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Diffusion of gases into the lung: How physics can help to understand physiology

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Abstract. In the human lung, the gas transfer between air and blood is achieved in terminal units that are called 'acini'. Whereas convection is still the predominant transport phenomenon at the acinus entrance, most of the acinar surface is in fact accessed by diffusion. The transition between convection and diffusion, and thus the size of the diffusion unit, depends on the air velocity at the acinus entrance. In this paper, we present a gas transport model which takes into account both the diffusion into the acinus and the diffusion across the alveolar membrane. It is shown that the physiological sizes of the diffusion unit in the lung, at rest or at exercise, can be explained by physical arguments. In that sense, diffusion is the 'dimensioning criterion' of the lung at the acinar level. This approach shows that, due to diffusional screening at inspiration and at rest, there exists a permanent spatial inhomogeneity of oxygen and carbon dioxide partial pressure which reduces the effective surface efficiency of the human acinus to a value of only 30 to 40%. This model casts a new light on the properties of this physiological transport system. It permits in particular to understand how several diseases among which pulmonary edema may remain asymptomatic in their early stages.

Keywords. Lung; diffusion; screening; efficiency; edema.

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1. Introduction

The human lung exhibits a complex geometry. In particular, its airway system can be represented as a dichotomous branching tree of 15 generations, terminated by 30,000 units called 'acini'. These units are in charge of the gas exchange between air and blood (figure 1). Gas exchange at the acinar level involves several physico-chemical phenomena, such as convection and diffusion. In order to exchange oxygen and carbon dioxide, blood and air are brought into close contact over a large surface area. In the mammalian lung, the gas exchange occurs in the most peripheral generations of the branched airway tree that form the acini [1]. Below the convection–diffusion transition, oxygen diffuses as a quasi-static gas and then eventually crosses the alveolar membrane to be finally bound by hemoglobin.

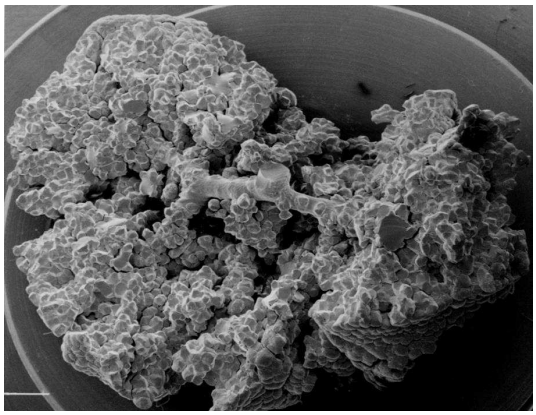

Figure 1. Microscopic view of a human acinus. The entrance is at the center. One can observe the branched structure in the first generations and the alveolar sacs openings on the acinar duct (courtesy of E R Weibel).

2. The convection–diffusion transition in the acinus

The transition between convection-dominated and diffusion-dominated transport is rather sharp. From that point, oxygen molecules diffuse in the alveolar gas to eventually reach the alveolar membrane where they are transferred into the blood. Conversely, carbon dioxide is extracted from the venous blood and brought back by diffusion up to the transition region between diffusion and convection.

The size of the diffusion unit considered above depends on an extra variable, which does not appear directly in the above product: It is the air velocity at the acinus entry that we call U. A change in U will induce a change in the convection–diffusion transition and a modification of the size of the zone where diffusion governs the gas transport, as shown in figure 2. For a given gas velocity U at the acinus entrance, one may define the bronchial tree bifurcation $Z(U)$ below which the corresponding subacini work under diffusion limited conditions, while the part of the acinus with $Z = Z(U)$ will work under the entrance partial pressure. To find $Z(U)$ one introduces an 'acinus Peclet number' $P(Z)$ which compares the flow velocity at Z with the mean diffusion velocity to reach, from Z, the deeper regions of the acinus. At any branching Z, the distance to cross to the end of the sacs is of order $(Z_{\max} - Z) \times \lambda$ where λ is the mean length of an acinar duct (figure 2). The 'acinus Peclet number' $P(Z)$ is defined as

$$P(Z) = \frac{U(Z)(Z_{\max} - Z)\lambda}{D(\mathrm{O_2})_{\mathrm{air}}}, \tag{1}$$

where the flow velocity $U(Z)$ at stage Z is found from the airway morphometry (Weibel 1985). Depending on whether $P(Z)$ is larger or smaller than 1, the transport is due to convection or diffusion. At rest in the healthy human lung, the transition occurs within the acinus, three generations after the entrance. The diffusion unit to be considered is thus the 1/8 subacinus. During exercise, the air velocity

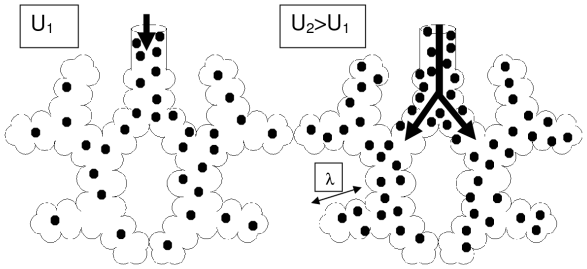

Figure 2. Schematized representation of diffusion screening and its dependence on the convection–diffusion transition represented by the arrowhead. The dots represent oxygen molecules. For small entrance velocity, the transition is close to the acinus entry and a non-uniform oxygen partial pressure may exist in the deeper regions. For a larger entrance velocity, the transition is deeper and the zones in which a partial pressure gradient may exist are smaller to the point that they may work in a quasi-uniform manner.

entrance increases and the transition moves deeper into the structure, around the 21st generation [2].

3. Diffusional screening in the acinus

Inside the region of the acinus where the gas transport is mostly diffusive, physiological parameters, geometrical characteristics and transport coefficients act in a complex way. For some values of these parameters, the system may exhibit 'screening effects' due to diffusion. Diffusional screening occurs when it is easier for oxygen molecules to cross the alveolar membrane near the entrance of the diffusion cell than to diffuse down to the more terminal regions of the acinus.

The existence of screening effects can be summarized into one number η ($0 < \eta < 1$) called the surface efficiency. It is the ratio of the real flux divided by the flux for infinite gas diffusivity. It measures the equivalent fraction of the acinus surface that can be considered as 'active'. So the total flux of oxygen in this model can be written as

$$\text{Flux} = S_{\text{lung}} \times W \times \eta \times (P_{\text{entrance}} - P_{\text{blood}}), \tag{2}$$

where S_{lung} is the developed acinar surface in the lung, P_{entrance} is the partial pressure of oxygen at the entrance of the acinus, and P_{blood} is the partial pressure of oxygen in the venous blood.

The surface efficiency of the acinus considered as a gas exchanger is then a crucial issue for respiration. A simple discussion of the process can be made by comparing the conductance to reach the surface by diffusion with the permeation conductance to cross the complex acinus surface. The parameters involved in these processes are the oxygen diffusivity, D and the membrane permeability, W. Consider a part of the acinus surface of area A and diameter L (diameter of the smallest sphere surrounding this part). The conductance to reach the surface is of order

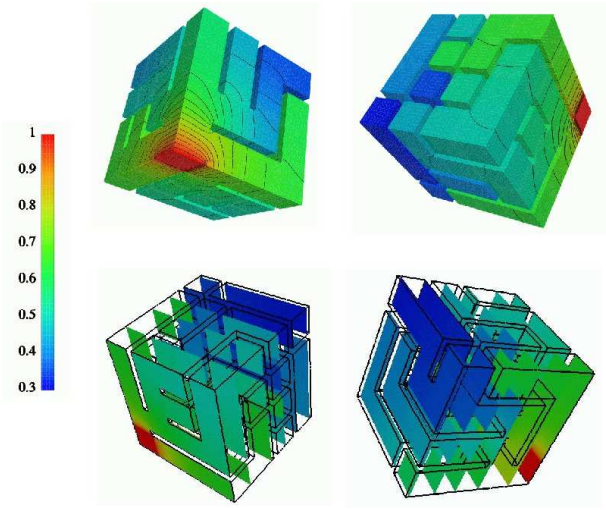

Figure 3. Three-dimensional simulations of the steady-state diffusion of oxygen in Kitaoka's model geometries of the human acinus at rest. The different shades represent various oxygen partial pressures. One can observe the non-uniform distribution of oxygen due to diffusion screening.

$Y_{\text{reach}} \approx DL$ whereas the conductance to cross $Y_{\text{cross}} = WA$. If the conductance to reach is larger than the conductance to cross ($Y_{\text{reach}} > Y_{\text{cross}}$), the surface works uniformly. But for a large enough system, the surface increases more rapidly than the diameter and one can have a situation where $Y_{\text{reach}} < Y_{\text{cross}}$. In that case, diffusion in the volume is a limiting step and the less accessible regions will receive little flux. In the language of physics theses regions are 'screened'. The transition between the screened and unscreened regimes is obtained when $Y_{\text{reach}} \approx Y_{\text{cross}}$, or equivalently $D/W \approx A/L$. The ratio $A/L = L_{\text{p}}$ is roughly the length of a planar cut of the surface, which is defined as the 'perimeter' of the surface. The length $\Lambda = D/W$ is called the unscreened perimeter length because a part of the surface that has its A/L value smaller than Λ will work uniformly.

For the normal values $D(\text{O}_2)$ and $W(\text{O}_2)$ in the healthy human lung, $\Lambda(\text{O}_2)$ is equal to 28 cm and the morphometrical data gives $L_{\text{p}} \approx 30$ cm for the 1/8 acinus. It has been shown that these two parameters are of the same order in many other mammals [2,3]. The fact that the purely physico-chemical length is comparable to the purely morphological perimeters of the acini of several mammals gives a clear evidence that screening should play a role in mammals' respiration. In particular, note that if the acini were too large, a major part of their surface would be inactive. This is the physical reason why the lungs have to be divided into a large number of small acini.

The surface efficiency of the human acinus at rest can be estimated either analytically [4], or through numerical simulations of the steady-state diffusion equation (figure 3) in a model geometry [5] that reproduces the key geometrical features of the acinus. The obtained values range from 30 to 40%, depending on the exact topology of the realization [6].

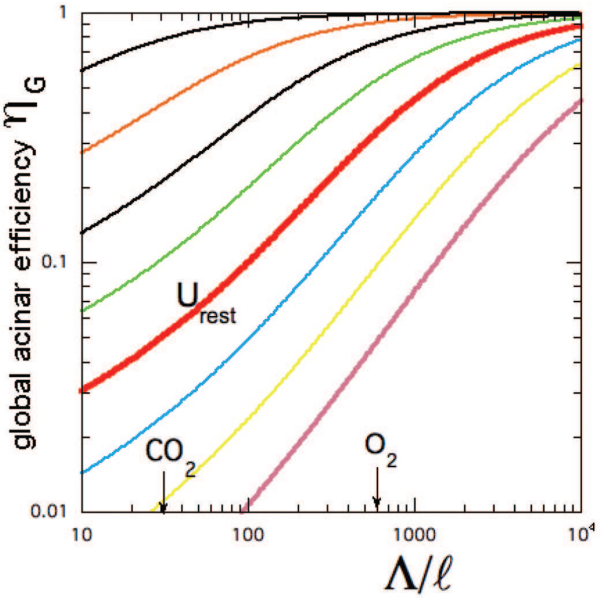

Figure 4. Global acinar efficiency as a function of the screening length for various air velocities at the acinus entrance. The unit length ℓ is equal to twice the alveoli diameter. The various curves correspond to entrance velocities increasing from $U_{\rm rest}/8$ by factors 2 up to $16U_{\rm rest}$. At rest velocity, the global efficiency for oxygen uptake is found to be equal to 0.32.

The global (unscreened + screened) flux can then be obtained together with the global acinus efficiency for various velocities at the acinus entrance [7]. The results are shown in figure 4. One observe that for the normal healthy lung the efficiency is about 30% at rest, and about 90% at exercise in which the entrance velocity is around 10 times the rest velocity.

One can summarize these results by saying that the nearness between the morphometric length $L_{\rm p}$ and the physical length Λ allows the acinus to work at 'the edge' of the diffusional screening: at rest, the acinus works with a reduced surface efficiency, of the order of 30%, while at exercise, the whole transfer capacity of the acinus is used [8]. This partial use of the transfer capacity of the acinar surface plays an important role, in particular in pulmonary diseases, as it procures a safety factor which may hinder the diagnosis of these diseases in their mild forms or in their early stages.

4. The impact of screening in pulmonary diseases

4.1 *Asthma or COPD*

In the case of severe asthma or COPD, the entrance velocity decreases and the efficiency decreases rapidly as shown in figure 4. On the other hand, for mild

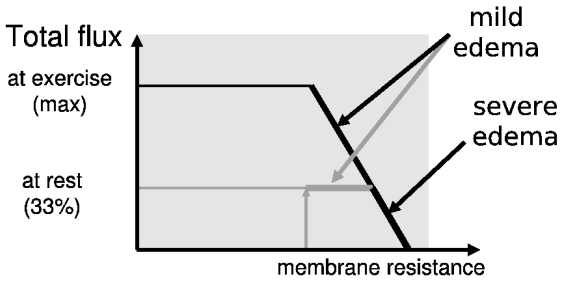

Figure 5. Schematic representation of the dependence of the net oxygen flux on an increase of the membrane resistance due to edema. The effect is very different at rest and at exercise (in the latter case, screening effects are small).

forms, if one assumes that the gas flux is kept constant (because muscular effort keeps the acinus inflation constant), although the diameters of the last bronchioles are reduced, the air velocity at the acinus entrance is increased. In that case, the diffusion source for oxygen enters more deeply into the acinus and the diffusion cell is smaller. This increases the diffusion efficiency and globally the oxygen uptake may remain approximately constant. Screening can then be seen as giving some natural protection against mild COPD. This could explain why COPD may remain silent: the patient can compensate the increase of the airway resistance by a stronger inspiratory effort. The same facts should apply to mild asthma.

4.2 *Emphysema*

In the frame of our model, mild emphysema can be modeled here as a loss of acinar surface. In the context of screening, it implies that a smaller surface works in a more uniform manner by increasing its efficiency. As a consequence, the two factors that determine the flux change in opposite sense. The very existence of screening gives a protection to respiration against mild emphysema, which can remain asymptomatic. This is no more true during exercise when the entire surface is working: the loss of exchange surface decreases the gas flux accordingly.

4.3 *Pulmonary edema*

In pulmonary edema the alveolar membrane permeability decreases. The permeability deterioration has two opposite effects: it decreases the flux directly, but at the same time, this is compensated by an increase of efficiency, at least at rest (see eq. (2) and figure 4). The combined effect of these factors for oxygen is schematically indicated in figure 5 where the global flux is given as a function of the ratio of the deteriorated membrane resistance to its value for the healthy case.

This means that the screening, to some extent, creates a protective effect for respiration. At the same time, it also means that mild edema may remain asymptomatic at rest. Let us mention that if one attributes the resistance increase to the

growth of a water film over the lung surface of order of 100 m^2, the quantity of water that would produce a diminution of the oxygen flux by a factor 2 is about 300–400 cm^3, a value consistent with clinical observations.

5. Conclusion

The oxygen transfer in the acinus has been analysed in this paper in a steady-state model, which is essentially valid during the peak inspiration phase. Screening effects play an even stronger role if one takes into account the complete respiratory cycle [9].

In summary, we have shown that diffusion is the 'dimensioning ruler' of the lung at the acinar level. The dimension of the acinus is such that diffusion screening exists at rest while it almost disappears at exercise. The very existence of this diffusion screening, which limits the efficiency of gas exchange at rest, provides the human respiration with a natural physical protection against mild aspects of several pulmonary diseases. The general qualitative statement arising from this fact is that, due to this natural safety factor, many of these diseases may remain asymptomatic. In a broader perspective, this phenomenon can be seen as a type of passive control for respiration.

Acknowledgments

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