■ Inicialization

FITTING BIOASSAY DATA AND PERFORMING UNCERTAINTY ANALYSIS WITH BIOKMOD

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Sanchez, Guillermo
Resumen en; http://www.health-physics.com/pt/re/healthphys/abstract.00004032-200701000-00009.htm

Summary

Here it is described the features included in the computer code BIOKMOD related with the ICRP Models. BIOKMOD has been applied to analyze several sources of uncertainties in the evaluation of internal exposures using the bioassay data: (i) Multiple constant and random intakes in occupational exposures taking into account periods without intake (weekends, holidays, etc.) are evaluated, and they are compared with the chronic intakes showing that the chronic approximation is not always good; (ii) An analytical method to evaluate the statistical uncertainties associated with the biokinetic model is described; (iii) Non linear techniques are applied to estimate the intakes using bioassay data, where not only the quantities intaken are assumed unknown but also other non linear parameters (AMAD, f1, etc). The methods described are accompanied with examples. Some of the most usual features of BIOKMOD can be run directly, using BIOKMOD WEB, at the web site:
http://www3.enusa.es/webMathematica/Public/biokmod.html

Introduction

Biokinetic modeling is widely used in internal dosimetry and to evaluate bioassay data. All current ICRP models, compiled in the ICRP Database of Dose Coefficients (ICRP 2001), can be represented by compartmental systems with constant coefficients. The conceptual model used by ICRP is represented in Fig. 1. It can be summarized as it follows. The human body can be divided in three systems:

a) The human respiratory tract model (HRTM). This model is applied for modeling the intake of radioactive aerosols by inhalation. The detailed description is given in ICRP 66 (1994). If a person inhales instantaneously a quantity I, it is deposited directly in some compartments of the HRTM. The fraction deposited in each compartment is called Initial Deposition Fraction or IDF. It is a function of Activity Median Aerodynamic Diameter (AMAD), which includes size, shape, density, anatomical and physiological parameters as well as various conditions of exposure. The IDF values may be calculated either following the procedure described in ICRP 66 (1994) or obtaining it from the Annex F of ICRP 66 (1994). The general model of the HRTM is common to any element except the absorption rates $\{s_{\rm pt}, s_p, s_t\}$ which are related to the chemical form of the element. ICRP gives default values of absorption rates according to types F, M or S.

b) The gastrointestinal tract (GI).- This is applied for modeling the intake of particles in the GI tract following the model provided in ICRP 30 (ICRP 1979) . Particles can be introduced in the GI Tract directly by ingestion, or from the RT. Deposition is in the stomach (ST). Part or all the flow is transferred, through SI, to the blood (B). The rate transfer from SI to B, is given by $\lambda_B = f_1\ \lambda_{\rm SI}/(1 - f_1)$, where f_1 is the fraction of the stable element reaching the blood (or body fluids). If $f_1 = 1$ all flows from the stomach it goes to B. The value of f1 is associated to the element and their chemical form The GI tract model will be replaced by the called Human Alimentary Tract Model (HATM), but it is not published yet.

c) Systemic compartments.- . They are specific to an element or groups of elements (ICRP 2001). ICRP 78 (1997) establishes three generic groups: (i) hydrogen, cobalt, ruthenium, caesium, and californium, (ii) strontium, radium, and uranium and, (iii) thorium, neptunium, plutonium, americium, and curium. For other elements not included in ICRP78, the ICRP 30 model is applicable and they have the same generalized compartmental model as group (i). For the elements of each group the same model is applied although some parameters are specific to the element. From a mathematical point of view we can establish two groups: a) Elements whose biokinetic model does not involve recycling, this includes the group (i) and the elements where ICRP 30 is still applicable, and b) elements whose biokinetic models involve recycling, this includes group (ii) and (iii).

A few computer codes have been developed to estimate intake and calculate internal dose using biassay data. The main characteristics of most of then are summarized by Ansoborlo et al (2003). BIOKMOD. has the following features to our knowledge are not included in any other.

a) 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 (Loevinger et al. 1988) 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, f_1, etc.) can be assumed unknown.

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

f) The user himself can build compartmental models in a very easy way generating automatically the system of differential equations and their solutions [Sanchez 2005].

We have applied BIOKMOD to the evaluation of internal exposures using bioassay data. In particular we will refer to the random intakes in occupational exposures and their implication in the bioassays, the application of analytical methods to evaluate the uncertainties associated with the biokinetic model parameters, and the use of non linear regression techniques to the bioassay data fitting. The methods described are accompanied with examples.

BIOKMOD is a tool box developed using Mathematica (Wofram Research, Inc. Champaign, IL) It includes several Mathematica packages (or subprograms). To run BIOKMOD with all capability it is necessary Mathematica, however, some of the most usual features of BIOKMOD can be run directly at: http://www3.enusa.es/webMathematica/-Public/biokmod.html. It is possible thanks to an interface, called, BiokmodWeb, which we have developed using webMathematica (Wofram Research, Inc) and Java (by Sun Microsystems, Inc.).

Solving ICRP models

General description

All current ICRP models, compiled in ICRP Database of Dose Coefficients (ICRP 2001), can be represented by compartmental systems with constant coefficients. The conceptual model used by ICRP is represented in figure 1. It can be summarized as it follows. The human body can be divided in three systems:

a) The human respiratory tract model (HRTM).- It is applied for modeling the intake of radioactive aerosols by inhalation. The detailed description is given in ICRP 66. If a person intakes by inhalation instantaneously a quantity I, it is deposited directly in some compartments of the HRTM. The fraction deposited in each compartment is called Initial Deposition Factor or IDF. It is a function of Activity Median Aerodynamic Diameter (AMAD), which includes size, shape, density, anatomical and physiological parameters as well as various conditions of exposure. The IDF values may be calculated either following the procedure described in ICRP 66 (1994) or obtaining from the Annex F of ICRP 66 (1994). AMAD value can be written and then the program computes the IDF. Another option is to directly write the IDF values for AI, $bb_{fast+seq}$, bb_{slow}, $BB_{fast+seq}$, BB_{slow}, ET1, and ET2. The general model of the RT is common to any element except the absorption rates $\{s_{pt}, s_p, s_t\}$ that are related with the chemical form of the element. ICRP gives default values of absorption rates according to types F, M or S. In BIOKMOD F, M or S can be chosen and the program will apply default values for absorption rates. Another option is to directly write the absorption rate parameters.

b) The gastro intestinal tract (GI).- This is applied for modeling the intake of particles in the GI tract following the model provided in ICRP 30 (ICRP 1979) . Particles can be introduced in the GI Tract directly by ingestion, or from the RT. Deposition is in the stomach (ST). Part or all the flow is transferred, through SI, to the blood (B). The rate transfer from SI to B, is given by $\lambda_B = f_1 \lambda_{SI}/(1 - f_1)$, where f_1 is the fraction of the stable element reaching the blood (or body fluids). If $f_1 = 1$ all flow from SI goes to B. The value of f_1 is associated to the element and their chemical form. In BIOKMOD f_1 must be introduced or a value by default (from ICRP 2001 and ICRP 1997) will be applied according with the element and the absorption rate previously chosen.

c) Systemic compartments.- . They are specific to an element or groups of elements (ICRP 2001). ICRP 78 (1997) establishes three generic groups: (i) hydrogen, cobalt, ruthenium, caesium, and californium, (ii) strontium, radium, and uranium and, (iii) thorium, neptunium, plutonium, americium, and curium. For other elements not included in ICRP78, the ICRP 30 model is applicable and they have the same generalized compartmental model as group (i). For the ele-

ments of each group the same model is applied although some parameters are specific to the element. From a mathematical point of view we can establish two groups: a) Elements whose biokinetic model does not involve recycling, this includes the group (i) and the elements where ICRP 30 is still applicable, and b) elements whose biokinetic models involve recycling, this includes group (ii) and (iii).

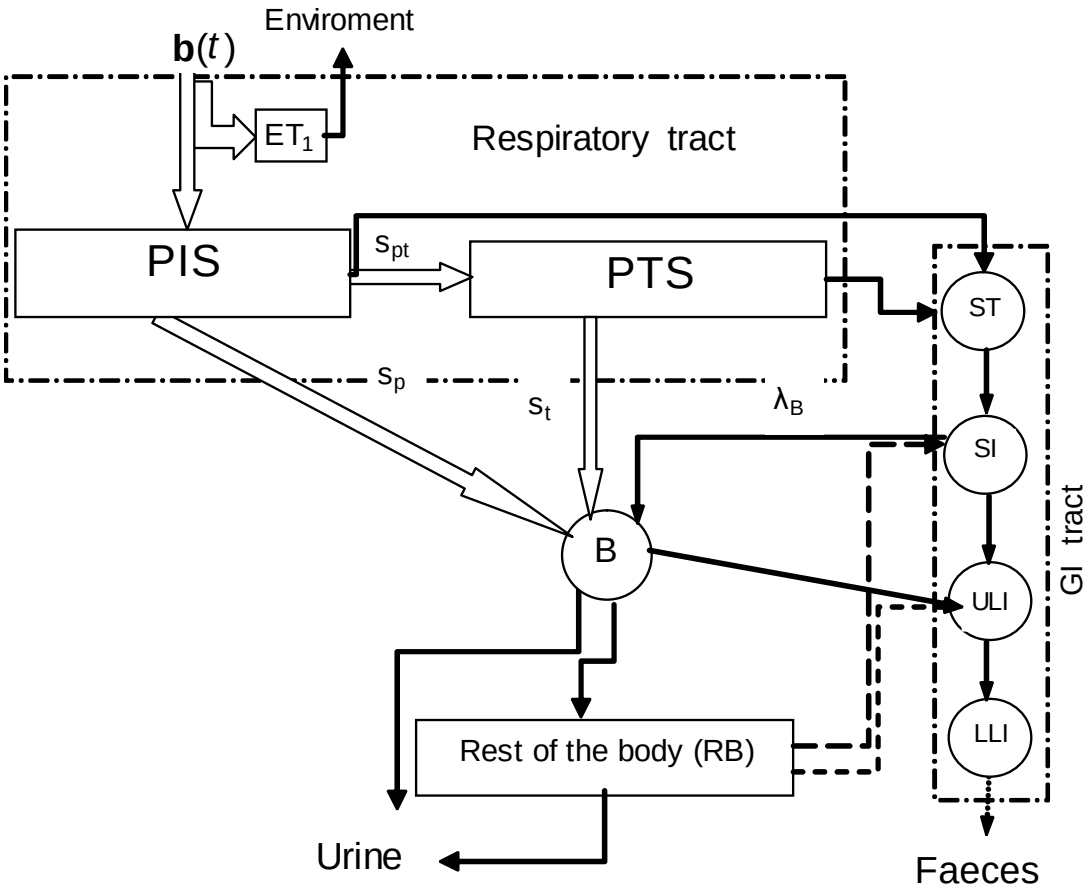


Fig. 1 Conceptual ICRP Model applied for particle intakes by inhalation. The particles are deposited in some compartments of the RT. From the RT the flow goes to the ST (Stomach) or to B. "Rest of Body" represents the systemic compartments, the detailed flow diagram is specific to each kind of element. The dashed arrows mean that the flow can be follow this way or not, depending on the characteristic of the element. The particles are eliminated through faecal or urine excretion. The disintegration can be considered as elimination from each compartment to away from the system; it is given by the disintegration constant of the isotope.

The format applied to introduce the inputs depends on whether it is used BIOKMOD directly or BiokmodWed, a friendly interface to run BIOKMOD using a web browser. The user can modify the respiratory tract and gastrointestinal tract parameters included by default. The reference worker parameters are used by default. Three kinds of intake way (injection, ingestion or inhalation) can be chosen. The day (d) will be used as unit of time. The radioactive decay constant, in day^{-1}, of the isotope must be introduced by the user. More details can be found in the BIOKMOD Help (more than 300 pages). We summarize below the equations used by BIOKMOD.

If we consider a single intake I at $t = 0$ then the content $q_i(t)$ in each compartment i of a n-compartmental system at time t, is given by

$$q_i(t) = I\, u_i(t) \qquad (1)$$

where $u_i(t)$ is usually called the unit impulse-response function. It can be represented with the following pattern

$$u_i(t) = F_i(l_1, \ldots, l_m, s_p, s_{pt}, s_t, f_1, \lambda_1, \ldots, \lambda_n, h_1 \ldots, h_r, \lambda_R, t) \quad (2)$$

where $l_i$denote the rate transfers for RT compartments, λ_i the rate transfers for GI compartments and $h_1, \ldots, h_r$ the rate transfers for systemic compartments, and λ_R is the decay constant of the isotope; $u_i(t)$ is a sum of exponentials [see e.g.:Sanchez and Lopez-Fidalgo 2003], that is

$$u_i(t) = \sum_{r=1} a_r \, e^{-k_r t} \quad (3)$$

The predicted value for a kind of bioassay m (lung retention, urine excretion, etc.) after an acute input "1" at $t = 0$, represented by $r_m(t)$, is obtained by the sum of the content of one or several compartments [Lopez-Fidalgo and Sanchez 2005]. It will also be a sum of exponentials

$$r_m(t) = \sum_{v=1} a_v \, e^{-d_v t} \quad (4)$$

where c_v and d_v are the coefficients obtained solving the model for the specific case.

This pattern is applicable for inhalation, ingestion or injection. In fact the ingestion can be considered a particular case of inhalation where the intake I happens directly in the stomach. In the same way, the injection is a particular case of ingestion where the intake I happens directly in the blood.

In the case of inhalation eqn(4) can be written as

$$r_m(t) = \sum_{j,v} \mathrm{IDF}_j(p) \, c_{j,v} \, e^{-d_{j,v} t} \quad (5)$$

The mathematical criteria applied to obtain $q_i(t)$ and $r_m(t)$ are described in Sanchez and Lopez-Fidalgo 2003. To simplify the notation we will write $r(t)$ instead of $r_m(t)$. We will call $r(t)$ standard retention function when we refer to an impulsive input "1" at $t = 0$. In other cases we will refer it as retention function, written $R(t)$. Below we summarize how $R(t)$ is computed for different cases.

