INFORMATION THEORY AND OTHERS FOR STEROIDS SEPARATION

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ABSTRACT
Chromatographic analysis, defined as techniques used for the separation of a mixture of compounds by their distribution between two phases, was introduced in 1901 by Russian botanist Mikhail Semyonovich Tsvet. Since then, the chromatography is used in chemistry, biology, medicine and other domains as analytical techniques. An original mathematical model for mobile phase optimization on High Performance Thin-Layer Chromatography has been developed and its performances on two sets of steroids are presented. The mobile phase optimization process proved to be able to provide accurate, precise and reproducible method useful in characterization and analysis of chromatographic parameters of studied steroids sets.

INTRODUCTION
Chromatographic analysis, defined as techniques used for the separation of a mixture of compounds by their distribution between two phases, was invented in 1901 by Russian botanist Mikhail Semyonovich Tsvet, during his research on plant pigments [1]. It is well known that an important task in separation of compounds from a mixture by chromatography is chousing of the proper mobile phase [2]. Researches were done for optimization of the column liquid chromatography [3] and of the high performance liquid chromatography [4].
Starting with results previous obtained in optimization of the mobile phase of chromatography separation [5,6], the aim of the research was to present the performances of an original mathematical model for mobile phase optimization and its application on High Performance Thin-Layer Chromatography.

MATHEMATICAL MODEL
The original optimization procedure start from the idea that into a mixture of three solvents the quantitative measure of the choused chromatographic parameter is dependent on composition of mobile phase through an equation of dependency with six or seven parameters, taking into consideration the molar fraction of the solvents.
The quantitative measure of a chromatographic parameter put in a mixture of three solvents depends on the composition of mobile phase. The dependence equation could be one with six or with seven parameters (eq. 1 and 2):

$$M6(x_1,x_2,x_3) = a_1x_1 + a_2x_2 + a_3x_3 + a_4x_1x_2 + a_5x_1x_3 + a_6x_2x_3 \quad (1)$$

$$M7(x_1,x_2,x_3) = a_1x_1 + a_2x_2 + a_3x_3 + a_4x_1x_2 + a_5x_1x_3 + a_6x_2x_3 + a_7x_1x_2x_3 \quad (2)$$

where x_1, x_2, x_3 are molar fraction of solvents used *(a number of three, where $x_1 + x_2 + x_3 = 1$)*, *M6* and *M7* are estimators and then predictors of choused chromatographic parameter, and a_1, a_2, a_3, a_4, a_5, a_6, a_7 are coefficients first determined based on the best estimation of choused chromatographic parameter and then used in prediction of used parameter for any composition of mobile phase.
Three chromatographic parameters were modeled starting from Eq. (1) and Eq. (2): the objective function (F_{ob}), the resolution for separation (RS), and retention factor (RF).

OPTIMIZATION MODEL
By applying of one out of three parameters used in optimization on a series of p experiments, there results a M_{ob} matrix with one row for each experiment. The elements of M_{ob} matrix represent the values of chromatographic parameter that is modeled by using Eq.(1) or Eq.(2). The optimization algorithm has a unique solution for $p \geq 6$ (Eq.(1)), and for $p \geq 7$ (Eq.(2)), respectively.
A system can be build for each row from M_{ob} matrix with p linear equations (where $p = 6$ (Eq.(1), and $p = 7$ (Eq.(2)), respectively):

$$M_{ob}(j) = a_1x_1 + a_2x_2 + a_3x_3 + a_4x_1x_2 + ... \quad (3)$$

where x_i are molar fractions of each solvent ($i = 1, 2, 3$) that enter into the composition of the e_j eluent ($j = 1, 2, \ldots, p$).
To the system presented in Eq.(3), the least squared method was applied for construction of the system with unique solution. Then, the Gaussian method was applied to found the solution. The solutions for the systems from Eq.(1) and Eq.(2) are:

$$A0 = (a_{01}, a_{02}, \ldots, a_{06}) \quad \text{- for Eq.(1)}$$
$$A0 = (a_{01}, a_{02}, \ldots, a_{07}) \quad \text{- for Eq.(2)} \quad (4)$$

The *A0* coefficients were used for prediction of the chromatographic parameter of interest by Eq.(1) or Eq.(2).

