Topic: Ionic equilibria and buffers

Subject: Physical pharmacyI

Class: S.Y.B.Pharm(Sem III)

Academic year: 2018-2019

Programme:2017-2021

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TEACHING LEARING OUTCOMES

- To understand Strong electrolytes and weak electrolytes, dissociation of weak electrolytes, dissociation constant pH, Sorensen's pH scale, pH determination (glass electrode)
- Applications of buffers, buffer equation (Henderson-Hasselbalch equation), buffer capacity, buffers in pharmaceutical and biological systems

MAPPING OF TLO WITH COS

Sr.no	Topic Learning Outcomes	COs	BL
1	To understand Strong electrolytes and weak electrolytes, dissociation of weak electrolytes, dissociation constant pH, Sorensen's pH scale, pH determination (glass electrode)	CO3	L2
2	Applications of buffers, buffer equation (Henderson-Hasselbalch equation), buffer capacity, buffers in pharmaceutical and biological systems	CO4	L3

CONTENTS

- Strong electrolytes and weak electrolytes.
- Dissociation of weak electrolytes, dissociation constant
- Define pH
- Sorensen’s pH scale
- pH determination (glass electrode)
- Define buffer
- Applications of buffers
- Buffer equation (Henderson- Hasselbalch equation)
- Buffer capacity
- Buffers in pharmaceutical and biological systems

Chapter 4
Ionic equilibria

Lecture 1

History

- The term PH was first used in 1909 by Soren Peter Lauritz Sorensen.
- He never mentioned what the little “P”stood for (H is obviously for the Hydrogen)
- No matter what the historical origin, it’s important to remember that the symbol pH now stands for the negative logarithm of the H ion concentration

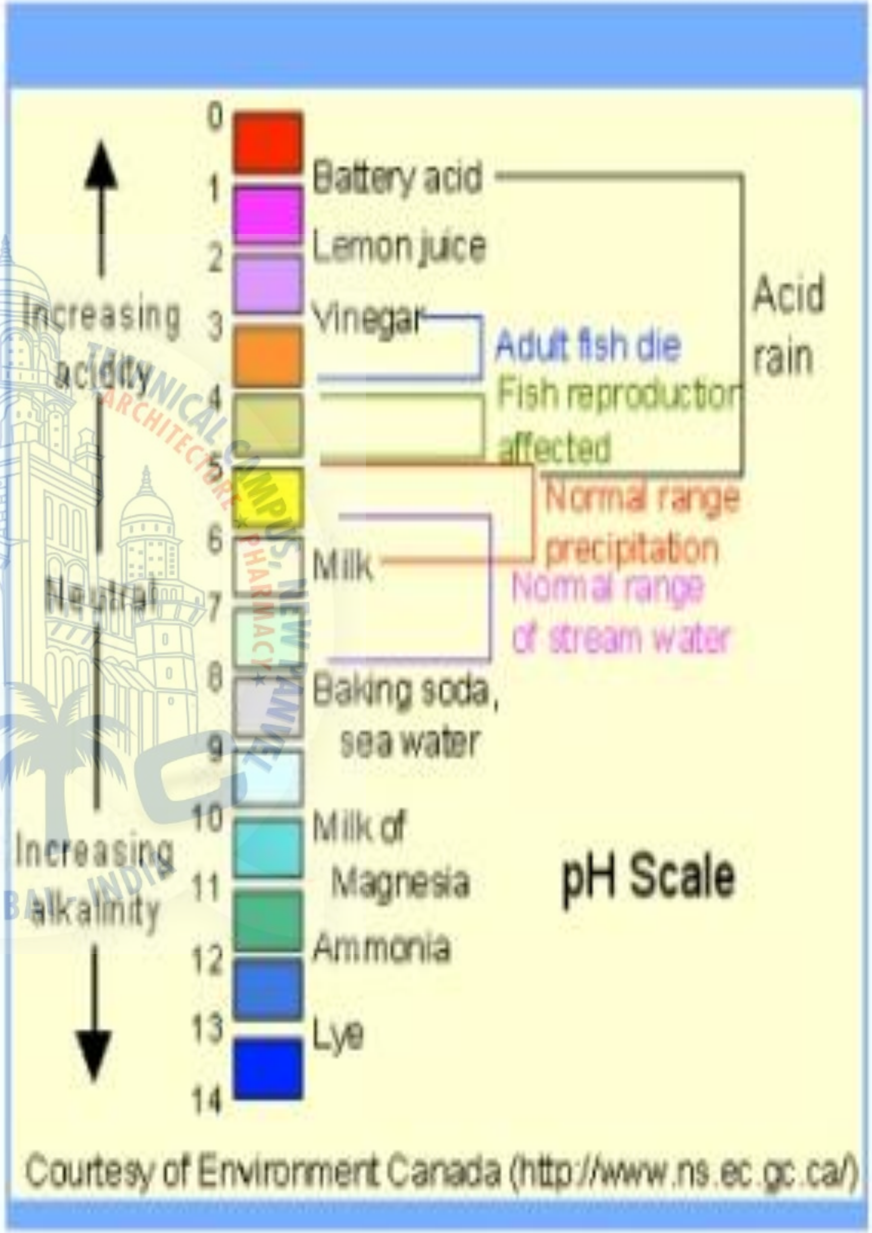
Soren Peter Lauritz Sorensen

Introduction

- Acidic and basic are two extremes that describe a chemical property chemicals.
- Mixing acids and bases can cancel out or neutralize their extreme effects. A substance that is neither acidic nor basic is neutral.

- pH = 7 means neutral.
- The region with pH values below 7 is designated as a acidic and above pH 7.0 is designated as basic (or alkaline).
- The pH numbers obtained by measuring solutions containing colloids and non aqueous solutions have little correlation on the activity scale.

- The pH scale measures how acidic or basic a substance is. The pH scale ranges from 0 to 14. A pH of 7 is neutral. A pH less than 7 is acidic. A pH greater than 7 is basic.



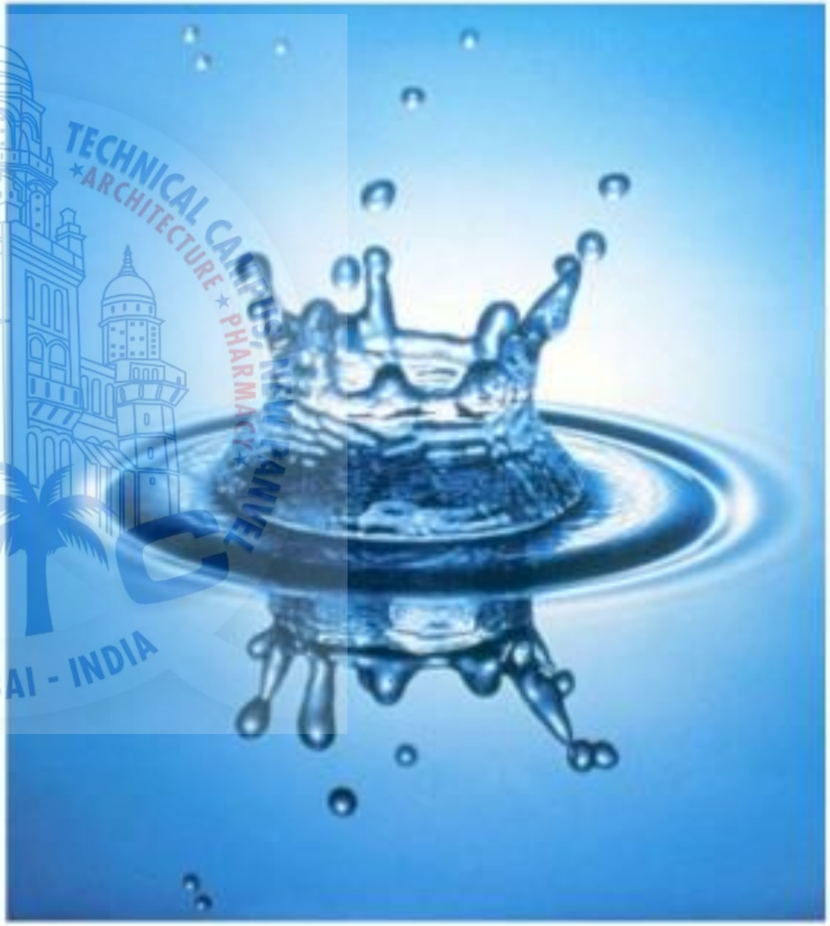
Courtesy of Environment Canada (http://www.ns.ec.gc.ca/)

How you measure the PH?

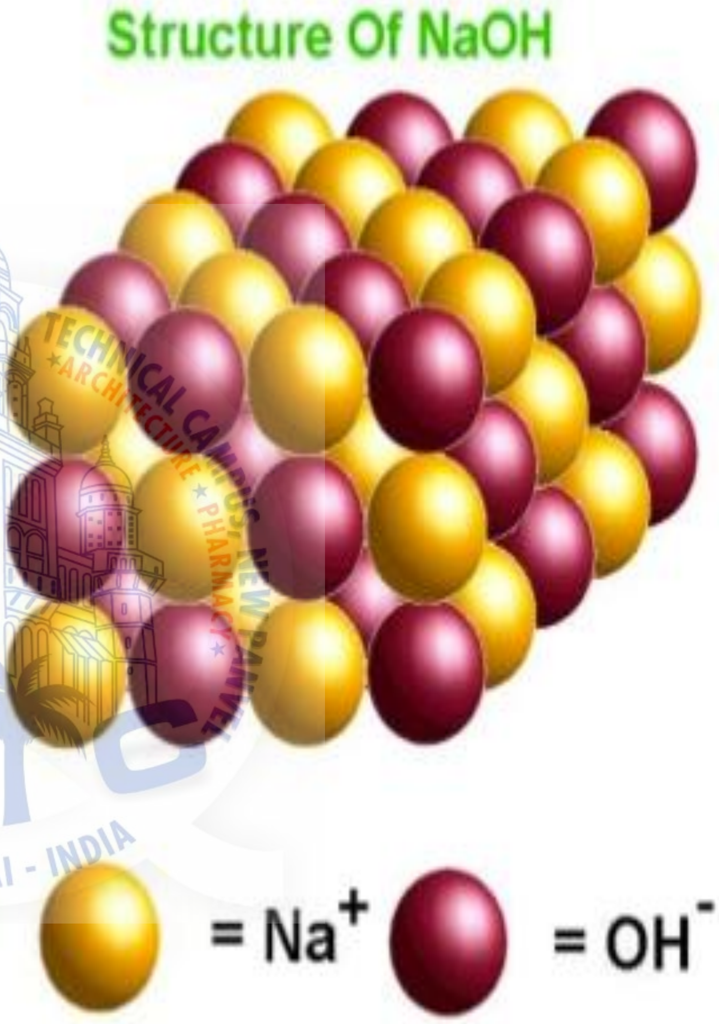
- The pH scale is logarithmic and as a result, each whole pH value below 7 is ten times more acidic than the next higher value.
- For example, pH 4 is ten times more acidic than pH 5 and 100 times (10 times 10) more acidic than pH 6.
- The same holds true for pH values above 7, each of which is ten times more alkaline (another way to say basic) than the next lower whole value.
- For example, pH 10 is ten times more alkaline than pH 9 and 100 times (10 times 10) more alkaline than pH 8.

Acid dissociation constants of weak acids

- Pure water is neutral. But when chemicals are mixed with water, the mixture can become either acidic or basic. Examples of acidic substances are vinegar and lemon juice. Lye, milk of magnesia, and ammonia are examples of basic substances.

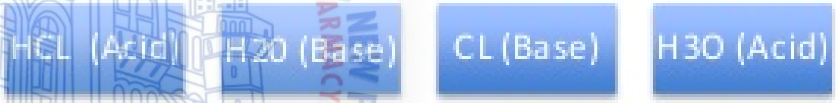


- Acids & bases that dissociate completrly in water, such as hydrochloric acid & sodium hydroxide, are called strong acids & strong bases



Let’s put an example

- We define an acid as a molecule that can donate a proton & a base, as a proton receptor.
- Acids & bases always come in pairs since for every proton donor thee must be a proton receptor
- Both sides of the dissociation reaction will contain an acid & a base


HCL (Acid)
H20 (Base)
CL (Base)
H3O (Acid)

pH and Sorensen's scale

- Electrolyte undergo dissociation in water producing ions.
- Acids undergo ionization in water giving hydrogen ions or hydronium ions.
- The thermodynamics definition for pH is
- pH is defined as negative logarithm of activity of hydrogen ions.
- Mathematically pH = -log a_{H+} -------------(1)
- where a_{H+} = activity of hydronium ion

- The activity of hydronium ion = hydronium ion concentration x rational activity coefficient .
- $a_{H^+} = c \times \gamma \pm$ ----------------(2)
- Substituting equation (2) in equation (1) gives
- $pH = -\log(c \times \gamma \pm)$ ------------------(3)

for practical purpose , activities are equal to concentration in dilute solution(when salts are not added) , because ionic strength is small. When neutral salt are added, the hydronium ions activity is affected and, hence activity coefficient should be employed, i.e. equation (3).

- Sorenson defined pH as the logarithm of the reciprocal of the hydrogen ion concentration.

Mathematically pH is expressed as a

$$pH = \log \frac{1}{[H_3O^+]} \text{ --------- } (4)$$

Equation (4) may be rearranged as:

$$pH = \log 1 - \log[H_3O^+] \text{ ---------------- } (5)$$

- Since log 1 is zero, equation (5) is written as :

$$pH = -\log[H_30^+] \text{-------------------}(6)$$

Thus , pH defined as negative logarithm of hydrogen ion concentration.

Sorensen established the term pH , to represent hydrogen ion potential. The term p used to express the negative logarithm .

The concentration of the H_30^+ is expressed in molarity, moles/liter etc.

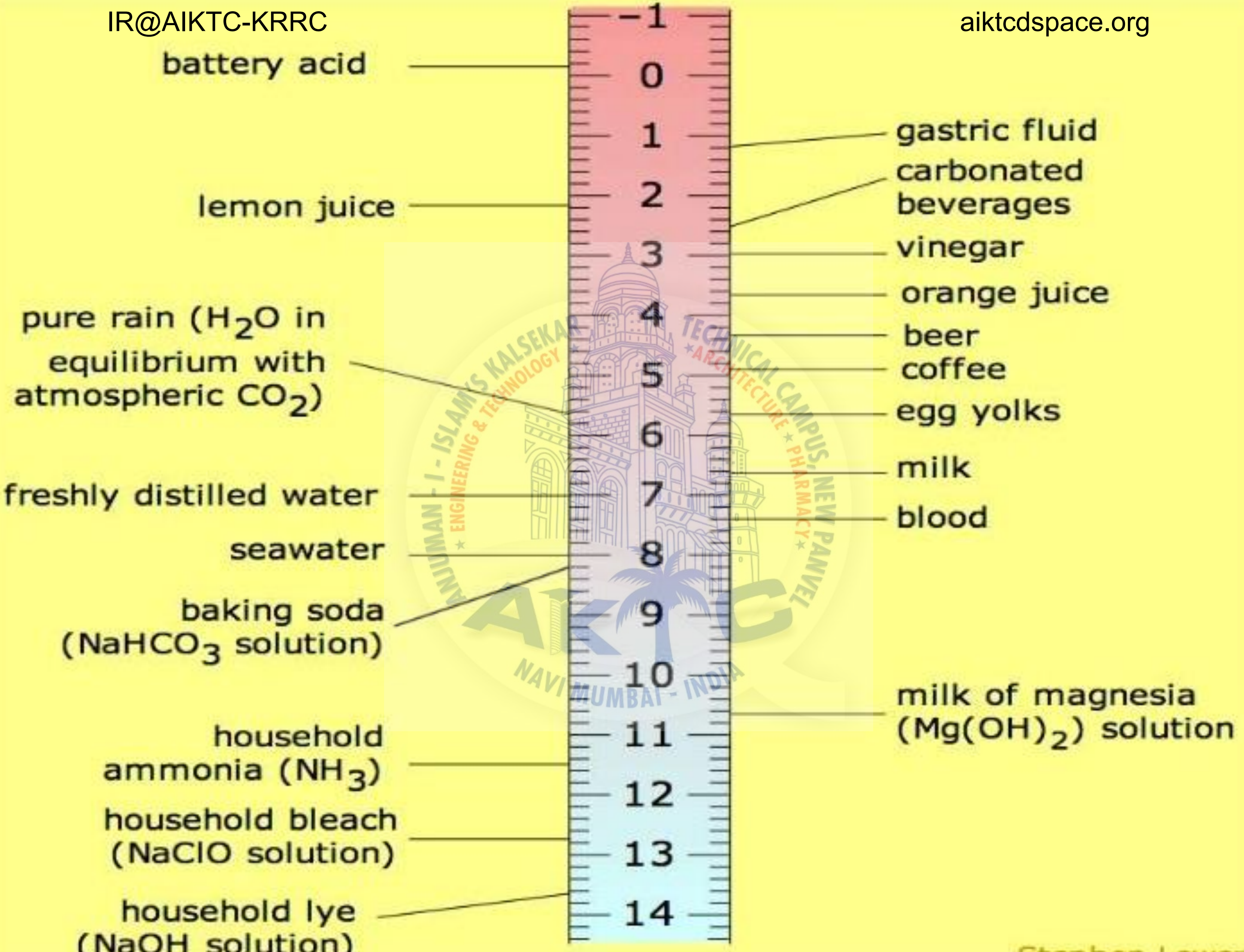
SORENSEN’S pH SCALE

Based on the pH values and different concentration of H_30^+ ions, a scale is devised and named after Sorenson, who had developed it.

The scale starts with a zero pH, i.e., hydrogen ion concentration is 1(or 10^0). It means the solution is strongly acidic.

At the other end of the scale , pH is 14 i.e., hydrogen ion concentration is 10^{-14} .It means the solution is strongly alkaline.

The central point pH in the scale is 7.0, because [H3O+] is equal to [OH], i.e., hydrogen ion concentration is 10^{-7}.



battery acid

lemon juice

pure rain (H_2O in equilibrium with atmospheric CO_2)

freshly distilled water

seawater

baking soda ($NaHCO_3$ solution)

household ammonia (NH_3)

household bleach (NaClO solution)

household lye (NaOH solution)

gastric fluid

carbonated beverages

vinegar

orange juice

beer

coffee

egg yolks

milk

blood

milk of magnesia ($Mg(OH)_2$) solution

Stephen Lower

Self-Ionization of Water

$H_2O + H_2O \rightarrow H_3O^+ + OH^-$

Though pure water is considered a non-conductor, there is a slight, but measurable conductivity due to "self-ionization"

K_w - Ionization Constant for Water

In pure water at 25 °C:

$[H_3O^+] = 1 \times 10^{-7}$ mol/L

$[OH^-] = 1 \times 10^{-7}$ mol/L

K_w is a constant at 25 °C:

$Kw = [H_3O^+][OH^-]$

$Kw = (1 \times 10^{-7})(1 \times 10^{-7}) = 1 \times 10^{-14}$

Calculating pH, pOH

$$pH = -\log_{10}(H_3O^+)$$

$$pOH = -\log_{10}(OH^-)$$

Relationship between pH and pOH

$$pH + pOH = 14$$

Finding $[H_3O^+]$, $[OH^-]$ from pH, pOH

$$[H_3O^+] = 10^{-pH}$$

$$[OH^-] = 10^{-pOH}$$

pH + pOH = 14

$$\begin{tikzcd}[column sep=huge, row sep=huge]
H^+ \arrow[r, shift left, "{[OH^-] = \frac{1\ x\ 10^{-14}}{[H^+]}}"] \arrow[d, shift left, "{pH = -\log[H^+]}"] & OH^- \arrow[l, shift left, "{[H^+] = \frac{1\ x\ 10^{-14}}{[OH^-]}}"] \arrow[d, shift left, "{pOH = -\log[OH^-]}"] \\
pH \arrow[u, shift left, "{[H^+] = 10^{-pH}}"] \arrow[r, shift left, "{pOH = 14 - pH}"] & pOH \arrow[l, shift left, "{pH = 14 - pOH}"] \arrow[u, shift left, "{[OH^-] = 10^{-pOH}}"]
\end{tikzcd}$$

APPLICATION OF pH:

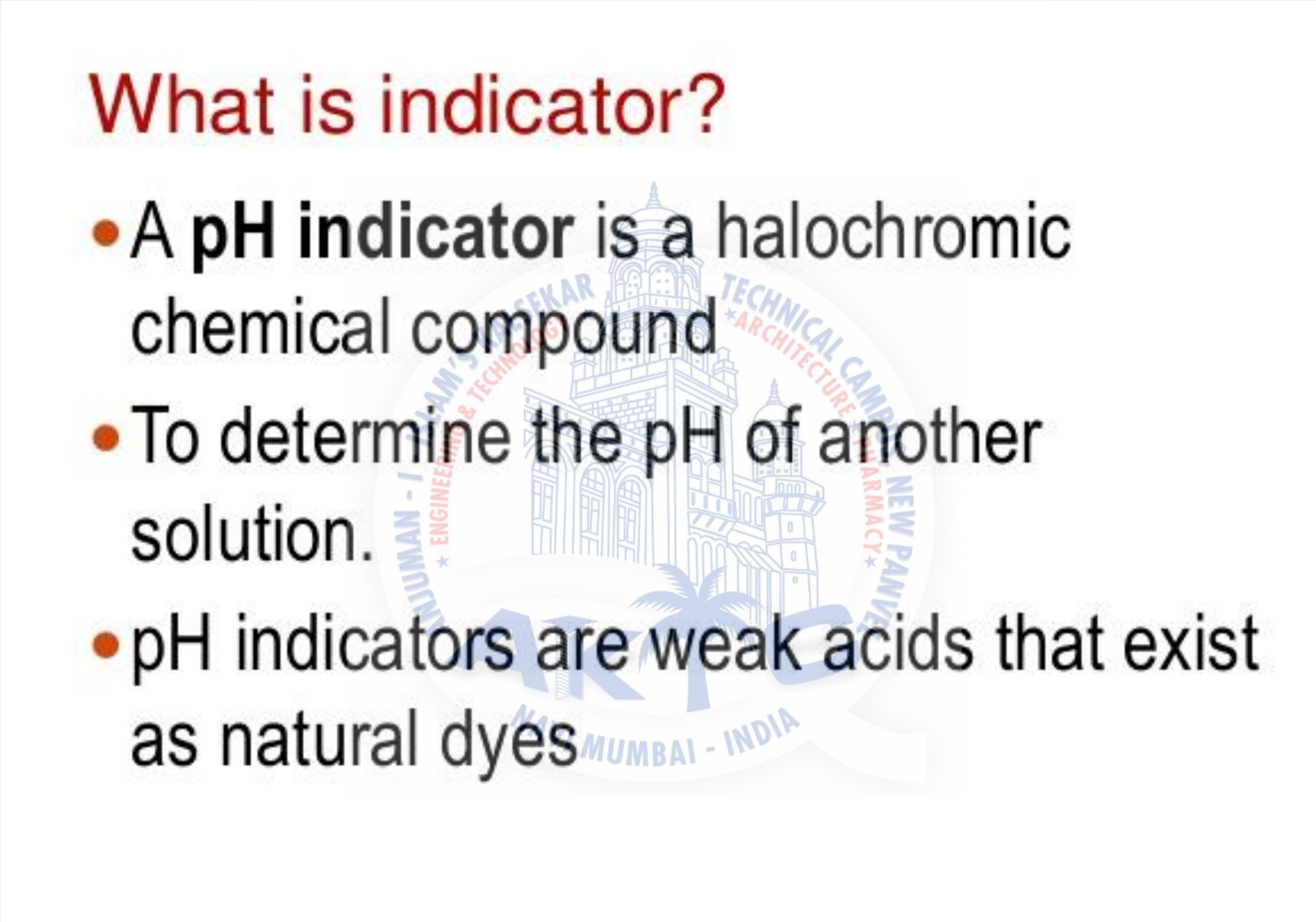
- Enhancing solubility
- Increasing stability
- Improving purity
- Optimizing biological activity
- Comforting the body
- Storage of products

pH indicators

Solution when added to a test solution produces a colour change, which helps in determining the pH of test solution.

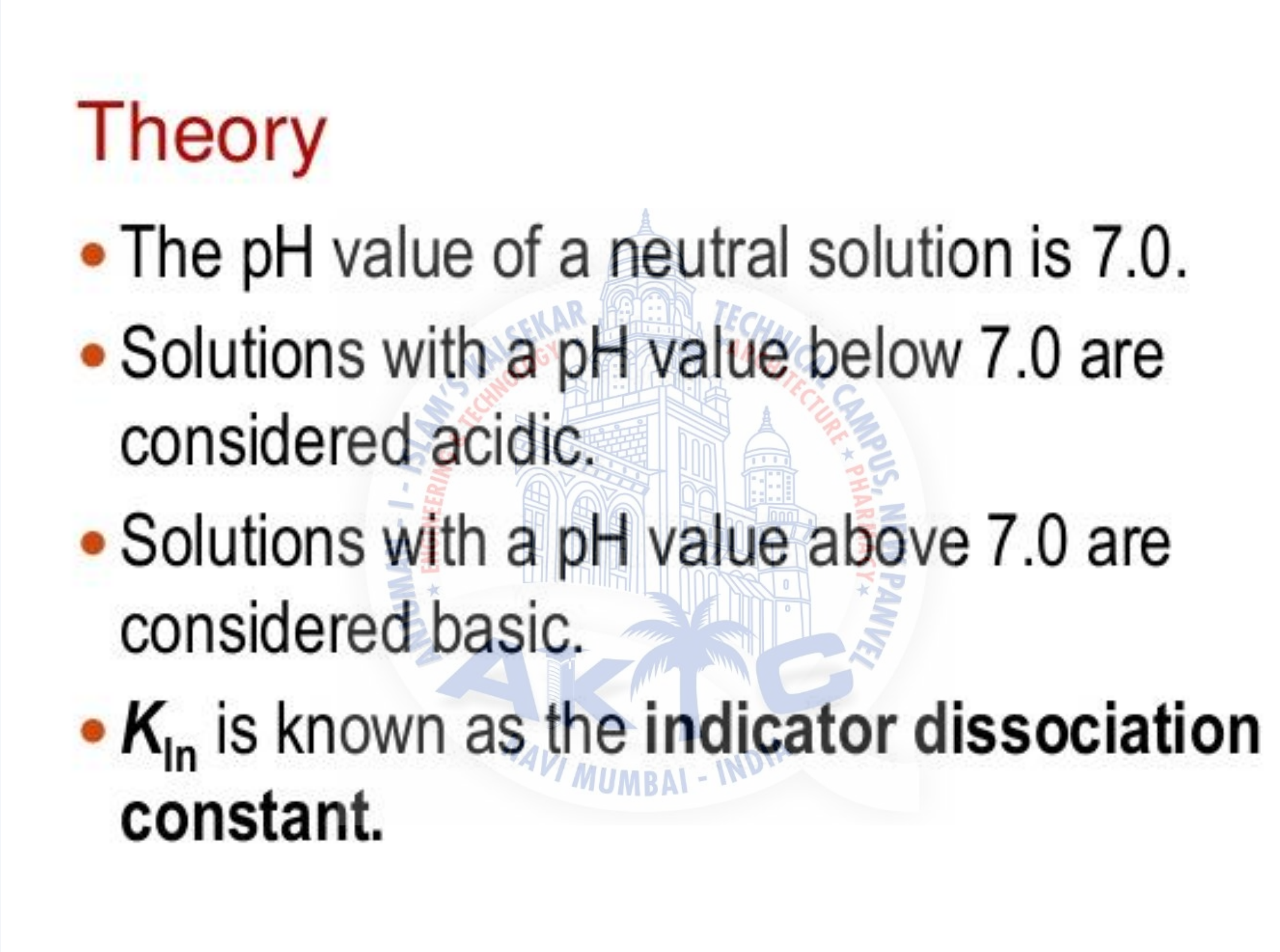
Universal indicator

Mixture of several indicators, which gives different colour shades as pH of solution varies, in particular pH range.



What is indicator?

