Detection and Quantitation: Understanding DL/LOD/LOQ

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Why Have Detection and Quantitation Limits?

- Define qualitative limits on data
  - Where can we assure (and be right 99% of the time) presence?
  - Where can we assure (and be right 99% of the time) absence?

- Define quantitative limits on data
  - At what concentration can we accurately tell how much is present?

- Ultimately: Define how data may (and may not) be appropriate for use.

WHAT ARE DL, LOD, AND LOQ?

A Quick Review

- Remember, the result (data) you get back from the laboratory should really be considered one point from a distribution of points.
- A probability distribution is a plot of the relative distribution of those results.

99.7% within 3 StDev

95% within 2 StDev

68% within 1 StDev

Probability

True Value
Concentration
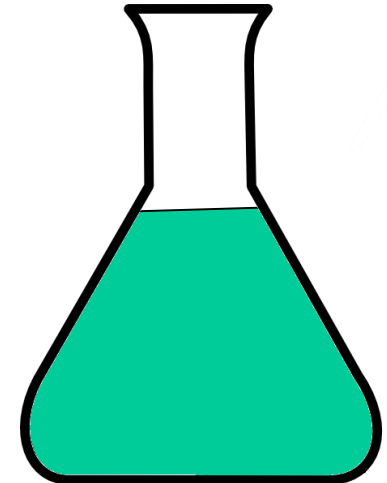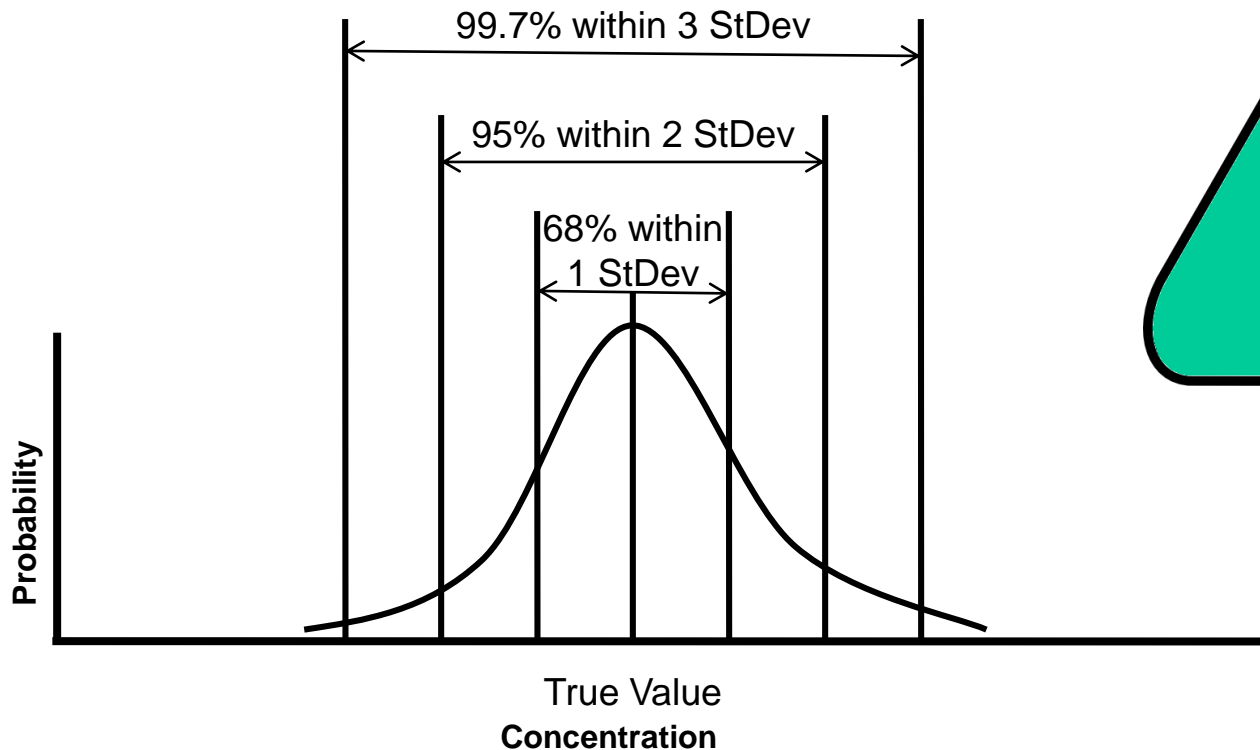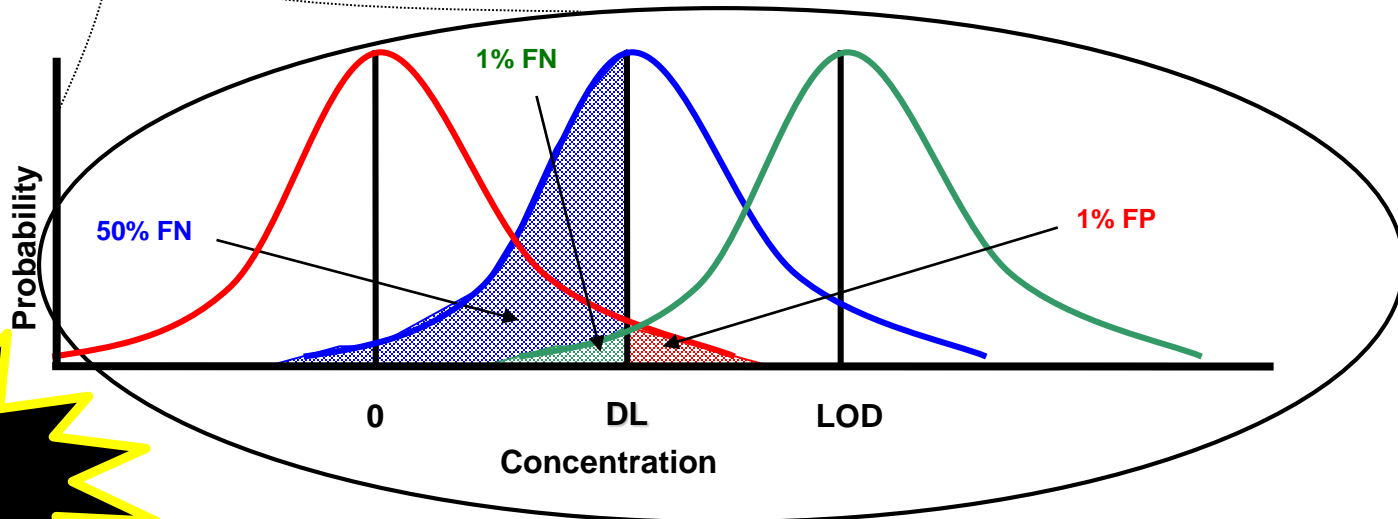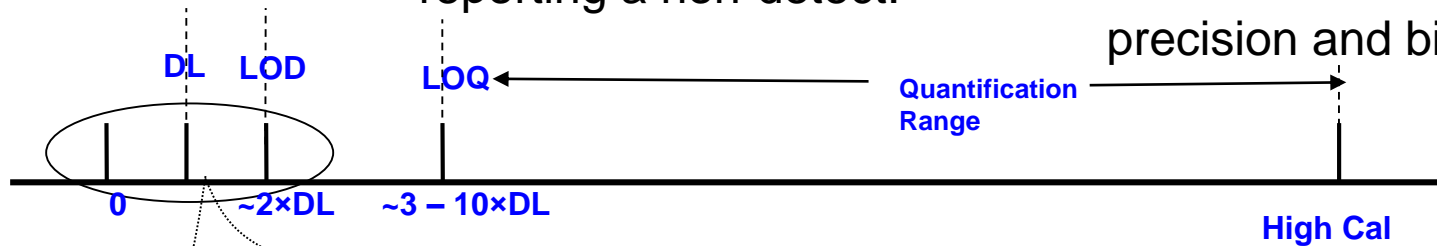
Defining Limits

Detection Limit (DL): False positive rate (Type I error) is 1%. Lowest concentration for reliably reporting a detection.

Limit of Detection (LOD): False negative rate (Type II error) is 1%. Lowest concentration for reliable reporting a non-detect.

Limit of Quantitation (LOQ): The smallest concentration that produces a quantitative result with known and recorded precision and bias.

DL LOD   LOQ ←   Quantification Range   →

0   ~2×DL   ~3 – 10×DL   High Cal

1% FN

50% FN   1% FP

Probability

0   DL   LOD

Concentration

What about MDL?

