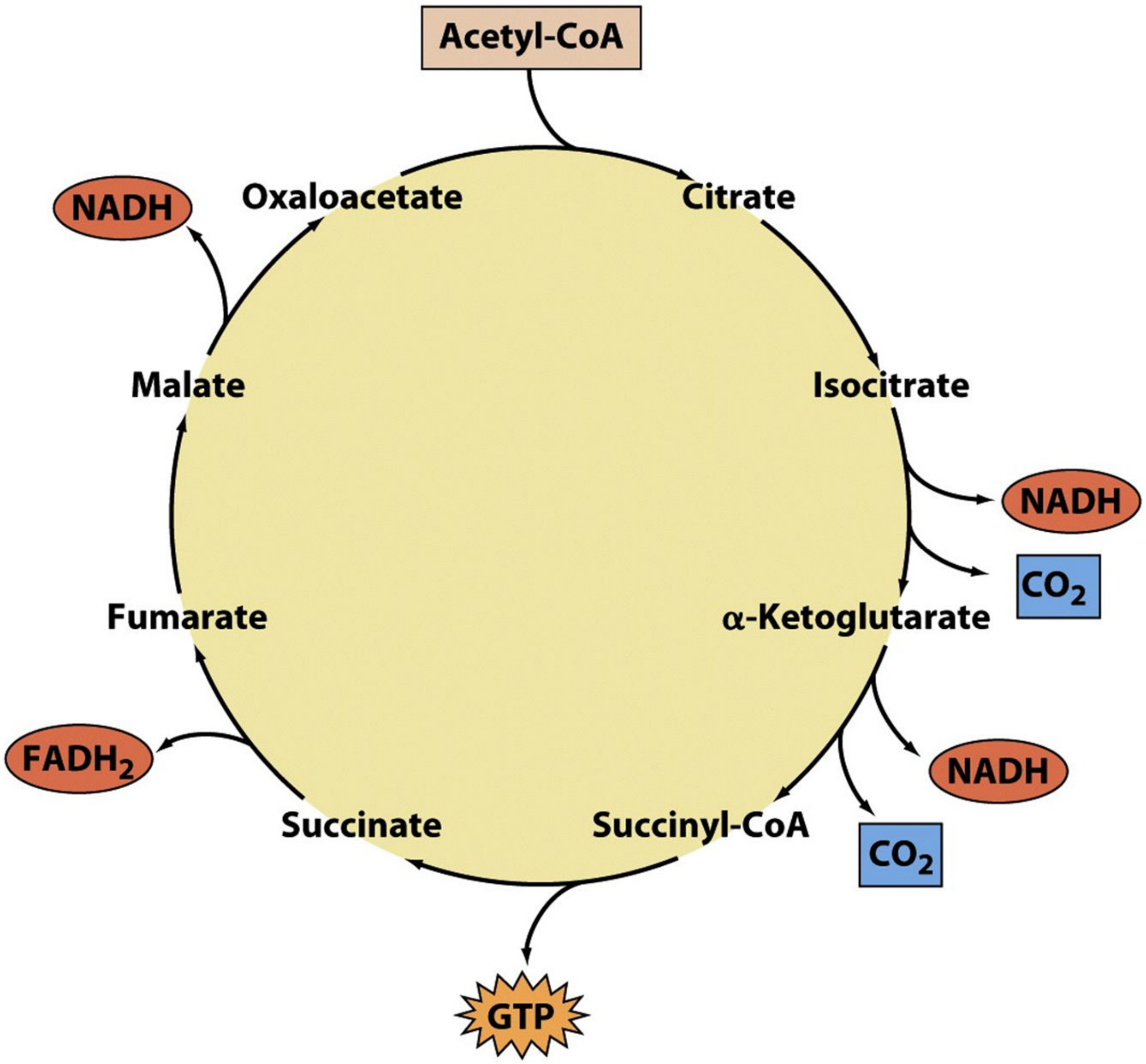
The oxidation of acetyl-CoA to CO_2 in the TCA cycle generates reduced cofactors



