

PRESSURE DROP IN CHROMATOGRAPHY COLUMNS

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1 Introduction

Biogen employs biochemical separation in chromatography columns as a processing step in the production of proteins. The output from a bioreactor is fed into a packed, vertical column, and the filtrate containing the desired product drawn from the bottom. The packing consists of resin-coated, agarose-based, relatively soft spherical particles, 50 – 150 microns in diameter. Laboratory experiments are typically performed in columns 20 cm in height and 5 cm in diameter, with a flow rate of about 200 cm/hr and pressure drop of the order of 20 psig. The objective is to scale-up to production level, where the columns are 60 – 100 cm in diameter, and estimate what pressure drops will be needed to sustain the same flow rate. The crucial factor inhibiting the flow appears to be the deformation of the packing material and the resulting compaction of the bed. The prohibitive cost of the resin-coated particles makes full-scale experiments impractical, and modelling attractive.

2 Modeling

We began with the working hypothesis that most of the bed would sag, thereby offering increased resistance to the flow, except for a thin layer adjacent to the wall of the column where wall friction would hold the particles up. However, the realization that the critical angle of friction for particle-to-particle contact is significantly larger (15°) than that for wall-to-particle contact (7°), followed by a simple kitchen experiment with salt particles in a plastic tube, convinced us that the bed would prefer to slide down the tube as a slug. This, in turn, suggested a model in which variations across the horizontal cross section of the bed could be neglected. Before any simplifications were made, however, it was deemed prudent to begin with the equations of two-phase flow, appropriate for a liquid flowing through a bed of solid particles:

$$(\alpha_s \rho_s)_t + \nabla \cdot (\alpha_s \rho_s \mathbf{v}_s) = 0, \quad (1)$$

$$(\alpha_l \rho_l)_t + \nabla \cdot (\alpha_l \rho_l \mathbf{v}_l) = 0, \quad (2)$$

$$\begin{aligned} (\alpha_s \rho_s \mathbf{v}_s)_t + \nabla \cdot (\alpha_s \rho_s \mathbf{v}_s \mathbf{v}_s) = & -\alpha_s \nabla p_s + \nabla \cdot (\alpha_s (\boldsymbol{\tau}_s + \boldsymbol{\sigma}_s)) \\ & + (p_{s_i} - p_s) \nabla \alpha_s + \mathcal{M}_s + \alpha_s \rho_s g \hat{\mathbf{e}}_x, \end{aligned} \quad (3)$$

$$\begin{aligned} (\alpha_l \rho_l \mathbf{v}_l)_t + \nabla \cdot (\alpha_l \rho_l \mathbf{v}_l \mathbf{v}_l) = & -\alpha_l \nabla p_l + \nabla \cdot (\alpha_l (\boldsymbol{\tau}_l + \boldsymbol{\sigma}_l)) \\ & + (p_{li} - p_l) \nabla \alpha_l + \mathcal{M}_l + \alpha_l \rho_l g \hat{e}_x, \end{aligned} \quad (4)$$

where the suffixes s and l denote the solid and the liquid phases, respectively; α_a denotes the volume fraction, ρ_a the density, $\mathbf{v}_a$ the velocity, $\boldsymbol{\sigma}_a$ the Reynolds or turbulent stress tensor, $\mathcal{M}_a$ the rate of interfacial momentum exchange, for species a , and g the acceleration due to gravity, directed along the unit vector $\hat{e}_x$. Further, the stress tensor $\mathbf{T}$ for each phase is decomposed as

$$\mathbf{T}_a = -p_a \mathbf{I} + \boldsymbol{\tau}_a, \quad (5)$$

where p is the spherical portion (pressure) and $\boldsymbol{\tau}$ the 'extra' part of $\mathbf{T}$. The interfacial value of p_a is denoted by p_{ai} . The volume fractions satisfy the saturation constraint

$$\alpha_s + \alpha_g = 1.$$

The following simplifications apply to the situation at hand:

