Supplementary Information: CHIMIA, 2022, 76, 127-132

Comparison of Plasma Ionization- and Secondary Electrospray Ionization-High Resolution Mass Spectrometry for Real-time Breath Analysis

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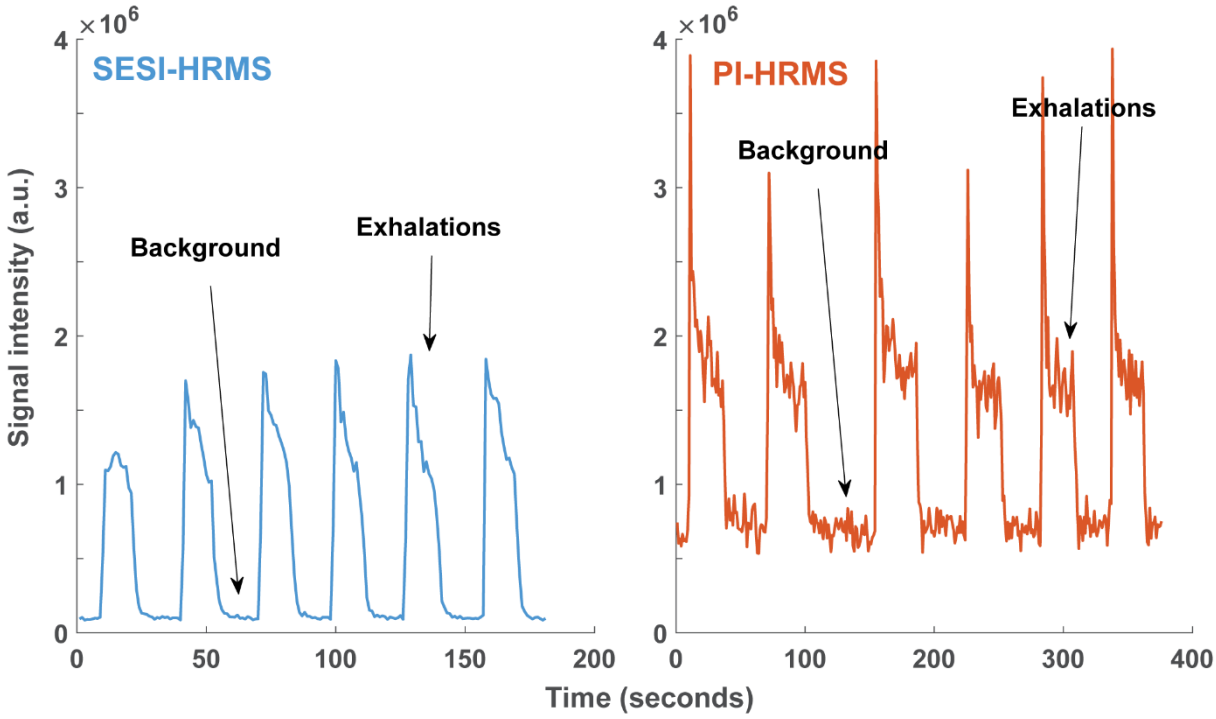


Figure S1: Time trace of $C_8H_{14}O$ for SESI-HRMS (left) and PI-HRMS (right). Each raw file contains 6 exhalations, the signal between two exhalations is consider as background signal. PI-HRMS shows higher background signal than SESI-HRMS and this led to the lower S/N ratio of PI-HRMS.

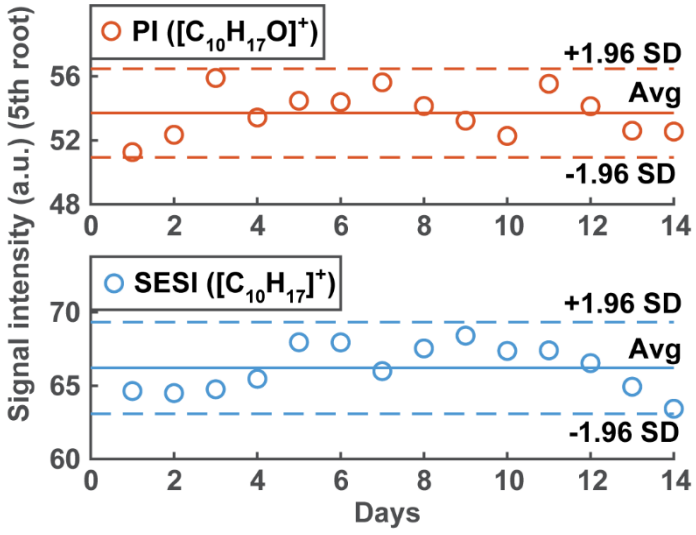


Figure S2. Signal intensity of α-terpinene detected by PI-HRMS and SESI-HRMS in 14 days. The coefficient of variation (CV) of the signal intensity of protonated α-terpinene ($[C_{10}H_{17}]^+$) with SESI-HRMS and signal intensity of protonated oxidized α-terpinene ($[C_{10}H_{17}O]^+$) with PI-HRMS during the two months that lasted the measurements (14 data points in total). We found

