

## Computer simulations of displacement chromatography of systems with species-dependent saturation capacities

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### ABSTRACT

Displacement chromatography of systems with Langmuir adsorption isotherms and species-dependent saturation capacities were analyzed and simulated with a general rate equation model. Conditions for the development of displacement train were derived and the effects of saturation capacity, initial slope and amount of the displacer on the displacement development were illustrated.

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### INTRODUCTION

Displacement chromatography has become an increasingly important column technique in the recovery and purification of biochemicals in large scale, because it is capable of producing concentrated products with high throughput. Recently, much effort has been devoted to the analyses of the column dynamics of displacement chromatography under ideal conditions [1–3] and non-ideal conditions [4–7]. These analyses provide useful guidelines for the design, scale up and optimization of displacement chromatography.

All the above mentioned studies have been restricted to systems with simple equilibrium isotherms. Standard Langmuir isotherms are used for adsorption and constant separation factors for ion exchange. It is generally required that the isotherm of the displacer lies above the isotherms of all solutes over the whole concentration range (Fig. 1D). The displacer has a higher affinity to the sorbent than all solutes, and it also has a higher or same saturation concentration [8]. For this reason, displacer components with small molecular weight are often used at high concentrations to effect the displacement.

The effects of species-dependent column capacities on the separation efficiencies in isocratic elution processes have been studied [9]. In this paper, the effects of species-dependent capacities on displacement development were analyzed. Langmuir adsorption kinetics with species-dependent saturation capacities and a general rate equation model, which includes axial dispersion, film diffusion, particle diffusion, and non-linear adsorption kinetics, were used to simulate the column dynamics in detail. Effects of saturation capacity, affinity, and amount of the displacer on the

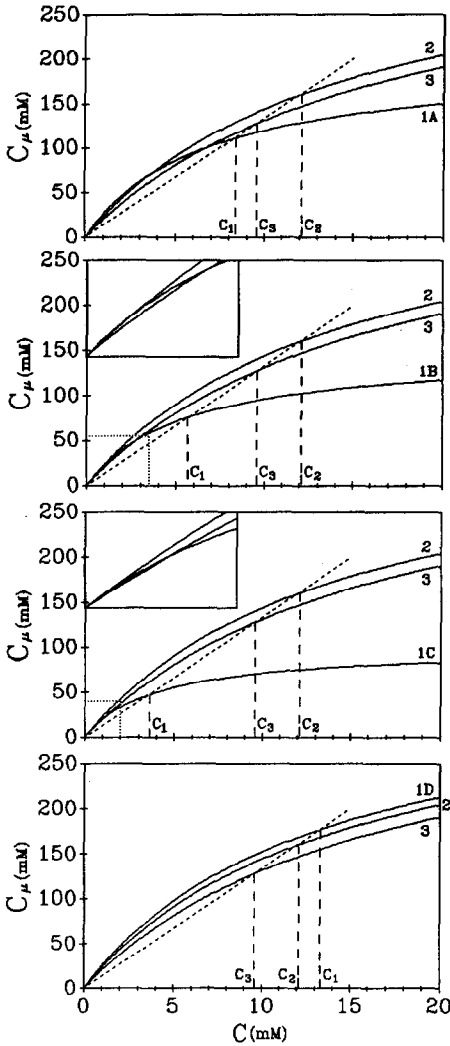


Fig. 1. Single component isotherms showing concentrations of fully developed displacement trains. All parameters are listed in Table I.

displacement train were illustrated with computer simulations. This study indicates that large molecules with low concentrations can also be used as displacers.

#### THEORETICAL ANALYSIS

##### *Rate equation model and adsorption kinetics*

A general rate equation model, which includes axial dispersion, film diffusion, particle diffusion, and adsorption kinetics, was used in the simulation of displacement chromatography. The details of the model description and solution procedure based

on the method of orthogonal collocation on finite elements were reported elsewhere [7], and the Langmuir adsorption kinetics with species-dependent saturation capacities were assumed in this study. The net rate of adsorption of solute  $i$  per unit solid volume of the stationary phase can be expressed as follows.

$$f(i) = k_a(i)C(i) \left( 1 - \sum_{j=1}^{NC} \frac{C_{\mu}(j)}{C_{\mu s}(j)} \right) - k_d(i) \left( \frac{C_{\mu}(i)}{C_{\mu s}(i)} \right) \quad (1)$$

When the adsorption and desorption rates are faster than the diffusion rate, the local equilibrium prevails. The expression describing this local equilibrium is

$$C_{\mu}(i) = \frac{C_{\mu s}(i)b(i)C(i)}{1 + \sum_{j=1}^{NC} b(j)C(j)} \quad (2)$$

where  $b(i) = k_a(i)/k_d(i)$ .

