NIIMBL® The National Institute for Innovation in Manufacturing Biopharmaceuticals

At-Line Nanoparticle Based Molecular Structure Analysis

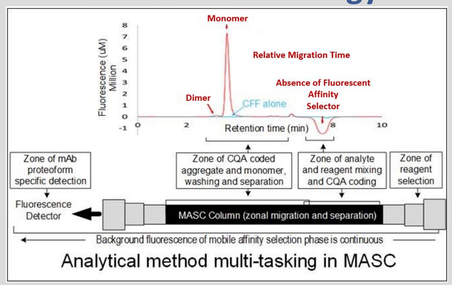
Introduction

Proteometer™ Project Overview

- ✓ BPL 4.0
- ✓ Successful Pilots
- ✓ Commercially Available Product

Methodology

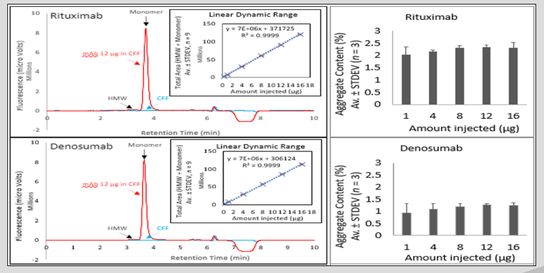
MASC™ Technology



Giving pharmaceutical companies better control of their batches

In-House Results

Proteometer-L™ In-House Results



Conclusion

Introducing Proteometer-L Kit

Offsite Results

Pilot Results & Opportunities

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Proteometer™, AKA "Proteoform Meter" Project Overview

➢T-mAb: At-line Proteoform Quantification Test <10 Min.

- ✓ Demonstrate proof of concept
- ✓ Test for Aggregate and mAb Titer in-house
- ✓ Complete Pilot Studies off-site and compare vs. in-house tests
- ✓ Purchase and assemble supplies for product release
- ✓ Reach BRL 4.0: Bio Readiness Level 4.0

The world's first technology for at-line molecular structure analysis

Notes: (1) All the above information is Novilytic Background IP, (2.) MASC, FRET Assay Technology, and Ligand Specific Labeling of HCP's are patented technology from Novilytic, LLC (USP 10,018,635 B2 ; USP 10,670,607 B2; USP 10,065,988), (3.) At-line Reactor Test hardware and technology is Patent Pending (F.E. Regnier, et.al. Novilytic, LLC)

