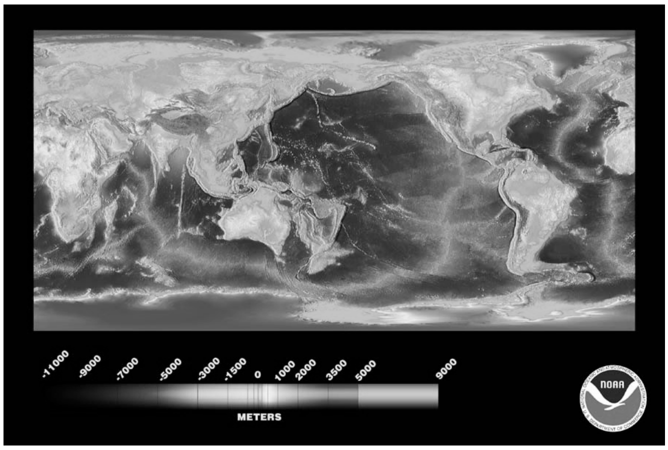
Organic and Biological Analytical Chemistry Group

CART Center for Analytical Research and Technology

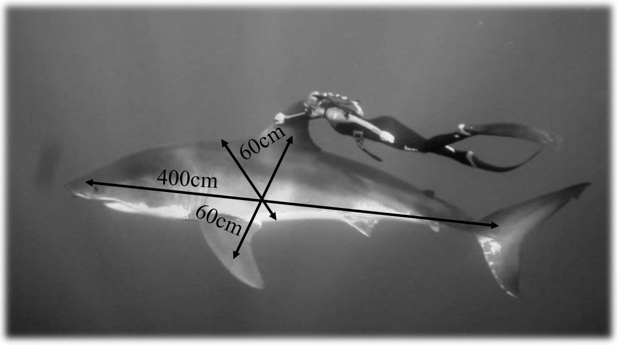
Université de Liège

Dioxins! Hunting the Great White Shark

J.-F. Focant et al.



⇨ 1,400 10^6 Km^3 of water



⇨ 1,4 m^3 of volume

1,400 10^6 Km^3 of water

1			10^3			10^6			10^9			10^{12}			10^{15}			10^{18}			10^{21}
Mm^3									km^3			hm^3			dam^3			m^3			dm^3
1	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0 L

1,4 10^{18} m^3 of volume

☝ 1 ppquint is 10^{-18}

⇨ 1 ppquint of ocean = 1,4 m^3

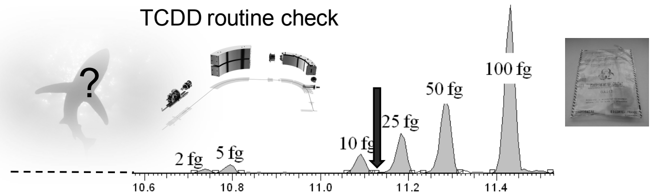
⇨ 1 great white is a ppquint in the Oceans

⇨ We are hunting the great white…

At the Dioxin Level

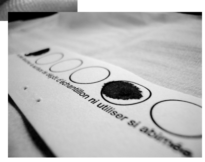
Quantity	Notation	Number of moles	Number of molecules
1 microgram (µg) or 10^{-6} g	ppm	3 nanomoles or 3.10^{-9}	2,000,000,000,000,000 (2.10^{15})
1 nanogram (ng) or 10^{-9} g	ppb	3 picomoles or 3.10^{-12}	2,000,000,000,000 (2.10^{12})
1 picogram (pg) or 10^{-12} g	ppt	3 femtomoles or 3.10^{-15}	2,000,000,000 (2.10^{9})
1 femtogram (fg) or 10^{-15} g	ppq	3 attomoles or 3.10^{-18}	2,000,000 (2.10^{6})
1 attogram (ag) or 10^{-18} g	ppquint	3 zeptomoles or 3.10^{-21}	2,000 (2.10^{3})
1 zeptogram (zg) or 10^{-21} g	ppsext	3 yoktomoles or 3.10^{-24}	2 (2.10^{0})
1 yoktogram (yg) or 10^{-24} g	ppsept	*Ghost mole*	0

TCDD routine check

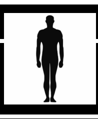


Why Going Lower ?

