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Physiological control of diving behaviour in the Weddell seal *Leptonychotes weddelli*: a model based on cardiorespiratory control theory

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Summary

Despite being obligate air breathers, many species of marine mammal are capable of spending most of their lives submerged in water. How they do this has been a subject of intense interest to physiologists for over a century, yet we still do not have a detailed understanding of the physiological mechanisms underlying this behaviour. What are the proximate mechanisms that trigger the 'decisions' to submerge and return to the surface? The present study proposes a model intended to address this question, based on fundamental concepts of cardiorespiratory control. Two basic hypotheses are examined by computer simulation, using a mathematical model of the mammalian cardiorespiratory control system with parameter values for an adult Weddell seal: (1) that the control of diving can be considered to be a respiratory control problem, and (2) that dives are initiated and maintained by disfacilitation of respiratory drive, not inhibition. Computer simulations confirmed the plausibility of these hypotheses. Simulated diving behaviour and physiological responses (ventilation, cardiac output, blood and tissue gas tensions) were consistent with published data from freely diving Weddell seals. Dives up to the estimated aerobic dive limit (ADL, 18–25 min) could be simulated without the need for active inhibition of breathing in this model. This theoretical analysis suggests that the most important physiological adjustments occur during the surface interval phase of the dive cycle and include hyperventilation accompanied by high cardiac output, appropriate regulation of cerebral blood flow and central chemoreceptor threshold shifts. During dives, cardiac output, distribution of peripheral blood flow, splenic contraction and peripheral chemoreflex drives were found to modulate physiological and behavioural responses, but were not essential for simulated dives to occur. The main conclusion from this study is that the central chemoreceptor may be an important mechanism involved in the regulation of diving behaviour, implying that CO_2, not O_2, is the key regulatory variable in this model. This model includes and extends the ADL concept and suggests an explicit mechanism by which the respiratory control system may play a central role in the regulation of diving behaviour. It is likely that respiratory mechanisms are an important component of a hierarchical behavioural control system and further studies are required to test the qualitative and quantitative validity of the model.

Key words: diving, Weddell seal, cardiorespiratory control, model, behaviour.

Introduction

Naturalists and scientists have long marveled at the ability of aquatic mammals to survive for prolonged periods without breathing, while acknowledging that these animals only occasionally display their prodigious breath-hold capacities under natural diving conditions. Indeed in most species, voluntary dives are usually observed to last only a fraction of the maximum breath-hold capacity. These short dives normally occur in bouts that may last several hours or even days, during which sequential dives are separated by brief intervals spent breathing at the water surface (Butler and Jones, 1997).

Several attempts have been made to understand the adaptive advantages that are realized by engaging in bouts of short dives *vs* other possible strategies, such as maximizing time underwater in each dive (Castellini et al., 1988; Fedak and Thompson, 1993; Kooyman et al., 1980). For example, following the pioneering study by Dunstone and O'Connor (1979), several investigators have exploited the basic principles of optimal foraging theory (Houston and Carbone, 1992; Kramer, 1988) to show that on average the diving tactics used by various species may improve the efficacy or efficiency of foraging, at least in terms of time and/or energy budgets. Despite their heuristic value, the validity of optimal diving models is currently open to debate because there remains considerable uncertainty about the physiological mechanisms involved in the proximate control of diving activities, which means that there is also uncertainty about the appropriate constraints to include in the models.

The most obvious and important constraints arise from the

fact that submerged mammals cannot breathe and there is a limit to breath-hold duration. This issue was addressed experimentally by Kooyman and others, and developed into the 'aerobic dive limit' (ADL) concept (Kooyman et al., 1983, 1980), defined as the maximum length of time that an animal can dive without significant elevation of post-dive plasma lactate concentrations. The ADL has also often been calculated in terms of the estimated O_2 storage capacity of the animal and its rate of O_2 consumption during dives (Kooyman and Ponganis, 1998), and a behaviour-based estimate of the ADL has also been attempted (Burns, 1999) using the correlation between post-dive surface interval and post-dive plasma lactate concentration (Kooyman et al., 1980). In most studies the majority of dives in the majority of species are observed to be of durations less than the ADL, and it is now widely accepted that routine foraging dives are a sustainable aerobic activity – a conclusion that represents an important and enduring contribution of the ADL hypothesis. The ADL concept (and models based upon it) assumes that oxygen supply is a limiting factor, but there is no explicit model that explains what actually triggers the initiation and termination of dives, especially those shorter than the ADL. It seems likely that numerous physiological, psychological and environmental factors govern the voluntary diving behaviours of marine mammals. The goal of this study was to determine whether the respiratory control system could, at least in principle, be an important component of this complex behavioural control system.

The ADL concept was never intended to be a model for the physiological regulation of diving behaviour, but in the absence of a better alternative it has often been used, at least implicitly, in that context. As a consequence, oxygen has been assigned a key role in most attempts to understand the physiological mechanisms underlying diving behaviour (Borg et al., 2004; Burns, 1999; Butler and Jones, 1997; Castellini et al., 1988; Fedak and Thompson, 1993; Kooyman and Ponganis, 1998; Kooyman et al., 1980). However, from the perspective of respiratory control this ADL-based approach is inadequate and should be elaborated, for several reasons. First of all, in mammals the peripheral chemoreceptors (principally the carotid body chemoreceptors) respond to partial pressure of oxygen in the arterial blood rather than O_2 content and there is a non-linear relation between partial pressure and content (i.e. the sigmoid blood oxygen dissociation curve). The aortic bodies may detect O_2 content of arterial blood (Lahiri et al., 1983), but there is no evidence that they have an important role in respiratory control in diving species (Daly et al., 1977; Jones and Purves, 1970). Secondly, the partial pressures of carbon dioxide in the arterial blood and brain tissue play a dominant role in the regulation of breathing in mammals (Phillipson et al., 1981). It can be argued that depletion of O_2 and accumulation of CO_2 are coupled during breath-hold dives, so that elevation of the partial pressure of CO_2 may indirectly indicate depletion of the O_2 store. However, this neglects the fact that partial pressures of O_2 and CO_2 both stimulate respiration, and these stimuli interact non-additively. A potential role for CO_2 in the regulation of dive and surface times has been suggested before (Boutilier et al., 1993, 2001; Butler and Stephenson, 1988; Halsey et al., 2003; Parkos and Wahrenbrock, 1987; Pasche, 1976b; Stephenson et al., 1986; Wilson et al., 2003), but there has not yet been a serious attempt to include this variable in a formal physiological model.

Finally, and perhaps most importantly, the ADL concept neglects the dynamic aspects of cardiorespiratory control. The chemoreflex control system is a negative feedback loop with significant circulatory delay between the effectors (internal and external gas exchange surfaces) and the sensory receptors. A controller of this type may induce changes in respiratory drive that are temporally out of phase with the changes in O_2 store (Cherniack and Longobardo, 1986; Khoo, 2000). Furthermore, neural feedforward inputs add to the chemoreflex inputs to modify respiratory drive (Shea, 1996). Hence to be fully explanatory, rather than merely descriptive, the ADL concept must be expanded to include information about changes in partial pressures of both O_2 and CO_2, chemoreflex characteristics (thresholds and sensitivities of both central and peripheral chemoreceptors), how they vary over time, and how they combine with non-chemoreflex inputs to affect overall respiratory drive.

It is often assumed that asphyxia develops with time under water and the diving animal remains submerged until a strong drive to breathe or some other stimulus triggers it to return to the surface (Castellini and Castellini, 2004; Davis et al., 2004; Milsom, 2000). As a dive progresses, the gradually increasing respiratory drive is assumed to be counteracted by inhibitory inputs arising perhaps from sensory receptors in the upper respiratory tract or from central neural origin. The present study was designed to evaluate an alternative hypothesis (Woodin and Stephenson, 1998); that apnoea is initiated and maintained during dives by disfacilitation of breathing, not active inhibition, and that under routine conditions a diving mammal is stimulated to return to the water surface by any positive value of net respiratory drive. That is, it is postulated that the threshold level of chemical respiratory drive that triggers an aquatic mammal to begin a dive and to return to the water surface is equivalent to zero net chemoreflex drive. The plausibility of this hypothesis was examined using a mathematical model of the cardiorespiratory control system, with parameter values derived from the literature for an average adult Weddell seal *Leptonychotes weddelli*. This species was chosen because it is a marine mammal species for which there is a reasonably complete set of parameter values available, it usually dives for durations less than the ADL and was the species upon which Kooyman based his original formulation of the ADL concept.

Materials and methods

A mathematical model of the mammalian cardiorespiratory control system was constructed in spreadsheet format (Microsoft® Excel version 2003) and simulations were executed with a time resolution of 0.6 s, which was found in preliminary tests to be short enough to avoid significant

artifacts in Weddell seal simulations (higher resolution would be required for simulations of smaller animals with shorter time constants). The model is a modified version of one published previously (Stephenson, 2004), which in turn was based on models developed by Cherniack and colleagues (Chonan et al., 1988; Longobardo et al., 2002, 1966), Khoo and colleagues (Khoo et al., 1991, 1982) and Duffin and colleagues (Duffin and Mahamed, 2003; Duffin et al., 2000). The cited publications should be consulted for a detailed description of the underlying concepts and assumptions.

The specific version of the model used in the present study is shown schematically in Fig. 1. It consists of six body compartments (alveolar lung, myocardium, brain, locomotor muscle, postural muscle and viscera) interconnected by the blood circulation. The locomotor and postural muscle compartments were treated as a combined compartment (i.e. assigned identical parameter values) in the present study.

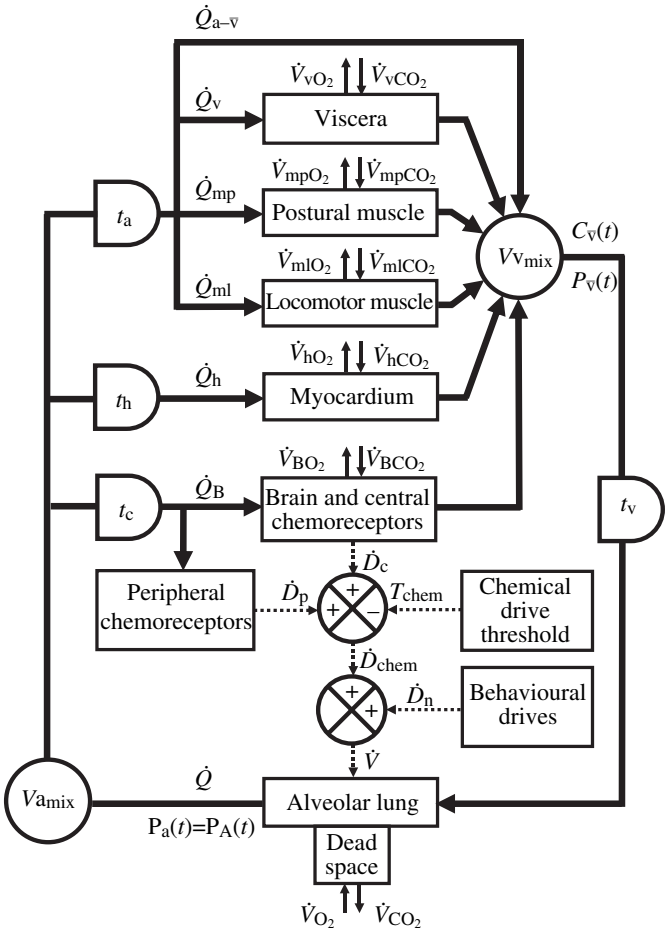

Fig. 1. Schematic diagram of the model. Six body compartments (rectangular boxes) interconnected by blood circulation (bold solid lines), with arterial and venous mixing compartments and circulatory lags (t_a, t_h, t_c and t_v). Compartmental blood flows are coupled to compartmental metabolic rate and oxygen delivery (local vascular regulation) and to respiratory drive (systemic vascular regulation). Fine solid arrows indicate internal and external gas exchange. Dotted arrows indicate neural respiratory drives. See text for a detailed description. Abbreviations are listed in Tables 1 and 2.

Parameter values used in computer simulations of diving in Weddell seals are given in Table 1. In all equations, volumes were expressed in litres, mass in kg, time in min, and partial pressures in mmHg (1 mmHg=0.133 kPa). Abbreviations are summarized in Tables 1 and 2.

The underlying assumption in this analysis is that respiratory drives represent a stimulus causing the animal to 'decide' to begin and end a dive.

Gas exchange

Mass balance equations were used to calculate exchange of gases between blood and atmosphere in the lung, and blood and tissues in the other model compartments. It was assumed that 'arterial' (i.e. pulmonary capillary) partial pressures of oxygen (Pa_{O_2}) and carbon dioxide (Pa_{CO_2}) and the respective alveolar partial pressures ($P_{A_{O_2}}$ and $P_{A_{CO_2}}$), were equivalent. It was also assumed that the partial pressures of gases in venous blood leaving the brain, heart, muscle and viscera compartments were equal to those in the respective tissues. O_2 was assumed to be obtained only from blood haemoglobin (i.e. dissolved O_2 was neglected) in all tissue compartments except muscle, which also included myoglobin saturation and desaturation. Blood and tissue CO_2 capacitances were assumed to be equal, so that CO_2 was added to tissue and blood in equal proportion by mass in all tissue compartments. Hence, the change in quantity of CO_2 and O_2 in one iteration ($dt=t-t_0$, where t is the current iteration and t_0 the previous one) is the sum of changes due to blood flow and metabolism:

$$\Delta CO_{2i} = dt\{\dot{Q}_i[Ca_{CO_2}(t-t_i) - C_{iCO_2}(t_0)] + \dot{V}_{iCO_2}(t)\} \quad (1a)$$

$$\Delta O_{2i} = dt\{\dot{Q}_i[Ca_{O_2}(t-t_i) - C_{iO_2}(t_0)] - \dot{V}_{iO_2}(t)\}\,, \quad (1b)$$

where ΔCO_{2i}, ΔO_{2i} are the changes in quantities of CO_2 and O_2 in compartment 'i', $Ca_{CO_2}(t-t_i)$, $Ca_{O_2}(t-t_i)$ are the concentrations of CO_2 and O_2 in arterial blood entering compartment 'i' after the relevant circulation lag time ($t-t_i$), and $\dot{V}_{iCO_2}(t)$, $\dot{V}_{iO_2}(t)$ represent aerobic metabolic rate of compartment 'i' in the current iteration (t), measured as rates of CO_2 production and O_2 consumption, respectively:

$$C_{iCO_2}(t) = C_{iCO_2}(t_0) + \Delta CO_{2i} / M_i \quad (2a)$$

$$C_{iO_2}(t) = C_{iO_2}(t_0) + \Delta O_{2i} / M_i\,, \quad (2b)$$

where M_i is the mass of compartment 'i'. This assumes that mass is numerically equivalent to tissue water volume.

