Triggering MALDI Time-of-Flight Mass Spectrometers with the *FASTFLIGHT*™ Digital Signal Averager

Although the ***FASTFLIGHT*** Digital Signal Averager is optimized for handling the ultra-high data rates encountered when an Electrospray Time-of-Flight Mass Spectrometer (ES TOF-MS) analyzes the output of a chromatograph, ***FASTFLIGHT*** can also enable higher data acquisition rates with most modern MALDI Time-of-Flight Mass Spectrometers (MALDI TOF-MS).

FASTFLIGHT uses a unique scheme* to minimize sampling jitter. This scheme also provides an economical means of achieving an effective 2-GSa/s sampling rate without any loss of the ion data that controls mass accuracy and sensitivity.[1,2] This performance is realized by synchronizing the trigger for the mass spectrometer with the 500-MHz sampling clock in the ***FASTFLIGHT***. In other words, ***FASTFLIGHT*** triggers the extraction pulse for the ion source in the mass spectrometer.

For ES TOF-MS this function is trivial to implement, because the acceleration of the ions at the source is initiated by an abrupt application of the accelerating voltage to the extraction electrode (sometimes referred to as the acceleration electrode, or the pusher electrode). In its normal operation, ***FASTFLIGHT*** delivers a trigger output pulse at the end of each scan. This pulse drives the electronics that abruptly applies the acceleration voltage to the extraction electrode. As a result, the acceleration of the ions is synchronized with the ***FASTFLIGHT*** sampling clock, and the synchronization jitter is less than 50 ps (FWHM).

Normally, ***FASTFLIGHT*** determines the extraction repetition rate by delivering the next Trigger pulse within 1 µs of the end of the previous scan. However, the Trigger Output can be held off until the mass spectrometer is ready for it by holding the Trigger Enable Input in the "disabled" state. Within 200 ns after returning the Trigger Enable Input to the "enabled" state, ***FASTFLIGHT*** delivers the next Trigger Output. Because ***FASTFLIGHT*** must synchronize the Trigger Output pulse with the sampling clock, there is a 34-ns jitter in this 200-ns delay. This jitter is of no consequence for an ES TOF-MS. Figure 1 shows the typical connections for the ES TOF-MS.

*U.S. Patent No. 6,072,388.

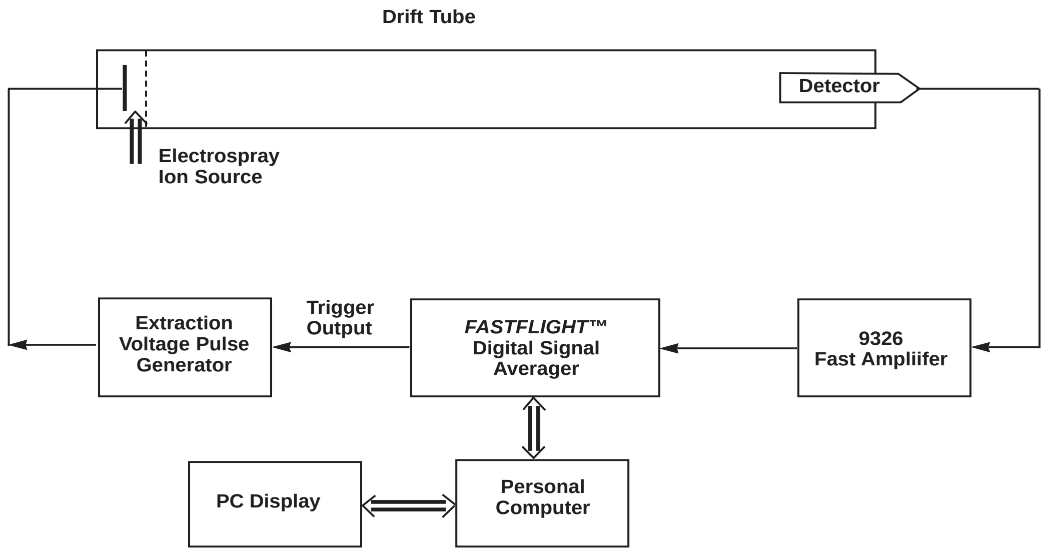

Figure 1. A Simplified Representation of an Electrospray TOF-MS Interfaced to the *FASTFLIGHT* Digital Signal Averager.

