Letter to the Editor

Influence of pressure on the maximum production rate in preparative liquid chromatography

Sir,

The influence of the available inlet pressure on the production rate in preparative chromatography is an important practical problem. It is critical that the users understand it properly. Snyder and Cox[1] have recently published a paper discussing the optimization of the experimental conditions for maximum production rate in preparative chromatography, in the touching band case. In this pedestrian reformulation of the classical treatment by Knox and Pyper[2], these authors make the following commentary: "Golshan-Shirazi and Guiochon[3] pointed out that there is an optimum pressure for a given preparative separation, which is true but misleading. Their optimum pressure corresponds to the case when the reduced velocity $v \ll 3$, which is never a good choice in practice [*i.e.*, this case corresponds to lower N_0 (column plate number for a small sample) and longer run time]. In any case, pressures larger than their "optimum" can in principle always be used to achieve higher production rate by using larger particles (so as to increase v). Of course practical considerations of various kinds impose very definite limits on maximum pressure". This statement prompts *two* comments on our part.

First, in our referenced paper[3], at the bottom of p. 1376, we have written: "It is seen [in Fig. 6c] that the production rate increases steadily with increasing pressure at which the equipment can operate, provided the optimum column is used". Similar comments can be found in other places, all underlining the gain in production rate associated with operating the column at high velocities and trading a reduction in the column efficiency for a decrease in the cycle time. In other words, our conclusions are precisely the opposite of what Snyder and Cox have incorrectly stated as being in our work.

To correct the record:

(i) The maximum production rate which can be achieved for any given separation increases with increasing available inlet pressure. This is illustrated in Fig. 6c of ref. 3. However, the optimum values of the column length, particle size, mobile phase velocity and sample size which permit the achievement of this maximum production rate vary also with the available pressure.

(ii) For a given column (*i.e.*, constant column length and particle diameter), there is an optimum inlet pressure, since there is an optimum mobile phase velocity[3]. The lowest value of v considered in Tables V–XI of ref. 3 is 55, a number considerably larger than the $v \ll 3$ misquoted by Snyder and Cox[1]. Fig. 11 of ref. 3 shows that, for a given column, the production rate increases with increasing v up to 100, where the plot stops.

(iii) In practice, for most separations and for a given value of the inlet pressure, the optimum value of v is very high, often several hundred. This result has been obtained by theoretical analysis of the solutions of the mass balance equations of chromatography[3], as well as by a Simplex optimization of the experimental conditions[4].

Secondly, we have always believed in the promise: "Then you will know the Truth, and the Truth will make you free"[5], a promise which applies well to science. It is difficult to understand how a truth may be misleading, unless it is presented deviously so as to mislead the reader as occurred in ref. 1. In their classical paper, Knox and Pyper[2] noted that their approach neglected the competition between the mixture components for interaction with the stationary phase. The authors of the present paper[1] suggest optimum conditions which are incorrect since we know that components interact in accordance with the displacement and tag-along effects[6,7], with experimental proof in refs. 8 and 9.

We are at a loss to understand the origin of the factual error made in ref. 1 and regret that the review process was unable to catch it.

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