massXpert 2: a cross-platform software environment for polymer chemistry modelling and simulation/analysis of mass spectrometric data

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SUMMARY
Since the middle of the 90s, mass spectrometry has evolved into an almost indispensable tool in structural studies on an ever-growing variety of (bio-)polymers, of which proteins, sugars and nucleic acids are the most prominent. Since the first public release of massXpert, the advances of mass spectrometry have motivated continuous and thorough maintenance of that software, in the form of two full software rewrites, culminating with massXpert 2, which we describe in this report. We shall describe the profound changes in mass spectrometry that were performed so as to keep up with the technical advances in mass spectrometry since a decade.

Availability: The massXpert 2 software is an open source and free software project hosted at http://www.massxpert.org.

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Supplementary information: Supplementary data are available at Bioinformatics online.

ABSTRACT

Summary: Since the middle of the 90s, mass spectrometry has evolved into an almost indispensable tool in structural studies on an ever-growing variety of (bio-)polymers, of which proteins, sugars and nucleic acids are the most prominent. Since the first public release of massXpert, the advances of mass spectrometry have motivated continuous and thorough maintenance of that software, in the form of two full software rewrites, culminating with massXpert 2, which we describe in this report. We shall describe the profound changes in mass spectrometry that were performed so as to keep up with the technical advances in mass spectrometry since a decade.

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1 INTRODUCTION

Since the introduction of large biopolymer analysis with soft ionization techniques, mass spectrometry as a whole has become a powerful combination of instrumentations, techniques and methodologies. Advances in each of these fields as well as in sample preparation methodologies have widened the scope of mass spectrometry from its main application field—biopolymer structure characterization—to other scientific areas, like cell science. We have witnessed these advances and practised them to some extent: our software development had to adapt to the new requirements set forward either by our own experiments, our collaborators, or according to feature requests by massXpert users [for a general account of mass spectrometry software, see Matthiesen (2008)]. In this report, we will review the main feature changes brought to massXpert 1 over a decade of development to ultimately yield massXpert 2, and relate these changes to the relevant technical evolutions in the field of mass spectrometry.

2 IMPLEMENTATION

2.1 Methods

The development of massXpert 2 was performed using the well-known cross-platform open source free software Qt libraries from Nokia (C++ language; software freely available at http://www.qtsoftware.com).

massXpert 2 was developed as an integrated environment in which four functional modules inter-relate: XpertDef for polymer chemistry modelling; XpertCalc for programmable desktop calculator-based calculations; XpertEdit for sequence editing and for all the biochemical and mass spectrometric simulations; XpertMiner for \((m/z, z)\) pair list-based data mining.

2.2 Results

2.2.1 Evolving computing landscape massXpert 1 was written at a time when the Microsoft Windows computing platform was overwhelmingly dominant. This domination has reduced since, which motivated the first Linux-based rewrite into GNU polyxmass (Rusconi, 2006 and references therein, for comparisons of program features with other existing software). A second rewrite leveraged on the experience gained during the first one, adding new features and most importantly adding native cross-platform support: massXpert 2 executes natively on all the common computing platforms and, in particular, may execute side by side with the software that drives the mass spectrometer. Indeed, massXpert was designed from the ground up to be used as a decision-making aid that should be harnessed while performing mass data acquisitions.

2.2.2 Increasing diversity of analysed polymers massXpert 1 only dealt with proteins, and almost all its data were internally hard-coded. The ever-increasing variety of polymers being analysed by mass spectrometry prompted us to perform a full software redesign so as to let users define polymer chemistries ex nihilo. The XpertDef module lets the user define any aspect of a polymer chemistry, from atoms through monomers and chemical modifications to cleaving agents and fragmentation patterns. massXpert 2 is shipped with definitions for proteins, saccharides and nucleic acids.

2.2.3 Electrospray ionization and multi-charged ions. When massXpert was first developed, MALDI-TOF mass spectrometry was predominant, hence the software only dealt with mono-protonated species. Because electrospray ionization was later widely adopted, massXpert 2 had to provide a way to configure ionization levels for any simulation. This new feature was considered essential, as GNU polyxmass and massXpert 1 were of almost no use in an

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electrospray ionization context, which is characterized by multi-charged ions.

2.2.4 \( (m/z,z) \) pair list-based data mining. The XpertMiner module features the ability to import mass data from outside massXpert 2, typically from the mass spectrometer data acquisition software, from spectrum display/analysis tools like mMass (Strohalm et al., 2008) or from databases. The imported datasets translate into \( (m/z,z) \) pair lists which are available for automated comparison with similarly created lists from massXpert 2-based simulations. Lists can be manipulated according to arbitrary parameters (add/remove masses or formulas, for example), and then used for peak-matching work with a configurable tolerance. Handling \( (m/z,z) \) pairs instead of \( m/z \) single values makes the whole data-mining process charge independent, which is essential with arbitrarily charged ions. The XpertMiner module is operated using simple drag-and-drop and copy/paste clipboard paradigms.

2.2.5 A completely new cross-link simulation framework. The new cross-link framework designed in massXpert 2 allows any number of cross-links to be set to a polymer sequence. For example, the Kunitz (1945) inhibitor—with its seven disulfide bonds—can be easily modelled. Figure 1 shows the Kunitz inhibitor loaded in the sequence editor with cross-linked cysteinyl residues displayed with the chromophore would involve specifying their positions as the ‘65:66:67’ list. Polymer sequence cleavage supports cross-links, even with partial cleavages.

2.2.6 Refactored chemical modification framework. A lot of progress has been made in the characterization of biopolymer chemical modifications and some modifications were found to be much more frequent and relevant than initially thought (methylation is a very important protein and DNA chemical modification). These advances prompted inclusion in massXpert 2 of a number of compelling improvements in its chemical modification framework, like being able to modify a given monomer in the sequence with any number of same or different modifications. Note that provisions set in the polymer chemistry definition ensure that the user does not inadvertently perform unrealistic simulations.

3 CONCLUSION

massXpert 1 was developed during the late 90s. Ten years of development and two rewrites later, massXpert 2 brings the improvements required by the evolution of mass spectrometric techniques. The most salient improvements are (i) the fact that scientists can model new polymer chemistries, which are then made available to the other modules in the software framework; (ii) a powerful cross-link framework allows the simulation of the most complicated situations; (iii) the sequence editor has new capabilities such as multi-region selections; (iv) a redesigned chemical modification framework ensures enough simulation flexibility for the most complex cases; (v) pervasive handling of multi-charged ions makes simulations more closely and reliably fit mass spectrometric experimental data; (vi) the data-mining module allows thorough comparisons of mass peak lists. Also of importance is the fact that the software is cross-platform and that a detailed (200 pp approximately) user manual in PDF format is available (see Supplementary information).

Finally, while massXpert 1 was released as proprietary no-cost software, the massXpert 2 software package is released under an open source free software license (GPLv3) so as to encourage collaborative development starting from current source code.

Conflict of Interest: none declared.

REFERENCES


