A vertical rectangular image on the left side of the slide. It features a light blue background with a white atomic symbol in the upper left. Below it, the chemical formula SiO_2 is visible. The center shows a 3D ball-and-stick model of a molecular structure. At the bottom, there are two smaller images: a multi-colored XRF spectrum on the left and a 2D diffraction pattern on the right.

Chemical TXRF: Advantages for Pharmaceutical and Food Testing

Michael E. Rider, Ph.D.

The Woodlands, TX

Michael.Rider@bruker-axs.com

Welcome

Today's Topics

- Introduction to XRF and TXRF
- The S2 PICOFOX Benchtop TXRF system
- Sample Preparations
 - Liquid
 - Suspensions
 - Solid Samples
 - Direct Analysis of Solid Samples
- Instrumental Measurements of Food, Pharmaceutical, and Medicinal Samples.

Contributing Authors

Alexander Seyfarth
Product Manager XRF, NA
Madison, WI USA



Dr. Hagen Stosnach
Applications Scientist TXRF
Berlin, Germany



Dr. Armin Gross
Global Product Manager TXRF
Berlin, Germany

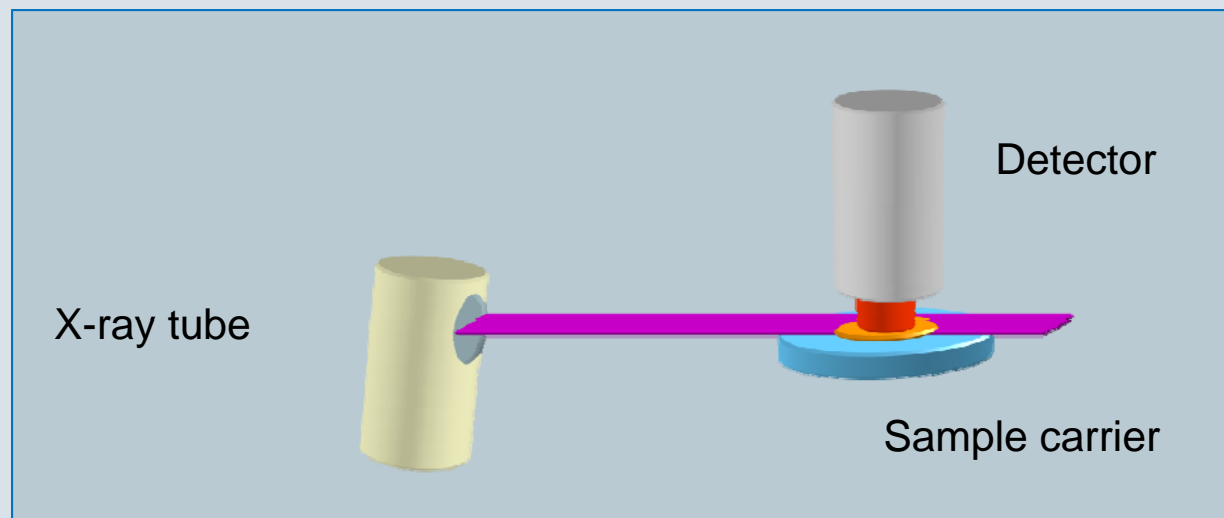




Introduction to XRF and TXRF

Principles of total reflection X-ray fluorescence (TXRF) spectroscopy

Total reflection X-ray fluorescence spectroscopy



Beam angle: $0^\circ / 90^\circ$

Principles of total reflection X-ray fluorescence spectroscopy

Samples for total reflection X-ray fluorescence spectroscopy:

- Powders: Direct preparation or as suspension
- Liquids: Direct preparation
- always as a thin film, micro fragment or suspension of a powder
- necessary sample amount:
Low μg respectively μl range



Principles of total reflection X-ray fluorescence spectroscopy

Quantification in total reflection X-ray fluorescence spectroscopy

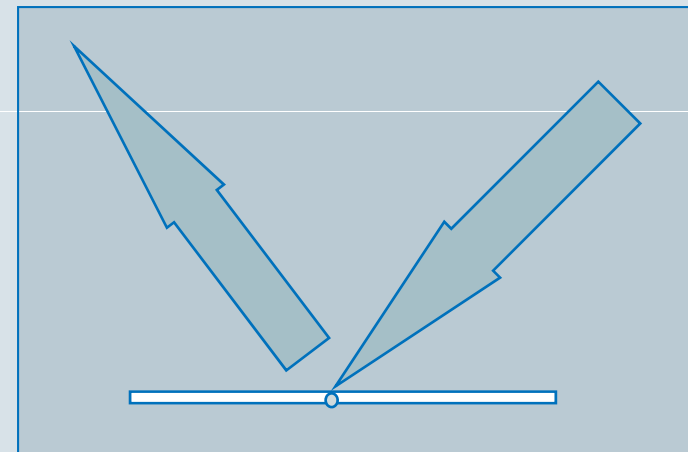
In TXRF the samples are prepared as thin films or layers

Therefore matrix effects are negligible

QUANTIFICATION IS POSSIBLE THROUGH

:

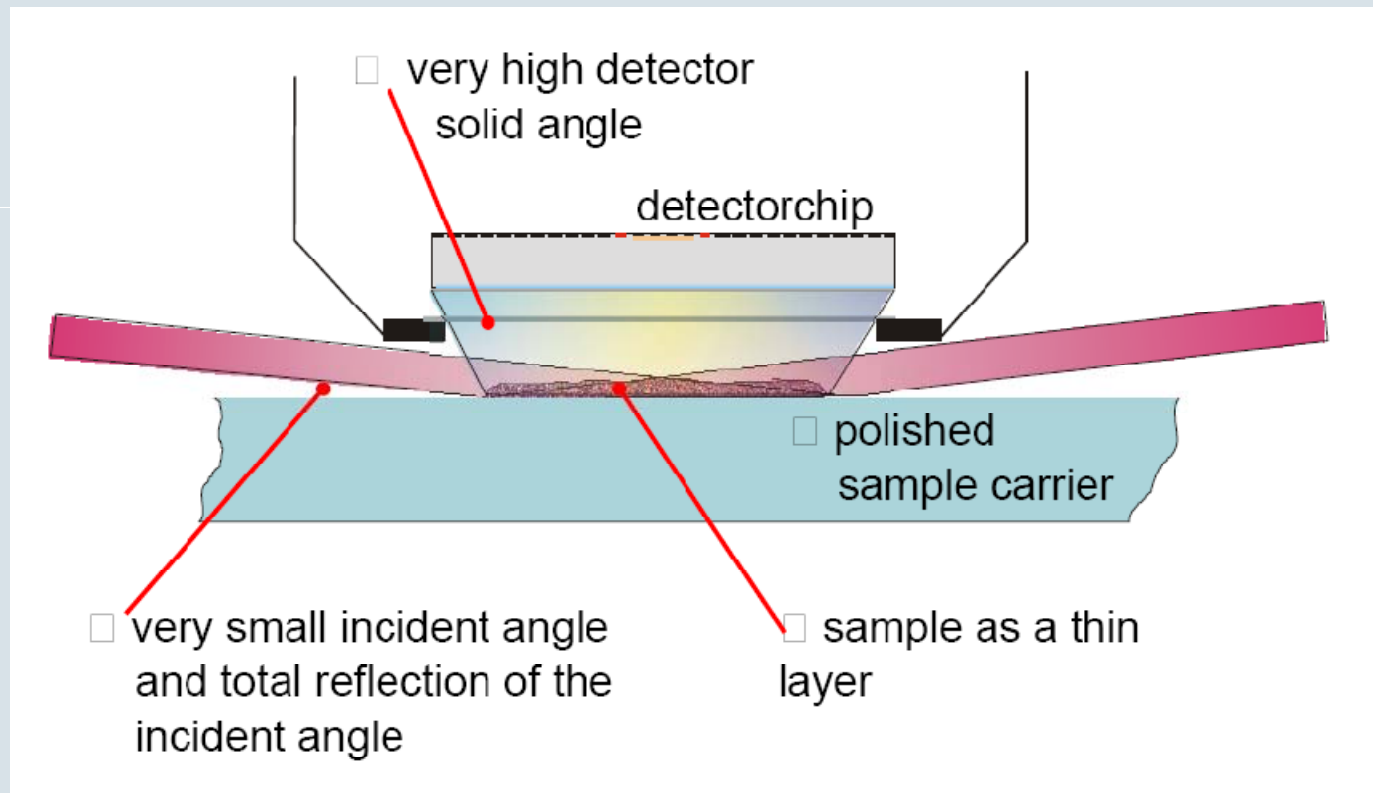
- Sensitivity of the instrument for element lines (energy-dependent)
- Net intensity of element lines
- Known concentration of an internal standard element



