

Critical Formulation, Foam-Structure, and Performance Attributes of Topical Foams

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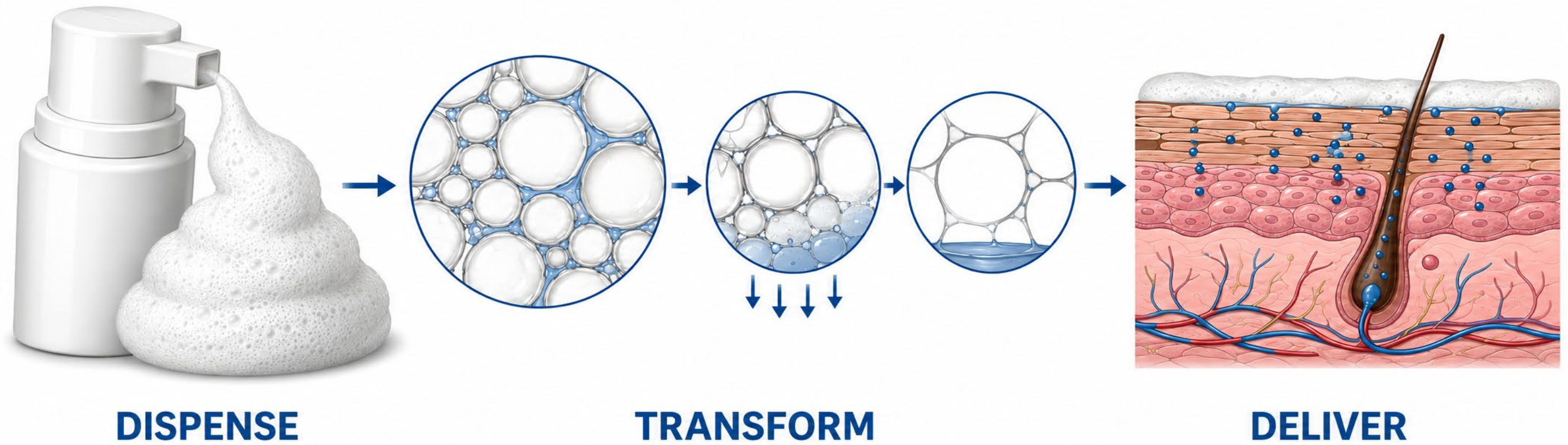
Advancing Generic Drug Development (AGDD) - Sep 10th, 2026
Modernizing Bioequivalence Approaches for Topical & Transdermal Products

Disclaimer

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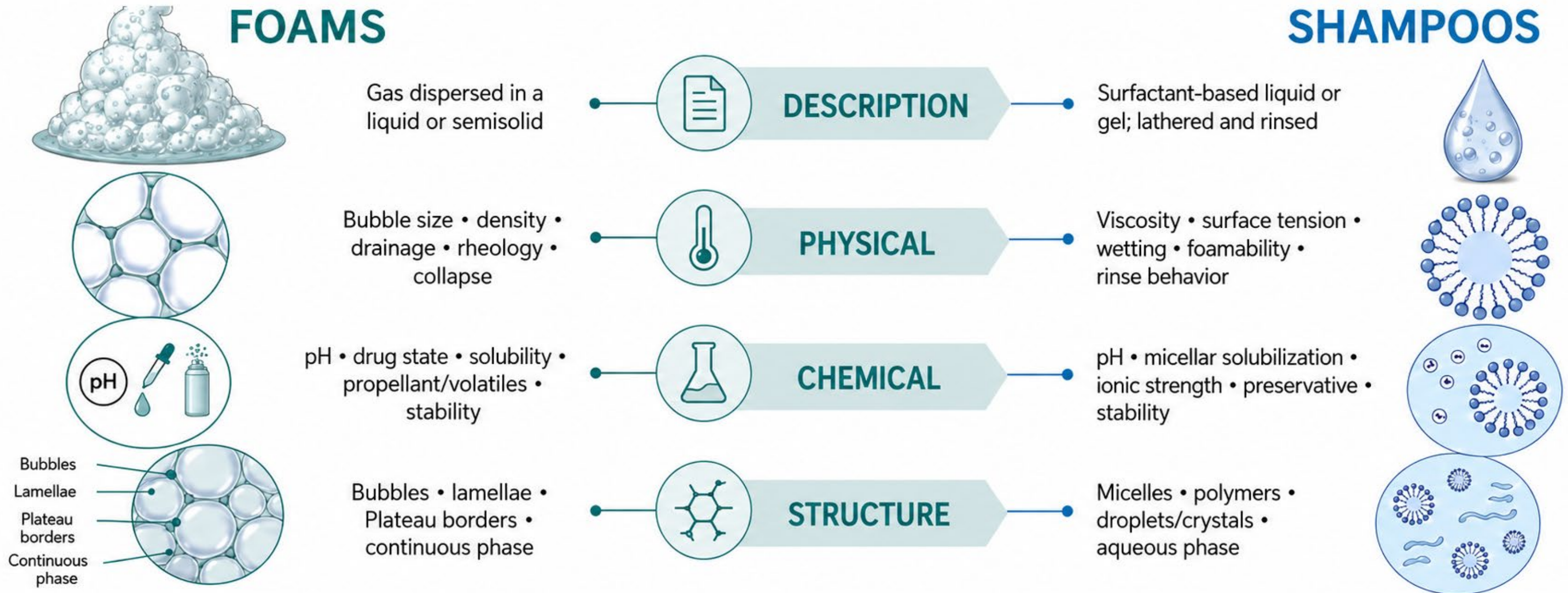
TOPICAL FOAMS

Dynamic dosage forms at the interface of formulation, device, and skin



Foams and shampoos

Attributes that govern topical performance



Foam generation: medicated foams vs medicated shampoos

Different generation mechanisms create different use-state structures and exposure conditions

Medicated foam

Foam generated during dispensing

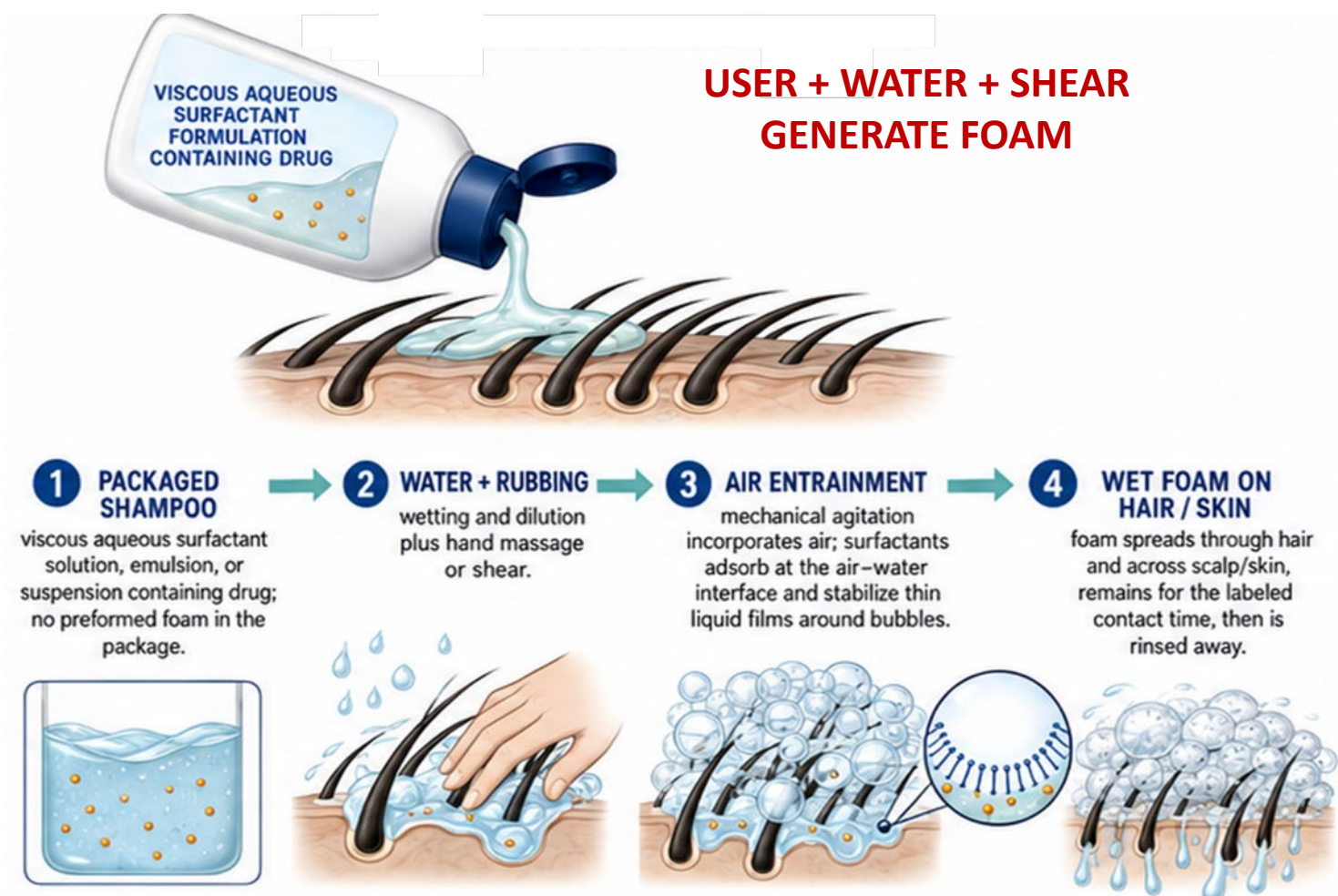
DEVICE / PACKAGE GENERATES FOAM



Medicated Shampoo

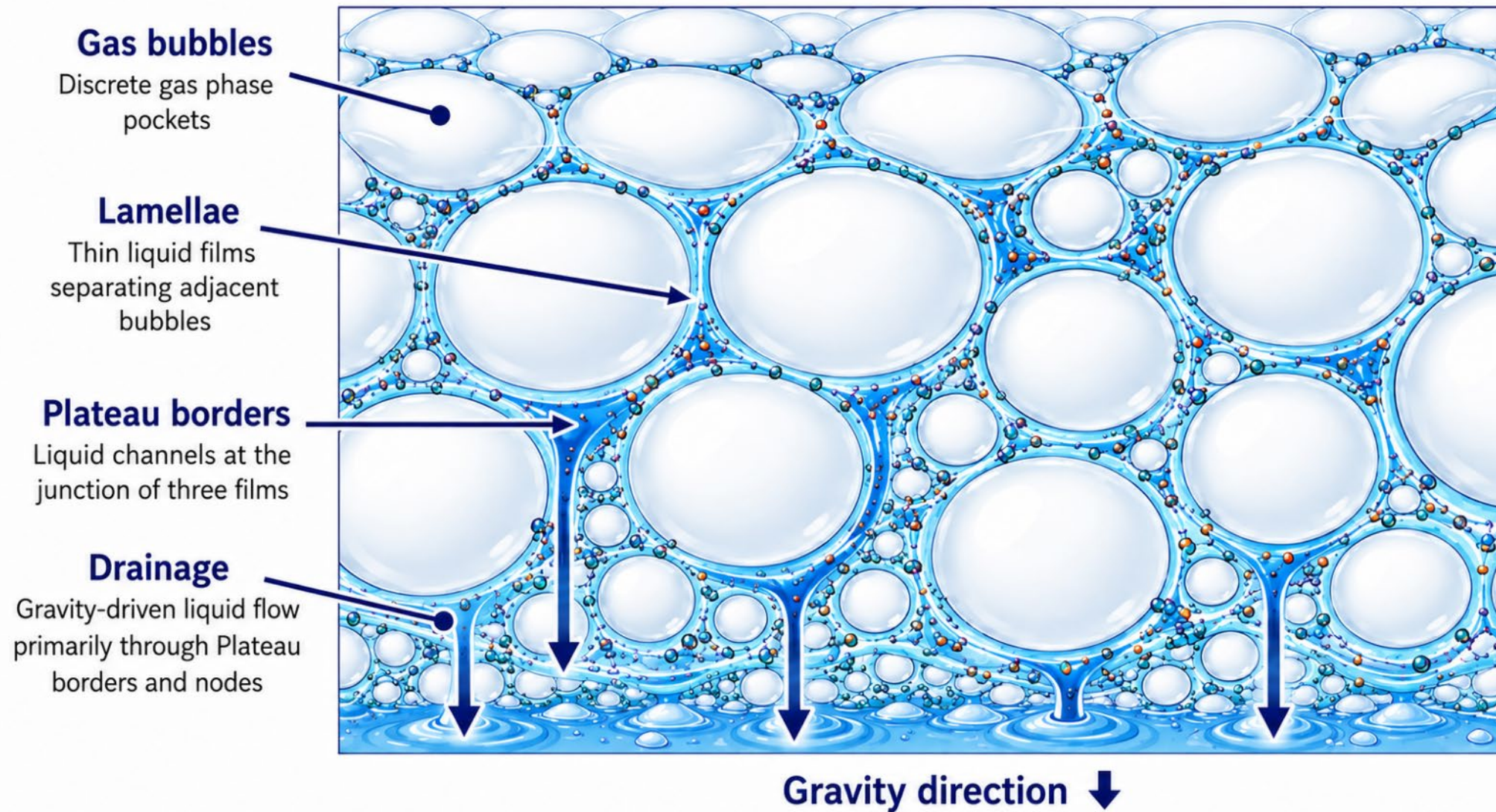
Foam generated in situ during use

USER + WATER + SHEAR GENERATE FOAM

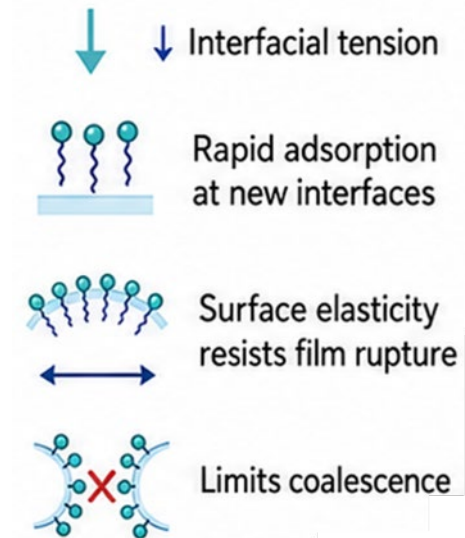


Microstructure and stabilization of topical foams

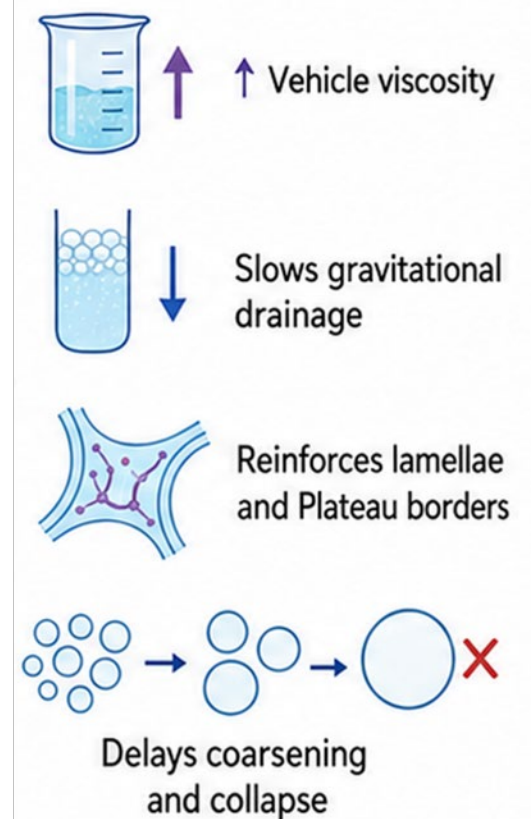
Conceptual foam microstructure (cross-section)



