Modeling Background Noise for Denoising in Chemical Spectroscopy

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Talk Outline

Problem Formulation

An Algorithm for Denoising
  Modelling the Noise
  Estimating Coefficients
  Segmentation
  Tikhonov Regularization

Numerical Results

Conclusions and Future Work
MALDI-TOF Mass Spectrometer

We will consider data sets obtained via Matrix Assisted Laser Desorption/Ionization Time Of Flight Mass Spectrometer.

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► Analyte sample is placed in a matrix solution.
► Pulsed laser fired at mixture, ionizing analyte.
► Analyte ions travel along a path of known length, striking a detector.
► Time of flight can be used to determine mass to charge ratio.
Mass Spectrum

Resulting data is a set of 50,000-100,000 data pairs (time/mass-to-charge ratio and intensity). Our spectra will be from SRM 2881, a polystyrene, obtained from NIST. Noise from various sources can lead to uncertainty (see Guttman, Flynn, Wallace, and Kearsley 2009).

![Figure: Analyte(red) and corresponding background(blue), low noise](image)

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Overview

- Fit background spectrum to stochastic differential model
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- Use Tikhonov regularization on each segment
Background Model

We fit the analyte-free spectrum to a Stochastic Differential Equation with time dependent coefficients

\[ dX_t = (a_0(t) + a_1(t)X_t)dt + b_0(t)X_t(t)dW_t \]

\( \{W_t\} \) is a Wiener Process, \( W_t - W_s \sim N(0, t - s) \), \( s < t \)
Discretization

Given the background data \( \{ X(i) \} \) at discrete points, we use Euler-Maruyama discretization:

\[
\Delta X(i) = (a_0(i) + a_1(i)X(i)\delta + b_0(i)X(i)\Delta W_i
\] (1)
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\]

(1)

Given a window size for regression \( h \), we use the Epanechnikov Kernel

\[
K_h(z) = \frac{3}{4h}(1 - z^2)
\]

for \( z \in (-1, 0) \) and \( K_h \equiv 0 \) off \((-1, 0)\).
Estimating $a_0, a_1$

In order to estimate $a_0, a_1$ at each $i$, we look to minimize

$$\min_{a_0, a_1} \sum_{j=1}^{N} \left( \frac{X(j + 1) - X(j)}{\delta} - a_0(i) - a_1(i)X(j) \right)^2 K_h \left( \frac{\delta(j - i)}{h} \right).$$

(2)
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(2)

For $Y(j) = X(j + 1) - X(j)$, $\tau_{ij} = \frac{\delta(j - i)}{h}$

$$\tilde{a}_0(i) = \frac{\sum Y(j)K_h(\tau_{ij}) - \delta a_1(i)K_h(\tau_{ij})}{\delta K_h(\tau_{ij})}.$$
Estimating $a_0, a_1$

In order to estimate $a_0, a_1$ at each $i$, we look to minimize

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\min_{a_0, a_1} \sum_{j=1}^{N} \left( \frac{X(j + 1) - X(j)}{\delta} - a_0(i) - a_1(i)X(j) \right)^2 K_h \left( \frac{\delta(j - i)}{h} \right).
$$

For $Y(j) = X(j + 1) - X(j)$, $\tau_{ij} = \frac{\delta(j-i)}{h}$

$$
\tilde{a}_1(i) = \frac{1}{\delta \left( \sum K_h(\tau_{ij}) \sum K_h(\tau_{ij})X(j)^2 - \left( \sum K_h(\tau_{ij})X(j) \right)^2 \right) \ast \left( \sum K_h(\tau_{ij}) \sum Y(j)X(j)K_h(\tau_{ij}) \right) - \sum Y(j)K_h(\tau_{ij}) \sum X(j)K_h(\tau_{ij})}
$$
Estimating $b_0$

Therefore $\Delta X(i) - (\tilde{a}_0(i) + \tilde{a}_1(i)X(i))\delta \approx b_0(i)X(i)\Delta W_i$,

We set

$$\tilde{E}_i = \frac{\Delta X(i) - (\tilde{a}_0(i) + \tilde{a}_1(i)X(i))\delta}{\delta}$$

Then we find $\tilde{b}_0(i)$ by maximizing at each $i$

$$-\frac{1}{2} \sum_{j=1}^{N} K_h(\tau_{ij})(\log(b^2X^2(i))) + \frac{\tilde{E}_i^2}{b^2X^2(i)}. \quad (3)$$

$$\tilde{b}_0(i) = \frac{\sum_{j=1}^{N} K_h(\tau_{ij})\tilde{E}_i^2 |X(i)|^{-2}}{\sum_{j=1}^{N} K_h(\tau_{ij})} \quad (4)$$
Mean and Variance

\[ E[X(t)] \] solves the initial value problem

\[ y'(t) = a_0(t) + a_1(t)y(t), \quad y(0) = X(0) \]

which we solve using a first order forward Euler scheme. The variance of the noise is given by

\[ \delta(b_0(t)X(t))^2 \]
We want to use denoising algorithms that take advantage of knowledge about the noise.
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Many assume constant variance of the noise.
Segmentation

- We want to use denoising algorithms that take advantage of knowledge about the noise.
- Many assume constant variance of the noise.
- We partition the data and take an approximation of the variance on each segment.
Segmentation

Given a number $L$ we partition the background spectrum into $L$ intervals, $I_\ell$, such that

$$\|\sigma(t)\|_{I_\ell} = \frac{1}{L} \|\sigma(t)\|_1$$

where $\sigma$ is the variance of the background spectrum.
We look to minimize

$$f_{\lambda,L}(x_{est}) = ||x_{est} - x_{obs}||_2^2 + \lambda||Lx_{est}||_2^2$$
Parameter Selection and Segmentation

UPRE is an unbiased estimator of the mean squared error of predictive error $P_\lambda$ of,

$$
\frac{1}{N} \| P_\lambda \|^2 = \frac{1}{N} \| x_\lambda - x_{true} \|^2,
$$
We use the following UPRE functional,

\[ U(\lambda) = E\left( \frac{1}{N} \| P_\lambda \|^2 \right) \]

\[ = \frac{1}{N} \| r_\lambda \|^2 + \frac{2\sigma^2}{N} \text{trace}(A_\lambda) - \sigma^2, \]

where \( r_\lambda \) is the residual and \( A_\lambda = (I + \lambda I)^{-1} \). We can take the mean of \( \sigma(t) \) for the above \( \sigma \).
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where \( r\lambda \) is the residual and \( A\lambda = (I + \lambda I)^{-1} \). We can take the mean of \( \sigma(t) \) for the above \( \sigma \). The optimal \( \lambda \) is defined to be,

\[ \lambda_{opt} = \min_{\lambda} \{U(\lambda)\}. \]
Algorithm Summary

Given $h, \epsilon, L$, background spectrum, and analyte spectrum:

1. Fit background spectrum to discreted stochastic model, using $h$ for regression
2. Partition time/mass-per-charge interval into segments
3. Use UPRE to establish on each corresponding segment of analyte spectrum an optimal $\lambda$ and use Tikhonov regularization
4. Repeat (2) and (3) with increased number of segments until improvement in normalized $L^1$ is less than $\epsilon$ or number of segments is equal to $L$. 
Noise Model

Figure: Simulated Background Spectrum from Noise model for 2nd Noisy Spectrum
Denoising Results

With $h = 10$, tolerance at .001, and max iterations 20,

**Figure: 1st Noisy Set**
Denoising Results

With $h = 10$, tolerance at .001, and max iterations 20,

Figure: 2nd Noisy set
Figure: Low Noise Spectrum divided by its $L^1$
Normalized Denoised Results

Figure: Low Noise Spectrum divided by its $L^1$

Figure: 2nd Noisy Spectrum, Denoised, similarly normalized
## Normalized Denoised Results

Normalized $L^1$ distance from Best Set and Noisy Spectrum

<table>
<thead>
<tr>
<th></th>
<th>Noisy</th>
<th>Denoised</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Set</td>
<td>0.5720</td>
<td>0.5682</td>
</tr>
<tr>
<td>2nd Set</td>
<td>0.4950</td>
<td>0.4912</td>
</tr>
</tbody>
</table>
We create a set of strategic points using the following algorithm

1. Set first and last data points as strategic points
2. Find data point with maximum orthogonal distance from line segment connecting two consecutive strategic points
3. This point becomes a new strategic point
4. Repeat until maximal orthogonal distance is below prescribed tolerance
Strategic Points

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Conclusions

- Modeled noise by SDE
- Created an algorithm to denoise spectrum by segmentation
- Smoothes without moving peak locations
Future Work

- Peak height is reduced, possibly fit strategic point height to pre-denoised level
- Investigate other regularization techniques
- Filter strategic points to remove insignificant peaks for better estimation of oligomer peaks
Thank You!