#### *Band concentrations and conditions of displacement development*

In fully developed displacement bands, all the solute bands have the same concentration velocity. The band concentrations can be determined from the single component isotherms and the displacer concentration, as illustrated in Fig. 1, where the isotherm parameters are listed in Table I. The band concentration of species  $i$  displaced by the displacer 1 is given by:

$$C(i)_{\text{BAND}} = \frac{C_{\mu s}(i)}{C_{\mu s}(1)} C(1) - \left( \frac{1}{b(i)} - \frac{C_{\mu s}(i)}{C_{\mu s}(1)b(1)} \right) \quad (3)$$

Eqn. 3 indicates that the band concentration of a solute increases with the displacer concentration and is independent of its feed concentration. The necessary conditions for displacement development can be also derived from the above equation. They are

$$b(1)C_{\mu s}(1) > b(i)C_{\mu s}(i) \quad (4)$$

TABLE I  
ISOTHERM PARAMETERS USED IN SIMULATION

Parameter	Value					
	1A	1B	1C	1D	2	3
$k_a$ (1/s)	15	18	25	7.714	7	6
$k_d$ (mM/s)	100	100	100	100	100	100
$b$ (1/mM)	0.15	0.18	0.25	0.07714	0.07	0.06
$C_{\mu s}$ (mM)	200	150	100	350	350	350
$bC_{\mu s}$	30	27	25	27	24.5	21

$$\frac{C(1)}{C_{\mu s}(1)} > \frac{C(i)_{\text{BAND}}}{C_{\mu s}(i)} + \left( \frac{1}{C_{\mu s}(i)b(i)} - \frac{1}{C_{\mu s}(1)b(1)} \right) \quad (5)$$

Eqn. 4 requires that the initial slope of the displacer must be higher than that of the solutes, while eqn. 5 gives the minimum displacer concentration to yield a band concentration of  $C(i)_{\text{BAND}}$  of the species  $i$ . This is equivalent to the classic condition that the chord slope of the displacer larger than the slope of the solute [2]. When  $C(i)_{\text{BAND}} = 0$ , eqn. 5 gives the minimum displacer concentration for the onset of any displacement development of the solute  $i$ , and when  $C(i)_{\text{BAND}} \geq C_r(i)$  a displacement factor higher than unity is achieved.

The third necessary condition for displacement development is a sufficient amount of displacer which maintains the displacer front in contact with the solutes. The minimum amount required can be determined from the slope and the chord slope of the displacer [3].

$$\Delta T_2 = \left( \frac{1 - \varepsilon_b}{\varepsilon_b} \right) (1 - \varepsilon_m) \left[ \left( \frac{C_\mu}{C} \right)_1 - \left( \frac{dC_\mu}{dC} \right)_1 \right] = \left( \frac{1 - \varepsilon_b}{\varepsilon_b} \right) (1 - \varepsilon_m) \left( \frac{b(1)C_{\mu s}(1)}{1 + b(1)C(1)} \right) \left( \frac{C(1)}{C_{\mu s}(1)} \right) \quad (6)$$

Finally, from eqn. 3, the band concentrations are calculated from the affinity constants and the saturation capacities of the displacer and the solutes.

Same band concentrations can be obtained with different displacers (1A and 1B) under the following equivalent displacer condition, which is derived from eqn. 3.

$$\left( \frac{b(1A)C_{\mu s}(1A)}{1 + b(1A)C(1A)} \right) = \left( \frac{b(1B)C_{\mu s}(1B)}{1 + b(1B)C(1B)} \right) \quad (7)$$

Eqn. 7 implies that, under ideal conditions, if the chord slopes of the displacer 1A and 1B are the same, identical displacement trains can be formed. Under those conditions, the minimum amount of the displacer required can also be compared. From eqns. 6 and 7, if the initial slope of the displacer 1A is larger [ $b(1A)C_{\mu s}(1A) > b(1B)C_{\mu s}(1B)$ ], the minimum amount of the displacer required will be larger [ $\Delta T_2(1A) > \Delta T_2(1B)$ ]. This will also leads to a longer tailing in the regeneration step.

