# One Compartment Model: Blood Flow

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Reference: [1].
Assumptions of compartment models in general (not just for one compartment):

1. Well-mixed.
2. Tracer amount.
3. Steady state. Mathematical meaning: rate constants do not change over time. Physiological meaning: tracer goes everywhere the tracee goes. (Verify this understanding. Compare Carson and Morris.)
4. No isotope effects.

## 1 Introduction

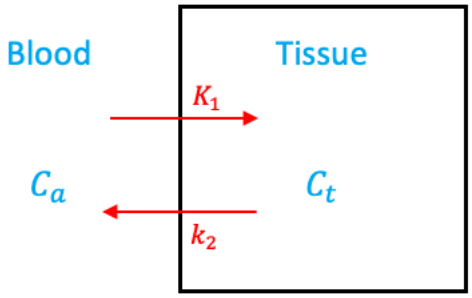


Figure 1: Basic one compartment model

The basic one compartment model is illustrated in Figure 1. It describes the bidirectional flux of tracer between tissue and blood. The only compartment represents the tissue. The model is characterized by the following elements:

- $C_a(t)$ and $C_t(t)$, the time-varying concentration of tracer in the arterial blood and tissue, respectively. For simplicity, sometimes we drop the time dependency and just write $C_a$ and $C_t$. The unit of both quantities is activity per volume, e.g. mCi/ml.
- $K_1$ and $k_2$, unknown constant parameters of the system, representing first-order kinetic rate constants. They are called *rate constants*, with unit $\frac{1}{\text{time}}$, e.g. $\text{min}^{-1}$.

- The concentrations and rate constants are related by a first-order differential equation

$$\frac{\mathrm{d}C_t}{\mathrm{d}t} = K_1 C_a - k_2 C_t \,, \tag{1}$$

with initial condition $C_t(0) = 0$, meaning there is no tracer in tissue at the beginning of experiment. The equation describes the dynamics of $C_t$: $K_1 C_a$ is the flux from blood to tissue and $k_2 C_t$ is the flux from tissue to blood. The unit of flux is mCi/ml/min.

Technically one can also write a DE for $C_a$. But in practice, the blood tracer concentration $C_a$ is measured (or more precisely, estimated), not calculated. So Equation (1) is sufficient.

If $C_a(t)$ is given and the parameters are known, $C_t(t)$ can be calculated by

$$C_t(t) = K_1 C_a(t) \otimes e^{-k_2 t} = K_1 \int_0^t C_a(s) e^{-k_2(t-s)} \,\mathrm{d}s \,. \tag{2}$$

(Note that the upper limit of the integral is $t$, not $\infty$.) In reality, the values of $K_1$ and $k_2$ are not known. $C_t$ can be measured by dynamic PET. The goal is to estimate $K_1$ and $k_2$. This can be done by treating it as a minimization problem. Some built-in Matlab packages can do curve fitting.

(TO-DO: Comment on the practical details of $C_t$ and $C_a$ measurements and the evaluation of the integral in Eq. (2)).

## 2 Parameter interpretation

The rate constants $K_1$ and $k_2$ can be interpreted in terms of physiological processes related to blood flow and tracer diffusion from blood to tissue.

### 2.1 $K_1$: product of blood flow and the first-pass extraction fraction

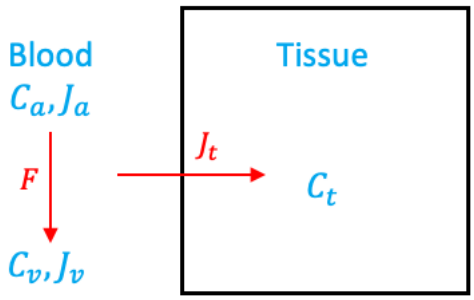


Figure 2: Zoom-in of the one compartment model in Figure 1, including blood flow and blood-to-tissue flux.

To give a physiological interpretation of $K_1$, we zoom in the compartment model and look at a single capillary and the tissue compartment in the immediate vicinity (Fig. 2). The tracer enters the capillary through arterial blood with concentration $C_a$ (unit mCi/ml), flux $J_a$ (unit mCi/min/ml) and flow rate $F$. Note that in tracer kinetic modeling, flow often means perfusion, thus the unit of $F$ is volume per unit time per mass/volume of **tissue**, i.e. ml/min/ml or ml/min/g. The in-flux $J_a$ leaves either through tissue extraction $J_t$ or venous circulation $J_v$. By Fick's principle (concentration of mass in steady state),

$$J_t = J_a - J_v \,.$$

Assuming that the flow rate $F$ is constant (reasonable because $F$ is a local rate), we have $J_a = FC_a$ and $J_v = FC_v$. It follows that

$$J_t = \frac{\mathrm{d}C_t}{\mathrm{d}t} = F(C_a - C_v)\,.$$

**Note:** The flow $F$ could be measured either in ml/min/ml or ml/min/g, depending on how the tissue is measured (in volume or in mass). If in mass, then $F$ is in ml/min/g, $C_a$ and $C_v$ are in mCi/ml, the unit of $J_t$ is then in mCi/min/g, the unit of $C_t$ is then in mCi/g, which is inconsistent with the unit of $C_t$ defined before. Zeyu's understanding is that, if so, then the unit of $C_t$ should be in mCi/g, as the tissue would be measured in mass rather than volume.

Next, we define the *unidirectional extraction fraction* $E$:

$$E = \frac{C_a - C_v}{C_a}\,,$$

the net fraction of the incoming tracer that is unidirectionally extracted into tissue during the first pass ot the tracer at this tissue site. $E$ is also called the *first-pass extraction fraction*. This fraction does not consider the tracer passing through the other direction (from tissue to blood), as in a first pass there is effectively zero tracer in the blood, i.e. $C_t = 0$. Combining all these with Eq. (1), we obtain

$$\frac{\mathrm{d}C_t}{\mathrm{d}t} = (FE)C_a = K_1 C_a\,.$$

Thus, $K_1$ can be interpreted as the product of the flow rate $F$ (in ml/min/ml) and first-pass extraction fraction $E$ (dimensionless).

A further interpretation of $E$ has been developed from the Renkin-Crone capillary model, which shows that

$$E = 1 - e^{-\frac{PS}{F}}\,,$$

where $P$ is the permeability of the tracer across the capillary membrane and $S$ is the capillary surface area per unit mass of tissue. The product $PS$ has the same unit as flow rate, e.g. ml/min/ml.

- If $PS \gg F$, then $E \approx 1$, $K_1 \approx F$.
- If $PS \ll F$, then $E \approx \frac{PS}{F}$, $K_1 \approx PS$.

Thus, when the extraction fraction $E$ is large (the capillary is highly permeable), $K_1$ is closely related to blood flow $F$.

### 2.2 $k_2$: related to $K_1$ and volume of distribution/partition coefficient

After sufficient time, the system described by Eq. (1) reaches *equilibrium*, where $C_a$ and $C_t$ become constants and the net flux between blood and tissue becomes zero. Thus $K_1 C_a = k_2 C_t$. At this point, the ratio between the tissue and blood concentrations is called the *equilibrium volume of distribution*, or *distribution volume*, or *partition coefficient*:

$$V_D = \frac{C_t}{C_a}\,. \tag{3}$$

For the one-compartment model, we easily see that $V_D = \frac{K_1}{k_2}$. For other compartment models, $V_D$ may be expressed in terms of the constant rates in other forms.

Even though $V_D$ is called a volume, it is actually a ratio, which is dimensionless. It is called a volume because it equals in value to the volume of *blood* that contains the same activity as 1ml of

tissue. For example, $V_D = 2$ means $C_t = 2C_a$, thus 2ml of blood contains the same activity of 1ml of tissue.

$V_D$ is relatively easier to measure. One method is to deliver tracer via continuous infusion in order to maintain $C_a$ at a constant level and measure $C_t$ using, say, PET. Then $V_D$ can be calculated by Eq. (3).

## References

[1] Evan D Morris, Christopher J Endres, Kathleen C Schmidt, Bradley T Christian, Raymond F Muzic, and Ronald E Fisher. Kinetic modeling in positron emission tomography. *Emission tomography: The fundamentals of PET and SPECT*, 46(1):499–540, 2004.