
**Separation Science and Technology**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

# Probabilistic Approach to Digital Simulation of Chromatographic Processes

J. B. Phillips[ab]; N. A. Wright[a]; M. F. Burke[a]
[a] DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ARIZONA TUCSON, ARIZONA [b] Department of Chemistry, Southern Illinois University, Carbondale, Illinois

**To cite this Article** Phillips, J. B. , Wright, N. A. and Burke, M. F.(1981) 'Probabilistic Approach to Digital Simulation of Chromatographic Processes', Separation Science and Technology, 16: 8, 861 — 884
**To link to this Article: DOI:** 10.1080/01496398108058133
**URL:** http://dx.doi.org/10.1080/01496398108058133

SEPARATION SCIENCE AND TECHNOLOGY, 16(8), pp. 861-884, 1981

# Probabilistic Approach to Digital Simulation of Chromatographic Processes

J. B. PHILLIPS*, N. A. WRIGHT, and M. F. BURKE

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF ARIZONA
TUCSON, ARIZONA 85721



**Abstract**

A unique system has been developed for the digital simulation of chromatographic processes. This system is based on a probabilistic approach to the discrete events of adsorption and desorption rather than using a continuous solution of the differential equations used to describe the rates of adsorption and desorption. The simulation system has been developed using a threaded code technique of programming which allows the user to interact with the high speed, microcoded internal portions of the system through a very high level specific language. The utility of the system for studying both linear and nonlinear chromatographic processes is demonstrated.

## INTRODUCTION

Digital computer simulation is a powerful technique useful as an aid in understanding the behavior of complex systems (*1*, *2*). A chromatographic column certainly qualifies as a complex system which is not well understood. Its behavior is basically determined by the chemistry of the adsorption–desorption processes occurring in the column. However, these processes are only indirectly connected to the chromatographic experimental results, such as retention time and peak shape. The connection must be made by a theory, or model, of the chromatographic process. Such models are usually expressed in mathematical terms.

Computer simulation provides a means of connecting the mathematics of a model to the experimentally measurable properties of a real system, showing how the assumptions made in a model logically determine its results. It is not always obvious what the behavior of a model, even a simple one, will be. A

*Present address: Department of Chemistry, Southern Illinois University, Carbondale, Illinois.

computer simulation is the most direct way to test a mathematical model and find out how it works. By comparing the results of simulation experiments on models to experiments on the corresponding chemical system, it is possible to derive information about the chemical system and its relationship to the models. This information may be qualitative determinations of the adequacy of models or quantitative estimates of the values of parameters that the chemical system and its model have in common.

Most of the basic processes involved in chromatography (for example, adsorption, diffusion, and gas flow) are fairly simple to model. But, when they are all put together, the resulting system behavior is much more complicated than any of the individual processes. It is the simultaneous interaction of all the processes which makes chromatography such a useful technique and a difficult system to model. A number of different models may be involved, each of which contributes in some way to the overall behavior of the system. A simulation is a way of performing experiments upon these models with the goal of developing an understanding of their simultaneous interactions and corresponding processes in chromatographic systems. The most important use of simulation in chromatography at this time is to distinguish between different models and combinations of models rather than to derive results for a particular model.



Modeling peak shapes with combinations of analytic functions is one form of simulation which has been applied to chromatography. For example, Chesler and Cram (*3*) generated simulated chromatograms by combining Gaussian, triangular, and exponential functions and used them in a study of moment analysis. Simulation using analytic functions has also been widely proposed as a method for recognizing and assigning areas to overlapping chromatographic peaks (*4–7*).

Chromatographic processes have been modeled using continuous system simulation. In this kind of simulation the model is described in terms of differential equations. Given a set of initial conditions for the variables, the computer then moves the system in simulated time, numerically solving the differential equations at each point in time. This kind of simulation has been widely used in testing theories of chromatography (*8–12*). But as the models become more complex and include nonlinear or nonequilibrium behavior, the simulations become more difficult and much slower.

## DISCRETE EVENT SIMULATION

In a discrete event simulation, the model is expressed in terms of mechanisms and event occurrence probabilities. The computer program produces random numbers to determine what events occur and collects statistics on the results.

Chromatography itself has not previously been simulated using the discrete event technique, but some of the physical processes which are involved in chromatographic systems have been. For example, Nakagawa has written computer programs to simulate both the Langmuir- and BET-type adsorption processes (*13*, *14*). In these programs a computer-simulated surface with 10,000 empty adsorption sites is placed in contact with a simulated gas. During each simulation time unit the computer generates a uniform distribution random number which is used to select one of the adsorption sites. A second random number is generated and compared with the probabilities for an adsorption and desorption event to make a decision on which type of event should occur. A record is kept of the total number of molecules adsorbed at each point in time during simulation.

This simulation is useful in that it very clearly illustrates what is happening during a nonlinear nonequilibrium process. It is possible to derive the same results mathematically though the derivation is not as simple and intuitive as the simulation. When additional features are added to the model, the mathematics involved can become much worse while the simulation program only becomes a little bigger but is still understandable. Nakagawa (*13*, *14*), using similar programs, also simulated the adsorption–desorption process for surfaces with two different kinds of sites and with access to some sites hindered by the presence of pores. The simulation with pores is especially interesting because it shows how a complex structure which is difficult to accurately describe in most theories of chromatography can be modeled using a computer program.

The three varieties of digital computer simulation (analytic functions, continuous, and discrete event) are useful in different situations and require different techniques for their implementation. The analytic functions approach is generally the simplest to implement since it just involves the evaluation of functions over a range of values of an independent variable. Continuous system simulation is more difficult because it has the problem of maintaining accuracy while simulating the passage of time in addition to the evaluation of functions. Discrete event simulation is the most difficult since, in addition, it has the problem of maintaining statistical significance. The amount of detail in an underlying model for a simulation varies in a similar fashion. A discrete event model is rich in descriptions of basic chemical mechanisms and is intuitively easy to think about and discuss. In a continuous model described by differential equations, much of the detail has been averaged out. Instead of describing individual events, the model describes the average result of many events. In an analytic function, the detail of how the system progresses with time has been removed. Another way of looking at it is that a continuous model can be derived from a discrete event model and an analytic function model can be derived from a continuous model.

The most important reason a discrete event model was chosen to simulate the behavior of the chromatographic system is because, of the three varieties, it is the most natural way of thinking about the basic chemical processes involved. Complex nonlinear adsorption and desorption mechanisms inside a chromatographic column are much easier to describe and understand in the form of discrete event computer algorithms than they are as differential equations. The mechanisms of adsorption and desorption are commonly visualized by chemists as individual molecules approaching and interacting with individual surface structures as illustrated by Fig. 1. Here a molecule flowing in the gas phase encounters the surface and with some probability becomes adsorbed. This is an adsorption event. Some time later, it happens to come loose and returns to the gas phase. This is a desorption event. This approach can lead to simple and understandable models of adsorption processes, as, for example, in the work of deBoer (*15*). It is an easy step from this visualization to defining a formal model which can be simulated by a computer. A discrete event simulation, however, requires the most work out of a computer and, therefore, the most care in the design of the simulation algorithms.



