

Monoisotopic Mass?

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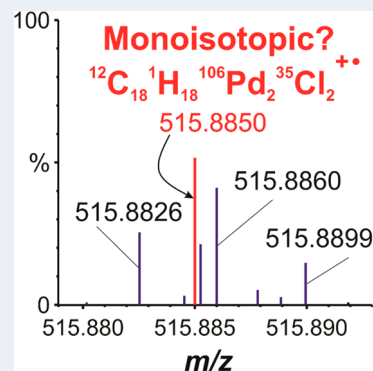


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ABSTRACT: The current IUPAC-recommended definition of the term “monoisotopic mass” of a chemical species is based on the most abundant isotopes of the constituent elements. It has even been proposed to constrain the definition to be based only on the atomic masses of the most abundant stable isotopes. Such an approach is flawed because in this way several elements and their compounds, in addition to isotopically enriched species, would not merit to be assigned a monoisotopic mass. Furthermore, for large molecules, such as proteins, the monoisotopic mass as currently defined loses its significance. Therefore, we propose to eliminate using the current definition altogether. Instead, the term isotopologue mass should be applied uniformly to every species denoted by a specific chemical formula.



INTRODUCTION

Several definitions are used in mass spectrometry to designate masses of ions.¹ Among them, *monoisotopic mass* is one widely used term in mass spectrometric discussions and publications. As expressed in the IUPAC compendium of mass spectrometry terminology, monoisotopic mass is the “exact mass of an ion or molecule calculated using the mass of the most abundant isotope of each [constituent] element.”^{2,3}

According to another definition for *monoisotopic mass*: “the monoisotopic mass of an element is the exact mass of the most abundant *naturally occurring stable* isotope determined relative to the mass of ¹²C, which is assigned the exact value of 12.0000 Da.”⁴ The monoisotopic mass of a molecule, ion, or radical is then the sum of the monoisotopic masses of all the atoms of its constituent elements.^{4,5} In a recent paper, it has been proposed to retain the descriptor *stable* in the monoisotopic mass definition for a molecule or an ion (see Table 1 in ref 6).⁶

If we accept the current definitions, D₂O *cannot* be assigned a monoisotopic mass because deuterium is *not* the most abundant isotope of the element hydrogen. Additionally, a mass spectrum of pure D₂O does not bear a peak for the *monoisotopic* species. The same argument applies to any isotope-enriched chemical species as well. Moreover, by this definition, no man-made element (not observed in nature) can be assigned a monoisotopic mass. In extreme cases, even some naturally occurring elements, such as bismuth, thorium, and protactinium, along with all their compounds without exception, cannot be allocated monoisotopic masses because their *sole* naturally occurring nuclides are unstable.

The term “monoisotopic” has been used differently in older literature: for example, as early as 1949, Norton⁷ and in 1957, Shapiro and Ditter,⁸ in their work with boranes, employed the term “monoisotopic spectrum” to designate spectra obtained

and calculated for *isotopically enriched* ¹⁰B and ²H compounds. None of those would be termed “monoisotopic spectra” by the current definition in the IUPAC “Gold Book,” which formulates the concept as “a spectrum containing only ions made up of the *principal* isotopes of atoms making up the original molecule.”^{9–13} The latter definition, however, is problematic also: even after disregarding that a mass spectrum is in fact a display of peaks, not ions, the IUPAC Gold Book “monoisotopic mass spectrum” definition implies that such a spectrum shows only the peaks representing ions constituted exclusively of the most abundant isotopes of the analyte, a spectrum practically impossible to generate directly in practice. At an early stage, Beynon did recognize that the use of the “monoisotopic mass spectrum” for isotopically enriched samples is problematic and recommended the term *principal* ion to be defined as a molecular or fragment ion made up of the most abundant isotopes of each of its atomic constituents.¹³ Thus, a monoisotopic mass spectrum is a spectrum containing only principal ions. However, principal ion is also a loose term, which leads to confusion.

The term “monoisotopic” is in fact self-contradictory when it refers to an element with a single (natural) nuclide because the prefix “mono” in Greek stands for “alone,” “only,” “sole,” and “single.” Thus, to speak of isotopes, as of twins, we need the existence of at least two nuclides.

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METHODS

The ultra-high-resolution mass spectrum of methionine was recorded on a Thermo Scientific Orbitrap Exploris 480 mass spectrometer (Thermo Fisher Scientific, Bremen, Germany). Data were acquired in positive ionization mode using a heated electrospray-ionization probe and external calibration (without a lock mass). Spectra were recorded in full-MS mode at scan range m/z 70–400, AGC = 100%, mild trapping, and mass resolution setting of 480,000. Methionine standard sample [Sigma-Aldrich Chemical Co. (St. Louis, MO)] dissolved in 10% acetonitrile/water (10 $\mu\text{g/mL}$) was infused at a flow rate of 10 $\mu\text{L/min}$ into an HPLC solvent stream (300 $\mu\text{L min}^{-1}$, solvent $\text{H}_2\text{O/ACN/formic acid}$ 90:10:0.09).

Isotopologue envelope simulations and exact-mass calculations for isotopologues were performed on the web-based isotope pattern calculator enviPat Web 2.4 (<https://www.envipat.eawag.ch>, last accessed 2021-03-09), at resolution setting 100,000 and isotope threshold 0.01, using the Elite_R240000@400 machine setting.

RESULTS AND DISCUSSION

First, we must ask ourselves whether a polyatomic molecule should in fact be referred to as monoisotopic at all. Molecules such as P_4 can indeed be called monoisotopic because phosphorus has only one naturally occurring nuclide (^{31}P), which constitutes all allotropes of the element. According to the guidelines provided by the Commission on Atomic Weights and Isotopic Abundances (CAWIA), an element is considered to be monoisotopic if it has one, and only one, isotope that is either stable or has a half-life greater than 1×10^{10} a (in passim, note that at times, the term “mononuclidic” has been used as a synonym for “monoisotopic”; we tend to agree strongly with the usage of the first over the second when single atoms or chemical elements in general are discussed because of the inherent contradiction lying in “monoisotopic” that we pointed out above).¹⁴ Thus, it is also acceptable to call $^{127}\text{I}_3^-$ or $^{79}\text{Au}_4^+$ monoisotopic ions. (N. B. Per CAWIA recommendations, bismuth and thorium would be termed monoisotopic [mononuclidic], because the half-lives of their sole naturally occurring nuclides ^{232}Th and ^{209}Bi are 1.4×10^{10} a and 1.9×10^{19} a, respectively, whereas ^{231}Pa , having a half-life of 32,760 a, would not be monoisotopic;¹² none of the three, or their compounds, could be monoisotopic by the “naturally occurring stable isotope” definition.)^{4–6} However, is it acceptable or logical to call $^{12}\text{H}_2^{16}\text{O}$, composed of a combination of isotopes of two elements, a monoisotopic molecule, whether its constituent nuclides are the most abundant isotopes or not? What does the “mono” stand for when a molecule is composed of more than one nuclide?

Second, at a very early stage, Yerger et al. did coin the term “monoisotopic mass” to designate the mass of the “molecular ion”, which is composed of the most abundant isotopes of the constituent elements.¹⁵ Although instruments with reasonable resolving power have been available since the 1930s,¹⁶ generally to assign molecular formulas to ions formed from small organic molecules, the most intense peak had to be resorted to, no matter whether it represented a homogeneous species with the most abundant isotopes. This was necessary because the peaks, e.g., for many organic analytes that represented the so-called $M + 1$ and $M + 2$ ions were composites of two or more isotopologues that could not be easily resolved to homogeneous signals with most instruments

available at that time. Thus, pivoting to a specific ion for the specific purpose of chemical formula determination historically made sense. However, with the advent of modern ultra-high-resolution mass spectrometry, most isotopologues (for small- to medium-sized molecules) can now be resolved to represent only one chemical formula.^{17,18} Consequently, the mass and the molecular formula of each individual ion can now be determined accurately. For example, the electrospray-ionization mass spectrum of protonated methionine shows several peaks for its isotopologues (Figure 1). The peak at m/z 150 in

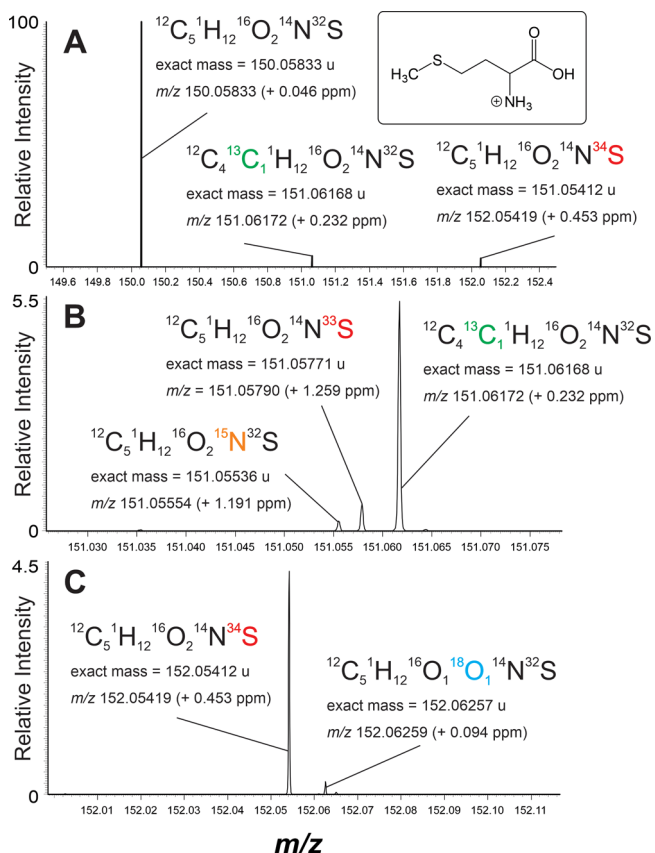


Figure 1. Mass resolution and accurate-mass determination of protonated methionine recorded on a Thermo Scientific Orbitrap Exploris Hybrid Quadrupole-Orbitrap mass spectrometer at the 480,000-resolution setting. The resolving power manifested at m/z 150 was about 550,000. (A) An expansion of the m/z 149.5–152.5 region. (B) An expansion of the m/z 151.025–151.080 section of the spectrum displaying resolved isotopologues $^{12}\text{C}_5^1\text{H}_{12}^{16}\text{O}_2^{14}\text{N}^{32}\text{S}$, $^{12}\text{C}_5^1\text{H}_{12}^{16}\text{O}_2^{14}\text{N}^{33}\text{S}$, and $^{12}\text{C}_4^{13}\text{C}_1^1\text{H}_{12}^{16}\text{O}_2^{14}\text{N}^{32}\text{S}$. (C) An expansion of the m/z 152.00–152.12 section of the spectrum displaying resolved isotopologues $^{12}\text{C}_5^1\text{H}_{12}^{16}\text{O}_2^{14}\text{N}^{34}\text{S}$ and $^{12}\text{C}_5^1\text{H}_{12}^{16}\text{O}_1^{18}\text{O}_1^{14}\text{N}^{32}\text{S}$.

Figure 1 is represented by a single formula, $^{12}\text{C}_5^1\text{H}_{12}^{16}\text{O}_2^{14}\text{N}^{32}\text{S}$. At a resolving power of about 550,000, three significant peaks were observed at m/z 151.05554, 151.05790, and 151.06172 for the m/z 151 isobaric ions (Figure 1B; N. B. a few minor isotopologue peaks such as that for $^{12}\text{C}_5^1\text{H}_{11}^2\text{H}_1^{16}\text{O}_2^{14}\text{N}^{32}\text{S}$ (m/z 151.0644) are also present but have not been labeled for clarity). Based on these accurate masses, the above-mentioned three peaks were attributed to the $^{12}\text{C}_5^1\text{H}_{12}^{16}\text{O}_2^{15}\text{N}^{32}\text{S}$, $^{12}\text{C}_5^1\text{H}_{12}^{16}\text{O}_2^{14}\text{N}^{33}\text{S}$, and $^{12}\text{C}_4^{13}\text{C}_1^1\text{H}_{12}^{16}\text{O}_2^{14}\text{N}^{32}\text{S}$ isotopologues, respectively. Analogously, the peaks at m/z 152.05419 and 152.06259 were recognized as those for $^{12}\text{C}_5^1\text{H}_{12}^{16}\text{O}_2^{14}\text{N}^{34}\text{S}$ and

