Human Decompression Modelling

Problem presented by

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Executive Summary

At present, no decompression algorithm is able to predict safe decompression for all dive scenarios. In practice, empirical adjustments are made by experienced organisations or divers in order to improve decompression profiles for the range of depths and durations needed on any particular dive. Bubble formation and growth in the human body are the fundamental causes of decompression sickness, and it is believed that there is significant scope for incorporating better modelling of these processes into the design of decompression algorithms.

VR Technology is a leading supplier of technical dive computers. The company is interested in expanding upon an existing algorithm (the Variable Gradient Model - VGM), which is used to design ascent profiles/decompression schedules and thereby mitigate the risk of decompression sickness in divers.

The Study Group took the approach of trying to extend the existing Haldane model to account more explicitly for the formation of bubbles. By extending the model to include bubble dynamics it was expected that some physical understanding could be gained for the existing modifications to some of the parameters.

The modelling that occurred consisted of first looking at the Haldane model and then considering a single small isolated bubble in each of the compartments and interpreting the predictions of the model in terms of decompression profiles.

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1 Introduction

1.1 Dangerous bubbles

(1.1.1) The amount of gas which can be dissolved in a liquid is an increasing function of pressure. If a liquid is saturated with gas at a given pressure and the pressure is suddenly reduced there is the potential for the explosive release of bubbles as gas comes out of solution (the so-called champagne bottle effect). This can lead to disastrous consequences for deep sea divers. As divers descend, their blood and tissues can become saturated with dissolved gases at the prevailing ambient pressure which is a linearly increasing function of depth. If divers then try to ascend too quickly it is possible for bubbles to form as the dissolved gas in their blood and tissues is forced out of solution. These bubbles can cause mechanical damage to tissues and can also block capillaries hence starving tissues of oxygen. This phenomena is known as decompression sickness or 'the bends' and it is potentially fatal. Divers can minimize the risk of decompression by performing a gradual ascent from depth which allows the dissolved gas content of their blood and tissues to slowly equilibrate with the ambient.

(1.1.2) VR Technology is a leading supplier of technical dive computers. The company is interested in expanding upon an existing algorithm (the Variable Gradient Model - VGM), which is used to design ascent profiles/decompression schedules and thereby mitigate the risk of decompression sickness in divers.

(1.1.3) At present, no decompression algorithm is able to predict safe decompression for all dive scenarios. In practice, empirical adjustments are made by experienced organisations or divers in order to improve decompression profiles for the range of depths and durations needed on any particular dive. Bubble formation and growth in the human body are the fundamental causes of decompression sickness, and it is believed that there is significant scope for incorporating better modelling of these processes into the design of decompression algorithms.

(1.1.4) The question that VR Technology brought to the Study Group was: How can we better model bubbles in the body to design decompression algorithms that work over the entire range of conditions that a diver might experience and to allow for a diver's physiology? How might we estimate the risks to the diver if the decompression requirements of the algorithm are not performed, owing to dive-dependent circumstances?

1.2 Beginner's guide to technical diving

(1.2.1) When a person dives below 30 meters or stays under the water for longer than 30 minutes, a decompression procedure is required before coming

back to the surface. This is due to the fact that breathing the compressed air or gas from diving cylinders under the water creates an elevated partial pressure of (inert) gas in the body tissues. The decompression is a controlled ascent where a diver stops at certain depths for certain times before continuing with the ascent. Decompression hopefully removes the extra (dissolved) gas in the divers body safely by using the blood to move gas from the tissues through the heart to the lungs where the gas is exchanged in the alveoli. Controlled ascent achieves this, ensuring the over pressure of gases in the tissues only gives rise to a manageable amount of sufficiently small bubbles.

(1.2.2) Standard air is composed of a mixture of 78% Nitrogen (N_2), 21% Oxygen (O_2) and 1% other gases. At increased depth, elevated partial pressures of Nitrogen can have a narcotic effect which can seriously inhibit the performance and judgement of divers. To avoid this divers switch to breathing Nitrox (a mixture of Oxygen and Nitrogen with a reduced N_2 concentration in comparison with air) or Trimix (a mixture of Oxygen, Nitrogen and an inert gas such as Helium (He).) The term "technical diving" refers to diving to depths where it is necessary to breath gas mixtures other than air.

