HOW DOES BODY TRANSPORT OXYGEN?

	K_D	# SITES	$\sim \Delta\theta$
MYOGLOBIN	2.6	1	-0.1
HYPOTHETICAL	44	1	-0.4
HEMOGLOBIN	26	4	-0.75
HEMOGLOBIN + BPG	>26	4	-0.95

$$\Delta\theta = \theta_2 - \theta_1$$

$$\Delta\theta = \frac{1}{1+K_D/L_2} - \frac{1}{1+K_D/L_1}$$

$$= \frac{1}{1+K_D/20} - \frac{1}{1+K_D/100}$$

SHOW HEME (Fe(II) IS ↔ ; INDUCED DIPOLE)
SHOW GOODSELL
START WITH STRUCTURE OF Mb ← THINGS TO NOTE:
  (PYMOL SCENE ∅)

  - α HELICAL STRUCTURE   1840s, SCHMIREL
  - HEME BINDS O_2 CHEM.
  - FIRST STRUCTURE SPERM WHALE   CRYSTAL

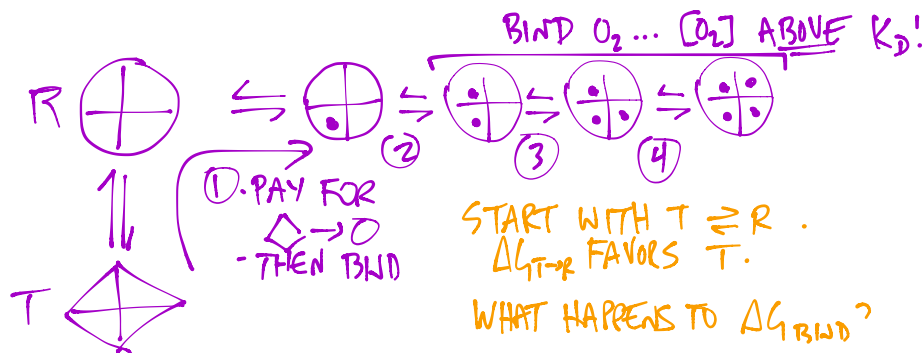$$\Delta\theta \sim 10\%$$

OKAY. LETS LOWER AFFINITY A BIT.

BEST K_D = 45 TORR
$\Delta\theta$ = 0.38

HOW CAN WE IMPROVE $\Delta\theta$?   MAKE CURVE STEEPER.

HOW DO YOU DO THIS?
  ⇒ MULTIPLE BINDING SITES
  ⇒ COUPLE THEM TOGETHER

BIND O_2 ... $[O_2]$ ABOVE K_D!

①. PAY FOR
  ◇ → ○
- THEN BIND

START WITH T ⇌ R.
$\Delta G_{T \to R}$ FAVORS T.
WHAT HAPPENS TO ΔG_{BIND}?

SHOW ORAGAMI.

ΔG_{BIND}

$$\Delta G_{LOAD}^{(1)} = \Delta G_{T \to R} + \boxed{\Delta G^{0'} + RT \ln \left(\frac{[Hb \cdot O_2]}{[Hb][O_2]} \right)} \leftarrow \text{AS } [O_2] \uparrow, \text{ GETS MORE \underline{NEGATIVE}.}$$
$$\hspace{3cm} \text{(POSITIVE)} \hspace{2cm} \underbrace{\hspace{5cm}}_{\text{DEPENDS.}}$$

EVENTUALLY ΔG_{BIND} WILL BE MORE NEGATIVE THAN ΔG_{TR} AND SYSTEM WILL LOAD.

$$\Delta G_{LOAD}^{(2)} = \cancel{\Delta G_{T \to R}} + \Delta G^{0'} + RT \ln \left(\frac{[Hb \cdot O_2]}{[Hb][O_2]} \right) \leftarrow \text{LOADS IMMEDIATELY!}$$
$$\hspace{2cm} \underline{\text{PREPAID}}$$

