Why non-target?

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‘Contaminants of emerging concern’

chemicals and other substances that have no regulatory standard, that have been recently “discovered” in the environment, and potentially cause deleterious effects in aquatic life at environmentally relevant concentrations.

…..not currently included in routine monitoring programs and may be candidates for future regulation.

……not necessarily new chemicals.

The challenge

- 72+ M known chemicals (14 M on the market)
- Tens of thousands of chemicals in the environment
- New chemicals entering the market (several thousand/year)
- Metabolism and transformation
- Toxic effects that are not explained by monitored chemicals
- Lack of correlation between chemical and ecological status

Hunts Needle in a Haystack

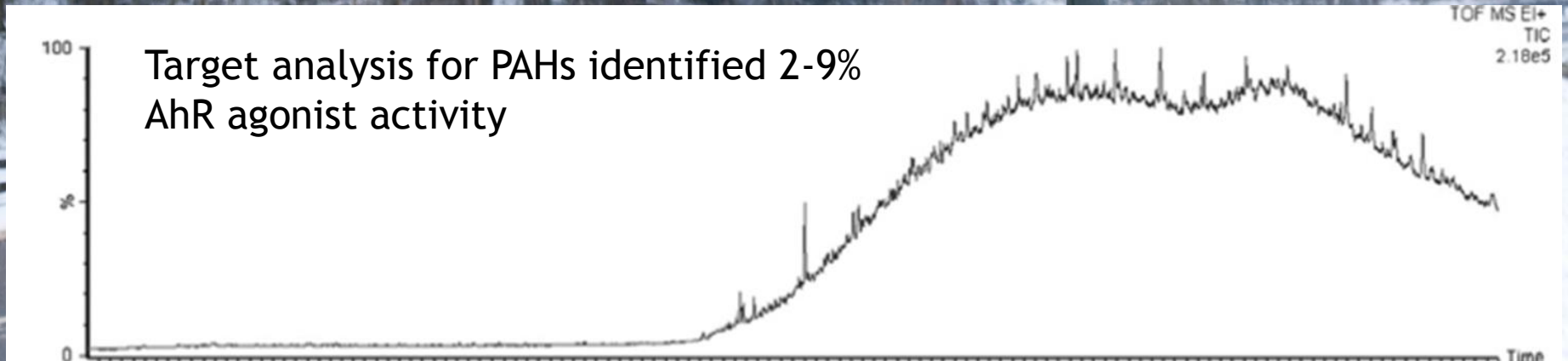
HOW LONG does it take to find a needle in a haystack? Jim Moran, Washington, D. C., publicity man, recently dropped a needle into a convenient pile of hay, hopped in after it, and began an intensive search for (a) some publicity and (b) the needle.

