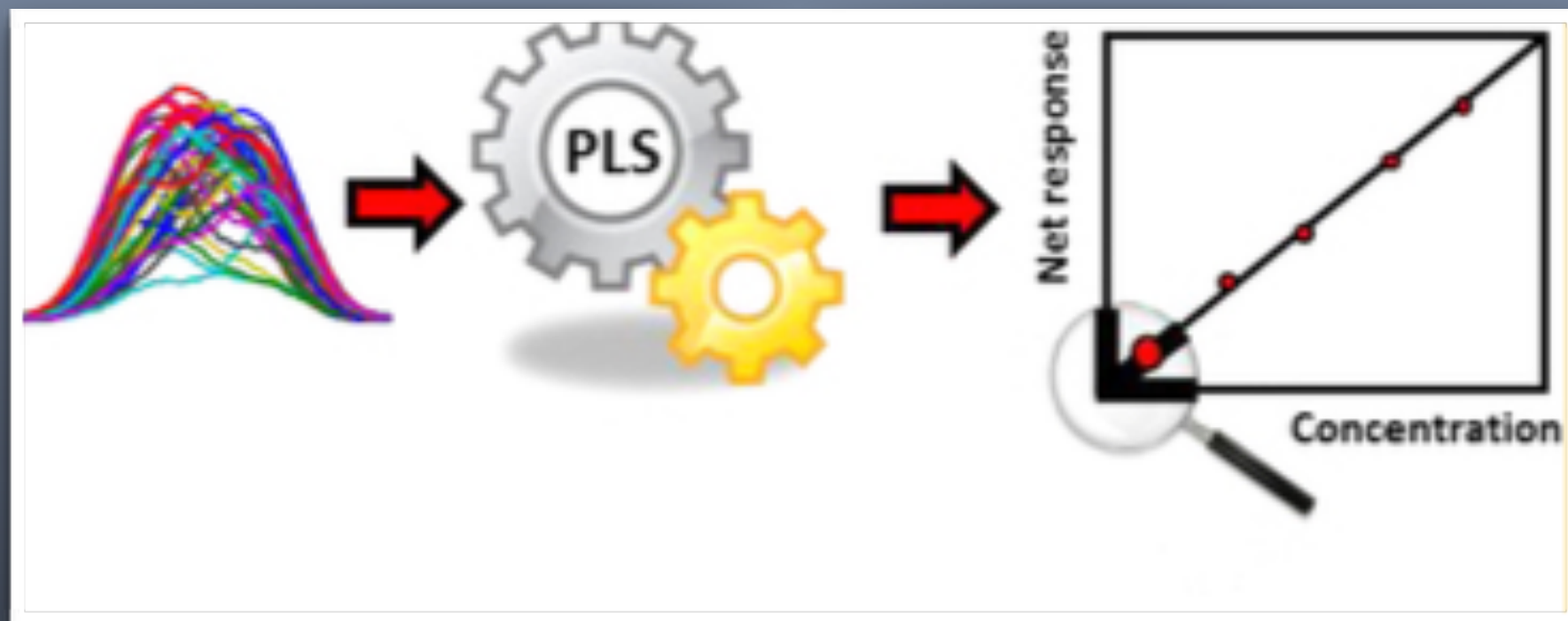




PARTIAL LEAST SQUARES CALIBRATION MODELING TOWARDS THE MULTIVARIATE LIMIT OF DETECTION FOR ENRICHED ISOTOPIC MIXTURES VIA LASER ABLATION MOLECULAR ISOTOPIC SPECTROSCOPY

Authors: Candace Harris¹, Luisa T.M. Profeta², Codjo Akpovo¹, Ashley C. Stowe³ and Lewis E. Johnson¹

¹Florida Agriculture & Mechanic University - CePaST, ²Alakai Defense Systems Inc., ³Y-12 National
Security Complex

- *Why do we need to set limitations on our detectors?*
- *How to account for all uncertainties?*
- *Every detector has their own calibration sets*

- INTRODUCTION
- **OUTLINE**
- PLS CALIBRATION SETS
- MULTIVARIATE LIMIT OF DETECTION

- PLS Calibration Sets
 - LAMIS on ^{10}B enriched Boric Acid mixtures
 - Chemical Mapping
 - LIBS on ^{235}U enriched Uranium Samples
 - Lorentz fits for predicted sample concentrations
 - PLS determinations
- Multivariate Limit of Detection

- **Y-CALIBRATION SET: ENRICHED BORIC ACID MIXTURES**
- **X-CALIBRATION SET**
- **PLS FEATURES**

- Cambridge Laboratory Isotopes ^{10}B boric acid ($\text{H}_3^{10}\text{BO}_3$ 99% ^{10}B atom, 0.01% ^{11}B atom) and ^{11}B boric acid ($\text{H}_3^{11}\text{BO}_3$ 99% ^{11}B atom, 0.01% ^{10}B atom)
- Each mixture was dissolved in 10mL of distilled water and was heated until solid consistency, then cooled to room temperature before becoming pelletized.
- 15 sample mixtures each weighing ~ 3g
- Pelletized **4 months** later - samples held in (desiccator with DRIERITE)
- Three pellets per mixture were used for sampling
- 5 mm thickness, 13 mm diameter and 500 mg each

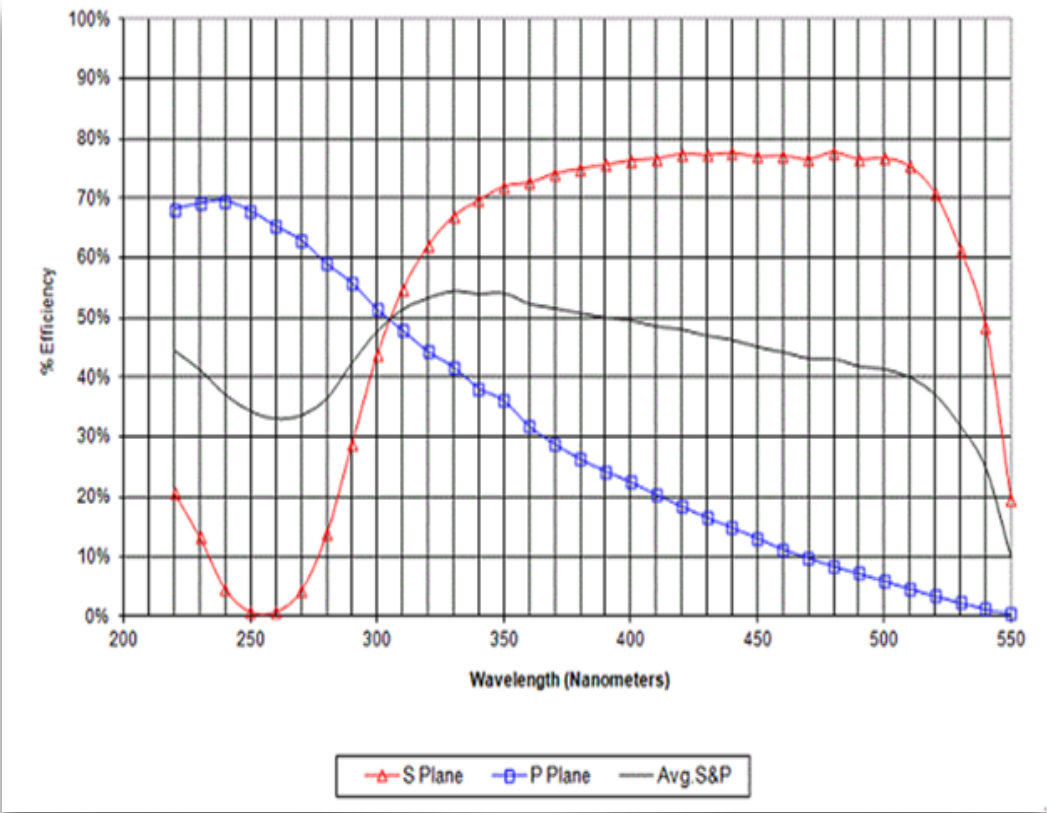
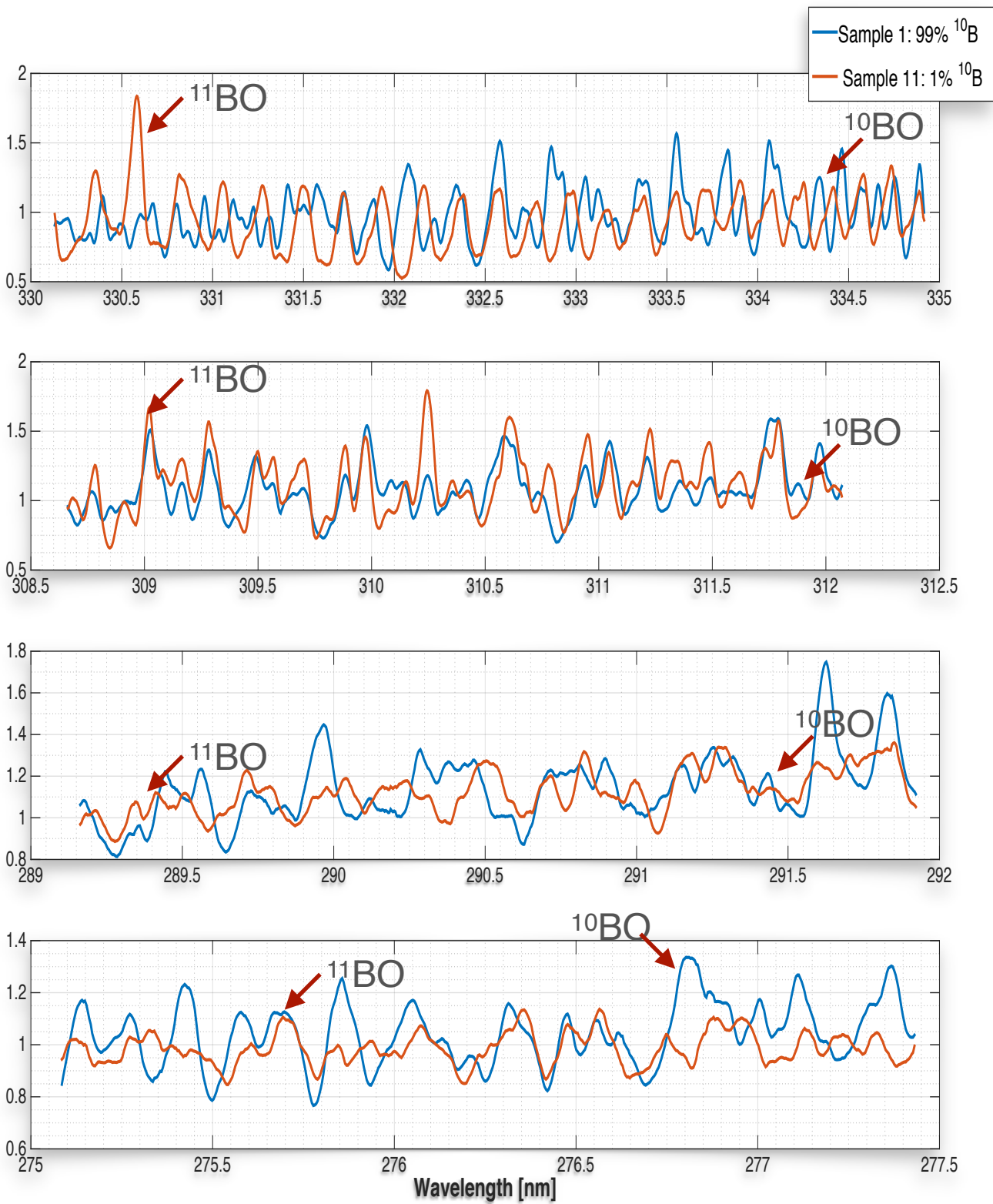
Label	$^{10}\text{B}/^{11}\text{B}$ Ratios
S1	99.00
S2	1.57
S3	1.07
S4	1.01
S5	0.89
S6	0.20
S7	0.80
S8	0.59
S9	0.12
S10	18.96
S11	0.01
S12	0.05
S13	4.77
S14	1.41
S15	8.18

