Supplementary Note

GameTag: A New Sequence Tag Generation Algorithm Based on Cooperative Game Theory

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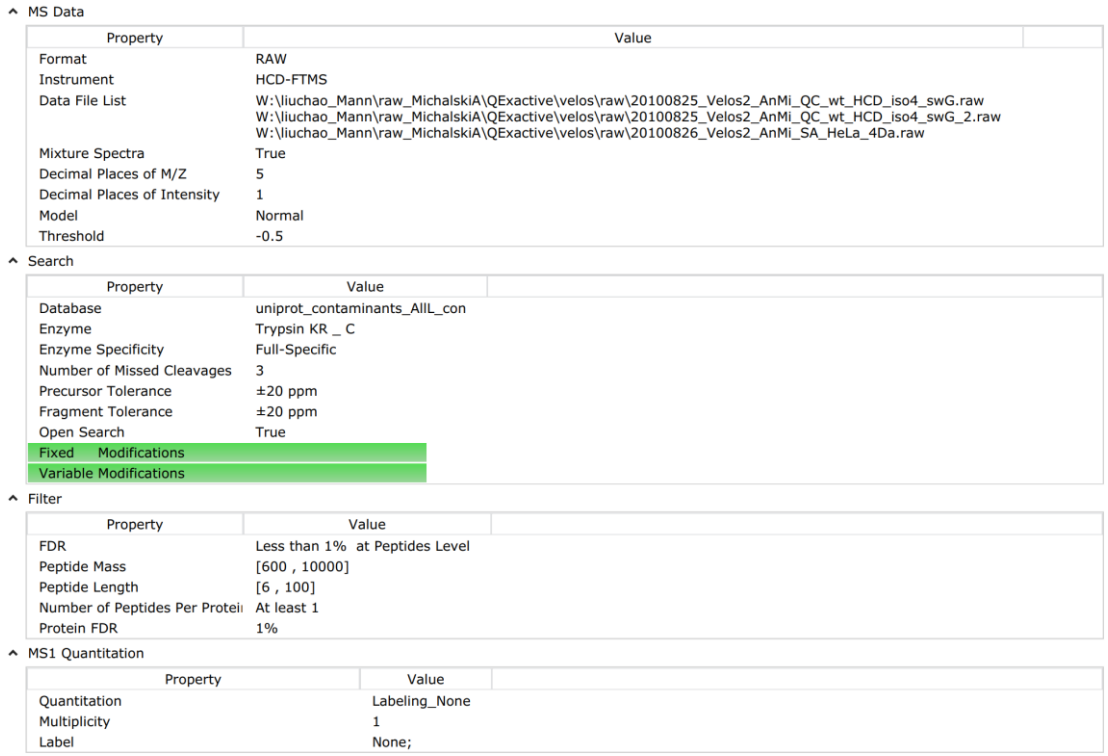
1. Dataset Annotation

In this section, we provide the detailed parameter settings of Open-pFind, PEAKS, and MSFragger, for dataset pre-processing and annotating. The intersection of identification results from the three can be considered as ground-truth PSMs. In practice, we employed `data_label_union.py` for intersection operation and result statistics.

1.1 Open-pFind

1) Tool download: http://pfind.ict.ac.cn/software/pFind3/index.html
2) Parameter setting interface:
   (Please note that no screenshots are all set by default)



MS Data

Property	Value
Format	RAW
Instrument	HCD-FTMS
Data File List	W:\liuchao_Mann\raw_MichalskiA\QExactive\velos\raw\20100825_Velos2_AnMi_QC_wt_HCD_iso4_swG.raw W:\liuchao_Mann\raw_MichalskiA\QExactive\velos\raw\20100825_Velos2_AnMi_QC_wt_HCD_iso4_swG_2.raw W:\liuchao_Mann\raw_MichalskiA\QExactive\velos\raw\20100826_Velos2_AnMi_SA_HeLa_4Da.raw
Mixture Spectra	True
Decimal Places of M/Z	5
Decimal Places of Intensity	1
Model	Normal
Threshold	-0.5

Search

Property	Value
Database	uniprot_contaminants_AllL_con
Enzyme	Trypsin KR _ C
Enzyme Specificity	Full-Specific
Number of Missed Cleavages	3
Precursor Tolerance	±20 ppm
Fragment Tolerance	±20 ppm
Open Search	True
Fixed Modifications	
Variable Modifications	