Current targeted approaches

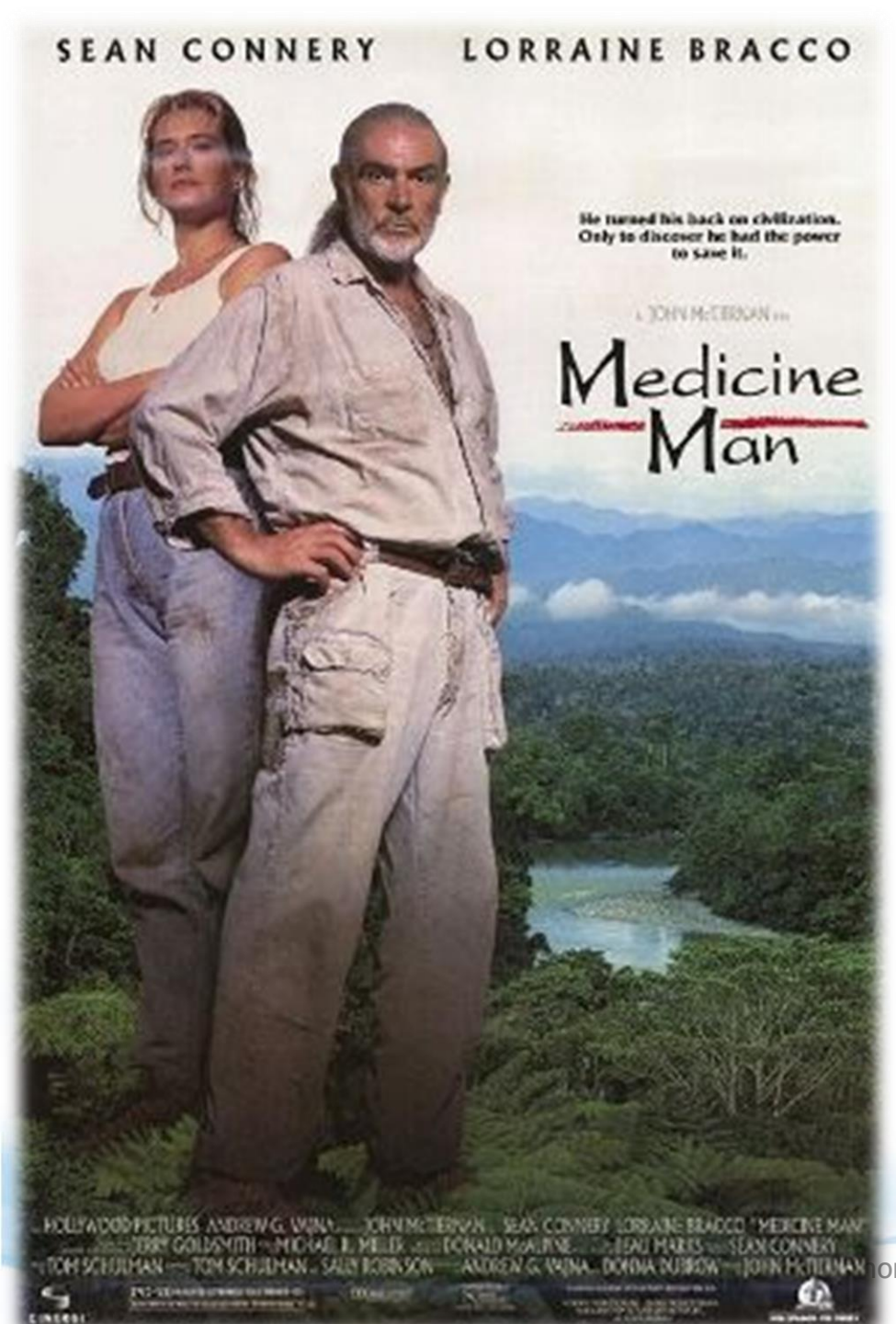
- Do they effectively select those chemicals to monitor and manage?

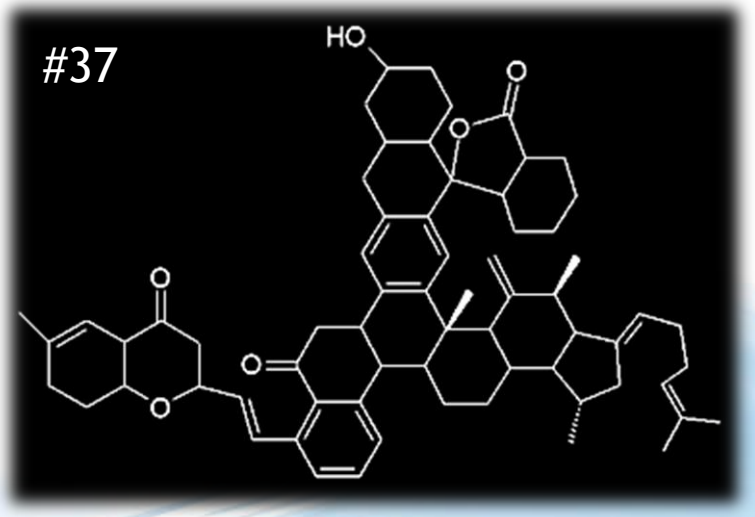
What to analyse?

