

Development of Tools for Probabilistic Uncertainty Analysis in Environmental Risk Assessment of Chemicals

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Why Tools for Probabilistic Environmental Risk Assessment of Chemicals?

- In EU, current focus is on the *deterministic* Risk Quotient, TGD (2003) :
 - $RCR = PEC / PNEC$ (Risk Characterisation Ratio)
 - Decisions as to whether RCR is below 1, between 1 and 10, between 10 and 100, etc.
- To address *uncertainty* aspects of RCR, we have to apply *probabilistic* Risk Assessment
- REACH CSA Scoping doc: '*RCR is not a true measure of Risk*' (Traas and Aldenberg, 2005)

Tools: Methods & Software

- Methods
 1. Uncertainty/ Sensitivity Analysis of Models
 2. Data Analysis, Statistics
 3. Risk Analysis
- Software
 1. Crystal Ball, @Risk, SimLab, ...
 2. R/ S-PLUS, SAS, SPSS, Matlab, ...
 3. *Any of above, Analytica, ..., Busy*

Methods for Probabilistic Environmental Risk Assessment

- Uncertainty Analysis/ Distribution Fitting
 - Exposure Concentration Distribution (ECD)
 - Species Sensitivity Distribution (SSD)
- Risk Characterisation
 - Overlap Plots
 - Joint Probability Curves
 - Ecological Risk

Risk Characterisation: PDF Overlap Plot

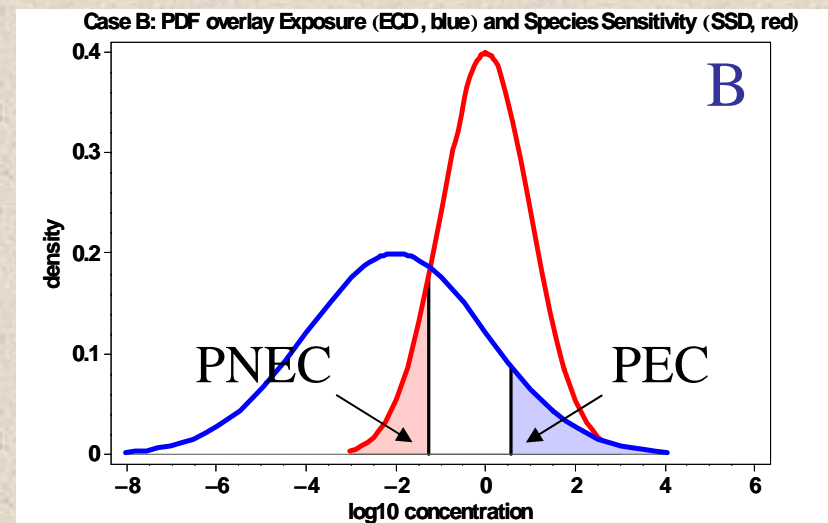
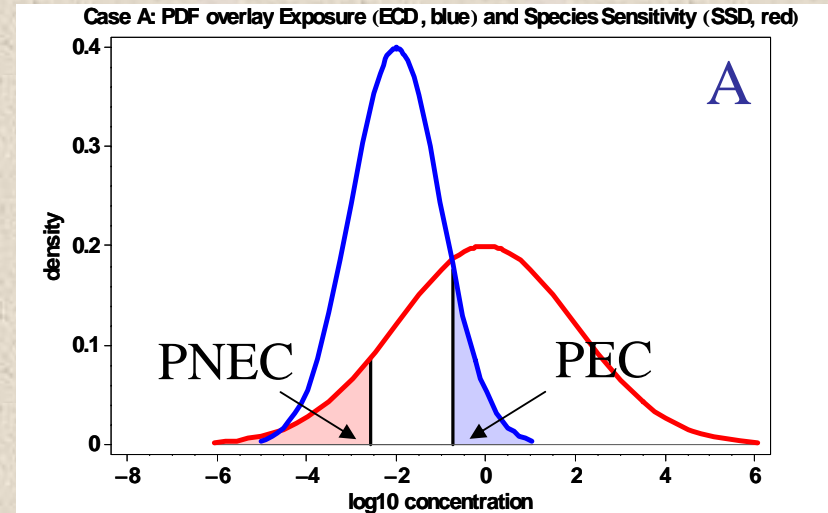
Exposure Concentration (*blue*) + Species Sensitivity (*red*)

PEC = 90th %-ile ECD

PNEC = 10th %-ile SSD

Illustrative example: *same* means, but standard deviations *interchanged*

- Case **A** (**wide** SSD)
 - ECD ~ Normal (-2, 1)
 - SSD ~ Normal (0, 2)
- Case **B** (**sharp** SSD)
 - ECD ~ Normal (-2, 2)
 - SSD ~ Normal (0, 1)



Deterministic Risk Quotient: $RQR = PEC/PNEC$

Exposure Concentration (*blue*) + Species Sensitivity (*red*)

$$RQR = PEC_{90}/PNEC_{10}$$

$$\log_{10}RQR = \log_{10}PEC_{90} - \log_{10}PNEC_{10}$$

- Case A:

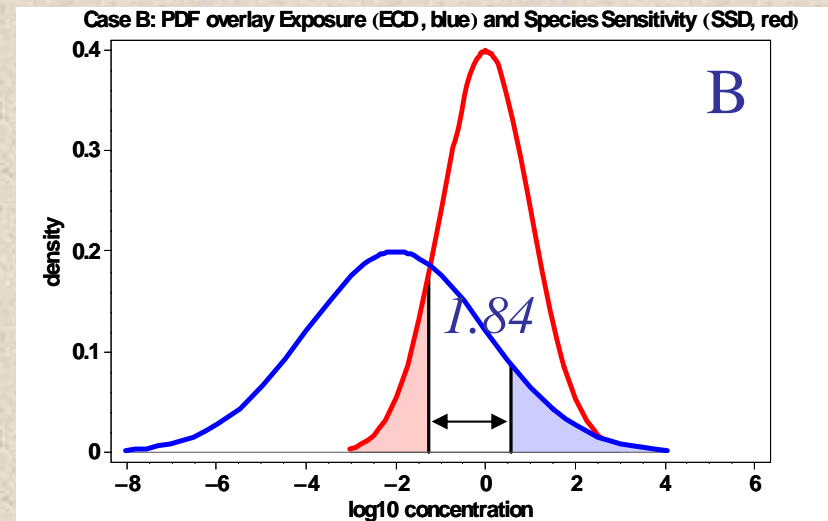
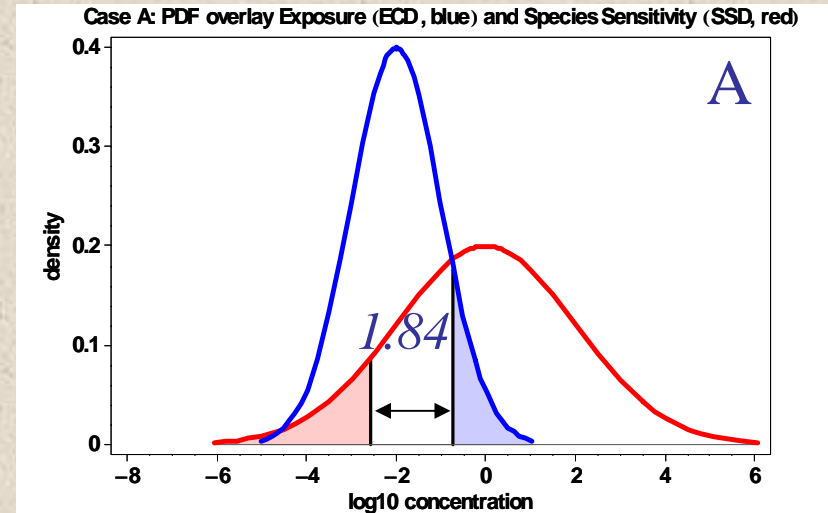
$$\log_{10}RQR = -0.72 - (-2.56) = 1.84$$

$$\rightarrow RQR = 70$$

- Case B:

$$\log_{10}RQR = +0.56 - (-1.28) = 1.84$$

$$\rightarrow RQR = 70$$



Probabilistic Risk Quotient

Aldenberg et al. (2002), Verdonck et al. (2003)