Filter

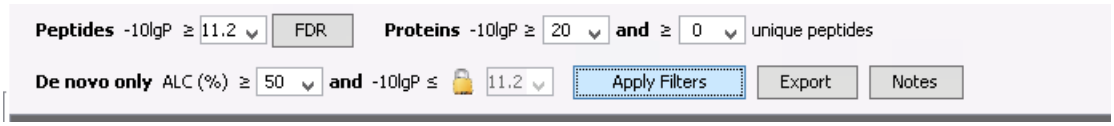
Property	Value
FDR	Less than 1% at Peptides Level
Peptide Mass	[600 , 10000]
Peptide Length	[6 , 100]
Number of Peptides Per Protei	At least 1
Protein FDR	1%

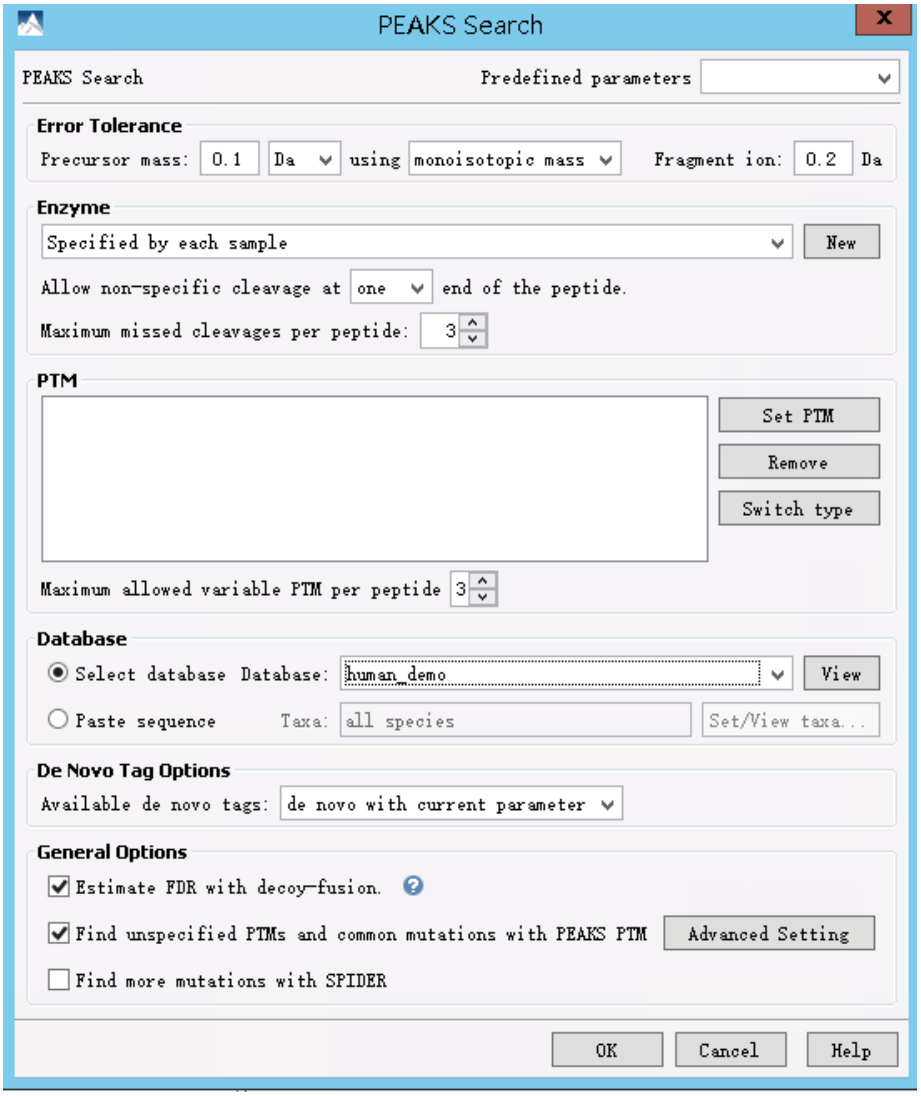
MS1 Quantitation

Property	Value
Quantitation	Labeling_None
Multiplicity	1
Label	None;

