New statistical tool for automated data processing of single particle ICP-MS for the size determination and quantification of gold nanoparticles

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1 Introduction

- Advances in the synthesis, stabilization, and production of nanoparticles (NPs) have fostered a new generation of NP-containing commercial products and intensified scientific investigation of these materials.
- Recently, single particle inductively coupled plasma-mass spectrometry (spICP-MS) has emerged as a highly valuable analytical technique for the characterization of aqueous NP suspensions.
- spICP-MS measurements on the millisecond scale typically generates sample measurement that contains tens of thousands of data points, of which only a small percentage contains a NP event. Because spICP-MS data analysis is time-intensive, instrument vendors and users have developed their own algoritms.
- A lack of sophistication and transparency in the algorithms used, restrictions due to software licenses, and in some cases, the need for extensive knowledge in programming can limit the applicability of these spICP-MS data analysis tools.

2 Research goal

Develop a new spICP-MS data processing tool with a user-friendly interface able to computing size, size distribution and number concentration as well as provide graphical display and statistical analysis of the data.

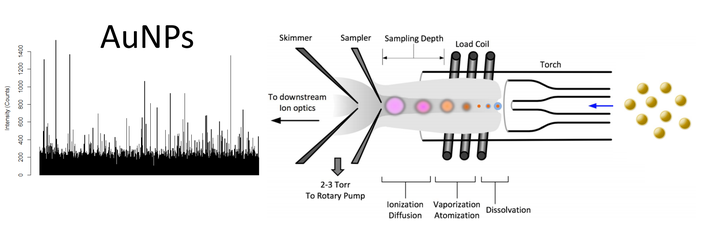
3 Materials and Methods


NIST RM AuNP


AuNP (vendor 1)


AuNP (vendor 2)

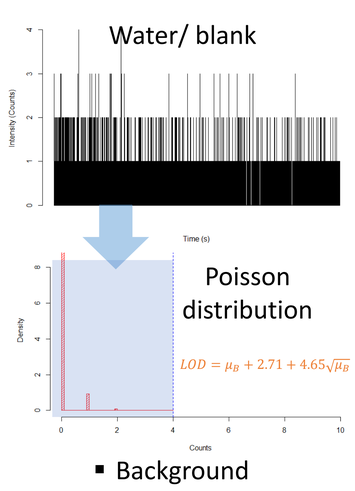
- AuNPs used in the spICP-MS determination



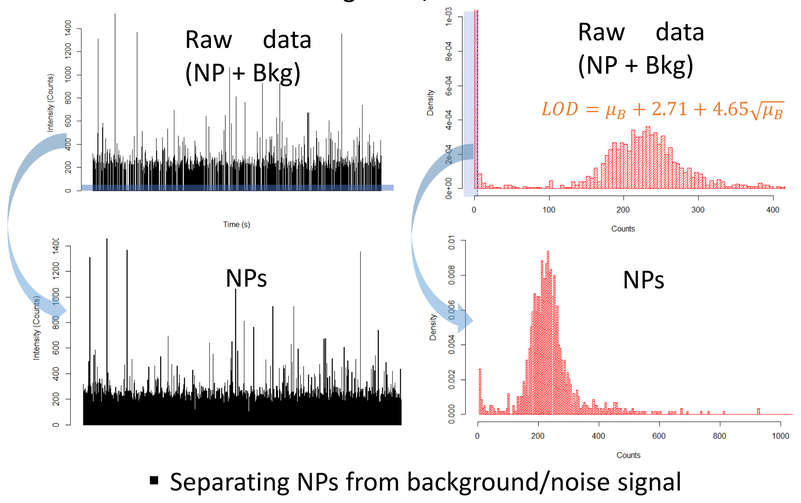
- Scheme of spICP-MS analysis, adapted [1]

4 Background signal

- Critical value (Lc) and Limit of detection (LOD) can be calculated using a Poisson-normal approximation [2]. LOD can be used as criterion to discriminate NPs from background/noise.