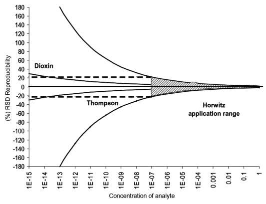
- ✓
- ✓
- ✓
- ✓ No fear
- ✓ Minimally invasive process
- ✓ Tiny volumes (20 – 100 µL)



How Big is the Challenge ?

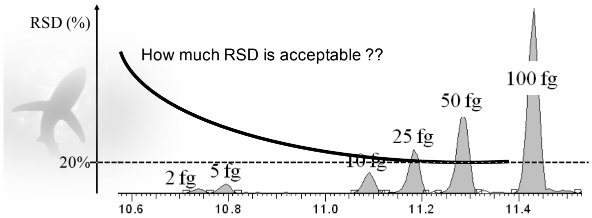


	pg/g fat	Quantity in 20 uL of blood	
2,3,7,8-TCDD	1	0,1 fg	
PeCDD/Fs	100	10 fg	✗
OCDD	300	30 fg	
CB-153	100 10^3	10 pg	
DDE	20 10^3	2 pg	✓
BDE-47	25 10^3	2,5 pg	



Analyte ratio	Units	Horwitz	AOAC	Thompson	Eppe
		% RSD_R	% RSD_R	% RSD_R	% RSD_R
1E−00	100%	2	1.3	–	–
1E−01	10%	2.8	1.8	–	–
1E−02	1%	4	2.7	–	–
1E−03	0.10%	5.7	3.7	–	–
1E−04	100 ppm	8	5.3	–	–
1E−05	10 ppm	11.3	7.3	–	–
1E−06	1 ppm	16	11	–	–
1E−07	100 ppb	22.6	15	22	–
1E−08	10 ppb	32	21	22	6.3
1E−09	1 ppb	45.3	30	22	7.9
1E−10	100 ppt			22	9.8
1E−11	10 ppt			22	12.3
1E−12	1 ppt			22	15.3
1E−13	100 ppq			22	19.1
1E−14	10 ppq			22	23.7

Eppe et al., Chemosphere (2008) 71, 379.



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Cryogenic zone compression for the measurement of dioxins in human serum by isotope dilution at the attogram level using modulated gas chromatography coupled to high resolution magnetic sector mass spectrometry

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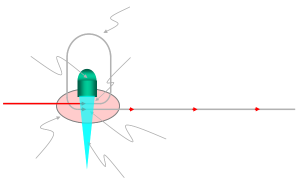
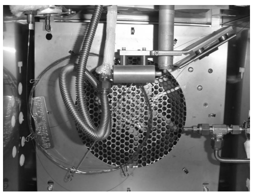
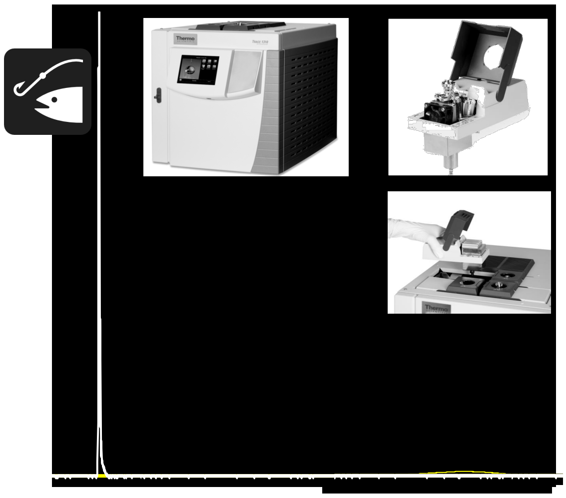
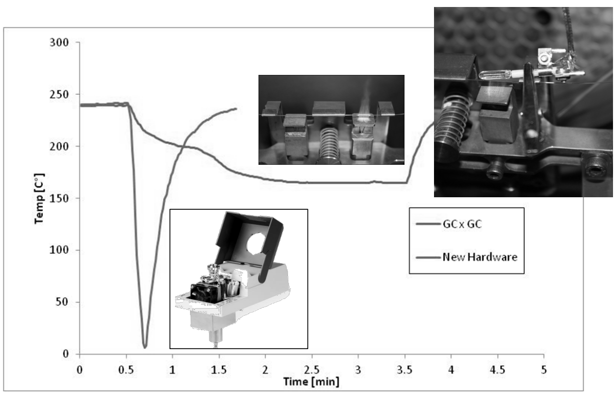


