Practical considerations for taking into account bioavailability and mixtures in environmental risk assessment of chemicals

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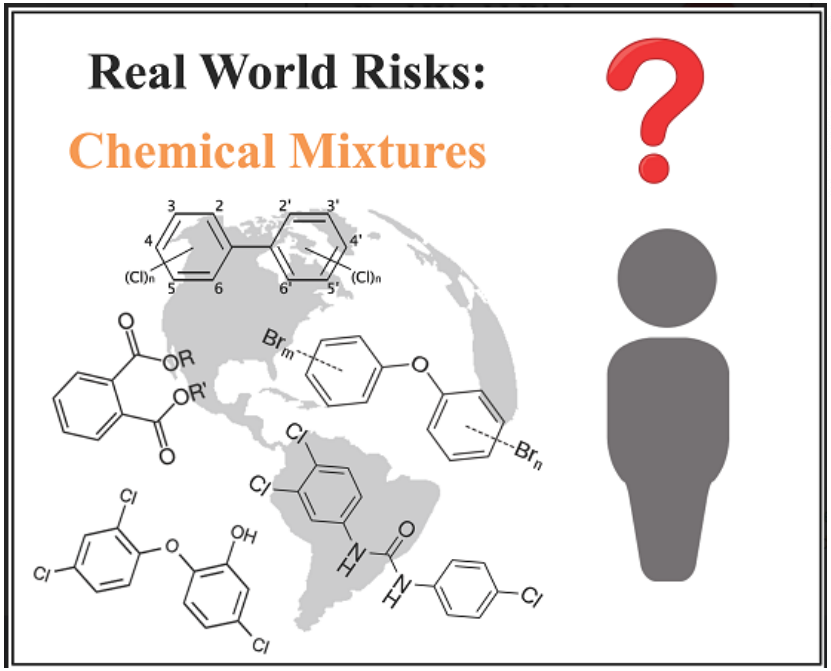
Challenges in the environmental samples

- Assessment based on single chemical threshold values

However,

- Unknown contaminants
- Typically mixtures
- Bioavailability

-> Risk?



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Challenges with the environmental samples

- **Mixture** toxicity
- Concentrations below thresholds, but still toxic samples
  - ”Something from nothing”
- Act together?
  - Concentration addition
- Are independent?
  - Synergism/antagonism

- **Bioavailability** of chemicals
- Only freely dissolved can pass cell membranes
- Total ≠ Dissolved (filtered) ≠ Bioavailable
- Usually not considered in the water quality criteria thresholds

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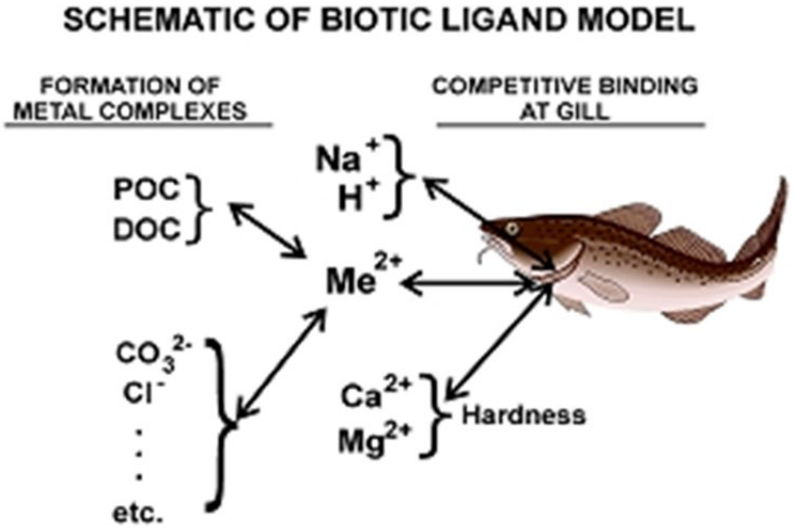
How to account for bioavailability?
Theory & practise for metals

