Multi-Parametric Ionomics of Single Yeast Cells with the icpTOF

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Metals and non-metals like S, P, Na, K, Ca, Mg, Mn, Fe, Cu, Zn, Se are essential building blocks of a living cell. Incorporated in the structure of proteins or as free ions, they control vital cell functions. For example, sulfur helps connect different proteins; phosphorous is present as phosphate in ATP, GTP, DNA, and RNA; sodium, chlorine, potassium and calcium are fundamental for nerve cells to send electrical signals; and other trace metals are required by enzymes and proteins to perform chemical reactions.

The distribution of elements in cells - often referred to as the cell ionome[1] - can be used to determine cells' states of development and growth rates. Changes in elemental composition can be utilized to study the response to toxic compounds or drugs, e.g. Pt-based compounds used in cancer therapy.

Traditionally, cell ionomic studies use ICP-MS after acid digestion of a cell pellet. This procedure usually requires a relatively large number of cells, expanding the analysis cost, and provides only the average results for a given cell population. The heterogeneity within the cell population is not considered and information on cell-to-cell variability is lost.

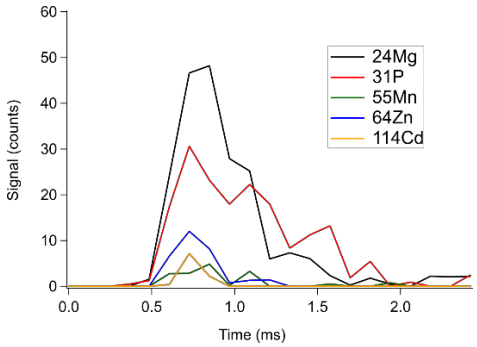

Figure 1 Example of a recorded signal for a single Wickerhamomyces anomalus yeast cell. Data were acquired with an integration time of 120 µs.

Every cell is, however, unique and analyzing single cells gives new insights into intracellular biochemistry and cell-environment interactions. Since many processes in a biological system are interconnected, accessing all elements in the cell increases the power and efficiency of the experiment, leading to better models and predictions. The TOFWERK icpTOF mass spectrometer

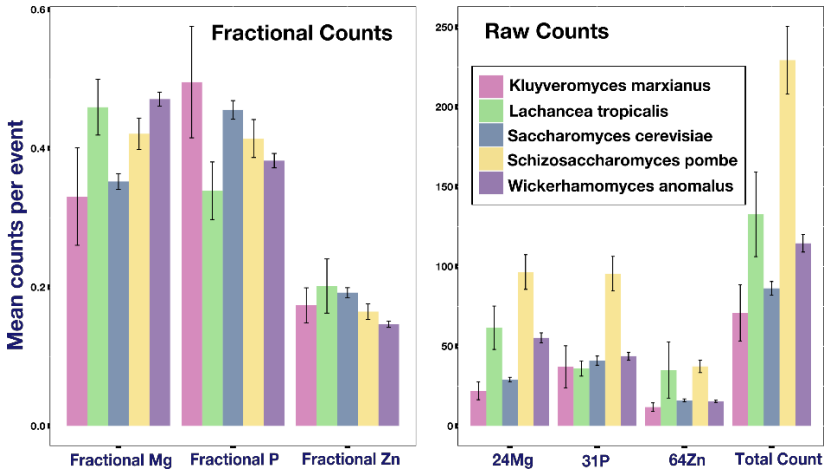

Figure 2 Left: Fractional mean counts of different elements in single cells (defined as counts of element X/Sum of counts of all elements). Right: Mean counts of different elements in single cells from different cell species. The difference in mean and fractional counts indicate the difference in element concentrations between different cell species.

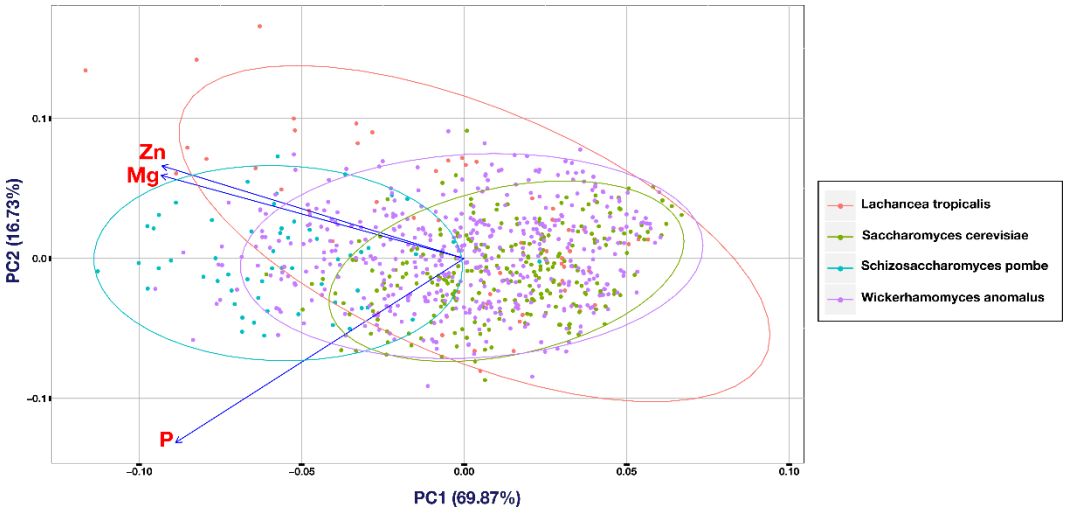

Figure 3 PCA plot for different species. The analysis shows no clear separation of cell populations from different species. There was just a minor difference between S. cerevisiae and S. pombe and S. pombe and W. anomalus detected.

enables the simultaneous detection of all elements in a single cell[2], making it an ideal and unique tool for multi-parametric ionomics.

In this study, we analyzed the cell ionome of different yeast cell species grown in Synthetic Complete Glucose Broth media spiked with Co, Ni and Cd. An icpTOF R was equipped with a conventional sample introduction system and run at an acquisition rate of 8250 spectra/s in triggered mode (120 µs integration time) or 550 spectra/s in

continuous mode (1.8 ms integration time). Signals of single cells were separated from the ionic background using the Particle Processing Module in TOFWERK's TofPilot software.

P, Mg and Zn were detected in every cell and K, Fe, Mn and Cd were detected in some cells, which were likely larger. Only the data of P, Mg and Zn were analyzed. A noticeable difference in average and relative concentrations of different elements in different species was observed (Figure 2). Based on results of Principal Component Analysis (PCA), however, it was concluded that it was not possible to separate cells from different species completely. There was just a minor difference between *S. cerevisiae* and *S. pombe* and *S. pombe* and *W. anomalus*.

This example demonstrates the power of the icpTOF technology for studying the cell ionome on an individual cell basis without any prior knowledge of the cell elemental composition.

References

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2. Hendriks, L.; Gundlach-Graham, A.; Hattendorf, B.; Günther, D., Characterization of a new ICP-TOFMS instrument with continuous and discrete introduction of solutions. *J. Anal. At. Spectrom.* **2017,** *32* (3), 548-561.

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