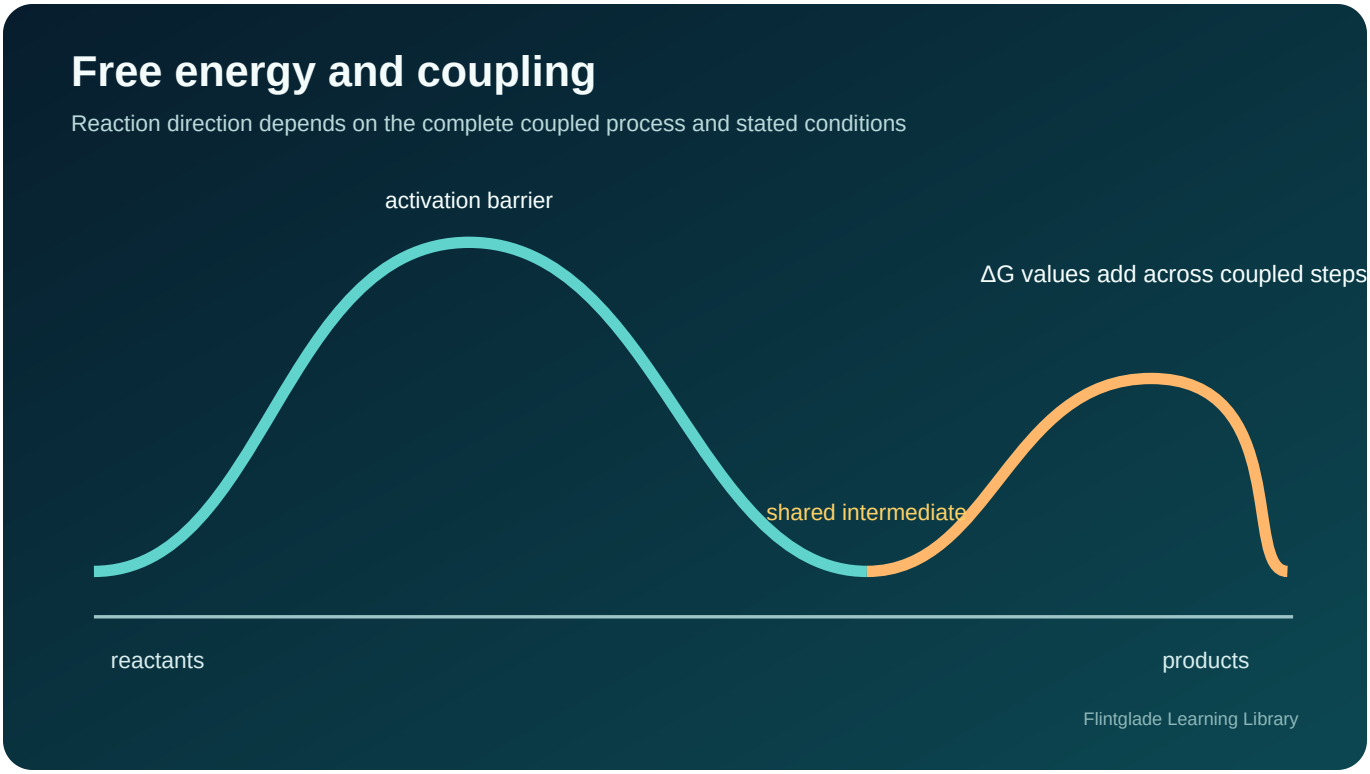
Activated Carriers in Metabolism

Flintglade Learning Library · General Biochemistry

Audience: Learners building an intuition for how cells move electrons, acyl groups, carbon dioxide, and phosphoryl groups.

MCAT connections: This guide can assist study of enzymes and kinetics, energetics and metabolism while keeping general biochemistry as its primary frame.



About this edition: This standalone edition organizes the material for independent reading with clear navigation, reusable reasoning frameworks, and print-ready presentation.

