AN AUTOMATED COMPUTATIONAL PIPELINE FOR RETENTION TIME ALIGNMENT ACROSS LC SYSTEMS

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SUMMARY

Retention time shifts in liquid chromatography (LC) are unavoidable. Absolute retention times are highly dependent on column and analysis conditions which can become an obstacle to comparing chromatographic data across LC systems. Here we demonstrate an automated approach for chromatogram alignment:

- **Employs a combination of digital signal processing techniques and nonlinear regression**
- **Constructs a projection model between retention times from one chromatogram to another**
- **Wavelet deconvolution provides an effective preprocessing step for noise & background removal**
- **The algorithm can align complex chromatograms, such as mAb Tryptic digests, across different LC systems.**

METHODS

The algorithm takes a set of raw chromatograms: sequences of regularly sampled retention time and intensity pairs. (Figures 2a & 3a)

It first applies some data preparation processing using wavelet deconvolution to simultaneously remove noise and any background matrix effects which might adversely influence downstream processing. (Figure 1)

An iterative approach is used to find and refine “mapping vectors”, where a mapping vector relates a raw retention time in one chromatogram to a raw retention time in another. (Figures 4a & 4b)

A generalized additive model (GAM) is used to model the nonlinear nature of the retention time mappings across chromatograms. (Figure 4c)

Finally, the resulting transform is used to map the retention times of the raw chromatograms into an aligned space. (Figures 2b & 3b)

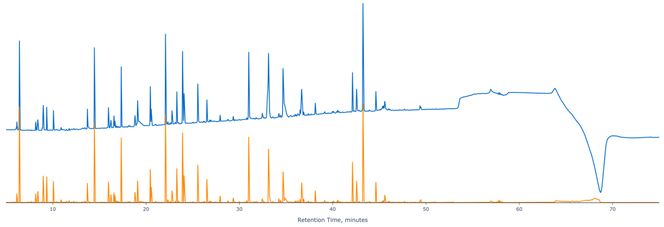

Figure 1: Noise & background removal. Raw chromatogram (Blue). Preprocessing (Orange)

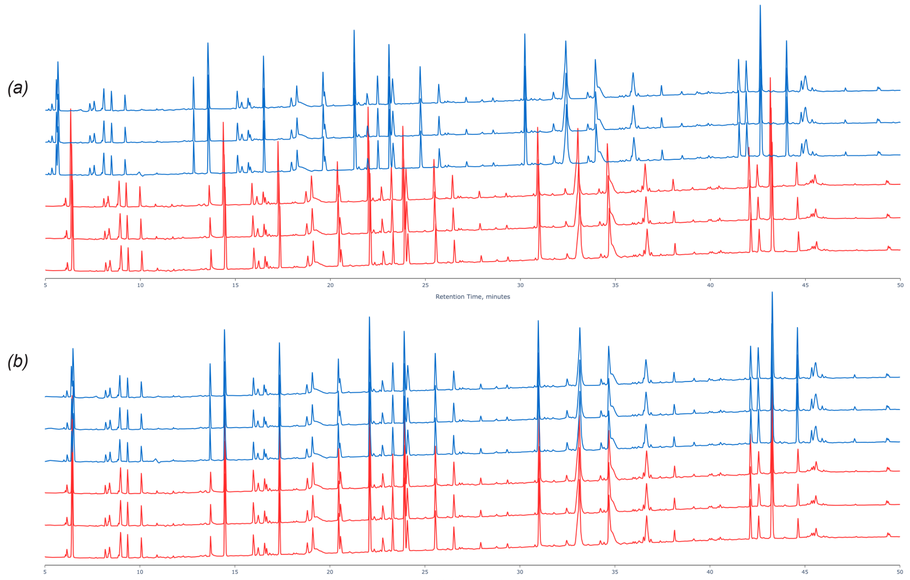

Figure 2. NIST mAb Tryptic digest chromatography data. ACQUITY™ PREMIER CSH™ (Waters Corporation) C18 1.7µm 2.1 x 100mm (Blue) ACQUITY CSH C18 1.7µm 2.1 x 100 mm (Red)
(a) Unaligned; (b) Aligned

