Islamic University
College of Pharmacy
Department of Pharmaceutics
Title of the course: ***Physical Pharmacy I*** Course number: **213**
Level: 2nd Class, 1st Semester
Credit hours: **Theory 3 hours Laboratory 1 hour**
Tutors: ***Prof.Dr. Falah Shareef Abed Suhail***
Reference text: ***Physical Pharmacy by Alfred Martin et al.***

Objectives:

- To understand the application of quantitative and theoretical principles of the physical characters of matter in the practice of pharmacy.
- It help the pharmacists in their trial to predict the solubility, compatibility and biological activity of drug products.
- As a result of this knowledge it will help in the development of new drugs and dosage forms as well as in improvement of various modes of administration.

No	Lecture title	hours
1.	**States of matter**: Introduction, binding forces between molecules, gases, liquids, solid and crystalline matters; phase equilibria and phase rule; thermal analysis.	10
2.	**Thermodynamics**: first law, thermochemistry, second law, third law, free energy function and applications.	8
3.	**Solutions of non-electrolytes**: properties, ideal and real solutions, colligative properties, molecular weight determination.	7
4.	**Solution of electrolytes**: properties, Arrhenius theory of dissociation, theory of strong electrolytes, ionic strength, Debye-Huchle theory, coefficients for expressing colligative properties.	5
5.	**Ionic equilibria**: modern theories of acids, bases and salts, acid-base equilibria, calculation of pH, acidity constants, the effect of ionic strength and free energy.	8
6	**Buffered and isotonic solutions**: Buffer equation; buffer capacity; methods of adjusting tonicity and pH; buffer and biological system.	7

Physical pharmacy

1- Introduction

Dimensions and units

The properties of matter are usually expressed by **3** fundamental dimensions:

Dimension	symbol	CGS Units	Si units
Length	L	Cm	m
Mass	M	g	Kg
Time	t	s	s

1metter= 1.65076373*10^{6} λ Kr ^{86}

1 Kilogarm= mass of platinum-Iridum block preserved at the Bureau of weights and measures in sevres, France

Fractions and multiples of units

Tetra(T),	Giga(G),	Mega(M),	Kilo(K)
10^{12}	10^{9}	10^{6}	10^{3}

Pico(P),	Nano(n),	Micro(*M*),	milli(m)
10^{-12}	10^{-9}	10^{-6}	10^{-3}

Descriptions

- Length m, cm, mm, . . .
- Area m^2, cm^2, mm^2, . . .
- Volume m^3, cm^3, mm^3, . . .
- Density = mass/volume in g/cm^3 or Kg/m^3, . . .
- Force = m*a in $g.cm.\ s^{-2}$ = dyne
- Pressure=F/A in $dyne.cm^{-2}$ or $N.m^{-2}$
- 1 atm=$1.0133*10^6$ $dyne.cm^{-2}$
- Work and energy 1erg= 1dyne.cm

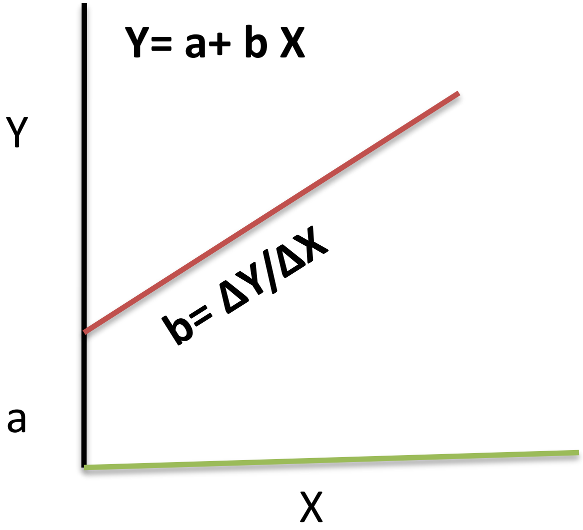
Linear relationship

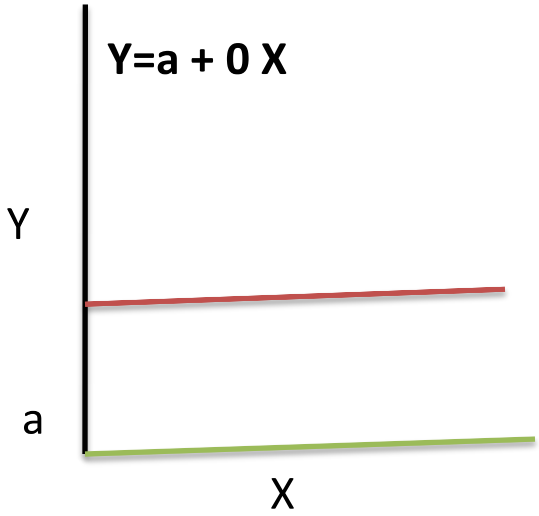
- The simplest variables between two variables, when the variables contain **no** exponents other than one (first degree equation),yields straight line when plotted on rectangular graph paper.
- The straight line or linear relationship is expressed as: **$Y= a + b X$**

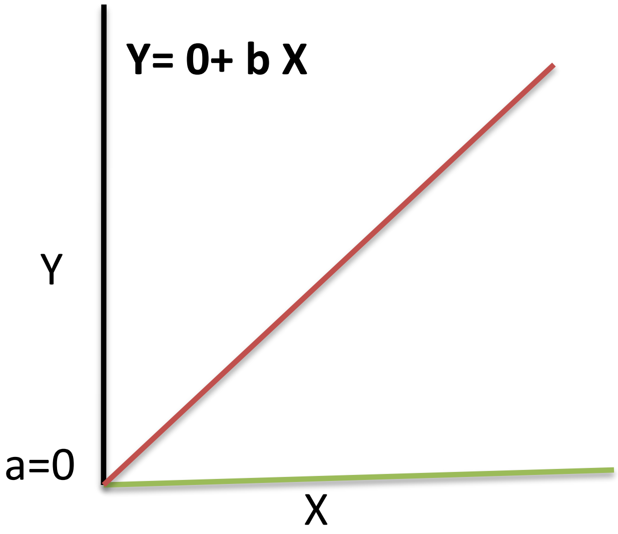
Y: dependant variable **X:** independent variable

