

Take-Home Message

Thermodynamics works everywhere

TD relates observables in experiments and between experiments and simulations

Sometimes details don't matter - then TD controls a system's behaviour

Universality of Thermodynamics

The law that [entropy](#) always increases, holds, I think, the supreme position among the [laws of Nature](#). If someone points out to you that your pet theory of the universe is in disagreement with [Maxwell's equations](#) — then so much the worse for Maxwell's equations. If it is found to be contradicted by observation — well, these experimentalists do bungle things sometimes. But if your theory is found to be against the [second law of thermodynamics](#) I can give you no hope; there is nothing for it but to collapse in deepest humiliation.

A. Eddington

Classical mechanics studies the motion of objects in the world, it finds relations between external mechanical coordinates (x_i, v_i, f_i) and time that determine the **KE and PE** that are consistent with Newton's laws.

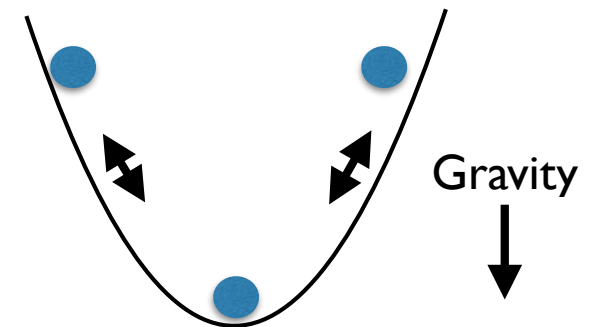
In classical mechanics, mechanical energy (or work) is conserved

But mechanical systems are observed to minimise their energy - why?

e.g., a ball rolls up and down a slope, but eventually stops at the bottom

Energy is lost due to friction, air resistance, sound, etc.

If there were no losses, the ball would oscillate forever.



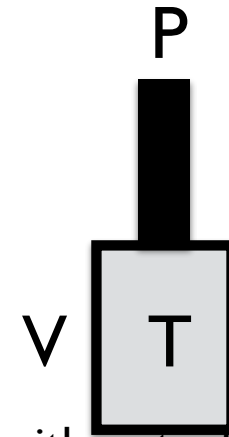
The motion of macroscopic objects (e.g., billiard balls) is usually unaffected by temperature

Q. What is the diffusion constant of a billiard ball? ($\eta_{\text{air}} = 18 \mu\text{Pa}\cdot\text{sec}$)

Q. How does its energy of motion compare to the thermal energy ($1/2 k_B T$)?

Classical thermodynamics

Classical thermodynamics studies the interior of a system using macroscopic coordinates (P , V , T) that determine the **Internal Energy** of the system, and finds relations among these coordinates that are consistent with the laws of thermodynamics.
It is a generalisation from every-day experience (involving heat, work, temperature, etc) to an ideal system that deals only with special states of a system called **Equilibrium States**.



It is an experimental result that equilibrium states of a system can be described with just a few experimental properties (*thermodynamic coordinates*),
e.g., a gas needs N , P , V , T not 10^{23} molecular coordinates.

Unlike classical mechanics, no energy is lost in thermodynamics - it just gets passed between different degrees of freedom

Q. Given a fixed mass of gas, with no chemical reactions, in a box of constant volume at constant temperature, how can its pressure be changed without altering V or T ?

Q. If we arbitrarily change P , V , T **adiabatically** and return to the initial state, is the system's internal energy the same as before?

Just as classical mechanics involves ideal objects (point particles, frictionless pulleys, rigid bodies, no air resistance, etc) so thermodynamics involves ideal processes:

- Frictionless pistons
- Infinitely-slow motion (quasi-static process)
- Infinitesimal temperature and pressure differences
- Heat reservoirs unaffected by any gain or loss of heat
- No turbulence or gradients in fluids, or inelastic deformations in solids
- Reversible processes

Whether or not these concepts apply to a system has to be determined by experiment. But when they are at least approximately true, we have a powerful means of predicting the behaviour of the system.

Not all idealisations are equivalent: we can imagine an adiabatic wall that prevents all heat transfer across it.

Q. Why cannot we imagine a wall that prevents the gravitational force crossing it?

Role of thermodynamics in cell biology? EPFL

Thermodynamics is concerned with understanding the properties of matter in so far as they are affected by changes of temperature.

Cells are isothermal - so what is the need for thermodynamics?

- TD gives relations between observable, macroscopic coordinates (P , V , T) that provide insight into experiments (cp point mass in classical mechanics)
- TD connects theory/simulations with experiments (**often the only connection!**)
- Many processes in a cell are near equilibrium because leaving eq. is energetically expensive
- Concepts of TD are applicable to cellular processes even if they are not *in* equilibrium but *near* equilibrium

Thermodynamics makes predictions

The usefulness of thermodynamics arises from its universality:

- all *dilute* gases obey the same ideal gas law: $PV = NRT$
- small particles suspended in water exhibit continual, random motion *independent* of their nature (Brownian motion)
- polymer properties are *independent* of monomer details (random walk)
- entropy dominates the shape fluctuations of the plasma membrane and vesicles because the membrane bending energy is small
- phase behaviour of mixtures of polymeric fluids depends on their physical chemical properties (we can often *ignore* atomic details):

concentration

molecular weight and shape

attraction / repulsion of monomers

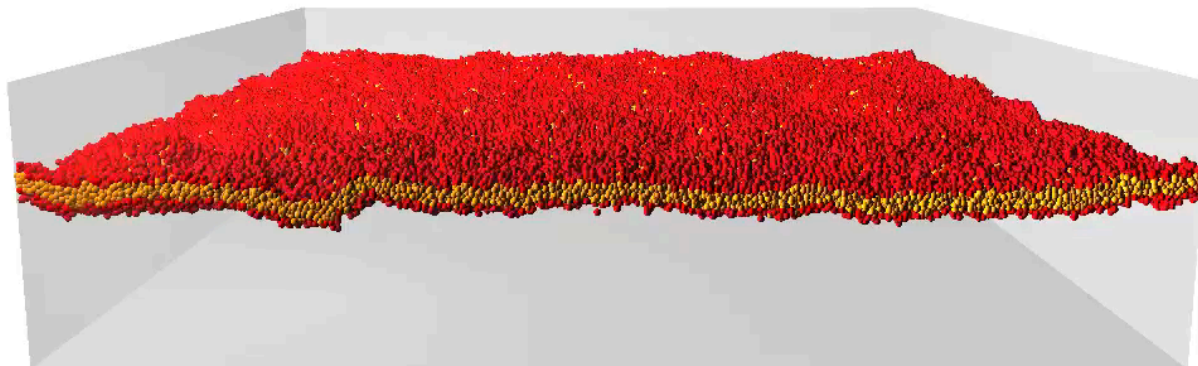
And when it is applicable, it is immensely powerful in predicting how a system behaves. If we can map a cellular function onto a thermodynamic model, we can predict a lot about it.

Q. How do we know these are the same?

Q. What tests could we do to prove it?



J. Ipsen, MEMPHYS, SDU



There are two approaches to thermodynamics:

Macroscopic:

- no assumptions about the structure of matter
- few coordinates needed (P, V, T, ...)
- usually suggested by our senses
- measurable
- sufficiently large compared to molecules that it is continuous

Experiments

Microscopic:

- assumes matter is made up of molecules
- many quantities ($\sim 10^{23}$ position + velocity) must be specified
- quantities not suggested by senses
- not measurable
- comparable to molecular size

Simulations

Whereas macroscopic thermodynamics deals only with observable coordinates and properties (P, V, T, etc), microscopic thermodynamics regards a system as composed of molecules in distinct states:

A **macrostate** is a specification of a few macroscopic coordinates: N, P, V, T, ...

A **microstate** is a specification of all 10^{23} $x(t)$ and $v(t)$ coordinates of the molecules

The molecules are assumed to obey some microscopic force law (either Newton's laws or Quantum Mechanics) that determines their motion, and the observable properties are obtained by averaging them over all accessible states of the system.

Statistical mechanics finds links between the macrostates observed in experiments and the (unobservable) microstates of the system by counting how many microstates make up each macrostate and averaging observables appropriately.

Computer simulations are a way of performing this averaging automatically - they generate a chain of microstates that, when averaged over, yield macroscopic observables.

A brief history of thermodynamics

Thermodynamics started as a practical question: **how to get work from heat**

- 1774 James Watt invented the first steam-engine (**Comment on efficiency**)
(except for Newcomen, 1712, Savery 1698, others, and Heron of Alexandria, 1st Century)
- 1790 Count Rumford (Benjamin Thompson) bored a cylinder under water and after 2 hours the water boiled: “bystanders were astonished to see water boil in the absence of a fire” *
- 1823 Sadi Carnot wrote “Réflexions sur la puissance motrice de feu”
(he thought heat was a substance, and a hot body contained a lot of it and a cold body little, but he still managed to get correct conclusions)
- 1839 Séguin showed that heat is energy
- 1842 Meyer calculated the conversion factor of work into heat
- ~1849 Joule wrote down the 1st Law of Thermodynamics (Energy is conserved)
- ~ 1850s Clausius and Kelvin independently wrote down the 2nd Law of Thermodynamics
(Heat flows spontaneously only from a hot body to a cold body)

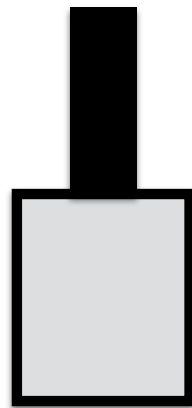
* Entropy and Low Temperature Physics, J. S. Dugdale
Hutchinson University Press, London, 1966

“A **phase** is an homogeneous region of matter bounded by surfaces across which its properties change discontinuously (e.g., solid, liquid or gas) “

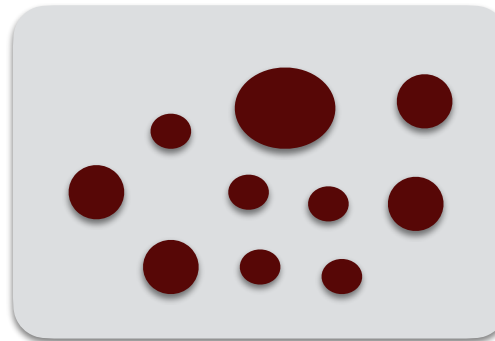
“An **equilibrium phase** has no internal gradients nor between it and its surroundings “



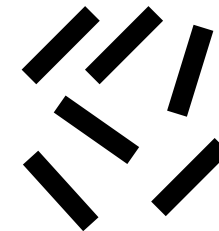
Water



Gas in isolated box
with a piston



Solution of micelles



Rodlike liq. crys. / TMV
in solution

“Homogeneous” contains an **implicit** average over a region of space, e.g., micelles in water.
NB. Molecular shape may or may not be relevant depending on concentration, cp. ideal gas.

There are distinct types of bounding surface (or wall):

Adiabatic = neither heat nor matter transport across the surface

Diathermal = heat transport but not matter

Open = heat and matter transport

A phase of a substance is in **thermodynamic equilibrium** if there are no spontaneous changes in its state.

Thermodynamic equilibrium = Mechanical + Chemical + Thermal equilibrium

Mechanical equilibrium = no unbalanced forces in a system nor across its boundaries

Chemical equilibrium = no chemical reactions, diffusion nor flow “

Thermal equilibrium = no spontaneous changes when in contact with a heat reservoir at the same temperature

If a system *can* make spontaneous changes *it will*, and will stop only when no more spontaneous changes can occur. They are driven by the tendency of the system to incessantly move through its phase space because its energy is continually being redistributed (equipartition theorem).

Once all macroscopic changes have ceased, the system is in equilibrium, and can be described using a few macroscopic coordinates (e.g., pressure, volume, temperature, ...)

Equilibrium does not mean static

Equilibrium does not mean static: it means *observable* properties do not change with time.

What doesn't change in the following examples?

