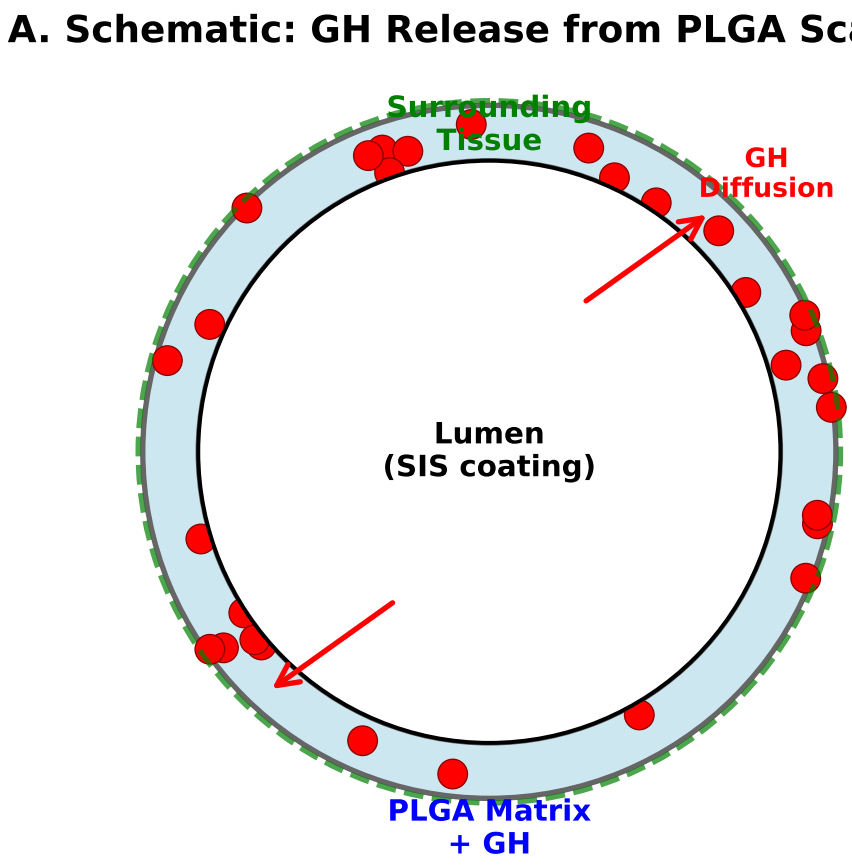
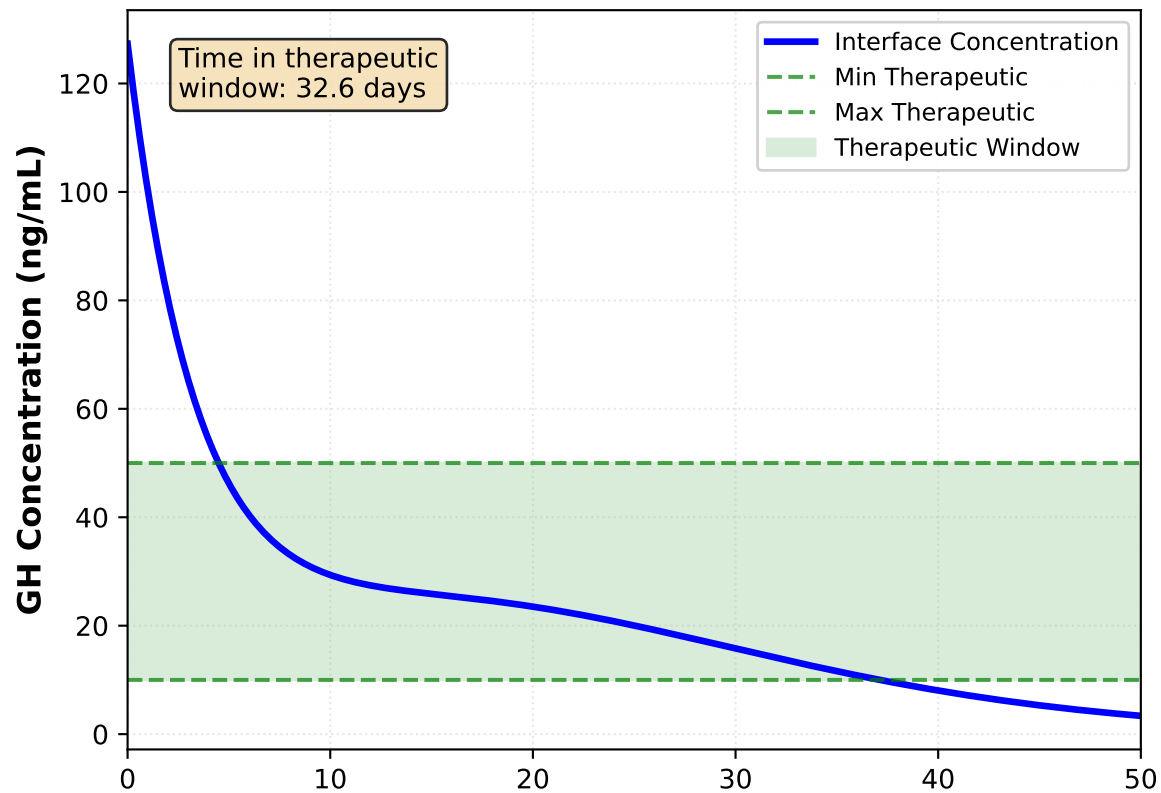