The situation for MALDI TOF-MS is more complicated, because the Laser pulse causes the desorption of the ions. Typically, the Laser cannot be triggered from an external source, or cannot be triggered with adequately low jitter. Fortunately, most modern MALDI TOF-MS utilize delayed extraction to improve the mass resolution.[3] Delayed extraction minimizes the loss of resolution caused by the ions exhibiting a range of velocities when they are desorbed from the sample. The typical arrangement is illustrated in Figure 2. The desired acceleration voltage is established between the sample holder and the grid at the entrance to the field-free drift tube. The delayed-extraction grid is located between the sample holder and the drift-tube entrance grid. By holding the delayed extraction grid at the same voltage as the sample holder, the ions experience no accelerating field when initially desorbed by the laser pulse. After a suitable time delay, the delayed extraction grid is abruptly changed to the appropriate voltage and the ions are accelerated into the drift tube. The extraction delay is typically in the range of 0.5 to 20 microseconds, and is adjusted to optimize the mass resolution. Delayed extraction improves the resolution by allowing time for the higher-velocity ions to move further towards the drift tube than the lower-velocity ions do. When the delayed extraction voltage is finally turned on, the lower-velocity ions experience a greater accelerating voltage than the higher-velocity ions do. By choosing the right delay time, the lower-velocity ions catch up to the higher-velocity ions of the same mass by the time the ions reach the detector at the end of the drift tube. This reduces the spread in arrival times, and improves the mass resolution.

As shown in Figure 2, the output pulse from the Laser drives the time delay generator, and the output of the delay generator initiates the delayed extraction pulse. ***FASTFLIGHT*** can be inserted into the system by breaking the dashed line between the delay generator and the input to the extraction pulse generator. The delay generator output is fed to the Trigger Enable Input on the ***FASTFLIGHT***, and the Trigger Output from the ***FASTFLIGHT*** connects to the input of the extraction pulse generator. This scheme synchronizes the delayed extraction pulse to the ***FASTFLIGHT*** sampling clock with less than 50 ps jitter, and permits a sequence of 0.5-ns Trigger-to-clock offsets to achieve 0.5-ns sampling resolution. The 34-ns jitter between the Trigger Enable Input and the Trigger Output will make a negligible contribution to the mass resolution, provided

