Elemental Metabolomics: Definition, determination of geographic, genetic and processing origin

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TERM	DESCRIPTION
Metabolite	An intermediate or final product of chemical reactions in an organism or a cell.
Metabolome	A complete set of small-molecules (molecular weight <1500 Da), that exist in a given biological tissues or sample
Metabolomics	Quantification of metabolome in target samples, monitoring their change, and characterization of phenotypes over time or in response to various stimuli.
Elemental metabolomics	Quantification and characterization of total concentration of chemical elements in biological samples and monitoring their changes for characterization of metabolic processes.
Elemental profiling	Quantification of chemical elements in a given sample or specimen.
Elemental fingerprinting	Classification of biological samples using their elemental profiles.
Elemental signature	Elemental composition derived from a representative selection of samples that represents some condition or status (e.g. geographic origin, genetic origin, or health status).

Applications of Elemental Metabolomics

Plant & Environmental Metabolomics

- **find association between genes and elements in plant tissues and responses to its environment (phenotype)**
- **assess gene function (genotype)**
- **improve plant health**
- **strategies for improved bioremediation**
- **decrease pesticide and herbicide use**

Food & Nutritional Metabolomics

- **analyze foods for elemental/compound profiles**
- **food authenticity**
- **biomarker-detection for food quality or safety**
- **complex toxicity studies**
- **food contaminants and their interactions**
- **Nutritional and environmental effects on animal health**

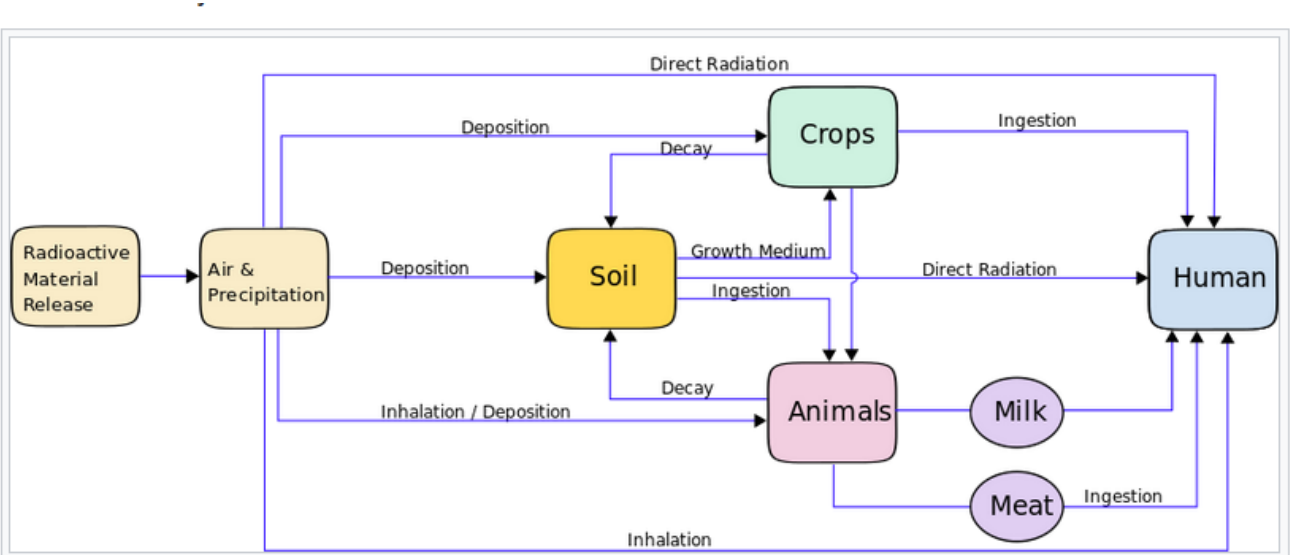
Clinical Metabolomics

Applications of Elemental Metabolomics

Clinical Metabolomics

- **biomarker-discovery and new laboratory tests development**
- **study of nutritional deficiencies and toxic exposure on human health**
- **chronic disease management and delay/prevention**
- **genomic/proteomic basis of effects of elemental homeostasis**

Example:



Airborne radioactive material can have an effect on humans via a range of routes.

Metabolites

How many?