- **Y-CALIBRATION SET**
- **X-CALIBRATION SET: LAMIS ON ENRICHED BORIC ACID PELLETS**
- **PLS FEATURES**

Laser Parameters	Q-Switched Nd:YAG 532 nm	Laser pulse energy ~42mJ	FL: 200 mm
Light Collection Paramters	oriented ~45 degrees relative to sample stage	Fiber Guide Ind. Collimator +Focus Guide	Andor 19 fiber optical bundle (200µm core)
Spectrometer Specifications	Andor 750 Shamrock (f = 750mm)	3600 gr/mm grating $\Delta\lambda = 0.02$ nm	iStar CCD DH740 2048x512
Acquisition Settings	Gain: 150	Gate Delay: 10µs	Gate Width: 50 µs

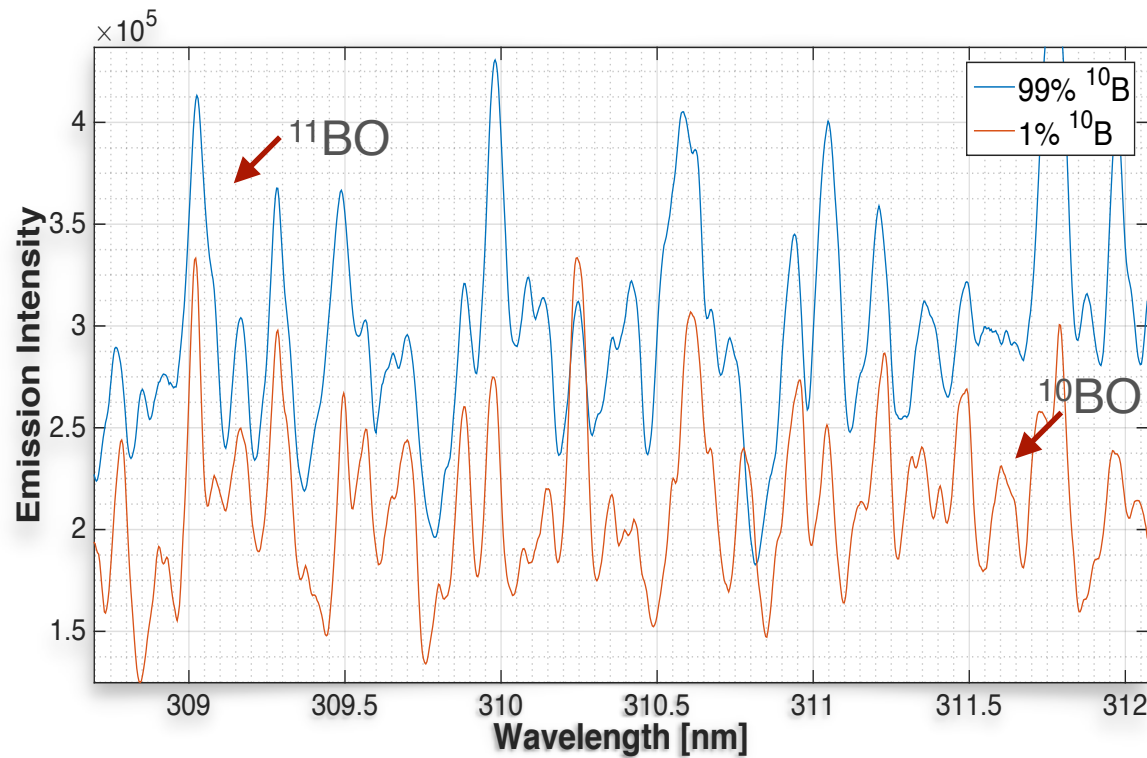
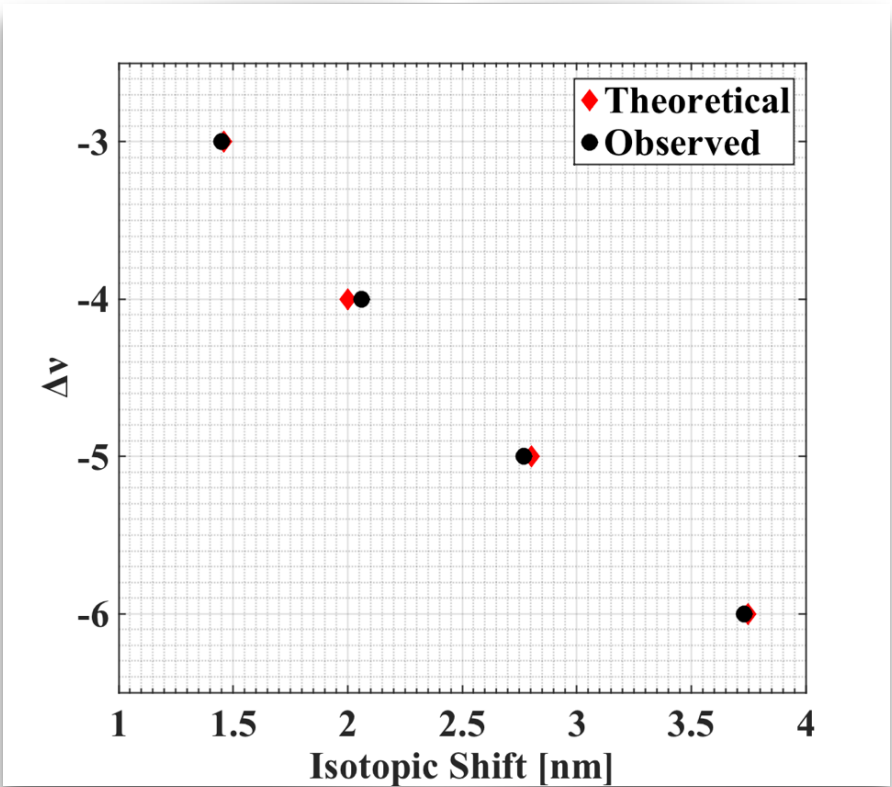
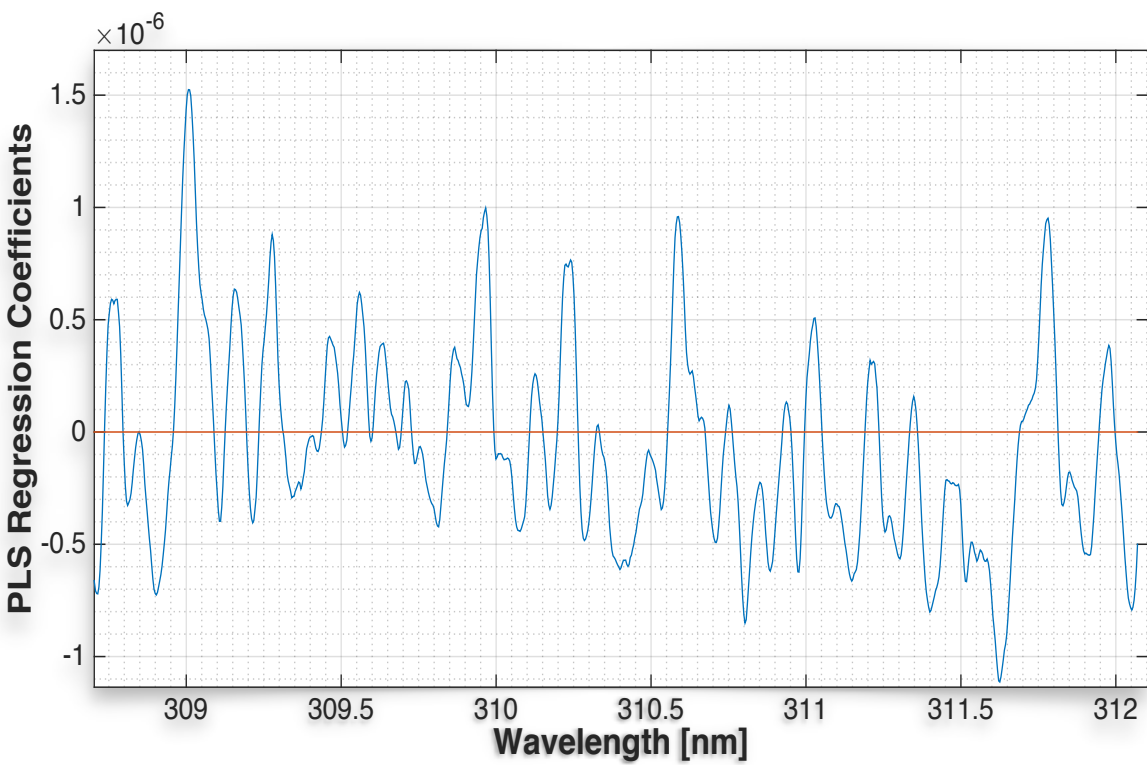
- Y-CALIBRATION SET
- X-CALIBRATION SET: LAMIS ON ENRICHED BORIC ACID PELLETS
- PLS FEATURES

Vibrational Transition ν	^{11}BO emission line [nm]	Plasma Arc Intensity *	^{10}BO emission line [nm]	Isoopic Shifts	Grating Quantum Efficiency
-6	330.67	8	334.43	3.76	50%
-5	308.98	9	311.78	2.80	50%
-4	289.34	10	291.34	2.00	40%
-3	275.45	9	276.91	1.46	30%

