Metallomic Scientific Network No. 11440027

Metallomics - What is it? - part I

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24. 4. 2015

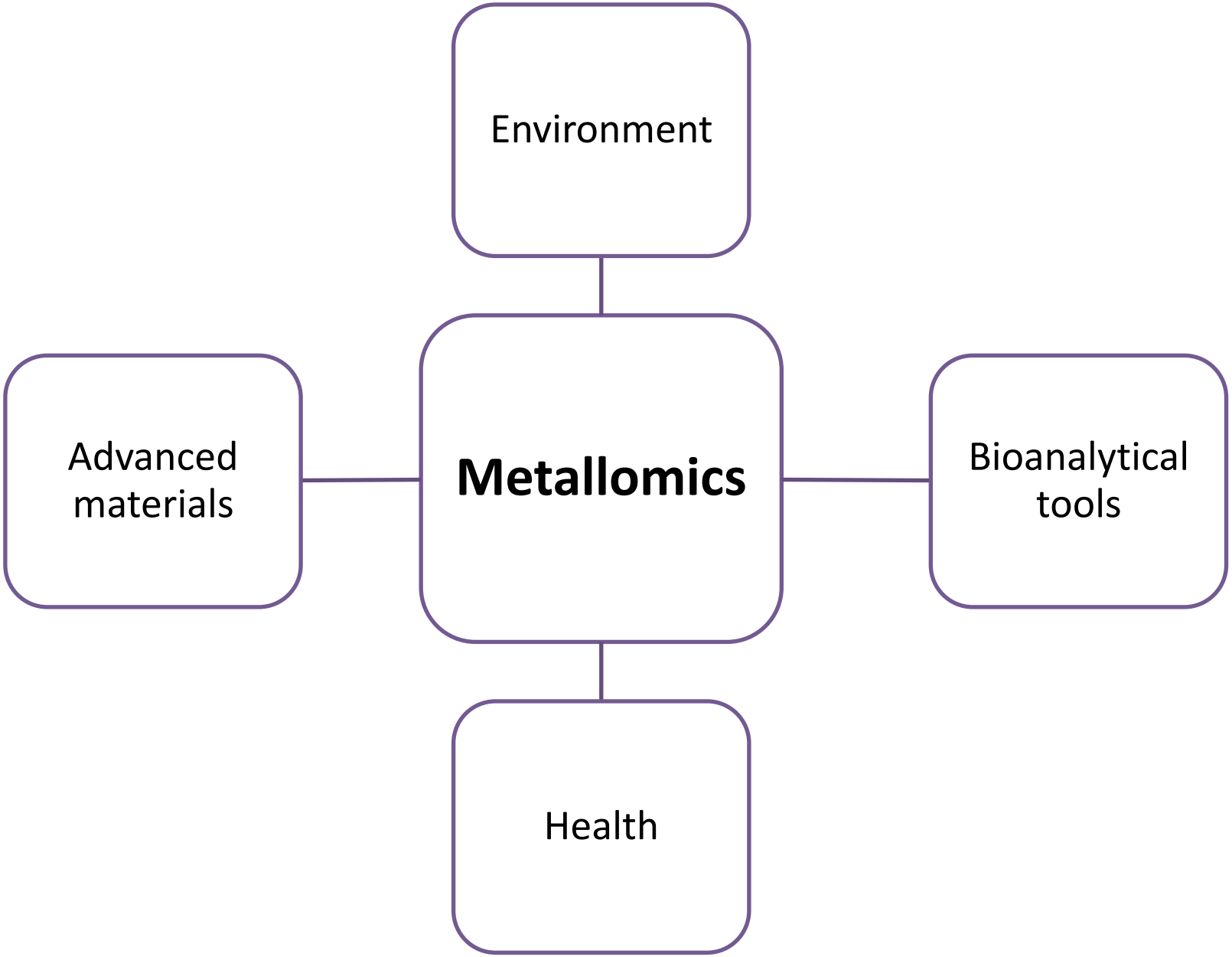
- Metallome
- Metallomics - definition
- Metalloproteomics
- Metalloproteins
- Analysis of metalloproteins

Metallome

- *by analogy with proteome*
  - Distribution of free metal ions in every one of cellular compartments (R.J.P. Williams)
- *alternative definition*
  - Metalloproteins or any other metal-containing biomolecules (H. Haraguchi)
- Considered as branch of metabolomics, even though the metals are not typically considered as metabolites
- Metallo -
  - transcriptome
  - proteome
  - metabolome
  - interactome

Metallomics - definition

- *Comprehensive analysis of the entirety of metal and metalloid species within a cell or tissue type* (J. Szpunar)
- *Study of metal-containing biomolecules* (H. Haraguchi)
- *Integrated biometal science* (H. Haraguchi)
  - Great significance in study of physiological and pathophysiological processes
  - Heavy metals-based nano- and micromaterials and their fate in the organisms and environment

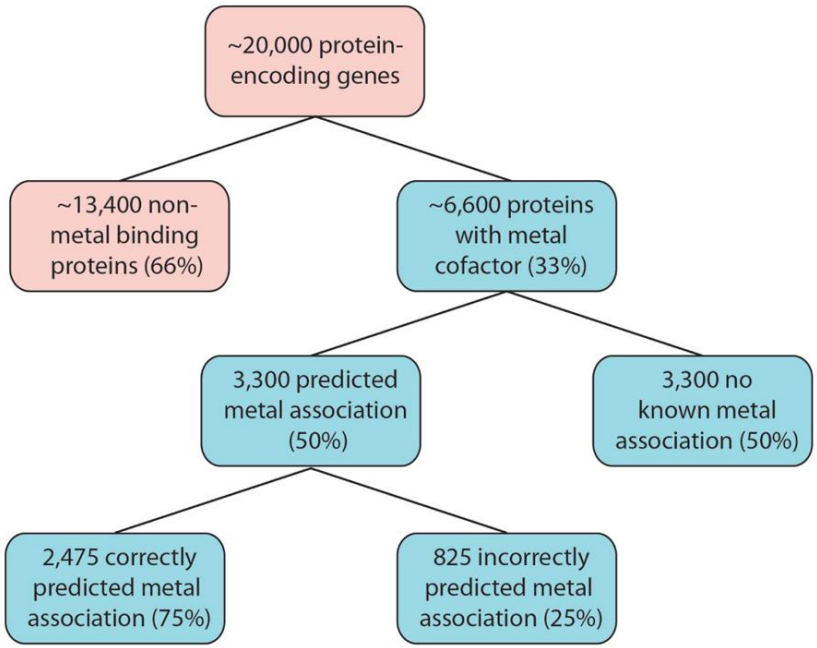

Environment
Advanced materials
Metallomics
Bioanalytical tools
Health

Metalloproteomics

- Relationship between metals and proteins
- About 30% of all proteins bind metal ions