- Gas molecules move in an isolated box: **the pressure does not change**
- Rigid liquid crystal molecules (or TMV) move and rotate in dilute solution: **density and orientational distributions**
- Chemical reaction $A + B \rightleftharpoons C + D$: **concentrations $[A]$, $[B]$, $[C]$, $[D]$**
- ATP molecules diffuse throughout the cytoplasm: **local concentration of $[ATP]$**
- A folded protein fluctuates about its lowest energy folded state: **mean shape**
- An intrinsically-disordered protein explores its (large!) conformational ensemble (recall the DPD polymer being stretched): **the ensemble doesn't change**

What motions are consistent with equilibrium? **EPFL**

A) A system may have **characteristic** motions in equilibrium that are the most important ones for a certain biological process:

e.g., gas molecules diffuse in a box, polymer conformational fluctuations, membrane shape fluctuations

These motions are what a good model should represent, which is why many polymers can be modelled as phantom chains, and membranes can be modelled as fluctuating elastic sheets ignoring lipid diffusion within them.

B) A system may exhibit some motions that **equilibrate rapidly** compared to other slower motions of interest:

e.g., ATP diffuses to all parts of the cytosol much faster than a motile cell crawls, so we can treat the ATP concentration as uniform in a model of cell crawling.

C) Unbalanced forces, accelerations, turbulence, flows, unbalanced chemical reactions, temperature gradients, are **not** consistent with equilibrium

Role of thermodynamics in cell biology? EPFL

Thermodynamics is concerned with understanding the properties of matter in so far as they are affected by changes of temperature.

- Temperature drives diffusion ($D = k_B T / 6\pi\eta a$, η = viscosity, a = sphere radius)
- Cells maintain gradients of ions, molecules: gradients relax by diffusion
- Some gradients relax faster than others (pressure, salt concentration, etc), once they have, they may be considered in equilibrium compared to slower processes of interest
- New properties appear (entropy, diffusion) that are typically unimportant on macroscopic scales.
- Concepts of *work* and *heat* take on new roles
- Adiabatic means “happens fast enough that no heat transfer occurs during process”
- Thermodynamics gives us relations between measurable quantities, a framework for understanding changes and distinguishing between fast and slow processes that allow us to focus on the relevant dynamics for the problem at hand (separation of scales)

Can P, V, T for a gas in a box in equilibrium take any values independently of each other?

Experimentally, it is found that the macroscopic thermodynamic coordinates of a system *in equilibrium* satisfy a relation (**equation of state**) although we may not be able to write it down:

$$f(P, V, T) = 0$$

- Classical thermodynamics cannot predict the equation of state of a system
- It must be determined from experiment or a microscopic model of a system
- It depends on the intermolecular forces, molecular shape, phase of the material (crystal, liquid, gas, etc), composition, macroscopic shape (long thin wire versus planar oil film), magnetic field, etc.
- But just knowing it exists gives us a lot of information and relationships

Difference between a model and reality: experimentally, a gas must have an equation of state, i.e., there must be a relation between P, V, T in equilibrium, but there are more than 60 equations describing gas/liquid-vapour/liquid regions and none of them work everywhere.

If a relation exists among three coordinates - $f(x, y, z) = 0$ - then we can write x as a function of y, z and y as a function of x, z , or z as a function of x, y .

$$dx = \left(\frac{\partial x}{\partial y} \right)_z dy + \left(\frac{\partial x}{\partial z} \right)_y dz$$

$$dy = \left(\frac{\partial y}{\partial x} \right)_z dx + \left(\frac{\partial y}{\partial z} \right)_x dz$$

$$dz = \left(\frac{\partial z}{\partial x} \right)_y dx + \left(\frac{\partial z}{\partial y} \right)_x dy$$

We then get:

$$\left(\frac{\partial x}{\partial y} \right)_z = 1 / \left(\frac{\partial y}{\partial x} \right)_z$$

and

$$\left(\frac{\partial x}{\partial y} \right)_z \left(\frac{\partial y}{\partial z} \right)_x \left(\frac{\partial z}{\partial x} \right)_y = -1$$

Classical thermodynamics is largely the application of relations like this to the internal energy of a system and its equation of state.