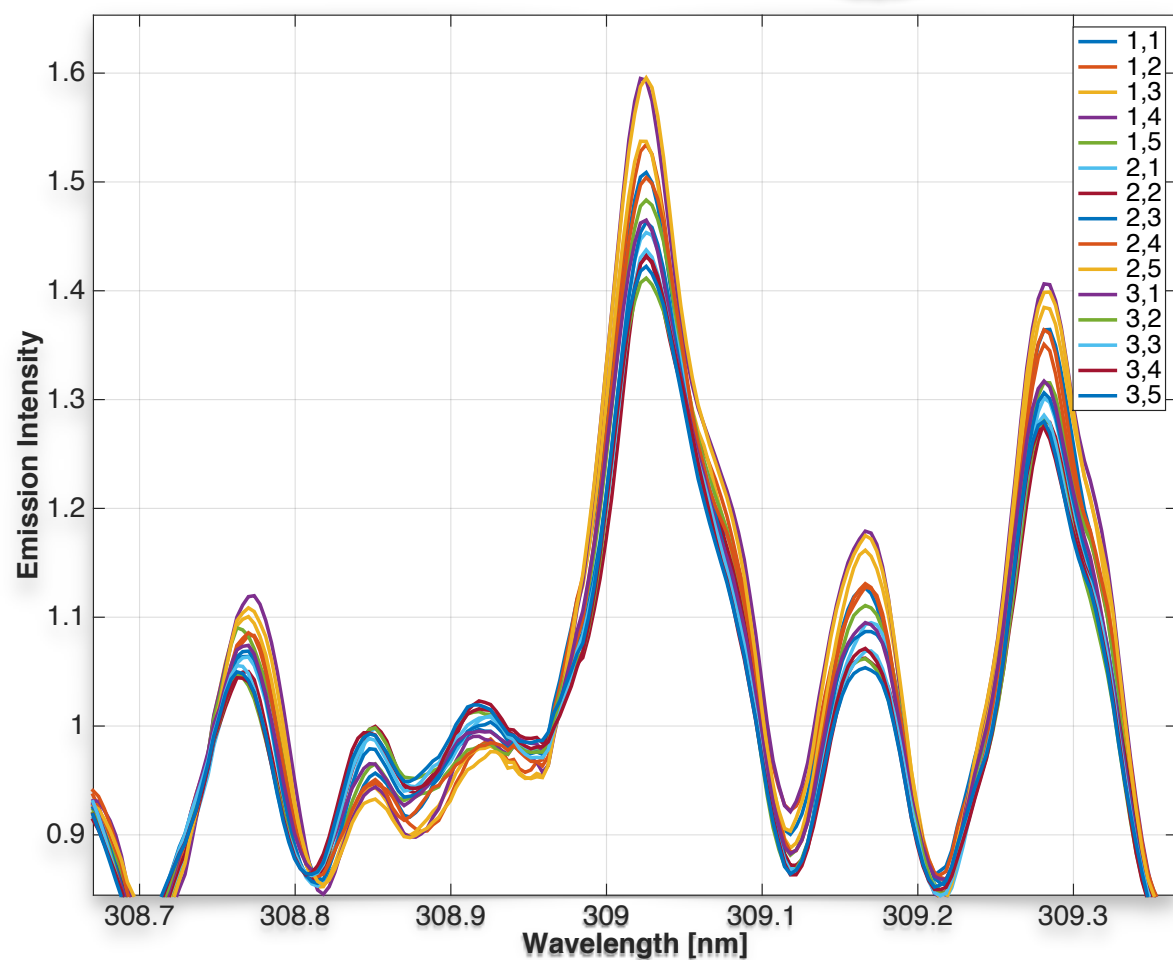
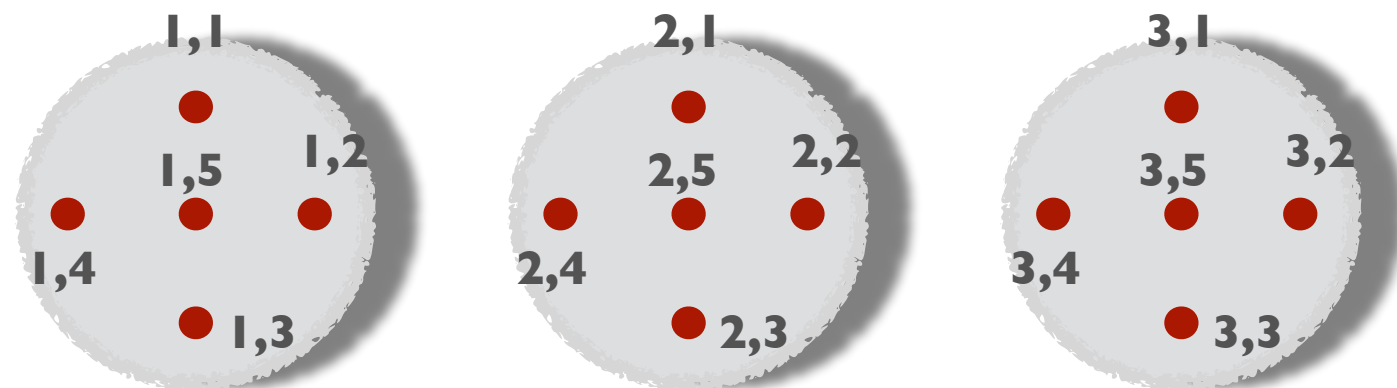


- Y-CALIBRATION SET
- X-CALIBRATION SET: MOLECULAR BANDHEAD IDENTIFICATION
- PLS FEATURES

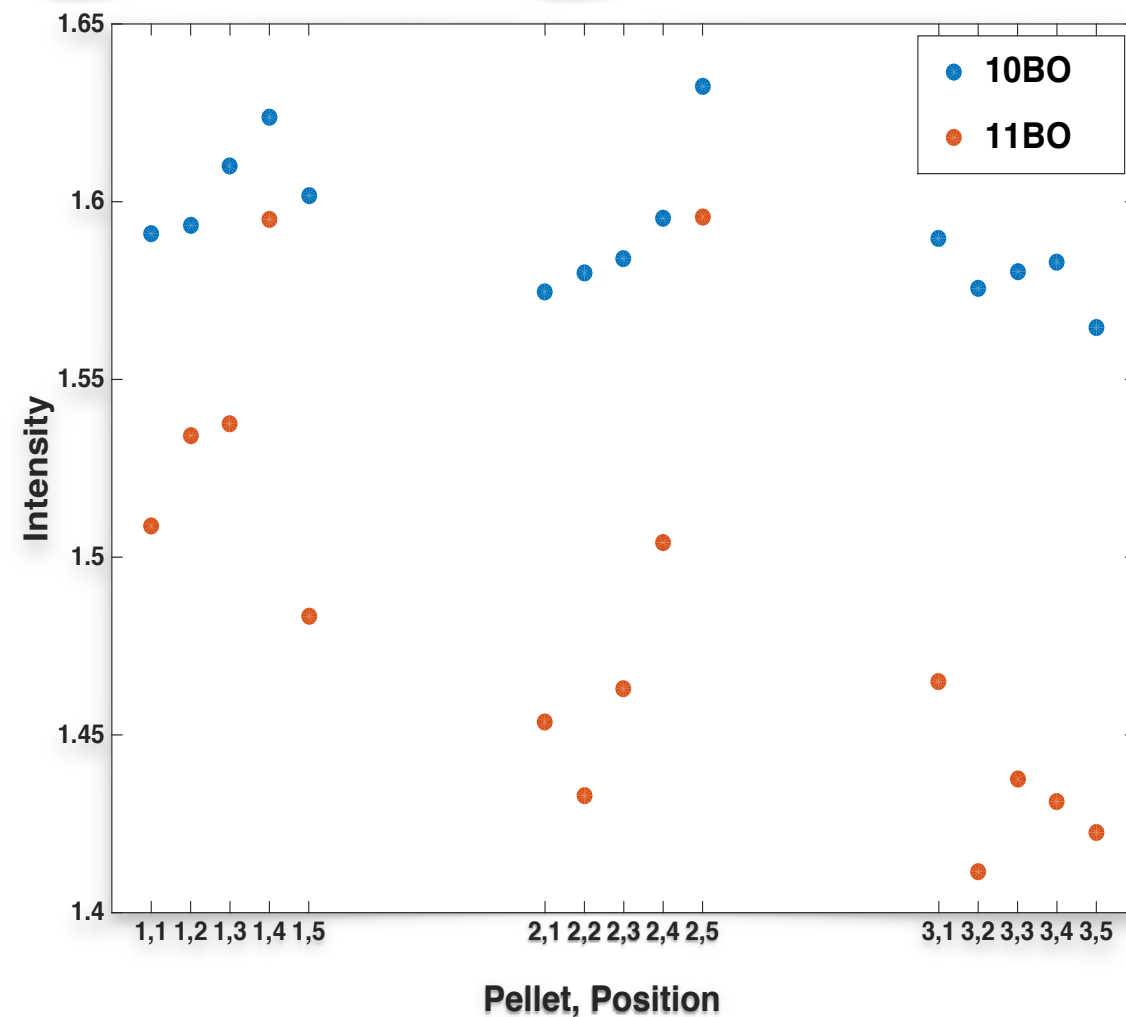
Vibrational Transition ν	^{11}BO emission line [nm]	Plasma Arc Intensity *	^{10}BO emission line [nm]	Isotopic Shifts	Grating Quantum Efficiency
-6	330.67	8	334.43	3.76	50%
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-4	289.34	10	291.34	2.00	40%
-3	275.45	9	276.91	1.46	30%



- Y-CALIBRATION SET
- X-CALIBRATION SET: CHEMICAL MAPPING
- PLS FEATURES



Sampled spectra consisted of 150-shot accumulations (30 shots per acquisition) in one quadrant position on each pellet.



Monitored ^{10}BO and ^{11}BO intensities and laser energy during sample stage translation

- **Y-CALIBRATION SET**
- **X-CALIBRATION SET**
- **PLS FEATURES: SAMPLE SPECTRA VARIANCE + PLS SCORES**

- **Scores**

Scores give the amount that each PC or component ("Latent Variable" or LV, generically) contributes to each sample. In models like Purity, MCR, and PARAFAC, this is theoretically proportional to chemical concentration or other quantitative property (depending on the physics of the measurements being analyzed.) This is the T term in the equation: $X = TP + E$

- **Outliers**

An observation with large residual.

An observation whose dependent-variable value is unusual given its values on the predictor variables.

An outlier may indicate a sample peculiarity or may indicate a data entry error or other problem.

