Oxygen Concentration of Blood: PO_2, Co-Oximetry, and More

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Objectives

- Define "O_2 Content", listing its 3 major variables
- Define the limitations of pulse oximetry
- Explain why a normal arterial PO_2 at sea level on room air is ~100 mmHg (13.3 kPa)
- Describe the major features of methemogobin and carboxyhemglobin

O_2 Concentration of Blood

- not simply PaO_2
  - Arterial O_2 Partial Pressure ~100 mm Hg (~13.3 kPa)
- not simply Hct (~40%)
  - or, more precisely, Hgb (14 g/dL, 140 g/L)
- not simply "O_2 saturation"
  - i.e., ~89%

O_2 Concentration of Blood

- rather, a combination of all three parameters
- a value labs do not report
- a value few medical people even know!

O_2 Content

(mm Hg) (g/dL)

$$= 0.003 * PaO_2 + 1.4 * [Hgb] * [\%O_2Sat]$$

$$= 0.0225 * PaO_2 + 1.4 * [Hgb] * [\%O_2Sat]$$

(kPa) (g/dL)

- normal value: about 20 mL/dL

Why Is the "Normal" P_aO_2 90-100 mmHg?

- $PAO_2 = (FiO_2 \times [Patm - PH_2O]) - (PaCO_2 / R)$
  - PAO_2 is alveolar O_2 pressure
  - FiO_2 is fraction of inspired oxygen (room air ~0.20)
  - Patm is atmospheric pressure (~760 mmHg at sea level)
  - PH_2O is vapor pressure of water (47 mmHg at 37 ^oC)
  - $PaCO_2$ is partial pressure of CO_2
  - R is the respiratory quotient (typically ~0.8)
  - ➔ 0.21 x (760-47) - (40/0.8)
  - ~100 mm Hg

- Alveolar–arterial (A-a) O_2 gradient is normally ~ 10,
  so PaO2 (arterial PO2) should be ~90 mmHg

NB: To convert mm Hg to kPa, multiply by 0.133

Insights from PAO_2 Equation (1)

- $PaO_2 \sim PAO_2 = (0.21x[Patm-47]) - (PaCO_2 / 0.8)$
  - At lower Patm, the PaO_2 will be lower
    - ➔ that's why airplane cabins are pressurized
  - At higher Patm, the PaO_2 will be higher
    - ➔ we'll exploit this later
  - Also:
    - "normal" PaO_2 in Boston is higher than in Denver
    - your PaO_2 is lower during a storm than on a sunny day

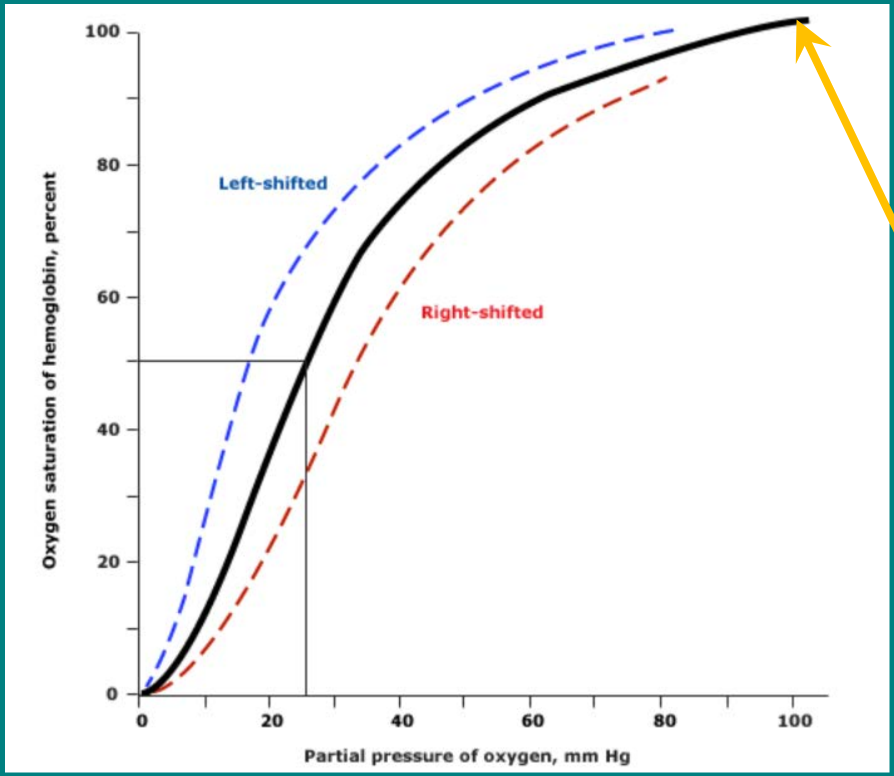
NB: To convert mm Hg to kPa, multiply by 0.133