(1.2.3) There are several main algorithms used to create decompression profiles in use today. Generally, they can be divided into Haldane type models [1,2], which split body into tissue types referred to as "compartments" and establish decompression times for each tissue, and bubble models [3], which study the formation of the bubbles and create decompression profiles that minimise the number and size of the bubbles during the ascent.

(1.2.4) It is worth noting that there is no scientific consensus on the exact causes of decompression sickness but there are strong evidences that the ultimate danger lies in bubbles. It is possible to create decompression profiles that exclude the creation of bubbles during the ascent altogether. However, these profiles give unrealistically long times of ascent and can not be used in practice. Experiments on animals [4] show that some number of bubbles are found in animals that did not suffer the symptoms of the decompression sickness. Therefore, it is accepted that some bubbles will be created during the human decompression.

(1.2.5) As bubble formation, growth and dynamics are clearly important in the onset of the decompression sickness, the Study Group decided to go down the route of studying the mechanisms that control how bubbles evolve.

(1.2.6) It is assumed that the lung's alveoli are efficient gas exchangers and the concentration of dissolved gas in the blood rapidly approaches that of the breathed gas mixture. The dissolved gas is then transported to different tissues in the body via the blood circulatory system. Some body tissues,

such as those in the central nervous system are perfuse with capillaries and the dissolved gas concentration in these tissues quickly equilibrates with that in the blood. Other tissue types, such as cartilage, contain considerable fewer capillaries, and it will take longer for the dissolved gas concentration in these tissue types to equilibrate with that in the blood. In a Haldane type model, the body is divided into a series of tissue types which are characterised by a 'half-time', the timescale over which the tissue equilibrates with the dissolved gas concentration of the blood.

2 The work of the Study Group

2.1 Outline

(2.1.1) The Study Group took the approach of trying to extend the existing Haldane model to account more explicitly for the formation of bubbles. The Haldane model separates the body into a variety of different tissue types (typically either 8 compartments or 16 compartments) and considers each to have a spatially uniform inert gas concentration. Exchange of gases from these compartments to the breathed gas is taken to be due to a simple mass transfer mechanism described by a mass transfer coefficient that is different for each tissue type. This coefficient is inversely proportional to the time scale, or "half life". Values of half life for different tissue types can be found in the literature, for example, see [2]. Decompression profiles are then determined by requiring that the gas pressure in all compartments stays within some tolerance of the total external pressure. By extending the model to include bubble dynamics it was expected that some physical understanding could be gained for the existing modifications to some of the parameters.

(2.1.2) The modelling that occurred consisted of first looking at the Haldane model and then considering a single small isolated bubble in each of the compartments. We start with a description of the Haldane model, then introduce the model of a bubble and subsequently consider how to interpret the predictions of the model in terms of decompression profiles.

2.2 The Haldane-type model

(2.2.1) Following Haldane we consider the body to be divided up into a number of compartments within each of which the gas concentration is taken to be spatially uniform. For simplicity we shall initially consider just one compartment and the case where the diver breathes air. We consider the following variables and parameter

- P_A - Total pressure in the gas breathed by the diver (assumed to be equal to the external pressure on the diver). It is typically between 10^5 N/m^2 (atmospheric pressure at sea level) and 10^6 N/m^2.

Pressure increases linearly with depth at a rate of approximately 1 atmosphere of pressure for every 10 meters of depth.

- P_{N_T} - Partial pressure of N_2 in the gas breathed by the diver (for air we have $P_{N_T} = 0.8P_A$)
- P_N - Partial pressure of N_2 in the compartment[1].
- k - Inverse of the timescale for mass transfer (typically this is in the range $\sim 10^{-3} - 10^{-5}\text{sec}^{-1}$).

