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LC-MS ESI Parameter Optimization with Bayesian Optimization for High Sensitivity Measurement

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1. Introduction

Electrospray Ionization (ESI) is one of the methods to ionize compounds in mass spectrometry (MS) (**Fig.1**). To realize high sensitivity, ESI parameters are optimized by measuring actual samples a few dozen times. It is important to reduce the number of measurements during optimization to save the time and the sample. In this study, we have analyzed sensitivity behavior for ESI parameters, and developed efficient optimization method.

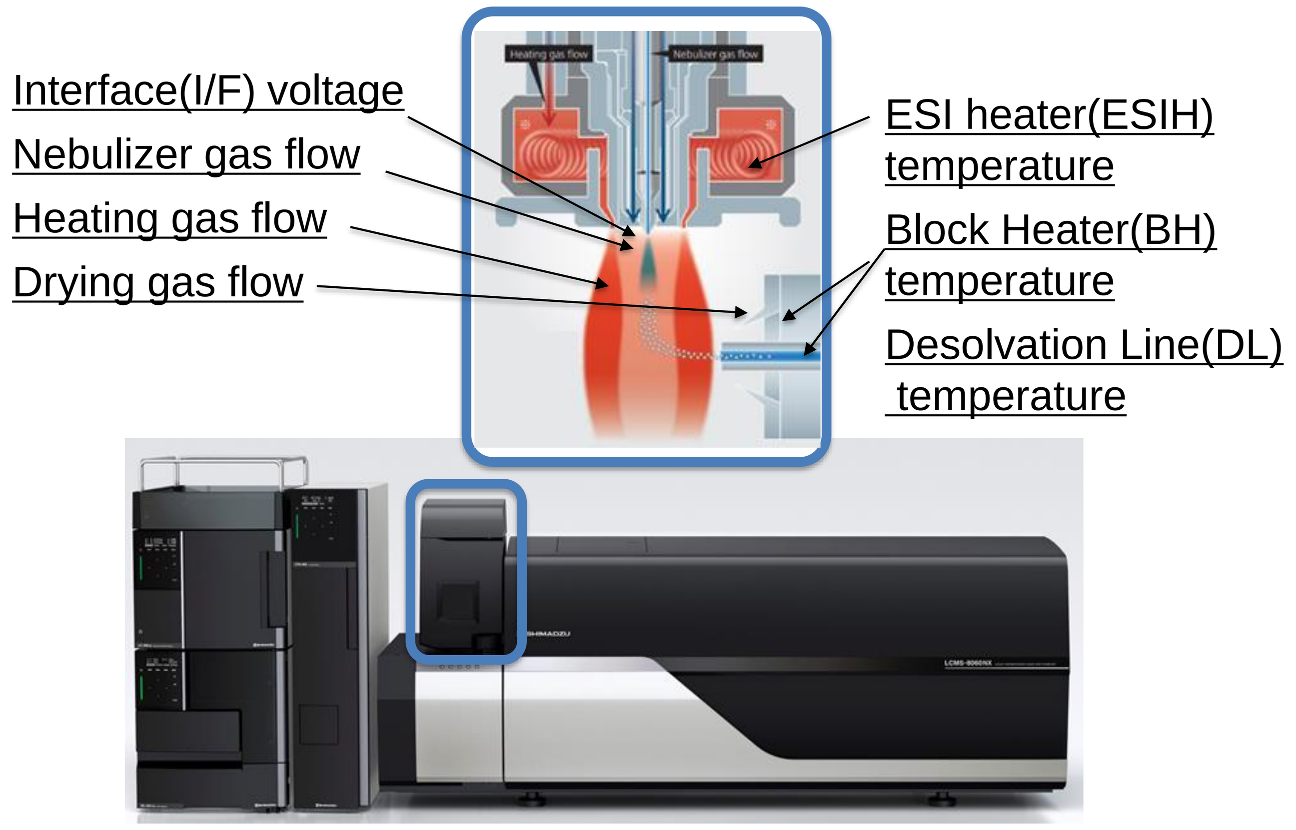

Figure 1 ESI parameters of LCMS-8060NX

2. Methods

○ Optimization Procedure

We have developed two step optimization procedure (**Fig. 2**). At the 1st step, three temperature parameters are combined to one parameter set, and the temperature parameter sets are optimized. At the 2nd step, other four parameters are optimized by Bayesian optimization (BO)[1]. To apply BO to ESI parameter optimization, we have developed noise-robust BO method in previous study[2]. This two step optimization procedure makes the latency time for temperature stabilization short, and enables to find the high sensitivity condition at a small number of measurement.

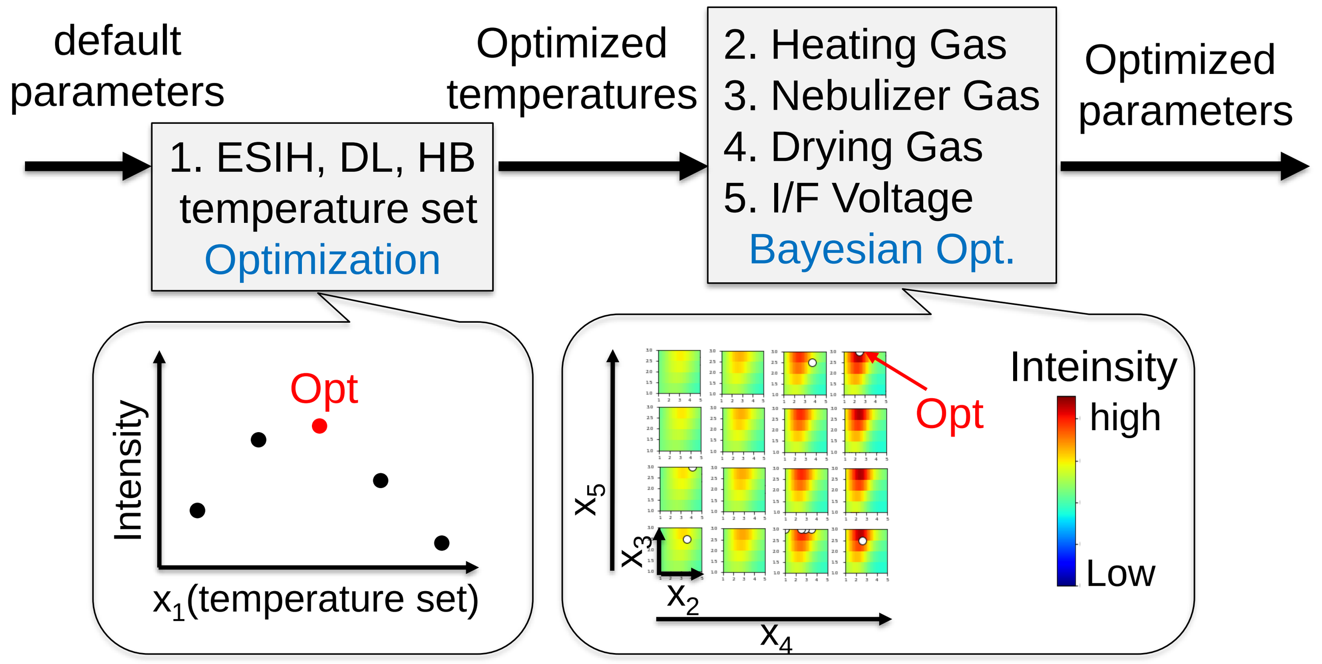

Figure 2 Optimization Procedure

○ Experimental Data Collection

To understand the true response surface for ESI parameters, we collected LC-MS data with 2,088 combinatorial conditions. Because full factorial design of 7 parameters is difficult to conduct, we conducted two patterns of combinatorial experiment (**Table 1**). Total 4 compounds (Angiotensin II, Atrazine, Dicamba and Flurbiprofen) are measured. In this experiment, Shimadzu HPLC (Prominence™) and LC-MS (LCMS-8060, of which ESI structure is very similar to LCMS-8060NX) are used.

