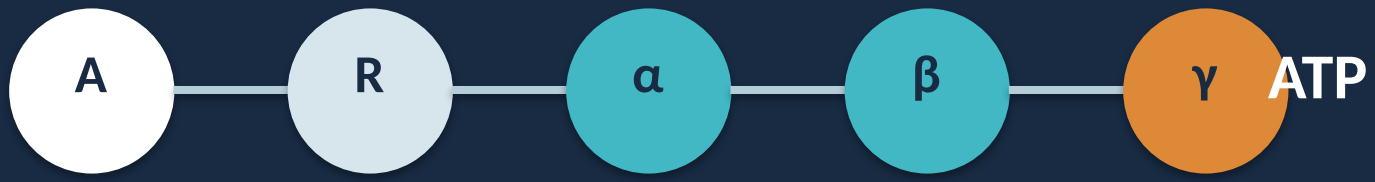
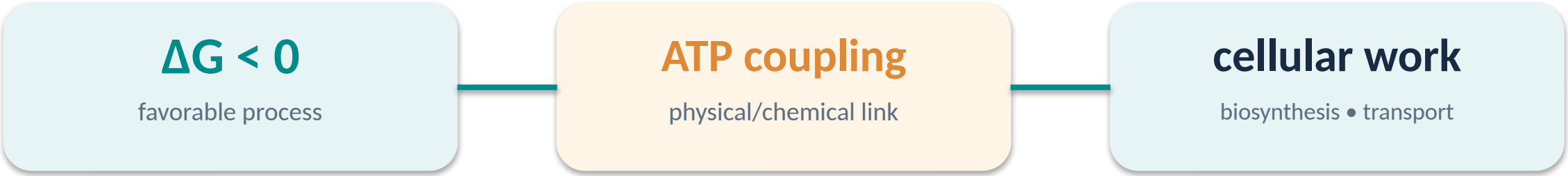
Lecture 3: ATP Chemistry. Physical Chemistry of ATP Hydrolysis.



chemical free energy ↔ cellular work

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From Thermodynamics to Cellular Work



- Previous lecture: ΔG tells us whether a process is thermodynamically favorable.
- Cells must also perform processes with positive ΔG.
- ATP allows favorable and unfavorable processes to be coupled so that ΔGtotal < 0.

Learning Objectives

- Explain why ATP hydrolysis is thermodynamically favorable.
- Distinguish $\Delta G^{\circ\prime}$ from the actual cellular ΔG.
- Explain ATP coupling in biosynthesis, transport and mechanical work.
- Calculate and interpret adenylate energy charge (AEC).
- Recognize ion-gradient coupling only as a preview for Lecture 5.

Module 1 • ATP Chemistry

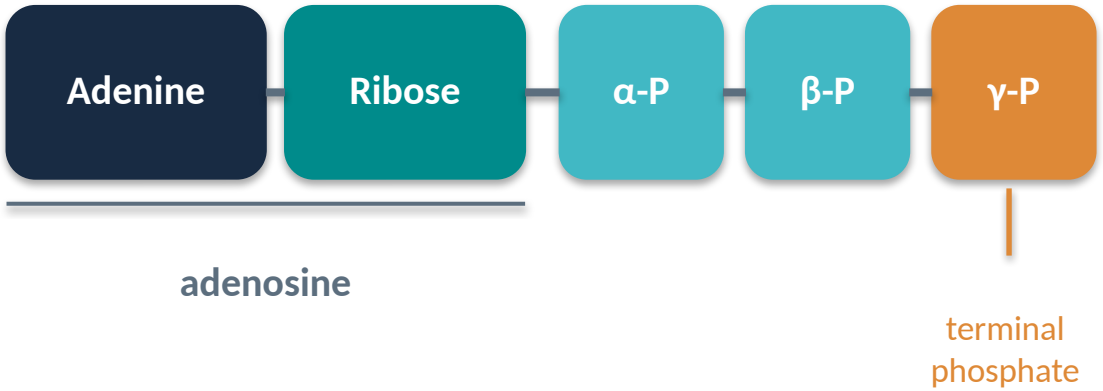
Adenine nucleotides and the bioenergetic role of ATP

Why ATP?

- Transferable intermediate between energy-yielding and energy-consuming processes.
- Can transfer a phosphoryl group or AMP, and can change protein conformation.
- Continuously regenerated: cells maintain ATP flux rather than a large static ATP reserve.

ATP Structure: Adenine + Ribose + Three Phosphates

- Adenine + ribose = adenosine.
- Phosphates are named α, β and γ from ribose outward.
- The γ-phosphoryl group is commonly transferred by kinases.



ATP, ADP and AMP: One Adenylate Pool



- ATP = three phosphates
- ADP = two phosphates
- AMP = one phosphate
- Interconversion of these nucleotides is central to energy homeostasis.

Phosphoester vs. Phosphoanhydride Linkages

Phosphoester

Ribose — O — Pα

Phosphoanhydride

Pα — O — Pβ — O — Pγ

- Ribose–O–Pα: phosphoester linkage
- Pα–O–Pβ and Pβ–O–Pγ: phosphoanhydride linkages
- “High-energy bond” is shorthand for high group-transfer potential — not energy stored inside one bond.