excellent and similar CVs for both techniques (2.4% for SESI-HRMS and 2.6% for PI-HRMS).

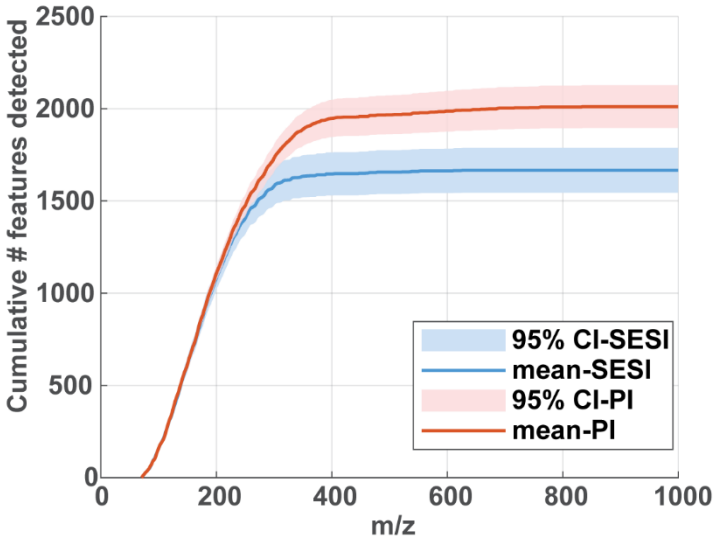


Figure S3. Cumulative correlating feature number of 58 breath files of each platform. The mean of PI-HRMS is 2011 with a 95% confidence interval (CI) of 1896 to 2127, and mean of SESI-HRMS is 1666 with a 95 % confidence interval (CI) of 1545 to 1788.

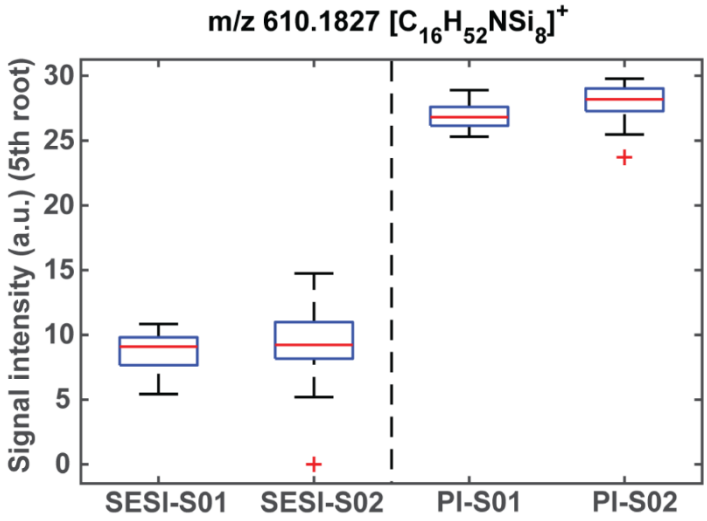


Figure S4. Boxplot of the feature with maximum loading in PC 1. This feature is a common contaminant $[C_{16}H_{52}O_8NSi_8]^+$ (m/z 610.1827), which showed two orders of magnitude stronger intensity in PI-HRMS than SESI-HRMS.