It was assumed that tissue respiratory quotient ($RQ=\dot{V}_{CO_2}/\dot{V}_{O_2}$) was equal to 1.0 in the brain compartment, where the tissues metabolize mainly glucose, and 0.85 in the other compartments.

In the lung compartment, change in quantities of CO_2 and O_2 in one iteration is the sum of changes due to blood flow (cardiac output $\dot{Q}$) and alveolar ventilation ($\dot{V}_A$):

$$\Delta CO_{2A} = dt\{\dot{Q}[C\bar{v}_{CO_2}(t-t_v) - Ca_{CO_2}(t_0)] - \dot{V}_A[F_{A_{CO_2}}(t_0) - F_{I_{CO_2}}(t)]\} \quad (3a)$$

$$\Delta O_{2A} = dt\{\dot{Q}[C\bar{v}_{O_2}(t-t_v) - Ca_{O_2}(t_0)] + \dot{V}_A[F_{I_{O_2}}(t_0) - F_{A_{O_2}}(t)]\}\,, \quad (3b)$$

where ΔCO_{2A}, ΔO_{2A} are the changes in quantities of CO_2 and O_2 in the alveoli, and $C\bar{v}_{CO_2}(t–t_v)$, $C\bar{v}_{O_2}(t–t_v)$ are mixed venous concentrations of CO_2 and O_2 entering the lung after venous lag time ($t–t_v$).

$$F_{A_{CO_2}}(t) = F_{A_{CO_2}}(t_0) + \Delta CO_2 / V_A \quad (4a)$$

$$F_{A_{O_2}}(t) = F_{A_{O_2}}(t_0) + \Delta O_2 / V_A\,, \quad (4b)$$

$$P_{A_{CO_2}} = F_{A_{CO_2}}(P_B–P_{H_2O}) \quad (5a)$$

$$P_{A_{O_2}} = F_{A_{O_2}}(P_B–P_{H_2O})\,, \quad (5b)$$

where P_A is alveolar partial pressure, F_A is alveolar fractional concentration, V_A is average alveolar volume, P_B is barometric pressure and P_{H_2O} is saturated water vapour pressure at 37°C (47 mmHg). Lung volume (V_L) could differ between surface respiration and apnoea onset. The respiratory exchange ratio (RER) was calculated as:

$$\mathrm{RER} = \frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}} = \frac{\dot{V}_A(F_{A_{CO_2}}–F_{I_{CO_2}})}{\dot{V}_A(F_{I_{O_2}}–F_{A_{O_2}})} = \frac{F_{A_{CO_2}} – F_{I_{CO_2}}}{F_{I_{O_2}} – F_{A_{O_2}}}\,, \quad (6)$$

Table 1. *'Standard' model parameter values for an average adult Weddell seal*

Parameter	Abbreviation	Value
Body mass (kg)	M_b	450.0
Brain mass (kg)	M_B	0.6
Heart mass (kg)	M_h	1.9
Skeletal muscle mass (kg)	M_m	157.5
Viscera and blood mass (kg)	M_v	290.0
Whole body oxygen consumption (l min^{-1})	$\dot{V}_{O_2}$	1.78
Brain oxygen consumption (l min^{-1})	$\dot{V}_{BO_2}$	0.0133
Myocardium oxygen consumption (l min^{-1})	$\dot{V}_{hO_2}$	0.225
Skeletal muscle oxygen consumption (l min^{-1})	$\dot{V}_{mO_2}$	0.432
Viscera oxygen consumption (l min^{-1})	$\dot{V}_{vO_2}$	1.11
Whole body carbon dioxide production (l min^{-1})	$\dot{V}_{CO_2}$	1.515
Brain carbon dioxide production (l min^{-1})	$\dot{V}_{BCO_2}$	0.0133
Myocardium carbon dioxide production (l min^{-1})	$\dot{V}_{hCO_2}$	0.191
Skeletal muscle carbon dioxide production (l min^{-1})	$\dot{V}_{mCO_2}$	0.367
Viscera carbon dioxide production (l min^{-1})	$\dot{V}_{vCO_2}$	0.944
Barometric pressure (mmHg)	P_B	760
Fractional inspired oxygen concentration	$F_{I_{O_2}}$	0.2093
Fractional inspired carbon dioxide concentration	$F_{I_{CO_2}}$	0.0004
Average lung volume (l)	V_L	16
Pulmonary dead space volume (l)	V_D	1.6
Tidal volume (l)	V_T	5.4
Standard resting lung ventilation (l min^{-1})	$\dot{V}_{rest}$	20
Maximum lung ventilation (l min^{-1})	$\dot{V}_{max}$	240
Central chemoreceptor threshold (mmHg CO_2)	T_c	37.4
Central chemosensitivity (l min^{-1} mmHg^{-1} CO_2)	S_c	12.29
Peripheral chemoreceptor threshold (mmHg CO_2)	T_p	37.4
Sp hypoxic shape constant (l min^{-1} mmHg^{-1} CO_2 mmHg^{-1} O_2)	K	350
Sp hypoxic asymptote (mmHg O_2)	A	15
Chemoreflex (apnoeic) threshold (mmHg CO_2)	T_1	43.7
Chemoreflex drive threshold (l min^{-1})	T_{chem}	103.4
Central neural drive (l min^{-1})	$\dot{D}_n$	0

Parameter	Abbreviation	Value
Maximum cardiac output (l min^{-1})	$\dot{Q}_{max}$	84.3
Maximum heart rate (beats min^{-1})	$f_{H_{max}}$	85
Standard cerebral blood flow (l min^{-1})	$\dot{Q}_{Brest}$	0.6
Minimum cerebral blood flow ($\times\dot{Q}_{Brest}$)	$\dot{Q}_{Bmin}$	0.4
Cerebrovascular CO_2 gain ($\times\dot{Q}_{Brest}$ mmHg^{-1})	Gq	0.05
Standard resting arterial carbon dioxide partial pressure (mmHg)	Pa_{CO_2rest}	44
Minimum arterial oxygen partial pressure (mmHg)	Pa_{O_2min}	15
Standard oxygen extraction coefficient – heart	$E^*_{hO_2rest}$	0.19
Standard oxygen extraction coefficient – muscle	$E^*_{mO_2rest}$	0.115
Maximum muscle oxygen extraction coefficient	$E^*_{mO_2max}$	10
Minimum muscle oxygen extraction coefficient	$E^*_{mO_2min}$	0.03
Standard oxygen extraction coefficient – viscera	$E^*_{vO_2rest}$	0.115
Maximum viscera oxygen extraction coefficient	$E^*_{vO_2max}$	0.8
Minimum viscera oxygen extraction coefficient	$E^*_{vO_2min}$	0.03
Arterio–venous blood shunt (l min^{-1})	$\dot{Q}_{a–v}$	0
Blood volume (l)	V_b	96
Arterial blood volume (l)	V_{b_a}	28.8
Venous blood volume (l)	V_{b_v}	67.2
Arterial effective mixed volume (l)	$V_{a_{mix}}$	4.3
Venous effective mixed volume (l)	$V_{v_{mix}}$	20.2
Haemoglobin concentration (kgHb l^{-1} blood)	C_{Hb}	0.26
Haemoglobin P_{50} (mmHg O_2)	P_{50Hb}	26.9
Hill coefficient	n	2.39
Standard resting haemoglobin saturation	Sa_{O_2rest}	0.975
Myoglobin concentration (kg Mb kg^{-1} muscle)	C_{Mb}	0.054
Myoglobin P_{50} (mmHg O_2)	P_{50Mb}	2.39
Minimum myoglobin O_2 saturation	Sm_{O_2min}	0.01
Pigment oxygen binding coefficient (l O_2 kg^{-1} pigment)	β_{Hb}, β_{Mb}	1.34

Data taken from Blix et al., 1983; Castellini et al., 1992; Cunningham et al., 1986; Davis and Kanatous, 1999; Duffin et al., 2000; Elsner et al., 1970; Fortune et al., 1992; Kooyman and Campbell, 1972; Kooyman et al., 1971, 1973, 1980; Lange et al., 1966; Ponganis et al., 1993; Zapol et al., 1979.

where $F_{I_{O_2}}$ and $F_{I_{CO_2}}$ are the inspired fractional concentrations of oxygen and carbon dioxide, respectively.

Blood circulation

Three main functional categories were quantified: blood flow, circulatory transfer functions and blood gases.

Blood flow

Cardiac output ($\dot{Q}$) was calculated as the sum of blood flows through each of the model tissue compartments (except lung) and the arterio–venous shunt ($\dot{Q}_{a-\bar{v}}$). $\dot{Q}_{a-\bar{v}}$ was an adjustable parameter that could differ between dive and surface intervals. It was assumed that changes in $\dot{Q}$ were associated with relatively large changes in heart rate (f_H, beats min^{-1}) and relatively smaller changes in cardiac stroke volume (V_S, litres), and the following relations were used, calculated from data in Davis and Kanatous (1999):

$$f_H = 1.1\dot{Q} + 5.0 , \quad (7a)$$

$$V_S = 0.005\dot{Q} + 0.6 . \quad (7b)$$

Maximum cardiac output ($\dot{Q}_{max}$) was varied in this model by adjusting maximum heart rate.

Brain blood flow ($\dot{Q}_B$) was assumed to be dependent on fractional oxygen saturation of arterial blood ($S_{a_{O_2}}$) and $P_{a_{CO_2}}$ in blood entering the brain (Fortune et al., 1992):

$$\dot{Q}_B = \dot{Q}_{Brest} + \{\dot{Q}_{Brest}Gq[P_{a_{CO_2}}(t-t_c)-P_{a_{CO_2rest}}]\} + \{\dot{Q}_{Brest}[S_{a_{O_2rest}}-S_{a_{O_2}}(t-t_c)]\} , \quad (8)$$

where $\dot{Q}_{Brest}$, $P_{a_{CO_2rest}}$ and $S_{a_{O_2rest}}$ are parameters representing standard 'resting' values, and Gq is a factor representing the relative cerebral vascular sensitivity to CO_2 (Fortune et al., 1992).

Myocardial, skeletal muscle and viscera compartment blood flows were subject to 'local regulation', modeled as follows:

$$\dot{Q}_i = \dot{V}_{iO_2} / [E^*_{O_2} \times C_{a_{O_2}}(t-t_i)] , \quad (9)$$

where $\dot{Q}_i$ is blood flow through compartment 'i', $\dot{V}_{iO_2}$ is oxygen consumption of compartment 'i', $C_{a_{O_2}}(t-t_i)$ is oxygen content of the arterial blood entering the compartment after the appropriate circulatory lag time ($t-t_i$) and $E^*_{O_2}$ is a 'target' blood oxygen extraction coefficient:

$$E^*_{O_2} = \frac{C_{a_{O_2}}(t-t_i) - C_{v_{O_2}}(t)}{C_{a_{O_2}}(t-t_i)} = \frac{\dot{Q}_i[C_{a_{O_2}}(t-t_i) - C_{v_{O_2}}(t)]}{\dot{Q}_i \times C_{a_{O_2}}(t-t_i)} = \frac{\dot{V}_{iO_2}}{\dot{Q}_i \times C_{a_{O_2}}(t-t_i)} , \quad (10)$$

where $C_{v_{O_2}}(t)$ is oxygen concentration of compartmental venous blood. Thus, compartmental blood flow was assumed to be dependent on metabolic rate of the tissue and arterial blood oxygen delivery.

For the myocardium, the target blood oxygen extraction coefficient was fixed at a value ($E^*_{O_2}$=0.19) that yielded published coronary blood flow under resting conditions (Zapol et al., 1979). Myocardial metabolic rate was assumed to change in direct proportion to cardiac output. This mechanism therefore ensured an adequate supply of oxygen to the heart muscle whenever blood oxygen content and heart work varied.

