QUALITY AND RELIABILITY IN ANALYTICAL CHEMISTRY

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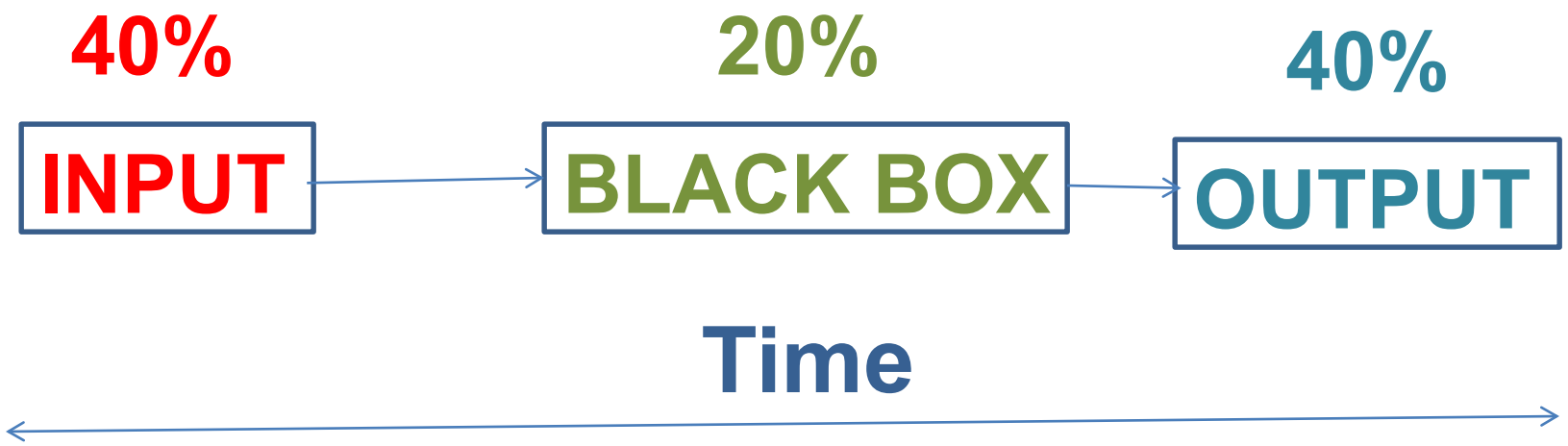
ANALYTICAL PROCESS

"The analytical laboratory of the future will be highly automated, particularly in quality control." (Swadesh JK, Kasouf CJ, Crit Rev Anal Chem, 25, 195, 1995)



PARAMETERS OF THE ANALYTICAL PROCESS

- **Rapidity**
- **Reproducibility**
- **Flexibility**
- **Reliability**

PARAMETERS OF THE ANALYTICAL PROCESSES: RAPIDITY

- **The time needed to develop an analytical process.**
- **One of the conditions for laboratory quality control;**
- **INFLUENCES THE COST OF THE ANALYSIS;**
- **Is dependent on the reliability of the analytical process and instrument;**
- **Utilization of computers and chemometrics for data processing.**

PARAMETERS OF THE ANALYTICAL PROCESSES: REPRODUCIBILITY

- "The closeness of agreement between independent test results obtained under stipulated conditions". (Fleming J et al, Accred Qual Assur 1, 87, 1996)
- The reproducibility of the sample and sampling will affect the reproducibility of the analytical information;
- Selectivity plays a very important role in the reproducibility of the analytical process

PARAMETERS OF THE ANALYTICAL PROCESSES: REPRODUCIBILITY

- Adequate software for chemometrics will make the data processing reproducible;
- Sensitivity of the method and instrument play a very important role in the reliability of the black box;
- e.g., determination of Cu^{2+}: $[HgI_4][Cu(en)_2]$ up to 10^{-6}g. For quantities lower than 10^{-6}g - radiochemical methods.

PARAMETERS OF THE ANALYTICAL PROCESSES: FLEXIBILITY

- The ability to be adaptable to ambient conditions.
- Must be an attribute to the operator, the method and the instrument;
- The method should be adapted to the sample (matrix and analyte) and to the instrument by correlation the operational parameters of the method with the functional parameters of the instrument.

PARAMETERS OF THE ANALYTICAL PROCESSES: RELIABILITY

- Reproducibility, rapidity, and flexibility of the analytical process assure its reliability.
- It represents a condition for automation.

STANDARDS AND STANDARDIZATION

- Standard and standardization play a major role in reliability assurance.
- Standardization refers to the compounds (standard compounds) and to analytical methods (standard methods).
- Standards act as a microdata bank.

