TOFpilot – Integrated Control Software for the icpTOF

Introduction

Inductively coupled plasma mass spectrometry (ICP-MS) has become a routine method for the elemental and isotopic analysis for a wide range of samples and applications. The advantages of combining ICP-MS with time-of-flight (TOF) mass analyzers include fast data acquisition and no limitations on the number of measured isotopes, thereby allowing quasi-simultaneous analysis of the entire mass spectrum. By measuring "all the elements, all the time" ICP-TOFMS instruments – such as TOFWERK's icpTOF – excel at the analysis of fast transient signals as produced by single particles (e.g., natural/ engineered nanoparticles and single cells) or signals produced by fast-washout (low dispersion) laser ablation cells.

In single-particle inductively coupled plasma mass spectrometry (sp-ICP-MS) the signals from individual nanoparticles (NPs) are detected. As the signal duration resulting from an individual NP is very short (usually < 0.5 ms), a high time resolution is required to fully characterize it. The same principle underlies the analysis of single cells by ICP-MS (sc-ICP-MS). The method of ICP-TOFMS is gaining attraction in these applications due to its wide quasi-simultaneous acquisition range, low full-spectrum acquisition time, and its high mass resolving power.

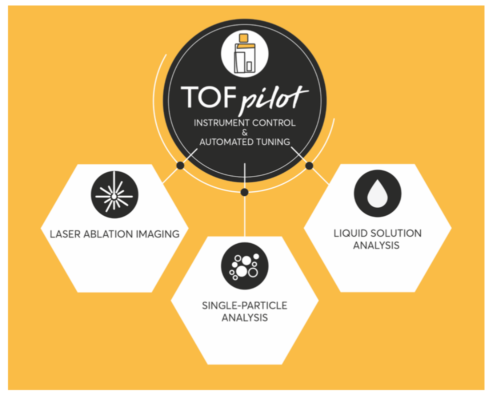

Figure 1: Schematic of TOFpilot. *The control software for the icpTOF allows for specialized workflows, including laser ablation imaging, single-particle analysis, and liquid solution analysis.*

In laser ablation (LA) ICP-MS, a solid sample is ablated via a UV laser inside an air-tight ablation cell and transported into the ICP-MS via a transport gas (e.g., He). With proper synchronization of the LA system and the mass spectrometer, element signals can be recorded at discrete positions on the sample in order to generate elemental or isotopic images. LA-ICP-MS imaging is increasingly applied in geological, biological, and medical studies. The combination of low dispersion ablation cells (with washout times on the order of milliseconds) and ICP-TOFMS significantly increases the speed of such imaging experiments, allowing to record hundreds of multi-elemental pixels per second.

Due to a wide range of applications, the icpTOF is designed to be compatible with various sample introduction methods. This flexibility in hardware drives the development of the integrated control software for the icpTOF – TOFpilot.

TOFpilot WorkFlows

TOFpilot is a control platform designed to operate all three models of the icpTOF (S2, R, and 2R). The icpTOF is based on the iCAP RQ (Thermo Scientific), and TOFpilot has full control over both the iCAP front-end and the TOF mass analyzer. The software greatly simplifies the workflow for the user by integrating control of the icpTOF with various sample introduction systems, such as different laser ablation systems (e.g., Teledyne CETAC and Elemental Scientific Lasers), autosamplers for solution analysis, and a TOFWERK micro-droplet generator (MDG) for the analysis of single particles/cells. TOFpilot operates on a module-basis (see Figure 1) which allows the user to set up different workflow sequences, including plasma startup, instrument tuning (manual or automated), liquid solution analysis, single particle and single cell analysis, laser ablation imaging (including real-time display), and single spot laser ablation analysis. In the following sections, the main workflows of TOFpilot are described.

Instrument Control

TOFpilot provides quick access to the status of the hardware and enables integrated control of the different system components, including the iCAP front-end and the time-of-flight (TOF) mass analyzer. From sample introduction, ion optics, CCT cell, to TOF parameters, TOFpilot seamlessly controls all operational instrument parameters within one program. The layout of the different functional blocks of adjustable parameters is fully configurable to the requirements of the user. Common operating steps include start/shutdown of the plasma and setting of voltages, gas flows, and torch position (see Figure 2).

