From Glucose to ATP

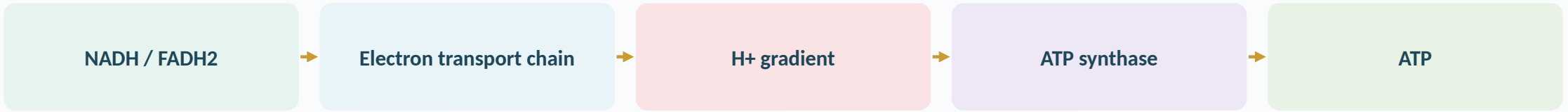
Cellular Respiration, Fermentation & Anaerobic Energy Metabolism

A biological, cell-centered pathway from nutrient oxidation to usable ATP

Glucose | Pyruvate | TCA | NADH | ETC | H+ gradient | ATP

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Bridge from last lecture



What you already know

Electron transfer through the respiratory chain creates a proton gradient across the inner mitochondrial membrane.

What ATP synthase uses

ATP synthase uses proton flow — not electron flow directly — to make ATP from ADP + Pi.

Quick retrieval: four questions

1 What carries electrons?

2 Where is the mitochondrial ETC?

3 What is the final electron acceptor?

4 What directly drives ATP synthase?

The new question: where do NADH and FADH2 come from?

Food molecules are oxidized → Electrons are transferred to carriers → Carriers deliver electrons to the ETC

Controlled oxidation lets cells capture energy step by step.

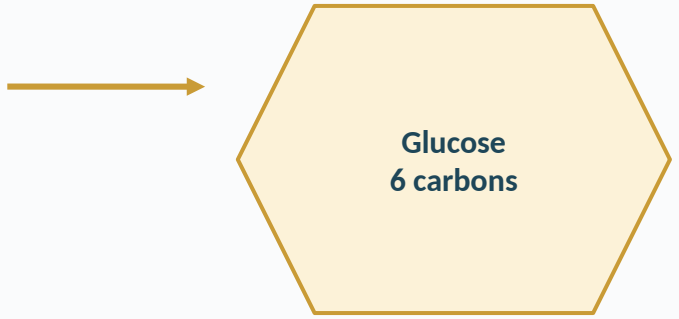
Key idea

Nutrient oxidation generates reduced electron carriers that feed the respiratory chain.

From food to one glucose molecule

1 • Carbohydrate food

Bread, rice, starch and other carbohydrates are digested into smaller sugars.



3 • Cellular fuel

Cells oxidize glucose in controlled stages instead of one uncontrolled step.

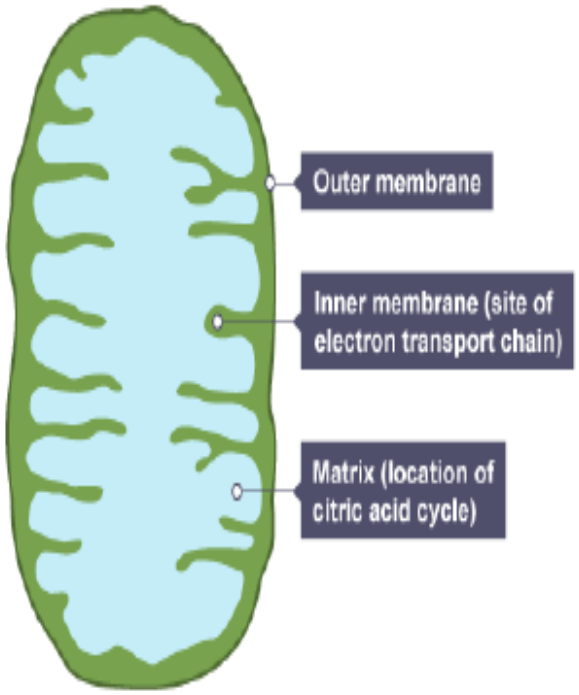
Why many steps?

Energy can be conserved in ATP and electron carriers instead of being released mostly as heat.

Bioenergetic perspective

Glucose is a carbon skeleton plus a source of transferable electrons.

Where does each stage occur?



Cytosol

Glycolysis converts glucose to pyruvate and produces ATP + NADH.