STANDARDS AND STANDARDIZATION

- Standards

✓ must be illustrative from a quality and quantity point of view;

✓ must possess good stability, homogeneity, and flexibility;

✓ must have a composition similar to the sample to be assayed.

AUTOMATION AND ROBOTICS

- Basic types of automation equipment:

➢ Automatic devices;

➢ Automated devices.

AUTOMATION AND ROBOTICS:
AUTOMATIC DEVICES

- "Automatic devices perform specific operations at a given point in an analysis, frequently the measurement step." (Christian GD, Anal Chem, 1994)
- **Objectivity**: it is assured by using a computer for selection and optimization of parameters of analytical method and for data processing of the analytical signal.

AUTOMATION AND ROBOTICS:
AUTOMATIC DEVICES

- **Rapidity**: more analytical information obtained using automatic devices – in a very short period of time. It is improved when combined with robotics.
- **Flexibility**: ability to optimize the operational parameters.
- **Reliability**: will increase by using automatic devices.

AUTOMATION AND ROBOTICS:
AUTOMATED DEVICES

- Automated devices can control and regulate a process without human intervention.
- Based on analytical methods with well known parameters;
- Necessary in process control;
- Heterogeneous teams of researchers are needed to build them;
- High quality and reliable analytical information are obtained.

QUALITY OF A SAMPLE

"Qualitative analysis is an art."

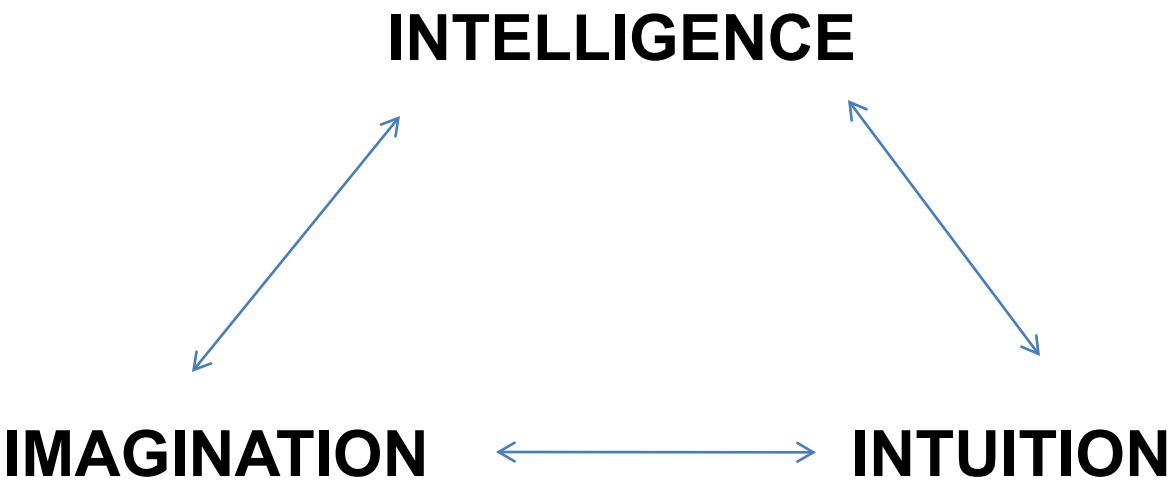
(Baiulescu, GE, 1983)

- Spectrometric methods;
- Dedicated organic reagents;
- MS
- Tandem techniques ICP/MS; HPLC/MS; GC/MS
- **STOCHASTIC SENSORS**

SENSITIVITY VS SELECTIVITY

QUALITY OF THE ANALYTICAL INFORMATION

BASIC ATTRIBUTES OF ANALYSTS



QUALITY OF THE ANALYTICAL INFORMATION

- ✓ **INTUITION:**

  - sample components, quantity and structure;

- ✓ **IMAGINATION:**

  - choosing the best method for the qualitative and quantitative analysis;