The MDL is an approximation of the DL – it protects against false positives only.

Defining Limits

Limit of Quantitation

- Limit of Quantitation (LOQ) (Clarification): The smallest concentration that produces a quantitative result with known and recorded precision and bias. For DoD/DOE projects, the LOQ shall be set at or above the concentration of the lowest initial calibration standard and within the calibration range.

- For DoD/DOE, at a minimum, the LOQ shall be verified quarterly. However, not all possible combinations of preparation and cleanup techniques are required to have LOQ verifications. If LOQ verifications are not performed on all combinations, the laboratory must base the LOQ verifications on the worst case basis (preparation with all applicable cleanup steps). In situations where methods are setup and used on an infrequent basis, the laboratory may choose to perform LOQ verifications on a one per batch basis in lieu of quarterly verification, prior to sample analysis. [Module 4 Section 1.5.2.2 e)]
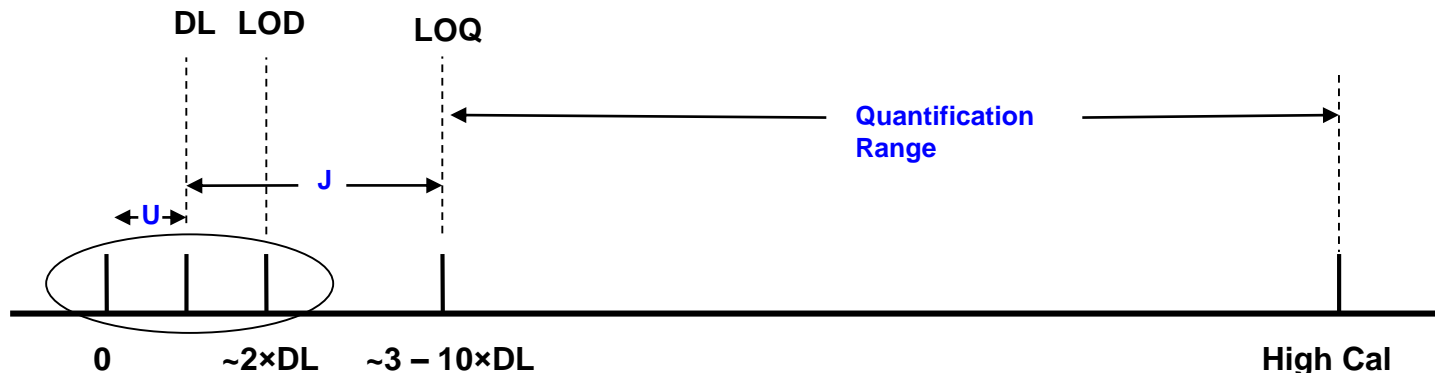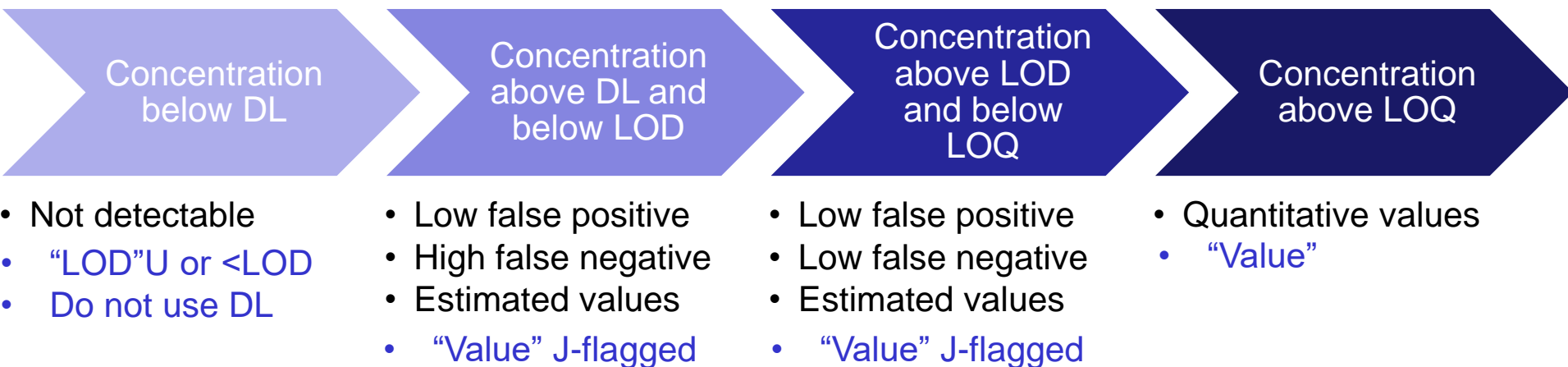
Defining Limits

