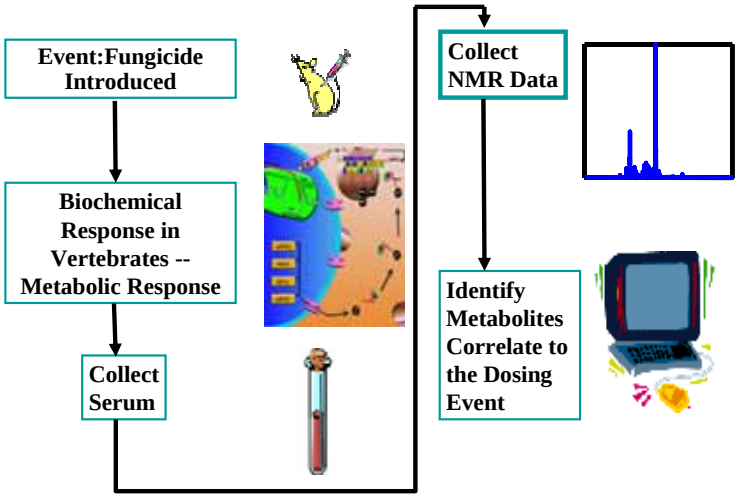
Multivariate Curve Resolution of Nuclear Magnetic Resonance Spectroscopy Metabonomic Data

M.K. Alam[1], T.M. Alam[1], D.R. Ekman[2]
[1]Sandia National Laboratories, Albuquerque, NM 87185
[2]NERL/ORD, Athens, GA 30605

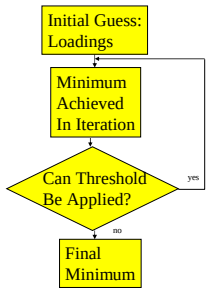
As part of EPA's effort in metabonomics, Sandia National Laboratories and EPA will collaborate on developing multivariate analysis tools for the interpretation of NMR spectroscopy data. Our goal is to correlate and interpret NMR response to the dosing by chemicals of interest.

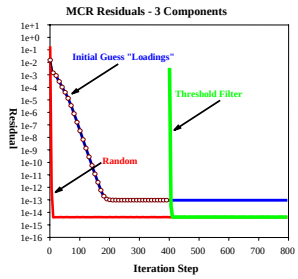


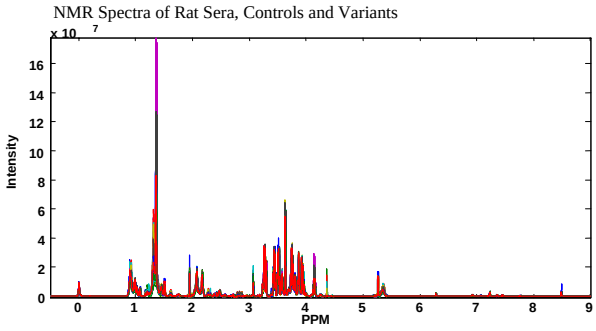
•Our work has focused on two tracks:

- 1) Using simulated data, discern performance of Multivariate Curve Resolution (MCR) programs used to estimate pure components.
- 2) Examine real NMR data set (from EPA) to determine separation efficiency, experimental issues, MCR performance.

Using simulated data, we have found that Two-Stage MCR reduces final error.







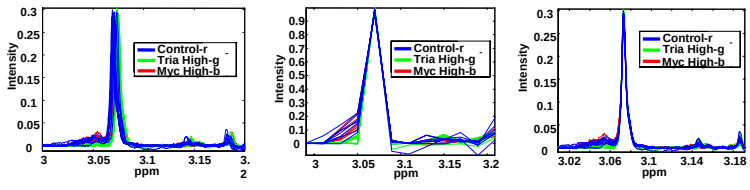
- NMR has been used to examine production of metabolites.
- In serum, there are 50 or more metabolites that can be detected using NMR.
- The resulting NMR profile in a typical metabonomics experiment can have 1000's of spectral lines.
- Experiments are typically 1) time course experiments, where sera samples are collected from a single host as a function of time, or 2) samples at a single time after an event from several hosts.
- *Goal of NMR experiments is to identify metabolites associated with a dosing event.*

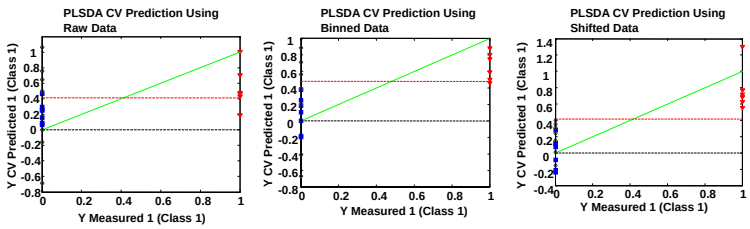
Data collected at EPA and analyzed at Sandia:

- Rats were dosed with two types of fungicide to induce metabolic changes (See D. Ekman poster).
- Sera samples were collected from dosed animals as well as control animals and analyzed using proton NMR spectroscopy.
- Can separation be detected between the three sets of samples?

Pre-processing Effects

- Variations in instrumental configuration, pH, sample chemistry and sample concentration can cause slight shifts in the NMR data.
- These spectral shifts can cause problems for classification. Common solution is to bin the data (0.02 ppm) such that shift is not apparent, but important information can be lost.
- Applying a shift algorithm that shifts to a common spectrum retains information and improves the classification results.





Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy's National Nuclear Security Administration under Contract DE-AC04-94AL85000.