(2.2.2) Assuming that the transfer between the breathed gas and the compartment is a simple linear process we have the equation

$$\frac{\mathrm{d}P_N}{\mathrm{d}t} = k(P_{N_T} - P_N), \tag{1}$$

which for the case of a diver breathing air is given by

$$\frac{\mathrm{d}P_N}{\mathrm{d}t} = k(0.8P_A - P_N), \tag{2}$$

(2.2.3) The initial data for this problem is usually given by assuming that the diver has had a long time to equilibrate with standard atmospheric conditions and hence $P_N = 8 \times 10^4$ N m^{-2} at time $t = 0$. This ODE problem can then be solved by conventional methods to predict the resulting pressure of gas in each tissue. In most dive computers this is done by a simple explicit Euler method with P_A given by the diver's depth below the surface. When considering a number of compartments each of these will have its own ODE to be solved and if there are several gases then there is an ODE for each gas in each compartment.

2.3 The bubble model

(2.3.1) We now consider a single small isolated bubble in each compartment and consider its dynamics. The first approximation that was made is that the bubble is so small that it does not significantly alter the overall amount of gas in each compartment. Note that if there is a large number of bubbles then this would not be true and the model would need modifying but this would also entail needing to model the number of bubbles in each compartment and, given the uncertainty in understanding of bubble behaviour, this was not done here. However, some preliminary calculations showed that to get similar quantities of nitrogen in bubbles and tissues, the bubble radii need to be about a quarter of the distance between bubbles.

(2.3.2) Looking at an isolated bubble, we shall consider: *(i)* a simple force balance to relate the external pressure, the internal bubble pressure and the bub-

[1]More precisely, P_N is the equilibrium partial pressure corresponding to the concentration in the tissue.

ble size; and *(ii)* how the amount of gas in the bubble changes through diffusion of gases into or out of the bubble. This flow is driven by concentration gradients between the bubble surface and the bulk of the surrounding compartment. The bubble and all the diffusion will be assumed to be spherically symmetric. For simplicity we assume that the only gas in the bubble is N_2.

(2.3.3) In developing this model we shall use the following variables and parameters:

- σ- surface tension of water ($\sim 10^{-1}$N/m)
- κ - Henry's constant ($\sim 6 \times 10^6$Nm/kg)
- L - ratio of density to pressure for N_2 ($\sim 10^{-5}$kg/Nm)
- D - diffusion coefficient of N_2 in water ($\sim 3.6 \times 10^{-9}$m^2/sec)
- C - concentration of N_2 in a compartment.
- P_B - partial pressure of N_2 in the bubble (and hence LP_B is the density of gas in the bubble).
- R - radius of the bubble.
- r, t - independent variables for radial distance from the centre of the bubble and for time.

2.4 Bubble dynamics

(2.4.1) The force balance on the bubble assumes that the external pressure exerted on the diver is balanced by pressure in the bubble and any surface tension force that may exist. The governing equation is therefore

$$P_B = P_A + \frac{2\sigma}{R}. \tag{3}$$

(2.4.2) We assume that the gas inside the bubble is in equilibrium with the gas immediately outside the bubble and that the two are related by Henry's law

$$P_B = \kappa C \qquad \text{at} \qquad r = R. \tag{4}$$

(2.4.3) The movement of gas near the bubble is controlled by diffusion. The variations of pressure are taken to be sufficiently slow so that the diffusion is quasi-steady. There is then a uniform flux of gas driven by the difference in gas concentration between the surrounding tissue in the compartment and the surface of the bubble. The governing equation is therefore

$$0 = D\nabla^2 C = \frac{D}{r^2}\,\frac{\partial}{\partial r}\left(\frac{1}{r^2}\frac{\partial C}{\partial r}\right), \qquad R < r < \infty, \tag{5}$$

with boundary conditions that

$$C \to \frac{P_B}{\kappa} \qquad \text{at } r = R, \qquad\qquad C \to \frac{P_N}{\kappa} \qquad \text{as } r \to \infty. \tag{6}$$

(2.4.4) Within the bubble the pressure is assumed to be spatially uniform and the rate of change of the total amount of gas in the bubble is given by the diffusive flux of gas across its surface. With the volume of the bubble being $4\pi R^3/3$ and its surface area being $4\pi R^2$,

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(\frac{4\pi}{3}R^3 L P_B\right) = 4\pi D R^2 \left.\frac{\partial C}{\partial r}\right|_{r=R}. \tag{7}$$

(2.4.5) We can solve equation (5) analytically, and after using (3) and (4), and substituting the solution into (7), we obtain the main governing equation for the bubble dynamics:

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(R^3(P_A + \frac{2\sigma}{R})\right) = \frac{3D}{L\kappa}R(P_N - P_A - \frac{2\sigma}{R}), \tag{8}$$

where $P_N = \kappa C_N$ is partial pressure of N_2 in the compartment.

