Thermal Analysis and Stability of Biomaterials

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Agenda

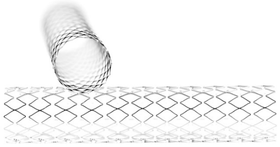
- **9 - 10:15am: Thermal analysis and stability of biomaterials**
- 10:15-10:30am: Break
- 10:30-noon: Using rheology to characterize flow and viscoelastic properties of hydrogels, adhesives and biopolymers
- 12-1pm: Lunch
- 1-2:15pm: Mechanical testing of medical devices
- 2:15-2:30 - break
- 2:30-3:15pm: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

What is a Biomaterial?

- Any synthetic material used to replace or restore function to a body tissue
  - Biomaterials are continuously in contact with body fluids
  - Exposure to body fluids implies that the biomaterial is placed within the interior of the body
    - This places restrictions on the types of biomaterials used

Ideal Biomaterial Properties

- Ideal material combination for biomaterials exhibits these qualities
  - A biocompatible chemical composition to avoid negative tissue reactions
  - Resistance to degradation
    - Corrosion resistance for metals
    - Resistance to biological degradation in polymers
  - Acceptable strength to sustain cyclic loading by the joint
  - A low modulus to minimize bone resorption
  - High wear resistance to minimize wear-debris generation

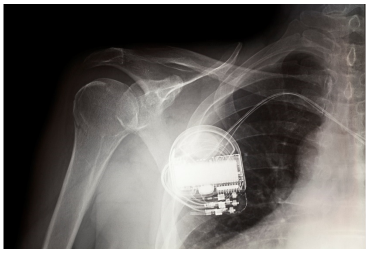


Types of Biomaterials

- Metals
  - Select metals are biocompatible and capable of long-term success as bodily implants
    - Nontoxic elements are used as alloying elements in biomedical alloys
    - Principal metals used: Stainless Steels, Pure titanium and titanium alloys, and Cobalt-base alloys
      - Ability to bear significant loads, withstand fatigue loading, and undergo plastic deformation prior to failure
  - Orthopedic surgeries commonly involve metallic implantation
    - Metallic implants are used in maxillofacial surgery, cardiovascular surgery and dental materials

Types of Biomaterials

- Polymers
  - Used for: facial prostheses, tracheal tubes, heart components, kidney components, liver components, dentures, hip and knees joints
  - Medical adhesives
  - Coatings and sealants



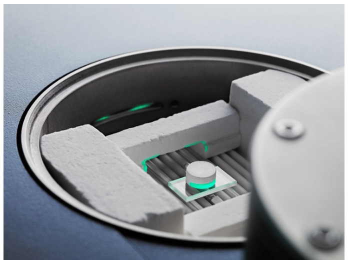
Application	Polymer Used
Knee, Hip, & Shoulder Joints	Ultrahigh molecular weight polyethylene (UHMWPE)
Finger Joints	Silicone
Sutures	Polylactic and Polyglycolic acid, Nylon
Tracheal Tubes	Silicone, Acrylic, Nylon
Heart Pacemaker	Acetal, Polyethylene, Polyurethane
Blood Vessels	Polyester, Polytetrafluoroethlene,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

Biopolymers

Polymer	Typical Use
Polyethylene	Tubing, Connectors and Bottles, Plastic Surgery Implants
Polypropylene	Disposable Syringes, Connectors, Finger-joint Prostheses, Nonabsorbable Sutures
Polytetrafluoroethylene, Polydifluoromethylene	Vascular Graft Prostheses, Heart Patches, Retinal Detachment Treatment
Polystyrene	Disposable Laboratory Items
Polymethyl methacrylate	Bone Cement, Artificial and Implanted Teeth, Denture Materials and Fillings, Intraocular Lens
Polyvinyl chloride	Disposable Medical Items, Blood Tubing Line, Cardiac Catheters, Artificial Limb Materials
Polydimethylsiloxanes (Silicone rubber)	Plastic Surgery Implants, Artificial heart and Heart-assist Pump Materials, Atrioventricular Shunts, Finger-joint Repair
Polyacrylonitrile	Membrane for dialysis
Polyurethane	Balloon for Intra-aortic Pump, Heart Valve Prostheses, Tubing
Polyvinyl alcohol	Drug-delivery System
Polyamides (nylons)	Nonabsorbable sutures, Tendon prosthesis, Drug-delivery System, Tracheal Tubes
Polyethylene terephthalate	Tendon and Ligament Reconstruction, Tracheal Replacement, Surgical Mesh Fabric
Hydrogels	Contact Lenses, Wound Dressings, Ophthalmic Implants, Drug-delivery System

Types of Biomaterials

- Ceramics
    - Ideal as biological implants; bone bonds well to them and they exhibit inertness within the body, high stiffness, and low friction and wear
        - Main drawback is their brittle nature, low impact resistance
    - Used for restorative materials in dentistry



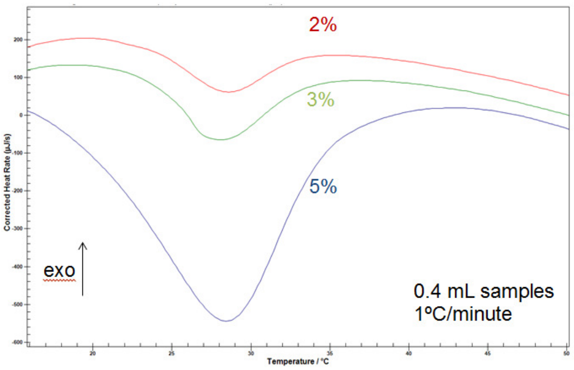
- Composites
    - Combination of low density/weight and high strength make them ideal for prosthetic limbs

Adhesives

- Adhesive biomaterials typically fall into three categories
    - Medical device assembly
        - Manufacturing of life-support equipment, sterile disposable items, sterile reusable items, and devices used for sensing, monitoring, and reporting
    - Hard tissue attachments
        - Orthopedics and dentistry
    - Soft tissue attachments
        - Wound closure

Hydrogels

- Hydrogels are flexible polymers used in a wide variety of applications including tissue engineering, drug delivery, contact lenses and superabsorbent materials.
- When a hydrogel is heated, the structure dissociates and the gel "melts" or collapses. Understanding and quantifying the chemistry of gelation on cooling and collapse on heating is important for consistent hydrogel formation.
- Hydrogels sense changes of pH, temperature, and concentrations of metabolite and these properties are used in their applications.



0.4 mL samples
1ºC/minute

TA Instruments – Thermal Analysis, Calorimetry, Rheology, Mechanical Testing

- Heat of Reactions
- Phase Changes
- Transition Temperatures
- Reaction Kinetics
- Thermal, Oxidative Stability

Calorimetry

- Residual Solvent Content
- Sorption/Desorption Profiles
- Thermal, Oxidative Stability
- Decomposition Kinetics, Lifetime Plots

Thermogravimetric Analysis

- Dimensional Changes
- Coefficient of Thermal Expansion
- Softening Point
- Annealing Characteristics

Dilatometry/Thermo-Mechanical Analysis (TMA)

- Visco-Elastic Properties
- Structure-Property Relationship
- Process Conditions
- End Product Performance

Rheology/Rubber Testing Products

- Fatigue Life
- Failure Analysis
- Viscoelastic Properties
- Physiologic Simulation

Mechanical Testing

- Thermal Diffusivity
- Thermal Conductivity
- Specific Heat Capacity
- Thermal Resistivity

Thermal Conductivity

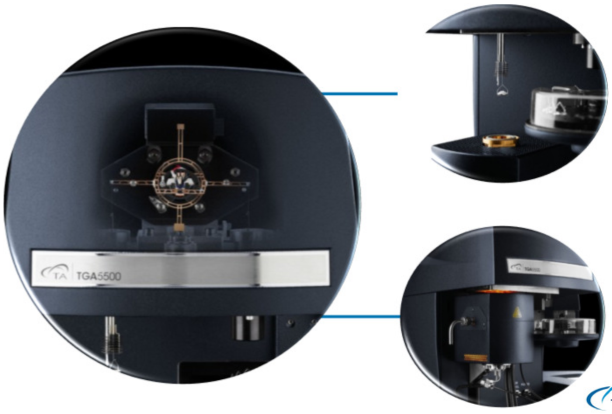
What is Thermogravimetric Analysis (TGA)?