SURFACTANTS — Interfacial stabilization



POLYMERS — Bulk-phase stabilization



Crystals



Solid crystalline particles

Micelles



Self-assembled surfactant aggregates

Oil droplets



Dispersed oil phase droplets

Engineered particles



Designed solid particles (varied size)

Polymer / surfactant structures



Chains, networks, or adsorbed layers

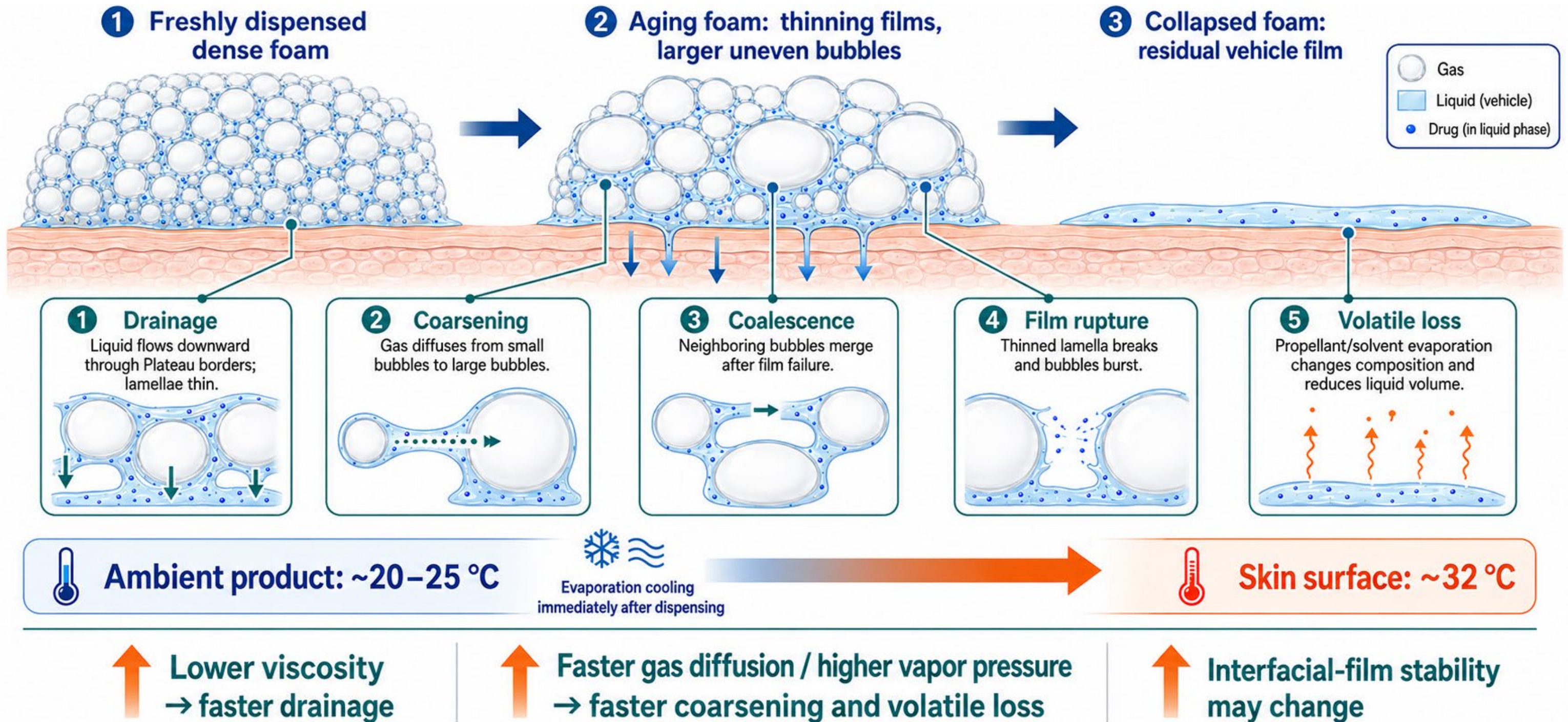
Combinations of these species



Multiple species coexisting

Possible dispersed species within topical foam systems

Mechanisms of topical foam collapse on skin



Net effect is formulation-dependent.

Surfactant redistribution during topical-foam collapse

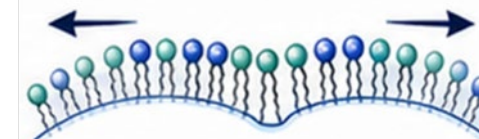
Why mixed surfactants stabilize foam



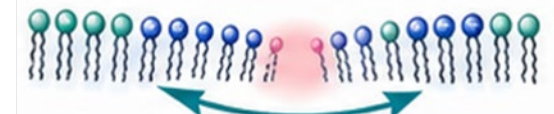
1 Synergistic molecular packing
reduced headgroup repulsion
and fewer interfacial defects.



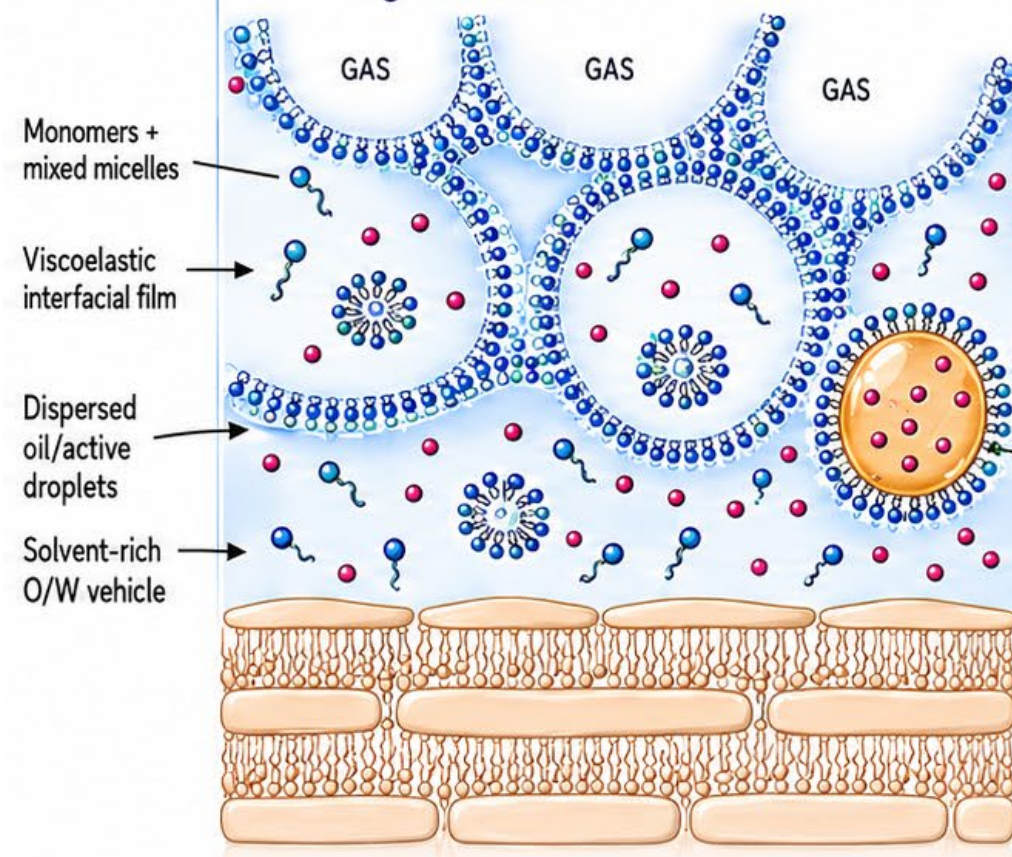
2 Interfacial viscoelasticity
cohesive film resists
deformation and rupture.



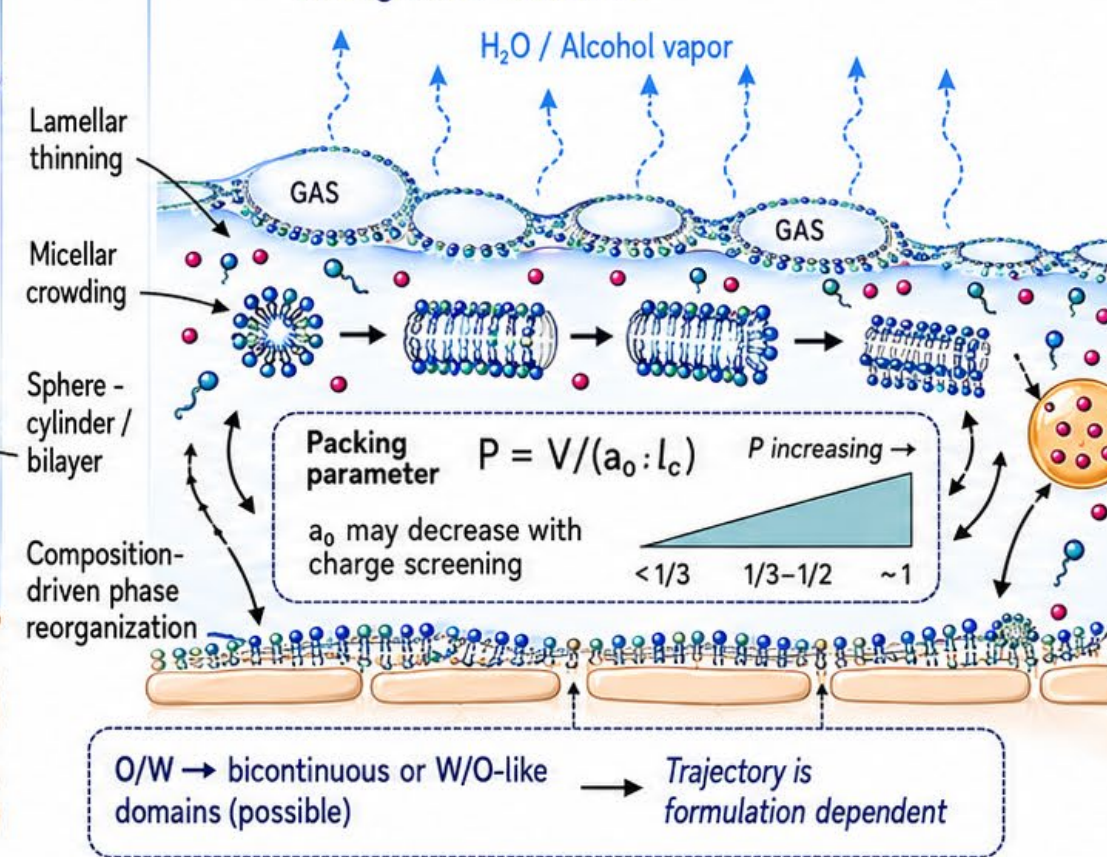
3 Marangoni repair
local surface-tension gradient
drives surfactant toward a
stretched, depleted region.



