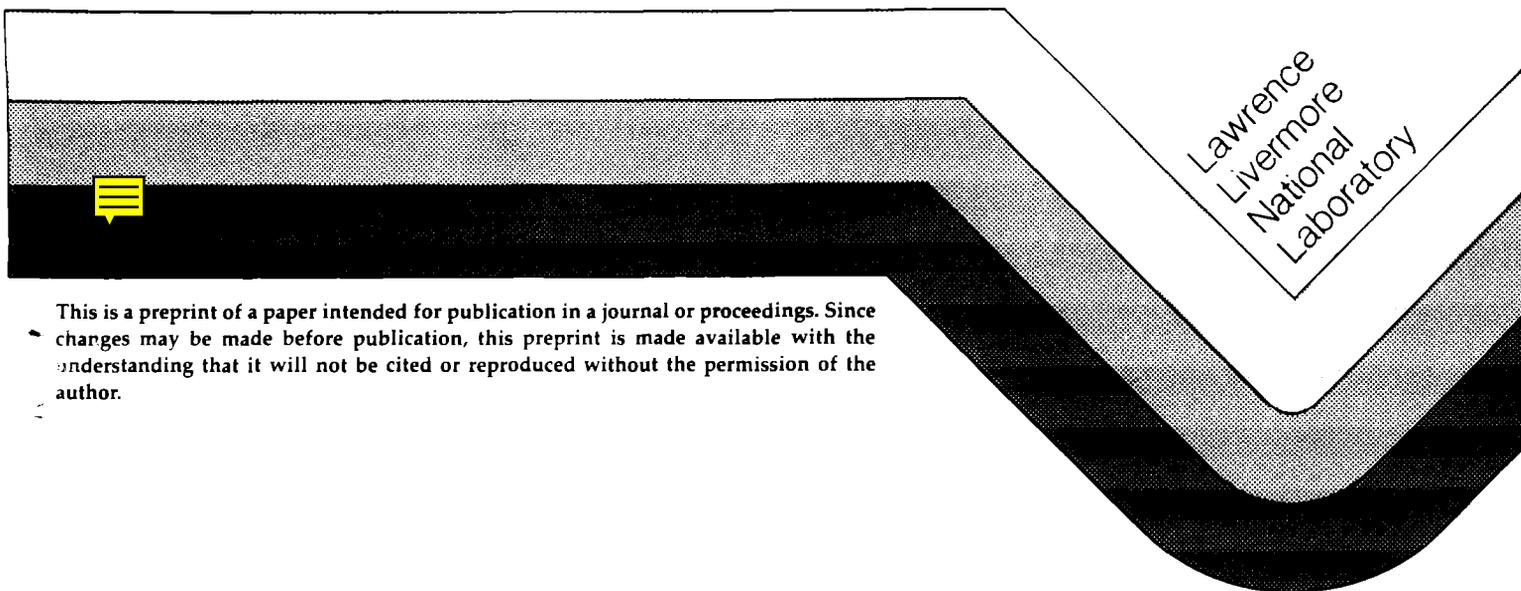


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Radionuclide-Body Burdens and Doses
from Discrete Stochastic Source Terms

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**Uncertainties in predicted radionuclide-
body burdens and doses from discrete stochastic
source terms**

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Abstract

Expressions are derived for the expectation and uncertainty of body burdens and doses calculated from a linear model of environmental transport and human metabolism in terms of expectation and uncertainty in soil concentrations. The soil concentrations were assumed to be discrete stochastic random variables. Three cases are compared to determine the relationship of the expectations and uncertainties under varying assumptions. This comparison allows us to set various input statistics in the simplest case to reproduce the output statistics of the more complex cases. The first case and the simplest (Highly Correlated) was for soil concentrations constant over the simulation period, T . In the two time-varying cases, it was assumed that N discrete samples were made of the soil concentration; each sample was constant during each time interval of length T/N . In one case (Discrete Random), the samples were assumed to be uncorrelated, and in the other (Discrete Autoregressive), they were assumed to be partially correlated with autocorrelation coefficient α . The expectation values of the body burdens and doses in the Highly Correlated case were identical to those in the Discrete Random case. The uncertainties of the body burdens and the doses in Highly Correlated case were identical in the limit of Rapid Metabolism to those of the Discrete Random case. In the limit of Slow Metabolism, the uncertainties of the body burdens and the doses in the Highly Correlated case were $N^{1/2}$ and $(3N/4)^{1/2}$, respectively, greater than those in the Discrete Random case. So to force the body burden or dose in the Highly Correlated case (constant input) to have the same statistics as the Discrete Random case requires that the soil concentration uncertainty be reduced by $N^{1/2}$ or $(3N/4)^{1/2}$, respectively. To force the Highly Correlated case to reproduce the expectation value of either the body burden in both the Slow and Rapid Metabolism limits or the dose in the Slow Metabolism and slow decay limit for the Discrete Autoregressive case requires setting the mean of the soil concentration to $\epsilon_m (1-\alpha)^{-1}$ where ϵ_m is the mean of the random component of the Autoregressive samples. To force the

Highly Correlated case to reproduce the uncertainty of the body burden in the Discrete Autoregressive case requires setting the uncertainty of the soil concentration to $\sigma_{\epsilon} (1-\alpha^2)^{-1/2}$ in the Rapid Metabolism limit and to $\sigma_{\epsilon} [(1-\alpha)(N^{1/2})]^{-1}$ in the Slow Metabolism limit. To force the Highly Correlated case to reproduce the uncertainty of the dose in the Discrete Autoregressive case requires setting the uncertainty of the soil concentration to σ_A in the Rapid Metabolism and rapid decay limit and to $\sigma_{\epsilon} [(1-\alpha)(N^{1/2})]^{-1} [2/(3^{1/2})]$ in the Slow Metabolism limit. That is, it is found that increasing the number of sampling periods decreases the uncertainty and increasing the autocorrelation increases the uncertainty. In these expressions, σ_{ϵ} is the uncertainty of the random component of the Autoregressive soil exposures and σ_A is the uncertainty of the initial exposure.

Introduction

Uncertainty in the fate and effects of radionuclides and other environmental pollutants is an important consideration in any assessment of risk. This paper considers the problem of the dependence of the output of models for computing body burdens of radionuclides and the associated dose on the uncertainty in the inputs (or forcing function). If the inputs are constant in time, this is not a difficult task because of the linear nature of the problem of exposure, body burden, and dose. However, this paper considers the case that the inputs or exposure may change over time with some uncertainty. This case requires that care must be used in the analysis.

There have been several discussions in the literature of the related problem of uncertainty in constant parameters of models for computing body burden of radionuclides (e.g., Garten 1980, Marivoet and Van Bosstraeten 1988, Breshears et al. 1989). Many authors have recommended a Monte Carlo approach to this problem, whether as a simple random design (Matthies et al. 1981, O'Neill et al. 1981, Schwarz and Hoffman 1980, Kercher and Anspaugh 1991) or as a stratified design such as Latin hypercube (Iman et al.

1981, Helton and Iman 1982, Iman and Shortencarier 1984). In the Monte Carlo approach, each parameter of the model is sampled from its distribution once before each run. By running the model many times, a distribution of the output results may be obtained. It is important to note that in most previous dose assessment schemes, each parameter is sampled only once per run. That is, the parameter is assumed to be constant during the run. A notable exception is the work of Unnikrishnan and Prasad (1987), who considered the case of continuous random fluctuations in air activity inputs in lung-model calculations. Their analysis will be used in our calculations in a companion paper on uncertainties due to continuous stochastic inputs (Kercher 1992).

The goal in this discussion is to show how the distribution of constant inputs may be chosen so that the resulting uncertainty in the distribution of outputs is the same as the distribution of outputs in the case of uncertainties in the time-varying input. For the purposes of our analysis, let us ignore the uncertainty in the other model parameters. However, in a specific assessment of a specific situation using the Monte Carlo method, one would include the uncertainty in model parameters as well as model inputs or source terms.

The analysis to follow was motivated by considerations of the model developed by Martin and Bloom (1980) for the Nevada Applied Ecology Group (NAEG) for application to the Nevada Test Site (NTS). For the NAEG model, Martin and Bloom assumed that a reference man (ICRP 1975) was living in a contaminated desert environment (grassland-shrubland vegetation), breathing air contaminated by soil resuspension, and eating vegetables that he had grown himself in the contaminated environment and milk and beef from cattle pastured in the same contaminated environment. All concentrations of radionuclides in air and foodstuffs are modeled as proportional to the soil concentration. There are many sources of variation in the man's intake including hour-to-hour variation in inhalation due to fluctuations in wind or movements on the farm; day-to-day variation in ingestion of differing types of foodstuffs or of foodstuffs having within-type variation due

to being grown in different parts of the farm; month-to-month variation due to differences in weather throughout the year or differences in the Man's activities at the farm; year-to-year variations due to differences in weather and the Man's activities; and decade-to-decade variations, which might consist of the relocations of the Man's living site. In this paper, let us consider only discrete fluctuations, and these will be classified into three cases: Highly Correlated (or Constant Input), Random, and Autoregressive. The continuous case is discussed in a companion document (Kercher 1992). For the Random and Autoregressive cases, let us assume that the simulation period is divided into N intervals of equal duration. In the Highly Correlated case, the simulation period itself is one interval and undivided. In all three cases, let us assume that the variation within intervals is negligible. The only significant variation occurs between intervals at the transition from one interval to another. That is, the distribution of the random variable is sampled once at the beginning of each time interval. In the Random case, the soil concentrations from one interval to the next are uncorrelated. In the Autoregressive case, the soil concentration from one interval to the next have correlation coefficient α . For example, for the man living on the farm, it might be imagined that the contamination on the farm is relatively homogeneous but that there is regional variation that is sampled by the Man's periodic relocation. In the Highly Correlated case, the initial location and exposures are decided upon (sampled) and then for the duration of the simulation the exposure remains constant. The Highly Correlated case is the easiest to simulate.

