MET-XAlign User Manual

(Beta version - last updated: 06/23/2015)

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MET-XAlign Description

MET-XAlign is a tool that can be used to align the extracted and annotated metabolite based on the analysis result of another tool MET-COFEA(For more details about MET-COFEA, pls refer to http://bioinfo.noble.org/manuscript-support/met-cofea/). In the in LC-MS based comparative metabolomics, the fragmentation pattern and retention time for the same metabolite can vary greatly, which greatly impeded the LC-MS based comparative metabolomics study. MET-COFEA and MET-XAlign together can solve this issue. The user can configure the optimal parameters for each biological experiment and run MET-COFEA separately to analyze the corresponding samples at pipeline mode, which will extract and annotate all of metabolites' associated feature list and output them as database files. Finally, all of the exported database files from MET-COFEA can be aggregated and analyzed in MET-XAlign according to the user configured alignment parameters. The approach that combination of MET-COFEA with MET-XAlign makes it possible to align the potential same metabolite compound(known or unknown) not only across different samples, but also across different biological experiments, different ESI models, even different instruments, which can in turn be expected to help the biomarker identification in comparative metabolomics. Fig.1 gives the flowchart of flowchart of comparative metabolomics study using MET-COFEA and MET-XAlign. MET-XAlign has been successfully developed with its core algorithm (compound based alignment) coding in C++ and visualization part coding in .NET.