Deterministic Risk Quotient employs percentiles:

$$\text{RCR} = \text{PEC}_{90} / \text{PNEC}_{10}, \text{ so:}$$

$$\log_{10} \text{RCR} = \log_{10} \text{PEC}_{90} - \log_{10} \text{PNEC}_{10}$$

Now consider the *Probabilistic Risk Quotient*, or log difference between *Exposure Concentration* and *Species Sensitivity*. Since both are Normal, the difference is Normal:

$$\log_{10} EC - \log_{10} SS \sim \text{Normal}(\mu_{\text{ECD}} - \mu_{\text{SSD}}, \sqrt{\sigma_{\text{ECD}}^2 + \sigma_{\text{SSD}}^2})$$

Probabilistic Risk Quotient:

$$\log_{10}RCR = \log_{10}EC - \log_{10}SS > 0 ?$$

- Case A

$$\log_{10}RCR \sim$$

$$\text{Normal}(-2, (1+4)^{1/2})$$

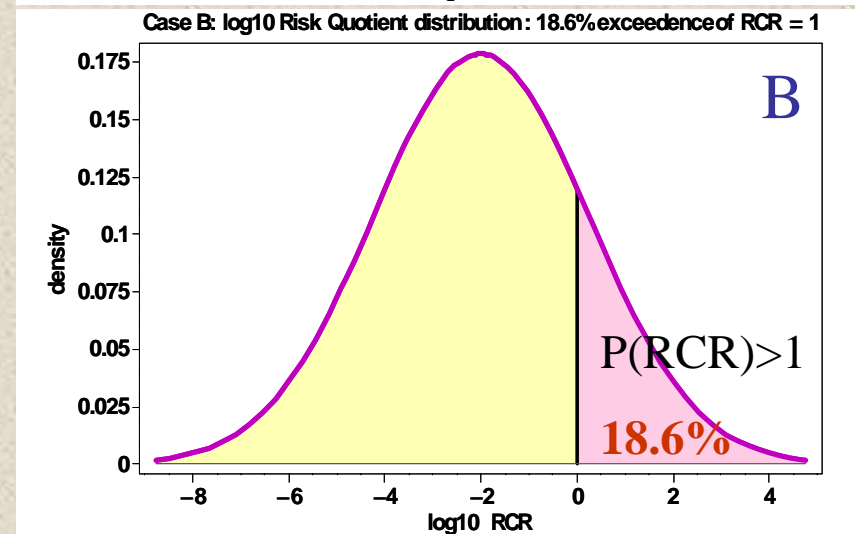
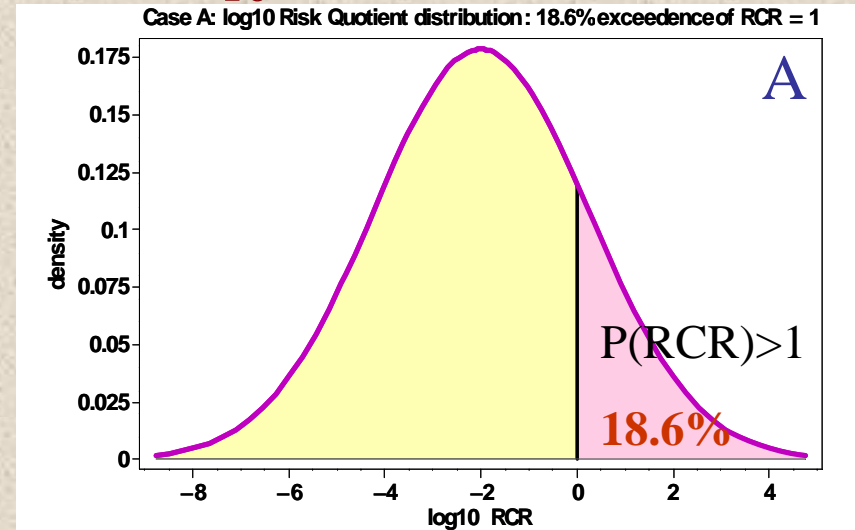
Exceeds 0 (RCR = 1) by **18.6%**

- Case B

$$\log_{10}RCR \sim$$

$$\text{Normal}(-2, (4+1)^{1/2})$$

Exceeds 0 (RCR = 1) by **18.6%**



Van Straalen Ecological Risk Overlap Plot

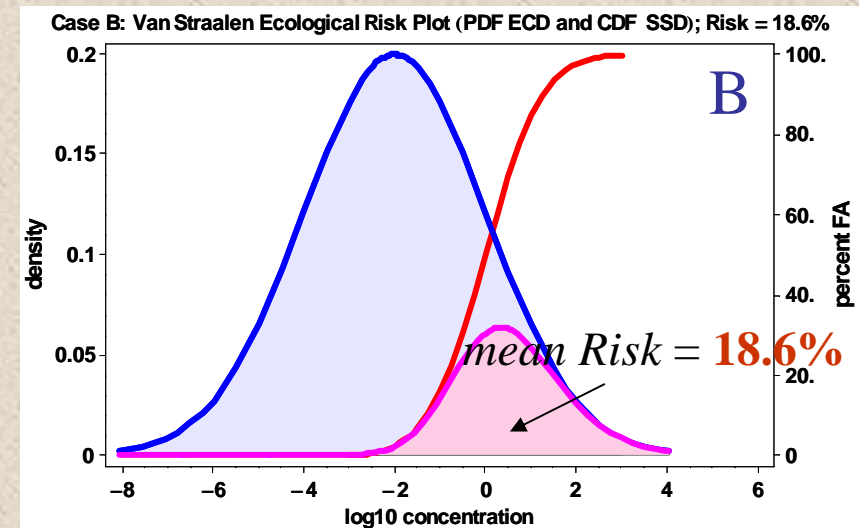
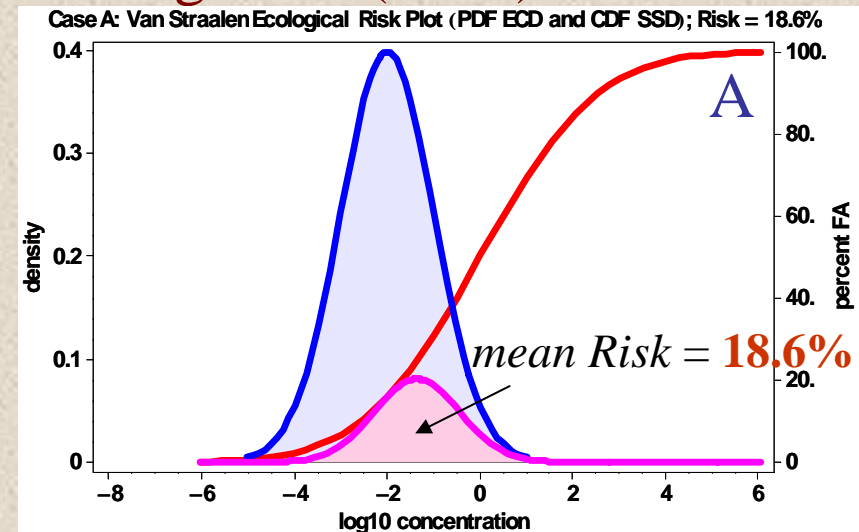
Van Straalen (2002), Aldenberg *et al.* (2002)

