Inverse solutions of the Severinghaus and Thomas equations which allow $P\mathrm{o}_2$ to be derived directly from $S\mathrm{o}_2$

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Abstract

Background. The motivation for this study was the need for inverse solutions of the Severinghaus and Thomas equations, in order to allow P_{O_2} to be derived directly from saturation and hence obviating the need to use an iterative method.

Methods. Both the Severinghaus equation (1979) and Thomas equation (1972) were investigated to see if convenient inverse solutions yielding P_{O_2} from S_{O_2} could be derived.

Results. Inverse solutions were derived for both equations, and tested using standard equation solving software. The derivations of the two solutions are presented.

Conclusion. The inverse solutions for P_{O_2} from S_{O_2} for these two equations represent a useful addition to the anaesthetist's mathematical 'toolbox'.

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1 Introduction

A recent paper by Hope *et al.* [1] described a non-invasive technique for estimating venous admixture using an iterative method for determining arterial oxygen tension (Pa_{O_2}) from haemoglobin saturation (Sa_{O_2}) using the Thomas equation [2]. The Thomas equation represents a significant improvement on a similar one derived by Kelman [3]. A slightly simpler equation with very similar functionality is that of Severinghaus [4].

Unfortunately however, both these equations are formulated to yield saturation from oxygen tension, and consequently an iterative computer method is currently required when performing the process in reverse, i.e. when determining oxygen tension from a known saturation. In view of this problem, and the increasing use of realtime computation in anaesthesia, it was decided to derive inverse solutions for these two useful equations, and these are presented in the present article.

2 The Severinghaus equation[2]

The oxyhaemoglobin dissociation curve is usually modeled from the set of saturation and oxygen tension data determined by Severinghaus [4,5,13] for human blood having a normal temperature, pH and P_{CO_2}, which represents the standard 'oxygen haemoglobin equilibrium curve' OHEC [6]. Severinghaus' modification [4] of the Hill equation is a cubic model of the *in vivo* oxyhaemoglobin dissociation curve. This equation was originally formulated as

$$s = (((p^3 + 150p)^{-1} \times 23400) + 1)^{-1} \tag{1}$$

for use with a calculator, where s is the fractional oxygen saturation (0–1) and p is the associated oxygen tension in mm Hg. Severinghaus clearly saw that the inverse equation would be useful (e.g. for determining P_{50}). Equation 1 was solved for PO_2 by Ellis [14] (1989).

Particular solution

Rearranging Equation 1 gives the following so-called '*reduced*' cubic equation

$$p^3 + 150p - 23400\left(\frac{s}{1-s}\right) = 0, \tag{2}$$

which can then be solved using a standard method [7]. The resulting exact physiological solution (the mathematically 'real' root), which gives the oxygen tension p as a function of the saturation s, is shown as Equation 3 (cf. Ellis [14] 1989),

$$p = \sqrt[3]{\frac{1}{2}\left(-y_N + \sqrt{y_N^2 - h^2}\right)} + \sqrt[3]{\frac{1}{2}\left(-y_N - \sqrt{y_N^2 - h^2}\right)}, \tag{3}$$

where

$$\begin{cases} h^2 = -500000, \\ y_N = -23400s/(1-s). \end{cases}$$

It is significant that Equation 2 has the same single real root configuration for the range $0 \le s \le 1$, and consequently Equation 3 holds throughout the physiological range.

[2]For some history and insight regarding this equation see Severinghaus' recent lecture on translational science (Severinghaus, 2009; p 726) [13], and also the revised version of his 1979 paper [4].

Results

Values returned from Equation 3 (see Table 1) were compared with those derived from Equation 2 using the Perl equation solving module *Math::Polynomial::Solve*[8], on a Mandrake-Linux PC using Perl v.5.8.1. These values were in complete agreement.