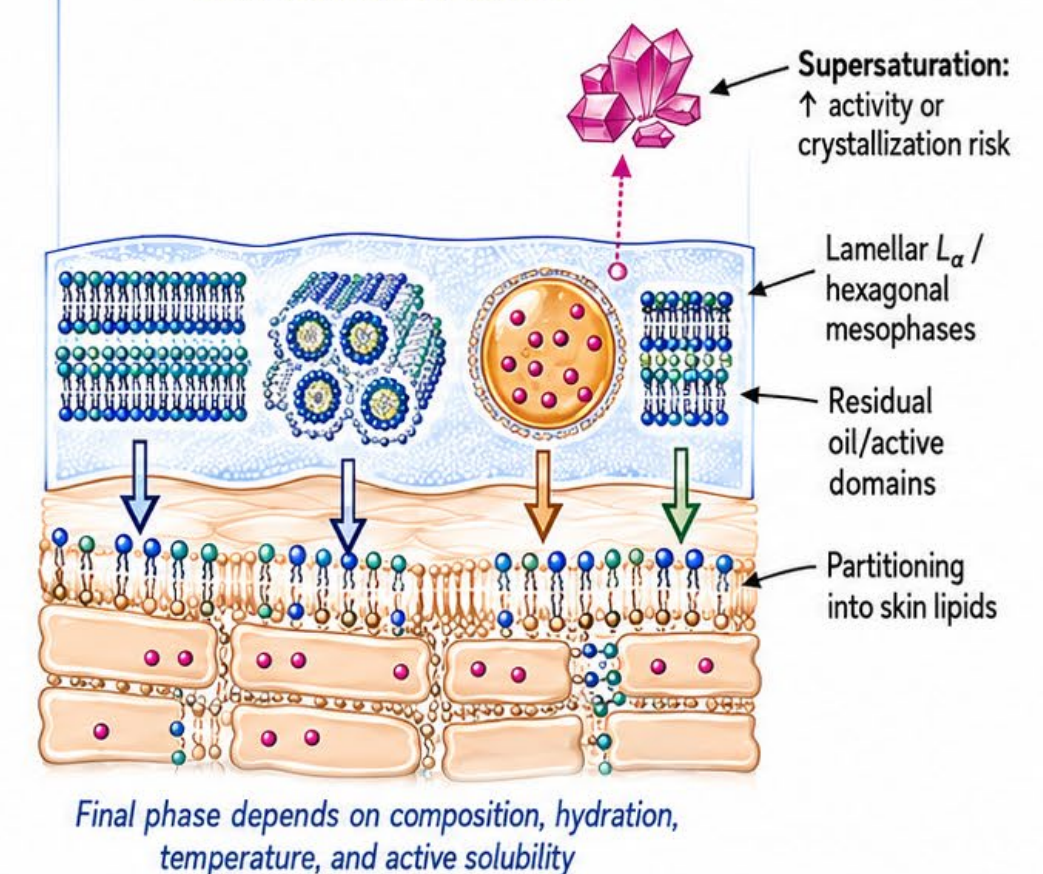
1 DYNAMIC FOAM High solvent volume



2 COLLAPSE + EVAPORATION Falling solvent volume



3 RESIDUAL FILM Ultra-low solvent volume



Solvent evaporation and film formation

Current PSG BE Pathways: Topical Foams and Shampoos

Three product-specific evidence architectures

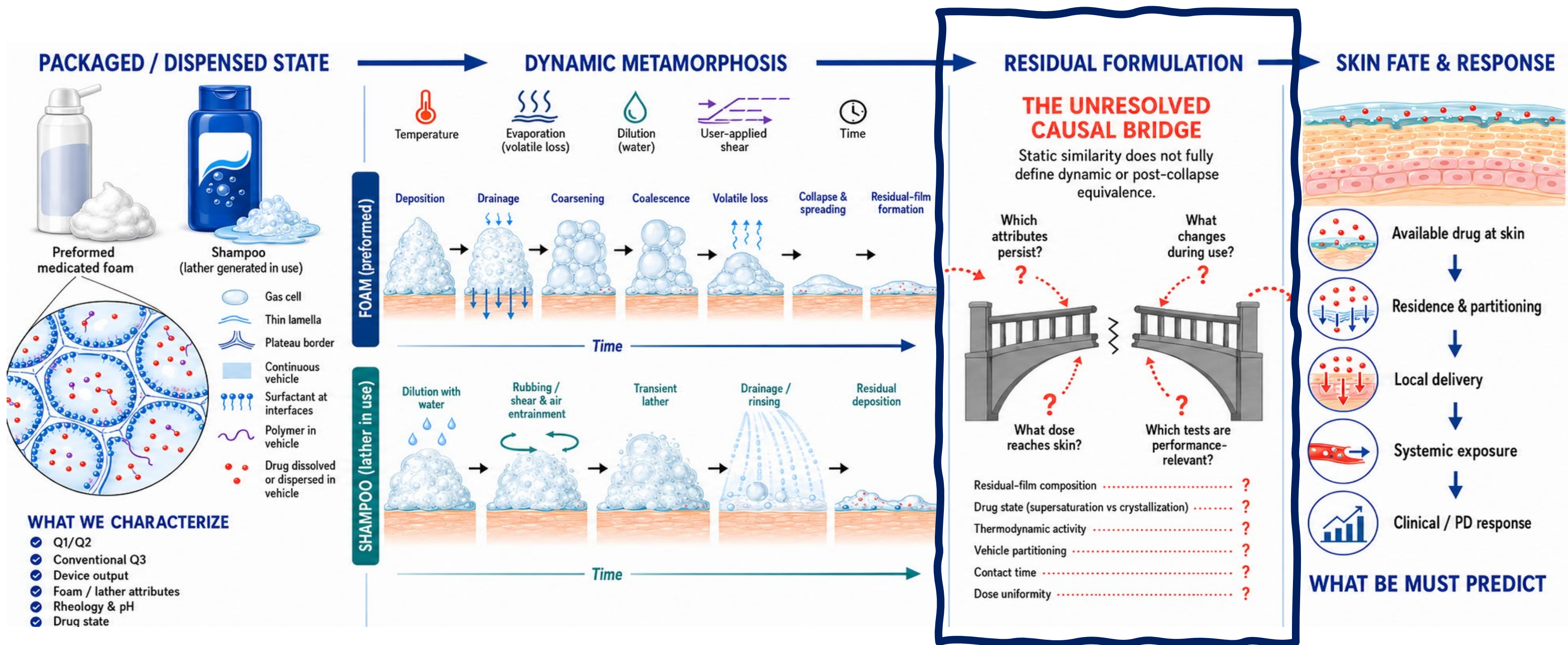
TARGETED WAIVER	CLINICAL / PD	STATE-AWARE IN VITRO
Formulation sameness Targeted use-state tests	Comparative clinical endpoint Vasoconstrictor PD for selected corticosteroids	Q1/Q2 + multi-state Q3 IVRT; IVPT for selected foams
Examples: Ketoconazole, clindamycin, minoxidil, and halobetasol foams; ciclopirox and clobetasol shampoos	Examples: Calcipotriene and tazarotene foams; betamethasone dipropionate/calcipotriene foam; ketoconazole shampoos	Examples: Roflumilast foam 0.3%; ketoconazole shampoos 1% and 2%; selenium sulfide shampoo 2.5%

SELECTED CONTEMPORARY PSG EXAMPLES

	TOPICAL FOAMS	TOPICAL SHAMPOOS
PATHWAY	Roflumilast foam 0.3%	Ketoconazole shampoos 1% and 2%
EVIDENCE	Uncollapsed → Collapsed	Dispensed → Diluted / Lathered → Residual
	Collapsed-state IVRT + IVPT	Multi-state Q3 + IVRT

No universal class-wide pathway — BE evidence remains product-specific.

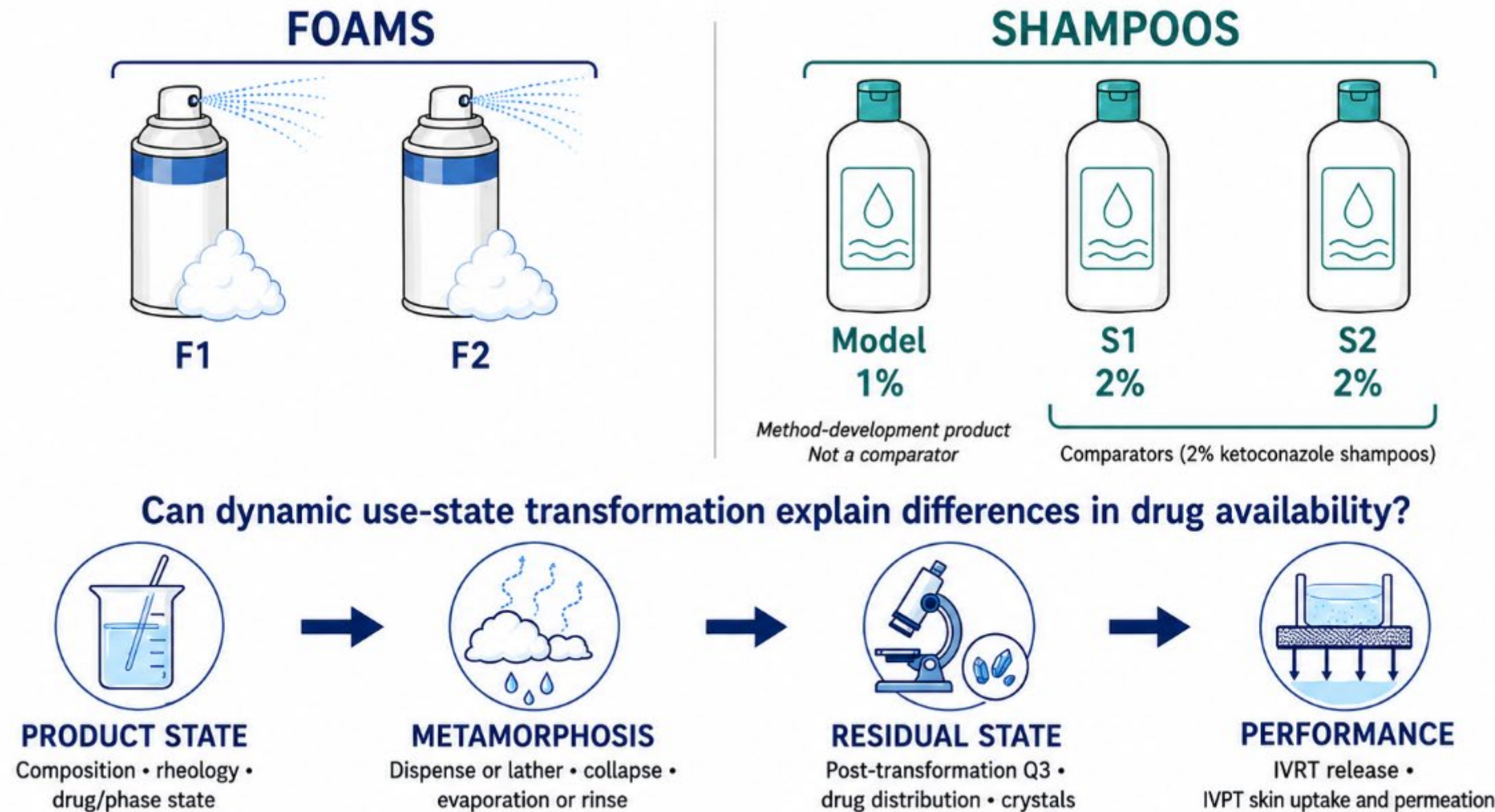
Scientific gap in BE assessment of topical foams and shampoos



The scientific gap is the linkage—not the absence of measurements.

Case-study: Ketoconazole foam and shampoo products

Five model products used to support method development for understanding and in vitro characterization of medicated foams and shampoo-generated foams



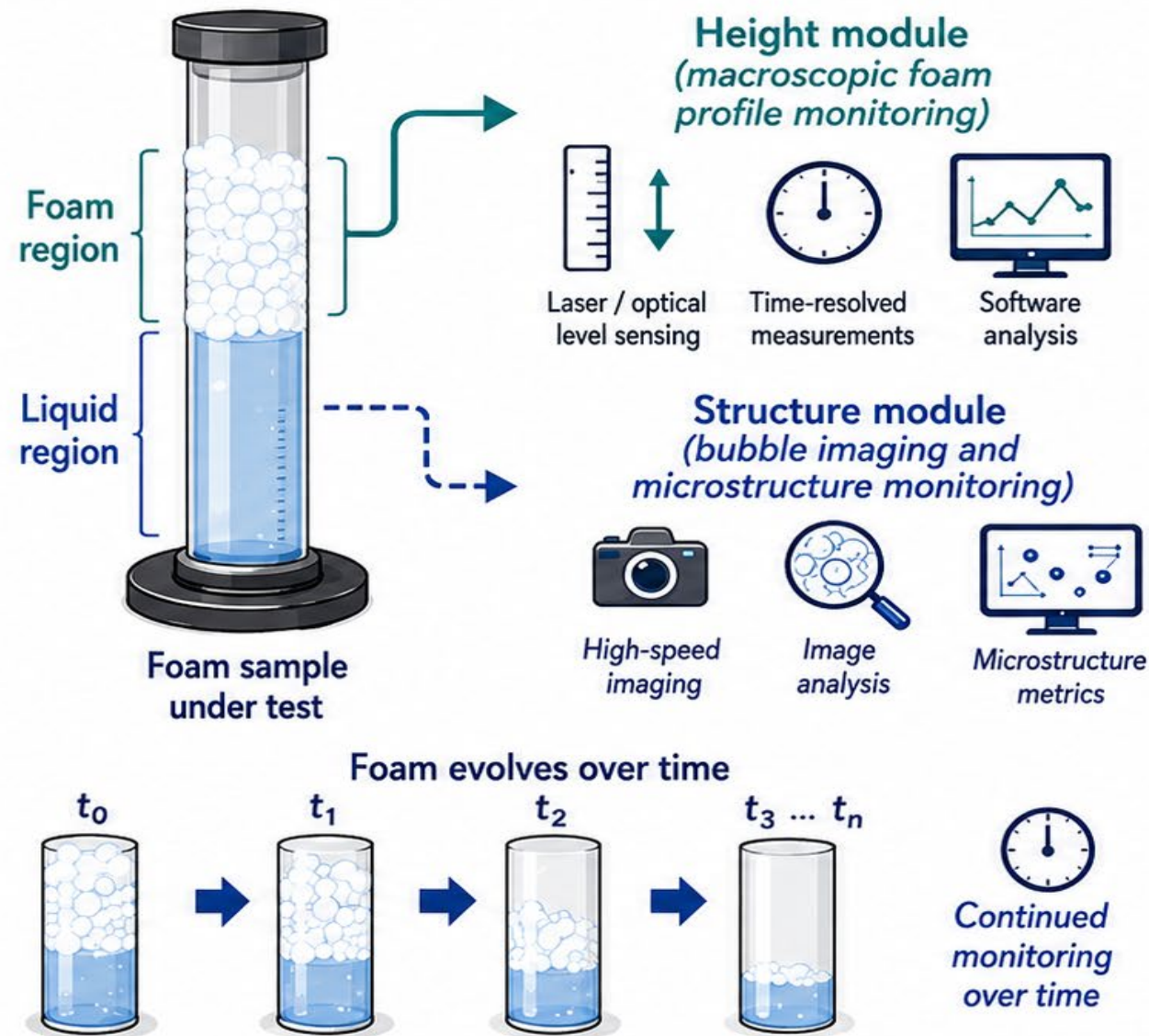
Q CASE-STUDY PURPOSE: Connect measurable transformation and residual-state attributes with comparative *in vitro* performance.

Products are compared within dosage form; foams and shampoos are not cross-dosage-form BE comparators.

Dynamic foam characterization of generated foams

Endpoint mapping based on foam height evolution and foam microstructure evolution

Representative characterization framework for dynamic foam analysis; endpoint availability may depend on the specific instrument setup and study design.



