Multiplexed High Pressure Ion Mobility-TOFMS: High Resolution, Sensitivity and Structural Information in One Package

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Introduction

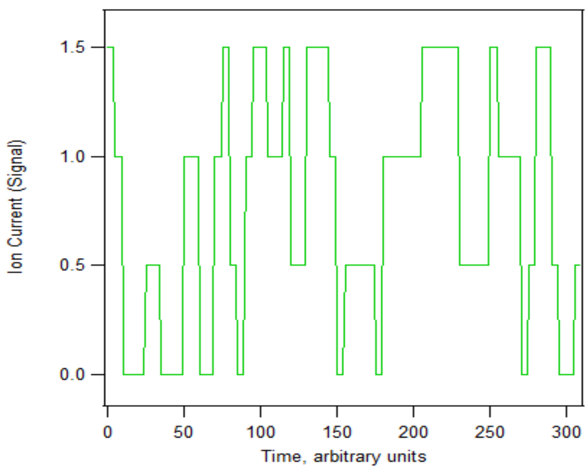
Classical drift tube ion mobility methods suffer from low sensitivity due to the narrow gate necessary for useful mobility resolution. Multiplexing methods such as Fourier or Hadamard transforms can theoretically resolve this dilemma, but have been problematic in practice. We report on development of a multiplexing strategy which achieves the desired performance in routine use. It has been implemented in a compact IMS-TOFMS instrument, including post-IMS collisional activation for structural elucidation.

Methods

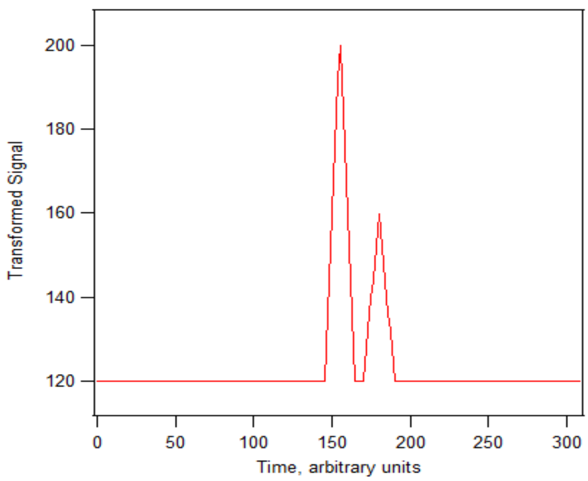
The IMS is a single piece atmospheric pressure conductive glass tube, enclosed for temperature and pressure control. Ions from the source, typically electrospray, are modulated into the tube with a Bradbury-Nielson gate, according to a preselected pattern. After the drift region the ions are passed through a 2-stage interface, with adjustable fields to control CID. The modulated ion signals are demodulated and enhanced in a separate postprocessing step.

Results

Multiplexing with Hadamard sequences can theoretically result in 50% duty cycle with no loss of resolution compared to conventional methods. An ideal example is shown below:

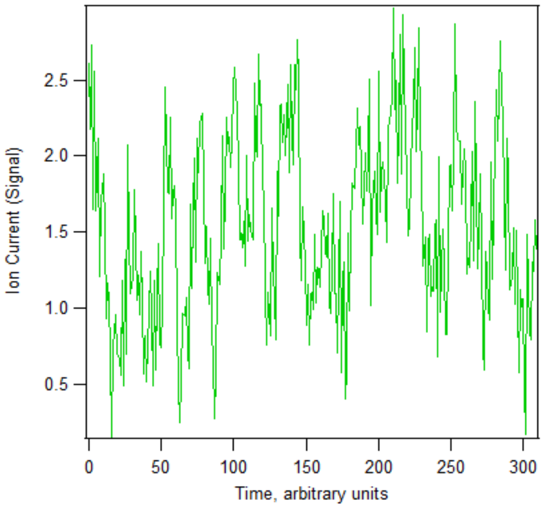


Modulated signal on detector

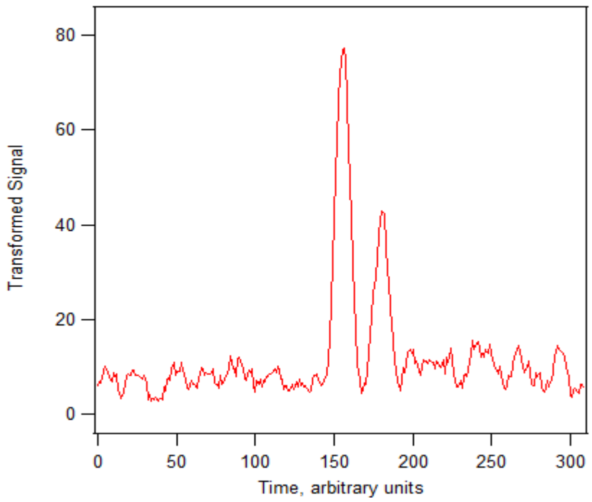


After inverse transform

However, multiplexing strategies can suffer from serious transform artifacts because the data is nearly always far from ideal as shown in the next figures:

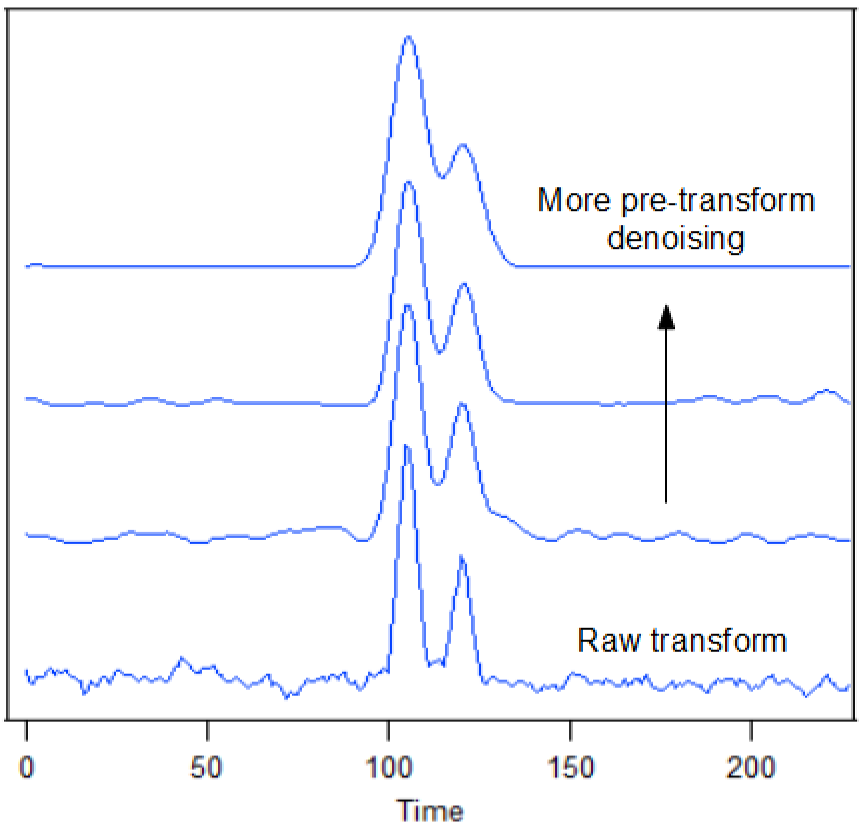


Modulated signal on detector



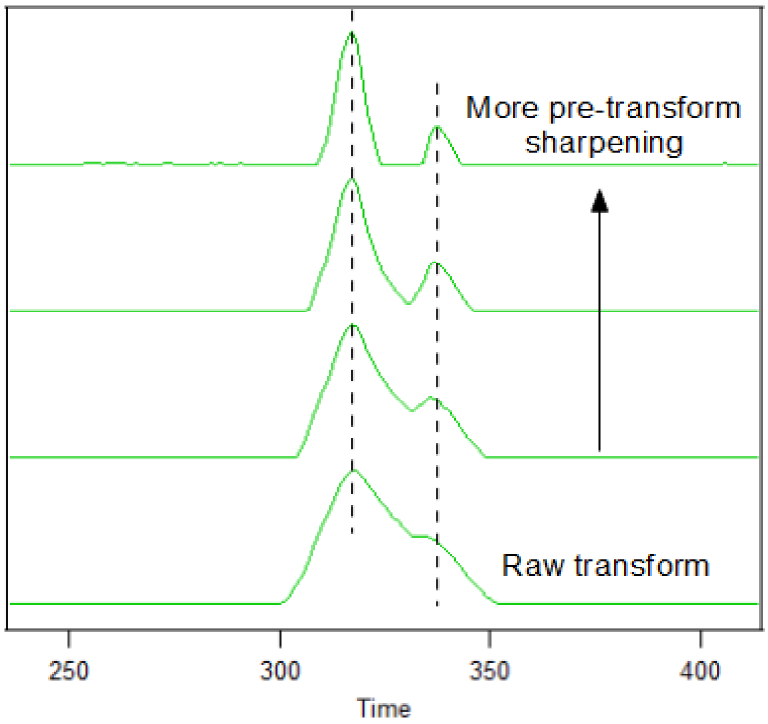
After inverse transform

This can negate the duty cycle advantage of multiplexing. Adaptive algorithms have been developed which progressively and dramatically reduce both systematic and random noise. The dynamic range of the multiplexed data is thereby regained. This "denoising" takes place in the multiplexed domain, which is more effective than smoothing after the inverse transformation:



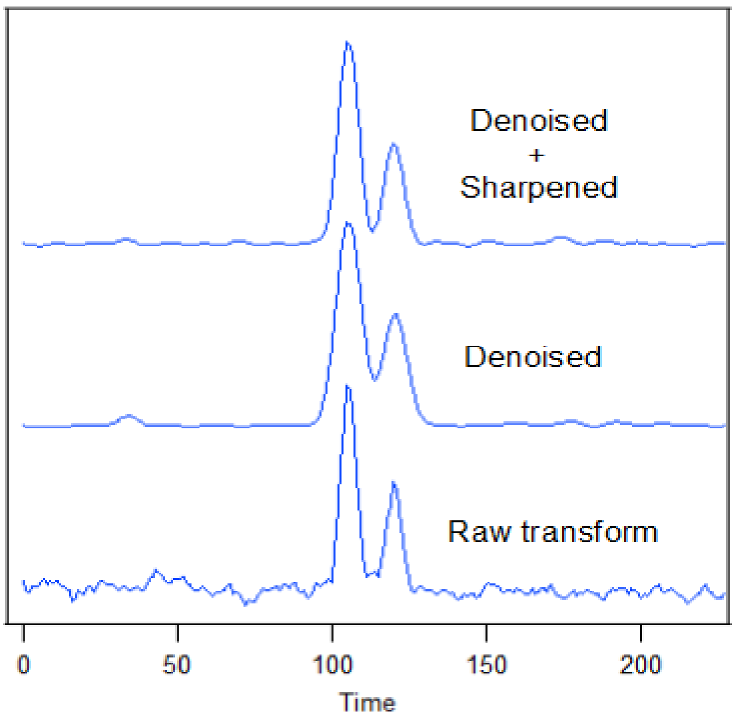
Example of denoising. Noise is decreased faster than peaks are broadened.

In addition, simultaneous optional enhancement of the peak shape can be performed, also in the multiplexed domain. The modulation is enhanced, which allows improvement of resolution, sometimes above the conventional limit:



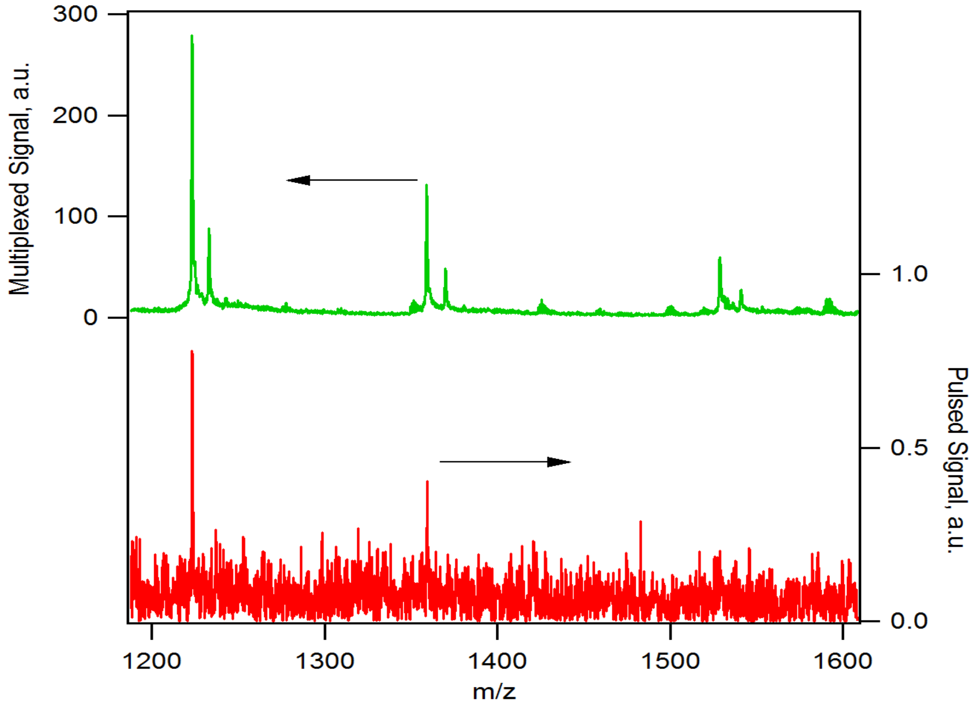
Example of the effect of sharpening in the multiplexed domain.
Peak positions and relative intensities are retained.

Sharpening and denoise are complementary, and can be used together:



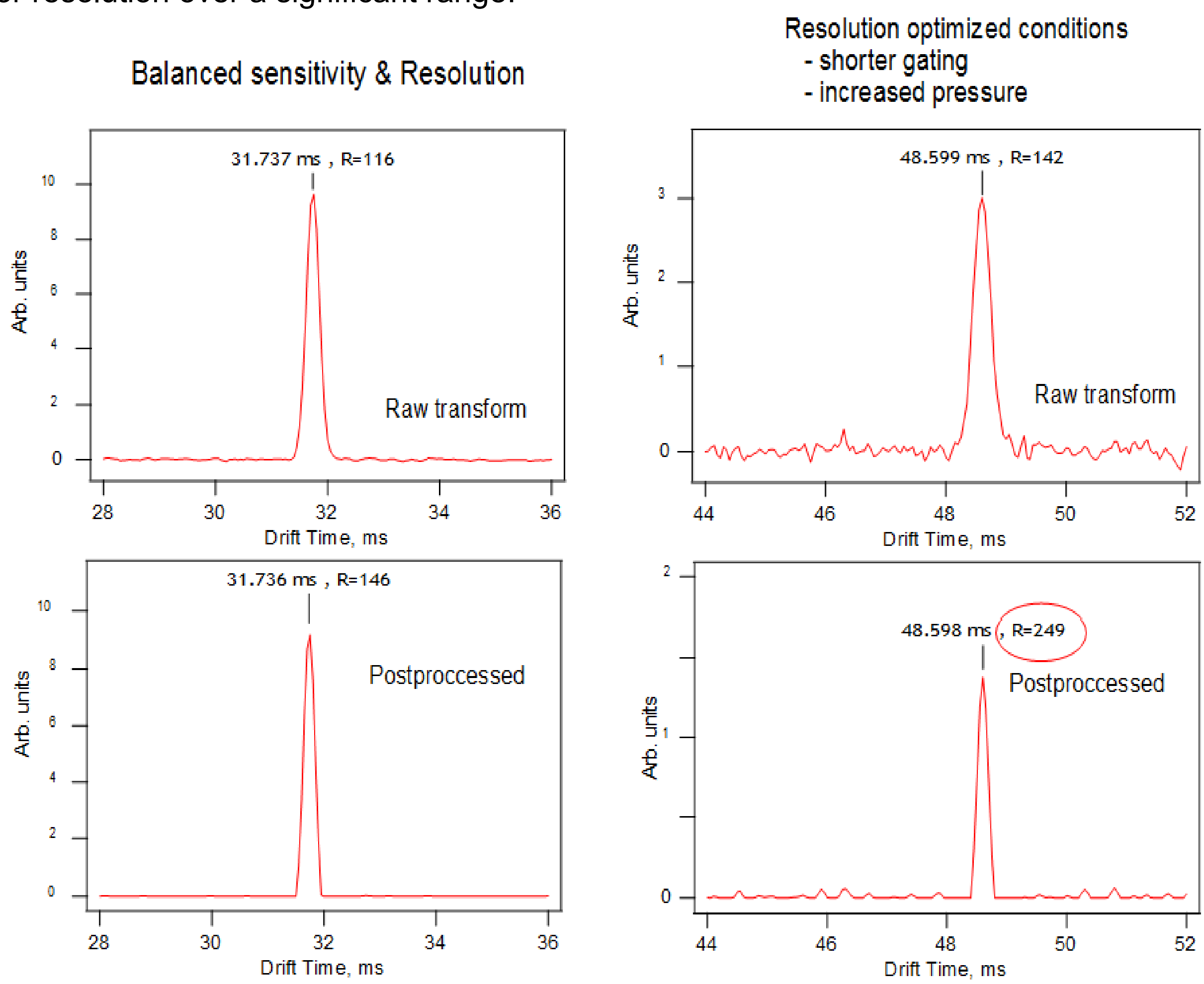
Example of combined denoise and sharpening. Denoise broadens, sharpening reduces S/N. Together, the final result is both resolved and has high S/N.

For mobility resolution near the practical maximum of our gating system, multiplexing typically delivers about 2 orders of magnitude increase in sensitivity:

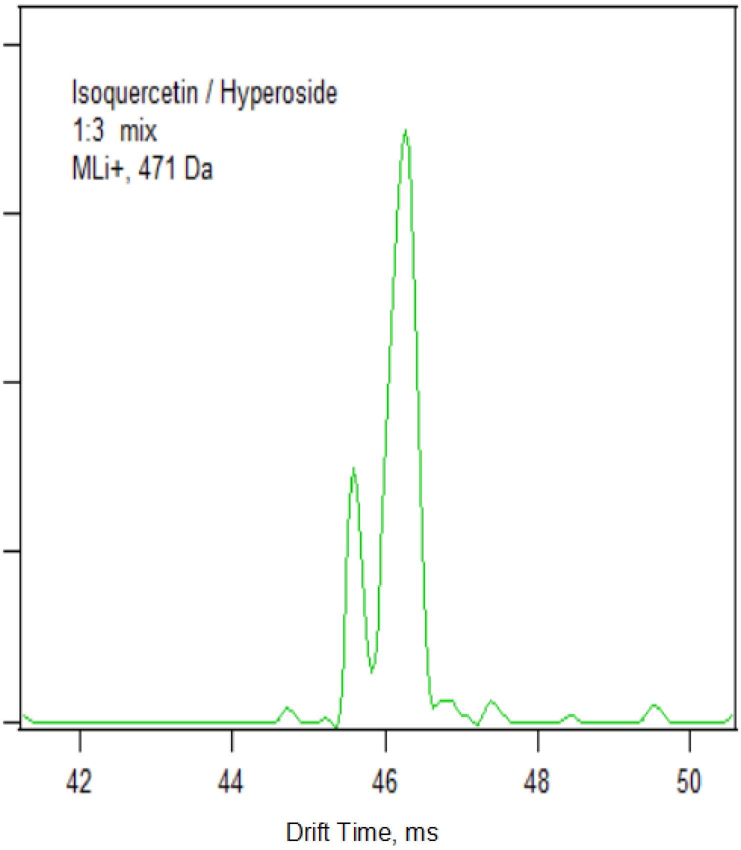


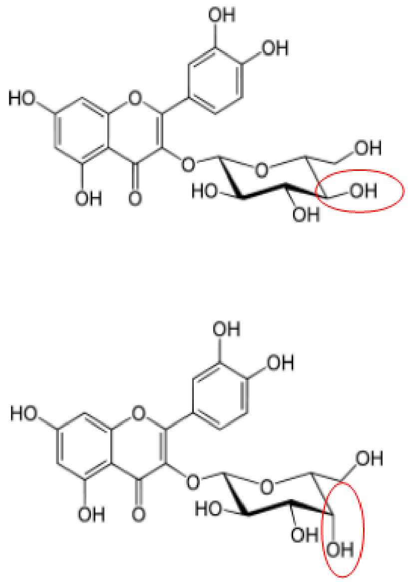
Cyctochrome C mass spectra measured in multiplexed (upper) and conventional modes.

Using postprocessing and varying instrumental conditions, it is possible, to trade sensitivity for resolution over a significant range:



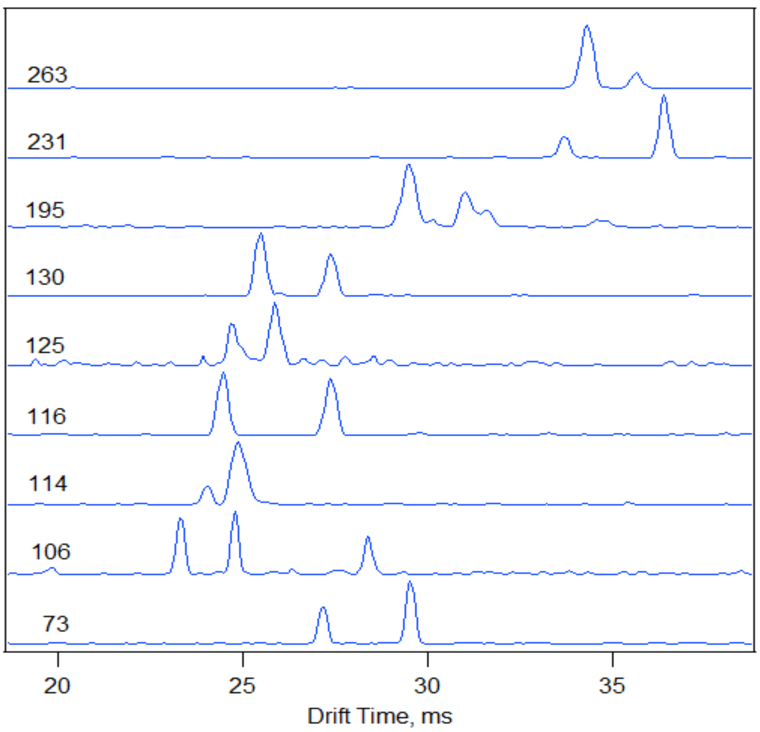
This allows successful separation of difficult mixtures, such as these diastereomers:





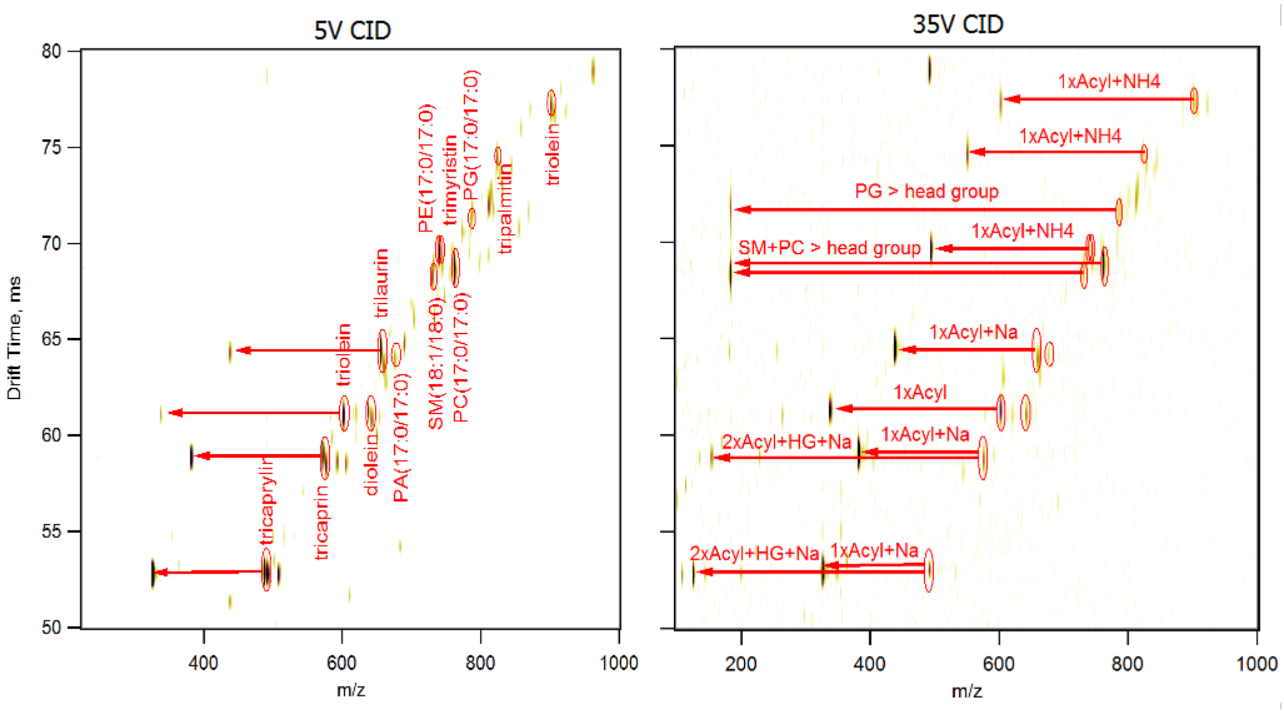
Samples courtesy of Prof. Wolfender, Universtiy of Geneva

Complex mixtures can be analyzed simultaneously. The next image shows substances detected in scotch whisky headspace vapor:



Whisky headspace IMS traces. The nominal masses are indicated. Each peak in each trace represents an isomer or isobar which was not resolvable in the mass spectrum.

Ions can be fragmented after the drift tube by changing voltages in the atmospheric pressure interface. Parent and daughter ions therefore have the same drift times. Since the drift times increase with m/z, the fragment ion region is always free of interferences, making assignments extremely straightforward. The next example shows a mixture of lipids.



Lipid mixture IMS-TOF diagram at low post-drift collision energy (left) and high collision energy (right). Relatively few fragments are observed at 5V, while characteristic side chain an headgroup fragments are abundant at 35 V. Due to drift time separation, assignments are easy and unique.

<u>Conclusions</u>

Hadamard multiplexing suffers from disadvantages if the data is not ideal. Pre-transform data treatment is able to minimize these drawbacks. Examples of successful multiplexed IMS-TOF measurements were shown, ranging from lipids to diastereomers to proteins. The characteristics of the Tofwerk IMS-TOF are summarized below.

MS resolution=4000 - 7000
IMS resolution= 150 raw, 250 postprocessed
Post-IMS CID
Room temperature to ~200° C
Pressure=sub ambient to 1.4 Bar

Finally, the utility of simultaneous high resolution and high sensitivity is qualitatively illustrated with an IMS-TOF plot of a whisky, in which hundreds of features are found: