Measurement error near the LoD and the estimation of geometric statistics in EGs

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The problem

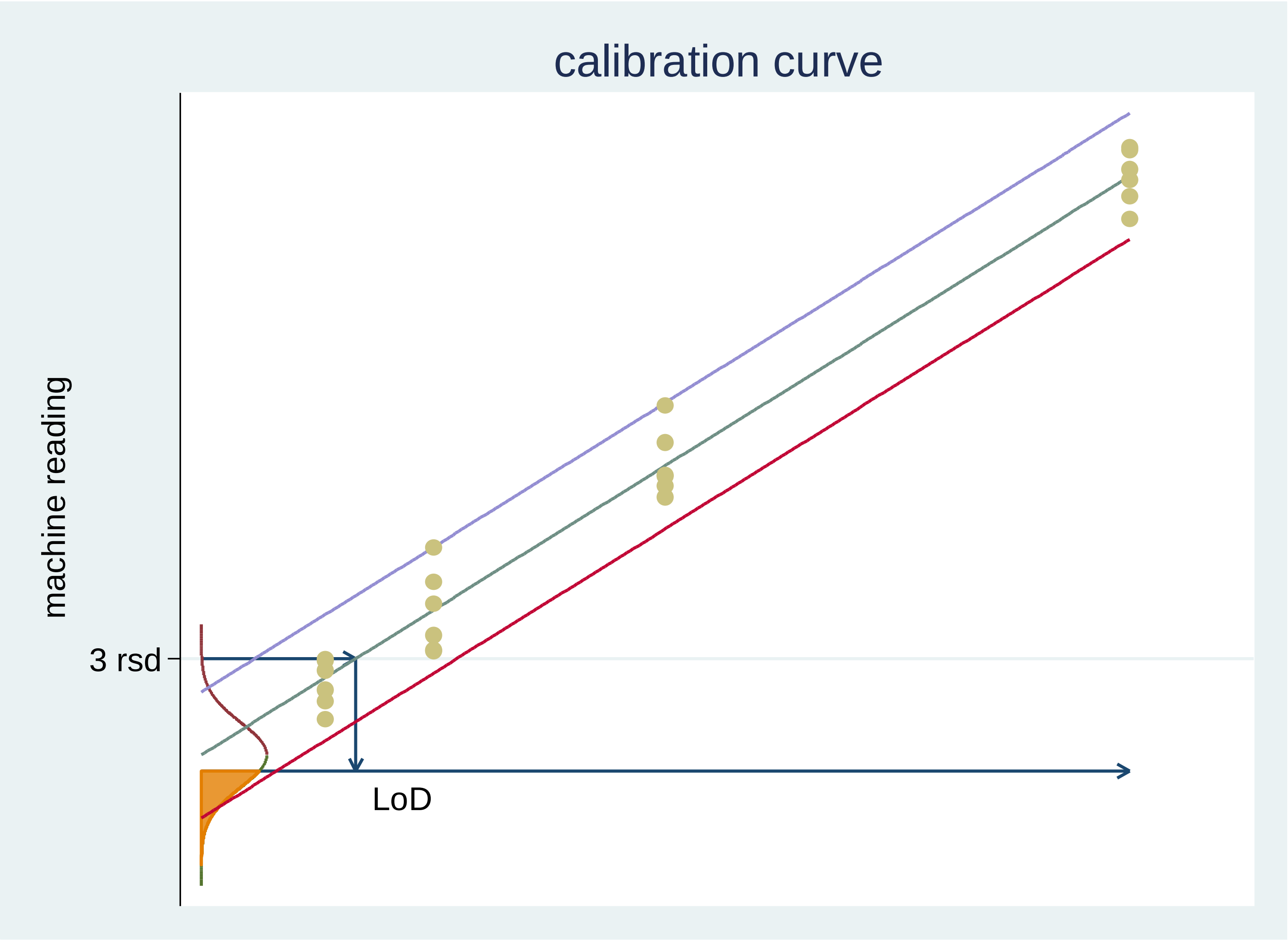
- Near the LoD exposure measurements have a poor relative precision and hence poor absolute precision on a log-transformed scale.
- Here we explore the consequences of this lack of precision on the estimation of geometric statistics (GM and GSD).

Estimating GM and GSD with measurements below LoD

- Standard statistical methods for accounting for censored values are
  - Replacing these values by LoD/2 or LoD/$\sqrt{2}$ – not recommended.
  - Maximum likelihood or Bayesian methods
  - Methods based on survival methods
- None accounts for the uncertainty in the LoD or the large measurement error near the LoD.

