THE THINGS
YOU CAN
NOT
SEE
CAN CHANGE
EVERYTHING
THE EVIDENCE IS CLEAR

Join those who have been making breakthrough discoveries, with
SYNAPT® Mass Spectrometry Systems – across all research disciplines.*#

Proteomics	 Biomarker	 Discovery	 Pharmaceutical	 l iPiDomics	 structural
e luciDation	 metaBonomics	 BioPharmaceuticals
structural	 Biology	 Polymers	 Petroleum	 characteri
zation	 imaging	 metabolite	 identification	 nanoParticles	 food	 research

SYNAPT G2-S now delivers more performance and capabilities than ever before –
transforming your capacity for discovery, understanding, and success.

* More than 150 peer reviewed papers published using T-Wave ion mobility
# More than 70 peer reviewed papers published using UPLC/MS² Technology
Join those who have been making breakthrough discoveries, with SYNAPT® Mass Spectrometry Systems – across all research disciplines.*

Proteomics  Biomarker  Discovery  Pharmaceuticals  
structural  elucidation  metabolomics  BioPharmaceuticals  
structural  Biology  Polymers  
imaging  metabolite  identification  nanoParticles  food  research
YOU LEAD THE DISCOVERY — WITH OUR LEADING TECHNOLOGY

High performance, versatility, and workflow efficiency of your MS system all play a crucial role in your ability to successfully reach your scientific and business goals — and that’s what drives the evolution of Waters SYNAPT technology.

SYNAPT G2-S combines revolutionary StepWave™ ion optics with proven Quantitative ToF (QuanToF™) and High Definition MS™ technologies to provide the highest levels of sensitivity, selectivity, and speed. With Waters leading MS Informatics, SYNAPT G2-S will help you efficiently extract the maximum information from your most challenging samples — in less time — so you can be first to discover, first to publish, first to succeed.
The ultimate in qualitative and quantitative performance
StepWave, QuanToF, and MS^3 'data independent' acquisition combine to provide the most comprehensive and confident untargeted identification and quantification of compounds with UPLC/MS/MS, at the lowest concentration levels in complex matrices.

Breakthrough SYNAPT High Definition MS™
Every scientist can extract unparalleled information content and make new discoveries not possible by any other method, by combining high efficiency ion mobility separations with high resolution exact mass tandem MS.

Maximum versatility
Serve the broadest range of applications with the most extensive range of targeted data acquisition methods, chromatographic inlet, and ionization source capabilities.

Instant efficiency
Realize maximum system usability and workflow efficiency across your organization through Waters design philosophy of Engineered Simplicity.™

Accelerated success
Maximize your success with complete system solutions backed by a superior applications and technical support network.
QuanTof Technology delivers an outstanding combination of performance attributes:

- Over 40,000 FWHM mass resolving power
- Exact mass (< 1 ppm RMS)
- Accurate isotope abundances
- In-spectrum dynamic range and linearity in detector response of up to $10^5$
- Up to 30 spectra/sec

QuanTof’s high-field pusher and dual-stage reflectron, incorporating high-transmission parallel wire grids, reduce ion turnaround times due to pre-push kinetic energy spread and improve focusing of high energy ions respectively. These innovative technologies combine to provide the highest levels of ToF performance. The unique ion detection system combines an ultra-fast electron multiplier and ‘hybrid ADC’ detector electronics to provide outstanding sensitivity and quantitative performance.
EXPERIENCE THE ULTIMATE IN QUALITATIVE AND QUANTITATIVE PERFORMANCE

When your progress is limited by missing information or the risk of false positive results in your analysis, the combination of StepWave ion optics, the QuanTof analyzer and MS\textsuperscript{E} ‘data-independent’ acquisitions will maximize your chances of success. By providing the best qualitative and quantitative performance attributes, these innovative technologies significantly increase compound coverage and confidence in identification, characterization, and quantitation for your most demanding applications.

