10.6 Nuclear Medicine

From FA Smith, Applied Radiation Physics

This title refers to the imaging of any radioactive material within a human body. Different applications include:

- Whole body imaging: The body can be either viewed when stationary by wide-angle detectors or moved slowly across the field of view of detectors which subtend a small solid-angle of a particular region. Two principal types of investigation exist - (a) the determination of small amounts of radioactive contamination *e.g.* the study of actinide ingestion of radiation workers for which detectors with high efficiency are required. (b) bone scans following the administration of bone-seeking radiopharmaceuticals. Isotopes employed are mostly ^{99m}Tc, but ^{67}Ga and ^{111}In are also used in particular cases. This technique is also known as γ-ray autoradiography.
- Single Photon Emission Computerized Tomography (SPECT): This uses the Anger Gamma Camera, or another dedicated system, and is the most widely-used technique. It can give two types of image – static or dynamic. The former gives a 2-dimensional histogram of total activity within the field of view of the camera face. The latter gives time-dependent information from a selected Region-of-Interest (ROI) of that view. Tomographic information is obtained by the rotation of the camera head about the body being imaged.

- Positron Emission Tomography (PET): Here, there is coincidence counting of annihilation photons at 511 keV by detectors placed either side of the body along a line through the region of interest. Each detector views this region of interest. Since the two photons are correlated, the spatial resolution is somewhat higher that in SPECT. The resolution in image space is limited by the smoothing necessary to reduce the noise due to poor counting statistics. Typical Full-Width-Half-Maximum image resolutions are 1 – 2 cm in SPECT and 7 – 9 mm in PET.

10.6.1 Compartmental analysis with radioisotope tracers

Compartmental Analysis is used to quantify the time-dependence of the uptake of a radiopharmaceutical. A model is constructed of the various organs (compartments)

involved in the transport within the body of an injected radiopharmaceutical. The complexity of the model increases with the number of compartments and on their nature. It matters, for example, whether the system is considered to be open or closed.

An appropriate model is used in conjunction with the clinical measurements to give information on the pathology of the organ systems. This information can be :

- rate constants which give information on the flow *between* organs,
- the distribution of transit times of blood flow *through* an organ,
- the total rate of blood flow *through* an organ.

As a rule, the half-life of the isotope is chosen to be roughly equal to the length of the scan in order to minimize dose to the patient. A correction for isotope decay is therefore required in the determination of time-dependent processes.

Consider a closed 3-compartment model.

10.6.2 Rate constants

The flow of activity between the compartments, Fig.(10.19), following the injection of amount q_0 into compartment 1 at time $t = 0$ is described by the following differential equations :