## EXPERIMENTAL

All computing involved in this project was done by a Hewlett-Packard 2100A minicomputer. The peripherals included an HP 7900A 2.5 million word disk drive, a Tektronics 4002A graphics terminal, a line printer, and a plotter. The computer included 32K of core memory, hardware floating point instruction set, and writable control store. Special microprograms stored in

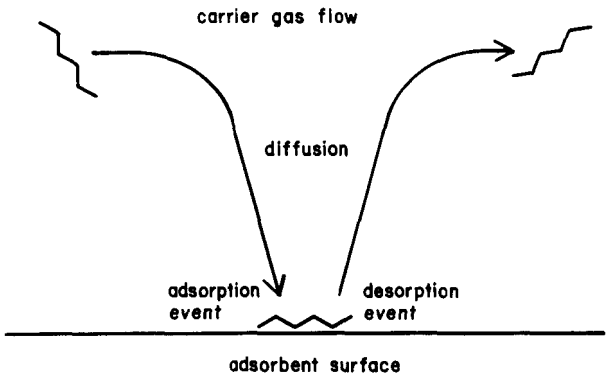


FIG. 1. An informal model of adsorption and desorption events.

writable control store greatly increase the speed of this computer. Typically, a simulation required 3–6 h of computer time.

A detailed description of the computer algorithms used will not be presented here. The concept of threaded programming as applied to these simulations has been dealt with previously (*16*). More details on the implementation of the simulation system algorithms are given elsewhere (*17*). A discussion of the general approach follows.

## DISCUSSION

The computer is very limited in the amount of memory available to record the state of the chromatographic system during a simulation and in the number of computations it can perform in a reasonable length of time. Therefore, the model chromatographic system must be drastically reduced in scale and in the amount of detail included. Only the minimum number of molecules necessary, performing only those events of immediate interest, are included in a simulation.



The models to be simulated are given as computer programs specifying the behavior of an individual molecule as it flows through the chromatographic column. The program is a model of the adsorption–desorption mechanism which determines the chromatographic system's behavior. All molecules in a simulation are executed with the same program and mechanism. The series of events and their timing, however, is determined by a random number generator and is different for each individual simulated molecule.

For events with constant probabilities of occurrence, such as desorption, the time to the next event may be determined with a random number from an exponential distribution. This is analogous to radioactive decay in which the waiting times between events are also exponentially distributed. For those events where a yes or no decision must be made at a fixed point in time, a uniformly distributed random number is required. A normally distributed Gaussian random number may be used to model the effect of diffusion between events. All of these random numbers are generated by high speed algorithms contained in subprograms.

Of course, more is involved in a chromatography experiment than just the adsorption and desorption processes. As a minimum, the model must provide for molecules being injected into a column, moving through the column while undergoing adsorption and desorption, and being detected as they reach the end of the column to produce a chromatogram. A flow chart modeling the behavior of a molecule in a chromatographic system is given in Fig. 2. The same model translated into a computer-understandable procedure (SIMULATE) is given in Fig. 3. This model is a simple linear chromato-

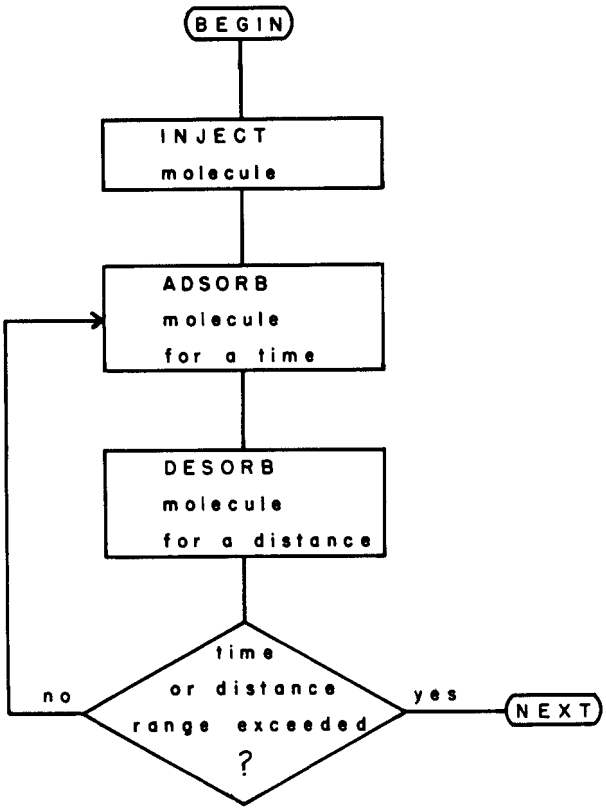


FIG. 2. Flow chart of a gas–solid chromatography model.



graphic system. A linear isotherm implies that there is no competition between molecules for adsorption sites.

At the beginning of the procedure, the molecule is injected into the column by utilizing another procedure, INJECT, which may be as simple or as complex as desired. Any kind of injection may be modeled by using an appropriate INJECT procedure. All of the simulations presented here use an exponential decay injection input profile. Once a molecule is injected into the column, it is repeatedly adsorbed and desorbed as specified by the ADSORB and DESORB procedures. When either the simulation column position or time exceeds the range allowed for the simulation, then an outside-of-range condition is detected and the computer exits from the adsorb-desorb loop.

The computer could simulate all the molecules simultaneously, executing the events in their correct order and switching around between different

```
* SIMULATE
*
* SIMULATE THE BEHAVIOR OF ONE MOLECULE PASSING THRCUGH
* A CHROMATOGRAPHIC SYSTEM.
*
LOCAL PROC SIMULATE BEGIN
INJECT          * INJECT A MOLECULE
DUP             * GET A COPY OF MOLECULE COUNT
POPSR           * DISPLAY COUNT IN SWITCH REGISTER
UNTILFAIL(REPEAT DO(ADSORB;DESORB;NEXT)) * MOVE A MCLECULE
DEL
DEL             * DELETE LEFT OVER DATA FROM STACK
DEL
NEXT
END
*
* INJECT
*
* SET MOLECULE COORDINATES TO INITIAL VALUES
*
LOCAL PROC INJECT BEGIN
INJRATE         * INJECTION RATE PARAMETER
R,EXP           * GENERATE EXPONENTIAL INJECTION DELAY
↑ TIME          * TIME AT WHICH MOLECULE ENTERS COLUMN
I,0             * PUT A ZERO ON DATA STACK
↑ COLUMN        * MOLECULE ENTERS COLUMN AT BEGINNING
NEXT
END
*
* ADSORB
*
* LINEAR ADSORPTION PROCEDURE
*
LOCAL PROC ADSORB BEGIN
COLUMN          * MOLECULE'S CURRENT COLUMN POSITION
HITRATE         * SURFACE ENCOUNTER RATE
R,EXP           * GENERATE EXPONENTIAL RANDOM NUMBER
I,+             * ADD IT TO COLUMN POSITION
↑ COLUMN        * UPDATE MOLECULE'S COLUMN POSITION
NEXT
END
*
* DESORB
*
* DESORPTION PROCEDURE
*
LOCAL PROC DESORB BEGIN
TIME            * MOLECULE'S CURRENT TIME
DESRATE         * AVERAGE DESORPTION RATE
R,EXP           * GENERATE RANDOM DESORPTION TIME
I,+             * ADD IT TO TIME COORDINATE
COLUMN          * CURRENT COLUMN POSITION
TIME            * MOLECULE'S TIME BEFORE ADSORPTION
ADSLINE 0       * RECORD ADSORPTION TIME IN DENSITY MAP
↑ TIME          * UPDATE MOLECULE'S TIME COORDINATE
NEXT
END
```

FIG. 3. Model of a chromatographic process.

molecules as required, or it could run a single molecule through the complete simulation before starting another one. The first technique is the more realistic one and is the way most discrete event simulations must be run in order to observe effects due to the interactions between events, but it is also very inefficient due to the record keeping required in switching around between molecules. The second technique is more efficient, easier to program, and results in more understandable programs and so should be used whenever possible. In linear chromatography models, there are no interactions between molecules anyway, so the event sequence can be rearranged to better suit the computer.

## Molecule Density Maps

The time at which each molecule emerges from the column is a very important simulation result because it is directly comparable to the results of a real experiment, e.g., the chromatogram. Information can be collected from a real chromatographic column only through an appropriate detector attached to the end of a column. There is no convenient way to observe the development of a peak as it moves down the column. In a simulation, however, the column position and time of each adsorption and desorption event is known, so statistical records can be kept of the simulation's behavior at any point in the experiment.

A molecule density map may be thought of as a two-dimensional array whose coordinates are time and chromatographic column position. The value of a point in this array is the relative density of molecules on the corresponding kind of adsorption site at that point in the simulation. A density map is stored in a binary tree structure rather than in an array, due to limitations of memory size and precision.

Each molecule of the simulation then has a trajectory in this two-dimensional space, moving in the column direction while in the gas phase and in the time direction while adsorbed on the surface. Statistics are collected from a simulation by recording the number of molecules passing through each point on the plane. A slice through this density map at a given column position is the chromatogram which would be recorded by an ideal detector at the end of a column of that length. A perpendicular slice at a given time is the molecular density along the column for that time. For example, the times at which molecules cross a series of points spaced along the column may be recorded producing, in effect, a series of chromatograms for various length columns. Alternatively, the column positions of all molecules at certain points in time may be recorded to produce plots of molecular density along

the column at specific times. Combining and generalizing these two ways of recording additional data leads to a two-dimensional representation of simulation results in which one axis is column position and the other axis is time.

These molecule position and time density maps provide a means of simulating nonlinear adsorption processes in a chromatographic column without running all the molecules simultaneously. The molecule density map provides an estimate of the density of molecules already adsorbed. In the case of a Langmuir isotherm, the molecule can become adsorbed only if it encounters an empty adsorption site. This is a nonlinear process because the probability of an empty site being available is determined by the number of molecules already adsorbed. In a simulation, the decision on whether a molecule is to be adsorbed or not at a given point along the column depends on the probability of the molecule encountering the surface at that point, on the density of available sites at that point, and on the density of molecules already adsorbed.

A nonlinear adsorption procedure for chromatographic simulation is broken up into two steps. First, the molecule being simulated moves down the column until it encounters the surface. The distance moved is sampled from the average surface encounter rate exponential distribution. A second procedure determines the density of molecules at the current column position and time, and, using a uniform distribution random number, makes a decision on whether the molecule will become adsorbed or not. If the density of molecules is high at this point, then the new molecule is not likely to find an available adsorption site and so will remain in the gas phase and it must try again. If the density of molecules is low, then the new molecule will most likely become adsorbed.

Information provided by a molecule density map is incomplete because it includes only information about molecules which have already been run through the simulation. The trajectories of molecules yet to be simulated cannot affect the behavior of those already done. This is an inescapable consequence of reordering the sequence of events. The reordering is necessary to make this discrete event simulation of chromatography practical, but it also affects the simulated behavior of nonlinear models. As the number of molecules simulated increases, the information provided by a molecule density map should become more accurate. To attain a given level of accuracy, more molecules must be simulated if the sequence of events is reordered than if all the molecules are simulated simultaneously. If the final density map converges to the same result as would be attained by a simultaneous simulation, then reordering the sequence of events is worthwhile even if it should require several times as many molecules.

## RESULTS

### Linear Chromatography Simulation

Figure 4 is a slice through a molecule density map at a fixed time. It shows the density of molecules in a linear simulation as a function of column position at one particular time. Plots may also be made at other values of the time coordinate to illustrate the development of the peak at earlier or later times in the simulated experiment. In addition, the density map may be sliced at any column position to give a plot of molecule density vs time.

The density map from which Fig. 4 was taken is the result of a simulation of the model given in Fig. 3. The peak matches the expected shape for a

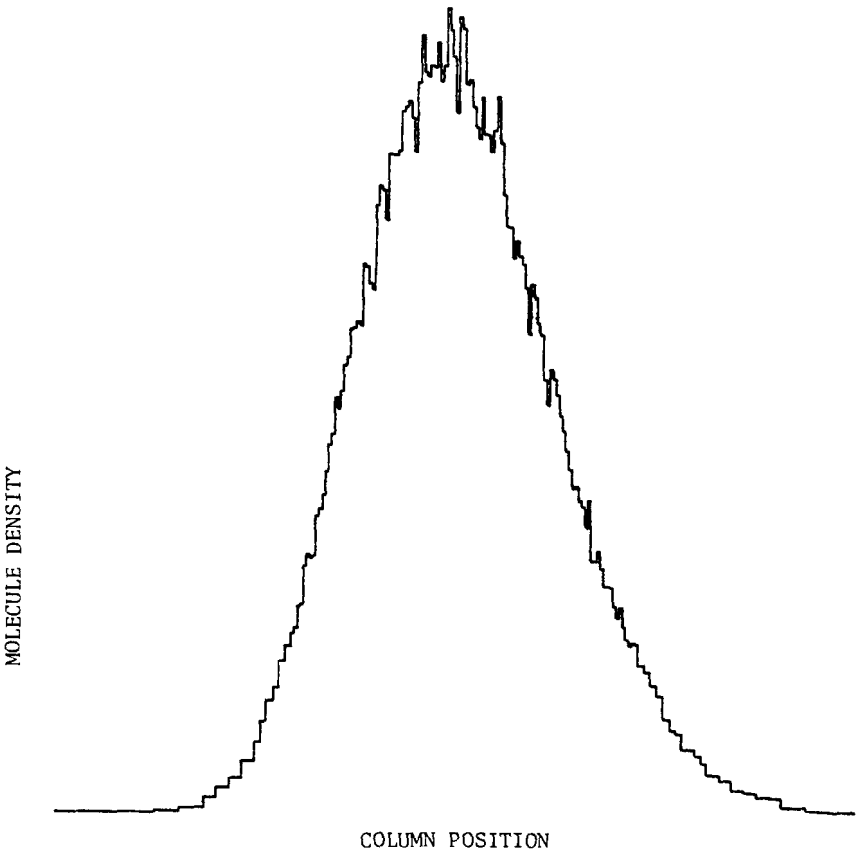


FIG. 4. Simulation of a linear chromatography model. Adsorption rate: 0.002; desorption rate: 0.002; plot time: 16,000.

linear chromatographic system with slow kinetics. It is not quite symmetrical because at this time in the simulated experiment the average molecule has been adsorbed and desorbed only 32 times. The symmetrical Gaussian peak shape is approached in a chromatographic system only after a long time and a large number of adsorption–desorption events. Most theories of chromatography must make a long time assumption, but this discrete event simulation actually works best at short times and, therefore, is especially useful in studying the initial stages of chromatographic elution.

Figure 5 is an example of a discrete event simulation used to observe the effect of injection profile on the initial development of a chromatographic peak. Plot A resulted from a near-ideal injection. Plots B and C resulted from

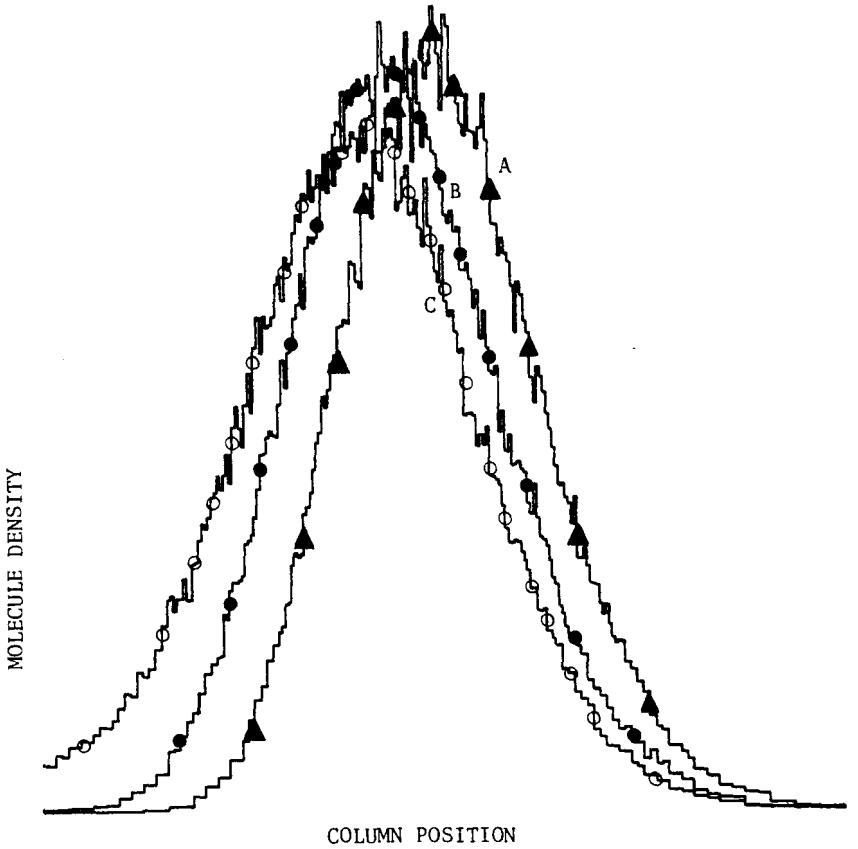


FIG. 5. Effect on injection port mixing on linear chromatography model. Adsorption rate: 0.002; desorption rate: 0.002; plot time: 16,000. Injection rates: 1.0, 0.0005, and 0.00025 for Plots A, B, and C, respectively.

progressively broader injection profiles. While the front or right side of Plots B and C are nearly as sharp as A, they are shifted left toward longer retention times simply because the average molecule enters the column later. The tailing side of Plot B is nearly as sharp as Plot A because the injection is sufficiently fast for all the molecules to get out of the injection port and undergo at least several adsorption and desorption events by this time. The overall shape of B is determined more by the chromatography than by the effect of a slow injection. Plot C has a more gentle slope on its tailing side. Not all of the molecules in Plot C have even entered the column, therefore the exponential decay of the injection port still has a large influence on the peak tail.

## Nonlinear Chromatography Simulation

A simple nonlinear model, Langmuir adsorption, can be simulated by replacing the ADSORB procedure in Fig. 3 with a more complex version which causes a molecule to become adsorbed only if a uniformly distributed random number exceeds the density map value at the current time and column position. This models the competition between molecules for a limited number of adsorption sites.

The results of a simulation of nonlinear Langmuir chromatographic model are presented in Fig. 6. Plots A through D show the simulated peak at four points during the experiment. Shortly after injection, Plot A, is still quite sharp but asymmetrical. The front is vertical while the back side is beginning to develop a tail. This asymmetry is the opposite of that observed in a linear model at short retention times (Fig. 4). In Plot B, the front has moved a considerable distance down the column but the tail has moved more slowly, resulting in a broader asymmetrical peak. The peak maximum just behind the sharp front is moving at a higher speed than the regions of lower concentration in the tail.

From the point of view of the individual molecules, there is a shortage of adsorption sites. Sometimes when a molecule encounters the surface and tries to become adsorbed, it finds that the adsorption site is already taken, so it must remain in the mobile phase and continue traveling down the column. This is more likely to happen in regions of high concentration such as exist in the peak soon after injection. So the average molecule and especially those in the part of the peak with the greatest concentration move down the column faster than they normally would until the peak spreads out and the concentration of molecules on the surface is reduced.

The faster moving peak maximum leaves the tail of the peak further behind as it moves down the column. The various parts of the tail move at speeds related to their local concentrations on the surface. Thus the tail stretches out

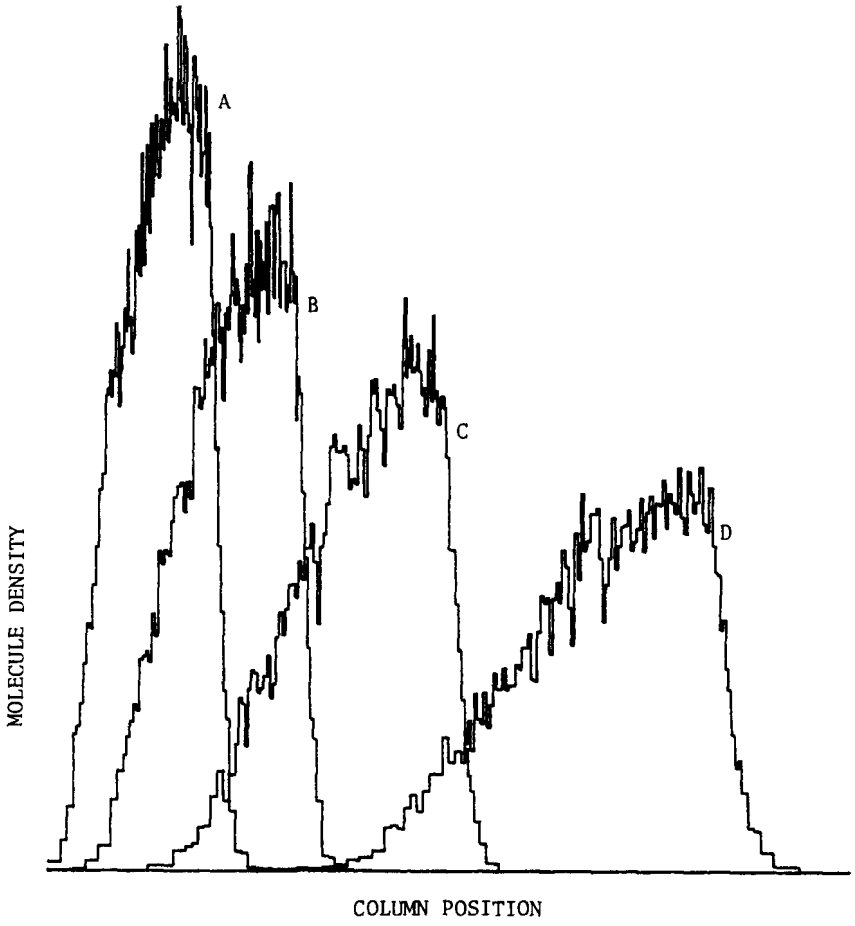


FIG. 6. Development of a nonlinear chromatographic peak. Surface encounter rate: 0.008; desorption rate: 0.004; sites per molecule: 16. Plot times: 4,000, 8,000, 16,000, and 32,000 for Plots A, B, C, and D, respectively.

further as long as any part of the peak contains enough molecules to cause a significant amount of competition for the available adsorption sites. This nonlinear mechanism is a very effective way of broadening a chromatographic peak.

