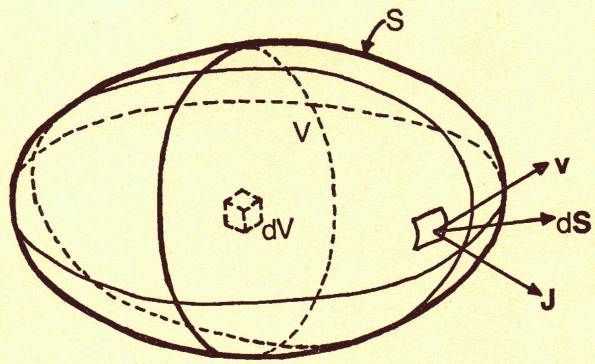
JAN-ERIK SIGDELL

A mathematical theory for the capillary artificial kidney



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The diffusion of a solute from a liquid flowing in a capillary tube is studied under different conditions. Starting with simple cases of plug flow and infinite permeability of the capillary wall, the treatment proceeds to the case of Poiseuille flow and limited permeability of the wall. In the analogous problem of heat transfer, this corresponds to a generalization of the Graetz problem to the case of a limited heat conductivity of the wall of the tube. Furthermore the approximative solution of Lévêque to the Graetz problem for low flows or short distances from the inlet end is generalized analogously. Finally a more general discussion of the case of a varying concentration outside the capillary follows. It is found that only one or two terms of the exact series solution need to be considered. In cases where more terms would be needed, the generalized Lévêque solution can be used instead. Therefore numerical calculations are not too difficult in themselves and diagrams of eigenvalues and coefficients greatly simplify practical applications. Optimization of the capillary dialyzer, the effects of ultrafiltration and recirculation and the relation to the total membrane area are discussed additionally. The mathematical treatment of the generalized Graetz problem is carried to much detail. Mathematical proofs are given for such things as the absolute and uniform convergence of the series solution. Of special interest in this respect is that the negligibility of the second axial derivative in the basic equation is proven mathematically, probably for the first time (hitherto authors refer to physical reasons only).

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Es handelt sich um eine gründliche und praktisch nützliche Studie über die Kapillarniere. Das Problem des Diffusionsaustausches zwischen zwei strömenden Flüssigkeiten, wobei die eine in einem rohrförmigen Gebilde fließt, ist hier eingehend behandelt. Neue Ergebnisse dabei sind: Lösung des erweiterten sogenannten Graetz-Problems, wobei eine begrenzte Durchlässigkeit der Rohrwand berücksichtigt wird (dies ist das Grundproblem der künstlichen Niere nach dem Kapillarprinzip) – Erweiterung der sogenannten Lévêque-Annäherung auf das obengenannte erweiterte Graetz-Problem – Studium des Einflusses einer Ultrafiltration durch die Wand – Studium des Einflusses der Konzentration außerhalb der Kapillaren – Allgemeine Folgerungen für die Kapillarniere – Mathematische Begründung und Beweisführung in sämtlichen Fällen – Diagramme und Annäherungsformeln erleichtern weitgehend die praktische Anwendung auf Diffusionsberechnungen in Kapillarnieren.

Interessenten des Buches sind: Praktisch und theoretisch tätige Nephrologen, Bioingenieure, Medizinmathematiker, „alle an der Diffusion und am Stoff- und Wärmeaustausch interessierten Personen und Institutionen."

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13 Figures and 2 Tables

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A note added in this scanned-in copy, written July 18, 2006

A few corrections have been entered in the text.

Chapter 16: "On the optimization of a capillary dialyzer" was written based on a no more actual presumption.

When the work was done in 1969-1970, there was a general hope that one may soon be able to operate hollow-fiber dialyzers without a blood pump, driven by the arterio-venous pressure difference. External shunts were still mostly used.

With the spread of internal shunts, this idea had to be dropped. With such a shunt, the pressure difference is insufficient fore an operation without a blood pump.

Therefore, quite different optimization criteria are valid under such circumstances. I have worked out a complete optimization procedure for this case, which I hope to describe on the webpage, on which this scanned-in text is made available as a PDF-file.

For this process, γ_b (see pages 62-63) has been calculated for the more general case.

I am aware that the English would have been a lot better if I had written this to day (36 years later)…

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Contents

1 Introduction

There are several reasons to expect a considerably better performance of a capillary dialyzer, where the blood (or the fluid to be dialyzed) is led through a large number of thin capillaries with semipermeable walls, as compared to other configurations of artificial kidneys which use sheets of membranes. Therefore some attempts have been made to construct such dialyzers. The true capillary artificial kidney employs true capillaries, i.e., a large number of separate, small diameter circular tubes of semipermeable material, connected in parallel, and not «capillary» channels formed, e.g., by folds of a membrane sheet. Here the performance of a true capillary kidney will be studied by theoretical analysis. The diffusion problem involved is related to the GRAETZ problem of heat conduction from a fluid flowing in a tube [11], but here the problem is complicated by the fact that the limited permeation of the tube wall has to be considered – the GRAETZ solution assumes a tube wall of (approximately) infinite heat conductivity; assuming an infinite permeation in the tube wall would here result in too rough an approximation.

Earlier studies. A few authors have been studying the performance of the capillary kidney, using simplifying assumptions. The analysis presented here is considerably more exact since such simplifying assumptions have been avoided to any extent practically possible.

One of the earlier works approaching a true capillary artificial kidney was presented by TWARDOWSKI in 1964 [40]. He constructed a dialyzer with four parallel units of 100 cellophane tubes each, 50 cm long and of 1 mm internal diameter. He also performed a calculation of the performance in general terms, not especially related to the capillary structure since it simply relates mean concentrations on both sides of any membrane in an approximative way.

Previous attempts to construct capillary dialyzers resulted, as TWARDOWSKI calls them, in «pseudocapillary» devices, utilizing membrane sheets pressed between grooved plates such that «pseudocapillary» ducts formed (KUHN, SAVINO, ZOSIN, LONGMORE – see [40]).

A more sophisticated attempt was that of STEWART et al., published in 1964 [36]. This dialyzer concept was developed at The Dow Chemical Company and the dialyzer is fabricated and sold by the Cordis Co., Miami, Fla. Some information on its construction and performance at prototype stages is given in [26], where the theoretical analysis is based upon a theoretical study by MICHAELS [27], which relates mean concentrations on both sides of a membrane in a somewhat more detailed way than in [40]. The dialyzers described in [26] have between 3200 and 14000 cellulose capillaries of internal diameters between 0.17 and 0.23 mm and lengths between 11.2 and 16.4 cm.

Some other attempts to the construction of capillary dialyzers are presented in the references [2, 14, 16].

A theoretical approach to the analysis of dialysis in an elliptical conduit was presented by YODER [41] [cf. 30] in 1963 and is applicable, within its limitations, on a capillary arrangement. Again, the mean concentration in the conduit is considered, neglecting the effects of the radial concentration variations like in the above mentioned analytical attempts.

An extensive work on capillary artificial kidneys is performed at the Monsanto Research Corporation, Dayton, Ohio [32]. The report [32] shows remarkable progress in techniques for the construction of capillary dialyzers, but uses the same theory as used in [26]. Prototypes evaluated *in vivo* have between 350 and 8000 heparinized polyacrylonitril capillaries, 6 or 15 cm long, with 0.25 mm internal diameter and 0.05–0.1 mm wall thickness.

Hence, as this brief review indicates, the theoretical studies of dialysis with capillary devices has hitherto relied on simplifying assumptions and approximative expressions, far below the level at which the equivalent problem of thermal diffusion from circular pipes (in heat exchangers, for example) has been studied. For excellent reviews of the theories of thermal convection, [8] and [39] are referred to. None of those theories does, however, treat the case of a limited wall conductivity for the heat – in practical cases it might well be appropriate to treat the tube wall as infinitely conductive. Such an approximation is, though, too rough in the corresponding dialysis problem (and this may perhaps be the reason why theories of thermal convection have not been «translated» to the dialysis from a capillary). In the present work, a simple and useful way to treat the influence of the limited wall permeation for diffusion is applied and the error of the approximation involved is investigated mathematically. The method for taking the wall permeation in account was found to be the same as the one used by GRIMSRUD and BABB [12] in the analysis of a conventional membrane sheet dialyzer. In the capillary dialyzer, studied in the present work, the mathematics are different and are here treated in a detailed and stringent way so as to provide a firm mathematical basis. The theory developed should be of interest also for applications to thermal convection problems involving circular tubes when a consideration of the effect of the wall conductivity is desired. Of special interest is the generalization of the LÉVÊQUE approximation, presented in Chapter 11, as this allows for simple treatments in cases where the exact series solution converges slowly.

Theories of conventional «flat conduit» dialyzers are somewhat easier and have been carried a lot further than for capillary dialyzers. An excellent example is given by ref. [12].

The advantages of capillary artificial kidneys and the general requirements on artificial kidneys are treated often enough in literature (see references) so that a repetition appears unnecessary here, especially as the scope is the mathematics of the device. In brief, the capillary kidney, through its geometry, allows for a better fulfilment of the requirement of the least possible blood space volume for a given performance (approximately the same as requiring the smallest blood volume with a given membrane surface area – for a capillary kidney the clearance is not exactly, but to a reasonable estimation, proportional to the membrane area).

General reviews on hemodialysis and artificial kidneys are given in the references [7, 9, 15].

The theory developed here should be of potential interest also for studies of diffusion exchange through the walls of capillary blood vessels in body tissues.

In the following, the diffusion out of a single capillary will be studied in a sequence of cases, going from the simplest case to the more exact study, which considers the velocity profile and the wall permeation. This will first assume zero concentration outside the capillary, so that the maximum performance results. The case of limited wash-off of the diffused substance outside the capillary will then be discussed.

The main part of the Chapters 1–13 of this work was done at J.R. Geigy, Ltd., from February 1969 till April 1970. I am indebted to the management of Ciba-Geigy, Ltd., Basle, Switzerland, for permitting the publication and, especially, to Dr. P. MOSER for invaluable aid with computer calculations and to Dr. R. VONDERWAHL and Professor H. WIRZ for pleasant stimulation.

The purpose of this work is to establish a well founded mathematical theory for the capillary dialyzer, since such a theory has hitherto been lacking (except for more or less rough approximations, indicated above). The growing interest for such dialyzers leads the author to hope that this theory will fulfil a certain need. Much to his regret, experimental verification has not been possible because (for certain reasons) facilities herefore were no longer available to him when the theoretical work had reached a state where such a verification would have been at place. Still, the well known (established and proven) theory of diffusion forms a firm enough basis, together with a careful mathematical treatment, so that such a verification would have been rather for the sake of completeness only. Therefore the real need for a confirmation appears more an academic than a practical question in this case.

2 The basic equation

The diffusion equation is in the literature usually given as referred to a specific coordinate system. It may be of interest to state the basic equation in general terms, not presupposing a specific frame of reference. A general derivation is quite simple and will here be given as a mathematical introduction.

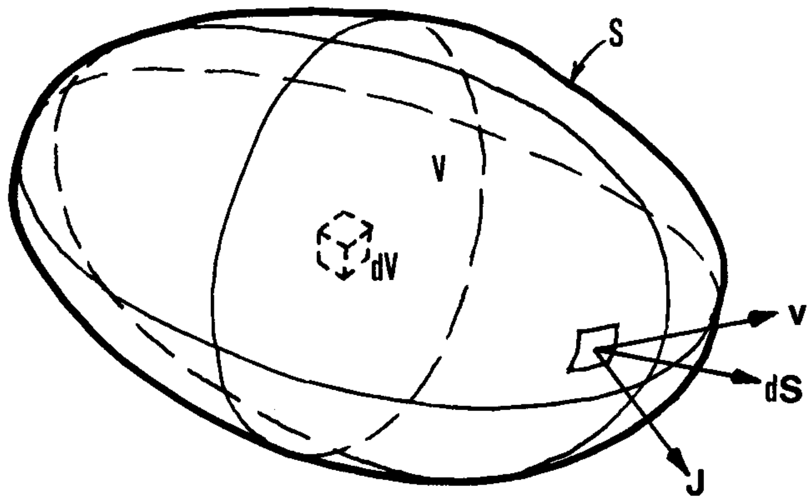

Fig. 1. An arbitrary volume in the flow field

The easiest derivation of the basic diffusion equation is achieved through the EULERian approach. Consider an arbitrary stationary volume V with the surface S in the flow field, as drawn in Fig. 1. To be studied is the diffusion of a single dissolved compound, the relative volume concentration of which will be denoted by C ($C=1$ meaning 100% concentration). Bold face types are used for vector notations: **v** is the velocity of the flowing fluid, **J** is the diffusion flux and **dS** is an oriented surface element of S ($\mathbf{dS} \perp S$, directed outwards). Any increase of the solute in V is caused by inflow through S:

$$\int_V \frac{\partial C}{\partial t}\, dV = -\oint_S (C\mathbf{v}+\mathbf{J}) \cdot d\mathbf{S}, \qquad (1)$$

or, applying the theorem of GAUSS:

$$\int_V \frac{\partial C}{\partial t}\, dV = -\int_V \nabla \cdot (C\mathbf{v}+\mathbf{J})\, dV, \qquad (2)$$

where the « del» or «nabla» symbol ∇ is used: $\nabla = grad$, $\nabla \cdot = div$, $\nabla^2 = \nabla \cdot \nabla =$ *div grad*.

Equation (2) must hold for any V (as long as the volume does not contain an essential boundary surface), therefore

$$\nabla \cdot (C\mathbf{v}+\mathbf{J})+\frac{\partial C}{\partial t}=0. \tag{3}$$

For the carrier fluid one has, analogously:

$$-\int_V \frac{\partial C}{\partial t}\,dV=-\oint_S [(1-C)\mathbf{v}-\mathbf{J}]\cdot d\mathbf{S}, \tag{4}$$

because the volume left behind by the dissolved compound, as it is shifted through diffusion, cannot remain as a «hole» but must be filled up with carrier fluid (solvent). As before we get from (4):

$$\nabla \cdot [(1-C)\mathbf{v}-\mathbf{J}]-\frac{\partial C}{\partial t}=0. \tag{5}$$

Eliminating $\mathbf{J}$ and $\partial C/\partial t$ from (3) and (5), of course, results in the equation of continuity:

$$\nabla \cdot \mathbf{v}=0. \tag{6}$$

Since

$$\nabla \cdot (C\mathbf{v})=\mathbf{v}\cdot \nabla C+C\nabla \cdot \mathbf{v}, \tag{7}$$

one gets from (6) and (3):

$$\mathbf{v}\cdot \nabla C+\nabla \cdot \mathbf{J}+\frac{\partial C}{\partial t}=0. \tag{8}$$

Now, FICKS first law of diffusion states

$$\mathbf{J}=-D\nabla C, \tag{9}$$

where D is the diffusivity or diffusion coefficient. Hence, from (8) and (9):

$$\mathbf{v}\cdot \nabla C+\frac{\partial C}{\partial t}=D\nabla^2 C. \tag{10}$$

The left side here is the «total time derivative» or the «time derivative following motion», which would have come out more directly if a LAGRANGEan derivation were used. Such a derivation is a little less easy to visualize, but, for completeness, the starting equation may be set up:

$$\int_V \left(\frac{\partial C}{\partial t}+\mathbf{v}\cdot \nabla C\right) dV=-\oint_S \mathbf{J}\cdot d\mathbf{S}, \tag{11}$$

where the left side is the increase in the (now moving) volume V, as given by the «total time derivative», including the effect of the movement of S along with $\mathbf{v}$, and the right side is the inflow through S trough diffusion, whereas there is no more a fluid flow through S. The derivation of (10) then follows analogously.

The full specification of a diffusion problem requires, besides (10), a specification of the conditions at a given boundary for the volume studied as well as the condition at a given time (initial condition). In a quite general case the boundary condition is of the type $\alpha C + \beta \nabla C \cdot \hat{n} = \delta$, where α, β and δ are constants, holding on a given boundary surface, which may have separate parts. $\hat{n}$ is a normal unity vector for the surface (of unity length, everywhere at right angles to the surface). The initial condition is generally a specification of C at a given time, usually defined as $t = 0$.

3 A simple limit case – uniform (bulk or plug) flow and infinitely permeable wall

This case has been treated in literature for the equivalent thermal problem, but with neglection of the term $\partial^2 C/\partial z^2$ in (12) below. The exact solution is not much more difficult and is derived in this chapter.

As the capillary structure is cylindrical, it is useful to introduce cylindrical coordinates, in which (10) takes the form

$$v_r \frac{\partial C}{\partial r} + v_z \frac{\partial C}{\partial z} + \frac{\partial C}{\partial t} = D\left(\frac{\partial^2 C}{\partial z^2} + \frac{\partial^2 C}{\partial r^2} + \frac{1}{r}\frac{\partial C}{\partial r}\right), \tag{12}$$

assuming fully developed straight tubular flow already at the entrance to the capillary so that there is rotational symmetry (independence of the angular coordinate). For application to a capillary kidney one may to a very good approximation assume the stationary case $\partial C/\partial t = 0$, since the rate of reduction of blood concentration of compounds to be excreted is very slow, compared to the «dwelling time» of blood in the kidney. A further assumption is negligible loss or gain of fluid through the capillary walls (the case of ultrafiltration will be discussed later, still the loss of fluid due to ultrafiltration occurs at a rate much slower than blood transport time and therefore is negligible when studying concentration profiles – a certain effect on the wall permeability will, however, be found later). This means (for a uniform capillary) that $v_r = 0$. The task is therefore to solve the equation

$$v \frac{\partial C}{\partial z} = D\left(\frac{\partial^2 C}{\partial z^2} + \frac{\partial^2 C}{\partial r^2} + \frac{1}{r}\frac{\partial C}{\partial r}\right), \tag{13}$$

putting $v_z = v$, assumed constant.

In this first, simple case the boundary conditions are

$$\begin{cases} C = C_0,\ z \leq 0, & (14a) \\ C = 0,\ r \geq r_1,\ z > 0, & (14b) \\ \dfrac{\partial C}{\partial r} = 0,\ r = 0, & (14c) \end{cases}$$

for zero concentration outside the capillary; here C_0 is the initial concentration, $z = 0$ the inlet end of the capillary and r_1 the inner radius of the capillary wall. (14*c*) follows from symmetry. To solve the equation according to the method of FOURIER, one sets as an intermediate solution to (13) alone:

$$C(r,z) = F_r(r)\ F_z(z), \tag{15}$$

giving, with (13):

$$\frac{vF_z' - DF_z''}{F_z} = D\,\frac{F_r'/r + F_r''}{F_r} = \lambda, \tag{16}$$

where λ must be a constant. The F_r-equation in (16) gives

$$F_r(r) = AJ_0\left(r\sqrt{-\frac{\lambda}{D}}\right) + BY_0\left(r\sqrt{-\frac{\lambda}{D}}\right), \tag{17}$$

where A and B are constants and J_0 and Y_0 the BESSEL functions of zero order and of first and second kind, respectively. Obviously, F_r must be limited for $|r| \leq r_1$ and therefore $B = 0$. This automatically fulfils (14*c*), but (14*b*) requires

$$\lambda = -D\left(\frac{\rho_k}{r_1}\right)^2, \tag{18}$$

where ρ_k, $k = 1.2, \ldots$ *ad infinitum*, are the positive zeroes of J_0. The special case $\lambda = 0$ does not fulfil the requirements, since this gives

$$F_r(r) = A \ln r + B, \tag{19}$$

which is not limited for $|r| \leq r_1$ unless $A = 0$, in which case (14*b*) also requires $B = 0$.

Hence the solution to (13) and (14) is a series of solutions (15):

$$C = \sum_{k=1}^{\infty} A_k(z)\ J_0\left(\rho_k \frac{r}{r_1}\right), \tag{20}$$

fitting (14*a*), since $J_0(\rho_k r/r_1)$ forms an orthogonal system for $|r| \leq r_1$. Putting this into (13) or (16) gives

$$vA_k' = D\left[A_k'' - \left(\frac{\rho_k}{r_1}\right)^2 A_k\right], \tag{21}$$

with the solution

$$A_k(z) = A_{ok} \exp\left\{-z\left[\sqrt{\left(\frac{v}{2D}\right)^2 + \left(\frac{\rho_k}{r_1}\right)^2} - \frac{v}{2D}\right]\right\} \tag{22}$$

(a solution with positive exponent is rejected since one must have $C \to 0$ as $z \to \infty$). To fulfill (14*a*), one has, from (20) and (22):

$$C_o = \sum_{k=1}^{\infty} A_{ok} J_o\left(\rho_k \frac{r}{r_1}\right), \tag{23}$$

from which

$$A_{ok} = \frac{2C_o}{\rho_k J_1(\rho_k)} \tag{24}$$

due to known properties of J_0 and the orthogonal system $J_0(\rho_k r/r_1)$ [38]. J_1 is the Bessel function of first order and first kind. The solution to (13) and (14) thus finally becomes

$$C = 2C_o \sum_{k=1}^{\infty} \frac{J_o(\rho_k r/r_1)}{\rho_k J_1(\rho_k)} \exp\left\{-z\left[\sqrt{\left(\frac{v}{2D}\right)^2 + \left(\frac{\rho_k}{r_1}\right)^2} - \frac{v}{2D}\right]\right\}. \tag{25}$$

More interesting for practical purposes is the mean concentration

$$\bar{C}(z) = \frac{1}{\pi r_1^2} \int_0^{r_1} 2\pi r\, C(r,z)\, dr, \tag{26}$$

for which (25) gives

$$\bar{C} = 4C_o \sum_{k=1}^{\infty} \frac{1}{\rho_k^2} \exp\left\{-z\left[\sqrt{\left(\frac{v}{2D}\right)^2 + \left(\frac{\rho_k}{r_1}\right)^2} - \frac{v}{2D}\right]\right\}. \tag{27}$$

The termwise integration, leading to (27), is allowed because the absolute values of the individual terms in (25) for large k are

$$\leq \text{const.} \frac{1}{\sqrt{k}} \exp\left(-\frac{\pi z k}{r_1}\right), \tag{28}$$

[17] which shows that the series (25) is absolutely and uniformly convergent. The larger the k, the faster the terms in (25) decay with z, due to the exponential functions. For larger z one may then approximate $\bar{C}$ with the first terms in the series (27). For sufficiently large z, the first term alone is sufficient as approximation of $\bar{C}$ (cf. Chapter 11).