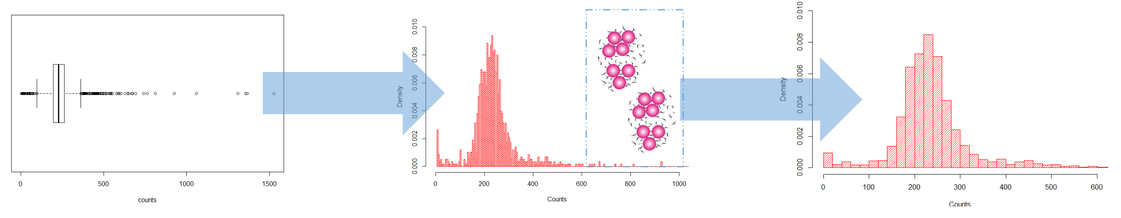
- Background



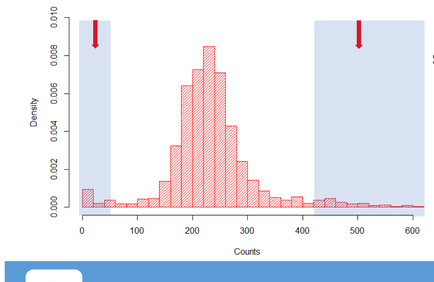
- Separating NPs from background/noise signal

5 Extreme outlier correction and signal estimation

- Extreme outliers significantly impact results and their graphical interpretation. A practical criterion based on the interquartile range reduce the influence of extreme outliers.



- Signal estimation was made using Hubers algorithm [3].



$$\mathbf{x}^T = [x_1 \quad x_2 \quad \Lambda \quad x_n]$$

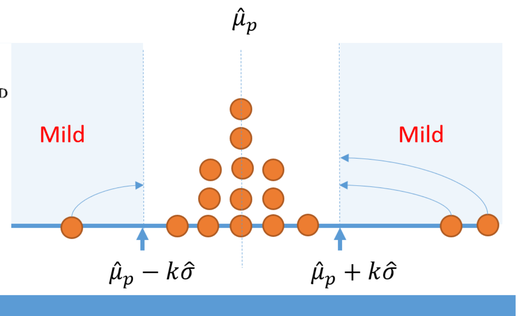
Set $1 < k < 2$, $p = 0$, $\hat{\mu}_0 = \text{median}$, $\hat{\sigma}_0 = 1.5 \times \text{MAD}$

$$\tilde{x}_i = \begin{cases} x_i & \text{if } \hat{\mu}_p - k\hat{\sigma}_p < x_i < \hat{\mu}_p + k\hat{\sigma}_p \\ \hat{\mu}_p - k\hat{\sigma}_p & \text{if } x_i < \hat{\mu}_p - k\hat{\sigma}_p \\ \hat{\mu}_p + k\hat{\sigma}_p & \text{if } x_i > \hat{\mu}_p + k\hat{\sigma}_p \end{cases}$$

$$\hat{\mu}_{p+1} = \text{mean}(\tilde{x}_i)$$

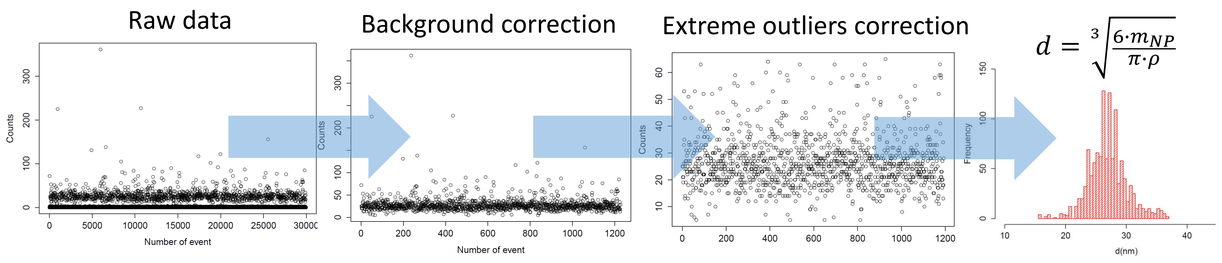
$$\hat{\sigma}^2_{p+1} = f(k)\,\text{var}(\tilde{x}_i)$$

If not converged, $p = p + 1$

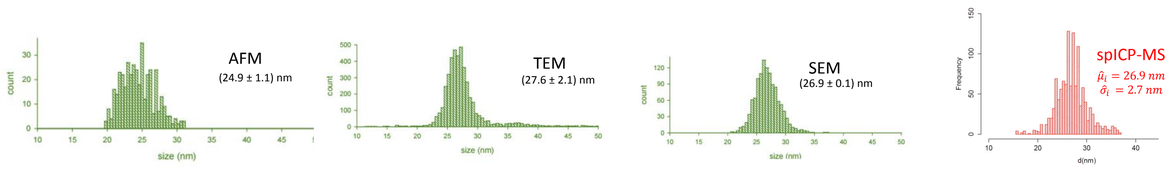


6 Results and visualization

- Visualization of the different process to separate particles events from the instrument background and to correct for extreme outliers.



