Using Rheology to Characterize Flow and Viscoelastic Properties of Hydrogels, Adhesives and Biopolymers

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Outline

- Basics in Rheology Theory

- TA Instruments Rheometers and DMAs
  - Instrumentation
  - Test methodologies

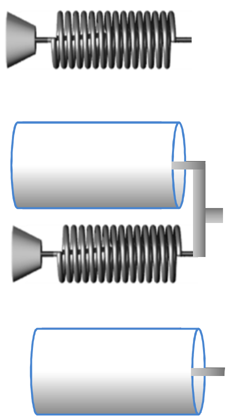
- Rheological Applications in Biopolymer and Biomedical Materials
  - Hydrogels and creams
  - Adhesives
  - Drug capsules
  - Polymers for medical devices

Rheology: An Introduction

Rheology is the science of *flow* and *deformation* of matter

Rheology: An Introduction

Rheology: The study of the relationship between a stress and deformation



Deformation F = F(x); F ≠ F(v)	Solid →		Purely Elastic
Deformation + Flow	Most material - - -		**Viscoelastic**
Flow F = F(v); F ≠ F(x)	Liquid →		Purely Viscous

$$\frac{Stress}{Strain} = Modulus$$

$$\frac{Stress}{Shear\ rate} = Viscosity$$

What does a Rheometer do?

- Rheometer – an instrument that measures both viscosity and viscoelasticity of fluids, semi-solids and solids

- It can provide information about the material's:
  - **Viscosity** - defined as a material's resistance to flow deformation and is a function of shear rate or stress, with time and temperature dependence

  - **Viscoelasticity** – is a property of a material that exhibits both viscous and elastic character. Measurements of G', G", tan δ with respect to time, temperature, frequency and stress/strain are important for characterization.

Who Will Need Help with Rheology Analysis?

Food

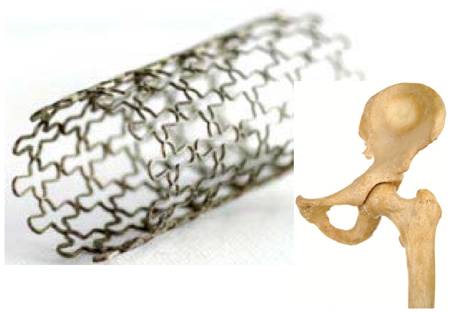
Personal Care

Pharmaceutical

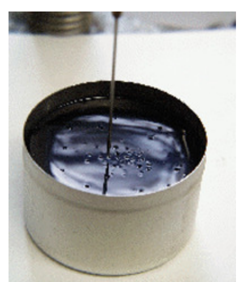
Polymers

Adhesives & coating

Automotive



Bio-medical devices



Asphalt

Aerospace

TA Instruments Rheometers and DMAs

- TA Rotational Rheometers
  - ARES-G2 and ARES (Strain Control – SMT)
  - DHR or AR (Stress Control – CMT)

- TA DMAs
  - RSA-G2 and RSA (Strain Control – SMT)
  - DMA Q800 (Stress Control – CMT)

Rotational Rheometers at TA

ARES G2

Controlled Strain
Dual Head
SMT

DHR

Controlled Stress
Single Head
CMT

Geometry Options

Concentric Cylinders

Very Low to Medium Viscosity

Cone and Plate

Very Low to High Viscosity

Parallel Plate

Very Low Viscosity to Soft Solids

Torsion Rectangular

Solids

Water → to → Steel

DMAs from TA Instruments

RSA G2	Q800	ARES G2 and DHR
		
Controlled Strain **SMT**	**Controlled Stress** **CMT**	**DMA mode** (oscillation)

DMA Clamps

S/D Cantilever

Tension-Film

Shear-Sandwich

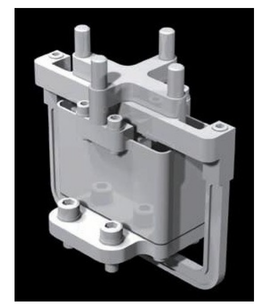
Submersible Compression

Submersible 3 Pt Bend

3-Point Bending

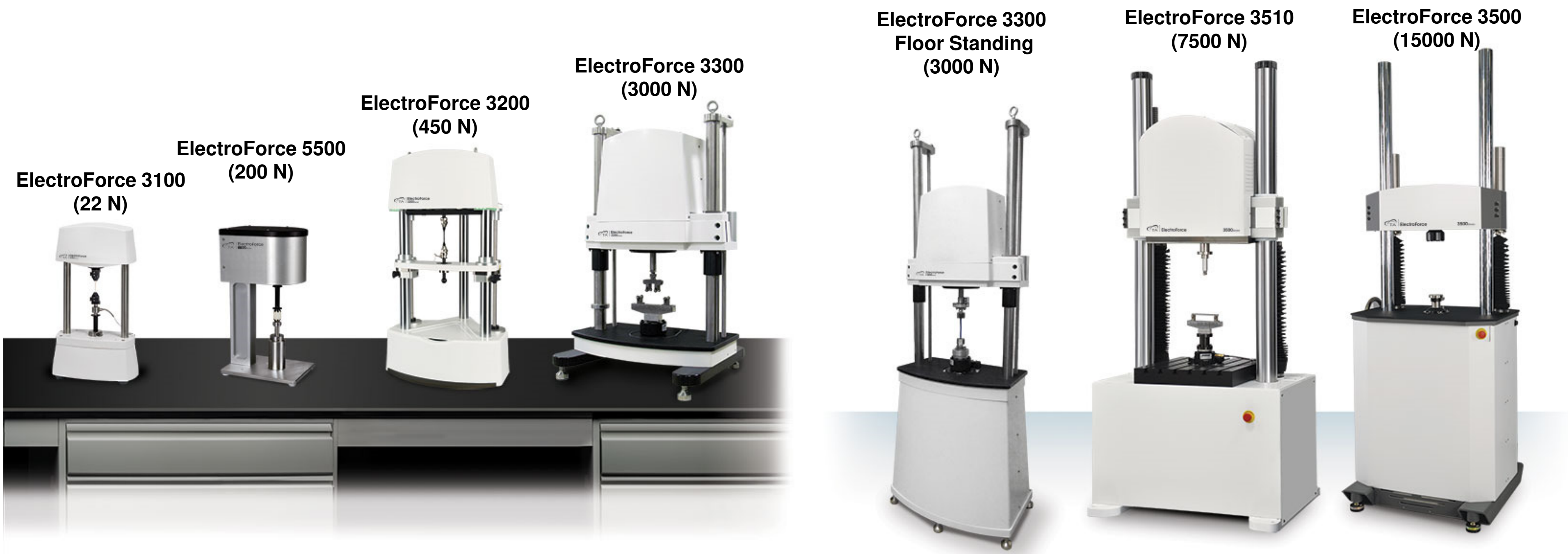
Tension-Fiber

Compression



Submersible Tension

ElectroForce Load Frames



Frequency to 300 Hz

Forces to 15kN

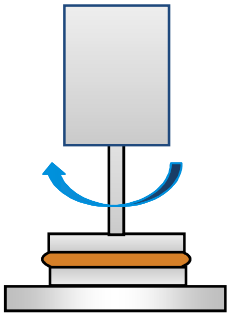
Interchangeable Fixtures

Common Rheological Experimental Methods

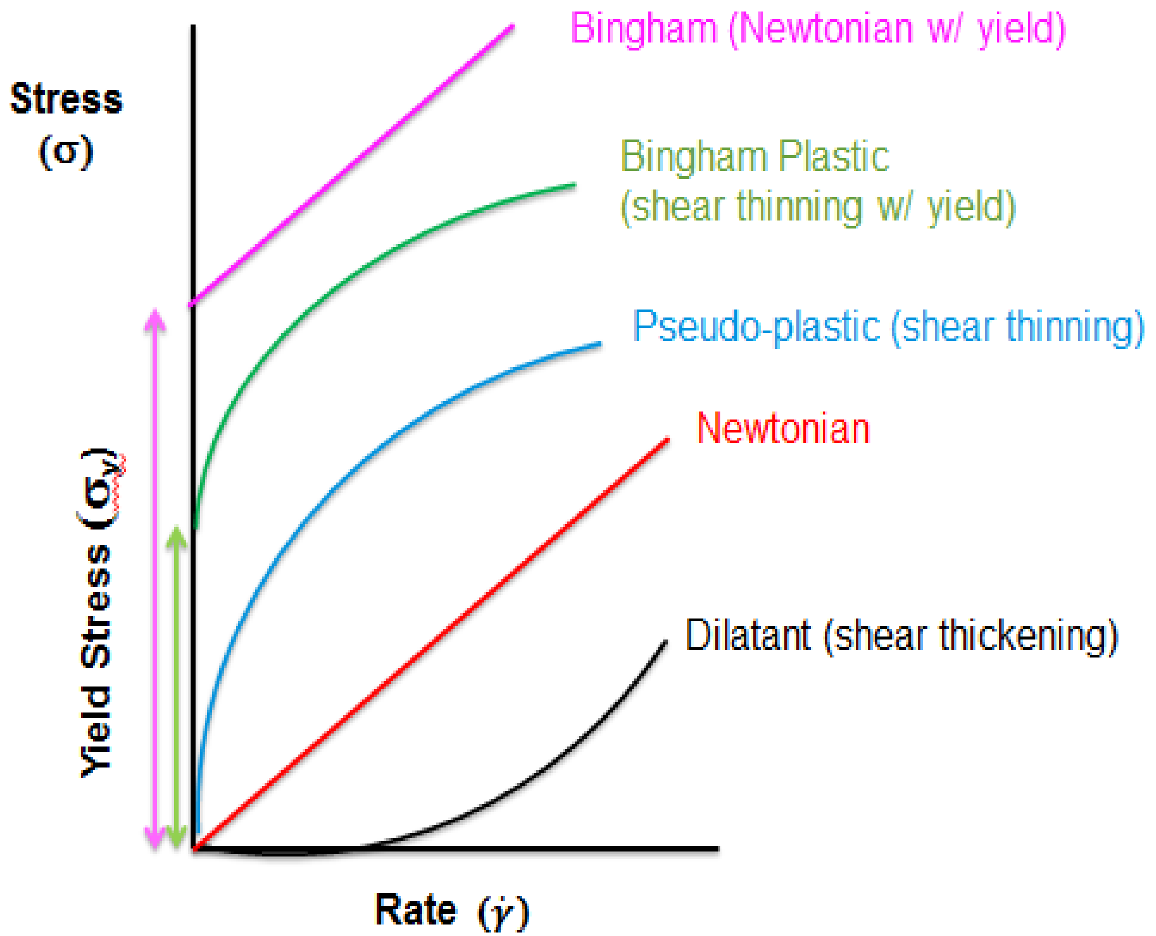
Flow Experiments

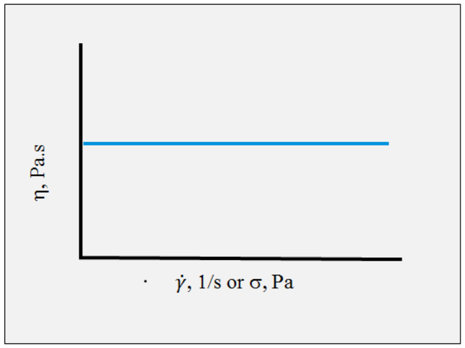
- What flow measures
  - Viscosity
    - “lack of slipperiness,” resistance to flow
    - The viscosity of water at room temperature is 1cP

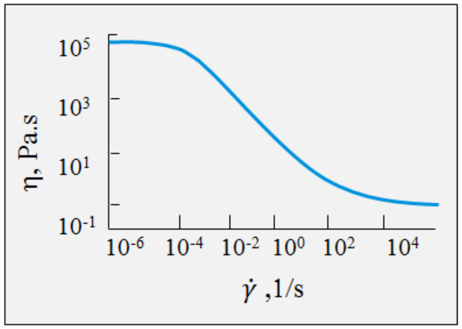
- Type of flow measurements on rheometer
  - Viscosity vs. time
    - Viscosity at single shear rate/stress
    - Time dependence (Thixotropy or Rheopexy)
  - Viscosity vs. shear stress or rate
    - Newtonian
    - Shear thinning, shear thickening,
    - Yield stress
  - Viscosity vs. temperature

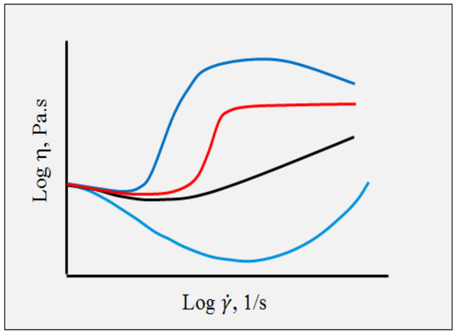


Flow Behaviors

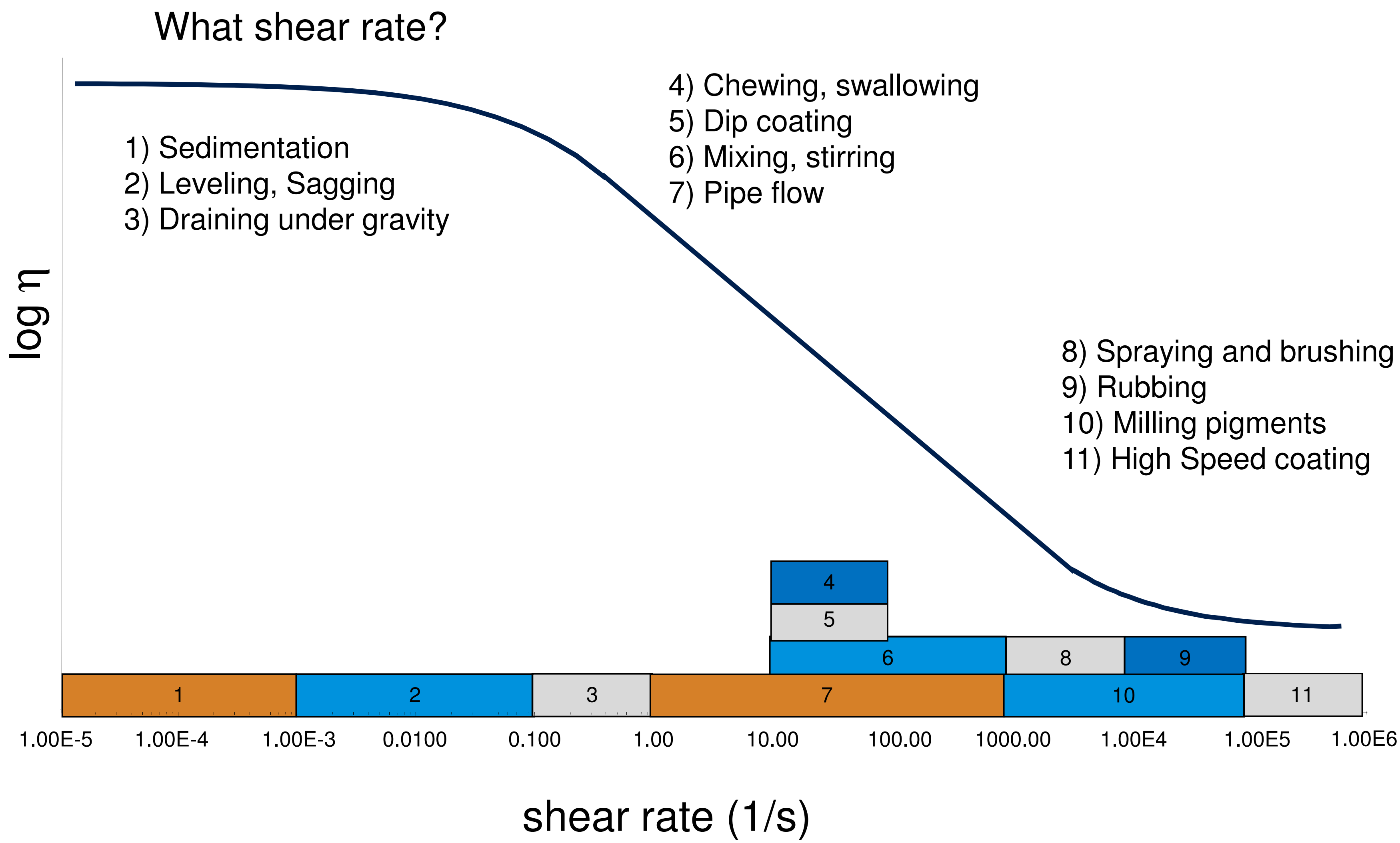




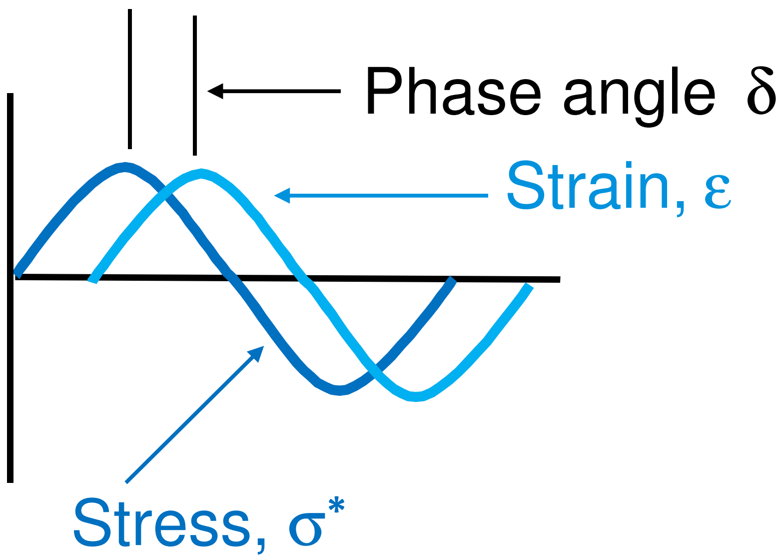


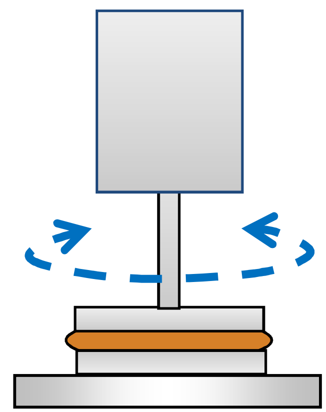


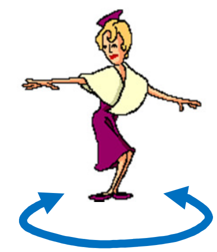
Information from a Flow Curve



Dynamic Oscillatory Tests







Dynamic stress applied sinusoidally

User-defined Stress or Strain amplitude and frequency

Viscoelastic Parameters

The Modulus: Measure of materials overall resistance to deformation.

