TSC II

Thermally Stimulated Currents

SETARAM Instrumentation
KEP Technologies

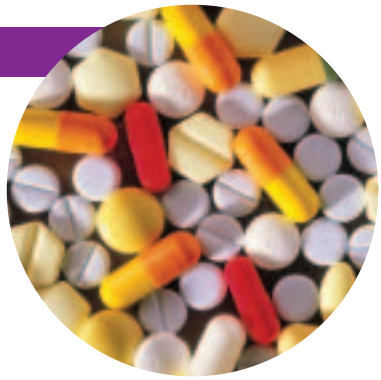
Excellence in thermal analysis and calorimetry

TSCII applications

... Introduction

This particular thermal analysis method uses **MOLECULAR MOBILITY** as a means of accessing structural information that cannot be obtained by any other techniques. It also gives access to dynamic parameters (ΔH, ΔS and relaxation time τ).

Pharmaceuticals

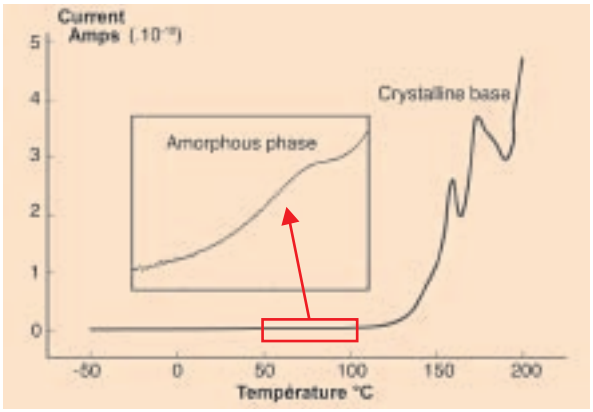


Examples of applications :

- **Polymorphism**
- Determination of **crystalline phase / amorphous phase ratio**
- Detection of **low levels of amorphous phase (< 1%)**
- **Influence of water** (plasticization)
- **Interactions** between active principle and excipient

• Purity of a crystalline compound: detection of an amorphous phase (< 1%)

The magnification of the curve at around 75°C shows the presence of a small amount of amorphous phase.

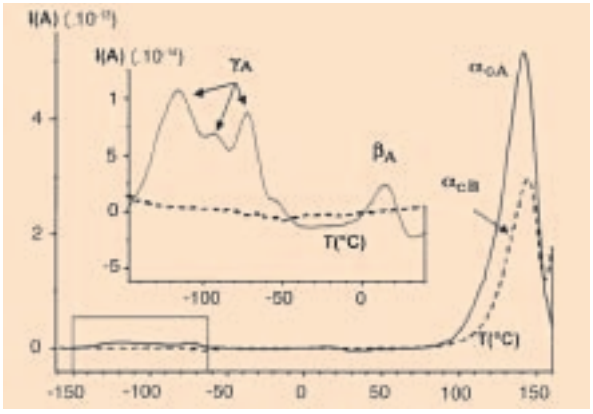


Complex TSC spectrum of a sample of 100% crystalline lactose

• Differentiation of 2 crystalline phases in Irbesartan

Irbesartan is a pharmaceutical product developed by Sanofi-Aventis and displaying two crystalline forms, A and B.

Peak between 100 and 150°C: molecular mobility associated (α_A, α_B) with precursor movements involved in the **fusion of the polymorphs A and B**. The fusion can also be observed in DSC (Differential Scanning Calorimetry). It is observed with TSC, as with DSC, that phase B is the more stable phase.



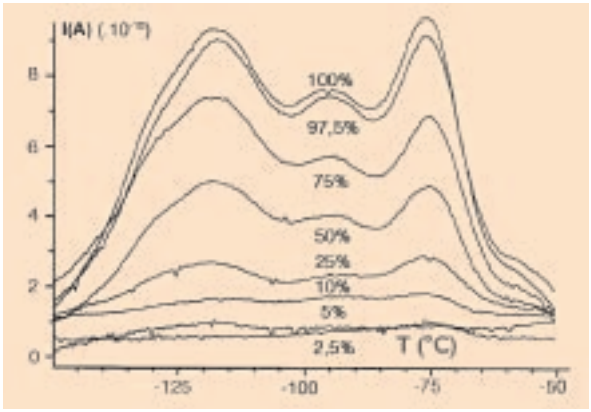
Complex TSC spectrum of Irbesartan

The peak between -150 and -50°C is only present for form A. This peak is attributed to the typical **molecular mobility** of the **channeled structure of form A** (HEXAGONAL crystalline system).

