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Tissue gas exchange models and decompression computations: a review

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Wienke BR. Tissue gas exchange models and decompression computations: a review. Undersea Biomed Res 1988; 15(6):53–89.—Mathematical models for inert gas transport and decompression are summarized. Both semi-infinite and finite media are treated, and resulting analytic expressions are obtained and compared against each other. One-dimensional plane and cylindrical geometries are considered, and limiting forms are explicitly detailed. Models are placed into three categories for discussion—bounded, bulk, and perfusion-diffusion. The intent is to collect treatments and techniques into one source for reference. Staging criteria, where appropriate to a model, are also included in the development. Bounded, bulk, and perfusion-diffusion models are described in supersaturation, statistical, and thermodynamic frameworks. Some strengths and weaknesses of deterministic and statistical models are noted. Today, models can be nested in hi-tech decomputers utilizing precision depth sensors and elapsed timers. The ability to solve equations and check criteria in an essentially continuous time mode imparts new dimensionality, enhancing capability and optimizing performance. However, there are limits on all computational models, both in theory and application, and herein we review range, physical correctness, and history of the algorithm.

mathematical models inert gas transport
decompression

The systematics (1–43) of gas exchange and decompression are so complicated that theories reflect only pieces of the puzzle. Computational algorithms and manned testing, however, are requisite in a spectrum of activities. This paper reviews a set of operational models and their correlations. Basic assumptions, mathematical techniques, solutions, and limiting forms are collected (44–49) and contrasted. Models are discussed within a historical, three-category framework chosen on the basis of dominant transport characteristics. The categories are bounded, bulk, and perfusion-diffusion. In underwater practice the continuous application of mathematical algorithms can be handled by small digital computers (decomputers), which monitor activity at regular time intervals (3–5 sec). Precise feedback loops between depth sensors and elapsed timers optimize calculations. Within such technology, model assumptions and bases also warrant comparison. The potential of electronic devices to process tables of information or detailed equations underwater is reaching maturity

(25–27), and virtually all algorithms described herein are amenable to digital implementation. Many algorithms, particularly those in the bulk category, are presently in commercial stages of development and distribution.

Although early researchers regarded critical tensions as limit points, separating bubble formation from nonformation, the data more aptly reflect dose response to a given set of predisposing conditions. Staging formats, correlated with testing and models, try to separate bends-provoking exposures from nonprovoking exposures with some measure of confidence. Accordingly, bubble formation is better viewed as symptomatic or subsymptomatic, instead of present or not present. Computational models, however, gain efficacy by their ability to track data, independent of physical interpretation (28). In this sense, the bottom line for computational models is utility, operational reliability, and reproducibility. A correct model can achieve such ends, but almost any model with sufficient parameter latitude could achieve the same ends.

For convenience, we place mathematical approaches into three transport categories, denoted simply as bounded, bulk, and perfusion-diffusion. Bounded models consist of solutions to the diffusion equation in media with finite extension and boundary conditions, and are spatially dependent. Bulk models employ solutions to the simple rate equation, usually assuming perfusion as a limiting factor, or solutions to the infinite media diffusion equation. Bulk models are generally spatially independent. Bulklike representations of bounded models can be generated by averaging equations over appropriate regions, eliminating the spatial dependencies. Spatially independent models are the simplest to use and program, and such representations are widely employed. Recent statistical models, which correlate global parameters and measurements with decompression risk, are also included in the bulk category. Perfusion-diffusion models are hybrids of predecessors, attempting to include both diffusion and perfusion in rate-limiting roles. Spatial dependencies in perfusion-diffusion model equations can also be averaged over regions of interest. Deterministic bounded and bulk models were first employed in decompression analyses, whereas perfusion-diffusion models are more recent and complex. Apart from nomenclature and broad categorization, no special significance is attached to the descriptors.

As is well known, computational models enjoy varying degrees of success and failure. More complex models address a greater number of issues but are harder to program for general use. The opposite is true for simpler models. Transport equations and decompression criteria are two related yet distinct considerations. Transport equations provide the vehicle to estimate gas tensions, apart from criticality. Decompression criteria are phenomenologic statements of permissible levels of dissolved or separated gas, effectively dictating staging procedures. Some criteria are based on first principles, but most are not. Both equations and criteria can be subjective in the absence of definitive data, the acquisition of which is tedious, sometimes controversial, and often ambiguous. When deterministic models are abandoned, statistical models can address the variability of outcome inherent to random occurrences, but only in grayer tones as far as specifying controlling mechanisms. The dose-response characteristics of statistical models are very attractive in the formulation of risk tables. Tables of comparative statistical risk offer a means of weighing exposure alternatives.

Despite shortcomings, the computational decompression lore has grown considerably. Much of the following is known qualitatively, but less quantitatively, and perhaps originality resides in the collection, derivation, synthesis, and presentation.

The intention is to draw scattered pieces of analyses together, replacing too deep a discussion here and too shallow an argument there, to give the reader a meaningful set of assumptions and equations within a uniform framework. An operational approach to the mathematics is adopted. All pertinent steps are described first, followed by intermediate and then final results. Details can thus be easily checked in standard handbooks, tables, or the included appendixes. Appendix A details the separation-of-variables technique used to solve the diffusion and Fick-Fourier second-order, differential equations, and includes useful integrals for series solutions. Appendix B generates power series expansions which are solutions to the differential equations and useful numerical representations for applications. Appendix C describes the method of maximum likelihood and probability.

TRANSPORT EQUATIONS

Tissue is usually separated into intravascular and extravascular regions for modeling purposes. Blood containing dissolved inert and metabolic gases passes through the intravascular zone, providing both initial and boundary conditions for subsequent gas transport through the extended extravascular zone. Three equations are applied to model transport, namely, a diffusion equation, a rate equation, and a combined diffusion-rate equation. All three attempt to quantify extravascular tensions in time, given a set of intravascular initial and boundary conditions. To simplify treatment of these three equations, we first scale solutions as follows.

Defining the instantaneous gas tension, p, given any constant tension, p_0, with the relative difference, $\Pi = p - p_0$, the diffusion equation is scaled by the substitution of Π for p,

$$(D\,\nabla)\,\Pi = \frac{\partial \Pi}{\partial t} \tag{1}$$

with ∇ the spatial gradient operator, t the time, and D the diffusion coefficient. The arbitrary tension, p_0, can always be chosen to yield homogeneous initial or boundary conditions, that is, $\Pi = 0$ initially, or on the boundary. Solutions to Eq. *1* depend on initial and boundary conditions and are most easily effected in the homogeneous case. Most calculations are performed in one-dimensional planar or cylindrical geometries. Furthermore, regarding tissue as uniform in composition, the diffusion coefficient, D, is constant and can be pulled outside of the divergence operator. Accordingly, in one-dimensional planar geometries, using the standard operator representation of $D\,\nabla^2$, we have,

$$\nabla \cdot (D\,\nabla)\,\Pi = D\,(\nabla \cdot \nabla)\,\Pi = D\,\nabla^2\,\Pi = D\,\frac{\partial^2 \Pi}{\partial x^2} \tag{2}$$

while in one-dimensional cylindrical geometries,

$$\nabla \cdot (D\,\nabla)\,\Pi = D\,(\nabla \cdot \nabla)\,\Pi = D\,\nabla^2\,\Pi = D\,\frac{\partial^2 \Pi}{\partial r^2} + \frac{D}{r}\,\frac{\partial \Pi}{\partial r} \tag{3}$$

with x and r the planar and cylindrical coordinates. Planar and cylindrical geometries are natural for modeling purposes. Two-dimensional geometries have been employed

in exchange calculations, but they often introduce unnecessary complexities or additional spatial terms that have small effect on solutions.

The scaled rate equation for gas transfer is similarly written, obviously with neither spatial dependencies implied nor boundary conditions required, by the solution,

$$\frac{\partial \Pi}{\partial t} = -\lambda \Pi \tag{4}$$

for λ some characteristic time constant for buildup or decay. Solutions to Eq. *4* depend only on the initial condition. This particular equation has been widely employed in decompression applications. It was originally suggested at the turn of the century by Boycott and coworkers (1) for caisson studies. As such, solutions to Eq. *4* are independent of position in tissue, obviously a simplification that requires rapid intercellular gas diffusion compared to time scales on the order of λ_1. The uniformity of gas loading, implicit to Eq. *4*, can also be effected in diffusion models by averaging spatial solutions over appropriate regions. Such simplifications provide analog expressions which can be compared with the perfusion solutions to Eq. *4* that depend only on time.

If diffusion, perfusion, and metabolic assimilation are included in the balance, the transport equation generalizes to the scaled Fick-Fourier expression,

$$\nabla \cdot (D \nabla) \Pi = \frac{\partial \Pi}{\partial t} + \kappa \Pi + Z(\Pi) \tag{5}$$

with Z the metabolic consumption rate and κ a perfusion time constant. For inert gases, obviously $Z = 0$. Solutions to Eq. *5* depend on both initial and boundary conditions, with simplification afforded in the homogeneous case, as with solutions to Eq. *1*. Clearly, the Fick-Fourier expression contains the diffusion and bulk rate equations as limiting subsets, but for historical and technical reasons both predecessors enjoy greater utility. In perfusion-dominated situations the rate equation is useful, whereas in diffusion-controlled applications the diffusion equation has greater utility. Perfusion-vs.-diffusion studies attempt to correlate theory and experiment, and in such analyses proponents invoke one or the other equation.

The transport solutions to Eqs. *1*, *4*, and *5* exhibit uptake and elimination symmetry provided gases remain dissolved, or phase inception and exchange mechanisms with existing free phases are neglected. If dissolved-free mechanisms are considered, the driving force for elimination can differ significantly from the uptake gradient, destroying the symmetry. Specific effects on elimination gradients will be quantified later. Obviously if gas separates and bubbles become entrained in the circulatory system, such loading will affect perfusion rates as well as gradients. Contemporary measurement and theory support nucleation, gas separation, and bubble growth mechanisms even below bends thresholds, considerations which lie outside most models but which get indirectly folded over model parameters and decompression criteria. The effects of such folding ultimately accommodate wide ranges in model interpretation, algorithm implementation, and parameter-value assignments.

The solutions to Eqs. *1*, *4*, and *5* can always be put into a general form,

$$p - p_0 = (p_i - p_0) F \tag{6}$$

with p_0 and p_i appropriate boundary and initial conditions, and the residue function, F, bounded in space and time (49),

$$0 \leq F \leq 1 \tag{7}$$

where F depends explicitly on position, x or r, and time, t. Additionally,

$$\lim_{t \to \infty} F = 0,$$
$$\lim_{t \to 0} F = 1 \tag{8}$$

The residue function, F, is also called the response, transfer, exchange, or tissue function. The fact that it is bounded, according to Eqs. *7* and *8* ensures that tensions are similarly bounded by p_i and p_0. In a series of excursions, p_0 and p_i represent extremes for the excursion, usually the arterial tension, p_a, or the venous tension, p_v, and the initial tension of the gas at the step. Steps are treated sequentially, with finishing partial pressures at one step representing initial partial pressures for the following step, and so on. In neglecting transit times between steps, such queuing is termed superposition. If transit times between stages are not neglected, the same residue functions can be averaged over the distance and absolute pressure. Alternatively, an exact equation with velocity-dependent terms appended can be employed to account for exposures between steps. In the following, functional and averaged forms for F are developed.