Reduced redox cofactors produced in glucose oxidation are used to make ATP

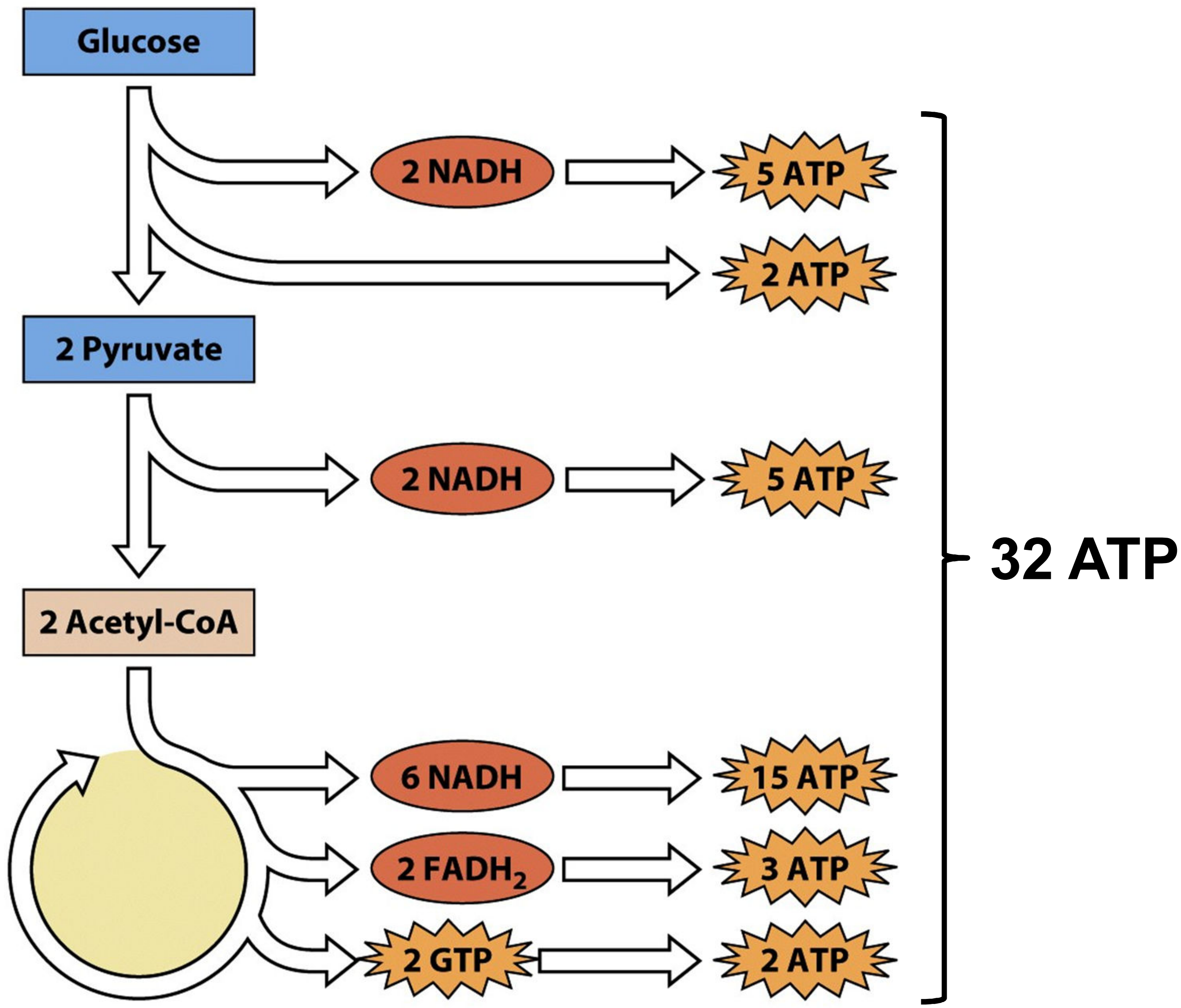


TABLE 16–1 **Stoichiometry of Coenzyme Reduction and ATP Formation in the Aerobic Oxidation of Glucose via Glycolysis, the Pyruvate Dehydrogenase Complex Reaction, the Citric Acid Cycle, and Oxidative Phosphorylation**

Reaction	Number of ATP or reduced coenzyme directly formed	Number of ATP ultimately formed*
Glucose ⟶ glucose 6-phosphate	−1 ATP	−1
Fructose 6-phosphate ⟶ fructose 1,6-bisphosphate	−1 ATP	−1
2 Glyceraldehyde 3-phosphate ⟶ 2 1,3-bisphosphoglycerate	2 NADH	3 or 5†
2 1,3-Bisphosphoglycerate ⟶ 2 3-phosphoglycerate	2 ATP	2
2 Phosphoenolpyruvate ⟶ 2 pyruvate	2 ATP	2
2 Pyruvate ⟶ 2 acetyl-CoA	2 NADH	5
2 Isocitrate ⟶ 2 α-ketoglutarate	2 NADH	5
2 α-Ketoglutarate ⟶ 2 succinyl-CoA	2 NADH	5
2 Succinyl-CoA ⟶ 2 succinate	2 ATP (or 2 GTP)	2
2 Succinate ⟶ 2 fumarate	2 $FADH_2$	3
2 Malate ⟶ 2 oxaloacetate	2 NADH	5
Total		30–32

*This is calculated as 2.5 ATP per NADH and 1.5 ATP per $FADH_2$. A negative value indicates consumption.

†This number is either 3 or 5, depending on the mechanism used to shuttle NADH equivalents from the cytosol to the mitochondrial matrix; see Figures 19–30 and 19–31.

How are reduced redox currencies (NADH, $FADH_2$) used to make ATP?

- Electrons spontaneously move from compounds of lower reduction potential to higher reduction potential
  - Reduction potential is a measure of electron affinity
  - Electron transfers are exergonic, releasing free energy
- The exergonic transfer of electrons can be coupled to endergonic processes to make them favorable
  - The transfer of electrons from NADH (or $FADH_2$) to O_2 is highly exergonic
  - ATP synthesis from ADP and P_i is endergonic
  - Electron transfers are coupled to ATP synthesis through the creation of an electrochemical proton gradient

Electron transfers drive H^+ gradient formation; gradient potential drives ATP synthesis

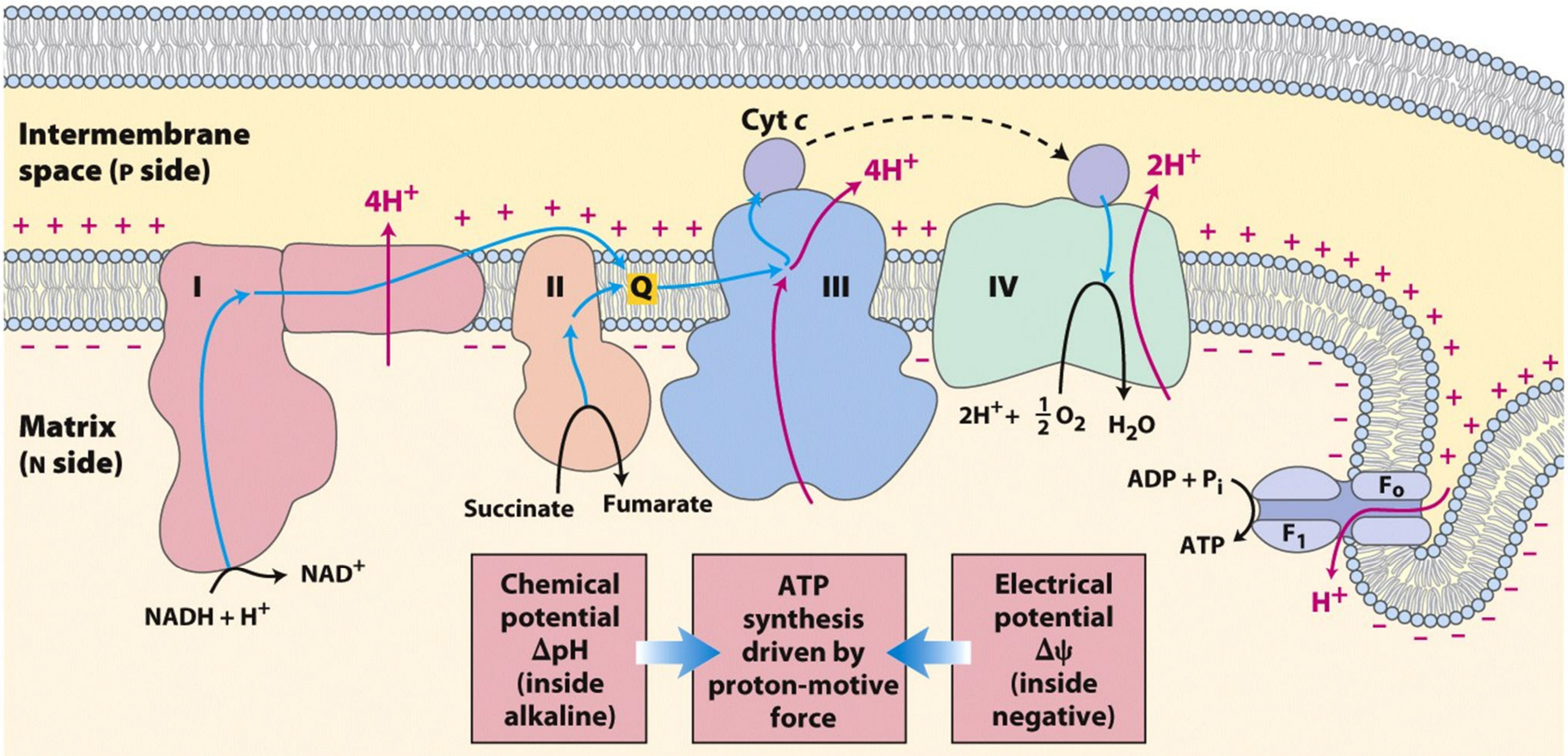
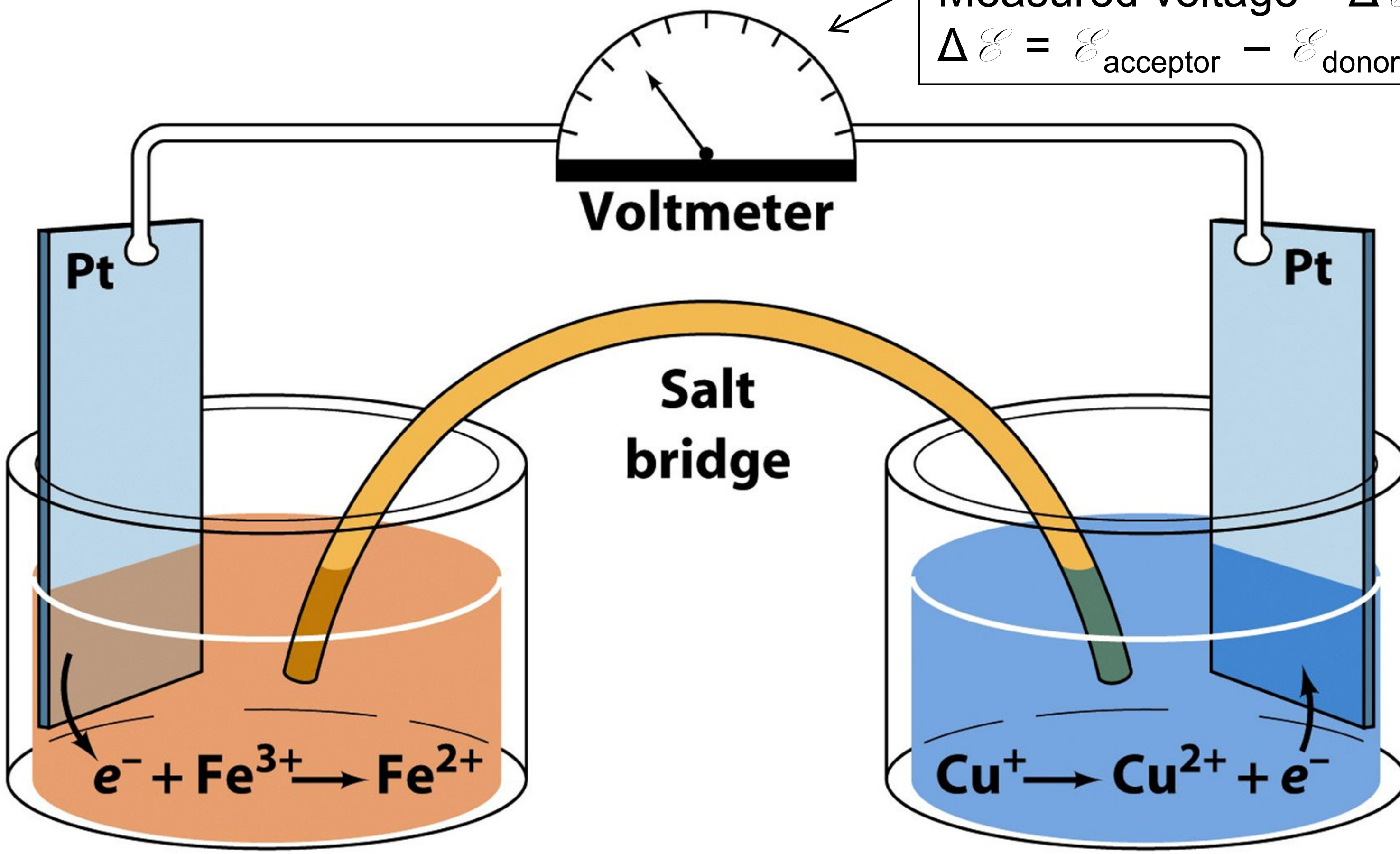


