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Application of Long Short-Term Memory Recurrent Neural Network in Chromatographic Separation

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Abstract. The chromatographic separation process is a continuous and discrete mixed system. It consists of a fixed bed of chromatographic columns or similar structures, with components separated by valve switching. System parameters need to be controlled during the separation process, making it susceptible to external interference. In actual production, deviations from optimal operating conditions often occur, hindering the full utilization of the SMB chromatographic separation process's capabilities. To unleash the potential of separation systems, results based on simulation models are crucial. This paper digitizes the simulation process, then utilizes Long Short-Term Memory (LSTM) neural networks to train simulation data, understanding the impact of observation parameters on outcomes. By identifying trends in complex parameter changes through LSTM learning, it establishes a foundation for verifying system controllability.

Keywords: Chromatographic, LSTM, SMB.

1. Introduction

Chromatographic separation exploits differences in compound distribution between a stationary phase and a mobile phase to separate mixtures. To achieve this separation, compounds are dissolved in a solvent and injected into a column under high pressure. Each component is driven by the mobile phase, penetrating into the stationary phase within the column. The extent of movement for each component depends on its distribution, as some components with weak interactions (adsorption forces) with the stationary phase are quickly flushed out of the column, while others with stronger interactions take longer to elute [1-3]. Continuous cyclic chromatography is a classic method for achieving continuity on a single-column basis. Fluid can be continuously recycled after separation by simply switching the four-way valve in the loop [4]. As the name suggests, the most typical counter-current device is the Continuous Circular Chromatography (CAC). The directions of motion for the stationary phase and eluent are vertically staggered. Martin was the first to propose such a device. The inlet and outlet are fixed at a point at the end of the loop, and the eluent leaves traces along the axis from all points on the loop, using packing material (stationary phase) within the loop. Thus, due to differences in the adsorption capacity of different components during the elution process, the retention times of the adsorbents also vary. After injecting the feedstock, as the stationary phase rotates, each component

moves along a helical path within the loop, leading to different components moving downward at different rates. The helical pitch of different parts varies, so the position of the helix at the bottom also differs. Finally, separation of different components can be achieved. Continuous sampling can be realized [5-6].

Counter-current separation can also achieve continuous separation. In the field of electrochemical system equipment, its typical mode is the true moving bed. In practical moving beds, it can fully utilize the stationary phase, increasing the utilization rate of the stationary phase. However, it also has its drawbacks: the wear of the bed and the energy consumption of counter-current movement require significant costs. The schematic diagram of its principle [7-8] is shown in Figure 1. The mobile phase circulates in the opposite direction to gravity through a circulation pump in the chromatographic column, while the solid adsorbent continuously moves from top to bottom due to gravity, creating a counter-current between the mobile phase and the stationary phase. This device not only improves separation efficiency but also enables continuous chromatography operations. Within the entire separation apparatus, each column's function can be divided into four functional zones, each playing a different role.

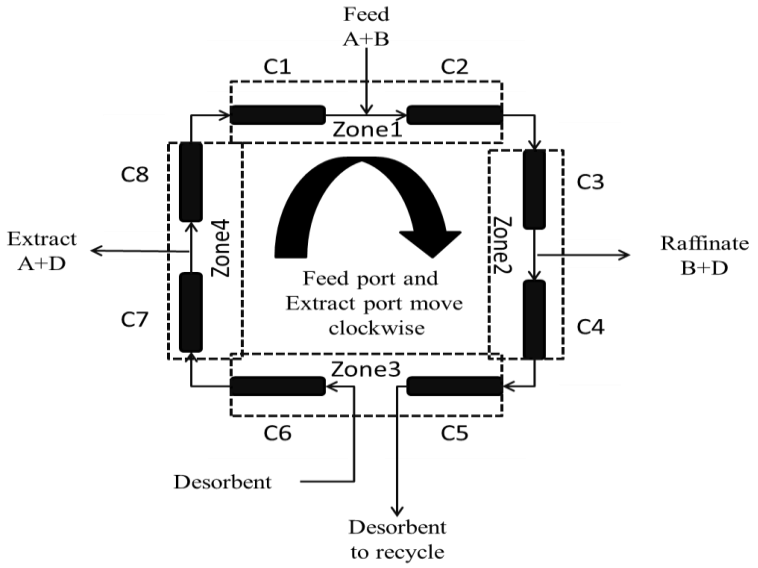


Figure 1. Separation process.

The advent of true moving bed technology has simplified continuous chromatographic operations and significantly improved separation efficiency. The processing capacity and production efficiency of materials have rapidly increased, making industrial chromatographic separation a reality. However, in counter-current systems, the solid adsorbent has moved from top to bottom, inevitably causing bed wear and generating a lot of powder. If these powders flow into the pipelines, they can block them and cause a decrease in flow rate [9-10]. To clean these powders, there are often inconveniences in practical operations, which in itself is adsorption. The loss of adsorbents is often expensive, adding unnecessary cost losses; moreover, it may also lead to pore formation. Changes in the journey may also cause uneven flow rates of the mobile phase, and even cause phenomena such as channeling and backflow, affecting separation quality.

Because of the problems of the real moving bed, people think whether the stationary phase can be truly fixed, and the separation effect can be achieved without the flow of adsorbents in the stationary phase. So in

the 1960s, Sorbax system developed by U.S. UOP company synthesized the advantages of previous beds and avoided their disadvantages. This is the early analog mobile bed. Because of the advantages of this system, it has been recognized by more and more people which is called simulated moving bed [11]. Chromatographic separation struggles to achieve a stable state, primarily due to factors such as system components, mechanical control disturbances, and the combination of adsorbents. Factors like flow leveling can affect the stability of SMB system separations, potentially leading to poor production outcomes. Hence, traditional SMB operations often require adjustments to ensure product yield, such as reducing production capacity and increasing solvent consumption. Therefore, this paper proposes using long short-term memory recurrent neural network intelligent technology for precision prediction of chromatographic separation systems. The main objective is to research precision control for multi-column chromatographic separation in subsequent steps [12-14].

2. Mathematical Model of Chromatographic Separation

Real moving bed of dynamic mathematical model is deduced by using TMB mathematical model for reference. Here, we give an overview of dynamic model, which is mentioned in literature [15]. For TMB, the mass balance of bulk phase is:

$$\frac{\partial C_{i,j}}{\partial t} = D_i \frac{\partial^2 C_{i,j}}{\partial x^2} - v_j^* \frac{\partial C_{i,j}}{\partial x} - \frac{1-\varepsilon}{\varepsilon} k_i (q_{ij}^* - q_{ij}) \tag{1}$$

$$\frac{\partial q_{i,j}}{\partial t} = \frac{\partial}{\partial x} u_s q_{ij} + k_i (q_{ij}^* - q_{ij}) \tag{2}$$

The relevant parameter descriptions are shown in Table 1. Therefore, the model can be converted to each other as follows:

$$\frac{\partial C_{i,j}}{\partial t} = D_i \frac{\partial^2 C_{i,j}}{\partial x^2} - v_j^* \frac{\partial C_{i,j}}{\partial x} - \frac{1-\varepsilon}{\varepsilon} k_i (q_{ij}^* - q_{ij}) \tag{3}$$

$$\frac{\partial q_{i,j}}{\partial t} = k_i (q_{ij}^* - q_{ij}) \tag{4}$$

(4) Substituted into (3), can get:

$$\frac{\partial C_{i,j}}{\partial t} = D_i \frac{\partial^2 C_{i,j}}{\partial x^2} - v_j^* \frac{\partial C_{i,j}}{\partial x} - \frac{1-\varepsilon}{\varepsilon} \frac{\partial q_{i,j}}{\partial t} \tag{5}$$

The adsorption equilibrium for both enantiomers is represented by Langmuir isotherms:

$$q(i,j) = \frac{q_m K_i C_{i,j}}{1 + \sum_{i=1}^{2} K_i C_{i,j}} \tag{6}$$

Table 1. The initial parameters.

Parameter	Nomenclature	Parameter	Nomenclature
$x(cm)$	Axial distance	$Q(cm^3\,\min^{-1})$	Volume flow rate
$k(gL^{-1})$	Comprehensive mass transfer constant	$t(\sec ond)$	Time
$v^*(cm\,\min^{-1})$	Effect velocity of body	$D(cm^2\,\min^{-1})$	Effective dispersion coefficient
$u_s(cm\,\min^{-1})$	Solid flow rate	ε	Bulk void fraction
$C(gL^{-1})$	Mobile phase concentration	i	Material index: A or B
$q(gL^{-1})$	Solid phase concentration	j	Column number: 1, 2, 3, 4, 5, 6, 7, 8
$q^*(gL^{-1})$	Solid phase concentration at equilibrium between solid phase and mobile phase		

3. Simulation and Prediction

3.1. Experimental Environment

The simulated digitization system contains 8 packed columns which was 2-2-2-2 model. The parameters of system were shown in Table 2.