Mitochondrial matrix

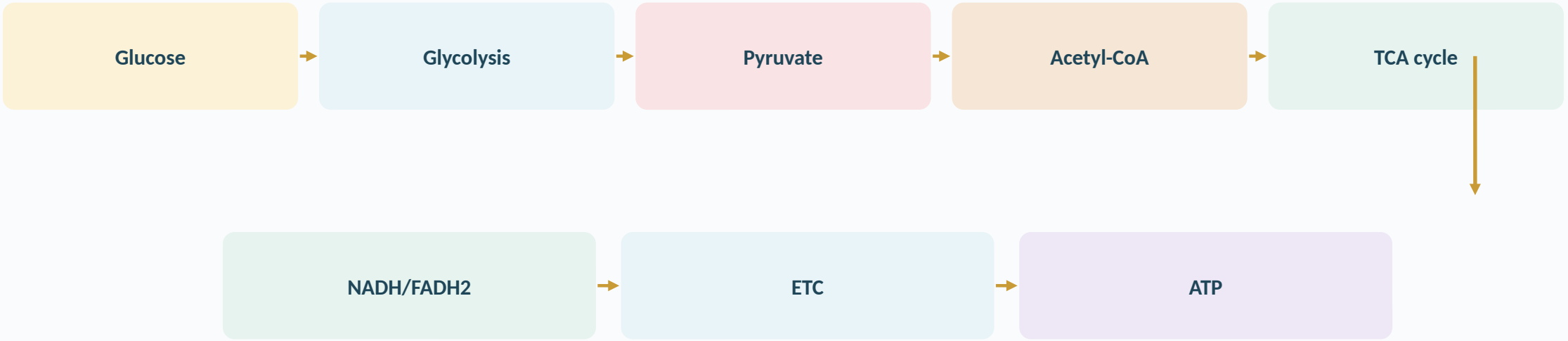
Pyruvate oxidation and the TCA cycle produce acetyl-CoA, CO_2, NADH and $FADH_2$.

Inner mitochondrial membrane

ETC and ATP synthase convert electron-transfer energy into most of the ATP.

Compartmentation makes the pathways easier to organize.

The whole pathway at a glance



Carbon story

Glucose carbon is progressively oxidized and released mainly as CO_2.

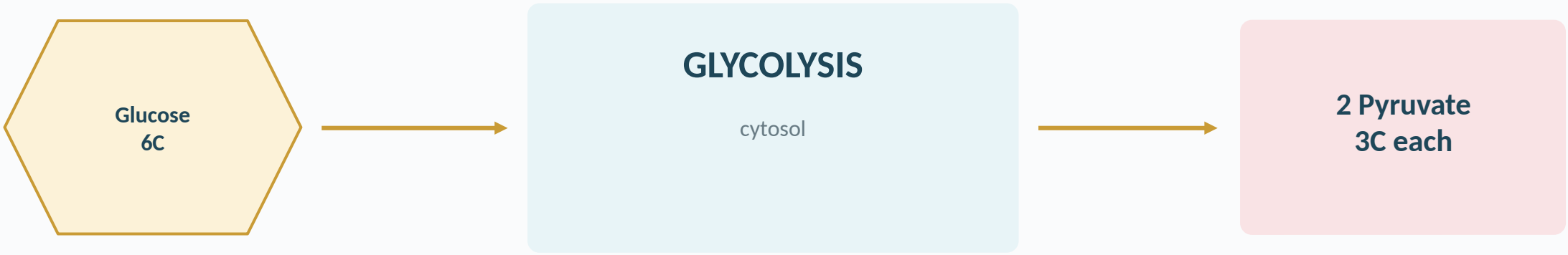
Electron story

Electrons are captured in NADH/$FADH_2$ and then used to make ATP.

Part I — Cellular respiration

Glucose → electron carriers → proton gradient → ATP

Glycolysis: the first stage



+ 2 ATP net

+ 2 NADH

first stage of glucose oxidation

Glycolysis in three simple phases

1 INVEST

ATP is used

− ATP

2 SPLIT

6C becomes two 3C molecules

6C → 3C + 3C

3 PAYOFF

ATP + NADH are produced

+ ATP + NADH

Net result per glucose: 2 pyruvate + 2 NADH + 2 ATP

Glycolysis balance sheet — per glucose

2 pyruvate	2 NADH	2 ATP net	2 H2O

Interpretation

The direct ATP yield is small; much of the captured energy is stored temporarily in reduced electron carriers.

Substrate-level phosphorylation

A phosphate is transferred directly to ADP

Direct phosphate transfer
from a metabolic intermediate
to ADP

No proton gradient required

Does not require the ETC

ETC creates a proton gradient
ATP synthase uses proton flow
to make ATP

Depends on membrane bioenergetics

Same product (ATP), different coupling mechanism.

Pyruvate: a metabolic crossroads

The fate of pyruvate depends on organism, redox state and metabolic conditions.



