

Metrology for Chemistry and Biology

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MATERIAL MEASUREMENT LABORATORY

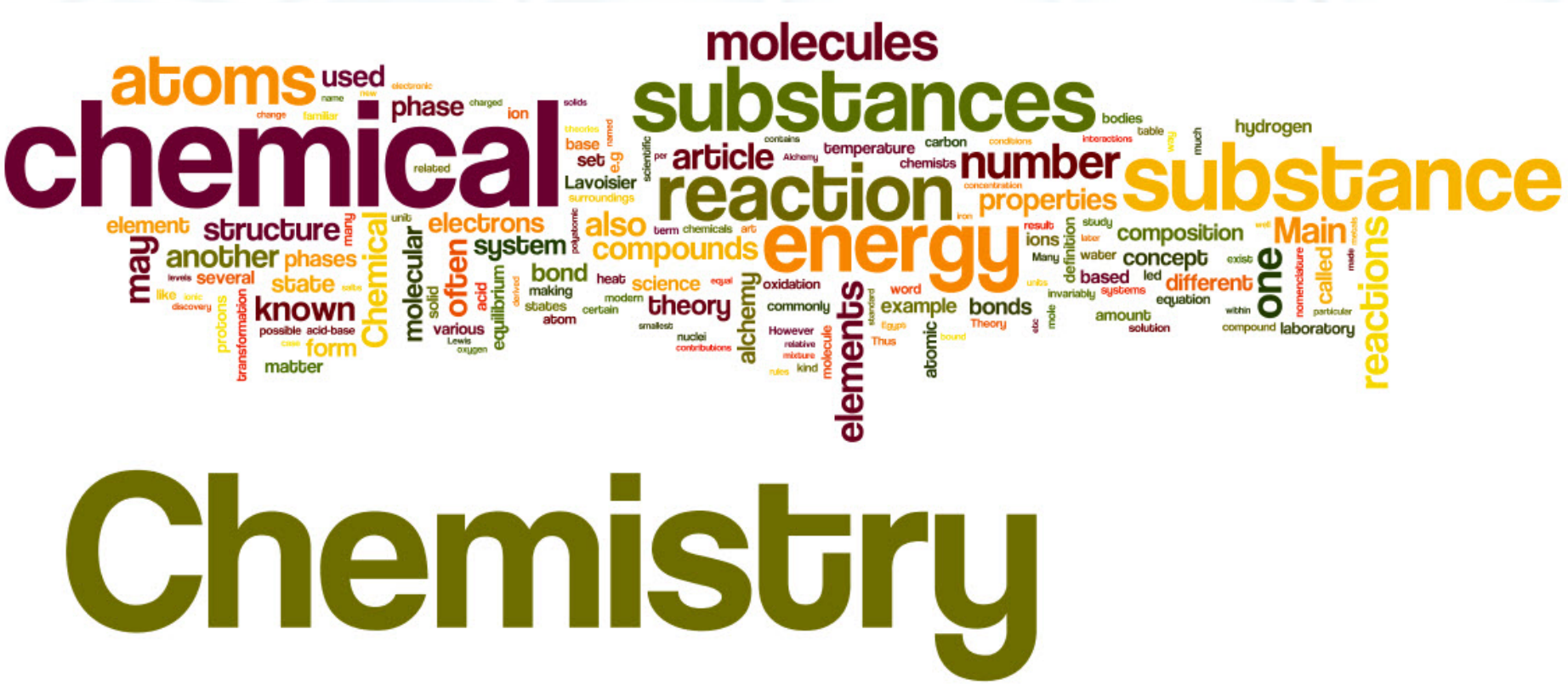
Metrological Context

CCAUV: Acoustics, Ultrasound & Vibration
CCEM: Electricity & Magnetism
CCL: Length
CCM: Mass & Related Quantities
CCPR: Photometry and Radiometry
CCQM: Amount of Substance - Metrology in Chemistry
CCRI: Ionizing Radiation
CCT: Thermometry
CCTF: Time and Frequency
CCU: Units

But What is Chemistry?