Negligible absorption of primary beam and fluorescence radiation

Principles of TXRF

X-ray Interaction with Sample



Principles of TXRF

Key to TXRF's High Signal to Low Background

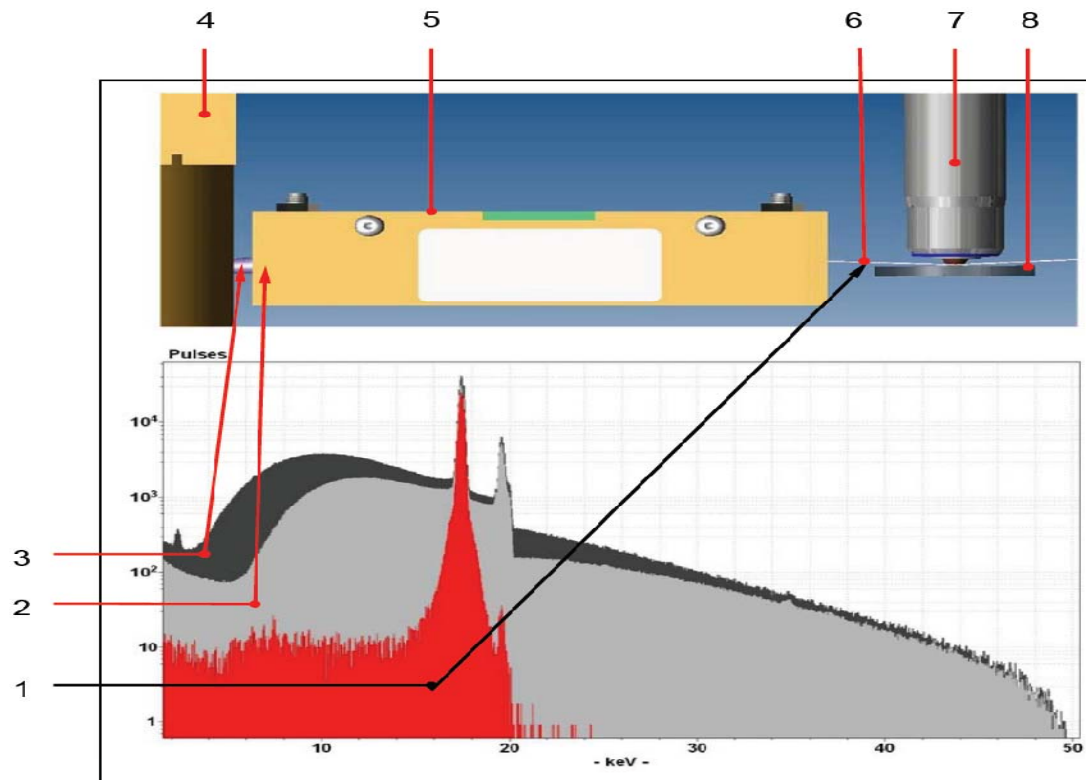


Figure 10: Monochromatization of the excitation radiation by means of a multilayer monochromator

- | | | | |
|---|----------------------------------------------------------------|---|---------------------------------|
| 1 | excitation spectrum | 5 | monochromator |
| 2 | spectrum after pre-filtration, filter component invisible here | 6 | monochromatized excitation beam |
| 3 | emission spectrum of the tube | 7 | detector |
| 4 | X-ray tube | 8 | sample carrier |

The Instrument S2 PICOFOX

Benchtop TXRF spectrometer
"S2 PICOFOX"

- Chemical TXRF Analyzer
- Metal-ceramic X-ray tube
 - Mo anode
 - air-cooled
 - optionally other tubes available
- Multilayer monochromator
- XFlash[®] Silicon Drift Detector
 - electro-thermally cooled
 - ≤ 149 eV @ 100 kcps
- Automatic version
 - 25 sample cassette





Chemical T-XRF units

Basic (commercially available) T XRF

- No vacuum chamber, no purge
- No moving monochromator or alignment
- SDD detector: high count rate, resolution and LN2 free!

Samples on substrate only

Designed for chemical analysis only

37 kg mobile use possible with 120V/230V

Elements Measured by the Mo PICOFOX

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	L	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra	A															
		L	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
		A	Ac	Th	Pa	U	Np	Pu	Am	Cm	Ek	Cf	Es	Fm	Md	No	Lr

- Impossible to measure
- Difficult to measure
- Measured using K-lines
- Measured using L-lines

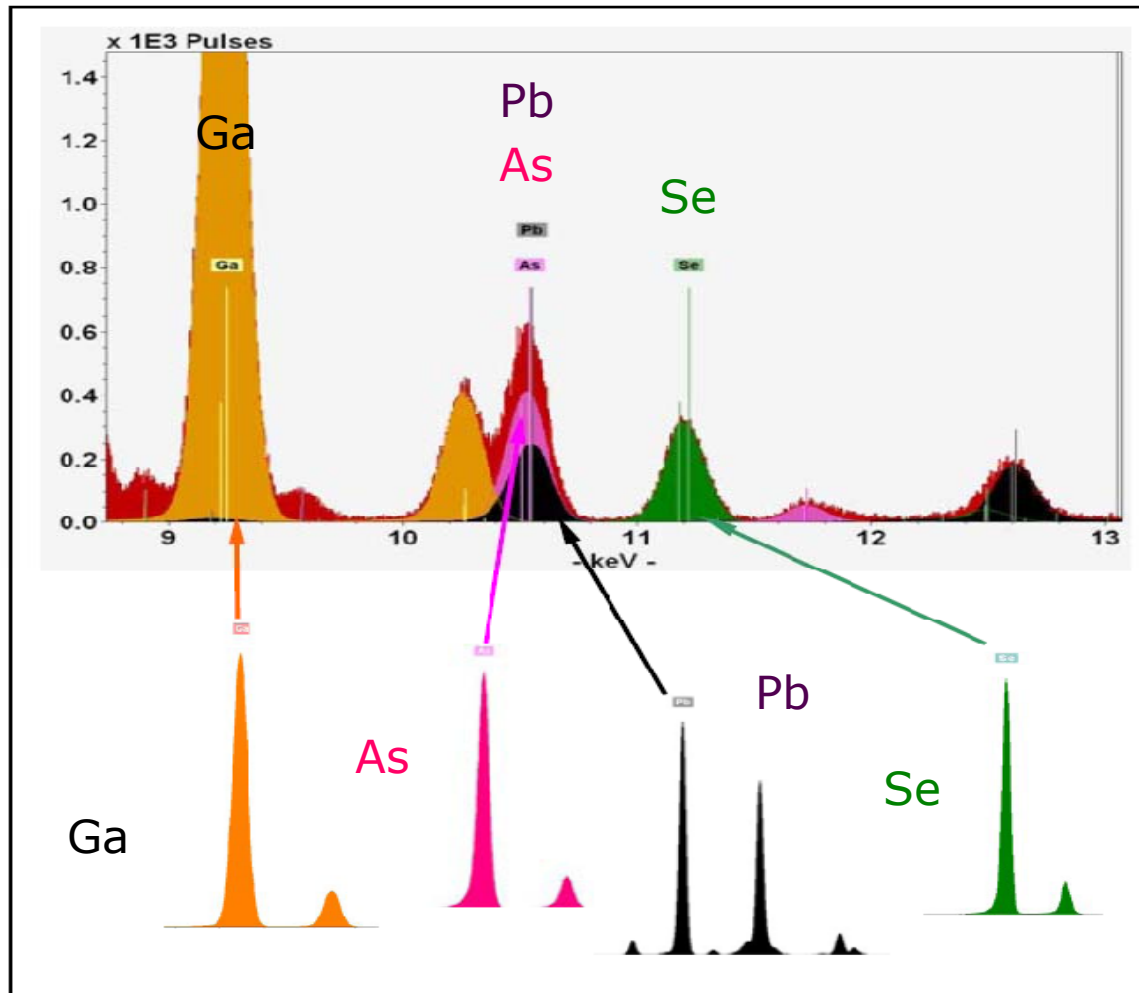
Elements Measured by the W PICOFOX

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	L	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra	A															
		L	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
		A	Ac	Th	Pa	U	Np	Pu	Am	Cm	Ek	Cf	Es	Fm	Md	No	Lr

