KBI BIOPHARMA

In Silico Formulation Design:

From Sequence to Optimized Formulation

Mechanistic predictions. Not a black box.

60-70%

fewer wet-lab samples vs conventional empirical DOE

3-6 mo

compressed early-formulation timeline to lock the operating window

1x

right-the-first-time formulation — fewer reformulations across clinical phases

Why In Silico Modeling Matters

Preclinical and IND-Enabling

Physics-Grounded Rationale: Defends chosen pH and ionic strength windows early—defensible in regulatory CMC sections without years of empirical justification.

Phase 1 and Phase 2

Scale-Up Stability: Operating window holds through scale-up; UF/DF Donnan offset is predicted, not discovered late. Avoids costly mid-clinical reformulations.

Phase 3 and BLA

Traceable Selection: Employs a TPP-driven decision tree, not a one-size-fits-all panel — supports control strategy and process validation.

Commercial Launch

Robust Formulation: Flexible for high-concentration and low-temperature presentations (i.e., SC autoinjector, lyo) because viscosity, opalescence, and frozen-state risks ere screened in silico early.

In Silico Workflow for Formulation, Developability, and Process Development

Initial Screening

Sequence, available structure and confidence metrics, plus a focused experimental pH profile.

Computational Assessment

Map charge, aggregation, colloidal stability, and interaction risk across pH and ionic strength.

Formulation Design

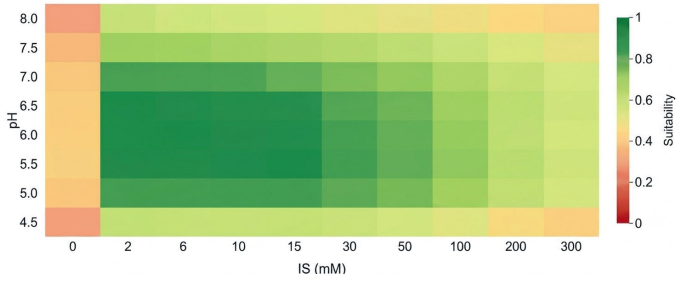
Recommend the design space, buffer, ionic strength, excipient strategy, and Donnan conditions.

Experimental Confirmation

Validate the highest-value conditions with a targeted laboratory panel and refine the window.

Example 1 — Models Built for Complex Molecules and Difficult Formulations

NISTmAb



Glycosylated Fc-fusion

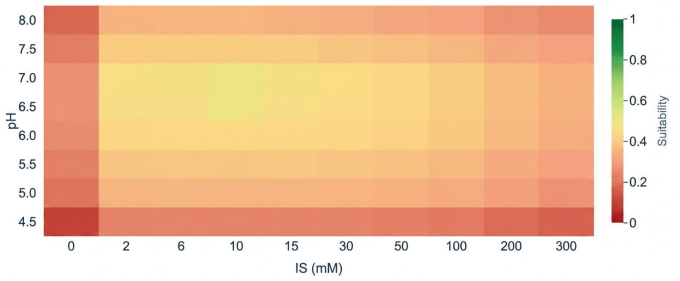
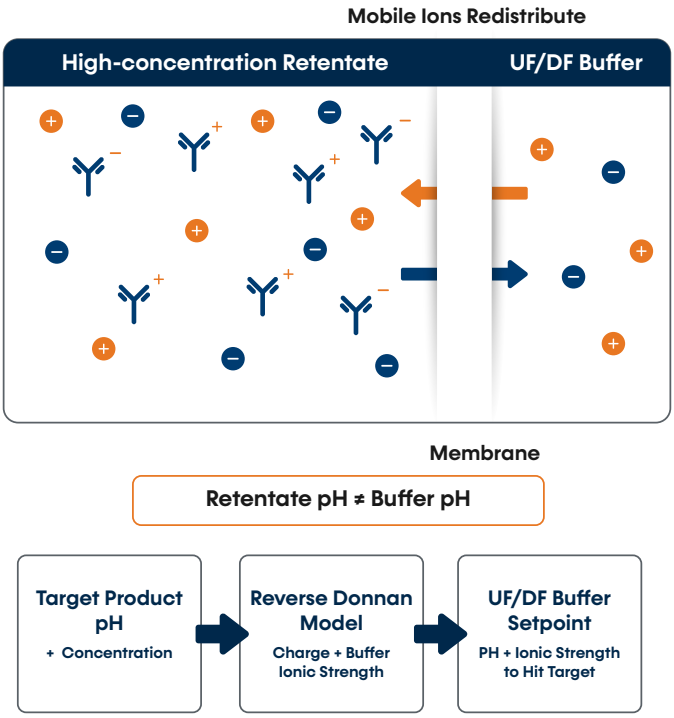


Figure 1. This glycosylated Fc-fusion's first thermal transition sits roughly 25 °C below that of a typical IgG1, so no condition offers the wider margin a stable mAb enjoys.

Key Take Away: Mechanistic modeling identifies the narrow operating window where a complex molecule is most likely to succeed, focusing experiments on the conditions that matter most.



Example 2 — Designing the UF/DF Buffer to Hit Target pH

Figure 2. Why the Donnan Effect Matters: At high protein concentration, Donnan partitioning can create a molecule- and condition-dependent pH offset between the UF/DF buffer and the protein retentate.

Key Take Away: Reverse Donnan modeling calculates the UF/DF buffer pH and ionic strength needed to reach the target final product pH, replacing iterative trial-and-error with a mechanistic setpoint.

Discover how physics-based formulation design can accelerate development.

Reach out to our team to explore your molecule.

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First Principles Biopharma