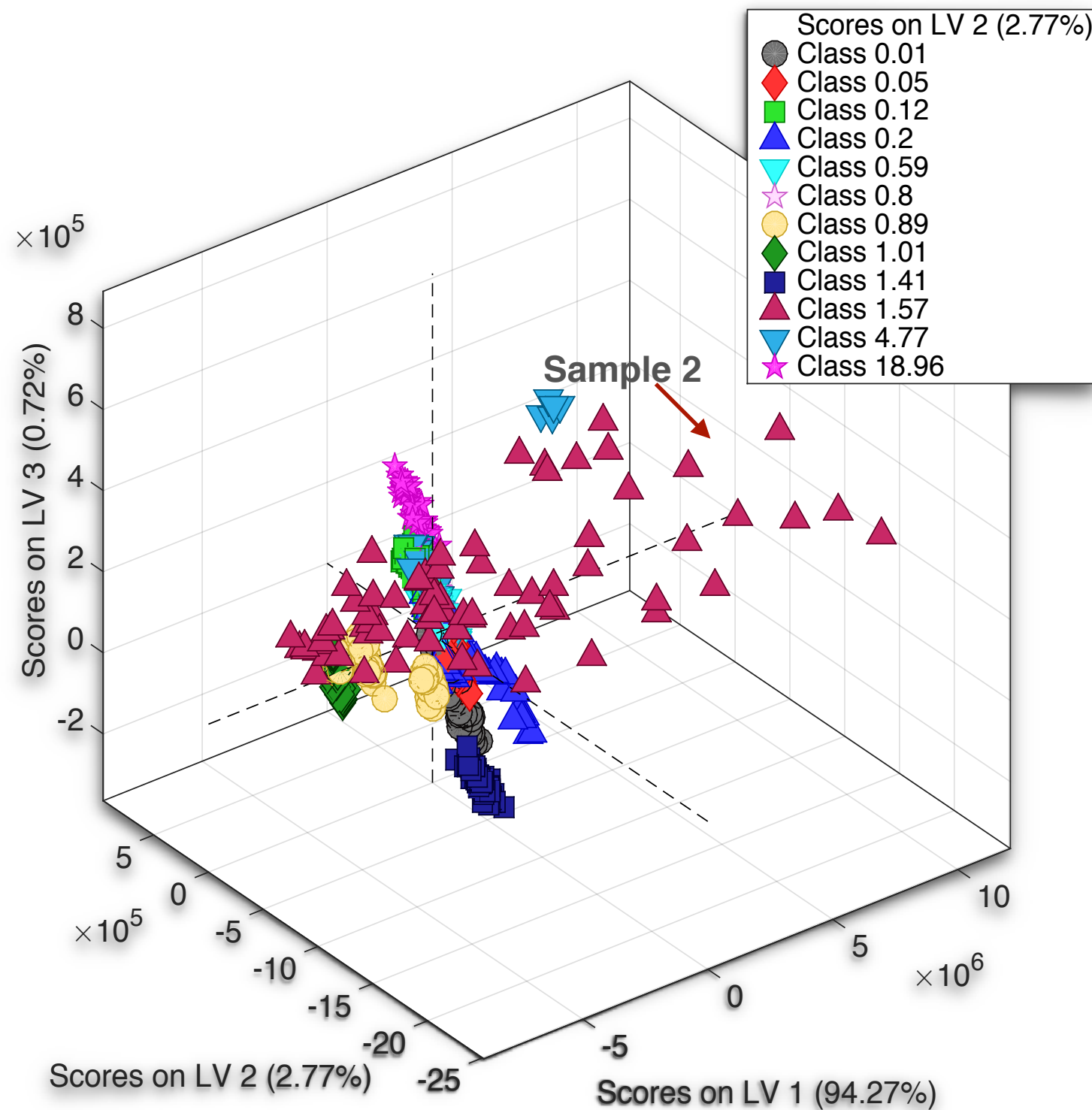
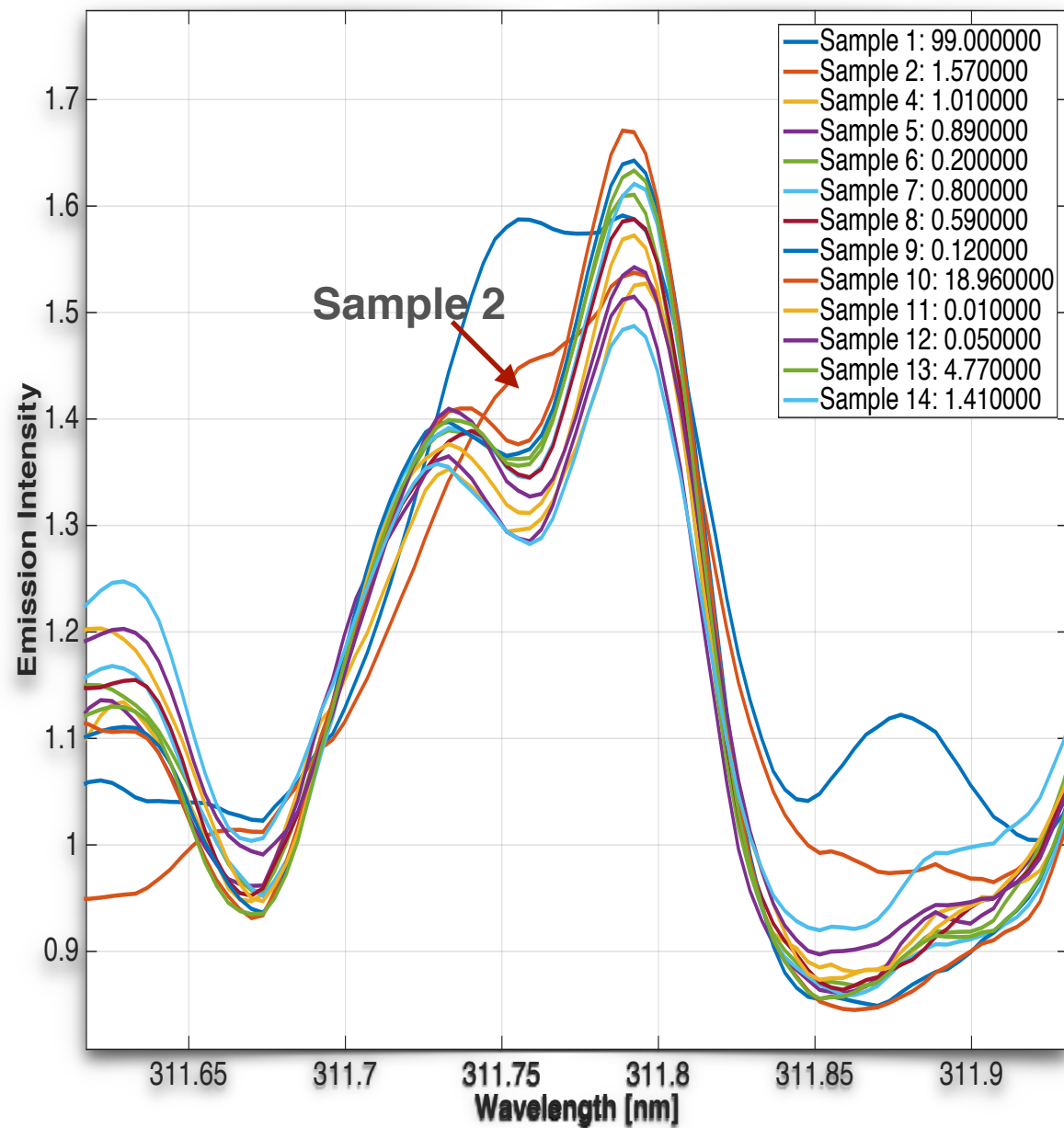
- **Leverage**

An observation with an extreme value on a predictor variable

Leverage is a measure of how far an independent variable deviates from its mean.

These leverage points can have an effect on the estimate of regression coefficients.

- Y-CALIBRATION SET
- X-CALIBRATION SET
- PLS FEATURES: SAMPLE SPECTRA VARIANCE + PLS SCORES



X-Calibration Spectra for ^{10}BO at 311.78 nm

3D Score plot

- Y-CALIBRATION SET
- X-CALIBRATION SET
- MULTIVARIATE LIMIT OF DETECTION

$$\text{LOD}_{\min} = 3.3[\text{SEN}^{-2} \text{var}(\mathbf{x}) + h_{0\min} \text{SEN}^{-2} \text{var}(\mathbf{x}) + h_{0\min} \text{var}(y_{\text{cal}})]^{1/2}$$

$$\text{LOD}_{\max} = 3.3[\text{SEN}^{-2} \text{var}(\mathbf{x}) + h_{0\max} \text{SEN}^{-2} \text{var}(\mathbf{x}) + h_{0\max} \text{var}(y_{\text{cal}})]^{1/2}$$

$$\text{LOD}_{\text{pu}} = 3.3 s_{\text{pu}}^{-1} [(1 + h_{0\min} + 1/I) \text{var}_{\text{pu}}]^{1/2}$$

