**SUPPLEMENTARY MATERIAL**

**Critical comparison of background correction algorithms used in chromatography**

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**S-1 – Overview of the experimental blank measurements**



**Figure S-1: Experimental blank measurements used as the drift component.**

In **Figure S-1** an overview is given of the different experimental measurements used as the drift component for the generated data. Note that in the present study difficult to correct sharp transitions such as those occurring near the end of the chromatogram were not taken into account as usually no peaks would be expected to elute near this region. The total length of the signals (in terms of number of data points) was (from background 1 to 5): 2400, 2400, 4801, 72001 and 187.

This is important because a lower number of data points will make it more difficult to distinguish between peaks and noise due to how we have generated the noise (addition of random numbers drawn from a normal distribution, not entirely realistic for short measurements). However in that case it is still valuable to see which methods can sufficiently distinguish between these.

**S-2 – Analysis of experimental peak shape**

**Table S-1: Height normalized SSE/MSE and AIC values for peaks 1-6 shown in Figure 2.**



**Table S-2: Determined Peak Parameters for MP-VII and EMG Distribution functions.**



**S-3 – Comparison of smoothing and drift correction methods**



**Figure S-2: Minimum RMSE surfaces for the different smoothing methods for backgrounds A, B, C, D, E (corresponding to the backgrounds 1-5 shown in Figure S-1) and previously drift corrected using either 1) LMV, 2) Backcor, 3) MM, 4) asLS, 5) arPLS or 6) airPLS.**



**Figure S-3: Minimum RMSE surfaces for the different drift correction methods for backgrounds A, B, C, D, E (corresponding to the backgrounds 1-5 shown in Figure S-1) and previously smoothed using either 1) WF, 2) WHIT, 3) FF, 4) SASS or 5) SG.**

In **Figure S-2** and **S-3** an overview is given of all the obtained minimum RMSE values. As shown, the “best” performing method is dependent on the baseline itself, however in most cases arPLS and LMV methods showed the lowest RMSE. Note also that the RMSE surfaces obtained in this way were (mostly) very close together.



**FIGURE S-4: A) RMSE surfaces obtained for the various drift-correction methods when no smoothing is performed prior to the drift correction for background 2 in Figure S-1. Methods are indicated by the coloured dots. B) Bottom view (lowest values) resulting from the overlaid RMSE surfaces.**



**FIGURE S-5: A) RMSE surfaces obtained for the various drift-correction methods when no smoothing is performed prior to the drift correction for background 2 in Figure S-1. Methods are indicated by the coloured dots. B) Bottom view (lowest values) resulting from the overlaid RMSE surfaces.**

In **Figure S-4** and **S-5** an overview is given of the obtained minimum RMSE values for the different drift correction methods as applied to background 2 in **Figure S-1**, without having performed prior smoothing. In **Figure S-4** the RMSE was calculated between the sum of known noise and drift components and the background estimated by the algorithm. In this case it is clear that the Autoencoder performed best as it was the only method capable of both smoothing and drift correction. For most other algorithms the RMSE increased with an increase in noise, which is expected as these could not perform smoothing, hence the increase in RMSE is directly due to the addition of the noise. In **Figure S-5** the RMSE was calculated between the known drift component and the background estimated by the algorithm. This highlights that most drift correction algorithms do no perform significantly worse in terms of determining the drift when high amounts of noise are present. The only exceptions were the LMV and airPLS methods.



**Figure S-6: Relative (%) errors in peak area versus SNR at different noise levels for the different methods. Corresponding to average SNR’s of: 55 ; 18 ; 11 ; 8 ; 6 at five different additive noise levels (1 to 5, corresponding to = 0.011 ; 0.033 ; 0.055 ; 0.077 and 0.1).**

In **Figure S-6** an overview is given of all the obtained relative errors for one of the signals from background 2, containing a peak coverage of 35.2% and variable noise intensity. This signal was initially smoothed using SASS. As shown, the different drift correction methods respond differently to the increasing noise intensity. Generally, only the peaks with low SNR are affected. While airPLS tends to start underestimating the drift in the presence of high noise, many of the other methods tend to begin overestimating the drift. It is also shown that with the addition of higher noise levels the low SNR peaks are completely removed when the autoencoder is used.