# Early Warning of Membrane Thickness Increase through Diffusing Capacity for CO

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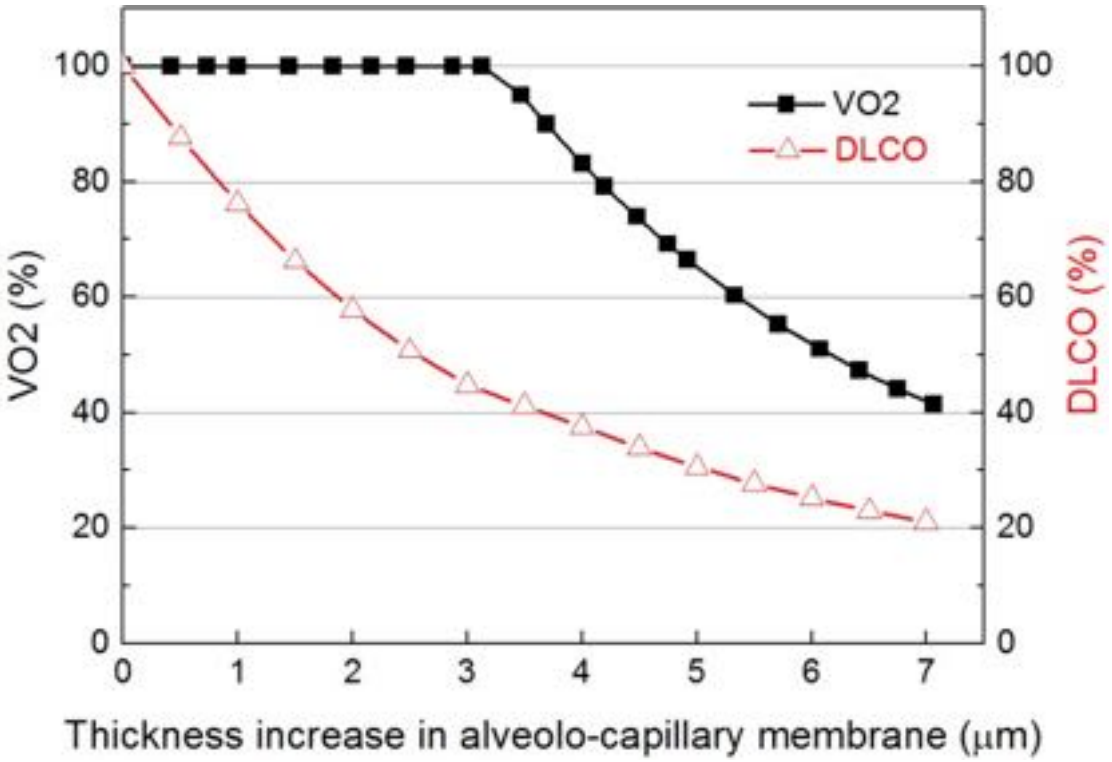