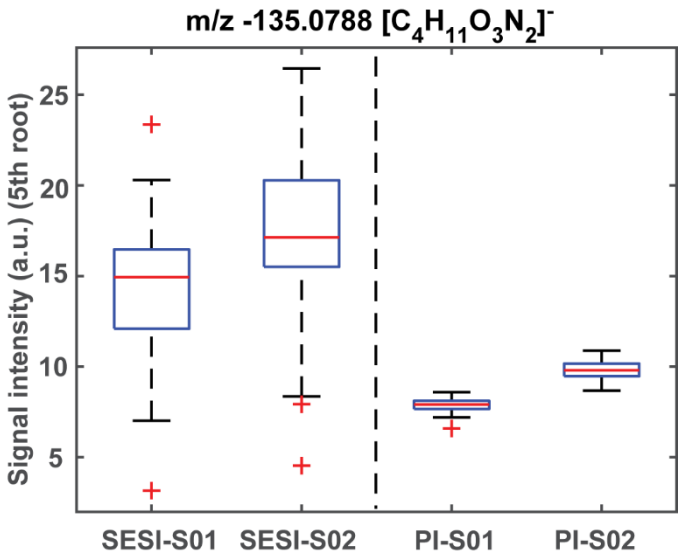
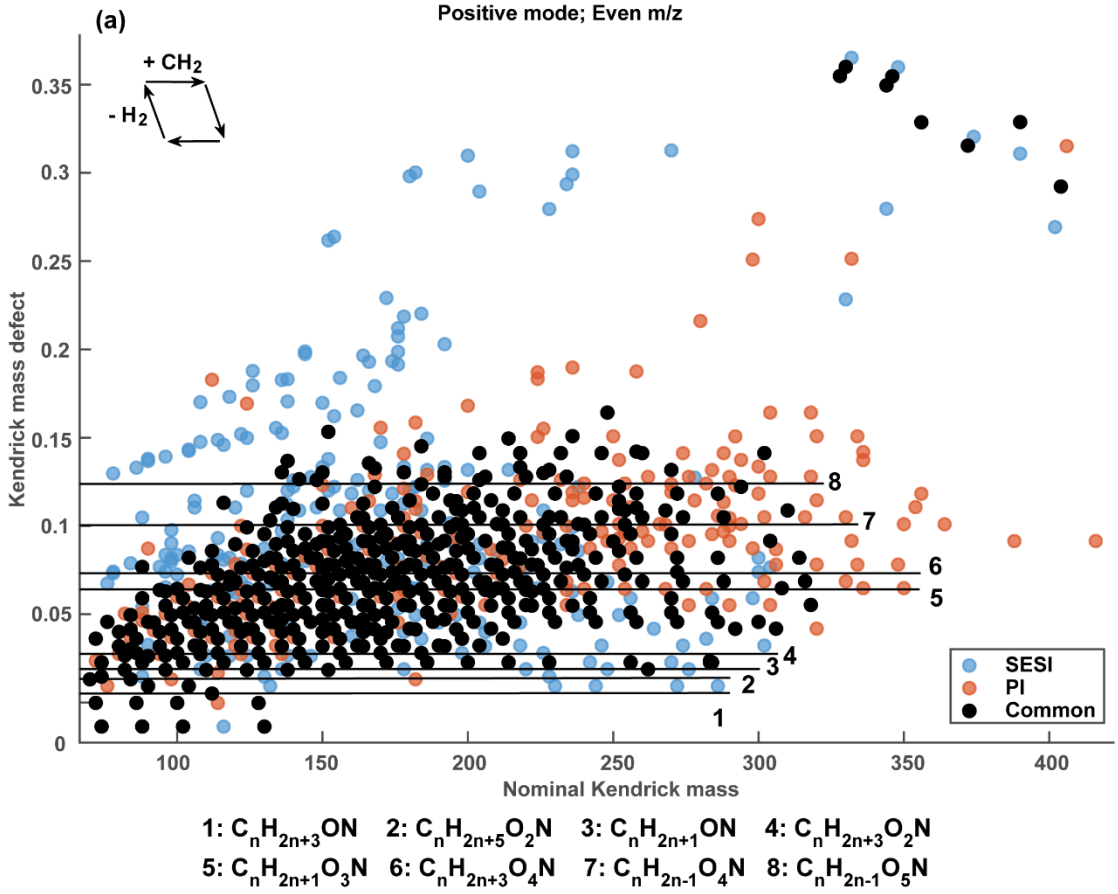


Figure S5. Boxplot of the feature with maximum loading in PC 2, $[C_4H_{11}O_3N_2]^-$ (m/z 135.0788) was found to be systematically more abundant for subject 2 in both platforms, and it was significant different between PI-S01 and PI-S02, but not between SESI-S01 and SESI-S02.



