Interactive Primer on Uncertainty Analysis for Exposure and Hazard Assessment

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Overview

- The Basics
  - variability, uncertainty, and value-of-information
- Discrete Bayesian methods
  - Role of priors, role of evidence
  - BBN's for synthesizing multiple evidence
- A BBN for "Is Naphthalene a Human Carcinogen at Low Doses"?
- Bayesian Hierarchical Models
  - Perchlorate effect on thyroid
  - Tox and EPI studies for low birth weight from DBP's

Variability

- Inherent variation
  - from location to location (spatial)
  - from year to year, month to month, or other (temporal)
  - from site to site
  - from individual to individual
- Variability characterized using empirical or mathematical distribution functions.
- Variability is not reduced with more information, but it can be better characterized.
- Variability can be reduced (or increased) through risk management actions.

Uncertainty

- Lack of scientific knowledge
- Can apply to the fundamental formulation of the risk model
  - Model (structure) uncertainty
  - All models are simplifications of reality
    - but may still be useful
- Can apply to model input values
  - Parametric uncertainty
  - Resulting from measurement error, disagreements in the literature on appropriate values or estimation procedures, mismatch in temporal or spatial scales for inputs, confounding variables

Characterization of Uncertainty

- Central estimates of key model outputs
  - with upper and lower plausible bounds
  - with variance (or standard deviation)
  - with confidence intervals
  - with full probability distribution function
- Identifying which uncertain model assumptions and inputs contribute most to uncertainties that matter
  - Value of Information (VOI)

Value of Information

- Scientific: Reduction in variance of important model output as information is obtained and the uncertainty in a model assumption or input is reduced
- Decision Analytic: Increase in the expected value of the optimal decision that will be made after the information is obtained and (as a result) the uncertainty in a model assumption or input is reduced.
  - Information only has value if the results of the study, experiment, field monitoring, etc. will lead to different management decisions, depending on the results.

Decision-Analytic Measures of VOI

- **EVPI** How much higher is the expected value of the best decision when there is no uncertainty?
- **EVPIX** How much higher is the expected value of the best decision when there is no uncertainty in Input X?
- **EVSI** How much higher is the expected value of the best decision that will be made contingent on a sampling program (with its associated measurement errors, FPR, FNR, etc.)?

Alternative Approaches for Simultaneous Characterization of Variability and Uncertainty

- Classical methods: use data to fit distributions, characterize uncertainty in parameters:
  - e.g., Frey and Burmaster: bootstrap methods or likelihood function distribution
    - → Applied to individual input variables, one at a time
- Bayesian methods: prior distribution for parameter values + data → posterior distribution for parameter values
  - Results cans differ from classical results when prior information is important, the study has low power (and/or a high false positive rate), small sample size, etc.
  - Conjugate distributions for uncertain parameters
  - Bayesian simulation (Markov Chain Monte Carlo)

BAYESIAN METHODS

Combine (prior) information, from expert knowledge or previous data-sets, with the information in observed data-sets

Readily distinguish between variability and uncertainty

Update probability and risk assessments as new information and data are acquired; and

Evaluate value-of-information to prioritize new research and data collection efforts

FUNDAMENTALS

Bayes Rule converts a prior probability for an event to a posterior probability:

$$P\,[\text{Event } A \mid \text{Observation } B] = \frac{P\,[\text{Observation } B \mid \text{Event } A] * P_o\,[\text{Event } A]}{P\,[\text{Observation } B]}$$

where:

- $P_o\,[\text{Event } A]$ **is the <u>prior</u> probability for the event;**
- $P\,[\text{Observation } B \mid \text{Event } A]$ **is the probability, or <u>likelihood</u> of observing B when A is true; and**
- $P\,[\text{Observation } B]$ **is the <u>total probability</u> of observing B (whether A is true or not)**

Example: Diagnosis of a Biased Coin

Event A_1 → an *unbiased* coin with $P(H) = P(T) = 0.5$
Event A_2 → a *biased* coin with $P(H) = 0.95$, $P(T) = 0.05$

What inference would we draw concerning these alternatives with the following evidence?

Observation B_1 → 5 heads out of 5 flips
Observation B_2 → 55 heads out of 60 flips
Observation B_3 → 55 heads out of 100 flips

That is, what is the probability that the coin is in fact biased (vs. unbiased), given each of the three experimental outcomes (B_1, B_2 or B_3)? . . . .

Example: Diagnosis of a Biased Coin (Continued)

→ **It depends on the priors!**

Consider two possible priors:

Prior_1 → "Noninformative" (or "vague") prior:

$P_o(A_1) = P_o(A_2) = 0.5$

(e.g., the coin of a magician in the circus)

Prior_2 → "Informed" prior:

$P_o(A_1) = 0.999 \quad P_o(A_2) = 0.001$

(e.g., after careful *prior* tests to ensure balance, or perhaps with a randomly selected coin from the bank)

Example: Diagnosis of a Biased Coin (Continued)

Results:

Prior	**Posterior Prob. Coin is biased = P(A_2),** given . . . B_1 (5 of 5)	B_2 (55 of 60)	B_3(55 of 100)
$P_o(A_2) = 0.5$ *(from magician)*	0.961	1.0 **(= 1 - 4.7×10^{-11})**	0.0 **(2.15×10^{-30})**
$P_o(A_2) = 0.001$ *(from bank)*	0.024	1.0 **(= 1 - 4.7×10^{-8})**	0.0 **(2.15×10^{-33})**

Bayesian Belief Network Model for Combining Multiple Strains of Evidence

- **VOI for scientific consensus among differing experts:**
  - Stiber, N.A., M. Pantazidou and M.J. Small. 1999. Expert system methodology for evaluating reductive dechlorination at TCE sites. *Environmental Science & Technology*, 33(17): 3012-3020.