- Study of the composition, properties, and behavior of matter

Chemistry: Diverse Aspects



Chemistry: Diverse Samples

Gases
Liquids
Solids

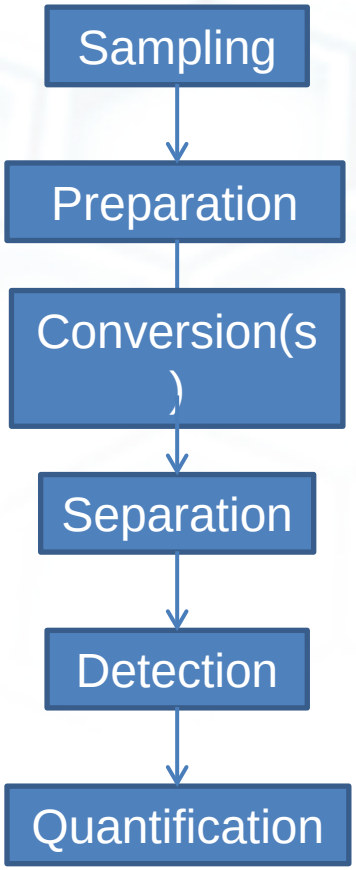
Stable
Reactive

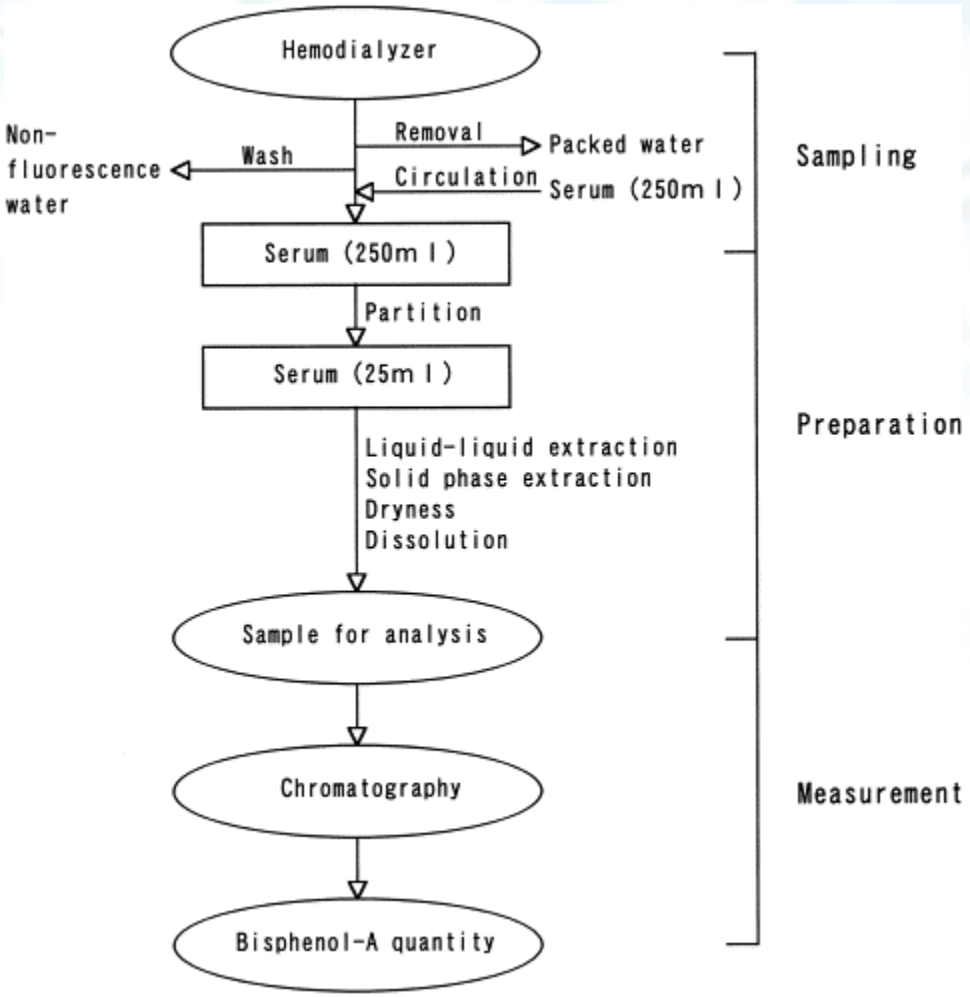
“Pure” materials
Mixtures
Impurities

Simple
Complex

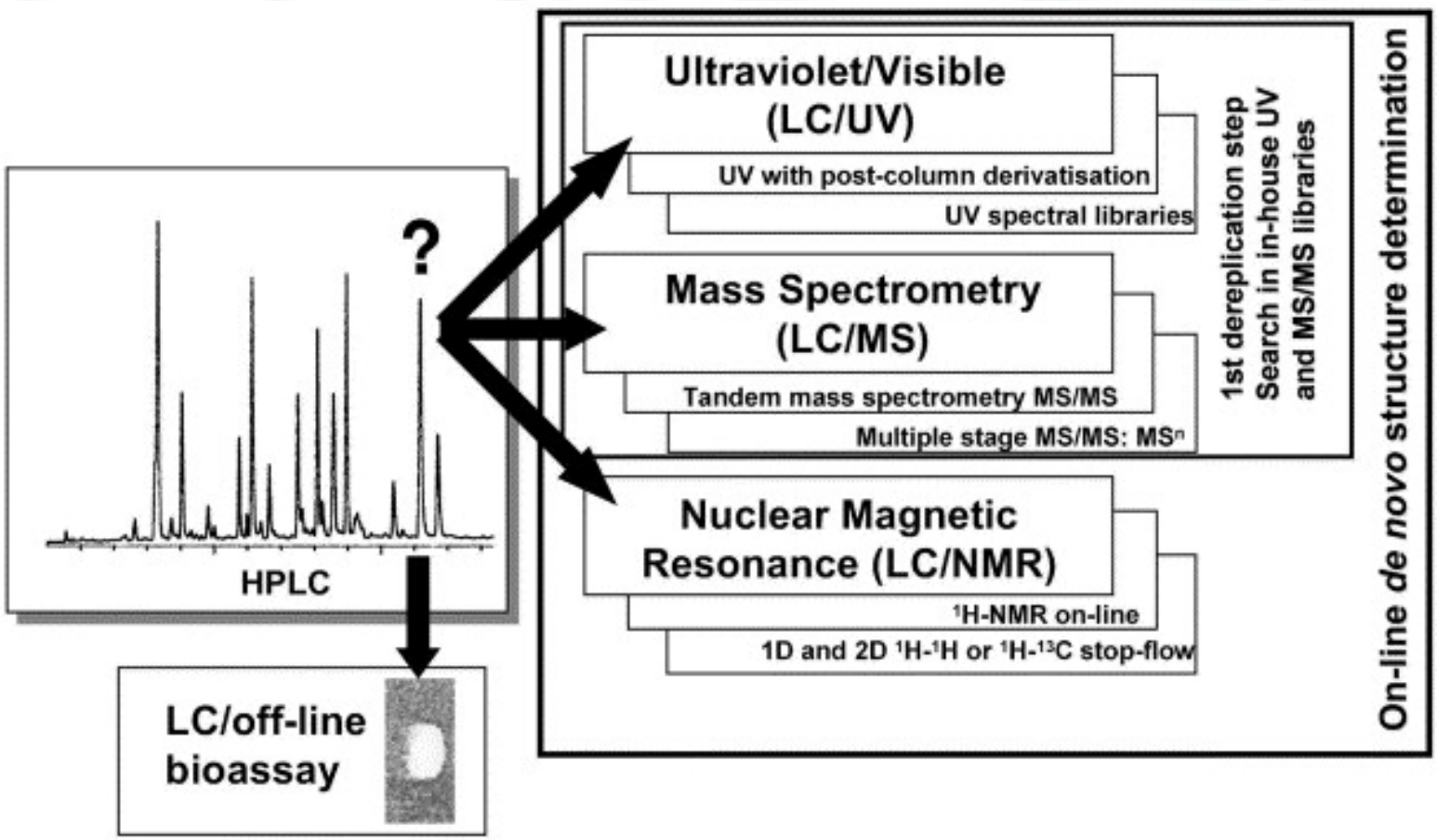
Foods
Metals
Minerals
Tissues

Analysis: Multiple Steps





Analysis: Many Techniques



Bottom Line: “Chemistry” Is (At Least) As Varied as “Physics”

Every measurement task (analyte, analyte quantity, sample matrix, amount of sample, and required accuracy) may present unique metrological challenges!

You’ve just had ≈3 days of metrology in various aspects of physics…

… so we’d best simplify a bit and hurry along.

Our View of Metrology

- Metrology is the stuff needed so data can support informed decision making.
  - in a good world, decisions are informed with data
    - which are the results of measurements!
- Calculus of Confidence
  - metrology is the ‘formal’ system that tells us how well we trust those data

Calculus of Confidence

- The tools of metrology:
  - Traceability
  - Uncertainty
  - Validation

- enable this **calculus of confidence** by which decisions are informed by measurement results with established confidence.

Tools of the Trade

- Measurement Uncertainty
  - is a non-negative parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used
- Metrological Traceability
  - is a property of a measurement result whereby the result can be related to a reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty
- Validation
  - is the provision of objective evidence that a given item fulfills specified requirements where the specified requirements are adequate for an intended use

http://www.bipm.org/en/publications/

Other Tools

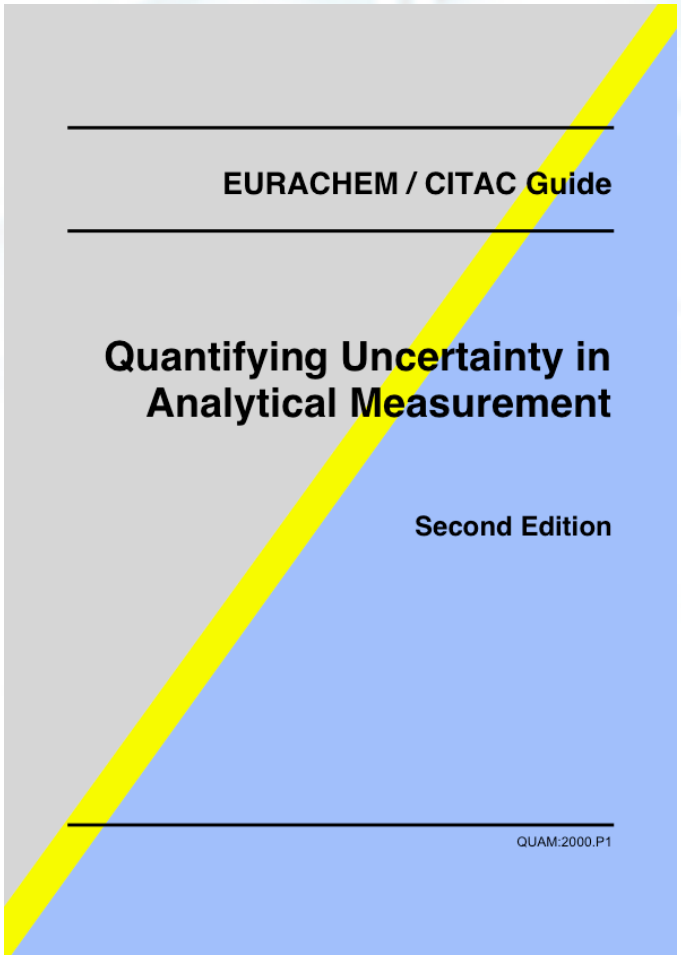
- Quality Management Systems
- Fitness for Purpose
- Data Analysis
  - Statistics and chemometrics
  - UncertaintyMachine
    - http://www.nist.gov/itl/sed/gsg/uncertainty.cfm
  - met*R*ology
    - http://www.nist.gov/itl/sed/gsg/metrology.cfm
- Measurement Process
  - Modularization
  - Filtering

EURACHEM Guides

EURACHEM is a Network of European organizations working to establish a system for the international traceability of chemical measurements and the promotion of good quality practices.

Useful publications include:

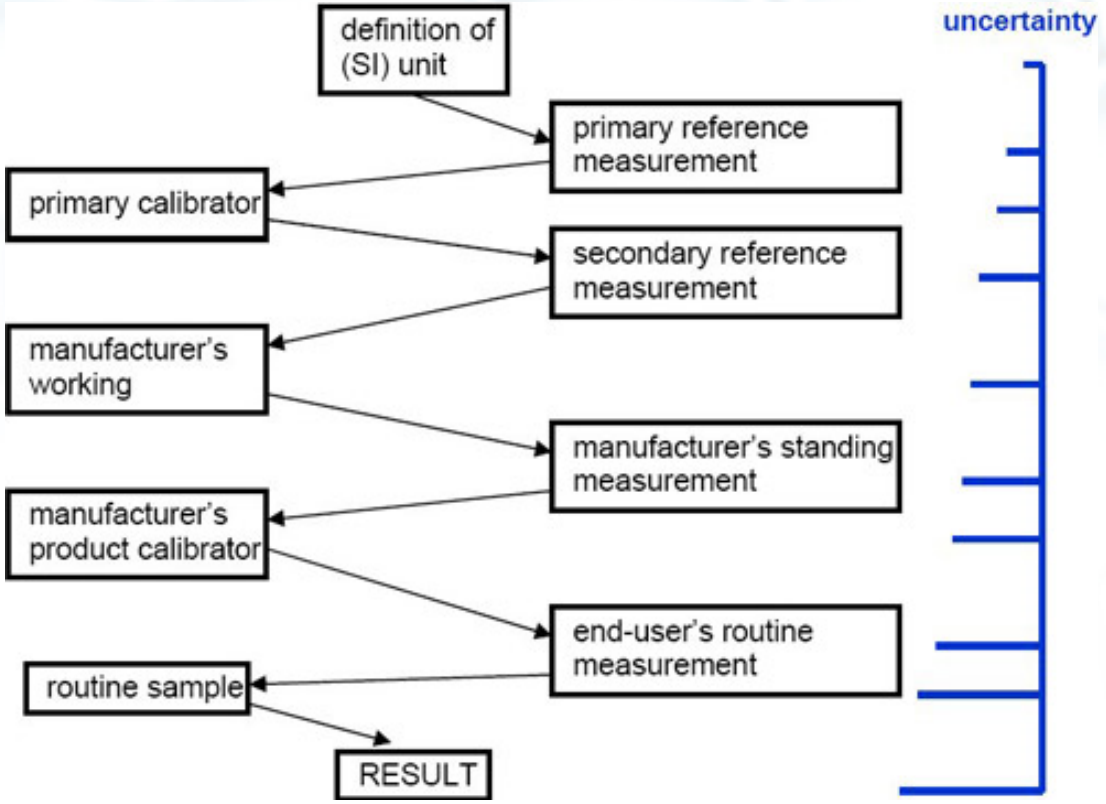
- Quantifying Uncertainty in Analytical Measurement (QUAM)
- Traceability in Chemical Measurement
- The Fitness for Purpose of Analytical Methods
- Guide to Quality in Analytical Chemistry
- see http://www.eurachem.org