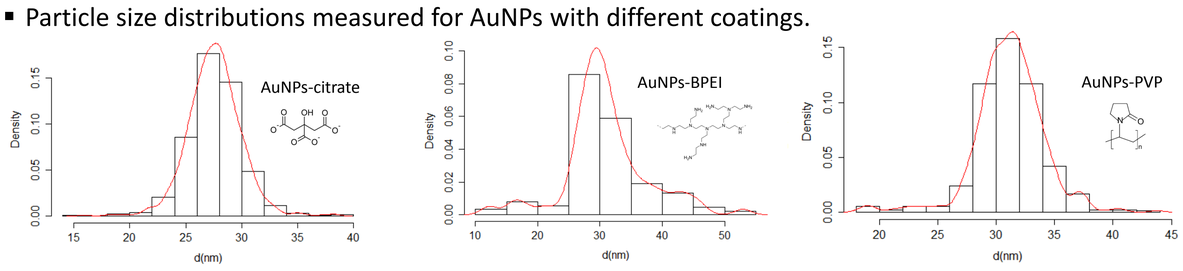
- Particle size reported in NIST RM 8012 and particle size obtained by the software.



- Results show an excellent agreement of the particle size and size distribution in comparison with the size reported for the NIST RM 8012.

7 Results

- Particle size distributions measured for AuNPs with different coatings.



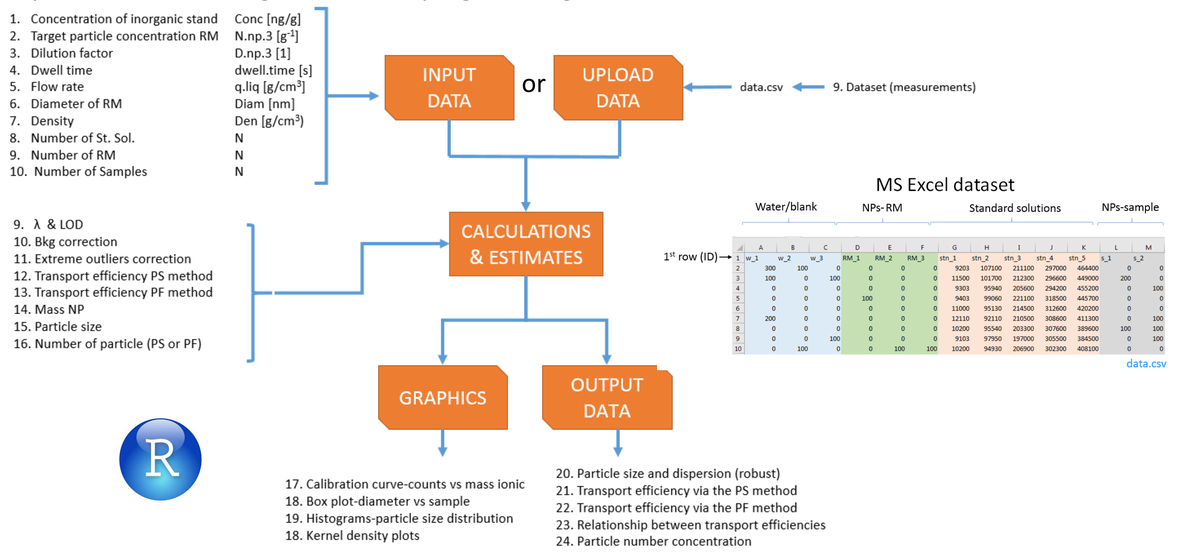
- Comparison between conventional calculations and the new approach.

Materials	Assigned value (TEM)	Conventional method*		New approach					
		Mean		Mean		Median		Huber	
ID	d(nm)	d (nm)	% diff fom TEM	d (nm)	% diff fom TEM	d(nm)	% diff fom TEM	d(nm)	% diff fom TEM
NIST RM8012-1	27,6 ± 2,1 (NIST)	27,1	-1,7	27,8	0,7	27,3	-1,1	27,4	-0,6
NIST RM8012-2		27,5	-0,3	27,8	0,8	27,1	-1,7	27,4	-0,9
NIST RM8012-3		27,8	0,7	28,2	2,2	27,3	-1,1	27,5	-0,5
AuNPs 1.1 (BPEI)	29,7 ± 2,6 (Vendor)	30,4	1,1	30,8	3,7	30,7	3,5	30,8	3,6
AuNPs 1.2 (BPEI)		30,4	1,1	31,1	4,6	31,0	4,4	31,0	4,3
AuNPs 1.3 (BPEI)		30,6	1,7	31,3	5,4	30,9	3,9	31,0	4,4
AuNPs 2.1 (PVP)	30,1 ± 2,6 (Vendor)	36,0	21,4	36,4	21,1	31,5	4,6	32,5	7,9
AuNPs 2.2 (PVP)		32,6	9,6	33,1	9,8	30,7	2,1	31,3	4,0
AuNPs 2.3 (PVP)		31,7	6,8	34,5	14,6	31,1	3,2	32,3	7,5