Learning goals

- Associate each carrier family with its transferable unit
- Explain why carrier structure supports its chemistry
- Avoid overgeneralizing carrier choice beyond a specific enzyme context

Navigate this guide

Part 0: What Problem Do These Molecules Solve?

Before defining any carrier, we need to understand why they exist at all.

Cells need to move chemical groups — acetyl groups, phosphoryl groups, CO_2 units, electrons — from one molecule to another. But most of these transfers are thermodynamically unfavorable on their own. The group being transferred is stable where it currently sits, and there is no driving force to move it somewhere else.

The solution: **activate** the group first. "Activation" means attaching the group to a special carrier molecule using a bond that stores energy. This bond is thermodynamically expensive to form but easy to break — meaning that when the carrier later donates the group to the final acceptor, the breaking of that high-energy bond releases energy that drives the transfer forward. The carrier is like a loaded spring: energy was spent to compress it (load the group), and that energy is recovered when it releases (donates the group).

Every carrier in this guide follows this same logic: **load → carry → donate.**

What is "high-energy" about a high-energy bond?

This phrase does not mean the bond itself is strong. It means the opposite — the bond is thermodynamically unstable relative to the products of its hydrolysis. When the bond breaks (by transferring the group to an acceptor), the system moves to a lower energy state, and the difference in energy is released. This released energy is what makes the transfer reaction favorable.

The most common types of high-energy bonds in carriers:

Thioester bonds (C(=O)–S): A carbonyl carbon bonded to a sulfur atom. Thioesters are high-energy because sulfur, unlike oxygen, does not donate its lone pair electrons into the carbonyl through resonance effectively. In a regular ester (C(=O)–O), oxygen's lone pair partially overlaps with the carbonyl, stabilizing it through resonance. Sulfur's 3p orbitals are too large and diffuse to overlap well with carbon's 2p orbital, so this stabilizing resonance is weak. The result: the thioester is less stable (higher energy) than an equivalent ester, and breaking it releases more energy.

Phosphoanhydride bonds (P–O–P): Two phosphate groups linked by a shared oxygen. High-energy because the products of hydrolysis (two separate phosphates) are stabilized by resonance, ionization, and relief of electrostatic repulsion between the negative charges that were forced to sit next to each other in the anhydride.

Phosphoester bonds (C–O–P): Generally lower energy than phosphoanhydrides but still carry useful activation energy in certain contexts.

N-carboxyl bonds (N–COO^-): As in biotin-CO_2. The CO_2 attached to biotin's nitrogen is activated — it is easier to transfer from biotin to an acceptor than it would be to grab free CO_2 from solution.

What does "carrier" mean concretely?

A carrier molecule has two parts:

1. **The business end** — the specific chemical group on the carrier where the transferred group attaches and detaches. This is where the chemistry happens. For CoA, it is the terminal thiol (-SH). For NAD^+, it is the nicotinamide ring. For ATP, it is the phosphate chain.
2. **The recognition handle** — the rest of the molecule, which does not participate in the chemistry but is recognized by enzymes. This is how enzymes distinguish CoA from NAD^+ from FAD. The adenine nucleotide portion of CoA, NAD^+, and FAD all look similar — they are built from ADP-like scaffolds — but each has a distinct structural feature that enzymes use to grab the right carrier and position it correctly.

This distinction matters because when you are asked "what does this carrier carry?" the answer is always about the business end, and when you are asked "how does the enzyme know which carrier to use?" the answer is always about the recognition handle.

Part 1: Activated Group Carriers

These carriers move chemical groups (non-electron transfers). Each entry below follows the same structure: what it carries, what the business end is, how the group is loaded, and how the group is donated.

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1. Thiamine Pyrophosphate (TPP)

What it carries: Two-carbon (2C) fragments, specifically "activated aldehydes." More precisely: TPP carries a hydroxyethyl group (–CH(OH)–CH_3) that is derived from the decarboxylation of an α-keto acid.