ECD PDF and SSD CDF scaled to the max of the ECD PDF

PDF and CDF are multiplied to get reduced PDF ('hump')

Ecological Risk is AUC of the product hump (*mean Risk*)

- Case A
 - AUC = **18.6%**
- Case B
 - AUC = **18.6%**



Risk Quotient and Mean (Ecological) Risk are not sufficient

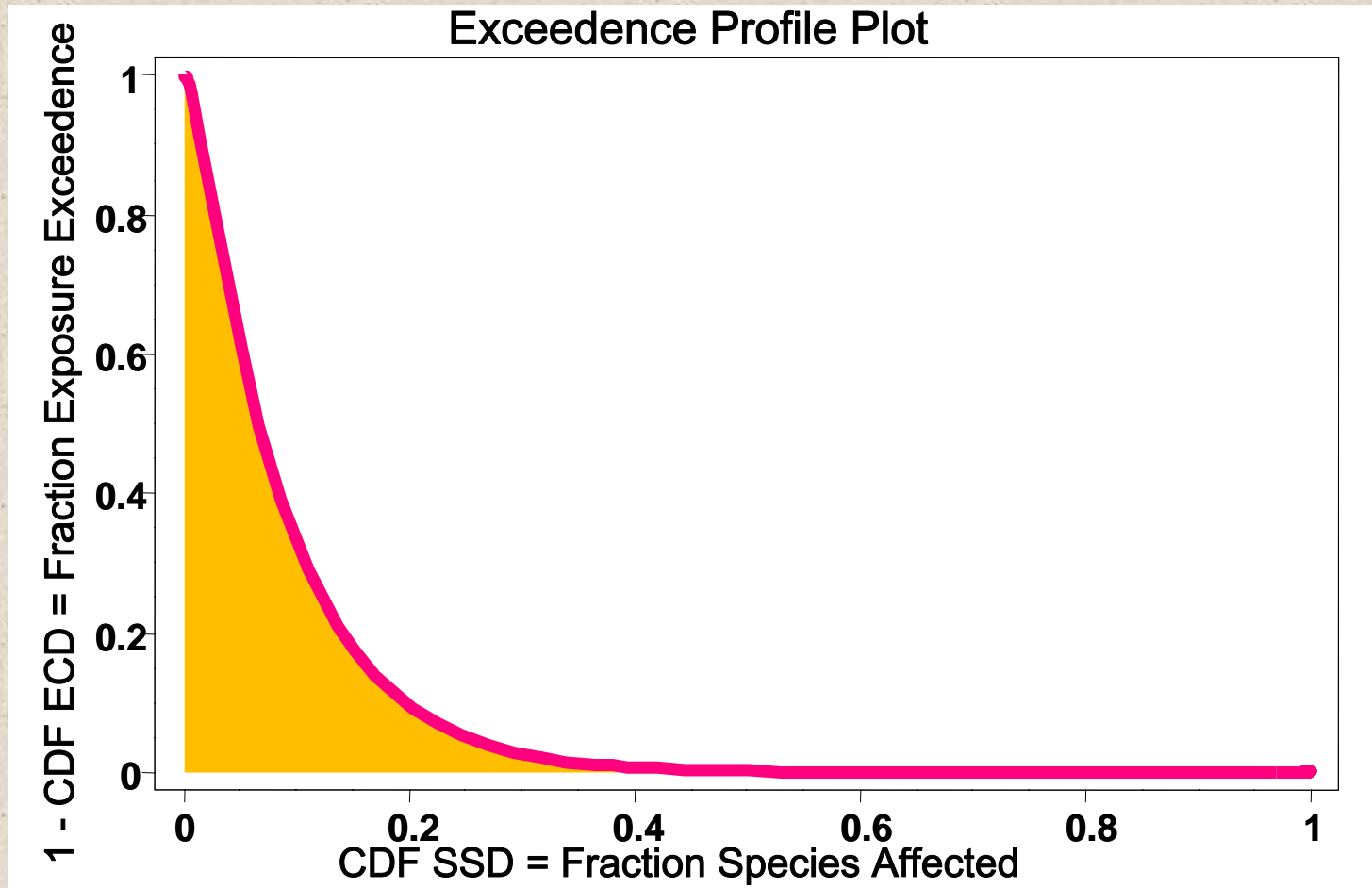
- Apparently the Risk Quotient, or RCR: Risk Characterisation Ratio, is *not sufficiently informative* to distinguish between Cases **A** and **B**
- The deterministic RCRs (**70**) are the same
- The probabilistic RCR distributions are identical, as are the exceedence probabilities of $\text{RCR} = 1$ (**18.6%**)
- The Van Straalen Mean Ecological Risk AUCs are the same too (**18.6%**)

Beyond Risk Quotient and Ecological Risk: Joint Probability Curves (JPCs)

- Are we stuck? No, we are not
- The solution is Joint Probability Curves (JPCs)
- There are 3 types of JPC:
 - Type 1: **Exceedence Profile Plot (EPP)**
 - Giesy et al. (1999), Solomon & Takacs (2002)
 - Type 2: **Cumulative Profile Plot (CPP)**
 - Aldenberg et al. (2002), Verdonck et al. (2003), ETX (2005)
 - Type 3: **Risk Distribution CDF Plot (RDCDF)**
 - Aldenberg (2007a,b), *Busy* (2007), EUFRAM (2007)
- These basically convey *the same information*, but Type 3 leads to the **Risk Distribution PDF** proper