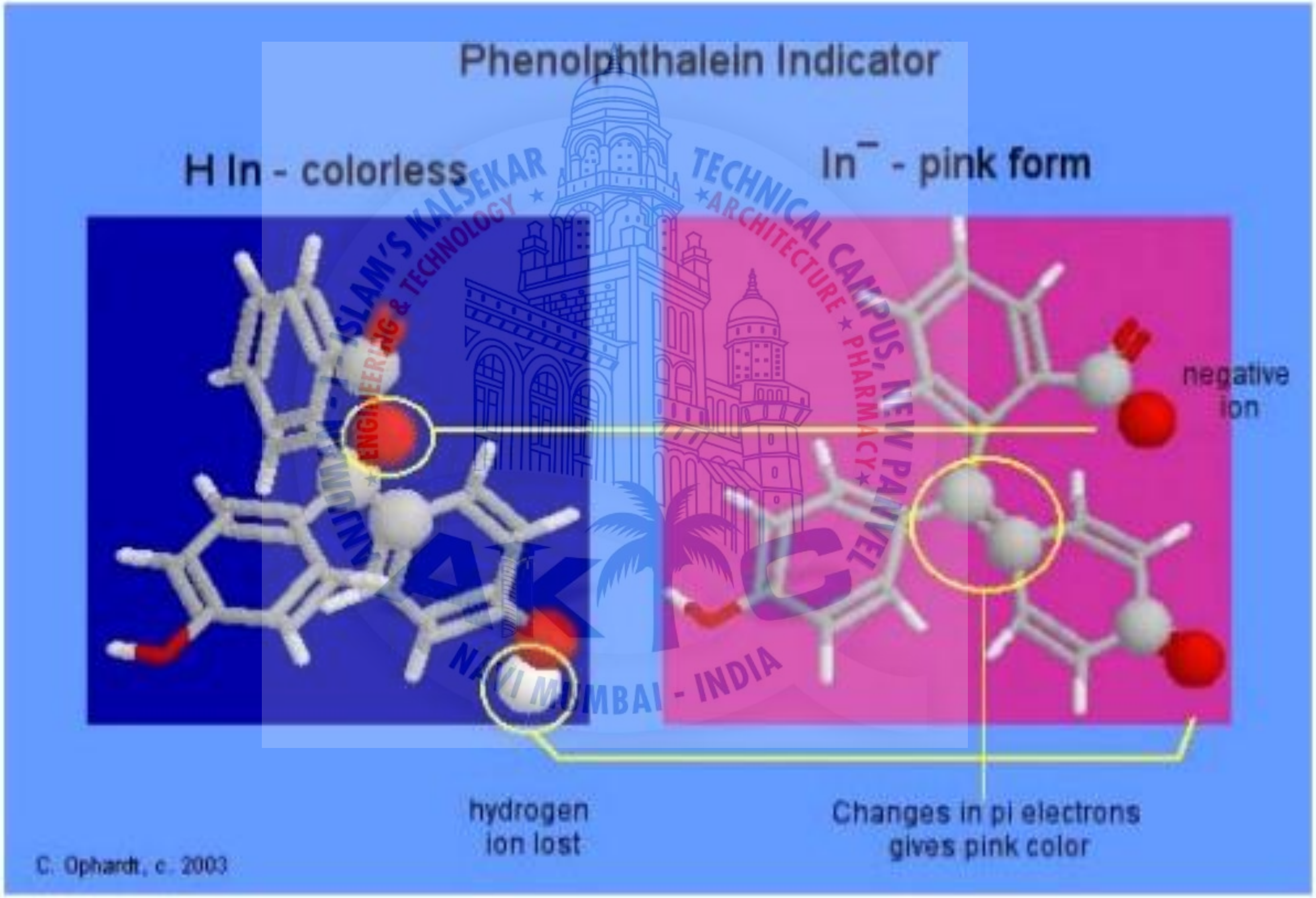
- A **pH indicator** is a halochromic chemical compound
- To determine the pH of another solution.
- pH indicators are weak acids that exist as natural dyes



Theory

- The pH value of a neutral solution is 7.0.
- Solutions with a pH value below 7.0 are considered acidic.
- Solutions with a pH value above 7.0 are considered basic.
- K_{In} is known as the **indicator dissociation constant.**

Molecular Basis for the Indicator Color Change:



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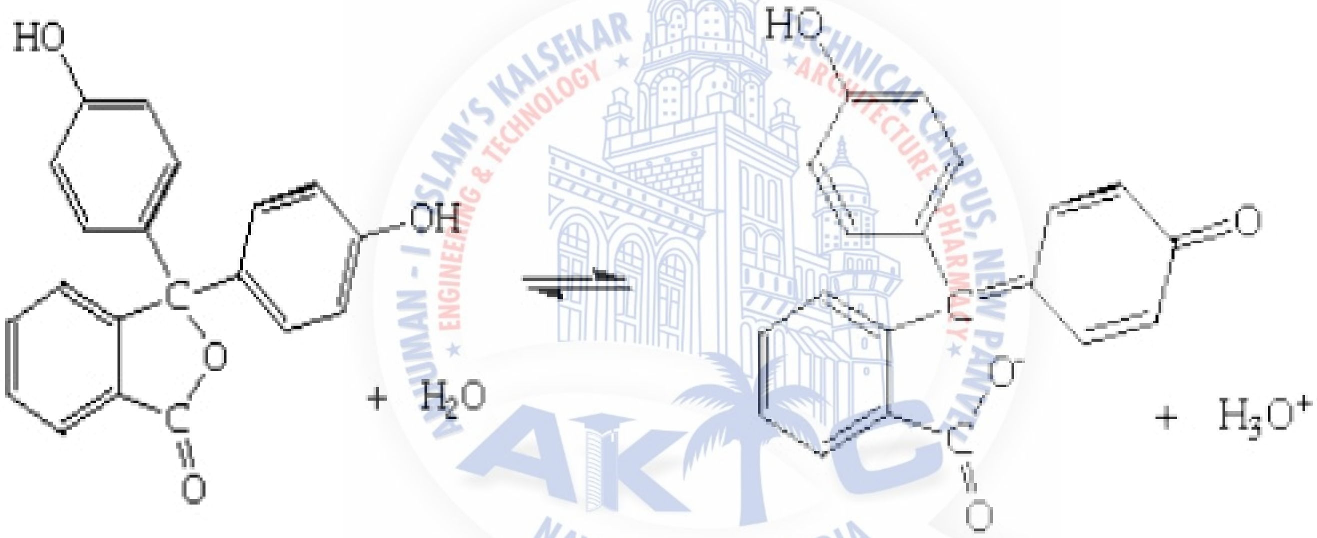
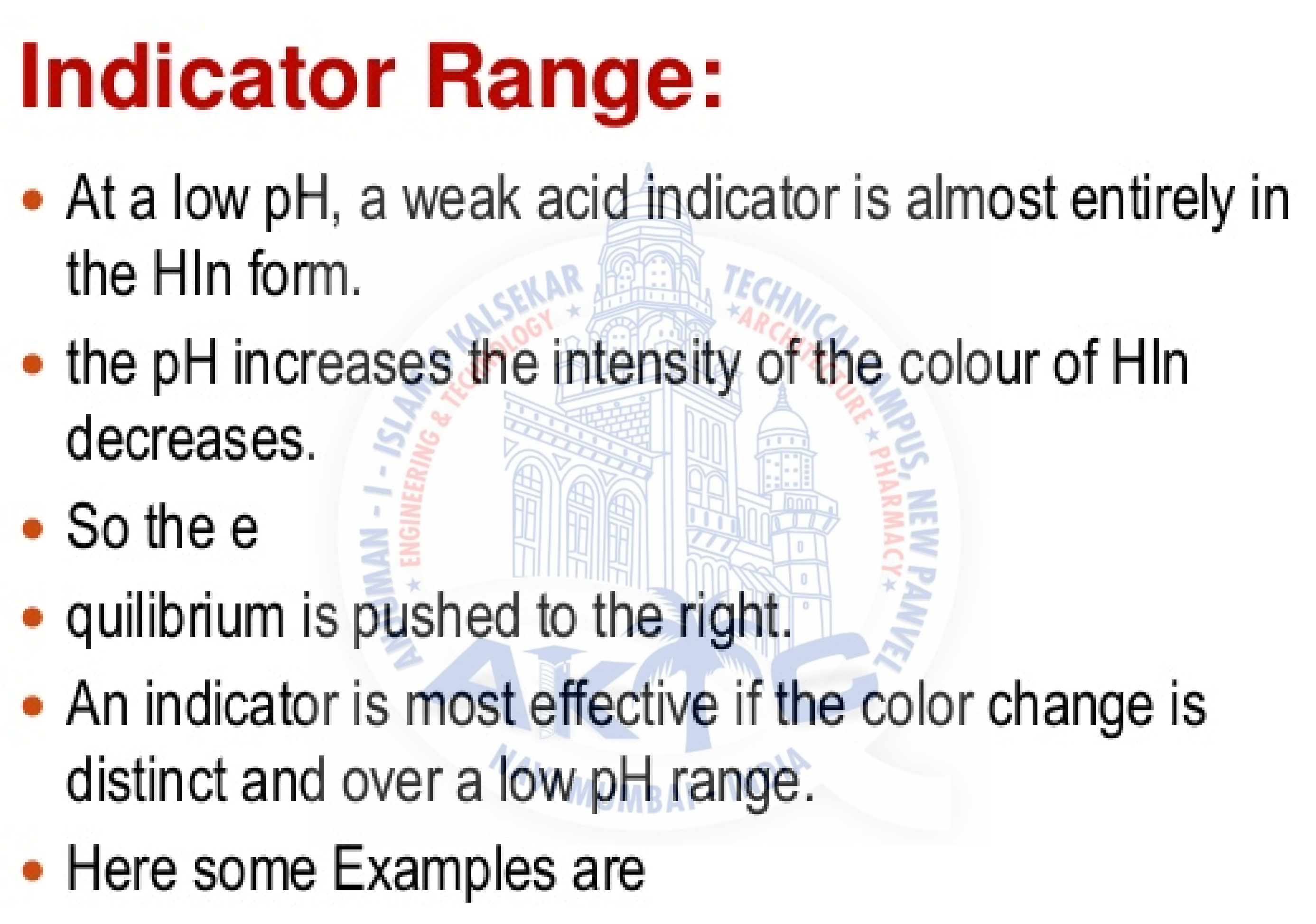
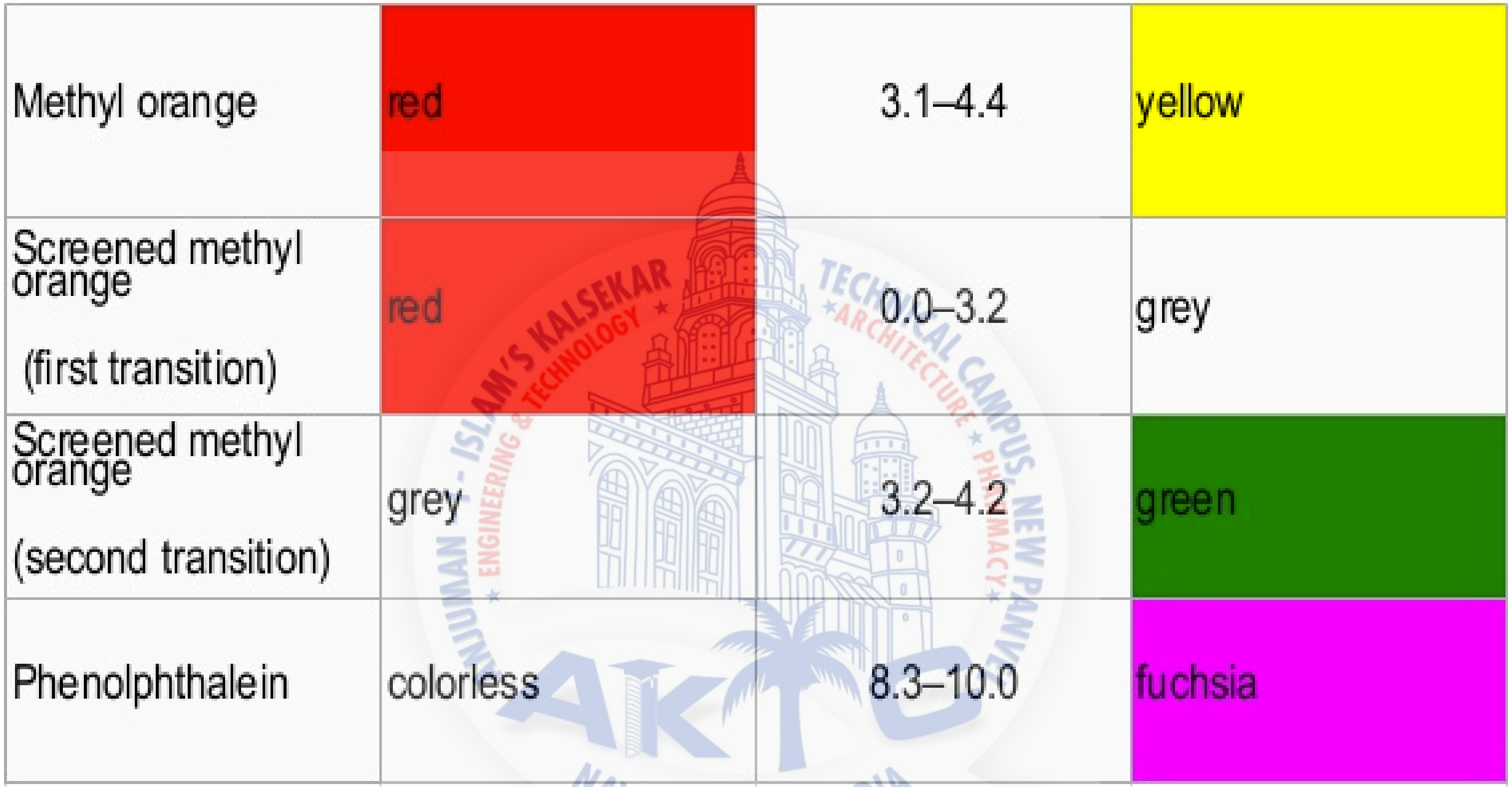


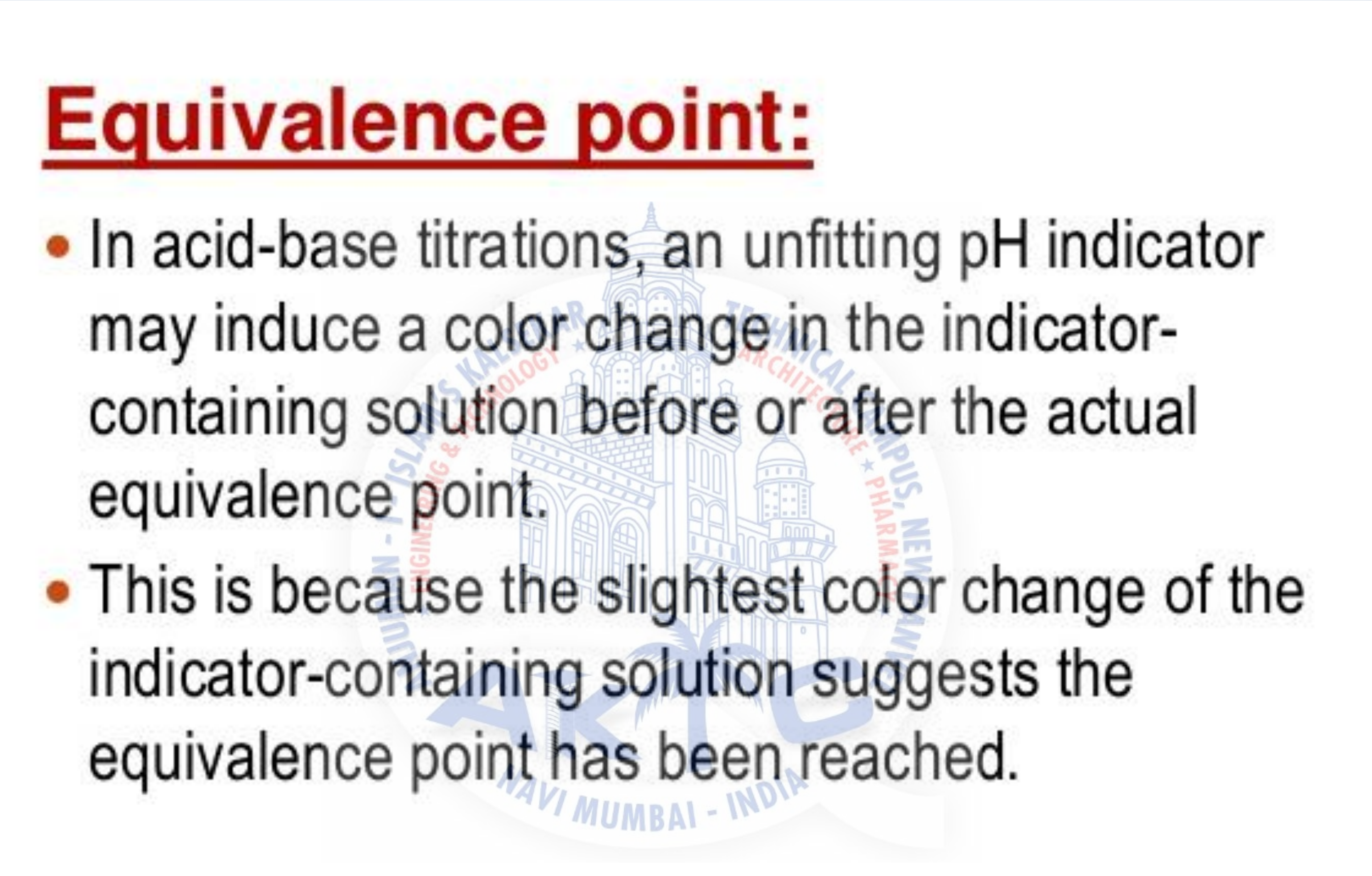


Indicator Range:

- At a low pH, a weak acid indicator is almost entirely in the HIn form.
- the pH increases the intensity of the colour of HIn decreases.
- So the e
- quilibrium is pushed to the right.
- An indicator is most effective if the color change is distinct and over a low pH range.
- Here some Examples are

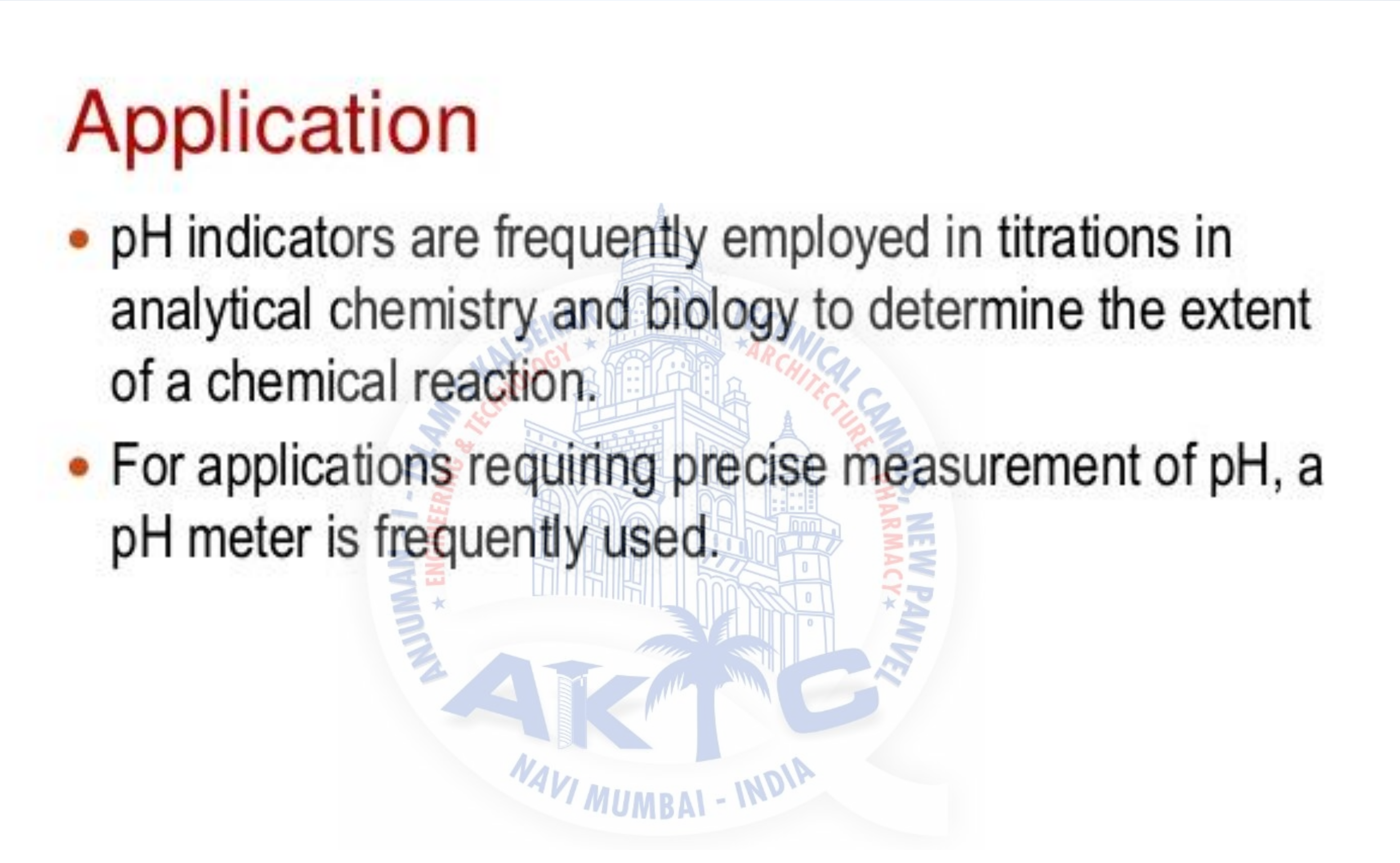


Methyl orange	red	3.1–4.4	yellow
Screened methyl orange (first transition)	red	0.0–3.2	grey
Screened methyl orange (second transition)	grey	3.2–4.2	green
Phenolphthalein	colorless	8.3–10.0	fuchsia



Equivalence point:

- In acid-base titrations, an unfitting pH indicator may induce a color change in the indicator-containing solution before or after the actual equivalence point.
- This is because the slightest color change of the indicator-containing solution suggests the equivalence point has been reached.



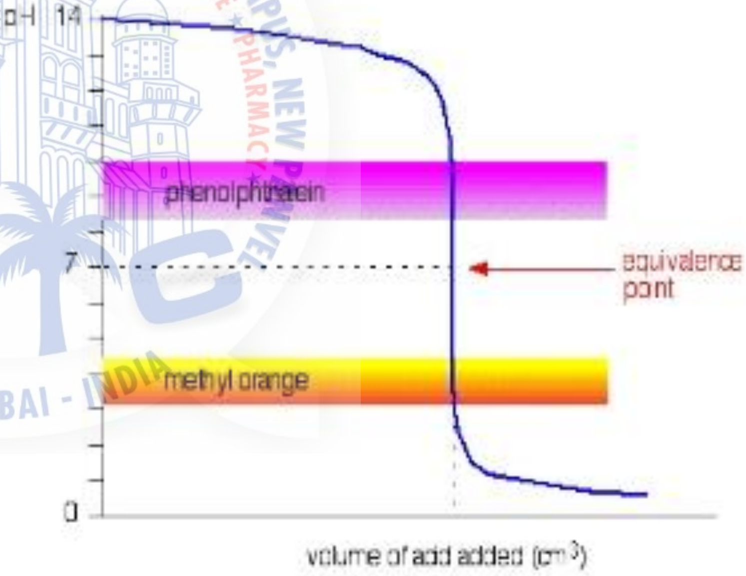
Application

- pH indicators are frequently employed in titrations in analytical chemistry and biology to determine the extent of a chemical reaction.
- For applications requiring precise measurement of pH, a pH meter is frequently used.

Choosing indicators for titrations:

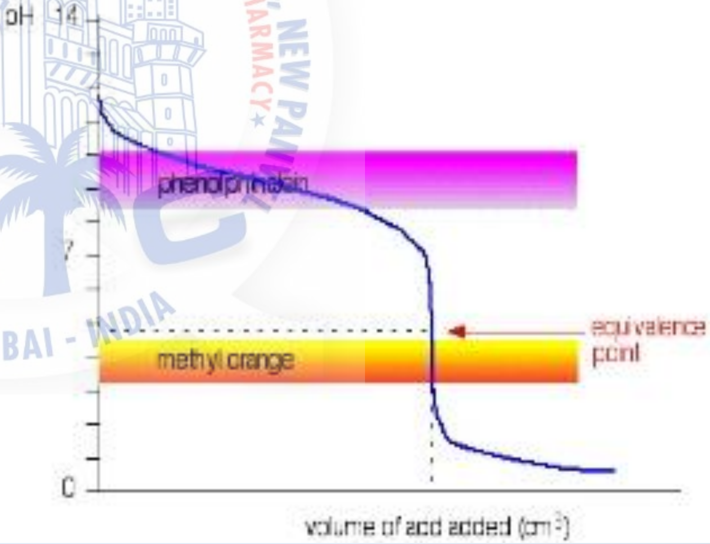
- **Strong acid v strong base.**

This diagram shows the pH curve for adding a strong acid to a strong base.



Cont…

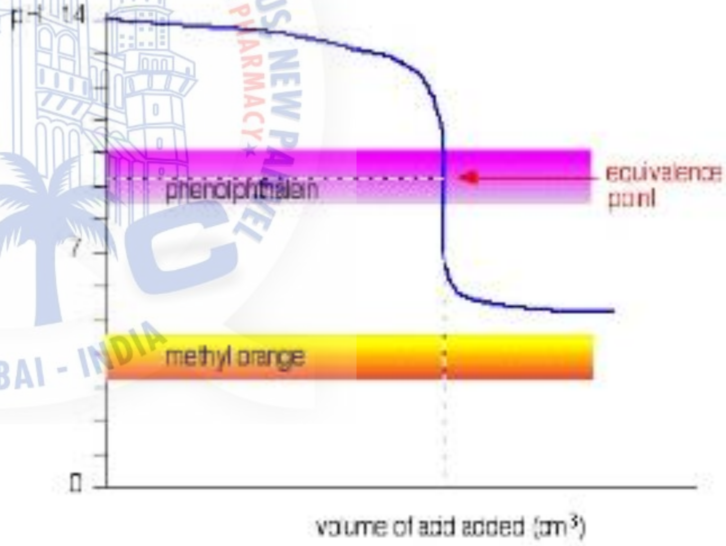
- **Strong acid vs weak base:** This time it is obvious that phenolphthalein would be completely useless. However, methyl orange starts to change from yellow towards orange very close to the equivalence point.



Cont…

- **Weak acid v strong base:**

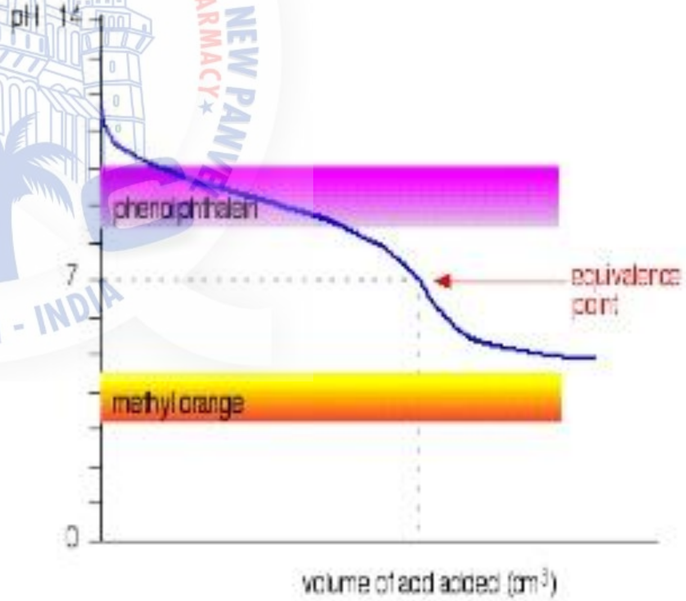
This time, the methyl orange is hopeless! However, the phenolphthalein changes color exactly where you want it to.

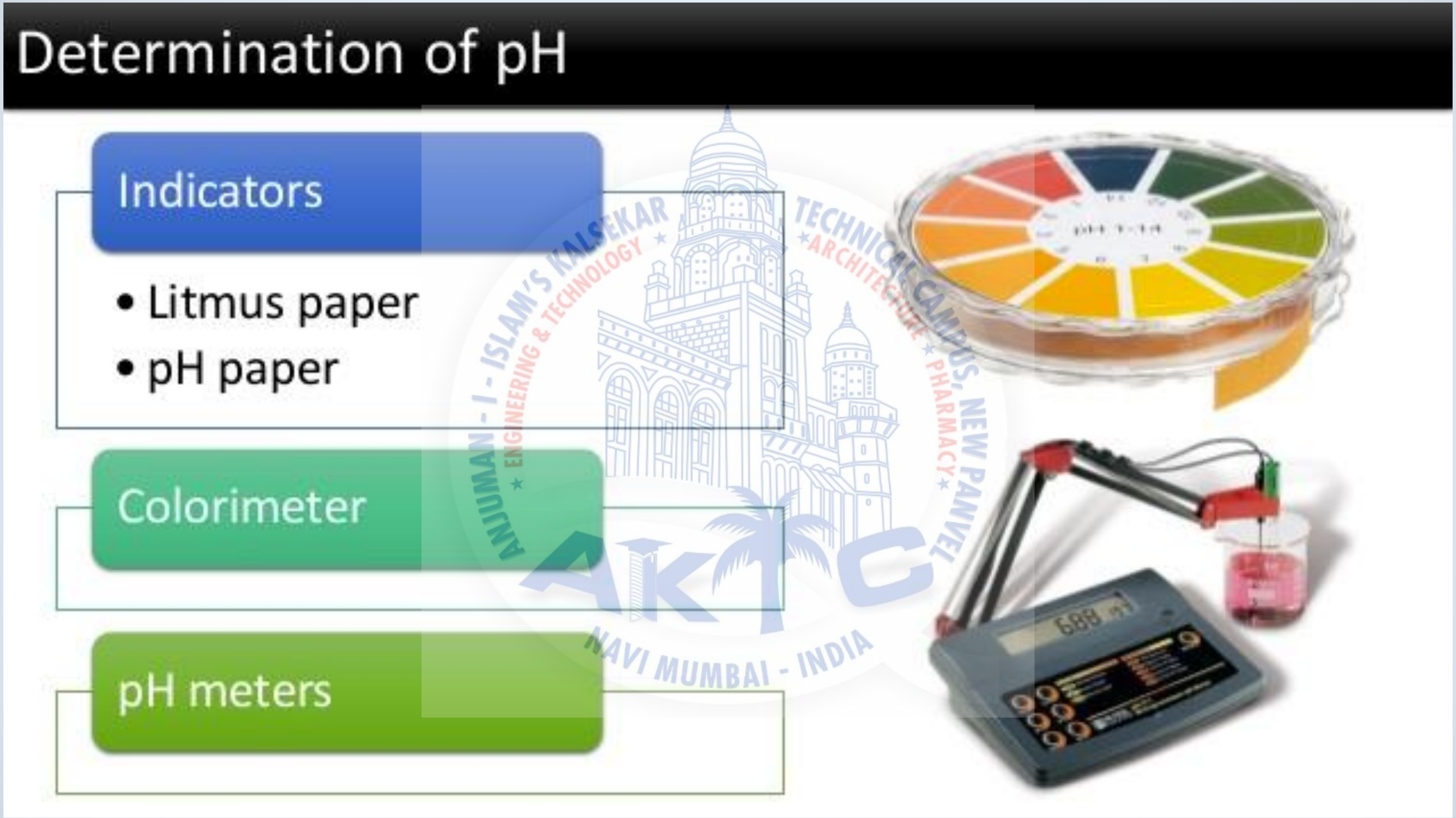


Cont…

- **Weak acid v weak base:**

The curve is for a case where the acid and base are both equally weak - for example, ethanoic acid and ammonia solution.





