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Solute diffusion out of a vesicle

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Abstract

Motivated by the problem of calculating the effusion time of solute from a spherical vesicle with an open pore, we present an analytical solution of a simpler problem in which solute particles are allowed to escape through a spherical cavity located at the center of the vesicle.

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1. Introduction

The time of efflux of solute through an open pore of a liposomal vesicle is an important practical problem of direct relevance to the design of efficient drug delivery systems [1,2]. There are a number of mechanisms involved in the leak-out. The osmotic pressure difference between the interior and the exterior of the vesicle produces an osmotic current through an open pore [3]. This flow also results in the transport of solute out of the vesicle [4,5].

Besides the osmotic current there is a diffusive efflux of solute. Since the concentration of solute outside the vesicle is much smaller than inside, a diffusive current through an open pore is established. To study the relative importance of effusion and osmosis, as a first order approximation we shall decouple the two effects.

The effusion of solute out of a vesicle is governed by the diffusion equation. The boundary condition on this equation is the vanishing of the diffusive current at the membrane surface and zero solute concentration inside the pore—recall that from the Fick's law, the diffusive current is proportional to the spacial derivative of the

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concentration. Unfortunately, because of the mixed nature of the boundary conditions—a combination of Neumann and Dirichlet—this problem is difficult to treat analytically. Therefore, in the hope of gaining further insight, we shall start by studying a simpler problem in which effusion of solute occurs through a spherical cavity located at the center of the vesicle.

2. Diffusion equation

We address the following problem. The particles confined to the interior of a hollow sphere $\mathbf{S}_1$ of radius R undergo a diffusive motion, with the diffusion constant D. At the center of $\mathbf{S}_1$ there is a concentric sphere $\mathbf{S}_2$ of radius $a < R$, which is a sink—when a solute particle enters into $\mathbf{S}_2$ it vanishes from the system. At time $t = 0$, N solute particles are uniformly distributed in the volume $a < r < R$. The question that we would like to answer is: What is the characteristic time for emptying $\mathbf{S}_1$?

The process of effusion is governed by the diffusion equation

$$\frac{\partial \rho}{\partial t} = D\nabla^2 \rho \; , \tag{1}$$

where $\rho(r,t)$ is the local density at distance r from the center of $\mathbf{S}_1$ at time t. At $t=0$

$$\rho(r,0) = \rho_0, \quad \text{for } a < r < R \; , \tag{2}$$

where

$$\rho_0 = \frac{3N}{4\pi(R^3 - a^3)} \tag{3}$$

is the initial density.

The boundary conditions are the vanishing of flux at the surface of $\mathbf{S}_1$,

$$\left.\frac{\partial \rho(r,t)}{\partial r}\right|_R = 0 \; , \tag{4}$$

and zero solute density at the surface of $\mathbf{S}_2$

$$\rho(a,t) = 0 \; . \tag{5}$$

It is easy to see why this problem is easier to study than the one in which a hole is located on the surface of the vesicle. In that case, the spherical symmetry of the boundary conditions Eqs. (4) and (5) is lost, and one has to solve the full mixed boundary value problem.

It is convenient to define

$$\varDelta(r,t) = \rho_0 - \rho(r,t) \; , \tag{6}$$

which satisfies the diffusion equation (1) with the boundary conditions

$$\left.\frac{\partial \varDelta(r,t)}{\partial r}\right|_R = 0 \tag{7}$$

and

$$\varDelta(a,t) = \rho_0 \; , \tag{8}$$

for all time. The initial condition is

$$\Delta(r,0) = 0, \quad \text{for } a < r < R \,. \tag{9}$$

Taking the Laplace transform of the diffusion equation and of the boundary conditions we find

$$s\tilde{\Delta}(r,s) = D\nabla^2\tilde{\Delta}(r,s)\,, \tag{10}$$

$$\tilde{\Delta}(a,s) = \frac{\rho_0}{s}\,, \tag{11}$$

$$\left.\frac{\partial\tilde{\Delta}(r,s)}{\partial r}\right|_R = 0\,, \tag{12}$$

where $\tilde{\Delta}(r,s)$ is the Laplace transform of $\Delta(r,t)$.

Eq. (10) with the boundary conditions (11) and (12) can be solved in terms of the spherical Bessel functions. The solution is

$$\tilde{\Delta}(r,s) = A\,\frac{\sin(kr)}{kr} + B\,\frac{\cos(kr)}{kr}\,, \tag{13}$$

where $k^2 = -s/D$ and

$$A = \frac{\rho_0[kR\tan(kR)+1]ka}{s\{[kR\tan(kR)+1]\sin(ka)+\cos(ka)[kR-\tan(kR)]\}}\,, \tag{14}$$

$$B = \frac{\rho_0[kR-\tan(kR)]ka}{s\{[kR\tan(kR)+1]\sin(ka)+\cos(ka)[kR-\tan(kR)]\}}\,. \tag{15}$$

Variation in the concentration of solute inside $\mathbf{S}_1$ follows from the inverse Laplace transform. Unfortunately, the exact inversion is not possible due to complexity of the expressions (14) and (15). The asymptotic form of the decrease in the number of solute particles inside $\mathbf{S}_1$ can, however, be determined from the leading pole (closest to $s=0$) of the Laplace transform. Note that the pole at $s=0$ corresponds to the stationary state $\Delta(r,\infty)=\rho_0$ or $\rho(r,\infty)=0$. Asymptotically, then, the number of solute particles inside $\mathbf{S}_1$ decays as

$$N(t) \sim \mathrm{e}^{-t/\tau}\,, \tag{16}$$

where $\tau = 1/(Dk_0^2)$ and k_0 is the root of

$$k_0R - \tan(k_0R) + [k_0R\tan(k_0R)+1]\tan(k_0a) = 0\,. \tag{17}$$

The scaled form of the inverse characteristic time for effusion obtained from the solution of Eq. (17) is plotted in Fig. 1. In the limit $a \to 0$ the characteristic time diverges as

$$\frac{D\tau}{R^2} \approx \frac{1}{3}\,\frac{R}{a}\,. \tag{18}$$

3. Conclusion

We have presented an analytical solution to an effusion problem in which particles are allowed to escape through a spherical cavity located at the center of a vesicle.

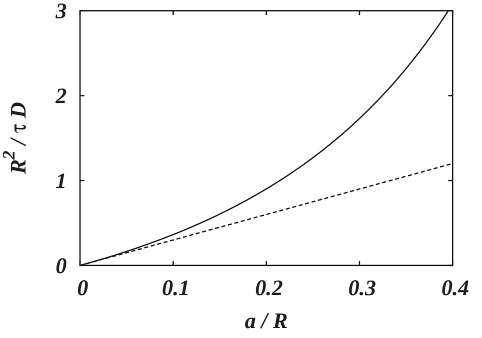

Fig. 1. The scaled form of the inverse characteristic time for effusion as a function of a/R. The dashed line is the asymptotic form given by Eq. (18).

In the limit that the radius of the cavity goes to zero, the effusion time diverges. Surprisingly, the divergence is proportional to $1/a$ instead of $1/a^2$—the surface area of the cavity—as one might have expected naively from a kinetic argument. At the moment, we do not have any simple explanation for this counterintuitive finding. We hope that the results presented in this contribution will help to shed more light on the problem of effusion of solute through an open pore of a real liposomal vesicle. Work in this direction is now in progress [6].

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