SYNAPT G2-S is equipped with a larger ion sampling orifice, an enhanced vacuum pumping configuration and revolutionary StepWave ion transfer optics. This groundbreaking dual-T-wave, off-axis design transfers ions from the ion source to the quadrupole MS analyzer with the highest possible efficiency, at the same time as ensuring undesirable neutral contaminants are actively filtered out. This dramatically increases MS ion intensities while minimizing background noise – significantly improving detection limits and the repeatability of quantitative assays.
Selectivity and accuracy
QuanTof delivers high resolution, exact mass, accurate isotope abundance, a wide dynamic range and speed of acquisition, without compromise, for UPLC separation of very complex samples.

Sensitivity and linearity
Stepwave and QuanTof provide LOD, LOQ’s at significantly lower concentrations than ever thought possible with high resolution MS, with exceptional linearity and reproducibility, even in the most complex matrices.

Maximum coverage
Eliminate the risk of incomplete analysis with UPLC®/MS², a simple patented method of data acquisition that comprehensively catalogs samples in a single analysis.²

Simple, complete assays
Quantify with all the benefits of oa-Tof and MS²:
- Quantify and confirm unlimited numbers of components in one analysis
- Eliminate or reduce time-consuming method development
- Interrogate archived datasets to detect, identify, and quantify new compounds
Accurate quantitation > 4 orders of linearity, with UPLC/MS$^E$

Simultaneous quantitation and identification with UPLC/MS$^E$. Every component is recorded with molecular (MS) and fragment (MS$^E$) ion spectra to aid compound identification. The mass spectral data shown is from 2.5 pg of Sulfadimethoxine on column.

Data shown is for Bovine Insulin (left) and [Glu1]-Fibrinopeptide B (right) at > 10,000X magnification.
BREAK THROUGH WITH SYNAPT HIGH DEFINITION MS

Ever wondered what components you might be missing because high mass resolution or your current tandem MS methods don’t provide enough selectivity? Frustrated that your existing MS techniques can’t address certain challenges?

The SYNAPT G2-S System provides a unique platform to further your discovery efforts by expanding on the capabilities of conventional MS instrumentation.

SYNAPT High Definition Mass Spectrometry is the combination of high-efficiency ion mobility measurements and separations with high-performance tandem MS, enabling the differentiation of samples by size, shape and charge, as well as mass.

By introducing the orthogonal dimension of gas-phase ion mobility separation, you can detect components that were previously undetectable, and access new research capabilities to overcome your toughest analytical challenges and accelerate your scientific understanding.

SYNAPT G2-S High Definition MS with Triwave Technology offers:

- Significant increases in analytical peak capacity
- Separation of isomers, isoforms, and isobaric compounds
- Enhanced conformational and structural characterization
- High ion mobility resolving power > 40 ($\Omega/\Delta\Omega$ full width half maximum)$^5$
- Exact mass measurement and wide dynamic range
- New Informatics tools to accelerate visualization, processing, and interpretation of multidimensional SYNAPT G2-S HDMS data

Why ion mobility?

Measuring the mobility, or drift time, of an ion can yield information about its structure, as compact ions with small collision cross-sections drift quicker than extended ions with large collision cross-sections. Mixtures of compact and extended ions can be separated in the gas phase.

SYNAPT G2-S: Enhanced IM separation power – the high ion mobility resolving power of SYNAPT G2-S enables a mixture of two reverse sequence peptides (GRGDS and SDGRG) differing in CCS ($\Omega$) by only 5%$^6$ to be easily separated. A mobility resolution in excess of 40 ($\Omega/\Delta\Omega$) is indicated.
For access to a unique range of experimental possibilities to improve identification, characterization or localization of specific compounds, Triwave is the key. Triwave employs three T-Wave™ ion guides, allowing ions to be trapped and accumulated, separated based on their mobility, and then transferred to the QuanTof analyzer for high-resolution analysis. Triwave’s innovative configuration also ensures that the introduction of IM is not made at the expense of sensitivity.