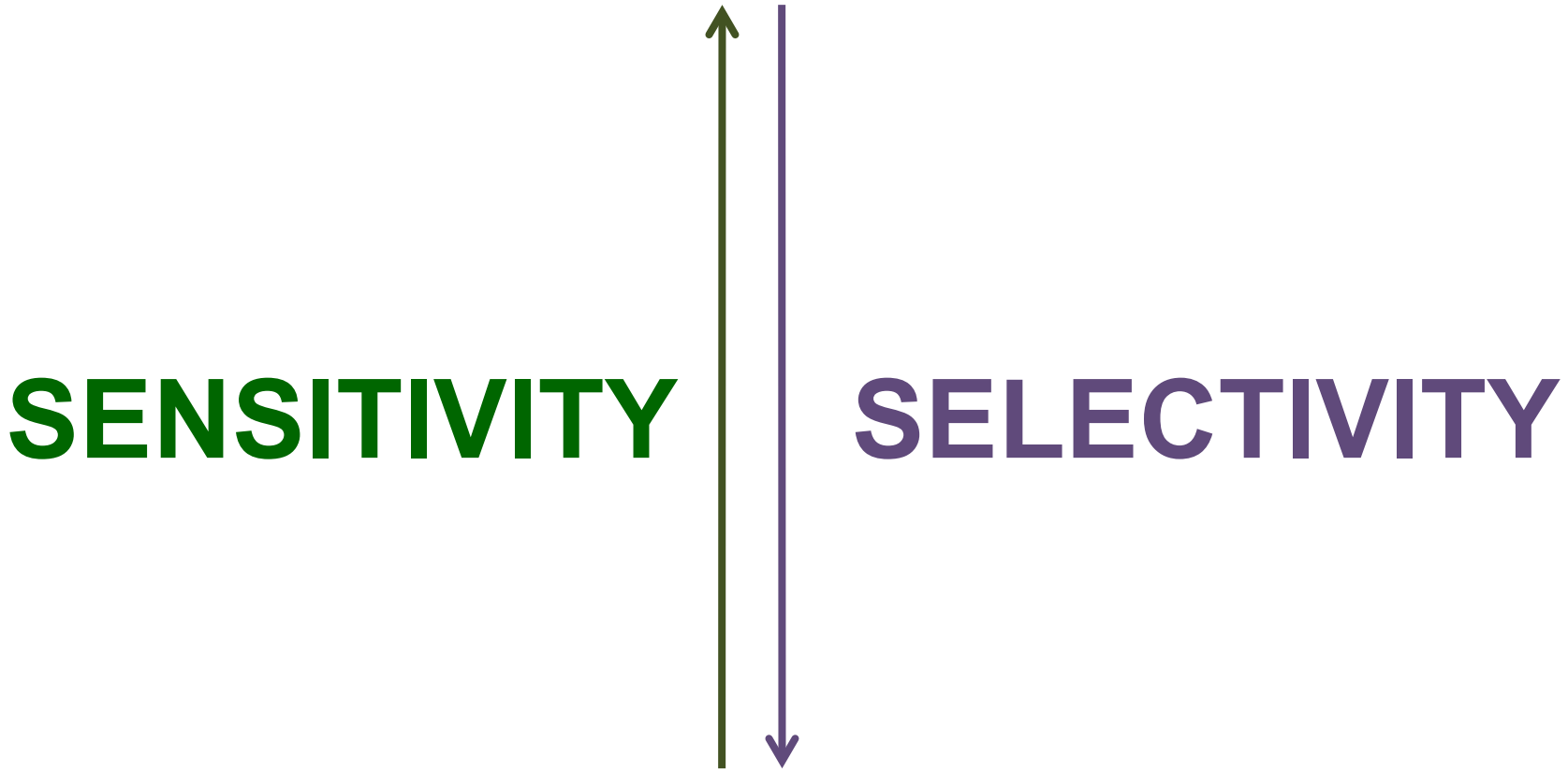
- ✓ **INTELLIGENCE: - FLEXIBILITY**

  - developing of experiments in good order.

QUALITY OF THE ANALYTICAL INFORMATION

- QUALITY OF THE SAMPLE & SAMPLING;
- QUALITY OF THE METHOD OF ANALYSIS;
- QUALITY OF DATA PROCESSSING.

SENSITIVITY vs SELECTIVITY



SENSITIVITY vs SELECTIVITY

SENSITIVITY vs SELECTIVITY

- Direct correlated with the complexity of the matrix of the sample;
- Masking the interfering species may help keeping a low sensitivity;
- The method of analysis should be chosen so that its sensitivity is correlated with the quantity of the species to be analyzed, and it should be free of interferences from the matrix.