For the skeletal muscle and viscera compartments, tissue metabolic rates were set as adjustable parameter values during dives and surface intervals. In addition to the 'local regulation' of blood flow described above, these compartments were also subject to 'systemic regulation' of blood flow, modeled by coupling target blood oxygen extraction coefficient ($E^*_{O_2}$) to net respiratory drive ($\dot{V}$). The extent of this cardiorespiratory coupling was independently adjustable for both dive and surface intervals in each compartment, and the gain of the coupling mechanism was normalized to standard resting lung ventilation ($\dot{V}_{rest}$):

if $\dot{V} > \dot{V}_{rest}$,

$$E^*_{O_2} = E^*_{O_2rest} - \dot{q}(E^*_{O_2rest} - E^*_{O_2min}) ; \quad (11a)$$

if $\dot{V} < \dot{V}_{rest}$,

$$E^*_{O_2} = E^*_{O_2rest} + \dot{q}(E^*_{O_2max} - E^*_{O_2rest}) , \quad (11b)$$

where $E^*_{O_2rest}$ is a standard resting blood oxygen extraction coefficient, and $E^*_{O_2max}$ and $E^*_{O_2min}$ are user-defined limits for the target oxygen extraction coefficient in each compartment. Within these limits, the 'relative coupling gain' ($\dot{q}$) caused compartmental target blood oxygen extraction coefficient ($E^*_{O_2}$) to vary in proportion to the relative change in lung ventilation:

if $\dot{V} > \dot{V}_{rest}$,

$$\dot{q} = (\dot{V} - \dot{V}_{rest}) / (\dot{V}_{max} - \dot{V}_{rest}) ; \quad (12a)$$

if $\dot{V} < \dot{V}_{rest}$,

$$\dot{q} = (\dot{V}_{rest} - \dot{V}) / (\dot{V}_{rest} - \dot{V}_{min}) , \quad (12b)$$

where $\dot{V}_{max}$ and $\dot{V}_{min}$ are maximum lung ventilation (a value determined in real animals by factors such as mechanical limitations on lung ventilation) and minimum ventilation (apnoea), respectively. In practice, the intensity of the 'systemic' cardiovascular response was adjusted by changing the degree of cardiorespiratory coupling *via* the $E^*_{O_2max}$ and $E^*_{O_2min}$ values (Eqn 11). In this study, all tissues were assumed to remain within the ADL (i.e. net anaerobic metabolism was excluded). Therefore in the viscera, which have no appreciable O_2 store, $E^*_{O_2max}$ never exceeded 0.8 (Davis and Kanatous, 1999). In skeletal muscle, however, nearly zero blood flow ($\dot{Q}_m$) could be achieved during apnoea by setting $E^*_{mO_2max}$ to a very high value (a value of 10 was used in this study). To satisfy the ADL constraint, if myoglobin oxygen saturation (S_{mO_2}) decreased to a minimum value (0.01), $E^*_{mO_2max}$ became 0.8 and muscle blood flow therefore became dependent on muscle metabolic rate ($\dot{V}_{mO_2}$) and arterial blood oxygen content [$C_{a_{O_2}}(t-t_a)$] for the remainder of the dive (Eqn 9).

Elevations in compartmental blood flows during surface intervals were constrained by maximum cardiac output and under limiting conditions, the competing drives for blood flow in the different compartments were resolved by imposing an arbitrary priority order: $\dot{Q}_B$=$\dot{Q}_h$>$\dot{Q}_m$>$\dot{Q}_v$. Thus, cerebral and

coronary oxygen delivery was always adequate, and skeletal muscle recovery was given priority over viscera to facilitate myoglobin reoxygenation. When present, the arterio–venous blood shunt ($\dot{Q}_{a-v}$) functioned as a fixed parameter and therefore assumed top priority, and because of this the maximum shunt flow was never set so high as to limit cerebral and coronary blood flows.

Circulatory transfer function

The arterial and venous transfer functions were each modeled as the sum of two components, a circulatory lag time and a mixing function (Lange et al., 1966). Circulatory lag times were assumed to be proportional to cardiac output and blood volume, and the latter was divided into arterial blood ($V\mathrm{b}_a$) and venous blood ($V\mathrm{b}_v$) in the volume ratio 3:7. The arterial lag time represents the average time taken for blood to flow from the lung to the muscles and viscera [$(t–t_a)$], and was calculated as:

$$(t–t_a) = V\mathrm{b}_a / \dot{Q} . \quad (13a)$$

It was assumed that circulatory lag time to the peripheral chemoreceptors and brain ($t–t_c$) was 70% of arterial lag time ($t–t_a$), and that the heart is half way between lung and brain (i.e. circulatory lag time to the myocardium ($t–t_h$) was 50% of chemoreceptor lag time ($t–t_c$). Venous circulatory lag time ($t–t_v$) was calculated similarly:

$$(t–t_v) = V\mathrm{b}_v / \dot{Q} . \quad (13b)$$

The mixing function was modeled as a simple first order system with time constant (τ_{mix}):

$$\tau_{mix} = V_{mix} / \dot{Q} , \quad (14)$$

where V_{mix} is the effective volume of the mixed sub-compartments of the arterial ($V\mathrm{a}_{mix}$) and venous ($V\mathrm{v}_{mix}$) systems (Fig. 1).

A step change in cardiac output cannot be modeled with a step change in circulation lag (i.e. in the referenced row of the spreadsheet) because in a real circulatory system a change in cardiac output is followed by a transition period lasting the duration of the new 'instantaneous steady-state' circulatory lag time. During this transition period the 'waveform' of blood gases at any given point in the circulation appears compressed or expanded when cardiac output increases or decreases, respectively. When cardiac output changes continuously, as it does during a diving bout, the circulatory delay is continuously in 'transitional' mode. To account for this, the appropriate lag time [expressed as the number of spreadsheet rows, $R(t)$] was calculated for each iteration as follows:

$$R(t) = R(t_0) + [R(t)^*–R(t_0)] / [(t–t_i^*)/\mathrm{d}t] , \quad (15)$$

where $R(t_0)$ is the number of rows representing the actual circulation lag time in the previous iteration, $R(t)^*$ is the number of rows equal to the calculated instantaneous steady-state circulation lag time [of duration $(t–t_i^*)$] in the current iteration and dt is the duration of each iteration (min).

Blood gases

Contents and partial pressures of blood gases were related by oxygen and carbon dioxide equilibrium curves. Bohr and Haldane effects were omitted. Temperature of the blood and tissues was assumed to be constant at 37°C. For oxygen, the Hill equation was used:

$$S_{O_2} = P_{O_2}^{\,n} / (P_{O_2}^{\,n}+P_{50}^{\,n}) \quad (16a)$$

$$P_{O_2} = [(S_{O_2}/1–S_{O_2})\times P_{50}^{\,n}]^{1/n} , \quad (16b)$$

where P_{50} is the P_{O_2} at 0.5 fractional saturation, n is the Hill cooperativity coefficient, and S_{O_2} is fractional saturation. The same relations hold for myoglobin, where n=1.

S_{O_2} was related to O_2 concentration (C_{O_2}) by:

$$C_{O_2} = S_{O_2}\times C_{Hb}\times\beta_{Hb} , \quad (17)$$

where C_{Hb} is the concentration of haemoglobin and β_{Hb} is the haemoglobin O_2 binding coefficient.

For carbon dioxide, a linear version of the carbon dioxide equilibrium curve was derived from data for human blood (Miyamura and Honda, 1978) and it was assumed to be the same for Weddell seal blood and tissue fluids:

$$C_{CO_2} = 0.0044P_{CO_2} + 0.2831 \quad (18a)$$

$$P_{CO_2} = 227.68C_{CO_2} – 64.374 . \quad (18b)$$

System controller

The ventilatory controller was based on Duffin's modification of the 'Oxford model' of respiratory control (Cunningham et al., 1986; Duffin et al., 2000), consisting of additive drives from central and peripheral chemoreceptors (feedback), and a central neural 'behavioural' drive (feedforward) that is independent of chemical stimuli. All respiratory drives were expressed in l min^{-1}.

This model assumes that central and peripheral chemoreceptors have a chemoreceptor threshold (T_c and T_p, respectively) for P_{CO_2}, below which chemoreceptors are functionally silent (Duffin et al., 2000). Chemoreceptor drives were assumed to increase as a linear function of P_{CO_2} above the respective chemoreceptor thresholds (T_c and T_p). The slopes of these relationships represent the central and peripheral chemosensitivities (S_c and S_p, respectively). Chemical respiratory drive ($\dot{D}_{chem}$) was computed as the sum of central and peripheral chemoreceptor drives ($\dot{D}_c$ and $\dot{D}_p$, respectively), and affected ventilation only when above a threshold (chemical drive threshold, T_{chem}). When chemical respiratory drive ($\dot{D}_{chem}$) fell below chemical drive threshold (T_{chem}), ventilation was determined solely by the behavioural drive ($\dot{D}_n$):

$$\dot{D}_{chem} = \dot{D}_c + \dot{D}_p ; \quad (19a)$$

if $\dot{D}_{chem} > T_{chem}$,

$$\dot{V} = \dot{D}_n + (\dot{D}_{chem}–T_{chem}) ; \quad (19b)$$

if $\dot{D}_{chem} \leqslant T_{chem}$,

$$\dot{V} = \dot{D}_n . \quad (19c)$$

The chemoreflex threshold (T_1) is the partial pressure of CO_2 at which chemical respiratory drive ($\dot{D}_{chem}$) is equal to chemical drive threshold (T_{chem}). In this study, $\dot{D}_n$ was set at user-defined values during surface intervals and fell to zero during dives. The chemoreflex threshold (T_1) and chemical drive threshold (T_{chem}) therefore both function as an 'apnoeic threshold' whenever behavioural drive ($\dot{D}_n$) is zero.

Central chemoreceptors were assumed to be (indirectly) sensitive to the partial pressure of carbon dioxide in the brain tissue compartment [$P_{BCO_2}(t)$; see Lahiri and Forster (2003) for a justification of this assumption] and peripheral chemoreceptors were assumed to be sensitive to Pa_{O_2} and Pa_{CO_2} in arterial blood flowing through the chemoreceptors [i.e. at time (t–t_c) after leaving the lung]:
if $P_{BCO_2}(t) > T_c$,

$$\dot{D}_c = S_c[P_{BCO_2}(t)–T_c] \; ; \tag{20a}$$

if $Pa_{CO_2}(t–t_c) > T_p$,

$$\dot{D}_p = S_p[Pa_{CO_2}(t–t_c)–T_p] \; . \tag{20b}$$

Central chemosensitivity (S_c) was a fixed parameter (Table 1), but peripheral chemosensitivity (S_p) was a variable (Table 2), varying as an inverse hyperbolic function of Pa_{O_2} (Duffin et al., 2000; Mohan and Duffin, 1997):

$$S_p = K / (Pa_{O_2}(t–t_c) – A) \; , \tag{21}$$

where K is a hyperbolic area constant and A is a Pa_{O_2} asymptote.

Reliable values for some respiratory control parameters ($\dot{D}_n$, T_c, T_p, S_c, S_p, K, A) are available only for adult male human beings. The corresponding values for an adult Weddell seal were estimated as follows. $\dot{D}_n$, S_c and S_p were estimated by defining a standard resting level of ventilation for both human and seal, and expressing $\dot{D}_n$, S_c and K, respectively, as multiples of standard ventilations. The value of A in Eqn 21 was assumed to be 15 mmHg, the same as the assumed lower critical Pa_{O_2} for cerebral viability in seals (Elsner et al., 1970).

It was assumed that there is a constant respiratory dead space volume in series with the alveolar compartment of the lung. Alveolar ventilation ($\dot{V}_A$) was derived from total ventilation ($\dot{V}$) as follows:

$$\dot{V}_A = \dot{V} – \dot{V}_D \; , \tag{22}$$

where $\dot{V}_D$ is dead space ventilation, and

$$\dot{V}_D = V_D \times f_R \; , \tag{23}$$

where f_R is respiratory frequency. To simplify the calculation of $\dot{V}_D$, respiratory tidal volume (V_T) was assumed to be constant.

Protocol

Standard model parameter values were derived from the literature or estimated as described above for an average adult male Weddell seal (Table 1). The primary objective was to determine whether the model could simulate variations in respiratory drive in a way that is consistent with the hypotheses outlined in the Introduction. These hypotheses predict that net respiratory drive will oscillate with amplitude large enough to induce apnoea. Furthermore, the durations of the simulated apnoeic and eupnoeic intervals must correspond to the range of durations reported for dive and surface intervals in freely behaving seals.

The basic approach used in each simulation was to set model parameters to desired 'resting' values and, with the model forced to remain at the surface, the system was allowed to reach a steady-state condition. The model was then switched to enable dive cycles so that parameter values automatically assumed 'surface' values when ventilating, and 'diving' values when apnoeic. Briefly, beginning at the water surface, if chemical respiratory drive ($\dot{D}_{chem}$) fell below chemical drive threshold (T_{chem}), a dive was initiated and model parameters assumed 'diving' values. When chemical respiratory drive subsequently increased above the chemical drive threshold, the dive was terminated and the model switched back to 'surface' parameter values. These studies were conducted with maximum dive depth set to 1 m to avoid any confounding effects of depth. This paper therefore describes simulations of a seal floating at the water surface and the effect of swimming to depth is to be examined in a subsequent study. To avoid any transients associated with the transition from steady state rest to diving mode, all analyses refer to dive cycles occurring in the interval 65–135 min after the onset of simulated diving behaviour.

An extensive series of simulations was conducted in which parameter values were systematically varied, alone and in combination, in order to determine the relative influence of each on respiratory stability. Only the most relevant tests are reported: (i) the effects of changes in behavioural respiratory drive, $\dot{D}_n$ (hyperventilation), (ii) the effects of variations in chemoreflex characteristics (T_c, T_p, S_c and S_p), (iii) the effects of cerebral blood flow, (iv) the effects of variation in the arterial and venous circulatory transfer functions, (v) the role of oxygen and (vi) the role of the spleen.

Hyperventilation

To examine the effect of hyperventilation the model was initially designed to include a timer function that enabled the user to specify a minimum ventilatory interval ($t_{s,min}$) between dives. This allowed an analysis of combinations of intensity ($\dot{D}_n$) and duration (t_s) of hyperventilation. The duration of apnoea (i.e. a shallow 'dive', t_d) was measured as a function of t_s at each of several values of $\dot{D}_n$. It was found in these tests that hyperventilation is necessary for apnoea, so a 'standard' value for the behavioural respiratory drive ($\dot{D}_n$=180 l min^{-1}) was used during the surface intervals in the subsequent simulations unless noted otherwise.