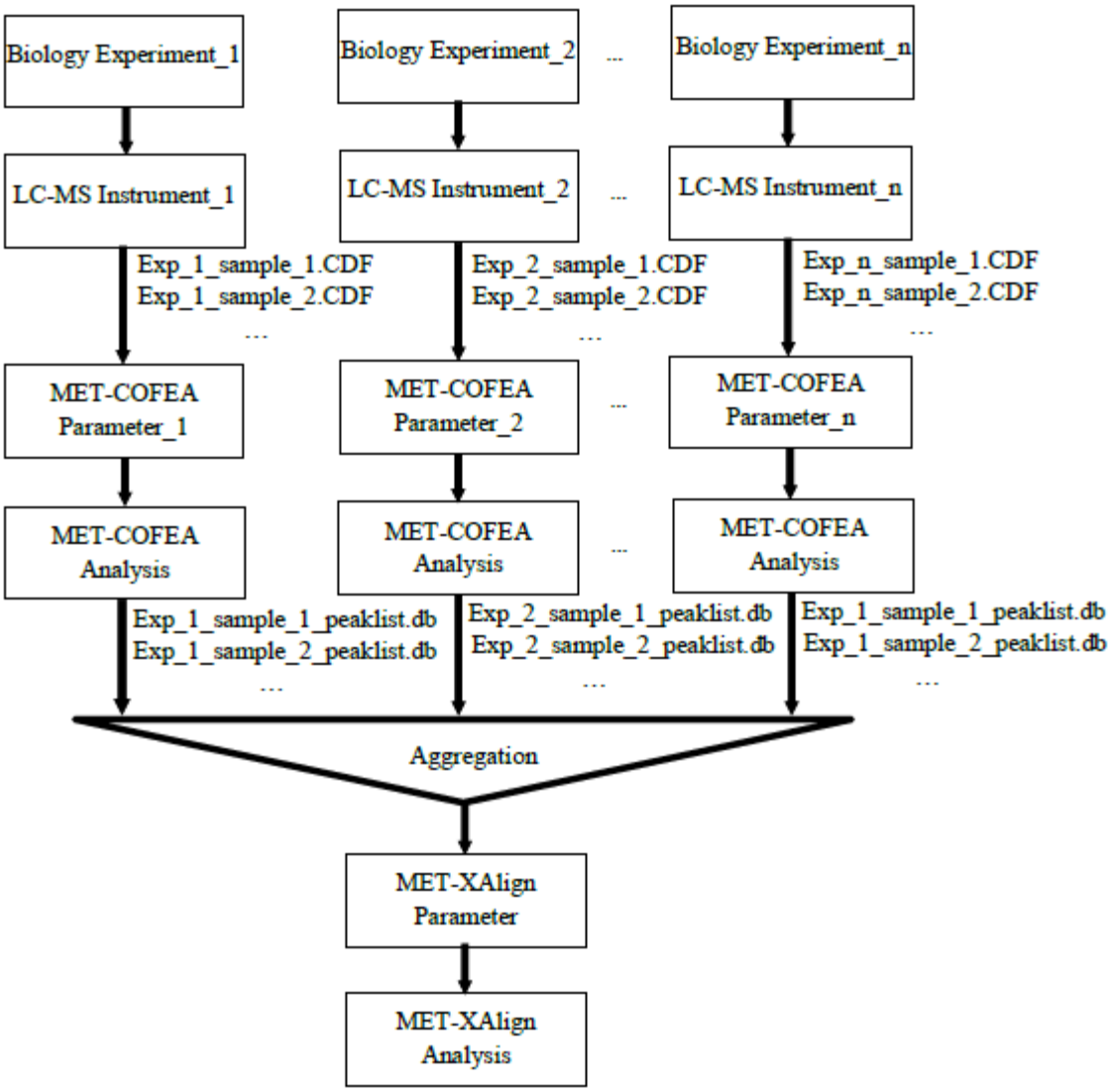

Fig. 1 Flowchart of Comparative Metabolomics study using MET-COFEA and MET-XAlign

MET-XAlign Application

Once the MET-COFEA's analysis for all the samples acquired from all biological experiments has finished, you can use MET-XAlign to align the same potential metabolites across all samples. Fig.2 is the screenshot of MET-XAlign software interface. All the application operation and parameters configuration can be finished by the software. There are 2 main parts (they are displayed as 2 item property page): **Align Process** for loading the analysis results from MET-COFEA and start alignment parameter configuration and alignment processing, **Align Visualization** for multiple sample's alignment results' visualization.

