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Model equations for common compartmental models

This document describes the mathematical equations needed to simulate the PET time-radioactivity concentration curves in compartmental models which have three tissue compartments, and equations for calculating the effect of blood radioactivity and the effect of blood flow on it. The approach of Kuwabara et al. [1] is used for partial solutions of the differential equations.

Compartments in series

When the compartment for arterial plasma (or blood, depending on the specific model), C_A, and all three tissue compartments, C_1, C_2, and C_3, are in series, the differential equations describing the concentration changes in the compartments and in the tissue without vasculature, C_T, can be written as:

$$C_T(t) = C_1(t) + C_2(t) + C_3(t) \quad (1)$$
$$dC_1(t)/dt = k_1 C_A(t) - (k_2 + k_3)C_1(t) + k_4 C_2(t) \quad (2)$$
$$dC_2(t)/dt = k_3 C_1(t) - (k_4 + k_5)C_2(t) + k_6 C_3(t) \quad (3)$$
$$dC_3(t)/dt = k_5 C_2(t) - k_6 C_3(t) \quad (4)$$

The integrated forms of equations (2-4) are:

$$C_1(T) = k_1 \int_0^T C_A(t)dt - (k_2 + k_3)\int_0^T C_1(t)dt + k_4 \int_0^T C_2(t)dt \quad (5)$$
$$C_2(T) = k_3 \int_0^T C_1(t)dt - (k_4 + k_5)\int_0^T C_2(t)dt + k_6 \int_0^T C_3(t)dt \quad (6)$$
$$C_3(T) = k_5 \int_0^T C_2(t)dt - k_6 \int_0^T C_3(t)dt \quad (7)$$

The concentration in venous blood, C_V^B, can be calculated from the arterial blood concentration, C_A^B, if blood flow (perfusion), f, is known. The required change in tissue concentration can be derived from the Eqs (1-4).

$$C_V^B(t) = C_A^B(t) - \frac{dC_T(t)/dt}{f} \quad (8)$$
$$dC_T(t)/dt = k_1 C_A(t) - k_2 C_1(t) \quad (9)$$
$$C_T(T) = k_1 \int_0^T C_A(t)dt - k_2 \int_0^T C_1(t)dt \quad (10)$$

The vascular volume, V_B (*ml/ml*), in PET radioactivity concentration per volume data, $C_{PET}(t)$, can then be included in the model by using the following equation, where r_A is the arterial fraction of V_B:

$$C_{PET}(t) = (1 - V_B)C_T(t) + V_B r_A C_A^B(t) + V_B(1 - r_A)C_V^B(t) \qquad (11)$$

By applying linear interpolation, the integral of radioactivity concentration in compartment n can be presented as in Eq. (12), and the compartmental concentration can be solved as in Eq. (13); Δt is the PET frame length (sample collection time):

$$\int_0^T C_N(t)dt = \int_0^{T-\Delta t} C_N(t)dt + \frac{\Delta t}{2} C_N(T - \Delta t) + \frac{\Delta t}{2} C_N(T) \qquad (12)$$

$$C_N(T) = \frac{1}{\Delta t/2} \int_0^T C_N(t)dt - \frac{1}{\Delta t/2} \left(\int_0^{T-\Delta t} C_N(t)dt + \frac{\Delta t}{2} C_N(T - \Delta t) \right) \qquad (13)$$

Substitution of Eq. (12) into Eq. (7) gives the equation for $C_3(T)$:

$$C_3(T) = \frac{k_5 \int_0^T C_2(t)dt - k_6 \left(\int_0^{T-\Delta t} C_3(t)dt + \frac{\Delta t}{2} C_3(T - \Delta t) \right)}{1 + \frac{\Delta t}{2} k_6} \qquad (14)$$

And equation for the integral of $C_3(t)$ can be derived e.g. by substitution of Eq. (13) into Eq. (7):

$$\int_0^T C_3(t)dt = \frac{k_5 \frac{\Delta t}{2} \int_0^T C_2(t)dt + \left(\int_0^{T-\Delta t} C_3(t)dt + \frac{\Delta t}{2} C_3(T - \Delta t) \right)}{1 + \frac{\Delta t}{2} k_6} \qquad (15)$$

Substitution of Eq. (15) in the Eq. (6), and then substitution of Eq. (12), gives the equation for $C_2(T)$:

$$C_2(T) = \frac{\left\{ \begin{array}{c} k_3 \int_0^T C_1(t)dt \\ - \left(k_4 + k_5 - \frac{k_5 k_6 \frac{\Delta t}{2}}{1 + \frac{\Delta t}{2} k_6} \right) \left(\int_0^{T-\Delta t} C_2(t)dt + \frac{\Delta t}{2} C_2(T - \Delta t) \right) \\ + \frac{k_6}{1 + \frac{\Delta t}{2} k_6} \left(\int_0^{T-\Delta t} C_3(t)dt + \frac{\Delta t}{2} C_3(T - \Delta t) \right) \end{array} \right\}}{\left\{ 1 + \frac{\Delta t}{2} \left(k_4 + k_5 - \frac{k_5 k_6 \frac{\Delta t}{2}}{1 + \frac{\Delta t}{2} k_6} \right) \right\}} \qquad (16)$$

Substitution of Eq. (15) in the Eq. (6), and then substitution of Eq. (13), gives the equation for the integral of $C_2(t)$:

$$\int_0^T C_2(t)dt = \frac{\left\{ \begin{array}{c} k_3 \frac{\Delta t}{2} \int_0^T C_1(t)dt \\ + \left(\int_0^{T-\Delta t} C_2(t)dt + \frac{\Delta t}{2} C_2(T-\Delta t) \right) \\ + \frac{\frac{\Delta t}{2} k_6}{1+\frac{\Delta t}{2} k_6} \left(\int_0^{T-\Delta t} C_3(t)dt + \frac{\Delta t}{2} C_3(T-\Delta t) \right) \end{array} \right\}}{\left\{ 1 + \frac{\Delta t}{2} \left(k_4 + k_5 - \frac{k_5 k_6 \frac{\Delta t}{2}}{1+\frac{\Delta t}{2} k_6} \right) \right\}} \qquad (17)$$

To derive the equation for $C_1(t)$, the Eq. (17) is substituted into Eq. (5):

$$C_1(T) = \frac{\left\{ \begin{array}{c} k_1 \left\{ 1 + \frac{\Delta t}{2} \left(k_4 + k_5 - \frac{k_5 k_6 \frac{\Delta t}{2}}{1+\frac{\Delta t}{2} k_6} \right) \right\} \int_0^T C_A(t)dt \\ + \left(k_3 k_4 \frac{\Delta t}{2} - (k_2 + k_3) \left\{ 1 + \frac{\Delta t}{2} \left(k_4 + k_5 - \frac{k_5 k_6 \frac{\Delta t}{2}}{1+\frac{\Delta t}{2} k_6} \right) \right\} \right) \left(\int_0^{T-\Delta t} C_1(t)dt + \frac{\Delta t}{2} C_1(T-\Delta t) \right) \\ + k_4 \left(\int_0^{T-\Delta t} C_2(t)dt + \frac{\Delta t}{2} C_2(T-\Delta t) \right) \\ + \frac{k_4 k_6 \frac{\Delta t}{2}}{1+\frac{\Delta t}{2} k_6} \left(\int_0^{T-\Delta t} C_3(t)dt + \frac{\Delta t}{2} C_3(T-\Delta t) \right) \end{array} \right\}}{\left\{ \left(1 + \frac{\Delta t}{2} \left(k_4 + k_5 - \frac{k_5 k_6 \frac{\Delta t}{2}}{1+\frac{\Delta t}{2} k_6} \right) \right) \left(1 + \frac{\Delta t}{2} (k_2 + k_3) \right) - k_3 k_4 \left(\frac{\Delta t}{2} \right)^2 \right\}} \qquad (18)$$

Compartments in parallel

When the compartments C_2 and C_3 are in parallel (e.g. specific and non-specific receptor binding), the differential equations describing the concentration changes in the compartments can be written as:

$$dC_1(t)/dt = k_1 C_A(t) - (k_2 + k_3 + k_5) C_1(t) + k_4 C_2(t) + k_6 C_3(t) \qquad (19)$$
$$dC_2(t)/dt = k_3 C_1(t) - k_4 C_2(t) \qquad (20)$$
$$dC_3(t)/dt = k_5 C_1(t) - k_6 C_3(t) \qquad (21)$$

The integrated forms of Eqs (19-21) are:

$$C_1(T) = k_1 \int_0^T C_A(t)dt - (k_2 + k_3 + k_5)\int_0^T C_1(t)dt + k_4 \int_0^T C_2(t)dt + k_6 \int_0^T C_3(t)dt \quad (22)$$

$$C_2(T) = k_3 \int_0^T C_1(t)dt - k_4 \int_0^T C_2(t)dt \quad (23)$$

$$C_3(T) = k_5 \int_0^T C_1(t)dt - k_6 \int_0^T C_3(t)dt \quad (24)$$

The Eqs. (1) and (8-13) apply also to this situation. Substitutions of Eq. (12) into Eqs. (23) and (24) give the concentrations of the second and third tissue compartment:

$$C_2(T) = \frac{k_3 \int_0^T C_1(t)dt - k_4 \left(\int_0^{T-\Delta t} C_2(t)dt + \frac{\Delta t}{2} C_2(T - \Delta t) \right)}{1 + \frac{\Delta t}{2} k_4} \quad (25)$$

$$C_3(T) = \frac{k_5 \int_0^T C_1(t)dt - k_6 \left(\int_0^{T-\Delta t} C_3(t)dt + \frac{\Delta t}{2} C_3(T - \Delta t) \right)}{1 + \frac{\Delta t}{2} k_6} \quad (26)$$

When the Eqs. (9) and (25) and (26) are substituted into Eq. (22), the concentration in the first tissue compartment can be calculated:

$$C_1(T) = \frac{\left\{ \begin{array}{c} k_1 \int_0^T C_A(t)dt \\ -\left(k_2 + \frac{k_3}{1+\frac{\Delta t}{2}k_4} + \frac{k_5}{1+\frac{\Delta t}{2}k_6} \right)\left(\int_0^{T-\Delta t} C_1(t)dt + \frac{\Delta t}{2} C_1(T-\Delta t) \right) \\ + \frac{k_4}{1+\frac{\Delta t}{2}k_4}\left(\int_0^{T-\Delta t} C_2(t)dt + \frac{\Delta t}{2} C_2(T-\Delta t) \right) \\ + \frac{k_6}{1+\frac{\Delta t}{2}k_6}\left(\int_0^{T-\Delta t} C_3(t)dt + \frac{\Delta t}{2} C_3(T-\Delta t) \right) \end{array} \right\}}{\left\{ 1 + \frac{\Delta t}{2}\left(k_2 + \frac{k_3}{1+\frac{\Delta t}{2}k_4} + \frac{k_5}{1+\frac{\Delta t}{2}k_6} \right) \right\}} \quad (27)$$

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.