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THEORY OF CO_2 EXCHANGE IN TROUT GILLS*

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INTRODUCTION

The complexity of the aqueous CO_2-bicarbonate-carbonate system and the lack of simple, precise methods for CO_2 measurement in cold water have prevented substantial progress in the study of CO_2 exchange and acid-base regulation in fish. One recent review (Albers, 1970) states that pH is regulated by ventilatory control of arterial P_{CO_2} (as in mammals), yet this has never been demonstrated. Recent experimental evidence contradicts that theory.

The rate of ventilation has now been shown to have no significant effect on arterial pH or CO_2 (Randall & Cameron, 1973*a*, *b*). Further, the concentration of CO_2 in the medium (water) does not greatly alter arterial pH (Cameron & Randall, 1972), nor the steady-state ventilation volume (Jannsen & Randall, unpublished data). These observations clearly indicate a CO_2-pH regulating system fundamentally different from that of the higher vertebrates.

Fish gills are commonly compared to countercurrent heat exchangers, and yet the dynamics of these exchangers are such that flux rates are only insensitive to flow at extreme capacity-rate ratios, i.e. given approximately equal capacities of the two fluids, only at greatly disparate flow rates. In a heat exchanger, heat loss from one fluid to a second will only be insensitive to flow of the second if that flow is much greater than flow of the hot fluid.

It is well established that capacity-rate ratios for oxygen in fish gills are near unity (Cameron & Davis, 1970; Lenfant & Johansen, 1972). Since the ventilation-perfusion ratio for rainbow trout is generally between 8:1 and 20:1 (Randall, 1970; Cameron and Davis, 1970) and CO_2 solubility is roughly equal in blood and water, it appears that the capacity-rate ratio for CO_2 in trout gills is very high, thus explaining the insensitivity to water flow observed experimentally (Randall & Cameron, 1973*b*).

The situation is unfortunately not as simple as that. The blood has a far larger reserve of chemically bound CO_2 than the water. If, for example, all this bound CO_2 were instantaneously interconvertible to dissolved CO_2, the effective capacity-rate of water is increased some 20-fold, as we will see below, and at a ventilation-perfusion ratio of 8:1 the resulting capacity-rate ratio is not 20:1, but 0·4:1. Obviously the true situation lies somewhere between these extremes, with the exact point determined by a wide range of quantitative factors.

The purpose of this paper is to present, using a simulation model, the total CO_2

