Introduction to isothermal calorimetry

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2009

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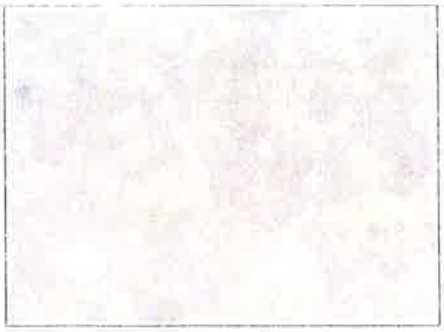

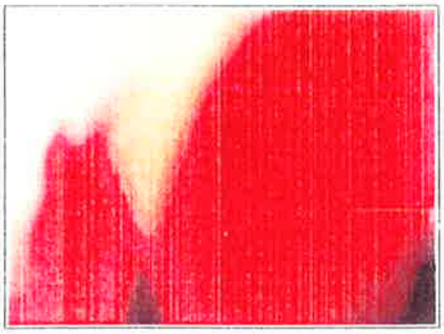

Introduction to Isothermal Calorimetry

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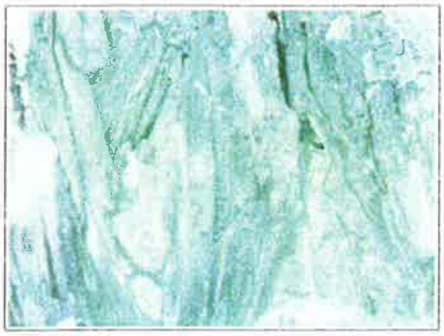
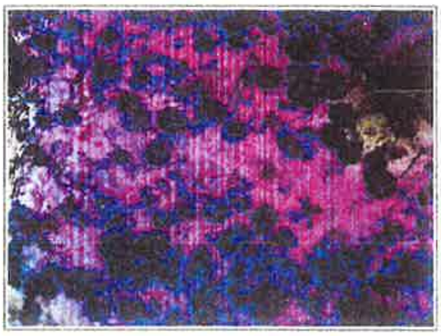










TVBM-7197 2009

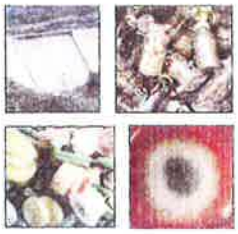
1. Course schedule
2. Introduction and some examples
3. Heat conduction calorimetry I
4. Cement calorimetry
5. Thermodynamics for calorimetry
6. Calibration
7. Different types of calorimeters
8. Kinetics and stability
9. Titration calorimetry
10. Thermochemistry
11. Pharmaceutical applications
12. Biological calorimetry
13. Heat conduction calorimetry II
14. Water vapor and calorimetry
15. Food Science
16. Sorption calorimetry
17. Papers

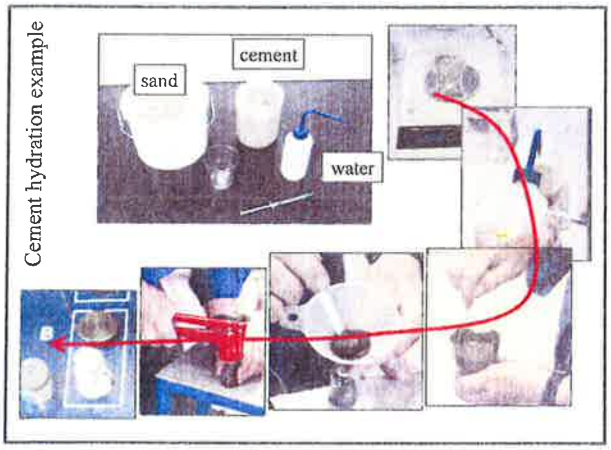
mold fungi sorption isotherms curing of adhesives
critical water activities vaporization enthalpies human
cells seed germination compatibility polymorphism
polymer reactions solution calorimetry cement
hydration vapor activity stability of explosives
crystallinity immersion yeast cells metal corrosion
titration sorption enthalpies ligand binding
degradation rot fungi vegetable respiration self-
discharge of batteries self-oxidation of fuels water
activity determination photocalorimetry student
calorimetry crystallisation microbiology tissue
cultures wetting crystal properties dissolution drug
targeting stability fermentation cement admixture
interaction polymer degradation insect activity
equilibrium constants polymer curing food-stuff
spoilage heat capacity recrystallisation oil oxidation

Lund Isothermal Calorimetry Group

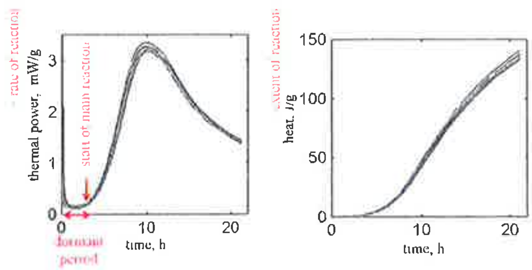
LICG

- Instruments and methods
- Measurements
- Teaching





Portland cement hydration result



Isothermal calorimetry is the measurement of thermal power (heat production rate) under constant temperature conditions.

This is a very general technique because almost all processes (physical, chemical, biological) produce heat.

Since nearly all processes produce heat, it is important to design isothermal calorimetry experiments so that only heat from the process under investigation is measured.

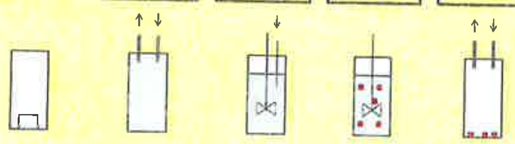
Different ways to systematize isothermal calorimetry

According to method: for example, ampoule and titration calorimetry

According to field of use: for example, cement and biological calorimetry

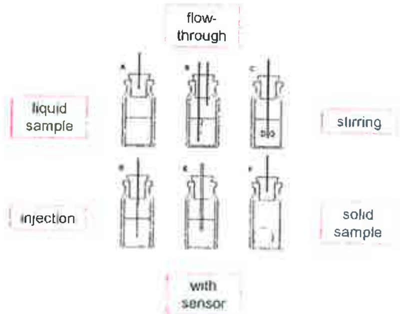
Examples of methods in isothermal calorimetry

Ampoule calorimetry | Perfusion calorimetry | Titration calorimetry | Solution calorimetry | Sorption calorimetry



All these methods (and many more) can be practiced in the same calorimeter; only the ampoules (vessels) change.

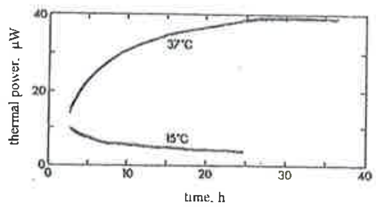
Example: use of glass ampoules (student experiments)



Examples of fields where isothermal calorimetry is used

- Stability of energetic compounds (explosives, fuels)
- Biological calorimetry
- Cement hydration calorimetry
- Polymer science
- Microbiological studies (yeast, bacteria)
- Food Science
- Physical Chemistry (sorption, mixing, solution, kinetics)
- Medicine
- Pharmaceutical technology
- Education
- Plant physiology
- Battery technology

Battery self-discharge

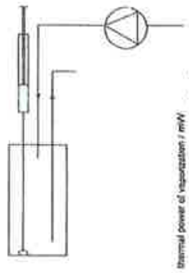


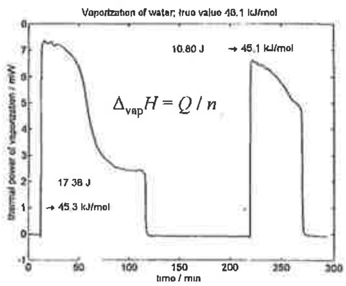
I. Wadsö

Why isothermal calorimetry?

1. General method
2. Often sensitive
3. Monitors processes
4. Non-destructive
5. Thermodynamics
6. Manipulate sample

Solvent vaporization enthalpy (student experiment)





For a certain application there are often many methods to from which to choose
It is important to choose the *best* method (cost, convenience, result...)

Mold activity as a function of relative humidity

Methods available from which to choose:

spore production
visual inspection (hyphal elongation, area)
mass change
toxin production
ATP-concentration
ergosterol content
chitin content
toxin production
heat production rate (isothermal calorimetry) ←

Problem: measure the activity of a fungi as a function of relative humidity (water activity)

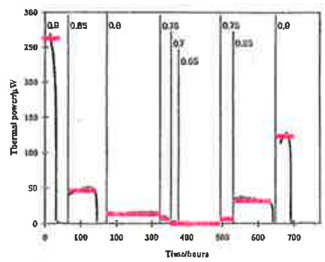


Fig. 3 Thermal powers measured for a bread sample half covered with *Penicillium* mould as a function of a_w (shown in the top of the figure). At the breaks in the curve no measurements were made as the sample was then in the humidity generator.

Markova and Wadsö (1998) Int. Biodeterioration Biodegradation 42 25-28

Mold activity as a function of relative humidity

Methods available from which to choose:

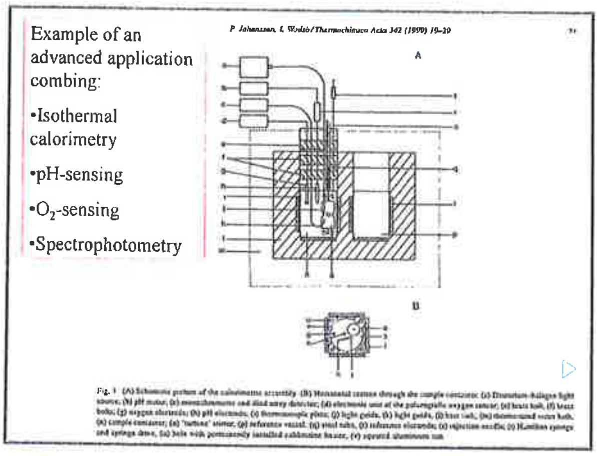
spore production
visual inspection (hyphal elongation, area)
mass change
toxin production
ATP-concentration
ergosterol content
chitin content
toxin production

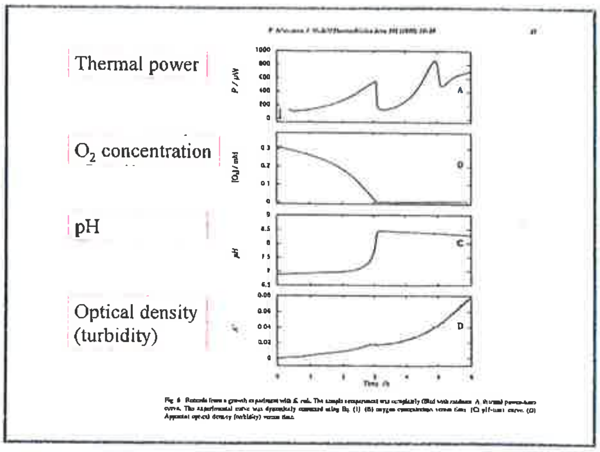
Expose to different climates and measure result after exposure

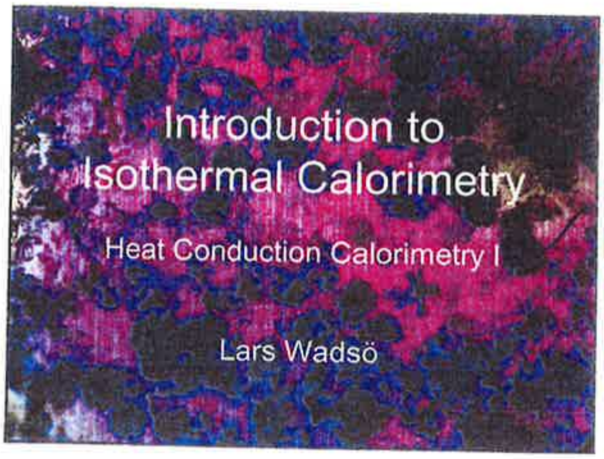
heat production rate (isothermal calorimetry) ← Continuously measure activity/response during measurement

Manipulate sample in calorimeter
Combine with other techniques

- Flow-through (perfuse) with a liquid or gas (dry or mixed with a liquid vapor)
- Inject a gas, liquid or solid
- Analyze gas or liquid leaving sample
- Stir (gases, liquids)
- Introduce light
- Combine with other sensors (pH, O_2, CO_2, RH...)


Example of an advanced application combing:
•Isothermal calorimetry
•pH-sensing
•O2-sensing
•Spectrophotometry
A
B


Thermal power
O2 concentration
pH
Optical density (turbidity)
A
B
C
D



Definitions

Isothermal calorimetry Measurements of heat and thermal power at (essentially) constant temperature conditions

Heat conduction calorimetry The most common measurement principle for isothermal calorimetry

This course is called "Introduction to Isothermal Calorimetry" and is a course on the theory and use of heat conduction calorimeters

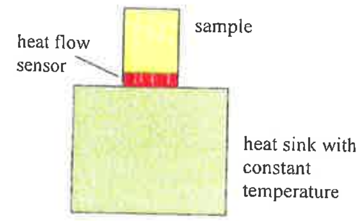
Heat "A form of energy present in all matter as kinetic energy of the atoms"

"Energy transferred from a hotter to a cooler body due to a temperature gradient"

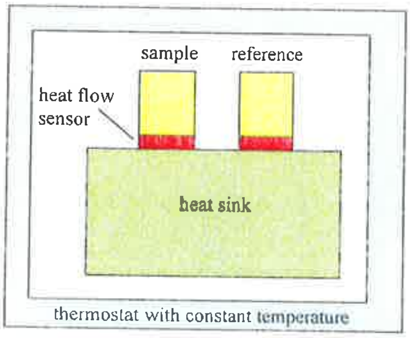
The SI unit of heat (and all other forms of energy) is the joule (J) The calorie (cal) is a non-SI unit of energy/heat, 1 cal = 4 18 J

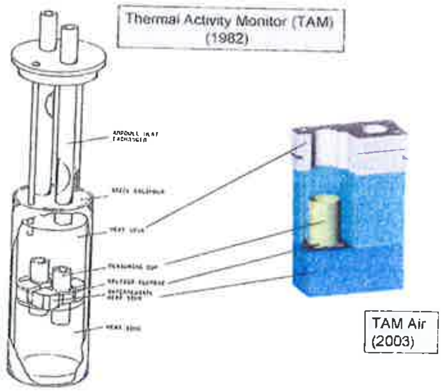
Thermal power, heat production rate, heat flow rate, heat flow all have the SI-unit watt (W). 1 W = 1 J/s In this course we will use the term "thermal power"

A Heat Flow Calorimeter 1



A Heat Flow Calorimeter 2





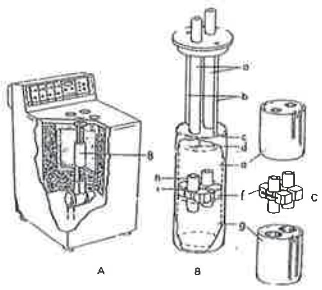
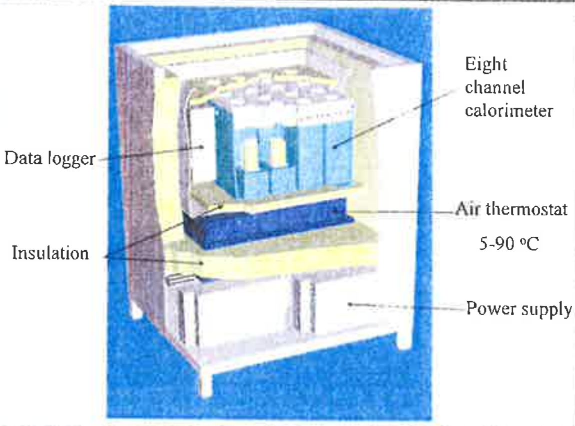
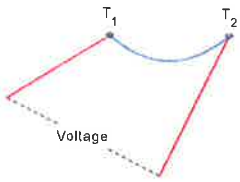


Figure 2. 4-channel TAM microcalorimeter (ThermoMetric, Sweden). A: Cut-away view of the instrument shown with one channel (B) positioned in the water bath B: One channel consists of the following parts: a, b: thin-walled steel tubes. c: steel cylin r. d: stic tube. e, g: aluminiu bolts ving as main heat sinks. f: aluminium block. h: aluminium tube (holder for ampule) thermocou-



Heat flow sensors are usually thermocouple plates

What is a thermocouple?



$T_1 = T_2 \Leftrightarrow$ Voltage=0

$T_1 \neq T_2 \Leftrightarrow$ Voltage≠0

<u>Peltier effect</u>
voltage applied ⇒ temperature difference

<u>Seebeck effect:</u>
temperature difference applied ⇒ voltage

Who invented the thermocouple?

Thomas Seebeck (1770-1831)
This Estonian born German scientist found in 1821 that a circuit made of two dissimilar metals with junctions at different temperatures deflected a compass magnet. He believed this was due to magnetism induced by the difference in temperature. He called the phenomenon "thermomagnetism" and believed that the earth's magnetic field was generated by temperature differences between the cold poles and the warm equator.

The Danish scientist **Hans Christian Ørsted** (1777-1851), who already in 1820 had proved that electrical fields influenced magnetic needles, followed Seebeck's work with interest and named the phenomenon the "thermoelectric effect".

Jean Peltier (1785-1845), a French watch maker, discovered in 1834 that a current through two dissimilar conductors generates heat at the junction of the two materials.

In 1838, **Emil Lenz** in St. Petersburg first froze and later melted a drop of water placed on a thermocouple junction, by reversing the current.

William Thompson (Lord Kelvin) described the interrelationship of the Seebeck and Peltier effects around 1860.

It was not until the 20th century that the thermoelectric effect found practical applications, for example through the work of Russian physicist **Abram Ioffe** (1880-1960).

Applications of Thermocouples

<u>To measure temperature with TC</u>
Type R, T, J for example
(T2 measured inside, cold junction)

<u>To cool/heat with thermocouple plates (TEC=ThermoElectric Cooler)</u>
Electronics in telecom, medical labs, aerospace, consumer products

<u>To measure heat flow</u>
Heat flow meters, heat flow calorimeters

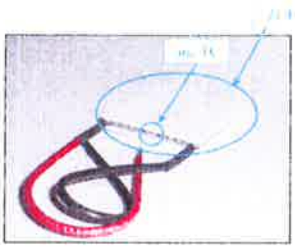
<u>In thermoelectric generators</u>
Used to convert heat from radioactive decay to electricity in space crafts (Apollo, Pioneer, Viking etc.)

A thermocouple thermometer

A Boeing 777 cockpit instrumentation system cooled with TEC's (www.marlow.com)

A portable heat flow meter (www.escscientific.com)

Heat flow sensors are usually made as thermocouple plates (Peltier cooling plates) containing many semiconductor thermocouples made of n- and p-doped bismuth-telluride (BiTe).



Φ	heat flow rate (W)
ΔT	temperature difference (K)
U	voltage (V)
P	thermal power (W)

Heat flows in response to temperature differences
$\Phi \sim \Delta T$

Voltage from thermocouple is proportional to temperature difference
$U \sim \Delta T$

Voltage output is proportional to heat flow through sensor
$U \sim \Phi$

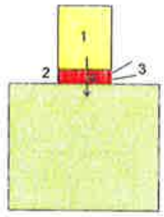
At steady-state (constant heat production), heat flow rate through the sensor is equal to the heat production rate (thermal power)
$P = \Phi$

Measured voltage is proportional to the thermal power
$U \sim P$

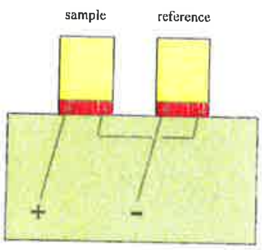
Note that the temperature differences should be small (essentially isothermal)

Four simultaneous processes

1. Heat is produced in the sample...
2. ...and a temperature difference develops across the heat flow sensor...
3. ...which results in a voltage output...
4. ...while heat flows out to the heat sink.



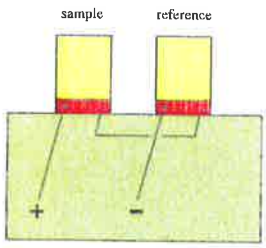
The reference



The reference is a sample with thermal properties similar to the sample, except that it does not produce any heat.

The measured signal is the difference between the sample-signal and the reference-signal.

Why use a reference?



1. Less noise from external disturbances
2. Measurement response is faster

Nomenclature

t	time	s
P	thermal power	W
Q	heat	J
U	voltage	V
ε	calibration coefficient	W/V
τ	time constant	s

At steady-state (constant thermal power):

$$P = \varepsilon \cdot U$$

\ calibration coefficient

At unsteady-state (thermal power is changing):

$$P = \varepsilon\,(U + \tau \cdot dU/dt)$$

\ time constant

At steady-state (constant thermal power):

$$P=\varepsilon \cdot U$$

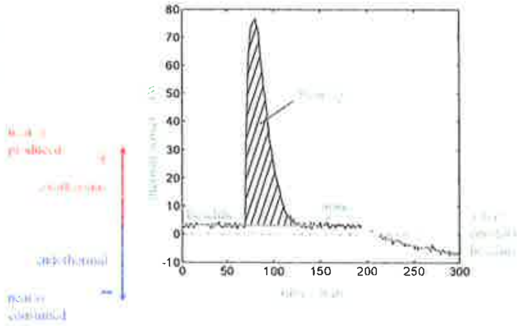
calibration coefficient

At unsteady-state (thermal power is changing):

$$P=\varepsilon\,(U+\tau \cdot dU/dt)$$

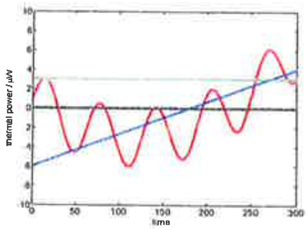
time constant

Correction for time-lag of calorimeter (Tian equation)



Baselines

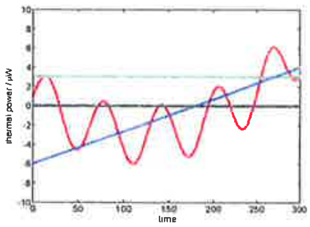
The ideal baseline is zero!



Note that one should always judge a baseline in relation to the measurement being made (duration of measurement, thermal power, acceptable spread in results etc.)

Baselines

Case 1 Measurement of microbial activity in carrot juice High thermal power and a large spread in sample properties makes baseline correction unnecessary



Case 2 Seven days measurement on heat of cement hydration made by integrating results over seven days of measurement A constant and correctly known baseline is very important

Case 3 Fast titration with one injection every 10 minutes and total experiment time of three hours Each peak is evaluated separately with baselines before and after that peak, and is not dependent on long-term behavior of baseline

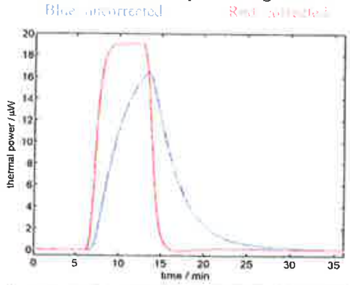
Tian correction

The measured signal is delayed with respect to the thermal power of the sample, and will therefore lag behind when thermal power changes (thermal inertia).

The Tian correction gives the thermal power from the delayed curve:

$P=\varepsilon\,(U+\tau \cdot dU/dt)$

Electrical calibration pulse for eight minutes



Note correction was not perfect because the Tian model is not perfect (but it is good enough for most purposes)

SUMMARY

Make a measurement

1 Baseline correction $U(t)=U_{mea}(t)-U_{BL}$
2 Apply calibration coefficient $P(t)=\varepsilon \cdot U(t)$
3 Apply Tian correction (if needed) $P_{corr}=P_{uncorr}+\tau \cdot dP_{uncorr}/dt$
4 Evaluate thermal powers and heats of interest

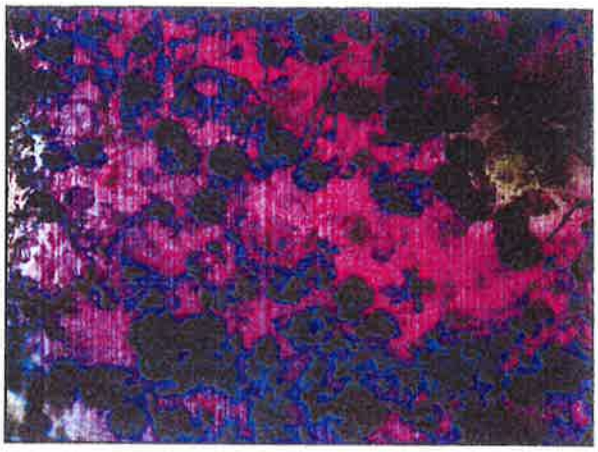
Note that many commercial instrument make the above corrections automatically However, it is always a good idea to know what the instrument and software are doing!

Manufacturers of isothermal calorimeters

Microcal (USA, www.microcalorimetry.com)

Setaram (France, www.setaram.com)

TA Instruments (USA, www.tainstruments.com)
(includes former CSC and Thermometric)



Introduction to Isothermal Calorimetry

Cement Hydration Calorimetry

Lars Wadsö

Important concept:

water/cement-ratio = mass of water / mass of cement

Low water/cement-ratio gives high quality: high strength and low permeability

w/c=0.6 normal concrete
w/c=0.35 high performance concrete
(w/c>1 sometimes used in the lab)

Additives (admixtures) used in concrete:

- Water reducing agents
- Plasticizers
- Retarders
- Accelerators
- Corrosion inhibitors
- Air entrainment agents*

* air pores of a certain size increases frost resistance

Current trends

- Decrease Environmental Impact
- High Performance Concrete
- Self-Compacting Concrete
- Self-Desiccating Concrete
- New Filler Materials
- Waste Materials Included

Major chemical compounds formed in the cement kiln:

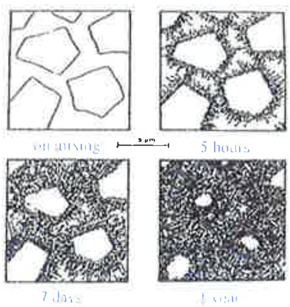
C_3S C_2S C_3A C_6A_2F/C_6AF_2

Complex reaction with water results in formation of a solid cement paste:

$$[C_3S,\ C_2S,\ C_3A,\ C_6A_2F/C_6AF_2] + H_2O \rightarrow C_kS_mH_n + CaOH + \ldots$$

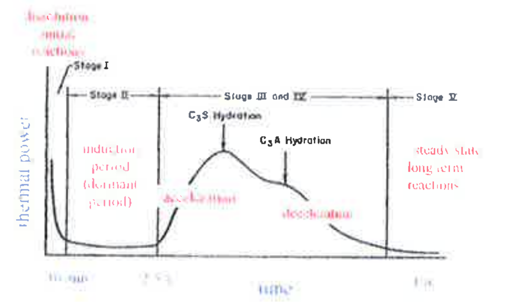
Note the cement chemist's shorthand notations

$CaO = C$ $SiO_2 = S$ $Al_2O_3 = A$
$Fe_2O_3 = F$ $H_2O = H$



Schematic picture of the setting and hardening process.

Taylor, H F W "Portland cement hydration products" in "Instructional Modules in Cement Science" Ed D M Roy, J Mater, Educ



Terms according to J F Young "Hydration of Portland Cement" in "Instructional Modules in Cement Science" Ed D M Roy J Mater Ed

Three types of cement/concrete calorimeters

Adiabatic Calorimetry (Semi-Adiabatic Calorimetry)

Sample temperature is measured on an insulated sample.

Solution Calorimetry

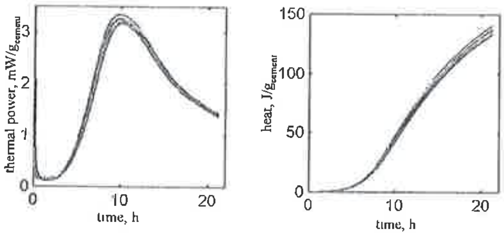
Heat of hydration is the difference between heat produced when a cement and a hydrated cement paste sample are each dissolved in strong acids.

Isothermal Calorimetry (conduction calorimetry)

Heat production rate is measured continuously at isothermal conditions.

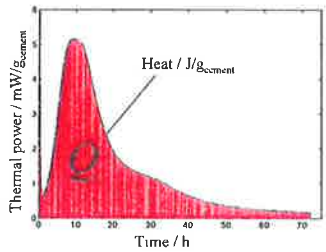
Cement hydration

Eight samples from the same mix

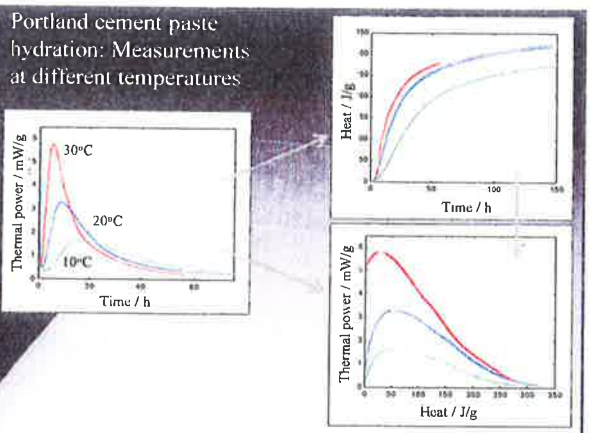


Note that thermal power and heat are given per g_{cement} (dry)

Heat of hydration measurement over three or seven days for the classification of cements.



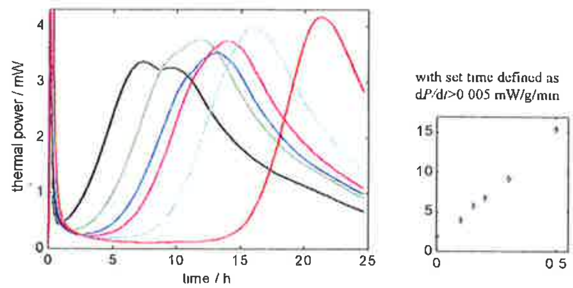
Portland cement paste hydration: Measurements at different temperatures



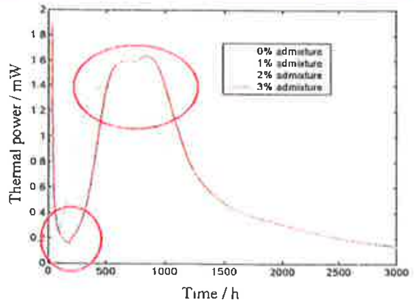
Cement hydration (retardation)

Six samples with 0 - 0.5% of an additive with retarding properties

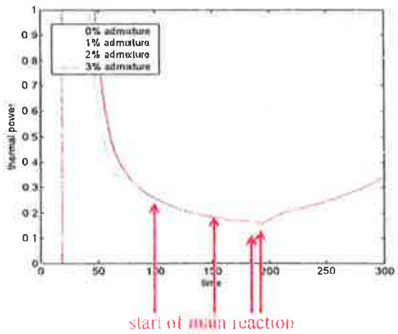
Closed glass ampoules at 20 °C



Note that isothermal calorimetry can show details in the hydration reactions (1)

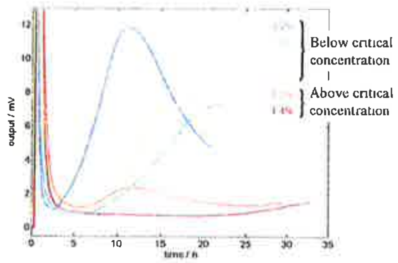


...details in the hydration reactions (2)



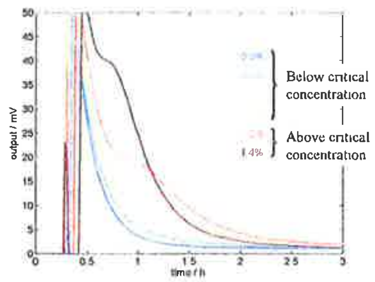
Cement-admixture interaction (1)

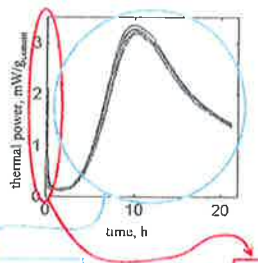
Abnormal hydration in low-sulfate cement with high admixture concentrations



Cement-admixture interaction (2)

Abnormal hydration in low-sulfate cement with high admixture concentrations (early reactions)





Main peak

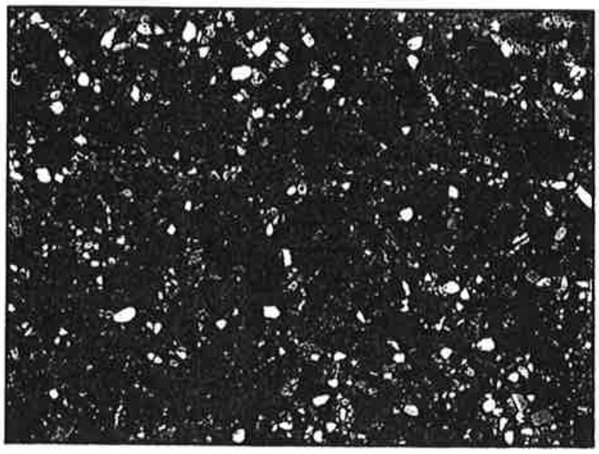
Mix outside and transfer to ampoule and calorimeter.

Early reactions

Mix inside ampoule in calorimeter (e.g., with admix-ampoule).

Isothermal calorimetry has a wide range of uses in cement/concrete science/technology, e.g.

- Heat of hydration
- Retardation
- Cement-admixture interactions
- Reaction rates as function of temperature
- Gypsum optimization
- Quality control



Introduction to Isothermal Calorimetry

Thermodynamics for Calorimetry

Lars Wadsö

Isothermal Calorimetry and Thermodynamics

Isothermal calorimetry can be used without any knowledge of thermodynamics. However, isothermal calorimetry is an excellent method to obtain data for thermodynamic calculations.

For example, with the help of thermodynamics, one can find in which direction a process tends to proceed and calculate properties that cannot be directly measured.

"SI-System"

Base units: m, kg, s, A, K, mol, cd

Derived units: Pa, J, W, V, Ω, °C ...

Prefixes: n, μ, m, k, M, G ...

Note: Mass is often expressed in grams (g) OK

Pressures are often *discussed* in units of bar or atm OK

Energy is sometimes expressed in calories ~~OK~~

Nomenclature

t	time	s
P	thermal power	$W = J\ s^{-1}$
Q	heat	J
W	work	J
ΔH	enthalpy change	$J\ mol^{-1}$
p	pressure	Pa
V	volume	m^3
n	amount substance	mol
R	gas constant (8 314)	$J\ mol^{-1}\ K^{-1}$
T	absolute temperature	K
C	heat capacity	$J\ K^{-1}$
also (but not used here)		
ΔU	internal energy	$J\ mol^{-1}$
ΔS	entropy	$J\ mol^{-1}\ K^{-1}$
ΔG	Gibbs energy	$J\ mol^{-1}$

Very important definitions

system	whatever we want to study
surrounding	the rest of the universe
open	transfer of matter possible
closed	no transfer of matter
isolated	no transfer of matter or heat
adiabatic	no transfer of heat
isothermal	no change of temperature
exothermic	heat is released ("warming")
endothermic	heat is consumed ("cooling")

The thermodynamic sign convention

Consider changes of thermodynamic properties from the point of view of the system

examples:

- Exothermic processes have ΔH<0
- Dissolution of salts in water can be exothermic or endothermic

	kJ/mol	
NaCl	3 88	slightly endothermic
LiCl	-37 03	exothermic
KCl	17 22	endothermic

Note that one can find the opposite definition in mechanical engineering the (useful) heat that comes out of a process (a machine) is there counted as positive

Note also that experimental results usually (but not always) are plotted with exothermic thermal powers as positive

ENERGY

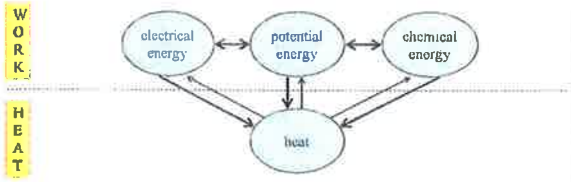
Energy exists in many forms: electrical energy, potential energy, heat etc

First law: Energy cannot be destroyed, only converted from one form to another

work ⇒ work

work ⇒ heat

heat ⇒ work + heat at lower temperature



Enthalpy, H (J/mol)

The enthalpy (H) is the energy content at constant pressure (the most common condition)

Only differences or changes in enthalpies (ΔH) can be measured, but one can define absolute enthalpies relative to the enthalpy of an arbitrary *standard state*, most commonly 25 °C, 1 atm

Enthalpy is the most commonly used thermodynamic property. Values of ΔH for different types of processes can be found in tables

A process (reaction) with an enthalpy change ΔH produces ΔH joules of heat per mol reacted at constant pressure conditions

For heterogeneous samples (such as cement, foodstuffs and polymer blends), the enthalpy can also be expressed in units of J/g (Δh)

$\Delta_x H$ is the change in enthalpy during a process of type x

Process x

$$X(\text{state}) \xrightarrow{\Delta_x H} Y(\text{state})$$

Examples of processes

vaporization	$\Delta_{vap}H$
condensation	$\Delta_{cond}H$
reaction	$\Delta_r H$
formation	$\Delta_f H$
combustion	$\Delta_c H$
solution	$\Delta_{sol}H$
transfer	$\Delta_{trans}H$
transition	$\Delta_{trs}H$
sublimation	$\Delta_{sub}H$
mixing	$\Delta_{mix}H$
ionization	$\Delta_{ion}H$
melting/fusion	$\Delta_{fus}H$

Enthalpy changes of formation ($\Delta_f H$) are most important!

$\Delta_f H$ is the enthalpy change associated with formation of a substance from the elements ($\Delta_f H$(an element)=0)

Common state specifiers:

gas	g
liquid	l
solid	s
aqueous solution	aq
solution	sln
crystalline	cr
infinite dilution	∞
saturation	sat

#1 The enthalpy change of a reaction can be calculated from the enthalpies of formation of the reactants and the products

$$A + B \rightarrow C \qquad \Delta_r H = \Delta_f H(C) - \Delta_f H(A) - \Delta_f H(B)$$

#2 Enthalpies of formation are given relative to a standard state. The most common standard state is 25 °C, 1 atm

$\Delta_f H^o$ ← standard state

examples: $\Delta_f H^o(\text{Na(s)}) = 0$ (by definition)

$\Delta_f H^o(\text{Na}^+\text{(aq)}) =$ -240.12 kJ/mol

#3 It is important to specify the state of a substance. Na(s), Na(l), Na(g), Na^+(aq) all have different enthalpies of formation

Enthalpy includes the volume work associated with volume changes, like pushing back the atmosphere to make room for evolved gas. For isothermal gas producing reactions, different amounts of heat are measured at constant pressure (open ampoule) and at constant volume (closed ampoule).

-Volume work $W = -p\,\Delta V$

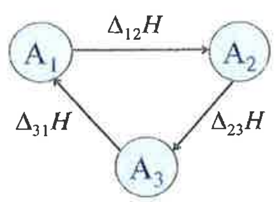
-Pressure work $W = -V\,\Delta p$

(from gas law: $pV=nRT$; for small changes in V and p)

This work is transformed to heat under isothermal conditions.

Example: An isothermal pressure increase from 1.0 to 1.1 atm in 20 mL produces 0.2 J heat

Hess law

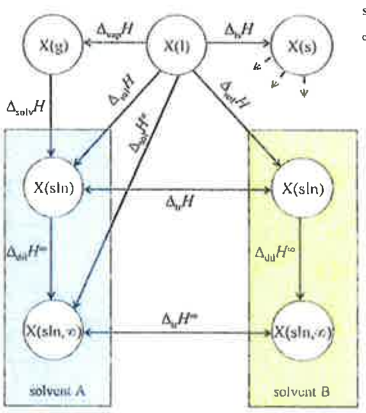


$$\Delta_{12}H + \Delta_{23}H + \Delta_{31}H = 0$$

$$\Sigma_{cycle}\Delta H = 0$$

All reactions need not be realizable in practice!

Hess law application



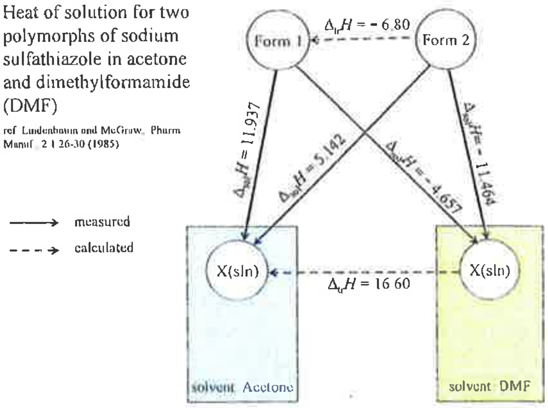
sln = solution

∞ = infinite dilution

for every cycle: $\Sigma\,\Delta H = 0$

Heat of solution for two polymorphs of sodium sulfathiazole in acetone and dimethylformamide (DMF)

ref Lindenbaum and McGraw, Pharm Manuf 2 1 26-30 (1985)



Gibbs energy (Free energy) ΔG J mol^{-1}

If ΔG<0 a process (reaction) is spontaneous, i.e moves towards equilibrium

Entropy ΔS J mol^{-1} K^{-1}

A measure of disorder; all real processes result in increase of the total entropy (system + surroundings)

$$\Delta G = \Delta H - T\Delta S$$

Heat capacity

When a heat Q (J) is supplied to an object with heat capacity C (J K^{-1}), its temperature will change by ΔT (K)

$$Q = C\,\Delta T$$

Heat capacity of an object (sample, part of a calorimeter) is the product of its specific heat capacity c (J g^{-1}K^{-1}) and its mass m (g):

$$C = c\,m$$

Total heat capacity of an object composed of several components with different heat capacities, is the sum of the heat capacities:

$$C_{tot} = \Sigma C_i$$

Heat Capacity Values for Some Common Materials

(approximate heat capacities (J g^{-1} K^{-1}) at 20 °C)

Brass	0.38
Steel	0 46
Quartz/sand	0 75
Cement	0 80
Minerals	≈0 8
Glass	0 84
Aluminum	0 90
Dry Wood	1 20
Water	4 18

Useful heat capacity calculations

The reference should have approximately the same heat capacity as the sample

If the sample is 5 g cement paste made from 3 g cement and 2 g water, what should be used as a reference?

1 Water? Heat capacity of sample 3·0 8 + 2·4 18 = 10 8 J K^{-1}

Mass of water with the same heat capacity 10 8 / 4 18 = 2 6 g

2 Sand? Heat capacity of sample, same as above

Mass of sand with the same heat capacity 10 8 / 0 8 = 14 3 g

Here, we have assumed that the heat capacity of cement paste equals that of its components

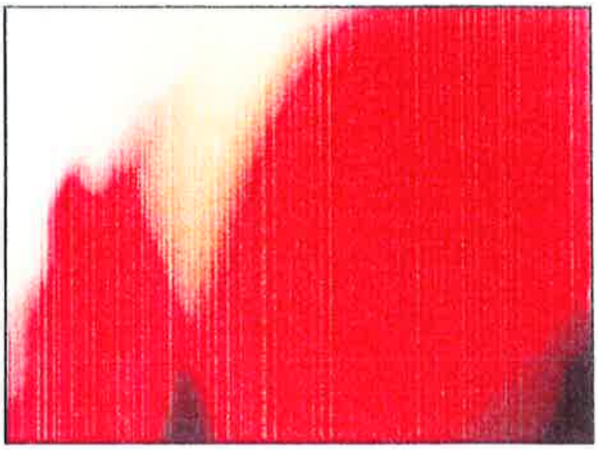
Approximate $\Delta_r H$ for different types of reactions

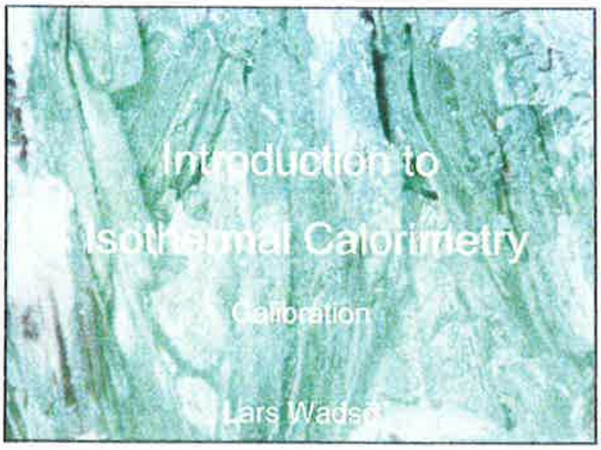
Useful for estimation of heats from a reaction *or* the reaction rate from measured thermal powers

		kJ mol^{-1}
Hydrolysis	$RCOOR' + H_2O \Rightarrow RCOOH + R'OH$	0
	$RNHCOR' + H_2O \Rightarrow RNH_2 + R'COOH$	+50
	$(RCO)_2O + H_2O \Rightarrow 2\ RCOOH$	-60
Decarboxylation	$RCOOH \Rightarrow RH + CO_2$	+30
Oxidation by O_2	$-CH_3 + 0.5\ O_2 \Rightarrow -CH_2OH$	-180
	$-CH_2- + 1.5\ O_2 \Rightarrow -COOH + H_2O$	-160
	$RCH_2OH + 0.5 O_2 \Rightarrow RCHO + H_2O$	-200
	$RCHO + 0.5 O_2 \Rightarrow RCOOH$	-290
	$2\ -SH + 0.5 O_2 \Rightarrow -S-S- + 0.5\ H_2O$	-260

Cox and Pilcher (1970) "Thermochemistry of Organic and Organometallic Compounds," Academic Press, London

Pedley et al. (1986) "Thermochemical Data of Organic Compounds," Chapman and Hall, London





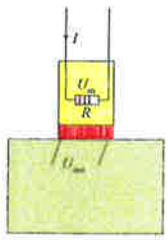
Calibration

= to introduce heat & measure response

Different types of calibration

1. Electrical calibration (convenient, most common)
2. Chemical calibration (valuable complement)
3. Radioactive sample (convenient, but obsolete)
4. Heat capacity NEW!
5. Diffusion cell NEW!

Electrical calibration theory



Nomenclature

U_{in}	voltage over heater	V
I	current through heater	A
R	heater resistance	Ω
U_{out}	output voltage from heat flow sensor	V
P	thermal power	W

Equations

$U_{in} = R \cdot I$ (Ohm's law)

$P = U_{in} \cdot I$ (Heat production rate in resistor)

$= U_{in}^2 / R$

$= I^2 \cdot R$

Note: the last equation is the best as the current is the same in the whole circuit, but U_{in} measured outside the calorimeter also includes voltage drops over the leads

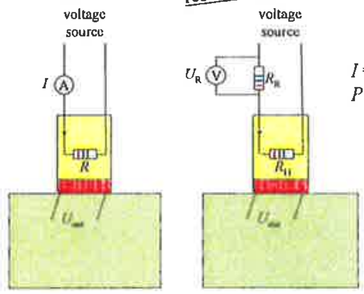
Electrical calibration in practice

with a mA-meter

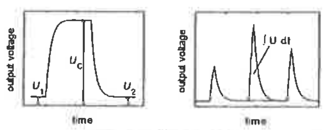
$P = I^2 \cdot R$

with an external reference resistor and a voltmeter

$I = U_R / R_R$
$P = I^2 \cdot R$



Two types of electrical calibration



	Steady State	Dynamic or Pulse
input	P	$Q = \int P\,dt = P \cdot \Delta t$
output	U	$\int U\,dt$
calibration coefficient	$\varepsilon = P/U$	$\varepsilon = Q/\int U\,dt$

Calibration coefficient

ε W/V

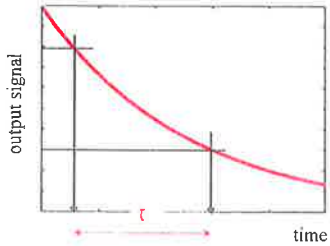
V does not need to be true volts, and could also be some other type of output from an amplifier or a data logger

Sensitivity

$1/\varepsilon$ V/W

The time constant, τ

The time constant is a measure of how rapidly a signal decreases when no heat is produced in the calorimeter. One simple way to find the calibration coefficient is to find the time it takes for the signal to decrease from any value to 37% of that value (e^{-1}). Normally this is done on the decaying part of a calibration curve



$$U(t) = U_0 \exp(-t/\tau)$$

Using the time constant, τ

$$P = \varepsilon\,(U + \tau \cdot \mathrm{d}U/\mathrm{d}t)$$ The Tian equation

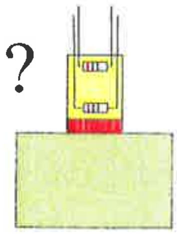
-The time constant is a model for time lag of a calorimeter.

-Some commercial calorimeters automatically make the Tian corrections.

-Sometimes more than one time constant is used, but this is usually not necessary.

Potential problems with electrical calibrations.

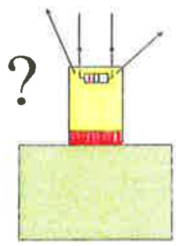
#1 Heater position



A calibration heater should ideally deposit the heat in the same place as heat is produced during a measurement.

Potential problems with electrical calibrations.

#2 Lead heat losses



A calibration heater always conducts some heat away through its leads. This is no problem if the leads are also there during measurements, but for insertion heaters, this can be a problem.

Chemical Calibration

The ideal way to calibrate an isothermal calorimeter for measurements is to run a similar type reaction with a well known enthalpy.

- aqueous dissolution and dilution of 1-propanol in water
- dilution of aqueous urea solutions
- dissolution of toluene in water
- hydrochloric acid – sodium hydroxide (acid + base) reaction
- sucrose hydrolysis
- binding of Ba^{2} to the cyclic ether 18-crown-6
- dissolution of potassium chloride in water
- hydrolysis of triacetin in imidazole-acetic acid buffers (long term)

ref. Wadsö, I and Goldberg, R N (2001) 'Standards in isothermal microcalorimetry' Pure Appl Chem 73 1625-1639

Chemical Calibration

Example: dissolution of a solid

Dissolution of crystalline potassium chloride (KCl) in water

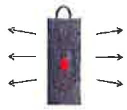
(1 mol KCl per 500 mol water)

ΔH=17.584±0.017 kJ/mol

Uncertainty is about 1/1000

ref. Wadsö, I and Goldberg, R N (2001) 'Standards in isothermal microcalorimetry' Pure Appl Chem 73 1625-1639

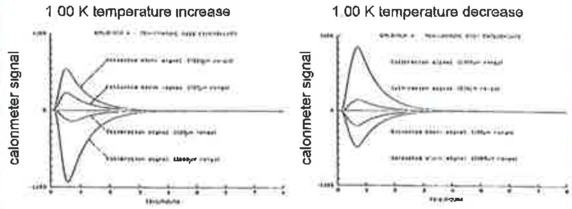
Radioactive Calibration



Ampoule with long-lived radioactive isotope will produce constant thermal powers over long periods of time.

Convenient, but restrictions on radioactive materials make the use of this type of devices very limited.

Heat Capacity Calibration



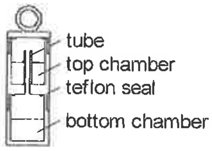
The calibration coefficient can be calculated from the output caused by a temperature step up/down with and without a known heat capacity sample (aluminum oxide, sapphire)

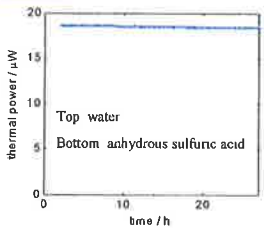
Interesting Based on fundamental physical principle Is anyone using it?

ref: Bunyan, P F (1999) Thermochim Acta 327 109-116

Diffusion Cell Calibration

The rate of water vapor diffusion in a fixed geometry between two solutions with constant water activities and constant enthalpies of vaporization will produce a constant thermal power





Not in use Can be of interest in large scale calorimeters

Wadsö L, Kocherbitov V (1999) *A new diffusion controlled calibration and test device for microcalorimeters* Presented at Workshop on the microcalorimetry of energetic materials, Leeds, UK

How good is a calorimeter/measurement?

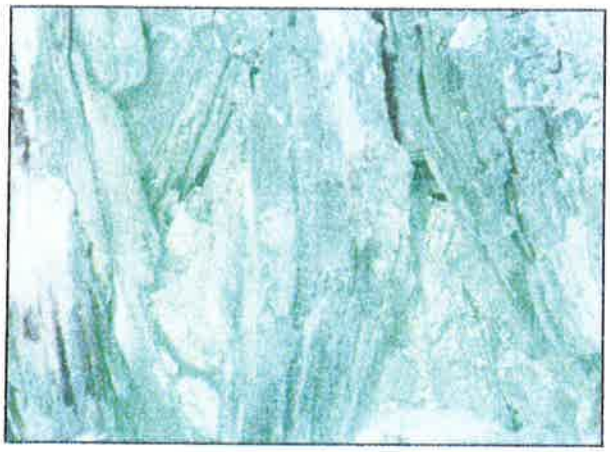
Repeatability (earlier *precision*) is a measure of the scatter (standard deviation) in a series of observations (around the measured mean) Report repeatability of experiments (not calibrations)

Uncertainty (earlier *accuracy*) is the difference between the measured mean and the true/accepted value. Run standard test reactions to calculate uncertainties (very difficult to calculate by combined uncertainties etc.)

Limit of detection is the smallest heat quantity (J) or thermal power (W) that can be determined with reasonable certainty (note: *sensitivity* is the inverse if the calibration coefficient).

Baseline. Calculate mean, slope and standard deviation

ref Wadsö, I and Goldberg, R (2001) Pure Appl Chem 73 1625-1639



Introduction to Isothermal Calorimetry

Different Types of Calorimeters

Lars Wadsö

CALORI-METER

Heat — Measure

There are many different types of calorimeters!

Different types of calorimeters

Scanning	Non-isothermal	Isothermal	Indirect calorimetry	Other types
The instrument changes the temperature	The process studied (the sample) changes the temperature	The temperature is (essentially) constant	Measure something else than heat, from which one can calculate the heat	Nuclear calorimeters
DSC (Differential Scanning Calorimeter)	Adiabatic cal	Heat conduction calorimeter	Respirometry	Semi-conductor radiation sensors
	Semi-adiabatic cal	Power compensation calorimeter		etc

Note: *not* colorimetry

DSC (Differential Scanning Calorimetry)

DSC measures the heat produced/consumed by processes that are initiated by the change in temperature

Examples
- melting-solidification
- dehydration
- degradation
- T_g-transition
- crystal transformation

DSC s are very common instruments

MDSC is a type of advanced DSC that can separate reversing (e.g. melting) and non-reversing processes (e.g. crystal transformation)

A DSC can be used in "isothermal mode," but specific sensitivity is lower than an isothermal calorimeter because of the small sample size required for DSC. Also, one cannot manipulate the sample during a measurement.

If you are used to DSC...

The world is quite isothermal and most processes (respiration, degradation, dissolution, oxidation...) take place even if the temperature is constant. It is not *temperature changes* that drive processes.

With isothermal calorimetry, we study processes under quite natural conditions.

Semi-adiabatic and Adiabatic Calorimeters

TA Instrument SolCal

A semi-adiabatic calorimeter is essentially an insulated sample in which the temperature is measured. It is necessary to compensate for heat lost by conduction and radiation.

In an adiabatic calorimeter, all heat produced by the sample heats the sample (adiabatic=no heat loss). This is usually accomplished by an adiabatic shield, meaning the surroundings are kept at exactly the same temperature as the sample OR measurements are made so quickly that no heat is lost

Examples: Bomb calorimeters, cement/concrete calorimeters, TA Instruments SolCal

In this group can be found (essentially) isothermal calorimeters that operate with small temperature changes (like the SolCal above), but also calorimeters with high temperature changes like most (semi-)adiabatic concrete calorimeters in which the temperature can rise 30-80 K during a measurement

Bomb Calorimeters

A bomb calorimeter is usually a semi-adiabatic calorimeter for heat of combustion measurement by reacting samples with an excess of oxygen

Bomb calorimeters of extreme precision were used to compile tables for heats of combustion of organic compounds. This application is now rare, since tabulated data for most simple compounds are available

Nowadays, simpler bomb calorimeters are used for measurement of heat contents of fuels, food and animal feed

Power Compensation Calorimeters

These are calorimeters in which the temperature is kept constant by addition or subtraction of heat. This is easiest to do by adding electrically produced heat to compensate an endothermic process, but can also be done by the Peltier effect to compensate for both exothermic and endothermic processes

Example: DSC, some titration calorimeters

Indirect Calorimetry

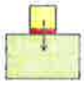
Another property which corresponds to heat produced can be measured and then used to calculate the heat

Example: Respirometry in which CO_2 production is measured and heat production is calculated based on the assumption that 470 kJ of heat is produced for each mole of CO_2 produced

Note that indirect calorimetry relies on knowledge of the correct heat (enthalpy) produced by the process as a function of the measured parameter

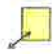
Isothermal calorimeters = calorimeters with essentially constant sample temperature

Heat conduction calorimeters



Heat flows to/from the sample by thermal diffusion

Power compensation



Temperature change is compensated by active heating/cooling

Some adiabatic calorimeters

The sample is insulated, but the temperature increase is made low

Essentially constant temperature?

Depends on process studied!

Kinetics (reaction rates) are more sensitive to temperature changes than determinations of total heats (such as titrations)

Determination of seven day heat of cement hydration	Determination of maximum rate of hydration of cement	Retardation of cement hydration for different additive concentrations
Liquid-liquid titration experiment	Determination of rate constant for enzymatic process	Comparison of effect of different drugs on a cell culture

"A measurement is isothermal if the temperature changes are so small they do not influence the results of the measurement"
LW

How large can an *isothermal* sample be?

5 g cement paste

5 mL water with animal (stirred)

5 g rubber sample

1000 g cement paste

1000 mL water with fish (stirred)

1000 g rubber sample

Whether or not a sample is isothermal depends on its size, volumetric heat production rate, thermal properties, and properties of the calorimeter. Most isothermal calorimeters use small samples (1-20 mL), but some very large devices (for example, a house with heat flow sensors) can also be considered to be isothermal calorimeters

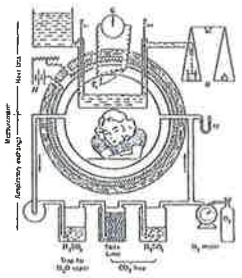
Isothermal calorimetry: size and thermal power ranges

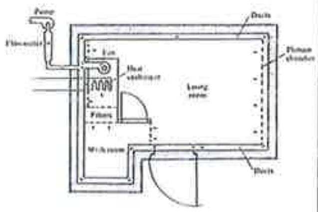
Size		Thermal power range
Huge	A house	MW
Large	Whole-body calorimeter	kW
		W
Small	A battery, cement paste	mW
Tiny	A few mg of a pharmaceutical substance	µW
		nW

Isothermal calorimetry: size and thermal power ranges

Size		Thermal power range
Small	A battery, cement paste	mW
Tiny	A few mg of a pharmaceutical substance	µW
		nW

Two large isothermal calorimeters





What is *microcalorimetry*?

'...a calorimeter designed for use in the microwatt (µW) range, under essentially isothermal conditions' (Wadsö, I and Goldberg, R N, 2001) (or a calorimeter using small samples)

A heat conduction calorimeter for measurement of low thermal powers

Typical applications areas

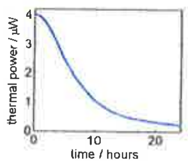
- titrations
- energetic compounds
- microbiology

Even more sensitive calorimeters are sometimes called *nanocalorimeters*

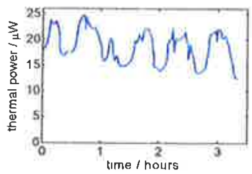
Sometimes 'microcalorimetry' is (unfortunately) used synonymously with 'isothermal calorimetry'

Microcalorimetry = 'microwatt isothermal calorimetry'

A 50 mm steel nail is bent and transferred into a microcalorimeter. The heat produced by the relaxation and reorganization of the atoms is clearly measurable for almost 24 hours



A 4 mm ant weighs only 1.5 mg. Still, it produces about 20 µW, with periods of activity and rest clearly evident



Organizations

International Confederation of Thermal Analysis and Calorimetry (ICTAC): www.ictac.org (European chapter: ESTAC, Nordic (not active) chapter: NOSTAC).

The Calorimetry Conference (CalCon): Annual conference

Journals in the field:

Thermochimica Acta

Journal of Thermal Analysis and Calorimetry

(Journal of Physical Chemistry)

Introduction to Isothermal Calorimetry

Kinetics and Stability

Lars Wadsö

Nomenclature

t	time	s
P	thermal power	$W = J\ s^{-1}$
Q	heat	J
ΔH, Δh	enthalpy change	$J\ mol^{-1}$, $J\ g^{-1}$
ν	rate	$mol\ s^{-1}$, $g\ s^{-1}$

Thermodynamics/ thermochemistry

How much heat is produced by a process when it goes to completion (or to a certain known state)?

Kinetics

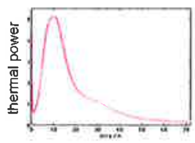
What is the reaction rate of a chemical process?

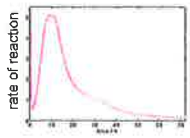
$$P = \Delta H \cdot \nu$$

Isothermal calorimeters can measure both enthalpies and kinetics (sometimes in the same experiment), but many measurements (especially on complex samples) give only kinetic information.

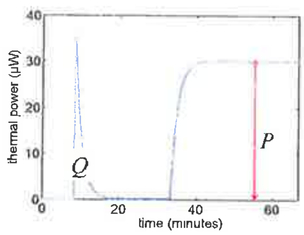
$$P = \Delta H \cdot \nu$$

The chemist	J/mol	mol/s
The material scientist	J/g	g/s





Note: ΔH is often unknown and many simultaneous and/or consecutive processes, each with a different ΔH value, may be occurring.

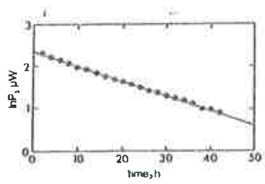


titration etc.
$n = Q / \Delta H$

kinetic measurement
$\nu = dn/dt = P / \Delta H$

Degradation of the Antibiotic Ampicillin in Water

"Textbook example"



First order kinetics predicts the rate of concentration change with time, dc/dt, is proportional to concentration c. Rate is proportional to thermal power that we measure. The rate equation can be expressed several ways

Exponential form	$c = c(0)\exp(-kt)$
Differential form	$dc/dt = -k\,c(0)\exp(-kt)$
Calorimetric form	$P / (\Delta H\ V) = -k\,c(0)\exp(-kt) \Rightarrow \ln(P) = -kt + const$

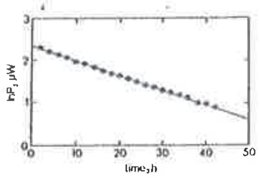
First order process: reaction rate is proportional to non-reacted mass/ (or amount)

1 First order rate law gives exponential solution
rate = $k \cdot m$ → rate = k_1 exp($-k_2 \cdot t$)

2 Thermal power is proportional to rate:
$P = \Delta H \cdot$ rate → $P = \Delta H \cdot k_1$ exp($-k_2 \cdot t$)

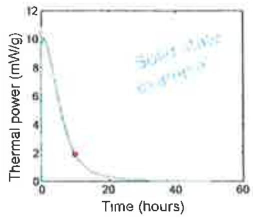
3 Take logarithm to find k_1 and k_2:
Ln(P) = ln($\Delta H \cdot k_1$) $- k_2 t$

4 Evaluate rate constant and enthalpy

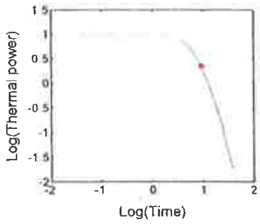


cf Wadsö & Li (2007)

Example: Epoxy curing

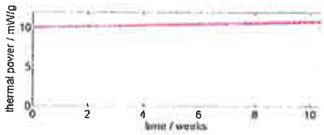


Calorimetric measurement



Kinetic model (mathematical or physiochemical)

Predicting kinetics is not trivial

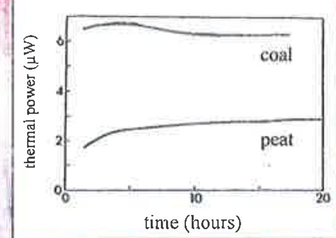


Suppose we had measured thermal power from a sample of an energetic compound with the results seen at the left.

What can we say about future development of the thermal power?

Is there a risk for a run-away situation (fire, explosion)?

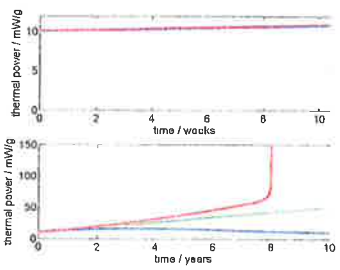
Self-heating of solid fuels



From P and knowledge of Δh, it is possible to calculate the annual loss of energy content (calorific value) by assuming for example constant thermal power.

L.Wadsö

Predicting kinetics is not trivial



Predictions of future *isothermal* heat production rates must be based both on measurements *and* information about the process

Predictions of the risk of a run-away situation must, in addition, be based on information and a model of the thermal situation (insulation, cooling)

Heat + amount degraded → enthalpy

Heat + enthalpy → degraded amount

$$Q = -(n(0) - n(t)) \cdot \Delta H$$

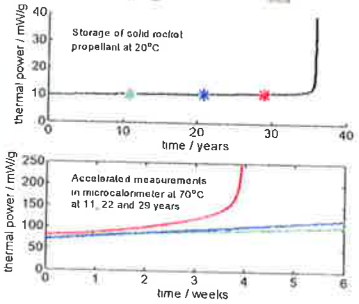
Thermal power + enthalpy → degradation rate

$$P = \frac{dn}{dt} \Delta H$$

Testing explosives

Explosives and other energetic compounds contain stabilizers that prevent autocatalytic (and accelerating) reactions

It is important to be able to make estimates of how long a batch of explosive can be stored before the stabilizers are consumed and the degradation reactions start to accelerate. Microcalorimetry is a standard method for this type of evaluation



Arrhenius' law

$$v = A \cdot \exp\left(-\frac{E_a}{RT}\right)$$

Nomenclature

v	rate of a process	g s^{-1} or mol s^{-1}
A	pre-exponential constant	g s^{-1} or mol s^{-1}
E_a	activation energy	J mol^{-1}
R	gas constant	J mol^{-1} K^{-1}
T	temperature	K
P	thermal power	W

Writing this law for two temperatures 1 and 2 and solving for E_a gives

$$E_a = \frac{R\ln(v_1 / v_2)}{\frac{1}{T_2} - \frac{1}{T_1}}$$

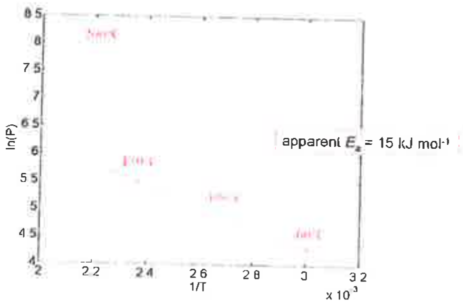
With isothermal calorimetry we measure thermal powers that are proportional to rates of processes. We can therefore also write the above equation as

$$E_a = \frac{R\ln(P_1 / P_2)}{\frac{1}{T_2} - \frac{1}{T_1}}$$

Note that

- The different measurements of thermal power must be made at the same conditions (except temperature)
- The Arrhenius law is not a natural law, it is a mathematical relationship found to be approximately valid for many processes.
- If different processes are active at different temperatures, the Arrhenius equation will give an activation energy that changes with temperature. The above two-point method is therefore quite dangerous. It is better to make measurements at more than two temperatures and plot the results in a Arrhenius diagram ln(rate) vs. 1/T

Example of Arrhenius' law application:
Heat production from wood pellets at elevated temperature



Hazardous evaluation

The picture shows a fire in a silo which contained paper, plastics and wood chips. This type of fire starts when the fuel is heated by microbial activity and is further catalyzed by oxidation of the fuel

fine chemicals
fossil fuels
bio-fuels
energetic materials
fertilizers
bleach

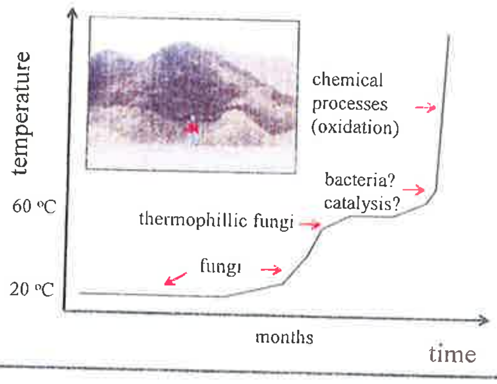
Methods:

HPLC

DSC-ARC-isothermal calorimetry

Note: stability is a chemical *and* physical property

Self-ignition in biofuel stacks



Shelf life evaluation

What determines the shelf life?

- Increased number of microorganisms
- Deteriorated mechanical properties (texture, crispiness...)
- Discoloration
- Lowered amount of active substance
- Increased amount of degradation product

Not only for foodstuffs!

Solid State Reactions

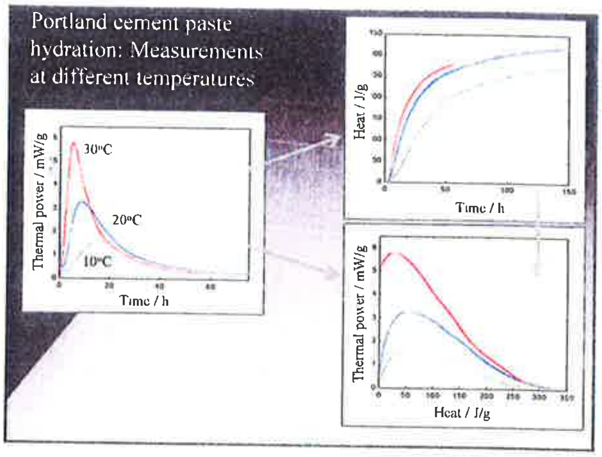
Reactants are not continuously mixed or not even in direct contact

Gases (oxygen) and vapors (water) may catalyze reactions

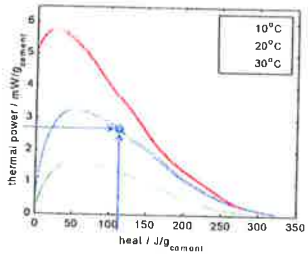
Many such reactions are diffusion controlled

Four point test
1. dry + nitrogen
2. dry + oxygen
3. wet + nitrogen
4. wet + oxygen

Portland cement paste hydration: Measurements at different temperatures



Isothermal calorimetry gives information both on rate and extent of reaction



P	J/s
Q	J
Δh	J/g
v	g/s
ξ	g/g
m	g

Thermal power is proportional to rate, v $P = \Delta h\ v$

Heat is proportional to how much cement has reacted (extent of reaction ξ)

$$Q = \Delta h\ \xi\ m$$

Note that this is a *general* method For the complex cement hydration reaction shown, Δh is not constant, but rather a function of the extent of reaction, $\Delta h(\xi)$

Kinetic models applied to calorimetric data

thermal power (dq/dt) ~ reaction rate

heat (q) ~ extent of reaction

reaction	rate equation	calorimetric rate equation
A — B	$dx/dt = k(A - x)^m$	$dq/dt = \Delta Hk(A - (q/\Delta H))^m$
A + B — C	$dx/dt = k(A - x)^m(B - x)^n$	$dq/dt = \Delta Hk(A - (q/\Delta H))^m(B - (q/\Delta H))^n$
A ⇌ C	$dx/dt = k(A/x_e)(x_e - x)$	$dq/dt = kA(\Delta H - (q/x_e))$
A + B ⇌ C	$dx/dt = k_1(A - x)(B - x)$	$dq/dt = k_1(A\Delta H - q)(B\Delta H - q) - (k_{-1}q)$
Ng equation[b]	$dx/dt = Ak(x/A)^m(1 - (x/A))^n$	$dq/dt = Ak\Delta H(q/A\Delta H))^m(1 - [q/(A\Delta H)])^n$
autocatalytic	$dx/dt = k(A - x)(x_0 + x)$	$dq/dt = k(A\Delta H - q)(x_0\Delta H + q)$
coagulation	$dx/dt = k(z - x)^2$	$dq/dt = k\Delta H(z - (q/\Delta H))^2$
Michaelis–Menten[c]	$d[ES]/dt = k(K_i[E][S])$	$dq/dt = k\Delta H(K_i[E][S] - (q/\Delta H))$

Wilson, R J, A E Beezer, J C Mitchell and W Loh (1995) "Determination of thermodynamic and kinetic parameters from isothermal heat conduction microcalorimetry applications to long-term-reaction studies", J Phys. Chem. 99 7108-7113

Example of how the Ng equation for solid state reactions can be transformed to a form suitable for calorimetric data

A solid state decomposition reaction may be written

$$A \rightarrow A_{dec} \qquad \Delta h$$

The Ng equation is:

$$\nu = k\xi^m(1-\xi)^n \qquad (10)$$

Here, ξ is the extent of reaction (fraction of compound degraded) that may be written.

$$\xi = \frac{m}{m_1} \qquad (11)$$

Now we introduce two important relations between the rate equation and the calorimetric experiments:

$$\nu = \frac{P}{\Delta h} \qquad (12)$$

i.e. the rate of a reaction is proportional to the thermal power

$$\xi = \frac{Q}{m_1\Delta h} \qquad (13)$$

i.e. the mass of substance reacted is proportional to the produced heat (we assume that all of the substance is degradet at infinite time).

We enter Eqs 12 and 13 into Eq. 10:

$$\frac{P}{\Delta h} = k\left(\frac{Q}{m_1\Delta h}\right)^m\left(1-\frac{Q}{m_1\Delta h}\right)^n \qquad (14)$$

k rate constant

v rate of reaction

ξ extent of reaction (0-1)

This is a way of transforming a rate equation so that it is written in terms of what can be measured with an isothermal calorimeter (P and Q)

continued

Known parameters (P and Q as functions of time)

$$\frac{P}{\Delta h} = k\left(\frac{Q}{m_1\Delta h}\right)^m\left(1-\frac{Q}{m_1\Delta h}\right)^n$$

Whether this can be solved depends on how good your data is and on how many measurements you have made You also need computer software to do the calculations

If you assume (or know) the values of, e g , x and y then you only have two unknown parameters left to solve for

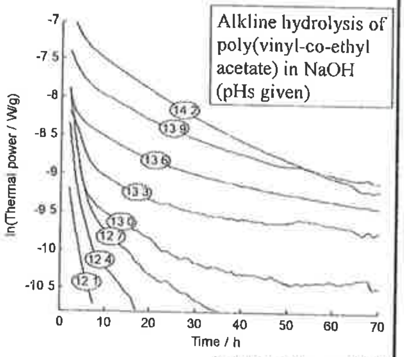
Wilson, R J, A E Beezer, J C Mitchell and W Loh (1995) "Determination of thermodynamic and kinetic parameters from isothermal heat conduction microcalorimetry: applications to long-term-reaction studies", J Phys. Chem 99 7108-7113

Willson, R J, A E Beezer and J C Mitchell (1996) "Solid state reactions studied by isothermal microcalorimetry; the solid state oxidation of ascorbic acid", Int J Pharmaceutics 132 45-51)

Degradation models

Calorimetric measurements can be used to test degradation models (kinetic models) and quantify the parameters (rate constant, activation energy etc.) in such models.

Alkline hydrolysis of poly(vinyl-co-ethyl acetate) in NaOH (pHs given)



Anderberg and Wadsö (2007)

Introduction to Isothermal Calorimetry

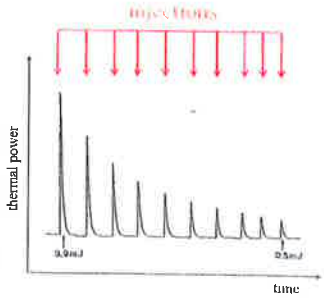
Titration Calorimetry

Lars Wadsö

Titration is the controlled addition (in steps or continuously) of one substance to another. Liquid-liquid titration is most common, but solid-liquid (dissolution) and gas-solid (sorption) can also be considered as titrations

Used for characterization of the interactions of all types of biological macromolecules with other compounds

… and for other types of studies where one is interested in adding one component to another, for example studies of enzyme kinetics



Equilibrium and equilibrium constants

$$A + B \rightleftharpoons C$$

$$K = \frac{[C]}{[A]\,[B]}$$

High K: A lot of C is formed

Low K: Little C is formed

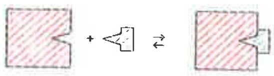
ΔH (J/mol)

Enzyme binding

$$A + B \rightleftharpoons AB$$

$$K = \frac{[AB]}{[A]\,[B]}$$

ΔH (J/mol)



Even seemingly simple processes can involve many steps

Binding of an alcohol (ROH) to α-cyclodextrin (α-CD) in aqueous solution

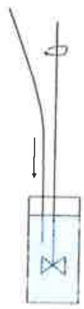
$$(\alpha\text{-CD}\cdot(H_2O)_n)_{aq} + (ROH)_{aq} \Rightarrow (\alpha\text{-CD}\cdot ROH\cdot(H_2O)_{n-x})_{aq} + x(H_2O)_{aq}$$

1. Dehydration of ROH
2. Solvation of ROH in cavity
3. Interactions between –OH and α-CD
4. Transfer of x H_2O from the cavity to bulk water
5. Conformational change of α-CD
6. Reduced mobility of the alkyl chain

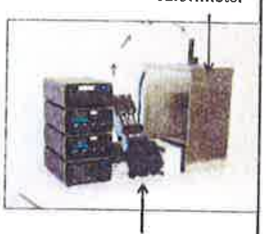
This whole complex process has one overall equilibrium constant and one overall enthalpy change

---

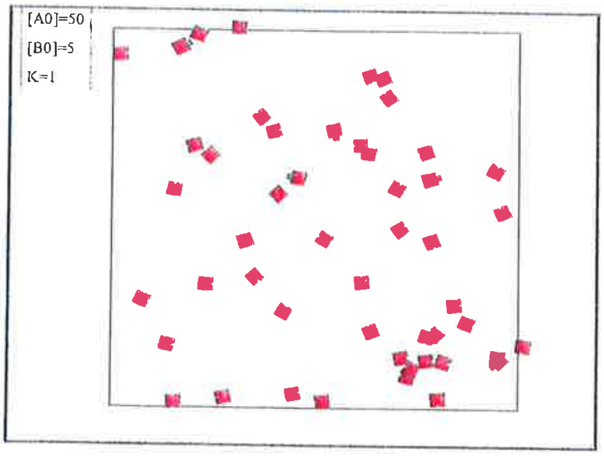
Isothermal titration calorimetry

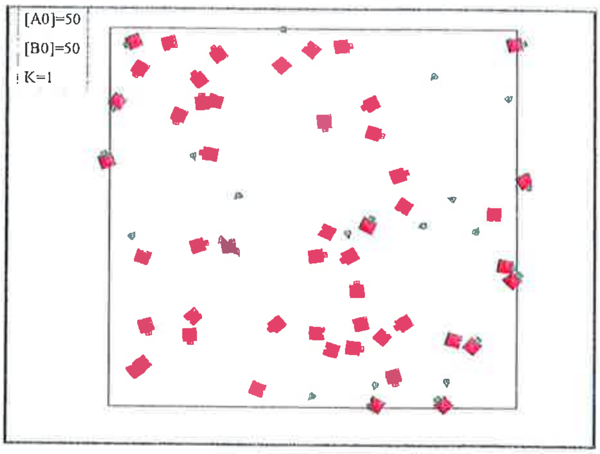


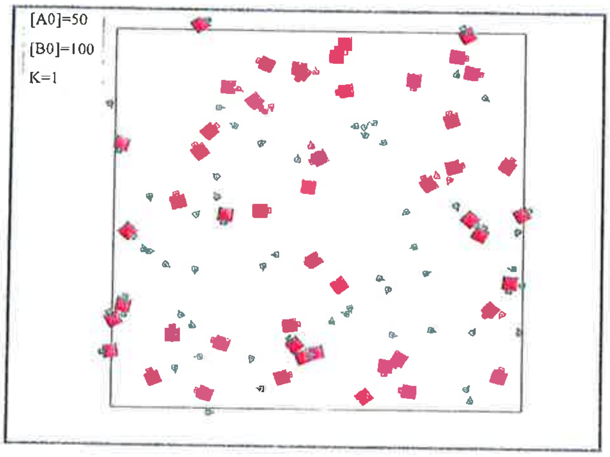
calorimeter

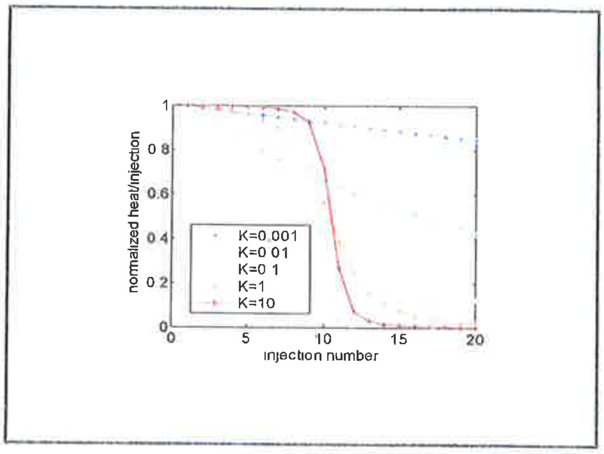


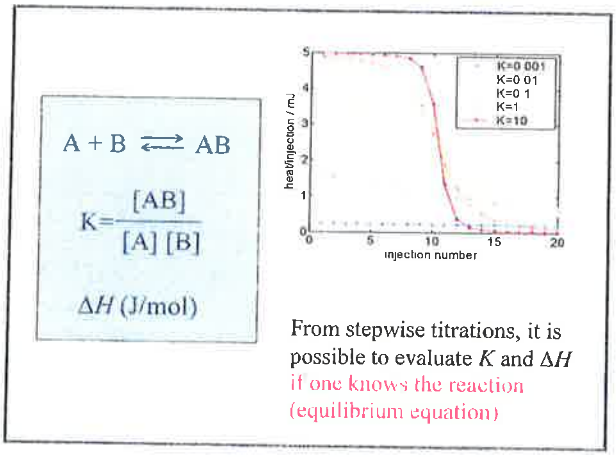
syringe pump

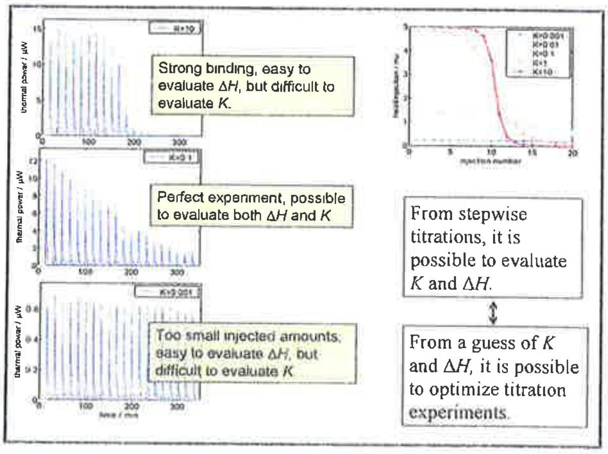

[A0]=50
[B0]=5
K=1


[A0]=50
[B0]=50
K=1

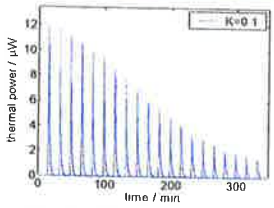

[A0]=50
[B0]=100
K=1


normalized heat/injection
injection number
K=0.001
K=0.01
K=0.1
K=1
K=10

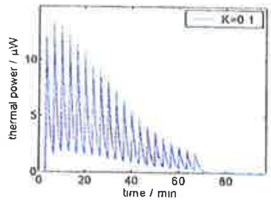

A + B ⇄ AB
K = [AB] / [A] [B]
ΔH (J/mol)
heat/injection / mJ
injection number
K=0.001
K=0.01
K=0.1
K=1
K=10
From stepwise titrations, it is possible to evaluate K and ΔH
if one knows the reaction (equilibrium equation)


Strong binding, easy to evaluate ΔH, but difficult to evaluate K.
Perfect experiment, possible to evaluate both ΔH and K
Too small injected amounts, easy to evaluate ΔH, but difficult to evaluate K
From stepwise titrations, it is possible to evaluate K and ΔH.
From a guess of K and ΔH, it is possible to optimize titration experiments.

