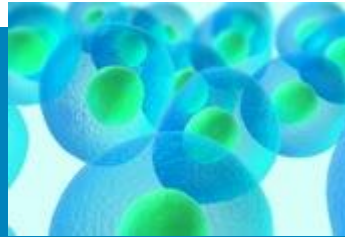
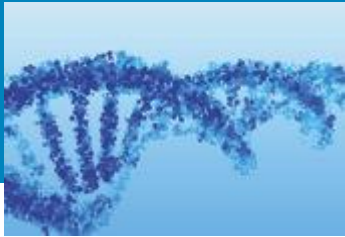




U.S. Manufacturing and Testing | **药明康德 WuXi AppTec**
Biologics · Advanced Therapies · Medical Devices



Optimization of TFF for Viral Vectors



Peter Lynch, M.S.
WuXi AppTec, Inc.

OUR JOURNEY

2017: Global Platform

2017

15,000+ employees worldwide

5 million ft² existing & upcoming R&D space
leading capability and technology platform



OUR PLATFORM

Comprehensive R&D Enabling Capabilities



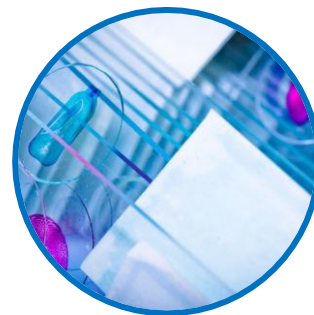
Small Molecules



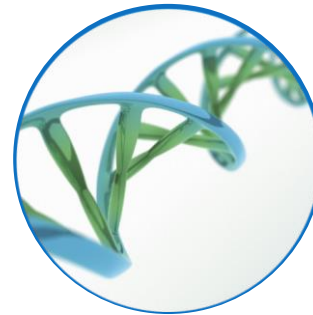
Biologics



Cell & Gene
Therapies



Medical Devices



Molecular Testing
and Genomics

Philadelphia Facilities

Cell / Gene Therapy Manufacturing and Testing

82,000 SF - *QC Testing, PD, Cell Therapy Manufacturing*



45,000 SF - *Manufacturing for Autologous / Allogeneic Cell Therapies*



150,000 SF - *CAR-T Cell Therapies and Gene Therapy Manufacturing*



WuXi Apptec Cell and Gene Therapy Services

- Tissue Acquisition
- Cell Banking
- cGMP manufacturing vector and cell therapies
- Process Development
- Media Screening, serum reduction
- Closed System Processing and QbD
- Viral Vector Manufacturing
 - Adherent Closed System up to >250L
 - Single-use Bioreactors 50 and 200L
 - Full Downstream including AKTA Pilot and Ready
- Cell Therapy
 - CAR-T viral and non-viral
 - XURI and GREX
 - KSEP and LOVO
- WUXI Lentiviral platform offerings
 - Production up to 250L
- Full Testing capabilities
- Process Validation and Commercialization



TangenX™ SIUS™ Single-use TFF Cassettes

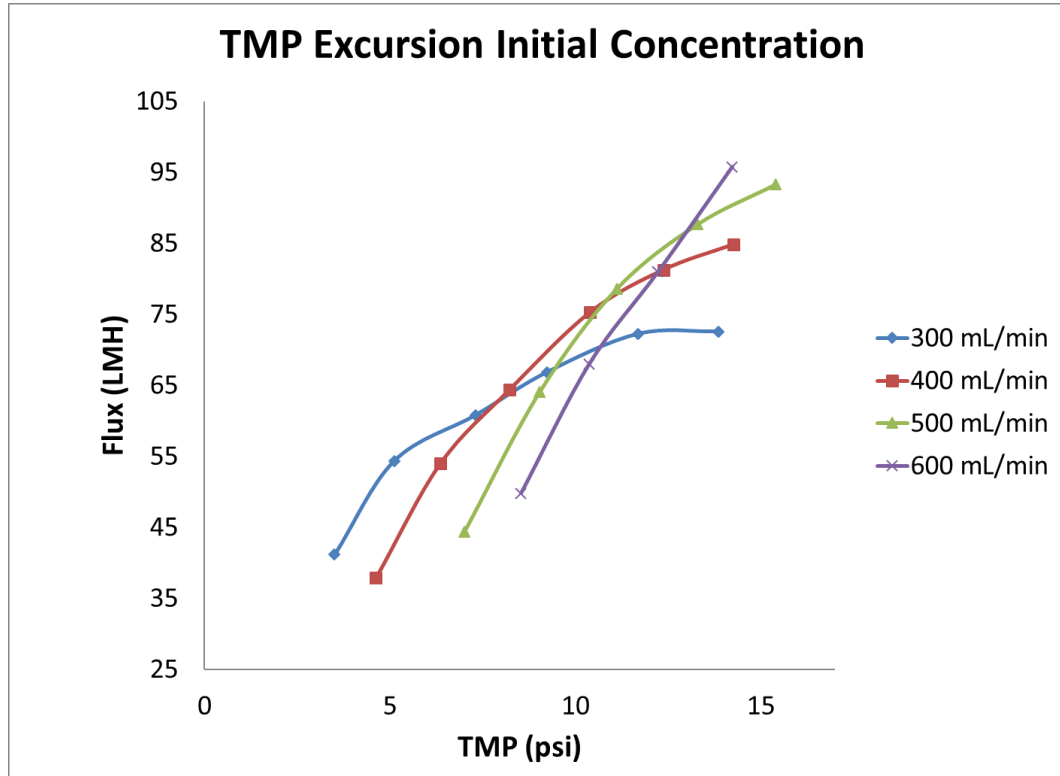
- Higher flux – better for processing large volumes in manufacturing
- Flexibility – More options to choose from
 - Pore size
 - Membrane surface area
- Less total membrane area needed for processing
- High yields
- Footprint at large scale
- Single use provides many advantages for a CMO dealing with multiple products from many different clients



