Supplementary Materials

Characterization of Drug-Polymer Adsorption Isotherms in Body-on-a-Chip Systems by Inverse Liquid-Solid Chromatography

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6 pages, 2 figures, and 1 tables

Numerical Algorithm

The experimental band profile was read into the program. Also loaded was a file containing the measured experimental parameters including the following:

- void time, t_0,
- flow rate, F, measured at the detector outlet with a graduated cylinder and stopwatch.
- Stationary phase mass, M_S,
- Column theoretical plates, N
- Column length, L
- Linear Calibration Curve Parameters

If the baseline was negative, the entire band profile was shifted in the positive direction by the amount of the negative deviation. Next, the detector calibration parameters were used to convert the band profile from units of detector response to concentration (as a function of retention time).

Next, the tail region of the band profile from the peak maxima to the peak baseline was identified and converted to specific retention volume corrected for the void time,

$$V_N = (t_R - t_0)\frac{F}{M_S}$$

Equation 18

Next, the isotherm was calculated according to the method of Elution at Characteristic Points [68].

Inherent in this method is the assumption that column efficiency is sufficiently high that the shape of the band profile is determined solely by the shape of the isotherm. Continuing from Equation 5 with the diffusion coefficient set to zero,

$$u\left(\frac{\partial[C]}{\partial z}\right) + \left(\frac{\partial[C]}{\partial t}\right) + \Phi\left(\frac{\partial[Q]}{\partial t}\right) = 0$$

Equation 19

Since [C] is a function both of z and t,

$$d[C] = \left(\frac{\partial[C]}{\partial z}\right)dz + \left(\frac{\partial[C]}{\partial t}\right)dt$$

Equation 20

At constant [C], Equation 20 may be rearranged to,

$$\left(\frac{\partial[C]}{\partial z}\right) = -\left(\frac{\partial[C]}{\partial t}\right)\left(\frac{\partial t}{\partial z}\right)$$

Equation 21

Combining Equation 19 and Equation 21 and rearranging,

$$\int_0^{t_R} dt = \int_0^L \frac{1}{u}\left\{1 + \Phi\frac{d[Q]}{d[C]}\right\}$$

Equation 22

After integrating,

$$t_R = \frac{L}{u}\left\{1 + \Phi\frac{d[Q]}{d[C]}\right\}$$

Equation 23

Since $L / u = t_0$ and $\Phi = M_S / (F \cdot t_0)$

$$[Q]([C]) = \int_0^{[C]} V_N d[C]$$

Equation 24

Another useful relationship may be derived from Equation 23. Consider the Langmuir equation,

$$[Q] = \frac{K_{eq}[S_0][C]}{1 + K_{eq}[C]}$$

Equation 25

Taking the first derivative with respect to concentration,

$$\frac{d[Q]}{d[C]} = \frac{K_{eq}[S_0]}{1 + 2K_{eq}[C] + K_{eq}^2[C]^2}$$

Equation 26

Now, in the limit as C goes to zero,

$$\lim_{[C]\to 0} \frac{\partial[C]}{\partial[C]} = K_{eq}[S_0]$$

Equation 27

Combining this result with Equation 23 and rearranging,

$$t_R = t_0\{1 + \Phi K_{eq}[S_0]\}$$

Equation 28

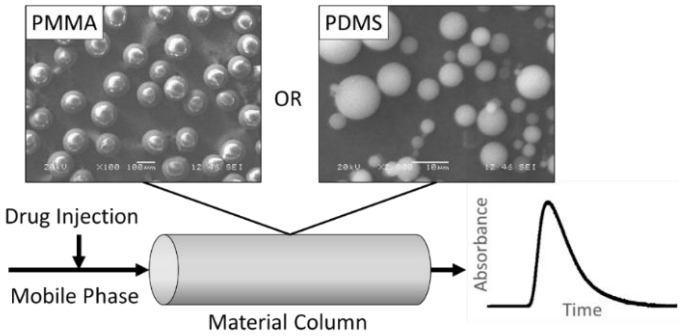
Following calculation of the approximate isotherm using the ECP method, the values K_{eq} and $[S_0]$ are estimated. The lowest concentration point in the band profile (at the end of the tail) corresponds to the highest energy point on the isotherm. The value of that point is used to estimate the $K_{eq}[S_0]$ parameter using Equation 28. The highest concentration point calculated from the ECP isotherm is taken as an estimate of the monolayer capacity, $[S_0]$. Then, using the earlier estimated value of $K_{eq}[S_0]$, the value of K_{eq} is calculated. These values of K_{eq} and $[S_0]$ are used as starting points for the optimization.