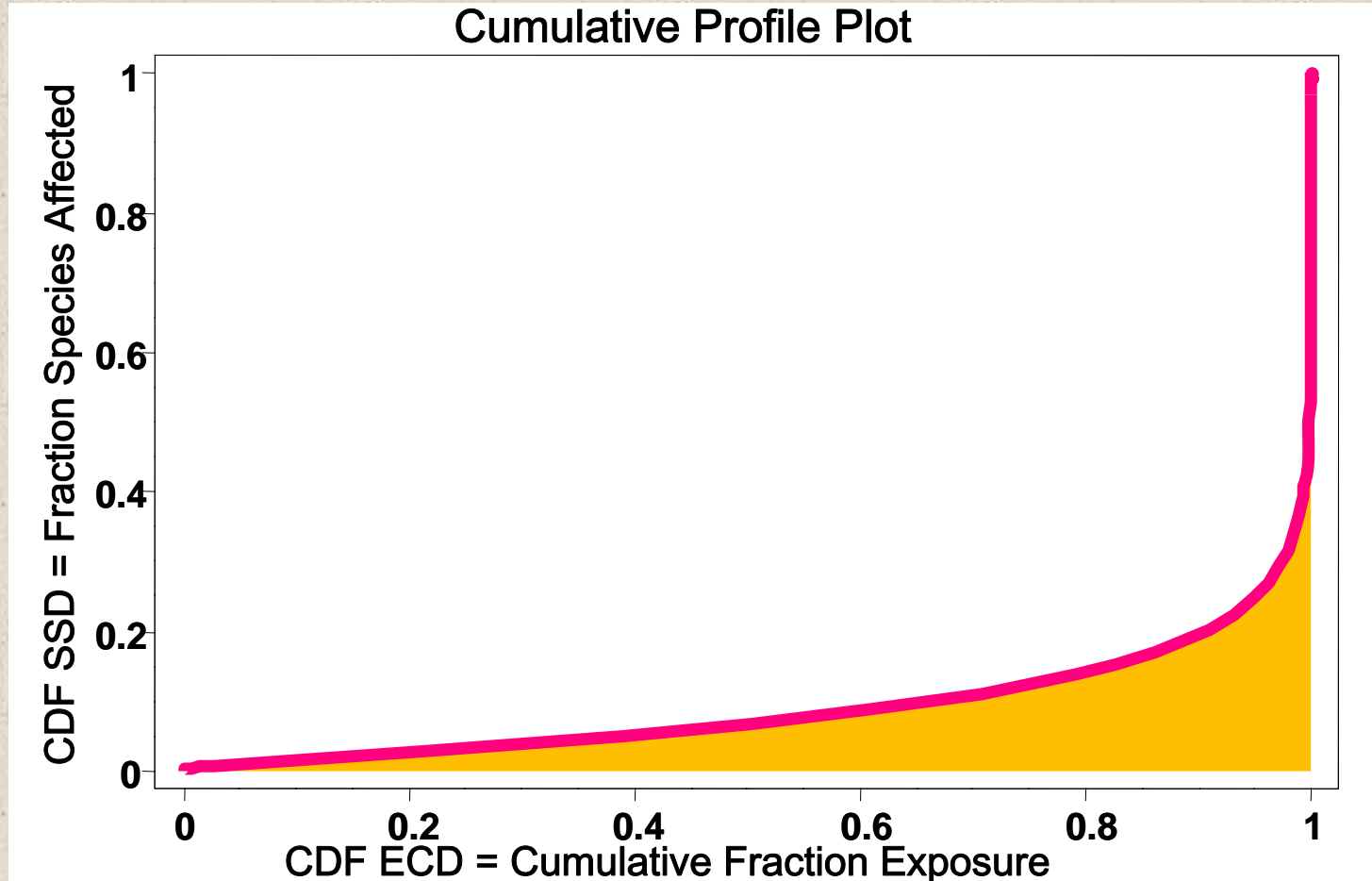
JPC Type 1: Exceedence Profile Plot (EPP)

Giesy et al. (1999), Solomon & Takacs (2002)



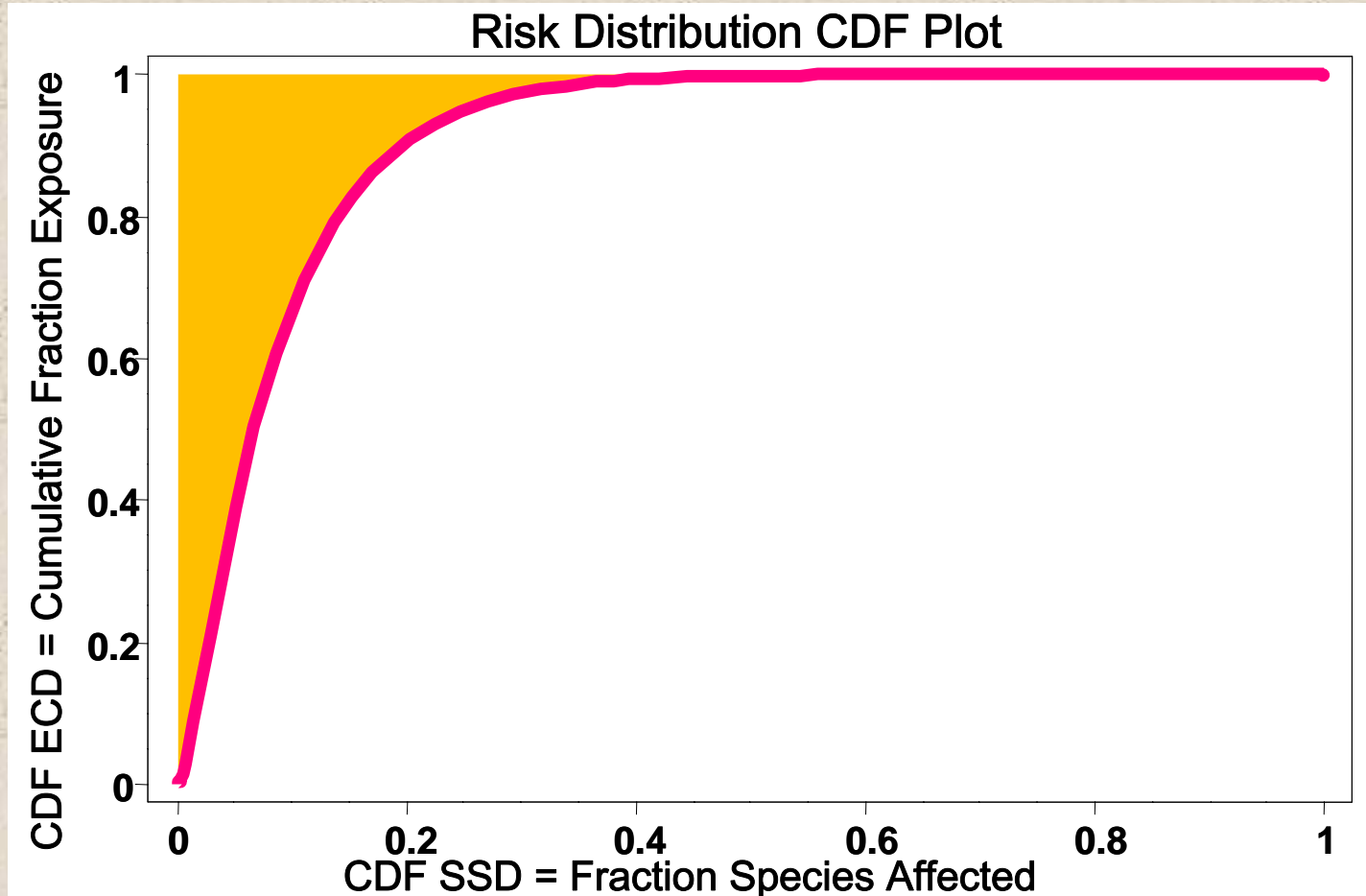
JPC Type 2: Cumulative Profile Plot (CPP)

Aldenberg et al. (2002), Verdonck *et al.* (2003), *E_TX* (2005)



JPC Type 3: Risk Distribution CDF Plot (RDCDF)

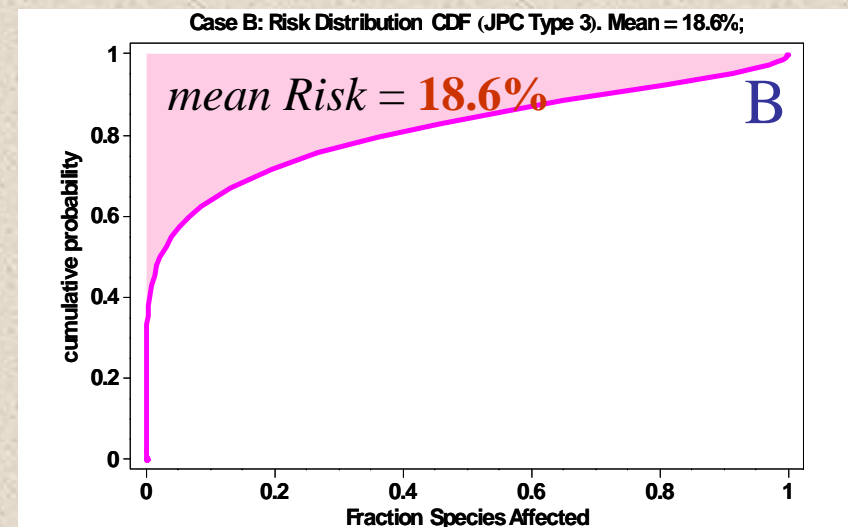
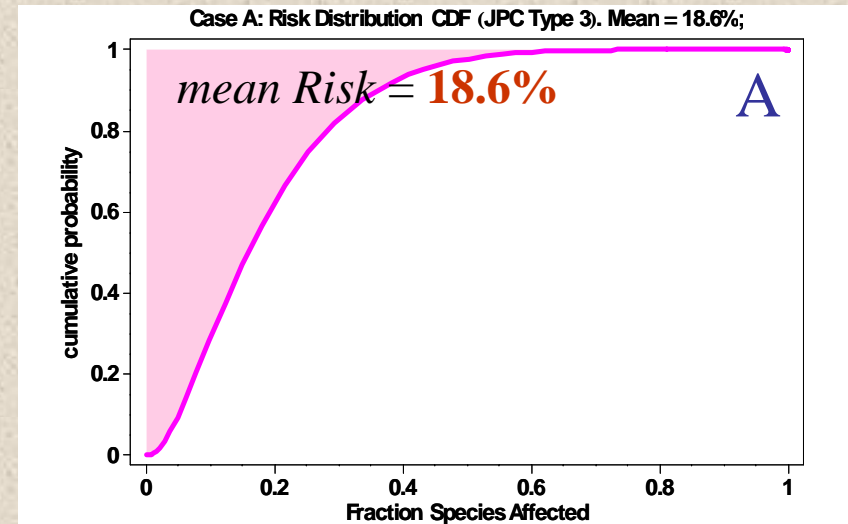
Aldenberg (2007a,b), *Busy* (2007), EUFRAM (2007)



JPC Type 3 Risk Distribution CDF (RDCDF)

Aldenberg (2007a,b), *Busy* (2007), EUFRAM (2007)

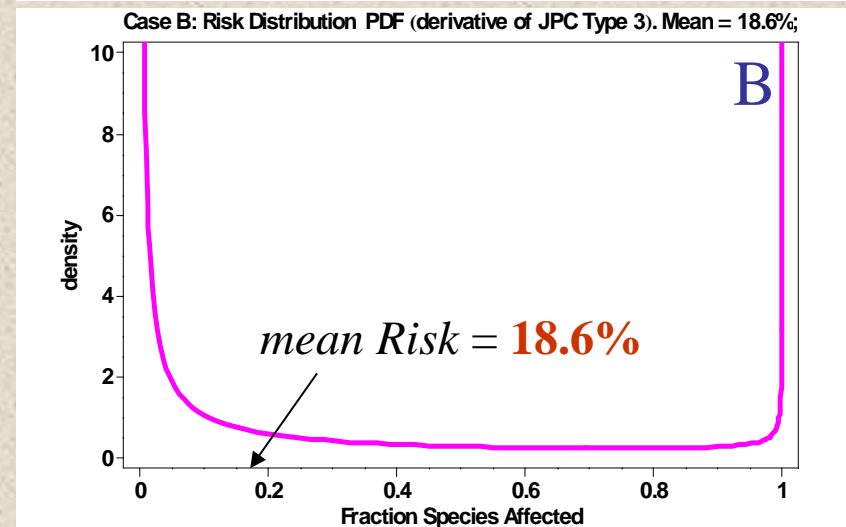
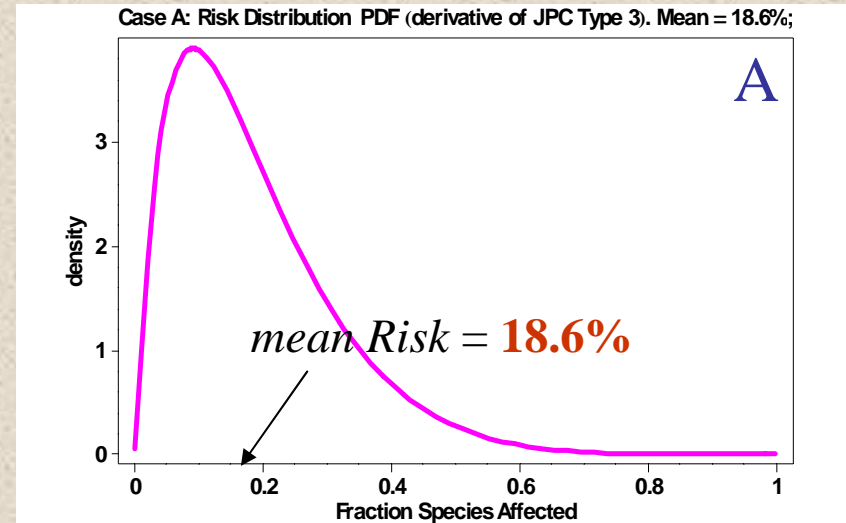
- The Type 3 JPC is the Exposure CDF plotted against the Toxicity CDF for the same concentrations
- The **upper** AUC is the *mean (Ecological) Risk*, or *mean Fraction Affected* (shaded).
 - Case A: **18.6%**
 - Case B: **18.6%**
- However, Risk Distribution CDFs are *different!*



Risk Distribution PDF is *derivative* of RDCDF

Aldenberg (2007a,b), *Busy* (2007)

