

# Probabilistic Reverse dosimetry Estimating Exposure Distribution

PROCEED

Version 1.0

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This Server-Side application (SSA), PROcEED v1.0, is a tool for performing two types of reverse dosimetry calculations. It is accessible through Firefox/Mozilla and Internet Explorer web-browsers upon successful installation on a server running Apache Tomcat, an open-access package available under the GNU public license. All calculations completed through the use of this tool are the responsibility of the respective end-users/modelers and are in no way endorsed by the authors or distributors of this application. The web-package provided (i.e., PROcEED.war) may be modified by the end-user under the condition that the original authors and source of this code be added as comments/references to the code (see citations below).

Output generated by the code may be used in public or private communications and publications, for personal, research or business related purposes provided that the accompanying citation is clearly added to the generated images/animations.

Georgopoulos P.G., Sasso A.F., Isukapalli S.S., Liroy P.J., Vallero D.A., Okino M., Reiter L. 2009.

Reconstructing population exposures to environmental chemicals from biomarkers: challenges and opportunities. *J Expo Sci Environ Epidemiol*,19: 149-171.

Tan Y.-M., Liao K.H., Conolly R.B., Blount B.C., Mason A.M., Clewell H.J. 2006. Use of a physiologically based pharmacokinetic model to identify exposures consistent with human biomonitoring data for chloroform. *J Toxicol Environ Health, Part A* 69: 1727-1756.

Tan Y.-M., Liao K.H., Clewell H.J. 2007. Reverse dosimetry: interpreting trihalomethanes biomonitoring data using physiologically based pharmacokinetic modeling. *J Expo Sci Environ Epidemiol*, 17: 591-603.

## Installation Requirements and Instructions for PROCEED Server-Side Application

### **User Requirements:**

- Understanding of basic commands, including but not limited to starting a web-daemon, and root access for installation.

### **Computer requirements:**

- Windows or Linux operating system (Installation instructions for windows included. For Linux installation, please discuss with the system administrator)
- Apache Tomcat web server available at <http://tomcat.apache.org> (preferably version 7... For new apache tomcat installations on Windows, the “32-bit/64-bit Windows Service Installer” is recommended)
- Internet Explorer or Mozilla Firefox web browser

### **Files:**

- PROCEED.war

### **Instructions:**

- Locate your apache tomcat folder (standard windows installation is at “C:\Program Files (x86)\Apache Software Foundation\Tomcat 7.0”)
- Place PROCEED.war in the “webapps” folder of your apache tomcat installation
- Restart the apache tomcat server (This can be done at Control Panel > System and Security > Administrative Tools > Services > Apache Tomcat 7.0)
- Access the webpage using your web browser at <http://your.host.ip:port/PROCEED> where <http://your.host.ip:port> is defined based on you tomcat installation (standard installation is at <http://localhost:8080>).

## PROcEED Quickstart Guide

It is recommended that upon installation, the following examples are run to ensure proper function of the application and to become familiarize with required inputs and outputs. Additional help documentation is available from the home page or at <http://my.host.ip:port/PROcEED/generalHelp.action>.

PROcEED can do two types of reverse dosimetry calculations. Both should be tested. Sample files are available in Examples.zip located in the installation package. These files should be extracted to an accessible folder referred to throughout this guide as the “examples folder”