RESULTS AND DISCUSSION
The mobile phase optimization application for chromatographic separation which used mixture's of three solvents was created, and is available at the following URL: http://vl.academicdirect.org/molecular_dynamics/mobile_phase_opt/
The optimization procedure was applied on two sets of steroids [6, 7], starting from the results obtained by high performance thin-layer chromatography with three solvents. The retention factor was considered as the most important parameter into chromatography and the results of optimization refer this factor.
For both sets of steroids the optimum mobile phase was obtained with the following generic equation:

$$\Delta RF = a_1x_1+a_2x_2+a_3x_3+a_4x_1x_2+a_5x_1x_3+a_6x_2x_3+a_7x_1x_2x_3 \quad (5)$$

The composition of the optimum mobile phase obtained previously and through optimization procedure are in Table 1.

Table 1. Characteristics of the optimum mobile phase

Abb.	Mobile phase composition	Optimum mobile phase	
		Prisma	Optimization
Ster_01	Chloroform – Methyl-Ethyl-Cetone – Cyclohexan	52 : 28 : 20	54 : 28 : 18
Ster_02	Chloroform – Cyclohexan – Methyl-Ethyl-Cetone	50 : 30 : 20	60 : 13 : 27

There were not identified statistically significant differences between experimental retention factor and the values obtained by the used of proposed optimization method, for none of studied sets of compounds ($p > 0.05$).
Applying the mathematical model to the experimental data the graphical representation of the retention factor at optimum mobile phase presented in figure 1 was obtained (Zmin = 0.06). The spots of dark color indicate the optimum mobile phase of obtained by the mathematical model.
A graphical representation of the retention factor estimated through optimization versus retention factor obtained from experimental data for one compound from Ster_02 set is presented in figure 2.

Figure 1. The diagram of the optimized retention factor (Ster_02 sample)

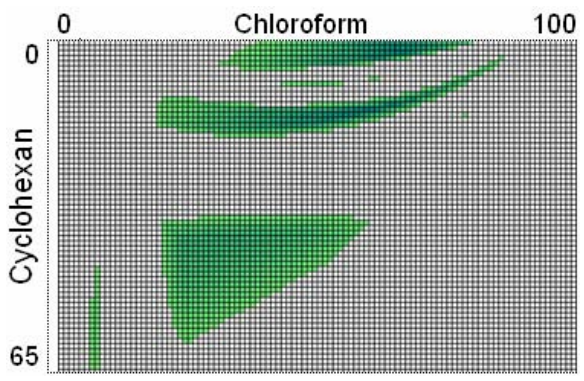
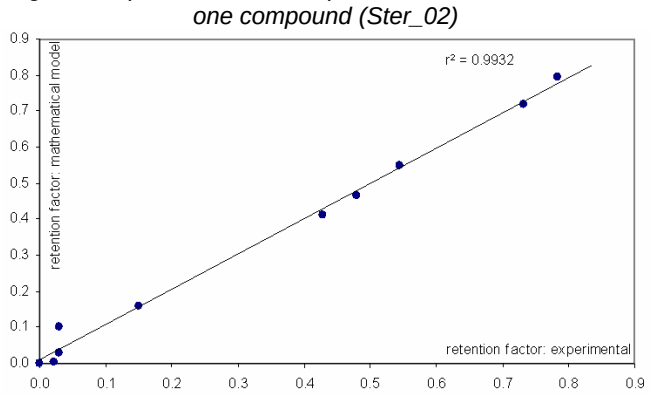


Figure 2. Optimized versus experimental retention factor for one compound (Ster_02)



CONCLUSIONS
The mathematical model proved to assure accurate results on analysis of the separation of both samples of steroids. More researches are necessary to be done in order to analyze the stability of the model.
The proposed mathematical model open a new pathway in separation of chemical compounds, and could become a useful method in separation of steroids biological or natural sources (as for example from drugs).

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The chromatography is used in chemistry [2], biology [3], and medicine [4] as an analytical technique.

An original mathematical model for mobile phase optimization on High Performance Thin-Layer Chromatography was developed and its performances on two sets of steroids are presented.

The mobile phase optimization process proved to be able to provide accurate, precise and reproducible method useful in characterization and analysis of chromatographic parameters of studied steroids sets.

Keywords: Information theory, Steroids, Optimization of Mobile Phase, High Performance Thin-Layer Chromatography

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