The analytical solutions given by the program can not be checked directly with other programs because in our knowledge there are no others with this capability. For this reason we have compared the numerical solution for acute intakes given by BIOKMOD for different times with the solutions given in the ICRP 78 obtaining a good match.

Single intake

The retention function $R_A(t)$ for a single or acute intake I_0 at $t = 0$ is given by

$$R_A(t) = I_0 \, r(t) \quad (6)$$

It can be computed using the BIOKMOD functions:

LungsRetention[Intake, IFD , FRA, t, λ, options] or **BioakdataReport[*element*, *"IntakeWay"*, *"IntakeType"*, *Report*,** *Intake, IFD , FRA, t, λ, options*] chosing as ***"IntakeType" -> Acute.*** It is also computed when the intake type it is not indicated.

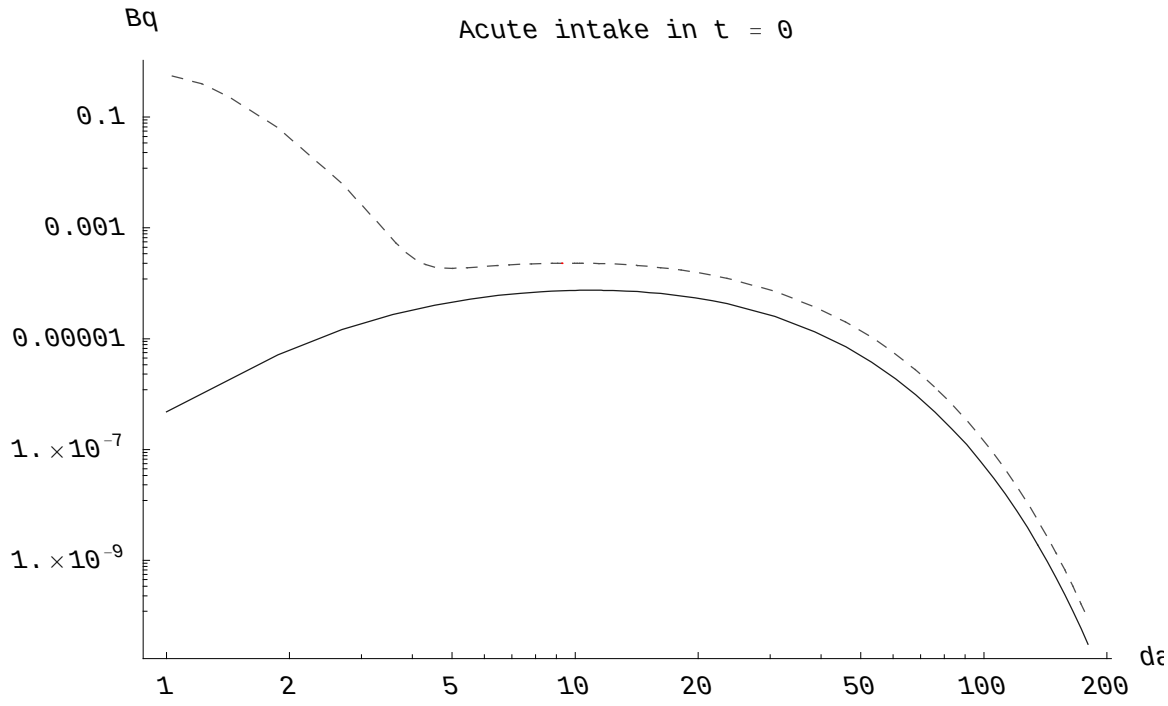
> *This example shows the lung retention as a function of initial deposition fraction (IDF) t days after an acute intake (I = 1 at t = 0) of radioactive aerosols type S and AMAD 5 μm.*

```
In[11]:= Collect[LungsRetention[1, {IDF_AI, IDF_"bb(fast+seq)",
           IDF_bbslow, IDF_"BB(fast+seq)", IDF_BBslow, ET_2, ET_1}, S, t, 0] // Chop,
         {IDF_AI, IDF_"bb(fast+seq)", IDF_bbslow, IDF_"BB(fast+seq)", IDF_BBslow, ET_2, ET_1}]
```

$$\begin{aligned}\text{Out[11]=}\ & (-0.000247754\, e^{-110.1\,t} + 0.00123877\, e^{-102.1\,t} + 6.98602\times10^{-6}\, e^{-100.1\,t} - \\ & 0.248002\, e^{-10.0001\,t} + 1.24001\, e^{-2.0001\,t} + 0.00699301\, e^{-0.0001\,t})\ IDF_{bb(fast+seq)} + \\ & (0.000991017\, e^{-110.1\,t} + 6.98602\times10^{-6}\, e^{-100.1\,t} + 0.992009\, e^{-10.0001\,t} + 0.00699301\, e^{-0.0001\,t})\ \\ & IDF_{BB(fast+seq)} + (1.65221\times10^{-7}\, e^{-110.1\,t} - 4.16099\times10^{-6}\, e^{-102.1\,t} + 0.000303031\, e^{-100.12\,t} + \\ & 0.000599161\, e^{-100.101\,t} + 0.0000831729\, e^{-100.1\,t} + 0.0000166334\, e^{-100.1\,t} + \\ & 0.000165387\, e^{-10.0001\,t} - 0.00416516\, e^{-2.0001\,t} + 0.303335\, e^{-0.0201\,t} + \\ & 0.599761\, e^{-0.0011\,t} + 0.0832562\, e^{-0.00022\,t} + 0.01665\, e^{-0.0001\,t})\ IDF_{AI} + \\ & (-1.25651\times10^{-6}\, e^{-110.1\,t} - 8.73253\times10^{-6}\, e^{-102.1\,t} + 0.00100101\, e^{-100.13\,t} + \\ & 6.98602\times10^{-6}\, e^{-100.1\,t} - 0.00125777\, e^{-10.0001\,t} - 0.00874127\, e^{-2.0001\,t} + \\ & 1.00201\, e^{-0.0301\,t} + 0.00699301\, e^{-0.0001\,t})\ IDF_{bbslow} + \\ & (-6.98602\times10^{-6}\, e^{-110.1\,t} + 0.000998003\, e^{-100.13\,t} + 6.98602\times10^{-6}\, e^{-100.1\,t} - \\ & 0.00699301\, e^{-10.0001\,t} + 0.999002\, e^{-0.0301\,t} + 0.00699301\, e^{-0.0001\,t})\ IDF_{BBslow}\end{aligned}$$

The below example represents the daily faecal and urine excretion for an acute intake $I = 1$ Bq at $t = 0$ of Iodine.

```
In[12]:= BiokdataReport[iodine, "Injection",
          "Acute", "GraphicReport", 1, 1, 180, Log[2] / 8.0]
```




```
Out[12]= - Graphics -
```

Chronic contant intake

The retention function $R_{Cr}(t)$ for a constant intake $I(t) = I_d$ (daily rate intake) for $0 \le t \le T$, at $t = T$ cease the intake, that is $I(t)$ for $t > T$, then the retention is given by

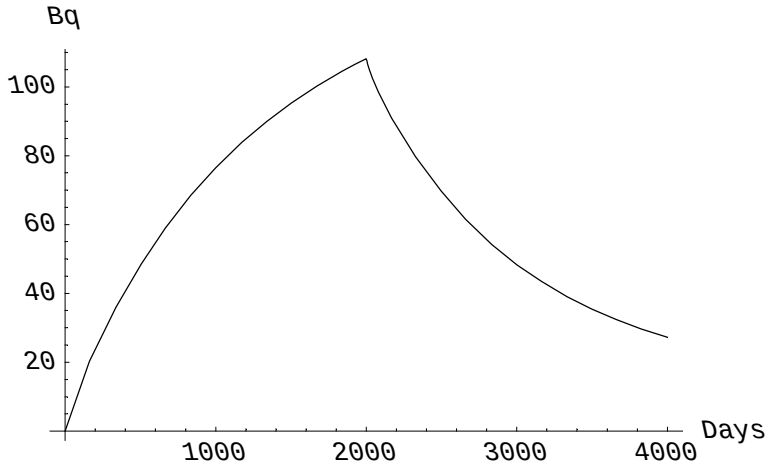
$$R_{Cr}(t) = I_d \int_0^t r(t)\,dt \text{ for } 0 < t \le T \text{ and } R_{Cr}(t) = I_d \int_{t-T}^t r(t)\,dt \text{ for } t > T \tag{7}$$

It is computed by the BIOKMOD function

qConstant[I_b,{$r[t]$, t}, t_i, T] gives the retention the day t_i after an intake I_b at $t = 0$ assuming that it cease the intake at $t = T$.

The below figure shows the lung retention for a worker that has been exposed from $t = 0$ to $t = 2000$ day to a chronic intake by inhalation of 3 BqU/day of UO_2 enriched aerosols type S and AMAD 5 μm. On the day $t = 2000$ xceases the intaken.(Note: The enriched uranium contains ^{238}U, ^{235}U and ^{234}U, for this isotopes $\lambda_R \to 0$)

```
In[13]:= qLungU5[t_] = LungsRetention[1, AMADAdultW[5], S, t, 0];

In[14]:= Plot[qConstant[3, {qLungU5[t], t}, t1, 2000],
           {t1, 0, 4000}, AxesLabel → {"Days", "Bq"}]
```




```
Out[14]= -Graphics-
```

Continuous variable intake

The retention function $R_C(t)$ for a continuous intake $I(t)$, is given by

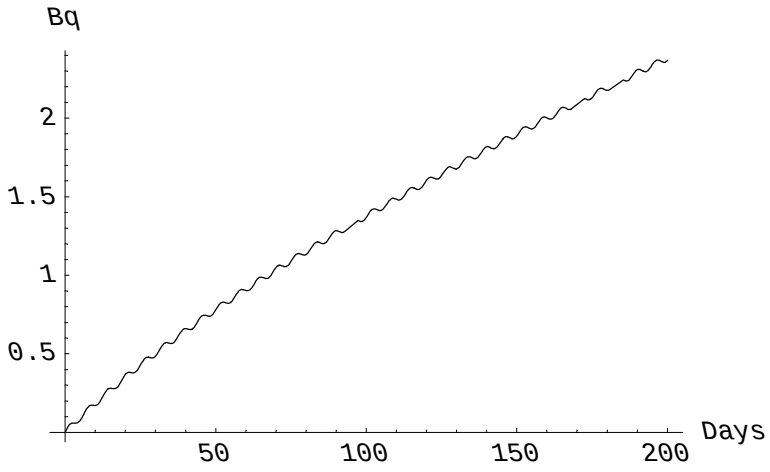
$$R_C(t) = \int_0^t I(\tau)\, r(t-\tau)\,d\tau \tag{8}$$

It is computed by the BIOKMOD function

qContinuous[$I(t)$,{$r[t]$}, t, t_i] gives the retention the day t_i after an intake $I(t)$ starting at at $t = 0$.

Here it is asumed the lung retention asuming an a continous intake given by $I(t) = 0.3 + 0.3\,\mathrm{Cos}[t]$

```
In[15]:= Plot[Evaluate[qContinuous[0.3 + 0.3 Cos[t], {qLungU5[t]}, t, t1]],
          {t1, 0, 200}, AxesLabel → { "Days", "Bq"}]
```




```
Out[15]= - Graphics -
```

It can be also used: **LungsRetention**[Intake, IFD , FRA, t, λ, options] or **BioakdataReport**[***element, "IntakeWay", "IntakeType", Report,*** *Intake, IFD , FRA, t, λ, options*] chosing as IntakeType→"Continuous".

The example represents a biexponential input (I(t) = 0.6 Exp[-10.2 t]+0.02 Exp[-6.0 t]) of iodo-131 by injection and the corresponding solution.It is been chosen that output gives the retention function for typical bioassays,but other output reports are available such as graphics representation,retention function for each compartment,or number of disintegrations accumulated in each compartment.

```
In[16]:= BiokdataReport[iodine, "Injection", "Continuous", "Automatic",
           {0.6 Exp[-10.2 t] + 0.02 Exp[-6.0 t] , t}, 1, t, Log[2] / 8.0] // Chop

Out[16]= {qDailyUrine[t] → 10999.2 ℮^-12.0866 t - 2461.2 ℮^-10.2 t - 1.52023 ℮^-6. t +
           1.20303 ℮^-2.85919 t - 0.000106687 ℮^-0.14679 t + 0.0000988393 ℮^-0.0929673 t,
         qDailyFaecal[t] → -3.88128 × 10^-6 ℮^-10.2 t - 8.52054 × 10^-8 ℮^-6. t +
           5.52234 × 10^-6 ℮^-2.85919 t - 0.0000124967 ℮^-1.88664 t - 8.4189 × 10^-7 ℮^-1.88664 t +
           0.0000135931 ℮^-1.08664 t - 0.0000408268 ℮^-0.14679 t + 0.0000355496 ℮^-0.0929673 t,
         qWholebody[t] → 0.0675817 ℮^-12.0866 t - 0.159095 ℮^-10.2 t - 0.00750263 ℮^-6. t +
           0.0802064 ℮^-2.85919 t - 2.47477 × 10^-6 ℮^-1.88664 t - 1.66722 × 10^-7 ℮^-1.88664 t +
           7.91086 × 10^-6 ℮^-1.08664 t - 0.00237953 ℮^-0.14679 t + 0.0211838 ℮^-0.0929673 t}
```

Multiple single intakes

For multiple single inputs: $\{I_1, \ldots, I_i, \ldots, I_n\}$ that happen at times: $\{t_0, t_1, \ldots, t_i, \ldots t_n\}$, where $t - t_i$ is the time since the input I_i occurred. Then, taken $t_0 = 0$, the retention function, $R_M(t)$ is given by .

