

RapidCode LFDA

Material for Discussion

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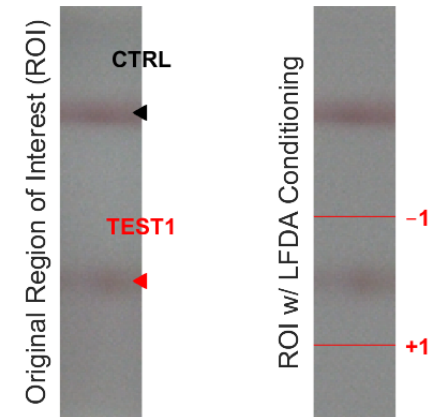
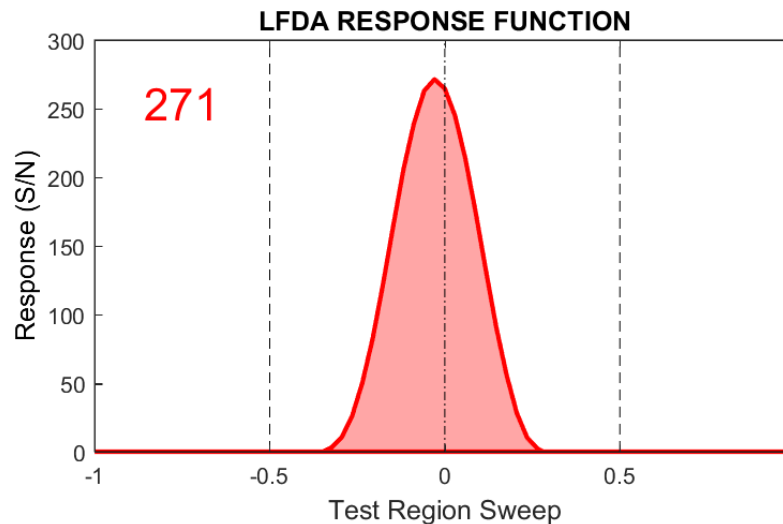
Ivans Chou

RapidCode, LLC

Sample LFDA Diagnostic Output

Sample LFDA Diagnostic Output

- Test with high S/N (~ 271) indicating strong negative for DOA
- RSA is the relative signal amplitude with respect to the on-strip reference line
- The expected value of purity (i.e. $\langle \text{PUR} \rangle$) is a function of S/N, while the measured value is formally independent of S/N
 - $0\% < \text{PUR} < 100\%$
 - $t\text{PUR} = (\text{PUR} - \langle \text{PUR} \rangle) / \sigma_{\text{PUR}}$
 - $\text{PUR} = \sim 96.1\%$
 - $\langle \text{PUR} \rangle = 99.3\%$
 - $t\text{PUR} = -1.59$ ("sigma")
- The horizontal structure function (HSF) is a metric which looks at variation across the width of the test line
 - $t\text{HSF} = (\text{HSF} - \langle \text{HSF} \rangle) / \sigma_{\text{HSF}}$
 - While $t\text{HSF}$ is ~ 6 sigma, anomaly over-ride in effect [o] because of high PUR value

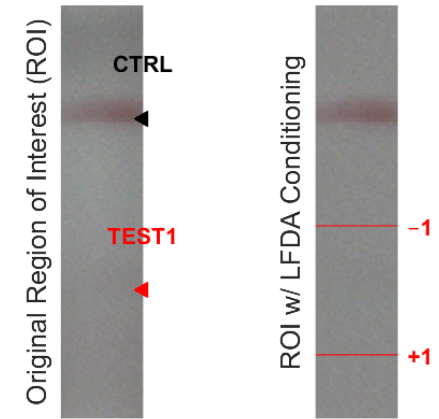
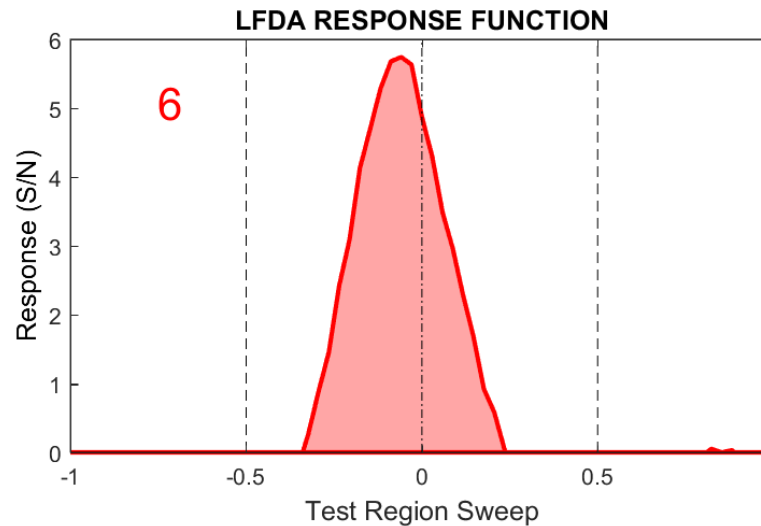


Filename: 50_05_01.jpg (Mode: on_strip_ref)

METRIC	CTRL	TEST1
Confidence	--	100.00%
SNR	834.39	271.43
RSA	--	57.04% \pm 1.75
PUR	--	96.08% \langle 99.31% \rangle
tPUR	--	-1.59
HSF	--	11.51 \langle 4.91 \rangle
tHSF	--	6.27 [o]

Sample LFDA Diagnostic Output

- Test with low S/N (~ 6) indicating a strong positive for DOA
- RSA = $\sim 9\%$, but with the low S/N has a large uncertainty of ~ 4 .
- Note tPUR indicate PUR is within 0.78 sigma of expected value
- Note tHSF indicates HSF is within 1.25 sigma of expected value
- Together, tPUR and tHSF indicate no anomaly in test