- Thermogravimetric Analysis (TGA) measures weight/mass change (loss or gain) and the rate of weight change as a function of temperature, time and atmosphere.

- Measurements are used primarily to determine the composition of materials and to predict their thermal stability. The technique can characterize materials that exhibit weight loss or gain due to sorption/desorption of volatiles, decomposition, oxidation and reduction.

Thermogravimetric Analyzers

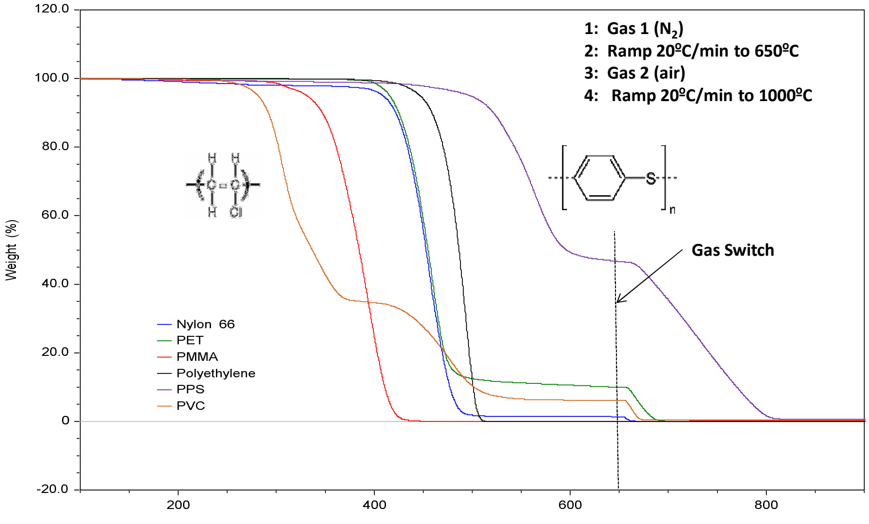
- A TGA must accurately:
  - control heating rate (furnace)
  - measure the change in temperature (thermocouple)
  - measure the mass of a sample and the change in mass as it is heated or held at an isothermal temperature (balance)



TGA Applications

- Thermal stability of materials
- Oxidative stability of materials
- Composition of multi-component systems
- Decomposition mechanism when coupled with evolve gas analysis techniques (FTIR, MS)
- The effect of reactive or corrosive atmospheres on materials
- Moisture and volatiles content of materials
- Estimated lifetime of a product
- Decomposition kinetics of materials

Thermal Stability of Polymers



1: Gas 1 (N_2)
2: Ramp 20ºC/min to 650ºC
3: Gas 2 (air)
4: Ramp 20ºC/min to 1000ºC

Gas Switch

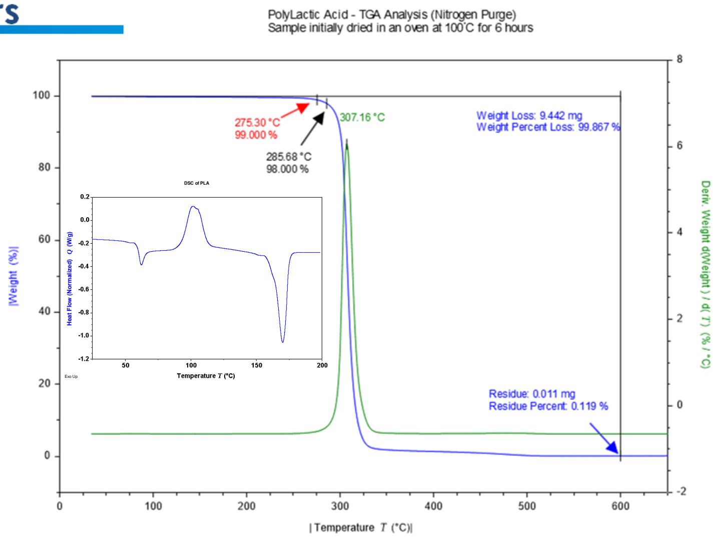
Thermal Decomposition and Degradation

- Solid polymeric materials undergo both physical and chemical changes when heat is applied. This usually results in undesirable changes to the properties of the material.
- ASTM provides a distinction to the terms thermal decomposition and thermal degradation:
  - **Thermal decomposition**: the process of extensive chemical species change caused by heat
  - **Thermal degradation**: a process whereby the action of heat or elevated temperature on a material, product or assembly causes a loss of physical, mechanical or electrical properties.

Thermal Stability of Polymers

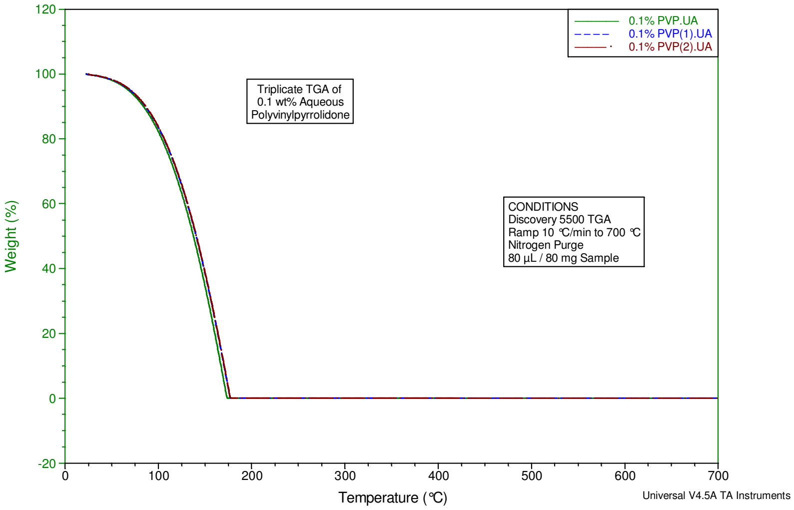
Upon degradation, typical property changes include:

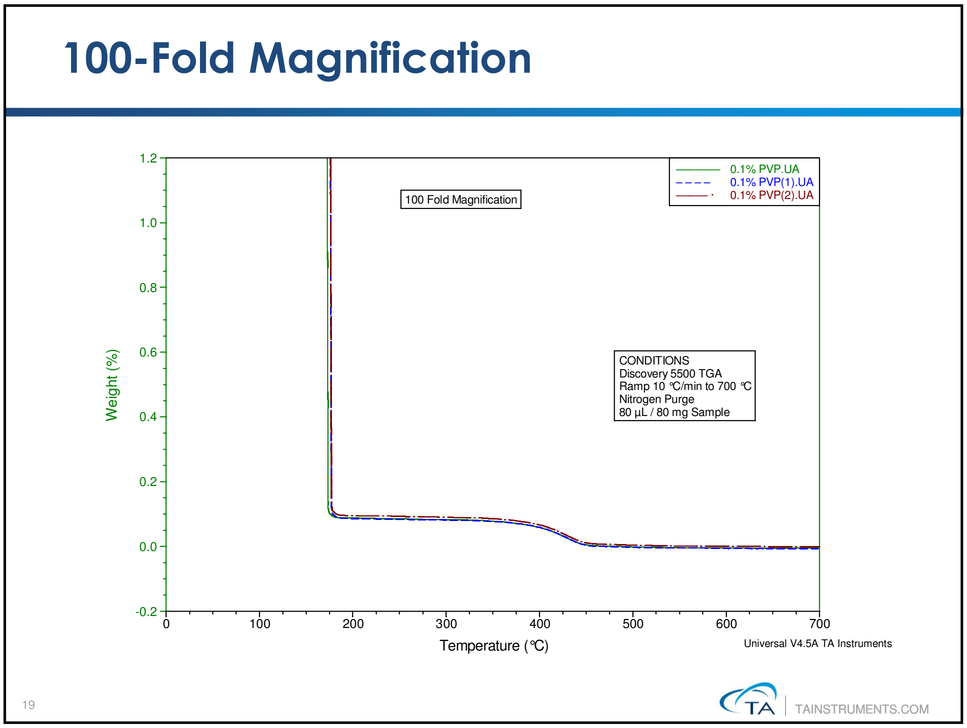
- Reduced ductility and embrittlement
- Chalking
- Color changes
- Cracking
- General reduction in most other desirable physical properties


PolyLactic Acid - TGA Analysis (Nitrogen Purge)
Sample initially dried in an oven at 100°C for 6 hours

Thermal degradation generally involves changes to the molecular weight (and molecular weight distribution) of the polymer.