### **Discretized Bayesian Approach (DBA)**

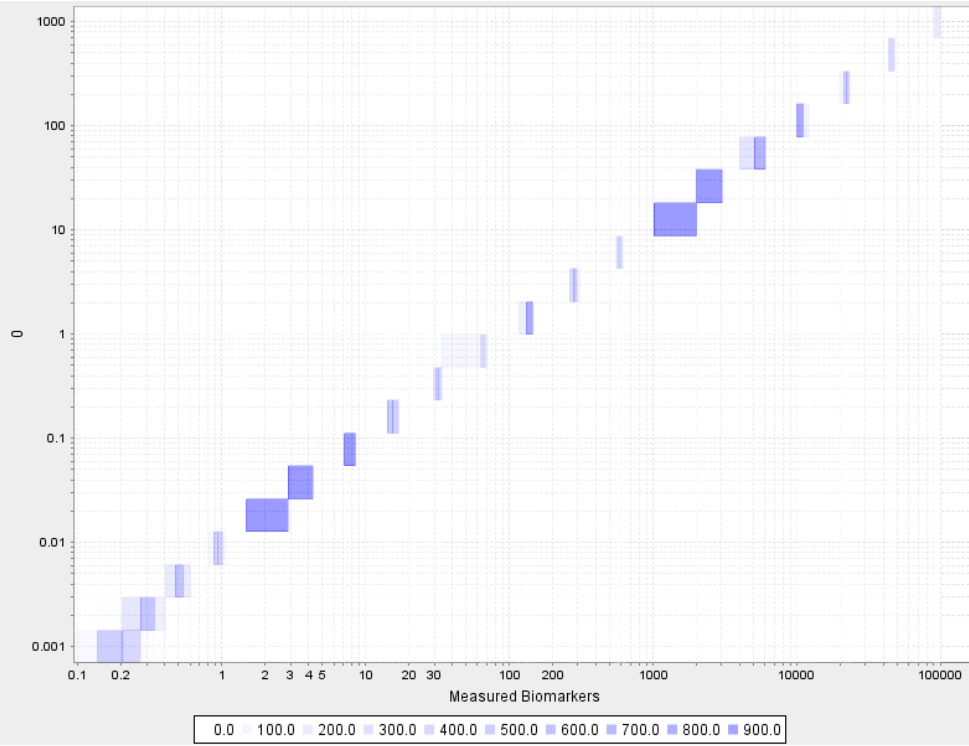
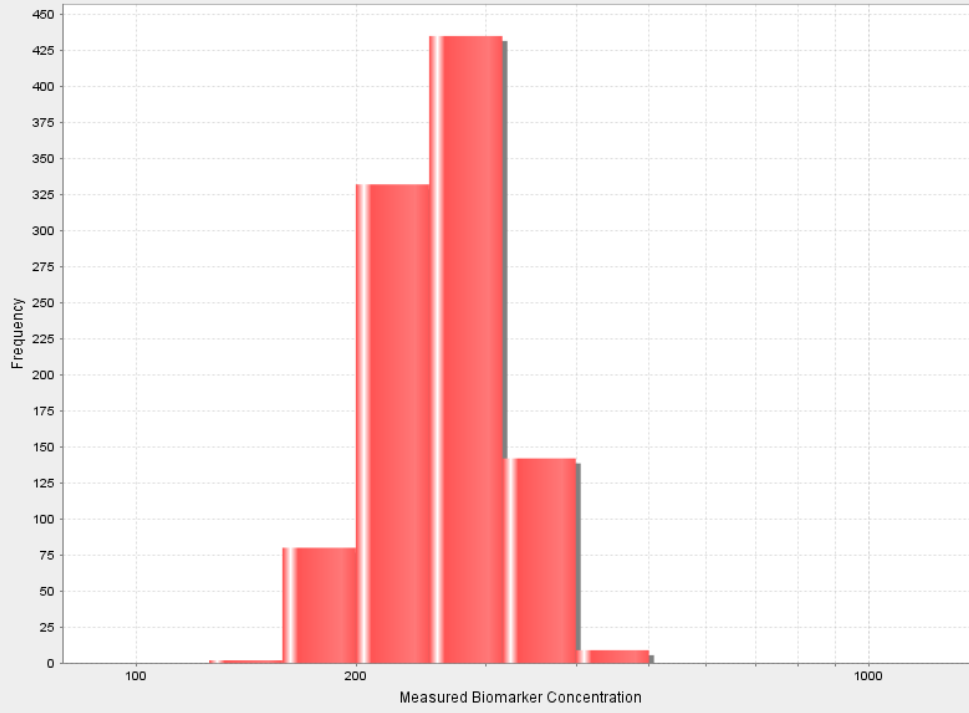
The first method to be applied is the discretized Bayesian approach. This approach requires at least two inputs: A dosimetry simulation file and a measured biomarker file. Further information on both of these files types is available in the help documentation.