- (a) The bed is at rest, i.e., $\mathbf{v}_s = 0$, and the Reynolds stress, $\boldsymbol{\sigma}_s = 0$.
- (b) The flow is steady.
- (c) The two phases are incompressible, so that $\rho_a = \text{constant}$.
- (d) Slow liquid flow causes the inertial terms in the liquid momentum equation to be small, and implies rapid pressure equilibration within each phase, allowing one to set $p_{ai} - p_a = 0$.
- (e) We take the packing material to behave as a linear elastic solid, albeit squishy, and hence characterized by a small Young's modulus E_Y . Recall that in terms of the Lamé constants, λ_s and μ_s , E_Y is given by

$$E_Y = \frac{\mu_s(3\lambda_s + 2\mu_s)}{\lambda_s + \mu_s}.$$

Smallness of E_Y leads to $\mu_s \ll \lambda_s$. That, in turn, implies that in the constitutive expression for the stress tensor,

$$\mathbf{T}_s \equiv -p_s \mathbf{I} + \boldsymbol{\tau}_s = \lambda_s \text{tr}(\mathbf{E}_s) \mathbf{I} + 2\mu_s \mathbf{E}_s,$$

where $\mathbf{E}_s$ is the deformation tensor, the diagonal components dominate, and to a first approximation, equal p_s . By the same token, the off-diagonal or shear components of $\boldsymbol{\tau}_s$ are small compared to p_s .

- (f) We ignore the contributions due to the viscous and Reynolds stress tensors, τ_l and σ_l respectively, in the liquid-phase momentum equation, arguing that during the tortuous motion of the liquid phase through the interstitial space, the dominant mechanism of momentum transfer from the liquid is the interphase force density, $\mathcal{M}_l$, rather than the molecular or eddy viscosity of the (water-like) liquid. Further, the primary contribution to $\mathcal{M}_l$ is taken to be in the form of Stokes drag. Thus, contributions such as virtual mass effects, significant in high-frequency transients, are neglected.
- (g) There are no azimuthal variations, and the flow is entirely axial, i.e., $\mathbf{v} = v\hat{e}_x$.
- (h) Buoyancy is removed by setting

$$p_a = \rho_a g x + P_a. \quad (6)$$

Under these simplifications, the equations reduce to the simple set considered in the next section. For details, see the rather considerable literature on filtration ([1], [2], [3], [4], [5] and [6]).

3 Governing Equations

The model used in analyzing the problem (see [7]) consists of an axial momentum equation for the solid phase,

$$\frac{d\bar{p}}{d\bar{x}} + \frac{d\bar{\sigma}}{d\bar{x}} + \frac{4B}{D}\bar{\sigma} = 0, \quad (7)$$

coupled with Darcy law as the momentum equation for the liquid,

$$\frac{d\bar{p}}{d\bar{x}} = -\frac{\mu}{\bar{K}}\bar{q}. \quad (8)$$

Here, $\bar{p}$ is the liquid pressure, $\bar{\sigma}$ the normal stress in the solid phase along the flow direction, $\bar{K}$ the permeability, μ the viscosity and B a stress factor (depending upon the angle of friction at the wall; see [7]), measuring the ratio between the shear and normal stresses in the solid phase at the wall of the column. D denotes the diameter of the column, and L its length, along which distance is measured by the axial coordinate $\bar{x}$. The liquid flux through the column is measured by $\bar{q}$. We use an overbar to denote dimensional variables, while symbols for parameters are left without overbars.

The permeability itself depends upon the state of stress in the solid, and is prescribed as

$$\frac{\bar{K}_0}{\bar{K}} = f(\bar{\sigma}/\bar{\sigma}_0), \quad (9)$$

where $\bar{\sigma}_0$ and $\bar{K}_0$ are constants. The dimensionless function f is monotonically increasing with $f(0) = 1$. The form for f is determined through experimental fitting; an example existing in the literature is $f(x) = e^x$ [7].