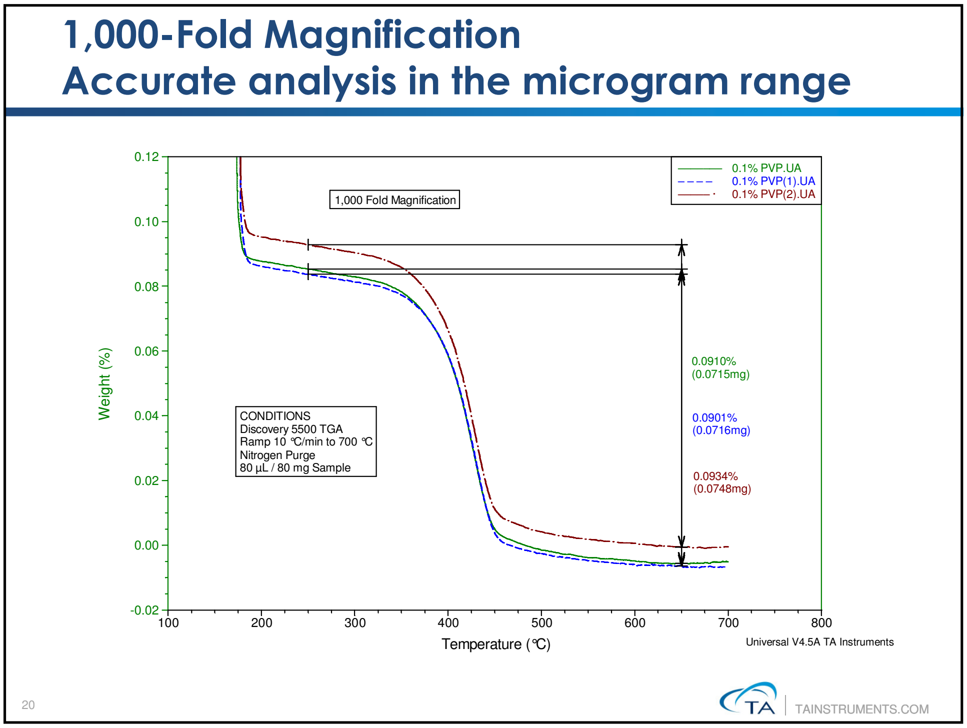
TGA of Polyvinylpyrrolidone (PVP) - Residual Content (Aqueous Polymer Solution)





100-Fold Magnification

CONDITIONS
Discovery 5500 TGA
Ramp 10 °C/min to 700 °C
Nitrogen Purge
80 µL / 80 mg Sample

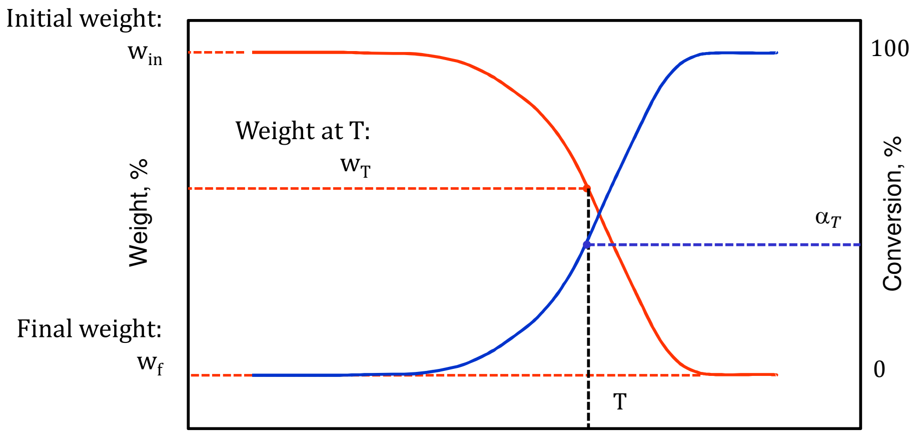


1,000-Fold Magnification
Accurate analysis in the microgram range

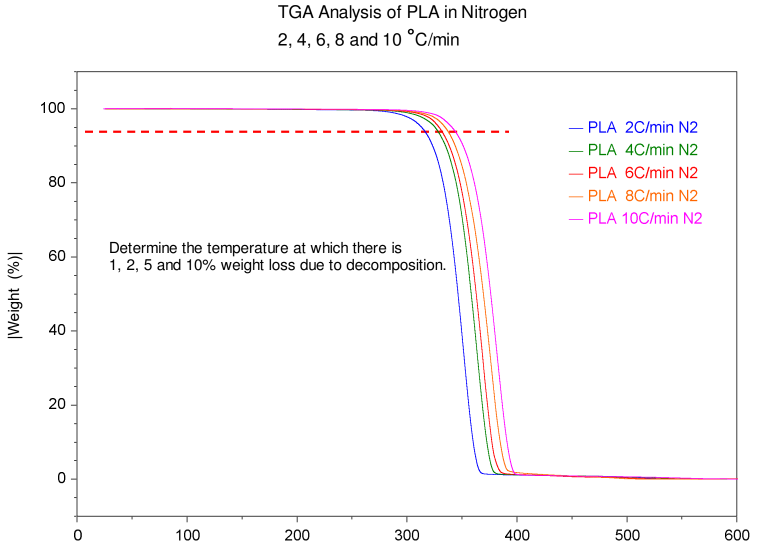
CONDITIONS
Discovery 5500 TGA
Ramp 10 °C/min to 700 °C
Nitrogen Purge
80 µL / 80 mg Sample

Kinetics by TGA

$$Conversion: \alpha = \frac{w_{in} - w_T}{w_{in} - w_f}$$

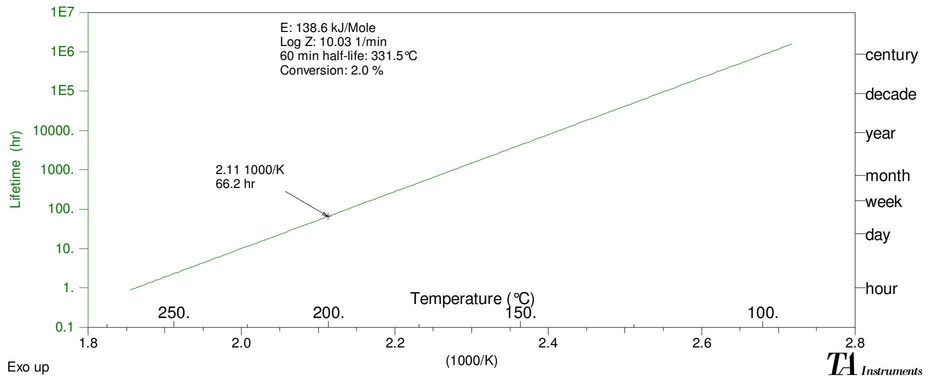


Polylactic Acid (PLA) Decomposition ASTM E1641 (Nitrogen Atmosphere)



Determine the temperature at which there is 1, 2, 5 and 10% weight loss due to decomposition.

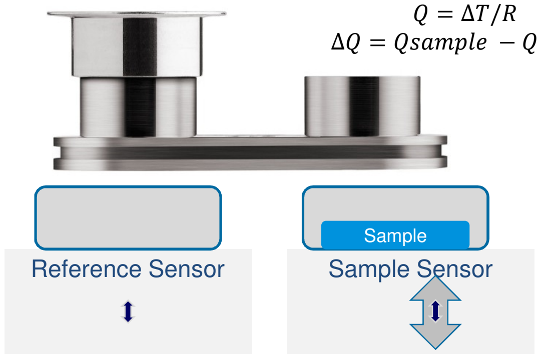
PLA Decomposition by ASTM E1641 Lifetime Plot Using a 2% Conversion



If processing is performed at 200℃ (above the melting temperature, under a nitrogen blanket), PLA is predicted to lose 2% weight due to decomposition if held for 66 hours at that elevated temperature.

Simple Heat Flux DSC Cell Schematic

$$Q = \Delta T / R$$
$$\Delta Q = Qsample\ - Qreference$$



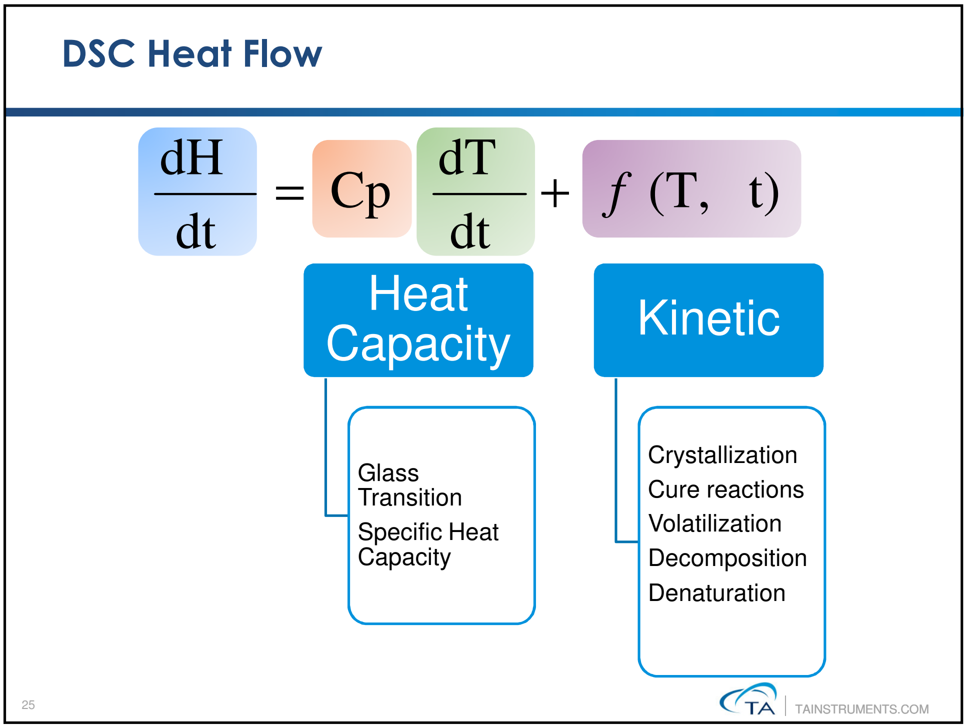
Reference Sensor

An empty pan on the reference sensor should react similarly to the pan on the sample sensor, thus canceling out any pan contribution

Sample Sensor

Heat **absorbed** by the sample gives an endothermic response

Heat **released** by the sample gives an exothermic response



DSC Heat Flow

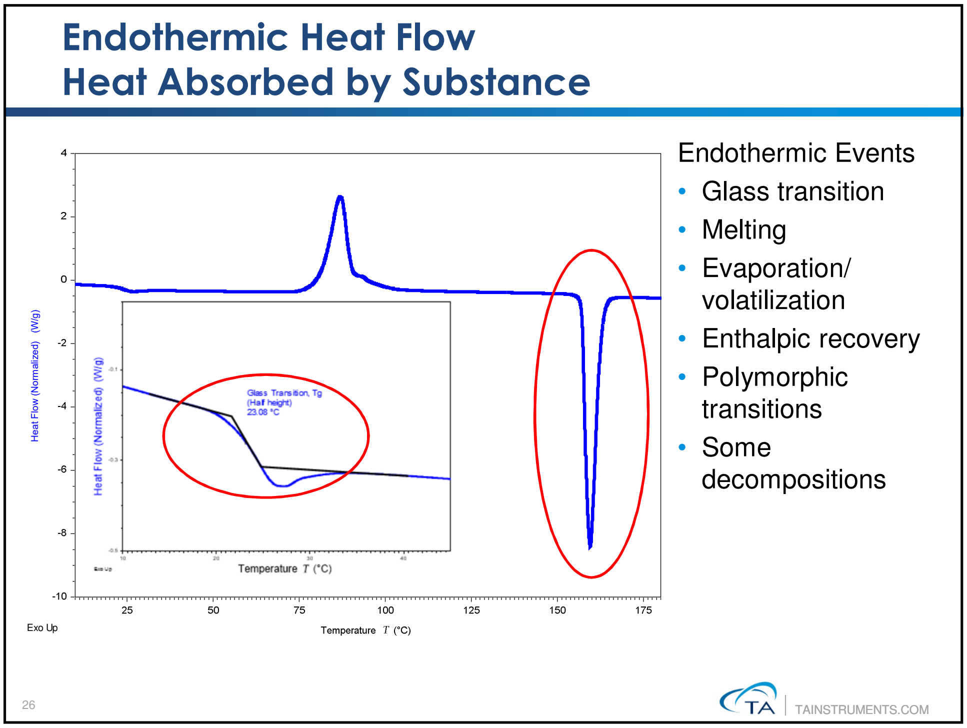
$$\frac{dH}{dt} = Cp\,\frac{dT}{dt} + f\,(T,\ t)$$

Heat Capacity

- Glass Transition
- Specific Heat Capacity

Kinetic

- Crystallization
- Cure reactions
- Volatilization
- Decomposition
- Denaturation

