BIOGNOSYS
NEXT GENERATION PROTEOMICS

APPLICATION NOTE

IMPROVE THE PERFORMANCE OF YOUR PROTEOMICS LC-MS FACILITY WITH QUIC

FEATURES

- An active queue of per-run QC analyses that supports real-time folder monitoring
- A multitude of readouts for main proteomics workflows based on iRT peptides
- For discovery proteomics workflows DIA and DDA a background library can be specified and additionally targeted to better QC the samples and sample processing
- Proper handling of corrupted files and duplicate run checking
- Intuitive visualization and customizable reporting for documentation
- Supports multiple instrument vendors

INTRODUCTION

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Over the last few years, mass spectrometry based proteomics has evolved into an extremely powerful enterprise. In discovery proteomics, using data dependent acquisition (DDA) or data independent acquisition (DIA), thousands of peptides and proteins can be identified in a single measurement.

In a different arena, targeted proteomics methods such as multiple or selected reaction monitoring (SRM/MRM) and parallel reaction monitoring (PRM) are widely used to quantify a few proteins very accurately over a very large sample cohort. Both discovery and targeted workflows rely on the performance of the entire liquid chromatography (LC)-mass spectrometer (MS) performance.

Thus, LC-MS performance has to be closely monitored to ensure high data quality and that the statistical analysis is delivering confident results about biological processes and not instrument performance.

The process of ensuring high data quality through monitoring of the LC-MS performance is called quality control (QC). Apart from ensuring high data quality, QC analysis further helps to increase the instrument up time in a facility between different experiments and is as such crucial to increase the economic aspect of mass spectrometry based analysis.

Therefore, both intra- and inter experimental QC analysis should be performed. As the market of mass spectrometers is heterogeneous and covered by multiple vendors there are no common practices established for QC. Moreover, different operators are measuring different parameters in complicated pipelines of specialized tools.

Therefore, inter- but also intra-laboratory comparisons about the performance of different LC-MS set-ups is not straightforward.

Tool	Interface	Operating System	Experiment Type	LC	MS	ID-free	ID-based
QuaMeter	Command-line	Windows, Linux	DDA	No	No	Yes	Yes
OpenMS	KNIME	Cross-platform	DDA	No	No	Yes	Yes
proteoQC	R	Cross-platform	DDA	No	No	No	Yes
PTXQC	R	Windows, cross-platform	DDA	No	No	No	Yes
SProCoP	Skyline	Windows	SRM&MRM	No	No	Yes	No
SimpatiQCo	Web	Windows	DDA	No	No	Yes	Yes
iMonDB	GUI	Windows	Any	No	Yes	No	No
QuiC	GUI	Windows	Any	Yes	Yes	Yes	Yes

Table 1. Summary of QC Tools. Adopted from (Bittremieux et al.).

Furthermore, mass spectrometry based proteomics consists of many different workflows which are often not analyzed together. This puts additional limitations on the readouts of QC metrics. Further, MS-based proteomics is moving more and more into the clinical and biological lab used as an analytical method, so mass spectrometers are no longer operated exclusively by the mass spectrometer experts. QC analysis must therefore be intuitive and easy to perform.

Lastly, the QC-ing of proteomics experiments should occur across the entire workflow from LC, instrument to the bioinformatics pipeline with ID-free and ID-based read outs. Looking at the currently available QC tools, one observes the only our software, QuiC, fulfills all the necessary requirements (***Table 1***).

QUIC

QuiC is a fast, easy-to-use (and install) QC monitor for any proteomics workflow such as DDA, DIA, SRM/MRM and PRM. QuiC is vendor independent and can thus be used to monitor an entire LC-MS facility within a single running instance of the application. It is developed to help maximize the full potential of any LC-MS facility by facilitating performance increases and up time of your instruments. It also serves as an aid in predicting instrument maintenance times. Using the event tag manager, QuiC records the interventions and maintenance of your LC-MS. QuiC provides readouts for the Mass Spectrometer, Panel Peptides (iRT), General parameters, Identifications and DDA Advanced for DDA-based QC readouts (***Figure 1***).