Metrological Traceability

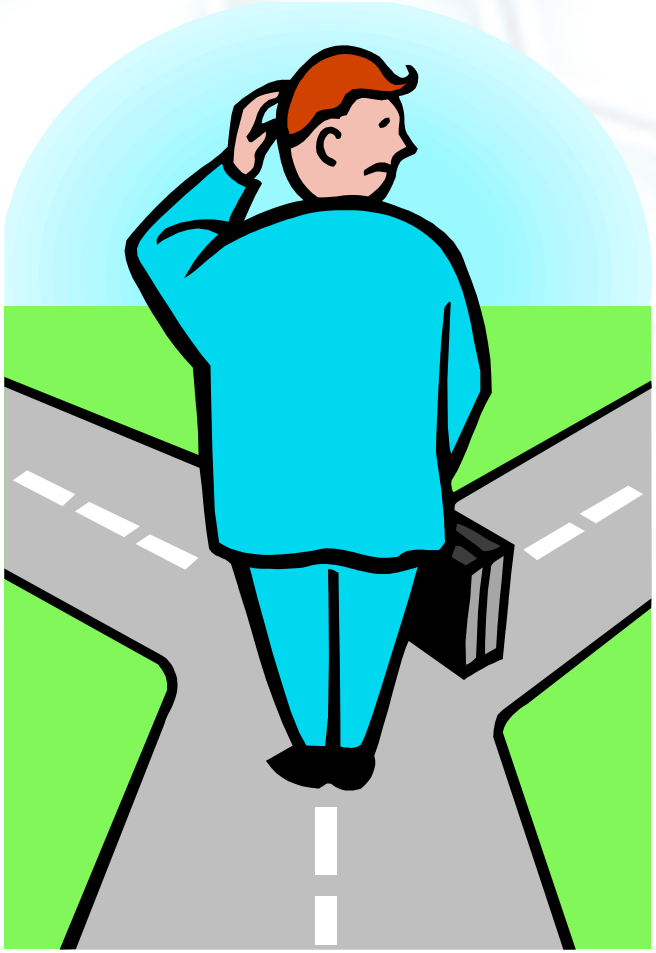
- *Traceability* is how you get units on your result
  - convert from units of your measurement tool to units of the 'standard'

$$C_{Unknown} = \frac{C_{Standard}}{S_{Standard}} S_{Unknown}$$

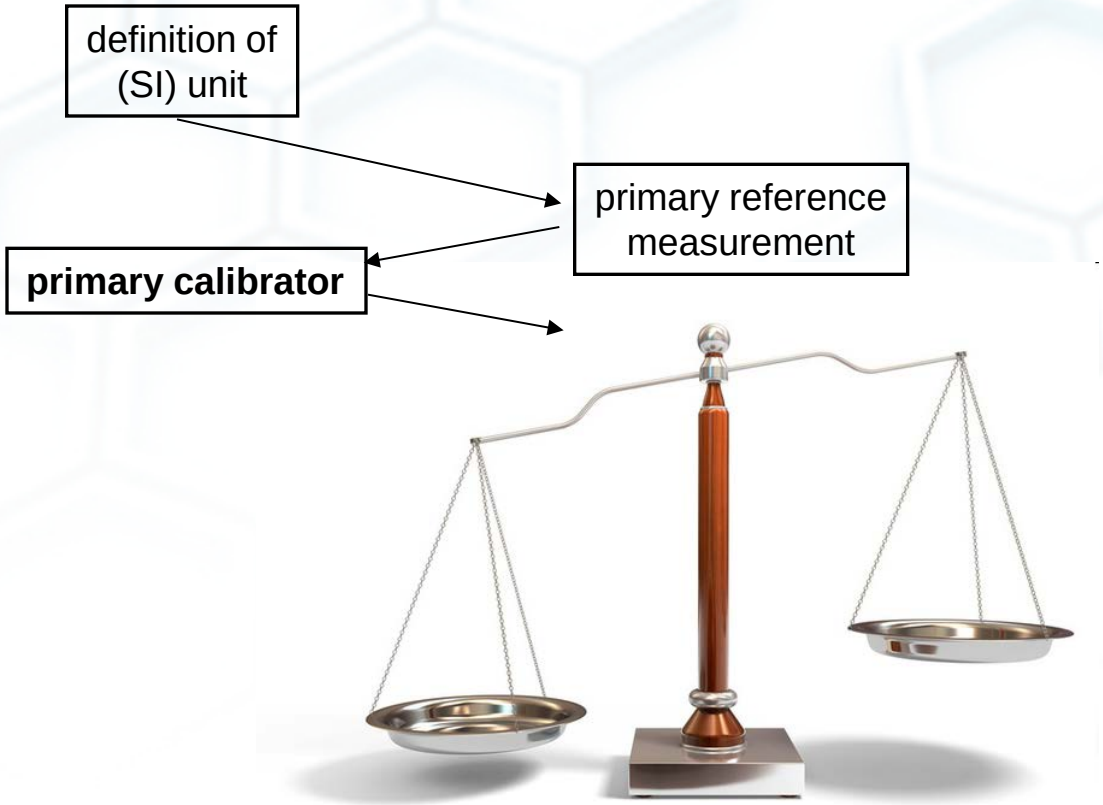


Traceability in chemistry…

- is different.
  - identity
    - what am I measuring, anyway?
  - interference
    - do I get the same response for analyte in my calibration material and in it's matrix?
  - morphology
    - is the analysis the same everywhere in my sample?



Given a “Primary Calibrator”



the rest is just a series of direct comparisons

But Primary **Chemical** Calibrators

Need to be chemically similar to the routine sample

These have the same mass...

...but **not** the same chemical properties

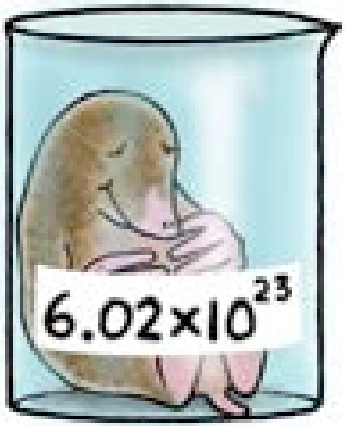
And There Are **Many** Different Chemical Entities

CAS Registry: ≈60,000,000

Commercial: ≈100,000

Commercially available **primary calibrators**: ≈100s

Units: Generally Just a Ratio…



~~Mole~~

$$\frac{\text{Mole analyte}}{\text{Mole sample}}$$

~~Kilogram~~

$$\frac{\text{Mass analyte}}{\text{Mass sample}}$$

“Pure” Materials

And the **primary calibrators** are “pure” materials

“… the determination of purity can never be a standardized procedure …”

W.M. Smit. *The concept of purity, and its bearing on methods used to characterize purity*. In: L.A.K. Stavely, ed., “The Characterization of Chemical Purity. Organic Compounds”, International Union of Pure and Applied Chemistry, Physical Chemistry Division, Commission on Physicochemical Measurements and Standards, Butterworth & Co. (Publishers) Ltd, London, UK (1971), pp. 7-10.

…but there is a process

1) Establish purpose and what constitutes fitness for purpose
2) Obtain suitable material and confirm identity of **primary component** (**PC**)
3) Determine PC with direct methods
4) Determine PC as 1-∑**impurity components** (**ICs**)
5) Harmonize and combine like values from independent sources
6) Combine results and estimate uncertainty

http://www.nist.gov/manuscript-publication-search.cfm?pub_id=901295

Method validation

- "checks the model"
  - tests completeness
  - tests assumptions
  - helps establish an uncertainty budget
- identifies relevant parameters to keep under control
- **tests** scope

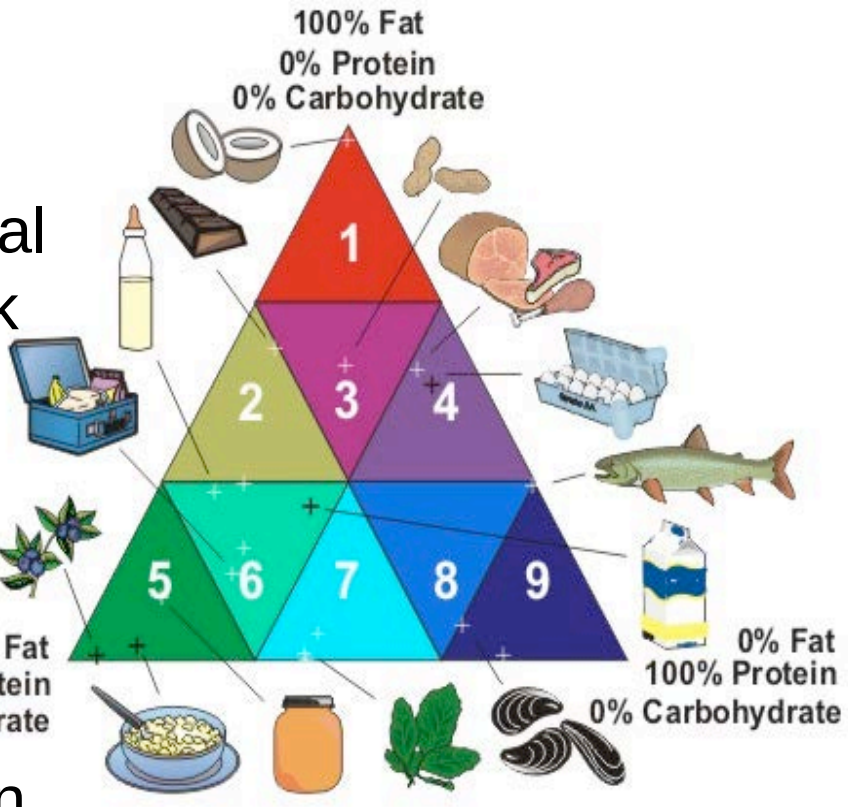
Validation in chemistry…

- is different.
  - **establish** scope
  - present a clear measurement model with objective evidence that…
    - the analyte is what's being measured
    - the result is robust with regard to interference