Respiration

Pyruvate → acetyl-CoA → TCA cycle

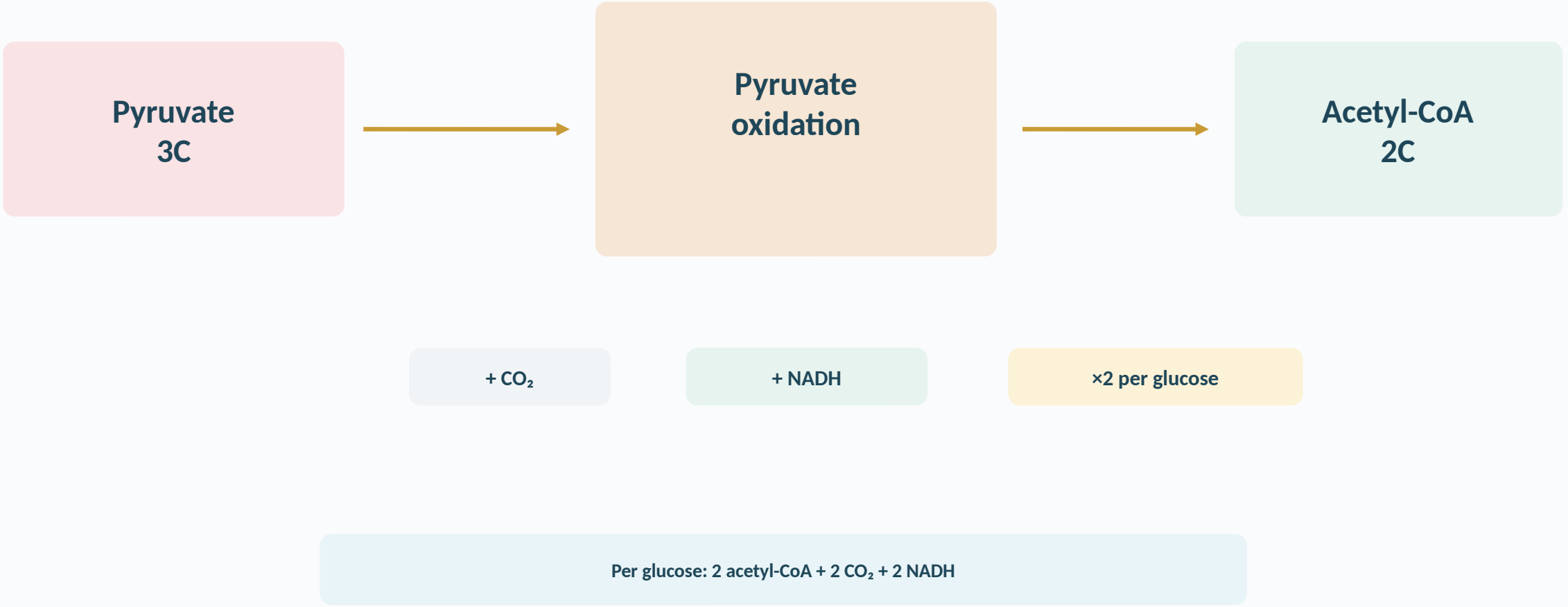
Fermentation

Pyruvate or a derivative receives electrons from NADH

Biosynthesis

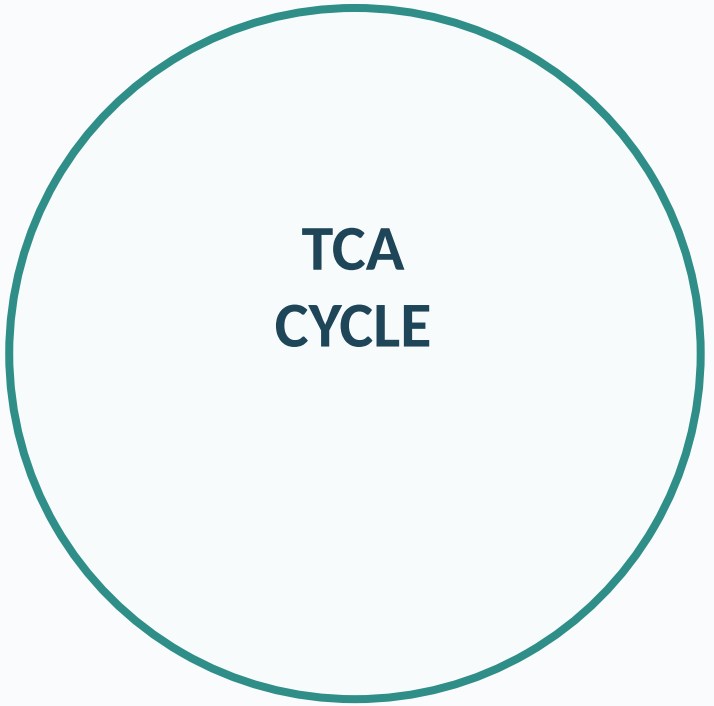
Carbon can be redirected into other cellular pathways

Pyruvate oxidation: the bridge to the TCA cycle



TCA cycle: what is its real purpose?