$^{12}\text{C}_5^{1}\text{H}_{12}^{16}\text{O}_1^{18}\text{O}_1^{14}\text{N}^{32}\text{S}$ isotopologues, respectively. In our opinion, these examples demonstrate that with ultra-high-resolution instrumentation, targeting only the so-called “monoisotopic ion” in order to determine a molecular formula for a compound that has lost its exclusiveness. The advances in technology now allow most, if not all, isotopologues of small molecules to be clearly resolved and treated as the separate entities that they are.

Third, the “monoisotopic mass” definition was historically practical and convenient when the most common elements in organic chemistry are involved—carbon, hydrogen, oxygen, nitrogen, sulfur, and phosphorus—because they are either mononuclidic or their most abundant isotope is of the lowest mass. Hence, in an isotopologue envelope, the “monoisotopic peak” would always have the lowest m/z value. But it does not seem practical in modern times to advocate the continuing use of this term. In fact, even Yergey et al. demonstrated that a monoisotopic ion thus defined would not be representative of large molecules because, using the example of polystyrene, “...monoisotopic mass is no longer the most abundant mass and may not, in fact, be visible in the spectrum because of its low probability of occurrence, 0.09% relative to the most abundant ions...”¹⁵ A simulated spectrum for a decaprotonated dimer of human insulin [$\text{C}_{514}\text{H}_{766}\text{N}_{130}\text{O}_{154}\text{S}_{12} + 10\text{H}$] $^{10+}$ shown in Figure 2 demonstrates this. The tendency for the

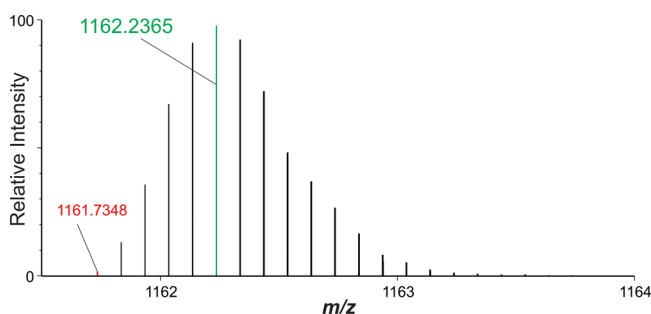


Figure 2. Simulated mass spectrum of decaprotonated dimer of human insulin [$\text{C}_{514}\text{H}_{766}\text{N}_{130}\text{O}_{154}\text{S}_{12} + 10\text{H}$] $^{10+}$. The so-called *monoisotopic* peak is shown in red (m/z 1161.7348), and the base peak for the most abundant (unresolved) isobaric isotopologue group is shown in green (m/z 1162.2365).

monoisotopic peak to decrease in significance is manifested with increasing analyte mass, and, as Gross has stated, “If the isotopic distribution is very broad and/or there are elements encountered that have a lowest mass isotope of very low abundance, recognition of the monoisotopic peak would become rather uncertain.”¹⁹

Even for certain small organic molecules with a high number of polyisotopic constituent elements, the isotopologue of the lowest mass may not be the most abundant. For example, in the simulated spectrum of decachlorobiphenyl molecular ion [$\text{C}_{12}\text{Cl}_{10}$] $^{+}$, the monoisotopic peak is the fifth most intense peak in the spectrum (Figure 3).

