

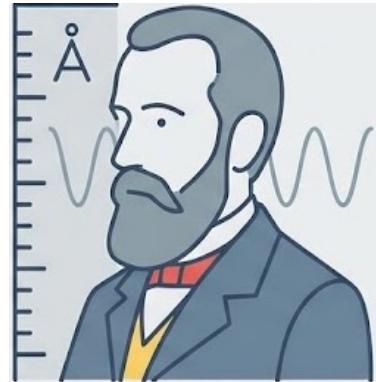
## **CHAPTER 2**

# **Water, Weak Bonds, and the Generation of Order Out of Chaos**

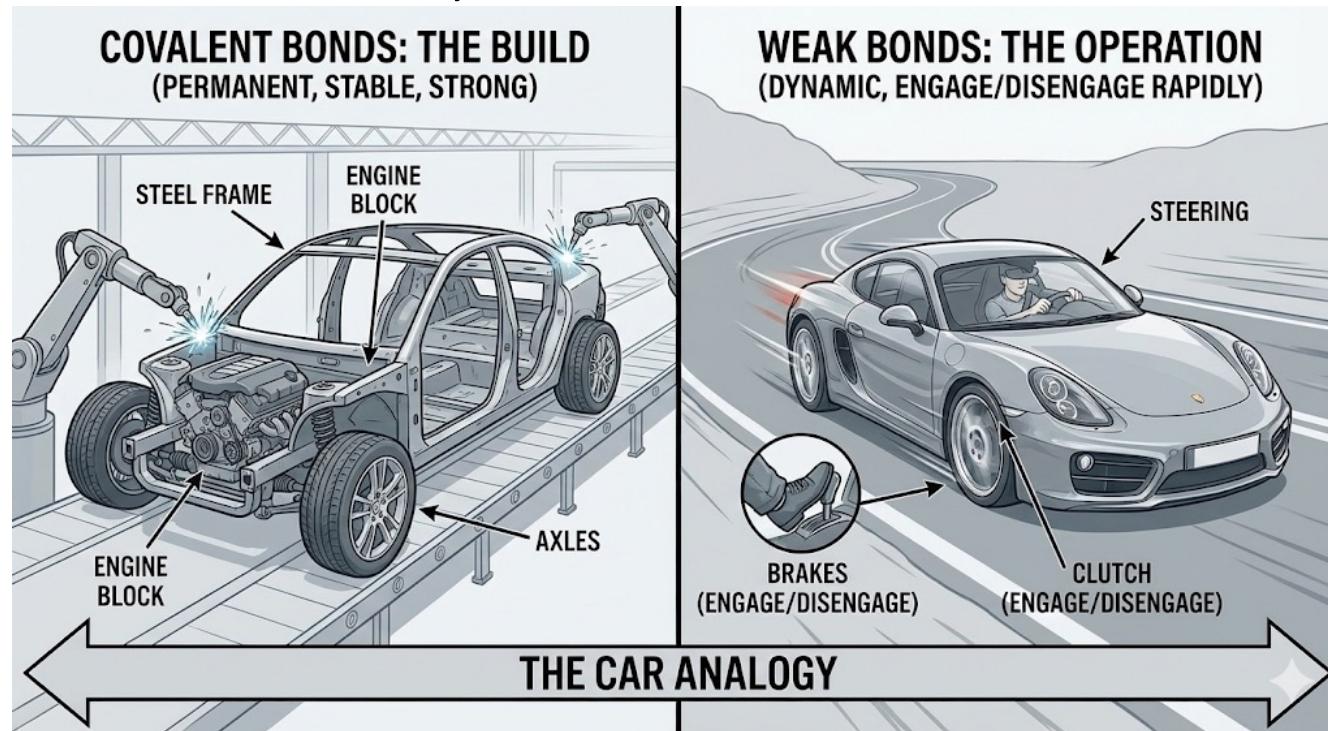
- **2.1 Thermal Motions Power Biological Interactions**
- **2.2 Biochemical Interactions Take Place in an Aqueous Solution**
- **2.3 Weak Interactions Are Important Biochemical Properties**
- **2.4 Hydrophobic Molecules Cluster Together**
- **2.5 pH Is an Important Parameter of Biochemical Systems**

# Introduction to Chapter 2

- 4 Ångströms is the distance where life happens, governed by weak, reversible interactions such as hydrogen bonds, van der Waals forces, and ionic bonds.
- Weak bonds permit dynamic interactions that form the basis of biochemistry and life itself.

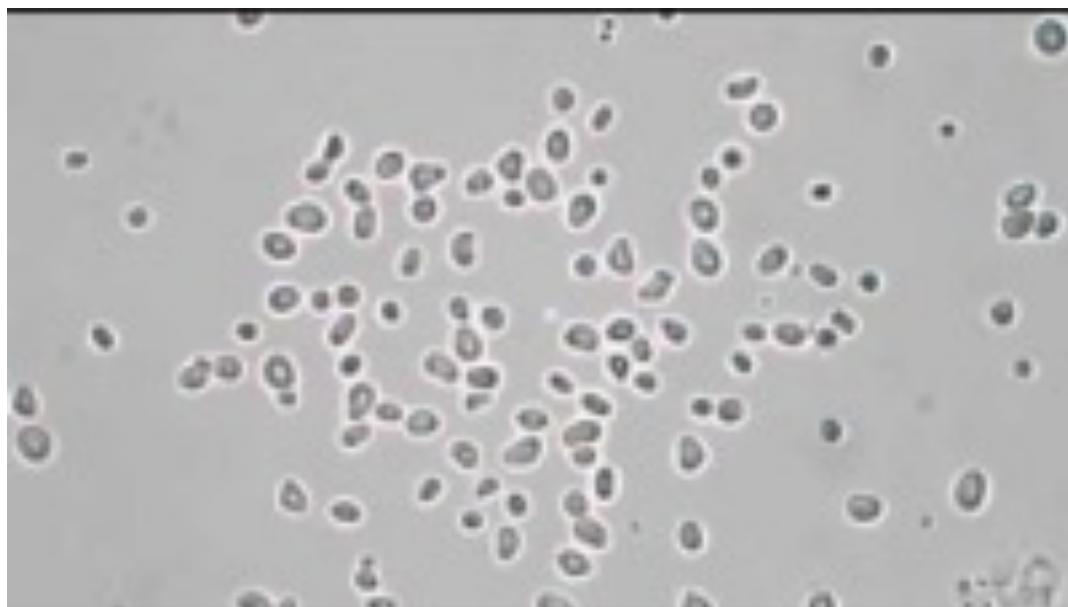
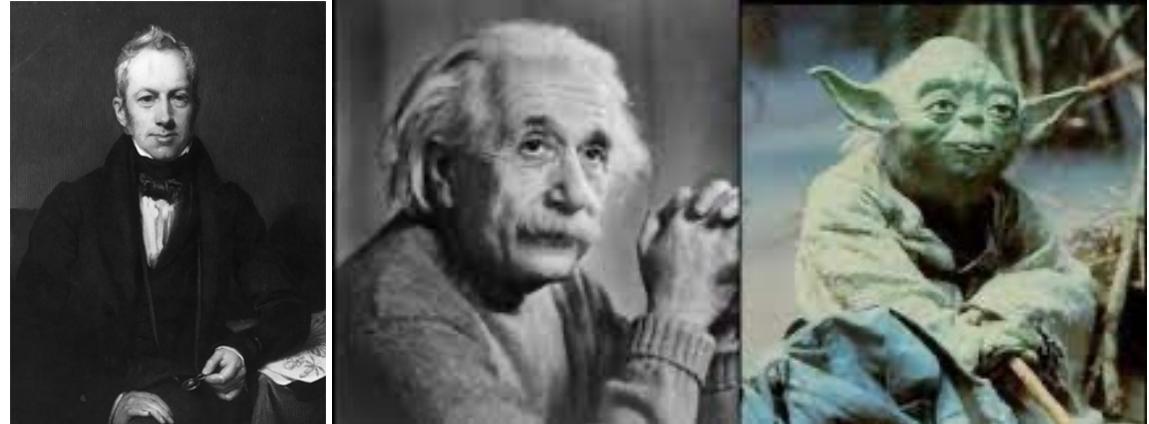


- One angstrom ( $\text{\AA}$ ) = 0.1 nanometer (nm) =  $1 \times 10^{-10}$  meter (m). It is named after Swedish physicist Anders Jonas Ångström (1814–1874), who expressed wavelengths as multiples of  $1 \times 10^{-10}$  meter. That length was subsequently named an angstrom.



# Section 2.1

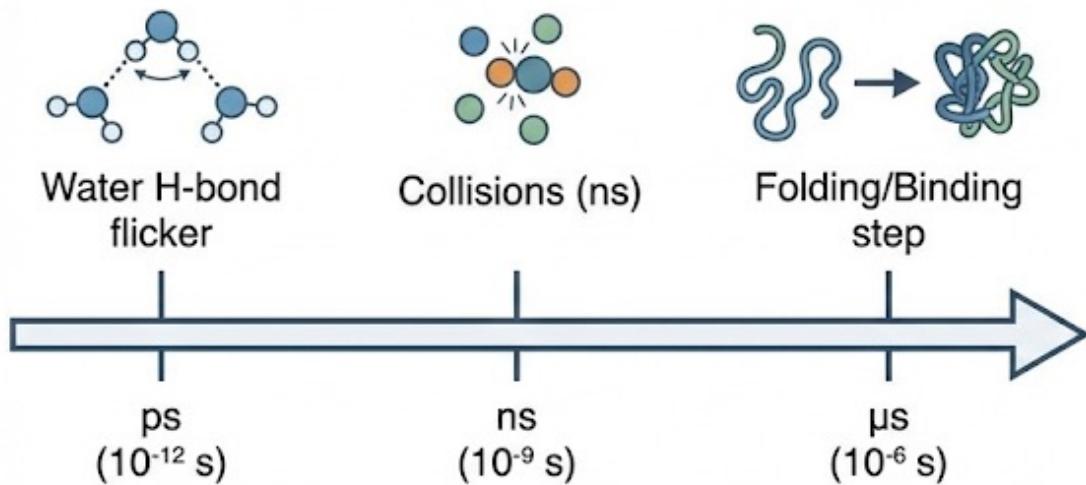
## Thermal Motions Power Biological Interactions



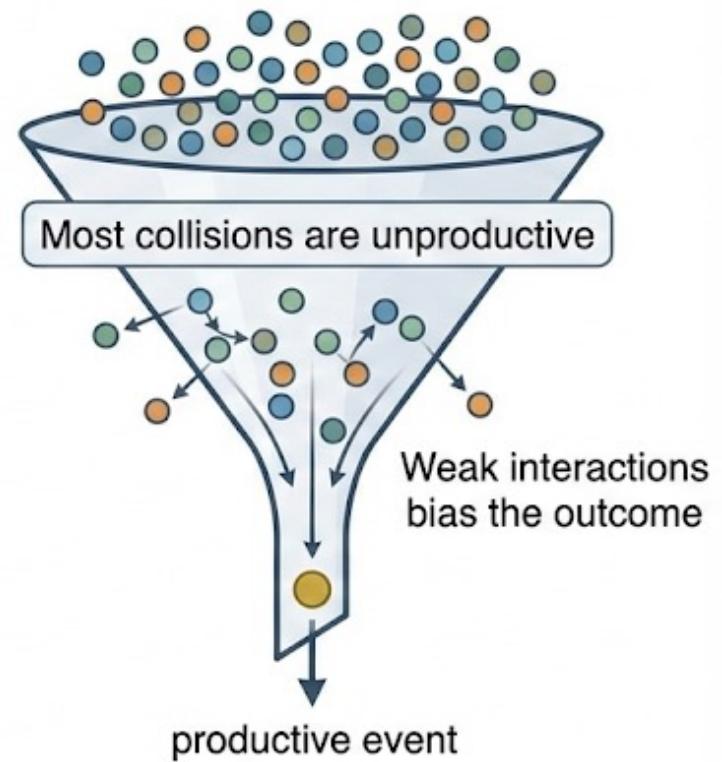
- Molecules are never still – Brownian motion is random jostling from thermal energy
- Water is ~60–70% of you, so this is the molecular stage where everything happens
- Thought experiment: What happens to life if the Brownian mosh pit stops?

# Collisions Are Cheap, Reactions Are Rare

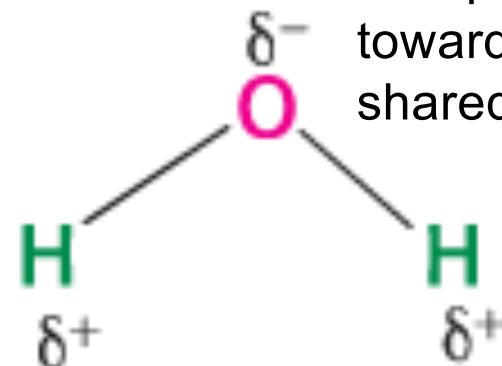
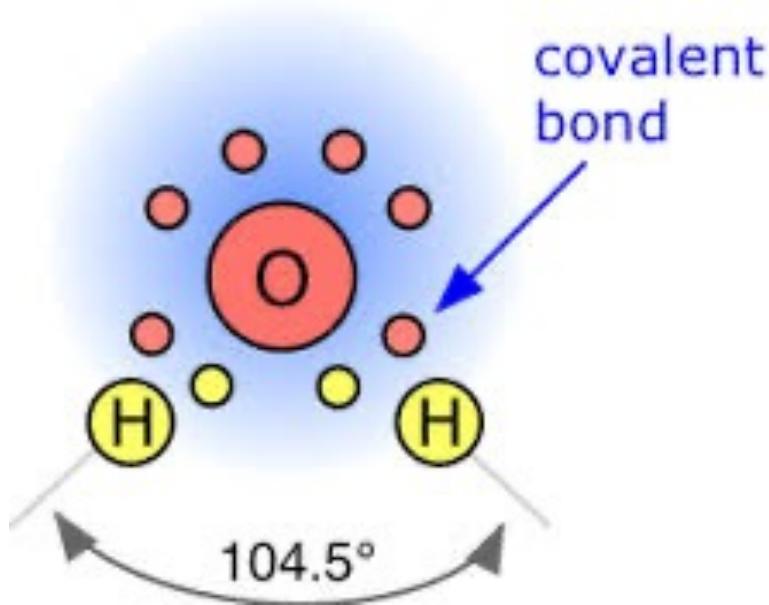
Typical biochemical timescale: ps to  $\mu$ s



Collisions: ~every nanosecond



Life is statistical mechanics  
wearing a lab coat.



Oxygen is electronegative, so it pulls electron density toward itself and hogs the shared electrons.

Something that looks neutral actually carries partial charges

## Section 2.2 Biochemical Interactions Take Place in an Aqueous Solution

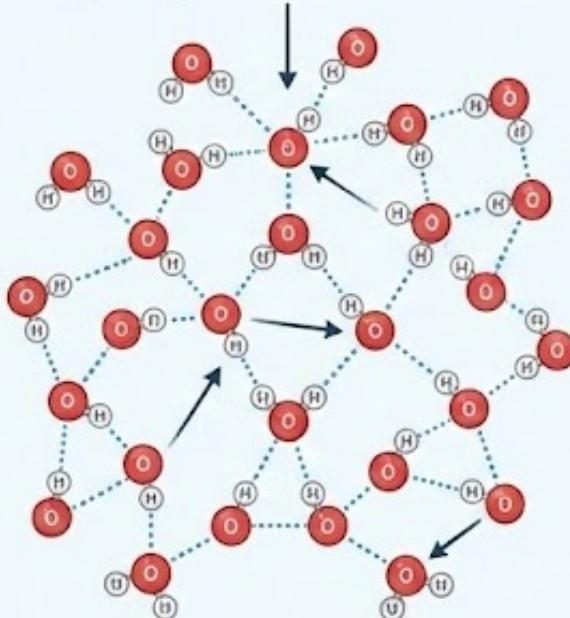
- Learning objective 4: Describe the chemical properties of water and explain how water affects biochemical interactions.
- Water is a polar molecule, with the oxygen atom carrying a slightly negative charge and the hydrogen atoms carrying slightly positive charges.
- Because charges are not evenly distributed it's polar

## 2.2 Three things that water does for biochemistry:



### 1. COHESION:

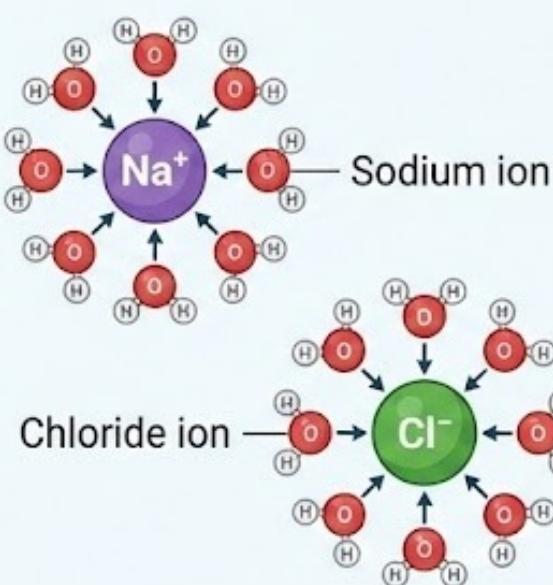
Hydrogen Bond Network



Water molecules attract each other through hydrogen bonds.

### 2. SOLVATION:

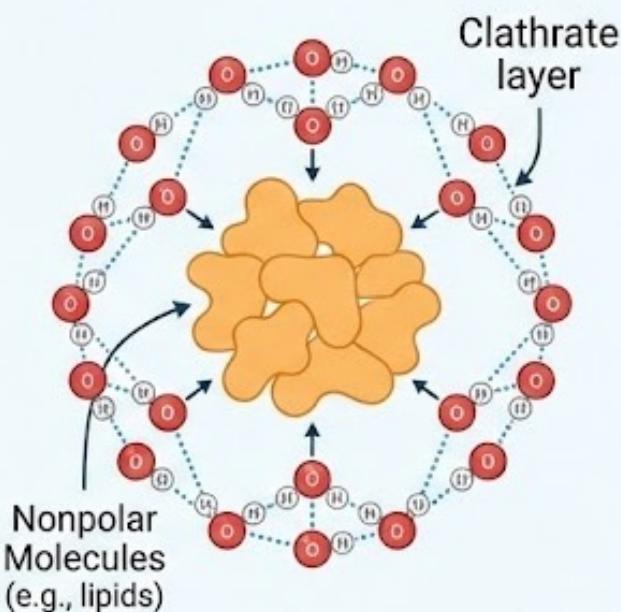
Hydration Shells of Ions



Water molecules surround and stabilize ions, forming hydration shells.

### 3. HYDROPHOBIC CLUSTERING:

Ordered Water Cage

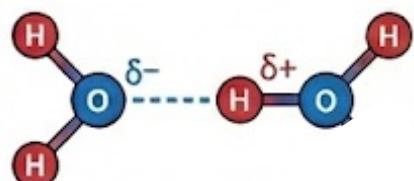


Nonpolar molecules aggregate, driving water to form an ordered cage around them.

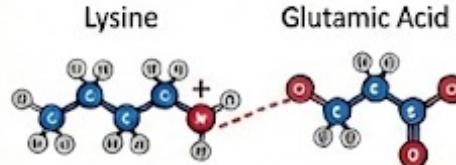
- Sticks to itself (cohesion via H bonds)
- Dissolves charged and polar molecules
- Rejects nonpolar molecules, which drives the hydrophobic effect”

## Section 2.3: Weak Interactions Are Important Biochemical Properties.

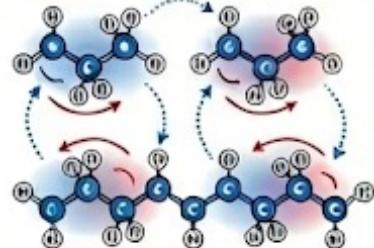
### Weak Interactions: Essential for Biochemical Dynamics



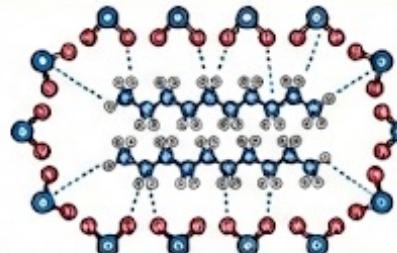
**Hydrogen Bonds:** Electrostatic attraction between  $\delta+$  H (bonded to O or N) and a  $\delta-$  electronegative atom like O or N.



**Ionic Bonds/Salt Bridges:** Electrostatic attraction between oppositely charged groups (e.g., + and - in amino acid side chains).



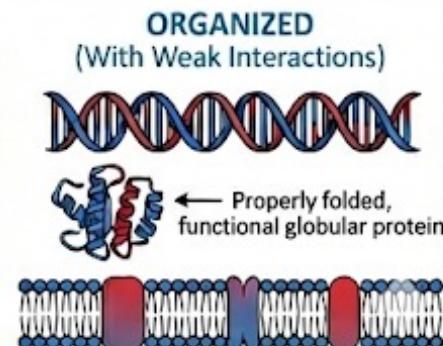
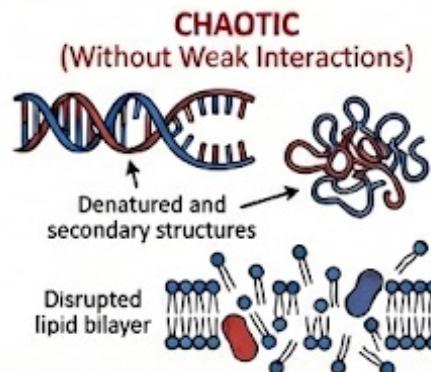
**Van der Waals Forces:** Temporary attractions from induced dipoles and electron fluctuations.



**Hydrophobic Interactions:** Entropy-driven clustering of nonpolar groups to exclude water.

- ✓ **Non-covalent and reversible**—enable dynamic processes like protein folding, DNA replication, and enzyme-substrate binding.
- ✓ Generate **order from chaos** in biological systems.

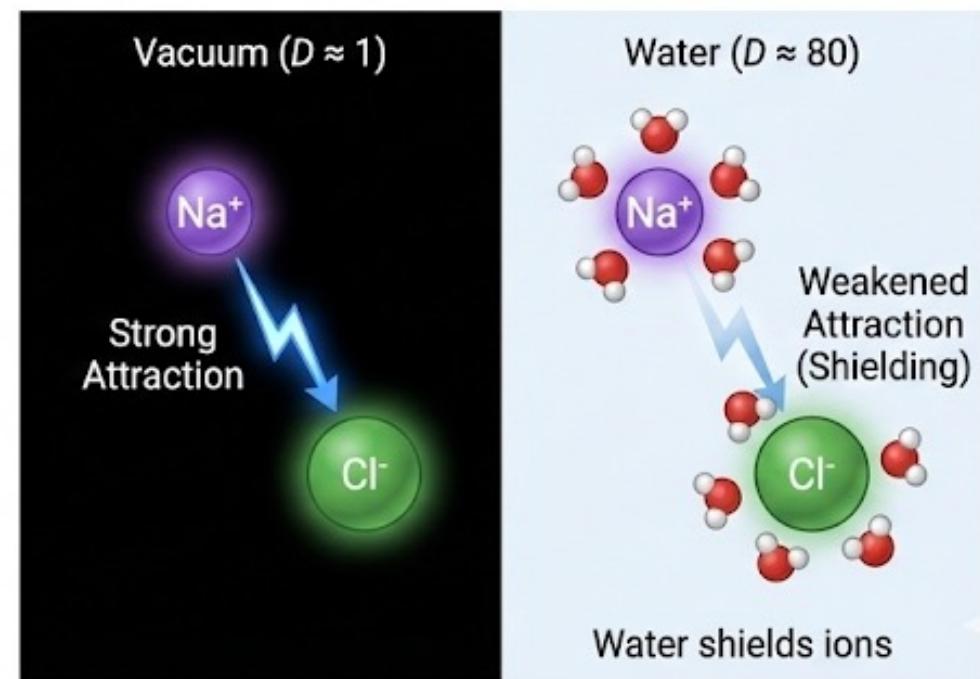
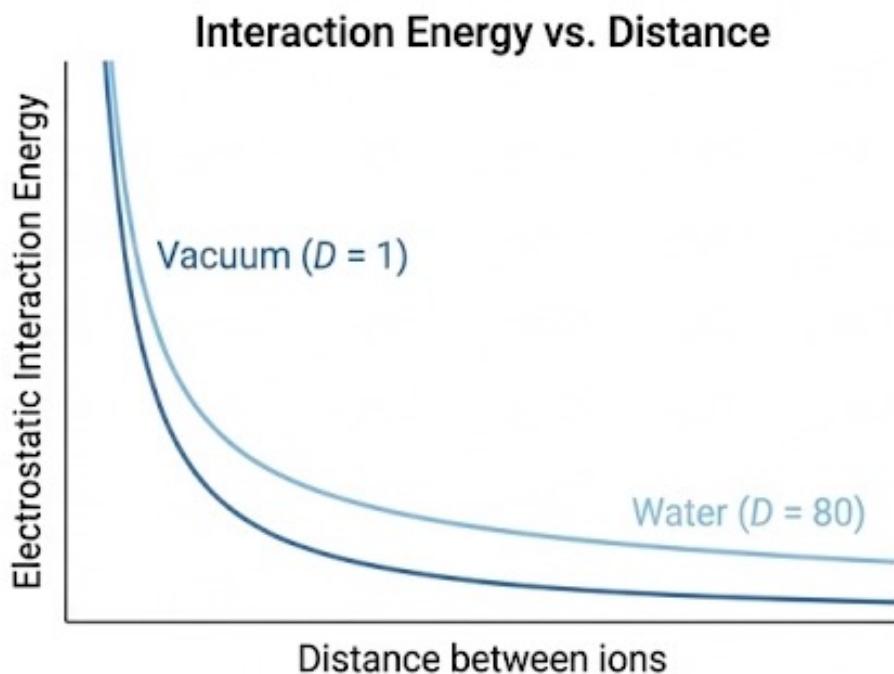
**What would life be like without reversible, weak interactions?**



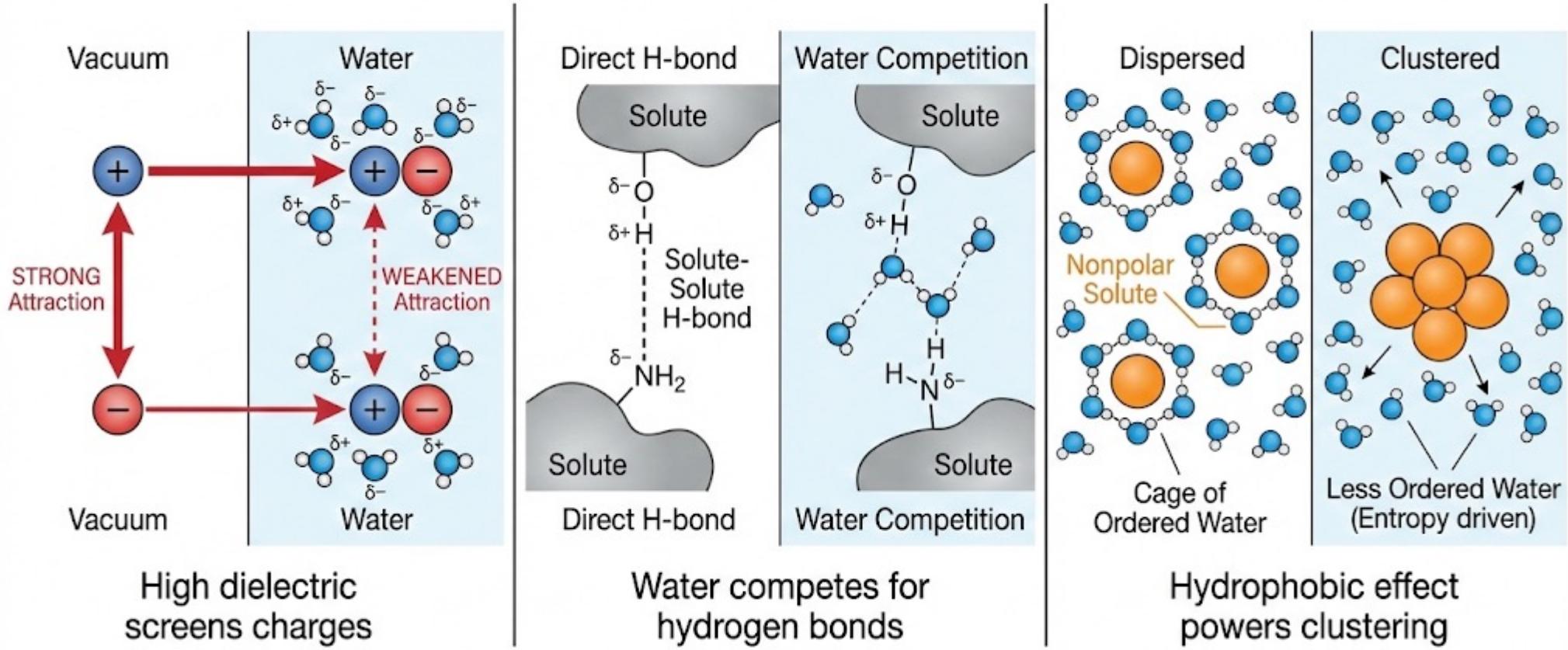
# The Role of Water: Shielding Ionic Interactions

$$E = \frac{kq_1q_2}{Dr}$$

- Energy falls with distance and with higher dielectric constant.
- Water's high dielectric constant weakens direct ion–ion attractions, allowing salts to dissolve.

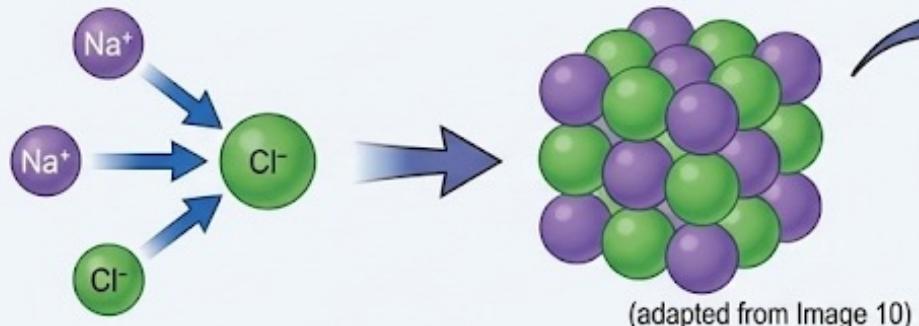


# Water Does Two Big Things to Weak Interactions



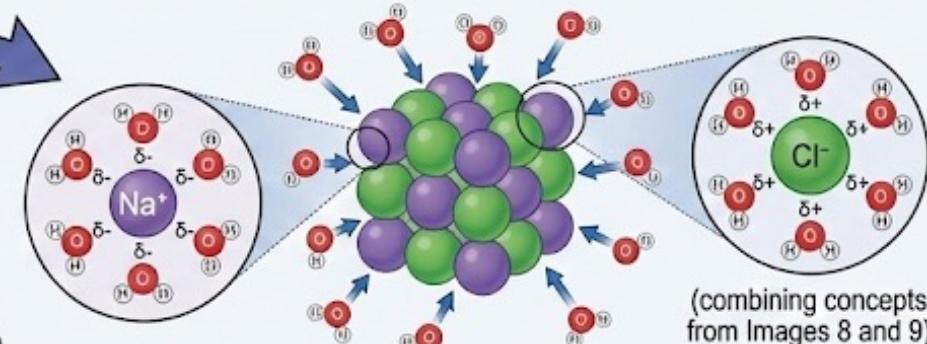
# Ionic Interactions: From Salt Crystals to Protein Structure

## 1. Strong Attraction Forms Crystals (Low Dielectric Environment)



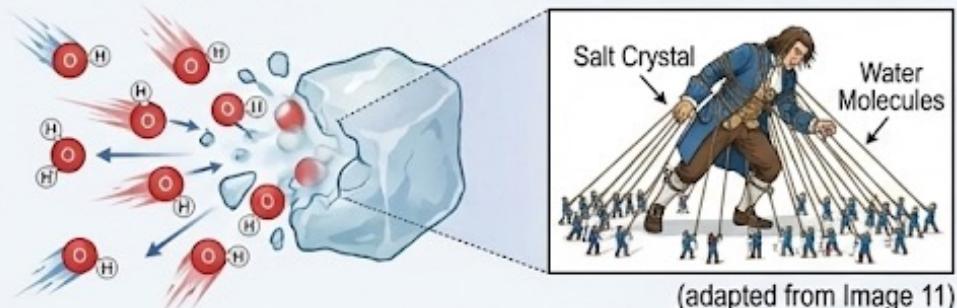
In the absence of water, electrostatic forces are strong, forming stable crystalline structures.

## 2. Water Weakens Interactions & Dissolves (High Dielectric $D \approx 80$ )



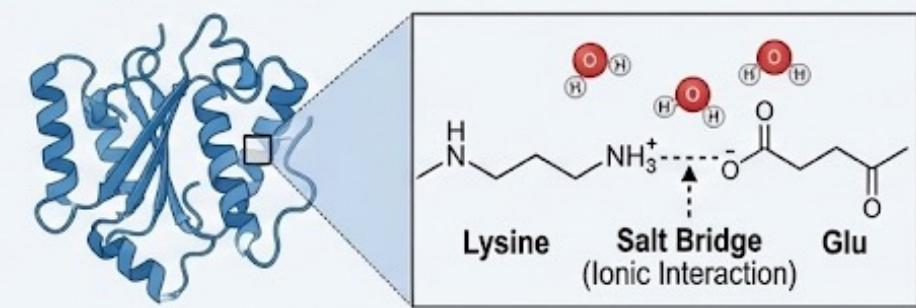
Water's high dielectric constant shields charges. Hydration shells replace ion-ion interactions, energetically allowing dissolution.

## 3. The Driving Force: Brownian Motion & The 'Gulliver' Effect



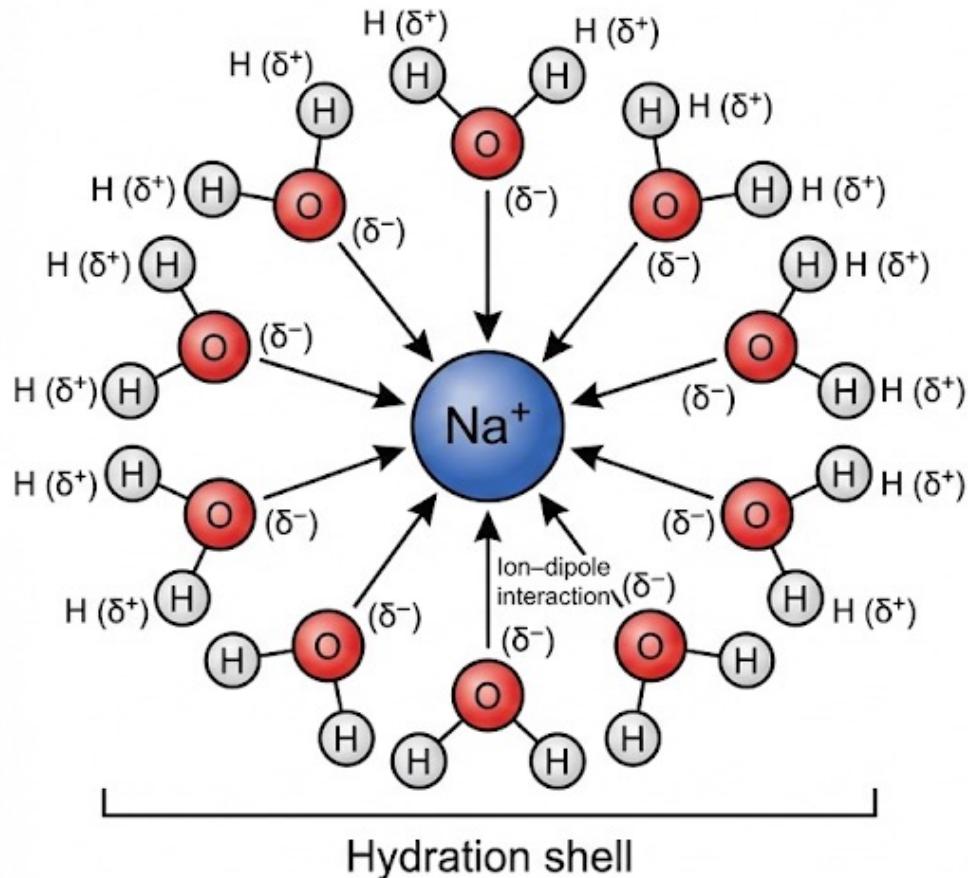
Thermal energy drives random collisions (Brownian motion). Like many small Lilliputians overpowering Gulliver, countless water collisions overcome the crystal lattice energy.