Input
Acetyl-CoA enters the cycle



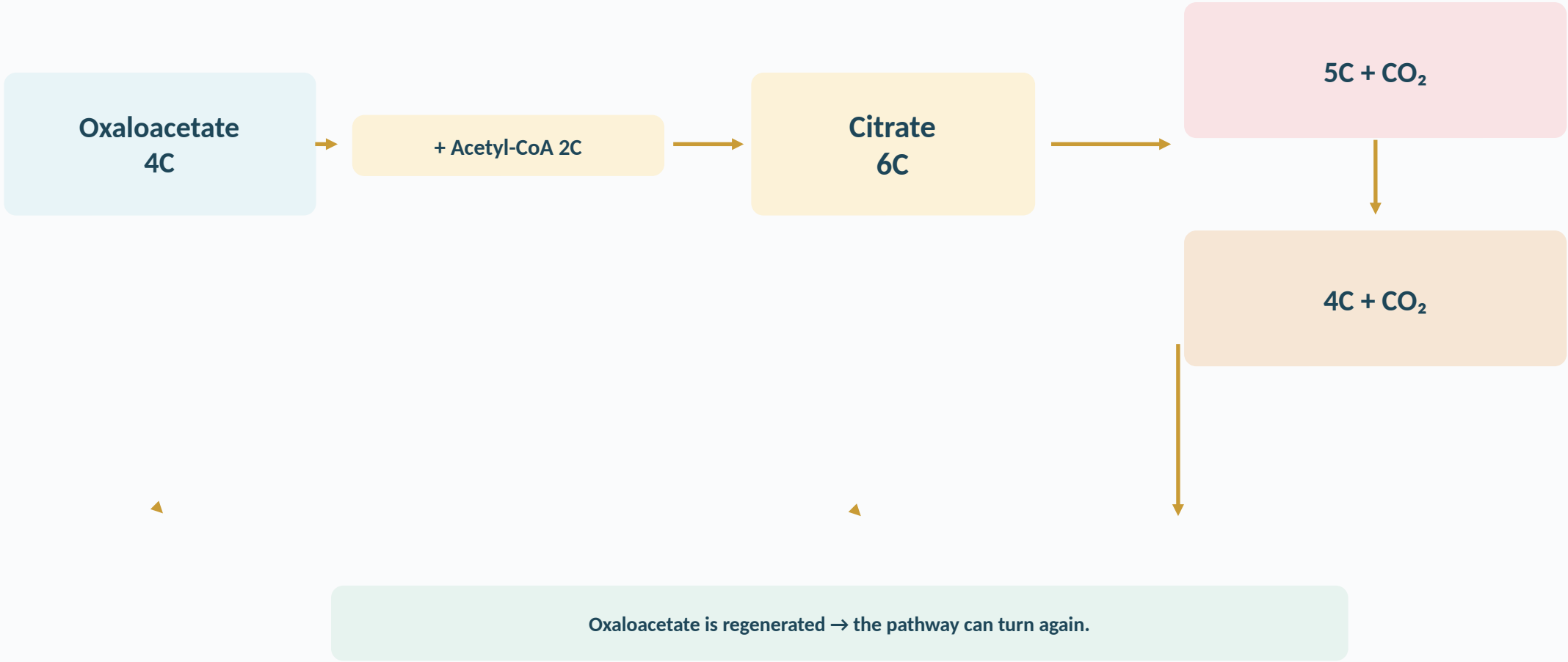
Major output
NADH + $FADH_2$ carry electrons

Cycle logic
Oxaloacetate is regenerated

Other outputs
CO_2 + small amount of GTP/ATP

Main bioenergetic role: produce reduced electron carriers.

Carbon flow through the TCA cycle



TCA cycle output — per acetyl-CoA

3 NADH	1 FADH2	1 GTP/ATP	2 CO2

Interpretation

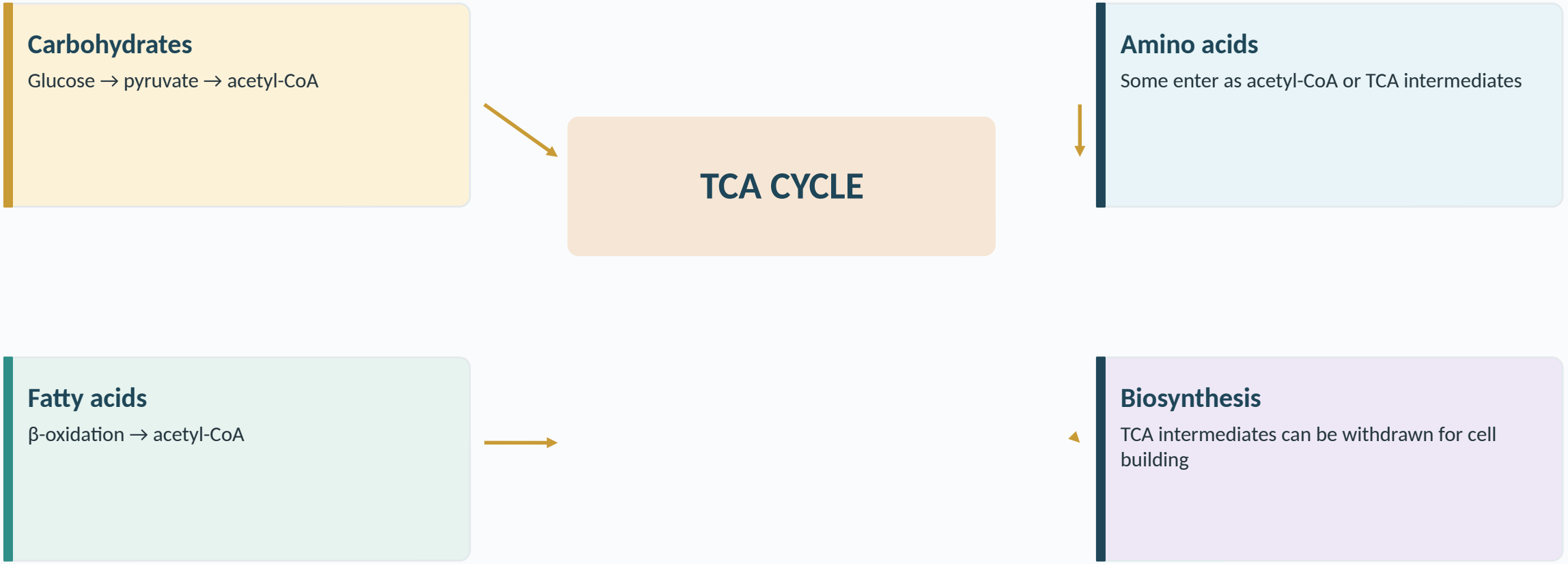
The direct ATP yield is small; much of the captured energy is stored temporarily in reduced electron carriers.

