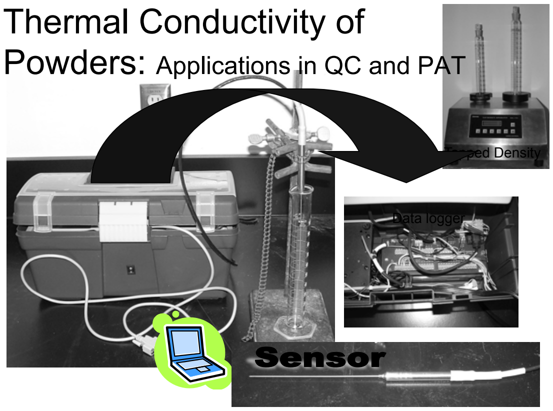
Thermal Conductivity of Powders: Applications in QC and PAT



Intensive / Extensive Property

- In physics and chemistry an intensive property of a system is a physical property of the system that does not depend on the system size or the amount of material in the system.
- By contrast, an extensive property of a system does depend on the system size or the amount of material in the system.
- However, some of the intensive properties are statistical in nature (e.g. viscosity) and are relevant only in aggregate scales.

- Examples of intensive properties include:
- temperature
- viscosity
- density
- electrical resistance
- melting point
- boiling point
- color (in solution)
- flammability

Examples of extensive properties include:
- mass
- volume
- entropy
- energy
- electrical resistance
- texture
- pressure

Thermal conductivity

- **Thermal conductivity** (λ) is the INTENSIVE PROPETY of a material which relates its ability to conduct heat.
- **Thermal conductivity** is the quantity of heat, Q, transmitted through a thickness L, in a direction normal to a surface of area A, due to a temperature difference ΔT, under steady state conditions and when the heat transfer is dependent only on the temperature gradient.
  - $\lambda = Q \times L / (A \times \Delta T)$
  - thermal conductivity = heat flow rate × distance / (area × temperature difference)

Definition

- The thermal conductivity of a material is defined as the rate at which heat flows through a certain area of a material and is given by Fourier's equation.
- $$\frac{dq}{dt} = -\lambda F \frac{dT}{dx}$$
- where q is the heat energy flowing in the x direction through the area F during time t, dT/dx is the temperature gradient, and λ is the thermal conductivity of the material

Examples of different Materials

	Thermal conductivity @20° C W/mK	Density @20° C Kg/m³	Volumetric heat capacity @20° C 10^6 J/m³K	Thermal diffusivity @20° C 10^{-8} m²/s
Air	0.025	1.29	0.001	1938
Glycerol	0.29	1260	3.073	9
Water	0.6	1000	4.180	14
Ice	2.1	917	2.017	104
Olive oil	0.17	920	1.650	10
Glass	0.93	2600	2.184	43
Gasoline	0.15	720	2.100	7
Methanol	0.21	790	2.500	8
Silicone oil	0.1	760	1.370	7
Alcohol	0.17	800	2.430	7
Sand (dry)	0.35	1600	1.270	28
Sand (saturated)	2.7	2100	2.640	102
Aluminium	237	2700	2.376	9975
Copper	390	8960	3.494	11161
Stainless Steel	16	7900	3.950	405

Effusivity

- Effusivity combines thermal conductivity, density and heat capacity into one value.
- Thermal Conductivity (k) = W/m*K
- Effusivity: $\sqrt{k\rho c_p}$
- Heat Capacity (c_p): J/kg*K

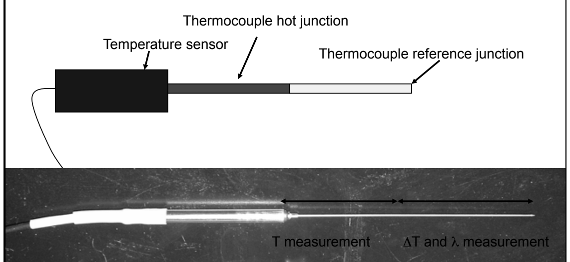
Effusivity

- Effusivity is a heat transfer property present in all materials in all formats – solid, liquid, pastes, powder and gas.
- Effusivity is the property that dictates the interfacial temperature when two semi-infinite objects at different temperature touch.

Non-Steady-State Probe Science

- The thermal conductivity of a medium can be determined by measuring the temperature response to heating.
- Generally, this method avoids the necessity of reaching a real thermal equilibrium with constant temperatures.
- Non-steady-state techniques are fast and also there is no need for careful sample preparation.

