RISK*e*Learning

Bioavailability – Metals, Organics, and Use at Hazardous Waste Sites

May 28, 2008 Session 1: "Metals"

Dr. Dominic Di Toro, University of Delaware
Environmental Control of Metal Bioavailability

Dr. Nicholas Basta, Ohio State University
Assessing Oral Contaminant Human (Bio)availability in Soil with *In Vitro* Gastrointestinal Methods:
Uncertainties, Data Gaps, and Research Needs

Environmental Control of Metal Bioavailability

Dominic M. Di Toro

Edward C. Davis Professor of Civil and Environmental Engineering
Center for the Study of Metals in the Environment
Department of Civil and Environmental Engineering
University of Delaware
Newark, DE

Superfund Basic Research Program
Webinar
EPA CLU-IN
28 May 2008

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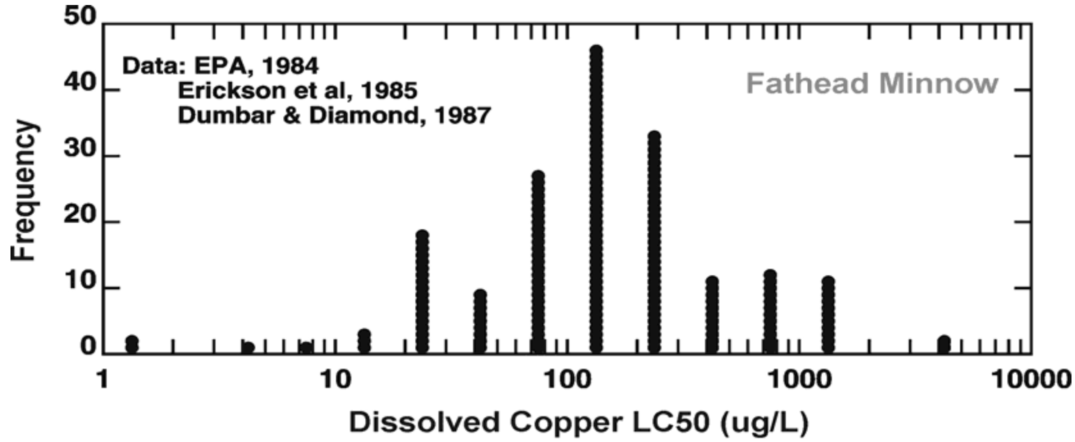
Bioavailability
No correlation between Total Cu and Biological Effects



LC50 = Concentration causing 50% mortality in 96 hrs

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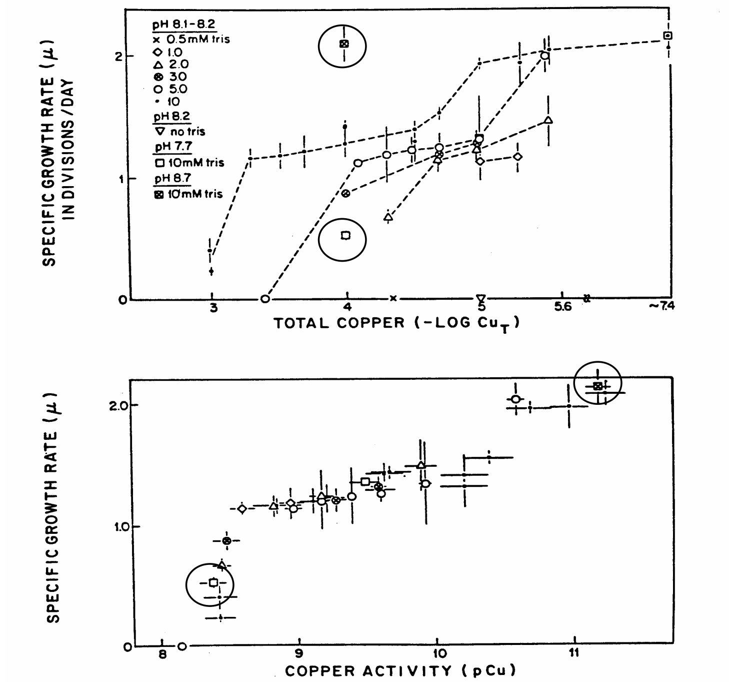
Free Ion
Activity Model

FIAM



Sunda, W., & Guillard, R. R. L. (1976). J. Mar. Res., 34, 511-529.

Campbell, P. G. C. (1995). Interactions between Trace Metals and Aquatic Organisms: A Critique of the Free-ion Activity Model. In A. Tessier & D. R. Turner (Eds.), Metal Speciation and Bioavailability in Aquatic Systems Wiley.

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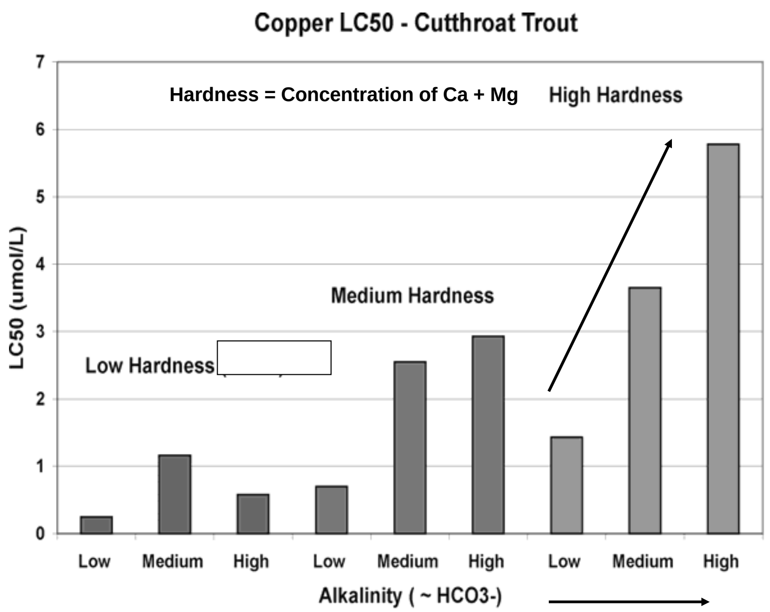
Speciation

Effect of Alkalinity and Hardness



Chakoumakos, C., Russo, R.C. Thruston, R.V (1979)
Environ. Sci. Technol. 13(2) 213