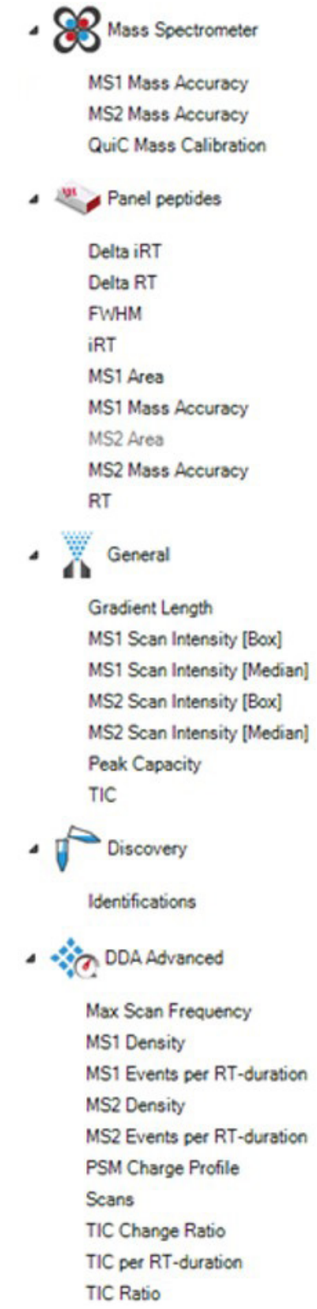

Figure 1: QC Parameters Monitored by QuiC.

DISCUSSION

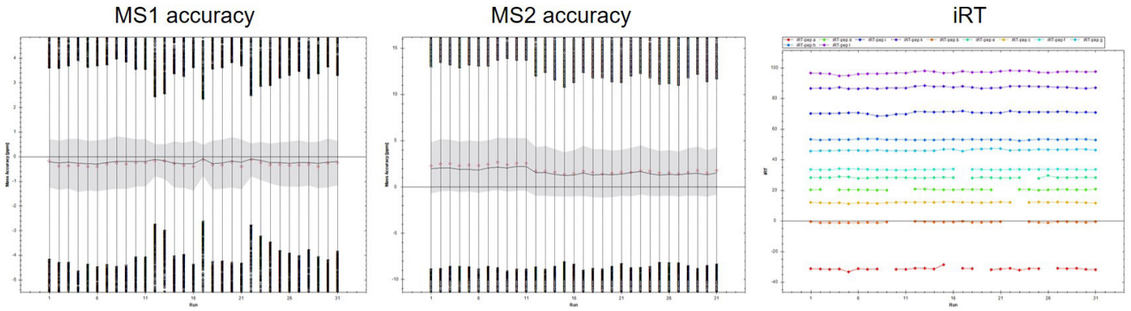

Figure 2: a) MS1 accuracy over the entire experimental set. B) MS2 accuracy over the entire data set c) iRT measurements for all Biognosys iRT peptides over the entire experimental set.

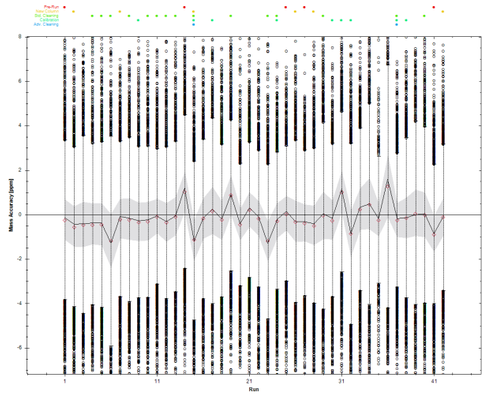

Figure 3: Inter-experimental QC history (Instrument1, Aug-Oct 2017, MS1 Accuracy) with tags to monitor MS performance and intervention events.