- Impossible to measure
- Difficult to measure
- Measured using K-lines
- Measured using L-lines

S2 PICOFOX

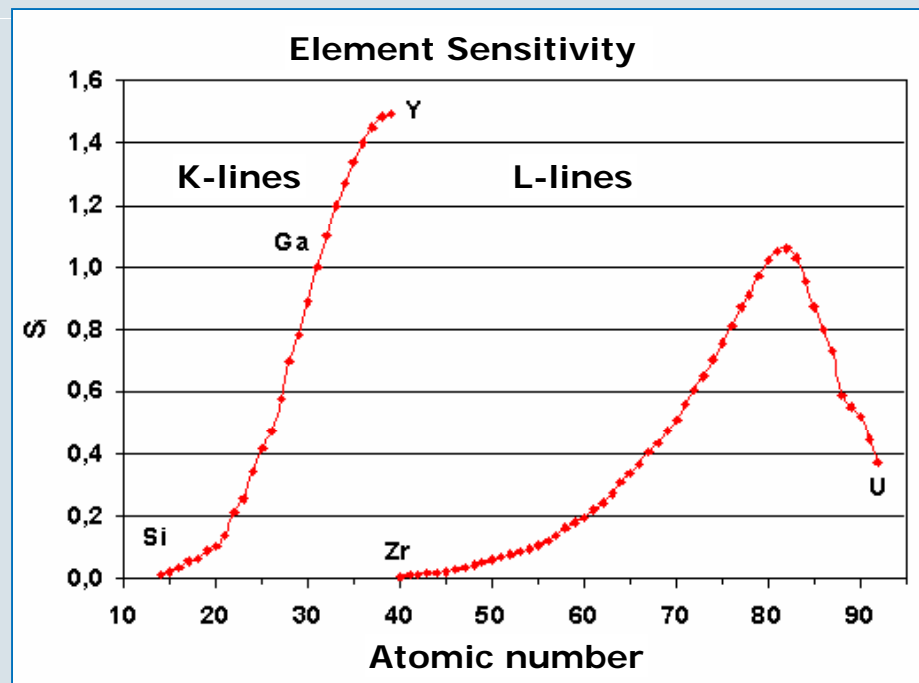
Overlapping Peaks Separated by Deconvolution



S2 PICOFOX

Element sensitivity

- The S2 PICOFOX detects elements from Na(11) to U(92)
- The element sensitivities depend on the atomic number
- The sensitivity factors are calibrated at factory





S2 PICOFOX

TXRF Measurement Time Considerations

The choice of measurement time is made in dependence of:

- Concentration ranges
- Necessary accuracy and reproducibility

Typical measurement times are:

- 120 s for a fast overview measurement
- 600 s for the analysis down to the low mg/kg respectively mg/l range
- 1000 s for the analysis in the sub-mg/kg respectively sub-mg/l range

Sample Carrier

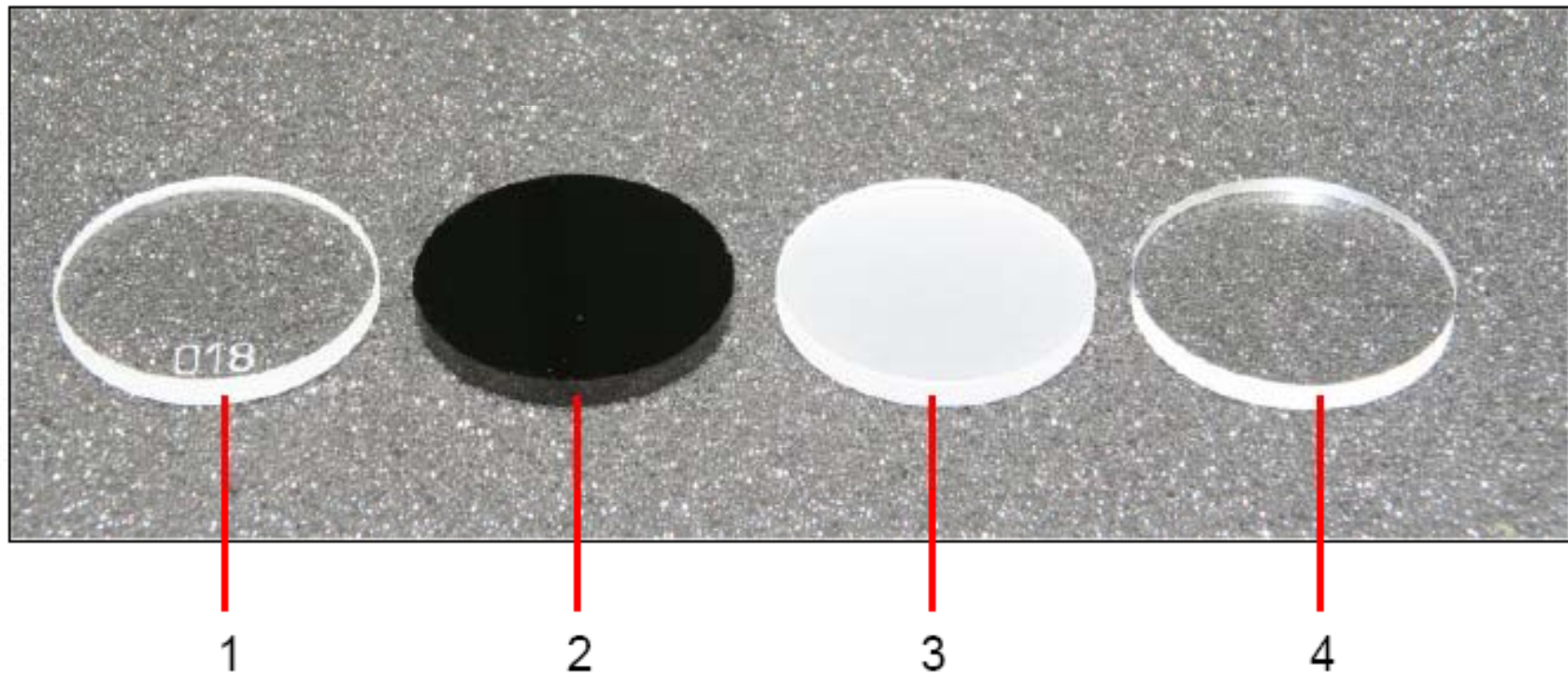
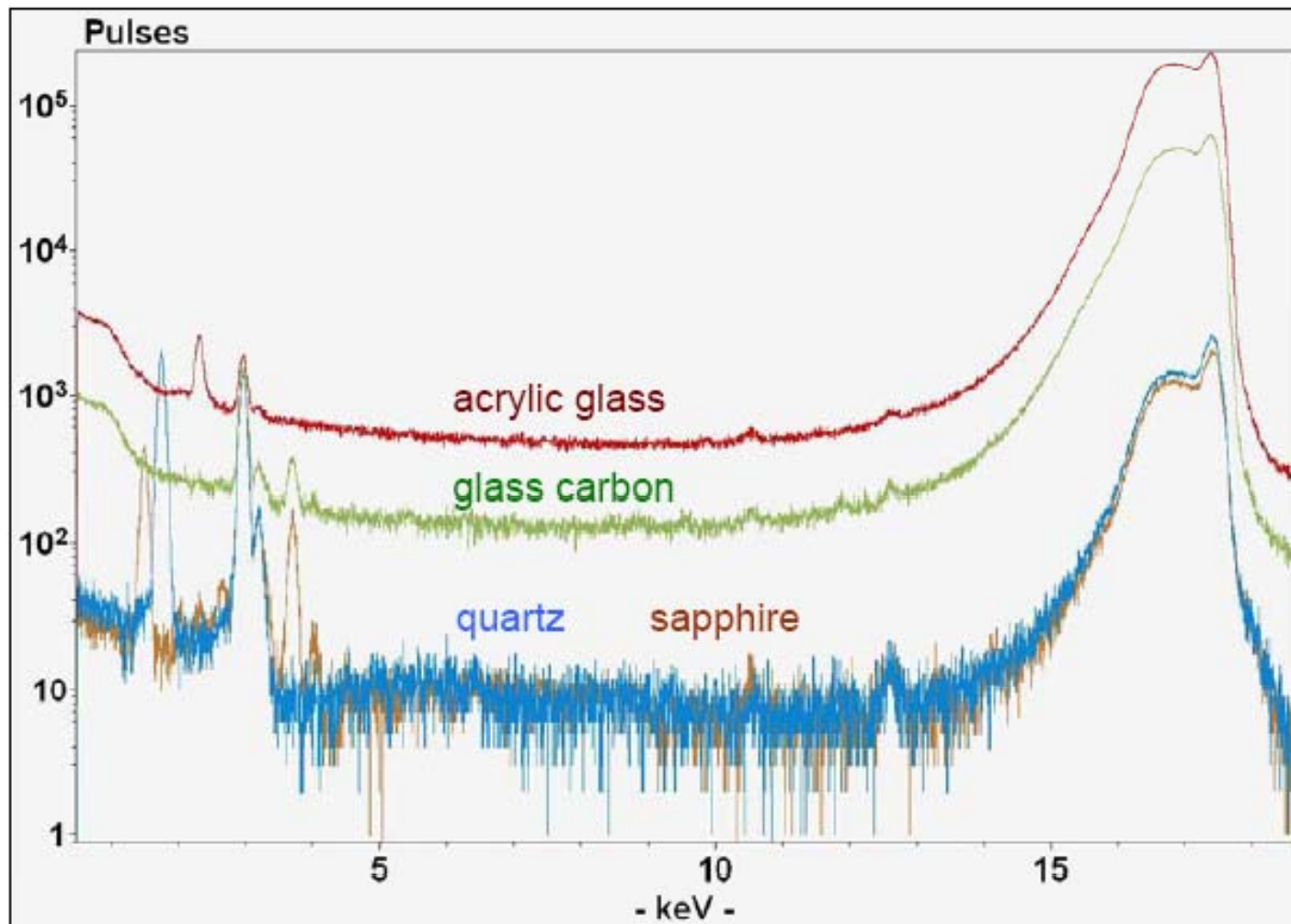


