Supplementary Information (SI) for Analyst.

Supporting Information For:

High Performance Charge Detection Mass Spectrometry without Ultra-High Vacuum

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Section S1. Statistical methods.

Individual Ion Statistics. The standard error of the mean, calculated by taking the standard deviation of the population divided by the square root of the sample size (in this case, the number of non-overlapping segments in the transient), is used to quantify the uncertainty of the measurement:

$$Std.\,Err.Mean = \frac{\sigma}{\sqrt{N}}$$

Where σ is the standard deviation, and N is the number of non-overlapping segments of the transient. The errors reported in the manuscript therefore represent the uncertainty in the average mass value over the transient and not the spread of individual segment-by-segment calculated masses in the STFT analysis. In the data shown in Figure 1c and 1f, the ions last the entire 1s trapping period. If a 10 ms segment length and a 5 ms overlapping segment are used to analyze the transient, the number of non-overlapping segments is simply obtained by dividing the total transient length (1 s) by the segment length (10 ms) and subtracting 2 to avoid STFT edge effects. Thus, N = 98 in this case, i.e., 98 independent determinations of the same ion's mass over the 1s transient.

Mass Histogram Statistics. Histograms are built from the combination of all individual ions mass measurements. The tables below listed number of ions used to build the histograms presented in Figures 4 (AAV9) and 5 (100 nm and 50 nm PS nanospheres, mAb).

	50 ms segment length	**10 ms segment length**
Figure number and panel	**Ion count**	**Ion count**
4a/f (1×10^{-8} Torr)	3369	2481
4b/g (1×10^{-7} Torr)	1381	1186
4c/h (3×10^{-7} Torr)	1763	1350
4d/i (6×10^{-7} Torr)	1017	953
4e/j (1×10^{-6} Torr)	/	1019

	100 nm PS (5a)	**50 nm PS (5b)**	**Pentamer mAb (5c)**
Pressure	**Ion count**	**Ion count**	**Ion count**
1×10^{-8} Torr	1435	5537	1217

1×10^{-7} Torr	704	2680	2660
5×10^{-7} Torr	/	/	1624
1×10^{-6} Torr	587	1660	/

The mass distributions observed in Figure 4 and Figure 5c are all well characterized using a Gaussian function:

$$y_i = a \times \exp\left[\frac{-(x_i - \mu)^2}{2\sigma^2}\right] + c$$

Where y_i and x_i are the data points, a is the amplitude, μ is the centroid of the Gaussian distribution, σ is the standard deviation of the Gaussian curve, and c is a fit offset constant.

The diameter distribution of the polystyrene nanospheres presented in Figure 5a and 5b are clearly non-Gaussian, so values of the error of the mean diameter are therefore reported as the full width at half maximum (FWHM) measured directly from the histogram bin values where counts cross 50% of the peak maximum.

Figure S1. Variability of the average frequency slopes of mAb pentamers, AAV9, 50 nm and 100 nm polystyrene nanospheres measured at different background pressures inside the electrostatic trap of a charge detection mass spectrometer. The variability is defined as the ratio of the standard deviation of the ion frequency slopes divided by the average ion frequency slopes for each different sample. The larger deviations observed in the averaged frequency slopes of smaller ions are therefore largely due to the larger initial frequency of these ions. In the case of the mAb pentamer sample, the presence of multiple ions species also results in higher variability.