Natural Matrix CRMs

"Yellow Light" standards

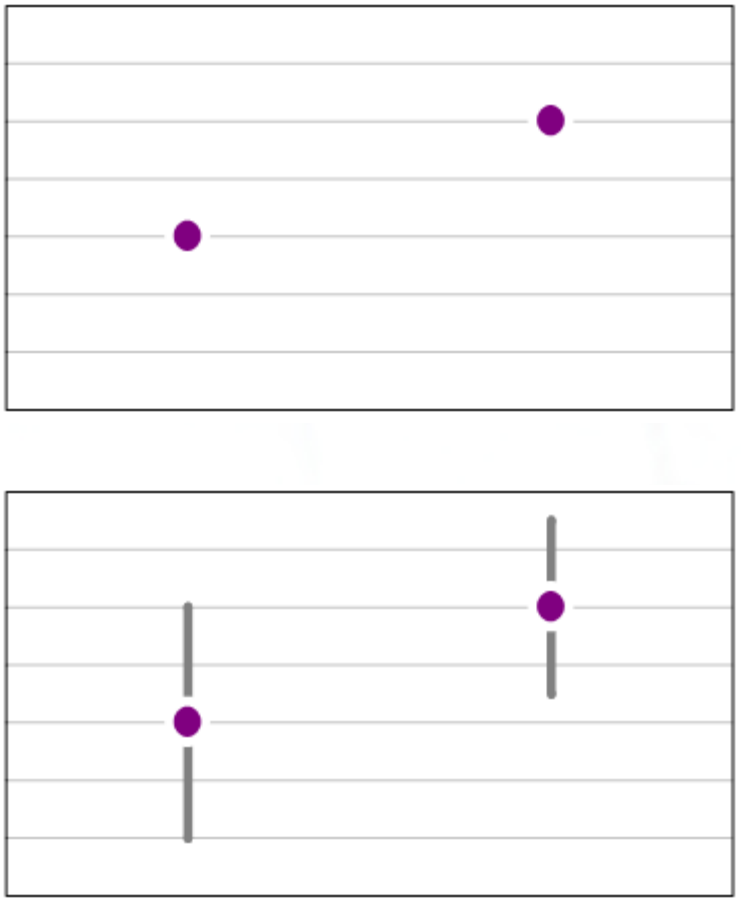
- CRMs with chemical/biological properties similar to your task
- Getting a "wrong" result for a CRM indicates your measurement process is inadequate
- Getting the "right" result increases confidence in your measurement process



AOAC Food Triangle

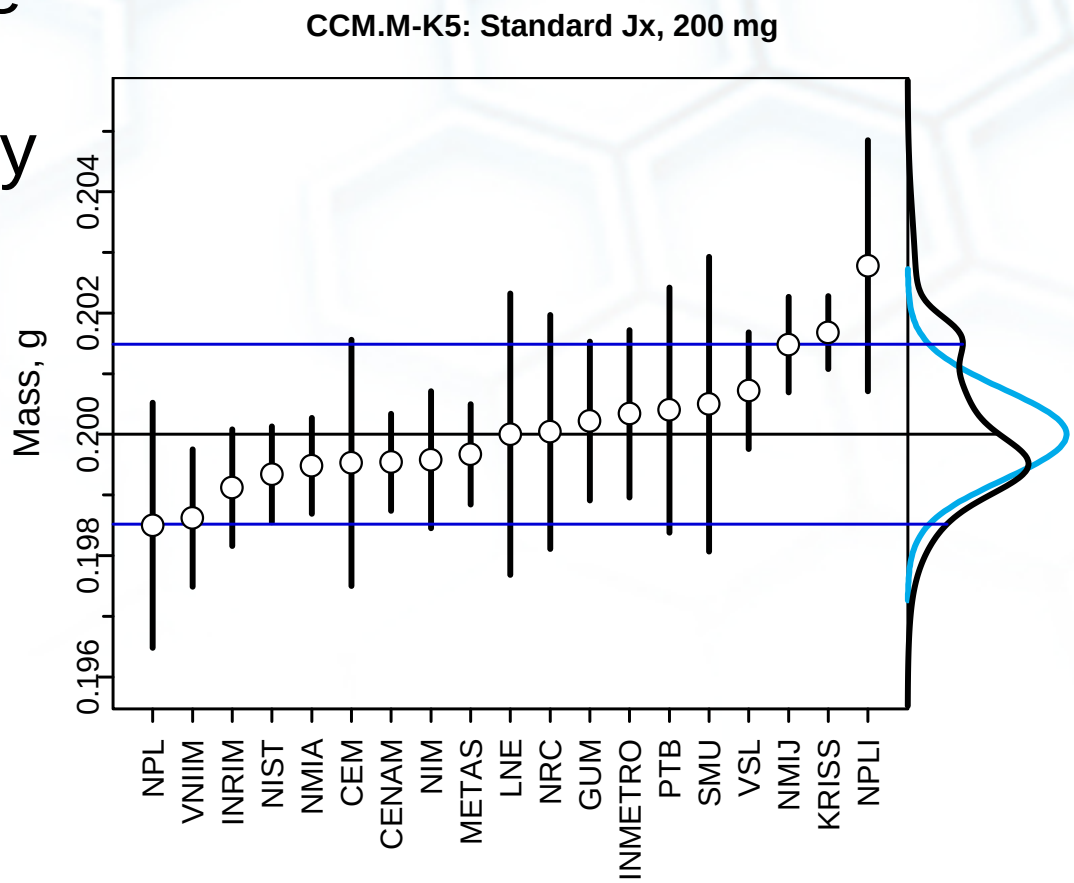
Measurement Uncertainty

- Are these results the same?
- how well do you know the result?
  - essential part of being able to compare!
- are these results good enough?
  - fit-for-purpose



Basic Stats: Dot&Bar Charts

Visual summary of the results, x_i and $U_{95}(x_i)$, from an interlaboratory comparison

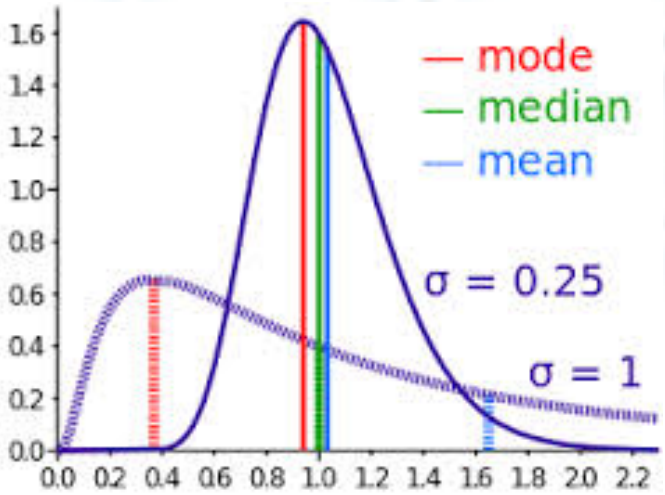


"Key Comparisons" are done by NMIs to help support calibration and measurement claims

http://www.bipm.org/en/cipm-mra/

Basic Stats: Robust Estimates

Median: estimate of location where
50 % of values are smaller,
50 % are greater



MADe: estimate of dispersion that approximates the standard deviation of the most consistent 50 % of the population

$$\text{MADe} = 1.4826 \times \text{Median}(|x_i - \text{Median}(x)|)$$

http://www.bipm.org/cc/CCQM/Allowed/10/CCQM04-15.pdf

Evidence from Key Comparisons

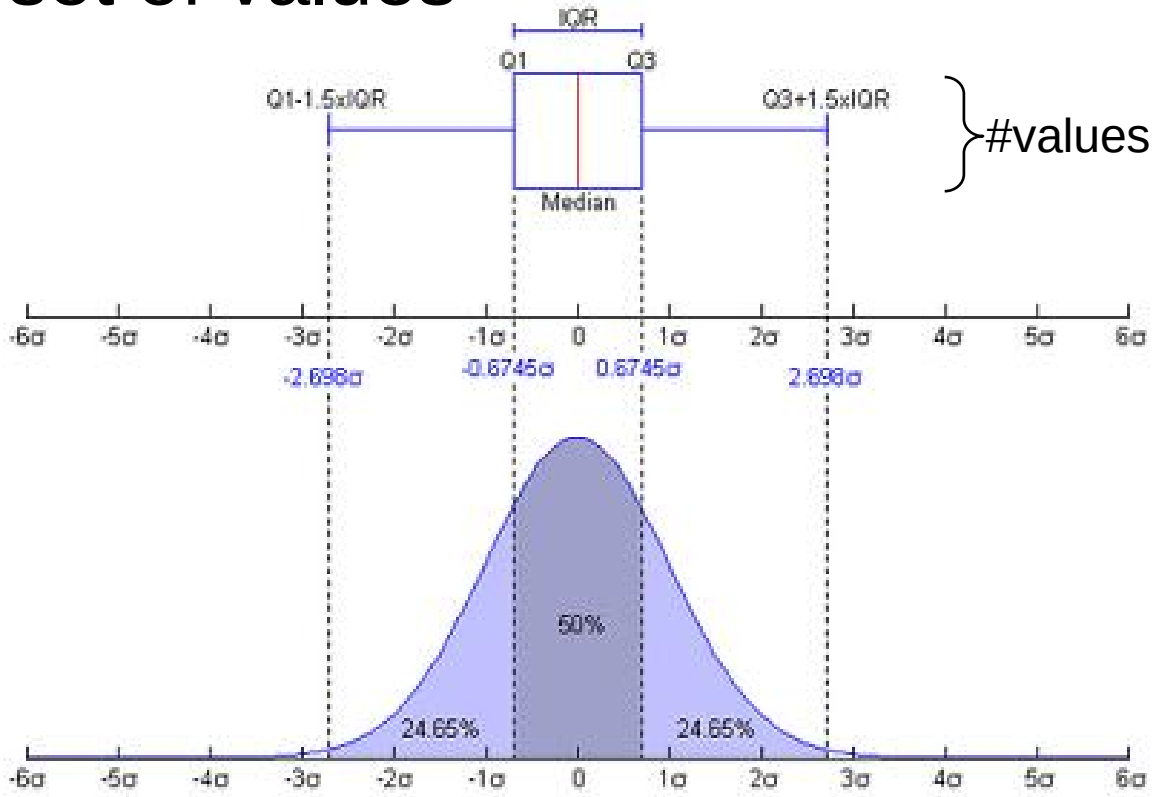
Comparison	#NMI	Median	MADe	MedianU	RelU	Cover	
CCM.M-K1: 1 kg standards in stainless steel, 1 kg	15	1000	7.42E-06	1.45E-05	7.42E-09	0.51	
CCM.M-K2: multiples of the kilogram, 100 mg	14	0.1	5.19E-07	4.75E-07	5.19E-06	1.09	
CCM.M-K2: multiples of the kilogram, 2 g	14	2	1.04E-06	1.00E-06	5.19E-07	1.04	
CCM.M-K2: multiples of the kilogram, 20 g	14	20	3.12E-06	3.45E-06	1.56E-07	0.90	
CCM.M-K2: multiples of the kilogram, 500 g	14	500	9.64E-06	9.50E-06	1.93E-08	1.02	
CCM.M-K3: Comparison, 50 kg	14	50000	2.97E-03	3.98E-03	5.93E-08	0.75	
CCM.M-K5: Standard Jx, 1 g	19	1	1.07E-03	8.20E-04	1.07E-03	1.30	
CCM.M-K5: Standard Jx, 2 kg	19	2000	6.08E-02	4.65E-02	3.04E-05	1.31	
CCM.M-K5: Standard Jx, 200 g	19	200	8.31E-03	6.30E-03	4.15E-05	1.32	
CCM.M-K5: Standard Jx, 200 mg	19	0.2	7.42E-04	5.65E-04	3.71E-03	1.31	
CCM.M-K5: Standard Jx, 50 g	19	50	4.15E-03	3.30E-03	8.31E-05	1.26	
CCM.M-K5: Standard Jy, 1 g	19	1	8.31E-04	8.80E-04	8.31E-04	0.94	
CCM.M-K5: Standard Jy, 2 kg	19	2000	7.86E-02	5.80E-02	3.93E-05	1.36	
CCM.M-K5: Standard Jy, 200 g	19	200	6.53E-03	6.25E-03	3.26E-05	1.04	
CCM.M-K5: Standard Jy, 200 mg	19	0.2	8.46E-04	5.10E-04	4.23E-03	1.66	
CCM.M-K5: Standard Jy, 50 g	19	50	3.41E-03	3.45E-03	6.82E-05	0.99	
					16	16	N
					4.28E-07	0.98	25 %
					3.60E-05	1.07	50 %
					2.70E-04	1.31	75 %

