Single-molecule protein sequencing on the Quantum-Si platform:
Advances in protein and proteoform identification and comparison with mass spectrometry

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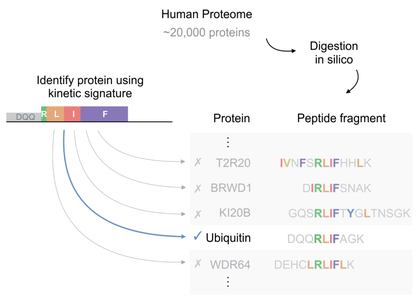
INTRODUCTION

Single-molecule protein sequencing is a transformational tool for protein science that will unlock new insights into the function of proteins in health and disease. Direct sequencing of single protein molecules offers the maximum possible detection sensitivity, with the potential to enable single-cell inputs, digital quantification based on read counts, detection of post-translational modifications (PTMs) and low-abundance or aberrant proteoforms, and cost and throughput levels that favor broad adoption.

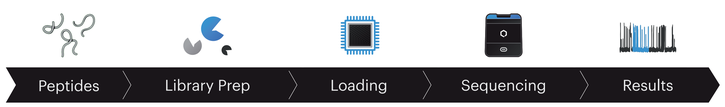
Quantum-Si developed the Platinum™ platform that has a small footprint and low cost with the aim of making protein sequencing accessible to the average research lab.

- Initial applications focus on purified or enriched protein samples and include comparing relative abundance of proteins or proteoforms, affinity reagent validation, discovery of PTMs, and digital barcoding based on peptide sequences.



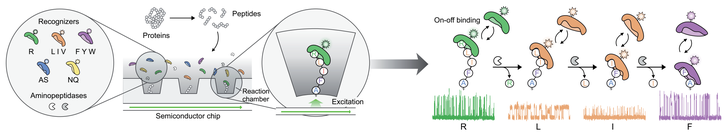
METHODS

- Easy workflow: 3 hours of hands-on work. Automatable.
- Upstream processing is similar to MS -> compatible with most single-cell workflows.



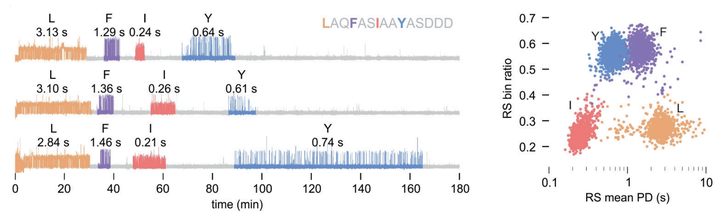
Peptides are conjugated and immobilized on a semiconductor chip

- **Real-time sequencing** is carried out in nanoscale reaction chambers.
- **Recognizers** reversibly bind to exposed N-terminal amino acids (NAAs).
- **Aminopeptidases** sequentially cleave one AA at a time from the N-terminus.
- **Binding kinetics** distinguish NAAs.
- **Fluorescence lifetime** differentiates dye-labeled recognizers.
- **Automated** signal processing and sequencing data analysis.

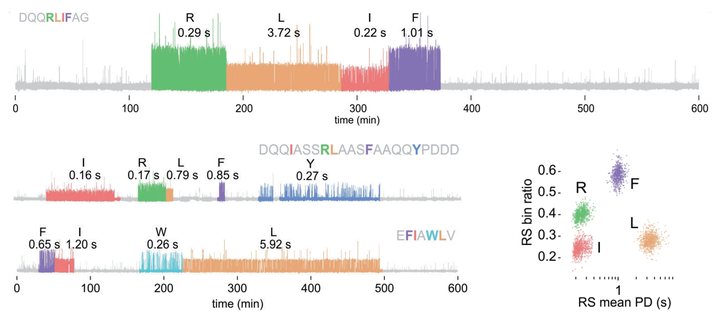


RESULTS AND DISCUSSION

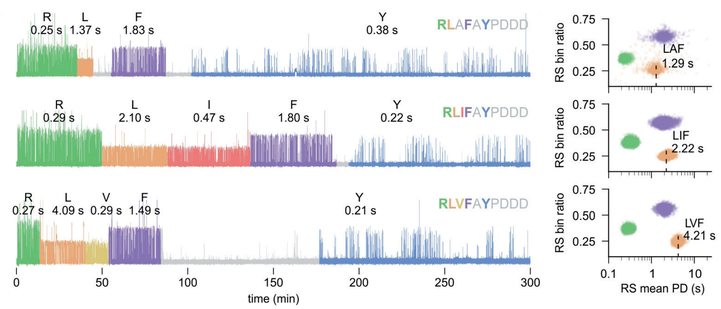
Different amino acids are distinguished by the distinct fluorescence properties and pulsing kinetics of the recognizers



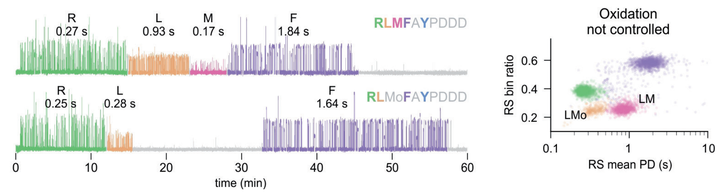
Dynamic sequencing of diverse peptides with high-precision kinetic outputs



Detection of single amino acid changes

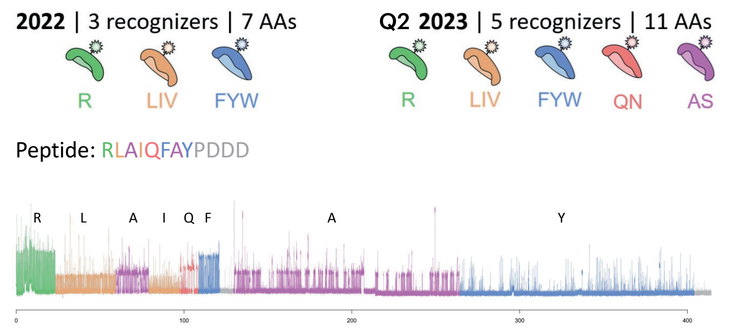


Detection of post-translational modifications

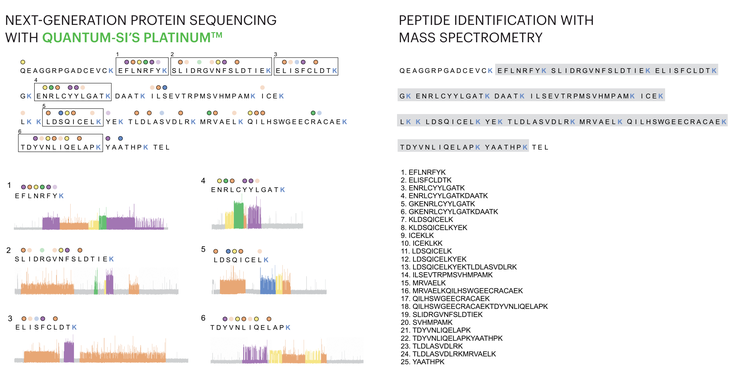


CONCLUSION AND OUTLOOK

New recognizers increase the number of amino acids detected



Advances in amino acid recognition enable accurate sequencing of more peptides and identification of more proteins



REFERENCE

Brian D. Reed et al, Science 2022, 378 (6166) 186–192.

TRADEMARKS/RESTRICTIONS

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