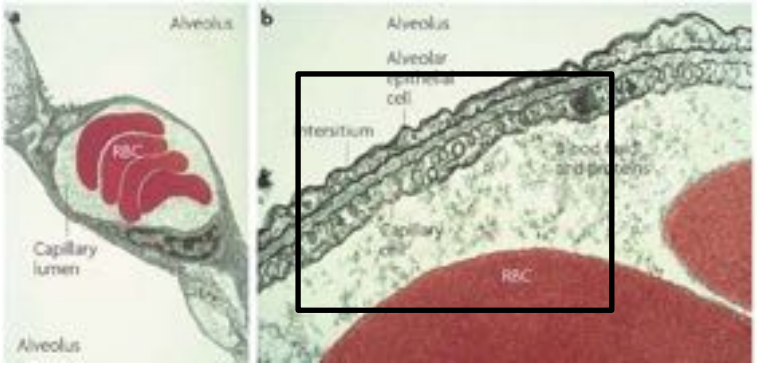
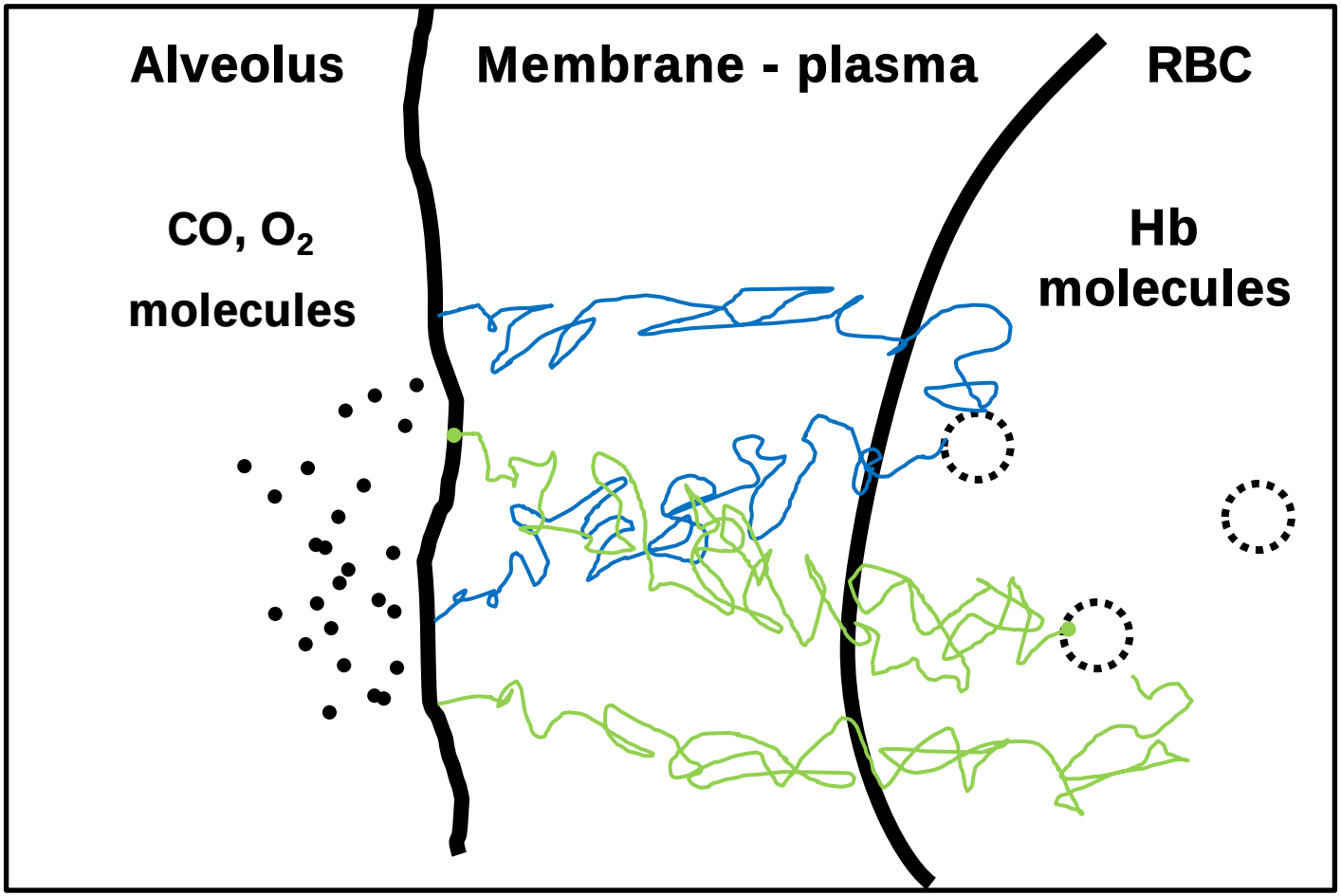
- **Time-based understanding of gas capture**
- **Quantitative prediction**
- **Difference between $O_2$ and CO**

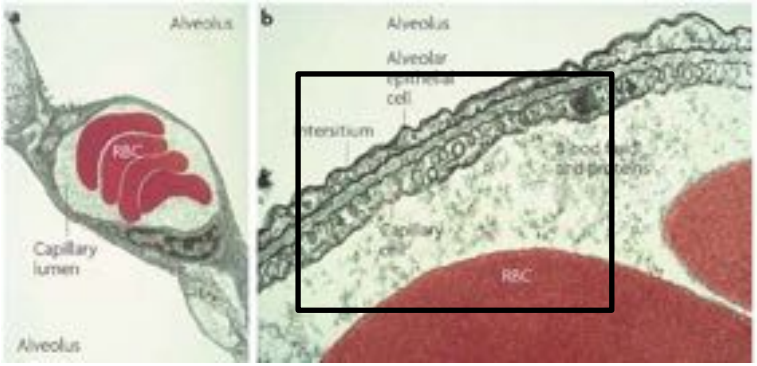



DLCO : CO diffusing capacity
VO2 : Volume of captured $O_2$




Patton and Byron (2007) *Nat Rev Drug Discov*



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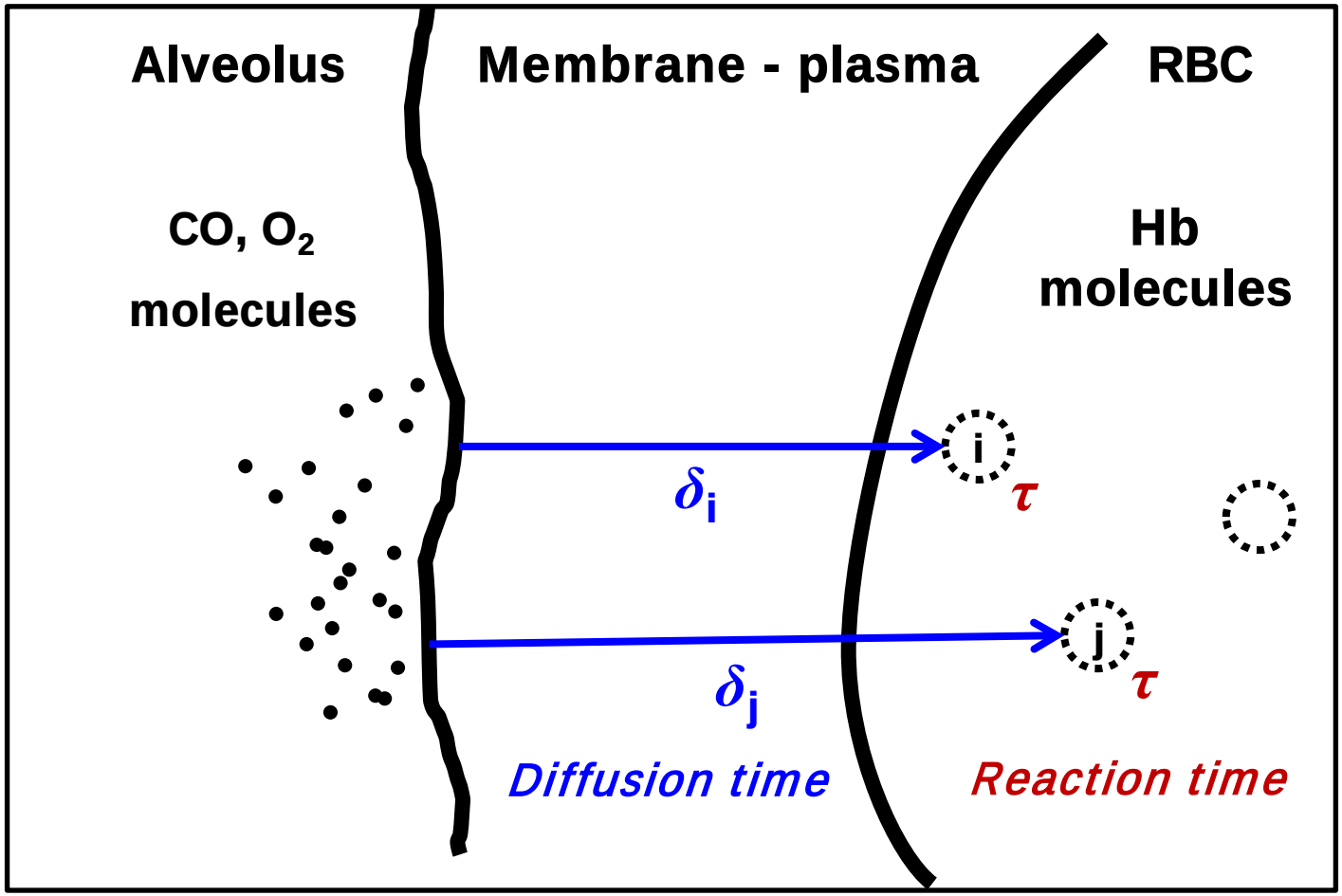


# CO Capture (Single breath measurement)

CO concentration at the membrane

Volume of RBCs in the pulmonary capillaries

$$\mathrm{DLCO} = \alpha C_g \frac{Vc \cdot Hct}{\delta_{Eq} + \tau}$$

**Average** diffusion time

Reaction time ~ 0.5 ms given by chemical kinetics

Roughton and Forster (1957)

$$\frac{1}{\mathrm{DLCO}} = \frac{1}{\mathrm{DMCO}} + \frac{1}{\theta_{CO} \cdot Vc}$$

DLCO : CO diffusing capacity
α : CO solubility in plasma
$C_g$ : CO concentration in alveolus
*Vc* : Capillary volume
*Hct* : Hematocrit

# *Hb* dependence

| | Before haemodilution | After | After/Before |
|---|---|---|---|
| Haemoglobin (g/L) | 149.4 ± 9.32 | 125.4 ± 9.32 | **0.84** |
| $DL_{CO}/VA$ at TLC (%th) | 91.3 ± 10.8 | 75.5 ± 13.4 | **0.83** |
| $DL_{CO}/VA$ at 70% TLC (%th) | 104.5 ± 15.5 | 88.5 ± 13.7 | **0.85** |
| $DL_{CO}/VA$ at FRC (%th) | 130 ± 20.2 | 107.6 ± 13.4 | **0.83** |
| Standard prediction (Roughton and Forster) | | | **0.93** |

Atfer *Le Merre et al. (1996) Can. J. Anaesth*

| Patients with sickle cell anaemia | Female (n = 29) | % normal | Male (n = 20) | % normal |
|---|---|---|---|---|
| Haemoglobin (g/dL) | 8.3 ± 0.8 | **62 ± 6** | 9.3 ± 1.6 | **64 ± 11** |
| Measured $DL_{CO}$ | | **54 ± 6** | | **61 ± 13** |
| Standard prediction (Roughton and Forster) | | **80** | | **81** |

Atfer *Delclaux et al. (2005) Chest*

# CO Capture (Single breath measurement)

CO concentration at the membrane

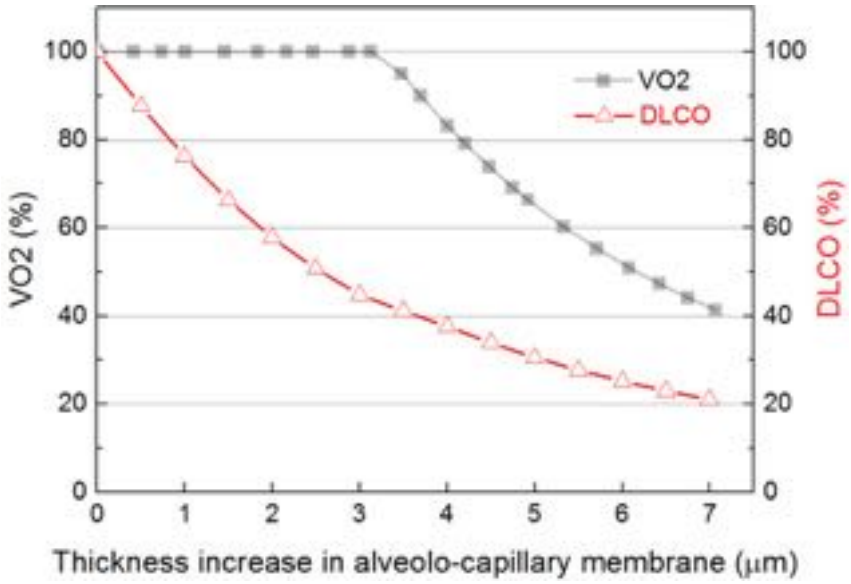
Volume of RBCs in the pulmonary capillaries

$$DLCO = \alpha C_g \frac{Vc \cdot Hct}{\delta_{Eq} + \tau}$$

$\delta_{Eq}$ ~ (thickness)$^{1.6}$

**Average** diffusion time

Reaction time ~ 0.5 ms
given by chemical kinetics




DLCO : CO diffusing capacity
α : CO solubility in plasma
$C_g$ : CO concentration in alveolus
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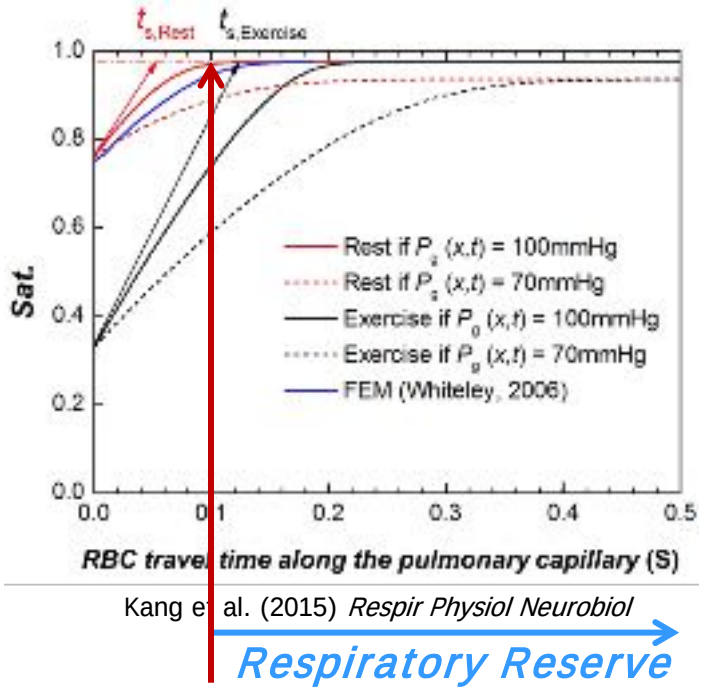
# Difference in $O_2$ Capture in the lung

1) Hb-$O_2$ saturation

**Time-evolution of RBC $O_2$ concentration**

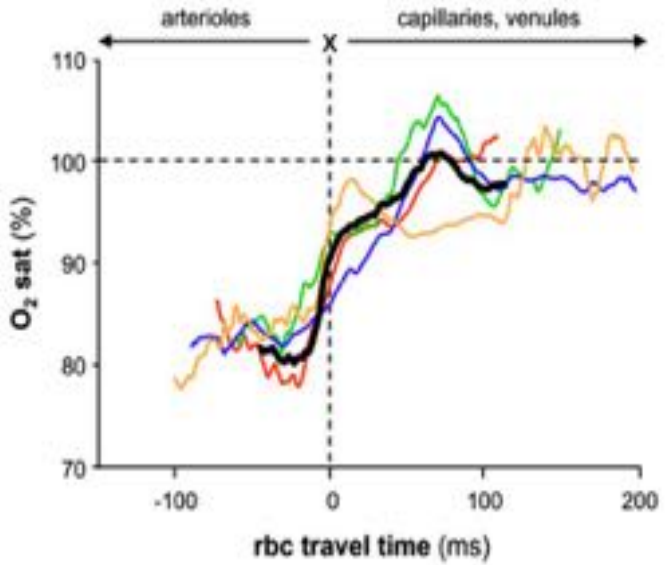
$$\frac{dC_{\mathrm{RBC}}(t)}{dt}+\frac{1}{\tau_{\mathrm{RBC}}+\alpha'\delta_{\mathrm{Ext}}}C_{\mathrm{RBC}}(t)=\frac{\alpha'\alpha C}{\tau_{\mathrm{RBC}}+\alpha'\delta_{\mathrm{Ext}}}$$

