Turku PET Centre Modelling report TPCMOD0010 2003-07-08
Vesa Oikonen

Modelling input function

This document reviews the input function models that are used in simulation or smoothing of the blood and plasma time-activity curves (TACs) in PET measurements. For now, this is mainly based on the study of Graham (1997).

Linear interpolation

A common approach, and applied by default in Turku PET Centre, is to use linear interpolation between the measured points.

Spline fitting

Measured input curve can be smoothed to avoid the non-physiological abrupt changes caused by measurement errors (sample timing, weighing or pipetting, and radioactivity counting). Several different spline fitting approaches have been used [Bassingthwaighte et al 1988; Beyer 1992].

Mathematical function fitting

Sum of exponential functions

A common approach is to fit a sum of two to three exponentials to the descending part of the bolus input curve, and to model the initial part either by linear interpolation, or by fitting another exponential function.

Thompson and Golish bolus input function

Bolus input function was modelled by Thompson et al. (1964); see Fig.1. Golish et al (2001) modified this function to include an asymptotic recirculation term:

$$C_p(t) = C_{\max}\left(\frac{\exp(1)}{\alpha\beta}(t-t_0)\right)^{\alpha}\exp\left(\frac{-(t-t_0)}{\beta}\right) \quad + \quad C_0\left(1-\exp\left(-(t-t_0)/\tau\right)\right)$$

The function with the recirculation term was developed for [^{13}N]NH_4^+ studies, but it seems to be suitable for fitting the blood curves which reach a steady level, e.g. [^{15}O]H_2O and [^{15}O]O_2 studies (Fig. 2.).

Gamma variate

Empirically determined curves for flow through vessels have been shown to correspond to gamma variate function, which can also be used to model the recirculation [Davenport 1983]. The expression of the gamma variate is

$$f(t) = \frac{t^{\alpha}e^{-t/\beta}}{\beta^{(\alpha+1)}\Gamma(\alpha+1)}$$

where α and β are parameters (α>-1), and Γ(α+1) is the gamma function defined by

$$\Gamma(\alpha+1)=\int_0^\infty x^\alpha e^{-x}dx$$

Kinetic models

Feng et al.

Feng et al. (1993) proposed and compared several different kinetic compartmental models for modelling the disappearance of tracers from the vascular space.

Graham

A somewhat different compartmental model was proposed by Graham (1997). This model depicts slowly varying plasma activity over several minutes, but is not intended to model the first-pass kinetics of tracers such as [^{15}O]H_2O [Graham 1997]. As Graham points out, all compartmental models will have a simple exponential behavior at late times, although many tracers tend to have a slight upward convexity long times after injection. This model cannot account for this phenomenon, nor the biphasic curves that may be caused by e.g. intravascular binding to blood cells [Graham & Nelp, 1980]. Appendix A contains the details of this model and an extension to it.

Maguire et al.

Maguire et al. (2003) developed further the compartmental models designed for [^{15}O]H_2O bolus studies, originally suggested by Bigler et al. (1981). The basic model consists of one central blood compartment, a fast exchanging compartment, and slow exchanging compartment. In the simplest model the slow exchanging compartment was removed, and in the optimum model the slow exchanging compartment was replaced by clearance term (no back-flux).

References

1. Bassingthwaighte JB, Chan IS, Goldstein AA. An efficient method for smoothing indicator-dilution and other unimodal curves. *Comput. Biomed. Res.* 1988; 21: 192-202.
2. Beyer RP. Fitting smooth curves to noisy indicator-dilution and other unimodal data. *Comput. Biomed. Res.* 1992; 25: 144-152.
3. Bigler RE, Kostick JA, Gillespie JR. Compartmental analysis of the steady-state distribution of $^{15}O_2$ and $H_2{}^{15}O$ in total body. *J. Nucl. Med.* 1981; 22: 959-965.
4. Feng D, Huang SC, Wang X. Models for computer simulation studies of input functions for tracer kinetic modeling with PET. *Int. J. Biomed. Comput.* 1993; 32: 95-110.
5. Davenport R. The derivation of the gamma-variate relationship for tracer dilution curves. *J. Nucl. Med.* 1983; 24: 945-948.
6. Golish SR, Hove JD, Schelbert HR, Gambhir SS. A fast nonlinear method for parametric imaging of myocardial perfusion by dynamic ^{13}N-ammonia PET. *J. Nucl. Med.* 2001; 42: 924-931.
7. Graham MM. Physiologic smoothing of blood time-activity curves for PET data analysis. *J. Nucl. Med.* 1997; 38: 1161-1168.
8. Graham MM, Nelp WB. Cardiac blood pool activity after in vivo and in vitro red blood cell (RBC) labelling. *J. Nucl. Med.* 1980; 21: P7.
9. Maguire RP, Spyrou NM, Leenders KL. Whole body [O-15]water pharmacokinetics measured in blood. *Physiol. Meas.* 2003; 24: 237-249.
10. Thompson JA, Starmar F, Whalen RE, McIntosh HD. Indicator transit time considered as a gamma variate. *Circ. Res.* 1964; 14: 502-515.

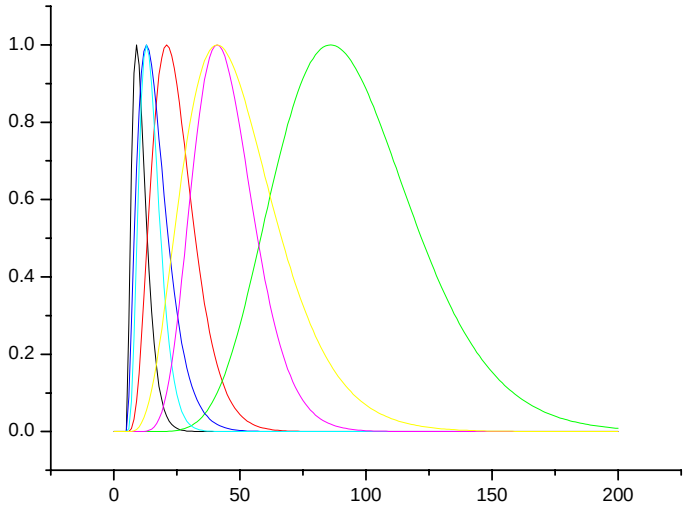

Fig. 1. Examples of Thompson's functions.

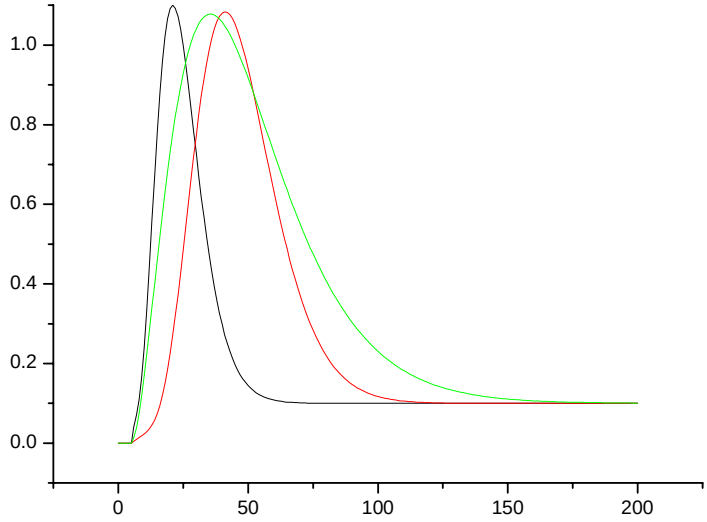

Fig. 2. Examples of Thompson's function with asymptotic recirculation term by Golish et al (2001).