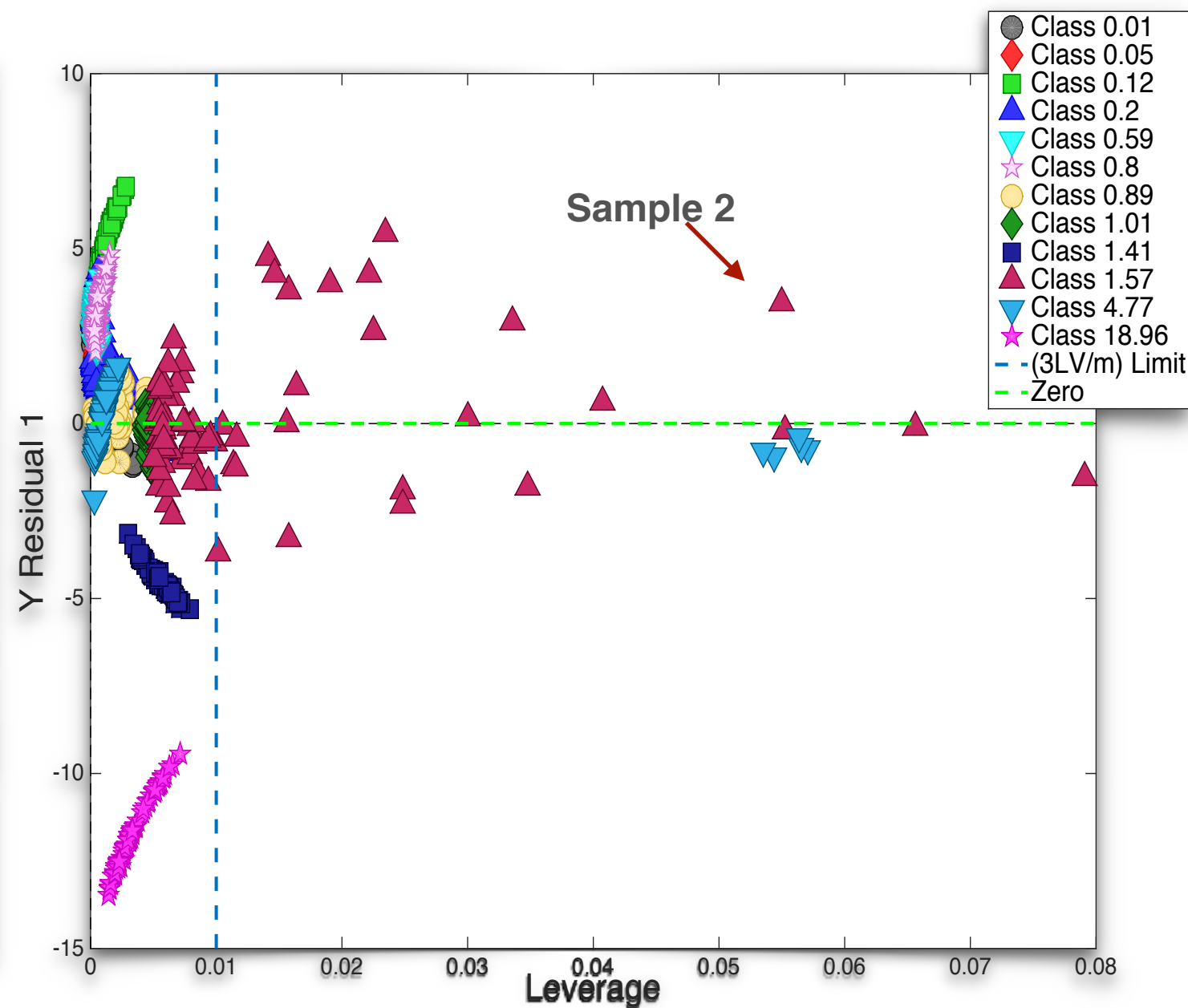
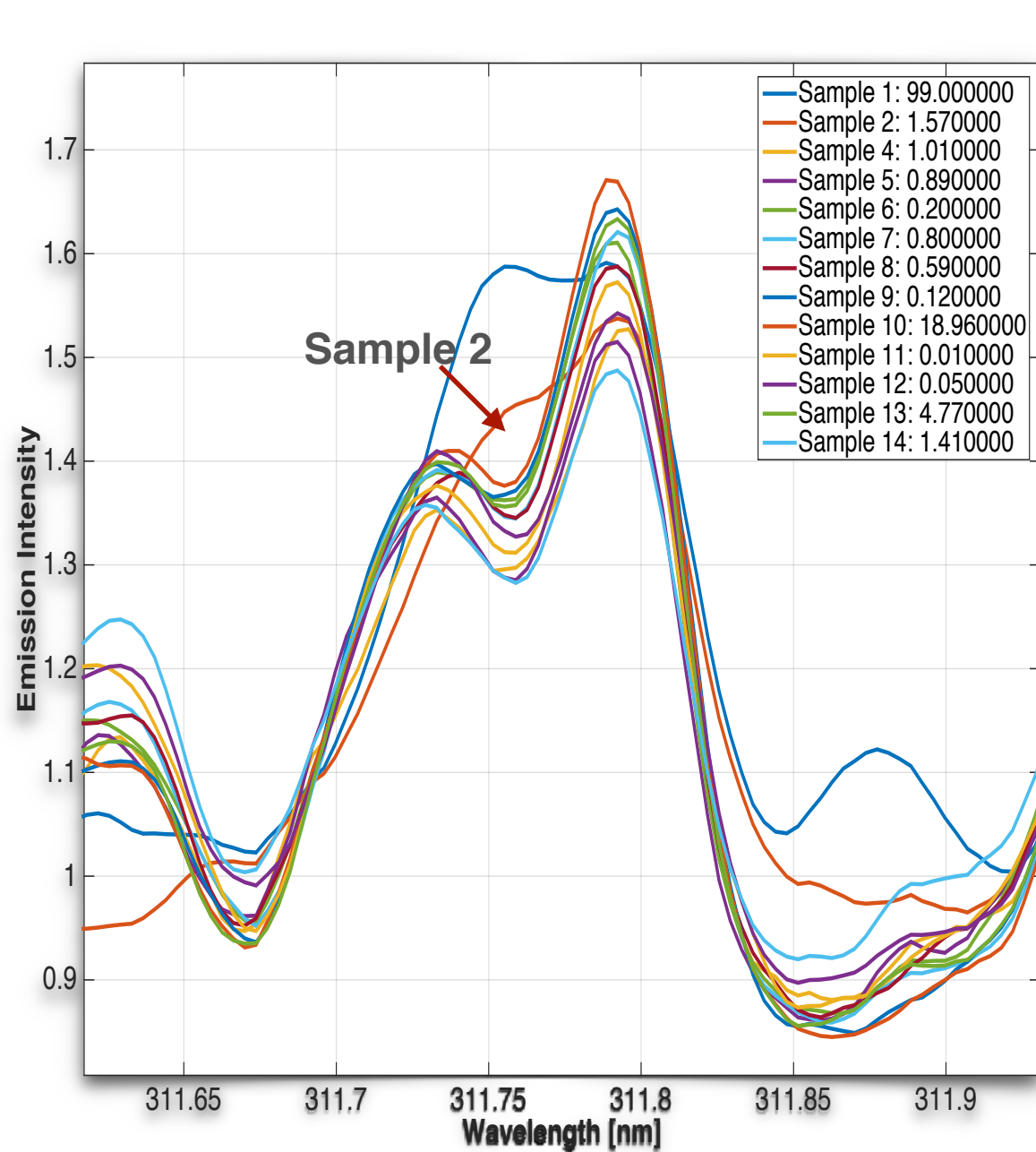
where *SEN* is the inverse of the regression vector, *var(x)* is mean of the instrumental signal variance, *var(y_{cal})* is calibration concentration variance, *h_{0min}* is minimum sample leverage *h_{0max}* is maximum sample leverage, *s_{pu}* is the slope of the pseudo univariate line, and *var_{pu}* is the regression residual variance.

Allegrini, F. and Olivieri, A. Anal. Chem. 2014, 86, 7858-7866

- Y-CALIBRATION SET
- X-CALIBRATION SET
- MULTIVARIATE LIMIT OF DETECTION

- SIMPLS Algorithm
- Mean center all data sets
- Venetian Cross Validation method - 7 splits

- Y-CALIBRATION SET
- X-CALIBRATION SET
- PLS FEATURES: SAMPLE SPECTRA VARIANCE + SAMPLE LEVERAGE



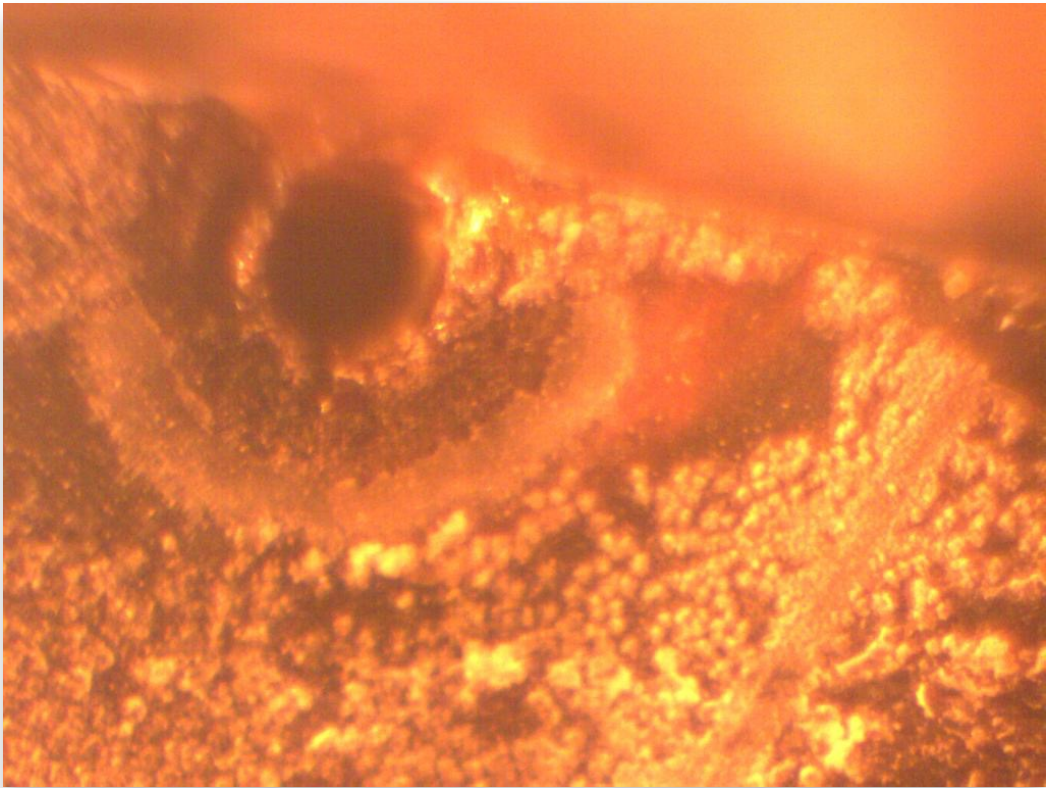
X-Calibration Spectra for ^{10}BO at 311.78 nm

Sample Leverage

- Y-CALIBRATION SET
- X-CALIBRATION SET
- MULTIVARIATE LIMIT OF DETECTION

Isoptic Shifts	#samples	# Spectra	# of PCs	var(x)	var(y)	LOD _{psu}	LOD _{min}	LOD _{max}
3.76	13	900	3	2.20E+09	0.001	1.65	0.10	0.11
2.80	13	900	3	1.82E+09	0.001	0.77	0.07	0.08
2.00	13	900	3	1.61E+09	0.001	0.84	0.06	0.07
1.46	13	900	3	1.58E+09	0.001	2.08	0.05	0.06

- **Y-CALIBRATION SET: ENRICHED URANIUM GLASSES + METALS**
- **X-CALIBRATION SET**
- **PLS FEATURES**



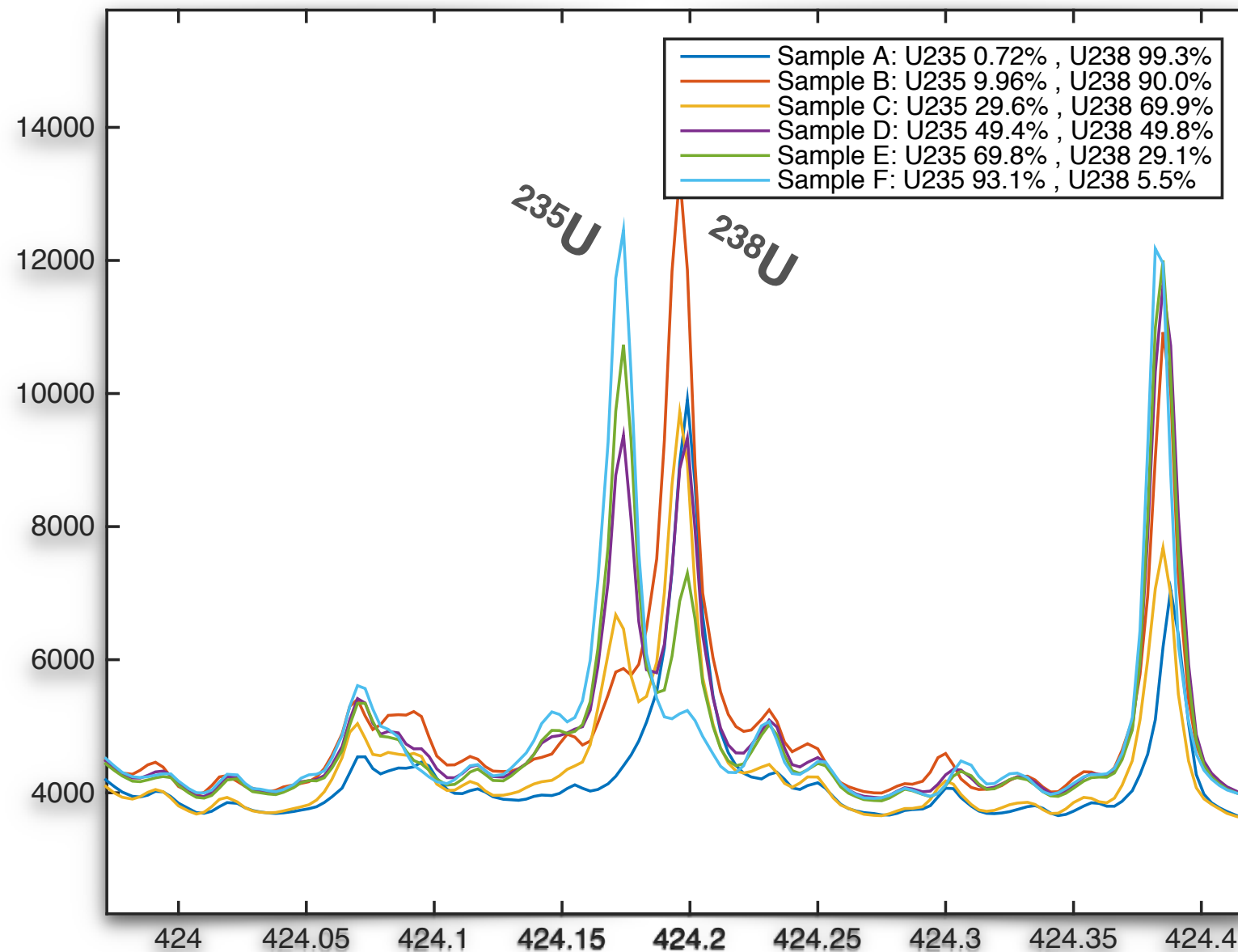
Samples enrichment by Y-12
National Security Complex
1)Triuranium (U_3O_8)Lithium
Borate Glass and 2)
isotopically enriched uranium
metal