A BBN Expert System for TCE Reductive Dechlorination

- Objective:
  - Develop an expert system to improve site evaluations for the reductive dechlorination of TCE in groundwater
  - By combining:
    - A causative model for the reductive dechlorination of TCE, built within a Bayesian Belief Network (BBN)
    - Expert knowledge obtained via an elicitation process
- Learn about:
  - reductive dechlorination processes
  - multi-expert elicitation and combining expert beliefs

BBN For Reductive Dechlorination

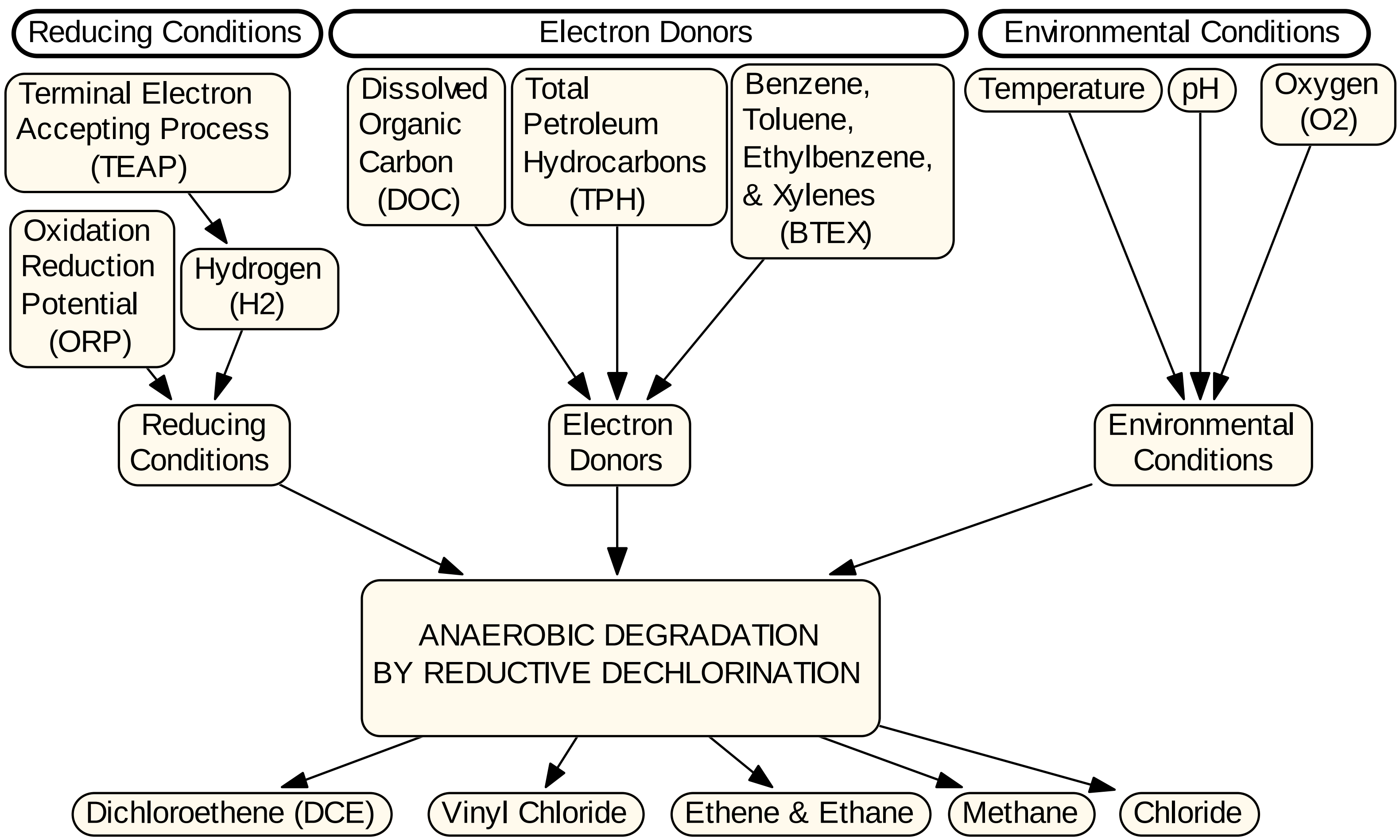


TABLE 1. Example of Prior Probabilities (Elicited from Expert L)

condition	prior probability (%)
terminal electron accepting process is denitrification	5
terminal electron accepting process is iron reduction	40
terminal electron accepting process is sulfate reduction	15
terminal electron accepting process is methanogenesis	40
oxidation reduction potential < 50 mV	90
[dissolved organic carbon] > 20 mg/L	70
[benzene, toluene, ethylbenzene, & xylenes] > 0.1 mg/L	70
[total petroleum hydrocarbons] > 1 mg/L	70
[dissolved oxygen] < 0.5 mg/L	80
0.5 mg/L < [dissolved oxygen] < 1 mg/L	15
[dissolved oxygen] > 1 mg/L	5
temperature > 15 °C (59 °F)	70
5 < pH < 9	80

TABLE 3. Example of Conditional Probabilities for Products of Reductive Dechlorination (Elicited from Expert L)

given that reductive dechlorination is ...	what is the probability that ...?	probability (%)
occurring	[*cis*-1,2-DCE] > 80% of [total 1,2-DCE]	90
not occurring	[*cis*-1,2-DCE] > 80% of [total 1,2-DCE]	10
occurring	vinyl chloride is detected	70
not occurring	vinyl chloride is detected	20
occurring	[ethene and ethane] > 0.01 mg/L	30
not occurring	[ethene and ethane] > 0.01 mg/L	10
occurring	[methane] > 0.1 mg/L	70
not occurring	[methane] > 0.1 mg/L	30
occurring	[chloride] > twice background	50
not occurring	[chloride] > twice background	10

