

An Analytical Method for Solving Biokinetic Particle Intake Models involving Recycling and Random Inputs: Application to Wrenn Uranium Model and to Evaluate Uncertainties in Retention for Workers Exposed to Radioactive Airborne

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1. Introduction

Compartmental modelling and simulation is widely applied in internal dosimetry and bioassay analysis prediction. In many occasions analytical solutions have been impractical so far. New computer programs that include symbolic capability, like *Mathematica* (Wolfram 1999), can be used in solving compartmental systems. We have developed an analytical method using *Mathematica* to solve a biokinetic particle intake model involving recycling and random intake. Size and solubility are variable. This method is applied to a uranium model based on ICRP 30/54 with Wrenn modifications (Wrenn *et al*, 1995). According to Wrenn this model is more appropriated for uranium than the newest ICRP 66 model, also the ICRP 66 only included the respiratory tract. The lung retention and the urinary and fecal excretion of inhaled uranium are calculated for acute and chronic intake. The acute solutions have been applied to simulation of the lung retention in workers that are exposed to random uranium airborne. The simulation shows the average lung retention as function of time and their statistical uncertainties. Experimental data of intakes, for workers moving in areas where the activity and the particle sizes are periodically monitored with air samplers, are used. The method can be applied to other models and other kind of radioisotopes. All these methods can be useful for the design and the conduct of the air control and for the bioassay monitoring.

2. The model

The models of ICRP 30, with Wrenn modifications, for the respiratory and gastrointestinal system were used. A detailed description can be found in Wrenn *et al* 1994 and 1995. A representation of the model is shown in Fig. 1 where **a, b, c, d, e, f, g, h**, represent the **Respiratory Tract (RT)** and **i** and **j** the lymphatic nodes, **ST, SI, ULI, LLI** represent the **Gastrointestinal (GI) System**, and **FEC** represents the fecal excretion. The flow goes from **RT** to **Urinary System (US)** that starts in **p** compartment where one fraction is recycling to skeletal (**O₁**) and one compartment called **O₂**, other is eliminated to compartments representative of Kidney (**K₁, K₂**) and other is eliminated to direct urine excretion **U**.

The main modifications to ICRP 30 are the following:

- a) **Respiratory Tract.**- The retention fractions, F_k , in **e** and **g** compartments have been modified for class Y airborne. Table 1 reflects these changes.

Table 1. Respiratory tract modifications for Class Y.

| Compartment | ICRP-30 Fraction | Modified Fraction |
|-------------|------------------|-------------------|
| e | 0.05 | 0.40 |
| g | 0.40 | 0.05 |

The depositions factor are the same as ICRP 30. We have found a fit to $D_M(x)$ and x (AMAD) given by eq. M are the regions $M = NP, TB$ and P .

$$D_M(x) = a_M + b_M \log x + c_M \log^2 x + d_M \log^3 x \quad (1)$$

where:

For $M = NP$, $a_{NP} = 0.311294$, $b_{NP} = 0.254937$, $c_{NP} = 0.0320926$, $d_{NP} = -0.0161474$,
 For $M = P$, $a_P = 0.251181$, $b_P = -0.12741$, $c_L = 0.0173474$, $d_P = 0$,
 For $M = TB$, $a_{TB} = 0.08$, $b_{TB} = 0$, $c_{TB} = 0$, $d_{TB} = 0$