What is an α-keto acid? An α-keto acid is a molecule that has a carboxylate group (–COO^-) and a ketone (C=O) on the carbon immediately adjacent to the carboxylate. The most important example is **pyruvate:** CH_3–C(=O)–COO^-. The carbon between the ketone and the carboxylate is called the α-carbon.

The business end: TPP's reactive part is its **thiazolium ring** — a five-membered ring containing both a nitrogen and a sulfur. The critical atom is the **carbon between the nitrogen and the sulfur** (called C2 of the thiazolium ring). This carbon is unusual: even though it is a carbon bonded to two heteroatoms (N and S), it can lose its proton to become a **carbanion** (a carbon with a lone pair and a negative charge). This carbanion is the nucleophile that attacks the substrate.

Why can this carbon lose its proton? Because the positive charge on the nitrogen of the thiazolium ring stabilizes the resulting negative charge on carbon. Additionally, the sulfur atom helps stabilize the carbanion through polarizability (sulfur's large electron cloud can accommodate nearby negative charge). The proton on C2 has a pKa around 17–19, but the enzyme environment lowers this further, making deprotonation feasible. This stabilized carbanion is sometimes called a **ylide** (a species with adjacent positive and negative charges on different atoms within the same molecule).

How it works as an "electron sink":

This is a critical concept. When TPP attacks the carbonyl carbon of pyruvate, the resulting intermediate needs to lose CO_2 (decarboxylation). After CO_2 leaves, the two remaining carbons would have an excess of electron density — specifically, a carbanion would form on what used to be the carbonyl carbon. Normally, carbanions on carbon are extremely unstable. But the thiazolium ring of TPP acts as an **electron sink**: the positive charge on the ring nitrogen and the resonance structures available within the ring pull electron density away from the carbanion, stabilizing it. Without this electron-sink capability, the decarboxylation would not occur because the intermediate would be too high in energy.

The mechanism in brief:

1. C2 of TPP is deprotonated → carbanion/ylide forms.
2. TPP carbanion attacks the carbonyl carbon (C2) of pyruvate. Arrow from the lone pair on TPP's C2 to the carbonyl carbon of pyruvate. The C=O electrons shift onto oxygen.
3. CO_2 is lost from the α-carboxylate. The electrons that held the C–COO^- bond stay on the α-carbon, forming a carbanion. The thiazolium ring stabilizes this carbanion (electron sink).
4. The resulting intermediate is the **hydroxyethyl-TPP** adduct — a 2C fragment (from pyruvate minus CO_2) covalently attached to TPP.
5. This 2C fragment can then be transferred to the next carrier (lipoamide) or released as an aldehyde, depending on the pathway.

Where you see it: Pyruvate dehydrogenase complex (PDH) — Step 1. Also in α-ketoglutarate dehydrogenase and transketolase.

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2. Lipoamide (Lipoic Acid)

What it carries: Acyl groups (specifically the acetyl group, –C(=O)–CH_3) and electrons. It is a dual carrier — it transfers a chemical group AND electrons simultaneously.

The business end: A **dithiolane ring** — a five-membered ring containing two sulfur atoms connected by a disulfide bond (S–S). This disulfide bond is the key. When the hydroxyethyl group is transferred from TPP to lipoamide, two things happen at once: (a) the 2C fragment is oxidized from a hydroxyethyl group to an acetyl group, and (b) the disulfide bond of lipoamide is reduced to two free thiols (–SH HS–). So lipoamide carries the acetyl group on one of its sulfur atoms (as a thioester: S–C(=O)–CH_3) while the other sulfur holds the electrons (as –SH) from the oxidation.

How the transfer works in the PDH complex:

1. Hydroxyethyl-TPP reacts with the disulfide of lipoamide.
2. The hydroxyethyl group is transferred and simultaneously oxidized to an acetyl group.
3. The disulfide (S–S) is reduced to two –SH groups, with the acetyl group now on one of them (S-acetyl).
4. The acetyl group is then transferred from lipoamide's sulfur to Coenzyme A's sulfur (thiol of CoA attacks the thioester on lipoamide → acetyl-CoA is produced, lipoamide now has two free –SH groups).
5. Lipoamide must be re-oxidized (–SH HS– → S–S) to be ready for the next round. This is done by dihydrolipoyl dehydrogenase (E3), which uses FAD and ultimately passes electrons to NAD^+.

