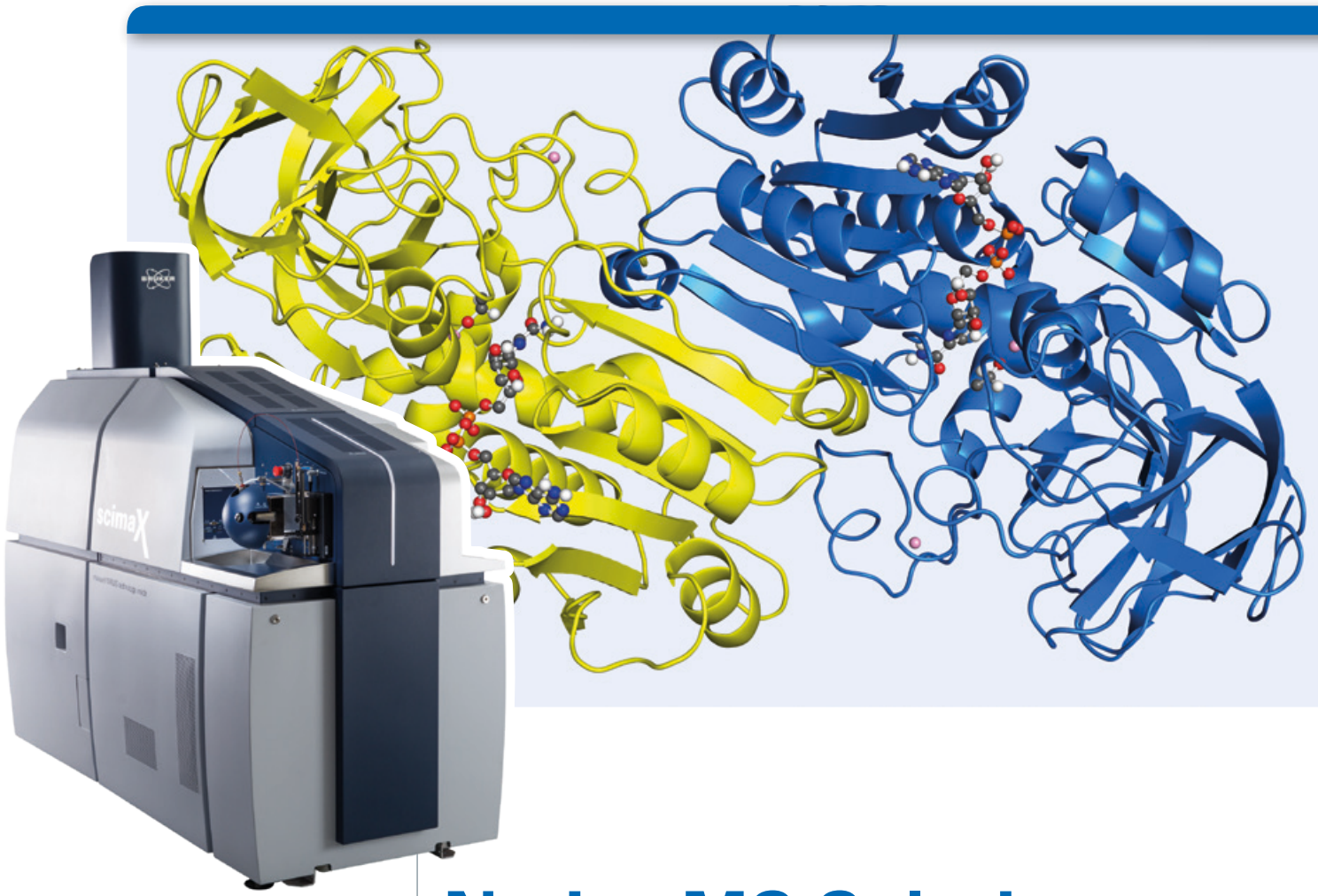
BRUKER



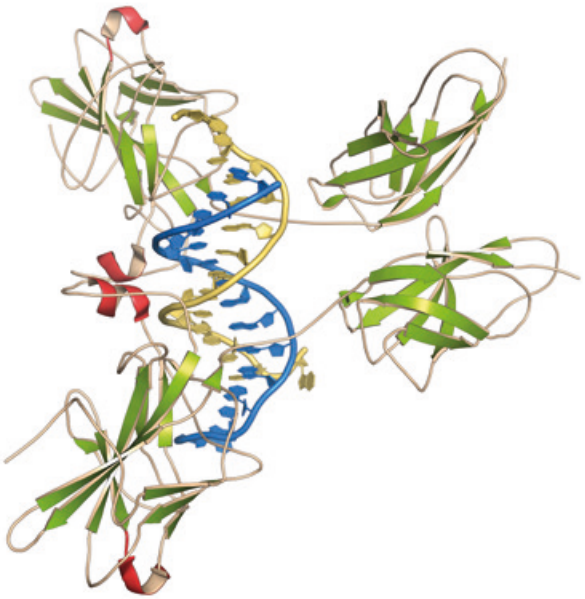
Native MS Solutions

- scimaX MRMS: Perfectly designed for Native MS

Innovation with Integrity

Mass Spectrometry

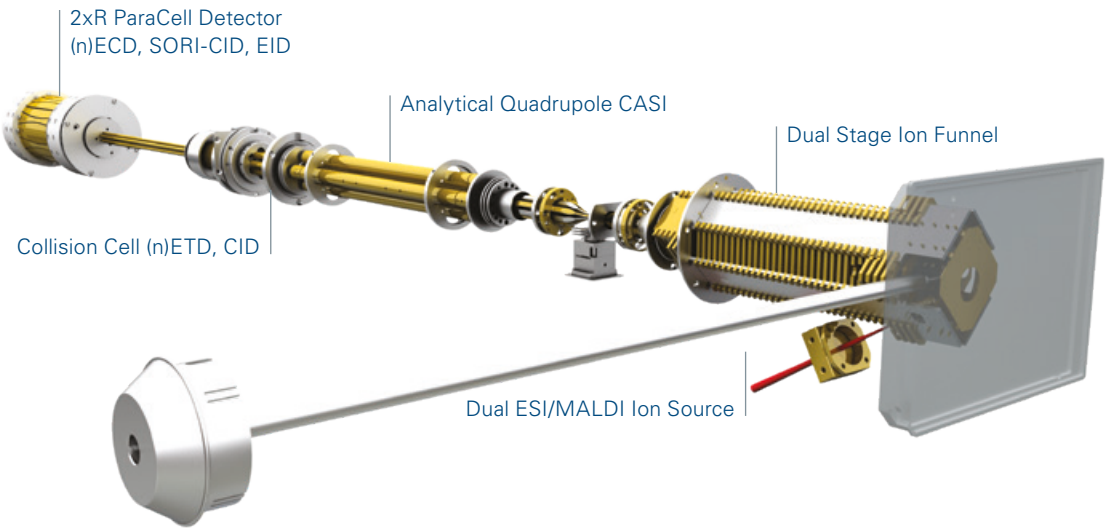
scimaX Ion Path – *Perfectly Balanced* for Native MS



The critical requirement for native MS is an optimal pressure gradient between the electrospray source and the mass analyzer. The ion path on the scimaX MRMS (magnetic resonance mass spectrometry) enables the transmission of intact biomolecular complexes into the ParaCell, allowing for extreme resolution analysis.

Now fragile fragment-protein, protein-substrate, multi-protein biomolecular complexes, membrane proteins with nanodiscs, mAbs, and native protein top-down analysis can all be analyzed on a standard (unmodified) scimaX.