Mass standard KCs published in the CIPM database

http://kcdb.bipm.org/AppendixD/default.asp

Basic Stats: Boxplot

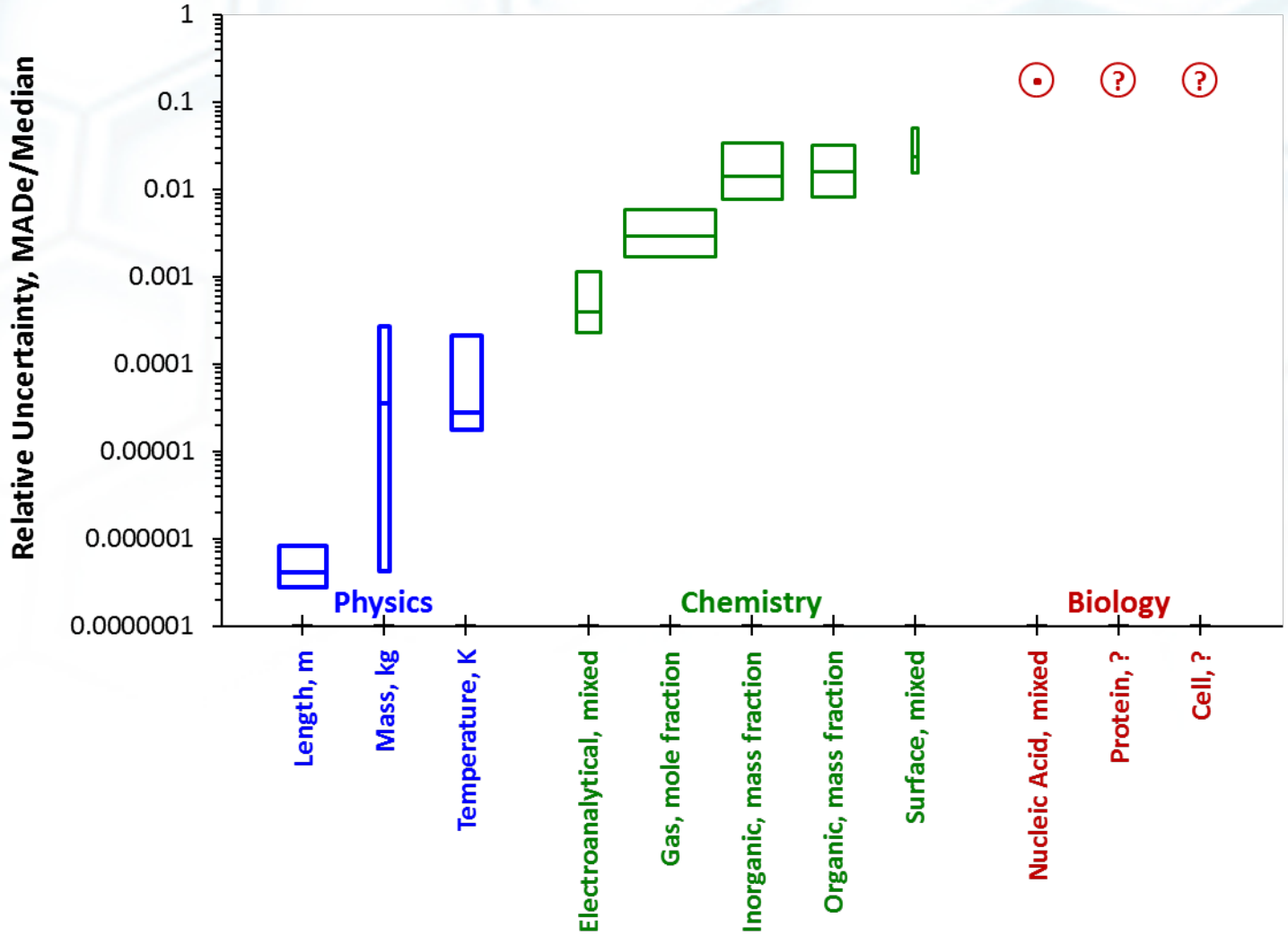
Visual summary of the distribution of a set of values



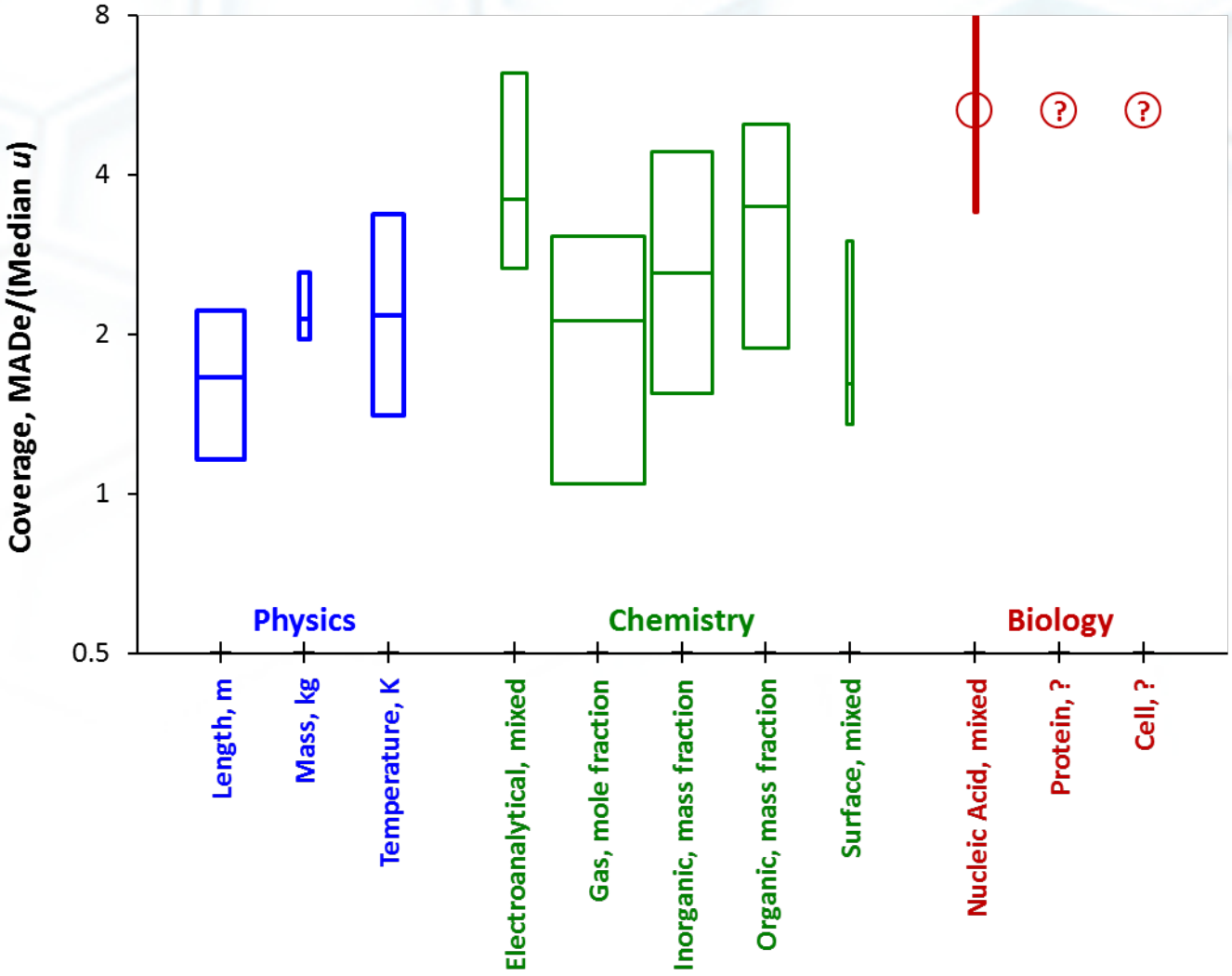
The View From the CCQM

- Working Groups
  - Electroanalytical (EAWG)
  - Gas (GAWG)
  - Inorganic (IAWG)
  - Organic (OAWG)
  - Surface (SAWG)
  - Bioanalysis (BAWG)
    - Nucleic acids
    - Proteins
    - Cells

