$$\hat{Q}_{\mathrm{m}}(s) = \frac{k_{\mathrm{m}} t_{\mathrm{ed}}}{\left(\sqrt{(s+k_{\mathrm{m}})t_{\mathrm{ed}}} - \sqrt{s t_{\mathrm{em}}}\right)} \left(\frac{\cosh\sqrt{(s+k_{\mathrm{m}})t_{\mathrm{ed}}}}{\cosh\sqrt{s t_{\mathrm{em}}}} - 1\right) \hat{Q}_{\mathrm{d}}(s) \tag{2.56}$$

where k_{m} is the rate of metabolism in the viable epidermis, $t_{\mathrm{ed}} = h_{\mathrm{e}}^2/D_{\mathrm{ed}}$, $t_{\mathrm{ed}} = h_{\mathrm{s}}^2/D_{\mathrm{sd}}$, $t_{\mathrm{em}} = h_{\mathrm{e}}^2/D_{\mathrm{em}}$, and first subscripts (s and e) denote the SC and the viable epidermis and the second subscripts (d and m) denote the drug and its metabolite, respectively. We note that the boundary conditions used in this work excluded the metabolite from diffusing back into the SC and the donor. This simplifies the solution for the metabolite, but could in some cases slightly overestimate its amount penetrating into the receptor. Two-layer diffusion of the viable epidermis and SC has been described more recently in {Todo, 2013 #1092}. The two-layer model can be described by Fick's second law of diffusion, where there is no impact from metabolism of the drug. Metabolism can occur in the SC layer, the viable epidermis and dermis [121, 122]. The model also compares results to experimental data that was taken in rat skin and within a silicone membrane.

2.1.9 DESORPTION

Although penetration (absorption) experiments are most common in studying percutaneous kinetics, desorption experiments have been used to study SC solute transport [28, 29]. In these desorption experiments, the membrane is initially saturated with the solute so that it is at equilibrium with the donor phase with concentration C_{d}. The membrane is then immersed into the receptor phase with no solute present at time $t = 0$. Assuming sink conditions in the receptor, the initial and boundary conditions for this case are:

$$C_{\mathrm{m}}(x, 0) = K_{\mathrm{m}} C_{\mathrm{d}} \tag{2.57}$$

$$C_{\mathrm{m}}\left(0, t\right) = 0 \tag{2.58}$$

$$C_{\mathrm{m}}\left(h_{\mathrm{m}}, t\right) = 0 \tag{2.59}$$

Solving Equation (2.5) with initial and boundary conditions [Equations (2.57 to 2.59)] in the Laplace domain yields for the amount of solute desorbed into the receptor phase:

$$\hat{Q}(s) = \frac{1}{s} \frac{A K_{\mathrm{m}} C_{\mathrm{d}} h_{\mathrm{m}}}{\sqrt{s t_{\mathrm{d}}}} 2 \tan\left(\frac{\sqrt{s t_{\mathrm{d}}}}{2}\right) \tag{2.60}$$

Equation (2.60) could be inverted to the time domain to yield an infinite series solution:

$$Q(t) = M_{\infty} \left\{1 - \frac{8}{\pi^2} \sum_{n=0}^{\infty} \frac{\exp\left[-(t/t_{\mathrm{d}})\pi^2 (2\pi+1)^2\right]}{(2n+1)^2}\right\} \tag{2.61}$$

where M_{∞} (= $C_{\mathrm{d}} K_{\mathrm{m}} A h_{\mathrm{m}}$) is the total amount of solute absorbed by the membrane. Equation (2.61) was used by Roberts et al. [29] to fit experimental desorption profiles for some solutes to yield t_{d} and K_{m}. These parameters could then be used to calculate the permeability coefficient:

$$k_{\mathrm{p}} = \frac{K_{\mathrm{m}} h_{\mathrm{m}}}{t_{\mathrm{d}}} \tag{2.62}$$

The desorption of hydrophilic drugs in the SC has been recently discussed in Miller et al. [1],where two phases of desorption were described. The fast phase happened within a matter of minutes while the slow-phase took a matter of hours. The fast phase was found to be negligible for lipophilic solutes while slow phase desorption was found to be dependent on molecular size, with desorption being slower for solutes that have a larger molecular weight [1].