BIOKMOD APPLIED TO EVALUATE BIOASSAY DATA

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Abstract. *Biokmod* is a tool box developed using *Mathematica* for solving compartmental models. It gives analytic an numeric solutions. *Biokmod* includes an specific package called *Humorap* to solve the current ICRP models. Acute, constant, continuous variable and multi-inputs intakes can be assumed. It gives urine and faecal excretion, lung retention and the content and the disintegrations (Us) in each compartment. All parameters (deposition factors, rate transfer coefficients, fractional rate of absorption, etc.) can be modified by users. *Humorap* can be used to establish bioassay programs. It can be also applied for evaluating unknown intakes fitting bioassay experimental data. A free version of *Biokmod* can be downloaded from http://web.usal.es/guillermo . There are a web version (*BiokmodWeb*) at http://www3.enusa.es/webMathematica/Public/biokmod.html .

1. INTRODUCTION

Biokmod is a program developed using *Mathematica* for solving compartmental models. Mathematical techniques applied in *Biokmod* are described in [1]. A free version of Biokmod can be downloaded from http://web.usal.es/guillermo . There are a web version (*BiokmodWeb*) at http://www3.enusa.es/webMathematica/Public/biokmod.html .

This program has the following capabilities:
a) It gives analytic solutions, apart from numeric.
b) All parameters (deposition factors, rate transfer coefficients, fractional rate of absorption, etc.) can be modified by users. It can be very useful for sensitivity analysis and for fitting experimental data.
c) Besides acute and constant inputs, it can practically be used for any kind of continuous inputs (exponentials, periodic, etc.), even for random inputs.
d) The user can build himself compartmental models in a very easy way.
e) The program uses symbolic computation (eigenvalues and eigensystem methods, laplace transform, analytic integration, etc.)

ICRP Models

Biokmod includes specific functions to solve the current ICRP models [2]. These models can be summarize as follows (Fig. 1):

Respiratory Tract Model.- The compartmental model of the human respiratory tract (RT) applied to the intake of radioactive aerosols by inhalation is described in ICRP 66. In this model the material is deposited in the respiratory tract: in compartments labeled "Particles in Initial State" (PIS) and in ET_1. From each PIS compartment the material is transferred into the body fluids, at an absorption rate s_p. It is also simultaneously transferred from PIS (at a rate s_{pt}) to a corresponding compartment labeled "Particles in Transformed State" (PTS). The flow goes from 1, in PIS, to 1, in PTS, from 2, in PIS, to 2, in PTS, and so on. The absorption rates $\{s_{pt}, s_p, s_t\}$ are related to the chemical form of the element. ICRP 66 [3] establishes three types of materials according to its absorption behavior: fast, F, moderate, M, and slow, S. The general model of RT is common to any element, changing the parameters values.

Gastro Intestinal and Systemic Compartments.- Other ICRPs (compiled in [2, 4]) expands ICRP 66 including all the compartments that take part in the metabolic process starting in the intake and ending in the faecal and urine excretion. The intake can be by inhalation, ingestion, or injection ICRP 78 applies for gastrointestinal tract (GI) the same model as in ICRP 30. The models are specific for groups of elements. ICRP 78 [4]establishes three generic groups: i) hydrogen, cobalt, ruthenium, caesium, and californium, ii) strontium, radium, and uranium (Fig. 5), and, iii) thorium, neptunium, plutonium,

americium, and curium. For the elements of each group the same model is applied. However, some parameters are specific of each element.

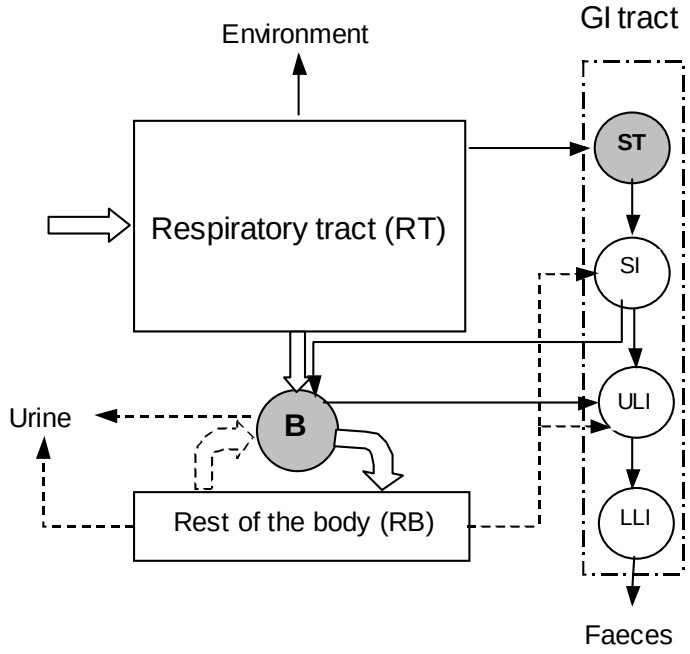

FIG 1 : *ICRP 78 Biokinetic Model. A dashed arrow means that the flow is possible for some isotopes and not for other. A hollow arrow means flow from a subsystem while a simple one means flow from a single compartmentment.*

2. HUMORAP

Biokmod includes an specific package called *Humorap* which current ICRP models. It provides several functions to calculate retention as function of time in each compartment or region given after a inhalation, ingestion or injection for acute, constant (chronic), continuous and multi simple intakes. Default values for standard worker are applied but many parameters (decay constants, initial depositions, clearances , absorption type factors, etc) can be modified by users. It is possible to obtain both numeric and analytical solutions.

The respiratory tract model has been developed according to ICRP 66 [3]. It is applied to compute the retention in regions AI, bb, BB, ET2, ET1 and Lungs. For Gastro Intestinal (GI) Tract ICRP 30 is applied. The full metabolic model, including systemic compartments, for some specific elements has been modeled applying [2] and [4]. The urine and faecal excretion, lung retention and the content in each compartment can be evaluated. The user not only can change the default values but also other models not include in the program can be built. The program can be used for evaluating unknown intakes fitting bioassay experimental data .

The content in RT compartments as function of the time *t* can be obtained with the *Humorap* function *RespiratoryTract[I_0, IDF, FRA, t, λ_R, options]* where *I* is the input, *IDF* are the initial deposition factors, *FRA* are the fractional rate of absorption and λ_R is constant decay. With *options* the default rate transfer can be modified. By default an acute intake is used, however other type of intake (constant and continuous) can be assumed. So *RespiratoryTract [3, AMAD5, S, t, 0]* gives content in each RT compartments for a reference worker t days (symbolic computation can be used) after having an acute intake 3 Bq of aerosols (class S (ej.: UO_2) and AMAD = 5 μm, λ_R is taken "0" because decay constant $\lambda_R \approx 0$ (ej.: for ^{238}U, ^{235}U, and ^{234}U).
The same example using a constant (chronic) intake of 3 Bq/day is written: *RespiratoryTract [3, AMAD5, S, t, 0,IntakeType → "Constant"]*. It also can be used the web version, as it is shown in the fig 2. and fig. 3.

3. BIOKDATA

Biokmod includes also a package called *Biokdata* with the parameters values and compartmental matrix for current ICRP Models. *BiomodWeb* uses *Biokdata* as it is shown in the fig. 4.