$$\mathbf{G^* = \left(\frac{Stress^*}{Strain}\right)}$$

The Elastic (Storage) Modulus: Measure of elasticity of material. The ability of the material to store energy.

$$G' = \left(\frac{Stress^*}{Strain}\right)\cos\delta$$

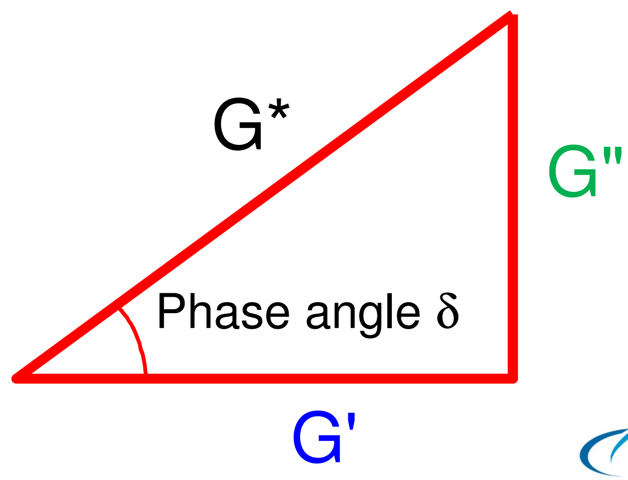
The Viscous (loss) Modulus:
The ability of the material to dissipate energy. Energy lost as heat.

$$G'' = \left(\frac{Stress^*}{Strain}\right)\sin\delta$$

Tan delta (phase angle):
Measure of material damping - such as vibration or sound damping.

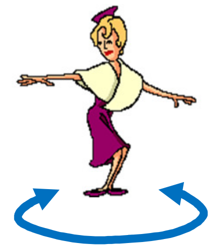
$$\tan\delta = \left(\frac{G''}{G'}\right)$$

The triangle relationship

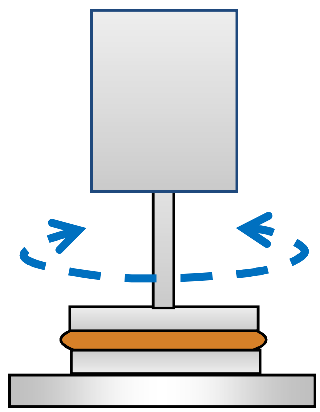


Understanding Oscillation Experiments

- What oscillation measures?
  - Viscoelastic properties (G'/E', G"/E", tan δ)



- Approach to Oscillation Experimentation
  - Stress and Strain Sweep
    - Measure linear viscoelastic region
    - Yield stress, stability
  - Time Sweep
    - Stability and structure recovery
    - Curing
  - Frequency Sweep
    - Measure polymer relaxation
    - Compare viscoelasticity of different formulations
  - Temperature Ramp
    - Measure glass transition,
    - Temperature operation range of a material



Rheology Applications in Biopolymers & Biomedical Materials

Purpose of a Rheological Measurement

Three main reasons for rheological testing:

- Characterization
  Structure-property relationship. MW, MWD, branching, state of flocculation, etc.

- Process performance
  Formulation stability, processing temperatures, extrusion, blow molding, pumping, leveling, etc.

- End product properties
  Mechanical strength, glass transition and sub-ambient transition temperatures, dimensional stability, settling stability, etc.

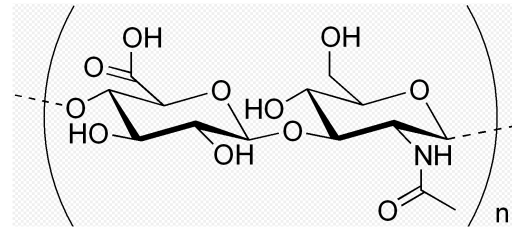
Hydrogels and Creams

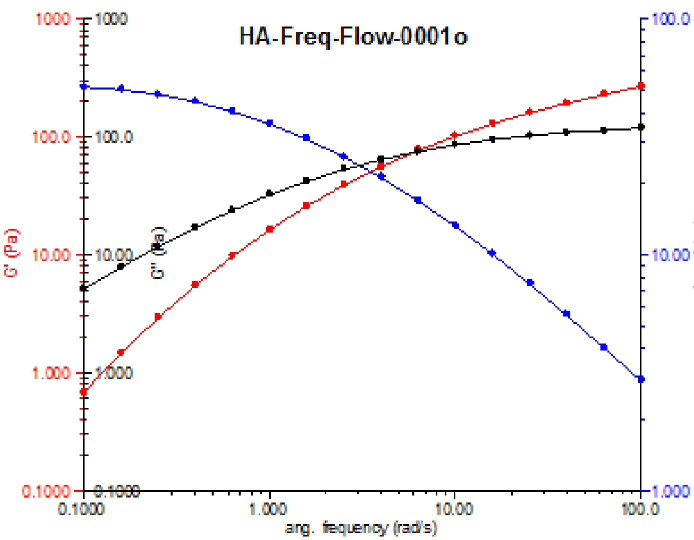
- Hydrogels and creams are soft matters that contain high level of liquids such as water or oil
- Hydrogels and creams are used in a wide variety of applications including tissue engineering, wound patch, drug delivery, contact lenses and superabsorbent materials
- Rheology can provide key information on gel formation and gel strength on different formulations

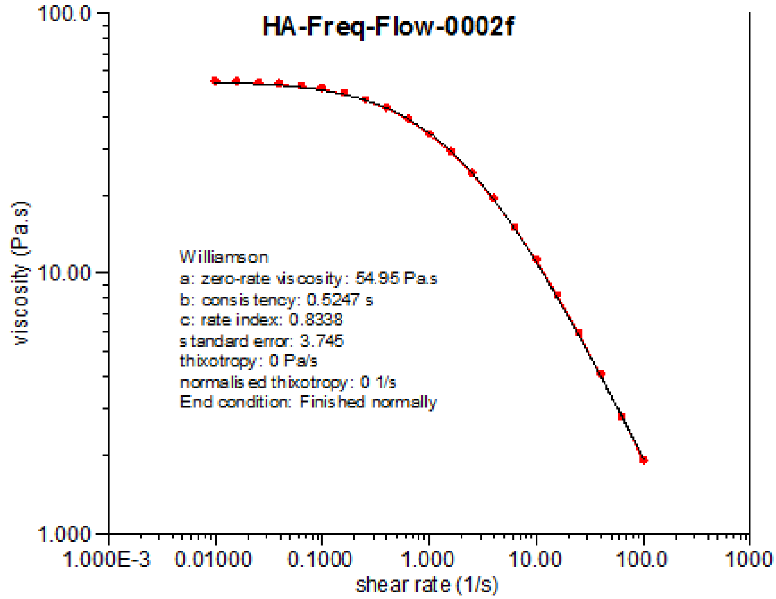


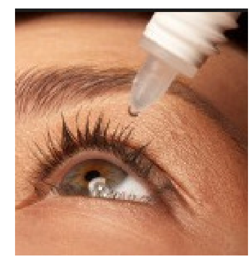
Natural Polymer: Hyaluronic Acid

- Hyaluronic acid is a natural polysaccharide, which is commonly used in pharmaceutical, biomedical and personal care
- Rheology can evaluate the visco-elastic properties as function of concentration, ionic strength, Mw, degree of crosslinking, formulations etc.



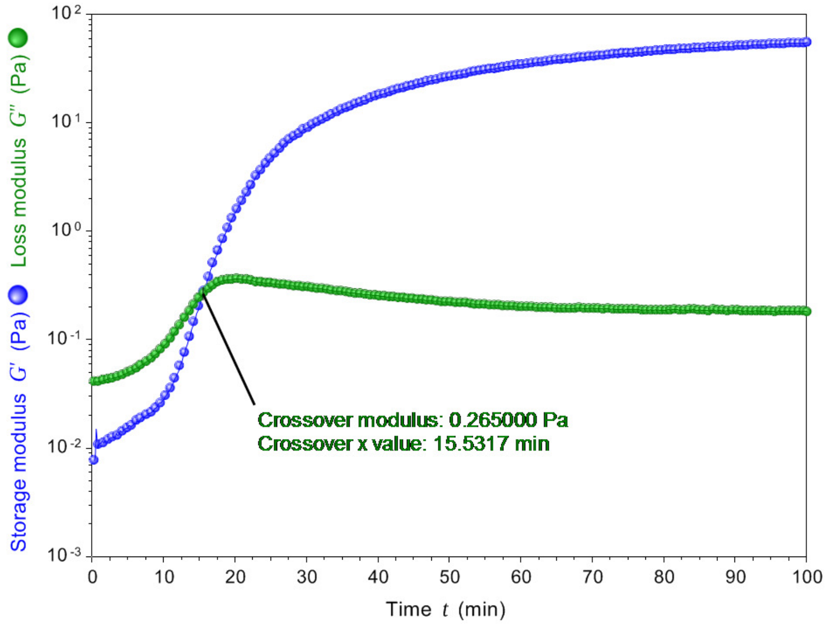


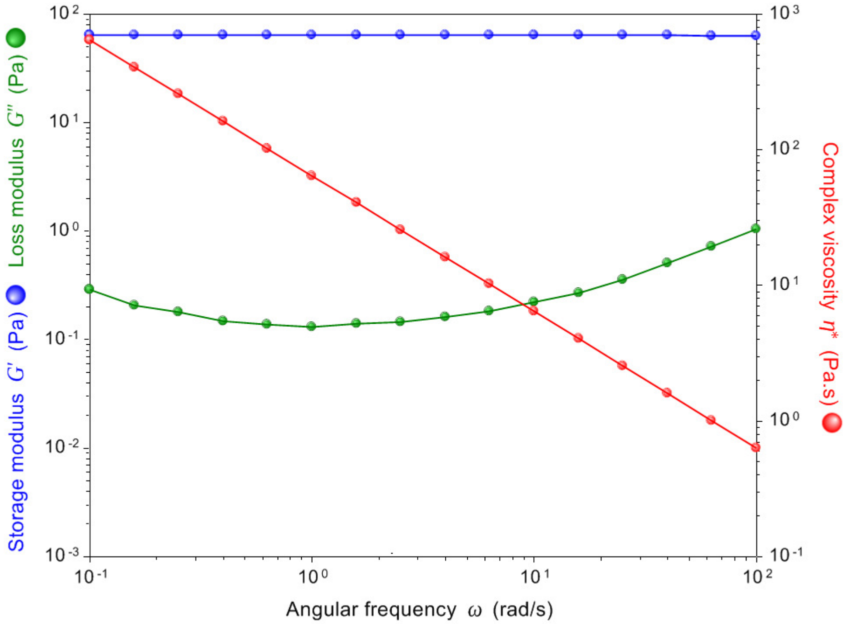




Hyaluronic Acid Gels:

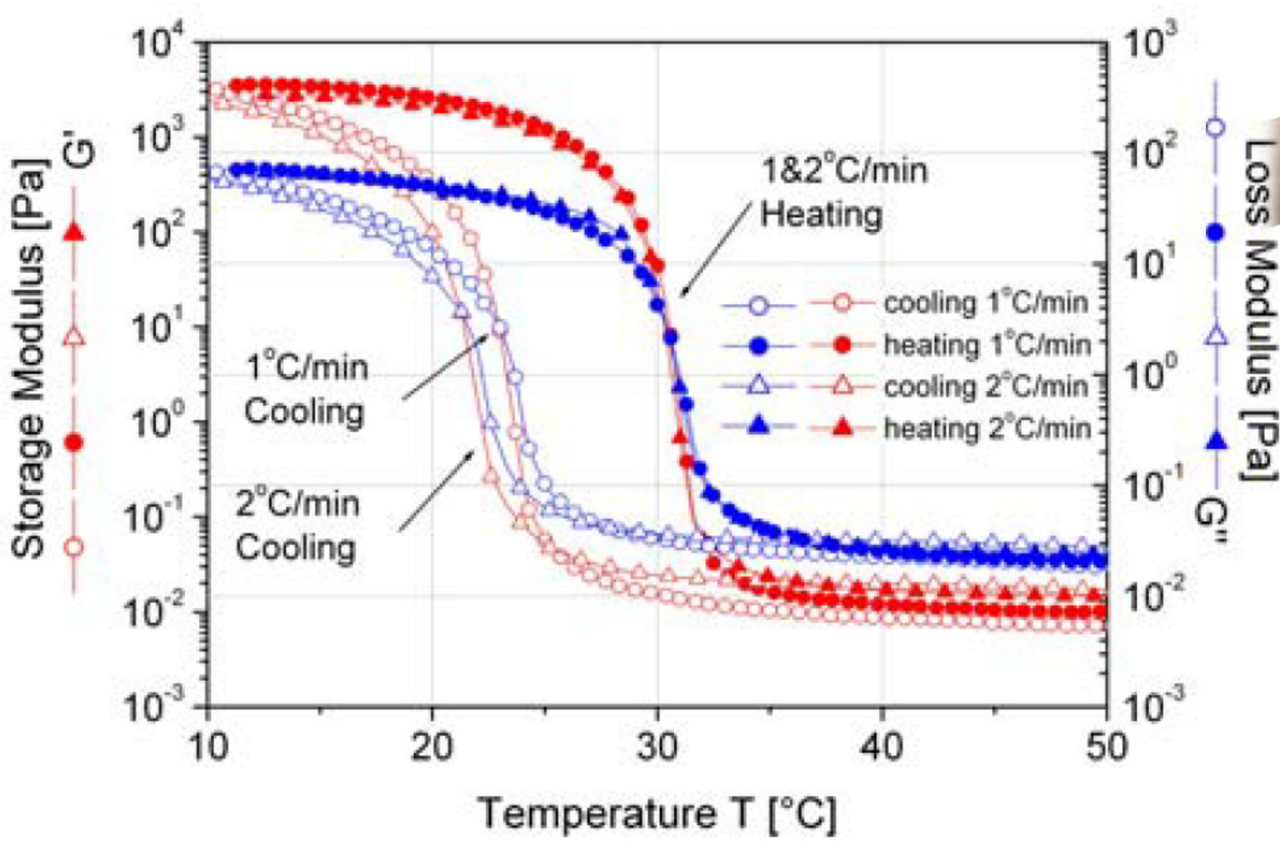
- Hyaluronic acid gels are used as lubricating agent during abdominal surgeries to prevent adhesion and also for join lubrication, wound healing etc.
- Rheology can monitor HA gelation and evaluate the gel strength





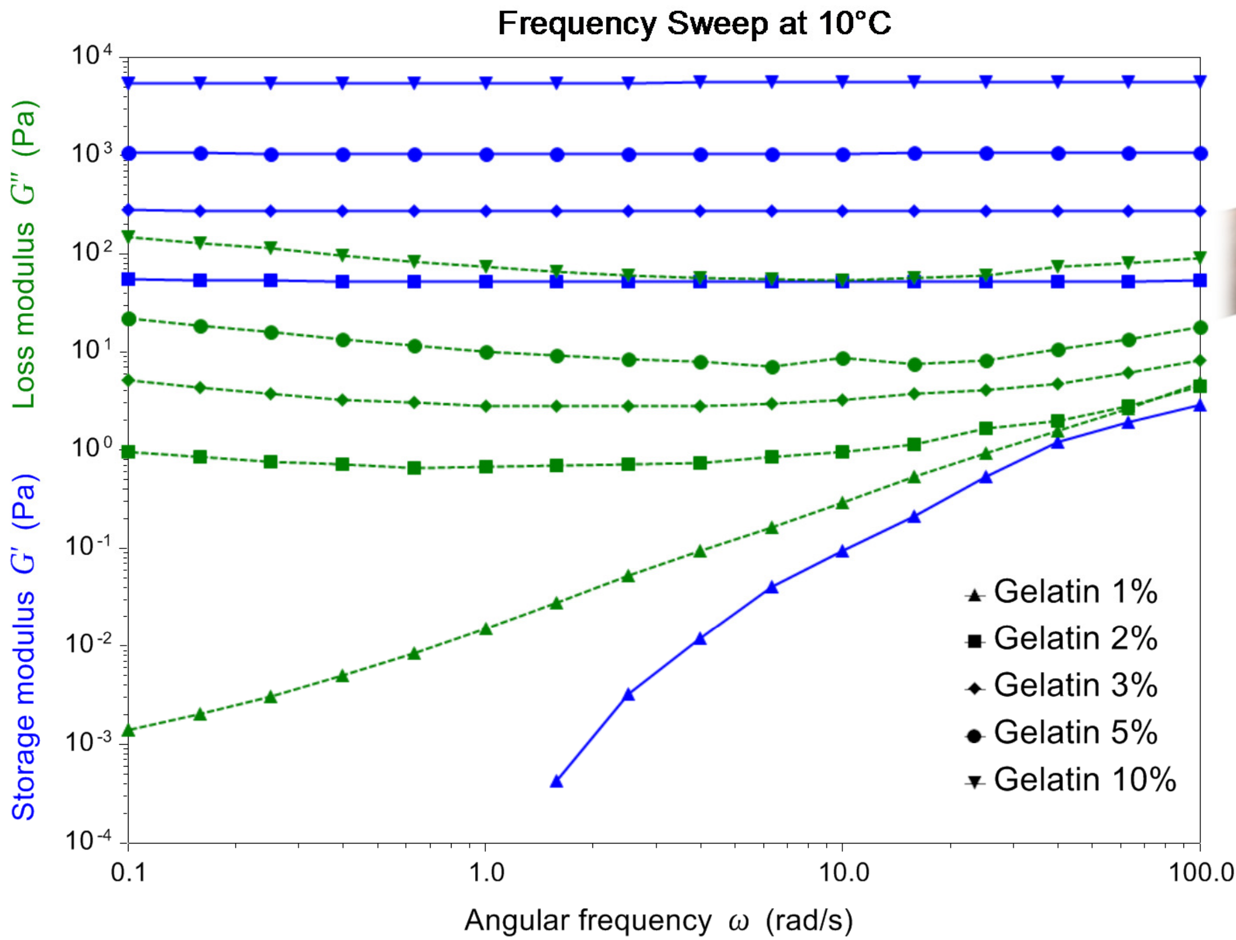
Gels: Gelatin Gelation vs. Temperature

- Thermal reversible gelatin gels:
  - Measure gelation and gel melt



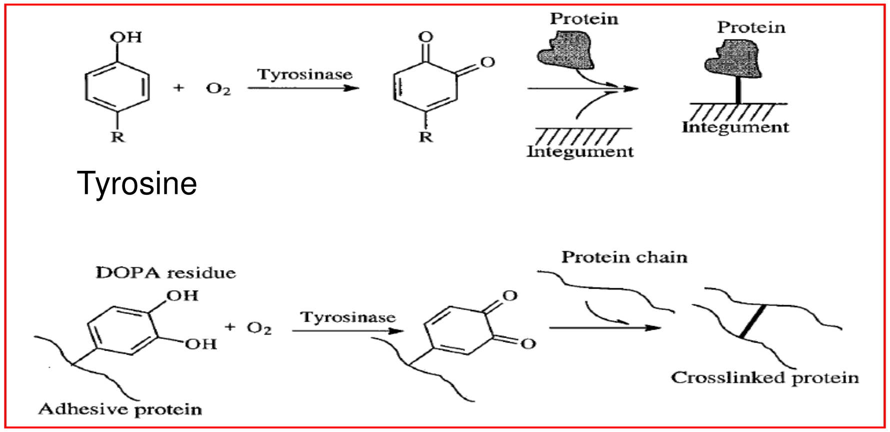
Gelatin Gel Strength at Different Concentration

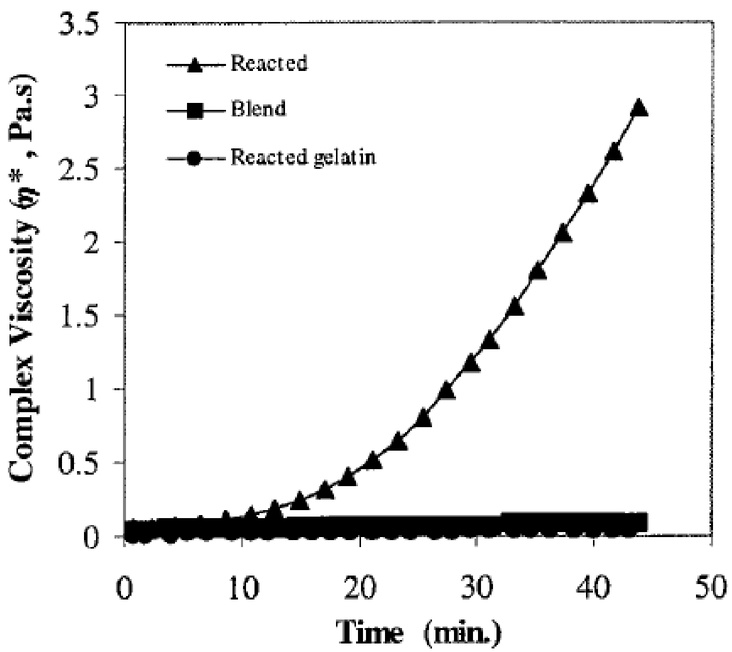
- A dynamic frequency sweep test can be used to compare gel strength at applications temperature

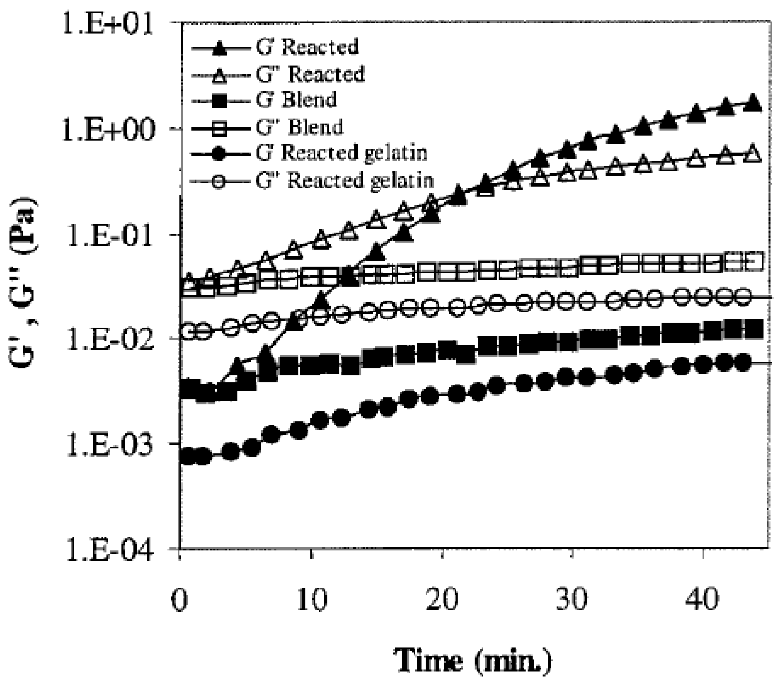


Gelatin/Chitosan Conjugation

- Use enzymatic approach to covalently graft gelatin to chitosan
- The conjugate exhibits interesting mechanical properties
- Applications as biomedical adhesives



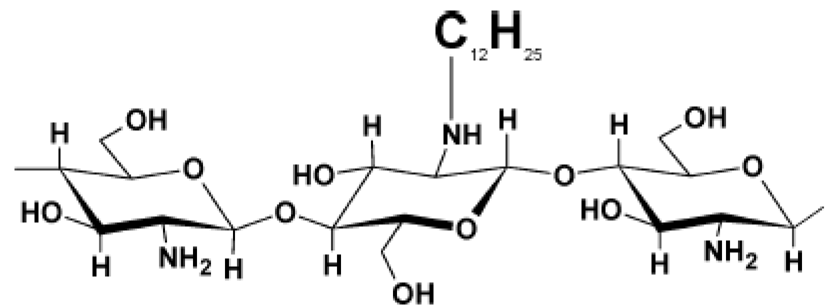




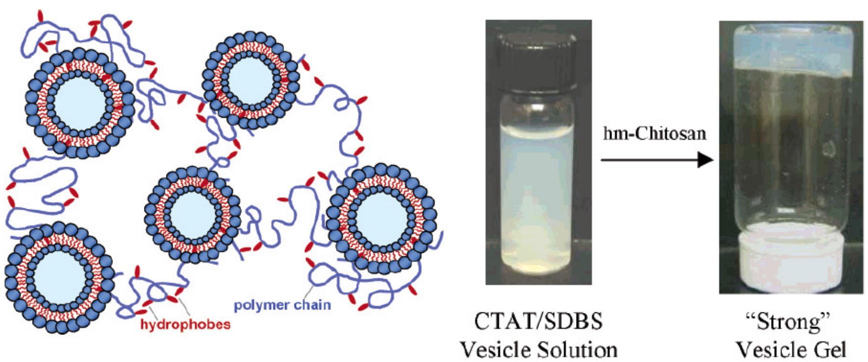
Chen et al. Biopolymers, Vol. 64, 292-302 (2002)

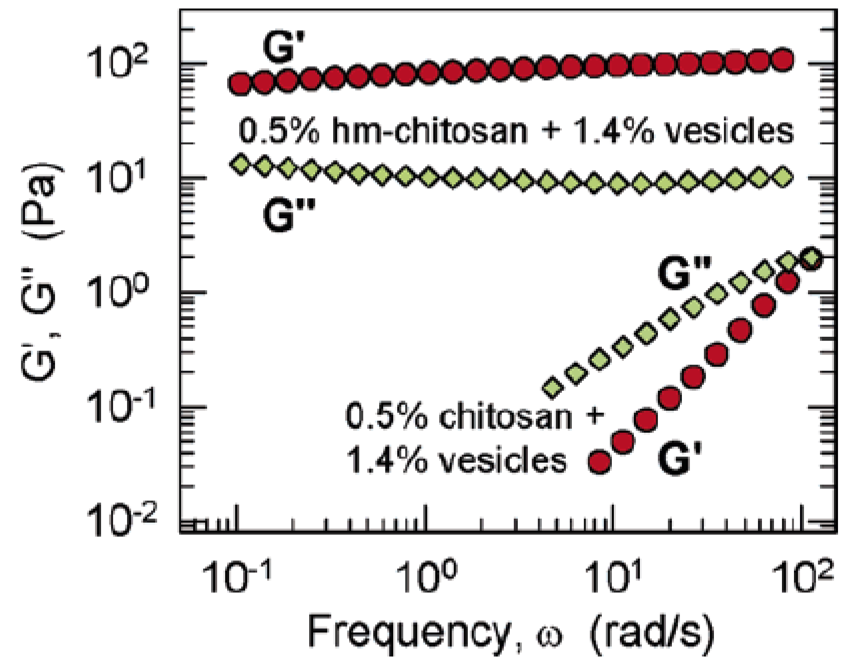
Vesicle-Biopolymer Gels

- Attach n-dodecyl tails to Chitosan backbone to obtain an associating biopolymer (HM-Chitosan)
- HM-Chitosan mixed with surfactant vesicle solution leads to a gel formation
- This hydrogel showed strong elasticity behavior and has potential applications in biomedical control release



HM-Chitosan

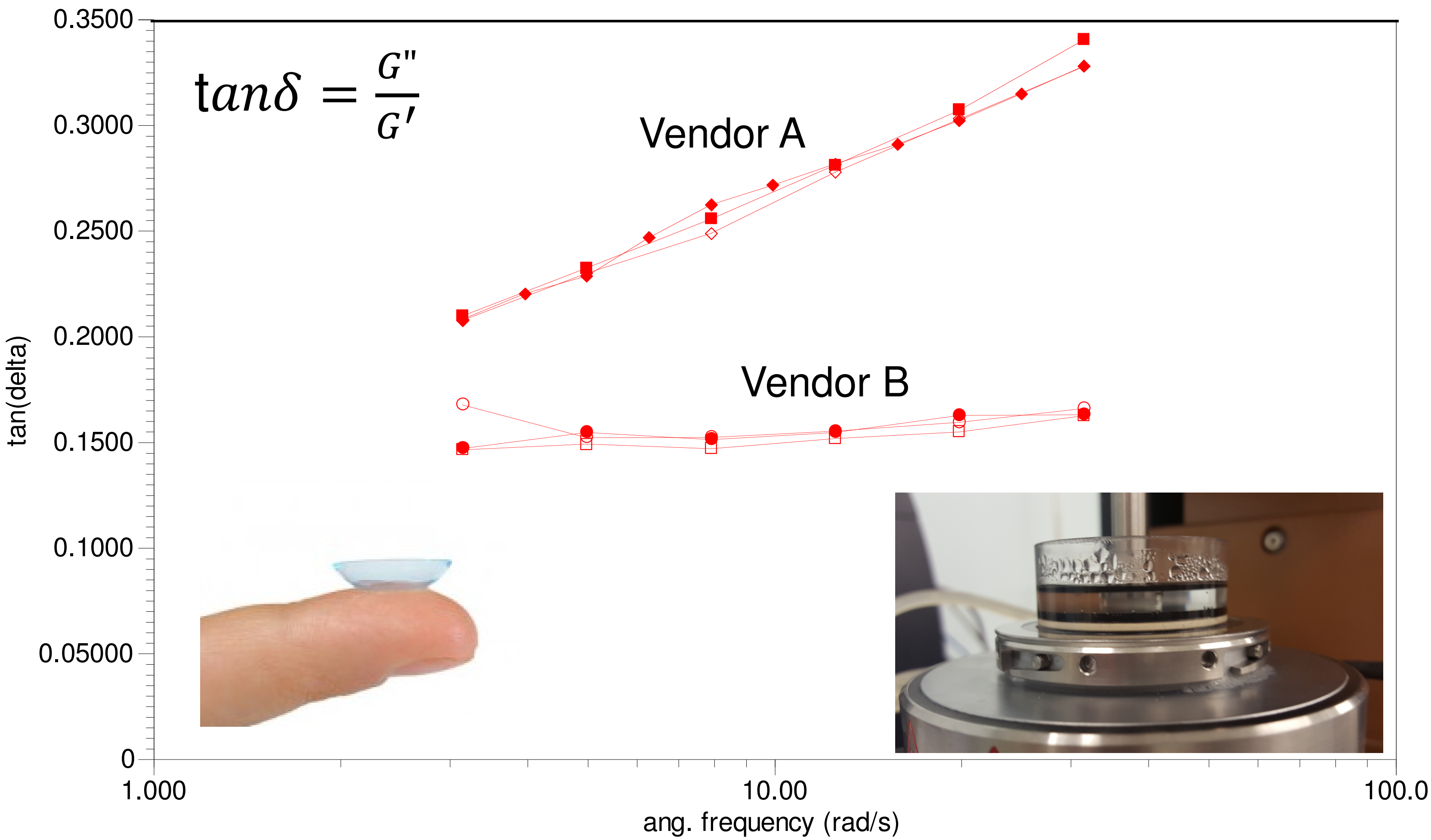




Chen T; Raghavan SR et al, Langmuir, 21, 26-33 (2005)