Determining the LoD

- All methods for determining the LoD rely on an estimation of the standard deviation of the measurement error at the blank.
- We consider here the method used by NIOSH (SOP 504 revised in 2004 – personal communication by Dr Neumeister) based on the linear regression of the calibration curve.



$$Y = sX + \varepsilon \quad \textit{with } \varepsilon \sim N(0, \sigma_B) \quad \textit{then } LoD = 3.\sigma_B/s$$

Theoretical measurement error as a function of the LoD

Let X_T a given (true but unknown) exposure concentration, the corresponding machine reading will be Y_{mes}=s X_T + *e*, where e is the measurement error in this reading

thus $X_{mes}=Y_{mes}/s = (s\ X_T + e)/s = X_T + e/s$

Thus we get the measurement error

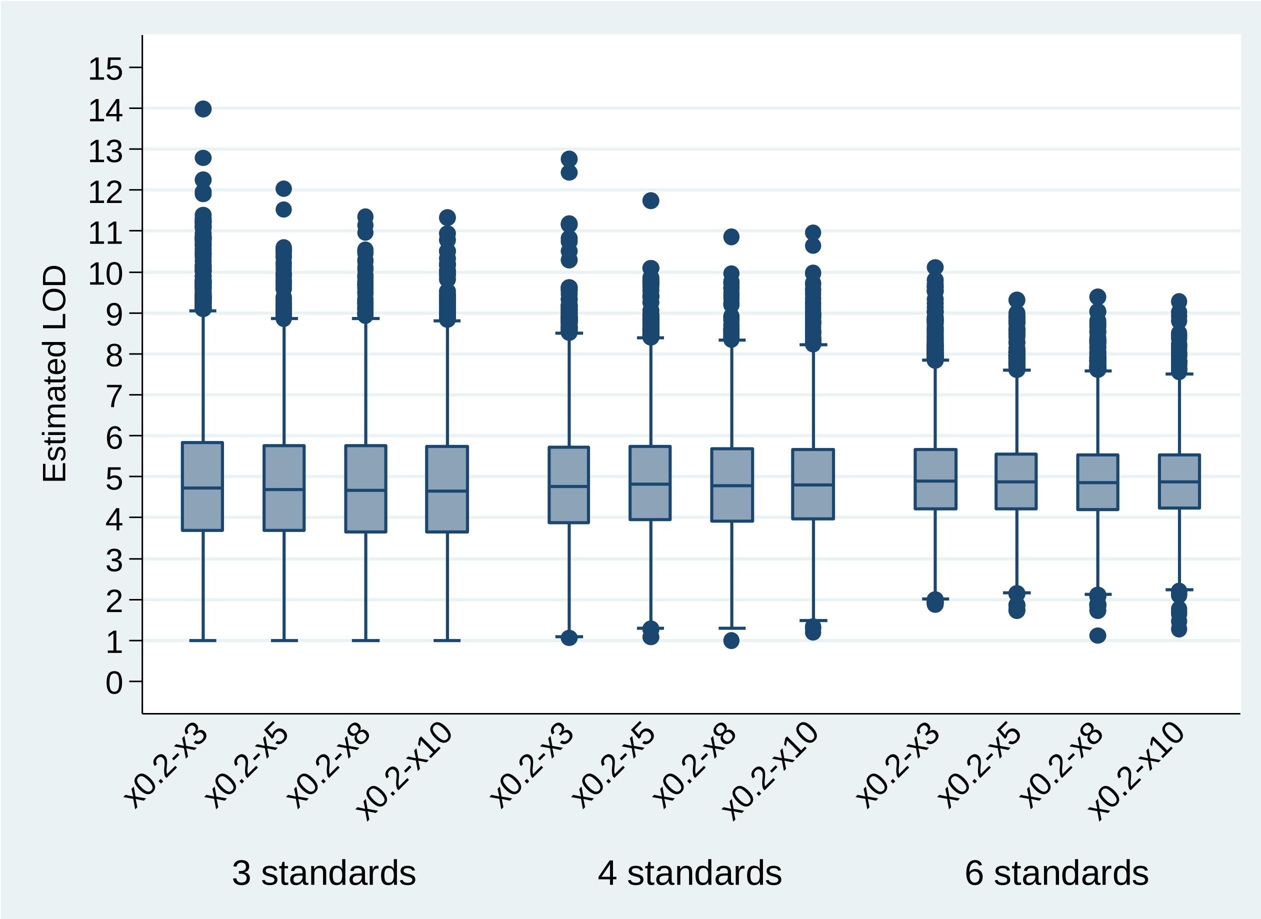
$X_{mes}-X_T = e/s$ with has a standard deviation σ_B/s

The minimal measurement error is thus LoD/3

Simulations of the SOP and the corresponding measurement error

- residual standard deviation σ_B =0.1, 0.5, 1
- LoD=5 (yields the slope as LoD= $3.\sigma_B/s$)
- Range of standards in the calibration curve 0.2 LoD-3xLoD, 0.2LoD-5xLoD, 0.2 LoD-10xLoD
- Number of triplicated standards :3, 4, 6