*Conventional method based in 3σ

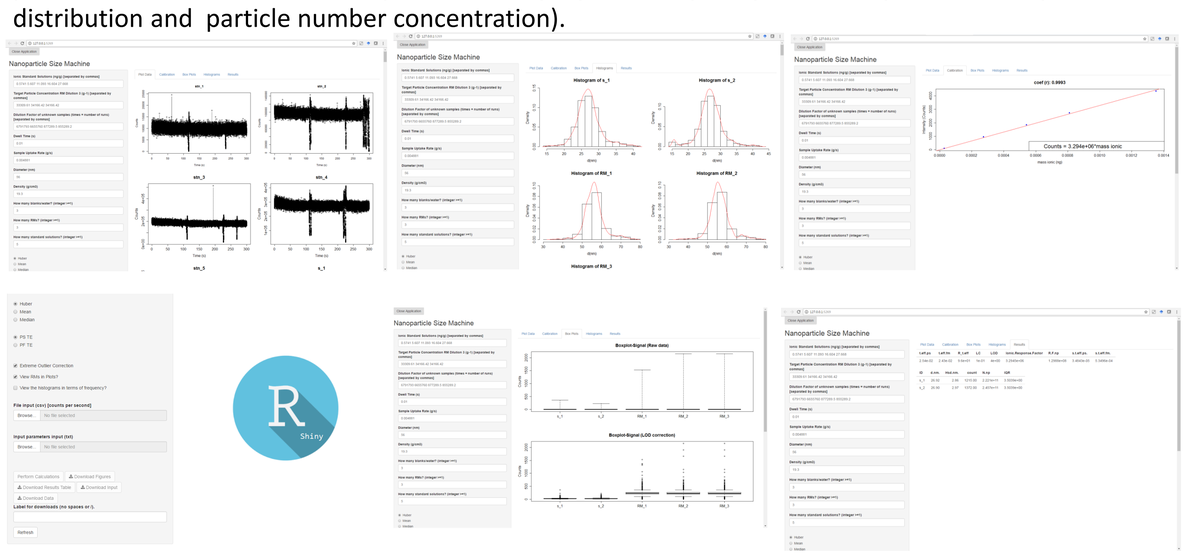
8 Software diagram

- The tool was developed with Rstudio and Shiny, [4,5] providing a user-friendly interface. Raw data files in csv format from any ICP-MS instrument vendor can be processed and results rapidly generated without sophisticated knowledge of R-studio programming.



9 Shiny app

- Critical information about spICP-MS measurements, graphics data analysis (plots, boxplots, calibration curve, histograms,) and results analysis (critical value, limit of detection, transport efficiency by the particle size method, and transport efficiency by the frequency method, particle size, particle size distribution and particle number concentration).



10 Conclusion and outlook

- This new statistical tool allows automated, fast and simultaneous spICP-MS sample data processing, reducing data analysis times from days to minutes.
- The tool provides results comparable with the conventional methods, and provides key information about the AuNPs properties (size, size distribution and particle number concentration).
- The tool demonstrates a method for accurate data processing of spICP-MS data. Huber algorithm provides an excellent approach to avoid mild outliers and accurately estimate the particle size.
- The application is currently limited to non-reactive NPs (i.e. NPS for which the ionic component is not significant). Efforts are currently under way to develop this software for application to all types of NPs measurable by spICP-MS analysis.

NIST
National Institute of Standards and Technology
Technology Administration, U.S. Department of Commerce

11 Reference

[1] Montaño, M. D., Olesik, J. W., Barber, A. G., Challis, K., & Ranville, J. F. (2016). Single Particle ICP-MS: Advances toward routine analysis of nanomaterials. Analytical and bioanalytical chemistry, 408(19), 5053-5074.

[2] Currie, L. (2008). On the detection of rare, and moderately rare, nuclear events. Journal of Radioanalytical and Nuclear Chemistry, 276(2), 285-297.

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