Insights from PAO_2 Equation (2)

- $PaO_2 \sim PAO_2 = (0.21x[Patm-47]) - (PaCO_2 / 0.8)$
  – On room air (FiO_2 = 0.21), at a given Patm,
    - As $PaCO_2$ decreases, PaO_2 increases
      – Patients who hyperventilate should have higher PO_2s
      – Don’t be surprised if a patient with a PCO_2 of 20 has a PO_2 of 120 – it’s expected!
    - As $PaCO_2$ increases, PaO_2 decreases
      – Patients with lung disease will have not only increased $PaCO_2$ but lower PaO_2
      – Don’t be surprised if a patient with a $PaCO_2$ of 60 has a PaO_2 of 150-80-10 = 70

NB: To convert mm Hg to kPa, multiply by 0.133

Why is the "Normal" "O_2 Saturation" ~95%?



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- sigmoid curve
- hemoglobin can bind
  ~ 1.4 mL O_2/g
  when fully saturated
- at PO_2 = 100 mmHg,
  100% saturated
- so, at a normal Hgb of
  ~14 g/dL), it holds
  1.4x14 = 19.6 mL/dL

NB: To convert mm Hg to kPa, multiply by 0.133

A Quick Review

- Under typical conditions, for the reasons given, PaO2 is ~100 mm Hg (~13.3 kPa)
- Based on the oxyhemoglobin dissociation curve, that PaO_2 corresponds to 100% "O_2 saturation", and each gram of Hgb can hold 1.4 mL of O_2
- So, returning to our O_2 content equation, we've explained the right-hand term

$$= 0.003 * PaO_2 + 1.4 * [Hgb] * [\%O_2Sat]$$

So, What's the Other Term?

- Actually, it's quite simple: dissolved O_2
- And the equation for it is equally simple:

  - 0.003 x PO_2 (mm Hg) [0.0225 X PO2 (kPa)]
    i.e., directly proportional to the partial pressure of O_2

  - at typical PO2's, it is negligible:
    0.003 x 100 mm Hg = 0.3 mL/dL
    0.0225 x 13.3 kPa = 0.3 mL/dL
    (vs Hgb-bound O_2 of 19.6 ml/dL,
    which we just calculated)

O_2 Concentration of Blood

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O_2 Content

$$= 0.003 * PaO_2 + 1.4 * [Hgb] * [\%O_2Sat]$$

dissolved	Hgb-bound
0.3	19.6

~ 20 mL O_2/dL

Different Scenarios Illustrating Oxygen Content Concepts

comments	PaO2	%O2Sat	Hgb	Hct	Dissolved Oxygen	Hgb-Bound O2	O2 Content
Normal	100	100	14	42	0.3	19.6	19.9
Low Hct	100	100	7	21	0.3	9.8	10.1
Low PaO2 (lung disease)	25	50	14	42	0.1	9.8	9.9
50% Methemoglobin	100	50	14	42	0.3	9.8	10.1
Very Low Hct No Transfusion	100	100	2	6	0.3	2.8	3.1
Hyperbaric Chamber	2200	100	2	6	6.6	2.8	9.4