As another example, we considered compounds composed of elements with several isotopes whose most abundant members are not the lightest. We present a simulated mass spectrum of the radical-cation of palladium(π -cinnamyl) chloride dimer $\text{C}_{18}\text{H}_{18}\text{Pd}_2\text{Cl}_2$, a.k.a. (bis[cinnamyl palladium-(II) chloride]), a widely used organometallic catalyst (Figure 4). It is a compound consisting of about 250 isotopologues (as reported in the simulated spectrum). According to the current

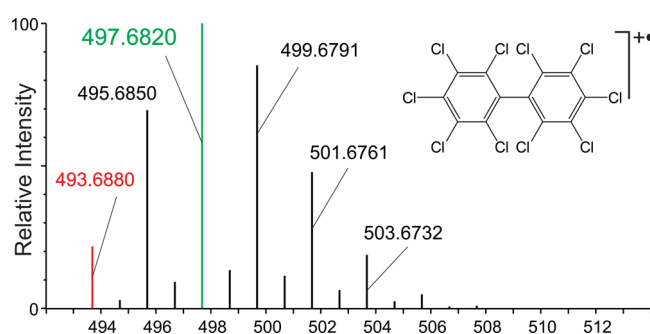


Figure 3. Simulated positive-ion mass spectrum of decachlorobiphenyl radical-cation [$\text{C}_{12}\text{Cl}_{10}$] $^{+}$. The so-called *monoisotopic* peak is shown in red (m/z 493.6880), and the base peak is shown in green (m/z 497.6820).

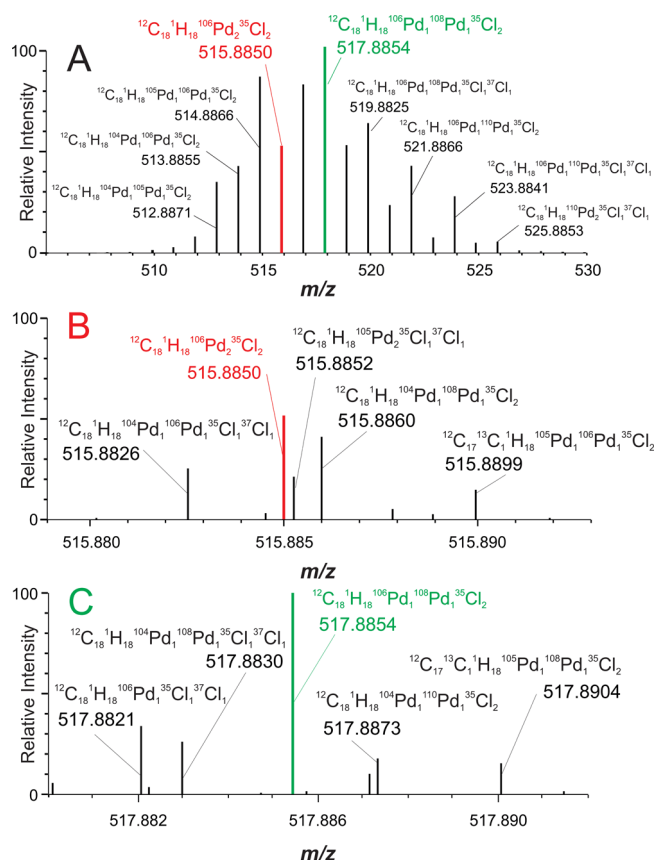


Figure 4. Simulated positive-ion mass spectrum of [$\text{C}_{18}\text{H}_{18}\text{Pd}_2\text{Cl}_2$] $^{+}$. (A); expansion of the “monoisotopic mass” region, m/z 515.879–515.893 (B); expansion of the m/z 517.880–517.892 section of the spectrum around the most abundant isotopologue (C).