Why lipoamide and not just transfer directly from TPP to CoA? The physical architecture of the PDH complex. Lipoamide is attached to a long, flexible lysine arm on the E2 subunit. This arm can swing between the E1 active site (where TPP is), the E2 active site (where CoA reacts), and the E3 active site (where lipoamide is re-oxidized). It is a molecular conveyor belt, physically shuttling the group between active sites that are too far apart for direct transfer.

Where you see it: Pyruvate dehydrogenase complex (E2 component), α-ketoglutarate dehydrogenase complex.

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3. Biotin

What it carries: Activated CO_2 (a carboxyl group, $–COO^-$).

The business end: A **ureido ring** — a five-membered ring containing two nitrogen atoms flanking a carbonyl (N–C(=O)–N). CO_2 is attached to one of the nitrogen atoms of this ring, forming **N-carboxybiotin** (biotin–N–COO^-). This N–C bond to CO_2 is the activated, energy-rich bond. The CO_2 is

more reactive here than free dissolved CO_2 because the N–COO^- bond is relatively weak and thermodynamically poised to transfer the carboxyl group to an acceptor.

How loading works — requires ATP:

1. Free CO_2 (as bicarbonate, HCO_3^-, in solution) is not reactive enough to carboxylate substrates directly.
2. ATP is consumed to activate the CO_2. Specifically: ATP reacts with bicarbonate to form **carboxyphosphate** (HO–CO–O–PO_3^{2-}), a mixed anhydride. This is the actual activated species. ADP is released.
3. The nitrogen of biotin's ureido ring attacks the carbonyl carbon of carboxyphosphate, displacing the phosphate. Arrow from the lone pair on biotin's nitrogen to the carbon of carboxyphosphate. Phosphate leaves.
4. Result: N-carboxybiotin. The CO_2 is now "loaded" onto biotin.

How donation works:

5. N-carboxybiotin swings (biotin is attached to a long lysine arm, just like lipoamide) to the acceptor substrate.
6. The carboxyl group is transferred from biotin's nitrogen to the acceptor (e.g., to pyruvate to make oxaloacetate, or to acetyl-CoA to make malonyl-CoA). Arrow from the acceptor's carbanion (generated by deprotonation) to the carbon of the –COO^- on biotin, with the N–C bond breaking.
7. Biotin is regenerated (decarboxylated), ready for the next round.

Where you see it: Pyruvate carboxylase (pyruvate → oxaloacetate), acetyl-CoA carboxylase (acetyl-CoA → malonyl-CoA). The signature clue is: **any ATP-dependent carboxylation reaction.**

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4. Coenzyme A (CoA)

What it carries: Acyl groups — most commonly the acetyl group (2 carbons), but also longer fatty acyl chains, succinyl groups, and others.

The business end: A terminal **thiol group (–SH)**. When CoA carries an acyl group, it forms a **thioester bond**: R–C(=O)–S–CoA. This is the high-energy bond. As explained in Part 0, thioesters are high-energy because sulfur does not stabilize the carbonyl through resonance as well as oxygen would, making the bond thermodynamically unstable and the acyl group easily transferable.

The recognition handle: CoA has a complex structure built from: a β-mercaptoethylamine unit (which carries the –SH), connected to pantothenate (vitamin B5), connected to a 3'-phospho-ADP moiety. The entire handle is recognized by enzymes, but none of it participates in the chemistry — only the terminal –SH does.

How it works:

Loading: The thiol (–SH) of CoA attacks an electrophilic carbonyl carbon (e.g., the thioester on lipoamide, or a carboxylate activated by ATP). Arrow from the lone pair on CoA's sulfur to the carbonyl carbon. A thioester bond forms.

