Vesa Oikonen, Marco Bucci

Model equations for parallel compartmental model with additional loss rate constant

This document describes the mathematical equations needed to simulate the PET time-radioactivity concentration curves in compartmental model which has one central tissue compartment, two parallel compartments attached to it, and possible loss from one of parallel compartments directly to venous plasma. The approach of Kuwabara et al. [1] is used for partial solutions of the differential equations.

The compartment for arterial plasma (or blood, depending on the specific model), and the first tissue compartment are represented by C_A and C_1, respectively. Parallel tissue compartments C_2 and C_3 are attached to C_1, and there is an additional loss rate constant, k_{loss}, representing loss from C_3 to venous plasma (blood) directly, without passing through compartment C_1. The differential equations describing the concentration changes in the compartments can be written as:

$$dC_1(t)/dt = k_1 C_A(T) - (k_2 + k_3 + k_5) C_1(T) + k_4 C_2(T) + k_6 C_3(T) \quad (A.1)$$
$$dC_2(t)/dt = k_3 C_1(T) - k_4 C_2(T) \quad (A.2)$$
$$dC_3(t)/dt = k_5 C_1(T) - (k_6 + k_{loss}) C_3(T) \quad (A.3)$$

The integrated forms of Eqs. (A.1-A.3) are:

$$C_1(T) = k_1 \int_0^T C_A(t)dt - (k_2 + k_3 + k_5) \int_0^T C_1(t)dt + k_4 \int_0^T C_2(t)dt + k_6 \int_0^T C_3(t)dt \quad (A.4)$$
$$C_2(T) = k_3 \int_0^T C_1(t)dt - k_4 \int_0^T C_2(t)dt \quad (A.5)$$
$$C_3(T) = k_5 \int_0^T C_1(t)dt - (k_6 + k_{loss}) \int_0^T C_3(t)dt \quad (A.6)$$

The Eqs. (1), (8) and (11-13) apply also to this situation. Because of additional loss rate constant, equations (9) and (10) now have to be written as:

$$dC_T(t)/dt = k_1 C_A(T) - k_2 C_1(T) - k_{loss} C_3(T) \quad (A.7)$$
$$C_T(T) = k_1 \int_0^T C_A(t)dt - k_2 \int_0^T C_1(t)dt - k_{loss} \int_0^T C_3(t)dt \quad (A.8)$$

Substitutions of Eq. (12) into Eqs. (A.5) and (A.6), with rearrangements, give the concentrations of the second and third tissue compartment:

$$C_2(T) = \frac{k_3\int_0^T C_1(t)dt - k_4\left(\int_0^{T-\Delta t} C_2(t)dt + \frac{\Delta t}{2}C_2(T-\Delta t)\right)}{1+\frac{\Delta t}{2}k_4} \qquad (A.9)$$

$$C_3(T) = \frac{k_5\int_0^T C_1(t)dt - (k_6 + k_{loss})\left(\int_0^{T-\Delta t} C_3(t)dt + \frac{\Delta t}{2}C_3(T-\Delta t)\right)}{1+\frac{\Delta t}{2}(k_6 + k_{loss})} \qquad (A.10)$$

Substitutions of Eq. (13) into Eqs. (A.5) and (A.6), give the integrals of concentrations of the second and third tissue compartment,

$$\int_0^T C_2(t)dt = \frac{k_3\frac{\Delta t}{2}\int_0^T C_1(t)dt + \int_0^{T-\Delta t} C_2(t)dt + \frac{\Delta t}{2}C_2(T-\Delta t)}{1+\frac{\Delta t}{2}k_4} \qquad (A.9)$$

$$\int_0^T C_3(t)dt = \frac{k_5\frac{\Delta t}{2}\int_0^T C_1(t)dt + \int_0^{T-\Delta t} C_3(t)dt + \frac{\Delta t}{2}C_3(T-\Delta t)}{1+\frac{\Delta t}{2}(k_6 + k_{loss})} \qquad (A.10)$$

which can be substituted into Eq. (A.1), and with the help of Eq. (12), the concentration in the first tissue compartment can be calculated:

$$C_1(T) = \frac{\left\{\begin{array}{c} k_1\int_0^T C_A(t)dt \\ -\left(k_2 + k_3 + k_4 - \frac{k_3 k_4\frac{\Delta t}{2}}{1+\frac{\Delta t}{2}k_4} - \frac{k_5 k_6\frac{\Delta t}{2}}{1+\frac{\Delta t}{2}(k_6 + k_{loss})}\right)\left(\int_0^{T-\Delta t} C_1(t)dt + \frac{\Delta t}{2}C_1(T-\Delta t)\right) \\ +\frac{k_4}{1+\frac{\Delta t}{2}k_4}\left(\int_0^{T-\Delta t} C_2(t)dt + \frac{\Delta t}{2}C_2(T-\Delta t)\right) \\ +\frac{k_6}{1+\frac{\Delta t}{2}(k_6 + k_{loss})}\left(\int_0^{T-\Delta t} C_3(t)dt + \frac{\Delta t}{2}C_3(T-\Delta t)\right) \end{array}\right\}}{\left\{1+\frac{\Delta t}{2}\left(k_2 + k_3 + k_4 - \frac{k_3 k_4\frac{\Delta t}{2}}{1+\frac{\Delta t}{2}k_4} - \frac{k_5 k_6\frac{\Delta t}{2}}{1+\frac{\Delta t}{2}(k_6 + k_{loss})}\right)\right\}} \qquad (A.11)$$

References

1. Kuwabara H, Cumming P, Reith J, Léger G, Diksic M, Evans AC, Gjedde A. Human striatal L-DOPA decarboxylase activity estimated in vivo using 6-[18F]fluoro-DOPA and positron emission tomography: error analysis and application to normal subjects. *J. Cereb. Blood Flow Metab.* 1993; 13:43-56.