The solutions to the diffusion and Fick-Fourier equations can be obtained by the standard separation of variables technique (44, 45). The differential equations are first separated into spatial and temporal parts, and each portion is then equated to the same constant (eigenvalue). Allowable values of this constant are determined by the boundary conditions. The full solution (46, 47) is a product of the spatial and temporal parts. The temporal parts are decaying exponentials, whereas the spatial parts in one-dimensional plane geometry are the trigonometric (sin, cos) functions, and the radial Bessel-Neumann (J_0, Y_0) functions in cylindrical geometry. The rate equation is solved easily in time, yielding decaying exponentials. Details and some integrals, expansions, and relationships are summarized in the appendixes.

It will be convenient to express ambient pressure, P, in units of feet of sea water (fsw), and gas partial pressures, p, as mole fractions of ambient pressure. All tables, decompression criteria, and residue functions are consistent with the convention.

BOUNDED TREATMENTS

If we treat the extravascular region as finite, maintaining the vascular boundaries at the arterial tension, that is, $p = p_a$ for $t > 0$, while for $t < 0$ we have $p = p_i$ uniformly, the boundary and initial conditions take the form in plane geometry,

$$\Pi(x,0) = p_i - p_a = \Pi_i,$$
$$\Pi(a,t) = p_a - p_a = 0,$$
$$\Pi(b,t) = p_a - p_a = 0 \tag{9}$$

while in cylindrical geometry for symmetric capillary spacing, the corresponding set is appropriate,

$$\Pi(x,0) = p_i - p_a = \Pi_i,$$
$$\Pi(a,t) = p_a - p_a = 0,$$
$$\frac{\partial \Pi(c,t)}{\partial r} = \frac{\partial (p - p_a)}{\partial r} = 0 \qquad (10)$$

for a and b the inner and outer boundaries of the extravascular region, and $c = b/2$. This set of boundary conditions offers the bases for a bounded class of diffusion solutions, as well as their bulk extensions, used in early studies. As the thickness of the extravascular region increases, bounded solutions approach bulk expressions asymptotically. Derivative boundary conditions at $c = b/2$ impart reflection symmetry to the solutions in the extravascular region. Here, a can be regarded as the capillary thickness, b some representative intercapillary spacing appropriate to the geometry, and c the midpoint of the extravascular zone.

Planar model

In one-dimensional slab geometry (3, 9) separating variables with α^2 the eigenvalue, the formal solution satisfying the inner boundary condition at a is written (appendixes A and B),

$$\Pi = \sum_{n=1}^{\infty} A_n \sin[\alpha_n (x - a)] \exp(-\alpha_n^2 D t) \qquad (11)$$

with A_n and α_n determined from initial and boundary condition at b. Applying the boundary condition at b requires that $\sin[\alpha_n (b-a)] = 0$ for all n so that,

$$\alpha_n = \frac{n\Pi}{(b-a)} \qquad (12)$$

Multiplying both sides of Eq. *11* by $\sin[\alpha_m (x - a)]$, applying the initial condition at $t = 0$, and integrating both sides of the equation over (a,b) yields,

$$\Pi_i \frac{2(b-a)}{(2n-1)\pi} = A_{2n-1} \frac{(b-a)}{2} \qquad (13)$$

Collecting terms, the slab solution reduces to the expression,

$$p - p_a = (p_i - p_a) E(x,t) \qquad (14)$$

$$E(x,t) = \sum_{n=1}^{\infty} \frac{4}{(2n-1)\pi} \sin[\alpha_{2n-1}(x-a)] \exp(-\alpha_{2n-1}^2 D t) = \sum_{n=1}^{\infty} E_{2n-1}(x,t) \qquad (15)$$

Averaging the response function, E, over the cellular domain (a,b),

$$\bar{E}(t) = \frac{\int_a^b E(x,t)dx}{\int_a^b dx} \qquad (16)$$

gives a bulklike response, depending on time and tissue thickness,

$$\bar{E}(t) = \frac{8}{\pi^2} \sum_{n=1}^{\infty} \frac{1}{(2n-1)^2} \exp(-\alpha_{2n-1}^2 D t) = \sum_{n=1}^{\infty} \bar{E}_{2n-1}(t) \qquad (17)$$

Slab algorithms have seen extensive application in Royal Navy studies (3, 9), with the decay constant, K,

$$K = \frac{\pi^2 D}{(b-a)^2} \tag{18}$$

adjusted to exposure data,

$$K = 0.007928 \text{ min}^{-1} \tag{19}$$

Because only one parameter, K, is employed, the model is aptly single tissue. Single tissue expressions such as Eq. *17* are employed in bounce applications, but one-parameter exponentials cannot model a broader exposure spectrum well. Single exposures, down to near 180 ft, satisfy a simple depth-time law which can be derived from a more general extension of Eq. *15*, as will be demonstrated.

Denoting the absolute pressure, P, fixed gradient theory (2, 6, 13) limits tissue saturation by a critical difference, L, so that,

$$p - 0.79 \text{ P} \leq L \tag{20}$$

In early air applications, $L \approx 24$ fsw for most exposures. In supersaturation approaches to staging, this value is conservative for deep, and liberal for shallow exposures. More recently (13), a depth-dependent ratio, Q, supplanting the fixed gradient, L, has been introduced to limit exposures,

$$\frac{p}{\text{P}} \leq Q \tag{21}$$

with the depth-dependent ratio given by,

$$Q = \frac{709}{\text{P} + 404} \tag{22}$$

taking the nitrogen mole fraction (air) to be 0.79, and absolute pressure, P, in fsw. At the surface at sea level (P = 33 fsw), $Q = 1.62$, for compressed air. At a depth of 460 ft (P = 493 fsw), a limiting $Q = 0.79$, and staging cannot be effected. The depth-dependent ratio approach lies somewhere between fixed gradient and multitissue schemes. Today, based on bubble formation studies in decompressed gelatin, Strauss (41) has suggested that the number of bubbles and their total volume can be decreased, and hence decompression time shortened, if L is taken in the neighborhood of 10 fsw.

Cylindrical model

If we wrap the plane geometry of the previous section into a hollow cylinder, we generate Krogh (10) geometry. The hollow cylindrical model retains all features of planar models and additionally includes curvature (26) for small a and b. For large a and b curvature effects become asymptotically small and cylindrical solutions relax to their planar counterparts. In one-dimensional geometry, denoting the separation

constant as β^2, the solution satisfying the inner boundary condition at a can be cast (appendixes A and B),

$$\Pi = \sum_{n=1}^{\infty} A_n \, U_0(\beta_n r) \exp(-\beta_n^2 D t) \tag{23}$$

for,

$$U_0(\beta_n r) = J_0(\beta_n r) Y_0(\beta_n a) - Y_0(\beta_n r) \, J_0(\beta_n a) \tag{24}$$

the cylinder function, J and Y Bessel and Neumann functions, and A_n and β_n to be determined from the initial and outer boundary condition at b, as in the slab case. Applying the outer derivative boundary condition, Eq. *10*, at $c = b/2$ requires,

$$J_1(\beta_n c) Y_0(\beta_n a) - Y_1(\beta_n c) \, J_0(\beta_n a) = 0 \tag{25}$$

so that β_n are the roots of the equation. Multiplying both sides of Eq. *23* by $U_0(\beta_n r)$, applying the initial condition at $t = 0$, and integrating both sides of the equation over the cellular region (a,c), yields,

$$\Pi_i \frac{2}{\pi \beta_n^2} = A_n \frac{2[J_0^2(\beta_n a) - J_1^2(\beta_n c)]}{\pi^2 \beta_n^2 \, J_1^2(\beta_n c)} \tag{26}$$

Combining Eqs. *24* and *26* produces the cylindrical result,

$$p - p_a = (p_i - p_a) \, E(r,t) \tag{27}$$

$$E(r,t) = \pi \sum_{n=1}^{\infty} \frac{J_1^2(\beta_n c)}{[J_0^2(\beta_n a) - J_1^2(\beta_n c)]} \, U_0(\beta_n r) \exp(-\beta_n^2 D t) = \sum_{n=1}^{\infty} E_n(r,t) \tag{28}$$

Again averaging the response function over the cellular region (a,c),

$$\overline{E}(t) = \frac{\int_a^c E(r,t) r dr}{\int_a^c r dr} \tag{29}$$

gives a corresponding bulk analog, depending on time and regional boundaries,

$$\overline{E}(t) = \frac{4}{(c^2 - a^2)} \sum_{n=1}^{\infty} \frac{1}{\beta_n^2} \frac{J_1^2(\beta_n c)}{[J_0^2(\beta_n a) - J_1^2(\beta_n c)]} \exp(-\beta_n^2 D t) = \sum_{n=1}^{\infty} \overline{E}_n(t) \tag{30}$$

for the hollow cylindrical case.

Shrinking the capillary radius with respect to the capillary separation, that is, taking $a \to 0$ with $b/a \to \infty$, we can simplify Krogh geometry. Under such conditions, the hollow cylinder collapses to a solid cylinder, with solutions to the diffusion equation only involving Bessel functions, J_0, and not Neumann functions, Y_0, which are indeterminate at the origin (appendix A). Accordingly, with $a = 0$ we first write,

$$\Pi = \sum_{n=1}^{\infty} A_n \, J_0(\beta_n r) \exp(-\beta_n^2 D t) \tag{31}$$

but, because of the loss of the inner boundary condition and reduced model flexibility, the initial and outer boundary conditions must be more generally posed,

$$\Pi\,(x,0) = p_i - p_a = \Pi_i$$
$$h\,\Pi\,(c,t) + \frac{\partial \Pi\,(c,t)}{\partial r} = h\,(p - p_a) + \frac{\partial\,(p - p_a)}{\partial r} = 0 \qquad (32)$$

with h any nonzero constant. The eigenvalues, β_n, from the second of the boundary conditions, are the roots of the relationship,

$$hJ_0\,(\beta_n c) - \beta_n\,J_1(\beta_n c) = 0 \qquad (33)$$

in analogy with Eq. *25*. In this case, requiring just refection symmetry about the tissue midpoint, c, is an incomplete mathematical statement without an inner boundary, and hence the need for a more general condition at some point $r > 0$. Evaluating the Bessel coefficients, A_n, from the initial condition at $t = 0$ by multiplying both sides of Eq. *31* by $J_0(\beta_n r)$ and integrating gives,

$$\Pi_i \frac{bJ_1(\beta_n c)}{\beta_n} = A_n \frac{c^2}{2\beta_n^2}[h^2 + \beta_n^2]\,J_0^2\,(\beta_n c) \qquad (34)$$

so that the solid cylindrical response function takes the final form,

$$E(r,t) = \sum_{n=1}^{\infty} \frac{2h}{c(\beta_n^2 + h^2)} \frac{J_0(\beta_n r)}{J_0(\beta_n c)} \exp\,(-\beta_n^2 Dt) = \sum_{n=1}^{\infty} E_n(r,t) \qquad (35)$$

Similarly, the averaged solution has the simple form,

$$\overline{E}(t) = \frac{4h^2}{c^2} \sum_{n=1}^{\infty} \frac{1}{\beta_n^2(h^2 + \beta_n^2)} \exp\,(-\beta_n^2\,Dt) = \sum_{n=1}^{\infty} \overline{E}_n\,(t) \qquad (36)$$

in analogy with Eq. *17*. Alternatively, the solid cylindrical results can be obtained from the hollow cylindrical results by using limiting forms of the Bessel and Neumann functions as $a \to 0$, but with more effort. The solid forms given above are useful when the extravascular zone is thick with respect to the capillary radius. In such cases, the reflection symmetry about the tissue midpoint is not maintained, as witnessed by a trivial (zero or constant) solution in Eqs. *35* and *36* as $h \to 0$.