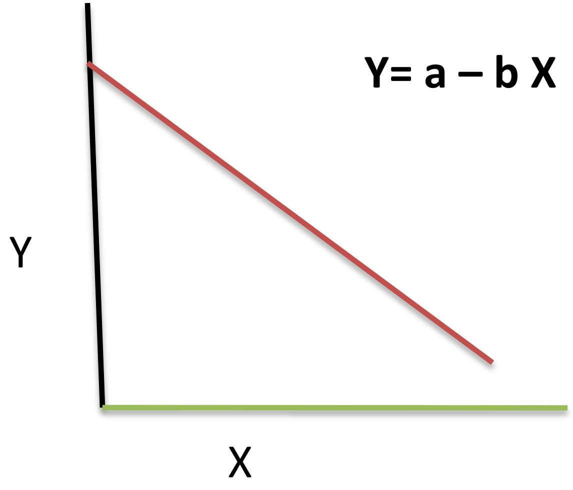
a: The Y independent **b:** the slope of line, may be +ev or –ev

For example $\ln C = \ln C_0 - Kt$ $Y=\ln C$, $X=t$, $a=\ln C_0$, $b= -k$


Y= a+ b X
Y
b= ΔY/ΔX
a
X

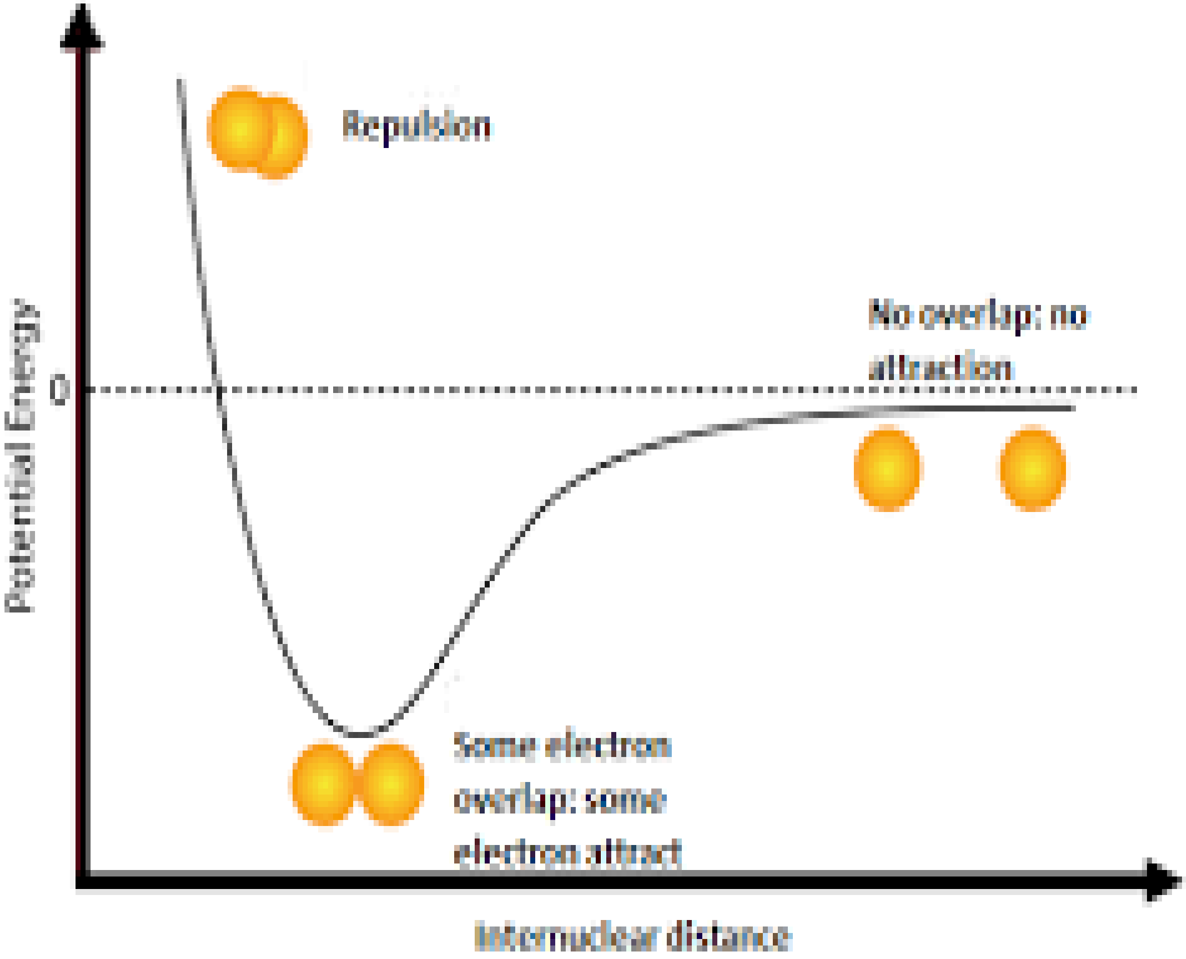

Y=a + 0 X
Y
a
X


Y= 0+ b X
Y
a=0
X


Y= a – b X
Y
X

Intermolecular force

- An **intermolecular force** is the force that mediates interaction between molecules, including the electromagnetic forces of attraction or repulsion which act between atoms and other types of neighboring particles, e.g. atoms or ions.
- Intermolecular forces are weak relative to **intramolecular forces** – the forces which hold a molecule together. For example, the covalent bond, involving sharing electron pairs between atoms, is much stronger than the forces present between neighboring molecules.


Repulsion
No overlap: no attraction
0
Potential Energy
Some electron overlap: some electron attract
Internuclear distance

The investigation of intermolecular forces starts from macroscopic observations which indicate the existence and action of forces at a molecular level.

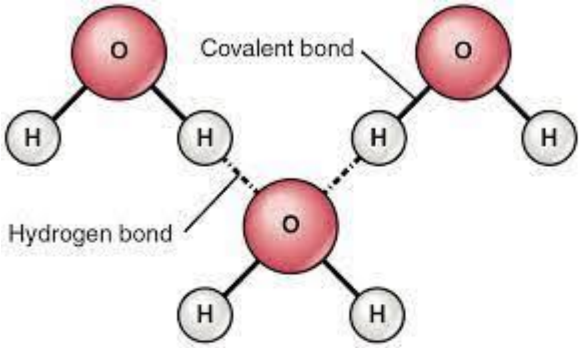
These observations include non-ideal-gas reflected by vapor pressure, viscosity, superficial tension, and absorption data.