definition, out of the 250 candidates, the [$^{12}\text{C}_{18}^{1}\text{H}_{18}^{106}\text{Pd}_2^{35}\text{Cl}_2$] $^{+}$ isotopologue (m/z 515.8850) must be termed the monoisotopic species. This ion is neither the most abundant isotopologue (relative intensity 51.64), nor does its integer mass (516 u) correspond to a single isotopologue. The most abundant isotopologue of this compound is the [$^{12}\text{C}_{18}^{1}\text{H}_{18}^{106}\text{Pd}_1^{108}\text{Pd}_1^{35}\text{Cl}_2$] $^{+}$ species (Table S1). Since the integer mass (i.e., the nominal mass after the definition proposed by Attygalle and Pavlov^{20,21}), 516 u, represents about 20 isotopologues (Table S1), labeling one of them as the monoisotopic species is of no practical benefit. As pointed out before, assigning a *monoisotopic* species made

sense and had practical value when it specified a *homogeneous* species. In the palladium(π -cinnamyl) chloride dimer peaks envelope, the peak that represents nominal mass 508 corresponds to an isotopically homogeneous ion ($^{12}\text{C}_{18}^{1}\text{H}_{18}^{102}\text{Pd}_2^{35}\text{Cl}_2$). As shown in Table S1, the 509, 529, and 530 peaks appear to correspond to isotopically homogeneous ions ($^{12}\text{C}_{17}^{13}\text{C}_1^{1}\text{H}_{18}^{102}\text{Pd}_2^{35}\text{Cl}_2$, $^{12}\text{C}_{17}^{13}\text{C}_1^{1}\text{H}_{18}^{110}\text{Pd}_2^{37}\text{Cl}_2$, $^{12}\text{C}_{16}^{13}\text{C}_2^{1}\text{H}_{18}^{110}\text{Pd}_2^{37}\text{Cl}_2$, respectively). However, even these peaks are not homogeneous if the contributions of deuterium isotopologues are included in the computation. Although these ions are not monoisotopic by the current definition, in practice they can still be used to obtain reasonable formulas by accurate-mass measurements because the interference from deuterium isotopologues is negligibly small (Table S1). Clearly, if several isotopic isobars share the same nominal mass, instruments with ultrahigh resolving power are needed to determine accurate masses and assign formulas to each isobaric species. Thus, calling one member of these isobaric mixtures by a unique name is redundant.

For easy reference, we present a list of our proposed changes to relevant terminology, as discussed above, in a format closely following that of IUPAC entries. Terms we propose to be avoided are marked with an asterisk (*). New definitions and statements we ourselves propose are marked herein with a double asterisk (**).

■ PROPOSITIONS FOR RELEVANT TERMINOLOGY

Exact Mass. Calculated mass of an ion or molecule with specified isotopic composition.^{2,22}

**Note 1: This term should be applied uniformly to all *isotopologues*.

Note 2: The current definition is retained.

Isotopically Enriched Ion. Ion enriched in an isotope in which the abundance of the particular nuclide is increased above the abundance at which it occurs in a reference, usually a naturally occurring sample.^{2,9,10,23}

Note: The current definition is retained.

***Isotopically Homogeneous Species. *Isotopically Pure Species.** Neutral or charged chemical species made up of a specific set of isotopes of the constituent chemical elements (not formally defined in the “Gold Book”¹⁰).

**Note 1: Only species such as $^{31}\text{P}_4$ or $^{31}\text{P}_4^{\bullet-}$ can be properly termed monoisotopic.

**Note 2: The definition is implied from common usage; the terms are not formally defined by IUPAC.^{2,10}

**Note 3: Both terms to be superseded by *isotopolog-(ue)*.

***Isotopic Ion.** Any ion containing one or more of the less abundant naturally occurring isotopes of the elements that make up its structure, e.g., CH_2D^+ .¹¹

**Note 1: The term is not warranted, and it is to be deprecated.

***Isotopic Molecular Ion.** *Molecular ion* containing one or more of the less abundant naturally occurring isotopes of the atoms that make up the molecular structure. Thus, for ethyl bromide there exist isotopic molecular ions such as $^{13}\text{CCH}_3\text{Br}^+$, $\text{C}_2\text{H}_4\text{DBr}^+$, $\text{C}_2\text{H}_5^{81}\text{Br}^+$, $^{13}\text{C}_2\text{H}_5^{81}\text{Br}^+$, etc.^{9,11}

**Note 1: The term is not warranted, and it is to be deprecated. See *molecular ion*.

Isotopolog(ue). A molecular entity that differs only in isotopic composition (number of isotopic substitutions), e.g., CH_4 , CH_3D , CH_2D_2 .¹⁰

Deprecated: isotopically homogeneous/pure species, isotopic molecular ion.