We render the problem dimensionless by employing L as the reference length, $\bar{\sigma}_0$ as the reference stress, $\bar{K}_0$ as the reference permeability and $\bar{q}_0$ as the reference flux, where

$$\bar{q}_0 = \frac{\bar{K}_0 \bar{\sigma}_0}{\mu L}. \quad (10)$$

Nondimensional variables retain their symbols, but without the overbars. Then the system assumes the dimensionless form

$$\frac{dp}{dx} + \frac{d\sigma}{dx} + R\sigma = 0, \quad (11)$$

$$\frac{dp}{dx} = -qf(\sigma), \quad (12)$$

with

$$\frac{1}{K(\sigma)} = f(\sigma). \quad (13)$$

The dimensionless quantity R appearing above is a modified aspect ratio, given by

$$R = \frac{4BL}{D}. \quad (14)$$

Equations (11) and (12) may be combined to yield

$$\frac{d\sigma}{dx} = R \left(\frac{q}{R} f(\sigma) - \sigma \right), \quad (15)$$

an equation that describes, for given q , the evolution of solid stress along the length of the column. The appropriate initial condition for this equation is¹

$$\sigma(0) = 0. \quad (16)$$

We may also combine (12) and (15) to obtain

$$\frac{dp}{d\sigma} = -\frac{q}{R} \frac{f(\sigma)}{\left(\frac{q}{R} f(\sigma) - \sigma \right)}, \quad (17)$$

which, in conjunction with the initial condition

$$p(0) = 0, \quad (18)$$

can be solved for the pressure drop down the column as a function of σ .

¹If a heavy plate is placed at the top of the bed, then the initial condition may be $\sigma(0) = \sigma_0 > 0$.

4 Solution

For a given flux q , and a given value of the modified aspect ratio R , equations (15) and (16) yield the stress profile down the length of the column as

$$Rx = \int_0^\sigma \frac{d\sigma}{\frac{q}{R}f(s) - s}. \quad (19)$$

Then, the fluid pressure can be computed by integrating (17) and (18) to get

$$p(x) = -\frac{q}{R} \int_0^{\sigma(x)} \frac{f(s)}{\frac{q}{R}f(s) - s} ds. \quad (20)$$

The full pressure drop across the column corresponds, of course, to $p(1)$.

For the purposes of the remaining discussion, we make the choice

$$f(s) = e^s. \quad (21)$$

We note immediately the existence of critical constants λ_c and σ_c , defined by

$$\lambda_c f(\sigma_c) = \sigma_c, \quad \lambda_c f'(\sigma_c) = 1,$$

i.e.,

$$f(\sigma_c) - \sigma_c f'(\sigma_c) = 0 \quad \text{and} \quad \lambda_c = \frac{1}{f'(\sigma_c)}. \quad (22)$$

Note that λ_c is determined entirely by the permeability function f , and for $f(x) = e^x$, the critical constants are

$$\sigma_c = 1 \quad \text{and} \quad \lambda_c = \frac{1}{e}. \quad (23)$$

For

$$\frac{q}{R} > \lambda_c, \quad (24)$$

the integral in (19) is bounded when its upper limit is set to ∞ . In other words, the stress σ becomes unbounded at a finite value of x , say x_∞ ; the larger the value of q , the smaller the value of x_∞ . Setting $x_\infty = 1$ gives the limiting value of q , say q_{lim} , corresponding to the value of flux at which the stress just becomes unbounded at the downstream end of the column. Implicitly, q_{lim} is defined as a function of the modified aspect ratio R by the integral expression

$$R = \int_0^\infty \frac{d\sigma}{\frac{q_{\text{lim}}}{R}f(s) - s}. \quad (25)$$

Figure 1 shows the graph of $q_{\text{lim}}(R)$. We reiterate that this is the maximum flux that a column of given dimensions can sustain; as expected, the fatter the column, the smaller is the limiting flux through it.

When $q < q_{\text{lim}}$, (19) shows that the end of the column will experience only a finite value of stress σ . In that case, as already indicated, pressure drop across the column may be computed from (20). Specifically, we set $x = 1$ in (19) and compute the corresponding value of $\sigma(1)$ for the given q . Then, on setting $\sigma(1)$ as the upper limit in (20), we compute the pressure drop $p(1)$. Figure 2 shows q as a function of pressure drop for various values of the modified aspect ratio R . This completes the solution.

