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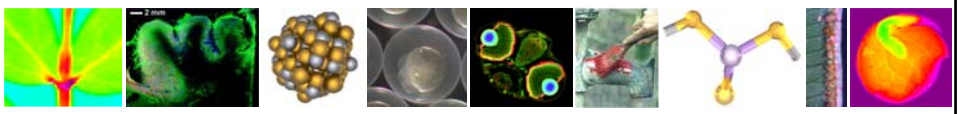
Applications of X-ray Absorption Spectroscopy in Life Sciences



Ingrid J. Pickering

University of Saskatchewan,
Saskatoon, Canada

ingrid.pickering@usask.ca

National School on Neutron and X-ray Scattering
Argonne National Laboratory
Oak Ridge National Laboratory
June 17, 2015

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Molecular and Environmental Science Group
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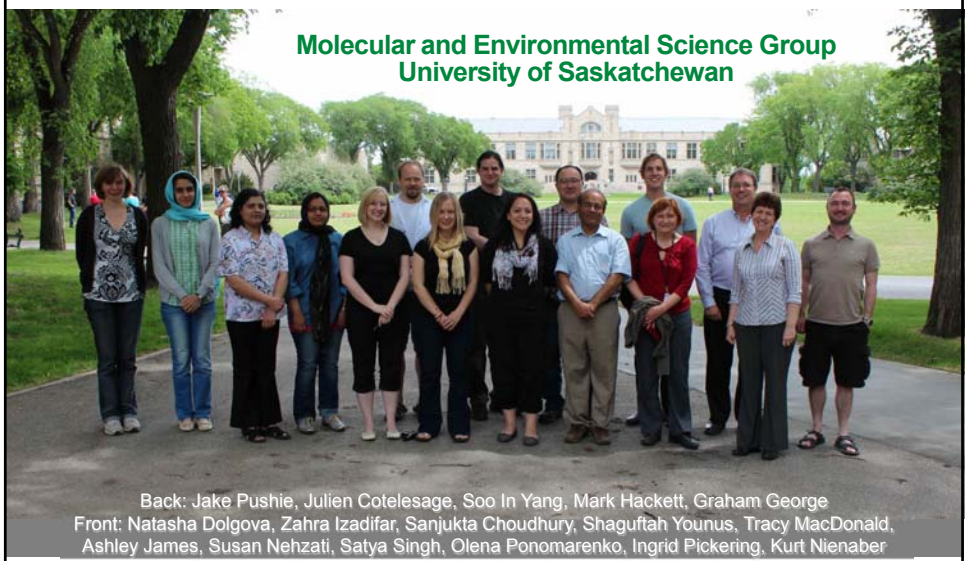

Back: Jake Pushie, Julien Cotelesage, Soo In Yang, Mark Hackett, Graham George
Front: Natasha Dolgova, Zahra Izadifar, Sanjukta Choudhury, Shaguftah Younus, Tracy MacDonald, Ashley James, Susan Nehzati, Satya Singh, Olena Ponomarenko, Ingrid Pickering, Kurt Nienaber

Graham George and Ingrid Pickering Research Group

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Acknowledgements

- National School on Neutron and X-ray Scattering (organizers, sponsors)

Canada Research Chairs
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HEART & STROKE FOUNDATION OF CANADA
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Canada Research Chairs Program
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CIHR Training Grant in Health Research Using Synchrotron Techniques
Heart and Stroke Foundation of Canada/CIHR Team Grant in Synchrotron Medical Imaging
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SSRL

Beamlines and their personnel

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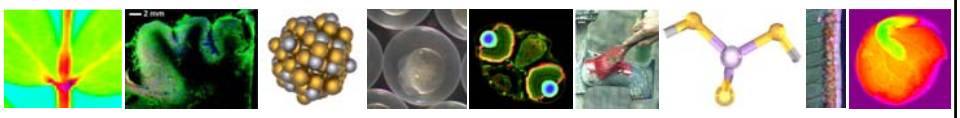
Overview



- Why use X-ray absorption spectroscopy in life sciences?
- X-ray absorption spectroscopy combined with X-ray fluorescence imaging
- Case studies:
  - Arsenic in plants
  - Mercury in zebrafish as vertebrate model
  - Mercury in human brain
  - Arsenic, selenium and Bangladesh

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Synchrotron Facilities in Canada and USA

(those used in my talk!)

CLS:
Canadian Light Source
(Saskatoon, SK)

SSRL:
Stanford Synchrotron Radiation Lightsource
(Stanford, CA)

APS:
Advanced Photon Source
(Argonne, IL)

http://johomaps.com/na/na2.html

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Sources of Metals in our Environment

Manmade sources

Natural sources

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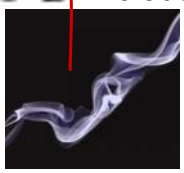
Sources of Human Exposure to Metals



food


drinking water


contact



inhalation

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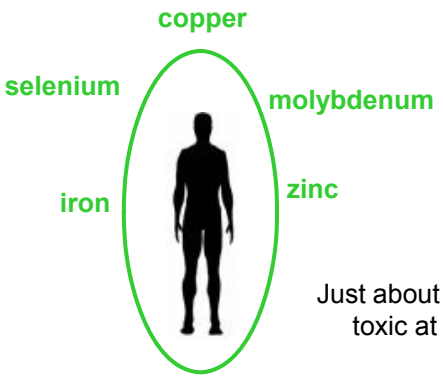
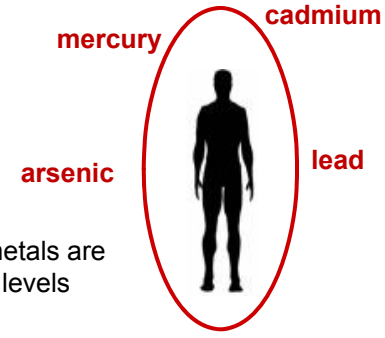
Elements in Humans (and other organisms)

Essential elements



Toxic elements



Just about all metals are toxic at high levels

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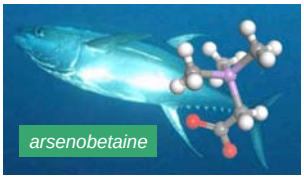
Chemical form matters!

Example: Arsenic

- Arsenic is infamous as a poison
  - *e.g.* Lewisite – war gas known as "dew of death"

- However, not all arsenic is poisonous!
  - *e.g.* Arsenobetaine (0.02 wt% in seafood) is not toxic at all



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X-ray Absorption Spectroscopy in Life Sciences

- Chemical form affects the element's properties, e.g.
  - Solubility and mobility in groundwater
  - Bioavailability to organisms
  - Toxicity or benefit to higher organisms including humans
- Samples are often heterogeneous, e.g.
  - Organisms, tissues, cells
  - Food, soil, sediment
- Need to know the chemical form of a potentially toxic or beneficial element in a complex matrix
  - X-ray absorption spectroscopy can do this

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X-ray Absorption Spectroscopy in Life Sciences

- XAS gives local structural information around central absorbing atom
  - Atomic property so no confusion over which element
- Due to X-ray properties, XAS can be used for almost any matrix:
  - Purified protein solution (simple)
  - Biological tissues, sediments, etc. (complex)
- Analyzes all forms of the element with no "hidden" phases, e.g.
  - Crystalline or amorphous solids, aqueous solutions, gases…
  - Can provide information on mixtures of chemical species
- XAS is very amenable to investigating metals and other elements in biological and environmental samples
  - One of few "*in* situ" probes, little pre-treatment required

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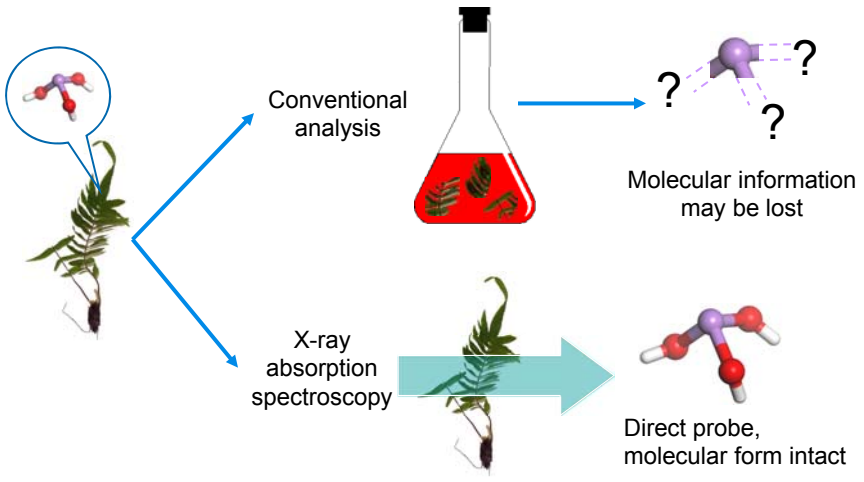
X-ray Absorption Spectroscopy: Direct and Potentially Non-Destructive



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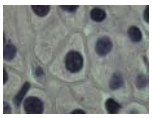
Imaging Chemical Species in Biological Samples

- Many complex samples have spatial structure
- Questions we may want to answer:
  - How is an **element** distributed?
  - What is an element's **chemical form** in a particular location?
  - How is a **chemical species** distributed?
- We would like to do this:
  - For **dilute levels** of elements (use fluorescence)
  - Sometimes on **intact living** specimens
- Answer these questions using
  - **X-ray fluorescence imaging** in combination with
  - **X-ray absorption spectroscopy**

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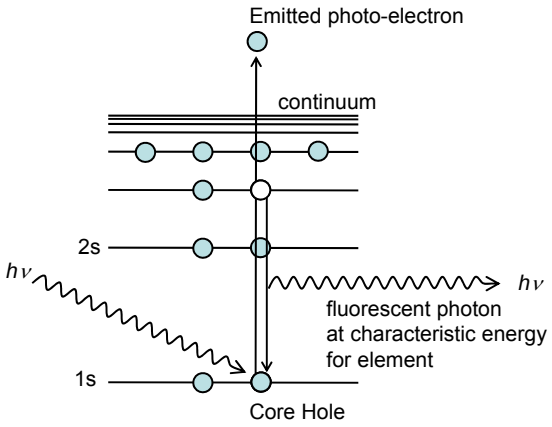
X-ray Fluorescence



- An X-ray fluorescent photon is emitted when an electron is absorbed
- Measuring fluorescence on a thin/dilute sample
  - Is equivalent to measuring absorbance
  - Is much more sensitive to dilute species
- It is also the basis of X-ray fluorescence imaging

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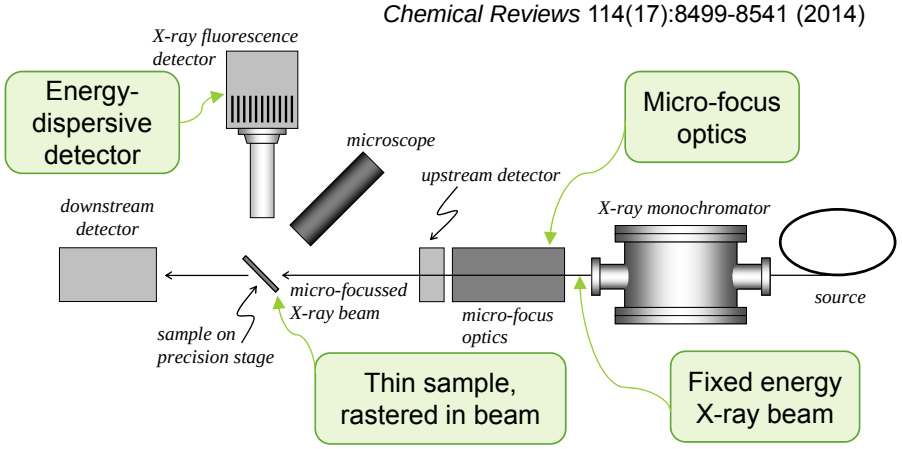
X-ray Fluorescence Imaging

Pushie, Pickering, Korbas, Hackett & George,
Chemical Reviews 114(17):8499-8541 (2014)



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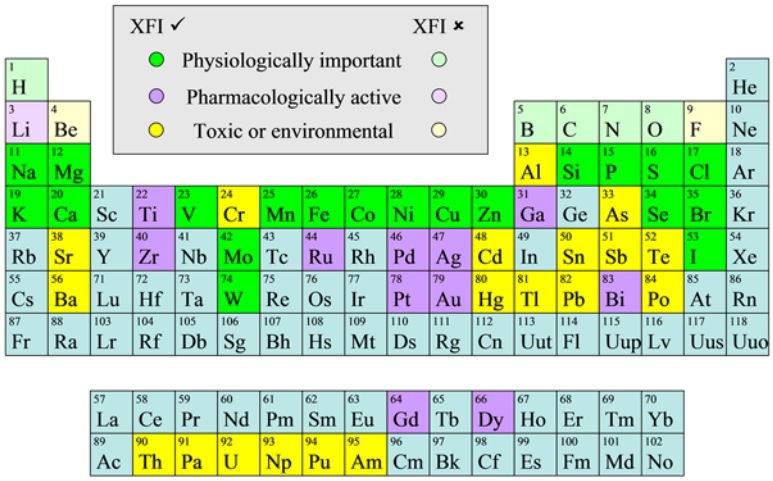
Elements Accessible by X-ray Fluorescence Imaging



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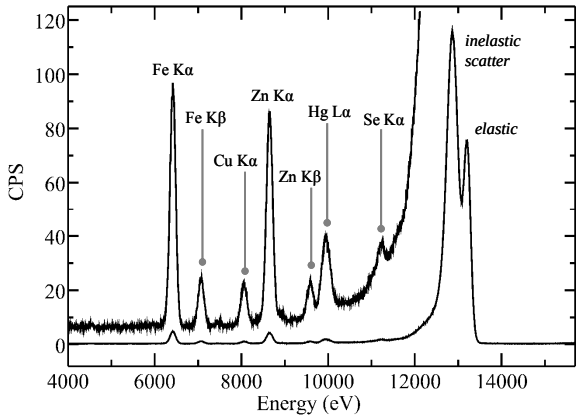
X-ray Fluorescence Imaging

X-ray fluorescence emission spectrum from energy-dispersive detector



Human cerebral cortex, individual poisoned through skin exposure to dimethylmercury, Canberra LeGe detector, analog electronics, Gaussian shaping amplifier, shaping time 2 μs, incident X-ray energy 13 200 eV. SSRL 9-3.

Pushie, Pickering, Korbas, Hackett & George
Chemical Reviews 114(17):8499-8541 (2014)

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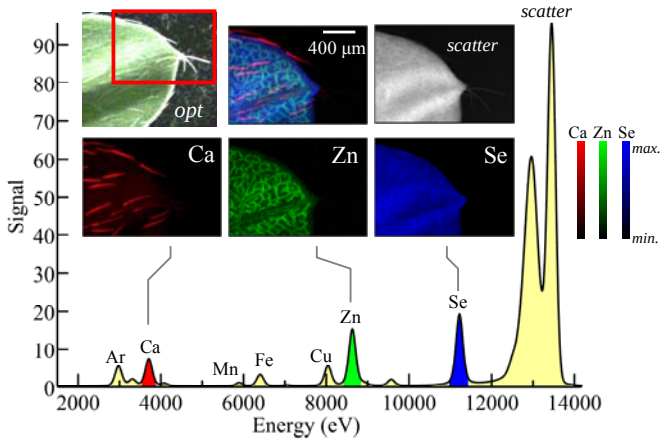
X-ray Fluorescence Imaging



Pushie, Pickering, Korbas, Hackett & George
Chemical Reviews 114(17):8499-8541 (2014)

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X-ray Fluorescence Imaging

- Fixed energy above absorption edge(s) of elements of interest
- Micro-focused ("pencil") beam
- Spatially raster sample in beam
- Measure fluorescence emission spectrum at each pixel
- Produces **elemental maps**
- Can be combined with X-ray absorption spectroscopy to provide **chemical** information

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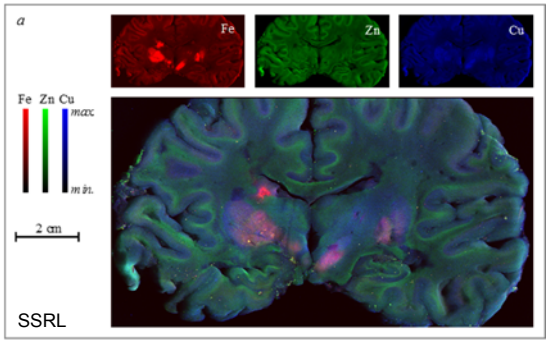
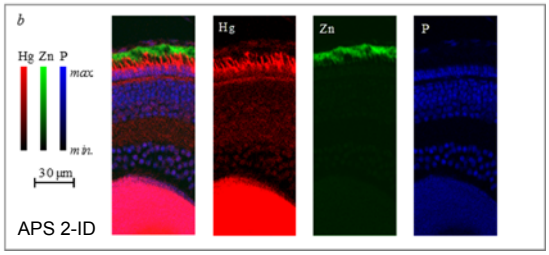
Spatial Resolution

- Spatial resolution of X-ray fluorescence imaging should be tuned to the object of interest
- Microfocus optics (to make a small beam)
  - (Apertures)
  - Kirkpatrick-Baez (K-B) mirror pair
  - Glass capillaries
  - Zone plates





Pushie, Pickering, Korbas, Hackett & George *Chemical Reviews* 114(17):8499-8541 (2014)

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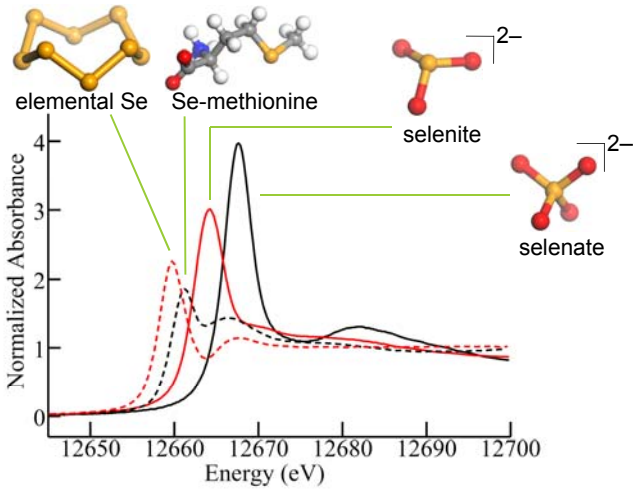
X-ray Absorption Spectroscopy

Near–edge (XANES) is sensitive to chemical form



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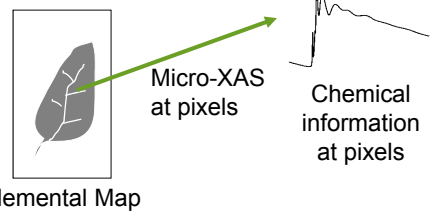
Simultaneous Spatial and Chemical Information

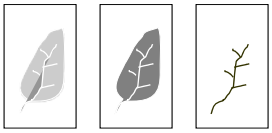
Two routes to information

1. X-ray Fluorescence Imaging Plus Micro-XAS



Elemental Map

2. Chemically Specific Mapping (Tune incident energy to peaks)



Chemical Maps

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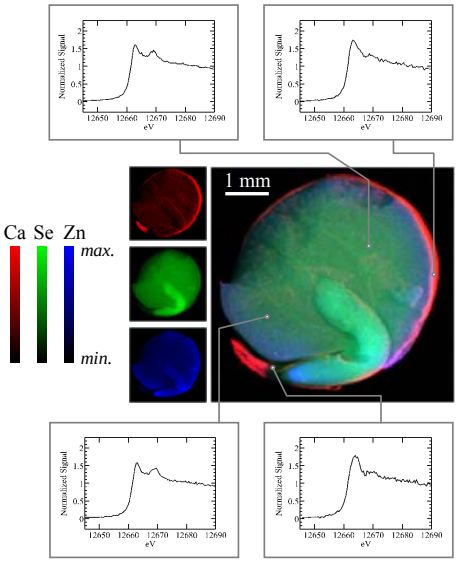
Micro-XAS

- Complete fluorescence map
- Select pixel of interest
- Scan incident energy
- Also called μ-XAS, μ-XANES, μ-XAFS

- Gives complete spectrum, but at limited points



Pushie, Pickering, Korbas, Hackett & George
Chemical Reviews 114(17):8499-8541 (2014)

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XAS Applications

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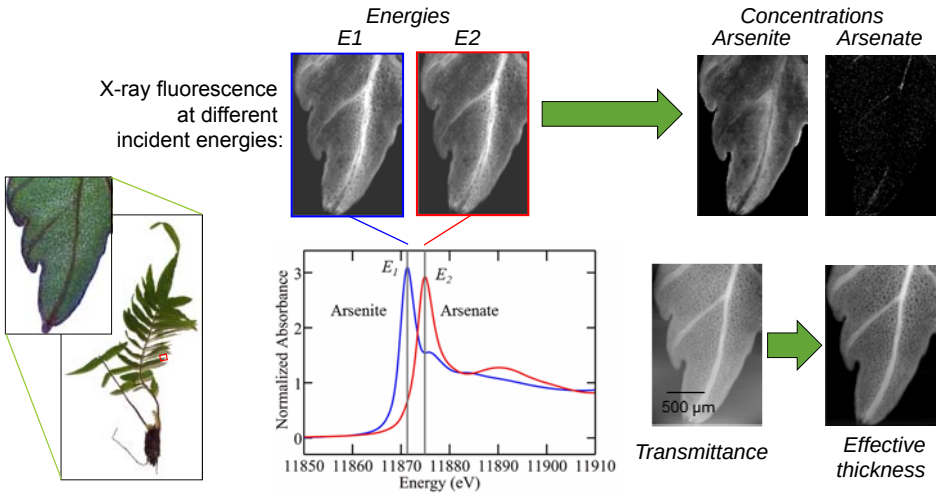
Chemically Specific Imaging

Map at two or more energies to generate chemical species maps



Pickering et al., *PNAS* **97**(20) 10717-10722

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XAS Applications

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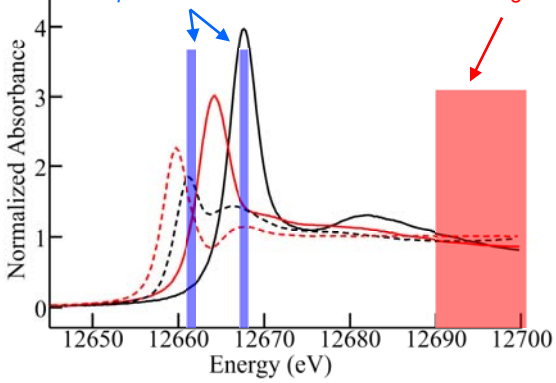
Chemically Specific Imaging *vs.* XFI

Differences lie in the incident energy

Chemical Specific Imaging
Energy at the edge:
Image *chemical species*

X-ray Fluorescence Imaging
Energy above the edge:
Image *element(s)*



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Choice of Chemically Specific Imaging

- X-ray Fluorescence Imaging plus micro-XAS:
  - ✓ Gives entire spectrum at selected points
  - × May miss spatial detail
  - × Longer dwell time at those pixels
- Chemically Specific Imaging:
  - × Need to know which species to look for
  - × Need good spectral contrast
  - ✓ Gives complete spatial maps of each species
  - ✓ Shorter dwell times

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Case Study: An Arsenic-Loving Fern

Pickering, I. J.; Gumaelius, L.; Harris, H. H.; Prince, R. C.; Hirsch, G.; Banks, J. A.; Salt, D. E.; George, G. N. *Environmental Science & Technology* (2006) *40,* 5010-5014.

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An Arsenic-Loving Fern

- *Pteris vittata:* a hyperaccumulator of arsenic
  - Takes up, stores and tolerates arsenic in tissues
  - High tissue concentration compared with soil
  - Can store up to 2% dry weight As

- Arsenic is a major environmental problem in many countries
- *Pteris vittata* shows potential in arsenic **phytoremediation**
  - Use of plants to remove arsenic from contaminated areas
  - (Either *Pteris vittata* itself or its pathways in engineered plants)

I. J. Pickering, L. Gumaelius, H. H. Harris, R. C. Prince, G. Hirsch, J. A. Banks, D. E. Salt and G. N. George *Environ. Sci. Technol.* (2006) **40**:5010-5014

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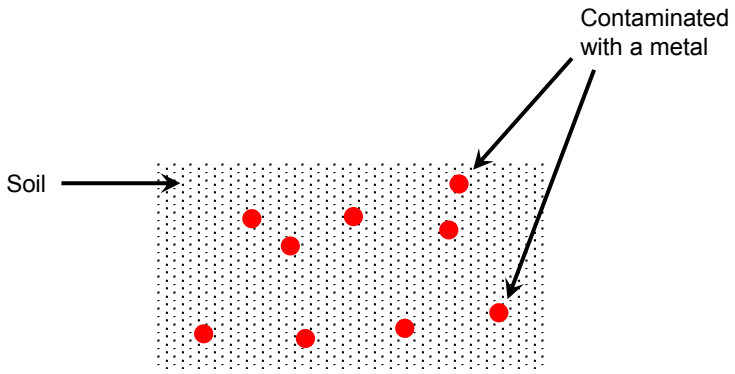
Phytoremediation

Soil contaminated with a metal – how do we clean this up?



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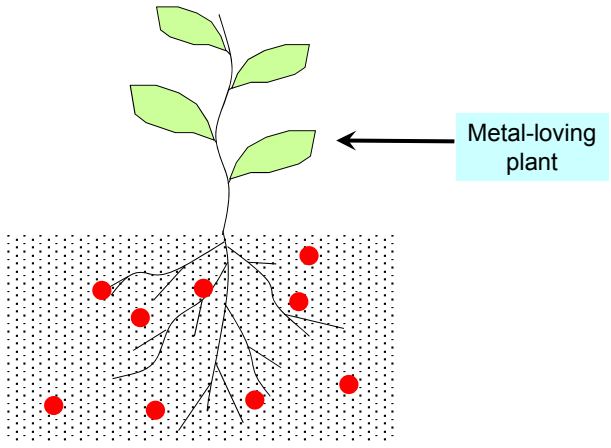
Phytoremediation

Grow plants which take up the metal…



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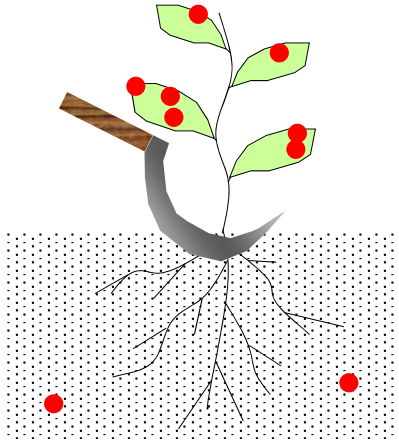
Phytoremediation

Harvest the plants and remove the contamination!



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Pteris vittata - Questions

- Unanswered Questions –
  - What chemical forms of arsenic are present?
  - What biotransformations of arsenic are taking place?
  - Where does biotransformation occur?
  - How does the plant avoid poisoning itself?

- Need a direct probe of arsenic chemical form within living plant tissues
  - X-ray absorption spectroscopy to determine speciation
  - Chemically specific mapping to determine localization

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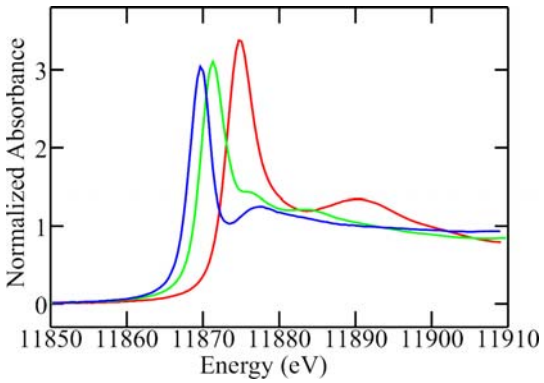
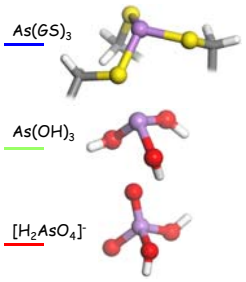
Pteris vittata – X-ray absorption spectroscopy

Use As K-edge XAS of standards as a fingerprint of chemical form





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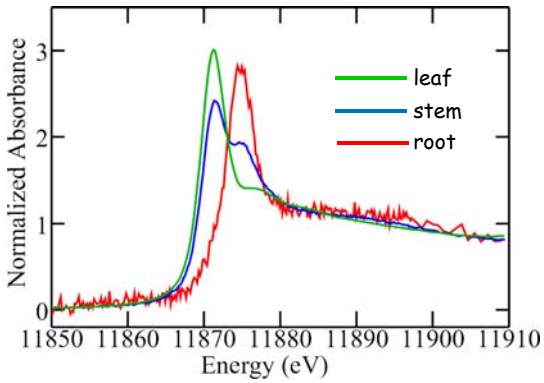
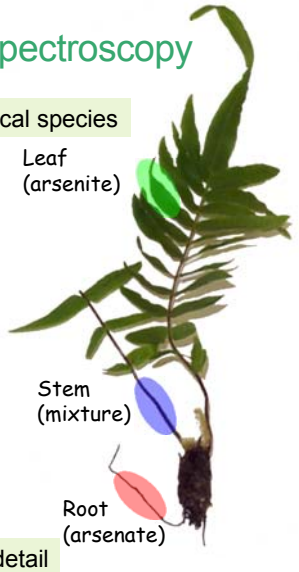
Pteris vittata – X-ray absorption spectroscopy

Different locations in fern show different As chemical species





Use chemically-specific imaging to provide more detail

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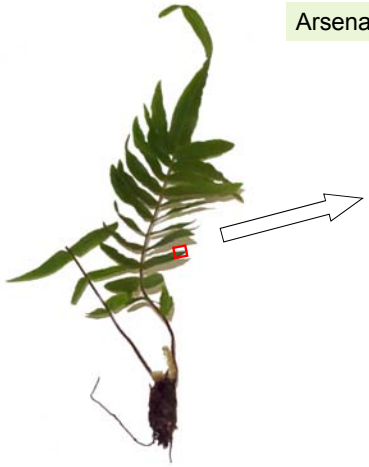
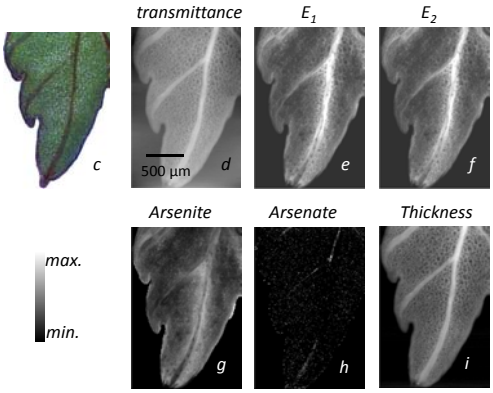
Pteris vittata: Chemically Specific Mapping of Leaflet (Pinna) Tip



Arsenate localized in leaf vein, arsenite high in leaf blade



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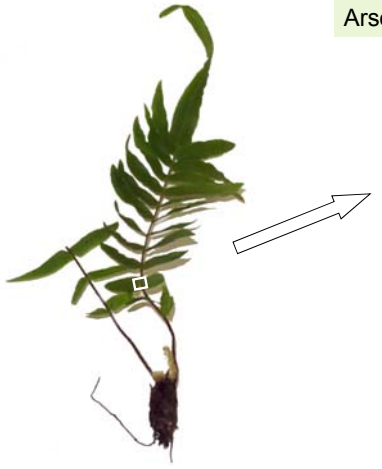
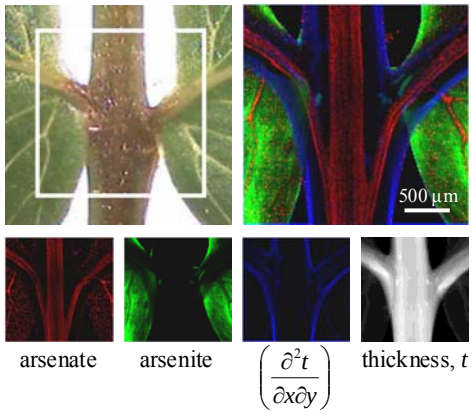
Transport vessels reveal arsenate and arsenite



Arsenite high in leaf blade. Arsenate visible in xylem



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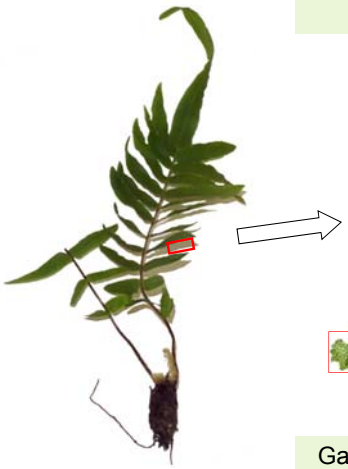
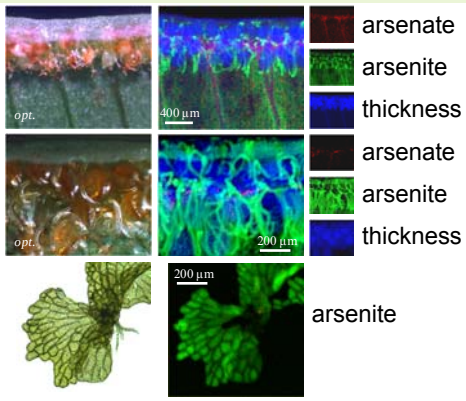
Reproductive Tissues Show Exclusion of Arsenic



Sporangia: arsenic in paraphyses, not spores



Gameophyte: arsenic absent from reproductive area

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What About Sulfur ?

- Arsenic loves sulfur coordination
- Cells are full of available sulfur
- Why isn't arsenic coordinated by sulfur???

Well actually,
maybe it is…

- Bulk near-edge and EXAFS shows borderline evidence for thiolate-coordinated species
- Use 3-component Chemically Specific Imaging to attempt to localize As-thiolate species

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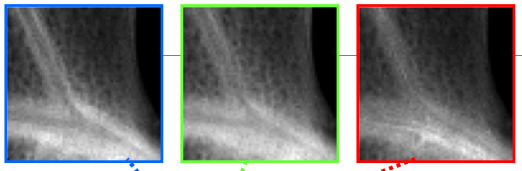
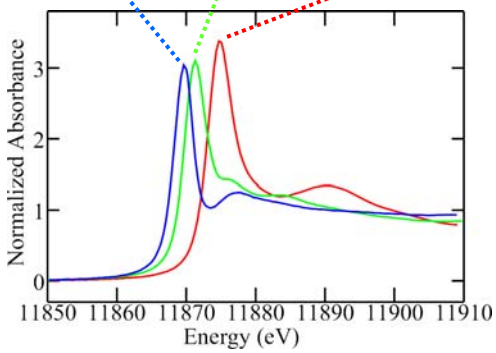
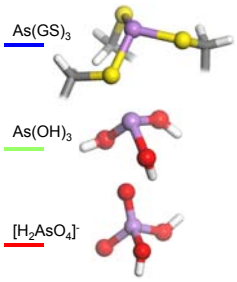
Use 3-Energy Chemically Specific Imaging



Collect images at energies sensitive to arsenic chemical species





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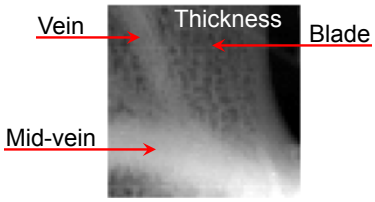
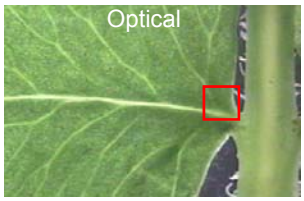
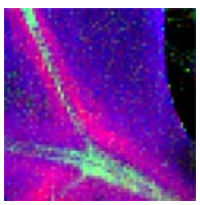
Arsenic-Sulfur Species Revealed Near Vein





Sulfur may be implicated in reduction



Arsenite: stored in blade

Arsenate: in veins (xylem)

Arsenic-thiolate: surrounds veins

As-thiolate
Arsenate
Arsenite

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Arsenic in Fern - Summary

- Sporophytes:
  - Arsenate is transported in the xylem to the leaves
  - In leaves, arsenite is stored at high levels
  - Thiolate-coordination may be implicated in reduction
- Reproductive tissues:
  - Arsenic is excluded

I. J. Pickering, L. Gumaelius, H. H. Harris, R. C. Prince, G. Hirsch, J. A. Banks, D. E. Salt and G. N. George *Environ. Sci. Technol.* (2006) **40**:5010-5014

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Mercury

In collaboration with Graham George, University of Saskatchewan

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Mercury

- Mercury is one of the most toxic elements to which humans are commonly exposed
- Acute exposure of organomercury leads to severe consequences, especially in children or fetuses

- microcephaly
- cerebropalsy
- seizures
- mental retardation
- blindness
- quadriparesis

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Minamata Japan

- Caused by dumping of mercury-containing industrial waste by Chisso Corporation* into Minamata Bay in the 1950's and 60's
- Local fish became heavily contaminated with methylmercury compounds
- First victim was a 5-year old girl in 1956
- Final death toll approached 2,000 people
- Discovery that organo-mercury compounds affect foetal development

* http://www.chisso.co.jp/english/index.asp (http://www.jnc-corp.co.jp/english/)

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Mercury in our food

Fish are a significant source of mercury in our diets and a major source of potentially neurotoxic methylmercury species.