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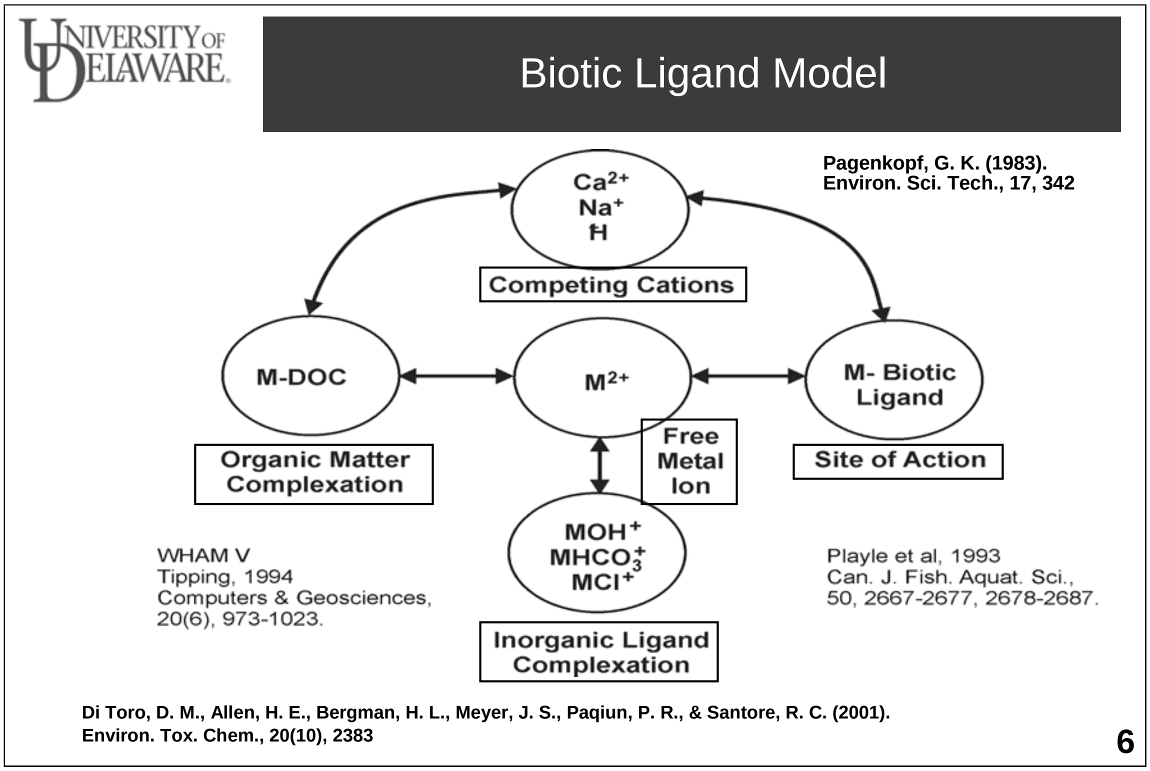


Overview of Biotic Ligand Model Framework:

The essence of the overall BLM framework (above) was first proposed by Pagenkopf (1983) as the Gill Site Interaction Model (GSIM).

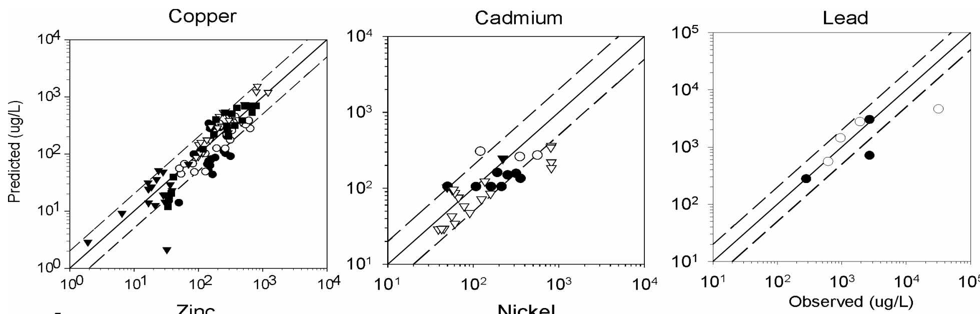
- Chemical equilibrium basics will not be discussed here. However, such models are not new and are generally well accepted by the scientific community.

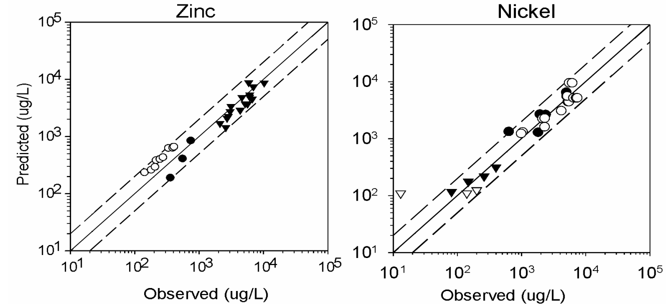
The BLM consists of 3 main types of interactions:

- Metal-Inorganic Ligand Interactions-
  - Chemical Equilibrium in Soils and Solutions (CHESS) (Santore and Driscoll, 1995) serves as the basis of the speciation computations and was adapted to include the metal-OM and metal-biotic ligand interactions described below.
- Metal-Organic Mater (OM) Interactions-
  - Based on the Windermere Humic Aqueous Model (WHAM), Version 5 (Tipping, 1994)
- Biotic Ligand Interactions-
  - Adapted from Playle et al., 1993a,b.

Each of these will be discussed in turn.

Daphnia Magna BLM LC50 Concentrations





Di Toro, D. M., McGrath, J. M., Hansen, D. J., Berry, W. J., Paquin, P. R., Mathew, R., Wu, K. B., & Santore, R. C.

Predicting Sediment Metal Toxicity Using a Sediment Biotic Ligand Model: Methodology and Initial Application.

Environ Tox. Chem., (2005).

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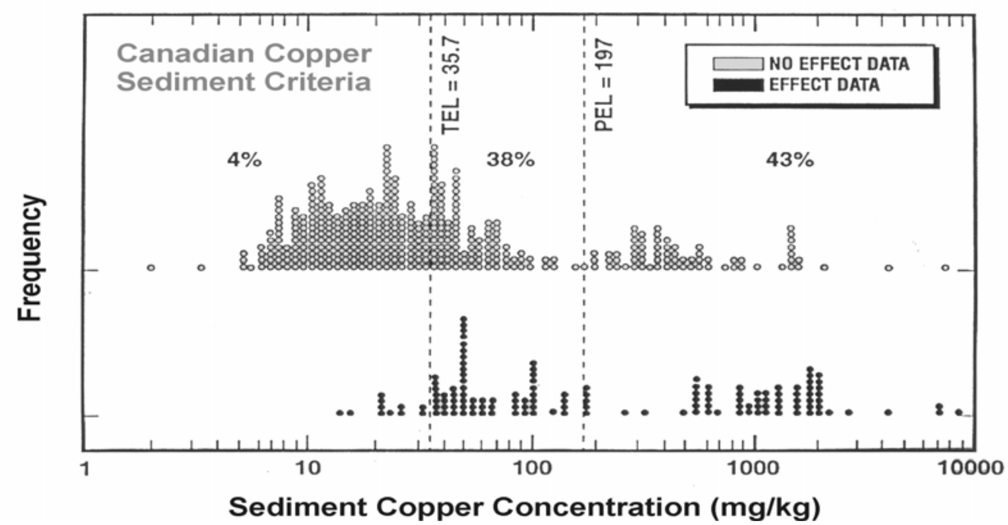
Bioavailability
No correlation between Total Cu and Biological Effects



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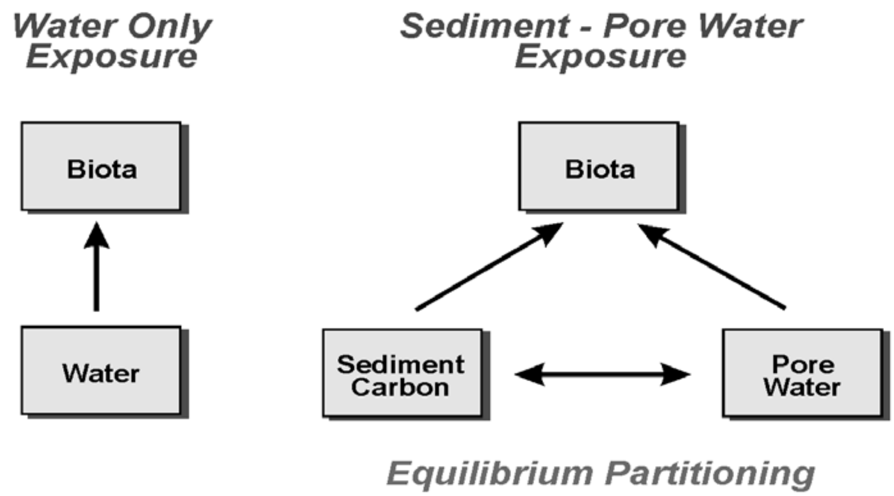
Equilibrium Partitioning Model of Sediment Toxicity



Di Toro, D. M., C. S. Zarba, D J. Hansen, W J Berry, R C. Swartz, C E. Cowan, S P. Pavlou H E. Allen, N A Thomas, P R Paquin. (1991). Environ. Toxicol. Chem. 11(12): 1541-1583.