Label	$^{235}U/^{238}U$ Ratios
A	0.72
B	9.96
C	29.98
D	50.10
E	70.80
F	94.49
G	0.20
H	94.49

- **Y-CALIBRATION SET**
- **X-CALIBRATION SET: LIBS ON ENRICHED URANIUM SAMPLES**
- **PLS FEATURES**

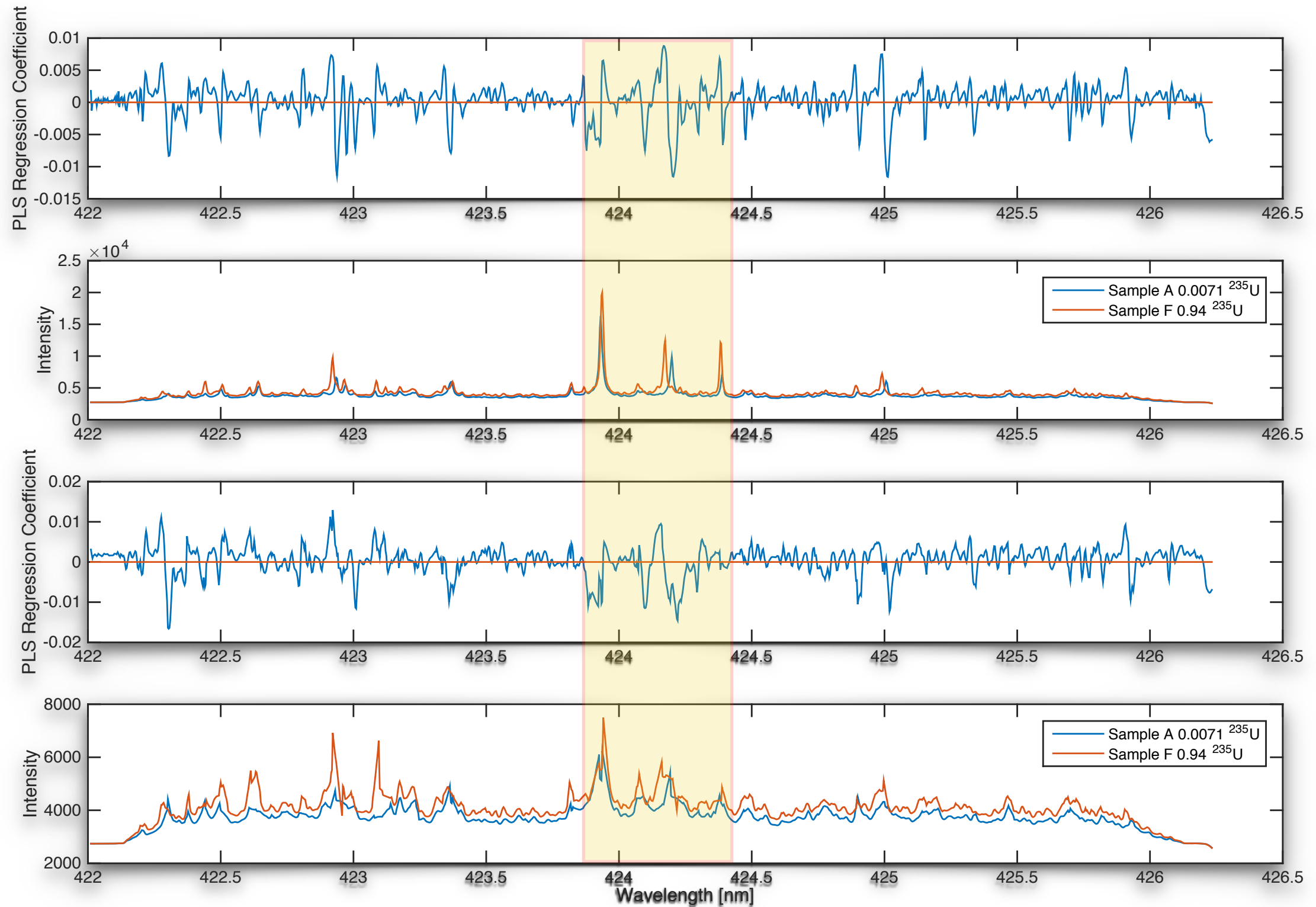
Laser Parameters	Q-Switched Nd:YAG 1064 nm	Laser pulse energy ~ 100 mJ	FL: 75 mm
Light Collection Parameters	oriented ~90 degrees relative to sample stage	collimator to fiber optic cable	19 fiber optical bundle
Spectrometer Specifications	Horiba Jobin Yvon Spectrometer (f = 1.25 m)	3600 gr/mm grating $\Delta\lambda = 0.02$ nm	PI Max iCCD 1340 X 1300
Acquisition Settings	1000 shot accumulation (20 shots/image 50 images total) per position	Gate Delay: 20 μ s	Gate Width: 2 μ s

- Y-CALIBRATION SET
- X-CALIBRATION SET: LIBS ON ENRICHED URANIUM SAMPLES
- PLS FEATURES



LIBS ONLY-12 U SAMPLES AT LBNL
GRADUATE STUDENTS: JIAOJIAN SONG AND CANDACE HARRIS

- Y-CALIBRATION SET
- X-CALIBRATION SET: ISOTOPIC SHIFT IDENTIFICATION
- PLS FEATURES



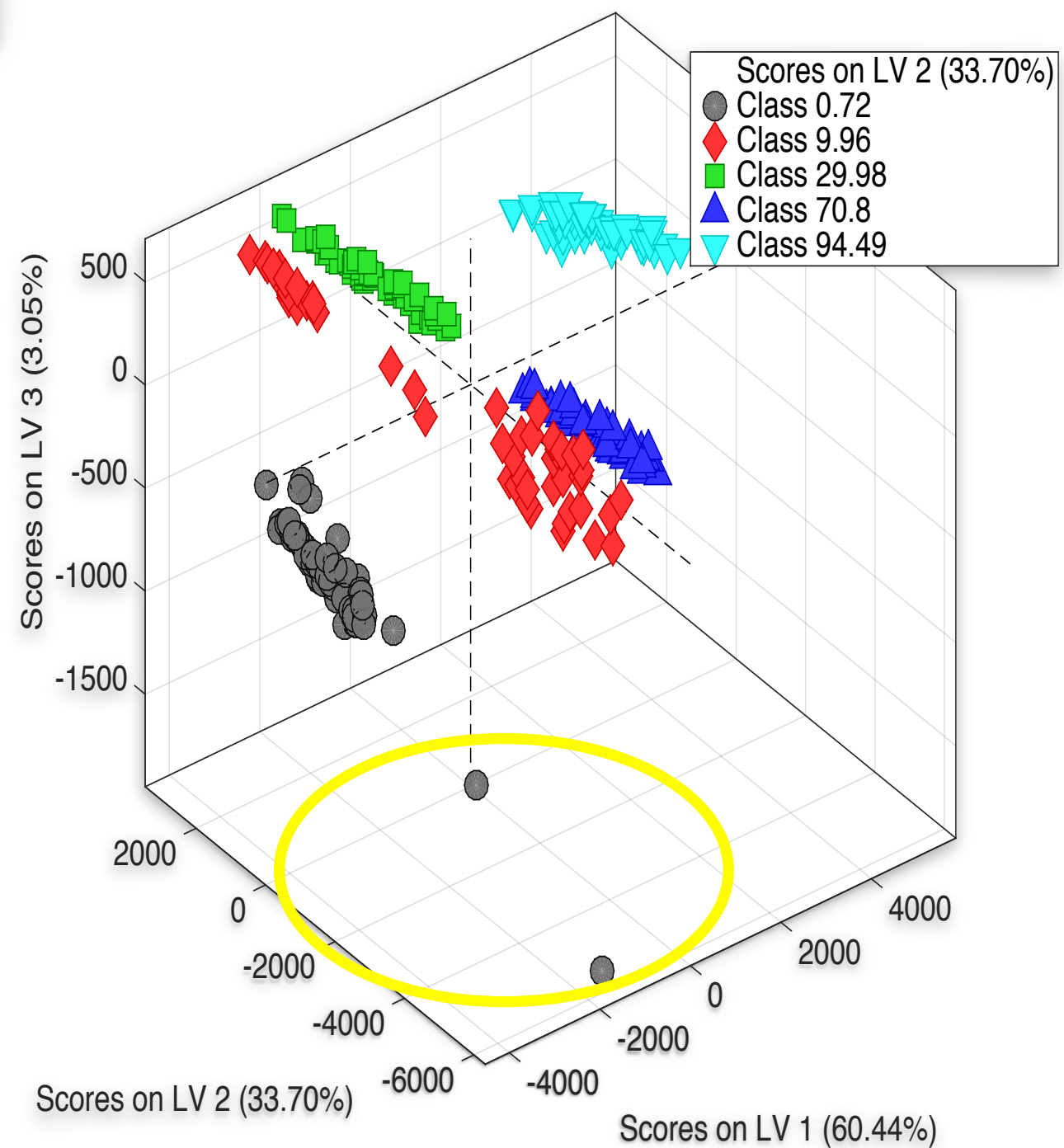
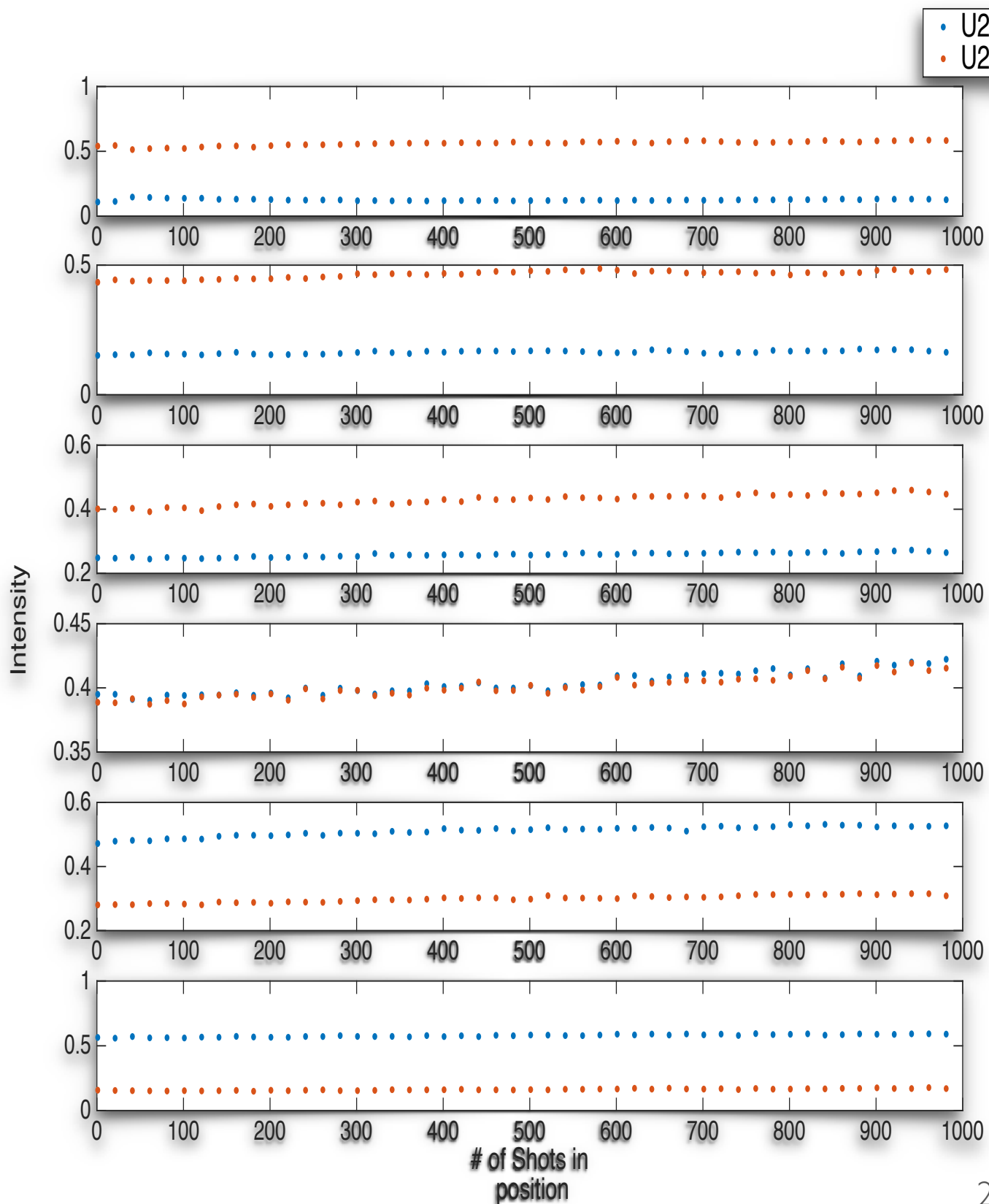
- **Y-CALIBRATION SET**
- **X-CALIBRATION SET**
- **MULTIVARIATE LIMIT OF DETECTION**