Determination of pH

Indicators

- Litmus paper
- pH paper

Colorimeter

pH meters

Colourimetric method

- Used to determine the pH of the solution upto +- 0.2 units in range of pH 3 to 11.0 based on colour change

Principle:

1. Capillators: buffer solution and universal indicator are mixed in capillary tubes. Small volume
2. Comparators. buffer solution and universal indicator are mixed in test tubes. large volume

METHOD

- Standard buffer solution 3-11.0
- Few drops of universal indicator
- Different colour produced
- Few drop of universal indicator in test solution
- Colour compared
- Then pH determined ex. 5 then again buffer solution of pH between 4-6 is made with interval of 0.2
- Then final exact pH determined.

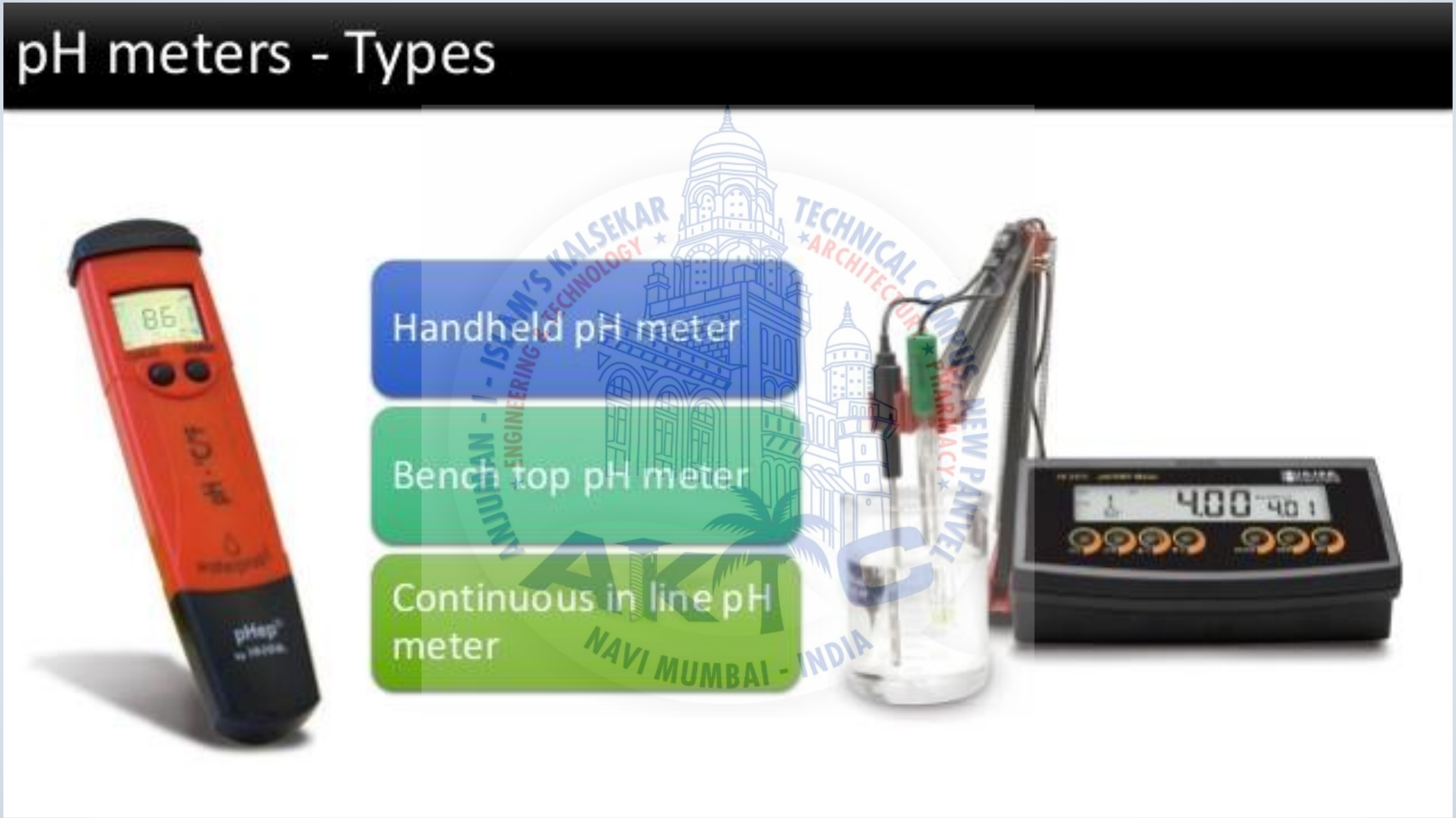
pH meters - History

Arnold Orville Beckman
(1900-2004)

pH meter or Electrometric method

pH determined by means of an electrode, whose potential depends on hydrogen ion activity

Electrodes like glass and hydrogen is used.



pH meters - Types

- Handheld pH meter
- Bench top pH meter
- Continuous in line pH meter

pH meters – pH Electrode

- Glass electrode
- Reference electrode
- Combination electrode
- 3 in 1 electrode

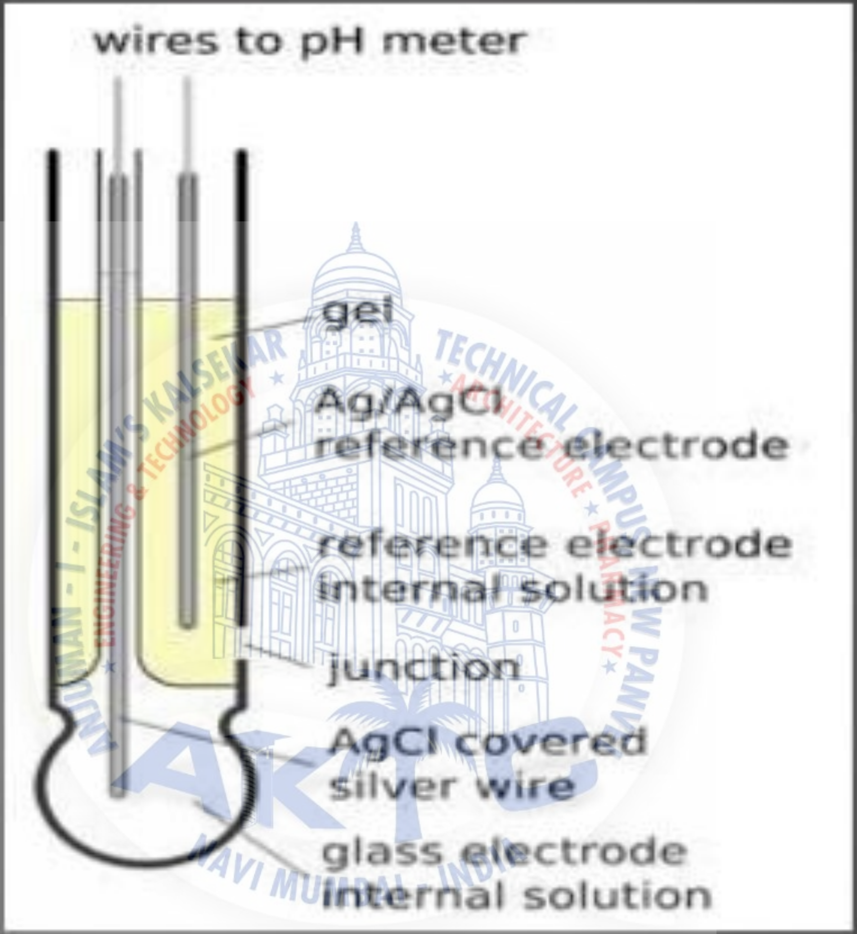


Figure : Combination gel electrode

Source : [http://www.ph-meter.info/pH-electrode-flow

pH meter -- Glass Electrode

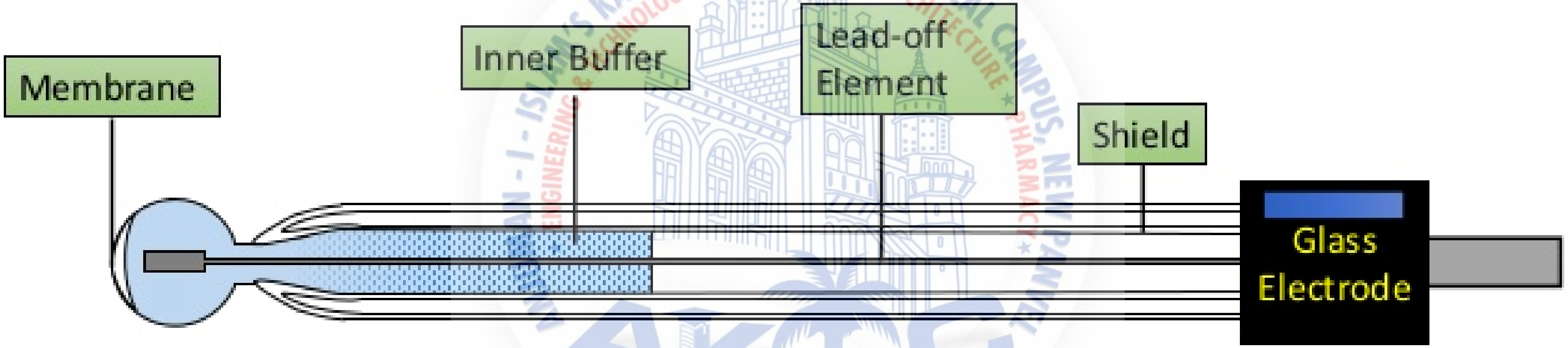


Fig Measuring (Glass) electrode

pH Reference Electrode

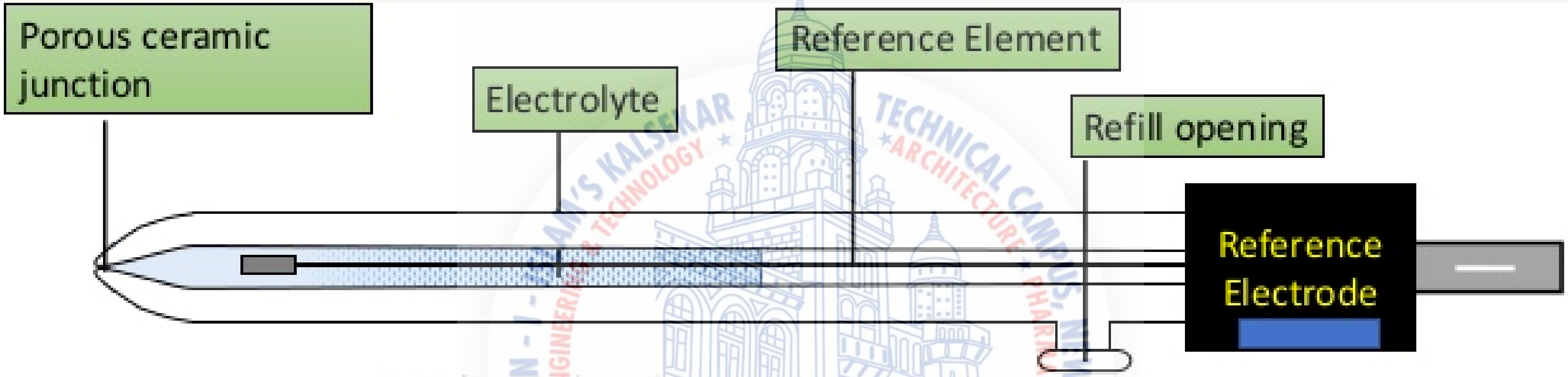


Fig Reference electrode

Reference electrolyte
- Inert
- High ion concentration → Low electrical resistance
- Contact with measuring solution

Popular Reference Systems
- Mercury/calomel
- Silver/Silver chloride

pH meter – Combination Electrode

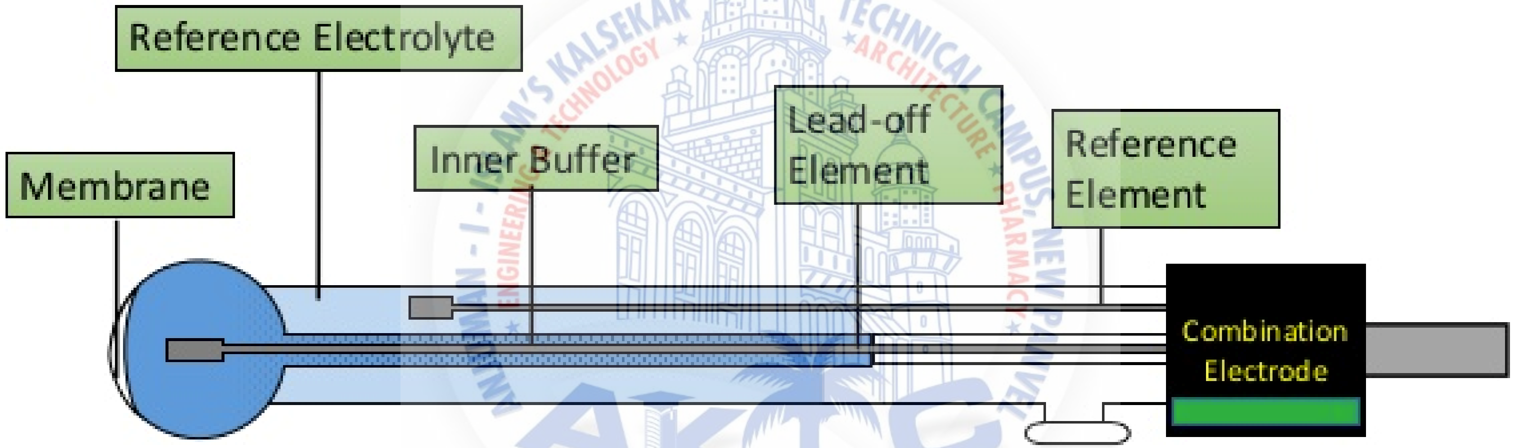


Fig Combination electrode

pH meter- Working principle

The potential of glass electrode is measured against that of reference electrode

$$E = E^0 + \boxed{\frac{2.303\,RT}{nF}}\log a_{H+}$$

Standard potential when $a_{H+} = 1 mol/L$

Nernst potential (E_N)/Slope factor
Change in potential per pH unit.
Depends on absolute temperature

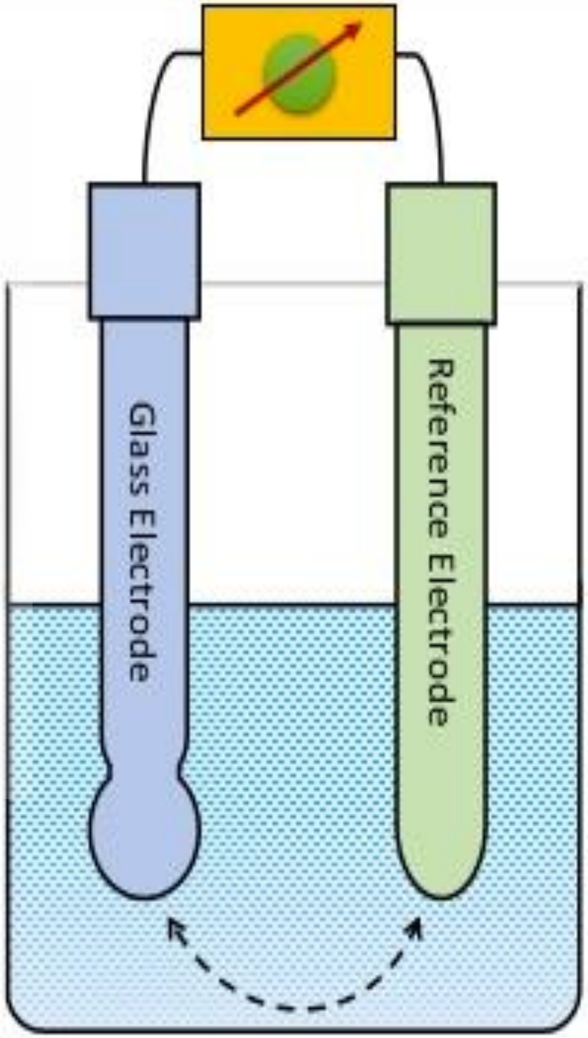
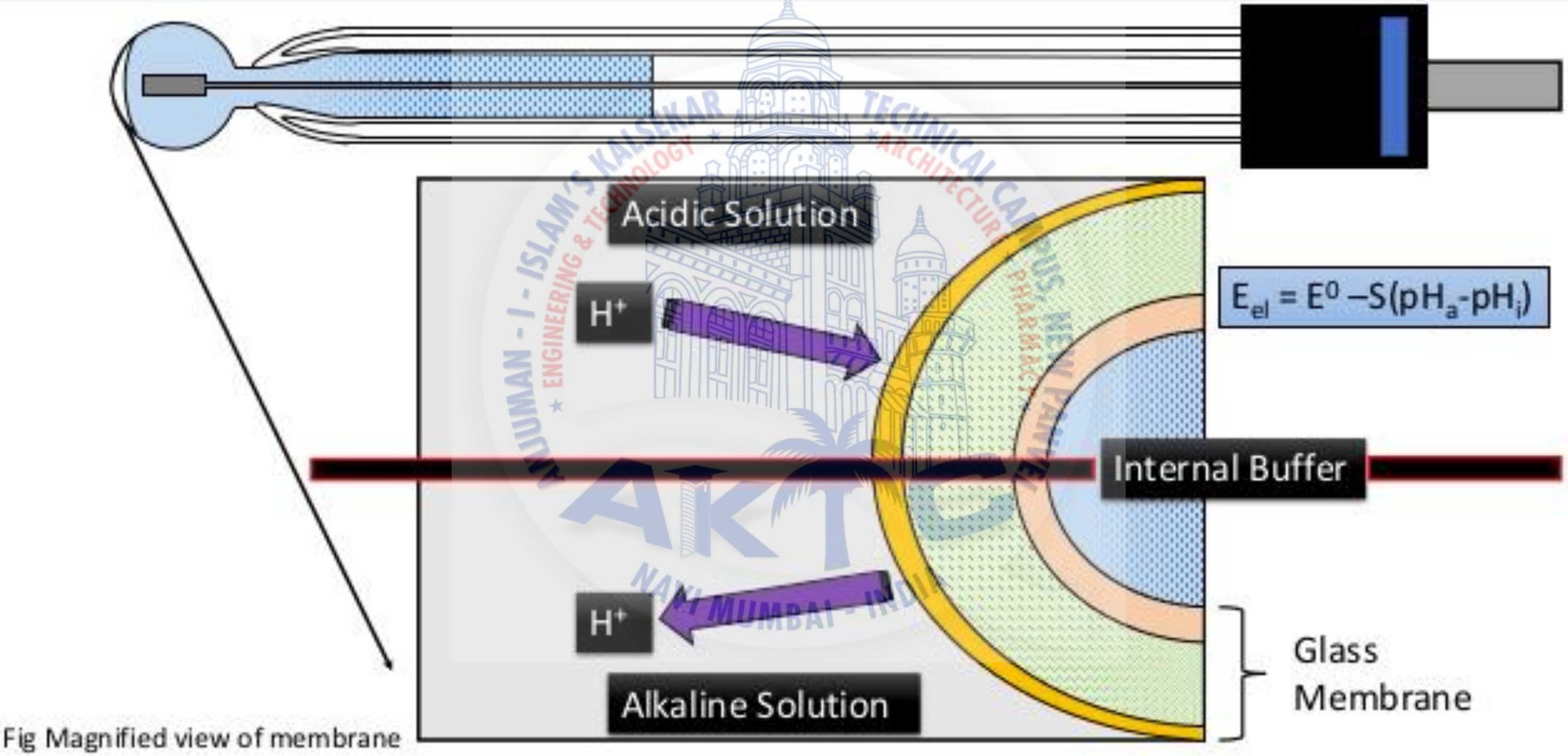


Fig Closed circuit of pH meter

pH Electrode – Working principle



$E_{el} = E^0 - S(pH_a - pH_i)$

Fig Magnified view of membrane

pH meter – working principle

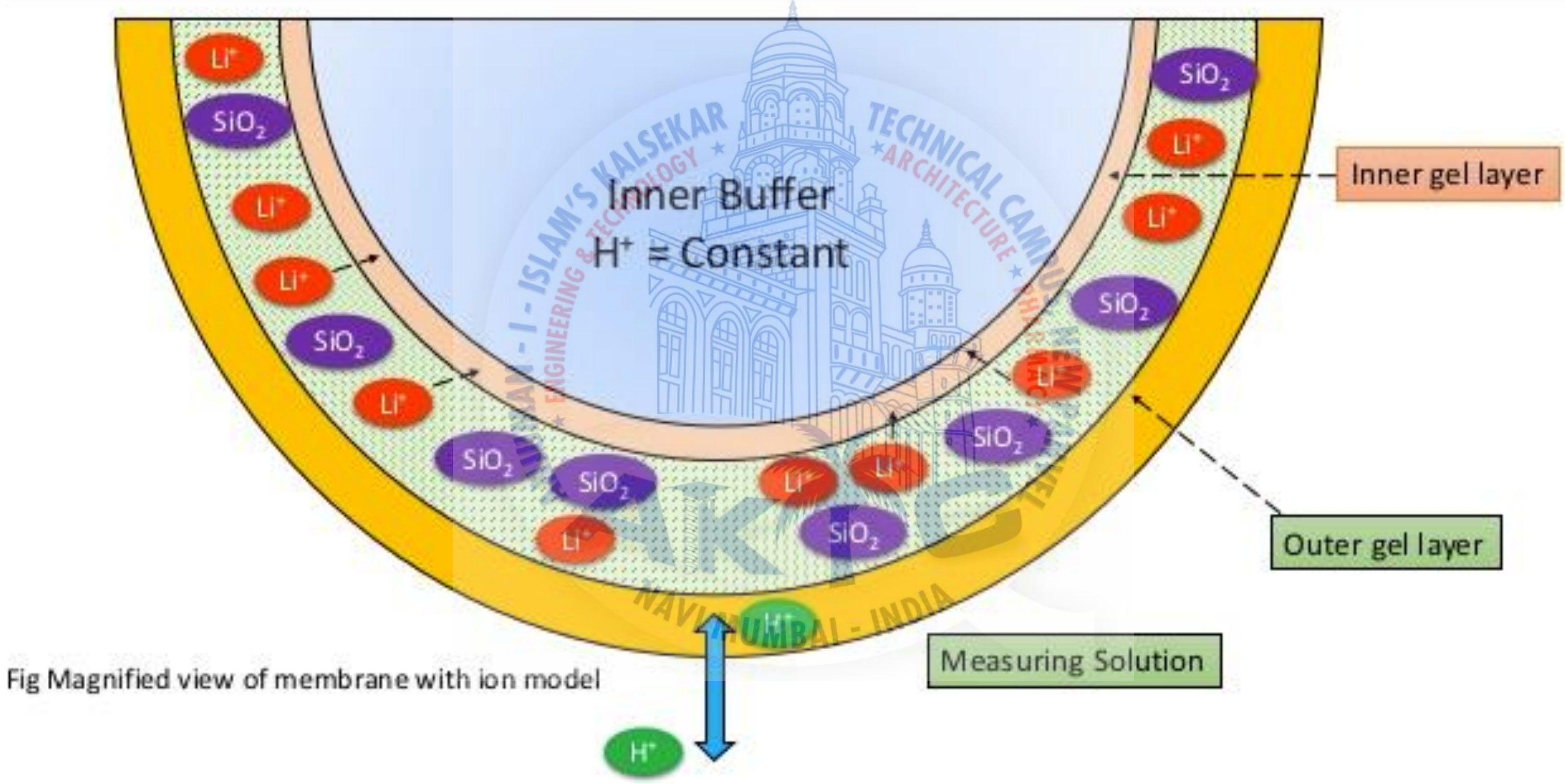
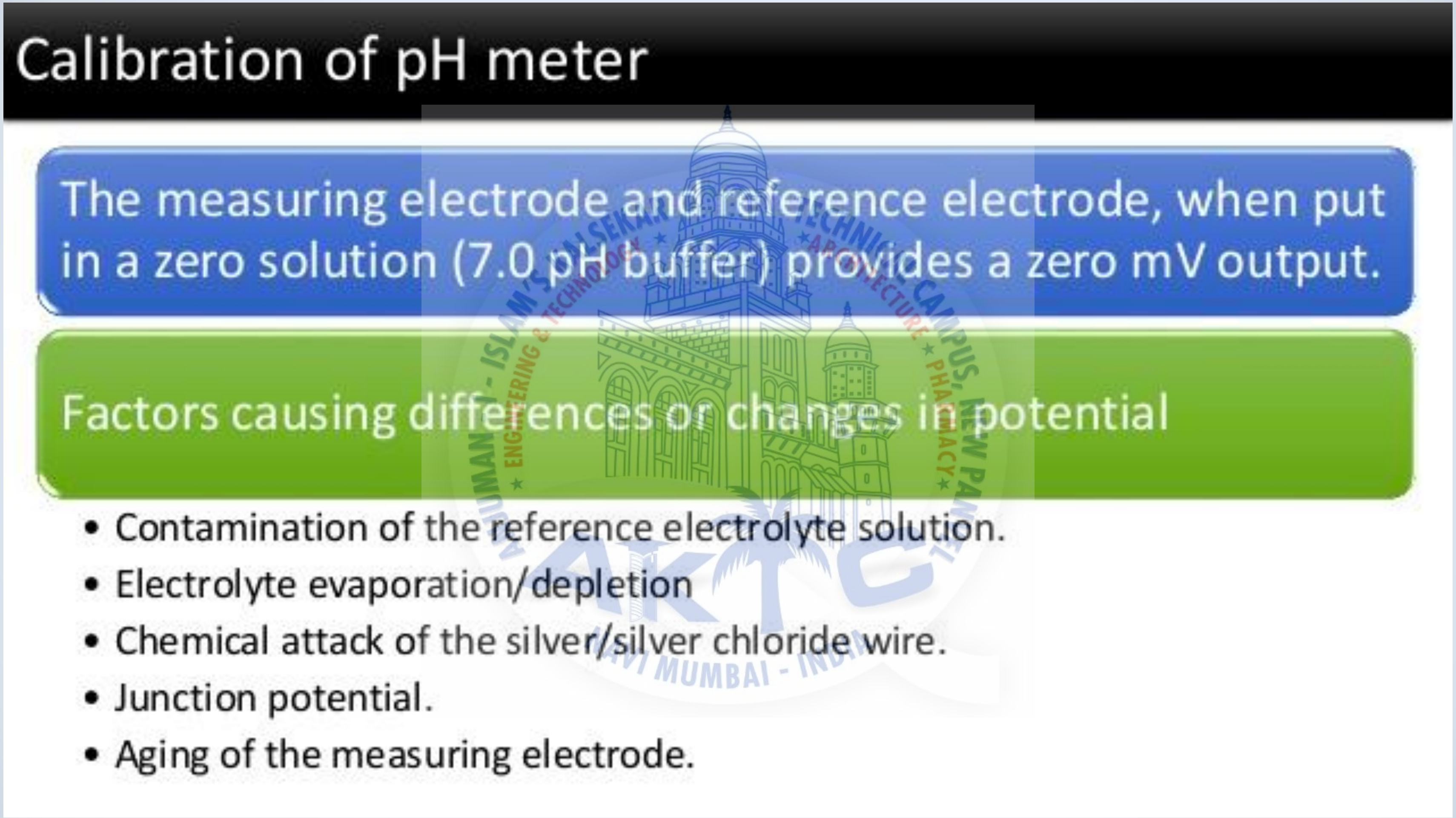


Fig Magnified view of membrane with ion model



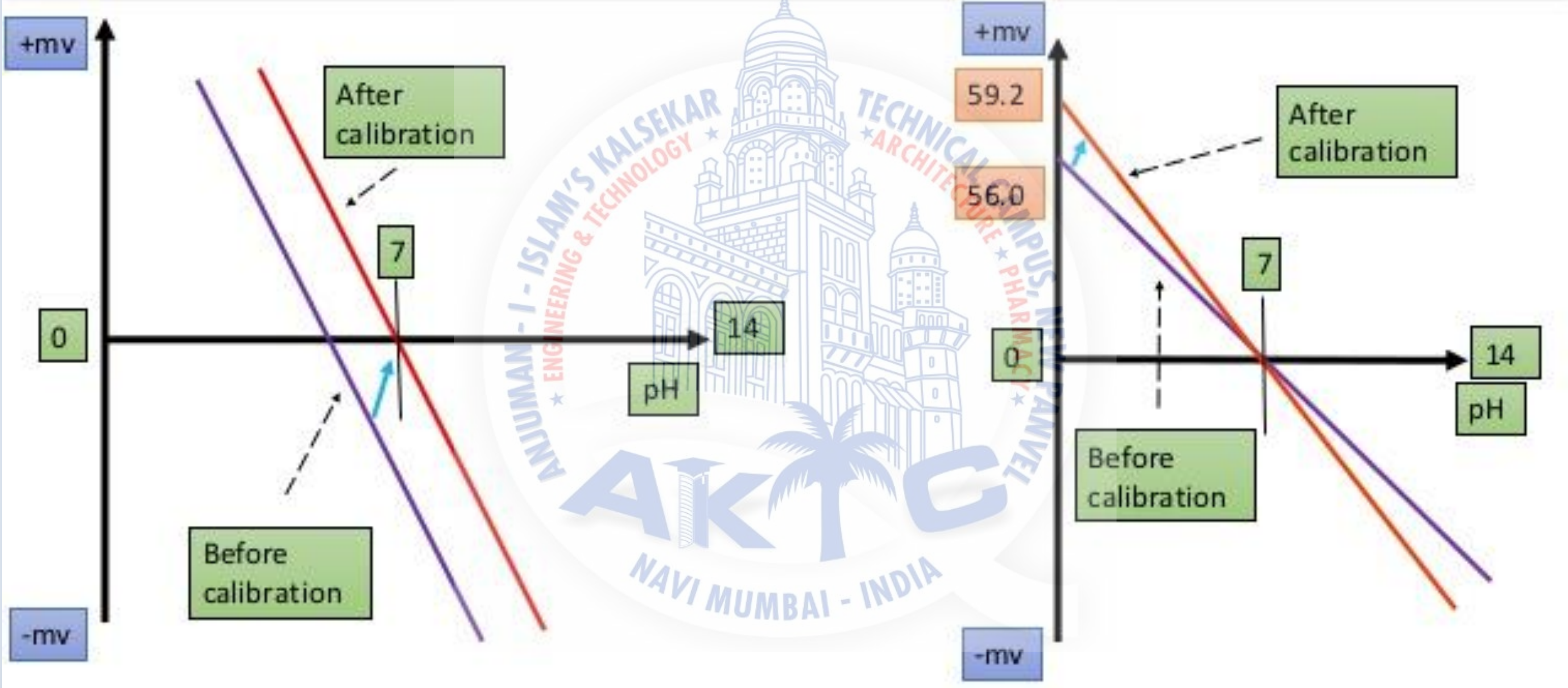
Calibration of pH meter

The measuring electrode and reference electrode, when put in a zero solution (7.0 pH buffer) provides a zero mV output.