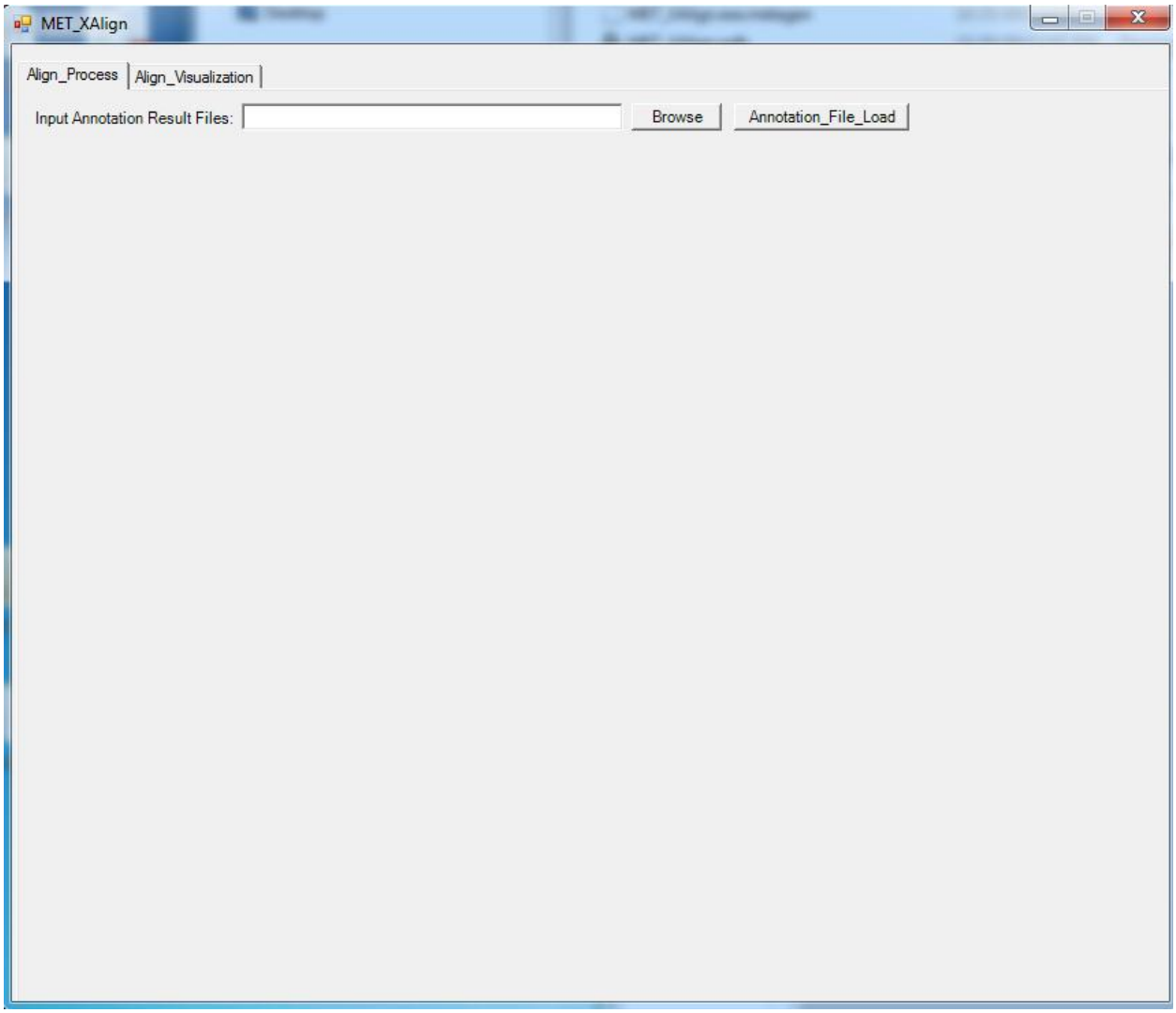

Fig. 2 screenshot is MET-XAlign software interface

Align Process

This property page let user to select the analysis result files (database file) outputted from MET-COFEA and load them into MET-XAlign and select some of them to align. Additionally, this property page also let user to configure the parameter for alignment. Fig.3 is the snapshot of property page of Align Process. The following is the normal procedures for this property page:

1. Click the button 'Browse' to select the MET-COFEA's analysis result database files.
2. Click the button 'Annotation_File_Load' to load these file name list into MET-XAlign.
3. Select all of them by click the radio button 'Align' or select some of them by click the corresponding radio button for alignment.
4. Configure the compound based alignment parameters.
5. Click the button 'Align', wait until it finished.