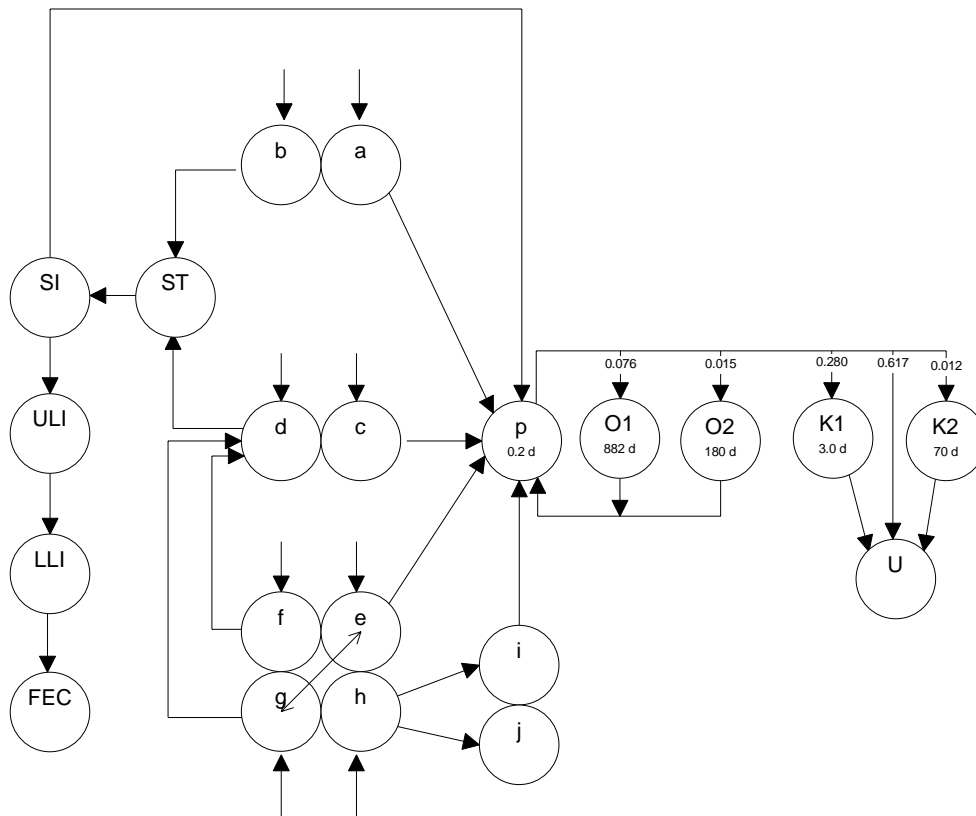


Figure 1. Modified ICRP 30 Model (Wrenn 1995)

b) **f₁ factor modifications** - Table 2 shows the modification of ICRP 30.

Table 2.- f₁ factor modifications

| Class | ICRP-30/54 | Modified factor |
|-------|------------|-----------------|
| D,W | 0.05 | 0.007 |
| Y | 0.002 | 0.002 |

c) **Urinary System.**- The metabolic model of ICRP has been changed as it is shown on the left side of Fig.1. We can see that the new model consists of:

- i) One input compartment **p** from **Respiratory Tract**. The biological half-time of **p** is 0.2 days. A fraction (0.617) is eliminated from **p** directly to urine, and the rest goes to other compartments.
- ii) A single skeletal compartment (**O₁**) that has a biological half-time of 882 days with a fractional deposition of 0.076 and Other (**O₂**) that has a biological half-time of 180 days with a fractional deposition of 0.015.
- iii) Two compartments **K₁** and **K₂**, that represent the kidney. **K₁** has a biological half-time of 3 days and a fractional deposition of 0.280 and **K₂** has a biological half-time of 70 days and a fractional deposition of 0.012.

3. Mathematical formulation

The set of differential equations for **Respiratory Tract** and **Gastrointestinal (GI) System** are the same as the ones of ICRP 30 (see also Bertelli and Lipstein 1987).

For **Urinary system** (**p, O₁, O₂, K₁, K₂** and **U**) the ordinary system of equation are (2) to (6) where:

$q_k(t)$ represents the amount of the radionuclide R accumulated in the compartment k as function of time t .
 $k = a, c, e, i, p, K_1, K_2, O_1, O_2$,
 λ_k is the biological clearance rate from compartment k . It is function of class of solubility.
 λ_R is the radioactive decay constant of radionuclide R.
 f_k is the fraction going to compartment k

For the plasma

$$\begin{aligned} \frac{d}{dt} q_p(t) = & \lambda_a q_a(t) + \lambda_c q_c(t) + \lambda_e q_e(t) + \lambda_i q_i(t) \\ & + \lambda_B q_{SI}(t) - (\lambda_p + \lambda_R) q_p(t) + \lambda_{O1} q_{O1}(t) + \lambda_{O2} q_{O2}(t) \end{aligned} \quad (2)$$

For the organs O1 and O2

$$\frac{d}{dt} q_{O1}(t) = f_{O1} \lambda_p q_p(t) - (\lambda_{O1} + \lambda_R) q_{O1}(t) \quad (3)$$

$$\frac{d}{dt} q_{O2}(t) = f_{O2} \lambda_p q_p(t) - (\lambda_{O2} + \lambda_R) q_{O2}(t) \quad (4)$$

For kidney compartments

$$\frac{d}{dt} q_{K1}(t) = f_{K1} \lambda_p q_p(t) - (\lambda_{K1} + \lambda_R) q_{K1}(t) \quad (5)$$

$$\frac{d}{dt} q_{K2}(t) = f_{K2} \lambda_p q_p(t) - (\lambda_{K2} + \lambda_R) q_{K2}(t) \quad (6)$$

The rate of urinary excretion dq_U/dt is given by:

$$\frac{d}{dt} q_U(t) = f_U \lambda_p q_p(t) + \lambda_{K1} q_{K1}(t) + \lambda_{K2} q_{K2}(t) - \lambda_R q_U(t) \quad (7)$$

where $q_U(t)$ is the total amount accumulated in urine.