## 4. Biological Context: Salt Bridges in Proteins

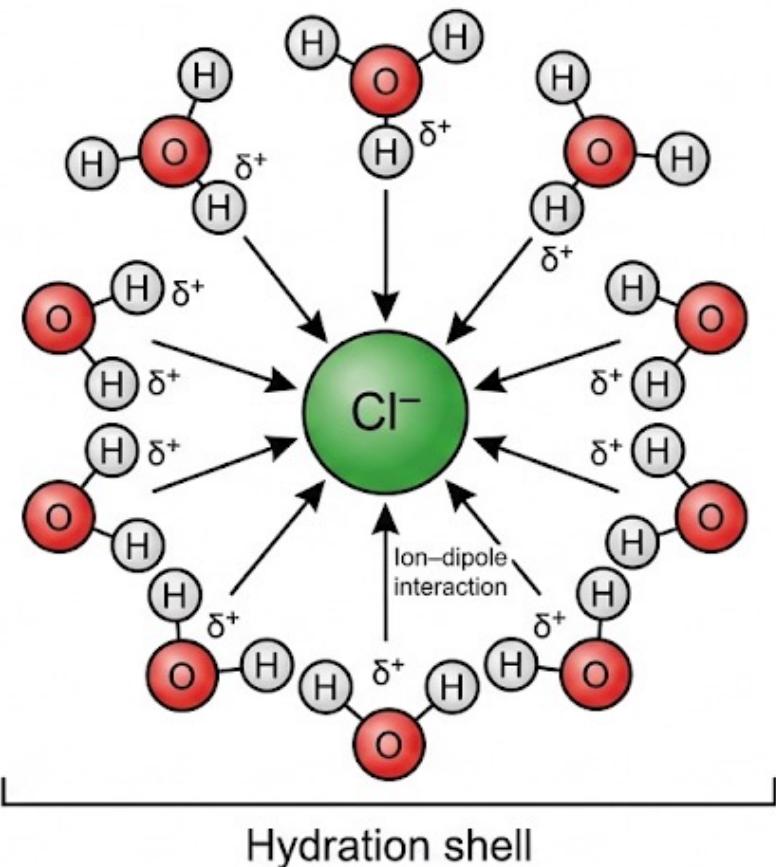


Ionic bonds between charged residues stabilize protein structures. These 'salt bridges' are often on the surface and are dynamic due to competition with water.

## $\text{Na}^+$ Hydration Shell



## $\text{Cl}^-$ Hydration Shell



Water dipole:  $\delta-$  on O,  $\delta+$  on H

# Quick Check: When Are Ionic Interactions Strongest?

- Pick all that increase electrostatic attraction

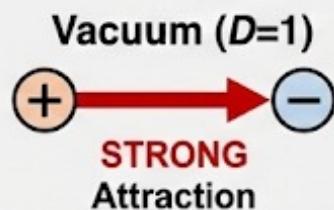
- Lower dielectric ( $D$ )
- Shorter distance ( $r$ )
- Larger charges ( $q_1, q_2$ )
- Water weakens ion–ion attraction compared to nonpolar environments

$$F \propto \frac{q_1 * q_2}{D * r^2}$$

Dielectric      Distance

Strongest electrostatics:  
high charge, close  
distance, low dielectric.

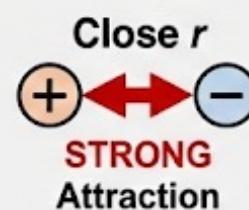
## Dielectric Comparison



Lower  $D \rightarrow$  stronger attraction

Water (high  $D$ ) weakens ionic interactions

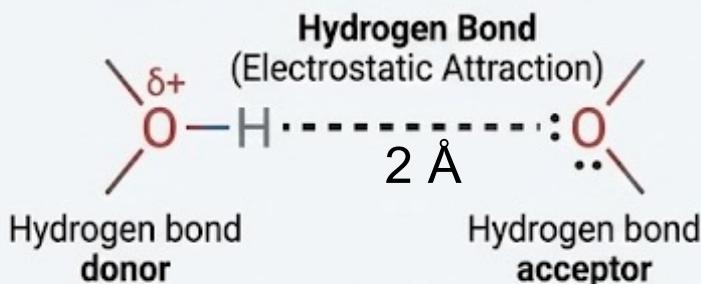
## Distance Comparison



Smaller  $r \rightarrow$  stronger attraction

Pick all that apply

# Hydrogen Bonds: Directional Weak Interactions & Their Biological Significance

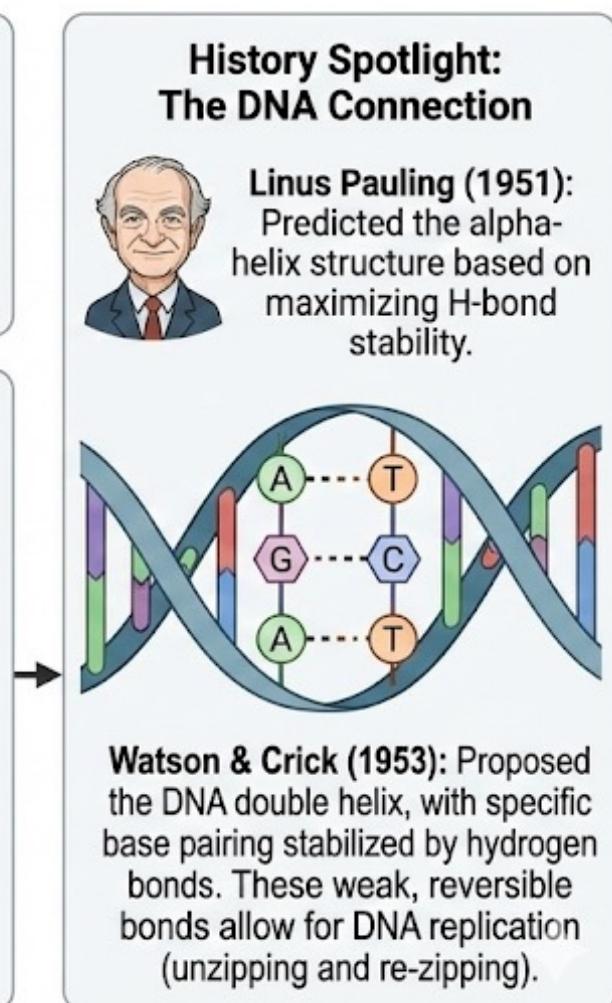
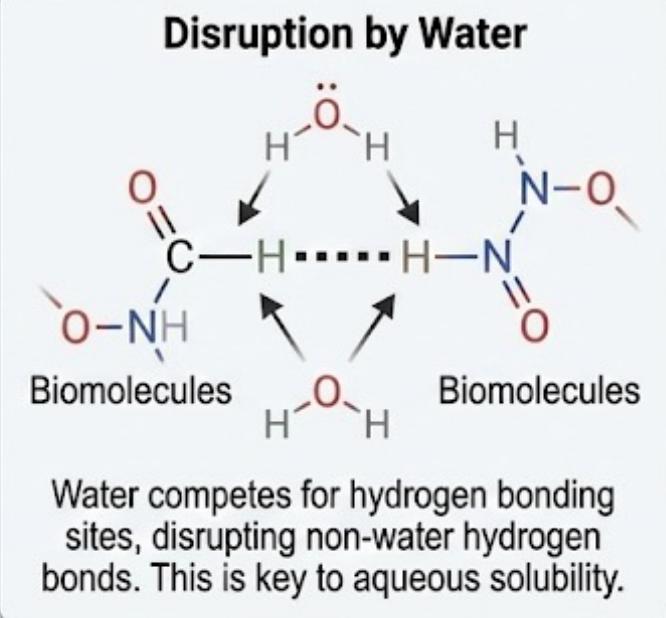
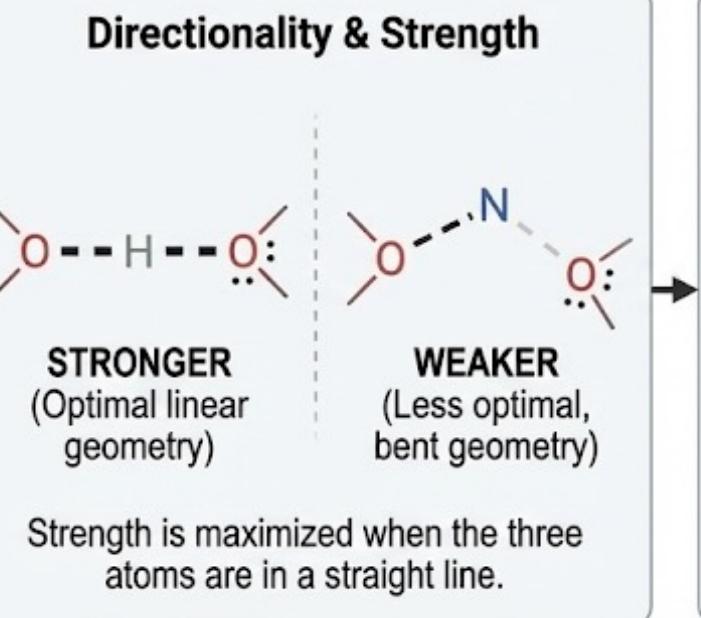


**Hydrogen Bond Donor**  
Interaction between a hydrogen atom covalently bound to an electronegative atom and a lone pair on another electronegative atom.  
Crucial for structure & function.

## History Spotlight: The DNA Connection



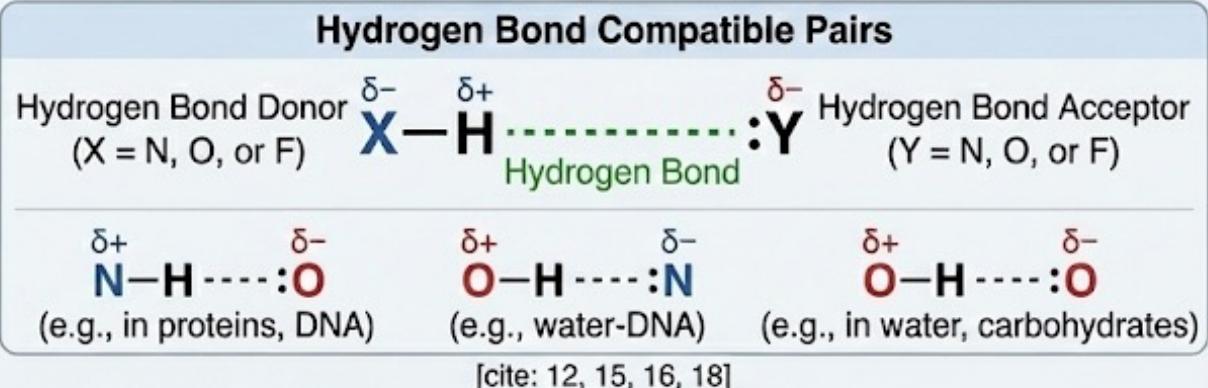
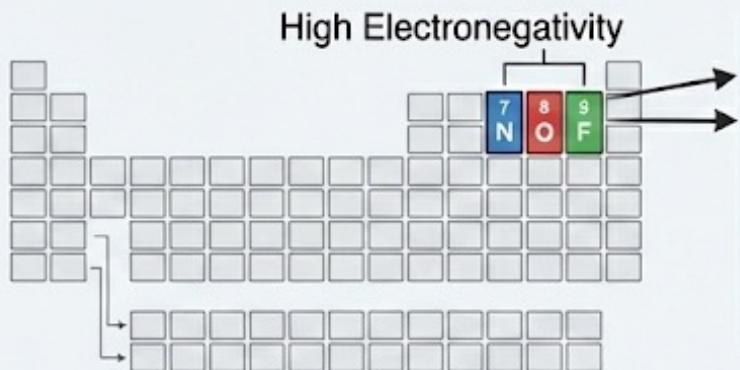
**Linus Pauling (1951):** Predicted the alpha-helix structure based on maximizing H-bond stability.



# Hydrogen Bonds: Key Players, Compatibility, and Characteristics

**Definition:** An electrostatic attraction between a hydrogen atom (covalently bonded to a highly electronegative atom) and a lone pair of electrons on another electronegative atom (**acceptor**) [cite: 16, 18].

## The Players: Electronegative Atoms & Compatibility



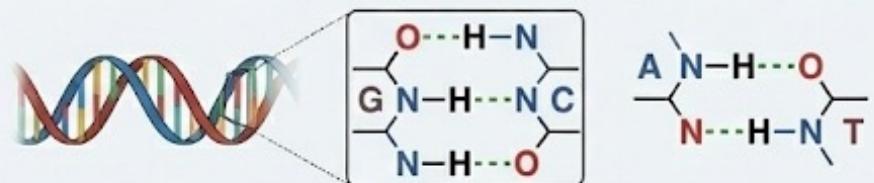
## Protein-Protein Hydrogen Bonding

(e.g., Secondary Structure)



H-bonds between backbone atoms stabilize alpha-helices and beta-sheets [cite: new].

## DNA Strand Hydrogen Bonding (Base Pairing)



Specific H-bonds between complementary bases hold the two DNA strands together [cite: new].

# True or False: Every Functional Group Can H-Bond

- False. Strong H-bonds usually require O or N
- Donor: H covalently bound to electronegative atom
- Acceptor: lone pair on electronegative atom
- C–H groups generally do not donate meaningful H-bonds
- Sulfur and phosphorus are typically poor H-bond participants (relative to O/N)

If the H is not strongly polarized, it is not a useful H-bond donor.

Legend: [Blue: Donor] [Green: Acceptor] [Purple: Both] [Grey: Neither]

$\text{R}-\text{OH}$ Alcohol Both	$\text{R}-\text{NH}_2$ $\text{NH}-\text{R}$ Amine Both	$\text{R}-\text{C}(=\text{O})-\text{R}$ Carbonyl Acceptor
$\text{R}-\text{C}(=\text{O})-\text{OH}$ Carboxylic acid Both (protonation dependent)	$\text{R}-\text{SH}$ Thiol Weak Donor/Acceptor (Verify)	$\text{R}-\text{CH}_3$ Hydrocarbon Neither
$\text{R}-\text{P}(\text{O}^{\text{2-}})-\text{O}^{\text{3-}}$ Phosphate (when deprotonated)	$\text{R}-\text{O}-\text{R}$ Ether Acceptor	$\text{R}-\text{C}(=\text{O})-\text{NH}_2$ Amide Both
$\text{R}-\text{C}(=\text{O})-\text{O}-\text{R}$ Ester Acceptor	 Aromatic Ring Neither	$\text{R}-\text{X}$ Halogen Neither

Strong H-bonds: mostly O and N

# Van der Waals Interactions: Weak Forces from Transient Charge Asymmetry

## 1. Nonpolar Molecules (Symmetric)

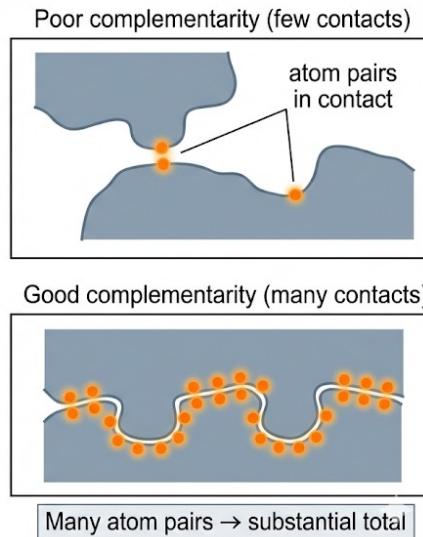
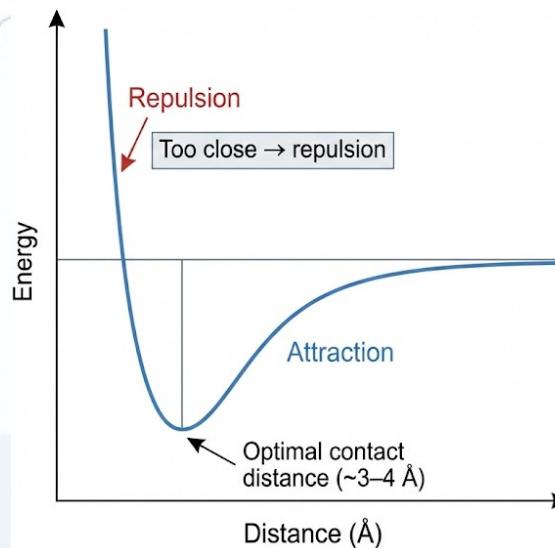
Symmetric electron distribution

## 2. Transient & Induced Dipoles (Asymmetric)

$\delta-$        $\delta+$

Van der Waals Attraction

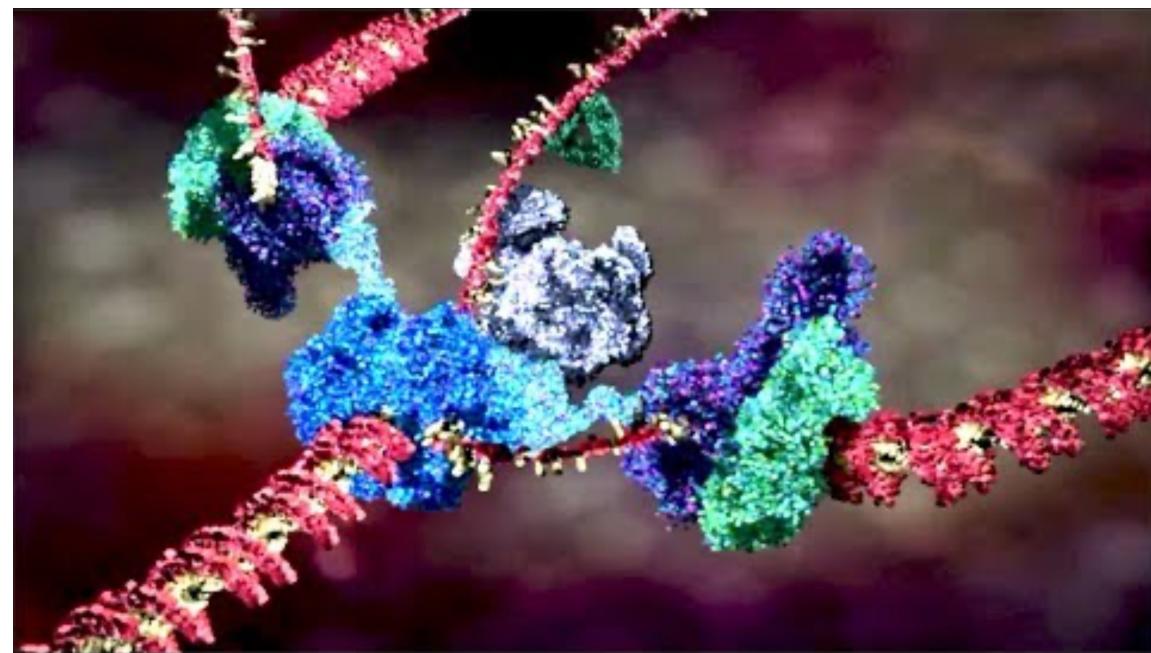
Nonpolar molecules can interact through temporary asymmetric electron distributions that induce complementary dipoles in nearby molecules [cite: 17].