TFF Process Development & Optimization

Sequence	Purpose
1. TMP Excursion at Initial Concentration	<ul style="list-style-type: none">• Determine TMP for UF/DF• Determine Feed Flow for UF/DF• Demonstrate Flux Stability• Confirm Retention of Product
2. Concentration / Volume Reduction	<ul style="list-style-type: none">• Determine Flux as Function of Concentration• Determine Placement of Diafiltration Step• Determine Flux as Function of Buffer Conditions
3. TMP Excursion at Final Concentration	<ul style="list-style-type: none">• Determine TMP for UF/DF• Determine Feed Flow for UF/DF• Confirm Retention of Product
4. Diafiltration Exchange	<ul style="list-style-type: none">• Determine Diafiltration Requirement• Confirm Retention of Product during DF
5. Product Recovery	<ul style="list-style-type: none">• Crude Assessment of Step Yield• Product Quality Evaluation

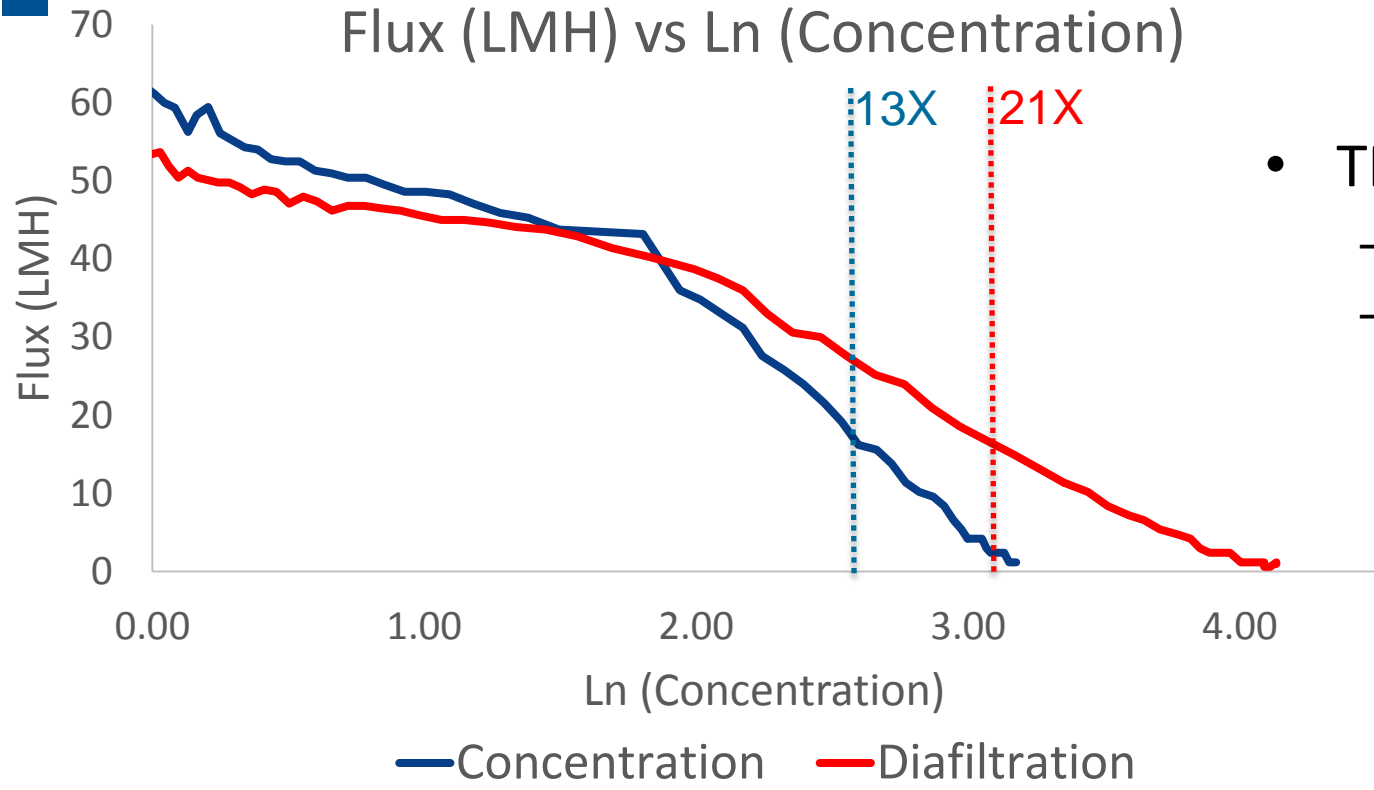
TMP Excursion at Initial Concentration



Note: Manual collection of flux samples were taken over 30 second time intervals. Filter area = $0.1M^2$

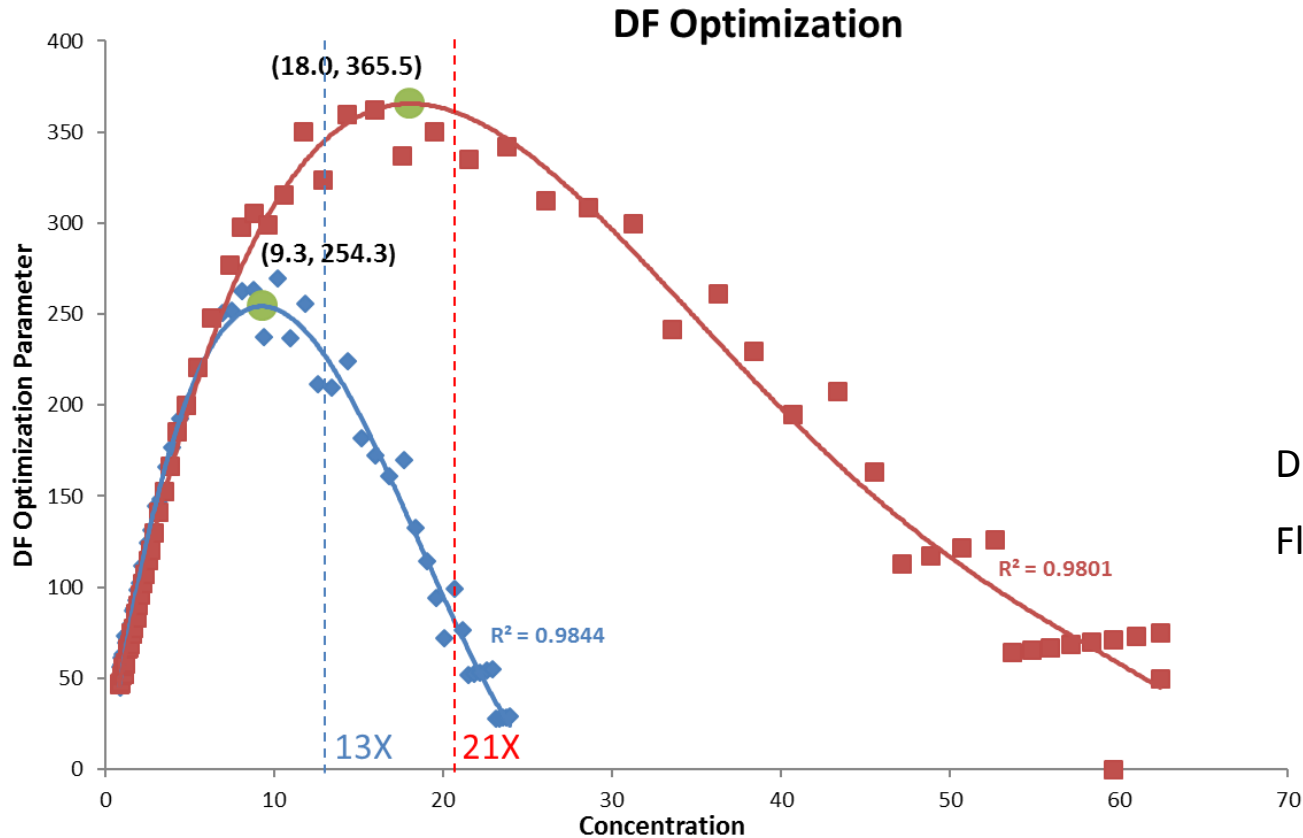
- Conclusions
 - **Flow Rate**
 - 5LMM
 - **TMP Range**
 - 8.8 – 11
 - Higher feed flow rates achievable if system safety concerns addressed.
 - No Impact to product recovery