$$R_M(t) = I_1\, r(t) + I_2\, r(t-t_1) + \ldots + I_n\, r(t-t_{n-1}) = \sum_{i=1}^{n} I_i\, r(t-t_{i-1}) \tag{9}$$

If the time is considered to be a discrete variable measured in days and I_j represents the intake that happened on the day j, then the previous equation can be written:

$$R_M(t) = I_1\, r(t) + I_2\, r(t-1) + \ldots + I_n\, r(1) = \sum_{j=1}^{t} I_j\, r(t-j+1) \tag{10}$$

It is computed by the BIOKMOD function **qMultiple.**

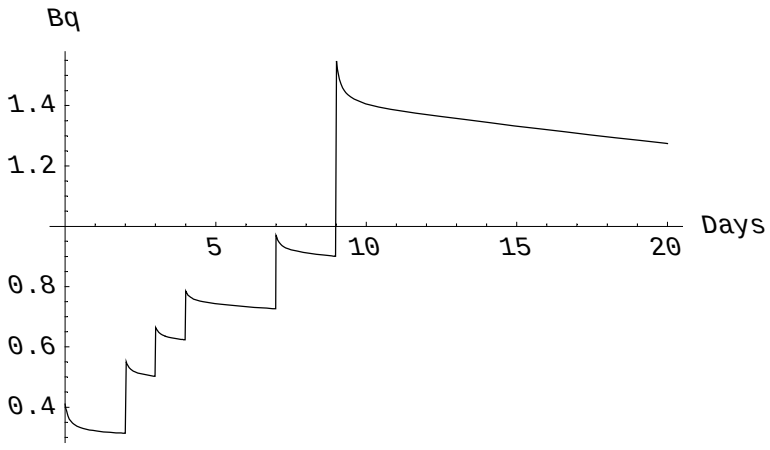
```
In[17]:= ?qMultiple

         qMultiple[inputsdata,{u[t],t}, tt] gives the  retention the
           time tt for multiples(constant:{...,{bi,ti,Ti},...} and singles
           {...,{bi,ti},...})inputs,being u[t] the unit-inpulse response
```

Example.- A worker started to work in an area exposed to UO2 (AMAD 5 μm and type S) radioactive aerosols starting the day $t = 0$. The quantities intaken since then has been $\{I,\ t\}$:

```
In[18]:= intakendata1 = {{5, 0}, {3, 2}, {2, 3}, {2, 4} , {3, 7} , {8, 9} };
```

So, the estimated lung retention since the started the first inkake can be represented as follows:

```
In[19]:= Plot[Evaluate[qMultiple[intakendata1, {qLungU5[t], t}, t1]],
          {t1, 0, 20}, AxesLabel→ { "Days", "Bq"}]
```




```
Out[19]= - Graphics -
```

It can be also used:

LungsRetention[Intake, IFD , FRA, τ, λ, options] or **BioakdataReport[*element, "IntakeWay", "IntakeType", Report,* *Intake, IFD, FRA, τ, λ, options*]** chosing as IntakeType→ "MultiInputs" give the retention or excretion τ days after the last intake $\{I_n\ ,\ t_n\}$ happened

In the same example, the lung retention for $\tau = 5$ is

```
In[20]:= LungsRetention[intakendata1, AMADAdultW[5], S, 5, 0, IntakeType → "MultiInputs"]

Out[20]= 1.34442
```

It can be compared with the obteinded using qMultiple (taking into account that $\tau = t - t_n$)

```
In[21]:= qMultiple[intakendata1, {qLungU5[t], t}, 9 + 5]

Out[21]= 1.34442
```

Multiple constant intakes

In many situations the intake I_j happens for a few hours every day. However, from a practical point of view it can be assumed that I_j is an acute intake. But if we want to consider $\{I_0, \ldots, I_i, \ldots, I_n\}$ as multiple constant intakes that happen at times: $\{t_0, t_1, \ldots, t_i, \ldots t_n\}$ during a time $\{T_0, \ldots, T_i, \ldots, T_n\}$, where $\tau_i = t - t_i$ is the time since the input I_i occurred.

We want consider the case where it happens multiple constant inputs $\{b_0, \ldots, b_i, \ldots, I_n\}$ that start at times: $\{t_0, t_1, \ldots, t_i, \ldots t_n\}$ during a time $\{T_0, \ldots, T_i, \ldots, T_n\}$.

We call $r(t)$ the unit function for a constant input

$$r(t,\ T_i) = \left\{0\ ,\ t < 0,\ \int_0^t u(t)\,dt \ \text{for}\ 0 < t \le T_i \ \text{and} \int_{t-T_i}^t u(t)\,dt \ \text{for}\ t > T_i\right\}$$

Then, the retention function for multiple constant inputs is given by

$$q_{\mathrm{MC}}(t) = \frac{b_0}{T_0}\, r(t-t_0) + \frac{b_1}{T_1}\, r(t-t_1) + \ldots + \frac{b_n}{T_n}\, r(t-t_n) = \sum_{i=1}^{n} \frac{b_i}{T_i}\, r(t-t_i) \qquad (11)$$

This equation is implemented in the BIOKMOD function **qMultiple**. This function can be used also for multiple acute inputs even for combination multiples acute and constant inputs.

> *Example.- A worker works in an area expose to UO2 (AMAD 5 μm and type S) radioactive aerosols during the last 2000 days. He works 5 days per week 8 hours a day, he also has 4 holiday weeks per year (with these criteria 2000 days are 1330 working days). It is estimated that in this time he has intaken 13300 BqU. We want to calculate the lung retention evolution. Regular weekends and holidays will be assumed.*

We will need the single-impulse function for lung

```
In[22]:= qLungU5S[t_] = LungsRetention[1, AMADAdultW[5], S, t, 0];
```

The lung retention for a single intake 1 Bq/day with $T_i = T = \frac{8h}{24h} = \frac{1}{3}$ is given by

```
In[23]:= days = 2000; Ti = 1 / 3;

In[24]:= lungret = 1 / Ti qConstant[1, {qLungU5S[t], t}, #, Ti] & /@ Range[days];
```

The average intake during this period conisdering all days is

```
In[25]:= totalintake = 13300; avgintake = totalintake / days;
```

Now we want calculated the number of working days.

```
In[26]:= workingdays = Flatten[
           Table[If[Mod[n, 7] == 0 || Mod[n, 7] == 6 || Mod[n, 365] == 0 || Mod[n, 365] == 364 ||
              Mod[n, 365] == 363 || Mod[n, 365] == 362 || Mod[n, 365] == 361 ||
              Mod[n, 365] == 360 || Mod[n, 365] == 359 || Mod[n, 365] == 358 ||
              Mod[n, 365] == 357 || Mod[n, 365] == 356 || Mod[n, 365] == 355 ||
              Mod[n, 365] == 354 || Mod[n, 365] == 353 || Mod[n, 365] == 352 ||
              Mod[n, 365] == 351 || Mod[n, 365] == 350 || Mod[n, 365] == 349 ||
              Mod[n, 365] == 348 || Mod[n, 365] == 347 || Mod[n, 365] == 346 ||
              Mod[n, 365] == 345 || Mod[n, 365] == 344 || Mod[n, 365] == 343 ||
              Mod[n, 365] == 342 || Mod[n, 365] == 341 || Mod[n, 365] == 340 ||
              Mod[n, 365] == 339 || Mod[n, 365] == 338, 0 , 1], {n, days}]];

In[27]:= wdays = Total[workingdays]

Out[27]= 1330
```

The average daily intake considering only the working days is

```
In[28]:= avgintakewd = totalintake / wdays

Out[28]= 10
```

The lung retention take in into accound the period where there are not intake is

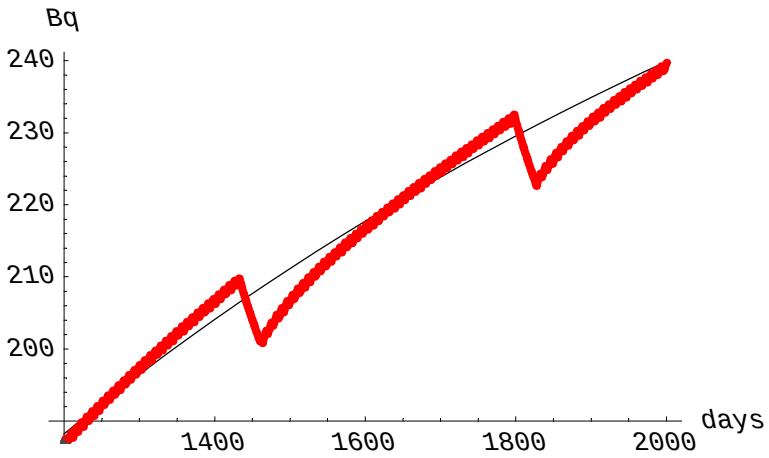
```
In[29]:= dailylungret = Transpose[
           {Range[days], ListConvolve[ workingdays, avgintakewd * lungret, {-days, 1}, 0]}];
```

The lung retention assuming a chronic intake is

```
In[30]:= qLungU5SCr[t_] = LungsRetention[1, AMADAdultW[5], S, t, 0, IntakeType → "Constant"];
```

Both solutions are plotted below

```
In[31]:= fig2 = Plot[avgintake qLungU5SCr[t], {t, 1200, days}, AxesLabel → {"days", "Bq"},
            Epilog → {Hue[0], PointSize[0.012], Map[Point, dailylungret]}]
```




```
Out[31]= - Graphics -
```

> *It can be observed that the differences between both methods are negligible in the middle of periods between two holiday seasons, and maxima just after the holiday periods, but even in these cases they are not too important (lower than 5%)*

The estimated lung retention different days after the intaken started it can be made directy using the BIOKMOD function **qMultiple**

```
In[32]:= ?qMultiple

         qMultiple[inputsdata,{u[t],t}, tt] gives the  retention the
           time tt for multiples(constant:{...,{bi,ti,Ti},...} and singles
           {...,{bi,ti},...})inputs,being u[t] the unit-inpulse response

In[33]:= dailyinputs = Transpose[{workingdays, Range[2000], Table[1 / 3, {2000}]}];

In[34]:= TableForm[Map[{#, avgintakewd qMultiple[dailyinputs, {qLungU5S[t], t}, #]} &,
           {100, 500, 1000, 1500, 2000}],
          TableHeadings → {None, {"Time after intake in days", "Lung retention"}}]

  Out[34]//TableForm=
       Time after intake in days     Lung retention
       100                           32.4497
       500                           107.734
       1000                          172.687
       1500                          206.337
       2000                          239.481
```

Random Intakes

In real situations, such as workers being exposed to radioactive aerosols during the working days, the individual daily intake I is usually a random variable. In a previous article we found (Lopez-Fidalgo and Sanchez, 2005) that in some occasions the daily intake $\{I_1, \ldots, I_i, \ldots, I_n\}$ can be fitted by a log-normal distribution LN(μ, σ^2), where μ and σ^2 are the mean and variance of the corresponding normal distribution. We showed that the retention function $R_{\text{rand}}(t)$ and the corresponding probability bands are given by

$$R_{\text{rand}}(t) = \mu_I \sum_{j=1}^{t} r(j) \pm z_{\frac{\gamma+1}{2}} \sigma_I \sqrt{\sum_{j=1}^{t} r^2(j)} \qquad (12)$$

being $\hat{\mu}_I = \frac{1}{N} \sum_t I_t$, $\sigma_I^2 = \frac{1}{N-1} \sum_t (I_i - \hat{\mu}_I)$ and z is the $100\,(\gamma+1)/2$ -quantile of the standard normal distribution.

If in eqn. (10) I is a random variable, then $I_j\, r(t-j+1)$ usually will take small values, and considering a large number (<100) of single inputs Ii then eqn. (10) will be a sum of random and independent variables. In this case eqn.(13) can be used without requiring that $\{I_1, \ldots, I_i, \ldots, I_n\}$ can be fitted to any distribution. It is a consequence of the Central Limit Theorem. We have also checked it by simulation using different distributions to generate $\{I_1, \ldots, I_i, \ldots, I_n\}$ and testing that eqn (13) is verified.

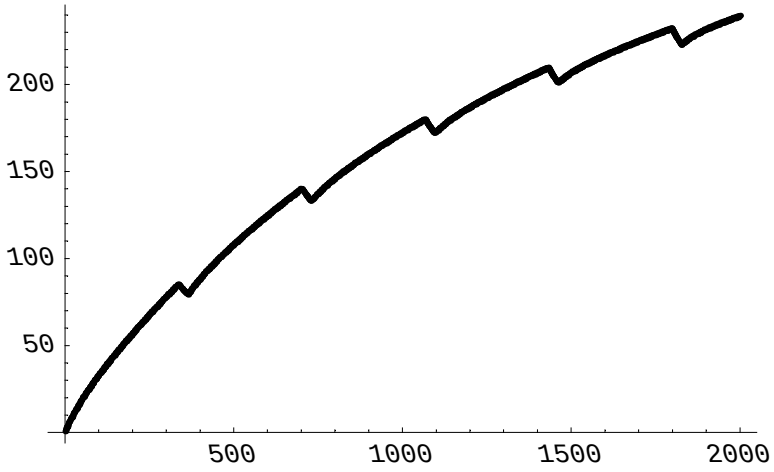
> *Example.-In the previous example we known from historical data that the relative standard deviation of the daily intakes for workers of this area is about 20%, that is $\sigma_I / \mu_I = 0.2$.*

Eqn (13) is applied (with $\gamma = 0.95$) for computing the upper and lower limit {uL,lL}

```
In[35]:= rr1 = ListConvolve[ workingdays, lungret, {-days, 1}, 0];
         rr2 = ListConvolve[ workingdays, lungret, {-days, 1}, 0]^2;
```

```
In[37]:= {uL, avg, lL} = Module[{z, s, k, d},
          z = 2; s = 0.2 avgintakewd; k = z * s * √rr2;
            d = Range[days]; {Transpose[{d, avgintakewd rr1 + k}],
             Transpose[{d, avgintakewd rr1}], Transpose[{d, avgintakewd rr1 - k}]}];
```

```
In[38]:= ListPlot[avg]
```




```
Out[38]= - Graphics -
```

```
In[39]:= Fig3 = FilledListPlot[lL, uL, AxesLabel → {"days", "Bq"}];
```

On the day 2000 the average, upper and lower limits are

```
In[40]:= {Last[uL], Last[avg], Last[lL]}
```

```
Out[40]= {{2000, 335.62}, {2000, 239.728}, {2000, 143.837}}
```

That it is $\mu_I = 10$; $\sigma_I = 0.2\ \mu_I = 2$; $\sum_{j=1}^{t} r(j) = 23.97$; $\sum_{j=1}^{t} r^2(j) = 574.70$; them the estimated lung content is BqU (computed with a confidence interval of 95%, z ≈ 2), and hence 143.8 BqU ≤ $RA_{Lung}(2000)$ ≤335.6 BqU.