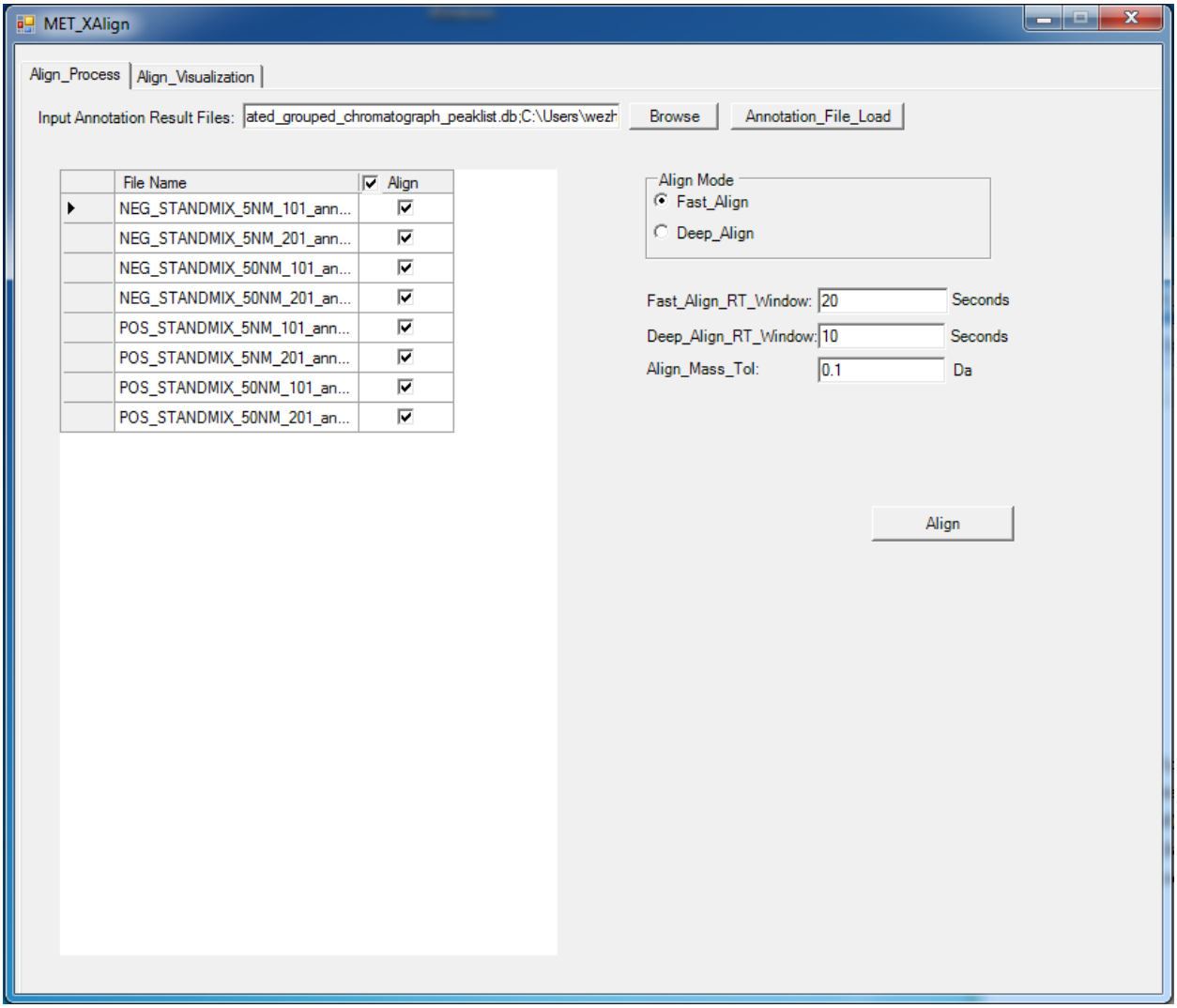

Fig. 3. Snapshot of MET-XAlign's Align_Process property page

Align Visualization

This property page allows the user to check the alignment results by visualizing the peaklist with the same Align_ID across different samples, different experiment sets. From the visualization (see Fig.4), all of the peaks with the same Align_ID across different samples are plotted and the peaks from the same Sample are plotted with one specific color (Right top panel). Additionally, the peak associated with the mouse click can also be plotted individually, or with the associated peaklist with the same Compound_ID, Group_ID (Right bottom panel). So, in this property page, the user can clearly know the relationship of the same compound associated peaks across different samples, even different experiment, and the relationship between the individual peak and the peaklist with the same Compound_ID, Group_ID.

The following is the normal procedures for this property page:

1. Select the alignment result file name "aligned_annotated_grouped_chromatograph_peaklist.aligndb". (This database file will be generated and stored in .\Result, once alignment finished.
2. Switch the retention time mode between RT_Original and RT_Corrected to check the alignment results.
3. Click a cell in the table to visualize the peaklist that have been aligned into the same Align_ID across different sample files. Figure.4 A and B gives the fragment pattern peaks for the same metabolite 'Glycyrrhetinic acid, 18 beta- Pygenic acid' at ESI(+) and ESI(-) respectively.