If z is such, that one may approximate $\bar{C}$ with the first n terms in (27), and one for $k \leq n$ also has $v/2D \gg \rho_k/r_1$, one can further approximate by setting

$$\bar{C} \approx 4C_o \sum_{k=1}^{n} \frac{1}{\rho_k^2} \exp\left[-\frac{Dz}{v}\left(\frac{\rho_k}{r_1}\right)^2\right], \tag{29}$$

which applies in most practical cases. The latter approximation in the exponent also results when $\partial^2 C/\partial z^2$ is neglected in (13), as is usual in literature. In a later study the latter simplification will be used but it will then also be shown that it leads to a negligible error in almost all practical cases.

For a non-zero concentration C_1 outside the capillary, (25) still holds if C is replaced by $C-C_1$ and C_0 by C_0-C_1, as is obvious from superposition. This assumes a constant C_1 but may also be applied as approximation when C_1 varies sufficiently slowly with z, if the mean value of C_1 over z is inserted. For more general cases the solution may be obtained in analogy to [39].

4 Another simple case – the opposite limit case of very high wall resistance to diffusion

Here one may assume an arbitrary velocity distribution v(r) in (13) and calculate the mean concentration $\bar{C}$ in (13) before solving the equation. In this case the concentration varies very little over the cross-section, $C(r,z) \approx \bar{C}(z)$. Therefore

$$\bar{v}\,\frac{\partial \bar{C}}{\partial z} \approx D\,\frac{\partial^2 \bar{C}}{\partial z^2} + \frac{D}{\pi r_1^2}\int_0^{r_1} 2\pi r \left(\frac{\partial^2 C}{\partial r^2} + \frac{1}{r}\frac{\partial C}{\partial r}\right) dr, \tag{30}$$

with the mean velocity $\bar{v}$ defined in analogy to (26). This approximation is better, the higher the diffusion resistance of the wall. In the limit (infinite resistance) it becomes an equality.

The integral term in (30) is

$$\frac{2}{r_1^2}\int_0^{r_1} r \left(\frac{\partial^2 C}{\partial r^2} + \frac{1}{r}\frac{\partial C}{\partial r}\right) dr = \frac{2}{r_1^2}\int_0^{r_1} d\left(r\,\frac{\partial C}{\partial r}\right) = \frac{2}{r_1}\left[\frac{\partial C}{\partial r}\right]_{r=r_1}, \tag{31}$$

using (14c). Because $C \approx \bar{C}$, the boundary condition is

$$D\frac{\partial C}{\partial r} \approx -\gamma \bar{C},\; r = r_1, \tag{32}$$

for zero concentration outside the capillary. Here γ is the permeation of the capillary wall (cf. Chapter 6). Combining (30), (31) and (32), it follows:

$$\bar{v}\,\frac{\partial \bar{C}}{\partial z} \approx D\,\frac{\partial^2 \bar{C}}{\partial z^2} - \frac{2}{r_1}\gamma \bar{C}, \tag{33}$$

from which

$$\bar{C} \approx C_0 \exp\left\{-z\left[\sqrt{\left(\frac{\bar{v}}{2D}\right)^2 + \frac{2\gamma}{Dr_1}} - \frac{\bar{v}}{2D}\right]\right\}, \tag{34}$$

since (14a) still holds and the term with a positive exponent must be rejected in order to have $\bar{C} \to 0$ for $z \to \infty$.

In practice one often has $\bar{v}/2D \gg \sqrt{2\gamma/Dr_1}$, in which case (34) becomes

$$\bar{C} \approx C_0 \exp\left(-\frac{2\gamma z}{\bar{v} r_1}\right), \tag{35}$$

which is also obtained if $\partial^2 C/\partial z^2$ is neglected in (30) (cf. [22]). Again, (34) applies to a constant concentration C_1, instead of zero, outside the capillary if $\bar{C}$ is replaced by $\bar{C}-C_1$ and C_0 by C_0-C_1.

5 Capillary with infinitely permeable wall and Poiseuille flow

Newtonian fluids in laminar flow within a tube have a Poiseuille distribution of the velocity:

$$\begin{cases} v_z = v = 2\bar{v}\left[1-\left(\frac{r}{r_1}\right)^2\right], & |r| \leq r_1, \\ v_r = 0, \end{cases} \tag{36}$$

where $\bar{v}$ is the mean velocity

$$\bar{v} = \frac{1}{\pi r_1^2}\int_0^{r_1} 2\pi r v \, dr. \tag{37}$$

To obtain the concentration distribution in this case, one may consult literature. With the notations introduced in this work inserted, one finds from [18] in the case when $\partial^2 C/\partial z^2$ is neglected [see (13)],

$$\frac{C}{C_0} = 1.477\, e^{-3.658\, Dz/\bar{v}r_1^2}\, R\left(\beta_1, \frac{r}{r_1}\right) - 0.810\, e^{-22.178\, Dz/\bar{v}r_1^2}\, R\left(\beta_2, \frac{r}{r_1}\right)$$
$$+ 0.385\, e^{-53.05\, Dz/\bar{v}r_1^2}\, R\left(\beta_3, \frac{r}{r_1}\right) - \ldots \; . \tag{38}$$

Here $R(\beta,x)$ is a solution of

$$\frac{d^2R}{dx^2}+\frac{1}{x}\frac{dR}{dx}+\beta^2(1-x^2)R=0, \tag{39}$$

which gives

$$R(\beta,x)=\sum_{n=0}^{\infty}B_{2n}x^{2n}, \tag{40}$$

with

$$\begin{cases} B_0=1, \\ B_2=-\dfrac{\beta^2}{4}, \\ \vdots \\ B_{2n}=\dfrac{1}{(2n)^2}\beta^2(B_{2n-4}-B_{2n-2}), \\ \vdots \end{cases} \tag{41}$$

β_k in (38) is the k:th positive root of

$$R(\beta,1)=0, \tag{42}$$

i.e., $\beta_1=2.70436$, $\beta_2=6.6791$, $\beta_3=10.3$, . . . according to [8].

In [33] an approximative general relation is derived as $\beta_k\approx 4k-4/3$, the better the higher k. This solution, given by (38)—(42), was first derived by GRAETZ [11].
When the velocity distribution is no more uniform, the «mixing cup concentration» C_m is of more interest than the mean concentration $\bar{C}$ according to (26). In steady state this is the concentration obtained when the fluid is collected and mixed in a «mixing cup» at the output end of a tube of length z:

$$C_m(z)=\frac{1}{\pi r_1^2\bar{v}}\int_0^{r_1}2\pi r\ v(r,z)\ C(r,z)\ dr. \tag{43}$$

In the previously studied cases one had $C_m=\bar{C}$; in the first case exactly since v was constant, in the second case approximately since C was almost constant with r. According to [18], one finds for the «mixing cup concentration»:

$$\begin{aligned}\frac{C_m}{C_0}&=0.820\ e^{-3.658\ Dz/\bar{v}r_1^2}+0.0972\ e^{-22.178\ Dz/\bar{v}r_1^2}\\ &\quad+0.0135\ e^{-53.05\ Dz/\bar{v}r/_1^2}+\ldots.\end{aligned} \tag{44}$$

A useful graph of this solution can be found in [18] (his Fig. 22—6).
After having studied these three simpler cases, a study considering the effect of the limited wall permeation is at place. In a first following case a uniform velocity

distribution will be assumed, which is of interest for estimations since the solution then contains well known functions and therefore is easier to handle. An exacter study must consider that the blood flow in a small vessel has a velocity profile which is almost parabolic (POISEUILLE flow – this holds well enough down to very thin capillaries, as discussed in a later chapter, and also for the mean velocity in a linear tube like an artificial kidney capillary in the case of pulsatile flow).

The case of turbulent flow within the capillary will not be treated as such a flow condition should be avoided, because it increases the risk for hemolysis and clotting. The case of turbulent flow (at thermal diffusion) with an infinitely conductive wall is treated in [19].

Before proceeding further with the cases mentioned, the diffusion in the capillary wall will be studied in the following chapter.

6 Diffusion in the capillary wall

In the simplest case, the plane case with diffusion through a membrane with constant concentrations on both sides as sketched in Fig. 2, the diffusion equation is $y'' = 0$, which gives

$$C = C_w \left(1 - \frac{y}{h}\right), \tag{45}$$

with notations defined in the Figure. The corresponding diffusion flux is

$$J = -D_w \frac{dC}{dy} \hat{y} = \frac{D_w C_w}{h} \hat{y}, \tag{46}$$

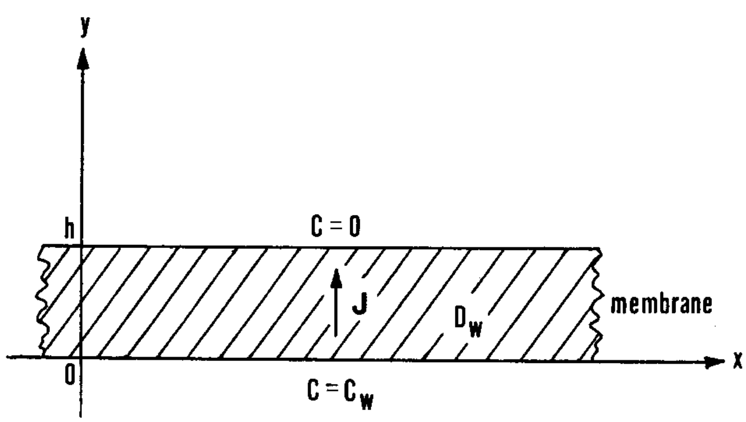

Fig. 2. Diffusion in a plane membrane

where D_w is the diffusion coefficient for the wall material and $\hat{y}$ the unity vector in the y-direction. This indicates that one may define a permeation γ of the membrane as

$$J = \gamma C_w \hat{y}, \tag{47}$$

so that

$$\gamma = \frac{D_w}{h} \tag{48}$$

in this case.

In a cylindrical geometry on has in an analogous case

$$\frac{\partial^2 C}{\partial r^2} + \frac{1}{r}\frac{\partial C}{\partial r} = 0, \tag{49}$$

which with the corresponding boundary conditions $C = C_w$ at $r = r_1$ and $C = 0$ at $r = r_2$ (outer radius of the wall) gives

$$C = C_w \frac{\ln r_2/r}{\ln r_2/r_1} \tag{50}$$

in the wall, which leads to the permeation

$$\gamma = \frac{D_w}{r_1 \ln r_2/r_1} \tag{51}$$

from the definition $\mathbf{J} = \gamma C_w \hat{r}$, in analogy to (46). For $r_2 - r_1 = h \ll r_1, r_2$ this reduces to (48).

A more detailed discussion of diffusion in the capillary wall will be given in Chapter 12.

If the capillary wall is very thin, as compared to the radius of the capillary, one easily realizes that axial diffusion within the wall is negligible. In Chapter 12 is actually shown that this holds even for quite thick walls. Therefore the influence of the wall can generally be given as

$$\mathbf{J}_w(z) = \gamma[C_w(z) - C_1(z)]\,\hat{r}, \tag{52}$$

where $\mathbf{J}_w$ is the local diffusion flux through the wall, C_w the concentration at the inside of the wall and C_1 the concentration at the outside. As shown in Chapter 12, the variation of C_w with z in the case $C_1 = 0$ does not ruin the validity of (52) and therefore this relation will hold also for a similar smooth variation of C_1 (such as an exponential variation).