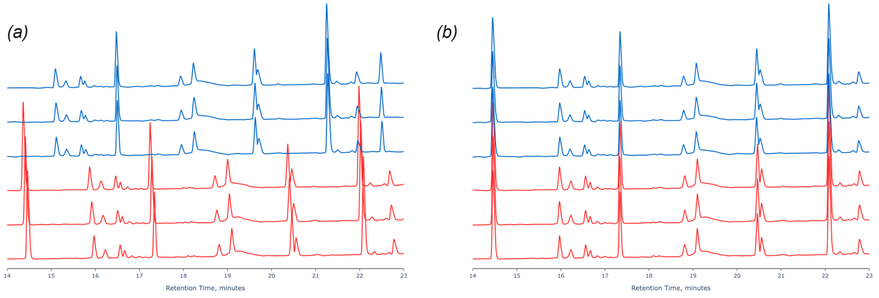

Figure 3. Zoomed area of data from Figure 2
(a) Unaligned; (b) Aligned

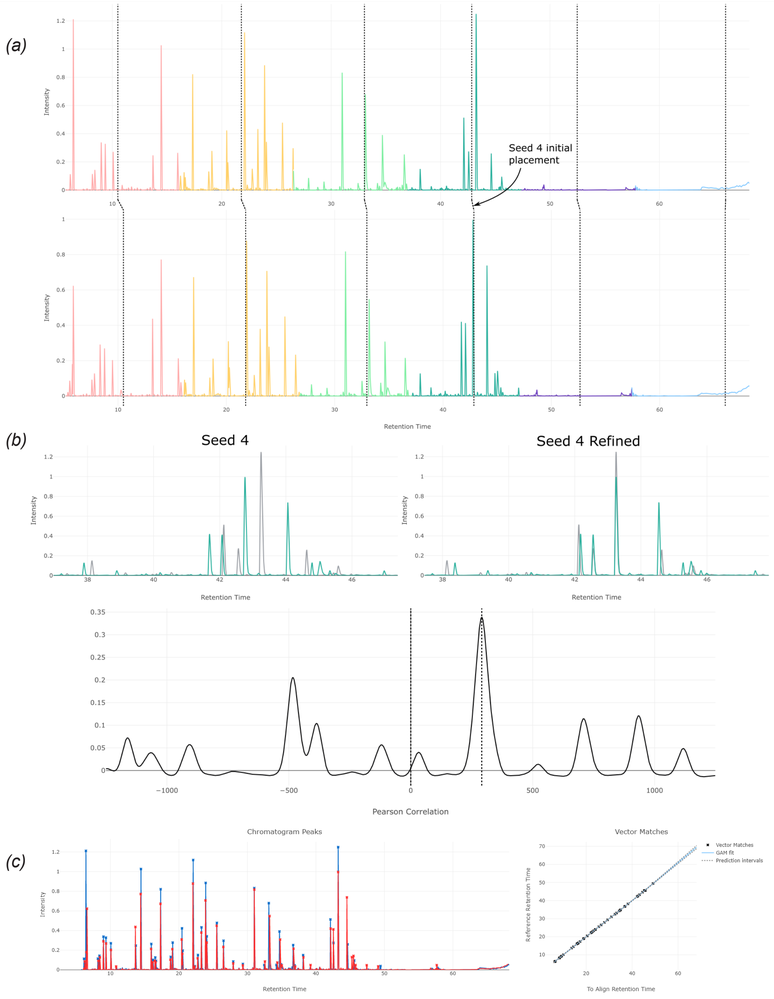

Figure 4. Intermediate stages of the processing pipeline
(a) Seed vector placement; (b) Seed vector refinement; (c) GAM fitting

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