Table 1 Data collection conditions

		Condition 1		Condition 2
I/F vol. [kV]		5 levels: 0.2,1.5,3.0, 4.0, 5.0		Fixed to optimal of condition 1
gas flow [L/min]	Neb.	4 levels: 0.5,1.5,2.5, 3.0		
	Heat.	5 levels: 3,5,7,10,15	<20	
	Dry.	5 levels: 3,5,7,10,15		
tempe rature [℃]	ESIH	5 sets: (IF, DL, BH) (100,100,100), (170,150,200), (240,200,300), (300,250,400), (400,300,500)		5 levels: 100,170,240,300,400
	DL			5 levels: 100,150,200,250,300
	BH			5 levels: 100,200,300,400,500

3. Results

○ Evaluation of Optimization Performance

We evaluated two optimization performances, our method and one factor at a time(OFAT) method. To evenly compare these two optimization performances, we used same experimental data collected as mentioned before as a ground truth. As a result, our method could search for the high sensitivity condition about half number of the measurement compared to OFAT method (**Fig. 3**). In 4 compounds, our method was 49% efficient on average.

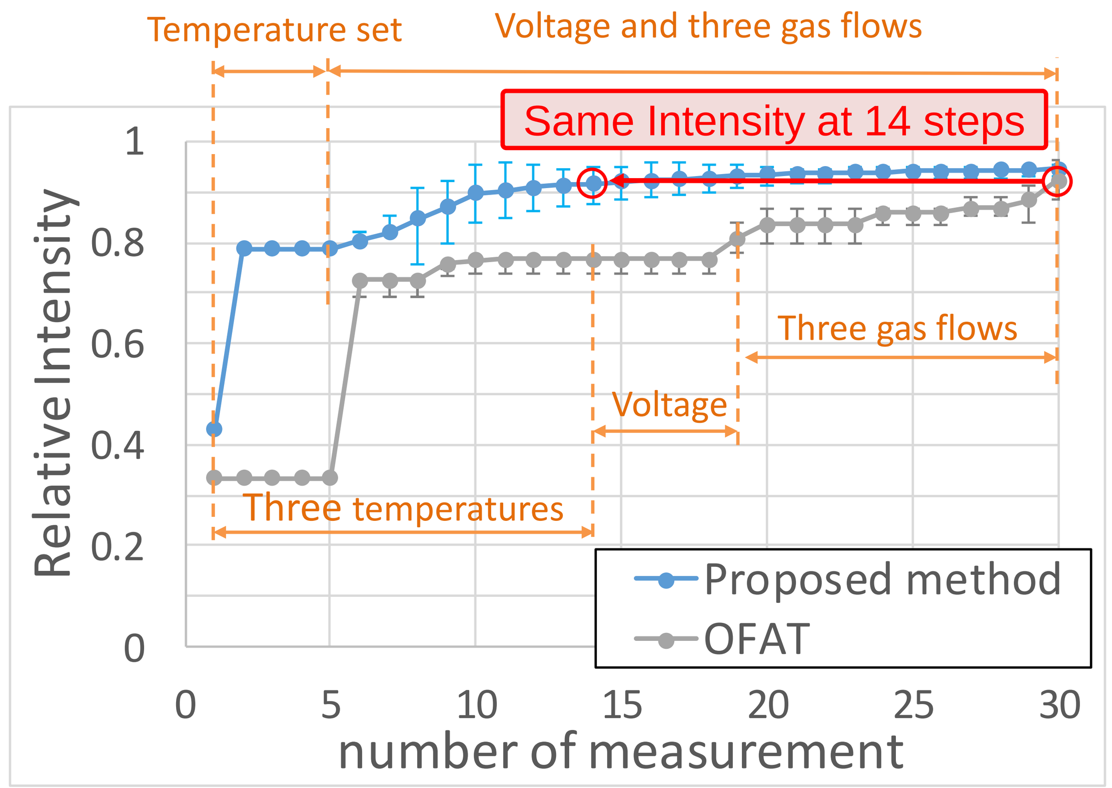

Figure 3 Evaluation of Optimization Performance (Flurbiprofen)

○ Investigation of Appropriate Default Parameter

We built response surface models for ESI parameters from the collected experimental data (**Fig. 4**).