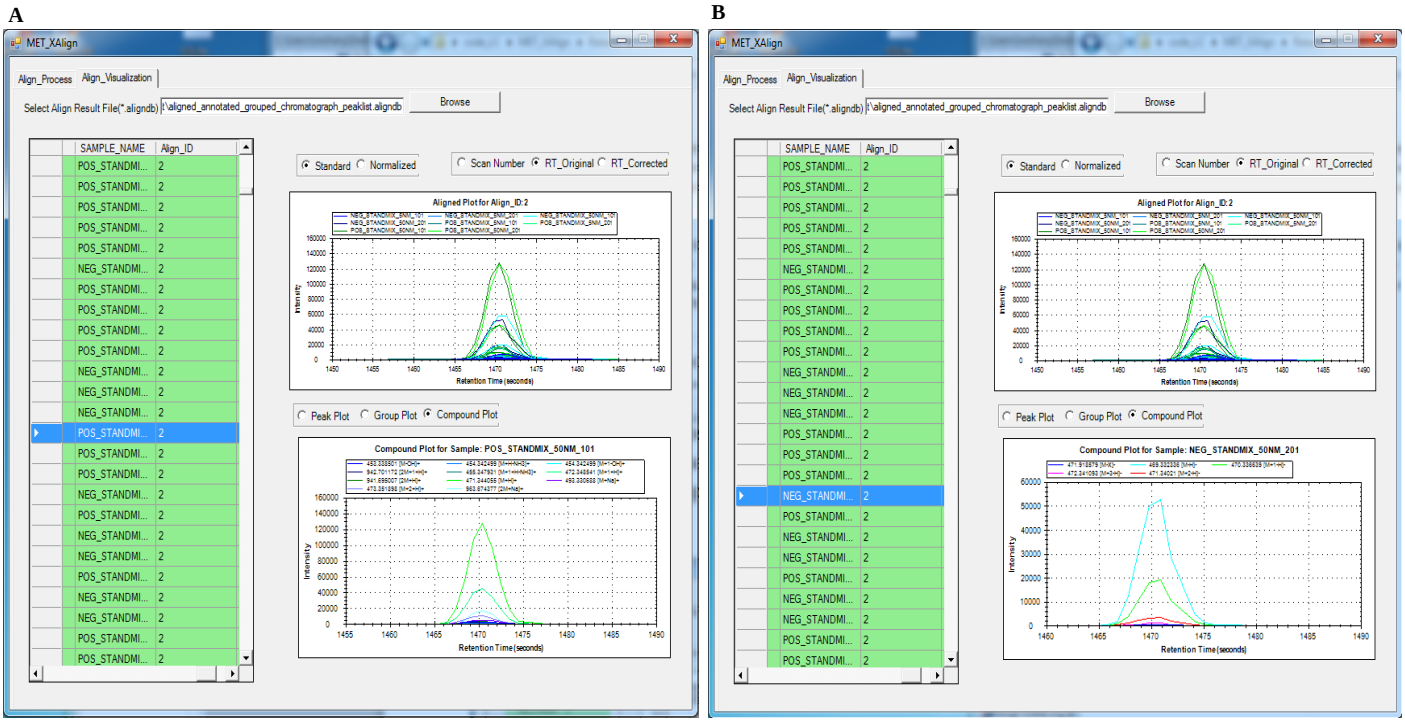

Fig. 4. Visualization of alignment result of MET-XAlign for the same metabolite named as '18 beta- Glycyrrhetinic acid' and marked by its unique Align_ID=2. A: The annotated metabolite's fragment peaks from sample POS_STANDMIX_50NM are plotted in the right bottom panel. B: The annotated metabolite's fragment peaks from sample NEG_STANDMIX_50NM are plotted in the right bottom panel