# DESIGN AND OPTIMIZATION OF AN ALTERNATIVE HIGH EFFICIENCY SAMPLE INTRODUCTION SYSTEM FOR SINGLE PARTICLE ICP-MS ANALYSIS

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## Abstract
In this study we present the development process of an alternative sample introduction system for inductively coupled plasma mass spectrometers (ICP-MS) with the aim of improving the efficiency and capabilities of single particle ICP-MS measurements. The system consists of a high efficiency pneumatic nebulizer, and a low memory effect, high transport efficiency on-axis spray chamber which are currently under manufacturing utilizing a high resolution, multijet (MJP) 3D printer. Both part underwent several fluid dynamic simulations to debunk potential design flaws and to assess their optimal operating conditions before their production.

## Introduction
The relatively novel technique of single particle inductively coupled plasma mass spectrometry (spICP-MS) is a powerful tool for the characterization of nanoparticle (NP) or cell dispersions. This technique can provide information regarding elemental or isotope composition of individual particles, as well as the size distribution and particle number concentration (PNC) of their dispersions with great statistical relevance. However, the standard ICP-MS sample introduction system – which usually consists of a concentric nebulizer and a Scott-type double-path spray chamber – hardly exceeds 5% transport efficiency and shows significant memory effects which makes its sample consumption suboptimally high for efficient single particle or single cell analysis [1,2]. It has been shown that by utilizing low sample consumption, high transport efficiency nebulizers which facilitate monodisperse droplet formation, coupled with low volume spray chambers, the performance and efficiency of the spICP-MS technique can be further enhanced. The higher sensitivity, lower limit of detections, and decreased sample consumption these accessories provide, come in handy considering the ever-increasing demand for determining the above mentioned characteristics of cell or NP dispersions using lower sample volumes and concentrations [3,4].
Also, as 3D printing technologies advanced in the past years, their minimum feature size (MFS) reached the few tens of microns regime, which makes them a great tool for producing parts which require high spatial resolution and precision such as nozzles and microchannels [5].

## Experimental
The connectors of the nebulizer and the spray chamber was designed to be compatible with our Agilent 7700X ICP-MS (Agilent Technologies, Santa Clara, CA, USA) instrument. The 3D models of the nebulizer and the spray chamber was made utilizing AutoCAD 2022 software (Autodesk Inc. San Rafael, CA, USA). The fluid dynamic simulations were carried out using COMSOL Multiphysics software (COMSOL Inc. Burlington, MA, USA). The production of the parts was done by utilizing ProJet MJP 3600 high precision 3D printer equipped with VisiJet M3 resin (3D Systems, Rock Hill, SC, USA).

**Results and discussion**

The operational principle and geometry of the nebulizer and the spray chamber was chosen to fulfil three requirements with no or relatively minor changes on the general design. (1) Their geometry (connections, size), and supplies (gas flows, liquid pumps) needed for operation should be compatible with our ICP-MS instrument. (2) Their geometry is relatively simple, does not include such small details (except the nozzle head, which inevitably on the edge of the capabilities of 3D printing) that are too challenging for the used 3D printing technique. (3) According to the literature, their efficiency is the reasonably high.

With those in mind, for the nebulizer we decided on a concentric pneumatic nebulizer. The changes we made compared for the general designs were the reduction of the inner volume and nozzle bore size as much as the design itself and the production technology allowed. As for the spray chamber, an on-axis type, low volume spray chamber with sheath gas flow was chosen, on which minor adjustments were made, decreasing its inner volume. Also, both the nebulizer and the spray chamber got equipped with connectors that are compatible with the tubing of the original nebulizer and spray chamber of the instrument. They are meant to be operated using only argon gas flows so that the plasma of the instrument remains relatively undisturbed. The application of the two chosen designs together was already reported in the literature a few times, they showed reasonably high, more than once near 100% transport efficiencies [2,6].

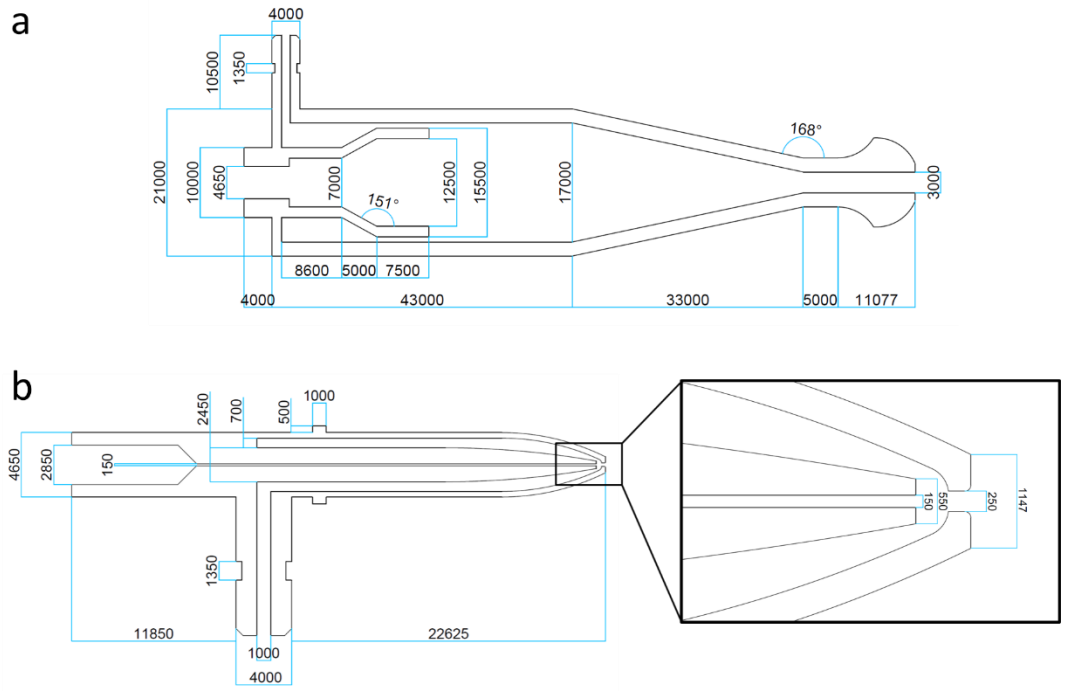


Figure 1. The final designs of the a) on-axis spray chamber b) concentric nebulizer. Values are given in µm units.