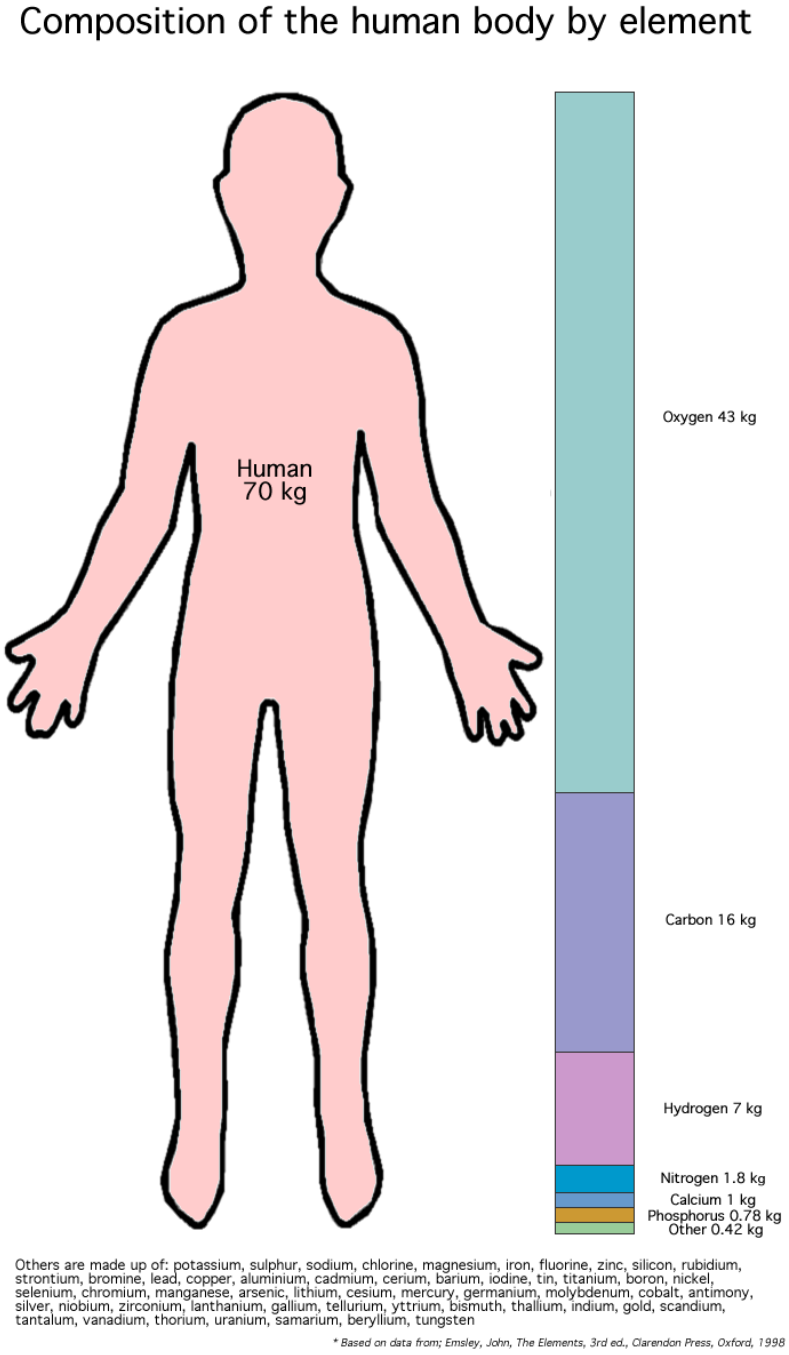
3,000 to 6,000 metabolites of interest .
The Human Metabolome Database (HMDB) has some 42,000 metabolites (SEP 16).
>200,000 metabolites are present in the plant kingdom

Human Metabolome Project (Wishart *et al*., 2007)

2500 metabolites, 1200 drugs and 3500 food components

High-throughput metabolomics

300 to 800 metabolites in a sample per minute



http://www.derekshirlaw.co.uk/the-elemental-composition-of-the-human-body/

Mega elements
C, H, N, O 96%

Essential macroelements
Ca, Cl, K, Mg,
Na, P, S 3%

Essential microelements
Co, Cu, Cr, Fe,
I, Mn, Mo, Se, Zn

Modulating microelements
As, Br, Ni, Si, Sn,
Sr, V, B, Cd, Li, Pb

Other elements
Al, Ba, Rb, Ti

Toxic elements
As, Be, Cr, Cd, Hg, Pb

Approximately 96% of elemental composition of human body, by mass, consists of four elements (C, H, N and O), we term them **“mega elements”**.

