The University of Manchester
Wolfson Molecular Imaging Centre

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Input Functions in PET

PET Oncology Meeting

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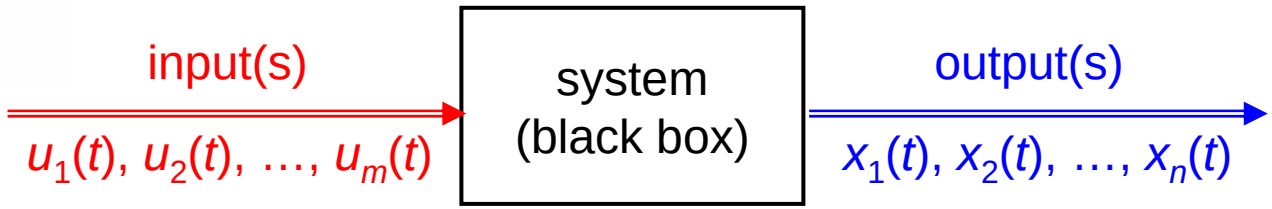
GENERAL

EXAMPLE

Input function: What is it and Why is it needed?

The concept of a *dynamical model*:

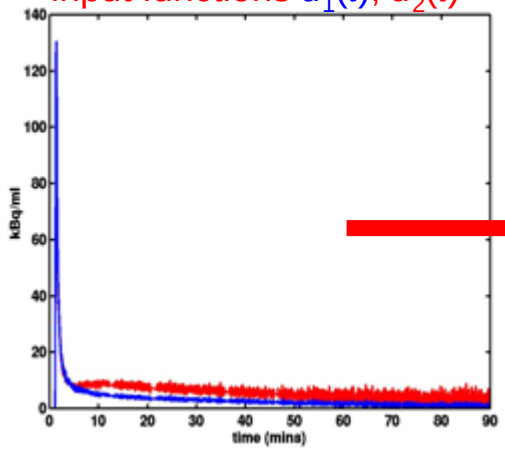


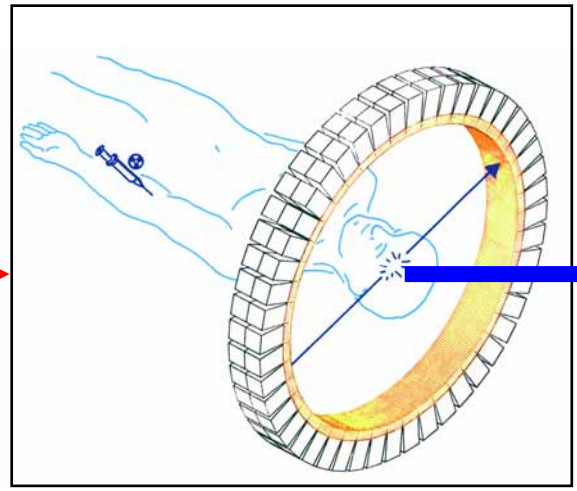
System identification:

perturb the system with an *input function*, observe the *system response* and try to infer the *system parameters* from the time series.

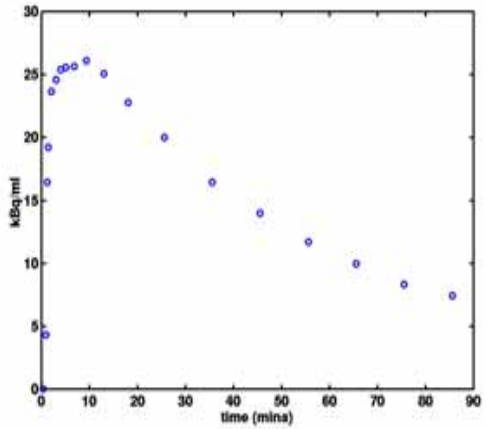
In PET:

input functions $u_1(t)$, $u_2(t)$





system response $x(t)$



Input function: What is it and Why is it needed?

In PET, the mathematical models are classified by their type of input in:

- plasma input models,
- reference tissue input models.

