Mass Spectrometry Data Center
NIST
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Enhancements to NIST MS Interpreter for Modeling High Mass Accuracy Tandem Mass Spectra

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Introduction

For over 20 years, MS Interpreter has been a freely available software tool for quickly examining the possible origin of EI mass spectra for GC/MS and more recently ESI-Tandem Spectra for LC/MS. After input of a structure and a spectrum, it assigns peaks to plausible molecular substructures based on a set of thermochemical estimates and fragmentation mechanisms based on known chemical structure (connection table)information. This work describes changes made to both the user interface and fragmentation logic to both improve reliability and accommodate high resolution spectra of positively or negatively singly charged ions. The software can be found at https://chemdata.nist.gov

MS Interpreter Operation

MS Interpreter can work in Low Resolution and High Resolution mode. The Low Resolution mode is designed for GC/MS EI mass spectra, and the high resolution mode primarily for LC/MS ESI-Tandem spectra.

Fig.1 shows the low-resolution mass spectrum of Cholesterol. Three types of peaks are represented: black for peaks having known fragmentation reactions; white for undetermined ones and yellow for 'unspecified' (unclassified) reactions. The proposed chemical origin of black and yellow peaks are shown in red in the structures Fig. 2. Peak types are represented as small tics above each mass in the Mass Spectrum view for observed and, optionally, predicted peaks with no abundance. For example, a peak with 301 corresponds to the theoretical one 301.25259 corresponding even-electron fragment. In high-res mode, if multiple peaks overlap, a black arrow is displayed on the top of the overlapped peak group/pair, which can be expanded by double clicking.

There are three peaks of different reaction type illustrated in Fig.1: (a) 301 m/z, rate 70, dissociation type; (b) 231 m/z, rate 67, type H-loss-in-ring and (c) 275 m/z, rate 18, type 1,2,-ring-dissociation. Peaks shown as dotted yellow lines are of reaction unspecified type fragmentation, with corresponding blue tic at the top. All tics on the top correspond to theoretical peaks calculated by the fragmenter. A green color shows parent ions and their isotopes.

The MS Interpreter fragmenter not only predicts fragments, but also shows the structures and broken bonds involved. This is shown on the Fig. 2 for the three peaks, described above.

Fig.3 shows and explains two peaks in the high resolution ESI-Tandem of Fentanyl. Shown are nominal m/z, exact m/z, formula, loss, reaction type, rates, ppm, abundance and odd or even electron state: (a) 180.1444 m/z, rate 97, type H-Displacement; (b) 281.2027 m/z, rate 90, type H-loss-in-ring.

Fig.4 shows how to use a mass difference calculator. After selecting two peaks, the difference in mass is sent to the formula calculator to find possible neutral losses.

The fragmenter computes possible fragments, with their m/z are shown on the top each peak. A fragmentation process may consists of any many as three bond breaking steps. Thermodynamics is used throughout to estimate rough rates of reaction, with the weakest bond (or fastest reaction) assigned the highest rate. On Fig.1 and Fig.2 are shown peaks and corresponding structures, where one bond is broken (a), (b) two and (c) – three.

All possible reaction types and their distributions are shown on Fig.5.

The assignment of peaks determination uses a set of rules based on bond strengths in the precursor ion. These rules account for various structural factors including bond strengths, protonation, and permit selected unspecified losses of stable molecules, including CO, NO, SO, OH, water, ammonia, CH_3, SO_2, CHN, C_2H_2, SH, N_2, CNO_2, CO_2, CF_2, O, S_2, CH_3N, C_2H_3N, C_2H_4O, C_2H_2O,S, and CS. The new fragmenter is able to determine several losses simultaneously, as it is showed on the Fig.4(b) for peak of 241.049 m/z, where the summary loss is $CO+CO_2+H_2O$.

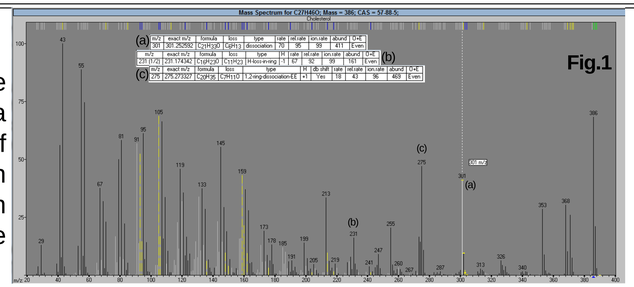

Fig.1 EI-GC mass spectrum of Cholesterol. Several peaks are annotated: (a) – 301 m/z, rate 70, dissociation type; (b) – 231 m/z, rate 67, type H-loss-in-ring and (c) – 275 m/z, rate 18, type 1,2,-ring-dissociation. Peaks shown as dotted yellow are for 'unspecified' reactions. All tics on the top are theoretical peaks, calculated by the fragmenter. A green color shows parent ions and its isotopes, yellow shows peaks of unspecified dissociation type.