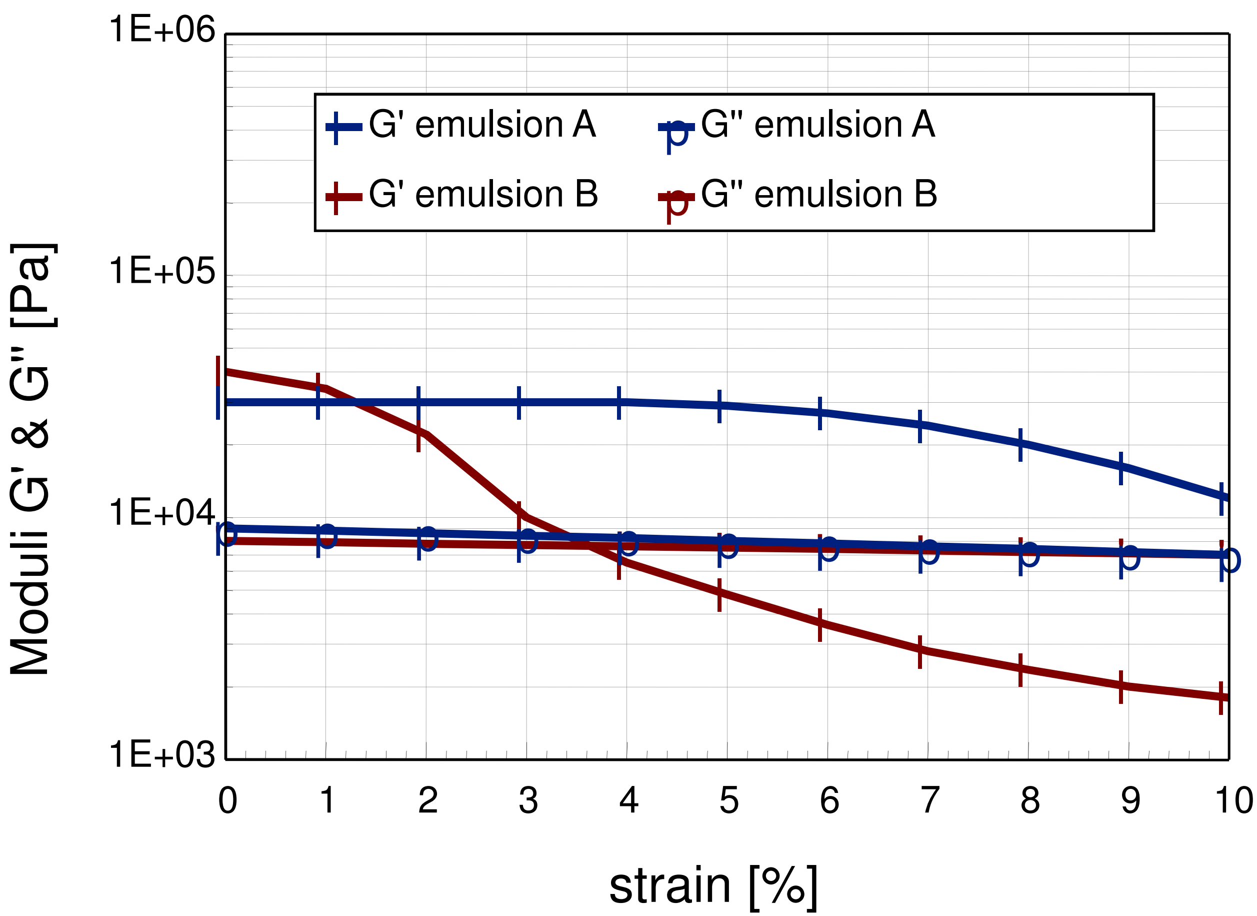
Contact Lens Visco-elasticity

- Compare frequency dependency of contact lens elasticity



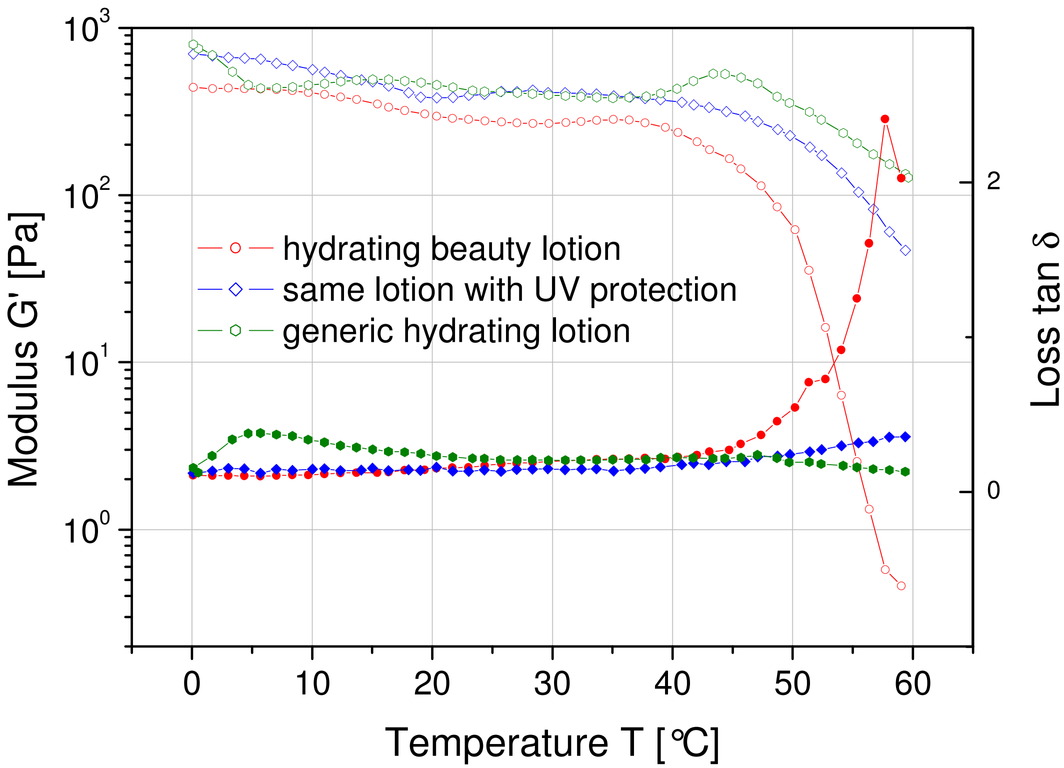
Creams/Lotions: Stability Testing

Stability, phase separation of a cosmetic cream



High Temperature Performance of Lotions

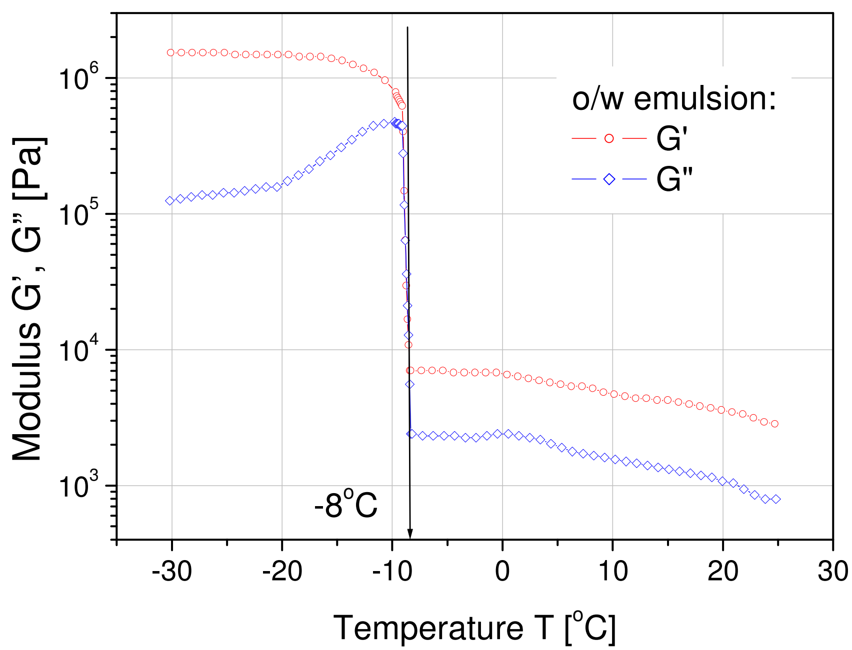
A: Hydrating Lotion B: UV Protection C: Generic Brand

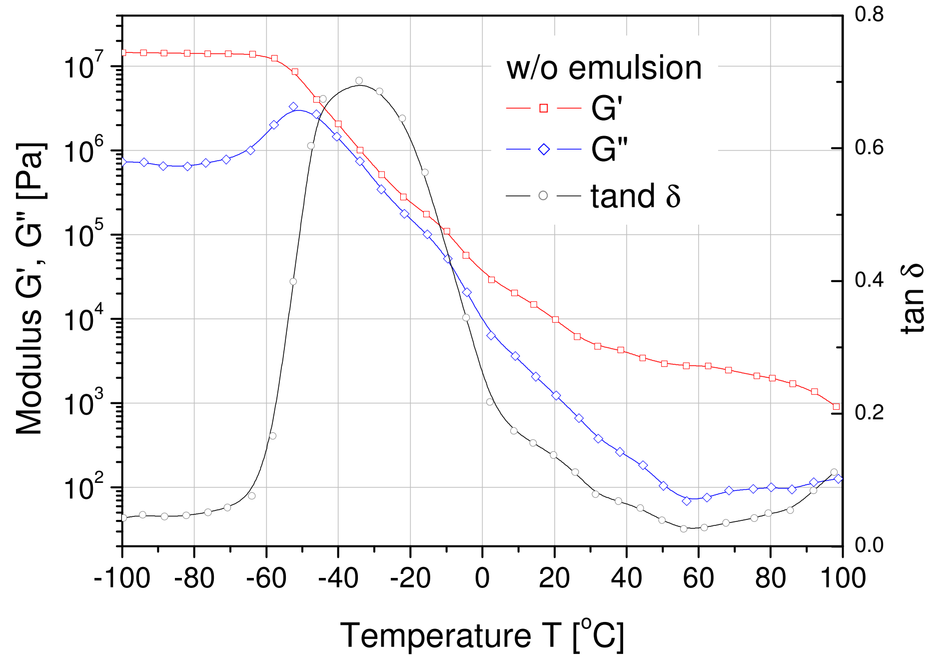


Ming L. Yao; Jayesh C. Patel Appl. Rheol. 11,2,83 (2001)

- G' for A decreases at 37°C
- G' for B withstands higher temperature =>used at higher temperature conditions (beach)
- G' for lotion C increases before dropping; tan δ decreases => phase separation for lotion C
- Tan δ for A & B increases above 37°C=> wax crystals melt and lower the modulus

Low Temperature Performance of Lotions





- In an o/w emulsion the freezing point of water is depressed due to the dispersed oil phase. Cooling below the freezing point has a major effect on temperature stability
- In an w/o emulsion, the dispersed water droplets freeze, but not the matrix. These emulsions do not have a sharp freezing point

R.Brummer Rheology essentials of Cosmetics Springer ISBN: 3-540-25553-2

Emulsion Temperature Stability

- Cycle temperature to evaluate temperature stability of emulsions

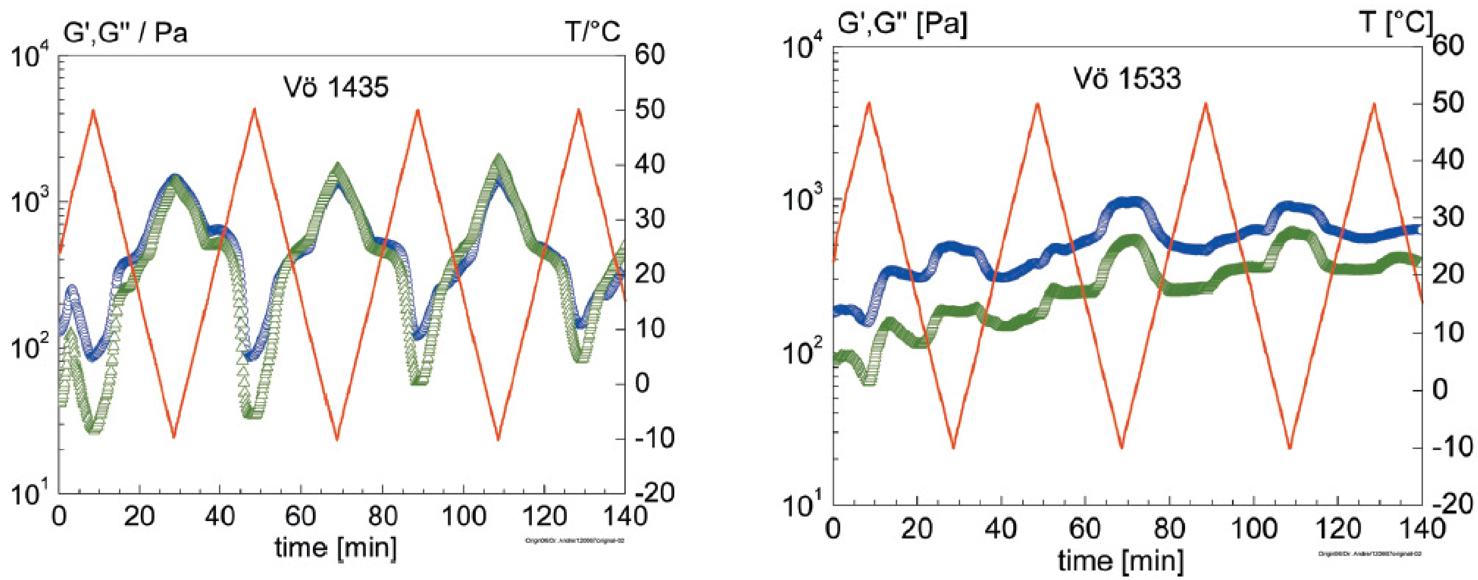
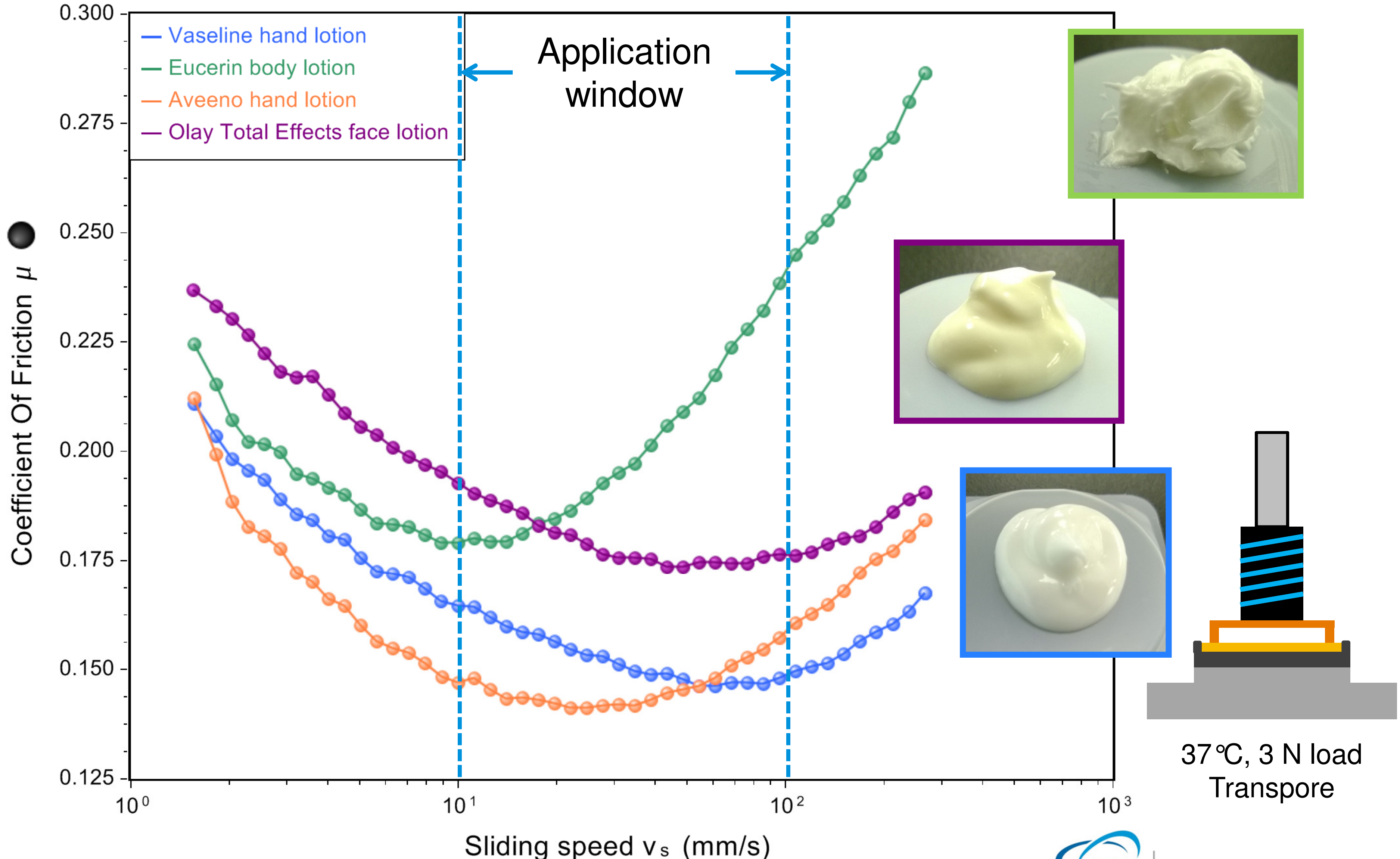