Donation: An acceptor nucleophile (another –SH, an –OH, or a carbanion) attacks the carbonyl carbon of the thioester. Arrow from the acceptor's lone pair to the thioester carbonyl carbon. CoA's sulfur departs as the leaving group ($–S^-$, thiolate), which is a good leaving group because the thioester is high-energy. CoA-SH is regenerated.

The central metabolic currency for acyl groups. Acetyl-CoA sits at the intersection of carbohydrate, fat, and amino acid metabolism. It feeds into the citric acid cycle, fatty acid synthesis, ketone body synthesis, and cholesterol synthesis. Every time you see "acetyl-CoA" in a pathway, CoA is the carrier that brought the acetyl group there.

Where you see it: Pyruvate dehydrogenase (product), citric acid cycle (citrate synthase — acetyl-CoA + oxaloacetate → citrate), fatty acid oxidation (product of each β-oxidation cycle), fatty acid synthesis (acetyl-CoA carboxylase — acetyl-CoA → malonyl-CoA).

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5. Adenosine Triphosphate (ATP)

What it carries: Phosphoryl groups ($–PO_3^{2-}$).

The business end: The **phosphate chain** — specifically, three phosphate groups linked by two phosphoanhydride bonds (α–β and β–γ). The γ-phosphate (the outermost one) is transferred most commonly, but the β-phosphate and even the α-phosphate can be transferred depending on the reaction.

What are the transfer modes?

- **Transfer of γ-phosphate only (phosphoryl transfer):** ATP → ADP + P_i. This is the most common. The enzyme uses the energy of the γ-phosphoanhydride bond to drive a phosphorylation reaction. Example: hexokinase phosphorylates glucose using ATP's γ-phosphate.
- **Transfer of pyrophosphate (β + γ phosphates together):** ATP → AMP + PP_i. The entire pyrophosphate unit (two linked phosphates) is released. This happens in reactions that need more driving force, because the subsequent hydrolysis of PP_i → $2P_i$ by pyrophosphatase makes the reaction essentially irreversible. Example: fatty acid activation (fatty acid + CoA + ATP → fatty acyl-CoA + AMP + PP_i).
- **Transfer of AMP (adenylyl transfer):** The α-phosphate stays bonded to the adenosine, and the whole AMP unit is transferred to the substrate. This creates an adenylated intermediate. Example: amino acid activation for translation (amino acid + ATP → aminoacyl-AMP + PP_i).

Why is ATP "high-energy"?

Four reasons, all working together:

1. **Electrostatic repulsion relief:** Three negatively charged phosphate groups are forced together. Hydrolysis separates them, reducing repulsion.
2. **Resonance stabilization of products:** ADP and P_i each have more resonance forms available than they did when locked together in ATP.
3. **Hydration stabilization:** The products (ADP and P_i) are better solvated by water than ATP is.
4. **Ionization:** At physiological pH, the products ionize to more stable charge states.

Where you see it: Everywhere. Kinases (transfer phosphoryl groups to substrates), synthetases (use ATP hydrolysis to drive bond formation), motor proteins, ion pumps.

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6. Uridine Diphosphate (UDP)

What it carries: Activated sugars (most commonly glucose → UDP-glucose, but also galactose, glucuronic acid, N-acetylglucosamine, and others).

The business end: The sugar is attached to the UDP through a **phosphoester bond** at the anomeric carbon (C1) of the sugar. Specifically, the anomeric -OH of the sugar attacks UTP (uridine triphosphate), displacing pyrophosphate (PP_i). The product is UDP-sugar + PP_i. Just like with ATP → AMP + PP_i reactions, the subsequent hydrolysis of PP_i → $2P_i$ makes this activation irreversible.

Why does the sugar need to be activated? Free sugars are not reactive enough for glycosidic bond formation. The hydroxyl group at C1 of a free sugar is a poor leaving group. By attaching UDP to C1, the enzyme now has a good leaving group (UDP, a stable nucleoside diphosphate) that departs when a new glycosidic bond forms. The analogy to CoA is exact: just as the thioester in acetyl-CoA makes the acetyl group transferable, the UDP-sugar bond makes the sugar transferable.

How donation works:

An acceptor molecule (another sugar's –OH, or a protein's Ser/Thr –OH) attacks the anomeric C1 of the UDP-sugar. UDP departs as the leaving group. A new glycosidic bond (or O-linked glycosylation) is formed.

Where you see it: Glycogen synthesis (UDP-glucose + glycogen chain → extended glycogen + UDP, catalyzed by glycogen synthase). Glucuronidation (detoxification pathway in the liver — UDP-glucuronic acid conjugates to drugs/toxins to make them water-soluble for excretion).

Part 2: Electron and Redox Carriers

These carriers move electrons (and their associated protons), not chemical groups. The chemistry here is oxidation-reduction (redox).

Quick redox reminder from first principles:

- **Oxidation** = loss of electrons. A molecule is oxidized when it loses electrons (or loses hydrogen atoms, which carry electrons with them, or gains oxygen). Mnemonic: OIL (Oxidation Is Loss).
- **Reduction** = gain of electrons. A molecule is reduced when it gains electrons (or gains hydrogen atoms, or loses oxygen). Mnemonic: RIG (Reduction Is Gain).
- Every oxidation is coupled to a reduction. If molecule A loses electrons, molecule B must gain them. The carrier is molecule B.

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7. NAD^+ / NADH (Nicotinamide Adenine Dinucleotide)

What it carries: A hydride ion (H^-), which is a hydrogen atom plus one extra electron — so it is equivalent to carrying two electrons and one proton as a package.

The business end: The **nicotinamide ring** — a six-membered aromatic ring derived from niacin (vitamin B3). In the oxidized form (NAD^+), the ring has a positive charge on its nitrogen and is aromatic. When NAD^+ accepts a hydride, two electrons and one proton are added to the C4 position of the ring. The ring loses its aromaticity and becomes non-aromatic — this is NADH. The remaining proton from the substrate (since a substrate typically loses 2H: one as H^- to NAD^+, and one as H^+ to solution) goes to the solvent.

The mechanism of hydride transfer:

This is a single-step, direct transfer. No radicals, no intermediates.

1. The substrate has a C–H bond that will be broken. This carbon is being oxidized.
2. The hydrogen leaves the substrate as H^- (it takes both electrons from the C–H bond with it).
3. H^- is delivered directly to the C4 position of the nicotinamide ring of NAD^+. Arrow from the C–H bond on the substrate to C4 of NAD^+. The positive charge on the ring nitrogen is neutralized by the incoming electrons.
4. A second hydrogen from the substrate (from an -OH or -NH group) is released as H^+ to solution.

Result: The substrate has been oxidized (lost 2H, or equivalently, lost 2 electrons). NAD^+ has been reduced to NADH (gained 2 electrons as H^-).

The recognition handle: An ADP moiety — adenine ring + two phosphates + ribose. This is what enzymes grab. The nicotinamide ring (the business end) sticks into the active site near the substrate.

Metabolic role — catabolic (breakdown) pathways:

NAD^+ is used primarily in catabolic reactions where substrates are being oxidized for energy extraction. NADH produced by catabolism carries its electrons to the electron transport chain (ETC) in the mitochondrial inner membrane, where the electrons flow through Complexes I → III → IV and ultimately reduce O_2 to water. The energy released during this electron flow drives ATP synthesis.

Key reactions that produce NADH: glycolysis (glyceraldehyde-3-phosphate dehydrogenase), pyruvate dehydrogenase, citric acid cycle (isocitrate dehydrogenase, α-ketoglutarate dehydrogenase, malate dehydrogenase).

8. $NADP^+$ / NADPH (Nicotinamide Adenine Dinucleotide Phosphate)

What it carries: A hydride ion (H^-) — identical chemistry to NAD^+/NADH.

