Simulation of Bubble Growth in Tissues during the Decompression Sickness

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Abstract

Decompression sickness (DCS) is a dangerous and sometimes deathful condition caused by nitrogen bubbles that form in the tissues of divers who surface too quickly. The subject of decompression theory in general is the study of pressure changes in blood and tissues.

This paper presented a model that combined by three important aspects of DCS: gas exchange between the capillary bed and the tissue, gas exchange between tissue and a single bubble and bubble growth in the tissue.

The used modelling methodology was based on hierarchical composition of process. This method was contained of physical, species and equation topology that helped to have a physical insight of process during modelling.

The mathematical model was solved by a computer-aided modelling tool named *Modeller* that implemented by using the *BlackBox 1.4* and runs in *Matlab* programming language.

The model was able to predict the pressure changes in blood and tissues during decompression and bubble size. It was possible to evaluate the important effective factors on DCS process such as type of tissue and duration of residence in depth. Four case studies were provided to present detail of the derived model.

Introduction

During a dive, the water pressure is greater than the air pressure at sea level. Thus, the pressure of nitrogen in the breathing gas is increased and the diver takes in more nitrogen than usual with each breath. On the way up, the water pressure drops or decompression occurs. Therefore, the extra dissolved nitrogen gradually diffuses out of the tissues and is delivered by the bloodstream to the lungs, which expel it from the body. If the diver surfaces too quickly, the nitrogen bubbles can be formed in the tissues, which are reason of decompression sickness. A bubble is defined as a volume of gas in a tissue. The bubble's size is a key to determine whether it will be shrink or grow.

Mathematical models of bubble evolution in tissue have recently been used as risk functions for predicting the incidence of DCS. The theory behind decompression modeling is very complex, but the calculations must be in practice realisms of diving. Most models do not address directly bubbles in tissues. However, they derive diving tables to minimize the chances of experiencing DCS by offering safety stops and ascent rate.

In particular, Haldene [1] developed a model of decompression for the Royal Navy by testing many dive profiled in a decompression chamber. Most of theory has been found empirically. However, theory was further developed during the years. Today, there are more conservative diving table models that recommended for sport and scientific divers. Nonetheless, the bubble equations have been omitted in most of models to facilitate running of model by computer.

Formation of bubble during decompression has been studied for the last three decades to have insight in the principles of decompression. This has resulted in new theories like the varying Permeability Model (VPM) by Yount [2] and Reduced Gradient Bubble Model (RGBM) [3]. Bubble theories do not only take into account the dissolved gas (like Haldane models), but also the free gas in the diver body.

By attention to studies and existing theories about mechanism of decompression sickness, the evolution of a single bubble decompression is considered in this paper. The mathematical model uses a new method that introduced by

Westerweele [4]. According to this method, a big model is divided to a few sub models. Thus, it facilitates the modeling, and shows a new clear physically view of decompression process in body. Besides, it is very easy to change assumptions of model and evaluate of the results. The output of simulation results is graphically with quick access to changes of all included variables of process such as partial pressure of dissolving gas in tissue and bubble size.

Glossary

α_B : Solubility of nitrogen gas in blood, ml/ml blood

α_t : Solubility of nitrogen gas in tissue, ml/ml tissue

D_t : Diffusion Constant of gas in tissue, cm^2/min

h : Boundary layer thickness , μm

$\dot{Q}$: Blood flow to tissue compartment, lit/min

$\hat{p}_{N_2}$: The partial nitrogen pressure flow rate, bar/min

$p_{N_2,amb}$: Initial partial nitrogen pressure in ambient pressure at beginning of decompression, bar

$p_{N_2,blood}$: Partial nitrogen pressure in the blood, bar

$p_{N_2,tissue}$: Initial partial nitrogen pressure in the tissue at starting decompression, bar