'Slow' Titrations versus 'Fast' Titrations

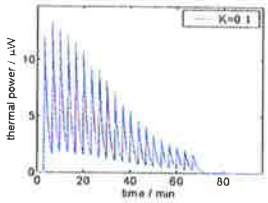


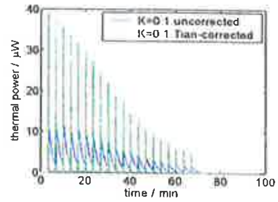
Analyze by integrating each peak between baselines (taken before and after the peak)



It is not possible to integrate the peaks without first using the Tian correction

Fast Titration





$$P = \varepsilon(U + \tau \frac{dU}{dt})$$

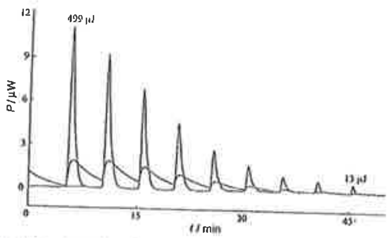
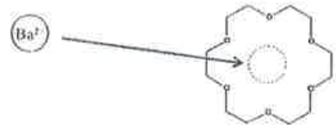
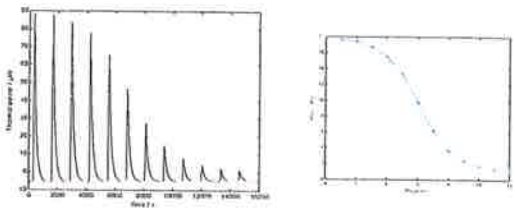


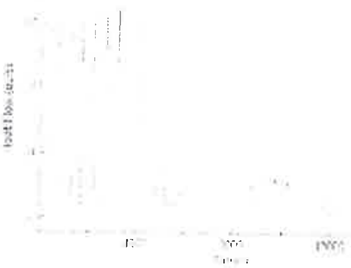
Fig. 1 Stepwise titration of ribonuclease A (ca. 60 µmol) by 2'-cytidine monophosphate using a heat conduction titration microcalorimeter (stainless steel reaction vessel, volume 2 ml, τ = 210 s). A 'dynamic correction' technique was employed and the time between injections was reduced to 4 min. Two curves are shown: the one with low and rounded peaks is the experimental curve, the curve with sharp peaks is the corrected curve. (Courtesy of Thermometric AB)

Ba^{2+} and 18-crown-6 titration





How does a drug molecule bind to the target (or to a non-target)?



Actinomycin D binds to single stranded DNA

Du et al (2007) Thermochimica Acta 452 31-35

Isothermal titration calorimetry (ITC)

+

ITC is a generic method.

No immobilization of the reactants

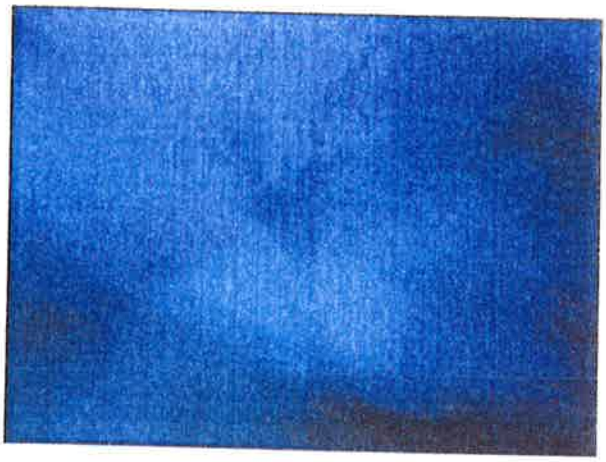
No modification of the reactants needed

No molecular weight restrictions

–

Time consuming (an experiment takes a few hours)

Not applicable to the studies of tight binders



Introduction to Isothermal Calorimetry

Thermochemistry

Thermochemistry – measurements of enthalpies

Process x
X(state) → Y(state)
$\Delta_x H$

Examples of processes:

vaporization	$\Delta_{vap}H$
condensation	$\Delta_{cond}H$
reaction	$\Delta_r H$
formation	$\Delta_f H$
combustion	$\Delta_c H$
solution	$\Delta_{sol}H$
transfer	$\Delta_{trans}H$
transition	$\Delta_{trs}H$
sublimation	$\Delta_{sub}H$
mixing	$\Delta_{mix}H$
ionization	$\Delta_{ion}H$
melting/fusion	$\Delta_{fus}H$

Enthalpy changes of formation ($\Delta_f H$) are most important!

$\Delta_f H$ is the enthalpy change associated with formation of a substance from the elements ($\Delta_f H$(an element)=0).

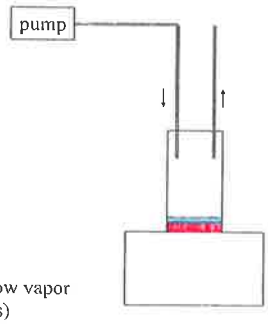
Common state specifiers:

gas	g
liquid	l
solid	s
aqueous solution	aq
solution	sln
crystalline	cr
infinite dilution	∞
saturation	sat

Enthalpy of vaporization

1. Constant thermal power of vaporization and mass change rate

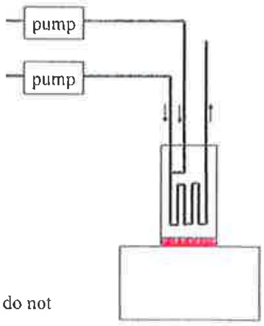
2. Heat of vaporization of a known amount



Problematic: substances with low vapor pressures (sublimation of solids)

Enthalpy of mixing

Flow calorimeter

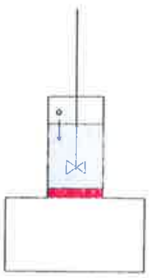


Problematic: substances that do not mix easily

Enthalpy of dissolution

1. Solid injection (solid-liquid titration)

(2. SolCal - a semi-adiabatic calorimeter)



Problematic: substances that do not dissolve easily or that have low solubilities

vaporization	vaporization ampoule
condensation	vaporization ampoule
reaction	different types of ampoules
formation	bomb calorimeter
combustion	bomb calorimeter
solution	solution ampoule or SolCal
transfer	calculated…
transition	-
sublimation	vaporization ampoule
mixing	mixing ampoule
dilution	titration calorimeter
ionization	calculated…
melting	DSC
solidification	DSC

Heat capacity

Drop-c_p calorimeter	$c = \dfrac{Q}{n\Delta T}$
Enthalpy determinations at different temperatures	$c_p = \left(\dfrac{dH}{dT}\right)_p$
DSC, micro-DSC	$c = \dfrac{Q - Q_0}{n\Delta T}$

Introduction to Isothermal Calorimetry

Pharmaceutical application areas

OVERVIEW

Polymorphism

Crystallinity - amorphicity

Stability

Compatibility

Biological applications

Titration calorimetry

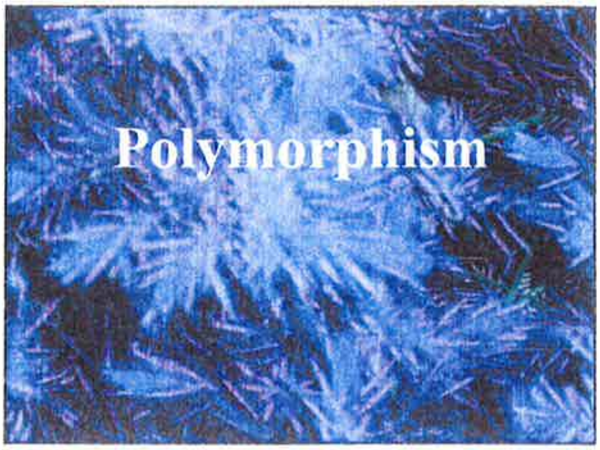
Isothermal calorimetry in the pharmaceutical field

Drug discovery
- Screening of drug candidates, target validation

Pre-formulation
- Crystallinity (amorphicity)
- Polymorphism
- Drug stability

Formulation development
- Drug/excipient compatibility

Production control
- Qualitative/quantitative analysis of amorphicity, polymorphism, stability… .



Terminology

Polymorphism is the tendency of a substance to crystallize into different crystalline states

Polymorphs are crystalline modifications

Amorphous materials are non-ordered (no long range order)

Crystalline materials have long-range order

Glassy materials liquefy by undergoing a glass transition

Solvates are substances that have absorbed solvents as part of their structure

Hydrate is a solvate with water

Pseudo-polymorphism is when a substance has different hydrates/solvates

The study of polymorphic behaviour of drugs and excipients is an important part of preformulation work in pharmacy because polymorphism affects:

- bioavailability mediated via dissolution
- solid state reactions (stability)
- hygroscopicity
- mechanical stability
- compactability
- batch and source variation

Are there different polymorphic forms?

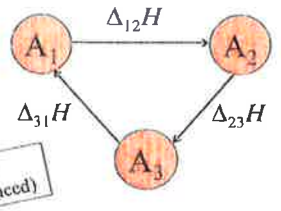
Do I have form A or form B (or a mixture of both)?

drug substance

What should we do to always get polymorph A?

How can we prove that we have control of the polymorphic form in our drug?

Hess law



ΔH is the enthalpy change (heat produced)

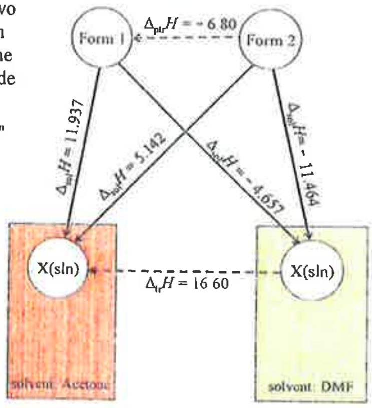
$$\Delta_{12}H + \Delta_{23}H + \Delta_{31}H = 0$$

$$\Sigma_{cycle}\Delta H = 0$$

All reactions need not be realizable in practice!

Heat of solution for two polymorphs of sodium sulfathiazole in acetone and dimethylformamide (DMF)

ref. Lindenbaum and McGraw. Pharm. Manuf. 2 1 26-30 (1985)



Which direction does a transformation go?

Answer: most likely is the direction for which $\Delta_{ptr}H_m < 0$ (exothermic)

if $\Delta_{ptr}H_m = \Delta_{sol}H_{m,A} - \Delta_{sol}H_{m,B} < 0$
then A is more stable than B

if $\Delta_{ptr}H_m = \Delta_{sol}H_{m,A} - \Delta_{sol}H_{m,B} > 0$
then B is more stable than A

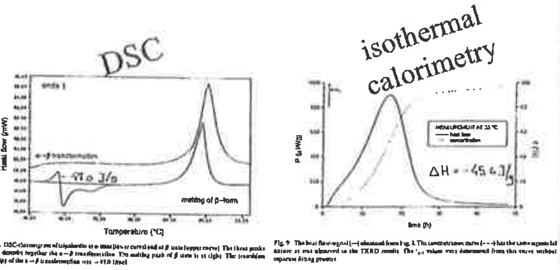
Polymorphic transformations can occur by two different mechanisms

Directly via molecular rearrangements in the dry state

or

Via a solvent phase, i.e. solvent-mediated polymorphic trans-formation (SMPT)

Comparison of DSC and Microcalorimetry for the α→β Transformation of Tripalmitin



Hongisto et al. (1996) Thermochim. Acta, 276, 229

Thermodynamics - kinetics?

Correlation of dissolution rate and heat of solution of a drug

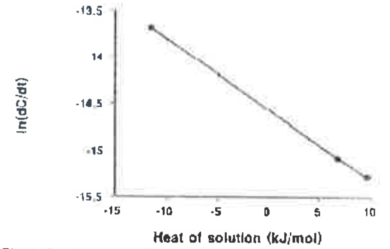
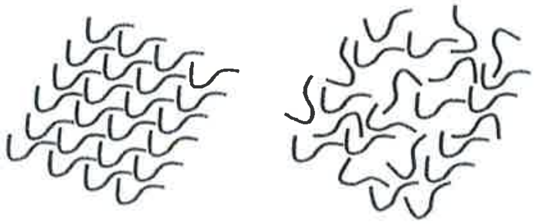


Fig. 2. Relationship between heat of solution and logarithm of initial dissolution rate of indomethacin polymorphs and glass at 25°C

Terada, K et al. (2000) Pharmaceutical Res 17(8) 920-924

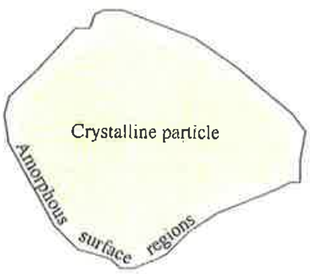
Crystallinity - Amorphicity



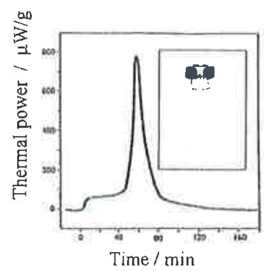
Long range order   No long range order

Crystallinity - Amorphicity of particles

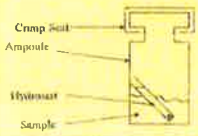
Milling and other operations create amorphous surface regions



Amorphous to Crystalline Transition in Hydrophobic Solids



The hydrostat is the small tube containing a saturated salt solution with a small excess of the corresponding salt It is used as a humidity source in the ampoule



Detecting Small Amounts of Amorphous Material in a Hydrophobic Powder

Comparison of Micronized to Ball Milled Drug

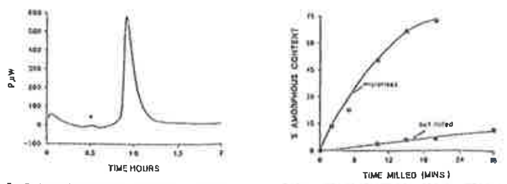
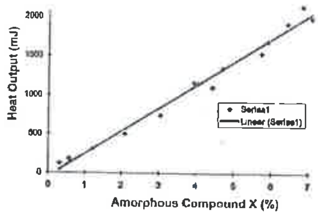


Fig. 2 A typical response (power as a function of time) obtained using the isothermal microcalorimeter where the amorphous sample has been exposed to ethanol vapour in a sealed vial.

Fig 6 The relationship between amorphous content induced during processing and time in the mill.

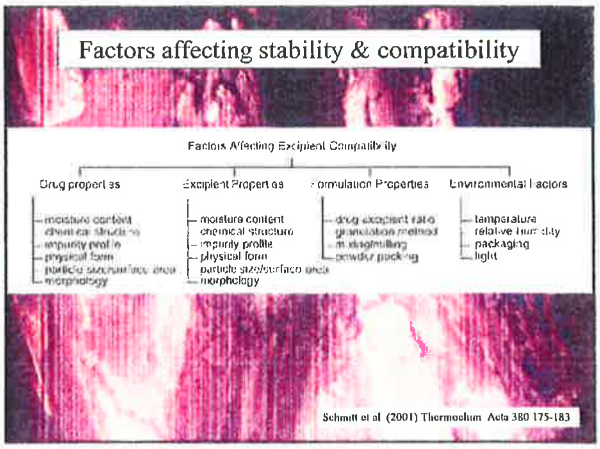
Ahmed Buckton & Rawlins,
International Journal of Pharmaceutics 130, p 195, 1996

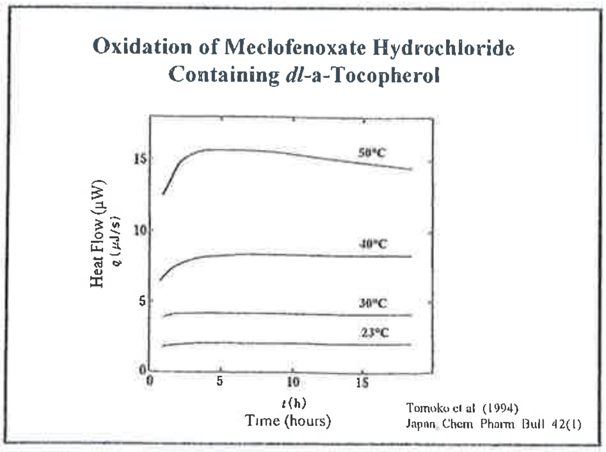
Quantifying low levels of amorphous material in a micronized drug

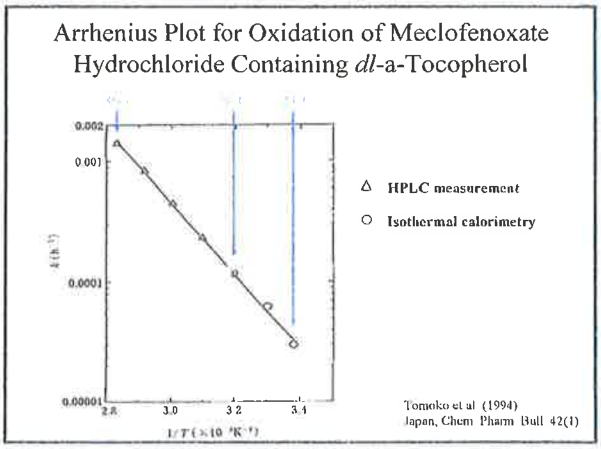


Mackin et al , Int J of Pharmaceutics, 231 (2002) pp 227-236

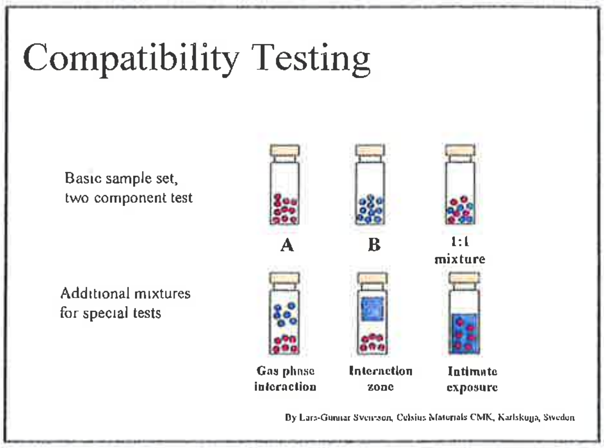

Stability


Factors affecting stability & compatibility
Factors Affecting Excipient Compatibility
Drug properties
Excipient Properties
Formulation Properties
Environmental Factors
moisture content
chemical structure
impurity profile
physical form
particle size/surface area
morphology
temperature
relative humidity
packaging
light
Schmitt et al (2001) Thermochim Acta 380 175-183


Oxidation of Meclofenoxate Hydrochloride Containing dl-a-Tocopherol
Heat Flow (µW)
q (µJ/s)
50°C
40°C
30°C
23°C
t (h)
Time (hours)
Tomoko et al (1994)
Japan. Chem Pharm Bull 42(1)

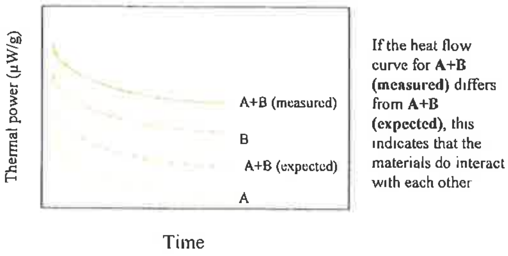

Arrhenius Plot for Oxidation of Meclofenoxate Hydrochloride Containing dl-a-Tocopherol
HPLC measurement
Isothermal calorimetry
Tomoko et al (1994)
Japan, Chem Pharm Bull 42(1)


Compatibility
Interactions in Mixtures of Solids


Compatibility Testing
Basic sample set,
two component test
A
B
1:1
mixture
Additional mixtures
for special tests
Gas phase
interaction
Interaction
zone
Intimate
exposure
By Lars-Gunnar Svensson, Celsius Materials CMK, Karlskoga, Sweden

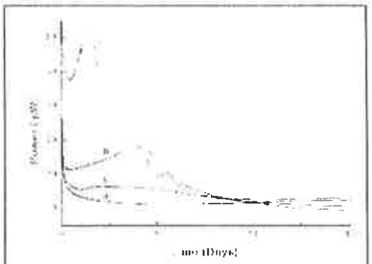
Evaluation of Compatibility

A 1:1 mixture of two components, A and B



If the heat flow curve for **A+B (measured)** differs from **A+B (expected)**, this indicates that the materials do interact with each other

Pharmaceutical compatibility testing in practice



Schmitt et al (2001) Thermochim Acta 380 175-183

Table
Summary of interaction power between ARI-527 and various excipients

Functional class	Excipient	Interaction power (μW)
Diluents	Dibasic calcium phosphate	[illegible]
	Microcrystalline cellulose	2.92
	Lactose monohydrate	[illegible]
	Pregelatinized starch	[illegible]
Lubricants	Calcium stearate	[illegible]
	Sodium stearyl fumarate	[illegible]
	Magnesium stearate	[illegible]
	Zinc stearate	2.05
	Hydrogenated cottonseed oil	[illegible]
	Stearic acid	0.812
	Colloidal silicon dioxide	[illegible]
Binders and disintegrants	Sodium starch glycolate	[illegible]
	Povidone K-30	2.59
	Crospovidone	[illegible]
	Hydroxypropyl methylcellulose	[illegible]
	Hydroxypropyl cellulose	1.55

Schmitt et al (2001) Thermochim Acta 380 175-183

Optimize protocols

Add water (vapor)

Compress components

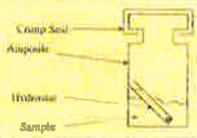
Increase temperature

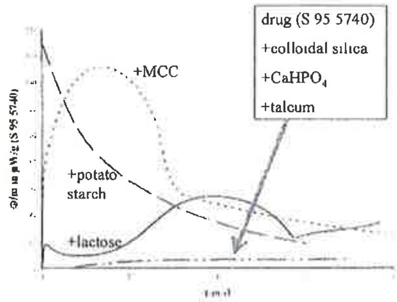
Experimental Design for Compatibility Screening

The sample preparation technique must be strictly followed in order to obtain reproducible and reliable data For the data presented, the following design was used

- A sample weighing 800 mg (or 400 mg of each component for two component mixture) was added to a vibratory ball mill
- Sample was milled for 10 minutes
- Sample (~500 mg) was loaded into a vial with hydrostat and placed in a heating block set at 50 °C The sample cap was crimped after the sample reached 50 °C
- Crimped ampoule was placed in an oven at 50 °C to equilibrate for 1-4 days prior to analysis This gives sufficient time for the sample to equilibrate with water vapor inside the vial
- Heat flow measured in microcalorimeter for 15 hours

The hydrostat is the small tube containing a saturated salt solution with a small excess of the corresponding salt. It is used as a humidity source in the ampoule





Selzer et al (1998) Int J Pharmaceutics 171 227-241

Biological calorimetry in the pharmaceutical field

Clinical Research
- Cell proliferation
- Apoptosis
- Metabolic effect on cultivated cells
- Receptor activation / cell signaling in cultivated cells

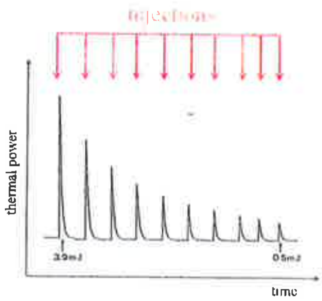
Drug Development
- Effect of primary hit compounds on cultivated cells
- Assay Development

Protein Production
- Identification of High-producing Clones
- Optimization of Culture Conditions

From www Symcell.se

Titration Calorimetry (ITC)

Titration is the controlled addition (in steps or continuously) of one substance to another. Liquid-liquid titration is most common, but solid-liquid (dissolution) and gas-solid (sorption) can also be considered as titrations.