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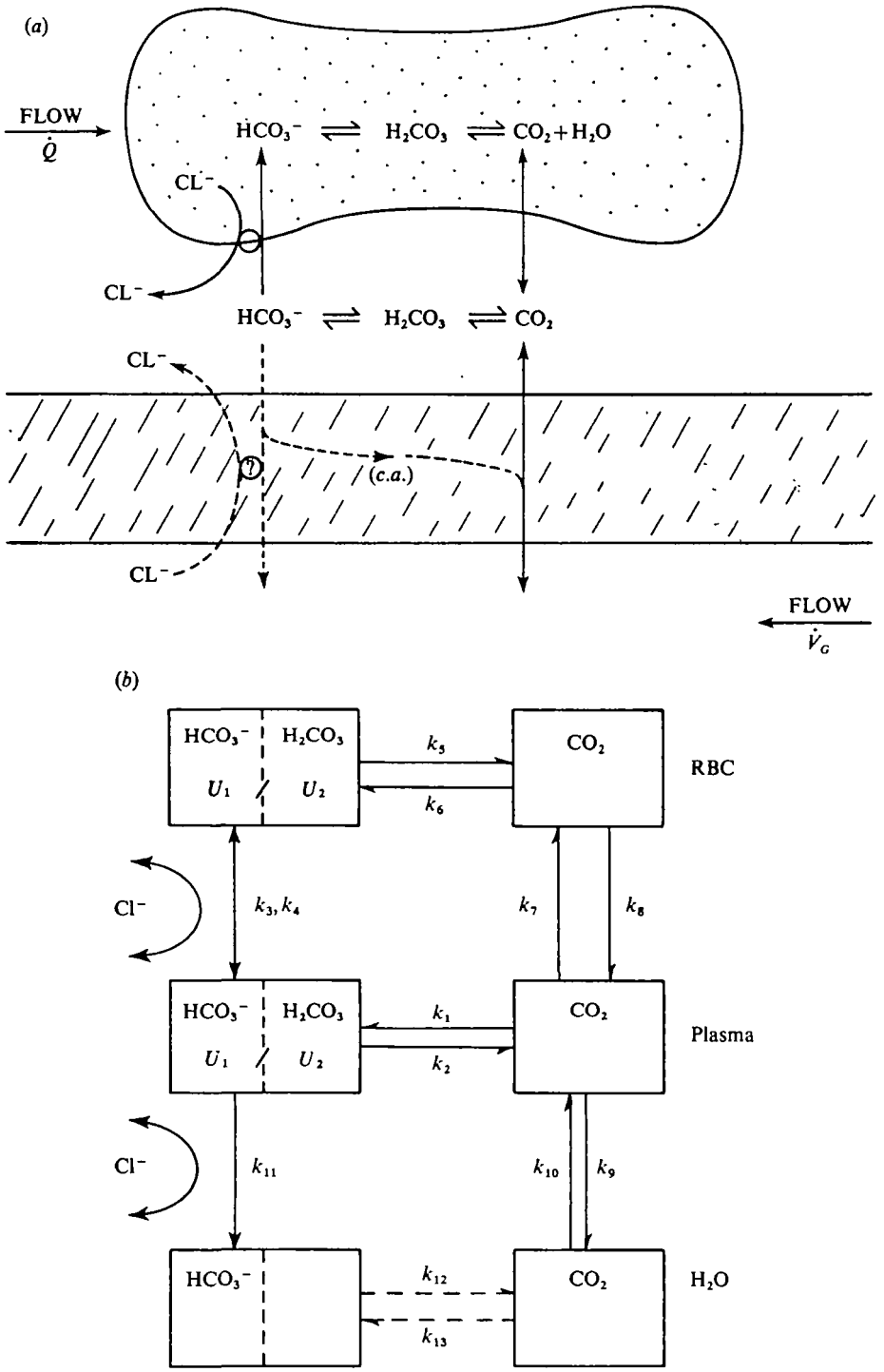

Fig. 1. (*a*) Diagrammatic representation of the principal methods of CO_2 loss and reaction in the blood of fish. The letters *c.a.* stand for carbonic anhydrase catalysis, and the coupled arrows with Cl^- indicate exchange diffusion reactions. (*b*) Diagram of the compartment model used to simulate pathways outlined above. Numbered *k*-values refer to rate constants.

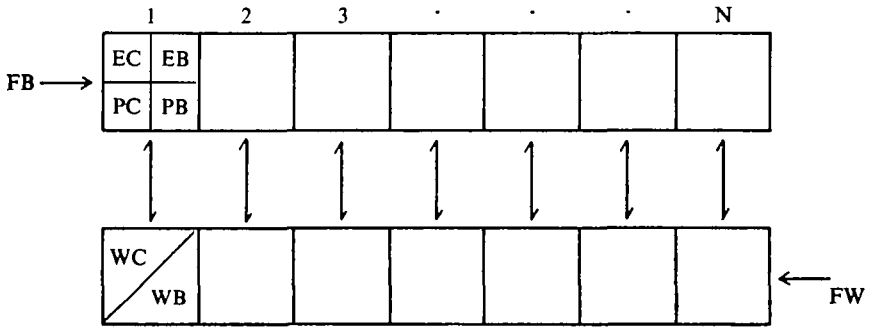

Fig. 2. Block diagram of computer simulation, showing compartmentalization used for simulating spatial aspects of countercurrent flow.

exchange system, and to try to point out what sets of conditions will reconcile theory and observation. We were also interested in collecting existing quantitative data on CO_2 kinetics, and in showing which processes have the greatest potential effect on CO_2 elimination through the gill.

CONSTRUCTION OF THE MODEL

The pathways of CO_2 movement or reaction that we considered to be significant are outlined in Fig. 1(*a*). The exclusion of carbamino and various protein-bound CO_2 pools was necessary, as scarcely anything at all is known about these pools in poikilotherms, but we did not expect them to be large.

Corresponding to Fig. 1(*a*), a compartment model was constructed (Fig. 1*b*), reaction or diffusion pathways were identified, and the modules were replicated to simulate the spatial aspects of countercurrent exchange (Fig. 2). Within each spatial block of the model concentrations are the product of inflow, reaction within the block, and outflow. Generally 10 spatial blocks were used in the simulation runs, but 20 or more were tried with essentially identical results.