- Cationic metals (Me^{2+}) interact mainly as ions
- Form complexes
- Compete with other ions
- Only a fraction in water is bioavailable
  - Uptake by biota



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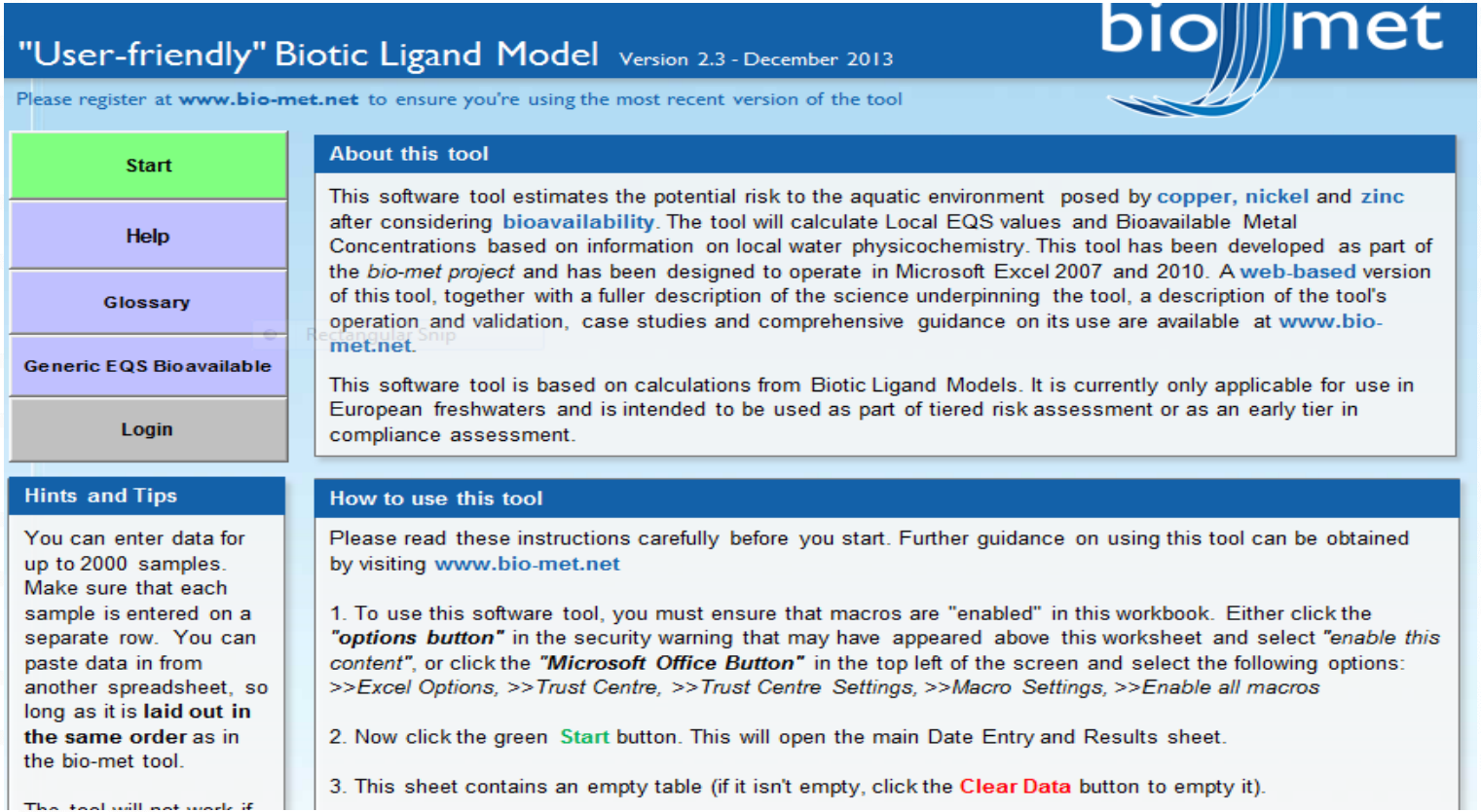
Metal bioavailability models in practise (1)
Freshwater only