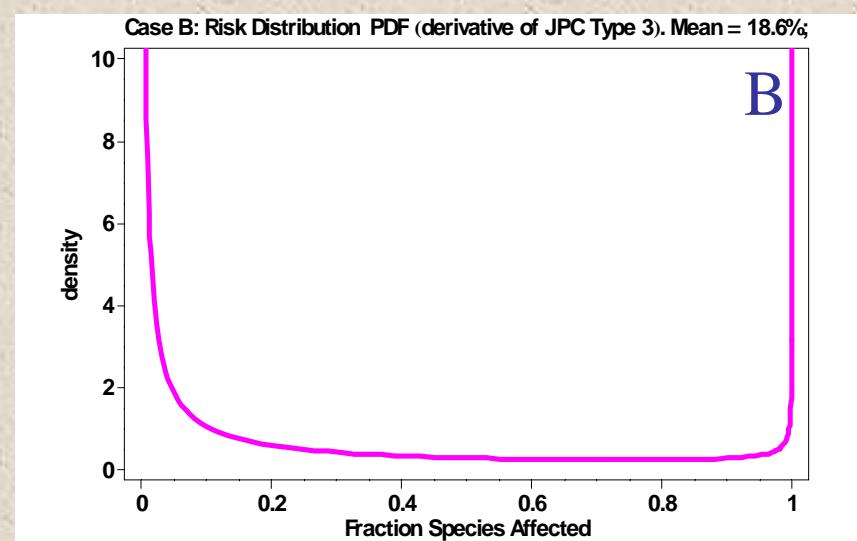
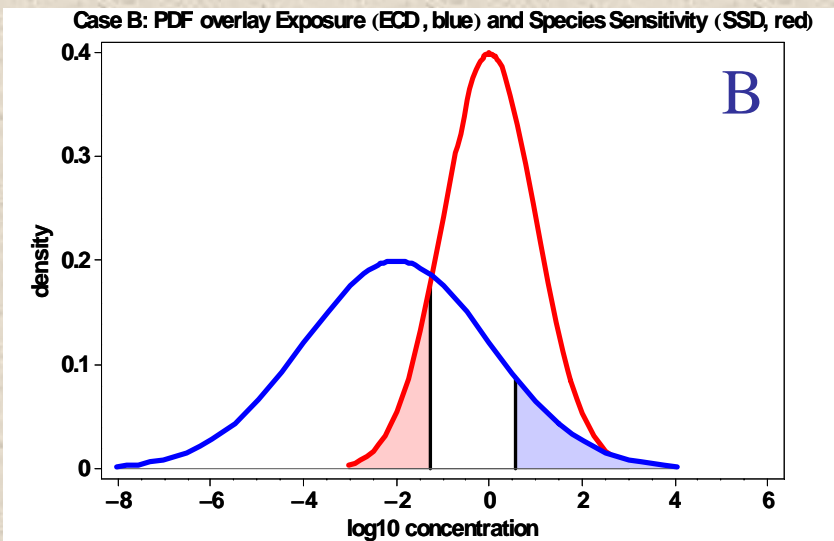
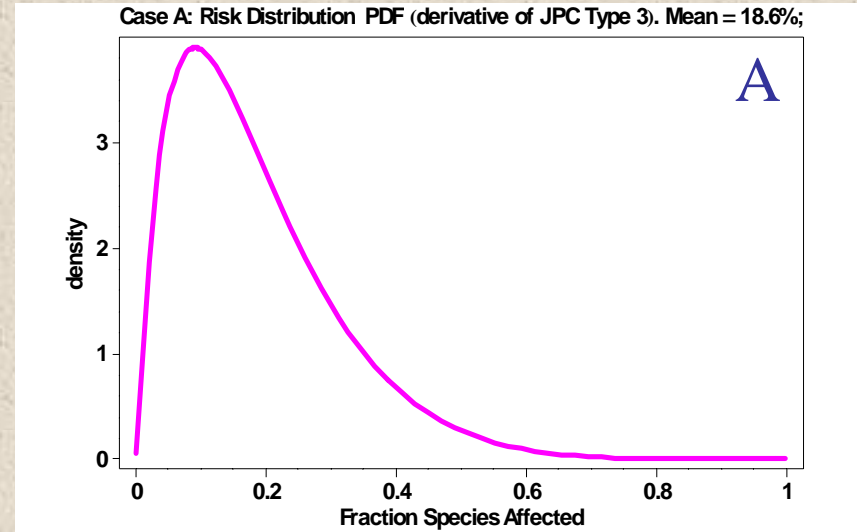
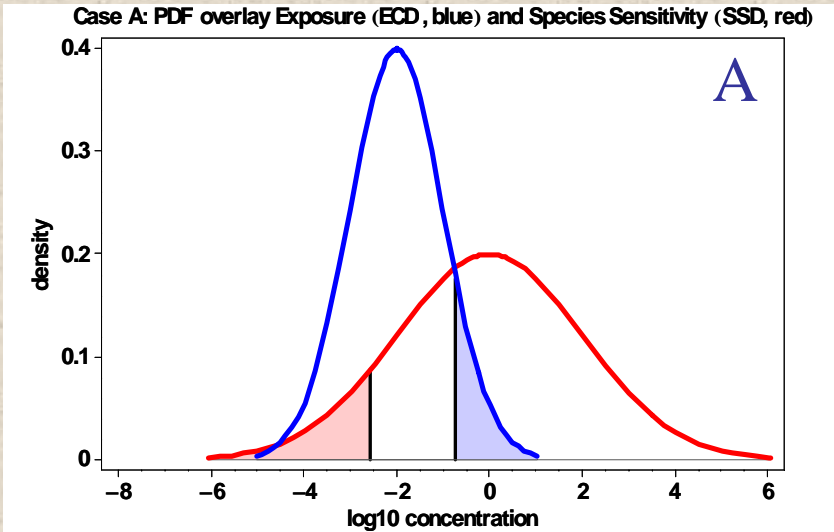
- The Risk Distribution PDF is the *derivative of RDCDF* (maths in *Busy*, 2007)
- Risk Distribution PDF over Fraction Affected *differs*:
 - Case A: PDF *Unimodal*
 - Case B: PDF *Bimodal*, with *asymptotes* at FA = 0 and 1
- Expected Risk, i.e. the *mean* of the *Fraction Affected Distribution* (FAD), is **18.6%** in both cases A and B
- However, Risk Distributions differ substantially



Cases A and B Revisited

PDF Overlap Plot + \log_{10} RCR

Risk Distribution PDF Plot



Software: *Busy* 1.1a

- *Busy* 1.1a (Bayesian Uncertainty System) is a software package running under Mathematica[®] 5.2
- *Busy* 1.1a available through:
 - Mail busymath@gmail.com
 - Web <http://busymath.googlepages.com>
- Currently, you *need* Mathematica to run it
 - Trial version (15 days) at Website Wolfram Research <http://wolfram.com/products/mathematica/trial.cgi>

Busy 1.1a User Interface

- User interface: Mathematica[®] Notebooks
 - Advanced Technical Documents
 - Manual, Guides, Toolboxes, and Templates
- Excel Link[®] for Mathematica
- Under development: *web*Mathematica[®] version to run *Busy* over the web
 - Provider hosting *web*Mathematica
 - Java Server Pages

Busy Notebook Interface

- Mathematica[®] Notebooks are technical documents divided into ‘cells’
- Cells may contain:
 - Input statements
 - Numerical output
 - Graphics
 - Explanatory text, with Greek and maths symbols
- See: flexible SSD fit for a pesticide (insect species)

BusySheet [SSD=Pesticide n=23] 10a57.nb *

Input

Our flexible kernel fit for this pesticide shows a quite well behaved distribution. There does not seem any heterogeneity (multi-modal shape) in the data. The unit is log₁₀ gram Active Substance per hectare.

```
In[102]= dens = pdfDataPlot[LogDens, {"Pesticide n = 23, PDF Plot and Histogram",  
"log10 gAS per ha", "Density"}];
```

Pesticiden = 23, PDF Plot and Histogram

So, we feel confident to overlay the histogram, the data dotPlot for the pesticide, and the flexible kernel fit. Note that we colored the two key species with a cyan color to stand out. They do not seem to take a special position in the Species Sensitivity Distribution (SSD):

```
In[103]= Show[dens, hist2, dens, dat2, Background -> tonePastel[penYellow]];
```