MONOMER

$\Delta \theta \sim 75\%$ DUMPED.
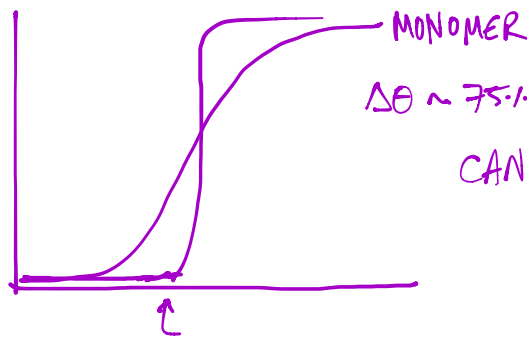
CAN BE DESCRIBED W/ HILL EQN:

$$\theta_{HILL} = \frac{L^n}{L^n + (K_D)^n} \xleftarrow{} \text{STEEPNESS (OFTEN \#SITES)}$$
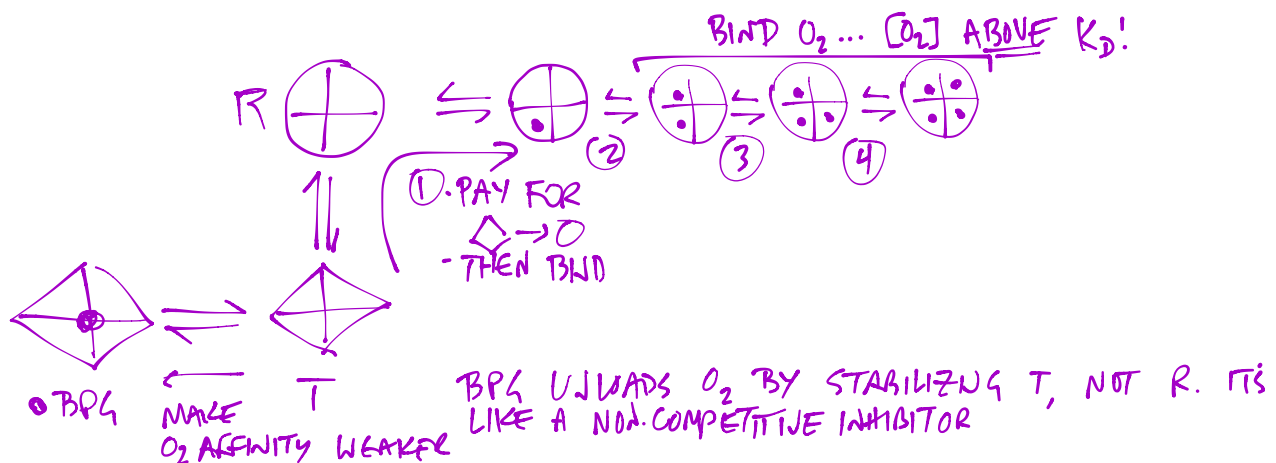
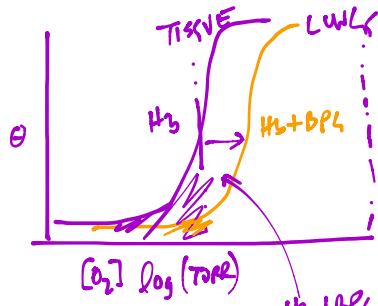MOST IMPORTANT FACT ABOUT Hb VS Mb BINDING CURVE?
  - STEEPER. BETTER LOADING AND UNLOADING

WHY DOES CURVE GET STEEPER?
  - HARDER TO LOAD INITIALLY (TAKES HIGHER $[O_2]$ TO BIND BECAUSE HAS TO PAY FOR $T \to R$ TRANSITION), BUT AFTER THIS IS PAID Hb IS ABOVE K_D AND COMPLETELY LOADS.

HOW DOES BPG BINDING ALTER O_2 LOADING AND UNLOADING?
  - BPG BINDS TO T, STABILIZING IT AND CAUSING O_2 AFFINITY TO GO DOWN.

BIND O_2 ... $[O_2]$ ABOVE K_D!

R

① PAY FOR
◇ → ○
- THEN BND

② ③ ④

BPG

MAKE O_2 AFFINITY WEAKER

T

BPG UNLOADS O_2 BY STABILIZING T, NOT R. ITS LIKE A NON-COMPETITIVE INHIBITOR

Hb + BPG unloads better because T state stabilized. Less O_2 affinity