Metal bioavailability models in practise (2)
Freshwater only

- www.Bio-met.net is for Ni, Cu, Zn, Pb

Optional	Optional	Required	Required	Required
Measured Nickel Conc (dissolved) [µg/L]	Measured Zinc Conc (dissolved) [µg/L]	pH	DOC [mg/L]	Ca [mg/L]
22		6,5	20	1

RESULTS (Nickel)				
Local EQS (dissolved) [µg/L]	BioF	Bioavailable Nickel Conc (µg/L)	RCR	Notes
28,93	0,14	3,04	0,76	Y

- www.PNEC-Pro.com is a Dutch version
- EU has bioavailable Environmental Quality Standards for Ni, Pb. Some member states apply also Zn and Cu EQSs

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Component-based mixture risk assessment

Concentration addition model

- A case where concentrations of chemicals are analysed
- Chemicals have either threshold values (PNECs) or Effective Concentrations (EC_{xx})
- Risk ratios can be summed up
- ≥ 1 indicates risk

When based on water quality criteria (thresholds):

$$\sum_i \frac{MEC_i}{EQS_i} \qquad \sum_i \frac{MEC_i}{PNEC_i}$$

When based on effective concentrations (EC50s, NOECs, EC10s etc.):

$$\frac{MEC_i}{ECx_i} = TU \qquad \text{SUM TU} = \sum_{i=1}^{n} \text{TU}_\text{i}.$$

TU's separately for e.g. algae, invertebrates, fish

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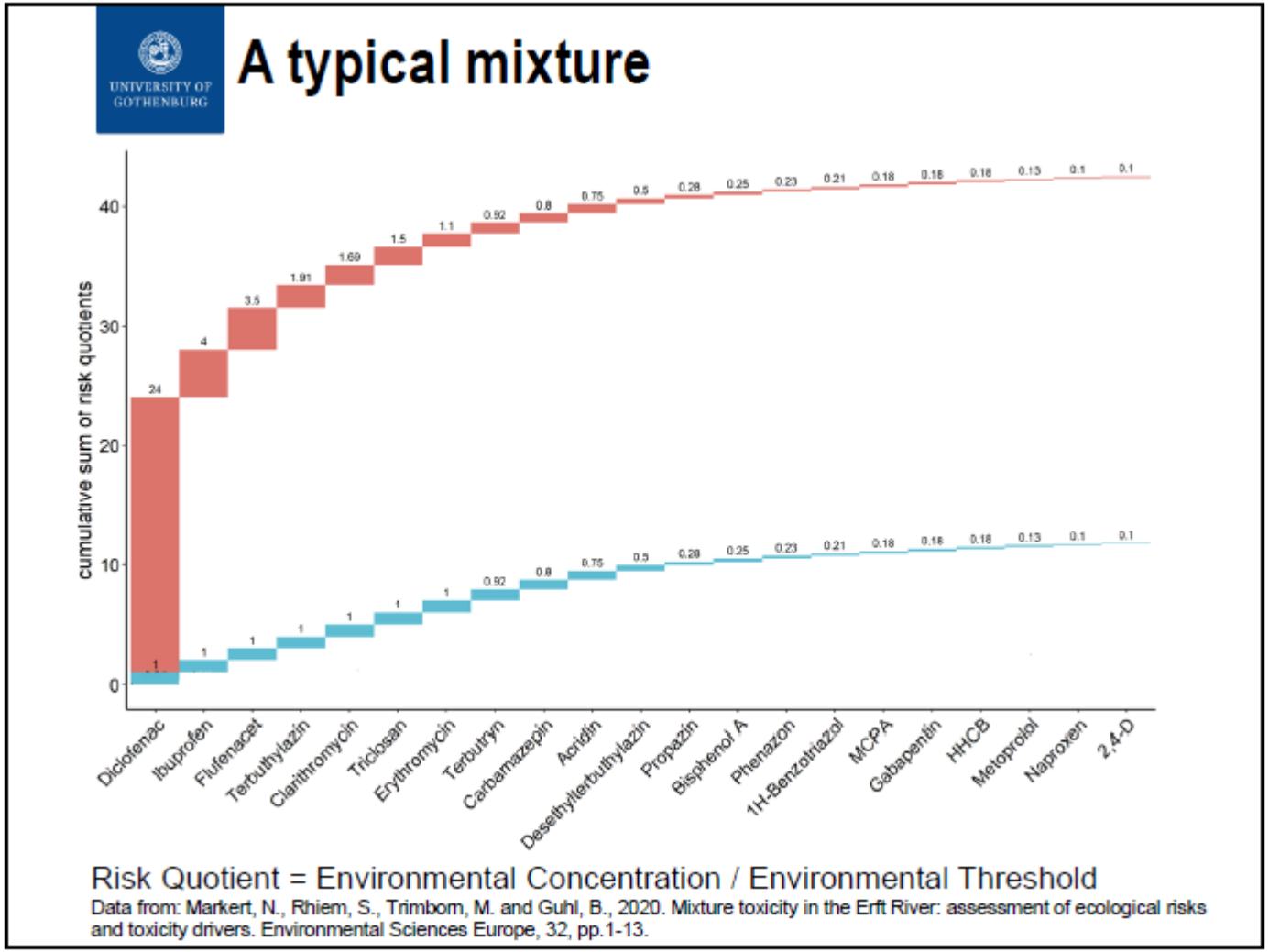
Example, Risk ratio (Risk quotient; Hazard quotient)