Various types of attractive intermolecular forces classified ass following:

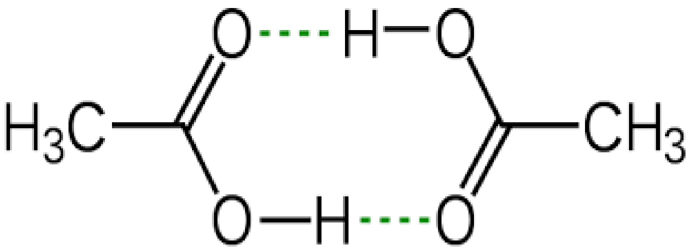
1-Hydrogen bonding

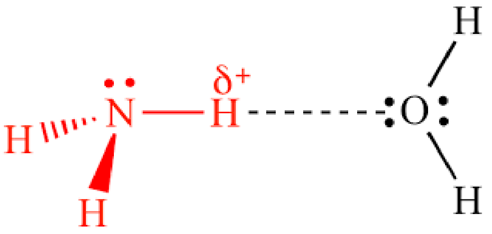
A *hydrogen bond* is an extreme form of dipole-dipole bonding, referring to the attraction between a hydrogen atom that is bonded to an element with high electronegativity, usually nitrogen, oxygen, or fluorine. The hydrogen bond is often described as a strong electrostatic dipole–dipole interaction.

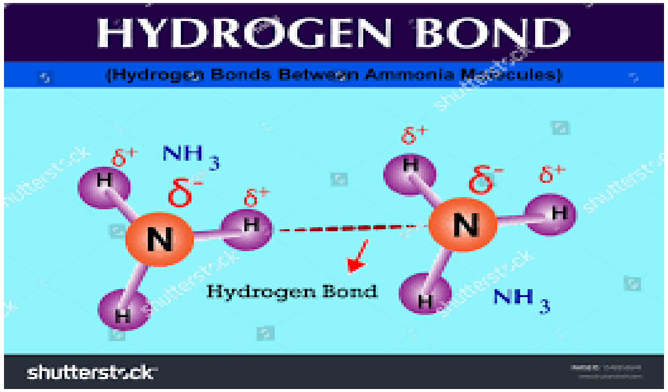
- The number of active pairs is equal to the common number between number of hydrogen the donor has and the number of lone pairs the acceptor has.