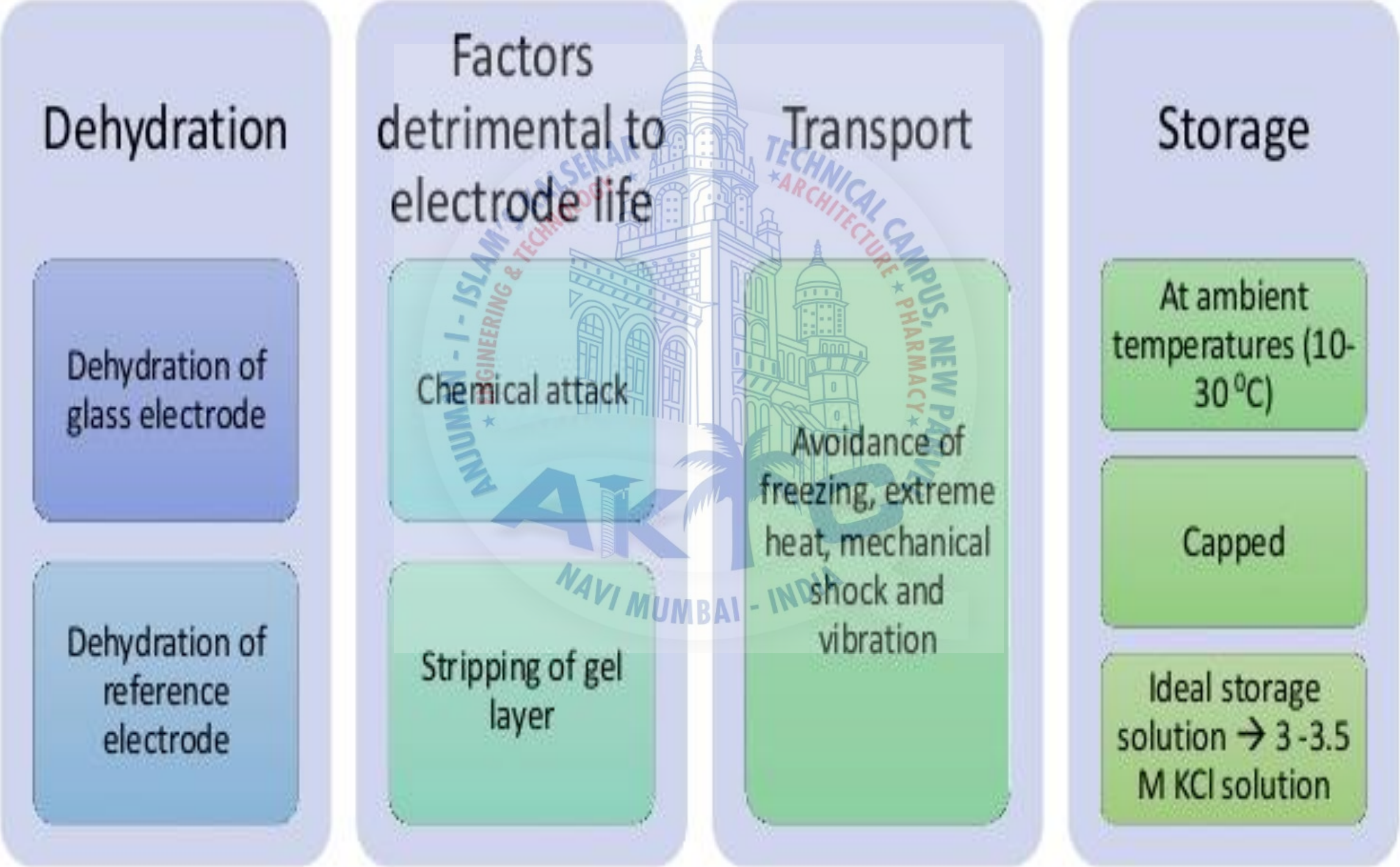
Factors causing differences or changes in potential

- Contamination of the reference electrolyte solution.
- Electrolyte evaporation/depletion
- Chemical attack of the silver/silver chloride wire.
- Junction potential.
- Aging of the measuring electrode.

Calibration of pH meter



Maintenance & Storage of pH electrode



Dehydration
- Dehydration of glass electrode
- Dehydration of reference electrode

Factors detrimental to electrode life
- Chemical attack
- Stripping of gel layer

Transport
- Avoidance of freezing, extreme heat, mechanical shock and vibration

Storage
- At ambient temperatures (10-30 ^{0}C)
- Capped
- Ideal storage solution → 3 -3.5 M KCl solution

pH Meter

Introduction

- A pH meter is an electronic instrument used for measuring the pH (acidity or alkalinity) of a liquid (though special probes are sometimes used to measure the pH of semi-solid substances). A typical pH meter consists of special measuring probes (a glass electrode and a reference electrode) connected to an electronic meter that measures and displays the pH reading.

Source : http://en.wikipedia.org/wiki/PH_meter

pH strips

Litmus dye is a natural pH indicator . Litmus paper is a small strip of paper that has dyes in it. When it touches a base or a dye then the litmus paper changes colors depending on , either it is a base or it is an acid. If a litmus paper is exposed to an acid it either changes its colour to pink or red. If a strip of litmus paper touches a base then the paper changes to a shade of blue.

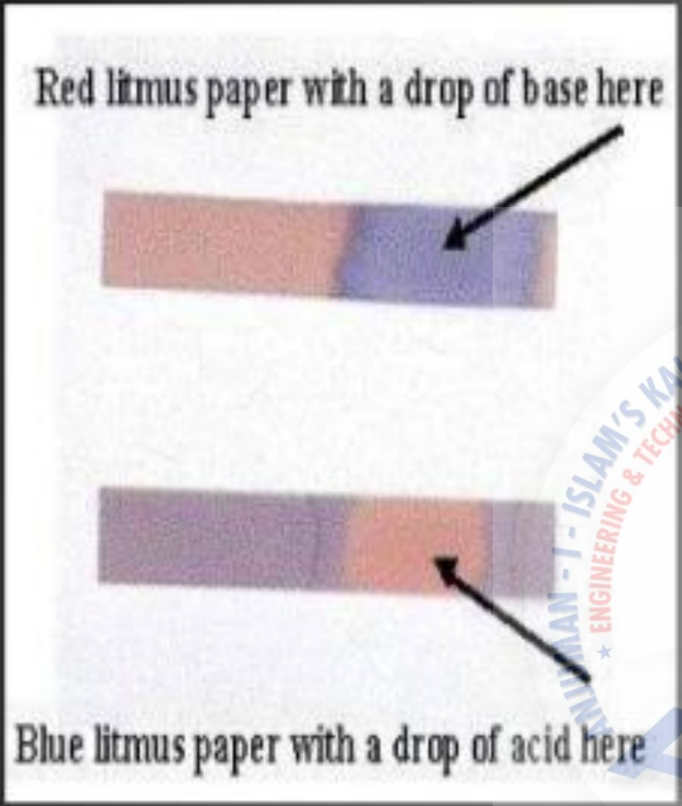
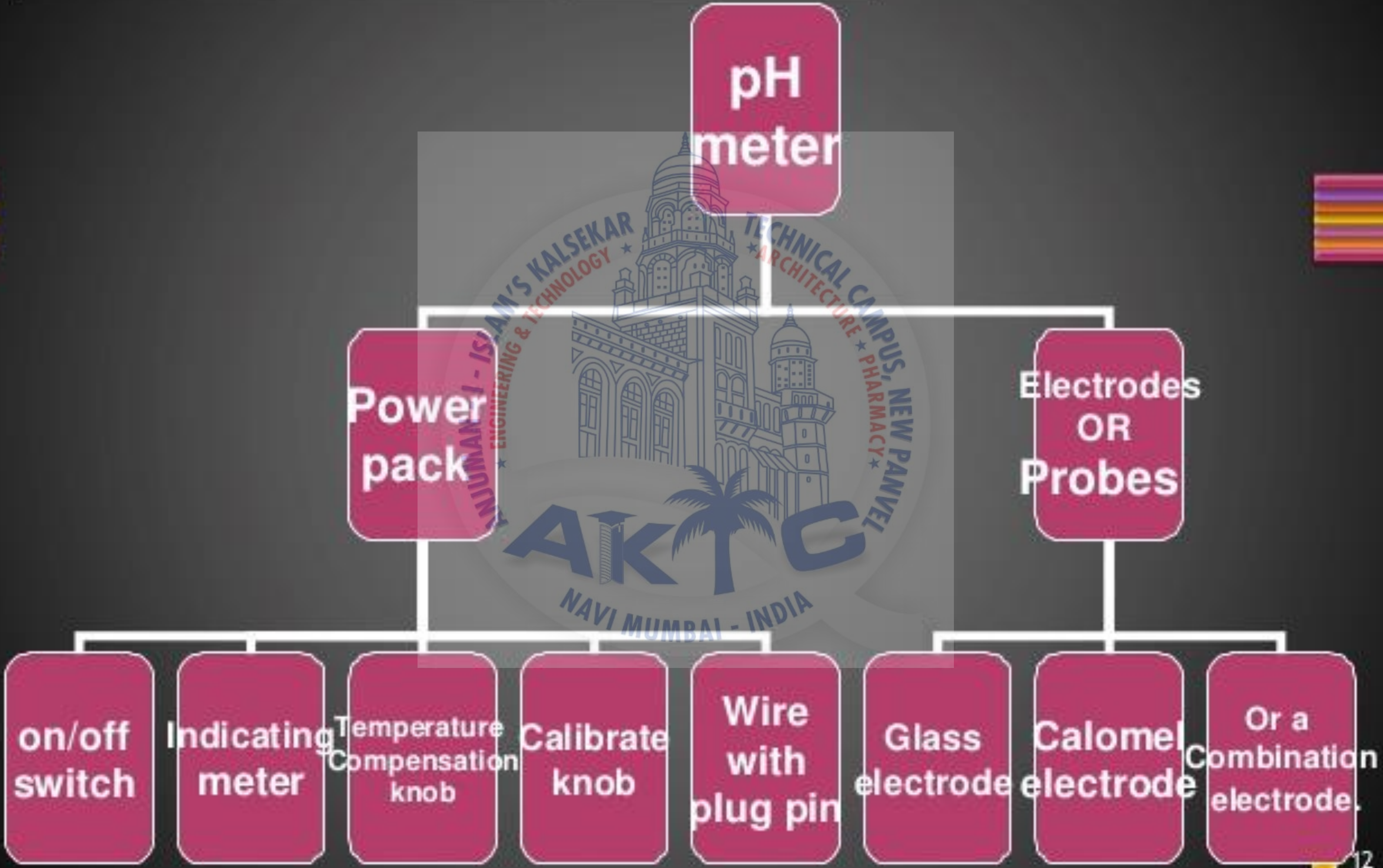


Figure : litmus test

Figure : pH values of different sample

Construction of pH meter



pH meter

Power pack

Electrodes OR Probes

on/off switch

Indicating meter

Temperature Compensation knob

Calibrate knob

Wire with plug pin

Glass electrode

Calomel electrode

Or a Combination electrode.

Types of pH meter

- Manual pH meter
- Digital pH meter

- A manual pH meter

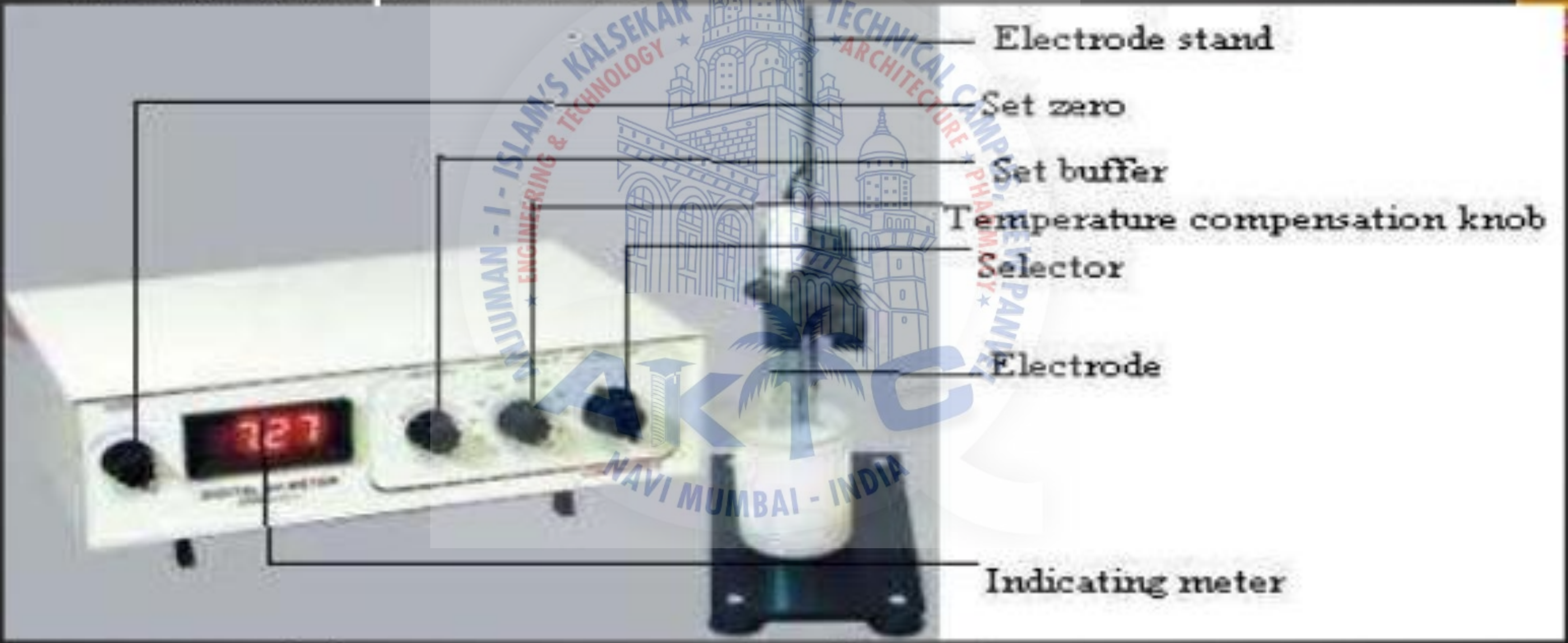


Figure : manual pH meter

Source : http://doubleroptics.tradeindia.com/deluxe-ph-meter-226808.ht

Types of probe

1. Glass electrode
2. Reference electrode
3. Combination gel electrode

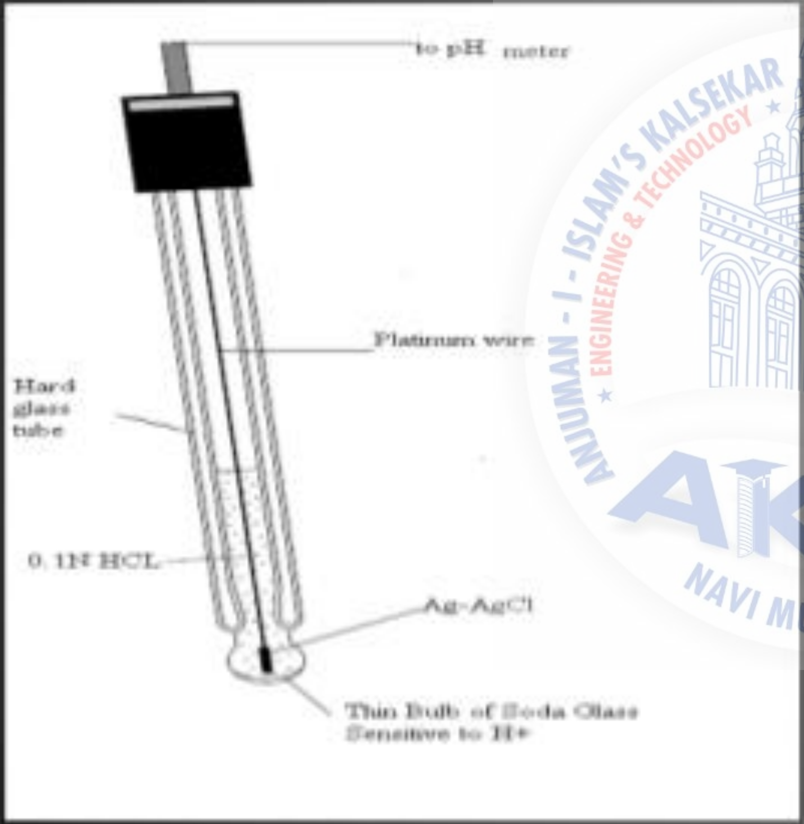


Figure :Glass electrode

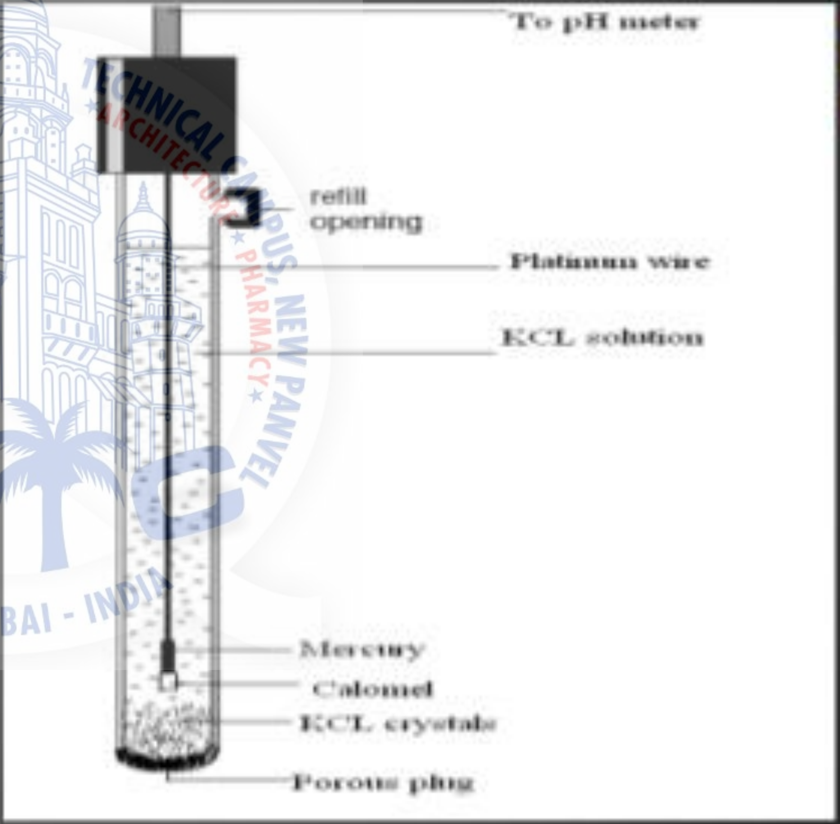


Figure : Reference electrode

Source :http://www.alliancets.com/site/files/408/29497/109873/159912/Guide_to_pH_Measurer

Calibration

- Calibration should be performed with at least two standard buffer solutions that span the range of pH values to be measured.
- For general purposes buffers at pH 4 and pH 10 are acceptable.
- The pH meter has one control (calibrate) to set the meter reading equal to the value of the first standard buffer and a second control (slope) which is used to adjust the meter reading to the value of the second buffer.
- A third control allows the temperature to be set.

Source :http://en.wikipedia.org/wiki/PH_meter

Measurement of pH

- The zero of the dial is set mechanically.
- The knob for temperature compensation is fixed for the temperature of the solution.
- The electrodes are dipped into a standard buffer solution of known pH.
- Adjustment is made so that the dial reads the value of the buffer solution.
- The electrodes are removed and washed well with distilled water.
- The electrodes are dipped into the sample solutions.
- The dial shows the pH value of the sample solution.

Applications of pH meter

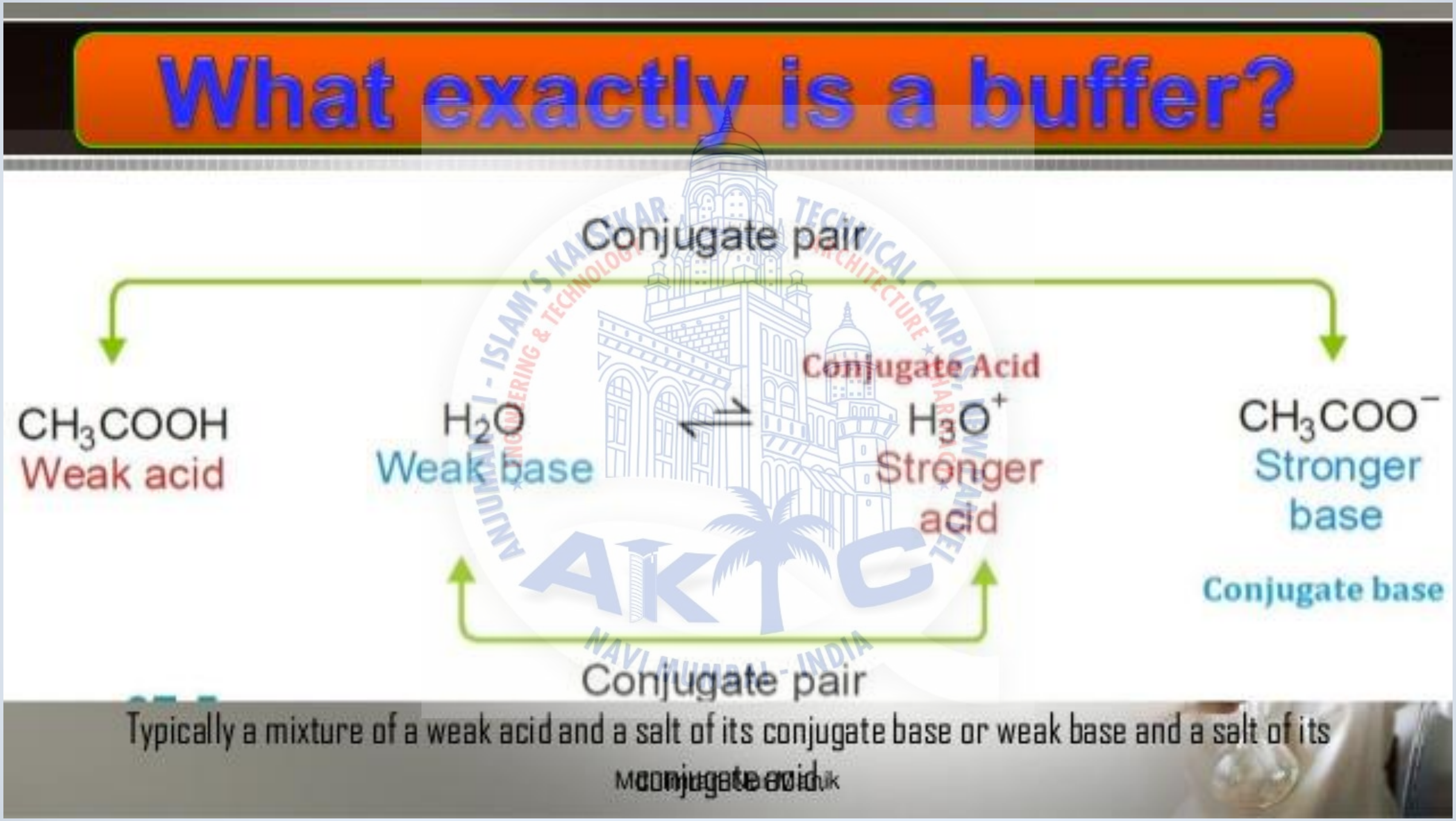
- For the diagnosis of various disorders in human body
- Agriculture
- Brewing
- Corrosion Prevention
- Dyeing
- Jam and Jelly Manufacturing
- Printing
- Pharmaceuticals

Conclusion

- A pH meter is an electronic instrument used for measuring the pH of a liquid/semi-solid substances. We exploited the properties of this indicator to determine with precision the acidity or alkalinity of various substances. pH meter is more useful than the other pH indicators because it gives accurate reading (e.g. , for detection of blood pH) and can measure the ph of a liquid as well as a semi-solid substance.

Chapter 4

Lecture 2



What exactly is a buffer?

Conjugate pair

Conjugate Acid

$CH_3COOH \quad H_2O \rightleftharpoons H_3O^+ \quad CH_3COO^-$

- CH_3COOH: Weak acid
- H_2O: Weak base
- H_3O^+: Stronger acid
- CH_3COO^-: Stronger base

Conjugate base

Conjugate pair

Typically a mixture of a weak acid and a salt of its conjugate base or weak base and a salt of its conjugate acid

Buffer are defined as compound or mixture of compounds that by their presence in solution resist changes in pH upon the addition of small quantities of acid or alkali.