Another 3.25% consists of **macro elements** (Ca, Cl, K, Mg, Na, P, and S)

The remaining are called **trace elements** (Al, As, B, Ba, Br, Cd, Ce, Co, Cs, Cu, Cr, F, Fe, Ge, Hg, I, Li, Mn, Mo, Ni, Pb, Rb, Se, Si, Sn, Sr, Ti, and Zn) or

ultratrace elements (Ag, Au, Be, Bi, Ga, Hf, In, Ir, Nb, Os, Pd, Pt, Re, Rh, Ru, Sb, Sc, Ta, Tc, Te, Th, Tl, U, V, W, Y, Zr, and the 14 lanthanides).

A human body of 75 kg would have approximately 72.5 kg of four mega elements, 2.5 kg of seven macro elements (Ca and P make ~1.9 kg), **15 g of trace (total of 28)**, and **1 mg of ultra-trace (total of 41)** elements

Instrumentation for elemental profiling **PAST**

ICP-OES

Flame-AAS

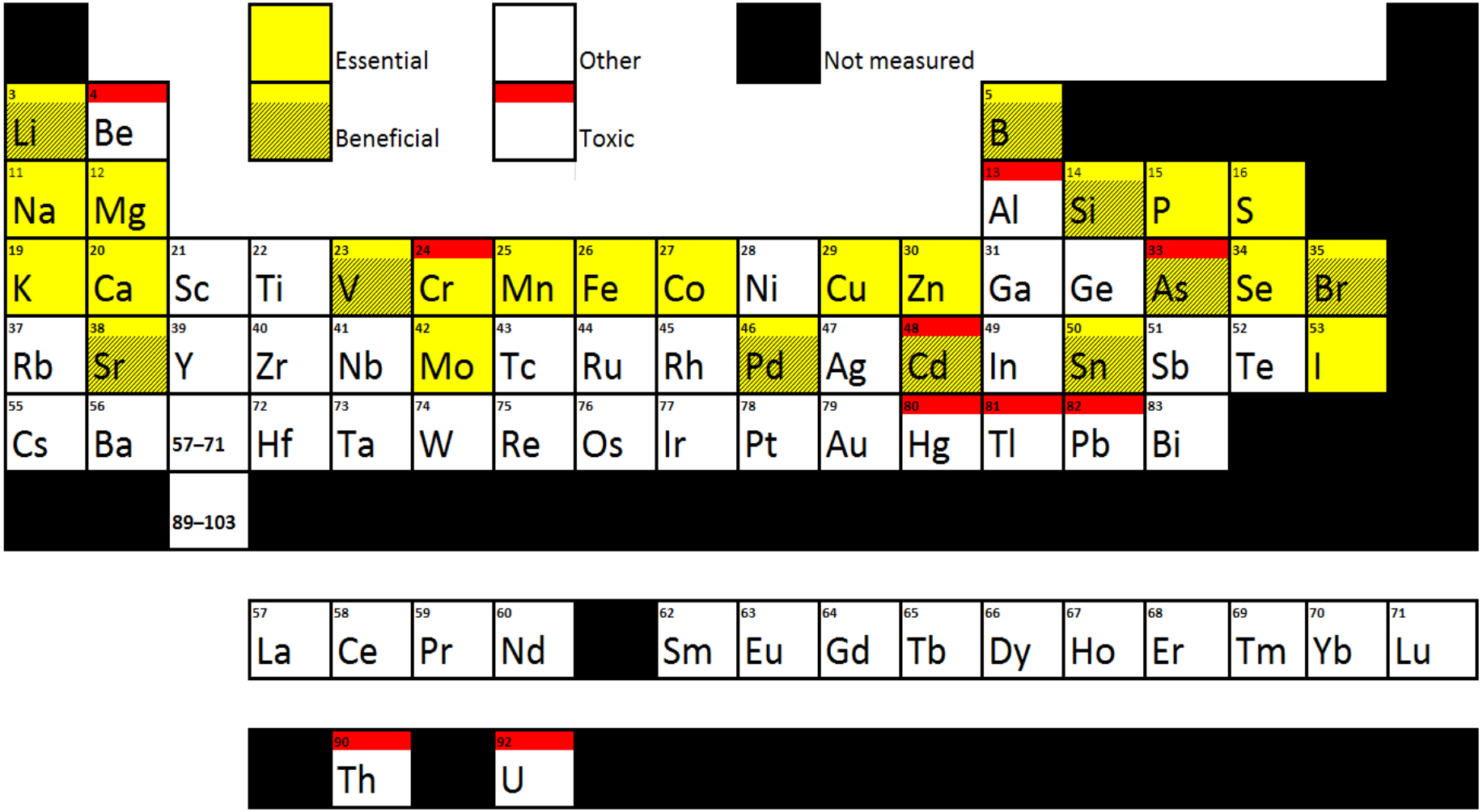
GF-AAS

400-800 measurements/8 hours

Instrumentation for elemental profiling **NOW**

ICP-MS

>70 elements, 6-17,000 measurements/8 hours



Common elemental analytes detectable and measurable by ICP-MS are shown. Groupings into essential, beneficial, common without clearly defined function, and toxic elements are somewhat arbitrary. For example, the toxicity-essentiality duality of chromium is related to speciation – trivalent Cr(III) is an essential nutrient considered non-toxic, while hexavalent Cr(VI) is considered toxic and carcinogenic.

