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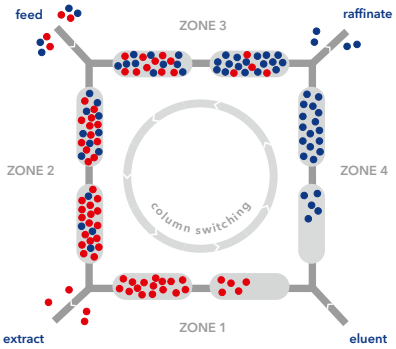
Simulated Moving Bed (SMB) inline sampling



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SUMMARY

During the development of a SMB method, it is helpful to determine the concentration profiles in the four SMB zones. An inline sampling was established in addition to the sampling at the extract and raffinate outlet. Therefore, a manual injection valve was implemented as sampling valve before the inlet of column 1 in the AZURA lab SMB system. With this setup a separation method of paracetamol and caffeine was optimized, and samples were taken in all four zones. The resulting concentration profiles help optimizing the method.

INTRODUCTION

In the development process of a SMB method it is necessary to determine the target substances in extract and raffinate. As the complexity of the SMB process is higher than the classical batch process, the development of the method comes with higher demands on process design and control. One way of monitoring the SMB process is the collection of both raffinate and extract for one switch or a whole cycle and determination of target substance distribution. This process is easily applied in small, lab-scale SMB processes and helpful for SMB method development (Rev. 1: TechNote VTN00012). This approach is more challenging in larger scale SMB as the volumes of the two outlets will significantly increase and sample taking could be more difficult due to constructional reasons. Another way of monitoring the SMB process is the inline sampling. Here, a sample is taken at a defined time point between two switches. For this inline sampling, a valve is implemented before the inlet of one column and it will be moved through the system with that column, see **Fig. 1**. With this valve a sample of the stream can be taken. This enables the composition of the liquid phase at one point of every switch and in all four zones to be determined.

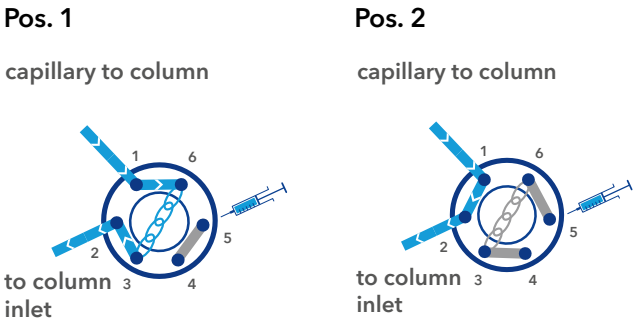

Fig. 1 Operation mode of the valve for the inline sampling (6-port 2-position).

Simulated Moving Bed (SMB) inline sampling

RESULTS

The manual valve was integrated in the flow path before the inlet of column 1. The operation mode of the valve is shown in **Fig 1**. The used SMB set-up was a 2:2:2:2 configuration with two columns in each of the four zones **(Fig. 2)**. An SMB process for the optimization of caffeine and paracetamol separation was run for ten cycles to reach a steady state. In the eleventh cycle samples were taken in the middle of the separation time between two switches. **Fig. 2** shows the SMB system setup with two columns in every zone. Chromatograms are positioned at the corresponding position of the flow path. The chromatograms and the corresponding position in the system help finding possibilities to optimize the method. The chromatograms in zone 4 show that both columns do not contain any raffinate. Additional to that no extract enters zone 3. This indicates that there is still room for improvement regarding the effectiveness of the separation. Higher flow rates in zone 2 and 3 could lead to a better performance of the system. Further, a higher feed flow rate could be realized and thus increase the productivity of the process. During cycle 14 two samples were taken between two switches, the first sample after 0.5 min and the second sample after 1.5 min. In **Fig. 3** the resulting concentration profile of paracetamol and caffeine is shown. This overview also shows the potential areas of improvement regarding the SMB process.