Quantitation Range

- Quantitation Range: The range of values (concentrations) in a calibration curve between the LOQ and the highest successfully analyzed initial calibration standard. The quantitation range lies within the calibration range.
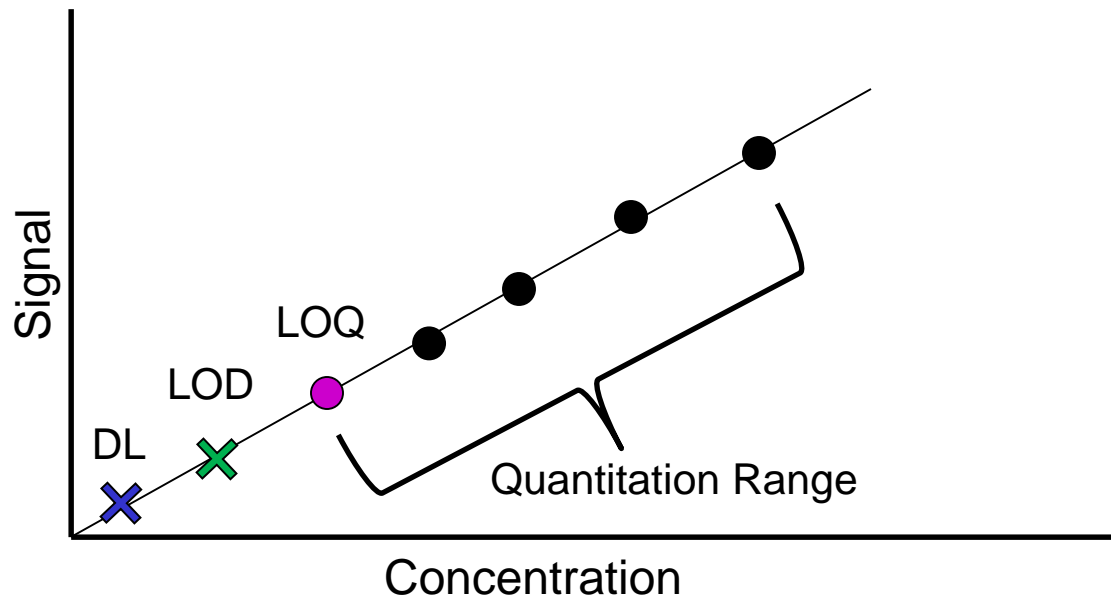
Data Quality and Reporting

- What does all this mean for data quality around these limits?
- How should data be reported around these limits?

Concentration below DL	Concentration above DL and below LOD	Concentration above LOD and below LOQ	Concentration above LOQ
• Not detectable • "LOD"U or <LOD • Do not use DL	• Low false positive • High false negative • Estimated values • "Value" J-flagged	• Low false positive • Low false negative • Estimated values • "Value" J-flagged	• Quantitative values • "Value"

DL **LOD** **LOQ**

Quantification Range

J

U

0   ~2×DL   ~3 – 10×DL   High Cal

Reporting – An Example

- In this example, DL = 2, LOD = 4, LOQ = 20 and the project Reporting Limit = 30.

- The following are the data and corresponding results:

Sample	Analytical Result	Reported Result
1	Non-detect	
2	2	
3	10	
4	20	
5	30	

- Data Qualifiers:
  - U – Analyte was not detected and is reported as less than the LOD or as defined by the customer. The LOD has been adjusted for any dilution or concentration of the sample.
  - J – The reported result is an estimated value (e.g. matrix interference was observed or the analyte was detected at a concentration outside the calibration range).

