Respiratory Physiology & Neurobiology 205 (2015) 109–119

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

A new approach to the dynamics of oxygen capture by the human lung

Min-Yeong Kang[a], Ira Katz[b,c], Bernard Sapoval[a,d,*]

[a] Physique de la Matière Condensée, CNRS, Ecole Polytechnique, 91128 Palaiseau, France
[b] Medical R&D, Air Liquide Santé International, Centre de Recherche Paris-Saclay, 78534 Jouy-en-Josas, France
[c] Department of Mechanical Engineering, Lafayette College, Easton, PA 18042, USA
[d] Centre de Mathématiques et de leurs Applications, CNRS, UniverSud, 94235 Cachan, France

ARTICLE INFO

Article history:
Accepted 3 November 2014
Available online 7 November 2014

Keywords:
Oxygen capture
Ventilation–perfusion
High altitude
Pulmonary edema
CO and NO diffusing capacity

ABSTRACT

Oxygen capture in the lung results from the intimate dynamic interaction *between* the space- and time-dependent oxygen partial pressure that results from convection-diffusion and oxygen extraction from the alveolar gas *and* the space and time dependence of oxygen trapping by the red blood cells flowing in the capillaries. The complexity of the problem can, however, be reduced due to the fact that the systems obey different time scales: seconds for the gas phase transport and tenths of seconds for oxygen trapping by blood. This results first from a dynamical study of gas transport in a moving acinus and second from a new theory of dynamic oxygen trapping in the capillaries. The global solution can be found only through a self-consistent iterative approach linking the two systems. This has been accomplished and used to quantify oxygen capture in various situations: at rest, during exercise, ventilation–perfusion mismatching, high altitude and pulmonary edema.

1. Introduction

The scientific understanding of oxygen capture has changed over time based on the conceptual and experimental tools that were available (West, 2004). Now, numerical tools exist that allow us to investigate the dynamic nature of oxygen capture in an unsteady realistic environment and complex geometry. Thus, herein a theory is presented that takes into account the complexity of the lung morphology, and the dynamics of respiration and oxygen trapping. It will be shown that because of the different characteristic time scales of oxygen transport in gas and blood, it is possible to study both separately although oxygen capture finally depends on their complex interaction.

In earlier studies, the possible non-uniformity of the oxygen concentration (also called incomplete gas mixing or stratification, Scheid and Piiper, 1980) was related to the finite diffusivity of oxygen (Dutrieue et al., 2000; Felici et al., 2003, 2005; Grebenkov et al., 2005; Hou et al., 2010; Mayo et al., 2012; Paiva and Engel, 1985, 1987; Sapoval et al., 2002a, b; Swan and Tawhai, 2011; Tawhai and Hunter, 2001; Weibel et al., 1981, 2005). To study the system from the *gas* point of view, we developed the concept of a "machine acinus" (Foucquier et al., 2013). This machine has realistic morphology and dynamics (Haefeli-Bleuer and Weibel, 1988; Weibel, 1984) but with an unknown permeability Ω, hereafter called the "integrative permeability". We suppose that in the artificial machine, blood acts as a *perfect sink*. The development determines the Ω values that give the same oxygen capture as the real acinus does under an oxygen partial pressure of approximately 100 mmHg.

Of course, saturation does really intervene and we show, by studying the *blood* point of view, how saturation evolves in time allowing us to determine the value of Ω. Our results are different from those derived from the conventional approach which uses, for oxygen, the formalism introduced by Roughton and Forster (1957) for the carbon monoxide case. This difference comes from the previous misinterpretation of the time scales involved in the establishment of dissolution.

Respiration results from the complex interaction between gas dynamics and blood saturation depending on the distribution of oxygen partial pressure. It is then only by combining the gas and blood approaches in a self-consistent manner that we are able to build a quantitative theory of oxygen capture with no adjustable parameters. This general approach can be applied to the quantification of many situations such as ventilation–perfusion heterogeneity, respiratory response to altitude, the existence of a respiratory reserve and a decrease of arterial oxygen partial pressure in pulmonary edema.

The theory for oxygen capture by blood can be also applied to other gases. Herein we consider the diagnostic and

* Corresponding author at: Physique de la Matière Condensée, CNRS, Ecole Polytechnique, 91128 Palaiseau, France. Tel.: +33 169334725.
E-mail address: bernard.sapoval@polytechnique.edu (B. Sapoval).

