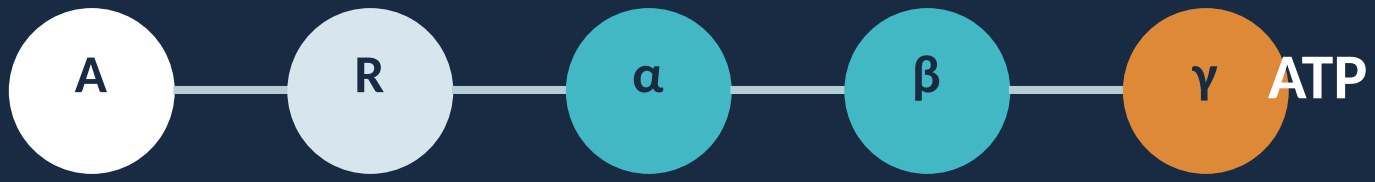
Lecture4: ATP-Dependent Energy Coupling. Cellular Energy Homeostasis



chemical free energy ↔ cellular work

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Module 3 • ATP-Dependent Energy Coupling

How ATP makes unfavorable cellular processes possible

Coupling

Energy Coupling: The Thermodynamic Logic

Endergonic step

$\Delta G_1 > 0$

ATP-linked step

$\Delta G_2 < 0$

Coupled process

$\Delta G\text{total} < 0$

$$\Delta G\text{total} = \Delta G_1 + \Delta G_2$$

The enzyme creates the physical/chemical link.

Mechanism 1: Direct Phosphoryl-Group Transfer

- ATP donates a phosphoryl group to a substrate.
- The phosphorylated product may be more reactive or have altered binding properties.
- Kinases are a major enzyme class using this strategy.

Example: ATP Drives Glucose Phosphorylation

Glucose + Pi → glucose-6-P

unfavorable alone

ATP + H_2O → ADP + Pi

favorable

↓ coupled by hexokinase ↓

Glucose + ATP → glucose-6-P + ADP

$\Delta G^{\circ\prime} \approx -16.7\ kJ \cdot mol^{-1}$

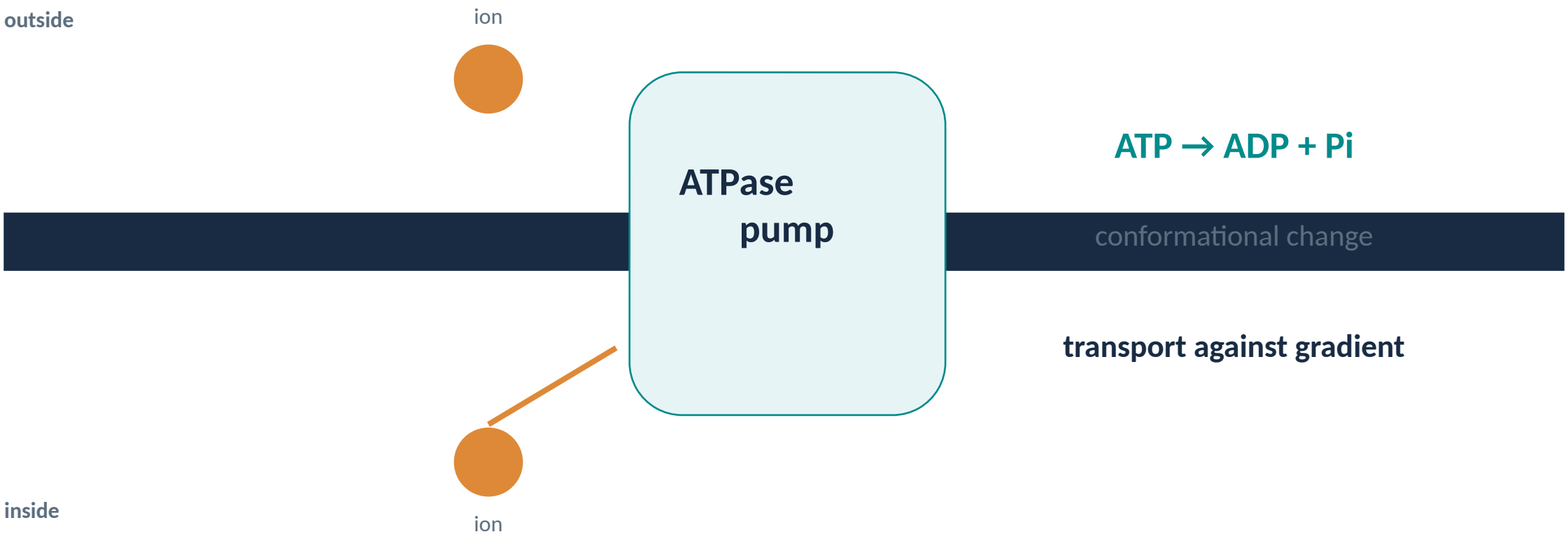
Mechanism 1b: ATP Creates an Activated Intermediate