It can be compared with the value obtaining assuming an chronic constant intake

```
In[41]:= avgintake * LungsRetention[1, AMADAdultW[5], S, 2000, 0, IntakeType → "Constant"]
```

```
Out[41]= 239.883
```

```
In[42]:= Clear[qLungs5S, days, totalintake, inputdata,
          avgintake, avgintakewd, workingdays, rr1, rr2, uL, avg, lL]
```

The program has a specific input and output for random intakes. The estimated daily intakes average and their standard deviation, calculated using historical data, must be introduced. It will also be indicated the number of working days per week, so if the worker rests at the weekend the program will take $I_j = 0$ for $j = 7k$ and $j = 7k-1, k = \{1, 2, \ldots\}$.

> *Predicted urine excretion (BqU/day) for a worker where he will work during 5 days per week in an area being exposed to uranium aerosols (type S, AMAD 5 μm and $\lambda_R \to 0$). The estimated average daily intake in this area is 3.3 BqU with a standard deviation of 5.1 BqU. The worker was previously exposed to a total intake of 5100 BqU from 1995-05-13 to 2005-10-13. The effect of the weekends without exposures can be observed.*

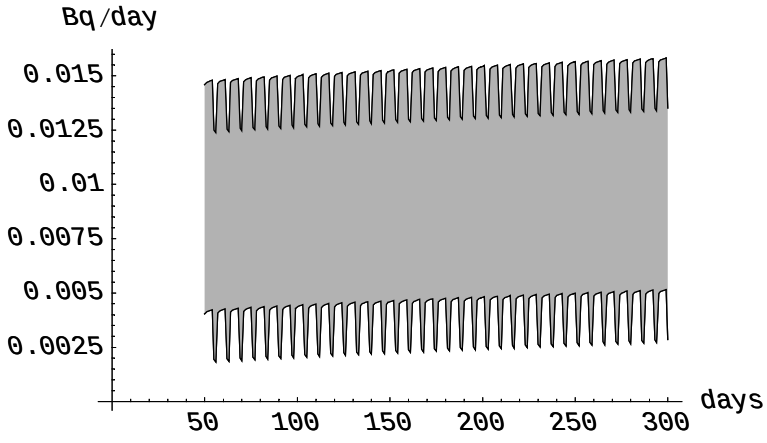
```
In[43]:= {urineExc, faecalExc, wholebodyRet} =
           {qDailyUrine[t], qDailyFaecal[t], qWholebody[t]} /. BiokdataReport[uranium,
            "Inhalation", "Acute", "Automatic", 1, AMADAdultW[5], S, 0.002, t, 0];

In[44]:= totaltime = Round[
           (FromDate[{2005, 10, 13, 0, 0, 0}] - FromDate[{1995, 5, 13, 0, 0, 0}]) / (3600 * 24)];
```

Now it is applied the function **qRandom** (See in Biokmod Help: Advance function)

```
In[45]:= sol = qRandom[5100, totaltime, urineExc, 3.3, 5.1, 1.96, 300, 5, t];

In[46]:= {days, me, int, ul, ll} = Transpose[sol];
```

The blue color represents the confidence interval for the daily urine excretion, it can be observed the effect of the weekeng where there are not intakes.

```
In[47]:= FilledListPlot[Transpose[{days, ll}],
           Transpose[{days, ul}], AxesLabel → {"days", "Bq/day"}];
```



Disintegrations

The nuclear transformations $U_i(t)$ that will happen up to time τ in a compartment i as consequence of the isotope content given by $q_i(t)$ are calculated using the eqn. (14)

$$U_i(\tau) = f_c \int_0^t q_i(t)\, dt \qquad (13)$$

where f_c is a conversion factor applied to give the nuclear transformations in the desired units. So fc = 8.65×10^{-4} (in s d^{-1}) to give $U_i(\tau)$ in Bq when t is in days and $q_i(t)$ is in Bq.

$U_i(t)$ is widely used in internal dosimetry, for example to calculate the commitment dose. In some publications (examples: apart. 9.4 in ICRP 66 or Loevinger 1988) $U_i(t)$ is usually computed using the mean residence times corrected with some mathematical tricks. It is already an approximated method. BIOKMOD computes analytically the eqn. (14) obtaining the exact solution.

Here they are given the evolution of accumulated disintegrations in the different comparments for iodine 131 ($t_{1/2}$ = 8.0 *d*)

```
In[48]:= Disintegrations["I", "Ingestion", 1, 1, t , Log[2] / 8] // Chop

Out[48]= {{ST, 3587.05 - 3587.05 e^-24.0866 t}, {SI, 0}, {B,
    30366.2 + 4055.57 e^-24.0866 t - 34166.3 e^-2.85919 t + 496.248 e^-0.14679 t - 751.665 e^-0.0929673 t},
   {ULI, 97.3654 - 0.0000264787 e^-24.0866 t + 0.389808 e^-2.85919 t -
    1.3581 e^-1.88664 t + 193.414 e^-0.14679 t - 289.811 e^-0.0929673 t},
   {LLI, 161.283 + 2.07224 ×10^-6 e^-24.0866 t - 0.395846 e^-2.85919 t + 3.05573 e^-1.88664 t -
    9.38874 e^-1.08664 t + 370.424 e^-0.14679 t - 524.979 e^-0.0929673 t}, {Thyroid,
    265014. - 140.606 e^-24.0866 t + 10282.2 e^-2.85919 t - 8017.6 e^-0.14679 t - 267138. e^-0.0929673 t},
   {UB_Content, 4876.05 - 655.925 e^-24.0866 t + 3007.06 e^-12.0866 t -
    7186.21 e^-2.85919 t + 80.6647 e^-0.14679 t - 121.634 e^-0.0929673 t}, {Other,
    15900.8 + 0.0508832 e^-24.0866 t - 32.8161 e^-2.85919 t + 29129. e^-0.14679 t - 44997.1 e^-0.0929673 t}}
```

Now the accumulated disintegrations for *t* = {{1.0, 10, 100, 365.35*50} days are obtained

```
In[49]:= Disintegrations["I", "Ingestion", 1, 1,
          {1.0, 10, 100, 365.35 * 50}, Log[2] / 8, DisintegrationReport → "True"]
```

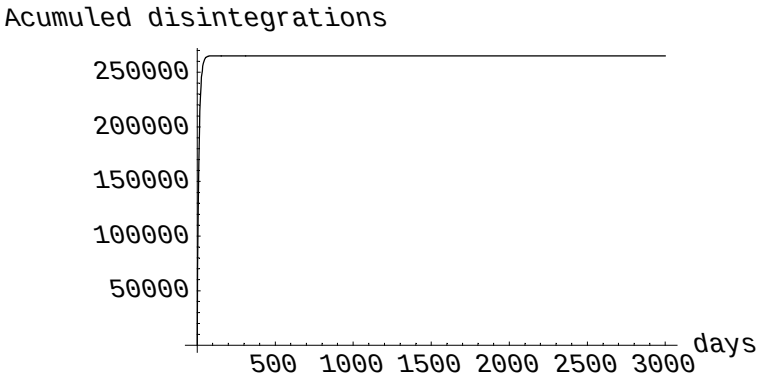
Out[49]//TableForm=

Compartment	1. day	10 day	100 day	18267.5 day
ST	3587.05	3587.05	3587.05	3587.05
SI	0.	0.	0.	0.
B	28151.5	30183.9	30366.1	30366.2
ULI	0.107423	27.5461	97.3389	97.3654
LLI	0.0357653	39.4318	161.235	161.283
Thyroid	15258.	157732.	264989.	265014.
UB_Content	4423.	4846.63	4876.04	4876.05
Other	48.7374	4852.82	15896.7	15900.8

Here it is shown the accumulated disintegration in the thyroid of I 131 as function of the time.

```
In[50]:= disThyIodine131[t_] = q2[t] /. BiokdataReport[iodine,
            "Ingestion", "Acute", "Disintegrations", 1, 1, t, Log[2] / 8];
```

```
In[51]:= Plot[disThyIodine131[t], {t, 0, 3000}, PlotRange → All,
          AxesLabel → {"days", "Acumuled disintegrations"}]
```




```
Out[51]= - Graphics -
```

Sensitivity and uncertainty analysis

The estimation of isotope content in a compartment or region involves many uncertainties even assuming that the ICRP metabolic models are a good representation of the real behaviour of the particles intake in the human body. This is so because most of the true values of the parameters at a real situation are unknown. The parameters usually applied are based on the reference values given in ICRPs.

Let's be $r(t)$ expressed as function of certain parameters $\{k_1, \ldots, k_r\}$ with their associated uncertainties: $\{u(k_1), \ldots u(k_r)\}$, then

$$r(t) = F(k_1, \ldots, k_n, t) \pm u_C(t) \qquad (14)$$

being $u_C(t)$ the combined standard uncertainty.

Assuming that $\{k_1, \ldots, k_r\}$ are uncorrelated and taking the first-order Taylor series terms of $F(k_1, \ldots, k_n, \lambda, t)$, then $u_C(t)$ can be evaluated using

$$u_c^2(r(t)) = \sum_{i=1}^{r} \left(\frac{\partial F}{\partial k_i}\right)^2 u^2(k_i) \qquad (15)$$

This is the expression used by BIOKMOD.

Of course, eqn (16) can be only applied when we can obtain the analytical solution of the model as function of the parameters $\{k_1, \ldots, k_r\}$, but it is only possible when the model not involve recycling and in some particular cases of models with recycling. No recycling models can be discomposed in catenary branches (Skrable et al, 1974), then, when $\{k_i \neq k_j\}$, the solution can be expressed as function of the parameters $\{k_1, \ldots, k_r\}$.

The HRTM is a non recycling model. So, eqn (16) can be use to study the HRTM uncertainties as it is shown in some of the examples below.

Also, it included an example where the eqn (16) is applied in a non recycling model.

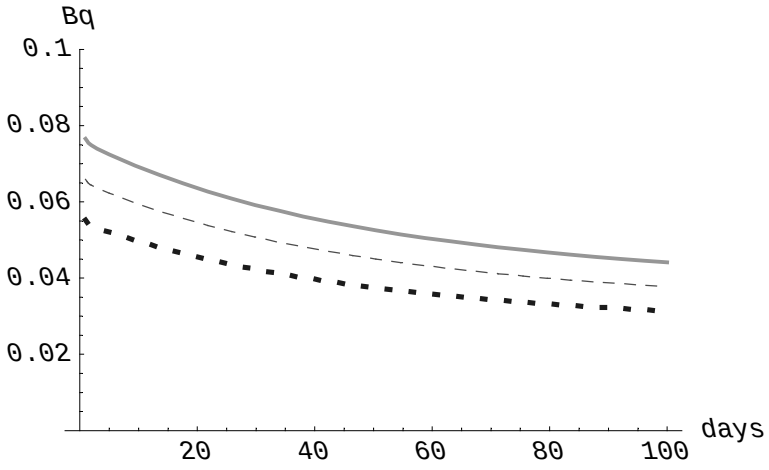
Example 1 .- Lung retention uncertainties associated with AMAD *p* and u_p

Lung retention predicted for a single intake of 1 Bq at $t = 0$, type S, decay constant negligible ($\lambda_R \to 0$) and AMAD p = 5 μm and $u_p = s_p = 0.5$ μm . The dashed lines represent the confidence interval (95%) associated with the AMAD uncertainties.

```
In[52]:= rLung[p_, t_] = LungsRetention[1, AMADfit[p], S, t, 0] // Chop;
```

The evolution of the content with their associated uncertainties for a coverage factor $k = 2$ is computed and represented as follow

```
In[53]:= yu[t1_] =
           {"mean", "uL", "lL"} /. Uin[rLung[p, t1], {p} , {σp} , 2] /. {p → 5, σp → 0.5};

In[54]:= Plot[Evaluate[yu[t]], {t, 1, 100}, PlotRange → {0, 0.1},
          AxesLabel → {"days", "Bq"}, PlotStyle → styles]
```




```
Out[54]= - Graphics -
```

It can be observed that a small difference in the AMAD value has an important consequence in the lung retention predicted. For this reason, when the value for AMAD is used to evaluate bioassay data and it it is not known then the intake estimated could have important uncertainties.

Example 2 .- Lung retention uncertainties associated with IDF_i and u_{IDF_i}

We want to evaluate for a reference worker the lung retention after an acute intake ($I = 1$ at $t = 0$) of radioactive aerosols type S and $\lambda_R \approx 0$ assuming a relative standard deviation of 10% of the IDF_i (that is $\sigma_i / IDF_i = 0.1$).