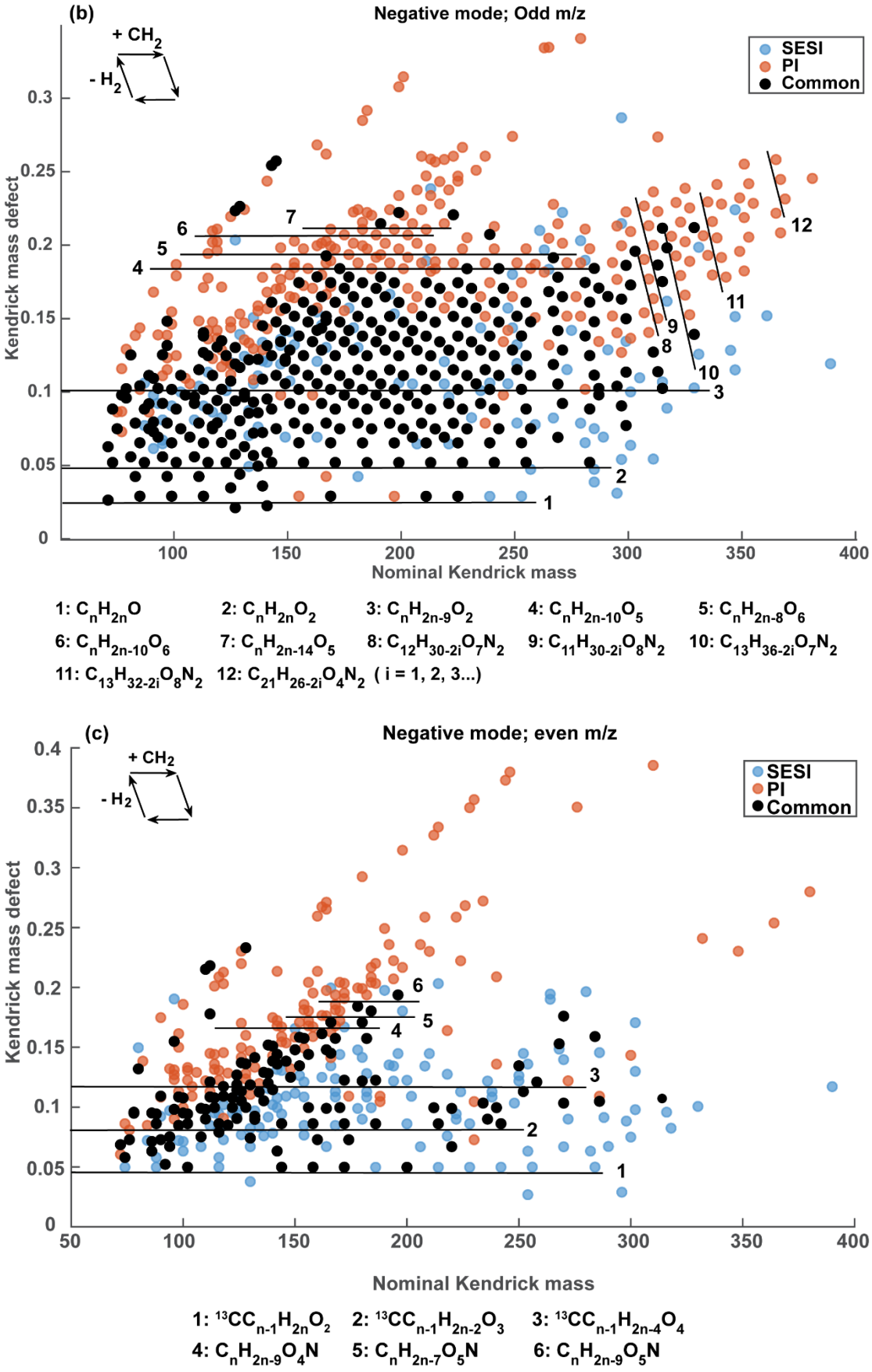


Figure S6. Kendrick Mass Defeat plot of breath features found by PI-HRMS and SESI-HRMS.

The orange dots are the ions only detected by PI-HRMS, the blue dots are only by SESI-HRMS and the black dots are overlap. There are some possible homologous series compounds (differ by the number of CH_2 unit) shown above, the features of same homologous series laid on a horizontal line. (a) Positive even m/z, 8 homologous series of N-containing compounds were assigned. (b) Negative odd m/z, 12 homologous series compounds have been found. Features in series 8 to 12 differ by the number of H_2 unit on an oblique direction. (c) Negative even m/z, 3 homologous series of N-containing compounds and 3 homologous series of isotope compounds were found.