Figure 18: Sample carrier types

1 quartz glass
2 glass carbon

3 sapphire
4 acrylic glass

Sample Carrier





Why Wait for Sample Prep!

Ease of Use and Versatility of
TXRF Analysis



S2 PICOFOX

Sample Types Overview

Sample type

- Liquids
- Suspensions
- Solids, powders

Application

Orange Juice/ Rum Analysis
Tap Water

Blood and serum testing
Medical Testing

Wheat Samples
Pharmaceutical Samples

Sample Preparation

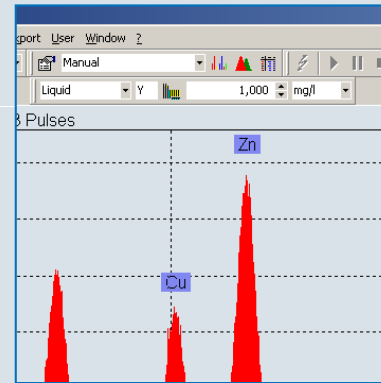
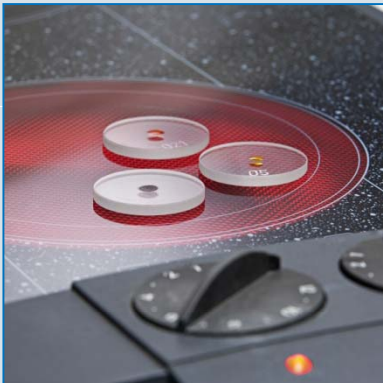
Liquid Samples

You'll need just a few steps for the preparation of liquid samples



- Fill sample in micro tube
 - Add internal standard
 - Homogenize
- Pipette on carrier

Sample Preparation Final Steps



- Dry by heat / vacuum
 - Load the instrument
 - Start data acquisition

Getting the Lead out (or knowing where it is...)

Sample

- Rum, 18 years old

Comparison between

- Flow-injection hydride-generation atomic absorption spectrometer with flame-quartz atomizer (FI-HG-AAS)
- S2 PICOFOX TXRF spectrometer

Source:

Latif Elçia, Zikri Arslanb & Julian F. Tyson (2009):
Determination of lead in wine and rum samples by flow injection-
hydride generation-atomic absorption spectrometry,
Journal of Hazardous Materials, Volume 162, Issues 2-3,



TXRF on RUM

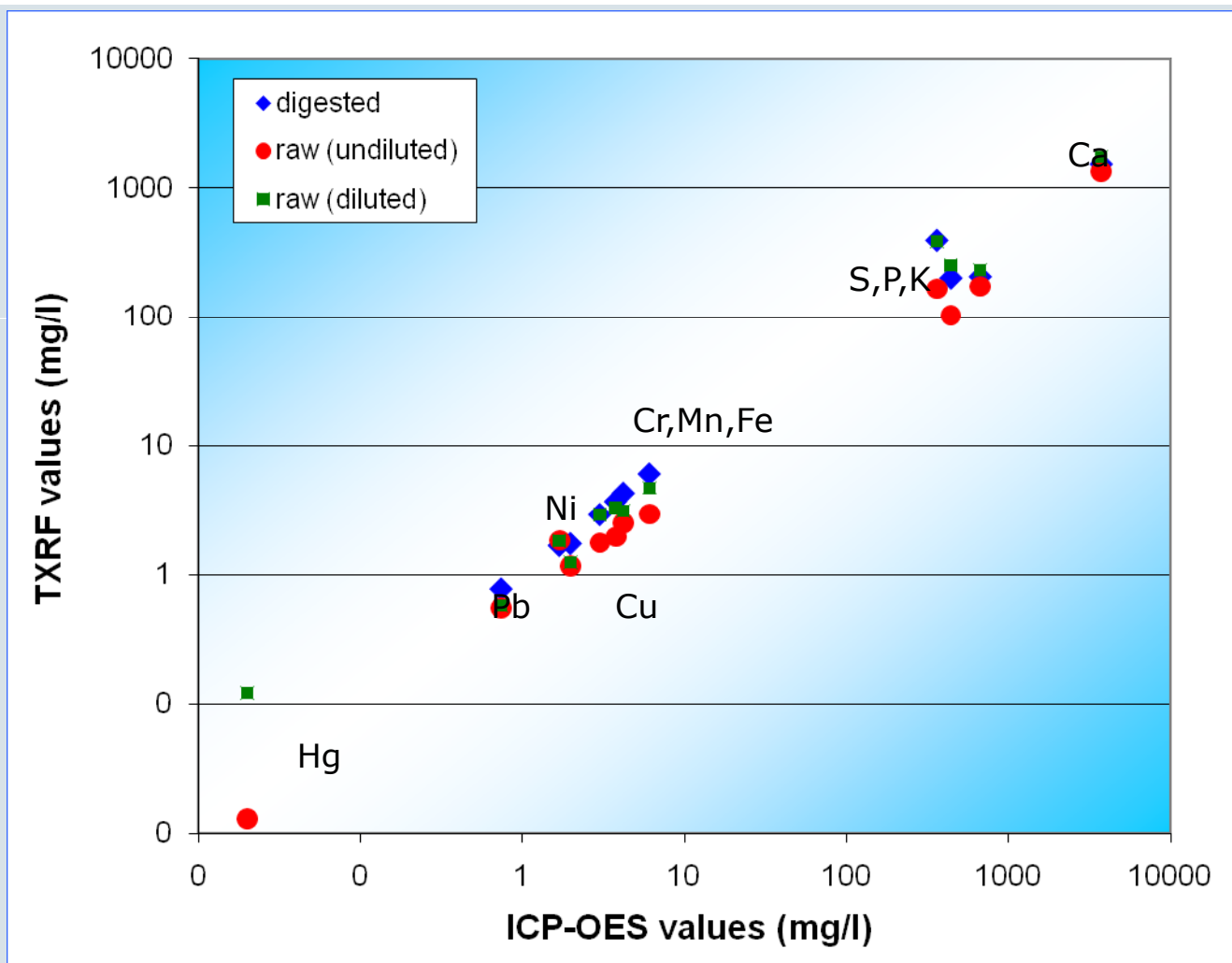
	TXRF	FI HG AAS
Sample preparation	<ol style="list-style-type: none"> 1. addition of Ga standard to 1 ml rum 2. 10 µl sample on quartz carrier 	<ol style="list-style-type: none"> 1. acidification of 170 µl rum to 0.30 Vol-% HCl, 2. addition of 3% solution of oxidant $K_3Fe(CN)_6$ in HCl 3. Neutralisation with $NaBH_4$ formation of lead hydride (PbH_4)
Measurement	1000 s measurement time	<ol style="list-style-type: none"> 1. calibration 2. measurement