Further developments for the one-dimensional hollow or solid cylindrical models parallel the foregoing planar model. The main advantage of both cylindrical models over planar models is their ability to fold tissue curvature into the treatment. In actual calculations, effects of cylindrical vs. planar geometry are not overwhelming, perhaps in the 5–10% range for zone-averaged expressions.

BULK TREATMENTS

Bulk regions are tissue zones of considerable thickness, zones where boundary effects are neglected, zones of average tissue-blood content, or regions where finite solutions are mathematically averaged to eliminate spatial dependencies (as seen earlier). Bulk treatments try to minimize complexity by focusing on controlling macroscopic features of gas exchange, be that diffusion or perfusion. Bulk models are simpler to use and program, often permitting considerable leeway in parameter

definition and thus correlations with experiments. The limiting features of bulk diffusion can be gleaned from an analysis of gas penetration into a thick (open side) extravascular zone, given one boundary condition at the vascular interface (closed side) and the initial condition.

Semi-infinite model

If $p = p_i$ uniformly for $t < 0$, and we maintain the inner boundary of a semi-infinite region at $p = p_a$ for $t \geq 0$, the boundary and initial conditions are written,

$$\begin{aligned} \Pi\,(x,0) &= p_i - p_a = \Pi_i \\ \Pi\,(a,t) &= p_a - p_a = 0 \end{aligned} \tag{37}$$

in analogy with Eq. 9. The open side ($x = \infty$) acquires the asymptotic behavior of the solution. The semi-infinite diffusion problem can be solved with Green's function or integral transform techniques (46, 47), but since we have already generated finite solutions in both slab and cylindrical geometries, it is easier to obtain the semi-infinite result by letting $b \to \infty$ and then replace the sums by integrals. Slab geometry suffices for the extension.

For simplicity, we first let $a = 0$ while taking $b \to \infty$. Replacing the summation over n in Eq. *15* with an integral as $b \to \infty$, one obtains,

$$\begin{aligned} &\lim_{b\to\infty} \sum_{n=1}^{\infty} \frac{4}{(2n-1)\pi} \sin(\alpha_n x) \exp(-\alpha_n^2 Dt) \\ &= \frac{2}{\pi} \int_0^{\infty} \frac{1}{n} \sin(\alpha_n x) \exp(-\alpha_n^2 Dt)\, dn \end{aligned} \tag{38}$$

Defining $s^2 = \alpha_n^2 D$, and using the integral representation (47) for *erf*,

$$erf\,[x/(4Dt)^{1/2}] = \frac{2}{\pi} \int_0^{\infty} \frac{1}{s} \sin(sx/D^{1/2}) \exp(-s^2 t)\, ds \tag{39}$$

the semi-infinite relationship follows from Eqs. *14* and *38*.

$$p - p_a = (p_i - p_a)\, E(x,t) \tag{40}$$

and with,

$$E(x,t) = erf\,[x/(4Dt)^{1/2}] \tag{41}$$

still exhibiting explicit dependence on the penetration, x, diffusivity, D, and time, t. Analogous extensions can be effected in cylindrical geometry, but are not recounted here. Averaging E over the extravascular interval $(0,b)$,

$$\bar{E}(t) = \frac{\int_0^b E\,(x,t)\, dx}{\int_0^b dx} \tag{42}$$

gives the two-term result (48) containing the response, Eq. *41*, at b,

$$\bar{E}(t) = erf\,[b/(4Dt)^{1/2}] + \frac{(4Dt)^{1/2}\,[\exp\,(-b^2/4Dt) - 1]}{b\pi^{1/2}} \tag{43}$$

The full expression for $\bar{E}(t)$ includes all exposures, that is, $0 \leq t \leq \infty$. For short or long times the residue function can be simplified using asymptotics. Limiting (46) forms of the error function are well known. For large values of the argument, $z = b/(4Dt)^{1/2}$, the error function can be expanded,

$$erf\,(z) = 1 - \frac{\exp\,(-z^2)}{z\pi^{1/2}}\left[1 - \frac{1}{2z^2} + \frac{3}{4z^4} - \frac{15}{8z^8} + \ldots\right] \tag{44}$$

The error is less than the value of the last term used. For $z < \infty$, we have a general expansion that is useful for small values of the argument,

$$erf\,(z) = \frac{2z}{\pi^{1/2}}\left[1 - \frac{z^2}{3} + \frac{z^4}{10} - \frac{z^6}{42} + \ldots\right] \tag{45}$$

For short times, or large values of $b/(4Dt)^{1/2}$, the averaged function is given by using Eq. *44*,

$$\bar{E}(t) \approx 1 - \frac{(4Dt)^{1/2}}{b\pi^{1/2}} \tag{46}$$

For long times, or small values of $b/(4Dt)^{1/2}$, we similarly find,

$$\bar{E}(t) \approx \frac{b}{(4\pi Dt)^{1/2}} \tag{47}$$

using Eq. *45*. Clearly $\bar{E}$ is bounded by 0 and 1.

Hempleman (3, 13) limited bounce exposures with a depth-time law,

$$dt^{1/2} \leq 475 \text{ fsw} - \text{min}^{1/2} \tag{48}$$

with d the depth. Based on venous gas emboli (VGE) measurements and desired reductions in count, Spencer (7) later recommended that the constant in the above equation be reduced to 465 fsw $\text{min}^{1/2}$. Using Eqs. *40*, *46*, and *48*, while taking $d = (p_a - p_i)/0.79$ as the bounce condition, gives for short times,

$$p - p_i \approx \frac{d(4Dt)^{1/2}}{b\pi^{1/2}} \leq 950\,\frac{D^{1/2}}{b\pi^{1/2}}\,fsw \tag{49}$$

The quantity D/b^2 is not fixed on principles and is treated as an exposure parameter, reflecting a recurring problem with diffusion-based models. A computational value for D/b^2 is suggested by Eq. *19*, with Eq. *49* relating the limiting behavior of the response function directly to the decompression criterion of Eq. *48*. The $t^{1/2}$ behavior of the response function is characteristic of bulk diffusion. The agreement between Eq. *48* and the no-decompression (U. S. Navy) limits are summarized in Table 1. Using the fixed gradient criteria of Eq. *48*, that is $p - p_i = 24$ fsw as the limit point, Eq. *49* predicts a bulk inverse time scale of D/b^2 on the order of $0.002 \cdot \text{min}^{-1}$, close to the slab parameter, K, of Eq. *46*. The $t^{1/2}$ criterion has been employed in constructing short duration tables (9, 13). However, the criterion breaks down for long times, $t \to \infty$, if the full exponential expression, Eq. *41*, does not enter computations. Actual

TABLE 1
DEPTH-TIME BOUNCE LAW AND NO-DECOMPRESSION LIMITS

Depth, fsw	Time Limit, min	Predicted Limit, min
35	310	185
40	200	141
50	100	90
60	60	62
70	50	46
80	40	35
90	30	28
100	25	23
120	15	16
140	10	12
180	5	7

time limitations are close to 100 min in air and mixed gas applications (10). Good agreement between Eq. *48* and the no-decompression time limits is seen in Table 1. Yet there are inconsistencies. Using Eq. *18*, with rough intercapillary spacing of 20 μm and radii of 4 μm, diffusion coefficients near $10^{-10} \cdot cm^{-2} \cdot sec^{-1}$ are predicted. Such values are five orders of magnitude smaller than the homogeneous diffusivity of water (tissue), $10^{-5} \cdot cm^{-2} \cdot sec^{-1}$. Cellular diffusivities on the order of $10^{-10} \cdot cm^{-2} \cdot sec^{-1}$ do raise rate-limiting questions regarding the role of perfusion vs. diffusion. Blood perfusion has been widely accepted as the rate-limiting process for the exchange of inert substances between the blood and extravascular tissue, yet most of the facets of blood-tissue exchange have been shown (23) to be equally compatible with a diffusion-contributing model if tissues are regarded as heterogeneous on the microscale.

Nishi (12) introduced a variant of the model by breaking the extended zone into four tissue regions of the same bulk diffusivity, D, but different critical ratios, Q, taken constant for all depths and correlated with VGE measurements. For relatively short exposures, the exponential response function, Eq. *44*, has a limiting form resembling the multitissue expressions discussed in the next segment. The averaged response, Eq. *43*, in each serial compartment then suggests a time constant, λ,

$$\lambda = \frac{4D}{\pi b^2} = 0.033 \text{ min}^{-1} \qquad (50)$$

when employing the exponential form, Eq. *44*, for tissue with assumed half-life near 20 min.

Although competing mechanisms remain masked and ambiguities persist, bulk model tables have been implemented. Operational success, of course, underscores all table-implemented models, of which the multitissue perfusion model is the most famous, enjoying widespread use. The multitissue algorithm also provides bases for a modern generation of electronic decomputers, differing in staging data but operating on the same premises. The numerical simplicity of the algorithm is very attractive for digital implementation (12, 14, 25–27).

Multitissue model

The multitissue model, originally proposed by Boycott et al. (1), is not based on a diffusion equation, but rather on a bulk perfusion rate equation. Classical and modern multitissue approaches to decompression are based on assumptions of limited supersaturation, with the transport of matter across regions of varying concentration, or pressure, driven by the local gradient, and gas uptake and elimination limited by blood flow rates. As discussed, the rate equation is given by Eq. *4*, with λ a set of phenomenological (tissue) constants. Scaling initial tissue tension with the arterial tension, p_a,

$$\Pi(0) = p_i - p_a = \Pi_i \tag{51}$$

and integrating Eq. *4* subject to the above yields (appendix B),

$$p - p_a = (p_i - p_a) \exp(-\lambda t) \tag{52}$$

The time for $p - p_a$ to decrease to half its immediate value, after reduction in p_a, is the tissue half-life, τ,

$$\tau = \frac{\ln 2}{\lambda} \tag{53}$$

As many as 10 (hypothetical) compartments with 2.5, 5, 10, 20, 40, 80, 120, 180, 240, and 360-min half-lives are employed in applications, and half-lives, τ, are routinely assumed to be independent of p_a. Compartments are just computational entities, and direct anatomic linkages are neither intended nor implied. Much detail is obviously buried in these tissue parameters, since they are not correlated with critical tissue equilibration rates (11, 21). Differences between computational λ and perfusion rates parallel previous differences between computational D and tissue (water) diffusivity in some ways.

Given absolute pressure, P, multitissue theory postulates that the degree to which any compartment tolerates nitrogen saturation is limited by a critical ratio, R,

$$\frac{p}{\mathrm{P}} \leq R \tag{54}$$

having a modern range, $1.10 < R \leq 3.20$, popularized by the U.S. Navy. Realistically, R (and L, Q) depends on many factors, not always discernible. Alternatively, the values of p for which the equalities hold in Eqs. *21* and *54* are the critical tensions, M. The correlated critical pressures collected by Buhlmann (4) and Workman (5) for specific compartments at various depths, as well as the later phenomenological compilation of Schreiner and Kelley (6) and VGE analysis of Spencer (7), provide a staging criterion. Surfacing ratios, R_0, critical pressures, $M_0 = R_0\mathrm{P}_0$, and depth ratios, R_∞, $(x \rightarrow \infty)$ are shown in Table 2 for six compartments. As a function of altitude, z, measured in feet, atmospheric pressure, P_0, is conveniently represented (15) by the barometerlike expression,

$$\mathrm{P}_0 = 33 \exp(-\xi z) \tag{55}$$

with,

$$\xi = 0.000038119 \text{ ft}^{-1} \tag{56}$$

TABLE 2
SURFACING AND DEPTH RATIOS, CRITICAL AND FITTED NITROGEN PRESSURES (P_0 = 33 fsw)

Half-Life, min	Surface Ratio	Critical Pressure, fsw	Fitted Pressure, fsw	Depth Ratio
5	3.15	104	104	2.27
10	2.67	88	87	2.01
20	2.18	72	73	1.67
40	1.76	58	60	1.34
80	1.58	52	52	1.26
120	1.55	51	49	1.19

The extension of the critical surface pressures and ratios in Table 2 to altitude has been a study in itself. Linear (16) and exponential (15) extrapolations of the critical pressures back to zero have been proposed. As at sea level, altitude measurements (4, 16, 29–30) are necessary in any multitissue extrapolation scheme. Buhlmann (4) and Boni et al. (30) have performed extensive measurements over a wide range of ambient pressures, resulting in critical pressure parameterizations for 16 compartments up to 3500 m in altitude. Four ranges, 0–700, 700–1500, 1500–2500, and 2500–3500 m above sea level, are employed in their altitude-compensated tables. Similarly, Bell and Borgwardt (16) tabulated linearily extrapolated schedules to 15,000 ft.

A few-parameter fit (14) to the critical pressures, expressed as linear functions of absolute pressure, also suggests that intercepts and slopes vary inversely as the fourth root of the compartment half-life, τ. Or, in other words, the critical pressures increase linearly with depth and scale as the inverse fourth power of the half-life, as depicted by the fitted critical pressures of Table 2. The fit to the surfacing critical tensions has the form, $M_0 = 155\ \tau^{-.25}$ fsw. The original set of Haldane assumptions amount to a bubble-free hypothesis, but their presence or nonpresence does not really affect the algorithm, since expressions link λ to phenomenological criteria.

Critical ratios are larger for faster tissues and lesser pressures, yet range of variation is not large, especially within compartments. Depending on the method used to extend critical pressures to altitude (reduced pressure), however, the surface values can change dramatically while the values at depth remain unchanged. Indeed, near and surfacing values are the principal concerns in many staging regimens. Blood rich, well-perfused, aqueous tissues are usually assumed to be *fast* (small values of τ), while blood poorer, scarcely perfused, lipid tissues are assumed to be *slow* (large values of τ). Sixteen compartments have been proposed by Bennett and Vann (31) for some applications, with variable ratios at 10-ft increments producing 736 degrees of freedom (fit parameters) to characterize the data. The proliferation of tissue compartments underscores the lack of detail in bulk models, particularly transport and bubble physics, but highlights their considerable flexibility and range.

The multitissue model addresses dissolved gas transport, with saturation gradients driving the interchange between blood and tissue. In the presence of free gas phases, transport mechanisms outside the multitissue model framework are enabled. Free-dissolved and free-blood gas gradients (discussed in Elimination Gradients) can now

compete with dissolved-blood gradients. If gas nuclei are entrained in the circulatory system, blood perfusion rates are effectively lowered, an impairment with impact on all gas exchange processes. To account for the presence of some separated phase, Thalmann and Spaur (25) suggested a modification to the multitissue algorithm which slows nitrogen elimination. Instead of exponential uptake and elimination functions as given in Eq. *52*, exponential uptake but linear elimination functions are used in calculations. Another obvious approach is to increase the assigned half-lives of compartments for gas elimination over those values assigned to the compartments on gas uptake (40), employing exponential response functions in both instances.

Maximum likelihood model

A correlated statistical approach, based on principles of maximum likelihood (48) which circumvent deterministic critical parameters and transport mechanisms, was developed by Weathersby et al. (8). Maximum likelihood applies any model to the data and adjusts parameters until theoretical predictions and data are in the closest possible statistical agreement. In a likelihood approach, dose-response statistics are folded into random parameters taken as decompression indicators, measured for instance by tissue saturation, number of VGE, volume of separated gas, depth-exposure time, etc. The greater the number of trials used in construction of the likelihood function over arbitrary risk measures, the more meaningful the estimation process, or the greater the statistical confidence level of the information.

In a series of N independent trials, each with individual probability, ρ_n, the likelihood of an outcome, Φ, is the product of the separate trial probabilities,

$$\Phi = \prod_{n=1}^{N} \rho_n \tag{57}$$

with Π denoting product multiplication. The logarithm of the likelihood, ψ, is more simply the sum of the individual probability logarithms,

$$\psi = \ln \Phi = \sum_{n=1}^{N} (\ln \rho_n) \tag{58}$$

The ρ are empirical risk (or success) functions, constants, tabular data, or integral measures over time, that is, $\rho = \rho(q)$, with q any convenient set of critical parameters. As a function of q, the maximum likelihood, ψ_{max}, occurs at the local maxima of ψ, or Φ equivalently (appendix C),

$$\left[\frac{\partial \psi}{\partial q}\right]_{q=q_{max}} = 0 \tag{59}$$

for all independent q. In analyzing sets of decompression data, the object of likelihood analysis is to maximize ψ by adjusting q, and hence ρ. The statistical confidence of the likelihood estimation process, as reflected in the sharpness of Φ, or ψ, peaks when plotted against q, will increase with the number of trials. For simple probability functions, ρ, of single value, q, the maximization process can be carried out analytically through the above equation. As the complexity of the probability function, or the number of independent parameters, q, increases, machine algorithms (14) become

more attractive. Depending on the number of trials and fit, the q_{max} can then be assigned statistical importance as critical indicators.

An integral measure of instantaneous risk, ζ, can be provided by the global probability measure, ρ,

$$\rho(\Delta t) = 1 - \exp\left[-\int_{\Delta t} \zeta(t')\, dt'\right] \tag{60}$$

with Δt any time interval. In decompression application, the integration of risk over the course of dive and postdive intervals differs fundamentally from the standard practice of avoiding a critical point at every instant during the dive. Implicit is the assumption that a given decompression stress, ζ, is more likely to produce symptoms if it is sustained in time. Certainly in Eq. *60*, $\rho \rightarrow 1$ as $\Delta t \rightarrow \infty$ for positive ζ, while $\rho = 0$ at $\Delta t = 0$. Also, a large number of distinct decompressions may culminate in the same probability, ρ, after integration. Using empirical forms of ζ, mainly ratios of inert gas supersaturation to ambient pressure at each stage, i, with arbitrary decay constant, λ,

$$\zeta_i(t') = \frac{(p_{i-1} - p_i) \exp(-\lambda t')}{P_i} \tag{61}$$

for tension, p, and ambient pressure, P, at appropriate stages, i or $i-1$, Weathersby et al. (37, 38) and Hays and colleagues (39) have re-analyzed much existing data for air and gas mixtures, and compiled a statistically based set of decompression tables using Eqs. *60* and *61*. Confidence levels of 5 and 1% have been established for the dose-response characteristics of the data.

A distribution of minimum bends depths has been obtained by Crocker et al. (34) in systematically increasing the pressure, N, at which a diver has been saturated before rapid decompression to threshold pressure, P. Similar trials on aviators have been reported by Gray et al. (35), and experiments on goats have been reported by Davidson et al. (36). In addressing all data, Hills (18) determined that the frequency of minimum bends depths fits a Weibull distribution, similar in form to the above stress function. If the cumulative fraction of bends cases up to N is ρ, the survivor fraction satisfies the criterion,

$$\xi = 1 - \rho = \exp\left[-[(H - 14.3)/25.1]^{4.73}\right] \tag{62}$$

with minimum bends differential, H, measured in fsw,

$$H = N - P \tag{63}$$

As the differential grows, the survivor fraction approaches zero exponentially, that is, $\xi \rightarrow 0$ as $H \rightarrow \infty$. At the cutoff, the survivor fraction is one, that is, $\xi = 1$, when $H = 14.3$ fsw. The midpoint fraction, $\xi = 0.5$, occurs at $H = 37.5$ fsw. The smallest differential for bends provocation is 14.3 fsw and the odds-even differential occurs at 37.5 fsw, reflecting dose-response statistics. The Weibull failure distribution is

extensively used in reliability studies linked to a multiplicity of fault factors. Cumulatively weighted moments of interest are the mean, $\overline{H}$,

$$\overline{H} = \frac{\int_{14.3}^{\infty} H\,\xi\,dH}{\int_{14.3}^{\infty} \xi\,dH} = 26.5 \text{ fsw} \tag{64}$$

the mean square, $\overline{H^2}$,

$$\overline{H^2} = \frac{\int_{14.3}^{\infty} H^2\,\xi\,dH}{\int_{14.3}^{\infty} \xi\,dH} = 758.1 \text{ fsw}^2 \tag{65}$$

and the variance, Σ^2,

$$\Sigma^2 = \frac{\int_{14.3}^{\infty} (H - \overline{H})^2\,\xi\,dH}{\int_{14.3}^{\infty} \xi\,dH} = 58.3 \text{ fsw}^2 \tag{66}$$

Accordingly, the standard deviation, Σ, and root mean square differential, $(\overline{H^2})^{1/2}$, have the values, 7.6 and 27.5 fsw, respectively. The mean and root mean square differentials differ only by 1 fsw, and at 27 fsw the survivor fraction is 0.96, more conservative than the odds-even (fraction midpoint) differential of 37.5 fsw. Roughly 67% of survivor fractions fall in the exposure limits of 26.5 ± 7.6 fsw.

PERFUSION-DIFFUSION TREATMENTS

Questions of whether perfusion or diffusion are rate limiting in tissue, whether bounded or bulk models are sufficiently representative for decompression analyses, how are free-dissolved gas interactions quantified, and why are seemingly dissimilar models successful in applications, prompted studies with a broader kinetic perspective. By the early 1970s, accessibility to high-speed computers permitted the numerical resolution of extremely complex problems, augmenting analyses on the computational side. Perfusion-diffusion models are an offspring of such studies.

Thermodynamic model

One approach, suggested by Hills (11) and extended by Hennessy (21), is more comprehensive than earlier models, addressing a number of additional issues. The

thermodynamic model is based on phase equilibration of dissolved and separated gases, with temporal uptake and elimination of inert gas into tissue limited by perfusion and diffusion. From a boundary (vascular) zone of thickness, a, gases diffuse into the cellular region. Cylindrical, one-dimensional symmetry is assumed (11) for simplicity in the extended zone. The radial equation and formal solution were treated in Eqs. *23–30*, but new boundary conditions of the form are now employed,

$$\Pi(r,0) = p_i - p_v = \Pi_i$$
$$\Pi(a,t) = p_v - p_v = 0$$
$$\frac{\partial \Pi(c,t)}{\partial r} = \frac{\partial (p - p_v)}{\partial r} = 0 \qquad (67)$$

with the venous tension, p_v, a time-dependent boundary condition linking blood flow rate and gas solubility to the mass flux across the vascular boundary according to a balance equation shortly described. The derivative boundary condition at $c = b/2$ again imparts reflection symmetry to the spatial solution. Accordingly, following earlier development, we write,

$$p - p_v = (p_i - p_v)\, R(r,t) \qquad (68)$$

for,

$$R(r,t) = \pi \sum_{n=1}^{\infty} \frac{J_1^2(\beta_n c)}{[J_0^2(\beta_n a) - J_1^2(\beta_n c)]} U_0(\beta_n r) \exp(-\beta_n^2 D t) = \sum_{n=1}^{\infty} R_n(r,t) \qquad (69)$$

with U_0 defined in Eq. *24* and the derivative boundary condition at the midpoint, $r = c$, requiring,

$$J_0(\beta_n a) Y_1(\beta_n c) - Y_0(\beta_n a)\, J_1(\beta_n c) = 0 \qquad (70)$$

for which the eigenvalues, β_n, are the roots of the zonal equation. The transport model also assumes a fully stirred, extended vascular zone from which venous blood leaves in equilibrium with respect to all gases, while arterial blood either diminishes or replenishes gases in the zone. Perfusion-limiting is applied as a boundary condition through the venous tension, p_v, by enforcing a mass balance across both the vascular and cellular regions at $r = a$,

$$S_b \frac{\partial p_v}{\partial t} = -\kappa S_b [p_v - p_a] - \frac{3}{a} S_c D \left[\frac{\partial p}{\partial r}\right]_{r=a} \qquad (71)$$

for κ a perfusion time constant, S_c and S_b the nitrogen cellular and blood solubilities, and p_a, the arterial gas tension. Clearly, Eqs. *68* and *71* bootstrap the tissue tension p, venous tension p_v, and arterial tension p_a in a complex feedback loop. Hennessy (21) has shown that the solution to the coupled set, Eqs. *69–71*, in various limits contains the solutions to all deterministic models hitherto described for gas exchange. Solutions to the coupled set, Eqs. *67–70*, are most easily handled numerically. In the following section an analytic solution to the Fick-Fourier model will be presented that has some common features with the thermodynamic approach, but is less complex.

One can couple the volume fraction, χ, of separated gas to mass balance under worse-case conditions. With cellular solubility, S_c, the separated gas fraction, with zero gas elimination, follows from the balance equation,

$$\chi \, P_{N_2} = S_c \, [p - P_{N_2}] \tag{72}$$

which states that the amount of separated gas is the difference between the original amount of nitrogen in solution before decompression and the amount left in solution. Employing the perfusion boundary tension, p_v, the balance equation takes the form,

$$\chi \, P_{N_2} = S_c \, [p_v + (p_i - p_v) \, \overline{R}(t) - P_{N_2}] \tag{73}$$

with the spatially averaged response function given by,

$$\overline{R}(t) = \frac{4}{(b^2 - a^2)} \sum_{n=1}^{\infty} \frac{1}{\beta_n^2} \frac{J_1^2(\beta_n c)}{[J_0^2(\beta_n a) - J_1^2(\beta_n c)]} \exp(-\beta_n^2 D t) = \sum_{n=1}^{\infty} \overline{R}_n(t) \tag{74}$$

which permits evaluation of the separated gas fraction, χ, for arbitrary exposures provided the partial pressure, P_{N_2}, is known. Both are limited for the phase algorithm in the following way.

Denoting, v, the volume of separated gas in tissue volume, V, and $\chi = v/V$, the separation fraction, Inman and Saunders (17) argued that they could induce bends-like pain in connective tissue using a local injection of Ringer's solution. Pain was not correlated with the volume of injected fluid, but rather with the injection pressure, δ. Thresholds varied between 0.4323 fsw and 1.1286 fsw injection differential. A criterion for decompression pain might also be provided by pressure differentials between separated gas and surrounding tissue. If the differential pressure, δ, exceeds the critical threshold, δ', pain occurs,

$$\delta > \delta' \tag{75}$$

or from Boyle's law and the tissue modulus, K,

$$K\chi \geq \delta' \tag{76}$$

with,

$$0.43 \leq \delta' \leq 1.13 \text{ fsw} \tag{77}$$

Accepting this threshold as a criterion for bending nerve endings, one bubble, or coalesced composite, would suffice to cause pain. Such thresholds would correspond to separated gas fractions, employing a nominal value (11) for K,

$$0.0039 \leq \chi \leq 0.0093 \tag{78}$$

which are small, yet not insignificant. The identification of the separated gas fraction, χ, as a critical indicator is a significant development. Hennessy and Hempleman (22) established a linear titration curve between saturation and safe decompression pressures, assuming that the same critical volume of released gas provokes mild attacks of decompression sickness. Their analysis also offers explanations for changes in signs and symptoms which follow changes in the nature of the exposure to pressure. Tables based on the volume of separated gas can be constructed (11, 22, 33).

A free phase in tissue introduces another dimension to gas exchange models. But as a critical indicator the separated fraction, χ, is a natural flag since it can be linked

systematically to the varied and complex mechanisms of bubble formation, bubble growth, and bubble elimination, as outlined by Epstein and Plesset (24), Yount and Strauss (20), and others. Bubbles, which are unstable, are thought to grow from stable, very small, micronuclei which resist collapse due to elastic skins of surface-activated molecules or possibly reduction in surface tension at tissue interfaces. Large pressures (on the order of 1000 atm) are necessary to crush these micropockets. On decompression, the micronuclei are surrounded by dissolved gases at high tensions and subsequently grow as surrounding gas diffuses into them. At some point a critical volume of separated gas is established and symptoms of decompression sickness become increasingly probable. Bubble mechanics are fairly well understood (28), but formation and stabilization mechanisms for micronuclei are not. The introduction of bubble mechanics into decompression theory has enhanced our understanding but taxed our numerical perseverance, as usual with complex phenomena. The computational issues of bubble formation, growth, and elimination are outside this scope.

Although inert gas tensions vary dramatically with depth, oxygen, carbon dioxide, and water vapor, tensions are fairly constant under normal conditions. Worse-case separated nitrogen pressure, P_{N_2}, as a function of ambient pressure is suggested by Hills (11),

$$P_{N_2} = P + 3.21 \text{ fsw} \tag{79}$$

Here, separated nitrogen is assumed to take up the difference between total hydrostatic pressure and the sum of metabolic gas and water vapor pressures. Arterial nitrogen equilibrates with alveolar nitrogen in less than a minute. At equilibrium, the nitrogen tissue tension, p_{N_2}, venous, p_v, and arterial, p_a, tensions are all equal to the alveolar partial pressure, p_{N_2}, which can be written, accounting for water vapor dilution (1.61 fsw),

$$p_{N_2} = 0.79\ P - 1.61 \text{ fsw} \tag{80}$$

taking 0.79 as the nitrogen mole fraction. The pressure difference, Δ, between ambient pressure and the sum of dissolved gases is the biological inherent unsaturation (11), or the oxygen window (19),

$$\Delta = P - p_{O_2} - p_{CO_2} - p_{H_2O} - p_{N_2} = 0.21\ P - 3.85 \text{ fsw} \tag{81}$$

taking the sum of dissolved and separated oxygen, water vapor, and carbon dioxide to be the same, according to Hills (11),

$$p_{O_2} + p_{CO_2} + p_{H_2O} = 5.47 \text{ fsw} \tag{82}$$

Such unsaturation occurs because carbon dioxide produced by metabolism is more soluble in tissue water than oxygen consumed, and exerts a lower partial pressure. This inherent unsaturation, quantifying the amount of tissue undersaturation (relative to ambient), is a factor in thermodynamic staging. Staging formats and tables have been designed by Behnke (19) and by Hills (11) to take up the inherent saturation while maintaining gas elimination gradients as maxima.

Values and ranges of relevant biophysical constants employed in the Hills-Hennessy approach are listed for completeness:

$$0.40 \leq \delta \leq 1.20 \text{ fsw}$$
$$0.049 \leq a \leq 3.5 \ \mu\text{m}$$
$$10.0 \leq b \leq 20.0 \ \mu\text{m}$$
$$0.020 \leq D \leq 0.060 \ \mu\text{m}^2/\text{s}$$
$$K \approx 3.7 \times 10^6 \text{ dyne/cm}^2 \qquad (83)$$

with 1 μm = 10^{-6} m. The radii are reasonable when compared with capillary diameters near 8 μm and intercapillary separations of 20–40 μm. The value of D is still five orders of magnitude smaller than the homogeneous diffusion coefficient of water, whereas the tissue modulus, K, does lie within experimental limits. Some transient measurements of the value of D given above have been reported (11, 21), with the assumption of a heterogeneous extravascular zone. Such heterogeneous effects on the diffusivity would be clearly rate-limiting, as noted.

Fick-Fourier model

The Fick-Fourier model employs Eq. *5*, which is the diffusion equation with a perfusion term, $\kappa\Pi$, included. The presence of the perfusion term will force all tensions to approach the arterial tension, p_a, over long-time scales, that is, $\Pi = p - p_a$ and when time derivatives and diffusion gradients vanish, Eq. *5* requires that $\kappa\Pi \rightarrow 0$, or $p \rightarrow p_a$ equivalently. If we include a $\kappa\Pi$ term in the diffusion equation directly, all foregoing bulk and bounded solutions append an additional $\exp(-\kappa t)$ multiplier to the solutions already generated for the same boundary and initial conditions. Perfusion is thus included as a balance term in the equation, and not as a boundary condition. Mathematical developments parallel the foregoing models with the inclusion of an additional term in the transport equation. Appendixes A and B summarize solutions to the Fick-Fourier equation in these cases. But in the context of the thermodynamic model, a set of inhomogeneous initial and boundary conditions will ensue. Such cases can be solved with the methods described once the problem is properly transformed. The transformations and solutions are most easily effected in slab geometry, and the development proceeds as follows.

From the vascular boundary, gases diffuse into the cellular zone according to the Fick-Fourier equation. Planar, one-dimensional symmetry is assigned in the extended zone. We first change variables under the substitution,

$$\Pi = V \exp(-\kappa t) \qquad (84)$$

with perfusion constant, κ, defined,

$$\kappa = f\mu \qquad (85)$$

for f the blood-tissue fraction and μ the perfusion rate. The initial and boundary conditions, allowing venous tensions at the boundaries to relax to arterial tensions at some rate, σ, slower than the perfusion rate, that is, $\sigma \leq \kappa$, are taken to be

$$\Pi(x,0) = p_i - p_a = \Pi_i$$
$$\Pi(a,t) = (p_v - p_a)\exp(-\sigma t) = \Pi_0 \exp(-\sigma t)$$
$$\Pi(b,t) = (p_v - p_a)\exp(-\sigma t) = \Pi_0 \exp(-\sigma t) \qquad (86)$$

constituting an inhomogeneous set. The substitution of Eq. *84* into Eq. *5* eliminates the perfusion team, yielding a diffusion equation for V in plane geometry,

$$D\frac{\partial^2 V}{\partial x^2} = \frac{\partial V}{\partial t} \tag{87}$$

with initial and boundary conditions,

$$\begin{aligned} V(x,0) &= \Pi_i \\ V(a,t) &= \Pi_0 \exp[(\kappa-\sigma)t] \\ V(b,t) &= \Pi_0 \exp[(\kappa-\sigma)t] \end{aligned} \tag{88}$$

A general method (46) can be invoked to solve Eqs. *87* and *88*. The solution, V, is broken into two parts, X and W,

$$V = X + W \tag{89}$$

with associated boundary conditions

$$\begin{aligned} X(x,0) &= \Pi_i \\ X(a,t) &= 0 \\ X(b,t) &= 0 \end{aligned} \tag{90}$$

and,

$$\begin{aligned} W(x,0) &= 0 \\ W(a,t) &= \Pi_0 \exp[(\kappa-\sigma)t] \\ W(b,t) &= \Pi_0 \exp[(\kappa-\sigma)t] \end{aligned} \tag{91}$$

for a dual set of diffusionlike equations,

$$D\frac{\partial^2 X}{\partial x^2} = \frac{\partial X}{\partial t} \quad D\frac{\partial^2 W}{\partial x^2} = \frac{\partial W}{\partial t} \tag{92}$$