Besides leaving a tail behind, the faster moving peak maximum moves continuously into new parts of the column with completely empty adsorption sites. Those molecules which happen to be in the forefront for the peak encounter this fresh surface and become adsorbed with no competition for adsorption sites. Their speed down the column must be at a slower rate for as

long as they remain in the lead. But the peak maximum following close behind is moving faster and quickly overtakes them. Any individual molecules which, because of the statistical variation in their individual adsorption and desorption behavior, happen to drift ahead of the main body of the peak are slowed down by the availability of adsorption sites and kept close to the peak maximum. The peak cannot spread in the forward direction as a linear chromatography peak would. This self-sharpening front behavior for non-linear peaks is predicted by nonlinear theories of chromatography (*18*, *19*). A nonequilibrium Langmuir isotherm treatment by Zhitomirskii et al. (*19*) shows nonvertical self-sharpening fronts very similar to these simulation results.

Figure 7 presents the results of a series of simulations run with identical parameters except for the size of the injected samples. The smallest peak resulted from an injection whose concentration was small enough to give essentially linear chromatographic behavior. Each successively larger peak



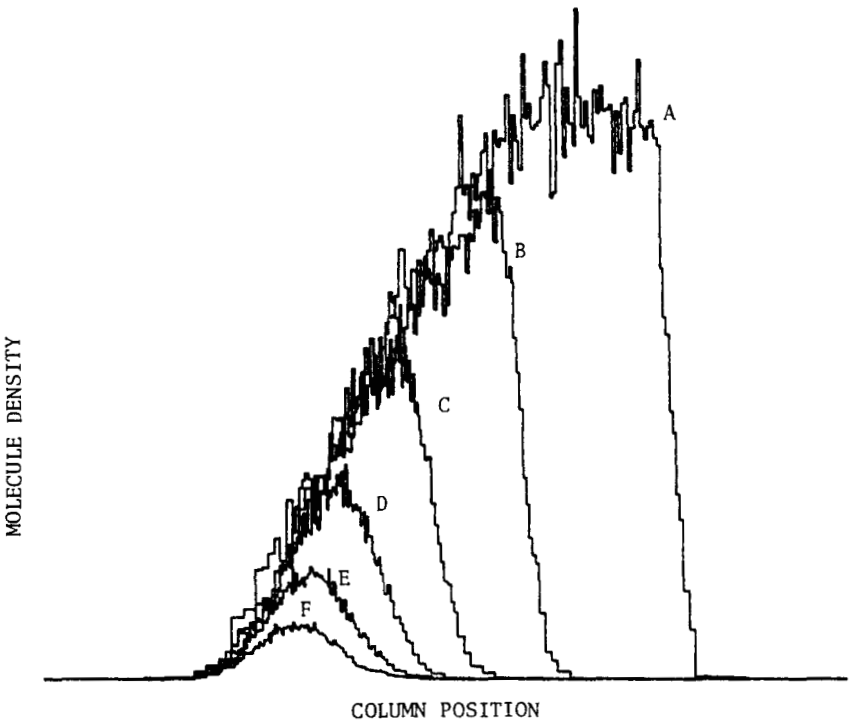


FIG. 7. Effect of sample size variation on simulation of a non-linear chromatography model. Surface encounter rate: 0.008; desorption rate: 0.004; plot time: 20,000. Sites per molecule: 8, 16, 32, 64, 128, and 256 for Plots A, B, C, D, E, and F, respectively.

resulted from an injection of twice the previous sample concentration. All peaks are plotted at the same point in simulated time and on the same scale relative to the number of available adsorption sites in the column.

The second smallest peak appears to be quite symmetrical and Gaussian in shape. It looks like a linear peak, but its peak maximum is shifted a little toward shorter retention times and it is a little broader than the smallest peak. A truly linear peak should be identical to all smaller peaks except for a scale factor. This second smallest peak behaved as a linear peak at the time this plot was made in the simulation and has been linear for most of its retention time. But for a short time after injection it had a large enough concentration to move faster than normal and develop a small tail.

The next two peaks are more obviously nonlinear. They have the expected asymmetry with a sharper front and a tail at the rear. The fronts are no longer self-sharpening as they were for a while after injection, and the smaller of the two is well on its way to the Gaussian shape. The two largest peaks still have self-sharpening fronts. The distance a nonlinear peak can travel and still maintain a self-sharpening front is determined by the size of the injection.

All of the nonlinear peaks in Fig. 7 follow the same curve on the tail side of the peak. This is a result of the faster average movement of molecules in regions of higher concentration. A molecule in the tail of a peak moves at a rate determined by the number of available adsorption sites which is determined by the local concentration of molecules. Molecules further up the tail are in regions with higher concentration and are, therefore, moving faster and must be on the average pulling away from the rest of the tail. Since molecules in the front are moving away from those in the back, they cannot have any influence on the behavior of those left behind. Thus molecules in the tail cannot tell how big a peak they belong to and must have the same behavior regardless. This argument assumes that spreading due to diffusion processes is insignificant in comparison with spreading due to nonlinearity.



## Nonuniform Surface Models

So far all models simulated have assumed that the solid surface consists of identical discrete adsorption sites. This uniformity of surface structure is an often-stated goal in the design of chromatographic systems (*20*, *21*), but real surfaces are always more complicated. For example, a modified Porasil surface intended for gas–solid chromatography was prepared and characterized (*22*). It was shown to have three distinct kinds of structures on the surface which could act as adsorption sites for molecules of various types. Any realistic gas–solid chromatography simulation must be able to include these and other nonuniform surface models.

It is quite easy to modify the nonlinear adsorption model used for Fig. 7 to include the possibility of the molecule becoming adsorbed on a second kind

of site with different characteristics. One such nonuniform surface model is as follows. Upon encountering the surface, a decision is made as to which of the two types of sites is present. In this particular model it is assumed that the molecules encounter the sites in proportion to their occurrence frequency on the surface. This may not always be the case, since adsorption kinetics may differ between site types. Once the site type has been determined through the use of a uniformly distributed random number, the molecule attempts to adsorb on it. Each type of adsorption site in a chromatographic model has its own density map. It is possible that one of the two kinds of sites may be nearly full in some particular region while the other is almost empty. Whether a molecule becomes adsorbed or not would then depend largely upon which type of site it encountered on the surface. The DESORB procedure for this two-site model generates an appropriate desorption time depending upon which of the two sites the molecule was adsorbed on.

Adding a second type of adsorption site greatly increases the range of possible chromatographic behavior of a model surface. The two individual kinds of sites can have different concentrations and adsorption–desorption kinetics. A molecule in the column can be involved in a larger variety of events and may interact with other molecules in a peak in more complex ways. The explanations for the chromatographic behavior of a system on a molecular level can become much more obscure than the single-site type examples have been.



For example, Fig. 8 illustrates the effect of varying the proportions of two distinct kinds of adsorption sites on the retention and shape of a chromatographic peak. All plots were made at the same simulation time and on the same density scale. The only variation among these simulations was in the amount of higher energy sites present in the column. A higher energy site is one which has a higher activation energy for desorption and, therefore, a slower desorption rate. In this particular example, the higher energy site desorption rate was slower than the low energy site by a factor of 10. In all of these simulations the low energy site was present in sufficient concentration to have essentially linear behavior.