$p_{N_2,tissue}$: Partial nitrogen pressure in the tissue, bar

P_{bubble}: Total pressure inside the bubble, bar

$p_{N_2,bubble}$: Partial pressure of nitrogen gas in the bubble, bar

R : Rate of change of ambient pressure (decompression rate), bar/min

r : Bubble radius, μm

$\dot{n}_{N_2}$: The accumulation of the nitrogen mass in system, mole/min

$\hat{n}_{N_2}$: Molar mass flow of mass connection, mole/min

n_{bubble} : Total mole of gas in the bubble, mole

V_{bubble} : Volume of a bubble, lit

V_{blood} : Volume of blood in compartment, lit

V_{tissue} : Volume of tissue in compartment, lit

τ : Tissue half-time, min

σ : Surface tension , dyne/cm

x : Fraction of nitrogen in equilibrium with the tissue

Material and Methods

The aim is to model of a bubble in tissue during decompression. The mechanism of this process is based on three important aspects of decompression process, i.e. Gas exchange between blood-tissue and between tissue-bubble with bubble growth in tissue. To have better insight of model, the detailed mechanism can be considered as following:

When we breathe a breathing gas that contains an inert gas (gases that do not take part in the Oxidative metabolisms, or are not used by the body) like nitrogen (N_2), this gas is dissolved in the blood via gas exchange in the lungs. Blood takes the dissolved gas to the rest of the bodily tissue. Tissue takes up dissolved gas from the blood. The mechanism of gas exchange of blood is based on three assumptions:

1) The gas can diffuse freely through the whole surface of walls of capillaries.
2) The concentration of inert gas in blood is in equilibrium with the dissolved gas in the tissue.
3) Diffusion in the lungs is very rapid so that equilibrium is established between the gas and the blood.

As a result, it is assumed that the partial pressure of blood is always equal to partial pressure in lungs.
The representation of tissue is resembled of two propounded theories;

1) Mapleson theory
2) Bühlman theory

As first issue [5], the body is divided into a number of tissue compartments such that the blood flow rate is the same into each compartment. It is not necessary to have a separate compartment for each tissue, but if the tissues are grouped into a few compartments, the blood flow per unit of volume of tissue must be same through the compartment.
In contrast, according to Bühlmann theory [6], our entire body absorbs nitrogen under pressure. However, some areas of body absorb gas faster than others do.
Decompression tissues are categorized by how fast they uptake gas as a compartment. A compartment can be charactrized by a variable called " half-time" that is a measure for inert gas uptake. Bühlmann improved and developed ZH-12L and ZH-16L model. Although tissue compartments do not correspond one to one with anatomic tissue, they do reference existing decompression areas that behave alike.
In any case, we have a bubble inside a tissue compartment, which is considered as a volume of nitrogen gas that follows the phenomenological laws of ideal gases, diffusion and surfaces tension. Because of decompression, bubble might grow in tissue compartment.
It is proposed different theories about forming of bubbles during decompression. In our model, a bubble is presented according to varying permeability model (VPM). This theory assumes that there are tiny bubbles (nuclei) in body. These short-lived nuclei can be continuously created by stresses in muscles and joints. Nonetheless, there is a minimum bubble number can be tolerated without DCS. These tiny bubbles will be growth during DCS. An average size of nuclei is used as initial size of bubble in our model.
According to the described mechanism, the model is derived by the following method.

Method of Modeling

The used method for modeling growth of a single bubble gas in tissue during decompression phenomena is based on the hierarchical decomposition of process into networks of elementary systems and physical connections.
This method is introduced by Westerweele and consists of five steps:

1) Physical Topology that describes the physical structure of the process based on two participle components systems and connections.
2) Species topology that state which chemical or biochemical species are present in which part of the process.
3) Generation of dynamic part of the process model is done by defining balance equations for each system and each extensive quantity.
4) Following last step, equation Topology is completed by introducing system equations such that transport rates, thermodynamic equilibrium.
5) If necessary, control is added.

In any case, for constructing of a model is not needed all five steps to be done in this sequence, but the results always would be a differential algebraic system.

Modeling of Decompression Sickness

The aim is to construct model of growth of a single bubble in a tissue compartment during decompression and based on described mechanism. The model would able to consider dynamic behavior of all included parts in process due to decompression theories such as partial pressure of dissolved gas in tissue and bubble size.

1. Physical Topology

According of described mechanism, the process is divided to three systems (blood, tissue and bubble). The diffusion paths are assumed bi-directional mass connections between blood-tissue and tissue- bubble system so that there is never contact directly between bubble-blood.