- Constructed 5-9 calibration sets
- Mean center all data sets
- Venetian Cross Validation method - 7 splits
- Used suggested PCs each model

- Y-CALIBRATION SET
- X-CALIBRATION SET
- MULTIVARIATE LIMIT OF DETECTION

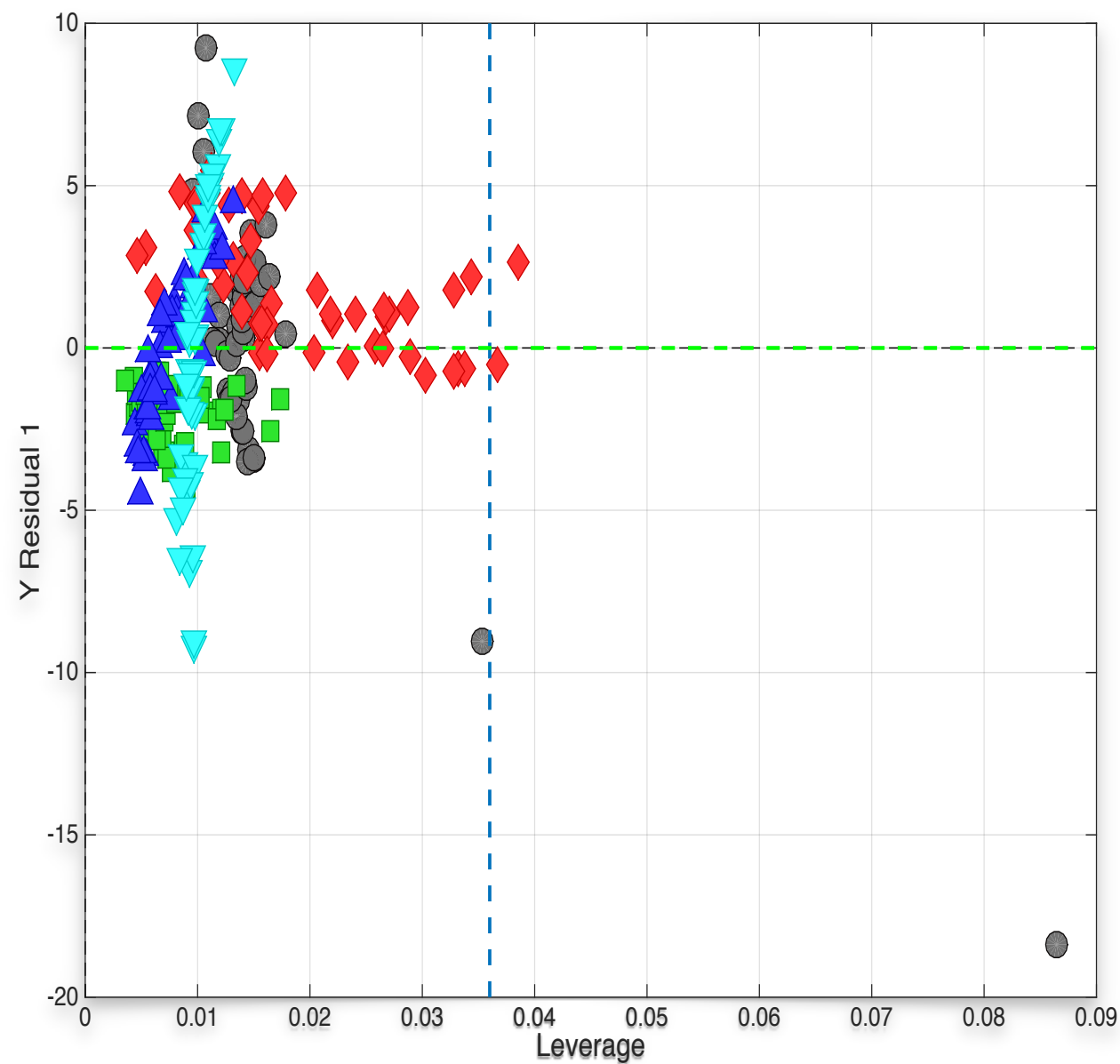
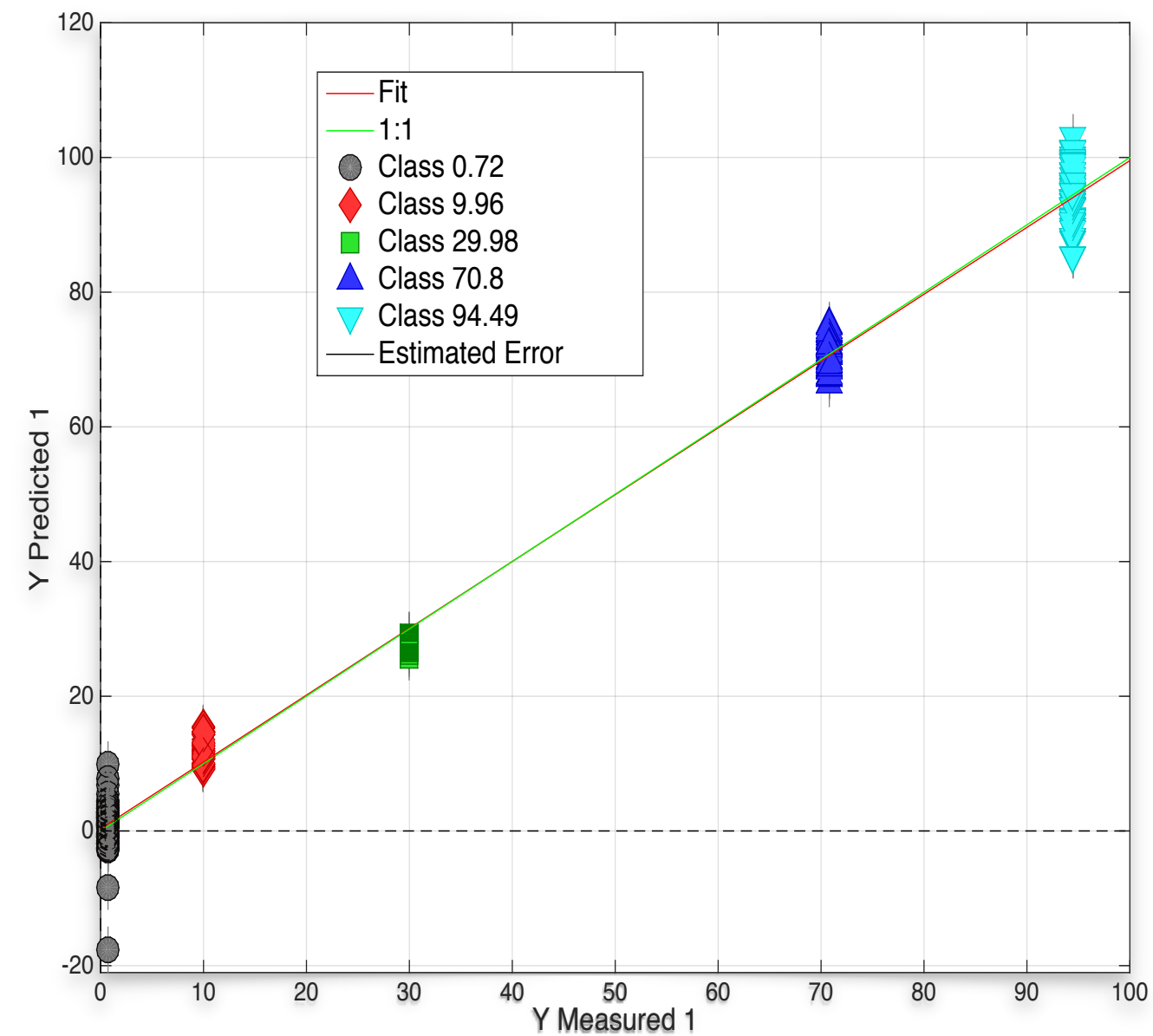
	Raw Spectra	Summed & Selected range $\Delta\lambda = 424.11-424.26$	Summed & Intensity Calibration	Summed and Deresolved	Summed Spectra	Mean Spectra	Mean & Deresolved	Intensity Calibration & Deresolved
No. of PCs'	3	2	2	4	3	3	3	2
RMSECV'	3.80	0.03	6.88	4.61	2.95	2.95	3.58	7.50
var(x)'	6773.89	867447.41	12072.87	71233.82	164882.26	6595.29	5123.46	8281.98
var(y)'	1090.74	1105.52	1105.52	1105.52	1105.52	1105.52	1105.52	1105.52
LOD min'	6.87	179.48	15.81	22.07	20.49	16.52	15.92	15.89
LOD max'	25.47	195.22	33.88	49.15	49.07	47.30	49.74	34.64
LOD psu'	12.54	9.70	23.63	12.65	9.41	9.41	11.53	24.80