Figure 19-19
Lehninger Principles of Biochemistry, Fifth Edition

Reduction potentials are measured using an electrochemical cell

Measured voltage = $\Delta\mathscr{E}$
$\Delta\mathscr{E} = \mathscr{E}_{acceptor} - \mathscr{E}_{donor}$



Under standard conditions, measurement against the standard hydrogen half cell ($1M\ H^+$, $1ATM\ H_2$) gives standard $\mathscr{E}$ ($\mathscr{E}^\circ \equiv 0$ for $H^+ + e^- \rightarrow \frac{1}{2} H_2$)

Table 14-5 Standard Reduction Potentials of Some Biochemically Important Half-Reactions

Half-Reaction	$\mathscr{E}^{\circ\prime}$ (V)
$\frac{1}{2}O_2 + 2H^+ + 2e^- \rightleftharpoons H_2O$	0.815
$NO_3^- + 2H^+ + 2e^- \rightleftharpoons NO_2^- + H_2O$	0.42
Cytochrome a_3 (Fe^{3+}) + e^- $\rightleftharpoons$ cytochrome a_3 (Fe^{2+})	0.385
$O_2(g) + 2H^+ + 2e^- \rightleftharpoons H_2O_2$	0.295
Cytochrome *a* (Fe^{3+}) + e^- $\rightleftharpoons$ cytochrome *a* (Fe^{2+})	0.29
Cytochrome *c* (Fe^{3+}) + e^- $\rightleftharpoons$ cytochrome *c* (Fe^{2+})	0.235
Cytochrome c_1 (Fe^{3+}) + e^- $\rightleftharpoons$ cytochrome c_1 (Fe^{2+})	0.22
Cytochrome *b* (Fe^{3+}) + e^- $\rightleftharpoons$ cytochrome *b* (Fe^{2+}) (*mitochondrial*)	0.077
Ubiquinone + $2H^+ + 2e^-$ $\rightleftharpoons$ ubiquinol	0.045
Fumarate$^-$ + $2H^+ + 2e^-$ $\rightleftharpoons$ succinate$^-$	0.031
FAD + $2H^+ + 2e^-$ $\rightleftharpoons$ $FADH_2$ (*in flavoproteins*)	~0.
Oxaloacetate$^-$ + $2H^+ + 2e^-$ $\rightleftharpoons$ malate$^-$	−0.166
Pyruvate$^-$ + $2H^+ + 2e^-$ $\rightleftharpoons$ lactate$^-$	−0.185
Acetaldehyde + $2H^+ + 2e^-$ $\rightleftharpoons$ ethanol	−0.197
FAD + $2H^+ + 2e^-$ $\rightleftharpoons$ $FADH_2$ (*free coenzyme*)	−0.219
$S + 2H^+ + 2e^- \rightleftharpoons H_2S$	−0.23
Lipoic acid + $2H^+ + 2e^-$ $\rightleftharpoons$ dihydrolipoic acid	−0.29
$NAD^+ + H^+ + 2e^-$ $\rightleftharpoons$ NADH	−0.315
$NADP^+ + H^+ + 2e^-$ $\rightleftharpoons$ NADPH	−0.320
Cysteine disulfide + $2H^+ + 2e^-$ $\rightleftharpoons$ 2 cysteine	−0.340
Acetoacetate$^-$ + $2H^+ + 2e^-$ $\rightleftharpoons$ β-hydroxybutyrate$^-$	−0.346
$H^+ + e^- \rightleftharpoons \frac{1}{2}H_2$	−0.421
$SO_4^{2-} + 2H^+ + 2e^- \rightleftharpoons SO_3^{2-} + H_2O$	−0.515
Acetate$^-$ + $3H^+ + 2e^-$ $\rightleftharpoons$ acetaldehyde + H_2O	−0.581

Source: Mostly from Loach, P.A., *In* Fasman, G.D. (Ed.), *Handbook of Biochemistry and Molecular Biology* (3rd ed.), Physical and Chemical Data, Vol. I, pp. 123–130, CRC Press (1976).