The Determination of Breath Biomarkers for Disease and Health Identifiers to Create a Non-Invasive Rapid Screen using Portable Mass Spectrometry

Dr. Guido F. Verbeck

Departments: Chemistry and Biological Sciences

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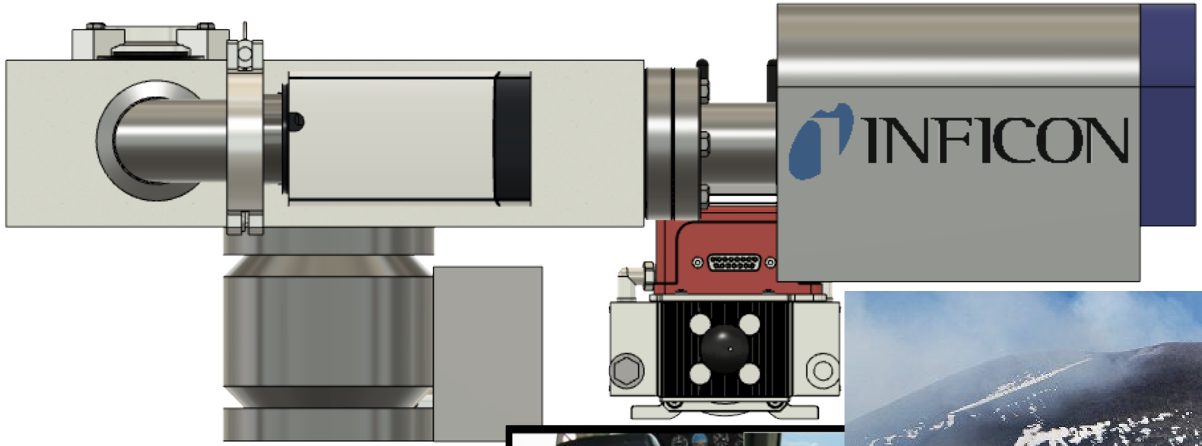
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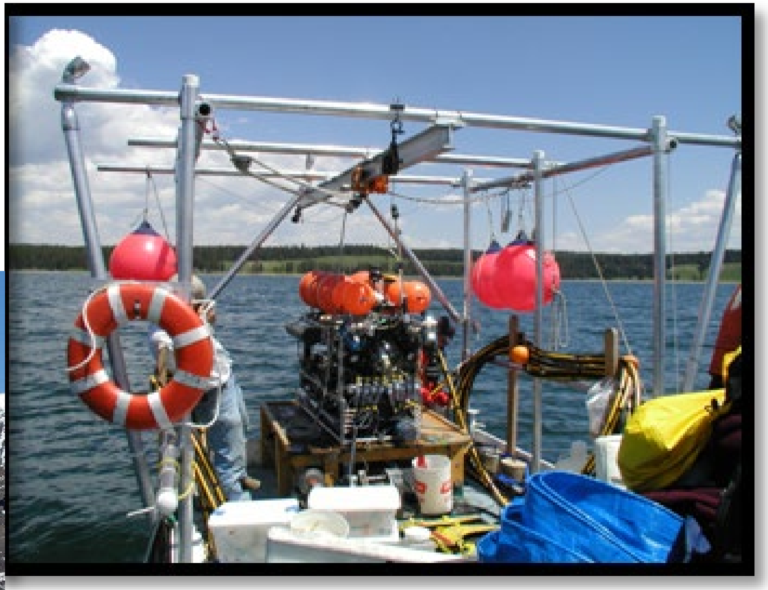
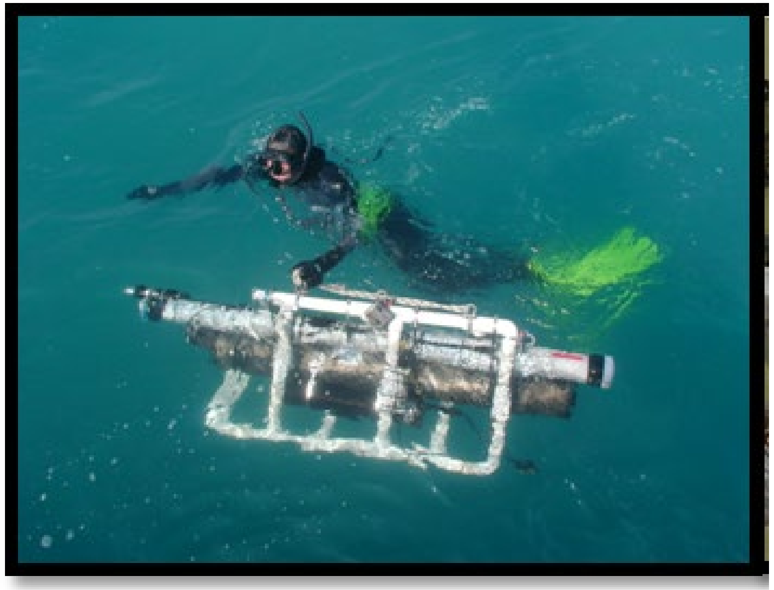
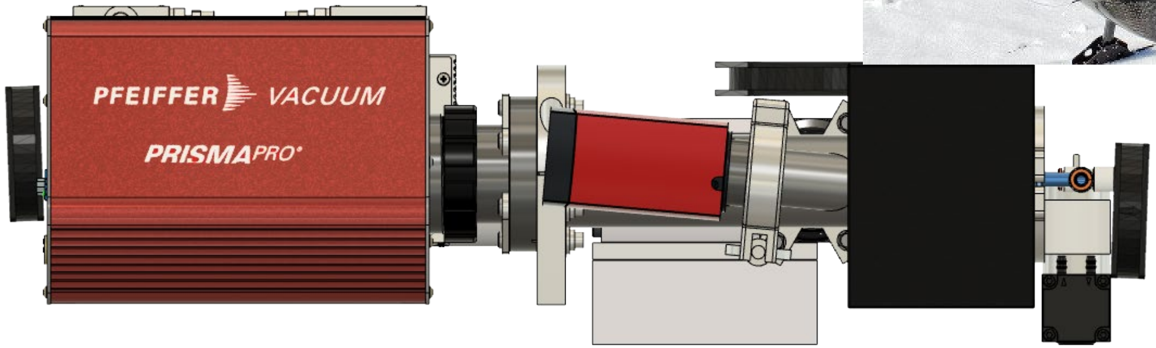
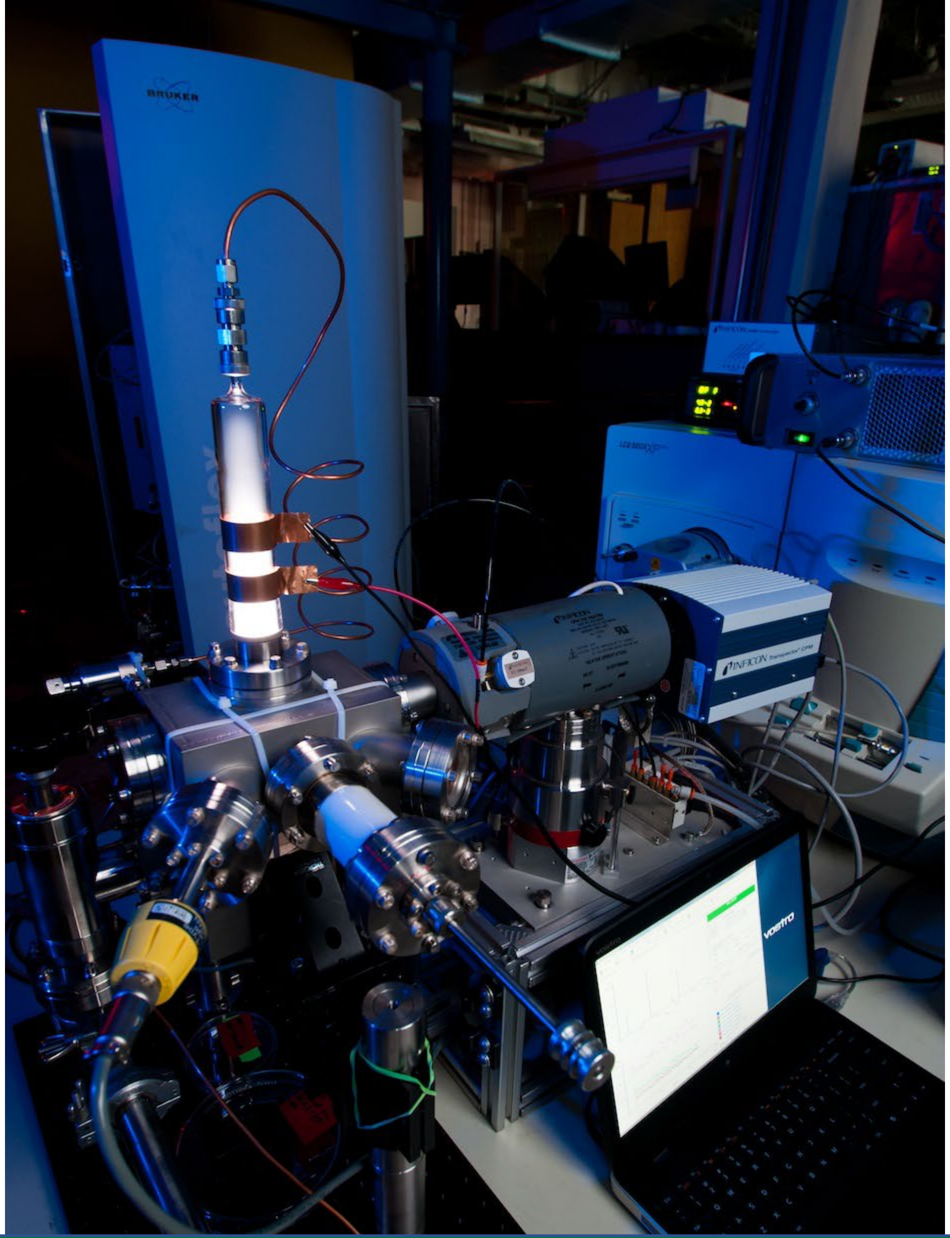





PFEIFFER VACUUM
PRISMAPRO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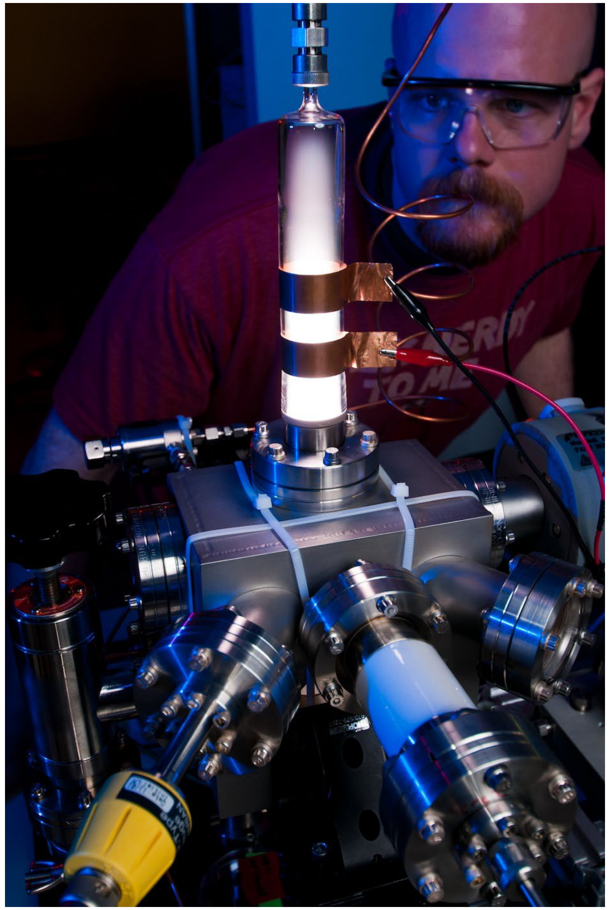

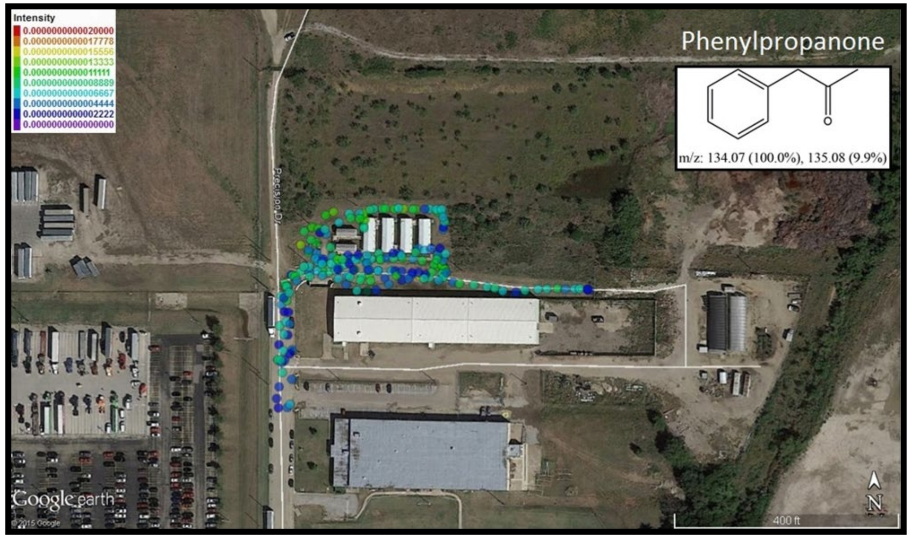

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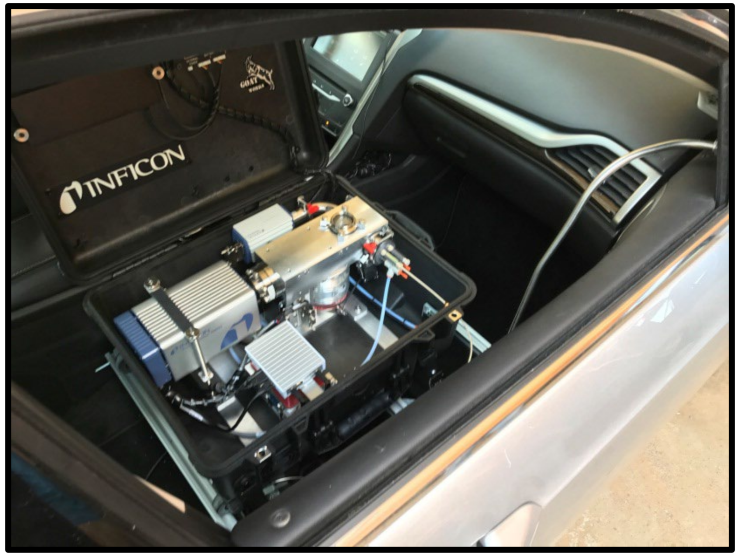

Mach, P.M.; McBride, E.M.; Sasiene, Z.J.; Brigance, K.R.; Kennard, S.K.; Wright, K.C.; Verbeck, G.F., “Vehicle-Mounted Portable Mass Spectrometry System for the Covert Detection via Spatial Analysis of Clandestine Methamphetamine Laboratories”, *Anal. Chem.*, 87 (2015) 11501-11508

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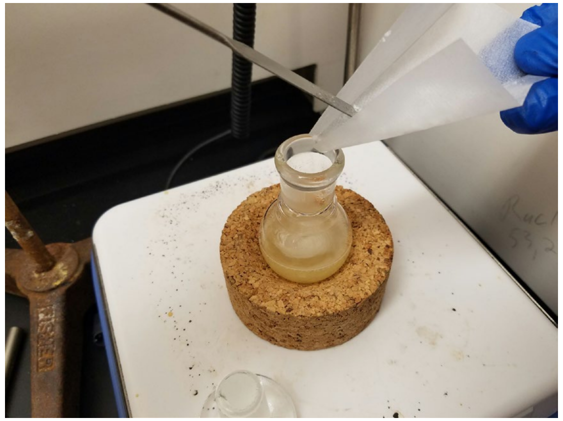
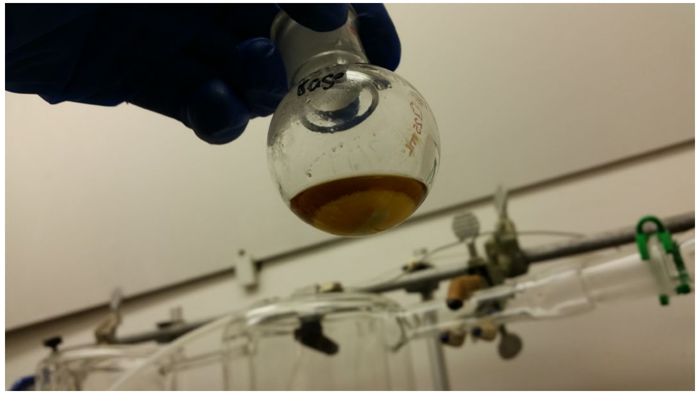
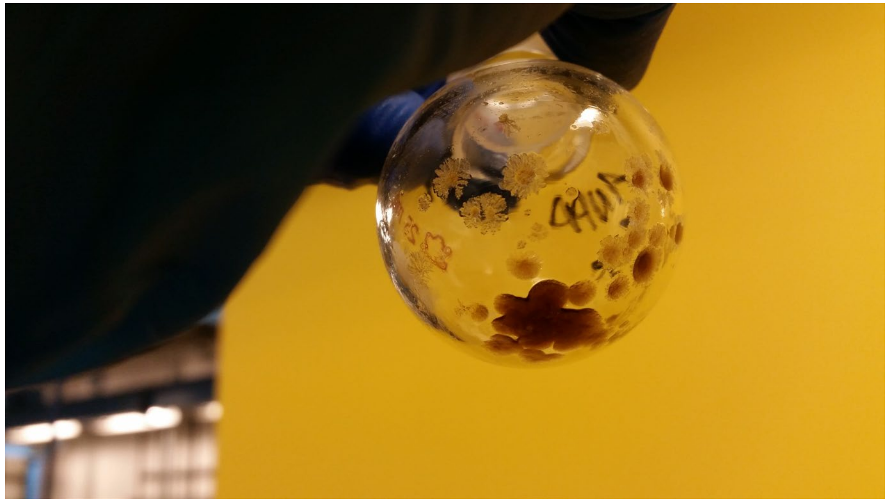
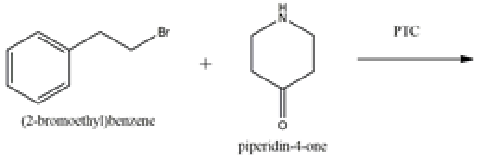


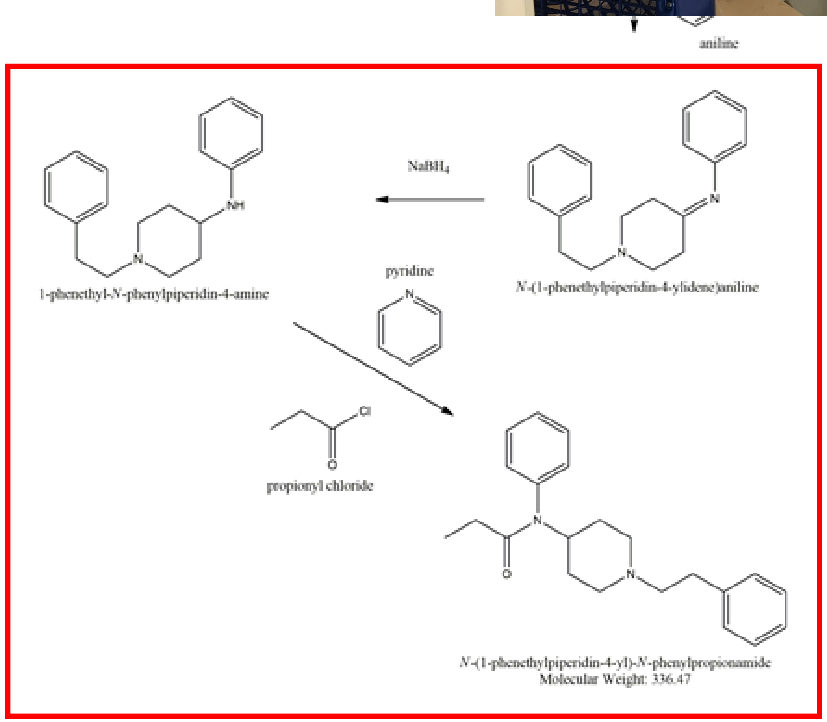
Addition of $NaBH_4$

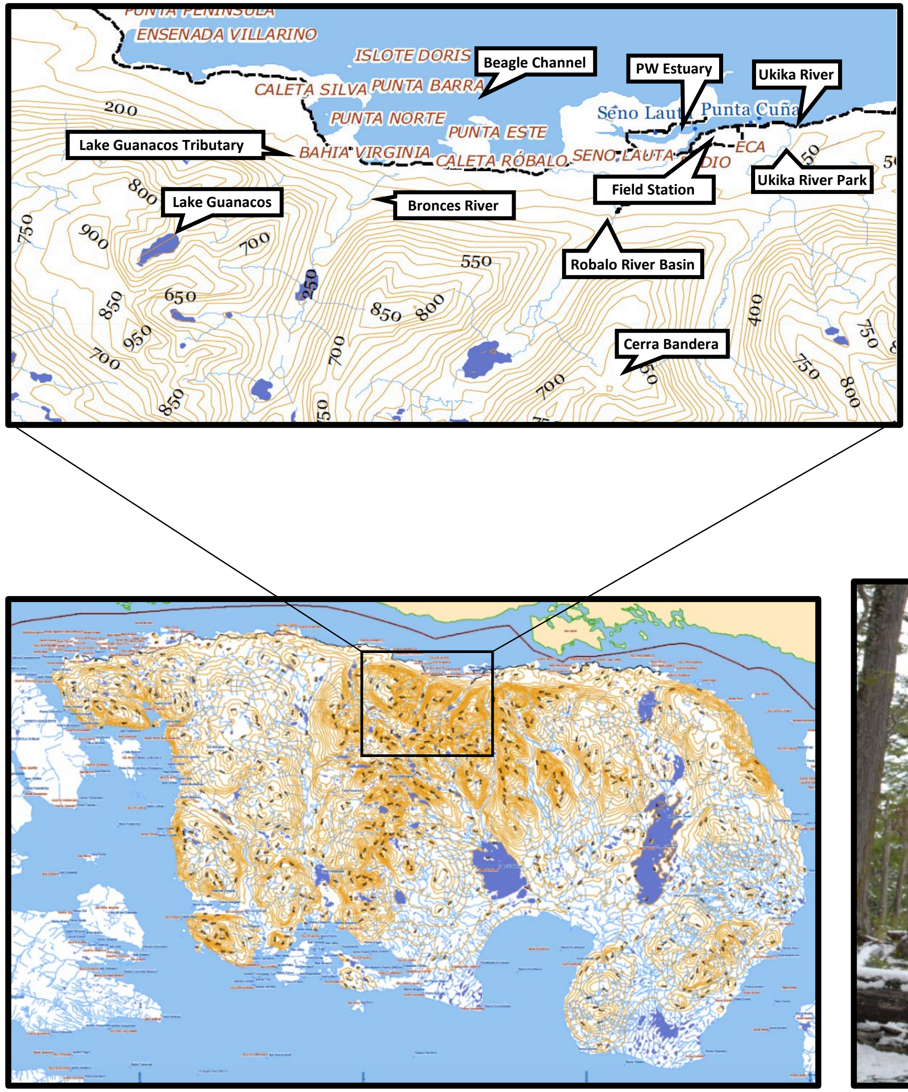


Final Product









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Mach, P.M.; Winfield, J.L.; Aquilar, R.A.; Wright, K.C.; **Verbeck, G.F.,** "A Portable Mass Spectrometer Study Targeting Anthropogenic Contaminants in Sub-Antarctic Puerto Williams, Chile" *Int. J. Mass Spectrom.* 422 (2017) 148-153.

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MIMS System Flat Membrane Analysis (cont.)

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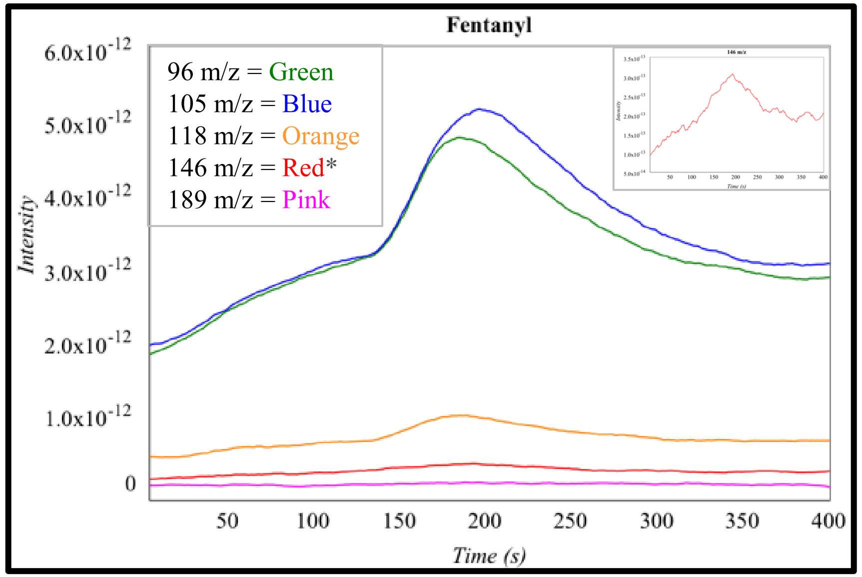
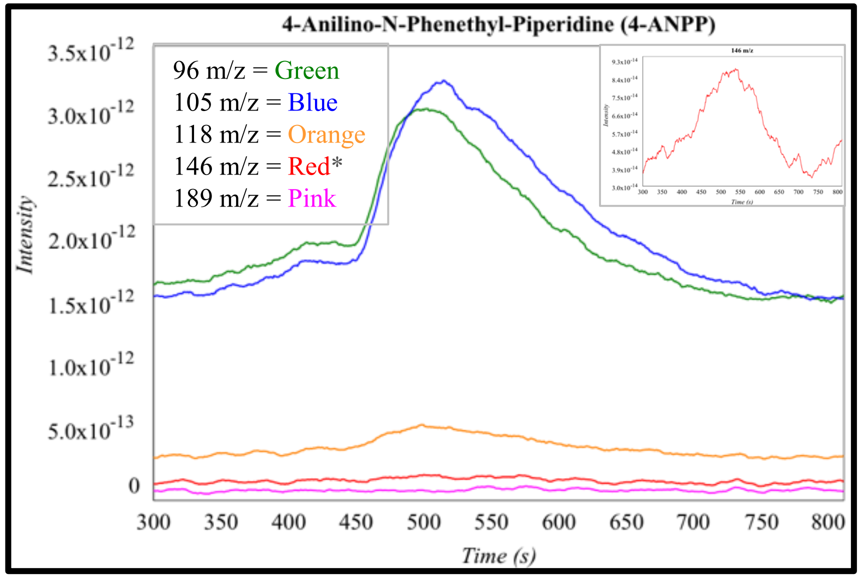
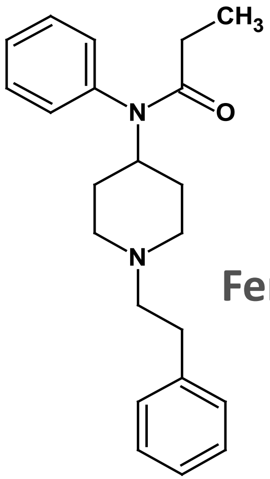
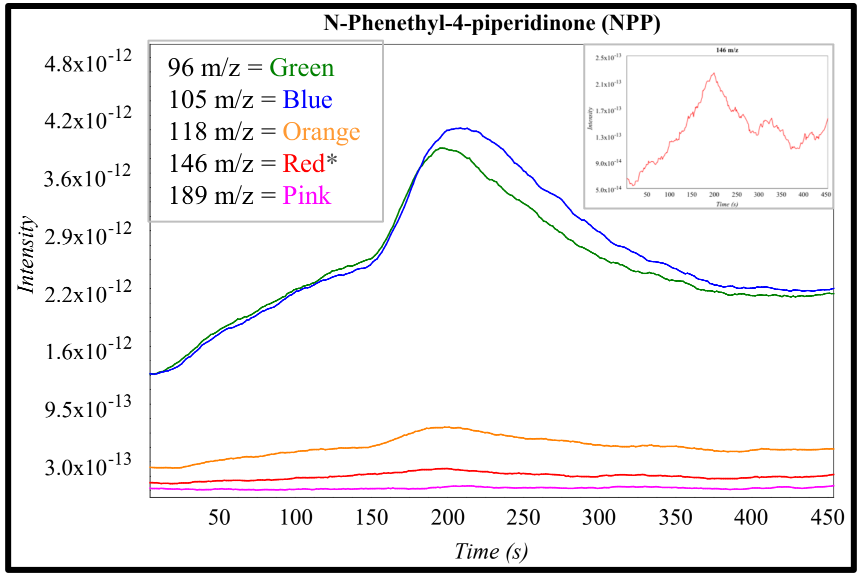
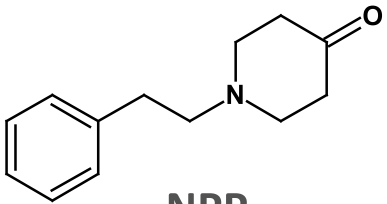




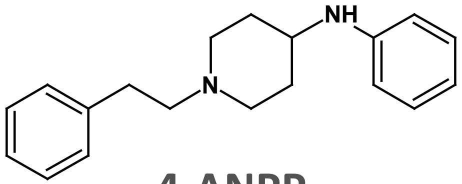


Fentanyl





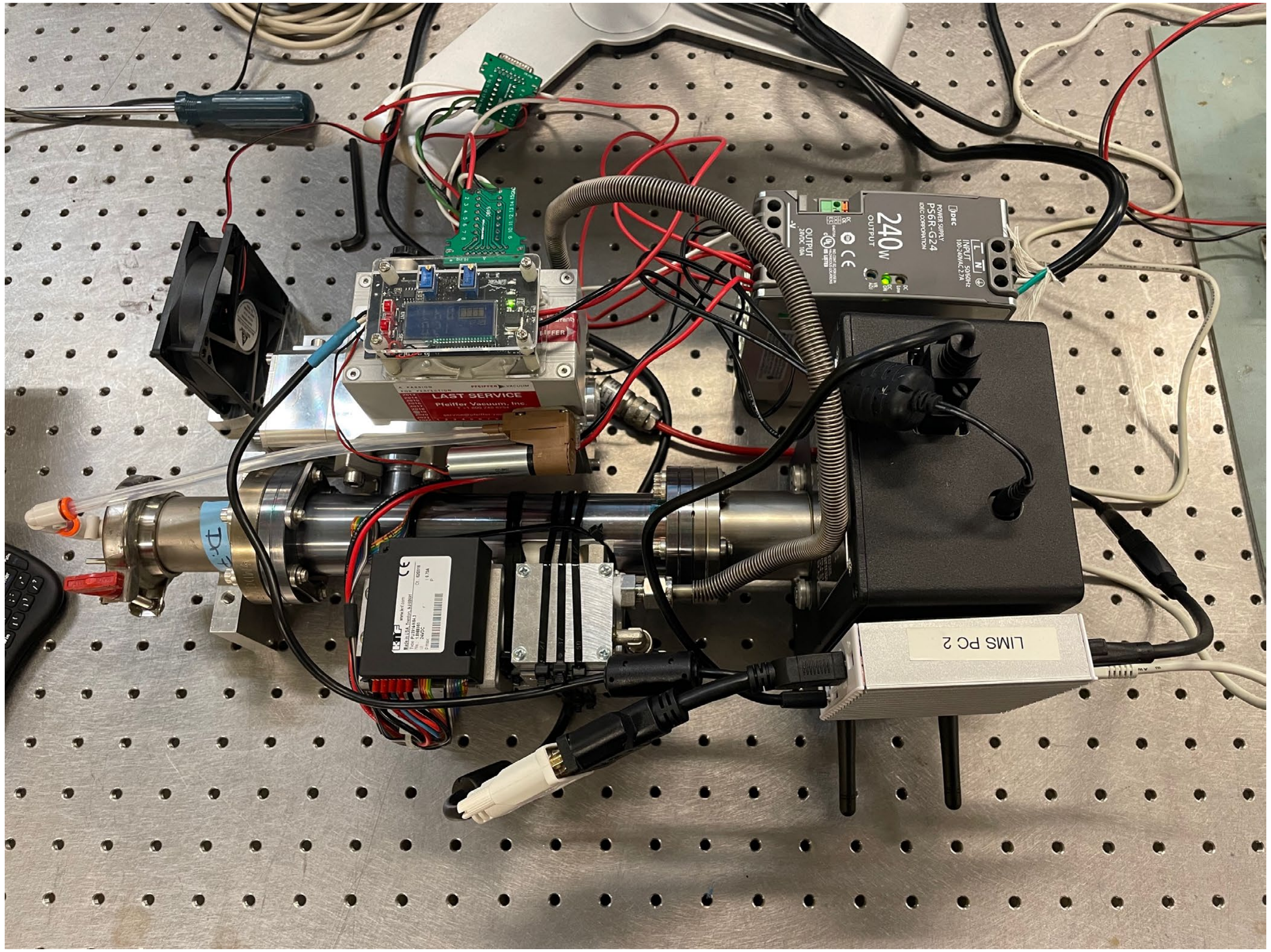
NPP



4-ANPP

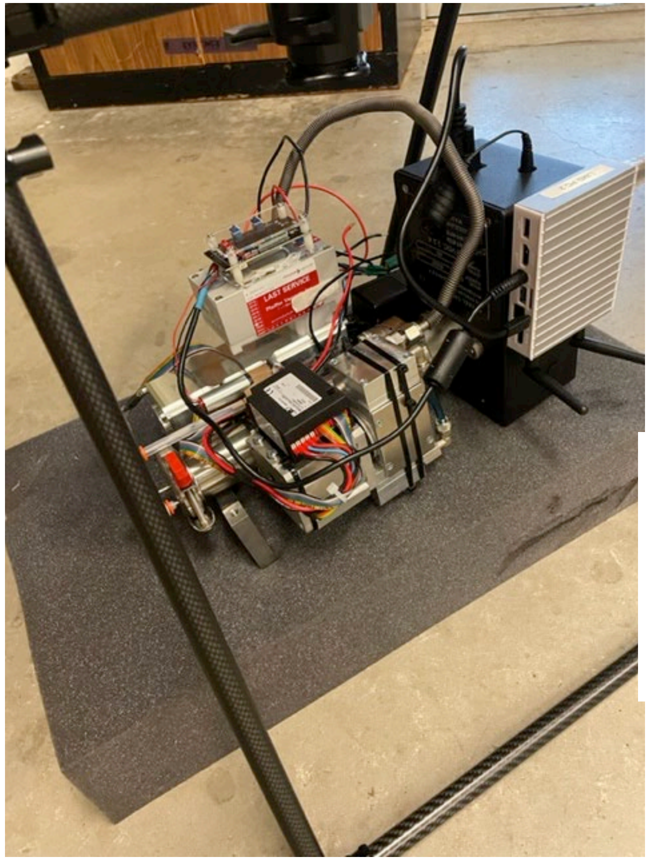
Figure 1. *CAD drawing for the Portable Mass Spectrometer drone system*

Figure 2*. CAD drawing for the Portable Mass Spectrometer drone system analyzing smoke chemistry*



crux

AFWERX



crux

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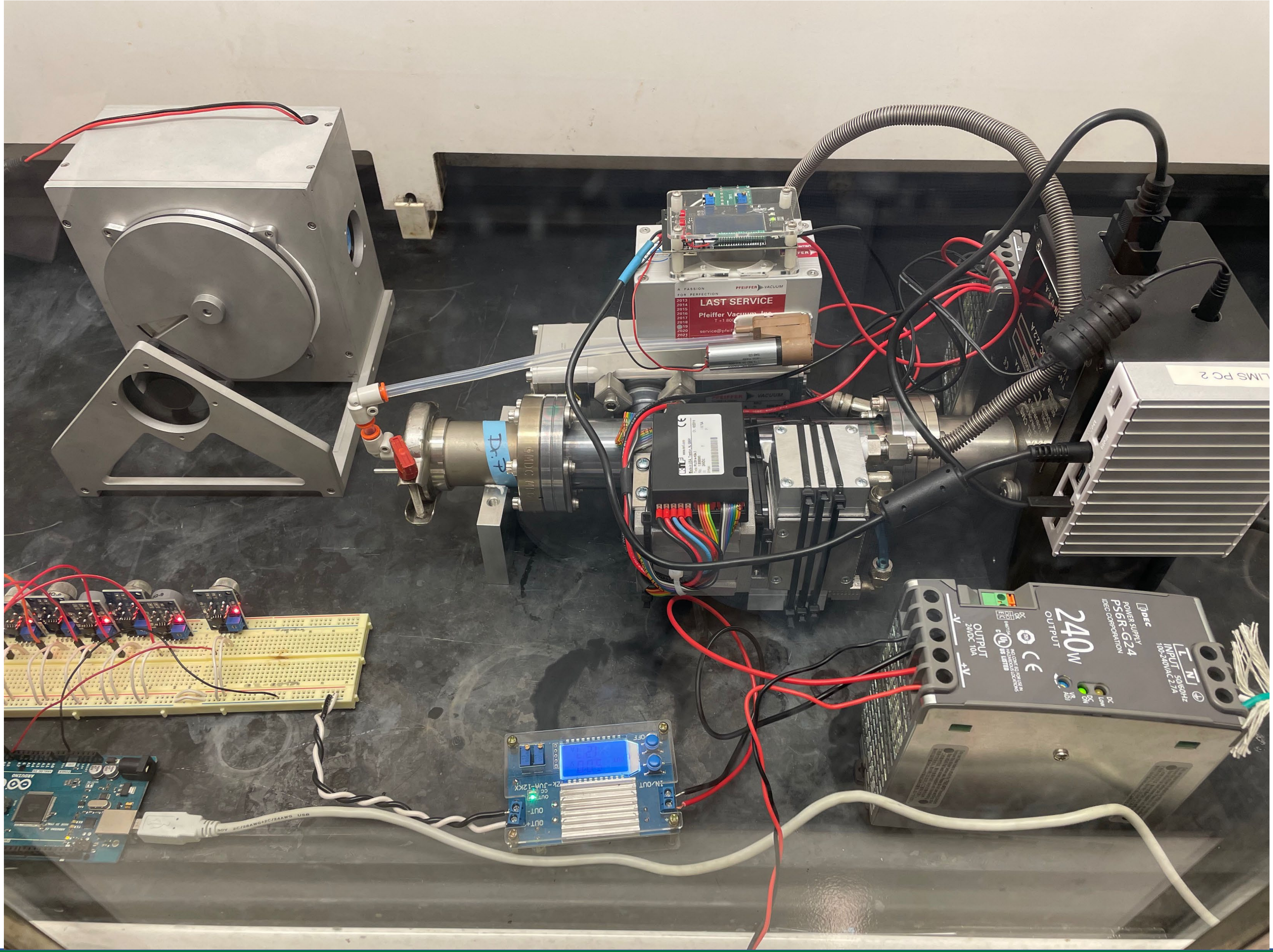

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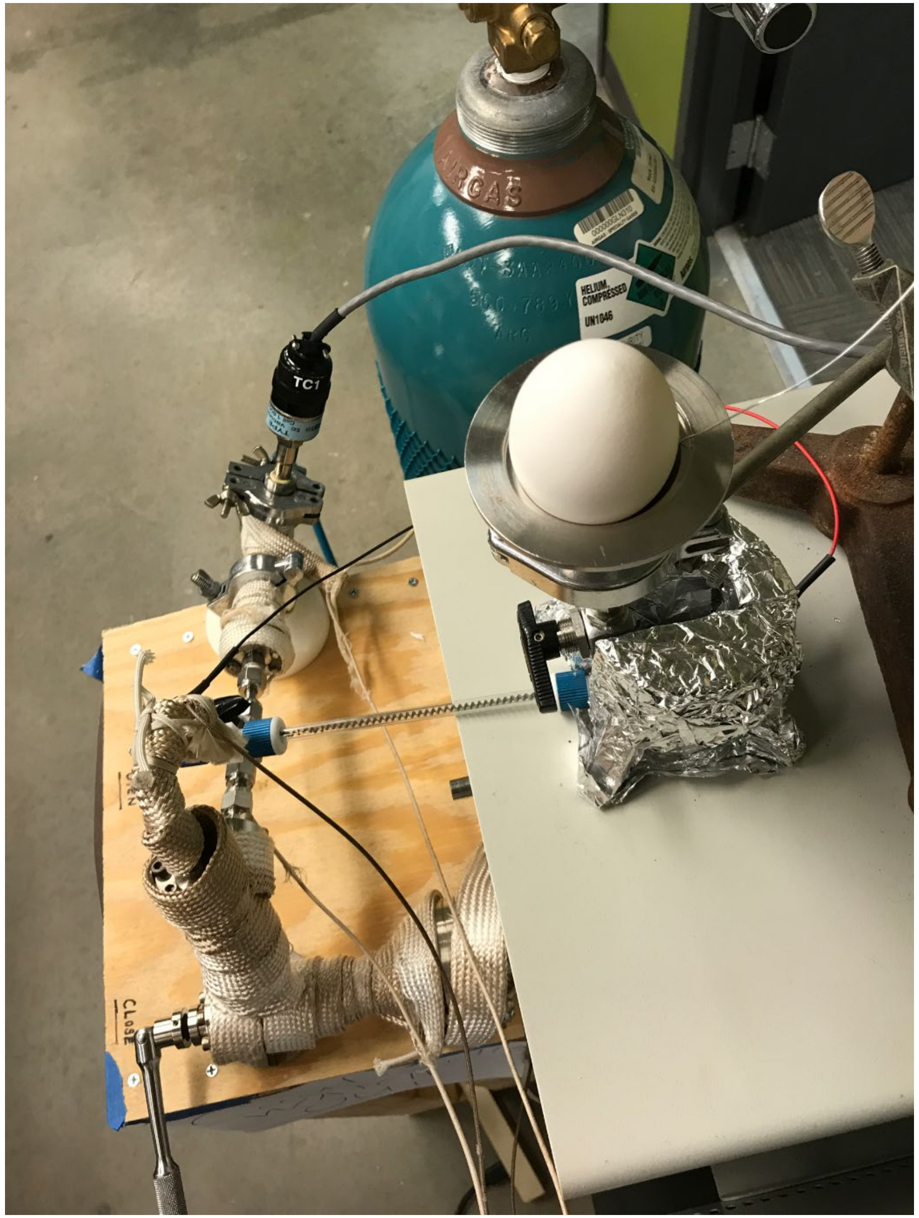
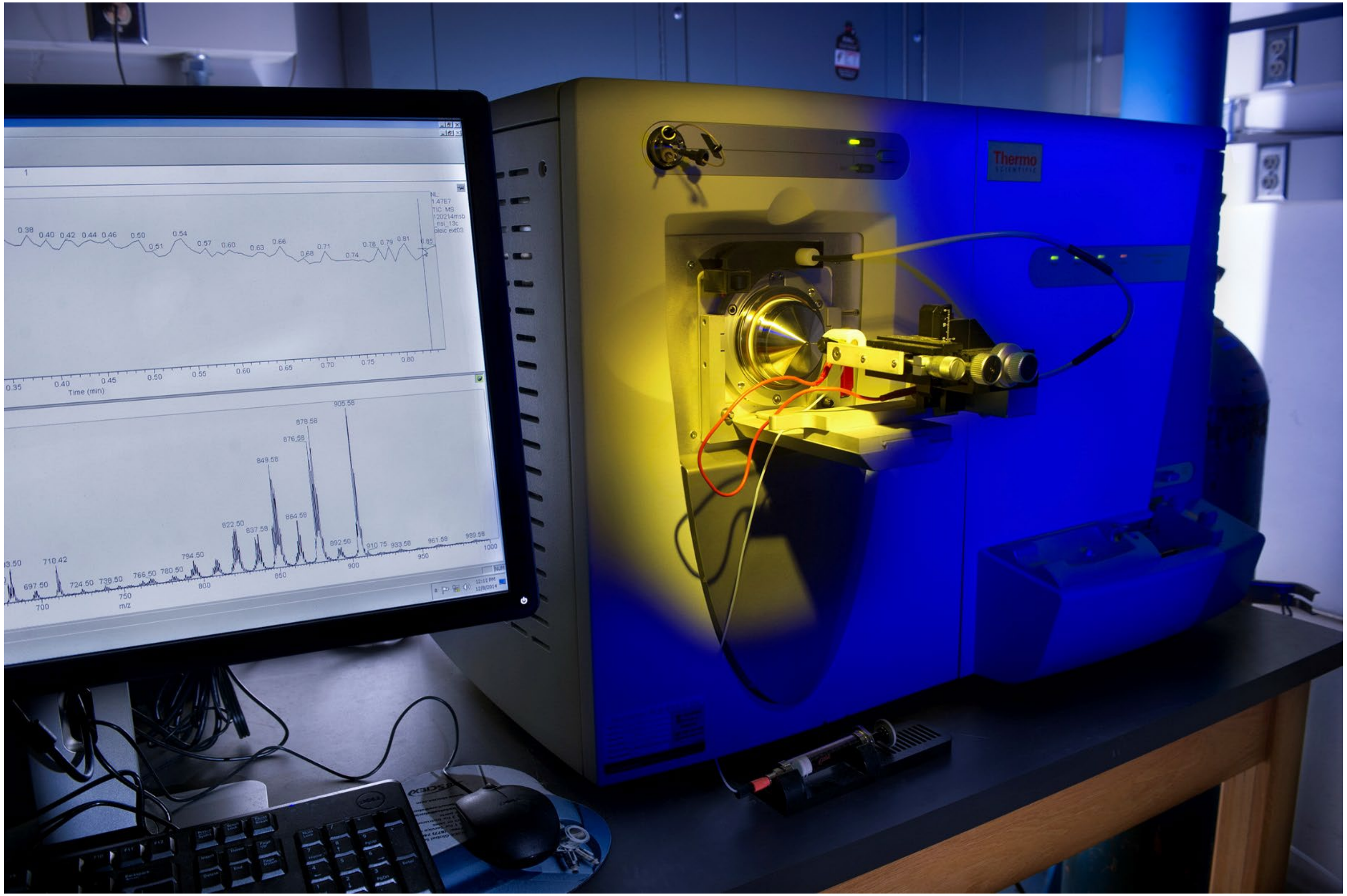
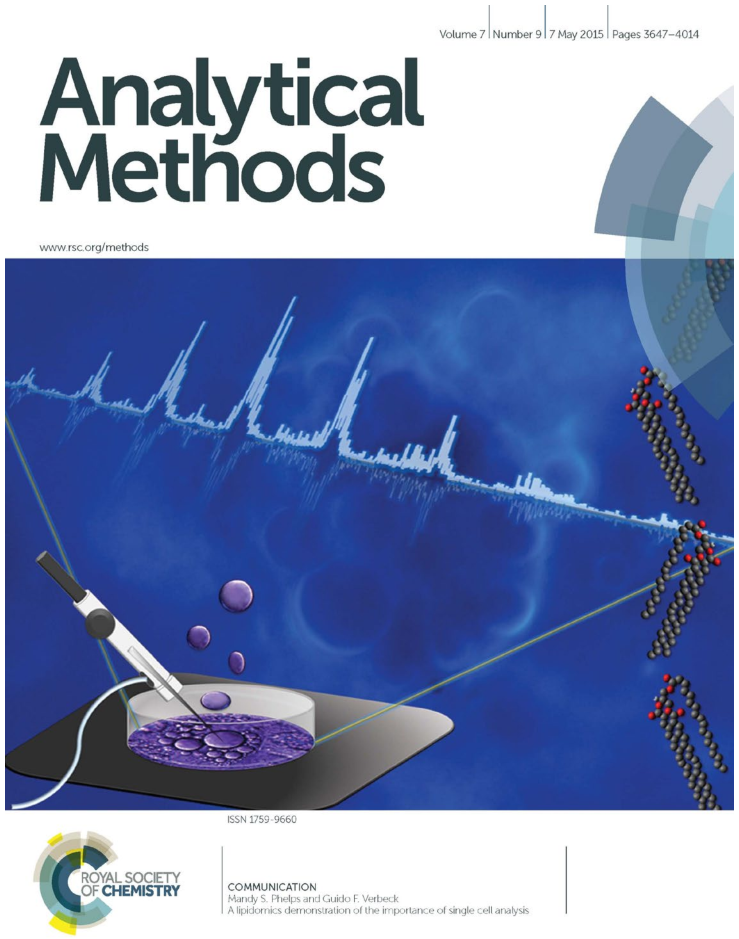
TC1


TC1


Thermo

Chemistry at the True One-Cell Limit



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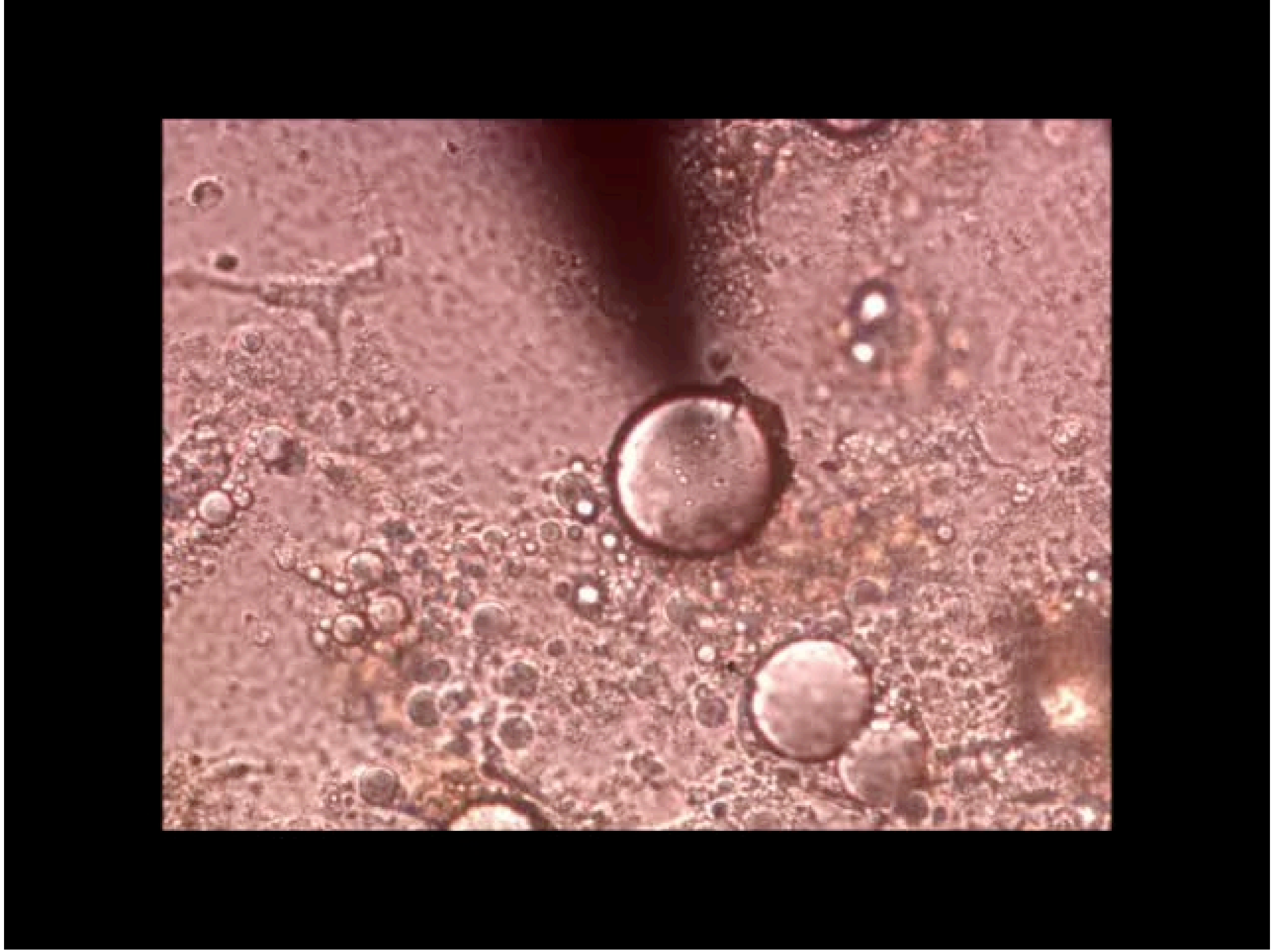
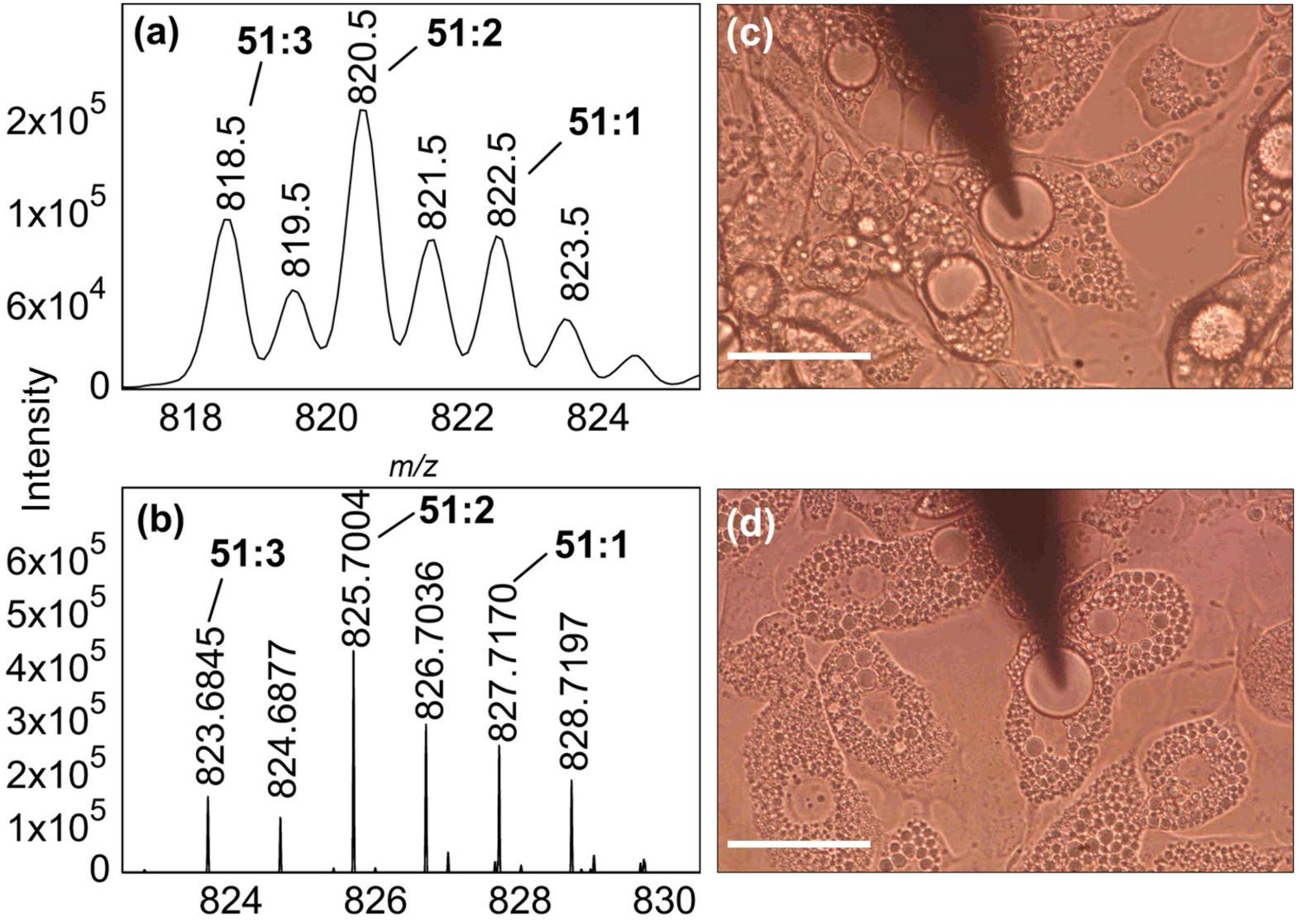
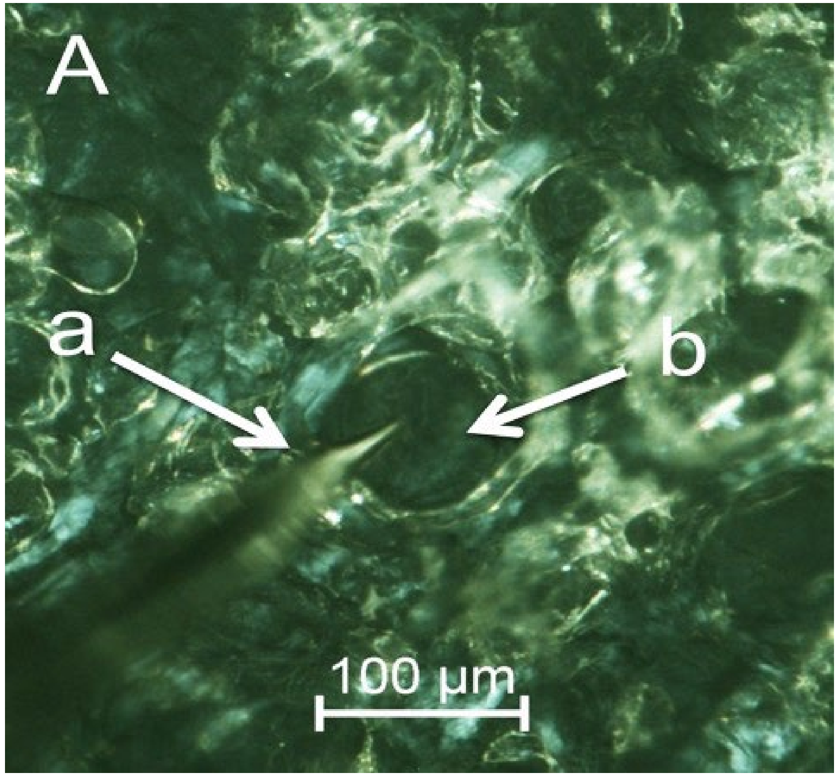




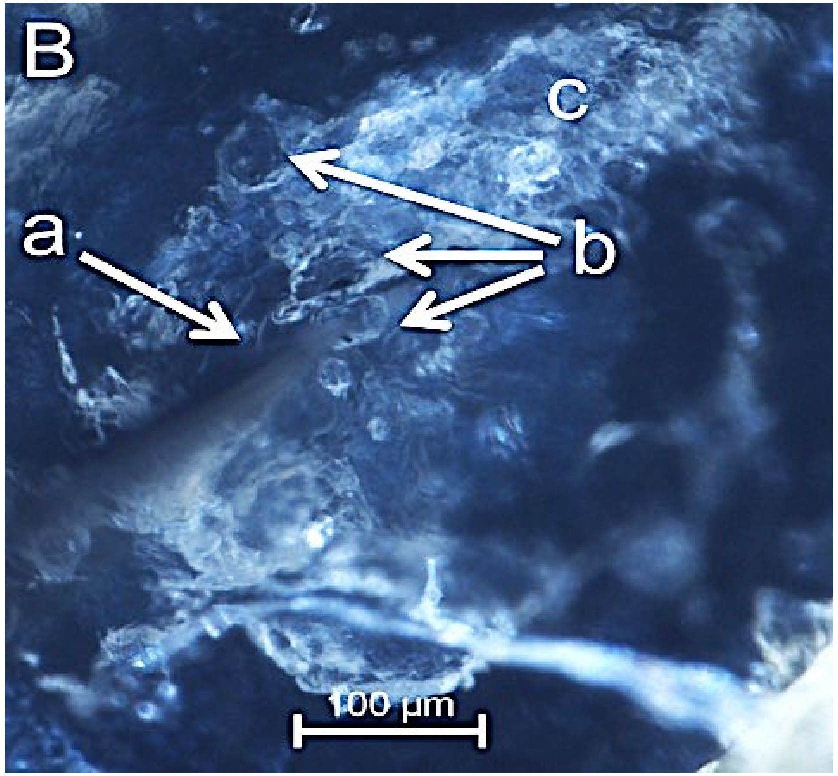
(a) Mass spectrum of the 51 carbon TAG range obtained from nanoextraction of the lipid droplet shown in (c) using NSI in a linear ion trap mass spectrometer with ammonium adduct $[M+NH_4]+$. (b) Mass spectrum from nanoextraction of the lipid droplet shown in (d) from MALDI in a hybrid linear ion trap- orbitrap mass spectrometer with sodium adduct [M+Na]+. Images are 40x differential interference contrast with scale bar of 50 μm.

Breast Tissue: Extraction of Lipid Body



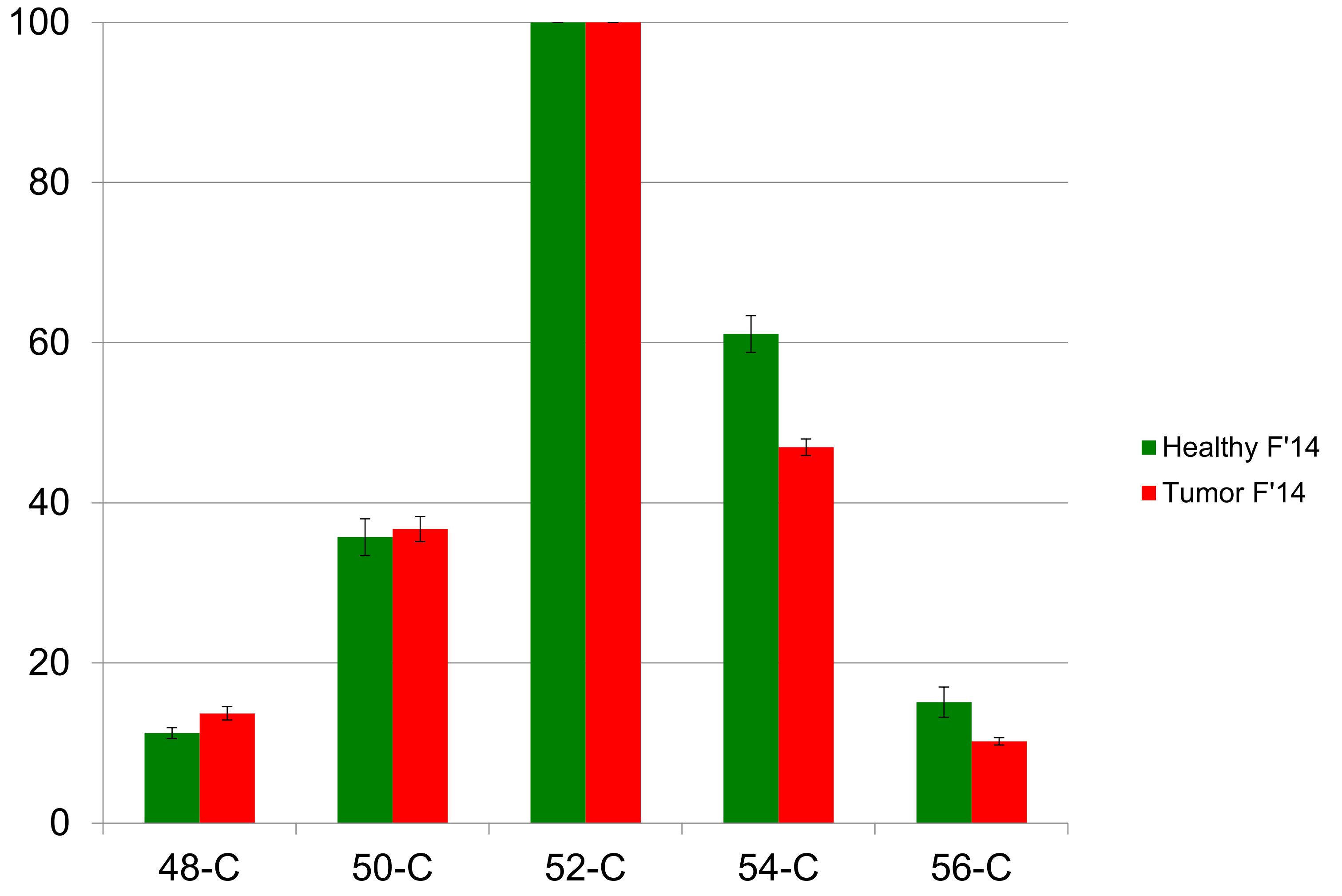
A. Healthy

Emitter tip (a) entering lipid body (b).



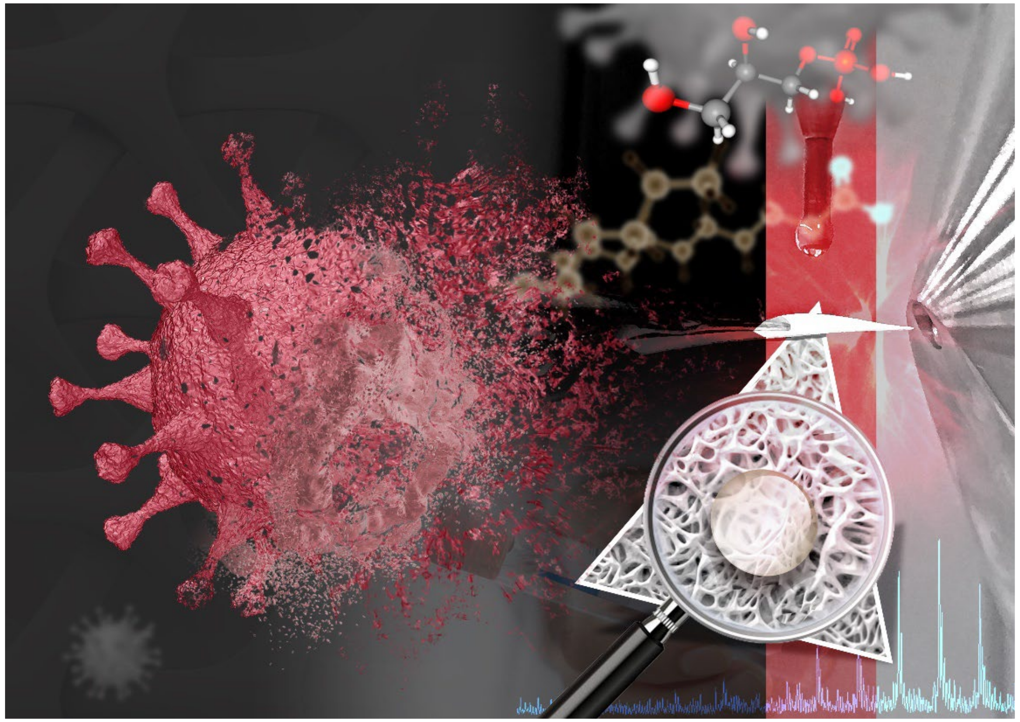
B. Tumor

Emitter tip (a) entering lipid body (b) within surrounding cancerous cells (c).