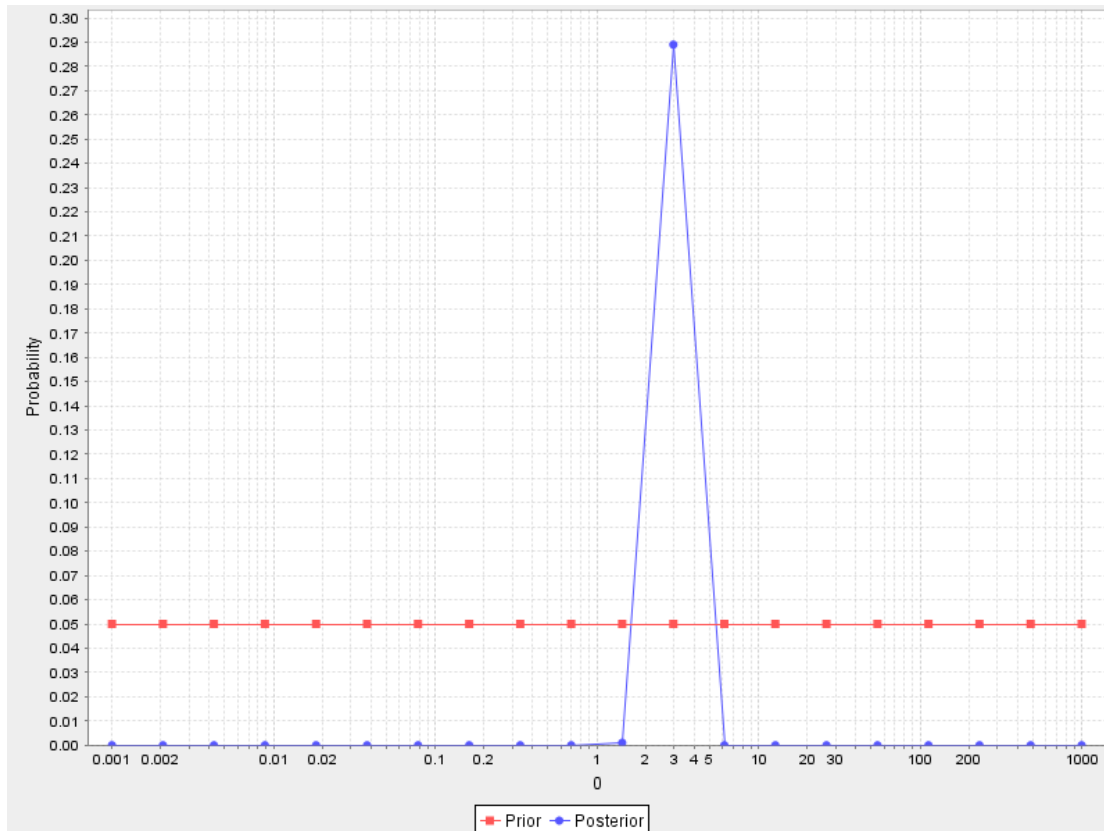
- 1) Access PROcEED at <http://my.host.ip:port/PROcEED>.
- 2) Choose Discretized Bayesian as the method.
- 3) For your Dosimetry Simulation File, select “dosimertyBinnedDBA.csv” from your examples folder.
- 4) Since this is a binned datafile, put a check in the appropriate checkbox.
- 5) For your Measured Biomarker File, select “biomarkerVector.csv” from your examples folder.
- 6) Submit

Upon submitting the form, PROcEED reads the biomarker data and the simulation file and summarizes them in the in the first two graphics below. It also assumes a uniform prior and estimates the probability distribution for the various exposures that may have occurred to exhibit the experimentally measured biomarker data. This distribution is shown in the third graph.

Your results from the steps above should match the graphics shown. Additional files are contained in the

**Biomarker Histogram**





## Exposure Conversion Factors (ECF)

The second method to be applied is the exposure conversion factor approach. This approach requires at exactly two inputs: A dosimetry simulation file and a measured biomarker file. Further information on both of these files types is available in the help documentation.

- 1) Access PROcEED at <http://my.host.ip:port/PROcEED>.
- 2) Choose Exposure Conversion Factors as the method.
- 3) For your Dosimetry Simulation File, select “dosimetryUnbinnedECF.csv” from your examples folder.
- 4) For your Measured Biomarker File, select “biomarkerVector.csv” from your examples folder.
- 5) Submit

Upon submitting the form, PROcEED reads the biomarker data and the simulation file. From the simulations file, it calculates exposure conversion factors and then samples the set of conversion factors/biomarker pairings to estimate the exposures that may have occurred to exhibit the experimentally measured biomarker data. The biomarker distribution is shown in the first graph and the exposure distribution in the second.

Additional example files are available in the example folder with self-explanatory names for testing the various system options.