For example, if $s = 0{\cdot}5$ then $s/(1-s) = 1$ and so $y_N = -23400$. Substituting these in Equation 3 gives $p = 28{\cdot}604 - 1{\cdot}747 = 26{\cdot}857$ mm Hg, which agrees exactly with Severinghaus' observation[4] that "P_{50} *with Equation 1 is* 26·86*, compared with* 26·67 *in the standard curve*". The exact values in mm Hg for the case $s = 0{\cdot}5$ are as follows:

Equation 2 : 26·856
Equation 3 : 26·856

3 The Thomas equation

The Thomas modification[2] of the Kelman equation[3] is a quartic model for the *in vivo* oxyhaemoglobin dissociation curve. The Thomas equation[2] gives the fractional haemoglobin saturation s (0–1) as a function of oxygen tension p (mm Hg), as follows,

$$s = \frac{p^4 + Ap^3 + Bp^2 + Cp}{p^4 + Ap^3 + Dp^2 + Ep + F}, \tag{4}$$

where $p = -P\mathrm{a}_{\mathrm{O}_2} \times 10^{0{\cdot}48(\mathrm{pH}-7{\cdot}4)-0{\cdot}024(T-37)-0{\cdot}0013(BE)}$, $A = 15$, $B = 2045$, $C = -2000$, $D = 2400$, $E = 31100$, and $F = 2400000$.

The inverse solution of Equation 4, giving the oxygen tension p for a given fractional saturation s, is shown as Equation 5 (see Figures 1-4)

$$p = p_N + \sqrt{r_1} - \sqrt{r_2} - \sqrt{r_3} \tag{5}$$

where p_N, r_1, r_2, r_3 are parameters derived from s and the coefficients A–F (see Appendix for derivation).

Values returned from Equation 5 (see Table 1) were compared with those derived from Equation 4 (using Equation 6) using the method described in Section 2, and found to be in complete agreement. For example, the exact values in mm Hg for the case $s = 0{\cdot}5$ are as follows (note that the negative sign arises from the way Thomas originally formulated his equation).

Equation 4 : −26·907
Equation 5 : −26·907

Table 1: Data generated by the derived inverse equations of Severinghaus (Equation 3) and Thomas (Equation 5).

	Oxygen tension (mm Hg)	
Saturation	Severinghaus [4]	Thomas [2]
0	0	0
0·10	10·21900	10·31184
0·20	15·26876	15·07883
0·30	19·25613	19·10322
0·40	22·99020	22·94330
0·50	26·85680	26·90743
0·60	31·21584	31·30776
0·70	36·61968	36·63698
0·75	40·04036	39·94493
0·80	44·30276	44·01368
0·85	50·01306	49·41240
0·90	58·65543	57·60025
0·91	61·04142	59·88959
0·92	63·78672	62·55021
0·93	67·00533	65·71481
0·94	70·87137	69·59593
0·95	75·66809	74·56080
0·96	81·89811	81·31437
0·97	90·57305	91·43363
0·98	104·18789	109·41959
0·99	131·93953	155·47307

4 Discussion

The required inverse solution to the Thomas equation represents only one particular root of the general solution (the negative real root). We are fortunate that throughout the physiological range of fractional saturation, the inverse Thomas equation ($F(p) = 0$) has the same geometric discriminant [8] and hence root configuration (two real roots and two complex roots), and consequently we are able to identify a particular solution which holds in all cases of interest.

Since the Severinghaus and Thomas equations were originally derived using 'best-fit' methodology while working in mm Hg, it was felt best to retain the same units. If translation to kPa is required, this is optimumly performed as a one-step final conversion; a suitable conversion factor being 7·50062 mm Hg/kPa given by Kaye and Laby [12] (see line 28 in the Perl program in the Appendix).

5 Appendix (Thomas eqn)

5.1 Solution

Equation 4 can be rewritten as follows.

$$F(p) \equiv (1-s)p^4 + A(1-s)p^3 + (B-sD)p^2 + (C-sE)p - sF = 0. \qquad (6)$$

Let $a = (1-s)$, $b = A(1-s)$, $c = (B-sD)$, $d = (C-sE)$, $e = -sF$, giving

$$F(p) \equiv ap^4 + bp^3 + cp^2 + dp + e = 0, \qquad (7)$$

with roots p_1, p_2, p_3, p_4, (let p_1 denote the required root, i.e., the negative real root), and [9]

$$\begin{cases} p_{_N} = \dfrac{-b}{4a}, \\ \varepsilon^2 = \dfrac{(3b^2-8ac)}{48a^2}, \\ I = 12ae - 3bd + c^2, \\ J = 72ace + 9bcd - 27ad^2 - 27eb^2 - 2c^3. \end{cases} \qquad (8)$$

