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The PicoChip™: A Robust, Easy-to-use Solution for Nanospray Enabled LC-MS

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Introduction

Nanospray ionization, in combination with nanobore liquid chromatography tandem mass spectrometry (nLC-MS/MS), has been the method of choice for protein/peptide biomarker discovery in the life sciences. These qualitative methods have typically featured very small (75 to 100 µm) inside diameter (ID) columns running at flow rates typically between 300 to 1,000 nL/min. Columns are typically either self-made by the analyst or commercially available in the form of 360 um outside diameter (OD) fused-silica tubing. Given the small ID and OD of the tubing, and the low column volume, there are numerous challenges in the implementation of these tools for successful LC-MS analysis. The traditional laboratory solution has been a heavy investment in the education and skill set of the analyst. Key to success are critical skills in making "perfect" connections, tuning the nanoelectrospray source, and deep experience in system troubleshooting. Injection-to-injection cycle times are typically long (> 30 minutes), so time lost to instrumental difficulties carries a high economic cost. Given the system and plumbing complexity, the ability to automate these processes has been limited. The growing need for analysis in the areas of protein quantification and biomarker validation places new demands on robustness, ease-of-use, and suitability for automation.

New Objective has developed an integrated system for nanobore LC-MS that alleviates the need for specialized expertise in nano-scale separations. The novel design of a "PicoChip" solution combines the functionality of the nanospray emitter, nanobore separation column, high-voltage contact, and autosampler transfer line into a single consumable device. The comfortable design of the consumable package makes it exceptionally easy to handle and eliminates the risk of emitter or column breakage. A new high-voltage contact with every column change means consistent and stable spray ionization. Pre-assembly and testing of the assembled device in a production setting ensures results in the customer's lab.

Format

PicoChip columns are available with a variety of column ID and tip opening geometries to accommodate any target flow rate. Like the PicoFrit® column, the PicoChip can be packed with any of our in-house chemistries, as well as custom packed.

- Column ID: 50 µm - 150 µm
- Tip opening: 10 µm - 30 µm (depending on column ID)
- Chromatography media: Can be packed with nearly any material available
- Bed length: Up to 100 mm length

Zero-dead-volume liquid-junction high-voltage connection

+

High-performance PicoFrit column

+

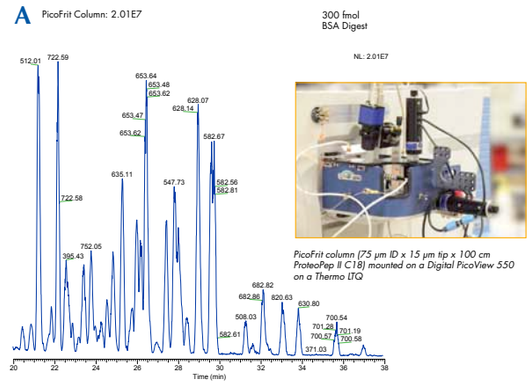
Tool-free set-up and operation

=

PicoChip column

Proven technologies are integrated into the PicoChip design: PicoClear zero-dead-volume high- voltage connection, high-performance of the PicoFrit column, tool-free set-up and operation.

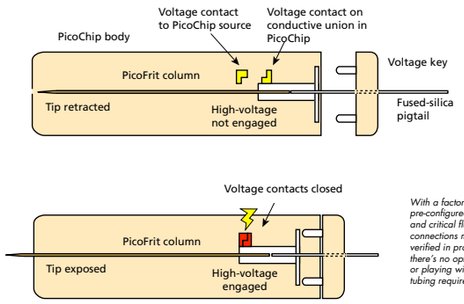
High-Performance



PicoFrit column (75 µm ID x 15 µm tip x 100 cm ProteoPep II C18) mounted on a Digital PicoView 550 on a Thermo LTQ

PicoChip column (75 µm ID x 15 µm tip x 100 cm ProteoPep II C18) on a Thermo LTQ

Comparison of PicoFrit column to PicoChip. The integrated format retains the high-performance capability of the PicoFrit column, but is far easier to use. Inconsistencies inherently introduced in conventional plumbing by different end-users during installation is virtually eliminated.



With a factory pre-configured stage and critical fluidic connections made and verified in production, there's no optimization or playing with capillary tubing required.

Triple-PicoChip System "The PicoSlide" mounted onto Thermo LTQ. Quad-PicoChip sources will also be available.

What is It?

PicoChip combines industry-proven technologies in a factory-configured format. The complex assembly of tubing, voltage connectors, columns and emitters is all done by production certified technicians to ensure consistent, reliable performance.

Advanced Applications

Adding automation and multiple PicoChip positions provide advanced and increased functionality. Three- and four-position PicoChip sources increase throughput and duty-cycle from 40% to <95%.

Conclusions

- Change-over can be accomplished by an inexperienced user in a matter of minutes.
- The interior design complexity of the PicoChip means that the nanospray source itself is exceptionally simple and low-cost.
- The PicoChip design is readily adapted to front-end automation. A newly developed four-channel source enables a facile nLC-MS/MS workflow and improves instrument duty cycle from 40% for a single channel system to greater than 95%.
- The enclosure of the nanobore column in the PicoChip housing protects the emitter from damage until ready for use. It also isolates the column from changes in ambient temperature and enables further temperature control such as column heating.

Future Work

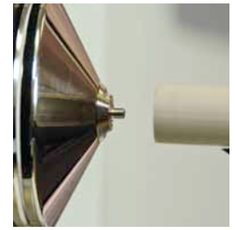
- Extended column bed lengths
- Built-in column heating
- Trap column integration

How does it work?

Attach PicoChip source

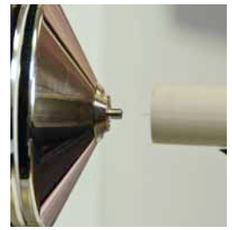
Place PicoChip onto magnetic stage

Connect feed line



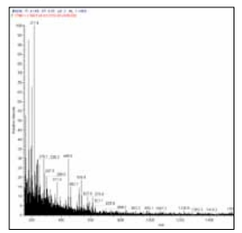
Tip is retracted until...

Activation key is inserted



Tip is exposed and voltage circuit completed

Close interlock



Collect data