4. Mathematical solution assuming accurate and chronic intake

The solutions of **Respiratory Tract (RT)** and **Gastrointestinal (GI)** System are well known. The analytical resolution technique of eigenvalues and eigenvectors or the Skrable method (Skrable *et al.*, 1979) can be applied. We have used the symbolic capability of *Mathematica*. To obtain a solution as a function of size of airborne (AMAD) we have divided the set of equation in three separate subsystems depending on contain $D_{NP}(x)$, or $D_{TB}(x)$ or $D_P(x)$. The final solution will be the sum solution of each subsystem. The solutions for an accurate intake in $t=0$ (with a determined AMAD, $x = x_s$ and class of compound S (S=D, W, Y in ICRP 30) always of the form:

$$q_k(t, x, S)_{x=x_s, S=S_c} = I(x, S)_{x=x_s, S=S_c} \left(\sum_{M,i} D_M(x, S) C_{NP,S}^h e^{a_{h,S} t} \right)_{x=x_s, S=S_c} \quad (8)$$

where $D_M(x)$ is given by eq(1). (It is not true when two subsequent compartments have the same half-time, but in this case we applied the usual criterion to overcome by attributing a little difference (<5%) in the half-time of these compartments).

The solutions for chronic intake are derived directly from accurate solutions by integration.

We have resolved the model for a size of airborne x (AMAD) and class of solubility S that we have supposed to

be constants. We have expressed the solutions as function of x and S . We can obtain the solution for a specific x and S values introducing in the equation the x value and by substituting the transfer factors for this class of solubility S .

Following these criteria we have developed a *Mathematica* program to obtain the analytical solutions for a accurate intake and for a continuous intake as function of time. The airborne size (AMAD), the biological half-time, and the fraction of transference can be changed.

In many occasions we are interested in the Intake Retention Fraction (*IRF*) corresponding to a type of measurement (**Lung retention, fecal or urinary excretion**). It is defined as follow.

$$IRF(t) = \frac{Q(t)}{I} \quad (9)$$

$Q(t)$ = Lung deposition or daily excretion rate (urine or feces) estimated by computation or by experimental measurement.

I = Estimated of intake with units the same as $Q(t)$.

4.1 Respiratory tract

The solution to RT is given by

$$q_{TR}(t, x)_{x=x_s} = I(x)_{x=x_s} [D_{NP}(x)_{x=x_s} TR_{NP}(t) + D_{TB} TR_{TB}(t) + D_P(x)_{x=x_s} TR_P(t)] \quad (10)$$

where

$$TR_{NP} = F_a e^{-\lambda_a t} + F_b e^{-\lambda_b t}$$

$$TR_{TB} = F_c e^{-\lambda_c t} + F_d e^{-\lambda_d t}$$

$$TR_P = F_f \frac{\lambda_f}{\lambda_d - \lambda_f} (e^{-\lambda_f t} - e^{-\lambda_d t}) + F_g \frac{\lambda_g}{\lambda_d - \lambda_g} (e^{-\lambda_g t} - e^{-\lambda_d t}) + F_e e^{-\lambda_e t} + \\ + F_f e^{-\lambda_f t} + F_g e^{-\lambda_g t} + F_h e^{-\lambda_h t} + F_h F_i \frac{\lambda_h}{\lambda_i - \lambda_h} (e^{-\lambda_h t} - e^{-\lambda_i t}) + F_h F_j (I - e^{-\lambda_h t})$$

(For the classes D and W, according to ICRP 30, $F_j=0$, and so the last term is „0,,)

The **lung retention**, $q_L(t, x)$, is given by the deposition in the regions TB and P. Then:

$$q_L(t, x)_{x=x_s} = I(x)_{x=x_s} [D_{TB} TR_{TB}(t) + D_P(x)_{x=x_s} TR_P(t)] \quad (11)$$

To ICRP 30 with Wrenn modified factors, to $x=1$, and $I=1$ the lung deposition (we can interpreted also as the *IRF*(t) for lung) are:

$$q_L^Y(t, x)_{x=1} = 0.1507 2^{-t/500} + 0.125 2^{-t} \quad (12)$$

$$q_L^W(t, x)_{x=1} = 0.1507 2^{-t/50} + 0.0004 e^{-0.01386 t} \quad (13)$$

$$q_L^Y(t, x)_{x=1} = 0.2511814 e^{-1.3863 t} \quad (14)$$

Integrating the acute expressions we obtain the solutions for continuous intake.