Instrument Tuning

Instrument tuning is performed either manually through access to the instrument parameters, or through autotuning modules. Autotuning of detector sensitivity, ICP settings, and ion optics is possible at this stage (see Figure 3). After successful completion of the tuning module, tune settings are saved with a fully documented history of parameter changes. A pdf-report summarizing the changes and the output of each optimization step (including graphs) is automatically generated.

Liquid Solution Analysis

The Liquid–External Calibration module in TOFpilot allows the setup of measurement sequences containing calibration standards and samples with unknown concentration.

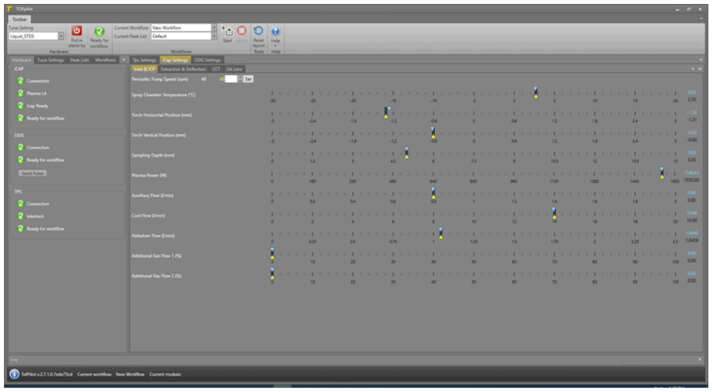

*Figure 2: **TOFpilot Instrument Control gives access to parameters from both the iCAP front-end and the TOF.** The current view displays the different parameters of the inlet and ICP from the iCAP settings. On the left tab, the status of all components is shown for rapid overview. At the top, the large red button (Put in stand-by) allows to switch off all voltages and the plasma. Additional hardware information can be accessed under the Tune Settings, Peak Lists, and Workflows tabs.*

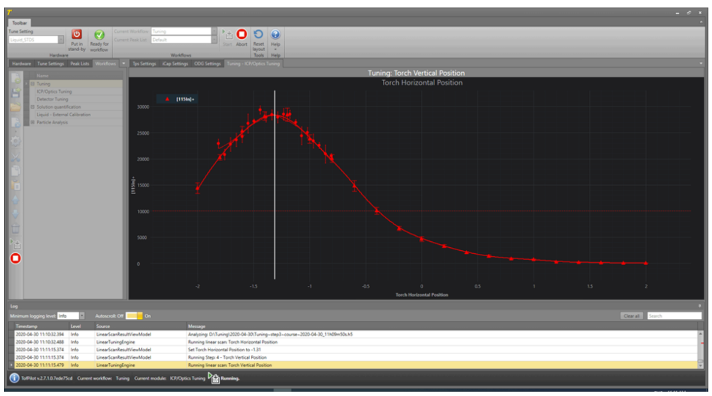

*Figure 3: **TOFpilot Autotuning window.** In this example, the signal of ^{115}In in a tuning solution is optimized by varying the torch position.*

Quantification is performed automatically after building and fitting of the calibration curve. TOFpilot simplifies the workflow for routine analysis and is compatible with different autosamplers for fast and automated sample introduction. A complete sequence comprising different types of vials (e.g., blanks, calibration standards, samples), as well as experimental parameters (e.g., integration time and dilution factor) can be set up and run (see Figure 4). Once the workflow is started, an overview window is displayed showing the progress of the analysis. Once the data have been measured, they can be re-processed at any time in the liquid re-processing module. Results can be published as a pdf-report or as csv-files for further post-processing.

Single Particle Analysis

TOFpilot features a fully integrated single particle workflow, which includes experiment setup and subsequent data processing and quantification. Like in the Liquid Solution Analysis workflow, the different types of vials (e.g., blanks, ionic standards, nanoparticle

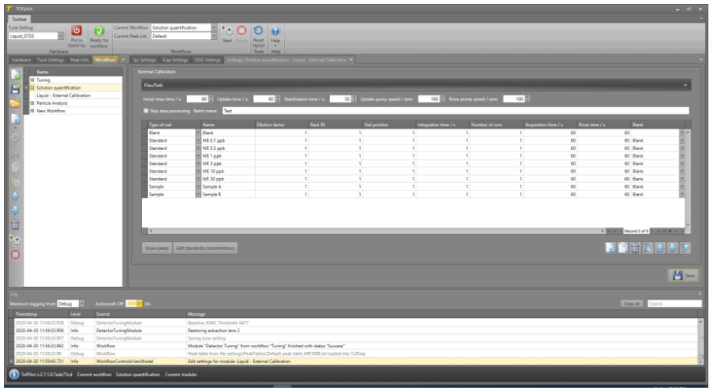

__Figure 4: TOFpilot Liquid Solution Analysis with external calibration.__ The editor allows setup of the sequence by specifying the types of vials (e.g., blank, standard, sample), the timing (e.g., rinse, uptake, stabilization), as well as standard concentrations for the respective analytes.