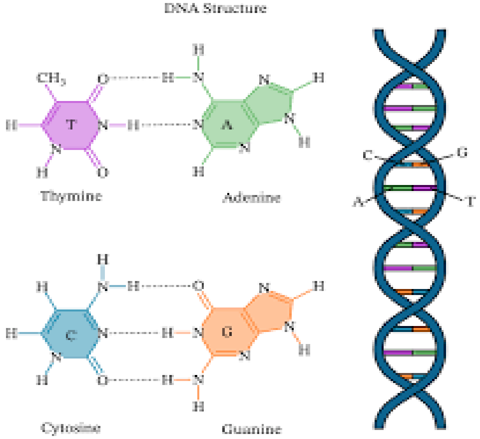


Hydrogen bonding in water

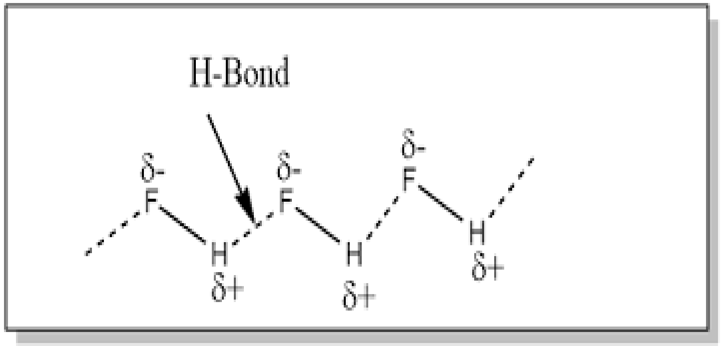


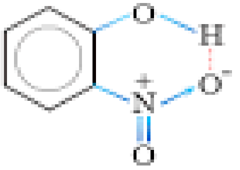




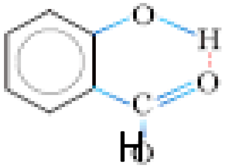


Intramolecular hydrogen bonding examples





ortho-nitrophenol



ortho-hydroxybenzaldehyde

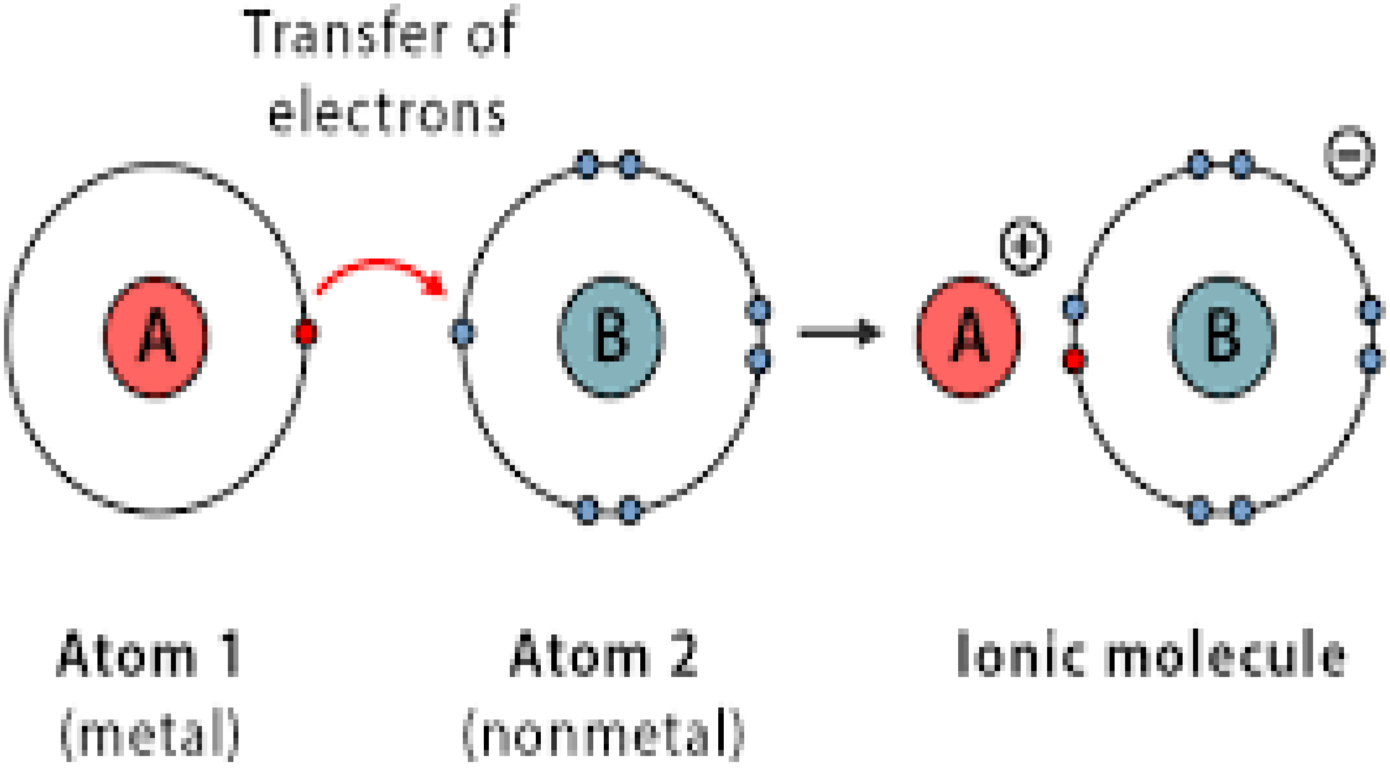
Priyamstudycentre.com

Ionic bonding

The attraction between cationic and anionic sites is a noncovalent, or intermolecular interaction which is usually referred to as ion pairing or salt bridge.

It is essentially due to electrostatic forces, although in aqueous medium the association is driven by entropy and often even endothermic. Most salts form crystals with characteristic distances between the ions.

Ionic Bond



Transfer of electrons

Atom 1
(metal)

Atom 2
(nonmetal)

Ionic molecule

ChemistryLearner.com

Dipole–dipole and similar interactions

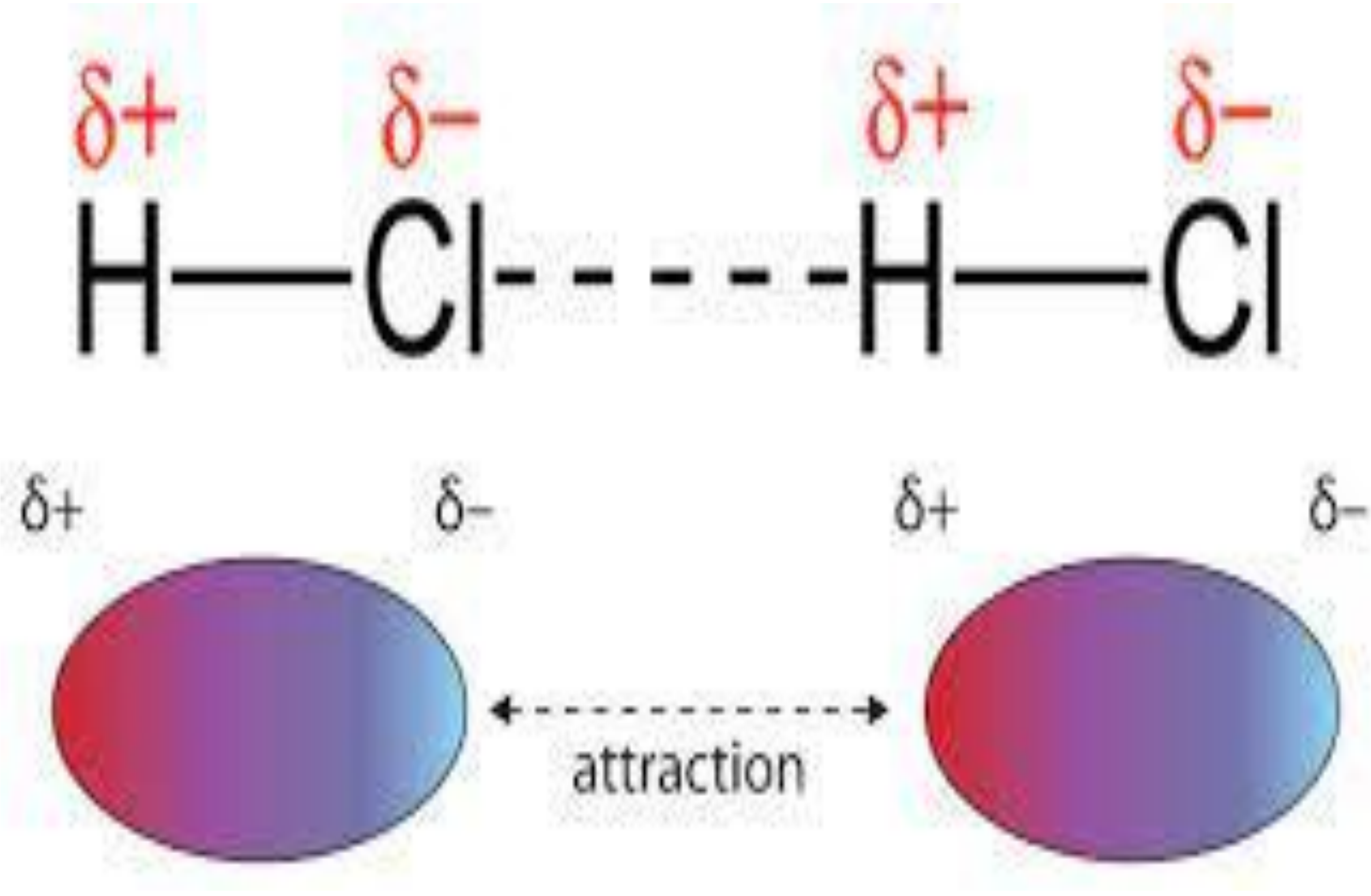
Dipole–dipole interactions (or Keesom interactions) are electrostatic interactions between molecules which have permanent dipoles. This interaction is stronger than the London forces but is weaker than ion-ion interaction

An example of a dipole–dipole interaction

hydrogen chloride (HCl): the positive end of a polar molecule will attract the negative end of the other molecule and influence its position.