Figs 2, 3 and 4 show the solution (*IRF*(t) for lung) for accurate and continuous intake for different class of compounds and AMADs (*IRF*(t) for lung)

4.2 Gastrointestinal and fecal excretion

The complete solutions are too long to be shown here (the *Mathematica* program is available by <mailto:gsl@fab.enusa.es>).

Figs.5 to 6 show the solution (*IRF(t)* for fecal) for accurate and continuous intake for different class of compounds and AMADs.

4.3 Urine excretion

The solution in this case is more complicated because it involves recycling. We have used Laplace Transform. The flow to **p** from compartments **a**, **c**, **e**, **i** and **SI**, are known because $q_a(t)$, $q_c(t)$, $q_e(t)$, $q_i(t)$, $q_{SI}(t)$ have been previously evaluated. They have the usual form $q_m(t) = a_j D_M(x) \text{Exp}(b_i t)$. For this reason we can regroup in eq(2) as follows

$$\lambda_a q_a(t) + \lambda_c q_c(t) + \lambda_e q_e(t) + \lambda_i q_i(t) + \lambda_B q_{SI}(t) = I(x)_{x=x_s} \times \left(D_{NP}(x)_{x=x_s} \sum_i C_{NP}^g e^{a_{gi}t} + D_{TB} \sum_j C_{TB}^j e^{a_j t} + D_P(x)_{x=x_s} \sum_l C_P^l e^{a_{hl}t} \right) \quad (15)$$

Substituting in eq(2) and doing $I(x) = 1$ (To acute $I_o = 1$ usually Bq or mg, and to continuous $I_c = \text{Bq d}^{-1}$ or mg d^{-1}).

$$\frac{d}{dt} q_P(t) = D_{NP}(x)_{x=x_s} \sum_i C_{NP}^g e^{a_{gi}t} + D_{TB} \sum_j C_{TB}^j e^{a_j t} + D_P(x)_{x=x_s} \sum_l C_P^l e^{a_{hl}t} - (\lambda_P + \lambda_R) q_P(t) + \lambda_{O1} q_{O1}(t) + \lambda_{O2} q_{O2}(t) \quad (16)$$

We can divide eq(10) in several eqs., one for each exponential term, getting the following form:

$$\frac{d}{dt} q_P^r(t) = c_r D_M e^{-a_r t} - \lambda_P q_P^r(t) + \lambda_{O1} q_{O1}(t) + \lambda_{O2} q_{O2}(t) \quad (17)$$

We have the subsystem given by equations (17), (3)- (6) that we have solved using Laplace Transform. We obtain $q_P^r(t)$ that is the amount of the radionuclide R accumulated in compartment **p** due to the contribution of term $c_r D_M \text{Exp}(-a_r t)$. The total quantity accumulated in **p** will be:

$$q_P(t) = \sum_r q_P^r(t, x) \quad (18)$$

hence

$$\frac{d}{dt} q_U(t) = f_U \lambda_P q_P(t) + \lambda_{K1} q_{K1}(t) + \lambda_{K2} q_{K2}(t) - \lambda_R q_U(t) \quad (19)$$

that is the rate of urinary excretion.

Figs. 7 an 8 show the solution to accurate and continuous intake for class Y and $I = 1$ (or *IRF(t)* for urine) for different AMADs.

4.4 Solutions for different class of compounds and AMADs

We have obtained the solutions for a determined size and class of compound S. His extension to consider several sizes and classes of compound S is easy. We only need to evaluate x and S for each specific value and sum the results.

$$q_T(t) = \sum_{x,S} I(x,S)_{x,S} \left(\sum_{M,i} D_M(x,S) C_{NP,S}^h e^{a_{h,S}t} \right)_{x,S} \quad (20)$$

5. Mathematical solution to irregular or random intake

We can evaluate an irregular or random intake by treating it as a multiple accurate intake. We suppose that the retention function, $q(t)$, for an accurate intake is known. The total amount accumulated in a compartment or region $Q(t)$ assuming an accurate intake I_j in each instant $t = j$ -for convenience we chose t in days and j (integer) = 1, 2, ..., d - with $Q(0)$ en $t = 0$ is given by:

$$\begin{aligned} \text{For } t = 1 & \quad Q^{(k)}(1) = I^{(k)}_0 q(1) \\ \text{For } t = 2 & \quad Q^{(k)}(2) = I^{(k)}_0 q(2) + I^{(k)}_1 q(1) \\ \text{For } t = 3 & \quad Q^{(k)}(3) = I^{(k)}_0 q(3) + I^{(k)}_1 q(2) + I^{(k)}_2 q(1) \\ \dots \dots \dots & \\ \text{For } t = d & \quad Q^{(k)}(d) = I^{(k)}_0 q(d) + I^{(k)}_1 q(j-1) + \dots + I^{(k)}_{j-1} q(2) + I^{(k)}_j q(1) \end{aligned} \quad (21)$$

To calculate $Q(t)$ for irregular intake is enough substitute the I_j values in (21).