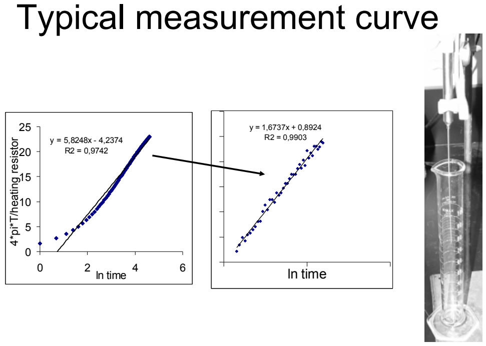
Temperature sensor TP02



Non-Steady-State Probe Science

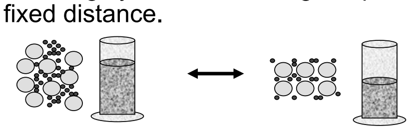
- **Non-Steady-State Probe**
- The main principle is that after an initial transient period, the temperature rise only depends on the heating power, Q, and the thermal conductivity , l.
- $U - U0 = A * \ln t + B$ (*equation 1)*
- $A = Q / 4 * \pi * L$ (*equation 2)*
- B is a constant depending on the sensor size, the properties of the surrounding material.
- From these equations L can easily be deducted also without knowing B.

Typical measurement curve



Powder Density USP

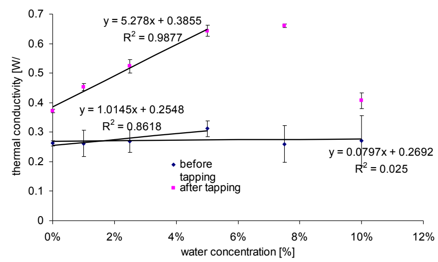
- The bulk density often is the bulk density of the powder “as poured” or as passively filled into a measuring vessel.
- The tapped density is a limiting density attained after “tapping down,” usually in a device that lifts and drops a volumetric measuring cylinder containing the powder a fixed distance.



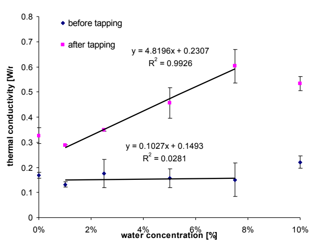
Comparison of the thermal conductivity of bulk vs. tapped density of powders

- The aim of this study was to evaluate a non steady state needle sensor to determine the thermal conductivity (λ) of powders and their blends.
- We investigated how λ of different powders was influenced by
  - 1) bulk vs. tapped density
  - 2) humidity grade of the powders and
  - 3) blending time of different powders.

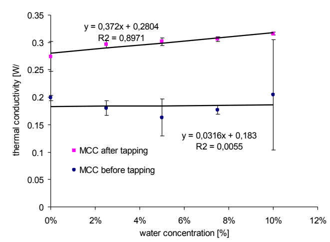
FlowLac 100 at different moisture content (w/w)



GranuLac 200 at different moisture content (w/w)



MCC at different moisture content (w/w)



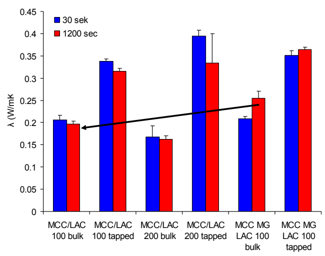
Summary of the Results

- The result shows that the values of λ are highly depended on the bulk and tapped density (ρ) of the powders.
- Bulk density measurements were generally sensitive to differentiate between different powders.
- However they were not sensitive to detect the water content within a powder.
- The tapped density measurements were reliable and highly reproducible and could differentiate between the nature of a powder and powder humidity.

Effusivity in QC

- To be able to use thermal conductivity measurements as quality control measure the "bulkiness" of a powder under investigation must be defined.
- Valid values of λ can not be determined if the density of the powder is not known.
- This can be overcome by determining λ in tapped powders.
- The results of bulk powders vs. tapped powders clearly demonstrate that reliable effusivity measurements can only be achieved using the tapped density of a powder because λ depends on the powder density.
- Therefore, it is possible to use effusivity as an additional powder characteristic in pharmaceutical quality control.

Thermal conductivity of powder blends after 30 and 1200 seconds



MCC/LAC 100 is a 1:1 mixture of microcrystalline cellulose and FlowLac 100; MCC/LAC 200 is a 1:1 mixture of microcrystalline cellulose and GranuLac 200; MCC/MG/LAC 100 is a 49.5:1:49.5 mixture of microcrystalline cellulose, Mg-stearate and FlowLac 100

PAT Tools

- The FDA guideline for process analytical technologies (PAT) states that PAT:
- “measurements collected from these process analyzers need not be absolute values of the attribute of interest. The ability to measure relative differences in materials before (e.g., within a lot, lot-to-lot, different suppliers) and during processing will provide useful information for process control”
- Our results showed that thermal conductivity measurements were sensitive to the blending process and addition of Mg-stearate.

Thermal Conductivity as PAT tool

- Measurements of λ were able to monitor powder blending.
- Thermal conductivity as measure in Process Analytical Techniques (PAT) seems to be feasible concept and can add valuable information to the process under investigation.