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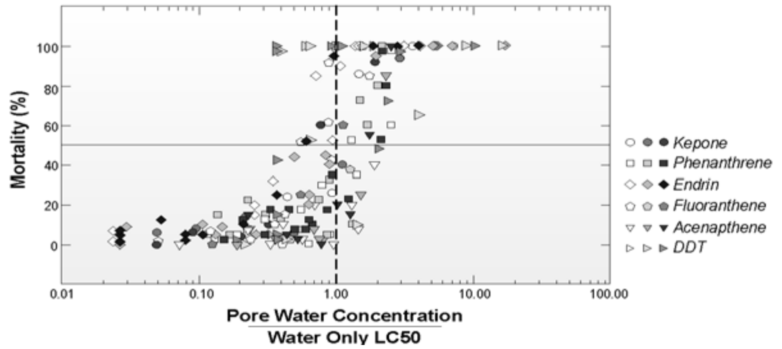
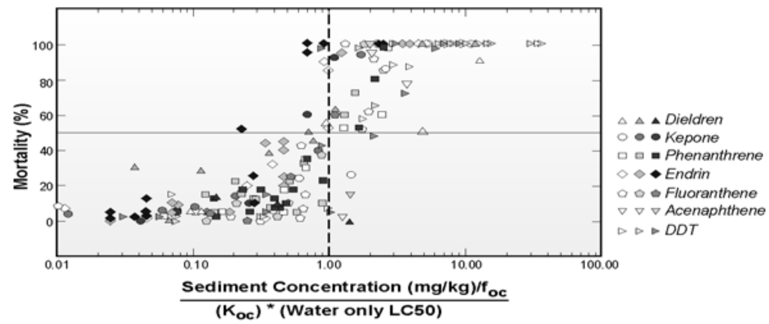
Sediment
Toxicity
Prediction

Pore Water



Organic
Carbon
Normalized



USEPA (2000). Draft Technical Basis for the derivation of Equilibrium Partitioning sediment guidelines (ESG) for the protect of benthic organisms: Nonionic organics No. EPA-822-R-00-001)

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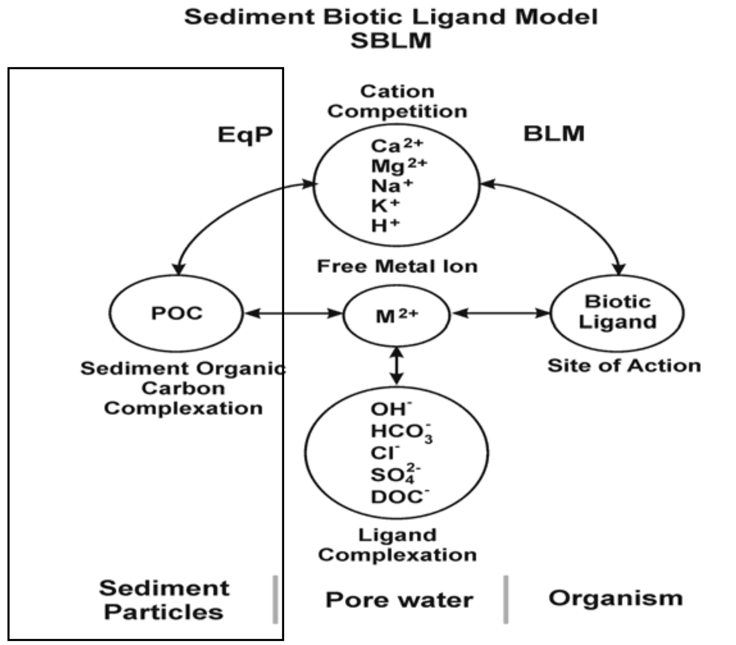
Application
to
Sediments

Sediment POC
Modeled
as Humic Acid



Di Toro, D. M., McGrath, J. M., Hansen, D. J., Berry, W. J., Paquin, P. R., Mathew, R., Wu, K. B., & Santore, R. C. Predicting Sediment Metal Toxicity Using a Sediment Biotic Ligand Model: Methodology and Initial Application. Environ Tox. Chem., (2005).

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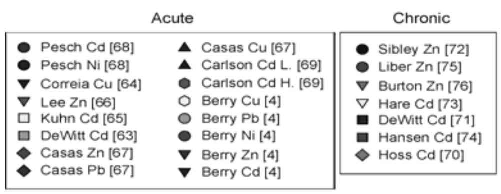
Predicting Sediment Metal Toxicity

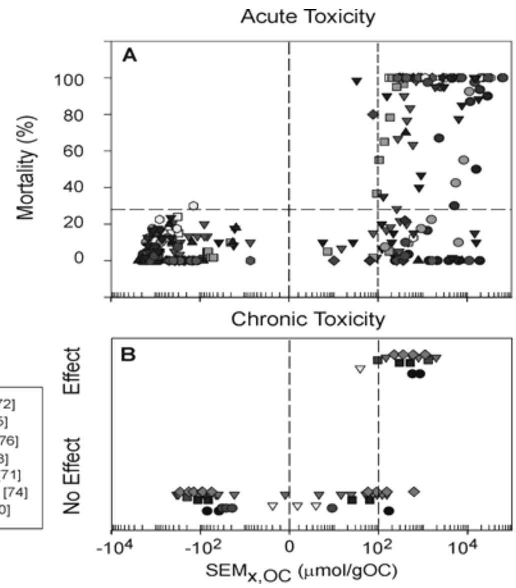
Organic Carbon Normalized Excess SEM

$SEM_{x,oc} = (SEM - AVS)/f_{oc}$

Observed Toxicity Boundary

$SEM_{x,oc} = 100\ \mu mol/gOC$





Di Toro, D. M., McGrath, J. M., Hansen, D. J., Berry, W. J., Paquin, P. R., Mathew, R., Wu, K. B., & Santore, R. C. Predicting Sediment Metal Toxicity Using a Sediment Biotic Ligand Model: Methodology and Initial Application. Environ Tox. Chem., (2005).

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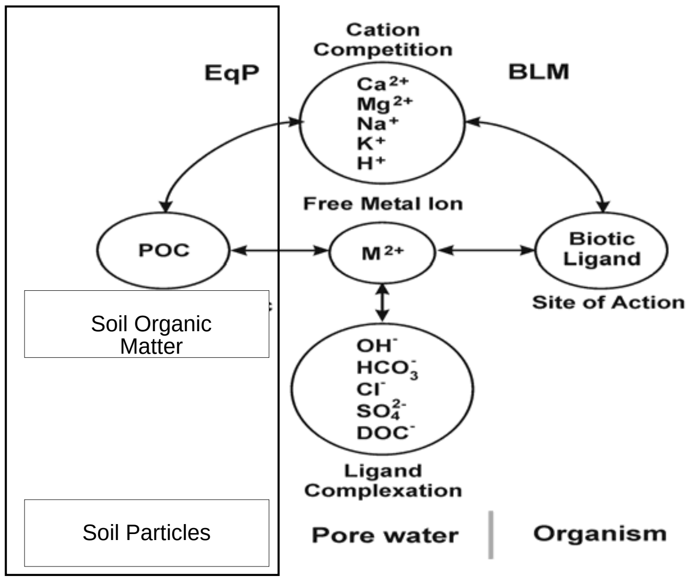
Terrestrial BLM

Application
to
Soils

Soil POC
Modeled
as Humic Acid



Thakali, S., Allen, H. E., Di Toro, D. M., Ponizovsky, A. A., Rooney, C. P., Zhao, F.-J., and McGrath, S. P. "A terrestrial biotic ligand model I: Development and application to Cu and Ni toxicities to barley root elongation in soils." Environ. Sci. Tech., 40(22) (2006): 7085-7093.

