ON-LINE CHARACTERIZATION OF NANOPARTICLES BY SINGLE PARTICLE ICP-MS UTILIZING MICROFLUIDIC DEVICES

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Abstract
In this study, polydimethylsiloxane (PDMS) - glass microfluidic chips (MCs) were designed and fabricated using moulds prepared by a professional 3D printer. The prepared chips were used for the dilution, counting and characterization of nanoparticles (NPs) performing single particle inductively coupled plasma mass spectrometry (spICP-MS) measurements.

Introduction
Single particle inductively coupled plasma mass spectrometry is a novel technique for the rapid characterization of the dispersions of nano- and submicron particles. The technique can provide information on the presence, size and size distribution, number concentration, elemental and isotope composition of nanodispersions [1, 2]. An outstanding advantage of spICP-MS is the low (10^3-10^5 mL^{-1}) optimal particle number concentration (PNC), which can be prepared from sub-microgram amounts of sample [3]. This advantage can be best exploited by a sample introduction system capable for the introduction of low-volume samples. The sample preparation procedure of spICP-MS is simple, requiring only the dilution of nanodispersions. Nevertheless, in case of real-life samples, where the PNC can be hardly estimated accurately, it can be work- and time-consuming to find the right dilution to achieve single particle detection. MCs are well-established state-of-the-art devices suitable for the handling of low-volume solution and dispersion samples. These tools often serve capillary electrophoresis but are exploited in other fields of analytical separation and sample preparation techniques as well. Most microfluidic devices are prepared utilizing polydimethylsiloxane (PDMS) and glass/quartz microscope slides as these materials are cost-effective and easy to produce [4]. MCs also bear the possibility for automation which makes them even more attractive.
The aim of our study was to develop microfluidic devices for on-line spICP-MS sample preparation. In this contribution, we present some of our experimental results.

Experimental
An Agilent 7700X inductively coupled plasma mass spectrometer (ICP-MS) was used in all experiments. Sample introduction was performed by utilizing Gilson Minipuls 3 peristaltic pumps (Gilson Inc. Middleton, WI, USA) and a Micro Mist type nebulizer equipped with a Peltier-cooled spray chamber (standard Agilent 7700x accessories). The sample uptake rate was 600 µL/min. The data acquisition software was used in Time Resolved Analysis (TRA) mode. The integration time was set to 500 ms for the measurement of solution samples and 6 ms for nanodispersions, whereas the acquisition time was set to 60 s. All measurements were repeated three times and the error bars in the following graphs indicate their standard deviation.
The microfluidic chip moulds were fabricated utilizing a Form 3 professional 3D printer using „High Temp” resin material (Formlabs, Somerville, MA, USA). Utilizing the moulds, the MCs

were prepared by using Sylgard 184 silicone elastomer and curing agent (Dow Corning, Midland, MI, USA) and sealing the PDMS to a flat glass microscope slide. Detailed description of the preparation of the MCs can be found in one of our earlier publications [5].
Before dilution and also directly before aspiration into the ICP-MS, the dispersions were sonicated in an ultrasonic bath for 5 min (Bransonic 300, Ney, Danbury, CT, USA) in order to minimize particle aggregation.
Co and Ag sample solutions were prepared from 1000 mg/L CertiPUR monoelemental standards (Merck GmbH, Darmstadt, Germany). In spICP-MS measurements, commercially available NP standard dispersions were used. Ultra uniform polyethylene-glycol-capped 47.8 (1.8) nm gold nanospheres were purchased from Nano-Composix (San Diego, California USA), Pelco NanoXact tannic acid-capped 43.4 (3.2) nm silver NPs were obtained from Ted Pella (Redding, California, USA). Trace-quality de-ionized labwater from a MilliPore Elix 10 device equipped with a Synergy polishing unit (Merck GmbH, Darmstadt, Germany) was used for the preparation of all solutions and dispersions. Ismatec S3 E-LFL Tygon tubings (IDEX Health & Science GmbH, Wertheim, Germany) of 0.27 and 0.48 mm inner diameter were used for the aspiration of liquid samples. To drive the liquid samples to and from the MCs, stainless steel capillaries with 1.2 mm outer diameter, fabricated from medical needles, were placed in the inlet and outlet ports. For the connection of peristaltic tubing, the inlet and outlet needles and the ICP-MS nebulizer, PFA tubing with 0.3 mm inner diameter (part number 5042-0953, Agilent Technologies, Santa Clara, California, USA) and patches prepared from silicone tubing with 1.0 mm inner diameter (Deutsch & Neumann GmbH, Berlin, Germany) were applied.
All data processing was performed within the Agilent MassHunter (Agilent Technologies, Santa Clara, California, USA) and OriginLab Origin (Northampton, Massachusetts, USA) software.

