Solution 1: Neuron activation

a) The a-v before the increase of CBF: $C_a - C_v = \frac{MR}{F}$

The a-v after the increase of CBF: $C_a - C_v = \frac{MR}{1.5 * F}$

(Metabolic rate (MR) and arterial oxygen concentration (C_a) are constants. F is the original flow.)So there is a 33.3% decrease in the a-v during an 50% increase of CBF.

b) As shown in a), when CBF is increased by 50%, C_v will increase. So the concentration of the deoxyhemoglobin in the veins will decrease.

This decrease in deoxyhemoglobine concentration during neuron activations allows to image activation of the brain using magnetic resonance (MR). The basic principle of that measurement is to image changes of deoxhyemoglobine concentrations, which is a paramagnetic compound influencing magnetic fields, hence the MR signal.

Solution 2: Car exchange

a) For any time, the system is described by the following differential equations:

$$\frac{dL^*(t)}{dt} = V\frac{G^*(t)}{G} - V\frac{L^*(t)}{L}$$
$$\frac{dG^*(t)}{dt} = -V\frac{G^*(t)}{G} + V\frac{L^*(t)}{L}$$

Where V is the car flux between Geneva and Lausanne in each direction, G and L are the total amount of cars in Geneva and Lausanne (assumed to be constant), respectively and G* and L* are the number of red cars in Geneva and Lausanne, respectively. In the following notations, the explicit time dependency will be omitted.

b) These two linear differential equations can be written as a differential system in the following way:

$$\frac{d}{dt}\begin{pmatrix} L^* \\ G^* \end{pmatrix} = \begin{pmatrix} -\frac{V}{L} & \frac{V}{G} \\ \frac{V}{L} & -\frac{V}{G} \end{pmatrix}\begin{pmatrix} L^* \\ G^* \end{pmatrix}$$

We need first to find the eigenvalues and eigenvectors of the matrix defining the differential system. The characteristic polynomial is:

$$\left(-\frac{V}{L} - \lambda\right)\left(-\frac{V}{G} - \lambda\right) - \frac{V^2}{GL} = 0$$

From this, we find the two eigenvalues :

$$\lambda_1 = 0$$
$$\lambda_2 = -\left(\frac{V}{G} + \frac{V}{L}\right)$$

The corresponding eigenvectors are:

$$\boldsymbol{u}_1 = \begin{pmatrix} L \\ G \end{pmatrix}$$
$$\boldsymbol{u}_2 = \begin{pmatrix} 1 \\ -1 \end{pmatrix}$$

So, the basis vectors of the solutions of this differential system are:

$$\boldsymbol{y}_1 = e^{\lambda_1 t}\begin{pmatrix} L \\ G \end{pmatrix} = \begin{pmatrix} L \\ G \end{pmatrix}$$
$$\boldsymbol{y}_2 = e^{\lambda_2 t}\begin{pmatrix} 1 \\ -1 \end{pmatrix} = e^{-\left(\frac{V}{G}+\frac{V}{L}\right)t}\begin{pmatrix} 1 \\ -1 \end{pmatrix}$$

Any solution is a combination of these two vectors. However, a single combination is respecting the initial conditions, which are $L^*(0) = 0$ and $G^*(0) = G_0^* = 50000$:

$$\begin{pmatrix} L^* \\ G^* \end{pmatrix} = a\begin{pmatrix} L \\ G \end{pmatrix} + b\, e^{-\left(\frac{V}{G}+\frac{V}{L}\right)t}\begin{pmatrix} 1 \\ -1 \end{pmatrix}$$
$$= \begin{pmatrix} aL + b\, e^{-\left(\frac{V}{G}+\frac{V}{L}\right)t} \\ aG - b\ \ e^{-\left(\frac{V}{G}+\frac{V}{L}\right)t} \end{pmatrix}$$

With $\begin{pmatrix} L^*(0) \\ G^*(0) \end{pmatrix} = \begin{pmatrix} 0 \\ G_0^* \end{pmatrix}$, we get for *a* and *b* :

$$a = \frac{G_0^*}{G+L}$$
$$b = -\frac{G_0^* L}{G+L}$$

So, finally, the solution for the labeling is:

$$L^*(t) = \frac{G_0^* L}{G+L}\left(1 - e^{-\left(\frac{V}{G}+\frac{V}{L}\right)t}\right)$$
$$G^*(t) = \frac{G_0^* G}{G+L} + \frac{G_0^* L}{G+L} e^{-\left(\frac{V}{G}+\frac{V}{L}\right)t}$$

c) For $t \to \infty$, we have :

$$L^*(\infty) = \frac{G_0^* L}{G+L} = 14286\ red\ cars$$
$$G^*(\infty) = \frac{G_0^* G}{G+L} = 35714\ red\ cars$$

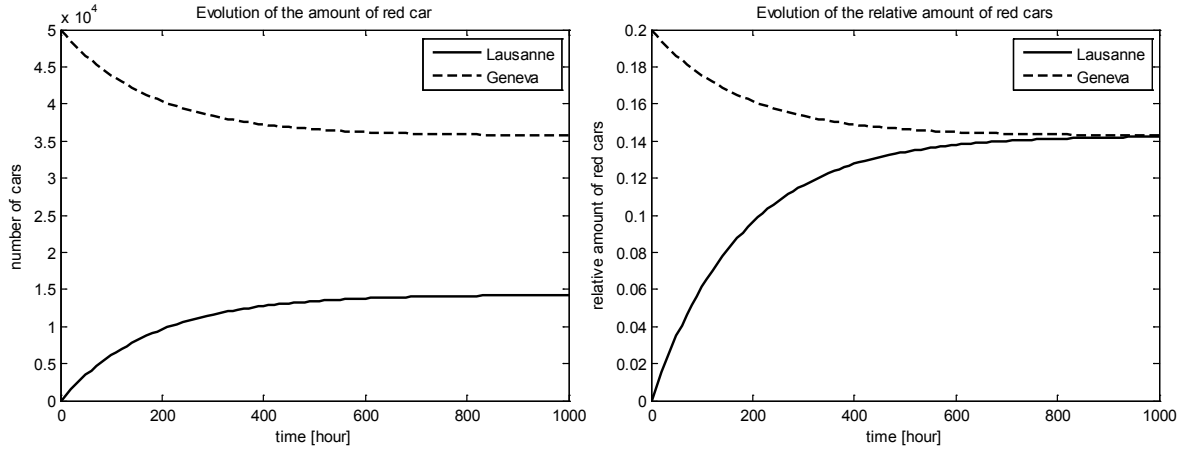
d) Let's name t_{8000} the time needed to have more than 8000 red cars in Lausanne. The condition is then:

$$L^*(t_{8000}) = \frac{G_0^* L}{G+L}\left(1 - e^{-\left(\frac{V}{G}+\frac{V}{L}\right)t_{8000}}\right) = 8000$$
$$-\left(\frac{V}{G}+\frac{V}{L}\right)t_{8000} = ln\left(1 - \frac{G+L}{G_0^* L}8000\right)$$
$$t_{8000} = \frac{-1}{\left(\frac{V}{G}+\frac{V}{L}\right)} ln\left(1 - \frac{G+L}{G_0^* L}8000\right) = 147\ hours$$

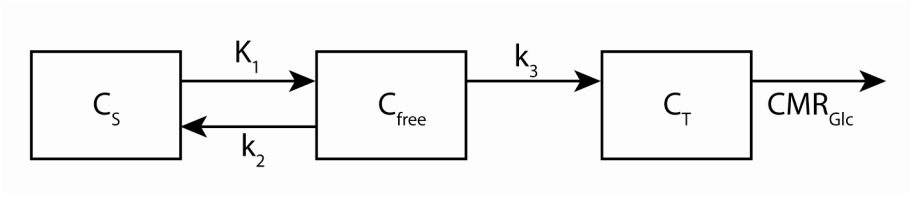
e) The percentage of red cars in Lausanne and Geneva after a very long time is given by:

$$\frac{L^*(\infty)}{L} = \frac{G_0^*}{G+L} = 14.3\%$$
$$\frac{G^*(\infty)}{G} = \frac{G_0^*}{G+L} = 14.3\%$$

They are equal. The system reaches its equilibrium when they are as many red cars leaving Geneva than those leaving Lausanne per unit of time. The total amount of cars per minute driving from or to Geneva is the same. In order to have the equilibrium for the red cars, the probability of finding a red car leaving Lausanne or Geneva must be the same. This probability is given by the amount of red car over the total amount of cars in each city. This value is often called fractional enrichment.



Solution 3: FDG-PET modeling / (brain) glucose metabolism



a) The differential equations describing the evolution of the total concentration in each pool are:

$$\frac{d}{dt}C_{free} = K_1 C_S - (k_2 + k_3)C_{free}$$
$$\frac{d}{dt}C_T = k_3 C_{free} - CMR_{Glc}$$

We assume constant total concentrations, which means that the differentials written above are equal to zero. We have:

$$C_{free} = \frac{K_1 C_S}{(k_2 + k_3)}$$
$$CMR_{Glc} = k_3 C_{free}$$

Which gives:

$$CMR_{Glc} = C_S \frac{K_1 k_3}{(k_2 + k_3)}$$

b) We can evaluate α and β using the plasma tracer concentration. To estimate the two parameters, we need two measurements. A good idea is to take the ones with the higher signal (5 and 15 min) (the third one can be used as verification):

$$\begin{cases} \alpha\, e^{-\frac{5}{\beta}} = C_S^*(5min) & (1) \\ \alpha\, e^{-\frac{15}{\beta}} = C_S^*(15min) & (2) \end{cases}$$

$$\rightarrow e^{\frac{10}{\beta}} = \frac{C_S^*(5min)}{C_S^*(15min)}$$

$$\rightarrow \frac{10}{\beta} = ln\left(\frac{C_S^*(5min)}{C_S^*(15min)}\right)$$

$$\rightarrow \beta = \frac{10}{ln\left(\frac{C_S^*(5min)}{C_S^*(15min)}\right)} = 10\ min$$

We can reuse one of the two equations (1) or (2) to extract α:

$$\alpha\, e^{-\frac{5}{\beta}} = C_S^*(5min)$$

$$\rightarrow \alpha = e^{\frac{5}{\beta}} C_S^*(5min) = 2000 \frac{kBq}{ml}$$

The Patlak formula to calculate the metabolic rate of glucose is:

$$CMR_{Glc} = \frac{C_S}{LC} \frac{C_T^*(T)}{\int_0^T C_S^*(t)dt}$$

We have the tissue tracer concentration at 40 min, where the contribution of free tracer in the tissue voxel can be neglected. We need then to calculate the integral of the plasma tracer concentration from 0 to 40min.

$$\int_0^T C_S^*(t)dt = \int_0^1 \alpha\, e^{-\frac{1}{\beta}}\, t\, dt + \int_1^T \alpha\, e^{-\frac{t}{\beta}}\, dt$$

$$= \alpha\, e^{-\frac{1}{\beta}} * \frac{1}{2} - \alpha\beta \left[e^{-\frac{t}{\beta}}\right]_1^T$$

$$= \frac{1}{2}\, \alpha\, e^{-\frac{1}{\beta}} - \alpha\beta \left(e^{-\frac{T}{\beta}} - e^{-\frac{1}{\beta}}\right) = 18635\ \frac{kBq}{ml} min \qquad for\ T = 40min$$

Finally, we find for the given values:

$$CMR_{Glc} = \frac{C_S}{LC} \frac{C_T^*}{\int_0^T C_S^*(t)dt} = \mathbf{0.124}\ \frac{\boldsymbol{\mu mol}}{\boldsymbol{g\ min}}$$

(we assume a tissue density of 1g/ml)

Solution 4: Model Fitting Pitfalls

This problem intends to make you aware of the pitfalls in experimental practice. In order to derive meaningful physical parameters (i.e. time constants) from experimental data, one often has to fit to a model function. This fitting is not trivial and can be error-prone.

In a PET experiment, we want to measure a saturation curve $A(1-e^{-\lambda t})$. The experiment takes 50 minutes and we can measure every 5 minutes, obtaining the following values:

min	**5**	**15**	**25**	**35**	**45**
value	0.0472	0.1964	0.4149	0.4259	0.6265

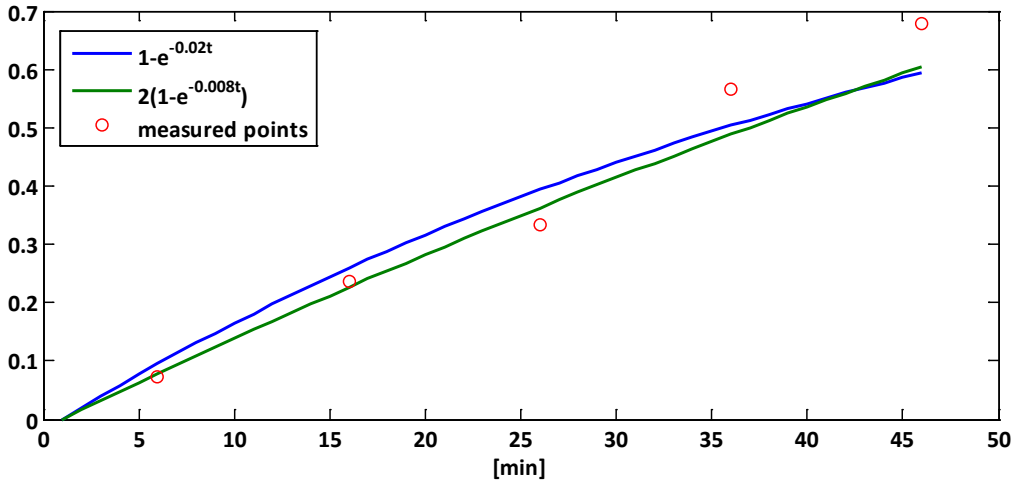
fct [1]	0.0942	0.2592	0.3935	0.5034	0.5934
res [1]	0.0479	0.0628	-0.0214	0.0775	-0.0331
fct [2]	0.0784	0.2262	0.3625	0.4884	0.6046
res [2]	0.0312	0.0297	-0.0524	-0.0625	-0.0219

Now we want to fit to our model function. Consider the following two:

$$1 - e^{-0.02t} \qquad [1]$$
$$2 \cdot (1 - e^{-0.008t}) \qquad [2]$$

a) RMSE function 1 = 5.23 %
RMSE function 2 = 4.61 %

b)



c) Measure longer, reduce the measurement noise. Here's the curve if we measured 180 min: