**Trachea (Generation #1)**

**Primary Bronchi (Generation #2)**

**Conducting Airways Generations 1-16**

**2nd Bronchi (Generation #3)**

**Respiratory Zone Generations ~17-23**

**Alveoli**

**O2**

**CO2**

**venous**

**arterial**

**PB=0**

**PA<0**

**Atmospheric Air**

- **High O2 (150 mmHg)**
- **CO2 ~ 0**

**Inspiration**

**O2**

**CO2**

**venous**

**arterial**

**PB=0**

**PA>0**

**Alveolar Air**

- **O2 ~100 mmHg**
- **CO2 ~ 40 mmHg**

**Expiration**

**Fick's law**

\[ J = DA \left( \frac{\Delta C}{\Delta X} \right) \]

**Lung**

**Chest Wall**

- **Stuck**
- **Together**

- **Air leak**
- **Pneumothorax**
- **Lung collapses**
- **& Chest expands**

**Hemoglobin-O2 Binding Curve**

- **Venous**
- **Arterial**

- **HbO2 content (ml O2 /dl)**

- **% Hb Saturation**

- **PaO2 (mm Hg)**

- **HbO2 content (ml O2 /dl)**
PO2 = 100 mm Hg
O2
P(O2) = 100 mm Hg
0.3 ml O2/dL
P(O2) = 100 mm Hg
14 ml O2/dL

VT
Total Lung Capacity
Expiratory Reserve
Inspiratory Reserve
FRC
Inspiratory Capacity
V_t
Exp
Res

Vital Capacity
4.5 L
500 ml
2.6 L
1.5 L
4.5 L
~6 L

Forced Vital Capacity

Flow-Volume Curves

V. A Few Terms (for Your Convenience)

Eupnea - Normal breathing.
Apnea - cessation of respiration (at FRC).
Apneic - cessation of respiration (in the inspiratory phase).
Apneic breathing - Apnea interrupted by periodic exhalation.
Hyperpnea - increased breathing (usual ↑VT).
Tachypnea - increased frequency of respiration.
Hyperventilation - increased alveolar ventilation (PACO2 <37 mm Hg).
Hyperventilation - decreased alveolar ventilation (PACO2 >43 mm Hg).
Atelectasis - closed-off alveoli, typically at end exhalation.
Cheyne-Stokes Respiration - Cycles of gradually increasing and decreasing VT.
Dyspnea - Feeling of difficulty in breathing.
Orthopnea - Discomfort in breathing unless standing or sitting upright.

PPl - Intrapleural pressure (pressure in space between visceral and parietal pleura).
Pl - Transpulmonary pressure (dissensory pressure of airway).
Paw - Alveolar pressure (pa) (partial pressure of CO2).
PaO2 - Arterial PO2.
PaCO2 - Arterial PCO2.
PaCO2 - venous PO2.
PvO2 - venous CO2.
PECO2 - PCO2 of exhaled air.

VE - Expired volume (liters)

VE = Alveolar ventilation (liters/min)
Q = Blood Flow (liters/min)
Some Typical Normal Values for Some Key Pulmonary Parameters

- FRC: 2.6 L
- RV: 1.5 L
- TlC: 6.0 L
- FVC: 4.5 L
- VT: 500 ml
- FEV1.0 / FVC >75%
- Frequency: 10-12/min
- V_a (norm) ± 0.5 L/min
- V_E (norm) ± 7 L/min
- Max. exp flow: 6-9 L/sec
- Compliance: 60-100 mL/cm Hg
- P_{aO2}: 100 mm Hg
- P_{aO2} (21% O2): 90-95 mm Hg
- P_{aO2} (100% O2): >500 mm Hg
- V_{E} (max): 120-150 L/min
- Max. exp flow: 7-10 L/sec
- [Hb]: 14-15 g/dL

Balance of Forces Determines FRC

Hooke's Law: \( F = -kx \)

Intrapleural space:
- Increasing volume: \( P_{pl} = -5 \)
- Decreasing volume: \( P_{pl} = 0 \)