Note: The current definition is retained.

Isotopolog(ue) Ions. Ions that differ only in the isotopic composition of one or more of the constituent atoms.^{2,10}

Note 1: For example, CH_4^+ and CH_3D^+ or $^{10}\text{BF}_3^+$ and $^{11}\text{BF}_3^+$, or the ions forming an isotope cluster corresponding to the natural isotopic abundances of the constituent atoms.

Note 2: Isotopolog is an abbreviation of isotopic homologue.

Note 3: The current definition is retained.

****Isotopolog(ue) mass.** Exact mass of an *isotopolog(ue)*.

Deprecated: monoisotopic mass.

**Note 1: The term is currently not defined as a distinct entity by IUPAC.^{2,10}

**Note 2: The definition is proposed herein.

**Note 3: Supersedes *monoisotopic mass*.

Molecular Ion. Ion formed by the removal of one or more electrons from a molecule to form a positive ion or the addition of one or more electrons to a molecule to form a negative ion.²

**Deprecated: isotopic molecular ion.

**Note 1: To be applied equally to possible *isotopologues* constituting molecular ion clusters, with specification of *isotopologue* composition. All *isotopologues* produce their respective molecular ions. For example, $^{31}\text{P}^{\bullet-}$ has only one molecular ion but Br^+ has three molecular ions.

**Note 2: All *isotopologues* can produce molecular ions, and the term should not be constrained only to denote a molecular ion made of the most abundant isotopes of the constituent atoms.

***Monoisotopic.** [The term is not formally defined by IUPAC as a standalone entity.]^{2,10}

**Note 1: Deprecated.

**Note 2: Only a few polyatomic species such as $^{31}\text{P}_4$ can be considered to be monoisotopic.

***Monoisotopic Element.** Element that has one and only one isotope that is either stable or has a half-life greater than 1×10^{10} a.¹²

Note 1: At various times, the term “mononuclidic” has been used synonymously with “monoisotopic”; similarly, radioactive isotopes have been referred to as “radio-nuclides” or “radioisotopes”. Thus, CAWIA considers Th to be monoisotopic because ^{232}Th has a half-life of 1.4×10^{10} a, and the half-lives of the other isotopes of Th are all less than 1×10^{10} a. In contrast, Pa is not classified as a monoisotopic element because the half-life of the most abundant isotope ^{231}Pa is only $3.25(1) \times 10^4$ a.¹²

**Note 2: The term is deprecated and is to be superseded by *mononuclidic element*. Technically, the prefix “mono” becomes redundant if an element is composed only of one nuclide; “mono” and “iso” are furthermore mutually exclusive in this case.

****Monoisotopic Ion.** Ion constituted of one isotope; e.g., $^{31}\text{P}^{\bullet}$ or $^{197}\text{Au}_3^-$.

Note 1: Although not constituted of the most abundant isotope (^{35}Cl), $^{37}\text{Cl}^{\bullet}$ is a monoisotopic ion.

Note 2: *Monoisotopic* is deprecated; only a few polyatomic species such as $^{31}\text{P}_4$ can properly be considered to be monoisotopic.

Note 3: *Monoisotopic mass spectrum* is deprecated; a mass spectrum is a display of peaks, not ions. A peak can be assigned to an ion that could be monoisotopic. But the peak or the spectrum itself should not be called monoisotopic.⁹

**Note 4: The term is currently not defined as a distinct entity by IUPAC.^{2,10}

**Note 5: The definition is proposed herein.

***Monoisotopic Mass.** Exact mass of an ion or molecule calculated using the mass of the most abundant isotope of each element.²

**Note: Deprecated; obsolete. To be superseded by *isotopologue mass* applied uniformly to every species constituting an isotopologue envelope. According to the proposed amendment, a mass can be assigned to any species defined by a chemical formula.

