

The robust and reliable LC-MS platform for high-throughput proteomics



I need to run extended, large cohort studies to advance my research. How can the Thermo Scientific™ Orbitrap Exploris™ 480 mass spectrometer system address this need?

Designed and manufactured for exceptional robustness, everyday reliability, and reproducibility from one instrument to another, the Orbitrap Exploris 480 mass spectrometer maximizes uptime and productivity to meet large-scale-study and sample-throughput requirements, while reducing everyday hassles. Rigorous testing at every stage of the manufacturing process ensures the quality of every system that leaves the factory. It works right out of the box!

“The Orbitrap Exploris 480 mass spectrometer has become our go-to system for large cohort studies. Over six months of constant operation, the instrument in our lab has delivered very high performance, and has required minimal effort to maintain these high levels. The robustness of the system is excellent, both with and without the use of the FAIMS Pro interface, and for DIA studies which utilize high ion current.”

— Prof. Jesper Olsen, Novo Nordisk Foundation Center for Protein Research, University of Copenhagen

“With its ability to perform robustly and reliably for extended periods, the Orbitrap Exploris 480 mass spectrometer is optimally suited for large-scale studies.”

— Dr. Alexander Harder, Sr. Product Manager,
Life Science Mass Spectrometry

What are the design innovations that provide the new levels of robust and reliable LC-MS performance day after day?

To meet the needs of large-scale studies, Thermo Fisher Scientific designed the Orbitrap Exploris 480 mass spectrometer system and its components for sustained cleanliness, streamlined maintenance, maximum uptime, and inter-and intra-instrument reproducibility. Rigorous testing was carried out to verify instrument reliability. For example, more than 50 turbo-pumps were run continuously to establish the long-term reliability of this component. (Figure 1). The six-stage pumping system controlled by a single turbo pump streamlines planned maintenance.



Figure 1. The turbo pumps used in the Orbitrap Exploris 480 mass spectrometer system were tested extensively for long-term performance.

Figure 2 summarizes the design innovations that contribute to the extraordinary levels of everyday mass spectrometer uptime and performance. First, the easy-to-clean, ultra-robust Thermo Scientific™ OptaMax NG Electrospray

ion source with probe capillary and ion transfer optics reduces quadrupole contamination to sustain sensitivity over multiple analyses. In addition, the active beam guide prevents neutrals from entering the quadrupole and improves robustness by eliminating the effects of local charging.

One robust calibration covers the entire mass range from m/z 40 to 6,000 (or optionally extended to m/z 8,000) with sub one-ppm mass accuracy, making it remarkably easy to achieve consistently excellent mass accuracy for highest-quality data and confidence in results. The standard Thermo Scientific™ EASY-IC™ source with automated internal calibrant delivery enables constant one-ppm mass accuracy, while providing ease of use and high-confidence mass calibration for at least five days. The source delivers calibrant ion as a lock mass, and the instrument control software uses the known mass-to-charge ratio of the calibrant mass peak to provide real-time fine adjustment of the mass calibration.

Advanced Quadrupole Technology (AQT) with novel, patented Configuration Switch Mode (CSM) extends quadrupole maintenance intervals up to 200% without compromising performance, while automatic bake-out following a power cycle saves time, getting you up and running samples faster. Robustness is further improved with Thermo Scientific™ Ion-Routing Multipole (IRM) trapping, which focuses and routes ions very effectively. The IRM facilitates dynamic, extended ion trapping and performs higher-energy collisional dissociation (HCD) fragmentation.