1.2 PEAKS

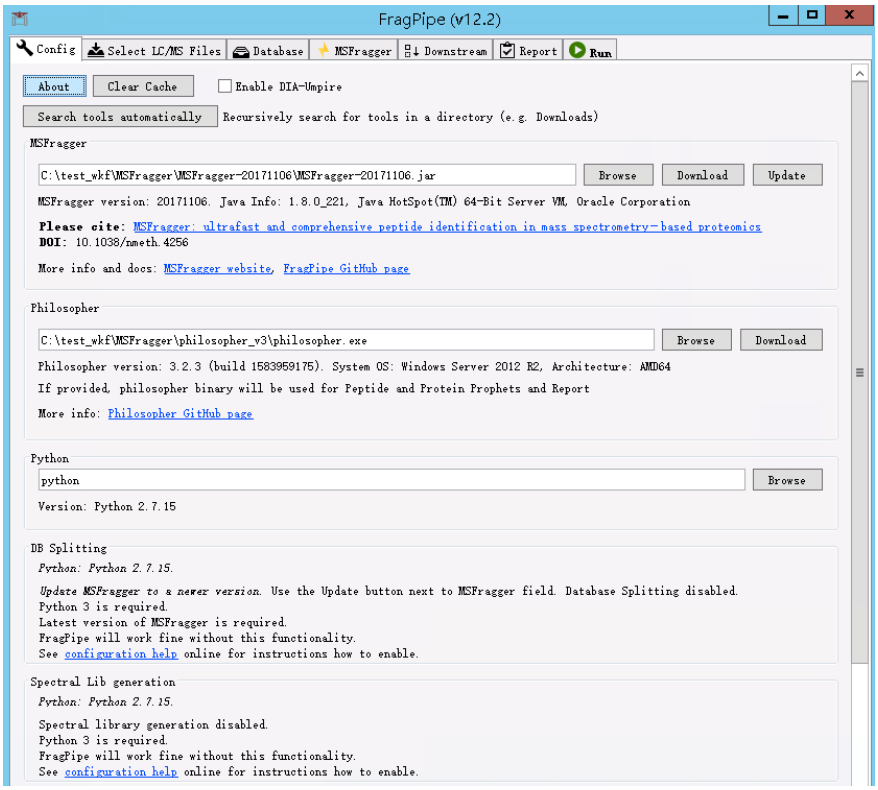
1) Homepage: https://www.bioinfor.com/download-peaks-studio/
2) Parameter setting interface:

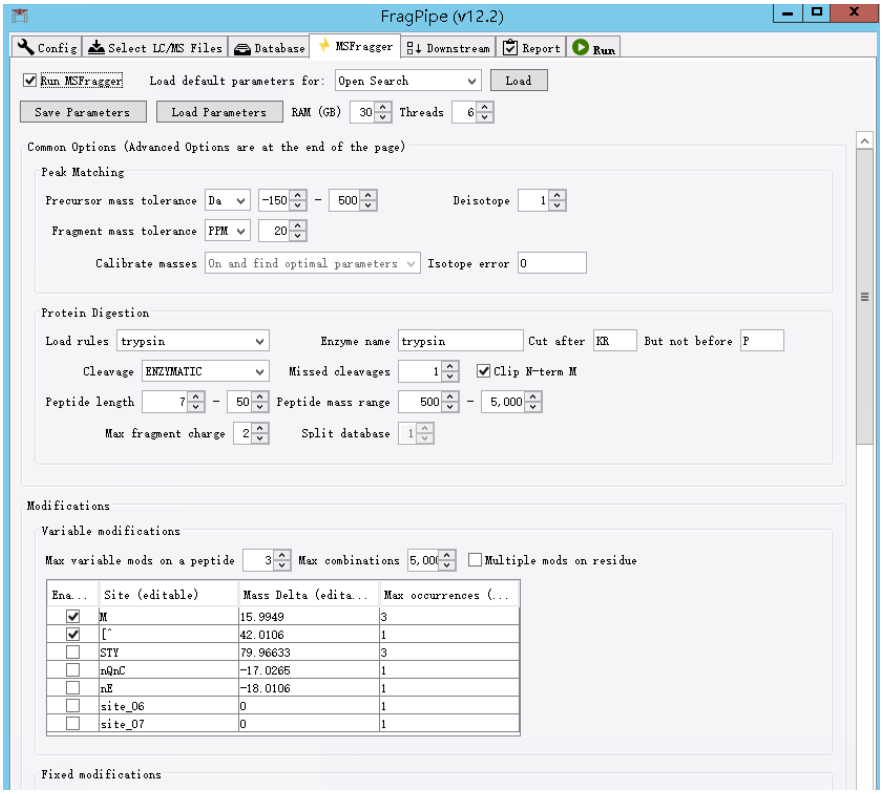




1.3 MSFragger

1) Tool download: http://msfragger.nesvilab.org/
2) Parameter setting interface:





2. Baseline Setting

In this section, we give the parameter setting for the baselines employed in the experiments for tagging performance comparison.