(2.4.6) *Initial conditions.* One consequence of equation (8) is that if the external pressure is sufficiently large then the bubble radius will collapse to zero in a finite amount of time. In addition the model shows that once a bubble has reached zero radius it will remain at this size independently of what pressures are applied. This problem has been noted many times previously and if bubbles are to be predicted then it is necessary to introduce some model of nucleation in order to get physically realistic predictions. One of the simplest model of nucleation is to assume that there is some mechanisms that prevents bubbles from completely collapsing [3]. This may be due to lipid layers on the interface that provide some mechanical strength (as outlined in figure 1) or due to small particles in the tissue around which the bubble can form. For the purposes of our modelling here we introduce the concept of a minimum radius R_c. Computationally we impose this condition by calculating the derivative of the radius from the ODE (8), which we denote by R'_{ODE} and then imposing the complementarity condition on the function $R(t)$ that

$$R - R_c \geq 0 \qquad \frac{dR}{dt} - R'_{ODE} \geq 0 \qquad (R - R_c)(\frac{dR}{dt} - R'_{ODE}) = 0. \tag{9}$$

From experimental data, it is estimated that $R_c \sim 10^{-6}$m but, given the uncertainty of this, we need to check that any predictions of the eventual model would be insensitive to this precise value. (Note that $R_c \sim 10^{-6}$m makes $2\sigma/R_c$ comparable with P_A.)

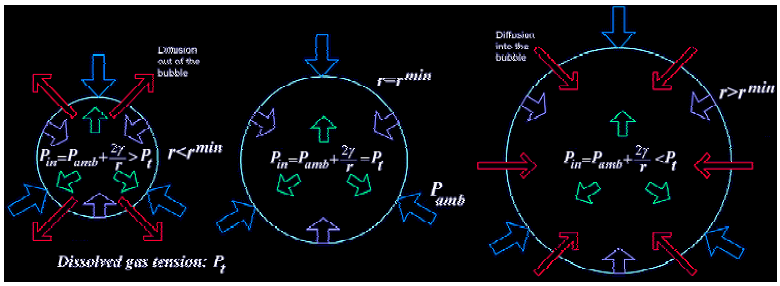

Figure 1: The meaning of R_c (This figure came from a website Deep Ocean Diving's Diving Science: Decompression Theory - Bubble Models, although the same ideas are in [3]).

(2.4.7) One useful point to note is that the time scale for the bubbles to respond to pressure variations can easily be determined by nondimensioanalisation and shown to be $t \sim \frac{L\kappa}{3D}R^2 \sim (10^{10}\text{ s m}^{-2})R^2$. With a bubble radius of order 10^{-4}m, this gives a time scale of minutes, similar to the lengths of stops divers make on ascents. Having the same time scales for decompression profiles and bubble evolution, indicates that bubble dynamics is an important consideration when constructing these profiles.

(2.4.8) For each tissue type the variations in the gas concentration and the bubble size is therefore determined by the two equations 8 and 2. For different tissue types, this pair of equations hold with different parameters k and σ and all other parameters remaining the same. For each additional gas that is considered there will need to be an additional equation similar to (2) and the total pressure in the bubble will need to be modified. The initial data for the problem will typically be that all the gases are in equilibrium with atmospheric conditions and bubbles in all compartments are at their minimum size.

2.5 Numerical solutions

(2.5.1) The problem as outlined can be considered as a "forward problem" where the external pressure experienced by the diver, P_A is given as a function of time time t and the ODEs then solved to determine how P_N and R vary with t. A Matlab code using the "chebfun" package (see www.comlab.ox.ac.uk/projects/chebfun/) allowed extremely accurate solutions to be found to these ODEs and these are presented here. The code assumes the diver to be breathing air, so there is a single inert gas, N_2, and eight different types of tissue are considered. The data used for the mass transfer timescales for the different compartments was taken from [2] and the other constants had the values given earlier in this report. The numerical predictions of the equations (8) and (2) are shown in Figures 2 and 3.