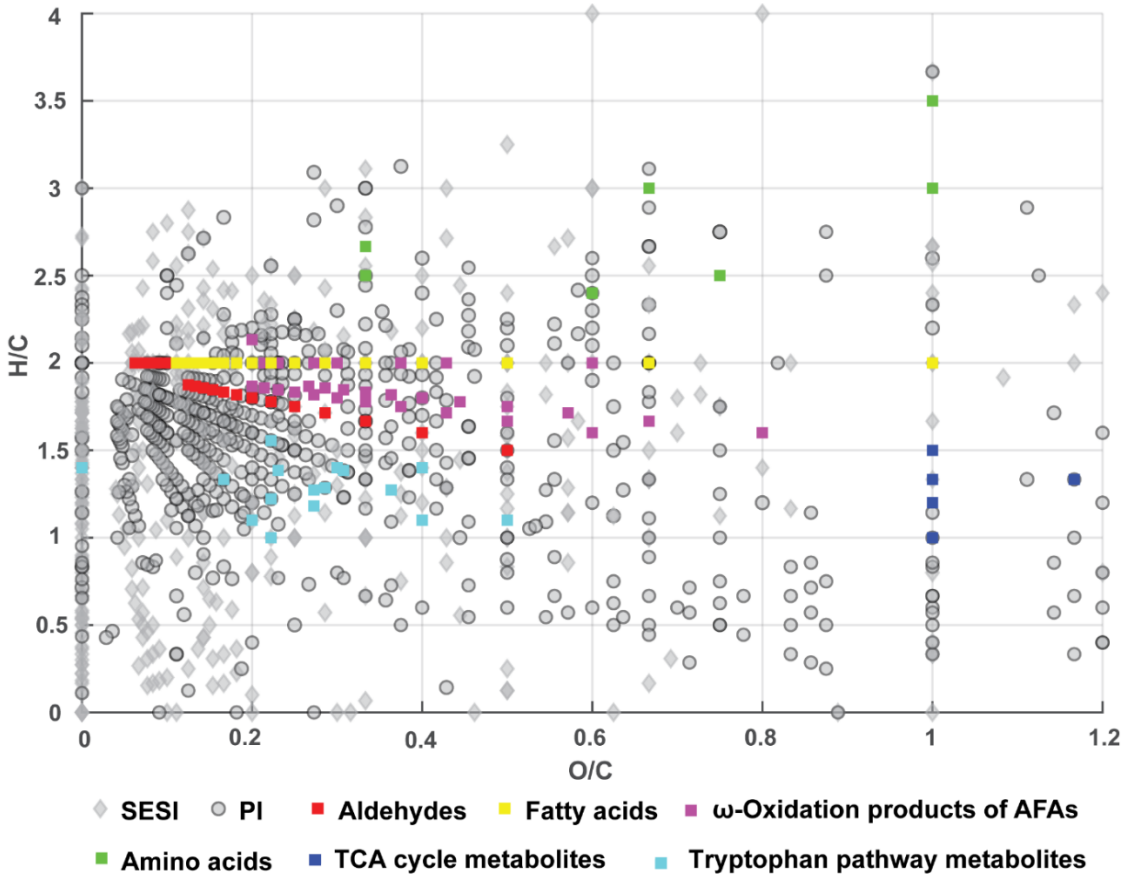


Figure S7. The van Krevelen diagram of assigned formula features. The gray diamonds are the features of SESI-HRMS and the gray dots are the features of PI-HRMS. The colored square are the human breath metabolites which were confirm by previous research[1]. Among these features, 91.51 % of the PI-HRMS features contain at least one oxygen atom and of SESI-HRMS features it is 85.48 %. Most of the fatty acid and its oxidation products, aldehydes and tryptophan pathway metabolites are distributed in the area where H/C is less than or equal to 2 and O/C is

less than 0.8 where many PI-HRMS features were distributed. The features detected by SESI-HRMS are more in the region with O/C less than 0.2, and a considerable part of them are ions that do not contain oxygen atoms.