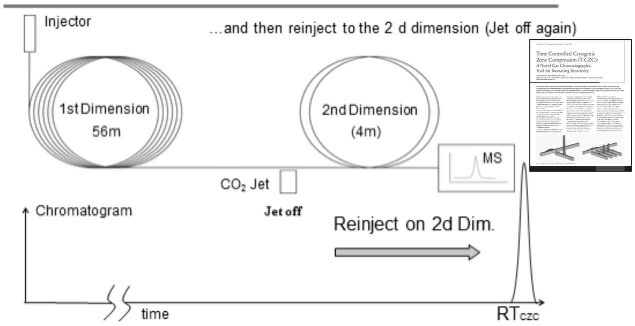




Hardware Evolution

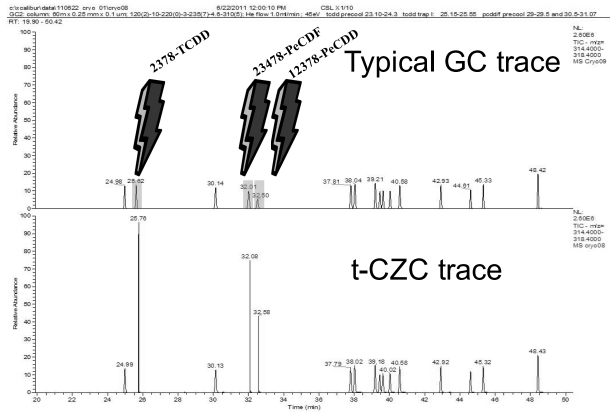


timed-CZC



Krumwiede and Mehlmann, Chromatogr. Today (2012) March.