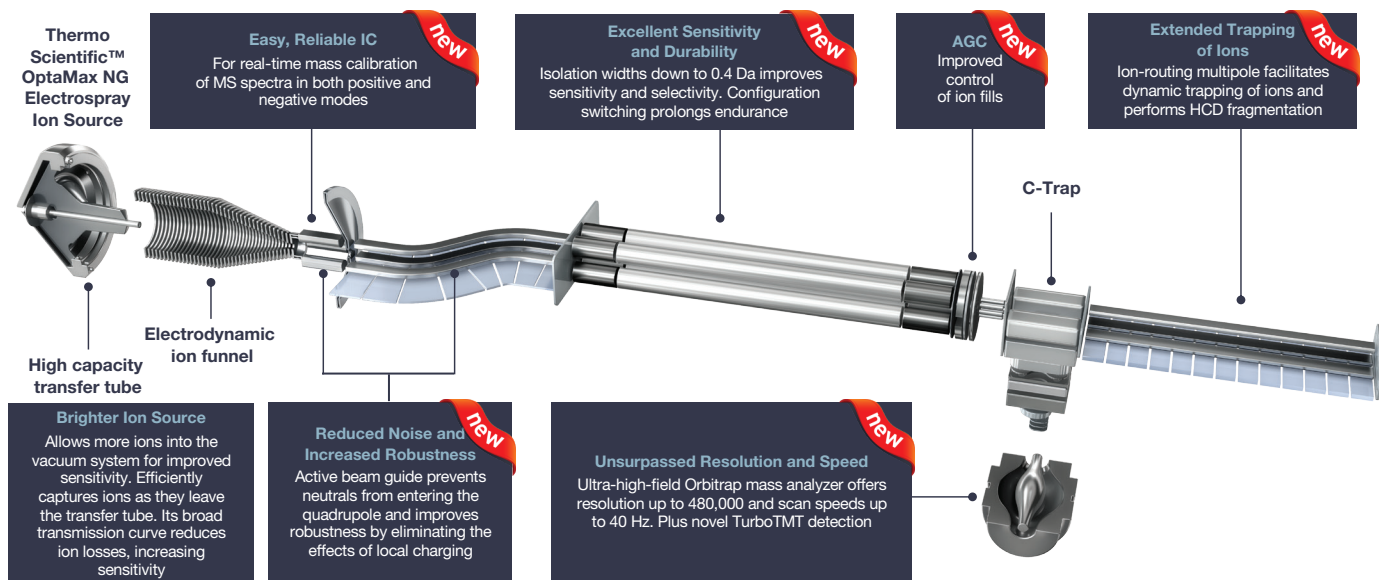


Figure 2. Schematic of Orbitrap Exploris 480 mass spectrometer, showing the design innovations that contribute to the extraordinary levels of reliability and robustness.

Even the most reliable mass spectrometer will eventually require maintenance. What has Thermo Fisher Scientific done to make maintenance procedures faster and easier?

The Orbitrap Exploris 480 mass spectrometer incorporates several innovations, including simplified calibration routines and an intuitive user interface for instrument operation and performance diagnostics that provide exceptional ease of use and maintenance. Shown in Figure 3, the instrument control software includes a diagnostics library that can be used to perform various system checks, such as ion optics and quadrupole maintenance checks, to ensure they are performing within specifications and ready for analyses.

Though AQT with CSM extends quadrupole maintenance time intervals, when maintenance is needed, the quadrupole assembly is easily accessed for cleaning or switching by trained users without time-consuming disassembly and reassembly procedures (Figure 4). The analyzer components are self-aligning and use conductive pins rather than cabling that could be damaged or attached incorrectly during maintenance.

- A cleaning kit with tools and consumables is included with the system
- Automatic bake-out following a power cycle saves time, getting you up and running samples faster
- Cleaning the ultra-robust ion source can be accomplished in just two to three hours

- Performance maintenance can be accomplished directly by the user or through a warranted maintenance contract

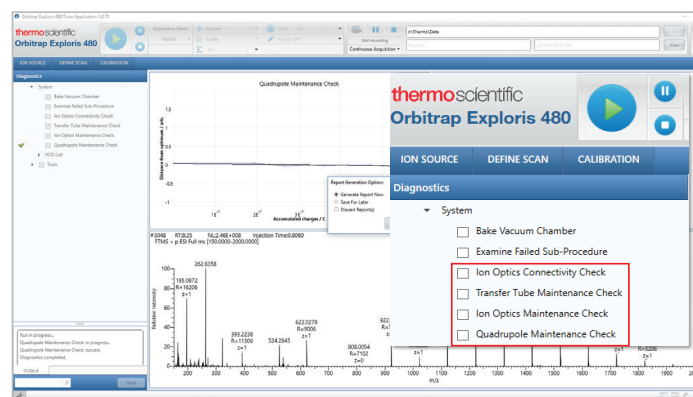


Figure 3. Orbitrap Exploris 480 mass spectrometer diagnostics are provided in the instrument control software.

