



A Brain Uptake Constant for Mathematical Modeling of Cerebral Radiopharmaceutical Uptake: A Synthetic Computational Study

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Abstract

Compartmental and tracer-kinetic models are widely used to describe radiopharmaceutical uptake in brain PET and SPECT, but in simple analytical models the fraction of transferred activity that reaches the brain is seldom isolated as a parameter of its own. This study defines a dimensionless Brain Uptake Constant, ψ , as the uptake fraction in a two-stage first-order model of cerebral radiopharmaceutical activity and examines its behaviour in a purely synthetic setting. Activity in the systemic pool, $A(t)$, is lost at a first-order rate k ; cerebral activity, $A_c(t)$, receives a source term $\psi k A(t)$ and is lost at an effective decay rate λ . The closed-form solution was evaluated directly for $A_0 = 100$ MBq, $k = 0.25 \text{ min}^{-1}$, $\lambda = 0.05 \text{ min}^{-1}$ and $\psi = 1.00, 0.75, 0.50$ and 0.25 over 0-60 min. Deterministic Gaussian fields were used to show the spatial effect of ψ as surface plots and heat maps. Each curve rises, passes through a single maximum at $t_{\text{peak}} = 8.047$ min and then decays. The peak time does not depend on ψ , whereas the peak

activity (66.87 MBq for $\psi = 1$) and the 0-60 min time-integrated activity scale linearly with ψ . In the spatial fields, ψ changes the amplitude but not the prescribed Gaussian widths. No clinical, PET or SPECT data were used, so the results say nothing about clinical validity. The model is offered as a simple parameterization that still has to be tested against measured dynamic imaging data with independently estimated kinetic parameters.

Keywords: Brain Uptake Constant, radiopharmaceutical kinetics, mathematical modeling, synthetic simulation, PET, SPECT.

1 Introduction

Mathematical models are used routinely in nuclear medicine to describe radiopharmaceutical kinetics, to quantify time-activity curves and to support the interpretation of PET and SPECT measurements. Brain PET studies usually rely on kinetic models and on an input-function strategy to estimate quantities such as influx, distribution volume and binding potential. Non-invasive approaches have been developed to avoid arterial sampling, although their applicability depends on the tracer and on the disease studied [1].



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Compartmental and biomathematical models offer another established way of describing radioligand transport and tissue uptake. Guo et al. [2] developed a one-tissue-compartment framework for central nervous system radioligands in which influx and efflux are treated separately and model parameters are linked to molecular and physiological descriptors. Other authors have described radiopharmaceutical transport and accumulation with differential equations that include uptake, elimination and radioactive decay [3]. Continuous distributions of rates have also been proposed as an alternative to single- and multi-exponential descriptions of radiopharmaceutical and radionuclide kinetics [4, 5].

Multi-rate-constant compartmental equations have been used to describe the kinetics of cerebral tracer uptake and to derive time-activity curves in human subjects [6], and compartmental models have been applied more broadly to the kinetics of other radionuclide systems [7]. Uptake models have even been built into probabilistic MR-PET reconstruction [8]. Explicit uptake and transport mechanisms are therefore already part of quantitative nuclear medicine, and the present work does not claim that cerebral uptake has not been modelled before.

The aim here is narrower. We introduce a dimensionless parameter ψ that scales the first-order transfer of activity into a synthetic cerebral compartment, while the transfer rate k and the decay constant λ are kept as separate quantities. Compared with a single-compartment mono-exponential baseline, this makes the uptake fraction appear explicitly in the source term, so that its effect on peak activity and on time-integrated activity can be studied analytically. The model is synthetic and low-dimensional by design. It is meant as a starting point for later comparison with measured time-activity curves, not as a disease-specific or clinically validated model.

Specifically, the study (i) derives the closed-form solution of the two-stage model, (ii) establishes its limiting and peak properties, (iii) quantifies the temporal outputs for four values of ψ , (iv) constructs deterministic synthetic spatial fields that illustrate the role of ψ , and (v) outlines how ψ could be estimated from imaging data.