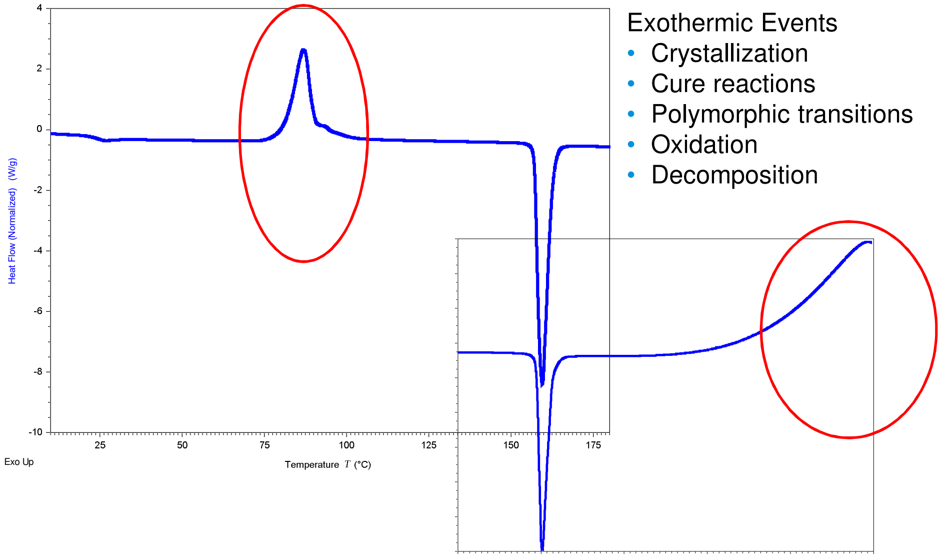


Endothermic Heat Flow
Heat Absorbed by Substance

Endothermic Events

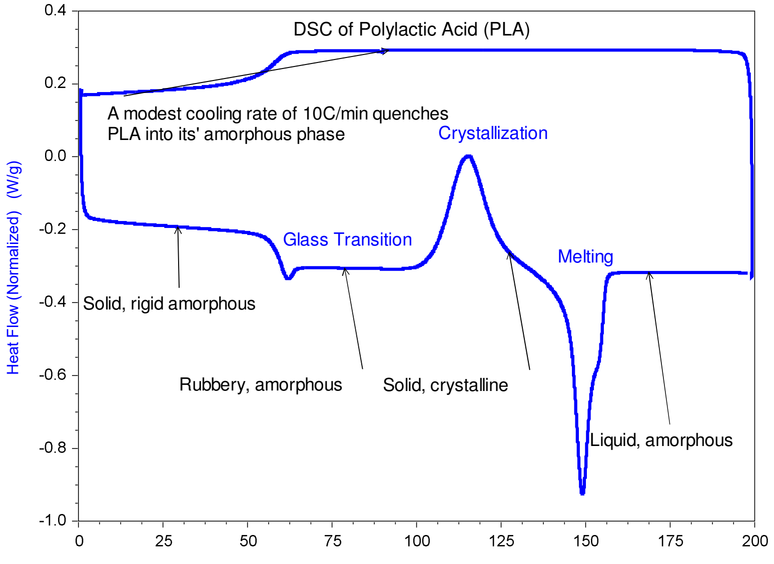
- Glass transition
- Melting
- Evaporation/ volatilization
- Enthalpic recovery
- Polymorphic transitions
- Some decompositions

Exothermic Heat Flow
Heat Released by Substance



Exothermic Events
- Crystallization
- Cure reactions
- Polymorphic transitions
- Oxidation
- Decomposition

Morphology of Polymers:
Amorphous and Semi-Crystalline

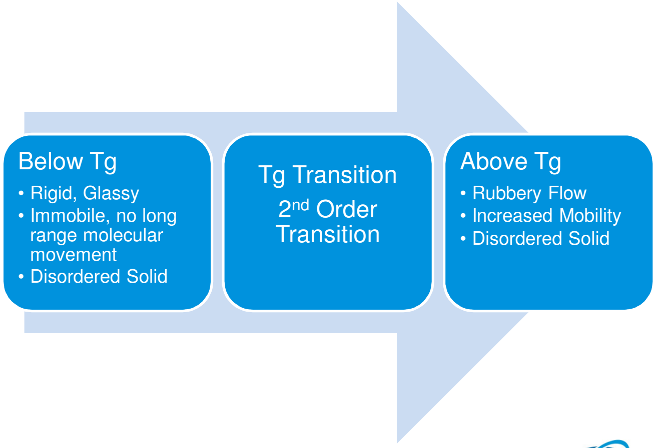


Determining the Glass Transition Temperature, Tg

- ASTM Standards
  - E3418 Standard test method for transition temperatures and enthalpies of fusion and crystallization of polymers by differential scanning calorimetry
  - E1356 Standard test method for assignment of the glass transition temperatures by differential scanning calorimetry
- ISO Standard
  - ISO11357-2 Determination of glass transition temperature and glass transition step height

The Glass Transition (Tg)

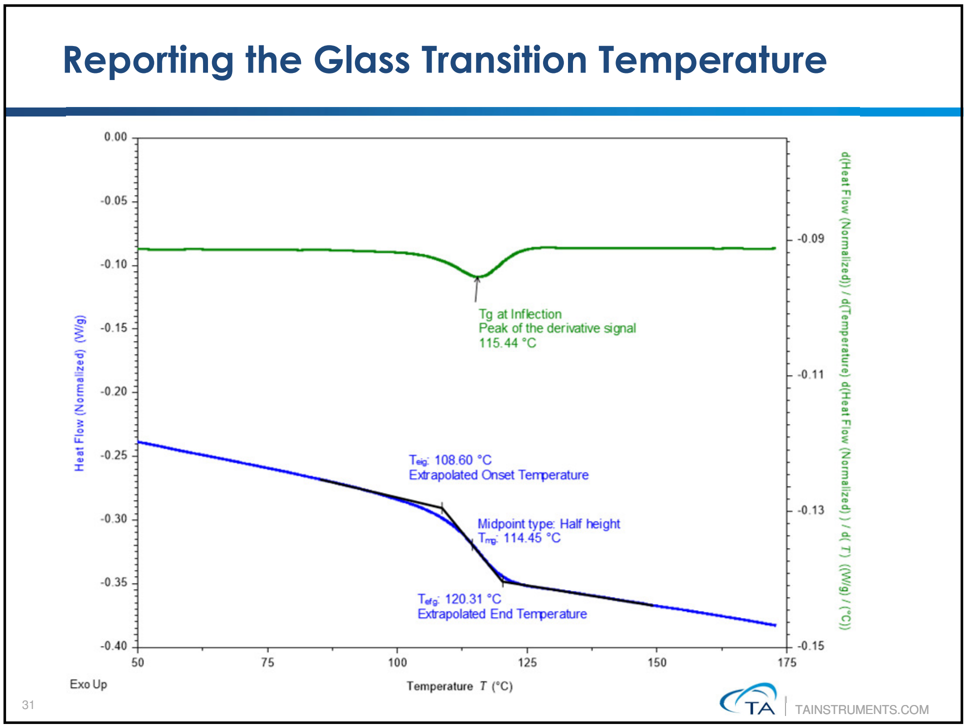
- The glass transition is a change in the free volume and molecular mobility in the amorphous phase of a material that results in a step change in heat capacity.



Below Tg
- Rigid, Glassy
- Immobile, no long range molecular movement
- Disordered Solid

Tg Transition
2^{nd} Order Transition

Above Tg
- Rubbery Flow
- Increased Mobility
- Disordered Solid



Reporting the Glass Transition Temperature

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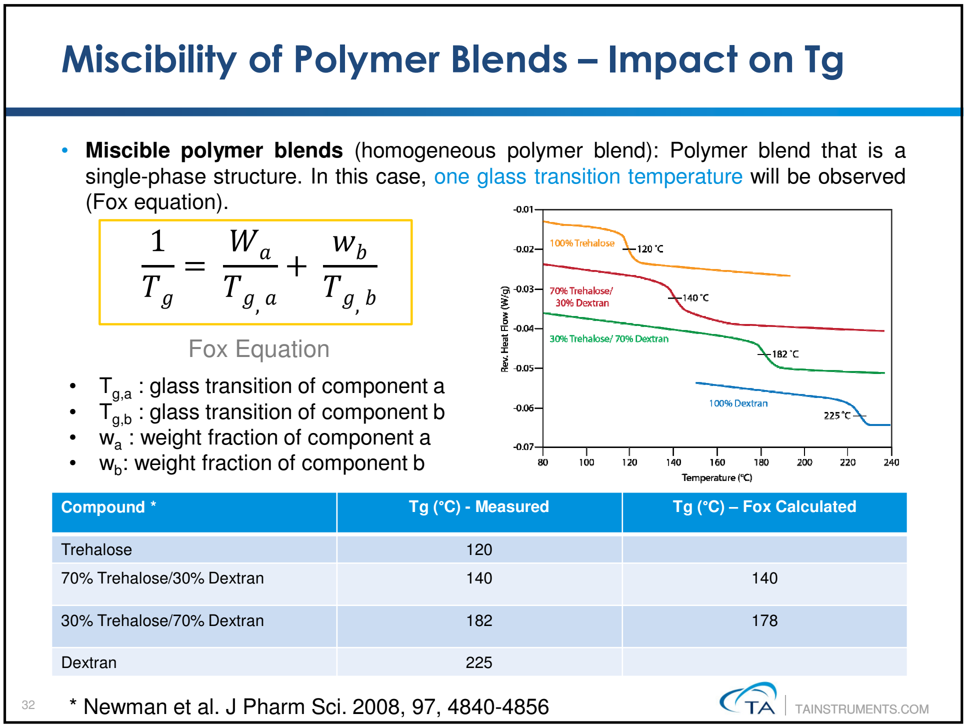

Miscibility of Polymer Blends – Impact on Tg

- **Miscible polymer blends** (homogeneous polymer blend): Polymer blend that is a single-phase structure. In this case, one glass transition temperature will be observed (Fox equation).

$$\frac{1}{T_g} = \frac{W_a}{T_{g,a}} + \frac{w_b}{T_{g,b}}$$

Fox Equation

- $T_{g,a}$: glass transition of component a
- $T_{g,b}$: glass transition of component b
- w_a : weight fraction of component a
- w_b: weight fraction of component b

Compound *	Tg (°C) - Measured	Tg (°C) – Fox Calculated
Trehalose	120	
70% Trehalose/30% Dextran	140	140
30% Trehalose/70% Dextran	182	178
Dextran	225	

* Newman et al. J Pharm Sci. 2008, 97, 4840-4856

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What Affects the Glass Transition?