Causes of Low Oxygen Concentration

- anemia (low hemoglobin/hematocrit)
  - what most physicians focus on
  - probably the most frequent cause
- low PaO_2 → low “O_2 saturation”
  - e.g., lung disease
- low “O_2 saturation” despite normal PO_2
  - i.e., carboxyhemoglobin or methemoglobin

Hemoglobin Species

- Oxyhemoglobin
  - ***oxygenated***
- Reduced (Non-Oxygenated) Hemoglobin
  - ***capable of becoming oxygenated***
- Carboxyhemoglobin (carbon monoxide)
  - ***cannot be oxygenated***
- Methemoglobin (oxidized Fe moiety)
  - ***cannot be oxygenated***

- How do we measure/distinguish them?

Spectrophotometry

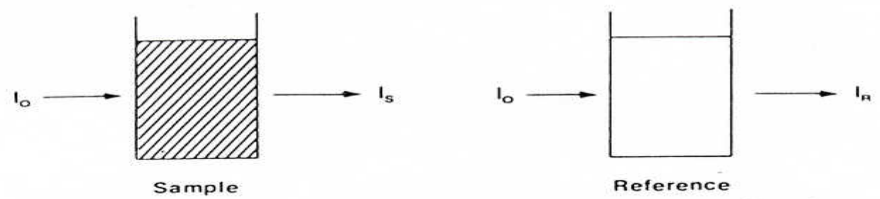


Figure 2-2. Transmittance of light through sample and reference cells. Transmittance of sample versus reference $= I_S/I_R$.

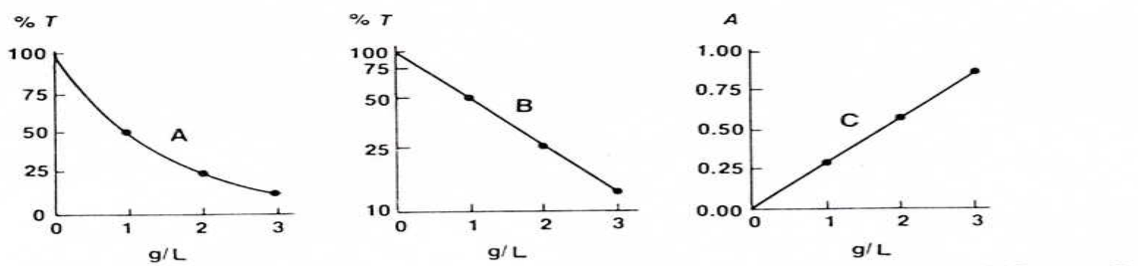


Figure 2-3. Transmittance and absorbance as a function of concentration. *A*. Per cent *T*, linear scale. *B*. Per cent *T*, logarithmic scale. *C*. Absorbance, linear scale.

$$A = -\log I_S/I_R = -\log T = \log \frac{1}{T} = \log \frac{100\%}{\text{per cent } T}$$
$$= \log 100 - \log \text{per cent } T = 2 - \log \text{per cent } T$$

Tietz NW (Ed). Fundamentals of Clinical Chemistry. 2nd Edition. 1976.

With One Measurand, Life is Simple

- $A = \varepsilon * b * C$ (or A=abc)
- Absorbance =
  (Molar Absorbtivity)*(Pathlength)*(Concentration)

- Two ways to calculate C from measured A
  - Know ε and b
    - co-oximeter
  - Run standard(s) to calculate $\varepsilon * b$
    - most assays

Absorbances Are Additive

- If two species (M and N) are present, and each has absorbances at two wavelengths, you can solve two simultaneous equations to determine their concentrations

b = known pathlength

- $A_{\lambda 1} = (\varepsilon_{M\lambda 1})(b)([M]) + (\varepsilon_{N\lambda 1})(b)([N])$
- $A_{\lambda 2} = (\varepsilon_{M\lambda 2})(b)([M]) + (\varepsilon_{N\lambda 2})(b)([N])$

