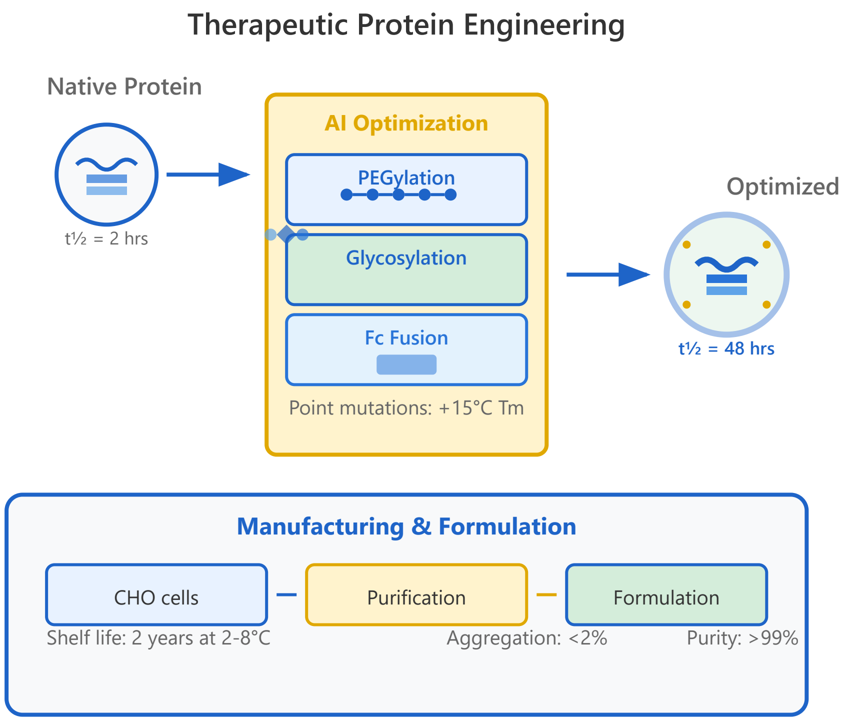
Therapeutic Proteins



Stability engineering
Thermal & chemical stability

Half-life extension
PEGylation, Fc fusion

Immunogenicity reduction
T-cell epitope removal

Formulation prediction
Aggregation prevention

Manufacturing optimization
Yield & quality improvement

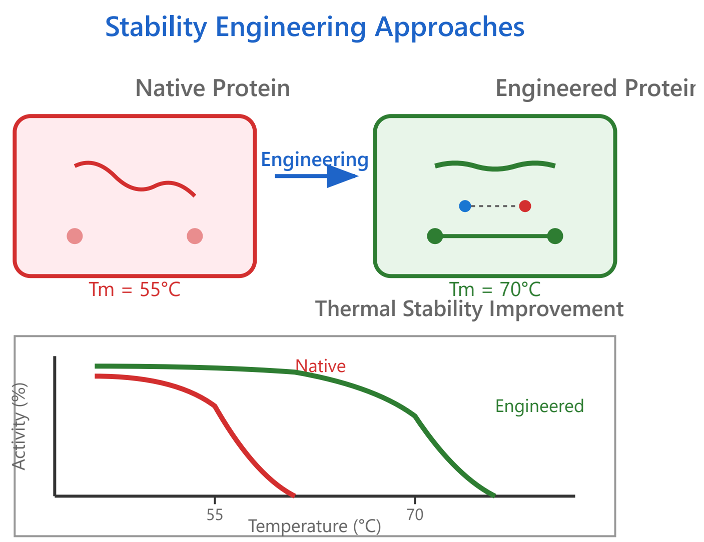
1. Stability Engineering

Thermal & Chemical Stability Enhancement

Objective: Improve protein resistance to temperature, pH changes, and chemical degradation to extend shelf life and maintain therapeutic efficacy.

Key Strategies:

- **Disulfide bond engineering** - Introduce strategic cysteine pairs to stabilize protein structure
- **Salt bridge optimization** - Enhance electrostatic interactions between charged residues
- **Hydrophobic core packing** - Improve interior residue arrangement to prevent unfolding
- **Surface charge modification** - Reduce aggregation-prone patches



Clinical Example: Enzyme Replacement Therapy

Recombinant human α-glucosidase (Pompe disease treatment) was engineered with strategic mutations increasing thermal stability from 55°C to 70°C, enabling room temperature storage and reducing cold-chain logistics requirements by 40%.