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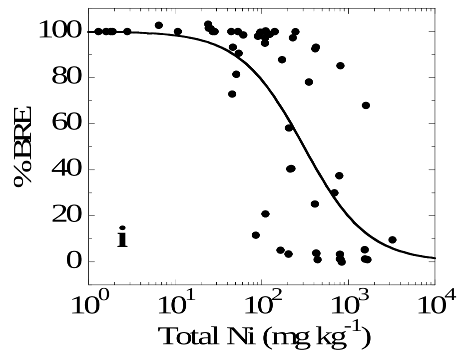
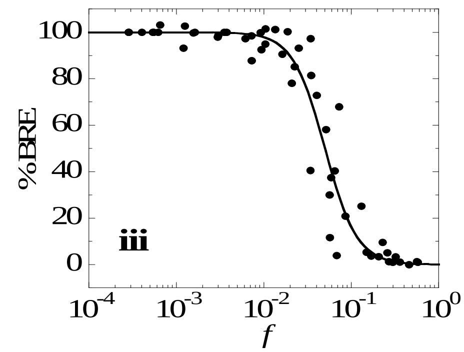
Ni Toxicity – Barley Root Elongation

Total Ni



BLM



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A terrestrial biotic ligand model I: Development and application to Cu and Ni toxicities to barley root elongation in soils."
Environ. Sci. Tech., 40(22) (2006): 7085-7093.

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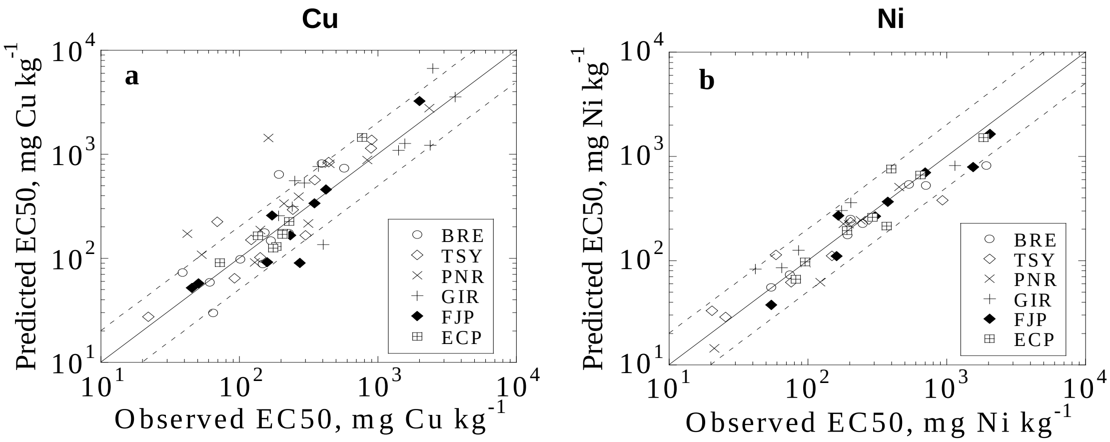
Terrestrial BLM
Predicted vs. Observed EC50
Various Endpoints



Thakali, S., Allen, H. E., Di Toro, D. M., Ponizovsky, A. A., Rooney, C. P., Zhao, F.-J., and McGrath, S. P. "
A terrestrial biotic ligand model I: Development and application to Cu and Ni toxicities to barley root elongation in soils."
Environ. Sci. Tech., 40(22) (2006): 7085-7093.

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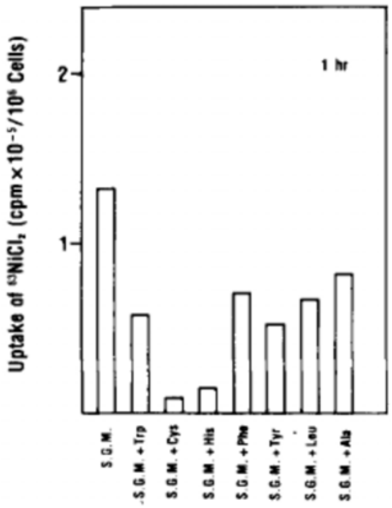
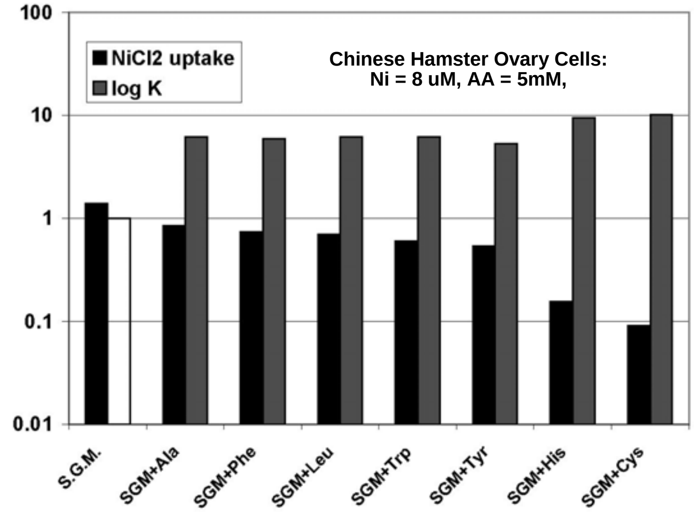
$NiCl_2$ Uptake and Ni^{2+} Binding Constants
Ni + Amino Acids





The Regulation of Ionic Nickel Uptake and Cytotoxicity by Specific Amino Acids and Serum Components
MARIA P. ABBRACCHIO, R. MARK EVANS, J. DANIEL HECK, ORAZIO CANTONI, AND MAX COSTA
BIOLOGICAL TRACE ELEMENT RESEARCH 4, 289-301 (1982)

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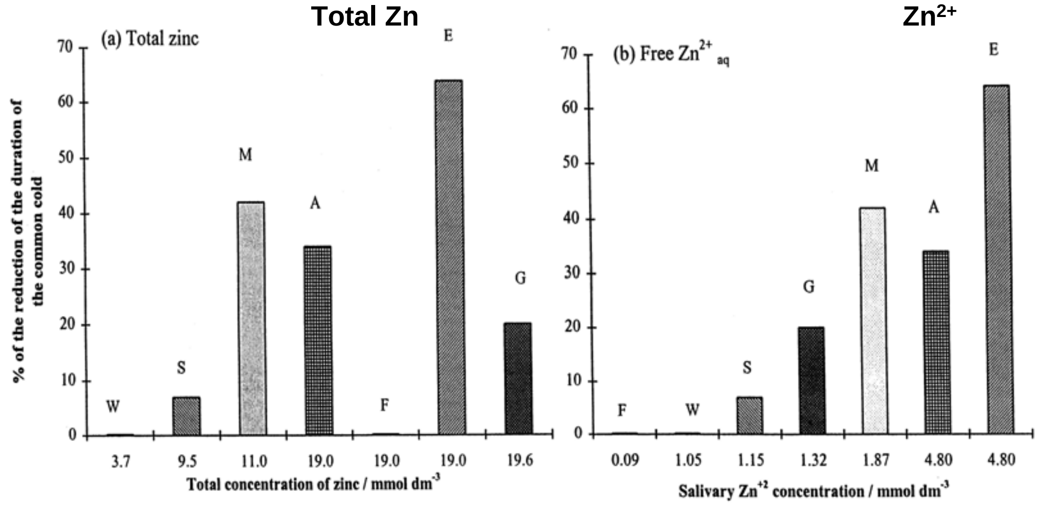
Free Ion Activity Model (FIAM)