Let the quartic's reduced form $Z(x)$ (with roots z_1, z_2, z_3, z_4) be generated by the translation [9] $(p - p_{_N}) \mapsto x$,

$$Z(x) \equiv F(x + p_{_N}) \equiv ax^4 - 6a\varepsilon^2 x^2 + y_{N_{Z'}} x + y_{N_Z},$$

where $y_{N_Z} = F(p_{_N})$ and $y_{N_{Z'}} = F'(p_{_N})$. Let its resolvent cubic $R(x)$ have an unscaled reduced form $S(x)$, which is typically scaled to the form $T(x)$, as follows [9]:

$$S(x) \equiv x^3 - \frac{I}{48a^2}x + \frac{J}{1728a^3} = 0,$$

$$T(x) \equiv x^3 - 3Ix + J = 0,$$

with roots t_i $(i = 1,2,3)$. Since it turns out that for the saturation range $0 \le s \le 1$ the equation $T(x) = 0$ has only a single real root, then the real [7] root (t_1) and complex [10] roots (t_2, t_3) are as follows.

$$t_1 = \sqrt[3]{\frac{1}{2}\left(-J + \sqrt{J^2 - 4I^3}\,\right)} + \sqrt[3]{\frac{1}{2}\left(-J - \sqrt{J^2 - 4I^3}\,\right)},$$

$$t_2, t_3 = \frac{-t_1}{2} \pm j\frac{\sqrt{3}}{2}\sqrt{t_1^2 - 4I}.$$

where $j^2 = -1$.

If the roots of $R(x) = 0$ are r_i $(i = 1,2,3)$, then it can be shown [9] that $r_i = \varepsilon^2 + t_i/12a$. The required root p_1 is then given by $p_1 = p_{_N} + z_1$ where $z_k = \pm\sqrt{r_1} \pm \sqrt{r_2} \pm \sqrt{r_3}$ $(k = 1,2,3,4)$. We just need to determine which of the four possible mathematical roots z_k is the appropriate root for our purposes, say, z_1 (see below).

Since the algebraic discriminant $4I^3 - J^2$ of the reduced quartic $Z(x)$ remains negative for the whole saturation range $(0 \le s \le 1)$ it follows that the quartic root configuration also remains constant for the whole saturation range. Equation $T(x)$ will therefore also maintain the same root configuration for the whole saturation range, and closer inspection reveals that this configuration is one positive real root and two negative complex roots.

After some experimentation, the required root of the reduced quartic (the negative real root z_1) is found to be given by

$$z_1 = \sqrt{r_1} - \sqrt{r_2} - \sqrt{r_3}, \tag{9}$$

where

$$\begin{aligned} r_1 &= \varepsilon^2 + (t_1/12a), \\ r_2 &= \varepsilon^2 + (t_2/12a), \\ r_3 &= \varepsilon^2 + (t_3/12a). \end{aligned}$$