ELEMENTAL METABOLOMICS

Comprehensive Elemental profiling, >70 elements,
High throughput, up to 17,000 cost efficient measurements/8 hours

Elemental signatures, databases

Bioinformatics, algorithms & tools for Big Data, scaling to reference materials

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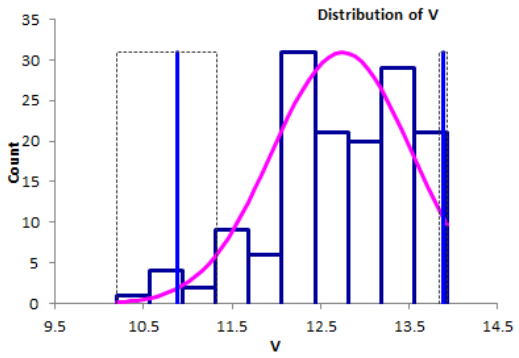
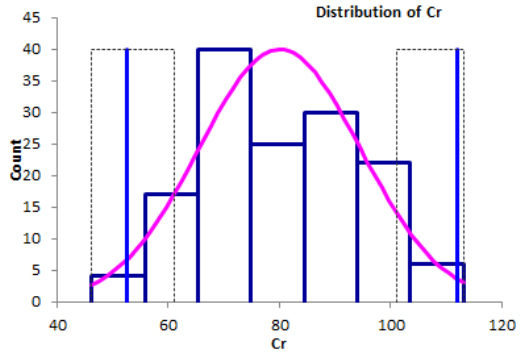
Paper

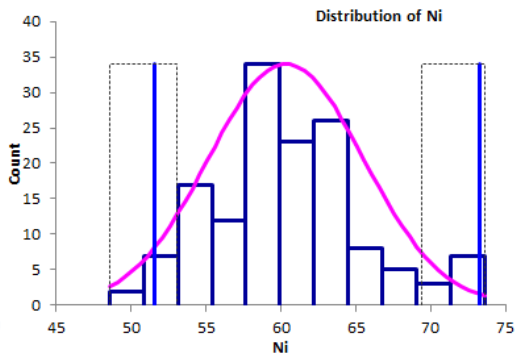
Elemental metabolomics

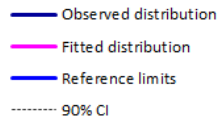
Ping Zhang, Constantinos A. Georgiou and Vladimir Brusic