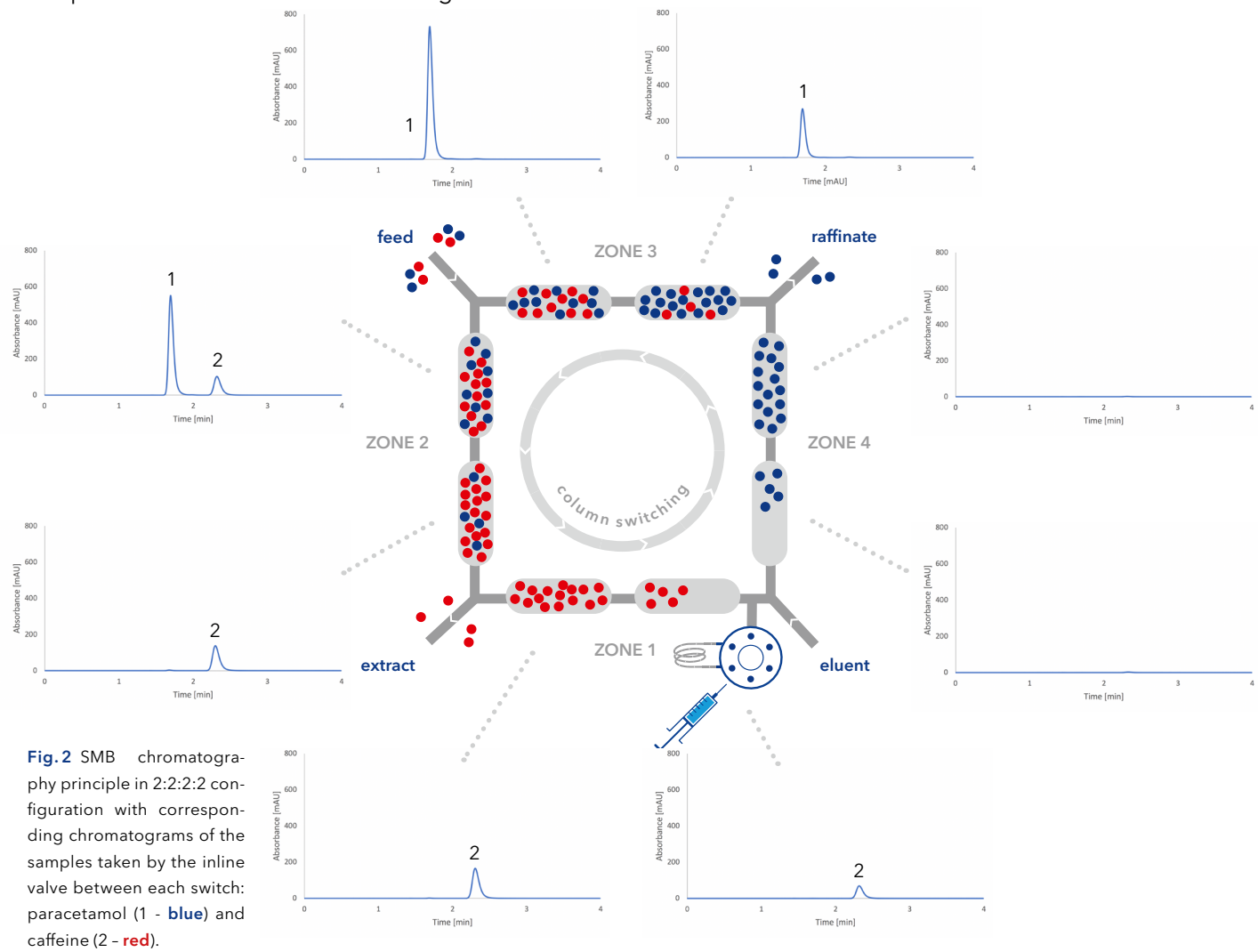

Fig. 2 SMB chromatography principle in 2:2:2:2 configuration with corresponding chromatograms of the samples taken by the inline valve between each switch: paracetamol (1 - **blue**) and caffeine (2 – **red**).

SAMPLE PREPARATIONS

In the beginning of the sampling the sample valve **(Fig. 1)** is in position 2 and the sample loop is implemented in the flow path. At the time of sampling the valve is switched manually to position 1. The switching must happen very fast to prevent high back pressure. With a syringe the liquid is pushed out of the loop into a sample vial. Then the loop is filled with eluent before it is switched back into the flow.

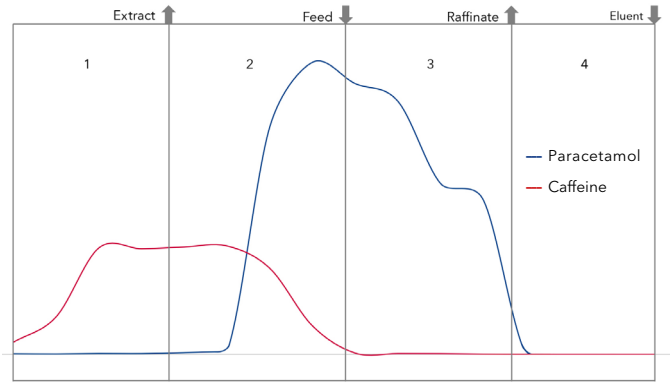

Fig. 3 Concentration profile of paracetamol and caffeine in the 4 SMB zones.

CONCLUSION

The inline sampling facilitates the process of sample taking during the SMB method development tremendously. Compared to samples taken from the outlets, the sample volume is much smaller as it only depends on the size of the sample loop used in the valve. It is possible to take samples at different points in the flow path and to gain knowledge of the concentration profiles of the two target substances in all four zones. This fastens the process of developing and optimizing a new SMB method.

MATERIALS AND METHODS

Tab. 1 Method parameters

	Feed (ml/min)	Eluent (ml/min)
In	0.2	4
Column temperature	ambient	
Cycle time	18.8 min	

Tab. 2 Material

Standard	CAS	Feed concentration (g/l)
Caffeine	58-08-2	1
Paracetamol (Acetaminophen)	103-90-2	6

Tab. 3 System configuration

Instrument	Description	Article No.
AZURA lab SMB system	SMB, biocompatible system, lab scale	A29100
Flow meter	3x M13 1x M12	A29800 A5394
Column	8x Eurospher II C8 150x8 mm, 100-15, 15 µm	15GE081E2Q
Software	Purity MCC	included in A29100

RELATED KNAUER APPLICATIONS

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