## Gecko Adhesion: A Biological Example

Geckos use millions of microscopic foot hairs to maximize surface area, harnessing collective van der Waals forces to climb surfaces like glass [cite: 17].

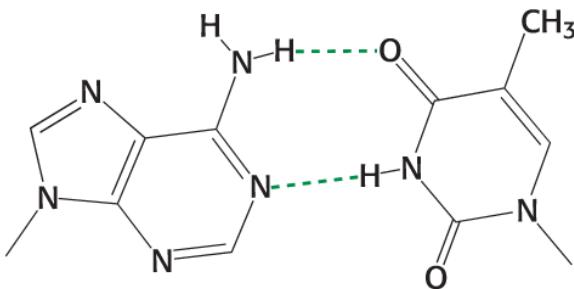
# Weak Bonds Permit Repeated Interactions



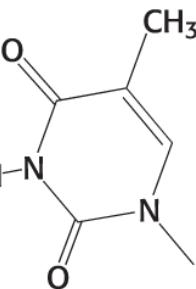
- Why is weak good?
  - Enable rapid binding and unbinding.
  - Allow proofreading and regulation.
  - Let enzymes unzip DNA on demand.

What would happen if we made all of the weak bonds about 40 times stronger?

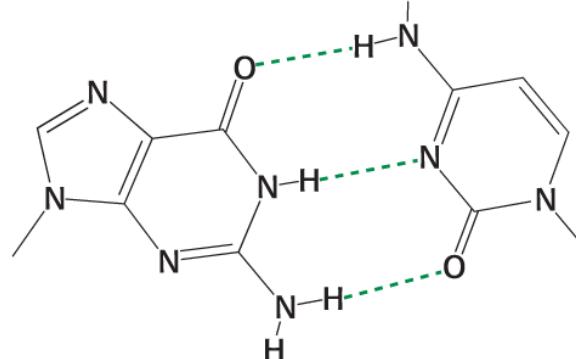
How can we do it?



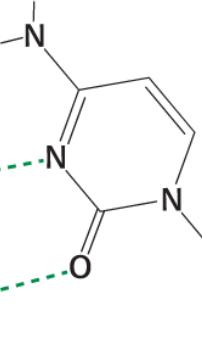
Adenine (A)



Thymine (T)

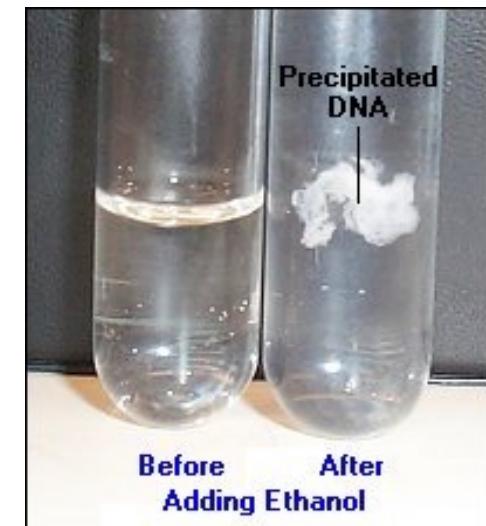


Guanine (G)



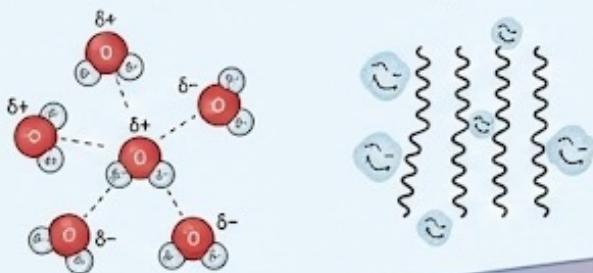
Cytosine (C)

Tymoczko et al., *Biochemistry: A Short Course*, 4e, © 2019 W. H. Freeman and Company

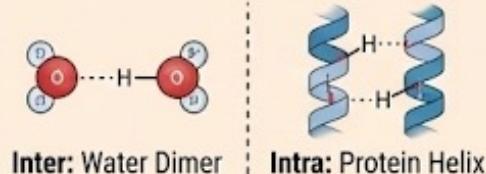


# Intermolecular & Intramolecular Forces: A Spectrum of Strengths

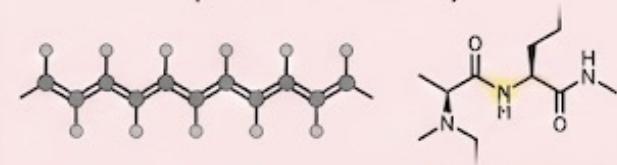
## Intermolecular Forces (Between Molecules)



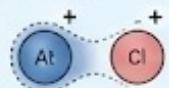
## Overlap: Can be Intra- or Intermolecular



## Intramolecular Forces (Within Molecules)



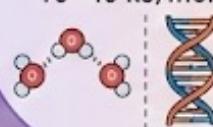
### Dispersion (London) 0.05–40 kJ/mol



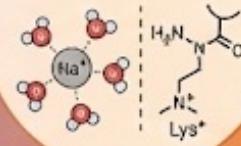
### Dipole-Dipole 5–25 kJ/mol



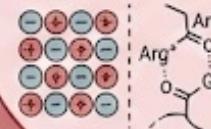
### Hydrogen Bonding 10–40 kJ/mol



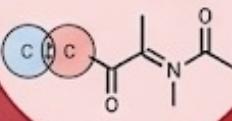
### Ion-Dipole 15–50 kJ/mol



### Ion-Ion 100–400 kJ/mol



### Covalent Bonds 100–1000+ kJ/mol



Increasing Strength

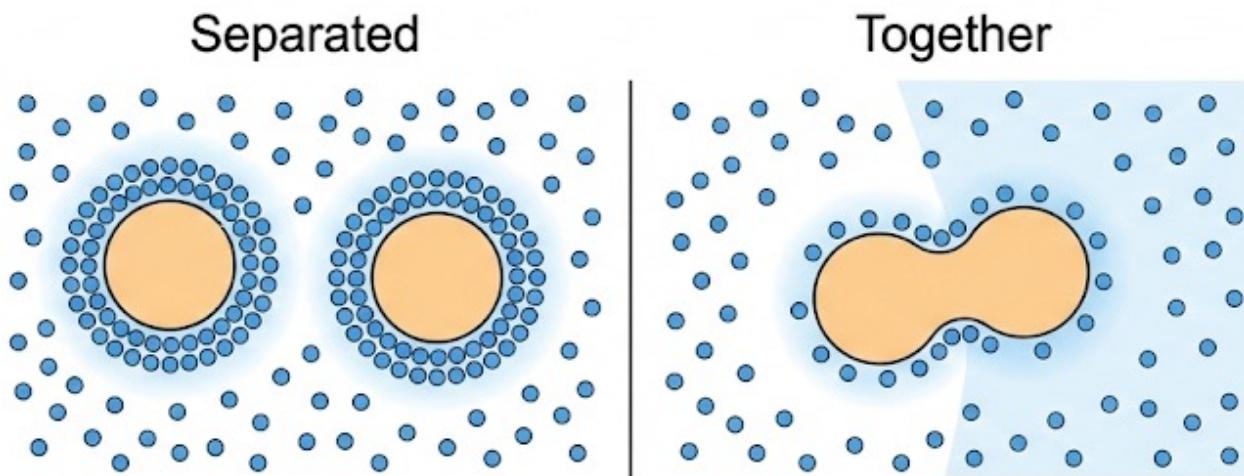
**Dispersion:**  
Hydrophobic cores in proteins  
& Membrane fluidity

**Covalent:**  
Peptide bonds, Disulfide bridges,  
Enzyme-substrate intermediates

Strengths approximate per interaction and vary by context (e.g., molecular size, polarizability, solvent, temperature).  
Zero attraction only possible with ideal gases. Always assess conditions for governing force.

# What About Hydrophobic Interactions?

- 1) H-bonds
- 2) Ionic
- 3) van der Waals
- 4) Hydrophobic



- We've covered H-bonds, ionic, van der Waals
- But hydrophobes don't really attract each other
- So what's pushing them together?
- Hint: it's not the hydrophobes...



- **QUICK QUIZ 1** What is a key biochemical advantage of the use of weak bonds in biochemistry?

Break

# The Hydrophobic Effect: An Entropy-Driven Biological Imperative

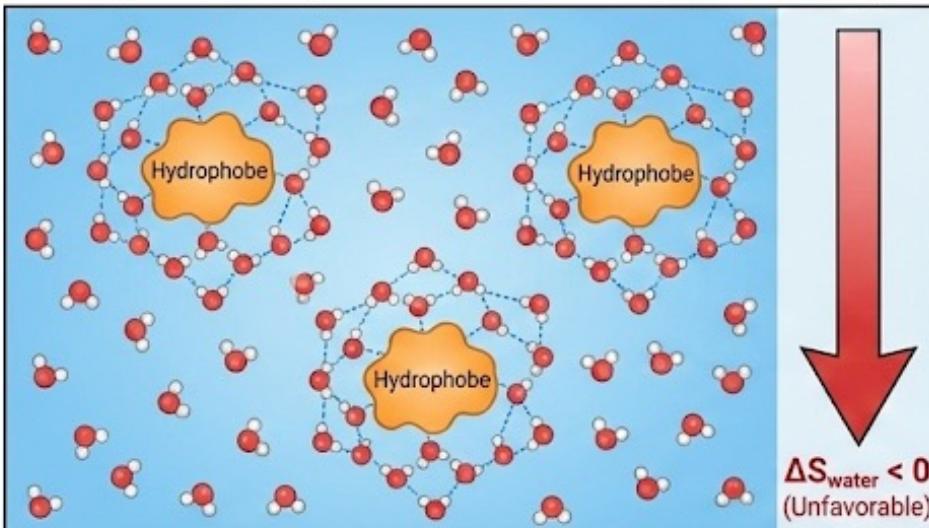
Question hook: Why do oil droplets round up in water, and what does that have to do with protein folding?



## The Thermodynamic Driver: Second Law

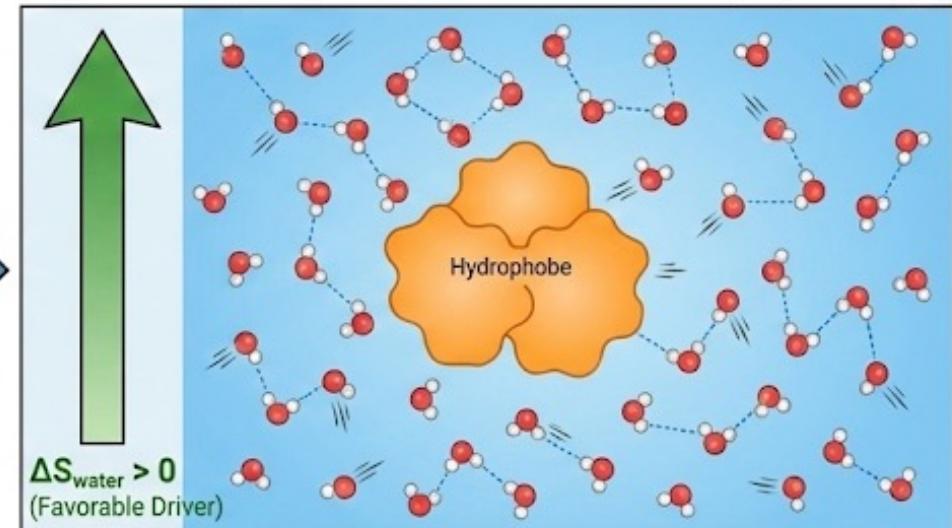
**Second Law of Thermodynamics:** The total entropy (disorder) of an isolated system always increases over time.

### 1. Separate Hydrophobes & Ordered Water (Low Entropy)



Water forms highly ordered "cages" around each individual nonpolar molecule to maintain H-bonding, decreasing water's entropy.

### 2. Clustered Hydrophobes & Disordered Water (High Entropy)



Clustering minimizes nonpolar surface area. The ordered water cages are disrupted, freeing water molecules to move chaotically, increasing overall entropy.



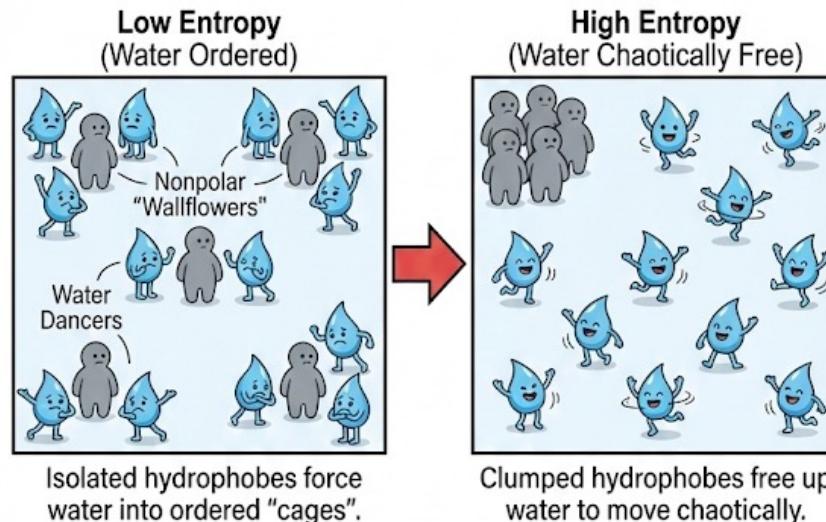
## Biological Significance & Organizing Force

The **Hydrophobic Effect** drives **protein folding** (burying hydrophobic cores) and the formation of cell membranes, powering biological organization. [cite: 23, 26, 27]

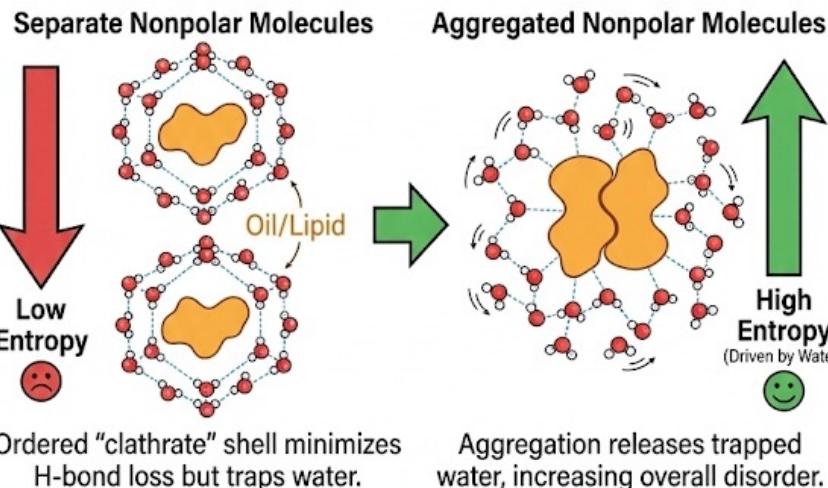
# The Exception: The Hydrophobic Effect

Driven by Entropy (Water's freedom), not Attraction

## The Crowded Dance Floor Analogy



## Molecular Mechanism: The Water "Cage"

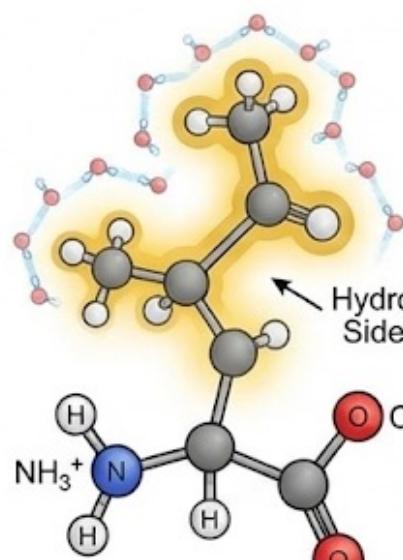


**Summary:** The "force" is not attraction between nonpolar groups, but the system maximizing entropy by freeing up water molecules from ordered cages.

