Dual channel microflow LC-MS: investigation of high sensitivity and high throughput

ABSTRACT

A dual gradient microflow liquid chromatography (LC-MS) system has been coupled with a triple quadrupole mass spectrometer (MS) in a high-sensitivity mode to achieve the performance of thin-film systems while allowing high-throughput separations. The system uses two separate gradient solvents with fixed and variable gradients to achieve separation efficiencies exceeding a single gradient system. The columns share a single column oven which is directly coupled to a stream selector valve mounted immediately at the electrospray orifice. Microfluidic injectors are used to provide fast dispensing. The use of low volume solvent mixing coupled with the reduction of solvent consumption results in reduced solvent consumption for improved sensitivity. Multiple reaction monitoring (MRM) transitions for triazines have been configured to allow multiplexed samples to be run. Initial experiments show an ability to gain nearly 2x in throughput over a single channel experiment, while maintaining good peak shapes and performance. In the examples below, the separations were conducted using 4 minute methods composed of a 1 minute gradient at the beginning of the 4 minute gradient. The column selector valve directly at the MS source, high performance microflow separations are maintained while nearly doubling the throughput of the instrumentation system overhead (both from software and initialization) nearly the full 2x improvement in throughput was demonstrated.

INTRODUCTION

Microfluidic LC-MS has proven to be a valuable tool for improving sensitivity while monitoring or optimizing throughput for high-sensitivity and high-throughput applications, including in drug discovery and development. The addition of a dual channel system has been shown to provide higher sensitivity while maintaining the critical performance of low-sensitivity microfluidic separations while dramatically increasing the throughput of the instrument. A high throughput dual channel LC system with a high-speed solvent pump that preserves the critical performance of low-sensitivity microfluidic separations while dramatically increasing the throughput of the instrument. Reduced solvent consumption for improved sensitivity. Multiple reaction monitoring (MRM) transitions for triazines have been configured to allow multiplexed samples to be run. Initial experiments show an ability to gain nearly 2x in throughput over a single channel experiment, while maintaining good peak shapes and performance. In the examples below, the separations were conducted using 4 minute methods composed of a 1 minute gradient at the beginning of the 4 minute gradient. The column selector valve directly at the MS source, high performance microflow separations are maintained while nearly doubling the throughput of the instrumentation system overhead (both from software and initialization) nearly the full 2x improvement in throughput was demonstrated.

MATERIALS AND METHODS

Two microflow gradient pumps (SCIEX Model 200) have been coupled with a custom flow controller and software configuration that allows coordination of the pumping from channel along with the required solvent systems. The pumping system is combined with a high-sensitivity quadrupole (Q1) and an electrospray (ESI) high-speed washing; CTC Analytics) equipped with two, independent, small port injection valves and separation columns. At an average time of just over 2 minutes per chromatogram (using a 4 minute method), the 14 consecutive chromatograms of triazines conducted in just under 30 minutes. Chromatograms are synchronized between the two columns is directed through a stream selection valve to the MS source. Through careful control of the injection and separation columns. The effluent from the stream selector valve is directed at the Q1 MS source to allow fast and low dispersion stream selection. The flow path of the stream selector valve is configured with a microfluidic valve (IDEX) in the TurboSource®

RESULTS

Microfluidic chromatography of both small molecule triazines and peptide (galactosidases and protein digest) combinations is demonstrated in the current configuration. The dual systems/pumps allow gradient separations of small molecule and large molecule combinations. The 2 min gradient is used in two independent, high flow rate (75uL/min). Note that the intensities of the two samples is considerably different. To the right is shown a blow up of one pair of sequential chromatograms. A high throughput implementation of micro LC-MS has been demonstrated using a dual channel LC-MS system with two independent gradient pumping systems, sample injection valves, and separation columns. The effluent of the two columns is directed through a stream selection valve to the MS source. Through careful control of sample injection and separation, the ability of both the column oven and the stream selection valve directly to the MS source high performance microflow separations are maintained while nearly doubling the throughput of the instrument. Such a approach provides the benefit of microLC/MS sensitivity while maintaining high flow rate (100uL/min). Reduced solvent consumption, and reduced solvent load to the MS source in high-throughput, high-performance workflow.

CONCLUSIONS

In the examples below, the separations were conducted using a 4 minute methods composed of a 1 minute gradient at the beginning of the 4 minute gradient. The column selector valve directly at the MS source, high performance microflow separations are maintained while nearly doubling the throughput of the instrument. Two microflow gradient pumps (SCIEX Model 200) have been coupled with a custom flow controller and software configuration that allows coordination of the pumping from channel along with the required solvent systems. The pumping system is combined with a high-sensitivity quadrupole (Q1) and an electrospray (ESI) high-speed washing; CTC Analytics) equipped with two, independent, small port injection valves and separation columns. Two microflow gradient pumping systems (SCIEX microLC 200) have been coupled in a custom hardware and software configuration that allows coordination of the pumping from channel along with the required solvent systems.

TRADEMARKS/LICENSING

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