Concentration / Volume Reduction



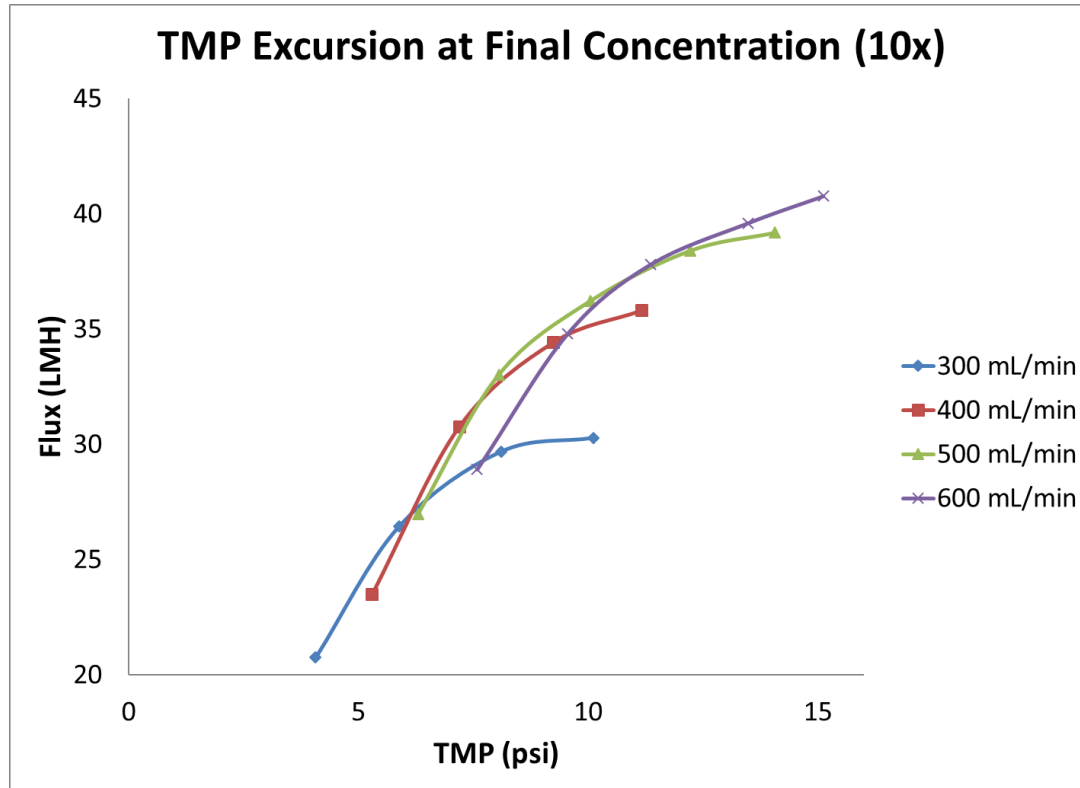
- TMPs > 11 psi
 - Initial Buffer: 13X
 - DF Buffer: 21X

Concentration / Volume Reduction



DF Optimization Parameter =
Flux x Concentration

TMP Excursion at Final Concentration



- Parameters
 - Flow Rate
 - 5LMM
 - TMP Range
 - 7.2 – 9
 - 6LMM is feasible
 - No change in flow rate for MFG simplicity

Note: Manual collection of flux samples were taken over 30 second time intervals. Filter area = $0.1M^2$

Optimized Process with TangenX™ SIUS™ Single-use TFF Cassettes

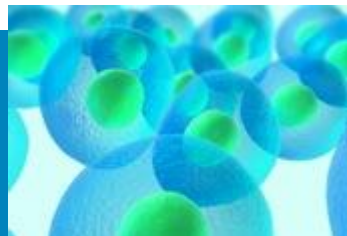
- Selected Parameters: 5 LMM, TMP 8.8 – 11 psi
- 3 Lots of 30 x HYPERstack-36
 - > 90% Recovery
- Similar Data from other vectors
 - TangenX™ SIUS™ Single-use TFF Cassettes
 - Recoveries 91-95%



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THANK YOU

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