2 Mathematical formulation

2.1 Activity compartments

Let $A(t)$ be the activity in the administered (systemic) pool that can feed the cerebral uptake pathway, and let $A_c(t)$ be the activity in the cerebral compartment. A_0 is the initial activity of the available pool, in MBq. All numerical results assume that the cerebral compartment is initially empty, $A_c(0) = 0$, because the curves are meant to show the appearance of uptake after administration; the general solution with a non-zero initial value is nevertheless given below. The systemic pool obeys

$$\frac{dA(t)}{dt} = -kA(t), \quad A(0) = A_0, \quad (1)$$

where k is a first-order input/transfer rate constant (min^{-1}). It is neither a fraction nor the Brain Uptake Constant. Solving Eq. (1) gives

$$A(t) = A_0 \exp(-kt). \quad (2)$$

The cerebral compartment receives a fraction ψ of the transfer flux $kA(t)$, and the activity in that compartment decays with rate λ :

$$\frac{dA_c(t)}{dt} = \psi kA(t) - \lambda A_c(t). \quad (3)$$

The Brain Uptake Constant ψ is dimensionless and is interpreted only as an uptake fraction, with $0 \leq \psi \leq 1$ in all simulations. It does not modify the decay rate and therefore does not enter the exponent of the decay term. The constant λ (min^{-1}) is an effective decay constant chosen for the synthetic calculation; no specific radionuclide is assigned to it.

2.2 Analytical solution

Substituting Eq. (2) into Eq. (3) gives the linear non-homogeneous equation

$$\frac{dA_c}{dt} + \lambda A_c = \psi k A_0 \exp(-kt). \quad (4)$$

With the integrating factor $\exp(\lambda t)$,

$$\frac{d}{dt} [A_c \exp(\lambda t)] = \psi k A_0 \exp((\lambda - k)t), \quad (5)$$

and integration from 0 to t gives, for $k \neq \lambda$,

$$A_c(t) = A_{c,0} \exp(-\lambda t) + \psi A_0 \frac{k}{k - \lambda} [\exp(-\lambda t) - \exp(-kt)]. \quad (6)$$

With $A_{c,0} = 0$, as in all simulations,

$$A_c(t) = \psi A_0 \frac{k}{k - \lambda} [\exp(-\lambda t) - \exp(-kt)]. \quad (7)$$

Equation (7) was used to generate the temporal curves. It also explains the initial rise: at $t = 0$ the cerebral compartment is empty while the source term is positive; as the available activity falls, the source weakens and decay eventually dominates.

The case $k = \lambda$ follows from the limit $k \rightarrow \lambda$ of Eq. (6):

$$A_c(t) = A_{c,0} \exp(-\lambda t) + \psi A_0 \lambda t \exp(-\lambda t), \quad (8)$$

so the solution stays finite when the two rates coincide.

2.3 Analytical properties

In the regime studied, $k > \lambda > 0$ and $0 < \psi \leq 1$. The bracket $\exp(-\lambda t) - \exp(-kt)$ is then non-negative for $t \geq 0$, so Eq. (7) gives $A_c(t) \geq 0$, and since both exponentials vanish as $t \rightarrow \infty$, $A_c(t) \rightarrow 0$. The trajectory is therefore bounded, non-negative and decays to zero.

Differentiating Eq. (7),

$$\frac{dA_c}{dt} = \psi A_0 \frac{k}{k - \lambda} [-\lambda \exp(-\lambda t) + k \exp(-kt)]. \quad (9)$$

Setting this derivative to zero yields a single interior maximum for any $k \neq \lambda$ with $k, \lambda > 0$:

$$t_{\text{peak}} = \frac{\ln(k/\lambda)}{k - \lambda}. \quad (10)$$

The parameter ψ does not appear in Eq. (10); with k and λ fixed, changing ψ alters the height of the curve but not the time of its peak. The peak activity is

$$A_{\text{peak}} = \psi A_0 \left(\frac{\lambda}{k} \right)^{\lambda/(k-\lambda)}, \quad (11)$$

and the time-integrated cerebral activity over $[0, T]$ is

$$\tilde{A}_c(T) = \psi A_0 \frac{k}{k - \lambda} \times \left[\frac{1 - \exp(-\lambda T)}{\lambda} - \frac{1 - \exp(-kT)}{k} \right]. \quad (12)$$

Equations (10)-(12) serve as direct checks on the numerical implementation. Because the closed-form solution is evaluated directly at 600 equally spaced time points, no ODE solver, step-size tolerance or convergence criterion is involved.

2.4 Baseline comparison

A natural baseline is the single-compartment mono-exponential model

$$A_{c,\text{base}}(t) = A_{c,0} \exp(-\lambda t). \quad (13)$$

For $A_{c,0} > 0$ it decreases monotonically and has no source term describing transfer from the systemic pool; for $A_{c,0} = 0$ it is identically zero. The proposed model differs in one respect: it adds the source term $\psi k A(t)$ and keeps λ as the loss rate of the cerebral compartment. In the governing equation ψ therefore scales a transfer flux rather than a plotted amplitude, even though, for $A_{c,0} = 0$, the resulting solution is simply proportional to ψ . The model remains much simpler than full compartmental or tracer-kinetic formulations and is not proposed as a substitute for them.

2.5 Notation, units and parameter ranges

Table 1 lists the symbols, units and values used. Note that the symbols here do not follow the consensus nomenclature for brain PET kinetic parameters [11]: in particular, k is the overall first-order loss rate of the systemic pool and should not be read as the rate constants K_1 or k_2 of a one-tissue compartment model.

Table 1. Notation, units and parameter ranges.

Symbol	Definition	Unit	Value/range used
$A(t)$	Activity available to the cerebral uptake pathway	MBq	$A_0 \exp(-kt)$
$A_c(t)$	Cerebral-compartment activity	MBq	≥ 0
A_0	Initial available (administered) activity	MBq	100
$A_{c,0}$	Initial cerebral activity	MBq	0 in simulations; ≥ 0 in general
k	First-order input/transfer rate constant	min^{-1}	0.25
λ	Effective decay constant of the synthetic model	min^{-1}	0.05
ψ	Brain Uptake Constant (dimensionless uptake fraction)	-	$0 \leq \psi \leq 1$
t	Time	min	0-60
x, y	Synthetic spatial coordinates	a.u.	see Section 4.2
$U_\psi(x, y), H_\psi(x, y)$	Normalized synthetic uptake fields	a.u.	0-2 (plotted scale)

Table 2. Computational environment and fixed simulation settings.

Component	Implementation	Fixed settings
Temporal solution	Direct evaluation of Eq. (7)	$A_0 = 100$ MBq; $k = 0.25 \text{ min}^{-1}$; $\lambda = 0.05 \text{ min}^{-1}$; $\psi \in \{1, 0.75, 0.50, 0.25\}$; 0-60 min; 600 points
Figure 2 spatial field	Two Gaussians, Eqs. (14)-(16)	$x \in [-4, 4]$ a.u.; $y \in [-3, 3]$ a.u.; 180×160 grid
Figure 3 heat maps	Two Gaussians $\times$ elliptical mask, Eqs. (17)-(19)	$x \in [-5, 5]$ a.u.; $y \in [-4.5, 4.5]$ a.u.; 500×450 grid; hot; bicubic
Randomness	None	Deterministic calculations
Software	Python / NumPy / Matplotlib	Python 3.13.5; NumPy 2.3.5; Matplotlib 3.10.8

Table 3. Temporal outputs calculated analytically from Eqs. (7) and (10)-(12).

ψ	Peak activity (MBq)	Time to peak (min)	Integrated activity, 0-60 min (MBq·min)	Activity at 60 min (MBq)
1.00	66.87	8.047	1875.53	6.22
0.75	50.16	8.047	1406.65	4.67
0.50	33.44	8.047	937.77	3.11
0.25	16.72	8.047	468.88	1.56

3 Computational implementation

All computations were carried out deterministically in Python (Table 2). The supplementary scripts use Python 3.13.5, NumPy 2.3.5 and Matplotlib 3.10.8. No random numbers are drawn in any simulation, so no random seed is needed.

4 Numerical results

4.1 Temporal activity

Figure 1 was generated directly from Eq. (7), without a numerical ODE solver. All four scenarios start from $A_c(0) = 0$, rise while the source term $\psi k A(t)$ dominates, peak at the time given by Eq. (10), and then decline as both the available input and the cerebral activity decrease.

The values in Table 3 follow the scaling predicted by the analytical solution. The peak time is the same for every ψ because ψ cancels from the stationarity condition, whereas the peak activity, the integrated activity and the activity at 60 min are all proportional to ψ . For $\psi = 1.00$ the peak activity is 66.87 MBq and the 0-60 min integrated activity is 1875.53 MBq·min.

4.2 Synthetic spatial model

To show the spatial meaning of ψ without implying any anatomical resolution, a two-dimensional field is built from two Gaussian components. It is not a three-dimensional brain volume. Figure 2 plots this

two-dimensional field as a surface, with dimensionless coordinates x and y and normalized uptake on the vertical axis:

$$G_L(x, y) = \exp \left\{ - \left[\frac{(x + 1.15)^2}{2 \cdot 1.25^2} + \frac{y^2}{2 \cdot 1.35^2} \right] \right\}, \quad (14)$$

$$G_R(x, y) = \exp \left\{ - \left[\frac{(x - 1.15)^2}{2 \cdot 1.25^2} + \frac{y^2}{2 \cdot 1.35^2} \right] \right\}, \quad (15)$$

$$U_\psi(x, y) = \psi [G_L(x, y) + G_R(x, y)]. \quad (16)$$

The Gaussian centres and widths are fixed (Table 4), so ψ changes only the amplitude of the field. The vertical axis is fixed at 0-2 a.u. in all four panels; any apparent shrinkage of the visible region at lower ψ is a consequence of the lower amplitude, not of a change in the Gaussian widths. The surface colours, by contrast, are scaled to the maximum of each panel and should not be compared across panels.

4.3 Synthetic heat maps

Figure 3 uses a separate two-dimensional parameterization, evaluated on a 500×450 grid and multiplied by an elliptical mask that stands for a simplified brain-shaped domain. Coordinates are again dimensionless and uptake values are in normalized arbitrary units; no physical length or activity calibration is implied. The heat-map field uses

Temporal evolution of cerebral activity under the proposed uptake model

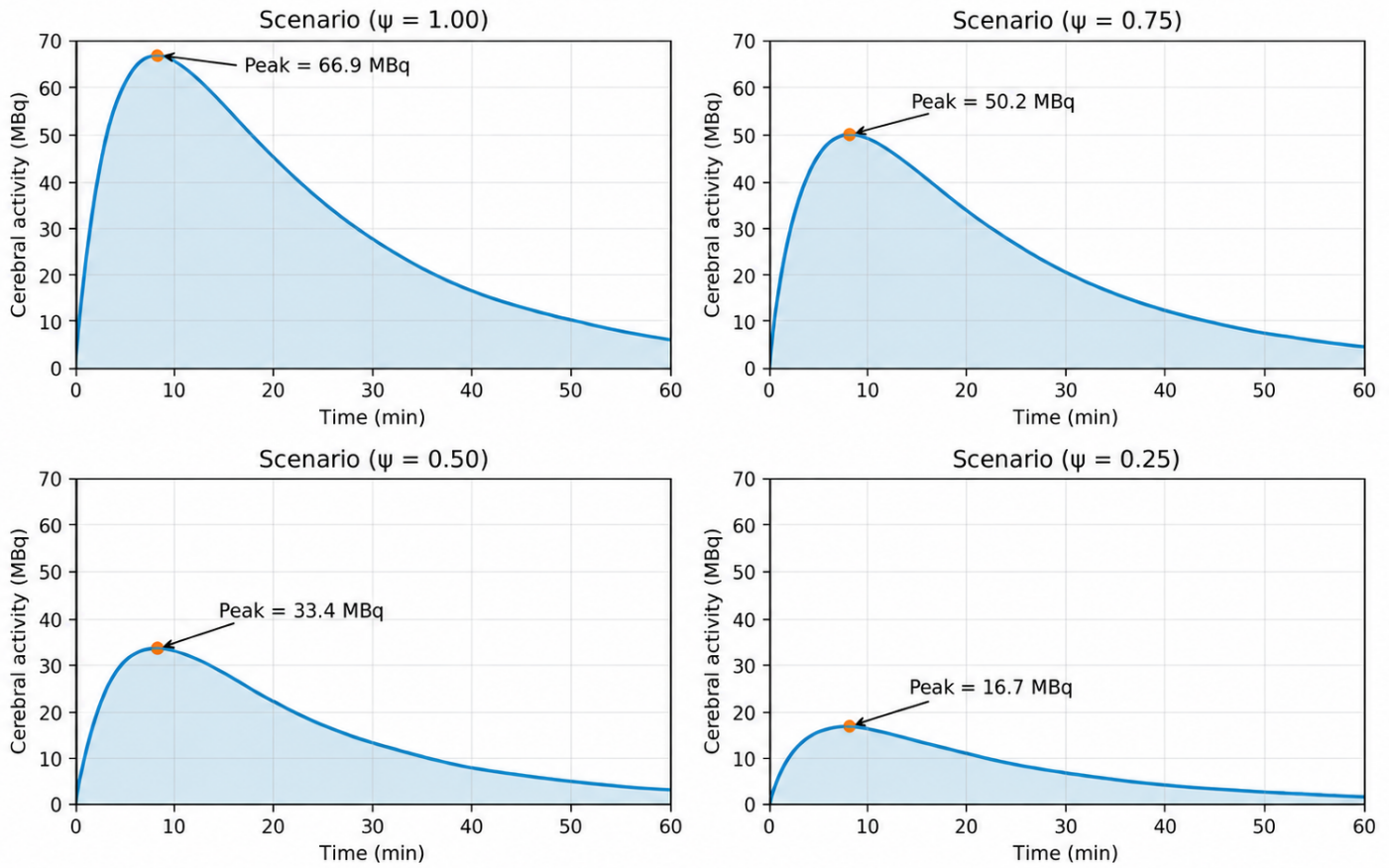


Figure 1. Synthetic cerebral activity obtained from Eq. (7) with $A_0 = 100$ MBq, $k = 0.25 \text{ min}^{-1}$, $\lambda = 0.05 \text{ min}^{-1}$, $A_c(0) = 0$ and $\psi = 1.00, 0.75, 0.50$ and 0.25 over 0-60 min. The peak time is $t_{\text{peak}} = 8.047$ min in all four panels. The shaded area under each curve corresponds to the 0-60 min time-integrated activity listed in Table 3.

Table 4. Parameters of the synthetic surface in Figure 2.

Quantity	Value
Gaussian centre, left	$x_0 = -1.15 \text{ a.u.}, y_0 = 0$
Gaussian centre, right	$x_0 = +1.15 \text{ a.u.}, y_0 = 0$
σ_x	1.25 a.u.
σ_y	1.35 a.u.
Spatial domain	$x \in [-4, 4] \text{ a.u.};$ $y \in [-3, 3] \text{ a.u.}$
Grid	180×160
Peak of unscaled field	1.310 a.u.
Effect of ψ	Amplitude scaling only

its own pair of Gaussians,

$$H_{L,R}(x, y) = \exp \left\{ - \left[\frac{(x \pm 1.25)^2}{2 \cdot 1.20^2} + \frac{y^2}{2 \cdot 1.35^2} \right] \right\}, \quad (17)$$

where the upper sign gives H_L and the lower sign H_R , together with the mask

$$M(x, y) = \begin{cases} 1, & (x/4.6)^2 + (y/4.1)^2 \leq 1, \\ 0, & \text{otherwise,} \end{cases} \quad (18)$$

$$H_\psi(x, y) = \psi M(x, y) [H_L(x, y) + H_R(x, y)]. \quad (19)$$

All four panels share the colour limits 0-2.00 a.u., with the colour bar placed outside the panels (Table 5). Since the widths are fixed, ψ again changes the intensity and not the spatial width.

5 Discussion

The model separates five quantities: the systemic activity $A(t)$, the cerebral activity $A_c(t)$, the transfer rate k , the decay constant λ and the dimensionless uptake fraction ψ . The rise-peak-decay shape of Figure 1 follows directly from the balance between source and decay in Eq. (3); no additional mechanism is needed to explain it.

Synthetic two-dimensional spatial field shown as a three-dimensional surface

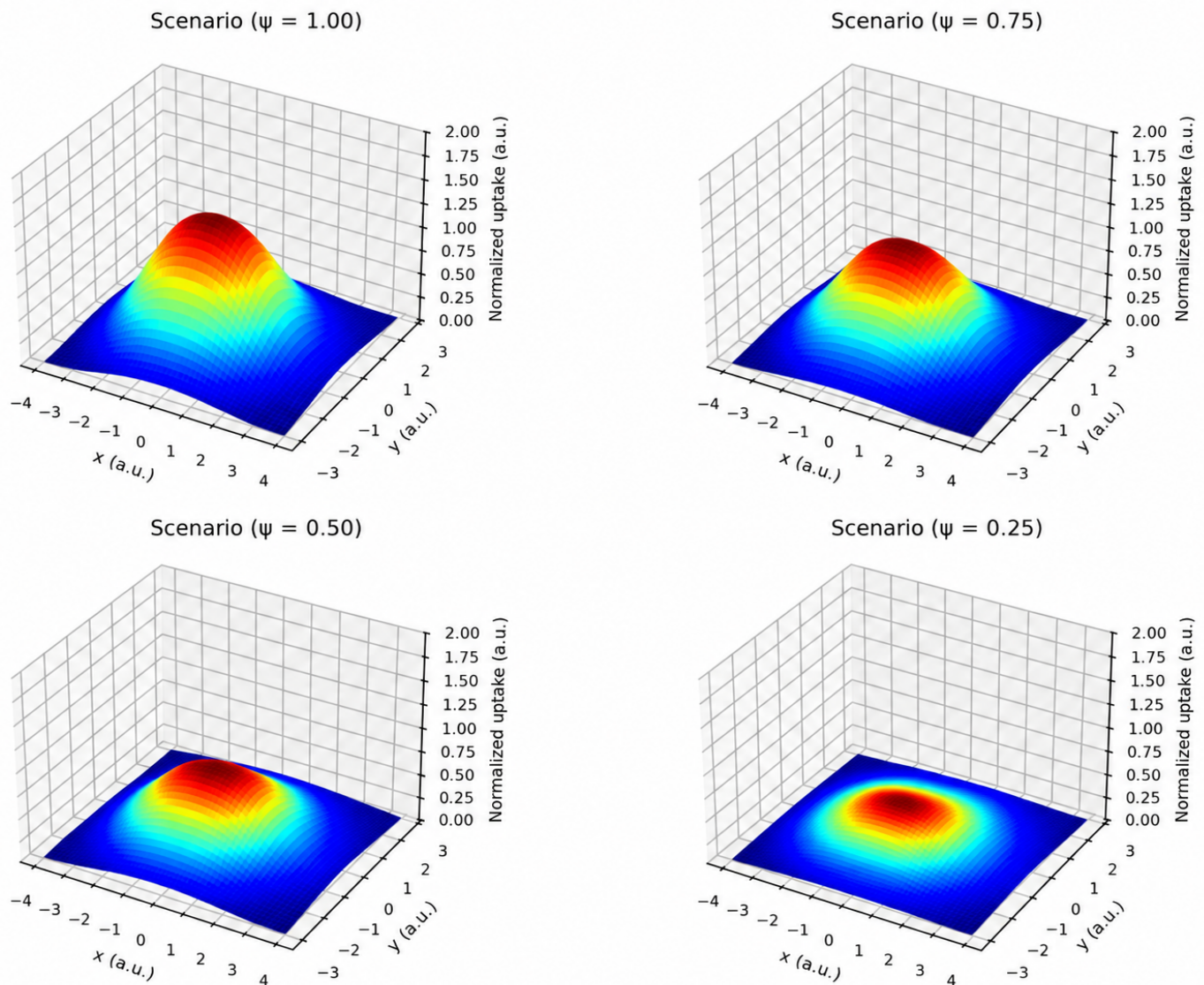


Figure 2. Synthetic two-dimensional uptake field of Eqs. (14)-(16) plotted as a surface for $\psi = 1.00, 0.75, 0.50$ and 0.25 . Parameters are given in Table 4. The plot does not represent an anatomically resolved brain.

5.1 Comparison with established kinetic formulations

PET and SPECT kinetic models may include one or more tissue compartments, transfer rates, receptor-binding terms, input functions and clearance processes [1, 2, 9, 10]. The present formulation is much simpler; what it adds is an explicit dimensionless uptake fraction ψ multiplying the transfer flux $kA(t)$. Relative to the mono-exponential baseline of Eq. (13), the size of the cerebral uptake (ψ) is thus separated from the rate of transfer (k) and from decay (λ). This separation is convenient for sensitivity analysis and for future parameter estimation, but it does not imply that existing compartmental models lack uptake mechanisms.

Unlike models built for quantitative PET pharmacokinetics, the present one has fewer compartments and contains no arterial input function, receptor binding, blood-brain barrier transport, perfusion or tracer-specific physiology [1, 2, 10]. Unlike the transport model for $^{99m}\text{Tc-MIBI}$ [3] and the continuous-rate approaches [4, 5], it is not fitted to experimental biodistribution data. It should therefore be read as a simplification suited to controlled synthetic experiments, not as an alternative to established kinetic analysis.

5.2 Limiting cases of ψ

For $\psi = 0$, Eq. (7) gives $A_c(t) = 0$ when $A_{c,0} = 0$: no activity is transferred to the cerebral compartment. For $\psi = 1$, the whole first-order transfer flux $kA(t)$ goes to

Synthetic cerebral uptake heat maps

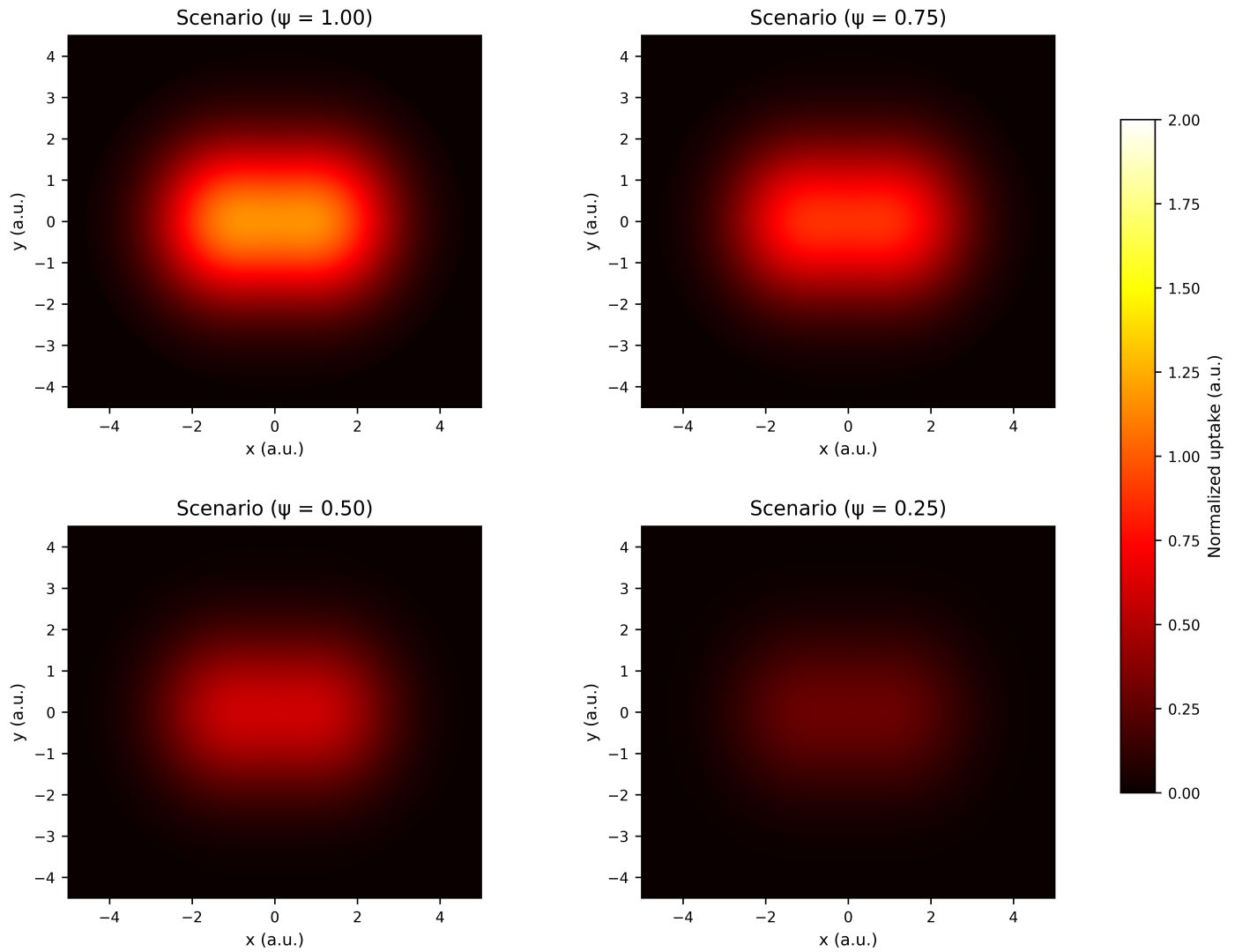


Figure 3. Synthetic cerebral uptake heat maps of Eq. (19) for $\psi = 1.00, 0.75, 0.50$ and 0.25 , drawn with the hot colour map, common limits of 0-2.00 a.u. and bicubic interpolation; parameters are given in Table 5. These are two-dimensional illustrations, not anatomical PET/SPECT images.

that compartment, and intermediate values scale the cerebral response linearly. Because ψ does not appear inside an exponential, it leaves the decay constant λ and the transfer time scale $1/k$ unchanged and only sets the share of the transfer flux assigned to the brain.

5.3 Estimating ψ from observations

Suppose dynamic imaging provides cerebral activities $A_{c,obs}(t_i)$ and that A_0 , k and λ are known or constrained independently. With

$$f(t) = A_0 \frac{k}{k - \lambda} [\exp(-\lambda t) - \exp(-kt)], \quad (20)$$

the observation model is linear, $A_c(t_i) = \psi f(t_i)$, and the least-squares estimate of ψ is

$$\hat{\psi} = \frac{\sum_i f(t_i) A_{c,obs}(t_i)}{\sum_i f(t_i)^2}, \quad (21)$$

restricted to $0 \leq \hat{\psi} \leq 1$ when ψ is interpreted as a fraction. If A_0 is unknown, only the product ψA_0 is identifiable from this model, and ψ cannot be separated from A_0 without further information. If k is estimated from the same time-activity curve, ψ and k may be correlated, because k shapes the curve while ψ sets its amplitude. Independent knowledge of A_0 and of at least one rate constant, or sufficiently informative longitudinal data, is therefore needed before ψ can be interpreted as a physiological quantity.

Table 5. Parameters of the synthetic heat maps in Figure 3.

Quantity	Value
Grid	500 × 450
Domain	$x \in [-5, 5]$ a.u.; $y \in [-4.5, 4.5]$ a.u.
Elliptical semi-axes	4.6 a.u. and 4.1 a.u.
Gaussian centres	$x_0 = -1.25$ and $+1.25$ a.u.; $y_0 = 0$
Gaussian widths	$\sigma_x = 1.20$ a.u.; $\sigma_y = 1.35$ a.u.
Colour map	hot
Interpolation	Bicubic
Common colour limits	0-2.00 a.u.
Peak of unscaled field	1.168 a.u.

5.4 Numerical illustration versus validation

All results in this paper are deterministic synthetic calculations. They show the mathematical consequences of the model but do not validate any physiological interpretation of ψ . No patient data, disease-specific images or measured cerebral uptake curves were used; the spatial figures are mathematical fields, not anatomical reconstructions, and the temporal parameters are illustrative rather than measured for a particular radionuclide.

A validation study would need dynamic PET or SPECT data acquired with a specified radionuclide and protocol, independent estimates or constraints for the kinetic parameters, and a comparison of predicted and observed time-activity curves using goodness-of-fit and out-of-sample criteria. The value of ψ should be tested across subjects and tracers.

5.5 Limitations

The main limitations are the low-dimensional compartment structure, the synthetic parameter values, the absence of imaging data and the absence of a disease-specific biological mechanism. The spatial fields use prescribed Gaussian widths and an elliptical mask and do not represent real cerebral anatomy or heterogeneity measured with MRI, PET or SPECT. The parameter λ is an illustrative effective decay constant not tied to a named radionuclide. Radioactive decay of the systemic pool is not modelled separately: k is treated as the overall loss constant of that pool, while λ lumps together physical decay and any biological clearance from the cerebral compartment. Likewise, the range $\psi = 0.25$ -1 was chosen to display the linear scaling and does not correspond to the brain uptake

fractions of clinical tracers.

6 Conclusion

A two-stage synthetic model of cerebral radiopharmaceutical activity was formulated in which the Brain Uptake Constant ψ is a dimensionless fraction multiplying the first-order transfer flux. Its closed-form solution, peak time, peak activity and integrated activity were derived and used to generate the temporal simulations.

With the chosen parameters, cerebral activity is non-negative and follows a rise-peak-decay course. The peak occurs at 8.047 min for all four values of ψ , while the peak activity and the 0-60 min integrated activity are proportional to ψ . In the spatial figures ψ modulates the amplitude of fixed Gaussian fields; it does not change anatomical extent, and the figures are not an anatomically resolved brain model.

The study is a mathematical and computational demonstration, not a clinical validation and not an analysis specific to Alzheimer’s disease or any other condition. The next step is to estimate ψ from measured dynamic PET or SPECT time-activity data under independently constrained kinetic assumptions, and to test whether it carries reproducible information beyond that provided by established compartmental and kinetic models.

Data Availability Statement

The results are fully deterministic and can be regenerated from the equations and parameter values reported here. No experimental dataset is associated with this study.

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Conflicts of Interest

The author declares no conflicts of interest.

AI Use Statement

The authors declare that no generative AI was used in the preparation of this manuscript.

Ethical Approval and Consent to Participate

Not applicable.

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