Table 2. The standard parameters for the separation.

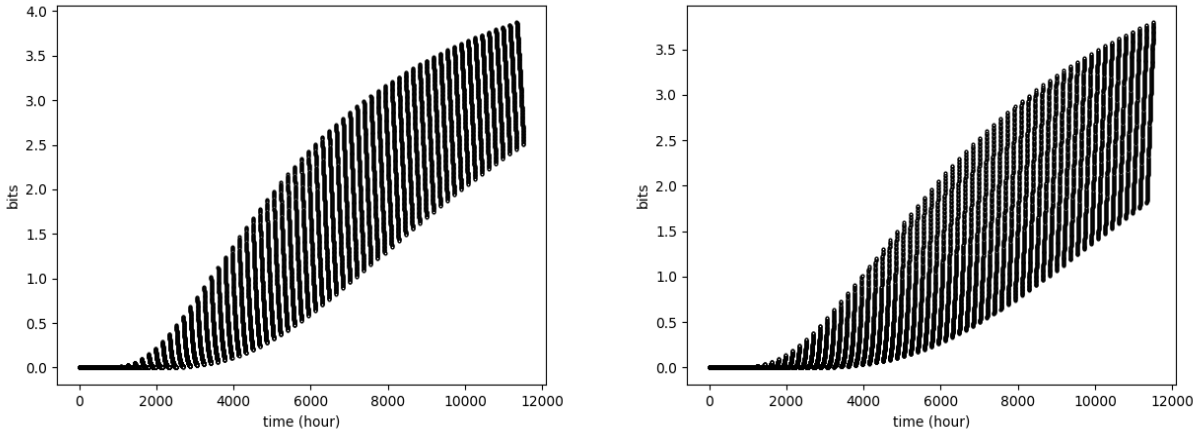
Parameter	Value	Parameter	Value
$L(cm)$	30	$C_{f,i}(gL^{-1})$	5
$d(cm)$	0.46	$\theta(\min)$	3
$q_m(gL^{-1})$	0.8	$Q_I(cm^3\,\min^{-1})$	6.980
$K_A(gL^{-1})$	0.05	$Q_{II}(cm^3\,\min^{-1})$	6.808
$K_B(gL^{-1})$	0.10	$Q_{III}(cm^3\,\min^{-1})$	8.716
$D_A(cm^2\,\min^{-1})$	0.23	$Q_{IV}(cm^3\,\min^{-1})$	4.619
$D_B(cm^2\,\min^{-1})$	1.25	ε	0.8

All computations were performed in MATLAB R2016a on a PC equipped with an Intel Core i7-3770K 3.53GHz processor, 16GB RAM, and running Windows 10. Simulation process data were written into data text documents via MATLAB file pointers, ensuring the experimental data's authenticity, reproducibility, and potential for public disclosure.

3.2. LSTM Training

Due to the nonlinear nature of the separation system and the multitude of parameters involved, which are highly sensitive, we employed 64 switching cycle data rounds to train the long short-term memory neural network for weight training in this process, aiming to determine the predictability of the system.

There is a total of 12,000 data points, with 90% used for training and 10% for testing. The original images are shown in Figure 2, while the testing results are depicted in Figure 3 and 4. The training results indicate that despite the complexity of the process, the testing data fits the data trends well. For material B, the total Mean Squared Error (MSE) for the training data is 0.012, and for the testing data is 0.016. For material A, the total Mean Squared Error (MSE) for the training data is 0.0193, and for the testing data is 0.0610. Thus, the prediction results are accurate, providing a foundation for achieving controllability.



(a) Extract Material B **(b)** Raffinate Material A

Figure 2. The purity of material B and A by the time.