Additional Things to Keep in Mind

- Limits are specific to analyte, matrix, test method, instrumentation, and analyst
  - DL/LOD determined in laboratory water matrix is a lowest possible value
  - Spikes at the LOD in the matrix of concern may be helpful in understanding your data quality and needs

- Limits are adjusted with dilution of sample
  - i.e., if an analysis with a LOD of 2 is performed on a sample that has been diluted 3x, the LOD for that sample is 6. Therefore, a non-detect, would be reported as 6U *not* 2U.

- DL is statistically determined; LOD is empirically verified

Should Project Goals = LOQ?

- Why Not?
  - Precision and bias are only defined at and above the LOQ
  - The laboratory's DL, LOD, and LOQ are typically defined in a clean matrix, and so are a lowest possible value.
  - The laboratory LOQ does not take into consideration any of the uncertainty derived from sampling procedures.
  - Remember, data is a distribution. Consider tolerable decision error along with measurement error when determining project goals.
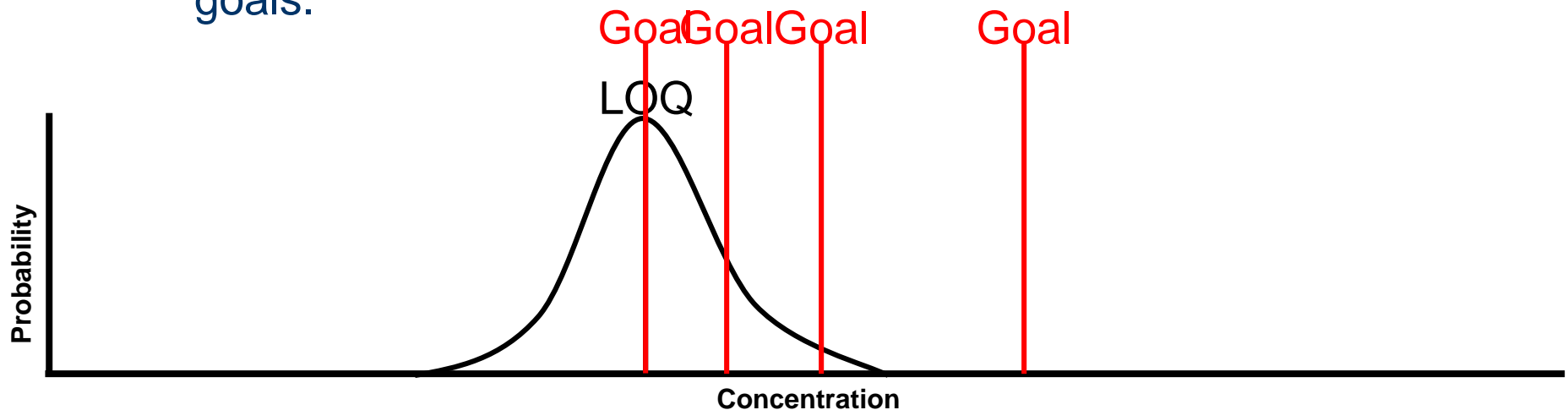
References

- EDQW Detection and Quantitation Fact Sheet (October 2017)
- DoD Quality System Manual 5.1 (January 2017)

Definitions

- Detection Limit (DL) – The smallest analyte concentration that can be demonstrated to be different from zero or a blank concentration with a 99% confidence. At the DL, the false positive rate (Type I error) is 1%. A DL may be used as the lowest concentration for reliably reporting a detection of a specific analyte in a specific matrix with a specific method with 99% confidence.

- Limit of Detection (LOD) (Clarification): The smallest concentration of a substance that must be present in a sample in order to be detected at the DL with 99% confidence. At the LOD, the false negative rate (Type II error) is 1%. A LOD may be used as the lowest concentration for reliable reporting a non-detect of a specific analyte in a specific matrix with a specific method at 99% confidence.

