Medical Biochemistry

Curated preclinical study track (not a medical degree, no licensure claim). Original explanations and practice only, following the reviewed course handout.

Filling the cell with chemistry

- Proteins and enzymes first, then energy (**glycolysis**, oxidative engine), then storage and traffic (**glycogen**, lipids, nitrogen), then the whole ledger.
- Every ATP count, enzyme constant and fuel flow is recomputed - and every clinical link names the broken step.

Structure levels and the sigmoid

1. **Levels** Primary sequence $\rightarrow$ secondary helix/sheet $\rightarrow$ tertiary fold $\rightarrow$ quaternary assembly; Hb is the reference tetramer: $\alpha_2\beta_2$, 64.5 kDa, 4 O_2.
2. **Cooperativity** Each O_2 shifts T$\rightarrow$R so binding helps binding (Hill n $\approx$ 2.8): full load in lungs, ~25% unloaded at rest and over 60% in working muscle.
3. **Capacity** 15 g Hb/dL $\div$ 64 500 g/mol $\times$ 4 sites $\approx$ 930 µmol O_2/dL $\approx$ 20.8 mL/dL in theory; measured 20.1 (1.34 mL/g).

Saturation and the constants

1. **Equation** $v = V_{max} \cdot [S]/(K_m+[S])$; K_m is $[S]$ at half-V_{max} - low K_m means high apparent affinity.
2. **Data** $v = 33$ at $[S]=1$, $v = 60$ at $[S]=4$: $33(K+1) = 15(K+4) \Rightarrow K_m = 1.5$ mM, $V_{max} = 82.5$ µmol/min ✓.
3. **Straight line** Lineweaver-Burk: y-intercept $1/V_{max}$, x-intercept $-1/K_m$ - the diagnostic transform.

Bioenergetics and glycolysis: split a sugar, bank ATP

1. **Ledger** Glucose $\rightarrow$ 2 pyruvate: invest 2 ATP, get 4 back + 2 NADH - net 2 ATP + 2 NADH, oxygen-free.
2. **Gates** Hexokinase -16.7, **PFK-1** -14.2 (committed), pyruvate kinase -31.4 kJ/mol - only these are irreversible.
3. **Control** PFK-1 reads the cell: AMP/ADP on, ATP/citrate off, fructose-2,6-bP strongly on.

TCA and oxidative phosphorylation: electrons down

1. **Cycle** Per acetyl-CoA: 3 NADH + 1 $FADH_2$ + 1 GTP; two turns per glucose.
2. **Pumps** I+III+IV pump 10 H^+ per NADH, 6 per $FADH_2$; **ATP synthase** charges ~4 H^+ per ATP $\Rightarrow$ 2.5 and 1.5.
3. **Total** Per glucose with EVERY carrier: 2 + 5 + 5(PDH) + 2 GTP + 15 + 3 = 32 ATP (malate shuttle) or 30 (glycerol-P).

Two banks, one polymer

1. **Banks** Liver ~100 g exports glucose (has the phosphatase); muscle ~400 g keeps it (lacks the enzyme).
2. **Switch Insulin**: both store. **Glucagon**: liver only breaks down - muscle has no receptor.
3. **Cost Gluconeogenesis**: 4 ATP + 2 GTP + 2 NADH per glucose (6 high-energy bonds) - storage in reverse costs.

Lipid metabolism: the freight map of fat

1. **Oxidation** Palmitate C16: 7 cycles $\rightarrow$ 8 acetyl-CoA + 7 $FADH_2$ + 7 NADH = 80 + 10.5 + 17.5 − 2 = 106 ATP ✓.
2. **Freight** Chylomicrons (gut), VLDL (liver), LDL (deliver), HDL (return) - the **lipoprotein** classes by route.
3. **Ketones** Fasting: acetyl-CoA diverted to **ketone bodies**; about a third of brain energy by day 3, up to two-thirds after weeks.