SENSITIVITY vs SELECTIVITY

Examples:

1. **Design of immunosensors for clinical analysis**

$$Ag + Ab \longleftrightarrow [Ag...Ab]$$

high selective and sensitive

- **Potentiometric transducer NO**
- **Amperometric transducer YES**

SENSITIVITY vs SELECTIVITY

2. Selectivity of the ion-selective, membrane electrodes

- **Based on the stability of the complexes formed at the membrane-solution interface:**

$$A + L \longleftrightarrow [AL] \quad K_{AL}$$

$$I + L \longleftrightarrow [IL] \quad K_{IL}$$

$$K_{AL} >> K_{IL} \text{ selectivity}$$

$$\text{Slope(A)} >> \text{Slope(I) sensitivity}$$

SENSITIVITY vs SELECTIVITY

3. Fluorescence and chemiluminescence sensors

- **Classified as the most sensitive sensors;**
- **Well known for their sensitivity;**
- **Only certain species can be determined using these types of sensors;**
- **Selectivity may be improved using Ab or enzymes.**

Sensitivity, selectivity, and complexity of the matrix

Selectivity ⟷ **Complexity of the matrix**

Environmental Clinical Food Pharmaceutical Analysis

Decreases the complexity of the matrix

Sensitivity, selectivity, and complexity of the matrix

Selectivity & sensitivity of

Sampling ⟷ **Analytical method**

e.g., dissolution process of solid samples - microwave diggestion + blank analysis

Sensitivity, selectivity, and complexity of the matrix

e.g., separation methods:

- **Chromatographic methods – high selectivity, still low sensitivity;**
- **Membrane separation – good selectivity; low sensitivity; recovery of the analyte less than 90%.**

Enantioselectivity

VERY IMPORTANT FOR PHARMACEUTICAL ANALYSIS AND CLINICAL ANALYSIS!!!

- **Enantiomers of the same chiral compound have different pathways in the body;**
- **Enantiomers of the same chiral compound can be biomarkers for different diseases, enantioselective analysis playing an important role in medical diagnosis.**

Enantioselectivity

Example

Determination of L-T_3 and L-T_4 in serum samples and pharmaceutical compounds

- **Serum samples – use immunosensors based on anti-L-T_3, and anti-L-T_4**
- **Pharmaceutical compounds – use either immunosensors or biosensors based on L-AAOD.**

Enantioselectivity

- ✓ **The technique which became a fact in enantioseparation is capillary zone electrophoresis, but it did not have a good sensitivity;**
- ✓ **Amperometric immunosensors exhibits high enantioselectivity and high sensitivity.**

RELIABILITY

THE MAINTENANCE OF QUALITY THROUGH TIME.

$$R_{AI} = f(R_S, R_M, R_I, R_{DP})$$

- **The sample acts as a "glue" between the method and the apparatus.**

RELIABILITY

Reliability ⟷ S/N

- **S/N must be kept constant and at the highest value possible.**
- **Automation – a solution.**

RELIABILITY OF THE SAMPLE

- **HISTORY OF THE SAMPLE;**

- **VERY IMPORTANT**
- **Will help to predict the composition as well as the quantity of the analytes in a matrix;**

RELIABILITY OF THE SAMPLE

- **Homogeneity of the sample.**

- **Ensuring the homogeneity of the sample is a sine qua non for obtaining reliable analytical information.**
- **very important for solid samples;**
- **The sampling must be selected accordingly with the complexity of the sample.**

RELIABILITY OF THE ANALYTICAL METHOD

"No analysis is better than the sample itself."

(Baiulescu, GE)

- **The analytical method should be selected accordingly with the complexity of the matrix and the nature of the analytes to be determined;**
- **The analysis is following the sampling process; a good correlation between sampling and analytical method should be achieved.**

RELIABILITY OF THE ANALYTICAL METHOD

- Most of the electrochemical methods required a very simple sampling, e.g., dissolution of the sample in water or in an organic solvent;
- Improvement of selectivity of these methods can be done by using an enzymatic reaction or an immunoreaction.

RELIABILITY OF THE ANALYTICAL METHOD

Examples:

1. **Environmental analysis**

- **Air and water analysis – no dissolution sample required;**
- **Soil analysis – dissolution of the sample required;**
- **Most of the analytes should be separated from the matrix (extraction, chromatography).**

RELIABILITY OF THE ANALYTICAL METHOD

Examples:

1. **Environmental analysis**

- **Inorganic analysis – ICP/MS; AAS; diamond paste based amperometric sensors;**
- **Organic analysis: spectrometry – UV/Vis, fluorescence, chemiluminescence; electrochemistry – amperometric sensors; biosensors; immunosensors; stochastic sensors.**

- **Immunosensors & biosensors – group selectivity.**

RELIABILITY OF THE ANALYTICAL METHOD

2. Food analysis

- The matrix is more simple than in the environmental analysis, and most of the time known.

✓ Applications of sensors and biosensors increased.