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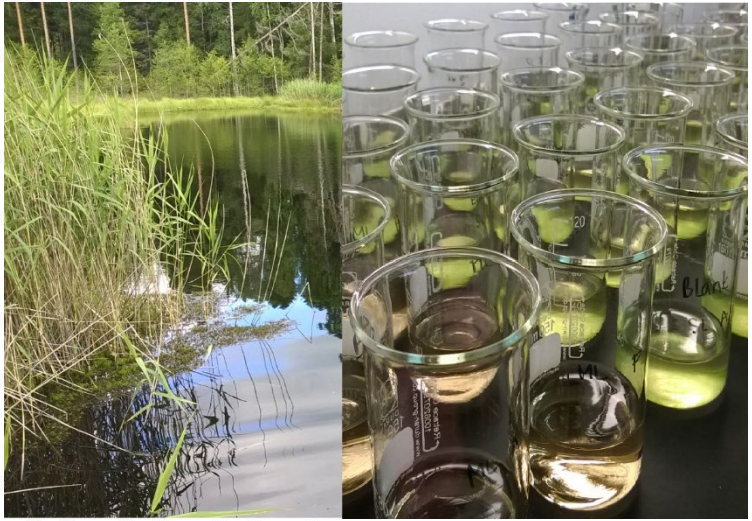
Whole mixture assessment
Effect-based methods (EBMs)



- *Biotests*
  - *In vivo/in vitro* lab tests
- *Biomarkers*
  - *In situ* exposed biota
- *Ecological indicators*
  - Quality indices; species, abundance

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EBMs are gaining support in the EU adminstration

"In the WFD review, a more holistic approach, taking into account the presence of mixtures of chemicals acting together (for example through the use of effect-based tools in addition to group EQSs), could be considered, to provide a more accurate assessment of risks and a more appropriate targeting of monitoring and measures"

(*from discussion document later endorsed by the water directors*)

Wernersson AS, Maggi C, Carere M. Technical report on aquatic effect-based monitoring tools. Technical Report 2014–077.