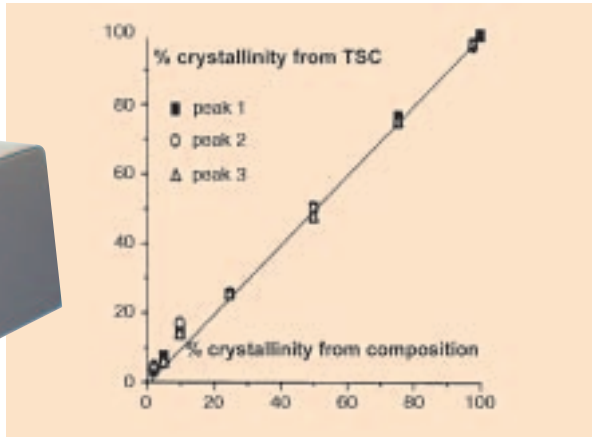
• Determination of crystalline/amorphous phase rate

By determining a **characteristic peak of crystalline form A** (between –150 and –50°C), it is possible to establish **a calibration curve** that allows the quantity of crystalline phase A in an unknown crystalline/amorphous phase mixture to be determined (area under the peak associated with the crystalline percentage).

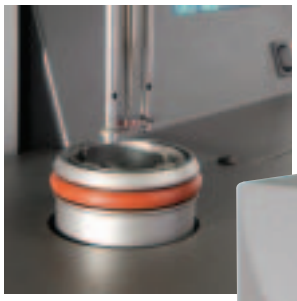
On the basis of peaks between –150 and –50°C of different mixtures at known levels of phase A and amorphous phase, it was possible to plot the calibration curve and thus determine very low crystallinity levels (<2.5%).

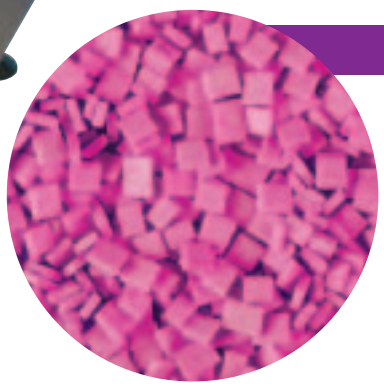


Complex TSC spectra of different phase A / amorphous phase mixings



Calibration curve





Biology

Examples of applications:

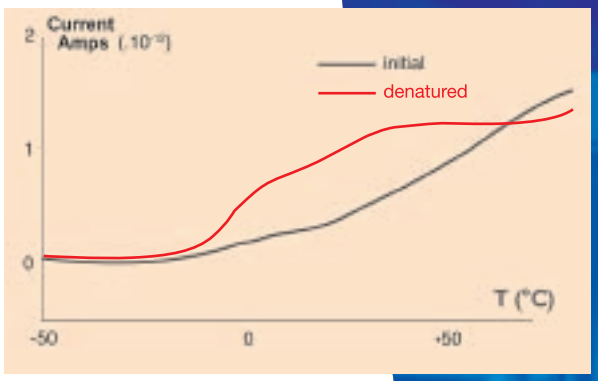
- Tracking the aging of tissue
- Testing tissue functionality and integrity
- Testing the efficiency of pharmaceutical treatments

• Collagen

Study of collagen: Laboratory of Polymer Physics - Toulouse, France – V. SAMOUILLAN

Denatured collagen displays a characteristic phenomenon, namely the increase of current intensity between 0 and 50°C. This relaxation mode has been associated with **molecular movements of Tropocollagen** (constituent units of collagen) and more specifically the breaking of hydrogen bonds between the CO and NH groups of two neighboring chains.