Prediction




Kang et al. (2015) *Respir Physiol Neurobiol*

Experiment



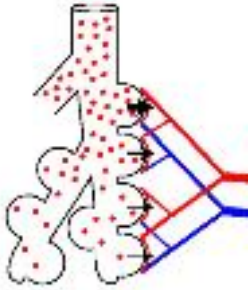

Tabuchi et al. (2013) *Am J Respir Crit Care Med*

*Respiratory Reserve*

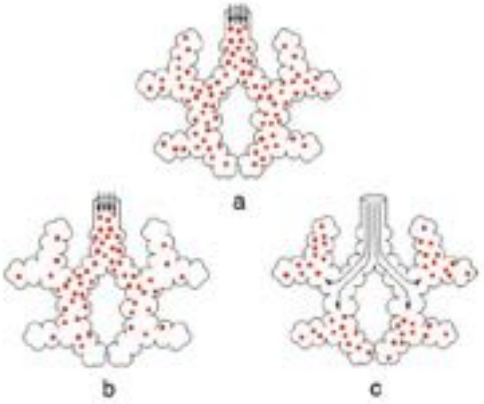
*100 ms*

## 2) Non-uniform distribution in airways

Diffusion screening



Convection / Diffusion




Sapoval et al. (2002) *PNAS*

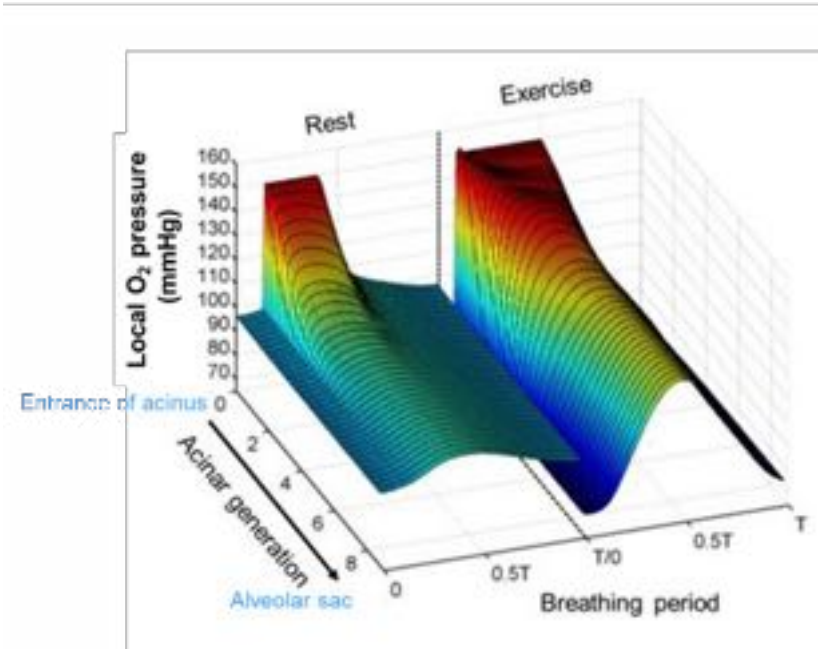
$O_2$ concentration distribution in airways

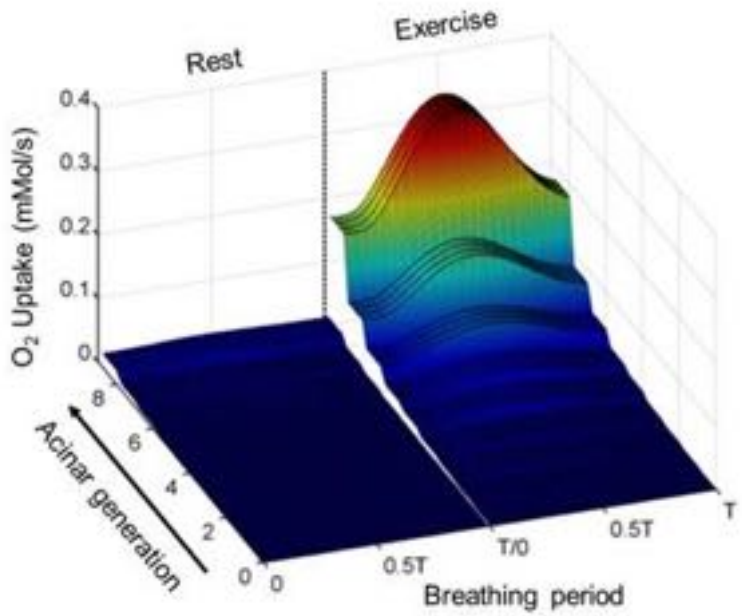
$$\frac{\partial C(x,t)}{\partial t} = D\frac{\partial^2 C}{\partial x^2} - \frac{\partial}{\partial x}(C \cdot U) - \Omega\frac{S}{V}(C - C_V/\alpha)$$

***Diffusion*** ***Convection*** ***Permeation (Capture)***

Foucquier et al. (2013) *Respir Physiol Neurobiol*

# Spatial – temporal distribution of $O_2$ pressure and Capture



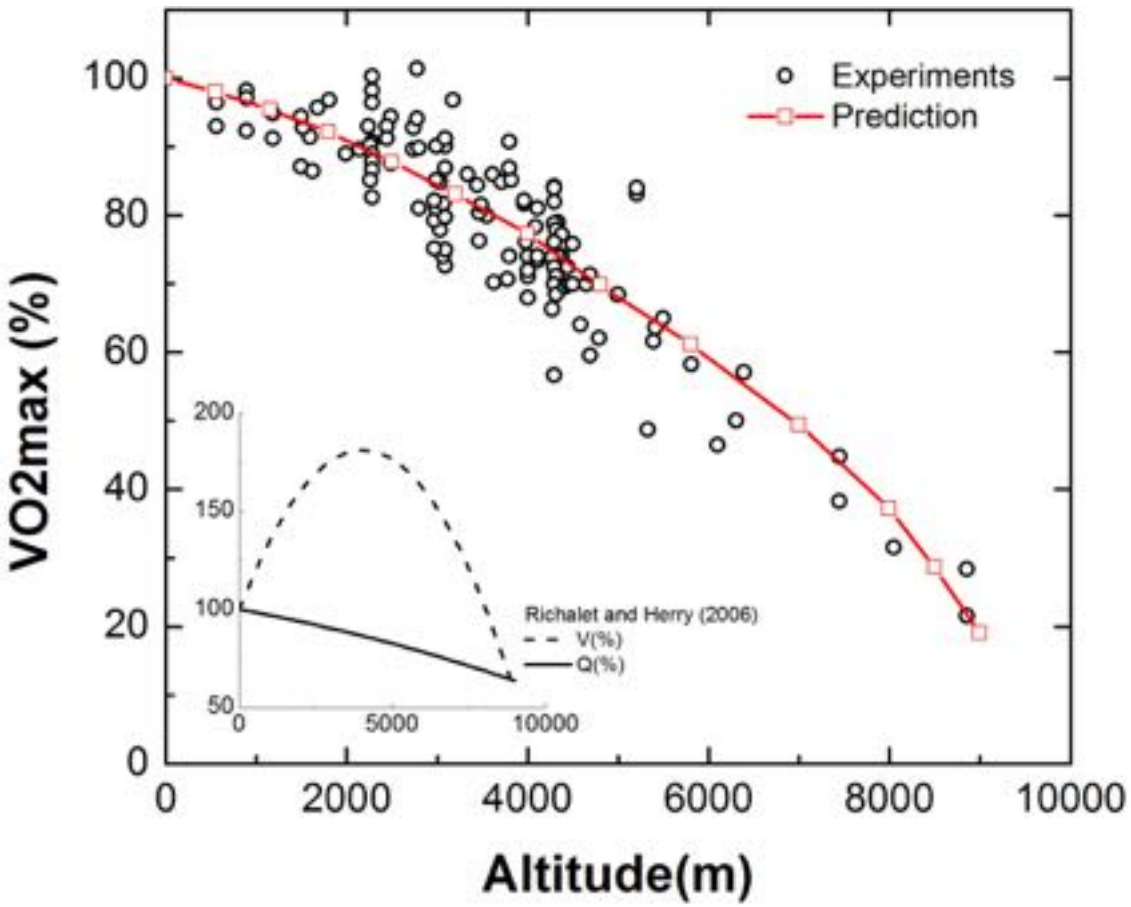

Kang et al. (2015) *Respir Physiol Neurobiol*

Alveolar $O_2$ pressure (**$P_AO_2$**) = Average local $O_2$ pressure for a period ***T***