5.1 Random Intake

We are interested in evaluating the average retention $\langle Q(t) \rangle$ and their uncertainties (I_0) when the intake I is a random variable. We have applied the following procedure:

- To collect experimental data of I . We had used the daily intake of worker moving in areas where the activity and the particle sizes are periodically monitored with air sample (Sanchez, 1998)
- To find a statistical model to fit the data. We have found that our data can be fitted to a lognormal distribution (Sanchez, 1998).
- To reply the procedure of eq(21) k times simulating the $I^{(k)}$ data with the random distribution found in b) and supposing periodic interval without intake to consider weekend and annual vacations. We have used calculated the lung retention function to UO₂ (Class Y), and AMAD 1 mm given by (12). We have compared the random solution with continuous intake, with a daily intake average $\hat{I} = I_T/d$. Fig. 4 represents the result.

5.2 Application to define the period of bioassay

The result of section 5.1 can be used to estimate the period of application of a bioassay. According with 4.3 of R.G. 8.9 rev 1(Draft 1993) that say: „In general, spot samples should be collected on a frequency corresponding to no more than a 30% increase in the accumulated fractions over any time period,„ The period Δt between two bioassays (one assay in $t = t_i$ and the next $t = t_{i+1}$) in can be estimated as follow:

$$\Delta t = t_{i+1} - t_i = Q^{-1}(t_{i+1}) - t_i \quad (22)$$

with

$$Q(t_{i+1}) = Q(t_i)(1 + \Delta f)$$

where:

$Q(t)$ function of retention (it is assumed that $Q(t) = 0$, in $t = 0$) that is given by eq(21). In many occasions we can approximate using the function of retention for a continuous intake.

$Q(t_i)$ retained activity in t_i . This amount is known because it is measured. If we don't know his true value because it is above the low level detection limit (LLD) we can estimated it teorically using the appropriated retention function $Q(t)$.

Df = the increase of retention required to make a bioassay.

Example.- The lung retention of uranium Class Y and AMAD = 1 μm for a continuous intake is given by $Q_c(t) = \hat{I}(108.9 - 0.180 2^{-t} - 108.7 2^{-t/500})$ (see Sanchez 1998) if we have a measure of the lung retention in the day $t_i = 600$ since it started the intake, and we chose an increment for lung retention of 30% ($Df = 0.3$) to make the next lung measured we obtain $Dt = 350$ days. In other word: the next measured with body counter should be made in 350 days.

6. Conclusion

It has been implemented a program developed in *Mathematica* (Wolfram 1999) to solve analytically the Wrenn uranium model. That involve recycling, we have extended to included random intake. We have obtained the solutions to lung retention and urinary and fecal excretion as function of the size and solubility of airborne. The method could be applied for other compartment models (ex.: ICRP66), and radionuclides.

Simulation techniques has been presented to calculate random lung retention for workers moving in areas where the activity and the particle sizes are periodically monitored with air samplers. The main conclusion is that assuming continuous intake is usually more restrictive that a random intake of the same activity.

We suggest how statistical criteria could be used to determine when a bioassay are required and their frequency.

7. References

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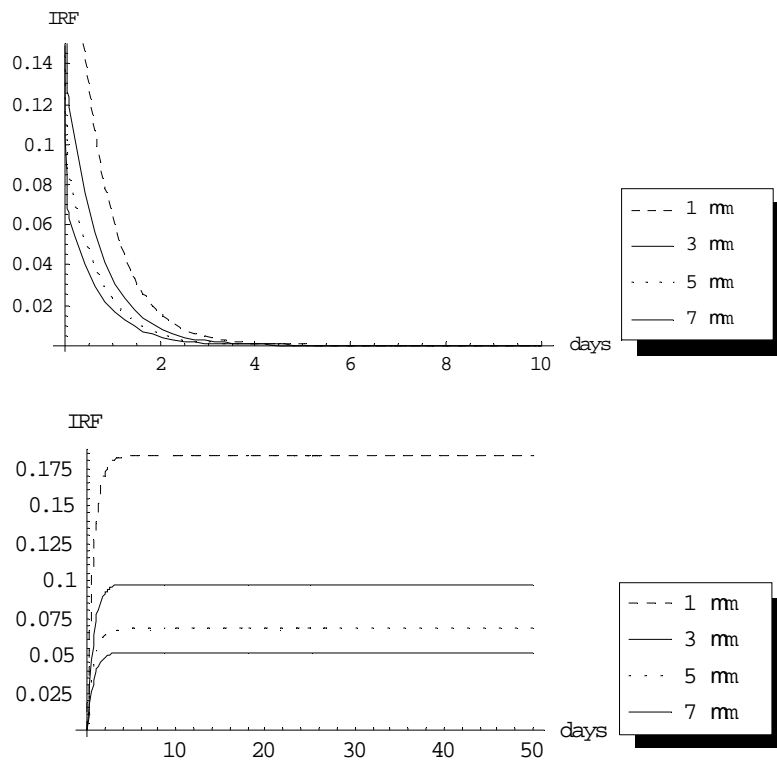


