results give an effective diffusion coefficient that can be used for finite element analysis [13]. The idea of multiscale modelling is one that has great potential in the future, as molecular simulations may be able to predict pharmacokinetic variables that are hard to come by in in vivo simulations.

2.1.11 Slow Binding in SC

Slow binding in the SC that may occur when molecules diffuse into the corneocytes. Once inside the corneocytes, the molecules may bind and unbind to the keratin fibers that are present before exiting through an arbitrary location on the boundary of the corneocyte. [16]However, the process of slow binding in the corneocytes is highly variable from molecule to molecule and difficult to determine experimentally. By approximating the transport in the SC by not considering the corneocyte diffusion, the following expressions for the unbound and bound concentration can be determined.

$$\frac{\partial C_u}{\partial t} = D\frac{\partial^2 C_u}{\partial x^2} - k_{on}C_u + k_{off}C_b$$

$$\frac{\partial C_b}{\partial t} = k_{on}C_u - k_{off}C_b$$

where C_u is the concentration unbound, C_b is the concentration bound to keratin fibers, k_{on} is the binding rate and k_{off} is the unbinding rate.

By assuming that the donor has a much larger volume than the SC, it could be estimated that the amount of solute at the top of the membrane will be close to the initial amount. Then the unbound concentration at the upper boundary of the SC could be approximated to be:

$$C_u(0,t) = K_{eff} f_u C_o$$

where f_u is the fraction of unbound solute and can be determined by the expression

$$f_u = \left(1 + \frac{k_{on}}{k_{off}}\right)^{-1}$$

Meanwhile at the bottom of the SC, [16] assumed a sink condition so:

$$C_u(h,t) = 0$$

Solving the system in the Laplace domain gives the following expression for the unbound concentration.

$$\hat{C}_u(x,s) = \frac{K_{eff} f_u C_0}{s} \times \left(cosh\left(\sqrt{\mathrm{g(s)t_d}}\,\frac{x}{h}\right) - \frac{sinh\left(\sqrt{g(s)t_d}\,\frac{x}{h}\right)}{tanh\left(\sqrt{g(s)t_d}\right)} \right)$$

When the results of this model were compared to experimental data and water absorption in the SC, it could be seen that the amount of solute desorbed in the skin affected concentration more than slow binding [16, 17]. Another analysis of slow binding was performed in [18] but is instead solved for two layers and not just the one that was used in the previous model.

2.1.12 SC Heterogeneity

A homogeneous membrane model is assumed for the majority of the mathematical analysis of solute transport in SC in this chapter and in most of the literature. In reality the SC consists of at