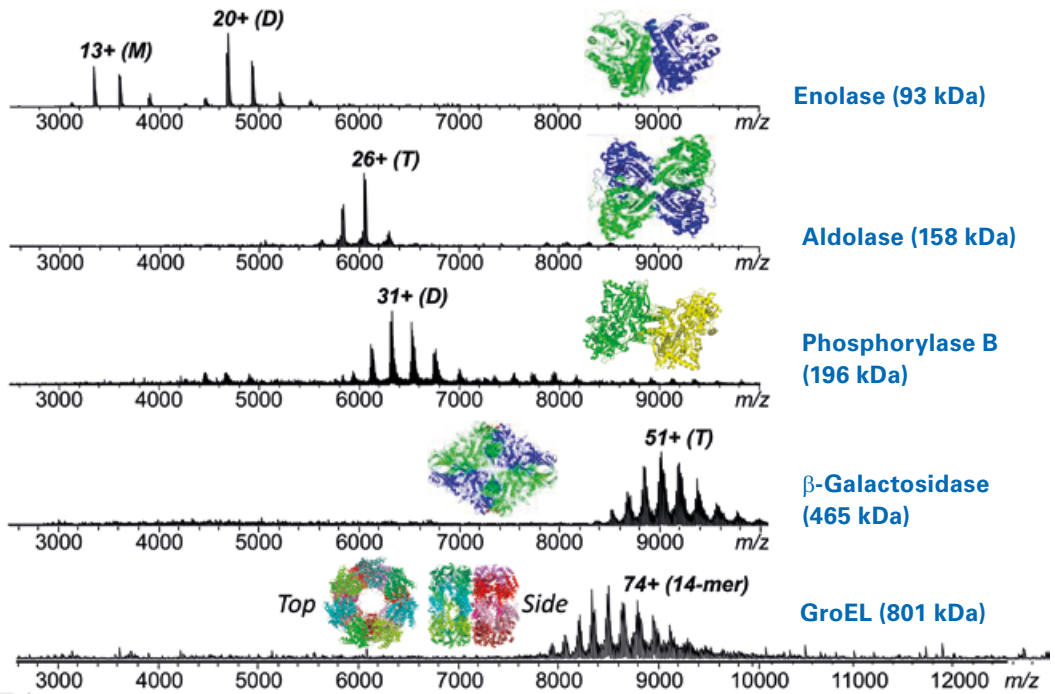
Standard features with scimaX



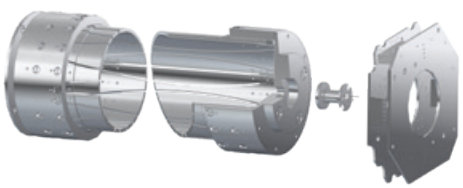
- CID: collision induced dissociation
- ECD: electron capture dissociation
- EID: electron induced dissociation
- ETD: electron-transfer dissociation
- SORI-CID: sustained off-resonance irradiation collision-induced dissociation
- CASI: continuous accumulation of selected ions

Native Mass Spectrometry: An Essential Tool for Modern Structural Biology

Native MS of Protein Complexes (15T MRMS)



Native Protein Complexes using MRMS - Courtesy Joe Loo, UCLA



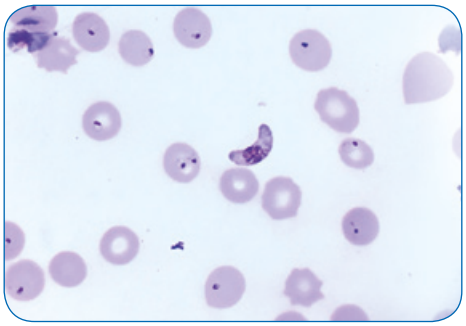
Proprietary ParaCell detector with patented magnetron control technology. Superior trapping capacity for high m/z, highly charged ions.

Successful analysis of large proteins and their complexes requires three key conditions to be met. First, the proteins must be transmitted and detected without breaking intramolecular bonds. Secondly, the protein must be sufficiently desolvated to allow observation of the free protein ions. Finally, the extraordinary amount of charge on the molecules must not overwhelm the detector leading to space charge or coalescence issues. The scimaX and ParaCell technologies were designed with these goals in mind and are proven in labs worldwide for native MS experiments.

Professor Joe Loo, University of California, Los Angeles, USA
"Native mass spectrometry and top-down proteomics are starting to impact studies in structural biology and medicine – and Bruker has all of the tools necessary for these growing technologies."

