



An expanded cellular automata model for enantiomer separations using a β -cyclodextrin stationary phase



Darren DeSoi*, Lemont B. Kier, Chao-Kun Cheng, H. Thomas Karnes

Virginia Commonwealth University, School of Pharmacy, Department of Pharmaceutics, 410 North 12th Street, P.O. Box 980533, Richmond, VA 23298-0533, USA

ARTICLE INFO

Article history:

Received 4 January 2013
Received in revised form 15 March 2013
Accepted 21 March 2013
Available online 26 March 2013

Keywords:

Cyclodextrin
Cellular automata
Chiral separations
Modeling

ABSTRACT

Chromatographic scale enantiomer separation has not been modeled using cellular automata (CA). CA uses easy to adjust equations to different enantiomers under various chromatographic conditions. Previous work has demonstrated that CA modeling can accurately predict the strength of one-to-one binding interactions between enantiomers and β -cyclodextrin (CD) [1]. In this work, the model is expanded to a chromatographic scale grid environment in order to transform model output into HPLC chromatograms. The model accurately predicted the lack of chromatographic selectivity of mandelic enantiomers (1.05 published, 1.01 modeled) and the separation of brompheniramine enantiomers (1.13 published, 1.12 modeled) previously modeled in one-to-one interactions. By examining cyclohexylphenylglycolic acid (CHPGA) enantiomers, the model accurately predicted both the selectivity and resolution of the enantiomer peaks at varying chromatographic temperatures. Modeled changes in mobile phase pH agree with laboratory outcomes when examining peak resolution and selectivity. Changes in injection volume resulted in an increase in retention time of the modeled enantiomers as was observed in the published laboratory results.

© 2013 Elsevier B.V. All rights reserved.

1. Introduction

Contrasting models that simulate enantiomeric interactions at a one-to-one scale to study binding energies, the expansion to model a chromatographic environment using cellular automata (CA) allows for the generation of model chromatograms. CA allows for the easy determination of equations based on fundamental binding energies (van der Waals, hydrogen bonding, hydrophobicity) to calculate probabilities and factors that guide ingredient interactions. Once chromatograms are predicted, then the degree of separation of enantiomers can be more accurately compared to laboratory results. Additionally, chromatographic conditions that are traditionally altered in the laboratory to improve peak separation can be modeled to see their impact on the degree of chromatographic separation: mobile phase temperature and pH, and injection volume.

Chromatographic retention of analytes in a β -cyclodextrin (CD) HPLC column involves multiple interactions with the CD stationary phase. This is incorporated into the model environment along

with the addition of a dual solvent mobile phase. Along with the new ingredient cells (enantiomers, mobile phase, and multiple CD sites), new interactions had to be accounted for. In addition to the enantiomer-CD interactions, mobile phase interactions with the enantiomers, CD stationary phase, and enantiomer are incorporated into the model.

The chromatographic model is tested to verify that chromatograms of mandelic acid and brompheniramine enantiomers agree with selectivity from the first one-to-one model [1]. Model rules are then adjusted to examine the enantiomeric separation of CHPGA. Changes to modeled HPLC column temperature, mobile phase pH, and sample injection volume are compared to published laboratory results.

2. Experimental

2.1. Software

The cellular automata model is written in Java™ and executed using Eclipse (version 3.1.2, The Eclipse Foundation) as an integrated development environment. All calculations and plots are performed using Microsoft Office Excel 2003 (Microsoft Corporation).

* Corresponding author at: Virginia Commonwealth University, School of Pharmacy, Department of Pharmaceutics, 410 North 12th Street, Richmond, VA 23298-0581, USA. Tel.: +1 804 852 6033; fax: +1 804 335 2087.

E-mail address: desoidj@mymail.vcu.edu (D. DeSoi).

2.2. Computer

Model runs are performed on a Toshiba Satellite™ A305 laptop, with Intel Core™ Duo CPU 1.83 GHz, 3.00 GB RAM, on a Windows 7 32-bit operating system.

2.3. Cellular automata model environment design

Cellular automata models are designed around a grid of cells, ingredient(s) location and amount, rules governing the interactions and movement of ingredients, and a specified runtime (iterations). Thousands of interactions occur between many analyte and stationary phase molecules depending on the amount of sample injected onto the chromatographic column and the column's design. Thousands of interactions are impractical to model, as this would vastly slow down the model and require substantial computational power. There may be no benefit in expanding the model to this degree, since the model is designed to predict chiral separations in an efficient manner and not replicate the physical environment of a chromatographic column. The number of analytes and β -CD stationary sites needs to be increased in a manner that allows multiple site interactions as the analytes move through the column. β -CD stationary sites are evenly spaced in an alternating manner to avoid possible solvent channels so that the analytes will have stationary phase interaction and not move through the column without interaction.

Analytes are placed randomly at the beginning of the modeled column, prior to the stationary phase, to represent the beginning of an injection of sample onto a HPLC column. Two different types of cellular automata cells are used representing enantiomer pairs. At the beginning of each run the analyte cells are randomly intermixed and have the ability to rotate as they move, which plays a part in their separation behavior since they are variegated cells.