Common Misconception: “Breaking the ATP Bond Releases Energy”

MISCONCEPTION

“Breaking the terminal phosphate bond releases energy.”

BETTER MODEL

Hydrolysis is favorable because the complete products are better stabilized.

Bond breaking costs energy; the full reaction releases net free energy.

Module 2 • Physical Chemistry of ATP Hydrolysis

Why hydrolysis is favorable and why cellular ΔG differs from ΔG°′

ATP Hydrolysis Under Biochemical Standard Conditions

$$ATP + H_2O \rightarrow ADP + Pi$$

$$\Delta G^{\circ\prime} \approx -30.5\ kJ \cdot mol^{-1}$$

- $ATP + H_2O \rightarrow ADP + Pi$
- $\Delta G^{\circ\prime} \approx -30.5\ kJ \cdot mol^{-1}$
- The prime symbol indicates a biochemical transformed standard state, commonly referenced near pH 7.

Why Is ATP Hydrolysis Favorable?

1

Electrostatic relief

Phosphate charge crowding is reduced.

2

Resonance

Pi is strongly resonance-stabilized.

3

Hydration

Products interact differently with water.

4

Environment

Mg^{2+}, pH and ionization shift energetics.

ΔG°′ Is a Reference; ΔG Is the Cellular Driving Force

ΔG°′

Reference quantity
Useful for comparing reactions
Standardized biochemical conditions

ΔG

Actual driving force
Depends on ATP, ADP, Pi and conditions
What the cell “feels” thermodynamically

Reference state ≠ cellular state

Actual Free Energy: $\Delta G = \Delta G^{\circ\prime} + RT \ln Q$

$$\Delta G = \Delta G^{\circ\prime} + RT \ln Q$$

$$Q \approx ([ADP]/c^{\circ})([Pi]/c^{\circ}) / ([ATP]/c^{\circ})$$

- $R = 8.314\ J \cdot mol^{-1} \cdot K^{-1}$
- T is absolute temperature (K)
- Concentrations are often used as a practical approximation to activities in teaching examples.

Worked Example: A Well-Energized Cell

DATA

37°C
ATP 5 mM
ADP 0.1 mM
Pi 10 mM

$$Q \approx 2 \times 10^{-4}$$

$$RT \ln Q \approx -22\ kJ \cdot mol^{-1}$$

$$\Delta G \approx -52\ kJ \cdot mol^{-1}$$

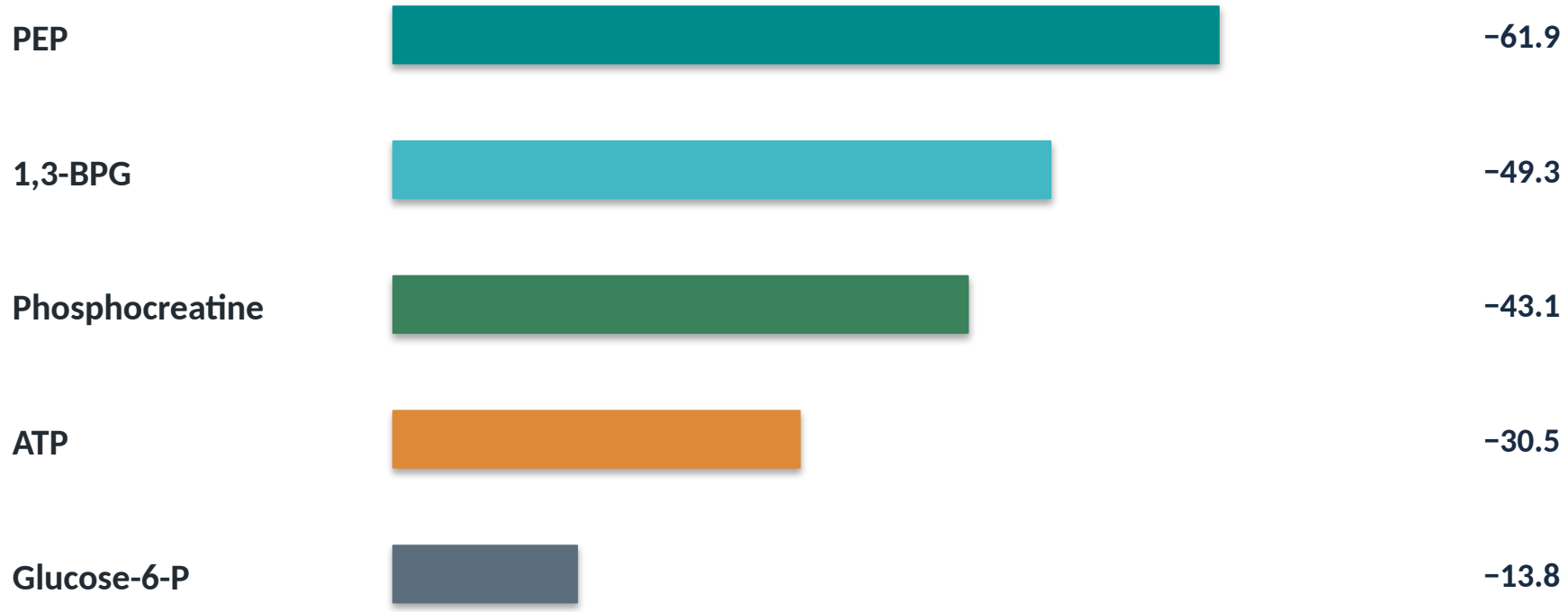
Cellular driving force > $|\Delta G^{\circ\prime}|$