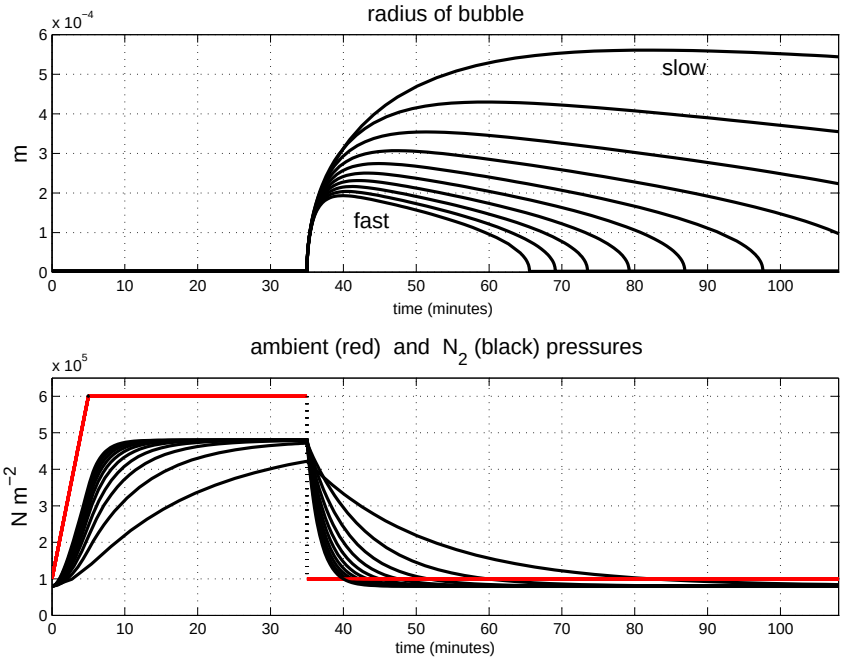

Figure 2: Numerical solutions that show how bubble's size and the N_2 pressure in the compartments change during the ascent from a 50 meter deep dive.

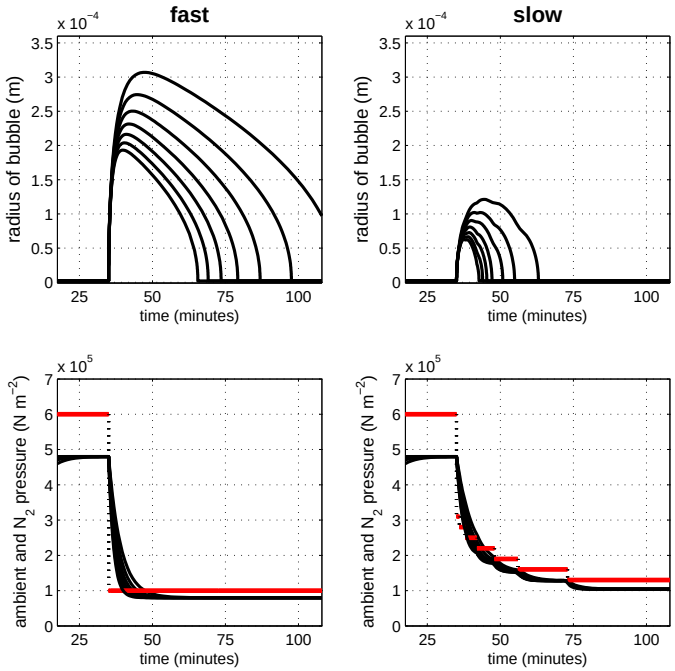

Figure 3: Numerical solutions that show how a bubble grows, and how nitrogen concentrations change, during an immediate ascent (left) and during a staged ascent allowing for decompression (right).