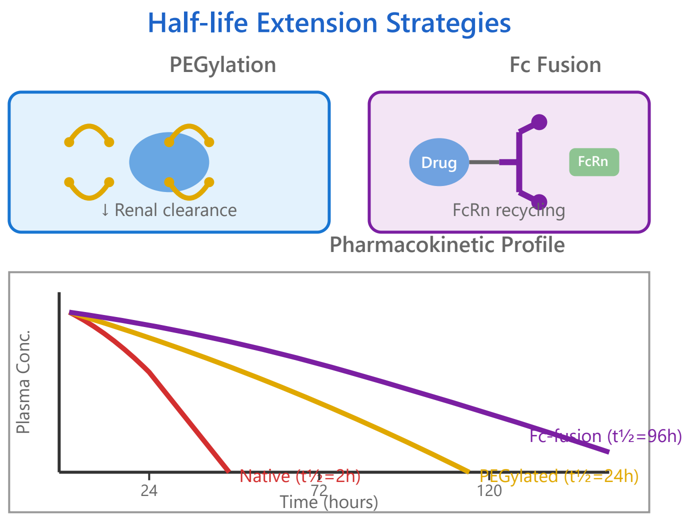
2. Half-life Extension

Prolonging Therapeutic Circulation Time

Objective: Extend protein residence time in circulation to reduce dosing frequency and improve patient compliance.

Major Approaches:

- **PEGylation** - Attachment of polyethylene glycol (PEG) chains increases hydrodynamic radius
- **Fc fusion** - Linking to IgG Fc domain enables FcRn-mediated recycling
- **Albumin fusion** - Leverage albumin's long half-life (19 days)
- **Polysialylation** - Attach polysialic acid chains for stealth effect



Clinical Examples:

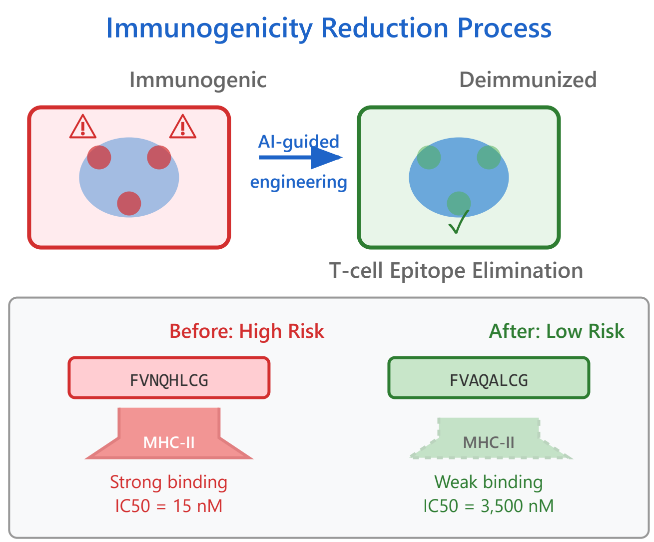
Pegfilgrastim (Neulasta®): PEGylated G-CSF extends half-life from 3.5 hours to 42 hours, reducing injections from daily to once per chemotherapy cycle.

Etanercept (Enbrel®): TNF receptor-Fc fusion achieves 102-hour half-life, enabling twice-weekly dosing for rheumatoid arthritis treatment.

3. Immunogenicity Reduction

Minimizing Unwanted Immune Response

Objective: Reduce the risk of anti-drug antibodies (ADAs) that can neutralize therapeutic effect or cause adverse reactions.



Key Strategies:

- **T-cell epitope removal** - Identify and eliminate MHC-II binding sequences using computational tools
- **Humanization** - Replace non-human sequences with human framework regions
- **Deimmunization** - Strategic mutations to disrupt epitope binding without affecting function
- **Glycosylation engineering** - Shield immunogenic surfaces with glycan

coverage

Clinical Success Story:

Factor VIII for Hemophilia A: Computational deimmunization reduced T-cell epitopes from 26 to 4, decreasing immunogenicity by 73% in preclinical models. Clinical trials showed a 5-fold reduction in inhibitor antibody formation compared to first-generation products, significantly improving treatment outcomes.