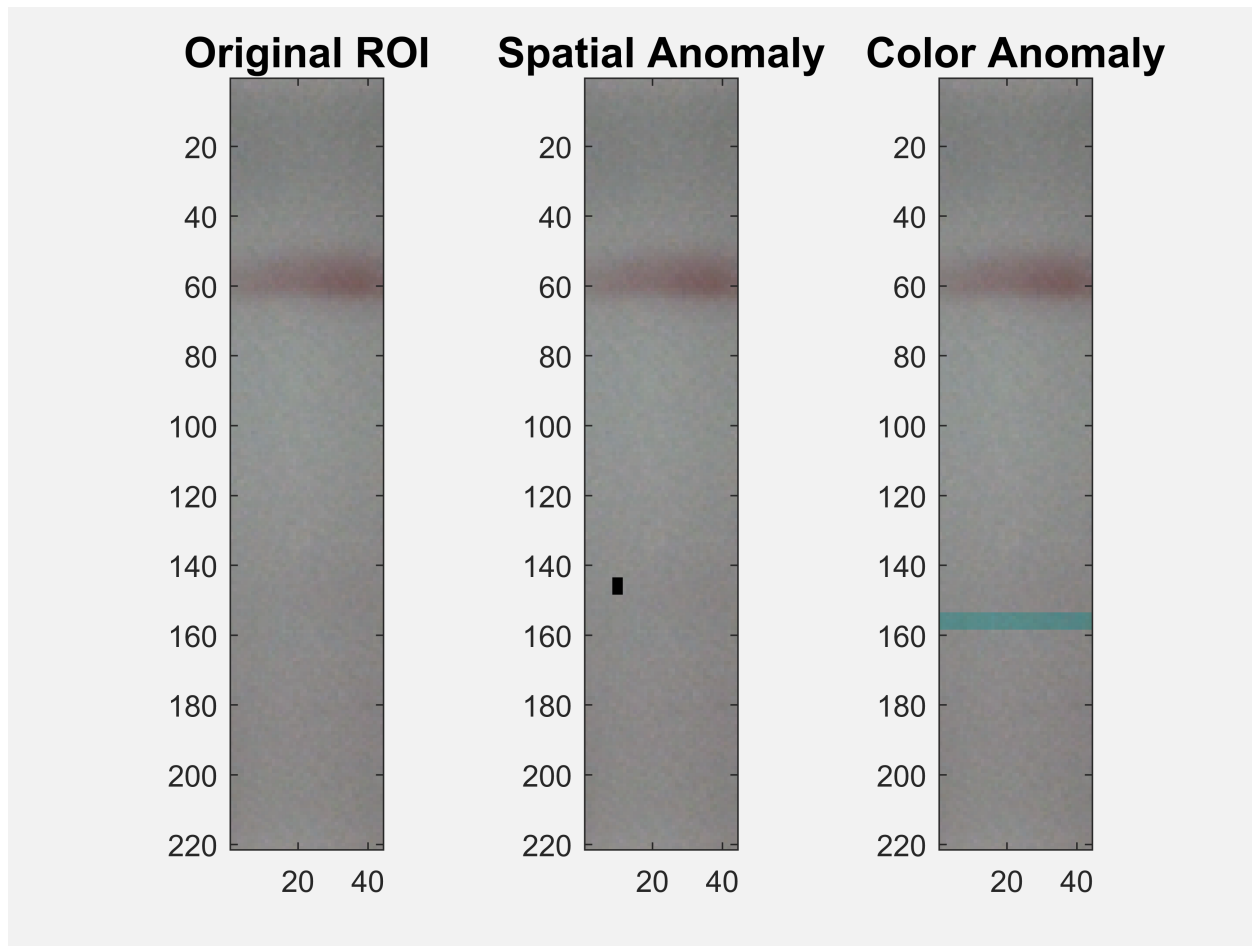
Filename: 50_02_03.jpg (Mode: on_strip_ref)

METRIC	CTRL	TEST1
Confidence	--	37.65%
SNR	693.53	5.74
RSA	--	9.10% \pm 4.26
PUR	--	60.26% <70.34%>
tPUR	--	-0.78
HSF	--	3.53 <4.76>
tHSF	--	-1.25

LFDA Anomaly Detection Metrics

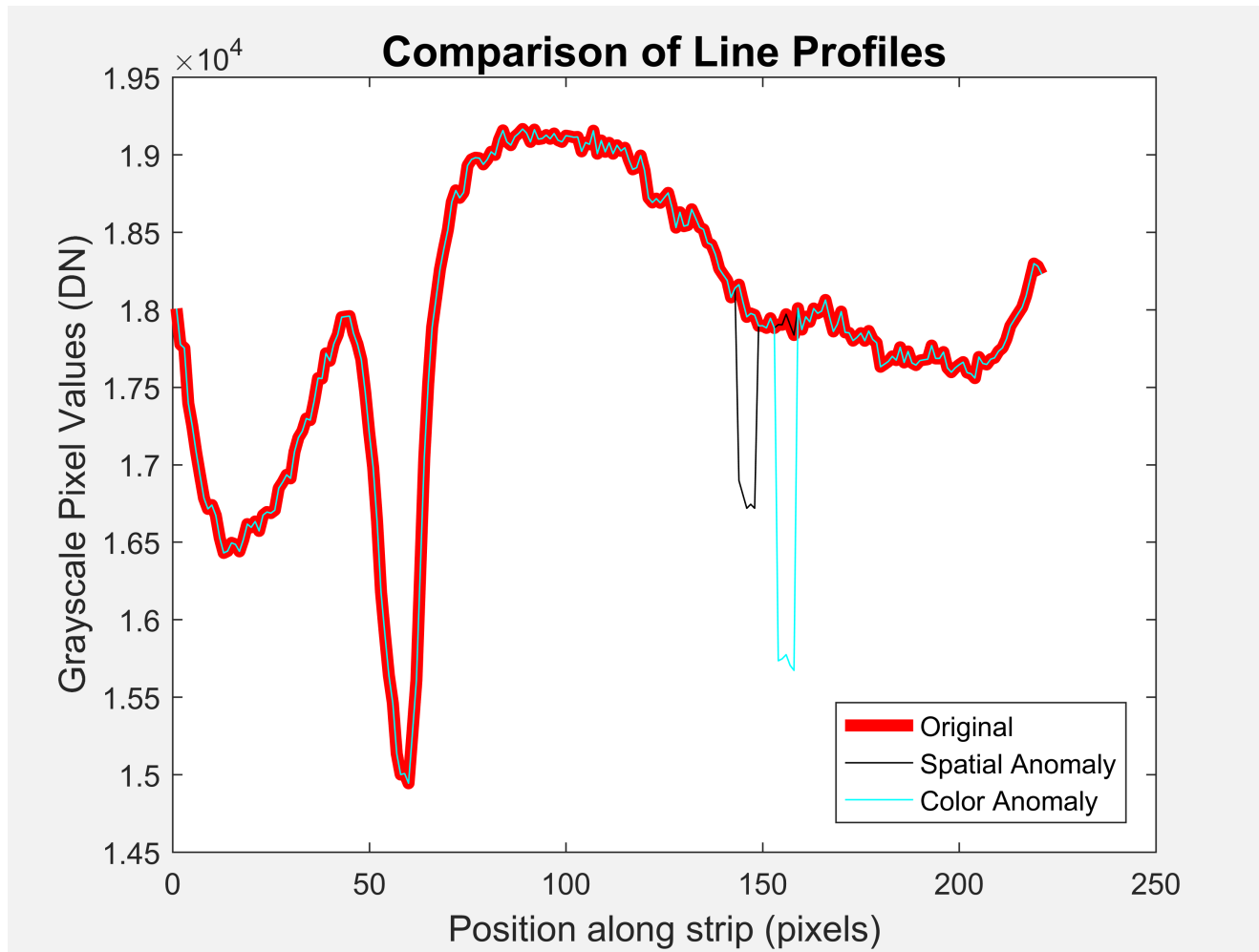
Dealing with Anomalies

- Insertion of anomaly onto strip image
 - Middle panel: technician will notice anomalous spot, but still call test a strong DOA positive
 - Right panel: technician may/may not notice that the response is the wrong color



Dealing with Anomalies

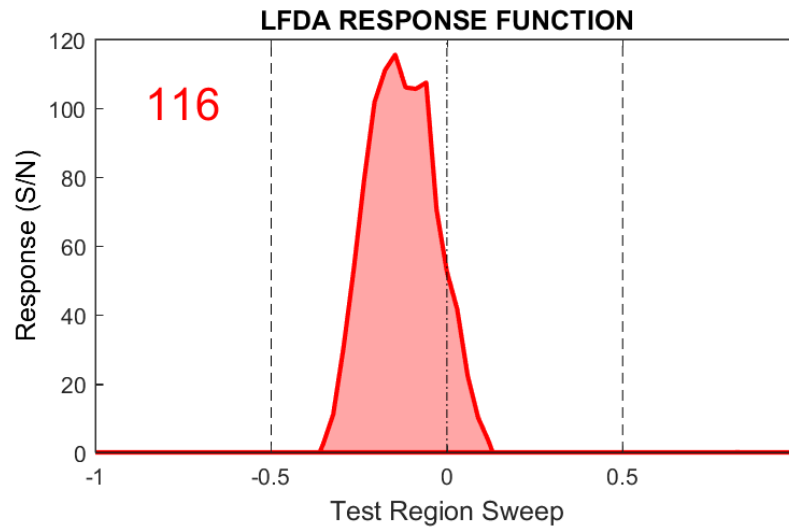
- Standard line profile analysis → strong response for both types of anomalies
 - → DOA negative → False negative