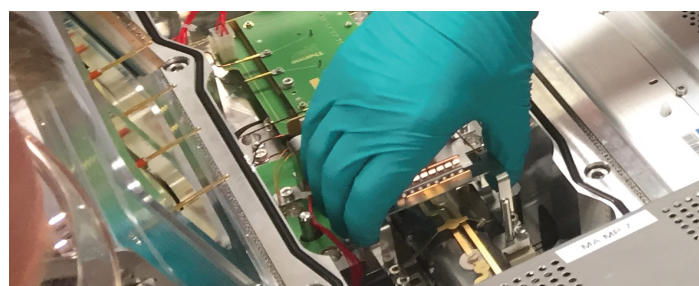


Figure 4. Fast quadrupole access allows easy end-user or service engineer maintenance and reduces downtime. Simply turn off the instrument, remove the top cover, and open the lid to access the ion optics and quadrupoles. Reassembly is easy with self-aligning components.

Most manufacturers claim that their instruments are robust and reliable. Do you have any data that supports your claims?

Thermo Fisher Scientific performed extensive applications testing of the Orbitrap Exploris 480 mass spectrometer. To determine instrument robustness and reliability, Thermo Scientific scientists assessed the performance characteristics of many different instruments in three longitudinal studies using the workflow shown in Figure 5. Protein and peptide identification were evaluated over ten repetitive injections of 1- μ g plasma in data-dependent acquisition (DDA) mode. This was followed by three DDA QC checks by injection of a low concentration sample: 200 ng Thermo Scientific™ Pierce™ HeLa digest standard with Pierce™ Retention Time Calibration (PRTC) Mixture. The PRTC Mixture is designed for optimization and confirmation of correct LC-MS operation, while the 200 ng HeLa digest was used to assess instrument performance.

The first two studies used the same Orbitrap Exploris 480 mass spectrometer (Instrument 1). In the first study, Instrument 1 ran the experimental workflow until the QC results exceeded \pm 10% peptide spectra matched (PSM), or the system diagnostics reported a failure. In preparation for the second study, Instrument 1 was cleaned following

the standard user maintenance procedure. Then the experimental workflow was repeated until the QC results exceeded \pm 10% PSM. To ensure the system continued to perform at a high level, regular maintenance checks were done using the system diagnostics shown in Figure 3. No calibration was required after cleaning, and importantly, the performance returned to the level achieved in the first study.

The third study was run on another Orbitrap Exploris 480 mass spectrometer (Instrument 2), with the same experimental workflow repeated until the QC results exceeded \pm 10% PSM. All tests were run at a chromatographic flow rate of 1 μ L/min, with a daily sample load of approximately 17 μ g over 16 hours.

Each system ran without significant loss of performance for over 125 days, with over 2,000 μ g material injected on average (Figure 5). Performance levels were fully restored after maintenance and held over an additional 137 days and 2000 μ g injected (Figures 6 and 7). These results show that, for typical high-throughput workflows, users can expect to load about 2000 μ g of sample before performance maintenance is needed. In addition, as shown in Figure 7, both Instruments 1 and 2 provided the same reliable performance, demonstrating inter-system reproducibility.