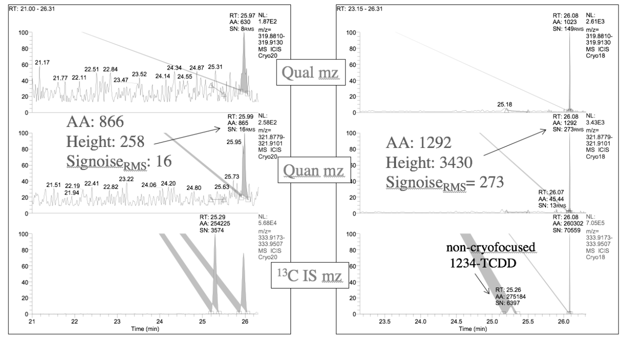
timed-CZC



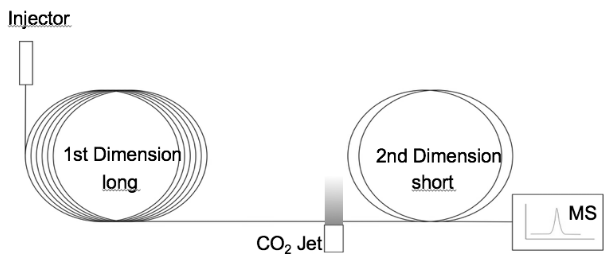
timed-CZC

standard GC-HRMS vs. CZC GC-HRMS

pooled blood sample on DFS (HRMS) – **2378-TCDD** ca. 10 fg



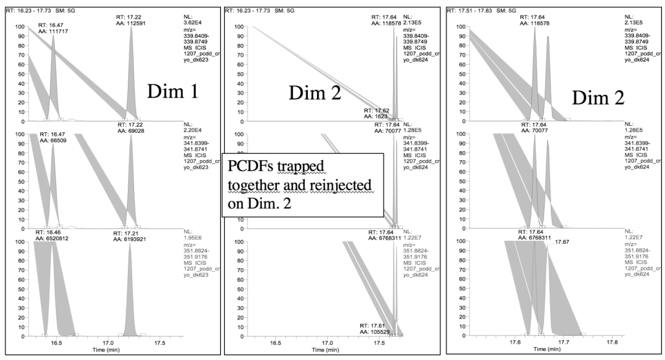
^{2}D is Still There…



5% type phase
30m

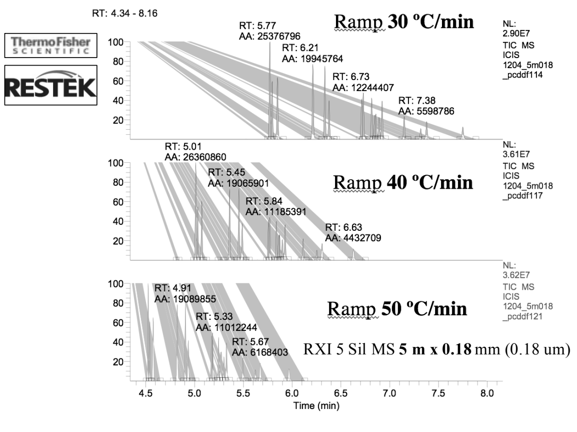
Polar type phase
<5m

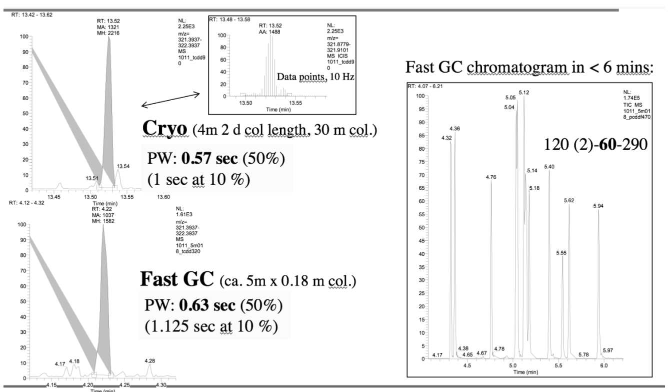
^{2}D is Still There…



Fast-GC type separation in ^{2}D…

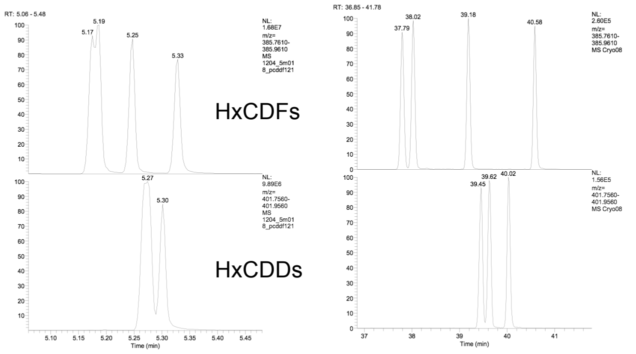
CZC But Why Not Just FGC?





Possibly a lot of time saved here…

FGC But…



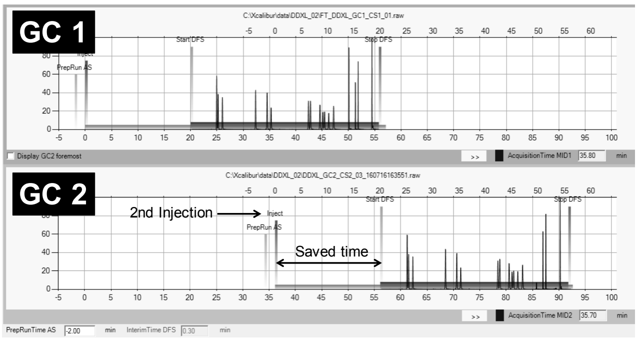
5m FGC 60m CZC

FGC *vs* t-CZC

	t-CZC	FGC
Fast	-	X
Simplicity	-	X
Flexibility	X	-
Inj. Volumes	X	-
Chrom. Resolut.	X	-
GCxGC	X	-
Cheaper	-	X

So, we have to go for the 'slow' option…

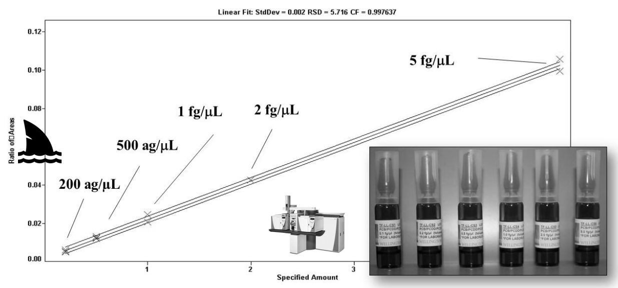
Unless We Do Dual Data…



92 min *vs* 2x57 (+10) min for 2 runs (16% saved)

timed-CZC

Triplicate five point calibration curve of TCDD (4uL injected) using t-CZC.