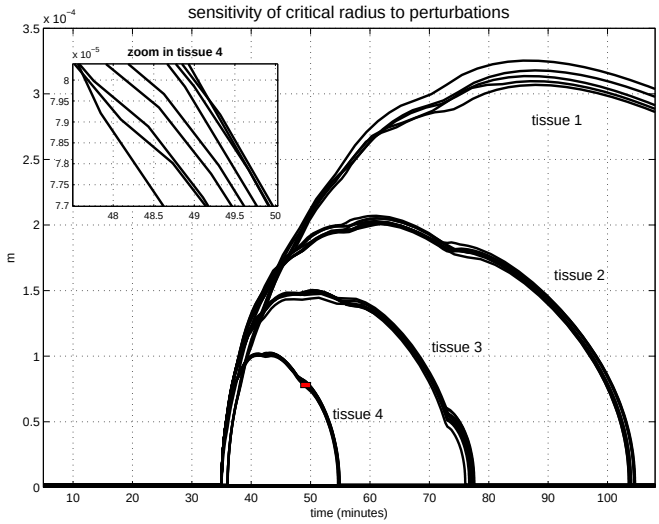

Figure 4: The sensitivity of the critical radius to perturbations

(2.5.2) As mentioned previously it is important to examine how sensitive the predictions of bubble size are to the assumed minimum radius. This is shown in Figure 4.

2.6 Decompression profile calculations

(2.6.1) Having examined the forward problem the study group then considered how this might be exploited to determine a decompression profile. The basic underlying mechanisms controlling the decompression profile was anticipated to be the size of the bubbles in the tissue. It was thought that the size might be a good indicator of the damage that would occur to the tissue. Hence a decompression profile should be found so that at all times the maximum size of bubble occurring in any compartment was less than some given contact R_{max}. This does determine a possible route for finding a decompression profile but the Study group did not pursue this as it requires the implementation of the full set of compartments and care with the resulting numerical methods.

(2.6.2) Instead the Study Group examined a simpler problem where it was found that some progress could be made relatively easily. We considered the case of a single compartment with a bubble and sought a decompression profile that ensured the bubble did not get larger than R_{max}. In fact the problem was examined by finding the external pressure P_A that ensures that the bubble radius remains at exactly R_{max} during the entire decompression. Hence we solve (2)and (8) for P_A and P_N when $R = R_{max}$. Hence the equations become

$$R_{\max}^3 \frac{\mathrm{d}P_A}{\mathrm{d}t} = \frac{3DR_{\max}}{L\kappa}\left(P_N - P_A - \frac{2\sigma}{R_{\max}}\right), \tag{10}$$

$$\frac{\mathrm{d}P_N}{\mathrm{d}t} = k(0.8P_A - P_N)\,. \tag{11}$$

This is a linear pair of ODEs with constant coefficients and therefore readily solvable. Let us analyse this pair of equations first.

(2.6.3) There are five parameters k, α, P, B and ϵ. k is related to the time scale for the rate of change of the pressure, $\alpha = 3D/({R_{\max}}^2 Lk)$ is related to the time scale for the rate of change of the bubble size, P is the initial pressure at the starting depth and $B = 2\sigma/R_{\max}$ is a constant depending on the maximum bubble size. The Study Group did not have the exact definitions and representative values for these quantities. ϵ is related to the nitrogen content being $\epsilon = 1 - [N_2]$, where $[N_2]$ is the fraction of nitrogen in the air (the percentage of nitrogen in the air expressed as a fraction). For normal air this gives $\epsilon = 1/5$. The two differential equations relate to the problem of determining P_N and P_A given a bubble of a constant maximum size.

(2.6.4) There are two different exponentials with different time scales

$$e^{-\left(\alpha+k+\sqrt{\alpha^2+2k\alpha+k^2-4\alpha k\epsilon}\right)t/2}$$

which is approximately

$$e^{-(\alpha+k)t} \equiv e^{\theta_1 t},$$

for the fast exponential decrease and

$$e^{-\left(\alpha+k-\sqrt{\alpha^2+2k\alpha+k^2-4\alpha k\epsilon}\right)t/2}$$

which is approximately

$$e^{-k\alpha\epsilon t/(\alpha+k)} \equiv e^{\theta_2 \epsilon t},$$

for the slow exponential decrease. The ratio of these rates of decrease is $(k\alpha\epsilon)/(\alpha+k)^2$ which is always $\leq \epsilon/4$ (occurs when $\alpha = k$) and can be considerably smaller if $\alpha << $ or $>> k$.