Note that bicarbonate and carbonic acid are combined into single compartments in plasma, erythrocytes and water. This was necessary because the reaction rates are orders of magnitude larger than any others in the system, so they must be considered instantaneous as a matter of computational expedience.

A system of six differential equations in six unknowns (the compartment masses) describes the behaviour of any block of the system. For example, the equation describing plasma CO_2 concentration in the N spatial blocks of compartment PC is:

$$\frac{d}{dt}PC(N) = k_7 \cdot \frac{V_p}{V_e} \cdot EC(N) + k_2 \cdot U_2 \cdot PB(N) - (k_1 + k_2 + k_g) \cdot PC(N) + F_b \cdot [PC(N-1) - PC(N)] + k_{10} \cdot WC(N)$$

where the k-values are rate constants identified in Fig. 1(*b*), F_b is the flow of blood into block N, and the U-values are the ratios of bicarbonate to carbonic acid in the PB compartment. To activate the simulation, initial (equilibrium) values for the upstream blood and water compartments were selected, rate constants were set, and the

Table 1. *Basic attributes of the 'standard' (basically salmonid) fish*

Symbol	Variable	Value	Derivation
	Weight	175 g	Arbitrary
$\dot{V}_{O_2}$	Oxygen consumption	0·113 ml/min	Cameron & Davis (1970)
$\dot{V}_{CO_2}$	CO_2 production	0·113 ml/min	From assumption that $RQ = 1$
$\dot{Q}$	Cardiac output	3·24 ml/min	Cameron & Davis (1970)
	Temperature	10 C	—
Pa_{CO_2}	Arterial CO_2 tension	1·8 torr	Cameron & Randall (1972)
Pv_{CO_2}	Venous CO_2 tension	3·8 torr	Cameron & Randall (1972)
P_{I,CO_2}	Inspired CO_2	0	Arbitrary (measured 0·5)
P_{E,CO_2}	Expired CO_2	0	Arbitrary (see text)
Ca_{CO_2}	Total art. CO_2	3·0 mM	Cameron & Randall (1972)
Cv_{CO_2}	Total venous CO_2	4·4 mM	Cameron & Randall (1972)
pH	Art. pH	7·90	Cameron & Randall (1972)
	Blood volume	5 % (8·75 ml)	Satchell (1971)
GBV	Gill blood volume	0·148 ml	See text calculations
D	Diffusion coefficient for CO_2	41×10^{-5}	Randall (1970)
$\dot{V}_G$	Ventilation volume	30 ml/min	Cameron & Davis (1971)
αW_{CO_2}	CO_2 solubility at 10°	1·70 ml/l/torr	Randall (1970)
αPl_{CO_2}	Plasma CO_2 solubility	1·47 ml/l/torr	Randall (1970)
Hct	Haematocrit	25 %	Cameron & Davis (1971)
A	Total gill surface	59,325 mm²	Calculated; Hughes (1966)
d	Diffusion distance	3 μ	Hughes & Grimstone (1965); Newstead (1967)

equation-solving computer program was 'turned on' and allowed to run until all compartments reached steady state. A modified Euler method was used for step-wise generation of time solutions of the equations, employing a very small time step.

DERIVATION OF RATE CONSTANTS AND INITIAL CONDITIONS

We selected the rainbow trout for our simulation since a large body of information is available for this species. Occasionally, however, data from other species (or phyla) had to be used for lack of the appropriate information for trout; we have noted this accordingly in the text.

Pertinent experimental data needed for various calculations is listed in Table 1. Gill area data are adapted from Hughes' (1966) work on *Salmo trutta*.

Initial (equilibrium) compartment concentrations are given in the text-table below,

Compartment	Symbol	Amount (M)	Conc. (mM/l)
Dissolved plasma CO_2	PC	$2{\cdot}282 \times 10^{-4}$	0·266
Dissolved RBC CO_2	EC	$3{\cdot}808 \times 10^{-5}$	0·266
Water dissolved CO_2	WC	0	0
Plasma $HCO_3^- + H_2CO_3$	PB	$3{\cdot}590 \times 10^{-3}$	4·19
RBC $HCO_3^- + H_2CO_3$	EB	$5{\cdot}994 \times 10^{-4}$	4·19
Water $HCO_3^- + H_2CO_3$	WB	0	0

along with identifying symbols used in this paper. Total system volume was considered in 1 ml units, of which 0·25 ml was erythrocytes (RBCs). Since the RBCs have approximately one-half the solubility coefficient of the plasma, the effective volumes used were 0·857 ml for plasma (V_p) and 0·143 ml for RBCs (V_e). Concentrations in the above table are derived by dividing the amounts by the appropriate volume.