AhR agonists in roadside snow (Unresolved complex mixtures)



Target analysis for PAHs identified 2-9% AhR agonist activity


SEAN CONNERY
LORRAINE BRACCO
He turned his back on civilization.
Only to discover he had the power
to save it.
Medicine
Man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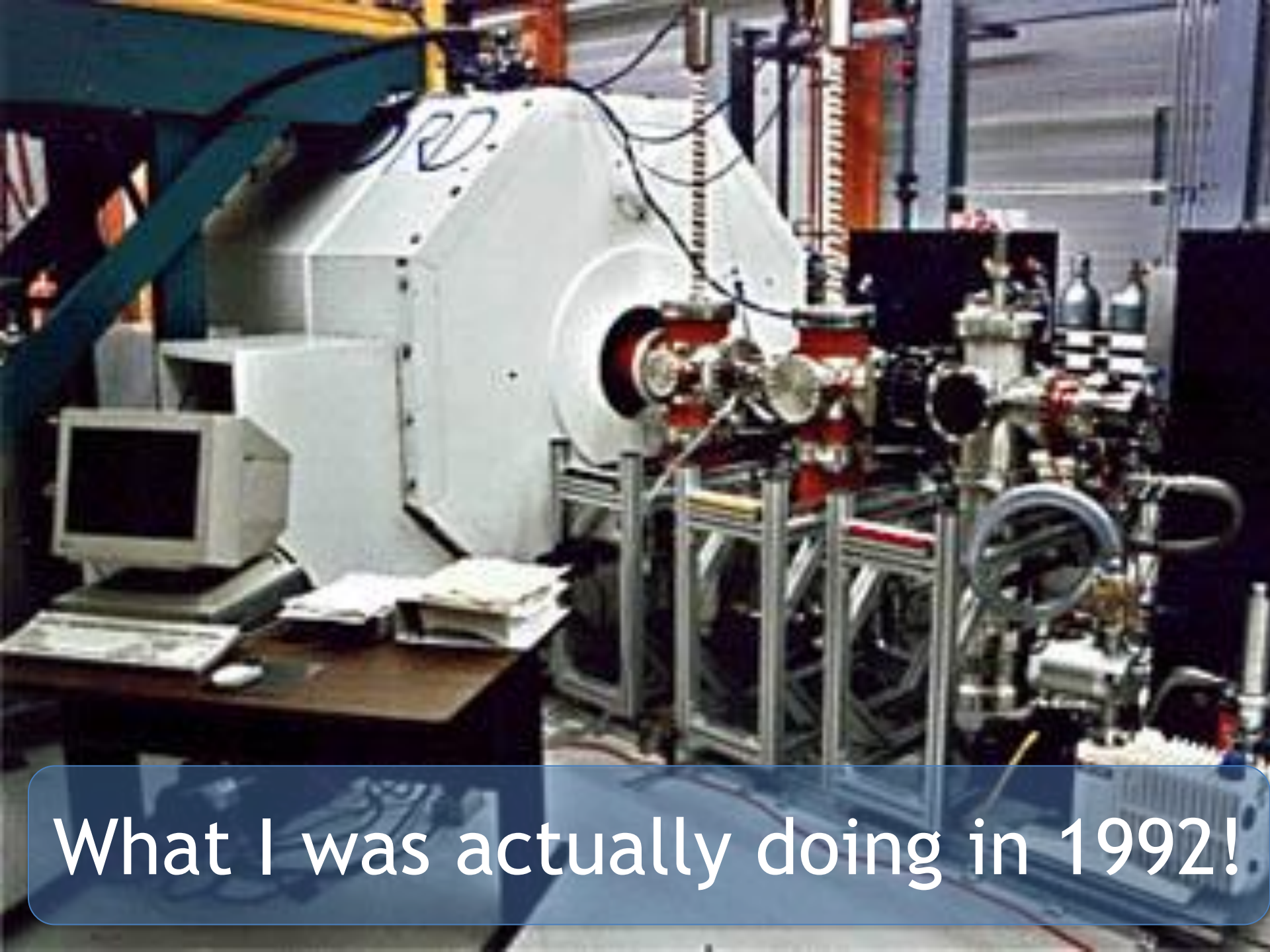

What I was actually doing in 1992!