From one glucose: carrier production before the ETC

Stage	NADH	$FADH_2$
Glycolysis	2	0
Pyruvate oxidation	2	0
TCA cycle	6	2
TOTAL	**10**	**2**

Most captured energy is still in reduced carriers — not yet in ATP.

Why the TCA cycle matters beyond glucose



The TCA cycle links energy metabolism with biosynthesis.

Reconnect to Lecture 4–5: carriers feed the ETC

NADH → Complex I → FADH2-linked electrons → Complex II → Electron flow → H+ pumping → H+ gradient → ATP synthase

Lecture 6 answers

Where the reduced electron carriers come from.

Lecture 4–5 answered

How mitochondria convert carrier electrons into a proton gradient and ATP.

Carbon oxidation → electron carriers → membrane bioenergetics → ATP

Two ways cells make ATP

Substrate-level phosphorylation

Direct phosphate transfer
from a metabolic intermediate
to ADP

No proton gradient required

Oxidative phosphorylation

ETC creates a proton gradient
ATP synthase uses proton flow
to make ATP

Depends on membrane bioenergetics

Same product (ATP), different coupling mechanism.

Approximate ATP yield from one glucose

Glycolysis: 2 ATP net

TCA substrate-level step: 2 GTP/ATP

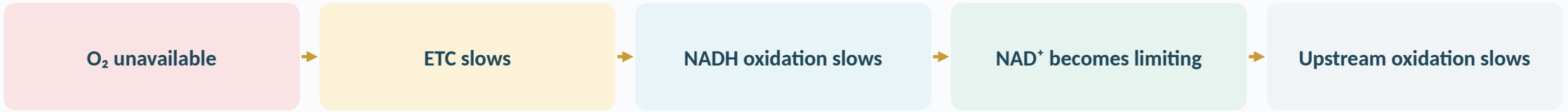
Oxidative phosphorylation: ~26–28 ATP

Total in many eukaryotic cells: ~30–32 ATP

Interpretation

The direct ATP yield is small; much of the captured energy is stored temporarily in reduced electron carriers.

Why oxygen matters



Direct role

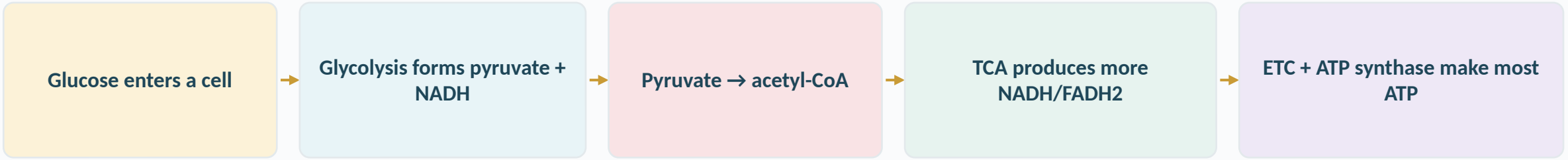
O_2 accepts electrons at the end of the aerobic respiratory chain.

Indirect consequence

By allowing NADH oxidation, respiration helps keep NAD^+ available for metabolism.

This sets up the need for fermentation.

Integrated case: what happens to glucose after a meal?



Energy transformation

Food chemical energy is transferred first to carriers and then to ATP.