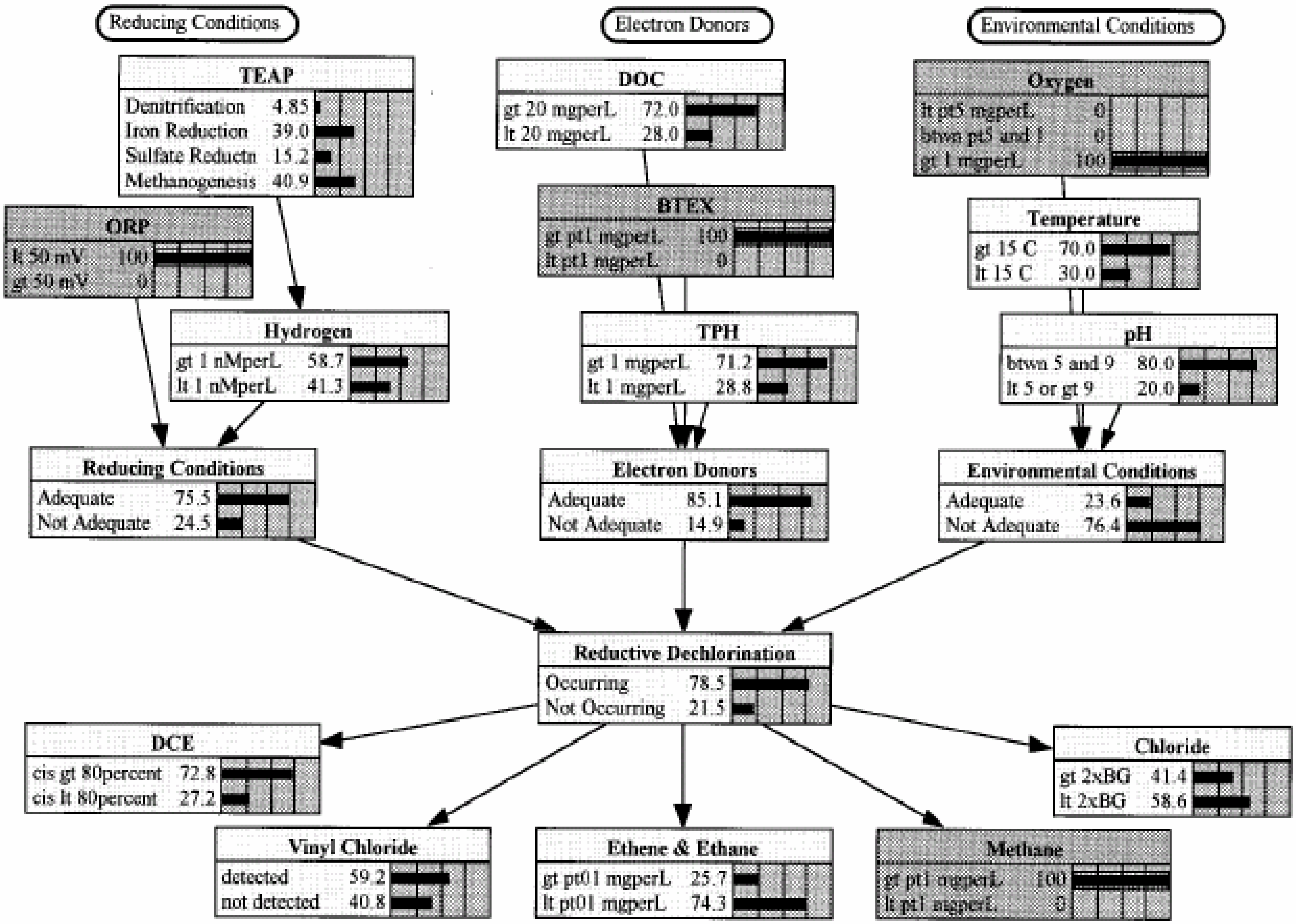


FIGURE 2. Example Netica output. Expert L's model with evidence: ORP < 50 mV, BTEX > 1 mg/L, oxygen > 1 mg/L, and methane > 0.1 mg/L.

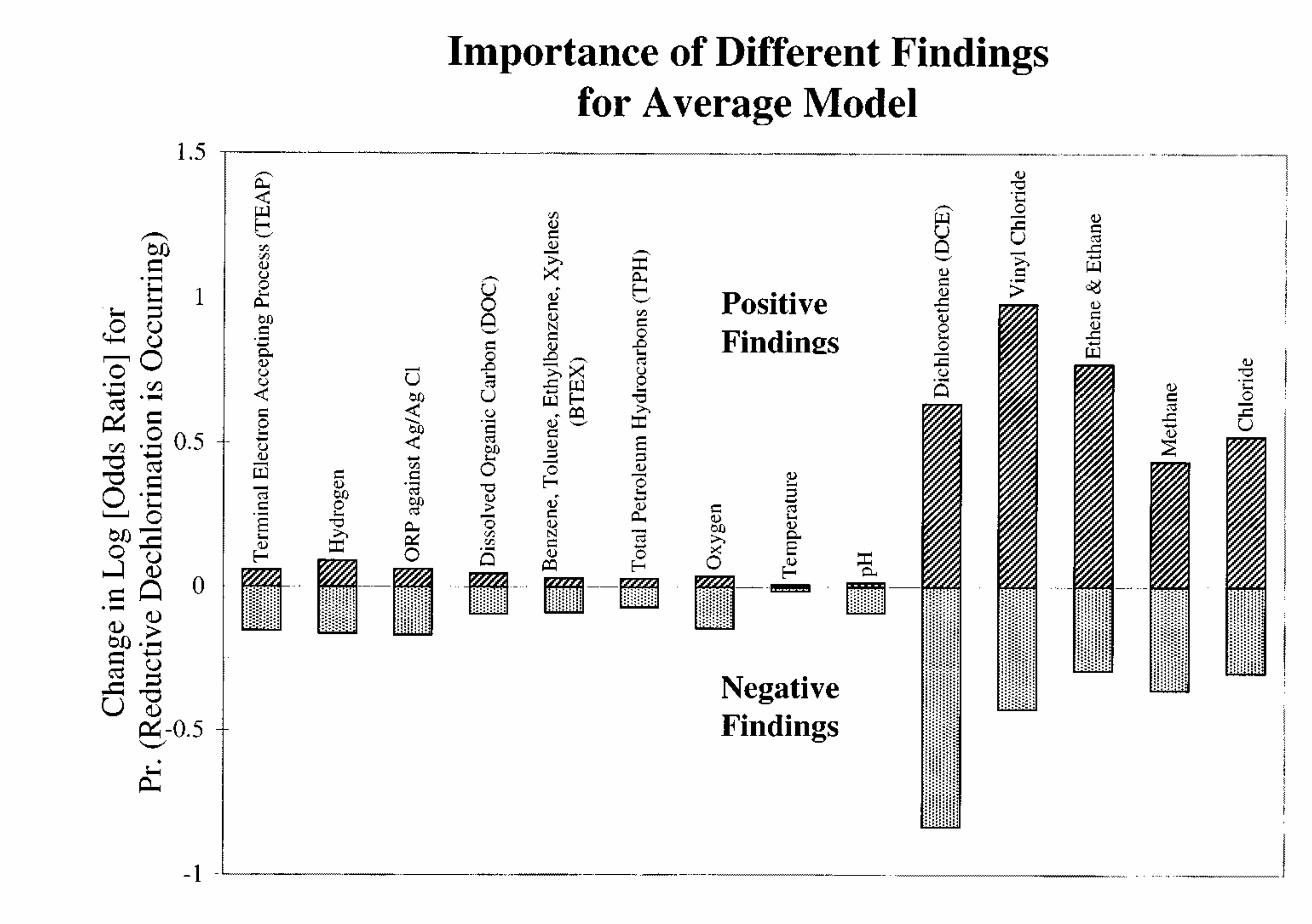
Comparison of Value of Information (VOI) for Different Types of Evidence