Endpoint Map: Extracted Foam Dynamic Characteristics

Foam evolves over time → Dynamic endpoints are derived from this evolution

A. Height and drainage endpoints

Height module	
	Foam height / foam volume
	Liquid height / liquid volume
	Drainage behavior
	Initial foamability
	Foam stability over time
	Relative foam decay
	Time to break / collapse time
	Drainage half-life
	Weight loss / weight remaining (complementary stability metric)

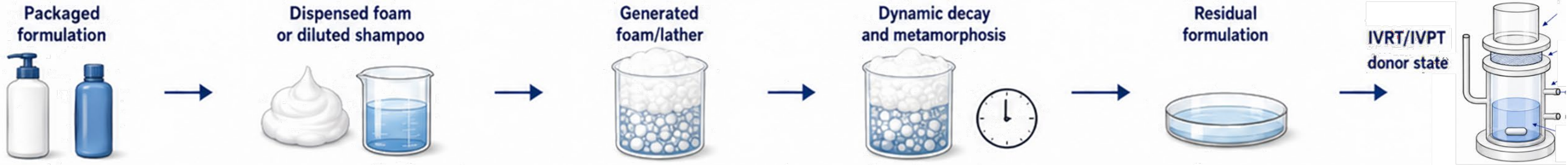
B. Bubble microstructure endpoints

Structure module	
	Bubble count / mm ²
	Mean bubble area
	Average bubble radius
	Bubble-size distribution over time
	Coarsening behavior
	Bubble-count decay
	Bubble-count half-life
	Change in mean bubble area over time
	Change in average bubble radius over time

Integrated dynamic picture of foam evolution (macroscopic + microstructure)

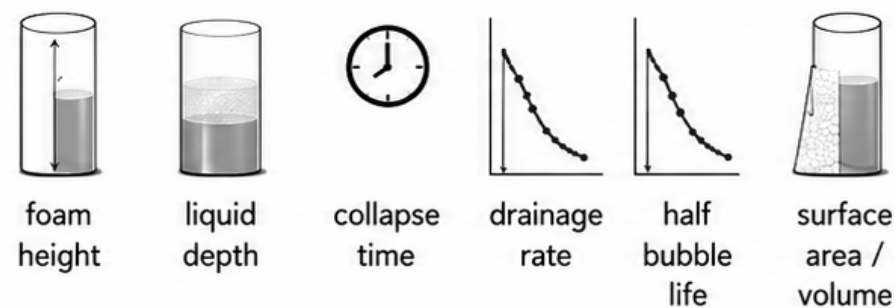
Assessment of foam performance attributes

Complementary tools for understanding microstructure, metastability, and performance-relevant behavior under the tested conditions

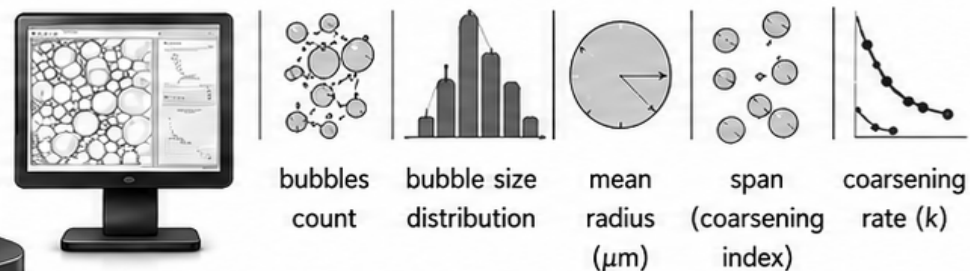


1. Dynamic Foam Analysis

A) Height-based analysis

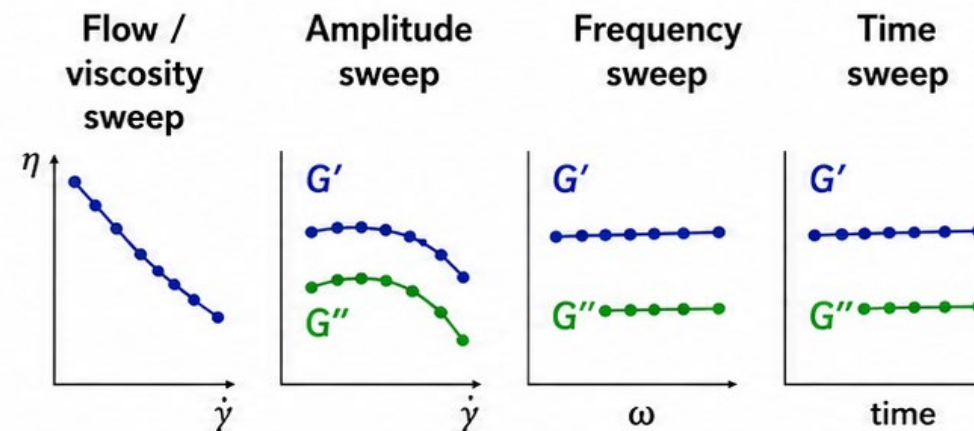


B) Foam Structure Module



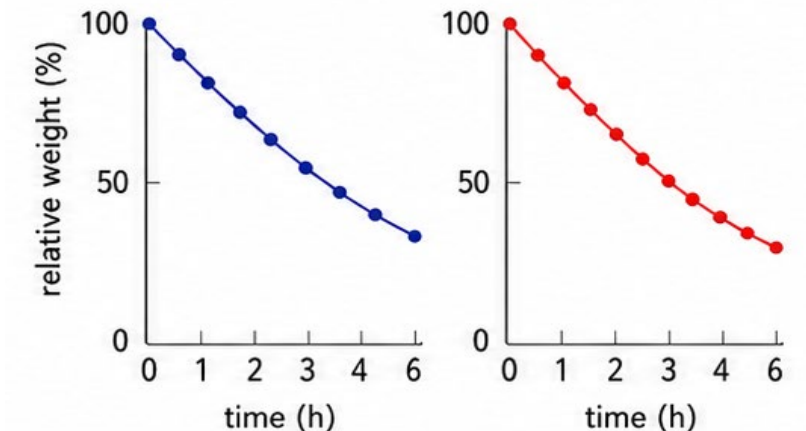
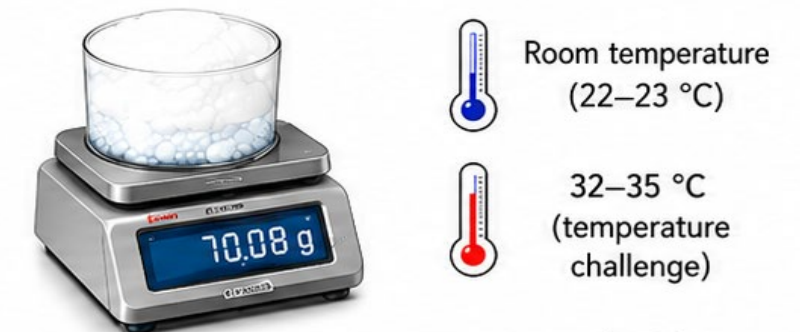
Model system and test conditions: dilution 1:25, 1:100, 1:400
gas flow 1.28, 0.92, 0.59 L/min, pressure 1.56, 1.17, 0.78 psi
test time 15 min, temperature 22–23 °C, volume 15 mL

2. Rheology Assessment



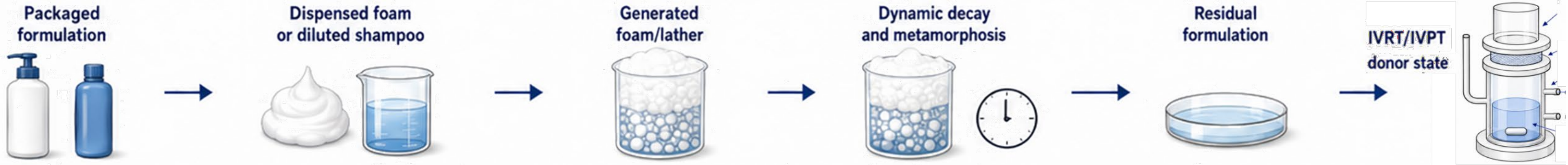
- 25 mm sand-blasted parallel-plate Peltier geometry; 1000 μm gap; 22–23 °C
- **Flow sweep:** $\dot{\gamma}$ shear rate 0.0001–10 s^{-1}
- **Amplitude sweep:** 1 Hz; strain 0.01–100%
- **Frequency sweep:** strain 0.1%; angular frequency 0.1–100 rad/s
- **Time sweep:** 1 Hz; strain 0.1%; duration 15 min

3. Foam Weight Loss and Metamorphosis



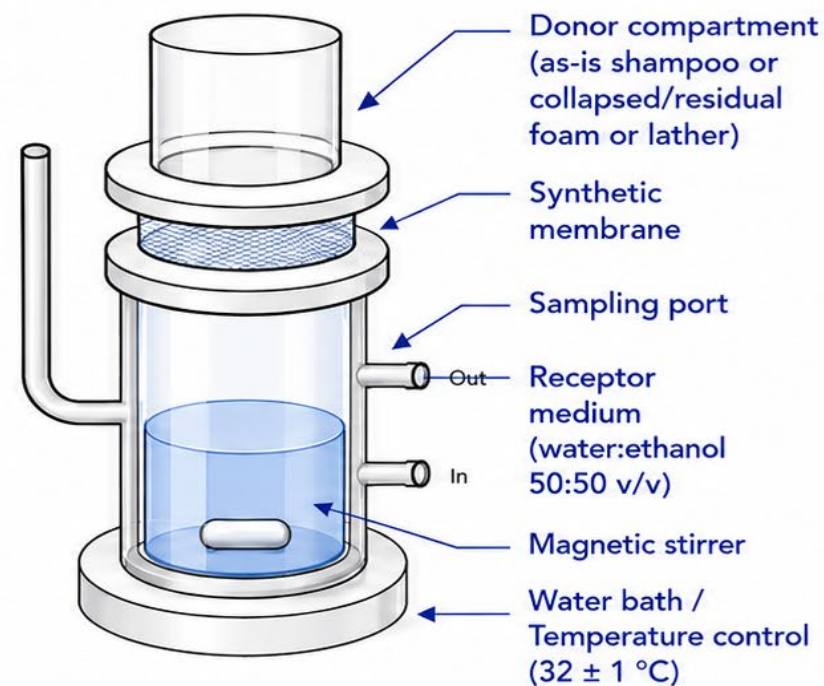
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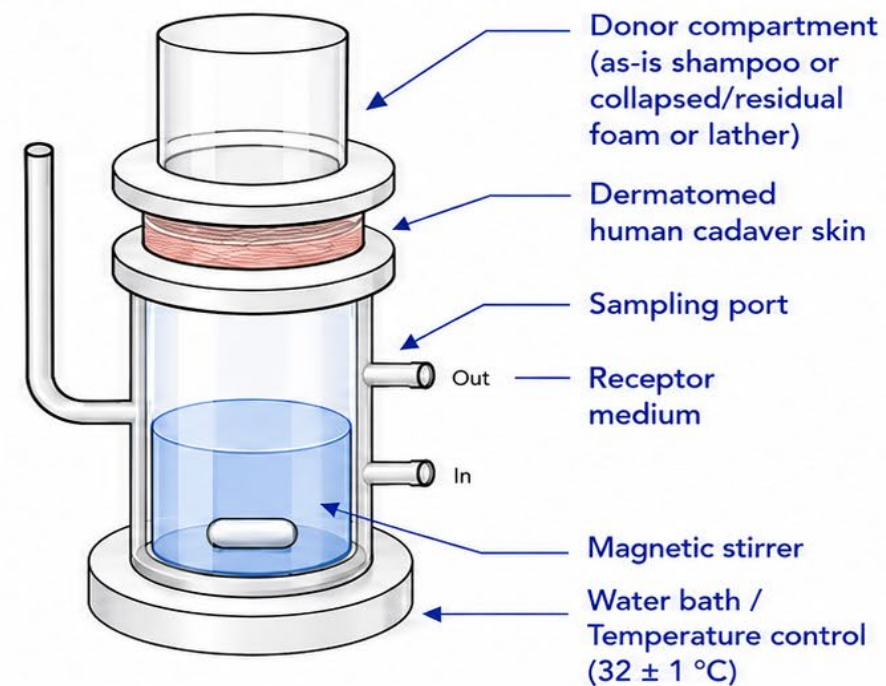
4. In Vitro Release Testing (IVRT)

Franz vertical diffusion cell assembly with synthetic membrane separating donor and receptor compartments.



5. In Vitro Permeation Testing (IVPT)

Franz vertical diffusion cell assembly with dermatomed human cadaver skin separating donor and receptor compartments.



Why conventional IVRT/IVPT requires a post-metamorphosis donor state?