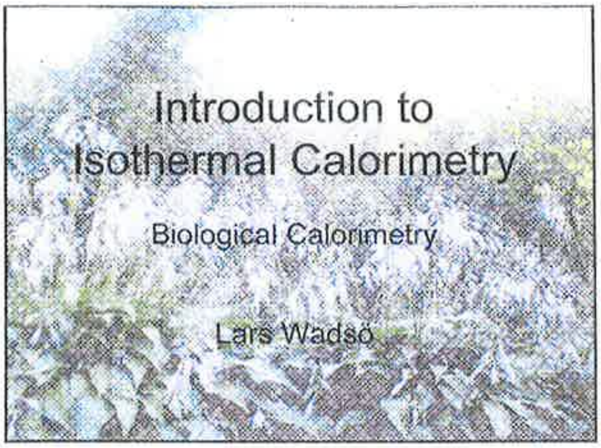
The result of ITC measurements

Stochiometry (1:1, 1:2 etc)

Binding constant (affinity)

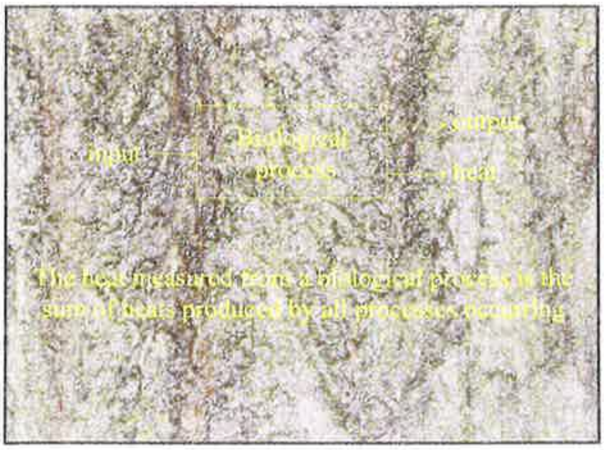
Thermodynamics (ΔH, ΔG, ΔS, Δc_p)

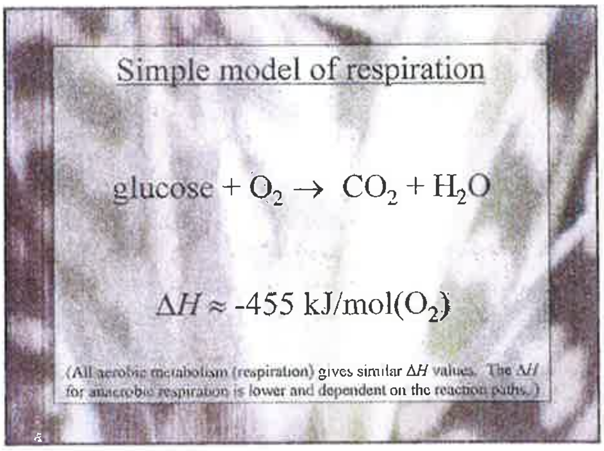
ΔH heat released
ΔG equilibrium constant
ΔS measure of order in system
Δc_p measure of temperature dependence of ΔH

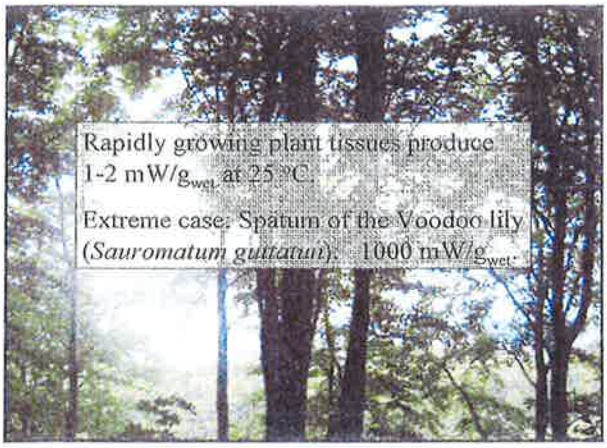


Biological Calorimetry

- Botany
- Zoology
- Mycology
- Microbiology
- Food science
- Ecology
- Building Materials
- Agriculture
- Forestry



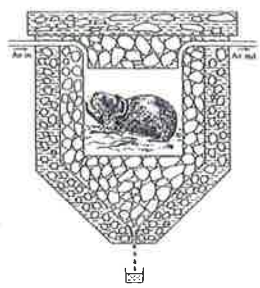




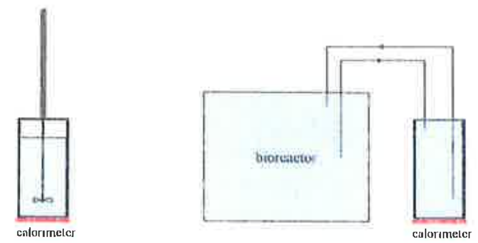
Measurement of heat produced by a guinea pig was measured by Lavoisier and Laplace in 1780.

The instrument is called a *Bunsen Ice Calorimeter*. Quantity of ice that melts is a measure of heat produced by the animal

Note that the calorimeter is isothermal at 0 °C, but the animal (also isothermal) is at about 37 °C



In *microbiological calorimetry,* the samples are usually cells in aqueous solution



ampoule calorimetry with stirring

isothermal flow calorimetry

Microbiological calorimetry

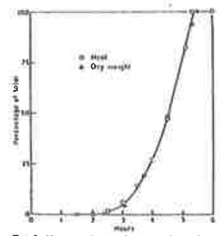


Fig. 2 Heat production by a growing culture of *Streptococcus faecalis*, with glucose as energy source [52]

Exponential phase – heat production rate is proportional to bacterial mass

The percentage of the total heat produced is shown on the y-axis

From review by Gustafsson, L (1991) Thermochim Acta 193 145-171 (measurements by Forrest, W W et al (1961) J. Bacteriol 82 685-690)

Microbiological calorimetry

Simultaneous measurement of several parameters in a bioreactor combined with a flow calorimeter.

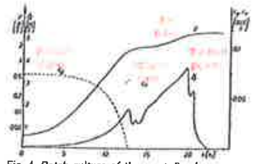


Fig. 4. Batch culture of the yeast *Saccharomyces cerevisiae* growing in a synthetic glucose medium. $\dot{Q}$, rate of heat production; X, dry mass, c_g, glucose concentration; c_e, ethanol concentration of the culture [62]. ($\dot{Q}$ in the text dQ/dt).

From review by Gustafsson, L (1991) Thermochim. Acta 193 145-171 (measurements by Brettel, R et al (1981) Eur J. Appl Microbio Biotechnol 11 205-211)

Microbiological calorimetry

Addition of substances during a measurement can give interesting information

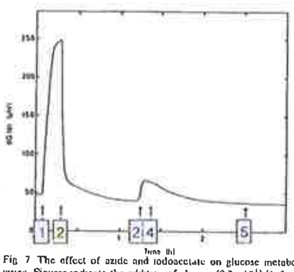


Fig. 7 The effect of azide and iodoacetate on glucose metabolizing *Saccharomyces cerevisiae*. Figures indicate the addition of glucose (0.2 g l^{-1}) (1, 3 and 5), azide (1 mM) (2) and iodoacetate (1 mM) (4) [46]

Azide – respiratory chain inhibitor

Iodoacetate – glycolytic inhibitor

Glucose

dQ/dt is the thermal power

Gustafsson, L (1991) Thermochim Acta 193 145-171

Measurements can also be made on larger samples. Here is an example with a 25 g fish in a 1 liter calorimeter

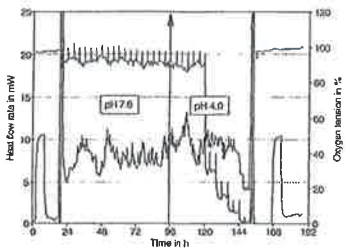
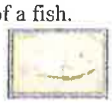


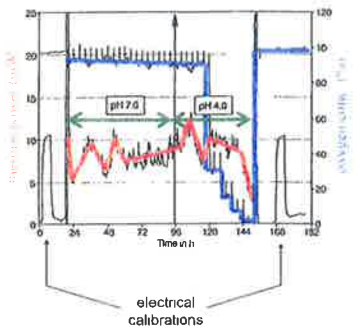
Fig. 1. Registration of an eight-day experiment with one single tilapia (*Oreochromis mossambicus* Peters). After 4 days the water was slowly acidified at an acidification rate of 3.6 pH units over 240 min. The fifth day the animal was exposed to a graded hypoxia load (40% AS, 25% AS, 15% AS and 5% AS) for 8 h per hypoxia level. The top signal alternating between reference and measurement position, is the oxygen tension signal. The irregular line is the heat production signal.

Heat flow rate is the thermal power

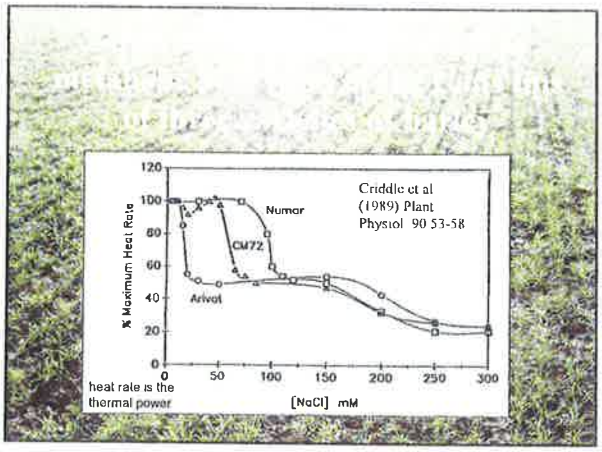
van Ginneken, V J T et al (1996) Thermochim Acta 276 7-15 (fish photo from www aquanic org)

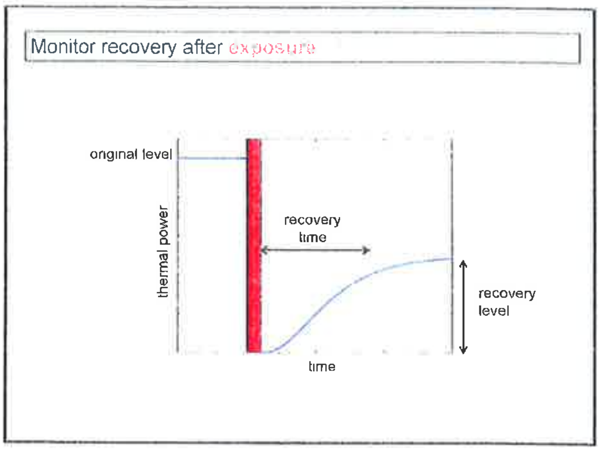
The effect of *acidification* (lower pH) and *hypoxia* (low oxygen concentration) on the activity and respiration of a fish.

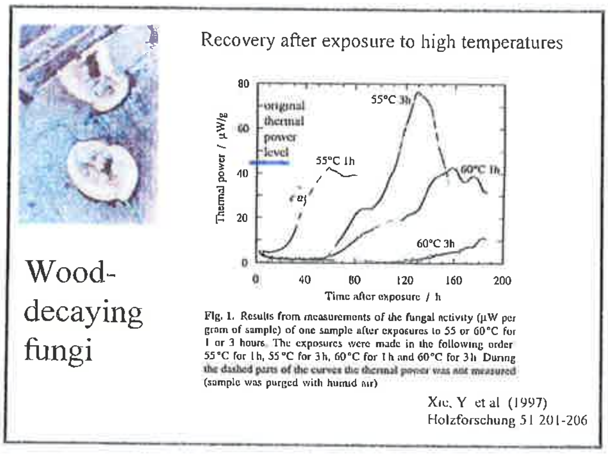


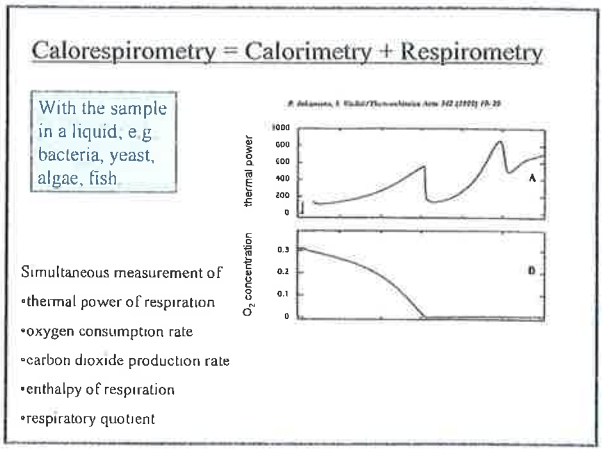


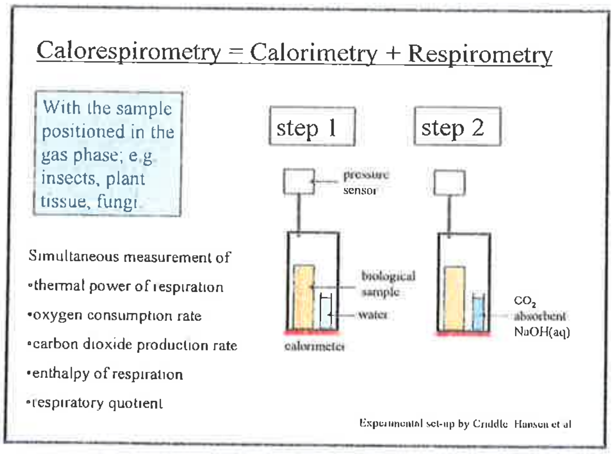
van Ginneken, V J T et al (1996) Thermochim Acta 276 7-15 (fish photo from www aquanic org)

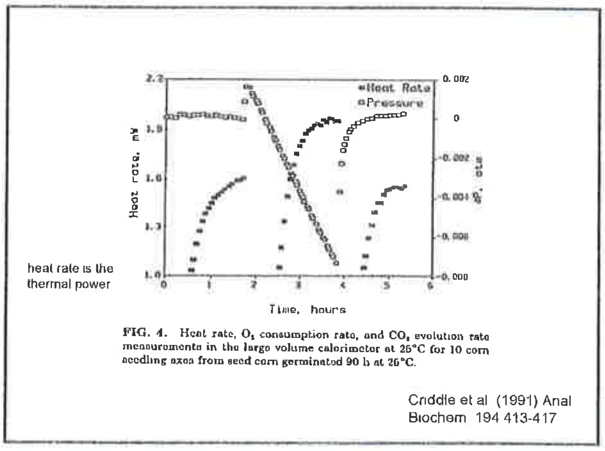

% Maximum Heat Rate
Criddle et al (1989) Plant Physiol 90 53-58
Numar
CM72
Arivat
heat rate is the thermal power
[NaCl] mM
0
50
100
150
200
250
300
20
40
60
80
100
120


Monitor recovery after exposure
original level
thermal power
recovery time
recovery level
time


Recovery after exposure to high temperatures
Wood-decaying fungi
Thermal power / μW/g
original thermal power level
55°C 3h
55°C 1h
60°C 1h
60°C 3h
Time after exposure / h
Fig. 1. Results from measurements of the fungal activity (μW per gram of sample) of one sample after exposures to 55 or 60°C for 1 or 3 hours. The exposures were made in the following order 55°C for 1h, 55°C for 3h, 60°C for 1h and 60°C for 3h. During the dashed parts of the curves the thermal power was not measured (sample was purged with humid air)
Xie, Y et al (1997) Holzforschung 51 201-206


Calorespirometry = Calorimetry + Respirometry
With the sample in a liquid, e.g. bacteria, yeast, algae, fish
thermal power
O2 concentration
Simultaneous measurement of
•thermal power of respiration
•oxygen consumption rate
•carbon dioxide production rate
•enthalpy of respiration
•respiratory quotient


Calorespirometry = Calorimetry + Respirometry
With the sample positioned in the gas phase; e.g. insects, plant tissue, fungi
step 1
step 2
pressure sensor
biological sample
water
calorimeter
CO2 absorbent NaOH(aq)
Simultaneous measurement of
•thermal power of respiration
•oxygen consumption rate
•carbon dioxide production rate
•enthalpy of respiration
•respiratory quotient
Experimental set-up by Criddle Hansen et al


Heat Rate
Pressure
Heat rate, mW
Time, hours
heat rate is the thermal power
FIG. 4. Heat rate, O2 consumption rate, and CO2 evolution rate measurements in the large volume calorimeter at 25°C for 10 corn seedling axes from seed corn germinated 90 h at 26°C.
Criddle et al (1991) Anal Biochem 194 413-417

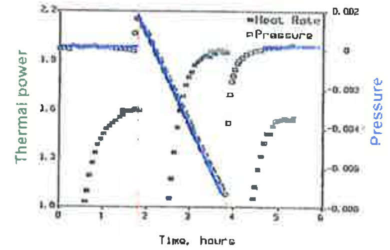


FIG. 4. Heat rate, O_2 consumption rate, and CO_2 evolution rate measurements in the large volume calorimeter at 25°C for 10 corn seedling axes from seed corn germinated 90 h at 25°C.

Criddle et al (1991) Anal Biochem. 194 413-417

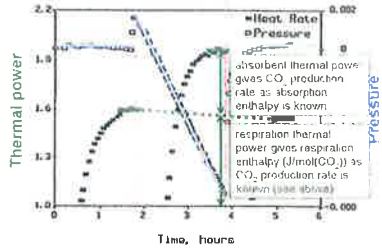


FIG. 4. Heat rate, O_2 consumption rate, and CO_2 evolution rate measurements in the large volume calorimeter at 25°C for 10 corn seedling axes from seed corn germinated 90 h at 25°C.

Criddle et al (1991) Anal Biochem. 194 413-417

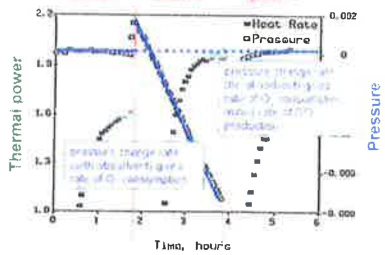


FIG. 4. Heat rate, O_2 consumption rate, and CO_2 evolution rate measurements in the large volume calorimeter at 25°C for 10 corn seedling axes from seed corn germinated 90 h at 25°C.