High ion mobility resolution has been achieved through increased operating pressure in the Triwave device (via the addition of a novel Helium filled entry cell in the IMS T-Wave). The TRAP and TRANSFER T-Wave regions can be used independently or together as collision cells, with (HDMS mode) or without (TOF mode) ion mobility separations, providing a unique and diverse range of experimental possibilities for improved and more complete structural characterization.
TRANSFORM YOUR CAPACITY TO DISCOVER

Uncovering unknown compounds fuels discovery and progress in scientific understanding. If you want to be able to see what others never have, the unique geometry of SYNAPT systems provide an unrivalled discovery advantage.7

PEAK CAPACITY
By combining high-efficiency ion mobility separations with a high resolution time-of-flight analyzer, SYNAPT G2-S provides a higher peak capacity and greater information content than is available with the highest chromatographic or mass resolution alone.

ION MOBILITY SEPARATION
The orthogonal separation afforded by high-efficiency IM separation dramatically increases the number of detectable and identifiable components in complex mixtures by rapidly separating molecules of the same mass-to-charge ratio, while also providing measurements related to their gas-phase conformation.

HDMS² WORKFLOW
To provide unambiguous confirmation of compound identity, the combination of ion mobility and MS² ‘data independent’ acquisition (HDMS²) means fragment ion information is attainable for every detectable component and with new ProteinLynx™, BiopharmaLynx™, High Definition Imaging, DynamX™ (HDX), and MS² data viewer informatics you can now access all these benefits quickly and easily across a wide range of applications.

Peak capacity is unparalleled
The HDMS data cube illustrates the increase in information content by introducing another dimension of ion mobility (dt) separation that provides a rapid and robust alternative to traditional 2D chromatographic methods.

A fully nested, parallel acquisition methodology is the key to harnessing the full power of UPLC (secs), high-efficiency IM separation (msecs), and high resolution TOF MS (µsecs). The three separation techniques provide seamless capability for separating the most complex mixtures.
Ion Mobility Separation gives an increase in analytical peak capacity with UPLC/IMS/MS

(A) UPLC separation of complex tangerine juice sample where (B) 6 isomers are detected using exact mass extracted ion chromatograms, and (C) 10 isomers are detected with UPLC and IMS combined. (D) Drift time versus m/z data for two isomers at the same retention time and m/z.

ION MOBILITY WORKFLOWS ARE SIMPLE, GENERIC, HIGHLY SELECTIVE, AND COMPREHENSIVE

MS® and HDMS® provide a simple, generic method to enable comprehensive profiling of the most complex datasets so you don’t have to redesign experiments for different sample sets. High quality molecular and fragment ion spectra are generated for every detectable component using retention time and/or (ion mobility) drift time alignment. The comprehensive nature of every dataset means that you can simply re-interrogate your data, not re-analyze your sample. The extra selectivity afforded by ion mobility separations provides more identifications and overall coverage for the most complex mixtures.
SYNAPT G2-S provides a unique and extensive range of analytical capabilities, making it possible to target and characterize specific molecules or families of components in more detail than ever before.

**Collision cross section — because shape matters**

Determining molecular conformation by traditional methods has its limits. SYNAPT High Definition MS (with travelling wave ion mobility) provides a unique method to complement traditional structural determination methods such as X-ray crystallography, electron microscopy, nuclear magnetic resonance, and tandem mass spectrometry.

Travelling wave ion mobility with tandem MS provides rapid separation of molecules on the basis of size, shape and charge and enables structural analysis for compounds that are not amenable to traditional methods.

- Separation of individual isomers, isoforms, and isobaric compounds
- Accurate conformational measurement at physiological concentrations
- Analysis of heterogeneous samples
- Wide mass range capability

The determination of CCS from SYNAPT HDMS data is a simple process, using the IM calibration tool within DriftScope™ enabling accurate conformational measurements to be determined using chromatographic or non-chromatographic data, from small molecules to large protein complexes.