Non-target techniques

- GC-HRToFMS
- GCxGC ToFMS
- LC-QToFMS
- LC-Orbitrap

Multiple choice

Mass spectrometry users have several options for mass analysers with high resolving power

Table 1 Comparison of commercial mass analyzers in LC-MS instruments. Typical values for an m/z range of 300–400 are given; specific instruments or configurations might achieve better figures of merit

Mass spectrometer	Resolving power[a] (FWHM)	Mass accuracy (ppm)	Linear dynamic range	Sensitivity[c] (absolute mass)
Triple quadrupole (QqQ)	Unit resolution[b]	50	10^4	Femto- to picogram (SRM)
Quadrupole ion trap (QIT)	10,000	50	10^3	Femto- to picogram (SRM, full scan)
Time-of-flight (TOF)	20,000	3	10^2–10^3	Picogram (full scan)
Orbitrap	100,000	2	10^3–10^4	Femto- to picogram (full scan)
Fourier transform ion cyclotron resonance (FT-ICR)	1,000,000	≤1	10^4	Picogram (full scan)

[a] Resolving power depends on *m/z* range and scan speed on most instruments

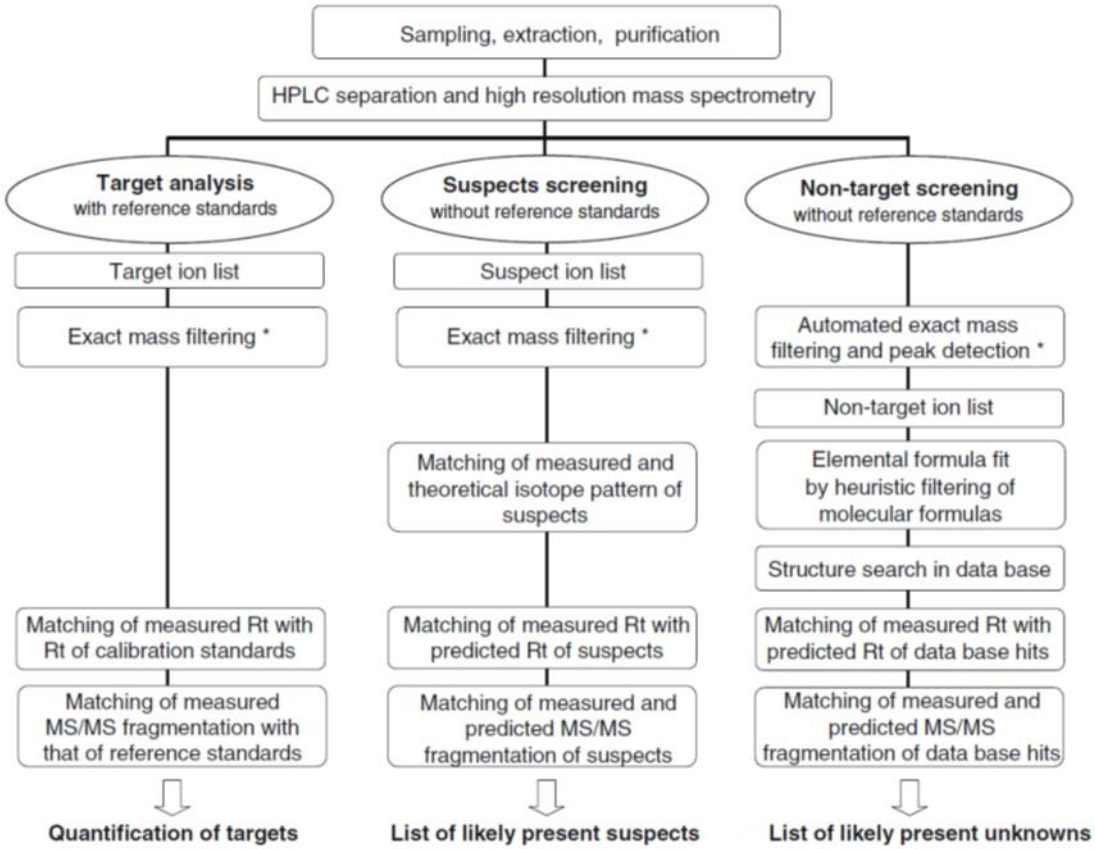
[b] Unit mass resolution is the resolution for standard quadrupole instruments; with special hyperbolic quadrupole instruments a resolving power of 5,000 and a mass accuracy of 5 ppm can be achieved without a major loss of signal intensity