Results and discussion

The design of the MCs (number of inlet ports, the angle between the inlet channels) has a strong impact on flow conditions. Chips with different sample and diluent inlet patterns (presented in Figure 1) were prepared and their performance for the on-line mixing/dilution of solutions was investigated both in computer simulations and in experiments.
In one of the first tests, we investigated how accurately can dilution be performed on the chips. We pumped Co standard solution and water into the input ports in a calculated microflow ratio and monitored the diminishing of the Co ICP-MS signal. According to our results, presented in Figure 2, the achieved dilution showed a good agreement with the theoretical dilution for “W” design, while the other two patterns provided less accurate dilution factors. This phenomenon can be probably explained by less favorable flow conditions at the junction when the diluent is introduced in only one channel. Thus, all further spICP-MS experiments were carried out using only the W design. Please also note the small error bars in the graph (and all later graphs), which indicate that the joint action of the chip, nebulizer and spray chamber, the overall mixing of the liquids in the system take place with very good efficiency.

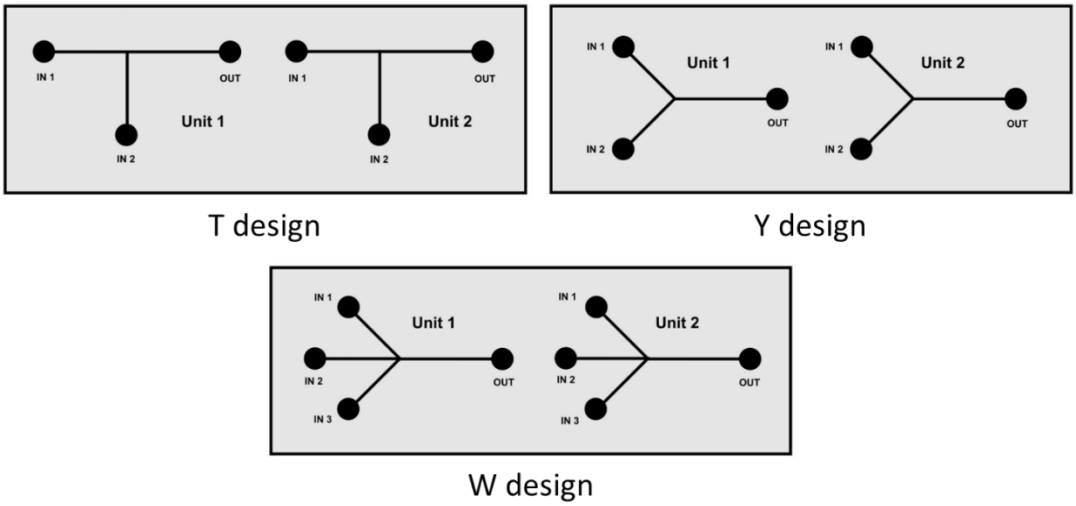

Figure 1. The various designs of the fabricated microfluidic chips

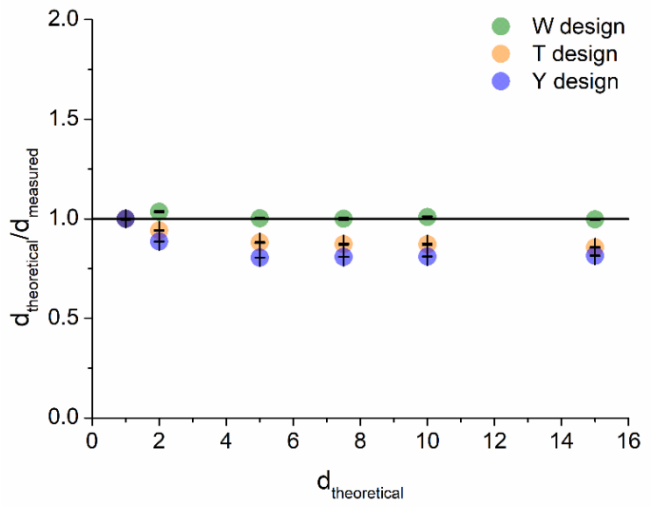

Figure 2. Investigation of the dilution accuracy of the different microfluidic chip designs

A typical task during spICP-MS analysis of unknown dispersions is to find the optimal PNC by performing dilution of the sample. The goal is to find a dilution where the maximum number of particles can be measured to obtain reliable statistical data but individual particle detection is still ensured. In practice this means that several diluted dispersions have to be prepared in relatively large volumes which is a time- and chemical-consuming process. Utilization of MCs for the on-line dilution of nanodispersions can make the process