- Heating Rate
- Heating & Cooling
- Aging
- Molecular Weight
- Plasticizer (compatibility)
- Filler
- Crystalline Content
- Copolymers
- Side Chains
- Polymer Backbone
- Hydrogen Bonding

Anything that effects the mobility of the molecules, affects the Heat Capacity and, in turn, the Glass Transition

Study of melting/crystallization using a DSC

- Melting is the process of converting solid, crystalline structure (lower energy) to a liquid amorphous structure (higher energy).
- Crystallization – The process of converting either solid amorphous structure (cold crystallization on heating) or liquid amorphous structure (cooling) to a more organized solid crystalline structure
- Melting:
  - low energy state → high energy state; requires input of energy; Endothermic peak
- Crystallization:
  - high energy state → low energy state; releases energy; Exothermic peak
- We integrate these peaks, <u>on a time basis</u> to determine the Heat of Fusion (melting) and Heat of crystallization

Experimental Method

A Heat Cool Ramp Method

1) Ramp 10℃/min to -90℃ or Equilibrate to -90℃*
2) Ramp 10℃/min to 200℃
3) Ramp 10℃/min to -90℃ or Equilibrate to -90℃*
4) Ramp 10℃/min to 200℃

- Start test at least 30℃ below the expected Tg
- End test at least 50℃ above the expected Tg for amorphous solids; stay below the decomposition temperature
- Increase heating rate and/or mass if Tg is barely detectable; this increases sensitivity

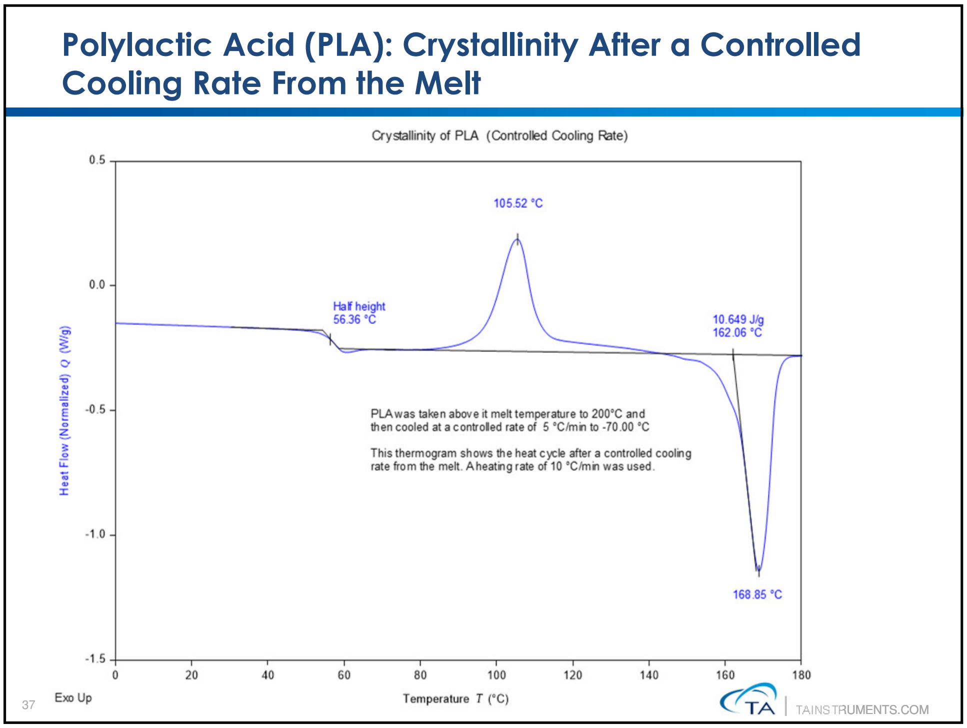
Basis of Multiple Heat Cool Heat Cycles

- 1st heating scan: Called the initial run. It reveals information about the current condition of the specimen; i.e., the thermal and mechanical history as influenced by processing conditions, crystallinity and curing, service temperatures etc.

- Cooling scan: Subsequent controlled cooling rates create a new, known specimen history

- 2nd and 3rd heating scans: Used for determining the characteristic properties of the material. In the case of reactive resins, a third heat cycle may be performed to validate the completion of the reaction.

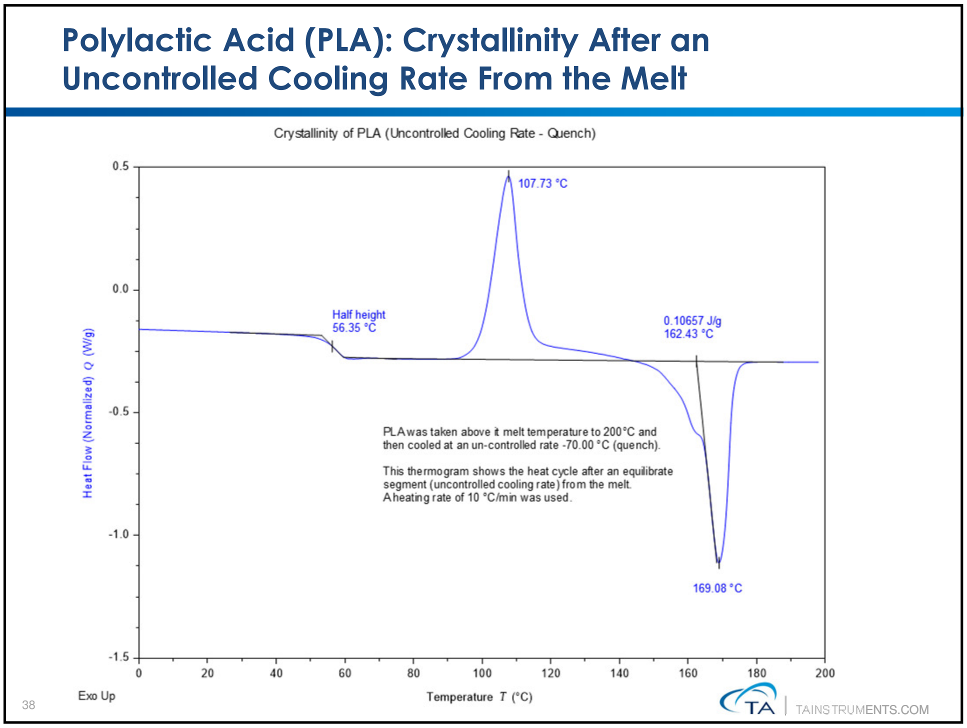
* Reference: *Thermal Analysis of Plastics: Theory and Practice* by G.W. Ehrenstein, G. Riedel, P. Trawiel 2004



Polylactic Acid (PLA): Crystallinity After a Controlled Cooling Rate From the Melt

PLA was taken above it melt temperature to 200°C and then cooled at a controlled rate of 5 °C/min to -70.00 °C

This thermogram shows the heat cycle after a controlled cooling rate from the melt. A heating rate of 10 °C/min was used.