Finally, since $p_1 = p_N + z_1$, we obtain

$$p_1 = p_N + \sqrt{r_1} - \sqrt{r_2} - \sqrt{r_3}. \tag{10}$$

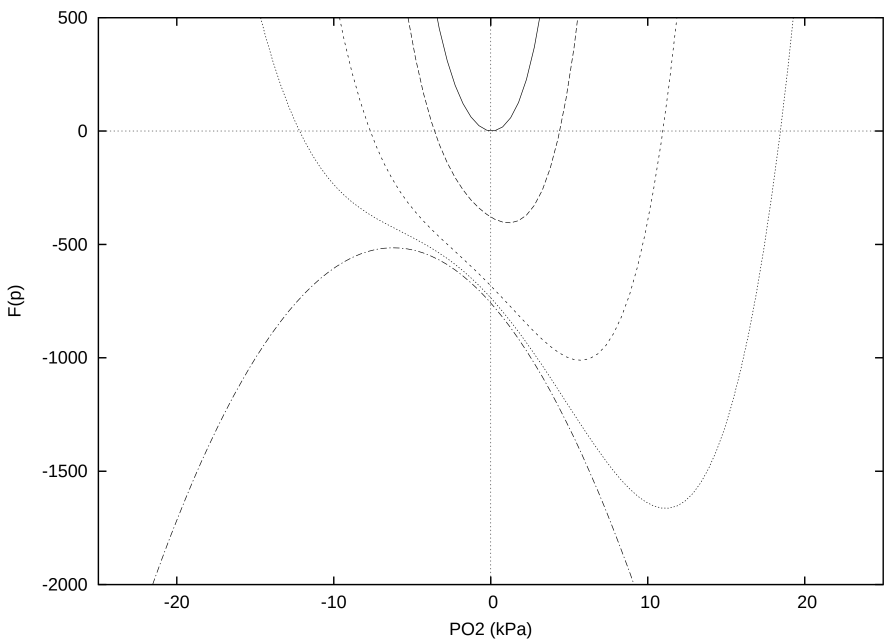

Figure 1: Quartic $F(p)$ for values of $s = 0, 0{\cdot}5, 0{\cdot}9, 0{\cdot}97, 1{\cdot}0001$ (from above down respeectively). Note that the root configuration (two real roots; two complex roots) is the same for $0 < s < 1$, since within this range of s the sign of the quartic discriminant remains the same. The significance of this is that for a given quartic solving program the required root, say r_1 will keep the same position in the root array, and hence greatly facilitates extraction of the correct root. Note that the curve inverts for $s > 1$ since the leading coefficient a is then negative as $a = 1 - s$ (see Equation 6).

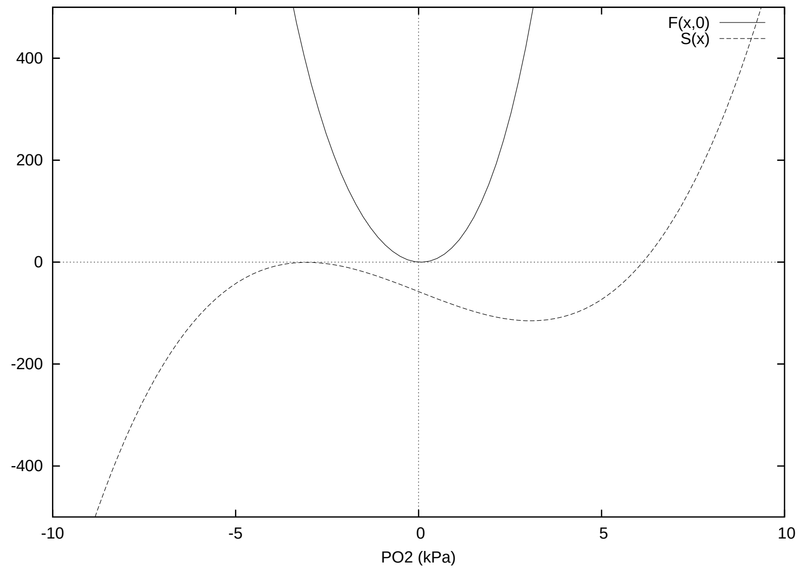

Figure 2: $F(p)$ and $S(x)$ for $s = 0$.

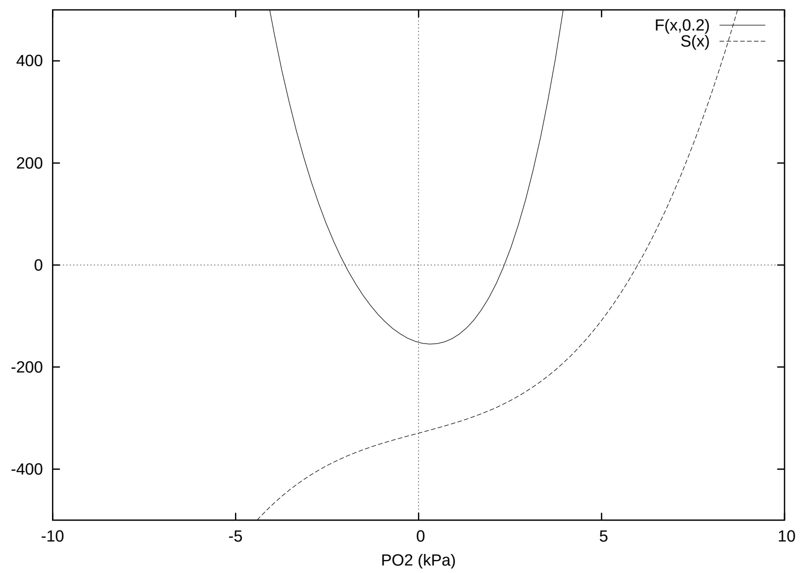

Figure 3: $F(p)$ and $S(x)$ for $s = 0{\cdot}2$.

5.2 Program

The following Perl 5 program solves the inverse Thomas equation using the *Math* :: *Polynomial* :: *Solve* module [11] (line 6).

```
1  #!/usr/bin/perl
2  # thomas-eqn.pl
3  #--------------------
4  -w;      #warning switch
5  use Math::Complex;    #complex maths library
6  use Math::Polynomial::Solve qw(quartic_roots);
7  #----------------------
8  $AA=15, $BB=2045, $CC=-2000, $DD=2400, $EE=31100,
      $FF=2400000;
9  print "sat (s), p (mmHg), p (kPa)\n";
10 # range 0.1-0.9
11   for($s=0.1;$s<=0.89;$s=$s+0.1){sat($s)};
12 # range 0.91-0.99
13   for($s=0.9;$s<=0.99;$s=$s+0.01){sat($s)};
14 # range 0.991-0.999
15   for($s=0.99;$s<1;$s=$s+0.001){sat($s)};
16 #--------------------------------
17 sub sat{
18       my ($s) = @_;
19       my $k=7.50062;   ##mmHg to kPa
20       # solve the quartic F(p)=0;
21       $a=(1-$s), $b=$AA*(1-$s), $c=$BB-$s*$DD,
            $d=$CC-$s*$EE, $e=-$s*$FF;
22       ($x1, $x2, $x3, $x4) =
            quartic_roots($a,$b,$c,$d,$e);
23       $x4kpa = $x4/$k; # required root is x4
24       print "$s, $x4, $x4kpa\n";
25         }
```

Notes:

—line 8: the constants determined by Thomas.

—lines 10–15: a series of **for** statements for calling the `sat()` subroutine for each range of saturation (s) values.

—lines 17–25: the subroutine which solves the quartic for a given value of stauration (s).

—line 19: the constant for converting mmHg to kPa.

—line 22: solving the quartic: the roots are placed in the array x_1–x_4. Note that since the sign of the discriminant remains the same for the whole saturation range ($0 < s < 1$) then the required root will always be the same one—x_4 in this particular case as determined by some initial experimentation).

—line 23: the value x_4 (in mmHg) is converted to kPa.

5.3 Results

```
using M::P::Solve = version 2.12
using Math::Complex = version 1.54

Thomas equation
sat (s),  p (mmHg),        p (kPa)
0.1, -10.3118413594488, -1.37479853124792
0.2, -15.0788301616509, -2.01034449974148
0.3, -19.1032293500069, -2.54688670403339
0.4, -22.9433035257091, -3.05885427147477
0.5, -26.9074365885018, -3.58736165656996
0.6, -31.3077609839598, -4.17402307862015
0.7, -36.6369882213363, -4.88452797519889
0.8, -44.0136836554275, -5.86800606555558
0.9, -57.6002520295602, -7.67939877364274
0.91, -59.8895976421806, -7.98461962373519
0.92, -62.5502106169618, -8.3393386969293
0.93, -65.7148179129474, -8.76125145827244
0.94, -69.5959304947859, -9.27869036090162
0.95, -74.5608031892216, -9.94061866741971
0.96, -81.3143718398646, -10.8410200543241
0.97, -91.4336374115412, -12.1901439363068
0.98, -109.41959580099, -14.5880734927233
0.99, -155.473070010936, -20.7280291510483
0.991, -164.665392103243, -21.9535707852475
0.992, -175.727554456875, -23.4284038461988
0.993, -189.315503679396, -25.2399806521856
0.994, -206.448597837887, -27.5242043774898
0.995, -228.820748459624, -30.5069112232887
0.996, -259.518189495934, -34.599565035415
0.997, -304.970870613725, -40.6594215696469
0.998, -381.808147071796, -50.9035449165264
0.999, -556.081895296556, -74.1381239546273
```

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