Resistance to change in pH is known as **buffer action.**

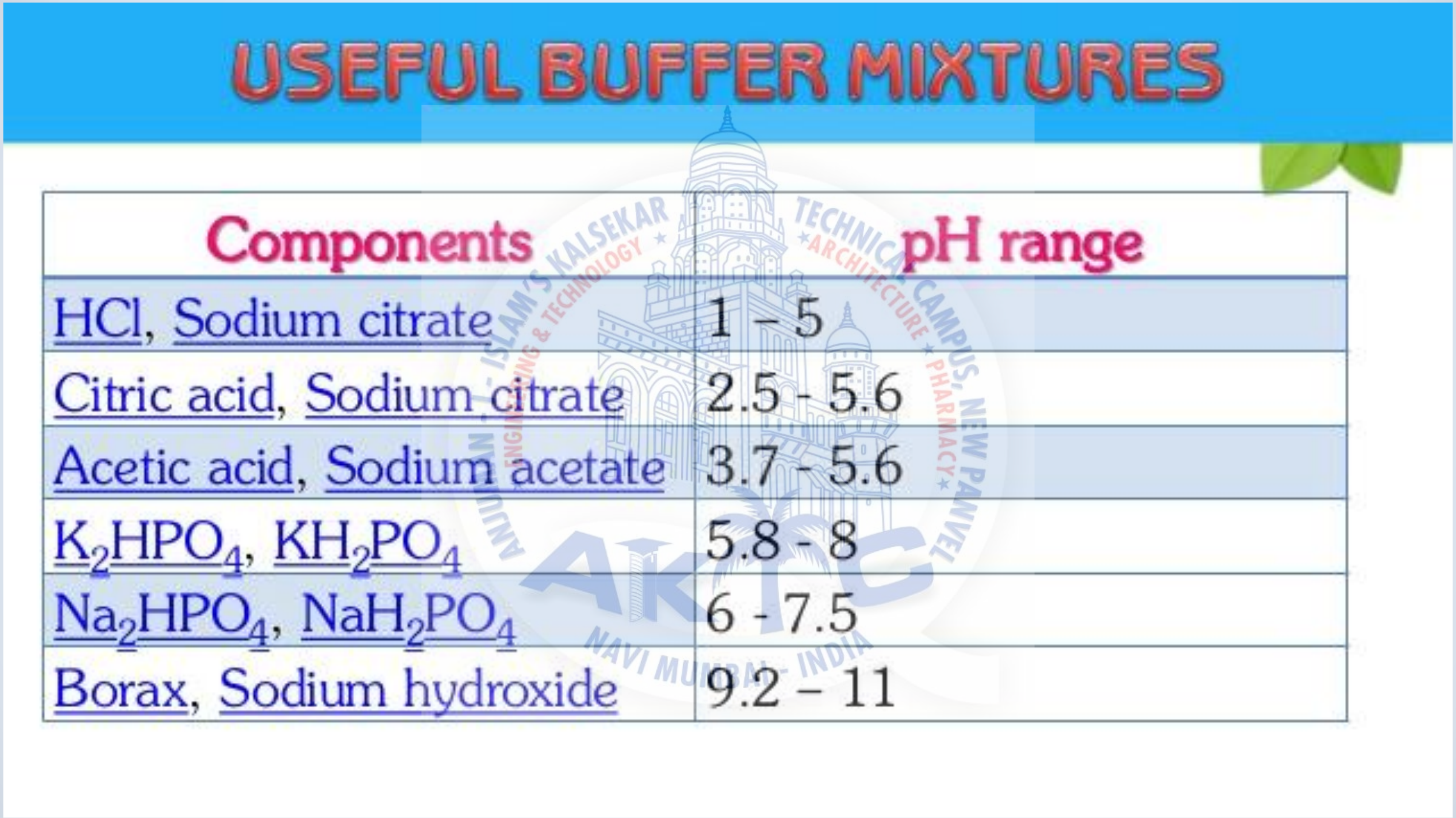
The amount of acid/base required to produce a unit change in pH in the solution is known as **buffer capacity.**

Characteristic of buffers

1. Buffers have a definite pH value

2. The pH value of buffer does not alter either on keeping for long periods or on dilution.

3. The pH value of buffer is very slightly altered by the addition of small quantities of acids and



USEFUL BUFFER MIXTURES

Components	pH range
HCl, Sodium citrate	1 – 5
Citric acid, Sodium citrate	2.5 - 5.6
Acetic acid, Sodium acetate	3.7 - 5.6
K_2HPO_4, KH_2PO_4	5.8 - 8
Na_2HPO_4, NaH_2PO_4	6 - 7.5
Borax, Sodium hydroxide	9.2 – 11

Buffer systems-composition and examples

- Weak acid and its conjugate base i.e the salt of weak acid with strong base. Ex: solution containing acetic acid sodium acetate
- Weak base and its conjugate acid i.e the salt of weak base with a strong acid. Ex: solution containing ammonium hydroxide and ammonium chloride

Buffer systems-composition and examples

- Two salts acts as acid-base pair which can function in manner either as 1 0r 2 ex: solution of monobasic potassium phosphate (KH_2PO_4) and dibasic potassium phosphate(K_2HPO_4)
- Amphoteric electrolytes act as buffer systems. Ex: solution of glycine
- Solutions of strong acids and solution of strong bases exhibit buffer action by virtue of relatively high concentration of hydronium ions and hydroxyl ions

Some important buffer systems

- HCl and KCl—1.2-2.2
- HCl and potassium hydrogen phthalate---2.2-4
- Sodium hydroxide and potassium hydrogen phthalate--- 4.2-5.8
- Boric acid, sodium hydroxide and potassium chloride ---- 8-10

BUFFER SOLUTION

- A buffer solution is one which maintains its pH fairly constant even upon the addition of small amounts of acid or base.

- There are two types of buffer solution.

1. Acidic Buffer
2. Basic Buffer

Acidic Buffer:

A weak acid together with a salt of the same acid with a strong base.These are called Acidic Buffer.

For Example.

$CH3COOH + CH3COONa$.

Basic Buffers:

A weak base and its salt with a strong acid.These are called Basic Buffers.

For Example.

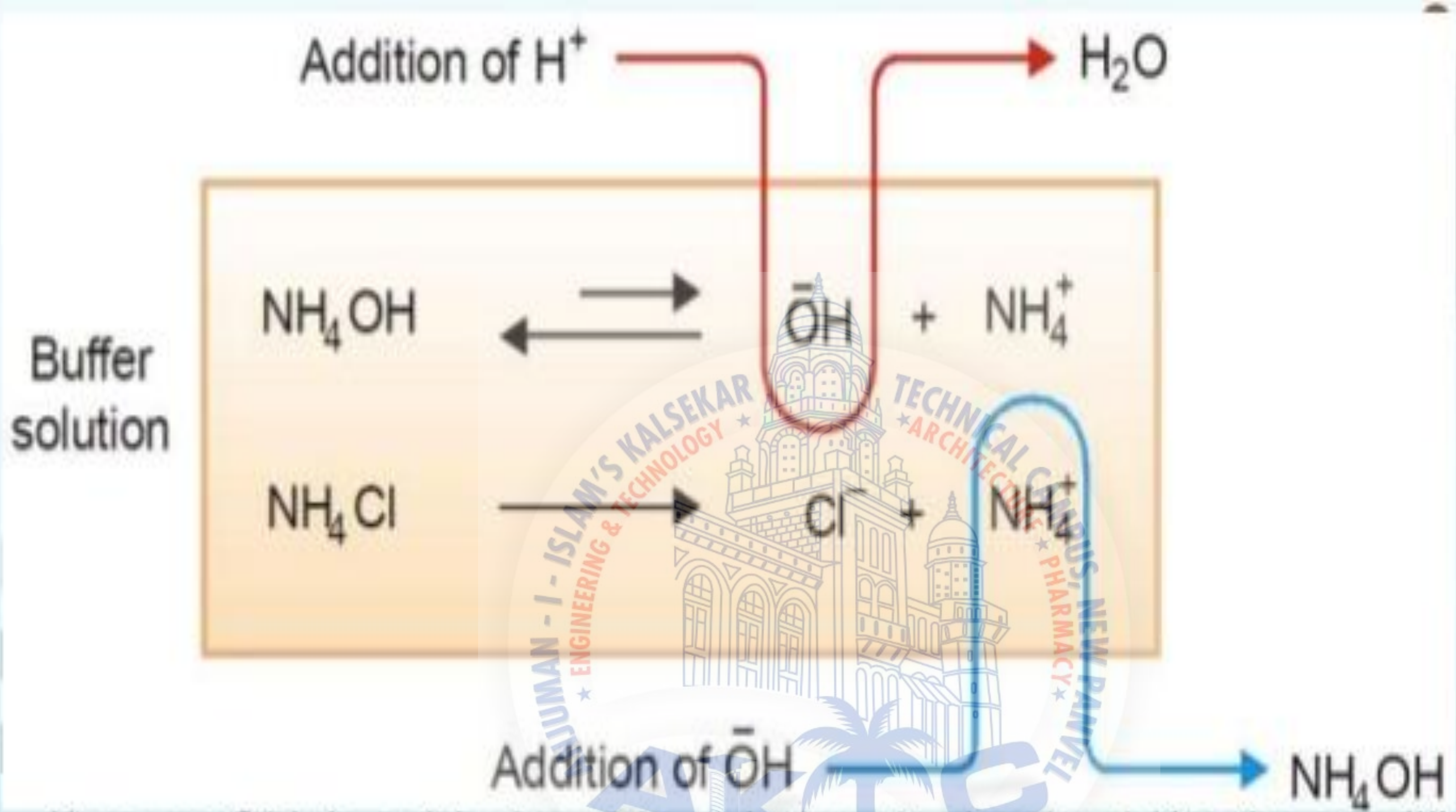
$NH4OH+NH4CL$

Let us illustrate buffer action by taking example of a common buffer system consisting of solution of acetic acid and sodium acetate.

$$CH3COOH \rightleftharpoons H^+ + CH3COO^-$$

$$CH3COONa \longrightarrow Na^+ + CH3COO^-$$

Since the salt is comletely ionized,it provides the common ion CH3COO in excess.



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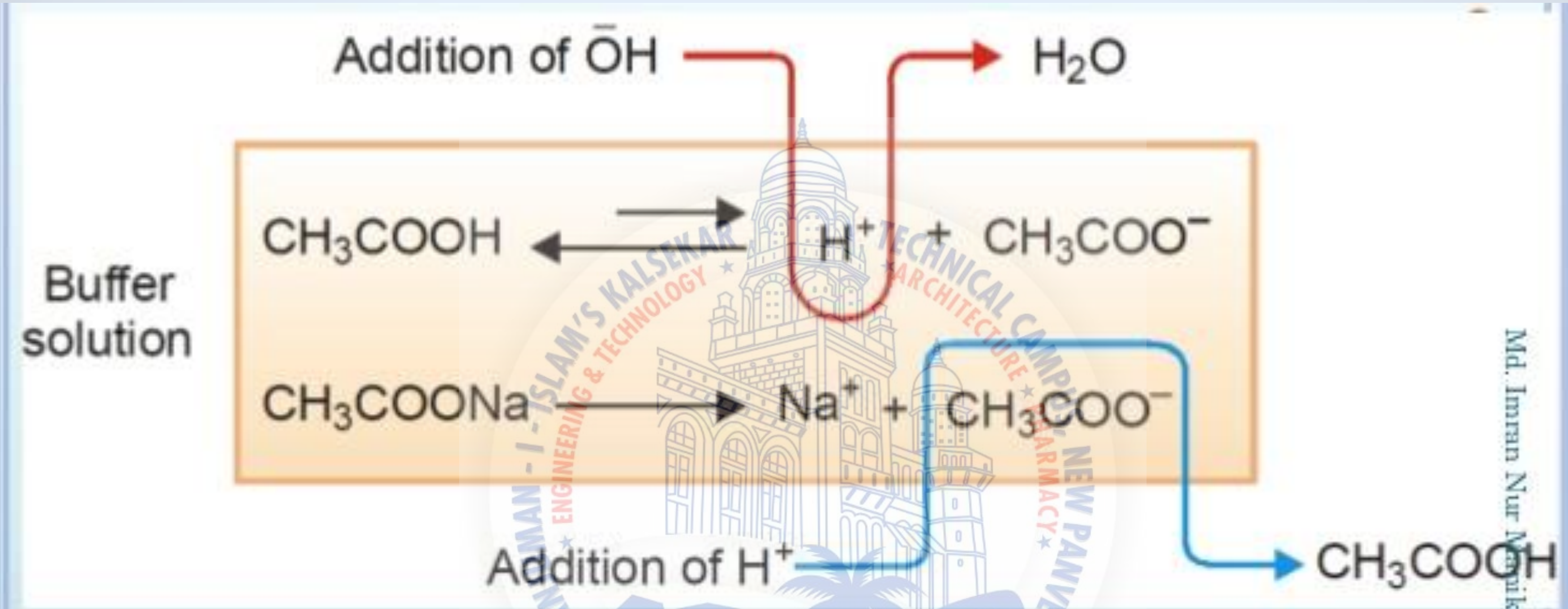
- If more OH^- is added to this solution, it simply shifts the equilibrium to the left, absorbing OH^-, so the $[OH^-]$ remains unchanged.

- If OH^- is removed (e.g. by adding H^+) then the equilibrium shifts to the right, releasing OH^- to keep the pH constant



Addition of $\bar{O}H$ → H_2O

Buffer solution

$CH_3COOH \rightleftharpoons H^+ + CH_3COO^-$

$CH_3COONa \longrightarrow Na^+ + CH_3COO^-$

Addition of H^+ → CH_3COOH

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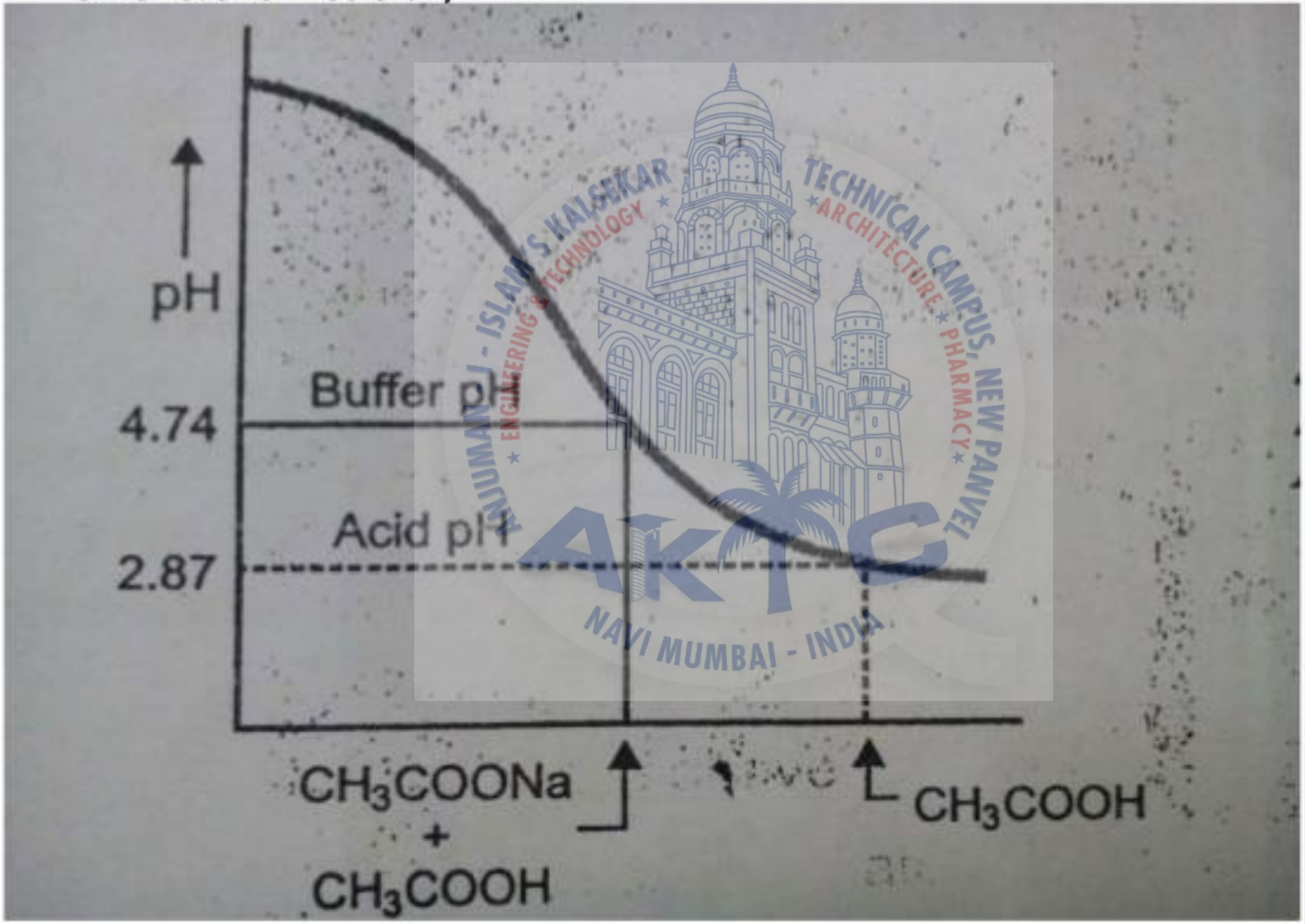
- If more H^+ is added to this solution, it simply shifts the equilibrium to the left, absorbing H^+, so the $[H^+]$ remains unchanged.
- If H^+ is removed (e.g. by adding OH^-) then the equilibrium shifts to the right, releasing H^+ to keep the pH constant

NH_2CH_2COOH glycine amphoteric electrolyte.

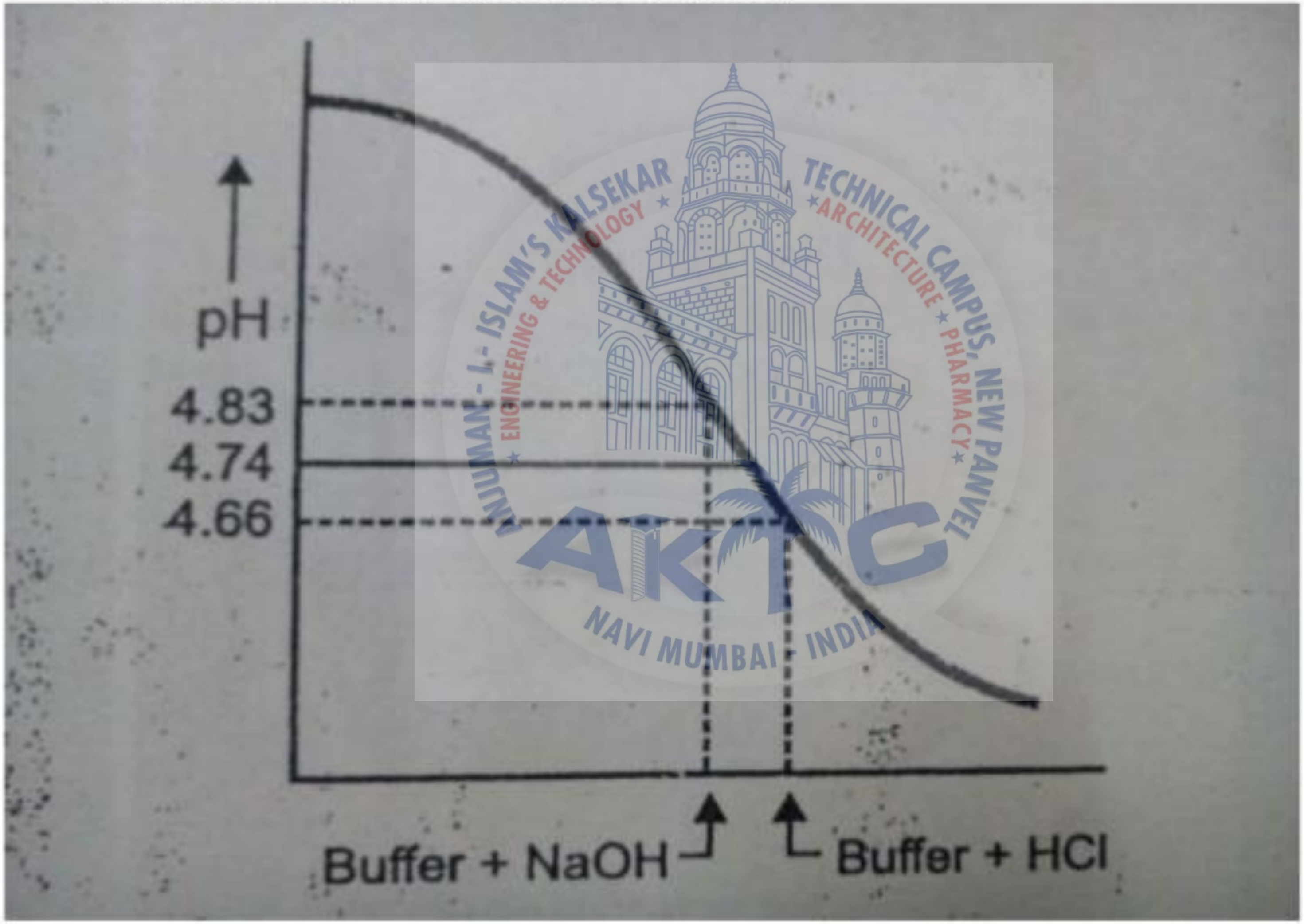
$$NH_2CH_2COOH + H_2O \longrightarrow NH_2CH_2COO^-$$

$$NH_2CH_2COOH + H_3O^+ \longrightarrow {}^+NH_3CH_2COO$$

The Buffer solution has a higher pH than the acid itself;

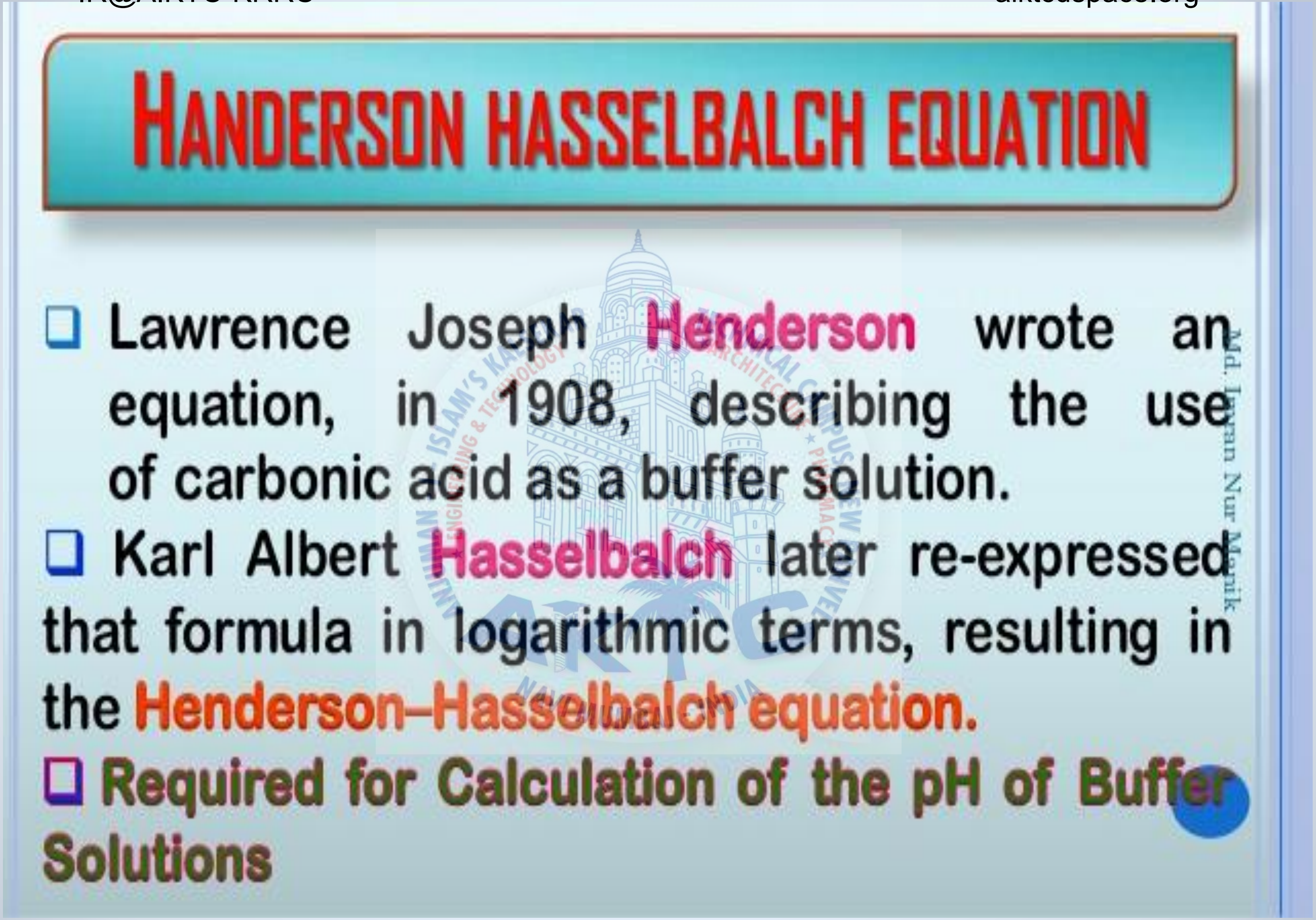


The pH of Buffer changes only slightly upon addition of an acid or base;



Application of buffer

1. Enhancing solubility
2. Increasing stability
3. Improving purity
4. Optimizing biological activity
5. Comforting the body.



HANDERSON HASSELBALCH EQUATION

- Lawrence Joseph **Henderson** wrote an equation, in 1908, describing the use of carbonic acid as a buffer solution.
- Karl Albert **Hasselbalch** later re-expressed that formula in logarithmic terms, resulting in the **Henderson–Hasselbalch equation.**
- **Required for Calculation of the pH of Buffer Solutions**

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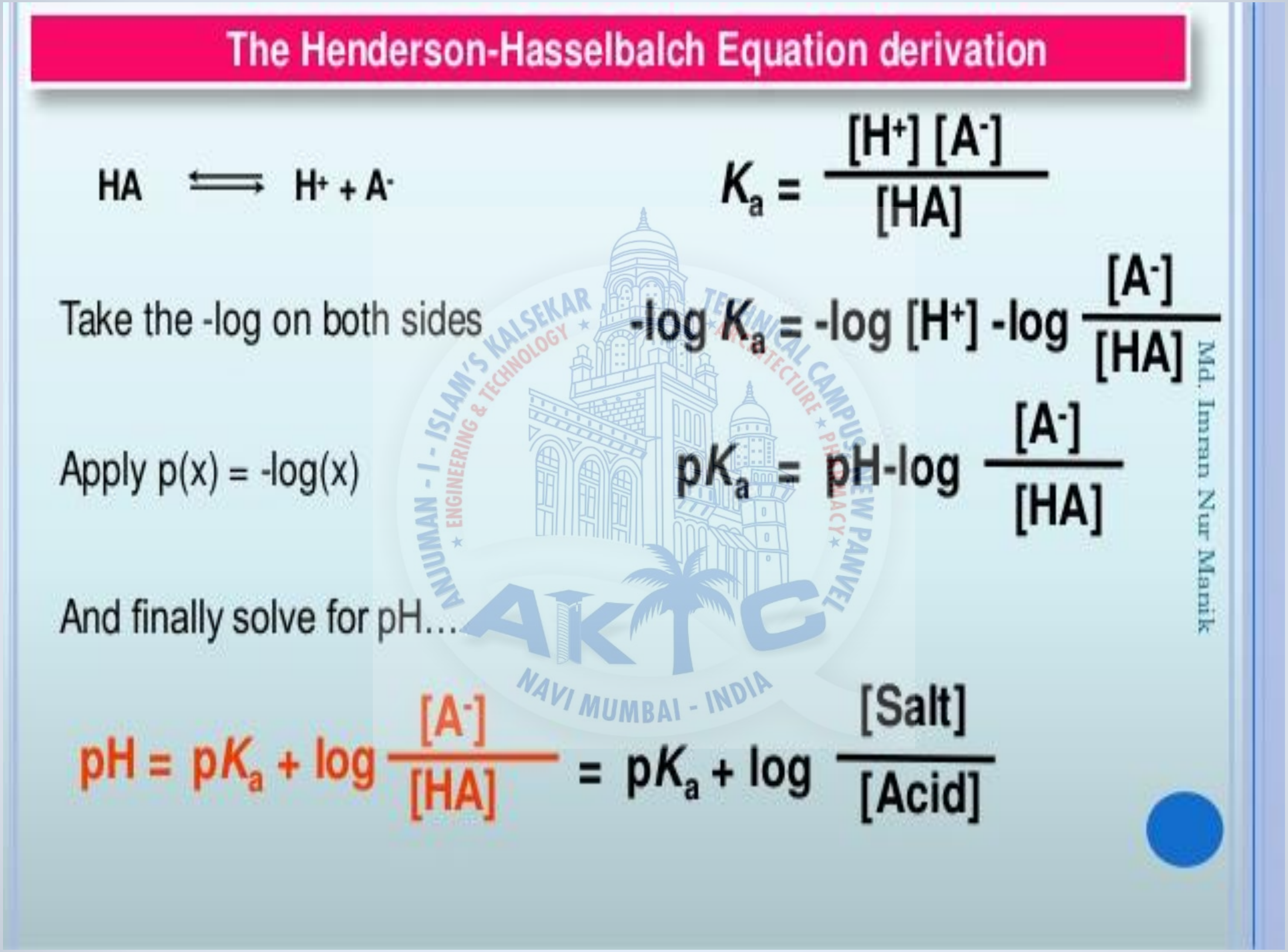

The Henderson-Hasselbalch Equation derivation

$$HA \rightleftharpoons H^+ + A^- \qquad K_a = \frac{[H^+][A^-]}{[HA]}$$

Take the -log on both sides $$-\log K_a = -\log [H^+] - \log \frac{[A^-]}{[HA]}$$

Apply p(x) = -log(x) $$pK_a = pH - \log \frac{[A^-]}{[HA]}$$

And finally solve for pH…

$$pH = pK_a + \log \frac{[A^-]}{[HA]} = pK_a + \log \frac{[Salt]}{[Acid]}$$

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For Acid Buffers:

The pH of acid buffer can be calculated from the dissociation constant, Ka of the weak acid and the concentrations of the acid and salt used.

- The dissociation expression of the weak acid can be represented as:
- $HA \leftrightarrow H^+ + A^-$
- Ka = [H+] [A-] / [HA]
- Or
- $[H^+] = Ka [HA] / [A^-]$ ----------- (1)

- A weak acid is only slightly dissociated, and its dissociation is further depressed by the addition of the salt (XA) which provides A^- ion (common ion effect) as a result the equilibrium concentration of the unionized acid is nearly equal to the initial concentration of the acid. The equilibrium concentration of A^- is assumed to be equal to the initial concentration of the salt added since it is completely dissociated. Therefore, in above equation (1), we represent concentration of A- by salt concentration.

- $[H^+] = Ka . [Acid] / [Salt]$ -------- (2)
- Taking log on both sides, we get:
- $\log[H^+] = \log Ka + \log [Acid] / [Salt]$
- multiplying both sides by –ve sign,
- $-\log[H^+] = -\log Ka - \log [Acid] / [Salt]$
- As $-\log[H^+] = pH$ & $-\log Ka = pka$
- $pH = pka - \log[Acid] / [Salt]$ OR

$$pH = pka + \log[Salt] / [Acid] \quad \text{---------} \quad (3)$$

Eq. (3) is called as Henderson – Hasselbalch equation.

It helps in calculating the pH value of buffer solution,

if the concentrations of acid as well as that of the salt are known.

For Basic Buffers:

Buffer equation for basic buffer can be calculated in same way as that for acidic buffers.