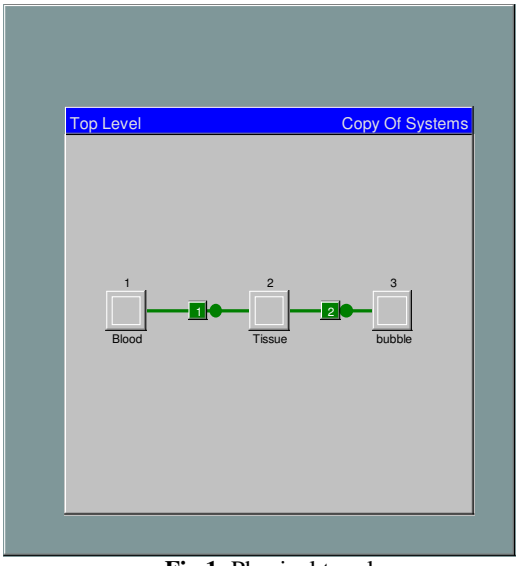

Fig.1: Physical topology

2. Species Topology

Definition of the species topology requires the definition of the species participated in decompression sickness process. Nitrogen is only diffusing gas that exchange between three systems during compression/decompression.

3. Equation Topology

3.1 Balance Equation

The energy balance is not relevant for this problem. Thus, only the mass balances of each system are required. Since nitrogen is only specie that is exchanged between three systems in this process, therefore the component mass balance for each system is needed as following:

3.1.1 Blood system

The mass balance for nitrogen is based on the assumption that the inert gas diffuses freely through the whole surface of the walls the capillaries.

$$\dot{n}_{N_2,blood} = -\hat{n}_{N_2,blood/tissue} \quad (1)$$

3.1.2 Tissue system

Accumulation of nitrogen in tissue is the amount carried by blood per unit time less the flux into the gas bubble.

$$\dot{n}_{N_2,tissue} = \hat{n}_{N_2,blood/tissue} - \hat{n}_{N_2,tissue/bubble} \quad (2)$$

3.1.3 Bubble system

It is assumed the gas inside a bubble involves only the inert gas. The accumulation of gas in bubble is equal to mass flow rate between tissue and bubble.

$$\dot{n}_{N_2,bubble} = \hat{n}_{N_2,tissue/bubble} \quad (3)$$

3.2 Connection equations

The mass flows through the mass connection m1 and m2 are considered to be Bi-directional and with different pressure are given by:

$$\hat{n}_{N_2,m_i} = K_i \cdot \hat{p}_{N_2,m_i} \quad (4)$$

(i=1, 2)

The pressure flow rate of both connections is modelled as the difference in partial pressure between the gas target and the gas origin:

$$\hat{p}_{N_2} = \left(p_{or} - p_{tar}\right) \quad (5)$$

Besides, K constant related to connection between blood and tissue systems (m1) can be calculated by two ways. According discussed mechanism, we are going to use of two theories basis for tissue compartment.

Due to Mapleson theory, rate of gas exchange between blood and tissue is stated as a empirical equation:

$$\hat{n}_{N_2,m1} = \frac{\alpha_B \dot{Q}}{\alpha_B V_{blood} + \alpha_T V_{tissue}} (p_{N_2,blood} - p_{N_2,tissue}) \quad (6)$$

By comparing Eq. (6) to Eq. (4), K_1 is defined as:

$$K_1 \cong \frac{\alpha_B \dot{Q}}{\alpha_B V_{blood} + \alpha_t V_{tissue}}$$

(7)

Provided that, second theory (Bühlmann model) K_1 is derived as:

$$K_1 \cong \frac{\ln(2)}{\tau} \quad (8)$$

Since the Fick equation describes diffusion of gas through tissue; thus, the rate of change of molar concentration of gas in the bubble equals the molar flux of gas through the bubble surface [9].

$$\hat{n}_{N_2,m2} = \frac{4\pi}{h} D_t.\alpha_t.r^2\left(p_{N_2,tissue} - p_{N_2,bubble}\right) \quad (9)$$

By comparing Eq. (9) and Eq. (4) , K_2 is found:

$$K_2 \cong \frac{4\pi}{h}.D_t.\alpha_t.r^2 \quad (10)$$

3.3 System Equations

The connections dictate that the secondary variables *p, v* should be defined. If the temperature of the process is assumed constant, the following definitions could be resulted.