- Difference in the log of the odds ratios =

$$\text{Log}\left[\frac{\text{Probability}(\text{true}\,|\,\text{evidence})}{\text{Probability}(\text{false}\,|\,\text{evidence})}\right]-\text{Log}\left[\frac{\text{Probability}(\text{true})}{\text{Probability}(\text{false})}\right]$$

- Average Model
  - Using average probabilities from all 22 expert elicitations

Comparison of Value of Information (VOI) for Different Types of Evidence: Average Model



Comparison of Value of Information (VOI) for Different Types of Evidence for Different Experts

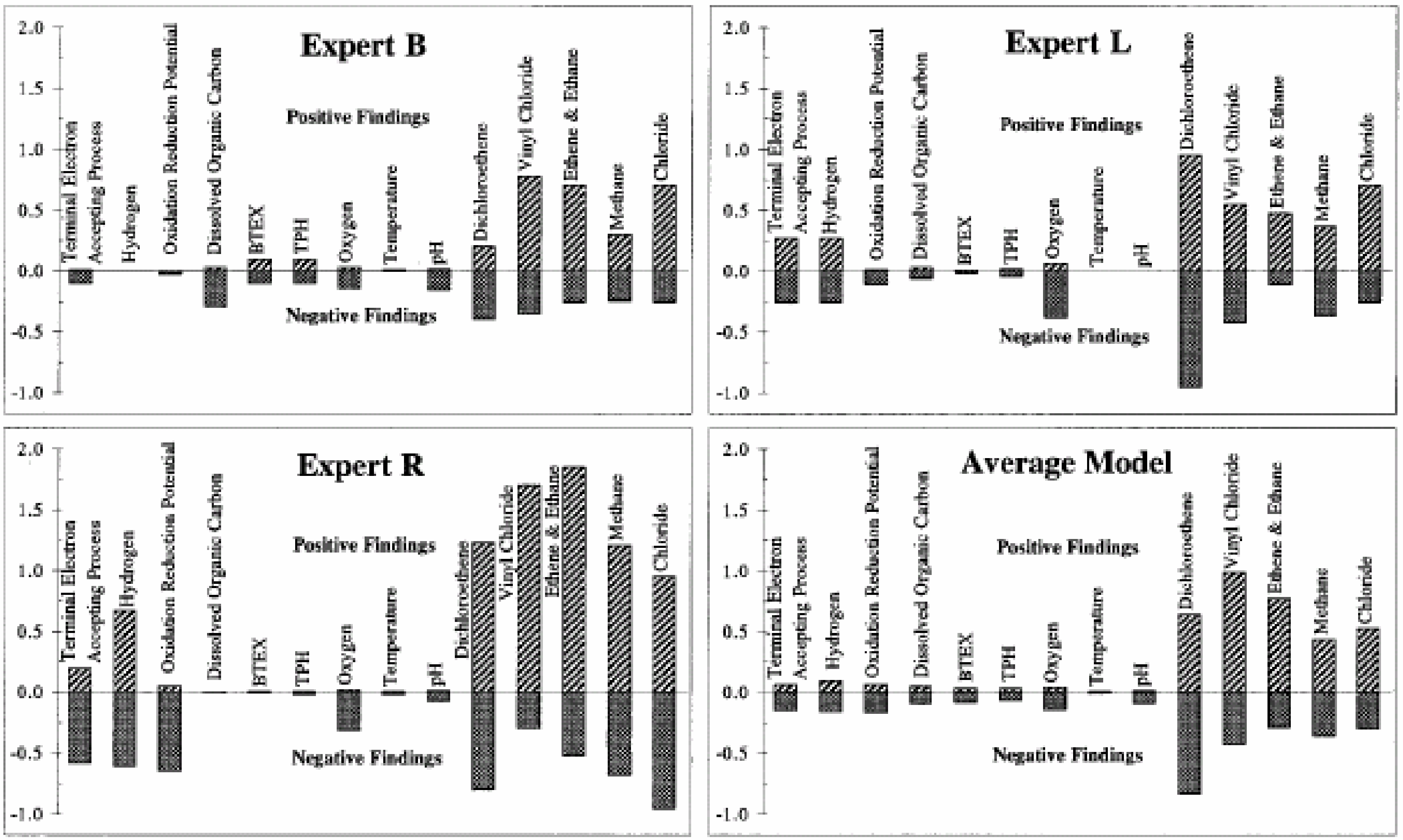
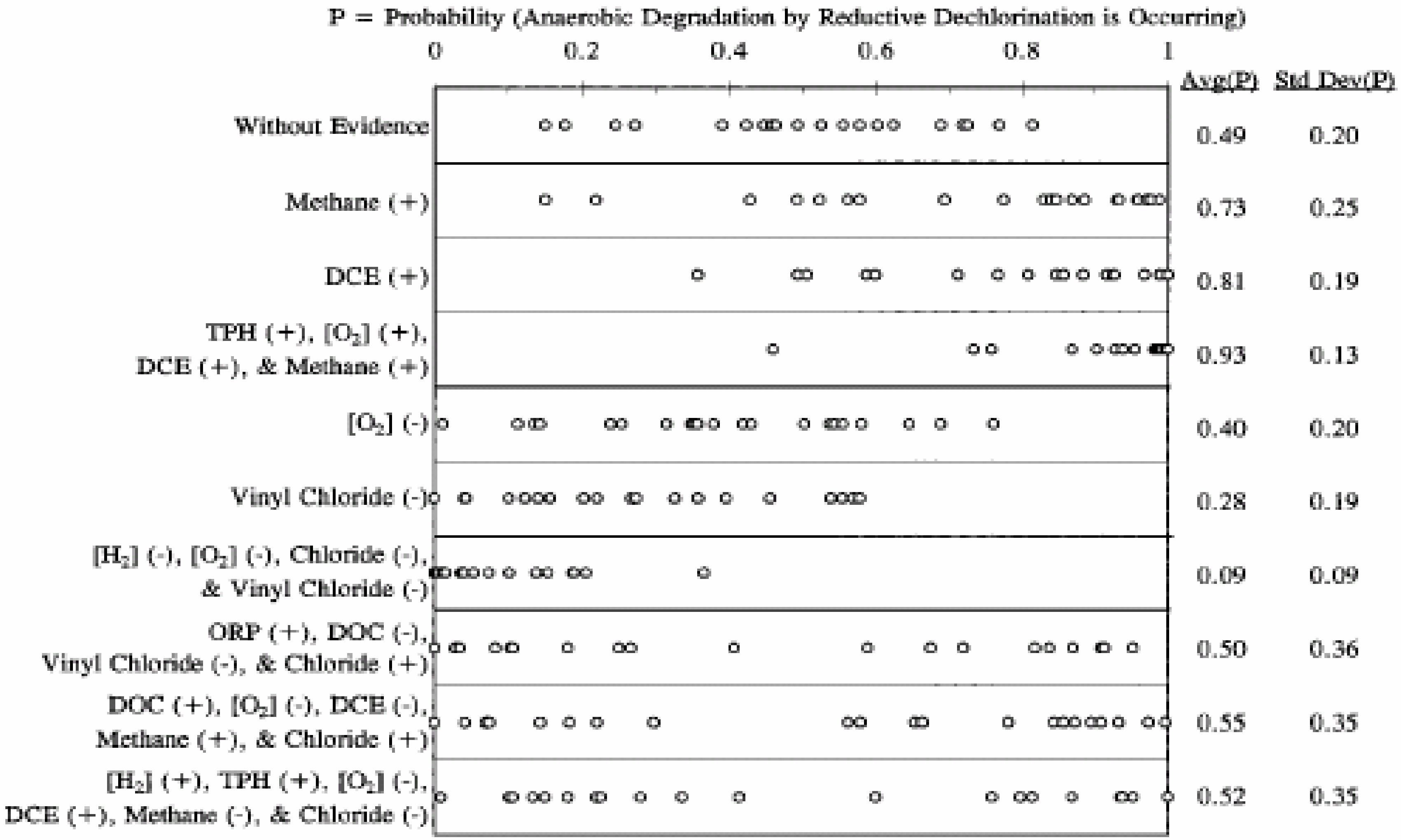