MgATP: The Form Many Enzymes Actually Recognize

- ATP strongly complexes Mg^{2+} in cells.
- Mg^{2+} changes charge distribution and phosphate geometry.
- Many ATP-dependent enzymes bind MgATP rather than fully uncomplexed ATP.
- Precise thermodynamic values depend on Mg^{2+} conditions.

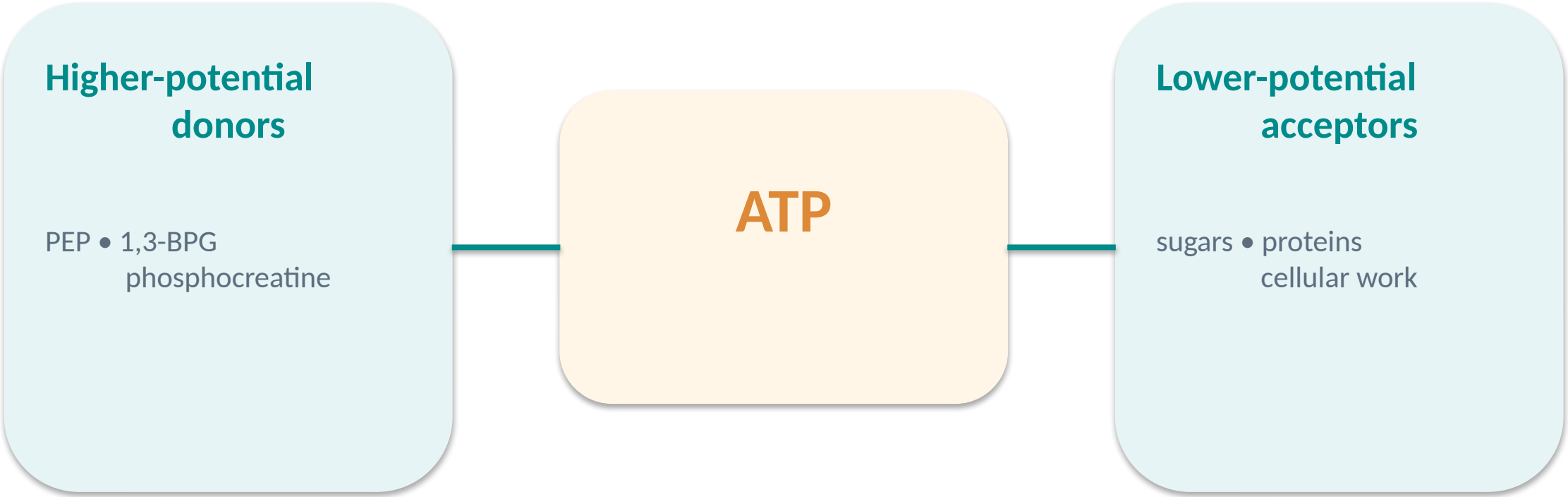
Phosphoryl-Transfer Potential: ATP Is in the Middle

Approximate $\Delta G^{\circ\prime}$ of hydrolysis ($kJ \cdot mol^{-1}$)



ATP = useful middle

Why the “Middle Position” Matters



ATP links energy-yielding metabolism to energy-consuming work.

How Is ATP Regenerated?

energy-yielding processes → **ADP + Pi** → **ATP** → **cellular work**

Detailed mechanisms are intentionally deferred to Lectures 4–6.

- Cells use energy-yielding reactions or ion gradients to re-form ATP.
- Detailed redox carriers are Lecture 4.
- Detailed membranes, proton gradients, ETC and ATP synthase are Lecture 5.
- Cellular respiration is Lecture 6.

Break + Retrieval Practice



5 min break

Then: retrieval practice — no notes.

Calculate the actual ΔG of ATP hydrolysis in an energy-stressed cell.

Retrieval Exercise: Energy-Stressed Cell

DATA

37°C
ATP 1 mM
ADP 2 mM
Pi 20 mM

YOUR TASK

- Compute Q
- Calculate ΔG
- Interpret sign and magnitude
- Compare with the previous −52 $kJ \cdot mol^{-1}$ example

Exercise Answer: ΔG Becomes Less Negative

Q	≈ 0.04
RT ln Q	≈ −8.3 kJ·mol^{-1}
ΔG	≈ −38.8 kJ·mol^{-1}

Hydrolysis remains favorable, but the driving force is reduced.