Amount of captured $O_2$ (**$VO_2$**) = Sum of local $O_2$ capture for a period ***T***

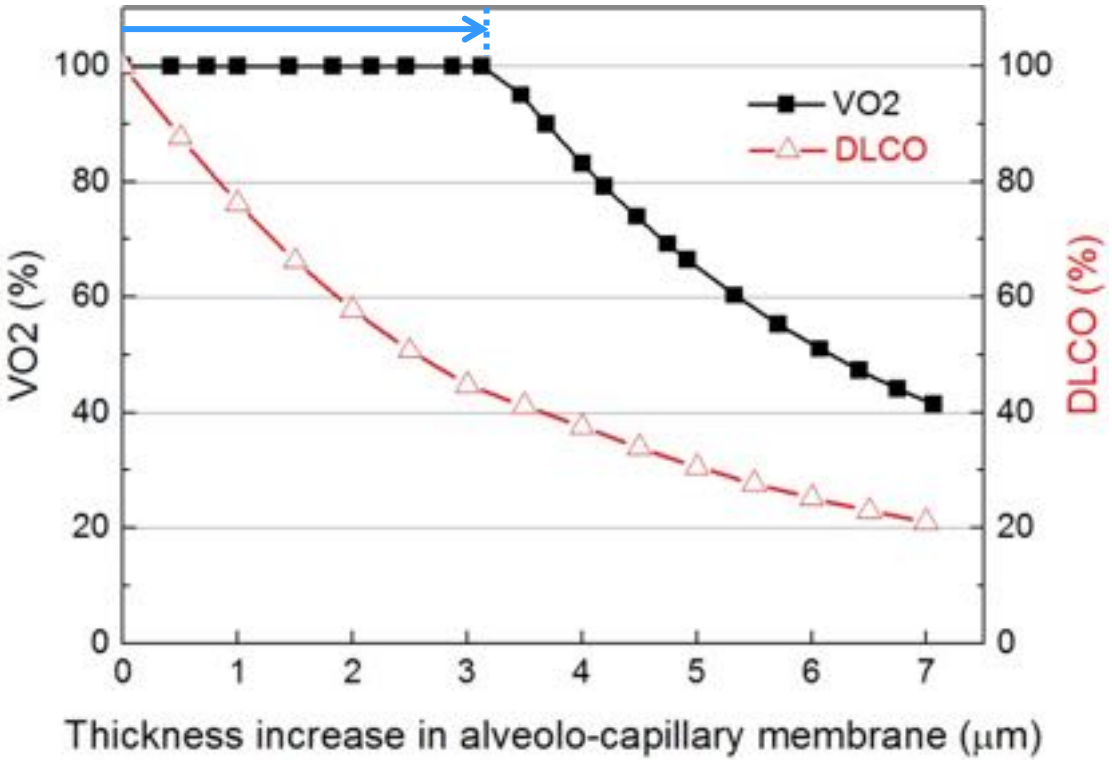
| | **$VO_2$** in mMol/min<br>Prediction (Experiment) | **$P_AO_2$** in mmHg<br>Prediction (Experiment) |
|---|---|---|
| Rest | 11.7 (9 - 13.4) | 96 (95 – 105) |
| Exercise | 107 (100 – 150) | 101 (95 – 105) |

# $O_2$ Capture at high altitudes




US Army Technical Bulletin MED 505 (2010)

*Respiratory reserve for $O_2$ capture*



# SUMMARY

- A new **time-based** understanding of gas capture in the lung is proposed, which allows for quantitative prediction of the capture.

- Mild thickening of the alveolar – capillary membrane would not be noticed due to the **respiratory reserve** for $O_2$ capture.

- On the contrary, DLCO shows **immediate response** to the thickening. So it could be indicative of early development diseases related to the thickening.