The business end: The exact same nicotinamide ring as NAD^+. The hydride transfer mechanism is identical.

Then what is different? One single phosphate group. $NADP^+$ has an extra phosphate esterified to the 2'-OH of the adenine ribose sugar. That is the only structural difference between NAD^+ and $NADP^+$ — one phosphate group on the recognition handle.

Why does one phosphate group matter? Because enzymes can tell them apart. Enzymes that use NAD^+ have binding pockets shaped to accommodate the 2'-OH (no phosphate). Enzymes that use $NADP^+$ have binding pockets shaped to accommodate the 2'-phosphate. This allows the cell to maintain two completely separate pools of electron carriers serving two different purposes, even though the chemistry they perform is identical.

Metabolic role — anabolic (biosynthetic) pathways:

NADPH is used primarily in anabolic reactions where electrons are being donated to build molecules. Fatty acid synthesis, cholesterol synthesis, nucleotide synthesis, and detoxification reactions (cytochrome P450) all consume NADPH. The cell keeps the NADPH/$NADP^+$ ratio high (reduced form dominant) so that NADPH is always available as an electron donor for biosynthesis. Conversely, the cell keeps the NADH/NAD^+ ratio low (oxidized form dominant) so that NAD^+ is always available to accept electrons during catabolism.

Where NADPH is produced: The pentose phosphate pathway (glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase) is the primary source. Also malic enzyme and isocitrate dehydrogenase (the cytoplasmic isoform).

The one-phosphate rule for this guide: NAD^+ = catabolism = oxidation of substrates = feeds electrons to ETC. $NADP^+$ = anabolism = reduction of substrates = provides electrons for biosynthesis. Same chemistry, different metabolic destination, distinguished by one phosphate.

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9. FAD / $FADH_2$ (Flavin Adenine Dinucleotide)

What it carries: Electrons and protons — but unlike NAD^+, FAD can carry them **one at a time or two at a time.**

The business end: The **isoalloxazine ring system** — a tricyclic (three fused rings) structure derived from riboflavin (vitamin B2). The N1 and N5 positions of this ring system are where the electrons and protons are accepted.

What makes FAD fundamentally different from NAD^+:

NAD^+ can only do **two-electron chemistry** (it accepts a hydride, H^-, period). FAD can do:

- **Two-electron, two-proton reduction:** FAD + 2H → $FADH_2$. Both hydrogens add to the ring. This is the standard pathway.
- **One-electron reduction:** FAD + $1e^-$ + $1H^+$ → FADH• (a semiquinone radical). The dot (•) means an unpaired electron — a radical. This is a stable radical, which is unusual and important. It means FAD can participate in reactions where electrons are transferred one at a time, acting as a stepping stone between two-electron donors and one-electron acceptors (or vice versa).

This one-electron capability is why FAD is used in the electron transport chain (Complex II) and in reactions involving molecular oxygen (which itself is a diradical and prefers to accept electrons one at a time).

Another key difference — FAD is often permanently bound:

NAD^+ is a freely diffusing cosubstrate. It binds, gets reduced to NADH, dissociates, and carries its electrons elsewhere. FAD, in contrast, is usually a **prosthetic group** — it is permanently attached to its enzyme (covalently or very tightly bound) and does not leave. This means FAD must be re-oxidized in place. The enzyme that reduces FAD must also have a mechanism to re-oxidize it, typically by passing the electrons to another acceptor (like ubiquinone/CoQ in the ETC, or directly to O_2 in oxidases).

The mechanism of FAD reduction (two-electron path):

1. The substrate has a bond that will be oxidized — commonly a C–C single bond being converted to a C=C double bond (as in succinate → fumarate), or a C–N or C–O bond oxidation.
2. Two hydrogens are removed from the substrate: one from each carbon of the bond being oxidized. These are transferred to FAD at the N5 and N1 positions (or C4a) of the isoalloxazine ring.
3. FAD is reduced to $FADH_2$. The substrate is oxidized (it now has a double bond where the single bond was).

