Calculation of hemoglobin oxygen saturation in the presence of CO – HbO2CO.doc

L. Hoofd – 29 October 2013

Oxygen and carbon monoxide compete at the same heme binding locations so that the saturation curve can be used – assuming the Hill curve here – with a combined pressure:

$$F = \frac{(P_{O2} + M\,P_{CO})^n}{P_{50}^n + (P_{O2} + M\,P_{CO})^n} \tag{1}$$

where F is the fraction of Hb occupied with either gas, P_{50} is the 50% saturation pressure of oxygen (under normal, CO-free circumstances), n is the Hill parameter of cooperativity, and M is binding strength factor (about 250 for human Hb). Note, that the CO's $P_{50,CO}$ is P_{50}/M. The relation between the amounts of O_2Hb and COHb is given by:

$$\frac{[COHb]}{[O_2Hb]} = \frac{M\,P_{CO}}{P_{O2}} \tag{2}$$

Full deoxygenation is reached for $P_{O2} = 0$ so that in that case the CO fraction is

$$F_{CO} = \frac{(M\,P_{CO,0})^n}{P_{50}^n + (M\,P_{CO,0})^n} = \frac{P_{CO,0}^n}{(P_{50}/M)^n + P_{CO,0}^n} \tag{3}$$

When oxygen binds to the hemoglobin, P_{CO} will be increased above $P_{CO,0}$ due to the competition of O_2 and CO. However, the amounts of CO involved are very small – because of the large M - so that F_{CO} remains virtually unchanged. Therefore, the combined binding can be handled with a fixed F_{CO} and the results expressed in terms of that fraction.

Then, the amount available for O_2 is $1-F_{CO}$ and 50% saturation is reached for a total bound fraction of $F = F_{CO}+F_{O2} = F_{CO} + ½(1-F_{CO}) = ½(1+F_{CO})$ so that the apparent 50% saturation pressure P^*_{50} is determined by:

$$½(1+F_{CO}) = \frac{(P^*_{50} + M\,P^*_{CO})^n}{P_{50}^n + (P^*_{50} + M\,P^*_{CO})^n} \tag{4}$$

where P^*_{CO} is the corresponding CO pressure; according to eq.(2):

$$\frac{F_{CO}}{½(1-F_{CO})} = \frac{M\,P^*_{CO}}{P^*_{50}} \tag{5}$$

Eq.(4) can be reworked as:

$$P^*_{50} + M\,P^*_{CO} = P_{50}\left(\frac{1+F_{CO}}{1-F_{CO}}\right)^{1/n} \tag{6}$$

which can be combined with eq.(5):

$$P^*_{50} + M\,P^*_{CO} = P^*_{50} + \frac{F_{CO}}{½(1-F_{CO})}\,P^*_{50} = P^*_{50}\left(\frac{1+F_{CO}}{1-F_{CO}}\right) = P_{50}\left(\frac{1+F_{CO}}{1-F_{CO}}\right)^{1/n} \tag{7}$$

so that:

$$\boxed{P^*_{50} = P_{50}\left(\frac{1-F_{CO}}{1+F_{CO}}\right)^{1-1/n}} \tag{8}$$

is the apparent oxygen P_{50} of the complex.

The Hill constant is defined from the slope of the saturation curve at half saturation. From eq.(1):

$$\frac{dF}{dP_{O2}} = \left(1 + M\frac{dP_{CO}}{dP_{O2}}\right)\frac{n\,P_{50}^n\,(P_{O2} + M\,P_{CO})^{n-1}}{\{P_{50}^n + (P_{O2} + M\,P_{CO})^n\}^2} \tag{9}$$

so that, also using $F = F_{O2}+F_{CO}$ in the left-hand term:

$$(P_{O2} + M\,P_{CO})\frac{dF_{O2}}{dP_{O2}} = \left(1 + M\frac{dP_{CO}}{dP_{O2}}\right) n\,F\,(1-F) \tag{10}$$