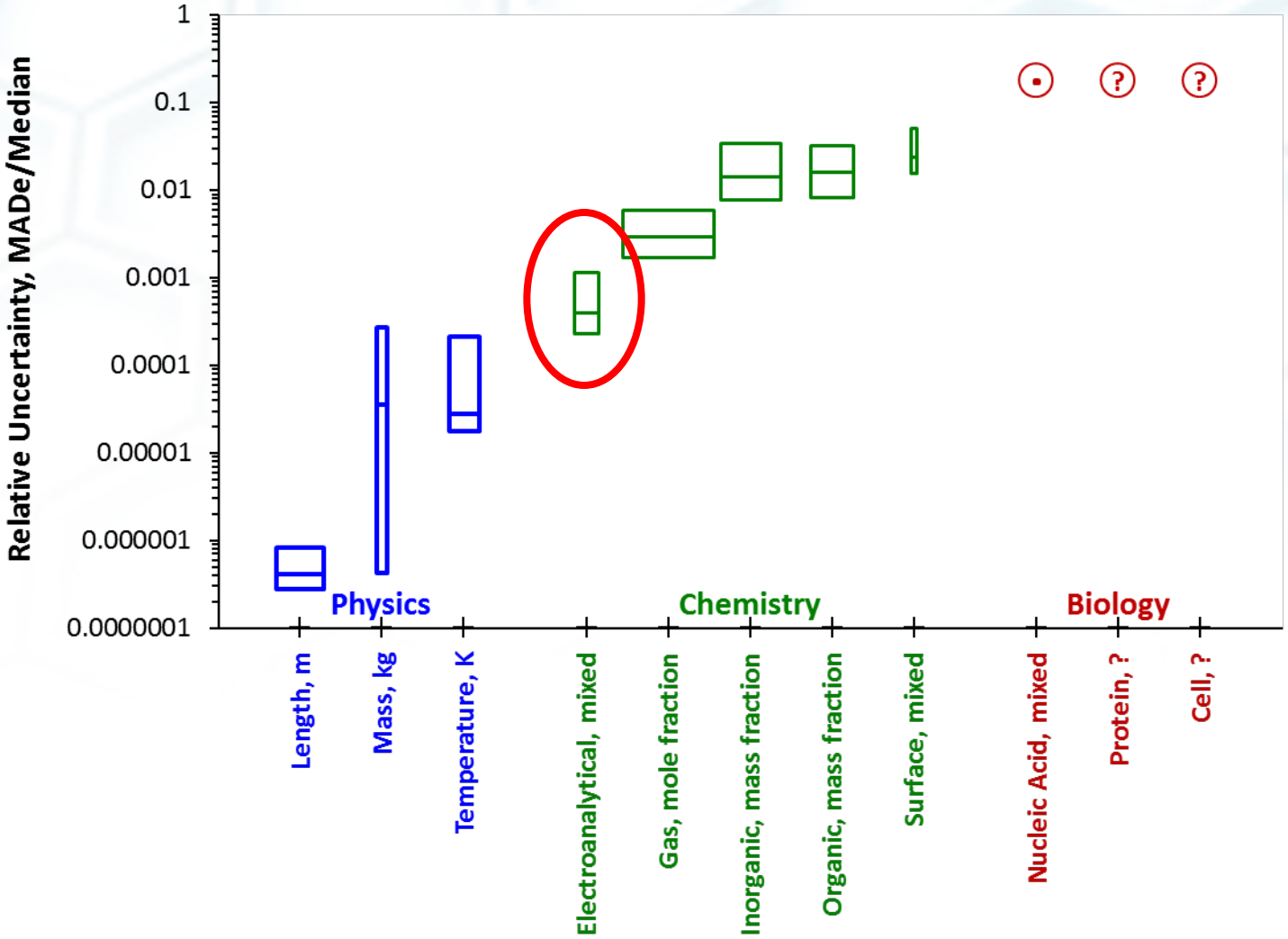
Relative Uncertainties: SD(pop)/*x*



Uncertainty Coverage: *u*(pop)/*u*(*x*)



So What's Going On?



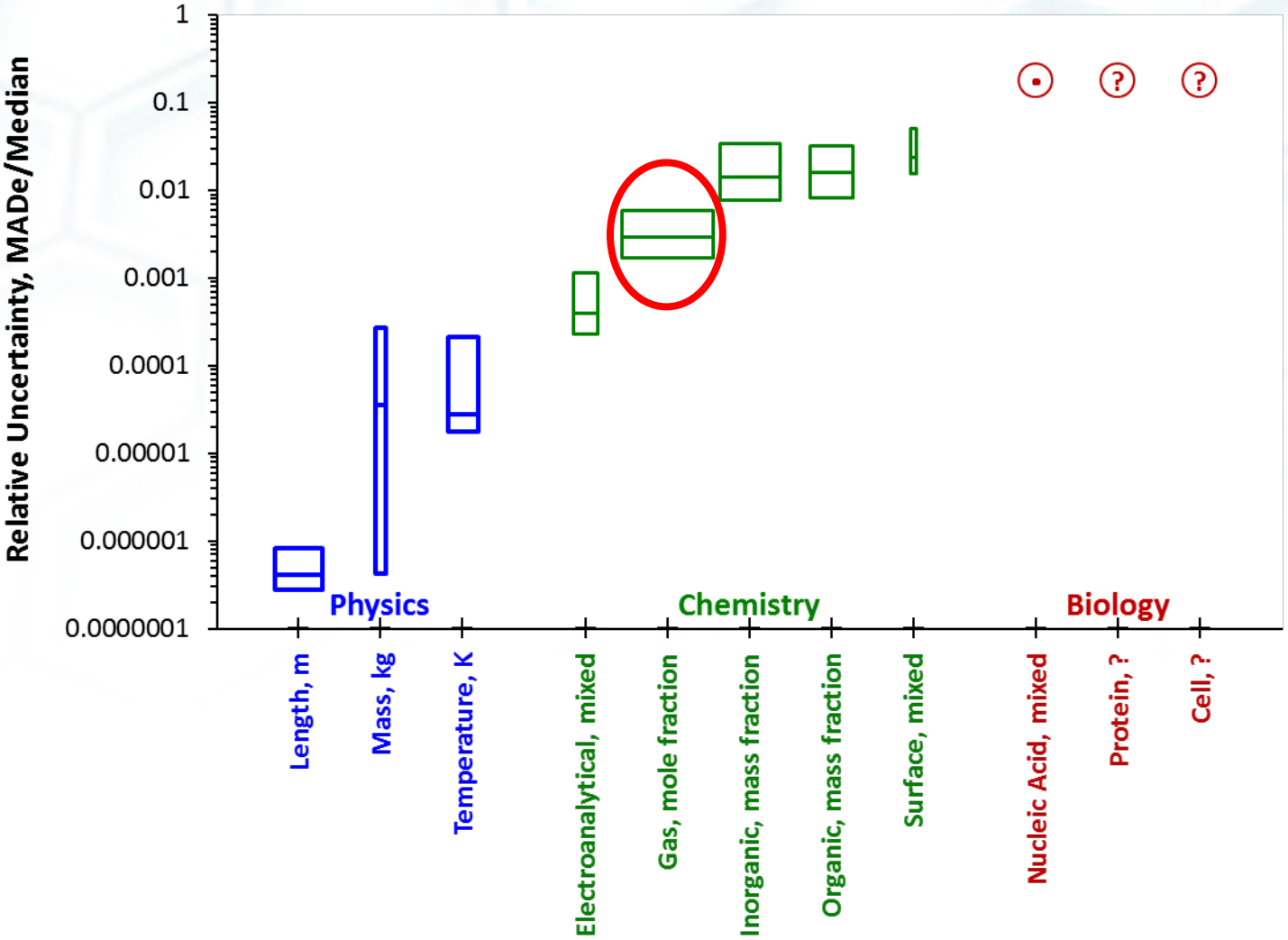
Electroanalytical (EAWG)

Responsible for studies of

- pH
- Electrolytic conductivity
- Titrametric standards
- Reductometric standards

Simple measurands
Simple samples
“Physics-like” measurement processes

So What's Going On?



