Abstract

Mass spectrometry (MS) is one of the highly sensitive and highly selective analytical methods for biochemical samples including DNAs, peptides, and proteins. Presently, MS plays a key role in the health and life sciences research such as the drug discovery, biomarker measurements for medical diagnosis, and proteomics. On the other hand, miniaturized analytical devices based on the lab-on-a-chip technologies also contribute to the progress of the life science researches.

In this work, the key components for the on-chip mass spectrometry including a vacuum pump, an ionization source, and an ion lens for time-of-flight (TOF) mass analysis were miniaturized toward the highly sensitive detection of versatile biomarkers. Conventionally, MS requires a high vacuum at about 10^{-4} Pa. However, the conceptual step to significantly miniaturize the mass spectrometer into a microchip is to operate it in a low vacuum using microfluidic channel. First, the vacuum generation method using the gas-liquid phase transition on a chip was studied. Next, the pulse-heating ionization source developed herein enables the ionization of a peptide and a protein in the presence of 2,5-dihydroxybenzoic acid as a matrix without laser, high voltage, or ambient gases. TOF mass spectrometry was performed with the pulse-heating ionization chip and a relatively small TOF mass analyzer. To realize highly sensitive analysis without abundant fragment ions, the effects of matrix and solvent for sample formation on the pulse-heating ionization was investigated. The combination of highly volatile matrix like 2,5-dihydroxyacetophenone and thin-layer method with highly volatile solvent like acetone was effective to reduce fragment ions as compared conventional matrix assisted laser desorption/ionization (MALDI) MS. Analyzed sample amount by the single pulse-heating ionization was briefly estimated about 750 amol. The miniaturized ion lens composed of a series of micro electrodes for on-chip TOF mass analyzer was integrated with the miniaturized ionization source. Ion motion in the miniaturized TOF mass analyzer was studied by numerical simulation of the ion trajectory controlled by the electric fields with micro electrodes. Finally, on-chip TOF mass spectrometry of bovine serum albumin as a protein analyte was firstly reported using the pulse-heating ionization and the 5 mm length of TOF mass analyzer with the electrostatic ion lens.

Keywords: Lab on a chip, Mass spectrometry, Miniaturized ionization source, On-chip ion lens, On-chip vacuum pump