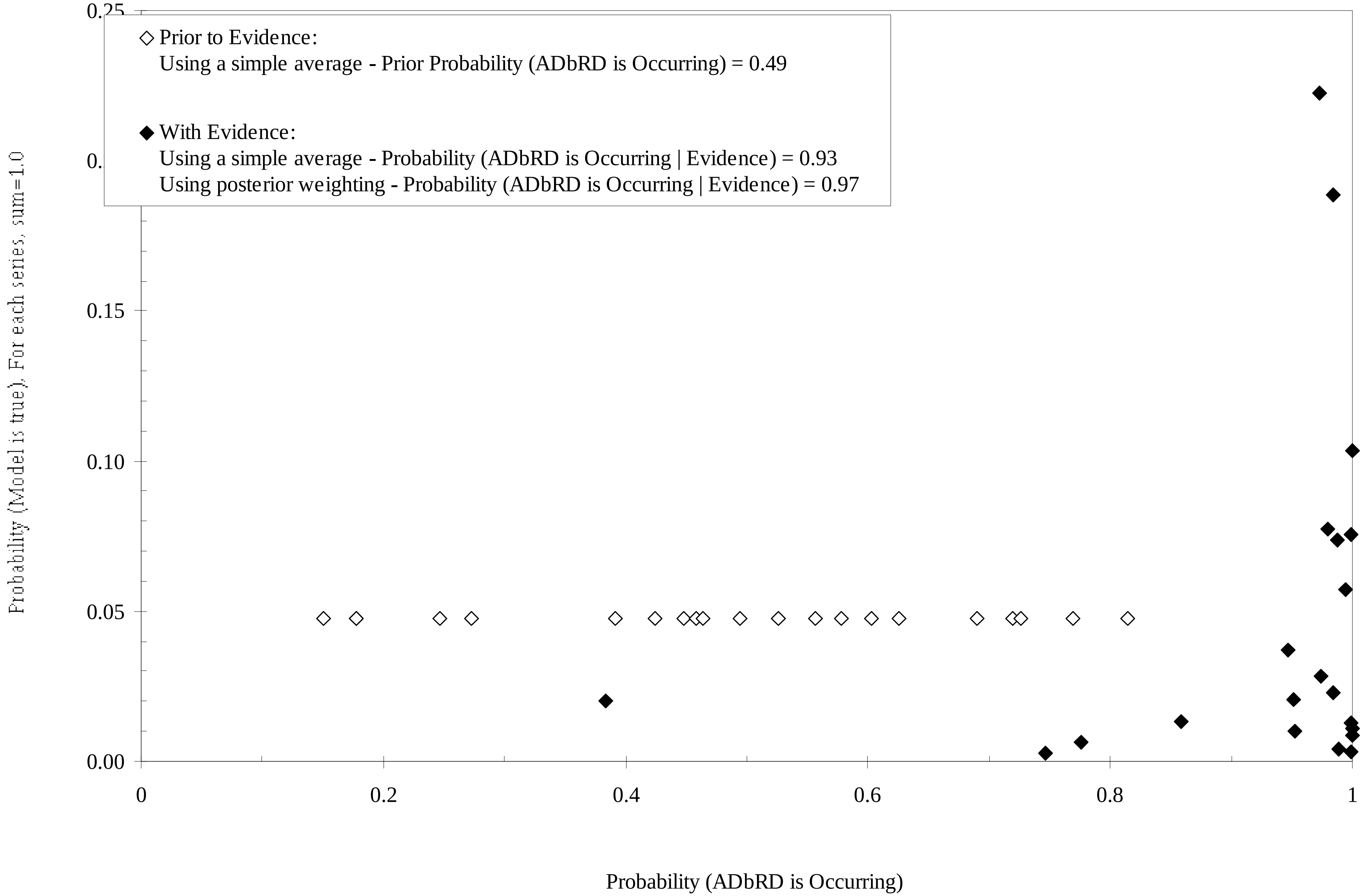
FIGURE 4. Importance of different findings for three expert models and the average model. Measured by ΔLOR(P) = change in log (odds ratio) for probability (anaerobic degradation by reductive dechlorination is occurring).