Chemoreflex parameters

When $t_{s,min}$ is used as in the above preliminary simulations, the duration of surface intervals is an independent variable. This was considered to be an unsatisfactory approach in the absence of any well-defined physiological analogue to the

arbitrary mathematical 'timer' ($t_{s,min}$). Further tests were therefore conducted to determine whether surface and dive durations could both be modeled as dependent variables using conventional respiratory control mechanisms. Specifically, on the basis of factors that are known to influence respiratory stability during sleep–wake cycles (e.g. Khoo, 2000), it was hypothesized that differences between dive and surface parameter values of the chemoreflex thresholds and/or chemosensitivities might provide a mechanism for modulation of t_s. The surface and diving values for thresholds and sensitivities (slopes) of both peripheral and central chemoreflexes were adjusted individually and in combination over a limited range around the nominal resting levels. The role of the peripheral chemoreceptors was tested by systematic changes in peripheral chemoreceptor threshold (T_p) in combination with variation in the peripheral chemoreceptor hypoxic asymptote (A). In these and all subsequent simulations, the $t_{s,min}$ function was inactivated (i.e. kept constant at zero) so that dive duration (t_d) and surface intervals (t_s) could both be assessed as dependent variables. On the basis of these tests a 'standard' set of chemoreflex parameter values was defined and used in all subsequent simulations unless noted otherwise.

Cerebral blood flow

Cerebral blood flow ($\dot{Q}_B$) was manipulated by adjusting the model parameter values for cerebrovascular CO_2 gain (Gq in Eqn 8) and the minimum cerebral blood flow ($\dot{Q}_{Bmin}$), separately and in combination.

Circulatory transfer functions

The effects on simulated surface intervals (t_s) and dive durations (t_d) of variation in arterial and venous transfer functions were examined by systematic adjustment of the two components, circulatory lag time and time constant of the mixing function.

The circulatory lag time was dependent on blood volume and cardiac output (Eqn 13). In these tests, blood volume was held constant and cardiac output ($\dot{Q}$) was varied either during dives ($\dot{Q}_d$) or during surface intervals ($\dot{Q}_s$). Mean $\dot{Q}_d$ was manipulated in two ways; by altering arterio–venous shunt flow ($\dot{Q}_{a-\bar{v}}$) during simulated dives or by altering the degree of cardiorespiratory coupling *via* changes in $E^*_{O_2max}$ during dives. Mean $\dot{Q}_s$ was manipulated by combined changes in maximum cardiac output ($\dot{Q}_{max}$) and arterio–venous blood shunt ($\dot{Q}_{a-\bar{v}}$) during surface intervals.

The time constants of arterial and venous mixing were adjusted by systematic changes in the effective volumes of the mixed circulatory sub-compartments ($V\mathrm{a}_{mix}$ and $V\mathrm{v}_{mix}$). Values of $V\mathrm{a}_{mix}$ and $V\mathrm{v}_{mix}$ were varied separately and in combination over the range 2–50% of arterial and venous blood volumes, respectively, and the effects of this on simulated dive and surface durations were noted. On the basis of these tests, 'standard' values for the effective volumes of the mixed circulatory sub-compartments ($V\mathrm{a}_{mix}$ and $V\mathrm{v}_{mix}$) were defined and used in all subsequent simulations (Table 1).

The role of oxygen

The oxygen concentration of inhaled air was adjusted over the range 10% to 100% O_2 ($F_{I_{O_2}}$=0.1–1.0). This was then repeated after elimination of oxygen-sensitive mechanisms in the model. First of all, peripheral chemoreceptor threshold (T_p) was increased sufficiently to abolish peripheral chemoreflex drive ($\dot{D}_p$), thereby simulating acute carotid body denervation (CBD). Secondly, the cerebrovascular O_2-sensitivity was deleted from Eqn 8 so that cerebral blood flow was solely dependent on arterial P_{CO_2}. Finally, alveolar volume at the start of a dive was set to zero to eliminate any effect of O_2 storage in the lung compartment. With all of the above manipulations applied concurrently the 'local regulation' component of tissue compartment blood flow (Eqn 9) remained as the only mechanism by which altered $F_{I_{O_2}}$ could have an effect on simulated diving behaviour in this model.

Oxygen store (V_{O_2store}) was calculated for the first iteration of a dive, and used in conjunction with the rate of oxygen consumption during dives ($\dot{V}_{O_2d}$) to estimate the aerobic dive limit in the convention manner: ADL= $V_{O_2store}/\dot{V}_{O_2d}$. O_2 content of the lung was calculated as the product of fractional alveolar oxygen concentration and alveolar volume ($F_{A_{O_2}}*V_A$), O_2 contents of arterial and venous blood were taken as the average concentration over the number of spreadsheet rows corresponding to the current arterial and venous circulatory lag times multiplied by the respective arterial and venous blood volumes, and muscle O_2 content was calculated as the product of muscle O_2 carrying capacity and myoglobin fractional oxygen saturation.

The role of the spleen

All of the above simulations were carried out using blood volume (Vb) and haemoglobin concentration (C_{Hb}) values corresponding to a seal with spleen contracted. To examine the functional significance of splenic contraction in the present model, standard diving parameters (Table 1) were entered with corrections to simulate an absence of splenic contraction: Vb=76 l, C_{Hb}=0.15 kg l^{-1}. The roles of Vb and C_{Hb} were examined separately and in combination.

Cardio-respiratory responses

Diving behaviour, lung ventilation, cardiac output, heart rate, regional blood flows, contents and partial pressures of O_2 and CO_2 in blood and tissue compartments and the chemoreflex drives were all calculated as dependent variables of the model. The dynamic responses of these variables were plotted and their interactions examined.

Results

Using the parameter values shown in Table 1, and with the model constrained to remain in 'surface' mode, all dependent variables eventually settled to stable steady-state values (Table 2). These 'resting' values represent the pre-dive starting conditions for all simulations, and all parameter values

Table 2. *Steady-state values of model dependent variables under surface 'resting' conditions, representing the starting conditions for diving simulations*

Variable	Abbreviation	Value
Alveolar ventilation (l min^{-1})	$\dot{V}_A$	24.7
Cardiac output (l min^{-1})	$\dot{Q}$	44.7
Heart rate (beats min^{-1})	f_H	53.2
Cerebral blood flow (l min^{-1})	$\dot{Q}_B$	0.54
Coronary blood flow (l min^{-1})	$\dot{Q}_h$	1.87
Skeletal muscle blood flow (l min^{-1})	$\dot{Q}_m$	11.83
Viscera blood flow (l min^{-1})	$\dot{Q}_v$	30.42
Arterial blood oxygen saturation	Sa_{O_2}	0.96
Venous blood oxygen saturation	$S\bar{v}_{O_2}$	0.85
Muscle oxygen saturation	Sm_{O_2}	0.96
Arterial blood partial pressure of oxygen (mmHg)	Pa_{O_2}	100.9
Mixed venous blood partial pressure of oxygen (mmHg)	$P\bar{v}_{O_2}$	55.9
Brain partial pressure of oxygen (mmHg)	P_{BO2}	64.0
Myocardium partial pressure of oxygen (mmHg)	Ph_{O2}	45.4
Muscle and viscera partial pressure of oxygen (mmHg)	Pm_{O_2}, P_{VO_2}	56.4
Arterial blood partial pressure of carbon dioxide (mmHg)	Pa_{CO_2}	41.6
Mixed venous blood partial pressure of carbon dioxide (mmHg)	$P\bar{v}_{CO_2}$	48.9
Brain partial pressure of carbon dioxide (mmHg)	P_{BCO_2}	47.2
Myocardium partial pressure of carbon dioxide (mmHg)	Ph_{CO_2}	53.9
Muscle and viscera partial pressure of carbon dioxide (mmHg)	P_{mCO_2}, P_{vCO_2}	48.7
Peripheral chemosensitivity (l min^{-1} mmHg^{-1} CO_2)	S_p	4.08
Peripheral chemoreflex drive (l min^{-1})	$\dot{D}_p$	17.1
Central chemoreflex drive (l min^{-1})	$\dot{D}_c$	123.9

Parameter values as given in Table 1.

remained unchanged during dive cycles unless noted otherwise.

Hyperventilation

As mentioned above, the model parameters shown in Table 1 gave rise to a dynamically stable control loop, and the model therefore did not develop spontaneous oscillatory behaviour. Hence, hyperventilation induced by an elevated feedforward 'behavioural' respiratory drive ($\dot{D}_n$) was needed to force chemical respiratory drive ($\dot{D}_{chem}$) below chemical drive threshold (T_{chem}) and thereby initiate and sustain cycles of apnoea (simulated dives) and ventilation (simulated surface intervals).

With the timer mechanism deactivated ($t_{s,min}$=0), surface intervals (t_s) decreased from 2 min at moderate behavioural respiratory drive ($\dot{D}_n$=60 l min^{-1}) to 1.3 min at high behavioural respiratory drive ($\dot{D}_n$=200 l min^{-1}). Similarly, dive duration (t_d) was short and only slightly affected by intensity of hyperventilation, rising from 1.5 min at $\dot{D}_n$=60 l min^{-1} to 3.1 min at $\dot{D}_n$=200 l min^{-1}.

The $t_{s,min}$ function was then used to examine the effect of increased duration of hyperventilation on subsequent dive duration. Dive duration (t_d) was found to be influenced by both duration ($t_{s,min}$) and intensity ($\dot{D}_n$) of hyperventilation. For surface intervals less than 3 min, no amount of hyperventilation (up to $\dot{V}_{max}$) could induce long duration dives. At any given $\dot{D}_n$ there was a critical $t_{s,min}$ that marked an abrupt increase in t_d, and this critical $t_{s,min}$ decreased with increasing $\dot{D}_n$.

Chemoreflex characteristics

Central chemoreceptor threshold (T_c) was found to be the only factor that could, when manipulated on its own, induce long-period dive cycles. Specifically, long duration simulated dives occurred when the central chemoreceptor threshold was lower during surface intervals than during dives (ΔT_c). There was a critical ΔT_c (–3.4 mmHg) that marked a transition between short-period and long-period dive cycles (Fig. 2).

When adjusted individually, the central and peripheral chemosensitivities (S_c and S_p, respectively), and peripheral chemoreceptor threshold (T_p), had negligible effects on simulated dive and surface intervals. Furthermore, combinations of changes in peripheral chemoreceptor threshold (T_p), and central and peripheral chemosensitivities (S_c and S_p) without concurrent changes in central chemoreceptor threshold (T_c) had little effect on simulated dive and surface intervals. However the peripheral chemoreflex was not completely without influence because the ΔT_c mechanism was found to be influenced by peripheral chemoreceptor threshold (T_p) (Fig. 2). Specifically, the effect of ΔT_c on simulated diving behaviour was attenuated when T_p was lower than the nominal resting value (i.e. when the peripheral chemoreceptors were more active).

Variation of the peripheral hypoxic asymptote (A) in the range 15–30 mmHg O_2 had only a small negative linear effect on dive and surface intervals. For example, at the standard T_c and T_p (see below), t_s decreased by 2.1 s and t_d decreased by 7.9 s per mmHg increase in A. Using these preliminary data as a guide, 'standard' chemoreflex parameter values were defined and used in all subsequent simulations, except where noted otherwise. Thus, the resting values (see Table 1) for T_p, S_p, A and S_c were used for both dives and surface intervals, and the resting T_c was used during dives together with a ΔT_c of –5.1 mmHg during surface intervals. These chemoreflex parameter values substituted for the $t_{s,min}$ function and allowed both t_s and t_d to be treated as dependent variables in all subsequent simulations.

Cerebral blood flow

When cerebral blood flow ($\dot{Q}_B$) was constrained to remain constant at resting levels, simulated dive and surface intervals were short (1.4 min and 3.4 min, respectively). When this constraint was relaxed, cerebral blood flow tended to rise during apnoea and fall during hyperventilation. Cerebrovascular CO_2 chemosensitivity (Gq) affected the rate

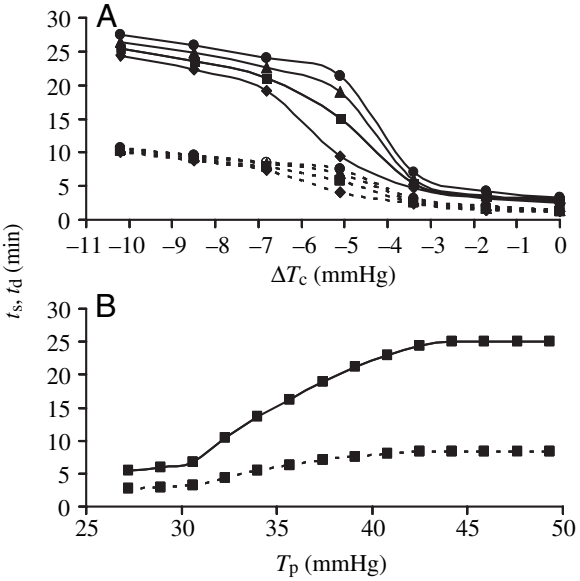

Fig. 2. The effects of varying chemoreceptor thresholds on durations of dives (t_d, solid lines) and surface intervals (t_s, broken lines). (A) The effect of decreases in central chemoreceptor threshold (T_c) during surface hyperventilation (ΔT_c, mmHg) at each of four different levels of peripheral chemoreceptor threshold (T_p, mmHg). T_c during dives was always 37.4 mmHg. T_p was constant across the dive cycle: circles, T_p=39.1 mmHg; triangles, T_p=37.4 mmHg; squares, T_p=35.7 mmHg; diamonds, T_p=34 mmHg. (B) The effect of variation in T_p on t_s and t_d at constant ΔT_c (–5.1 mmHg). Note that increasing T_p represents decreasing peripheral chemoreceptor responsiveness to CO_2 and O_2.

