Proteome dynamics in vivo from lc-ms and heavy water metabolic labelling.

Chantal Alharbi*

Laboratory of Pharmaceutical Biotechnology, Ghent University, Belgium

Abstract

A dynamic equilibrium between protein synthesis and degradation leads to protein homeostasis. It is crucial for the proper operation of all organs and is frequently linked to illnesses like non-alcoholic fatty liver disease and neurodegenerative diseases. Using liquid chromatography, mass spectrometry, and heavy water metabolic labelling together provides a potent method for studying proteostasis in vivo with high throughput. In time-course investigations, stable isotope incorporation is often estimated using intact peptide signals. The protein decay rate constant is derived from the time-course of label incorporation. A reliable estimate of label incorporation is often provided by intact peptide signals, which are computed from integration in chromatographic time and mass-to-charge ratio domains. The peptide signals could be negatively impacted by sample complexity, a small dynamic range, and a low signal-to-noise ratio, though. By altering peak shape in the chromatographic time and m/z domains, these artefacts make the DRC estimations more difficult. On the other hand, fragment ions are less susceptible to these distortions and may be an excellent tool for supporting DRC estimations. Here, we demonstrate that the isotope enrichment during metabolic labelling with heavy water is reflected in the label incorporation encoded into the isotope distributions of fragment ions. In order to create useful methods for DRC estimations, we investigate the label incorporation statistics.

Keywords: Protein synthesis, Chromatographic, Fragmentations.

Introduction

The cellular proteome is constantly being generated and destroyed, and it is in a state of dynamic equilibrium. The proper operation of cellular proteins depends on protein homeostasis. Examples of transitions to new equilibria include organismal growth, differentiation, and illness [1]. The strong combination of metabolic labelling and LC-MS allows researchers to examine how proteins are used by living things. Modern mass spectrometers have improved in resolution, mass accuracy, sensitivity, and scanning speed, making it possible to study hundreds of proteins at once. Experimentally, deuterium labelling with heavy water is straightforward due to the availability of enhanced water for drinking. The body's water quickly reaches equilibrium throughout. Other metabolic labelling methods can be used to assess the dynamic proteome in vivo. In order to completely label the proteins in the pulse phase and track their elimination in the chase phase, the stable isotope labelling of mammals (SILAM) technique involves metabolic labelling by an essential amino acid. The tagged amino acid diet is pricey, and SILAM depends on a specific amino acid in a peptide to assess its turnover. The provision of labelled diet is another metabolic labelling strategy [2].

The isotope profiles of intact peptides are frequently used in modern bioinformatics approaches to assess proteome dynamics from metabolic labelling. However, co-eluting species and other aberrations might cause the isotope distributions to be distorted. The tandem mass spectra's (MS/MS) fragment ions offer supplementary data on label incorporation and can enhance DRC estimate [3]. The SILT and SRM techniques can only quantify peptides that contain the labelling amino acid since they rely on amino acid-based labelling. The heavy water labelling approach is applicable to a larger population of peptides and labels all non-essential amino acids. By calculating fragment ion abundances from the MS/MS spectra of labelled and unlabelled peptides, SILT measures label incorporation. Peptide fragmentation must occur twice, once for tagged peptide and once for unlabelled peptide. Our method measures the label incorporation from a single MS/MS at each labelling time point. To extract DRCs, the depletion's time-course metabolic labelling dimension is applied. As will be demonstrated further below, data from this approach has problems with spectrum accuracy, changes in isotope distributions of fragment ions, and sensitivity of changes in isotope distributions to the quantity of exchangeable hydrogens in a fragment [4].

***Correspondence to:** Chantal Alharbi, Laboratory of Pharmaceutical Biotechnology, Ghent University, Belgium, E-mail: alharbichantal@gmail.com

***Received:** 04-Nov-2022, Manuscript No. AASBPR-22-81769; **Editor assigned:** 05-Nov-2022, PreQC No. AASBPR-22-81769(PQ); **Reviewed:** 17-Nov-2022, QC No. AASBPR-22-81769; **Revised:** 19-Nov-2022, Manuscript No. AASBPR-22-81769(R); **Published:** 26-Nov-2022, DOI: 10.35841/aasbpr-3.6.127*

***Citation:** Alharbi C. Proteome dynamics in vivo from lc-ms and heavy water metabolic labelling. J Syst Bio Proteome Res. 2022;3(6):127*

We will research experimental and data processing strategies that will address the concerns mentioned above in a subsequent work. In order to obtain quantitative data about the rate constants, we will develop methods of simulating the incorporation of isotopes into fragment ions. The method will be automated so that it may be used with larger datasets and increase the statistical significance of the results. We didn't include MS/MS spectra from precursors that weren't monoisotopic in our investigation. We will examine and model these spectra in a subsequent paper so that they can be used in DRC computations. We will also investigate the impact of MS parameters NCE, number of micro scans for each MS/MS, offset location, and isolation window length on the distributions of fragment ion isotopes [5].

Conclusion

Peak detection and integration in the chromatographic time and domains are required for the quantification of label incorporation from MS scans. In contrast, MS/MS quantitation is less complicated. Additionally, the ion abundances can be averaged or the median value employed, just like in this work, if a peptide has been selected for fragmentation in DDA more than once. Peptides that have been selected for quantification pass a number of filtering requirements throughout the subsequent data processing, such as identifications at various time periods of incorporation with a specific, modest FDR. These parameters lead to the selection of peptides in MS/MS that have numerous fragment ions.

References

1. Baiceanu A, Mesdom P, Lagouge M, et al. Endoplasmic reticulum proteostasis in hepatic steatosis. Nat Rev Endocrinol. 2016;12:710-722.
2. Claydon AJ, Beynon R. Proteome dynamics: Revisiting turnover with a global perspective. Mol Cell Proteomics. 2012;11:1551-1565.
3. Price JC, Holmes WE, Li KW, et al. Measurement of human plasma proteome dynamics with (2)H(2)O and liquid chromatography tandem mass spectrometry. Anal Biochem. 2012;420:73-83.
4. Rauniyar N, McClatchy DB, Yates JR. Stable isotope labeling of mammals (SILAM) for in vivo quantitative proteomic analysis. Methods. 2013;61:260-268.
5. rice JC, Guan S, Burlingame A, et al. Analysis of proteome dynamics in the mouse brain. Proc Natl Acad Sci. 2010;107:14508-14513.

Citation: *Alharbi C. Proteome dynamics in vivo from lc-ms and heavy water metabolic labelling. J Syst Bio Proteome Res. 2022;3(6):127*