TABLE II  
PHYSICAL PARAMETERS USED IN SIMULATION

Parameter	Value			Parameter	Value
	1A-1D	2	3		
$C_t$ (mM)	3.3	4	4	$u$ (cm <sup>2</sup> /s)	0.004
$D_p$ (cm/s)	$8 \cdot 10^{-7}$	$8.5 \cdot 10^{-7}$	$9 \cdot 10^{-7}$	$L$ (cm)	25
				$\varepsilon_b$	0.35
				$\Delta T$	2
				$R_p$ ( $\mu$ m)	20
				$\varepsilon_m$	0.3

## RESULTS AND DISCUSSION

In this section, detailed column dynamics of displacement chromatography were simulated to illustrate the effects of operational parameters. The physical parameters used in all the simulations are listed in Table II, unless otherwise stated.

The effects of displacer concentrations on the displacement development are similar to those in literature [5,6]. The effects of the affinity ( $b_1$ ), saturation capacity ( $C_{\mu s1}$ ), and initial slope ( $b_1 C_{\mu s1}$ ) were given in eqn. 3 and illustrated in Fig. 2a-c. For a given solute, its band concentration increases with decreasing  $C_{\mu s1}$  and  $b_1 C_{\mu s1}$  values. In Fig. 2a-c, both  $C_{\mu s1}$  and  $b_1 C_{\mu s1}$  were reduced and hence the displacement effect increases. In Fig. 2c, the solute 3 band is affected by the non-ideal effects (mass transfer resistances) where the band concentration is lower than that predicted by the ideal theory (eqn. 3).

The displacement effluent histories under the equivalent displacer conditions are shown in Fig. 3a-c. The initial slopes of the displacers in Fig. 3a and b are the same; hence the effluent histories are identical. In Fig. 3c, the initial slope of the displacer is

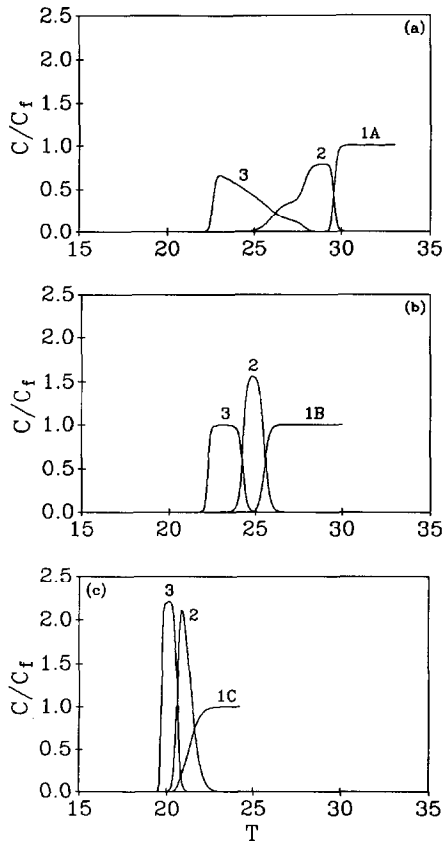


Fig. 2. Effect of displacer affinity on effluent histories. (a)  $C_{\mu s} = 200 \text{ mM}$ ;  $b_1 = 0.15 \text{ mM}^{-1}$ ; (b)  $C_{\mu s} = 150 \text{ mM}$ ,  $b_1 = 0.18 \text{ mM}^{-1}$ ; (c)  $C_{\mu s} = 100 \text{ mM}$ ,  $b_1 = 0.25 \text{ mM}^{-1}$ .