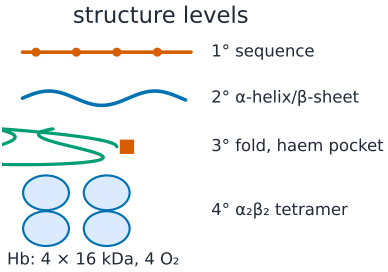
Nitrogen metabolism: two nitrogens, one ticket

1. **Funnel Transamination** moves amino groups onto α-ketoglutarate as **glutamate**; brain and muscle taxi N as **glutamine** and alanine.
2. **Cycle** Liver, 2 compartments, 5 enzymes: $NH_3 + CO_2 \rightarrow$ carbamoyl-P $\rightarrow$ citrulline $\rightarrow$ arginine $\rightarrow$ urea + ornithine back.
3. **Cost** 3 ATP (4 high-energy bonds) per urea, exporting 2 N; ~30 g urea/day $\approx$ 14 g N ✓ matches the diet.

Integration of metabolism: one lever, four organs

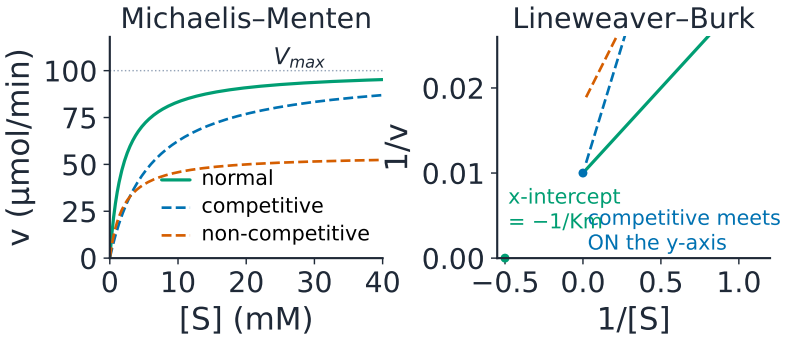
1. **Timeline** Hours 0-4 absorbed fuel; 4-12 liver **glycogen**; 12-24 **gluconeogenesis** ramps; day 3 brain about a third on ketones, weeks up to two-thirds.
2. **Switch Insulin** sets every organ to store; glucagon (liver-only) opens the banks - one signal, coherent arrows.
3. **Tape** HbA1c $\geq$ 6.5%: glycation integrates glucose over the ~120-day red-cell life - recorder, not snapshot.

From sequence to sigmoid



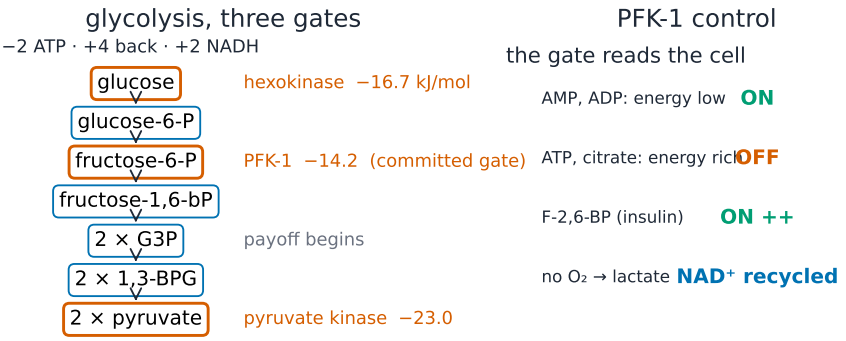
Hb: 4×16 kDa ≈ 64.5 kDa; **sigmoid** O_2 binding with Hill n ≈ 2.8 - myoglobin hyperbolic, **haemoglobin** cooperative.

Which line moved



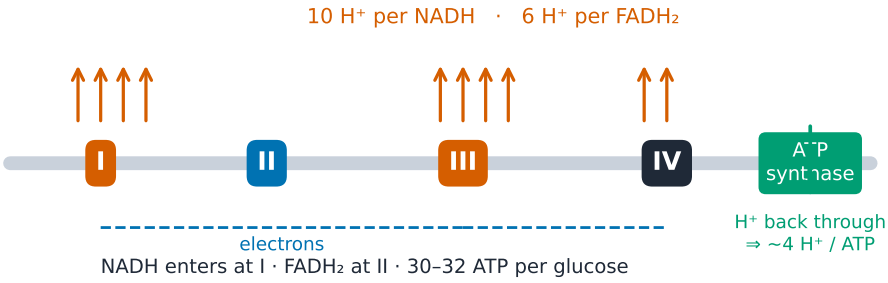
Competitive: Km up, Vmax same (lines meet on the y-axis). Non-competitive: Vmax down, Km same (x-axis).