  ~ 6600 predicted proteins with metal cofactor in human proteome

- Combination approaches that address the expression of metaalloproteins and their changes in biological time and space

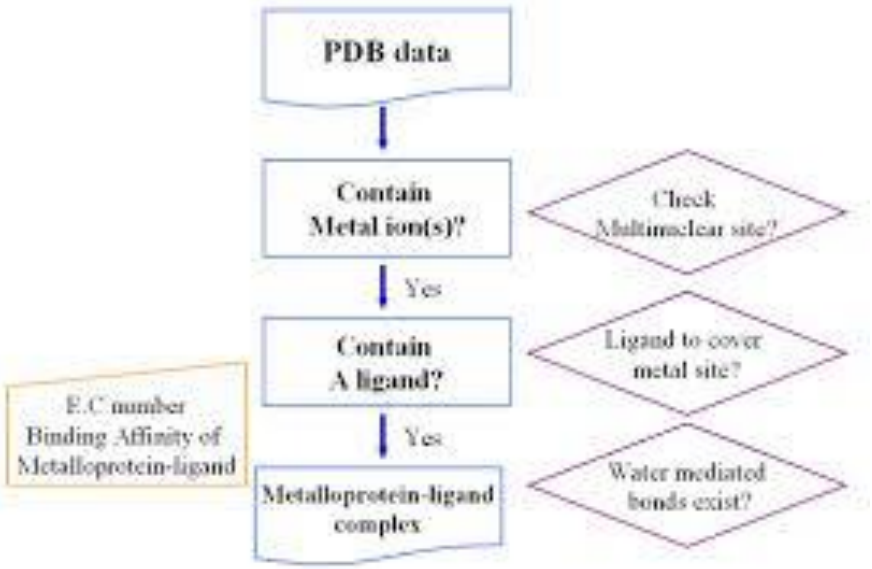


http://www.frontiersin.org/files/Articles/55343/fnagi-05-00035-HTML/image_m/fnagi-05-00035-g001.jpg

Metalloproteins

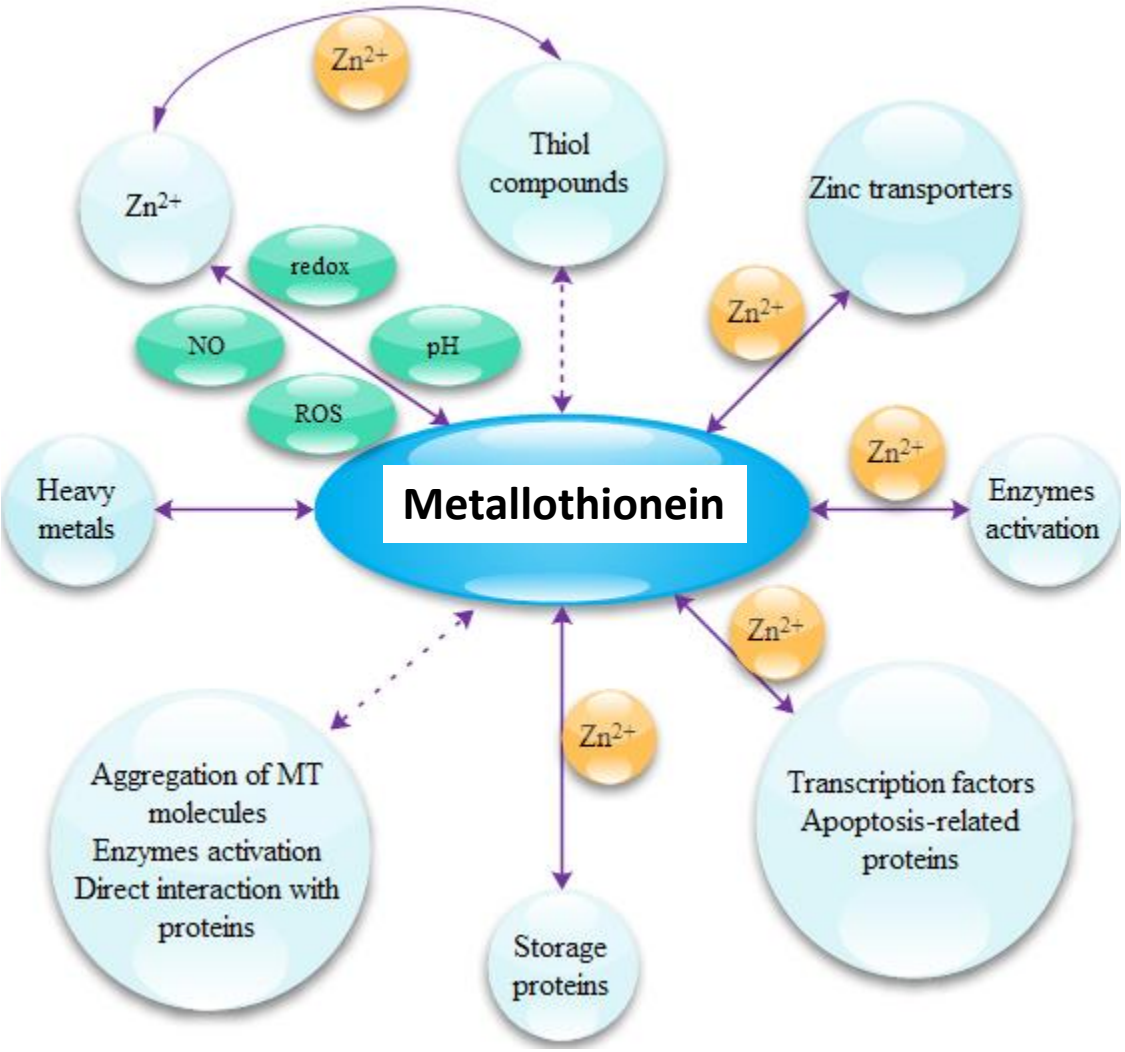
- Metalloenzymes
- Signal-transduction metalloproteins
  - Calmodulin
  - Transcription factors
- Storage and transport
  - Metallothioneins

Metalloprotein Ligand Interaction Database



http://silver.sejong.ac.kr/metligdb/home.html

Metallothioneins and essential metal ions



Krizkova, S.; Ryvolova, M.; Hrabeta, J.; Adam, V.; Stiborova, M.; Eckschlager, T.; Kizek, R. *Drug Metab. Rev.* **2012**, *44*, 287.