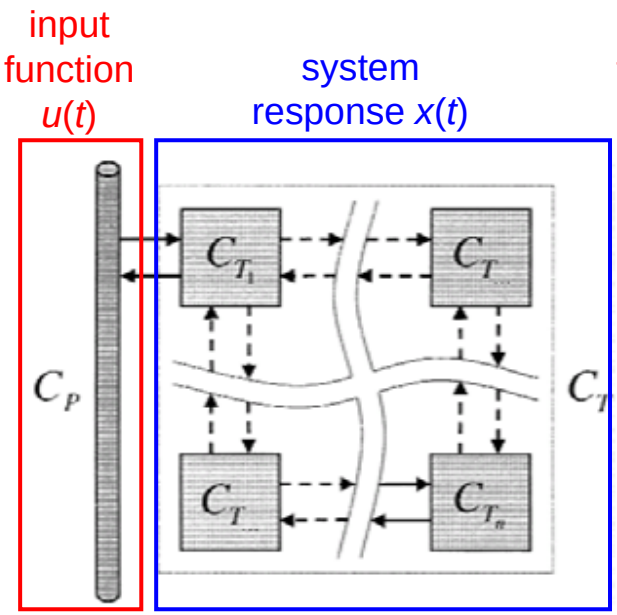


FIG. 2. Reversible tissue model.

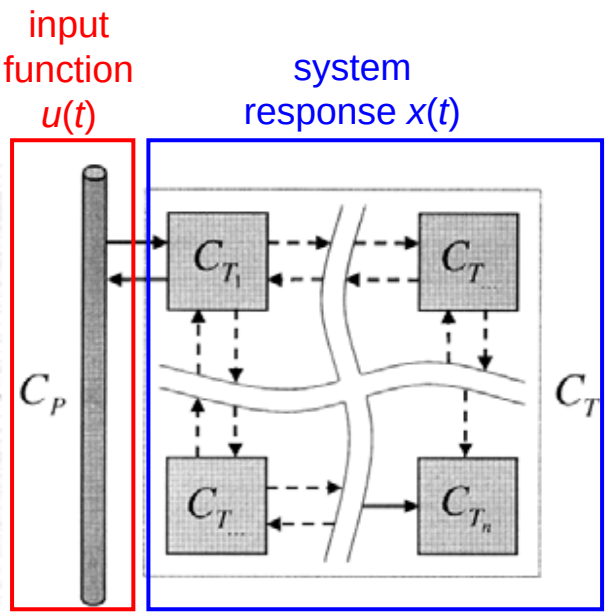


FIG. 3. Irreversible tissue model with a single trap.

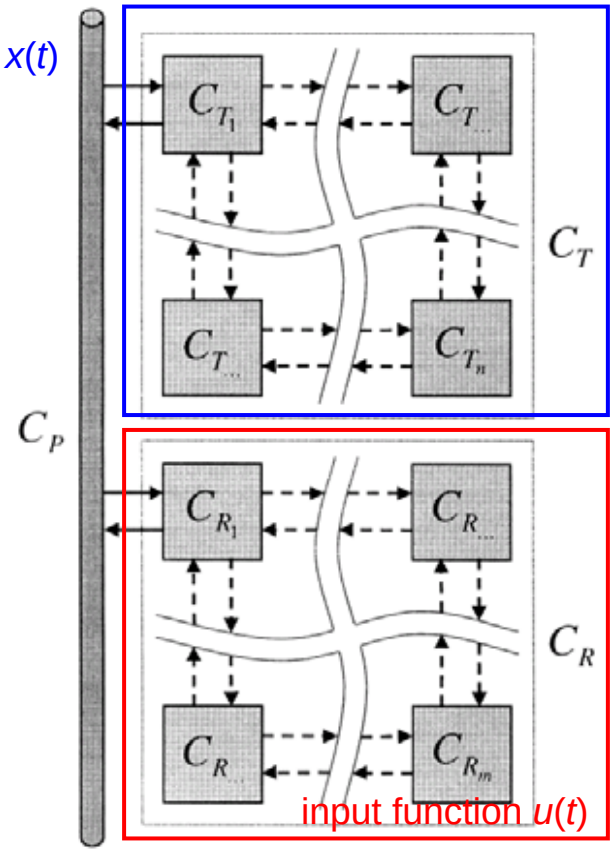


FIG. 4. Generalized reference tissue model.

For a comprehensive review:

Gunn, R.N. *et al*. J. Cereb. Blood Flow Metab. **21** (2001), 635-52.