Gas Analysis (GAWG)

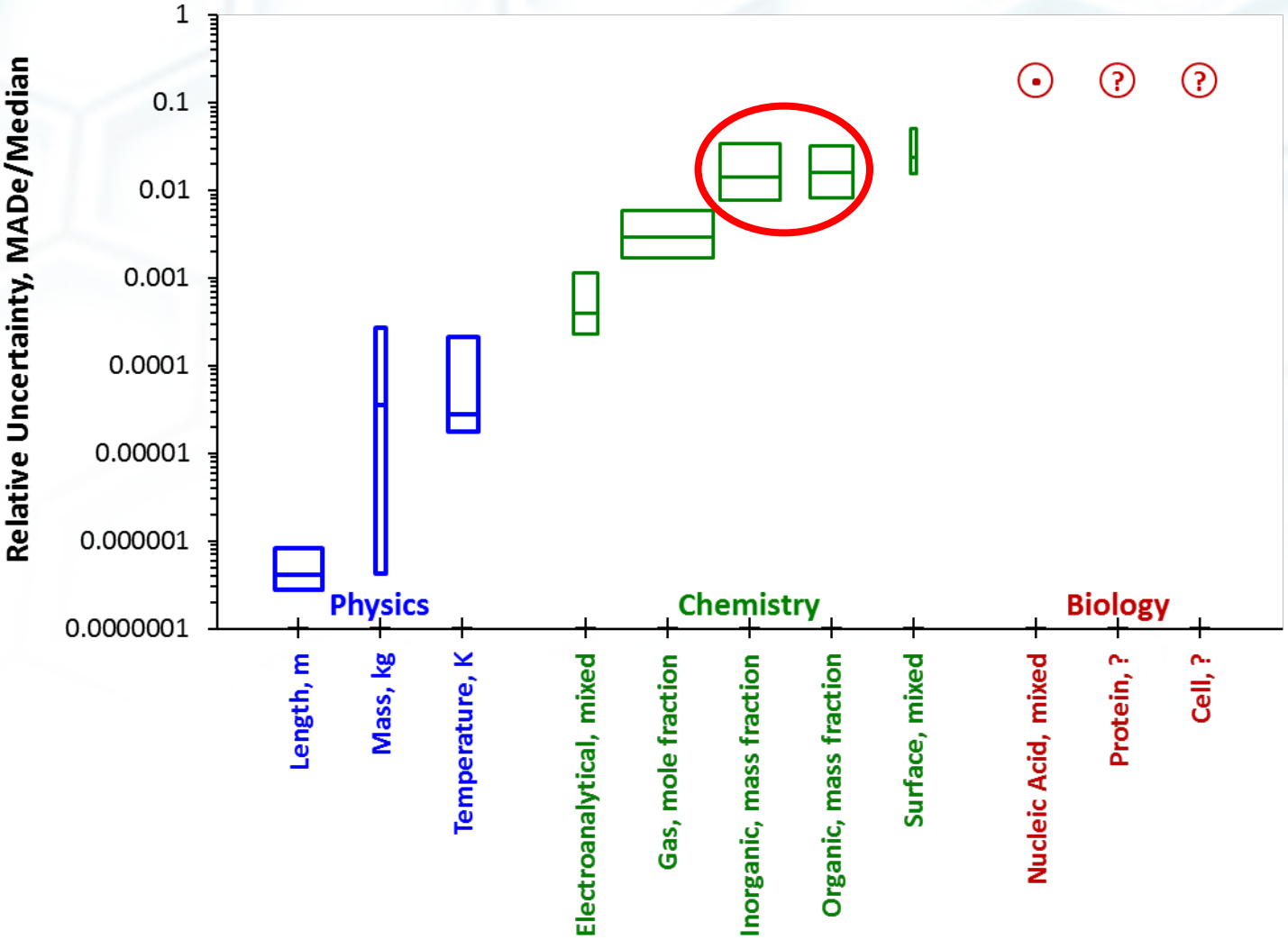
Responsible for studies of

- Stable gases (e.g., methane)
- Reactive gases (e.g., ozone)

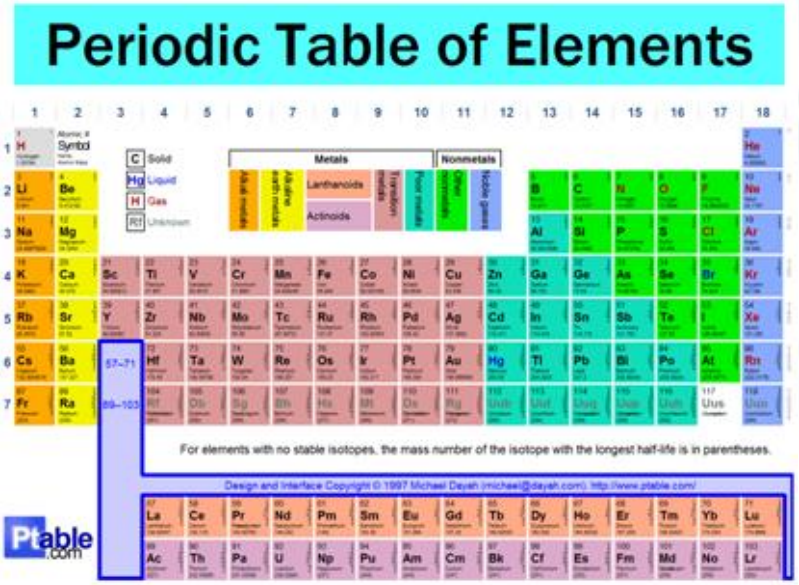
in N_2, air, natural gas

Relatively simple measurands
Relatively simple samples
Relatively simple measurement processes

So What's Going On?



Inorganic Analysis (IAWG)



Responsible for studies of

- Elemental composition
- Isotopic composition
- Valence speciation

in alloys, foods, minerals, sediments, soils, tissues, …

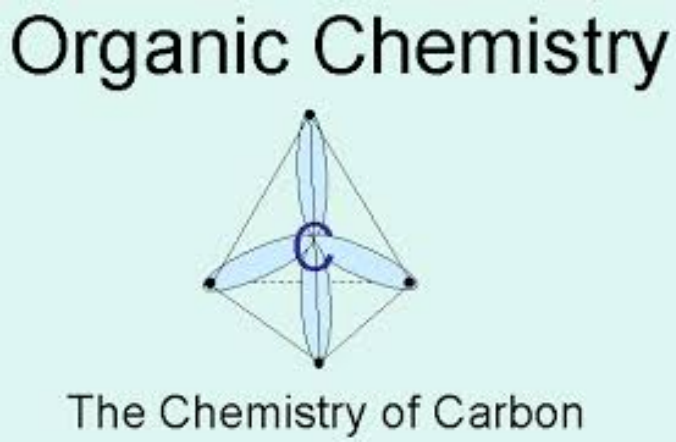
Simple to complex measurands
Simple to complex samples
Simple to complex measurement processes

Organic Analysis (OAWG)

Responsible for studies of

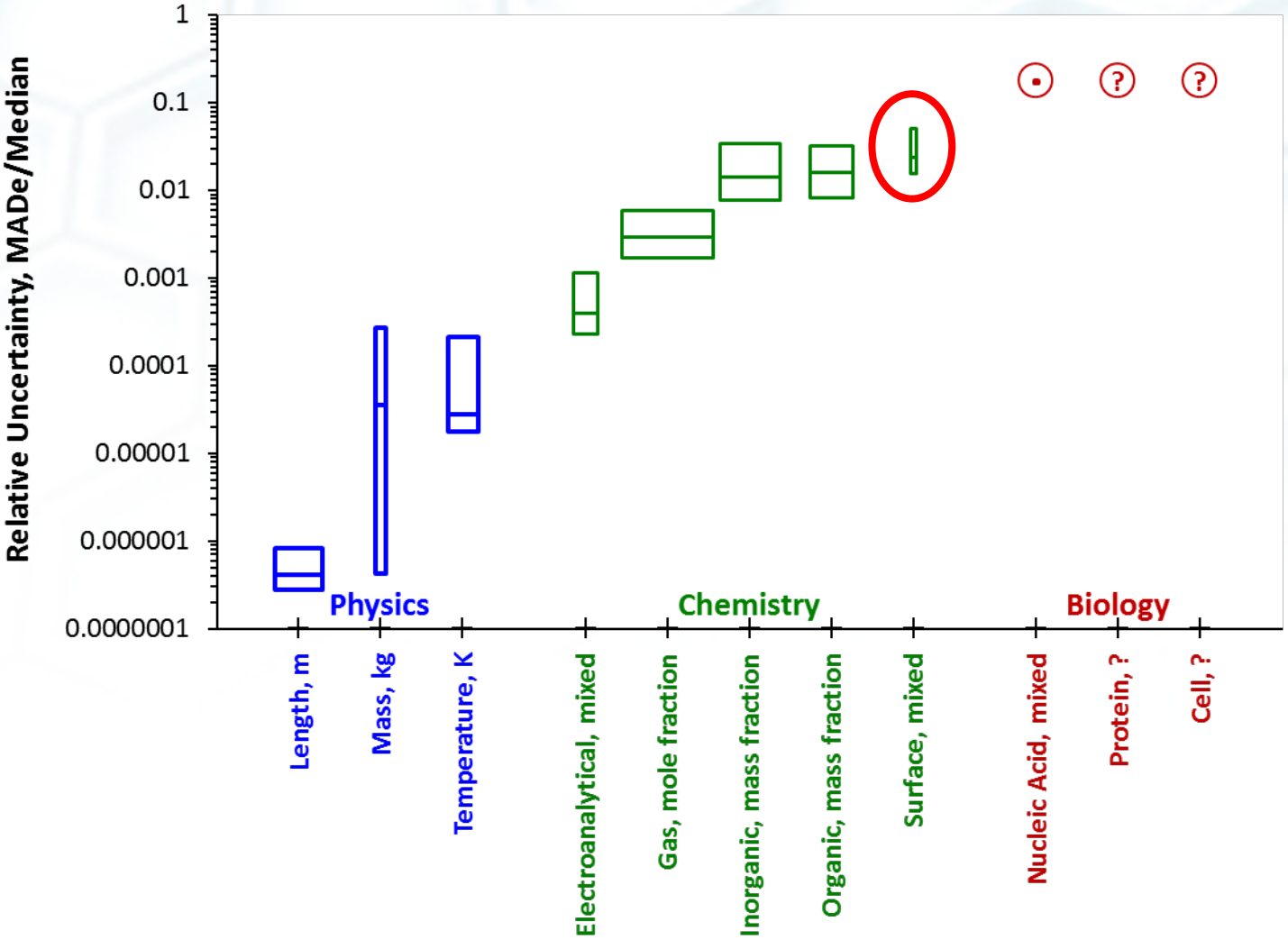
- Liquids, solids, solutions
- Relatively small molecules (< 1000 amu)

in “pure” materials and foods, sediments, soils, tissues, …



Simple to complex measurands
Simple to complex samples
Simple to complex measurement processes

So What's Going On?