3.3.1 Bubble system

By attention to this assumption that the gas inside of the bubble is considered ideal and the bubble is formed by only nitrogen, the definitions can be:
Total pressure is equal with partial pressure inside bubble.

$$p_{N_2,bubble} = P_{bubble} \quad (11)$$

$$P_{bubble} = \frac{n_{bubble}.R.T}{V_{bubble}} \quad (12)$$

$$r = \sqrt[3]{\frac{3.V_{bubble}}{4\pi}} \quad (13)$$

Effects of surface tension at the gas-liquid interface of the bubble are incorporated through use of the Laplace equation, which, neglecting tissue viscoelastic effects.

$$P_{bubble} = P_{amb} + \frac{2\delta}{r} \quad (14)$$

3.3.2 Blood system

The system equations are based on a few assumptions from studied theories. By attention to mentioned assumptions for this system, the partial pressure of the blood equal to partial pressure of breathing gas.

$$P_{N_2,blood} = P_{amb}.x \quad (15)$$

3.3.3 Tissue system

By attention to two different issues about dissolved inert gas in tissue, we can define system equations to tissue in two ways:
1-*Mapleson's* theory

$$P_{N_2,tissue} = \frac{n_{N_2,tissue}.R.T}{V_{N_2,tissue}} \quad (16)$$

$$V_{N_2,tissue} = (V_{tissue}\alpha_T + V_{blood}\alpha_B).x \quad (17)$$

2-*Half-time* theory

$$P_{N_2,tissue} = P_{N_2,amb} + R\left[t - \frac{1}{k}\right] - \left[P_{N_2,amb} - P_{N_2,tissue^o} - \frac{R}{K}\right]e^{-Kt} \quad (18)$$

$$K = \ln(2)/\tau \quad (19)$$

Simulation Method

For solving process modelling, it is used of a computer tool called *Modeller*. This computer tool has been developed based on the described modelling methodology by Westerweele. The *Modeller* aims to contribute in the development of the process models and facilitate hierarchical modelling of process plants through a user-friendly interface. The *Modeller* is implemented by using of the BlackBox Component Builder1.4.
The *Modeller* constructs the process models from primitive building blocks that are simple thermodynamic systems and connections. The *Modeller* generates symbolic models in the form of differential-algebraic equations consisting of mass and/or energy balances, completed with transfer laws, physical and geometrical property relations and/or kinetic laws.
With the information on the physical and species topology *Modeller* can automatically generate balances of fundamental extensive quantities (mass, energy and momentum) of every elementary system. In order to describe

the behaviour of the process other equations are added.
The output consists of mathematical equations are linked to *Matlab* and are shown graphically.
The model of decompression sickness is constructing by *Modeller*. The balance equations for three systems; i.e. blood, tissue and bubble is generate as Eq. (1), (2) and (3). The connection and system equations are defined for *Modeller* according to derived equations in last section.
The bubble growth and partial pressure in the tissue during decompression are evaluated by using the derived model with parameter values shown in Table I. It is assumed the bubble grows from nuclei of 10-µm radius that is present in the tissue.

Table I. Model parameter value used in simulation

Parameter	Ref.	Value
σ	9	30 dyne/cm
D_t	9	1.32×10^{-6} cm^2/min
α_t	9	0.0125 cm^2 /cm^2
α_b	9	0.0125 cm^2 /cm^2
h	9	3 µm
$\dot{Q}$	5	0.66 and 1.42 lit/min
V_T	5	4.67 and 0.171 lit
V_B	5	0.41 and 0.88 lit
τ	6	30 and 360 min
r	9	10 µm
R	6	0.5 and 1 atm/min