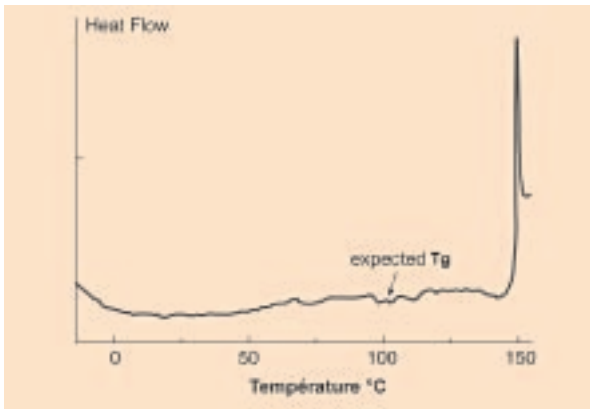
This phenomenon can therefore be attributed to the breakdown of the triple Helix (α) structure which leads to an increase in molecular mobility. This specific denaturation can be observed in **aging** and illnesses.
Consequently, this peak can be used as a means of evaluating the aging of tissue or to check the efficacy of pharmaceutical treatments on collagen denaturation.



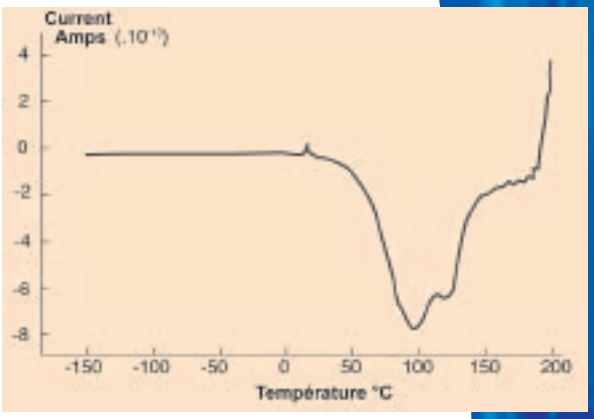
Complex TSC spectra of healthy collagen and denaturated collagen

• Proteins

The **glass transitions (Tg)** of proteins are usually studied using DSC (Differential Scanning Calorimetry).
In the temperature range at which the glass transition of an amorphous globular protein is expected, it is particularly difficult to clearly determine the heat capacity jump characteristic of this event.
The complex TSC spectrum was obtained by applying a specific procedure, namely quenching the sample down to -150°C followed by a linear rise in temperature while maintaining the static electric field E while recording the signal up to a temperature of 200°C.
A negative peak corresponding to the dielectric manifestation of the glass transition Tg is observed.



DSC curve of amorphous globular protein



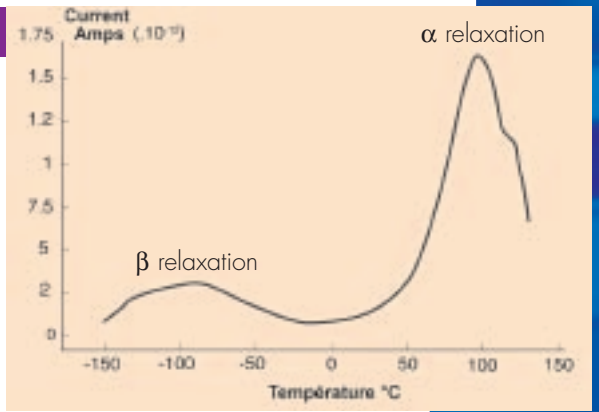
Complex TSC spectrum of an amorphous globular protein: detection of Tg temperature

Polymers

Examples of applications:

- Better transition resolution compared with DSC
- The possibility of studying surface treatments on finished products
- The study of plasticizing and oxidation phenomena

The following curve shows the β and α mode relaxation phenomena of Poly(ethyleneterephtalate). With DSC it is impossible to see observe the β mode.