Impact of Positive, Negative, and Mixed Evidence on Experts' Assessment of Prob(Reductive Dechlorination Occurring)



Aggregation of Multiple Experts

- Can multiple opinions be combined?
- How should multiple opinions be combined?
- Simple average
  - equitable and good performance
- Many methods of weighting and calibrating
- Bayesian approaches
  - compelling theoretical foundation
  - BBN allows aggregate posterior probability for each expert model (consistency with evidence)

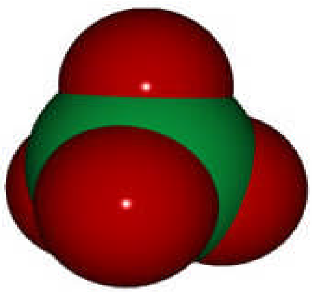

◇ Prior to Evidence:
Using a simple average - Prior Probability (ADbRD is Occurring) = 0.49
◆ With Evidence:
Using a simple average - Probability (ADbRD is Occurring | Evidence) = 0.93
Using posterior weighting - Probability (ADbRD is Occurring | Evidence) = 0.97
Probability (Model is true). For each series, sum=1.0
0.25
0.15
0.10
0.05
0.00
0
0.2
0.4
0.6
0.8
1
Probability (ADbRD is Occurring)

A BBN for Synthesizing Evidence Regarding the Carcinogenicity of Naphthalene to Humans (at non-cytotoxic concentrations)

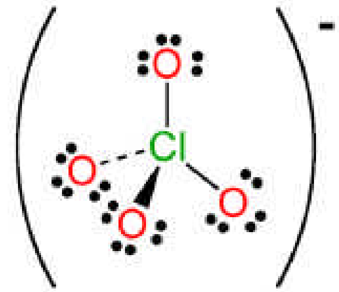
- Identify structure and determine conditional probabilities for, for example
  - false positive and false negative rates for key studies
  - Strength of relationship between animal and human results
- Develop as a consensus effort, or elicit conditional probabilities from multiple experts?

Bayesian Hierarchical Models

- Especially well suited for combining information from multiple studies:
  - Dose-response parameters from each study are sampled from a distribution (with hyperparameters that are also estimated) for all studies
    - **Bayesian Meta Analysis**
  - Dose-response parameters for a given animal model sampled from a distribution for all like animals
  - Within a study, dose-response parameters for one gender sampled from distribution for both genders