**Investigation and differentiation of the drug Ondansetron and metabolite structures using travelling wave ion mobility mass spectrometry (both MS and MS/MS data) and molecular modelling.**

![Image of Ondansetron and GR90315 structures](image1)

**Ondansetron**
- Theoretical: 107.7 Å²
- T-Wave: 107.4 Å²

**GR90315**
- Theoretical: 109.8 Å²
- T-Wave: 110.4 Å²

**GR63418**
- Theoretical: 111.2 Å²
- T-Wave: 111.5 Å²

**GR60661**
- Theoretical: 111.4 Å²
- T-Wave: 111.7 Å²
Time Aligned Parallel (TAP) fragmentation – for more complete structural elucidation

Confident structural characterization of components, from small organic molecules to modified peptide species demands the best in structural coverage and data quality. TAP fragmentation provides a distinct advantage for building a complete structure, through superior fragment ion coverage, sensitivity and accuracy compared to traditional MS^n or MS/MS techniques.

Multiple components of interest can be individually selected for TAP fragmentation in a UPLC gradient and then subjected to two stages of CID which provide extensive fragmentation with high resolution and exact mass to aid unambiguous structural elucidation.

Ion mobility separation plays a key enabling role, separating first generation fragments and second generation fragments and then, through ‘drift time’ values, aiding the automated association of fragments within the MS^n data viewer software.
Electron Transfer Dissociation – when CID isn’t enough

When analyzing post-translational modifications and top-down sequencing are all important, Electron Transfer Dissociation (ETD) complements collision induced dissociation (CID). Developed specifically to maximize confidence, flexibility, and ease-of-use, the optional ETD capability of SYNAPT G2-S is a uniquely powerful feature for sequencing of biomolecules.

- **High performance** – high resolution, Exact Mass data and high reaction efficiency generate the highest quality sequence data
- **Flexible** – to utilize a range of high-efficiency reagents as well as employ Ion Mobility Separations with ETD for advanced fundamental studies
- **Easy-to-use and maintain** – easy, stable introduction and quick replenishment of ETD reagent to the MS through the simplicity of the ETD glow discharge source

<table>
<thead>
<tr>
<th>TRAP T-WAVE</th>
<th>IMS T-WAVE</th>
<th>TRANSFER T-WAVE</th>
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<tr>
<td>ETD</td>
<td>No IMS</td>
<td>CID Supplemental Activation</td>
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Triwave provides a very flexible analytical platform for ETD studies.

Characterization of o-linked glycosylated peptide from Erythropoietin using LC/MS/MS with ETD. The ETD spectrum shown here exhibits fragment ions of the peptide ion enabling location of modification to be determined.

Supplemental activation is employed routinely to deliver high levels of ETD fragmentation for enhanced sequence coverage. The data shown here is for the phosphopeptide at m/z 688 from a digest of bovine Beta-Casein. Mixed mode CID/ETD DDA analysis provides high quality sequence information on the basis of charge state.
If you need to maximize the number of identifications in complex mixtures or quantify with isotope labelling, SYNAPT G2-S will help you maximize data quality and coverage of components at the lowest concentrations.

The combination of high sensitivity from StepWave and enhanced fast spectral acquisition rates (30 spectra/sec) with the intelligent decision making of FastDDA maximized the number of target compounds that can be detected and analyzed.

UPLC/FastDDA is an advanced, intelligent and automated MS/MS acquisition method that now utilizes embedded algorithms to more rapidly interrogate MS survey spectra for co-eluting precursor ions, selecting them for MS/MS analysis based on threshold intensity, charge state and pre-defined exact mass include/exclude lists.

The collision energy for each spectrum is optimized according to precursor charge state and m/z, resulting in high quality exact mass MS/MS spectra for further processing, interpretation, and database searching.