Application

Sewage & Fresh Water Analysis



Results



Mercury in Tap Water and Orange Juice

Situation

- Sources for mercury release
 - natural sources (volcanoes)
 - industrial activities (coal-fired power plants, gold production, cement, non-ferrous metal industry)
- Maximum contamination levels (MCL) for Hg in drinking water
 - 1 $\mu\text{g/l}$ European Community (directive 98/83)
 - 2 $\mu\text{g/l}$ US-EPA (Safe Drinking Water Act, 1974)





Foodstuff

Hg is difficult

Hg is volatile and easily lost due to heat during preparation or DIGESTIONS!

TXRF Instrumentation can readily detect the Hg! But preparation is very important..

E.g. fish/wheat (FDA limit 1 ppm Hg)

- FREEZE DRYING and GRINDING followed by mixing with IS and AIR drying
- (achievable as well with WD and ED XRF but calibration is difficult!)

Mercury in Tap Water and Orange Juice

Samples

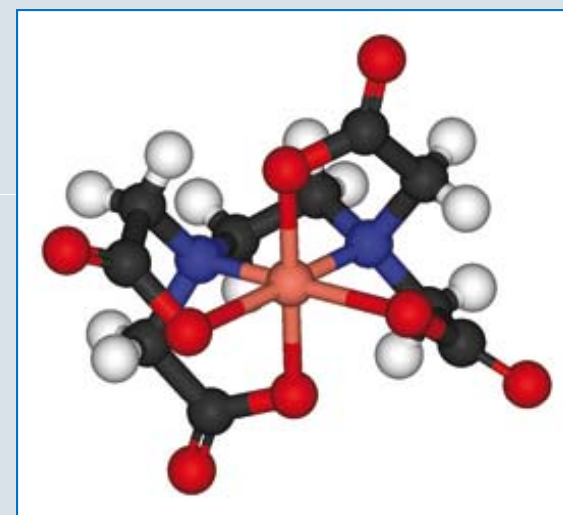
- tap water and orange juice, spiked with Hg (50 – 500 µg/l)

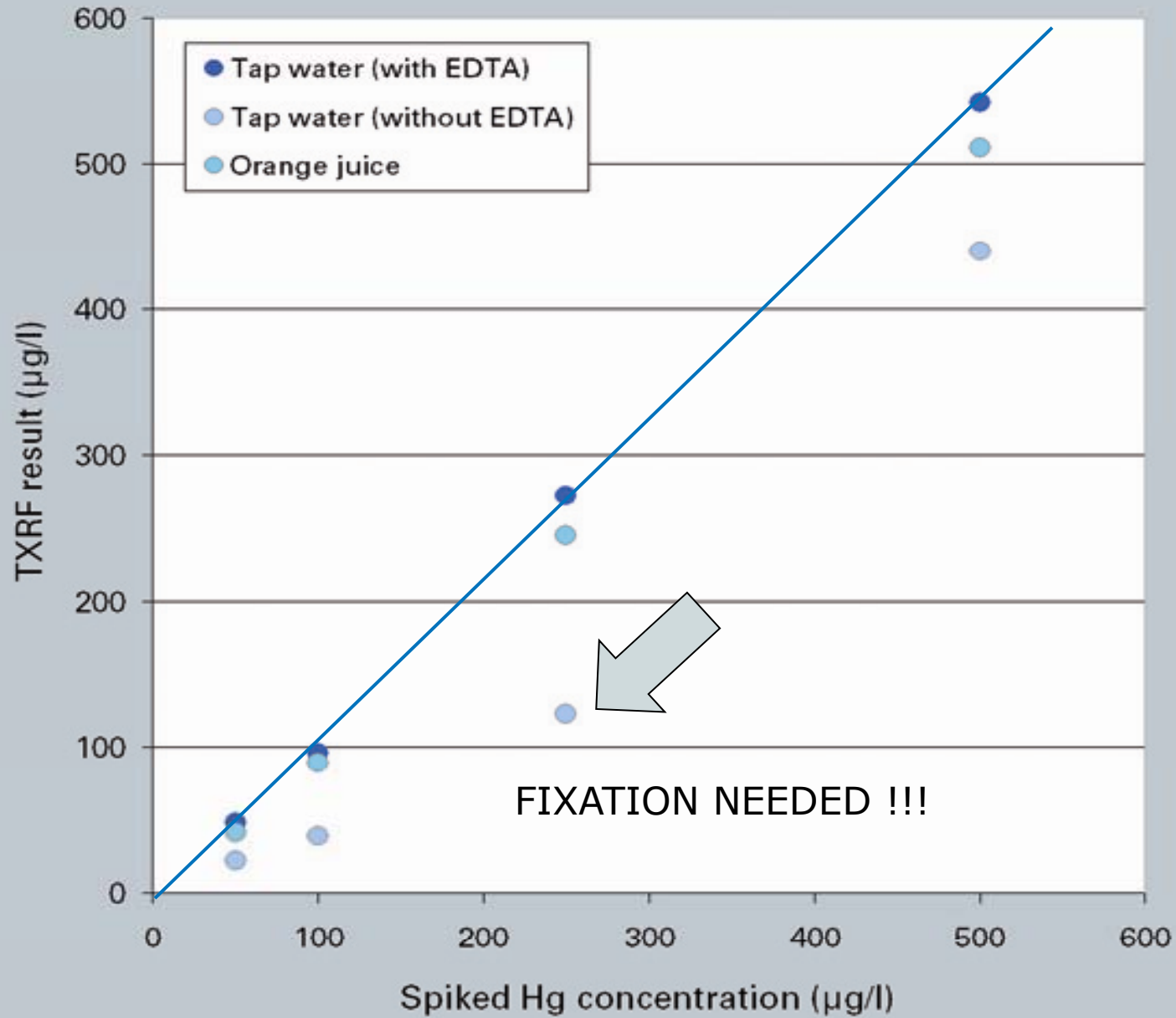
Sample preparation

- mixing with concentrated EDTA-solution (Hg-fixation)
- internal standardization