Results

The dynamic of bubble growth during decompression from depth to sea level were computed by the model with parameter values shown table I. The pressure profile consisted of 30 m dive during 3 min for all simulations to a residence by defined bottom time and surfing to sea level. The effect of bottom time, type of tissue, and surfacing rate were analyzed. These simulations should confirm existing expectations for dive profiles from a single bubble. The partial nitrogen pressure of dissolving gas in tissue is evaluated during decompression. This factor can show amount of gas expel from tissue (or chance to grow the bubble). Effect of some parameters on decompression process can be studied by dynamic partial pressure of tissue.
In first case, the effect of bottom time (time step ate the depth) is considered in Fig.2 that plots partial pressure in tissue with two different bottom times during decompression. The condition of simulation is same for two tissues except their residence in depth. Both tissues are exposed to same decompression rate. It predicts that more stop time causes more uptake inert gas in tissue. In other word, gas keeps on dissolving in tissue until the partial pressure of the dissolved gas is equal to the partial pressure of the blood, through the entire body that called saturation, if tissue has enough time in compression.

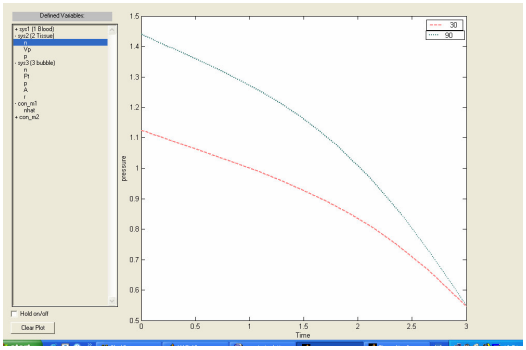

Fig. 2: Partial Nitrogen pressure (bar) in tissue with two different bottom time (30 and 90 min)

Furthermore, the reduction of ambient pressure or decompression rate can be slow or fast. In a constant initial case after 90 min bottom time in 30 m depth, two different decompression rates are considered. It is clear partial pressures of tissue in two cases are equal. Now for considering of rate of decompression, this aspect is shown on size of bubble in Fig.3. It is found that surfacing faster cause more bubble growth. This approves theory DCS.

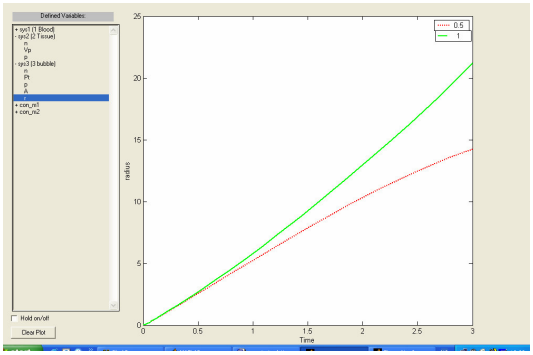

Fig. 3: Radius growth of the bubble in two different decompression rate 0.5 and 1 atm/min

Just as it was mentioned, theory behind of DCS is complex and there are different views to describe this process. To represent of tissue in our model, we referred to two propounded theories. Since, one of advantages of our model is to change of assumptions of model quickly. It is easy to switch the basis of model.
In the case that representation of tissue resembles of Bühlmann theory, the effect of half-time of tissue compartment (a characterization for rate of inert gas dissolving in tissue) is shown in Fig.4. The model predicts the faster tissue (like abdominal organs which take fast nitrogen of blood) expels the nitrogen gas fast during decompression contrary to slow tissue (like fatty marrow) at the same condition. In contrast, the bubble grows in slow tissue more that in fast tissue as Fig.5.