Up to **30 MS/MS** per survey scan
VERSATILITY—BECAUSE YOUR CHALLENGES DEMAND IT

SYNAPT G2-S MS and MALDI SYNAPT G2-S MS are next-generation quadrupole orthogonal acceleration Time-of-flight systems, which can be upgraded on site to incorporate next generation HDMS functionality.

System upgradability – Future proof your lab
Because you never know what challenges are around the corner, more inlet choices will serve you better:

- The ACQUITY UltraPerformance LC® family of products is proven to be the most powerful and flexible chromatographic inlet for mass spectrometry based analysis today, featuring 2D RP/RP, Hydrogen Deuterium Exchange (HDx) and ‘plug and play’ nanoTile™ Technology.

- Waters Universal Ion Source Architecture, engineered to take maximum advantage of UPLC®, allows the widest range of ionization techniques as well as the very latest innovations in ionization technologies.

Also compatible with DESI (Prosalia), DART (IonSense), LDTD (Phytronix), and TriVersa NanoMate (Advion) sources.
INSTANT EFFICIENCY AND ACCELERATED SUCCESS WITH ENGINEERED SIMPLICITY

High performance is key to productivity, but why should you have to work any harder to take advantage? Central to the design of SYNAPT G2-S is Engineered Simplicity. This means that while SYNAPT G2-S is engineered to handle your most complex applications, it’s also engineered to add simplicity and automation throughout your entire workflow.

Simplicity starts with IntelliStart

Get up and running quickly and the discoveries come even faster! SYNAPT G2-S features IntelliStart™ Technology, an intuitive interface that automates routine tasks. This technology ensures that all levels of scientist can operate the instrument quickly and confidently, to generate reproducible UPLC/MS data of the highest quality.

Be Assured. Choose Waters Global Services

Waters Global Services helps customers optimize laboratory operations by providing superior service, support, upgrades, training, and Waters Quality Parts.® For more information, go to www.waters.com/services.
WHY LEADING RESEARCHERS ARE LEADING WITH SYNAPT HIGH

To reach beyond the boundaries of conventional mass spectrometry, you can access the extra dimension of high-efficiency ion mobility separation offered by SYNAPT G2 HDMS, across a wide range of applications. When leading researchers are saying the benefits of the SYNAPT Mass Spectrometry Systems are this good, can you risk being out of the game?

Enhancing qualitative and quantitative proteomic analysis
“The Waters SYNAPT G2 with ion mobility has greatly enhanced selectivity for proteomic analysis. An orthogonal measure, ion mobility dramatically improves the label-free MS² methodology used in our research. Relative to earlier technology, the new G2 HDMS² platform enables detailed fragment ion determination with well characterized chromatographic measures, producing more accurate peptide sequence determination with precise, reproducible quantification.”

ANDREW K. OTTENS, Ph.D.
Assistant Professor of Anatomy & Neurobiology and Biochemistry, Virginia Commonwealth University, VA, USA

Increasing efficiency in pharmaceutical research and discovery
“We didn’t expect the results to be as good as they are. If we had to synthesize just these three metabolites, it would probably have taken several months, whereas the ion mobility LC-MS experiment and modeling calculations is probably around a week’s worth of work.”

DRUG METABOLITE ID MADE EASY
Chemistry World, July 2010
www.chemistryworld.org

Transforming characterization of challenging compounds in lipiddomics research
“TAP fragmentation for lipidomic analysis provides a very powerful approach for structural identification where fatty acyl fragmentation and localization of double bonds is achievable from the on-line UPLC analysis of plasma and tissue samples. With SYNAPT G2, scientists can, for the first time, combine high resolution, accurate mass, and ion mobility to provide a comprehensive and robust method for the unequivocal structural assignment of lipids.”

THOMAS HAKENMEIER, Ph.D.
Professor of Analytical Bioscience, Leiden/Amsterdam Center for Drug Research, Leiden University and Scientific Director of the Netherlands Metabolomics Centre, Netherlands

Helping understand the role of structure in biopharmaceutical characterization
“It is shown that IMMS reveals 2 to 3 gas-phase conformer populations for IgG2s. In contrast, a single gas-phase conformer is revealed using IMMS for both an IgG1 antibody and a Cys-232 Ser mutant IgG2, both of which are homogeneous with respect to disulfide bonding. This provides strong evidence that the observed IgG2 gas-phase conformers are related to disulfide bond heterogeneity. Additionally, IMMS analysis of redox enriched disulfide isoforms allows unambiguous assignment of the mobility peaks to known disulfide structures. These data clearly illustrate how IMMS can be used to quickly provide information on the higher order structure of antibody therapeutics.”

BAGAL D., ET AL.

success
**DEFINITION MASS SPECTROMETRY**

Images acquired by conventional MS can be a composite of the distribution of multiple ions (left).

Imaging with ion mobility allows the determination of the true distribution of the ion of interest (right) free of interfering isobaric components (middle).

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Expanding scientists ability to better characterize polymer microstructure

“IMS/MS is starting to attract devotees among analytical scientists who recognize the decisive benefits that come from coupling mass analysis with shape-dependent ion separation. As Prof. [Jim] Scrivens (from the University of Warwick, UK) put it, “The ability to track families of ions is one extraordinarily powerful aspect of this technique.” More generally, he added, IMS/MS offers a platform “for separating and visualizing all of these different types of compounds in one high-information-content experiment that is superior to other approaches.””

**DOUBLING UP ON MASS ANALYSIS**

*Chemical & Engineering News.*

March 29, 2010 Volume 88, Number 13 pp. 35-37.

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Structural Biology: Unique insights into biological mechanisms

Providing a totally new dimension, SYNAPT is the MS platform of choice for the rapid structural analysis of large heterogeneous protein complexes. Dozens of papers have been published based on the unique abilities of SYNAPT High Definition MS.¹

**Enhancing structural characterization of proteins with HDX and ion mobility**

“Importantly, ion mobility separations provided an orthogonal dimension of separation in addition to the reversed-phase high-performance liquid chromatography (RP-HPLC). The additional dimension of separation allowed for the deconvolution of overlapping isotopic patterns for co-eluting peptides and extraction of valuable deuterium incorporation data for those peptides. Taken together, these results indicate that including ion mobility separation in HX MS analyses further improves the mass spectrometry portion of such experiments.”

**IACOB R. E., ET AL.**


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**Enhanced spatial localization in tissues: High Definition Imaging (HDI) MALDI**

To determine the efficacy of a drug, it is critical to understand how it’s distributed within plant or animal tissue. Imaging by MALDI MS provides this capability. Whether you want to determine the location of peptides, lipids, drugs, or drug metabolites, HDI™ MALDI – the combination of high-efficiency ion mobility separations and MALDI – uniquely offers the ability to determine the distribution of your target compound without interference from simultaneously ionized background ions.

“… imaging IM-MS provides several unique advantages including (1) selective imaging of isobaric species (i.e. lipids versus peptides) or structural/conformational subpopulations of the same species on the basis of IM, (2) separation/rejection of undesirable endogenous chemical noise, (3) reduction of ion suppression effects in the source of the Tof-MS, by temporal IM separation of analytes, and (4) potential utility for nearly simultaneous IM-MS/MS of all analytes at a particular pixel coordinate.”

**McLEAN J. A., RIDENOUR W. B., CAPRIOLI R. M.**

*J Mass Spectrom.*

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Augmented Reality is a new technology that displays multidimensional computer-generated graphics in real time, enhancing what you can perceive on screen. Like SYNAPT G2-S, it opens up a world of possibilities in the kind of information you can see.

Use the picture marker on the left with your computer’s webcam to see our cutting-edge system technology come to life. Visit www.waters.com/SynaptAR for more information.

www.waters.com/synaptg2s
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