5 Conclusions

The figures tell the complete story. Figure 1 displays the maximum dimensionless flux rate q_{lim} , related to the dimensional value $\bar{q}_{\text{lim}}$ by

$$q_{\text{lim}} = \frac{\bar{q}_{\text{lim}}}{\bar{q}_0} = \frac{\bar{q}_{\text{lim}} \mu L}{\bar{K}_0 \bar{\sigma}_0},$$

as a function of the modified aspect ratio $R = 4BL/D$. The actual flux must be smaller than this limiting value.

Figure 2 displays how, for a given flux, the needed pressure drop increases as D is increased to scale up from experiment to production level. Note the crucial role played by the wall stress-factor B ; larger the B , the smaller the pressure drop for a given L/D .

The calculations shown here correspond to the choice e^x for the scaled permeability function. This function probably represents the greatest uncertainty, and needs to be measured accurately for the particle beds under use.

Workshop Contributors

This report was prepared by Ash Kapila (Rensselaer) and Alistair Fitt (Southampton) with the assistance of Brian Aufderheide and Deepak Nagrath (Rensselaer).

References

- [1] G.G. CHASE AND M. L. WILLIS, *Compressive cake filtration*, Chem. Engng. Sci., 47, (1992), pp. 1373–1381.
- [2] M.S. WILLIS, R.M. COLLINS AND W.G. BRIDGES, *Complete analysis of non-parabolic filtration behavior*, Chem. Eng. Res. Des., 61 (1983), pp. 96–109.

- [3] M.S. WILLIS AND I. TOSUN, *A rigorous cake filtration theory*, Chem. Engng. Sci., 35 (1980), pp. 2427-2438.
- [4] M.S. WILLIS, I. TOSUN AND R.M. COLLINS, *Filtration mechanisms*, Chem. Eng. Res. Des., 63 (1985), pp. 175-183.
- [5] K.H. PARKER, R.V. MEHTA AND C.G. CARO, *Steady flow in porous, elastically deformable materials*, Trans. ASME, 54 (1987), pp. 794-800.
- [6] M.S. WILLIS, *A multiphase theory of filtration*, in Progress in Filtration and separation, R.J. Wakeman, ed., Elsevier, New York (1983).
- [7] P.A. DAVIES AND B.J. BELLHOUSE, *Permeability of beds of agarose-based particles*, Chem. Engng. Sci., 44 (1989), pp. 452-455.