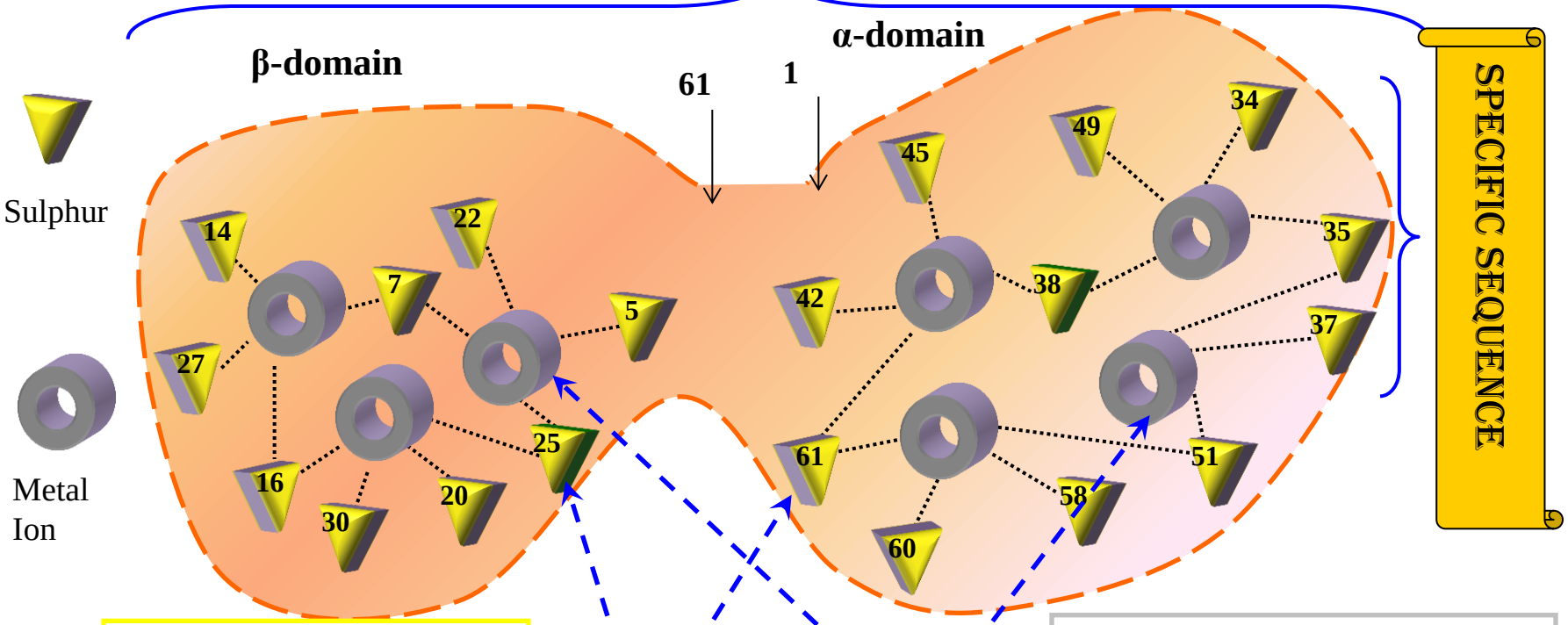
Overview of Methods Used for Analysis of MT

Quantity: Matrix-assisted laser desorption/ionization mass spectrometry with time of flight ionization (MALDI-TOF-MS), mass spectrometry with electrospray ionization (ESI-MS)

A PROTEIN

Structure: nuclear magnetic resonance, electron paramagnetic resonance (EPR), Raman spectroscopy, circular dichroism (CD), magnetic circular dichroism, Mossbauer spectroscopy and X-ray techniques

enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), Western blotting



Cyclic, differential pulse and square wave voltammetry, chronopotentiometric stripping analysis

SULPHUR

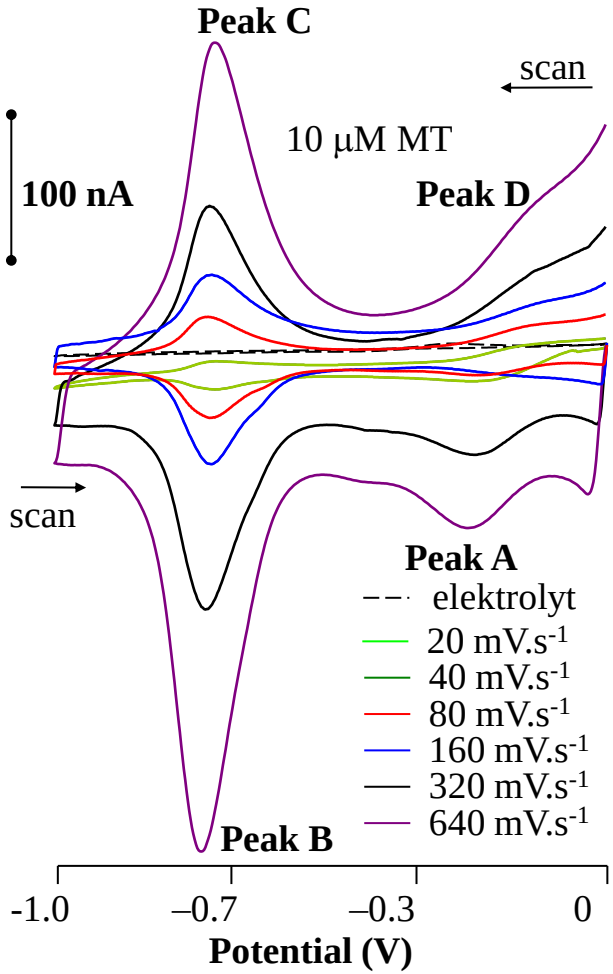
METAL

Saturation techniques (Hg (II), Ag (I) and Cf (II)), mass spectrometry with inductively coupled plasma (ICP-MS)