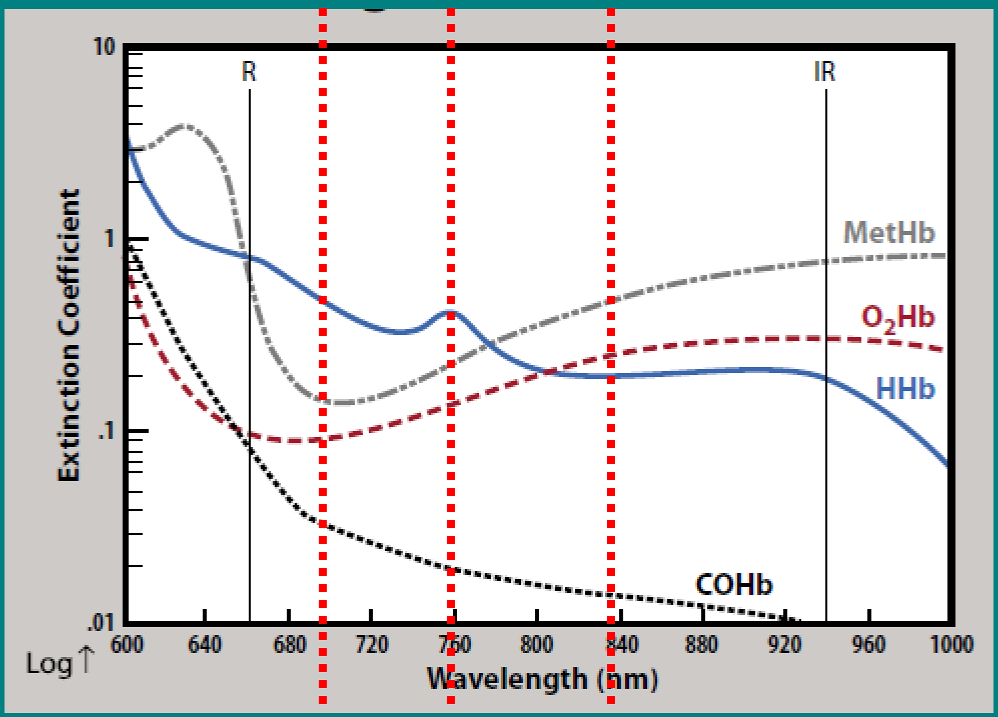
known molar absorbtivities

- $0.845 = 0.0265\ [M] + 0.0543\ [N]$
- $0.675 = 0.0453\ [M] + 0.0277\ [N]$

➔ $[M] = 7.9$, $[N] = 11.7$

Absorbances Are Additive: General Principle

- To measure n species,
  you need measurements at n wavelengths
- Pulse oximeters: 2 wavelengths → 2 species



Adapted from:
Haymond S. Oxygen saturation. Clinical Laboratory News. February, 2006.