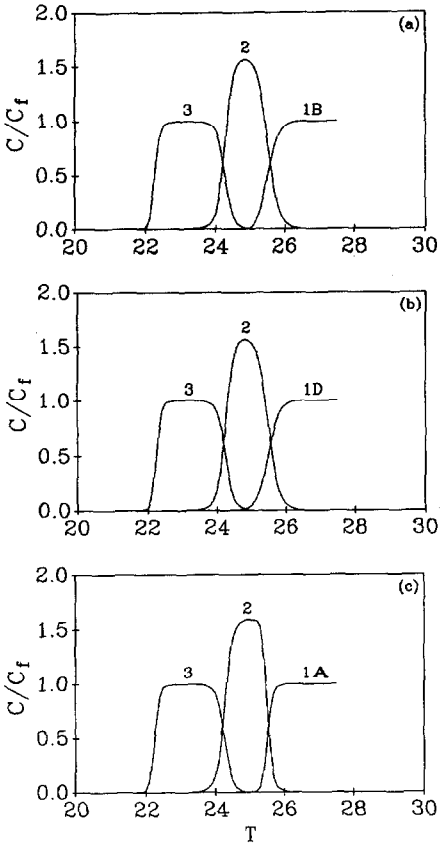


Fig. 3. Displacement under equivalent displacer conditions. (a)  $C_{\mu s} = 150 \text{ mM}$ ,  $b_1 = 0.18 \text{ mM}^{-1}$ ,  $C_1 = 3.3 \text{ mM}$ ; (b)  $C_{\mu s} = 350 \text{ mM}$ ,  $b_1 = 0.077 \text{ mM}^{-1}$ ,  $C_1 = 7.7 \text{ mM}$ ; (c)  $C_{\mu s} = 200 \text{ mM}$ ,  $b_1 = 0.15 \text{ mM}^{-1}$ ,  $C_1 = 5.141 \text{ mM}$ .

larger than those used in Fig. 3a and b. The breakthrough curve of the displacer in Fig. 3c is slightly sharper. The band of solute 2, which is in contact with the displacer, is also slightly sharper. On the other hand, the band of solute 3 is the same as those observed in Fig. 3a and b.

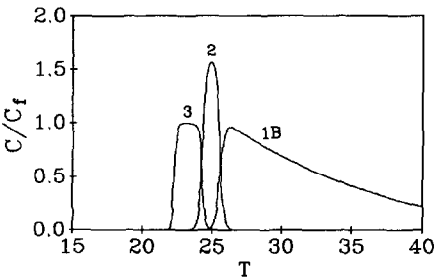


Fig. 4. Displacement under minimum amount of displacer.  $\Delta T_2 = 9$ .

Fig. 4 shows the displacement effluent histories when the minimum amount of the displacer (eqn. 6) is used. This minimum amount is needed to maintain the displacement bands as in Fig. 3a–c. A lesser amount of the displacer will cause the displacement bands to be degraded into elution peaks, while a larger amount only contributes to a longer regeneration time.

## CONCLUSIONS

Displacement chromatography of systems with species-dependent saturation concentrations were analyzed and computer simulations with a general rate equation model were used to illustrate the effects of displacer saturation capacity and initial slope on the displacement dynamics.

Displacement can be developed only when the initial slope of the displacer is larger than those the solutes (eqn. 4), the displacer concentration is high enough (eqn. 5), and the displacer amount is large enough (eqn. 6). Under equivalent displacer conditions (eqn. 7), similar displacement profiles can be developed with different displacers and lower displacer concentration can be used if the displacer has a smaller saturation capacity. A displacer with a smaller initial slope will require less amount of the displacer and shorter regeneration time.

## SYMBOLS

$b(j)$	Langmuir affinity constant of component $j$ ( $=k_a(j)/k_d(j)$ )
$C(j)$	concentration of component $j$ in fluid phase
$C_u(j)$	concentration of component $j$ in solid phase
$C_f(j)$	feed concentration of component $j$
$C_{us}(j)$	saturation concentration of component $j$ in solid phase
$D_p(j)$	effective diffusivity of component $j$
$f(j)$	net rate adsorption of component $j$ per unit solid volume
$k_a(j)$	adsorption rate constant of component $j$
$k_d(j)$	desorption rate constant of component $j$
$L$	column length
NC	number of components
$R_p$	particle radius
$t$	time
$T$	dimensionless time $= tu/L\varepsilon_b$
$u$	superficial velocity
$\Delta T$	dimensionless feed volume
$\Delta T_2$	dimensionless amount of displacer
$\varepsilon_b$	bed void fraction
$\varepsilon_m$	particle porosity

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