Both can now be solved independently using the techniques described in appendixes A and B. Unlike the thermodynamic case, the tissue, arterial, and venous tensions are not bootstrapped by both the mass balance and transport equations, obviously a numerical simplification. Solving Eqs. *90–92* and multiplying the solution V by $\exp(-\kappa t)$ according to Eq. *84* yields,

$$p - p_a = (p_v - p_a)\,G(x,t) + (p_i - p_a)\,H(x,t) \tag{93}$$

for,

$$G(x,t) = \sum_{n=1}^{\infty} \frac{4}{(b-a)} \frac{\alpha_{2n-1}D}{(\alpha_{2n-1}^2 D + \kappa - \sigma)} \sin[\alpha_{2n-1}(x-a)][\exp(-\sigma t) - \exp(-\alpha_{2n-1}^2 Dt - \kappa t)] = \sum_{n-1}^{\infty} G_{2n-1}(x,t),$$

$$H(x,t) = \sum_{n=1}^{\infty} \frac{4}{(2n-1)\pi} \sin[\alpha_{2n-1}(x-a)]\exp(-\alpha_{2n-1}^2 Dt - \kappa t) = \sum_{n=1}^{\infty} H_{2n-1}(x,t) \tag{94}$$

and eigenvalues, α, defined by,

$$\alpha_{2n-1} = \frac{(2n-1)\pi}{(b-a)} \tag{95}$$

Obviously for large perfusion and/or diffusion rates the response function decays very rapidly in time. The perfusion terms, $\exp(-\kappa t)$ and $\exp(-\sigma t)$, scale the sum of all Fourier diffusion components. But because only a single equation is employed, perfusion and diffusion cannot be sequenced in a two-step process, as in the preceding thermodynamic treatment. Denoting the vascularity, $\epsilon = a/b$, the blood-tissue partition coefficient, f, from Eq. *85* is taken (21) in this model with $S_p = S_b/S_c$,

$$f = \frac{1}{\epsilon^2 + (1 - \epsilon^2) S_p} \tag{96}$$

and $S_p = 1$ for aqueous tissue, and $S_p = 5$ for lipid tissue. Vascularity, ϵ, has the range, $1/15 \leq \epsilon \leq 1/5$, so that for most applications $f \approx 1/S_p$. The balance equation takes the analogous form to Eq. *73*,

$$\chi \, P_{N_2} = S_c \left[p_a + (p_v - p_a)\, \overline{G}(t) + (p_i - p_a)\, \overline{H}(t) - P_{N_2}\right] \tag{97}$$

with averaged response functions given by,

$$\overline{G}(t) = \frac{8}{(b-a)^2} \sum_{n=1}^{\infty} \frac{D}{(\alpha_{2n-1}^2 D + \kappa - \sigma)} [\exp(-\sigma t) - \exp(-\alpha_{2n-1}^2 D t - \kappa t)] = \sum_{n=1}^{\infty} \overline{G}_{2n-1}(t) ,$$

$$\overline{H}(t) = \frac{8}{\pi^2} \sum_{n=1}^{\infty} \frac{1}{(2n-1)^2} \exp(-\alpha_{2n-1}^2 D t - \kappa t) = \sum_{n=1}^{\infty} \overline{H}_{2n-1}(t) \tag{98}$$

The functions $\overline{H}$ and $\overline{G}$ broadly reflect diffusion and perfusion exchange in opposite limits, although effects get folded together by virtue of decaying exponentials involving both κ and D. Exchange is clearly perfusion-controlled whenever $\alpha_{2n-1}^2 D >> \kappa$, and then $\overline{H} < \overline{G}$. But, when $\alpha_{2n-1}^2 D << \kappa$, diffusion can compete with $\overline{H} > \overline{G}$. The net effect is rather complicated, depending on the summation, p_v, p_i, and p_a in addition to κ, D, b, and a. Similar analyses can be applied to radial models, with additional complications induced by eigenvalue equations involving both Bessel and Neumann functions. To give a better feeling for the net effects of κ and D on the exchange, consider the lowest order ($n = 1$) terms in the expansion given by,

$$\overline{G}(t) \approx \frac{8}{(b-a)^2} \frac{D}{\alpha_1^2 D + \kappa - \sigma} [\exp(-\sigma t) - \exp(-\alpha_1^2 D t - \kappa t)],$$

$$\overline{H}(t) \approx \frac{8}{\pi^2} \exp(-\alpha_1^2 D t - \kappa t) \tag{99}$$

For large D,

$$\overline{G}(t) \to \frac{8}{\pi^2} \exp(-\sigma t),$$

$$\overline{H}(t) \to 0 \tag{100}$$

while for small D,

$$\overline{G}(t) \to \frac{8}{(b-a)^2} \frac{D}{D + \kappa - \sigma} [\exp(-\sigma t) - \exp(-\kappa t)],$$

$$\overline{H}(t) \to \frac{8}{\pi^2} \exp(-\kappa t) \tag{101}$$

so that the response depends on D for small D, and on κ and σ for large D. When D and κ are of similar magnitude, perfusion and diffusion bootstrap each other, with neither one nor the other predominating.

Opposing limits of $\overline{G}$ and $\overline{H}$ suggest that effective half-lives, $\bar{\tau}$, can be defined which depend inversely on D and κ, that is,

$$\bar{\tau}_{2n-1} = \frac{\ln 2}{\bar{\lambda}_{2n-1}} \tag{102}$$

with,

$$\frac{1}{\bar{\lambda}_{2n-1}} = \frac{1}{\alpha_{2n-1}^2 D} + \frac{1}{\kappa} \tag{103}$$

exhibiting the limiting form as $D \rightarrow \infty$,

$$\bar{\lambda} \rightarrow \kappa \tag{104}$$

or as $\kappa \rightarrow \infty$,

$$\bar{\lambda} \rightarrow \alpha_{2n-1}^2 D \tag{105}$$

Higher order diffusion terms, that is terms with $n >> 1$, damp out rapidly by virtue of Eq. *103*. Thus in the two extremes, $\bar{\tau}$ is determined by diffusion or perfusion time scales. In between, effects interfere, as first noted by Hennessy (21) and by Hills (23). Tables 3 and 4 contrast lipid and aqueous half-lives for various values of $\Theta = D/a^2$, and f, fixing $\epsilon = 1/5$ for illustration, and taking the lowest order diffusion term, $n = 1$, which makes the largest contribution to the functions $\overline{G}$ and $\overline{H}$. Values of $\Theta = D/a^2$ represent the two extremes of homogeneous (water) and heterogeneous (cellular) diffusion, that is $D \approx 10^{-5} \cdot \text{cm}^{-2} \cdot \text{sec}^{-1}$ and $D \approx 10^{-10} \cdot \text{cm}^{-2} \cdot \text{sec}^{-1}$. In the last columns, the Haldane half-lives, $\tau_H = \ln 2/\kappa$, are also listed. For small value of Θ, both perfusion and diffusion contribute to $\bar{\tau}$, whereas for large values of Θ only perfusion matters in both tables. An overlap between $\bar{\tau}$ and the Haldane half-life, τ_H, is exhibited for smaller values of the perfusion, μ, in all the above cases. Accepting the water (tissue) value of $\Theta = 10^4 \cdot \text{min}^{-1}$, perfusion is the controlling mechanism for gas uptake and elimination.

TABLE 3

AQUEOUS TISSUE HALF-LIVES AND PERFUSION-DIFFUSION SPECTRUM ($S_p = 1$).

μ, min^{-1}	$\bar{\tau}$, min $\Theta = 0.10{,}000$, min^{-1}	$\bar{\tau}$, min $\Theta = 10{,}000$, min^{-1}	τ_H, min
0.0001	6942.7	6931.4	6931.5
0.0010	704.4	693.1	693.2
0.0100	80.6	69.3	69.3
0.1000	18.2	6.9	6.9
1.000	11.9	0.7	0.7
10.00	11.3	0.07	0.07
100.0	11.2	0.007	0.007

TABLE 4
LIPID TISSUE HALF-LIVES AND PERFUSION-DIFFUSION SPECTRUM (S_p = 5).

μ, min^{-1}	$\bar{\tau}$, min Θ = 10,000, min^{-1}	$\bar{\tau}$, min Θ = 10,000, min^{-1}	τ_H, min
0.0001	33559.0	33548.0	33548.0
0.0010	3366.0	3354.8	3354.8
0.0100	346.7	335.4	335.5
0.1000	44.8	33.5	33.5
1.000	14.6	3.4	3.4
10.00	11.6	0.34	0.34
100.00	11.2	0.034	0.034

As seen, simultaneous treatment of combined perfusion-diffusion is tedious. Yet results clearly recover previous models in opposite limits and shed considerable light in regions where mechanisms compete. Complexities in transport solutions and decompression criteria mitigate cookbook staging formats, and digital implementation is more difficult.

ELIMINATION GRADIENTS

If there has been no gas separation in a particular tissue with tension, p, the driving force for gas elimination, Δp_{N_2}, is provided by the tissue-arterial gradient,

$$\Delta p_{N_2} = p - p_{N_2} = p - 0.79\ P \qquad (106)$$

incorporating Eq. *80* for the arterial tension. The rate of elimination is thus greatest for the lowest ambient pressure, as usually assumed in classical approaches. However, if gas has separated from solution, tissue gradients do not entirely drive gas transfer, and elimination and uptake functions based on these gradients will be asymmetric. Because of surface tension, tissue compliance, and dynamics (28) of mixed phases, separated gas partial pressures exceed tissue tensions, and the driving force for elimination, ΔP_{N_2}, depends on the gradient between separated and arterial gas,

$$\Delta P_{N_2} = P_{N_2} - p_{N_2} = 0.21\ P + 3.21\ fsw \qquad (107)$$

which, using Eqs. *80* and *81* and assuming that under limiting conditions the inherent unsaturation takes up the excess (free) gas pressure, suggests,

$$\Delta P_{N_2} = \Delta + 8.68\ fsw \qquad (108)$$

Gas elimination rates are now greatest at the highest ambient pressure, driven by the inherent unsaturation. As such, Eq. *107* obviates a worst-case change in staging procedures, reversing the upward haul dictated by any saturation gradient, Eq. *106*.

When the full inherent unsaturation gradient is not employed, weighted terms can be employed in constructing an effective (28) elimination gradient, Γ. Separated and

dissolved gas gradients are then fractionated by a simple factor, γ, consistent with multiphase flow partitioning.

$$\Gamma = \gamma\,(P_{N_2} - p) + (p - 0.79\,P) \qquad (109)$$

with $0 \leq \gamma \leq 1$. Rewriting Eq. *109*, using Eqs. *106* and *107*, there results,

$$\Gamma = \gamma\,P_{N_2} + (1 - \gamma)\,p - 0.79\,P = \gamma\,\Delta P_{N_2} + (1 - \gamma)\,\Delta p_{N_2} \qquad (110)$$

serving to link model extremes by a phenomenological fraction. Use of a split gradient implies that only a portion of tissue gas has separated, leaving the remainder dissolved. Knowing or being able to estimate free and dissolved partial pressures, Eq. *110* could then be employed for staging. More precisely, Eq. *110* could replace any of the elimination gradient terms multiplying the residue functions in the foregoing treatments, imposing uptake and elimination asymmetry of the tissue functions in the process. The empirical practices of Hawaiian (42) and Australian (43) diving fishermen also seem to correlate with the deeper staging regimens suggested by Eq. *107*.