Below, this will be applied on the calculation of the concentration inside the capillary under consideration of the limited wall permeability. Thereby a considerable simplification is reached. A more stringent analytic solution from solving partial differential equations in two regions – blood and wall (and possibly also in a third region outside the capillary) would become extremely complicated and hardly useful for practical applications. The results in Chapter 12 will verify the good validity of the simplification thus introduced. In this way the problem is again reduced to a generalized STURM-LIOUVILLE problem, where the wall permeation only enters in the boundary condition. (The term «generalized STURM-LIOUVILLE problem» is used because the original STURM-LIOUVILLE problem only allows for coefficient functions which neither become zero nor infinity inside the actual interval or at its boundaries).

The discussion was here based on an idealized membrane with also microscopic homogeneity and with a linear concentration profile in Fig. 2. Obviously, though, (52) holds for any membrane structure, with an appropriate value of γ — the effective or equivalent value.

7 Limited wall permeation and uniform (bulk, plug) flow

Here (13) is to be solved with the boundary conditions

$$\begin{cases} C = C_0,\ z \leq 0, & (53a) \\ \dfrac{\partial C}{\partial r} = -\dfrac{\gamma}{D} C,\ r = r_1 & (53b) \end{cases}$$

where (53*b*) follows from the above discussion in Chapter 6, assuming zero concentration outside the capillary wall. Putting $C(r,z) = F_r(r)\,F_z(z)$ one finds in the same way as in Chapter 3:

$$C = \sum_{k=1}^{\infty} a_k\, J_0\left(s_k \frac{r}{r_1}\right) \exp\left\{-z\left[\sqrt{\left(\frac{v}{2D}\right)^2 + \left(\frac{s_k}{r_1}\right)^2} - \frac{v}{2D}\right]\right\}, \quad (54)$$

where a_k, $k = 1, 2, \ldots$, are constants and s_k the positive roots of

$$\frac{\gamma r_1}{D} J_0(s) = s J_1(s), \quad (55)$$

resulting from (53*b*) when the relation $J_0' = -J_1$ is used [17].

This is a FOURIER-BESSEL series of the second kind [38] for which (53*a*) gives

$$a_k = C_0 \frac{\int\limits_0^{r_1} r J_0\left(s_k \frac{r}{r_1}\right) dr}{\int\limits_0^{r_1} r J_0^2\left(s_k \frac{r}{r_1}\right) dr} = \frac{2 C_0 J_1(s_k)}{s_k\,[J_1^2(s_k) + J_0^2(s_k)]}, \tag{56}$$

or, using (55),

$$a_k = \frac{2\,C_0}{s_k\,J_1(s_k)\left[1 + \left(\frac{D s_k}{\gamma r_1}\right)^2\right]}, \tag{57}$$

to be inserted in (54). (54) with (57) approaches (25) as $\gamma \to \infty$.

For practical use it is of interest to find an approximative expression simplifying the application of these equations. In practical cases (for not too short capillaries) it is to be expected that C can be sufficiently well approximated by the first term in (54) alone (cf. Chapter 11). For this reason one may search for an approximative solution of (55) for the first eigenvalue s_1 in a more handy form. This may be found by approximation of $J_0(x)$ and $J_1(x)$ in the range $0 \leq x \leq \rho_1$, in which s_1 falls (ρ_1 is the first positive zero of J_0). Near zero, $x \approx 0$, one may approximate these functions by their power series, using only the first terms. Instead of adding more terms, the range of applicability of the approximations may be increased by altering the coefficients slightly, at the cost of a reduced but still acceptable accuracy at the origin. Doing this in such a way that exactness is required for $x = 0$, 1 and 2, one finds

$$\begin{cases} J_0(x) \approx 1 - 0.2484\,x^2 + 0.0136\,x^4, & \text{(58a)} \\ x J_1(x) \approx 0.4907\,x^2 - 0.0506\,x^4. & \text{(58b)} \end{cases}$$

The BESSEL functions themselves and their approximations are drawn in the diagrams of Fig. 3 and Fig. 4, showing good approximations within the whole actual range ($\rho_1 = 2.4048$ [17]).

These approximations give, with (55),

$$s_1^2 \approx 4.84\,\frac{1 + 0.506\,w - \sqrt{1 + 0.169\,w + 0.0304\,w^2}}{1 + 0.269\,w}, \tag{59}$$

where $w = \gamma r_1/D$. For very small w one has, from the true series expansions, the approximation $s_1^2 \approx 2w$.

For large k, one has $s_k \approx \rho_{1k}$, where ρ_{1k} are the zeroes of J_1, as is seen from (55). Using known approximations of ρ_{1k} and $J_0(\rho_{1k})$ [17] one finds that the absolute values of the individual terms in (54) for large k are

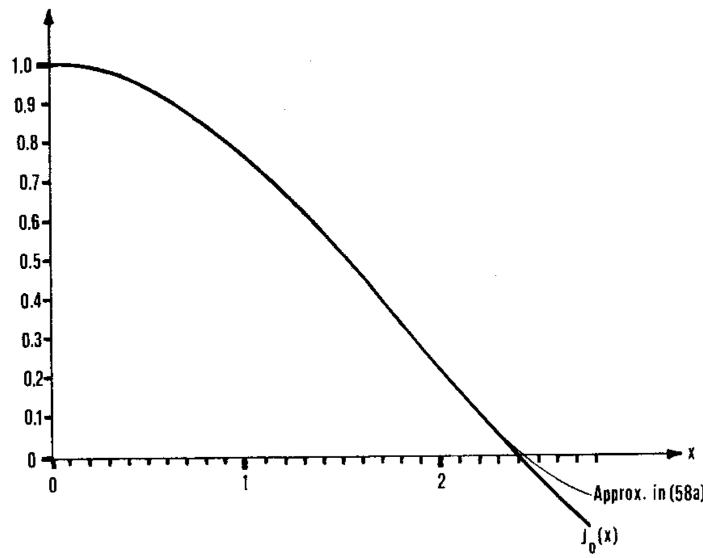

Fig. 3. Comparison of the Bessel function $J_0(x)$ with its approximation in eq. (58*a*)

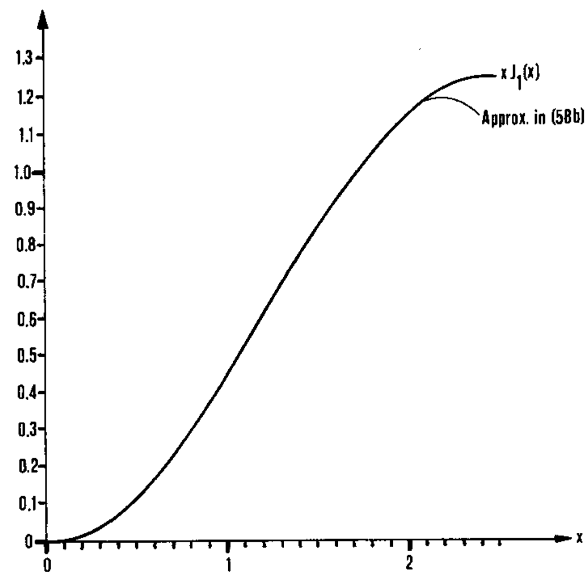

Fig. 4. Comparison of the function $xJ_1(x)$ with its approximation in eq. (58*b*)

$$\leq \text{const. } w \frac{J_0(\pi k r/r_1)}{w^2 + \pi^2 k^2} \sqrt{k}\, e^{-\pi z k/r_1}, \tag{60}$$

showing that the series (54) is absolutely and uniformly convergent. Therefore the series can be integrated termwise to give the mean concentration $\bar{C} = C_m$:

$$\bar{C} = 4\, C_0 \sum_{k=1}^{\infty} \frac{1}{s_k^2(1 + s_k^2/w^2)} \exp\left\{-z\left[\sqrt{\left(\frac{v}{2D}\right)^2 + \left(\frac{s_k}{r_1}\right)^2} - \frac{v}{2D}\right]\right\}, \tag{61}$$

where, again, $w = \gamma r_1/D$. For very small w this gives, using $s_1^2 \approx 2w$ and assuming a large v (for simplicity):

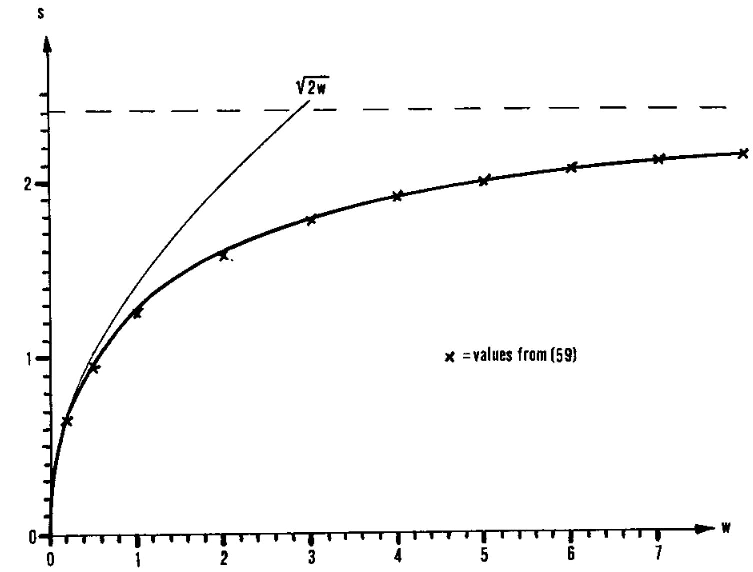

Fig. 5. Comparison of the exact solution $s_1(w)$ of eq. (55) with the general approximation in eq. (59) and the special approximation $s_1^2 = 2w$ for small w

$$\bar{C} \approx C_0\, e^{-2zwD/vr_1^2} + 4C_0 \frac{w^2}{3.8^4}\, e^{-3.8^2 zD/vr_1^2} + \dots, \tag{62}$$

since then $s_2 \approx \rho_{12} \approx 3.8$, etc. As $w \to 0$ this reduces to the first term, which is identical with (35).

Again one may use only the first terms in (54) for a sufficiently large z, as mentioned above. If $z \gg r_1$ and $vr_1 \gg 2s_1D < 4.8\ D$ one may actually write

$$\bar{C} \approx \frac{4\ C_0}{s_1^2(1 + s_1^2D^2/\gamma^2r_1^2)}\, e^{-Dzs_1^2/vr_1^2}, \tag{63}$$

where s_1 may be taken from (59). A graph of s_1, compared to the approximations (59) and $s_1^2 \approx 2w$ is shown in Fig. 5. It seems to be a good rule to use (59) for $w \geq 0.2$ and $s_1^2 \approx 2w$ for $w < 0.2$.

As in the previous cases, the simplified exponents in (62) and (63) correspond to neglecting the second z-derivative of C in (13).

The coefficient before the exponential function in (63), denoted as

$$\vartheta = \frac{4}{s_1^2(1 + s_1^2D^2/\gamma^2r_1^2)}, \tag{64}$$

is drawn in Fig. 6.