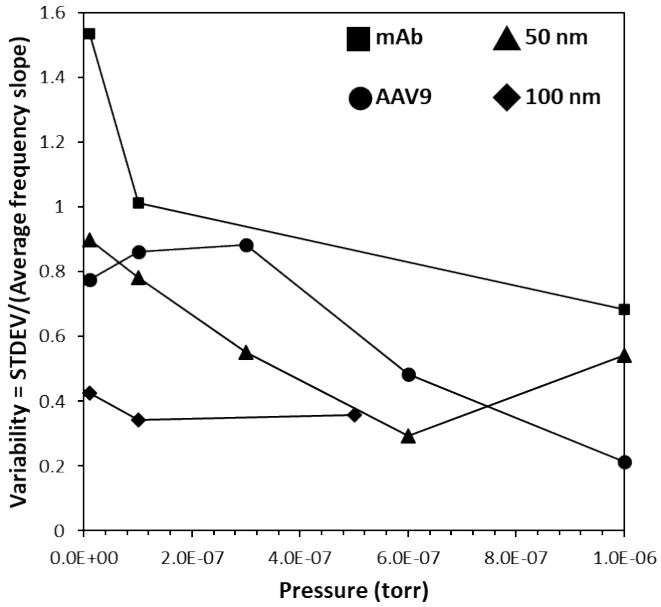

Table S1. Fitting equations for the average frequency slopes presented in Figure 2.

Analytes	Slope (Hz/s/torr)	Intercept (Hz/s)
mAb	5E+09	125.98
AAV9	1E+09	93.51
50 nm PS nanosphere	3E+08	20.89
100 ns PS nanosphere	7E+07	11.86

Figure S2. Mass distribution of 50 nm and 100 nm polystyrene nanospheres measured in the electrostatic trap of a charge detection mass spectrometer. Ions were measured for 1 s at 1 × 10^{-8} Torr, 1 × 10^{-7} Torr, 5 × 10^{-7} Torr, and 1 × 10^{-6} Torr. Input energy was set at ~220 eV/z at the entrance of the electrostatic trap. The mass distributions are composed of ions that lasted the entire trapping period (1 s).

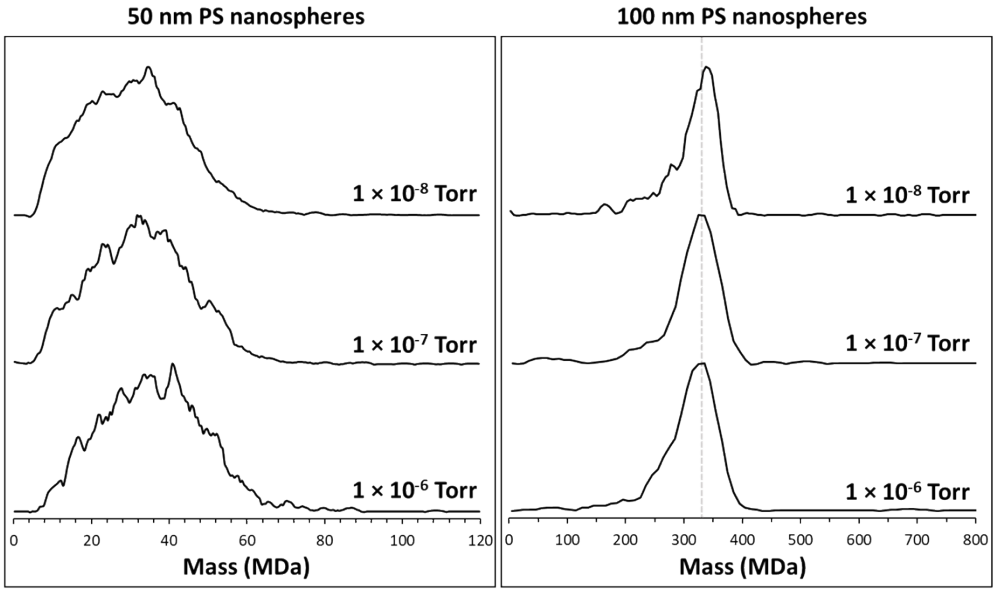

Figure S3. Mass distribution of mAb pentamers as measure for 1 s in the electrostatic trap of a charge detection mass spectrometer at a pressure of 5×10^{-7} Torr. Two input ion energy settings were evaluated: 220 eV/charge (black line) and 250 eV/charge (red line). The mass distributions are composed of ions that lasted a minimum of (a) 985 ms, *i.e.*, the entire trapping period, and (b) 500 ms in the electrostatic trap.