Native MS Applications for Fragment Based Drug Discovery

MRMS takes on the challenge of discovering new drugs for Malaria



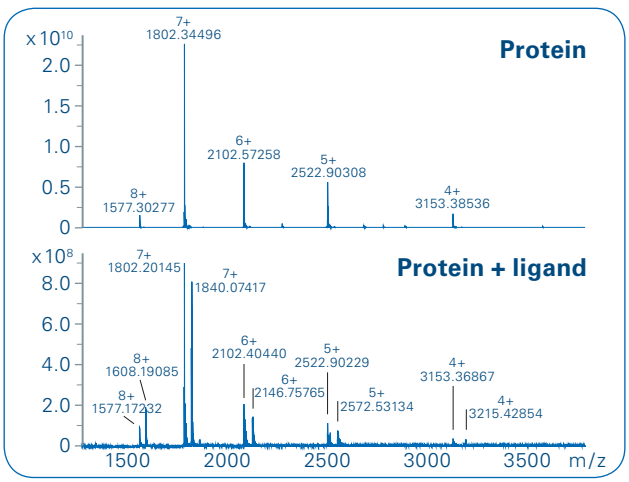
Malaria causing, crescent shaped *Plasmodium falciparum* gametocyte in blood smear

Advancing the frontiers of Fragment-Based Drug Design (FBDD), Professor Ron Quinn and co-workers of the Griffith Institute for Drug Discovery, analyzed a specially curated natural products fragment library of over 600 unique compounds against 62 separate potential malaria drug protein targets.[1] Using MRMS, 79 fragments were identified interacting with 31 proteins and later shown to have *in vitro* activity against *Plasmodium falciparum*, a parasite that induces severe malaria in humans. 13 of these compounds had IC_{50} values less than 45 µM, which is uncommon for leads from fragment libraries.

Professor Ronald Quinn, Griffith Institute for Drug Discovery, Brisbane, Australia

"Our first experiments worked beautifully. Bruker MRMS retains weak non-covalent complexes and also easily handles screening of pools of compounds. The high resolution is perfect to resolve the complex mixtures."

Observe free and bound protein target



Weak binding (K_d > 10 µM) interactions typical in FBDD are routinely preserved and observed by MRMS. The balanced ion optics require no special modifications for native MS.

[1] Fragment-Based Screening of a Natural Product Library against 62 Potential Malaria Drug Targets Employing Native Mass Spectrometry. Vu H, Pedro L, Mak T, McCormick B, Rowley J, Liu M, Di Capua A, Williams-Noonan B, Pham NB, Pouwer R, Nguyen B, Andrews KT, Skinner-Adams T, Kim J, Hol WGJ, Hui R, Crowther GJ, Van Voorhis WC, and Quinn RJ. *ACS Infectious Diseases* 2018 **4** (4), 431-444. DOI: 10.1021/acsinfecdis.7b00197.

Six Proven Reasons for Using the scimaX MRMS for Native MS

1 Ion path leaves fragile non-covalent interactions intact

Bruker's perfectly balanced MRMS ion optics have always been the most efficient in the industry for native MS – no changes to vacuum or a separate, special instrument needed. Complexes are desolvated but not disrupted.

2 Only instrument to offer broadband extreme resolution

Only Bruker MRMS offers the ability to detect molecules at 200 m/z at 20 million resolution and ppb mass accuracy while also providing resolving power in the hundreds of thousands at 5000 m/z.

3 Extreme Sensitivity

Protein concentrations ranging from 100 µM to 10 nM have been observed, enabling a wide range of ligand affinities to be studied and compared (> 100 µM often results in aggregation).

4 scimaX easily interfaces to multiple ion sources including cIEF

Bruker's sources are at ground allowing easy interface of most custom ion sources.

5 The ultimate companion for HTS and FBDD – eliminate your false positives

Native MS on scimaX is the best tool for distinguishing specific and non-specific interactions as well as determining stoichiometry of binding.

The scimaX MRMS is built on conduction cooling technology. It does not require liquid cryogens or a vent line for operation.

6 scimaX is the most flexible instrument in the industry with native MS capabilities

scimaX not only excels at native MS, but also MALDI Imaging, isotopic fine structure, metabolomics, petroleomics, and more.