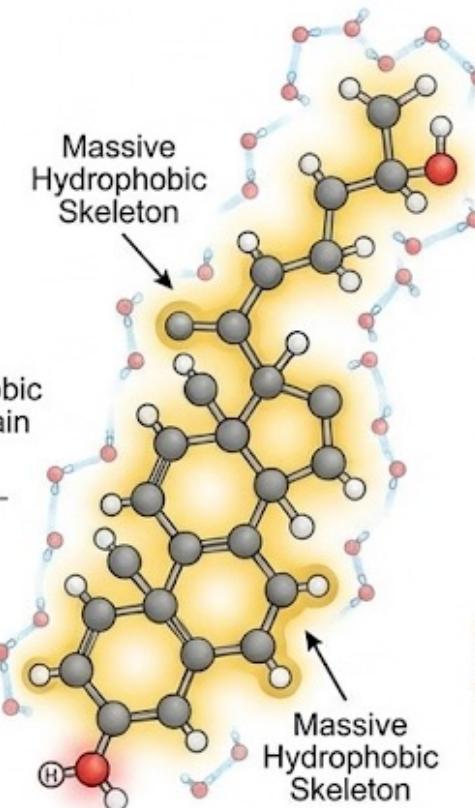


Key for Membrane Formation & Protein Folding

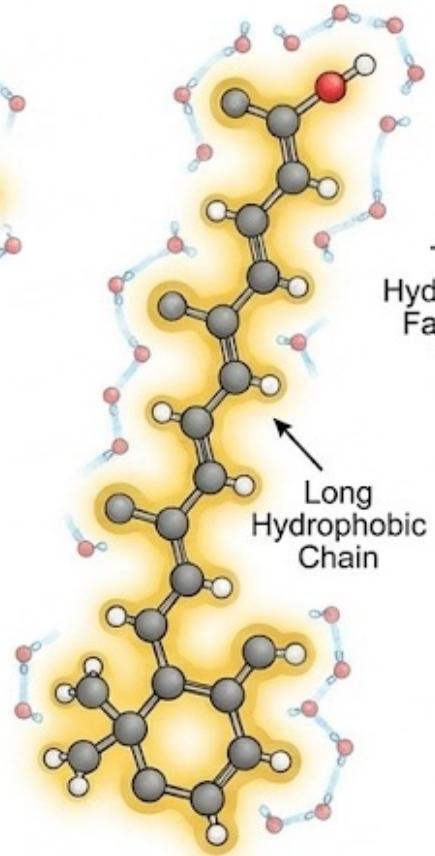
# Examples of hydrophobic biomolecules.



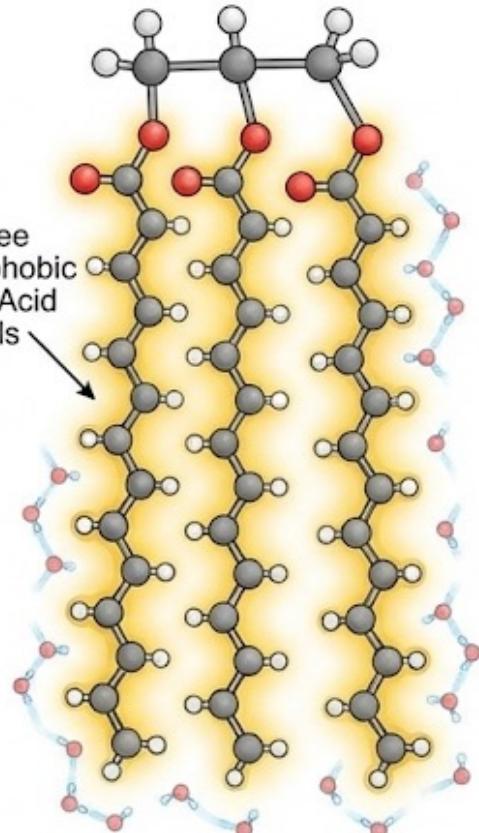
Leucine  
ball and stick structure



Cholesterol  
ball and stick structure



Vitamin A (Retinol)  
ball and stick structure

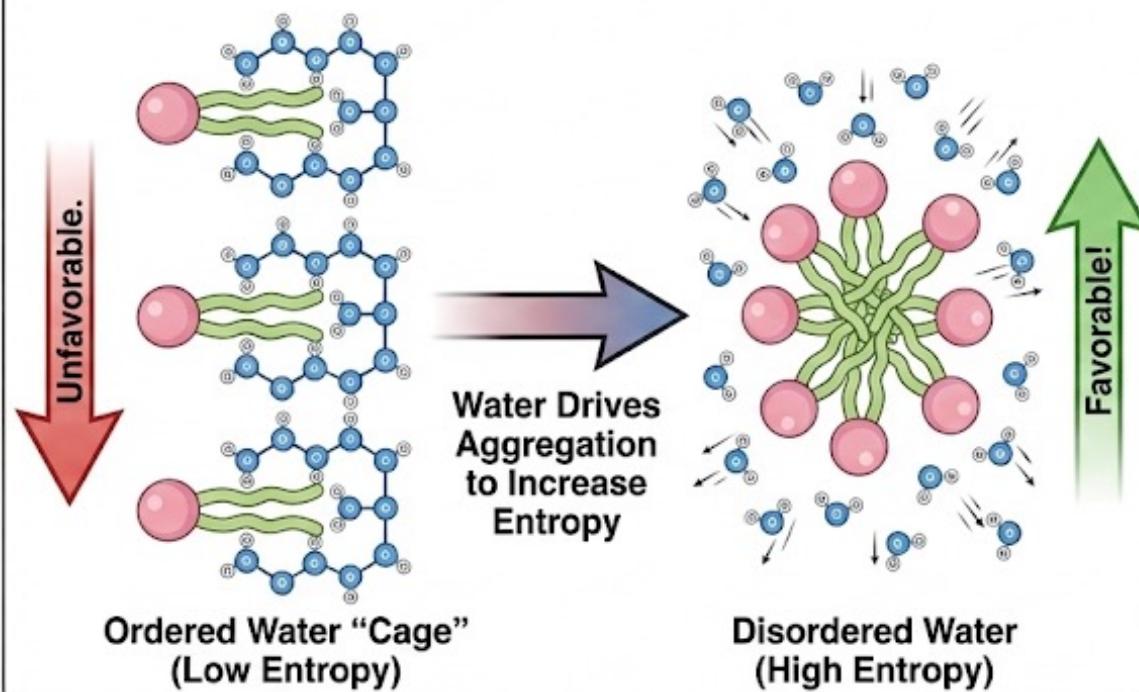


Triglyceride  
ball and stick structure

# The Hydrophobic Effect: How Water ‘Pushes’ Membranes into Shape

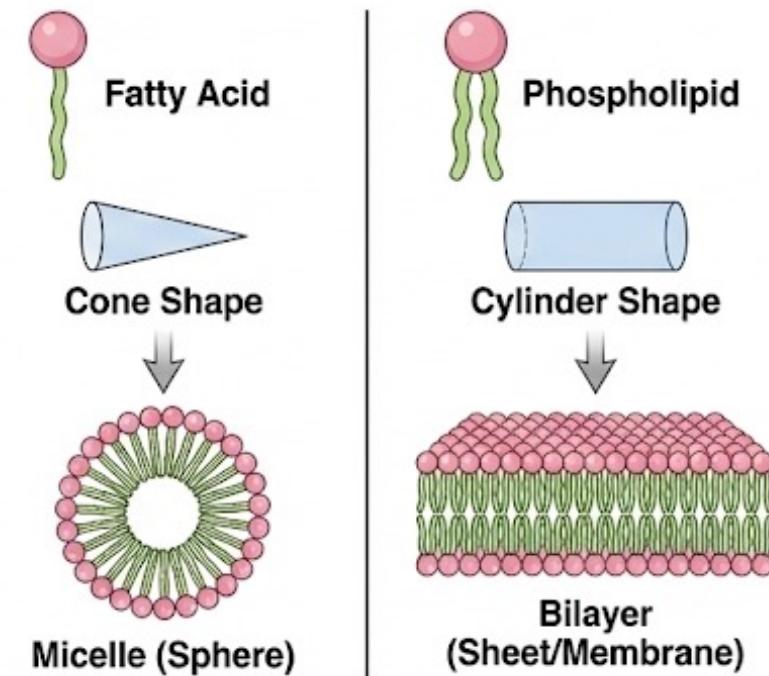
## The Thermodynamic Driver (Entropy)

### 1. Water Cages & The Entropic Push



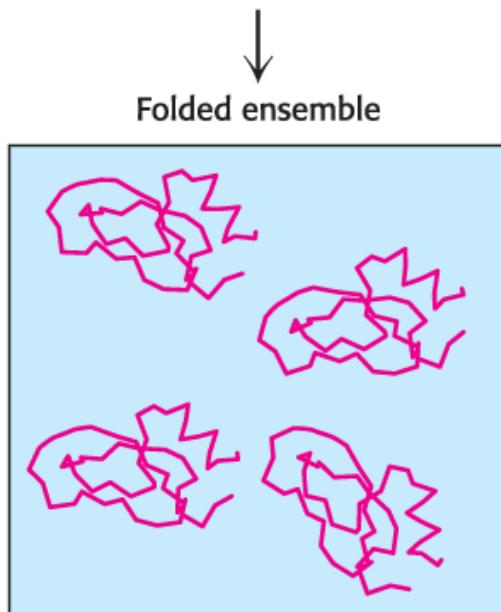
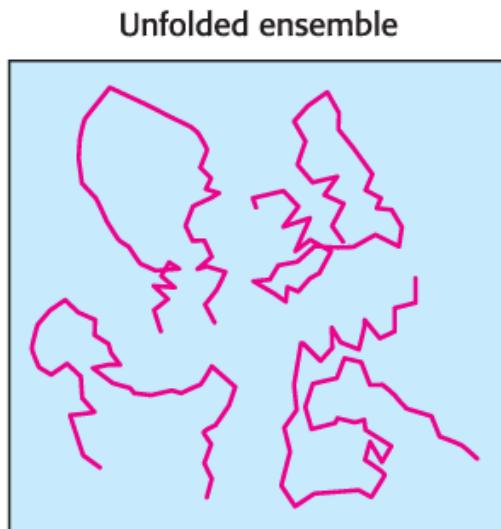
## The Geometric Constraint (Structure)

### 2. Geometry Dictates the Final Form

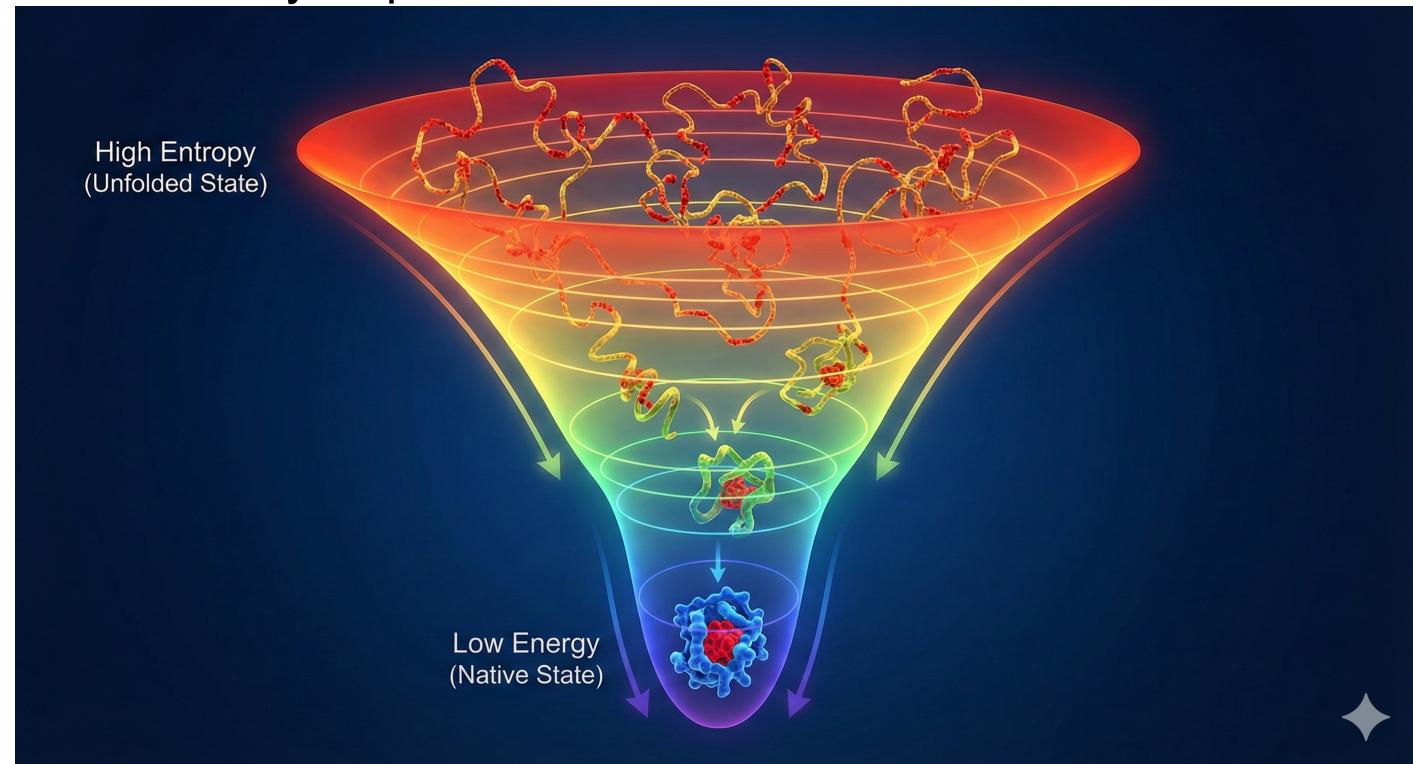


Bulky two-tailed phospholipids cannot fit into a micelle, forcing them to form the extensive bilayers that build cells.

# Protein Folding is Powered by the Hydrophobic Effect

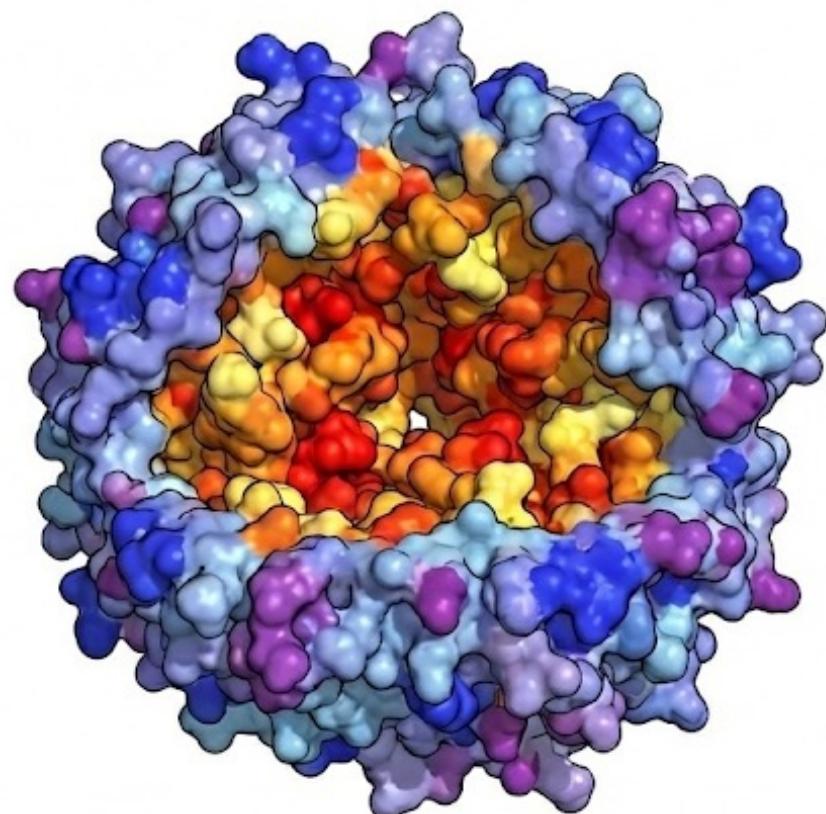


- Proteins have all the information they need to fold properly without additional energy
- But here we're going from disordered to ordered. Isn't this a violation of the second law?
- This is also a hydrophobic effect driven by hydrophobic amino acids.



On a protein shaped like a rock, where will the hydrophobic amino acids be? Where will the charged amino acids be?

## Think-Pair-Share: Hydrophobic Core & Charged Surface in a Protein



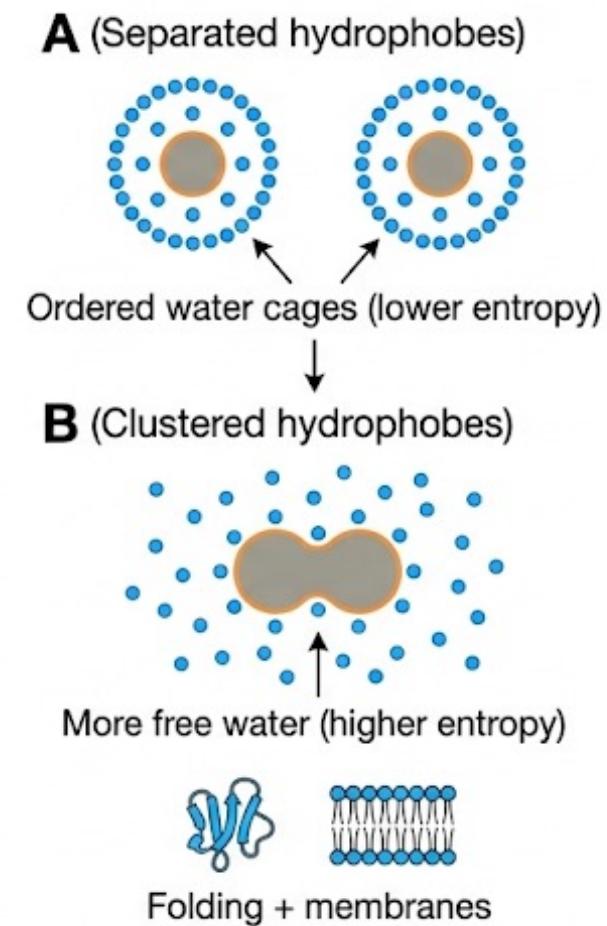
### Question & Activity

THINK   PAIR   SHARE/CLICK

In this **cross-section of a protein**, point to the **hydrophobic core** and the **charged/polar surface**.