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In vivo biotests

Individual level effects, either acute or chronic

- Can be related to population level responses
- Acute; mortality, immobility, Chronic; growth, reproduction

Respond to all stress factors (also other than contaminants)

Can be chemical group specific (algae; herbicides)

Typical standard species; green algae, water flea, fish

- Many standards (ISO, OECD, ASTM, CEN)
- Baltic sea specific; brackish water species

Test matrices; water, sediment, extracts

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In vitro biotests

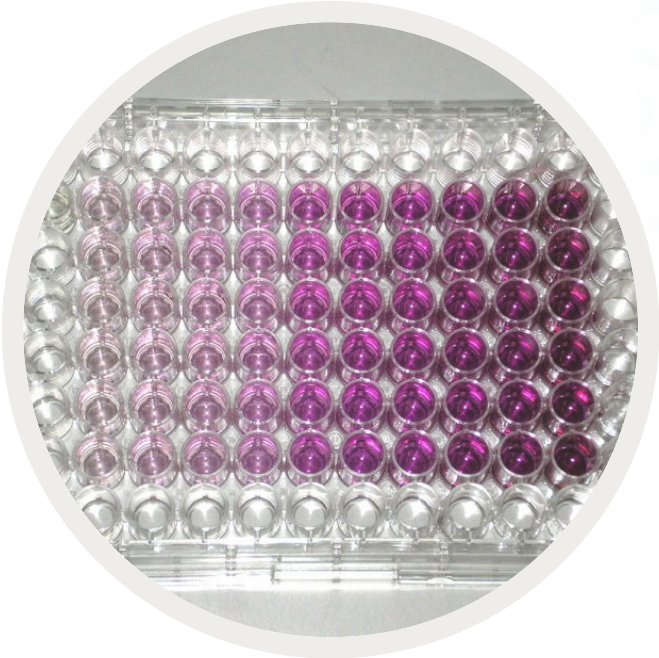
Typically cell line or single cell species tests

Measure molecular level responses, receptor bindings etc.

Usually fast, high through-put tests, e.g. apply well plate/light emission

Chemical group specific responses

- Mutagenicity, endocrine disrupters, neurotoxicity, many receptor binding tests etc.



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Using ”water quality criteria” of a specific *in vitro* response (1)

Trigger values for environmental samples

- Effect-based trigger value = ”Environmental quality standard”
  - Test specific!
  - For screening and risk assessment (pass/fail)
- Available for several response types
  - Escher ym. 2018. Sci. Tot. Env. 628-629:748-
- Most advanced is endocrine disruption (ISO standards)
  - Receptor binding tests ER-CALUX, YES, A-YES

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Using ”water quality criteria” of a specific *in vitro* response (2)

Trigger values for environmental samples

- Assumptions:
  - Reference chemical and unknows bind to the same receptor
  - Reference chemical (E2 hormone) effect level concentration is known = trigger value (e.g. 0,4 ng E2/L)
  - Sample response is normalized to reference chemical response (x ng E2 equivalents/L)
  - Exceedance indicates risk of unknowns endocrine disrupters in a sample

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Recommendations for a monitoring or environmental risk assessment program

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Comprehensive risk assessment is made of combination of chemical analysis and effect-based methods

- Perform chemical analysis (suspect screening)
- Find the most abundant chemicals ≠ hazard
- Do the component-based risk assessment ≈ hazards
- Complement chemical analyses with EBMs
  - Select chemical matching biotests if specific chemical group is in interest
  - At least use basic *in vivo* tests to see mixture effects
  - A battery of different EBM approaches is recommended
  - Possibly study local biota for biomarkers

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An example of environmental risk assessement

Case gypsum ($CaSO_4$) on fields

Effect of sulfate on riverine biota

- Chemical analysis
  - On site online sensor
- Lab tests
  - Mussel behaviour
  - Mussel glochidia survival
  - Moss growth
- Field *in situ* exposures
  - Perifyton colonization & growth
  - Trout egg incubation
- Field surveys
  - Mussel abundance before-after
  - Fish abundance before-after

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Thank you!

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