[c] Sensitivity depends strongly on the ionization efficiency of the compound in the ion source

Krauss et al., 2010

Terminology

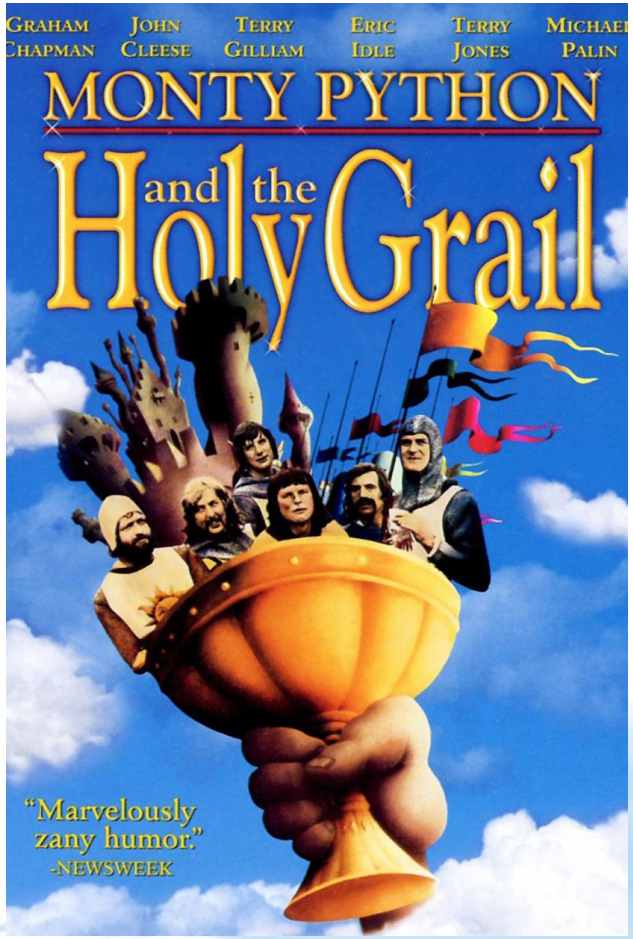
ID procedure



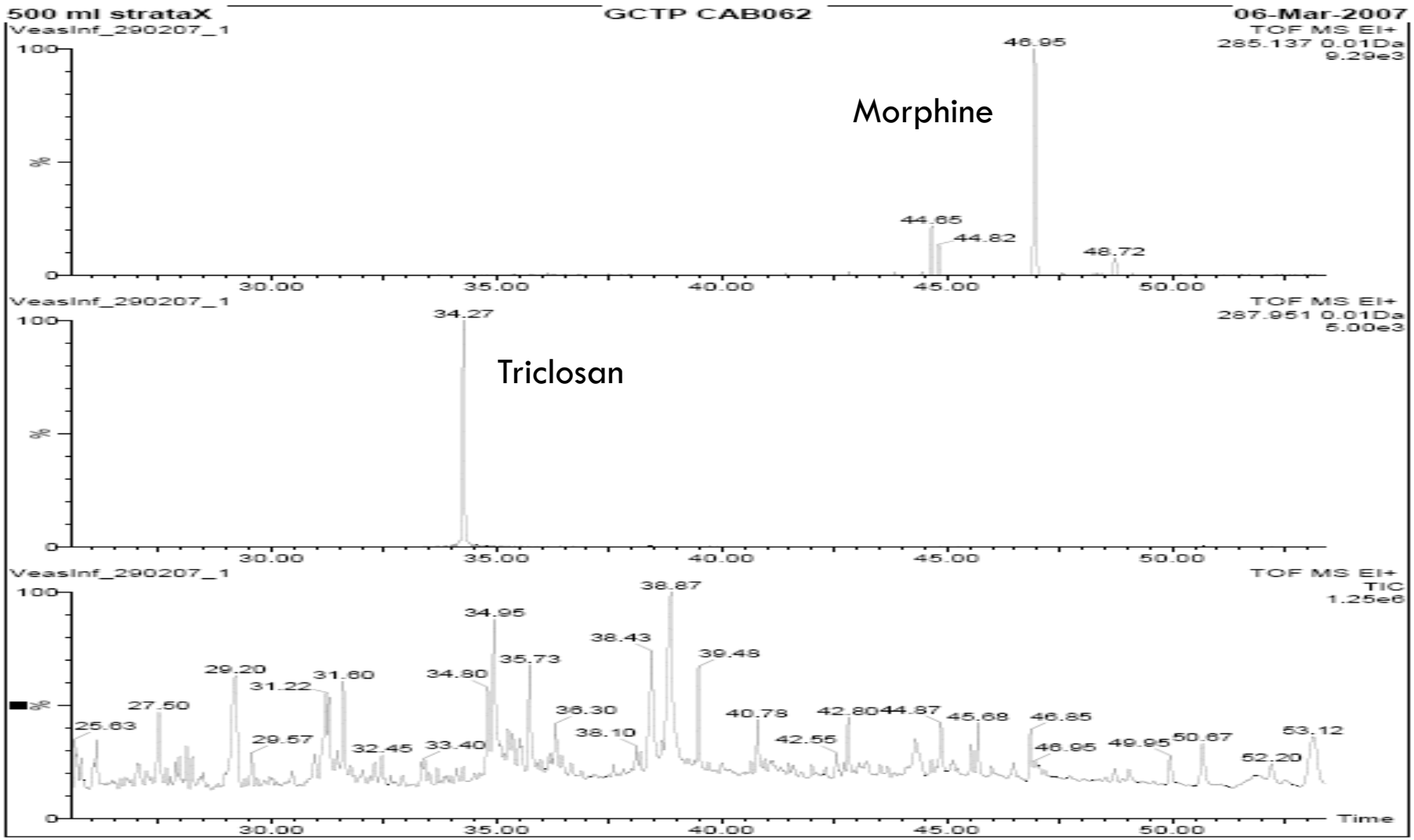
Krauss et al., 2010

Potential of the approach

- Comprehensive characterisation of environmental samples
- Combination with bioassays and chemometric techniques
- Identifying new contaminants of emerging concern
- Retrospective assessments



Retrospective analysis

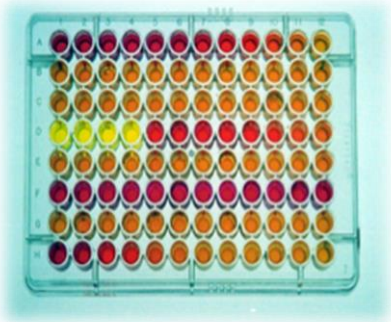


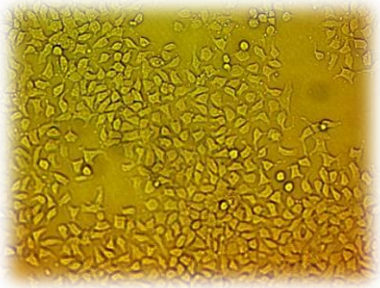
Virtual sample banking

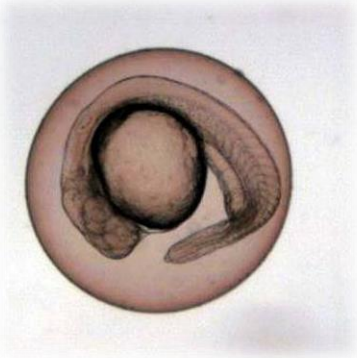
- Retrospective analysis
- Spatial and temporal assessments
- Major considerations
  - Storage solutions
  - Accessibility
  - Ownership
  - Future-proofing
  - Security
  - Sustainability

Use with a battery of EDA bioassays

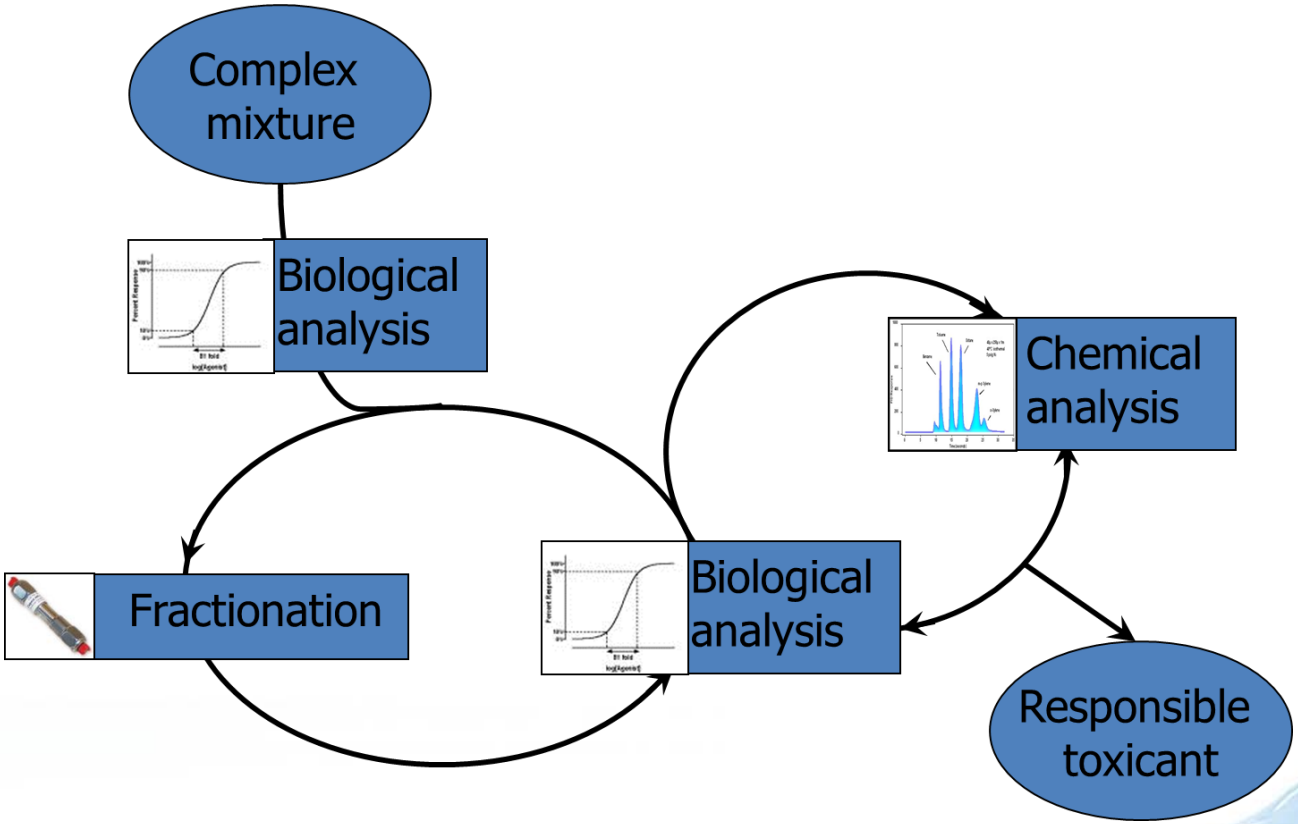
- Daphnia immobilisation
- Algal growth
- Fish embryo toxiciy (FET)
- YES/YAS assay
- Transthyretin (TTR) assay
- AMES fluctuation test
- GR-CALUX