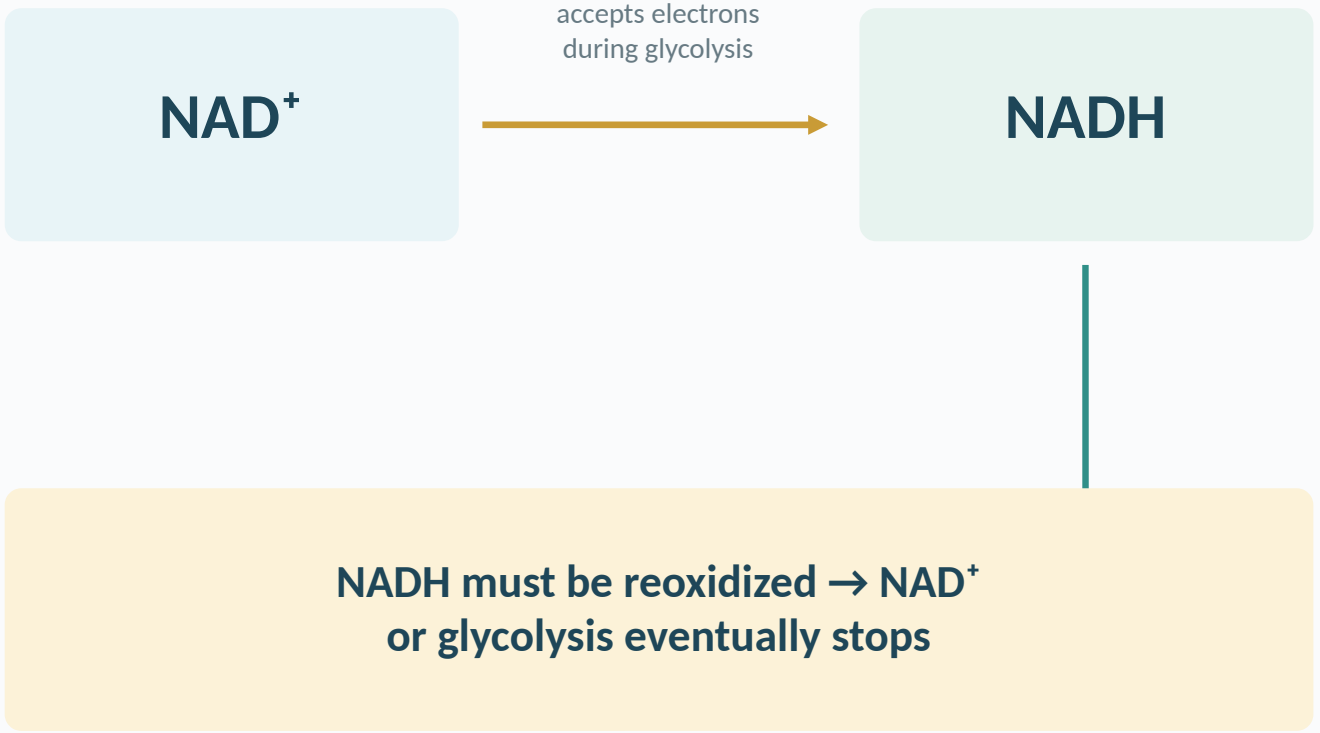
Cellular work

ATP can then support transport, synthesis, movement and homeostasis.

Part II — What if oxidative phosphorylation cannot keep up?

High glycolytic demand

Why NAD+ regeneration is essential



Respiration

ETC reoxidizes NADH indirectly.

Fermentation

An organic molecule accepts electrons from NADH.

The limited NAD pool must be recycled.

Fermentation: the core idea

No respiratory ETC is required

ATP comes mainly from glycolysis

NADH is reoxidized to NAD+

Organic products receive the electrons

Main purpose: regenerate NAD^+ so glycolysis can continue.

Lactate fermentation



ATP source

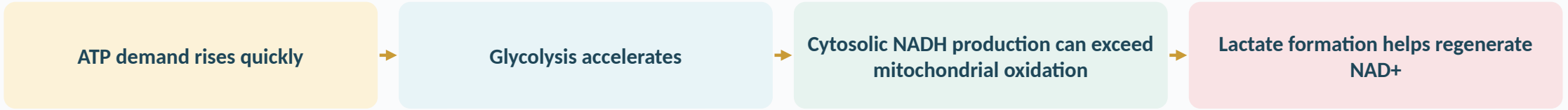
The lactate-forming step does not make extra ATP. ATP comes from glycolysis.

Why it helps

Regenerated NAD^+ lets glycolysis continue producing ATP.

Fermentation solves a redox problem first.

