Introduction

BIOKMOD is a Mathematica toolbox for modeling biokinetic systems with special application for solving ICRP Models and bioassay data evaluation.

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Last update of this help: 2013-10-30

$Version

9.0 for Microsoft Windows (32-bit) (January 24, 2013)

This version of BIOKMOD includes (i) a package to solve system of ordinary linear differential equations (SOLDE) with special application to compartmental and physiological models; (ii) A package for fitting data, it can be applied to fit the transfer rates using experimental data; (iii) A specific package for optimal design; iv) Some packages for solving the current ICRP Models, they have special applications to calculate internal dose and bioassay data evaluations. Some tutorials are included about: i) Compartmental and physiological modeling (linear and non linear), ii) Random intakes in occupational exposures and their implication in the bioassays, iii) Analytical methods to evaluate the uncertainties associated with the biokinetic model parameters, iv) Non linear regression techniques to the bioassay data fitting, v) Optimal design applied to perform bioassay programs.

To run BIOKMOD with all capability it is necessary Mathematica 9 (most of the functions run also in version 6, 7 or 8). Some of the most usual features of BIOKMOD can be run directly using a web browser at http://www3.enusa.es/webMathematica/Public/biokmod.html.

Summary

BIOKMOD has the following features to our knowledge are not included in any other.

a) The user himself can build compartmental models in a very easy way generating automatically the system of differential equations and their solutions.

b) It gives analytical and numerical solutions (other codes only give the numerical). Even the solutions can be given as function of some parameters. The accumulated disintegrations in a compartment or region can be computed exactly by analytical integration, what is more precise than the method of the mean resident time often applied for other codes.

c) Apart from acute, chronic and multi-inputs, it can practically be used for any kind of
continuous inputs (exponentials, periodic, etc.), even for random inputs.

d) The intakes can be estimated fitting bioassay data where not only the intake quantities but also other parameters (AMAD, f1, etc.) can be also assumed unknown. For non linear fitting are applied the optimization algorithm included in Mathematica and a specific package included in BIOKMOD.

e) Analytical expressions instead of simulation can be used for sensitivity and uncertainty analysis.

f) Optimal design tools.

g) The full version included practically all Currents ICRP Models.

The help includes many examples.

To install BIOKMOD:


2. Extract the file "biokmodXX.zip" with a zip utility (ex:winzip). It will create a folder called Biokmod. Copy this folder in Mathematica directory'AddOns\Applications

3 Open Mathematica then in the toolbar chose Help-> Documentation Center , you find in the bottom “Add-ons and Packages” then click, and you will open a new item called Biokmod where is included the help where the usage of BIOKMOD is described.

**Examples**

In the toolbar chose Evaluation Evaluate ⇒Notebook

```mathematica
Needs["Biokmod`SysModel`"]
SysModel, version 1.5 2013-09-02
```

**Iodine model**
In this model, $k_{24} = k_{10} = 1.9404$ (compartment 4 is not taken into account), $k_{30} = 0.01155$ and $k_{31} = 0.0462$; also is assumed that the input is of Iodine 131 (disintegration constant $\lambda = \frac{\log(2)}{8.02}$ day$^{-1}$). Then the model is:

\[
\text{iodine131matrix} = \text{CompartMatrix}[3, \\
\{\{1, 2, k_{12}\}, \{1, 0, 1.9404\}, \{2, 3, k_{23}\}, \\
\{3, 0, 0.01155\}, \{3, 1, 0.0462\}\}, \log(2) / 8.02];
\]

A input $b_1 = 27.13e^{-24.08t} + 27.13e^{-2.86t} - 0.02e^{-0.147t} + 0.0194e^{-0.093t}$ happens in compartment 1, and $b = 0$ in the others

\[
binput = \{-27.13e^{-24.08t} + 27.13e^{-2.86t} - \\
0.020e^{-0.147t} + 0.0194e^{-0.093t}, 0, 0\};
\]

\[
\{x_1, x_2, x_3\} = \{x_1, x_2, x_3\} /.
\text{ParametricSystemNDSolve}[\text{iodine131matrix}, \\
\{0, 0, 0\}, \text{binput}, \{t, 0, 100\}, x, \{k_{12}, k_{23}\}];
\]

The model is plotted as function of parameter $k_{12}$ and $k_{23}$.
Example 2

It is assumed that are taken samples of iodine in compartment 1

\[
\text{dataIodine} = \{(0, 0.002), (50, 0.106), (100, 0.077),
(150, 0.056), (200, 0.041), (250, 0.032), (300, 0.023),
(350, 0.018), (400, 0.011), (450, 0.011), (500, 0.007)\};
\]

An input to the compartment 1 is given by

\[
\text{iodo129h} = 34.4 \cdot e^{-200. \cdot t} + 1.09 \cdot e^{-110. \cdot t} +
0.808 \cdot e^{-102. \cdot t} + 6.414 \cdot e^{-100. \cdot t} + 5.458 \cdot e^{-24. \cdot t};
\]

We wish fit the coeff. k12 and k23 of the models

\[
\text{model}[{t_1} \text{ ? NumberQ}, {k12} \text{ ? NumberQ}, {k23} \text{ ? NumberQ}] :=
\frac{x_2[t]}{. \text{SystemNDSolve[}
\text{CompartMatrix}[3, \{(1, 2, k12), (1, 0, 1.9404),
(2, 3, k23), (3, 0, 0.01155), (3, 1, 0.0462)\}],
\{0, 0, 0\}, \{\text{iodo129h, 0, 0}\}, \{t, 0, 500\}, t1, x];
\]
Example 3

Current ICRP models are included.

Here it is plotted the lung retention a time t (in days) after an acute intake as function of intake, size of particles intaken (AMAD) and type of metabolism. (Note: Disintegration constant lambda, in days\(^{-1}\) by default = 0, but it can be modified by user).

Needs["Biokmod`Resptract`"]

Resptract 1.2 2005-05-16
References

Some studies has been published where BIOKMOD has been used (some available at the author website: http://diarium.usal.es/guillermo).


Lopez-Fidalgo J Rodriguez-Diaz J.M.,Sánchez G; G., Santos-Martin M.T. Optimal designs for compartmental models

Sánchez G; Fitting bioassay data and performing uncertainty analysis with BIOKMOD  Health Physics..  92(1) :64-72. 2007. ISSN/ISBN: 0017-9078