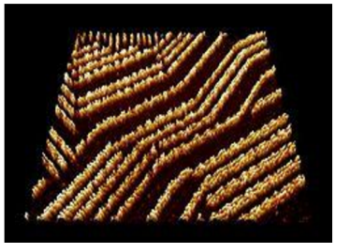


Surface Analysis (SAWG)

Responsible for studies of **Surface Chemistry**

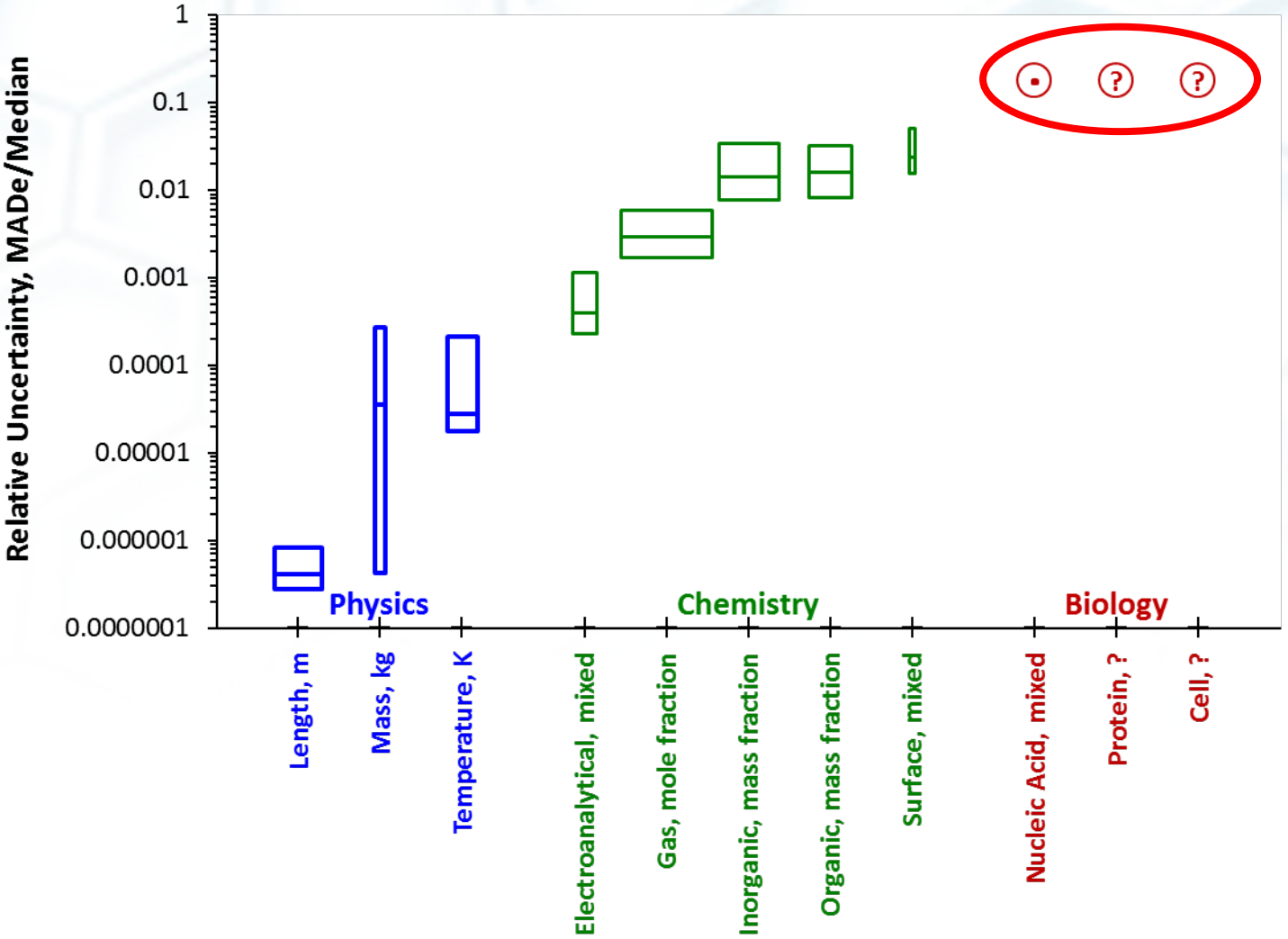
the study of physical and chemical phenomena that occur at the interface of two phases, including solid-liquid interfaces, solid-gas interfaces, solid-vacuum interfaces, and liquid-gas interfaces

Note: very few published KCs



Simple to complex measurands
Relatively complex measurement processes
Relatively complex samples

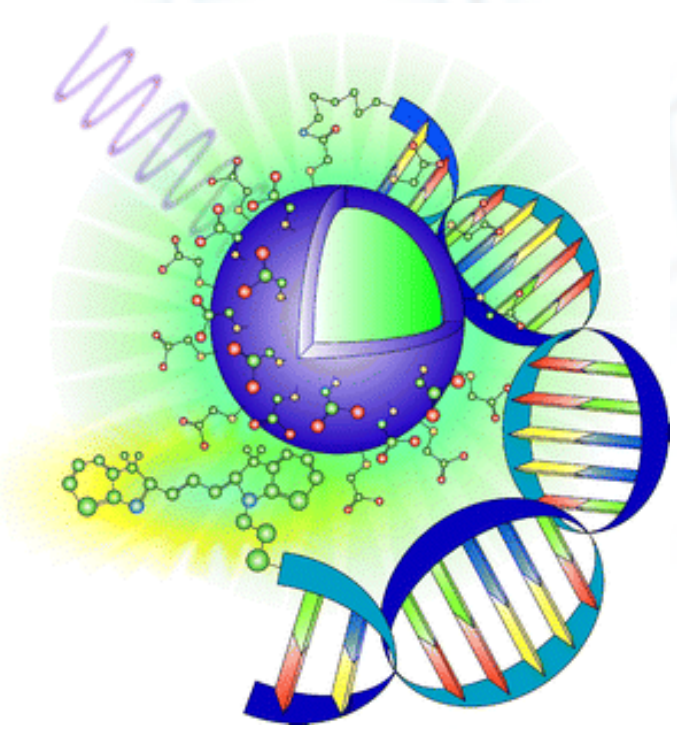
So What's Going On?



Bioanalysis Analysis (BAWG)

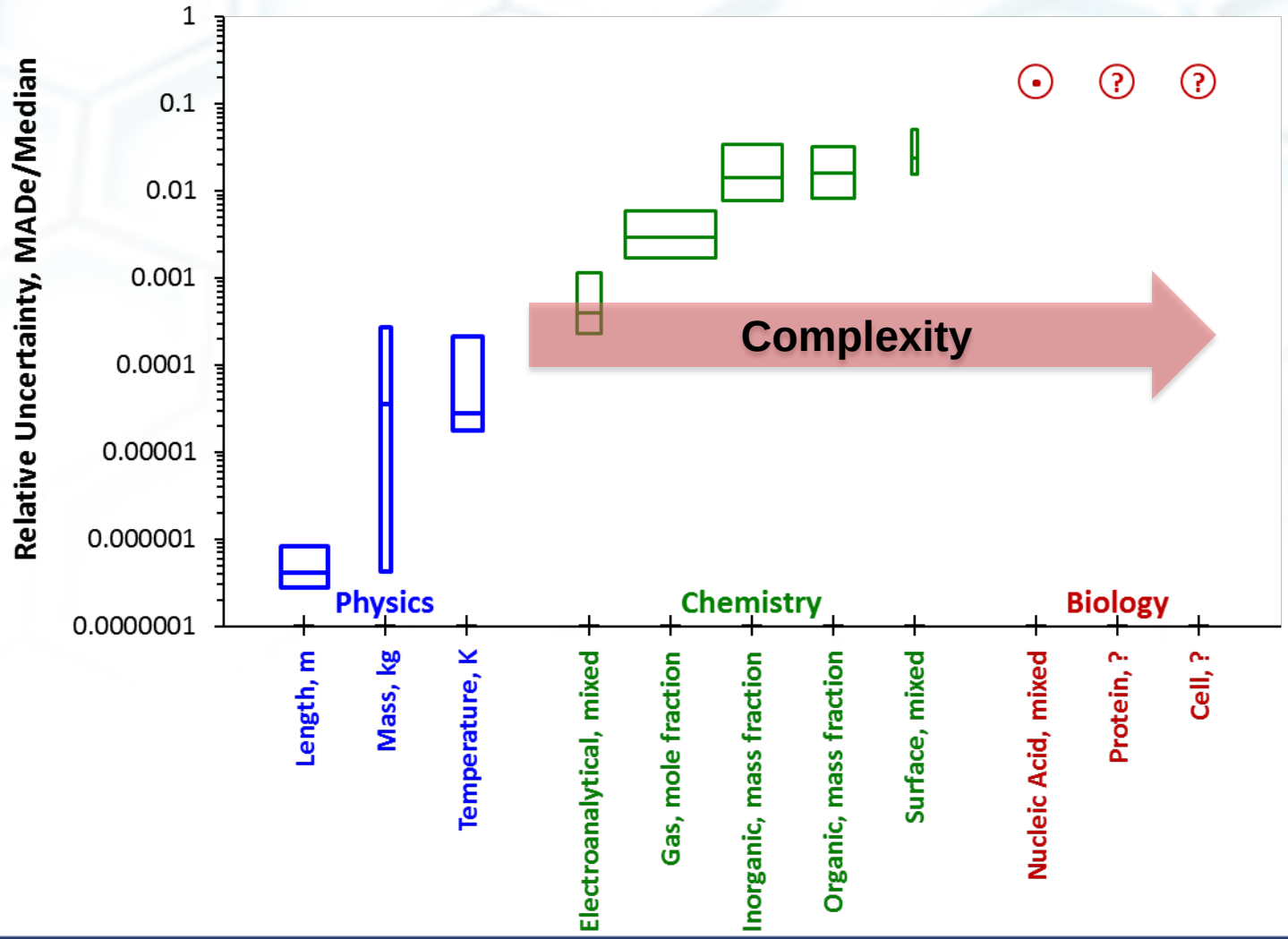
Responsible for studies of

Everything Else



Complex measurands
Complex measurement processes
Complex samples

So What's Going On?



Break Time!