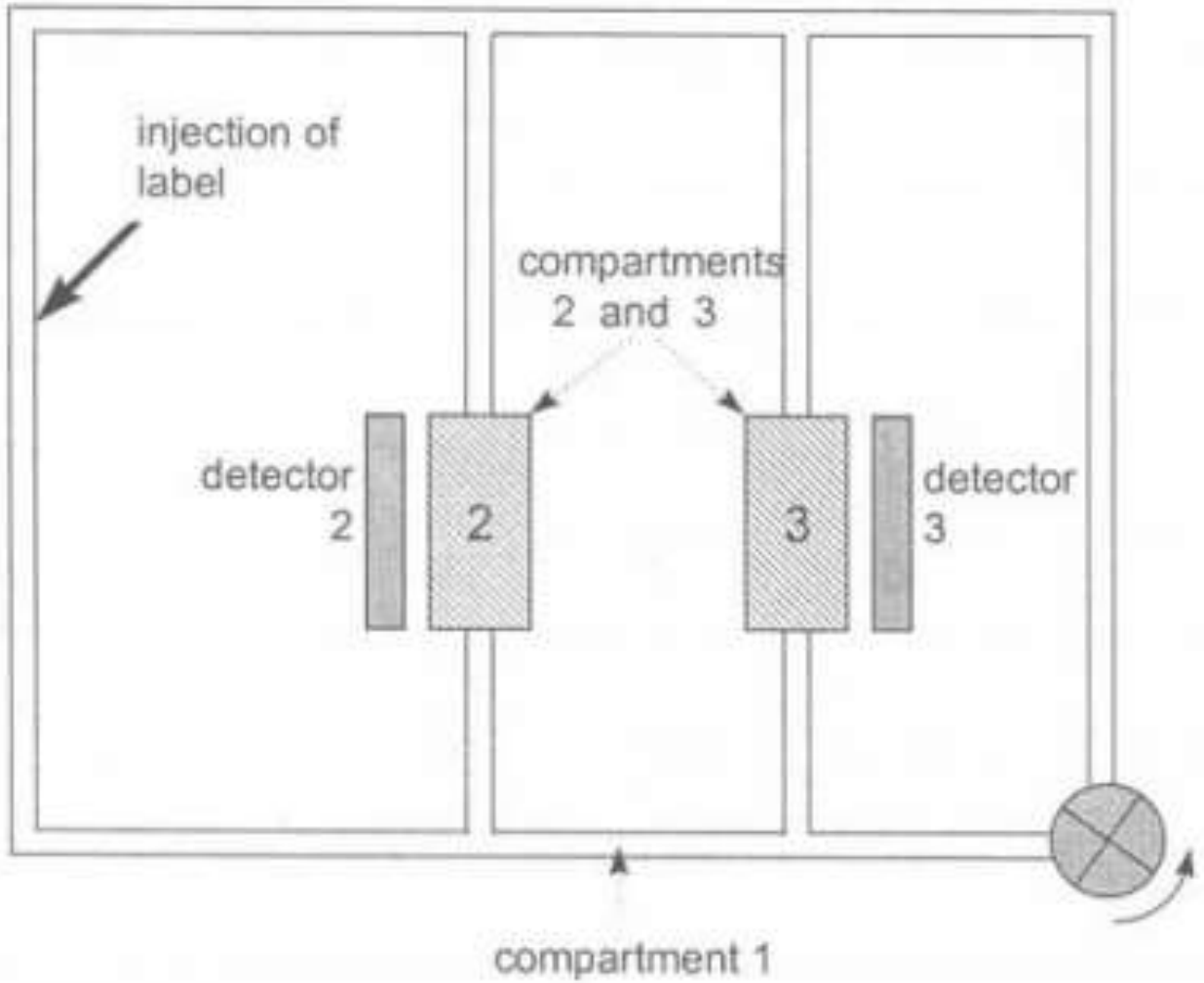

Fig.(10.19) Illustration of a 3-compartment closed system. At t = 0, radioactivity is injected into compartment 1. Compartments 2 and 3 can take up radioactivity from 1 with rate constants K_{12} and K_{13}. The radioactivity can be returned to 1 from the respective compartments with rate constants K_{21} and K_{31}. Uptake is monitored in each compartment by detectors d2 and d3.

$$\frac{dq_1}{dt} = K_{21}q_2 + K_{31}q_3 - K_{12}q_1 - K_{13}q_1$$

$$\frac{dq_2}{dt} = K_{12}q_1 - K_{21}q_2$$

$$\frac{dq_3}{dt} = K_{13}q_1 - K_{31}q_3$$

The rate constant K_{xy} expresses the transfer from compartment x to compartment y. The limiting conditions at time t = 0 are $q_1 = q_0$, $q_2 = q_3 = 0$. For an isotope with decay constant λ in a closed system, we also have the amount of circulating activity given by, $q_{0t} = q_0 \, exp(-\lambda t)$.

When there is no reversible transfer of activity from compartments 2 and 3 back to 1 (i.e. $K_{21} = K_{31} = 0$) the general solutions of the above equations are :

$$q_2 = \frac{-K_{12}}{K_{12} + K_{13}} q_0 e^{-Kt} + C_2 \qquad (10.10)$$

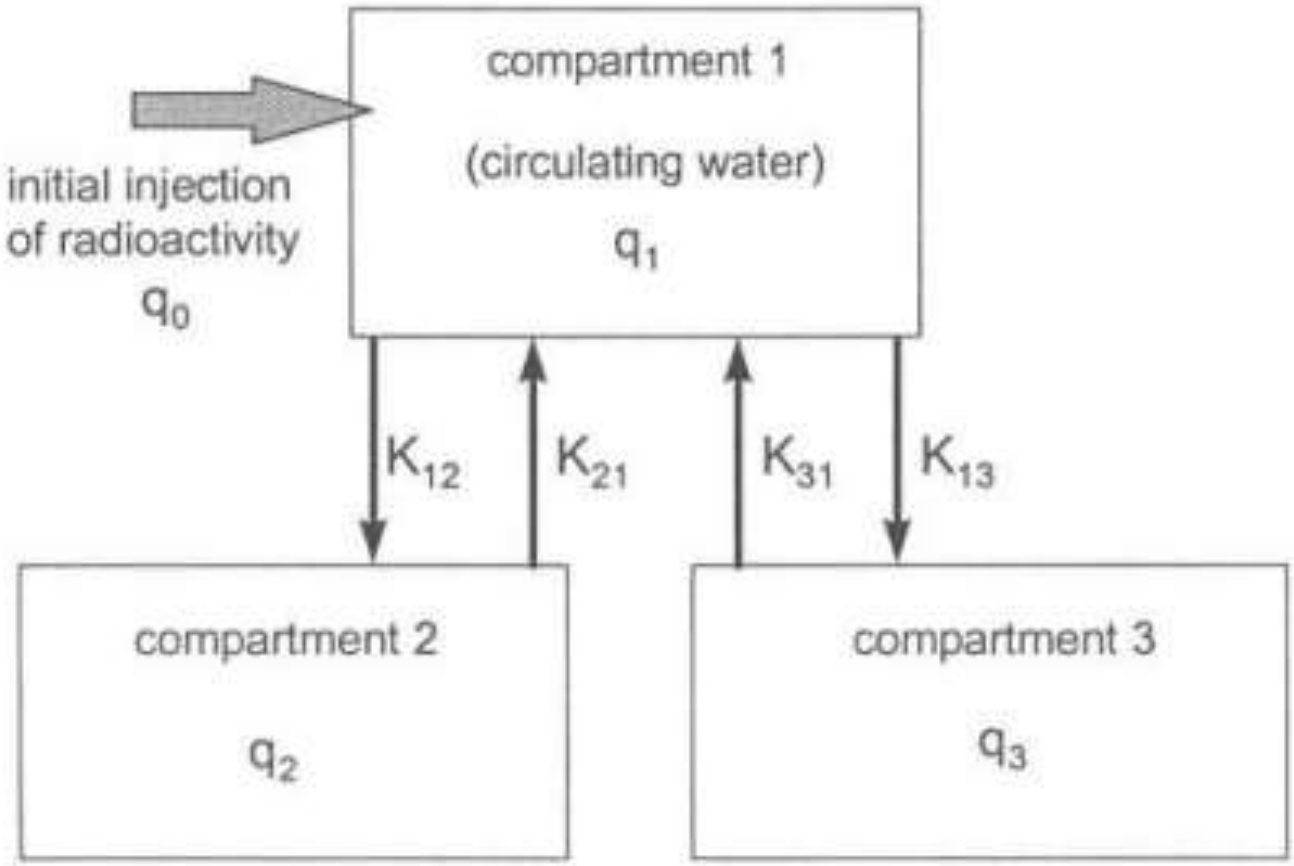

Fig.(10.20) The model of a closed three-compartment system as represented in Fig.(10.19). An initial injection of radioactive material, q_0, is made at time t = 0. At a later time the quantities in each of the three compartments are q_1 , q_2 and q_3 .

$$q_3 = \frac{-K_{13}}{K_{12} + K_{13}} q_0 e^{-Kt} + C_3 \qquad (10.11)$$

where $K = K_{12} + K_{13}$. The constants of integration, C, represent the amounts of activity in each of the two compartments as t approaches infinity, and are obtained from the limiting conditions at t = 0. Under the restrictions imposed by the need to minimize dose, however, the isotope lifetime should never be significantly greater than the time required for the clinical investigation. Except in cases where the decay constant of the isotope, λ, approaches zero, therefore, the values of :

$$C_2 = \frac{K_{12}}{K_{12} + K_{13}} q_{0t} \quad \text{and} \quad C_3 = \frac{K_{13}}{K_{12} + K_{13}} q_{0t} \qquad (10.12)$$

are not constant but have a time-dependence due to the radioactive decay of the isotope. Substituting Eqs.(10.12) into Eqs.(10.11) and (10.10), we get :

$$q_2 = q_0 e^{-\lambda t} \frac{K_{12}}{K} \left[1 - e^{-Kt}\right] \text{ and } q_3 = q_0 e^{-\lambda t} \frac{K_{13}}{K} \left[1 - e^{-\lambda t}\right] \qquad (10.13)$$

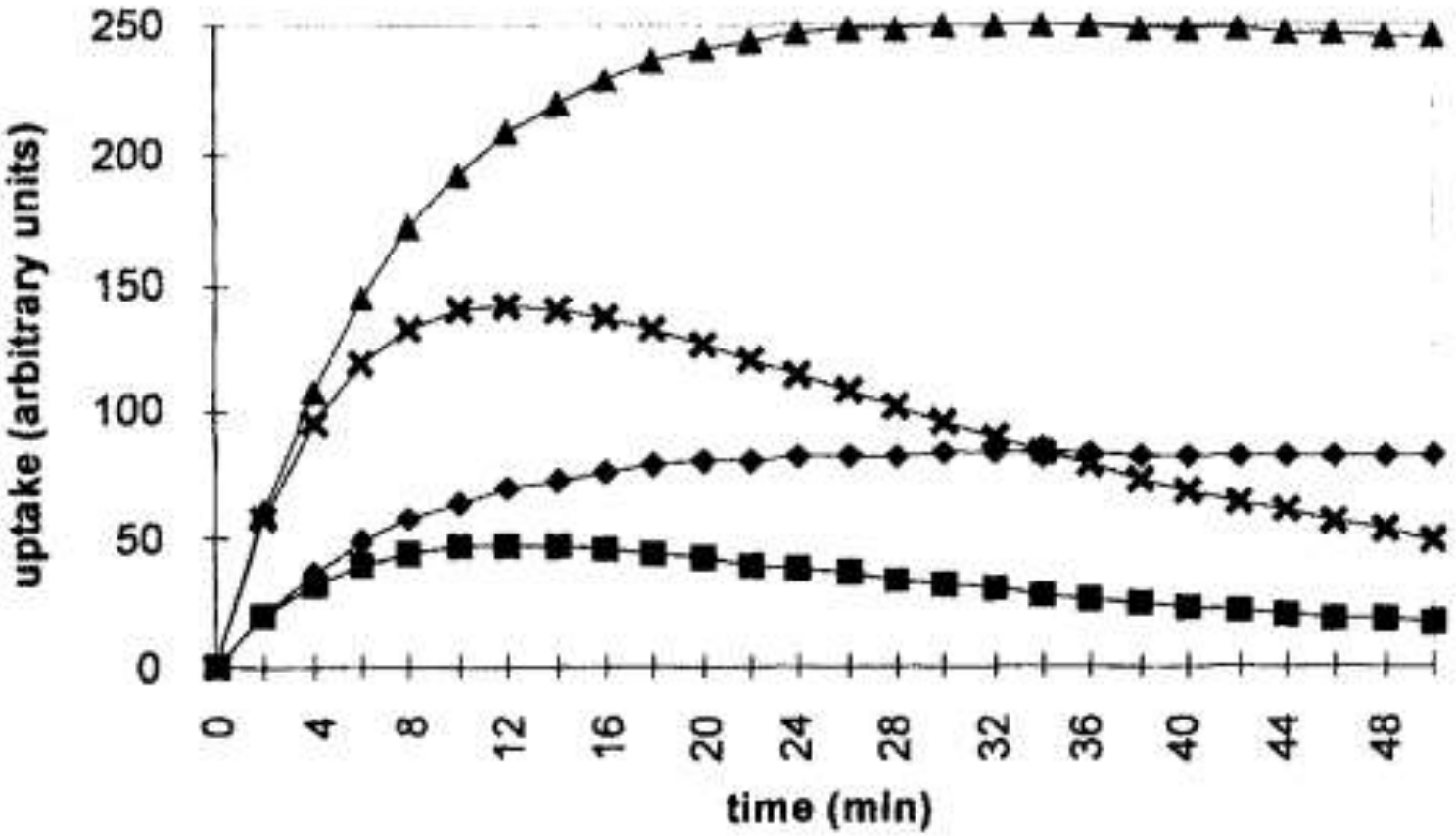

Fig.(10.21) The uptake in compartments 2 and 3 using Eqs.(10.13) for ^{99m}Tc and ^{11}C. Values assumed for the rate constants are : $K_{12} = 0.0325\ min^{-1}$, $K_{13} = 0.0975\ min^{-1}$, $K = 0.13\ min^{-1}$. Decay constants are : ^{99m}Tc, $\lambda = 0.00192\ min^{-1}$: ^{11}C, $\lambda = 0.034\ min^{-1}$: $q_0 = 360$ arbitrary units. ◆ q_2 ^{99m}Tc : ▲ q_3 ^{99m}Tc : ■ q_2 ^{11}C : ✖ q_3 ^{11}C.

10.6.3 Transit times

Another important aspect of dynamic tracer studies is the study of the distribution o transit times of blood through an organ or through the vascular bed of a tissue Mathematical modelling of such studies generally assumes :

- that the input into the system of a radioactive label occurs instantaneously (i.e it is a delta function),Fig.(10.22),

- the output from the system (organ, tissue…) will be the summation of flow of the label through all the pathways available.

Under these circumstances, a distribution of transit times will be observed at the output. The Mean Transit Time is the mean value of the transit time distribution of the outflow curve h(t). Thus :

$$\bar{T} = \frac{\int_0^\infty t\ h(t)\ dt}{\int_0^\infty h(t)\ dt} \qquad (10.14)$$

The denominator of Eq.(10.14) is unity if there is no loss of label in the system (*i.e.* it is a conservative system) when the mean transit time becomes :

$$\bar{T} = \int_0^\infty t\ h(t) dt \qquad (10.15)$$

The amount of activity retained by the system at any time t is the system retention function *R(t)* :

$$R(t) = 1 - \int_0^t h(t)\ dt$$

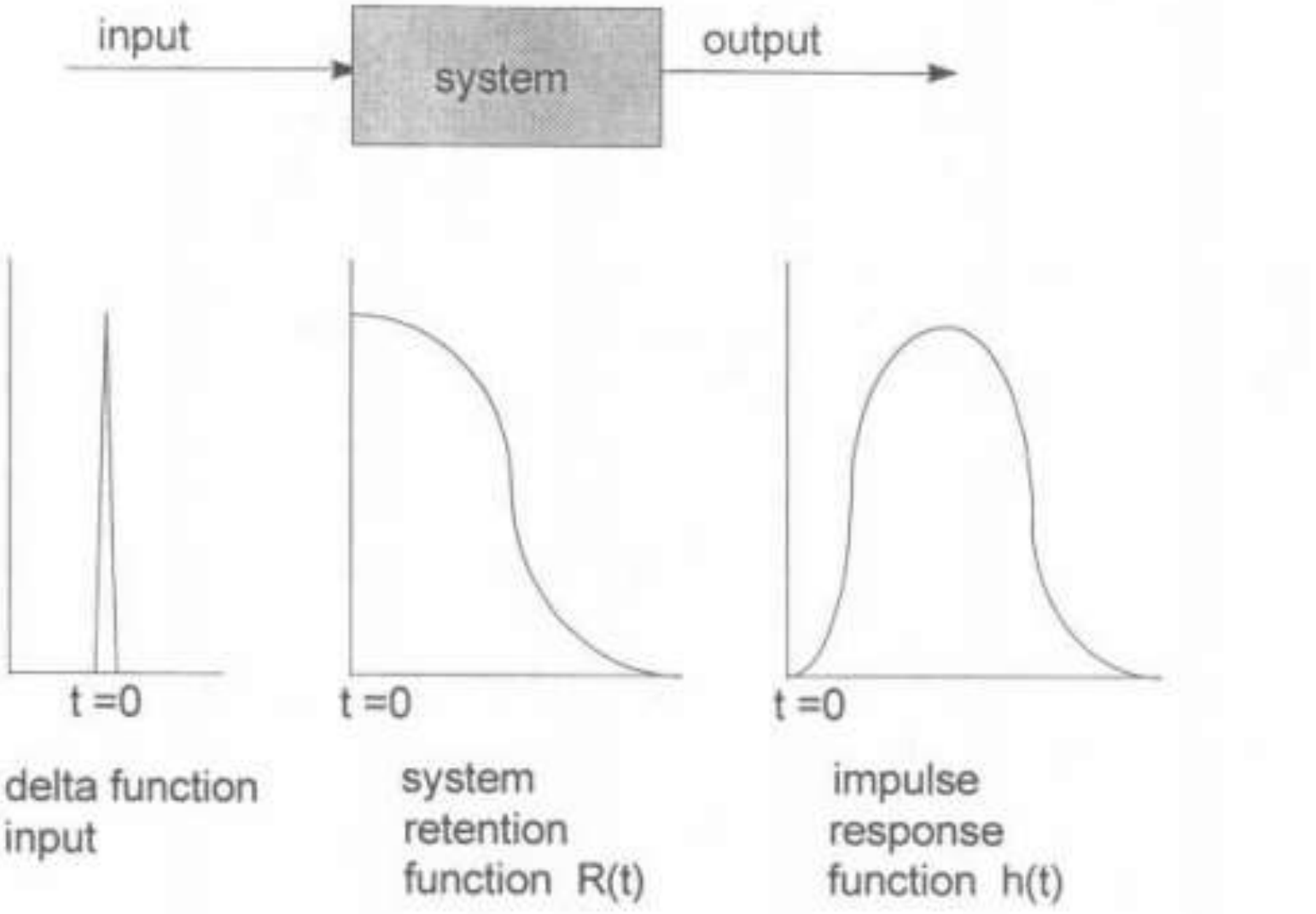

Fig.(10.22) Time-dependent functions that describe the passage of radioactive tracer through a system.

giving $h(t) = -dR/dt$. Integrating Eq.(10.15) by parts, with $u = t$, $dv/dt = h(t)$ and $v = (1-R(t))$, we have :

$$\bar{T} = uv - \int v \, du / dt$$

$$\bar{T} = \int_0^\infty R(t)dt \qquad (10.16)$$

The mean transit time is therefore the total area under the system retention function.

In general, the input is not a delta function but will have a distribution $I(t)$. The output is then described by a function $O(t)$ which is the convolution of $I(t)$ with the impulse response function $h(t)$.

$$O(t) = I(t) * h(t)$$

10.6.4 Flow rates through a single channel

Blood flow through vessels and its perfusion of organs and tissues is a widely used investigation in nuclear medicine. In a simple analogue system such as Fig.(10.19) a known amount of tracer, Q, is injected into compartment 1 as a bolus with a time distribution assumed to be a delta function. A sample volume dV withdrawn downstream from the injection point at a time t following the injection, has a tracer concentration, $C(t) = dQ/dV$. If the sample is collected over a time dt, the flow rate is:

$$F = \frac{dV}{dt} = \frac{dQ}{C(t)dt}$$

Under the assumption that the mixing is uniform, the sample is representative of the whole system such that :

$$\frac{dQ}{Q} = \frac{C(t)dt}{\int_0^\infty C(t)dt}$$

The flow-rate then becomes :

$$F = \frac{Q}{\int_0^\infty C(t)dt} \qquad (10.17)$$

Eq.(10.17) embodies the Stewart-Hamilton principle of indicator-dilution. Its application in an investigation of cardiac output, for example, entails the measurement of an activity:time curve, proportional to $C(t)$, over the heart following an intravenous injection. In this case, blood recirculation ensures that $C(t)$ reaches an equilibrium value over a measurement time period which is much shorter that the isotope half-life.

The flow-rate generated by the heart, F, can then be determined by measuring the equilibrium value of the output curve, C_{eq}, and equating it to Q/V' where V' is a blood sample volume taken at equilibrium. Thus Eq.(10.17) is modified to :

$$F = \frac{C_{eq}}{\int_0^\infty C(t)dt} V' \qquad (10.18)$$

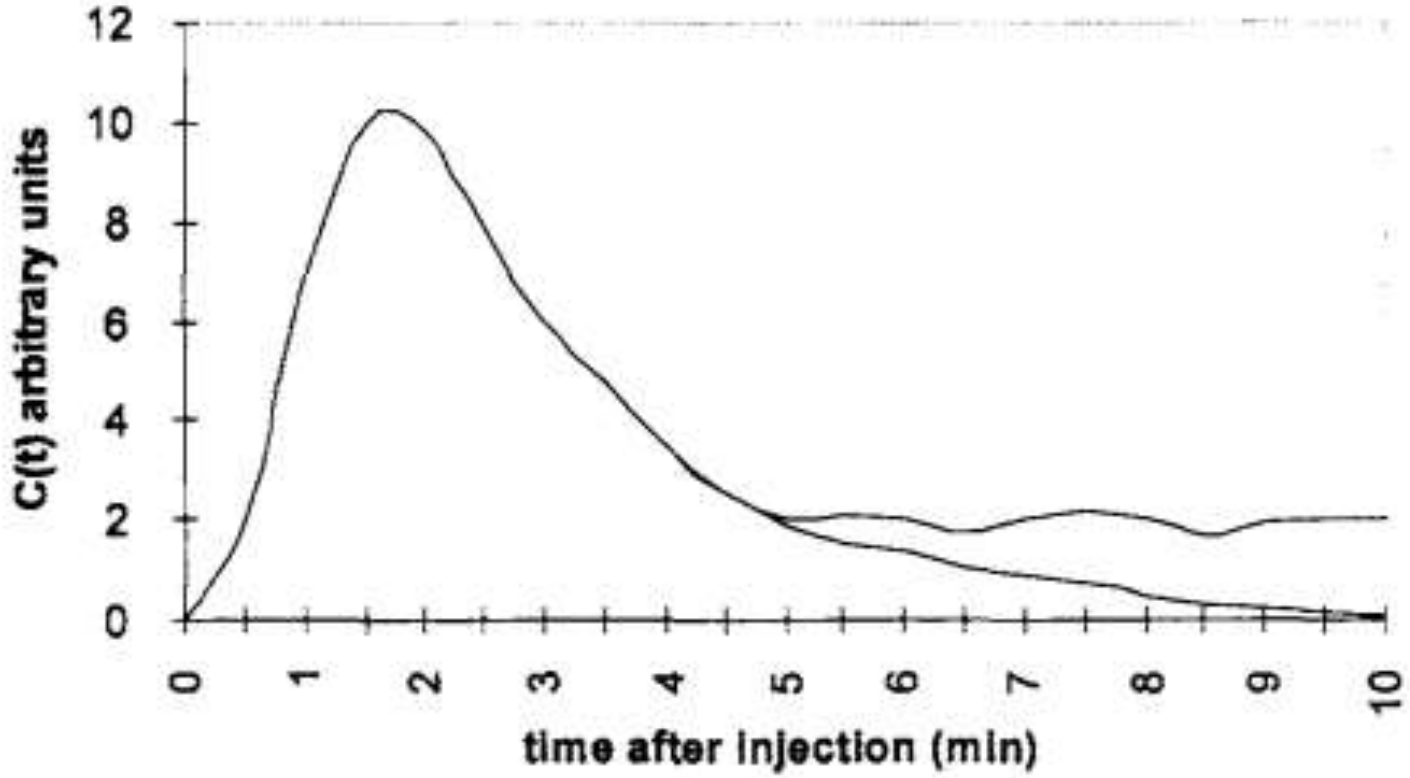

Fig.(10.23) A typical activity:time curve, proportional to *C(t)*, measured over the heart. The lower curve would be observed without any recirculation of the injected activity, for example, when the blood volume is infinitely large and there is only one pass of the activity through the heart. The upper curve shows the equilibrium value, C_{eq}, achieved when the injected activity becomes uniformly distributed.

The numerator of Eq.(10.18) must be the integrated area of the lower curve in Fig.(10.23) – that is, C(t) corrected for recirculation.

10.6.5 Flow through an organ having multiple channels

The complex micro-circulation within an organ can be modelled as a system of parallel elements which start at the input and end at the output. At the boundary of the organ at A, Fig.(10.24), the tracer input, Q, divides in proportion to the flow in each channel. Thus :

$$\frac{dQ}{Q} = \frac{dF}{F}$$

From the Stewart-Hamilton principle, Eq.(10.17) :

$$dF = \frac{F}{Q} dQ = \frac{dQ}{\int_0^\infty C(t)dt} \qquad (10.19$$

The fluid volume which arrives at the output B from each channel in time t is $dV = dF$. Substituting Eq.(10.19) we have :

$$dV = \frac{tdQ}{\int_0^\infty C(t)dt}$$

Since dQ is the quantity of tracer delivered at the output between times t and $t\ dt$ in each channel, $dQ = C(t)\ F\ dt$ so that :

$$dV = \frac{C(t)Ftdt}{\int_0^\infty C(t)dt} \qquad (10.20$$

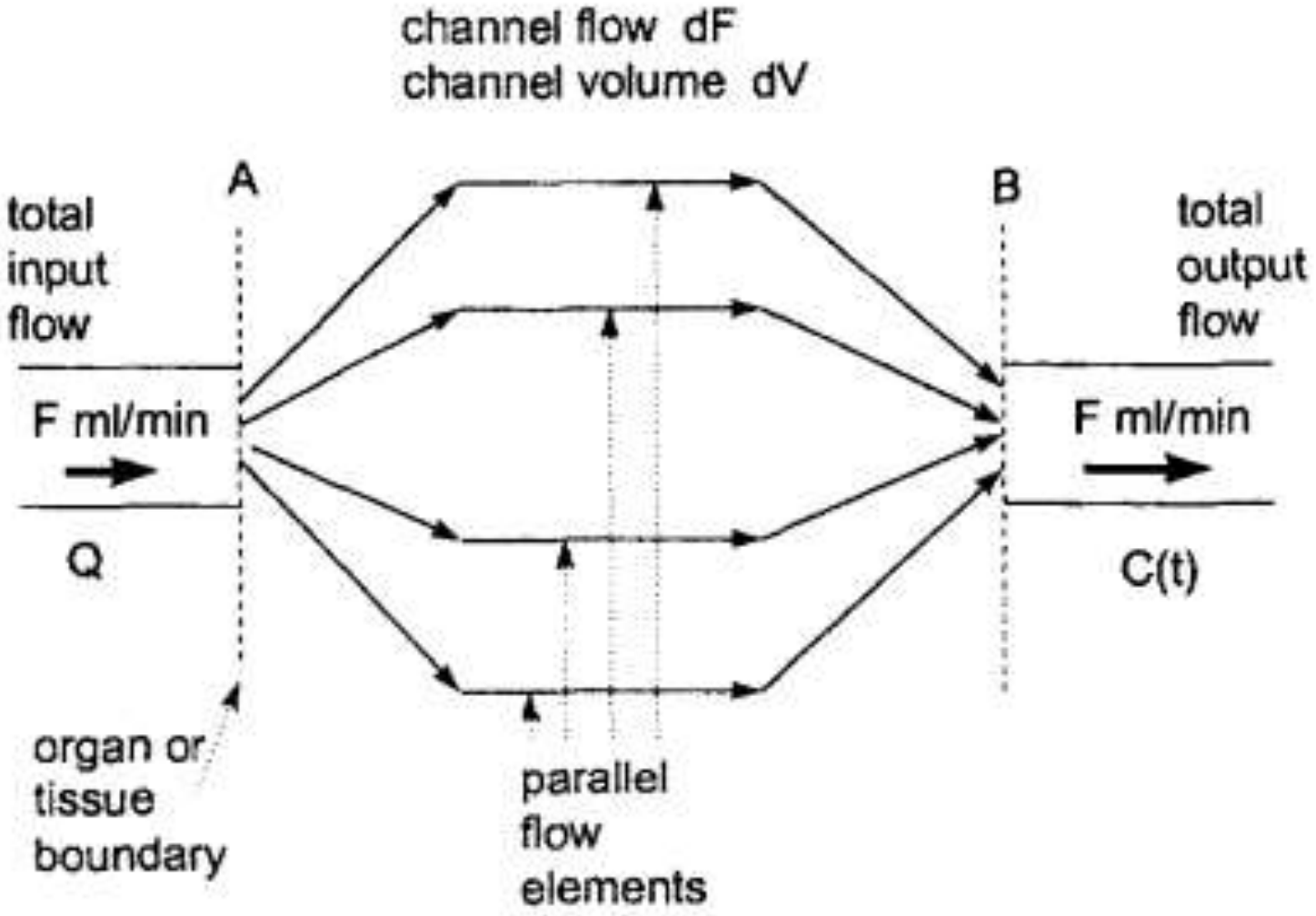

Fig.(10.24) Model of parallel flow through an organ or tissue.

The total volume, V, is the sum of all individual channel volumes :

$$V = \frac{F \int_0^\infty tC(t)dt}{\int_0^\infty C(t)dt}$$

When the tracer input is delivered as a delta function, $C(t)$ can be replaced by the impulse response function $h(t)$,

$$V = \frac{F \int_0^\infty th(t)dt}{\int_0^\infty h(t)dt} = F\bar{T} \qquad (10.21)$$

The mean transit time in Fig.(10.25) is defined as :

$$\bar{T} = \frac{\sum_i t_i N_i \Delta t}{\sum_i N_i \Delta t} \qquad (10.22)$$

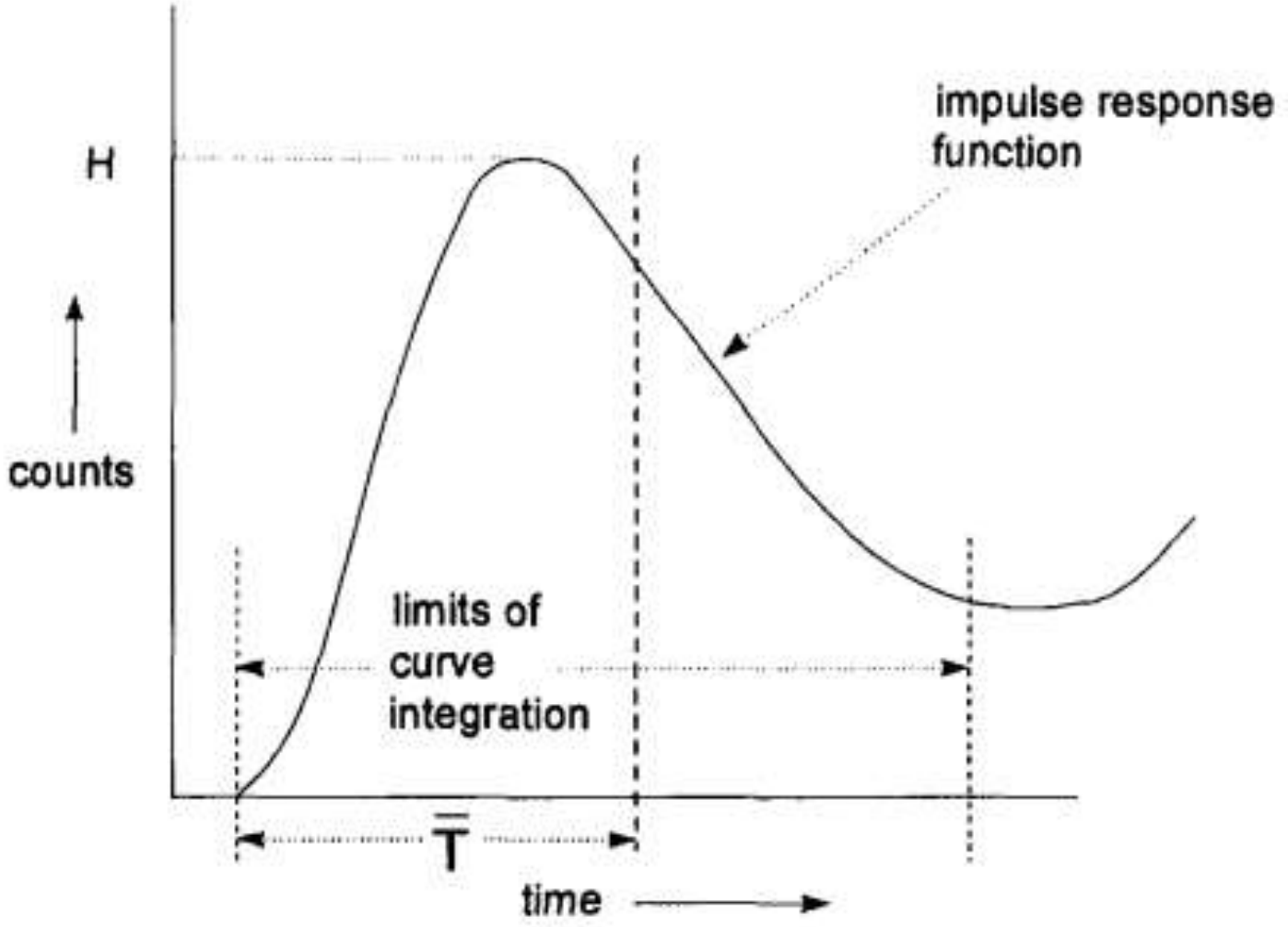

Fig.(10.25) An impulse response function *h(t)*. Counts N_i are recorded at time t_i in the time interval Δt — that is, between t_i and $t_i + \Delta t$.