Criddle et al. (1991) Anal Biochem 194 413-417

International Society for Biological Calorimetry
ISBC
www.biocalorimetry.org

Introduction to Isothermal Calorimetry

Heat Conduction Calorimetry II

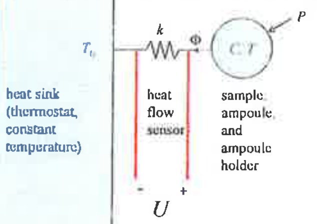
Lars Wadsö

Nomenclature

C	heat capacity (J/K)
E	Seebeck coefficient* (V/K)
k	thermal conductance* (W/K)
P	thermal power (W)
T	temperature (K)
ΔT	temperature difference (K)
U	voltage (V)
ε	calibration coefficient (W/V)
Φ	heat flow rate (W)

* of heat flow sensor

The simplest model of a heat conduction calorimeter



$$\begin{cases} \Phi = k(T - T_0) \\ \dfrac{dT}{dt} = \dfrac{(P - \Phi)}{C} \\ U = E(T - T_0) \end{cases}$$

$$P = \varepsilon\left(U + \tau\frac{dU}{dt}\right)$$

$$\varepsilon = \frac{k}{E}$$

$$\tau = \frac{C}{k}$$

Tian:

$$P = \varepsilon\left(U + \tau\frac{dU}{dt}\right)$$

$$\varepsilon = \frac{k}{E} \qquad \tau = \frac{C}{k}$$

k and E are instrument parameters

C is an instrument + sample-parameter

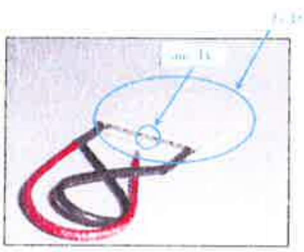
Typical values

k	thermal conductance	0.4 W/K
E	Seebeck coefficient	0.03 V/K
C	heat capacity of sample	30 J/K (empty ampoule)
		80 J/K (water filled ampoule)

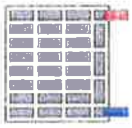
calibration constant: $\varepsilon \approx 10$ W/V

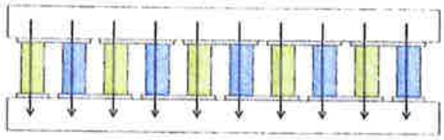
time constant: $\tau \approx 100$ s (empty), 200 s (water filled)

The thermocouple plate



The thermocouple plate (TCP)



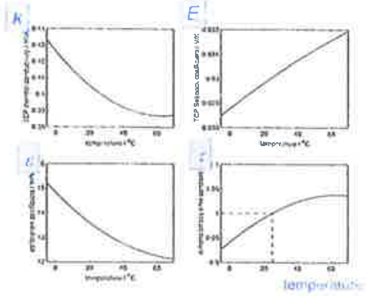


Heat flows through all the thermocouple parts in parallel

The measured voltage is the sum of the voltages over all thermocouples

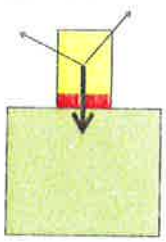
$$\varepsilon = \frac{k}{E} \qquad \tau = \frac{C}{k}$$

Thermocouple properties depend on temperature



One normally recalibrates heat conduction calorimeters when the temperature is changed (also because other changes may take place)

Not all heat produced in a sample leaves through the heat flow sensor



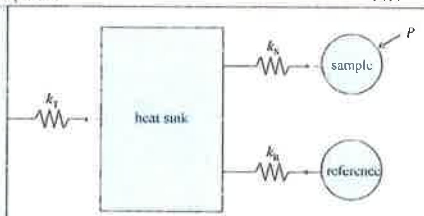
Heat losses are acceptable provided they are reasonably low and the same for calibration and measurement

It is therefore important to calibrate so that

- heat is produced in the same position as during an experiment
- heat conduction paths are the same as during an experiment

A more complete model of a heat conduction calorimeter

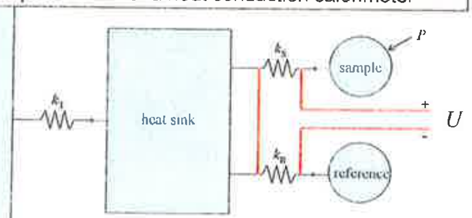
thermostat constant temperature



In a real heat conduction calorimeter, heat produced in the sample will influence temperature of the heat sink

A more complete model of a heat conduction calorimeter

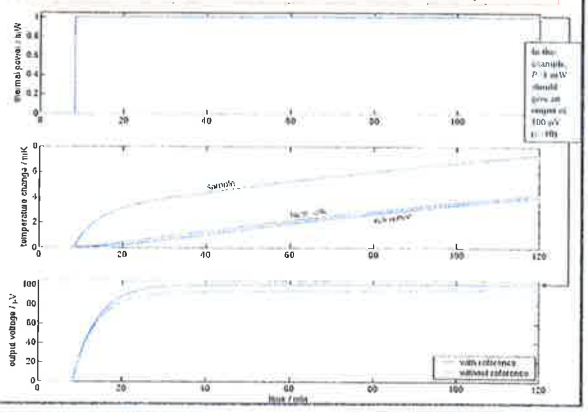
thermostat constant temperature



Why use a reference?

1. Decrease effects of external disturbances that tend to influence both sample and reference in the same way
2. Decrease the effect of temperature changes in the heat sink (gives more rapid response)

Simulated example of the positive effect of a reference on response time



Two potential problems with isothermal calorimetry

1. High thermal power may produce a significant temperature change in the sample
2. High heat output (high thermal power and/or long time) may give significant temperature changes in heat sink

Both these effects will cause the measurement to take place at a temperature other than that of the heat sink. Whether or not this is a problem depends on the type of measurement being made

An *approximate* equation for temperature increase in the sample caused by factor 1 above:

$$\Delta T = \frac{P}{k}$$

A *worst case approximate* equation for temperature increase in the whole calorimeter (factor 2 above), assumes no heat leaks out of the calorimeter (in other words, is valid only for short times). Note: C is heat capacity of the heat sink

$$\Delta T = \frac{Q}{C} = \frac{P \cdot \Delta t}{C}$$

An *approximate* equation for the temperature increase in the sample caused by factor 1 above

$$\Delta T = \frac{P}{k}$$

Example: A thermal power P of 4 mW in a calorimeter with a heat flow sensor thermal conductance k of 0.4 W/K gives a temperature change of 0.01 K

(cf. Wadsö L. (2000) Temperature changes within samples in heat conduction calorimeters. Thermochim. Acta 366 121-127)

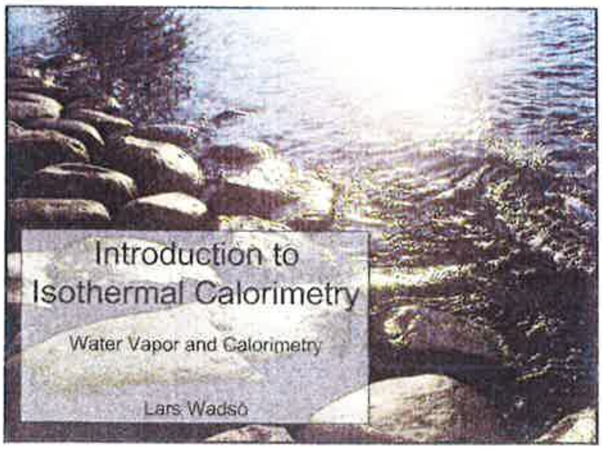
A *worst case approximate* equation for the temperature increase in the whole calorimeter (factor 2 above) assuming that no heat leaks out of the calorimeter, i.e. valid for short times (C is the heat capacity of the heat sink):

$$\Delta T = \frac{Q}{C} = \frac{P \cdot \Delta t}{C}$$

Example: A thermal power P of 10 mW for 60 minutes (Δt) in a calorimeter with a heat capacity (C) of 500 J/K gives a temperature change of 0.07 K

Temperature changes caused by heat production in the sample

Sensitive to temperature changes	kinetic measurements
	biological measurements
	qualitative measurements
	comparative measurements
Not sensitive to temperature changes	titrations (transient T-changes)



Temperature
Humidity
Oxygen
Light

→ speed up degradation

There is often a synergetic effect!

"Critical Relative Humidity"

Steel corrosion >50% RH
Mold growth >75% RH
Flooring adhesive failure >90% RH

Too simple to be generally good

For [illegible] no *generally* "safe RH-levels" exist

Each formulation has to be studied separately and humidity is only one aspect (although an often very important one) that needs to be considered.

Important humidity considerations for stability testing

Formation of hydrates

Deliquescence

Humidity level for stability/compatibility testing

Water Vapor and Calorimetry

1. Chemical and biological processes are often dependent on water
2. Sorption properties can be measured by calorimetry
3. Water is a common source of problems in isothermal calorimetry

Nomenclature

a_w	water activity
A	area (m^2)
c	moisture content ($g\ g^{-1}$)*
D_p	diffusion coefficient of water vapor in air ($g\ Pa^{-1}\ s^{-1}\ m^{-1}$)
P	thermal power (W)
v	vapor content ($g\ m^{-3}$)
ϕ	relative humidity ($Pa\ Pa^{-1}$)

* gram water per gram dry material

Relative Humidity (RH) ≈ Water Activity (a_w)

Relative humidity is the vapor pressure divided by the saturation vapor pressure and is thus primarily defined for gaseous systems

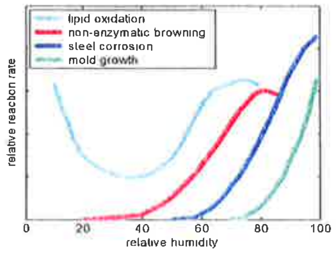
Water activity has a stricter thermodynamic definition and is defined for all types of systems (gaseous, liquid, solid)

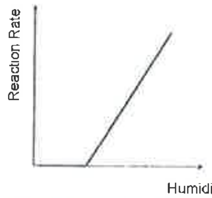
Some people also use RH for liquid and solid systems. Such systems are assigned the RH that a gas phase *in equilibrium* with the system would have had

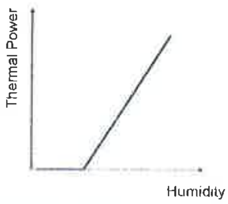
RH values are often given as %, while water activities are given as fractions (always use fractions in calculations)

1

Reaction rates often depend on how much water is available (low RH ⇒ low availability of water)

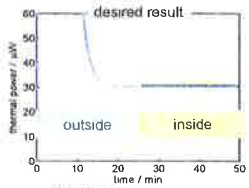






Two principally different methods of measuring thermal power (reaction rate) as a function of moisture state

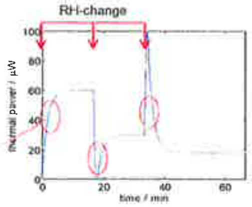
Change RH outside calorimeter



Change RH inside calorimeter

desired result

adsorption effect



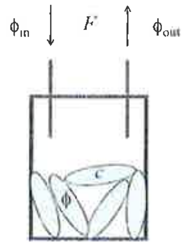
Air contains very little water, even at 100% RH

At 25 °C, 150 mL of air saturated with water vapor holds 3.5 mg water.

Hygroscopic solids can hold large amounts of water

At 25 °C, 150 mL wood will absorb 5 g of water when taken from 60 to 80% relative humidity

The ideal situation when we humidify a sample (100% efficiency)



ϕ relative humidity

c moisture content

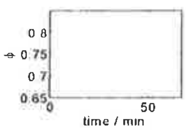
F gas flow rate (m³/s)

Example
At start of RH change

ϕ=0.70

ϕ_{in}=0.80

ϕ_{out}=0.70



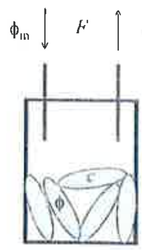
Example
At end of RH change

ϕ=0.795

ϕ_{in}=0.80

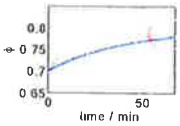
ϕ_{out}=0.795

The real situation when we humidify a sample (less than 100% efficiency)



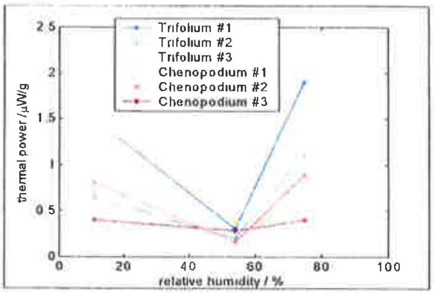
ϕ relative humidity
c moisture content
F gas flow rate (m³/s)

Example
At start of RH change
ϕ=0 70
ϕ_{in}=0 80
ϕ_{out}=0 75



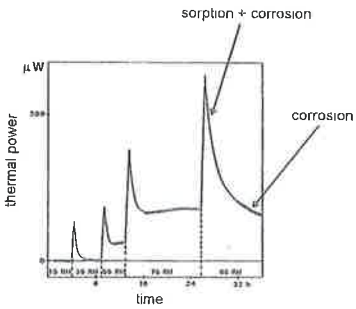
Example
At end of RH change
ϕ=0 78
ϕ_{in}=0 80
ϕ_{out}=0 795

Thermal power from (degradation?) processes in seeds as a function of relative humidity (water activity)



Corrosion of Mild Steel in Humid Air

Problems
What oxide is formed?
What is the enthalpy change?



Paulsson et al Thermometric Application Note TM001

2

One can use isothermal calorimetry in two ways.

because we are interested in the heat/enthalpy
1 Enthalpy of vaporization
2 Sorption enthalpies
3 Dissolution enthalpies
4 Fermentation (process heat)
5 Cement hydration (risk of cracking)
etc

or because we use the heat to calculate other things
1 Sorption isotherms
2 Stability and compatibility (annual degradation)
3 Vapor pressures
4 Biological activity
etc

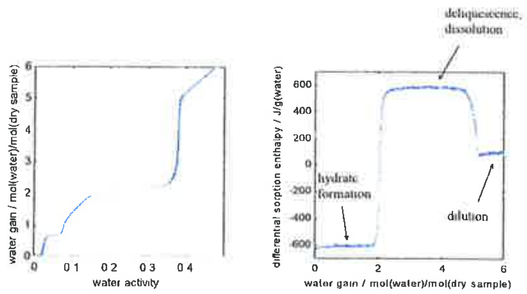
---

textiles
foodstuffs
chemical products
packaging materials
wood, pulp and paper
building materials
pharmaceuticals
drying agents
polymers
catalysts

Sorption is of great practical interest

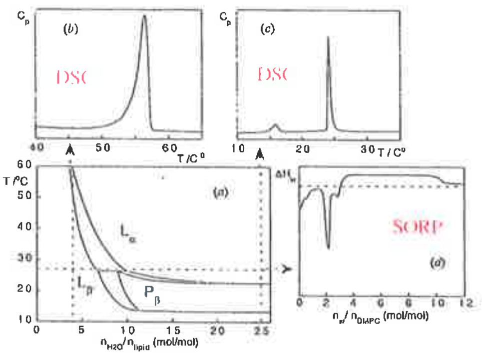
Sorption is a way to investigate materials (surface chemistry, porosity...)

Sample X Measured with SORP: Evaluated Result



SORP results phospholipids (DMPC)

N Markova, E Sparr, L Wadsö, H Wennerström, (2000), J Phys Chem 104 8053-8060



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③ Water Vapor?

in the air

in our bodies (perspiration, exhalation)

titration into aqueous solution

biological materials

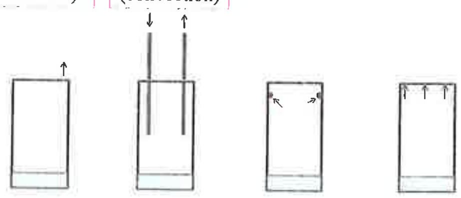
sorption calorimetry

cement hydration

etc.

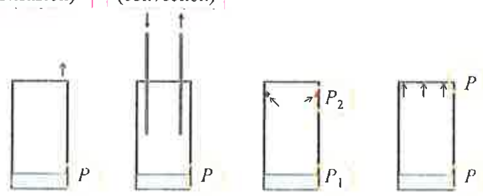
What types of problems can one have?

Vaporization (diffusion) | Vaporization (convection) | Absorption | Condensation



What types of problems can one have?

Vaporization (diffusion) | Vaporization (convection) | Absorption | Condensation



Enthalpy of ...

vaporization

condensation

absorption

adsorption

desorption

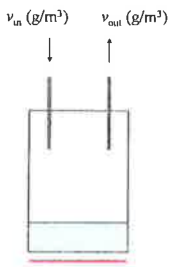
...

Δh (J/g)

Forced Convection

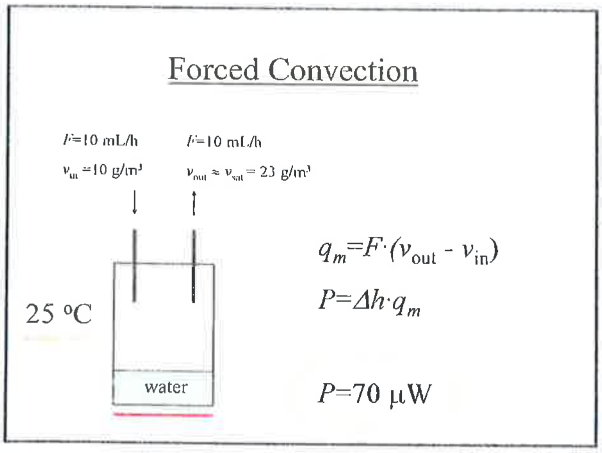
F gas flow rate (m^3/s) $\quad v$ vapor content (g/m^3)

q_m resulting mass transfer rate (g/s)

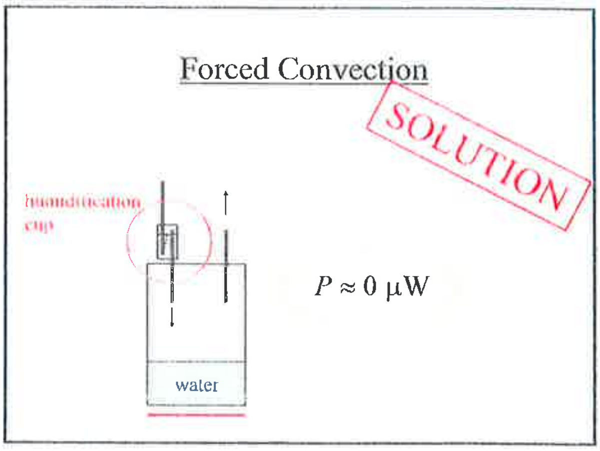


$$q_m = F \cdot (v_{out} - v_{in})$$

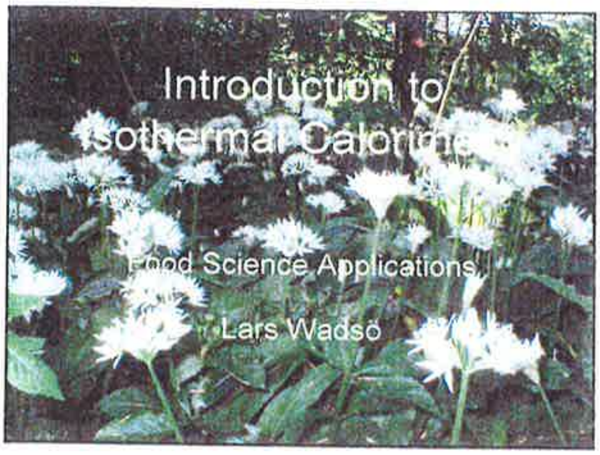
$$P = \Delta h \cdot q_m$$

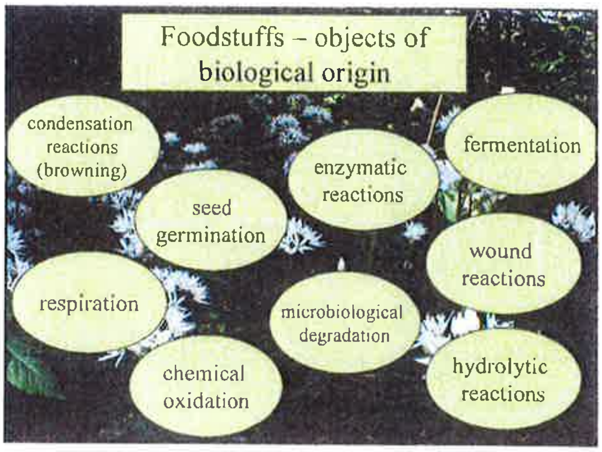


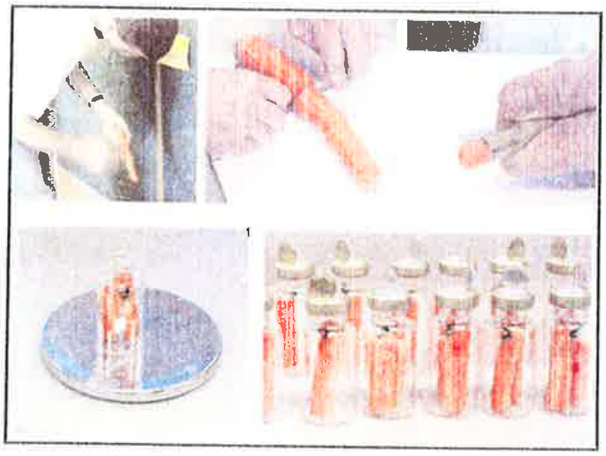
Forced Convection
F=10 mL/h
v_{in}=10 g/m³
F=10 mL/h
$v_{out} \approx v_{sat}$ = 23 g/m³
25 °C
water
$q_m = F \cdot (v_{out} - v_{in})$
$P = \Delta h \cdot q_m$
P=70 μW

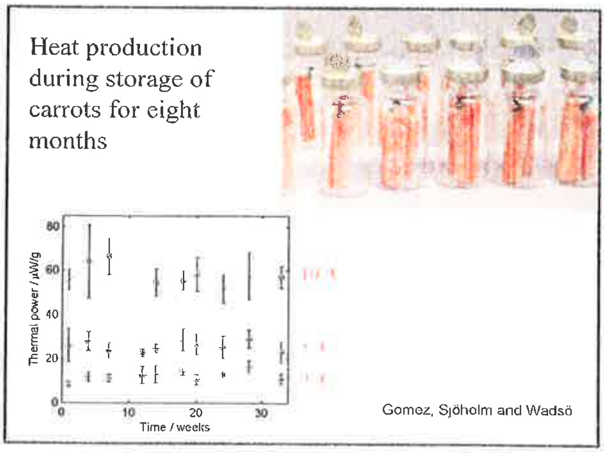


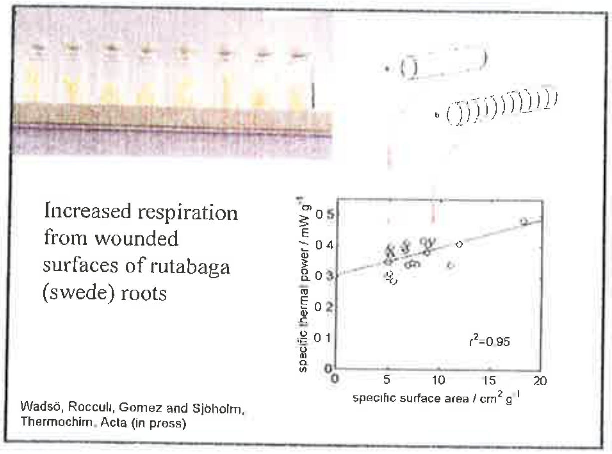
Forced Convection
SOLUTION
water
$P \approx 0$ μW