In this example we evaluate the lung uncertainties associated with IDF_i: {IDF_{AI}, $IDF_{bb\ (fast+seq)}$, IDF_{bbslow}, $IDF_{BB(fast+seq)}$, IDF_{BBslow}}

```
In[55]:= rLung[{idfAI_, idfbbfs_, idfbbslow_, idfBBfs_, idfBBslow_, ET2_, ET1_}, t_] =
           Collect[LungsRetention[1,
              {idfAI, idfbbfs, idfbbslow, idfBBfs, idfBBslow, ET2, ET1} , S, t, 0] // Chop,
            {idfAI, idfbbfs, idfbbslow, idfBBfs, idfBBslow}];
```

Calling

```
In[56]:= idf = {IDF_AI, IDF_bb (fast+seq), IDF_bbslow, IDF_"BB(fast+seq)" , IDF_BBslow, ET2, ET1};
```

```
In[57]:= idf1 = {IDF_AI, IDF_bb (fast+seq), IDF_bbslow, IDF_"BB(fast+seq)", IDF_BBslow};
```

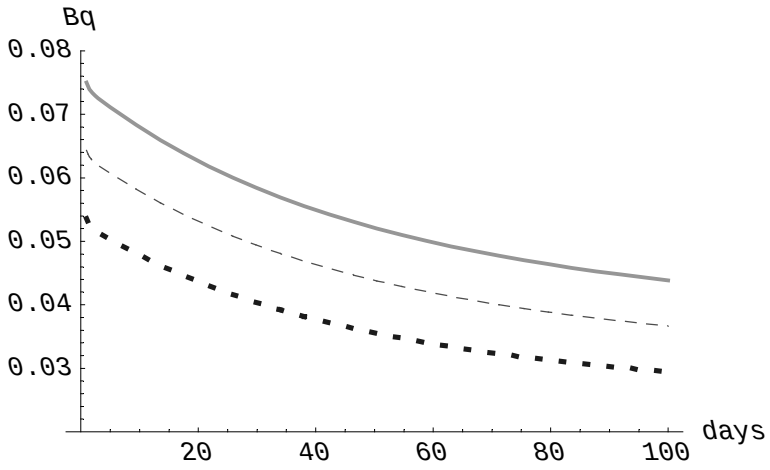
Note that $F_{\mathrm{Lung}}(t, p) = \sum_{i=1}^{5} A_i(t)\,\mathrm{IDF}_i(p)$

```
In[58]:= rLung[idf, t]
```

```
Out[58]= (0.000991017 e^-110.1 t + 6.98602×10^-6 e^-100.1 t + 0.992009 e^-10.0001 t + 0.00699301 e^-0.0001 t)
           IDF_BB (fast+seq) + (1.65221×10^-7 e^-110.1 t - 4.16099×10^-6 e^-102.1 t + 0.000303031 e^-100.12 t +
             0.000599161 e^-100.101 t + 0.0000831729 e^-100.1 t + 0.0000166334 e^-100.1 t +
             0.000165387 e^-10.0001 t - 0.00416516 e^-2.0001 t + 0.303335 e^-0.0201 t +
             0.599761 e^-0.0011 t + 0.0832562 e^-0.00022 t + 0.01665 e^-0.0001 t) IDF_AI +
           (-1.25651×10^-6 e^-110.1 t - 8.73253×10^-6 e^-102.1 t + 0.00100101 e^-100.13 t +
             6.98602×10^-6 e^-100.1 t - 0.00125777 e^-10.0001 t - 0.00874127 e^-2.0001 t +
             1.00201 e^-0.0301 t + 0.00699301 e^-0.0001 t) IDF_bbslow +
           (-6.98602×10^-6 e^-110.1 t + 0.000998003 e^-100.13 t + 6.98602×10^-6 e^-100.1 t -
             0.00699301 e^-10.0001 t + 0.999002 e^-0.0301 t + 0.00699301 e^-0.0001 t) IDF_BBslow +
           (-0.000247754 e^-110.1 t + 0.00123877 e^-102.1 t + 6.98602×10^-6 e^-100.1 t -
             0.248002 e^-10.0001 t + 1.24001 e^-2.0001 t + 0.00699301 e^-0.0001 t) IDF_bb (fast+seq)
```

```
In[59]:= idfu[t1_] = {"mean", "uL", "lL"} /. Uin[rLung[idf, t1], idf1, 0.1 idf1, 2] /.
           Thread[idf → AMADAdultW[5]];
```

```
In[60]:= fig4 = Plot[Evaluate[idfu[t]], {t, 1, 100},
           PlotRange → {0.02, 0.08}, AxesLabel → {"days", "Bq"}, PlotStyle → styles];
```



Example 3 .- Whole body uncertainties of ^{60}Co intake by ingestion associated with f_1.

The uncertainties of the retention functions associated with the rate transfer factors is other interesting topic to be investigated using analitycal methods. Howerver, it is not always posible to obtain the analitical expresion of a model as function of one o several rate transter factors k_i. In fact, it is only posible when the model not involve recicling and in some particular cases of model with recycling. The no recycling models can be descomposed in catenary branches (Skrable el al, 1988). Then, when it is verified that $k_i \neq k_j$, the retention function after an acute intake I_0 at $t = 0$ has the pattern that follows (Sanchez and Lopez -Fidalgo 1988):

$$r(I, k_1, \ldots, k_n, \lambda_R, t) = I_0 \left(\sum_{r=1}^{q} A_r(k_1, \ldots, k_n)\, e^{-a_r(k_1, \ldots, k_n)\, t} \right) e^{-\lambda_R t}$$

being $A_r(k_1, \ldots, k_n)$ and $a_r(k_1, \ldots, k_n)$ the coefficients obtained solving the model for the specific case.

```
In[61]:= K1 = k1 + K1; K2 = k2 + K2; K3 = k2 + K3;
```

```
In[62]:= ff[t_] = Catenary[b, 3, t, K, k, 0] // Simplify
```

$$\text{Out[62]}= b\,k_1\,k_2\left(\frac{e^{-t\,(K1+k_1)}}{(K1-K2+k_1-k_2)\,(K1-K3+k_1-k_2)}+\frac{e^{-t\,(K2+k_2)}}{(K2-K3)\,(-K1+K2-k_1+k_2)}+\frac{e^{-t\,(K3+k_2)}}{(-K2+K3)\,(-K1+K3-k_1+k_2)}\right)$$

We wish estimated the associated uncertainty for ^{60}Co whole body content retention, after an acute intake $I_0 = 1$ by ingestion, for fractional absorption $f_1 = 0.1$ with an associated uncertainty of $\sigma = 20\%\, f_1$.

The first step is obtained the whole body content as function of I_0 and f_1. It can be made as follows

```
In[63]:= CompartNumbers[cobalt]
```

```
Out[63]//TableForm=
1     Blood
2     Systemic A
3     Systemic B
4     Systemic C
5     Bladder
6     Urine
7     ULI
8     LLI
9     FEC
```

The GI compartments much be added

Bladder (n-4) to urine (n-3)	k[n-4,n-3] ->	12
ULI (n-2) to LLI (n-1)	k[n-2,n-1] ->	k_{ULI}
LLI (n-1) to FEC (n)	k[n-1,n] ->	k_{LLI}
SI (n+1) to ULI (n-2)	k[n+1,n-2] ->	k_{SI}
ST (n+2) to SI (n+1)	k[n+2,n+1] ->	k_{ST}
SI (n+1) to B (1)	k[n+1,1] ->	$f_B\,k_{SI}$

Then the cobalt compartmental matrix as function of f1 is

```
In[64]:= cobaltextended =
          Join[ icrp30Model[6 / 7, 1 / 7, {6, 60, 800}, {3 / 10, 1 / 10, 1 / 10}, 1 / 2],
            {{11, 10, k_ST}, {10, 1, f_B k_SI}, {10, 7, k_SI}}] /. Rationalize[Options[qGI]]
```

$$\text{Out[64]}= \left\{\left\{1, 2, \frac{3\,\text{Log}[2]}{5}\right\}, \left\{1, 3, \frac{\text{Log}[2]}{5}\right\}, \left\{1, 4, \frac{\text{Log}[2]}{5}\right\}, \left\{1, 5, \frac{6\,\text{Log}[2]}{7}\right\},\right.$$
$$\left\{1, 7, \frac{\text{Log}[2]}{7}\right\}, \left\{2, 5, \frac{\text{Log}[2]}{7}\right\}, \left\{3, 5, \frac{\text{Log}[2]}{70}\right\}, \left\{4, 5, \frac{3\,\text{Log}[2]}{2800}\right\},$$
$$\left\{2, 7, \frac{\text{Log}[2]}{42}\right\}, \left\{3, 7, \frac{\text{Log}[2]}{420}\right\}, \left\{4, 7, \frac{\text{Log}[2]}{5600}\right\}, \{5, 6, 12\},$$
$$\left.\left\{7, 8, \frac{9}{5}\right\}, \{8, 9, 1\}, \{11, 10, 24\}, \left\{10, 1, \frac{6\,f1}{1-f1}\right\}, \{10, 7, 6\}\right\}$$

The content in each compartment, for $I = 1$, is given by

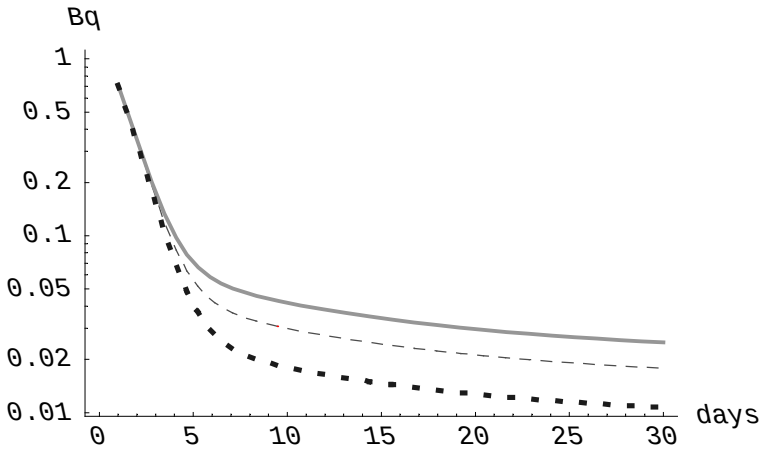
```
In[65]:= qWB =
           MatrixExp[CompartMatrix[11, cobaltextended], t].{0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1};
```

Finally, the whole body content as function of f_1 and t is (note are obtained sum all compartment content except compartment 6 (urine) and 9 (fecal)

```
In[66]:= rWBCo[fn1_, tt_] = Total[Drop[Drop[qWB, {6}], {8}]] /. {f1 → fn1, t → tt};
```

Them Uin function is applied to obtain the whole body rentencion and their associated uncertainty for $f_1 = 0.1$, $\sigma = 20\% f_1$, and taking γ =95% (then z = 2). It is been account that the half-life for ^{60}Co is 5.27 year.

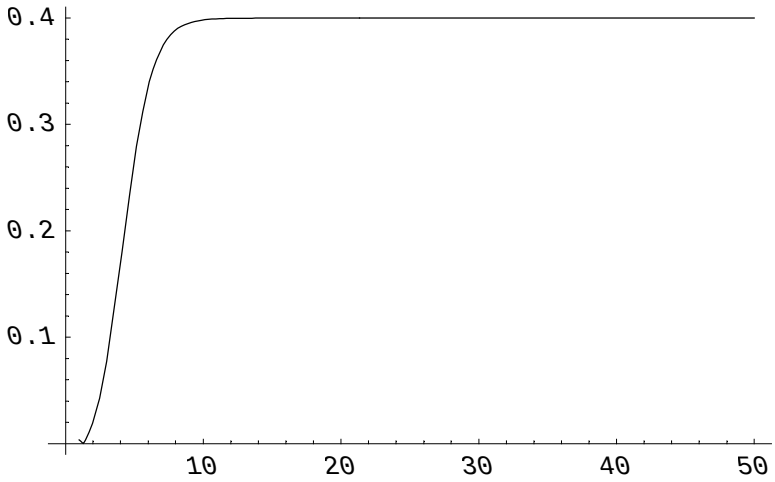
```
In[67]:= WBCou[t1_] =
           {"mean", "uL", "lL"} /. Uin[rWBCo[fn1, t1] Exp[-Log[2] / (5.27 * 365.24) t1],
              {fn1}, {0.2 fn1}, 2] /. fn1 → 0.1;

In[68]:= LogPlot[Evaluate[WBCou[t]], {t, 1, 30},
          AxesLabel → {"days", "Bq"}, PlotStyle → styles]
```




```
Out[68]= - Graphics -
```

It can be observed that the uncertainty is almost constant for t>10 days

```
In[69]:= Plot[(WBCou[t][[2]] - WBCou[t][[1]]) / WBCou[t][[1]], {t, 1, 50}]
```




```
Out[69]= - Graphics -

In[70]:= med[t_] = rWBCo[0.1, t] Exp[-Log[2] / (5.27 * 365.24) t] ;
```

Note: The solution has been tested with the given using BiokdataReport[cobalt, "Ingestion", "Acute", "BioassayTable", 1, 0. 1, 180, Log[2]/(5.27*365.24)]//Chop

```
In[71]:= Clear[cobaltextended, rWBCo, WBCou]
```

Fitting bioassay data

Basic equations

The bioassay measurements can be used to estimate the intake and, then, infer the internal dose.

Let's suppose a single intake I_0 (unkown) in $t = 0$ of radioactive particles, whose characteristics (AMAD, solubility, etc) are known, by a worker with a metabolism that responds to the ideal model for the standard worker. At time t after the intake, a bioassay is made obtaining a measurement m, with negligible uncertainties. Then, taken $m = R_A(t)$ and using eqn (4), I_0 will be calculated. However, it is an unrealistic situation; in the real world the evaluation of internal exposures using the bioassay data involves a lot of uncertainties. In fact, in an intercomparation exercise where the same cases, using the same data, have been evaluated by different experts, large discrepancies have been obtained (Doerfel 1999).

The features included in BIOKMOD can be used to evaluate and minimize the uncertainties.