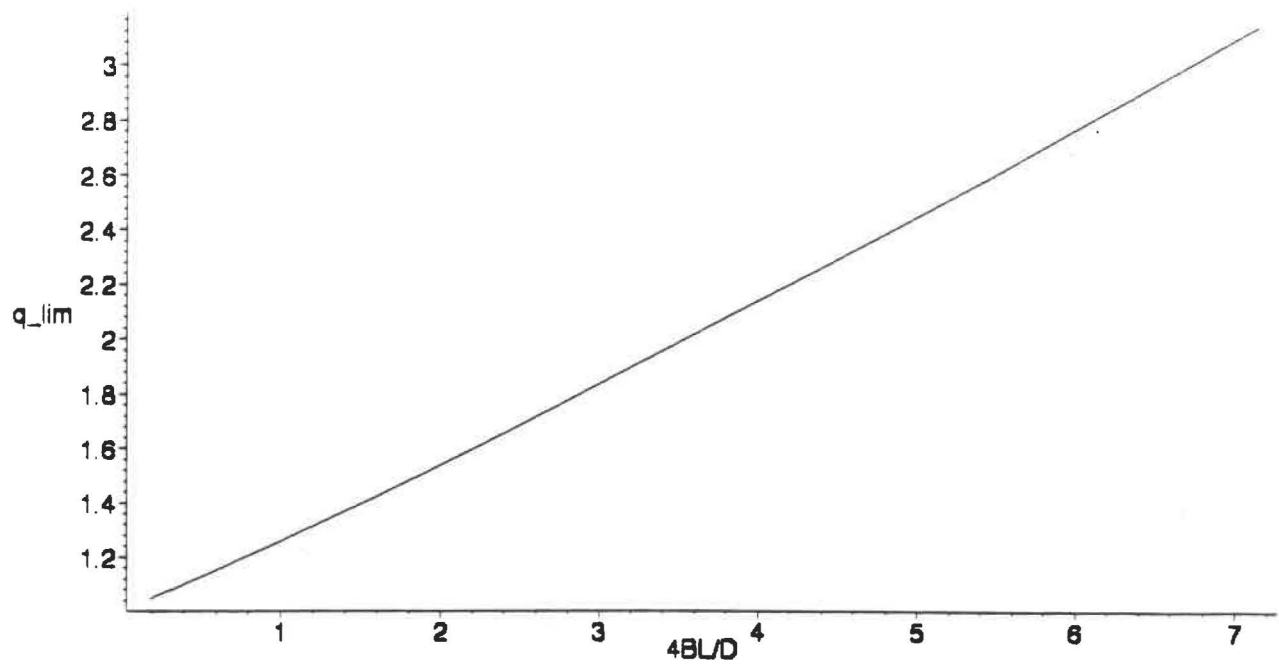


Figure 1. Limiting Flux q_{lim} versus modified aspect ratio $4BL/D$.

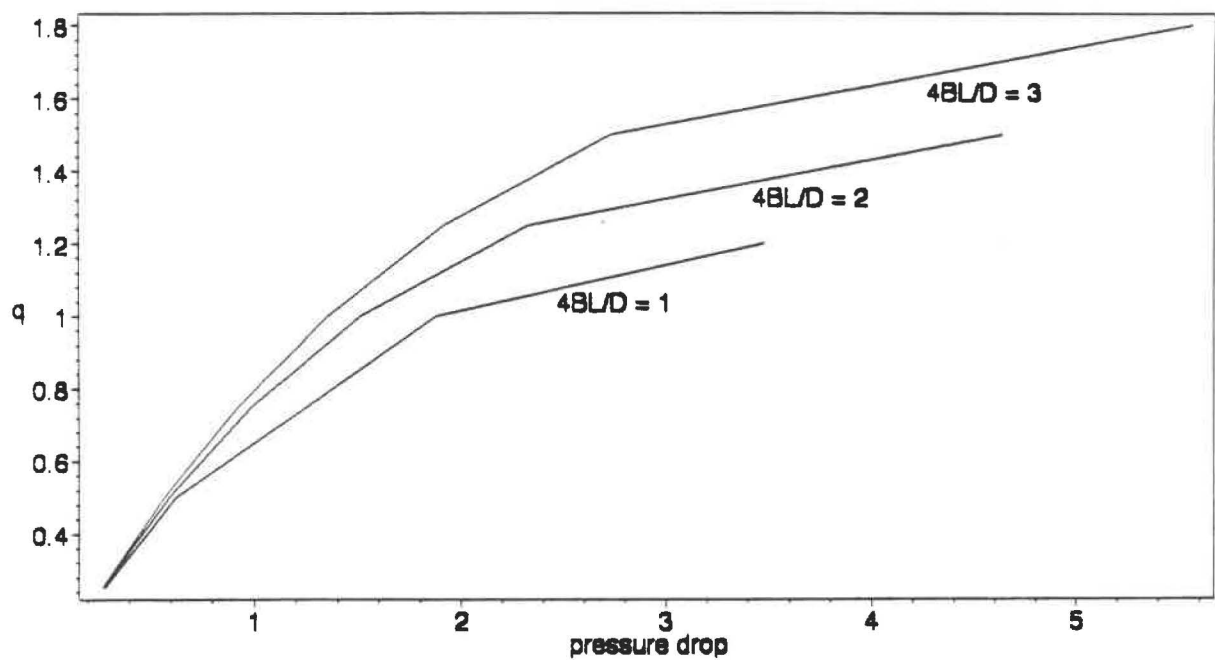


Figure 2. Discharge versus pressure drop for various values of $4BL/D$.