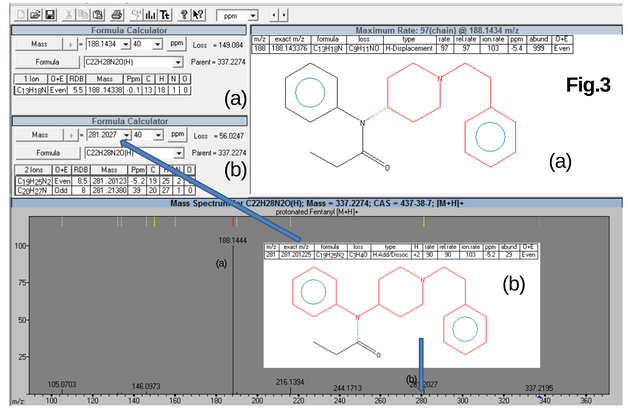

Fig.3 A high resolution ESI-Tandem of Fentanyl. Two peaks are shown assigned fragmentation results: exact m/z, formula, loss, reaction type, rates, ppm, abundance and Odd or Even state: (a) – 180.1444 m/z, rate 97, type H-Displacement; (b) – 281.2027 m/z, rate 90, type H-loss-in-ring.

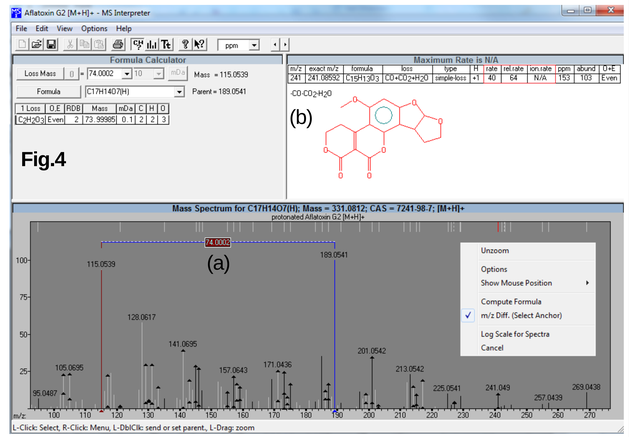

Fig.4 A high resolution ESI-Tandem of Aflatoxin. A new feature shows mass loss between two mass spectrum peaks. It is especially useful in high resolution mode. (a) – The difference between two main peaks 189.0541 and 115.0539 m/z corresponds loss of $C_2H_2O_3$ with 0.1 mDa precision. (b) – the new fragmenter is able to assign molecular losses. For 241.049 m/z the loss is $CO+CO_2+H_2O$.

Fig.2 Several peaks from Fig 1: (a) – 301 m/z, rate 70, dissociation type, (b) – 231 m/z, rate 67, type H-loss-in-ring and (c) – 275 m/z, rate 18, type 1,2,-ring-dissociation

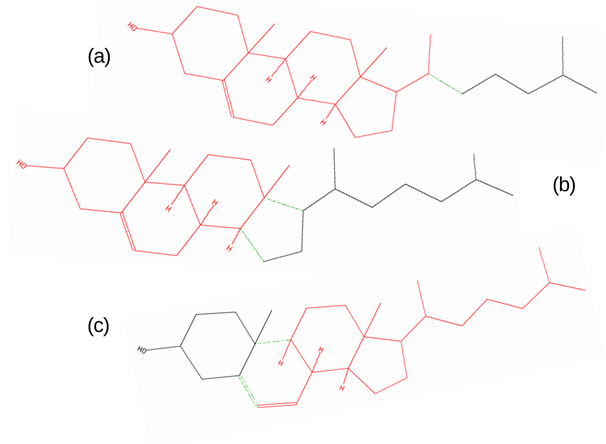

Fig.5 Current set of fragmentation reactions and numbers of assigned largest fragment ions for EI-GC and ESI-Tandem

Fragment Type	EI-GC	ESI-Tandem
1,1,2-dissociation-unspec	2193	7
1,1,3-dissociation-unspec	491	5
1,1-nonring-dissociation	1041	-
1,1-ring-dissociation	1355	35
1,2,3-break-ion	562	7
1,2,3-break-neutral	174	5
1,2,n-break-ion	583	7
1,2,n-break-neutral	2075	33
1,2-nonring-diss.-EE/OE	6941/559	35/-
1,2-ring-diss.-EE/OE	3791/6527	268/-
1,3-me-rearrangement	9	-
1,3-ring-dissociation	1613	70
2-bond-cleavage-EE/OE	22800/3807	212/-
2H-shift/diss	1540	-
acetyl-losses	27	-
diss./(-H)/+	113075/5003/2592	547/-/29
diss.-in-ring-EE/OE	711/408	35/-
doubly-charged	75	-
g-shift/diss	4165	-
H-Add/Dissoc	-	1368
H-Displacement	-	4113
H-gain-in-complex	8394	3
H-loss-in-complex	7184	-
H-loss-in-ring	7000	98
No Annotation	13049	1574
ortho-effect	480	-
simple-loss	2177	730
Si-rearrangement	7	-
TMS-rearrangement	419	-
Unspecified	755	12
Grand Total	**216579**	**8098**