✓ Separation methods for the most complex matrices is recommended

RELIABILITY OF THE ANALYTICAL METHOD

3. Pharmaceutical analysis

- The matrix is simple and well known.

✓ Applications of sensors and biosensors is recommended.

✓ Separation methods is recommended for complex matrices, or analytes presenting similar chemical properties.

RELIABILITY OF THE ANALYTICAL METHOD

4. Clinical analysis

- **The matrix is simple and well known. History of the sample is very important for a successful analysis.**

✓ **Applications of sensors and biosensors is recommended, especially for *in vivo* analysis.**

✓ **High sensitive methods (e.g., chemiluminescence) are combined with immunoassay**

RELIABILITY OF THE INSTRUMENT

"The choice of the instrument is imposed by the sample and its matrix." (Baiulescu, GE)

"the selection of analytical methods and of the corresponding instrumentation is a consequence of correct knowledge of the sample's history and homogeneity"

- ✓ **The operational parameters of the method must be connected with the functional parameters of the instrument.**

RELIABILITY OF THE INSTRUMENT

- Evolution of the method of analysis required the evolution of the instrument;
- Evolution of the instrument is connected with the evolution of material science, electronics, technology.

$$P = f(\text{concentration})$$

P = physical property

RELIABILITY OF THE INSTRUMENT

- Accuracy of the analytical balance and pipets.
- Sensitivity of the instrument must be correlated with the sensitivity of the analytical method.
- Automation will assure the best objectivity of the analysis and the highest reliability.
- Dedicated instruments may be created for clinical, and food laboratories, but not for research.

RELIABILITY OF THE DATA PROCESSING

- The signal obtained from the instrument is converted into the analytical information using an interface and dedicated programs;
- Chemometrics are used to process the analytical information;
- The computer must process data, store data, and transmit data to the operator;
- The software used for data acquisition and data processing is essential;

RELIABILITY OF THE DATA PROCESSING

- **The performance of the computer must be correlated with the number, speed, and complexity of the signals that are obtained from the analytical instrument.**

METHOD DEVELOPMENT

THE KEY: ANALYTICAL INFORMATION OBTAINED MUST BE CHARACTERIZED THROUGH QUALITY AND RELIABILITY.

- **SAMPLING PROCESS MUST BE CORRELATED WITH ANALYTICAL METHOD.**
- **SAMPLE IS THE "GLUE" BETWEEN METHOD AND INSTRUMENT.**

METHOD DEVELOPMENT

- KNOWLEDGE ABOUT THE HISTORY OF THE SAMPLE ARE NECESSARY IN ORDER TO SELECT THE BEST ANALYTICAL PROCESS;
- MINIMIZING THE TIME OF ANALYSIS IS ESSENTIAL ESPECIALLY IN CLINICAL ANALYSIS;
- AUTOMATION OF THE BEST ANALYTICAL PROCESSES WILL INCREASE THEIR QUALITY AND RELIABILITY.

METHOD DEVELOPMENT

- **A METHOD DEVELOPED FOR DETERMINATION OF AN ANALYTE IN A MATRIX MAY NOT EXHIBIT THE SAME QUALITY AND RELIABILITY FOR ITS DETERMINATION IN A DIFFERENT MATRIX.**

Example:

Determination of thyroid hormones in pharmaceutical formulations and serum samples with biosensors based on L-AAOD.

METHOD DEVELOPMENT

- **THE SAME METHOD USED IN TWO INSTRUMENTS: ONE OF HIGH SENSITIVITY AND THE OTHER OF LOW SENSITIVITY - MAY NOT WORK IN BOTH INSTRUMENTS.**

Example: utilization of the amperometric sensors based on diamond paste needs high sensitive instruments.

METHOD DEVELOPMENT

- KEEPING SAMPLING PROCESS AT MINIMUM NR. OF STEPS WILL INCREASE THE RELIABILITY OF THE METHOD.

- UTILIZATION OF DEDICATED SOFTWARE FOR INSTRUMENT DRIVING, DATA ACQUISITION, AND PROCESSING WILL INCREASE THE RELIABILITY OF THE ANALYTICAL INFORMATION.

METHOD DEVELOPMENT

Validation of method is necessary.

- **Can be done vs standard methods and/or using standard samples;**
- **Utilization of chemometrics is essential in the validation process.**

QUALITY AND RELIABILITY IN ANALYTICAL CHEMISTRY

References

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2. D.C. Springer, R.I. Stefan and J.F. van Staden, *"Laboratory Auditing for Quality and Regulatory Compliance", Taylor & Francis, Nw York, USA, 2005.*