Quantum SI - Platinum
The Power of Next-Generation Protein Sequencing

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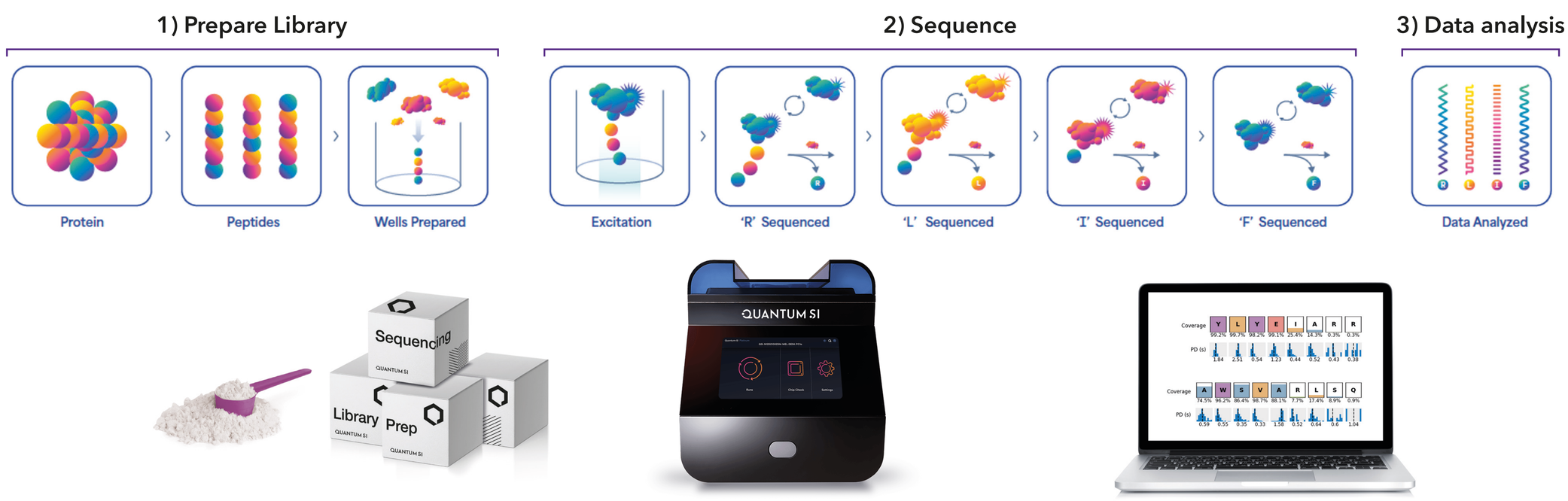
Sequencing proteins and linking amino acid variations to biological function is essential for advancing our understanding of health and disease. Historically, these efforts relied on mass spectrometry, requiring specialized and costly instrumentation. Quantum SI's Platinum system introduces Next-Generation Protein Sequencing (NGPS), offering single-molecule resolution with a streamlined workflow. At the core of this technology are recognizer molecules, which specifically bind peptides, enabling precise protein sequencing on a benchtop platform. This approach eliminates the need for expensive equipment, allowing advanced proteomic analysis in standard laboratory settings. In our study we demonstrate the successful preparation and sequencing of a peptide library from lyophilized BSA (bovine serum albumin), validating Platinum's robust capabilities in protein identification and alignment.

Technology and Method

In the present study, a protein library was prepared from lyophilized bovine serum albumin (BSA) using Quantum-Si's Library Preparation Kit: the input sample consisted of a 5 µM BSA solution in 100 µL. The proteins in the sample were reduced, alkylated, and digested with LysC to generate peptides. These peptides were then functionalized, conjugated, and immobilized onto wells of Quantum-Si's proprietary semiconductor chip. Subsequently, sequencing was performed with Quantum-Si's Sequencing Kit: fluorescently labeled N-terminal amino acid (NAA) recognizers and aminopeptidases were introduced to the chip, where binding events were monitored for fluorescence lifetime, intensity, and kinetic properties. This process generated unique kinetic signatures, which were converted into amino acid calls for peptide and protein identification.
The comprehensive workflow, encompassing library preparation, sequencing, and data analysis via Quantum-Si's Platinum cloud-based software, was successfully completed within a span of two and a half days, showcasing the efficiency of this Next-Generation Protein Sequencing platform.

