

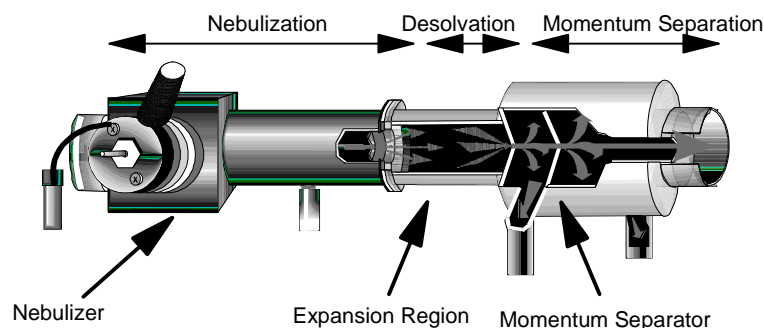
Waters® Integrity® LC/MS System Advancements in Particle Beam (PB) Technology Featuring Waters ThermaBeam™ LC/MS Interface

Waters has improved upon existing particle beam interface technology to increase sensitivity and handle the full range of HPLC conditions. As a result, ThermaBeam, an advanced, patented PB interface featured in the Integrity LC/MS System, offers many advantages over traditional PB interfaces.

Coupling a liquid chromatograph to a mass spectrometer has fostered much research regarding interface design and dynamics. Difficulties arise when interfacing a liquid flow to the high vacuum and high temperatures of a mass spectrometer ion source. The analyte, which is dissolved in the flowing mobile phase, must be desolvated, vaporized and ionized as it passes through regions of increasing vacuum and temperature. This process must also be accomplished with minimal sample loss and degradation.

The particle beam interface, which was developed circa 1984, coupled a wide range of LC separations to an Electron Ionization (EI) mass spec source that produces a unique fragmentation pattern (i.e. "fingerprint") for each analyte. In order to discuss some of the improvements over traditional PB technologies, it is important to first understand how the PB interface works. Transfer of neutral analytes from the HPLC to the EI source is accomplished solely by aerodynamic means. There are three stages to this process: aerosol formation (nebulization), desolvation and momentum separation as detailed in below:

Figure 1: Cut-Away View of One Example of a Particle Beam Interface



Particle Beam Theory: The nebulizer disperses the mobile phase into a fine mist of droplets. The resulting aerosol then passes through a desolvation chamber where the volatile solvent evaporates. The analyte then condenses to form small, solid particles. The resulting particles, solvent and helium carrier are drawn into a pumped chamber causing a rapid expansion. The larger solute particles will gain momentum due to the expansion while the low-momentum solvent and helium will undergo radial expansion. The solute particles will continue through a small orifice in a linear "beam" leaving the lighter components to be pumped away. The high-velocity particle beam will then pass into the EI ion source of the mass spectrometer. The heated walls of the MS source provide thermal energy for flash vaporization followed by electron ionization of the analyte in the gas phase.

Figure 2 below illustrates a traditional PB interface. Following aerosol formation from the HPLC effluent, the aerosol is desolvated at near atmospheric pressure and at ambient temperature. A two-stage momentum separator is used to remove solvent vapor and helium from the particle beam. Transport efficiency is poor. Note that in this

design nebulization occurs at ambient temperature, rather than utilizing any heat in this process. This interface also relies on numerous adjustments, such as the amount of capillary extension beyond the end of the nebulizer tube, in order to optimize performance. Other disadvantages include an inability to handle high HPLC flow rates, high aqueous mobile phases, and marked differences in performance at the extreme ends of a gradient separation.

Figure 2: Traditional Particle Beam Interface

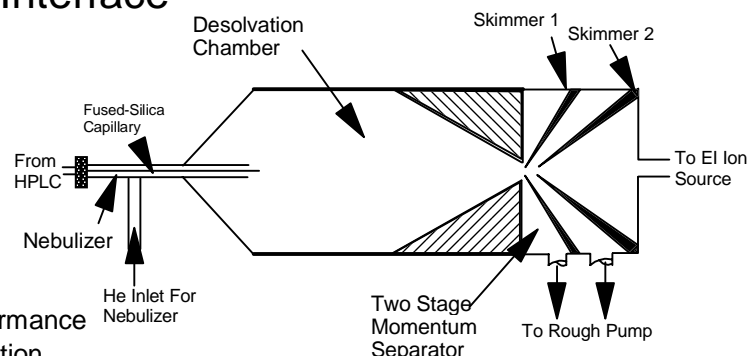
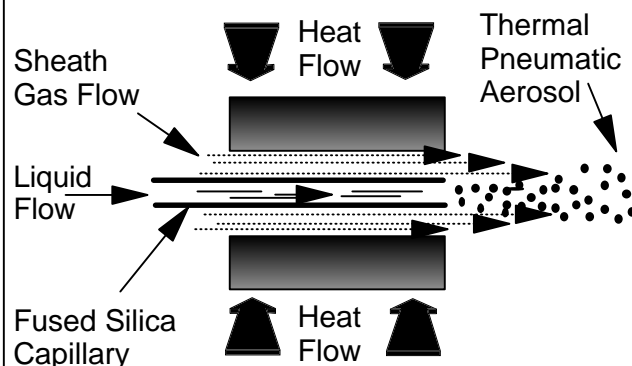


Figure 3: Highly Efficient, Thermal Concentric Nebulizer



Waters' unique thermal concentric nebulizer design, which uses both heat and concentric sheath gas (helium) for aerosol formation, is shown in Figure 3. A flow of helium around the fused-silica capillary transfers heat from the heated nebulizer to the HPLC flow through the capillary thus creating a very fine aerosol of uniform droplet size. The result is increased transfer efficiency of sample through the interface to the ion source. The expansion region in the Waters ThermaBeam interface has also been modified. It is shorter than in older designs, thus reducing the distance required in the expansion region, which decreases the dispersion of the particle beam.

Benefits of Waters ThermaBeam Technology over Traditional PB Interfaces

- * Decreased dispersion during desolvation results in increased detection sensitivity due to reduced sample loss, minimal band broadening and better peak symmetry
- * Greater efficiency of solvent evaporation allows for wider range of HPLC operating conditions (e.g., flow rates up to 1ml/min with up to 100% aqueous eluents)
- * Due to improved aerosol formation, less helium gas is consumed thus decreasing cost of operation
- * Improved ruggedness of the interface requires less attention and maintenance by the user

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