$$\Delta\tau/\tau << \Delta v_o/v_o$$

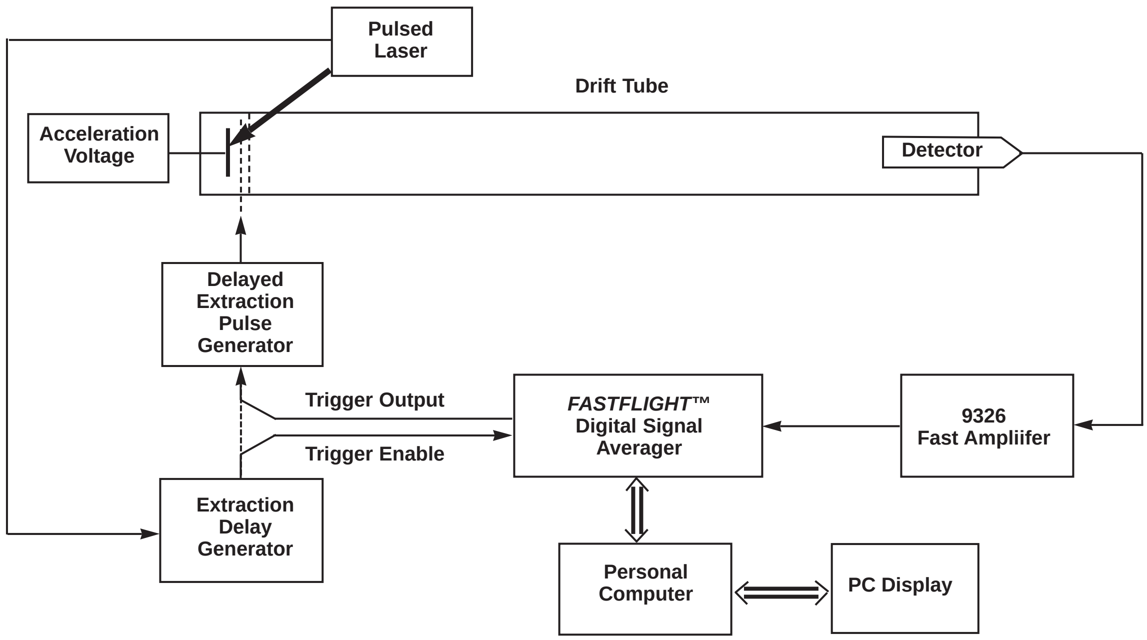

Figure 2. A Simplified Illustration of a MALDI TOF-MS with a Delayed Extraction Grid Interfaced to the *FASTFLIGHT* Digital Signal Averager. In this schematic representation, the sample holder is operated at the accelerating voltage, and the delayed extraction grid is located between the sample holder and the grounded grid at the entrance to the drift tube. The laser flash desorbs and ionizes the ions at the sample holder. The delayed extraction grid resides at the accelerating voltage until pulsed to a lower voltage by the delayed extraction pulse generator. The dashed line is the normal connection. Solid lines show the connections necessary for the ***FASTFLIGHT*** interface.

where $\Delta\tau = 34$ ns is the jitter in the extraction delay caused by ***FASTFLIGHT,*** τ is the average value of the extraction delay, v_o is the average value of the initial ion velocity immediately following desorption and ionization, and Δv_o is the width of the initial velocity distribution (FWHM). This condition is easily fulfilled, because normally $\Delta v_o/v_o \sim 1$ and typically $\tau >> 100$ ns.

With ***FASTFLIGHT*** incorporated as shown in Figure 2, the Laser pulse period controls the repetition rate. Most older MALDI TOF-MS use a Laser repetition rate in the range of 10 to 20 Hz, because of limitations in the Laser. These spectrometers typically use digital sampling oscilloscopes to read out the detected signal record after each Laser pulse. Averaging multiple records improves the signal-to-noise ratio, and the averaging is usually performed in a supporting computer. Both the slow readout speed for the oscilloscope and the averaging in software limit the repetition rate.

FASTFLIGHT enables drastically higher repetition rates, because it performs averaging in its hardware memory as each record is acquired. The dead times at the end of each scan and at the end of each averaged spectrum are less than 1 µs. This means that ***FASTFLIGHT*** can process scans having a 99-µs length at Laser repetition rates up to 10 kHz, and can stream full-length, averaged spectra to hard disk at a sustained rate of 10 spectra per second. This permits Laser repetition rates in MALDI TOF-MS to be increased more than 100-fold into the kHz range. To prevent rapid sample burn-off, the Laser intensity in each pulse can be reduced,[4] and/or the sample can be scanned to distribute the Laser pulses over a wide area of the sample. The latter technique provides a more representative measurement, and a more efficient use of the sample.

References

[1] ***FASTFLIGHT*** Brochure, ORTEC, Sept. 2000.

[2] ***FASTFLIGHT*** Instruction Manual, ORTEC, Sept. 2000.

[3] Marvin Vestal and Peter Juhasz, *Resolution and Mass Accuracy in Matrix-Assisted Laser Desorption Ionization Time-of-Flight*, Journal of American Society for Mass Spectrometry, 1998, 9, 892–911.

[4] G. Westmacott, W. Ens, A.N. Krutchinsky, and K.G. Standing, *Measurements of Ion Yield Vs. Laser Fluence Using Orthogonal-Injection MALDI/TOF With Collisional Cooling and Single-Ion Counting*, Proceedings of the 46th ASMS Conference on Mass Spectrometry and Allied Topics, May 31–June 4, 1998, Orlando, Florida, 937.

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