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A highly charged topic

Philip Lössl tells of mass spectrometry's struggles to come to terms with terminology.

When Joseph John Thomson (pictured) wrote the final sentences of his book, *Rays of Positive Electricity and Their Application to Chemical Analysis,* one detects a sense of pride: "The positive rays thus seem to promise to furnish a method of investigating the structure of the molecule, a subject certainly of no less importance than that of the structure of the atom"[1].

Indeed, after discovering the electron in his cathode ray experiments, Thomson's work with positive rays allowed him, for example, to determine the mass-to-charge ratios of hydrogen and helium, and detect stable isotopes of neon[2]. Despite his pride and optimism, Thomson likely did not foresee that the analytical discipline he founded — mass spectrometry — would become a widespread method used in physical, chemical, biological and even medical research. And he surely would not have predicted that — more than 120 years after his first experiments — the terms and units used to report mass spectrometric results would still be under debate.

Considering that mass spectrometry measures mass-to-charge ratios, one might expect it to report measurements of m/e in the combined SI unit kg C^{-1}. Indeed, the IUPAC Analytical Chemistry division mentions kg C^{-1} in their recommendations[3] but explicitly links it to the term "ratio of mass to charge". In contrast, the mass-to-charge ratio should be considered a dimensionless quantity and always be abbreviated as m/z, representing "the ratio of the mass of an ion to the unified atomic mass unit" (m) divided by the charge number z.

One can imagine these definitions causing confusion, not least because m is the SI-recommended symbol for mass and the elementary charge e is much more common than the charge number z. To add to the unit tangle, mass spectrometrists traditionally express masses in units of the Dalton (Da) or unified atomic mass unit (u). As such, it is unsurprising that mass-spectrometric nomenclature is a somewhat wayward field. While most data are reported using the dimensionless quantity m/z, one will also find mass spectra labelled with m/e, u/z and

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even Da, u, or atomic mass units (amu)[4], and hear people referring to the measured mass-to-charge ratio simply as mass measurement. Until the 1980s, the incoherent use of mass terminology and units to discuss mass-to-charge ratios was often based on the implicit assumption that the detected ions will almost always be singly charged[5], making the m/z scale highly similar to the mass scale.

This hand-wavy justification became invalid with the emergence of electrospray ionization (ESI), which allows ionizing large polymers and even intact proteins[6]. ESI nowadays is one of the most widely used ionization methods, particularly in biological mass spectrometry where it has become the mainstay for protein analysis. One peculiarity of ESI mass spectrometry is that macromolecules are detected as a series of multiply charged ion species. Consequently, m/z and mass scales become very different, with the m/z value of a, say, ten-fold charged species being just about one tenth of the species' mass.

To end the confusion about the units, it seemed appropriate to invoke the name of mass spectrometry's founding father. Shortly after the first reports of ESI mass spectra of multiply charged ions, the Thomson (Th) was proposed as the unit for mass-to-charge ratio with the mass given in u and using the charge number z (ref. [5]). According to this definition, z — and thus the value in Th — could be positive or negative, depending on whether cations or anions were measured. Unfortunately, the career of Thomson the unit was far less successful than that of Thomson the physicist. Although adopted in some standard works[7], the Thomson never earned community-wide acceptance. IUPAC now advises against using the Thomson[3], adding it to the lengthening list of controversial terms in mass spectrometry.

Mass spectrometry has not been gentle to its controversial expressions; some have even been put in the realm of Lewis Carroll's Humpty Dumpty, where a word "means just what I choose it to mean — neither more nor less"[8,9]. But this categorization would seem unfair toward the Thomson, which in principle offers a workable solution to report m/z values and distinguish cations from anions. Some mass spectrometrists are still reporting their m/z values in Th and will likely continue to do so. However, as mass spectrometry is becoming an increasingly popular method in many areas of science, and a fully coherent terminology is not in sight, the field might just as well take a leaf out of Humpty Dumpty's book and make extra sure to define their terms and units for non-specialists, because "of course you don't [know] — till I tell you"[9]. ❐

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