Supporting Information

A Novel Strategy for Extracted Ion Chromatogram Extraction to Improve Peak Detection in UPLC–HRMS

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1. Experimental Part.

Dataset 1.

Sample treatment for tobacco plant and tea samples. Tobacco plant and tea samples are grounded to powder before analysis. About 20 mg sample was weighted in a 2.0 mL tube and added with 1.5 mL solvent of CH_3OH and H_2O (70/30, v/v). A 2 min volute, followed by a 30 min ultra-sounded with 40 KHz treatment utilized for components extraction. The tube was centrifuged at 13000 rpm for 10 min, and 1 μL of supernatant was injected into an Agilent 1290-6540 UPLC-QTOF.

An ultra-performance Agilent C18 column was used for tobacco plant sample analysis. The mobile phase consists of (A) water and (B) ACN with 0.1% Formic acid. A flow of 0.2 mL min^{-1} was used. The phase (A) is started from 85% and reduces to 0% within 15 min and maintains for 5 min. QTOF parameters are: Gas temperature, 350 °C; gas flow, 12 L min−1; nebulizer, 40 psi; sheath gas temperature, 350 °C; sheath gas flow, 10 L min−1; Vcap, 3500 V; and mass range, 50–1000.

An ultra-performance Waters T3 column was used for tea sample analysis. The mobile phase is the same as tobacco plant sample. The mobile phase started with 100% A and then declined to 70% within 10min, to 10% within 15 min, followed by a decrement to 0% at 17 min and held for 4 min. The QTOF parameters are the same as tobacco plant sample.

Sample treatment for wine sample. 100 μL wine sample are pooled with 900 μL solvent (CH_3OH/H_2O, 70/30, v/v). 1 μL sample was injected into the Agilent 1290-6545 UPLC-QTOF with C18 column. Instrumental condition is the same as tobacco plant sample.

Dataset 2.

Calibration samples. Nineteen compounds, including *Metformin hydrochloride, Phenformin hydrochloride, Telmisartan, Clonidine hydrochloride, Atenolol, Metoprolol, Tolbutamide,*

Lovastatin, Simvastatin, Gliclazide, Felodipine, Rosiglitazone maleate, Prazosin Hydrochloride, Candesartan, Cilexetil, Gliquidone, Reserpine, and *Nifedipine* were prepared in methanol. Calibration samples were obtained by diluting the mixture with CH_3OH. Concentrations for each compound are 8, 12, 16, 20, 24, and 28 ng mL^{-1}. These calibration samples were analyzed on an Agilent 1290-6545 UPLC-QTOF. The instrumental parameters are the same as tobacco plant sample.

Tea mixture samples. The standard compound solutions were mixture with tea extraction (see tea sample treatment) to test quantification capability of AiCN-EIC for analyzing complex samples. Concentrations in these samples are the same as calibration samples. Tea mixture samples were analyzed on an Agilent 1290-6545 UPLC-QTOF with instrumental parameters optimized the same as tobacco plant sample.

2. Data Analysis Part

Data analysis parameters for XCMS Online, Mzmine2/ADAP, and MS-DIAL. The following parameters were used for these methods:

Method	Parameters
XCMS Online	Using parameters that have been optimized for UPLC-QTOF on the web version.
Mzmine2/ADAP	**Ion chromatogram extraction.** *ADAP Chromatogram Builder; m/z tolerance*: *0.01 Da or 20 ppm.*
	Peak Detection. *Peak deconvolution: wavelets (ADAP); Min highest intensity: 100.*
	Peak Alignment. *method: RANSAC; m/z tolerance*: *0.01 Da or 20 ppm; RT tolerance: 0.5 min*.
MS-DIAL	**Data Collection.** *Centroid parameter: MS1 tolerance 0.01 Da.*
	Peak Detection. *Mass slice width: 0.1 Da;*
	Peak Alignment. *Retention time tolerance: 0.5 min; MS1 tolerance: 0.01 Da.*

Circle 1

Step 0

	scan	m/z	Bleft	Bright	min(Bleft,Bright)	side	cluster
1	1	100.001	Inf	**0.001**	0.001	right	0
2	5	100.002	**0.001**	0.0015	0.001	left	0
3	2	100.0035	0.0015	**0.0005**	0.0005	right	0
4	6	100.004	**0.0005**	0.0015	0.0005	left	0
5	3	100.0055	0.0015	**0.0005**	0.0005	right	0
6	7	100.006	**0.0005**	0.001	0.0005	left	0
7	4	100.007	**0.001**	0.001	0.001	left	0
8	8	100.008	**0.001**	Inf	0.001	left	0

i=1

	scan	m/z	Bleft	Bright	min(Bleft,Bright)	side	cluster
1	1	100.001	Inf	Inf	0		**1**
2	5	100.002	Inf	**0.0015**	0.0015	right	**1**
3	2	100.0035	0.0015	**0.0005**	0.0005	right	0
4	6	100.004	**0.0005**	0.0015	0.0005	left	0
5	3	100.0055	0.0015	**0.0005**	0.0005	right	0
6	7	100.006	**0.0005**	0.001	0.0005	left	0
7	4	100.007	**0.001**	0.001	0.001	left	0
8	8	100.008	**0.001**	Inf	0.001	left	0

When i=2, no merge! continue

i=3

	scan	m/z	Bleft	Bright	min(Bleft,Bright)	side	cluster
1	1	100.001	Inf	Inf	0		1
2	5	100.002	Inf	**0.0015**	0.0015	right	1
3	2	100.0035	**0.0015**	Inf	0.0015	left	**2**
4	6	100.004	Inf	0.0015	0.0015	left	**2**
5	3	100.0055	0.0015	**0.0005**	0.0005	right	0
6	7	100.006	**0.0005**	0.001	0.0005	left	0
7	4	100.007	**0.001**	0.001	0.001	left	0
8	8	100.008	**0.001**	Inf	0.001	left	0

When i=4, no merge! continue

i=5

	scan	m/z	Bleft	Bright	min(Bleft,Bright)	side	cluster
1	1	100.001	Inf	Inf	0	right	1
2	5	100.002	Inf	**0.0015**	0.0015	right	1
3	2	100.0035	**0.0015**	Inf	0.0015	left	2
4	6	100.004	Inf	0.0015	0.0015	left	2
5	3	100.0055	0.0015	Inf	0.0015	right	**3**
6	7	100.006	Inf	**0.001**	0.001	right	**3**
7	4	100.007	**0.001**	0.001	0.001	left	0
8	8	100.008	**0.001**	Inf	0.001	left	0

i=6

	scan	m/z	Bleft	Bright	min(Bleft,Bright)	side	cluster
1	1	100.001	Inf	Inf	0	right	1
2	5	100.002	Inf	**0.0015**	0.0015	right	1
3	2	100.0035	**0.0015**	Inf	0.0015	left	2
4	6	100.004	Inf	0.0015	0.0015	left	2
5	3	100.0055	0.0015	Inf	0.0015	right	**3**
6	7	100.006	Inf	Inf	0		**3**
7	4	100.007	Inf	0.001	0.001	right	**3**
8	8	100.008	**0.001**	Inf	0.001	left	0

i=7

	scan	m/z	Bleft	Bright	min(Bleft,Bright)	side	cluster
1	1	100.001	Inf	Inf	0	right	1
2	5	100.002	Inf	**0.0015**	0.0015	right	1
3	2	100.0035	**0.0015**	Inf	0.0015	left	2
4	6	100.004	Inf	0.0015	0.0015	left	2
5	3	100.0055	**0.0015**	Inf	0.0015	left	**3**
6	7	100.006	Inf	Inf	0		**3**
7	4	100.007	Inf	Inf	0		**3**
8	8	100.008	Inf	Inf	0	left	**3**

Circle 2

i=1

	scan	m/z	Bleft	Bright	min(Bleft,Bright)	side	cluster
1	1	100.001	Inf	Inf	0	right	**1**
2	5	100.002	Inf	Inf	0		**1**
3	2	100.004	Inf	Inf	0		**1**
4	6	100.004	Inf	**0.0015**	0.0015	right	**1**
5	3	100.006	**0.0015**	Inf	0.0015	left	3
6	7	100.006	Inf	Inf	0		3
7	4	100.007	Inf	Inf	0		3
8	8	100.008	Inf	Inf	0	left	3

When i=2, no merge! continue

When i=3, no merge! continue

i=4

	scan	m/z	Bleft	Bright	min(Bleft,Bright)	side	cluster
1	1	100.001	Inf	Inf	0	right	**1**
2	5	100.002	Inf	Inf	0		**1**
3	2	100.004	Inf	Inf	0		**1**
4	6	100.004	Inf	Inf	0		**1**
5	3	100.006	Inf	Inf	0		**1**
6	7	100.006	Inf	Inf	0		**1**
7	4	100.007	Inf	Inf	0		**1**
8	8	100.008	Inf	Inf	0	left	**1**

When i=5, no merge! continue

When i=6, no merge! continue

When i=7, no merge! continue

When i=8, no merge! continue

End

Figure S1. Graphical illustration of the developed EIC construction algorithm. At first, ions are sorted based on m/z values. The boundary of each ion is calculated to select matched *side*.

Two ions will be merged if the *side* of the *i*th is right and the *i*+1th is left. For the clustered ions, the matched *side* is recalculated.