- ATP can activate a substrate before product formation.
- Example principle: carboxylate + ATP → activated acyl-phosphate or adenylate intermediate.
- The activated intermediate then reacts in biosynthesis.

Mechanism 2: Conformational Coupling

- ATP binding and hydrolysis change protein conformation.
- Different conformations have different affinities for substrates or ions.
- The ATPase cycle imposes directionality on transport or movement.

Example: ATP-Driven Membrane Pump



Example: Molecular Motors Convert ATP Turnover into Movement

- ATP binding changes motor–filament affinity.
- Hydrolysis and product release advance the mechanochemical cycle.
- Repeated cycles produce directional movement and force.

Mechanism 3: Ion-Gradient Coupling — Preview Only

electrochemical ion gradient → coupled membrane work → ATP / transport

PREVIEW ONLY

Detailed Δp, ETC and ATP synthase mechanisms are Lecture 5.

- Cells can store free energy as an electrochemical ion gradient.
- Ion flow can be coupled to ATP synthesis or membrane transport.
- Detailed proton gradient, ETC and ATP synthase mechanisms belong to Lecture 5.

Three Ways to Couple Free Energy to Cellular Work

Chemical

phosphoryl transfer
activated intermediate

Conformational

transport
mechanical work

Ion-gradient

membrane bioenergetics
Lecture 5 preview

Same thermodynamic principle — different physical link.

Module 4 • Cellular Energy Homeostasis

Adenylate energy charge, adenylate kinase and energy sensing

Adenylate Energy Charge (AEC)

$$AEC = ([ATP] + 0.5[ADP]) / ([ATP] + [ADP] + [AMP])$$



higher AEC → ATP-loaded adenylate pool

- Range: 0 to 1
- Higher AEC means a larger fraction of the adenylate pool is ATP-loaded.
- AEC is a descriptor of energetic state — not the only molecular sensor.

AEC Worked Example

ATP 4.5 mM
ADP 0.5 mM
AMP 0.05 mM

AEC

$$(4.5 + 0.25) / 5.05$$

$$\approx 0.94$$

strongly ATP-loaded

Adenylate Kinase Links ATP, ADP and AMP

$$2\ ADP \rightleftharpoons ATP + AMP$$

- Buffers changes in adenine nucleotide pools
- Makes AMP particularly sensitive to a fall in energetic state

AMP can change markedly when the adenylate pool becomes stressed.

What Happens When Energy Demand Increases?



Energetic state links thermodynamics to regulation.

Energy Sensing: AMPK as a Eukaryotic Example

- AMPK responds to energetic stress in many eukaryotic cells.
- Activation favors ATP-generating processes and restrains some ATP-consuming biosynthesis.
- Bacteria and other organisms use different regulatory systems.

ATP Is Compartmentalized and Locally Consumed

- Whole-cell ATP concentration does not describe every local process.
- Organelles and microdomains can have different ATP/ADP ratios.
- Transport, diffusion and local enzyme organization shape ATP availability.

Case Study: Energy Stress and an ATP-Dependent Pump

Well-energized

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

larger thermodynamic margin

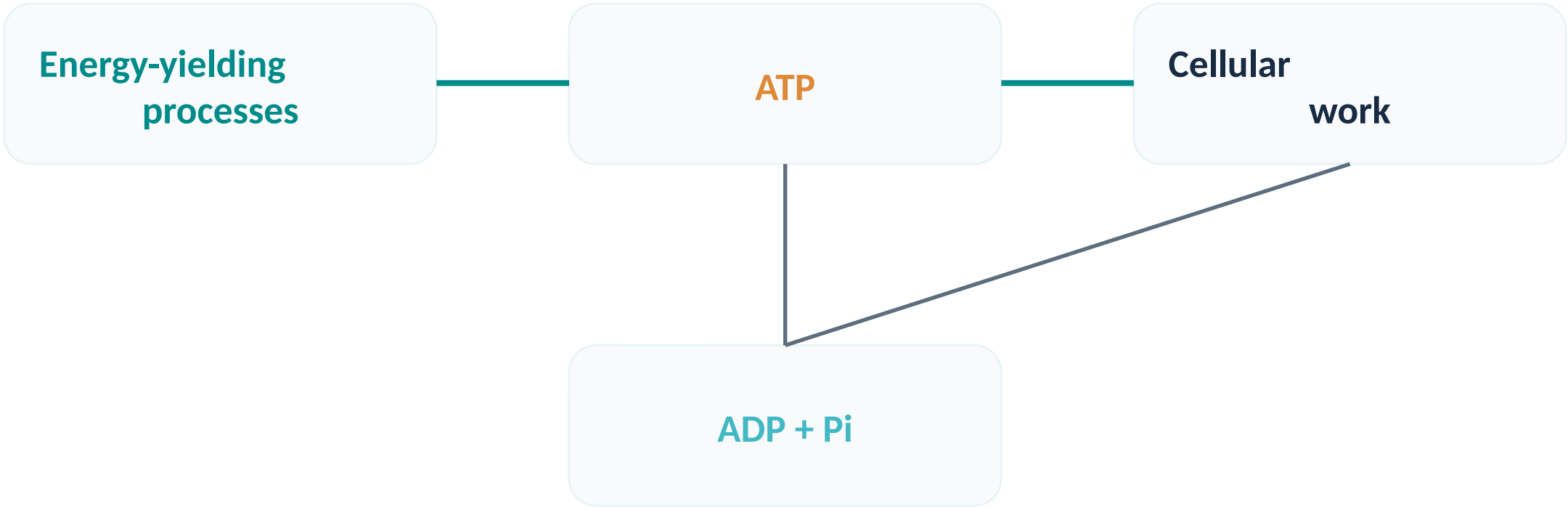
Energy-stressed

$$\Delta G_{ATP} \approx -39\ kJ \cdot mol^{-1}$$

smaller thermodynamic margin

Actual pump performance depends on the complete coupled system.

Integrating the Lecture: ATP as a Dynamic Energy Intermediate



regulation balances ATP production and ATP demand

Take-Home Messages

- ATP hydrolysis is favorable because the products are better stabilized — not because bond breaking itself releases energy.
- $\Delta G^{\circ\prime}$ is a reference; cellular ΔG depends on ATP, ADP, Pi, temperature and conditions.
- ATP drives work through enzyme-mediated coupling.
- AEC summarizes the adenylate pool but does not replace local thermodynamic and regulatory information.
- Key texts: Lehninger Principles of Biochemistry (8th ed.); Panov, Functional Bioenergetics.

Next Lecture: Oxidation–Reduction Reactions and Electron Carriers

Oxidation–Reduction Reactions and Electron Carriers

- What is oxidation and reduction?
- How do electron donors and acceptors work?
- NAD^+/NADH, $NADP^+$/NADPH and FAD/$FADH_2$
- How is electron transfer related to free energy?