

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 O₂.
- 2 Cooperativity** Each O₂ shifts T $\rightarrow$ R so binding helps binding (Hill $n \approx 2.8$): full load in lungs, ~35% unloaded in tissues.
- 3 Capacity** $15 \text{ g Hb/dL} \div 64\,500 \text{ g/mol} \times 4 \text{ sites} \approx 930 \text{ } \mu\text{mol O}_2/\text{dL} \approx 20.8 \text{ mL/dL}$ ✓ - the textbook number recomputed.

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 $[S]=4$: $33(K+1) = 15(K+4) \Rightarrow K_m = 1.5 \text{ mM}$, $V_{\max} = 82.5 \text{ } \mu\text{mol/min}$ ✓.
- 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 -23.0 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: $3 \text{ NADH} + 1 \text{ FADH}_2 + 1 \text{ GTP}$; two turns per glucose.
- 2 **Pumps** I+III+IV pump 10 H^+ per NADH, 6 per FADH_2 ; **ATP synthase** charges $\sim 4 \text{ H}^+$ per ATP $\Rightarrow 2.5$ and 1.5 .
- 3 **Total** Per glucose with EVERY carrier: $2 + 5 + 5(\text{PDH}) + 2 \text{ GTP} + 15 + 3 = 32 \text{ ATP}$ (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:** $4 \text{ ATP} + 2 \text{ GTP} + 2 \text{ NADH}$ 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 FADH₂ + 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**; by day 3 the brain draws ~2/3 from them.

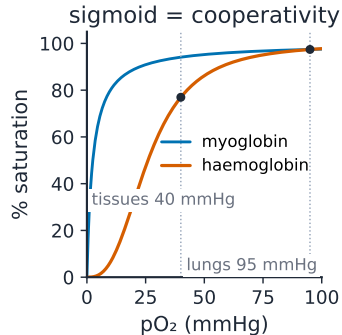
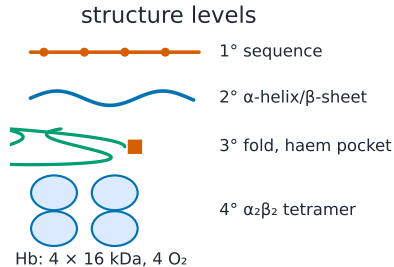
Nitrogen metabolism: two nitrogens, one ticket

- 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: $\text{NH}_3 + \text{CO}_2 \rightarrow \text{carbamoyl-P} \rightarrow \text{citrulline} \rightarrow \text{arginine} \rightarrow \text{urea} + \text{ornithine back}$.
- 3 **Cost** 3 ATP (4 high-energy bonds) per urea, exporting 2 N; $\sim 30 \text{ g urea/day} \approx 14 \text{ g N}$ ✓ matches the diet.

Integration of metabolism: one lever, four organs

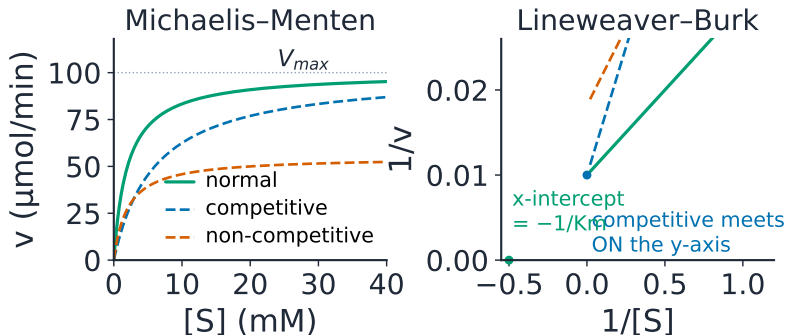
- 1 Timeline** Hours 0-4 absorbed fuel; 4-12 liver **glycogen**; 12-24 **gluconeogenesis** ramps; day 3+ brain on $\sim 2/3$ ketones.
- 2 Switch Insulin** sets every organ to store; glucagon (liver-only) opens the banks - one signal, coherent arrows.
- 3 Tape** $\text{HbA1c} \geq 6.5\%$: glycation integrates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

From sequence to sigmoid



Hb: 4 $\times$ 16 kDa $\approx$ 64.5 kDa; sigmoid O₂ binding with Hill $n \approx 2.8$ - myoglobin hyperbolic, **haemoglobin** cooperative.