If all parameters (AMAD, absorption parameters, etc.) of the model, except the quantities intakes, are assumed to be known, the only uncertainties will be the ones of the measurements, and then we have a linear statistical model. Eqn (17) and eqn (18) are applied to estimate I and its associated uncertainty. They are based on the method described by Skrable el al. (2002):

$$I = \frac{\sum_{i=1}^{N} r_{C,j}(t_i)\,\frac{m_i}{u_i^2}}{\sum_{i=1}^{N} \frac{r_{C,j}^2(t_i)}{u_i^2}} \tag{16}$$

$$u_I = \frac{1}{\sum_{i=1}^{N} \frac{r_{C,j}^2(t_i)}{u_i^2}} \tag{17}$$

where

t_i is the time from the start of the intake to the measurement i.

m_i and u_i are the measurement and their associated uncertainties (calculated with the same confidence level that u_I).

$r_{C,j}$(t), with C = {A (acute) or Cr (Chronic)} is the retention function, with $I_0 = 1$ or $I_d = 1$, associated with measurement m_i.and j is the type of bioassay (note: different kinds of bioassays can be applied simultaneously)

Eqs (17) and (18) are the apply by MLFit (See BIOKMOD Help)

Example: A worker has been exposed to an (unknown) acute intake of uranium aerosols (class S, Type S) by inhalation in $t = 0$. With a lung counter have been taken measured after the intake: {1, 10, 30, 60, 90, obtaining the values given by sampleLungUnc: $\{t_i, m_i.u_i\}$.

```
In[72]:= sampleLungUnc = {{1, 39, 5}, {10, 36, 5}, {30, 29, 5}, {60, 26, 5},
           {90, 23, 5}, {120, 22, 5}, {180, 20, 5}, {270, 18, 5}, {350, 14, 5}};

In[73]:= MLFit[sampleLungUnc, LungsRetention[1, AMADAdultW[5], S, t, 0], t]

Out[73]= {Mean → 608.545, s → 38.4612}
```

Other authors recommend (ICRP Draft 2006) the maximum likelihood method which uses the following eqn

$$\mathrm{Log}(\hat{I}) = \frac{\sum_{i=1}^{N} \left(\mathrm{Log}\left(\frac{m_{i,j}}{r_{C,j}(t_{i,j})}\right) \Big/ (\mathrm{Log}(\mathrm{SF}_{i,j})^2)\right)}{\sum_{i=1}^{N} (1/\mathrm{Log}(\mathrm{SF}_{i,j})^2} \tag{18}$$

being SF_i the scattering factor for m_i. If the bioassay data are log normally distributed then SF is the geometric standard deviation (SG) of the log-normal distribution.

```
In[74]:= MLFitLog[sampleLungUnc, LungsRetention[1, AMADAdultW[5], S, t, 0], t]

Out[74]= Mean → 603.899
```

When it is assumed, that not only the intake but also other parameters $\{k_1,\ldots, k_r\}$ are unknown (AMAD, f_1, etc.) then we have a problem of nonlinear fitting. BIOKMOD applies eqn (15) for fitting the bioassay data (It is minimized $\chi 2$):

$$(\hat{I}, k_1, \ldots, k_r): \operatorname{Arg}\operatorname*{Min}_{[I,k_1,\ldots k_r]}\left[\sum_{i=1}^{N}\left(\frac{I\, r_{C,j}(t_i, k_1, \ldots, k_r) - m_i}{u_i}\right)^2\right] \qquad (19)$$
$$\text{Restrictions: } I > 0,\ k_{1\,(\min)} \le k_1 \le k_{1\,(\max)},\ \ldots,\ k_{r(\min)} \le k_r \le k_{r(\max)}$$

If the bioassay data are log normally distributed then the below eqn is used

$$(\hat{I}, k_1, \ldots, k_r): \operatorname{Arg}\operatorname*{Min}_{[I,k_1,\ldots k_r]}\left[\sum_{i=1}^{N}\left(\frac{\operatorname{Log}[I\, r_{C,j}(t_i, k_1, \ldots, k_r)] - \operatorname{Log}[m_i]}{\mathrm{SG}_i}\right)^2\right] \qquad (20)$$
$$\text{Restrictions: } I > 0,\ k_{1\,(\min)} \le k_1 \le k_{1\,(\max)},\ \ldots,\ k_{r(\min)} \le k_r \le k_{r(\max)}$$

Eqn (20) or (21) are the apply by X2FitE (See BIOKMOD Help)

Note: If only a kind of bioassay is applied and all the uncertainties u_i are the same or they are not available can be used the specific *Mathematica* functions for fitting (e.g. FindFit)

Idenfication problems

In some occasions, using the same bioassay data, several solutions, mathematically equivalents can be obtained. For instance: For substances of type F (rapid absorption) and $f_1 = 1$ almost all particles deposited in the respiratory tract (excluded that returned directly to the environment) are transferred quickly into the blood (B). This means that in this case an intake I_0 in $t = 0$ of radioactive aerosols of AMAD p can be approximated by an instantaneous input b_B in B in t = 0 given by

$$b_B = I_0 \sum_i \mathrm{IDF}_i(p) \qquad (21)$$

$\sum_i \mathrm{IDF}_i(p)$ includes all de *IDF* factor except IDF_{ET1}.

If I_0 and p are unknown, and therefore IDF_i values will be also unknown, then eqn (20) will be verified for an infinitum number of values. So if we replace $b_B(t)$ at eqn (6) using eqn (19) it will be found that bioassay data m_i can be fitted to different values of I_0 and p. However the accumulated disintegrations, given by eqn (14), will be the same as long as that eqn.(20) be satisfied, and hence the committed effective dose E will be also the same. For instance: If it is has been obtained by fitting an intake I_1 assuming an AMAD p_1 and the true (unknown) value is I_2 with AMAD p_2, then it will be verified that $I_1 \sum_i \mathrm{IDF}_i(p_1) = I_2 \sum_i \mathrm{IDF}_i(p_2)$ and E1 ≈ E2 being $E_1 = I_1\mathrm{DCF}(p_1)$ and $E_2 = I_2\ \mathrm{DCF}(p_2)$ where $\mathrm{DCF}(p_i)$ is the dose conversion factor corresponding to an AMAD p_i.

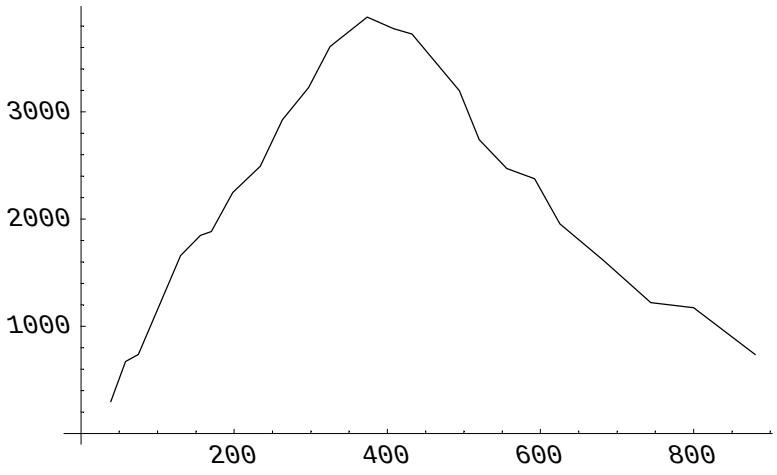
In the same way, an intake I_0 by ingestion with $f_1 = 1$ is practically equivalent to an instantaneous input $b_B = I_0$ in $t = 0$. Theses conclusions can be extended to not acute inputs as consequence of the convolution theorem.

Example 1

As a result of Chernobyl accident (26 april 1986) a male 39 years old and 80 kg (member of the public) has been exposed to continuous and unknown ingestion of Cs-137 (This data has been supplied by Ansoborlo)

The results of the whole body activity retention are given below : {time after the accident (d), activity (Bq)}

```
In[75]:= wholeData = {{39, 300}, {58, 671}, {75, 737}, {130, 1661}, {156, 1846},
          {170, 1882}, {198, 2247}, {234, 2493}, {263, 2926}, {297, 3224}, {325, 3608},
          {374, 3883}, {408, 3773}, {432, 3723}, {494, 3195}, {520, 2740}, {556, 2469},
          {592, 2375}, {625, 1954}, {682, 1614}, {744, 1221}, {800, 1174}, {880, 739}};

In[76]:= ListPlot[wholeData, PlotJoined → True]
```




```
Out[76]= - Graphics -
```

Here is evaluated the retention in the whole body for an acute intake "1" of Cs-137 in t=0 [More details in Help "Isotope"]

```
In[77]:= qWbCs137[t1_] = qWholebody[compartMatrix[caesium], 1, 1, t1, Log[2] / (30 * 365.24)]

Out[77]= -0.000177381 e^(-24.0001 t1) + 0.00165462 e^(-12.0001 t1) - 0.0230333 e^(-2.77265 t1) +
          0.0207699 e^(-1.80006 t1) - 0.0430482 e^(-1.00006 t1) + 0.139387 e^(-0.346063 t1) + 0.904447 e^(-0.00636326 t1)
```

This function supposes a daily chronic ingestion "inp" during a time t1. The ingestion of caesium stop in $t = T$, for $t > T$, inp = 0.

```
In[78]:= qConstant[1, {qWbCs137[t], t}, t, 2000]

Out[78]= { t1 must be non negative
           142.499 + 7.39086 × 10^-6 e^(-24.0001 t) - 0.000137884 e^(-12.0001 t) + 0.00830732 e^(-2.77265 t) - 0.011538
           0. - 7.39086 × 10^-6 e^(-24.0001 (-2000+t)) + 0.000137884 e^(-12.0001 (-2000+t)) - 0.00830732 e^(-2.77265 (-2000
```

It can be observed that the retention was increasing until T. We can suppose that the caesium ingestion happened until T, when it ceased. Now we can fit the experimental data to bearing in mind both periods.

```
In[79]:= model2[t1_?NumericQ, p_?NumericQ, tt_?NumericQ] := p
          qConstant[1,{qWbCs137[t],t}, t1, tt]
```

The funtion estimates the best fit for the intake I, in Bq/day, and the period T, in days

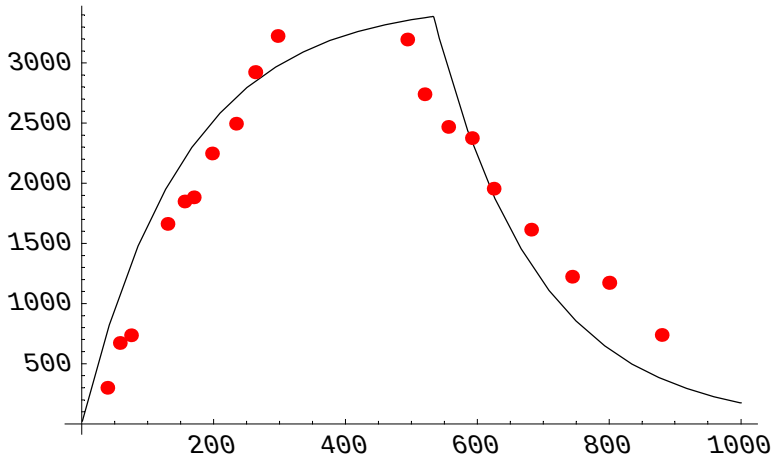
```
In[80]:= {input, timeIntake} = {p, tt} /. FindFit[wholeData, model2[t, p, tt], {p, tt}, t]

Out[80]= {24.5952, 533.961}
```

Then, the accumulated intake is

```
In[81]:= input timeIntake

Out[81]= 13132.9
```

It can be observed the good mach obtained

```
In[82]:= Plot[qConstant[input, {qWbCs137[t], t}, t1, timeIntake],
           {t1, 1, 1000}, Epilog→ {Hue[0.], PointSize[0.02], Map[Point, wholeData]}]
```




```
Out[82]= - Graphics -
```

Example 2

A researcher has been exposed to a single acute intake of ^{125}I. After the exposure it has been measured the ^{125}I in the thyroid obtaining: {Days after accidental intake, Thyroid activity measured (Bq)} = {{7, 5143},{14, 4773},{15, 4403},{21, 4070}, {28,3471}, {42, 2546}}. (Bioassay data taken from French C. S. et Al, 2003).

The data in French C. S are in nCi, they has been converted to Bq

```
In[83]:= sampleThy = {#1, 37 #2} & @@@
           {{7, 139}, {14, 129}, {15, 119}, {21, 110}, {28, 93.8}, {42, 68.8}}

Out[83]= {{7, 5143}, {14, 4773}, {15, 4403}, {21, 4070}, {28, 3470.6}, {42, 2545.6}}
```

Sol

The bioassay data have been fitted to the iodine thyroid retention function assuming an AMAD p_1 = 1 μm, p_2 = 5 μm, and p_3 = 10 μm. The solutions obtained have been (Fig. 5), respectively, I_1 = 57448.5 Bq, I_2 = 41412.1 Bq and I_3 = 46724.6 Bq. As $d_1 = \sum_i \mathrm{IDF}_i(1\ \mu\mathrm{m}) = 0.34665$; $d_2 = \sum_i \mathrm{IDF}_i(5\ \mu\mathrm{m}) = 0.480875$, $d_3 = \sum_i \mathrm{IDF}_i(5\ \mu\mathrm{m}) = 0.426196$, an hence $I_1\ d_1 = I_2\ d_2 = I_3\ d_3 = 19914$ Bq.