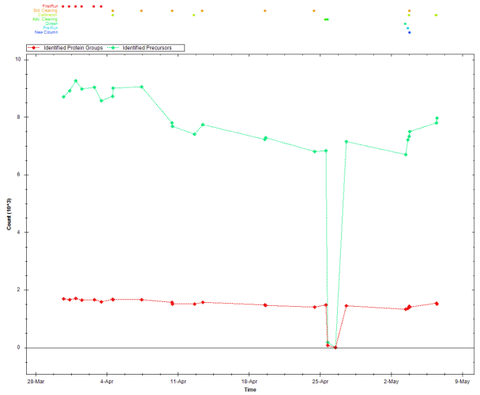

Figure 4: Inter-experimental QC history (Instrument 2, April/May 2017, Identifications) with tags to monitor MS performance and intervention events. Several interventions had to be made to bring the performance back up to an acceptable level.

INTRA-EXPERIMENTAL QC USING QUIC

Generally, intra-experimental QC gives information about the parameters relevant for a single experiment. These readouts can be used to judge the data quality and enable the researcher to exclude data sets from analysis due to bad LC-MS performance. In the experiment here, 30 DDA runs were analyzed using QuiC to see the performance of the LC-MS set up used in this study.

Both, on the MS1 and on the MS2 level the instrument showed excellent performance with no significant deviation of the mass accuracy (***Figure 2a and 2b***). The chromatography also showed good stability. As shotgun mass spectrometry suffers from missing values due to semi-stochastic selection for MS/MS some of the peptides are not identified in all runs. This is slightly more pronounced for the early eluting peptides when the gradient might not be fully established and stable (***Figure 2c***).

On top of instrument wide QC, QuiC also enables the user to look into individual runs. These features can be helpful when deciding about the potential issues a certain run had.

Even tags can be useful to see when changes to the setup have been made. In this case, the entire experiment could be measured with the same set up and without the need for recalibration or other interventions.

INTER-EXPERIMENTAL QC USING QUIC

The mass spectrometer should be analyzed with dedicated QC samples, either between experiments or on regular intervals in order schedule interventions such as transfer capillary exchange, calibration and tuning.

Again, this can help to increase the up time of the LC-MS set up, the ultimate goal of any LC-MS facility manager. Here in particular, the many different features of QuiC are helpful.

The storage of historical data further assists in evaluating current performance and performance evolution over time (***Figure 3***). As the QC samples always have same origin (complex C. elegans lysate with iRT spiked in), the identifications can be used to further monitor LC-MS stability. A continuous drop in identifications can inform the scheduling of interventions by looking at the recent history (***Figure 4***).

Interestingly, the first advanced cleaning did not help but made the issue worse. Only the second cleaning could restore the number of identifications back to the acceptable range and the instrument vendor had to be contacted to perform maintenance, which restored the performance to an acceptable level again.

CONCLUSIONS & REFERENCES

CONCLUSIONS

QuiC is a free, easy-to-use desktop application that provides a suite of proteomics quality control capabilities for scientists and mass spec facility managers. QuiC provides mass spectrometric and chromatographic readouts for all major proteomics workflows.

QuiC is an invaluable tool for tracking performance both over the course of a single experiment, but also across experiments over long periods of time. In the former case, this empowers researchers with the knowledge to determine what runs should be included in the final results and what runs fell below acceptable QC metric thresholds.

In the latter case, facility managers can track and predict instrument failures over medium to long terms to help mitigate wasted time on poor quality runs and to maximize total facility up-time.

REFERENCES

1. Bittremieux W, Tabb DL, Impens F, Staes A, Timmerman E, Martens L, Laukens K. Quality control in mass spectrometry-based proteomics. Mass Spectrom Rev. 2017 Sep 7. doi: 10.1002/mas.21544.

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