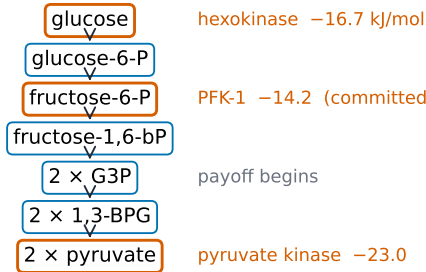
Which line moved



Competitive: K_m up, V_{max} same (lines meet on the y-axis). Non-competitive: V_{max} down, K_m same (x-axis).

The glycolysis gates

glycolysis, three gates
 $-2 \text{ ATP} \cdot +4 \text{ back} \cdot +2 \text{ NADH}$



PFK-1 control
 the gate reads the cell

AMP, ADP: energy low **ON**

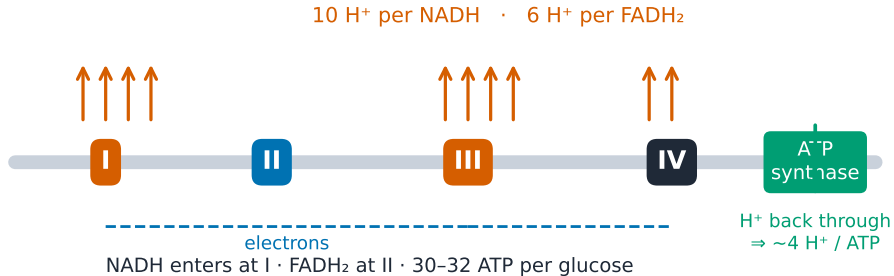
ATP, citrate: energy rich **OFF**

F-2,6-BP (insulin) **ON ++**

no $\text{O}_2 \rightarrow$ lactate **NAD^+ recycled**

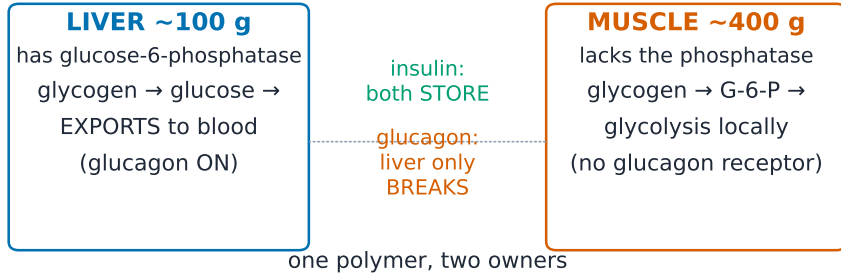
Invest -2 ATP , pay back $+4 \text{ ATP} + 2 \text{ NADH}$; **PFK-1** is the gate that reads AMP, ATP and fructose-2,6-bP.

The electron transport chain and ATP synthase



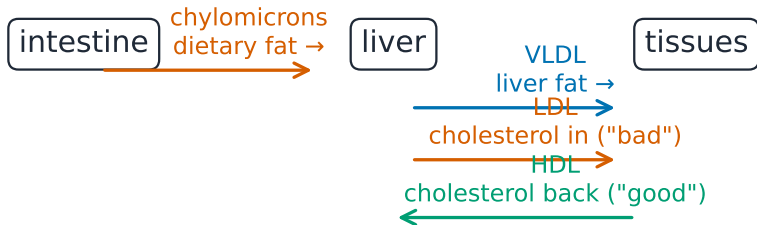
Electrons fall to O₂ through I, III, IV pumping 10 H⁺ per NADH; the return flow spins **ATP synthase** at ~4 H⁺/ATP.

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.

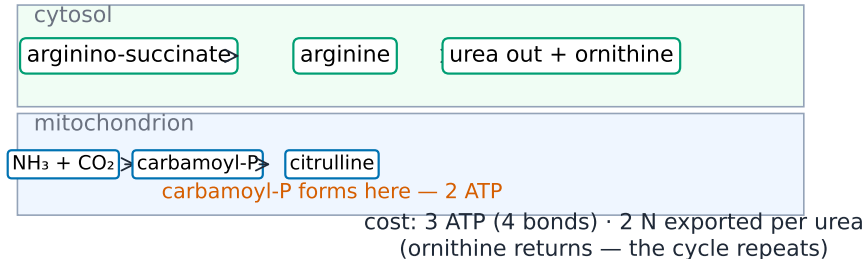
Lipoproteins: deliver and return



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



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; FADH₂ 1.5.)
- Palmitate total? (106 ATP.)
- HbA1c diabetes threshold? ($\geq$ 6.5 %.)