2.1 InsPecT

1) Tool download: http://proteomics.ucsd.edu/Software/Inspect/
2) Dataset format conversion (we use .mgf as spectrum file): http://tools.proteomecenter.org/wiki/index.php?title=Main_Page
3) Database Setup: run CMD as belows
   ```
   > python PrepDB.py FASTA [myDB.fasta]
   ```
4) Parameter InputFile:
   ```
   speactra, [FILENAME.mgf]
   protease, Trypsin
   mod, 57, C, fix
   TagCount, 100
   TagLength, 5
   ```
5) Run the InsPect:
   ```
   > InsPecT.exe -i InputFile.text -o OutputFile.txt
   ```

(In order to output the extracted tags, we can adopt the "DEBUG" module, more detail can be refer to document: http://proteomics.ucsd.edu/Software/Inspect/InspectDocs/)

2.2 PepNovo+

1) Tool download: https://github.com/jmchilton/pepnovo
2) Run the pepnovo+ with the below command:
   ```
   >PepNovo.exe -file [mgfPath] -model CID_IT_TRYP
   C+57:M+16 -digest NON_SPECIFIC -tag_length 5 -
   num_solutions 100 -fragment_tolerance 0.01 >
   [OutputFilePath]
   ```

(Note that we utilize the high-resolution data version for tag extraction. In practice, If the MS/MS spectra come from high-resolution instruments, the sequencing performance can be improved by manipulating the tolerances. For instance if the spectra have fragment tolerances of 0.01, this can be set with the flag: `-fragment_tolerance 0.01` .)

2.3 SVM:

1) Package download: https://www.csie.ntu.edu.tw/~cjlin/libsvm/
2) Parameter setting:

Input features	Peak intensity Edge mass error Node relevance degree
Feature Normalization	Yes
Kernel	RBF
C	512
Gamma	0.03125
Validation	5-fold cross-validation

(For convenience, the tag features produced by tag generator are used directly.)

3) Train the SVM model as:

```
>svm-train.exe -t 2 -g 0.03125 -c 512 -v 5 -s 1
[DatasetName] [ModelName]
```

4) Predict the results using the trained SVM model:

```
>svm-predict.exe [DatasetName] [ModelName] [OutputFile]
```

3. Additional Experimental Results

Due to the limitation of paper space, we will present some addition results here.

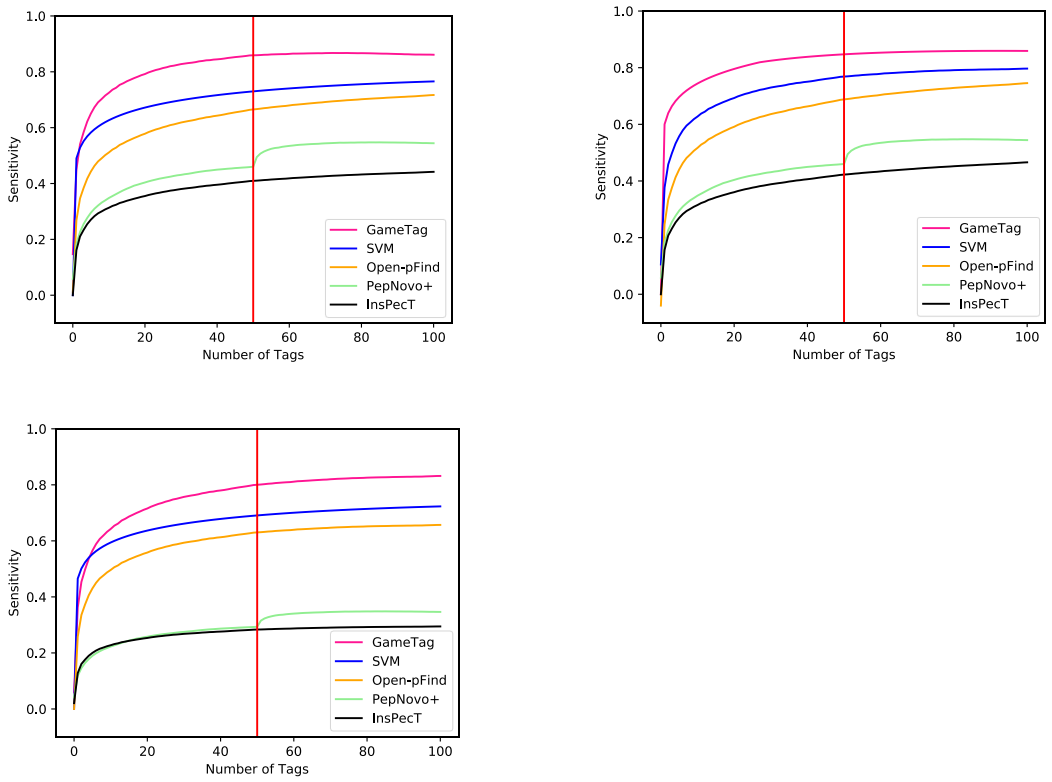


Figure S1: Sensitivity of different methods as a function of the number of tags considered for each spectrum on Gygi-Human-QE, Dong-Ecoli-QE, and Xu-Yeast-QEHF, respectively.