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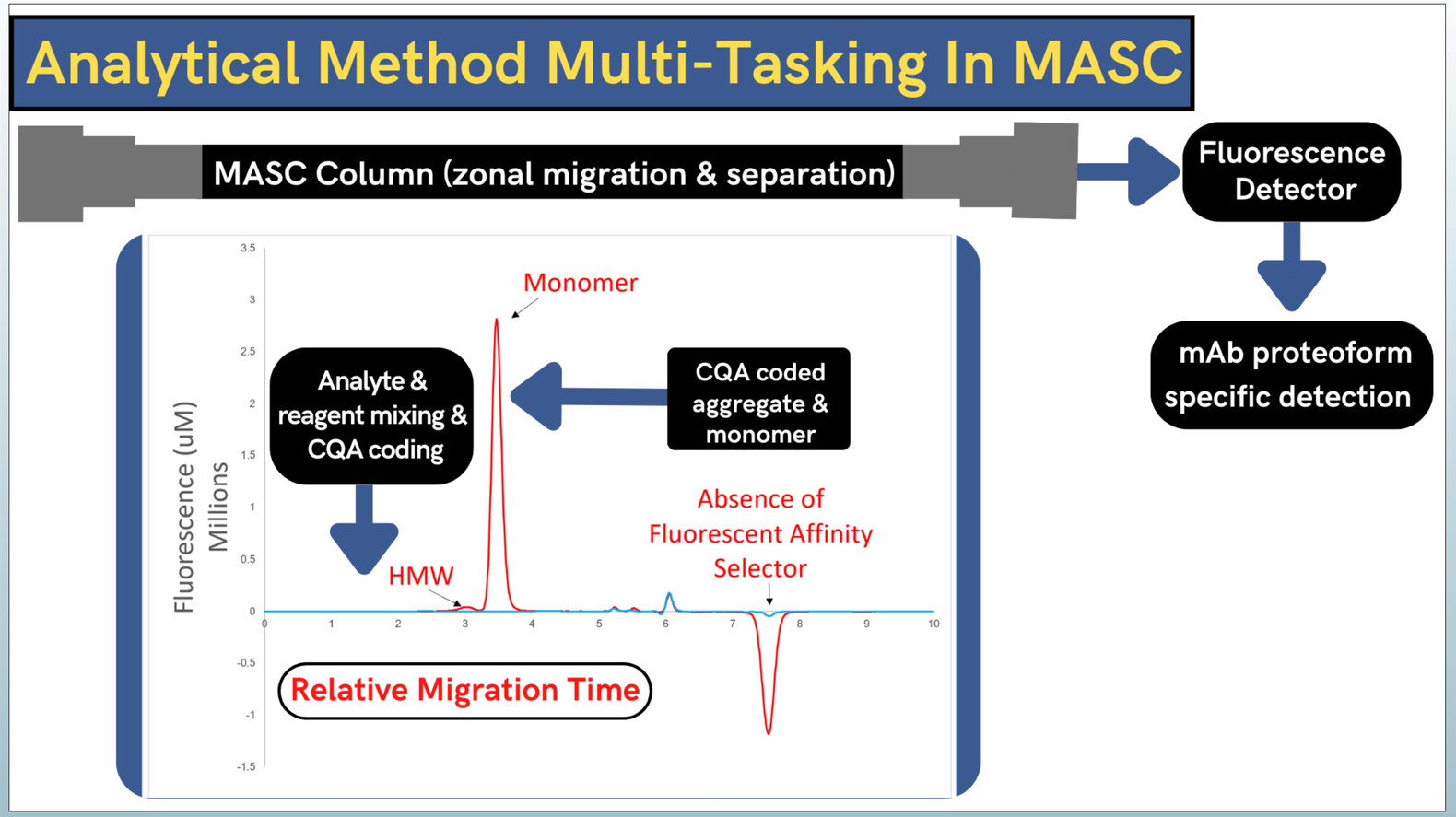
MASC™ Technology (Mobile Affinity Sorbent Chromatography)

How it works:

- Fluorescent labeled molecular coding agent is pumped through the column continuously.
- After injection of the mAb in crude culture filtrate, the band passes through fluorescent labeled molecular coding agent, where it selectively binds to sites on the mAb
- The mAb-coding agent complex has a higher molecular weight than unbound molecular coding agent, and different molecular weight than high molecular weight proteins and mAb fragments, resulting in separation
- The mAb-coding agent complex is continuously washed by additional mobile phase containing coding agent until it elutes
- Measurement of the complex by fluorescence detection results in highly accurate mAb Titer and Aggregate analysis
- Confirmed linear Titer from 0.5 - 16 µg in crude culture filtrate with broader linear range at lower concentrations than ELISA and 8x faster



Flow of molecular coding agent is shown from left to right in the figure above.