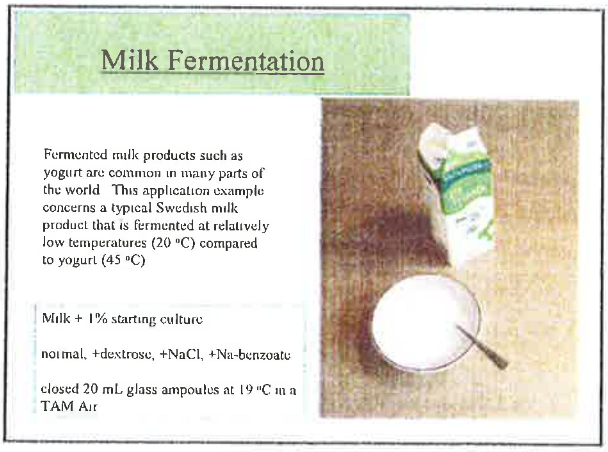

Introduction to Isothermal Calorim
Food Science Applications
Lars Wadsö


Foodstuffs – objects of biological origin
condensation reactions (browning)
fermentation
enzymatic reactions
seed germination
wound reactions
respiration
microbiological degradation
chemical oxidation
hydrolytic reactions

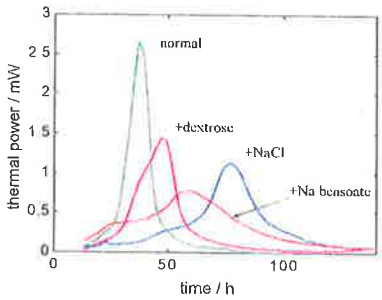



Heat production during storage of carrots for eight months
80
60
40
20
0
Thermal power / µW/g
0
10
20
30
Time / weeks
Gomez, Sjöholm and Wadsö


Increased respiration from wounded surfaces of rutabaga (swede) roots
specific thermal power / mW g⁻¹
0.5
0.4
0.3
0.2
0.1
0
0
5
10
15
20
specific surface area / cm² g⁻¹
r²=0.95
Wadsö, Rocculi, Gomez and Sjöholm, Thermochim. Acta (in press)


Milk Fermentation
Fermented milk products such as yogurt are common in many parts of the world. This application example concerns a typical Swedish milk product that is fermented at relatively low temperatures (20 °C) compared to yogurt (45 °C)
Milk + 1% starting culture
normal, +dextrose, +NaCl, +Na-benzoate
closed 20 mL glass ampoules at 19 °C in a TAM Air

Milk Fermentation

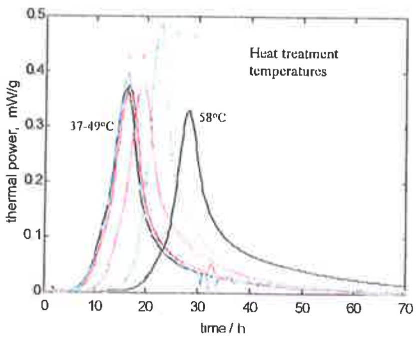


Carrot Juice Spoilage

Eight samples were heat treated at 37-58 °C

closed 20 mL glass ampoules at 25 °C (accelerated)

Carrot Juice Spoilage Measured at 25 °C

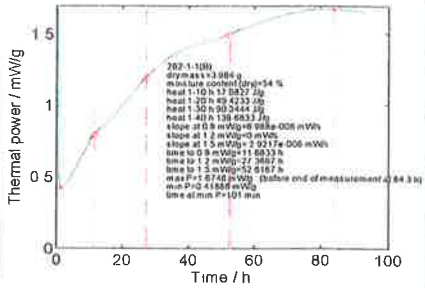


Barley Grain Germination (Malting)

steeping = water absorption to start germination

malting = germination

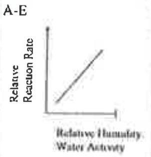
100 barley grains in 20 mL glass ampoule with free water in an absorbent pad, perfused with humidified air

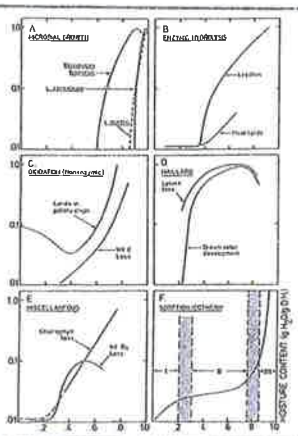


L. Wadso (unpublished work)

Water is a key factor in shelf-life

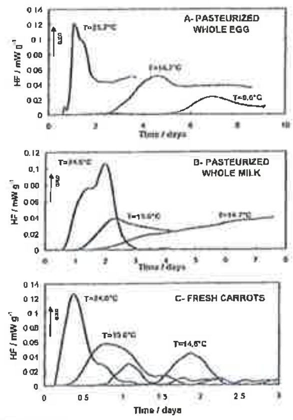
A-E





From Fennema Food Science

Shelf Life Evaluation



"Isothermal DSC traces at different temperatures" = isothermal calorimetry at different temperatures

"HF" = "Heat Flow" = thermal power

Riva et al. (2001) Thermochim Acta 370 73-81

Comparison of different measures of degradation (measured on parallel samples)

M. Riva et al./Thermochimica Acta 370 (2001) 73–81

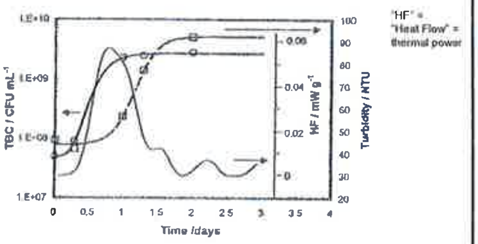


Fig. 5. Kinetics indices (heat flow, turbidity and Plate count) for packaged fresh carrots stored at 20°C.

"Microcalorimetry is a very useful tool for the measurement of the degree of aging of a product and also for the elucidation of the aging mechanism. This can sometimes be a formidable task in such a complex matrix as a food product".

Almqvist et al. (1991) Thermometric Application Note 22016

Introduction to Isothermal Calorimetry

Sorption calorimetry

The vapor state of a solid (how much vapor a substance has sorbed):

water content, vapor content, water gain

$g_{vapor}/g_{dry\ solid}$

$mol_{vapor}/mol_{dry\ solid}$

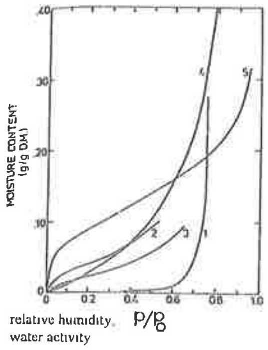
The vapor state of the gas surrounding of a solid

relative humidity, water activity

$Pa_{vapor}/Pa_{saturation}$

Sorption isotherm

Equilibrium sorption isotherm
Moisture sorption isotherm (MSI)



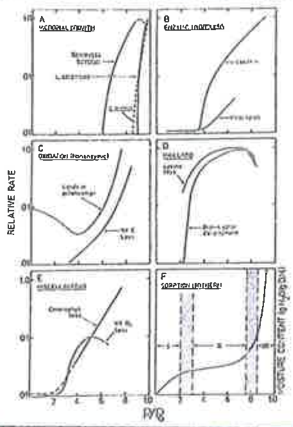
1 Confection (mainly sucrose)
2 spray-dried chicory extract
3 Roasted Columbian coffee
4 Pig pancreas extract powder
5 Native rice starch

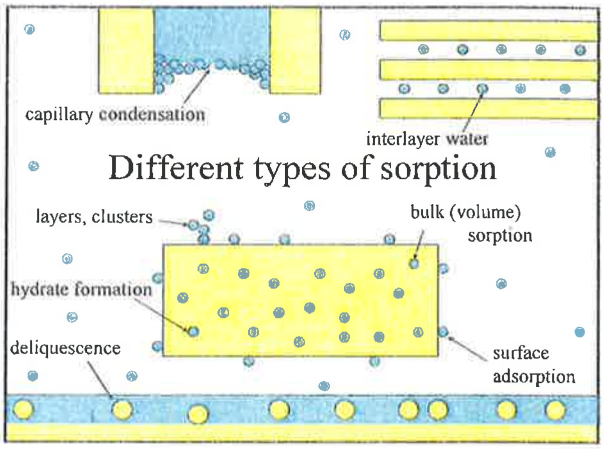
ref Fennema "Food Chemistry" 1996

Other processes that can take place during sorption

glass transition
crystallisation
conformational changes
swelling-shrinkage
chemical reactions, degradation

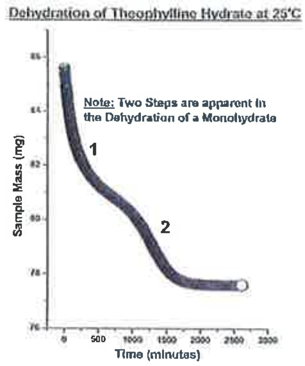
The importance of water activity in food science





Sorption processes often have complex kinetics

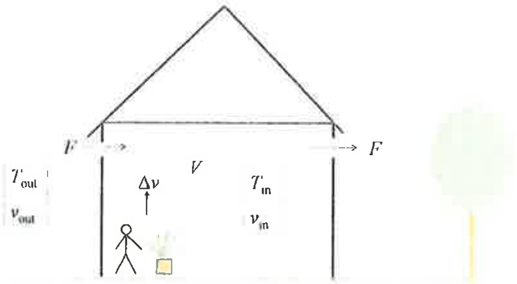
Solid-state kinetics is often complex, governed by diffusion etc.



Sokoloski, T
SmithKline
Beecham

	WINTER	SUMMER
INDOORS	RH=35% v=7 g/m^3 T=20°C	RH=68% v=13 g/m^3 T=20°C
OUTDOORS	RH=92% v=4 g/m^3 T=0°C	RH=72% v=11 g/m^3 T=15°C

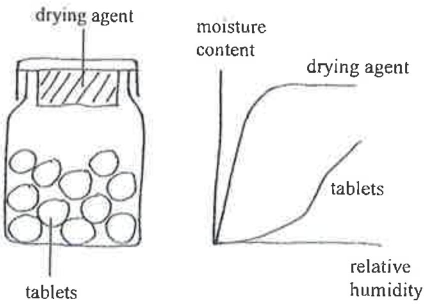
Typical values in Lund, Sweden

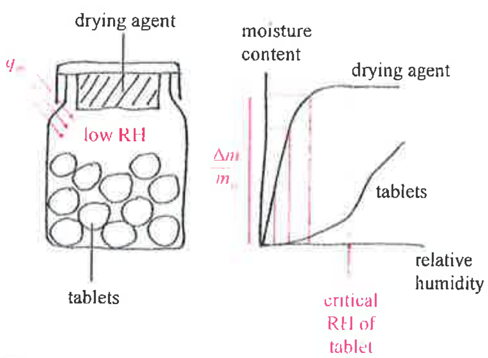


T temperature (°C)
F air flow rate (m^3/h)
n air changes per hour (ach, ACH) (1/h)
Δv humidity contribution indoors (g/m^3)
v vapor content (g/m^3)
V volume (m^3)

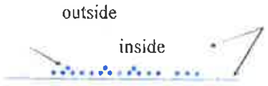
$n=F/V$

$v_{in}=v_{out}+\Delta v$

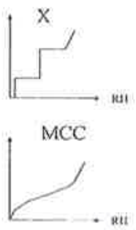




Problem: moisture transport into blister pack

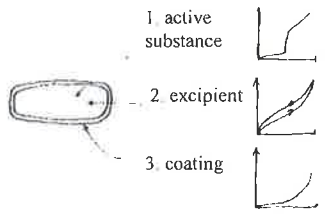


tablet 5 mg X dihydrate (M_m=162 g/mol)
95 mg microcrystalline cellulose MCC at a_w=0.15
permeability of blister pack 10^{-13} g/Pa/s
climate 1 30°C/90% RH (Singapore)
climate 2 20°C/60% RH (Sweden)
end of shelf life when 10% of X is pentahydrate



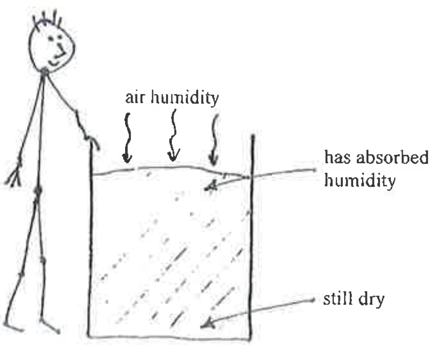
Calculate end of shelf life!

Moisture redistribution



	initial	
1. active substance	a_{w1}	m_1
2. excipient	a_{w2}	m_2
3. coating	a_{w3}	m_3

What will the final water activity be when equilibrium is established?



Examples of processes that produce heat:

sorption
crystallization
conformational changes
deliquescence
chemical reactions

Differential sorption enthalpy
J/g_{water}
(a function of RH/concentration)

the heat produced when one gram of liquid water is sorbed by a large sample

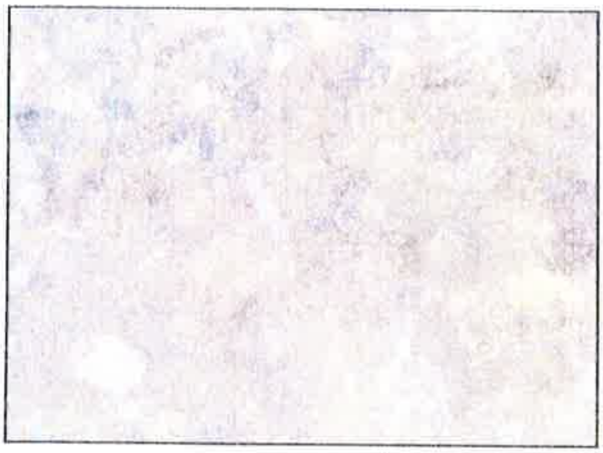
Integral sorption enthalpy
J/g_{sample}
(between two moisture states)

the heat produced when one gram of sample changes its moisture state

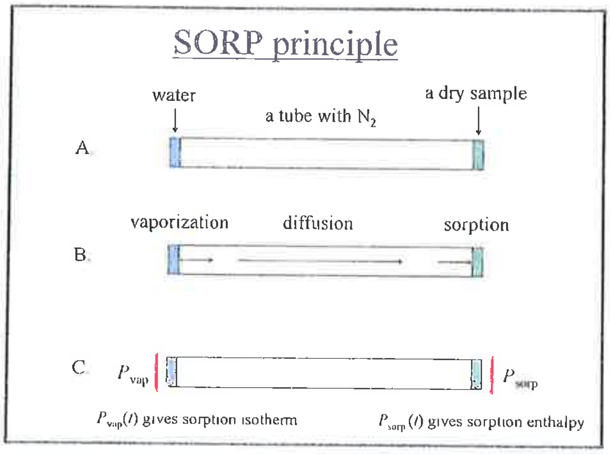
Why will two sorption methods sometimes not give the same result?

1. Method of drying
2. Mode of vapour transfer (step, ramp...)
3. Rate of moisture transfer
4. Sample size
5. Sample thickness etc.

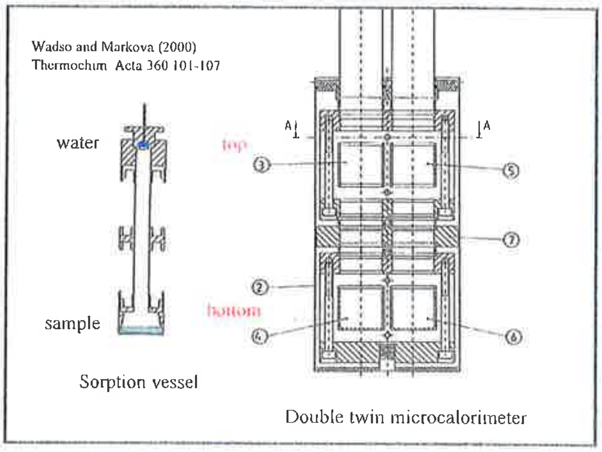
kinetics...



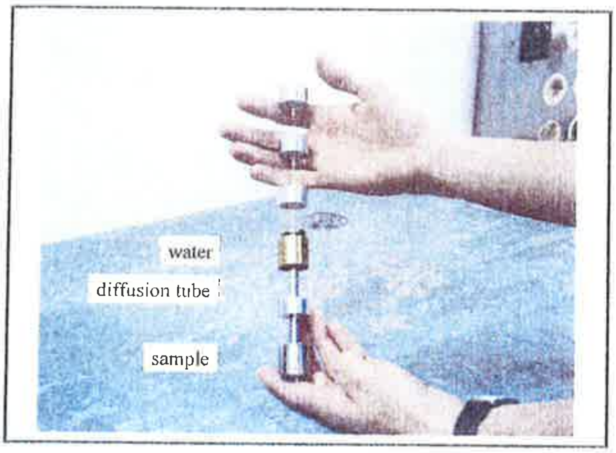
Sorption microcalorimeter
A SECOND GENERATION TWIN DOUBLE MICROCALORIMETER
Measurements of sorption isotherms, heats of sorption and sorption kinetics
A double twin isothermal microcalorimeter
Lars Wadsö, Natalia Markova
On application of an isothermal sorption microcalorimeter
N. Markova, F. Sparr, L. Wadsö



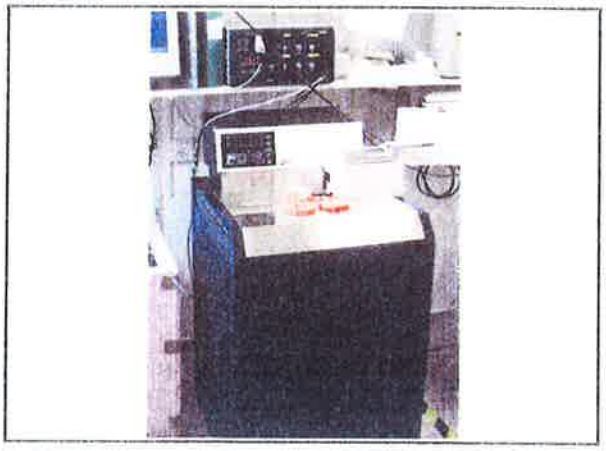
SORP principle
water
a tube with N2
a dry sample
A.
vaporization
diffusion
sorption
B.
C.
Pvap
Psorp
Pvap(t) gives sorption isotherm
Psorp(t) gives sorption enthalpy



Wadso and Markova (2000)
Thermochim Acta 360 101-107
water
sample
top
bottom
Sorption vessel
Double twin microcalorimeter

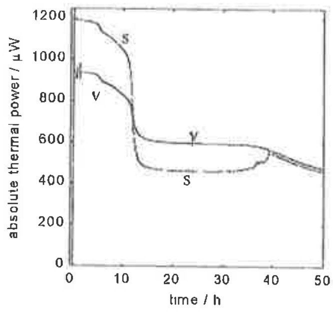


water
diffusion tube
sample

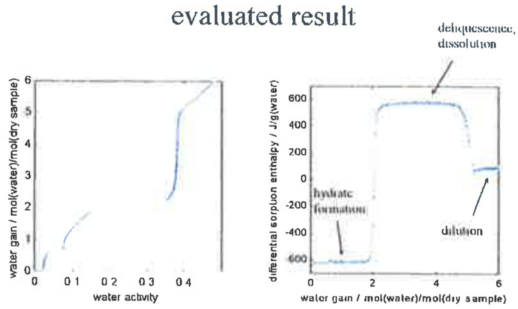


sample X measured with SORP

dried at room temp in vacuum, 37 mg, primary result



sample X measured with SORP: evaluated result

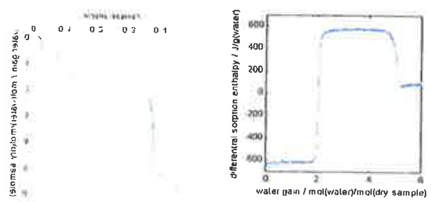


We measure triplets of

- water activity (often disturbed by kinetics)
- moisture content (robust)
- sorption enthalpy (robust)

sorption isotherm

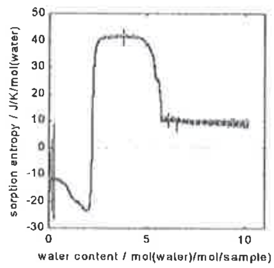
sorption enthalpy plot



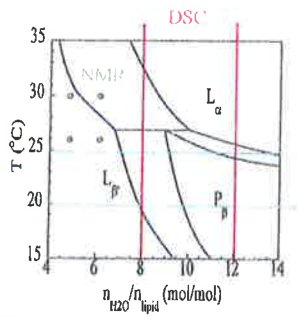
Sorption entropy

sample X measured with SORP

a_w and ΔH gives the entropy ΔS of the process



Phase diagram (DMPC)



N Markova, E Sparr, L Wadsö, H Wennerström, (2000), J Phys Chem 104 8053-8060