Physiological example: intense exercise



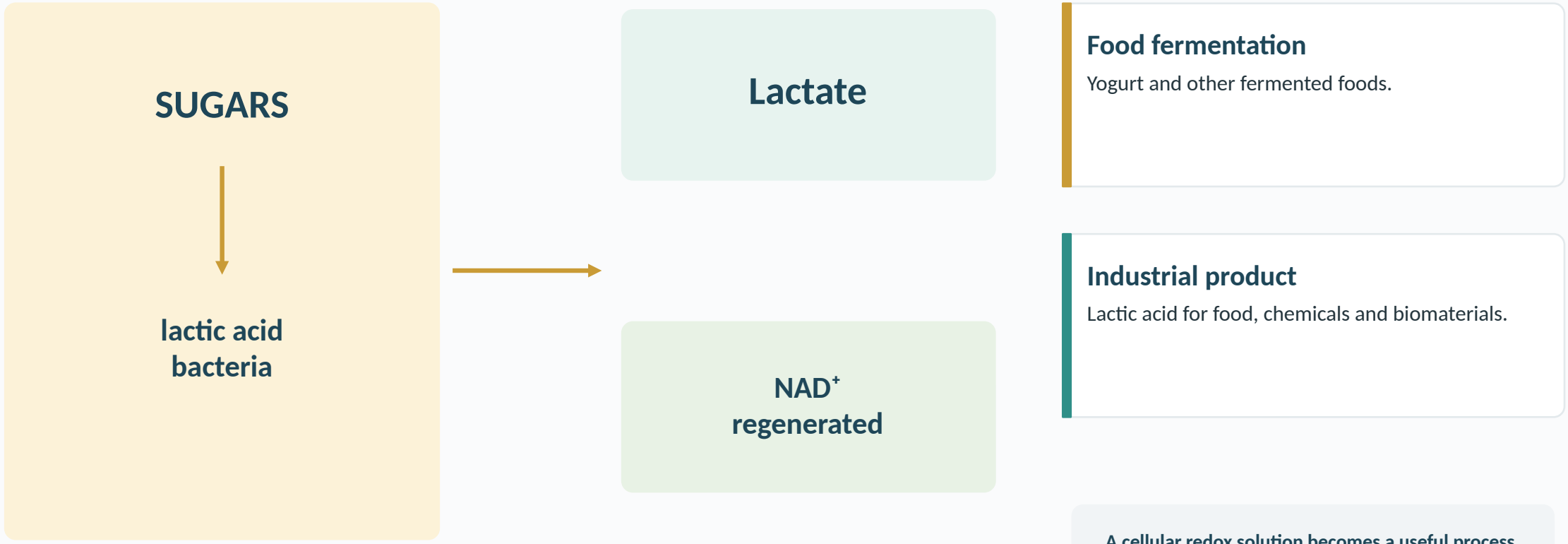
Important nuance

Lactate production does not mean that oxygen is absolutely zero.

Better explanation

High glycolytic flux can exceed the rate of mitochondrial oxidation of reducing equivalents.

Lactic acid bacteria: a microbial example



Food fermentation

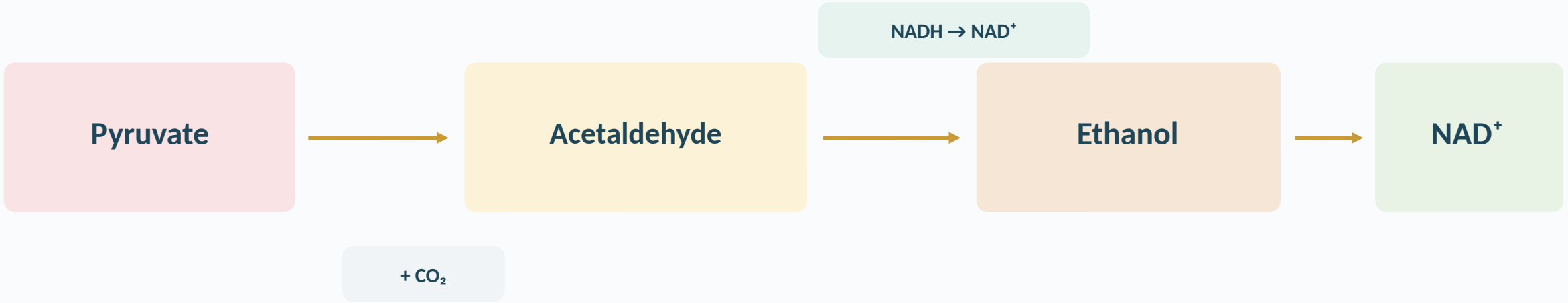
Yogurt and other fermented foods.

Industrial product

Lactic acid for food, chemicals and biomaterials.

A cellular redox solution becomes a useful process.

Alcoholic fermentation in yeast



Redox function

Acetaldehyde accepts electrons from NADH and becomes ethanol.

Energy function

Regenerated NAD^+ lets glycolysis continue making ATP.

Yeast in bread, beverages and bioethanol

Bread

CO_2 expands the dough

Saccharomyces

Beverages

Ethanol is a desired product

Saccharomyces

Bioethanol

Ethanol is recovered as a fuel product

Saccharomyces

Same redox pathway; different human use of its products.

Respiration, fermentation and anaerobic respiration

Aerobic respiration

Respiratory ETC
Terminal acceptor: O_2
Ion gradient + ATP synthase
High ATP yield

Fermentation

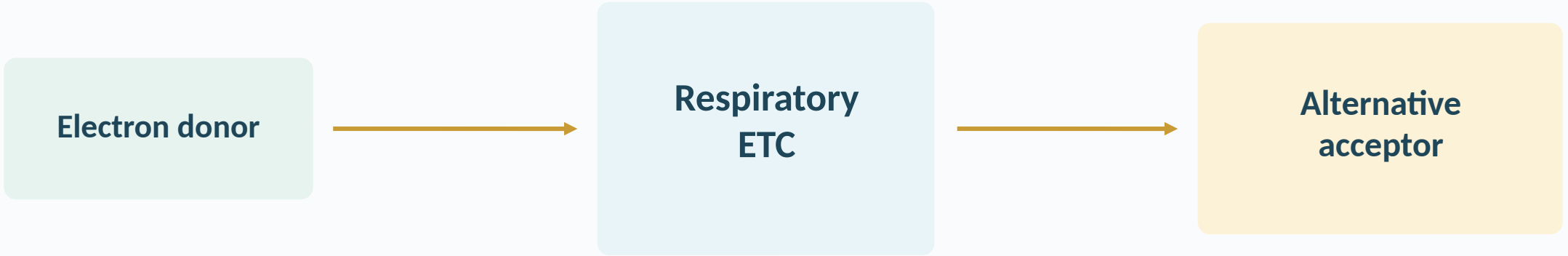
No respiratory ETC required
Organic electron acceptor
ATP mainly from glycolysis
NAD^+ regeneration

Anaerobic respiration

Respiratory ETC
Terminal acceptor ≠ O_2
Ion gradient often formed
Common in microbes

Key distinction: fermentation does not use a respiratory electron-transport chain.