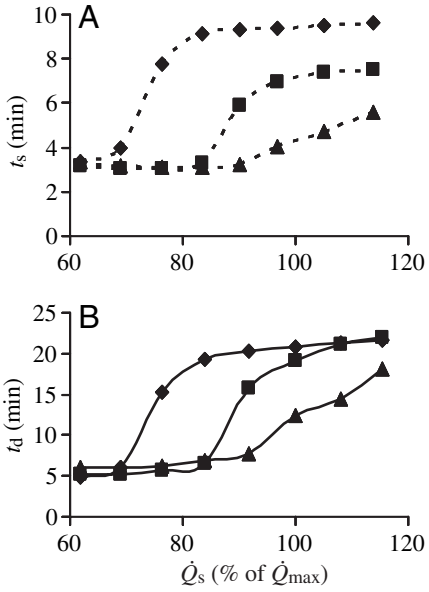

Fig. 3. The effect of mean cardiac output during surface intervals ($\dot{Q}_s$, expressed as a percentage of the nominal maximum cardiac output, $\dot{Q}_{max}$) on (A) surface intervals (t_s) and (B) dive durations (t_d). In this study $\dot{Q}_{max}$ was assumed to be 84.3 l min^{-1}, corresponding to a maximum heart rate of 85 beats min^{-1}. Simulations were conducted at three levels of hyperventilation ($\dot{D}_n$, expressed as a percentage of maximum ventilation, $\dot{V}_{max}$=240 l min^{-1}); diamonds, $\dot{D}_n$=58%; squares, $\dot{D}_n$=75%; triangles, $\dot{D}_n$=92%.

of change in cerebral blood flow, while minimum cerebral blood flow ($\dot{Q}_{Bmin}$) imposed a limit on the maximum possible decline during hyperventilation-induced hypocapnia. There were found to be thresholds in both parameters marking abrupt changes between long and short simulated dive and surface intervals. Long-period dive cycles occurred only if Gq exceeded a threshold of $0.035\dot{Q}_{Brest}$ mmHg^{-1}, together with $\dot{Q}_{Bmin} < 45\%$ of $\dot{Q}_{Brest}$.

Circulatory transfer function

Deletion of the arterial mixed sub-compartment from the model had relatively minor effects on simulated dive and surface intervals. In contrast, the venous mixed sub-compartment was found to be a necessary feature of the model, because without it blood gases and chemoreflex drives displayed unrealistic step transients associated with the large and rapid changes in ventilation and cardiac output over the course of a dive cycle. Nevertheless, the quantitative effects of variations in the time constants of the venous mixing function on simulated dive and surface intervals were small. Increases in $V\text{a}_{mix}$ and $V\text{v}_{mix}$ both caused surface intervals to increase by 0.05 min l^{-1} and dive durations to increase by 0.2 min l^{-1}. $V\text{a}_{mix}$ and $V\text{v}_{mix}$ had additive effects.

Systematic variation of mean cardiac output over the surface interval ($\dot{Q}_s$) (with mean diving cardiac output, $\dot{Q}_d$, held constant) had substantial effects on simulated dive (t_d) and surface (t_s) intervals (Fig. 3). There was a threshold value of $\dot{Q}_s$, below which dive cycles were always short (t_s ~3.5 min and t_d ~5 min) and independent of $\dot{Q}_s$. Above the threshold, t_s and t_d increased to an asymptote with further increases in $\dot{Q}_s$. In addition, Fig. 3 shows that the effect of suprathreshold $\dot{Q}_s$ was dependent on the intensity of hyperventilation ($\dot{D}_n$). As $\dot{D}_n$ increased, the $\dot{Q}_s$ threshold increased, asymptotic t_d increased slightly, and asymptotic t_s decreased substantially.

Systematic variation of mean cardiac output during dives ($\dot{Q}_d$) with $\dot{Q}_s$ held constant had non-linear effects on both simulated dive and surface intervals. Manipulation of $\dot{Q}_d$ by varying the arterio–venous shunt flow ($\dot{Q}_{a-v}$) caused damped oscillations (period approximately 6 min) in diving blood gas levels that gave rise to concomitant oscillations in chemical respiratory drive ($\dot{D}_{chem}$). This in turn led to fluctuating relations between t_s and t_d *vs* $\dot{Q}_d$ (Fig. 4). In contrast, when $\dot{Q}_d$ was varied by changes in cardiorespiratory coupling (i.e $E^*_{O_2max}$, see Eqn 11) the rapid oscillations in blood gases were absent, and dive and surface intervals were both linearly related to $E^*_{O_2max}$, indicating inverse hyperbolic relations (see Eqn 9) between simulated dive and surface intervals *vs* $\dot{Q}_d$ (Fig. 4). Arterio–venous blood shunt flow during dives caused a general increase in simulated dive and surface intervals at all but the lowest $\dot{Q}_d$ (Fig. 4).

The role of oxygen

With standard 'control' parameter values, simulated dive and surface intervals were reduced in hypoxia ($F_{I_{O_2}}$<0.21). For

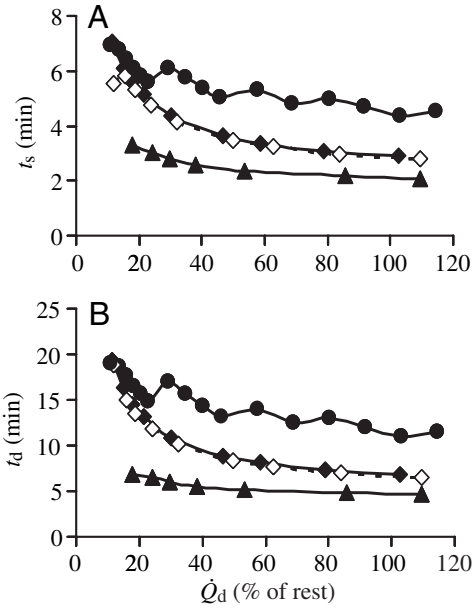

Fig. 4. The effect of mean cardiac output during dives ($\dot{Q}_d$, expressed as a percentage of nominal resting $\dot{Q}$) on (A) surface intervals (t_s) and (B) dive durations (t_d). Circles, effect of varying $\dot{Q}_d$ by changes in arterio–venous shunt flow ($\dot{Q}_{a-v}$); black diamonds, effect of varying $\dot{Q}_d$ by changes in cardiorespiratory coupling (*via* E^*_{O2max}, see text for details); white diamonds, effect of hypoxia (F_{IO_2}=0.15) on the responses to varying E^*_{O2max}; triangles, effect of elimination of splenic contraction on the responses to varying E^*_{O2max}.

example, simulated dive and surface intervals were reduced by 55% and 52%, respectively, when fractional inspired oxygen concentration (F_{IO_2}) was decreased from 0.21 to 0.1. When F_{IO_2} was less than 0.1, dives were aborted due to P_{aO_2} falling below the lower critical level for cerebral viability (assumed to be 15 mmHg). At F_{IO_2} in the range 0.1 to 0.15, simulated diving was unsteady, with long-term periodic modulation of simulated dive and surface intervals over two or more dive cycles. Simulation of hyperoxia (F_{IO_2}>0.21) had only slight effects on simulated dive and surface intervals. For example, dive duration increased by 7% when F_{IO_2} increased from 0.21 to 1.0.

Elimination of peripheral chemoreflex drive by increasing peripheral chemoreceptor threshold (T_p) to 47.6 mmHg modified the above responses to hypoxia and hyperoxia. Under these conditions, which were intended to mimic acute carotid body chemoreceptor denervation (CBD), there was an overall increase in both dive and surface intervals, as predicted from Fig. 2, and the hypoxia-induced decreases in simulated dive and surface intervals were strongly attenuated, but not abolished. Dive cycles continued to exhibit long-term (multiple dive cycle) periodicity during hypoxia (F_{IO_2}=0.1–0.15) in the absence of peripheral chemoreflex input.

Elimination of the cerebrovascular sensitivity to arterial blood oxygen saturation (see Eqn 8) resulted in stable dive cycles at all F_{IO_2} above 0.1, and reductions in simulated dive and surface intervals, an effect that progressively disappeared in hyperoxia. Furthermore, cerebrovascular insensitivity to O_2 partially reversed the effects of CBD alone, in that the CBD-induced overall increases in simulated dive and surface intervals were greatly reduced when cerebral blood flow was simultaneously rendered insensitive to arterial oxygen.

Finally, setting alveolar volume (V_A) at the start of the dive to zero had the effect of causing decreases in simulated dive and surface intervals at all F_{IO_2}, an effect that was also apparent when alveolar collapse was imposed concurrently with CBD and cerebrovascular O_2 insensitivity, leaving 'local' control of peripheral blood flow as the only functional O_2-sensitive mechanism remaining in the model. Under the latter conditions, dive cycles were stable but the effects of F_{IO_2} on simulated dive and surface intervals were otherwise virtually identical to control. This indirect effect of O_2 on dive duration (t_d) is illustrated in Fig. 4, where hypoxia *per se* can be seen to have little effect on the t_d *vs* $\dot{Q}_d$ relation.

Under standard control conditions, with F_{IO_2} at 0.21, $V_{O2store}$ was calculated to be 43.7 l at the onset of a simulated dive and, assuming that all of the O_2 is available for metabolism, calculated ADL was 24.6 min.

The role of the spleen

Splenic contraction was found to have a marked effect on simulated diving behaviour in this model, an effect that interacted with the cardiovascular diving response. Fig. 4 shows that splenic contraction altered the relations between simulated dive and surface intervals *vs* diving cardiac output ($\dot{Q}_d$). Splenic contraction caused increases in both simulated dive and surface intervals, and this effect was greater at lower $\dot{Q}_d$.

Simulations were compared at constant $\dot{Q}_d$ (20.8 l min^{-1}) with all four combinations of blood volume (V_b=96 and 76 l) and blood haemoglobin concentration (C_{Hb}=0.26 and 0.15 kg l^{-1}). There were direct correlations of simulated dive and surface intervals to both V_b and C_{Hb}, such that simulated dive and surface intervals were each directly proportional to total blood haemoglobin content ($V_b \times C_{Hb}$). Analysis of the integrated responses of blood and tissue gas tensions determined that the effect of haemoglobin concentration was mediated by variation in the rate of change of brain tissue P_{CO_2} during the surface interval due to changes in cardiac output. The latter occurred as a consequence of C_{Hb}-related variation in O_2 delivery to the tissue compartments and hence in the drive for peripheral blood flow. The effect of blood volume was mediated by altered rates of change in brain tissue P_{CO_2} due to V_b-induced variation in cardiovascular lag times and mixing time constants during both simulated dives and surface intervals.

Discussion

The model described here successfully simulated routine dive and surface times of the Weddell seal *Leptonychotes weddelli*. This study therefore supports the plausibility of the basic hypotheses that the cardio-respiratory control system

may play an important role in the regulation of diving behaviour and that apnoea can be initiated and maintained by disfacilitation of respiratory drive without the need for active inhibition of breathing.

This model proposes that diving behaviour may entrain to oscillations in respiratory drive, the period, duty cycle and amplitude of which are susceptible to modification *via* numerous factors. The model requires that respiratory drive be perturbed by hyperventilation, which causes an otherwise stable chemoreflex loop to oscillate; an example of induced respiratory instability. The temporal characteristics of the oscillating model system were found to be dependent on several key assumptions that will require empirical verification. These include differences between 'diving' and 'surface' values of the behavioural respiratory drive and central chemoreceptor threshold, and appropriate values for cerebrovascular chemosensitivity and cardiorespiratory coupling.

The model simulations demonstrated that active inhibition of breathing is not necessary to sustain apnoea during shallow dives up to the ADL in this species. However, the model does not preclude active inhibition of breathing, and indeed such inhibition will be required during the ascent phase of deeper dives. This model proposes that positive chemical respiratory drive triggers the decision to return to the water surface, and seals at depth must obviously delay respiration until the ascent phase is completed. This issue is to be addressed in more detail in a subsequent paper. Furthermore, it is highly likely that various other factors (emotional, volitional, physiological, etc) may modify diving behaviour (Fedak and Thompson, 1993) leading to delays in the termination of some individual dives, and active inhibition would be necessary under those circumstances. Nevertheless, the present study is consistent with the suggestion that in the absence of such extrinsic stimuli the animals will tend to remain at the surface as long as chemoreflex drive is positive, and they will usually remain submerged as long as the chemoreflex drive remains below the apnoeic threshold. In other words, diving behaviour is modeled as repetitive central apnoea with hyperventilatory surface intervals. Model simulations indicate that adjustment of the levels of hyperventilation and tachycardia at the water surface, and bradycardia during dives, provide powerful mechanisms by which a diving seal can adjust the dynamic characteristics of the cardiorespiratory system in the short term. Regulation of blood volume *via* splenic contraction represents an additional potential mechanism for longer-term regulation in Weddell seals. It is suggested on the basis of these results that diving behaviour and respiratory control are 'tuned' in such a way that the seals essentially ride an adjustable wave of respiratory drive (Woodin and Stephenson, 1998). This study therefore builds upon the ADL concept by using a more detailed model of the cardiorespiratory control system, enabling quantitative evaluation of the roles of a variety of physiological factors in the control of individual dives.