Polar molecules have a net attraction between them. Examples of polar molecules

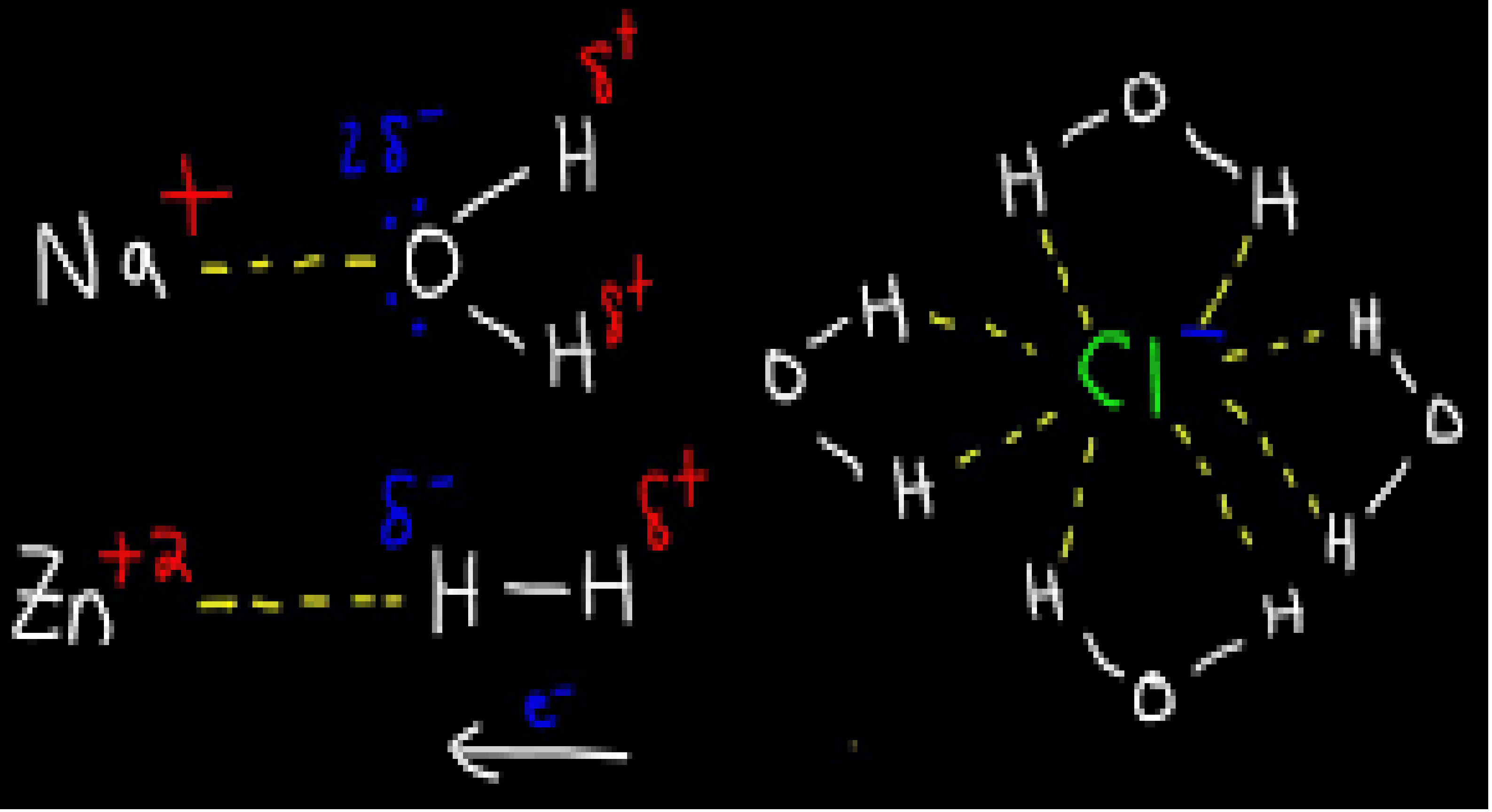
hydrogenchloride (HCl) and chloroform ($CHCl_3$).


δ+
δ−
δ+
δ−
H—Cl- - - - -H—Cl
δ+
δ−
δ+
δ−
attraction

Ion–dipole and ion–induced dipole forces

- Ion–dipole and ion–induced dipole forces are similar to dipole–dipole and dipole–induced dipole interactions but involve ions, instead of only polar and non-polar molecules. Ion–dipole and ion–induced dipole forces are stronger than dipole–dipole interactions because the charge of any ion is much greater than the charge of a dipole moment. Ion–dipole bonding is stronger than hydrogen bonding.