- Limit of Quantitation (LOQ) (Clarification): The smallest concentration that produces a quantitative result with known and recorded precision and bias. For DoD/DOE projects, the LOQ shall be set at or above the concentration of the lowest initial calibration standard and within the calibration range.
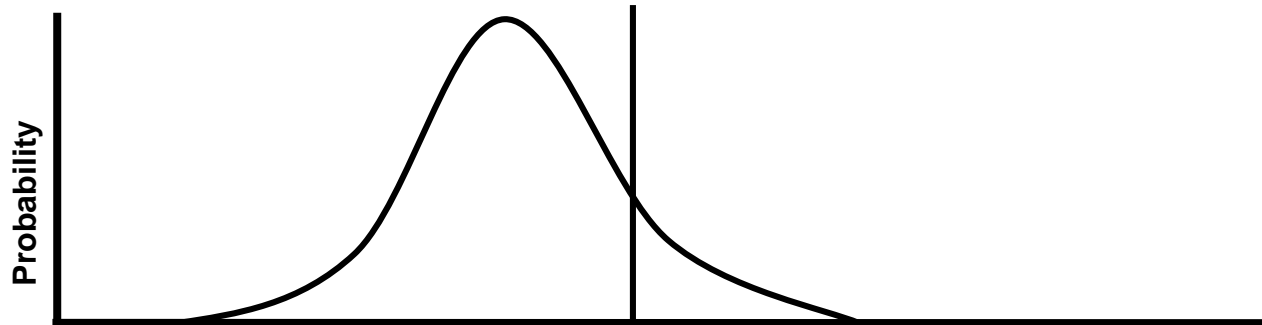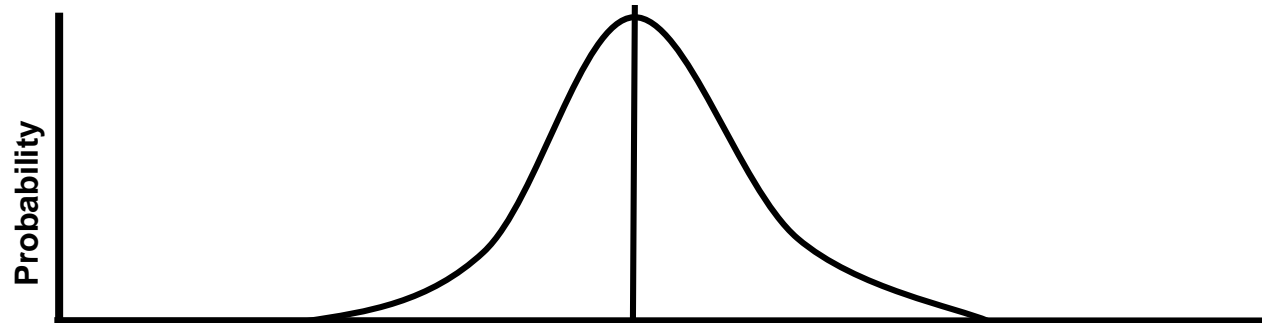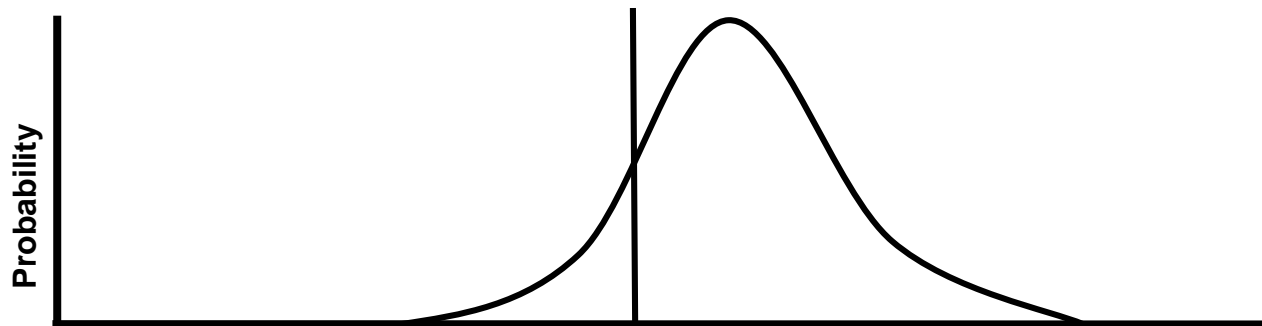
Signal-to-Noise