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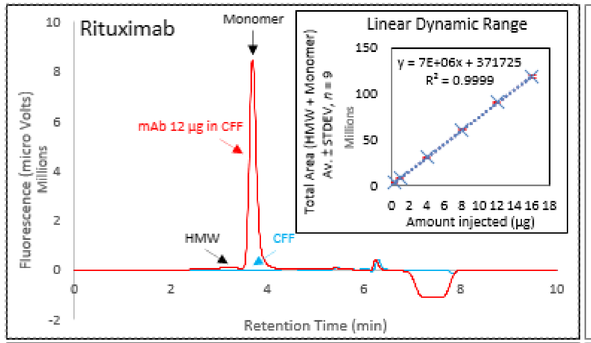
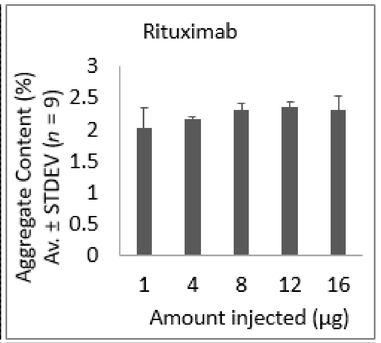
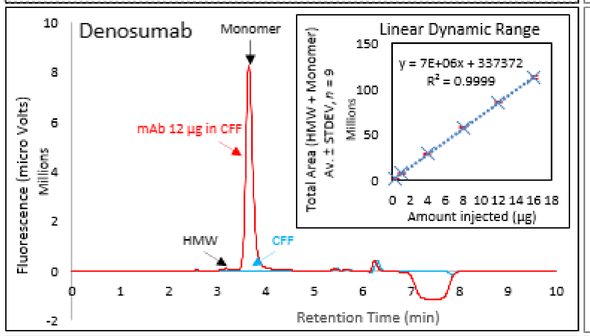
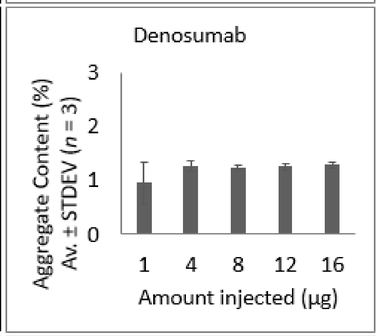
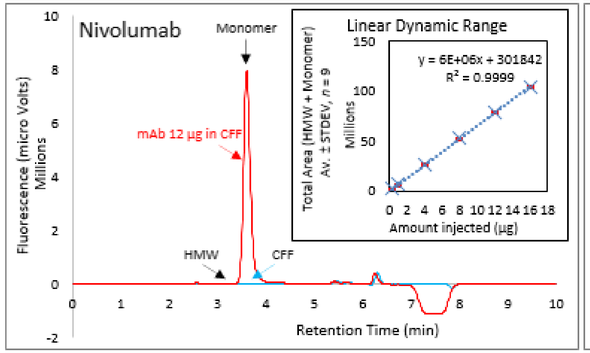
Proteometer-L Pilot Results (Johnson & Johnson)