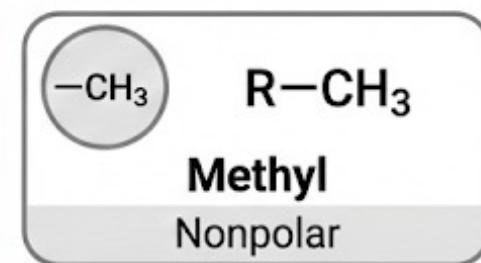
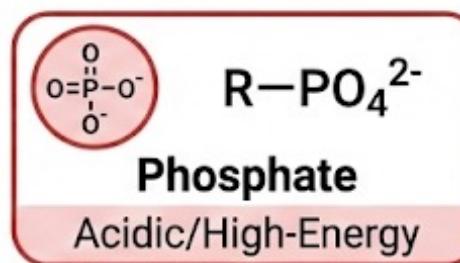
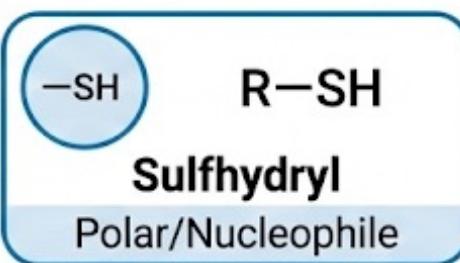
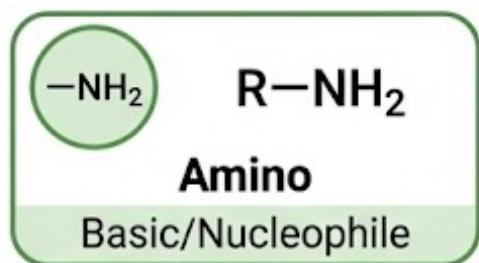
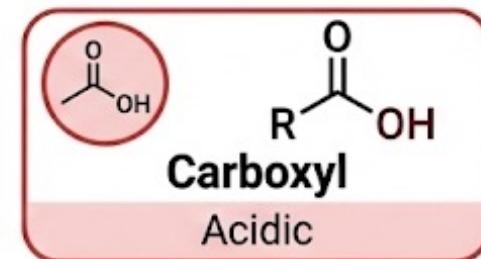
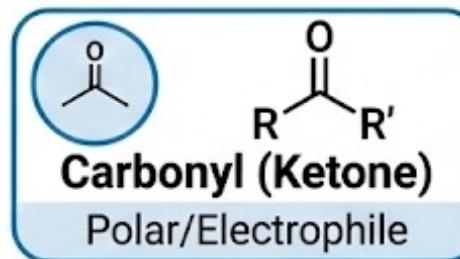
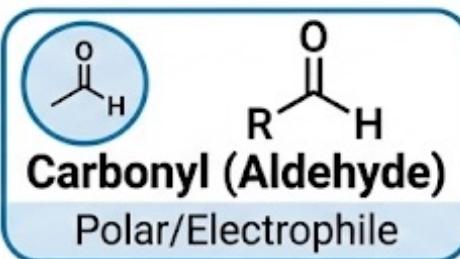
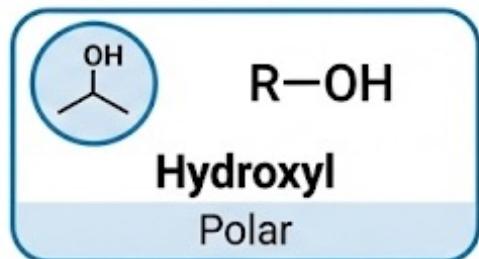
# Hydrophobic Effect: Bottom Line

- **NOT** attraction between nonpolar molecules
- **DRIVEN** by **entropy of water**
  - Water cages are unfavorable
  - Clustering **releases water, increases entropy**
- Drives protein folding and membrane formation



# Functional Groups: The Chemical Toolkit of Life

Specific chemical properties are conferred by distinct groups of atoms.



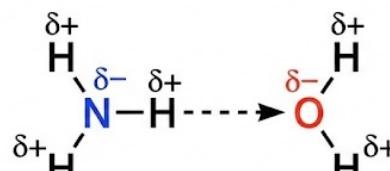
## Quick Quiz: H-Bond with Water?

Hydroxyl (-OH)

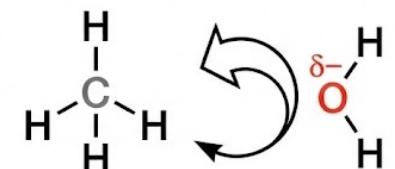
Amino (-NH<sub>2</sub>)

Carboxyl (-COOH)

Methyl (-CH<sub>3</sub>)



H-Bond Donor/Acceptor



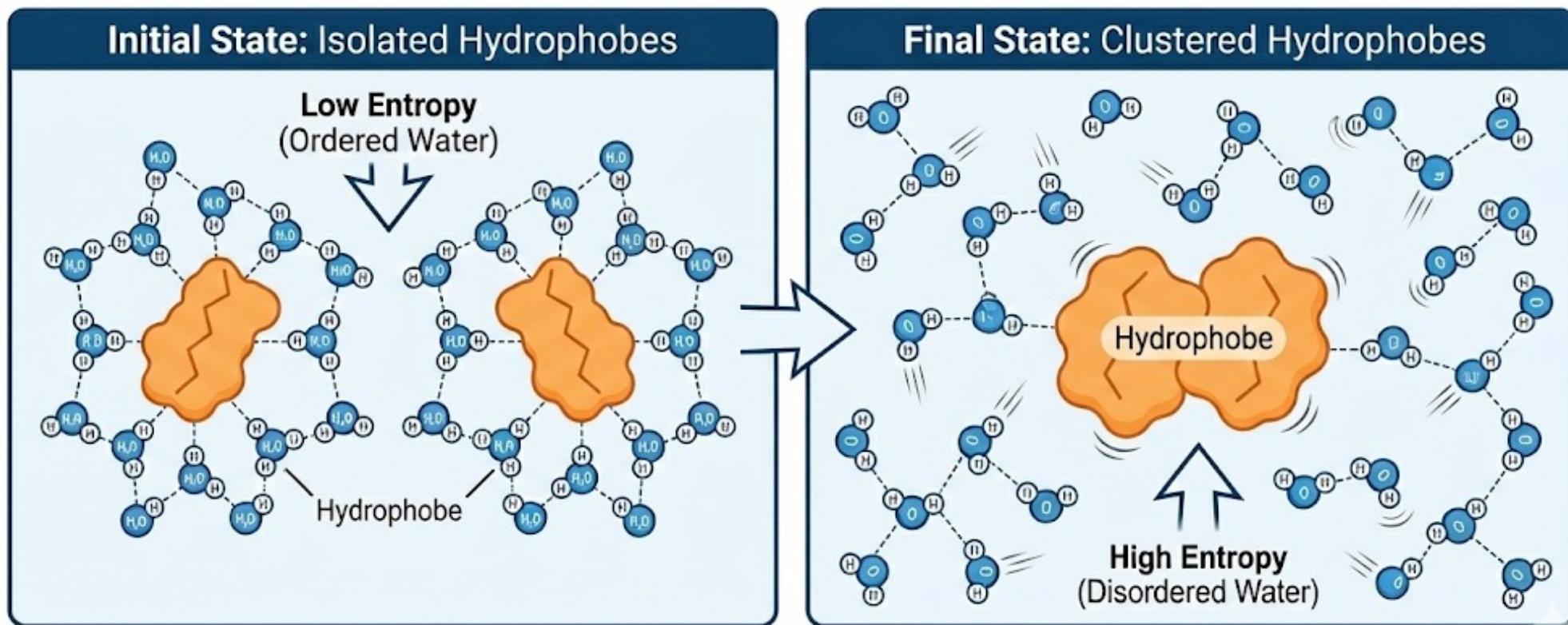
Hydrophobic / No Interaction

Key Concept: Only groups with Electronegative atoms (O, N) + H can play the H-bond game. Methyl is 'invisible' to H-bonds.

## Quick Quiz 2

## Quick Quiz 2

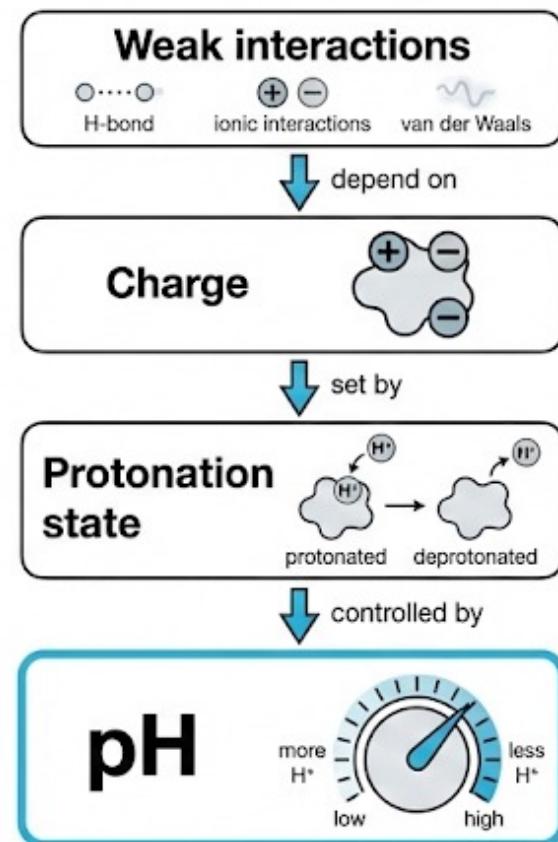
Question: Can order be generated by an increase in randomness?



"The Hydrophobic Effect: Increased Water Entropy Drives Clustering (Order)" [cite: 23, 26, 27, 30, 32, 36].

# From Weak Bonds to pH

- Weak interactions depend on charge
- Charge depends on protonation state
- Protonation depends on pH
- Therefore: pH is the master dial



# pH Basics: The Biochemical Thermostat of Life

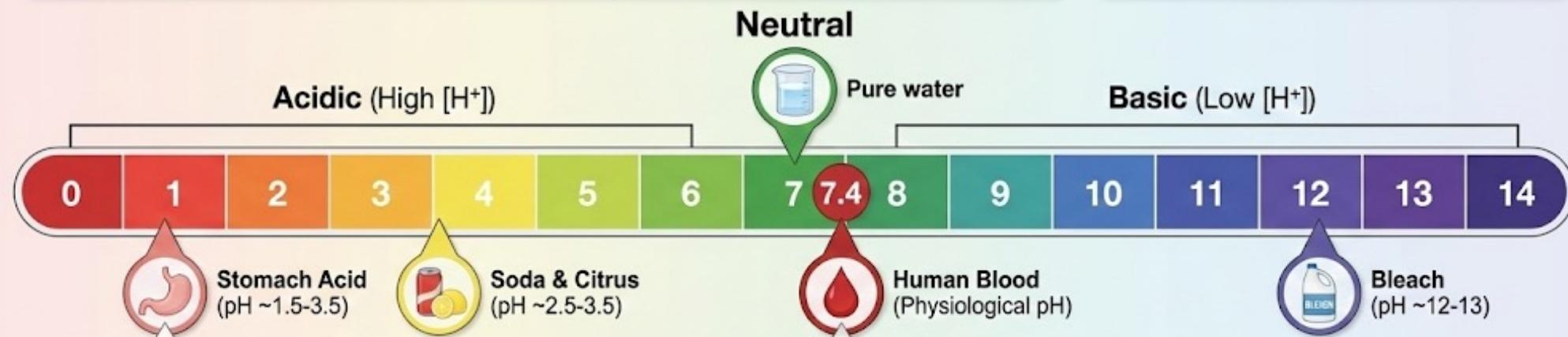
## Definition & Importance

$$\text{pH} = -\log[\text{H}^+]$$

pH is a logarithmic scale measuring proton concentration. Small changes in pH values mean large changes in  $[\text{H}^+]$ . This is critical because **pH dictates the protonation state of biological molecules, regulating their structure and function.**

## The “Biochemical Thermostat” Concept

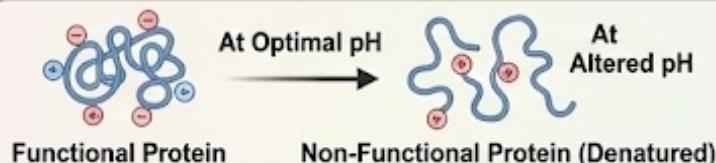
Just as a thermostat maintains a narrow temperature range for comfort, biological systems maintain a tight pH range for optimal biochemical activity. Enzymes and proteins are highly sensitive to pH changes.



### Clinical Touch: GERD

Gastroesophageal Reflux Disease (GERD) is the backflow of acidic stomach contents into the esophagus, causing damage and "heartburn".

Strictly regulated at pH 7.35 – 7.45.  
Deviations (acidosis or alkalosis) can be life-threatening, disrupting oxygen transport and enzyme function.



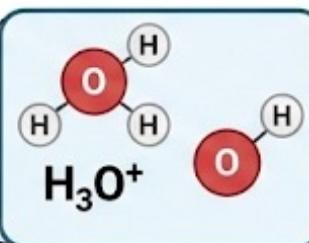
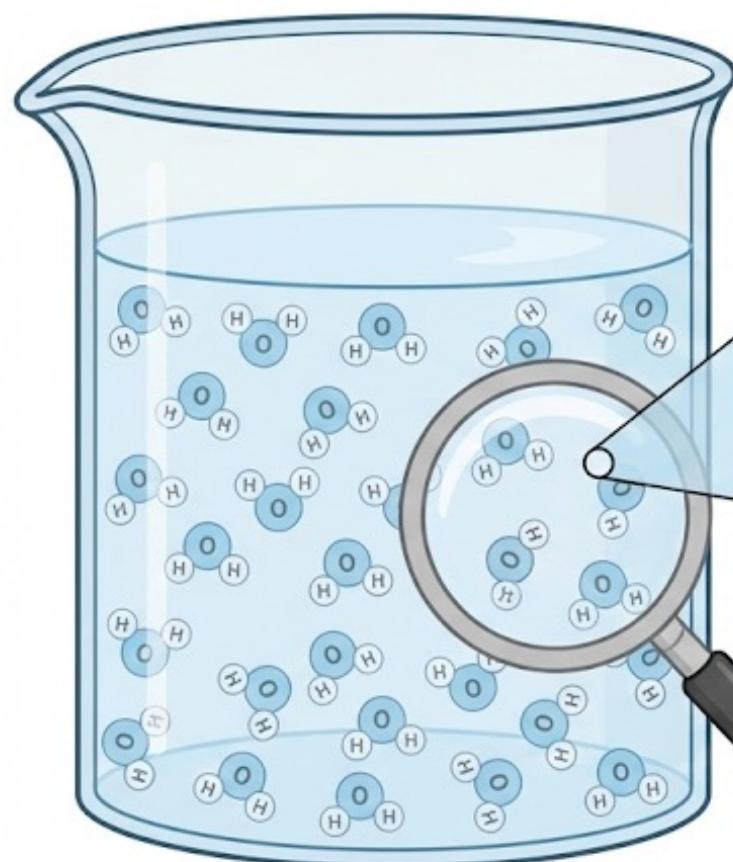
## Why it Matters: Protonation States

### The “thermostat” must be set correctly!

pH determines the charge on functional groups (e.g.,  $-\text{COOH}$  vs.  $-\text{COO}^-$ , protonation (e.g., excess protons protonating carboxyl,  $-\text{COO}^-$ ,  $-\text{NH}_2$  vs.  $-\text{NH}_3^+$ ), which dictates the intramolecular forces that hold proteins and DNA in their functional shapes.

# Water Ionization & The Ion Product ( $K_w$ ): A Tiny Fraction

Water is a **weak electrolyte**, undergoing slight self-ionization at equilibrium.



A Tiny Fraction Dissociates

At Neutral pH (7):  
 $[\text{H}^+] = 1.0 \times 10^{-7} \text{ M}$   
 $[\text{OH}^-] = 1.0 \times 10^{-7} \text{ M}$

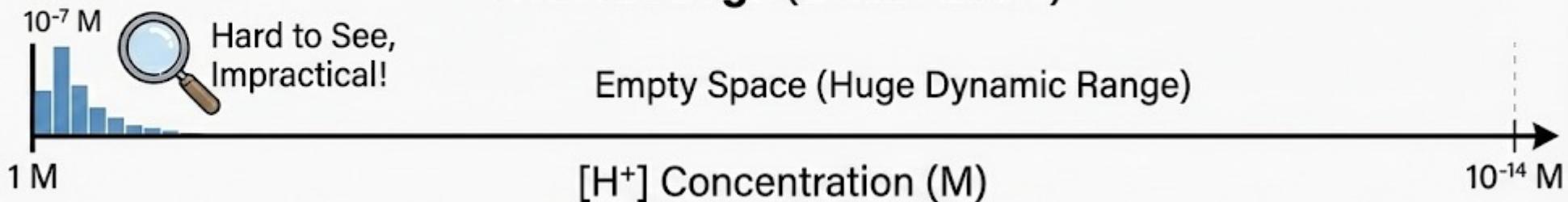
**Ion Product of Water ( $K_w$ ):**

$$K_w = [\text{H}^+][\text{OH}^-] = (1.0 \times 10^{-7})(1.0 \times 10^{-7}) = 1.0 \times 10^{-14} \text{ at } 25^\circ\text{C}$$

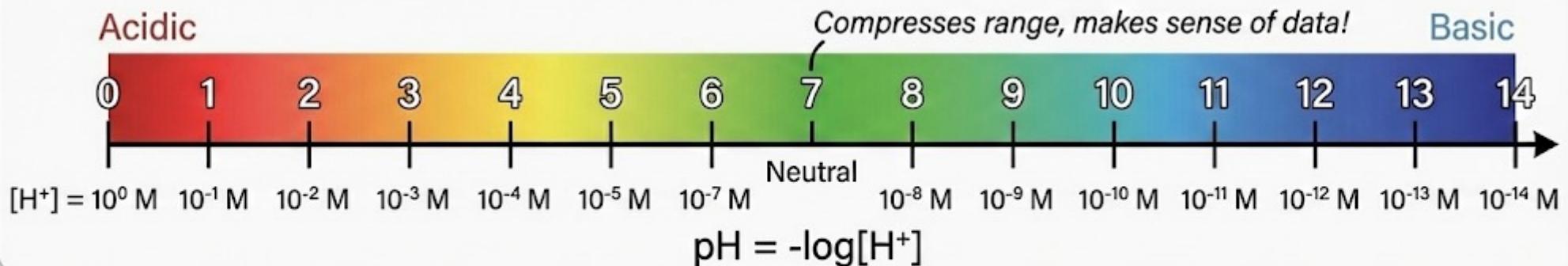
**Fun Fact:** Only about 1 in 10 million water molecules is "going through a phase" at any given time!

# The Logarithmic “Life Hack” for pH

## Without Logs (Linear Scale)



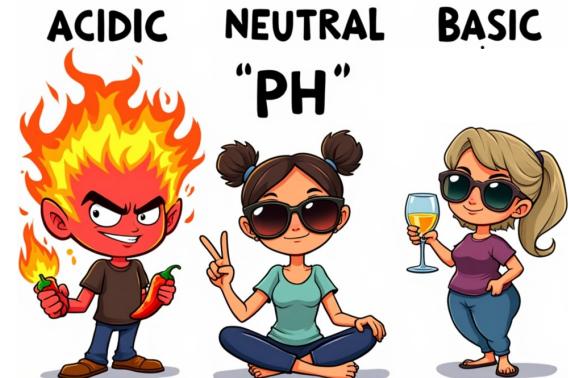
## With Logs (Logarithmic Scale - pH)



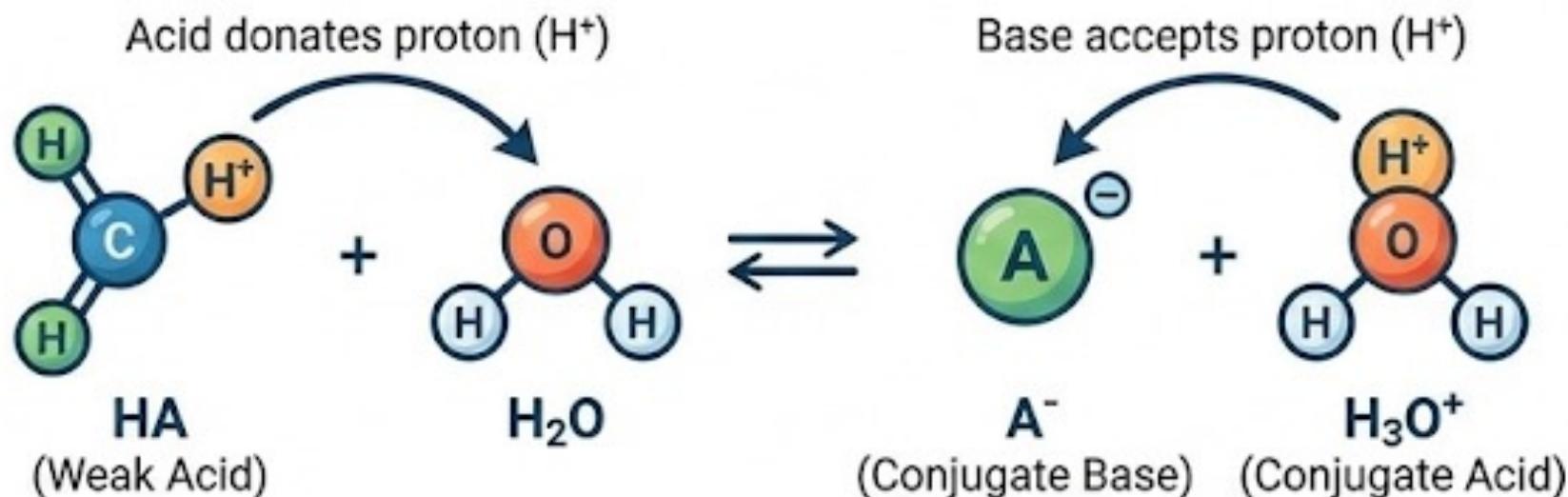
- Compresses a huge range ( $10^{14}$ ) into a manageable scale (0-14).
- Transforms multiplication into addition (Math Magic!). [cite: 37]

Using this hack we can now represent the ionization state of water or any water based solution as this:

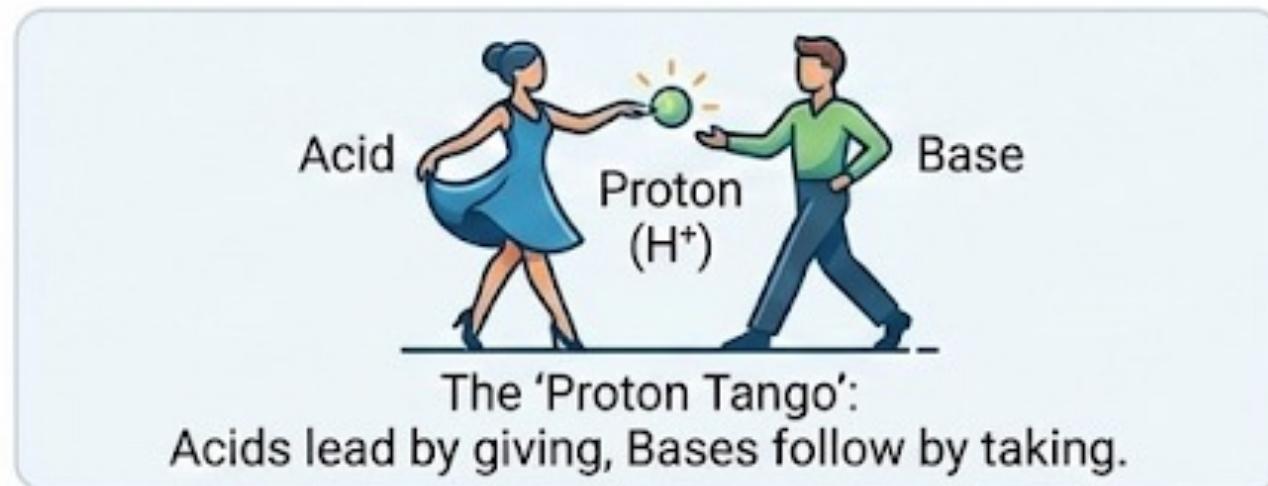
$$\text{pH} = \log_{10} \left( \frac{1}{[\text{H}^+]} \right) = -\log_{10} [\text{H}^+]$$



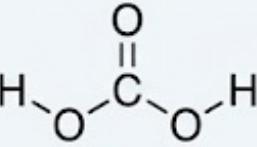
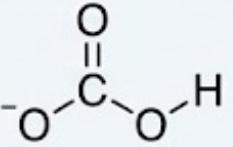
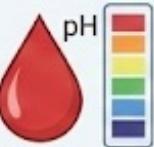
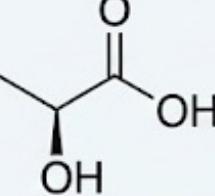
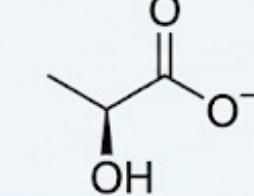
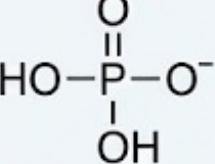
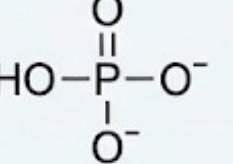
# Acids and Bases – The Proton Tango



- **Acids:** The proton donors (give away  $H^+$ ).
- **Bases:** The proton acceptors (take  $H^+$ ).



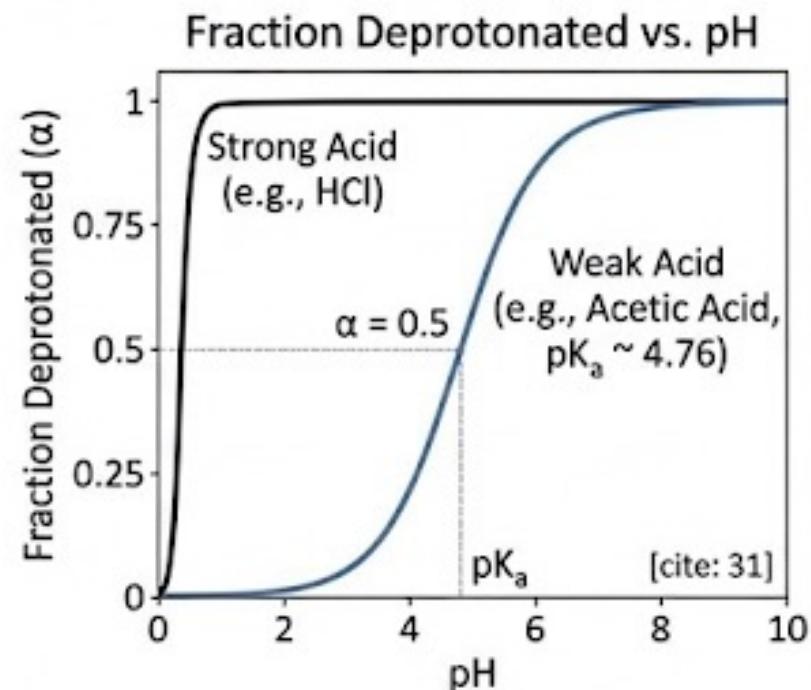
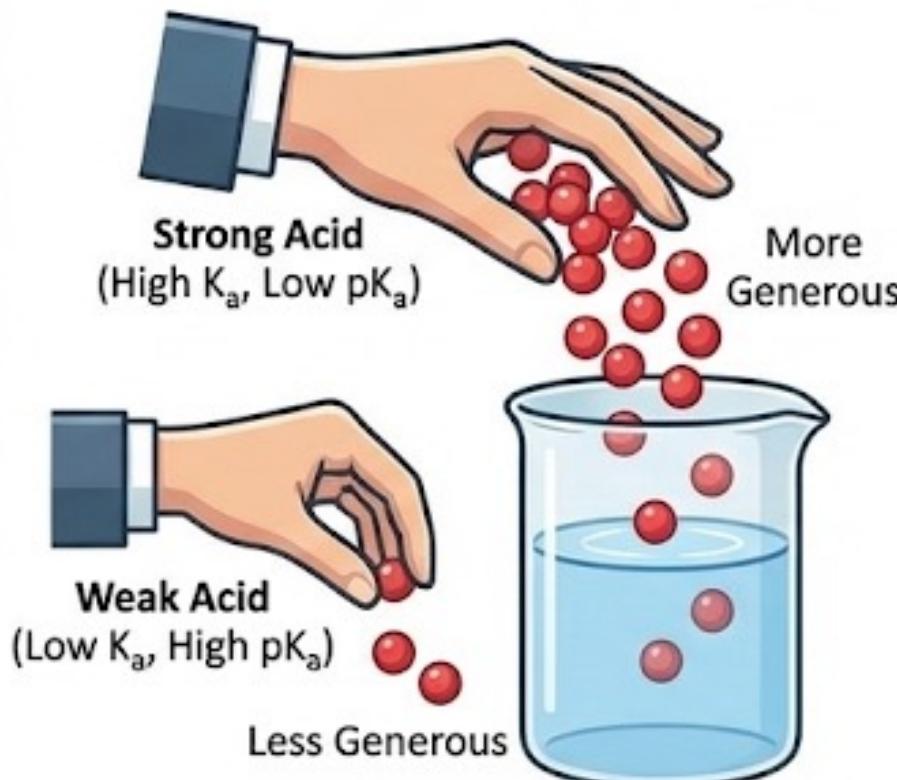
# Conjugate Acid-Base Pairs: The Proton-Swapping Partners

Acid (Proton Donor)	Conjugate Base (Formed after H <sup>+</sup> Loss)	Biological Importance
 Carbonic Acid (H <sub>2</sub> CO <sub>3</sub> )	 Bicarbonate (HCO <sub>3</sub> <sup>-</sup> )	 Blood pH buffering system (transport of CO <sub>2</sub> )
 Lactic Acid	 Lactate	 Produced during anaerobic muscle activity (exercise)
 Dihydrogen Phosphate (H <sub>2</sub> PO <sub>4</sub> <sup>-</sup> )	 Hydrogen Phosphate (HPO <sub>4</sub> <sup>2-</sup> )	 Intracellular pH buffering and DNA backbone component

"A conjugate acid-base pair consists of two species that differ by only one proton (H<sup>+</sup>). This reversible relationship is key to many biological buffers." [cite: 48, 51]

# Acid Strength: $K_a$ & $pK_a$ ("Generosity Score")

- **$K_a$  (Acid Dissociation Constant):** Measures tendency to donate protons. Higher  $K_a$  = Stronger Acid (more generous).
- **$pK_a$  (-log  $K_a$ ):** Lower  $pK_a$  = Stronger Acid (**chemists love logs to compress range!**).



# Useful Conversions – The Acid-Base Formula Toolkit

## ACID-BASE FORMULA TOOLKIT (at 25°C)



### pH and $[H^+]$

$$pH = -\log[H^+]$$



### pOH and $[OH^-]$

$$pOH = -\log[OH^-]$$



### The Relationship

$$pH + pOH = 14$$



### $pK_a$ and $K_a$

$$pK_a = -\log(K_a)$$



### Ion Product of Water ( $K_w$ )

$$K_w = [H^+][OH^-] = 1.0 \times 10^{-14}$$

## Why These Matter?

- Compress a wide range of concentrations into manageable numbers (the power of logs!).
- Allow for quick conversions between acidity, basicity, and dissociation constants.

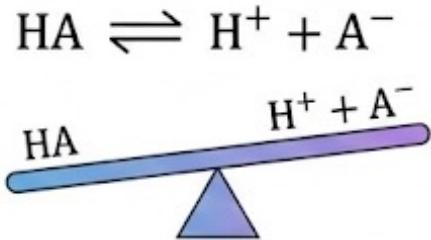
The ionization equilibrium of a weak acid:  $HA \rightleftharpoons H^+ + A^-$

$K_a$  (acid dissociation constant) =  $[H^+][A^-] / [HA]$

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

# The Henderson-Hasselbalch Derivation: A Step-by-Step Algebra Sequence

## 1. Starting Point: Acid Dissociation Equilibrium & $K_a$



$K_a$  measures the tendency of the acid (HA) to donate a proton.

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

## 2. Rearrange to Isolate $[\text{H}^+]$

$$[\text{H}^+] = K_a \times \frac{[\text{HA}]}{[\text{A}^-]}$$

We rearrange the equation to solve for the hydrogen ion concentration.

## 3. Take Negative Logs & Introduce pH/pKa

$$-\log[\text{H}^+] = -\log\left(K_a \times \frac{[\text{HA}]}{[\text{A}^-]}\right)$$

$$-\log[\text{H}^+] = -\log(K_a) - \log\left(\frac{[\text{HA}]}{[\text{A}^-]}\right)$$

Since  $-\log[\text{H}^+] = \text{pH}$

And  $-\log(K_a) = \text{pK}_a$

$$\text{pH} = \text{pK}_a + \log\left(\frac{[\text{A}^-]}{[\text{HA}]}\right)$$

This relates pH, pKa, and the ratio of conjugate base to acid, creating a powerful tool for understanding buffers. [cite: 36, 49]

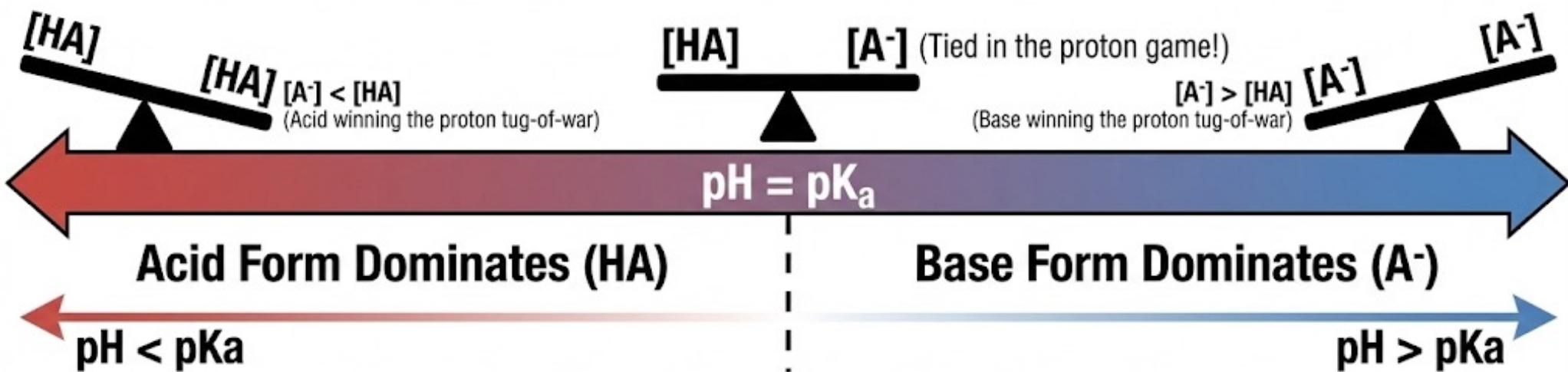
$$\text{pH} = \text{pK}_a + \log\left(\frac{[\text{A}^-]}{[\text{HA}]}\right)$$



Lawrence Joseph Henderson.

# Interpreting the Henderson-Hasselbalch Equation

$$\text{pH} = \text{pK}_a + \log([\text{A}^-]/[\text{HA}])$$



This equation helps predict the protonation state of biomolecules at a given pH, crucial for understanding their behavior in biological systems (e.g., around physiological pH 7.4). [cite: 36, 47, 49]

## “Henderson–Hasselbalch Worked Example”

Acetic acid buffer

$$pK_a = 4.76$$

$$pH = 5.76$$

Question: What is the ratio  $[A^-]/[HA]$  (base to acid)?



