A more general theoretical approach for dissolution modeling called the *Film-Model Theory* was postulated by Nernst (1904) and expanded upon by Brunner (1904) in an effort to deconvolute the components of the dissolution constant, k. Both Nernst and Brunner made the following assumptions:

1. The mass flux, that is, intrinsic dissolution rate, is governed by Fick's first law of diffusion:

$$J = \frac{\mathrm{d}m}{\mathrm{d}t}\left(\frac{1}{S}\right) = -D\left(\frac{\mathrm{d}c}{\mathrm{d}x}\right) \tag{17.12}$$

   where $\mathrm{d}c/\mathrm{d}x$ is the solute concentration gradient and D is the diffusivity (diffusion coefficient), and
2. The concentration gradient within the diffusion layer is constant, thus,

$$\frac{\mathrm{d}c}{\mathrm{d}x} = \frac{\left(c_\mathrm{t} - c_\mathrm{s}\right)}{h} \tag{17.13}$$

   where h is the thickness of the stagnant diffusion layer.

Substitution of Equation 17.13 into Equation 17.12 gives

$$J = \left(\frac{\mathrm{d}m}{\mathrm{d}t}\right)\left(\frac{1}{S}\right) = \frac{D\left(c_\mathrm{s} - c_\mathrm{t}\right)}{h} \tag{17.14}$$

This led to the following equation:

$$\frac{\mathrm{d}c}{\mathrm{d}t} = k_2\left(\frac{DS}{Vh}\right)\left(c_\mathrm{s} - c_\mathrm{t}\right) \tag{17.15}$$

where k_2 is the intrinsic dissolution rate constant.

Sink Conditions

Sink conditions refer to a special case where there is essentially no buildup of the solute, which is assumed to be the case for the absorption of a drug from the gastrointestinal tract. Two ramifications for this special case are that the concentration gradient ($c_\mathrm{s} - c_\mathrm{t}$) described in Equation 17.9 is not rate-limiting under any conditions and, if the surface area of the solute is kept constant, the rate of dissolution will follow zero-order kinetics. *In vivo* sink conditions can be approximated *in vitro* by ensuring that the concentration of the solute does not exceed 5%–10% of its solubility. In practice, this is accomplished by either using a large volume of the dissolution medium or continuously replenishing the dissolution medium under carefully controlled conditions. Under sink conditions, $c_\mathrm{s} \gg c_\mathrm{t}$, and Equation 17.15 can be rewritten as the limiting case:

$$\left(\frac{\mathrm{d}c}{\mathrm{d}t}\right)_{\mathrm{t}\to 0} = k_2\left(\frac{DS}{Vh}\right)c_\mathrm{s} \tag{17.16}$$

Since D, c_s, and k_2 are constants for a given solute, they can be combined into k_3, and Equation 17.16 can be further simplified into

$$\frac{\mathrm{d}c}{\mathrm{d}t} = k_3\left(\frac{S}{Vh}\right) \tag{17.17}$$