Proven MS technology for routine analysis of native protein complexes

Wongkongkathep P, Han JY, Choi TS, Yin S, Kim HI, Loo JA. (2018) ***Native Top-Down Mass Spectrometry and Ion Mobility MS for Characterizing the Cobalt and Manganese Metal Binding of α-Synuclein Protein***, Journal of the American Society for Mass Spectrometry, 10.1007/s13361-018-2002-2, **29** (9), 1870–1880

Vu H, Pedro L, Mak T, McCormick B, Rowley J, Liu M, Quinn RJ (2018) ***Fragment-Based Screening of a Natural Product Library against 62 Potential Malaria Drug Targets Employing Native Mass Spectrometry***, ACS Infectious Diseases, 0.1021/acsinfecdis.7b00197, **4** (4), 431-444

Lin Z, Guo F, Gregorich ZR, Sun R, Zhang H, Hu Y, Shanmuganayagam D, Ge Y (2018) ***Comprehensive Characterization of Swine Cardiac Troponin T Proteoforms by Top-Down Mass Spectrometry***, Journal of the American Society for Mass Spectrometry, 10.1007/s13361-018-1925-y, **29** (6), 1284–1294

Li H, Nguyen HH, Ogorzalek LRR, Campuzano IDG, Loo JA (2018) ***An Integrated Native Mass Spectrometry and Top-Down Proteomics Method that Connects Sequence to Structure and Function of Macromolecular Complexes***, Nature Chemistry, 10.1038/nchem.2908, **10** (2), 139–148

Chen B, Lin Z, Alpert AJ, Fu C, Zhang Q, Pritts WA, Ge Y (2018) ***Online Hydrophobic Interaction Chromatography-Mass Spectrometry for the Analysis of Intact Monoclonal Antibodies***, Analytical chemistry, 10.1021/acs.analchem.8b01865, **90** (12), 7135–7138

Campuzano ID, Netirojjanakul C, Nshanian M, Lippens JL, Kilgour DP, Orden SL, Loo JA (2018) ***Native-MS Analysis of Monoclonal Antibody Conjugates by Fourier Transform Ion Cyclotron Resonance Mass Spectrometry***, Analytical Chemistry, 10.1021/acs.analchem.7b03021, **90** (1), 745-751

Zhang J, Ogorzalek LRR, Loo JA (2017) ***Structural Characterization of a Thrombin-Aptamer Complex by High Resolution Native Top-Down Mass Spectrometry***, Journal of the American Society for Mass Spectrometry, 10.1007/s13361-017-1751-7, **28** (9), 1815–1822

Teruya K, Rankin G., Chrysanthopoulos PK, Tonissen KF, Poulsen S-A (2017) ***Characterisation of Photoaffinity-Based Chemical Probes by Fluorescence Imaging and Native-State Mass Spectrometry***, Chembiochem: a European journal of chemical biology, 10.1002/cbic.201600598 **18** (8), 739–754

Li H, Sheng Y, McGee W, Cammarata M, Holden D, Loo JA (2017) ***Structural Characterization of Native Proteins and Protein Complexes by Electron Ionization Dissociation-Mass Spectrometry***, Analytical chemistry, 10.1021/acs.analchem.6b02377, **89** (5), 2731–2738

Chrysanthopoulos PK, Mujumdar P, Woods LA, Dolezal O, Ren B, Peat TS, Poulsen S-A (2017) ***Identification of a New Zinc Binding Chemotype by Fragment Screening***, Journal of medicinal chemistry, 10.1021/acs.jmedchem.7b00606, **60** (17), 7333–7349

Cai W, Tucholski T, Chen B, Alpert AJ, McIlwain S, Kohmoto T, Jin S, Ge Y (2017) ***Top-Down Proteomics of Large Proteins up to 223 kDa Enabled by Serial Size Exclusion Chromatography Strategy***, Analytical chemistry, 10.1021/acs.analchem.7b00380, **89** (10), 5467–5475

For Research Use Only. Not for Use in Clinical Diagnostic Procedures.

Bruker Daltonik GmbH

Bremen · Germany
Phone +49 (0)421-2205-0

Bruker Scientific LLC

Billerica, MA · USA
Phone +1 (978) 663-3660

Scan the QR-Code for more details

ms.sales.bdal@bruker.com - www.bruker.com