Pesticide n = 23, PDF Plot and Histogram

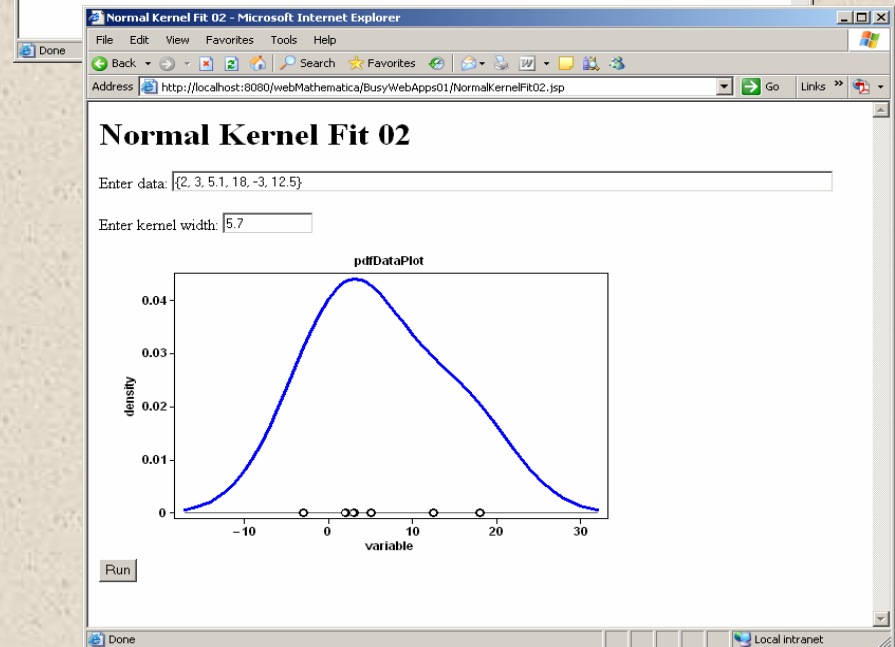
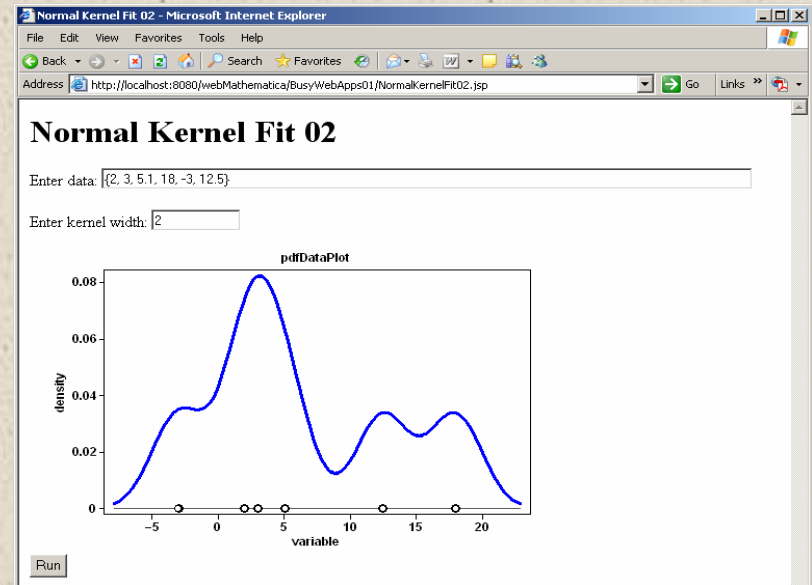
We might as well try the ordinary Gaussian (normal) distribution. Let's first see what the normal quantile fit looks like:

```
In[104]= normalQuantilePlotQuartileFit[LogData, Label];
```

normalQuantilePlotQuartileFit

web-based *Busy* experiment

- webMathematica[®] allows browser-based web applications
- Example: Normal Kernel Density fit on a small sample of points, running through MS Internet Explorer[®]

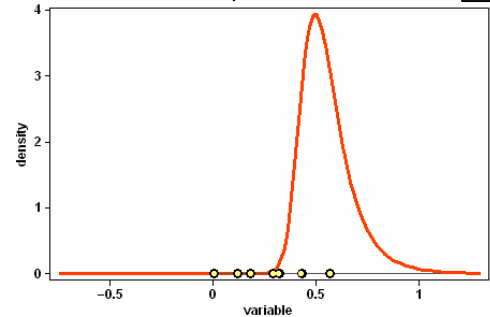
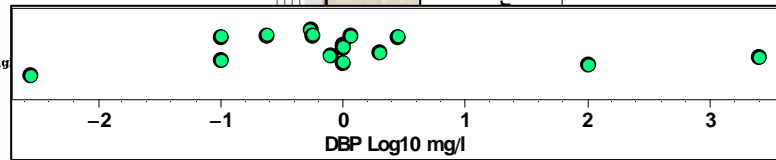
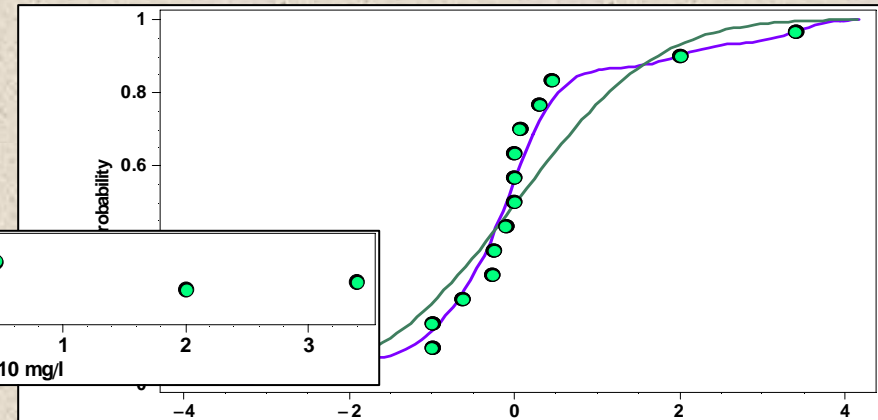


Busy Graphics Gallery (1)

```

BusyRefMan [Normal Reference Uncertainty] 10a50.nb *
Output
In[62]:= quantref90 = referenceQuantilePDistribution[normdat, 0.90]
Out[62]:= aNoncentralTLocationScaleDistribution-
In[63]:= setPlotRangeVar[quantref90, plims]
Out[63]:= {-0.744236, 1.29138}
In[64]:= setPlotLineColor[quantref90, penRedOrange]
Out[64]:= Hue[0.0416667]
In[65]:= setPlotSymbolFillColor[variableData[quantref90], penYellowLight]
Out[65]:= Hue[0.166667, 0.5, 1.]
In[66]:= pquantref90 = pdfDataPlot[quantref90, ""];

```



```

In[221]:= log10HC5 = quantile[toxNormalLog10, 0.05]
Out[221]:= -2.16653
In[222]:= log10HC5Kernel = quantile[toxNormalKernelLog10, 0.05]
Out[222]:= -2.31338

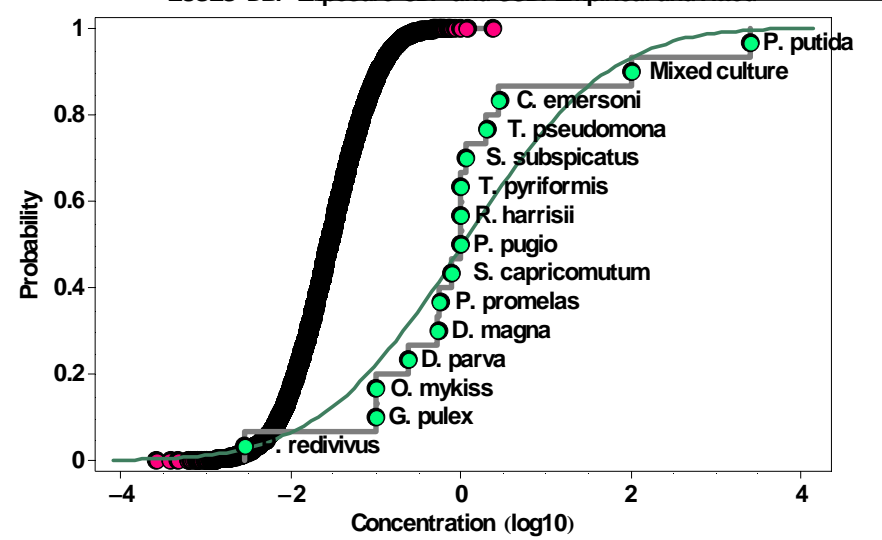
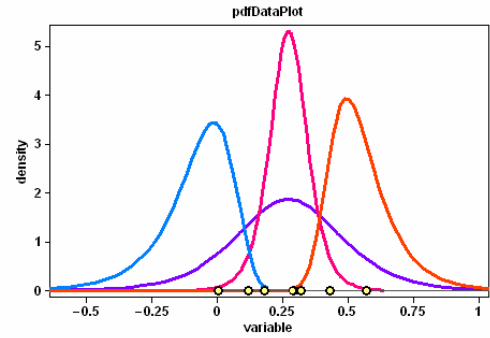
```