% Reduction of the duration of the common cold
vs

Total Zn **Zn^{2+}**



D.R. Williams : Coordination Chemistry Reviews 185–186 (1999) 177–188

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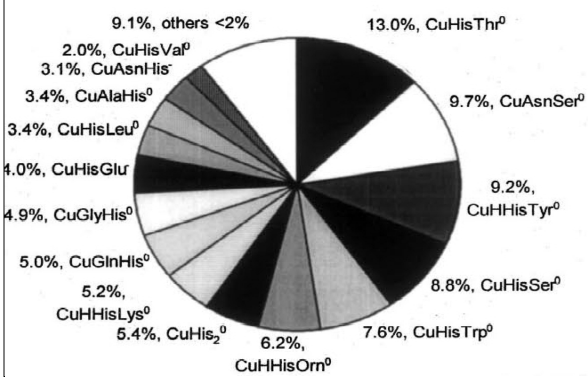
Speciation in Wound Fluid

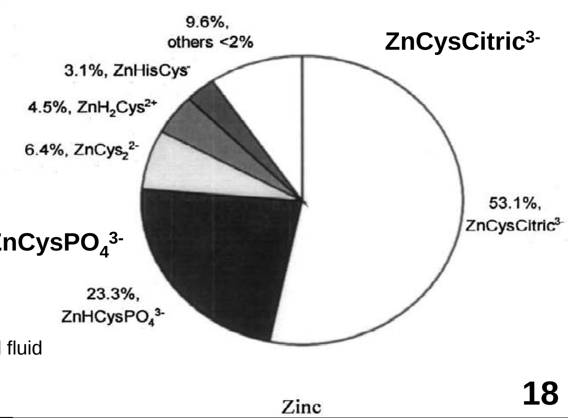


Cu
Mostly Neutral

Zn
Mostly Anonic

ZnCysCitric^{3-}

ZnCysPO$_4^{3-}$



Analysis and chemical speciation of copper and zinc in wound fluid
Paul W. Jones, David M. Taylor, David R. Williams
Journal of Inorganic Biochemistry 81 (2000) 1–10

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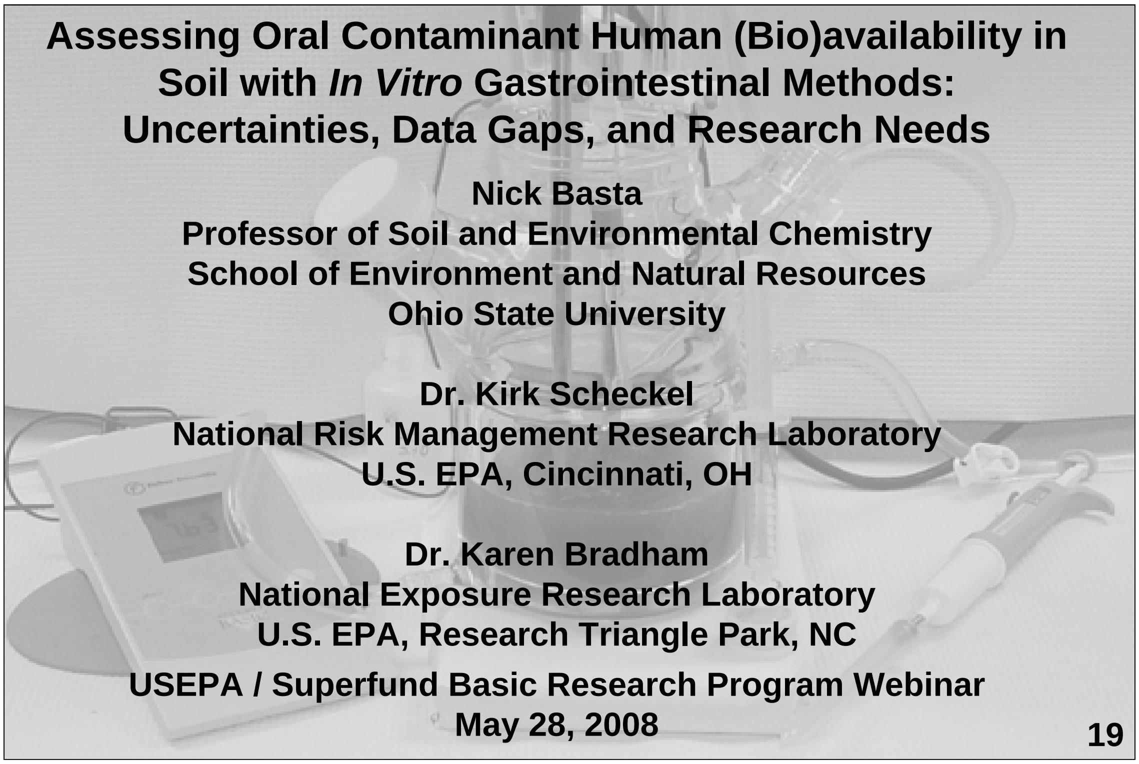
Assessing Oral Contaminant Human (Bio)availability in Soil with *In Vitro* Gastrointestinal Methods: Uncertainties, Data Gaps, and Research Needs
Nick Basta
Professor of Soil and Environmental Chemistry
School of Environment and Natural Resources
Ohio State University
Dr. Kirk Scheckel
National Risk Management Research Laboratory
U.S. EPA, Cincinnati, OH
Dr. Karen Bradham
National Exposure Research Laboratory
U.S. EPA, Research Triangle Park, NC
USEPA / Superfund Basic Research Program Webinar
May 28, 2008
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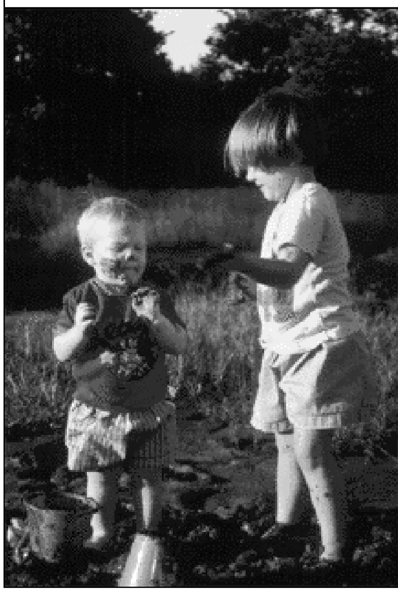
Using Bioavailability to Adjust Risk in the Soil Ingestion Pathway

"Soil Contaminant Oral Bioavailability"



$$\text{Risk} = [\text{Soil}] \frac{(EF)(ED)(IR)(BIO)}{(BW)(AT)}$$

How do we measure BIO for children?