faster and more practical. In order to test this, the online dilution of a gold nanodispersion with 47.8 nm particle size and initial PNC of $1 \cdot 10^5$ mL^{-1} was carried out in the dilution range of 1-100 folds. As Figure 3 shows, there is an excellent linearity between the number of detected NP events and the nominal PNC resulted by the on-line dilution in the range of $1 \cdot 10^3$ and $5 \cdot 10^4$ mL^{-1}. At the highest measured concentration ($1 \cdot 10^5$ mL^{-1}) the number of detected events falls below expectations, which is a clear indication of the detection of more than one NP during the same integration window.

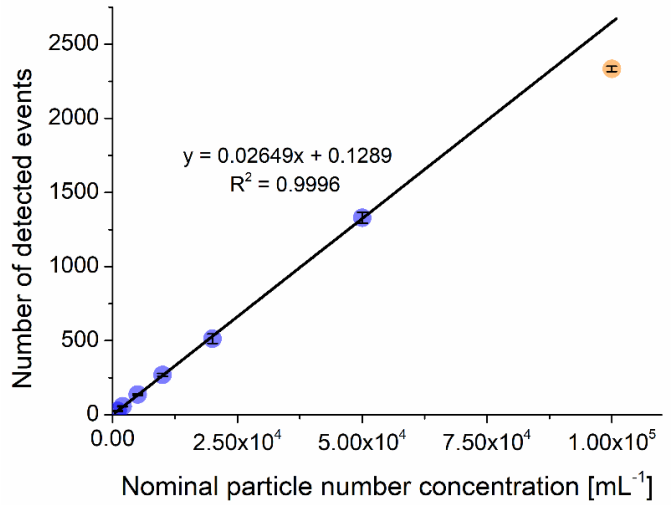

Figure 3. On-line dilution of Au nanodispersion with 47.8 nm particle size and initial PNC of $1 \cdot 10^5$ mL^{-1} in the 1-100 dilution range

Dissolved analyte content in nanodispersions can originate from either the matrix (presence of precursor residues or impurities of other synthesis reagents), or from the partial dissolution of the NPs. In either case, the dissolved analyte content generates a continuous background signal during the time-resolved spICP-MS measurements, which can bury the signal peaks of small NPs. A practical approach to tackle this interference is to dilute the dispersion, as it does not affect the signal originating from individual NPs, but it effectively diminishes the background signal. Utilization of MCs for this purpose is also favorable. Figure 4 shows our experimental results, which demonstrates the above discussed possibilities. A nanodispersion containing 43.4 nm Ag NPs with $1 \cdot 10^5$ mL^{-1} PNC and 1 ppb dissolved Ag was on-line diluted in the range of dilution factors 1 to 10. According to our results, a 5-fold dilution was optimal, as this resulted in a particle peak position that did not shift further to the left with additional dilution. The downside of this technique is that the total measurement time has to be increased in correspondence with the dilution factor in order to maintain the statistical relevance of the collected data.