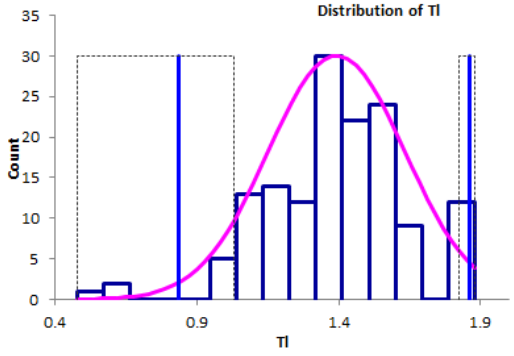
Egg yolk

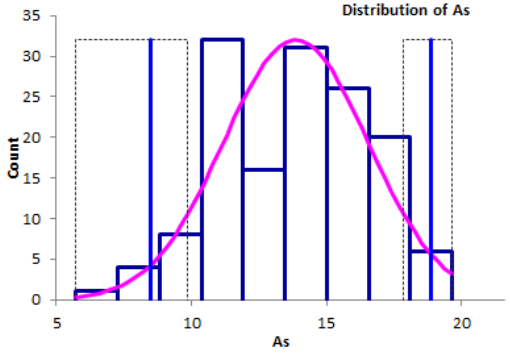


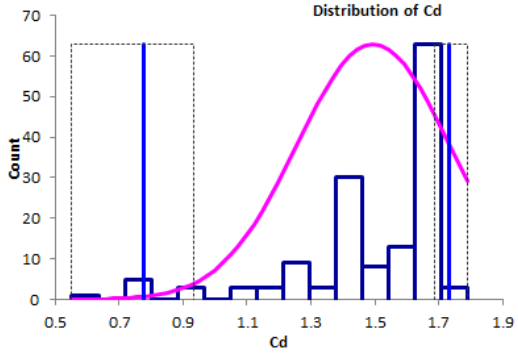


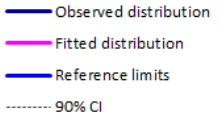




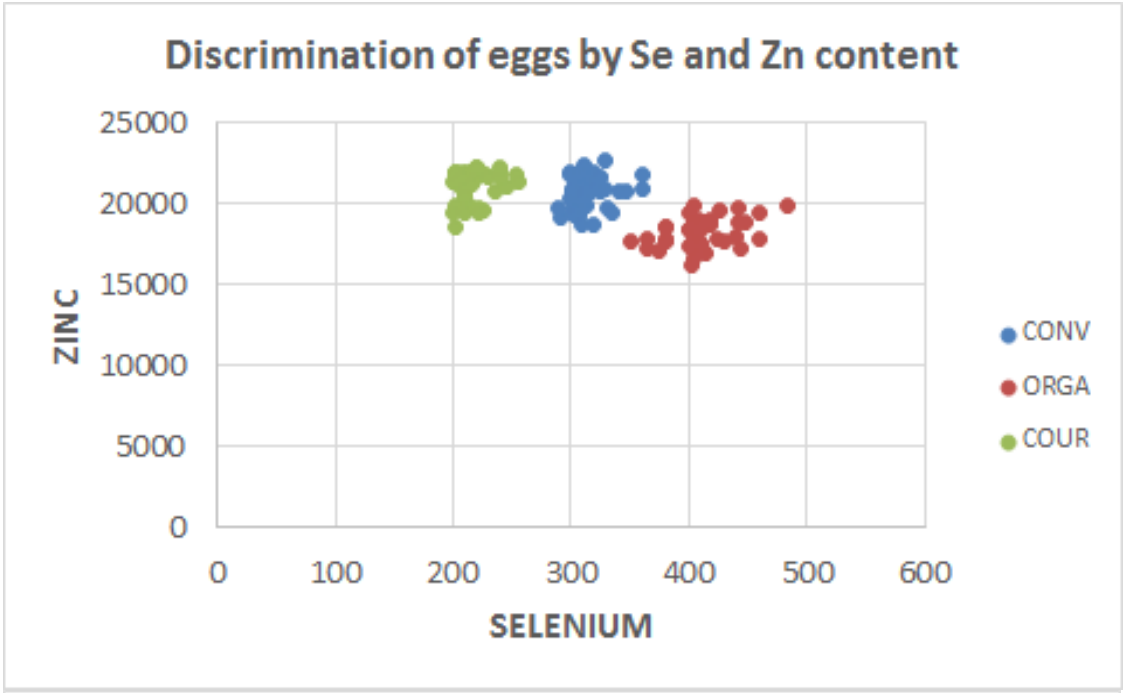


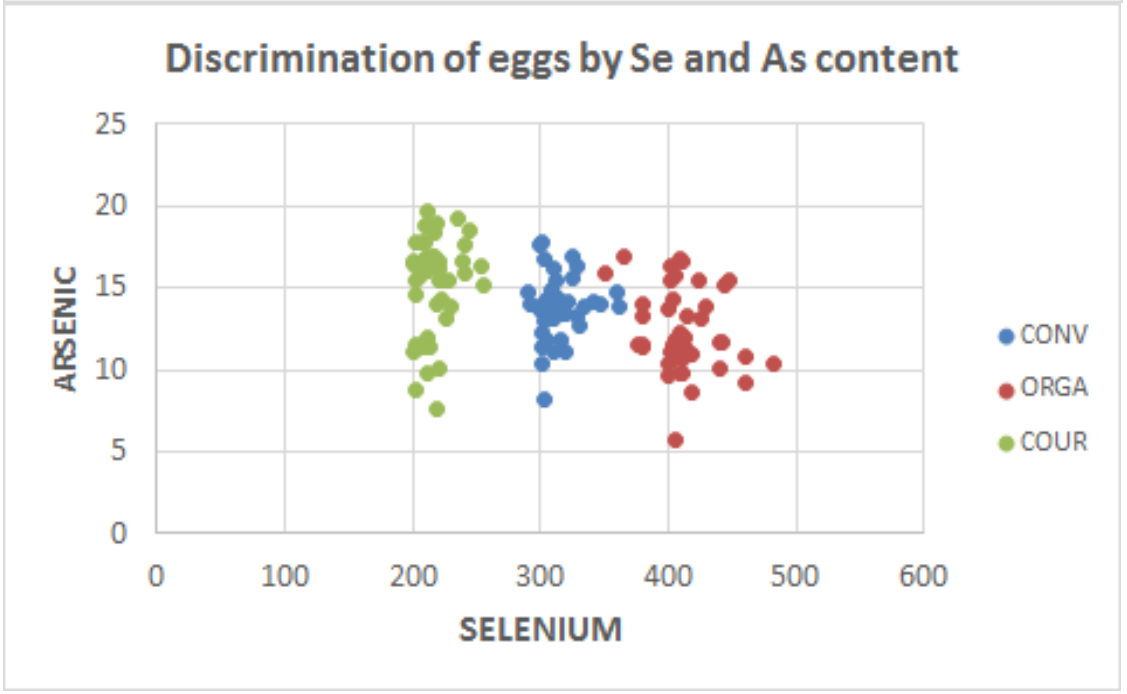






		Se	Zn	Mn	Co	Cu	Mo	V	Cr	Ni	Tl	As	Cd
MEDIANS	CONV	310	20705	837	4.52	1361	264	12.5	66.2	63.3	1.39	14.0	1.44
	ORG	409	18365	789	4.52	1243	245	13.4	84.0	58.5	1.49	11.7	1.65
	COUR	213	21475	698	4.91	1295	243	12.7	92.0	58.9	1.33	16.3	1.64
	COV	26%	8%	10%	9%	9%	8%	6%	18%	9%	17%	19%	16%


Discrimination of eggs by Se and Zn content
25000
20000
15000
10000
5000
0
ZINC
0
100
200
300
400
500
600
SELENIUM
CONV
ORGA
COUR


Discrimination of eggs by Se and As content
25
20
15
10
5
0
ARSENIC
0
100
200
300
400
500
600
SELENIUM
CONV
ORGA
COUR

ELEMENTAL METABOLOMICS
Determination of geographic, genetic and processing origin

Greek cheeses geographic & milk types

Elemental signatures & databases of Greek PDO chesses & milk types

Determination of Geographic and Genetic origin of Serbian Wines

Determination of rice Geographic and Genetic origin

Elemental signatures of Ukrainian cereals

Determination of eggs Geographic origin

Discrimination of production method:
- **-game meat**
- **-free range eggs**
- **-flooded vs unfolded rice**

AUA Elemental Metabolomics capacity

Big research infrastructure, 12/2016, partner in the foodomics.gr

Elemental Metabolomics partners

Academic

University of Boston, USA
University of Belgrade, Serbia
Nazarbayev University, Kazakhstan
Ukrainian academy of sciences, Kiev
Griffith's University, Australia
Kumamoto University, Japan

Institute of Quality Standard and Testing Technology for Agro-Products, Chinese Academy of Agricultural Sciences, Beijing
University of Jinan, Jinan, Shandong
Institute of Urban Environment, Chinese Academy of Sciences, Xiamen

Industrial

ChengduTongtian Food Ltd., Sichuan
Mountain River Medical Science and Technology Ltd, Yantai, Shandong
Shandong International Biotechnology Park, Luye Group, Yantai, Shandong

Elemental Metabolomics, Greek-China agri-food projects

Elemental metabolomics for authentication of milk and milk products

-Data base of elemental signatures of Greek and Chinese milk
-Dbase application for milk and milk products authentication
-Methods developed will be evaluated with authentic milk samples and also milk samples from the market at Greece and China
-Rapid methods for adulteration detection is important in view of the melamine and other food scandals involving milk in China
-Algorithms and methods for authentication of Greek cheeses will be developed

Elemental Metabolomics to enhance agri-food production through ultra-trace elements fortification: Utilization of mining byproducts for plant and meat production

-Assessment of ultra trace element bioavailability from Greek, Bosnian and Chinese byproducts, for plants and animals
-field evaluation of byproducts as
--fertilizers of different types of soils for major corps i.e. soy beans, corn and rice.
--feeds fortification

CONCLUSIONS

Elemental Metabolomics is an exciting new subfield of Metabolomics

Links multiple domains:

environmental, **agriculture**, food science, nutrition, **health** sciences, medicine

Numerous applications:

biomonitoring, food authentication, food reinforcement, optimization of agricultural practices, health applications (diagnosis, prognosis, etc.)

Danezis GP, Tsagkaris AS, Camin F, Brusic V, Georgiou CA. Food authentication: techniques, trends and emerging approaches. Trends in Analytical Chemistry 2016, 85; 123-132.

Danezis GP, Tsagkaris AS, Camin F, Brusic V, Georgiou CA. Food authentication: state of the art and prospects. Current Opinion in Food Science 2016, 10, 22-31.

Zhang P, Georgiou CA, Brusic V. Elemental metabolomics. Briefings in Bioinformatics (in press).

Zhang P, Georgiou CA, Brusic. Elemental metabolomics–linking environmental, food, nutrition and health sciences. In Book of Abstracts 10th International Conference Bioinformatics of Genome Regulation and Structure\Systems Biology, Novosibirsk, Russia, 2016, pp 347. (Abstract).

Zhang P, Georgiou CA, Brusic V. Elemental metabolomics for improving human health. In Mitic N. (editor), Book of Abstracts, Belgrade Bioinformatics Conference 2016, pp 7-8, ISBN 978-86-7589-108-6. (Abstract).

Instrumentation for elemental profiling **NEAR FUTURE**

LA-ICP-MS

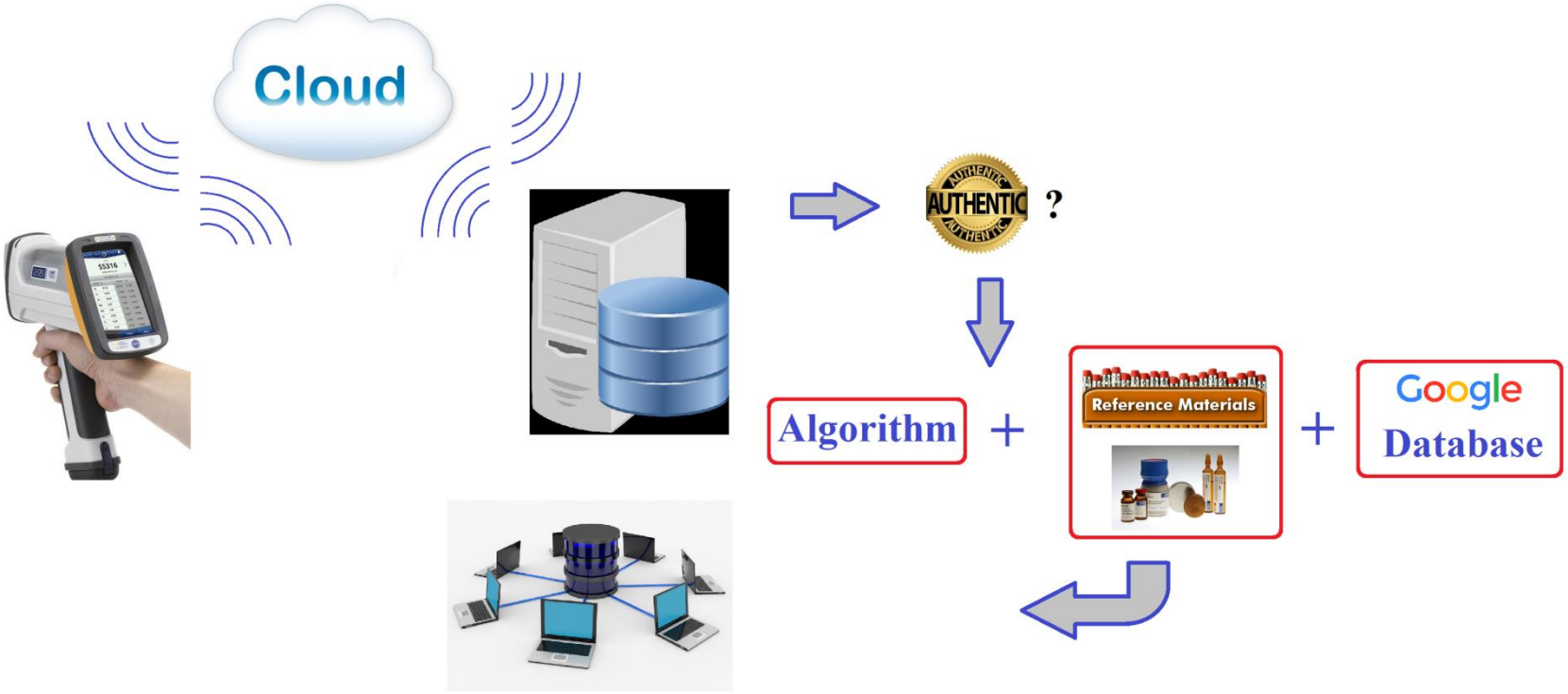
No sample digestion !!! & spatial analysis

MC-ICP-MS

~300 elements and stable isotopes

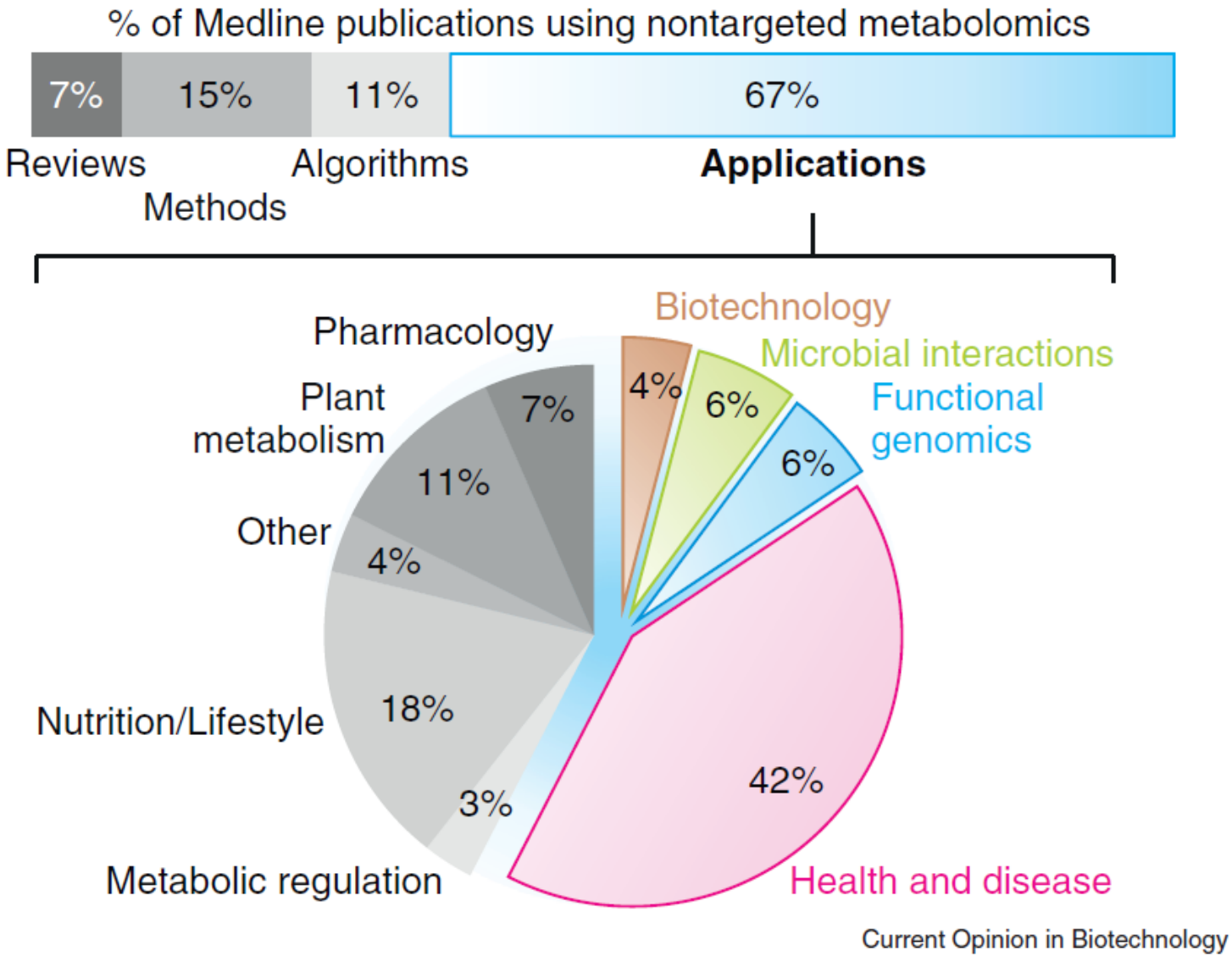
Instrumentation for elemental profiling **FAR FUTURE**

On site elemental profiling through portable Laser Ablation ICP-MS



Metabolomics is the endpoint of the Omics cascade:
genomics → transcriptomics → proteomics → metabolomics

Omics focuses on high-throughput measurements of molecular data and their interpretations that connect organism's genetic code with its phenotype and defines systems biology



Sevin, Kuehne, Zamboni and Sauer, 2015