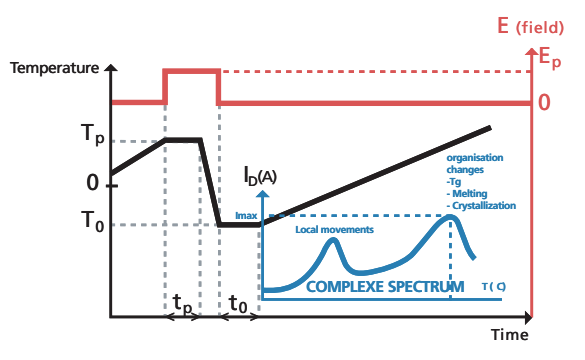
Complex TSC spectrum of Poly(ethyleneterephtalate: β and α relaxations

... principle

This technique which uses molecular mobility as a measurement probe is particularly suited to **materials having a polar character:** poly(methylmetacrylate), lactose, cellulose, protein…
At a given temperature T_P, a static electric field E_P is applied for a time t_P that is long enough to permit the different mobile entities of the material to orient themselves according to the field.

This configuration is then frozen by rapid decrease in temperature to a temperature T_0 low enough for the molecular mobility to be considered nil.

At T_0, the field is eliminated and the sample is short-circuited for time t_0 to eliminate the rapid space charge relaxation and stabilize the sample at this temperature.



During a linear temperature increase, the return to equilibrium of the previously oriented entities generates a **depolarization** current (I_d) which is recorded, as a function of temperature, with ahigh sensitivity electrometer (10^{-15} A= femto A).

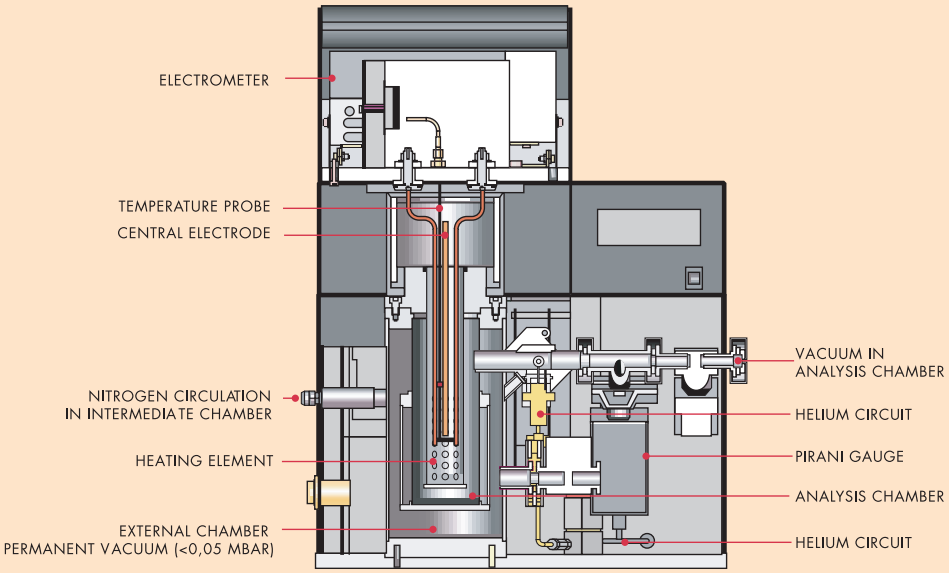
Each depolarization current peak is characterized by its position at temperature T_{max}, its intensity I_{max} and its width at mid-height. Its analysis enables it to be associated with a **sequence of mobile entities of a specific length.**

Different types of materials can therefore be studied with a TSC: films, powders, liquids, gels and pellets without **any prior preparation**, since electrodes adapted to different morphologies are available. The low equivalent frequency (10^{-4} - 10^{-2} Hz) of the TSC gives it good resolution and sensitivity, thereby allowing it to supplement the information obtained by Differential Scanning Calorimetry (DSC) and Dynamic Dielectric Spectroscopy.


Electrode for liquids


Calibration electrode


Electrode for films and pellets



TSCII CROSS SECTION

Specifications

Technical data	
Temperature (platinum probe):	Range: -170°C/350°C, accuracy ±0.12% Heating temperature gradient: 0 to 40°C/min Cooling temperature gradient: 0 to 40°C/min
Electrometer:	Range: 10^{-15} to 2.10^{-2} A Precision: ± 0.1% for the 20mA range ± 1% for the 20pA range
Applied voltage:	0 to 500V/mm, accuracy ± 0.15%
Pressure sensors:	Helium: 1100 mbar Vacuum: 10^{-4} mBar to 10 mbar
Sample:	Pellet, film: from 0.25 to 4 mm Liquid, powder: 20mg

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