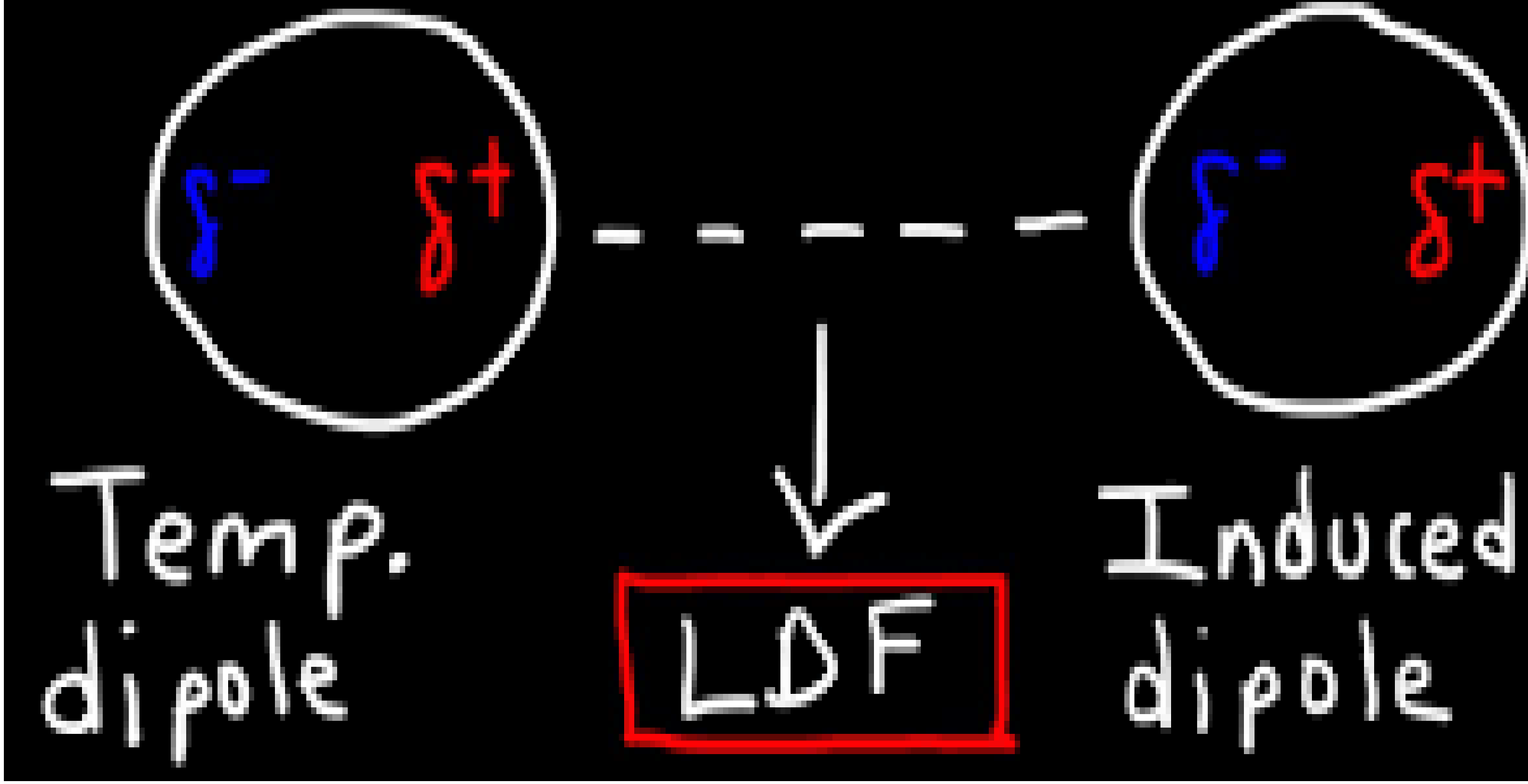
Ion - Dipole Forces



Van der Waals forces

The van der Waals forces arise from interaction between uncharged atoms or molecules, leading not only to such phenomena as the cohesion of condensed phases and physical absorption of gases, but also to a universal force of attraction between macroscopic bodies

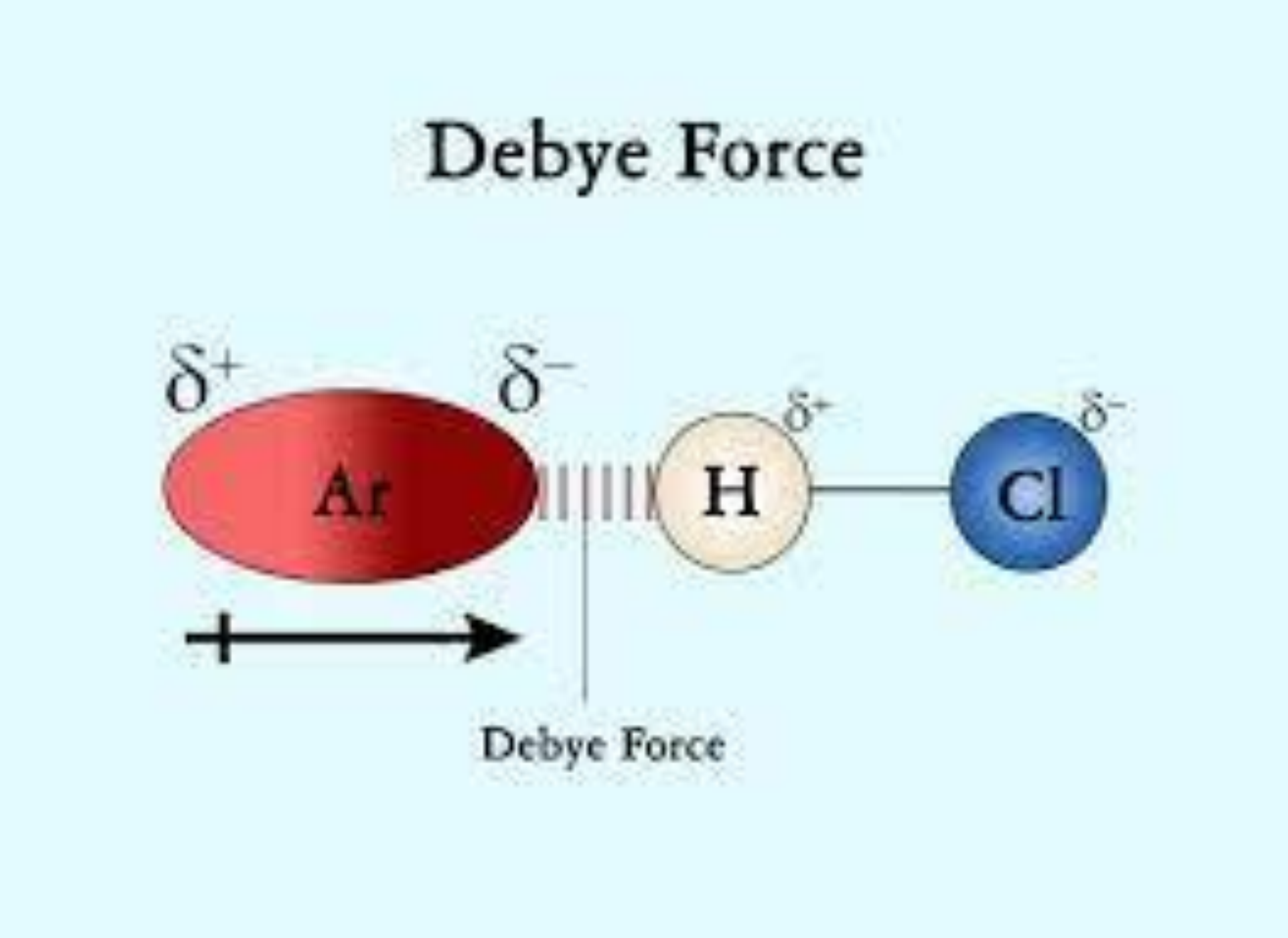
Van Der Waals Forces



Debye force

(permanent dipoles–induced dipoles)

The second contribution is the induction (also termed polarization) or Debye force, arising from interactions between rotating permanent dipoles and from the polarizability of atoms and molecules (induced dipoles). These induced dipoles occur when one molecule with a permanent dipole repels another molecule's electrons. A molecule with permanent dipole can induce a dipole in a similar neighboring molecule and cause mutual attraction. Debye forces cannot occur between atoms. The forces between induced and permanent dipoles are not as temperature dependent as Keesom interactions because the induced dipole is free to shift and rotate around the polar molecule.


Debye Force
δ+
δ−
Ar
H
δ+
Cl
δ−
Debye Force

The induced dipole forces appear from the induction (also termed polarization), which is the attractive interaction between a permanent multipole on one molecule with an induced (by the former di/multi-pole) 31 on another.