Fresh foam and shampoo lather are transient gas-liquid structures-not stable, reproducible donor doses



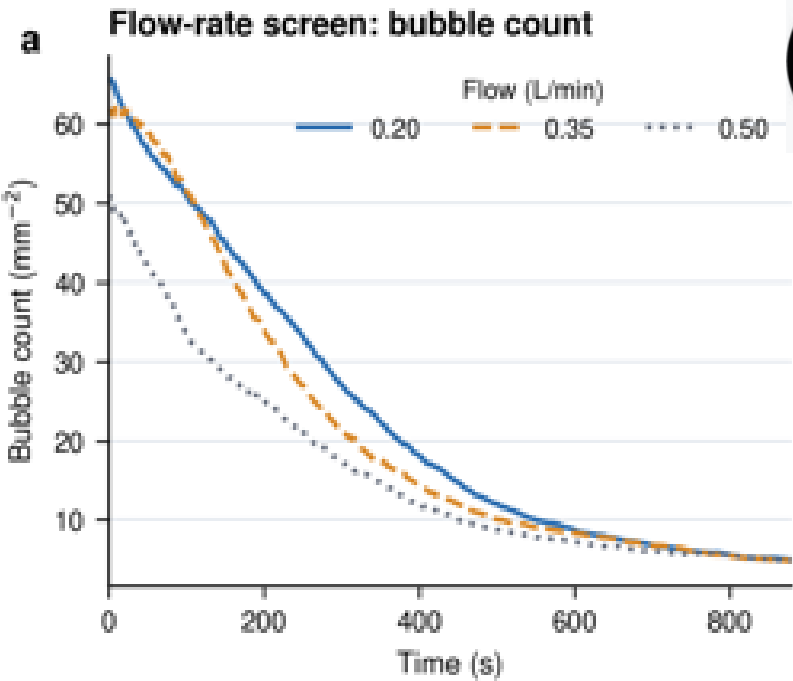
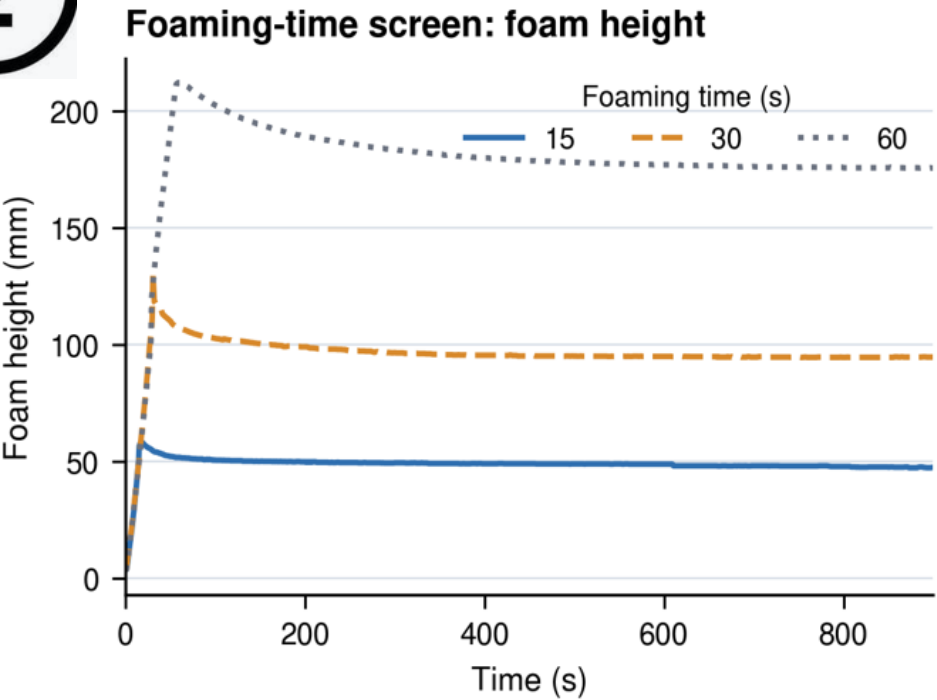
Foam columns collapsed at 32°C over time

Model shampoo: integrated results from foam analysis and IVRT

Foaming
time

2

1% ketoconazole model shampoo / method development and use-state residual release behavior



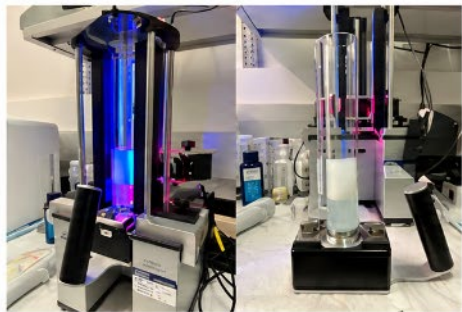
3

Sparging gas
flow rate

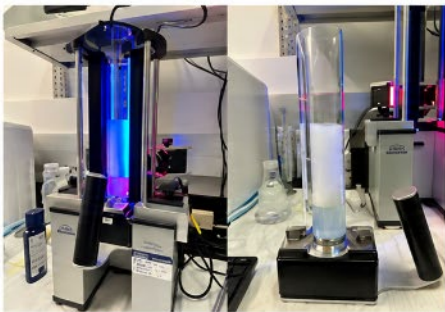
Foaming
time

2

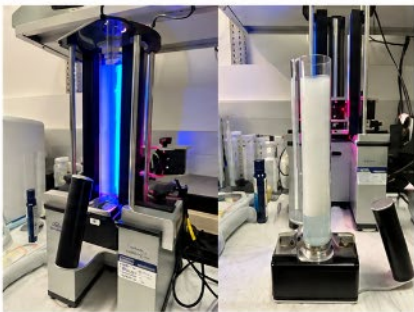
Effect of foaming time on foam and liquid heights



Foaming time = 15 seconds



Foaming time = 30 seconds

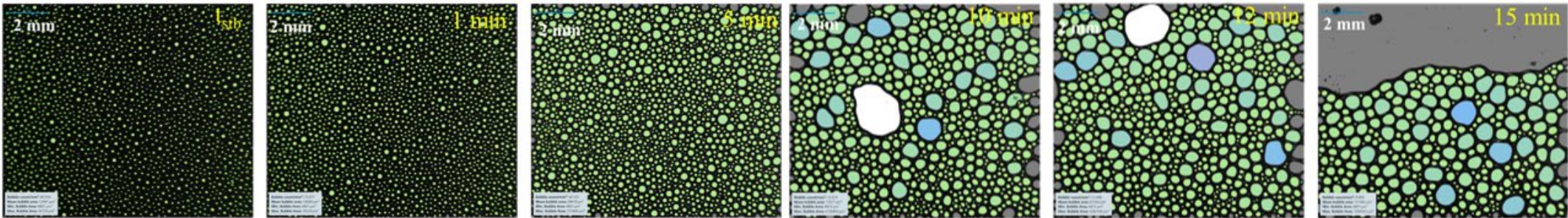
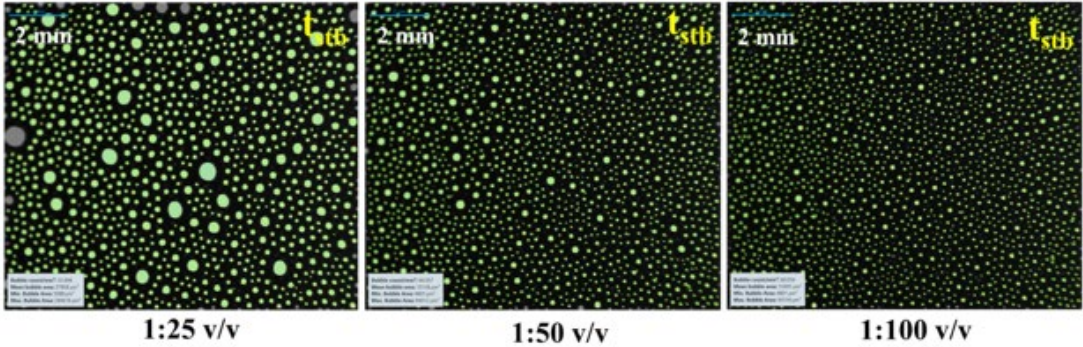


Foaming time = 60 seconds

Dilution

1

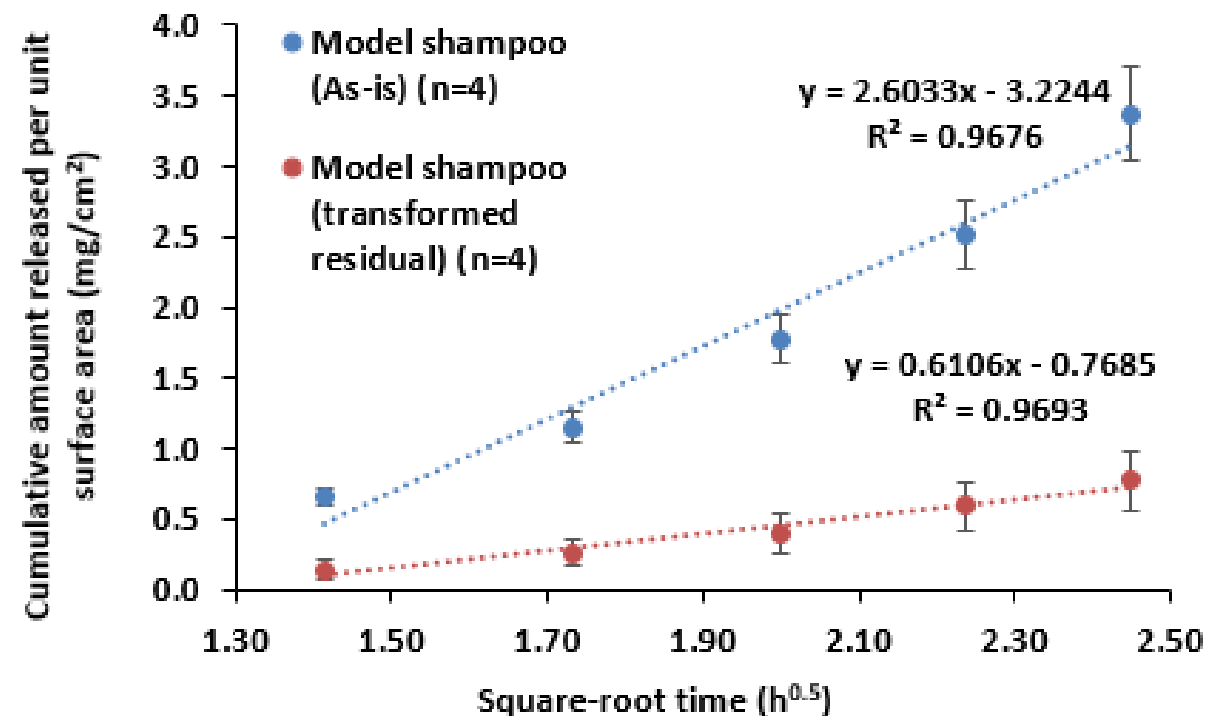
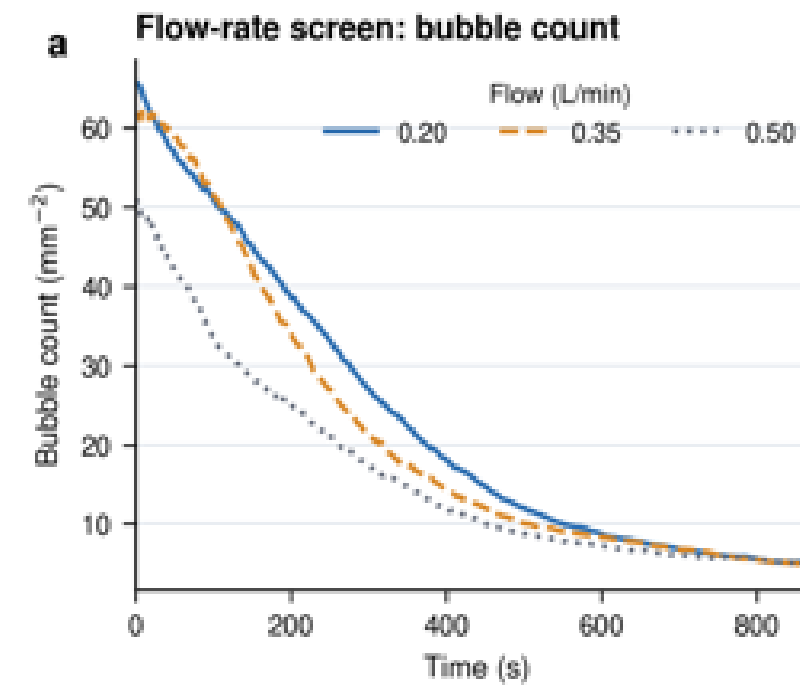
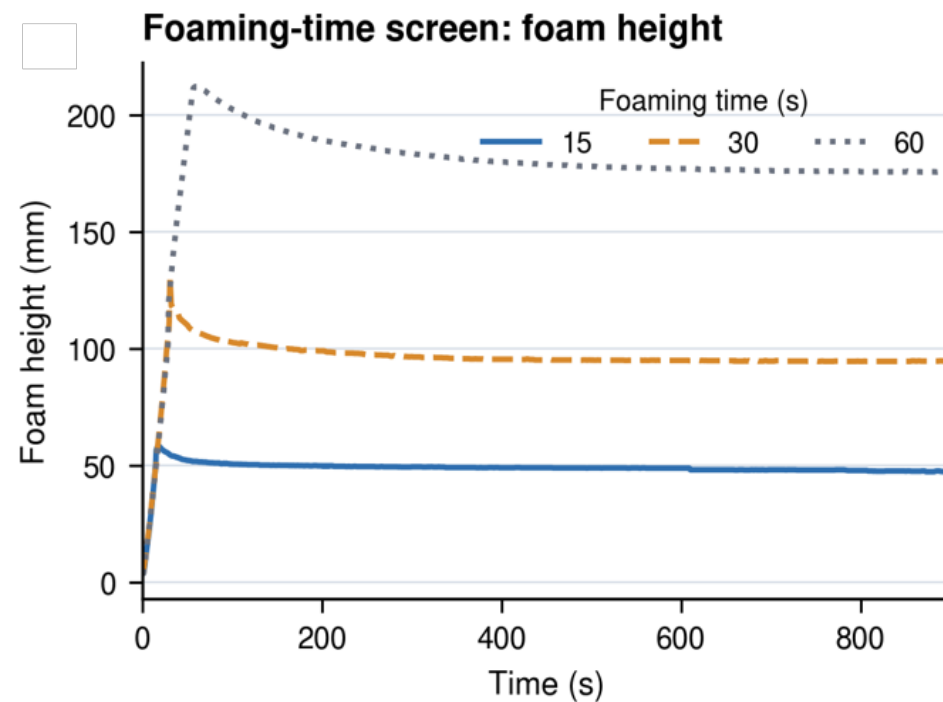
Effect of dilution on bubble size distribution



Foam collapse images over 15
minutes at 1:100 v/v dilution and foamed
by air flow rate of 0.20 L/min for 30 seconds.

Model shampoo: integrated results from foam analysis and IVRT

1% ketoconazole model shampoo / method development and use-state residual release behavior



2.603 ± 0.272

AS-IS SLOPE
n=4 • CV 10.4%

The intact polymer–surfactant structure can distribute ketoconazole among aqueous, micellar, polymer-associated, and structured domains.