Animal model dosing trials
- **costly, lengthy, not easily obtained data**

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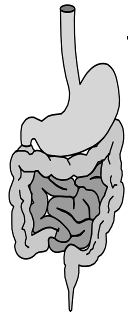
In Vitro Gastrointestinal Methods

An Inexpensive, Fast, Accessible Alternative



Sequential extraction, 37°C

all have a stomach phase
some have an intestinal phase

may have several intestinal simulations for duodenum, jejunum, colon, etc.

***in vitro* "(bio)availability" = dissolved contaminant**
= bioaccessible contaminant

bioaccessibility > bioavailability, so *in vitro* assumes worst case

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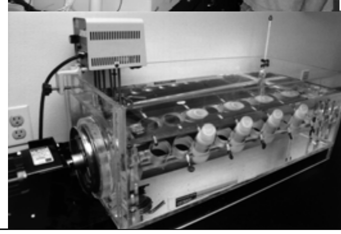
Types of IVG Methods

Based on contaminant
Inorganic Contaminants (Pb, As, Ni, Cd)
Organic contaminants (dioxin/furans, PAH, pesticides)

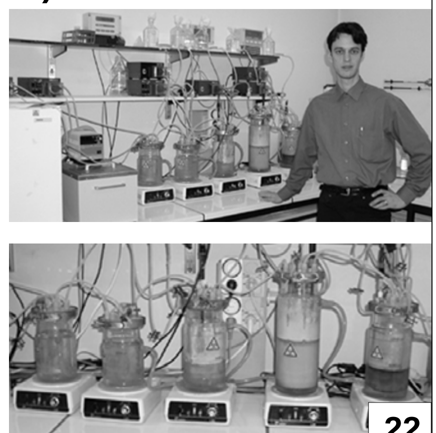
Based on Type / Complexity
batch (simple) vs. dynamic (complex)

OSU IVG batch

SBRC RBALP batch



SHIME dynamic



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Select Types of IVG Methods

Method	Type	Main application(s)
PBET / RBALP (Ruby, Drexler)	Batch, fasting	Pb
OSU IVG (Basta, Rodriguez)	Batch, fasting	Pb, As, Cd
RIVM, (Oomen, Sips)	Batch, fed	PAH / Pb, As
SERDP (Lowney)	Batch, fasting	Pb, As
SHIME (Van de Wiele)	Dynamic, fed	PAH, As
TIM, tiny TIM	Dynamic, fed	PAH

fasting vs. non-fasting
Inorganic / fasting: pH very important
organic / fed: bile, food used most important

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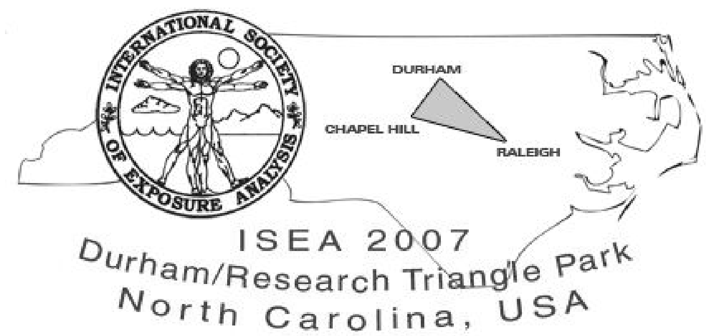
ISEA 2007 Conference

Use of In Vitro Bioaccessibility / Relative Bioavailability Estimates in Regulatory Settings: What is Needed?

Symposium chairs: K. Bradham, U.S.EPA, P. Rasmussen, Health Canada
R. Schoof, Integral Consulting, Inc., M. Cave, British Geological Survey

State of Science of IVG Methods
List of Data Gaps and Research Needs



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U.S. EPA
Guidance for Evaluating the Oral Bioavailability of Metals in Soils for Use in Human Health Risk Assessment
OSWER 9285.7-80, May 2007

Recommended Criteria for Validation of Test Methods adapted from ICCVAM

"Data generated adequately measure or predict the toxic endpoint of interest and demonstrate a linkage between either the new test and effects in the target species."

***In vitro* gastrointestinal (IVG) method must be correlated with an acceptable *in vivo* model**
IVG must be *predictive*

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Acceptable *In Vivo* Models

accurate
bioavailability

unlikely
model

acceptable model
for Pb, As, other
bioavailability

USEPA
Pb OK; As?

acceptable
model for
bioavailability

expensive
ethical issues

acceptable
bioavailability?

inexpensive
recent developments
Dave Thomas
USEPA RTP (ISEA 2007)

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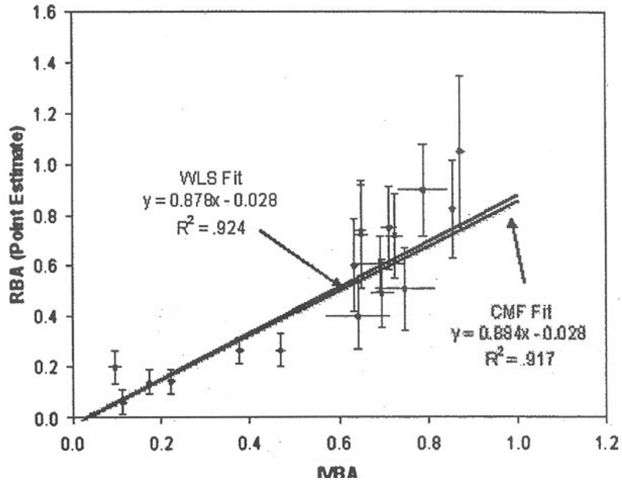
RBALP *in vitro* gastrointestinal method correlated with immature swine bioavailable Pb



Drexler and Brattin. 2007. Human Ecol. Risk Assess. 13:383-401.

Estimation of RBA of Pb in soil and soil-like materials using *In Vivo* and *In Vitro* Methods. OSWER 9285.7-77, May 2007

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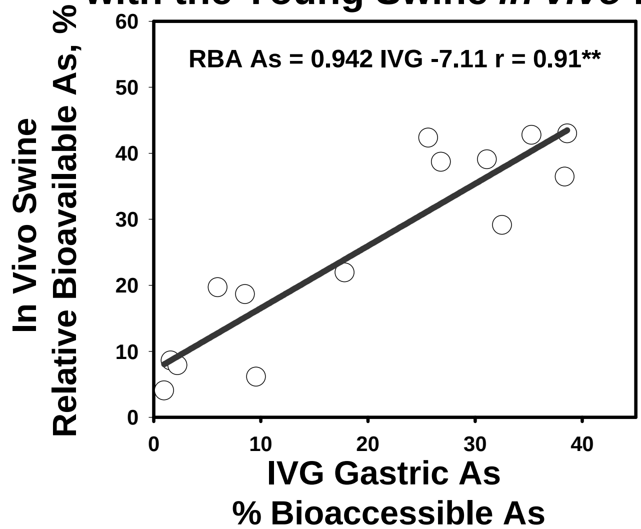
Correlation of OSU IVG method with the Young Swine *in vivo* model



Basta et al. 2003.
Grant R825410 Final Report.
submitted to U.S. EPA ORD

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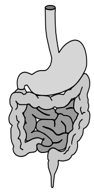
OSU *In Vitro* Gastrointestinal Method



Simulated GI extraction at 37^{o}C

Gastric bioaccessibility and
Intestinal bioaccessibility

Development of Chemical Methods to Assess the Availability of Arsenic in Contaminated Media, R825410

U.S. EPA, Office of Research and Development
National Center for Environmental Research

N.T. Basta, R.R. Rodriguez, and S.W. Casteel
Nov 1996 to October 2000.