As before, (54) and (61) are valid also for a constant concentration $C_1 \neq 0$ outside the capillary if C is replaced by $C - C_1$ and C_0 by $C_0 - C_1$.

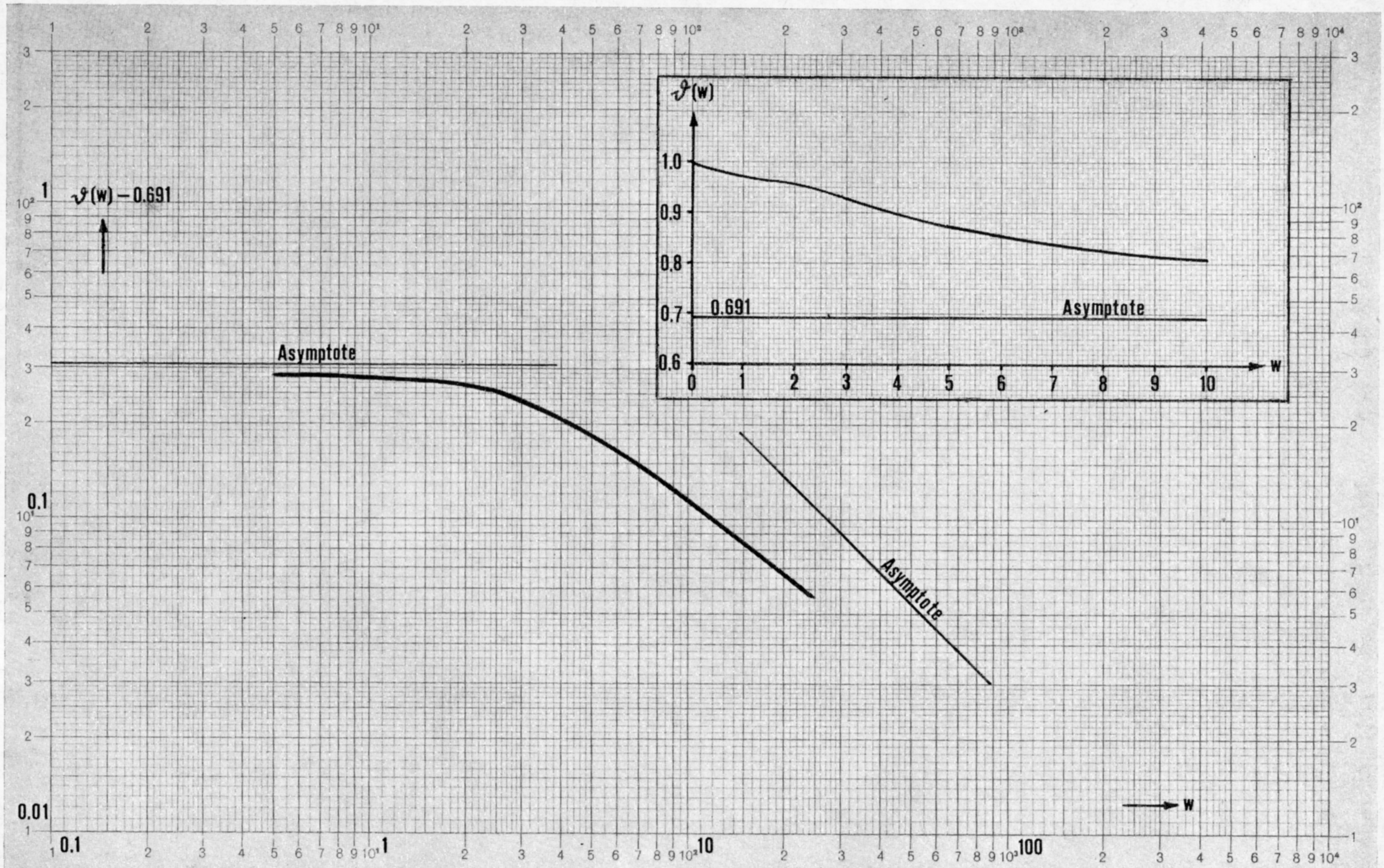

Fig. 6. The coefficient ϑ in eq. (63), defined by eq. (64), as a function of w

8 Limited wall permeation and POISEUILLE flow

In this case the problem is to solve (13) with the velocity distribution (36) and the boundary conditions (53). In order to avoid substantial mathematical difficulties, the term $\partial^2 C/\partial z^2$ will be neglected in (13):

$$2\bar{v}\left[1-\left(\frac{r}{r_1}\right)^2\right]\frac{\partial C}{\partial z}=D\left(\frac{\partial^2 C}{\partial r^2}+\frac{1}{r}\frac{\partial C}{\partial r}\right). \qquad (65)$$

The neglection of this term will be discussed in Chapter 10.

With the same technique as used in earlier chapters, the solution

$$C=\sum_{k=1}^{\infty} a_k P_k\left(\frac{r}{r_1}\right)\exp\left[-\frac{Dz}{2\bar{v}}\left(\frac{p_k}{r_1}\right)^2\right], \qquad (66)$$

results, where $P_k(x)$ is a solution of

$$xP_k''+P_k'+p_k^2\,x(1-x^2)\,P_k=0, \qquad (67)$$

using the symbols $'$ and $''$ for derivatives with respect to x. p_k, $k=1,2,\ldots$, in (67) are such that

$$-w\,P_k(1)=P_k'(1), \qquad (68)$$

where

$$w=\frac{\gamma r_1}{D}. \qquad (69)$$

In the next chapter it will be shown that the system $\{P_k\}$ forms a closed orthogonal set. The proof will verify that the coefficients a_k are given by

$$\begin{cases} a_k=\dfrac{C_o}{N_k}\displaystyle\int_0^1 x(1-x^2)\,P_k(x)\,dx, & (70a)\\[2ex] N_k=\dfrac{1}{2p_k}\left[\dfrac{\partial P}{\partial x}\dfrac{\partial P}{\partial p}-P\dfrac{\partial^2 P}{\partial x\,\partial p}\right]_{\substack{p=p_k\\x=1}}, & (70b)\end{cases}$$

which fulfils (53*a*). Here P symbolizes the general solution of (67) with an arbitrary parameter p instead of p_k.

The integral in (70*a*) can be calculated as follows, using (67):

$$\int_0^1 x(1-x^2)\,P_k\,dx=-\int_0^1\frac{1}{p_k^2}(xP_k''+P_k')\,dx=-\int_0^1\frac{d(xP_k')}{p_k^2}=-\frac{P_k'(1)}{p_k^2}. \qquad (71)$$

Again, and in the following, ′, ″, etc., are used to indicate derivatives with respect to x. In some cases derivatives with respect to p also arise [as in (70)] and the complete notations will then be used for all derivatives to avoid confusion.
It should be made clear that the P_k used here are not the same as the functions $R(\beta_k, r/r_1)$ used in Chapter 6 and [18], although they satisfy identical differential equations. The difference lies in the boundary conditions and therefore in the eigenvalues and leads to a different kind of orthogonal system in the present case. The difference is analogous to that between a FOURIER-BESSEL series of the first kind (cf. Chapter 3) and of the second kind (cf. Chapter 7). Nevertheless one may use the series expansion for R, given in [18], which in an obvious modification for P_k gives:

$$P_k(x) = \sum_{n=0}^{\infty} b_{2n} x^{2n}, \tag{72}$$

where

$$\begin{cases} b_0 = 1, \\ b_2 = -\dfrac{p_k^2}{4}, \\ \vdots \\ b_{2n} = \dfrac{p_k^2}{4n^2}(b_{2n-4} - b_{2n-2}), \\ \vdots \end{cases} \tag{73}$$

As will be seen, this series expansion converges too slowly with respect to x to be convenient for the calculation of the eigenvalues p_k. A somewhat different series expansion for the P_k, which is found to be more practical once it is derived, is a power series with respect to p_k, the coefficients being polynomes in x. Of course this is just a reorganization of (72), but an easier and direct way to find the coefficient functions will be shown below.
Putting

$$P_k = \sum_{m=0}^{\infty} p_k^{2m} f_m(x) \tag{74}$$

one finds, from (67),

$$f_0'' + \frac{1}{x} f_0' + \sum_{m=1}^{\infty} p_k^{2m} \left[f_m'' + \frac{1}{x} f_m' + (1 - x^2) f_{m-1} \right] = 0, \tag{75}$$

i.e., by termwise identification,

$$\begin{cases} f_0'' + \dfrac{1}{x} f_0' = 0, & \text{(76a)} \\ \vdots & \vdots \\ f_m'' + \dfrac{1}{x} f_m' = -(1 - x^2) f_{m-1}, & \text{(76m)} \\ \vdots & \vdots \end{cases}$$

with the solutions

$$\begin{cases} f_0 = A_0 \ln x + B_0, & (77a) \\ \vdots & \vdots \\ f_m = -\int \frac{1}{x} \int x(1-x^2)\, f_{m-1}\, dx^2, & (77m) \\ \vdots & \vdots \end{cases}$$

Since P must be limited when $x \to 0$, one has $A_0 = 0$. Integration of (77*m*) also yields logarithmic terms with arbitrary coefficients. For the same reason these must be zero. This gives

$$\begin{cases} f_0 = B_0, & (78a) \\ f_1 = B_1 - B_0 \left(\frac{x^2}{4} - \frac{x^4}{16}\right), & (78b) \\ f_2 = B_2 - B_1 \left(\frac{x^2}{4} - \frac{x^4}{16}\right) + B_0 \left(\frac{x^4}{4 \cdot 16} - \frac{5x^6}{16 \cdot 36} + \frac{x^8}{16 \cdot 64}\right), & (78c) \\ \vdots & \vdots \end{cases}$$

i.e., in general terms,

$$f_m = \sum_{j=1}^{2m} K_j x^{2j} + B_m. \tag{79}$$

with constant coefficients K_j. In order to fulfil the symmetry requirement (14*c*) and in order to standardize the functions, one desires

$$\begin{cases} P(0) = 1, & (80a) \\ P'(0) = 0. & (80b) \end{cases}$$

The first of these equations gives

$$\sum_{m=0}^{\infty} p_k^{2m} B_m = 1 \tag{81}$$

and the second is automatically fulfilled. (81) can be satisfied independently of p_k if one choses $B_0 = 1$ and $B_m = 0$ for $m \geq 1$. Now all constants are determined and (77) forms an algorithm for the generation of the f-functions, where A_0 and all integration constants are set to zero. This gives

$$\begin{cases} f_0 = 1, & (82a) \\ f_1 = -0.25\, x^2\, (1 - 0.25\, x^2), & (82b) \\ f_2 = 0.015625\, x^4 (1 - 0.555556\, x^2 + 0.0625\, x^4), & (82c) \\ f_3 = -0.434028\, x^6\, 10^{-3} (1 - 0.875\, x^2 + 0.2225\, x^4 - 0.015625\, x^6), & (82d) \\ f_4 = 0.678168\, x^8\, 10^{-5} (1 - 1.2\, x^2 + 0.487778\, x^4 - 0.0777551\, x^6 + & \\ \quad + 0.444444\, x^8\, 10^{-2}), & (82e) \\ f_5 = -0.678168\, x^{10}\, 10^{-7} (1 - 1.527778\, x^2 + 0.861111\, x^4 - & \\ \quad - 0.220911\, x^6 + 0.0253702\, x^8 - 0.111111\, x^{10}\, 10^{-3}), & (82f) \\ \vdots & \vdots \end{cases}$$

In Appendix 1 it is shown that the series (72) is absolutely convergent for any p_k and any x. Therefore one may reorganize the terms in (72) and still have an absolutely convergent series with the same sum. One such reorganization is (74), since this also generates a power series and both these series satisfy (80). [Making integration constants zero does not «remove terms» from the power series as this is done in order to avoid logarithmic terms which do not have such power series anyway and would not satisfy (80)]. Therefore (72) and (74) are identical since a function cannot have more than one power series expansion. The algorithm thus generates (72) reorganized after powers in p_k in an easier and more direct way than through using (73) and reorganize terms. This reorganized series will be found useful below.