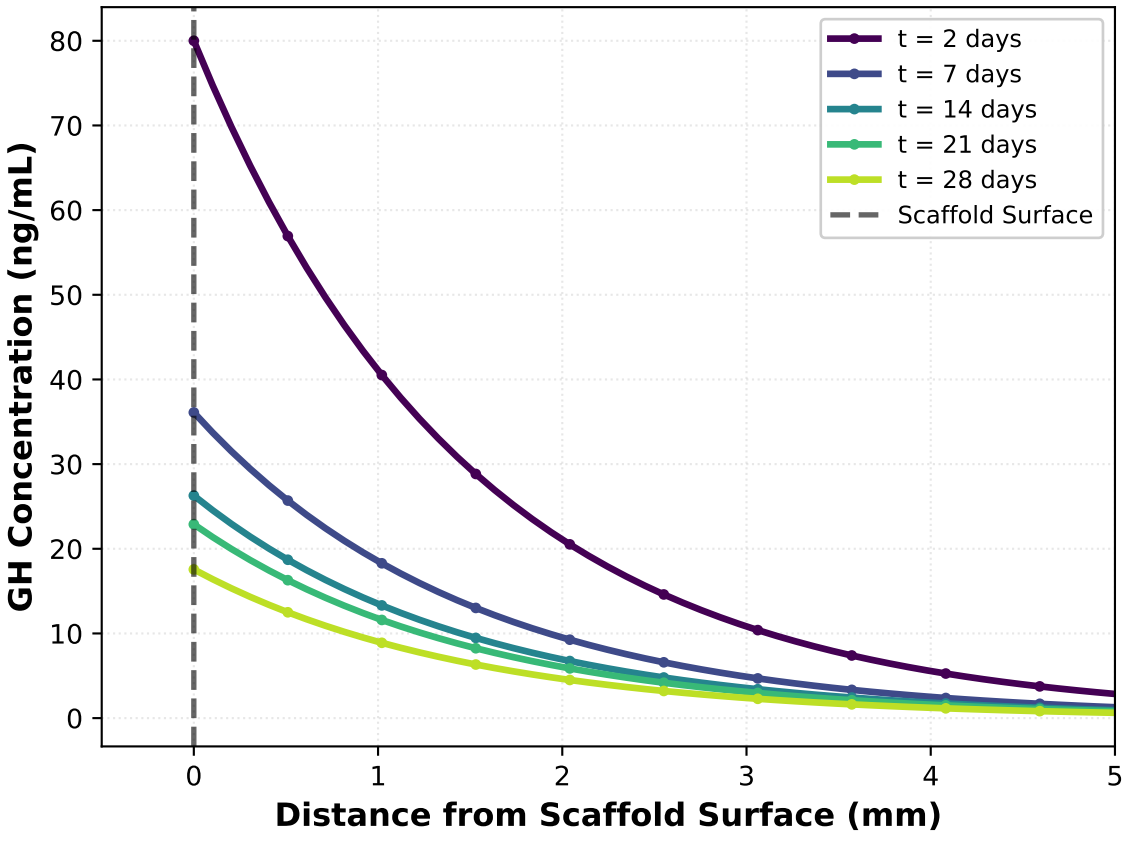
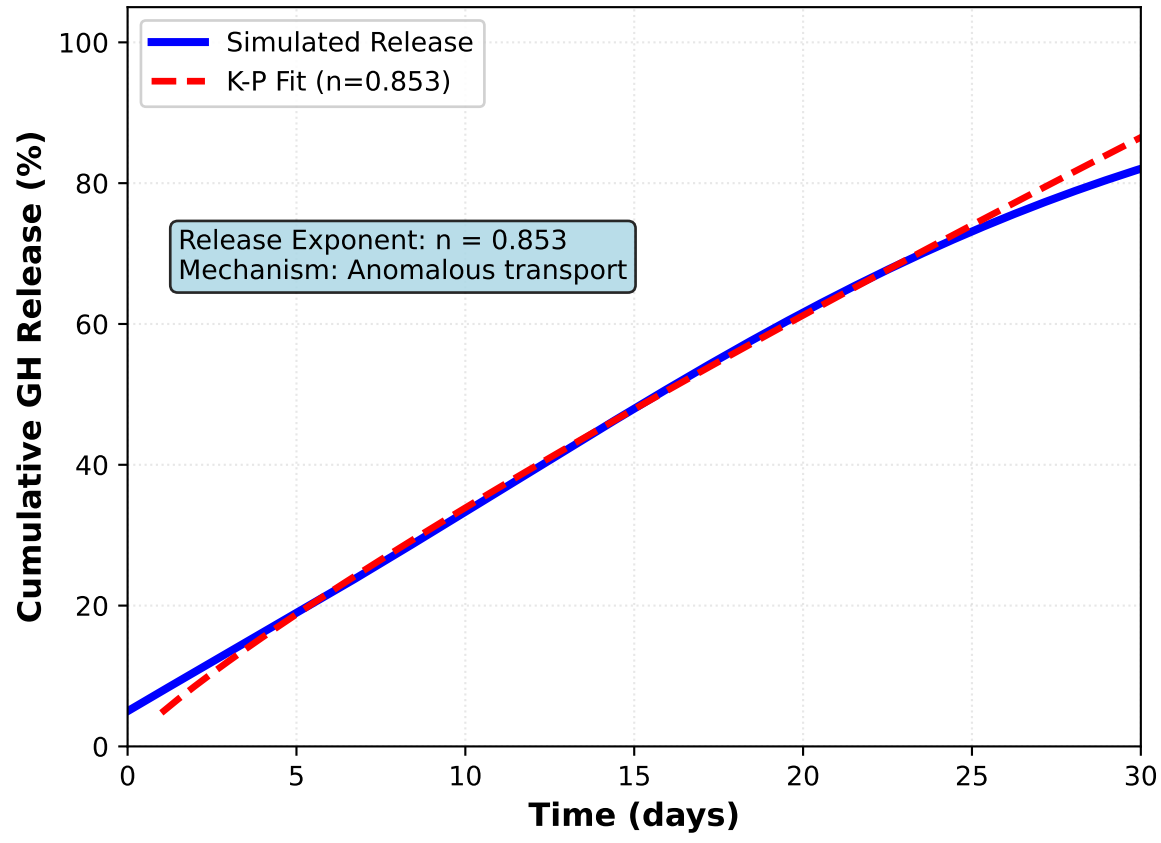
Figure 6.1: Growth Hormone Release from Prototype 3 PLGA/SIS Scaffold

