Towards a Noise Model of MALDI TOF Spectra

In recent years, matrix-assisted laser desorption/ionization time-of-flight (MALDI TOF) mass spectrometry has been investigated for early diagnosis of several types of cancer from blood samples. Noise in mass spectrometry may make it difficult to recognize the subtle pathological changes embedded in mass spectra of blood samples. Effective signal restoration using digital filters could be an important part of the successful application of MALDI TOF for early cancer diagnosis. In mass spectrometry, the signal is the relative abundance of detected ions and the noise is the unwanted interfering signal originating from sources unrelated to the biochemical nature of the disease. In order to design effective digital filters and to characterize the filter performance, the sources of noise must be identified and the statistical characteristics of the noise must be measured.

We hypothesize that there exist three types of noise in MALDI TOF spectra: Johnson noise, shot noise, and chemical noise. Johnson noise is generated by the random thermal motion of electrons in electrical systems. Johnson noise follows the Gaussian distribution and it can be expressed as an additive term in the noise model. Shot noise is caused by the randomness in ion arrival time at the TOF detector. Shot noise follows the Poisson distribution. Since the variance of shot noise is expected to be proportional to the number of ions arriving at the detector given a time interval, shot noise can be modeled as a multiplication of the signal intensity and a random variable. Chemical noise mainly originates from matrix clusters. Matrix is also ionized with the sample during MALDI process and these matrix ions form clusters. The monotonically decreasing baseline is due to the presence of small clusters of matrix material, since the likelihood of cluster formation decreases with cluster size. Moreover, occasional sharp peaks in the higher mass ranges can result from unusually large clusters of matrix material.

We have designed experimental procedures to measure the statistical characteristics of these types of noise. We used mass spectra from an empty plate to measure the characteristics of Johnson noise. Because Johnson noise comes from the electrical instrumentation systems, mass spectra from the empty plate contain only the component of Johnson noise. The power spectral density of the mass spectra was analyzed to determine frequency and variance information. We propose to investigate the contributions of shot noise using a sample containing several known proteins of different amounts and measuring the noise variance at the peak of each protein. Since the variance of shot noise can be expressed as a multiplication of the signal intensity and a random variable, measuring the noise variance at each protein peak will enable us to know the mean and variance of the random variable. Multiple mass spectra from a plate with only matrix material could be used to investigate the characteristics of chemical noise. Mass spectra from only matrix material are expected to enable us to model the baseline in the low mass range as a monotonically decreasing function and to estimate the frequency and location of sporadic peaks due to matrix clusters in the high mass range.