The two kinds of sites are assumed to exist independently on the surface, and molecules can interact with only one of them at a time. The adsorption rates for each of the two kinds of sites is determined by the surface encounter rate and by the fraction of each kind of site. The probability that a molecule attempts to become adsorbed on one kind of site rather than the other is determined solely by their relative availability and not by any chemical differences.

Plot A of Fig. 8 resulted from a simulation with no high energy sites. It provides a uniform surface standard against which the two-site models can be compared. Plot B resulted from an identical simulation except for high energy

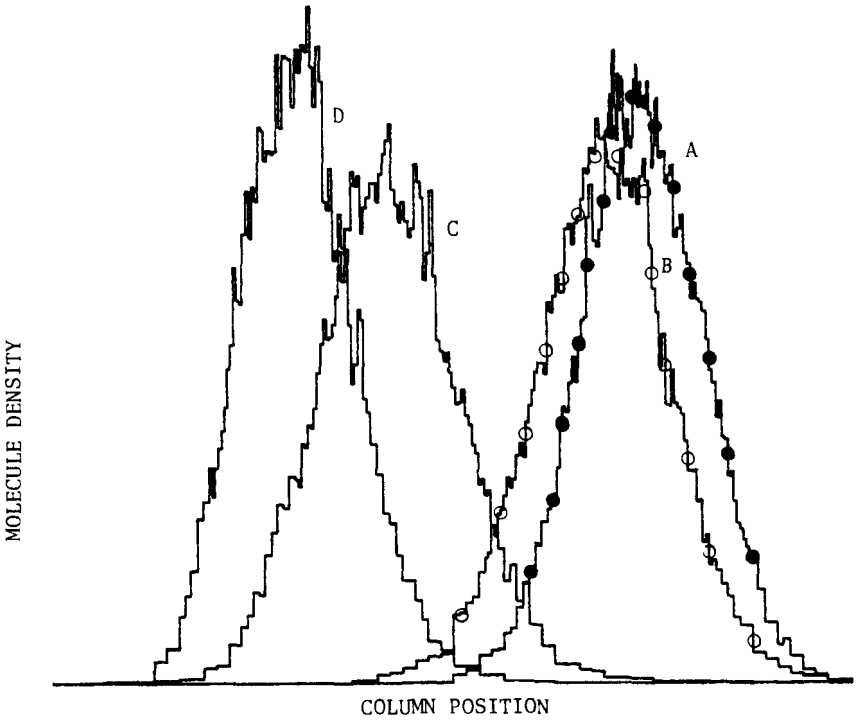


FIG. 8. Simulation of a nonlinear chromatography model with two types of adsorption sites. Surface encounter rate: 0.01; Sites 0 desorption rate: 0.01; Sites 1 desorption rate: 0.001; sites 0 premolecule: 1,000; plot time: 25,000. Sites 1 per molecule: 0, 10, 100, and 200 for Plots A, B, C, and D, respectively.



sites added at a concentration 1% as large as the low energy sites. The peak is retained slightly longer in the column and made slightly broader. The effect is not very large simply because at only 1% concentration the molecules do not run into a high energy site very often. With the high energy site concentration set at 10% of the low energy site concentration, Plot C results. Here the peak has about the same breadth as in Plot B, but it has moved only a little more than half as far down the column. The presence of the high energy sites is causing excessive peak broadening and poor column efficiency. At 20% high energy site concentration, Plot D, the peak retention has increased but the peak is also sharper than in Plot C. The column efficiency has not deteriorated further and may be even a little better as the chromatographic behavior of the column begins to be dominated by the high energy sites.

This simulation experiment confirms the rule that uniform surfaces are better than nonuniform surfaces for good, efficient gas–solid chromatography. It also demonstrates why it is so difficult to make reproducible chromatographic adsorbents. It is desirable to have low energy nonspecific adsorption as the major retention mechanism in a gas–solid chromatography column. This is often achieved by deactivating the surface through a chemical reaction to remove or cover up the specific interaction high energy adsorption sites. But, if the reaction is not 100% complete and a few high energy adsorption sites, say 5–10%, remain uncovered, then a situation like Plot C of Fig. 8 will result and the column efficiency will be much worse than expected. The results could be considerably worse than this if the high energy adsorption sites have slower desorption rates than were assumed in these models.

The simulation cannot prove that this model is the correct one. Others may give results just as close to the real experiment. But it does prove that the model is at least consistent with the experimental results. An indication of which models are consistent with experiments can be very valuable in the planning of further research. This is especially true for research involving complex systems such as chromatography where intuition is not enough.



The two-site model with independent sites is probably good enough if the two kinds of sites are not too different in chemical behavior or concentration. But it may not be adequate if the two sites have fundamentally different character, resulting in different mechanisms of adsorption and desorption. For example, one of the two sites may have a low energy nonspecific adsorption while the second can become involved in a specific interaction with a functional group on an adsorbed molecule. To become adsorbed, the molecule must encounter the surface with its functional group on the side toward the adsorption site. This must happen less often than simply hitting the surface as in a nonspecific adsorption event. Therefore, the kinetics of adsorption on a specific interaction site should be slower than the simple site encounter rate.

However, if there is a large concentration of nonspecific adsorption sites surrounding each specific site, then the molecule may be initially adsorbed on a neighboring nonspecific site until it eventually migrates to the specific site with its functional group in the proper position for adsorption. The activation energy for transfers between adsorption sites is likely to be smaller than for complete removal from the surface in a desorption event and, consequently, the rate of transfer between sites is likely to be faster than the rate of desorption. The adsorbed molecules may then act as a two-dimensional gas on the solid surface (*15*). While moving over the surface, a molecule could encounter a high energy adsorption site and become stuck on it. Either of these mechanisms involving first a nonspecific adsorption followed by

transfer to a specific interaction adsorption site should lead to improved kinetics for adsorption on high energy sites.

A two-site adsorption model involving transfer to high energy sites from neighboring low energy sites is given in Fig. 9. In this model it is assumed that a molecule must first become adsorbed on a nonspecific site in the usual fashion. It may then transfer to a neighboring specific interaction site if one is available and empty. It is assumed that on the average each specific interaction site has four nonspecific sites close enough to supply molecules.

```
* ADSORB1
*
* TRY TRANSFERRING MOLECULE FROM LOW TO HIGH ENERGY
* ADSORPTION SITE IF THERE IS ENOUGH ROOM.
*
LOCAL PROC ADSORB1 BEGIN
COLUMN        * GET COLUMN POSITION COORDINATE
TIME          * AND TIME COORDINATE
DENSITY 1     * DENSITY OF MOLECULES ALREADY HERE
F.(SCALE1 *)* MULTIPLY BY MOLECULES PER SITE 1 RATIO
R.>U          * ADSORB ON SITE 1 IF ROOM, ELSE LEAVE ON SITE 0
NEXT
END
*
* STUCK
*
* PROCEDURE TO TEST A MOLECULE AT THE SURFACE TO SEE IF
* IT WANTS TO STICK HERE.
*
LOCAL PROC STUCK BEGIN
DUP           * GET CURRENT COLUMN POSITION
TIME          * CURRENT TIME
DENSITY 0     * GET DENSITY OF MOLECULES ON LOW ENERGY SITES
F.(SCALE0 *)* MULTIPLY BY MOLECULES PER SITE 0 RATIO
R.>U          * MAKE ADSORPTION DECISION
NEXT
END
*
* ADSORB
*
* NONLINEAR ADSORPTION PROCEDURE FOR A TWO SITE SURFACE
* WITH MOLECULE TRANSFER BETWEEN SITES.
*
LOCAL PROC ADSORB BEGIN
COLUMN           * CURRENT COLUMN POSITION COORDINATE
REPEAT HITSURF * ENCOUNTER THE SURFACE
UNTIL STUCK      * TEST DENSITY & MAYBE BE ADSORBED
↑ COLUMN         * COLUMN POSITION AT ADSORPTION
IF F.(SITERATIO R.>U) * HIGH ENERGY SITE NEARBY ?
THEN PUSHF       * NO, KEEP IT ON SITE TYPE 0
ELSE ADSORB1     * YES, TRY ADSORBING ONTO IT
↑ SITEFLAG       * FLAG INDICATING EITHER SITE TYPE 0 OR 1
NEXT
END
```

FIG. 9. Nonlinear adsorption model for surfaces with two kinds of sites and surface transfer of molecules from low energy to high energy sites.