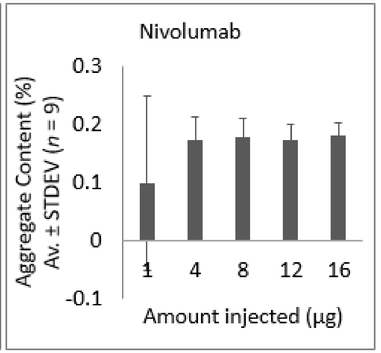


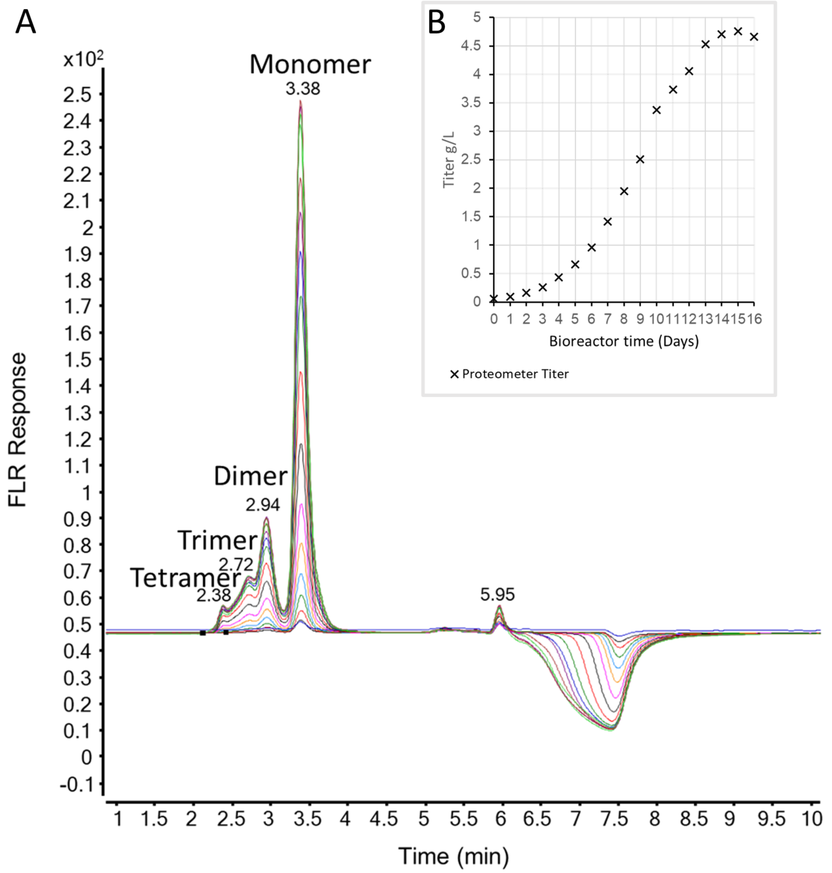


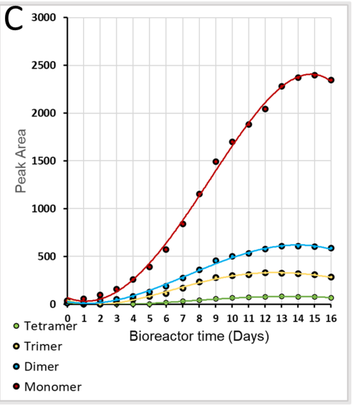


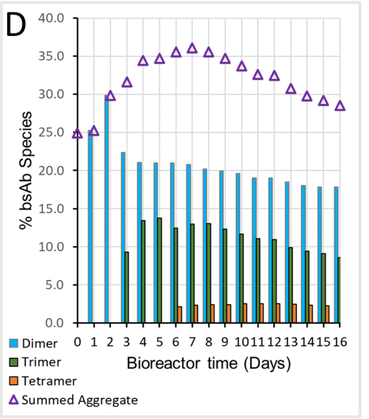












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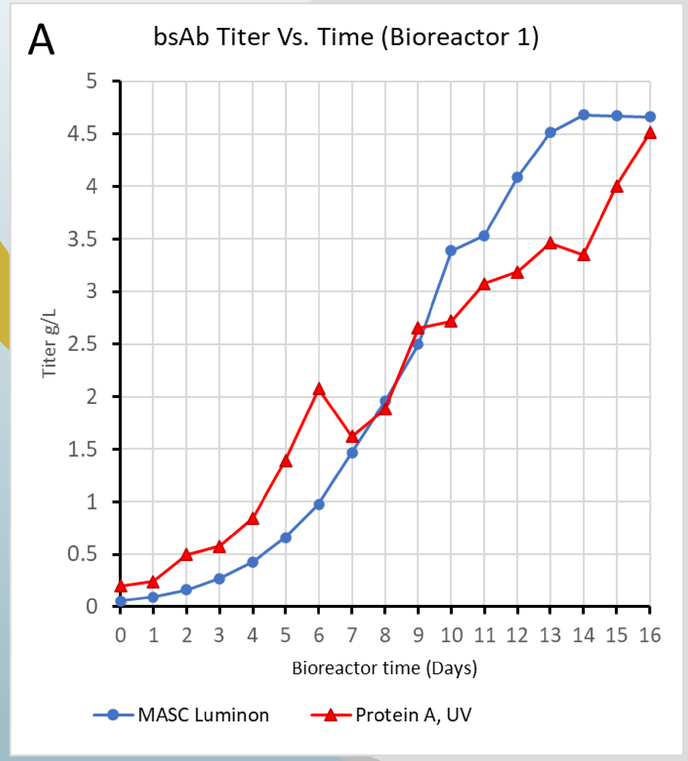
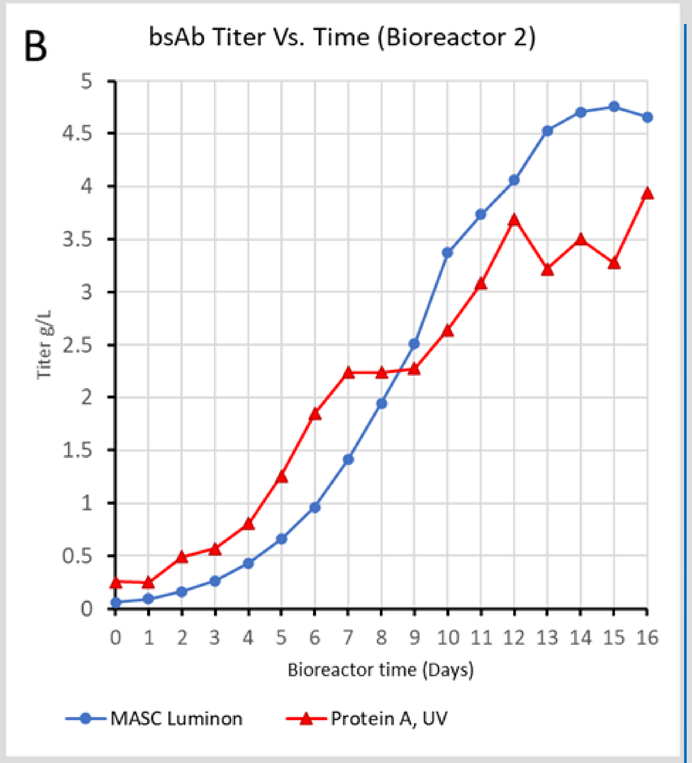
Pilot Testing Results (Johnson & Johnson)





Additional Pilot Opportunities:

- Contact
  - Paul C. Dreier, BSc., MBA
  - Mobile / WhatsApp!: +1.317.752.3116
  - Email: pdreier@novilytic.com

Pilots were completed with two major pharmaceutical manufacturers and one major instrument company.

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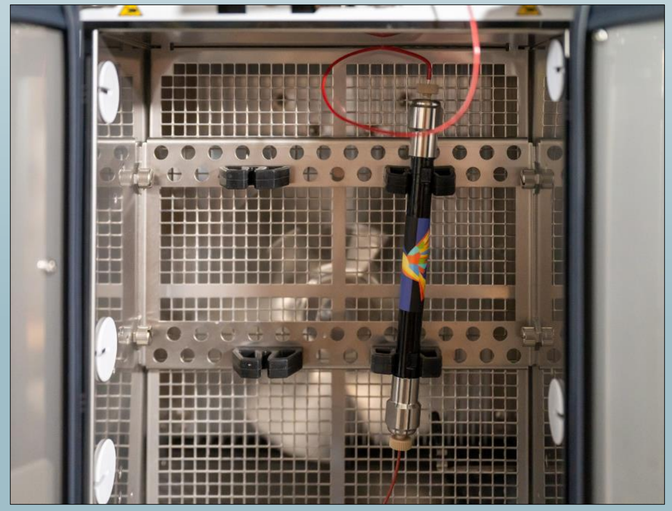
Proteometer-L Kit

At-Line Nanoparticle Based Molecular Structure Analysis

Minimum Viable Product Status – Complete!

- ✓ All Raw Materials Identified and Purchased
- ✓ All Supply Contracts Signed
- ✓ Proteometer-L Kit Designed and Assembled
- ✓ Application Notes and Kit Usage Instructions Completed
- ✓ Pilots 1 and 2 Completed
- ➢ Seeking Additional Pilot Testing Opportunities



Notes

Slide 3

Within the reactor, mAb's, and high molecular weight species (dimers, trimers, and tetramers) are coded, washed, and separated. In some cases, there may be a small amount of non-specific binding to fragments which contain an intact portion of the Fc region where the coding agent binds. The negative peak in the chromatogram results from the withdrawal of coding agent from the mobile phase during binding to the mAb, thereby decreasing the background fluorescence signal.

Slide 4

MASC testing is capable of efficiently separating IgG1, 2, and 4 monomers and aggregates (high molecular weight proteins) in crude culture filtrate, with linear results from 1-16 µg for each (Left). MASC is capable of separating bispecific antibodies and high molecular weight proteins, including dimers, trimers, and tetramers, with resolution of the individual high molecular weight species (Right).

Slide 5

The visual is a comparison of MASC testing (blue curves) versus typical Protein A purification (red curves) of a bispecific antibody from two bioreactors. With Protein A purification, we observe titer error of up to 10% versus expected for this antibody. However, using MASC testing, we observe more accurate titer values, with error of less than 2% versus expected.

Slide 6

Proteometer-L Kit Components:

- Proteometer-L Reactor
- Proteometer-L Reagent
- Proteometer-L Reconstitution Reagent
- Instructions for use