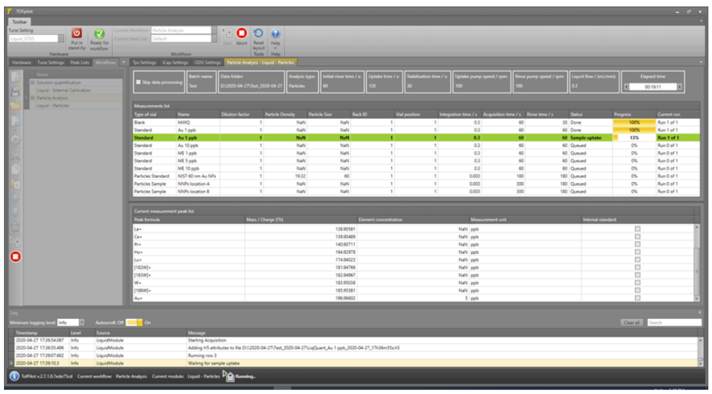

__Figure 5: TOFpilot Single Particle Analysis.__ Overview of a running sequence, where the first two vials (i.e, blank and 1 ppb Au standard) have already been measured and the 5 ppb Au standard is currently being taken up. Following the uptake, 30 s will be spent for stabilization before acquisition. The clock indicator in the top right gives an indication of the elapsed time, the remaining time, and the end time.

standards, and nanoparticle samples) as well as experimental parameters can be defined. Here again, the overview window shows the current state of the analysis (see Figure 5).

After measurement, the data is processed directly for particle number concentrations and particle mass distributions. The quantification is based on the approach developed by Pace H. E. and his coworkers (2011), using liquid standards for calibration and the particle size method for the determination of the transport efficiency. All results are summarized in a report and are exported as csv-files for further post-processing in third-party software. Note that this module may also be used for single cell analysis.

Laser Ablation Imaging

A Laser Ablation Imaging workflow with live preview is available within TOFpilot and currently supports any rectangular shape. The first step is to set the ablation parameters (e.g., fluence, repetition rate, spot size), the

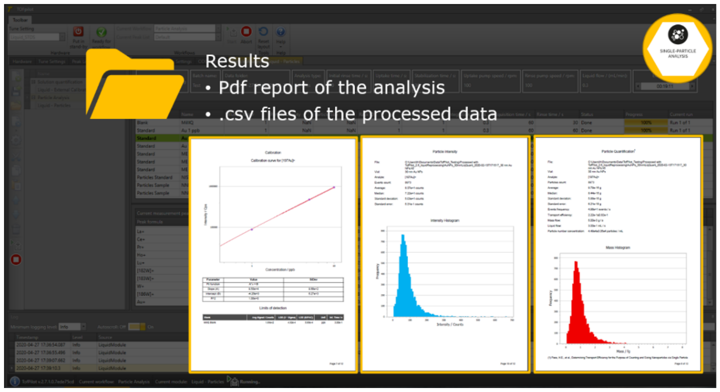

Figure 6: Export of processed single particle data. *The processed data can be saved as a pdf-report or as csv-files for further post-processing in third-party software.*

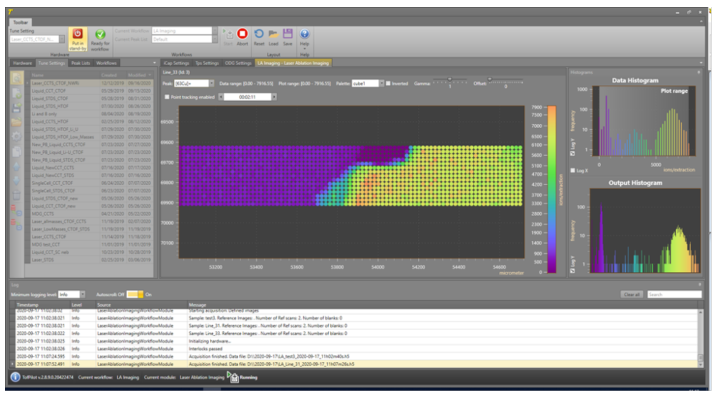

Figure 7: TOFpilot Laser Ablation Imaging. *Real-time display showing the construction of the image pixel by pixel and line by line. Each pixel contains a full mass spectrum. During image acquisition, different isotope channels and display settings can be selected.*