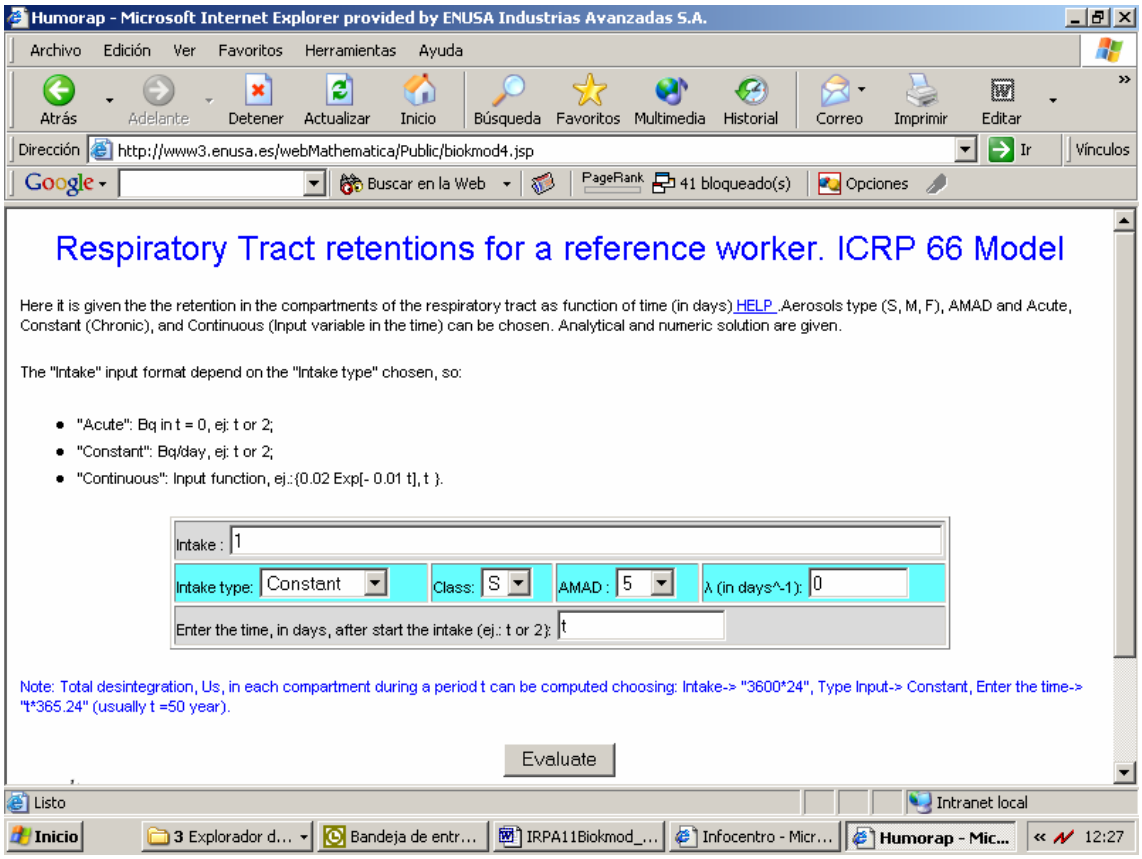

FIG 2. BiomodWeb computes the Respiratory Tract.

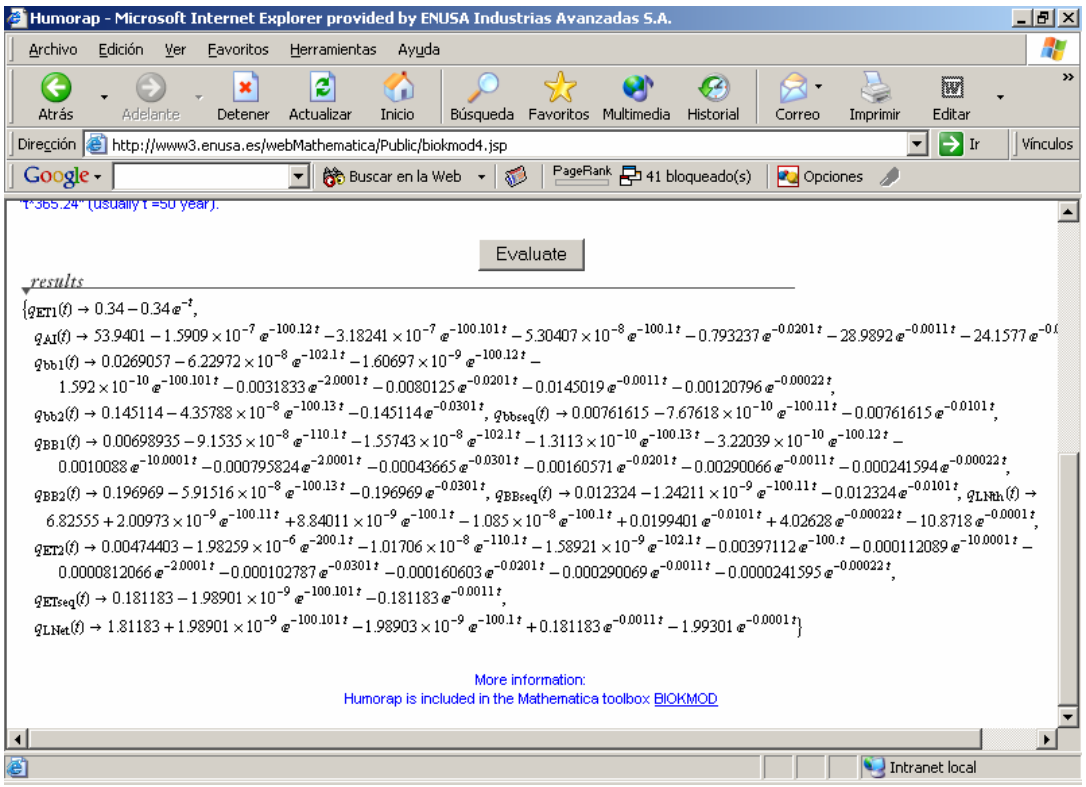

FIG. 3. *BiomodWeb output: Respiratory tract retention using the input of FIG. 2.*

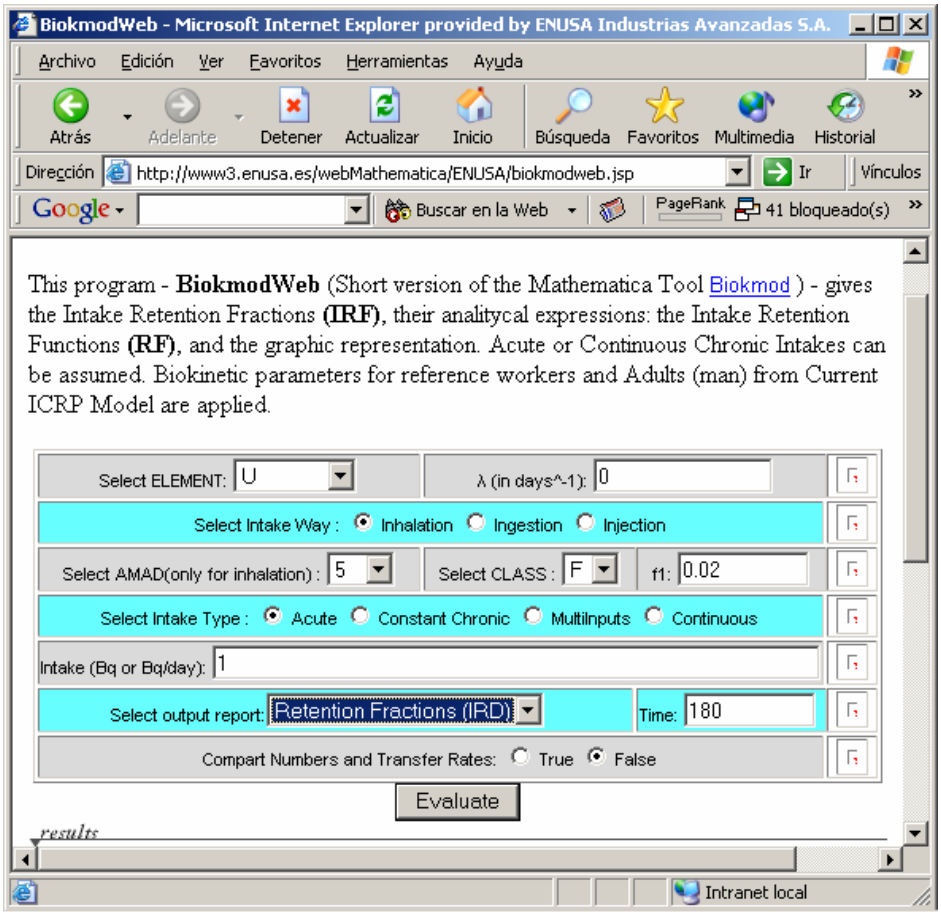

FIG. 4 . BiokmoWeb. Main Input

4. BUILDING MODELS YOUR SELF

Although BIOKMOD included the almost all current ICRP models, in some situations the user can be interested in defining himself the compartmental matrix (e.g., adding new compartments or modifying the rate of transfer default values). Here is an illustrative example that consists on solving the uranium model (UM). To include all compartments, apart from RT, the uranium model (UM), which is shown in Fig. 5, should be used.