First it is computed the thyroid retention as funtion of t an p (previously we need to know the number used by Biokmod for thyroid compartment)

```
In[84]:= CompartNumbers[iodine]

  Out[84]//TableForm=
       1     Blood
       2     Thyroid
       3     Rest
       4     Bladder
       5     Urine
       6     ULI
       7     LLI
       8     FEC
```

```
In[85]:= qThyAmad[t_, p_] := q2[t] /. BiokdataReport[iodine, "Inhalation",
            "Acute", "CompartmentContent", 1, AMADAdultW[p], F, 1, t, Log[2] / 60.14]
```

This function is applied to obtain the retention for p (in μm) = {1, 5 , 10}

```
In[86]:= {qThyAmad1[t_], qThyAmad5[t_], qThyAmad10[t_]} = Map[qThyAmad[t, #] &, {1, 5, 10}];
```

The bioassay data are fitted using AMAD p(in μm)={1,5,10} to obtain $I(p)$

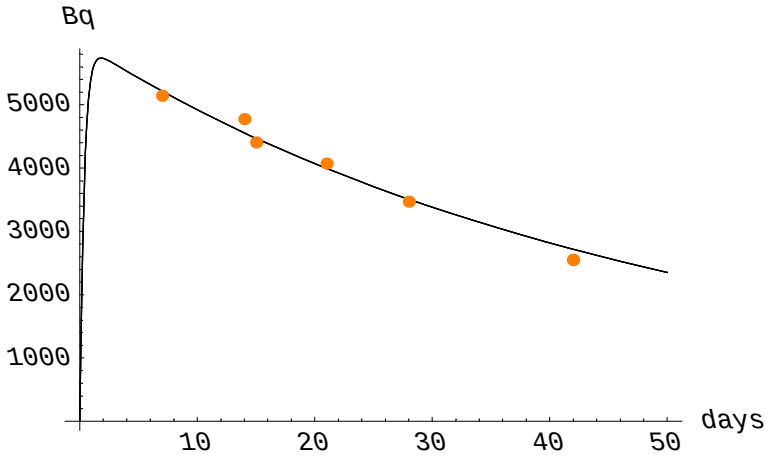
```
In[87]:= {f1, f5, f10} = Map[FindFit[sampleThy, intake #, {intake}, t] &,
            {qThyAmad1[t], qThyAmad5[t], qThyAmad10[t]}];
```

The intake $I(p)$ for p(in μm) = {1,5,10} are shown

```
In[88]:= {I1, I5, I10} = { intake /. f1, intake /. f5, intake /. f10}

Out[88]= {57448.5, 41412.1, 46724.6}
```

Fig. I-125 thyroid retention function fitted using the experimental data. The continuous line actually is three lines superposed corresponding to three combination of intakes and AMADs. It can be observed that they are indistinguishable

```
In[89]:= fig5 = Plot[{I1 qThyAmad1[t], I5 qThyAmad5[t], I10 qThyAmad10[t]},
            {t, 0, 50}, AxesLabel → {"days", "Bq"},
            Epilog :→ Map[{Orange, PointSize[.02], Point[##]} &, sampleThy] ]
```




```
Out[89]= - Graphics -
```

Now it is obtained the $\sum_i \mathrm{IRF}_i(p)$, being i = {AI, bb$_{\mathrm{fast+seq}}$, bb$_{\mathrm{slow}}$, BB$_{\mathrm{fast+seq}}$, BB$_{\mathrm{slow}}$, ET$_2$ } (It can be tested with the given in ANNEX F, Table F.1, of ICRP 66) for AMAD p (in μm) = {1,5,10}

```
In[90]:= {idf1, idf5, idf10} = Map[Plus @@ Drop[AMADAdultW[#], -1] &, {1, 5, 10}]

Out[90]= {0.34665, 0.480875, 0.426196}
```

Finally it is obtained $I(p) \sum_i \mathrm{IDF}_i(p)$ with p = {1,5,10}. It can be obserbed that $I(1) \sum_i \mathrm{IDF}_i(1) \approx I(5) \sum_i \mathrm{IDF}_i(5) \approx I(10) \sum_i \mathrm{IDF}_i(10)$.

```
In[91]:= {idf1, idf5, idf10} {I1, I5, I10}

Out[91]= {19914.5, 19914., 19913.8}
```

In the same way, taken into account that DCF for iodine 125 are DCF_1(1 μm) = 5.3 10^{-6} mSv/Bq , DCF_2 (5 μm) =7.3 10^{-6} mSv/Bq, and DCF_3 (10 μm) =6.5 10^{-6} mSv/Bq. Therefore $E_1 = I_1$ DCF_1 = 0.305 mSv; $E_2 = I_2$ DCF_2 = 0.303 mSv; $E_3 = I_3$ DCF_3 = 0.304 mSv; that is $E_1 \approx E_2 \approx E_3$.

Here are computed $E(p) = I(p)$ DCF_p . It can be observed that $E_1 \approx E_2 \approx E_3$. (being E_1= E(1); E_2= E(5); E_3= E(10));

```
In[92]:= {dcf1, dcf5, dcf10} = {5.3 10^-6, 7.3 10^-6, 6.5 10^-6};

In[93]:= {E1, E2, E3} = {I1 dcf1, I5 dcf5, I10 dcf10}

Out[93]= {0.304477, 0.302308, 0.30371}
```

Example 3

A worker has been exposed from $t = 0$ to $t = 2000$ day to a chronic intake by inhalation of 3 BqU/day of UO_2 aerosols type S and AMAD 5 μm. On the day $t = 2000$ he accidentally intakes by inhalation an unknown I quantity of UO_2. The uranium lung content has been measured using a lung body counter obtaining: {Days after accidental intake, Lung content (BqU)} ={{1,186}, {5,181}, {30,161}, {70,149}, {120,143}, {250,113}}. It is supposed that the measured uncertainties is 30 Bq with a conficence level of 95%. We wish to know the accidental quantity intaken.

Note.- The lung measurements have been simulated using a single intake of 1700 BqU with AMAD 7 μm with a random noise. The lung counters usually measure the ^{235}U but here it has been converted to give the data in BqU. The chronic and the accidental intakes are assumed to be from approximately the same enrichment (4.4% of ^{235}U).

Sol

If it is assumed an AMAD of 5 μm (recommended value by ICRP 66 when AMAD is unknown) then eqn (17) and eqn (18) can be applied. The solution obtained is that the accidental intake was 1205 ± 254 BqU. If it is supposed that the AMAD is unknown then the eqn (20) is applied obtaining 1875 BqU and AMAD 7.8 μm. These are nearer to the "true" values.

```
In[94]:= qLungU5[t_] = LungsRetention[1, AMADAdultW[5], S, t, 0];
```

The "measured" (it has been alredy simulated) data has been:

```
In[95]:= SeedRandom[101]

In[96]:= sampleLung1 = Map[{#, qConstant [3, {qLungU5[t], t}, # + 2000, 2000] +
              1700 LungsRetention[1, AMADAdultW[7], S, #, 0] +
              Random[NormalDistribution[0, 5]]} &, {1, 5, 30, 70, 120, 250}] // Round

Out[96]= {{1, 186}, {5, 181}, {30, 161}, {70, 149}, {120, 143}, {250, 113}}
```

Los calculoes estan realizados con los siguientes valores

```
In[97]:= sampleLung1 = {{1, 186}, {5, 181}, {30, 161}, {70, 149}, {120, 143}, {250, 113}};
```

The first step is subtracted the chronic intake

```
In[98]:= {timemeasured, measured} = Transpose[sampleLung1];
```

That is the lung retention due to the chronic intake

```
In[99]:= cronicLung =
          Map[{#, qConstant[3, { qLungU5[t], t}, # + 2000, 2000]} &, timemeasured] // Round

Out[99]= {{1, 108}, {5, 107}, {30, 104}, {70, 99}, {120, 95}, {250, 85}}
```

The total retention minus the chronic retention gives the lung retention due to the accidental intake

```
In[100]:=
      sampleLung2 = Transpose[{timemeasured, Transpose[sampleLung1 - cronicLung][[2]]}]

Out[100]=
      {{1, 78}, {5, 74}, {30, 57}, {70, 50}, {120, 48}, {250, 28}}
```

```
In[101]:=
Clear[int, p]

In[102]:=
model1[t_, int_, p_] = LungsRetention[int, AMADfit[p], S, t, 0];

In[103]:=
{inputAcute, pp} =
 {int, p} /. FindFit[sampleLung2, model1[t, int, p], {{int, 500, 1000}, {p, 3, 10}}, t]

Out[103]=
{1875.69, 7.83468}
```

Here is fitted adding the measured uncertainties (30 Bq)

```
In[104]:=
sampleLungUnc2 = Map[Append[#, 30] &, sampleLung2];

In[105]:=
sampleLungUnc2

Out[105]=
{{1, 78, 30}, {5, 74, 30}, {30, 57, 30}, {70, 50, 30}, {120, 48, 30}, {250, 28, 30}}
```

If the AMAD 5μm is assumed , then

```
In[106]:=
MLFit[sampleLungUnc2, LungsRetention[1, AMADAdultW[5], S, t, 0], t]

Out[106]=
{Mean → 1205.28, s → 253.809}
```

If the the AMAD fitted is assumed, then

```
In[107]:=
MLFit[sampleLungUnc2, LungsRetention[1, AMADAdultW[pp], S, t, 0], t]

Out[107]=
{Mean → 1900.98, s → 400.305}
```

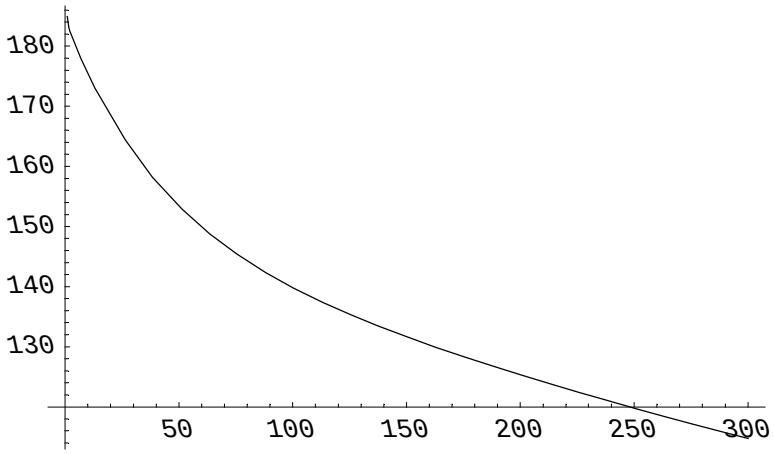
Note that the solution is the same. It happens becouse the uncertainties are the same for all the measurements.

```
In[108]:=
FindMinimum[X2FitE[{int, p}, sampleLungUnc2, model1[t, int, p], t],
 {int, 1000, 3000}, {p, 3, 8}]

Out[108]=
{0.11186, {int → 1875.69, p → 7.83468}}
```

> *Fig6..- Predicted lung retention after an acute intake assuming a previous chronic intake The dashed line represents the underlying contribution from the chronic intake.*

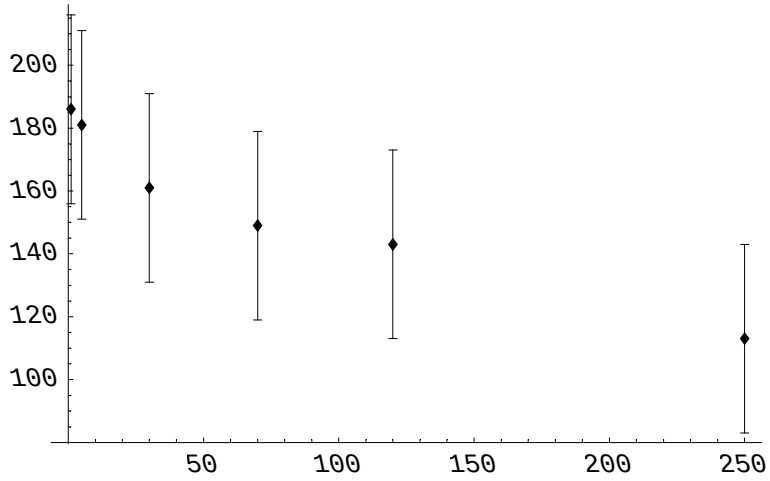
```
In[109]:=
qLungU7[t_] = LungsRetention[1, AMADAdultW[pp], S, t, 0];
```

```
In[110]:=
PlotLung1 = Plot[qConstant[3, { qLungU5[t], t}, t1 + 2000, 2000] +
    inputAcute qLungU7[t1], {t1, 1, 300}];
```



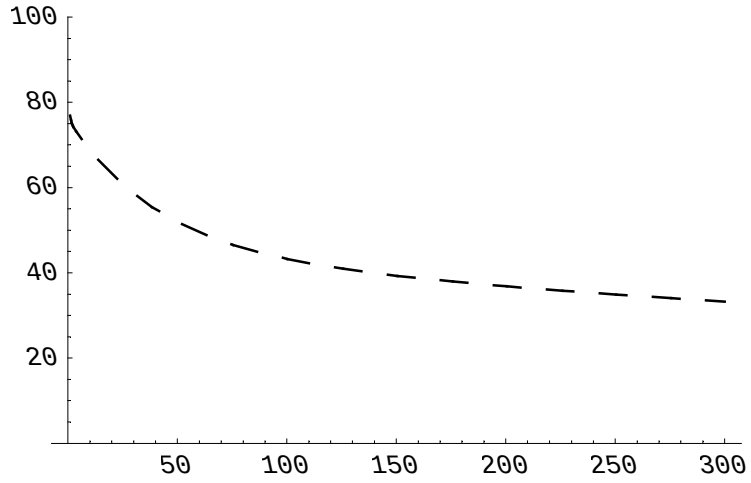

```
In[111]:=
sampleLung3 = Map[Append[{#}, ErrorBar[30 ]] &, sampleLung1];
```

```
In[112]:=
PlotLung2 = MultipleListPlot[sampleLung3]
```