. **Rodriguez et al. 1999. ES&T 33:642-649.**

Basta et al., 2007. J. Environ. Health Sci. Part A 42:1275-1181

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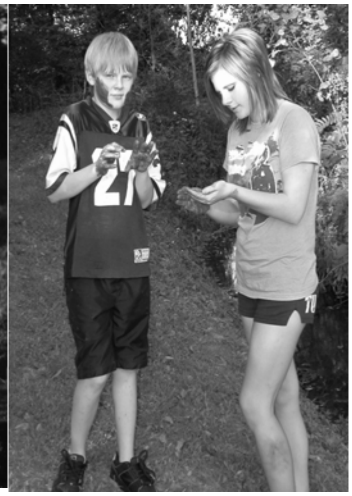
Research on OSU IVG still continuing after 10 yr

1997



2007

the soil isn't contaminated

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Correlation of "SERDP" method with Relative Bioavailable Arsenic

Lowney, presented at ISEA 2007
Primate (cynomolgus monkey) RBA As vs. "SERDP" As

"SEDRP" As: gastric bioaccessibility
0.4 M glycine/HCl pH 1.5 OR 0.4 M K_2HPO_4, pH 2.5

use larger bioaccessible As value of two methods

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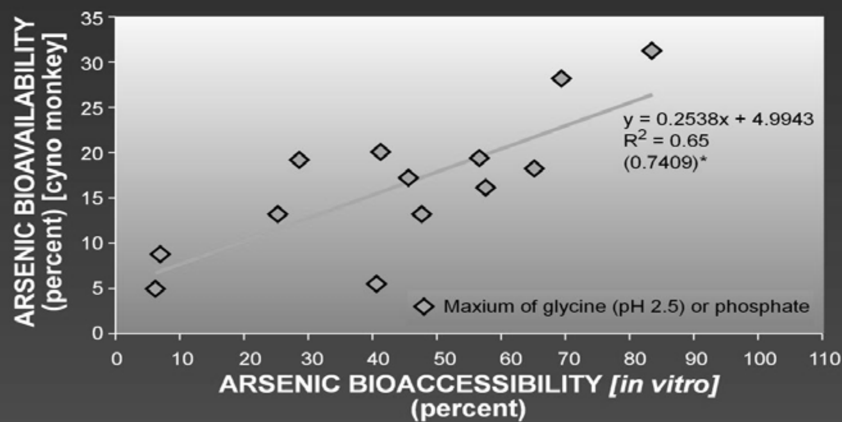
IV:IVC
Arsenic RBA in cynomolgus monkey Dual Extraction ("SERDP Method"): Maximum of Glycine or Phosphate



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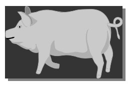
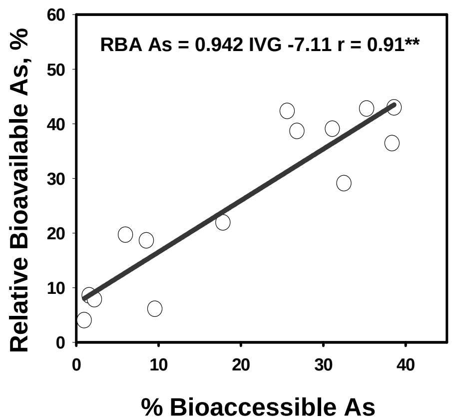
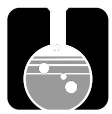
Can we use the same method for different contaminants?





Basta et al. 2003.
Grant R825410 Final Report.
submitted to U.S. EPA ORD



OSU IVG correlation with in vivo

As with dosing vehicle
Rodriguez et al. 1999.
ES&T 33:642-649

As without dosing vehicle
Basta et al., 2007. J. Environ. Health Sci. Part A 42:1275-1181.

Pb with/out dosing vehicle
Schroder et al., 2004
J. Environ. Qual., 33:513-521.

Cd with/out dosing vehicle
Schroder et al., 2003.
ES&T 37:1365-1370.

IVG Method Correlation Studies
Will the method work for other contaminated soils?

Most correlation studies conducted on highly contaminated wastes

often > 2,000 mg/kg contaminant of concern

Estimating RBA of Pb in Soil and Soil-like materials
(OSWER 9285.7-77, May 2007)
Most of 19 solid waste materials from smelter origin
Pb content: 1,590 to 14,200 mg/kg, median 7,225 mg/kg

Estimating RBA of Arsenic in Contaminated Soils and Solid Media
(Rodriguez et al., 1999)
As content: 233 to 17,500 mg/kg, median 1,460 mg/kg

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In Vitro Models
Method Validation Issues

Will the *in vitro* test work for all types contaminants/media?

Do we have to conduct validation studies for all contaminant sources?

mining waste, battery waste, paint, coal ash, etc.?

Better approach – contaminant speciation
SEM/EDX (J. Drexler); EXAFS (K. Scheckel)

Which species are bioavailable?
Does the *in vitro* test measure them?

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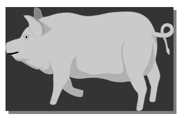
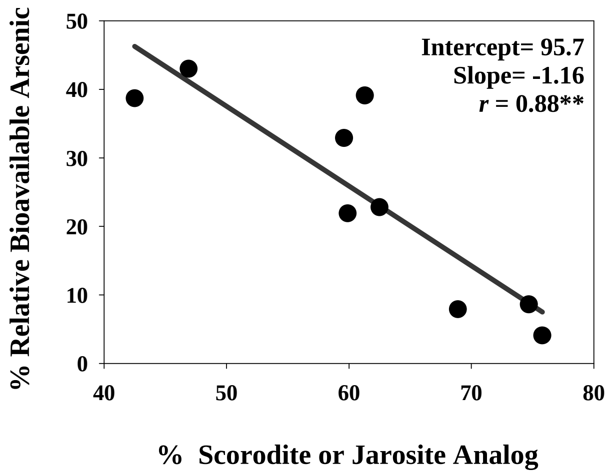
Bioavailable Arsenic and Solid Phase Speciation





Arsenic identified as Scorodite or Jarosite Analog inversely related to Relative Bioavailable Arsenic

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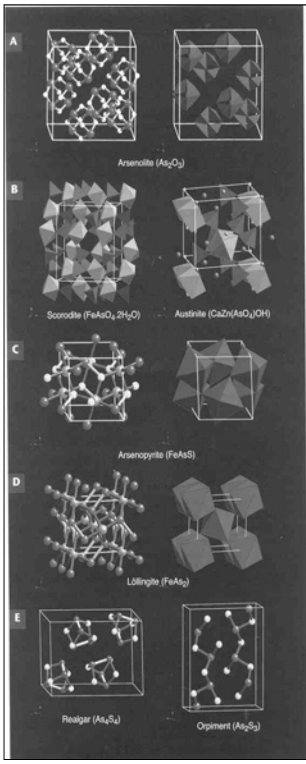

Arsenic Speciation, Mineralogy, Bioaccessibility, and Bioavailability

We could extrapolate the OSU IVG methods for highly contaminated smelter waste soils to soils/solid waste where scorodite / jarosite As-analog was the arsenic source term

More studies need to document relationship between Arsenic Speciation Bioaccessibility, and Bioavailability

Photo from Peggy A. O'Day. April 2006.
Elements 2:77-83.
Chemistry and Mineralogy of Arsenic

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Contaminant Concentration in Soil / Solid Waste
when will bioavailability adjustments be made?