Using various combinations of physiologically realistic parameter values, simulated surface intervals (t_s) varied from 1.33 to 10.66 min and simulated dive times (t_d) varied from 1.46 to 27.41 min. This corresponds well to the observed ranges of surface intervals and dive durations in unrestrained adult Weddell seals. For example, in the classic study by Kooyman and colleagues (Kooyman et al., 1980), time–depth recorders were deployed on 22 free-ranging seals. Over 97% of 4601 dives were less than 26 min in duration, and over half were less than 10 min. Fewer data are available for surface times of freely diving Weddell seals, but most reported observations are less than 10 min (Burns, 1999). The aerobic dive limit (ADL), measured or calculated in various ways, generally falls within the range 18–25 min for adult Weddell seals, and this was also the case in the present model. The model simulations suggest that several physiological factors may influence surface intervals and dive durations and the final behavioural pattern is determined by quantitative variations in the combination of these factors. The following discussion summarizes and integrates the key components of the model.

Dynamic modeling approach

The design of the model is based on previously published attempts to understand the physiological basis of periodic breathing, Cheyne–Stokes breathing and sleep apnoea in human beings (Cherniack and Longobardo, 1986; Khoo, 2000; Khoo et al., 1991, 1982; Longobardo et al., 1966, 1982). However, application of this approach to the control of diving required several modifications to accommodate the profound cardiovascular responses that sometimes occur during diving behaviour. The model described here also differs substantially from that described by Davis and colleagues (Davis and Kanatous, 1999; Davis et al., 2004), as do the objectives of the two studies. Specifically, the present model includes an external gas exchanger (lung), it emphasizes cardio-respiratory control mechanisms, and it treats the system as operating in an explicitly non-steady state during diving behaviour. In addition to blood and tissue gas contents, respiratory and cardiovascular convection are dependent variables in the present model. Diving behaviour, or more specifically the 'decisions' to begin a dive and to begin the ascent to the water surface at the end of a dive, are hypothesized to be dictated by respiratory drives, and as such are also dependent variables of the present model.

When the model was held in 'surface mode', all dependent variables eventually settled to a steady state, indicating that with the parameter values given in Table 1, the Weddell seal model system exhibits dynamic stability. Various factors can lead to the development of spontaneous instability (Khoo, 2000), and this was observed under certain conditions in the present model of the Weddell seal. For example, small decreases in resting cardiac output were sufficient to elicit spontaneous periodic breathing and intermittent apnoea. However a discussion of these results is beyond the scope of the present paper. The steady-state values for dependent variables are given in Table 2 and are in reasonable agreement with published data, although it is not clear whether true steady-state conditions have ever actually been studied in seals because even seals hauled out on ice often display intermittent

or periodic breathing, and full equilibration of CO_2 in the model viscera and skeletal muscle compartments required over an hour of constant resting ventilation and blood flow. Nevertheless it was necessary to define starting conditions for the simulations and it was felt that steady resting conditions were most appropriate because they were reproducible and facilitated a smooth transition to 'diving' mode.

Hyperventilation

It is hypothesized that diving apnoea is initiated and maintained by disfacilitation of respiration, which requires that the chemical drive to breathe falls below the apnoeic threshold for intervals up to the ADL (i.e. 20–25 min). Chemical respiratory drive can only be reduced by hyperventilation, which causes decreases in P_{CO_2} of the brain and arterial blood and increases in P_{O_2} of the arterial blood. Hyperventilation at a level sufficient to induce apnoea was therefore a necessary component of the model.

Kooyman et al. (1971) observed a resting ventilation of approximately 20 l min^{-1}, and this was adopted as the standard resting value against which chemoreflex parameters were scaled in this study. The model settled to a steady-state ventilation of 35 l min^{-1}, somewhat higher than the standard value but still within the range of resting values observed in seals breathing at an artificial ice hole. Kooyman et al. (1971) also reported a maximum single observation of post-dive ventilation of approximately 225 l min^{-1} and in the present study, the maximum possible level of ventilation ($\dot{V}_{max}$) was assumed to be slightly higher than this, at 12 times the standard resting level (i.e. 240 l min^{-1}). Most diving animals that have been studied have been found to hyperventilate between serial dives, including the Weddell seal. In the present study most simulations assumed a submaximal value of behavioural respiratory drive ($\dot{D}_n$=180 l min^{-1}), which is in the upper part of the range of values most commonly observed by Kooyman et al. (1971).

In addition to hyperventilation *per se*, the model predicted that it was also necessary to ensure that the surface interval lasted long enough to enable the venous blood to achieve relatively hypocapnic and hyperoxic blood gas levels. Only then was it possible to sustain long dive times without active inhibition of breathing. In initial tests, the role of hyperventilation was investigated using a feedforward drive ($\dot{D}_n$) to determine the 'intensity' of hyperventilation and a

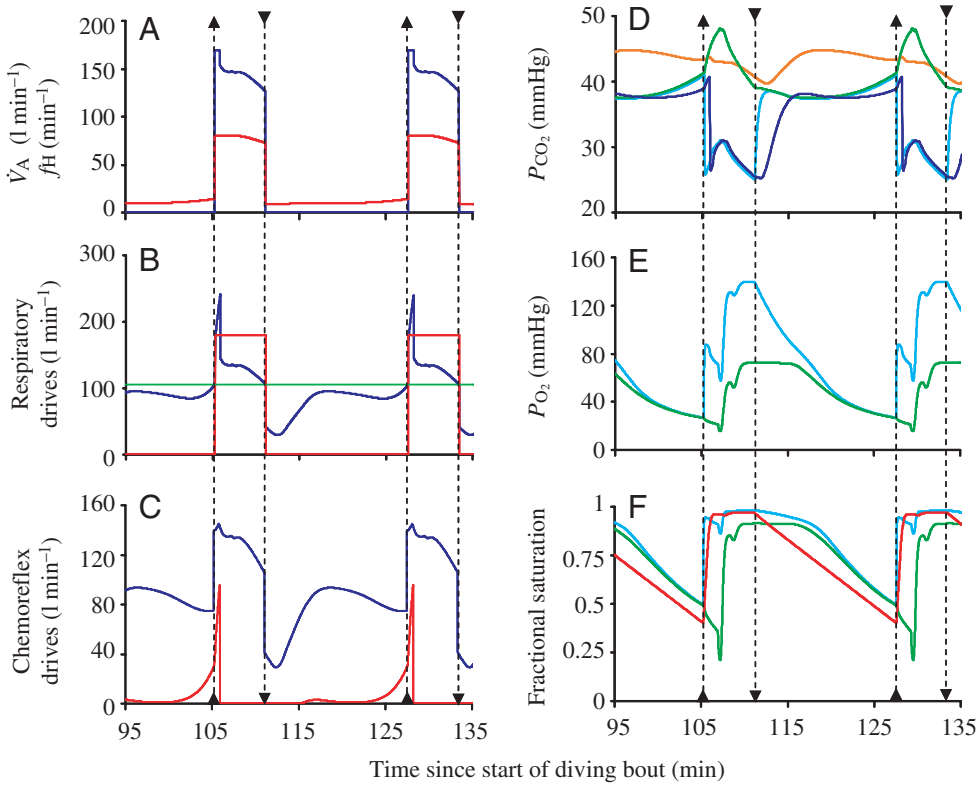

Fig. 5. Dependent variables during simulated shallow resting dive cycles in an adult Weddell seal model. A dive (onset indicated by downward broken arrows) and the preceding and succeeding surface intervals (onset at upward broken arrows) are shown. Parameter values were chosen for the purposes of illustration to yield a 16.4 min dive with 5.9 min surface intervals, typical diving behaviour for an adult Weddell seal: $\dot{D}_n$=75% $\dot{V}_{max}$, $\dot{Q}_s$=81.4 l min^{-1}, $\dot{Q}_d$=6.7 l min^{-1} (zero flow in muscle), corresponding to a mean surface heart rate of 146 beats min^{-1} and mean diving heart rate 10.5 beats min^{-1}. (A) Alveolar ventilation ($\dot{V}_A$, dark blue) and heart rate (f_H, red). (B) Total chemical respiratory drive ($\dot{D}_{chem}$, dark blue) and central neural respiratory drive ($\dot{D}_n$, red). Horizontal light green line is the chemical drive threshold (T_{chem}). Ventilation occurs only when $\dot{D}_{chem}$ and/or $\dot{D}_n$ are above T_{chem}, so that T_{chem} functions as an 'apnoeic threshold' of respiratory drive. $\dot{D}_n$ is assumed to be inhibited (e.g. by reflexes in the upper respiratory tract) during dives. (C) Central chemoreflex drive ($\dot{D}_c$, dark blue) and peripheral chemoreflex drive ($\dot{D}_p$, red), which represent the components of $\dot{D}_{chem}$. $\dot{D}_c$ is determined by partial pressure of CO_2 in the brain $P_{BCO_2}(t)$ and $\dot{D}_p$ is determined by partial pressures of both O_2 and CO_2 in the arterial blood flowing through the peripheral chemoreceptor [$Pa_{O_2}(t–t_c)$ and $Pa_{CO_2}(t–t_c)$, respectively]. (D) Partial pressures of CO_2 in various parts of the model system: orange, P_{BCO_2}[t] at the central chemoreceptor; light blue, $P_{ACO_2}(t)$ in the lung and pulmonary capillary blood; dark blue, $Pa_{CO_2}(t–t_c)$ at the peripheral chemoreceptor; dark green, $P\bar{v}_{CO_2}(t–t_v)$ in mixed venous blood at the lung. (E) Partial pressures of O_2 in various parts of the model system: light blue, $P_{AO_2}(t)$ in the lung and pulmonary capillary blood; dark green, $P\bar{v}_{O_2}(t–t_v)$ in mixed venous blood at the lung. (F) Oxygen saturation of 'arterial' blood in the pulmonary capillaries [$Sa_{O_2}(t)$, light blue], mixed venous blood at the lung [$S\bar{v}_{O_2}(t–t_v)$, dark green], and skeletal muscle myoglobin [$Sm_{O_2}(t)$, red].

'timer' function ($t_{s,min}$) to set the minimum duration of hyperventilation between dives. These studies uncovered a complex interaction between intensity and duration, shown in subsequent simulations to be also influenced by cardiac output (see below). Basically, for any given level of behavioural respiratory drive ($\dot{D}_n$) there was a critical surface duration below which subsequent dives were short and above which subsequent dives were long. The critical surface time varied in a non-linear inverse relation to $\dot{D}_n$.

The cause of the abrupt transition between long and short dive durations can be explained with reference to Fig. 5, which depicts some results of a typical model simulation. During apnoea the chemical drive to breathe ($\dot{D}_{chem}$) varied in an unexpected way over time, rising to an early broad 'peak' and then decreasing slightly before gradually rising again late in the dive. The short duration dives were cases where the early rise in brain tissue P_{CO_2} was sufficient to cause central chemoreflex drive ($\dot{D}_c$, and hence $\dot{D}_{chem}$) to exceed the chemical drive threshold (T_{chem}) so that the dives were terminated after approximately 2–8 min. In contrast, the long duration dives (14–24 min) represented cases where the early rise in $\dot{D}_c$ was insufficient to trigger ventilation so that the onset of breathing was delayed until brain tissue and arterial blood P_{CO_2} rose to the point where the combination of central ($\dot{D}_c$) and peripheral ($\dot{D}_p$) chemoreflex drives equaled the chemical drive threshold (T_{chem}).

The blood and tissue gas curves shown in Fig. 5 provide insight into the interdependence of the various components of the cardiorespiratory system. In particular, model simulations highlight the importance of the temporal (phase) relations between variables for the pattern of respiratory drive. For example, the rise in brain tissue (and hence central chemoreceptor) P_{CO_2} that occurred early in a simulated dive was induced by the rise in arterial blood P_{CO_2} [at (t–t_c) circulatory time lag] following the cessation of pulmonary gas exchange at the start of apnoea (Fig. 5D). When breathing stopped, alveolar P_{CO_2} rapidly increased until it came to equilibrium with mixed venous P_{CO_2}. Thus, mixed venous P_{CO_2} at the start of apnoea had an important indirect influence on the size of the initial rise in brain tissue P_{CO_2} (and hence $\dot{D}_{chem}$) during early apnoea, highlighting the important influence that venous P_{CO_2} is predicted to have on dive duration in this model. The subsequent (paradoxical) gradual decrease in chemical respiratory drive ($\dot{D}_{chem}$) following the initial peak during the early part of the dive is brought about by two related factors: (i) a delayed effect of hyperventilation from the previous surface interval making its way through the venous system and causing arterial blood to exhibit a delayed undershoot in P_{CO_2}, and (ii) the washout of CO_2 from the brain tissue as the blood and brain tissue gradually equilibrate in this closed (apnoeic) system. Finally, the initially slow, but accelerating rise in peripheral chemoreflex drive ($\dot{D}_p$), closely followed by a rise in central chemoreflex drive ($\dot{D}_c$) reflects the delayed effect of ongoing tissue respiration during apnoea working its way through the circulation to the peripheral and central chemoreceptors. It is the latter combination of $\dot{D}_c$ and $\dot{D}_p$ that eventually terminates the long dives.

In preliminary tests without the $t_{s,min}$ function it was found that only short period dive cycles could be induced because the resonant frequency of the system was predominantly determined by the lung to chemoreceptor delay time (t–t_c), as expected from similar observations in models of human Cheyne–Stokes respiration (Khoo et al., 1991; Longobardo et al., 1966). This prompted a search for a plausible mechanism for extending surface times. The importance of the venous blood gases at dive onset has already been mentioned, and preliminary studies in which a central venous chemoreceptor was included in the model successfully simulated long-period dive cycles. However, this approach was abandoned because there is no evidence for such a mechanism in mammals (Daly et al., 1977; Lahiri et al., 1983), and attention was turned instead to conventional chemoreflex mechanisms that have been shown to be implicated in human respiratory instability (Khoo, 2000; Smith et al., 2003).