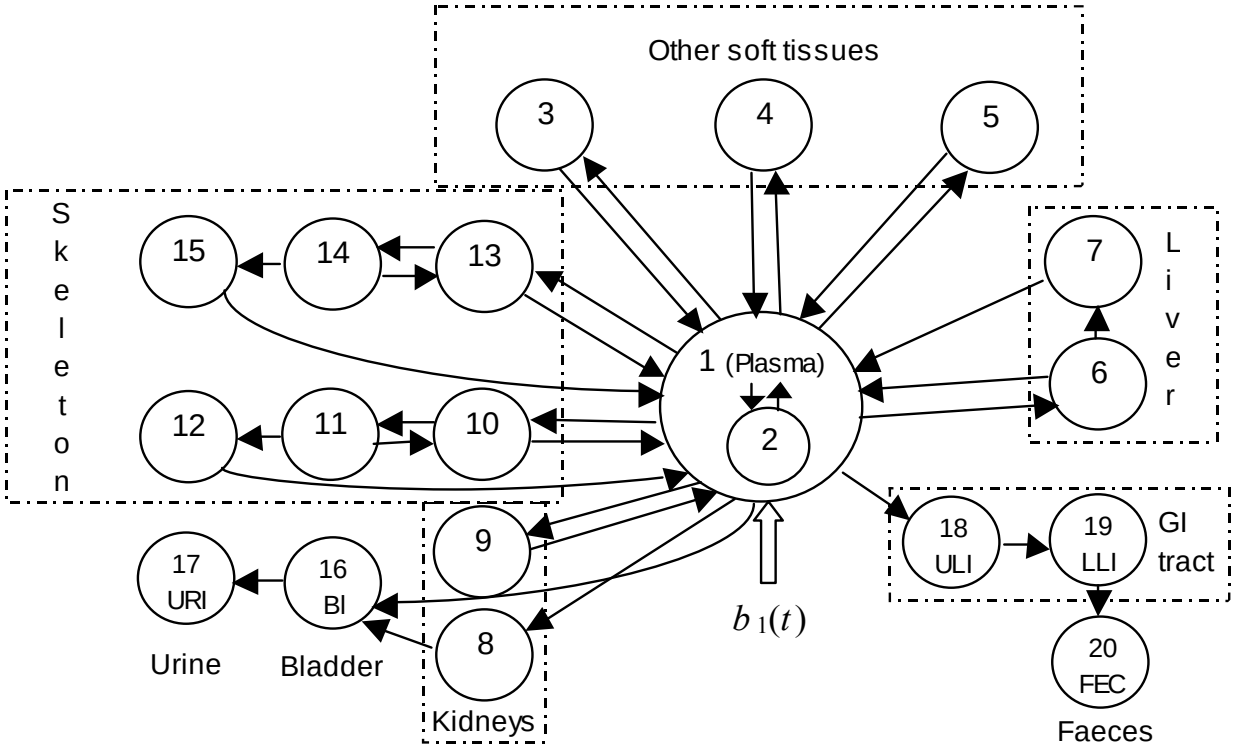

FIG 5. Biokinetic model for uranium, lead and strontium (based in figure 8 of ICRP 78).

The RT and UM are connected through ST and B as usual. In these cases it can be used the function *CompartMatrix*[*n*, {{*i, j, k_{ij}*}}],where *n* is the number of compartments and {*i, j, k_{ij}*} means flow from *i* to *j* with a rate of transfer k_{ij}. Using this function the compartmental matrix for UM will be given in the *Mathematica* style as,

CompartMatrix[22, {{1, 3, 10.5}, {1, 2, 0.245}, {1, 16, 15.43}, {1, 8, 2.94}, {1, 9, 0.0122}, {1, 18, 0.122}, {1, 6, 0.367}, {1, 4, 1.63}, {1, 5, 0.0735}, {1, 10, 2.04}, {1, 13, 1.63}, {3, 1, 8.32}, {2, 1, 0.347}, {8, 16, 0.099}, {9, 1, 0.00038}, {6, 1, 0.092}, {6, 7, 0.00693}, {4, 1, 0.0347}, {5, 1, 0.000019}, {13, 1, 0.0693}, {13, 14, 0.0693}, {7, 1, 0.00019}, {11, 12, 0.00578}, {12, 1, 0.000493}, {15, 1, 0.0000821}, {14, 13, 0.0173}, {14, 15, 0.00578}, {10, 1, 0.0693}, {11, 10, 0.0173}, {10, 11, 0.0693}, {16, 17, 12}, {18, 19, k_{ULI}}, {19, 20, k_{LLI}}, {21, 1, f_1 $k_{SI}/(1 - f_1)$}, {21, 18, k_{SI}}, {22, 21, k_{ST}}}],

where the number of compartments is given in Fig.5. and the rate of transfer, in d^{-1}, in Table A.10.1 of ICRP 78.