1000 calibration curves were simulated and LoDs and measurement error calculated for each combination of the above parameters



The measurement error standard deviation was found to be between 0.4 x LoD and 0.5 x LoD

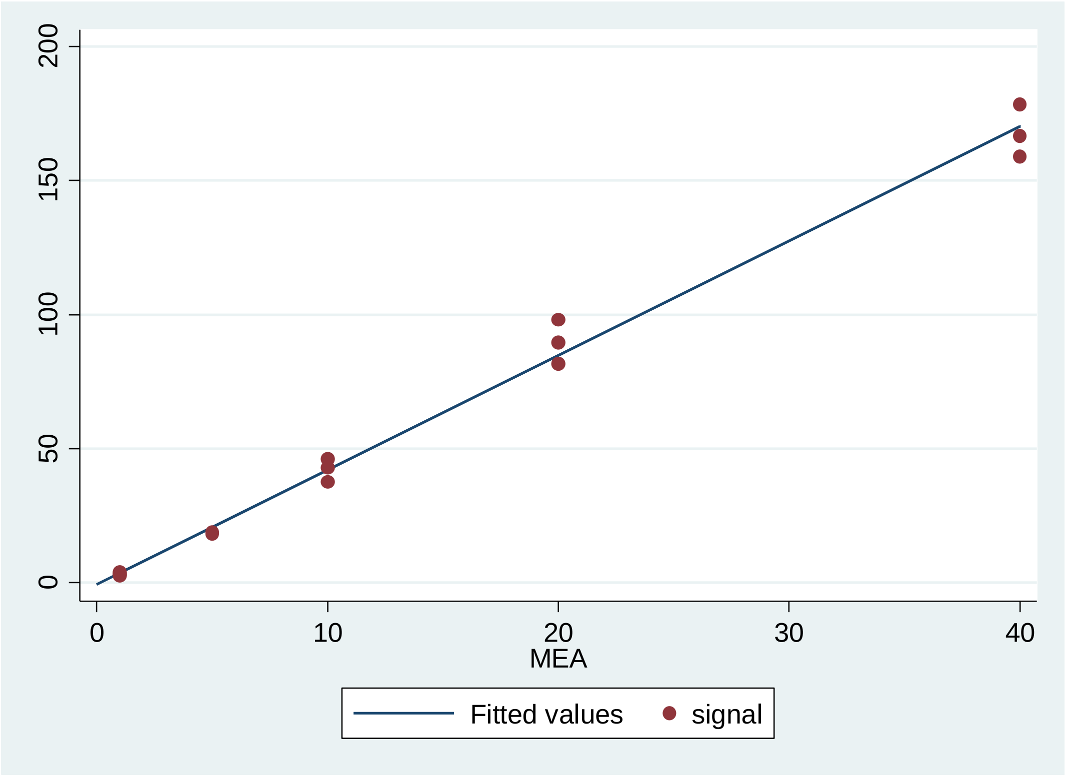
What are the consequences on the estimation of GM and GSD

- Results of other simulations
  - Virtually no consequence of measurement error when the percentage below LoD is lower than 30%
  - When more censored measurements, the GM is overestimated but moderately (10-20%)
  - The GSD on the other hand is underestimated but again moderately.

A real example :

measuring MEA in intensive floor cleaning (Gerster et al. 2014 Annals)

- A colleague set up a method for measuring Mono-ethanol-amine based on gas chromatography.
- He obtained a LoD= 1.3µg/filtre, based on a signal/noise ratio.



	Measured signals			All MEA standards			MEA standards<40			MEA standards<20		
EA	Rep 1	Rep 2	Rep 3	Slope	RSE	LOD	Slope	RSE	LOD	Slope	RSE	LOD
µg/filter	3.1	3.7	2.6									
µg/filter	17.9	18.4	18.6									
) µg/filter	42.6	37.5	46.1							4.3	2.6	**1.8**
) µg/filter	81.6	98.0	89.6				4.6	4.4	**2.9**			
) µg/filter	178.4	159.1	166.6	4.3	6.0	**4.3**						

Estimation of GM and GSD

- 37 measurements for 23 workers for intensive floor cleaning. We took a random sample of one meas. per subject , 9 < LD.
- The tasks were of variable length so that the LoDs varied
- With LoD=1.3, GM=0.038 g/m3, GSD=4.8
- With LoD=1.8, GM=0.045 g/m3, GSD=3.8

Conclusion

- The determination of LoDs is rather unstable and a LoD should not be considered a fixed value when computing geometric statistics.
- When describing data sets of measurements with a sizeable proportion of non detects, the value of the LoD should be augmented until results are stable.
- Measurement error does not appear to have a huge influence.

THANK YOU FOR YOUR ATTENTION