http://dx.doi.org/10.1016/j.resp.2014.11.001

a	radius of a red blood cell
C_E	oxygen concentration on the external surface of a red blood cell
C_g	local oxygen concentration in gas
C_p	oxygen concentration in the internal fluid assimilated with plasma
C_{RBC}	oxygen concentration in a red blood cell
C_S	oxygen concentration in air at sea level
Cv	oxygen concentration in mixed venous blood
D	diffusion coefficient of oxygen in air
D_{O_2}	diffusion coefficient of oxygen in plasma
D_{CO}	diffusion coefficient of carbon monoxide in plasma
D_{NO}	diffusion coefficient of nitric oxide in plasma
DL_{O_2}	diffusing capacity of the lung for oxygen
DL_{CO}	diffusing capacity of the lung for carbon monoxide
DL_{NO}	diffusing capacity of the lung for nitric oxide
Hb	hemoglobin molecule
Hct	hematocrit
k_{CO}	rate constant for carbon monoxide uptake
k_{NO}	rate constant for nitric oxide uptake
N_{ac}	number of acini in the lung
N_{Hb}	number of Hb molecules per red blood cell
N_{NO}	number of nitric oxide molecules leaving the alveolar volume
$N_{RBC,Lung}$	number of red blood cells in the lung
n	exponent of the Hill equation
P_A	average alveolar oxygen partial pressure
P_a	oxygen partial pressure of the arterial blood
P_b^*	barometric pressure
P_I	inspired oxygen partial pressure
P_g	local alveolar oxygen partial pressure
P_p	oxygen partial pressure in plasma
P_V	oxygen partial pressure of the mixed venous blood
P_{50}	P_p at 50% saturation
RBC	red blood cell
Q	cardiac output
S	gas exchange surface area
S_{Lung}	total lung surface area
Sat	oxygen saturation fraction of hemoglobin molecules
STP	standard temperature and pressure
T	duration of a respiratory cycle
t	time coordinate for gas during the respiratory cycle
t_B	time coordinate for oxygen trapping dynamics by blood
t_c	capillary transit time
t_s	saturation time for blood
U	gas convection velocity in airways
V	volume of an acinar branch
V_A	alveolar volume
V_{ac}	volume of an acinus
V_c	pulmonary capillary volume
V_p	plasma volume per red blood cell
V_{RBC}	volume of a red blood cell
$\dot{V}$	ventilation
$\dot{V}_{O_2}$	the amount of oxygen uptake of the lung
x	position in airways
α	liquid to gas partition ratio for oxygen
α_{CO}	liquid to gas partition ratio for carbon monoxide
α_{NO}	liquid to gas partition ratio for nitric oxide
α'	partition ratio of oxygen concentration between plasma and red blood cell
α'_{CO}	partition ratio of carbon monoxide concentration between plasma and red blood cell
α'_{NO}	partition ratio of nitric oxide concentration between plasma and red blood cell
δ_{Ext}	characteristic time for oxygen diffusion from alveolar space to the red blood cell surface
$\delta_{Ext,CO}$	characteristic time for carbon monoxide diffusion from alveolar space to the red blood cell surface
$\delta_{Ext,NO}$	characteristic time for nitric oxide diffusion from alveolar space to the red blood cell surface
δ_{Hb}	characteristic time for oxygen trapping by hemoglobin molecules
$\delta_{Hb,CO}$	characteristic time for carbon monoxide trapping by hemoglobin molecules
$\delta_{Hb,NO}$	characteristic time for nitric oxide trapping by hemoglobin molecules
λ	equivalent diffusion barrier thickness
Φ	oxygen flux across the gas exchange surface
ϕ	instantaneous oxygen flux per red blood cell
Ω	integrative permeability
$\Omega_{physiol}$	integrative permeability in physiological units ($ml_{STP}\,cm^{-2}\,min^{-1}\,mmHg^{-1}$)

therapeutic gases carbon monoxide (CO) and nitric oxide (NO). Thus, we propose a quantitative approach to determine the diffusing capacity of the lung for these gases, DL_{CO} and DL_{NO}. It is found that oxygen capture, although controlled by the same type of equations, is fundamentally different from CO or NO capture.

2. Methods

2.1. The gas phase transport: the machine acinus at rest and during exercise

If the oxygen (O_2) concentration is non-uniform, the differential oxygen flux across an element of the alveolar surface dS at position x and time t can be expressed by

$$d\Phi = \Omega\left(C_g(x,t) - \frac{C_v}{\alpha}\right) dS \quad (1)$$

where $C_g(x,t)$ is the local O_2 concentration, C_v is the mixed venous O_2 concentration in blood plasma (assumed to be constant during a breathing cycle) and α is the Ostwald partition ratio (dimensionless ratio of concentration in liquid to concentration in gas at equilibrium, 0.024 for oxygen in water and air). Units of flux are molecules/time and Ω is expressed in units of length/time or velocity. Note that the usual physiological units in terms of partial pressures obscure the fact that the permeability really measures an average molecular velocity that is explicit in this formulation. Permeability is usually measured in standard physiological units such as volume per unit surface per unit time per partial pressure (for instance $ml_{STP}\,cm^{-2}\,min^{-1}\,mmHg^{-1}$; where STP refers to standard temperature and pressure). Here we use the equivalent physical units, length divided by time or velocity units, to emphasize that the permeability is a measure of average molecule velocity. The equivalence between the physical and the physiological units of permeability is then given by $\Omega\,(cm\,s^{-1}) = 12.7 \times \Omega_{physiol}$ ($ml_{STP}\,cm^{-2}\,min^{-1}\,mmHg^{-1}$).

The O_2 concentration is space- and time-dependent because it is governed by convection, diffusion and permeation across the peripheral surface. Assuming that the transverse diffusion time across the acinar duct is negligible compared to the stream-wise transport during the respiratory cycle, the 1D convection–diffusion–permeation equation can be used to