At half-saturation, $P_{O2} = P^*_{50}$, this is, also using eq.(7):

$$P^*_{50}\left(\frac{1+F_{CO}}{1-F_{CO}}\right)\frac{dF_{O2}}{dP_{O2}}(P^*_{50}) = \left\{1 + M\frac{dP_{CO}}{dP_{O2}}(P^*_{50})\right\}\frac{n}{4}(1-F_{CO}^2) \tag{11}$$

so that in the case of no CO, $P_{CO} = F_{CO} = 0$, $P^*_{50} = P_{50}$ and $F_{O2} = S_{O2}$:❶

$$n = 4\,P_{50}\,\frac{dS_{O2}}{dP_{O2}}(P_{50}) \tag{12}$$

And consequently, for the CO case, $F_{CO} \neq 0$, where $S_{O2} = F_{O2}/(1-F_{CO})$:

---

❶ Strictly, this derivation has to be done not considering CO at all, since otherwise the term dP_{CO}/dP_{O2} might be problematic

$$n^* = \frac{4\,P^*_{50}}{1-F_{CO}}\,\frac{dF_{O2}}{dP_{O2}}(P^*_{50}) \tag{13}$$

To solve for n*, we also have to use eq.(2) now written as:

$$F_{CO}\,P_{O2} = F_{O2}\,M\,P_{CO} \tag{14}$$

and take the derivative to P_{O2}:

$$F_{CO} = \frac{dF_{O2}}{dP_{O2}}\,M\,P_{CO} + F_{O2}\,M\,\frac{dP_{CO}}{dP_{O2}} \tag{15}$$

Again, at half-saturation, with some rearrangement and substituting $F_{O2} = ½(1-F_{CO})$:

$$½(1-F_{CO})\,M\,\frac{dP_{CO}}{dP_{O2}}(P^*_{50}) = F_{CO} - \frac{dF_{O2}}{dP_{O2}}(P^*_{50})\,M\,P^*_{CO} \tag{16}$$

Now, the left-hand side can be substituted into eq.(11) also substituting eq.(5) for $M\,P^*_{CO}$:

$$P^*_{50}\left(\frac{1+F_{CO}}{1-F_{CO}}\right)\frac{dF_{O2}}{dP_{O2}}(P^*_{50}) = \frac{n}{4}(1-F_{CO}{}^2) + \frac{n}{2}(1+F_{CO})\left\{F_{CO} - \frac{dF_{O2}}{dP_{O2}}(P^*_{50})\,\frac{2\,F_{CO}}{1-F_{CO}}\,P^*_{50}\right\} \tag{17}$$

which can be rearranged to:

$$P^*_{50}\left(\frac{1+F_{CO}}{1-F_{CO}}\right)(1+n\,F_{CO})\frac{dF_{O2}}{dP_{O2}}(P^*_{50}) = \frac{n}{4}(1+F_{CO})^2 \tag{18}$$

so that for n*:

$$\boxed{n^* = n\,\frac{1+F_{CO}}{1+n\,F_{CO}}} \tag{19}$$

NOTE:

The above formulas have limited applicability since the Hill curve is an approximation only valid for the middle region of the saturation curve. For high F_{CO}, in the upper part of the curve, the P^*_{50} will have a minimum value according to the binding strength of the fourth oxygenation step of hemoglobin and the n* will approach 1 – and not 2n/(1+n) – because the last binding step is a simple non-cooperative binding. There will be an upper limit for F_{CO} which could be derived following the above treatment now using a four-step binding mechanism for hemoglobin such as the MWC scheme. However, such high F_{CO}s are unphysiologic (as are low P_{O2}s) so that in realistic situations the above formulas can be applied.

Also, nothing is said about the shape of the curve. It is an additional assumption that this is still adequately described also for saturations deviating form 50% – around 50%, it is proven to be correct.