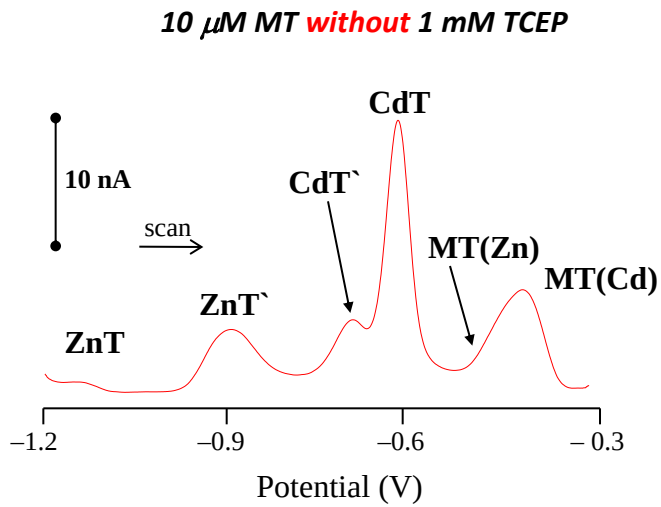
Adam, V., Fabrik, I., Eckschlager, T., Stiborova, M., Trnkova, L., Kizek, R., *TRAC-Trends Anal. Chem.* **2010**, *29*, 409-418.

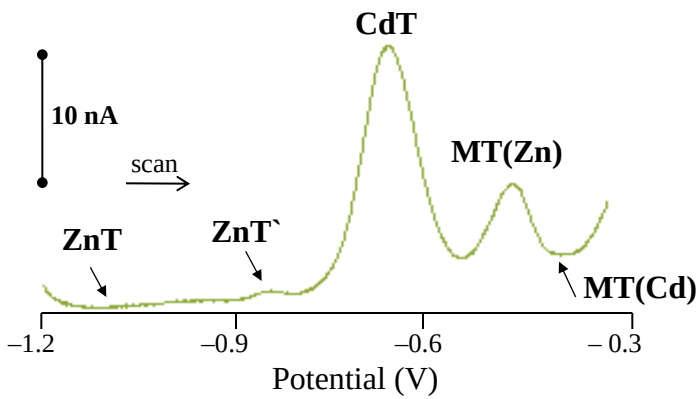
Electrochemical behaviour of metallothioneins I

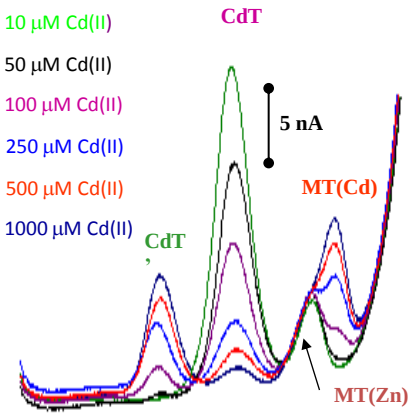
Cyclic voltammetry

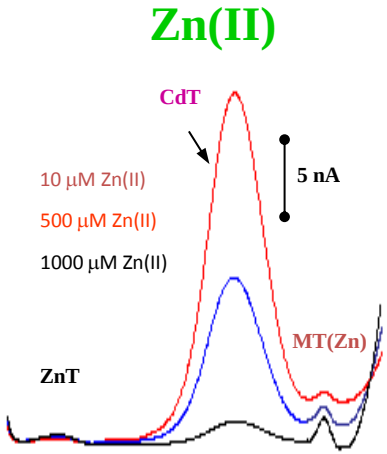


Differential pulse voltammetry





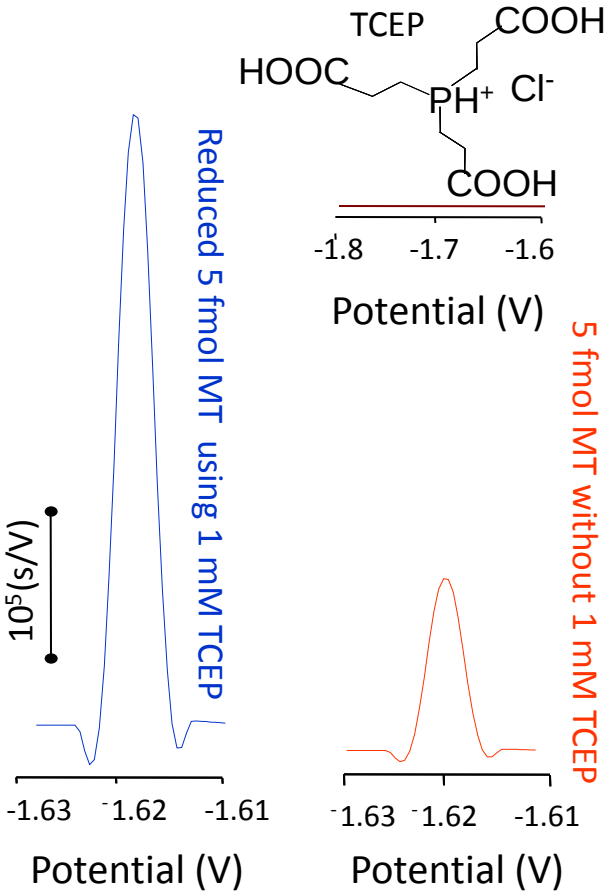


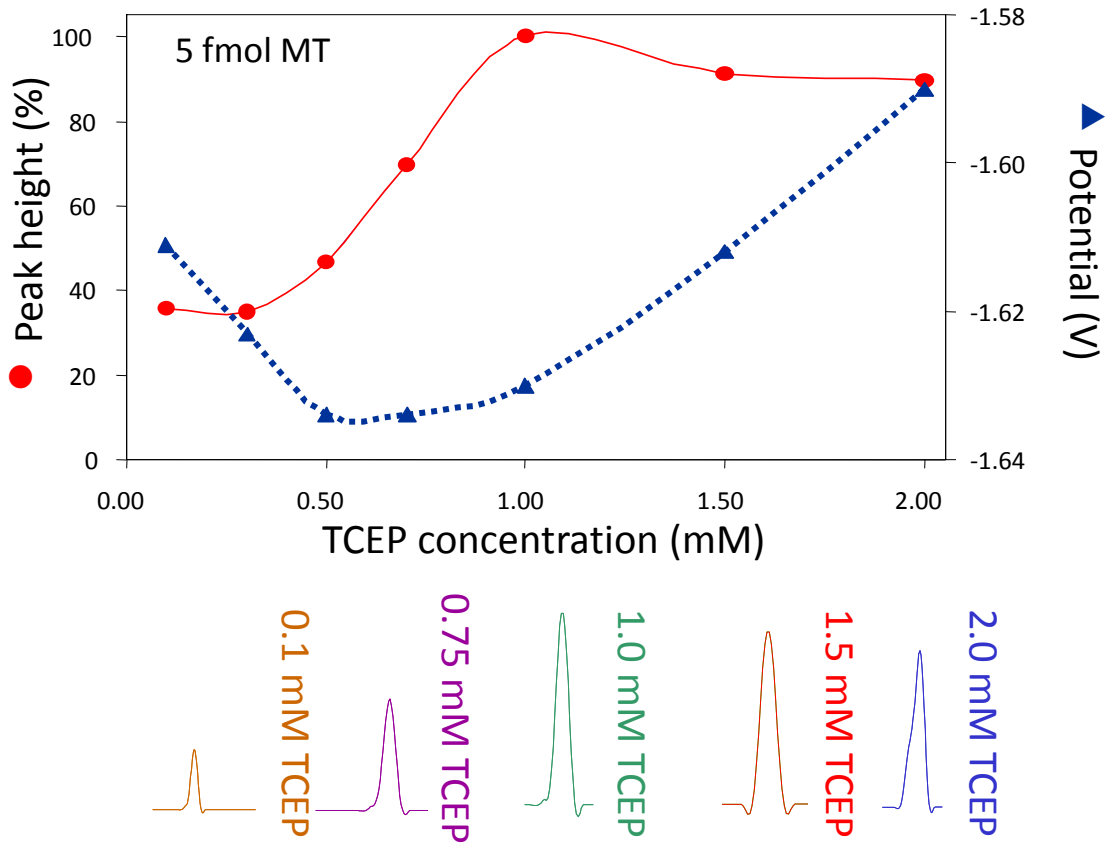


Petrlova, J.; Potesil, D.; Mikelova, R.; Blastik, O.; Adam, V.; Trnkova, L.; Jelen, F.; Prusa, R.; Kukacka, J.; Kizek, R. *Electrochim. Acta* **2006**, *51*, 5112.

Electrochemical behaviour of metallothioneins II

Chronopotentiometric stripping analysis



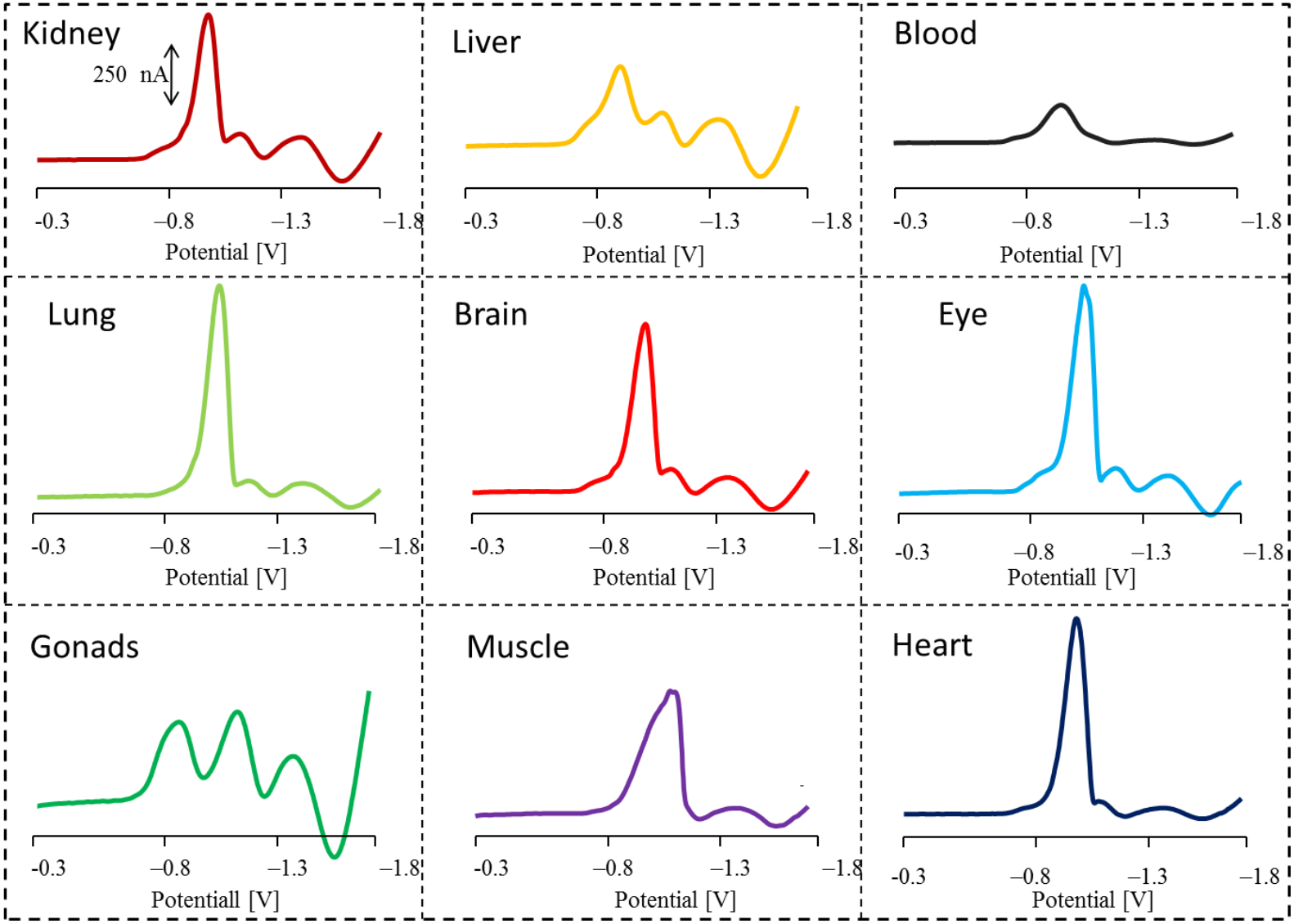


Adam, V.; Petrlova, J.; Wang, J.; Eckschlager, T.; Trnkova, L.; Kizek, R. *PLoS ONE* **2010**, *5*, e11441.

Application of Brdicka reaction for determination of metallothionein in real samples

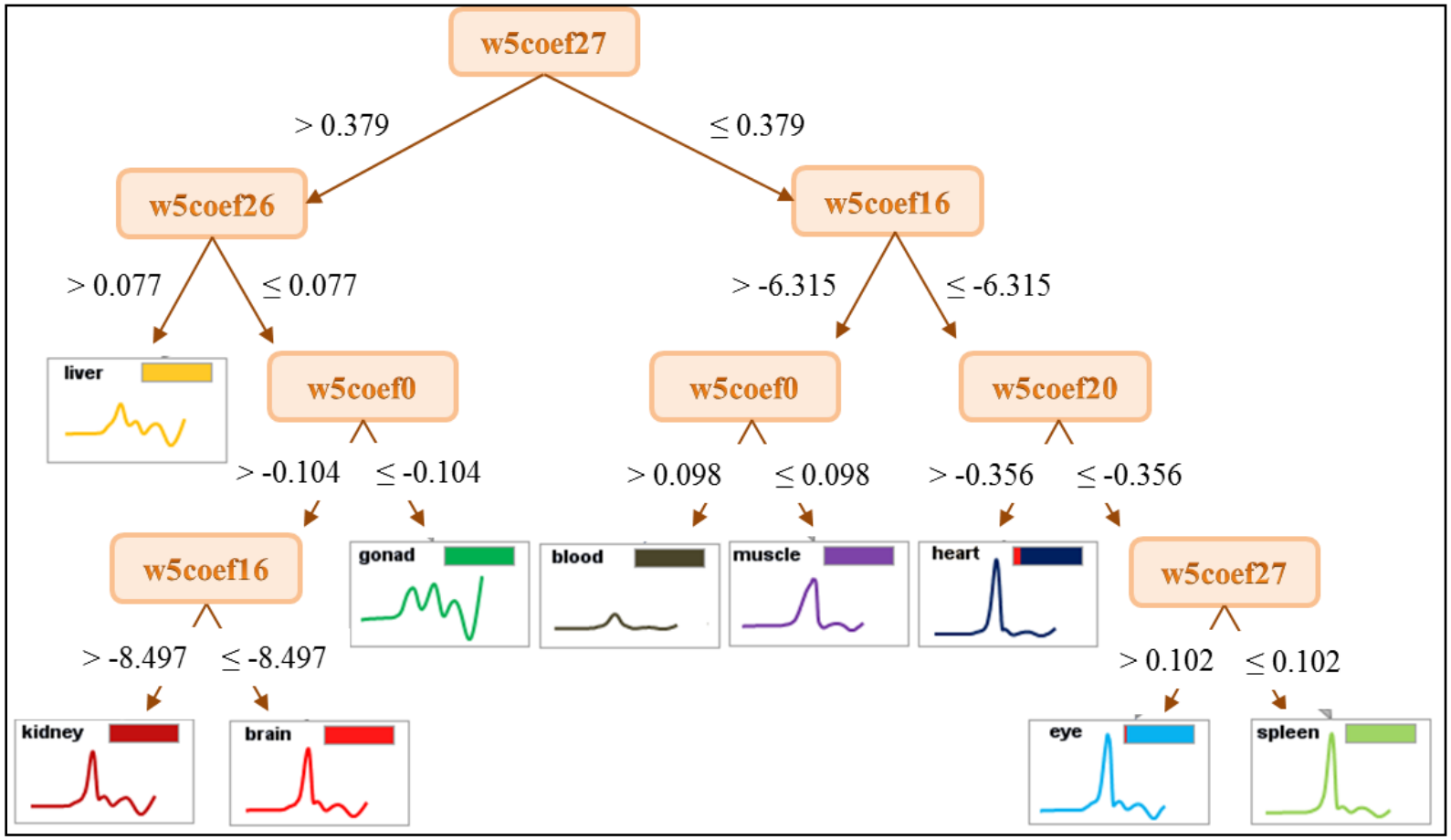
The content/concentration is not enough!

Animal tissue analysis



Sobrova, P.; Vyslouzilova, L.; Stepankova, O.; Ryvolova, M.; Anyz, J.; Trnkova, L.; Adam, V.; Hubalek, J.; Kizek, R. *PLoS ONE* **2012**, *7*, 1.

Mathematical processing



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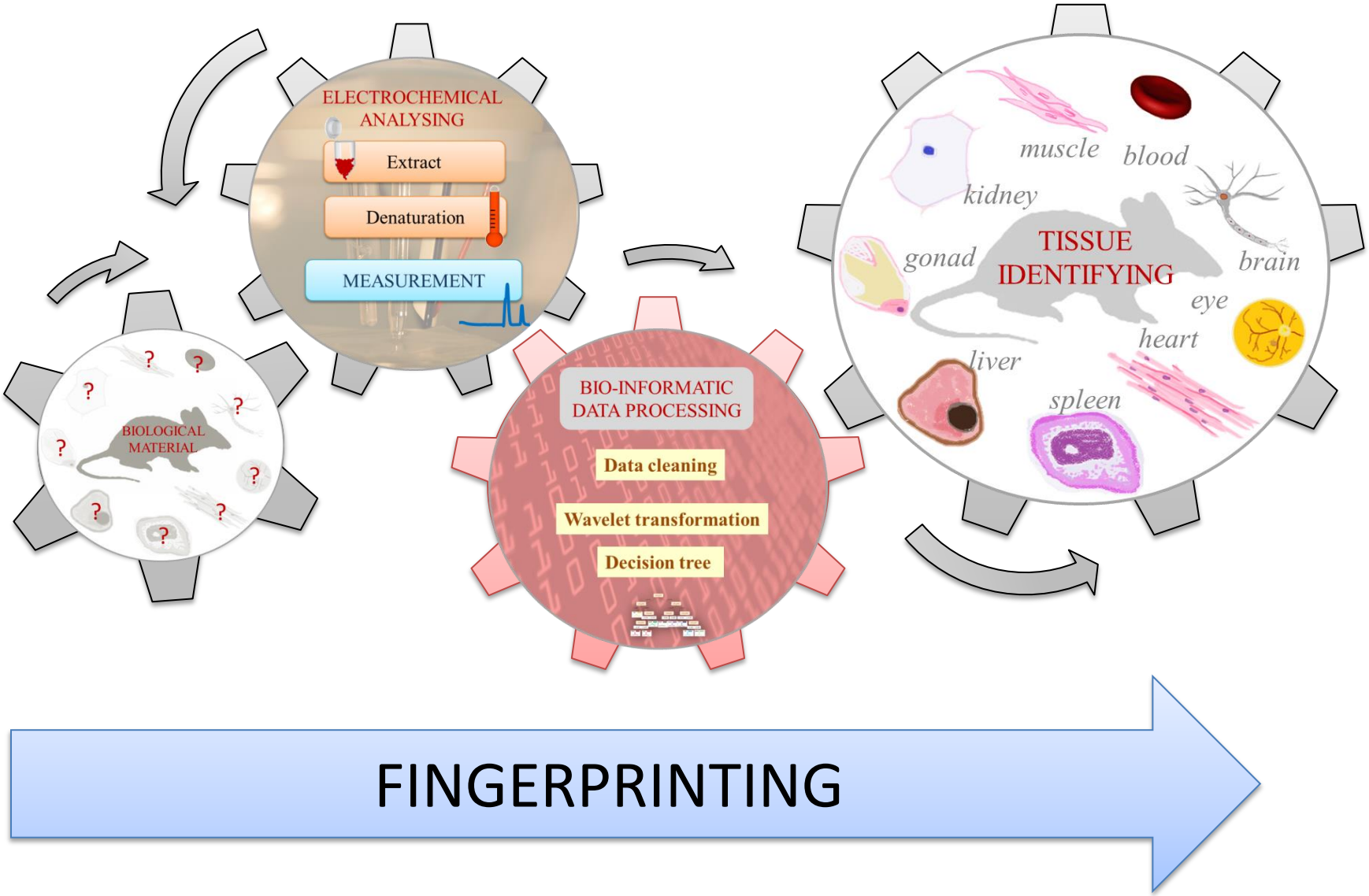
Tissue fingerprinting