Concentrations of CO_2 gas were derived by multiplying venous CO_2 tension (3·8 tor

Table 2. *Reaction rates employed in the simulation. Numbering refers to the scheme in Fig. 2(b), and the derivation is noted where appropriate*

(More detailed calculations are referred to in the text.)

Rate	Value	Source and notes
k_1, k_{12}	0·0175 sec^{-1}	Interpolated to 10 °C from Edsall (1969*a*); equivalent to his k_{CO_2}
k_2, k_{13}	7·0 sec^{-1}	Interpolated to 10 °C from Edsall (1969*a*): equivalent to his $K_{H_2CO_3}$
k_3, k_4	0·866 sec^{-1}	Piiper (1969) shows mean $t_{\frac{1}{2}}$ of 0·8, and $k = 0{\cdot}693/t_{\frac{1}{2}}$
k_5, k_6	var.	Same as k_1, k_2 times F, a catalysis factor for carbonic anhydrase activity
k_7, k_8	138·6 sec^{-1}	The $t_{\frac{1}{2}}$ for this equilibrium is given by Piiper (1969) as 0·005 sec, thus $k = 0{\cdot}693/0{\cdot}005 = 138{\cdot}6$
k_9, k_{10}	36·23	See text for calculation
k_{11}	var.	See text

times solubility for CO_2 (αPl_{CO_2}, Table 1) times conversion factors for ml to mM and an appropriate volume (V_p). Erythrocytic CO_2 (EC) was derived similarly, using V_e.

Values for bicarbonate plus carbonic acid were calculated by (1) subtracting dissolved CO_2 from the total CO_2 (Table 1) and (2) and by calculating equilibrium concentrations employing rate constants scaled to appropriate temperature from data of Forster (1969) and Edsall (1969). Both methods gave nearly identical results (above). Also from this second method, the ratio of bicarbonate to carbonic acid (U_1/U_2) was calculated.

Reaction rate constants were selected from values given in the literature, much of it necessarily mammalian. However, most of the reactions are simple chemical systems and should be the same at comparable temperatures. Rate constants used are given in Table 2, as well as sources for their derivation. Numbering of k-values corresponds to Fig. 1(*b*).

Values could be fairly easily selected for all but three of the k-values: k_5,k_6 and k_{11}. The mechanism of chloride-bicarbonate exchange with water in the gill (which leads to HCO_3^- efflux at rate k_{11}) is not sufficiently known. Kerstetter & Kirschner (1972) give data, however, from which it is possible to estimate the percentage of total CO_2 efflux resulting from this pathway under certain conditions, and so k_{11} can be 'fitted' by adjusting it to produce approximately this percentage. The remaining problem, selection of a catalysis factor (F) for carbonic anhydrase was solved by comparing the known output of the system ($\dot{V}_{CO_2}$, Table 1) with the simulated output at various values of F. We found by stepping F through values of 1, 10, 100, 500 and 1000 that a value of at least 500 was necessary to produce simulation output of the same order of magnitude as the observed $\dot{V}_{CO_2}$ of the fish. This does not seem unreasonable, as catalysis may increase other reactions by many orders of magnitude.

The calculation of diffusion rate constant was a matter of some detail, and was performed using the Fick equation:

$$f'(0) = -AD\,dc/dx$$

where A is the gill area, D is the diffusion coefficient for CO_2 in tissue (Table 1), and dc/dx is the concentration gradient across the gill. Replacing dc/dx by $[C_i - C_0]/d$,

where C_i = blood concentration of dissolved CO_2, C_0 = water concentration and d = diffusion distance in mm (Table 1), we have:

$$f'(0) = (593/2)(41 \times 10^5)(3{\cdot}8 - 0{\cdot}2)/(760 \times 0{\cdot}0003) = -1{\cdot}919 \text{ ml/min.}$$

The value for A is divided by 2 since Hughes (1966) estimates that only about one-half of the secondary lamellar surface is underlain by blood space. The value of $f(0)$ in ml is calculated as follows:

$$\begin{aligned} f(0) &= Pv_{CO_2}.\alpha Pl_{CO_2}.GBV \\ &= (3{\cdot}8)(1{\cdot}57 \times 10^{-3})(0{\cdot}148) \\ &= 8{\cdot}83 \times 10^{-4} \end{aligned}$$

and therefore:

$$\begin{aligned} k &= f'(0)/f(0) = 2173 \text{ min}^{-1} \\ &= 36{\cdot}23 \text{ sec}^{-1} \end{aligned}$$

where GBV is the gill blood volume.