Since the two identical series are shown to converge absolutely for any real x and any real p_k, they also converge uniformly for any complex x and any complex p_k. Therefore they may be integrated or differentiated termwise arbitrarily many times and this with respect to x, as well as with respect to p when used in (70b).

According to (68), (74) and (82) one may now determine the first eigenvalue p_1 to a very good approximation as the first positive root of

$$-p^{10}(0.421880\cdot 10^{-7} + w\,0.926930\cdot 10^{-8}) +$$
$$+ p^8(0.566862 + w\,0.145445)\,10^{-5} - p^6(0.450304 + w\,0.144043)\,10^{-3} +$$
$$+ p^4(0.0182292 + w\,0.00792101) - p^2(0.25 + w\,0.1875) + w = 0, \qquad (83)^*$$

where w is defined by (69). One here has $0 \leq p_1 \leq 2.6974$, where the upper limit (approached as $w \to \infty$) follows from Chapter 5. (83) also gives $p_1 \to 2.7048$ as $w \to \infty$. If the p^8-term in (83) is neglected, the first positive root instead approaches 2.697, i.e. already a somewhat had approximation for large w. For smaller w, however, higher powers of p may be neglected. Table 1 shows which powers have to be retained for different w with a required accuracy – as derived empirically from computer calculations.

Figs. 7 and 8 show p_1 as a function of w in log-log and lin-log diagrams. For very small w, (83) gives

$$p_1 \approx 2\sqrt{w}, \qquad (84)$$

which is also included in Table 1.

The FOURIER *coefficients and higher eigenvalues.* Before calculating the FOURIER coefficients a_k in (66), it is useful to simplify the expression. (70) and (71) give

$$a_k = -\frac{2\,C_0\,P_k'(1)}{p_k\left[\dfrac{\partial P}{\partial x}\dfrac{\partial P}{\partial p} - P\dfrac{\partial^2 P}{\partial x\,\partial p}\right]_{\substack{p=p_k\\x=1}}}. \qquad (85)$$

Now (68) gives

* With only terms up to p^8 in (83), p_1 $(w = \infty) = 2.70436$

$$\left[\frac{\partial^2 P}{\partial x\, \partial p}\right]_{x=1} = -\frac{\partial}{\partial p}[w\, P(1)] = -w\frac{\partial P(1)}{\partial p} - P(1)\frac{\partial w}{\partial p}, \tag{86}$$

from which, with (68) and (85),

$$a_k = \frac{2\, C_0\, w}{p_k\, P_k(1)\left[\frac{\partial w}{\partial p}\right]_{p=p_k}}. \tag{87}$$

Table 1. Accuracy of simplifications of (83) for different w

Highest power of p kept in (83)	Error in $p_1 \leq$ %	at $w <$
6	0.01	0.5
	0.05	1.5
	0.1	2.6
	0.3	∞
4	0.01	0.08
	0.05	0.2
	0.1	0.3
	0.5	0.7
	1	1.3
	2	2.6
	5	30
	5.35	∞
2	0.01	0.0005
i.e.	0.05	0.003
	0.1	0.006
	0.5	0.03
$p_1 \approx 4\sqrt{\frac{w}{4+3w}}$	1	0.07
	2	0.15
	10	1.7
	15	∞
$p_1 \approx 2\sqrt{w}$	0.01	0.0001
	0.15	0.001
	0.5	0.02
	1	0.04
	2	0.08
	5	0.2
	10	0.4

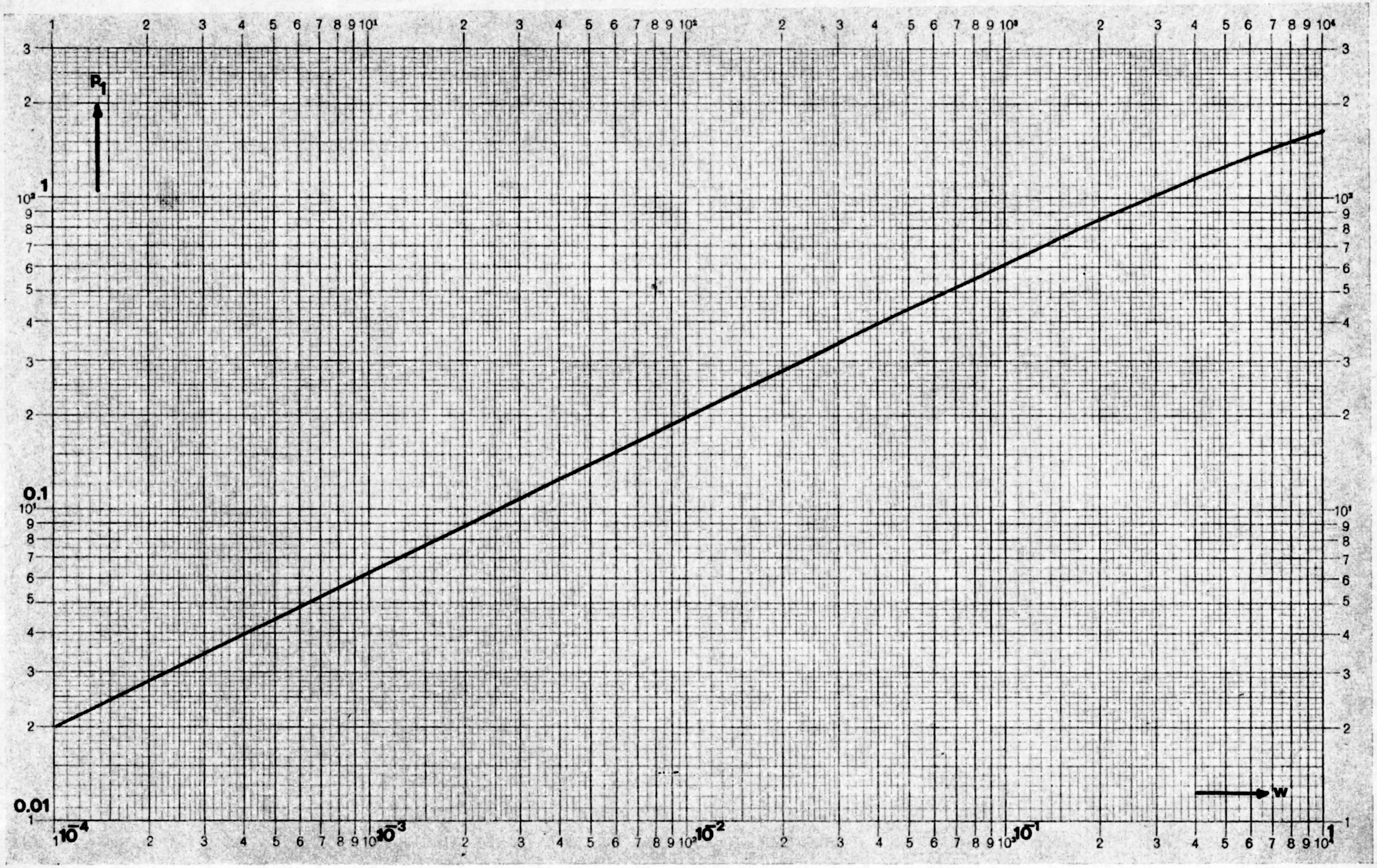

Fig. 7. The first eigenvalue p_1 as a function of w for lower values

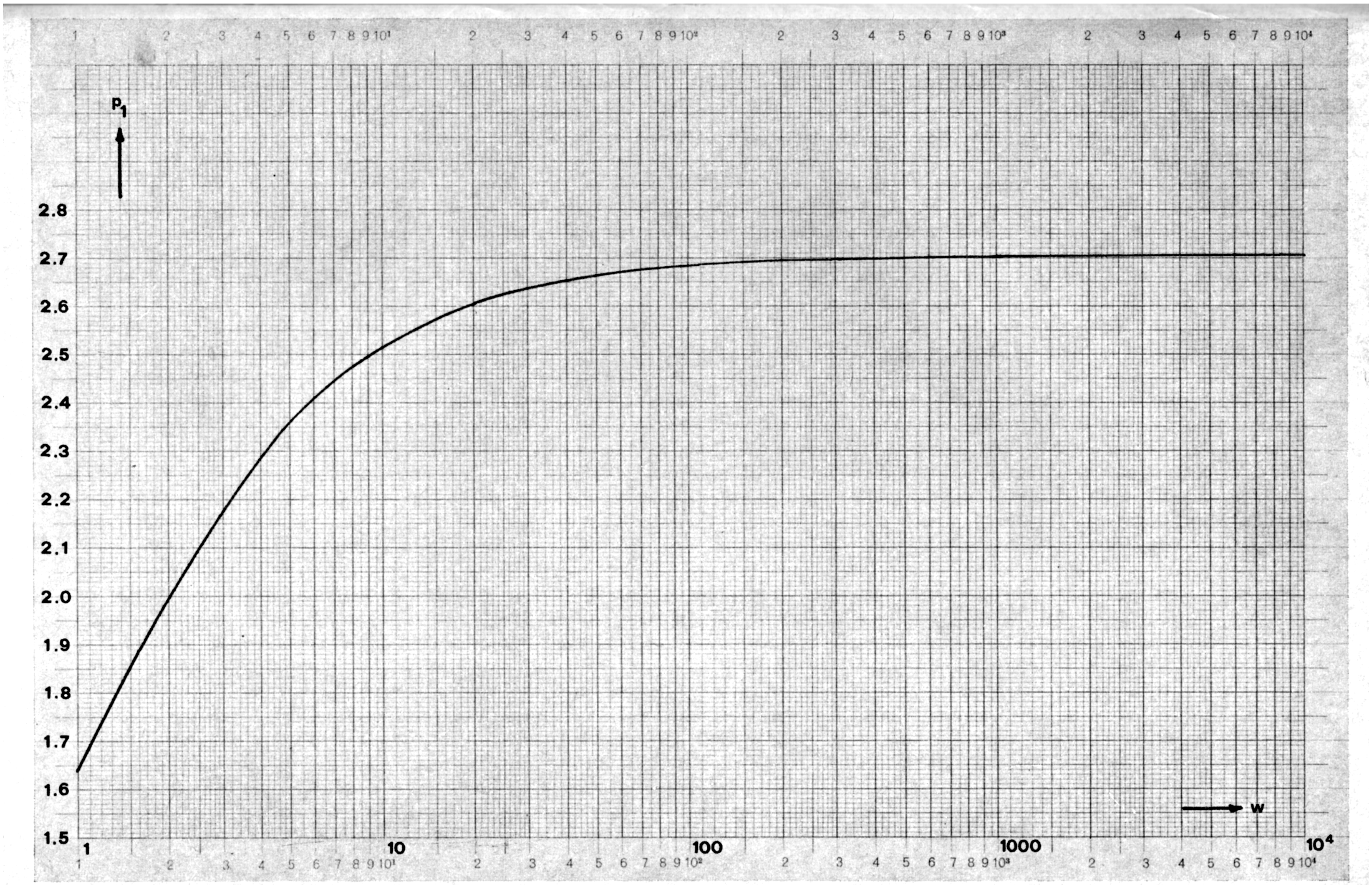

Fig. 8. The first eigenvalue p_1 as a function of w for higher values

This expression is to be inserted in (66) and $\partial w/\partial p$ for $p=p_1$ may be taken from (83). P_1 follows from (74) and (82). For higher values of k an approximative treatment will be given below.