(2.6.5) Both solutions P_N and P_A are of the form $a + be^{\theta_1 t} + ce^{\theta_2 \epsilon t}$, the initial conditions are $P_A = P, P_N = (1-\epsilon)P$. There is a rapid change on the fast time scale ($0 < t < 10$). (Note: For $t > 10$ there is a slow change to the steady state $P_N = -B/\epsilon, P_A = -B(1-\epsilon)/\epsilon$. However the model breaks down before this stage mainly because neither P_N nor P_A can get much below atmospheric pressure.)

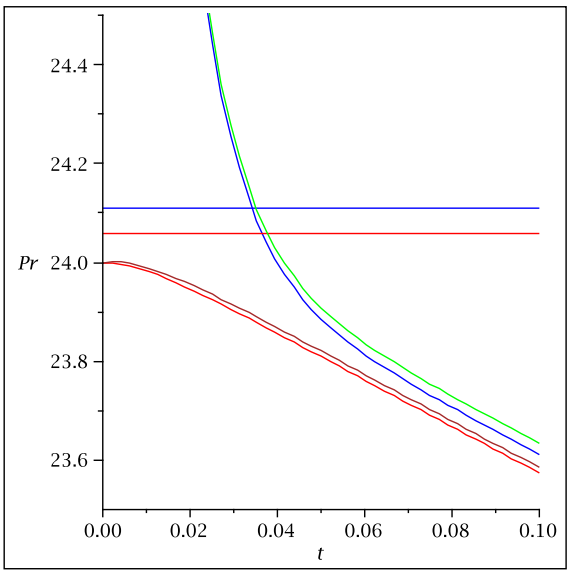

Figure 5: The red graph is the exact solution for P_A with $\epsilon = 1/5$, the brown graph is the series solution for P_A, correct to order epsilon squared with $\epsilon = 1/5$ and the red straight line is the asymptotic value as you come out of the boundary layer. The blue graph is the exact solution for P_N with $\epsilon = 1/5$, the green graph is the series solution P_N, correct to order epsilon with $\epsilon = 1/5$ and the blue straight line is the asymptotic value as you come out of the boundary layer. $k = 1, \alpha = 100, P = 30, B = 1/100, \epsilon = 1/5$.

(2.6.6) For illustrative purposes let us take $k = 1, \alpha = 100, P = 30, B = 1/100, \epsilon = 1/5$. The solutions are illustrated in Fig. 5. Generally, there will not be much difference in the overall shape of the graphs for different parameters but the time scale will be altered with values ranging from 20-30 minutes to as long as 4-5 days. In Fig. 5, $k = 1$, so the timescale is short, however if we take a much smaller $k = 1/630$, the timescale increases and becomes impractical to use in real dives, which is illustrated in Fig. 6.

(2.6.7) There are two obvious drawbacks to using (10) and (11). The first is that R will not, in general, be at our chosen value of $R_{\max}$ at the time ascent is started. There would have to be some initial stage of ascent during which bubbles could grow, see (c), below. Secondly, the strategy cannot be applied as it stands for multiple tissue types unless the radius for each is fixed at R_c. (There would be incompatibility between the different ODEs.)

(2.6.8) The following points should also be noted:

(a) Assuming that the diver does start ascending with bubble radius $R = R_{\max}$ as required, the time taken to reduce P_A to 1 atmosphere appears to be an increasing function of $R_{\max}$: the bubble size should be fixed as small as possible to get quickest ascent. (*E.g.* the initial size R_c, of 1 micron or so, if our supposition on this limiting

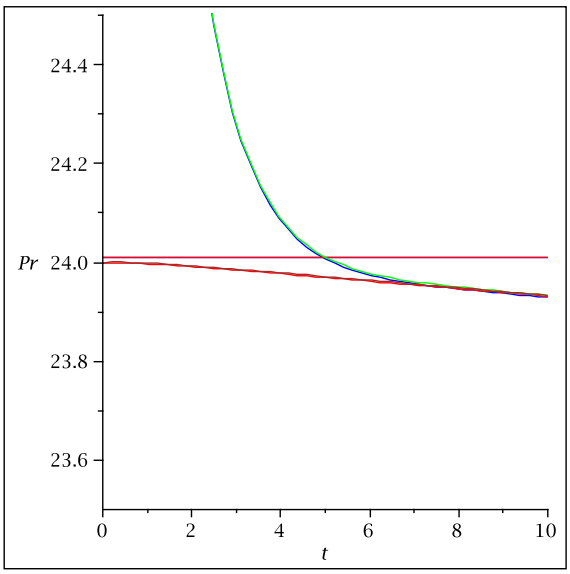

Figure 6: The same as in Fig. 5 but $k = 1/630, \alpha = 1$.

size is correct. This makes the strategy feasible in that we do not need some starting phase during which R increases up to our required maximum, again see (c). However, in practice this will give an unrealistically slow ascent.)