Gill blood volume (GBV) is calculated as follows. The number of lamellae is given by $2L/d'$, and the volume of each 2° lamella by $blx/2$, where x is the thickness of one lamellar space. Since only half of the lamellar surface is underlain by blood space, we have $GBV = (L)(1/d')(2)(\frac{1}{2}b)(l)(x)(\frac{1}{2}) = 0{\cdot}148$ ml. Gill water volume (GWV) is calculated similarly as $GWV = (L)(1/d')(d)(l)(b)(2) = 0{\cdot}6805$ ml. The first estimates of transit times, then, are 2·6 sec for blood (Table 1, $\dot{Q} = 3{\cdot}24$ ml/min) and 1·36 seconds for water (Table 1, $\dot{V}_G = 30$ ml/min) at a $\dot{V}_G/\dot{Q}$ ratio of 8·4:1.

Other authors (Stevens, 1968; Hoffert & Fromm, 1966) give higher estimates for gill blood volume, but their estimates include larger arterioles and arteries, while our calculations only take into account the blood space within the secondary lamellae.

There is one further complication that must be considered: shunt pathways have been proposed for the gills (Steen & Kruysse, 1964) and there is some evidence that not all the secondary lamellae are perfused in a normal resting fish (Davis, 1972). Indeed, Randall (1970) calculates that perhaps only 20% of the gill area need be utilized at rest. If it were the case that all blood flow at rest passed through 20% of the lamellae, we would have a transit time for blood of 0·5 sec, and a $\dot{V}_G/\dot{Q}$ ratio of 1·6:1 at these perfused lamellae. Consequently, behaviour of simulations was examined at transit times ranging from 2·6 down to 0·5 sec.

In addition to studying the behaviour of the countercurrent model, we simplified the model considerably in some additional trials to simply explore the effect of varying several of the rate constants on the rate of CO_2 efflux from the system. For this exercise we eliminated compartments WC and WB, reactions 10, 12 and 13 (Fig. 1*b*), and simply considered reactions 9 and 11 as going to infinite sinks. We then studied behaviour in a finite 'slug' of blood as it entered the gill at time 0 and remained for a transit time, t varying from 0·5 to 2·5 s.

RESULTS

Countercurrent model

Total rates of CO_2 efflux ($\dot{V}_{CO_2}$) are given in Table 3 for five trial runs of the simulation. In all cases rate constants and initial conditions were those given in Table 2 and the text (above), with $F = 10^3$. In the runs $\dot{V}_G$ and $\dot{Q}$ were varied

Table 3. *Total CO_2 output of the countercurrent flow model, with rate constants given in Table 2, F = 1000*

Blood flow is either 3·24 ml.min^{-1}, with residence time = 2·5 sec, or 6·48, giving t = 1·25 secs, as noted in the table. Expected $\dot{V}_{CO_2}$ was 0·113 ml.min^{-1} (Table 1).

Number	$\dot{Q}$ ml·min^{-1}	$\dot{V}_G$ ml·min^{-1}	$\dot{V}_{CO_2}$ ml·min^{-1}
1	3·24	15	0·051
2	3·24	30	0·093
3	3·24	60	0·145
4	6·48	30	0·080
5	6·48	60	0·158