The glycolysis gates



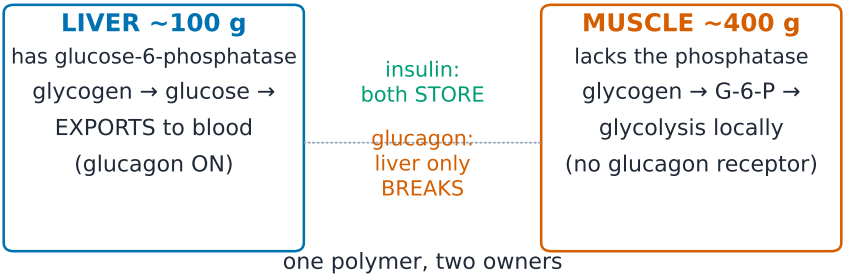
Invest −2 ATP, pay back +4 ATP + 2 NADH; **PFK-1** is the gate that reads AMP, ATP and fructose-2,6-bP.

The electron transport chain and ATP synthase



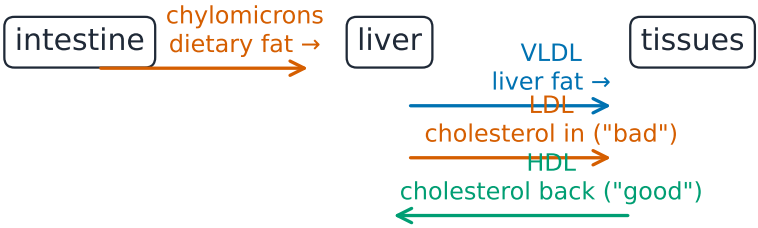
Electrons fall to O_2 through I, III, IV pumping 10 H^+ per NADH; the return flow spins **ATP synthase** at ~4 H^+/ATP.

Liver feeds, muscle keeps



Liver has glucose-6-phosphatase and exports; muscle traps G-6-P for itself - **insulin** stores both, **glucagon** opens only the liver.

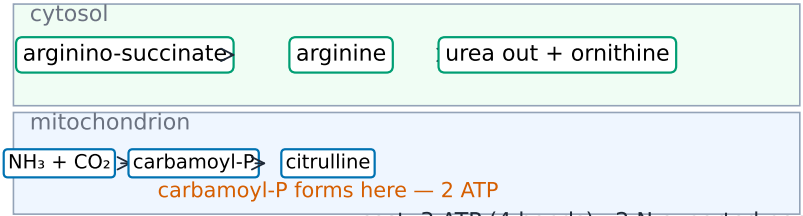
Lipoproteins: deliver and return



tissues take fat and cholesterol; only HDL brings it home

> Chylomicrons and VLDL deliver fat; LDL drops cholesterol off; HDL brings it home - the freight map.

The urea cycle across two compartments



cost: 3 ATP (4 bonds) · 2 N exported per urea
(ornithine returns — the cycle repeats)

Mitochondrial carbamoyl-P and citrulline, cytosolic arginine: five enzymes, 3 ATP, 2 N exported per urea.

Fed and fasting: the fuel-flow ledger

FED	insulin high — store
liver	glycogen ↑, fat ↑
muscle	glucose in, glycogen ↑
fat	take up, store TAG
brain	glucose (120 g/day)

FASTING	glucagon high — release
liver	glycogen → glucose out, then gluconeogenesis
muscle	export amino acids
fat	lipolysis → fatty acids
brain	glucose, then ketones

Fed: store everywhere. Fasting: liver releases, muscle exports, fat liberates, brain adapts - the same map, two settings.

Check yourself

- **Glycolysis** net ATP per glucose? (2, plus 2 NADH.)
- NADH $\rightarrow$ ATP (modern count)? (2.5; $FADH_2$ 1.5.)
- Palmitate total? (106 ATP.)
- HbA1c diabetes threshold? ($\geq$ 6.5 %.)