EUSES DBP E

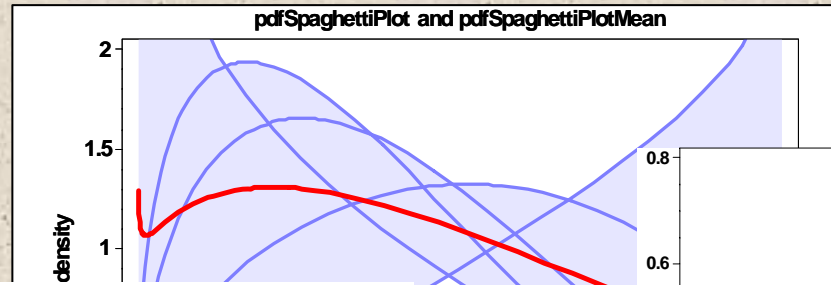
```

In[67]:= displayRange[{ppredref, pmuref, pquantref5, pquantref90}, {-0.6, 1.}];

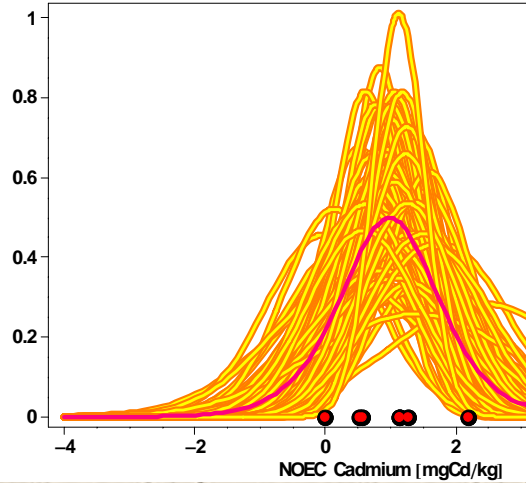
```



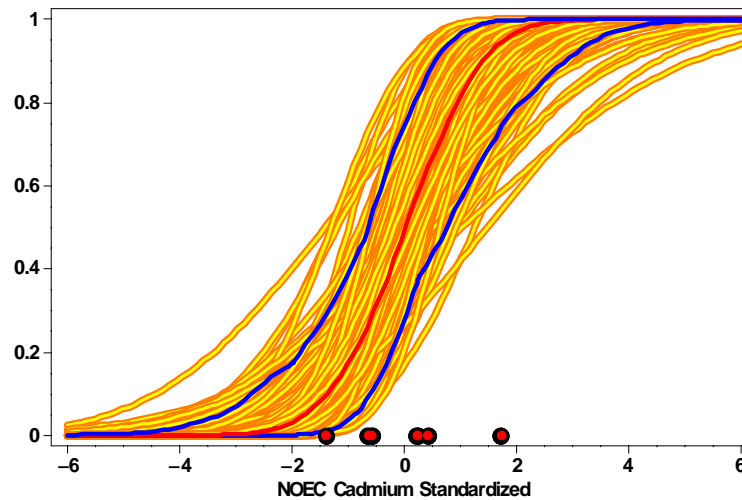
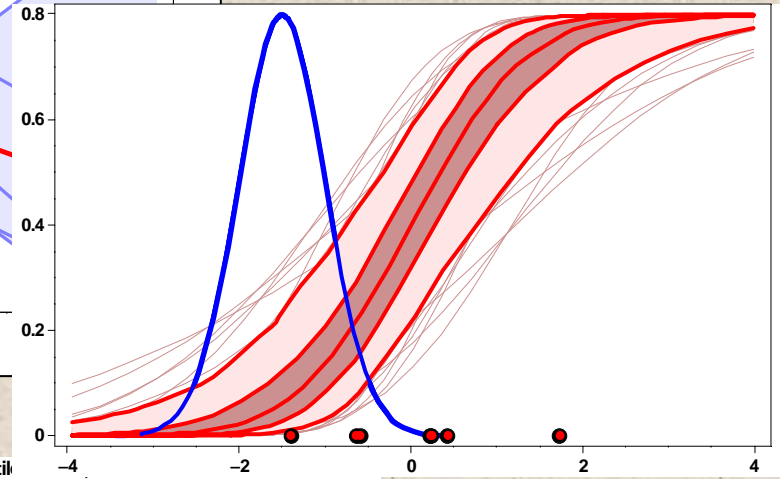
Busy Graphics Gallery (2)



SpaghettiPlot, n = 7



0.6
variable
Spaghetti Plot Percentil



References (1)

- Aldenberg, T. (2007a). Fractional Distributions in Risk Analysis. *Busy 1.1a* Reference Manual Appendix 2. Web <http://busymath.googlepages.com>
- Aldenberg, T. (2007b). Probabilistic Environmental Risk Assessment (PERA) through Second-Order Bayesian Normal Distributions and Fractional Risk Distributions. In: *Review of the State of the Science for Conducting Uncertainty Analysis in Ecological Risk Assessment*. (W.J. Warren-Hicks, D.R.J. Moore, and T. Aldenberg). Prepared for ACC.
- Aldenberg, T., and J.S. Jaworska (2000). Uncertainty of the hazardous concentration and fraction affected for normal species sensitivity distributions. *Ecotox. Environm. Safety*, **46**, 1–18.
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- ECOFRAM (1999). Report of the Aquatic Work group. Washington, D.C.: U.S. EPA, Office of Pesticide Programs.

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- Solomon, K.R., and P. Takacs (2002). Probabilistic risk assessment using species sensitivity distributions. In: *Species Sensitivity Distributions in Ecotoxicology* (L. Posthuma, G.W. Suter II, and T.P. Traas, eds.), Lewis Publishers, pp. 285–313.

References (3)

- TGD (2003). Technical Guidance Document on Risk Assessment. European Commission, Joint Research Centre, EUR 20418 EN/2.
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- Verdonck, F.A.M., T. Aldenberg, J. Jaworska, and P.A. Vanrolleghem (2003). Limitations of current risk characterization methods in probabilistic environmental risk assessment. *Env. Tox. & Chem.*, **22**, 2209–2213.
- Warren-Hicks, W.J., D.R.J. Moore, and T. Aldenberg (2007). Review of the State of the Science for Conducting Uncertainty Analysis in Ecological Risk Assessment. Prepared for the American Chemistry Council, in prep.