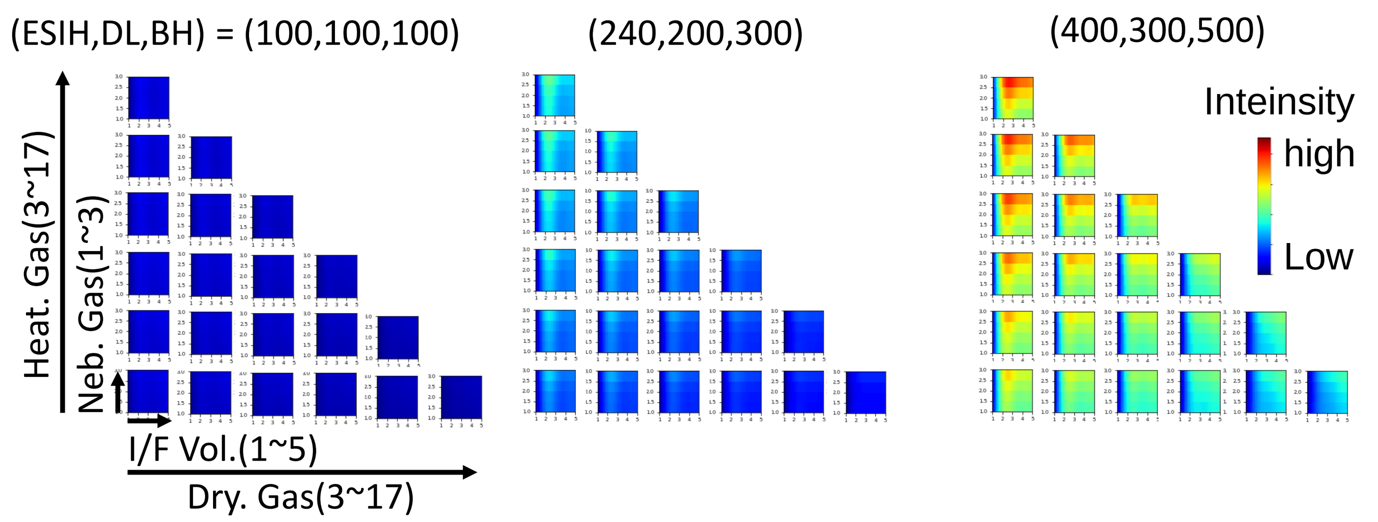

Figure 4 Examples of constructed response surfaces (Angiotensin)

Based on the response surfaces of several compounds, we changed default parameters in LCMS-8060NX. We demonstrated that new default parameters improved intensity about 2.6 times on average with various fields of compounds (**Fig. 5**).