The final designs are shown on Fig. 1, the inner volume of the spray chamber accessible for the produced aerosol and the dead volume for the sample in the nebulizer are ca. 9.2 mL and 0.51 µL respectively. In the design process, several fluid dynamic simulations were carried out using COMSOL Multiphysics software. Firstly, the pressure conditions were assessed inside of the two components. In case of both designs, we concluded that they are capable enduring the inside pressure in a wide range of introduced gas flow values, thanks to the axial symmetry of the design and the good mechanical resilience of the 3D printer resin. By examining the pressure and gas flow velocity distribution inside the simulated components a few iterations per design

were made. (1) To optimize the relative velocity of the nebulizer and the sheath gas flow by adjusting the size of the constriction through which the sheath gas is introduced. (2) To ensure the optimal and reproducible nozzle position inside the chamber to reduce the chance of droplet deposition on the walls.

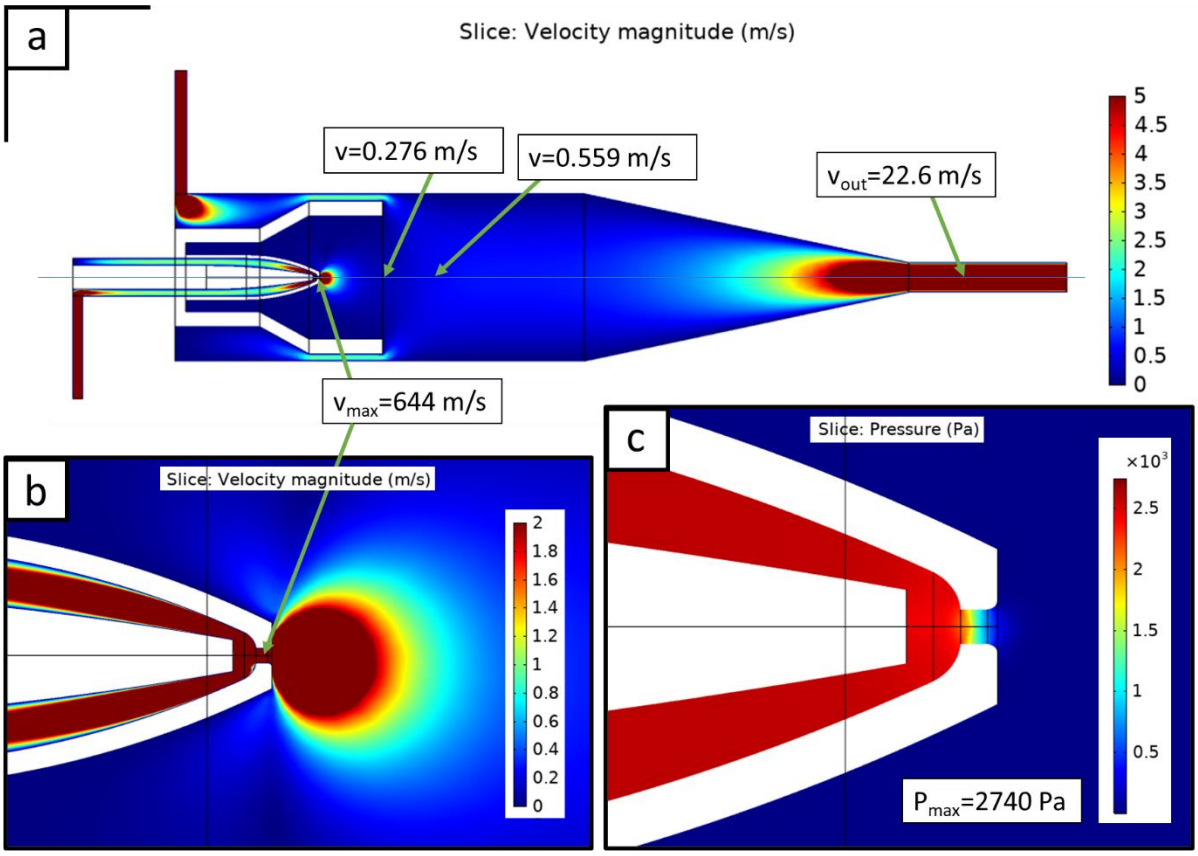


Figure 2. Simulation results showing the lateral gas velocity profiles a) on the whole model b) near the nozzle, while c) shows the lateral pressure distribution at the tip of the nozzle. All plotted in the mid-depth plane of the model.

## Conclusion

An alternative, 3D printed sample introduction system containing a concentric pneumatic nebulizer, and a low volume on-axis spray chamber equipped with sheath gas flow for ICP-MS was designed to enhance single nanoparticle or cell analysis. Its geometry was based on previously published reports of high efficiency nebulizers, spray chambers and several fluid dynamic simulations which the models underwent before finalization. As the continuation of this research, we are planning to characterize the capabilities of this custom sample introduction system experimentally. Examining its transport efficiency, primary and secondary droplet size distribution, and its effect on the efficiency of spICP-MS measurements when coupled with our instrument.

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