4. Formulation Prediction

Aggregation Prevention & Stability Optimization

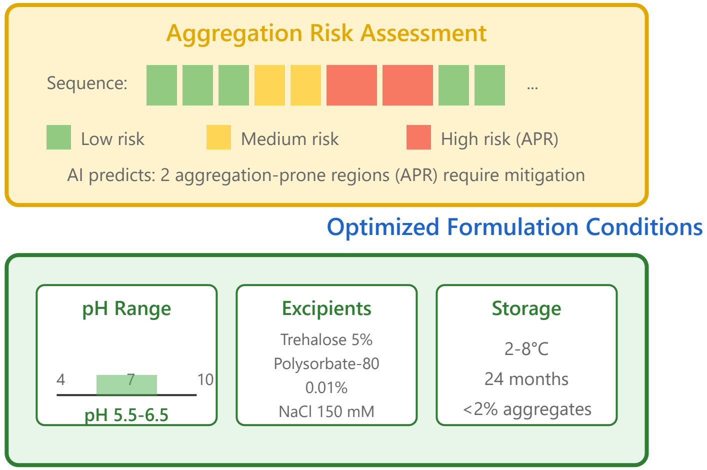
Objective: Design optimal formulation conditions to prevent protein aggregation, maintain stability during storage, and ensure consistent drug product quality.

AI-Driven Approaches:

- **Aggregation propensity prediction** - Identify aggregation-prone regions using ML models
- **pH optimization** - Predict optimal pH range for maximum stability

- Excipient screening - AI-guided selection of stabilizing agents (sugars, salts, surfactants)
- Concentration optimization - Balance high concentration needs with aggregation risk

Formulation Optimization Workflow



Real-World Application:

Monoclonal Antibody (150 mg/mL): Machine learning models predicted optimal formulation with histidine buffer (pH 6.0), 8% sucrose, and 0.02% polysorbate-80. This formulation achieved 36-month stability at 5°C with less than 1% high molecular weight species, eliminating the need for extensive empirical screening and saving 18 months of development time.

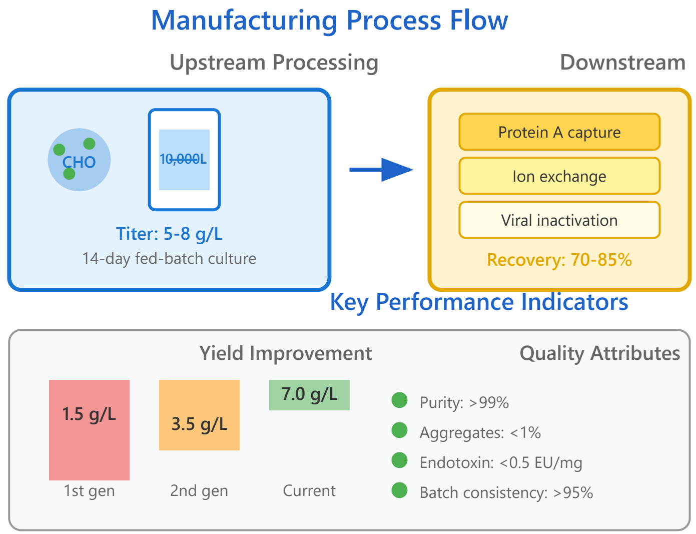
5. Manufacturing Optimization

Yield & Quality Improvement through Process Engineering

Objective: Maximize protein production efficiency, ensure consistent quality, and reduce manufacturing costs through bioprocess optimization.

Optimization Targets:

- **Cell line engineering** - CHO, HEK293, E. coli strain optimization for higher titers
- **Expression system** - Codon optimization, signal peptide design, secretion enhancement
- **Culture conditions** - Media composition, temperature, pH, dissolved oxygen
- **Purification strategy** - Chromatography sequences, yield optimization
- **Process analytics** - Real-time monitoring and AI-driven process control



Industry Example:

Adalimumab Biosimilar Production: Process optimization through AI-guided media design and cell line engineering increased volumetric productivity from 2.5 g/L to 7.2 g/L in CHO cells. This 3-fold improvement reduced cost of goods by 60% while maintaining product quality matching the reference product across all critical quality attributes. The optimized process enabled commercial-scale production in smaller bioreactors, significantly reducing capital expenditure requirements.