Dealing with Anomalies: Spatial

- LFDA analysis indicates **ZERO** confidence in spite of high S/N ratio (~116)

- At face value the high S/N indicates DOA negative response, while a visual examination suggests a DOA positive response
- However, LFDA indicates that the assay is ANOMALOUS and reports zero confidence in results in spite of high S/N:
 - Large value of HSF metric i.e. tHSF ~ 30 sigma
 - Low value of PUR wrt <PUR> i.e. tPUR ~ -18 sigma

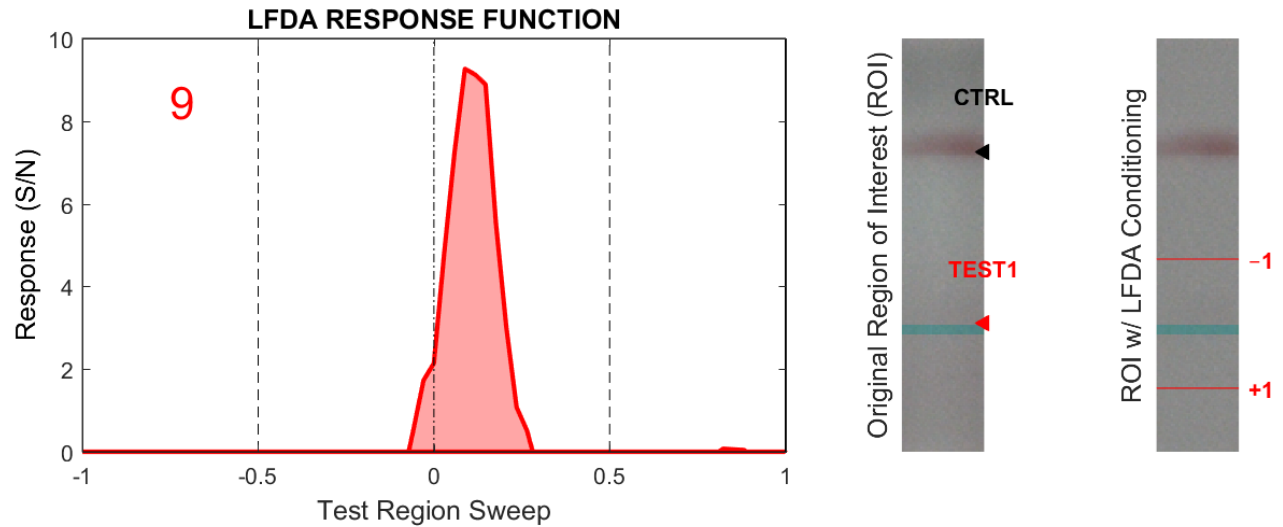


Filename: 50_02_03x.jpg (Mode: on_strip_ref)

METRIC	CTRL	TEST1
Confidence	--	0.00%
SNR	693.09	115.56
RSA	--	40.83% ± 20.38
PUR	--	59.77% <98.28%>
tPUR	--	-17.72 [x]
HSF	--	34.14 <4.76>
tHSF	--	29.56 [x]

Dealing with Anomalies: Color

- LFDA analysis indicates **ZERO** confidence result in spite of modest S/N ratio
- Extremely low PUR value ($\sim 1.4\%$ when expected value at $S/N \sim 9$ is $\sim 80.5\%$) indicates signal **does not "look" like the reference at all**
- HSF indicates a modest anomaly as well, with $tHSF \sim 7.6$ sigma

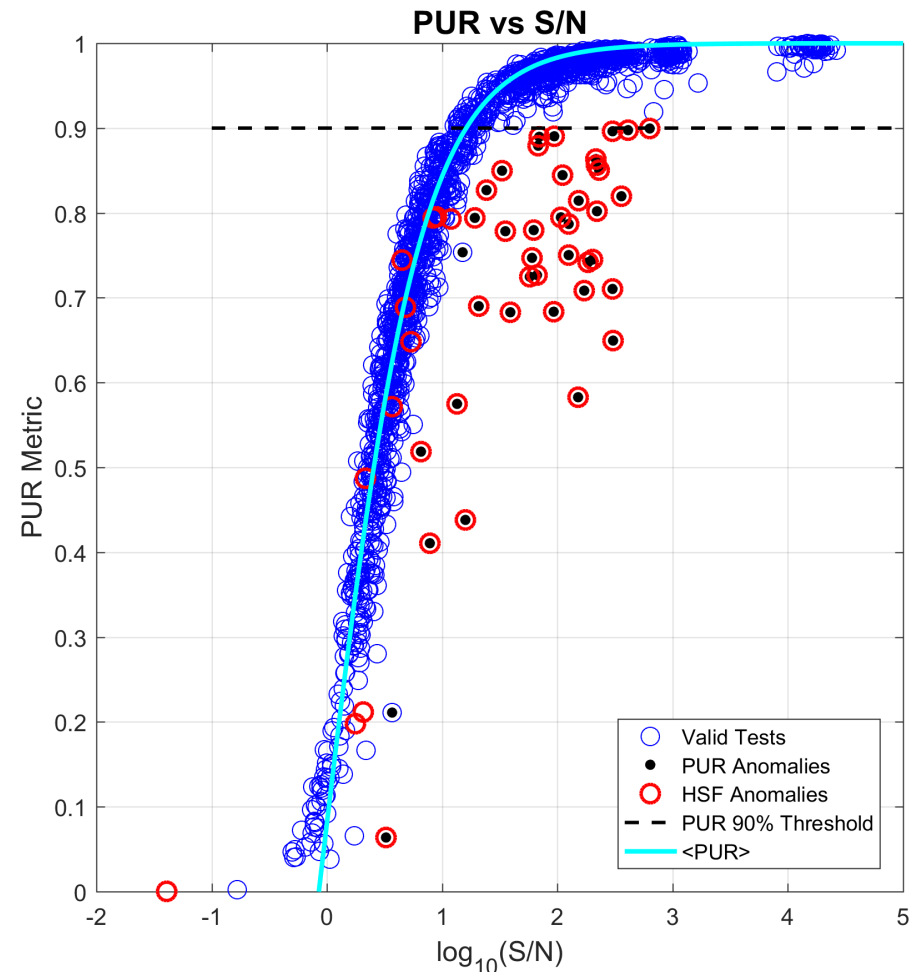


Filename: 50_02_03y.jpg (Mode: on_strip_ref)

METRIC	CTRL	TEST1
Confidence	--	0.00%
SNR	696.11	9.27
RSA	--	11.54% \pm 587.61
PUR	--	1.37% <80.54%>
tPUR	--	-8.74 [x]
HSF	--	12.27 <4.76>
tHSF	--	7.55 [x]