For practical applications, the «cup mixing concentration» C_m, defined by (43), is of more interest. Integration of (66) with use of (71) and (68) gives, with (87),

$$C_m(z) = 8\, w^2\, C_0 \sum_{k=1}^{\infty} \frac{\exp\left[-\dfrac{Dz}{2\bar{v}}\left(\dfrac{p_k}{r_1}\right)^2\right]}{p_k^3 \left[\dfrac{\partial w}{\partial p}\right]_{p=p_k}}. \tag{88}$$

The termwise integration, which has been applied here, is justified by Appendix 2. When $w=\infty$, corresponding to $p_1 = 2.705$, the first term in (88) is, with (83),

$$C_m = 0.82\, C_0\, e^{-3.658Dz/\bar{v}r_1^2} + \ldots, \tag{89}$$

in agreement with (44). When $w \approx 0$, (84) gives

$$C_m \approx C_0\, e^{-2Dzw/\bar{v}r_1^2}, \tag{90}$$

in agreement with (35).

To calculate $\partial w/\partial p$ at $p=p_1$ for use in (87) and (88) one may use (83) to a good approximation:

$$\begin{aligned}\frac{\partial w}{\partial p}&(-0.926930\, p^{10}10^{-8} + 0.145445\, p^8\, 10^{-5} - 0.144043\, p^6\, 10^{-3} + 0.00792101\, p^4 - \\ &- 0.1875\, p^2 + 1) = 0.421880\, p^9\, 10^{-6} - 0.4534896\, p^7\, 10^{-4} + \\ &+ 0.2701824\, p^5\, 10^{-2} - 0.0729168\, p^3 + 0.5\, p + w(0.926930\, p^9\, 10^{-7} - \\ &- 0.116356\, p^7\, 10^{-4} + 0.864258\, p^5\, 10^{-3} - 0.0316840\, p^3 + 0.375\, p).\end{aligned} \tag{91}$$

For further eigenvalues (83) is too approximative and one may instead derive another expression from an approximation for $P(x)$ at $x \approx 1$ according to [33] (which is developed and used in this reference for the eigenvalues of the «FOURIER-R»-series in Chapter 5, but may also be applied to the second kind «FOURIER-P»-series appearing here):

$$P(x) \approx \frac{2}{3}\sqrt{2y}\left[\sin\left(\frac{p\pi}{4}-\frac{\pi}{3}\right) J_{1/3}\left(\frac{p\sqrt{8}\, y^{3/2}}{3}\right) - \sin\left(\frac{p\pi}{4}-\frac{2\pi}{3}\right) J_{-1/3}\left(\frac{p\sqrt{8}\, y^{3/2}}{3}\right)\right], \tag{92}$$

where $y = 1 - x$ and J is the BESSEL function of the first kind and of orders indicated by the indices. With (68) and (92) one finds for the eigenvalue p_k, $k=2, 3, \ldots$, the k: th positive root of

$$w \approx -0.4593\, p^{2/3}\left[1 + \sqrt{3}\, \mathrm{cotg}\left(\frac{p\pi}{4} - \frac{2\pi}{3}\right)\right]. \tag{93}$$

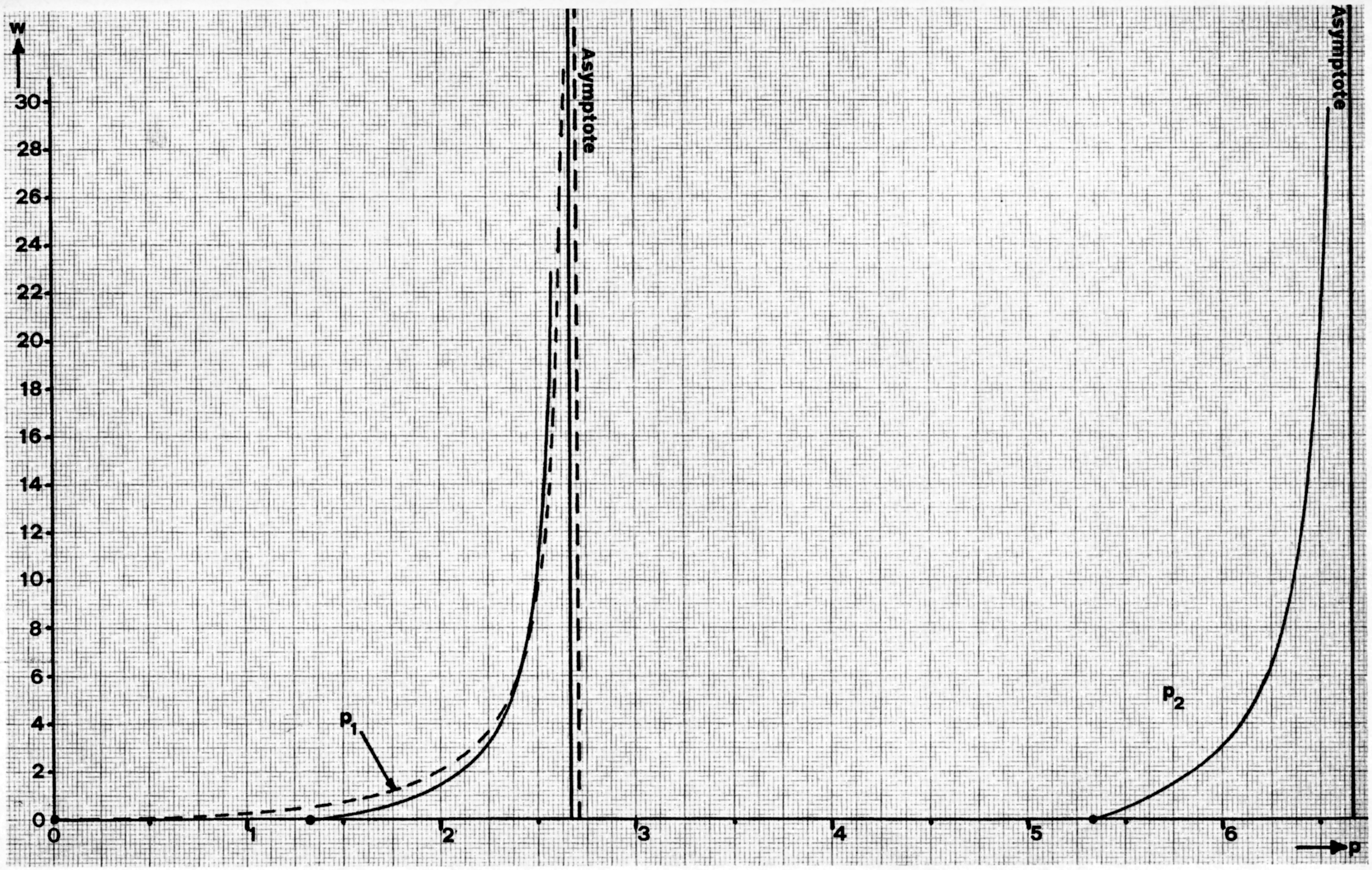

Fig. 9. The second eigenvalue p_2 as a function of w, also showing a comparison between p_1 and the first positive root of eq. (93)

A diagram for p_2 is given in Fig. 9, also showing a comparison between p_1 from (83) and the first positive root of (93). This formula also shows that $p_k \to 4/3 + 4(k-1)$ as $k \to \infty$ when $w < \infty$.
For use in (87) and (88) one also finds, from (93),

$$\frac{\partial w}{\partial p} \approx \frac{2w}{3p} + 0.62481\, p^{2/3} \left[1 + \operatorname{cotg}^2 \left(\frac{p\pi}{4} - \frac{2\pi}{3}\right)\right], \qquad (94)$$

which, again applying (93), may be written as

$$\frac{\partial w}{\partial p} \approx 0.83308\, p^{2/3} + w\left(\frac{2}{3p} + 0.9069\right) + 0.9873\, w^2 p^{-2/3}, \qquad (95)$$

to be used for p_k, $k = 2, 3, \ldots$.
When $w = \infty$, (93) gives $p_2 = 6.667$ in agreement with β_2 in Chapter 5 and with (89) and (95) one finds for the first two terms:

$$C_m(z) = 0.82\, C_0\, e^{-3.658\, Dz/\bar{v}r_1^2} + 0.0971\, C_0\, e^{-22.2\, Dz/\bar{v}r_1^2} + \ldots, \qquad (96)$$

in good agreement with (44). For $w \approx 0$ one finds, with (90), (93) and (95):

$$C_m(z) = C_0\, e^{-2Dzw/\bar{v}r_1^2} + 0.0207\, w^2 C_0\, e^{-14.2\, Dz/\bar{v}r_1^2} + \ldots, \qquad (97)$$

in quite good agreement with (62) in the second term – it is to be expected that the solutions of the cases in this chapter and in Chapter 7 approach each other when $w \to 0$, because the velocity distribution has less influence, the lower the w-value.

9 The functions P(p,x)

The eigenfunctions P_k used in Chapter 8 are solutions of (67) with parameters p_k, determined by (68). For a general discussion one may denote the parameter by p and the solution by $P(p,x)$. Two equivalent power series for this solution were developed in Chapter 8 – a series in powers of x [(72), (73)] and a series in powers of p [(74), (77), (81), (82)]. The functions P are closely related to the BESSEL wave functions $\mathfrak{J}_0(\alpha,\beta,\mathfrak{z})$ [28]; P is a special case of $\mathfrak{J}_0$ with $\alpha = ip$ and $\beta = p$:

$$P(p,x) = \mathfrak{J}_0(ip,p,x) = 1 - \frac{(xp)^2}{4} + \frac{(xp)^4}{64}\left(1 + \frac{4}{p^2}\right) - \frac{(xp)^6}{2304}\left(1 + \frac{20}{p^2}\right) + \ldots, \qquad (98)$$

as is also found from the above mentioned series expansions.