***Monoisotopic Mass Spectrum.** Mass spectrum containing only ions made up of the *principal isotopes* of atoms making up the original molecule.^{2,9,10}

**Note: Deprecated; obsolete. A mass spectrum is a display of peaks, not ions. A peak can be assigned to an ion that could be monoisotopic. But the peak or the spectrum itself should not be called monoisotopic.

***Monoisotopic Peak.** [The term is not formally defined by IUPAC.]^{2,10}

**Note 1: Monoisotopic peak is understood to denote the peak corresponding to the *principal ion* in an isotopic cluster.

**Note 2: Deprecated. To be superseded by *most intense peak* within an isotopic cluster of peaks. The proposed substitution is visually unambiguous and axiomatically self-evident.

***Monoisotopic Species.** [The term is not formally defined by IUPAC.]^{2,10}

**Note 1: A neutral or charged chemical species made up of the most abundant isotopes of the constituent chemical elements is generally viewed as the monoisotopic species.

**Note 2: Deprecated. To be superseded by *isotopolog(ue)*.

**Note 3: Only a very limited number of species such as $^{31}\text{P}_4$ or $^{31}\text{P}_4^{\bullet}$ can be considered monoisotopic.

****Mononuclidic Element.** Element that has one and only one natural nuclide that is either stable or has a half-life greater than 1×10^{10} a.¹²

Deprecated: monoisotopic element.

**Note: To supersede *monoisotopic element*.

***Principal Ion.** 1. Most abundant ion of an isotope cluster.²

2. A molecular or fragment ion which is made up of the most abundant isotopes of each of its atomic constituents. In the case of compounds that have been artificially [sic] isotopically enriched in one or more positions such as $\text{CH}_3^{13}\text{CH}_3$ or

CH_2D_2 the principal ion may be defined by treating the heavy isotopes as new atomic species. Thus, in the above two examples, the principal ions would be of masses 31 and 18, respectively.^{9,11}

**Note 1: Deprecated. To be superseded by *most abundant isotopologue* (with additional specification whether in a spectrum or a given isotopologue envelope, regardless of isotope enrichment).

**Note 2: According to the current definition, each molecule has only one *molecular ion*. Thus, it is ambiguous to say “isotopologue molecular ions”.

**Note 3: The attempt to introduce the term *principal ion* for isotopically enriched samples leads to additional complications. If an enriched sample generates a spectrum with two peaks of equal intensity, the distinction becomes problematic.

***Principal isotope.** [The term is not formally defined by IUPAC.]^{2,10}

**Note: Deprecated. To be replaced by the axiomatic term *most abundant isotope*.

Because we have followed the IUPAC definitions format as closely as necessary for this brief glossary, for the sake of completeness we include three additional entries to substitute other, more ambiguous current terms.

Most Abundant Isotope. Isotope of the greatest abundance.

Deprecated: principal isotope.

**Note 1: Supersedes *principal isotope*.

Most Abundant Isotopolog(ue). *Isotopolog(ue)* of the greatest abundance in an isotope cluster.

Deprecated: principal ion.

**Note 1: Supersedes *principal ion*.

Most Intense Peak. Peak of the greatest intensity in an isotopolog cluster or mass spectrum

Deprecated: monoisotopic peak.

**Note 1: Supersedes *monoisotopic peak*.

CONCLUSIONS

Considering all that has been stated above, we propose that we should refrain from using the terms “monoisotopic,” “monoisotopic mass,” and most of their derivatives altogether and instead simply use the exact mass of each individual isotopologue, on an equal footing, to determine its molecular identity (molecular formula) by accurate-mass measurements. The term “monoisotopic mass spectrum” should be used only to refer to the special cases of mass spectra of “true” monoisotopic isotopologues (e.g., $^{31}\text{P}_4^{\bullet}$).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jasms.1c00110>.

Formulas and exact masses of bis[cinnyl palladium(II) chloride] radical-cation isotopologues (Table S1) (PDF)

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<https://pubs.acs.org/10.1021/jasms.1c00110>

Notes

The authors declare no competing financial interest.

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