Measurements

- Mo-excitation
- Measurement times: 1000 s and 3600 s





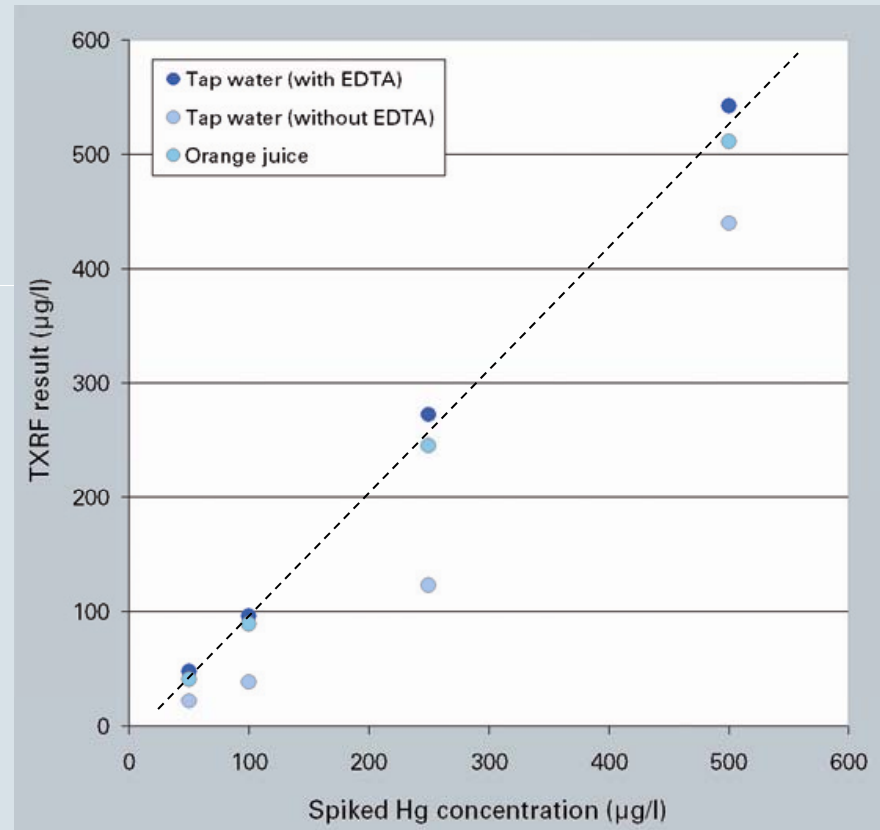
Stosnach, H;
The analysis
of orange
juice and
water by
TXRF;

Mercury in Tap Water and Orange Juice

Results

- Using fixation reagents, quantitative analysis of Hg in water and beverages is possible
- Sub-ppb detection limits are achievable

	Tap water (1000 s)	Tap water (3600 s)	Orange juice (1000 s)
LLD ($\mu\text{g/l}$)	1.20	0.58	7.90



Sample Preparation Suspensions

Suspensions can be analyzed just after dilution



- dilute sample with distilled water
 - add internal standard
 - homogenize
- pipette on carrier

Se analysis in Blood/Bodily fluids

Blood analysis



Precision and Accuracy

Element	Unit	Serum (ClinCheck L2)				Whole blood (Seronorm L2)			
		TXRF	s (n=5)	Reference ¹⁾	s	TXRF	s (n=5)	Reference ²⁾	s
Fe	mg/l	440	7,4	435	12	2,9	0,09	1,964	0,20
Cu	µg/l	66	2,2	62	2,1	1685	43	1562	312
Zn	µg/l	501	4,9	504	6,9	2194	118	2225	334
Se	µg/l	12	0,29	12	1,0	97	18	102	26

1): Sector-Field Inductively-Coupled Plasma Mass Spectroscopy

2): Atomic Adsorption Spectroscopy



Foodstuff

Hg is difficult

Hg is volatile and easily lost due to heat during preparation or DIGESTIONS!

TXRF Instrumentation can readily detect the Hg! But preparation is very important..

E.g. fish/wheat (FDA limit 1 ppm Hg)

- FREEZE DRYING and GRIDNING followed by mixing with IS and AIR drying
- (achievable as well with WD and ED XRF but calibration is difficult!)

Sample Preparation

Solid and Powder Samples I

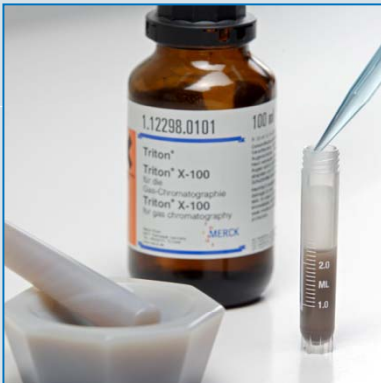
Solids are ground to fine particle size and resuspended for direct analysis without digestion



- Fill powder in mortar
 - Grind carefully
- Weigh about 20-50 mg
 - Transfer to tube

Sample Preparation

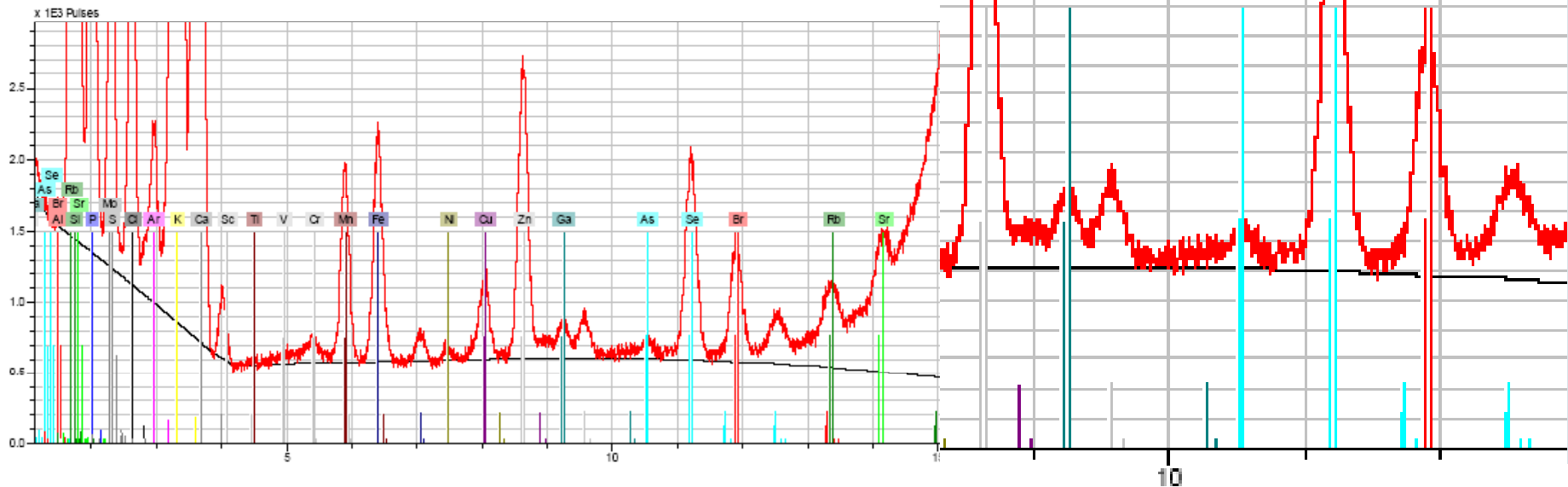
Solid and Powder Samples II

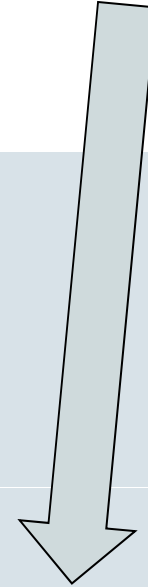


- Suspend in detergent solution
 - Add standard
- Homogenize
- Pipette on carrier