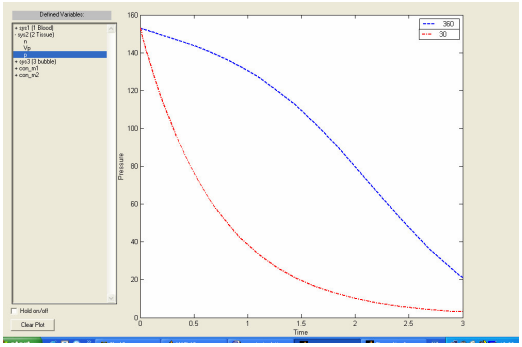

Fig.4: Partial Nitrogen pressure (bar) in tissue with half times 30 and 360 min

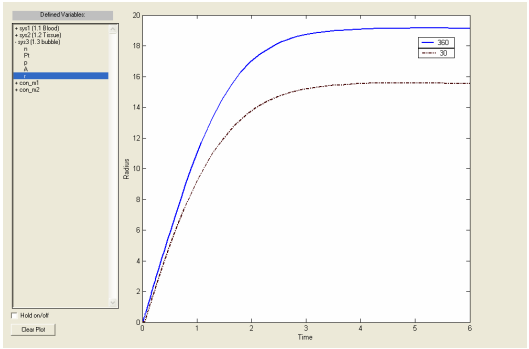

Fig.5: Radius growth (μm/min) of the bubble in two types of tissue with half time 30 and 360 min.

Mapleson theory looks at tissue compartments by different definition. As this issue, there is the same blood flow rate thought each compartment. Fig.6 shows the partial pressure of dissolving gas in two type tissue at same decompression condition. It predicts that by increasing of blood flow rate factor, the partial pressure of tissue decreased faster during decompression. Other interpretation is that bubble grows less in tissue compartments which have more blood flow rate.

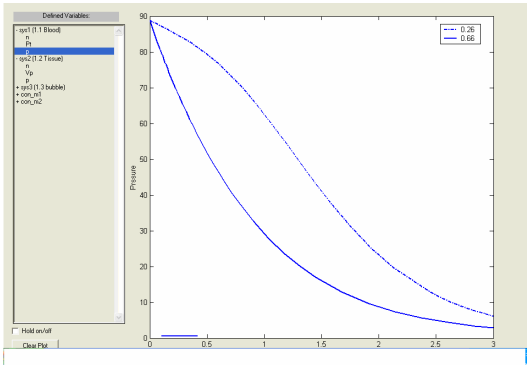

Fig.6: Partial Nitrogen pressure (bar) in two different types of tissues by blood flow rates 0.26 and 0.66 lit/min

Discussion

In this paper, it is attempted to gain a deeper understanding of bubble gas growth by investigating decompression model. The main property of this model is physical meaning of all equations. According to the used method model methodology, the process of decompression sickness is divided to three uniform distributed systems. These systems are connected by mass paths. Each system can be studied and modelled independent. This method helps to divide a big process to a series of small process that are linked each other by physical connections.
The focus of model is the growth of a single bubble in a tissue compartment. Three steps is considered to describe mechanism this process. In first part, blood exchanges nitrogen gas in lungs and takes it to tissues. Consequently, nitrogen is dissolved in tissues. Next step, the gas exchange is done between dissolved gas in tissue and bubble; and at last a bubble in tissue is growing.
In first part, partial nitrogen gas in blood is equal to partial nitrogen gas of breathing gas in lungs as stated assumptions. Second part of mechanism is related to definition of tissue.
Since, the one of purposes of this paper was to show how a complex process like decompression sickness can be easily divided to small parts. Also, it is possible to change assumptions and sub models without distribute the structure of model. We referred to two different issues for representing the tissue. Each one of two Mapleson and Bühlman

theories considers tissue compartment by attention to some factors. However, for switching the definition of tissue compartment is only enough to change a coefficient of mass connection equation (K_1). Last part of mechanism is bubble growth during decompression. Representation of forming bubble is based on VPM theory. It is assumed that bubble exists in tissue before decompression, so that it grows from a very small size during decompression.

The mathematical equations of model are divided to three sets. Mass balance equations of nitrogen component for each system, thermodynamic system equations and mass connection equations respect to partial pressure.

Simulation based on the derived model is achieved by the computer tool *Modeller*. The *Modeller* generates mass balance for each system same our model automatically. But, the system and connection equations are defined for *Modeller* as the derived model. After entering of all parameters, the model is run, and out put is considers in *Matlab.*

The result of four case study of our simulation is in agreement with decompression theory. The decompression rate, bottom time and change of type of tissue compartment are the interested factors in simulation case studies.

However, we do not have any experimental data to valid the model. It is found that the procedure of the results is corresponding with the decompression theory. By attention to effective applied method, the future work can be to develop a model for the growth of a range bubble sizes of bubbles.

Acknowledgment

I would like to thank Professor T.Hertzberg of Chemical Engineering Department at NTNU.

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