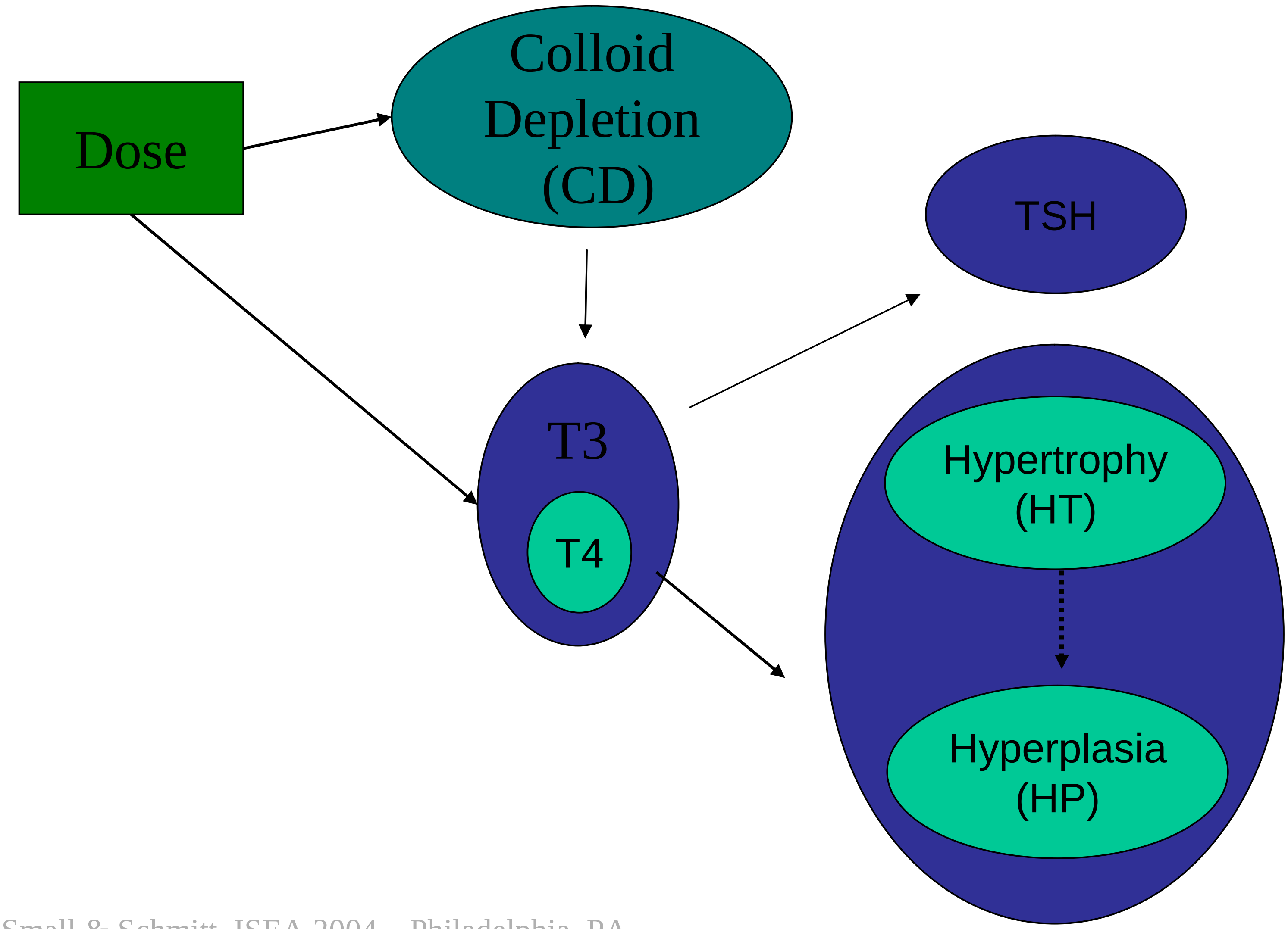


Chemical of Interest : Perchlorate Ion $[ClO_4]^-$

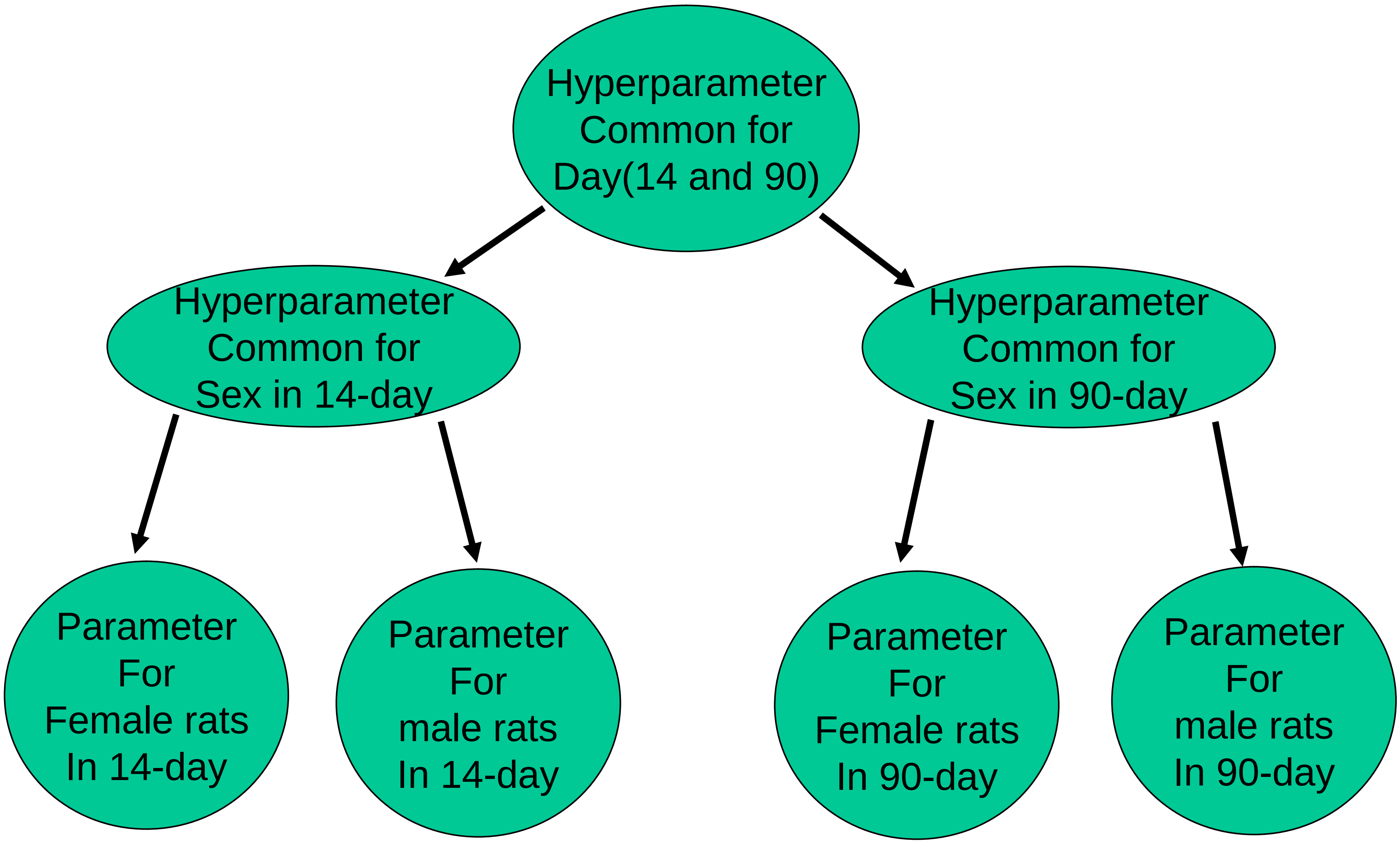


- Principal source
  - Ammonium Perchlorate
  - Rocket fuel booster
- Widespread reports of ground water contamination
- Future levels expected to increase