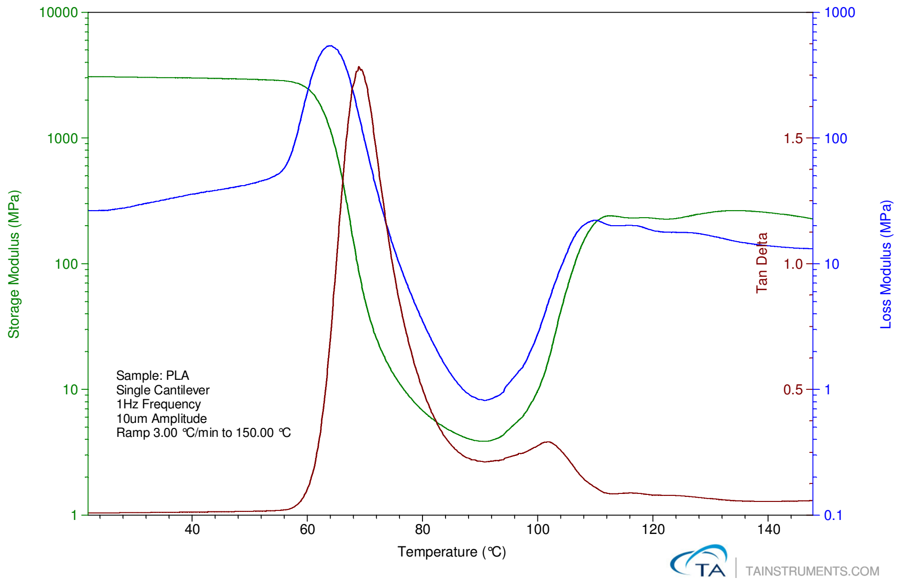


Polylactic Acid (PLA): Crystallinity After an Uncontrolled Cooling Rate From the Melt

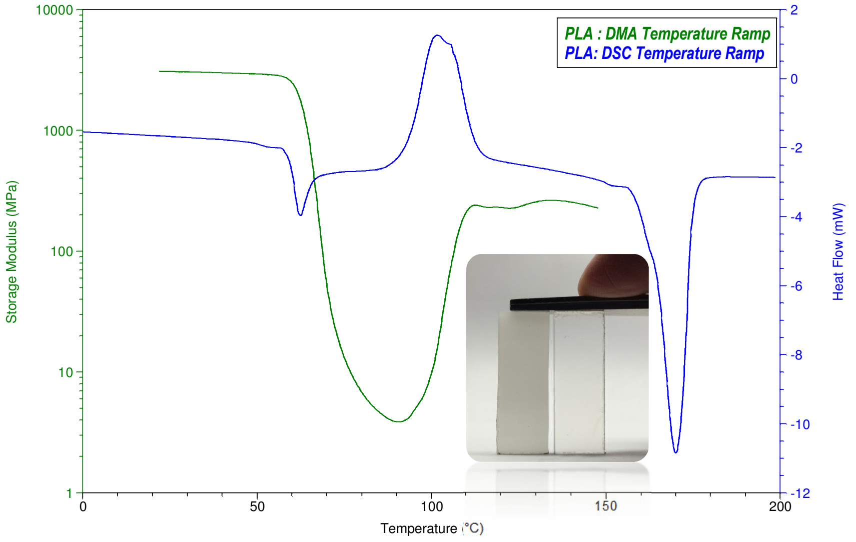
PLA was taken above it melt temperature to 200°C and then cooled at an un-controlled rate -70.00 °C (quench).

This thermogram shows the heat cycle after an equilibrate segment (uncontrolled cooling rate) from the melt. A heating rate of 10 °C/min was used.

Dynamic Mechanical Analysis (DMA) of PLA Glass Transition and Cold Crystallization



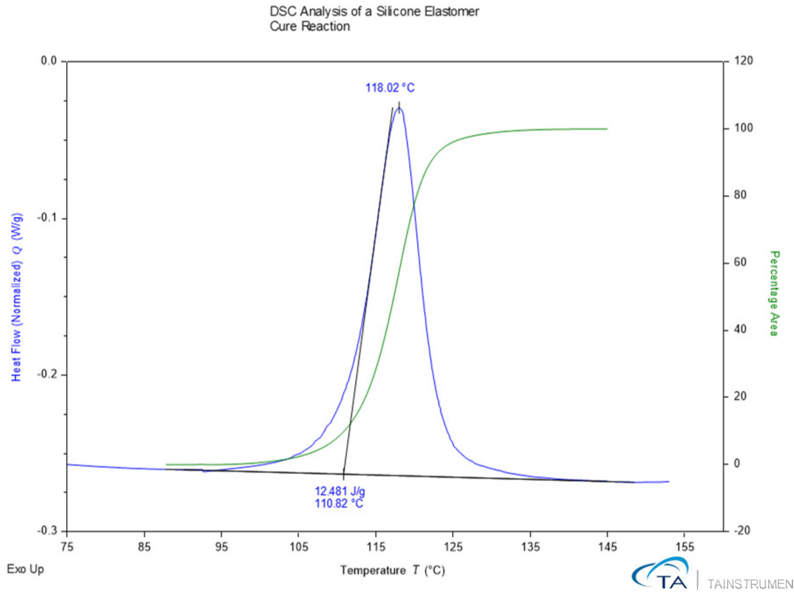
An Overlay of the Storage Modulus and Heat Flow of Polylactic Acid

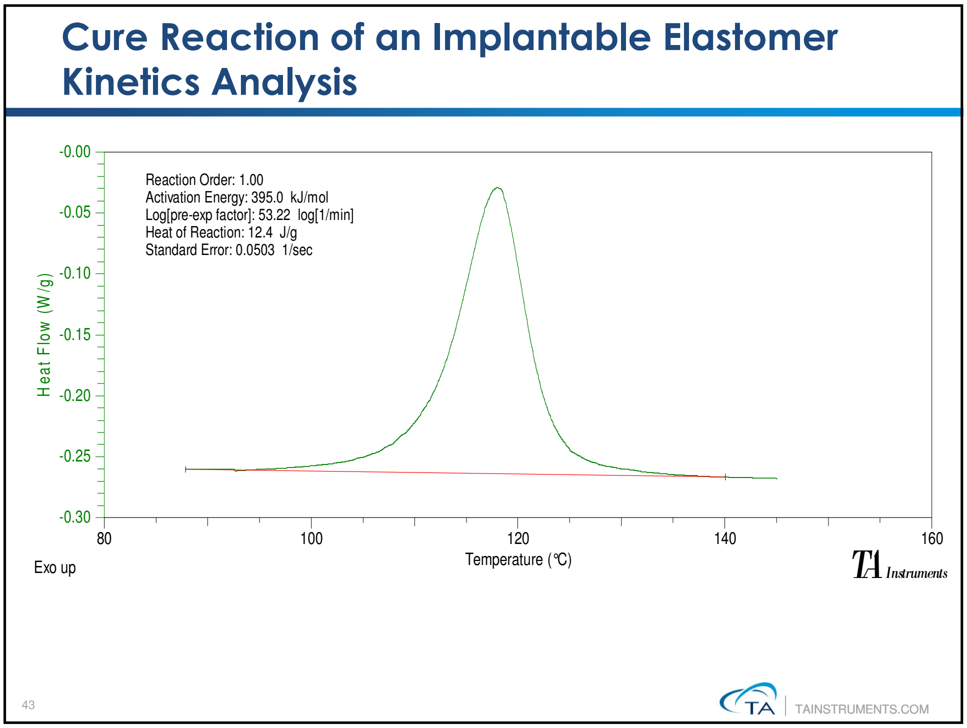


Crosslinking reactions – Cure of elastomers, adhesives and epoxies

- A “thermoset” is a cross-linked polymer formed by an irreversible exothermic chemical reaction.
- Crosslinking reactions are generally exothermic. As the chemical reaction takes place, it is almost always accompanied by a release of heat.
- The reactions can be easily monitored using a DSC
  - **Heat of reaction**
  - **Residual cure**
  - **Glass transition**
  - **Heat capacity**