Live calc: 3 minutes

Write these numbers down:  
pH 5.76,  $pK_a$  4.76

①  $pH = pK_a + \log_{10} ([A^-]/[HA])$

②  $5.76 = 4.76 + \log_{10}([A^-]/[HA])$

③  $5.76 - 4.76 = \log_{10}([A^-]/[HA])$

④  $1.00 = \log_{10}([A^-]/[HA])$

⑤  $10^{1.00} = [A^-]/[HA]$

$$[A^-]/[HA] = 10$$

“Base:Acid = 10:1”

# Why the Henderson–Hasselbalch Equation Is So Powerful

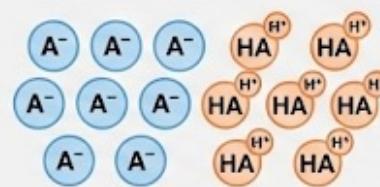
$$\text{pH} = \text{pK}_a + \log([\text{A}^-]/[\text{HA}])$$

pH tells you the ratio of deprotonated to protonated forms

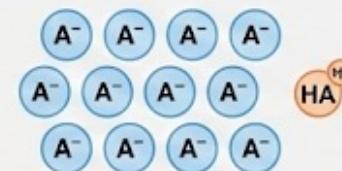
$$\text{pH} = \text{pK}_a - 1 \rightarrow 10:1 \text{ acid:base}$$



$$\text{pH} = \text{pK}_a \rightarrow 50:50$$



$$\text{pH} = \text{pK}_a + 1 \rightarrow 10:1 \text{ base:acid}$$



pH

pK<sub>a</sub>



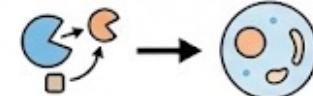
**Population, not magic**

pH reflects how molecules are distributed between forms



**Why buffers work**

Maximum buffering occurs near pK<sub>a</sub>



**Why biology loves it**

Small pH shifts cause big functional changes

# Diagram Depicting a Variety of Conjugate Acid–Base Pairs

## Monoprotic acids

Acetic acid  
( $K_a = 1.74 \times 10^{-5} \text{ M}$ )

Ammonium ion  
( $K_a = 5.62 \times 10^{-10} \text{ M}$ )

## Diprotic acids

Carbonic acid  
( $K_a = 1.70 \times 10^{-4} \text{ M}$ )

Bicarbonate  
( $K_a = 6.31 \times 10^{-11} \text{ M}$ )

Glycine, carboxyl  
( $K_a = 4.57 \times 10^{-3} \text{ M}$ )

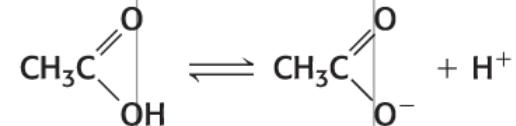
Glycine, amino  
( $K_a = 2.51 \times 10^{-10} \text{ M}$ )

## Triprotic acids

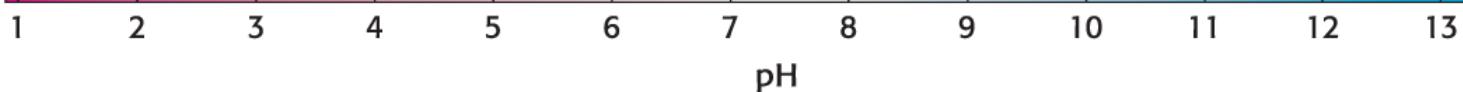
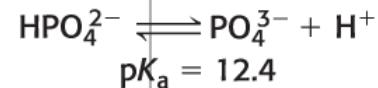
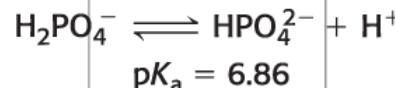
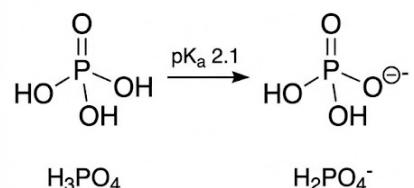
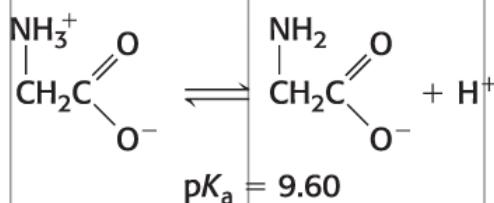
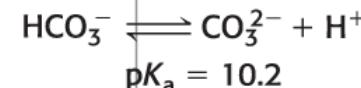
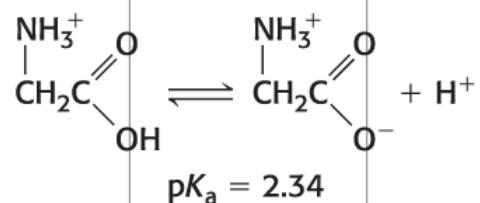
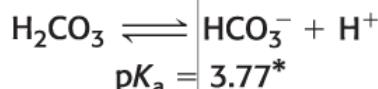
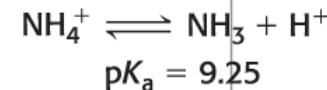
Phosphoric acid  
( $K_a = 7.25 \times 10^{-3} \text{ M}$ )

Dihydrogen phosphate  
( $K_a = 1.38 \times 10^{-7} \text{ M}$ )

Monohydrogen phosphate  
( $K_a = 3.98 \times 10^{-13} \text{ M}$ )

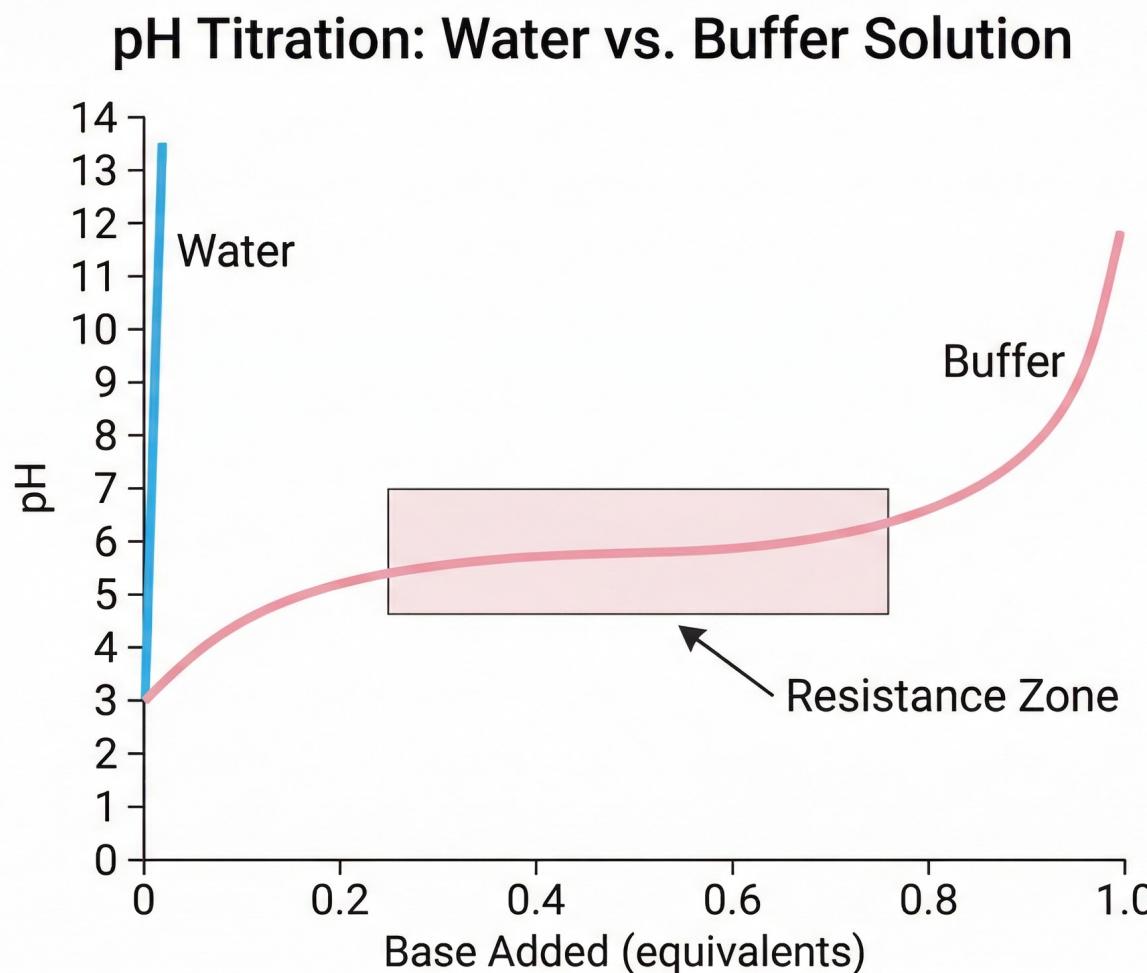


Conjugate acid  $pK_a = 4.76$



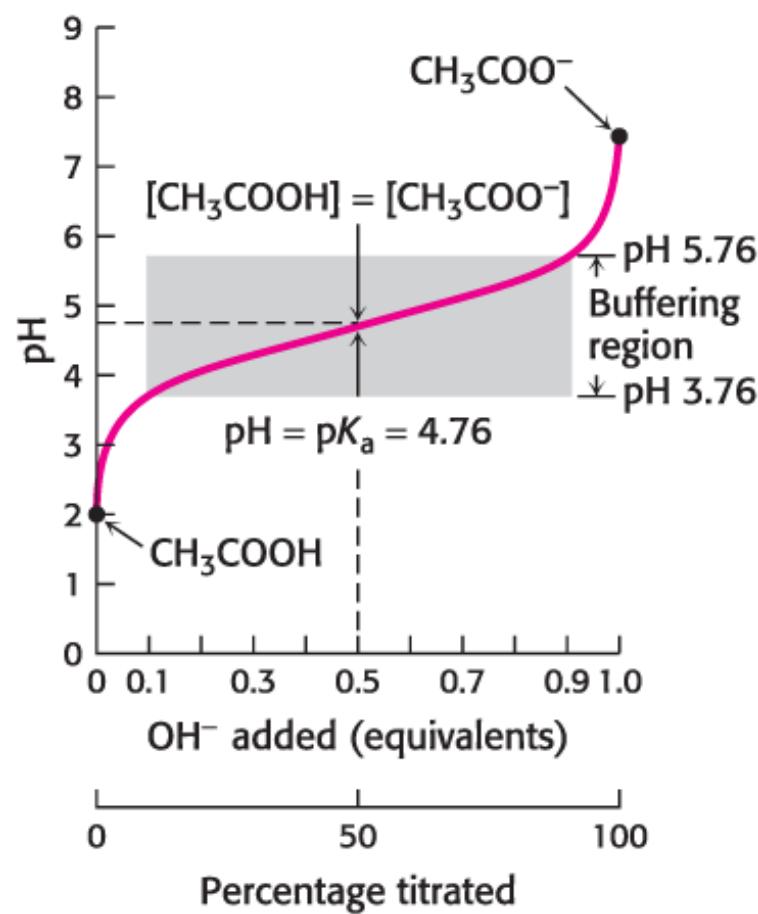
# Buffers Resist Changes in pH

- An acid–base conjugate pair resists changes in the pH of a solution.
- In other words, it acts as a buffer. A buffer is most effective at a pH near its  $pK_a$ . Rule of thumb is within one pH unit.

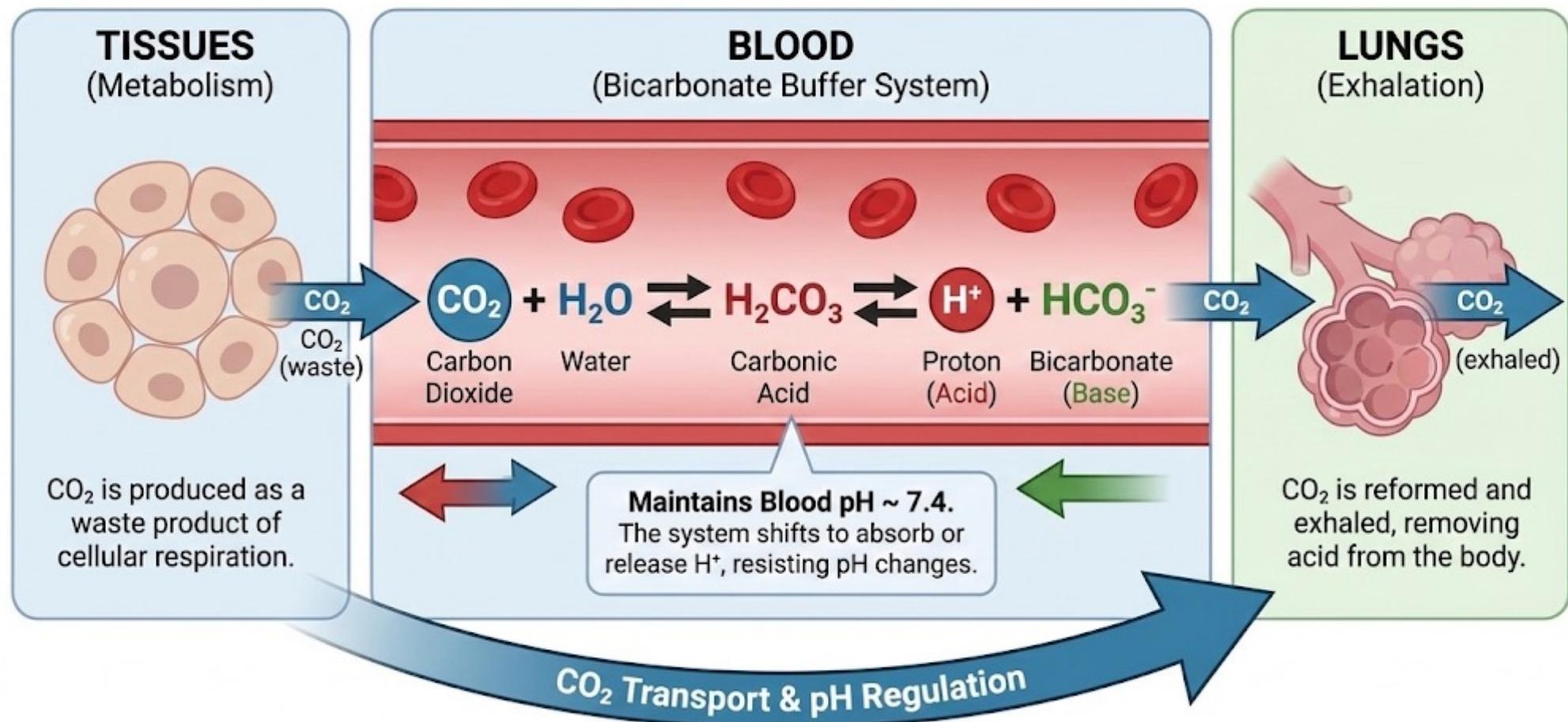


## Real-world examples

### Acetic acid



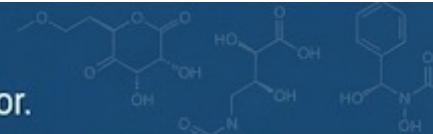
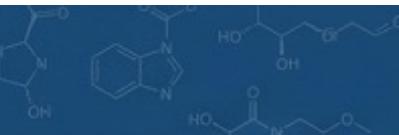
# Biological Buffers: The Bicarbonate System in Blood



Final thoughts.

# The Biochemist's Logarithm Survival Guide:

Intuitive tricks for pH and Henderson-Hasselbalch without relying on a calculator.



## 1. The Foundation – Logs are just “Zero Counters”

Log almost always means  $\log_{10}$ . It asks: “How many powers of 10?”



Exponent counter

$$\log(1) = 0 \quad (10^0)$$

$$\log(10) = 1 \quad (\text{one zero})$$

$$\log(100) = 2 \quad (\text{two zeros})$$

$$\log(0.1) = -1 \quad (10^{-1})$$

$$\log(0.01) = -2 \quad (10^{-2})$$



Biochem App: Ratio  $[\text{Base}]/[\text{Acid}] = 1 \rightarrow \log \text{ is } 0 \rightarrow \text{pH} = \text{pK}_a$ . Ratio is 10  $\rightarrow \text{pH is +1 unit from pK}_a$ .

## 4. Estimation Superpowers (No Calculator Needed)

Memorize TWO values to estimate almost anything.

$$\log(2) \approx 0.3$$

$$\log(3) \approx 0.47$$

(use 0.5)

Composite Rule:  $\log(A \times B) = \log(A) + \log(B)$

$$\text{Examples: } \log(4) = \log(2 \times 2) = 0.3 + 0.3 = 0.6$$

$$\log(6) = \log(2 \times 3) = 0.3 + 0.5 = 0.8$$

$$\log(5) = \log(10/2) = 1 - 0.3 = 0.7$$

‘Half-Unit’ Trick:

Ratio Base/Acid is 3:1  $\rightarrow \text{pH is } \sim 0.5 \text{ units above pK}_a$

## 2. The “pH Flip” (Negative Logs)

Why lower concentration means higher pH.

$$\text{pH} = -\log[\text{H}^+]$$

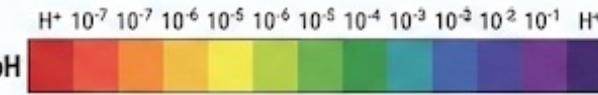
Inverter graphic  
Big NEGATIVE exponent on  $[\text{H}^+]$       Tiny Concentration      Flips to big POSITIVE pH

Shortcut Rule:

If  $[\text{H}^+] = 1 \times 10^{-X}$ , then  $\text{pH} = X$

$$1 \times 10^{-7} \text{ M} \rightarrow \text{pH } 7$$

$$1 \times 10^{-2} \text{ M} \rightarrow \text{pH } 2$$



## 5. The Real World pH Estimation Trick

Combine scientific notation with log(2) trick.

$$\text{Scenario: } [\text{H}^+] = C \times 10^{-E}$$

“Mantissa Subtraction” Hack:  
 $\text{pH} = E - \log(C)$

Example 1:

Find pH if  $[\text{H}^+] = 2 \times 10^{-5} \text{ M}$

1. Exponent (E): 5
2. Coefficient (C): 2
3. Recall  $\log(2) \approx 0.3$
4. Calculate:  
 $\text{pH} = 5 - 0.3 = 4.7$

Example 2:

Find pH if  $[\text{H}^+] = 4 \times 10^{-8} \text{ M}$

$$\begin{aligned} E &= 8, C = 4, \\ \log(4) &\approx 0.6, \\ \text{pH} &= 8 - 0.6 = 7.4 \quad (\text{physiological}) \end{aligned}$$

## 3. Henderson-Hasselbalch Ratio Tricks

Don’t flip out over flipped fractions.

$$\text{pH} = \text{pK}_a + \log\left(\frac{[\text{A}^-]}{[\text{HA}]}\right) \quad (\text{Base/Acid})$$

“Sign Flipper” Trick:  
 $\log(A/B) = -\log(B/A)$

$$\text{pH} = \frac{A}{B} - \log\left(\frac{A^-}{\text{HA}}\right)$$

$$\log\left(\frac{10}{1}\right) = +1 \rightarrow \text{pH} = \text{pK}_a + 1$$

$$\log\left(\frac{1}{10}\right) = -1 \rightarrow \text{pH} = \text{pK}_a - 1$$

## 6. Anti-Logs (The Reverse Gear)

Handling non-integer pH values.

Concept:  $\text{pH} = X \rightarrow [\text{H}^+] = 10^{-X}$ . Easy for whole numbers, hard for decimals.

“Split and Reverse” Trick: If pH = 7.4, find  $[\text{H}^+]$

1. Split negative pH into next \*more negative\* integer & positive decimal:  
 $-7.4 = -8 + 0.6$
2. Rewrite as product:  
 $[\text{H}^+] = 10^{-8} \times 10^{0.6}$
3. Reverse estimate positive decimal ( $\log(4) \approx 0.6$ ):  
 $10^{0.6} \approx 4$
4. Combine:  
 $[\text{H}^+] \approx 4 \times 10^{-8} \text{ M}$