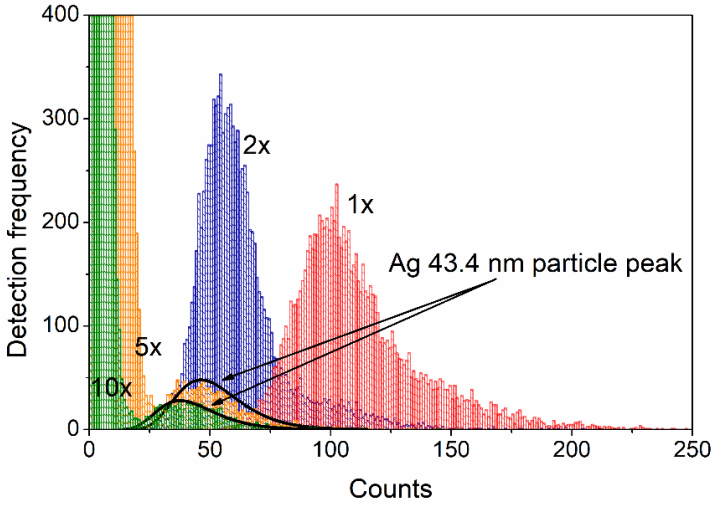

Figure 4. spICP-MS histograms of on-line diluted nanodispersion originally containing 43.4 nm Ag NPs with $1 \cdot 10^5$ mL^{-1} PNC and 1 ppb dissolved Ag

A particularly challenging situation in spICP-MS is when only a small amount of sample is available for analysis. As MCs are capable for handling of µL liquid samples with ease, they could be applied for the analysis of e.g. precious nanodispersion samples. We tested this concept by the injection of a few ten µL sample volumes and studied if the number of detected events is proportional to the PNC. As our results in Figure 5 indicate, the utilization of the fabricated MCs provided a good correlation with a reasonable standard deviation and accuracy.

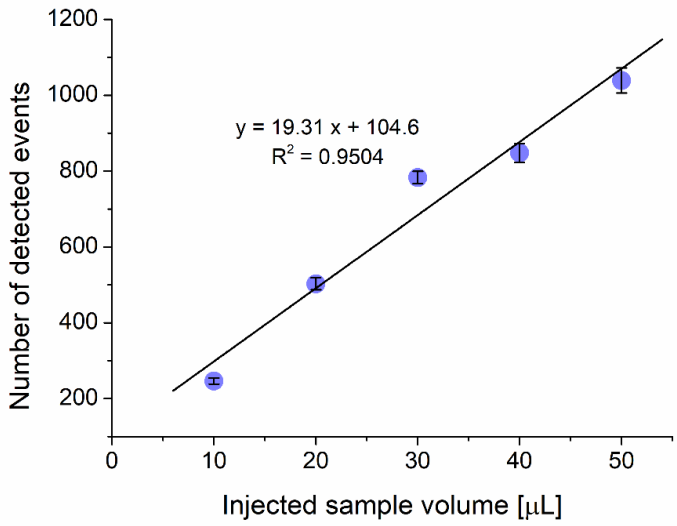

Figure 5. The number of detected events of low volume (10-50 µL) Au nanodispersions with 47.8 nm size and initial PNC of $5 \cdot 10^5$ mL^{-1} with 10-folds online dilution on the MC

Conclusion

PDMS-glass microfluidic chips were successfully applied for the on-line dilution and sample introduction of NPs for spICP-MS analysis. The utilization of the chips provides the prospect of automation (e.g. using electronically actuated microvalves and software control) that makes spICP-MS sample preparation fast and simple. We also demonstrated the feasibility of carrying out spICP-MS measurements on low (only a few tens of µL) sample volumes.

Acknowledgements

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