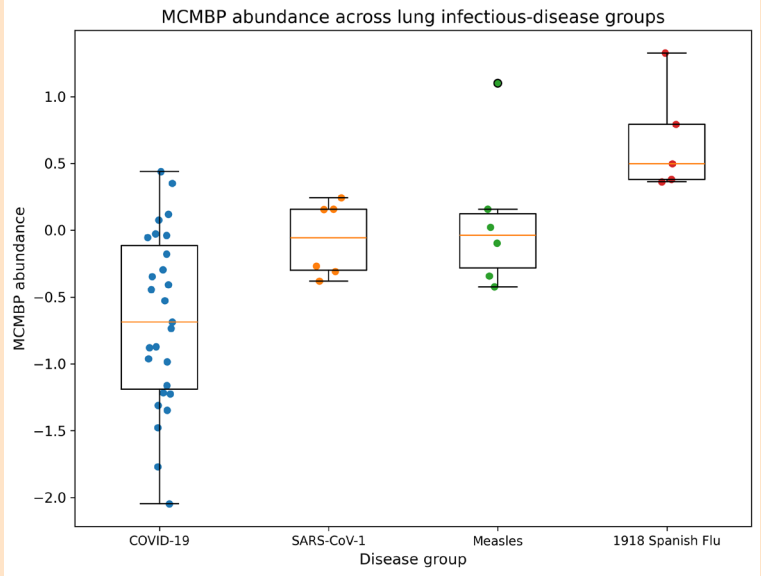
COVID-19 vs SARS-CoV-1 shows strongest proteomic divergence

1,740 proteins with significant differential expression p < 0.05



MCM Binding Protein

Elevated in 1918 Spanish Flu compared to modern viral infections



"OptiSpray democratizes electrospray ionization by eliminating the skill gap in emitter positioning, enabling routine users to achieve performance comparable to experienced mass spectrometrists."

Dr. Thomas Conrads
Dr. Brian Hood
Inova Health

Acknowledgments

Thermo Fisher Scientific

Eloy Wouters
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Runsheng Zheng
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Lukas Taujenis
Marius Mameniskis
Shanhua Lin
Khatereh Motamed

Collaborators at Inova Health

Dr. Brian Hood
Dr. Thomas Conrads









Thank you



Learn more at **thermofisher.com/optispray**

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