- Y-CALIBRATION SET
- X-CALIBRATION SET
- PLS FEATURES: SAMPLE SPECTRA VARIANCE + PLS SCORES



3D Score Plot for Sample D 50:50

- Y-CALIBRATION SET
- X-CALIBRATION SET
- PLS FEATURES: SAMPLE LEVERAGE+RESIDUALS

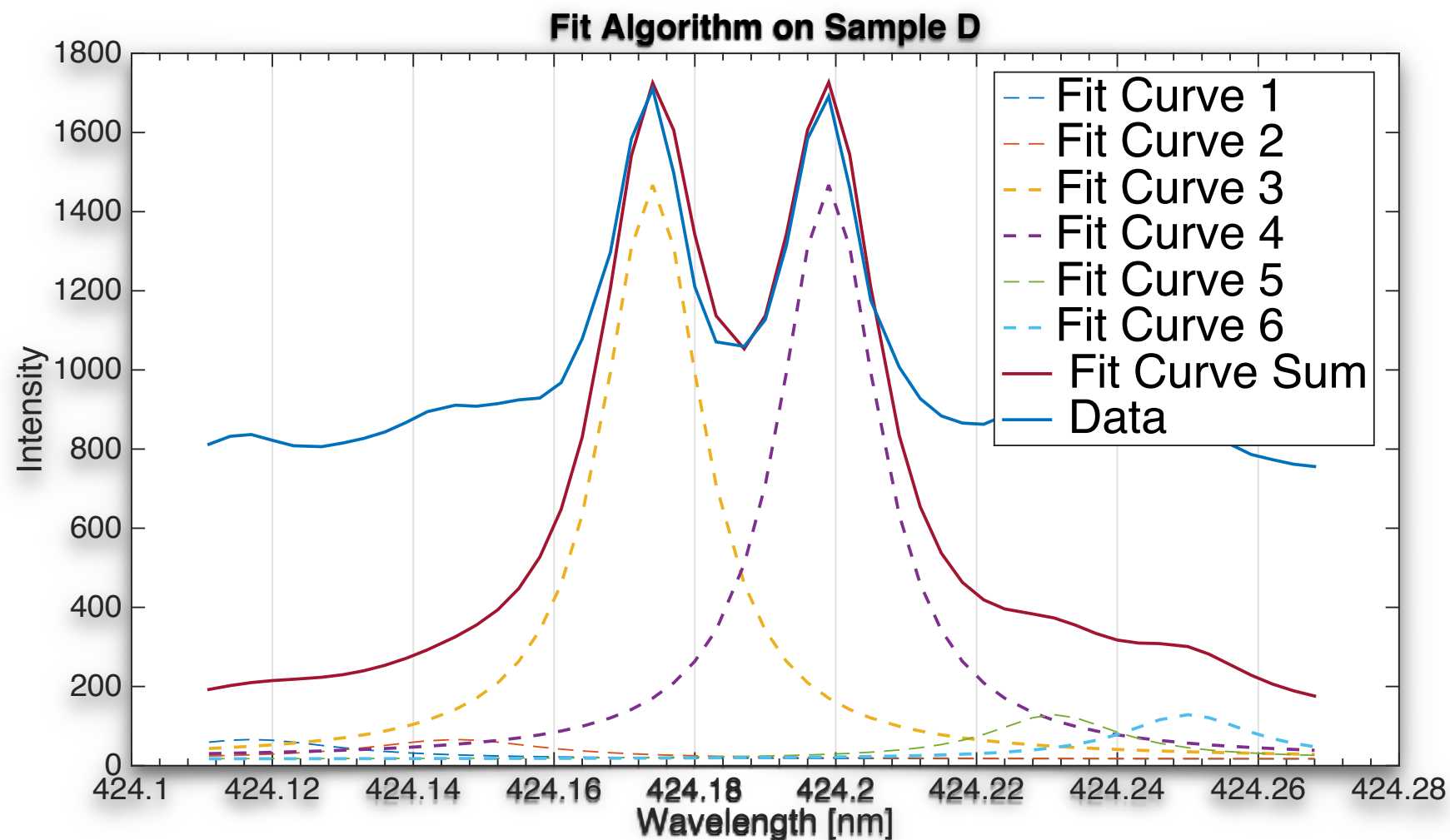


Calibration Set Sample D 50:50

- **Y-CALIBRATION SET**
- **X-CALIBRATION SET**
- **MULTIVARIATE LIMIT OF DETECTION**

Samples	# Spectra	# of PCs	var(x)	var(y)	LOD _{psu}	LOD _{min}	LOD _{max}
A	250	3	4.63E+04	885.61	11.64	7.60	20.85
B	250	3	4.11E+04	1051.86	10.37	7.45	38.88
C	250	3	4.52E+04	1270.92	10.01	8.63	32.10
D	250	3	4.24E+04	1296.47	10.70	10.31	35.73
E	250	3	4.25E+04	1119.15	10.84	8.86	29.00
F	250	3	4.26E+04	662.82	8.60	6.26	25.99
G	300	3	4.33E+04	1090.74	10.51	7.26	27.35
H	300	3	4.33E+04	1090.74	10.51	7.26	27.35

- MULTIVARIATE LIMIT OF DETECTION
- LORENTZ FITS LIBS ON URANIUM SAMPLE
- PLS SAMPLE DETERMINATION



SAMPLE D
 100 LASER SHOT AVERAGED
 U ISOTOPIC CONCENTRATION (%) ²³⁵U: 49.4048 ²³⁸U: 49.8389

Fit Results: $\frac{{}^{235}\text{U}}{{}^{235}\text{U} + {}^{238}\text{U}} = 50.248756$
 (Line Width 1.01 - *Ref. Chan*)

- **MULTIVARIATE LIMIT OF DETECTION**
- **LORENTZ FITS LIBS ON URANIUM SAMPLE**
- **PLS SAMPLE DETERMINATION**

Sample	Compositon	Actual ²³⁵ U relative abundance (%)	Lorentz fit determined ²³⁵ U relative	#of spectra fitted	RSD (%)	Uncertainty (%)
A	Enriched Uranium Glass	0.72	8.80	6	0.61	11.23
B	Enriched Uranium Glass	9.96	10.82	10	2.32	0.09
C	Enriched Uranium Glass	29.98	30.09	10	0.18	0.00
D	Enriched Uranium Glass	50.10	50.67	10	0.16	0.01
E	Enriched Uranium Glass	70.80	68.96	10	0.17	0.03
F	Enriched Uranium Glass	94.49	94.75	10	2.56	0.00
G	Enriched Uranium Metal	0.20	0.02	10	0.01	0.89
H	Enriched Uranium Metal	94.49	72.34	7	17.80	0.23

- **MULTIVARIATE LIMIT OF DETECTION**
- **LORENTZ FITS LIBS ON URANIUM SAMPLE**
- **PLS SAMPLE DETERMINATION**

Sample	Actual ²³⁵ U relative abundance (%)	PLS determined ²³⁵ U relative (abundance (%))	#of PCs	RMSECV	RSD	Uncertainty	Bias
A	0.72	2.86	6	2.01	3.21	2.98	0.01
B	9.96	13.44	3	3.21	2.01	0.35	-0.02
C	29.98	28.48	5	2.40	2.00	0.05	-0.04
D	50.10	49.77	3	3.28	1.63	0.01	-0.01
E	70.80	70.44	8	1.80	2.92	0.01	-0.02
F	94.49	94.85	8	1.64	3.31	0.00	-0.01
G	0.20	-87.65	7	2.10	12.46	176.40	-0.01
H	94.49	78.36	7	2.10	4.66	0.17	-0.01

- MULTIVARIATE LIMIT OF DETECTION
- LORENTZ FITS LIBS ON URANIUM SAMPLE
- LIMIT OF DETECTION + FIT RESULTS COMPARISON

Samples	Actual ²³⁵ U relative abundance (%)	Lorentz fit determined ²³⁵ U relative abundance (%)	PLS determined ²³⁵ U relative (abundance (%))	LOD _{psu}	LOD _{min}	LOD _{max}
A	0.72	8.80	2.86	11.64	7.60	20.85
B	9.96	10.82	13.44	10.37	7.45	38.88
C	29.98	30.09	28.48	10.01	8.63	32.10
D	50.10	50.67	49.77	10.70	10.31	35.73
E	70.80	68.96	70.44	10.84	8.86	29.00
F	94.49	94.75	94.85	8.60	6.26	25.99
G	0.20	0.02	-87.65	10.51	7.26	27.35
H	94.49	72.34	78.36	10.51	7.26	27.35

■ CONCLUSIONS

- With the limits determined, we can assume that the amount of analyte cannot be detected in a given test sample if its predicted concentration is below the LOD_{min} or that the analyte is present if its predicted concentration is above the LOD_{max} .
- As predicted, the β system (2,5) with $\Delta v = -3$ shows a LOD_{max} larger than the other systems, which could be interpreted in the fit for the calibration curve and only examined in the smallest observed isotopic shift.
- In addition to this, the pseudo univariate limit of detection was calculated to compare to the multivariate interval. Compared with results from the pseudounivariate LOD, the multivariate LOD includes other factors (i.e. signal uncertainties) and reveals the significance in creating models that not only use the analyte's emission line but also its entire molecular spectra.

■ FUTURE WORK

- Create more isotopically enriched sample sets
 - Zr-94 mixtures via LAMIS - femtosecond and nanosecond laser ablations
 - LAMIS-LIF
 - Simulated Spectra
- Compare Cambridge Isotope Laboratories calibration samples with other enriched isotope manufacturers
 - Sigma Aldrich
 - Trace Sciences
 - New Brunswick Laboratories