*Special certified Standards from Wellington Labs.

*Special Certified Standards**?**

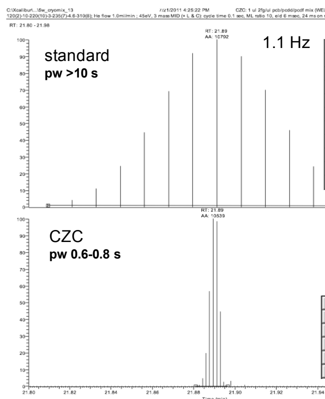
✓ ^{13}C standard solution purity?

✓ ^{13}C,^{12}C of different congeners co-modulated?

Specie	Mass	Required resolution	Ion in cluster	Isotope abundance	Level (pg/µl)	Specie ratio
^{12}C-2378-TCDD	321,8930	>8000	M+2	100%	0,05	1
^{13}C-2378-TCDF	321,9325		M+6	10%	50	100
^{12}C-2378-TCDD	319,8960	>8000	M	75%	0,05	1
^{13}C-2378-TCDF	319,9354		M+4	50%	50	650

✓ Not even talking about blank issues… (LOQs)

Get the Sector MS Speeded Up



Cycle [sec]: 0.90

Section 1	L/C	Mass	Gr.	Int.	Time[ms]
1		303.90160	1	1	163
2		305.89870	1	1	163
3	Lock	313.98336	1	20	8
4		315.94190	1	5	32
5		317.93890	1	5	32
6		319.89599	1	1	163
7		321.89304	1	1	163
8		331.93680	1	5	32
9		333.93390	1	5	32
10	Cali	363.98017	1	20	8

Cycle [sec]: 0.08

Section 2	L/C	Mass	Gr.	Int.	Time[ms]
1	Lock	313.98389	1	8	2
2		319.89599	1	1	18
3		321.89371	1	1	18
4		333.93381	1	2	9
5	Cali	363.98070	1	8	2

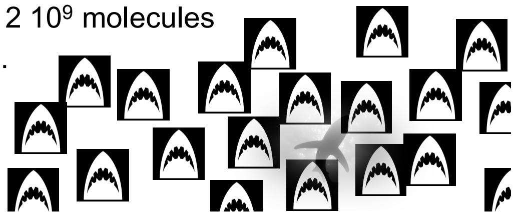
What About Ion Statistics ?

- ✓ Ppquint is about 2 10^3 molecules…
- ✓ Low % MS duty cycle
- ✓ A few ‘hundreds’ of molecules effectively analyzed

  - Lower mass resolution (5,000) ?
  - Use of other IS (1234-TCDD…) ?
  - MID optimisation ?
  - Less SIM descriptors ?
  - Reduce lock mass dwell time ?
  - Use quantum statistics ?

What About Blanks ?

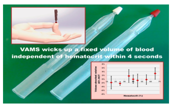
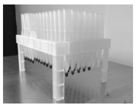
- ✓ Ppquint is about 2 10^3 molecules…
- ✓ Routine lab blank levels (large samples)
  - TCDF 130fg absolute from lab
    - ➢ 250 10^6 molecules
  - PCB 126 > 1pg absolute from lab
    - ➢ 2 10^9 molecules
  - …



Need for Microsampling 20 µL

- ✓ 20 µL sample sizes
- ✓ Moving from mL (L…) of solvent to µL…
- ✓ Dried-blood spots (DBS) & Micro-extraction by packed sorbent (MEPS) L'Homme and Focant, Anal. Methods (2015), DOI: 10.1039/c5ay00543d.
- ✓ Volumetric absorptive micro-sampling (VAMS) & Micro solid-phase extraction (SPE)



Take Home Message

- ✓ Chasing the ppquint is not easy
- ✓ t-CZC (Dual Data) has high potential
- ✓ PTV-LVI is to also be considered
- ✓ ‘Basic’ sectorMS approach to be revisited
- ✓ MIDs, lock mass, ion statistics, blanks…
- ✓ MEPS, VAMS,… need for ’small’ sample prep
- ✓ We will have to revisit our QC stds…

Acknowledgements

- ✓ D.G. Patterson Jr.
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