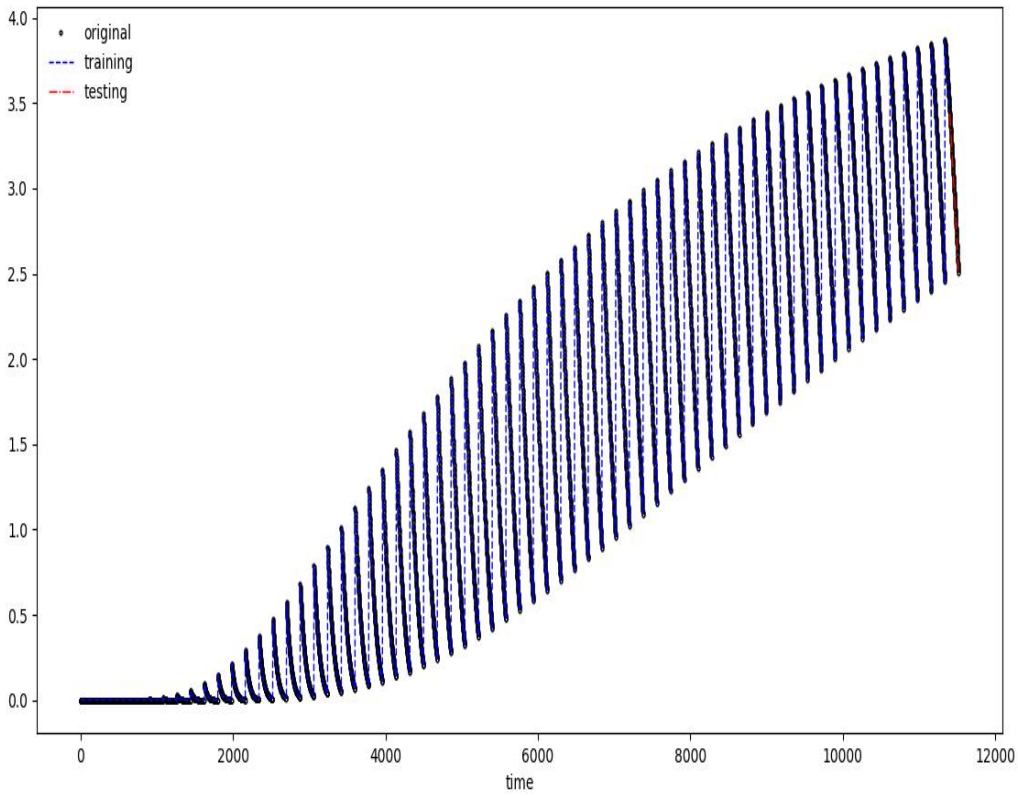


Figure 3. Using LSTM predict separation process of material B.

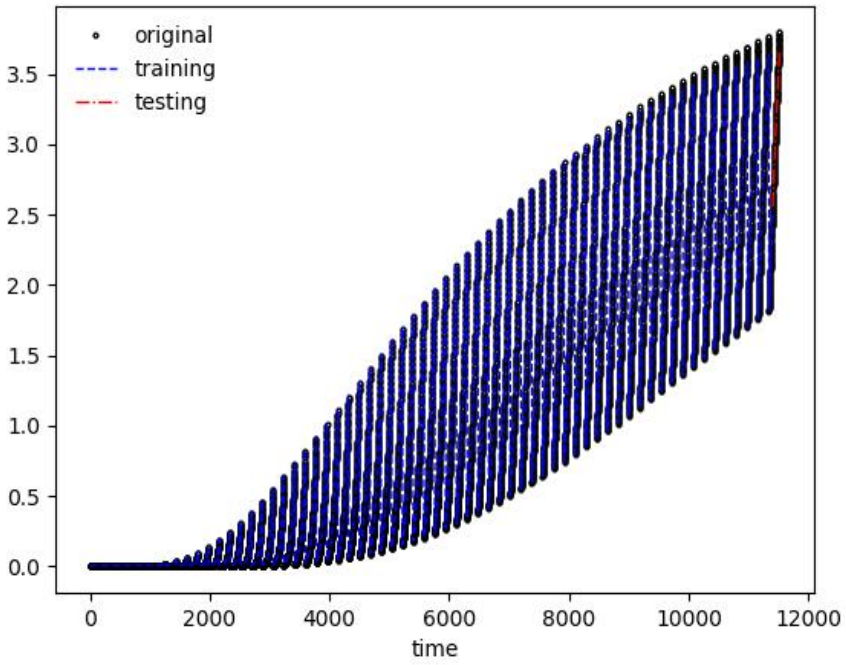


Figure 4. Using LSTM predict separation process of material A

4. Conclusion

Despite the complexity of the chromatographic separation process, influenced by numerous sensitive parameters, it is not inherently unpredictable. Through computer simulations and training with long short-term memory recurrent neural networks, it has been discovered that the system' s parameters and the solubility of the final extract and raffinate can be predicted, laying the groundwork for further control. Control based on deep neural networks will possess adaptability and robustness. Traditional parameters are adjusted through manual experience, thus optimal parameters cannot be found, whereas training and searching with deep neural networks undoubtedly bring significant economic benefits to the production process.

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