Figure 2. Lung retention fraction for acute and chronic intake. Class D

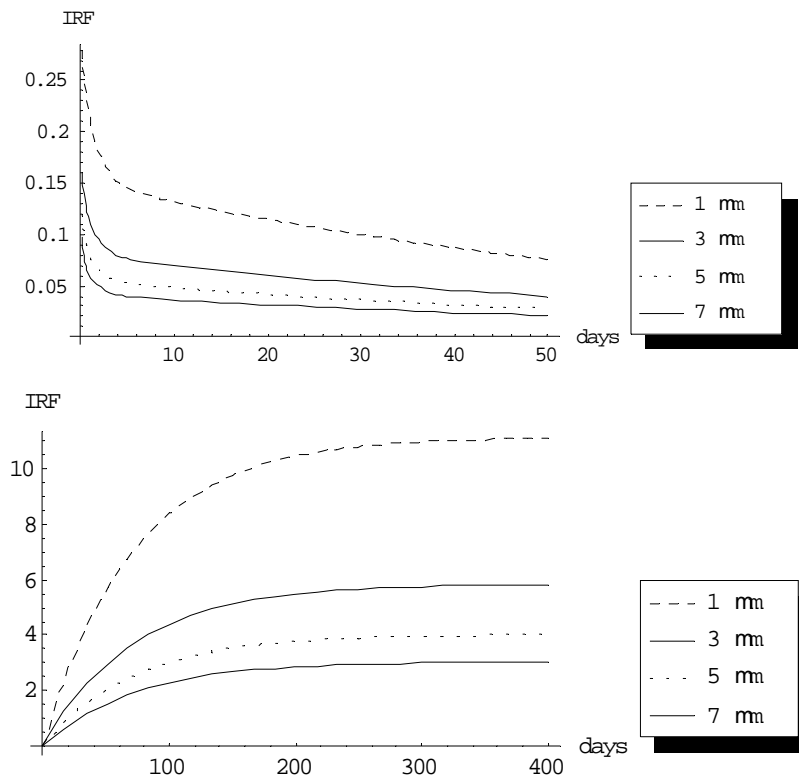


Figure 3. Lung retention fraction for acute and chronic intake. Class W

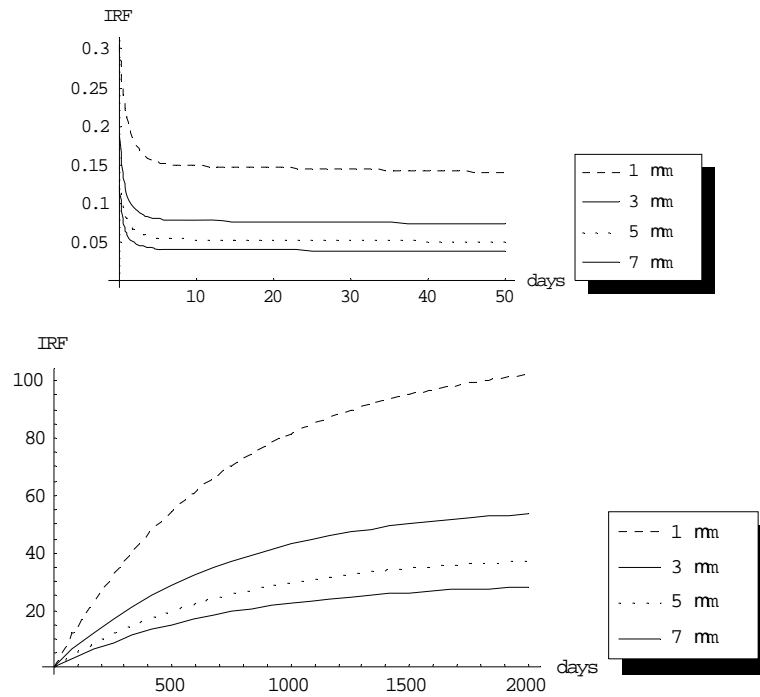


Figure 4. Lung retention fraction for acute and chronic intake. Class Y