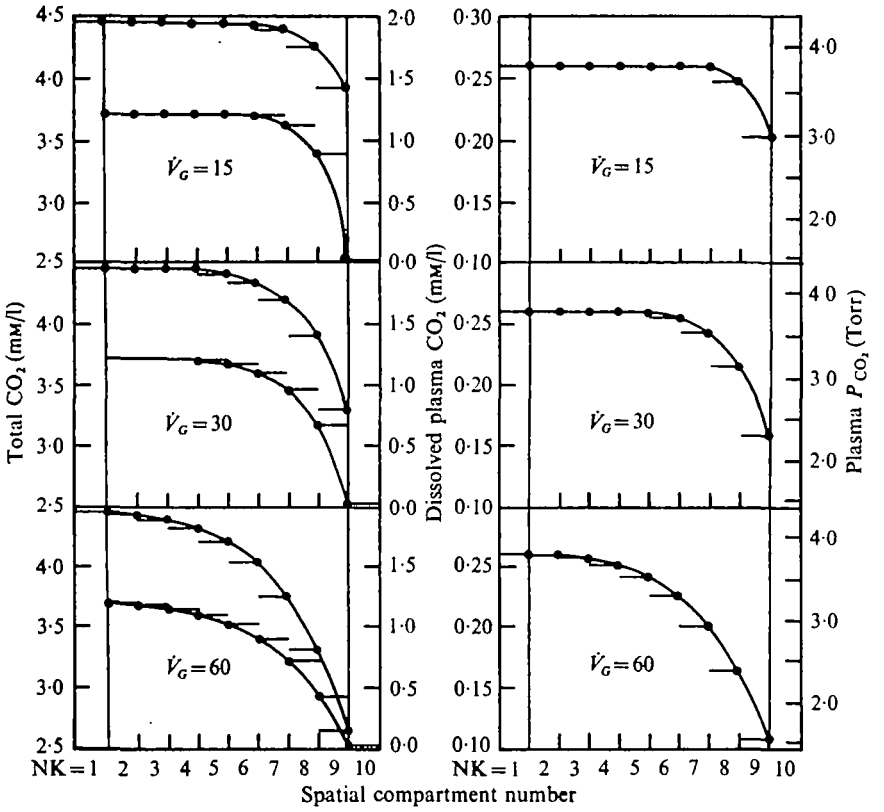

Fig. 3. Gradients of CO_2 across the secondary lamellae, as calculated using the countercurrent simulation. In all panels blood flows from left to right (top lines) and water from right to left (bottom lines). The right-hand panels show only blood P_{CO_2} values, since there was so little difference between blood and water.

shown. Output under these conditions (0·051–0·158 ml.min^{-1}) bracketed the expected value (0·113 ml.min^{-1}); this was also true when F = 500, but not when F was less than 500 or much greater than 1000. The rate of direct HCO_3^- efflux from plasma to water (k_{11}) was zero in these trials.

Gradients of total CO_2 in water and blood, and partial pressure of CO_2, are shown in Figure 3(*a*,*b*) for runs 1, 2 and 3 of Table 3. These graphs reveal that rather than

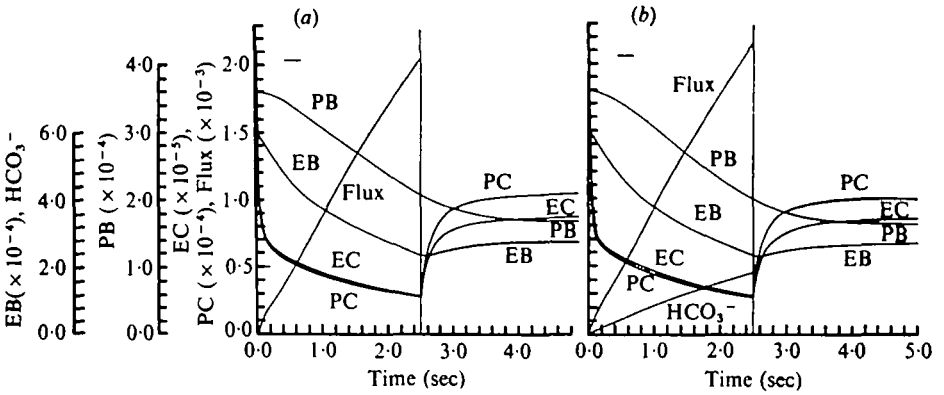

Fig. 4. Results of the simplified simulation, using external (water) concentrations as an infinite sink. All rate constants are as given in Table 2, except that in (*b*) the rate of direct HCO_3^- efflux (k_{11}) was increased from 0 to 0·0126. At 2·5 sec, loss from the blood was re-set to zero to simulate re-equilibration of the blood. The expected flux of 1·4 mM was reached in 1·65 and 1·58 sec for (*a*) and (*b*), respectively.