Ideal gas equation of state

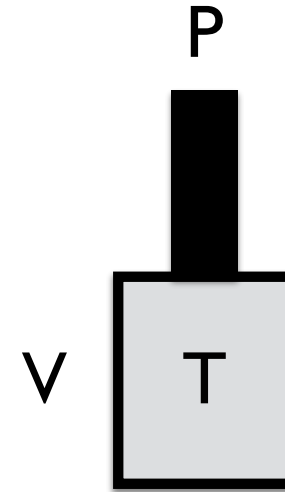
An ideal gas is defined by the two equations:

$$PV = NRT$$

$$U = U(T)$$

VdW gas is defined by:

$$(P + aN^2/V^2)(V - Nb) = Nk_B T$$



Nb is effectively the reduction in available volume due to the size of the N gas molecules

aN^2/V^2 is the extra pressure that must be added to compensate for inter-molecular attraction that tends to make them clump and reduce the pressure on the walls

When we think of a gas, it is tempting to think of an ideal gas: but it is not clear if this is accurate in a given experiment. In cellular structures like membranes, protein/lipid aggregates, ribosomes, etc. crowding, attractions, etc, we have to develop new intuition about the thermodynamic behaviour of the material.

Exercise: calculation of isothermal compressibility **EPFL**

Recall from the DPD lecture that the a_{ww} conservative parameter was set from the compressibility of water.

$$K_T = -1/V \left(\partial V / \partial P \right)_T$$

What are the units of P , V and K_T ?

A) What is the compressibility of an ideal gas? (Do this derivation)

$$PV = NRT$$

B) What is the dimensionless compressibility of a DPD fluid (Do this derivation)

$$P = \rho k_B T + \alpha a_{ww} \rho^2 \quad \alpha = 0.1 \text{ (Groot and Warren 1997)}$$

C) What is the compressibility of a Van der Waals gas? (Optional derivation)

$$(P + aN^2/V^2)(V - Nb) = Nk_B T$$

A thermodynamic **ensemble** is a specification of the constraints on a phase.

There are as many ensembles as there are combinations of constraints:
constant mass, volume, pressure, temperature, area, surface tension, length, force, etc.

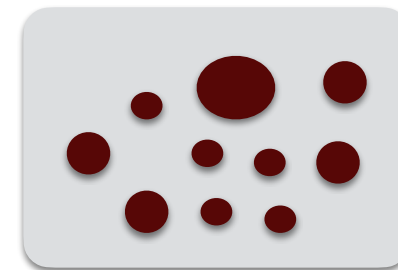
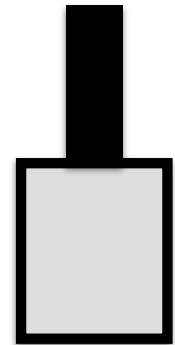
Most common ensembles for fluid systems are:

Microcanonical - N, V, E are constant

Canonical - N, V, T

Grand Canonical - μ, V, T

Gas in a box with a piston
clamped at constant
volume and diathermal
walls: N, V, T



Solution of micelles: V, T, N_{lipid}
(not number of micelles!)

How does a system move from one state to another?

An **adiabatic process** is one that takes place without any heat transfer ($Q = 0$)

- this does not mean that the system is isolated: the process could occur much faster than heat can be transported across its boundaries. This is relevant for cells. If a process is adiabatic it doesn't matter how the work is done, no energy is lost so the system ends up in the same state regardless of the path.

An **isothermal process** is one that takes place at constant temperature

- this does not mean that no heat is transferred: a heat gain could be exactly balanced by the performance of work or vice versa.

Other types of process exist (isobaric, isochoric, etc) or ones in which several variables change simultaneously.

“If a system is caused to change from an initial state to a final state by adiabatic means only, the work done is the same for **ALL** adiabatic paths connecting the two states.”

Work can take many forms depending on the type of system (all have units of energy and involve the product of an **intensive** variable and an **extensive** variable):

- $-P.dV$ for a gas subject to an applied pressure p
- $f.dL$ for a polymer whose length is changed by an amount dL by an applied force f
- $\sigma.dA$ for a thin liquid film whose area is increased by an amount dA against surface tension

An **intensive coordinate** is one that is independent of the mass or volume of the system, .e.g, pressure, temperature, magnetic field, etc.