Mobile phase cells are also added to the model. Two different types of cells are used so that dual solvents may be modeled. Their polarity and densities are incorporated into the model to best represent their chemical and physical properties under laboratory conditions. The mobile phase cells interact with analytes and stationary phase in various ways according to their chemical nature.

Flow (gravity factor in the model) is incorporated on analytes and mobile phase cells at equal values. The gravity parameter in the cellular automata model represents the tendency to move in a certain direction.

As in the one-to-one model, a β -CD is represented using several cells (see Fig. 1). The β -CD is now made of variegated cells that are divided into two types of sites, each having their own set of interaction rules. B0 sides represent the secondary hydroxyl groups located at carbon two of the β -CD in addition to the hydrophobic interior of the β -CD depending on what side of the analyte cell it is interacting with. B1 sides represent the hydrophobic interior of the β -CD, while B2 represent the primary hydroxyl groups of the β -CD at carbon six. The outside or exterior of the β -CD denote sites that have minimal interaction with analytes and are in yellow using the variable C.

There are two types of analyte cells in the model, A and D, to represent an enantiomer set. Analyte cells are variegated with 4 sides to represent a chiral molecule. Each side has its own set of interaction rules with stationary phase sites (B0–B2), mobile phase cells W1 or W2 (water and acetonitrile), and each other. Mobile phase cells are non-variegated and have the same set of interaction rules on each side.

The cellular automata model environment consists of a grid of cells 40 columns wide and 800 rows long for a total of 32,000 cells to represent a chromatographic column. This grid design evolved through several steps of runs and observations. The grid is designed

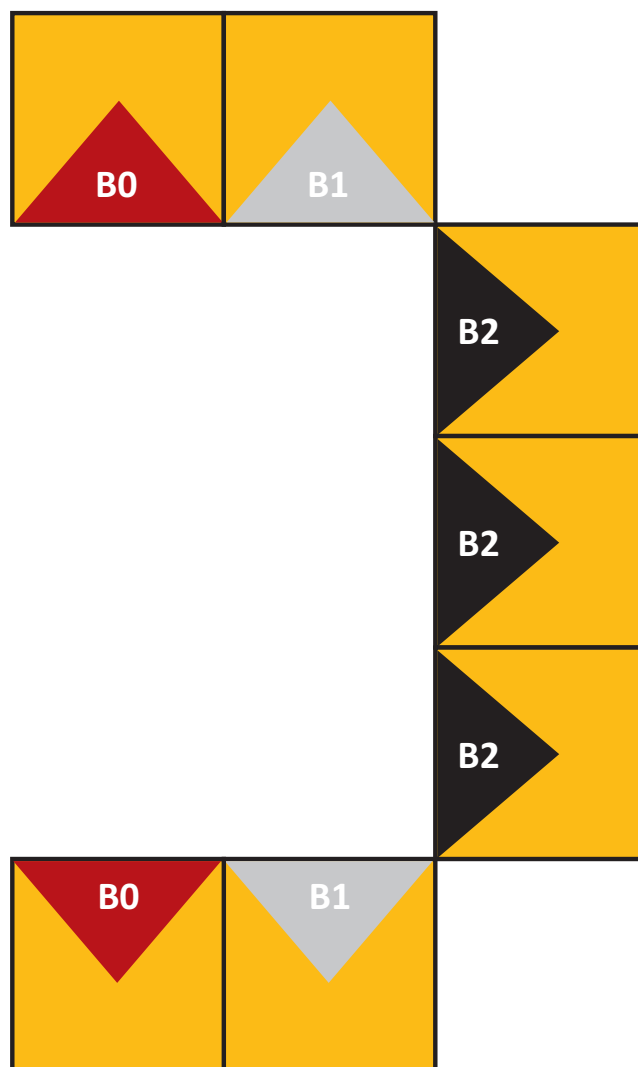


Fig. 1. The two dimensional, cellular automata grid representing a cyclodextrin ring with a variegated analyte cell for chromatographic scale.

as a torus with no edges so that ingredients may pass from one side of the grid to the other. The first 10 rows of the grid does not contain any CD cells so that analyte cells may start there at the beginning of each run to represent a sample injection. One hundred of each analyte are randomly placed within this space so that analytes are intermixed with each other and mobile phase cells.

β -CD cells begin at row 11 in the orientation as in Fig. 1. Oriented on its side the β -CD sites have analytes enter due to their attraction or lack thereof. The side direction that the β -CD faces does not matter since all moving cells may exit one side of the grid and reappear on the opposite side, eliminating analyte and mobile phase cell movement boundaries. β -CD sites were placed in a manner so that they are spaced five cells apart on any side. This type of placement continues until a total of 100 β -CD sites exist, so that stationary phase is present from rows 10 to 204. The remaining 595 rows are left empty for mobile phase at the start of each run. These rows provide an area for the analytes to move into after their interaction with the stationary phase sites. It is in these rows that the analytes will be examined, as in high performance liquid chromatography when analytes leave the column and continue onward to the detector.

Placement of mobile phase cells is random; however, several factors need to be considered to determine their concentration: empty space available in the grid after placement of stationary

Download English Version:

<https://daneshyari.com/en/article/1201211>

Download Persian Version:

<https://daneshyari.com/article/1201211>

[Daneshyari.com](https://daneshyari.com)