Figure 5a and 5b : Shear moduli G' and G'' versus time during subsequent heating and cooling cycles for sample 1435 (a) and 1533 (b).
Symbols: G' (blue line), G'' (green line), measured 24 h after sample preparation Red line: temperature

V. André, N. Willenbacher, H. Debus, L. Börger, P. Fernandez, T. Frechen, J. Rieger. **Prediction of Emulsion Stability: Facts and Myth . Cosmetics and Toiletries Manufacture Worldwide**

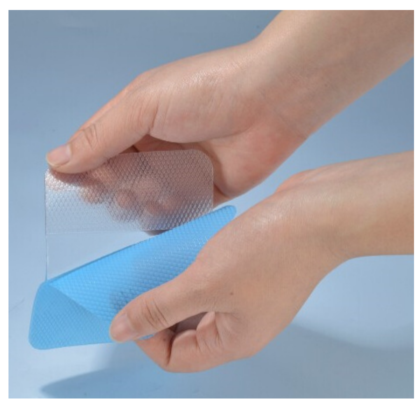
Lotions: Coefficient of Friction

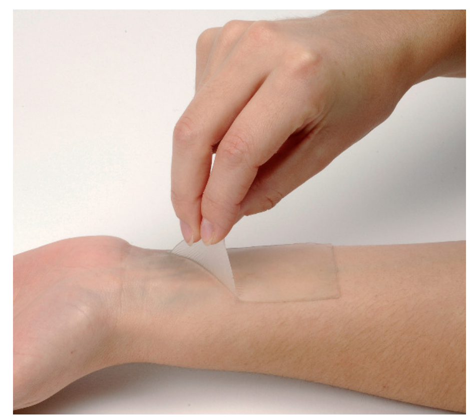


37 ℃, 3 N load
Transpore

Biomedical Adhesives

- Adhesives are used in biomedical device assembly; hard tissue or soft tissue attachments (e.g. dentistry or wound closure)
- Rheology helps to guide adhesive process
- Rheology measurements can correlate to the tack and peel performance of the finial products





Bio-adhesives Test Methodologies

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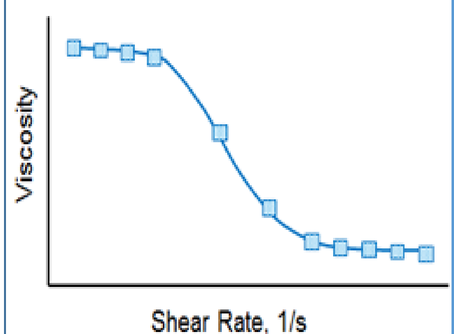
<td>
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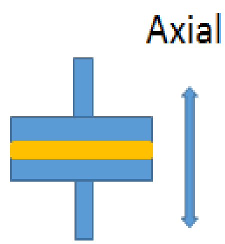
<td>
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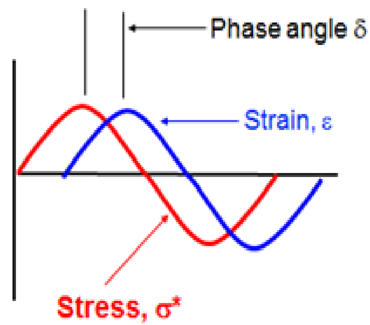
<td>
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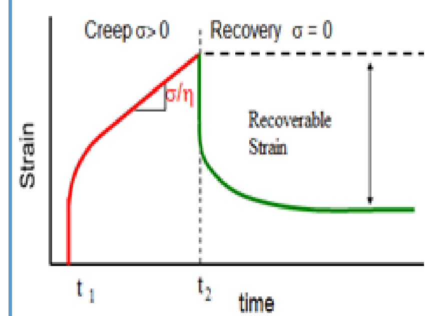
<td>
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<tr>
<td>• Measure solution viscosity
• Measure melt viscosity</td>
<td>• Measure tack and peel</td>
<td>• Measure transition temperatures
• G’ (cohesive strength)
• G” (tack strength)
• Tan delta (elasticity)
• Predict long time performance</td>
<td>• Measure cold flow
• Predict long time performance</td>
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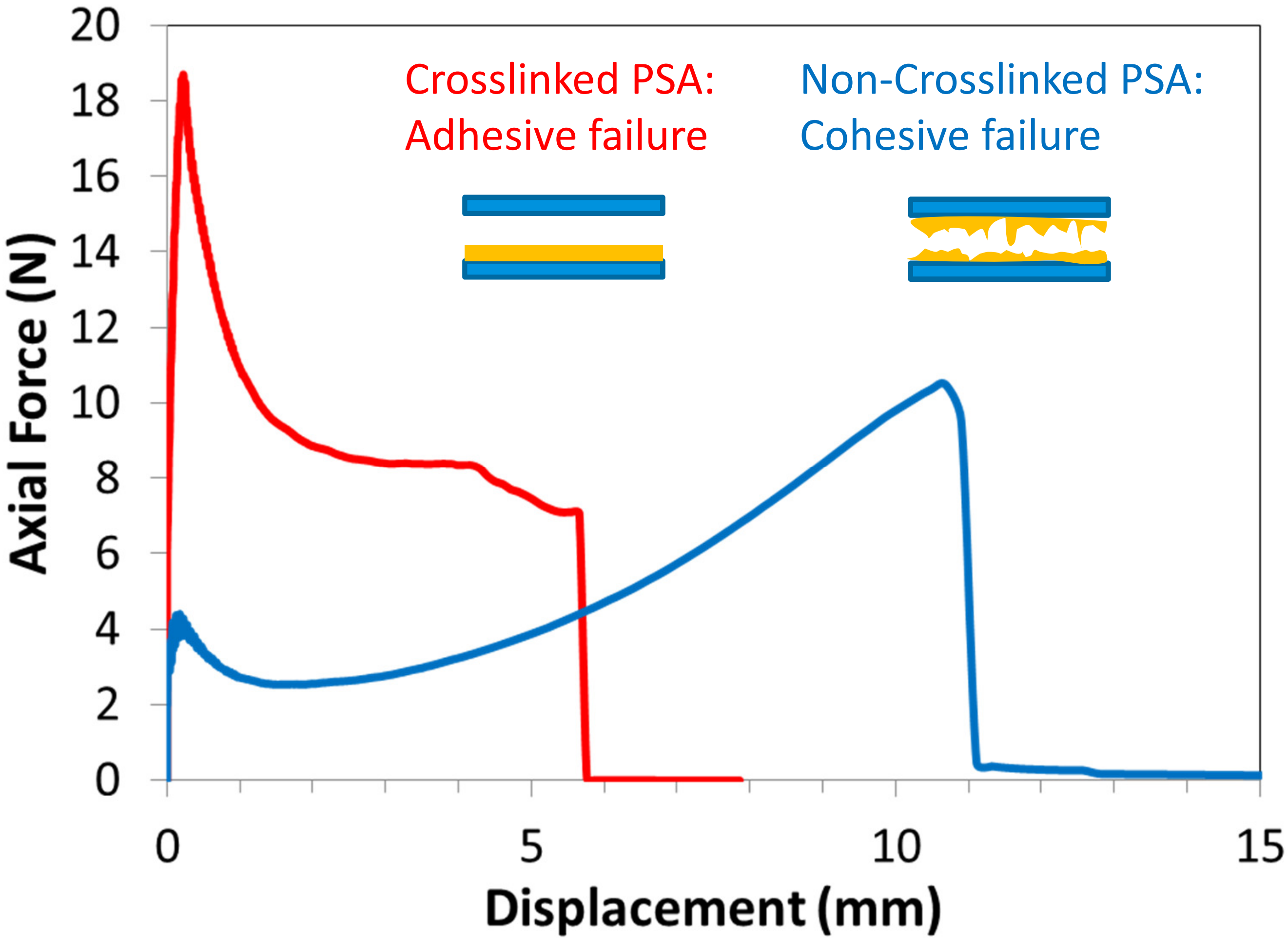
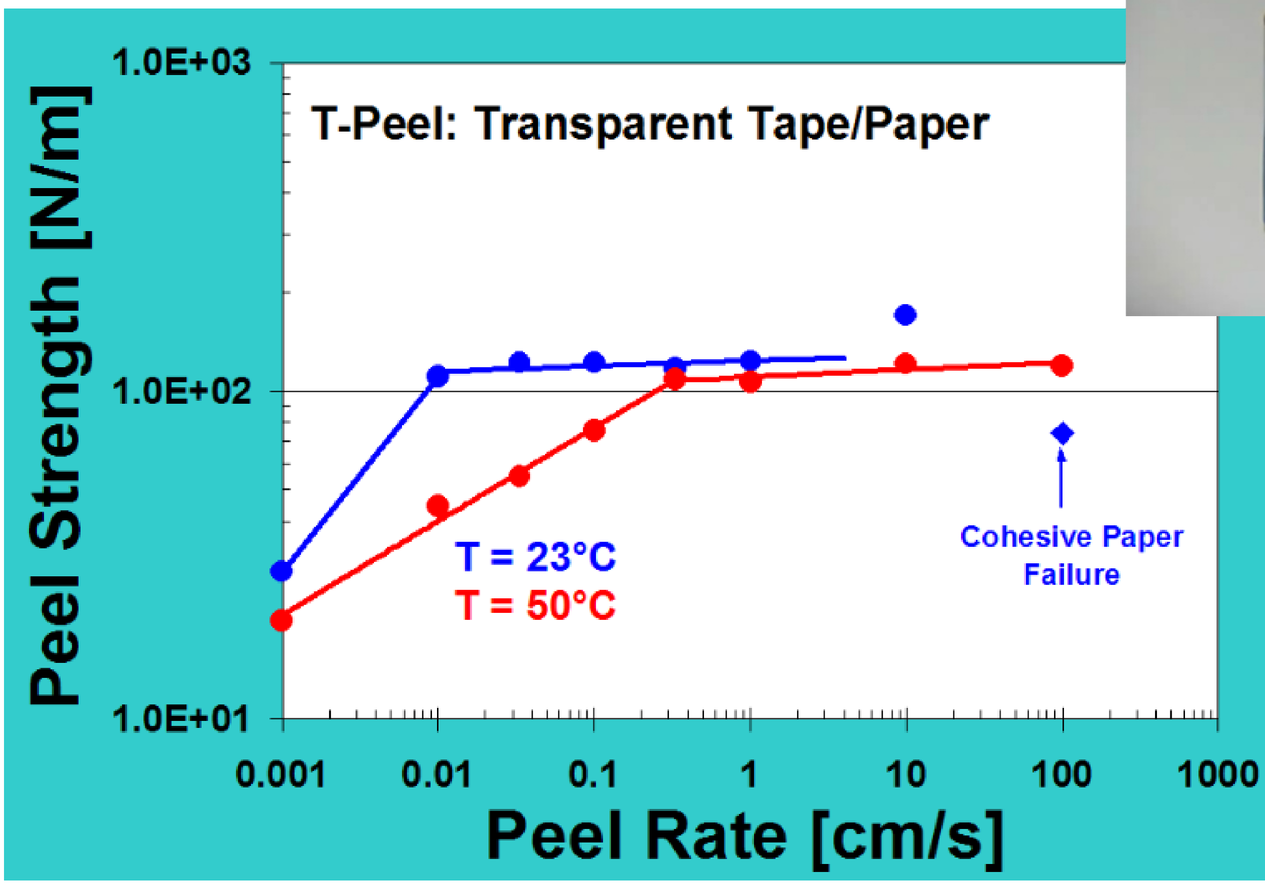
Adhesive Tack Testing

- Experimental:
  8mm parallel plate, Axial tensile at 0.1mm/sec



Adhesive 180 Degree Peel Test

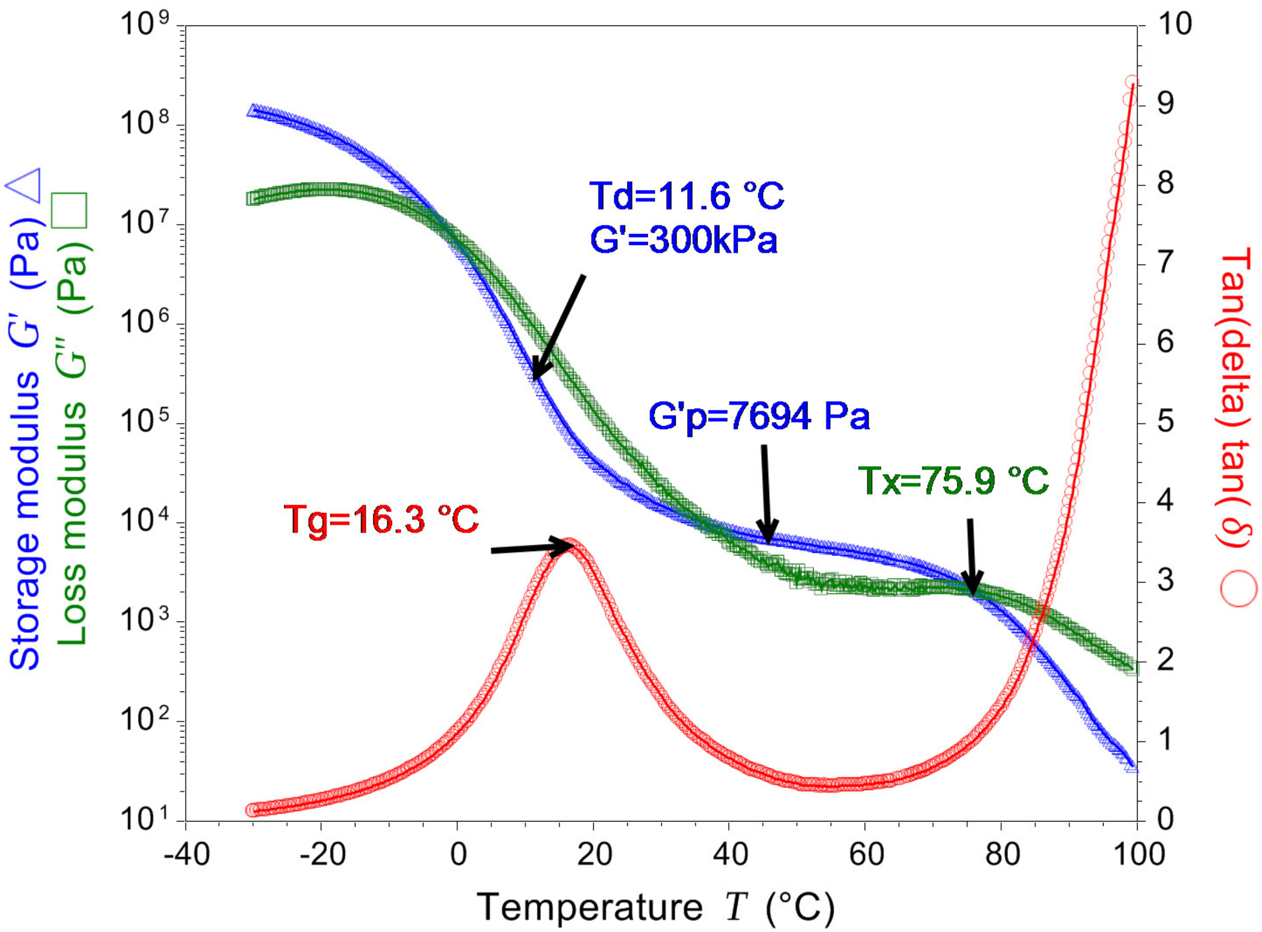
- The SER geometry on a rheometer can perform peel test at 180 degree angel.