No possibility of transfer between nonspecific adsorption sites is included in the model.

The result of a simulation of this model is given in Fig. 10. In this simulation there is only one high energy site for every 1000 low energy sites, but once a molecule is adsorbed on a high energy site, it stays there on an average 500 times as long as on a low energy site. The main part of the peak is about where it should be for approximately linear chromatography on the low energy adsorption sites; therefore, most of the molecules must be completely ignoring the high energy sites.

The peak tail has a very different shape than the tails resulting from simply overloading a single-site type column. It is much longer because of the very slow desorption kinetics of the high energy sites and lower in concentration because of the limited number of these sites. The adsorption kinetics are enhanced by the mechanism transferring molecules from low to high energy



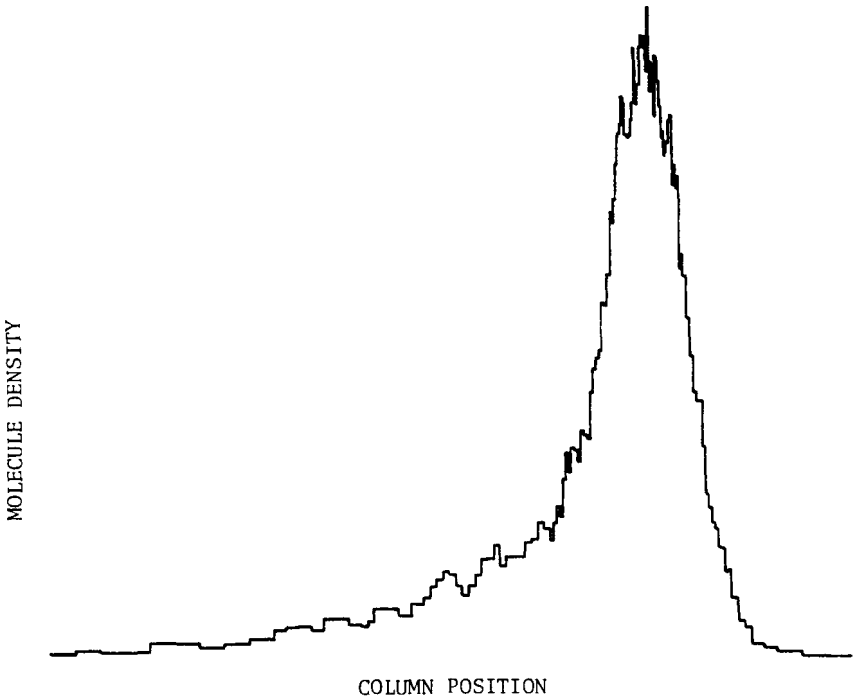


FIG. 10. Simulation of a nonlinear chromatography model with two types of adsorption sites and surface transfer of molecules from low energy to high energy states. Surface encounter rate: 0.02; Sites 0 desorption rate: 0.02; Sites 1 desorption rate: 0.001; Sites 0 per molecule: 400; Sites 1 per molecule: 4; plot time: 25,000.

sites. The high energy sites must be nearly saturated wherever there is a reasonably large concentration of molecules adsorbed on the low energy sites. As the main part of the peak passes over a section of the column, almost all of the high energy sites are filled. Then, after the peak has moved on, molecules slowly desorb from the high energy sites. But most of them will never catch up with the main peak because it is moving at a rate mainly determined by the low energy sites, while out on the tail the high energy sites are no longer completely saturated, and a molecule has an increased chance of becoming adsorbed once again and moving even further out in the tail.

This very low concentration of high energy sites continuously builds a tail on the chromatographic peak at a rate determined by the concentration of the sites. The length of the tail is determined by the desorption kinetics. To be effective tail producers, high energy sites must have some adsorption mechanism which increases the rate over what it would be if they became adsorbed by simply encountering the site directly from the gas phase.

Giddings (*23*) argued that in order to produce a distinct tail on a peak, a high energy site must have a desorption rate at least $10^5$ times slower than the low energy sites responsible for the main part of the peak. This is clearly not true for this model since the high energy site desorption rate is only 500 times the low energy site desorption rate. Giddings did not consider the possibility of a molecule being moved further out into the tail by additional adsorptions on the high energy sites. The enhanced rate of adsorption in this model makes these additional adsorptions in the tail an important part of the mechanism responsible for building the tail to a significant size. In a two-dimensional gas model, the rate of adsorption on the high energy sites might be even greater, resulting in a faster buildup of a tail.



Figure 11 illustrates the effect of changing the sample size on the model given in Fig. 10. Plot B in this figure is the same simulation presented in Fig. 10. Plot A is an increase in sample size by a factor of 4 and Plot C is a decrease by a factor of 4. The attenuations of Plots A and C are adjusted to the same scale as Plot B. All three simulations are plotted at the same simulation time.

Increasing the sample size four times causes the low energy adsorption sites to begin behaving nonlinearly. The result is a shift to shorter retention times and a larger column overloading tail. As expected, increasing the sample size is detrimental to the efficiency of this chromatographic column. But decreasing the sample size is also bad. Now the high energy tail-producing sites can take a larger proportion of the molecules from the main part of the peak and move them into the tail. This kind of tail is limited by the number of high energy sites, and as the total sample size is reduced, a small number of sites becomes proportionally more important. Giddings (*24* pp. 255–257) has previously observed and explained this kind of behavior.

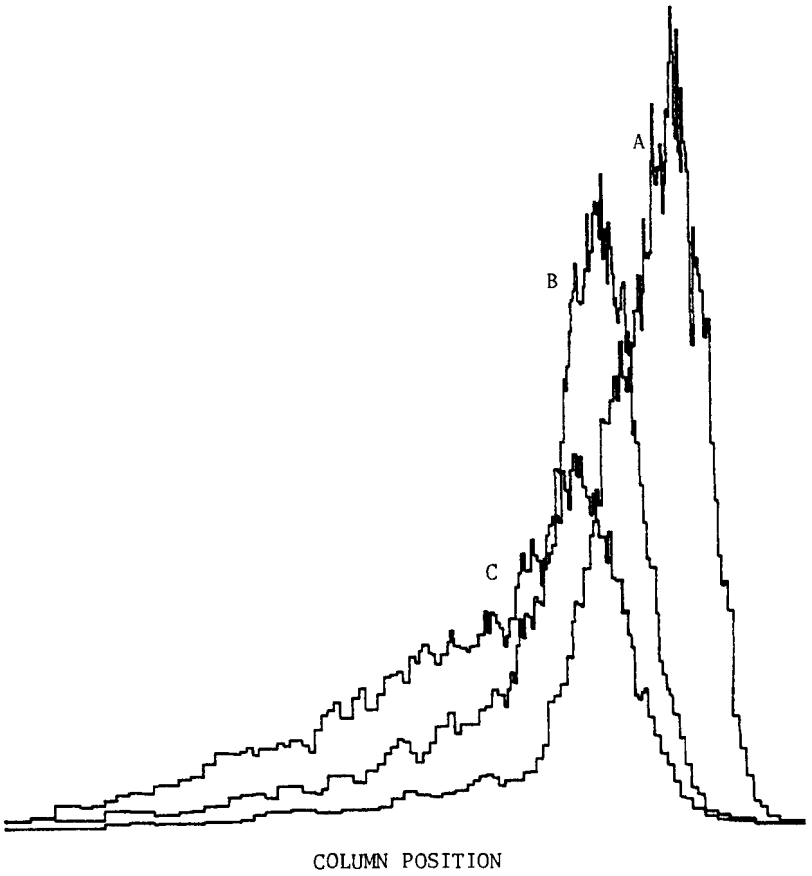


FIG. 11. Effect of sample size variation on simulation of a nonlinear chromatography model with two types of adsorption sites and surface transfer of molecules from low energy to high energy sites. Surface encounter rate: 0.02; Sites 0 desorption rate: 0.02; Sites 1 desorption rate: 0.001; plot time: 25,000. Sites 0 per molecule: 100, 400, and 1,600 and Sites 1 per molecule: 1, 4, and 16, for Plots A, B, and C, respectively.

## CONCLUSION

The simulation results presented here are intended as examples of the kind of chromatographic models which can be tested using this technique. These are by no means the only kind of chromatographic systems which may be modeled. The simulation is designed specifically for gas–solid chromatography, but it may be used to model other chromatographic systems with

little or no modification. Peripheral parts of a chromatographic system such as input profile and detector response may be included in models.

Any model or theory which can be expressed in terms of the discrete event algorithms and does not exceed the capacity of the available computer memory may be simulated. Many models which are difficult to express and solve analytically may be examined by this simulation procedure. The basic requirement is that the model be expressible in terms of mechanisms and probabilities. For example, diffusion of a molecule leaving a surface and returning to the gas phase and flowing through porous structures may be modeled by probability density functions derived from the geometry of gas flow through the porous structure. This case has been treated previously only by making very restrictive assumptions (*24*, pp 195–225). Such assumptions are not required by this simulation approach. The greatest value of these digital computer simulation techniques is in their use as qualitative aids to the understanding of models of chromatographic mechanisms. Informal models are a very important part of the thinking processes of all chemists engaged in research on new chemical systems. Very often, as in the case of chromatography, these informal models tend to be based on molecular interactions mechanisms. A discrete event simulation is a more formal way of expressing the same kind of molecular model. In exchange for the extra effort required in formally defining and writing down a model, the simulation provides a way of testing the logic of a model. The testing can provide evidence as to the feasibility of a model and so aid in the intelligent discussion and comparison of alternative models, leading to valuable insight into the behavior of corresponding real chromatographic systems.



## REFERENCES


1. A. M. Colella, M. J. O'Sullivan, and D. J. Carlino, *Systems Simulation*, Lexington Books, Lexington, Massachusetts, 1974.
2. J. S. Rosko, *Digital Simulation of Physical Systems*, Addision-Wesley, Reading, Massachusetts, 1972.
3. S. N. Chesler and S. P. Cram, "Effect of Peak Sensing and Random Noise on the Precision and Accuracy of Statistical Moment Analysis from Chromatographic Data," *Anal. Chem.*, *42*, 1922 (1971).
4. E. Grushka, M. N. Myers, and J. C. Giddings, "Moments Analysis for the Discernment of Overlapping Chromatographic Peaks," *Ibid.*, *42*, 21 (1970).
5. T. S. Buys and K. De Clerk, "Bi-Gaussian Fitting of Skewed Peaks," *Ibid.*, *44*, 1273 (1972).
6. S. N. Chesler and S. P. Cram, "Iterative Curve Fitting of Chromatographic Peaks," *Adv. Chromatog.*, *8*, 44 (1973).
7. E. Cuso, X. Guardino, J. M. Riera, and M. Gassiot, "Non-linear Fitting Method for Recorded Chromatographic Peaks," *J. Chromatogr.*, *95*, 147 (1974).
8. K. De Clark and T. S. Buys, "Moment Analysis in Non-liner Chromatography: I. The First Moment," *Ibid.*, *63*, 193 (1971).

9. T. S. Buys and K. De Clerk, "Moment Analysis in Non-linear Chromatography: II. The Second Moment," *Ibid.*, *67*, 1 (1972).
10. P. Valentin and G. Guiochon, "Propagation of Signals of Finite Concentration in Gas Chromatography. I. The Quasi-Ideal Model," *Sep. Sci.*, *10*, 245 (1975).
11. P. Valentin and G. Guiochon, "Propagation of Signals of Finite Concentration in Gas Chromatography. II. Study of the Discontinuities and their Conditions of Stability," *Ibid.*, *10*, 271 (1975).
12. K. Yanaoka and T. Nakagawa, "Moment Analysis of Non-linear Gas Chromatography Computer Simulation," *J. Chromatogr.*, *103*, 221 (1975).
13. T. Nakagawa, "Simulation of BET Type Adsorption," *Kolloid-Z. Z. Polym.*, *221*, 40 (1967).
14. T. Nakagawa, "Simulation of Langmuir Type Adsorption," *Ibid.*, *209*, 60 (1966).
15. J. H. deBoer, *The Dynamical Character of Adsorption*, Clarendon Press, Oxford, 1968.
16. J. B. Phillips, M. F. Burke, and G. S. Wilson, "Threaded Code for Laboratory Computers," *Software Pract. Exper.*, *8*, 257 (1978).
17. J. B. Phillips, "Computer Methods in the Study of Chromatographic Processes," PhD Dissertation, University of Arizona, 1977.
18. F. Helfferich and G. Klein, *Multicomponent Chromatography, Theory of Interference*, Dekker, New York, 1970.
19. B. M. Zhitomirskii, A. V. Agafonov, A. D. Berman, and M. I. Yanovskii, "Theoretical Approach to Gas–Solid Chromatography Applied to the Slow Attainment of Adsorption Equilibrium and to the Langmuir Isotherm," *J. Chromatogr.*, *94*, 1–12 (1974).
20. A. V. Kiselev and Y. I. Yashin, *Gas Adsorption Chromatography*, Plenum, New York, 1969, p. 40.
21. W. Rudzinski, A. Waksmundzki, R. Leboda, and M. Jaroniec, "New Possibilities of Investigating Adsorption Phenomena by Gas Chromatography: Estimation of Adsorbent Heterogeneity from the Pressure Dependence of Retention Data," *Chromatographia*, *7*, 663–668 (1974).
22. R. K. Gilpin and M. F. Burke, "Role of Tri- and Dimethylsilanes in Tailoring Chromatographic Adsorbents," *Anal. Chem.*, *45*, 1383–1389 (1973).
23. J. C. Giddings, "Theory of Gas-Solid Chromatography: Potential for Analytical Use and the Study of Surface Kinetics," *Ibid.*, *36*, 1170 (1964).
24. J. C. Giddings, *Dynamics of Chromatography, Part I, Principles and Theory*, Dekker, New York, 1965.

*Received by editor January 23, 1981*