Modeling Cooperative Binding with the Hill Equation

This page contains information extracted from one section of Integrating Concepts in Biology. There is a short introduction and then a data figure. Your task is to interpret and manipulate a mathematical model for the data in the figure by answering the Integrating Questions. This sample has been reformatted for this DIBS workshop.

Cooperativity is an emergent property of hemoglobin that increases its capacity to bind a lot of oxygen when the concentration of O_2 changes very little, as shown in Figure 13.1. Hemoglobin is able to bind oxygen cooperatively because it has four subunits. Once the first oxygen molecule has bound to a subunit of hemoglobin, the other three bind very rapidly. Archibald Hill developed an equation that closely fits the data in Figure 13.1 for oxygen saturation of a hemoglobin solution. The Hill equation has become one of the most famous and useful equations in biology, because it can be applied in any situation where ligands bind to receptors. This synopsis of BME 13.1 and the accompanying Excel file CH13_hemoglobin.xlsx lets you experiment with the Hill equation. If x is the concentration of oxygen, and y is the percent oxygen saturation of hemoglobin, the Hill equation says that $y = x^n/(k^n + x^n)$, where k is a positive constant. You will discover the role of k and n in the integrating questions.

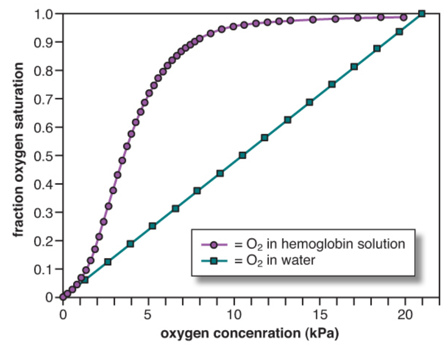

Figure 13.1 Solubility of gaseous O_2 in water and hemoglobin solutions. The units of oxygen concentration in the air over the liquids are kilopascals (kPa). Original Art with help from Durwin Striplin, Davidson College Chemistry Dept. Raw data from Severinghaus, 1979, his table I.

Bio-Math Exploration Integrating Questions

1. What percent oxygen saturation *(y)* is predicted by the Hill equation when the concentration of oxygen *(x)* is equal to *k?* In light of your result, what biological interpretation does the constant *k* have in the Hill equation?
2. Enter this Wolfram Alpha command to graph the Hill equation for k = 3 and n = 1, 2, 3 and 4. From these four curves, describe the effect that changing the value of *n* has on the shape of the Hill equation. Where do these four curves intersect? Why?
3. Open the Excel file CH13_hemoglobin.xlsx, which contains the data on oxygen saturation of hemoglobin from Figure 13.1 and a Hill equation model for the data. Change the values of *k* and *n* at the top of the sheet labeled "Hill equation" to find the best fit to the hemoglobin data, judging by the similarity of the two curves in the graph.

As you discovered in BME Integrating Question #1, the value of k is the concentration of oxygen for which the oxygen saturation is 50% (approximately 3.5), and all four graphs of the Hill equation went through that point because the value of n does not affect the value of y when $x = k$. The value of n is a measure of cooperative binding, and it controls the steepness of the curve. A large value of n produces a large increase in the percent of binding sites occupied for a relatively small increase in the amount of oxygen available. Mathematical models can help you make biological predictions. From the Hill equation, you can deduce that hemoglobin works through cooperative binding, and that it goes through transitions in its affinity for oxygen as the concentration of oxygen increases.