Why FAD for C–C → C=C oxidations instead of NAD^+?

Thermodynamics. The free energy change for oxidizing a C–C single bond to a C=C double bond is not large enough to reduce NAD^+ (NAD^+ has a more negative reduction potential, meaning it requires a stronger electron donor). FAD has a less negative reduction potential, meaning it accepts electrons from weaker donors. So FAD is matched to reactions with smaller energy drops, while NAD^+ is matched to reactions with larger energy drops (like alcohol → aldehyde or aldehyde → acid).

Quick reasoning rule: if the reaction is **removing two hydrogens from adjacent carbons to form a double bond**, the carrier is FAD. If the reaction is **oxidizing an alcohol to a carbonyl or a carbonyl to a carboxylate**, the carrier is NAD^+.

Where you see it: Succinate dehydrogenase (Complex II — succinate → fumarate, FAD → $FADH_2$), pyruvate dehydrogenase complex (E3 — dihydrolipoamide dehydrogenase reoxidizes lipoamide using FAD), acyl-CoA dehydrogenase (first step of fatty acid β-oxidation), monoamine oxidase.

Part 3: Quick-Reference Summary Table

Carrier	What it carries	Business end	Bond type	Key pathway(s)
TPP	2C fragment (activated aldehyde)	Thiazolium C2 carbanion	C–C bond to ring	PDH (E1), α-KG DH, transketolase
Lipoamide	Acyl group + electrons	Disulfide ring (S–S)	Thioester (S–C=O)	PDH (E2), α-KG DH
Biotin	Activated CO_2	Ureido ring nitrogen	N–COO^-	Pyruvate carboxylase, ACC
CoA	Acyl groups	Terminal –SH	Thioester (S–C=O)	PDH product, TCA, FA synthesis/oxidation
ATP	Phosphoryl groups	Phosphate chain (γ, β, α)	Phosphoanhydride (P–O–P)	Kinases, synthetases, pumps
UDP	Activated sugars	Anomeric C1–O–UDP bond	Phosphoester	Glycogen synthase, glucuronidation
NAD^+	Hydride ($H^- = 2e^- + 1H^+$)	Nicotinamide ring C4	—	Catabolic oxidations → ETC
$NADP^+$	Hydride ($H^- = 2e^- + 1H^+$)	Nicotinamide ring C4	—	Anabolic reductions (FA synthesis, PPP)
FAD	$2e^- + 2H^+$ (or $1e^-$ at a time)	Isoalloxazine ring N1/N5	—	C–C → C=C oxidations, ETC Complex II

Part 4: Pattern Recognition Key

recognition clue	Carrier
α-keto acid decarboxylation	TPP
"electron sink"	TPP (thiazolium ring stabilizes carbanion)
Swinging arm / lipoyl arm on E2	Lipoamide
Disulfide ↔ dithiol interconversion	Lipoamide
ATP-dependent carboxylation	Biotin
"activated CO_2"	Biotin
Thioester bond / acyl group transfer	CoA
Acetyl group entering TCA cycle	Acetyl-CoA
Phosphorylation of a substrate	ATP (γ-phosphate)
Reaction releases PP_i (pyrophosphate)	ATP (cleaved to AMP + PP_i)
Sugar activation for glycosidic bond formation	UDP-sugar

recognition clue	Carrier
Glycogen synthesis	UDP-glucose
Alcohol → carbonyl oxidation	NAD^+
Aldehyde → acid oxidation	NAD^+
Catabolic oxidation producing electrons for ETC	NAD^+ → NADH
Reductive biosynthesis (FA, cholesterol, nucleotides)	NADPH
Pentose phosphate pathway product	NADPH
C–C single bond → C=C double bond	FAD
One-electron chemistry / radical intermediate	FAD (semiquinone)
Prosthetic group (permanently bound to enzyme)	FAD
Freely diffusing cosubstrate for redox	NAD^+ or $NADP^+$