Our goals will be to compare the three cases by relating the body burdens, doses, and their uncertainties to each other. As a concomitant goal, the inputs for the Highly Correlated case will be determined such that the outputs reproduce the expectation and uncertainties of the Random and Autoregressive cases. For example, it will be shown how to chose the expectation and uncertainty in the soil concentration so the Highly Correlated case would produce the expectation and uncertainty of the body burden in the Random case. These comparisons will be made for the limits of Rapid and Slow Metabolism to

simplify the algebra. However, it should be emphasized that the solutions that are given here could be used to make comparisons for arbitrary metabolism and radioactive decay rates. Closed-form solutions are given to the general problem in each of the three cases. These solutions could be used numerically to relate expectations and uncertainties between the three cases for specific radionuclides.

The basic metabolism model for man of the International Commission on Radiological Protection (ICRP) (ICRP 1979) calculates body burdens of a particular radionuclide with the equation

$$\frac{dy_i}{dt} = \sum_{j=1}^n a_{ij} y_j + F_i(t) \quad (1)$$

where the a_{ij} are constant coefficients of transfers from compartment j to i (day^{-1}), y_i is the activity burden of the internal compartment i (Bq), and $F_i(t)$ is the intake (inhalation or ingestion) of the radionuclide to compartment i (Bq day^{-1}), and n is the number of compartments in the man model. The exception to this model is that of the alkaline earths (ICRP 1973) in which the a_{ij} are time-dependent. In the case of only one compartment and for $F_i(t)$ a random variable, eq. 1 is the Langevin equation, a discussion of its subtleties can be found in standard references on stochastic processes (e.g., Wang and Uhlenbeck 1945, Prabhu 1965). In our discussion that follows, let us simplify the mathematical details by assuming the matrix coefficients are constant, but suitable generalizations can be made for the time-dependent case. After eq. 1 is solved, the cumulative internal dose for the k th organ $H_k(t)$ (Sv) is then given formally by

$$H_k(T) = \sum_{j=1}^n \int_0^T B_{kj} y_j(t) dt \quad (2)$$

where the B_{kj} ($\text{Sv day}^{-1} \text{Bq}^{-1}$) are proportional to the SEE coefficients (ICRP 1979) for the k th target, j th source organ. So that one may write compact expressions, matrix notation will be used; for example eq. 1 becomes

$$\frac{d}{dt} \mathbf{y} = \mathbf{A}' \mathbf{y} + \mathbf{F}(t) \quad (3)$$

where the a_{ij} are the matrix elements of \mathbf{A}' , $y_i(t)$ the vector element of \mathbf{y} , and $F_i(t)$ the vector elements of \mathbf{F} .

The discussion in ICRP (1979) concentrates on an exposition of the \mathbf{A}' matrix. Other studies concentrate on radionuclide transport in the environment and delivery to man, i.e., the forcing function $\mathbf{F}(t)$ (Whicker et al. 1990, Whicker and Kirchner 1987, Hoffman et al. 1984). Some modeling efforts model both the \mathbf{A}' matrix and the \mathbf{F} vector (Martin and Bloom 1980, Kercher and Anspaugh 1991). Some uncertainty analyses have concentrated on uncertainties in \mathbf{A}' (Schwarz and Dunning 1982), whereas others concentrate on uncertainties in \mathbf{F} (Breshears et al. 1989, Unnikrishnan and Prasad 1987). In the discussions that follow, let us restrict our analysis of uncertainties to time-varying, stochastic \mathbf{F} .

Solutions to the Body Burden Equation

For constant matrix \mathbf{A}' , the formal solution to eq. 1 is

$$\mathbf{y}(T) = e^{\mathbf{A}'T} \int_0^T e^{-\mathbf{A}'t} \mathbf{F}(t) dt + e^{\mathbf{A}'T} \mathbf{y}(0) \quad (4)$$

For our discussion, let us consider the type of model in which the form of $F_i(t)$ is given by

$$F_i(t) = G_i(t) c_i(t) \quad (5)$$

where G_i is the i th component of the vector transfer function that models the transfer from the soil-to-man compartment i and $c_s(t)$ is the concentration of the radionuclide at the soil surface at time t . Models used by Kirchner et al. (1983), Kirchner and Whicker (1984), Martin and Bloom (1980), and Kercher and Anspaugh (1991) are examples of this type. For convenience, let us suppose that (1) \mathbf{G} is constant in time and (2) all radionuclides were deposited at time $t=0$, then let us assume that

$$c_s(t) = C_s(t) e^{-\lambda t} \quad (6)$$

where $C_s(t)$ is the time dependence of exposure independent of radioactive decay and λ is the radioactive decay rate of the radionuclide. Introduce a new matrix \mathbf{A} equal to $\mathbf{A}' + \lambda \mathbf{I}$ where \mathbf{I} is the identity matrix. See Appendix A for a discussion of the properties of the matrices \mathbf{A} and \mathbf{A}' . Let us also assume $\mathbf{y}(0) = 0$. Using eqs. 5, 6, and A.3, then eq. 4 becomes

$$\mathbf{y}(T) = e^{-\lambda T} e^{\mathbf{A}'T} \int_0^T e^{-\mathbf{A}'t} \mathbf{G} C_s(t) dt \quad (7a)$$

For some of the calculations to follow it is more convenient to write eq. 7a as

$$y_k(T) = \sum_{j,l=1}^n \Psi_{kj} e^{\lambda_j T} \int_0^T e^{-(\lambda_j + \lambda)t} \Psi_{jl}^{-1} G_l C_s(t) dt \quad (7b)$$

where the transformation from eq. 7a to eq. 7b is by use of eq. A.9. (Appendix A contains the definitions of λ_j and Ψ_{kj}). Equations 5 and 7 suggest that a sampling process is occurring in which a man continually samples his soil environment by his exposure to the radionuclide over time T . To get an idea of the uncertainty in dose due to this sampling,

one should consider an ensemble of such men, each sampling his environment over time T . As noted above, there are of course uncertainties in \mathbf{A} and \mathbf{G} and appropriate Monte Carlo methods for analyzing those uncertainties should be used (Iman and Shortencarier 1984). In the discussion here, let us concentrate on the uncertainties in $C_f(t)$.

In the discussion to follow, $C_f(t)$ is treated as a random variable. Appendix B states the mathematical properties of the functions used to characterize such distributions. Let us consider three separate cases: Highly Correlated, Discrete Random, and Discrete Autoregressive time series. The first two cases are special cases or limits of the third, but, in the interests of clarity of expression, let us discuss each of them separately.

Highly Correlated Case (Constant Input)

In the Highly Correlated case, the distribution of the random variable $C_f(t)$ may be sampled by the man several times over the time domain of simulation $[0, T]$, but let us assume for this case that, each time it is sampled, the value chosen is so close to the original value chosen that one may take as a good approximation that

$$C_f(t) = C_f(0) \tag{8}$$

As a result, the most important sampling is the first sampling, and it occurs at time $t=0$. This case might correspond to the situation assumed by Martin and Bloom (1980) in which the radionuclide is spread over the landscape as a smooth, slowly varying spatial function and once the man chooses a location, he remains in that location and grows his food in that location for the entire time of simulation. So the solution to eq. 1 becomes for constant matrix \mathbf{A}'

$$y(T) = e^{-\lambda T} C_s(0) e^{\lambda T} \int_0^T e^{-\lambda t} \mathbf{G} dt \quad (9)$$

or

$$y(T) = e^{-\lambda T} C_s(0) (e^{\lambda T} - \mathbf{I}) \mathbf{A}^{-1} \mathbf{G} \quad (10)$$

To characterize the distributions, the expectation function E and the standard deviation D (for the uncertainty) will be used with the usual definitions (e.g., Cramer 1955). (Appendix B provides a discussion of the properties of these statistics.) Using eq. B.1 through B.6, one finds the mean and standard deviation of $y_k(t)$ for the Highly Correlated case to be

$$E[y_k(T)] = e^{-\lambda T} E[C_s(0)] [(e^{\lambda T} - \mathbf{I}) \mathbf{A}^{-1} \mathbf{G}]_k = e^{-\lambda T} c_{HC} [(e^{\lambda T} - \mathbf{I}) \mathbf{A}^{-1} \mathbf{G}]_k \quad (11)$$

and

$$D[y_k(T)] = e^{-\lambda T} D[C_s(0)] [(e^{\lambda T} - \mathbf{I}) \mathbf{A}^{-1} \mathbf{G}]_k = e^{-\lambda T} \sigma_{HC} [(e^{\lambda T} - \mathbf{I}) \mathbf{A}^{-1} \mathbf{G}]_k \quad (12)$$

where c_{HC} is the mean of $C_s(0)$ and σ_{HC} is the standard deviation.

Calculate the cumulative dose at time T by integrating eq. 10 in eq. 2. The expectation and standard deviation are found as before:

$$H_k(T) = C_s(0) \left\{ \mathbf{B} \mathbf{A}^{-1} \left[(\mathbf{A} - \lambda)^{-1} (e^{(\mathbf{A} - \lambda)T} - \mathbf{I}) + \frac{e^{-\lambda T} - 1}{\lambda} \right] \mathbf{G} \right\}_k \quad (13a)$$

$$E[H_k(T)] = c_{HC} \left\{ \mathbf{B} \mathbf{A}^{-1} \left[(\mathbf{A} - \lambda)^{-1} (e^{(\mathbf{A} - \lambda)T} - \mathbf{I}) + \frac{e^{-\lambda T} - 1}{\lambda} \right] \mathbf{G} \right\}_k \quad (13b)$$

$$D[H_k(T)] = \sigma_{HC} \left\{ \mathbf{B} \mathbf{A}^{-1} \left[(\mathbf{A} - \lambda)^{-1} (e^{(\mathbf{A} - \lambda)T} - \mathbf{I}) + \frac{e^{-\lambda T} - 1}{\lambda} \right] \mathbf{G} \right\}_k \quad (13c)$$

Discrete Random Case

For both the Discrete Random and Discrete Autoregressive cases, let us suppose that the time period of simulation T is divided into N time intervals of length $D=T/N$. Let us suppose that for each of the N time intervals the sampled soil concentration $C_j(t)$ is highly correlated (constant) during that time interval but is random from one time interval to the next. That is, one assumes that for practical purposes $C_j(t)$ is constant C_i during the i th time interval. So eq. 7a integrates to

$$y(T) = e^{-\lambda T} e^{AT} (-A^{-1}) (1 - e^{A\Delta}) \left[\sum_{i=1}^N C_i e^{-Ai\Delta} \right] G \quad (14)$$

For the Discrete Random case, let us assume that for each of the N time intervals, the C_i is a random variable independent (uncorrelated) of any of the other C_i 's. For example, if the spatial distribution of the radionuclide were weakly varying on the landscape and the man were to move N times during the simulation period, then this would approximate the conditions for the Discrete Random case. Each move would have to result in a resampling of the environment independent of previous samples. Thus, the man could not move close by to his previous position, but instead, would have to move a large, random distance away. In the case of occupational exposure, if the man's work assignment were to change N times over his working life with equal time intervals for each assignment, one would approximate the Discrete Random case conditions. Alternatively, if conditions on the landscape were to change at random from one small time interval to the next, say, day to day, or month to month, one might also approximate the conditions for the Discrete Random case. A special case of changing environmental conditions is the seasonal effect that occurs at the beginning of each of the four seasons of the year; the seasonal effect results in a change in climatic conditions and produces a new exposure (sampling) that then remains constant over the season. (In the seasonal case, there is the complication that four different distributions are being sampled, so the results to follow

must be generalized before they can be applied.) Only nonseasonal effects will be considered here.