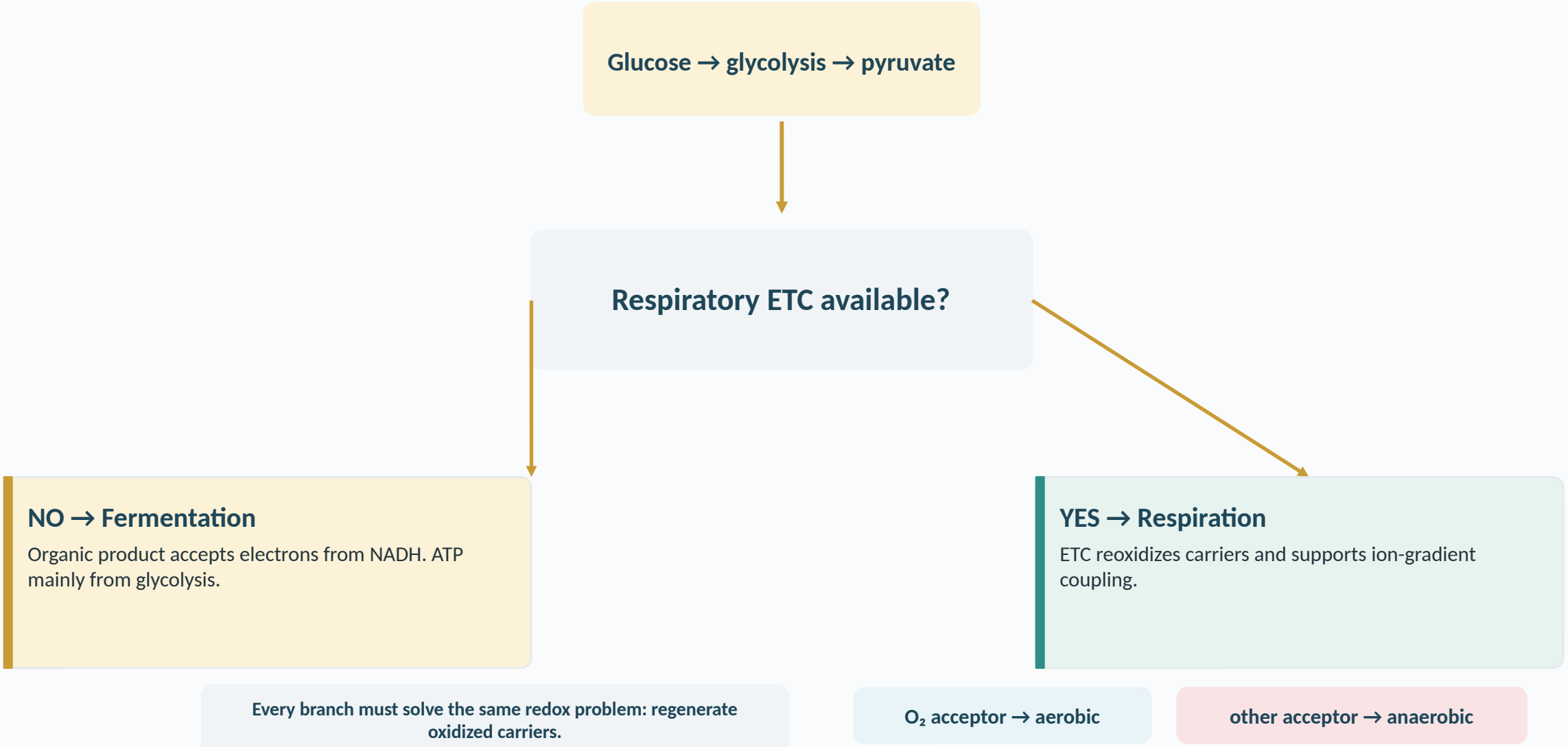
Anaerobic respiration: alternative electron acceptors



NO_3^- | SO_4^{2-} | Fumarate | others

Respiration is defined by an ETC, not by oxygen alone.

One decision map for energy metabolism



Take-home messages

1. Glycolysis begins glucose oxidation and makes pyruvate, ATP and NADH
2. Pyruvate oxidation + TCA produce most reduced carriers
3. ETC converts electron energy into a proton gradient
4. ATP synthase uses the gradient to make most ATP
5. Fermentation regenerates NAD+ without a respiratory ETC
6. Anaerobic respiration uses an ETC with a non-O2 terminal acceptor

References and recommended reading

1 Nelson & Cox — Lehninger Principles of Biochemistry, 8th ed.

2 Madigan et al. — Brock Biology of Microorganisms, 16th ed.

3 Arnold & Finley — Regulation and function of the mammalian tricarboxylic acid cycle

4

Recommended seminar reading: focus on figures and pathway logic before detailed regulation.