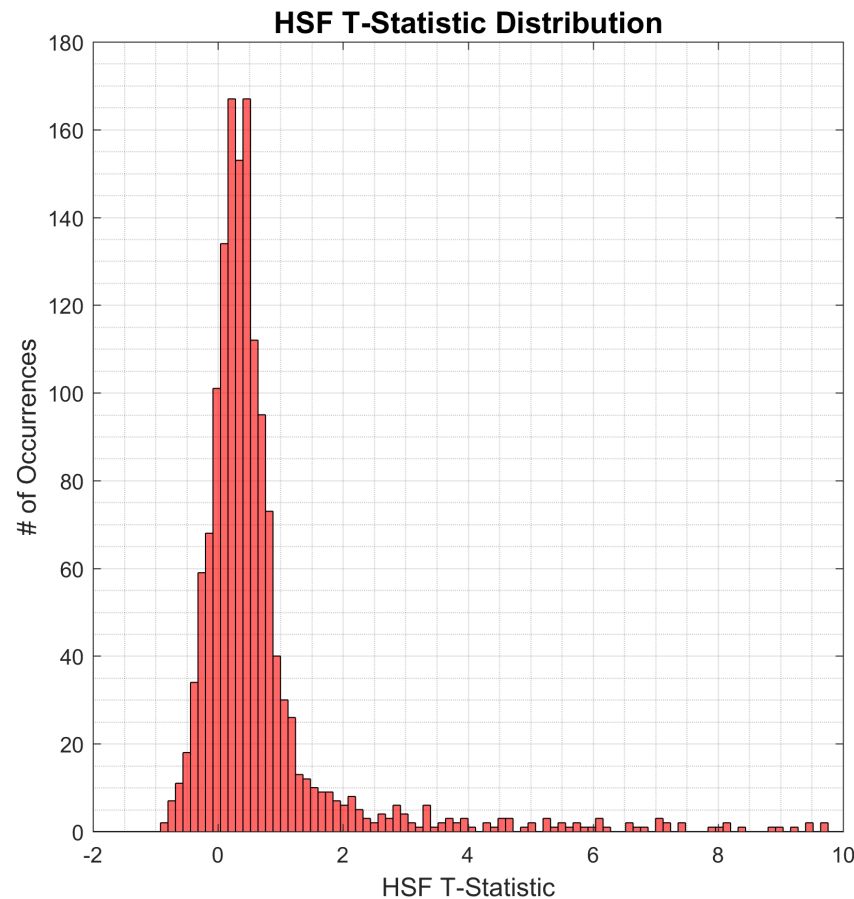
LFDA Anomaly Detection: PUR vs SNR

- LFDA results from a customer demonstration study with 1610 test strips
 - Blue circles – metric values for “normal” test results
 - Cyan line – $\langle \text{PUR} \rangle$ as a function of S/N
 - Red circles – HSF anomalies
 - Solid black dots – PUR anomalies



LFDA Anomaly Detection: HSF Metric

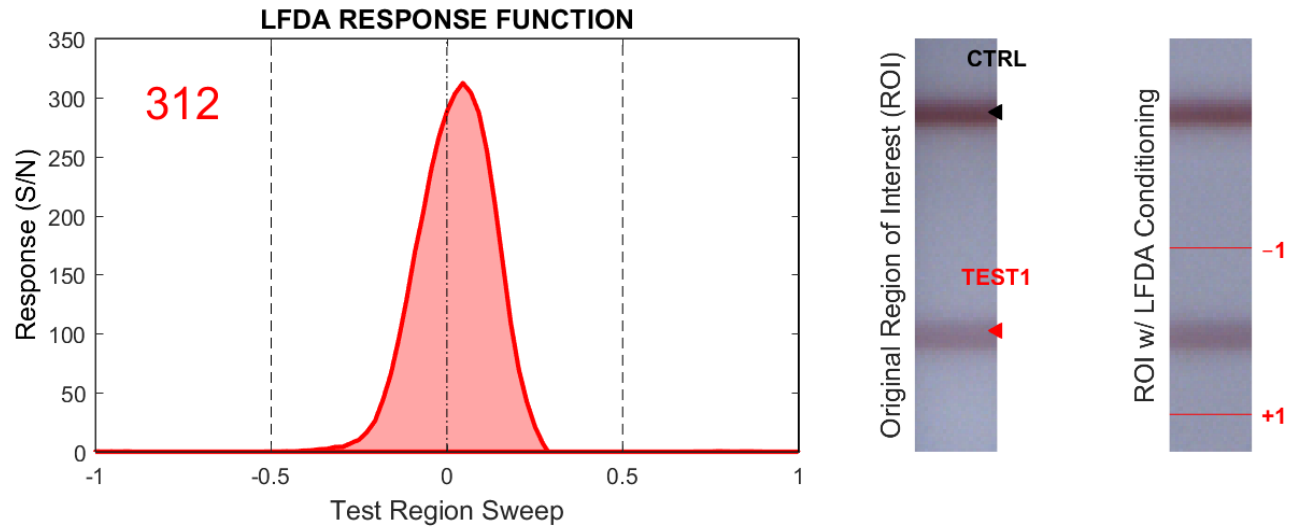
- LFDA results from a customer demonstration study with 1610 test strips
 - Distribution of HSF T-Statistic
 - Expectation is that this should be zero mean for a zero S/N test line (i.e. pure noise) test case, and the positive non-zero mean is due to the presence of test lines with finite S/N and imperfect horizontal uniformity



LFDA: On-chip & Template Reference Modes

Control Negative: On-chip Reference

- High S/N negative control with RSA signal level → ~50% of on-chip ref
- LFDA measured metrics and expected values consistent

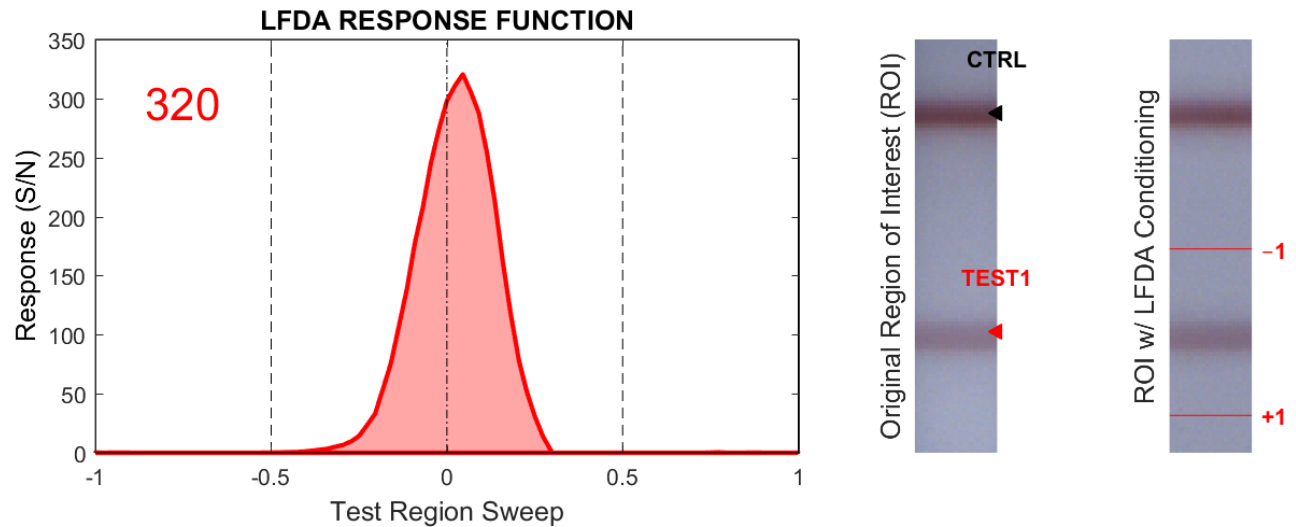


Filename: control neg.png (Mode: on_strip_ref)

METRIC	CTRL	TEST1
Confidence	--	100.00%
SNR	1196.01	312.20
RSA	--	51.09% ± 1.09
PUR	--	97.36% <99.36%>
tPUR	--	-0.99
HSF	--	6.45 <8.74>
tHSF	--	-0.78

Control Negative: Self-Reference Template

- Demonstration of RSA & PUR self-consistency using test strip itself as a reference template
- In the "template" mode, statistics for the control line are computed as well as for the test line



Filename: control neg.png (Mode: template_ref)

METRIC	CTRL	TEST1
Confidence	100.00%	100.00%
SNR	1199.72	320.49
RSA	100.15% ± 0.69	100.26% ± 0.89
PUR	100.00% <99.83%>	100.00% <99.38%>
tPUR	0.08	0.31
HSF	11.20 <8.74>	6.45 <8.74>
tHSF	0.84	-0.78

Non-Anomaly Sample Outliers – QC

Non-Anomaly Sample Outliers – QC

- Using LFDA as an automated detection algorithm provides a rapid method to obtain statistically significant assessment of QC from large sample studies
 - The table below shows a summary of LFDA results from ODI’s small sample DOA demonstration study

- Data sorted by RSA
- Note the clear separation by concentration ... except ...

... anomaly?

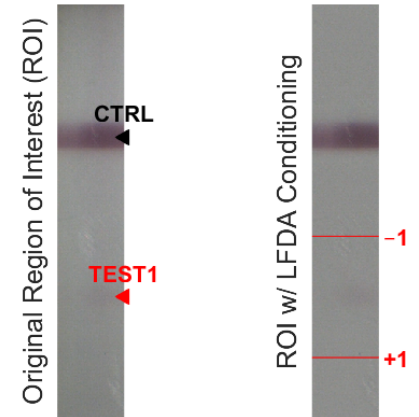
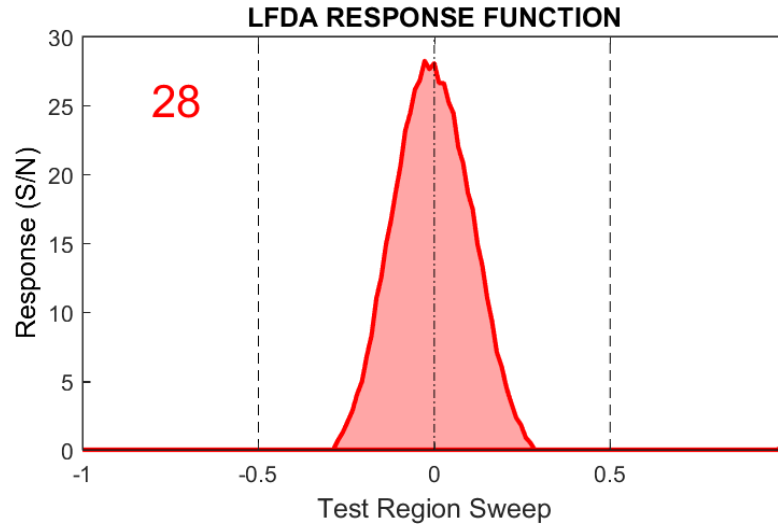
comparison

	A	B	C	D	E	F	G	H	I	J
1	FILE	CON	DOA	CONFIDENCE	SNR	RSA	PUR	PUR_T	HSF	HSF_T
2	3_2017-07-03-131836-0000.png	-50	BZO	100.0	66.2	12.2	93.2	-1.6	39.2	43.6
3	3_2017-07-03-131938-0000.png	-50	BZO	100.0	50.7	10.3	95.3	-0.3	4.4	-0.3
4	1_2017-07-03-131648-0000.png	-50	BZO	100.0	50.0	10.3	91.8	-1.7	5.3	0.9
5	3_2017-07-03-132049-0000.png	-50	BZO	100.0	42.1	9.3	92.7	-0.9	10.0	6.7
6	1_2017-07-03-140414-0000.png	-25	BZO	100.0	28.2	7.0	92.5	-0.2	9.5	6.2
7	2_2017-07-03-131737-0000.png	-50	BZO	100.0	19.6	6.9	88.9	-0.3	4.6	0.0
8	1_2017-07-03-140529-0000.png	-25	BZO	100.0	18.7	5.9	89.3	-0.1	4.6	-0.1
9	1_2017-07-03-140728-0000.png	-25	BZO	100.0	15.9	5.2	82.3	-1.0	7.4	3.5
10	1_2017-07-03-140627-0000.png	-25	BZO	96.1	9.0	4.5	75.9	-0.5	4.9	0.3
11	2_2017-07-03-135113-0000.png	25	BZO	97.7	9.1	4.1	77.3	-0.4	4.4	-0.4
12	2_2017-07-03-135425-0000.png	25	BZO	99.1	8.8	4.1	83.6	0.4	4.2	-0.5
13	2_2017-07-03-135219-0000.png	25	BZO	98.2	8.5	3.9	78.6	0.0	4.6	-0.1
14	1_2017-07-03-135023-0000.png	25	BZO	96.0	8.8	3.8	75.9	-0.4	4.0	-0.9
15	4_2017-07-03-132934-0000.png	50	BZO	86.0	7.3	3.4	71.8	-0.4	4.4	-0.3
16	2_2017-07-03-135316-0000.png	25	BZO	56.3	5.6	3.3	64.7	-0.4	3.8	-1.1
17	1_2017-07-03-140436-0000.png	-25	BZO	38.7	4.8	3.1	60.8	-0.3	4.2	-0.5
18	2_2017-07-03-132737-0000.png	50	BZO	74.3	4.7	2.9	69.8	0.3	3.9	-0.9
19	1_2017-07-03-132646-0000.png	50	BZO	32.1	3.6	2.7	60.0	0.2	4.1	-0.7
20	5_2017-07-03-133042-0000.png	50	BZO	0.0	3.0	2.4	41.4	-0.4	4.4	-0.3
21	3_2017-07-03-132836-0000.png	50	BZO	0.0	1.8	1.9	37.8	0.3	4.1	-0.7

Non-Anomaly Sample Outliers – QC

- Comparison for BZO outlier

- S/N good
- PUR very high and consistent with <PUR>
- HSF elevated wrt <HSF>
 - Close examination yields horizontal asymmetry in line response which is detected by HSF
 - tHSF overridden because of high PUR
- RSA of 7% above cutoff indicating expected response

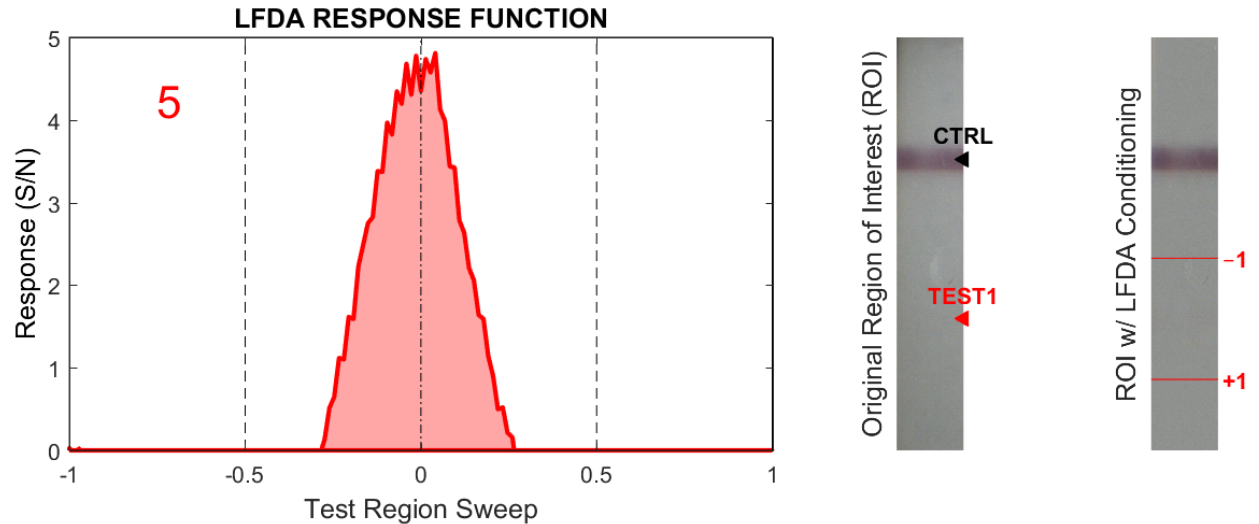


Filename: 1_2017-07-03-140414-0000.png (Mode: on_strip_ref)

METRIC	CTRL	TEST1
Confidence	--	100.00%
SNR	5782.16	28.22
RSA	--	6.99% ± 0.42
PUR	--	92.54% <93.20%>
tPUR	--	-0.17
HSF	--	9.52 <4.65>
tHSF	--	6.16 [o]

Non-Anomaly Sample Outliers – QC

- BZO outlier
 - RSA of 3% below cutoff → anomaly?
 - All LFDA metrics good
- *Strip/drug sample QC?*
 - Blink with previous chart
 - Notice clear absence of line
 - **LFDA correctly identified low signal for this test!**



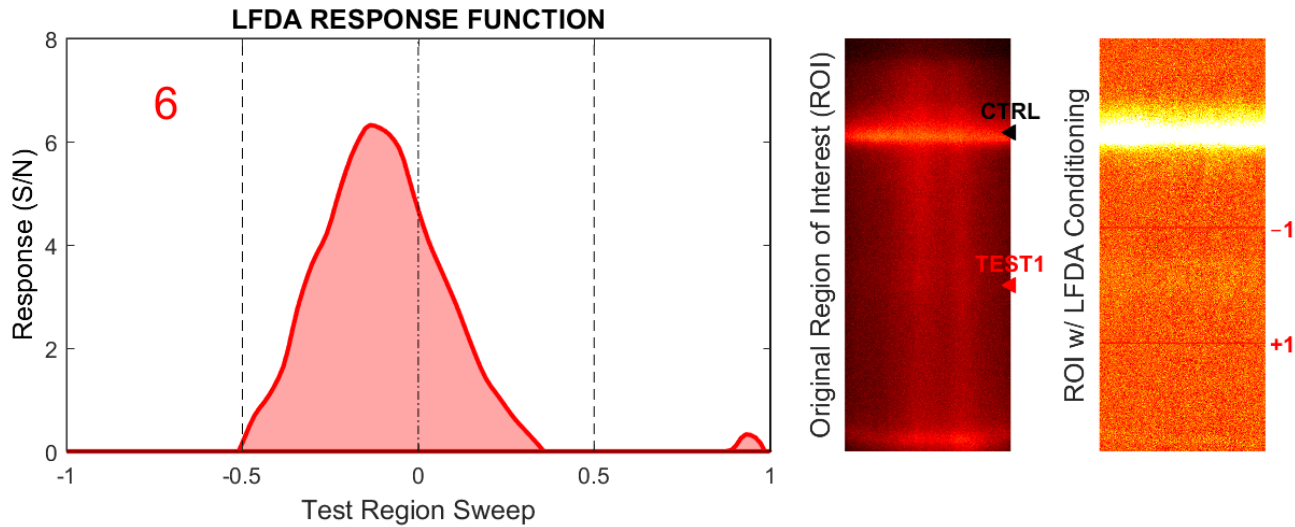
Filename: 1_2017-07-03-140436-0000.png (Mode: on_strip_ref)

METRIC	CTRL	TEST1
Confidence	--	38.71%
SNR	4910.66	4.81
RSA	--	3.13% ± 1.43
PUR	--	60.85% <65.58%>
tPUR	--	-0.32
HSF	--	4.24 <4.65>
tHSF	--	-0.52

LFDA Background Conditioning

- The following charts show some results illustrating the effectiveness of the LFDA background conditioning process

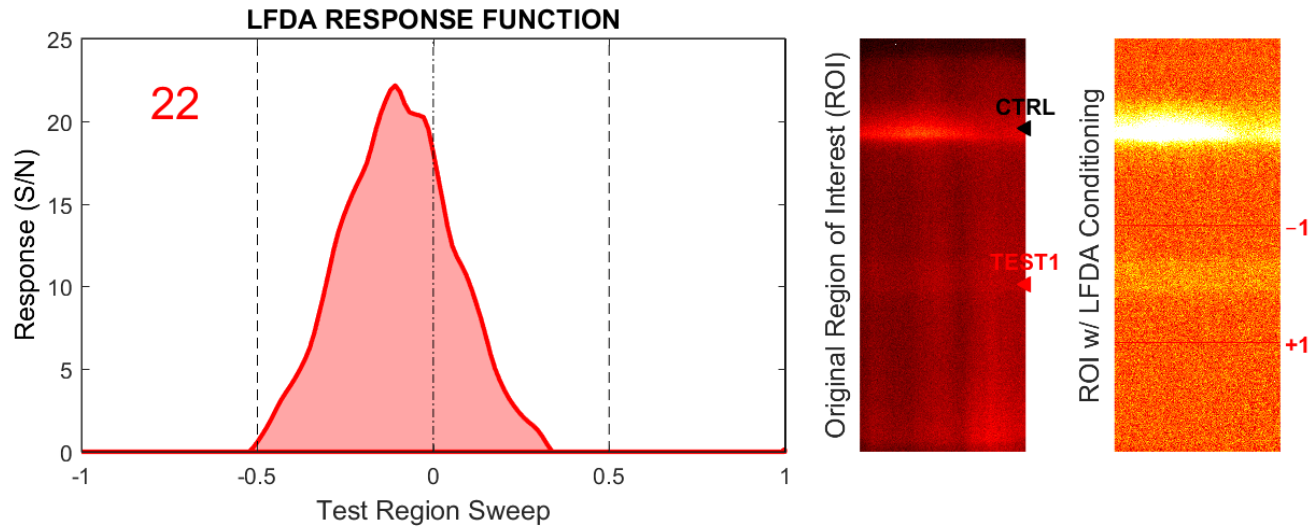
LFDA Background Conditioning



Filename: dev01_con11_rep03.raw

METRIC	CTRL	TEST1
Confidence	100.00%	92.49%
SNR	1665.12	6.32
RSA	80.26% ± 1.79	1.64% ± 0.39
PUR	97.00% <99.88%>	75.17% <72.70%>
tPUR	-1.44	0.20
HSF	12.16 <3.26>	3.31 <3.26>
tHSF	21.53 [o]	0.12

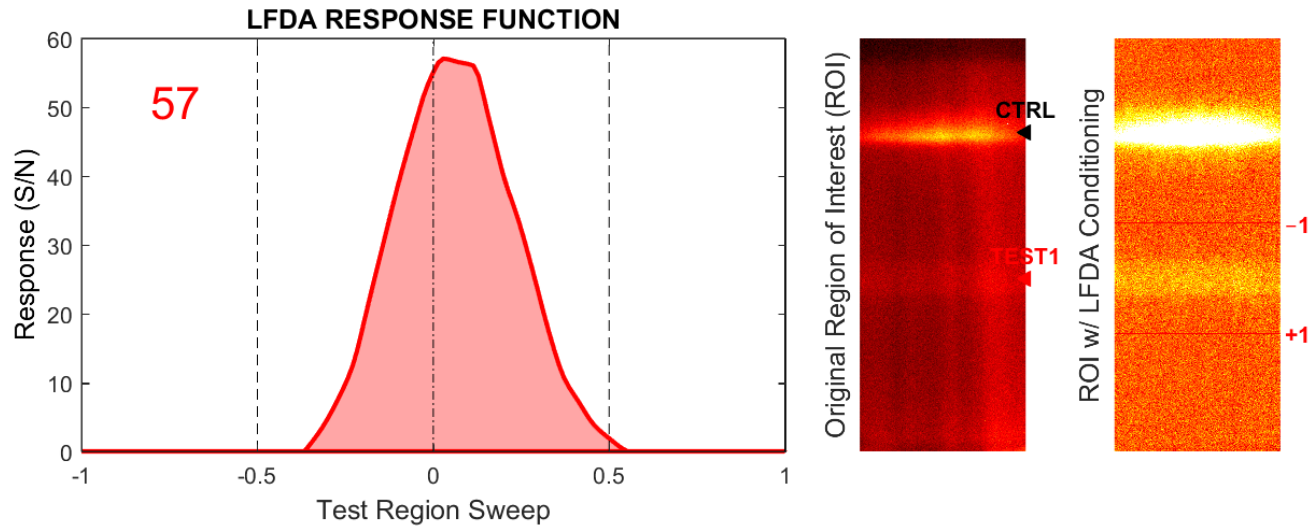
LFDA Background Conditioning



Filename: dev01_con20_rep03.raw

METRIC	CTRL	TEST1
Confidence	100.00%	100.00%
SNR	783.38	22.16
RSA	59.62% ± 1.36	3.33% ± 0.22
PUR	96.99% <99.75%>	92.00% <91.37%>
tPUR	-1.38	0.14
HSF	45.68 <3.26>	3.48 <3.26>
tHSF	102.58 [o]	0.53

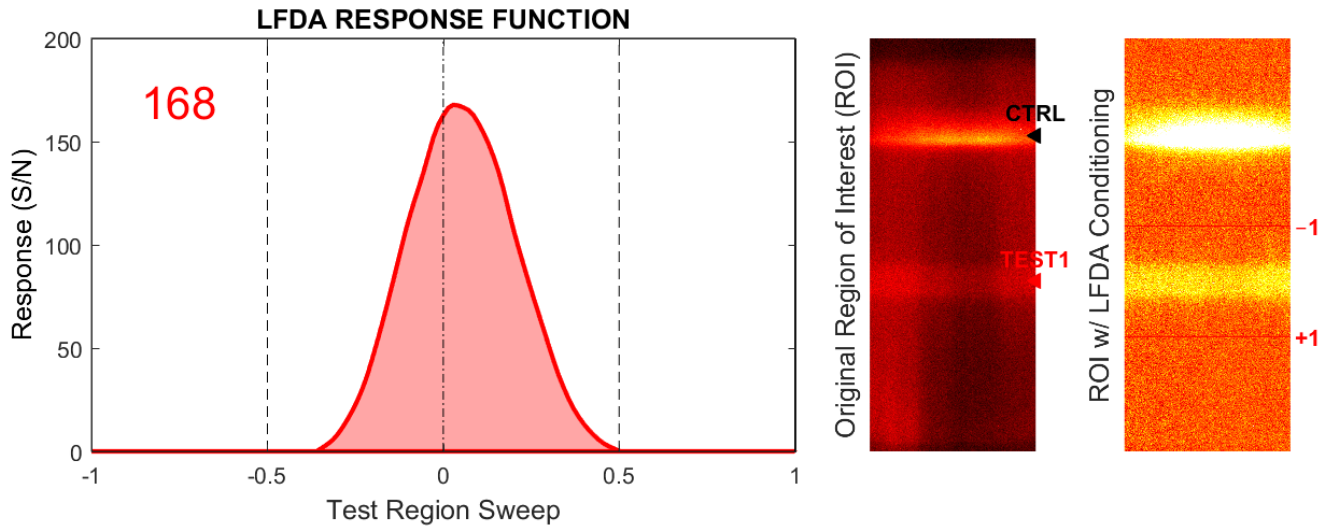
LFDA Background Conditioning



Filename: dev01_con21_rep01.raw

METRIC	CTRL	TEST1
Confidence	100.00%	100.00%
SNR	1884.09	57.05
RSA	83.02% ± 1.21	4.77% ± 0.14
PUR	98.10% <99.89%>	96.68% <96.59%>
tPUR	-0.89	0.04
HSF	50.28 <3.21>	3.22 <3.21>
tHSF	116.98 [o]	0.01

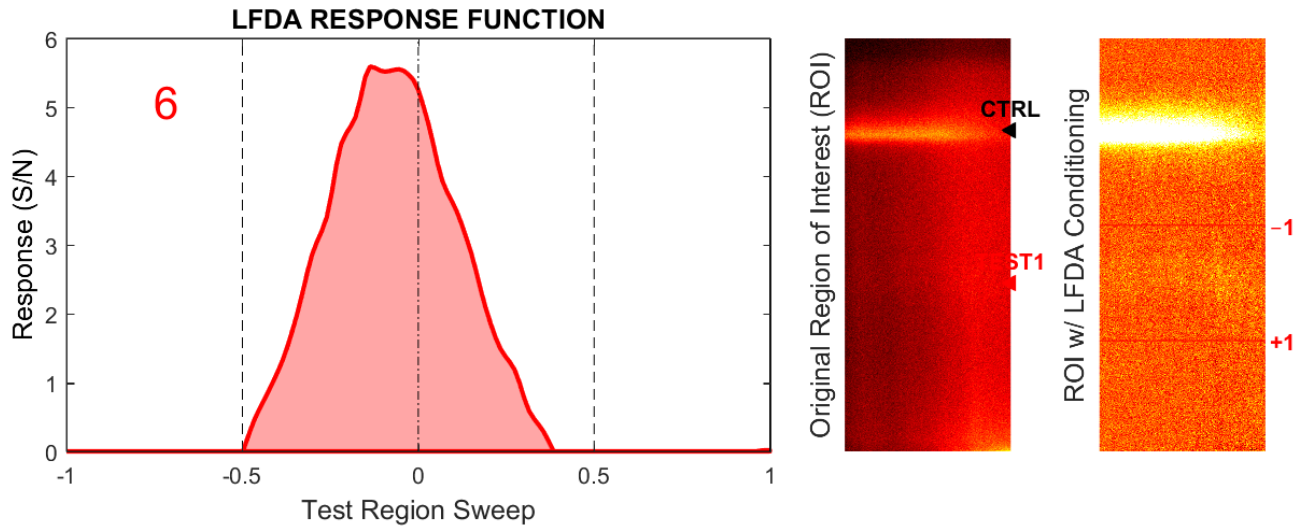
LFDA Background Conditioning



Filename: dev01_con24_rep04.raw

METRIC	CTRL	TEST1
Confidence	100.00%	100.00%
SNR	1725.32	167.80
RSA	82.79% ± 1.02	8.46% ± 0.11
PUR	98.50% <99.88%>	98.63% <98.82%>
tPUR	-0.69	-0.09
HSF	58.81 <3.21>	3.50 <3.21>
tHSF	138.19 [o]	0.71

LFDA Background Conditioning



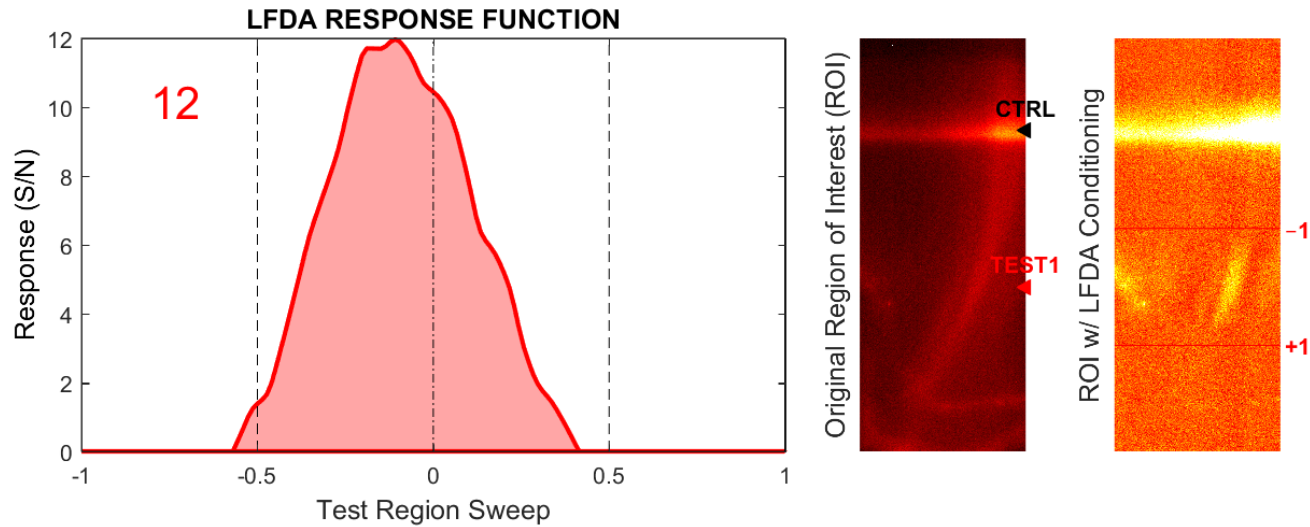
Filename: dev01_con30_rep03.raw

METRIC	CTRL	TEST1
Confidence	100.00%	92.75%
SNR	1102.00	5.59
RSA	69.54% ± 1.18	1.64% ± 0.36
PUR	97.84% <99.82%>	76.65% <70.32%>
tPUR	-0.99	0.49
HSF	62.61 <3.23>	3.67 <3.23>
tHSF	145.57 [o]	1.08

LFDA Sample Anomalies

- The following charts show some results illustrating the real sample anomalies

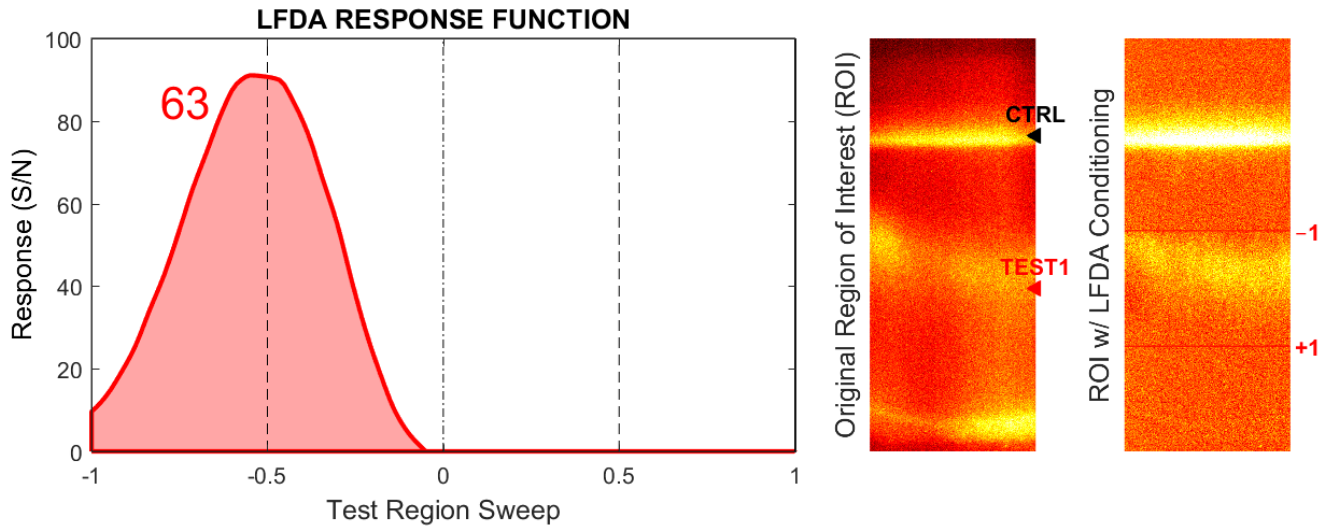
LFDA Sample Anomalies



Filename: dev01_con04_rep02.raw

METRIC	CTRL	TEST1
Confidence	100.00%	0.00%
SNR	997.29	11.97
RSA	54.74% ± 1.49	1.98% ± 0.37
PUR	96.41% <99.80%>	79.31% <84.66%>
tPUR	-1.69	-0.72
HSF	69.30 <3.30>	15.87 <3.30>
tHSF	155.10 [o]	29.52 [x]

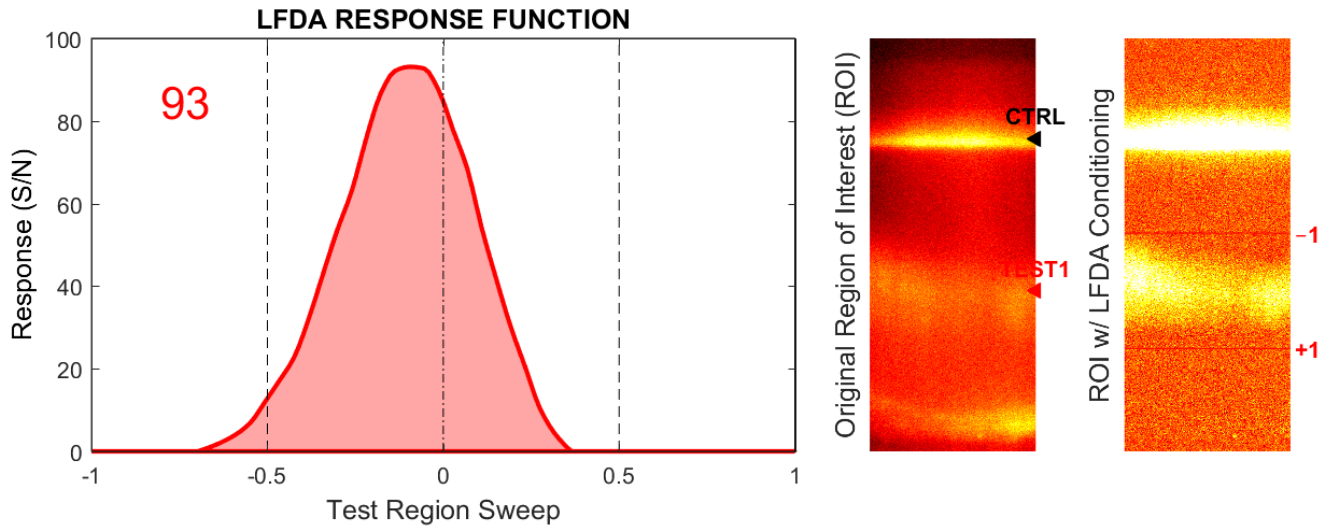
LFDA Sample Anomalies



Filename: dev05_con16_rep05.raw

METRIC	CTRL	TEST1
Confidence	100.00%	0.00%
SNR	778.86	62.52
RSA	51.63% ± 1.61	4.86% ± 0.97
PUR	95.84% <99.74%>	78.00% <96.85%>
tPUR	-1.95	-7.45 [x]
HSF	6.27 <3.30>	20.76 <3.30>
tHSF	6.97 [o]	41.03 [x]

LFDA Sample Anomalies



Filename: dev09_con12_rep03.raw

METRIC	CTRL	TEST1
Confidence	100.00%	0.00%
SNR	1648.90	93.11
RSA	104.57% ± 3.43	8.28% ± 2.71
PUR	95.58% <99.88%>	68.34% <97.88%>
tPUR	-2.15	-13.08 [x]
HSF	20.00 <3.35>	27.28 <3.35>
tHSF	37.99 [o]	54.59 [x]