(b) After P_A drops to 1 atmosphere (the diver reaches the surface), equations (8) and (2) will again apply. With the sudden change of equations, we have instantaneously increased $\mathrm{d}P_A/\mathrm{d}t$ and reduced $\mathrm{d}R/\mathrm{d}t$ from 0. This then indicates a shrinking of the bubbles, as desired.

(c) With a preliminary constant rate of ascent, so that $\mathrm{d}P_A/\mathrm{d}t = -a$, say, (8) can be solved approximately, subject to neglecting the last terms on each side, to find (in principle):

- the time at which bubbles start growing;
- their size after that time;
- when R reaches the chosen value of $R_{\max}$;
- the values of P_A and P_N then to be used as initial values for (10) and (11).

3 Conclusions

A simple extension of the conventional model of decompression has been developed. The inclusion of bubble dynamics in each of the different compartments has been performed accounting for local diffusion of gas to the bubble. The numerical solutions of these ODEs have shown realistic behaviour by including a minimum bubble diameter and the solutions appear insensitive to the precise value of this parameter. A simple decompression profile has been created for a single compartment model

that indicates the use of a criteria based on avoiding a maximum bubble size may give very realistic profiles.

The model we have presented is based on the Haldane model. Conventional implementations of this model are based on the work of Buhlmann who has two parameters for each of the compartments. In particular, according to Buhlmann, the ambient (local atmospheric) pressure P_A should not fall below

$$P_{\text{tol}i} = b_i(P_{Ni} - a_i) \tag{12}$$

with a_i and b_i the two parameters, and P_{Ni} the nitrogen pressure, for tissue type i, for any i. (For most compartments, b is close to 1.) The model developed by the Study Group can give an explanation for the sizes of a, as for example tabulated by Buhlmann, for different tissue types. Because it takes time for bubbles to grow to "dangerous" sizes, it is possible for P_N to exceed P_A, temporarily, without serious harm befalling the diver. Larger values of a can then be associated with smaller time constants, *i.e.* with tissues with larger values of k, because in such compartments P_N falls more rapidly. The use of the bubble model allows more careful dependence of the allowed pressure difference between tissue compartments and the external pressure. This gives a physical basis for understand the b values and also appears to indicate why, for example, the b values are sometimes modified for "long" dives as here the bubbles have had more time to equilibrate than in shorter dives.

3.1 Way forward

(3.1.1) The ideas in this report are worth following through but need to be validated against any data regarding bubble behaviour although this validation is very difficult..

There are a number of additional ideas that are worth pursuing.

(3.1.2) Can the compartmental model be avoided and replaced by simply considering a single slab of tissue and a more careful describing the diffusion within this tissue using a diffusion equation, rather than the Haldane approach?

(3.1.3) Are there other criteria that should be considered for avoiding damage to tissue other than bubble size? Can a critical size for damage be determined from other considerations? Is the controlling property the total volume of gas contained in all of the bubbles?

(3.1.4) The transfer of the gas from the bubbles into the tissue might be important, particularly during decompression as it would keep the tissue concentration higher than currently predicted. Our model does not allow for this. Can realistic models be made for determining the distribution of bubble nuclei in the various tissues?

(3.1.5) Is it realistic to use the same physical parameters for all tissue types (*e.g.*

surface tension, diffusivity) and are there data to allow these to be found by other means?

(3.1.6) It is worth exploring how to implement a simple numerical method to solve the control problem of finding a decompression profile that restricts the maximum bubble size in any compartment to the critical size.

(3.1.7) It is worth incorporating distributions of possible variability in the parameters into the predictions.

(3.1.8) Can we get our model to work not just on the maximum bubble size, but on predicting the parameters of a distribution of bubbles in the tissue?

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