Chest Wall Recoil Force
- Normal
- Emphysema + lung recoil
- Fibrosis + lung recoil
- Pneumothorax

Lung Wall Recoil Force
- Normal
- Emphysema + lung recoil
- Fibrosis + lung recoil
- Pneumothorax

As we remove air from pleural space the lung expands & the chest wall gets pulled in.
**Surface Area (relative)**

**Surface Tension (dynes/cm)**

- Water
- Detergent

**Lung Surfactant**

**Plasma**

- **Surfactant**
  - 40% Dipalmitoyl Lecithin
  - 25% Unsaturated Lecithins
  - 8% Cholesterol
  - 27% Apoproteins, other phospholipids, glycerides, fatty acids

**Hysteresis**

- **Surface Area** ∝ **↑ Surface Tension**

**1. Reduces Work of Breathing**
**2. Increases Alveolar Stability** (different sizes coexist)
**3. Keeps Alveoli Dry**

**Static Compliance Curves**

- Normal
  - PIP = -5
- Emphysema (high compliance)
  - ↓ lung recoil
- Fibrosis (low compliance)
  - ↑ lung recoil

**Balance of Forces Determines FRC**

- **Hooke’s Law**: \( F = -kx \)

- **Chest Wall Recoil Force**
- **Lung Wall Recoil Force**

**Balance of Forces in Emphysema and Fibrosis**

- **Pneumothorax**
- **Intrapleural Pressure, PIP** (cm H2O)
  - Normal: PIP = -5
  - Emphysema: ↓ lung recoil
  - Fibrosis: ↑ lung recoil

**Intrapleural Pressure and Lung Volume**

- **FRC**
- **VT**
- Normal FRC
The dashed trace is the PIP required to overcome recoil forces (or PTP taken from compliance curve). More PIP (solid curve) is required to overcome airway resistance to flow. N.B. \( \Delta P = P_A - P_B \) is required for flow.

Regional- Apex to Base Differences

Axes:
- PIP (cm H2O)
- Lung Volume

Legend:
- Apex
- Base
- Alveolar Volume
- Ventilation

Legend:
- ++
- +++

The figure shows the differences in lung volume between the apex and base under different PIP conditions. The dashed line represents the PIP required to overcome recoil forces, while the solid line shows the increased PIP needed to overcome airway resistance.

Apex to Base Differences

Axes:
- PIP (cm H2O)
- Lung Volume

Legend:
- Apex
- Base
- Alveolar Volume
- Ventilation

Legend:
- ++
- +++

This figure illustrates the lung volume changes at the apex and base under normal lung volume conditions.

Static Compliance Curves

Axes:
- Pleural Pressure, \( P_d \) (cm H2O)
- Lung Volume

Legend:
- FRC
- VT

Legend:
- Normal

The static compliance curves demonstrate the relationship between pleural pressure and lung volume. The normal curve is shown, indicating the typical compliance pattern.
The linear Dashed trace is the Ppl required to overcome recoil forces. More Ppl (solid curve) is required to overcome airway resistance to flow. N.B. $\Delta P = PA - PB \propto Resist \cdot Flow$. 

Lung Volume

Airway Resistance

Normal

\[ v = \frac{\text{Flow}}{A} \]

\[ R = \frac{\rho D v}{\eta} \]

\[ R = \frac{k \cdot \text{number}}{A^2} \]

N.B. this is total x-sectional area ($A_f = n^2 A_i$).

Dynamic Compression of Airways

Mild Expiratory Effort (P+13)

Normal at FRC

\[ P_{pl} = 0 \]

\[ P_{PA} = 0 \]

\[ P_{pl} = -5 \]

Normal at FRC

Dynamic Compression of Airways

Mild Expiratory Effort (P+13)

Normal at FRC

\[ P_{pl} = 0 \]

\[ P_{PA} = 0 \]

\[ P_{pl} = -5 \]
**Dynamic Compression of Airways**

- **Mild Expiratory Effort (P+13)**
  - Normal at FRC
  - Emphysema
  - Low V. & Basal Alv also like this

- **Strong Expiratory Effort (P+30)**
  - Normal at FRC
  - Emphysema
  - Pursed-lips
  - Hi Resist

**Equal Pressure Point**

- (in supported airways)
- PEEP=+5
- FRC

**Flow-Volume Curves**

- Effort Independent limb in forced expiration.
- Due to Dynamic Airway Compression and airway collapse.

**Forced Vital Capacity**

- Normal
- Obstructive
- Restrictive

- FEV₁<br>FVC<br>%
- FEV₁₀₀<br>FVC<br>%
- RV
PO2 = 100 mm Hg
14 ml O2/dL

PO2 = 100 mm Hg
0.3 ml O2/dL dissolved
20 ml O2/dL HB-O2

Bohr Shift Hb-O2 Curve

% Saturation of Hemoglobin

PaO2 (mm Hg)

Bohr Shift
↑ [H+]↑ CO2, ↑ Temp or DPG
↓ [H+]↓ CO2, ↓ Temp

Myoglobin
Normal Hb
Carbon Monoxide
Anemia

Hb-O2 content
(ml O2 /100 ml blood)

PaO2 (mm Hg)

Lungs
CO2 Unloading & O2 Loading

Tissue
CO2 Loading & O2 Unloading

Carbonmonoxyheme
O2 curve

Whole blood total CO2 Content (ml CO2/dl)

Both given PaCO2 CO2 content of blood increases as PaO2 falls (Haldane effect).
**HALDANE SHIFT**

Rest Venous

Arterial ($\uparrow$O$_2$)

$\uparrow$O$_2$ helps CO$_2$ unloading

---

**XIV. RESPIRATORY GAS CASCADE**

<table>
<thead>
<tr>
<th>Gas</th>
<th>$P_{in}$ mm Hg</th>
<th>$P_{out}$ mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air (dry)</td>
<td>760</td>
<td>0</td>
</tr>
<tr>
<td>Trachea (humidified: 760-47)</td>
<td>713</td>
<td>0</td>
</tr>
<tr>
<td>Alveolus (some O$_2$ absorbed by blood)</td>
<td>100</td>
<td>40</td>
</tr>
<tr>
<td>Arterial (R-L Shunt)</td>
<td>90</td>
<td>40+</td>
</tr>
<tr>
<td>Mixed venous (O$_2$ absorbed by tissues)</td>
<td>40</td>
<td>46</td>
</tr>
</tbody>
</table>

**CO is Diffusion Limited** (soaked up by Hb immediately)
Uptake depends on Diffusing Capacity

$\text{CO} + \text{Hb} = \text{Hb-Co} \quad [\text{CO}] = 0$

NO$_2$ doesn't bind $[\text{NO}_2] = [\text{NO}_2]$]

**NO$_2$ is Perfusion Limited** (Blood is quickly "saturated")
Uptake depends on how much blood goes by

Measuring Diffusion capacity, $D_i$ (or Transfer capacity) with CO

$J_{CO} = D_i \frac{\Delta P}{\Delta x}$

$\Delta P = P_{CO2} - P_{aCO2}$ and $P_{CO2}$ and $D_i$, $A$ & $\Delta x$ are lumped into $D_i$
$D_i = J_{CO} \frac{P_{CO2}}{\Delta P} \quad (\text{where} \ J_{CO} \text{is the rate of CO uptake measured})$

**Diffusion in Pulmonary Capillaries**

**O$_2$ Diffusion in Pulmonary Capillaries**

(transit time)
Expired Lung Volume (L)

<table>
<thead>
<tr>
<th>N₂ Concentration (%)</th>
<th>0</th>
<th>0.2</th>
<th>0.4</th>
<th>0.6</th>
<th>0.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar Plateau</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inspired O₂</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diluted by alveolar N₂</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fowler's Test
Area A = Area B

Alveolar Gas Equation

\[
V_{Alv} = \frac{P_{Alv} - P_{PA}}{RQ} + K
\]

\[
PAO_2 = PIO_2 - \frac{P_{Alv}}{RQ}
\]

\[
V_{O_2} = \frac{P_{O_2}}{P_{IO_2} - P_{EO_2}}
\]

\[
V_{CO_2} = \frac{P_{CO_2}}{P_{ACO_2}}
\]

\[
V_{A} = \frac{V_{O_2}}{FIO_2} (P_{ATM} - P_{H_2O}) - \frac{P_{CO_2}}{RQ} + K
\]

\[
V_{OE} = \frac{V_{CO_2}}{FIO_2} (P_{ATM} - P_{H_2O}) - \frac{P_{CO_2}}{RQ}
\]

\[
V_{AO} = \frac{V_{CO_2}}{FIO_2} (P_{ATM} - P_{H_2O}) - \frac{P_{CO_2}}{RQ} + K
\]

\[
V_{AE} = \frac{V_{O_2}}{FIO_2} (P_{ATM} - P_{H_2O}) - \frac{P_{CO_2}}{RQ}
\]

\[
RQ = \frac{V_{CO_2}}{V_{O_2}}
\]

The Bohr Equation

\[
V_{D1} = \frac{(P_{ACO_2} - P_{ECO_2})}{V_{T}}
\]

\[
V_{D2} = \frac{(P_{aCO_2} - P_{ECO_2})}{V_{T}}
\]

1. For \( V_T = 500 \text{ ml} \), \( f = 10/\text{min} \), \( V_A = 150 \text{ ml} \), what is \( \dot{V}_{CO_2} \)?

\[
\dot{V}_{CO_2} = \frac{500}{10} \times 150 = 500 \text{ ml/min}
\]

2. If \( \dot{V}_{O_2} \) is doubled by increasing \( V_T \), what is \( \dot{V}_{CO_2} \)?

\[
\dot{V}_{CO_2} = \frac{1000}{10} \times 150 = 1000 \text{ ml/min}
\]

3. If the same \( \dot{V}_{O_2} \) is obtained by doubling frequency, what is \( \dot{V}_{CO_2} \)?

\[
\dot{V}_{CO_2} = \frac{10000}{20} \times 150 = 7500 \text{ ml/min}
\]

Thus increasing \( V_T \) rather than frequency is more effective for \( \dot{V}_{CO_2} \).

XIX. RESPIRATORY EXCHANGE RATIO

\[
RQ = \frac{V_{CO_2}}{V_{O_2}}
\]

The relative amounts of O₂ consumed and CO₂ produced depends upon the fuel.

Carbohydrate: \( RQ = 1 \)

Fat: \( RQ = 0.7 \)

Protein: \( RQ = 0.8 \)

A typical "normal" \( RQ \) is 0.8

The partial pressures of O₂ and CO₂ are also affected.

\[
RQ = \frac{V_{CO_2}}{V_{O_2}} = \frac{P_{CO_2}}{P_{ACO_2}} = \frac{40}{50}
\]

Study Questions/Exercises

Q: Why does this ratio necessarily reflect the RQ?
Flow of Blood or Air

Perfusion

Ventilation

Flow of Blood or Air

Ventilation Perfusion Ratios

Low $V_A/Q$

Normal $V_A/Q$

High $V_A/Q$

Ventilation

Perfusion

Flow of Blood or Air

Region

$V_A$

$Q_A$

$Q_L$

$P_{CO_2}$

$P_{O_2}$

Apex

Base

++

++

+
Mechanisms of Hypoxemia
A. Hypoventilation
B. Diffusion Abnormalities
C. Right to Left Shunt
D. Ventilation/Perfusion Mismatch
E. Low inspired \( P_{O_2} \)

Mechanisms of Hypoxemia
<table>
<thead>
<tr>
<th>( P_{aO_2} )</th>
<th>( P_{aCO_2} )</th>
<th>( P_{aO_2} ) (A-a)</th>
<th>( P_{aO_2} ) with 100% O(_2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoventilation</td>
<td>low</td>
<td>High</td>
<td>Norm</td>
</tr>
<tr>
<td>Diffusion</td>
<td>low</td>
<td>norm-low</td>
<td>high</td>
</tr>
<tr>
<td>R-L Shunt</td>
<td>low</td>
<td>norm-low</td>
<td>high</td>
</tr>
<tr>
<td>( V_{A/Q} ) Imbalance</td>
<td>low</td>
<td>norm-bi-ni</td>
<td>high</td>
</tr>
</tbody>
</table>

Other Hypoxemias (without low \( P_{aO_2} \))
- Anemia
- Carbon Monoxide
- Hypoperfusion (CV problem)

Local Control
- Low \( P_{aCO_2} \) → vasoconstriction
- Low \( P_{aCO_2} \) → bronchoconstriction

Study Questions/Exercises:
Consider ½ of pulmonary blood flow going to regions where \( P_{aO_2} \) is 150 mm Hg and the other ½ to a region of \( P_{aO_2} = 40 \) mm Hg. Assume \( P_{aCO_2} = 30 \) and 50 mm Hg in these respective regions. How does \( P_{aCO_2} \) become less than normal while \( P_{aCO_2} \) is normal?

Hemoglobin-O\(_2\) Binding Curve
\[ \frac{(100+75)}{2} = 87.5 \]
\[ \frac{(20+15)}{2} = 17.5 \]

Hemoglobin-O\(_2\) Binding Curve
\[ \frac{(100+75)}{2} = 87.5 \]
\[ \frac{(20+15)}{2} = 17.5 \]

Simple Negative Feedback System
- Integrator in CNS (Medulla)
- Sensors Chemoreceptors Central & Peripheral
- Effectors Respiratory Muscles (e.g., Diaphragm)
- Control Variables \( P_{O_2}, P_{CO_2}, pH \)

Simple Negative Feedback System
- Integrator in CNS (Medulla)
- Sensors Chemoreceptors Central & Peripheral
- Effectors Respiratory Muscles (e.g., Diaphragm)
- Control Variables \( P_{O_2}, P_{CO_2}, pH \)
Peripheral Chemoreceptor Responsiveness

\[
\begin{align*}
\text{Peripheral Chemoreceptor Responsiveness} \\
\text{% maximal firing rate} \quad & \quad \text{Arterial } P_cO_2 \text{ (mm Hg)} \\
75 & \quad 50 & \quad 25 & \quad 50 & \quad 100 & \quad 500
\end{align*}
\]

Respiratory Acidosis ($T_{PCO_2}$)

\[
CO_2 \rightarrow HCO_3^- + H^+
\]

Metabolic Acidosis

\[
\text{Hyperventilation} \quad & \quad J_{PCO_2}
\]

CNS Alkalosis !!!

(then pump $HCO_3^{-}$ out)

CNS Acidosis

\[
\text{then } HCO_3^- \text{ is pumped in}
\]

(& restores $pH_{cNS}$ faster than kidneys can restore $pH_{systemic}$)

Plasma BBB CSF

\[
\begin{align*}
CO_2 & \rightarrow HCO_3^- + H^+ \\
HCO_3^- + H^+ & \rightarrow CO_2
\end{align*}
\]
Ventilatory Response to $O_2$

Ventilatory Response to $CO_2$

Ventilatory Response to $CO_2$

Ventilatory Response to $O_2$

Ventilatory Response to $CO_2$

Ventilatory Response to $CO_2$

Ventilatory Response to $CO_2$

Ventilatory Response to $CO_2$

Ventilatory Response to $CO_2$
**EFFECTS OF HIGH ALTITUDE**

**A.** At 10,000 ft $P_B$=525 mmHg inspired $P_{O2}$ is ~100 mmHg $\Rightarrow$ $P_{A,O2}$ is ~50 mmHg.

At 15,000 ft $P_B$=380 mmHg inspired $P_{O2}$ is ~70 mmHg $\Rightarrow$ $P_{A,O2}$ is ~20 mmHg.

At Mt Everest $P_B$=250 mmHg, inspired $P_{O2}$ is ~42 mmHg $\Rightarrow$ $P_{A,O2}$ is ~0 mmHg.

At 63,000 ft $P_B$=47 mmHg, inspired $P_{O2}$ is ~0 mmHg $\Rightarrow$ tissues boil, H$_2$O vapor.

**B.** Acclimatization and hyperventilation at 10,000 ft

<table>
<thead>
<tr>
<th>Time at High Alt.</th>
<th>$P_{A,O2}$</th>
<th>$P_{A,CO2}$</th>
<th>pH blood</th>
<th>pH CSF</th>
<th>$V_E$ [HCO$_3^-$]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Hr</td>
<td>low</td>
<td>low</td>
<td>high</td>
<td>high</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoxic drive is restrained by low $P_{A,CO2}$ and high pH.</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1-2 days</td>
<td>low</td>
<td>low</td>
<td>high</td>
<td>Norm</td>
<td></td>
</tr>
<tr>
<td></td>
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<tr>
<td>CSF chemoreceptors no longer limiting hyperventilation.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2-4 days</td>
<td>low</td>
<td>low</td>
<td>Norm</td>
<td>Norm</td>
<td></td>
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<tr>
<td></td>
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<tr>
<td>Peripheral alkalosis no longer restraining hyperventilation.</td>
<td></td>
<td></td>
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<tr>
<td>30 Yrs.</td>
<td>low</td>
<td>Norm</td>
<td>Norm</td>
<td>Norm</td>
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<td></td>
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<tr>
<td>Hypoxic response of chemoreceptors lost.</td>
<td></td>
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</tr>
</tbody>
</table>

**C.** Other adjustments

1. Polycythemia
2. Enhanced Diffusing Capacity
3. Increased Capillary Density
4. Right shift of HbO$_2$ curve
Equations

Old ones you already knew

\[ \Delta P = QR \quad \text{Ohm's Law} \]
\[ J = DA(\Delta C/\Delta x) \quad \text{Fick's Law} \]
\[ J_{CO_2} = DL_{CO_2} - COP_{CO_2} \]
\[ PV = nRT \quad \text{Universal Gas Law (Boyle's & Charles' Laws)} \]
\[ P_x = P_F \quad \text{Dalton's Law of Partial Pressures} \]
\[ C_x = P_x \cdot \text{Ksolubility} \quad \text{Henry's Law} \]
\[ P = 2T/r \quad \text{Law of LaPlace} \]
\[ F = -kx \quad \text{Hooke's Law} \]

\[ R = \frac{8 \eta l}{\pi r^4} \quad \text{Tubular resistance} \]
\[ N_R = \frac{\rho D v}{N} \quad \text{Reynold's Number} \]
\[ CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+ \]
\[ RQ = \frac{V_{CO_2}}{V_{O_2}} \quad \text{Respiratory Quotient} \]
\[ P_{trans} = P_T - P_F \quad \text{Transpulmonary P (Transmural)} \]

New ones!

\[ \Delta \frac{P_{CO_2}}{P_{O_2}} = \frac{P_{CO_2} - P_{O_2}}{P_{O_2}} \quad \text{Bohr Eqn} \]
\[ V_{A} = \frac{V_{E}}{P_{CO_2} - P_{O_2}} \quad \text{Helium Dilution} \]
\[ V_{A} = \frac{V_{E} \times P_{CO_2}}{P_{O_2}} \quad \text{Nitrogen Washout} \]

\[ \text{New Ones!} \]

\[ V_{A} = \frac{(P_{CO_2} - P_{O_2})}{P_{O_2}} \quad \text{Bohr Eqn} \]
\[ \text{New Ones!} \]

\[ \text{New Ones!} \]

\[ \text{New Ones!} \]

\[ \text{New Ones!} \]

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