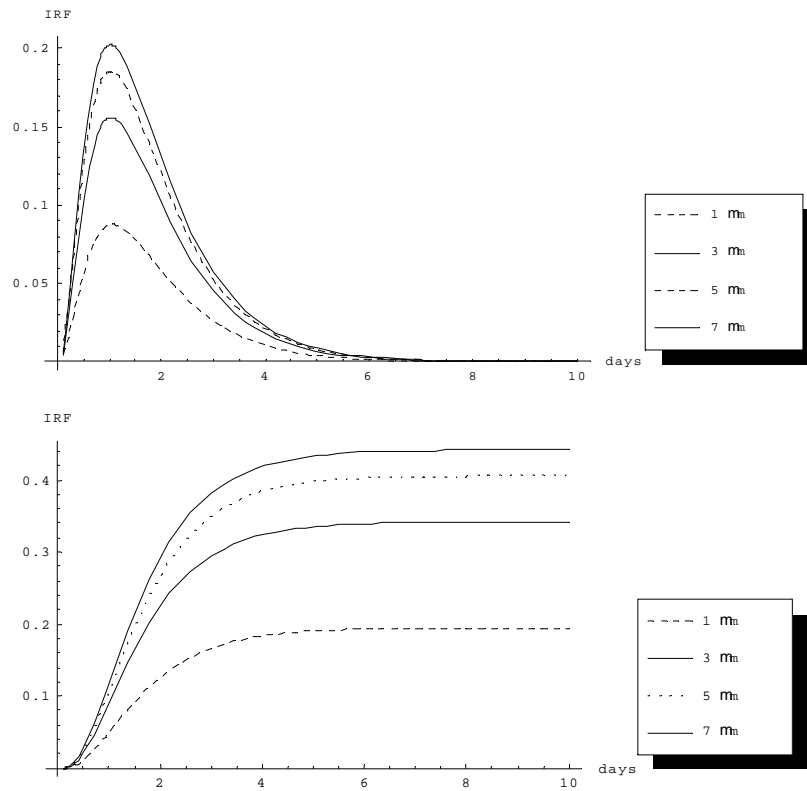


Figure 5. Fecal excretion fraction for acute and chronic intake. Class D

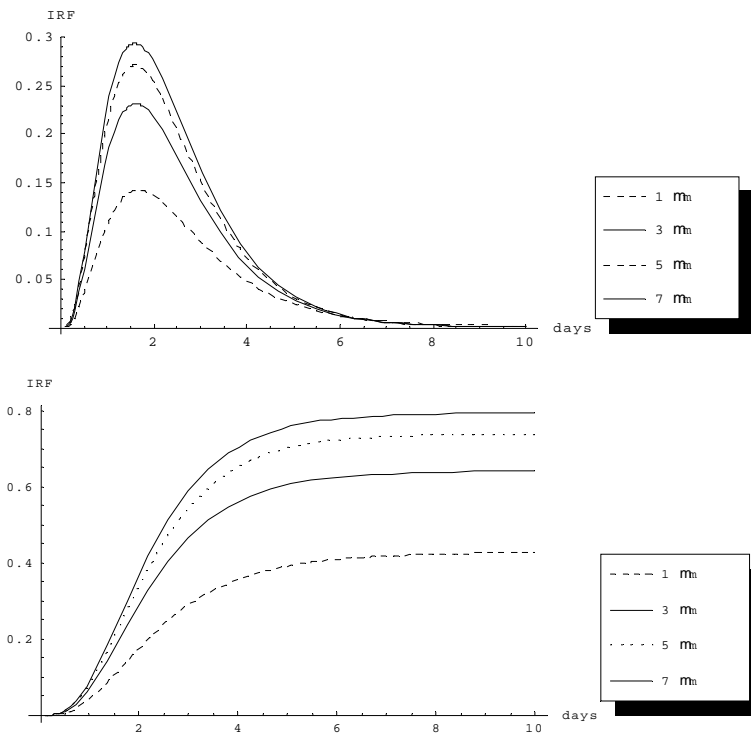


Figure 6. Fecal retention fraction for acute and chronic intake. Class W

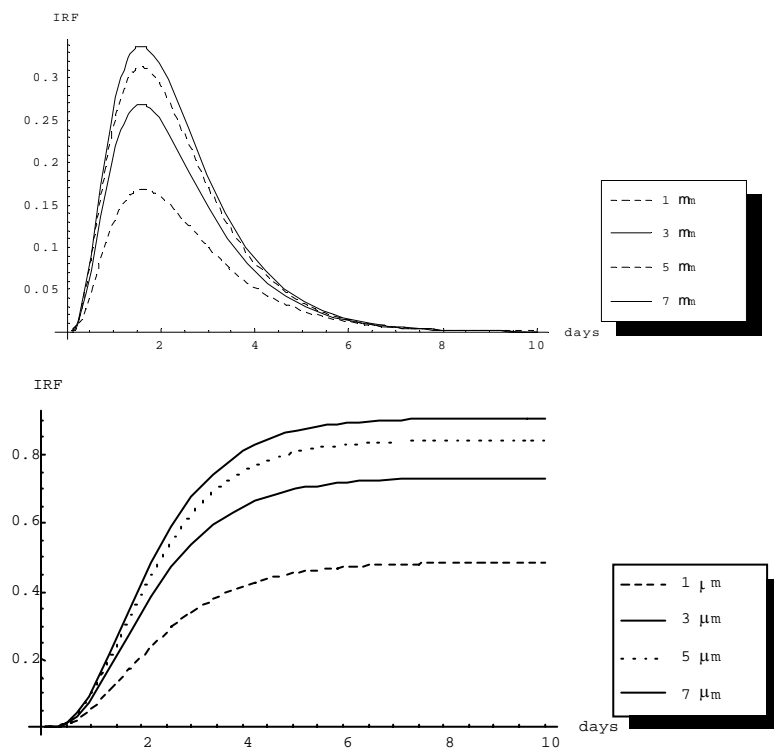


Figure 7. Fecal retention fraction for acute and chronic intake. Class Y

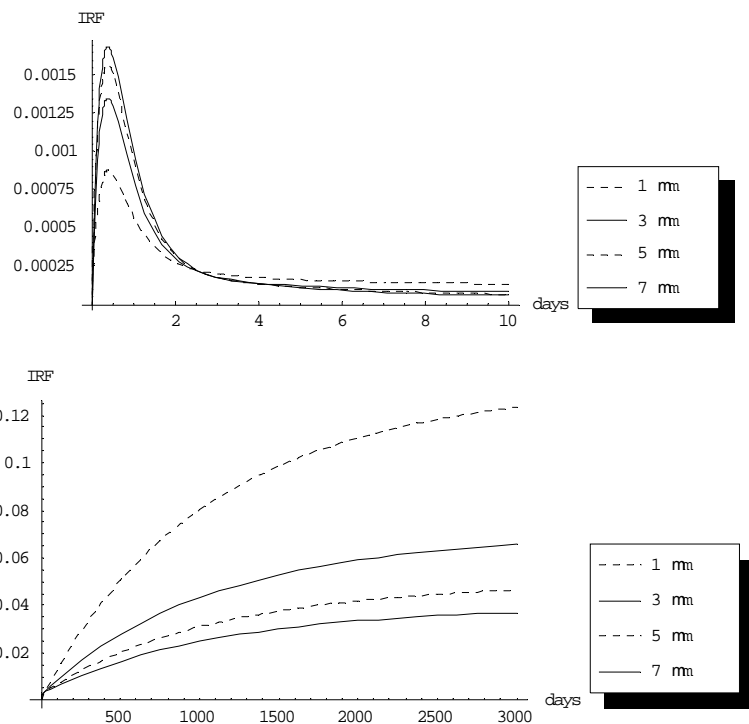


Figure 8. Urine retention fraction for acute and chronic intake. Class Y

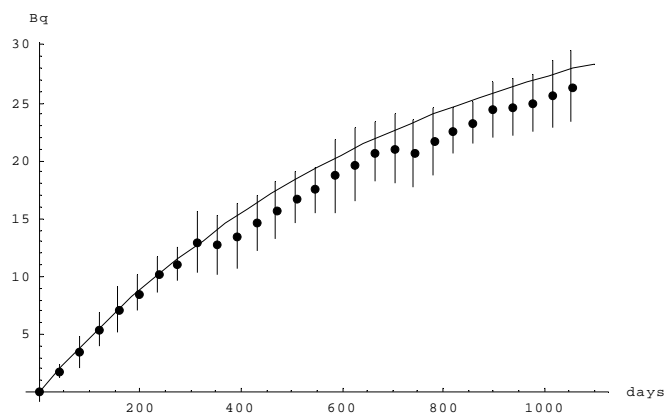


Figure 9. Lung retention for random (average and confidence interval) and chronic intake. Class Y