Gene expression

SanXoT: a modular and versatile package for the quantitative analysis of high-throughput proteomics experiments

Marco Trevisan-Herraz 1,2, Navratan Bagwan 1, Fernando García-Marqués 1,2, Jose Manuel Rodríguez 1, Inmaculada Jorge 1,2, Lakes Ezekurdia 1,2, Elena Bonzon-Kulichenko 1,2,*† and Jesús Vázquez 1,2,*†

1Vascular Pathophysiology Area, Cardiovascular Proteomics Laboratory, Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Madrid 28029, Spain and 2Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain

*To whom correspondence should be addressed.
†The authors wish it to be known that, in their opinion, the last two authors should be regarded as Joint Last Authors.

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Abstract

Summary: Mass spectrometry-based proteomics has had a formidable development in recent years, increasing the amount of data handled and the complexity of the statistical resources needed. Here we present SanXoT, an open-source, standalone software package for the statistical analysis of high-throughput, quantitative proteomics experiments. SanXoT is based on our previously developed weighted spectrum, peptide and protein statistical model and has been specifically designed to be modular, scalable and user-configurable. SanXoT allows limitless workflows that adapt to most experimental setups, including quantitative protein analysis in multiple experiments, systems biology, quantification of post-translational modifications and comparison and merging of experimental data from technical or biological replicates.

Availability and implementation: Download links for the SanXoT Software Package, source code and documentation are available at https://wikis.cnic.es/proteomica/index.php/SSP.

Contact: jvazquez@cnic.es or ebonzon@cnic.es

Supplementary information: Supplementary information is available at Bioinformatics online.

1 Introduction

Current high-throughput quantitative proteomics presents many bioinformatic challenges, especially in the case of stable isotope-based techniques. Several of these problems have been highlighted in the literature, such as the problem of undersampling (Nilsson et al., 2010), the need for a null hypothesis (Arntzen et al., 2011; Karp et al., 2010; Lin et al., 2006), the proteome dynamic range (Zubarev, 2013), the non-normality of protein abundance change distributions (Karp et al., 2010) and the need for quality control measures. Most of these issues were addressed by the weighted spectrum, peptide and protein (WSPP) statistical model (Bonzon-Kulichenko et al., 2011a; García-Marqués et al., 2016; Jorge et al., 2014; Navarro et al., 2014). WSPP models the error structure of the data generated by the mass spectrometer (spectrum level) and integrates the quantitative results into peptide values using weighted averages according to error propagation theory (higher weights are assigned to measurements with lower error). The peptide values are then integrated into protein values and finally the protein values are integrated to determine protein abundance changes. Thus, the data are analysed independently and sequentially at the spectrum, peptide and protein levels and the specific error sources are considered separately, allowing efficient detection of artefacts (Bonzon-Kulichenko et al., 2011a; Bonzon-Kulichenko et al., 2011b; Jorge et al., 2009). The
libraries are also available. Executables for this OS that do not require installation of any further Licence v2.0. It has been extensively tested in Windows, and portable developed in Python, and is publicly available under the Apache modularity, can be used in automated workflows. SanXoT has been applicability of the GIA. SanXoT is very flexible and, thanks to its software package to fully exploit therobustness, versatility and general and different experimental setups. Hence, we developed the SanXoT protein quantitation, able to cope with large number of experiments (García-Marqueś et al., 2014). This was, in turn, possible thanks to the use standardized variables that accurately follow normal distributions in a way unaffected by the undersampling typical of data-independent mass spectrometry approaches.

In addition—thanks to its modular design and the use of plain text files hierarchically structured at each level using relation tables—SanXoT can be easily integrated in other workflows that make use of network analysis or transcriptomics data, or are generated with label-free techniques. SanXoT is currently being adapted for use in parallel with integrated protein identification algorithms, allowing mutual feedback between peptide/protein identification and quantitative information.

4 Conclusion

The successful, extensive use of the SanXoT software package—in preliminary versions—in different biological contexts has demonstrated its utility in exploiting the specific characteristics of the WSPP model for quantitative proteomics analysis (see Refs in Supplementary Material). Perhaps the most notable feature is its robustness, which is mainly a consequence of the use of weighted averages and the estimation of variances from the global distribution of data at each level (Navarro et al., 2014). This was, in turn, possible thanks to the use standardized variables that accurately follow normal distributions in a way unaffected by the undersampling typical of data-independent mass spectrometry approaches.

The WSPP model for quantitative proteomics analysis (see Refs in Supplementary Material) demonstrated its utility in exploiting the specific characteristics of the WSPP model for quantitative proteomics analysis (see Refs in Supplementary Material). Perhaps the most notable feature is its robustness, which is mainly a consequence of the use of weighted averages and the estimation of variances from the global distribution of data at each level (Navarro et al., 2014). This was, in turn, possible thanks to the use standardized variables that accurately follow normal distributions in a way unaffected by the undersampling typical of data-independent mass spectrometry approaches.

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