- Co-Oximeters: >4 wavelengths → >4 species

Pulse Oximeters & Abnormal Hemoglobins

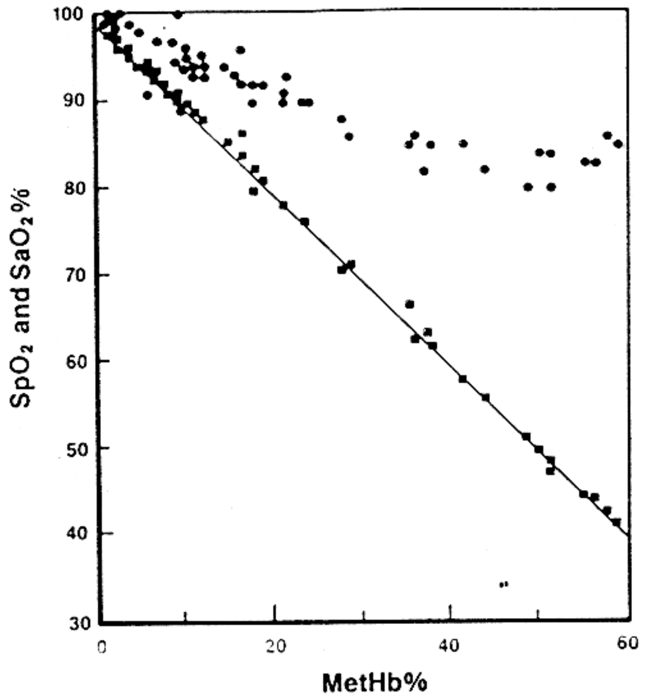


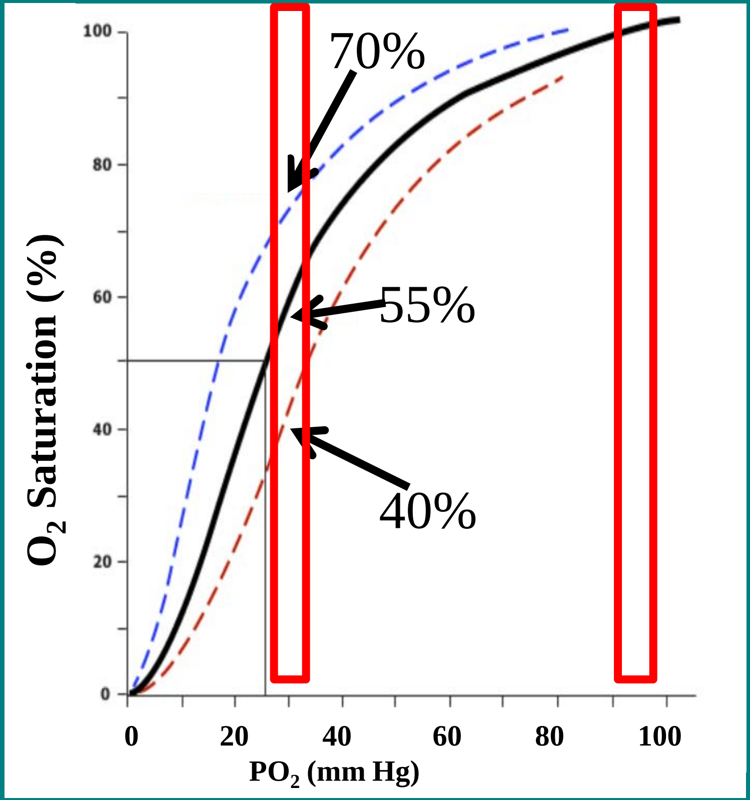
FIG. 1. Nellcor® Sp_{O_2} (●) and IL-282 Sa_{O_2} (■) *versus* MetHb% for FI_{O_2} = 1.0. Line shown is Sa_{O_2} = 100 − MetHb%.

Barker SJ et al. Anesthesiology 1989;70:112-117.

- "simplifying" assumption:
  only oxyhemoglobin
  and reduced hemoglobin
  are present
- works most of the time,
  but not all of the time
- tends to overestimate
  oxyhemoglobin,
  just what you don't want

Oxygen Delivered to Tissues

oxygen delivered = arterial O_2 content –venous O_2 content



Line	O2 saturation		O2 Content		O2
	Arterial	Venous	Arterial	Venous	Delivered
Black	95%	55%	18.9	11.1	7.8

P_{50} = PO_2 where O_2 saturation is 50%

Blue: 18 (left-shift)

Black : 25 (normal)

Red: 37 (right shift)

typical venous PO_2

typical arterial PO_2

Oxyhemoglobin Terminology

- Currently, there are 3 terms used for “oxygen saturation” (CLSI C-46, 2009)
  - hemoglobin oxygen saturation (SO_2)
  - fractional oxyhemoglobin (FO_2Hb)
  - estimated oxygen saturation (O_2Sat)

- in normal individuals, these values match closely
- but, in patients, they can be significantly different

- In general, physicians and other health care professionals
  - use the term O2sat (#3) to mean hemoglobin oxygen saturation (#1)
  - have never heard of the term fractional oxyhemoglobin (#2), though that is what co-oximeters “should” report

Oxyhemoglobin Terminology

- SO_2 is calculated as:
  - **oxyhemoglobin / (oxyhemoglobin + reduced hemoglobin)**
  - represents the percentage of hemoglobin *capable of being oxygenated* that is oxygenated
  - in other words, the denominator explicitly omits from consideration methemoglobin or carboxyhemoglobin

Oxyhemoglobin Terminology

- FO_2Hb
  - **oxyhemoglobin / (total hemoglobin)**
  - represents the percentage of ***all hemoglobin present*** that is oxygenated
  - when methemoglobin or carboxyhemoglobin is present, they are included in the denominator

Oxyhemoglobin Terminology

- O_2Sat
  - An estimate of what the oxyhemoglobin should be using the measured PO2 and the oxyhemoglobin dissociation curve, assuming that

    1) that the patient's blood sample is absolutely typical (pH, temperature, 2,3-DPG concentration, etc.), and

    2) that no methemoglobin or carboxyhemoglobin is present

  - This calculation, common on ABG analyzers, **should not be reported**

Example: Fireman Brought Into Emergency Room With Smoke Inhalation

- The facts:
  - PO_2 = 120 (hyperventilation)
  - hemoglobin fractions:
    oxy=80%, reduced=0%, carboxy=20%, met=0%
- The CLSI values:
  - SO_2 = 100% [80/(80+0)]
  - FO_2Hb = 80% [80/(80+0+20+0)]
  - O_2sat = 100% [at PO2= 100 mmHg, normal hemoglobin is 100% saturated]

- My practice (though it is technically incorrect), is to report the value as 80% and call it O_2Sat

- At a minimum, make sure your clinicians know how your lab is handling these values

Methemoglobin

- we all make methemoglobin continuously
- normal values are roughly 1%
- represents oxidation of heme Fe atom from ferrous (+2) to the ferric (+3) state
- normally, our bodies reduce methomoglobin back to hemoglobin
- with increased oxidative stress (e.g., drugs) or with defective enzymes, methemoglobin can increase to pathologic levels
- patients present with shortness of breath (low O_2 content) and cyanosis (blue color)
- arterial blood looks brown, despite high PO_2

Carboxyhemoglobin

- represents hemoglobin complexed with carbon monoxide (CO)
- causes:
  - fires (smoke inhalation)
  - using gas or charcoal grills indoors
  - smoking
  - air pollution (living in urban areas)
- every home should have a CO (as well as a smoke) detector!
- patients present with shortness of breath (low O2 content)
- in contrast to methemoglobin,
  - blood is “cherry red”
  - FO_2Hb (co-oximetry) is low despite high PO_2
  - pulse oximetry overestimates oxyhemoglobin

Self-Assessment Question 1

Which is the best indicator of oxygen concentration in blood?

A) PO_2

B) Hematocrit

C) O_2 content

D) O_2 saturation

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B) Hematocrit
C) O_2 content
D) O_2 saturation

Self-Assessment Question 2

Which of the following is true?

A) A normal alveolar PO_2 is higher in Denver than in Boston because the air is cleaner

B) A normal fractional oxyhemoglobin is higher in Denver than Boston because it has less air pollution

C) Typical pulse oximeters provide reliable measurements of “oxygen saturation” for use in patients with smoke inhalation

D) One must use arterial blood to get an accurate assessment of methemoglobin concentrations

Self-Assessment Question 3

What method principle is involved in measuring oxyhemoglobin percentages?

A) Gas chromatography
B) Ion selective electrodes
C) Beer's Law
D) O_2 electrode, followed by interpolation from oxyhemoglobin dissociation curve

Answers

1 (C) O_2 content

2 (B) A normal fractional oxyhemoglobin is higher in Denver than Boston because it has less air pollution

3 (C) Beer's Law