Table 4. *Summary of computer trials of the simplified simulation model, showing sensitivity to carbonic anhydrase catalysis and rate of direct efflux of* HCO_3^- *by exchange diffusion*

(The expected efflux was 1·4 mM (Table 1), and times taken to reach this total efflux are shown as well as the total efflux after 2·5 sec of gill exposure)

Trial number	*F*, carbonic anhydrase	k_{10} HCO_3^- loss rate	Time for 1·4 mM flux	Flux at 2·5 sec, × 10^{-4}
1	1	0	>2·5	0·22
2	10	0	>2·5	0·26
3	100	0	>2·5	0·63
4	500	0	2·25	1·54
5	1000	0	1·60	2·05
6	1000	0·0063	1·50	2·12
7	1000	0·0126	1·46	2·19
8	1000	0·0189	1·40	2·25
9	1000	0·0252	1·38	2·58
10	2000	0	1·30	2·46

being hyperventilated with respect to CO_2, the gills are, rather, hyper-perfused. CO_2 gradients and resulting efflux are strongly affected by flow of both water and blood.

Simplified model

Fig. 4 contains results from the simulation after simplification to eliminate spatial and counterflow characteristics. External (water) CO_2 was assumed to remain at zero. In this form we can manipulate various rate constants more easily to assess sensitivity of the total CO_2 efflux to them. In Fig. 4(*a*) all rate constants were the same as in Table 3, runs 1–3; and in Fig. 4(*b*) the same with k_{11} = 0·013, a rate resulting in approximately 20% of the total efflux by this pathway. At 2·5 sec k_9 was re-set to zero to simulate the re-equilibration of the blood after leaving the secondary lamellae.

In Table 4 results of varying F (for carbonic anhydrase catalysis) and k_{11} (for direct HCO_3^- excretion) are given. No combination of other rate constants could produc

e expected efflux ($\dot{V}_{CO_2}$, Table 1) in the calculated transit time of 2·5 sec when F was much less than 500.

The effects of acetazolamide treatment (to block carbonic anhydrase) were simulated by reducing F to 1 and then increasing all initial compartment concentrations to a level where CO_2 efflux was the same as without acetazolamide. We found that an approximately five-fold increase in initial concentrations was needed.

In general, the model was found to be highly sensitive to diffusion rate (k_9), transit time (t), and carbonic anhydrase catalysis (F, k_5 and k_6), It was less sensitive to changes in Cl^--HCO_3^- exchange between RBCs and plasma (k_3 and k_4), and was almost completely insensitive to changes in CO_2 diffusion between RBCs and plasma (k_7 and k_8) and rates of dissociation of H_2CO_3 (in compartments PB and EB).

DISCUSSION

What is the meaning of a simulation that contradicts experimental observations? In this case, how can the flow sensitivity of the countercurrent simulation be reconciled to the flow insensitivity found by Randall & Cameron (1973*a*, *b*)? Since the simulation is a much simplified model, we must return to some of the simplifying assumptions and ask what complicating factors could reconcile this apparent contradiction.

The simulation results make it clear that replacement of dissolved plasma CO_2 is sufficiently rapid to result in an effective αPl_{CO_2} much greater than αW_{CO_2}, hence a much lower capacity-rate for CO_2 than would be the case otherwise. These capacity-rates, however, are calculated on the basis of overall gill and water flows and do not take into account the true rates of flow at the surface of the secondary lamellae.

If a fish has an overall ventilation-perfusion ratio ($\dot{V}_G/\dot{Q}$) of 10:1, and if $\frac{1}{2}$ of the secondary lamellar surface is non-respiratory, then $\dot{V}_G/\dot{Q}$ drops to 5:1; the value is less if some of the water is spilled between hemibranchs, and since the gill musculature is capable of altering the amount of this spillage (Pasztor & Kleerkoper, 1962), $\dot{V}_G/\dot{Q}$ is a variable subject to local control. Furthermore, there is evidence (Davis, 1972) that not all secondary lamellae are perfused at rest. Whether the total blood flow is channelled through a reduced number of lamellae, or whether the flow in perfused lamellae remains the same with the balance of flow passing through by-pass shunts (Steen & Kruysse, 1964) is not known, but recent results favour the former hypothesis (Cameron & Randall, unpublished data). In the former case $\dot{V}_G/\dot{Q}$ at the secondary lamellae drops still further; in the latter it is unchanged. Measurements of arterial saturation would also indicate the former, since any large non-respiratory shunt would appreciably lower Pa_{O_2}.