Table S1. Detailed m/z list of each correlation network 1

Network No.	m/z	Network No.	m/z	Network No.	m/z
1	74.97534	1	111.0385	1	154.9074
1	76.01751	1	112.0463	1	154.9637
1	76.51917	1	113.0359	1	155.0315
1	77.00832	1	113.9785	1	155.9903
1	77.45764	1	114.0438	1	156.9744
1	77.95734	1	115.0067	1	158.9965
1	78.013	1	115.0366	1	161.0121
1	78.01394	1	115.4839	1	162.0155
1	78.99701	1	115.9836	1	163.0278
1	83.02153	1	116.0489	1	163.0452
1	84.01498	1	116.5505	1	165.0071
1	84.95969	1	117.0397	1	167.0316
1	85.02279	1	117.9586	1	169.0472
1	85.52445	1	118.9427	1	170.0424
1	85.96301	1	119.0283	1	171.0264
1	86.46293	1	120.9529	1	173.0057
1	86.95572	1	120.9809	1	173.0121
1	86.96258	1	121.9842	1	173.0785
1	86.9927	1	122.9769	1	174.0009
1	87.02784	1	122.9851	1	174.985
1	87.99348	1	123.0139	1	175.0004
1	88.04439	1	123.4891	1	175.0278
1	88.95255	1	123.9886	1	175.9845

1	88.99022	1	124.0734	1	175.9892
1	89.96245	1	124.4892	1	176.0051
1	89.96368	1	124.9738	1	176.9805
1	90.94768	1	124.9889	1	176.9892
1	92.98592	1	125.0114	1	177.007
1	93.02028	1	125.0542	1	177.9801
1	94.02811	1	130.979	1	179.0227
1	94.96756	1	131.0016	1	183.0176
1	95.01891	1	133.0172	1	183.9852
1	95.46822	1	133.9941	1	184.9693
1	95.96791	1	134.9578	1	186.1182
1	96.02358	1	134.9869	1	186.9356
1	96.03316	1	135.0502	1	191.0227
1	96.04197	1	135.9691	1	192.0114
1	96.53489	1	135.9992	1	192.9955
1	97.03526	1	136.0549	1	193.0019
1	98.01179	1	136.9532	1	193.0383
1	98.01923	1	138.0422	1	194.9912
1	98.02783	1	138.0505	1	195.0176
1	98.02963	1	138.9635	1	197.0121
1	99.00325	1	138.9914	1	198.9302
1	99.01183	1	139.0345	1	204.9461
1	102.97027	1	139.0365	1	205.0383
1	103.97285	1	139.0431	1	215.0162
1	103.9736	1	143.0016	1	216.9409
1	104.03063	1	143.9619	1	219.0903
1	104.47348	1	144.5048	1	228.9955
1	104.90783	1	145.0045	1	233.9676
1	104.96631	1	145.0172	1	234.9516

1	104.97323	1	145.0346	1	234.9671
1	104.97452	1	146.9965	1	235.9512
1	105.0033	1	147.0321	1	235.9644
1	105.03848	1	148.9896	1	236.9484
1	105.54015	1	149.0122	1	236.9558
1	106.00408	1	151.9079	1	237.1009
1	106.96315	1	152.0318	1	244.9484
1	106.97827	1	152.9068	1	248.9405
1	106.99195	1	153.0158	1	254.959
1	107.00083	1	153.0522	1	254.9664
1	107.97299	1	153.908		
1	108.95829	1	154.0098		

References

[1] a) J. F. n. d. l. M. Pablo Martı´nez-Lozano, *Analytical Chemistry* **2008**, *80*, 8210; b) M. T. Gaugg, T. Bruderer, N. Nowak, L. Eiffert, P. Martinez-Lozano Sinues, M. Kohler, R. Zenobi, *Anal Chem* **2017**, *89*, 10329, DOI: 10.1021/acs.analchem.7b02092; c) A. Tejero Rioseras, K. D. Singh, N. Nowak, M. T. Gaugg, T. Bruderer, R. Zenobi, P. M. Sinues, *Anal. Chem.* **2018**, *90*, 6453, DOI: 10.1021/acs.analchem.7b04600; d) D. Garcia-Gomez, T. Gaisl, L. Bregy, P. Martinez-Lozano Sinues, M. Kohler, R. Zenobi, *Chem Commun (Camb)* **2016**, *52*, 8526, DOI: 10.1039/c6cc03070j; e) D. Garcia-Gomez, T. Gaisl, L. Bregy, A. Cremonesi, P. M. Sinues, M. Kohler, R. Zenobi, *Clin. Chem.* **2016**, *62*, 1230, DOI: 10.1373/clinchem.2016.256909; f) D. Garcia-Gomez, P. Martinez-Lozano Sinues, C. Barrios-Collado, G. Vidal-de-Miguel, M. Gaugg, R. Zenobi, *Anal Chem* **2015**, *87*, 3087, DOI: 10.1021/ac504796p.