Highly Contaminated
unreasonable adjustment

Moderately Contaminated

reasonable adjustment

Background

High level: 7,000 mg/kg total As or Pb
Bioavailability has to be very very low
unreasonable adjustment

Moderate level: 300 mg/kg As
moderate bioavailability so
reasonable adjustment

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Assessing Bioavailability of Moderately Contaminated Soil

The greatest utility of IVG or *in vivo* methods may be to assess risk for soils with mod. level contamination Pb paint, pesticides, coal ash, CCA, cattle dips, etc.

Moderately contaminated urban and/or old industrial sites

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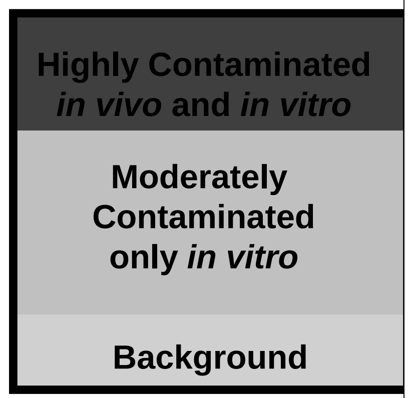
Bioavailable (*in vivo*) vs. Bioaccessible (*in vitro*) Method Detection Limits and Contaminant Levels

most *in vivo* dosing studies require highly contaminated soil
> 500 to 5,000 mg/kg contaminant

Moderately contaminated soil levels
could be < 1000 mg/kg Pb; < 100 mg/kg As
Below *in vivo* detection limits

Below *in vivo* working range but
easily measured by IVG methods



<u>A Strong Advantage</u> <u>of IVG methods</u>
is the ability to estimate
(bio)availability at moderate levels

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Are we confident to use IVG methods to Estimate Contaminant Bioavailability in Soil for Moderately Contaminated Soils?

Knowledge of chemical speciation is essential!

contaminant species in old orchard soil same as contaminant species in smelter soil (*in vivo* correlation study)?

Yes: then we are more confident to use the IVG (*in vitro*) method for the orchard soil

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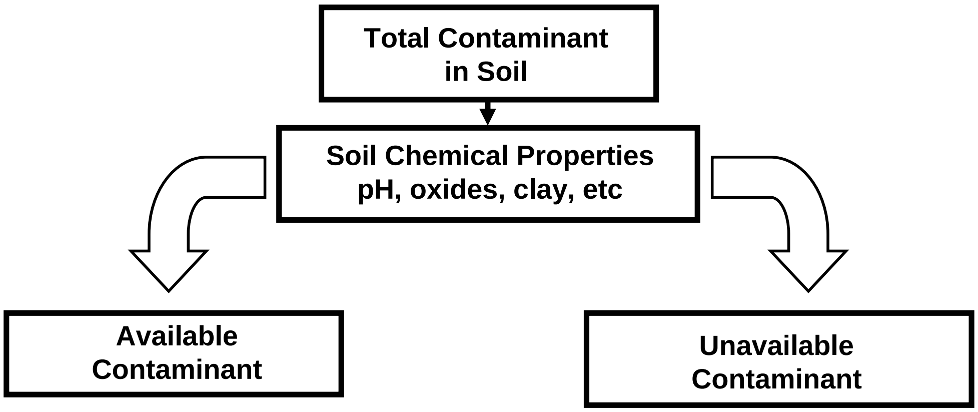
Does the Soil Type Affect Bioavailability?

Soil Chemistry Can Greatly Affect Contaminant Sequestration and Contaminant Bioavailability / Bioaccessibility



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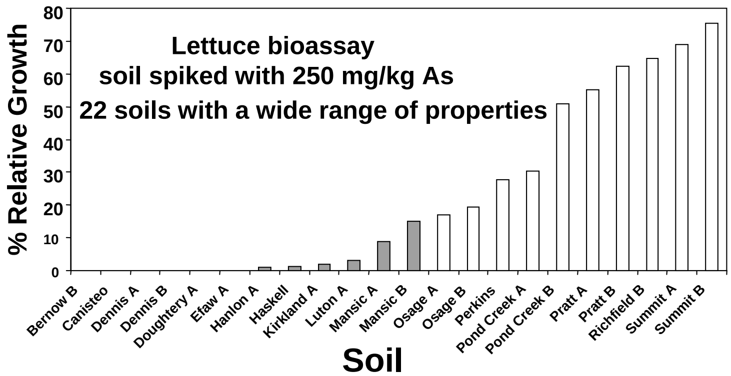
Soil Chemical Components and Properties greatly affect availability and toxicity



Soil properties greatly affect bioavailability / toxicity

Bradham et al. 2006. Environ. Tox. Chem. 25(3):769-775. earthworms Pb

Dayton et al. 2006. Environ. Tox. Chem. 25(3):719-725. lettuce Pb

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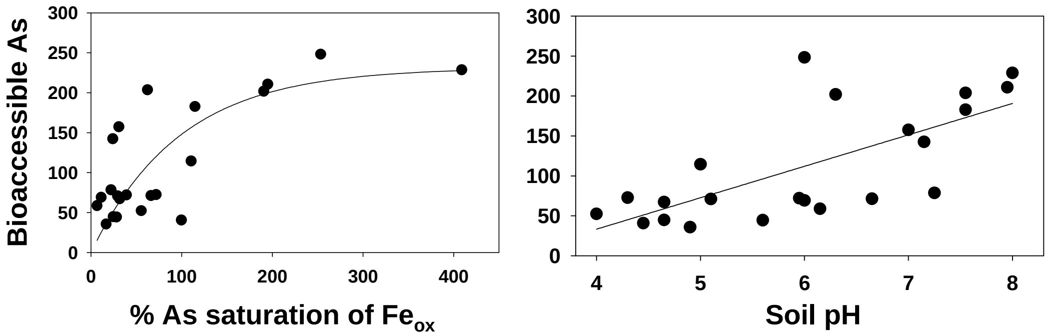
Soil Chemical Components and Properties greatly affect IVG Method As bioaccessibility



Bioaccessible As = 87 log ($\%As_{sat}$) + 31 (soil pH) - 223 R^2 = 0.7868

Similar results as
Yang, Barnett, Jardine, Basta, and Casteel. 2002. Environ. Sci. Technol. 36:4562-4569

Determine the ability of IVG methods to measure bioaccessibility in contaminated soils with a <u>wide range of soil chemical properties</u>

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U.S. EPA
Guidance for Evaluating the Oral Bioavailability of Metals in Soils for Use in Human Health Risk Assessment
OSWER 9285.7-80, May 2007

"A detailed protocol for the test method........., and a description of the known limitations of the test including a description of the classes of materials that the test can and cannot accurately assess."

- **Specify the contaminant chemical speciation and**
- **whether the IVG method has been correlated with *in vivo* for the contaminant species in the test material**
- **Measure soil chemical parameters that affect bioavailability**

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Summary
Uncertainties, data gaps, research needs

- ❖ Research leading to acceptance of existing / new *in vivo* models
- ❖ Document the relationship between arsenic speciation, bioaccessibility, and bioavailability
- ❖ Test the use of soil chemical / speciation methods to support IVG data when IVG is the only option
- ❖ Determine the ability of IVG methods to measure bioaccessibility in contaminated soils with a <u>wide range of soil chemical properties</u>

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Thank you for your attention
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Register now for the second and third presentations of the Bioavailability series:

"Bioavailability of Organic Compounds: Methods and Case Studies" – June 11th, and

"Use of Bioavailability Information at Hazardous Waste Sites" – June 18th

by following the registration link on the Risk e Learning web page.

For more information and archives of this and other Risk e Learning web seminars please refer to the Superfund Basic Research Program Risk e Learning web page:

http://tools.niehs.nih.gov/sbrp/risk_elearning/

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Thank You

Links to Additional Resources

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