Consider a basic buffer composed of a mixture of weak base (BOH) and its salt (BA). The dissociation constant for base can be written as,

$$BOH \leftrightarrow B^+ + OH^-$$

$$Kb = [B^+]\,[OH^-] \,/\, [BOH]$$

OR

$$[OH^-] = Kb\,[BOH] \,/\, [B^+] \quad \text{-----------} \quad (1)$$

- A weak base is only slightly dissociated, and its dissociation is further depressed by the addition of the salt (BA) which provides B^+ ion (common ion effect) as a result the equilibrium concentration of the unionized base is nearly equal to the initial concentration of the base. The equilibrium concentration of B^+ is assumed to be equal to the initial concentration of the salt added since it is completely dissociated. Therefore, in above equation (1), we represent concentration of B+ by salt concentration.

$[OH^-] = Kb.\ [Base] / [Salt]$ --------- (2)

Taking log on both sides, we get:

$\log[OH^-] = \log Kb + \log [Base] / [Salt]$

multiplying both sides by –ve sign,

$-\log[OH^-] = -\log Kb - \log [Base] / [Salt]$

As *-log[OH⁻] = pOH* & *-logKb = pkb*

$pOH = pkb - \log [Base] / [Salt]$

Or

$pOH = pkb + \log[Salt] / [Base]$ ---------- (3)

Significance of Henderson – Hasselbalch equation:

By this equation, the pH of a buffer solution can be calculated from the initial concentrations of the weak acid and the salt provided when ka is given. However, the Henderson equation for a basic buffer will give pOH, and so pH can be calculated as;

$$pkw = pH + pOH$$

or

$$pH = pkw - pOH$$

$$pH = 14 - PoH$$

Also, the dissociation constant of a weak acid (pka) or a weak base (pkb) can be calculated by measuring the pH of a buffer solution containing equimolar concentrations of the acid (or base) and the salt.

Buffer capacity

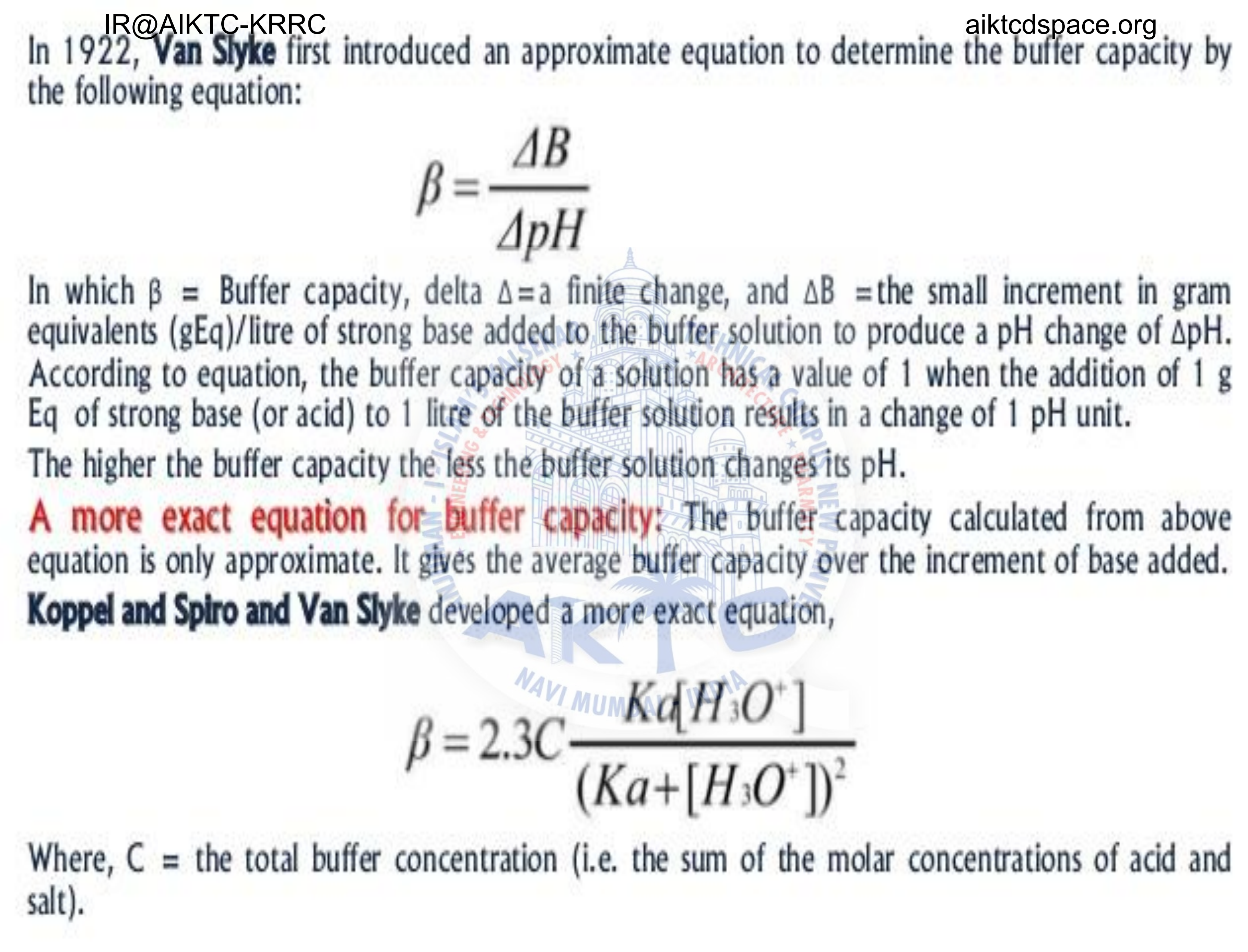
Buffer capacity is a measure of the efficiency of a buffer, in resisting changes in pH. The buffer capacity is defined as **the number of moles per litre of strong monobasic acid or base required to produce an increase or decrease of one pH unit in the solution.** It is also known as *buffer efficiency*, *buffer index*, and *buffer value*.

Conventionally, the buffer capacity (β) is expressed as **the amount of strong acid or base, in gram-equivalents, that must be added to 1 litre of the solution to change its pH by one unit.**

A buffer solution can resist a small amount of change of pH on adding acid or alkali to the solution. Buffer capacities ranging from 0.01-0.1 are usually adequate for most pharmaceutical solutions.

BUFFER CAPACITY

- The buffer capacity of a buffer solution is "a measure of its magnitude of its resistance to change in the pH on an addition of an acid or a base."
- Buffer capacity is also referred as *buffer index, buffer value, buffer efficiency or buffer coefficient.*
- The buffer capacity represented by 'β' may also be defined as:
- "The ratio of the increment (amount added) of strong acid or base to the small change in pH (ΔpH) brought about by this addition".
- $\beta = \Delta A$ or $\Delta B / \Delta pH$
-
- Where, ΔA or ΔB represents the small increment (in gram equivalents / litre of strong acid or base added) to the buffer to bring about a pH change of ΔpH.
- According to the above equation, a solution has a buffer capacity of 1 when one litre of it requires one gram equivalent of a strong acid or base to change the pH by one unit. So, smaller the pH change in a solution upon the addition of an acid or base, greater is the buffer capacity and vice versa.



In 1922, **Van Slyke** first introduced an approximate equation to determine the buffer capacity by the following equation:

$$\beta = \frac{\Delta B}{\Delta pH}$$

In which β = Buffer capacity, delta Δ=a finite change, and ΔB =the small increment in gram equivalents (gEq)/litre of strong base added to the buffer solution to produce a pH change of ΔpH. According to equation, the buffer capacity of a solution has a value of 1 when the addition of 1 g Eq of strong base (or acid) to 1 litre of the buffer solution results in a change of 1 pH unit.

The higher the buffer capacity the less the buffer solution changes its pH.

A more exact equation for buffer capacity: The buffer capacity calculated from above equation is only approximate. It gives the average buffer capacity over the increment of base added.

Koppel and Spiro and Van Slyke developed a more exact equation,

$$\beta = 2.3C\frac{Ka[H_3O^+]}{(Ka+[H_3O^+])^2}$$

Where, C = the total buffer concentration (i.e. the sum of the molar concentrations of acid and salt).

IMPORTANCE:

It is important in chemical as well as in biological term.

Buffer Capacity of water:

As the purity of fresh water increases,the buffer capacity decreases and 100 percent pure fresh water is no buffer at all.

What factors determined buffer capacity ?

The concentration of the buffer (the higher the concentration,the larger the buffering capacity) and how close the pka of buffer is compared to the pH of solution.

CHOICE OF A SUITABLE INDICATOR:

we may have the titration of:

- a strong acid with a strong base
- a weak acid with a strong base
- a strong acid with a weak base
- a weak acid with a weak base

Titration a strong acid with a strong base:

In this titration both methyl orange and phenophthalein are suitable indicators

Titration a weak acid with a strong base:

In this titration phenophthalein is a suitable indicator, while methyl orange is not.

Titration a strong acid with a weak base:

In this titration, evidently methyl orange and methyl red are suitable indicators.

Titration a acid with a weak base:

Under these condition, all indicators change colour only gradually and no indicator is suitable.

Chapter 4

Lecture 3

BUFFERS AND THE BODY

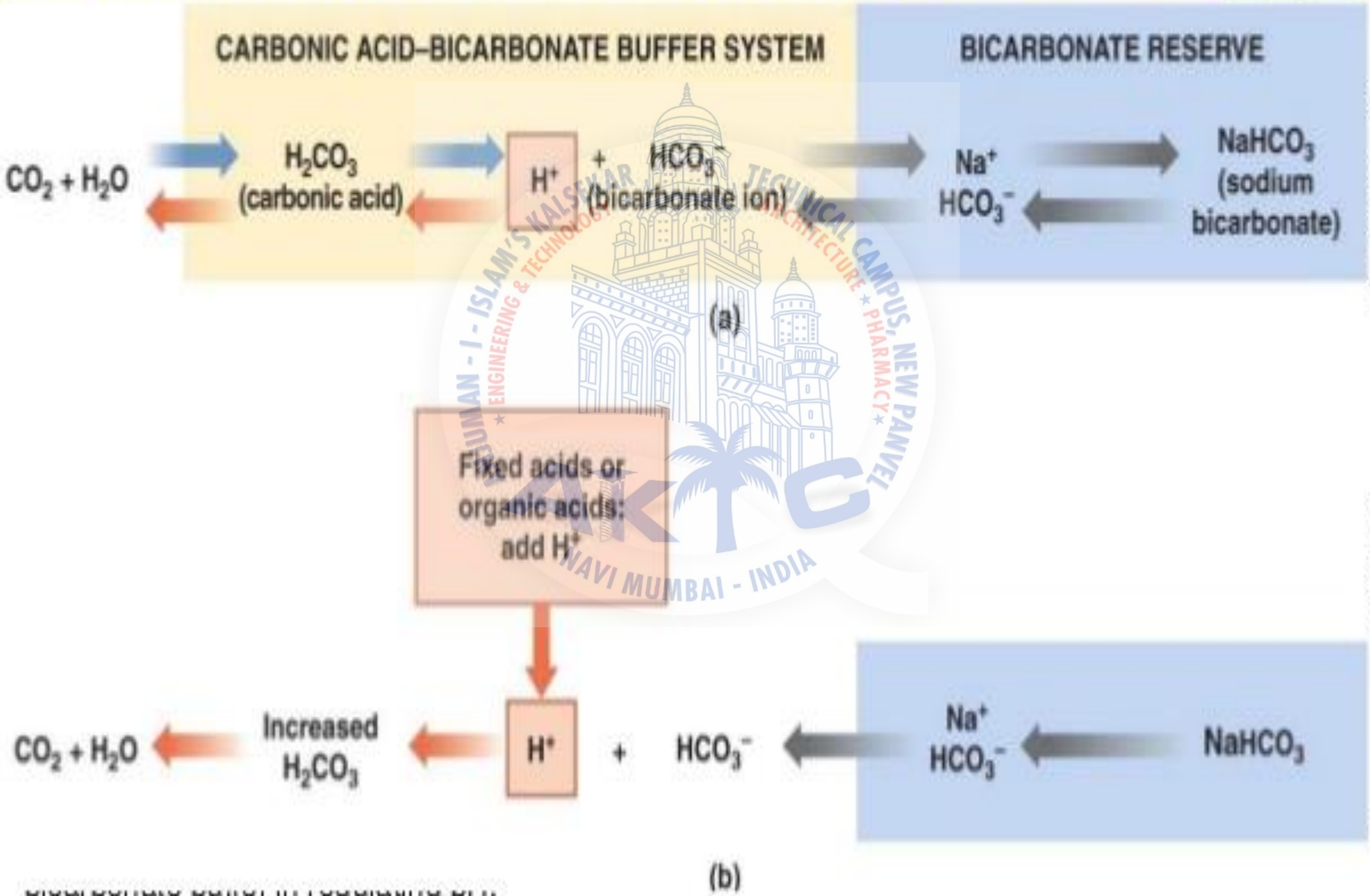
Body fluids contain buffering agents and buffer systems that maintain pH at or near pH=7.4. Important endogenous (natural) buffer systems include **carbonic acid/sodium bicarbonate and sodium phosphate** in the plasma and haemoglobin**, and potassium phosphate in the cells**.

An *in vivo* value of $pH < 6.9$ or $pH > 7.8$ can be life threatening. Pharmaceutical solutions generally have a low buffer capacity in order to prevent overwhelming the body's own buffer systems and significantly changing the pH of the body fluids. Buffer concentrations of between 0.05 and 0.5 M and buffer capacities between 0.01 to 0.1 are usually sufficient for pharmaceutical solutions.

In biological systems:

- The pH of blood is maintained at about 7.4 by two buffer systems. That are;
- ***a) primary buffers*** : these are present in plasma. The plasma contains;
- carbonic acid / carbonate & acid /alkali sodium salt of phosphoric acid.
- ***b) secondary buffers***: these are present in erythrocytes which are;
- oxy-haemoglobin / haemoglobin & acid / alkali potassium salts of phosphoric acid.

HOW IS THE PH OF THE BLOOD CONTROLLED? WHAT HAPPENS WHEN THE BLOOD PH IS NOT MAINTAINED?



bicarbonate buffer in regulating pH.

Lacrimal fluids have been found to have buffer capacity
pH of tears 7.4 with a range of 7-8
Pure conjectivial fluid is more acidic than tear fluids.

Factors influencing pH of buffer solution

- Temperature

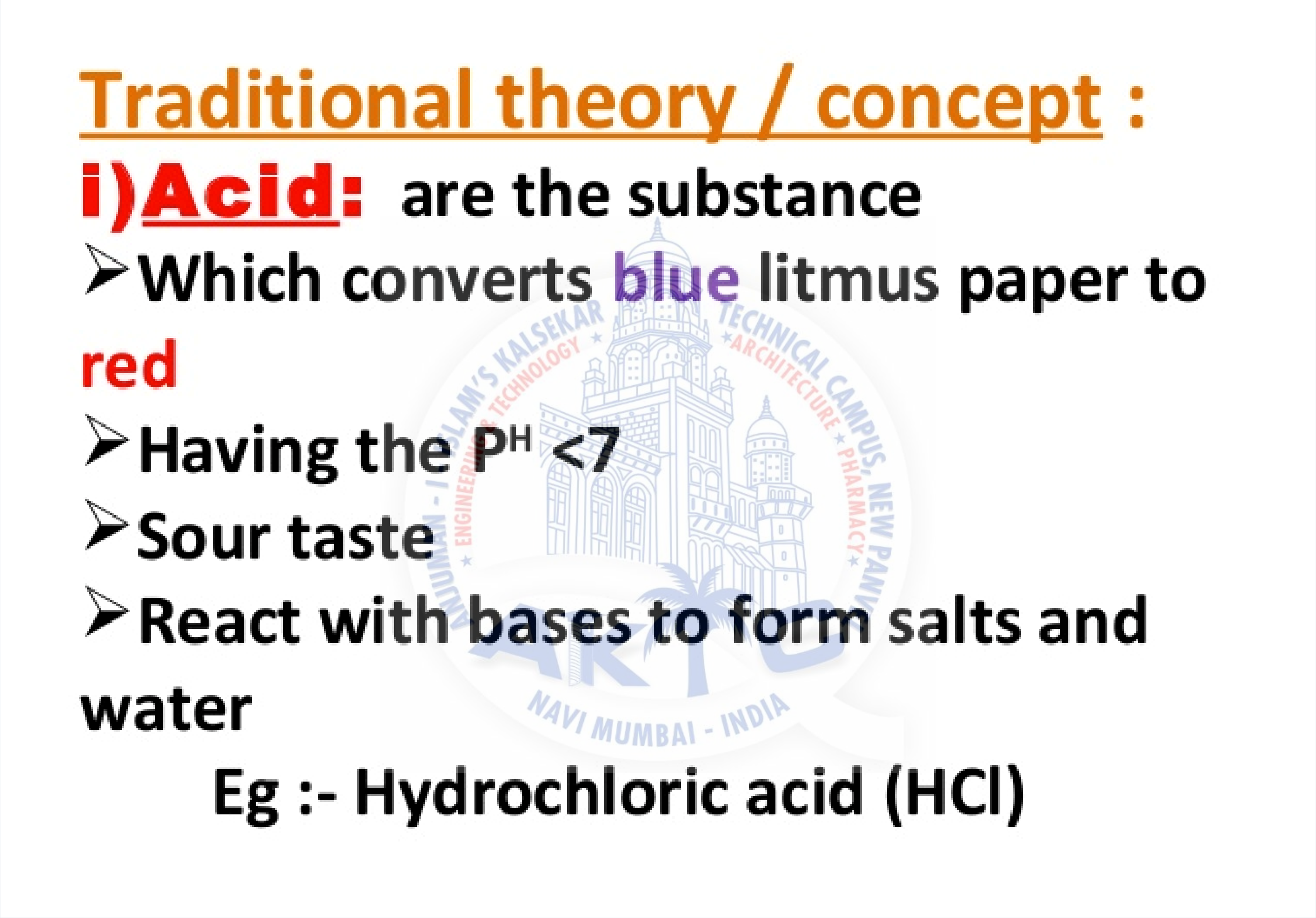
Temperature increases
-acetate buffers pH increases
-Boric acid sodium borate buffers pH decreases

- Ionic strength

-Addition of neutral salts to buffer solution changes the pH of solution due to altered ionic strength
-Extreme Dilution of buffers also changes pH due altered ionic strength. Therefore pH of buffer solution is mentioned.

Acids, Bases are defined by Four main theories,

a)Traditional theory / concept
b)Arrhenius theory
c)Bronsted and Lowry theory
d) Lewis theory

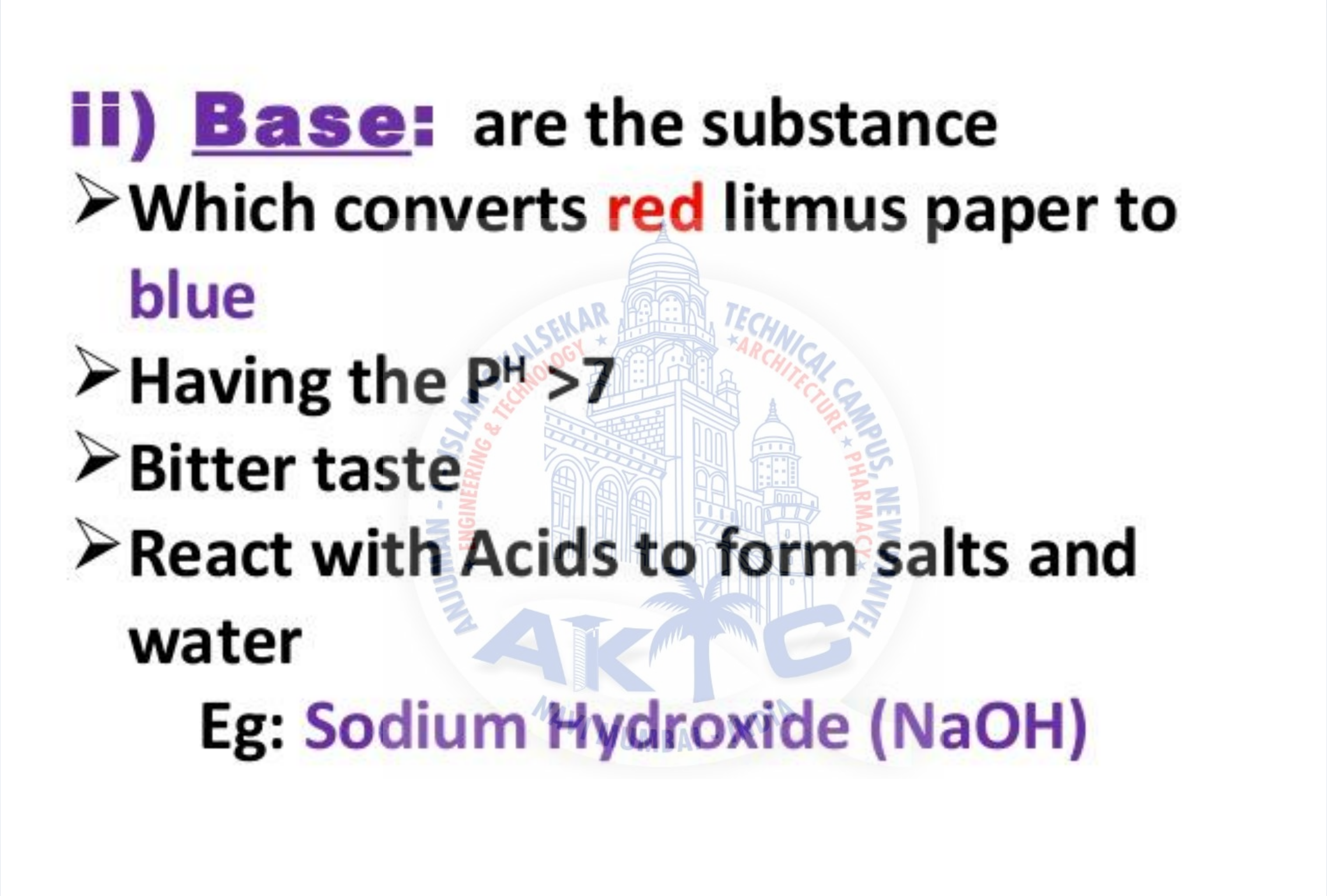


Traditional theory / concept :

i)Acid: are the substance

- Which converts blue litmus paper to red
- Having the $P^H < 7$
- Sour taste
- React with bases to form salts and water

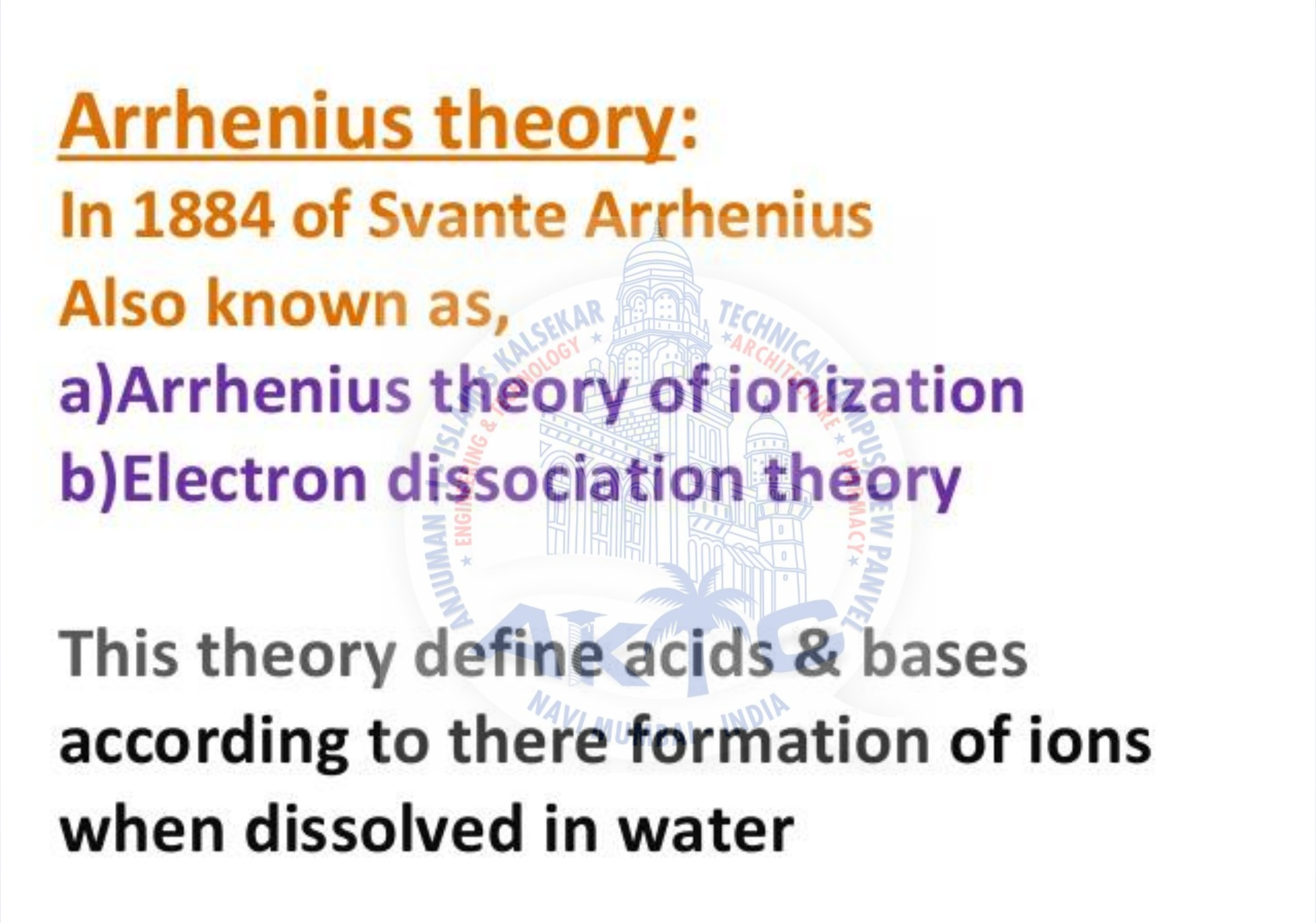
Eg :- Hydrochloric acid (HCl)



ii) Base: are the substance

- ➢ Which converts red litmus paper to blue
- ➢ Having the $P^H > 7$
- ➢ Bitter taste
- ➢ React with Acids to form salts and water

Eg: Sodium Hydroxide (NaOH)



Arrhenius theory:

In 1884 of Svante Arrhenius

Also known as,

a)Arrhenius theory of ionization

b)Electron dissociation theory

This theory define acids & bases according to there formation of ions when dissolved in water

Acids

"An Acid is a substance that can release hydrogen ion (H+) when dissolved in water"

(OR)

"A substance which when dissolved in water gives hydrogen ions (H^+) is known as acid"

Eg: Hydrochloric acid.

$$HCl \rightarrow H^+ + Cl^-$$

Base

"A Base is a substance that can release a Hydroxyl ion (OH^-) when dissolved in water"

(OR)

"A substance which when dissolved in water gives Hydroxyl ion (OH^-)is known as acid"

Eg : Sodium Hydroxide

$$NaOH \longrightarrow Na^+ + OH^-$$

Neutralization reaction

Acid react Base

↓

Salt & Water

Eg: Hydrochloric acid react sodium hydroxide

↓

Sodium chloride (Salt) & water

$$\mathrm{NaOH + HCl \longrightarrow NaCl + H_2O}$$

(base) (Acid) → (Salt)

According to Arrhenius theory,

“Neutralization as the process in which hydrogen ion and hydroxyl ion combine to form unionized molecule or water”

$$NaOH + HCl \longrightarrow NaCl + H_2O$$

i) $HCl \longrightarrow H^+ + Cl^-$

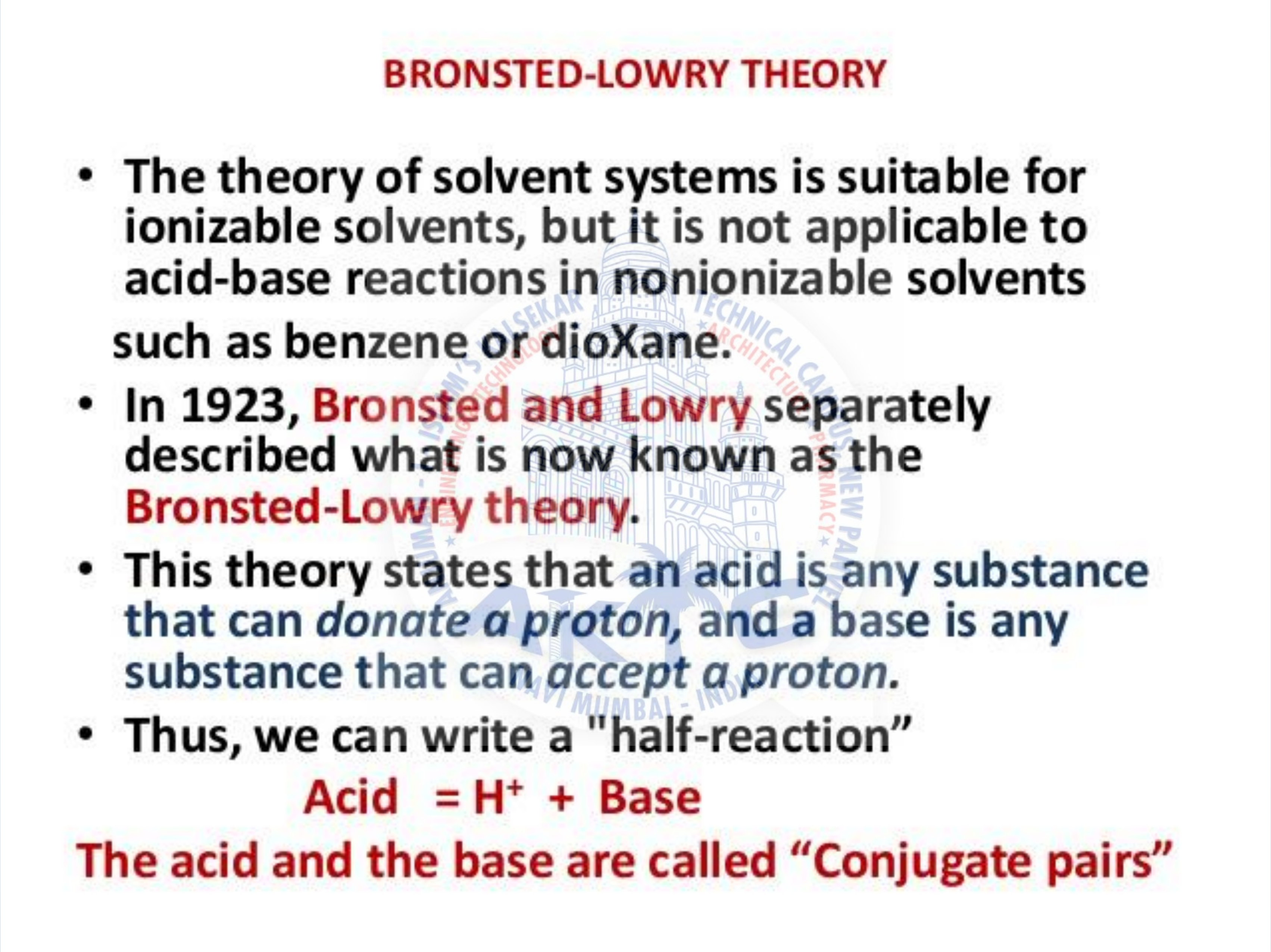
ii) $NaOH \longrightarrow Na^+ + OH^-$

$$H^+ + OH^- \longrightarrow H_2O$$

Limitations :