Breast Tissue: Heterogeneity of the Relative Triglyceride Distribution

Paper Spray Mass spectrometry utilizing Teslin® substrate for rapid detection of lipid metabolite changes during COVID-19 infection



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Rapid detection of lipid metabolite changes during COVID-19 infection

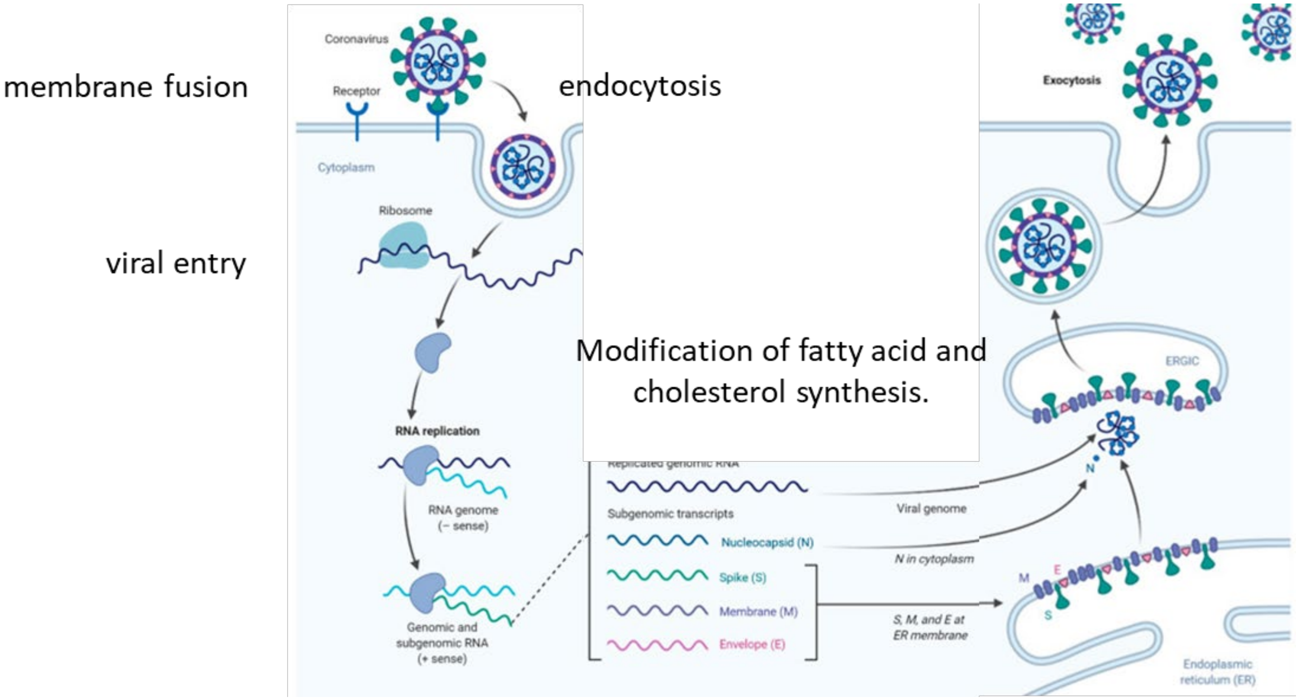
Current testing methods

- ✓ Polymerase Chain Reaction (PCR)- current viral infection
- ✓ Antibody test - previous infection (1-3 weeks to produce antibodies
- ✓ Negative identification is still vulnerable- Antibody test

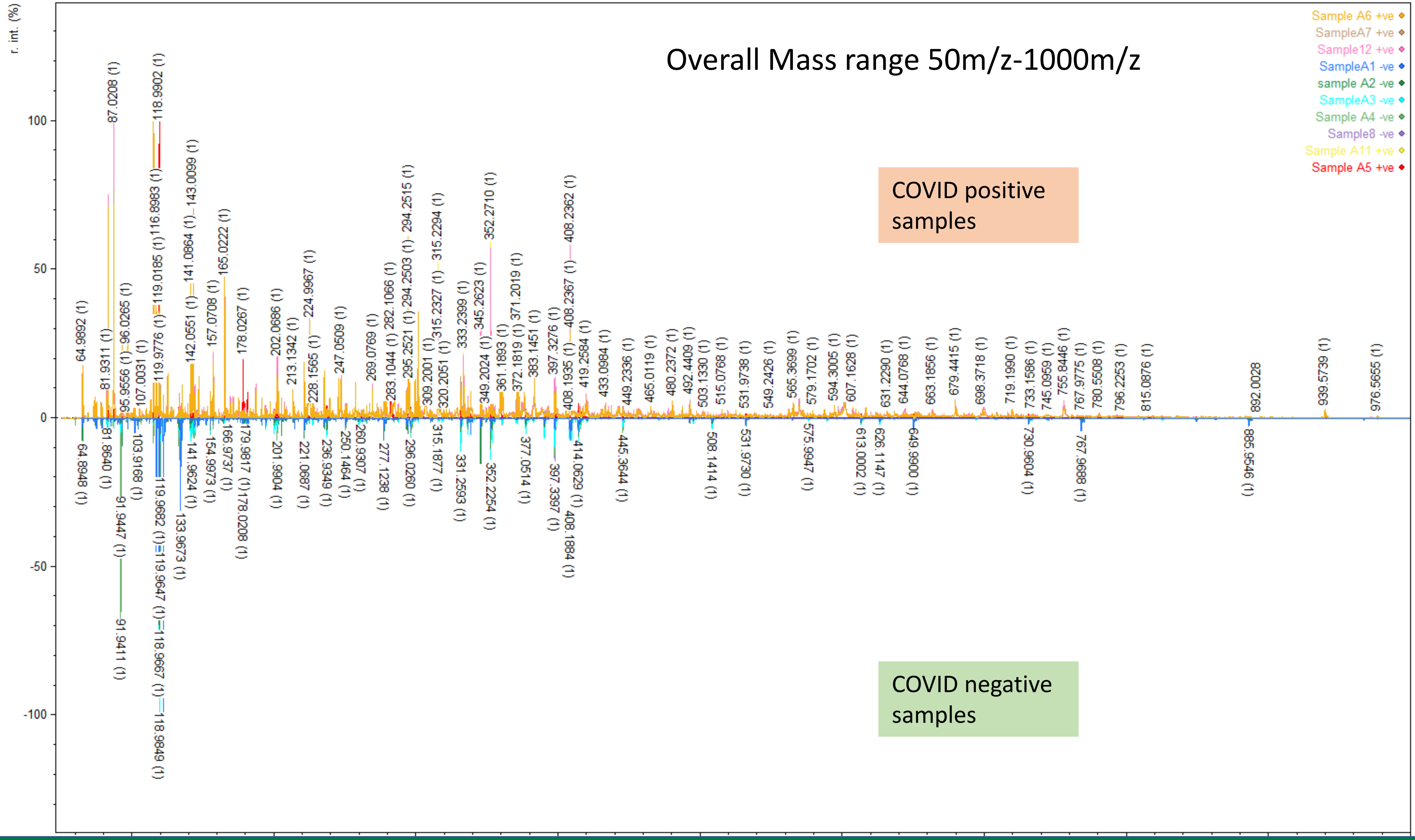
Challenges

- ○ Complexity
- ○ Time
- ○ Backlog of testing kits
- ○ The cost of testing
- ○ Risk with considerable uncertainty
- ○ cross-contamination
- ○ carryover contamination
- ○ mutation of the primer
- ○ improper sampling procedures and handling

The life cycle of SARS-COV2 and potential lipid modification



Abu-Farha, Mohamed et al. "The Role of Lipid Metabolism in COVID-19 Virus Infection and as a Drug Target." International journal of molecular sciences vol. 21,10 3544. 17 May. 2020, doi:10.3390/ijms21103544


Overall Mass range 50m/z-1000m/z
r. int. (%)
100
50
0
-50
-100
Sample A6 +ve
SampleA7 +ve
Sample12 +ve
SampleA1 -ve
sample A2 -ve
SampleA3 -ve
Sample A4 -ve
Sample8 -ve
Sample A11 +ve
Sample A5 +ve
COVID positive samples
COVID negative samples
64.9892 (1)
81.9311 (1)
87.0208 (1)
95.9556 (1)
96.0265 (1)
107.0031 (1)
116.8983 (1)
118.9902 (1)
119.0185 (1)
119.9776 (1)
141.0864 (1)
142.0551 (1)
143.0099 (1)
157.0708 (1)
165.0222 (1)
178.0267 (1)
202.0686 (1)
213.1342 (1)
224.9967 (1)
228.1565 (1)
247.0509 (1)
269.0769 (1)
282.1066 (1)
283.1044 (1)
294.2503 (1)
294.2515 (1)
295.2521 (1)
309.2001 (1)
315.2294 (1)
315.2327 (1)
320.2051 (1)
333.2399 (1)
345.2623 (1)
349.2024 (1)
352.2710 (1)
361.1893 (1)
371.2019 (1)
372.1819 (1)
383.1451 (1)
397.3276 (1)
408.1935 (1)
408.2362 (1)
408.2367 (1)
419.2584 (1)
433.0984 (1)
449.2336 (1)
465.0119 (1)
480.2372 (1)
492.4409 (1)
503.1330 (1)
515.0768 (1)
531.9738 (1)
549.2426 (1)
565.3699 (1)
579.1702 (1)
594.3005 (1)
607.1628 (1)
631.2290 (1)
644.0768 (1)
663.1856 (1)
679.4415 (1)
698.3718 (1)
719.1990 (1)
733.1586 (1)
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767.9775 (1)
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796.2253 (1)
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81.8640 (1)
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91.9411 (1)
103.9168 (1)
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119.9647 (1)
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118.9849 (1)
133.9673 (1)
141.9624 (1)
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179.9817 (1)
178.0208 (1)
201.9904 (1)
221.0687 (1)
236.9349 (1)
250.1464 (1)
260.9307 (1)
277.1238 (1)
296.0260 (1)
315.1877 (1)
331.2593 (1)
352.2254 (1)
377.0514 (1)
397.3397 (1)
408.1884 (1)
414.0629 (1)
445.3644 (1)
508.1414 (1)
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575.9947 (1)
613.0002 (1)
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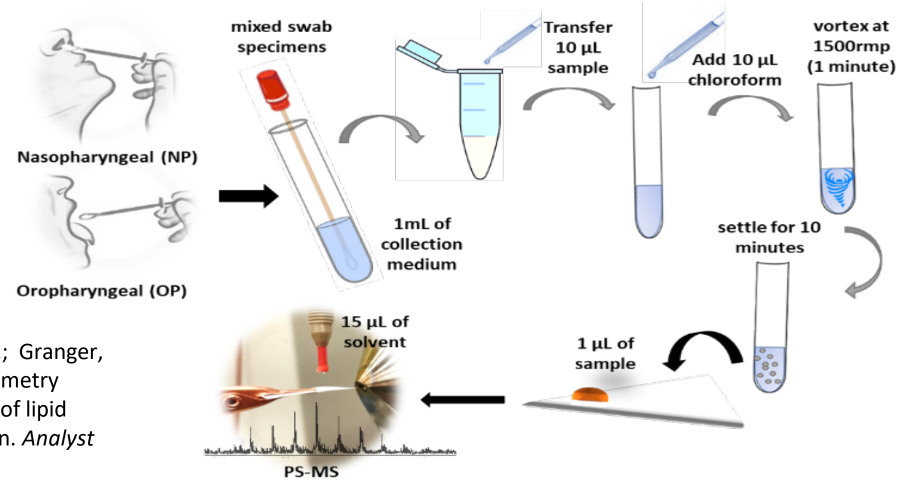
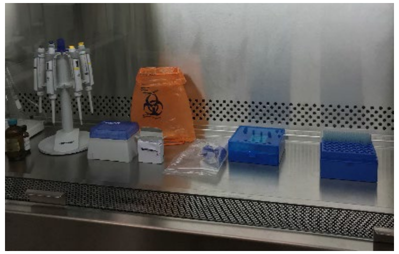
885.9546 (1)

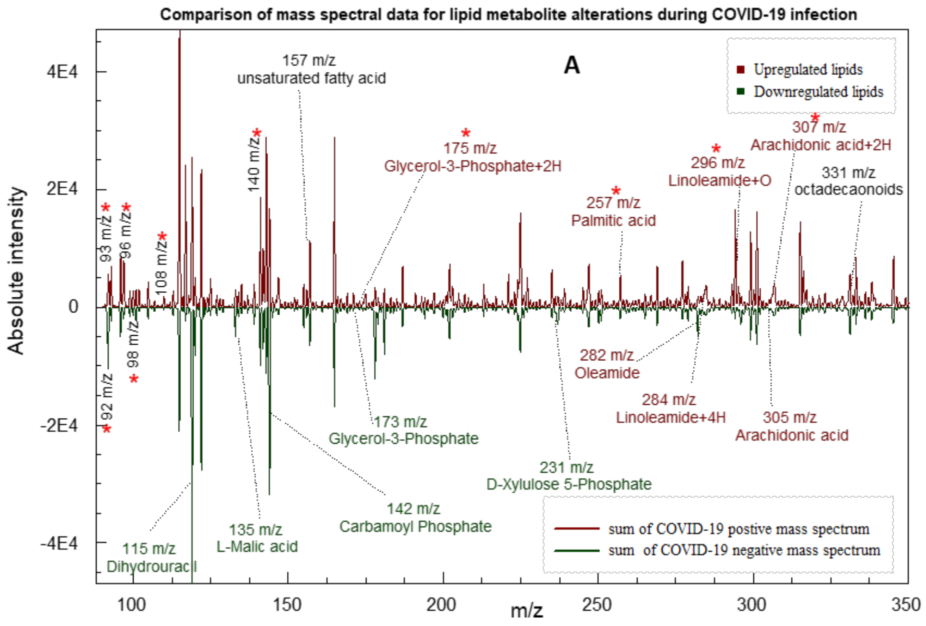
Rapid detection of lipid metabolite changes during COVID-19 infection

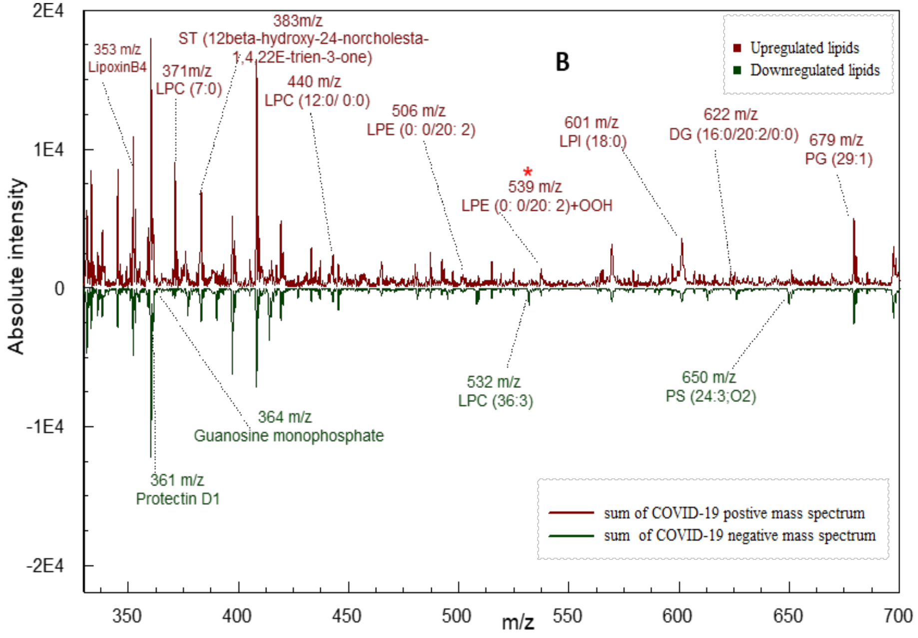


Sample Retrieval and preparation



De Silva, I. W.; Nayek, S.; Singh, V.; Reddy, J.; Granger, J. K.; Verbeck, G. F., Paper spray mass spectrometry utilizing Teslin® substrate for rapid detection of lipid metabolite changes during COVID-19 infection. *Analyst* **2020**





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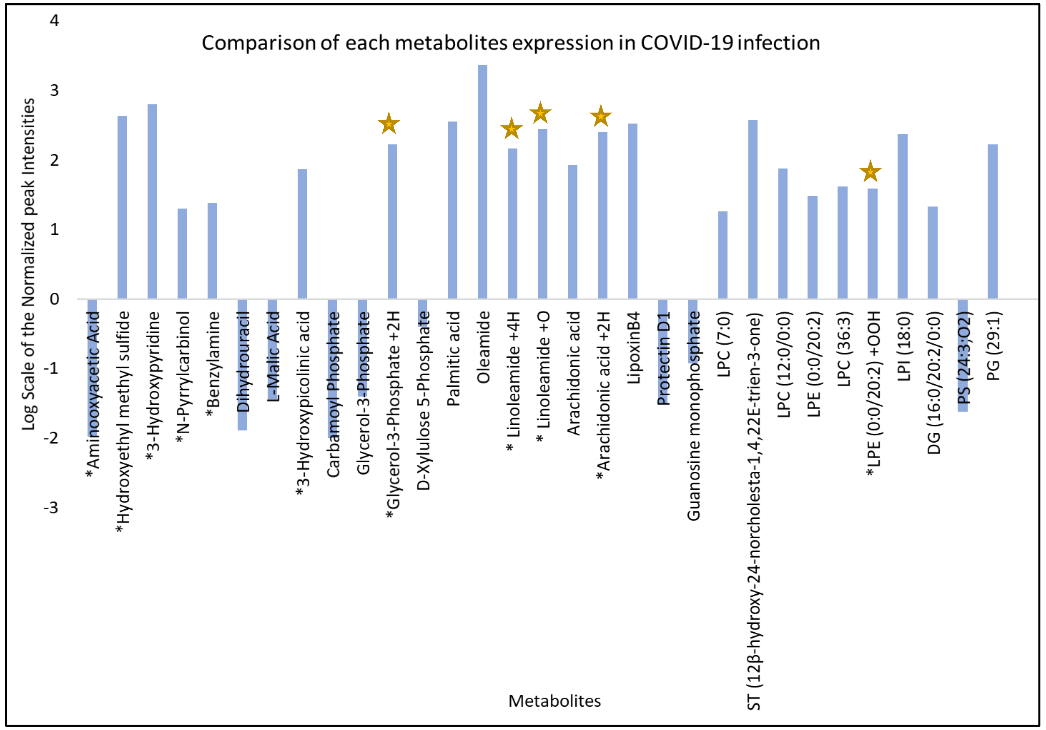
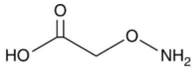
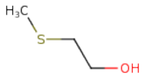
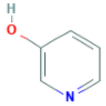
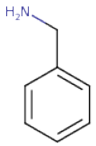
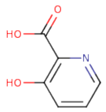
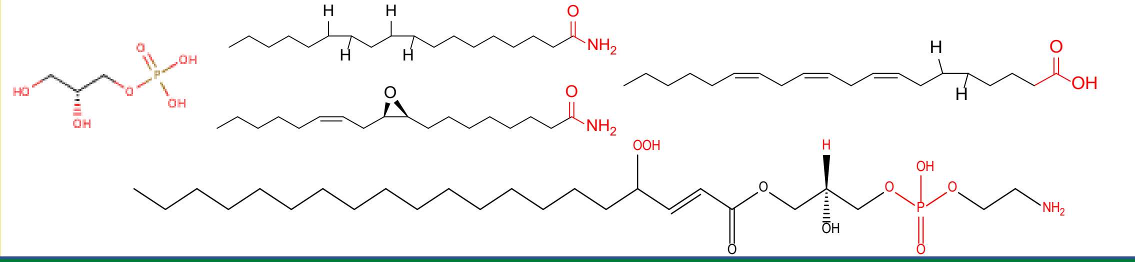


[M+H] +	m/z shown in the paper	Metabolite Name	CAS ID	Metabolite ID
92.0219	92	*Aminooxyacetic Acid	645-88-5	N/A
92.9862	93	*Hydroxyethyl methyl sulfide	5271-38-5	HMDB0032425
95.9931	96	*3-Hydroxypyridine	109-00-2	N/A
98.0835	98	*N-Pyrrylcarbinol	92776-61-9	N/A
108.0246	108	*Benzylamine	100-46-9	HMDB0033871
140.0816	140	*3-Hydroxypicolinic acid	874-24-8	HMDB0013188
175.0003	175	*Glycerol-3-Phosphate +2H	Oxidized form 57-03-4	Oxidized form HMDB0000126
284.0727	284	* Linoleamide +4H	Oxidized form 3072-13-7	Oxidized form HMDB0062656
296.1589	296	* Linoleamide +O	Oxidized form 3072-13-7	Oxidized form HMDB0062656
306.8391	306	*Arachidonic acid +2H	Oxidized form 506-32-1	Oxidized form HMDB0001043
539.151	539	*LPE (0:0/20:2) +OOH	N/A	HMDB0011513



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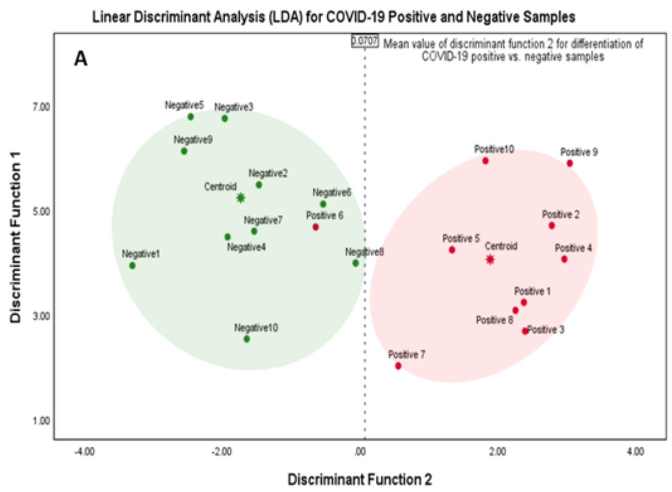
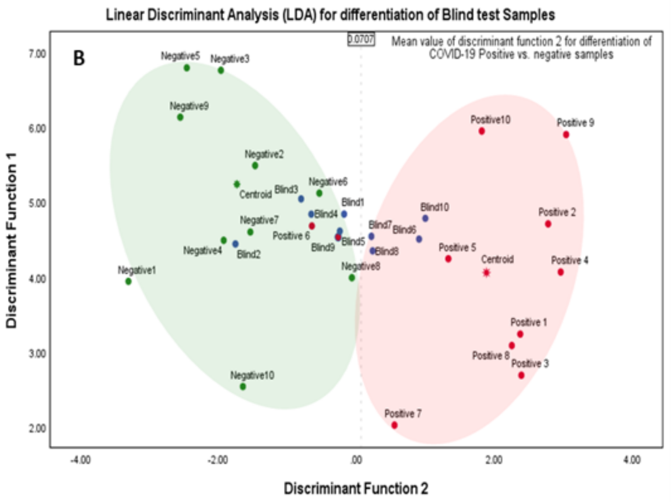
$discriminant\ function\ 1$

$$= 1.5 * (m/z92) - 2.66 * (m/z93) - 1.94 * (m/z96) + 2.07\ (m/z98)$$
$$- 1.1\ (m/z108) + 1.12(m/z140) - 2.22\ (m/z175) + 2.77\ (m/z257)$$
$$+ 6.41(m/z296) + 5.11(m/z307) - 0.14(m/z539)$$

$discriminant\ function\ 2$

$$= 0.12 * (m/z92) + 0.78(m/z93) - 1.24 * (m/z96) - 0.76(m/z98)$$
$$+ 0.74(m/z108) - 0.56(m/z140) + 0.10(m/z175) + 0.36\ (m/z257)$$
$$- 0.96(m/z296) + 1.05(m/z307) + 0.76(m/z539)$$





C **Summary of PS-MS Classification**

Sample Number	PCR Confirmation	PS-MS Clasification (Function2)		
Positive 1	COVID-19 Positive	●	2.380	Positive
Positive 2	COVID-19 Positive	●	2.780	Positive
Positive 3	COVID-19 Positive	●	2.390	Positive
Positive 4	COVID-19 Positive	●	2.960	Positive
Positive 5	COVID-19 Positive	●	1.330	Positive
Positive 6	**COVID-19 Positive**	●	**-0.650**	**Negative**
Positive 7	COVID-19 Positive	●	0.550	Positive
Positive 8	COVID-19 Positive	●	2.260	Positive
Positive 9	COVID-19 Positive	●	3.040	Positive
Positive10	COVID-19 Positive	●	1.820	Positive
Negative1	COVID-19 Negative	●	-3.310	Negative
Negative2	COVID-19 Negative	●	-1.470	Negative
Negative3	COVID-19 Negative	●	-1.970	Negative
Negative4	COVID-19 Negative	●	-1.930	Negative
Negative5	COVID-19 Negative	●	-2.460	Negative
Negative6	COVID-19 Negative	●	-0.540	Negative
Negative7	COVID-19 Negative	●	-1.540	Negative
Negative8	COVID-19 Negative	●	-0.070	Negative
Negative9	COVID-19 Negative	●	-2.560	Negative
Negative10	COVID-19 Negative	●	-1.650	Negative
Blind1	COVID-19 Negative	●	-0.180	Negative
Blind2	COVID-19 Negative	●	-1.760	Negative
Blind3	COVID-19 Negative	●	-0.800	Negative
Blind4	COVID-19 Negative	●	-0.650	Negative
Blind5	COVID-19 Negative	●	-0.240	Negative
Blind6	COVID-19 Positive	●	0.910	Positive
Blind7	COVID-19 Positive	●	0.220	Positive
Blind8	COVID-19 Positive	●	0.240	Positive
Blind9	**COVID-19 Positive**	●	**-0.260**	**Negative**
Blind10	COVID-19 Positive	●	1.000	Positive

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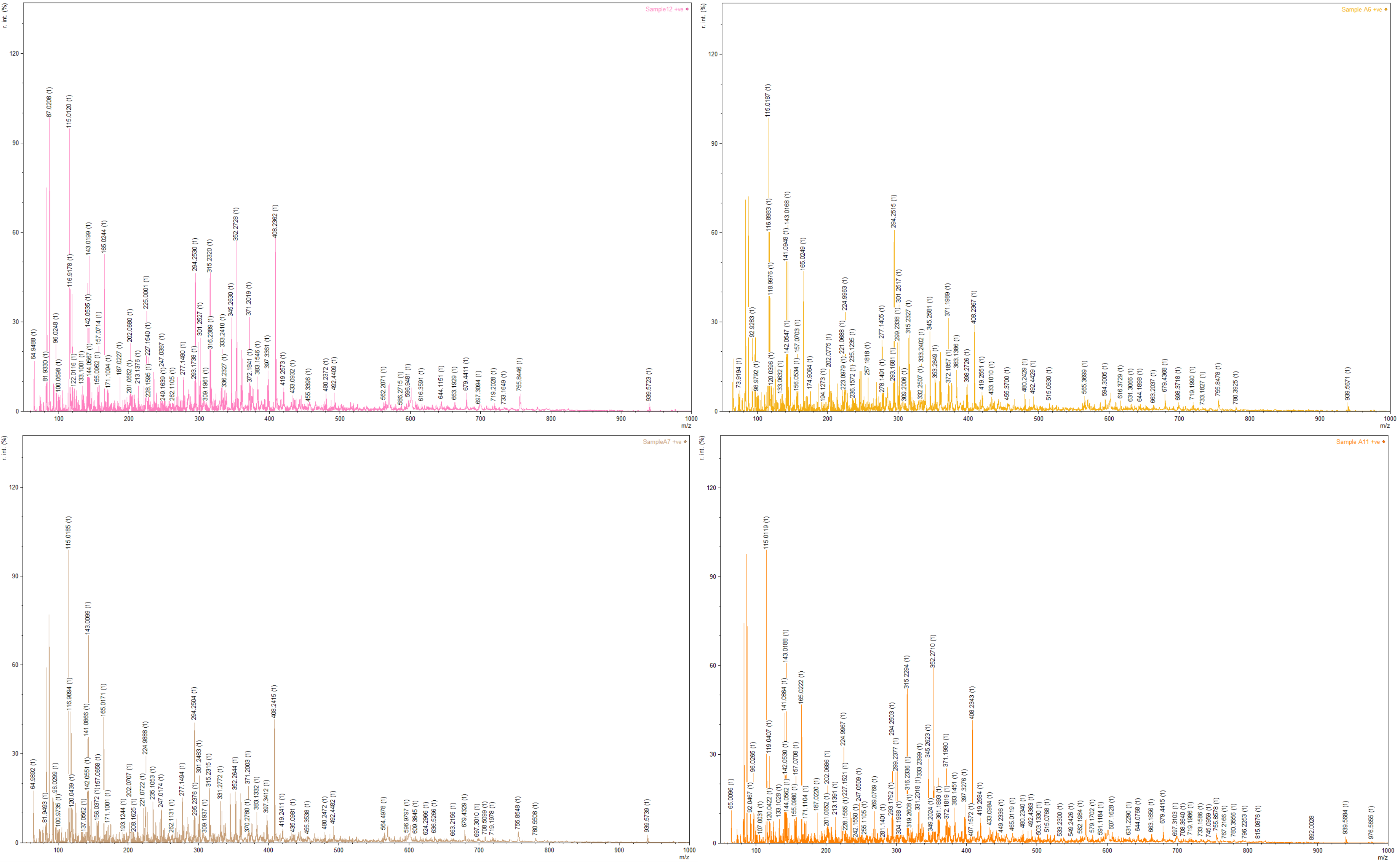
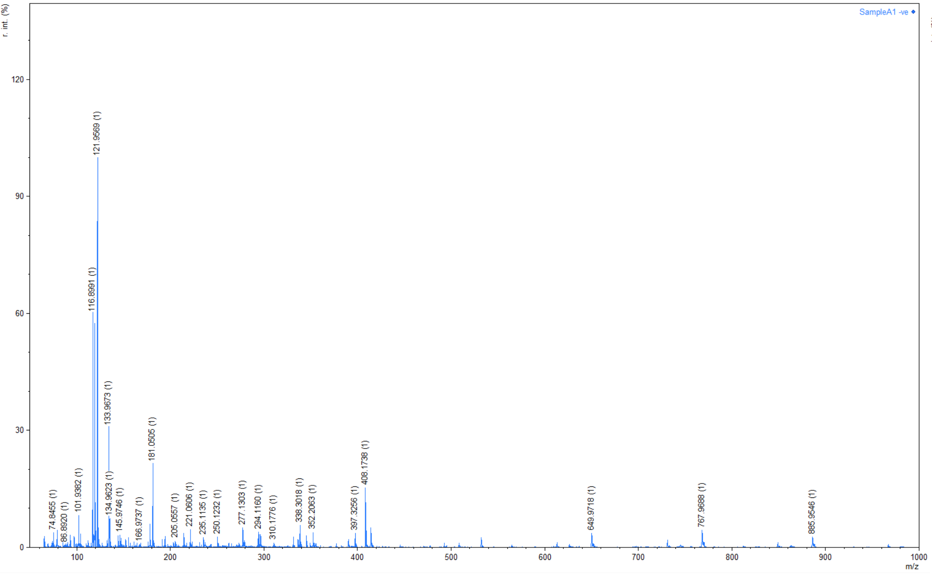
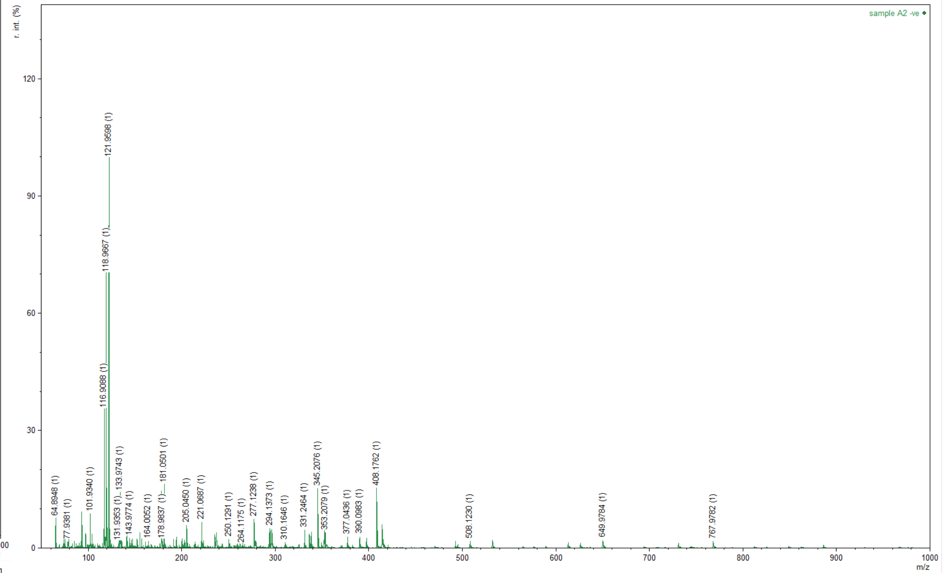
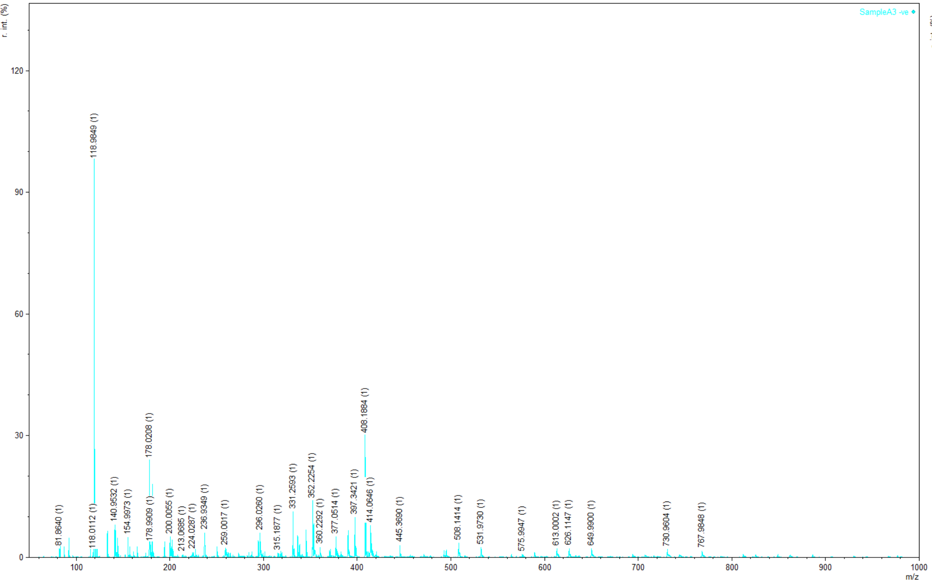
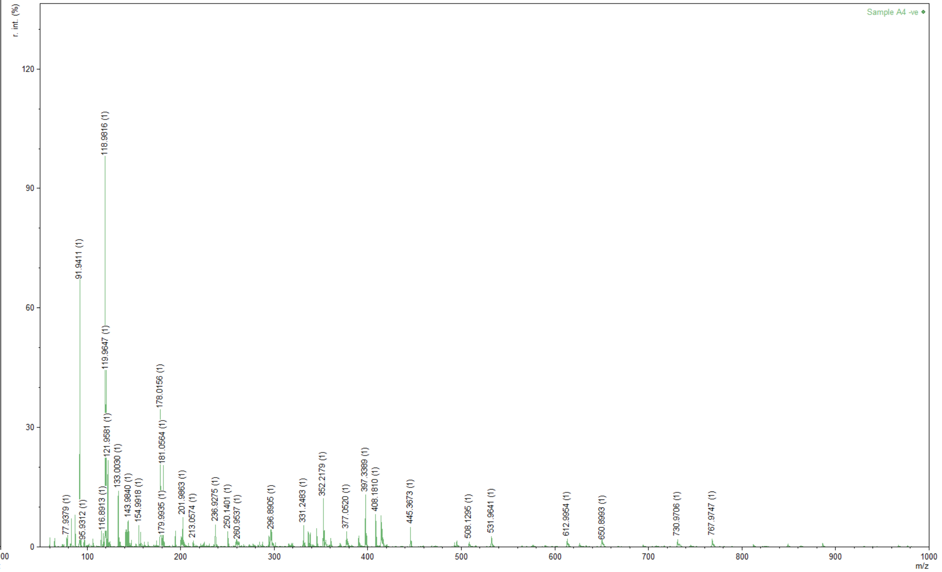


COVID positive samples









COVID negative samples

Unique Peaks common in ≥20% and ≥10% of spectra: Positive Cases (without Positive Case 1) and Negative cases

Unique Positive Peak(s) **NOT** including sample one (≥10%)		Unique Negative Peak(s) (≥10%)
m/z	m/z	m/z
65	294	181
83	295	
87	299	
96	301	
97	315	
115	316	
117	331	
141	333	
142	345	
143	352	
157	353	
165	360	
202	361	
225	371	
227	383	
235	408	
247		

Unique Positive Peak(s) **NOT** including sample one (≥20%)	Unique Negative Peak(s) (≥20%)
m/z	m/z
83	none
87	
115	
117	
141	
143	
165	
225	
294	
301	
408	

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Average Relative Intensities of Unique Peaks common in ≥10% of spectra: Positive Cases (without case 1) and Negative cases

Average Relative Intensity of Unique Negative Peaks (≥10%)	
m/z	Average Relative Intensity
181	18.28

- No matching duplicates between positive case 1 and positive cases 2 – 5.

Average Relative Intensity of Unique Positive Peaks **NOT** including sample one (≥10%)			
m/z	Average Relative Intensity	m/z	Average Relative Intensity
65	15.75	294	45.85
83	69.92	295	13.53
87	86.74	299	22.04
96	20.37	301	27.09
97	18.02	315	35.82
115	98.91	316	16.63
117	41.81	331	11.89
141	43.18	333	17.38
142	21.70	345	25.82
143	61.94	352	37.64
157	20.44	353	17.01
165	47.48	360	19.79
202	17.77	361	14.74
225	32.08	371	26.80
227	15.32	383	11.96
235	13.37	408	42.52
247	13.14		

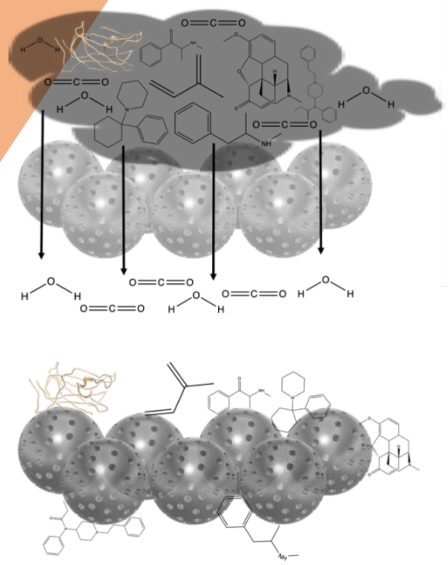
0.5ppb Concentration Acquisition

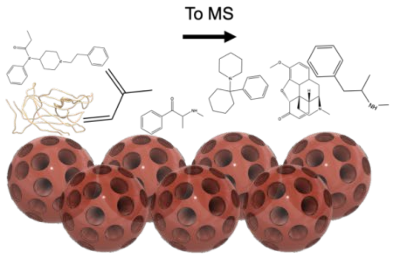
Standard Compounds: Aldehydes& Ketones

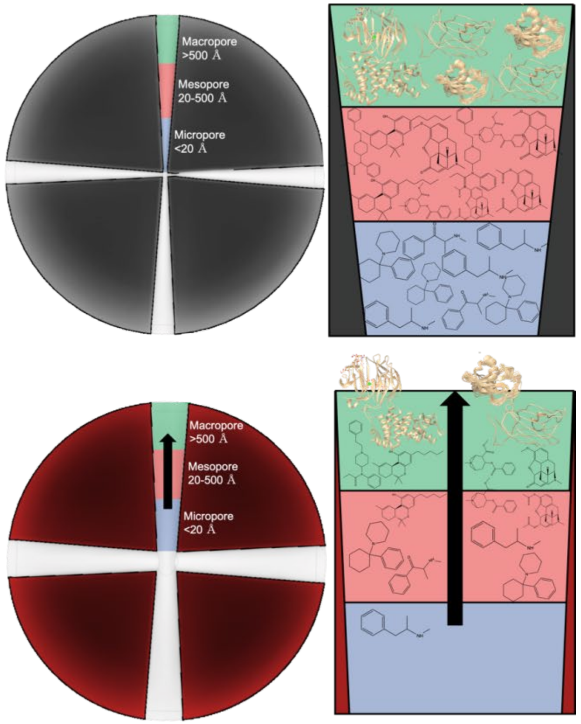
1. Formaldehyde: **29 m/z**
2. Acetaldehyde: 29 m/z (**15 m/z**)
3. Acrolein: **56 m/z**
4. Acetone: **43 m/z**
5. Propionaldehyde: **58 m/z**
6. Crotonaldehyde: **41 m/z**
7. Butyraldehyde: **44 m/z**
8. Benzaldehyde: **77 m/z**
9. Isovaleraldehyde: 44 m/z (**27 m/z**)
10. Valeraldehyde: 44 m/z (**57 m/z**)
11. o-Tolualdehyde: **91 m/z**
12. m-Tolualdeyde: **91 m/z**
13. p-Tolualdehyde: **91 m/z**
14. Hexanal: 44 m/z (**39 m/z**)
15. 2,5-Dimethylbenzaldehyde: **134 m/z**

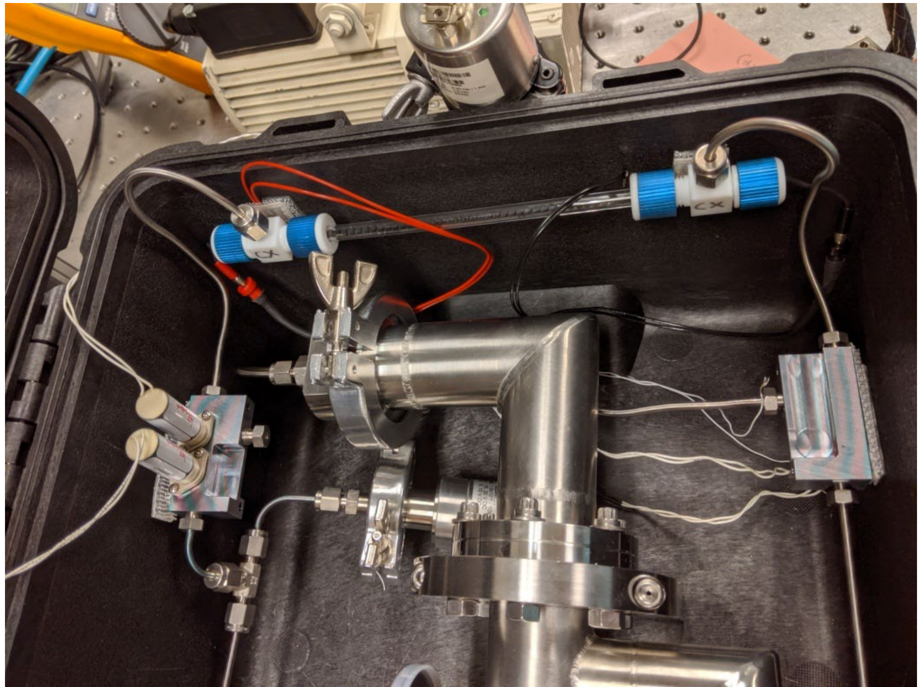
RED = Parent peak
BLACK = Daughter peak
BOLD = Tracked m/z value

Breathalyzer Portable Mass Spectrometry









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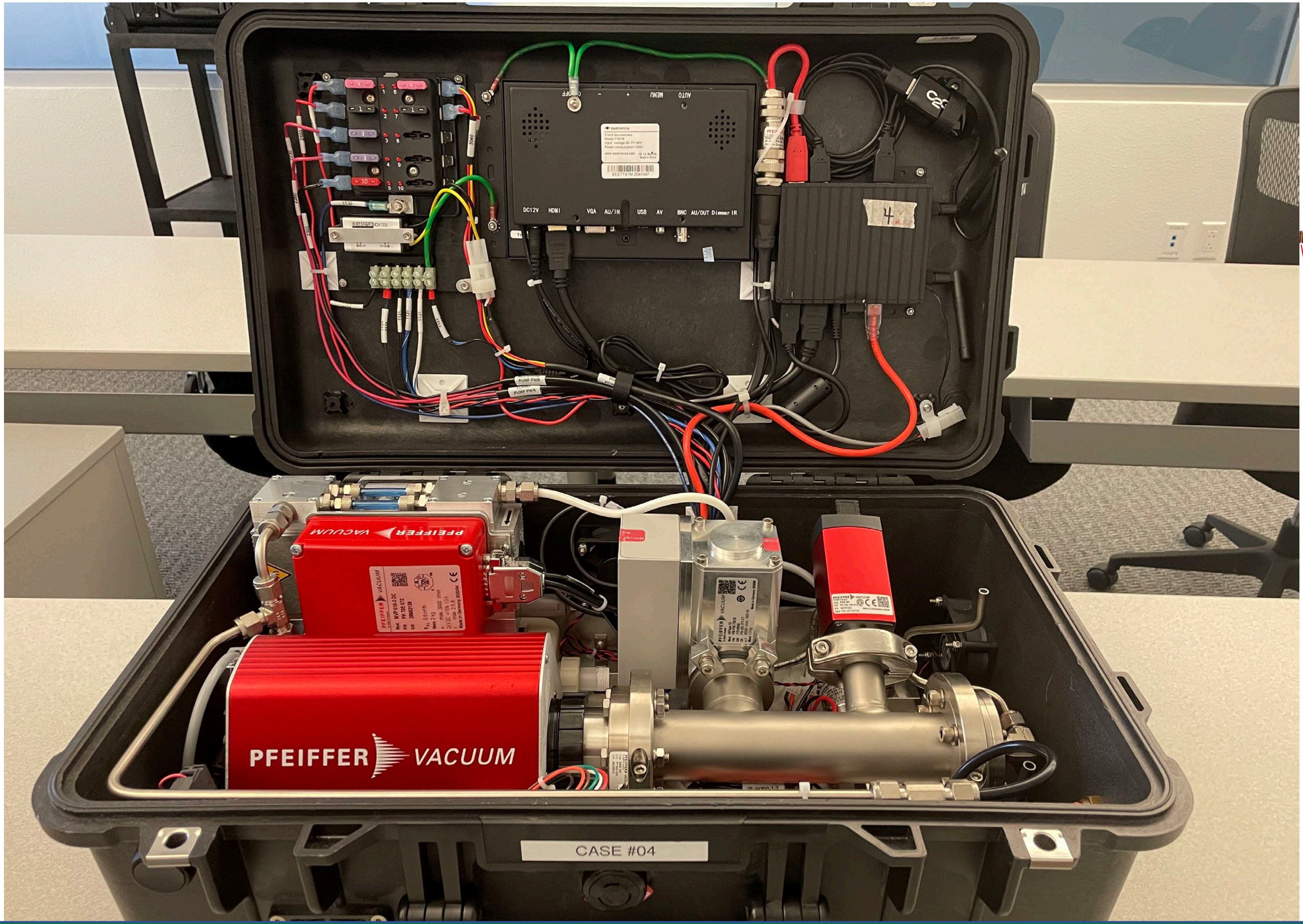
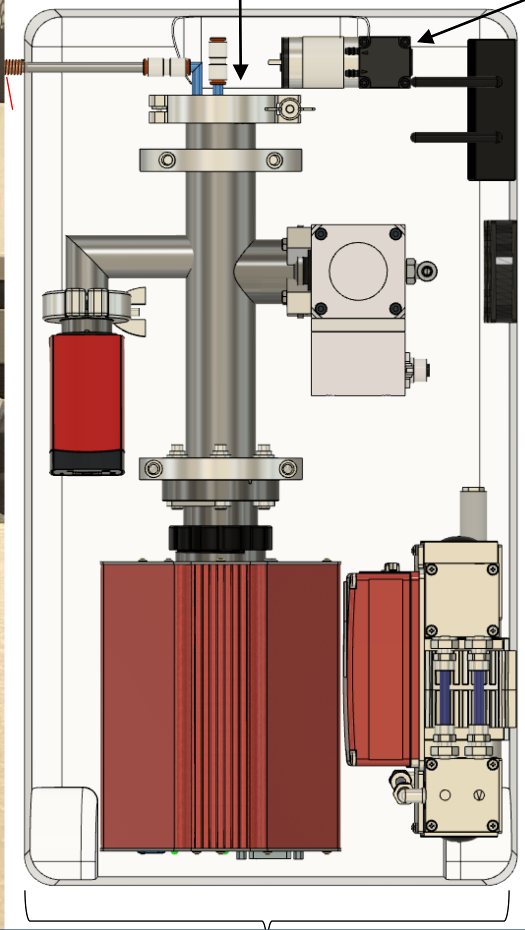
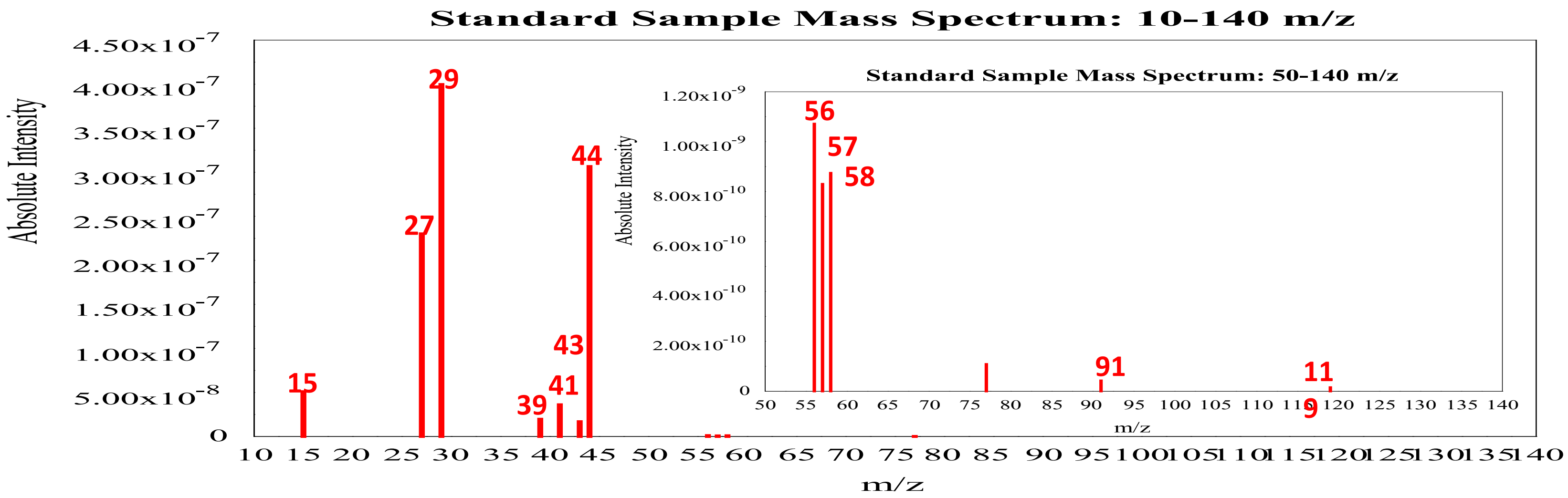
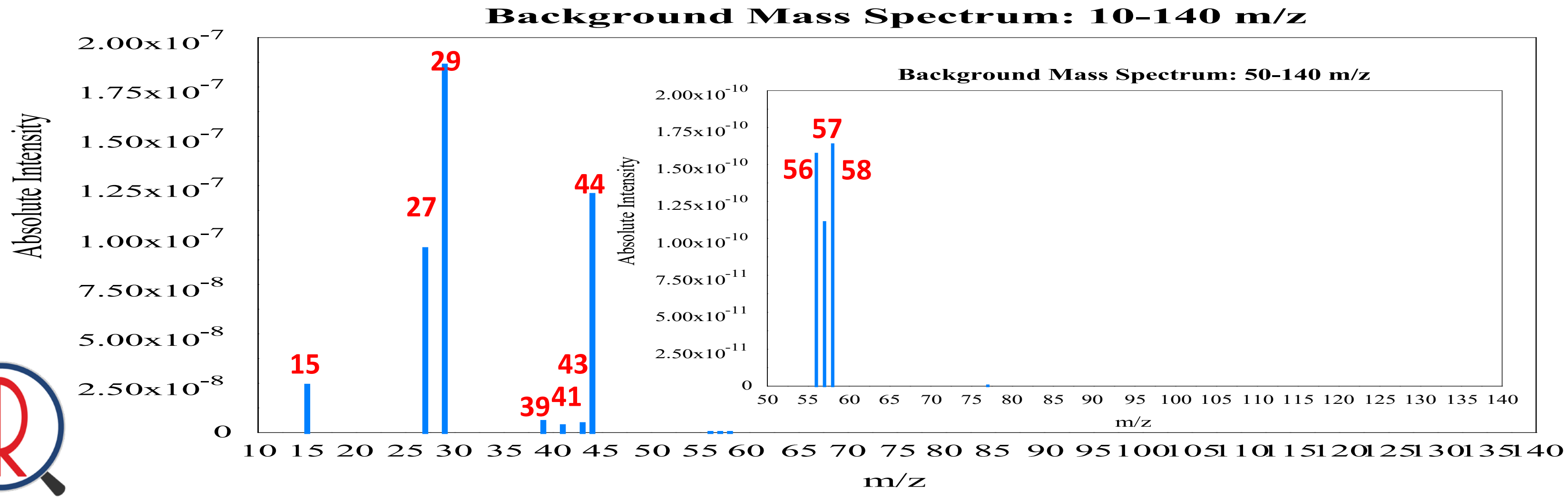




0.5ppb Concentration Acquisition VS Background Acquisition





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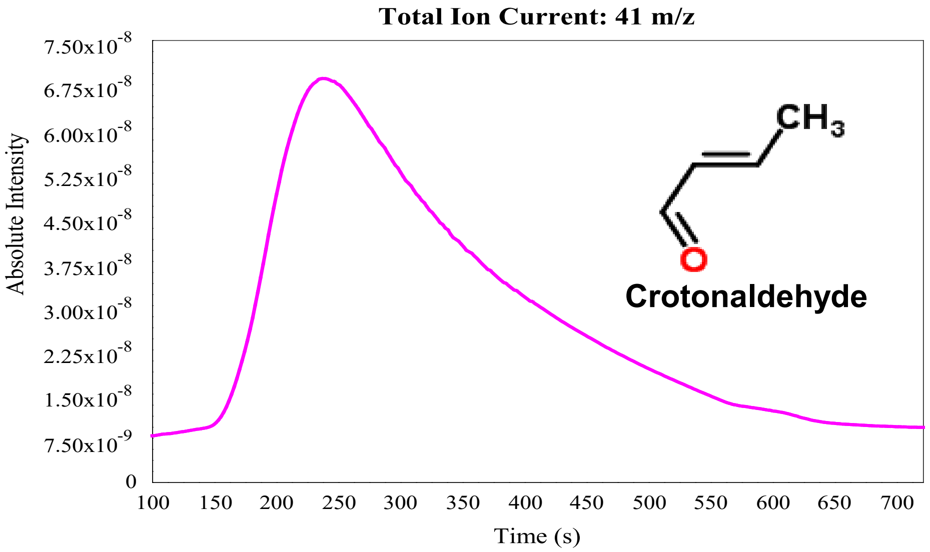
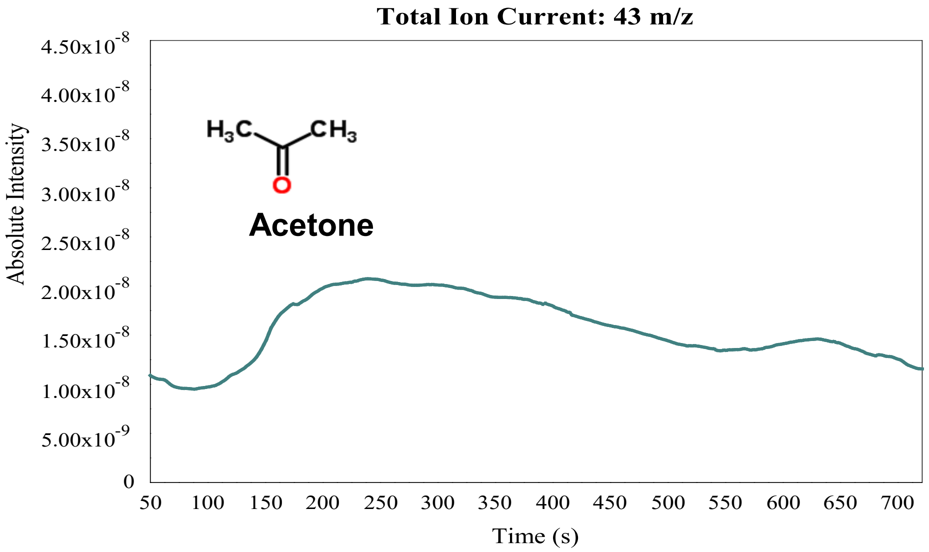
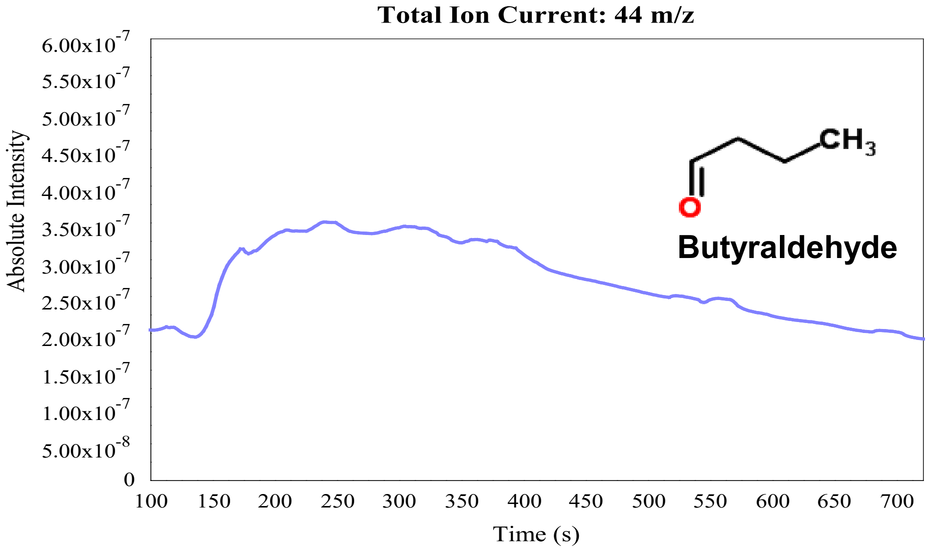
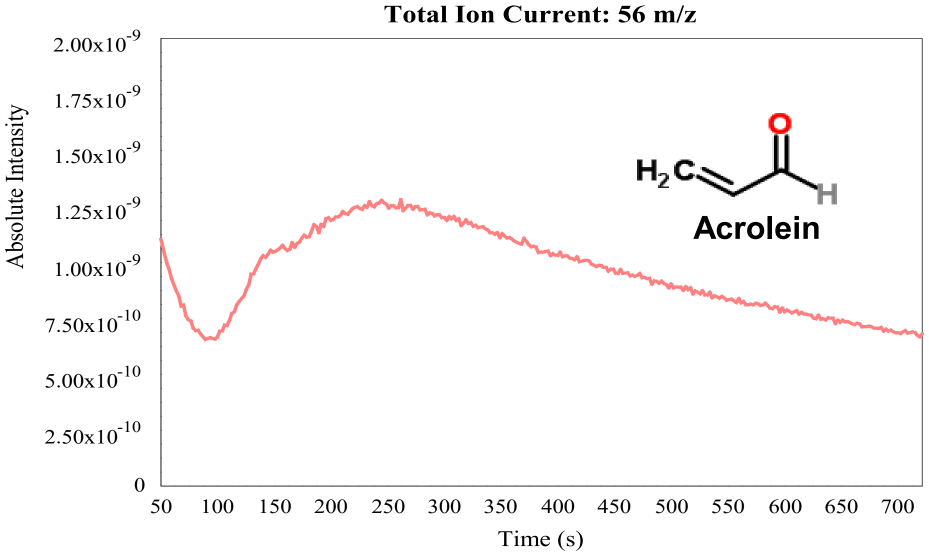
0.5ppb Concentration Acquisition

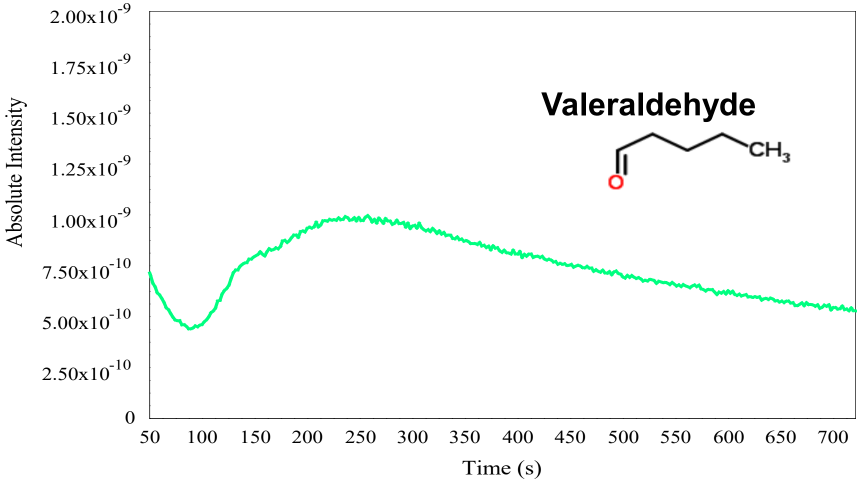




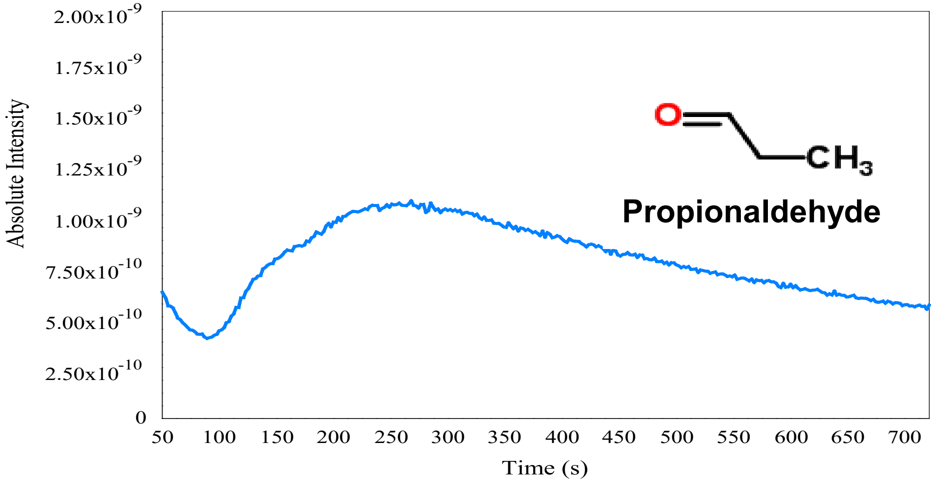




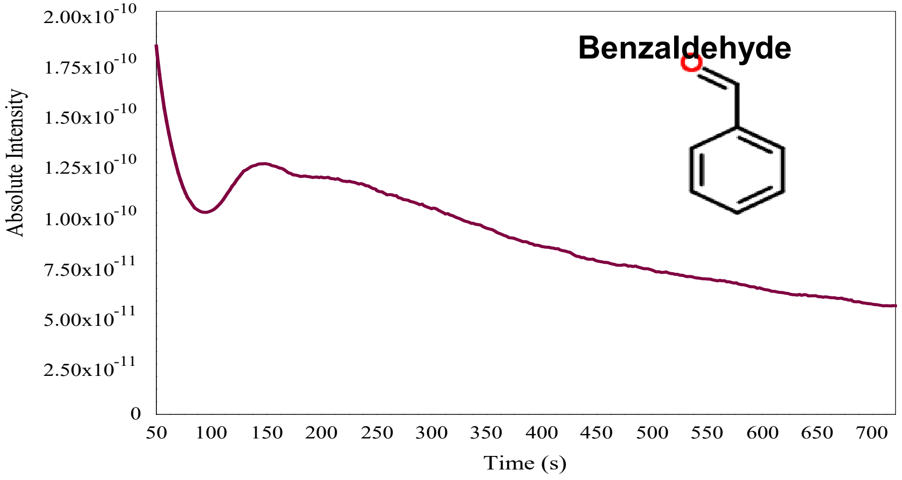
0.5ppb Concentration Acquisition



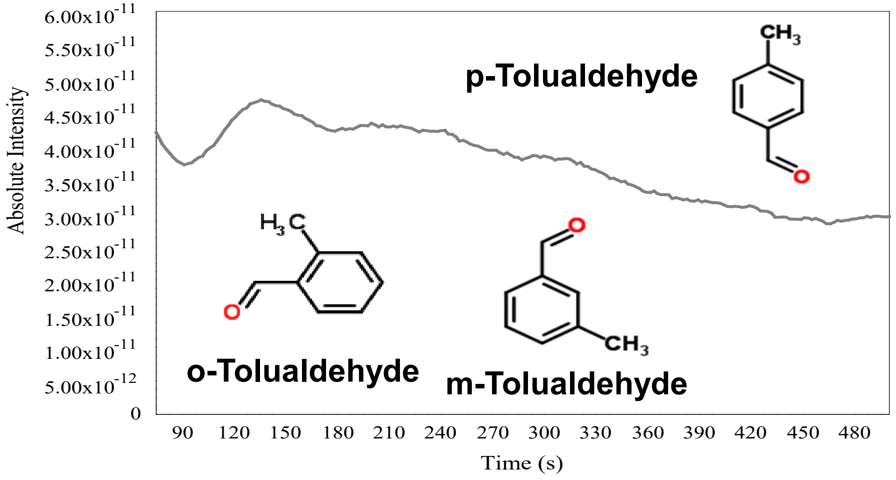
Total Ion Current: 57 m/z



Total Ion Current: 58 m/z



Total Ion Current: 77 m/z



Total Ion Current: 91 m/z

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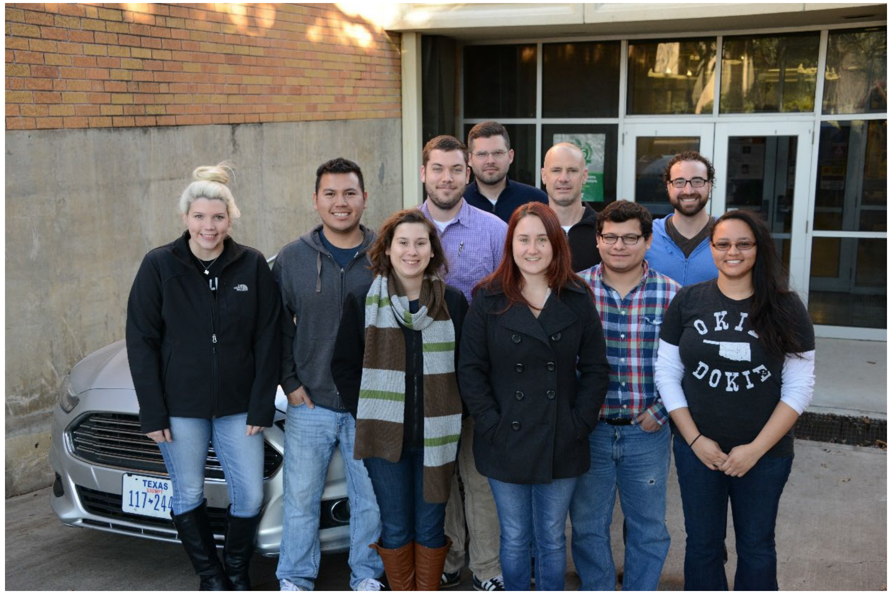

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