http://www.xpansioninstruments.com/results_peel.htm

Adhesive Temperature Ramp

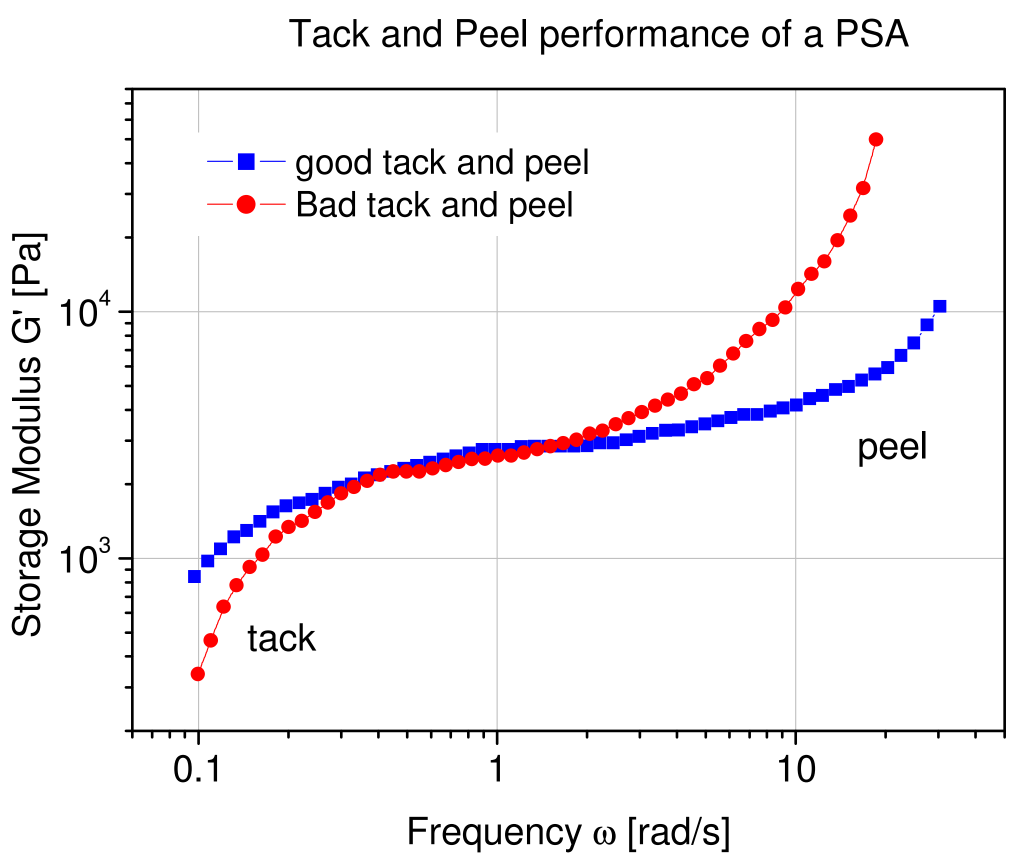
- Most popular test in adhesive industry
- The measurement results correlate to the performance of a PSA with temperature

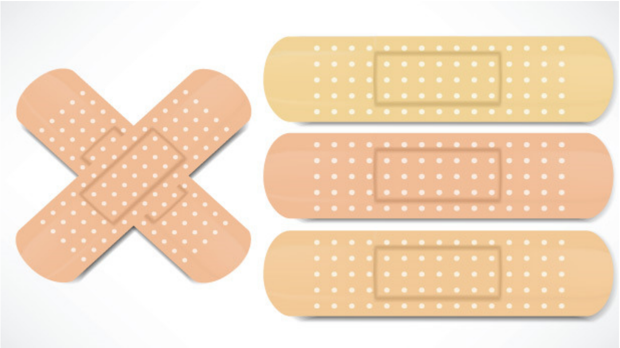


- Glass transition: Tg = 16.3°C
- G crossover: Tx = 75.9°C
- Dahlquist temperature: Td = 11.6°C
- Plateau modulus G'p = 7694 Pa

Adhesive: Tack and Peel Performance

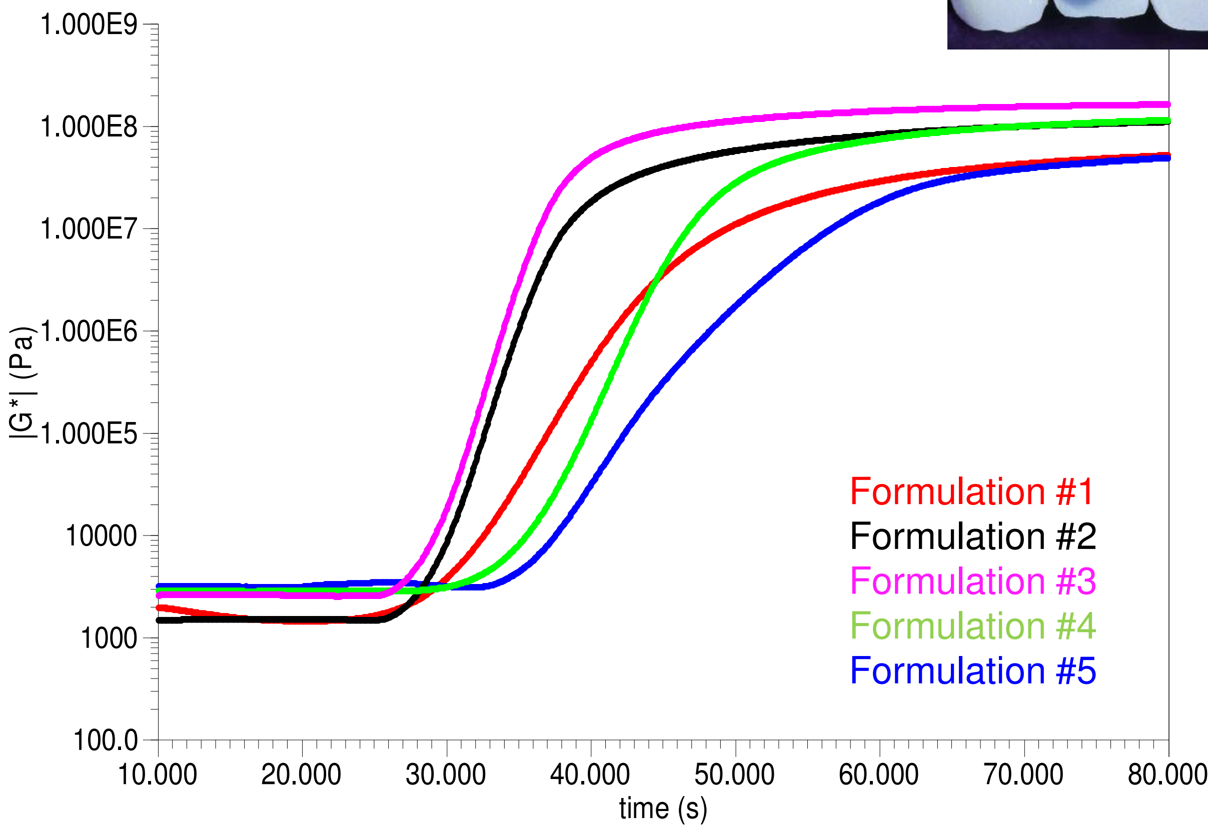
- A dynamic frequency sweep test results can correlates to tack and peel performance





Dental Adhesive UV Curing

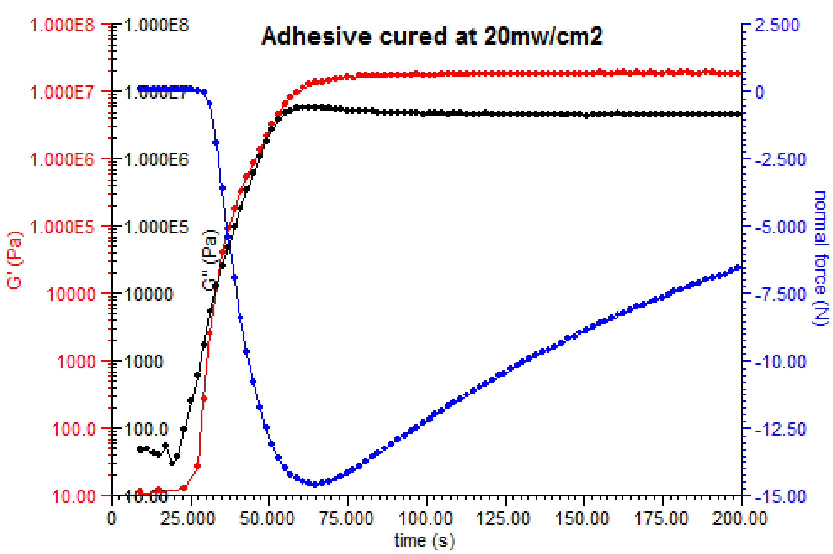
- Dental materials cure under blue light



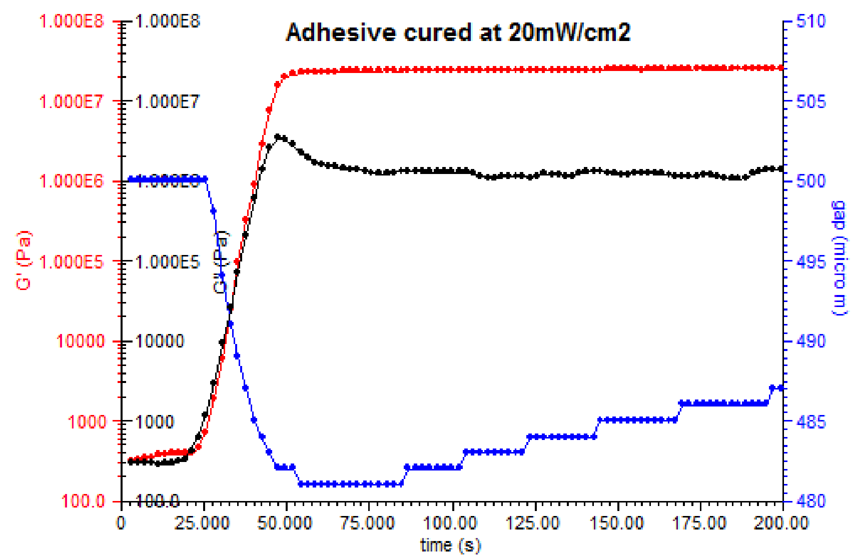
Adhesive Curing Shrinkage

- Adhesive curing shrinkage will cause fractures in process
- Using rheometer + UV curing accessory, we can quantitatively monitor the shrinking force during curing or the dimension shrinkage

Monitor force buildup

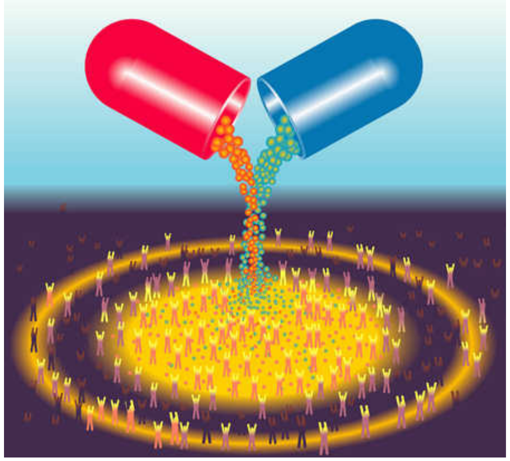


Monitor dimension/gap change



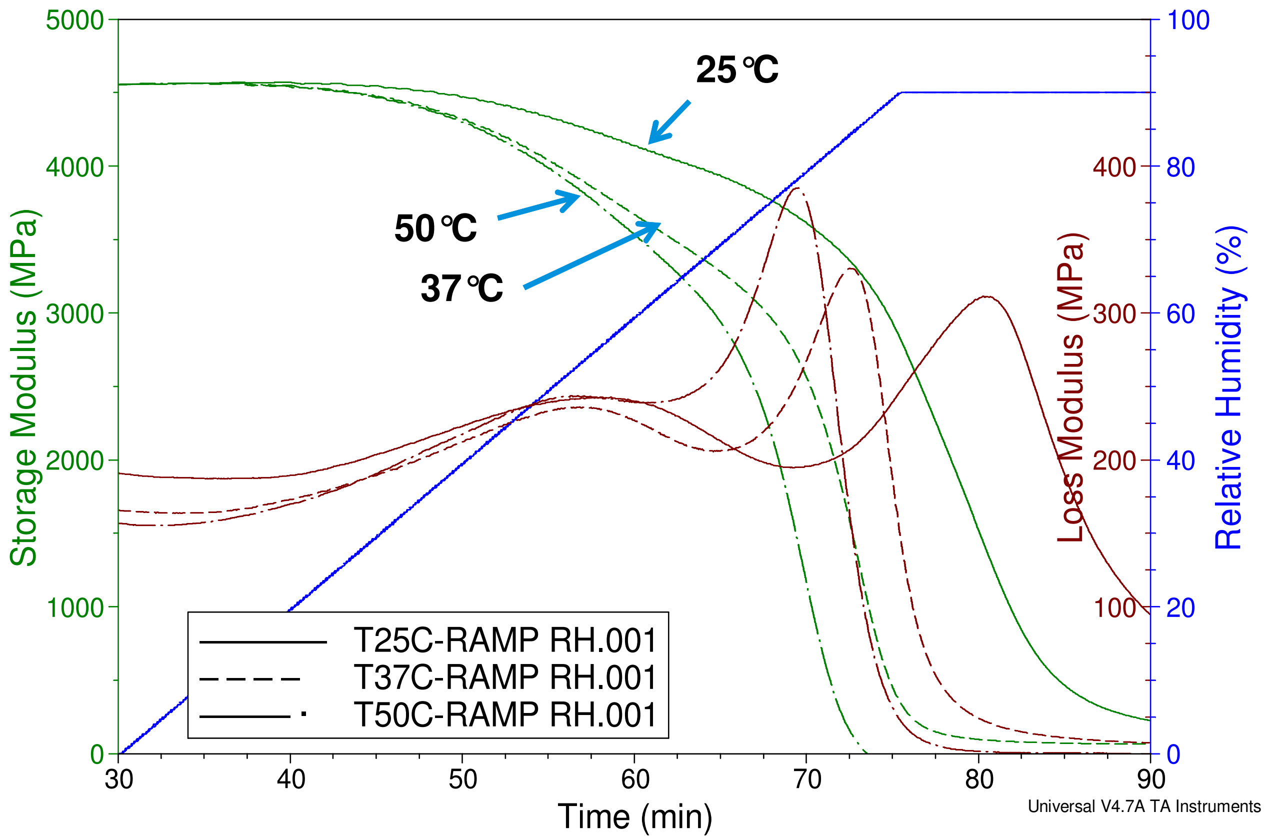
Drug Capsules

- Drug capsules are typically made from gelatin or polysaccharide such as (HPMC)
- Rheology and DMA can help to investigate the optimum capsule process conditions and also evaluate the capsule properties with a controlled temperature and humidity



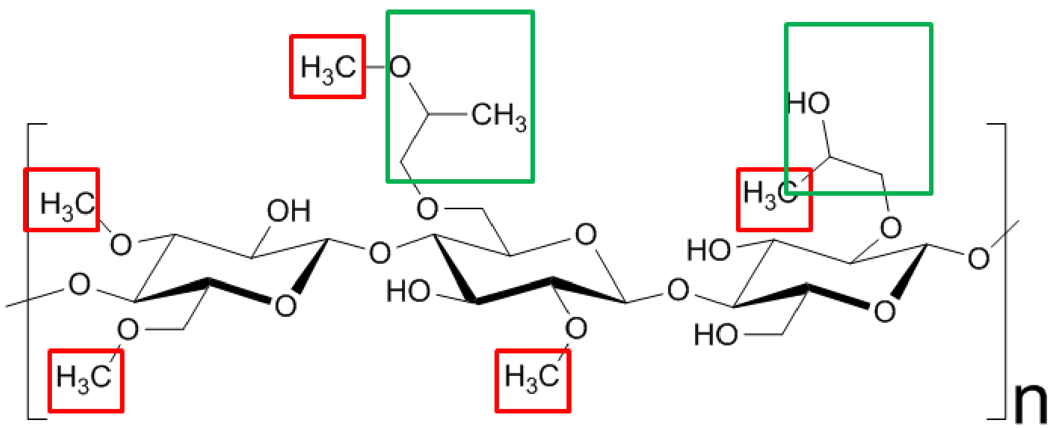
Gelatin Capsule: Mechanical Strength vs. Temperature and Humidity

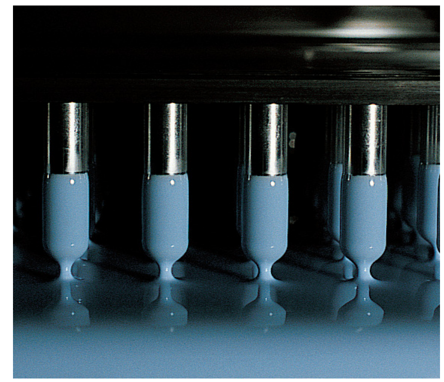
- A dynamic temperature or humidity ramp experiment can help evaluate the mechanical properties (stability) of gelatin capsules at different storage conditions (temperature and humidity).