To characterize the distribution of y_k , take the expectation of eq. 14 to get

$$E(y_k(T)) = e^{-\lambda T} c_R [A^{-1} (e^{\lambda T} - 1) G]_k \quad (15)$$

Details of the calculation are in Appendix C.

Now let us consider the standard deviation for the Discrete Random case. Begin with eq. 7b and employ the Discrete Random case assumptions outlined above to get

$$D^2(y_k) = \sigma_R^2 e^{-2\lambda T} \sum_{j,l,m,r=1}^n \Psi_{kj} \Psi_{km} e^{-(\mu_j + \mu_m)T} \Psi_{jl}^{-1} \Psi_{mr}^{-1} G_l G_r \left\{ \frac{(1 - e^{-\mu_j \Delta})(1 - e^{-\mu_m \Delta})}{\mu_j \mu_m} \frac{(1 - e^{-(\mu_j + \mu_m)T})}{(e^{-(\mu_j + \mu_m)\Delta} - 1)} \right\} \quad (16)$$

See Appendix C for details.

The dose calculation of the Discrete Random case is performed by integrating either eq. 14 or C.3b in eq. 2. to find

$$H_k(T) = \sum_{i=1}^N C_i \left\{ B(-A^{-1})(-A + \lambda)^{-1} \left[e^{-i\lambda \Delta} (1 - e^{-\lambda \Delta}) \frac{\Delta}{\lambda} - (1 - e^{-\lambda \Delta}) e^{(\lambda - \lambda)\Delta} e^{-i\lambda \Delta} \right] G \right\}_k \quad (17a)$$

with

$$E(H_k(T)) = c_R \left\{ B(-A^{-1})(-A + \lambda)^{-1} \left[(1 - e^{-\lambda T}) \frac{-A}{\lambda} - (1 - e^{\lambda T}) e^{-\lambda T} \right] G \right\}_k \quad (17b)$$

and

$$\begin{aligned}
D^2(H) = \sigma_R^2 \sum_{j,l,h,p,m,q} B_{kj} B_{kh} \Psi_{jl} \Psi_{hp} \frac{1}{\mu_l \mu_p (\mu_l + \lambda) (\mu_p + \lambda)} \Psi_{lm}^{-1} \Psi_{pq}^{-1} G_m G_q \\
\left[(1-e^{-\lambda\Delta})^2 \frac{\mu_l \mu_p}{\lambda^2} \frac{1-e^{-2\lambda\Delta N}}{e^{2\lambda\Delta}-1} + (1-e^{-\lambda\Delta}) \frac{\mu_l}{\lambda} (1-e^{-\mu_p\Delta}) e^{-(\mu_p+\lambda)\Delta N} \frac{1-e^{(\mu_p-\lambda)\Delta N}}{e^{(\lambda-\mu_p)\Delta}-1} \right. \\
+ (1-e^{-\lambda\Delta}) \frac{\mu_p}{\lambda} (1-e^{-\mu_l\Delta}) e^{-(\mu_l+\lambda)\Delta N} \frac{1-e^{(\mu_l-\lambda)\Delta N}}{e^{(\lambda-\mu_l)\Delta}-1} \\
\left. + (1-e^{-\mu_l\Delta}) e^{-(\mu_l+\lambda)\Delta N} (1-e^{-\mu_p\Delta}) e^{-(\mu_p+\lambda)\Delta N} \frac{1-e^{(\mu_l+\mu_p)\Delta N}}{e^{-(\mu_p+\mu_l)\Delta}-1} \right] \quad (17c)
\end{aligned}$$

Comparison of the Discrete Random and Highly Correlated Cases

In comparing the Discrete Random and Highly Correlated Cases, let us first consider the body burdens. Note that eq. 15 is exactly the same form for $E(y_k)$ that was determined for the Highly Correlated case, eq. 11. Thus for $E(C_S(0)) = E(C_i)$ or $c_{HC} = c_R$

$$E(y_k, \text{Highly Correlated}) = E(y_k, \text{Random}) \quad (18a)$$

Similarly, the expectation of the dose $E(H_k)$ for the Highly Correlated case, eq. 13b, is exactly the same as the expectation of the dose $E(H_k)$ for the Discrete Random case, eq. 17b, if it is assumed that $c_{HC} = c_R$

$$E(H_k, \text{Highly Correlated}) = E(H_k, \text{Random}) \quad (18b)$$

To compare eq. 16 and 17c, the uncertainties of the body burden and the dose, respectively, in the Discrete Random case with eq. 12 and 13c, the uncertainties in the Highly Correlated case, consider these equations in two opposite and extreme limits. The first limit is for extremely rapid metabolism of the radionuclide in all of man's compartment

organs; the second limit is for extremely slow metabolism in all compartments. These limits are taken for purposes of simplifying the comparison of these uncertainties. In any particular situation regarding a particular radionuclide, one would use the equations directly to make a comparison or to determine the adjustments necessary to simulate discrete fluctuations with a constant input.

Rapid Metabolism Limit

First, consider the variance of the body burdens. In the Rapid Metabolism limit, all μ_i are large such that $\mu_i \Delta \gg 1$. In this limit, eq. 16 becomes

$$D(y_k, \text{Random}) \rightarrow \sigma_R e^{-\lambda T} [-\mathbf{A}^{-1} \mathbf{G}]_k \quad (19)$$

See Appendix C for details. In the same limit, eq. 12 goes to

$$D(y_k, \text{Highly Correlated}) \rightarrow \sigma_{HC} e^{-\lambda T} [-\mathbf{A}^{-1} \mathbf{G}]_k \quad (20)$$

So in the limit of Rapid Metabolism and for $\sigma_R = \sigma_{HC}$

$$D(y_k, \text{Random}) = D(y_k, \text{Highly Correlated}) \quad (21)$$

Next consider the variance of the dose. To compare the variance of the dose in the Highly Correlated case with the Discrete Random case in the Rapid Metabolism limit, let us also assume that the decay is rapid ($\lambda \Delta \gg 1$). Then the variance of the Highly Correlated dose, eq. 13c, approaches

$$D(H_k, \text{Highly Correlated}) \rightarrow \frac{\sigma_{HC}}{\lambda} [\mathbf{B} (-\mathbf{A} + \lambda)^{-1} \mathbf{G}]_k \quad (22)$$

In this limit, the variance of the Discrete Random Dose, eq. 17 also approaches eq. 22 if $\sigma_R = \sigma_{HC}$. Thus

$$D(H_k, \text{Random}) = D(H_k, \text{Highly Correlated}) \quad (23)$$

Slow Metabolism Limit

Now consider the limit of Slow Metabolism. In this limit, all the μ_i are small, so $\mu_i T \ll 1$. First, examine the uncertainty in the body burdens. In Appendix C, this limit is found to be

$$D(y_k, \text{Random}) \rightarrow \frac{\sigma_R e^{-\lambda T} T}{\sqrt{N}} G_I \quad (24)$$

In the Slow Metabolism limit, the Highly Correlated uncertainty (eq. 12) becomes

$$D(y_k, \text{Highly Correlated}) \rightarrow \sigma_{HC} T e^{-\lambda T} G_I \quad (25)$$

Thus, in the limit of Slow Metabolism and for $\sigma_R = \sigma_{HC}$

$$D(y_k, \text{Random}) = \frac{D(y_k, \text{Highly Correlated})}{\sqrt{N}} \quad (26)$$

Alternatively, one could force

$$D(y_k, \text{Random}) = D(y_k, \text{Highly Correlated}) \quad (27)$$

by choosing σ_{HC} so that

$$\sigma_{HC} = \frac{\sigma_R}{\sqrt{N}} \quad (28)$$

Consider next the uncertainty in the dose. In addition to the Slow Metabolism limit, let us also assume that $\lambda T \ll 1$. In this limit, the uncertainty of the dose in the Discrete Random case (eq.17) approaches

$$D(H_k, \text{Random}) \rightarrow \sigma_R [B G]_k \frac{T^2}{\sqrt{3} N} \quad (29)$$

In this same limit, the uncertainty of the dose for the Highly Correlated case, eq. 13c, approaches

$$D(H_k, \text{Highly Correlated}) \rightarrow \sigma_{HC} [B G]_k \frac{T^2}{2} \quad (30)$$

So for Slow Metabolism and decay,

$$D(H_k, \text{Random}) = \frac{\sigma_R}{\sigma_{HC}} \frac{2}{\sqrt{3} N} D(H_k, \text{Highly Correlated}) \quad (31)$$

Equation 31 implies that in order to force equality

$$D(H_k, \text{Random}) = D(H_k, \text{Highly Correlated}) \quad (32)$$

one must choose

$$\sigma_{HC} = \frac{2}{\sqrt{3} N} \sigma_R \quad (33)$$

Comparing eq. 28 and 33, one sees that σ_{HC} can be adjusted to reproduce the uncertainty in the body burdens or the uncertainty in the dose but not both simultaneously.

Discrete Autoregressive Case

In the final case, the Discrete Autoregressive case, the closed form expression for y_k will be derived for the simplest linear autocorrelation between successive samples. The derived equations will contain the Discrete Random case and Highly Correlated case as special cases. The most general linear model of random variable X for time series X_t , the Autoregressive-Moving Average (ARMA) model (Kendall 1976, Chatfield 1975), is given by

$$X_t = \alpha_1 X_{t-1} + \dots + \alpha_m X_{t-m} + \beta_0 Z_t + \beta_1 Z_{t-1} + \dots + \beta_l Z_{t-l} \quad (34)$$

where X_i is the random variable at time $t = i$ and Z_i is another, independent random variable at time $t = i$. The terms with the α 's as coefficients make up the autoregressive part of the expression and the terms with the β 's as coefficients make up the moving average part of the expression. For purposes of exposition here, the simplest autoregressive model is sufficient. So consider the case of a first-order autoregression (also known as the Markov scheme):

$$X_t = \alpha X_{t-1} + Z_t \quad (35a)$$

or for the C_i in eqs. 14 and C.3b

$$C_i = \alpha C_{i-1} + \varepsilon_i \quad (35b)$$

where ε_i is a random variable independent of C_1 and ε_j for $i \neq j$. Note that it is well known that the autocorrelation function between C_i and C_{i+k} is α^k . In particular, the autocorrelation between neighboring time intervals is α . This is shown in Appendix C for our particular assumptions. Applying eq. 35b to the C_{i-1} term in eq. 35b successively $i-2$ times, one finds

$$C_i = \alpha^{i-1} C_1 + \sum_{j=0}^{i-2} \alpha^j \varepsilon_{i-j} = \alpha^{i-1} C_1 + \sum_{j=2}^i \alpha^{i-j} \varepsilon_j \quad i > 1 \quad (36)$$

First, consider the body burdens. In the Discrete Autoregressive case, the equation for the body burden output (eq. 14) becomes

$$y(T) = e^{-\lambda T} e^{AT} (-A^{-1}) (1 - e^{A\Delta}) \left\{ C_1 e^{-A\Delta} + \sum_{i=2}^N \left[\alpha^{i-1} C_1 + \sum_{j=0}^{i-2} \alpha^j \varepsilon_{i-j} \right] e^{-A\Delta i} \right\} \mathbf{G} \quad (37)$$

Calculate the expectation value of eq. 37 using $E(C_1) = c_A$ and $E(\varepsilon_{i,j}) = \varepsilon_m$ to get

$$E(y_k) = e^{-\lambda T} \left\{ e^{AT} (-A^{-1}) (1 - e^{A\Delta}) e^{-A\Delta} \left[c_A (1 - \alpha^N e^{-AT}) (1 - \alpha e^{-A\Delta})^{-1} + \frac{\varepsilon_m}{1 - \alpha} \left((e^{-A\Delta} - e^{-AT}) (1 - e^{-A\Delta})^{-1} - (\alpha e^{-A\Delta} - \alpha^N e^{-AT}) (1 - \alpha e^{-A\Delta})^{-1} \right) \right] \right\} \mathbf{G}_k \quad (38)$$

Note that in the limit $\alpha \rightarrow 0$, $\varepsilon_m \rightarrow c_A$, and $c_A \rightarrow c_R$, one recovers eq. 15 for the Discrete Random case. Also, note that in the limit $\alpha \rightarrow 1$, $\varepsilon_m \rightarrow 0$, and $c_A \rightarrow c_{HC}$, one recovers eq. 11 for the Highly Correlated case. However, for an arbitrary value of ε_m/c_A and $0 < \alpha < 1$, the expected value in the Discrete Autoregressive case differs from the Discrete Random and Highly Correlated cases.

To calculate the uncertainty in the distribution of y_k in the Discrete Autoregressive case, begin with eq. C.3b and manipulate as shown in Appendix E to get

$$\begin{aligned}
D^2(y_k) &= \left[e^{-\lambda T} e^{\Lambda T} (1 - e^{-\Lambda \Delta}) A^{-1} (1 - \alpha^N e^{-\Lambda T}) (1 - \alpha e^{-\Lambda \Delta})^{-1} G_k \right]^2 \sigma_A^2 \\
+ \sigma_\varepsilon^2 \sum_{j,l,i,h=1}^n & \Psi_{kj} e^{\lambda_j T} \Psi_{jl}^{-1} G_l \frac{1 - e^{-\mu_j \Delta}}{\mu_j} \Psi_{ki} e^{\lambda_i T} \Psi_{ih}^{-1} G_h \frac{1 - e^{-\mu_i \Delta}}{\mu_i} \frac{e^{(\mu_j + \mu_i) \Delta}}{(1 - \alpha e^{\mu_j \Delta})(1 - \alpha e^{\mu_i \Delta})} \\
& \left[\frac{e^{(\mu_j + \mu_i) \Delta} - e^{(\mu_j + \mu_i) T}}{1 - e^{(\mu_j + \mu_i) \Delta}} - \frac{e^{\mu_j T} \alpha e^{\mu_i T} - \alpha^N e^{\mu_j \Delta}}{e^{\mu_j \Delta} - \alpha} \right. \\
& \left. - \frac{e^{\mu_i T} \alpha e^{\mu_j T} - \alpha^N e^{\mu_i \Delta}}{e^{\mu_i \Delta} - \alpha} + e^{(\mu_j + \mu_i) T} \frac{\alpha^2 - \alpha^{2N}}{1 - \alpha^2} \right] \quad (39)
\end{aligned}$$

Note that in the limit $\alpha \rightarrow 0$ and $\sigma_\varepsilon \rightarrow \sigma_A$, one recovers eq. 16 for the Discrete Random case. Also, note that in the limit $\alpha \rightarrow 1$ and $\sigma_\varepsilon \rightarrow 0$, one recovers eq. 12 for the Highly Correlated case. However, for an arbitrary value of $\sigma_\varepsilon/\sigma_A$ and $0 < \alpha < 1$, the expected value of D^2 in the Discrete Autoregressive case differs from the Discrete Random and Highly Correlated cases.

Now consider the calculation of the dose for the Discrete Autoregressive case. Integrate either eq. 37 or E.3c in eq. 2 to arrive at the expression for the dose to organ k

$$\begin{aligned}
H &= B (-A^{-1}) (A - \lambda)^{-1} \left[\left\{ M(\lambda) \left(\frac{-A}{\lambda} \right) (1 - \alpha^N e^{-\lambda \Delta N}) + M(A) e^{(A - \lambda) \Delta N} (1 - \alpha^N e^{-A \Delta N}) \right\} C_1 \right. \\
& \quad + M(\lambda) \left(\frac{-A}{\lambda} \right) e^{\lambda \Delta} \sum_{i=2}^N \varepsilon_i (e^{-i \lambda \Delta} - \alpha^{N-i+1} e^{-\lambda \Delta (N+1)}) \\
& \quad \left. + M(A) e^{(A - \lambda) \Delta N} e^{A \Delta} \sum_{i=2}^N \varepsilon_i (e^{-i A \Delta} - \alpha^{N-i+1} e^{-A \Delta (N+1)}) \right] G \quad (40a)
\end{aligned}$$

where

$$M(x) = (1 - e^{x \Delta}) (e^{x \Delta} - \alpha)^{-1} \quad (40b)$$

The expectation of the dose is then given by

$$\begin{aligned}
E(\mathbf{H}) = & \mathbf{B}(-\mathbf{A}^{-1})(\mathbf{A}-\lambda)^{-1} \left\{ \left[M(\lambda) \left(\frac{-\mathbf{A}}{\lambda} \right) (1-\alpha^N e^{-\lambda \Delta N}) + M(\mathbf{A}) e^{(\mathbf{A}-\lambda)\Delta N} (1-\alpha^N e^{-\mathbf{A}\Delta N}) \right] c_A \right. \\
& - \frac{\varepsilon_m}{1-\alpha} \left(\frac{-\mathbf{A}}{\lambda} \right) (e^{-\lambda \Delta} - e^{-N\lambda \Delta} + M(\lambda) (\alpha e^{-\lambda \Delta} - \alpha^N e^{-\lambda \Delta N})) \\
& \left. - \frac{\varepsilon_m}{1-\alpha} e^{(\mathbf{A}-\lambda)\Delta N} (e^{-\mathbf{A}\Delta} - e^{-N\mathbf{A}\Delta} + M(\mathbf{A}) (\alpha e^{-\mathbf{A}\Delta} - \alpha^N e^{-\mathbf{A}\Delta N})) \right\} \mathbf{G} \quad (41)
\end{aligned}$$

To calculate the variance of the dose of the Discrete Autoregressive case, take D^2 of the eigenvalue-eigenvector form of eq. 40a and find after manipulation

$$\begin{aligned}
D^2(H_k) = & \sigma_\lambda^2 \sum_{l,j,m,q,p,r} B_{kl} B_{kj} \frac{\Psi_{lm} \Psi_{jq}}{\mu_m \mu_q} \left\{ M(\lambda) \left(\frac{\mu_m}{\lambda} \right) P(-\lambda) + M(-\mu_m) e^{-(\mu_m+\lambda)\Delta N} P(\mu_m) \right\} \\
& \left\{ M(\lambda) \left(\frac{\mu_q}{\lambda} \right) P(-\lambda) + M(-\mu_q) e^{-(\mu_q+\lambda)\Delta N} P(\mu_q) \right\} \frac{\Psi_{mp}^{-1} \Psi_{qr}^{-1} G_p G_r}{(\mu_m+\lambda)(\mu_q+\lambda)} \\
& + \sigma_\varepsilon^2 \sum_{l,j,m,q,p,r} B_{kl} B_{kj} \frac{\Psi_{lm} \Psi_{jq}}{\mu_m \mu_q} \left\{ M^2(\lambda) \frac{\mu_m \mu_q}{\lambda^2} \left[\mathcal{Q}(e^{-2\lambda \Delta}) - 2\alpha^N e^{-\lambda \Delta N} \mathcal{Q}\left(\frac{e^{-\lambda \Delta}}{\alpha}\right) \right. \right. \\
& + e^{-2\lambda \Delta N} \alpha^{2N} \mathcal{Q}(\alpha^{-2}) \left. \right] + M(\lambda) M(-\mu_q) \frac{\mu_m}{\lambda} e^{-(\mu_q+\lambda)\Delta N} \left[\mathcal{Q}(e^{(\mu_q-\lambda)\Delta}) - \alpha^N e^{-\lambda \Delta N} \mathcal{Q}\left(\frac{e^{\mu_q \Delta}}{\alpha}\right) \right. \\
& - \alpha^N e^{\mu_q \Delta N} \mathcal{Q}\left(\frac{e^{-\lambda \Delta}}{\alpha}\right) + e^{(\mu_q-\lambda)\Delta N} \alpha^{2N} \mathcal{Q}(\alpha^{-2}) \left. \right] + M(\lambda) M(-\mu_m) \frac{\mu_q}{\lambda} e^{-(\mu_m+\lambda)\Delta N} \\
& \left[\mathcal{Q}(e^{(\mu_m-\lambda)\Delta}) - \alpha^N e^{-\lambda \Delta N} \mathcal{Q}\left(\frac{e^{\mu_m \Delta}}{\alpha}\right) - \alpha^N e^{\mu_m \Delta N} \mathcal{Q}\left(\frac{e^{-\lambda \Delta}}{\alpha}\right) + e^{(\mu_m-\lambda)\Delta N} \alpha^{2N} \mathcal{Q}(\alpha^{-2}) \right] \\
& + M(-\mu_m) M(-\mu_q) e^{-(\mu_q+\mu_m+2\lambda)\Delta N} \left[\mathcal{Q}(e^{(\mu_m+\mu_q)\Delta}) - \alpha^N e^{\mu_m \Delta N} \mathcal{Q}\left(\frac{e^{\mu_q \Delta}}{\alpha}\right) - \alpha^N e^{\mu_q \Delta N} \mathcal{Q}\left(\frac{e^{\mu_m \Delta}}{\alpha}\right) \right. \\
& \left. \left. + e^{(\mu_m+\mu_q)\Delta N} \alpha^{2N} \mathcal{Q}(\alpha^{-2}) \right] \right\} \frac{\Psi_{mp}^{-1} \Psi_{qr}^{-1} G_p G_r}{(\mu_m+\lambda)(\mu_q+\lambda)} \quad (42a)
\end{aligned}$$

where

$$P(x) = 1 - \alpha^N e^{x\Delta N} \quad (42b)$$

and

$$\mathcal{Q}(x) = \frac{x - x^N}{1 - x} \quad (42c)$$

Comparison of the Discrete-Autoregressive Case to Highly Correlated Case

The Discrete Random and Highly Correlated cases have already been compared; therefore, let us restrict our comparison of the Discrete Autoregressive case to the Highly Correlated. Recall that a primary goal in this discussion is to determine how to choose the mean and uncertainty in the case of constant input (Highly Correlated case) to match the mean and uncertainty in the distribution of the actual case occurring in practice, which in this instance is presumed to be approximated by the Discrete Autoregressive case described above. To do this, compare the formulae for the Highly Correlated case (eqs. 11 and 12 for the body burden and eqs. 13b and 13c for the dose) with the statistics formulae for the Discrete Autoregressive case (eqs. 38 and 39 for the body burden and eqs. 41 and 42a for the dose). Because of the complexity of these equations, let us resort to the expedient of considering the two limits of Rapid and Slow Metabolism.

Rapid Metabolism Limit

In the limit of Rapid Metabolism, the expectation values of the body burden y_k for the Highly Correlated case and the Discrete Autoregressive case are found to be related as

$$E(y_k, \text{Autoregressive}) \rightarrow \left[\alpha^{N-1} + \frac{\epsilon_m}{c_A(1-\alpha)} (1 - \alpha^{N-1}) \right] \frac{c_A}{c_{HC}} E(y_k, \text{Highly Correlated}) \quad (43)$$

Details of this calculation are in Appendix E. So to force

$$E(y_k, \text{Autoregressive}) = E(y_k, \text{Highly Correlated}) \quad (44)$$

set

$$c_{HC} = c_A \left[\alpha^{N-1} + \frac{\epsilon_m}{c_A(1-\alpha)} (1 - \alpha^{N-1}) \right] \quad (45)$$

which for large N becomes

$$c_{HC} \approx \frac{\epsilon_m}{(1 - \alpha)} \quad (46)$$

Now consider the uncertainty of the body burden in the Rapid Metabolism limit. In this limit, it is shown in Appendix E that the uncertainties of the Highly Correlated case and the Autoregressive case are related by

$$D^2(y_k, \text{Autoregressive}) \rightarrow \frac{\sigma_A^2}{\sigma_{HC}^2} \left[\alpha^{2(N-1)} + \frac{\sigma_\epsilon^2 (1 - \alpha^{2(N-1)})}{\sigma_A^2 (1 - \alpha^2)} \right] D^2(y_k, \text{Highly Correlated}) \quad (47)$$

So, to force

$$D^2(y_k, \text{Autoregressive}) = D^2(y_k, \text{Highly Correlated}) \quad (48)$$

set

$$\sigma_{HC}^2 = \sigma_A^2 \left[\alpha^{2(N-1)} + \frac{\sigma_\epsilon^2 (1 - \alpha^{2(N-1)})}{\sigma_A^2 (1 - \alpha^2)} \right] \quad (49a)$$

which for large N becomes

$$\sigma_{HC}^2 \approx \frac{\sigma_\epsilon^2}{(1 - \alpha^2)} \quad (49b)$$

To calculate the expectation of the dose H_k in the Rapid Metabolism limit, let us also assume that the decay is rapid, too, i.e., let us assume $\lambda\Delta \gg 1$. In Appendix E, the expectations of the dose in the Discrete Autoregressive case and Highly Correlated case are calculated for this limit. They are related by

$$E(H_k, \text{Autoregressive}) = \frac{c_A}{c_{HC}} E(H_k, \text{Highly Correlated}) \quad (50)$$

so that $c_A = c_{HC}$ forces equality.

Now consider the uncertainty in the dose for the Rapid Metabolism and rapid decay limit. In this limit, in Appendix E it is shown that the uncertainty in the Autoregressive dose is related to the uncertainty in the Highly Correlated dose by

$$D(H_k, \text{Autoregressive}) = \frac{\sigma_A}{\sigma_{HC}} D(H_k, \text{Highly Correlated}) \quad (51)$$

To force equality, set $\sigma_A = \sigma_{HC}$.

Slow Metabolism Limit

In the limit of Slow Metabolism for the radionuclide in question, the expectation value of the body burden y_k for Highly Correlated case is related to that of the Autoregressive case by

$$E(y_k, \text{Autoregressive}) \rightarrow \left[\frac{\epsilon_m}{c_A(1-\alpha)} + \frac{1}{N} \frac{1-\alpha^N}{1-\alpha} \left(1 - \frac{\epsilon_m}{c_A(1-\alpha)} \right) \right] \frac{c_A}{c_{HC}} E(y_k, \text{Highly Correlated}) \quad (52)$$

as shown in Appendix E. To force

$$E(y_k, \text{Autoregressive}) = E(y_k, \text{Highly Correlated}) \quad (53)$$

requires that

$$c_{HC} = c_A \left[\frac{\epsilon_m}{c_A(1-\alpha)} + \frac{1}{N} \frac{1-\alpha^N}{1-\alpha} \left(1 - \frac{\epsilon_m}{c_A(1-\alpha)} \right) \right] \quad (54a)$$

which for large N approaches

$$c_{HC} \approx \frac{\epsilon_m}{(1-\alpha)} \quad (54b)$$

Note that this is the same condition to force equality of the body burdens in this limit.

The uncertainty of the dose for the Highly Correlated case in the Slow Metabolism (and decay) limit is related to that of the Autoregressive case by

$$D(H_{k, \text{ Autoregressive}}) = \frac{\sigma_{\epsilon}}{\sigma_{HC}(1-\alpha)} \frac{2}{\sqrt{3N}} D(H_{k, \text{ Highly Correlated}}) \quad (60)$$

To force equality of the variance of the two doses requires that

$$\sigma_{HC} = \frac{\sigma_{\epsilon}}{(1-\alpha)} \frac{2}{\sqrt{3N}} \quad (61)$$

Note that this differs from eq. 57 by the factor $2/(3^{1/2})$. Thus to adjust σ_{HC} to force the uncertainty of the Highly Correlated dose to match the uncertainty in the Discrete Autoregressive dose, the uncertainty in the final body burdens will differ. However, note that both formulae, eq. 57 and 61, contain the factor $1/[(1-\alpha)(N^{1/2})]$. These factors will be discussed in the next section.

Discussion

One sees by eqs. 18a and 18b that the expectation of the body burdens and doses, respectively, in the Highly Correlated and Discrete Random cases are equal. Recall that in the Highly Correlated case, every man in an ensemble of men samples the environment once at the beginning of a T -year exposure. In the Discrete Random case, every man samples the environment several times in the T -year time span with each sample being independent of all others. So, averaged over the ensemble of men, in both cases one gets the same average for body burden and for dose. In the Discrete Random case, the number of samples is N times that of the Highly Correlated case.

In comparing the Discrete Random case with the Highly Correlated case in the Rapid Metabolism limit, eqs. 21 and 23, one finds that the uncertainty in the body burdens and doses, respectively, is the same in both cases, is proportional to the uncertainty in the distribution of the radionuclide in the soil, and is independent of the number of samples taken. In the Discrete Random case in which many samples per run are made, the Rapid Metabolism has the effect of purging one sample from the system before the end of the next time period. On the other hand, in the Slow Metabolism limit, the effect of each sampling persists for the duration of the run. In this limit, for the same uncertainty for the radionuclide concentration in the soil for both the Discrete Random and Highly Correlated cases, one finds that the uncertainties in the body burdens and doses in the Discrete Random case is less than those of the Highly Correlated case by a factor of $N^{1/2}$ and $(3N/4)^{1/2}$, respectively. So, by sampling many times, for which the content of the sampling persists in the system, the variance in the content of the system decreases by a factor of N . The dependence of the uncertainty on N in the Slow Metabolism limit is analogous to that of the standard error of the mean of N if N were to represent the number of samples used to estimate the mean. Now, if one want to simulate the effect of the multiple samples in situations in which the environment is sampled only once at the beginning of the run, one may do so by decreasing the uncertainty in the soil distribution by $N^{1/2}$ for body burdens or $(3N/4)^{1/2}$ for doses. That is, one can use the model in the constant input mode to simulate a variable input of multiple samples if it is known that the multiple sampling occurs in N discrete, equal time intervals. Note that the factor of $3^{1/2}/2$ arises from the definition of dose as proportional to the time integral of body burden.

Now consider the Discrete Autoregressive case. The Discrete Autoregressive case corresponds to real-world situations in which each man makes N successive samples of the environment over the course $[0, T]$ of the simulation, but for which each sample is not independent of the previous samples. Instead, each sample is correlated with the previous sample with a correlation coefficient of α , correlated with the second previous sample by

α^2 , etc. An example might be that the man lives in an environment for which the radionuclide contamination is a spatial function with small spatial variation over the distances of possible moves by the man. In this example, the function of spatial contamination would have small scale, spatial noise associated with it. If the man moves a small distance in this environment N times, his exposure could approximate the conditions of the Discrete Autoregressive case. Alternatively, in an occupational setting, N reassignments during a working career in which each reassignment had some similarity with the previous assignment and some new additional features could also approximate the conditions of the Discrete Autoregressive case.

As N becomes large, the expectation of the body burden in the Highly Correlated case is a constant factor times the expectation for the Discrete Autoregressive case in both the Slow Metabolism limit and the Rapid Metabolism limit. This constant factor is the same in both limits and equals $\epsilon_m c_{HC}^{-1} (1-\alpha)^{-1}$. One finds this same constant factor in comparing the expectation of the dose for the Highly Correlated and Autoregressive cases in the Slow Metabolism and slow decay limit. In other words, the expectation of the body burdens for both the Rapid and Slow Metabolism limits and of the doses for the Slow Metabolism and slow decay limit for the Highly Correlated case can be made equal to the expectations in the Discrete Autoregressive case if c_{HC} is chosen to be $\epsilon_m (1-\alpha)^{-1}$. For the Rapid Metabolism and rapid decay limit, the expectation of the doses in the Highly Correlated and Autoregressive cases are related by c_A/c_{HC} . So, the expectation of the dose in the Highly Correlated case can be made equal to the expectation in the Autoregressive case if c_A is chosen to be c_{HC} . In the Rapid Metabolism and rapid decay limit the initial sample is the most important. However in the other limits, the initial sample c_A in the Discrete Autoregressive case becomes increasingly unimportant as N gets large because α^N (the correlation of the last sample with c_A) is small for $\alpha < 1$. Hence, the mean of the noise term in the sampling is the important factor in determining final body burdens. But because

any noise introduced in any sampling persists into further time intervals, the mean of the sampled noise is inflated by a factor of $(1-\alpha)^{-1}$.

In the Rapid Metabolism limit for large values of N , the uncertainty of the body burden in the Discrete Autoregressive case is equal to the uncertainty in the Highly Correlated case multiplied by a factor of $\sigma_\epsilon \sigma_{HC} (1-\alpha^2)^{-1/2}$. One finds that σ_A , the uncertainty in the first sample of the soil concentration, is unimportant in determining the uncertainty in the body burden in the Discrete Autoregressive case. However, in the Rapid Metabolism and rapid decay limit, the uncertainty of the dose in the Autoregressive case is related to the uncertainty of the dose in the Highly Correlated case by the factor σ_A/σ_{HC} . Hence σ_A is important to the dose in this limit. Also, see that for large N the asymptotic expressions for the uncertainty in both the body burdens and doses in the Discrete Autoregressive case in the Rapid limit is independent of N . The radionuclide activity taken up in each to the N time periods is turned over before the end of the next period. Thus, each sample's impact on the final burden due to persistence of radionuclide burden is minimal. So the uncertainty is independent of the number of samples. However, the value of the radionuclide sampled near the end of the simulation depend on previous samples because of the autocorrelation function α^k . The uncertainty in the body burden for the Discrete Autoregressive case is increased by a factor of $(1-\alpha^2)^{-1/2}$ because of this reduced independence. One can force the uncertainty of the body burden in the Highly Correlated case to match the uncertainty of the Discrete Autoregressive case by adjusting the variance in the original distribution so that σ_{HC}^2 is set to $\sigma_\epsilon^2 (1-\alpha^2)^{-1}$. However, in the Rapid Metabolism and rapid decay limit, the uncertainty in the dose is determined solely by the uncertainty in the initial exposure σ_A .

In the Slow Metabolism limit for large N , the uncertainty in the body burdens and doses for the Discrete Autoregressive case is equal to the uncertainty in the Highly Correlated case multiplied by a factor of $\sigma_\epsilon \sigma_{HC}^{-1} [(1-\alpha)(N^{1/2})]^{-1}$ and $\sigma_\epsilon \sigma_{HC}^{-1} [(1-\alpha)(N^{1/2})]^{-1} [(2/(3^{1/2}))]$, respectively. Because of the Slow Metabolism,

each sampled radionuclide concentration persists in the body burden. This persistence decreases the uncertainty in the final body burden by the factor of $N^{1/2}$. Again, Slow Metabolism produces a dependence on N similar to that of the standard error. The effect of the correlation of the samples from one time period to the next reduces the randomness between time intervals and increases the uncertainty in the body burden by the factor of $(1-\alpha)^{-1}$. To force the Highly Correlated case to match the uncertainty in the body burdens or the dose in the Discrete Autoregressive case requires that one adjusts the uncertainty in the soil concentration so that σ_{HC} is set to $\sigma_{\epsilon} [(1-\alpha)(N^{1/2})]^{-1}$ or $\sigma_{\epsilon} [(1-\alpha)(N^{1/2})]^{-1} [2/(3^{1/2})]$, respectively. The difference of a factor of $2/(3^{1/2})$ between these two expressions arises from the definition of dose as an integral of body burden.

Conclusion

The results of this paper indicate that the rate of metabolism has an important effect on the uncertainty in body burdens of radionuclides and doses in situations in which the exposure to the radionuclide changes over time in a stochastic way. Slow Metabolism tends to reduce uncertainty relative to those situations in which the soil concentration is sampled once and then held constant.

However, our results also suggest that if enough is known about the resampling over the simulation period, then the uncertainty distribution for the single-sample, constant-input case (Highly Correlated) can be adjusted so that simulations using constant inputs can simulate the uncertainty of the body burdens or doses in the resampled (Discrete Random or Discrete Autoregressive) cases. In particular, one needs to know the number of resampling periods; they must be of equal length. One needs to know or be able to estimate the degree of autocorrelation between the successive exposures. Finally, an estimate of the mean and uncertainty in the random portion of the exposure must be made. If these factors

are all satisfied, both the mean and uncertainty of the soil exposure distribution can be adjusted to reproduce the characteristics of the body burden or dose distribution resulting from periodic re-exposure. For some statistics, such as expectations in the Discrete Random case, both both body burden and doses can be simulated simultaneously. For others statistics, either the body burden or dose can be reproduced but not both simultaneously.

Appendix A. Properties of the Metabolic Transfer Matrix

The matrix A' defined by ICRP(1979) is a lower triangular matrix

$$a_{ij} = 0 \quad \text{for } i < j \quad (\text{A.1})$$

whose diagonal elements are in the form

$$a_{ii} = -\mu_i - \lambda \quad (\text{A.2})$$

where μ_i is the biological turnover rate of the radionuclide in the i th compartment. Thus, it will be convenient to introduce a new matrix A of just the biological parameters defined by

$$A' = A - \lambda I \quad (\text{A.3})$$

where I is the identity matrix. The j th eigenvalues of A' is denoted by λ_j and is chosen so that the j th eigenvalue of A is $-\mu_j$. Kercher (1983) discusses the solution of linear transport models of the form of eq. 1 using eigenvalues and eigenvectors. Let us assume that the

eigenvalues of A' are discrete (not degenerate) so that the eigenvectors of A' are linearly independent. Denoting the j th eigenvector of A' as ψ^j , the eigen equation for A' is

$$A' \psi^j = \lambda_j \psi^j \quad (\text{A.4})$$

Equation A.1 implies that the eigenvalues of A' are the diagonal matrix elements so that

$$\lambda_i = -\mu_i - \lambda \quad (\text{A.5})$$

which is substituted along with eq. A.3 into eq. A.4 to get

$$A \psi^j = -\mu_j \psi^j \quad (\text{A.6})$$

Thus the eigenvectors of A are the eigenvectors of A' and the eigenvalues of A are $-\mu_i$.

Equation A.4 can be written as

$$A' \Psi = \Psi \Lambda \quad (\text{A.7})$$

where Ψ is a matrix with elements $\Psi_{ij} = \psi_i^j$ and Λ is the diagonal matrix with diagonal elements $\Lambda_{ii} = \lambda_i$. Note that $\Lambda_{ij} = 0$ for $i \neq j$. Because the eigenvectors of A' are linearly independent, Ψ^{-1} exists and eq. A.7 implies

$$\Psi^{-1} A' \Psi = \Lambda \quad (\text{A.8})$$

and in fact

$$\Psi^{-1} f(A') \Psi = f(\Lambda) \quad (\text{A.9})$$

and for A one finds

$$\Psi^{-1} \mathbf{A} \Psi = \Omega \quad (\text{A.10})$$

where Ω is the diagonal matrix with diagonal elements $\Omega_{jj} = -\mu_j$ and $\Omega_{ij} = 0$ for $i \neq j$.

Appendix B. Properties of Uncertainty Distributions

In this paper, we are interested in the uncertainty distribution of $y_k(t)$. Let us use the usual functions to characterize the distribution, namely, the mean and standard deviation. For a random variable X , take the usual definitions of the expectation function $E(X)$ or mean of X (Cramer 1955) such that $E(X)$ has the properties

$$E(aX + b) = a E(X) + b \quad (\text{B.1})$$

and

$$E\left(\sum_{i=1}^k a_i X_i\right) = \sum_{i=1}^k a_i E(X_i) \quad (\text{B.2})$$

where a and b are scalars. The standard deviation function $D(X)$ is given by

$$D^2(X) = \sigma^2 = E((X - E(X))^2) = E(X^2) - E^2(X) \quad (\text{B.3})$$

with the property

$$D(aX + b) = |a| D(X) \quad (\text{B.4})$$

Use the result that if the random variables X_i are independent then

$$E\left(\prod_{i=1}^k X_i\right) = \prod_{i=1}^k E(X_i) \quad (\text{B.5})$$

and

$$D^2\left(\sum_{i=1}^k a_i X_i\right) = \sum_{i=1}^k a_i^2 D^2(X_i) \quad (\text{B.6})$$

Appendix C. Calculations for the Discrete Random Case

To characterize the distribution of y_k , take the expectation of eq. 14 to get

$$E(y_k(T)) = e^{-\lambda T} \left[e^{\mathbf{A}T} (-\mathbf{A}^{-1}) (1 - e^{\mathbf{A}\Delta}) \sum_{i=1}^N E(C_i) e^{-\mathbf{A}i\Delta} \mathbf{G} \right]_k \quad (\text{C.1})$$

Let us assume that each sampling is independent but from the same distribution (nonseasonal), hence $E(C_i) = c_R$ where c_R is the mean soil concentration with radioactive decay removed. So eq. C.1 is simplified to

$$E(y_k(T)) = e^{-\lambda T} \left[e^{\mathbf{A}T} (-\mathbf{A}^{-1}) (1 - e^{\mathbf{A}\Delta}) c_R \sum_{i=1}^N e^{-\mathbf{A}i\Delta} \mathbf{G} \right]_k \quad (\text{C.2a})$$

$$= e^{-\lambda T} \left[e^{\mathbf{A}T} (-\mathbf{A}^{-1}) (1 - e^{\mathbf{A}\Delta}) c_R (e^{-\mathbf{A}\Delta} - e^{-\mathbf{A}\Delta(N+1)}) (1 - e^{-\mathbf{A}\Delta})^{-1} \mathbf{G} \right]_k \quad (\text{C.2b})$$

This expression simplifies to eq. 15 in the text.

Now let us consider the standard deviation for the Discrete Random case. Begin with eq. 7b and employ the Discrete Random case assumptions outlined above so that eq. 7b becomes

$$y_k(T) = \sum_{j,l=1}^n \Psi_{kj} e^{\lambda_j T} \sum_{i=1}^N C_i \Psi_{jl}^{-1} G_l \int_{(i-1)\Delta}^{i\Delta} e^{-(\lambda_j + \lambda)t} dt \quad (\text{C.3a})$$

$$= \sum_{j,l=1}^n \Psi_{kj} e^{\lambda_j T} \Psi_{jl}^{-1} G_l \frac{1 - e^{(\lambda_j + \lambda)\Delta}}{(-\lambda_j - \lambda)} \sum_{i=1}^N C_i e^{-(\lambda_j + \lambda)\Delta i} \quad (\text{C.3b})$$

Interchange the summations in eq. C.3b and take D^2 of both sides of the equation. Then use eq. B.6 because the C_i are independent. One finds

$$D^2(y_k) = \sum_{i=1}^N D^2(C_i) \left[\sum_{j,l=1}^n \Psi_{kj} e^{\lambda_j T} \Psi_{jl}^{-1} G_l \frac{(1 - e^{(\lambda_j + \lambda)\Delta})}{(-\lambda_j - \lambda)} e^{-(\lambda_j + \lambda)\Delta i} \right]^2 \quad (\text{C.4a})$$

Using $D^2(C_i) = \sigma_R^2$, perform the sum over i in eq. C.4a, and also use eq. A.5 to find

$$D^2(y_k) = \sigma_R^2 e^{-2\lambda T} \sum_{j,l,m,r=1}^n \Psi_{kj} \Psi_{km} e^{-(\mu_j + \mu_m)T} \Psi_{jl}^{-1} \Psi_{mr}^{-1} G_l G_r \left\{ \frac{(1 - e^{-\mu_j \Delta})(1 - e^{-\mu_m \Delta})}{\mu_j \mu_m} \frac{(1 - e^{-(\mu_j + \mu_m)T})}{(e^{-(\mu_j + \mu_m)\Delta} - 1)} \right\} \quad (\text{C.4b})$$

Rapid Metabolism Limit

Let us first consider the variance of the body burdens. In the Rapid Metabolism limit, all μ_i are large such that $\mu_i \Delta \gg 1$. In this limit, the expression in the curly brackets in eq. C.4b approaches

$$\{\dots\}_{\text{eq. C.4b}} \rightarrow \left\{ \mu_j^{-1} \mu_m^{-1} e^{(\mu_j + \mu_m)T} \right\} \quad (\text{C.5})$$

so that eq C.4b approaches

$$D^2(y_k) \rightarrow \sigma_R^2 e^{-2\lambda T} \sum_{j,l=1}^n [\Psi_{kj} \mu_j^{-1} \Psi_{jl}^{-1} G_l] \sum_{m,r=1}^n [\Psi_{km} \mu_m^{-1} \Psi_{mr}^{-1} G_r] \quad (\text{C.6a})$$

$$\rightarrow \sigma_R^2 e^{-2\lambda T} [-A^{-1} \mathbf{G}]_k^2 \quad (\text{C.6b})$$

The square root of eq. C.6b is shown in the text, eq. 19.

Slow Metabolism Limit

Now consider the limit of Slow Metabolism. In this limit, all the μ_i are small so $\mu_i T \ll 1$. First, let us examine the uncertainty in the body burdens. In this limit, eq. C.4b goes to

$$D^2(y_k) \rightarrow \sigma_R^2 e^{-\lambda T} \sum_{j,l,m,r=1}^n \Psi_{kj} \Psi_{km} e^{-(\mu_j + \mu_m)T} \Psi_{jl}^{-1} \Psi_{mr}^{-1} G_l G_r \Delta^2 \frac{T}{\Delta} \quad (\text{C.7a})$$

$$\rightarrow \sigma_R^2 e^{-2\lambda T} \frac{T^2}{N} G_l^2 \quad (\text{C.7b})$$

The square root of eq. C.7b is shown in the text as eq. 24.

Consider next the uncertainty in the dose. In addition to the Slow Metabolism limit, assume that $\lambda T \ll 1$. In this limit, the variance of the dose in the Discrete Random case (eq. 17) approaches

$$D^2(H_k) \rightarrow \sigma_R^2 \sum_{j,l,h,p,m,q=1}^n B_{kj} \Psi_{jl} B_{kh} \Psi_{hp} \Psi_{lm}^{-1} G_m \Psi_{pq}^{-1} G_q \frac{\Delta^4 N(N-1)(N+1)}{3} \quad (\text{C.8a})$$

$$\rightarrow \sigma_R^2 [\mathbf{B} \mathbf{G}]_k^2 \frac{T^4}{3N} \quad (\text{C.8b})$$

The square root of eq. C.8b is given in eq. 29.

Appendix D. Autocorrelation in the Autoregressive Model

To give meaning to the parameter α introduced in eq. 35b, consider the autocorrelation function defined for a random variable X_t as

$$\rho(t, \tau) = \frac{\text{Cov}(X_t, X_{t+\tau})}{\text{Var}(X_t)} = \frac{E[(X_t - E(X_t))(X_{t+\tau} - E(X_{t+\tau}))]}{E[(X_t - E(X_t))(X_t - E(X_t))]} \quad (\text{D.1a})$$

So, the autocorrelation function of the C_i defined by eq. 35b is found by substituting eq. 36 into the definitions of the covariance and variance. For $i > 1$

$$\text{Cov}(C_i, C_{i+k}) = E \left[\left\{ \alpha^{i-1}(C_1 - c_A) + \sum_{j=2}^i \alpha^{i-j}(\epsilon_j - \epsilon_m) \right\} \left\{ \alpha^{i-1+k}(C_1 - c_A) + \sum_{j=2}^i \alpha^{i+k-j}(\epsilon_j - \epsilon_m) \right\} \right] \quad (\text{D.1b})$$

Now note that since C_1 is independent of ϵ_i

$$E[(C_1 - c_A)(\epsilon_j - \epsilon_m)] = E(C_1 - c_A) E(\epsilon_j - \epsilon_m) = 0 \quad (\text{D.2})$$

So that for $i > 1$

$$\text{Cov}(C_i, C_{i+k}) = \alpha^{2i-2+k} E[(C_1 - c_A)^2] + \sum_{j=2}^i \alpha^{i-j} \alpha^{i+k-j} E[(\epsilon_j - \epsilon_m)^2] \quad (\text{D.3a})$$

$$= \alpha^{2i-2+k} \sigma_A^2 + \sigma_E^2 \alpha^{2i+k} \sum_{j=2}^i \alpha^{-2j} \quad (\text{D.3b})$$

$$= \alpha^{2i-2+k} \left[\sigma_A^2 + \sigma_E^2 \frac{\alpha^{-2(i-1)} - 1}{1 - \alpha^2} \right] \quad (\text{D.3c})$$

Following the same procedure, the variance for $i > 1$ is given by

$$\text{Var}(C_i) = \alpha^{2i-2} \left[\sigma_A^2 + \sigma_\varepsilon^2 \frac{\alpha^{-2(i-1)} - 1}{1 - \alpha^2} \right] \quad (\text{D.4})$$

So

$$\rho(i,k) = \frac{\alpha^{2i-2+k} \left[\sigma_A^2 + \sigma_\varepsilon^2 \frac{\alpha^{-2(i-1)} - 1}{1 - \alpha^2} \right]}{\alpha^{2i-2} \left[\sigma_A^2 + \sigma_\varepsilon^2 \frac{\alpha^{-2(i-1)} - 1}{1 - \alpha^2} \right]} = \alpha^k \quad i > 1 \quad (\text{D.5})$$

The derivation for $i = 1$ is even simpler

$$\text{Cov}(C_1, C_{1+k}) = E \left[(C_1 - c_A) \left\{ \alpha^k (C_1 - c_A) + \sum_{j=2}^{1+k} \alpha^{1+k-j} (\varepsilon_j - \varepsilon_m) \right\} \right] \quad (\text{D.6a})$$

$$= \alpha^k E[(C_1 - c_A)^2] = \alpha^k \sigma_A^2 \quad (\text{D.6b})$$

and

$$\text{Var}(C_1) = \sigma_A^2 \quad (\text{D.6c})$$

So

$$\rho(1,k) = \alpha^k \quad (\text{D.7})$$

Therefore, for all i and k one finds

$$\rho(i,k) = \alpha^k \quad \text{for } i \geq 1, k \geq 0 \quad (\text{D.8})$$

Appendix E. Calculations in the Discrete Autoregressive Case

To calculate the uncertainty in the distribution of y_k in the Discrete Autoregressive case, begin with eq. C.3b, which is rewritten as

$$y_k(T) = \sum_{j,l=1}^n \Psi_{kj} e^{\lambda_j T} \Psi_{jl}^{-1} G_l \frac{1 - e^{-\mu \Delta}}{\mu_j} \left[C_1 e^{\mu \Delta} + \sum_{i=2}^N C_i e^{\mu_i \Delta} \right] \quad (E.1)$$

and substitute eq. 36 for C_i to get

$$y_k(T) = \sum_{j,l=1}^n \Psi_{kj} e^{\lambda_j T} \Psi_{jl}^{-1} G_l \frac{1 - e^{-\mu \Delta}}{\mu_j} \left[C_1 e^{\mu \Delta} + \sum_{i=2}^N \left(\alpha^{i-1} C_1 + \sum_{r=2}^i \alpha^{i-r} \varepsilon_r \right) e^{\mu_i \Delta} \right] \quad (E.2)$$

Then simplify by carefully interchanging summations and summing over i to get

$$y_k(T) = \sum_{j,l=1}^n \Psi_{kj} e^{\lambda_j T} \Psi_{jl}^{-1} G_l \frac{1 - e^{-\mu \Delta}}{\mu_j} \left[C_1 e^{\mu \Delta} \frac{1 - \alpha^N e^{\mu_j T}}{1 - \alpha e^{\mu \Delta}} + \sum_{r=2}^N \varepsilon_r e^{\mu_r \Delta} \frac{1 - \alpha^{N-r+1} e^{\mu \Delta (N-r+1)}}{1 - \alpha e^{\mu \Delta}} \right] \quad (E.3)$$

Take D^2 of both sides of eq. E.3 and since all the random variables in eq.E.3 are independent, apply eq. B.6 to get

$$D^2(y_k) = \left[\sum_{j,l=1}^n \Psi_{kj} e^{\lambda_j T} \Psi_{jl}^{-1} G_l \frac{1 - e^{-\mu \Delta}}{\mu_j} e^{\mu \Delta} \frac{1 - \alpha^N e^{\mu_j T}}{1 - \alpha e^{\mu \Delta}} \right]^2 D^2(C_1) + \sum_{i=2}^N D^2(\varepsilon_i) \left[\sum_{j,l=1}^n \Psi_{kj} e^{\lambda_j T} \Psi_{jl}^{-1} G_l \frac{1 - e^{-\mu \Delta}}{\mu_j} e^{\mu_i \Delta} \frac{1 - \alpha^{N-i+1} e^{\mu \Delta (N-i+1)}}{1 - \alpha e^{\mu \Delta}} \right]^2 \quad (E.4)$$

Using $D^2(C_1) = \sigma_A^2$ and $D^2(\varepsilon_i) = \sigma_\varepsilon^2$, perform the sum over i and this equation becomes eq. 39.

Rapid Metabolism Limit

In the limit of Rapid Metabolism, the expectation value of the body burden y_k for the Highly Correlated case, eq. 11, goes to

$$E(y_k, \text{Highly Correlated}) \rightarrow e^{-\lambda T} c_{HC} [-\mathbf{A}^{-1} \mathbf{G}]_k \quad (E.5)$$

whereas the expectation value for the Discrete Autoregressive case goes to

$$E(y_k, \text{Autoregressive}) \rightarrow \left[\alpha^{N-1} + \frac{\epsilon_m}{c_A (1 - \alpha)} (1 - \alpha^{N-1}) \right] e^{-\lambda T} c_A [-\mathbf{A}^{-1} \mathbf{G}]_k \quad (E.6)$$

These two equations are combined to produce eq. 43.

Now consider the uncertainty of the body burden in the Rapid Metabolism limit. In this limit, as before, the uncertainty of the Highly Correlated case (eq. 12) approaches

$$D(y_k, \text{Highly Correlated}) \rightarrow e^{-\lambda T} \sigma_{HC} [-\mathbf{A}^{-1} \mathbf{G}]_k \quad (E.7)$$

and the uncertainty in the Discrete Autoregressive case approaches

$$D^2(y_k, \text{Autoregressive}) \rightarrow e^{-2\lambda T} \sigma_A^2 \left[\alpha^{2(N-1)} + \frac{\sigma_\epsilon^2 (1 - \alpha^{2(N-1)})}{\sigma_A^2 (1 - \alpha^2)} \right] [-\mathbf{A}^{-1} \mathbf{G}]_k \quad (E.8)$$

Combining these two formulae one arrives at eq. 47 in the text.

To calculate the expectation of the dose H_k in the Rapid Metabolism limit, assume that the decay is rapid, too, i.e., assume $\lambda \Delta \gg 1$. Then the expectation of the dose in the Discrete Autoregressive case approaches

$$E(H_k) \rightarrow \frac{c_A}{\lambda} \left[\mathbf{B} (-\mathbf{A} + \lambda)^{-1} \mathbf{G} \right]_k \quad (E.9)$$

and the dose in the Highly Correlated case in the same limit also approaches

$$E(H_k) \rightarrow \frac{c_{HC}}{\lambda} \left[\mathbf{B} (-\mathbf{A} + \lambda)^{-1} \mathbf{G} \right]_k \quad E.10$$

These formulae can be combined to produce eq. 50 in the text.

Now consider the uncertainty in the dose for the Rapid Metabolism limit. In this limit, eq. 42a approaches

$$D^2(H_k, \text{Autoregressive}) \rightarrow \frac{\sigma_A^2}{\lambda^2} \left[\mathbf{B} (-\mathbf{A} + \lambda)^{-1} \mathbf{G} \right]_k^2 \quad (E.11)$$

just as the Highly Correlated case, eq. 13c, approaches

$$D(H_k, \text{Highly Correlated}) \rightarrow \frac{\sigma_{HC}}{\lambda} \left[\mathbf{B} (-\mathbf{A} + \lambda)^{-1} \mathbf{G} \right]_k \quad (E.12)$$

These two equations combine to produce eq. 51.

Slow Metabolism Limit

In the limit of Slow Metabolism for the radionuclide in question, the expectation value of the body burden y_k for Highly Correlated case, eq. 11, approaches

$$E(y_k, \text{Highly Correlated}) \rightarrow e^{-\lambda T} c_{HC} T G_k \quad (E.13)$$

and the expectation value of the body burden in the Discrete Autoregressive case, eq. 43, approaches

$$E(y_k, \text{Autoregressive}) \rightarrow \left[\frac{\epsilon_m}{c_A (1 - \alpha)} + \frac{1}{N} \frac{1 - \alpha^N}{1 - \alpha} \left(1 - \frac{\epsilon_m}{c_A (1 - \alpha)} \right) \right] e^{-\lambda T} c_A T G_k \quad (E.14)$$

Use these equations to get eq. 54a.

To calculate the uncertainty in the body burden y_k in the Slow Metabolism limit for the Highly Correlated case take the limit of eq. 12 to find, as before,

$$D(y_k, \text{Highly Correlated}) \rightarrow e^{-\lambda T} \sigma_{HC} T G_k \quad (E.15)$$

and the limit for the Discrete Autoregressive case, eq. 39 becomes

$$D^2(y_k, \text{Autoregressive}) \rightarrow \left[\frac{1}{N^2} \left(\frac{1 - \alpha^N}{1 - \alpha} \right)^2 + \frac{\sigma_\epsilon^2}{\sigma_A^2 N^2 (1 - \alpha)^2} \left\{ N - 1 - \left(\frac{1 - \alpha^N}{1 - \alpha^2} \right) (1 - \alpha^N + 2\alpha) \right\} \right] \sigma_A^2 e^{-2\lambda T} T^2 G_k^2 \quad (E.16)$$

These two equations can be combined to produce eq. 55 in the text.

The expectation of the dose for the Highly Correlated case in the Slow Metabolism (and decay) limit approaches

$$E(H_k, \text{Highly Correlated}) \rightarrow c_{HC} [\mathbf{B} \ \mathbf{G}]_k \frac{T^2}{2} \quad (E.17)$$

and the expectation of the dose in the Discrete Autoregressive case approaches

$$E(H_k, \text{Autoregressive}) \rightarrow \frac{\epsilon_m}{1 - \alpha} [\mathbf{B} \ \mathbf{G}]_k \frac{T^2}{2} \quad (E.18)$$

Use these two equations to produce eq. 58.

Recall that the uncertainty of the dose for the Highly Correlated case in the Slow Metabolism (and decay) limit, eqs. 13c and 30, approaches

$$D(H_k, \text{Highly Correlated}) \rightarrow \sigma_{HC} [B G]_k \frac{T^2}{2} \quad (E.19)$$

and the uncertainty of the dose for the Autoregressive case, eq. 42a, in this limit approaches

$$D^2(H_k, \text{Autoregressive}) \rightarrow \frac{\sigma_{\epsilon}^2}{(1 - \alpha)^2} [B G]_k^2 \frac{T^4}{3N} \quad (E.20)$$

Combining eq. E.19 and E.20, one gets eq. 60 which relates the uncertainties of the two doses.

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