- Water is essential
- Not explain acidity or basisity of non aqueous Solvent Eg :benzene
- Basisity of Ammonia (No OH^- ion) is not explained
- Acidity of BF_3,$AlCl_3$ (No H^+ ion) is not explained

- Acidity of oxides of P block element (CO_2) is not explained
- Basisity of oxides of S block element (Na_2o) is not explained
- Neutralization with out absence of solvent is not explained



BRONSTED-LOWRY THEORY

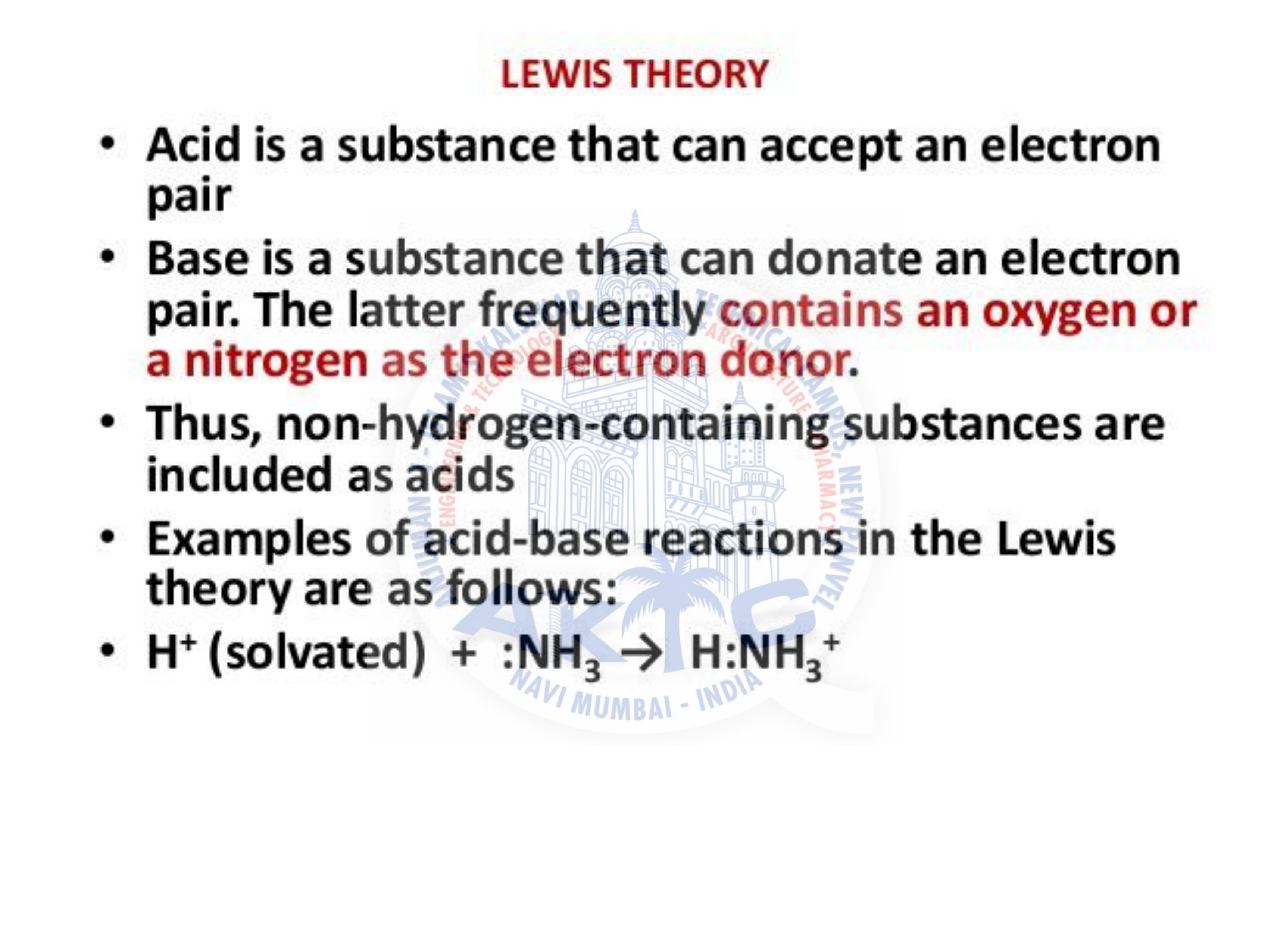
- The theory of solvent systems is suitable for ionizable solvents, but it is not applicable to acid-base reactions in nonionizable solvents

such as benzene or dioXane.

- In 1923, Bronsted and Lowry separately described what is now known as the Bronsted-Lowry theory.
- This theory states that an acid is any substance that can *donate a proton,* and a base is any substance that can *accept a proton.*
- Thus, we can write a "half-reaction"

$$\text{Acid} = H^+ + \text{Base}$$

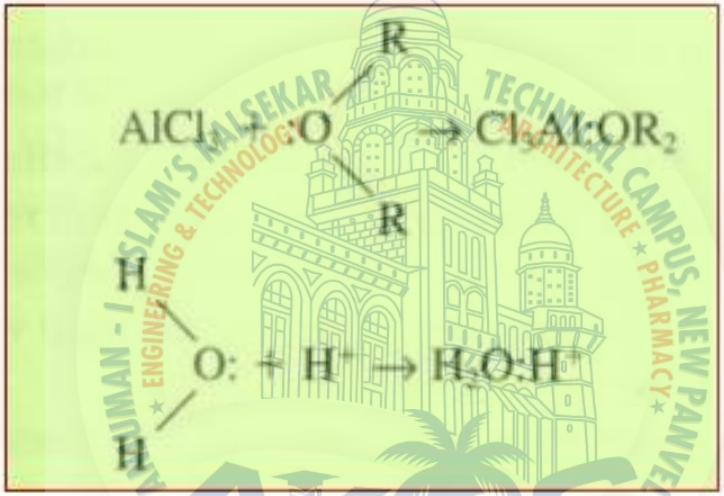
The acid and the base are called “Conjugate pairs”



LEWIS THEORY

- Acid is a substance that can accept an electron pair
- Base is a substance that can donate an electron pair. The latter frequently contains an oxygen or a nitrogen as the electron donor.
- Thus, non-hydrogen-containing substances are included as acids
- Examples of acid-base reactions in the Lewis theory are as follows:
- H^+ (solvated) + $:NH_3 \rightarrow H:NH_3^+$

Lewis Acid



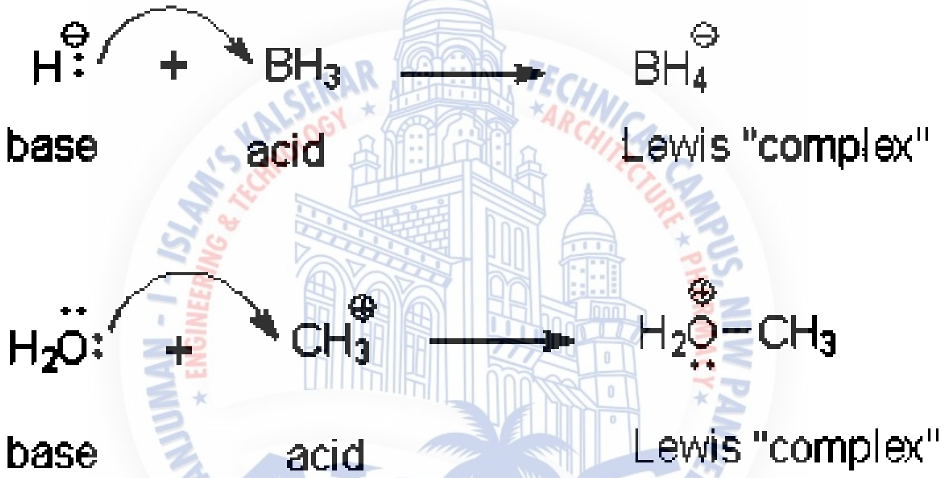
$$AlCl_3 + \overset{R}{\underset{R}{:O}} \rightarrow Cl_3Al:OR_2$$

$$\overset{H}{\underset{H}{O:}} + H^+ \rightarrow H_2O:H^+$$

$$H^+ + :OH^- \rightarrow H:OH$$

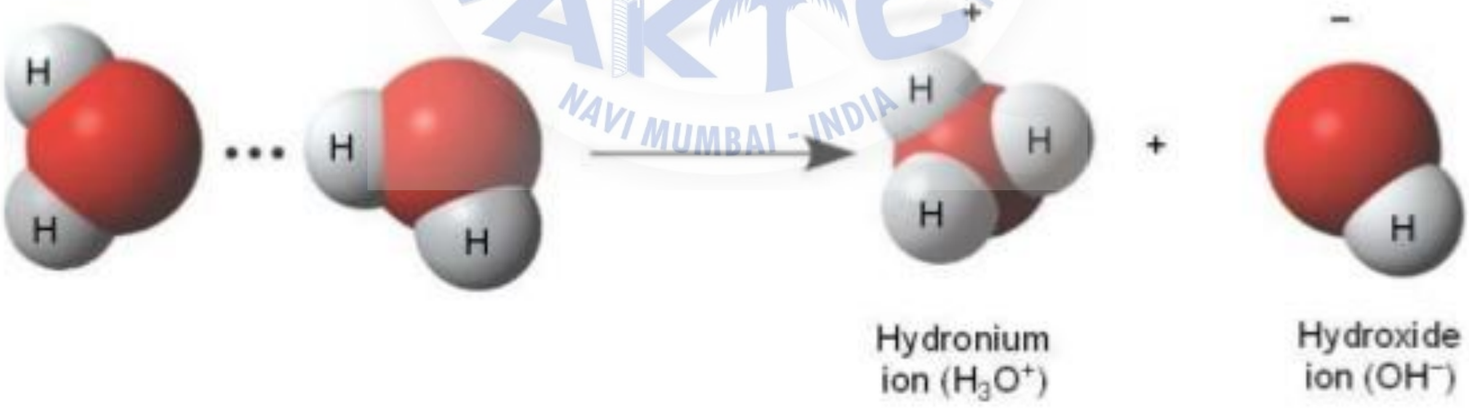
lewis acid base reaction

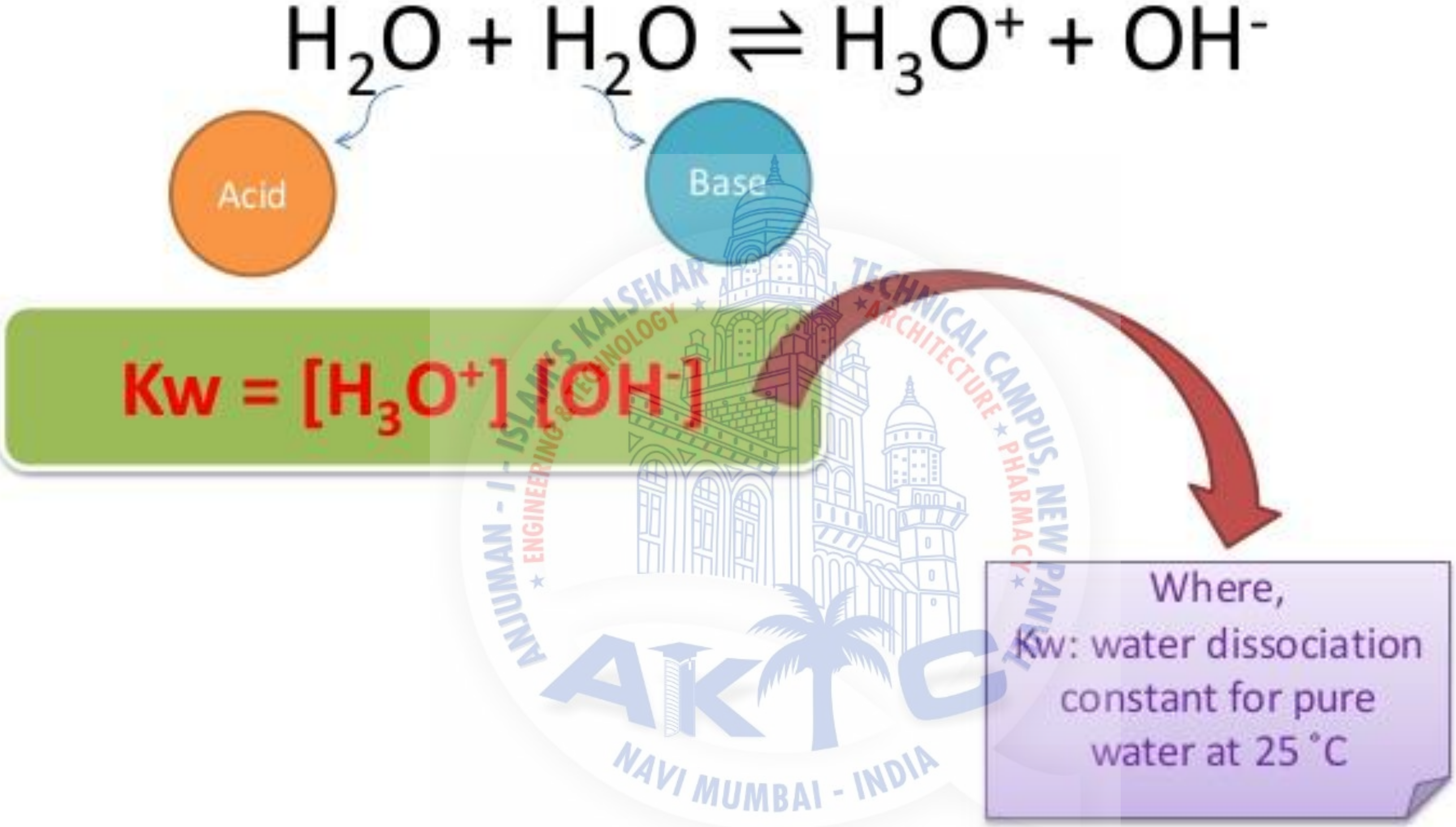
- From the definition of acid and base suggested by Lewis, we can write acid-base reactions like this:



- Characteristics of these reactions:
  - They are charge balanced – the total charge of all species is the same on both sides.
  - The product is sometimes described as a Lewis "complex".
  - Red arrows are used to show the how the bond between the acid and base is formed.
    - The tail sits on a pair of electrons.
    - The head sits on points to where these electrons will be in the product.

DISSOCIATION OF WATER





$$H_2O + H_2O \rightleftharpoons H_3O^+ + OH^-$$

$Kw = [H_3O^+]\,[OH^-]$

Where,
Kw: water dissociation constant for pure water at 25 °C

- $[H_3O^+] = [OH^-] = 1.0 \times 10^{-7}$ mol dm^{-3}
- Thus,

  Kw = [H3O+] [OH-]

  $= (1.0 \times 10^{-7})(1.0 \times 10^{-7})$ mol^2 dm^{-6}

  $= 1.0 \times 10^{-14}$ mol^2 dm^{-6}
- log [H3O+] + log[OH-] = log (1.0×10^{-14})

  log [H3O+] + log[OH-] = -14.0

  -log [H3O+] + log[OH-]= 14.0
- Thus, pH + pOH = 14.0

  or pH + pOH = pKw (-log = p)

The relation between Ka, Kb and Kw

- Weak acid :

$CH_3COOH_{(aq)} \rightleftharpoons H^+_{(aq)} + CH_3COO^-_{(aq)}$

Acid

Base

$$Ka = \frac{[H^+][CH_3COO^-]}{[CH_3COOH]}$$

* $CH_3COO^-{}_{(aq)} + H_2O \rightleftharpoons CH_3COOH{}_{(aq)} + OH^-$

$$Kb = \frac{[CH_3COOH][OH^-]}{[CH_3COO^-]}$$

- $Ka \, . \, Kb = \left(\frac{[H^+][\cancel{CH_3COO^-}]}{[\cancel{CH_3COOH}]}\right)\left(\frac{[\cancel{CH_3COOH}][OH^-]}{[\cancel{CH_3COO^-}]}\right)$

$$Ka \, . \, Kb = [H^+] \, [OH^-]$$

$$Ka \, . \, Kb = Kw$$

To obtain the value of K_b for the anion derived from a weak acid

-
- $K_b = \frac{K_w}{K_a}$, $K_a = \frac{K_w}{K_b}$
- For the hydrolysis of acetate ion (*),
- $K_b = \frac{1.0 \times 10^{-14} \quad Kw}{1.8 \times 10^{-5} \quad KQ} = 5.6 \times 10^{-10}$

Weak acid

- The degree of dissociation of weak acids and bases, ∝ less than 1 (or less 100%).
- The molarity of H_3O^+ ions is less than the molarity of the acid (HA).
-

$[H_3O^+] < [Acids]$

Acid dissociation constant, K_a

- Each weak acid has an acid dissociation constant (K_a).
- The relative strength of weak acids are deduced from the K_a values.
- Strong acids have higher K_a (lower pK_a) values than weaker acids.

$$K_a = \frac{[H_3O^+][A^-]}{[HA]}$$

Example ;
Methanoic acid (HCOOH); $K_a = 1.6 \times 10^{-4}$ mol dm^{-3}
$pK_a = 3.8$
Is a stronger acid than ethanoic acid (CH_3COOH); $K_a = 1.7 \times 10^{-5}$ moldm^{-3}
$pK_a = 4.8$

WEAK BASE

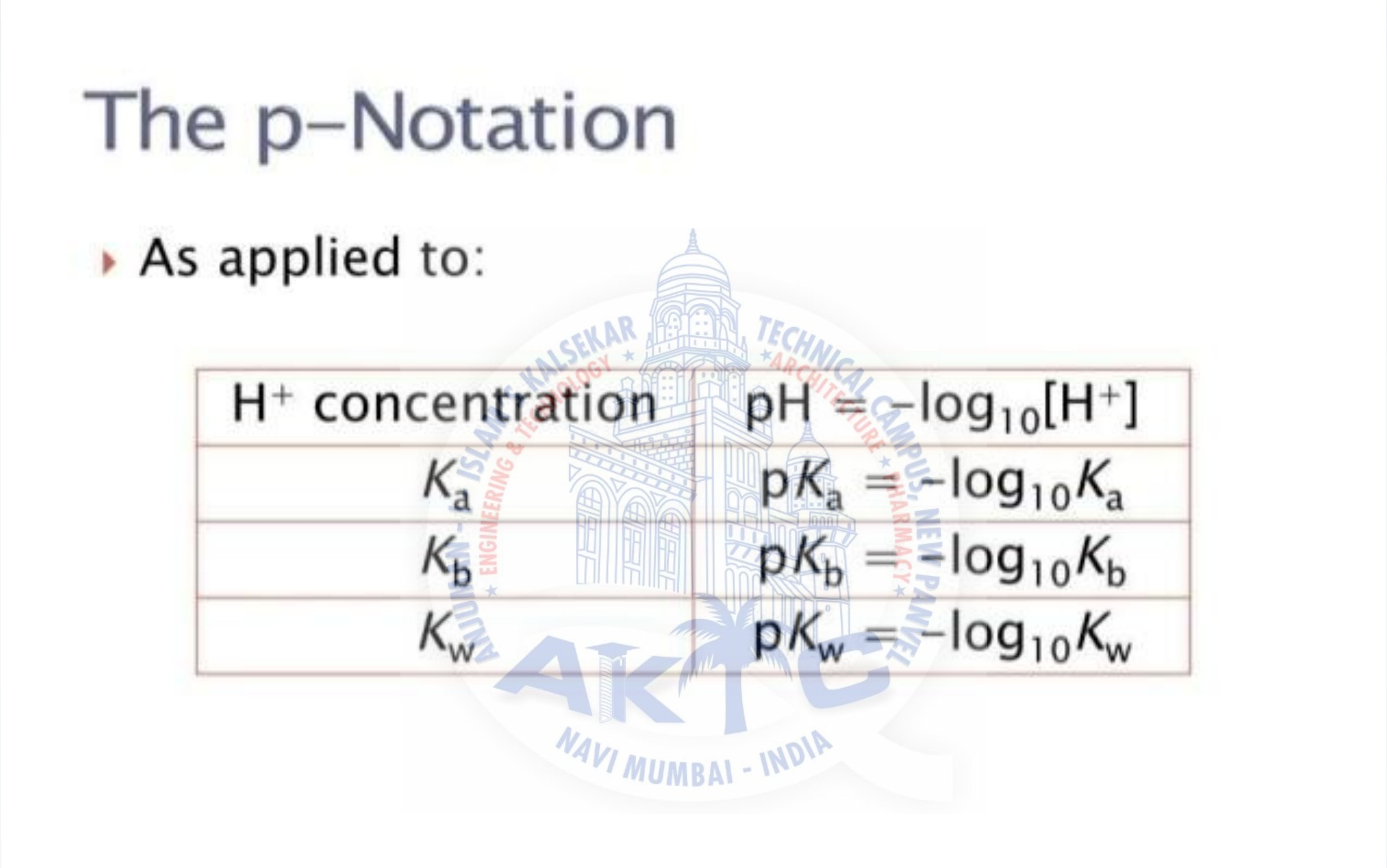
- The degree of dissociation of weak bases $\propto < 1$ ($< 100\%$).
- The molarity of OH^- ion is less than the molarity of undissociated base.

$$[OH^-] < [Base]$$

- The molarity of OH^- from weak bases (B) can be calculated using equilibrium law.

Base dissociation constant, K_b

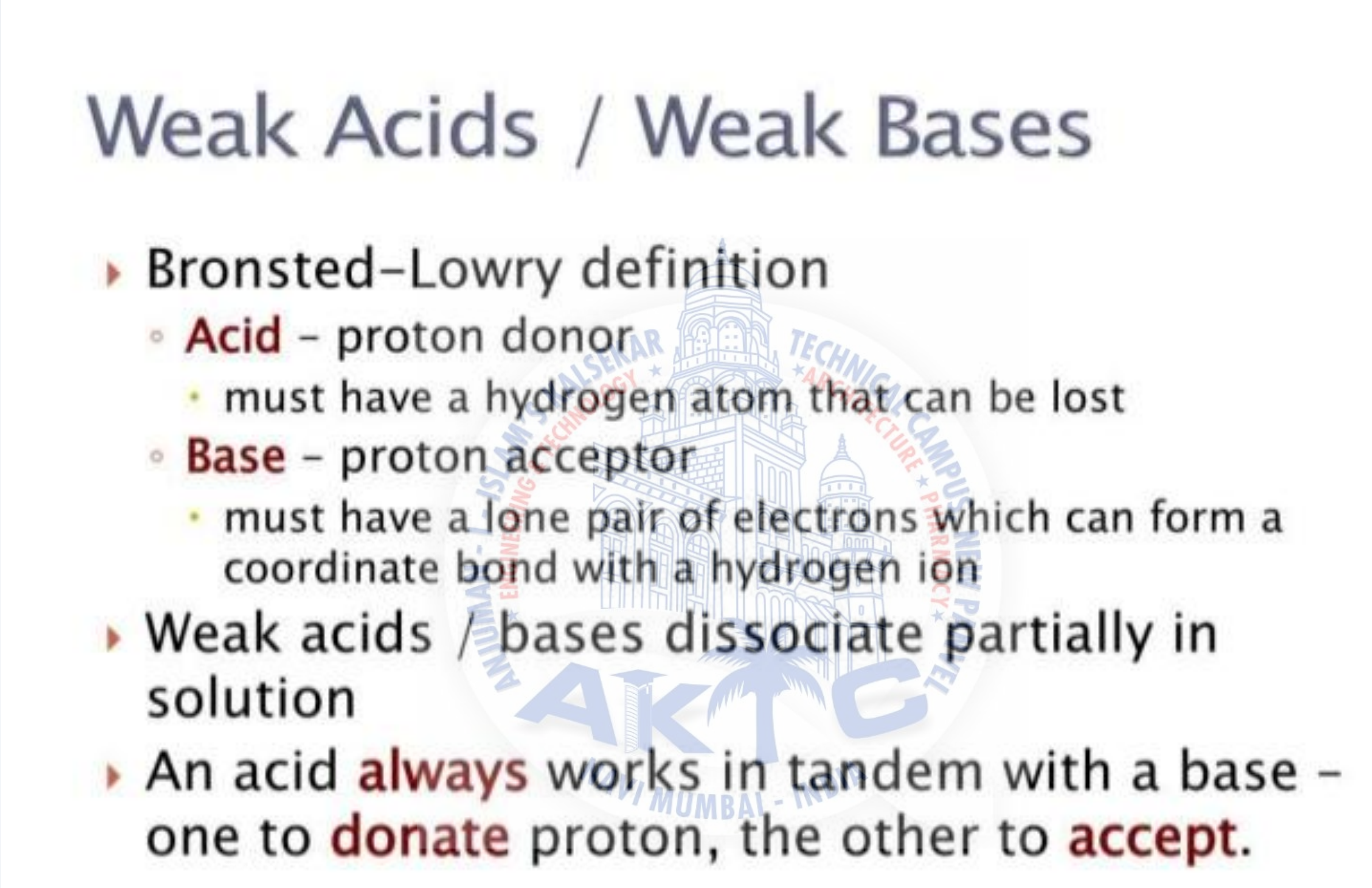
- Weak bases has a base dissociation constant, K_b.
- The relative strength of weak bases can be deduced by comparing the K_b values.
- Strong bases have higher K_b (lower pK_b) values than weaker bases.



The p–Notation

- As applied to:

H^+ concentration	$pH = -\log_{10}[H^+]$
K_a	$pK_a = -\log_{10}K_a$
K_b	$pK_b = -\log_{10}K_b$
K_w	$pK_w = -\log_{10}K_w$



Weak Acids / Weak Bases

- Bronsted–Lowry definition
  - **Acid** – proton donor
    - must have a hydrogen atom that can be lost
  - **Base** – proton acceptor
    - must have a lone pair of electrons which can form a coordinate bond with a hydrogen ion
- Weak acids / bases dissociate partially in solution
- An acid **always** works in tandem with a base – one to **donate** proton, the other to **accept**.

Weak Acids / Weak Bases

- Conjugate acid–base pairs

$$HA + H_2O \rightleftharpoons A^- + H_3O^+$$

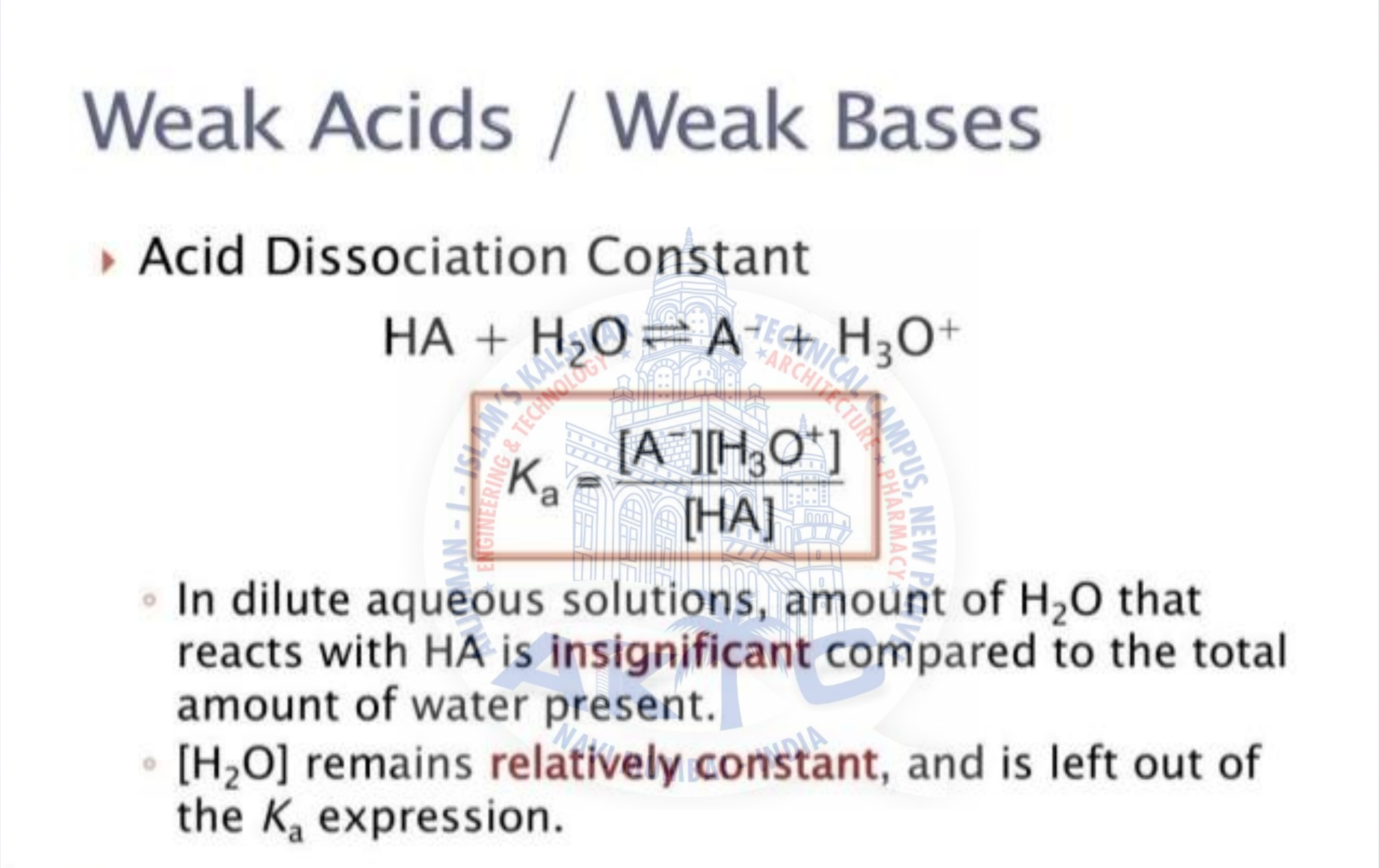
- This equation may be simplified as:

$$HA \rightleftharpoons A^- + H^+$$

Weak Acids / Weak Bases

- Conjugate acid–base pairs

$$B + H_2O \rightleftharpoons BH^+ + OH^-$$



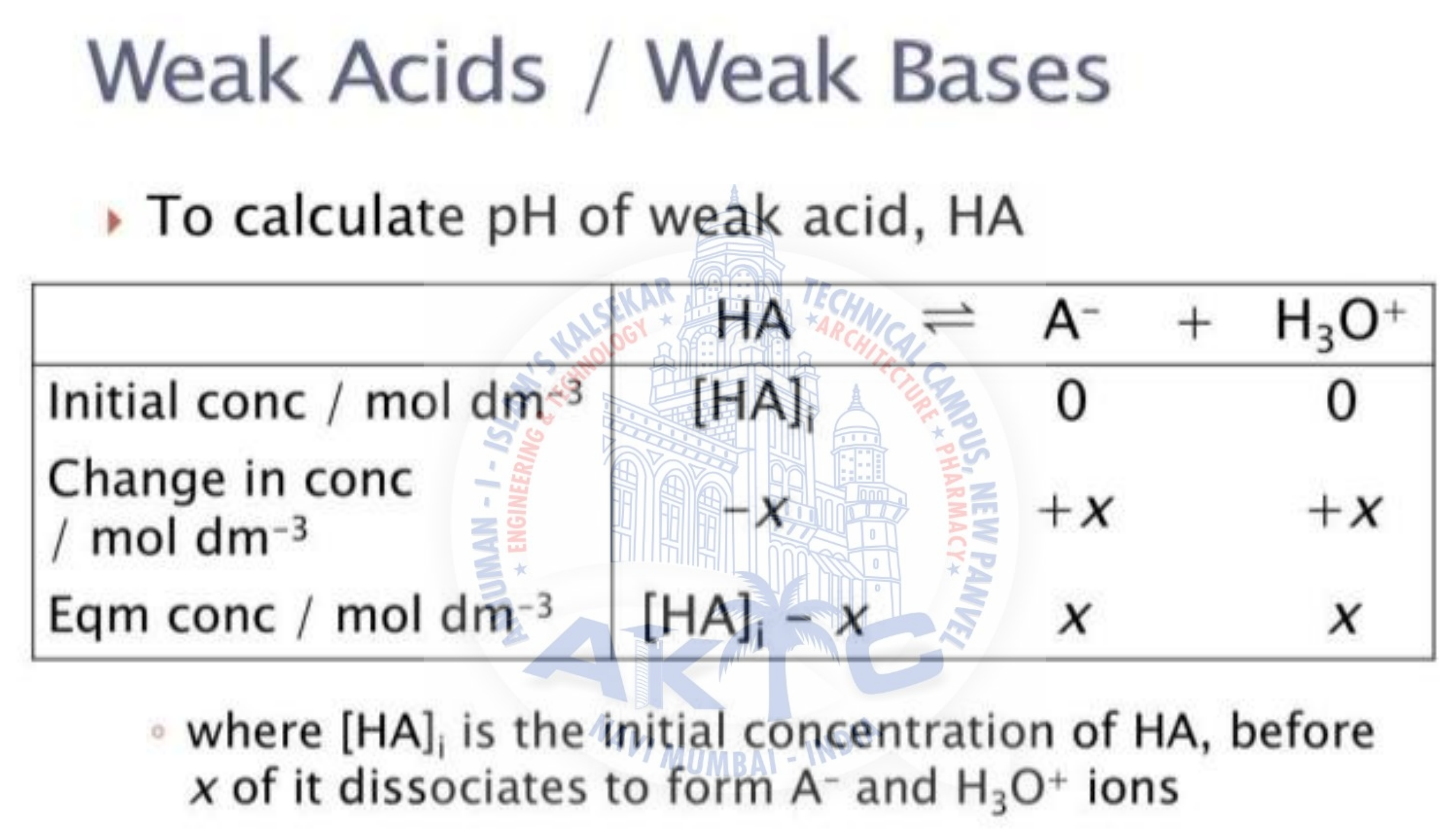
Weak Acids / Weak Bases

- Acid Dissociation Constant

$$HA + H_2O \rightleftharpoons A^- + H_3O^+$$

$$\boxed{K_a = \frac{[A^-][H_3O^+]}{[HA]}}$$

  - In dilute aqueous solutions, amount of H_2O that reacts with HA is insignificant compared to the total amount of water present.
  - $[H_2O]$ remains relatively constant, and is left out of the K_a expression.



Weak Acids / Weak Bases

- To calculate pH of weak acid, HA

	HA	$\rightleftharpoons$	A^-	$+$	H_3O^+
Initial conc / mol dm^{-3}	$[HA]_i$		0		0
Change in conc / mol dm^{-3}	$-x$		$+x$		$+x$
Eqm conc / mol dm^{-3}	$[HA]_i - x$		x		x

  - where $[HA]_i$ is the initial concentration of HA, before x of it dissociates to form A^- and H_3O^+ ions

Weak Acids / Weak Bases

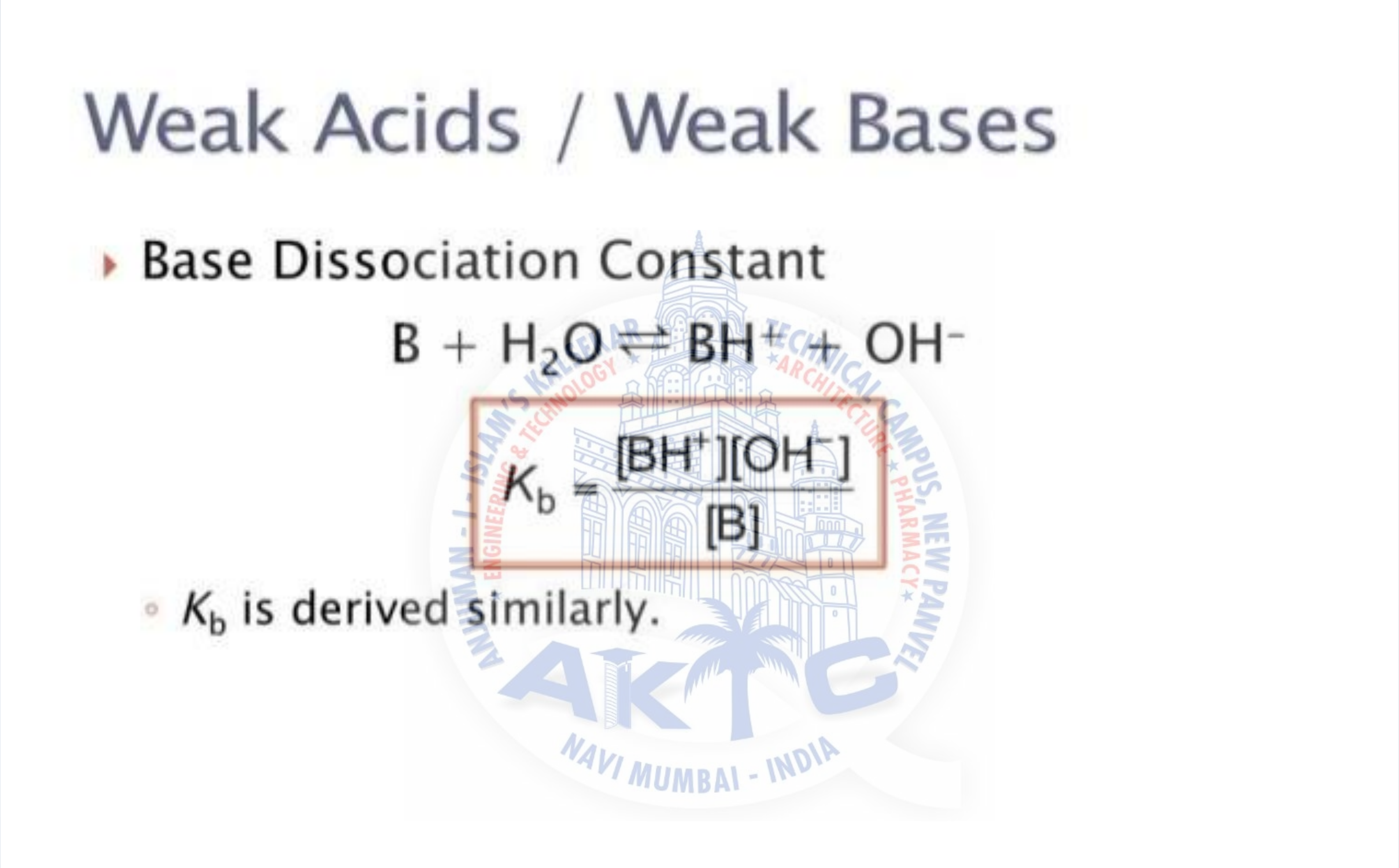
- To calculate pH of weak acid
  - Assuming degree of acid dissociation is small such that $[HA]_i >> x$, and $[HA]_i - x \approx [HA]_i$

$$K_a = \frac{[A^-][H_3O^+]}{[HA]} = \frac{x^2}{[HA]_i - x} \approx \frac{x^2}{[HA]_i}$$

$$\therefore x = [H^+] = \sqrt{K_a \times \{[HA]_i - x\}} \approx \sqrt{K_a \times [HA]_i}$$

equals to [HA]
at equilibrium

$$\boxed{\begin{gathered} pH = -\lg\sqrt{K_a \times [HA]} \\ \text{or} \\ pH \approx -\lg\sqrt{K_a \times [HA]_i} \end{gathered}}$$



Weak Acids / Weak Bases

- Base Dissociation Constant

$$B + H_2O \rightleftharpoons BH^+ + OH^-$$

$$\boxed{K_b = \frac{[BH^+][OH^-]}{[B]}}$$

  - K_b is derived similarly.

Weak Acids / Weak Bases

- To calculate pH of weak base, B

	B	$+$	H_2O	$\rightleftharpoons$	BH^+	$+$	OH^-
Initial conc / mol dm^{-3}	$[B]_i$		–		0		0
Change in conc / mol dm^{-3}	$-x$		–		$+x$		$+x$
Eqm conc / mol dm^{-3}	$[B]_i - x$		–		x		x

  - where $[B]_i$ is the initial concentration of B, before x of it dissociates to form BH^+ and OH^- ions

Weak Acids / Weak Bases

- To calculate pOH of weak base
  - Assuming degree of base dissociation is small such that $[B]_i >> x$, and $[B]_i - x \approx [B]_i$

$$K_b = \frac{[BH^+][OH^-]}{[B]} = \frac{x^2}{[B]_i - x} \approx \frac{x^2}{[B]_i}$$

$$\therefore x = [OH^-] = \sqrt{K_b \times \{[B]_i - x\}} \approx \sqrt{K_b \times [B]_i}$$

equals to [B] at equilibrium

$$\boxed{\begin{gathered} pOH = -\lg\sqrt{K_b \times [B]} \\ \text{or} \\ pOH \approx -\lg\sqrt{K_b \times [B]_i} \end{gathered}}$$

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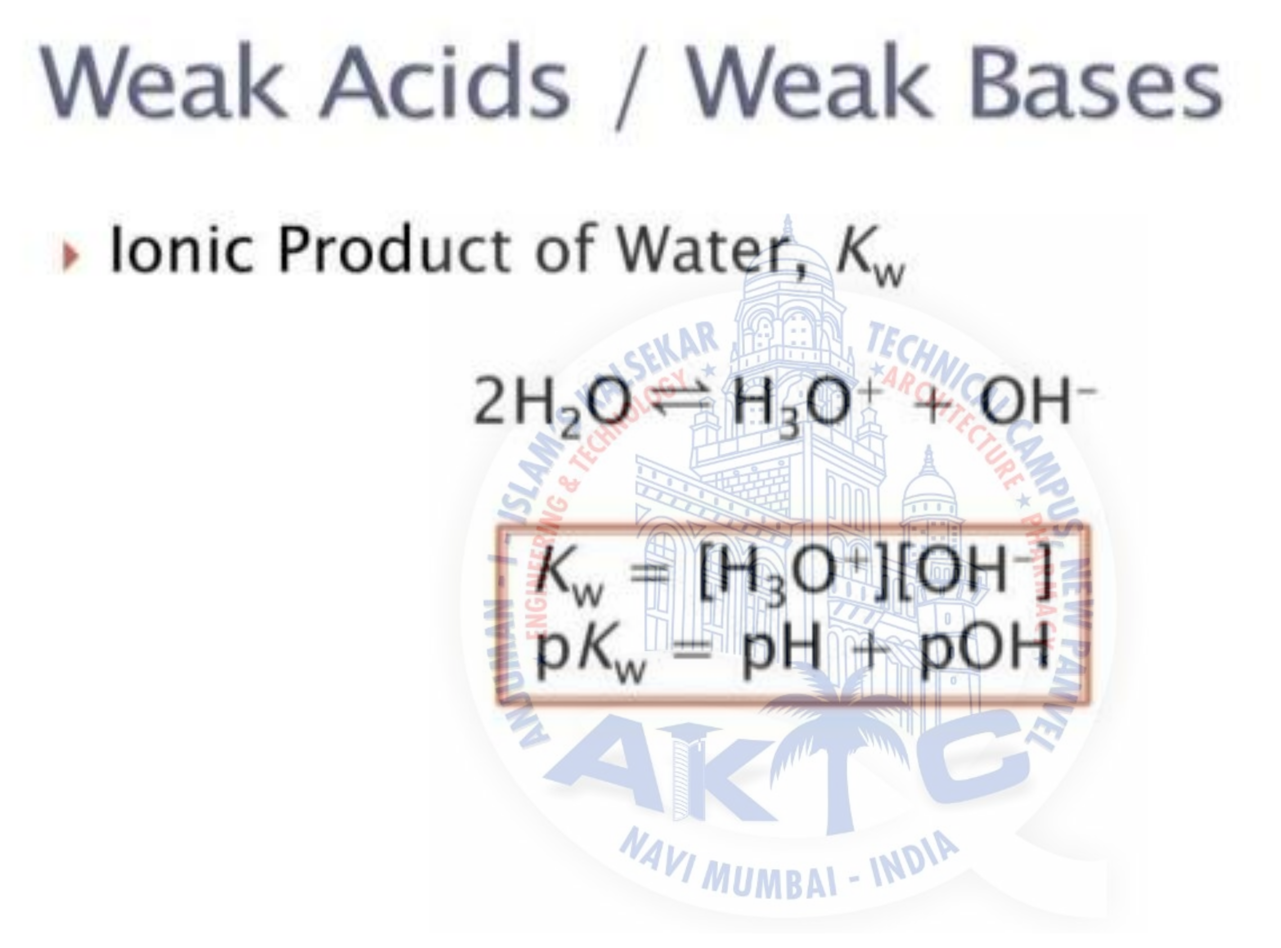


Weak Acids / Weak Bases

- Ionic Product of Water, K_w

$$2H_2O \rightleftharpoons H_3O^+ + OH^-$$

$$\boxed{\begin{array}{l} K_w = [H_3O^+][OH^-] \\ pK_w = pH + pOH \end{array}}$$

Weak Acids / Weak Bases

- Temperature dependence of K_w

Temperature / °C	K_w / x 10^{-14} mol² dm^{-6}	pK_w	[H^+] / 10^{-7} mol dm^{-3}	[OH^-] / 10^{-7} mol dm^{-3}	pH
0	0.114	14.9	0.338	0.338	7.47
25	1.01	14.0	1.00	1.00	7.00
50	5.48	13.3	2.34	2.34	6.63

- pH + pOH = 14 is **only** applicable at 25 °C!
- pH of pure water decreases with temperature as [H^+] increases. *Is water becoming more acidic?*

No, pure water remains neutral at **all** *temperatures even though pH changes, since [H^+] and [OH^-] are* **always equal** *at* **all** *temperatures.*

Weak Acids / Weak Bases

- Relationship between K_w, K_a and K_b
  - Consider a weak acid HA,

$$\underset{\text{acid}}{HA} + H_2O \rightleftharpoons \underset{\text{conjugate base}}{A^-} + H_3O^+$$

$$K_a = \frac{[A^-][H_3O^+]}{[HA]}$$

  - Its conjugate base, A^-, undergoes salt hydrolysis as follows:

$$A^- + H_2O \rightleftharpoons HA + OH^-$$

$$K_b = \frac{[HA][OH^-]}{[A^-]}$$

Weak Acids / Weak Bases

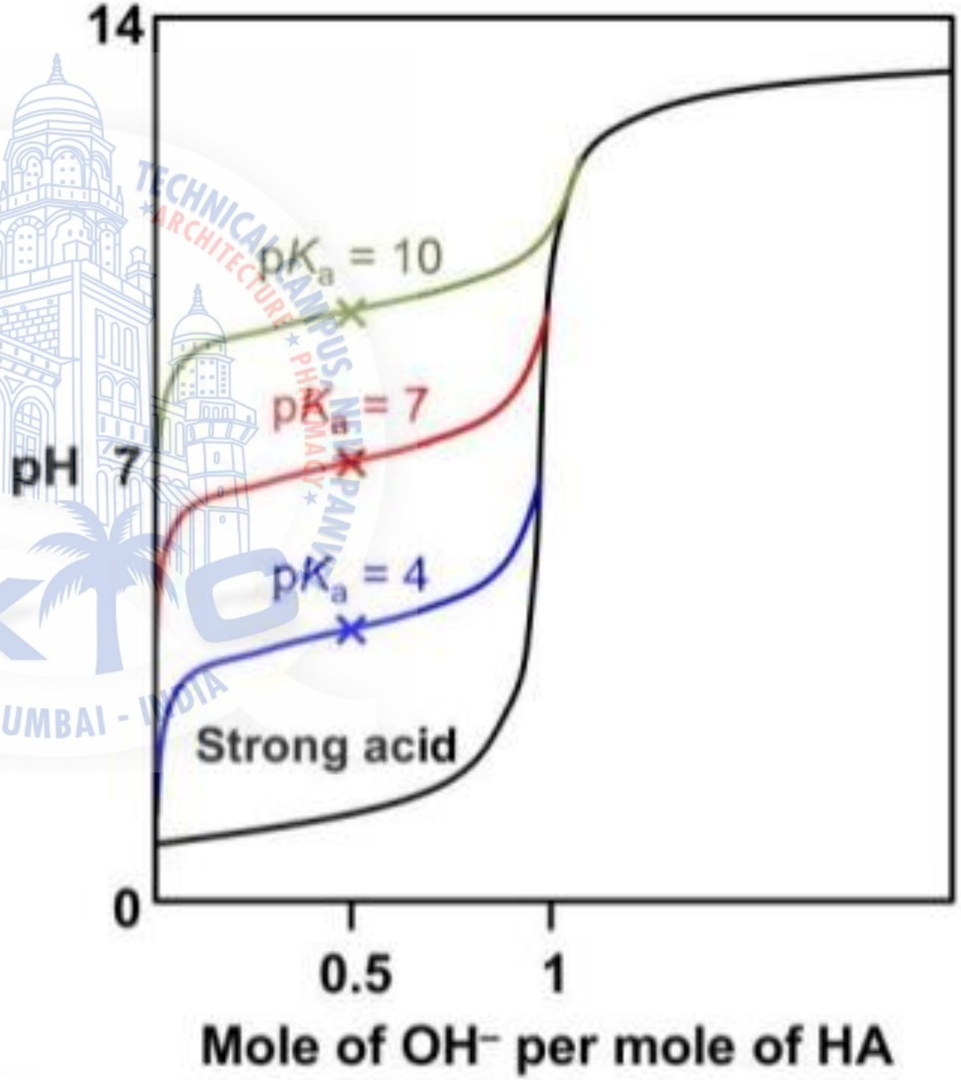
- Relationship between K_w, K_a and K_b

$$K_a \times K_b = \frac{\cancel{[A^-]}[H_3O^+]}{\cancel{[HA]}} \times \frac{\cancel{[HA]}[OH^-]}{\cancel{[A^-]}}$$

$$K_a \times K_b = [H_3O^+][OH^-] = K_w$$

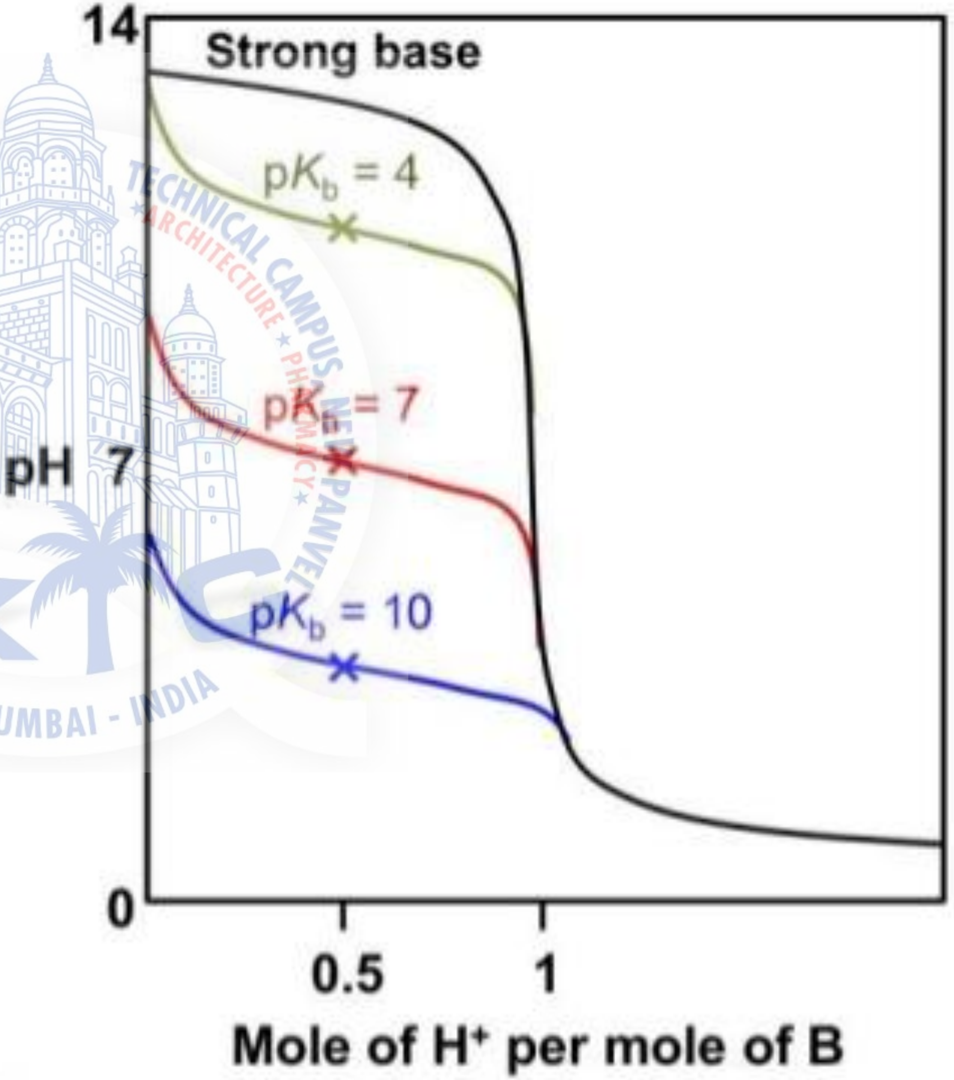
Weak Acids / Weak Bases

- pH Titration Curves
  - Weak acids titrated against a strong base



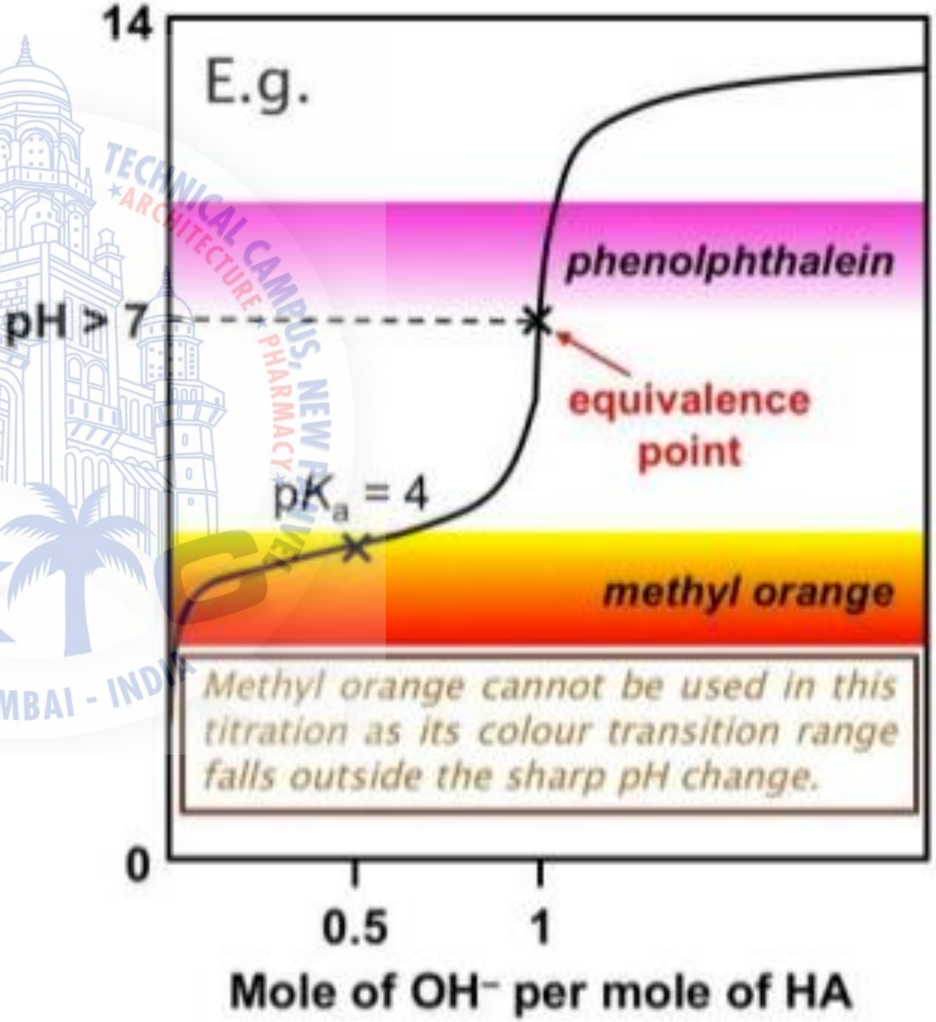
Weak Acids / Weak Bases

- pH Titration Curves
  - Weak bases titrated against a strong acid



Weak Acids / Weak Bases

- Choice of Indicator
  - pH transition range of chosen indicator should fall within the region where a sharp change in pH is observed on the titration curve.



Methyl orange cannot be used in this titration as its colour transition range falls outside the sharp pH change.

REFRENCES

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- Essentials of Physical Pharmacy , C.V .S Subrahmanyum, V allabh Prakashan

- Internet access (wikipedia)

QUESTION BANK

1. Define
- Buffer
- Buffer capacity
- pH
- pOH
- Dissociation constant

2. Explain in brief Henderson-Hasselbalch equation
3. Expalin application of Buffer in pharmaceutical and biological systems
4. Explain Sorensen's pH scale
5. Explian methods of determining pH
6. Give mechasims of working of buffers
7. Give concept of weak and strong electrolytes
8. Give structure of glass electrode