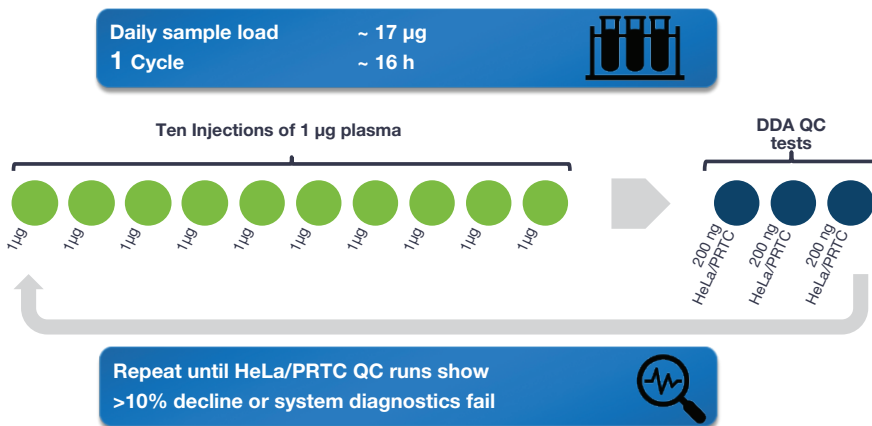


Figure 5. Experimental workflow used to study instrument robustness. Ten injections of 1- μ g plasma were followed by three DDA QC tests of 200 ng HeLa digest standard containing PRTC.

Orbitrap Exploris 480	Increasing sample load with constant performance				Comments
	0-600µg	601-1,200µg	1201-1,900µg	1,900-2,300µg	
Study 1, Instrument 1	1948 µg				125 days (~4 months) without performance decline
Study 2, Instrument 1	2130 µg				137 days (~4.5 months) without performance decline
Study 3, Instrument 2	2215 µg				142 days (~4.5 months) without performance decline

Figure 6. Longitudinal study results. In each study, Instruments 1 and 2 ran without decline in performance for more than 125 days. The performance of Instrument 1 was fully restored after maintenance and lasted for another 137 days and more than 2,000 µg injected.

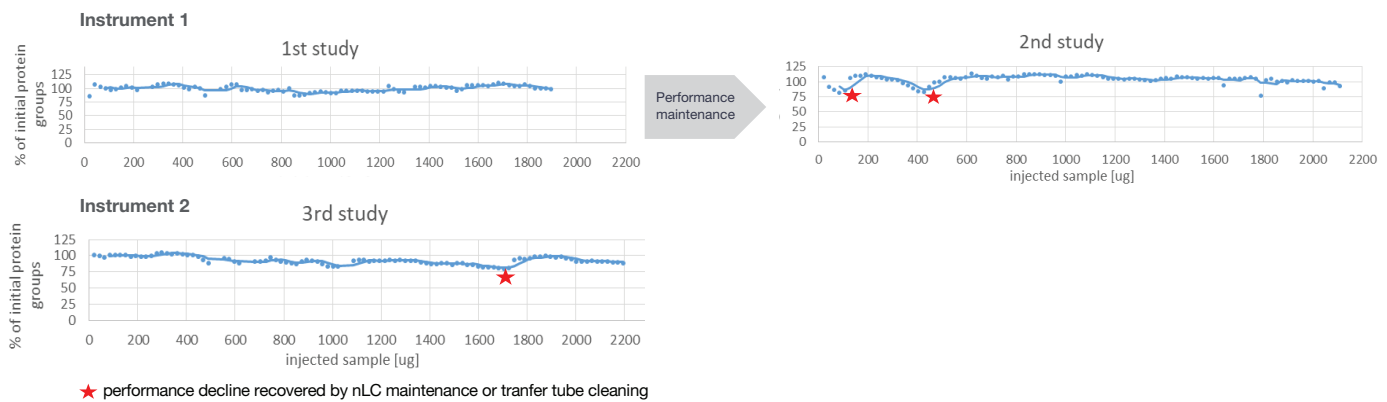


Figure 7. Another view of longitudinal study results. Performance was fully restored after maintenance and lasted for another 137 days and more than 2,000 µg injected. Instruments 1 and 2 yielded the same reproducible high-performance peptide and protein identification (% initial protein groups identified).

Conclusion

From simplified quadrupole assembly access and cleaning, to patented CSM, efficient IRM trapping, and intuitive user interface for performing diagnostics, the Orbitrap Exploris 480 mass spectrometer includes novel technologies that significantly enhance instrument robustness, reliability, and ease-of-maintenance. Intra- and inter-instrument reliability and robustness ensure that the Orbitrap Exploris 480 mass spectrometer will fully satisfy the needs of researchers who wish to run extended, large cohort studies.

Find out more at thermofisher.com/OrbitrapExploris480