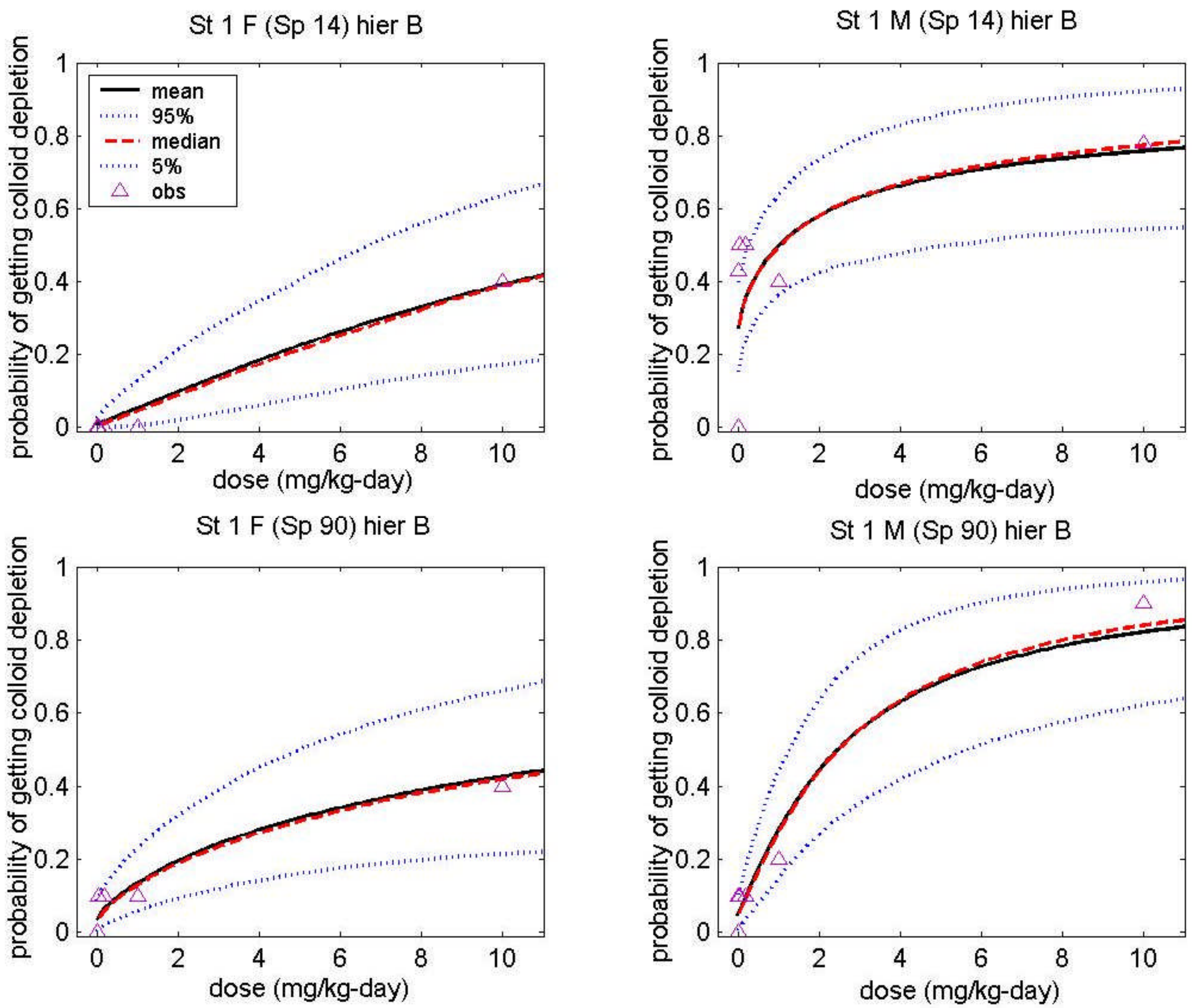
Model Structure - Mechanistic Model



Hierarchy for sex and time point (day)



Results – Step 1 (Hierarchical B)

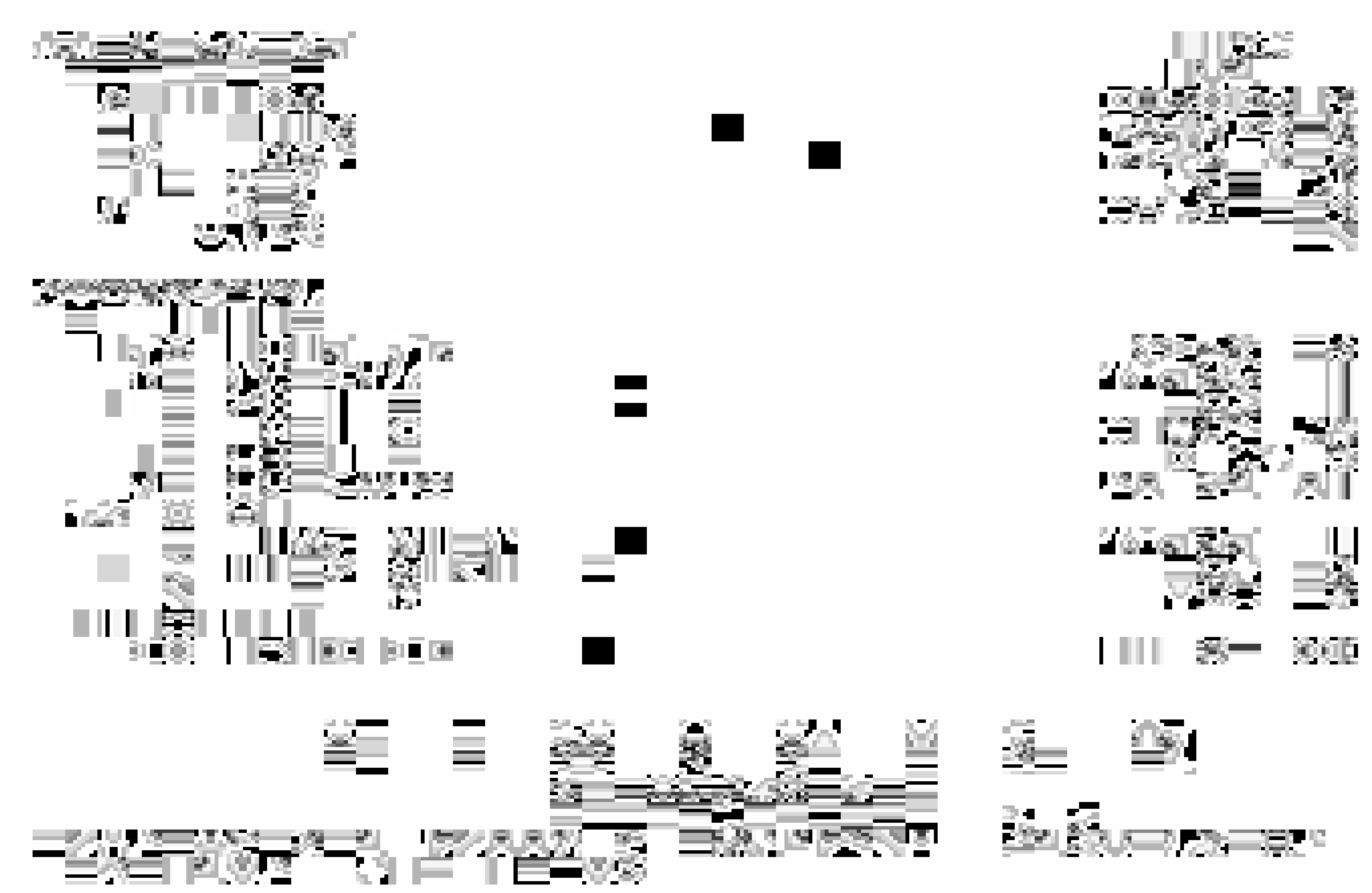


Example: DBP's and Reduced Birth Weight

Methods

Methods (Continued)

Results



Results (Continued)