Chemoreflex mechanisms

There are few data available on the central and peripheral chemoreflex thresholds and chemosensitivities of seals. These parameters are difficult to measure accurately and reliable estimates exist only for human subjects where carefully controlled studies have been conducted. The main difficulty concerns knowing the P_{CO_2} and P_{O_2} at the chemoreceptor sites and this is particularly problematic in animals such as seals where respiration is often intermittent, setting up large oscillations in blood gas tensions with substantial phase lags as demonstrated in this model analysis (see Fig. 5). In the present study it was assumed that chemoreceptor thresholds of the Weddell seal are 10% greater than the mean human value because studies involving inhalation of hypercapnic gases have shown fairly consistent right shifts in the responses of diving mammals compared with human beings and other terrestrial species (Craig and Pasche, 1980; Milsom et al., 1996; Parkos and Wahrenbrock, 1987; Pasche, 1976a). Note that this is a small deviation since it remains within the normal range of human central chemoreceptor threshold values, which are quite variable between individuals. The evidence for reduced CO_2 chemosensitivity (i.e. the slope of the response) in seals is weak (Skinner and Milsom, 2004), and normal human values were adopted, assuming that chemosensitivity can be scaled relative to standard ventilation. However, there is (slightly) stronger evidence for a blunted hypoxic ventilatory response in seals, and this was incorporated into the present model by setting the hypoxic asymptote (A, see Eqn 21) to 15 mmHg, equal to the assumed critical P_{O_2} for CNS viability (Parkos and Wahrenbrock, 1987; Pasche, 1976b). Simulations in which A was raised to 30 mmHg (the normal value for human subjects) had only a small effect on surface intervals and dive durations, a first clue as to the relatively small (but not negligible) role played by O_2 and the peripheral chemoreflexes in this model, discussed in more detail below.

It was found that a small decrease (–4 to –8 mmHg) in central chemoreceptor threshold (ΔT_c) during surface hyperventilation served to prolong surface time long enough

for venous hypocapnia to develop, enabling long-period dive cycles to occur. Short-term and long-term transitions in chemoreflex thresholds have been measured, mainly in human subjects, in a number of situations. These include slow changes over circadian (24 h) timescales (Stephenson et al., 2000), changes over several minutes in response to acute hypoxia (Duffin and Mahamed, 2003; Mohan and Duffin, 1997), and rapid changes over several seconds during transitions between sleep and wakefulness (Phillipson and Bowes, 1986). A decrease in the central chemoreceptor threshold is a left shift in the central chemoreflex response curve and therefore represents an increase in the responsiveness of the respiratory system to brain P_{CO_2} (*via* changes in brain pH; Lahiri and Forster, 2003) during surface hyperventilation. The underlying mechanisms are unknown but may involve excitatory neuromodulation or inhibitory disfacilitation at the chemoreceptors or at some other part of the chemoreflex neural pathway. Note that the standard ΔT_c used in this study (–5.1 mmHg) involved the threshold falling to only 5% below the mean value for normal human subjects, which remains within the normal range of human subject variability. Thus, the changes in T_c required by this model are not unreasonably large. Nevertheless, a hyperventilation-associated decrease in central chemoreceptor threshold has not been demonstrated (or even looked for) in seals or any other diving species, and represents an important untested prediction of the model.

It has been suggested that a central 'timer' mechanism for determining surface interval duration, simulated in the present model by the $t_{s,min}$ function, might exist in the form of descending influences on respiratory drive originating in a central neural pattern generator (CPG; Milsom et al., 1997). It was found, however, in the simulations involving $t_{s,min}$ that some $t_{s,min}$ durations gave rise to relatively unstable dive cycles, with long-term modulation of surface intervals and dive durations over several cycles. The two mechanisms used in this study to regulate the duration of surface intervals ($t_{s,min}$ and ΔT_c) are not necessarily mutually exclusive and it is possible to envisage a 'conditional' CPG whose timing signal is fine-tuned by chemical feedback in order to suppress long-term instabilities (Milsom et al., 1997). The latter scenario could work, for example, if the CPG exerted its effect *via* the ΔT_c mechanism, with the CPG determining the magnitude of ΔT_c at any given time. This of course is pure speculation at present and represents an intriguing topic for further experimental research.

Simulated carotid body chemoreceptor denervation caused increases in surface intervals and dive durations, indicating that the peripheral chemoreceptors are not necessary for simulation of long-period dive cycles in this model. This is in sharp contrast to the central role that the peripheral chemoreflex plays in the development of human periodic breathing and sleep apnoea (Smith et al., 2003). This suggests that despite the superficial similarities in the breathing patterns in diving (and sleeping) seals and human sleep apnoea patients that originally prompted the work described here (Stephenson et al., 1986; Woodin and Stephenson, 1998), there are some important fundamental mechanistic differences. Nevertheless, when present, the peripheral chemoreceptors served to modulate surface intervals and dive durations through a direct contribution to total chemical drive ($\dot{D}_{chem}$) at the end of dives. This can be understood with reference to Fig. 5, which shows that peripheral chemoreflex drive ($\dot{D}_p$) remained below threshold until late in the dive when the arterial blood gases began to change relatively rapidly, leading to a rapid surge in $\dot{D}_p$. This was the main factor that caused total chemical respiratory drive ($\dot{D}_{chem}$) to rise relatively suddenly above the apnoeic threshold to terminate the dive. Increased responsiveness of the peripheral chemoreceptors therefore had the effect of initiating the surge in $\dot{D}_p$ a little earlier, thereby reducing dive times, and *vice versa* (Fig. 2).

Cerebral blood flow

As discussed above, the early broad 'peak' in chemical respiratory drive ($\dot{D}_{chem}$) during dives (Fig. 5B) was found to be strongly related to brain tissue P_{CO_2}, and the central chemoreceptor threshold (T_c) was found to be the most influential chemoreflex characteristic affecting durations of apnoea and ventilation. These results point to a prominent role for the central chemoreceptors in the regulation of dive and surface intervals, a suggestion that was reinforced by the finding that surface intervals and dive durations were strongly dependent on regulation of cerebral blood flow ($\dot{Q}_B$). Cerebral blood flow has an important role in the regulation of central chemoreflex drive ($\dot{D}_c$) because brain tissue P_{CO_2} is determined by balancing the rates of brain CO_2 'delivery' (*via* metabolism and arterial blood) and CO_2 removal (*via* brain venous drainage and chemical buffering). Long-period dive cycles were abolished when constant cerebral blood flow was assumed, demonstrating the importance of appropriate adjustments of cerebral blood flow over the dive cycle in this model. This is supported by the finding that cerebral blood flow oscillated over dive cycles in freely diving rats (Ollenberger and West, 1998b). The model predicts that two factors are crucial; sensitivity of the brain vasculature to arterial P_{CO_2} (Gq, see Eqn 8), also supported by data in diving rats and apnoeic humans (Ollenberger and West, 1998a; Przbylowski et al., 2003), and the maximum degree of cerebral vasoconstriction that can occur in response to hypocapnia ($\dot{Q}_{Bmin}$). In this model, regulation of cerebral blood flow during the surface interval was of greater importance than that during dives because it played a prominent role in determining the rate of washout of brain CO_2, and therefore in the time taken for central chemoreflex drive ($\dot{D}_c$) to fall below threshold to initiate a dive. High cerebral blood flow during the surface interval led to rapid washout of brain CO_2 and a short surface interval. This in turn led to relatively high venous blood P_{CO_2} at dive onset and therefore short dive durations, as explained earlier. Conversely, low cerebral blood flow during the surface interval led to slow washout of brain CO_2, long surface interval and therefore long subsequent dive. High cerebrovascular chemosensitivity (Gq) allowed cerebral blood flow to fall

rapidly at the start of the surface interval, but when $\dot{Q}_{Bmin}$ was very low (<30% of $\dot{Q}_{Brest}$), washout of brain CO_2 was too slow and the surface interval was long enough for excessive venous hypocapnia to develop. This resulted in a subsequent dive in which oxygen stores were fully consumed before CO_2 built up sufficiently to initiate ventilation, and the simulated animal 'died'. Hence, the appropriate value of Gq was $0.05\dot{Q}_{Brest}$ $mmHg^{-1}$ CO_2, which is in the upper part of the normal range observed in human subjects, and a $\dot{Q}_{Bmin}$ of 40% of $\dot{Q}_{Brest}$ was adopted. These assumptions require experimental verification.

Cardiovascular responses

The circulatory transfer function describes the delay and distortion of the blood gas 'waveform' as the blood flows between tissue and alveolar gas exchangers (venous transfer function) and between the lung and chemoreceptors and tissues (arterial transfer function). There are absolute lag times, representing the time taken for blood to flow between effectors, that are dependent on blood volume and cardiac output, and there are arterial and venous mixing processes that 'smear' the blood gas waveform, and depend on the effective mixing volume and cardiac output. In humans, the arterial effective mixed blood volume ($V\mathrm{a}_{mix}$) is approximately 10–15% of arterial blood volume (calculated from data published by Lange et al., 1966). To my knowledge, comparable data are not available for pinnipeds. However there is anatomical and functional evidence for an expanded and compliant proximal aorta (Windkessel) in seals (Drabek, 1975; Molyneux and Bryden, 1978; Rhode et al., 1986; Shadwick and Gosline, 1995), which might be predicted to increase $V\mathrm{a}_{mix}$. It was therefore assumed that $V\mathrm{a}_{mix}$ was 15% of arterial blood volume (i.e. at the upper end of the normal human range) in the present simulations. Relative effective mixed volume for the venous system ($V\mathrm{v}_{mix}$) was arbitrarily assumed to be double that of the arterial system (i.e. 30% of $V\mathrm{b}_{v}$). Variations of both parameters led to only minor effects on surface intervals and dive durations, indicating that errors in these values will not significantly affect the overall conclusions of the study.

Cardiac output ($\dot{Q}$), which influences both components (mixing and lag) of the transfer function as well as the rates of gas exchange in the tissue compartments and lung, had an important role in the regulation of surface intervals and dive durations in these computer simulations. There was a strong interaction between the effects of cardiac output and the intensity of hyperventilation during the surface interval, on the durations of surface intervals and dives (Fig. 3). In general, higher hyperventilation enabled longer dives, but only when accompanied by high cardiac output. When mean surface cardiac output ($\dot{Q}_s$) was less than 90% $\dot{Q}_{max}$, variations in hyperventilation ($\dot{V}_n$) affected surface intervals and dive durations only when $\dot{V}_n$ was mild to moderate intensity (i.e. less than 75 $\dot{V}_{max}$). With $\dot{Q}_s$ near maximum (i.e. 90–110% of nominal $\dot{Q}_{max}$), variations in $\dot{V}_n$ had greater effects on surface intervals and dive durations. Thus the diving efficiency, expressed as the dive–pause ratio (t_d/t_s), increased with increasing hyperventilation at maximal $\dot{Q}_s$, but not when $\dot{Q}_s$ was less than 90% of maximum. This model assumed a constant behavioural respiratory drive ($\dot{V}_n$) during surface intervals, which is probably an oversimplification. It seems likely that the drive to hyperventilate may vary over time at the surface, incrementing, decrementing or perhaps exhibiting a biphasic or more complex pattern. Weddell seals have been reported to show a decrementing pattern of ventilation between dives (Kooyman et al., 1971). However the present simulations suggest that the observed decrease in ventilation over time at the surface is to some extent due to the falling chemoreflex drive (Fig. 5) and it is unclear whether $\dot{V}_n$ also varied over time in Kooyman's studies. Further research is needed to clarify this issue, and to understand how ventilation, $\dot{V}_n$ and $\dot{Q}_s$ are fully integrated during surface intervals in freely behaving animals.

The preceding discussion concerning the role of surface cardiac output ($\dot{Q}_s$) in the regulation of surface intervals and dive durations was based on simulations in which the 'intensity' of the diving response was always 'maximal' (i.e. minimal blood flow in muscle and viscera with correspondingly low cardiac output and heart rate). In simulations with fixed levels of hyperventilation and cardiac output during surface intervals ($\dot{V}_n$=75% of $\dot{V}_{max}$ and $\dot{Q}_s$=100% of $\dot{Q}_{max}$), surface intervals and dive durations were both inversely related to mean diving cardiac output ($\dot{Q}_d$). However, the effect was non-linear and variation in $\dot{Q}_d$ (*via* changes in the gain of cardiorespiratory coupling) had a significant influence on diving behaviour only when diving cardiac output was less than approximately 25% of resting levels. This provides a tentative explanation for the finding that pharmacological blockade of diving responses had little effect on short dives in captive harbour seals (Elliott et al., 2002), where bradycardia was not very intense even under control conditions.

The situation was a little more complicated when an arterio-venous blood shunt ($\dot{Q}_{a-v}$) was used to adjust mean diving cardiac output. Under these conditions, the accumulation of venous CO_2 was influenced by arterial admixture during the dive and this had two main effects: it caused oscillations in blood gas tensions during dives (carried over from the preceding surface interval), and it delayed the time taken to raise chemical respiratory drive ($\dot{V}_{chem}$) to the apnoeic threshold, which in turn led to increased dive durations. Furthermore, the longer dive led to greater production of CO_2 and greater depletion of O_2 in the tissues so that more time was required during the subsequent surface interval to drive chemical respiratory drive back below the apnoeic threshold. Diving cardiac output (as indicated by heart rate) has been observed to vary between and within voluntary dives (Butler and Jones, 1997; Kooyman and Campbell, 1972) but the fine control of peripheral blood flow has not been measured and it is not known whether an arterio–venous shunt or tissue perfusion, or a combination of both, contribute to the variation in $\dot{Q}_d$ during voluntary dives. Radioactive microsphere tracer studies in Weddell seals, spotted seals and grey seals found evidence for an increase in peripheral arterio–venous blood

shunting during forced submergence (Blix et al., 1983; Zapol et al., 1979) but the relevance of this to voluntary dives is unclear.