0.611 ± 0.150

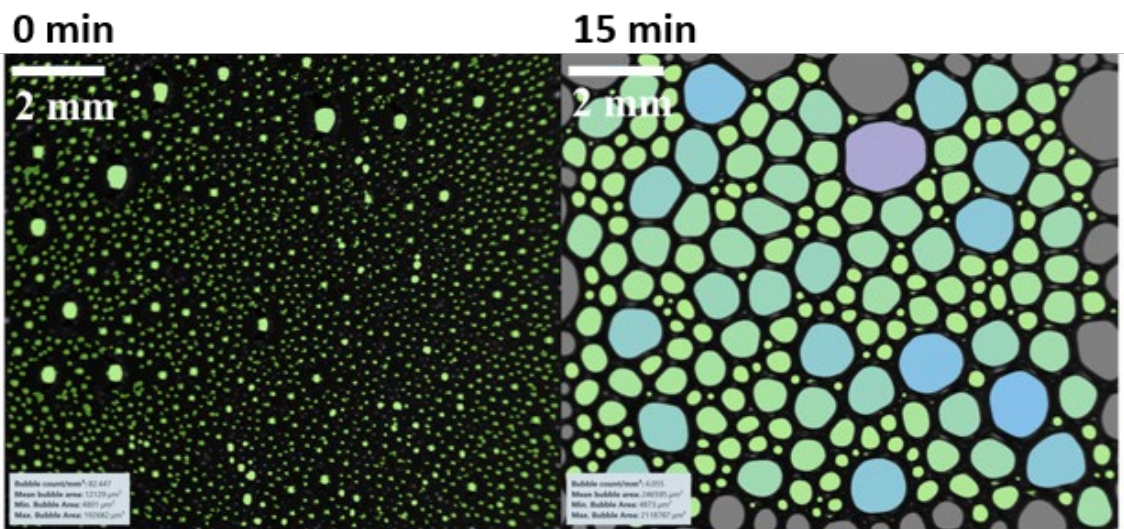
RESIDUAL SLOPE
n=4 • CV 24.6%

Dilution and collapse can reorganize micelles and polymer accessibility. The raw slope ratio is 0.235; dose-normalized interpretation remains exploratory.

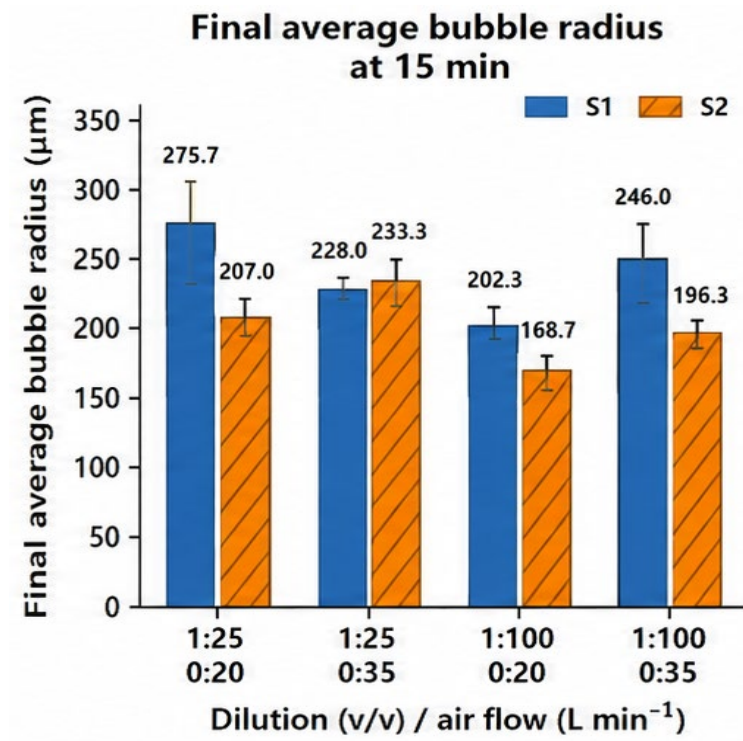
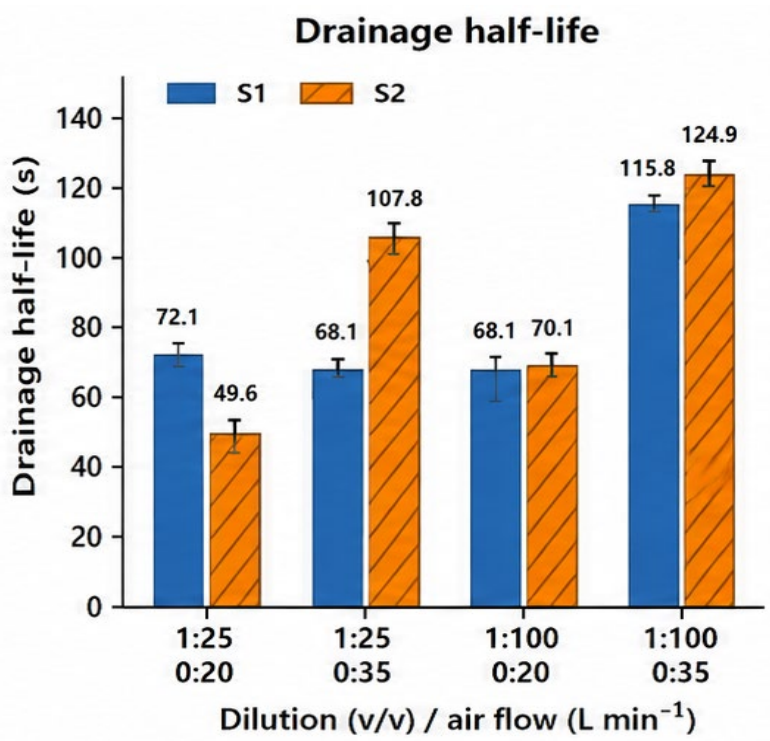
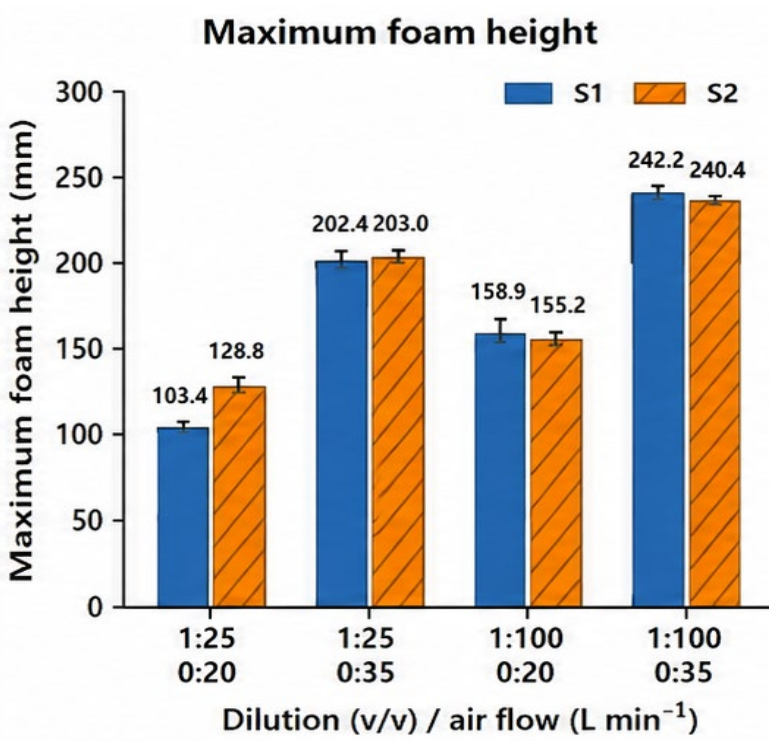
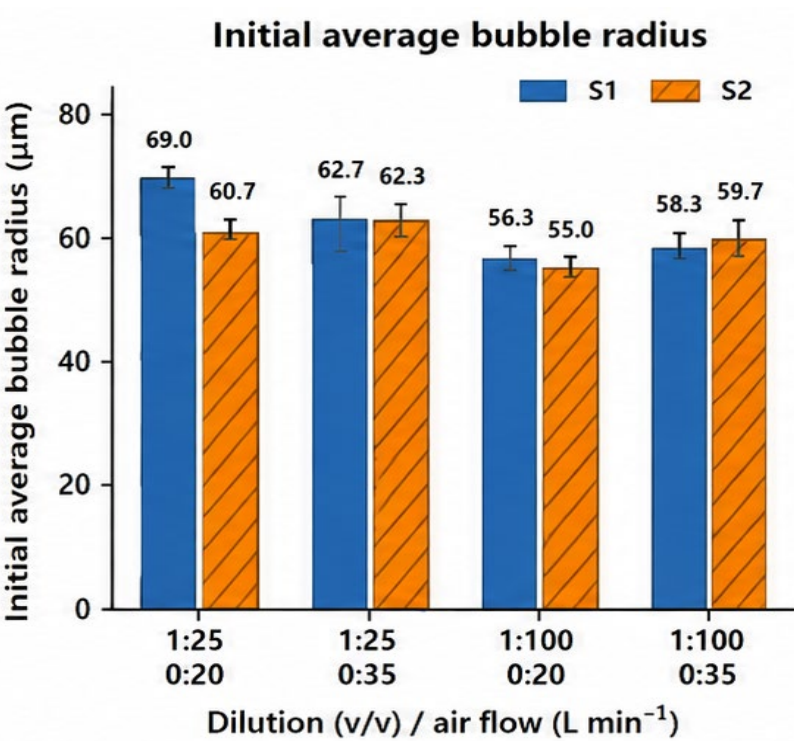
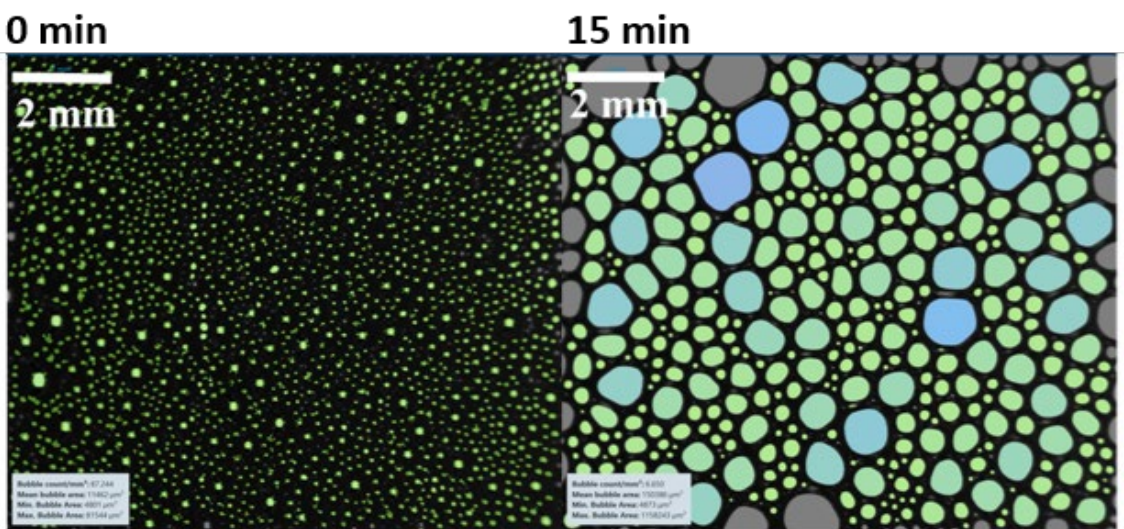
Shampoo products S1 and S2: results of foam analysis, rheology, and IVRT

2% ketoconazole shampoos / Q1, Q2, and Q3 different formulations / foaming behavior, flow properties, and residual-formulation release

Foam of shampoo S1

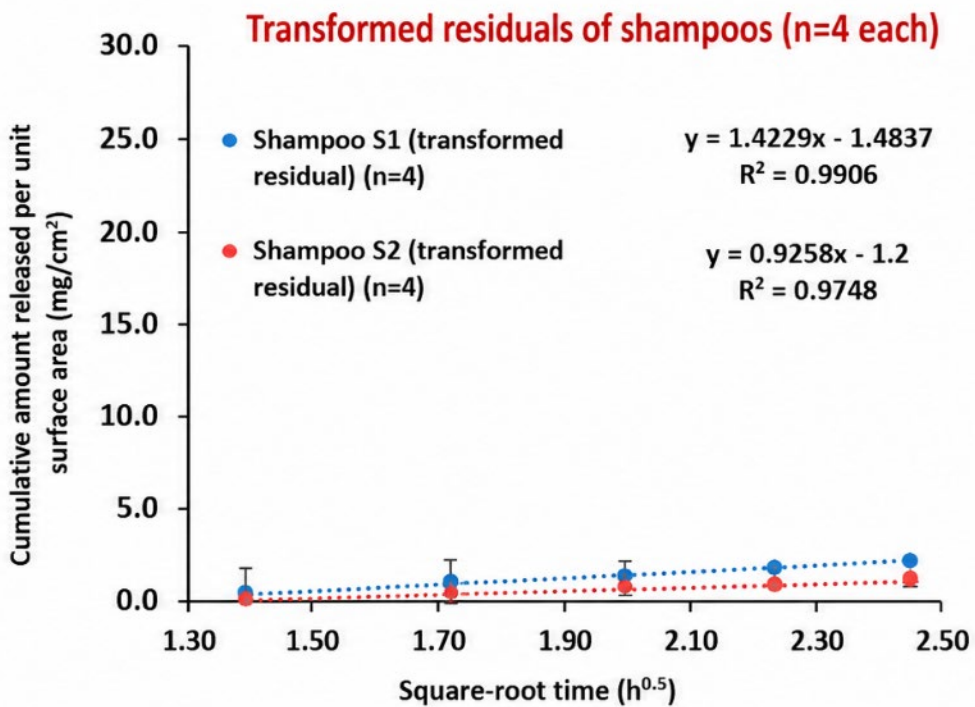
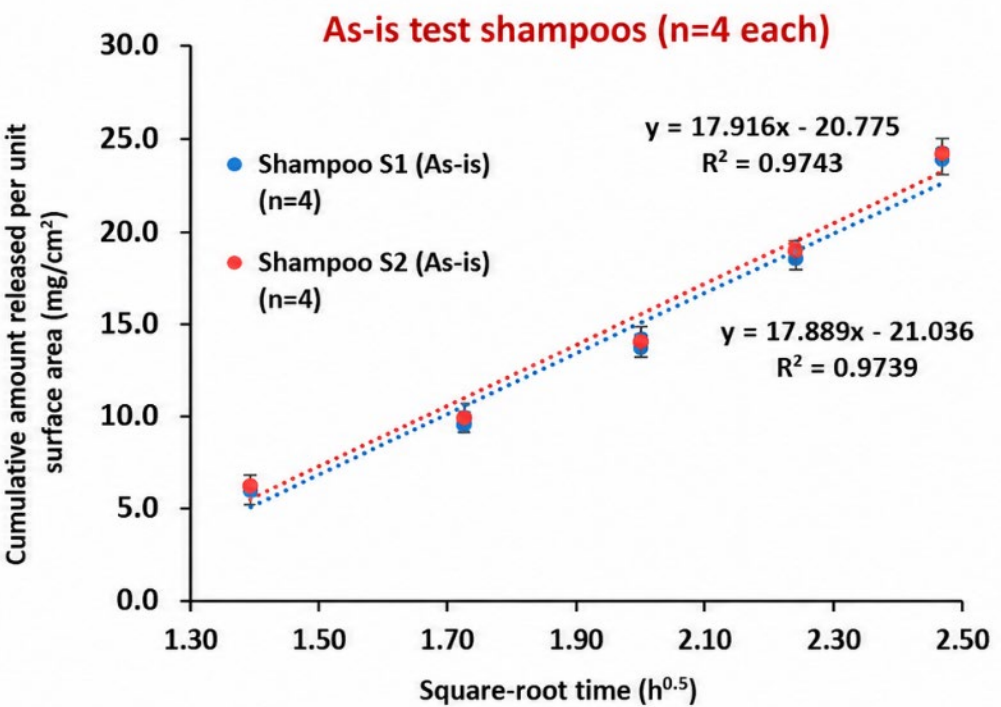
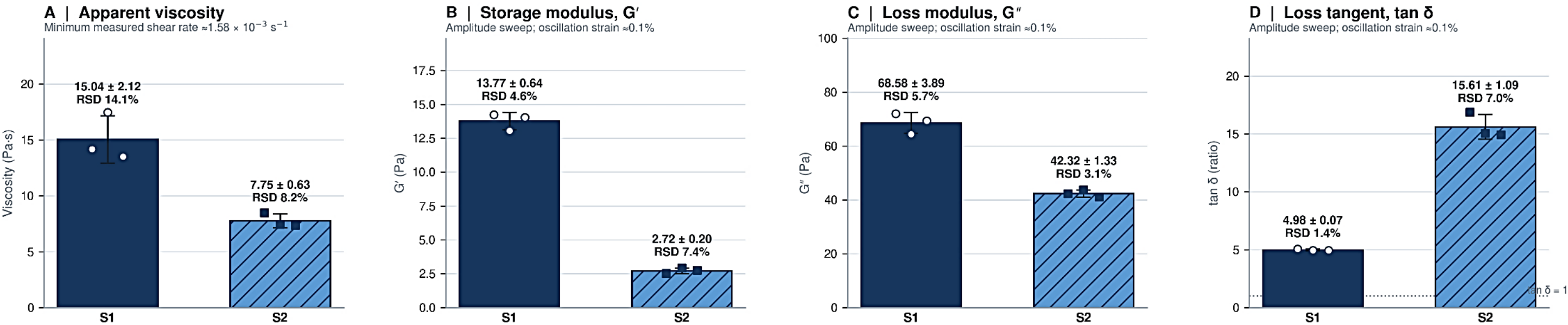