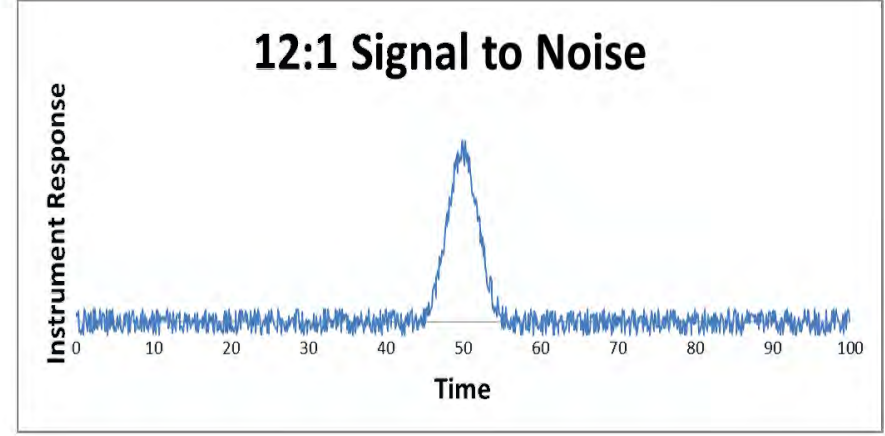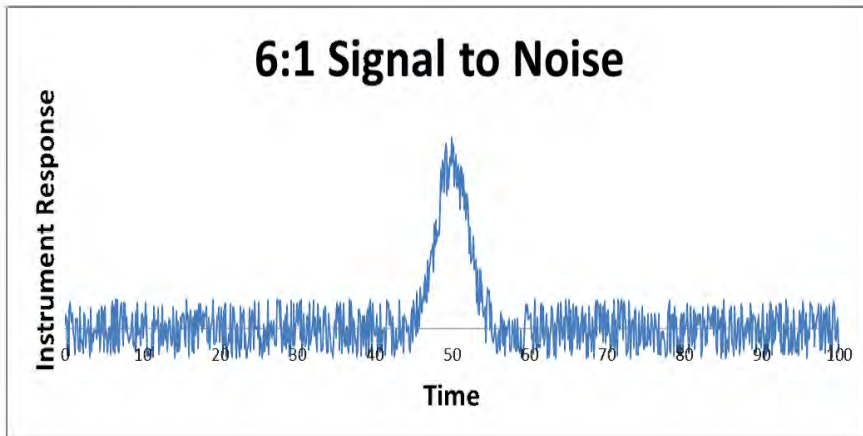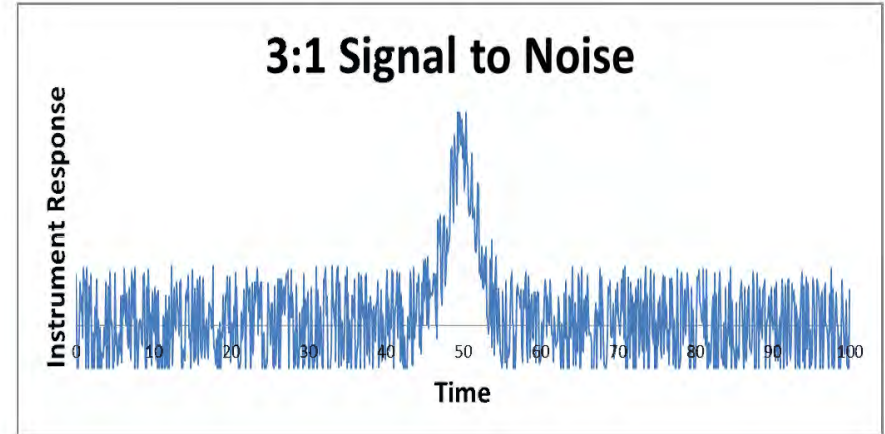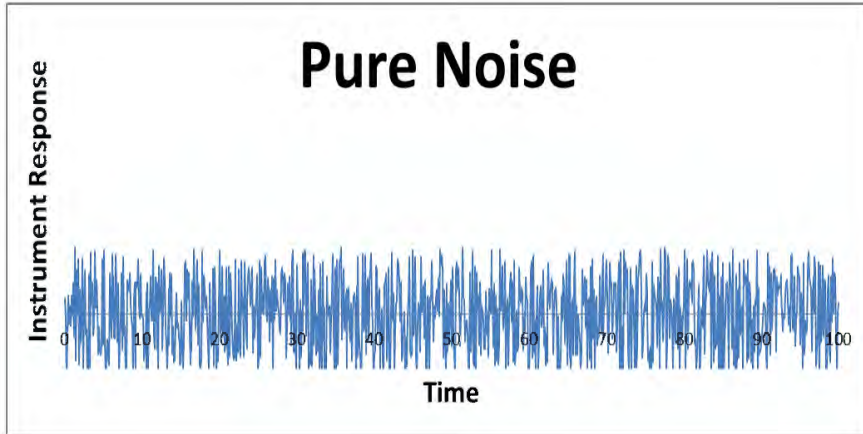
Precision
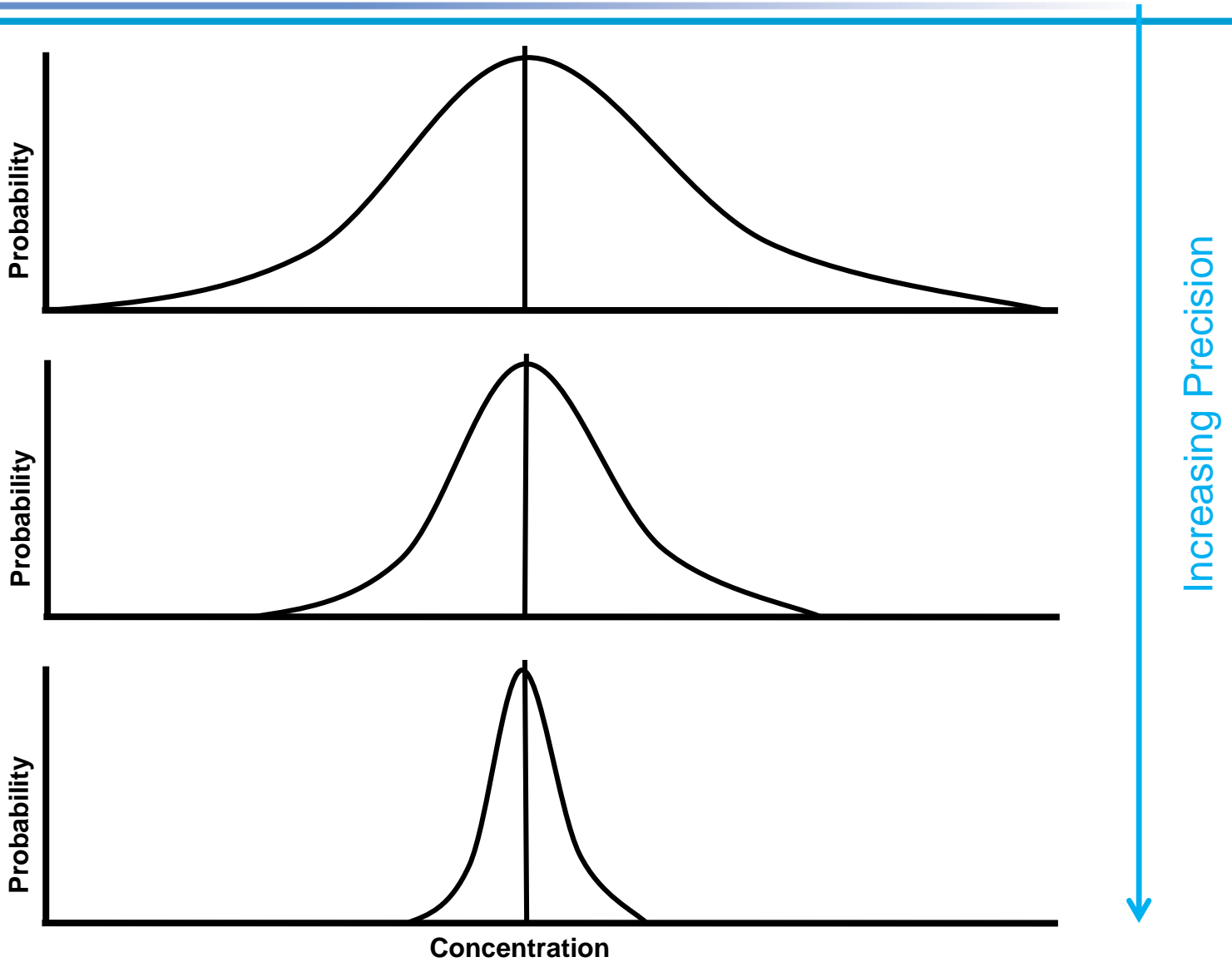
Bias

Low Bias

No Bias

High Bias

Concentration