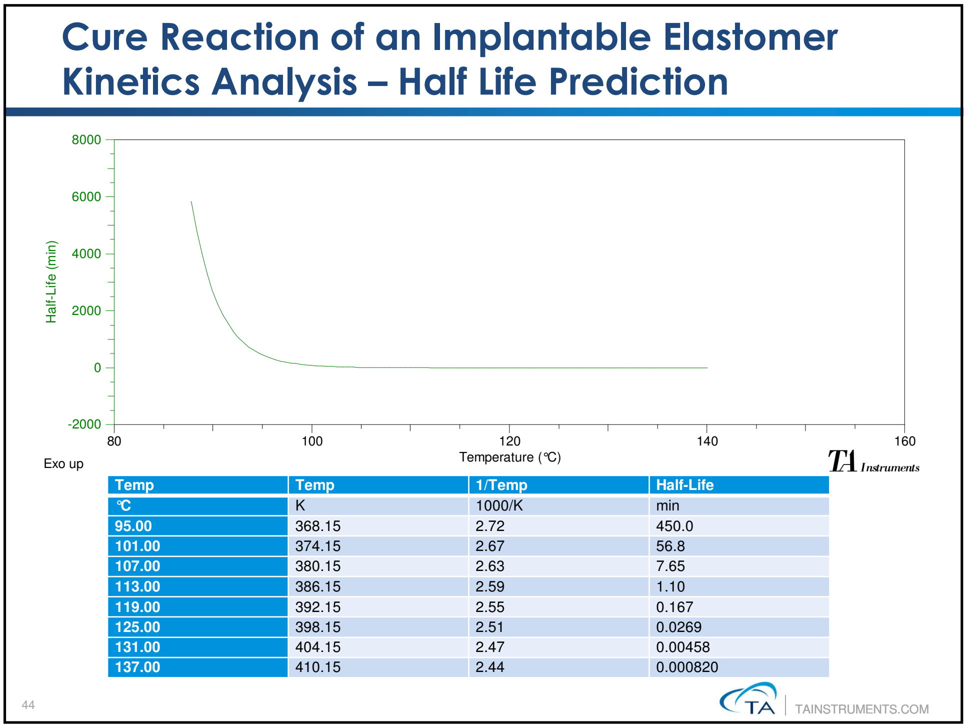
Cure Reaction of Liquid Silicone Elastomer Running Integral Analysis





Cure Reaction of an Implantable Elastomer Kinetics Analysis

Reaction Order: 1.00
Activation Energy: 395.0 kJ/mol
Log[pre-exp factor]: 53.22 log[1/min]
Heat of Reaction: 12.4 J/g
Standard Error: 0.0503 1/sec

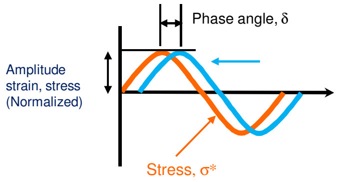


Cure Reaction of an Implantable Elastomer Kinetics Analysis – Half Life Prediction

Temp	Temp	1/Temp	Half-Life
℃	K	1000/K	min
95.00	368.15	2.72	450.0
101.00	374.15	2.67	56.8
107.00	380.15	2.63	7.65
113.00	386.15	2.59	1.10
119.00	392.15	2.55	0.167
125.00	398.15	2.51	0.0269
131.00	404.15	2.47	0.00458
137.00	410.15	2.44	0.000820

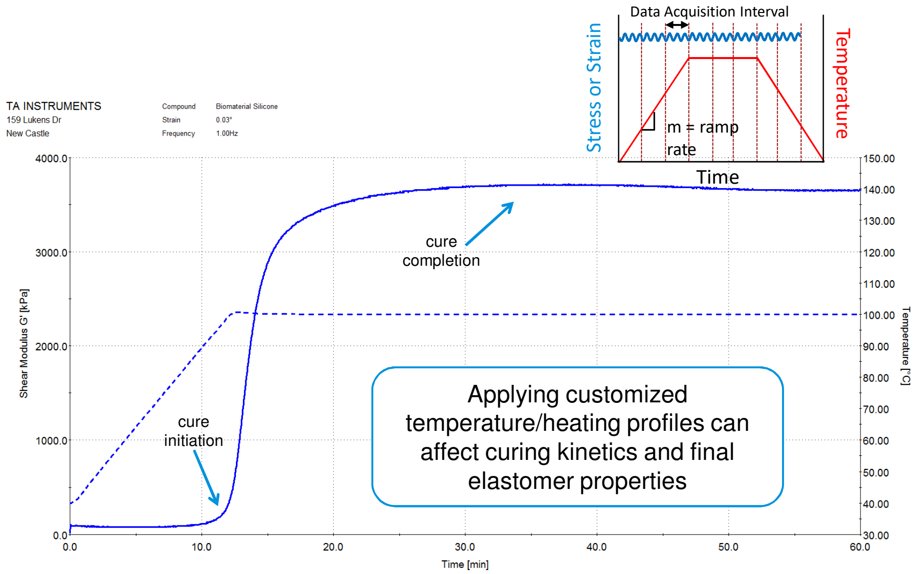
Cure Reaction on a Rubber Process Analyzer (RPA)

- Measures material response to shear deformation or force as a function of time, temperature, frequency, or deformation
    - Typically reports viscoelastic properties of storage modulus (G'), loss modulus (G"), and tan delta



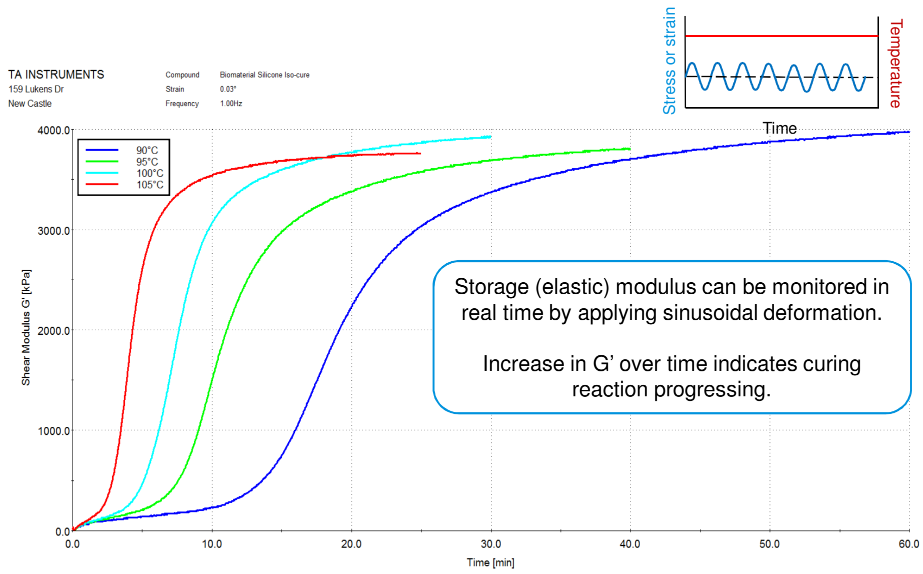
- Common Uses:
    - Complete pre and post cure viscoelastic characterization
    - Measure cure profile of materials during isothermal or anisothermal tests
    - Effects of filler/vulcanization network
        - Payne Effect
    - Identifying differences in viscoelastic material properties
        - Frequency dependence
        - Strain dependence
        - Stress relaxation

Cure Reaction of an Implantable Silicone Elastomer Physical Property Measurement – Anisothermal



Applying customized temperature/heating profiles can affect curing kinetics and final elastomer properties

Cure Reaction of an Implantable Silicone Elastomer Physical Property Measurement – Isothermal



Storage (elastic) modulus can be monitored in real time by applying sinusoidal deformation.

Increase in G' over time indicates curing reaction progressing.

Thermal Analysis Review

- Thermogravimetric Analysis
  - Stability
  - Volatile content
  - Decomposition kinetics
- Differential Scanning Calorimetry
  - Transition temperatures
  - Crystallinity
  - Heat of reactions
  - Reaction kinetics

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

The World Leader in Thermal Analysis, Rheology, and Microcalorimetry