Water Soluble Cellulose - HPMC

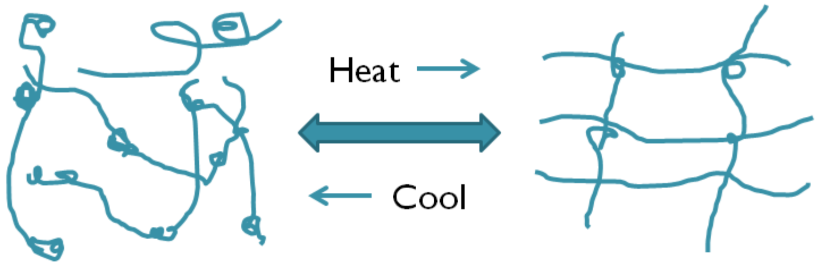
- Hydroxypropyl methylcellulose (HPMC)
- Soluble in cold water, insoluble in hot water. Gelation temperature and gel strength depending on the ratio of HP/MC and degree of substitution
- Cellulose based drug capsules

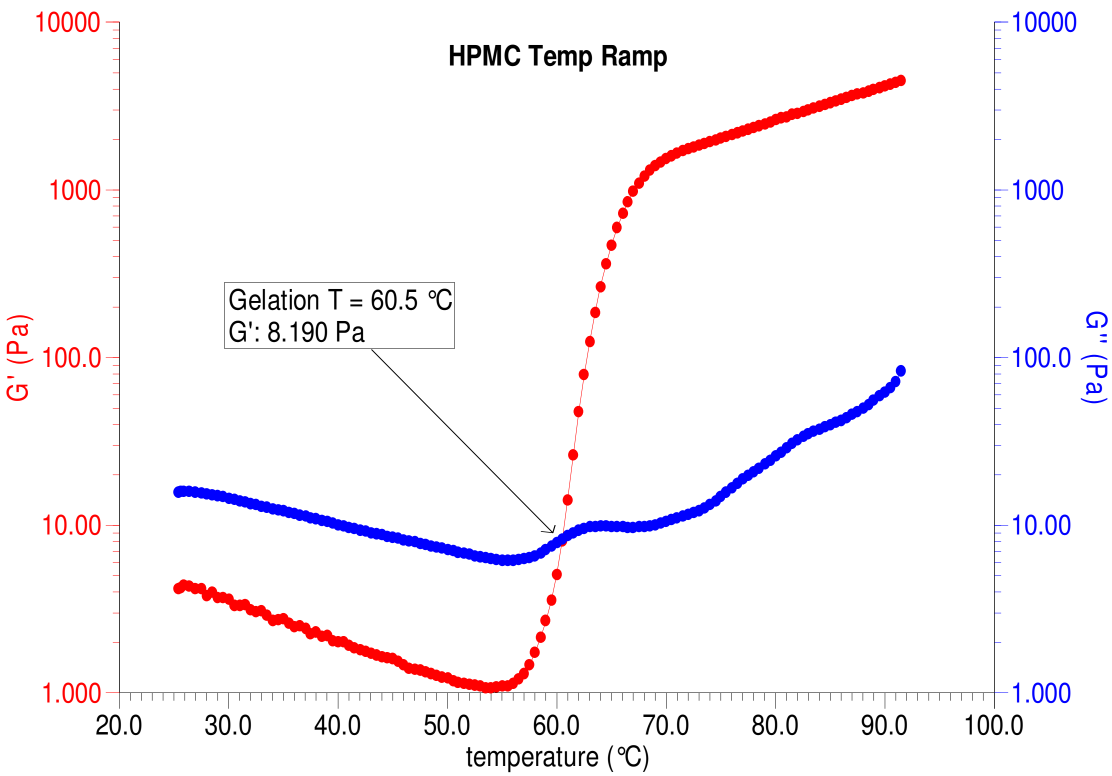




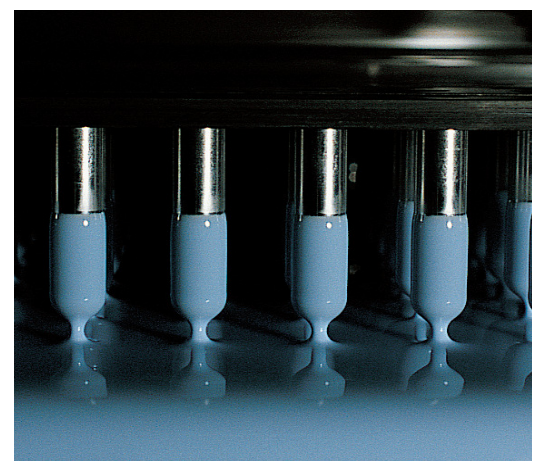
HPMC Gelation Mechanism

- Thermal reversible gel
- Transition from intra-molecular interaction to inter-molecular interaction





Capsule manufacturing process – a hot pin dipped into a cold solution



Polymers – Medical Devices

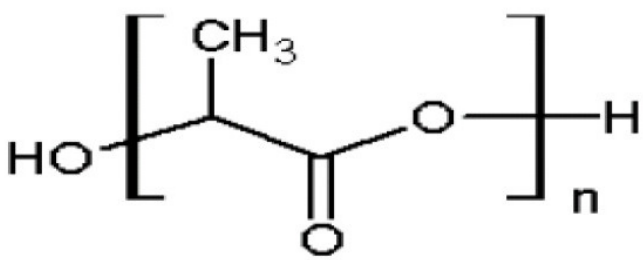
- Polymers are used as medical devices such as hips and knees joints, sutures, stents, and facial prostheses etc.

- Rheology helps to guide process conditions and evaluate end product performance

Application	Polymer Used
Knee, Hip, & Shoulder Joints	Ultrahigh molecular weight polyethylene (UHMWPE)
Finger Joints	Silicone
Sutures	Polylactic and Polyglycolic acid, Nylon
Tracheal Tubes	Silicone, Acrylic, Nylon
Heart Pacemaker	Acetal, Polyethylene, Polyurethane
Blood Vessels	Polyester, PVC, Polytetrafluoroethylene,
Gastrointestinal Segments	Nylon, PVC, Silicones
Facial Prostheses	Polydimethyl siloxane, Polyurethane, PVC
Bone Cement	Polymethyl methacrylate

Polylactic Acid (PLA)

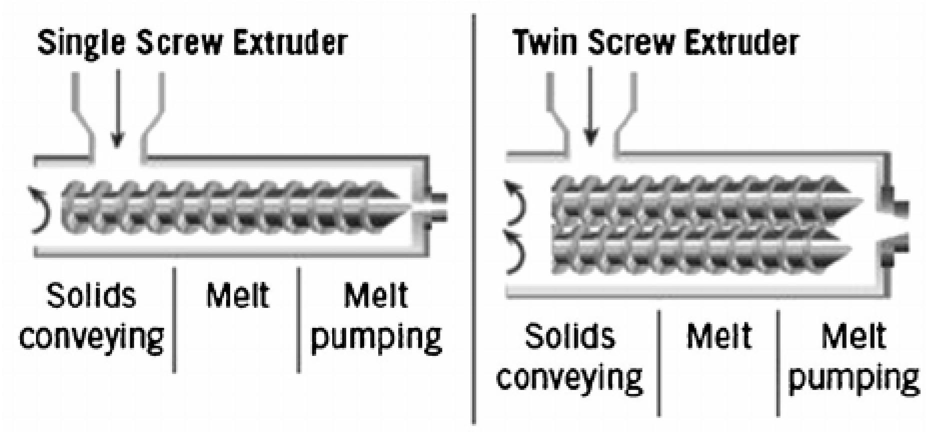
- Polylactic acid (PLA) and its composite materials are FDA approved synthetic degradable polymers. It shows many good characteristic features:
  - Biocompatibility
  - Biodegradability
  - Good process ability
  - Low cost
- PLA has been widely used in many biomedical applications such as
  - Orthopedics
  - Drug carriers
  - Stents
  - Tissue engineering
  - Antimicrobial agents



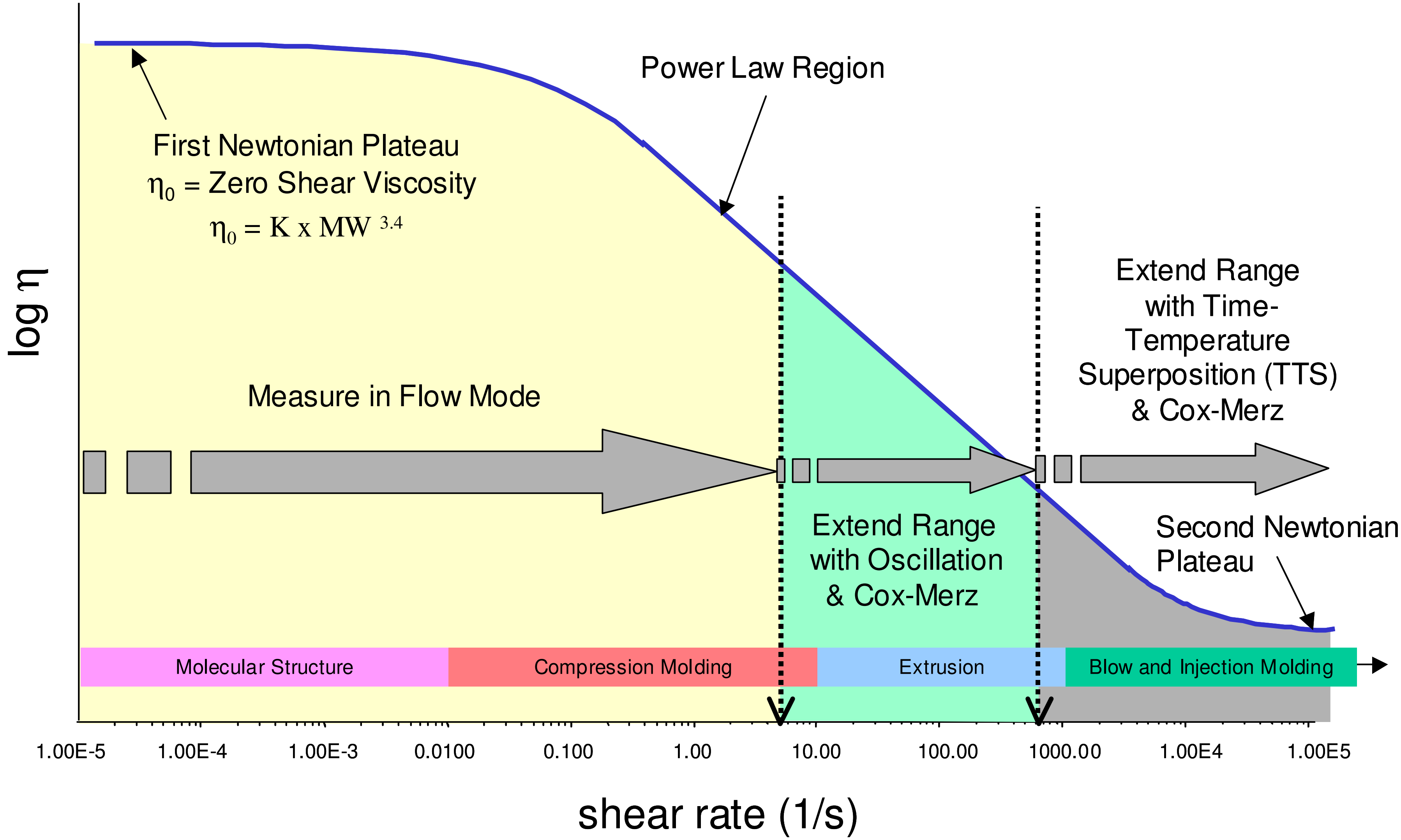
What Rheology Can Help?

- Rheology helps to investigate processing conditions (e.g. temperature and shear). Polymer processing technologies including extrusion, injection molding and blow molding.

- Rheology provides quantitative evaluation on the end unit performance of PLA based products. Such as influence of Mw, plasticizers, stabilizers, pigments and fillers etc.



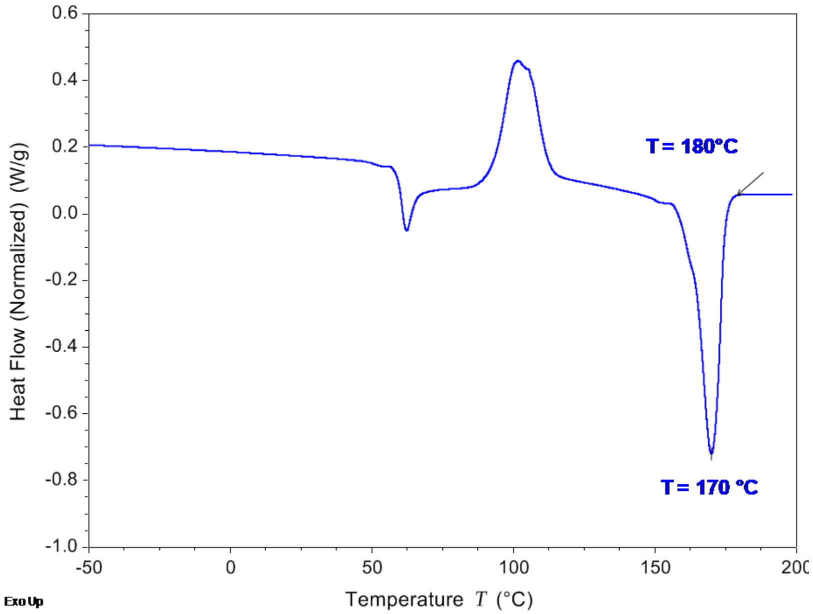
Idealized Flow Curve – Polymer Melts

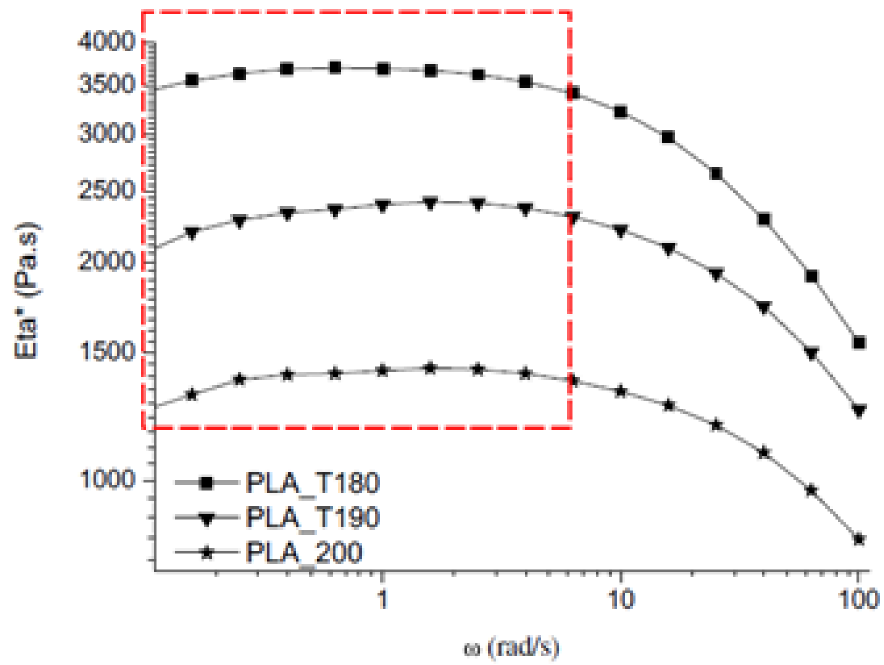


PLA Melt Flow Processing Temperature

- DSC Indicates PLA melt at 170℃. The extrusion process temperature needs to be greater than Tm (melt) but lower than Td (decomposition).