SUMMARY

Gas exchange and decompression in blood and tissue are governed by many factors, such as diffusion, perfusion, phase separation, nucleation and cavitation, membrane permeation, fluid shifts, and combinations thereof. Owing to the complexity of biological systems, multiplicity of tissues and media, and diversity of boundary conditions, it is difficult to solve the transport problem in vivo. Early decompression studies adopted the supersaturation viewpoint. A closer look at the physics of phase separation and bubbles in the mid-1970s and new insights into gas transfer mechanisms, culminated in extended kinetics and thermodynamic theories. Integration of both approaches can proceed on the numerical side because calculation techniques can be made equivalent. Thermodynamic models are more general than supersaturation models, incorporating their predictive capabilities as subsets. Statistical models, developed mostly in the mid-1980s, are intrinsically gray from a mechanistic viewpoint, but do provide the strongest correlations with actual experiments, and thus offer the best means to table fabrication. It is still fair to say that deterministic models admit varying degrees of computational license, that model parameters do not correlate as a complete set with the real world, and that many mechanisms are not addressed optimally. In the latter case, free-phase inception is particularly noteworthy.

Present notions of nucleation and cavitation suggest that phase inception is random yet highly probable in body tissue. Once established, a gaseous phase will further grow by acquiring gas from adjacent saturated tissues (mainly), according to the strength of the free-dissolved gradient. Although exchange processes are better understood, nucleation and stabilization mechanisms remain poorly understood and calculationally elusive. Stochastic Monte Carlo approaches are potentially powerful, but only in supercomputer environments, due to the large numbers of events required for meaningful statistics over simulation time spans. Transport models for entrained bubbles and coalescence dynamics are similarly complicated. In all cases, we need to know more about micronuclei and size distributions, bubble sites, and tissue thermodynamic properties before computing power can be applied efficiently.

Appendix A
Separation of Variables

Solutions to the second-order diffusion or Fick-Fourier equations can be effected with a straightforward technique (44, 45) that separates spatial and temporal differential terms in the full equation and equates each to the same constant. Although individual spatial and temporal terms differ in plane and cylindrical geometry, the approach is the same in each case. Separation-of-variables technique can be applied to any second-order differential equation with either homogeneous boundary or homogeneous initial conditions. Homogeneous initial conditions can always be transformed to homogeneous boundary conditions by simple change of dependent variable.

Plane geometry

The slab solution, Π, to the one-dimensional diffusion equation in plane geometry, Eqs. *1* and *2*, is assumed to be a product of space and time parts,

$$\Pi(x,t) = X(x)\,T(t) \qquad (A\text{-}1)$$

satisfying,

$$\frac{\partial^2 \Pi}{\partial x^2} = \frac{1}{D}\frac{\partial \Pi}{\partial t} \qquad (A\text{-}2)$$

subject to two boundary and one initial conditions. Inserting Eq. *A-1* into Eq. *A-2* and then dividing the result on each side by Π produces,

$$\frac{1}{X}\frac{\partial^2 X}{\partial x^2} = \frac{1}{DT}\frac{\partial T}{\partial t} \qquad (A\text{-}3)$$

The relationship holds simply when both terms are equal to the same constant, $-\alpha^2$, or set of constants (eigenvalues), that is,

$$\frac{\partial^2 X}{\partial x^2} + \alpha^2 X = 0$$

$$\frac{1}{D}\frac{\partial T}{\partial t} + \alpha^2 T = 0 \qquad (A\text{-}4)$$

with α^2 real eigenvalues. The solutions to Eqs. *A-4* are linear combinations of trigonometric functions in the spatial case, and decaying exponentials in time (appendix B),

$$X(x) = \frac{A}{C}\sin(\alpha x) + \frac{B}{C}\cos(\alpha x)$$

$$T(t) = C\exp(-\alpha^2 D t) \qquad (A\text{-}5)$$

with A, B, and C constants to be determined, only two of which are independent. Multiplying separate solutions gives the full expression,

$$\Pi(x,t) = [A \sin(\alpha x) + B \cos(\alpha x)] \exp(-\alpha^2 D t) \tag{A-6}$$

or, more generally for any set A_n, B_n, and α_n satisfying Eq. *A-2*,

$$\Pi(x,t) = \sum_{n=1}^{\infty} [A_n \sin(\alpha_n x) + B_n \cos(\alpha_n x)] \exp(-\alpha_n^2 D t) \tag{A-7}$$

The α_n are determined from one boundary condition, whereas A_n and B_n are obtained from the initial and remaining boundary conditions. Finite solutions evolve in time provided $\alpha_n^2 \geq 0$.

Repeating the analysis for the Fick-Fourier equation, Eqs. *5* and *3*, gives for inert gases, $Z = 0$,

$$\frac{1}{X}\frac{\partial^2 X}{\partial x^2} = \frac{1}{DT}\frac{\partial T}{\partial t} + \frac{\kappa}{D} \tag{A-8}$$

or, equating both sides to the same constant, $-\alpha^2$,

$$\frac{\partial^2 X}{\partial x^2} + \alpha^2 X = 0,$$

$$\frac{1}{D}\frac{\partial T}{\partial t} + \frac{\kappa}{D} T + \alpha^2 T = 0 \tag{A-9}$$

and thus in the general case,

$$\Pi(x,t) = \sum_{n=1}^{\infty} [A_n \sin(\alpha_n x) + B_n \cos(\alpha_n x)] \exp(-\alpha_n^2 D t - \kappa t) \tag{A-10}$$

with A_n, B_n, and α_n determined as before.

For small arguments, $\alpha_n x \leq 1$,

$$\sin(\alpha_n x) = \alpha_n x - \frac{(\alpha_n x)^3}{6}$$

$$\cos(\alpha_n x) = 1 - \frac{(\alpha_n x)^2}{2} \tag{A-11}$$

which are well-behaved as $x \to 0$, as on any interval, $-\infty \leq x \leq \infty$, while, with $\alpha_n^2 D t \leq 1$, or $\alpha_n^2 D t + \kappa t \leq 1$, it follows that,

$$\exp(-\alpha_n^2 D t) = 1 - \alpha_n^2 D t$$

$$\exp(-\alpha_n^2 D t - \kappa t) = 1 - \alpha_n^2 D t - \kappa t \tag{A-12}$$

Defining $u(\alpha_n x)$ for constant A_n and B_n,

$$u(\alpha_n x) = A_n \sin(\alpha_n x) + B_n \cos(\alpha_n x) \tag{A-13}$$

a useful integral on the interval (a,b) is given by,

$$\int_a^b u(\alpha_n x) u(\alpha_m x) dx = \frac{(b-a)}{2} (A_n^2 + B_n^2)\, \delta_{nm} \tag{A-14}$$

when the $u(\alpha_n x)$ are periodic in any multiple of 2π over the interval (a,b), with orthogonality expressed by the Kronecker δ,

$$\delta_{nm} = 0 \quad m \neq n$$
$$\delta_{nm} = 1 \quad m = n \tag{A-15}$$

Alternatively, Eq. *A-14* equivalently requires eigenvalues, α_n, which are integer multiples of $\pi/2(b-a)$.

Cylindrical geometry

The radial solution, Π, to the one-dimensional diffusion equation in cylindrical geometry, Eqs. *1* and *3*, is written,

$$\Pi(r,t) = R(r)\,T(t) \tag{A-16}$$

Performing the same steps as in the planar case yields,

$$\frac{1}{R}\frac{\partial^2 R}{\partial r^2} + \frac{1}{Rr}\frac{\partial R}{\partial r} = \frac{1}{DT}\frac{\partial T}{\partial t} \tag{A-17}$$

so that equating both sides to the separation constant, $-\beta^2$, or set of eigenvalues, produces,

$$\frac{\partial^2 R}{\partial r^2} + \frac{1}{r}\frac{\partial R}{\partial r} + \beta^2 R = 0$$
$$\frac{1}{D}\frac{\partial T}{\partial t} + \beta^2 T = 0 \tag{A-18}$$

with real β^2. The radial equation is satisfied by a linear combination of zero-order Bessel and Neumann functions, whereas the temporal part again requires decaying exponentials (appendix B),

$$R(r) = \frac{A}{C} J_0(\beta r) + \frac{B}{C} Y_0(\beta r)$$
$$T(t) = C \exp(-\beta^2 D t) \tag{A-19}$$

with A, B, and C constants. For any set A_n, B_n, and β_n, we find in analogy with Eq. *A-7*,

$$\Pi(r,t) = \sum_{n=1}^{\infty} [A_n J_0(\beta_n r) + B_n Y_0(\beta_n r)] \exp(-\beta_n^2 D t) \tag{A-20}$$

and similarly in the Fick-Fourier case,

$$\Pi(r,t) = \sum_{n=1}^{\infty} [A_n J_0(\beta_n r) + B_n Y_0(\beta_n r)] \exp(-\beta_n^2 D t - \kappa t) \tag{A-21}$$

with A_n, B_n, and β_n again determined from the initial and two boundary conditions, and $\beta_n^2 > 1$.

For small values of the argument, $\beta_n r \leq 1$,

$$J_0(\beta_n r) = 1 - \frac{(\beta_n r)^2}{4}$$

$$Y_0(\beta_n r) = \frac{2}{\pi}\left[\ln(\beta_n r/2) + 0.5772\right]\left[1 - \frac{(\beta_n r)^2}{4}\right] \qquad (A\text{-}22)$$

Obviously, J_0 remains finite as $r \to 0$, but Y_0 does not, asymptotically decreasing as the natural logarithm. As $r \to \infty$, however, both functions approach zero, that is, for $\beta_n r >> 1$,

$$J_0(\beta_n r) = \left[\frac{2}{\beta_n r}\right]^{1/2} \cos(\beta_n r)$$

$$Y_0(\beta_n r) = \left[\frac{2}{\beta_n r}\right]^{1/2} \sin(\beta_n r) \qquad (A\text{-}23)$$

For small values of the argument, the temporal expansions, Eqs. *A-12*, also hold in the cylindrical case.

Taking $U_0(\beta_n r)$,

$$U_0(\beta_n r) = A_n J_0(\beta_n r) + B_n Y_0(\beta_n r) \qquad (A\text{-}24)$$

for constant A_n and B_n, a useful integral involving the Bessel-Neumann functions on the interval (a,b) is given by,

$$\int_a^b U_0(\beta_m r) U_0(\beta_n r) r dr = \left[\frac{1}{2} r^2 [U_0^2(\beta_n r) + U_1^2(\beta_n r)]\right]_a^b \delta_{nm} \qquad (A\text{-}25)$$

provided β_n is a real zero of the boundary condition for h_1 and h_2 constants,

$$h_1 \beta_n U_1(\beta_n b) - h_2 U_0(\beta_n b) = 0 \qquad (A\text{-}26)$$

and real numbers k_1 and k_2, both not zero, exist such that,

$$k_1 \beta_n U_1(\beta_n a) - k_2 U_0(\beta_n a) = 0 \qquad (A\text{-}27)$$

with δ_{nm} defined by Eq. *A-15*. The first-order and zero-order Bessel and Neumann functions are connected by the simple relationships,

$$J_1(\beta_n r) = -\frac{\partial J_0(\beta_n r)}{\partial(\beta_n r)}$$

$$Y_1(\beta_n r) = -\frac{\partial Y_0(\beta_n r)}{\partial(\beta_n r)} \qquad (A\text{-}28)$$

Similarly,

$$\int_a^b U_0(\beta_n r) r dr = 2\frac{J_0(\beta_n b) - J_0(\beta_n a)}{\pi \beta_n^2 J_0^2(\beta_n a)} \qquad (A\text{-}29)$$

provided β_n is a root of the equation,

$$J_0(\beta_n a) Y_0(\beta_n b) - J_0(\beta_n b) Y_0(\beta_n a) = 0 \qquad (A\text{-}30)$$

or,

$$\int_a^b U_0(\beta_n r) r dr = \frac{2}{\pi \beta_n^2} \tag{A-31}$$

when,

$$J_0(\beta_n a) Y_1(\beta_n b) - Y_0(\beta_n a) J_1(\beta_n b) = 0 \tag{A-32}$$

If β_n is a simple root of the equation,

$$J_0(\beta_n b) = 0 \tag{A-33}$$

then,

$$\int_0^b J_0(\beta_n r) J_0(\beta_m r) r dr = \frac{b^2}{2} J_0^2(\beta_n b) \delta_{nm} \tag{A-34}$$

If β_n is a root of the expression,

$$h J_0(\beta_n b) - \beta_n J_1(\beta_n b) = 0 \tag{A-35}$$

the integral satisfies,

$$\int_0^b J_0(\beta_n r) J_0(\beta_m r) r dr = \frac{1}{2\beta_n^2} [b^2 h^2 + b^2 \beta_n^2] J_0^2(\beta_n b) \delta_{nm} \tag{A-36}$$

For any β_n and interval,

$$\int_0^b J_0(\beta_n r) r dr = \frac{b}{\beta_n} J_1(\beta_n b) \tag{A-37}$$

Appendix B
Solutions and Series Expansions

The exponential, trigonometric, and Bessel-Neumann function solutions to the rate and diffusion equations are known (46, 47). But to recover these solutions in a useful form for computation and application, we employ a power series expansion and adjust the coefficients to satisfy the differential equation.

First-order differential equations, such as Eqs. *4*, *A-4*, and *A-18*, are of the simple form,

$$\frac{\partial \Pi}{\partial t} + \lambda \Pi = 0 \tag{B-1}$$

for λ constant. The power series solution is written,

$$\Pi(t) = \sum_{n=0}^{\infty} c_n t^{s+n} \tag{B-2}$$

with s and c_n constants. In the case of a first-order differential equation, only one of

the c_n is independent. Substituting Eq. *B-2* into Eq. *B-1*, performing the indicated operations, multiplying the equation by t, and then collecting powers of t^{s+n} gives,

$$sc_0 = 0$$
$$(s+n)c_n + \lambda c_{n-1} = 0 \quad n \geq 1 \tag{B-3}$$

From the first of Eqs. *B-3*, $s = 0$, and all coefficients, c_n, for $n \geq 1$ are related to c_0 by the second of Eqs. *B-3*. Collecting coefficients and using the recursion relationship from Eq. *B-3*, we write, taking $C = c_0$,

$$\Pi(t) = C \sum_{n=0}^{\infty} (-1)^n \frac{(\lambda t)^n}{n!} \tag{B-4}$$

which is the usual exponential solution, since,

$$\sum_{n=0}^{\infty} (-1)^n \frac{(\lambda t)^n}{n!} = \exp(-\lambda t) \tag{B-5}$$

The plane and cylindrical solutions to Eqs *A-4* and *A-18* result in the exact same manner, that is, replace Π with T and λ with $\alpha^2 D$ in the planar case, or λ with $\beta^2 D$ in cylindrical case.

The plane and cylindrical (spatial) solutions to the second-order diffusion equation are more complex. The solutions, trigonometric and Bessel-Neumann functions, are well known, as above. We again employ the power series expansion in plane and cylindrical coordinates as follows.

The plane diffusion equation is written, as in Eqs. *2* and *A-4*,

$$\frac{\partial^2 X}{\partial x^2} + \alpha^2 X = 0 \tag{B-6}$$

with α constant. Expanding the solution as a power series in x,

$$X(x) = \sum_{n=0}^{\infty} d_n x^{s+n} \tag{B-7}$$

with d_n and s to be determined. In the second-order case, only two of the d_n are independent and the rest are obtained recursively. Inserting the power series into Eq. *B-6*, performing operations, multiplying the equation by x^2, and then equating to zero each coefficient of x^{s+n} requires,

$$s(s-1)d_0 = 0$$
$$sd_1 = 0$$
$$(s+n)(s+n-1)d_n + \alpha^2 d_{n-2} = 0 \quad n \geq 2 \tag{B-8}$$

Trivially, this implies that $s = 0$, or $s = 1$ for d_0 nonzero from the first of Eqs. *B-8*, $s = 0$ from the second of Eqs. *B-8* for d_1 nonzero, and the remaining d_n are recursively related to d_0 or d_1 from the last of the three equations. The solution then splits into

two independent series, one involving d_0 and d_{2n}, and the other involving d_1 and d_{2n-1}. Taking $s = 0$ using the recursion from the last of Eqs. *B-8*, there results,

$$X(x) = A \sum_{n=1}^{\infty} (-1)^{n-1} \frac{(\alpha x)^{2n-1}}{(2n-1)!} + B \sum_{n=0}^{\infty} (-1)^n \frac{(\alpha x)^{2n}}{2n!} \qquad (B\text{-}9)$$

with $A = \alpha d_1$ and $B = d_0$. The usual trigonometric results are recovered by noting,

$$\sum_{n=1}^{\infty} (-1)^{n-1} \frac{(\alpha x)^{2n-1}}{(2n-1)!} = \sin(\alpha x)$$

$$\sum_{n=0}^{\infty} (-1)^n \frac{(\alpha x)^{2n}}{2n!} = \cos(\alpha x) \qquad (B\text{-}10)$$

The cylindrical solution is expanded in a power series in r^{s+n},

$$R(r) = \sum_{n=0}^{\infty} f_n r^{s+n} \qquad (B\text{-}11)$$

and is inserted into the radial expression, Eqs. *3* and *A-8* for instance, with β constant,

$$\frac{\partial^2 R}{\partial r^2} + \frac{1}{r}\frac{\partial R}{\partial r} + \beta^2 R = 0 \qquad (B\text{-}12)$$

Repeating the same steps as in the planar case yields,

$$s^2 f_0 = 0$$

$$(s+1)^2 f_1 = 0$$

$$(s+n)^2 f_n + \beta^2 f_{n-2} = 0 \quad n \geq 2 \qquad (B\text{-}13)$$

as the general recursion scheme. Here, $s = 0$ is a repeated root of the first of Eqs. *B-13*, but not of the second equation, as was the previous case. The solution requires $f_1 = 0$ in the above, so that all higher order coefficients f_{2n-1} are also zero from the second of Eqs. *B-13*. The series involving f_0 and f_{2n}, for $s = 0$, gives one independent solution of the radial equation. The second independent solution can be obtained by differentiating the first solution and evaluating the result at $s = 0$. The recursion relationships remain the same in both cases, namely Eqs. *B-13* with $s = f_1 = 0$. Evaluating both solutions and adding them together, we find, with $A = f_0$ and B any constant, or multiple of A,

$$R(r) = [A + B \ln(\beta r)] \sum_{n=0}^{\infty} (-1)^n \left[\frac{(\beta r)^n}{2n!}\right]^2 + B \sum_{n=0}^{\infty} (-1)^{n-1} \left[\frac{(\beta r)^n}{2n!}\right]^2 \eta(n) \qquad (B\text{-}14)$$

for,

$$\eta(n) = 1 + \frac{1}{2} + \frac{1}{3} + \cdots + \frac{1}{n}$$

$$\eta(0) = 0 \qquad (B\text{-}15)$$

The usual form,

$$R = A J_0(\beta r) + B Y_0(\beta r) \qquad (B\text{-}16)$$

is recovered by noting that the series expansions define J_0 and Y_0,

$$\sum_{n=0}^{\infty} (-1)^n \left[\frac{(\beta r)^n}{2n!}\right]^n = J_0(\beta r)$$

$$\ln(\beta r)J_0(\beta r) + \sum_{n=0}^{\infty} (-1)^{n-1} \left[\frac{(\beta r)^n}{2n!}\right]^2 \eta(n) = Y_0(\beta r) \qquad (B\text{-}17)$$

Appendix C
Probability and Maximum Likelihood

Elementary probability theory and statistical methods (48) can often be applied to complicated failure-success data with considerable payoff in the fabrication of occurrence tables. Probabilistic measures can be backed out of the data with very few assumptions about controlling mechanisms and sequence. A simple approach is described in the following.

The probability of any random occurrence, ρ, can be a complicated function of many parameters, $q = q_1, q_2, \ldots, q_K$. The only constraint is,

$$0 \leq \rho(q) \leq 1 \qquad (C\text{-}1)$$

for appropriate values of q. If the probability of nonoccurrence is ξ, then by conservation of probability,

$$\rho(q) + \xi(q) = 1 \qquad (C\text{-}2)$$

over the same range of q. Similarly,

$$0 \leq \xi(q) \leq 1 \qquad (C\text{-}3)$$

Popular single-valued ($K = 1$) functions for ρ take the general forms,

$$\rho(q) = q \quad 0 \leq q \leq 1$$

$$\rho(q) = \frac{1}{1+q} \quad 0 \leq q \leq \infty$$

$$\rho(q) = \exp(-q) \quad 0 \leq q \leq \infty$$

$$\rho(q) = \sin^2(q) \quad 0 \leq q \leq \pi/2 \qquad (C\text{-}4)$$

as well as power law extensions of the basic function set. Linear combinations of the above set, with appropriate (constant) multipliers to satisfy Eq. *C-1*, are also employed. Multivalued functions, $\rho(q_1, q_2, \ldots, q_K)$, are also easily constructed. The form of ρ can be dictated by theory, or observation over many trials. In decompression applications, the parameters, q, may well be the bubble-nucleation rate, number of VGE, degree of saturation, amount of sudden pressure reduction, volume of separated gas, etc., and combinations thereof. The parameters q may also be integrated over all time in any sequence of events. Such integrated measures are more difficult to both construct and analyze over arbitrary numbers of trials. Complexities in the separate probability functions ultimately transfer to the likelihood estimators over all outcomes.

The likelihood of any outcome, Φ, of N trials is a product function of the individual probability measures of the form,

$$\Phi = \rho^n (1 - \rho)^m \qquad (C\text{-}5)$$

given n failures and m successes (n cases of decompression sickness and m cases without decompression sickness), with,

$$n + m = N \qquad (C\text{-}6)$$

The logarithm of the likelihood, Ψ, is similarly cast,

$$\Psi = \ln \Phi = n \ln \rho + m \ln (1 - \rho) \qquad (C\text{-}7)$$

and is maximized,

$$\frac{\partial \Psi}{\partial \rho} = 0 \qquad (C\text{-}8)$$

when, from Eq. *C-7* for appropriate value of ρ, n, and m,

$$\frac{n}{\rho} - \frac{m}{1-\rho} = 0 \qquad (C\text{-}9)$$

Solving trivially gives,

$$\rho = \frac{n}{n + m} = \frac{n}{N} \qquad (C\text{-}10)$$

or

$$\xi = 1 - \rho = \frac{m}{n + m} = \frac{m}{N} \qquad (C\text{-}11)$$

Thus the likelihood function is maximized when the failure probability, ρ, is the ratio of actual failures to trials, and similarly in the case of successes.

For any multivalued probability function, $\rho(q_1, q_2 \ldots, q_K)$, the maximization requires,

$$\frac{\partial \Psi}{\partial \rho} = \sum_{i=1}^{K} \frac{\partial \Psi}{\partial q_i} \frac{\partial q_i}{\partial \rho} = 0 \qquad (C\text{-}12)$$

The condition is satisfied when all $\partial\Psi/\partial q_i$ are identically zero, with the $\partial q_i/\partial\rho$ arbitrary, but well-behaved, bounded functions. The K-coupled homogeneous set,

$$\frac{\partial \Psi}{\partial q_i} = 0 \quad i = 1, 2, \ldots, K \qquad (C\text{-}13)$$

can be solved by analytic or numerical methods on a computer. For single-valued probability functions, the differentiation and reduction are usually simple. Multivalued expressions are more difficult.

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