Integration with bioassays: EDA



Environmental Science & Technology

Article

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Chemometrics-Assisted Effect-Directed Analysis of Crude and Refined Oil Using Comprehensive Two-Dimensional Gas Chromatography–Time-of-Flight Mass Spectrometry

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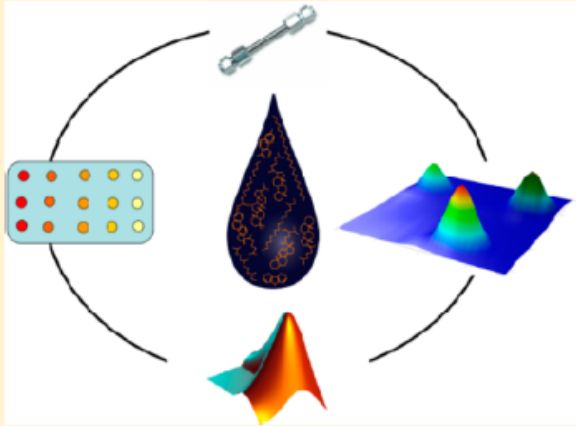
Supporting Information

ABSTRACT: An effect-directed analysis (EDA) of fresh and artificially weathered (evaporated, photooxidized) samples of North Sea crude oil and residual heavy fuel oil is presented. Aliphatic, aromatic, and polar oil fractions were tested for the presence of aryl hydrocarbon receptor (AhR) agonist and androgen receptor (AR) antagonist, demonstrating for the first time the AR antagonist effects in the aromatic and, to a lesser extent, polar fractions. An extension of the typical EDA strategy to include an *N*-way partial least-squares (*N*-PLS) model capable of relating the comprehensive two-dimensional gas chromatography–time-of-flight mass spectrometry (GC × GC–TOFMS) data set to the bioassay data obtained from normal-phase LC fractions is proposed. The predicted AhR binding effects in the fresh and artificially weathered aromatic oil fractions facilitated the identification of alkyl-substituted three- and four-ring aromatic systems in the active fractions through the weighting of their contributions to the observed effects. A *N*-PLS chemometric model is demonstrated as a potentially useful strategy for future EDA studies that can streamline the compound identification process and provide additional reduction of samples' complexity. The AhR binding effects of the suspected compounds predicted by *N*-PLS and identified by GC × GC–TOFMS were confirmed using quantitative structure–activity relationship (QSAR) estimates.



First i.d. of a new party drug

- Identification criteria: retention time (0.2 minute tolerance), mass accuracy of the parent ion (3 mDa tolerance) and mass accuracy of the fragment ions (3 mDa tolerance).

Identification criterium

- European Commision (2002) Commision Decision 2002/657/EC implementing Council Directive 96/23/EC
- MS techniques measuring specific ions are valued according to information points (IP)
- IP >4 = I.D.
- Are these criteria sufficient, do they need to be more precise?
- Should they be reconsidered as resolving power improves?

Management use

- CEC identification
- Retrospective assessments
- Advanced screening studies
- Metabolites/TPs
- Chemical/discharge regulation
- Regulation (REACH (CoRAP))

Potential policy use

- Strengthening priority lists
- Reinforce a substance based approach
- Potential shift from emission- to recipient based policy?

Summary

- An exciting technique in infancy
- Expert knowledge
- Few guidelines at present
- QA/QC procedures
- Intercalibration in its infancy (Norman 2013/2014)
- Unknowns
- Extraction techniques?
- Not chemicals will be amenable
- Identification criterium?
- Suspect screening and retrospective approaches
- Huge potential!

Hunts Needle in a Haystack

HOW LONG does it take to find a needle in a haystack? Jim Moran, Washington, D. C., publicity man, recently dropped a needle into a convenient pile of hay, hopped in after it, and began an intensive search for (a) some publicity and (b) the needle. Having found the former, Moran abandoned the needle hunt.