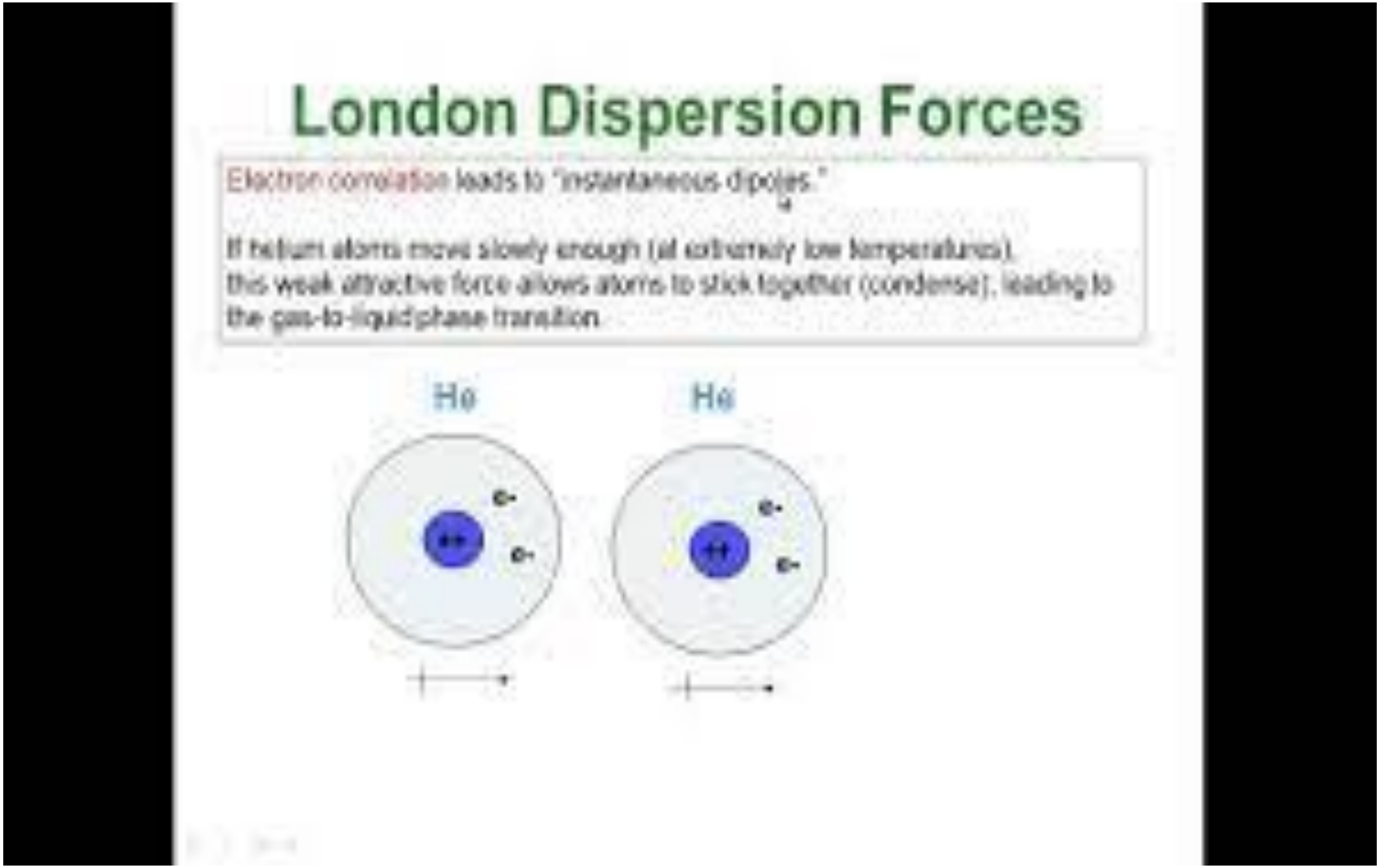
This interaction is called the *Debye force*, named after Peter J. W. Debye.

One example of an induction interaction between permanent dipole and induced dipole is the interaction between HCl and Ar. In this system, Ar experiences a dipole as its electrons are attracted (to the H side of HCl) or repelled (from the Cl side) by HCl.

London dispersion force

(fluctuating dipole–induced dipole interaction)

The third and dominant contribution is the dispersion or London force (fluctuating dipole–induced dipole), which arises due to the non-zero instantaneous dipole moments of all atoms and molecules. Such polarization can be induced either by a polar molecule or by the repulsion of negatively charged electron clouds in non-polar molecules. Thus, London interactions are caused by random fluctuations of electron density in an electron cloud. An atom with a large number of electrons will have a greater associated London force than an atom with fewer electrons. The dispersion (London) force is the most important component because all materials are polarizable, whereas Keesom and Debye forces require permanent dipoles.



London Dispersion Forces

Electron correlation leads to "instantaneous dipoles."

If helium atoms move slowly enough (at extremely low temperatures), this weak attractive force allows atoms to stick together (condense), leading to the gas-to-liquid phase transition.

London interaction is universal and is present in atom-atom interactions as well. For various reasons, London interactions (dispersion) have been considered relevant for interactions between macroscopic bodies in condensed systems. Hamaker developed the theory of van der Waals between macroscopic bodies in 1937 and showed that the additivity of these interactions renders them considerably more long-range.

Relative strength of forces

Bond type	Dissociation energy (kcal/mol)[	Dissociation energy(kJ/mol)	Note
Ionic lattice	250–4000	1100–20000	
Covalent bond	30–260	130–1100	
Hydrogen bond	1–12	4–50	About 5 kcal/mol (21 kJ/mol) in water
Dipole–dipole	0.5–2	2–8	
London dispersion forces	<1 to 15	<4 to 63	Estimated from the enthalpies of vaporization of hydrocarbons

States of matters

Gasses, liquids, crystalline solids and liquid crystalline are four states or phase of matter.

Each state depend on the intermolecular interaction

Gaseous state

Gas molecules had a very small intermolecular interaction, travel in random paths and frequently colliding with one another and with walls of container.

Hence, they exert a pressure and volume depend on **T**

A- Ideal gases

No interaction between atoms or molecules and has infinite volume of molecules.