The solution given for an impulse intake "1" in $t = 0$ for workers exposed to inhalation of uranium aerosols UO_2 (class S) and AMAD 5 μm is shown below

$$q_{Lungs}[Uranium, AMAD5, S, t, 0] =$$

$$= 0.0100881\, e^{-10.0\, t} + 0.007959\, e^{-2.00\, t} + 0.01031\, e^{-0.0301\, t} + 0.01614\, e^{-0.0201\, t} + 0.03191\, e^{-0.0011\, t} + 0.00443\, e^{-0.00022\, t} + 0.001087\, e^{-0.0001\, t}$$

$$q_{Urine}[Uranium,\ AMAD5,\ S,\ 0.002,\ t,\ 0] =$$

$$= -1.53\ e^{-10.0\ t} - 1.70\ e^{-6.01\ t} + 1.11\ e^{-5.38\ t} + 0.000163\ e^{-2.00\ t} + 2.70 \times 10^{-6}\ e^{-0.344\ t} + 3.48 \times 10^{-6}\ e^{-0.139\ t} + 6.40 \times 10^{-7}\ e^{-0.0990\ t} + 1.63 \times 10^{-5}\ e^{-0.0973\ t} + 3.17 \times 10^{-6}\ e^{-0.0301\ t} + 2.11 \times 10^{-6}\ e^{-0.0201\ t} + 1.04 \times 10^{-6}\ e^{-0.0126\ t} + 3.07 \times 10^{-6}\ e^{-0.0011\ t} + 4.32 \times 10^{-7}\ e^{-0.00022\ t} + 1.17 \times 10^{-7}\ e^{-0.0001\ t}$$

$$q_{Faecal}\ [Uranium,\ AMAD5,\ S,\ 0.002,\ t,\ 0] =$$

$$= 20.7\ e^{-6.01\ t} + 0.000558\ e^{-5.38\ t} + 0.761\ e^{-2.00\ t} - 4.85\ e^{-1.80\ t} + 2.07\ e^{-1.00\ t} + 0.000331\ e^{-0.0301\ t} + 0.000337\ e^{-0.0201\ t} + 0.000319\ e^{-0.0011\ t} + 5.34 \times 10^{-7}\ e^{-0.00022\ t}$$

5. SUMMARY

Biokmod is a tool box developed using *Mathematica* for solving compartmental models. It gives analytic an numeric solutions. *Biokmod* includes an specific package called *Humorap* to solve the current ICRP models. Acute, constant, continuous variable and multi-inputs intakes can be assumed. It gives urine and faecal excretion, lung retention and the content and the disintegrations (Us) in each compartment. All parameters (deposition factors, rate transfer coefficients, fractional rate of absorption, etc.) can be modified by users. *Humorap* can be used to establish bioassay programs. It can be also applied for evaluating unknown intakes fitting bioassay experimental data . A free version of *Biokmod* can be downloaded from http://web.usal.es/guillermo . There are a web version (*BiokmodWeb*) at http://www3.enusa.es/webMathematica/Public/biokmod.html .

6. REFERENCIAS

1 Sánchez G., López-Fidalgo J. *Mathematical techniques for solving analytically large compartmental systems,* in *Health Phys*. 85:184-193 (2003).

2 International Commission on Radiological Protection. *ICRP Database of Dose Coefficients: Workers and Members of the Public* v. 2.0.1 (CD-ROM).

3 ICRP66 International Commission on Radiological Protection, *Human Respiratory Tract Model for Radiological Protection*. ICRP publication 66. Oxford: Pergamon Press (1994).

4 International Commission on Radiological Protection, *Individual monitoring for internal exposure of workers*. ICRP Publication 78.