THE OXYGEN-CARRYING FLASK: A REPRESENTATIONAL TRANSFORM OF THE OXYGEN DISSOCIATION CURVE OF HEMOGLOBIN

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The teaching of oxygen transport by hemoglobin is supported by a graphic depiction of the sigmoid $O_2$ dissociation curve of hemoglobin. However, a reconstruction of the same curve into an alternate paradigm, the “$O_2$-carrying flask,” affords a visual demonstration of the significance of its sigmoid shape and the implications of its shifts, which should be useful in elucidating certain aspects of $O_2$ transport to undergraduate students of physiology. This article provides a mathematical justification for the flask design.


Key words: oxyhemoglobin-dissociation; analogue model; teaching method

The $O_2$ saturation of hemoglobin at different partial pressures of $O_2$ ($P_{O_2}$) is ubiquitously depicted graphically by, and most physiology students are familiar with, the family of sigmoid $O_2$ dissociation curves (Fig. 1). However, the inadequacy of such a graphic representation for undergraduate teaching is demonstrated by the following problem: hemoglobin with high 2,3-diphosphoglyceric acid content, i.e., with a right-shifted $O_2$ dissociation curve, undergoes greater $O_2$ desaturation in the tissues but is less saturated with $O_2$ in the alveoli. What then is the net effect on the $O_2$ delivery to the tissues: an increase or a decrease? The answer depends on the arterial $P_{O_2}$ (Fig. 2). The cause of such a bimodal (increasing and decreasing) effect on $O_2$ delivery is not readily apparent from the conventional family of curves. It is here that the physical analogues of the curves, the “$O_2$-carrying flasks” (Fig. 3), provide a simple explanation. The pressure volume relationship of any fluid in these flasks of specific shapes would replicate the familiar sigmoid $O_2$ dissociation curves of hemoglobin with mathematical precision.

METHOD

The shapes of the flasks have been deduced from the formula relating the percentage of $O_2$ saturation of hemoglobin to the $P_{O_2}$ (1).

After the $O_2$ saturation-$P_{O_2}$ relationship has been differentiated, the values of saturation increments ($dS$) are halved and plotted symmetrically about the abscissa

$$\%\text{saturation (S)} = \frac{(1/kP_{O_2} + 1)^3 + m - 1}{(1/kP_{O_2} + 1)^3 + m - 1}$$

where $k$ and $m$ are variables that change with shifts in the $O_2$ dissociation curve.

Differentiating

$$dS/dP_{O_2} = \frac{R^6 + 4R^3(m - 1) - 3R^2}{[kP_{O_2}^2(R^4 + m - 1)^2]}$$

where $R = 1/kP_{O_2} + 1$

USING THE MODEL

The shape thus obtained can be utilized in several ways. The simplest method would be to calculate the volume of fluid in the flask when filled to different heights and plot a pressure-volume curve. For volume calculation, the area in the flask under the fluid level may be measured by the simple
O₂ dissociation curves of hemoglobin (left-shifted, normal, and right-shifted), plotted using Margaria's equation (1). Shifts have been deliberately exaggerated so that corresponding "flasks" (Fig. 3, A and C) have distinct contours. Pₒ₂, partial pressure of O₂.

graphic method. With the assumption that the flask has flat opposing surfaces, the volume of the flask would be proportional to the area measured out. Alternatively, the shape of the flask can be built into an apparatus giving direct readouts of the pressure head as well as the volume of fluid flowing in or out of the flask. The same effect can also be achieved through a computer simulation.

It may be noted that the absolute values of pressure and volume are irrelevant in the present context; what is important here is the sigmoid relation between the two, irrespective of their absolute values and units. Nevertheless, it should not be difficult to generate from these flasks a set of values of pressure and volume that correspond numerically to the familiar values encountered in the conventional discussion of O₂ transport. This can be done either by manipulating the actual dimensions of the flasks (keeping the relative widths at different heights unchanged) or by choosing a fluid with a suitable specific gravity. Such latitudes also make it possible to use the flask for denoting the O₂ carried by different quanta of hemoglobin (e.g., 1 g of hemoglobin, 100 ml of blood, or 5 liters of blood) as preferred by individual teachers.

"O₂-carrying flasks" representing hemoglobin with left-shifted (A), normal (B), and right-shifted O₂ dissociation curves (C). Widths and heights of flasks are represented in abscissa and ordinate, respectively, in arbitrary scales. Width scale is inconsequential (any scale would suffice); hence none is shown. Lines I and II indicate relative levels to which O₂ at partial pressures of 95 mmHg (normal arterial Pₒ₂) and 40 mmHg (normal venous Pₒ₂), respectively, would fill up flask.
CONCLUSION

The concept of the “O₂-carrying flask” lends a picturesque insight to the O₂-carrying capacity of hemoglobin. For instance, it may be stated that the normal O₂ requirements of the body can be met with the O₂ present in the slender neck of the flask. The bulk of the O₂ is stored in the capacious base of the flask to meet the exigencies of hypoxia. The arterial Po₂ determines the level to which the flask is filled up with O₂, and the venous Po₂ determines the level to which it is emptied. In mildly to moderately hypoxic hypoxia, which occurs at high altitudes, it is advantageous to have a flask with a wider neck at the expense of a less capacious base (Fig. 3C), a difference which would show up graphically as a right shift of the O₂ dissociation curve. In more severe hypoxia, as faced by the fetus in utero, the neck of the flask is not filled. It then becomes more advantageous to increase the capacity of the base at the expense of constricting the neck (Fig. 3A). This would be equivalent to a left-shifted O₂ dissociation curve, as indeed it is in fetal hemoglobin.

Experiences in the classes and the feedback obtained from the students suggest that a representational transform such as this is a useful adjunct to conventional graphs in understanding the dynamics of O₂ transfer by hemoglobin.

Reference


Teachers and their students may find the following article from News In Physiological Sciences useful when exploring the physiology of the preceding paper: