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Mathematical Analysis of Drug Diffusion in Tissues

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Abstract

A drug released at a tissue boundary may diffuse through extracellular space while simultaneously binding to tissue constituents, entering cells, undergoing metabolism or being removed by microvessels. Mathematical models link these processes to spatial concentration and exposure. This article develops a one-dimensional diffusion–reaction model from conservation of mass and Fick's law, states its boundary conditions and analytical steady-state solution, and explains characteristic timescales and penetration length. A constructed example compares normalized concentration profiles under three first-order removal rates. With the same diffusivity and thickness, larger removal rates yield lower concentrations deeper in the modeled tissue. The illustration is not a fitted experiment and cannot determine any drug's therapeutic dose or safety. Extensions cover reversible binding, vascular exchange, heterogeneous tissue and numerical solution. Reported data, tissue-specific parameters and validation are essential before translating such calculations to clinical use. Foundational diffusion theory and published drug-transport studies support the modeling framework [1–4].

Keywords: drug diffusion; tissue transport; Fick's law; reaction–diffusion equation; penetration depth; drug delivery; mathematical modeling

1 Introduction

Drug concentration within tissue need not equal the concentration applied at its surface or measured in blood. Concentration gradients cause molecules to move; uptake and clearance change how much remains at each depth. This matters for topical treatment, local implants, brain delivery and tumor penetration. A mathematical model can separate the effects of diffusion, tissue loss and exposure time, provided its simplifying assumptions are explicit.

Higuchi's classic analysis connects release from an ointment vehicle to diffusion under specified sink and suspension assumptions [2]. A model of tissue penetration addresses a subsequent transport domain and should not treat formulation release and tissue uptake as identical processes. Reviews of diffusion-controlled delivery emphasize that geometry, initial concentration, solubility and device structure determine which equation is appropriate [3]. Local brain delivery models likewise demonstrate the need to represent transport in both delivery material and surrounding tissue [4].

2 Governing equation from mass conservation

Let $C(x,t)$ denote freely mobile drug concentration in a planar tissue region $0 \le x \le L$, in units of amount per tissue volume. In one dimension, the diffusive flux is $J = -D\,\partial C/\partial x$, where D is an effective diffusion coefficient (length^2/time). For constant D, mass conservation with a distributed source S and first-order removal kC gives $\partial C/\partial t = D\,\partial^2 C/\partial x^2 - kC + S(x,t)$. Here k has units time^{-1}. A term called "removal" can represent irreversible uptake, metabolism or a lumped local clearance, but combining mechanisms into one fitted k limits interpretation.

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A more general heterogeneous model writes $\partial(\varphi C)/\partial t = \partial[\varphi D(x)\ \partial C/\partial x]/\partial x - \varphi k(x)C + q(x,t)$, with accessible volume fraction φ. Different definitions of C (interstitial concentration versus amount per bulk tissue volume) require consistent factors of φ. When a vascular concentration drives exchange, a source such as $P_s a_v(C_v - C/K_p)$ may be added, where $P_s a_v$ is permeability–surface-area product per tissue volume and K_p is a partition factor. Such extensions require their own measured parameters.

3 Initial and boundary conditions

A partial differential equation is incomplete without initial and boundary conditions. For the illustrative slab, $C(x,0) = 0$, $C(0,t) = C_0$ for $t > 0$, and $\partial C/\partial x(L,t) = 0$. The first boundary represents a maintained surface concentration; the last represents no net flux at the distal face. Other experiments may need a prescribed flux, a finite surface transfer coefficient, or a vascular sink. The sudden change at $x = 0$, $t = 0$ is an idealization and does not specify the microscopic application transient.

Table 1. Alternative boundary descriptions; their signs depend on the chosen positive spatial direction. Use the condition matching the experimental device.

Condition	Mathematical form	Physical interpretation
Fixed concentration	$C(0,t) = C_0$	Maintained donor or reservoir
Prescribed flux	$-D\ C_x(0,t) = J_0$	Known input rate per area
Permeable interface	$-D\ C_x(0,t) = h(Cd - C(0,t))$	Finite interfacial mass transfer
No flux	$C_x(L,t) = 0$	Impermeable or symmetry boundary

4 Analytical steady-state solution

For constant C_0, D and k, with S = 0, the steady-state problem is $D\ d^2C/dx^2 - kC = 0$. The two boundary conditions yield $C(x)/C_0 = \cosh[(L - x)/\ell]/\cosh(L/\ell)$, where $\ell = \sqrt{(D/k)}$ is a characteristic penetration length. At k = 0 the no-flux steady solution is spatially uniform, $C = C_0$. The parameter ℓ is not an absolute cutoff: it describes the competition between diffusion and removal. For L much larger than ℓ, concentrations at the far edge can be small even when the boundary concentration remains fixed.

Two nondimensional measures clarify this competition. The removal-to-diffusion ratio $Da = kL^2/D = (L/\ell)^2$ is a Damköhler-type number. The diffusive timescale is $tD = L^2/D$, while the removal timescale is $tk = 1/k$. When Da is large, removal acts strongly before drug traverses the slab. At small Da, diffusion can smooth concentration differences across the thickness. These are model-based descriptions, and an actual effective diffusivity can vary with tissue architecture and compound chemistry [1,3].

5 Illustrative parameters and concentration profiles

For the constructed example, choose L = 0.10 cm (1 mm), $D = 1.0 \times 10^{-6}$ cm²/s and $k = 1.0 \times 10^{-4}$, 4.0×10^{-4} or 1.0×10^{-3} s⁻¹. These numbers are selected only to expose mathematical sensitivity; they are not measurements from a named drug or tissue. The corresponding diffusion time L^2/D is 10,000 s (about 2.78 h). Steady state may require several timescales depending on the mode of observation. Figure 1 and Table 2 evaluate the exact steady-state formula, so there is no discretization error in the plotted profile itself.

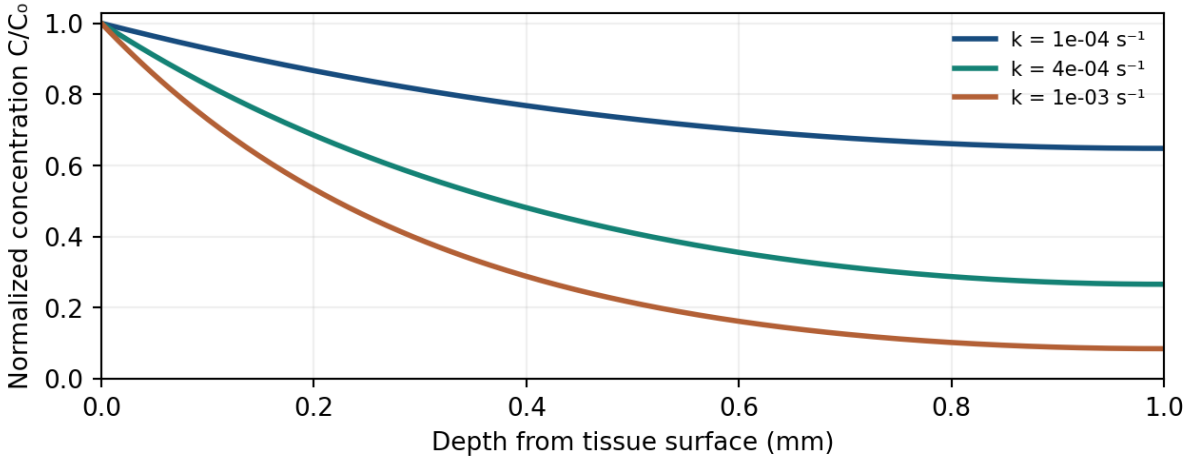


Figure 1. Illustrative, normalized steady-state concentration versus depth for three removal rates. $D = 10^{-6}$ cm²/s and L = 0.10 cm are fixed; no patient or laboratory observations are shown.

Table 2. Derived values for Figure 1. The distal concentration falls as the selected removal rate rises, under the stated fixed-concentration and no-flux boundary conditions.

k (s^{-1})	ℓ (mm)	Da	$C(L)/C_0$
1e-04	1.000	1.0	0.648
4e-04	0.500	4.0	0.266
1e-03	0.316	10.0	0.085

The plotted effect is a mathematical consequence of the chosen model: changing k while holding the boundary C_0 fixed changes both ℓ and the shape of C(x). It does not establish that stronger clearance alone governs penetration in a real tissue. A measured spatial profile might also reflect heterogeneity, nonlinear binding, perfusion, tissue necrosis or a concentration-dependent boundary input.

6 Extensions and numerical implementation

Reversible binding requires at least a second state variable. If B is bound concentration and Bmax the available binding capacity, a simple system is $\partial C/\partial t = D\,C_{xx} - kon\,C(Bmax - B) + koff\,B - kC$, and $\partial B/\partial t = kon\,C(Bmax - B) - koff\,B$. The sum C + B conserves mass with respect to binding alone; metabolism or vascular removal must be represented separately. Rapid-equilibrium binding may permit a reduced equation, but the reduction must be derived for the experimental concentration range.

For a radially symmetric depot or vessel, geometry changes the diffusion operator: $\partial C/\partial t = D\,r^{-2}\,\partial(r^2\partial C/\partial r)/\partial r - kC$ for a sphere, or $D\,r^{-1}\,\partial(r\partial C/\partial r)/\partial r - kC$ for a cylinder. At r = 0 a regular solution has zero radial gradient. Piecewise tissue layers require continuity of concentration adjusted by partition coefficients and continuity of flux at interfaces. A model with spatially variable perfusion often requires numerical methods rather than the closed-form slab expression.

Finite differences can approximate the transient slab model at interior node i: $(C_i^{n+1} - C_i^n)/\Delta t = D(C_{i+1}^n - 2C_i^n + C_{i-1}^n)/\Delta x^2 - kC_i^n$. This explicit method is subject to time-step restrictions; for diffusion alone $D\Delta t/\Delta x^2 \le 1/2$ in one dimension. Implicit or Crank–Nicolson schemes allow larger time steps but still require convergence checks. Preserve nonnegative concentrations, track boundary flux and verify a mass-balance residual when a computational solution is used [1].

7 Model calibration and interpretation

Calibration requires data that can identify D, k and the boundary input. A single terminal tissue concentration generally cannot separate all three. Time-resolved concentrations at several depths, independent measurements of diffusivity or clearance, and the donor concentration history improve identifiability. Fit parameters on one dataset, test predictions on held-out observations and report uncertainty. If exposure drives a pharmacological response, the tissue transport model can be coupled to a separate concentration–effect model; concentration alone does not establish efficacy or toxicity.

A useful reporting checklist includes specimen geometry, tissue preparation, temperature, assay method, definition of free versus total drug, experimental input, units, loss mechanisms, optimization criterion and numerical convergence. When a simplified slab cannot explain the data, refine the physical structure before adding arbitrary terms. The goal is an interpretable model with a clearly stated range of validity, not merely a close fit.

8 Conclusion

Fickian reaction–diffusion equations provide a transparent starting point for analyzing how drug spreads through tissue and is locally removed. Their analytical penetration length and dimensionless removal ratio expose the assumptions governing spatial exposure. In the illustrative slab, larger k produces steeper concentration decay with depth. Real drug–tissue systems may additionally involve binding, vessels, layered geometry and changing boundary concentrations. Model parameters and clinical implications therefore require experimental validation for each compound, tissue and administration route.

References

[1] Crank, J. (1975). The Mathematics of Diffusion (2nd ed.). Clarendon Press, Oxford. https://staff.bath.ac.uk/ensdasr/PAPERS/Crank-The-Mathematics-of-Diffusion.pdf

[2] Higuchi, T. (1961). Rate of release of medicaments from ointment bases containing drugs in suspension. Journal of Pharmaceutical Sciences, 50(10), 874–875. https://doi.org/10.1002/jps.2600501018

[3] Siepmann, J., & Siepmann, F. (2012). Modeling of diffusion controlled drug delivery. Journal of Controlled Release, 161(2), 351–362. https://doi.org/10.1016/j.jconrel.2011.10.006

[4] Siepmann, J., et al. (2006). Local controlled drug delivery to the brain: Mathematical modeling of the underlying mass transport mechanisms. International Journal of Pharmaceutics, 314(2), 101–119. https://pubmed.ncbi.nlm.nih.gov/16647231/

Article type: explanatory mathematical review with a constructed steady-state example; no new clinical or experimental measurements are claimed.