- After melt, extrusion temperature may need to be adjusted to reach ideal shear viscosity

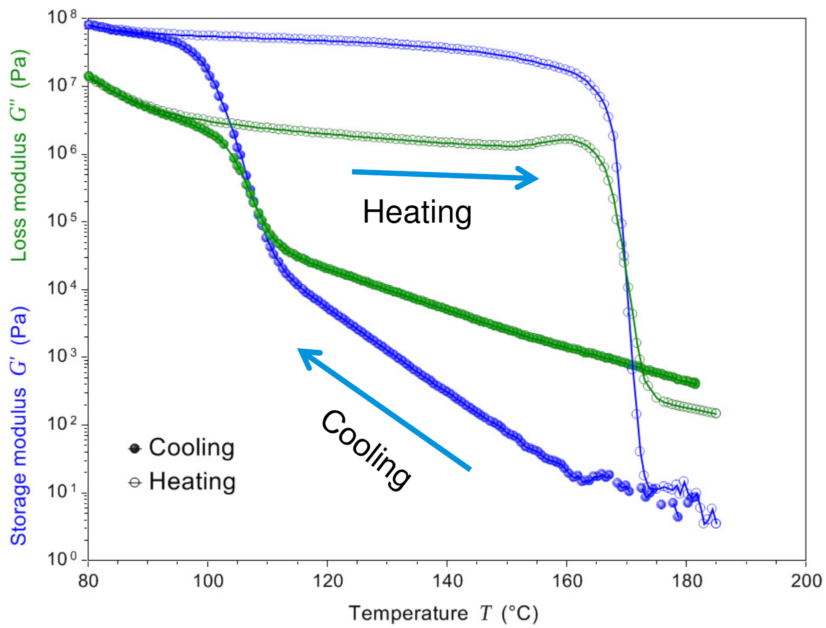


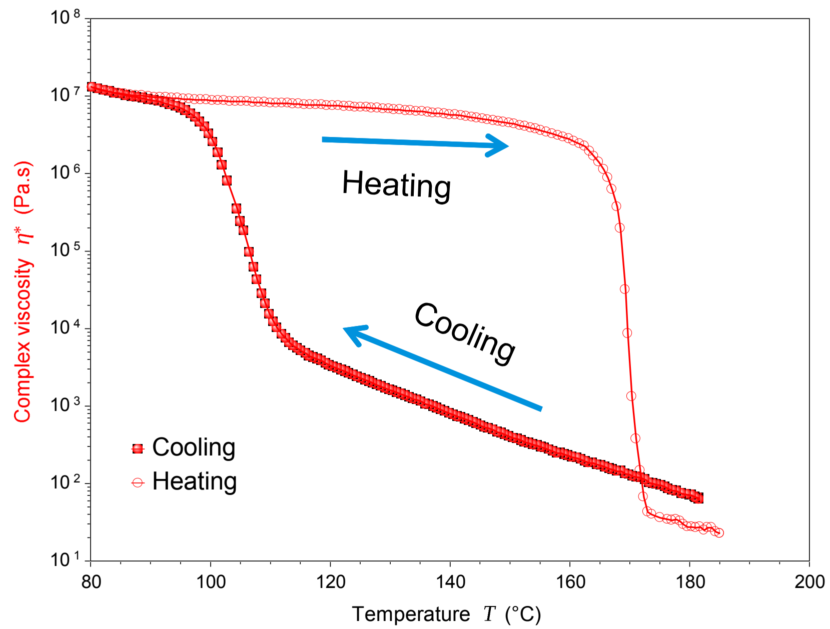


R. Al-Itry et al. / Polymer Degradation and Stability 97 (2012) 1898e1914

PLA Melt Temp Ramp Test on a Rheometer

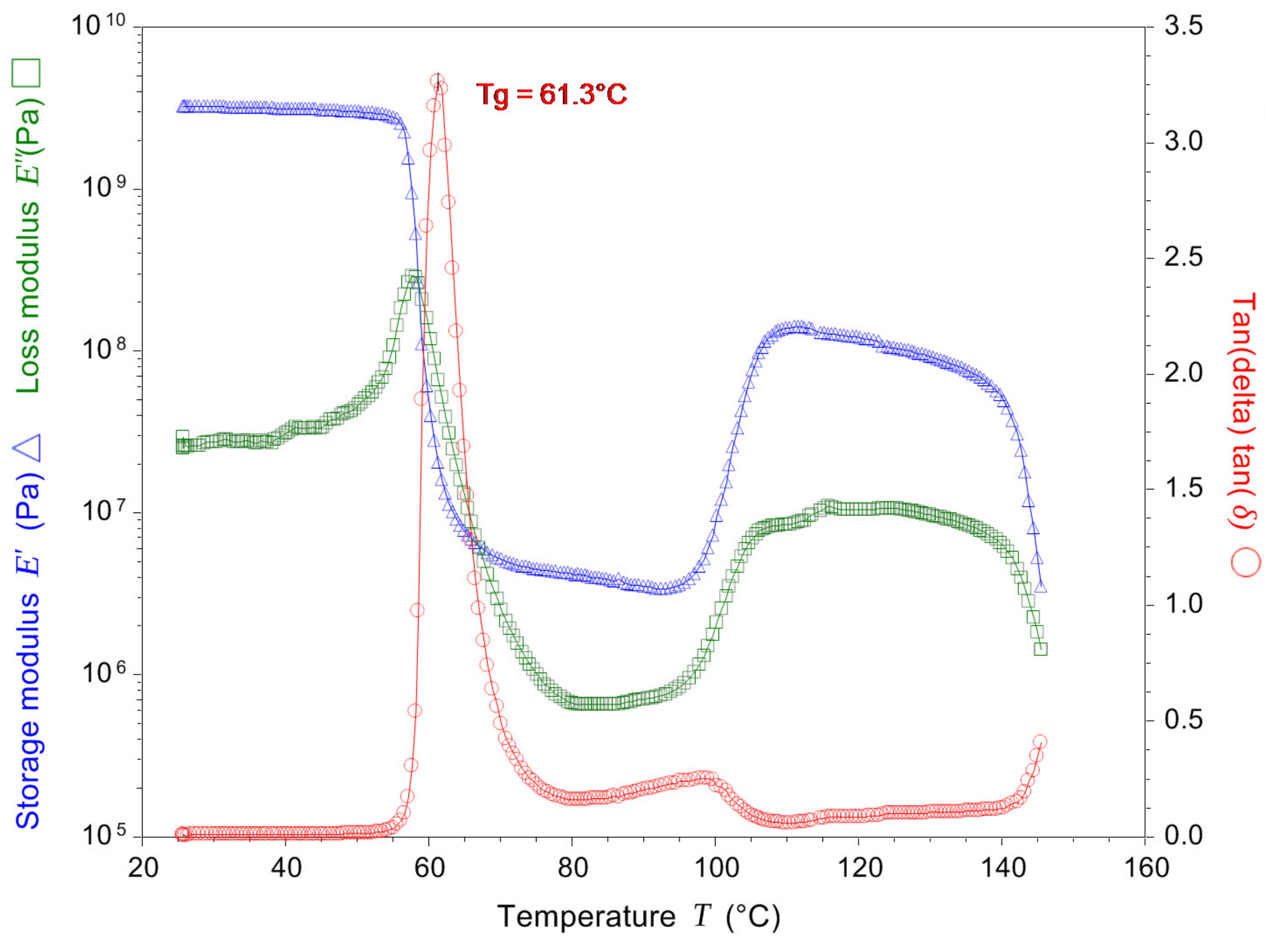
- A dynamic temperature ramp test on rheometer can help to investigate appropriate extrusion temperature and also cooling conditions





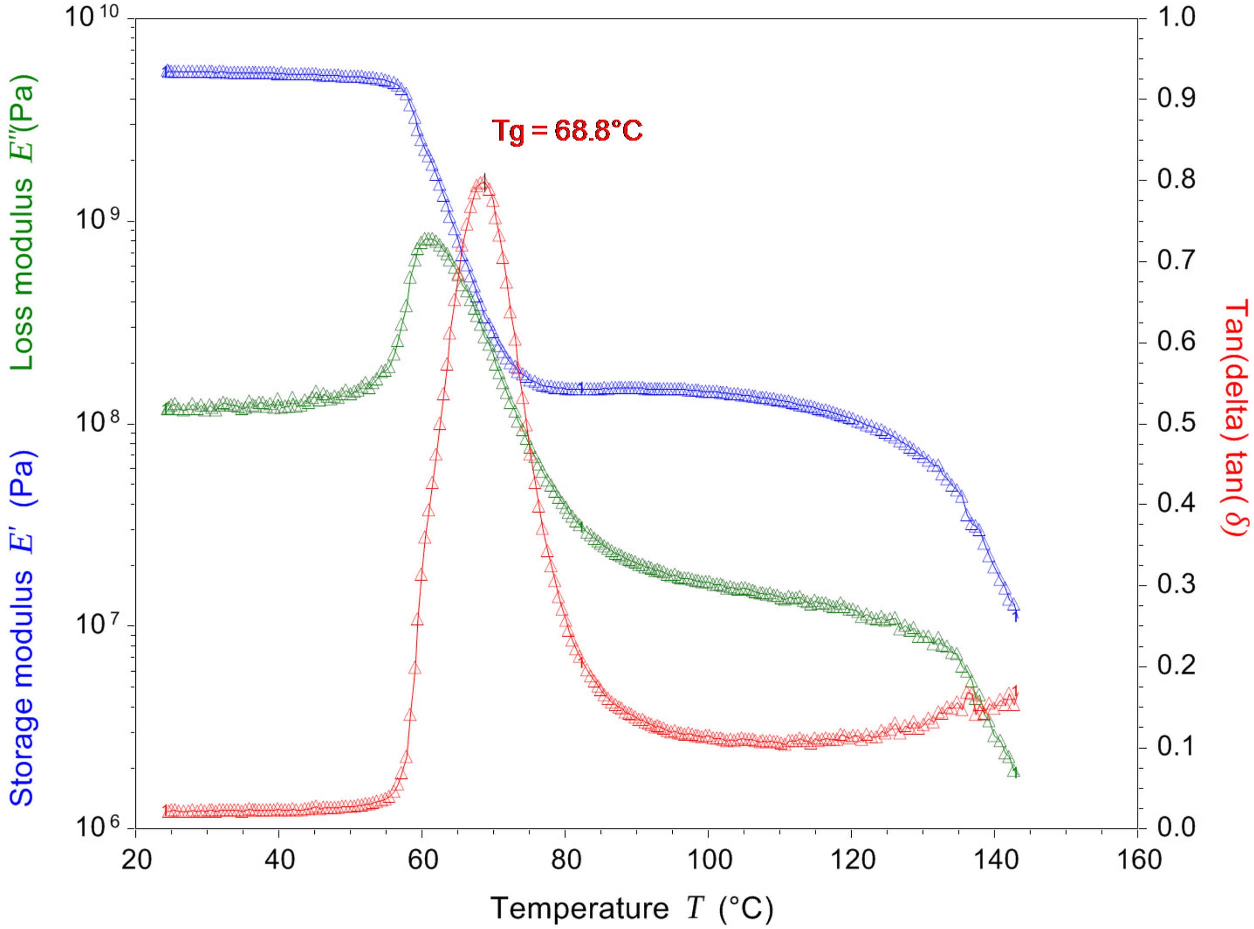
PLA End Product Performance-Fast Cooling

- PLA fast cooling after extrusion

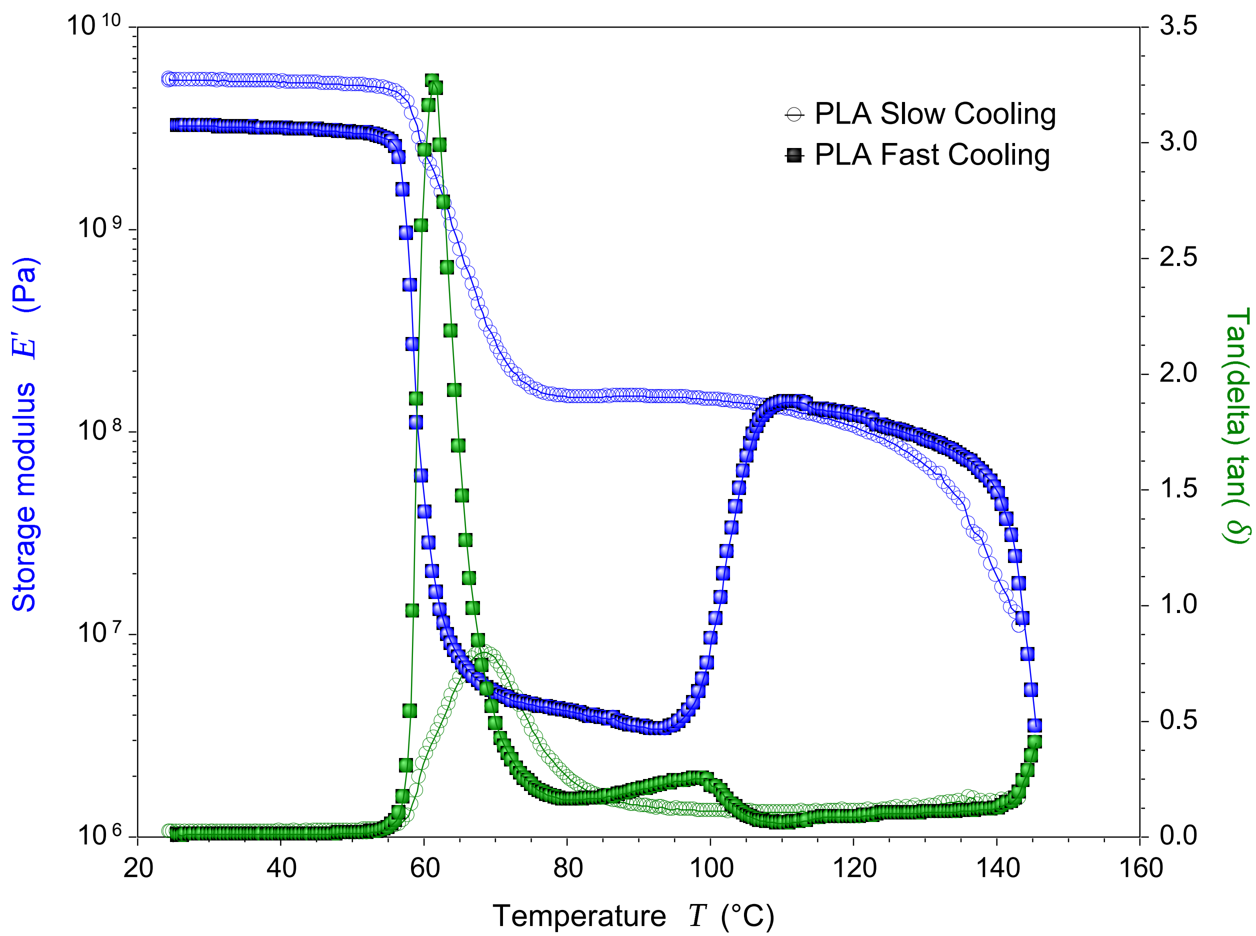


PLA End Product Performance-Slow Cooling

- PLA slow cooling after extrusion



PLA – Compare Different Process Conditions



Summary

- Rheology is a powerful tool for investigating viscosity and viscoelastic properties of biopolymer materials and biomedical devices

- Materials evaluated by rheological techniques can be either liquids, semi-solids, gels, or solids. The viscoelastic properties can be monitored as a function of time, temperature, frequency, shear rate and shear stress

- The rheological measurement information can be used for
  - Basic research and product development
  - Trouble shooting manufacturing problems
  - General QC analysis, distinguish batch to batch variation

Agenda

- 9 - 10:15am: Thermal analysis and stability of biomaterials
- 10:15-10:30am: Break
- 10:30-noon: Using rheology to characterize flow and viscoelastic properties of hydrogels, adhesives and biopolymers
- **12-1pm: Lunch**
- 1-2:15pm: Mechanical testing of medical devices
- 2:15-2:30 - break
- 2:30-3:15pm: Mechanical testing of engineered tissues and biomaterials
- 3:15-4pm – Q&A with TA Instruments Applications Engineers

Thank you for your attention!

Instruments