An **extensive coordinate** is one that is proportional to the mass or volume, e.g., volume, magnetisation, length of a wire, etc.

Whenever a quantity depends only on the initial and final states, an important conclusion follows:

there is a function of the thermodynamic coordinates - the **Internal Energy U** - whose value at the final state minus its value at the initial state is equal to the adiabatic work done.

$$U = -W$$

The sign is chosen so that if a system *does* work, W is positive and its internal energy decreases, e.g., if a gas under pressure p expands by an amount dV (> 0), then $W = p dV$, and U decreases.

Internal energy is a function of the thermodynamic coordinates - $U(T, V)$, $U(T, P)$ $U(P, V)$ - and is similar to the *potential energy* of a mechanical system that is a function of its external mechanical coordinates.

cp. Potential energy of a body in a gravitational field (or a charge in an E field) depends only on its position, and the change in PE is equal to the work done on the body independently of the path it follows.

“When a system whose surroundings are at a different temperature, and on which work may be done, undergoes a process, the energy transferred by non-mechanical means, equal to the difference between the internal energy change and the work done is called Heat.”

1st Law of Thermodynamics

$$Q = U - (-W)$$

or

$$U = Q - W$$

1st law means more than just energy is conserved:

- it asserts the existence of an **internal energy function U** whose value at the final state minus its value at the initial state equals the adiabatic work done in going from the initial to the final state (when $Q = 0$) or $Q - W$ if not
- energy is conserved when heat is included
- heat is energy in transit by virtue of a temperature difference

Thermodynamics assumes frictionless pistons, perfectly adiabatic walls, no energy loss, etc, and a **reversible process** is an idealisation of a physical change. All natural processes are irreversible.

A reversible process -

is **quasi-static** - so all changes proceed infinitely slowly

has **no dissipative effects** - no friction, heat loss, hysteresis or inelastic effects, etc.

When a system undergoes a reversible process both the **system** and its **surroundings** can be brought back to their original state without any extra work being done or heat being transferred: everything is exactly as it was before the change.

Question. Why does the Krebs cycle have so many steps?

In order to keep the energy changes (heat released) small so that the system remains **close to equilibrium** as it passes through all its stages. If all the heat were released in a single, complex chemical reaction it would be very inefficient.

A car is inefficient because temperature and pressure gradients waste energy in heat loss.

For infinitely small changes, we can replace the macroscopic quantities, U , Q , W by infinitesimal quantities, dU , dQ , and dW .

$$dU = dQ - dW$$

dU is the differential of an actual function - the internal energy U - so it can be expanded as Taylor series in its coordinates - P, V, T :

$$dU(T, V) = \left(\frac{\partial U}{\partial T} \right)_V dT + \left(\frac{\partial U}{\partial V} \right)_T dV$$

It is an **exact** differential. (Question: why only 2 arguments and not all 3 of p, V, T ?)

But dW and dQ are NOT differentials of any functions there are NO functions $W(P, V, T)$ and $Q(P, V, T)$ of the TD coordinates, and dW and dQ are **inexact differentials**.

The performance of work and the flow of heat are simply methods by which the internal energy of a system can be changed. The internal energy **cannot** be separated into a thermal and mechanical part.

Cellular world is different from the ours, but thermodynamics is the same.

TD answers questions: 1) what can a system possibly do, 2) what is it most likely to do?

- **1st Law** - Only processes that conserve energy are observed, and systems in equilibrium have an internal energy that depends only on their macroscopic coordinates (if E increases in a sim. you have a problem; if you pump E into a sim. where does it go?)
- **2nd Law** - Of processes that conserve energy, which ones occur? (Heat never spontaneously flows up a temperature gradient)
- TD provides *the* quantitative link between simulations and experiments: in experiments we want to change 1 parameter and observe effects, we cannot do this if other properties are changing as well: diff. calculus gives the rules relating such changes.
- Leaving equilibrium is energetically expensive so cells tend to stay close to equilibrium and equilibrium thermodynamics can relate observations