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Note

Elution and washing in fixed bed affinity chromatography

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The recent paper[1] and detailed review article[2] by Chase highlighted the inadequate theoretical understanding of the sequential stages of adsorption, washing and elution, involved in fixed bed affinity chromatography[3]. The equations presented by Chase[1,2] for the adsorption stage were based on earlier work by Thomas[4] and by Hiester and Vermeulen[5], and applied to the simple reaction kinetic model:

$$\underset{\text{adsorbate}}{\mathrm{A}} \quad + \quad \underset{\begin{pmatrix}\text{biospecific binding}\\ \text{site on adsorbent}\end{pmatrix}}{\mathrm{B}} \quad \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \quad \underset{\begin{pmatrix}\text{non-covalent}\\ \text{complex}\end{pmatrix}}{\mathrm{A \cdot B}} \tag{1}$$

Subject to certain constraints it is in fact possible to derive analytical and semi-analytical solutions for the elution and washing stages. These are presented here.

ADSORPTION

Following the work of Thomas[4], the relevant equations for adsorption (using the symbols described in the notation section) are:

$$C = \frac{I_0(2\sqrt{rst}) + \varphi(t,rs)}{I_0(2\sqrt{rst}) + \varphi(t,rs) + \varphi(s,rt)} \tag{2}$$

$$Q = \frac{\varphi(t,rs)}{I_0(2\sqrt{rst}) + \varphi(t,rs) + \varphi(s,rt)} \tag{3}$$

ELUTION

For the general case where elution takes place at a different volumetric flow rate and under different values of the reaction rate constants, from the adsorption stage, the problem is not amenable to analytical solution. If, however, elution takes place under conditions such that: $\dot{V}' = \dot{V}$, $k'_1 = k_1$, and $k'_2 = k_2$, then an analytical

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solution is possible, and has been derived by Hiester and Vermeulen[6]. However, the equations they presented contain some, presumably typographical, errors. The relevant equations in their correct form are:

$$C' = \frac{\exp(-t_{ad})\,[\varphi(t_{ad}+t',rs)+2I_0\sqrt{rs(t_{ad}+t')}] - [\varphi(t',rs)+2I_0\sqrt{rst'}]}{\exp(-t_{ad})\,\{\varphi(t_{ad}+t',rs)+2I_0\sqrt{rs(t_{ad}+t')}+\varphi[s,r(t_{ad}+t')]\}+[\varphi(rt',s)-\varphi(t',rs)]} \quad (4)$$

$$Q' = \frac{\exp(-t_{ad})\,\varphi(t_{ad}+t',rs) - \varphi(t',rs)}{\exp(-t_{ad})\,\{\varphi(t_{ad}+t',rs)+2I_0\sqrt{rs(t_{ad}+t')}+\varphi[s,r(t_{ad}+t')]\}+[\varphi(rt',s)-\varphi(t',rs)]} \quad (5)$$

Furthermore, if adsorption is allowed to take place until equilibrium is attained in the bed, these equations reduce to the solution originally proposed by Thomas[7,8]:

$$C' = \frac{\varphi(rs,t')}{\varphi(rs,t') + I_0(2\sqrt{rst'}) + \varphi(rt',s)} \quad (6)$$

$$Q' = \frac{I_0(2\sqrt{rst'}) + \varphi(rs,t')}{\varphi(rs,t') + I_0(2\sqrt{rst'}) + \varphi(rt',s)} \quad (7)$$

If $r \to 1$, these relations in turn reduce to:

$$C' = \exp[-(s + t')]\varphi(s,t') \quad (8)$$

$$Q' = 1 - \exp[-(s + t')]\varphi(t',s) \quad (9)$$

Although the general case cited above is intractable, a reasonable simplifying assumption is that during elution the rate of the adsorption reaction is negligible (*i.e.* $k'_1 \to 0$). It is then possible to show that:

$$C' = (k'_2 q_0/c_0 \dot{V}) \cdot \exp(-t') \int_0^x \mathrm{F}(x)\,\mathrm{d}x \quad (10)$$

$$Q' = \exp(-t') \cdot \mathrm{F}(x) \quad (11)$$

where

$$\mathrm{F}(x) = \frac{\varphi(t_{ad},x)}{I_0(2\sqrt{\lambda x t_{ad}}) + \varphi(t_{ad},\lambda x) + \varphi(\lambda x/r,rt_{ad})} \quad (12)$$

It is clear that the integral of F(x) requires a numerical solution method, but this is a considerably less onerous task than numerical solution of the partial differential equations of the general case.

WASHING

The equations applicable to the washing stage depend on the operational conditions assumed to apply. If flow rate and reaction kinetics are as for adsorption, then eqns. 4 and 5, 6 and 7, or 8 and 9 are applicable, and there is no distinction between washing and subsequent elution. However, if no leakage of the adsorbed species occurs during washing (*i.e.* $k_2'' \rightarrow 0$), then:

$$C'' = 0, \text{ for } t'' \geqslant 0 \tag{13}$$

and

$$Q'' = Q(t = t_{\text{ad}}) \tag{14}$$

DISCUSSION

The above equations may prove useful in some limited cases. Unfortunately, a fully general analytical solution of the elution stage is not possible for the kinetics adopted here. An examination of the even more simple "linear kinetics" case of Thomas[7,8] shows that this too defies general analytical solution. The principal reason for this in both instances is that the initial condition applicable to the elution or washing stage, with respect to the variable Q' (or Q''), is always a complicated one.

NOTATION

a	ultimate capacity of the bed for adsorbate (kg/kg).
c	concentration of adsorbate in liquid phase (kg/m^3).
c_0	concentration of adsorbate in feed solution to adsorption stage of process (kg/m^3).
C	dimensionless adsorbate concentration in liquid phase [= c/c_0].
k_1	rate constant for binding reaction between adsorbent and adsorbate (m^3/kg sec).
k_2	rate constant for breakdown of adsorbent–adsorbate complex (1/sec).
K_{de}	dissociation constant for adsorbent–adsorbate complex [= k_2/k_1] (kg/m^3).
q	amount of adsorbate bound to adsorbent, per unit mass of adsorbent (kg/kg).
q_0	amount of adsorbate bound to adsorbent, per unit mass of adsorbent, at equilibrium (kg/kg).
Q	dimensionless amount of adsorbate bound to adsorbent [= q/q_0].
r	dimensionless parameter [= $1/(1 + (c_0/K_{\text{de}}))$].
s	dimensionless parameter [= $k_1ax/\dot{V}$].
t	dimensionless parameter [= k_2y/r].
t_{ad}	specific value of t at end of adsorption stage [= $k_2\theta_{\text{ad}}/r$].

$\dot{V}$ volumetric flow-rate of liquid stream (m^3/sec).
x mass of adsorbent in bed from inlet to point under consideration (kg).
y time elapsed after inert components have first arrived at bed outlet [$= \theta - (\varepsilon x/\dot{V})$] (sec).

Greek letters
ε voidage of bed of adsorbent (m^3/kg).
θ time (sec).
θ_{ad} duration of adsorption stage (sec).
λ parameter [$= rk_1 a/\dot{V}$] (1/kg).

Superscripts
none variables refer to adsorption stage.
$'$ variables refer to elution stage.
$''$ variables refer to washing stage.

Functions
$I_0(2\sqrt{z})$ modified Bessel function of zero order $\left\{= \sum_{m=0}^{\infty} [z^m/(m!)^2]\right\}$.

$\varphi(u,v)$ Thomas's[4] function [$= \exp(u) \int_0^u \exp(\xi) \cdot I_0(2\sqrt{v\xi})\, d\xi$].

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