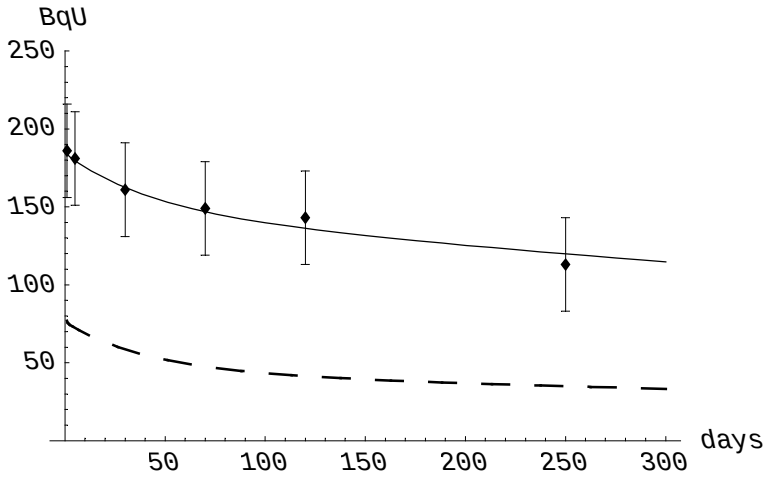

```
Out[112]=
- Graphics -
```

```
In[113]:=
PlotLung3 = Plot[inputAcute qLungU7[t], {t, 1, 300}, PlotRange → {0, 100},
  PlotStyle → {AbsoluteThickness[1], AbsoluteDashing[{10, 10}]}]
```




```
Out[113]=
- Graphics -
```

```
In[114]:=
fig6 = Show[PlotLung1, PlotLung2,
   PlotLung3, PlotRange → {0, 250}, AxesLabel → {"days", "BqU"}];
```



Example 4

An operator has been exposed to an simple accidental intake by inhalation of ^{60}Co. The cobalt form was metal and oxide. A program of in-vivo monitoring was carried out ten days after the event and continued up to 3 years (Table 2). Urine samples were also taken (Table 2). Additional information: It is recommended to assume that the whole body and urine measurements be approximated by a log-normal distribution with a geometric standard deviation of 1.07 Bq and 1.8 Bq

(Data from ICRP (Draft 2006): Draft guidance document: Bioassay data interpretation (Annex B) http://www.icrp.org/news_guidance.asp [Accessed 15 june 2006])

sol 1

This is a case where multiple data sets must be fitted to a nonlinear model.

The default parameter recommended by ICRP 78 for cobalt oxide values are: AMAD 5 μm, absorption Type S, f1 value 0.05. If we applied the chi squared test ($\chi 2$) the goodness of the data fitted is very bad. For this reason we used the eqn (21) assuming that p (AMAD value in µm), the absorption rates: $\{s_{pt}, s_p, s_t\}$ and f1 are unknown. This is a case where multiple data sets must be fitted to a nonlinear model. To avoid a too long time of computation some restrictions about the parameters fitted were established. Also the number of step to find the minimum of eqn (21) was limited. The best fit obtained corresponds to 398.5 kBq with AMAD 5.5 μm, $\{s_{pt}, s_p, s_t\}$ ={10, 90, 0.0007} and f1 = 0.1. The committed effective dose, E(50) calculated using these values is: 4.5 mSv.

The method applied in ICRP (Draft 2006) is different. There is taken as AMAD 5 μm, then is applied the eq. (19) several times: One set with with f1= 0.1 testing mixture of absorption Types S and M other repeating the procedure with f1 = 0.05. In each test is obtained the Ji2 value. Finally is chosen the solution where the Ji2 is smallest one. The computation has been made using IMBA Professional. The solution reported is 404 kBq and 5 mSv

```
In[115]:=
     sampleWBCo60 =
       {{10, 23900}, {14, 29200}, {17, 20100}, {20, 18200}, {27, 21600}, {40, 19800},
        {60, 21600}, {80, 17500}, {190, 11600}, {370, 8100}, {747, 4800}, {1010, 2700}};
```

Table 1 Whole body activity measurement

```
In[116]:=
     TableForm[sampleWBCo60,
      TableHeadings→ {None, {"Time of measurement\n after intake in days",
         "Whole body\n activity of 60Co (Bq)"}}]
```

```
Out[116]//TableForm=
     Time of measurement       Whole body
      after intake in days      activity of 60Co (Bq)
     10                        23900
     14                        29200
     17                        20100
     20                        18200
     27                        21600
     40                        19800
     60                        21600
     80                        17500
     190                       11600
     370                       8100
     747                       4800
     1010                      2700
```

```
In[117]:=
     sampleUriCo60 =
       {{14, 709}, {27, 64}, {40, 71}, {60, 37}, {80, 29}, {190, 11}, {370, 1.7}};
```

Table 2.- Urine activity measurement

```
In[118]:=
TableForm[sampleUriCo60,
 TableHeadings→ {None, {"Time of measurement\n after intake in days",
    "Daily urinary excretion\n rate of 60Co (Bq)"}}]
```

```
Out[118]//TableForm=
Time of measurement       Daily urinary excretion
 after intake in days      rate of 60Co (Bq)
14                        709
27                        64
40                        71
60                        37
80                        29
190                       11
370                       1.7
```

```
In[119]:=
sampleWBCo60L = {{10, Log[23900], Log[1.2]}, {14, Log[29200], Log[1.2]},
   {17, Log[20100], Log[1.2]}, {20, Log[18200], Log[1.2]},
   {27, Log[21600], Log[1.2]}, {40, Log[19800], Log[1.2]},
   {60, Log[21600], Log[1.2]}, {80, Log[17500], Log[1.2]},
   {190, Log[11600], Log[1.2]}, {370, Log[8100], Log[1.2]},
   {747, Log[4800], Log[1.2]}, {1010, Log[2700], Log[1.2]}};
```

```
In[120]:=
sampleUriCo60L = {{14, Log[709], Log[1.8]}, {27, Log[64], Log[1.8]},
   {40, Log[71], Log[1.8]}, {60, Log[37], Log[1.8]}, {80, Log[29], Log[1.8]},
   {190, Log[11], Log[1.8]}, {370, Log[1.7], Log[1.8]}};
```

The parameters to be fitted are Intake, AMAD p, $f_1, s_{pt}\, s_p\, s_t$.

```
In[121]:=
fitType[p_, f1_, s1_, s2_, s3_, t_] :=
 Module[{x1, x2}, {x1, x2} = {qWholebody[t1], qDailyUrine[t1]} /.
    BiokdataReport[cobalt, "Inhalation", "Acute", "Automatic", 1,
     AMADAdultW[p], {s1, s2, s3}, f1, t1, Log[2] / (5.27 * 365.24)];
  FindMinimum[X2FitE[{int}, sampleWBCo60L , Log[int x1] /. t1 → t,
    sampleUriCo60L , Log[int x2] /. t1 → t, t], {int, 10^5, 10^6}]]
```

```
In[122]:=
todos =
  Table[Flatten[{p, f1, s1, s2, s3, fitType[p, f1, s1, s2, s3, t]}], {p, 4.5, 5.5, 0.5},
   {f1, 0.06, 0.1, 0.04}, {s1, 9, 10}, {s2, 90, 100, 10}, {s3, 0.0002, 0.002, 0.0005}];
```

```
In[123]:=
todos1 = Flatten[todos, 4]; ji2 = Transpose[todos1][[6]]; ps = Position[ji2, Min[ji2]];
```

The best fit obtained correspond to

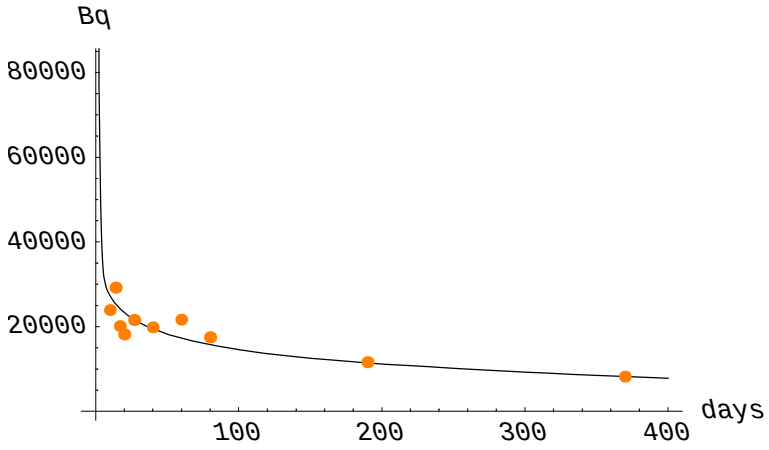
```
In[124]:=
{amadp, ff1, s1, s2, s3, min, inp} = Extract[todos1, ps][[1]]
```

```
Out[124]=
{5.5, 0.1, 10, 90, 0.0007, 15.5141, int → 398551.}
```

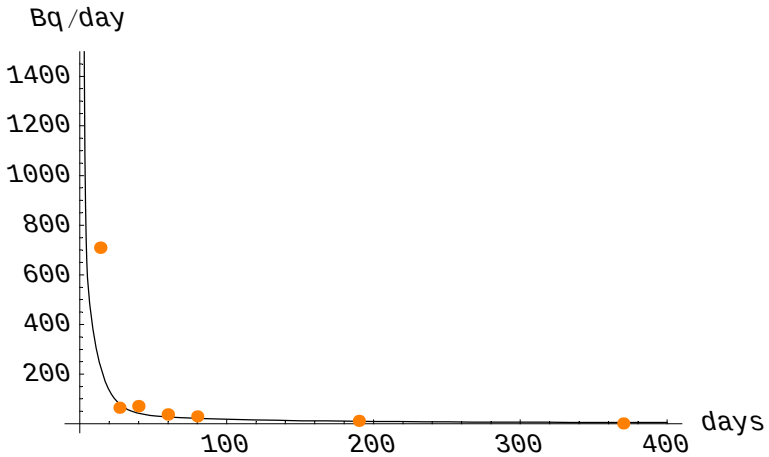
{amadp, ff1,s1,s2,s3,min,inp} = {5.5, 0.1, 10, 90, 0.0007, 15.92, int→ 398551};

Here are compared the "experimental" data with the fitted functions

```
In[125]:=
     I1 = int /. inp;

In[126]:=
     {cobaltwb[t_], cobaltURI[t_]} =
       {qWholebody[t], qDailyUrine[t]} /. BiokdataReport[ cobalt, "Inhalation", "Acute",
         "Automatic", 1, AMADAdultW[amadp] , {s1, s2, s3}, ff1, t, Log[2] / (5.27 * 365.24)];

In[127]:=
     Plot[I1 cobaltwb[t1], {t1, 1, 400}, AxesLabel → {"days", "Bq"},
      Epilog :> Map[{ Orange, PointSize[.02], Point[##]} &, sampleWBCo60]]
```




```
Out[127]=
     - Graphics -

In[128]:=
     Plot[I1 cobaltURI[t1], {t1, 1, 400}, AxesLabel → {"days", "Bq/day"},
      Epilog :> Map[{ Orange, PointSize[.02], Point[##]} &, sampleUriCo60]]
```




```
Out[128]=
     - Graphics -
```

Then we can computed the equivalent doses using the **Doses** package included in the new version of **Biokmod**. . It can be used for computing, over a period τ, the acumulated disintegration $U_s(\tau)$, the committed effective doses $e(\tau)$ and the equivalent doses $H(\tau)$. The SEE factors, require for computing $e(\tau)$ and $H(\tau)$, are included for some selected isotopes,

in the other cases the SEE factors can be introduced as input data (It can be obtained using DCAL (SEECAL). It can be downloaded at http://ordose.ornl.gov/downloads.html).

```
In[129]:=
     {amadp, ff1, s1, s2, s3, inp} = {5.5,  0.1, 10, 90, 0.0007, 398551};

In[130]:=
     CommittedDose["Co 60", "Inhalation", inp,
      AMADAdultW[amadp], {s1, s2, s3}, ff1, 50 * 365.25]
```

Accumulted disintegration, in Bq, as function of the time

Compartment	18262.5 day
AI	1.47604×10^6
bb1	1349.24
bb2	10178.3
bbseq	512.246
BB1	390.742
BB2	13944.5
BBseq	847.09
ET2	371.238
ET1	29607.7
ETseq	7546.29
LNth	18869.5
LNet	7118.45
ST	1546.8
SI	5568.19
B	5171.07
ULI	19104.9
LLI	34377.3
Other	663196.
Liver	0.
UB_Content	493.267

Dose accumulated, in Sv, as function of the time

Sv/Bq	18262.5 day
Testes	0.000647195
Ovarius	0.00124167
Red Marrow	0.00188664
Colon	0.00203449
Lungs	0.0237358
St Wall	0.00193433
Bladder Wall	0.000860611
Mama	0.00290778
Liver	0.00232751
Oesophagus	0.00344612
Thyroid	0.00162156
Skin	0.000975408
Bone Surface	0.00161858
Muscle	0.00160571
Brain	0.000729113
Small intestine	0.00132312
Kidneys	0.0015073
Pancreas	0.00232831
Spleen	0.00233603
Thymus	0.00344612
Uterus	0.00101719
Adrenals	0.00288376
Extrathoracic airways	0.0203698
Effective, e(50)	0.00446216

The committed effective dose, E(50) calculated using these values is: 4.46 mSv

Conclusion

There are some good computer codes that can be applied in the interpretation of bioassay data. We have developed a new one, BIOKMOD, with some innovations that can be useful mainly for advanced studies. The standard version of BIOKMOD is available for free download at the author web side: http://web.usal.es/guillermo. Furthermore there is a web version (available at http://www3.enusa.es/webMathematica/Public/biokmod.html , sponsored by ENUSA Industrias Avanzadas. S.A) and therefore it can be used everywhere where an internet connection exists.

BIOKMOD has been used in the evaluation of internal exposures using the bioassay data: Multiple constant and random intakes in occupational exposures taking into account periods without intake (weekends, holidays, etc.) has been described; an analytical method to evaluate the statistical uncertainties associated with the biokinetic model has been developed; non linear techniques have been applied to estimate the intakes using bioassay data.

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