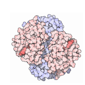
Lecture-00-Hemoglobin

Quantitative Biochemistry

- My name is Dr Philip Fowler and my undergraduate was in Physics, my PhD in Chemistry and I spent ten years in the Department of Biochemistry before moving up to the John Radcliffe to establish my own research group investigating antibiotic resistance.
- I took this course over in 2020 from Professor Elspeth Garman who gave this course and developed it over 25 years. About ten years ago I was a class tutor on this course.
- Please feel free to email me with any suggestions (or any other thoughts). My email is philip.fowler@ndm.ox.ac.uk.
- This term we have 12 lectures to introduce you to the mathematics you need for biochemistry. Next term someone else will introduce the statistics you need.

Hemoglobin



Hemoglobin (Hb) has four oxygen binding sites so we can write

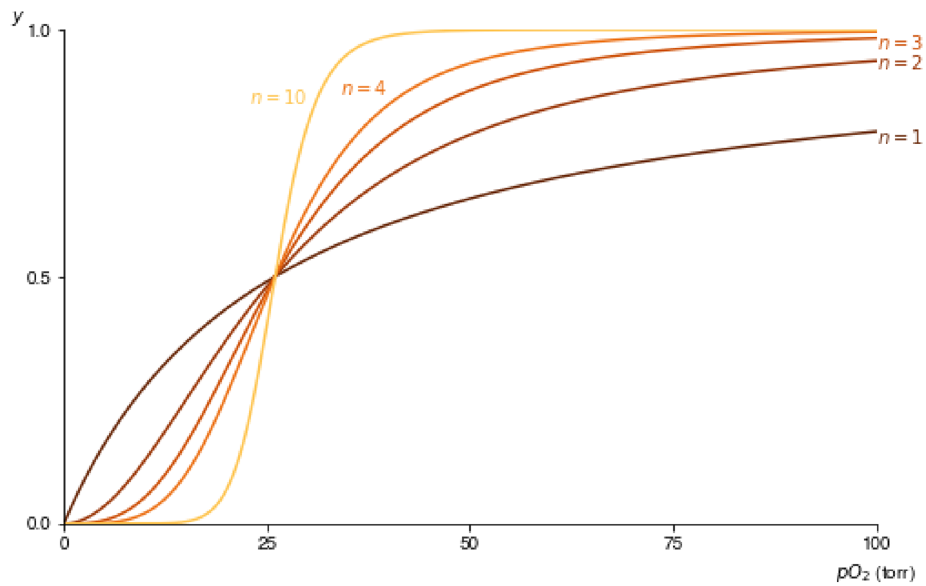
$$Hb(O_2)_n \leftrightharpoons Hb + nO_2$$

where $n \leq 4$

The binding of oxygen to hemoglobin is described by the *Hill equation*

$$Y = \frac{(pO_2)^n}{(pO_2)^n + (P_{50})^n}$$

where Y is the fraction of binding sites occupied by oxygen molecules, pO_2 is the partial pressure of oxygen (analogous to concentration) and P_{50} is a measure of affinity.



How we measure n?

I can't draw curves like those above – we **always** have to convert the function into the form of a straight line and then measure the gradient and y-intercept.

$$
\begin{aligned}
Y &= \frac{(pO_2)^n}{(pO_2)^n + (P_{50})^n} \\
Y &= \frac{\left(\frac{pO_2}{P_{50}}\right)^n}{\left(\frac{pO_2}{P_{50}}\right)^n + 1} \\
Y\left(\left(\frac{pO_2}{P_{50}}\right)^n + 1\right) &= \left(\frac{pO_2}{P_{50}}\right)^n \\
Y &= \left(\frac{pO_2}{P_{50}}\right)^n (1 - Y) \\
\frac{Y}{1 - Y} &= \left(\frac{pO_2}{P_{50}}\right)^n
\end{aligned}
$$

Hmm, is that simpler?? Well if we take the logarithms of both the LHS and RHS and apply the log laws (more later!) we can simplify it…

$$
\begin{aligned}
\ln\left(\frac{Y}{1-Y}\right) &= \ln\left(\frac{pO_2}{P_{50}}\right)^n \\
&= n\ln\left(\frac{pO_2}{P_{50}}\right) \\
\ln\left(\frac{Y}{1-Y}\right) &= n\ln(pO_2) - n\ln(P_{50})
\end{aligned}
$$

this looks like

$$y = m.x + c$$

i.e. if we plot $\left(\frac{Y}{1-Y}\right)$ against $\ln(pO_2)$ the gradient is n and the y-intercept is $-n\ln(P_{50})$.

We are now in position where we can take measurements in an experiment and, by plotting a graph in the form above, can estimate n and P_{50}!