Ideal gas lows:

1- Boyel's law:- The V and P of given mass of gas at constant T are relates

$P \alpha 1/V$, $PV = K$ constant

2- Gay-Lussas Law:- V and T of a given mass of gas at constant P are directly proportional

$V \alpha T$, $V/T = K$ constant

General ideal gas law

Combination of Boyle's and gay-Lussac to

$$P_1V_1/T_1 = P_2V_2/T_2$$

thus PV/T is constant can be expressed $PV/T=R$

R:- is molar value constant

So $PV=RT$ for 1 mole and **$PV=nRT$** for n mole

At S.T.P stander temperature and pressure

$T=273.15\ ^0K$, $P=1$ atm, $\tilde{V}=22.414\ L.mol^{-1}$

R= *1atm*22.414 L.mole^{-1}/273.15^{0}K=* ***0.08205*** *L.atm.^{0}K^{-1}.mol^{-1}*

- $PV=nRT$, $n=W/Mw$
- $PV=(W/Mw)RT$
- $Mw= W*RT/PV$
- $P*Mw=(W/V)RT$
- $P*Mw= \boldsymbol{\rho}\,RT$ **$\boldsymbol{\rho}$:-** density $g.L^{-1}$
- $P= \boldsymbol{\rho'}RT$ **$\boldsymbol{\rho'}$** :-molecular density $mol.g.L^{-1}$

Example 2-2

Calculation of Volume Using the Ideal Gas Law

What is the volume of 2 moles of an ideal gas at 25°C and 780 mm Hg?

$$(780 \text{ mm}/760 \text{ mm atm}^{-1}) \times V$$
$$= 2 \text{ moles} \times (0.08205 \text{ liter atm/mole deg}) \times 298 \text{ K}$$
$$V = 47.65 \text{ liters}$$

Molecular Weight

The approximate molecular weight of a gas can be determined by use of the ideal gas law. The number of moles of gas *n* is

P.24

replaced by its equivalent *g/M*, in which *g* is the number of grams of gas and *M* is the molecular weight:

$$PV = \frac{g}{M}RT \qquad (2\text{–}7)$$

or

$$M = \frac{gRT}{PV} \qquad (2\text{–}8)$$

Example 2-3

Molecular Weight Determination by the Ideal Gas Law

If 0.30 g of ethyl alcohol in the vapor state occupies 200 mL at a pressure of 1 atm and a temperature of 100°C, what is the molecular weight of ethyl alcohol? Assume that the vapor behaves as an ideal gas. Write

$$M = \frac{0.30 \times 0.082 \times 373}{1 \times 0.2}$$
$$M = 46.0 \text{ g/mole}$$

The two methods most commonly used to determine the molecular weight of easily vaporized liquids

B- Real gas

They are composed of molecules of a finite volume tend to attract one another.

These factors affect the volume and pressure terms in the *Ideal gas equation* of state.

for n moles of real gas

$(P+an^2/v^2)\ (V-nb) = nRT$

a: for pressure resulting from mole of interaction ($L^2.atm.mol^{-2}$)

b: the volume of mole molecules

$a = 27R^2Tc^2/64Pc$, $b = RTc/8Pc$

Pc, Tc: critical pressure and temperature

gas	*a*	*b*
H_2	0.244	0.0266
O_2	1.36	0.0318
CH_4	2.253	0.0428
H_2O	5.464	0.0305
$HCCl_3$	15.17	0.1022

Example 2-5

Application of the van der Waals Equation

A 0.193-mole sample of ether was confined in a 7.35-liter vessel at 295 K. Calculate the pressure produced using (*a*) the ideal gas equation and (*b*) the van der Waals equation. The van der Waals *a* value for ether is 17.38 liter^2 atm/mole^2; the *b* value is 0.1344 liter/mole. To solve for pressure, the van der Waals equation can be rearranged as follows:

$$P = \frac{nRT}{V - nb} - \frac{an^2}{V^2}$$

(*a*)

$$\begin{aligned} P &= \frac{0.193 \text{ mole} \times 0.0821 \text{ liter atm/deg mole} \times 295 \text{ deg}}{7.35 \text{ liter}} \\ &= 0.636 \text{ atm} \end{aligned}$$

(*b*)

$$\begin{aligned} P &= \frac{0.193 \text{ mole} \times 0.0821 \text{ liter atm/deg mole} \times 295 \text{ deg}}{7.35 \text{ liter} - (0.193 \text{ mole}) \times (0.1344 \text{ liter/mole})} \\ &\quad - \frac{17.38 \text{ liter}^2 \text{ atm/mole}^2 \, (0.193 \text{ mole})^2}{(7.35 \text{ liter})^2} \\ &= 0.626 \text{ atm} \end{aligned}$$

Example 2-6

Example 2-6

Calculation of the van der Waals Constants

Calculate the pressure of 0.5 mole of CO_2 gas in a fire extinguisher of 1-liter capacity at 27°C using the ideal gas equation and the van der Waals equation. The van der Waals constants can be calculated from the critical temperature T_c and the critical pressure P_c (see the section Liquefaction of Gases for definitions):

$$a = \frac{27R^2T_c^{\,2}}{64P_c} \quad \text{and} \quad b = \frac{RT_c}{8P_c}$$

The critical temperature and critical pressure of CO_2 are 31.0°C and 72.9 atm, respectively. Using the ideal gas equation, we obtain

$$
\begin{aligned}
P &= \frac{nRT}{V} = \frac{0.5\ \text{mole} \times 0.0821\ \text{liter atm/deg mole} \times 300.15\ \text{deg}}{1\ \text{liter}} \\
&= 12.32\ \text{atm}
\end{aligned}
$$

Using the van der Waals equation, we obtain

$$
\begin{aligned}
a &= \frac{27 \times (0.0821\ \text{liter atm/deg mole})^2 \times (304.15\ \text{deg})^2}{64 \times 72.9\ \text{atm}} \\
&= 3.608\ \text{liter}^2\ \text{atm/mole}^2
\end{aligned}
$$

$$
\begin{aligned}
b &= \frac{(0.0821\ \text{liter atm/deg mole}) \times 304.15\ \text{deg}}{8 \times 72.9\ \text{atm}} \\
&= 0.0428\ \text{liter/mole}
\end{aligned}
$$

$$
\begin{aligned}
P &= \frac{nRT}{V - nb} - \frac{an^2}{V^2} \\
&= \frac{(0.5\ \text{mole} \times 0.821\ \text{liter atm/deg mole}) \times 300.15\ \text{deg}}{1\ \text{liter} - (0.5\ \text{mole} \times 0.0428821\ \text{liter/mole})} \\
&\quad - \frac{(3.608\ \text{liter}^2\ \text{atm/mole}^2) \times 0.5\ \text{mole}^2}{(1\ \text{liter})^2} \\
&= 11.69\ \text{atm}
\end{aligned}
$$