How much mercury in your diet is safe?

In the USA, the FDA, the AHA and the EPA disagree

- EPA: “eat no more than two fish meals a week” “do not eat fish that are high in mercury”
- FDA: “nutritional benefits of eating fish outweigh the risks from mercury”
- AHA: “healthy people should eat fish at least twice a week”

How much fish in our diet is safe?

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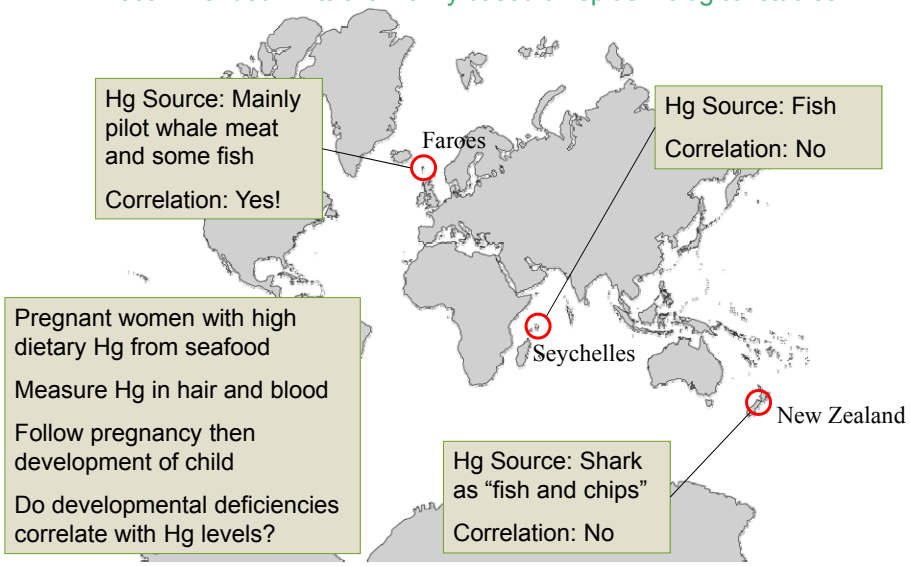
Recommended limits are mainly based on epidemiological studies



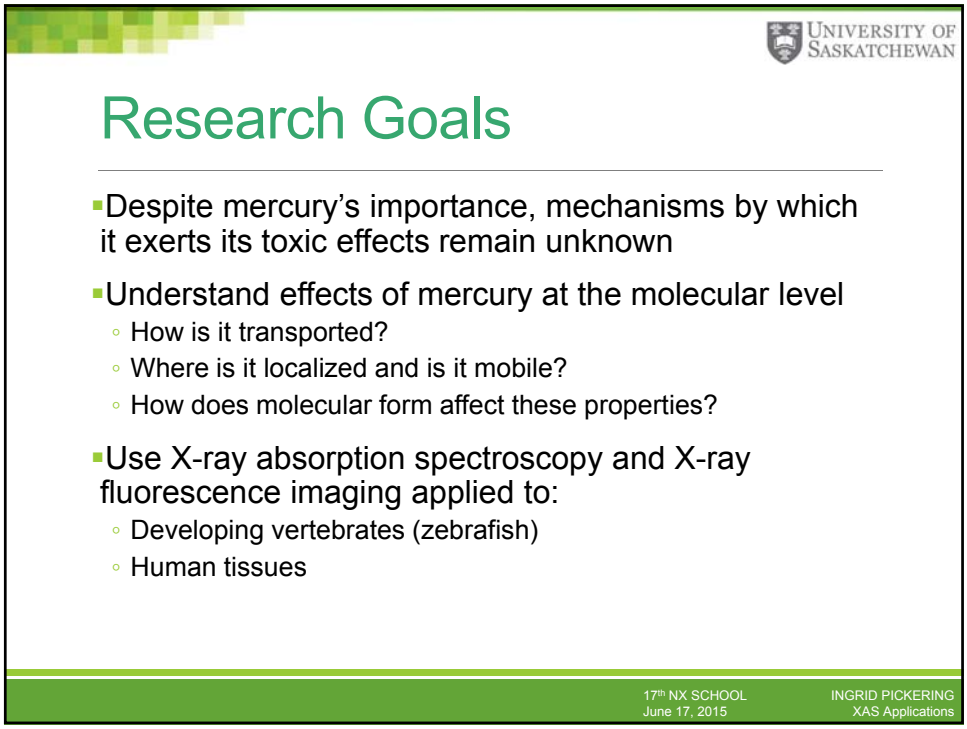
Pregnant women with high dietary Hg from seafood

Measure Hg in hair and blood

Follow pregnancy then development of child

Do developmental deficiencies correlate with Hg levels?


Banning Fish will Impact World Health
The United Nations Food and Agriculture Organization estimates that over one billion people depend on marine fish as primary daily nutrition
If the West passes legislation declaring fish unsafe to eat then other countries may follow suit
This could significantly and negatively impact world health
17th NX SCHOOL June 17, 2015
INGRID PICKERING XAS Applications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Research Goals
Despite mercury's importance, mechanisms by which it exerts its toxic effects remain unknown
Understand effects of mercury at the molecular level
How is it transported?
Where is it localized and is it mobile?
How does molecular form affect these properties?
Use X-ray absorption spectroscopy and X-ray fluorescence imaging applied to:
Developing vertebrates (zebrafish)
Human tissues
17th NX SCHOOL June 17, 2015
INGRID PICKERING XAS Applications

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Mercury in Zebrafish Larvae

M. Korbas, S. R. Blechinger, P. H. Krone, I. J. Pickering and G. N. George. Localizing organomercury uptake and accumulation in zebrafish larvae at the tissue and cellular level. *PNAS* **105**(34), 12108-12112 (2008)

M. Korbas, T. C. MacDonald, I. J. Pickering, G. N. George and P. H. Krone. Chemical form matters: differential accumulation of mercury following inorganic and organic mercury exposures in zebrafish larvae. *ACS Chemical Biology*, **7**(2) 410-419 (2012)

Advanced Photon Source (20-ID)

Argonne NATIONAL LABORATORY

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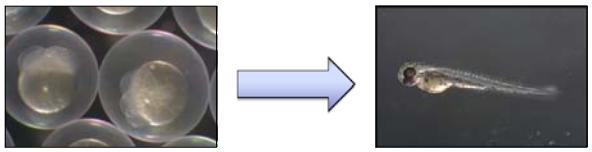
Mercury in Zebrafish

- Mercury is well known as a toxic element but different forms show widely different toxic effects
  - Methyl mercury species considered neurotoxic
- Use zebrafish to study how different mercury forms accumulate
  - Zebrafish are a well-established vertebrate model
  - Easy to maintain, quick growth, well characterized staging series



Korbas M et al (2008) PNAS 105:12108–12112
Korbas M, MacDonald TC et al (2012) *ACS Chem Biol* 7:410-419

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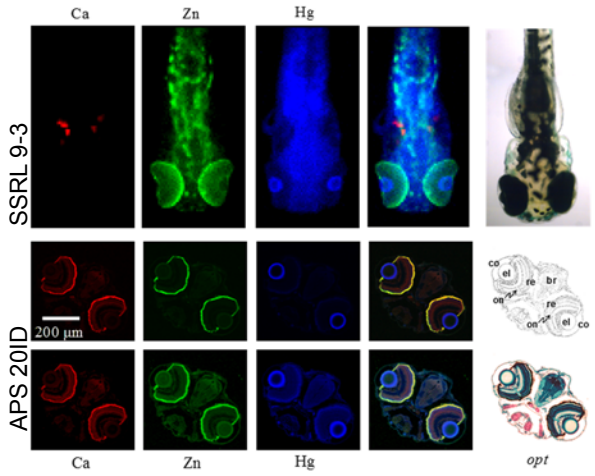
Zebrafish and Methylmercury L-Cysteine

- Treat with 100 μM CH_3Hg(L-Cys)
  - 24 h exposure
  - 3.5 dpf
- Organic mercury accumulates preferentially in outer layers of eye lens



Korbas M et al (2008) PNAS 105:12108–12112
Korbas M, MacDonald TC et al (2012) *ACS Chem Biol* 7:410-419

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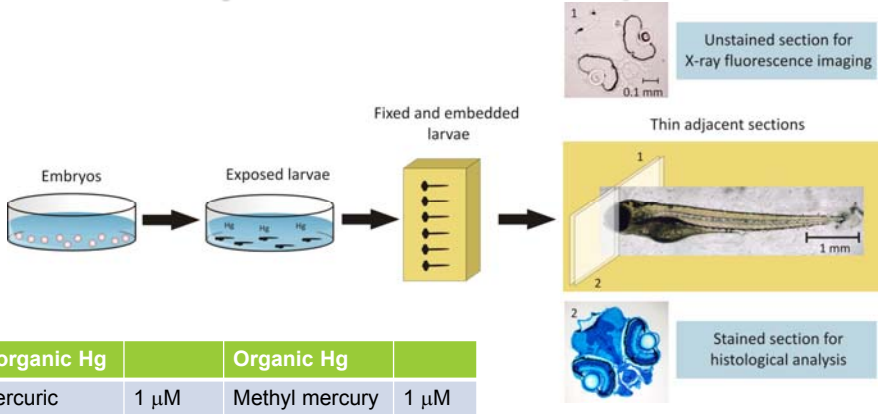
Mercury in Zebrafish: Exposure



Inorganic Hg		Organic Hg	
Mercuric chloride	1 μM	Methyl mercury chloride	1 μM
Mercury bis-L-cysteinate	100 μM	Methyl mercury L-cysteineate	2 μM

Korbas M et al (2008) PNAS 105:12108–12112
Korbas M, MacDonald TC et al (2012) *ACS Chem Biol* 7:410-419

Chemical Form Results

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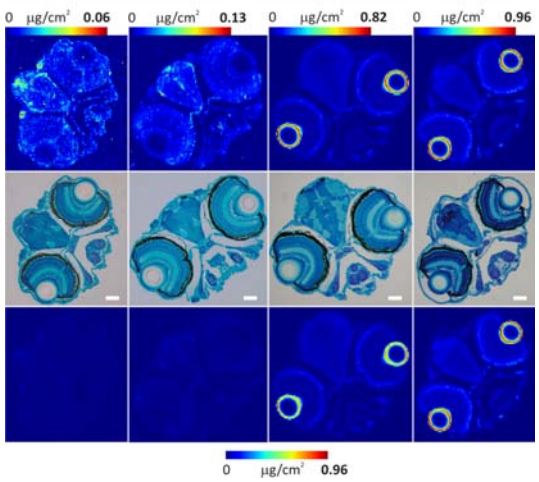
	Inorganic		Organic	
Eyes & Brain	$HgCl_2$	$Hg(L\text{-}Cys)_2$	CH_3HgCl	$CH_3Hg(L\text{-}Cys)$



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Korbas M et al (2008) PNAS 105:12108–12112
Korbas M, MacDonald TC et al (2012) *ACS Chem Biol* 7:410-419

Chemical Form Results

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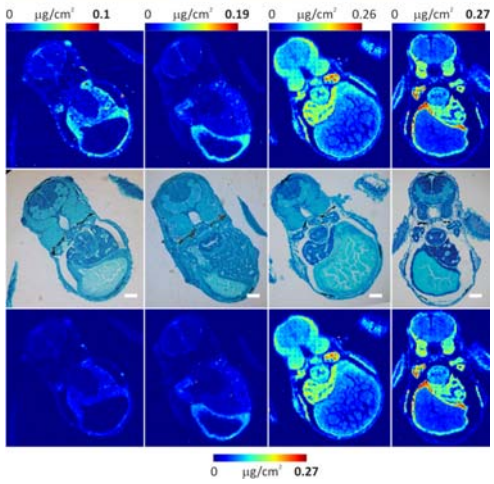
	Inorganic		Organic	
Liver & Kidney	$HgCl_2$	$Hg(L\text{-}Cys)_2$	CH_3HgCl	$CH_3Hg(L\text{-}Cys)$



Advanced Photon Source (20-ID)

Argonne

Korbas M et al (2008) PNAS 105:12108–12112
Korbas M, MacDonald TC et al (2012) *ACS Chem Biol* 7:410-419

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Conclusions from Zebrafish

- Chemical form plays an important role in toxicity
- Preferential accumulation:
  - *Organomercury* in eye lens epithelium, skeletal muscle, gut tube
  - *Inorganic mercury* in brain ventricular region
  - *Both* accumulate in sensory organs and brain
- Organomercury mostly accumulates to higher levels
- Zebrafish: model system to study toxic metals

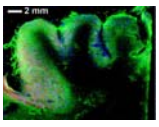
Korbas M et al (2008) PNAS 105:12108–12112
Korbas M, MacDonald TC et al (2012) *ACS Chem Biol* 7:410-419

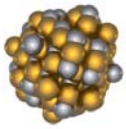
University of Saskatchewan

Mercury, Selenium and Human Brain

M. Korbas[a], J.L. O'Donoghue[b], G.E. Watson[b], I.J. Pickering[a], S.P. Singh[a], G.J. Myers[b], T.W. Clarkson[b], and G.N. George[a]

ACS Chemical Neuroscience, 2010, *1* (12), 810-818
[a] *University of Saskatchewan*
[b] *University of Rochester*






Gosia Korbas

SSRL
Stanford Synchrotron Radiation Lightsource

Objective

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To investigate the molecular nature of **mercury** and **selenium** in human brain samples

Case	1	2	3	4	5
Gender	F	F	M	F	F
Age (yrs)	29	48	60	76	67
Cortex	frontal	occipital	occipital	occipital	occipital
Mercury Exposure	acute poisoning at age 8 yrs	acute poisoning, 10 months to death	fish consumption	fish consumption	none known
Toxicant	CH_3Hg-X	$(CH_3)_2Hg$	CH_3HgS(thiol)	CH_3HgS(thiol)	n/a
Hg(ppb)	1179	2670	324	120	0.06
Pathology	severe atrophy	severe atrophy	normal	normal	normal

Korbas et al. *ACS Chem. Neurosci.* (2010) **1**:810-818
Slide courtesy of Gosia Korbas

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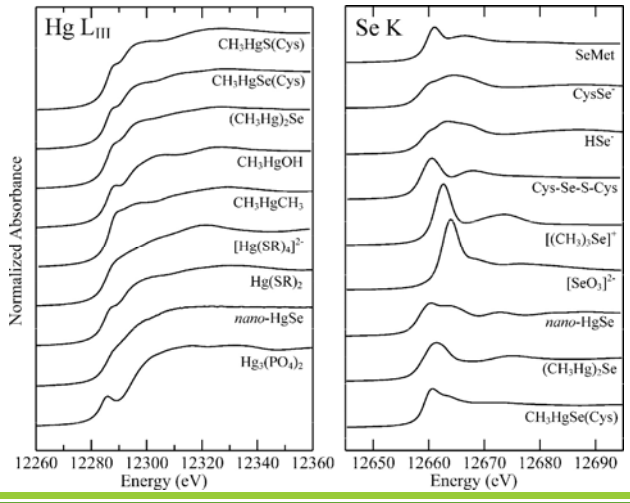
Near-edge spectra as chemical fingerprints



Korbas et al. *ACS Chem. Neurosci.* (2010) **1**:810-818

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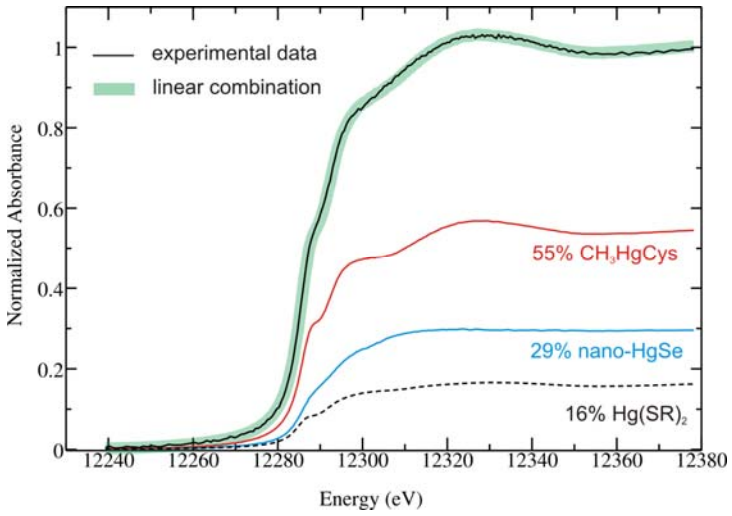
CASE 2

Chemical speciation - mercury



Korbas et al. *ACS Chem. Neurosci.* (2010) **1**:810-818
Slide courtesy of Gosia Korbas

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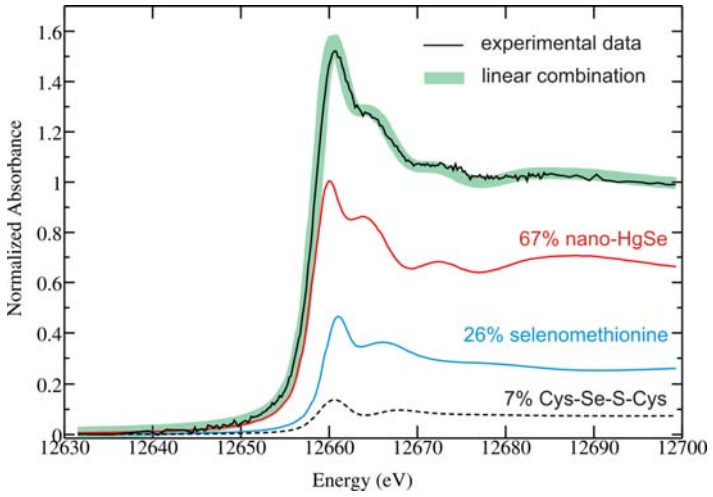
CASE 2

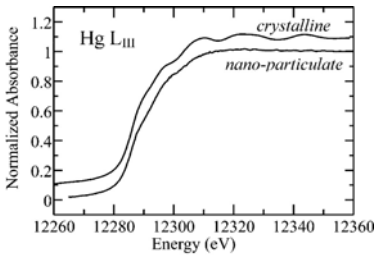
Chemical speciation - selenium

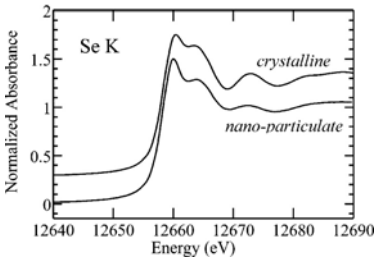


Korbas et al. *ACS Chem. Neurosci.* (2010) **1**:810-818
Slide courtesy of Gosia Korbas

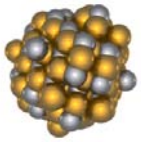
University of Saskatchewan

Nano-HgSe Shows Damped Features





- Spectra are similar compared with crystalline
  - Similar maxima, but much less pronounced
  - Indicates greater disorder due to truncation effects



Korbas et al. *ACS Chem. Neurosci.* (2010) **1**:810-818

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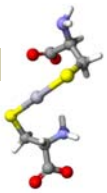
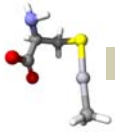
Mercury in brain

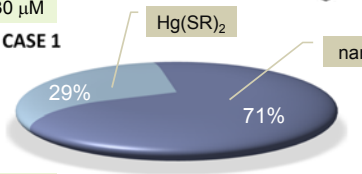
Three main Hg species


nano-HgSe

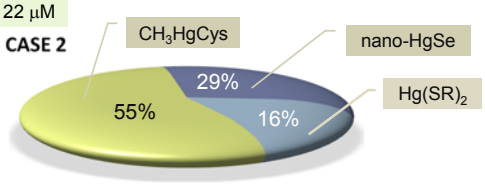

$Hg(SR)_2$


CH_3HgCys

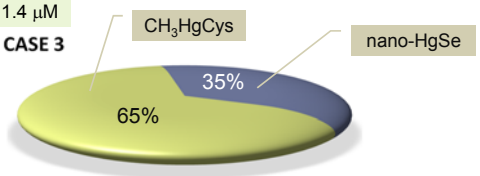
Total Hg: 30 μM
CASE 1



Total Hg: 22 μM
CASE 2



Total Hg: 1.4 μM
CASE 3



Korbas et al. *ACS Chem. Neurosci.* (2010) **1**:810-818
Slide courtesy of Gosia Korbas

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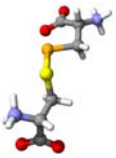
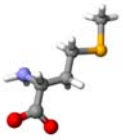
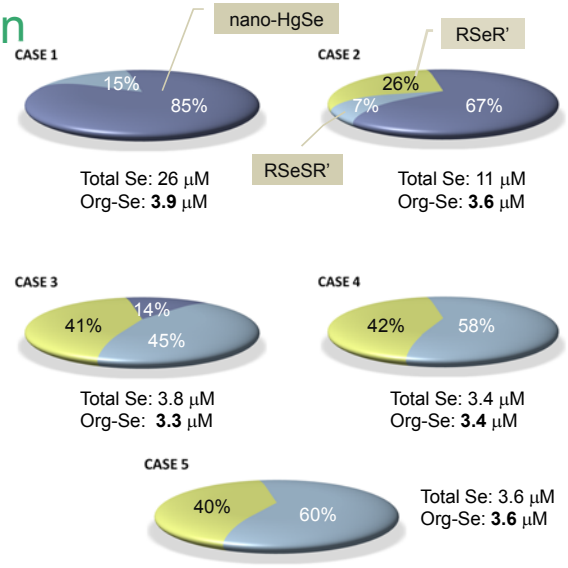
Selenium in brain

Three main Se species


nano-HgSe


RSeSR'


RSeR'



Korbas et al. *ACS Chem. Neurosci.* (2010) **1**:810-818
Slide courtesy of Gosia Korbas

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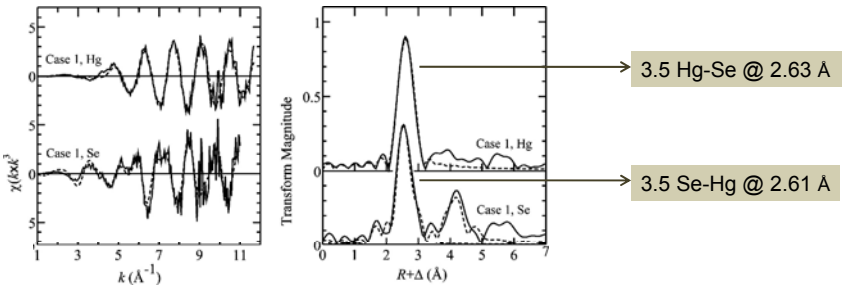
EXAFS Shows Evidence for HgSe Species

Extended X-ray absorption fine structure (EXAFS)

Fourier transforms



Korbas et al. *ACS Chem. Neurosci.* (2010) **1**:810-818

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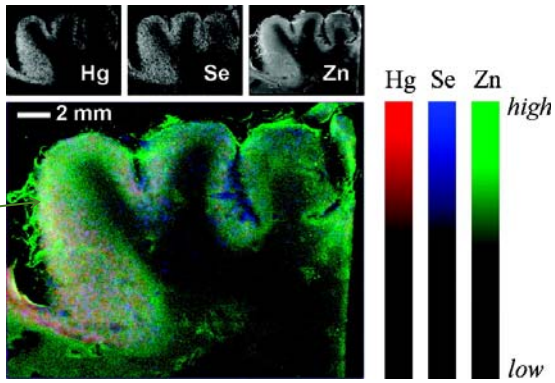
Hg and Se are Co-localized

CASE 2



Majority of Hg and Se co-located in grey matter

X-ray fluorescence imaging

Korbas et al. *ACS Chem. Neurosci.* (2010) **1**:810-818

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Selenium and Mercury in Brain: Summary

- Nano-HgSe seen in all higher exposures
  - Likely an inert species involved in detoxification
- Total brain Hg is not good measure of Hg toxic potential
- Se distributed between
  - organic selenium: remarkably constant
  - nano-HgSe: increases with Hg levels
- "Organic" brain average Se level is not depleted
- Se may redistribute from other structures to bind Hg

Korbas et al. *ACS Chem. Neurosci.* (2010) **1**:810-818

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Case Study: Arsenic and Selenium in Bangladesh


Paul LaPorte
Emory University


Jürgen Gailer
University of Alberta


Roger Prince
ExxonMobil BioMedical Sciences


Graham George
University of Saskatchewan


Olena Ponomarenko
University of Saskatchewan


Mohammad Alauddin
Wagner College


Selim Admed
Bangladesh


Habibul Ahsan
University of Chicago


Julian Spallholz
Texas Tech University

SSRL
Stanford Synchrotron Radiation Lightsource

Gailer, George, Pickering *et al*. (2000) *J. Am. Chem. Soc.* **122**:4637-4639

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Arsenic and Selenium

Arsenic has no confirmed biological function
Selenium is an essential trace element

H																	He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra	Ac															

Lanthanides
Actinides

Metals Non-metals

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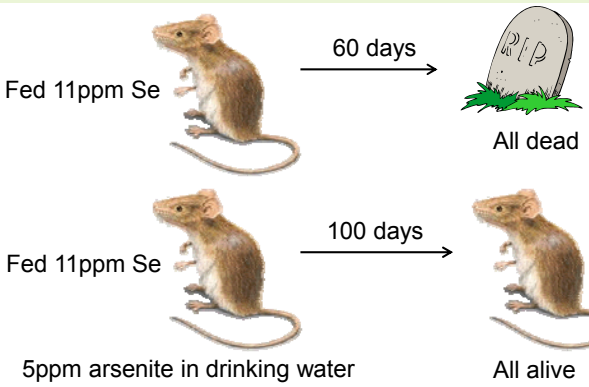
Two Wrongs that *do* Make a Right: Arsenic and Selenium

Moxon (1938) – Arsenite completely protected rats fed upon selenized wheat



"The feeding of arsenic to livestock to prevent selenium poisoning is not recommended on the basis of these results…"

A lethal dose of arsenite (or selenite) can be completely counteracted by an equal and otherwise lethal dose of selenite (or arsenite).

Moxon AL (1938) *Science* 88(2273): 81

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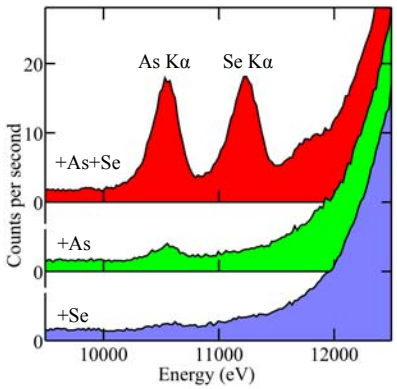
Arsenic and Selenium in Bile

- Inject rabbit with arsenite and selenite
- As and Se: excreted in bile only when both are present
- As:Se 1:1 in bile



- Suggests an arsenic-selenium molecule responsible for mutual detoxification

Gailer et al., *J. Am. Chem. Soc.* **122**, 4637-4639 (2000).