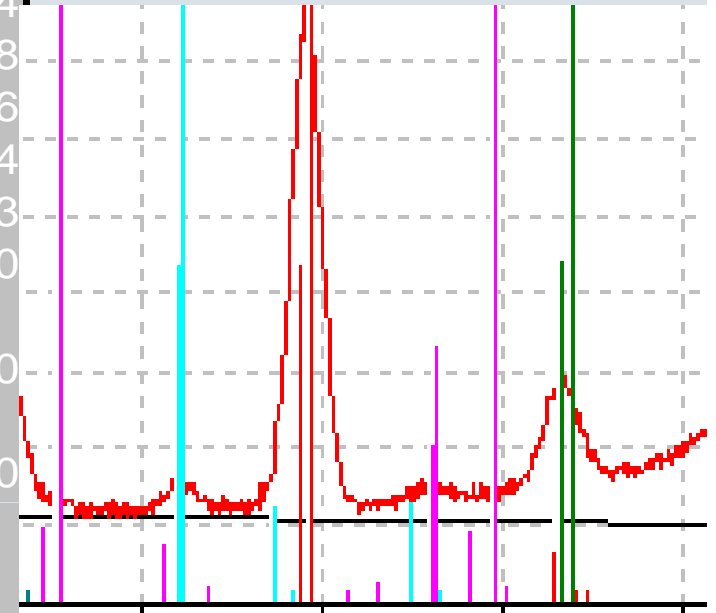
Se signal with TXRF (Wheat)

More details on wheat analysis from
 Craig Lacher
 USDA
 North Dakota
 Correlating TXRF technique
 with Hydride and GFAAS
 LLD 0.1 mg/kg (1000 sec)
 Repeatability of prep < 10% at 10 mg/kg level





No.	Element	Line	Energy (keV)	Conc. (mg/l)	SigmaC (mg/l)	LLD (mg/l)
1	Si	K12	1.740			
2	S	K12	2.309	683.160	2.015	1.346
3	Cl	K12	2.622	2465.922	4.705	0.750
4	Ar	K12	2.958			
5	K	K12	3.314	698.757	1.427	0.259
6	Ca	K12	3.692	56.361	0.193	0.129
7	Sc	K12	4.093			
8	Ti	K12	4.512			
9	V	K12	4.953	0.061	0.023	0.049
10	Cr	K12	5.415	0.169	0.019	0.039
11	Mn	K12	5.900	0.035	0.014	0.030
12	Fe	K12	6.405	1.115	0.015	0.024
13	Ni	K12	7.480	0.049	0.009	0.018
14	Cu	K12	8.046	1.153	0.011	0.016
15	Zn	K12	8.637	0.793	0.009	0.014
16	Ga	K12	9.251	5.000	0.018	0.013
17	As	K12	10.543	0.032	0.005	0.010
18	As	L1	1.282			
19	Se	K12	11.224	0.085	0.005	0.010
20	Se	L1	1.379			
21	Br	K12	11.924	1.823	0.009	0.010
22	Br	L1	1.481			
23	Mo	K12	17.480			
24	Mo	L1	2.292			



Se Analytical Issues

ICP-MS

Isotope	Mass	Abundance [%]	Corrections	Potential Interferences
⁷⁴ Se	73.9225	0.89	-1.317357 * ⁷² Ge	Ge, ArS, Nd ²⁺ , Sm ²⁺ , Sm ²⁺
⁷⁶ Se	75.9192	9.37	-0.276325 * ⁷² Ge	Ge, ArS, Ar ₂ , Sm ²⁺ , Eu ²⁺ , Gd ²⁺
⁷⁷ Se	76.9199	7.63		ArCl, Ar ₂ H, Sm ²⁺ , Gd ²⁺
⁷⁸ Se	77.9173	23.77	-0.030461 * ⁸³ Kr	Kr, Ar ₂ , Dy ²⁺ , Gd ²⁺
⁸⁰ Se	79.9165	49.61	-0.198433 * ⁸³ Kr	Kr, Ar ₂ , BrH, Dy ²⁺ , Gd ²⁺ , Dy ²⁺
⁸² Se	81.9167	8.73	-1.007833 * ⁸³ Kr	Kr, Ar ₂ H, BrH, SO ₃ , Dy ²⁺ , Ho ²⁺ , Er ²⁺

Hydride generation atomic absorption

- Se(IV) then Hydride generation
- Matrix interferences from Fe

GF AAS

Matrix interferences

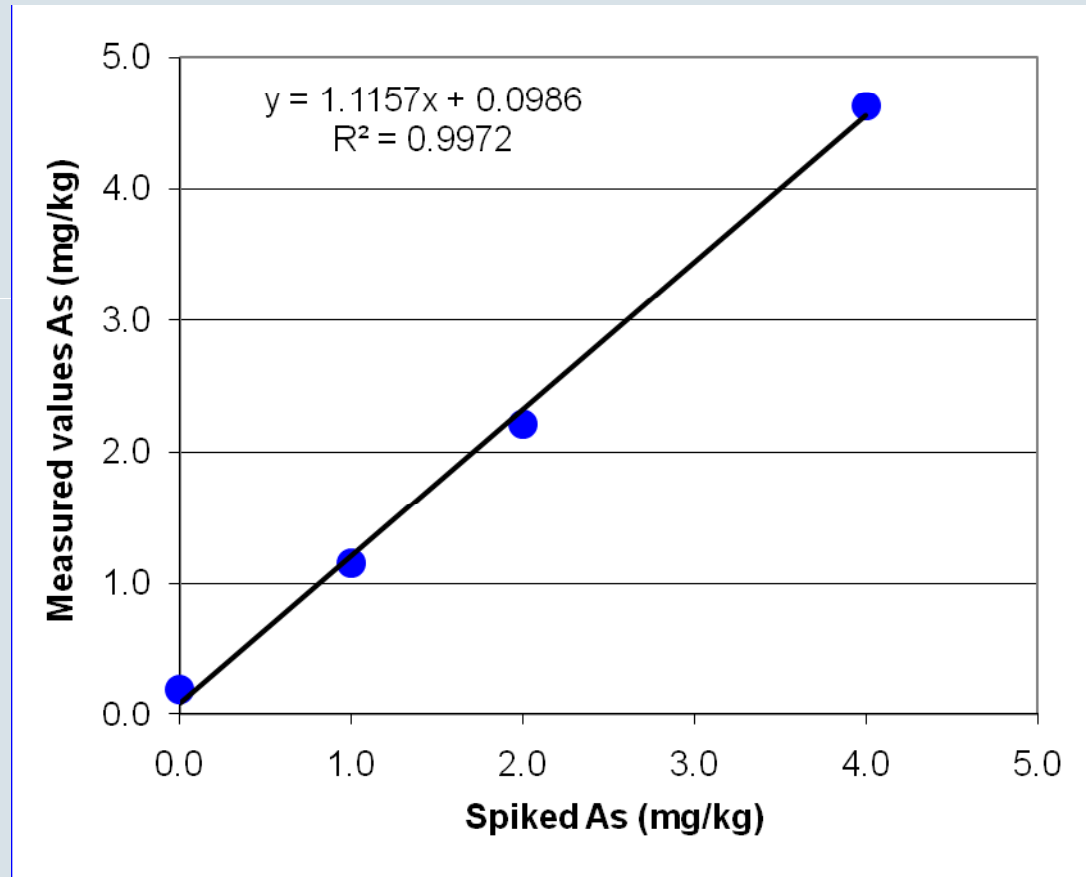
Application

Pharmaceuticals - Purity Control



Recovery results:

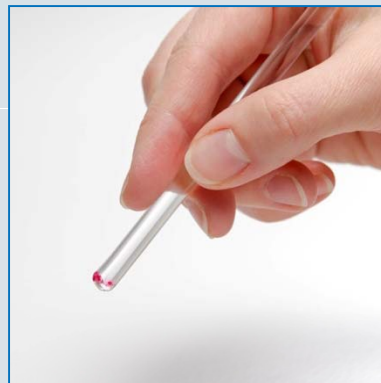
Trace element concentrations of Ca, Ti, Cr, Fe, Ni, Cu, Zn and Br were determined simultaneously



Qualitative Solid Sample Preparation

Pharmaceutical & Forensic Analysis

Microparticles are measured semi-quantitatively and non-destructively



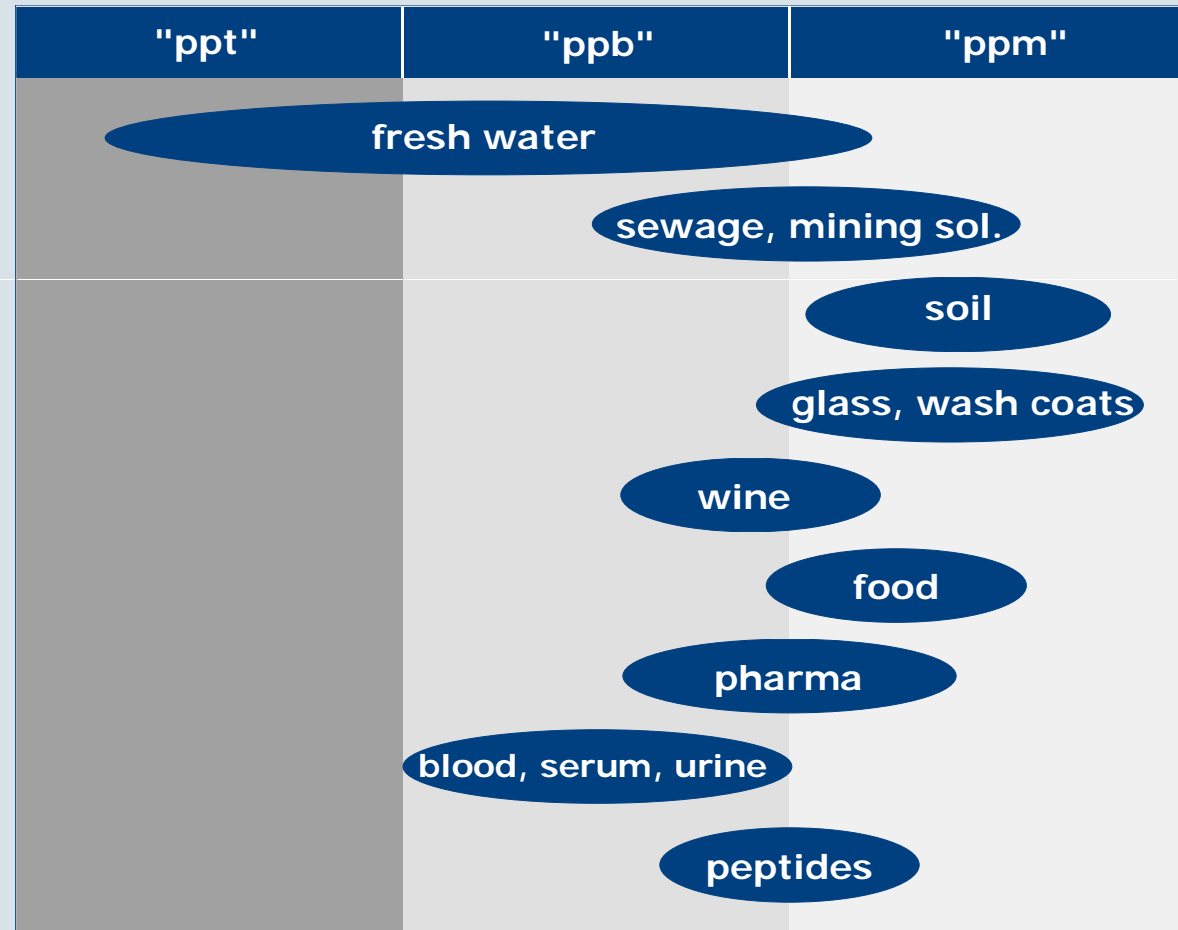
- Dab vacuum grease on carrier
 - Pick-up some particles with a (glass) rod
 - Drop particles on grease

TXRF Applications Summary

3 σ Detection Limits



Low background
 \approx low detection limits



Summary

PPB-PPM sensitivity range for various elements

Quantify inorganic content of phytochemical standards using affordable sample quantity

Fastest sample preparation

Non-destructive & automated

Very good for Se, Hg

Good for As,Pb

Can screen for the ABSENCE!



Conclusion

Chemical TXRF is a great tool for Food and Nutritional Supplements analysis :

CON (Nutritional supplements):

As per FDA guideline 21 CFR 111 T XRF will need 2 sources to fulfill guidelines (the big three instead of big four for Mo!)

AOAC needs still needs to approve methodology

PRO (ALL)

Large elemental range for screening % to ppb!

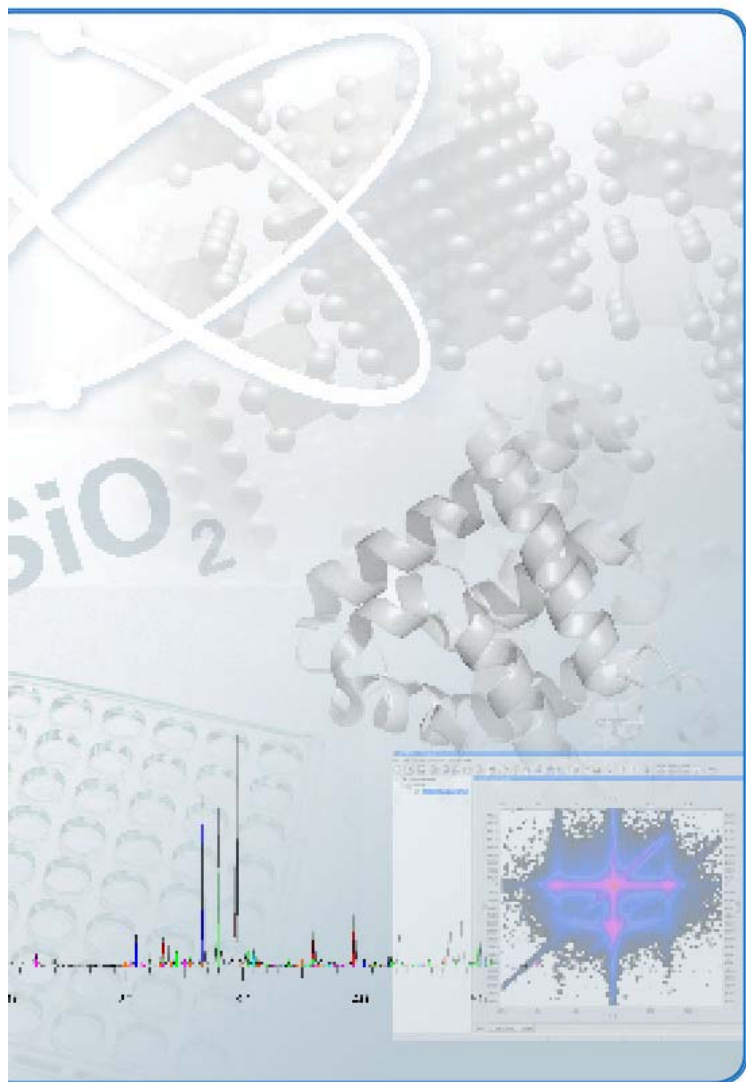
Fastest and easiest sample preparation

Fingerprinting to determine "reasonable" contaminants and origin control

ICP MS throughput and "uptime" help

Hg and Se are KEY elements for T XRF use

Cost savings for Screening in Labs ...



Thank You for Your Attention.

Any Questions?

Michael.Rider@bruker-axs.com