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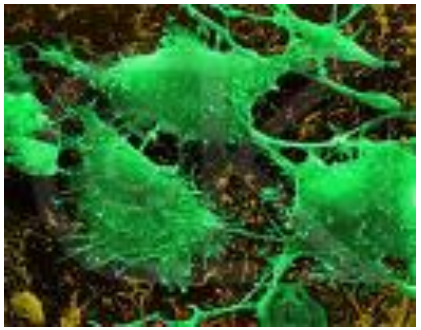
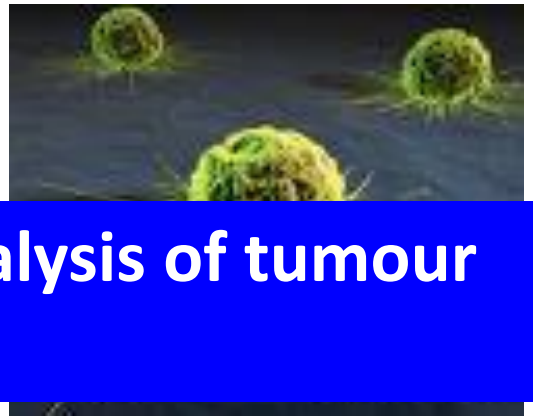
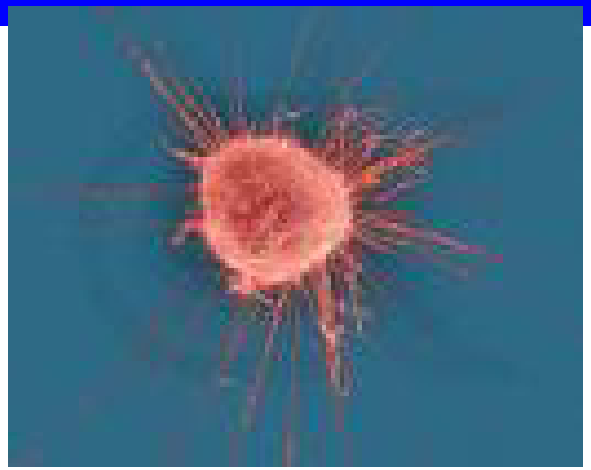
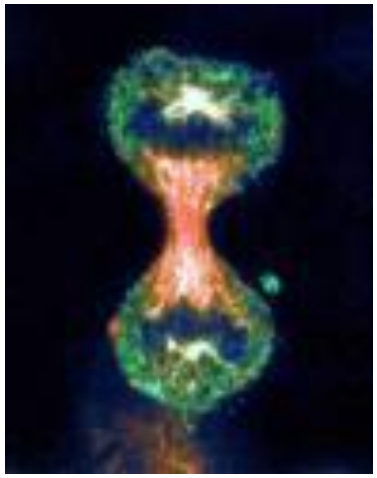




Can we use the same procedure for analysis of tumour diseases?

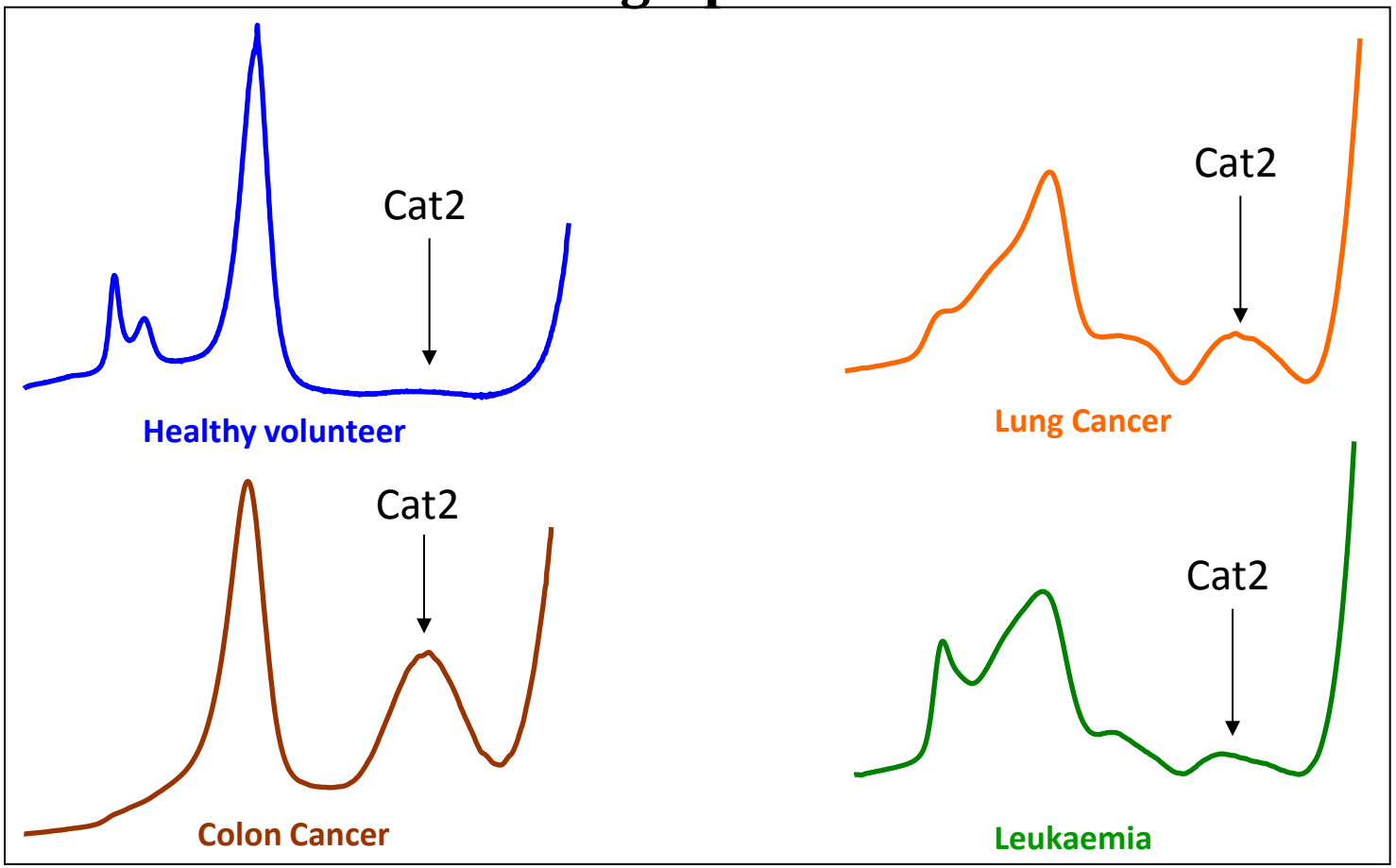




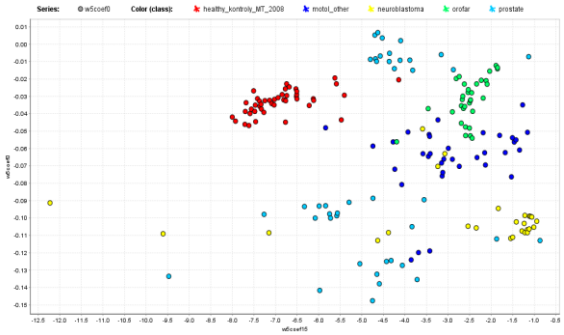
Tumour disease fingerprinting?

DP voltammograms of blood serum samples from patients with various types of cancer differed according to type of the cancer.

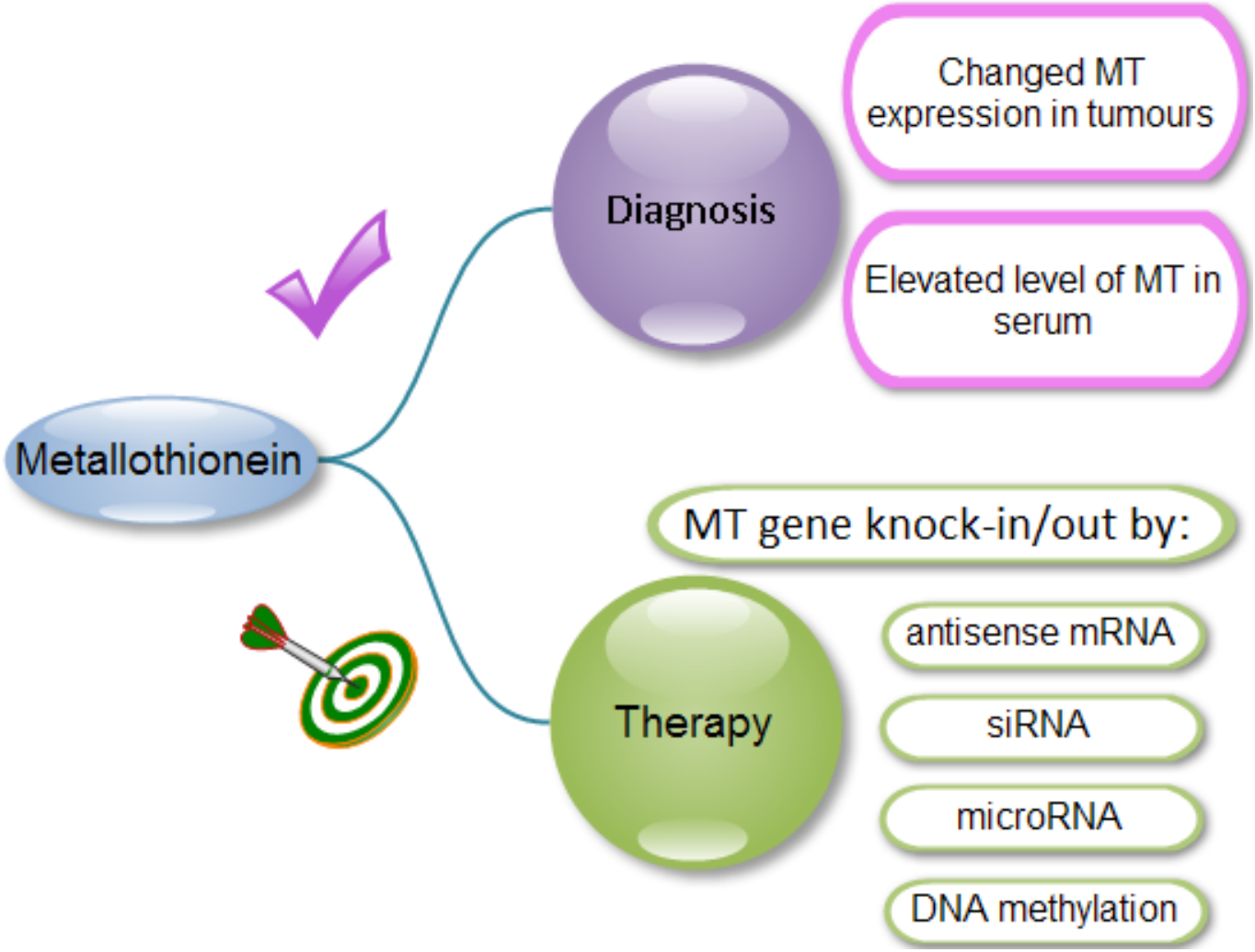
=> Electrochemical Fingerprint of a tumour disease



Tumour disease fingerprinting?



Conclusion


Metallothionein
Diagnosis
Changed MT expression in tumours
Elevated level of MT in serum
Therapy
MT gene knock-in/out by:
antisense mRNA
siRNA
microRNA
DNA methylation

Acknowledgement

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