ZipChip

What they are and how they work

WHAT IT IS

The ZipChip® system is a microfluidic device that integrates capillary electrophoresis (CE) with electrospray ionization. The system employs zone electrophoresis, where analytes are injected as a small band and are then separated in an electric field. The analytes separate due to differences in electrophoretic mobility, which is simply a function of the charge and size of the analyte. Separation occurs freely in solution without the use of a gel matrix or ampholyte mixture. ZipChip processes a wide range of analytes from small molecules to intact proteins. In just minutes biological samples are quickly separated, providing sharp well-defined peaks backed by the power of MS analysis.

Each chip is a single piece of glass, about the same size and shape as a common microscope slide. These chips are fabricated using photolithography and wet chemical etching to produce microfluidic channels in a glass substrate. A schematic diagram of a ZipChip is shown in Figure 1. The design and operation of the chip can be thought of as the seamless integration of 3 major functional elements: sample injection, electrophoretic separation, and electrospray ionization (ESI). Sample injections utilize the cross feature shown in the top of Figure 1; the separation occurs in the longer, serpentine channel; and ESI occurs at the lower right corner of the device. Integration of these components on a single microfluidic chip eliminates junctions, connectors and dead volume between individual functions. These limitations cause increased analysis time and decreased separation resolution in other liquid separation approaches.

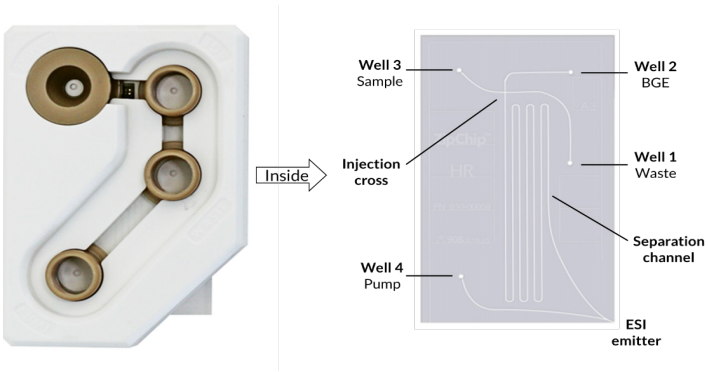

Figure 1: Image of a chip in its cartridge (left) and the schematic of the microfluidic channels of the chip (right). The glass chips are housed in a plastic cartridge to create fluid wells and for ease of handling.

HOW IT WORKS

Injection: ZipChip uses a novel sample injection method that utilizes pressure-driven flow to precisely deliver aliquots of sample into the separation channel with no injection bias. Figure 2 shows a schematic that describes this injection method. This schematic represents a close up look at the injection cross labeled in Figure 1. The sample to be injected is placed in the sample reservoir labeled "Well 3", in Figure 1. The background electrolyte (BGE) is placed in the reservoir labeled "Well 2". To introduce sample into the separation channel, head pressure is applied to Wells 2 and 3, for a period of time called the loading step. The duration of the loading step is computer-controlled to deliver precise amounts of nanoliter sample volumes. A brief clearing step utilizing the flow of clean BGE from Well 2 leaves a cleanly defined plug of sample in the separation channel. At this point voltage is applied to perform the electrophoretic separation.

Separation: Immediately following the sample injection sequence, voltage is applied to Wells 2 and 4. These voltages dictate the electrical field strength for the CE separation and the ESI voltage. Analytes migrate down the separation channel in the electric field toward the ESI orifice where they are then ionized and introduced into the mass spectrometer.

ESI: The bulk flow necessary to support ESI is provided by fluid flow from Well 4 (Pump) to the ESI corner. Typical ESI flow rates for ZipChip are about 150 nL/min to achieve

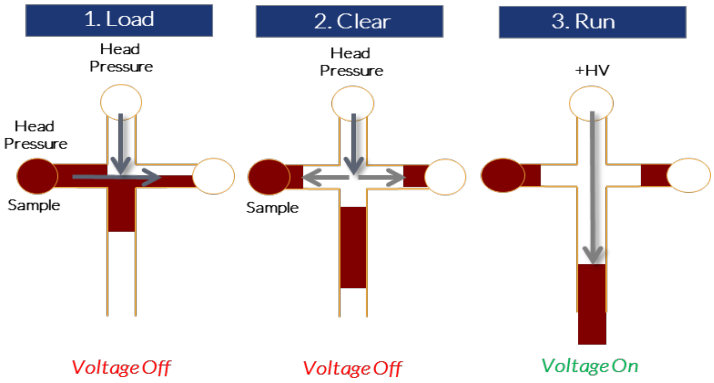

Figure 2: The pressure-driven injection scheme.

Figure 4: The ZipChip interface and autosampler installed on a Thermo Scientific mass spectrometer.

the best combination of sensitivity and robustness. The ESI emitter of the chip is formed directly on the corner of the microfluidic device. This corner is diced so that the terminal end of the separation channel is centered on this corner. Figure 3 shows an image of a chip spraying towards the inlet of a mass spectrometer. At such low flow rates the ESI plume is not visible with normal lighting, so a green diode laser is used for illumination. The opening of the microfluidic channel is more like a wide, shallow slit than a typical cylindrical emitter. The depth of the channel is the critical dimension defining performance that is very similar to that of a 10µm fused silica emitter.

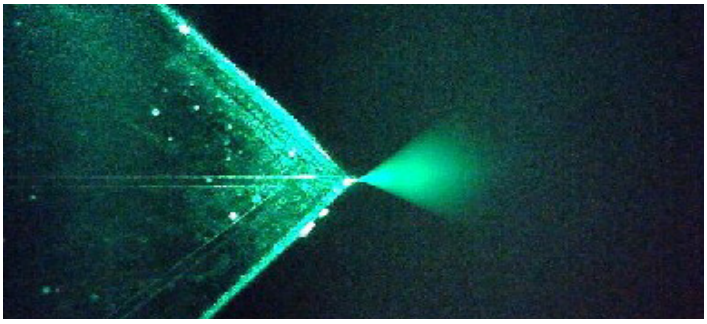

Figure 3. Image taken from the ZipChip optical system showing the ESI plume illuminated with a green laser.

ZipChip Platform: The ZipChip system consists of the interface, an autosampler, and control software. Figure 4 shows the interface and autosampler installed on a Thermo Scientific orbitrap mass spectrometer. The interface uses standard mounting to attach to conventional mass spectrometers and simplifies the analysis of samples with ZipChip. All of the valving and electrical components needed to perform separations are contained in the interface box and no adjustment of the chip position or ESI voltage is ever necessary. The autosampler sits to the side of the interface and is connected to it via two transfer tubes. With the autosampler, fluids can be delivered to the chip for chip priming, well rinsing, and BGE refreshes as well as sample delivery. The software automates system and chip priming with just the click of a button and facilitates data collection for either single analysis runs or longer sequence ques. Users need only define a few method parameters, like injection volume and separation field strength. The ZipChip system simplifies CE-MS analysis with setup that is simple and fast so users can focus on data collection and interpretation.

Zip Chip Benefits:

- Quick and easy system setup
- Fast Analysis
- Analyze a wide Range of Analytes – small molecules and amino acids, peptides, intact proteins, antibodies and antibody drug conjugates (ADCs)
- Analyze a wide Range of Matrices – Cell lysates, growth media, plasma, blood, urine, biopharma end-product etc.
- Minimal sample Prep – dilute and shoot for many applications

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