For the data reported in this paper, either a single Langmuir or Bi-Langmuir model was used. For the cases when the experimental results did not accurately fit a single Langmuir model, a Bi-Langmuir was then tried. The starting points for the bi-Langmuir parameters were set by simply dividing the single Langmuir $[S_0]$ term by two and setting both $[S_0]_1$ and $[S_0]_2$ to this value. $K_{eq,1}$ and $K_{eq,2}$ were both set to the same value.

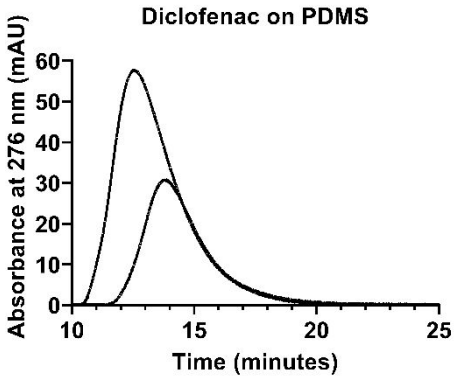
All calculations were done using Python and extensive use was made of the Scientific Python libraries.[69] The non-oscillatory Akima cubic spline[70] was used from the Scientific Python Interpolation Module for interpolation in several stages of the algorithm. Because preliminary investigations using just Nelder-Mead optimization[71] resulted in obviously local minima, the following two-stage optimization strategy was utilized:

First, optimization toward the minima was done using the Nelder-Mead algorithm from the Scientific Python optimization package. After each time the Nelder-Mead algorithm resolved, the optimizer would then iterate through a grid of nearby values in the problem domain within a specified range built around the Nelder-Mead solution (a total of 15^2 points for a single Langmuir optimization or 5^4 for a Bi-Langmuir). Each of these points were evaluated by the function and the lowest score was then used as the starting point for the next Nelder-Mead

optimization. If the optimization routine resolved to the same solution five times, that point was deemed as the solution. For each iteration, the evaluated function would load in the assumed Langmuir or Bi-Langmuir parameter values and experimental parameters for the column and analyte, then generate a simulated band profile using the Godunov algorithm. The simulated band profile was then compared against the experimental data by interpolating to a common time line and tabulating the sum of squares of the residuals between the two curves which was returned to the optimizer. In the event that negative Langmuir parameters were predicted, a sum of squares value of infinity was simply returned (no simulation was performed).



Supplemental Figure S1. Overview of the Inverse Liquid-Solid Chromatographic Process.



Supplemental Figure S2. Overlapping curves of diclofenac at $2x10^{-4}$ M and $1x10^{-4}$ M concentrations, demonstrating the virtual peaks covered by the Elution by Characteristic Points (ECP) method.

Supplemental Table S1. Nomenclature

Symbol	Units	Description
$\mathbf{A_g}$	mm^2	Column Cross Section of (mobile phase permeable portion)
[C]	$\mu mol \cdot mL^{-1}$	Concentration of the solute in the mobile phase
D	$cm^2 \cdot min^{-1}$	Apparent diffusion coefficient of the solute in the mobile phase
F	$mL \cdot min^{-1}$	Volumetric flow rate of mobile phase
H	cm	Column Height Equivalent of a Theoretical Plate (HETP)
L	cm	Column length
$\mathbf{m_g}$	$g \cdot cm^{-1}$	Mass of stationary phase per unit column length
$\mathbf{M_S}$	g	Mass of stationary phase
N	unitless	Column theoretical plate number
[Q]	$\mu mol \cdot g^{-1}$	Concentration of the adsorbed solute
$\mathbf{[S_0]_i}$	$\mu mol \cdot g^{-1}$	The ith adsorbent/solute monolayer saturation capacity
t	min	Time
$\mathbf{t_0}$	min	Unretained compound void time
$\mathbf{t_R}$	min	Solute retention time
u	$cm \cdot min^{-1}$	Mobile phase linear velocity in the z direction
$\mathbf{V_M}$	mL	Volume of mobile phase
$\mathbf{v_g}$	$mL \cdot cm^{-1}$	Volume of mobile phase per unit column length
$\mathbf{V_N}$	mL	Specific retention volume
z	cm	Linear position of solute, measured from the column inlet
Φ	$g \cdot mL^{-1}$	Phase ratio expressed as stationary phase mass per mobile phase volume