There are possible explanations, then, for the apparent contradiction: that Randall and Cameron (1973) altered the overall $\dot{V}_G/\dot{Q}$ (or $\dot{V}_G/\dot{V}_{O_2}$) ratio, but did not alter $\dot{V}_G/\dot{Q}$ at the secondary lamellae, due to spillage of the increased flow between hemibranchs; alteration of the gill perfusion pattern; changes in shunting; or a combination of these. Artificial gill ventilation was shown earlier to lower the effectiveness of gas transfer (Davis & Cameron, 1970), and although increased ventilation was accomplished by a less unnatural technique by Randall and Cameron (1973*b*) there is no way of knowing the fine details of water distribution under these conditions.

A further factor which may be significant is that Randall & Cameron (1973*a*, *b*)

were concerned only with steady-state measurements, and found no difference in P_{CO_2} or pH several hours after changing the ventilation. During this time a number of adjustments could have taken place, including an increase in diffusion distance (d) by mucus production in the gill epithelium (Randall, 1970), changes in shunt pathways under neuro-endocrine control (Steen & Kruysse, 1964), changes in physical conformation of the gills (Pasztor & Kleerkoper, 1962), or gross changes in blood distribution by the afferent gill arteries (Cameron, Randall & Davis, 1971).

Or let us consider the following: an increase in $\dot{V}_{O_2}$ at constant $\dot{V}_{CO_2}$ in tissues would lead to an immediate increase in CO_2 efflux (Fig. 3), increase in pHa, and a decrease in Pa_{CO_2}. Since this lost CO_2 would not be completely replaced in the next circuit of the body, initial concentrations of all CO_2 species at the time of next gill entry would be proportionately reduced, bringing $\dot{V}_{CO_2}$ back into balance. The increased pH might then cause a change in either Na^+/H^+ or Cl^-/HCO_3^- exchange (Kerstetter & Kirschner, 1972), restoring the original pHa. The net long-term change in P_{CO_2} and pH would therefore be small, as Randall and Cameron (1973*b*) observed. Data of Dejours (1969) and Lloyd & White (1967) indicate that this re-adjustment of buffering is a slow (many hour) process. Our simulation is only constructed to deal with acute changes at constant initial concentrations, and therein may be the difference.

The results of the simulation, as well as study of the dynamics of heat exchangers, demonstrate that insensitivity to flows can occur only at grossly disparate capacity-rates of the two fluids. Examination of the best available data does not seem to show that this is the case in the fish gill, either for oxygen or carbon dioxide. There must, then, be additional factors to consider in order to arrive at the true flow characteristics at the secondary lamellae, which are the ones that matter for gas exchange.

From Fig. 4 it is also apparent that if, for example, only 20% of the secondary lamellae are perfused at rest (cf. Randall, 1970), and no blood is shunted through other pathways, then the blood residence time is reduced from 2·5 to 0·5 sec, with a resulting drastic decrease in total CO_2 efflux.

A second function of the simulation exercise, then, is to point out the special importance of more accurate determinations of the residence time of blood in the gills, and of the catalysis factor for carbonic anhydrase. The former will be a variable influence by changes in perfusion pattern, as discussed above. The latter factor has not been investigated at all in fish blood, but there is certainly the possibility that this rate, too, is under biochemical control, via inactivation of enzyme, production of inhibitors, and so forth.

We hope that this exercise will serve to focus critical thinking on the many variables which affect rates of CO_2 transfer in the gills, and stimulate research into long-neglected areas of CO_2 excretion and acid-base balance in aquatic poikilotherms.

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SUMMARY

1. A computer simulation of countercurrent CO_2 exchange in fish gills was constructed to examine effects of variations in blood and water flow rates.

2. CO_2 output was sensitive to both blood and water flow rates, contrary to experimental data.

3. Various explanations of the contradiction are discussed, including patterns of gill perfusion and possible shunting of blood.

4. A simplified version of the model was also used to demonstrate extreme sensitivity of CO_2 efflux to variations of the residence time of blood in the gills.

5. Data from the literature on reaction rate constants for the CO_2/carbonate/bicarbonate system are summarized, and the importance of some of these reactions is examined.

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