Workflow



Results

The sequencing run of the prepared protein library achieved a total of 3753 peptide alignments, all of which were aligned with the reference BSA sequence. Among the identified peptides, three sequences (YLY, AWS, TVM) demonstrated false discovery rates (FDR) below 0.1, highlighting the high specificity of the analysis (Fig. 1). The kinetic summary of aligned reads (Fig. 2) illustrates the coverage and unique pulse duration (PD) patterns for each amino acid in the identified peptides. Notably, YLY and AWS exhibited high sequence coverage, while TVM showed lower coverage but retained distinct kinetic signatures. These results confirm the presence of BSA in the sample, underscoring the platform's capacity to deliver high-confidence protein identifications.

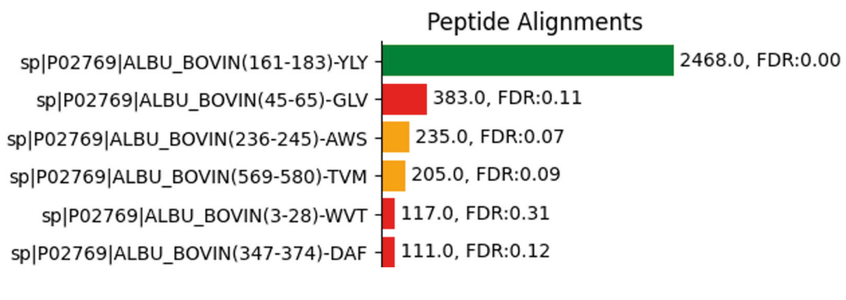


Fig 1. Peptide alignments demonstrate the detection and confidence levels of six peptides from bovine serum albumin (BSA). The YLY peptide achieved the highest alignment count (2468) with an FDR of 0.00, confirming high reliability. Only peptides with the highest number of alignments are shown.

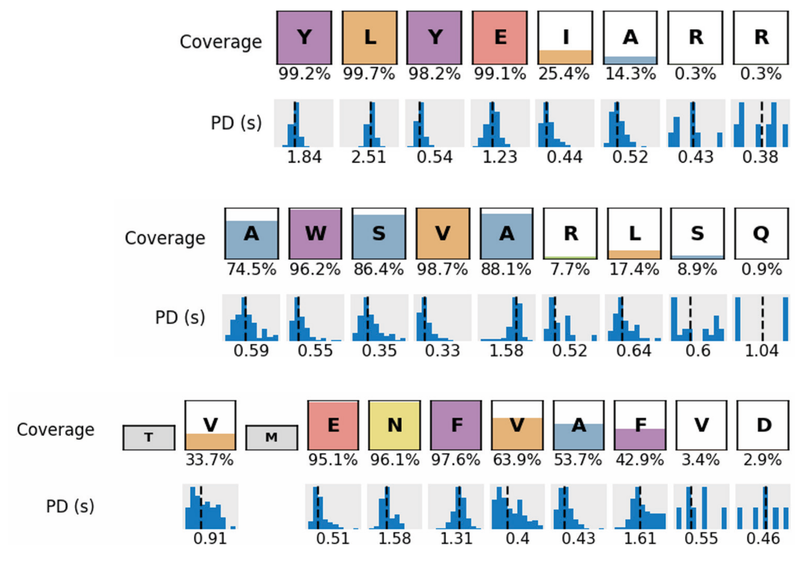


Fig 2. Kinetic summary of aligned reads displays sequence coverage and pulse duration (PD) distributions for each amino acid in identified peptides. The data reveal unique recognition patterns for YLY, AWS, and TVM peptides, reflecting precise amino acid identification.

Conclusion

The findings underscore the capability of Quantum SI's protein sequencing technology to provide detailed insights into bovine serum albumin (BSA), demonstrating its potential to advance proteomics research. Utilizing single-molecule sequencing, the platform achieves exceptional accuracy in peptide alignment and protein quantification. Its flexibility and efficiency make it a valuable tool for diverse applications, including the analysis of proteins in complex mixtures, multiplexed studies using peptide tags, biomarker discovery, investigation of protein variants, antibody characterization (such as glycosylation analysis), and post-translational modification mapping. At GeneTiCA, we are equipped with this cutting-edge technology to support advanced proteomic analyses and can facilitate its integration into laboratory workflows for broader research applications.