image size and shape in the laser software. TOFpilot then downloads all image data, including coordinates and ablation parameters, and creates a corresponding grid in the preview window. The user can start the ablation (i.e., image rastering) in TOFpilot, which fills the grid pixel by pixel and line by line with data from the icpTOF enabling real-time imaging. Different isotope channels and display settings (e.g., color palettes, gamma) can be selected during the construction of the image. Each pixel in the image contains a full mass spectrum along with the laser metadata (see Figure 7). The final image can be exported for post-processing. Quantification is possible with third-party software, including Iolite (University of Melbourne) or HDIP (Teledyne CETAC) provided that gas blanks and suitable calibration reference materials were recorded along with the image on the sample.

Summary and Outlook

The TOFpilot software greatly simplifies the workflow for the user by integrating control over the icpTOF (including iCAP front-end and TOF analyzer) and different sample introduction systems (e.g., autosamplers and laser ablation systems). TOFpilot operates on a module-basis which allows the user to set up different workflow sequences.

The Single Particle Analysis module including experiment setup, subsequent data processing and quantification further advances the icpTOF as a method for single particle and single cell analysis. The Laser Ablation Imaging module enables real-time display of multi-element images, thereby reducing the risks associated with recording images "blindly".

The goal of TOFpilot is to guide the user through the entire analytical session, from plasma startup and instrument tuning, over data acquisition and display, to processing and export of (quantitative) data. New modules to be added include a Laser Ablation Spot Analysis Module and a module to control TOFWERK's microdroplet generator (MDG).

Acknowledgements

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Further Reading From TOFWERK

Knowledge post: What is Single Particle ICP-MS? (https://www.tofwerk.com/single-particle-icp-ms/)

Knowledge post: What is Laser Ablation ICP-MS Imaging? (https://www.tofwerk.com/laser-ablation-icp-ms-imaging/)

Knowledge post: Advantages of Time-of-Flight Mass Spectrometry Over Quadrupole MS (https://www.tofwerk.com/advantages-time-of-flight-mass-spectrometry-over-quadrupole-ms/)

Perspective Article on Single-Cell Analysis with ICP-TOFMS in Spectroscopy, October 2020 (https://www.tofwerk.com/single-cell-analysis-tofms-october-2020-spectroscopy/)

Perspective Article on Multielemental Imaging with Laser Ablation ICP–TOFMS in Spectroscopy, May 2017 (https://www.tofwerk.com/la-icptofms_imaging_spectroscopy_2017/)

Recent Peer-Reviewed Publications Using the icpTOF and TOFpilot

Theiner S. et al. Laser ablation-ICP-TOFMS imaging of germ cell tumors of patients undergoing platinum-based chemotherapy. Metallomics 2020. DOI: 10.1039/D0MT00080A

Van Malderen, S., Van Acker, T., Vanhaecke, F. Sub-μm nanosecond LA-ICP-MS imaging at pixel acquisition rates above 250 Hz via a low-dispersion setup. Analytical Chemistry 2020. DOI:10.1021/acs.analchem.9b05056 von der Au, M. et al. Single cell-inductively coupled plasma-time of flight-mass spectrometry approach for ecotoxicological testing. Algal Research 2020. DOI:10.1016/j.algal.2020.101964

Bussweiler, Y. et al. Trace element mapping of high-pressure, high-temperature experimental samples with laser ablation ICP time-of-flight mass spectrometry–Illuminating melt-rock reactions in the lithospheric mantle. Lithos, 2020. DOI: 10.1016/j.lithos.2019.105282

Bevers, S. et al. Quantification and Characterization of Nanoparticulate Zinc in an Urban Watershed. Frontiers in Environmental Science: Biogeochemical Dynamics 2020. DOI: 10.3389/fenvs.2020.00084

For a complete list of icpTOF publications, see https://www.tofwerk.com/products/icptof/

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