The role of oxygen

Overall, the model simulations point to an important role for the central chemoreceptors in the development of long-period cycles of intermittent ventilation, which implies that CO_2 is a dominant influence in this model. So what is the role, if any, of O_2? Oxygen is involved in several aspects of the present model. First of all, the ADL (i.e. O_2 store) places an absolute limit on dive durations. Anaerobic metabolism represents a biochemical alternative that would have implications for respiratory control and may extend the behavioural options of the diving animal (Fedak and Thompson, 1993). Future modeling studies that include anaerobiosis would therefore be instructive. In addition to its role as a limiting factor, oxygen has several direct roles in the regulation of respiration and circulation. Peripheral chemosensitivity is potentiated by arterial hypoxia, and the present study suggests that increased peripheral chemoreflex drive is inversely related to dive durations (Fig. 2). However, the finding that elimination of peripheral chemoreflexes (simulated carotid body denervation) did not prevent the simulation of long-period dive cycles, indicates that the peripheral chemoreflex is not an essential factor in the regulation of diving behaviour in this model.

The effects of atmospheric hypoxia on simulated diving behaviour are in broad agreement with direct observations of diving seals, where dives were shortened and considerably less frequent when inspired oxygen concentration ($F_{I_{O_2}}$) was decreased, and only slightly affected by hyperoxia (Parkos and Wahrenbrock, 1987; Pasche, 1976b). However, although diving was suppressed, it was not completely abolished at 10% inspired O_2, as the model has predicted. Two factors missing from the model simulations may explain this discrepancy; acute hypoxia may induce a hypometabolic response (Frappell et al., 1992) resulting in an elevated ADL, although recent data do not support such a scenario in elephant seals (Kohin et al., 1999), or anaerobiosis may be important over the course of an experimental exposure to extreme hypoxia. Unfortunately, anaerobic metabolites have not been measured during hypoxic diving in seals.

Elimination of peripheral chemoreflex drive (simulated carotid body denervation, CBD) had the effect of modifying the simulated behavioural responses to hypoxia and hyperoxia. Durations of dives and surface intervals were increased, relative to control, at all except the highest $F_{I_{O_2}}$, and the hypoxia-induced decrease in dive duration was suppressed (but not abolished). Elimination of the O_2-sensitive component of the mechanism regulating cerebral blood flow caused small decreases (relative to control) in simulated surface intervals and dive durations under hypoxia, and it significantly reduced the effect of concurrent CBD. Thus, in this model O_2 has effects on dive durations *via* two antagonistic mechanisms; peripheral chemoreceptors (carotid bodies) tend to decrease dive durations and cerebrovascular oxygen sensors tend to increase dive durations. Simulated lung collapse at dive onset eliminates the alveolar stores of O_2 and CO_2 and this had an overall effect of decreasing dive durations at most $F_{I_{O_2}}$. This effect was independent of CBD and cerebrovascular O_2-sensitivity and did not alter the overall effect of $F_{I_{O_2}}$.

Thus, elimination from the model of all of the above O_2-sensitive mechanisms had surprisingly little impact on the responses to hypoxia, leading to the conclusion that the primary effect of hypoxia on dive duration was mediated by variations in viscera compartment blood flow, the only remaining avenue by which O_2 could exert an effect on the system in this model. In these simulations the muscle blood flow was essentially insensitive to O_2 because the 'full' diving response had been invoked by setting the 'target' oxygen extraction coefficient ($E^*_{mO_2max}$) to 10, as explained in the Materials and methods.

The role of the spleen

Several investigations have concluded that Weddell seals and other pinnipeds raise the oxygen carrying capacity of the blood during diving activities by contraction of the spleen (Hurford et al., 1996; Kooyman et al., 1980; Qvist et al., 1986). An obvious advantage of this is the consequent increase in ADL, but the present study has found that there are also indirect effects that may play a significant role in the regulation of dive and surface times. Specifically, changes in blood haemoglobin concentration (C_{Hb}) and/or blood volume (Vb) led indirectly to variation in the rate of change in brain tissue P_{CO_2} during surface intervals and/or dives. The splenic expansion of blood volume affected brain tissue P_{CO_2} mainly through increases in circulatory lag times, analogous to the effects of changes in cardiac output. Indeed, this model analysis (Fig. 4) revealed that Weddell seals are able to greatly extend their dive times as a result of the co-evolution of an intense diving response (bradycardia and vasoconstriction) and splenic contraction. The combined effects of these two adaptations were far greater than the sum of the individual effects. For example, in the absence of splenic contraction, the diving response alone resulted in simulated dive duration increasing by 53%, from 4.5 min to 6.9 min, while splenic contraction in the absence of a diving response caused a similar increase in simulated dive duration (Fig. 4). However, when both factors were combined, simulated dive duration was increased by 440%, from 4.5 min to 19.7 min. The effects of the haemoglobin concentration component of splenic contraction on simulated diving behaviour were also mediated by changes in circulatory lag time, but in this case *via* the 'local regulation' of peripheral blood flow. In this model, increased haemoglobin concentration enabled O_2 delivery to be achieved at lower blood flow, which decreased diving cardiac output and, therefore, increased circulation lag times and simulated dive duration. Qvist et al. (1986) observed that when dives were separated by relatively long surface intervals, haemoglobin concentration varied across the dive cycle, rising to a maximum during longer dives and falling toward resting values during longer surface intervals, implying that spleen

volume is under dynamic control. For simplicity, the present study assumed constant blood volume and haemoglobin concentration in any given dive bout, as was observed by Castellini et al. (1988).

The above discussion concludes that the mechanism used in this model for the regulation of peripheral blood flow (Eqn 9) represents the main way in which O_2 exerted an effect on diving behaviour. This approach to modeling the regulation of peripheral blood flow was adopted to ensure that the ADL is not exceeded in any peripheral tissue compartment by matching blood flows to metabolic rates and arterial O_2 content. The model also features coupling between local and systemic cardiovascular control mechanisms on the one hand, and cardiovascular and respiratory mechanisms on the other (Eqns 11 and 12). In defence of this approach, there is strong experimental evidence that tissue perfusion is regulated by a combination of autoregulatory (local) mechanisms and autonomic and/or endocrine (systemic) mechanisms in mammals (Marshall, 1999). Furthermore, central mechanisms that integrate cardiovascular and respiratory reflexes normally ensure that these two systems are coupled (Daly, 1986).

It must be acknowledged, however, that the cardiovascular control system is far more complex than this simple model implies. While O_2 has been shown to play an important role in the regulation of capillary blood flow (Marshall, 1999; Mohrman and Regal, 1988), many other mechanisms are also involved that may modify the regional and global distribution of tissue blood flow (Marshall, 1999; Thomas and Segal, 2004). For example, there is evidence for some degree of independence of respiratory and circulatory 'drives' (e.g. variability of heart rate during dives (Kooyman and Campbell, 1972; Qvist et al., 1986) that could not be modeled in the present study. Nevertheless, as a first approximation the present scheme captures the essential characteristics of the system, and has yielded insights that would not have emerged had a simpler approach been adopted, such as the assumption of constant tissue blood flow. A more sophisticated model of cardiovascular control may yield further insights in future studies.

So how well does the model simulate the behaviour and physiology of freely diving Weddell seals? The elegant field studies conducted by Kooyman and colleagues (Castellini et al., 1988, 1992; Kooyman and Campbell, 1972; Kooyman et al., 1983, 1971, 1973, 1980; Ponganis et al., 1993) and Qvist et al. (1986) provide data for comparison. Overall, they indicate that the dependent variables calculated by the model are remarkably consistent with those measured experimentally, although there are some noteworthy deviations. Hyperventilation and tachycardia during the surface intervals between serial dives are essential parameters in the model (Fig. 5A), without which the 'disfacilitation' hypothesis would fail. Both were observed in freely diving seals (Kooyman and Campbell, 1972; Kooyman et al., 1971; Qvist et al., 1986). Fig. 5D indicates that the model predicts low alveolar and arterial P_{CO_2} during the surface interval as a consequence of hyperventilation, and while only a few measurements were taken, both end-tidal P_{CO_2} and arterial blood P_{CO_2} were as low as 30 mmHg (Kooyman et al., 1971, 1980; Qvist et al., 1986). These experimental observations are slightly higher than the model predictions, probably because the levels of hyperventilation and tachycardia chosen for the model simulations are near the maximum values observed experimentally. The model predicts that arterial P_{CO_2} remains close to the resting value (the actual level is determined by the venous P_{CO_2} at the end of the surface interval and early in the dive) until relatively late in a dive, when it rises progressively. This was observed during both long and short dives in the field (Kooyman et al., 1973; Qvist et al., 1986), prompting the authors to suggest that this implies a difference in metabolic rate in long and short dives. The present simulations suggest that this explanation may not be correct because the same result is obtained when simulated dive times are adjusted (at constant metabolic rates) by changes in factors such as hyperventilation, surface tachycardia, diving bradycardia, and the relative distribution of blood flow between tissues and arterio–venous anastomoses. The highest arterial blood P_{CO_2} is predicted by the model to occur at some time (depending upon the position of the blood sampling catheter) just after the onset of the surface interval, and this also was observed experimentally (Qvist et al., 1986).

The model also replicated observed changes in P_{O_2} with reasonable success. High alveolar and arterial P_{O_2} (>120 mmHg) were recorded after approximately 3 min of post-dive recovery, immediately before a dive and during approximately the first minute of a dive (Kooyman et al., 1973, 1980; Qvist et al., 1986). This was simulated by the model, although again, for the reasons given above, the peak P_{O_2} calculated by the model (Fig. 5E) was slightly higher than observed values. Arterial blood P_{O_2} decreased to as low as 18.2 mmHg at 1 min before the end of a 27 min dive (Qvist et al., 1986), just above the lower critical value (15 mmHg) assumed in this study. Low values were observed in long and short dives, and this is also apparent in the model simulations. Furthermore, arterial blood oxygen content was found to remain constant for approximately half of the dive duration (Qvist et al., 1986), a finding also replicated in the present model simulations (Fig. 5F).

It has been suggested on the basis of direct measurements of end-tidal P_{CO_2} and P_{O_2} in the grey seal and harbor porpoise that the duration of the surface interval is mainly determined by the dynamics of CO_2 elimination (Boutilier et al., 2001). A progressive rise in respiratory exchange ratio (RER) was observed in diving grey seals (Reed et al., 1994), and this was also simulated in the present model. The rise in RER is dependent on the level of hyperventilation and reflects the difference in the slopes of the O_2 and CO_2 blood equilibrium curves. The slope of the O_2 equilibrium curve decreases as haemoglobin becomes saturated, whereas the slope of the CO_2 equilibrium curve was assumed to be constant in this model. The latter assumption probably led to a small overestimation of predicted RER toward the end of the surface interval in the

present study. Furthermore, 'U-shaped' changes in end tidal P_{CO_2} and P_{O_2} were observed in grey seals (Reed et al., 1994) and attributed by the authors to a limitation in oxygen consumption from lung or blood during dives (see also Butler and Jones, 1997). The present model supports their conclusion that the above result is not an experimental artifact (Fig. 5D,E) but suggests that the U-shaped curves may reflect a phase lag in venous blood gas tensions, rather than a limited O_2 uptake, highlighting again the importance of the dynamic aspect of cardiorespiratory control.

In conclusion, this study presents a model for the proximate control of diving behaviour in the Weddell seal. It remains to be seen whether the model can be generalized to other species of diving mammals and birds. The model expands on the aerobic dive limit concept and is based on fundamental principles of cardiorespiratory control. The majority of parameter values were derived from direct measurements in Weddell seals as published by Kooyman and others, and unknown parameters were estimated conservatively from human data. The latter mainly concerned chemoreflex characteristics and represent an area in need of further investigation in pinnipeds and other diving animals. The study supports the plausibility of the basic hypotheses set out in the Introduction: that the control of diving can be modeled in terms of respiratory control and that the apnoeic threshold can trigger the initiation and termination of dives without the need to resort to active inhibition of breathing. This analysis suggests that CO_2 is an important factor regulating diving behaviour, with O_2 relegated to secondary modulatory roles. The model also underscores the importance of the dynamic aspects of the cardiorespiratory system during dive cycles, with phase relationships between lung, arterial and venous blood, brain and other tissues playing a key role in the overall integrated behaviour of the system and of the animal.

While this model emphasizes a role for the respiratory control system in the regulation of diving behaviour, it must be stressed that this does not imply that the respiratory control system is the only factor involved. It is envisaged that the present model represents one part of a hierarchical behavioural control system that also includes input from factors such as volitional, appetitive, emotional, arousal and circadian drives. It is suggested that the cardiorespiratory control system is a core component of the overall control system, assuming primary control of diving behaviour under routine conditions when other inputs are weak or absent, and responding to and modulating the effect of other inputs when they are present. The model also suggests that in most dives the animals are not necessarily fighting against a powerful drive to breathe, and that once the urge to breathe does reappear, the animal will be stimulated to 'decide' to return to the surface, unless some other priority intervenes (such as predator avoidance or imminent capture of prey etc). Hence, it is proposed that there is a reciprocal interaction between behaviour and cardiorespiratory control, with diving behaviour responding to cardiorespiratory inputs and the cardiorespiratory system responding to overriding behavioural drives. This model is intended to facilitate further research by providing a conceptual framework for the investigation of how diving animals control their behaviour, and by providing a tool for the development of testable quantitative predictions. Computer simulations have confirmed the plausibility of the model, but they cannot confirm or refute its validity without experimental investigation. To this end, the model was constructed in spreadsheet format so that it will be useful to as many researchers as possible. A copy of the spreadsheet is freely available from the author upon request.

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