Plasma input function measurements

withdrawal times → pot weights

Foot Switch

Balance

Well Counter (NaI)

Automatic Gamma Counter

Centrifuge

discrete blood samples

whole blood

plasma

Blood Trolley (BGO)

Metabolite Analysis

Computer

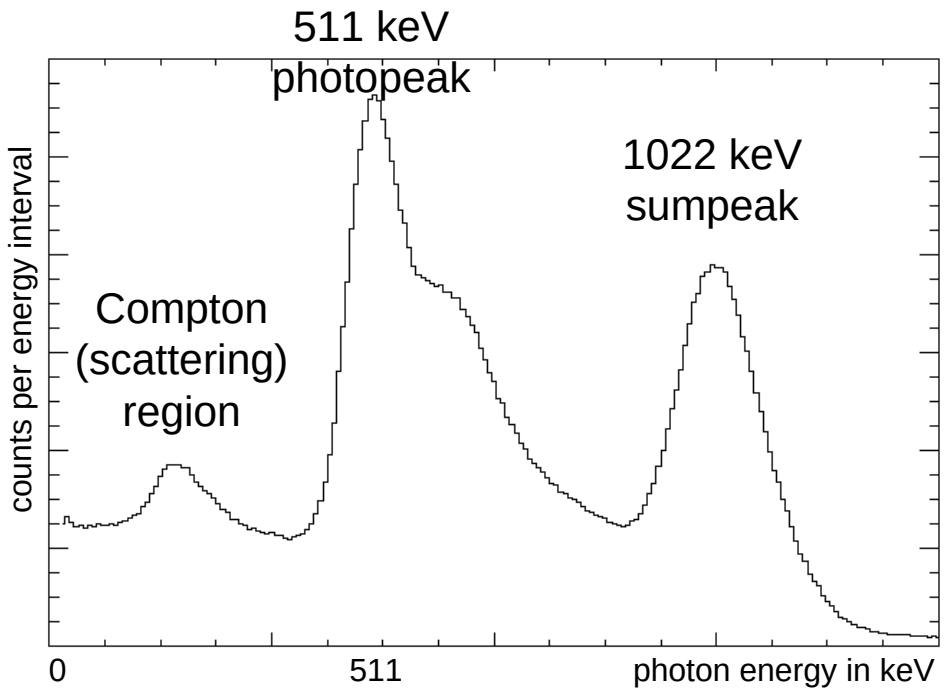
Continuous whole blood

Inorganic scintillation detectors

Scintillator properties

	Sodium iodide NaI(Tl)	Bismuth germanate BGO	Lutetiumoxy orthosilicate LSO(Ce)
density	3.7 g·cm^{-3}	7.1 g·cm^{-3}	7.4 g·cm^{-3}
effective atomic number	51	75	66
relative scintillation efficiency	100	15	75
scintillation decay time	230 ns	300 ns	fast: 12 ns slow: 40 ns

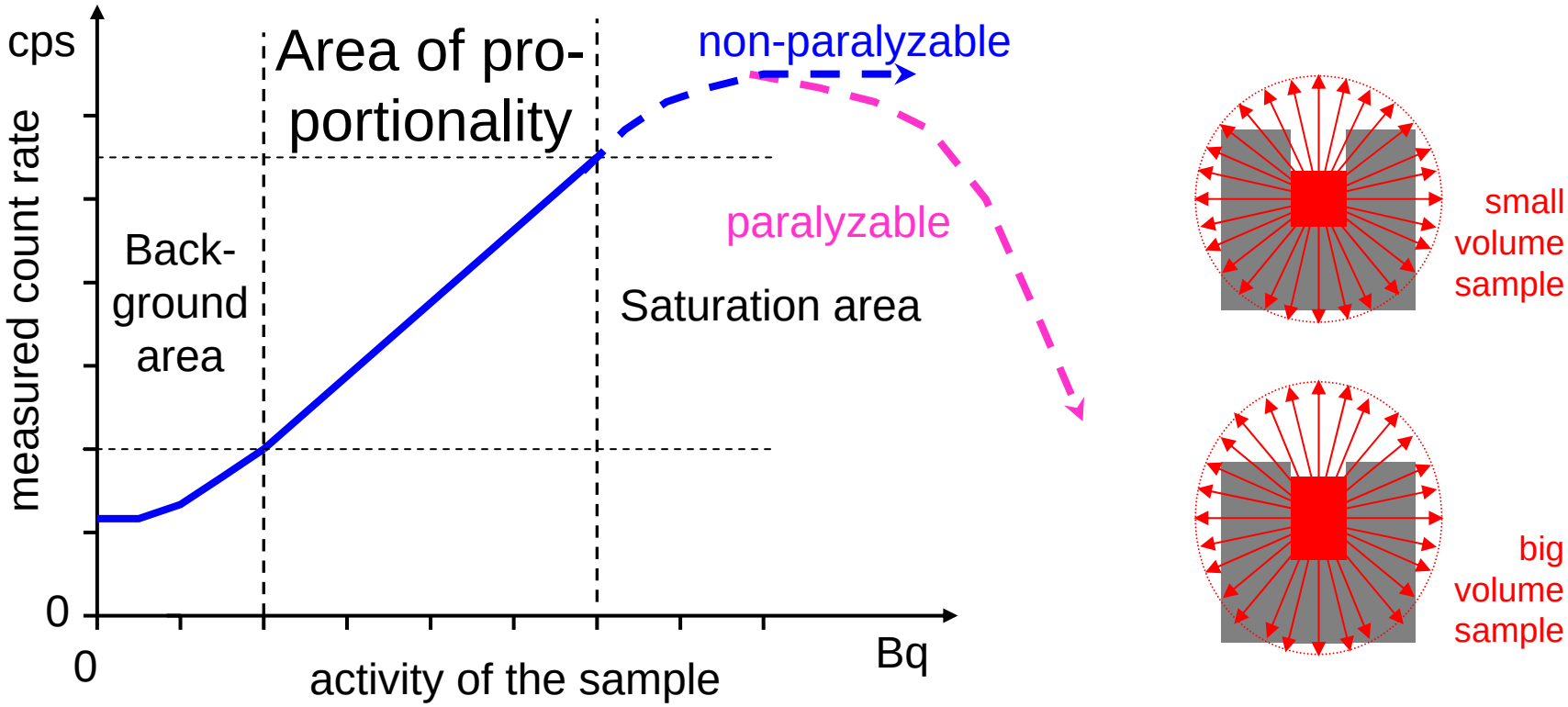
Energy spectrum from a β^+ emitting isotope



Radiation detection

The measured count rate has to be corrected for:

- background (and crosstalk on the Automatic Gamma Counter),
- deadtime losses,
- geometrical factors (volume effect),
- radioactive decay.



Analysis of the discrete samples

Foot Switch

Radio controlled clock

Scan start time and sample withdrawel times

Whole blood and plasma activity concentration in kBq/ml (decay corrected to scan start time)

Well counter

Background, deadtime, geometry and decay correction

Corrected count rates

Balance

Pot weights (empty & full)

Sample weights

Sample volumes

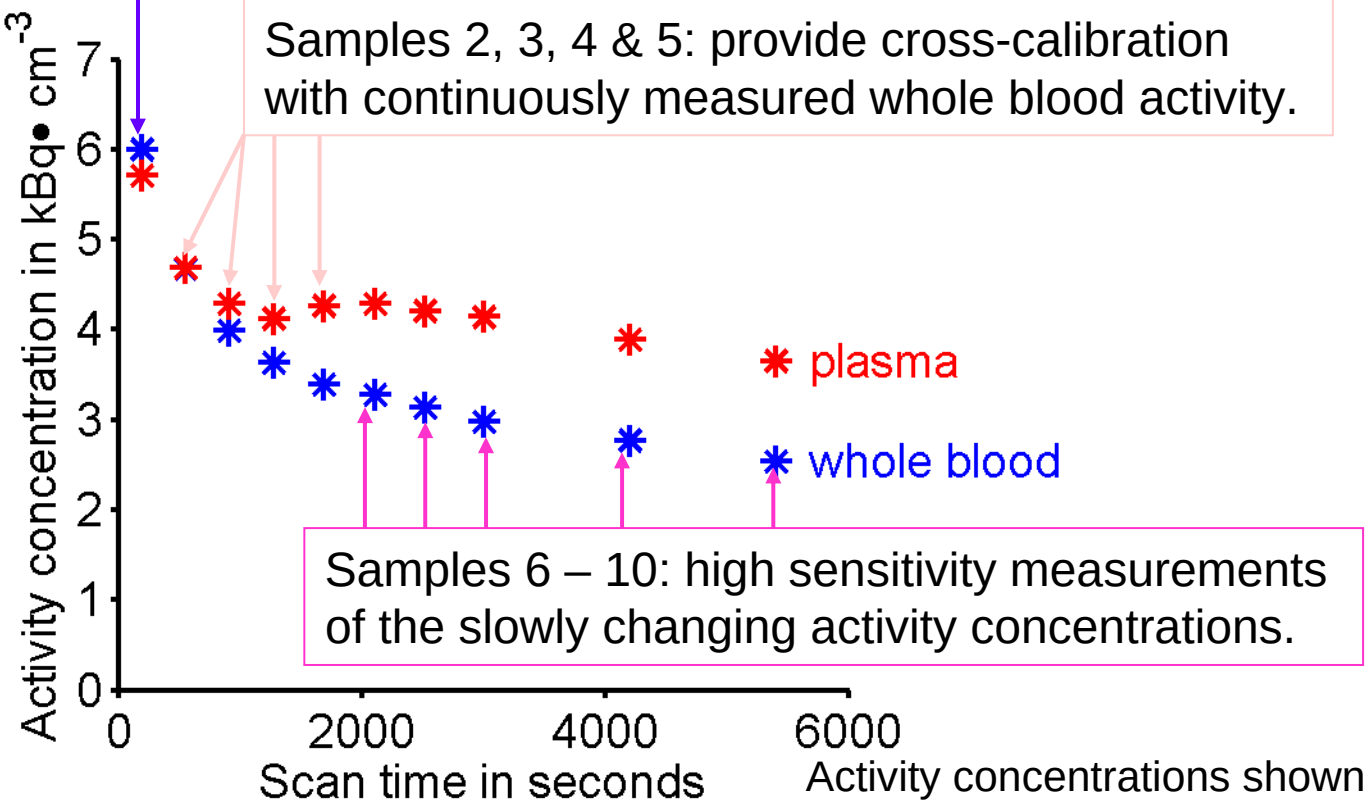
Blood and plasma density (g/ml)

Analysis of the discrete samples

Example: serotonin transporter radioligand [^{11}C]DASB study

First sample: important time point for determination of parent fraction. No cross-calibration with on-line blood detector measurements possible (too early).

Samples 2, 3, 4 & 5: provide cross-calibration with continuously measured whole blood activity.



Samples 6 – 10: high sensitivity measurements of the slowly changing activity concentrations.

Sampling protocol

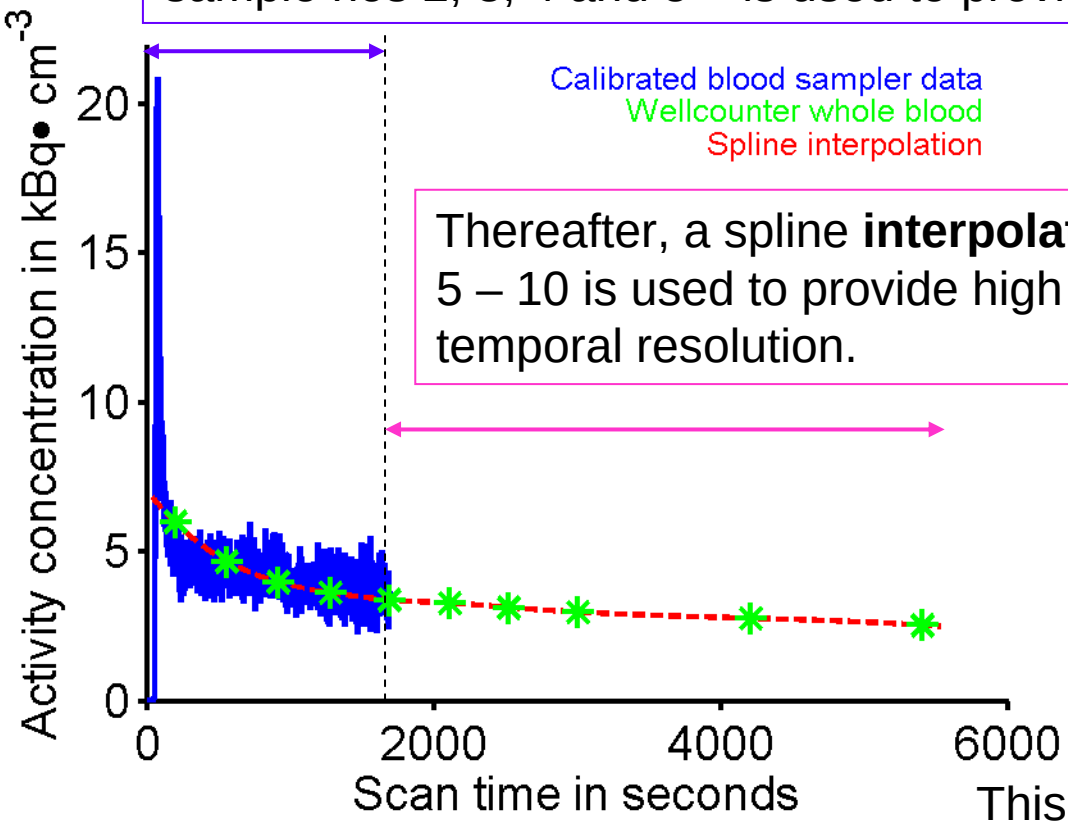
no	time
1	3 min
2	9 min
3	15 min
4	21 min
5	28 min
6	35 min
7	42 min
8	50 min
9	70 min
10	92 min

Activity concentrations shown in the plot are corrected for radioactive decay and were obtained in a healthy volunteer after a 529 MBq bolus injection.

Combination of the discrete samples with the on-line whole blood measurements

Activity concentration of whole blood

For the first 28 minutes of the scan, the continuous measurement of whole blood activity concentration – cross-calibrated with the discrete sample nos 2, 3, 4 and 5 – is used to provide good temporal resolution.



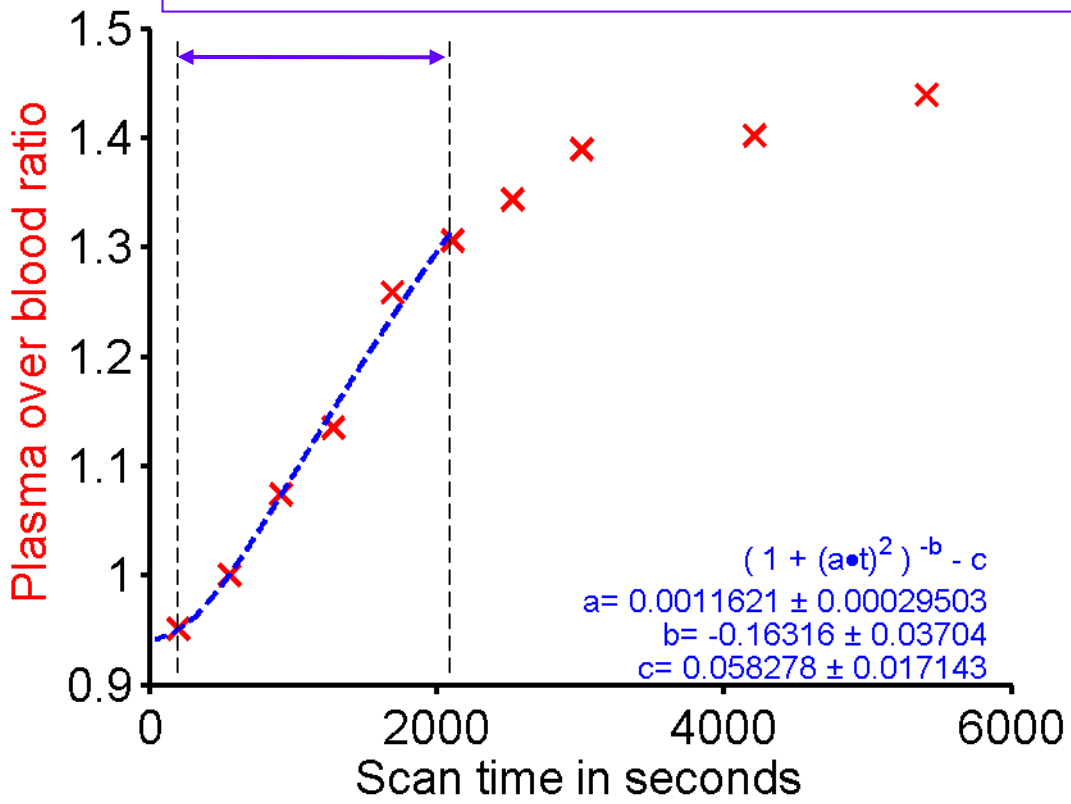
Thereafter, a spline **interpolation** of the discrete samples 5 – 10 is used to provide high sensitivity albeit poor temporal resolution.

Last sample **after the end** of the image acquisition.

This input function is often used to estimate the ***fractional blood volume***.

Plasma-over-whole blood (POB) activity concentration ratio

A model function is used for the **interpolation** of the time course of the POB ratio between the measured discrete samples during the first 35 min of the scan.



What to do with the first minutes of the scan?

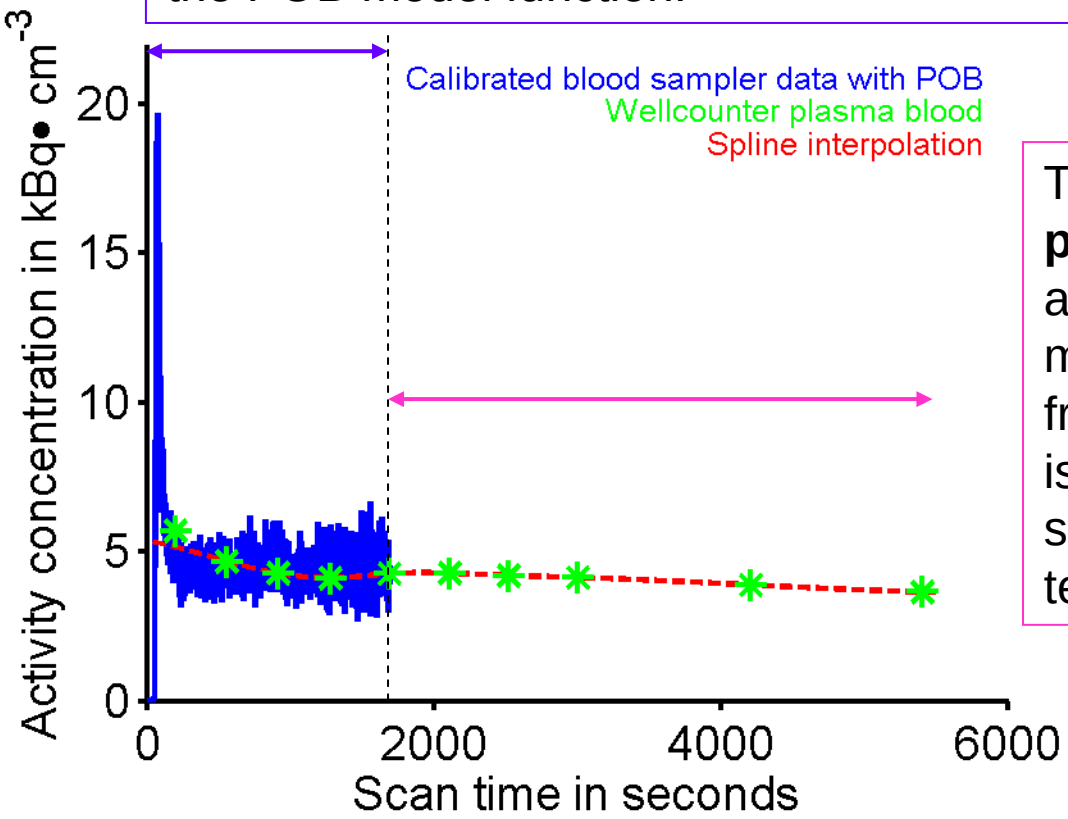
Is it appropriate to **extra-polate** with the model function towards zero?

Normally, the peak of the input function occurs during that period.

Plasma input function

Total activity concentration of plasma

For the first 28 minutes of the scan, the cross-calibrated continuous measurement of whole blood activity concentration is multiplied with the POB model function.



Thereafter, a spline **inter-polation** of the plasma activity concentration measurements obtained from discrete samples 5 – 10 is used to provide high sensitivity albeit poor temporal resolution.

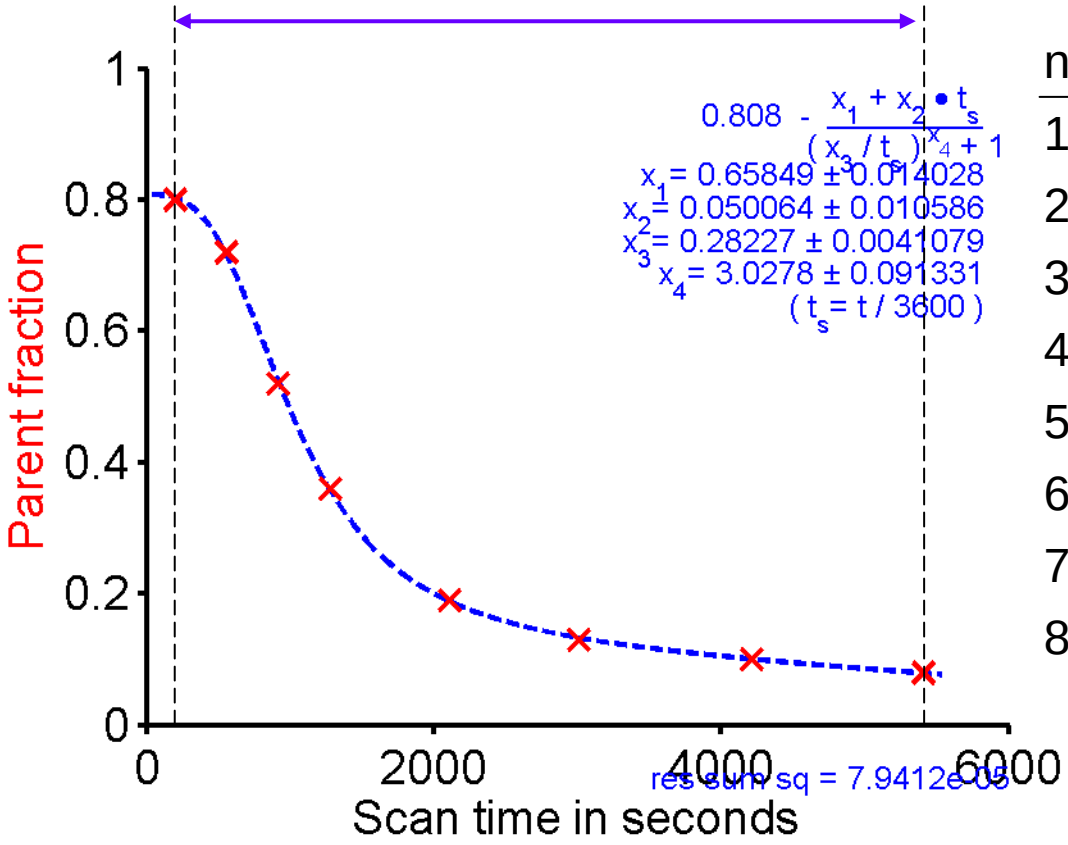
Determination of parent fraction in plasma

A model function is used for the **interpolation** of the time course of the parent fraction between the measured discrete samples during the entire scan.

What to do with the first minutes of the scan?

Is it appropriate to **extra-polate** with the model function towards zero?

Normally, the peak of the input function occurs during that period.

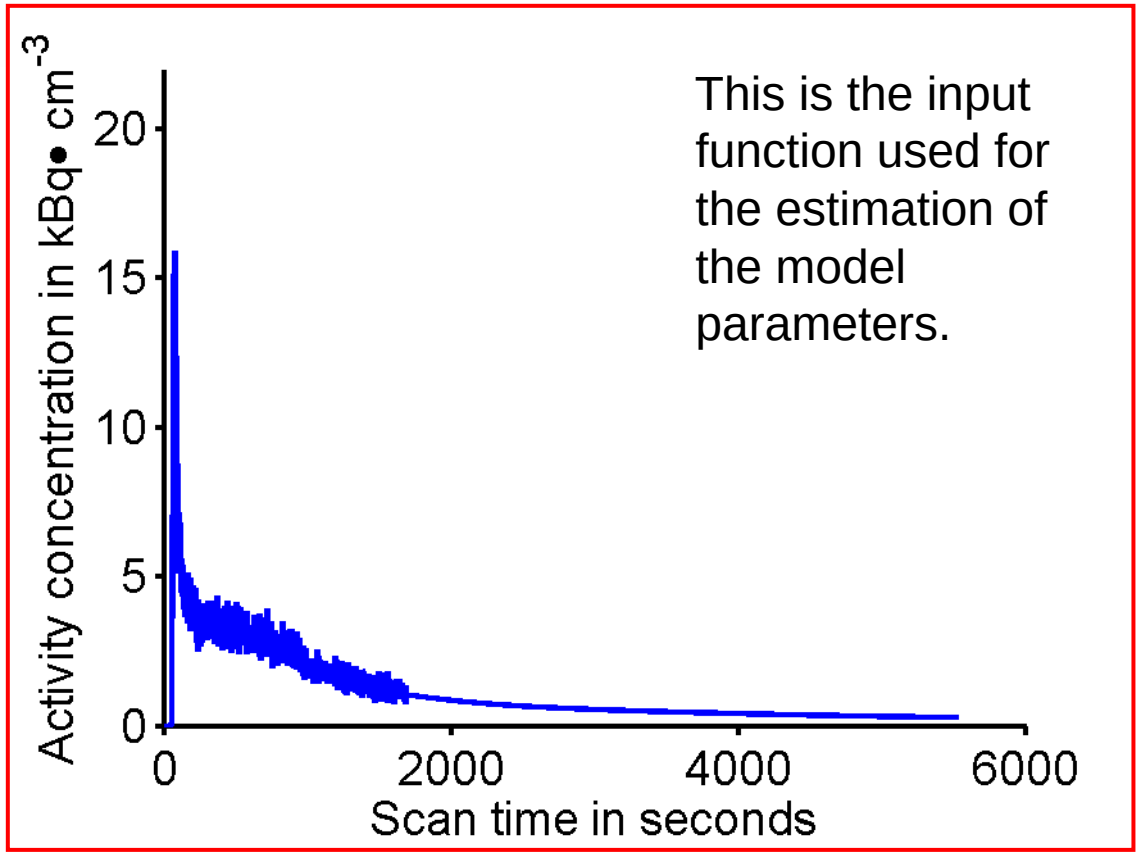


Sampling protocol

no	time
1	3 min
2	9 min
3	15 min
4	21 min
5	35 min
6	50 min
7	70 min
8	92 min

Parent in plasma input function

Activity concentration due to unmetabolised parent compound in plasma



Further material will appear on
http://personalpages.manchester.ac.uk/staff/Rainer.Hinz