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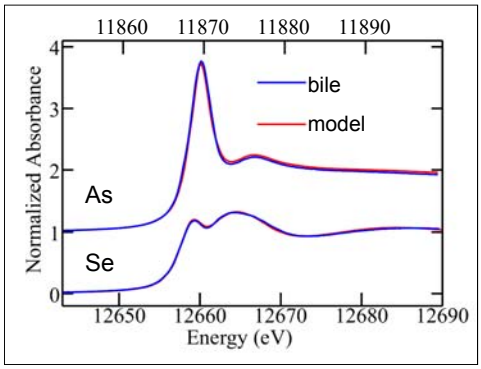
Arsenic-Selenium Antagonism

- Bile As and Se K near-edge spectra identical with model synthesized from arsenite, selenite and glutathione



Gailer, George, Pickering *et al*. (2000) *J. Am. Chem. Soc.* **122**:4637-4639 17th NX SCHOOL June 17, 2015 INGRID PICKERING XAS Applications

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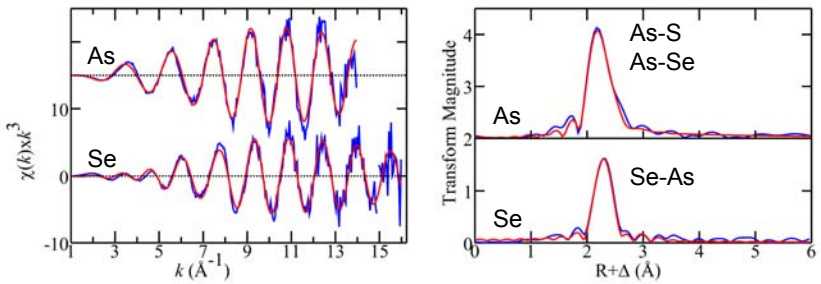
Arsenic-Selenium Antagonism

• Bile As and Se EXAFS used to structurally characterize species in bile



As EXAFS:	2 As-S	@ 2.25 ± 0.02 Å
	1 As-Se	@ 2.32 ± 0.01 Å
Se EXAFS:	1 Se-As	@ 2.31 ± 0.02 Å

Gailer, George, Pickering *et al*. (2000) *J. Am. Chem. Soc.* **122**:4637-4639 17th NX SCHOOL June 17, 2015 INGRID PICKERING XAS Applications

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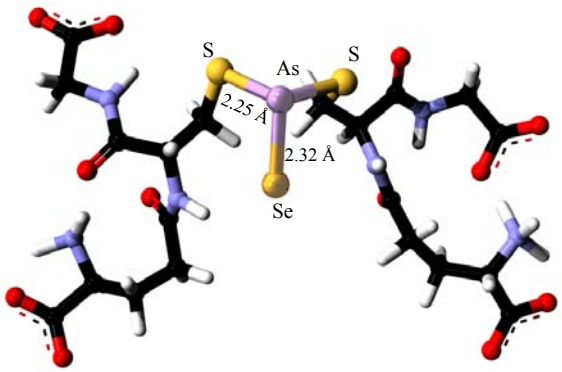
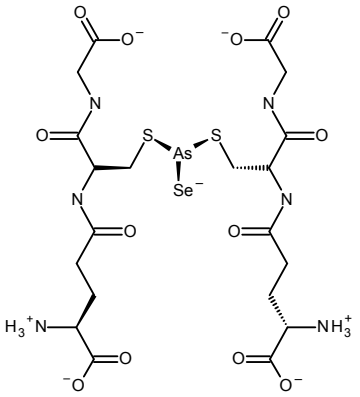
As-Se Species Identified in Bile

- An unusual molecule with 1:1 Se:As - the seleno-*bis*(S-glutathionyl) arsinium ion





Energy minimized DFT optimized geometry

Gailer, George, Pickering *et al*. (2000) *J. Am. Chem. Soc.* **122**:4637-4639

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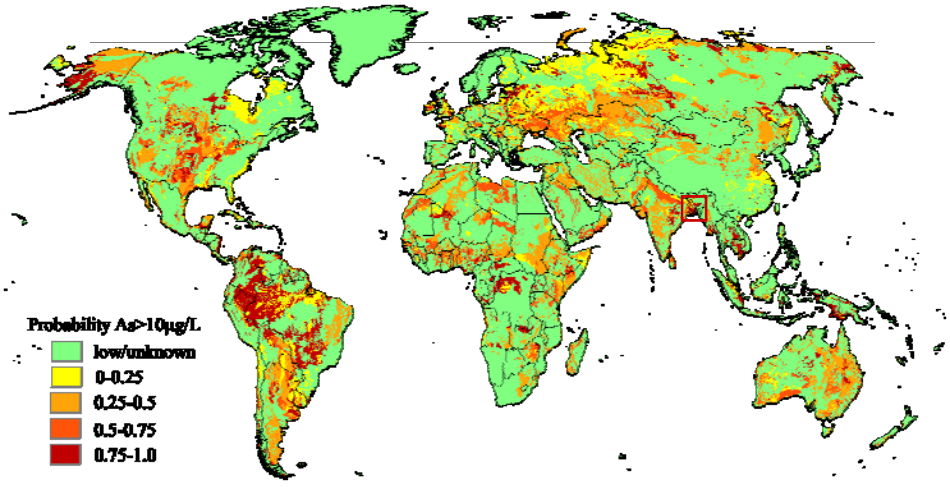
Arsenic water contamination



Amini *et al.*, 2008, *Env. Sci. Technol.* **42**:3669-75

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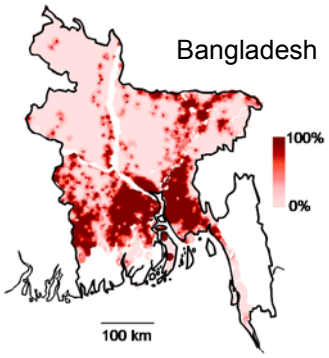
Arsenic Poisoning in Bangladesh

- In Bangladesh & parts of India, tube wells are contaminated with arsenic
- Leads to "arsenicosis"
  - Dermatitis and skin disorders
  - Malignant tumors
  - Death
- 25% of all deaths in affected areas now due to arsenicosis
- Between 35 and 85 million people are affected*



Percentage of wells measuring >50 ppb As in water
data from British Geological Survey Report WC/00/19

* Estimated by World Health Organization

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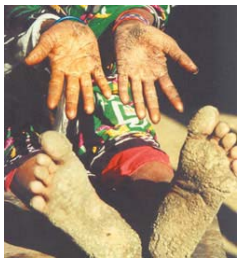
Arsenic Poisoning in Bangladesh

- Puzzles:
  - Not all people drinking from same well get sick
  - Other areas in the world have high arsenic but not the same symptoms



- Clues:
  - Bangladesh is low in dietary selenium
  - Very low selenium levels in livers of victims
  - Other arsenicosis areas also have low selenium

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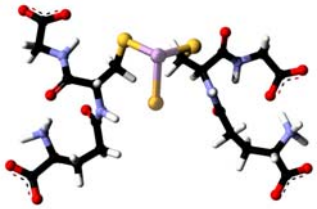
A Selenium-Arsenic Hypothesis

- Formation of $[(GS)_2AsSe]^-$ is a mechanism to that serves to mutually detoxicify As and Se
  - $[(GS)_2AsSe]^-$ is rapidly excreted to bile
- Selenium is an essential trace element
  - For every atom of As removed, one atom of Se is lost too
- Diet in arsenicosis areas is low in Se
  - Is the arsenicosis an As-induced Se deficiency?
  - Chronic Se deficiency can cause symptoms similar to arsenicosis
- First suggestion of a palliative role for Se in arsenicosis



Gailer, George, Pickering *et al*. (2000) *J. Am. Chem. Soc.* **122**:4637-4639

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Clinical Trial of Selenium Supplementation

www.bangladesh-selenium.org

- Benefits observed in only ~15% of patients
- No statistical demonstration of benefits
- Selenium levels appeared *synchronized* in a significant number of patients…

Patients	819
Duration	48 weeks
Location	Upazilla, Bangladesh
Dose	200 µg Se/day or placebo
Endpoints	Dermatological

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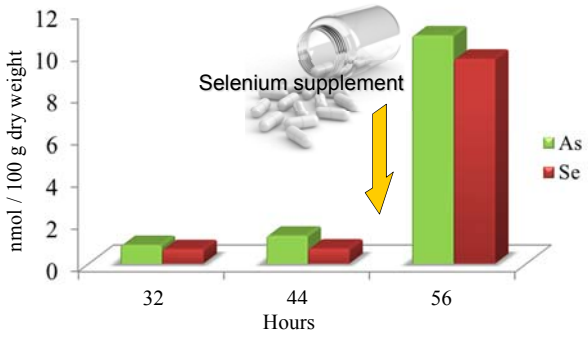
Preliminary Results, Pilot of New Clinical Trial



- Selenium supplement promotes fecal arsenic excretion

Grand Challenges Canada
Grands Défis Canada

- New clinical trial now funded by Grand Challenges Canada

https://youtu.be/D_845FQL0c8

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Closing Remarks

- X-ray absorption spectroscopy provides chemical information on heavier elements in the life sciences
  - Often complex, heterogeneous systems
- Combined with X-ray fluorescence imaging, provides spatial resolution of chemical information