Foam of shampoo S2



Shampoo products S1 and S2: results of foam analysis, rheology, and IVRT

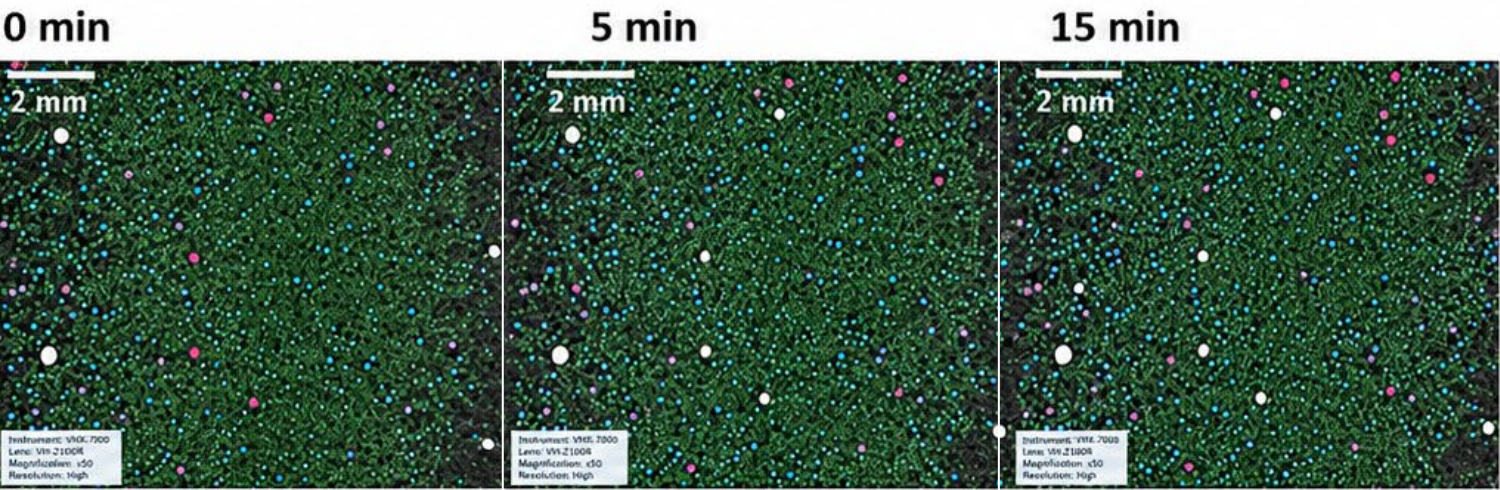
2% ketoconazole shampoos / Q1, Q2, and Q3 different formulations / foaming behavior, flow properties, and residual-formulation release



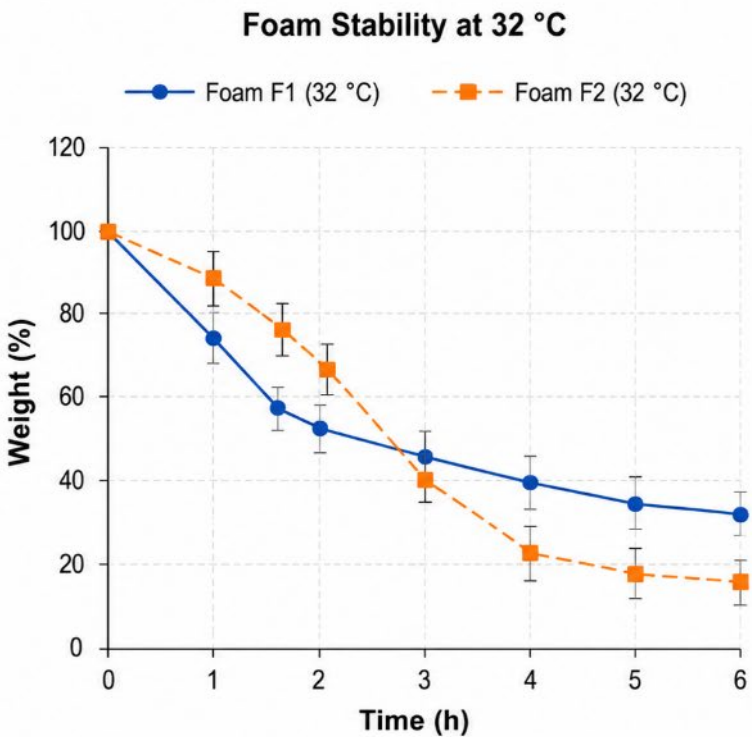
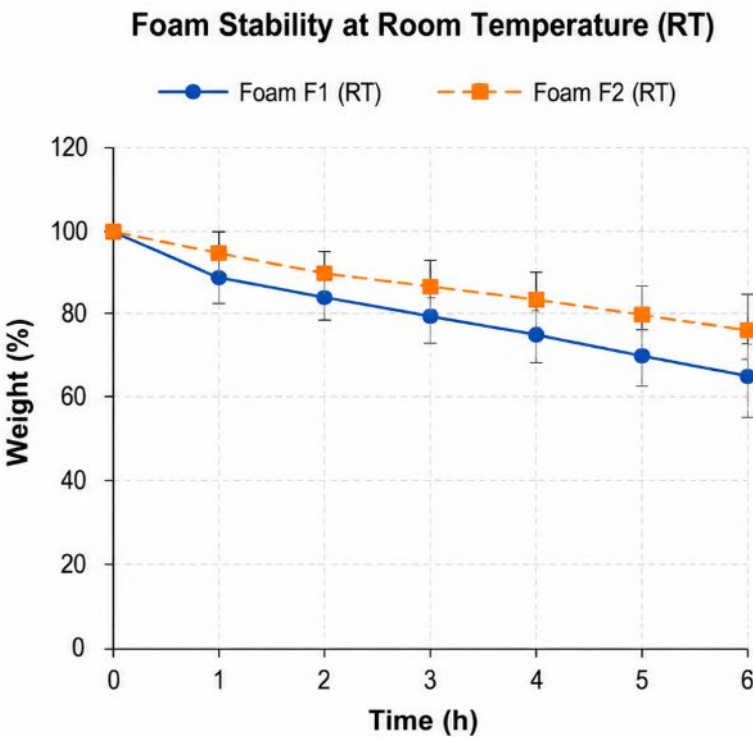
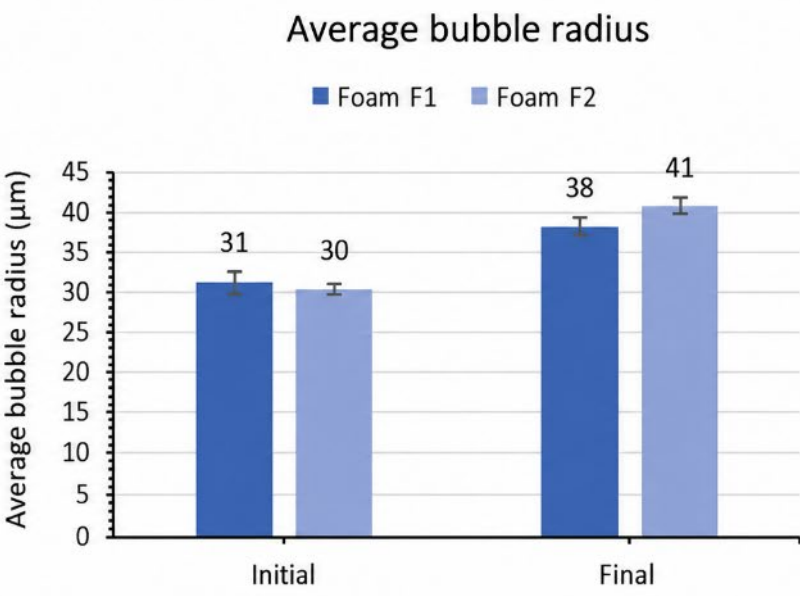
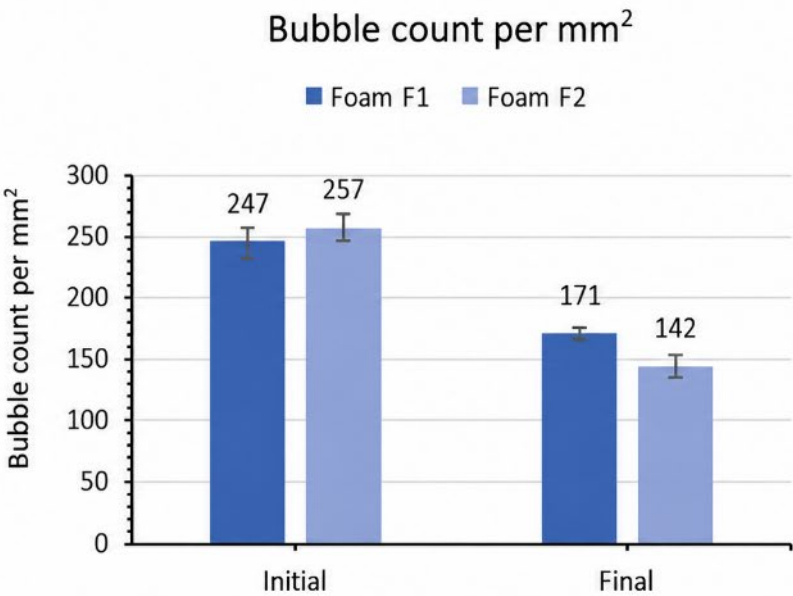
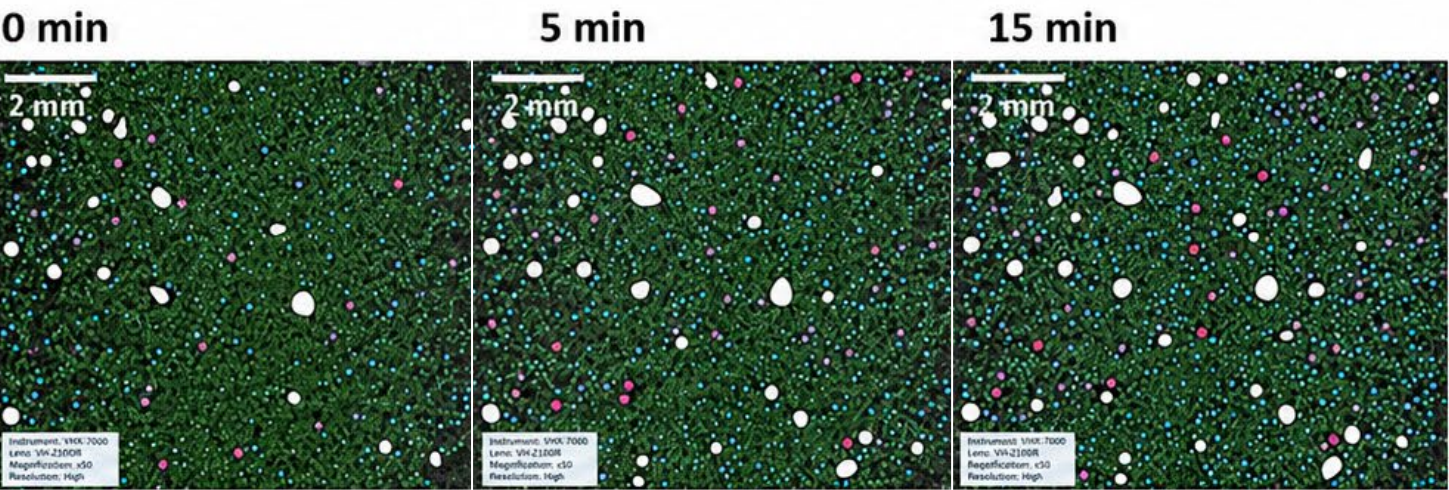
Foam products F1 and F2: results of foam analysis, rheology, and IVRT

2% ketoconazole foams | Q1, Q2, and Q3 similar formulations | dispensed-foam microstructure, decay behavior, flow properties, and residual-formulation release

Foam F1

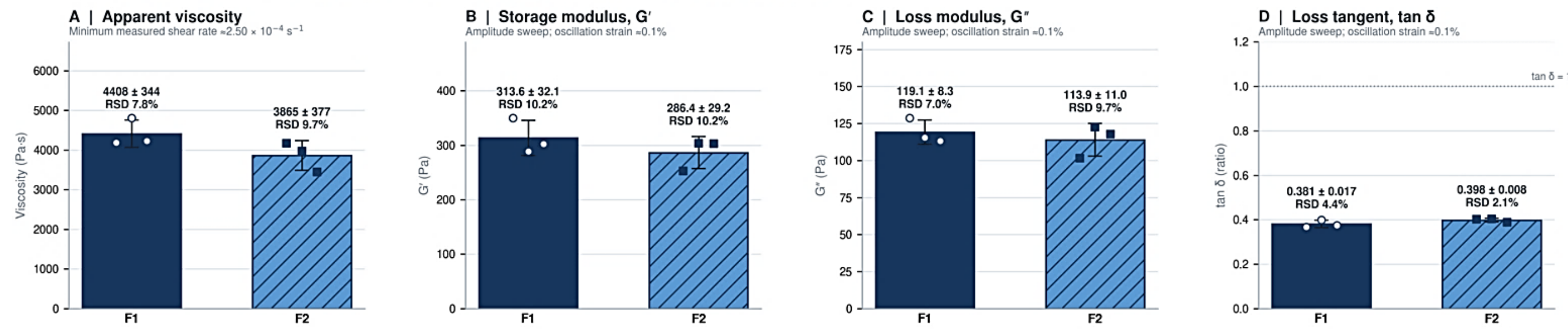


Foam F2

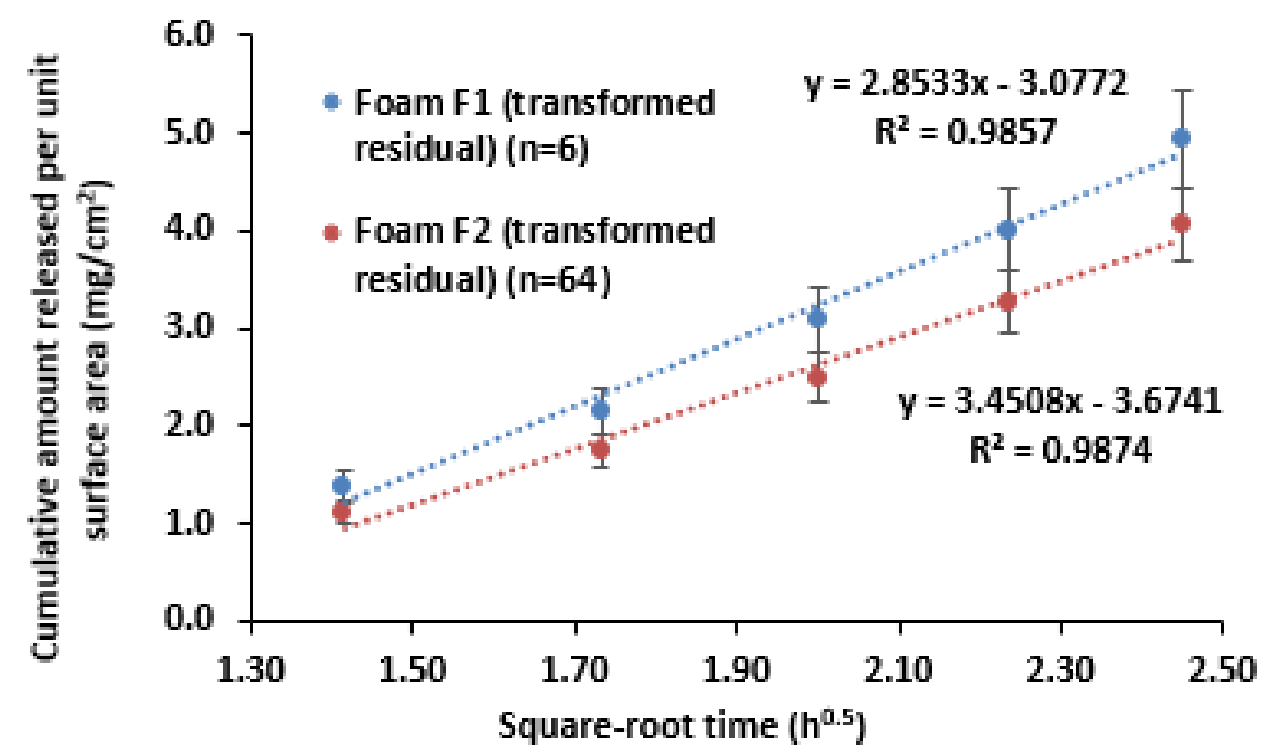


Foam products F1 and F2: results of foam analysis, rheology, and IVRT

2% ketoconazole foams / Q1, Q2, and Q3 similar formulations / dispensed-foam microstructure, decay behavior, flow properties, and residual-formulation release



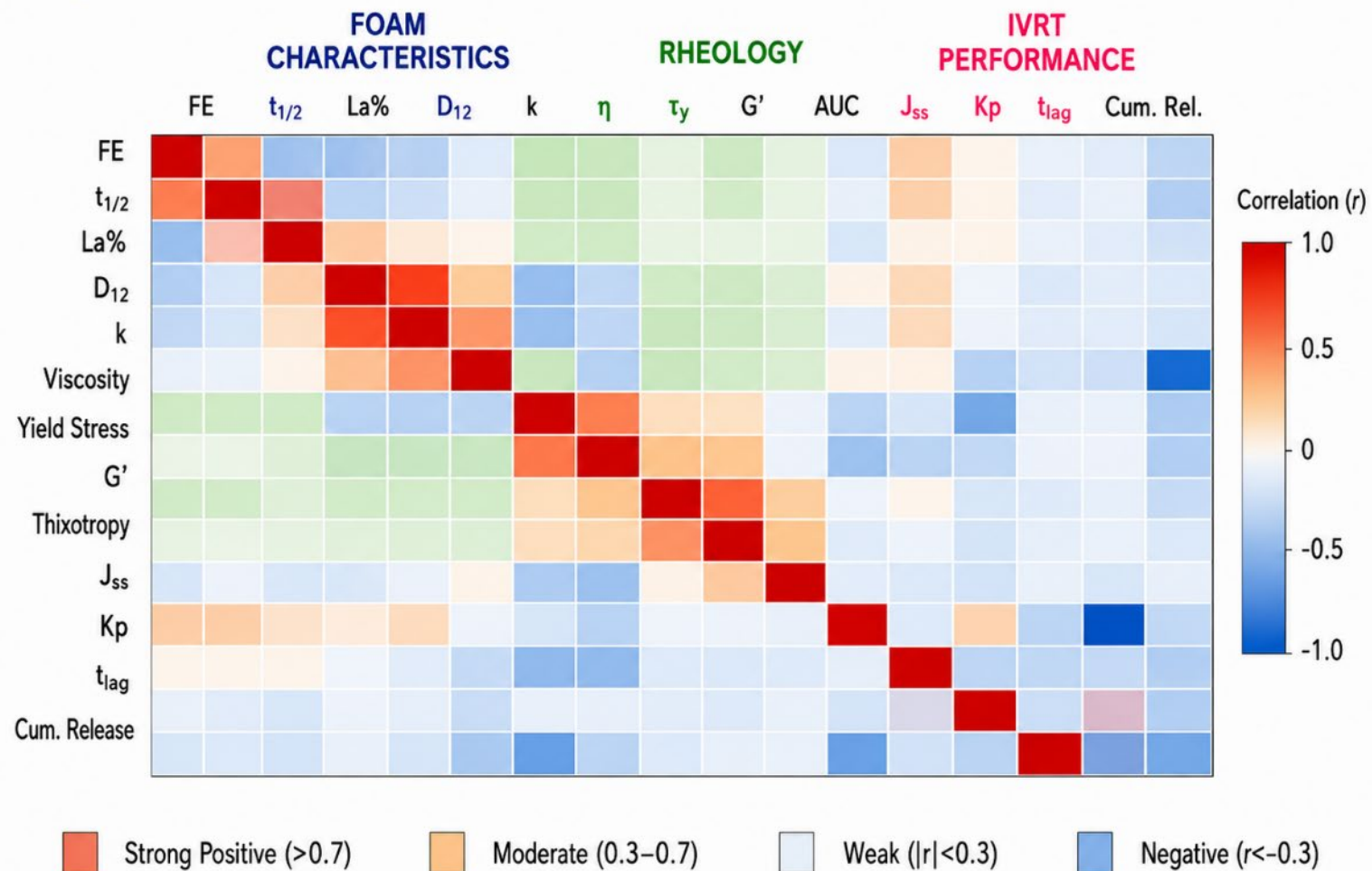
Transformed residuals of Foams (n=6 each)



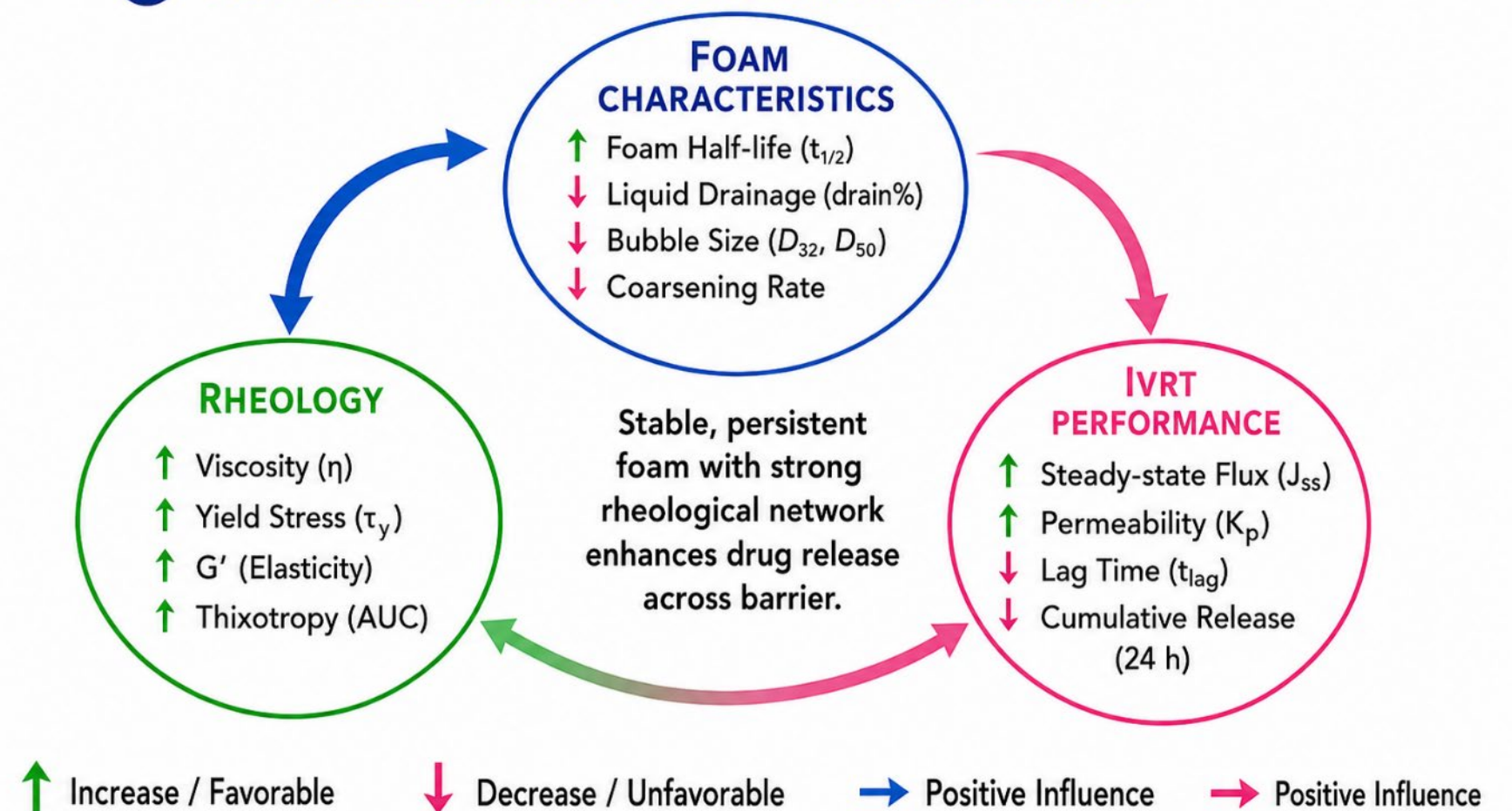
Integrated foam performance profile

*Linking Foam Characteristics, Rheology and In Vitro Release (IVRT)
Comprehensive Data Interpretation, Relationships and Regulatory Implications*

4 RELATIONSHIPS BETWEEN DATA SETS (Correlation Heatmap)



5 KEY RELATIONSHIPS & MECHANISTIC LINKS



TAKE-HOME MESSAGE

For topical foams and shampoo-generated foams, the critical question is not only whether formulations appear similar at the packaged state, but whether the generated foam and post-collapse residual state behave similarly in ways that are relevant to **drug release and skin delivery**.

A MULTI-STATE, MECHANISTICALLY INFORMED EVALUATION IS ESSENTIAL

1. Dynamic foam behavior

Foamability, drainage, coarsening, and collapse matter.

2. Residual state matters

The post-collapse donor can govern release performance.

3. Orthogonal tools

DFA, rheology, and IVRT provide complementary insight.

4. Integrated evidence

Multi-dimensional profiling supports stronger mechanistic interpretation.

5. Regulatory relevance

Supports future performance-based assessment frameworks.

ACKNOWLEDGMENTS



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Thank You

Q&A