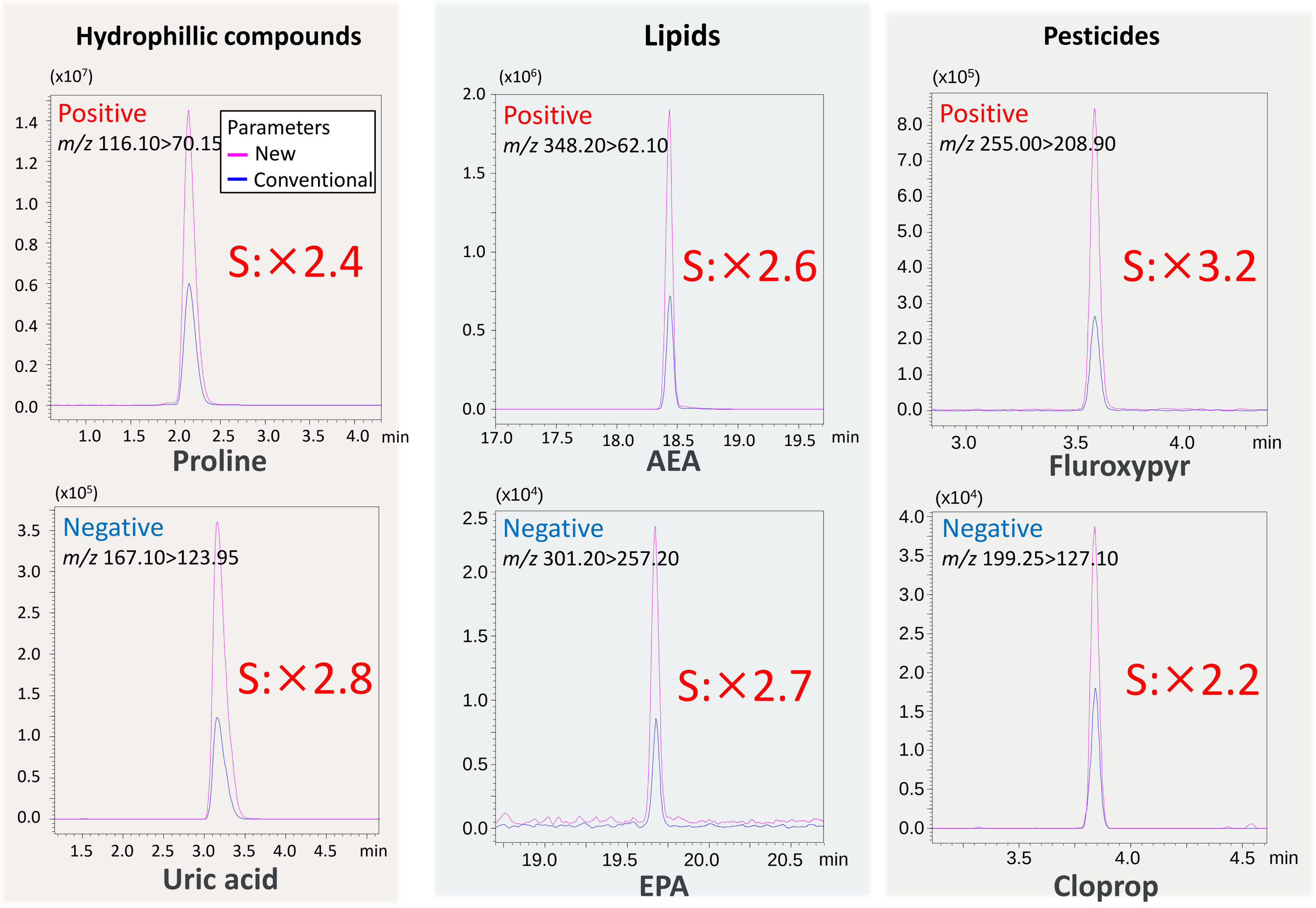

Figure 5 Analyses of various samples with new default ESI parameters

4. Conclusion

We've developed efficient ESI parameter optimization method. In the process of this study, we found an ESI parameter set which enable high signal intensity with various fields of compounds.

Based on this study, We set this new ESI parameter set as default parameters in LCMS-8060NX. By LCMS-8060NX, users can obtain good measurement result without making complicated analytic condition search, and decrease their workload.

References

[1] Snoek et al., Practical Bayesian Optimization of Machine Learning Algorithms, Proc. NIPS, Vol. 2, 2012

[2] Tagawa et al., LC-MS Interface Parameter Optimization for High Sensitivity Measurement, Shimadzu Review, Vol. 75, 2018