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Letter to the Editor

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

Reply to the letter of S. Golshan-Shirazi and G. Guiochon

Sir,

We welcome the opportunity to comment on the letter of Golshan-Shirazi and Guiochon[1] with respect to our previous paper[2]. These authors cite a specific passage from ref. 2 and then proceed to generalize on the remainder of that article. Concerning the specific passage (which deals with their own published work[3]), we can say that (a) the passage represents a misinterpretation on our part of Fig. 6 for ref. 3, and (b) this error was further compounded by an intuitive —but totally wrong— analysis of the misinterpretation. Unfortunately two "wrongs" did not make a "right". We are also surprised that this obvious error was not caught during inhouse reviews or its subsequent processing by three outside reviewers for the journal. However, the text in question appears in ref. 2 as a footnote which in no way compromises the remaining discussion or conclusions of that paper.

The more important issue raised by Golshan-Shirazi and Guiochon deals with the pertinence of our treatment[2] for separations which involve "... the competition between the mixture components for interaction with the stationary phase". They assume that the existence of this competition invalidates the various conclusions reached by Knox and Pyper[4] in their elegant treatment of preparative liquid chromatographic separation as a function of sample weight and volume, column efficiency and mobile phase strength. We disagree with this conclusion.

We have reported modeling studies[5] and supporting experimental data[6] which treat the case of the 2-compound sample in preparative liquid chromatography. This work shows for moderately overloaded columns (and consequent "touching band" separations as discussed by Knox and Pyper[4]) that sample interaction leads to a significant increase in allowable sample size *vs.* the case where interaction effects are ignored. This in turn increases the predicted production rate (grams per hour of purified product) by a constant factor (so-called "blockage effect") for a given value of the separation factor α), but it has little affect on the optimum value of the plate number N (for maximum production rate). For this case, therefore, the treatment of ref. 2 is still appropriate; our conclusions with regard to production rate as a function of column conditions, maximum allowable pressure, etc. are still valid.

We have since extended the conclusions of refs. 5 and 6 (see also ref. 7) to the case of more heavily overloaded separations —where the two bands leaving the col-

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umn overlap more or less extensively[8]. Again we find that interaction effects lead to higher sample loadings than are predicted in the absence of interaction, but the effect on conditions for maximum production rate is parallel to that shown by Knox and Pyper[4] for touching-band separations with no interaction. Thus, for recovery of a certain fraction of product charged to the column (50, 95 or 99%), a larger sample weight can be separated and a lower plate number is required. However, the optimum choice of column conditions (particle size, column length, flow-rate) is still understandable in terms of the treatment of ref. 2. These optimum column conditions depend on two factors: the value of α for the separation in question and the desired recovery of purified product.

The simplifications suggested by the Knox-Pyper treatment[4] have since been found[9] to provide a comparable picture of preparative liquid chromatographic separations that use gradient elution. However, these advances in our understanding of preparative liquid chromatography necessarily involve some compromise. A more rigorous treatment as developed by Guiochon and his collaborators in several dozen recent papers should in principle be more accurate for specific cases. Our aim has instead been the uncovering of more general (and more approximate) recommendations that can facilitate the practical development of liquid chromatography methods for preparative separation. Similar differences in approach characterize much of chromatography; practical chromatographers have generally benefitted from both the complex, rigorous treatment and its simplified, more approximate counterpart. We welcome quantitative comparisons of these two approaches, so that any limitations of the simplified treatment can be made known.

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