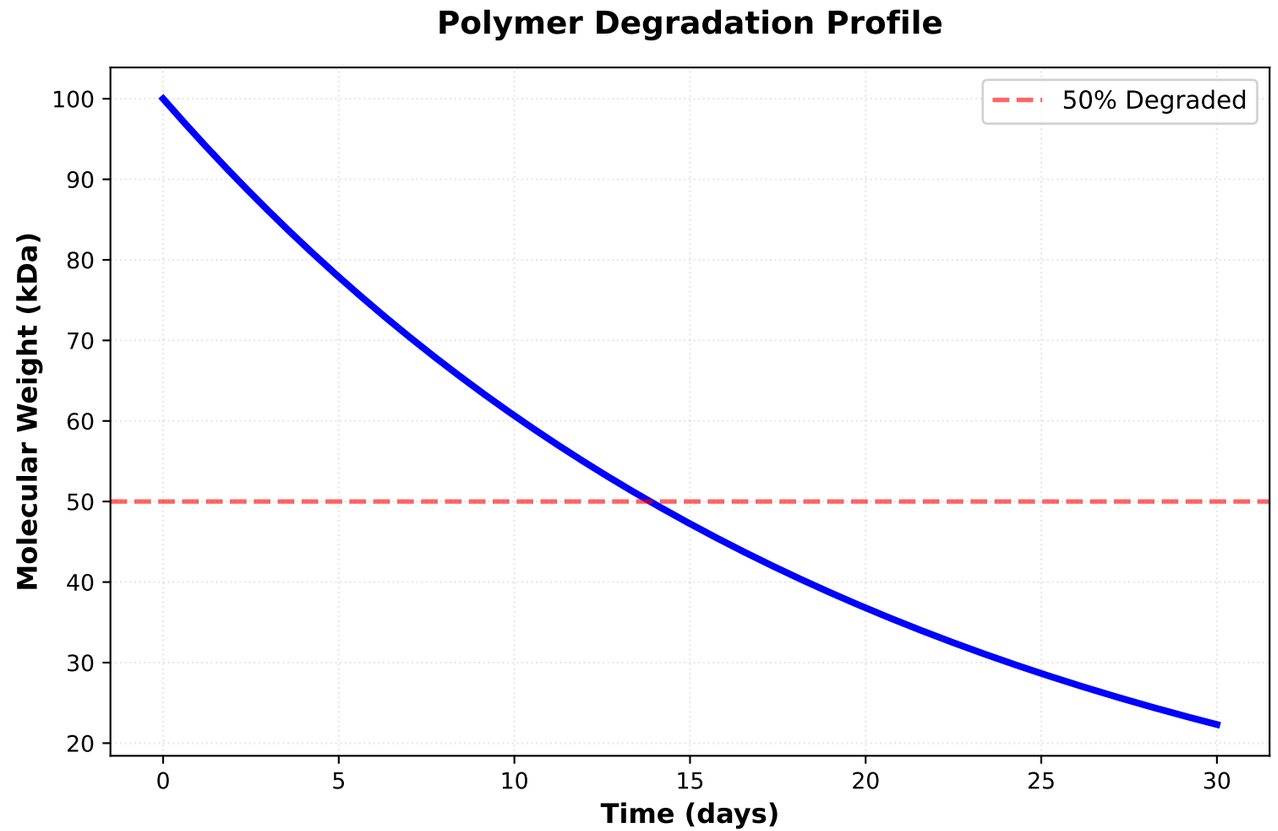


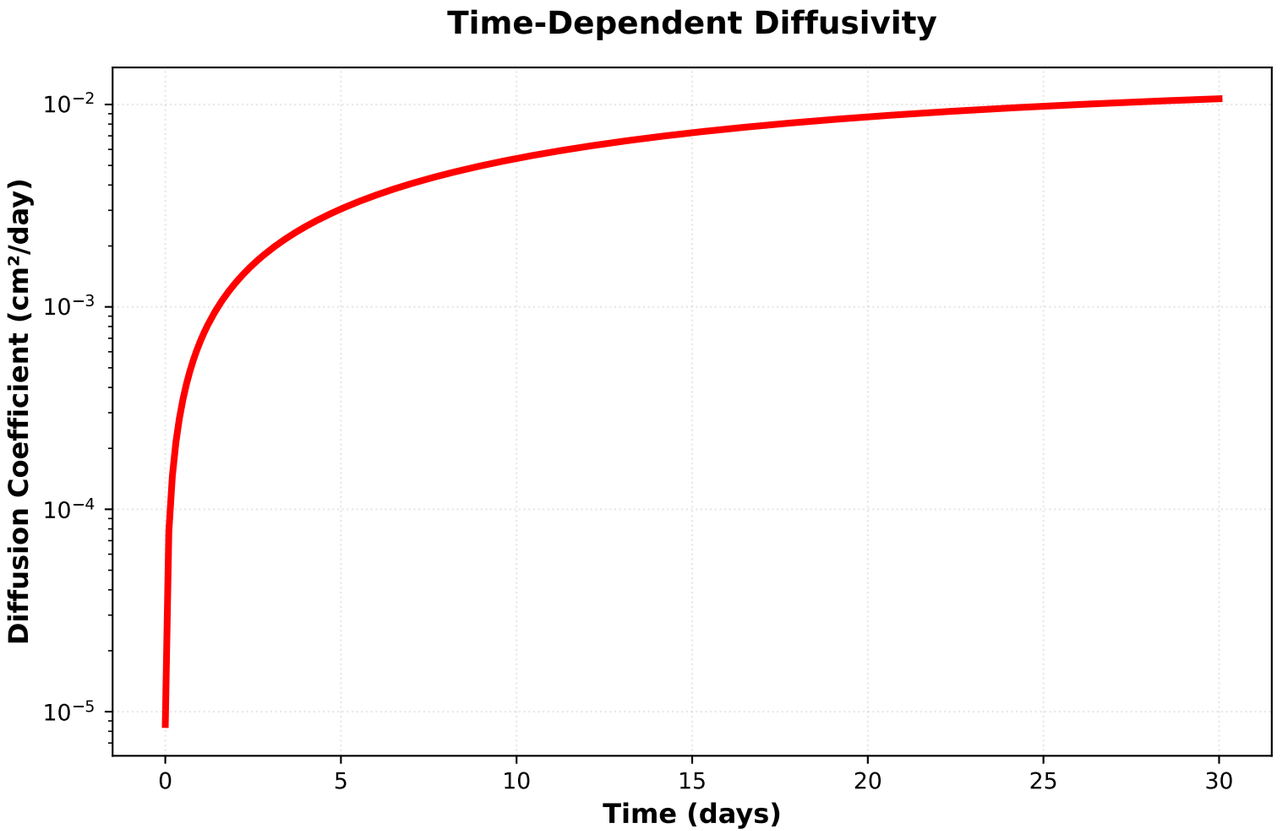






Supplementary Figure S1: Polymer Degradation and Diffusivity Evolution





MODEL 5: BIOACTIVE AGENT DELIVERY FROM DEGRADING SCAFFOLD
Growth Hormone Release from PLGA/SIS Scaffold - Simulation Results

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SCAFFOLD PARAMETERS
• Outer Radius: 1.25 cm
• Inner Radius: 1.05 cm
• Wall Thickness: 0.20 cm
• Graft Length: 15.0 cm
• Scaffold Volume: 21.677 cm^3

PLGA PROPERTIES
• Lactide:Glycolide Ratio: 75:25
• Degradation Rate Constant: 0.05 day^{-1}
• Initial Molecular Weight: 100.0 kDa

GROWTH HORMONE LOADING
• Initial GH Loading: 0.15 mg
• Initial Concentration: 0.0069 mg/cm^3 (6.92 $\mu g/cm^3$)

THERAPEUTIC WINDOW ANALYSIS
• Target Range: 10.0 - 50.0 ng/mL
• Maximum Interface Concentration: 127.32 ng/mL
• Time Above Minimum (10.0 ng/mL): 37.2 days
• Time Within Therapeutic Window: 32.7 days

RELEASE KINETICS
• Total Release at 30 days: 97.4%
• Remaining in Scaffold: 3.86 µg
• Average Release Rate: 3.25%/day

KORSMEYER-PEPPAS MODEL FIT
• Release Rate Constant (k): 0.0476
• Release Exponent (n): 0.853
• Release Mechanism: Anomalous (non-Fickian) transport

FEASIBILITY ASSESSMENT

✓ FEASIBLE: Therapeutic concentration maintained for ≥3 weeks
  Prototype 3 with 0.15 mg GH loading is suitable for advancement.

  The tri-phasic release profile (burst → diffusion → erosion) is evident
  from the simulation results, confirming the expected behavior of PLGA-based
  delivery systems.

DESIGN RECOMMENDATIONS

The modeling results support the following design considerations:
1. PLGA 75:25 provides controlled degradation kinetics
2. SIS coating effectively prevents luminal GH loss
3. Scaffold geometry (tubular) enables radial diffusion to tissue
4. Time-dependent diffusivity captures degradation-enhanced release

Next Steps:
• Validate model predictions with in vitro release studies
• Conduct biocompatibility and stability assessments
• Evaluate tissue penetration depth in ex vivo models
• Optimize loading based on target therapeutic duration

Generated: Model 5 Simulation
Date: October 28, 2025