The P-functions are close relatives to the BESSEL functions. It may therefore be of interest to develop P in a series of such functions. First put $\xi = px$ and $P(p,x) = Q(p,px)$ and insert in (67):

$$Q'' + \frac{1}{\xi} Q' + \left(1 - \frac{\xi^2}{p^2}\right) Q = 0. \tag{99}$$

Trying [1]

$$Q = \sum_{n=0}^{\infty} a_n \xi^n J_n(\xi), \tag{100}$$

one finds that such a development can be realized with

$$\begin{cases} a_0 = 1, \\ a_1 = 0, \\ a_2 = \dfrac{1}{2p^2}, \\ \vdots \\ a_n = \dfrac{n-1}{np^2} a_{n-2} - \dfrac{1}{2np^2} a_{n-3}, \\ \vdots \end{cases} \tag{101}$$

if one choses $P(p,0) = Q(p,0) = 1$. For large n this means that $a_n \approx a_{n-2}/p^2$. This gives

$$P(p,x) = J_0(px) + \frac{x^2}{2} J_2(px) - \frac{px^3}{6} J_3(px) + \frac{3x^4}{8} J_4(px) - \dots \tag{102}$$

From (102) one sees that

$$P(p,x) \approx J_0(px) \tag{103}$$

for $0 \leq x \ll 1$, as is also found directly from (67) or (99). According to [33] one further has

$$P(p,x) \approx \sqrt{\frac{2}{\pi px}} \, \frac{\cos\left[\frac{p}{2}\left(x\sqrt{1-x^2} + \arcsin x\right) - \frac{\pi}{4}\right]}{\sqrt[4]{1-x^2}} \tag{104}$$

for a «medium x», $0 < x < 1$, and (92) for $0 < y \ll 1$, where $y = 1 - x$. Here (104) and (92) are asymptotic and therefore hold for large p only ($p \geq p_2$ in practice). (It is interesting to note that (92) reminds strongly on the NICHOLSON formulae [17]. Actually, as an alternative to the derivation in [33], one may divide the last term in (67) by $x^2 \approx 1$ when $x \approx 1$ and obtain a differential equation with the solution $A\, J_{ip}(ipx) + B\, Y_{ip}(ipx)$, from which (92) may be derived by using the NICHOLSON formulae). For $p = p_1$, the first eigenvalue, an approximating polynominal was instead used in Chapter 8, being the first terms of the power series expansion.

A necessary condition for the usefulness of the P-functions is that they form an orthogonal set for $p=p_1, p_2, \ldots$. This will now be proven, especially because the proof also delivers the orthogonality relation which determines the coefficients in a «FOURIER-P»-series. The orthogonality has been proven before for the R-functions of Chapter 6 [11], but the proof will here be extended to their generalizations into the P-functions.

For $P_n = P(p_n, x)$ and $P_m = P(p_m, x)$ one has, from (67),

$$\begin{cases} xP_n'' + P_n' + p_n^2\, x\,(1-x^2)\, P_n = 0, & (105) \\ xP_m'' + P_m' + p_m^2\, x\,(1-x^2)\, P_m = 0, & (106) \end{cases}$$

from which

$$\frac{d}{dx}\,[x(P_n'P_m - P_m'P_n)] = (p_m^2 - p_n^2)\, x\,(1-x^2)\, P_nP_m. \qquad (107)$$

Integration of (107) gives

$$P_n'(1)P_m(1) - P_m'(1)P_n(1) = (p_m^2 - p_n^2)\int_0^1 x(1-x^2)P_nP_m dx, \qquad (108)$$

since P_n and P_m and their derivatives are limited for $x \approx 0$, according to (103). The boundary condition in Chapter 8 is a special case of the more general expression

$$a\, P(1) + b\, P'(1) = 0, \qquad (109)$$

from which

$$b\,(P_n'P_m - P_m'P_n) = 0, \qquad (110)$$

which directly shows that the left side of equation (108) is zero if $b \neq 0$, but this also holds when $b=0$ since (109) then shows that $P(1)=0$. Therefore

$$\int_0^1 x(1-x^2)\, P_nP_m\, dx = 0 \qquad (111)$$

if $n \neq m$. (108) may also be written as

$$\left[\frac{P_n'}{p_m+p_n}\,\frac{P_m-P_n}{p_m-p_n} - \frac{P_n}{p_m+p_n}\,\frac{P_m'-P_n'}{p_m-p_n}\right]_{x=1} = \int_0^1 x(1-x^2)P_nP_m\, dx, \qquad (112)$$

from which, as $p_m \to p_n$,

$$\int_0^1 x(1-x^2)\, P_n^2\, dx = \frac{1}{2p_n}\left[P_n'\,\frac{\partial P}{\partial p} - P_n\,\frac{\partial P'}{\partial p}\right]_{\substack{p=p_n,\\ x=1}} \qquad (113)$$

where P' still means the derivative with respect to x. (111) and (113) may be combined in

$$\int_0^1 x(1-x^2)\,P_nP_m\,dx = \frac{\delta_{nm}}{2p_n}\left[\frac{\partial P_n}{\partial x}\frac{\partial P}{\partial p} - P_n\frac{\partial^2 P}{\partial p\,\partial x}\right]_{\substack{p=p_n,\\ x=1}} \tag{114}$$

where δ_{nm} is the KRONECKER symbol ($\delta_{nm}=1$ if $n=m$ and 0 if $n\neq m$). Hence the P_k-functions of Chapter 8 are orthogonal and (114) gives the relation (70).
That the functions p_k form a closed orthogonal set can be shown in full analogy to the proof that the functions of the FOURIER-BESSEL series of the second kind (cf. Chapter 7) form a closed set (as well as the fact that there is an enumerable infinity of eigenvalues), such as the proof in [20].
For that purpose one may, in analogy to [20], transform (67) with (68) into an integral equation

$$P(x) = p^2\int_0^1 K(x,\xi)\,(1-\xi^2)\,P(\xi)\,d\xi, \tag{115}$$

where the kernel K is the symmetrical GREEN function

$$K = \begin{cases} \dfrac{1}{w} - \ln\xi, & 0\leq x\leq\xi\leq 1, \\[2ex] \dfrac{1}{w} - \ln x, & 0\leq\xi\leq x\leq 1, \end{cases} \tag{116}$$

or, equivalently,

$$\mathfrak{P}(x) = p^2\int_0^1 \mathfrak{K}(x,\xi)\,\mathfrak{P}(\xi)\,d\xi, \tag{117}$$

where

$$\mathfrak{P}(x) = P(x)\sqrt{x(1-x^2)} \tag{118}$$

and

$$\mathfrak{K}(x,\xi) = K(x,\xi)\sqrt{x\,\xi(1-x^2)(1-\xi^2)}. \tag{119}$$

For the detailed proof, [20] is referred to*, merely needing obvious and simple modifications of its proof for the BESSEL functions.
Some further relations for $P(p,x)$ are given in Appendix 4.

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* A correction to [20]: the equation for «p» on page 87 should have $k\Delta$ instead of Δ in the denominators of the integrands.

10 On the neglection of $\partial^2 C/\partial z^2$

According to (13), the following equation holds in the case of POISEUILLE flow in the capillary:

$$2\bar{v}\left[1-\left(\frac{r}{r_1}\right)^2\right]\frac{\partial C}{\partial z}=D\left(\frac{\partial^2 C}{\partial z^2}+\frac{1}{r}\frac{\partial C}{\partial r}+\frac{\partial^2 C}{\partial r^2}\right), \tag{120}$$

taking v from (36). The «cup mixing concentration», defined by (43), here becomes

$$C_m(z)=4\int_0^1 x(1-x^2)\,C(xr_1,z)\,dx. \tag{121}$$

If (120) is integrated, after multiplication by $x=r/r_1$, one has

$$2\bar{v}\frac{\partial C_m}{\partial z}=4D\frac{\partial^2}{\partial z^2}\int_0^1 x\,C(xr_1,z)\,dx-\frac{4\gamma}{r_1}C(r_1,z), \tag{122}$$

where the last term follows from

$$\int_0^{r_1} r\left(\frac{1}{r}\frac{\partial C}{\partial r}+\frac{\partial^2 C}{\partial r^2}\right)dr=\int_{r=0}^{r_1} d\left(r\frac{\partial C}{\partial r}\right)=\left[r\frac{\partial C}{\partial r}\right]_0^{r_1} \tag{123}$$

and the boundary condition (53b).
In (122) one has $\partial C_m/\partial z<0$, $\partial^2 C/\partial z^2\geq 0$ and $C>0$ when $\gamma<\infty$ (except in the entrance region, where the second derivative may be negative, but here the generalized LÉVÊQUE solution will later be applied – see Chapter 11). Therefore the influence of $\partial^2 C/\partial z^2$ is negligible when

$$\frac{\partial^2}{\partial z^2}\int_0^1 x\,C(xr_1,z)\,dx\ll\frac{\gamma}{r_1 D}C(r_1,z). \tag{124}$$

If this inequality is not satisfied, $\partial^2 C/\partial z^2$ cannot be neglected. So far, (124) is a necessary condition. It remains to find out if it is also sufficient when one inserts the solution of (65), which already neglects the actual second derivative.
As $\partial C/\partial z<0$ and $\partial^2 C/\partial z^2\geq 0$ in the actual region, one finds from (120) that the neglection of the second derivative with respect to z leads to a certain underestimation of the concentration at the «downstream» end of the capillary, i.e., it leads to a certain overestimation of the dialysis performance of the capillary. This is the result of a somewhat exaggerated decay of the concentration along the axis, which further leads to a certain overestimation of the second derivative in a region

of lower z-values but a certain underestimation for higher z-values. Still, the boundary concentration $C(r_1, z)$ is everywhere somewhat underestimated. Clearly, (124) is strictly sufficient when the solution of (65) is inserted in the region where the second derivative is overestimated. For higher z-values one can anyway rely on the fact that (124) is well satisfied by the approximative solution if it is so by the exact one. This is what makes (124) a necessary condition, but the exponential nature of the solution indicates that the relative errors in the approximative solutions for concentration and its second derivative should tend to similar values as z grows, so that their influences on (124) tend to cancel. Before almost equal relative errors are reached, the second derivative should be less underestimated than the boundary concentration, exaggerating (124) if the approximative solution is inserted, again making it a sufficient condition.*

If the above discussed approximative solution of (65) is inserted, according to Chapter 8, it turns (124) into

$$\sum_{k=1}^{\infty} a_k \left(\frac{Dp_k^2}{2\bar{v}r_1^2}\right)^2 e^{-Dzp_k^2/2\bar{v}r_1^2} \int_0^1 xP_k(x)\,dx \leqslant \frac{\gamma}{Dr_1} \sum_{k=1}^{\infty} a_k\, e^{-Dzp_k^2/2\bar{v}r_1^2} P_k(1). \tag{125}$$

In the case where the approximation of the two series through their first terms is sufficient (cf. Chapter 11), one finds

$$\left(\frac{Dp_1^2}{2\bar{v}r_1^2}\right)^2 \leqslant \frac{\gamma}{Dr_1} \frac{P_1(1)}{\int_0^1 xP_1(x)\,dx}. \tag{126}$$

According to Chapter 8, one may here put

$$\int_0^1 x\,P_1(x)\,dx \approx 0.5 - 0.0520833\,p_1^2 + 0.00161675\,p_1^4 - 0.238393\,p_1^6\,10^{-4} + \\ + 0.203327\,p_1^8\,10^{-7} - 0.115077\,p_1^{10}\,10^{-8} \tag{127}$$

and

$$P_1(1) \approx 1 - 0.1875\,p_1^2 + 0.00792100\,p_1^4 - 0.144043\,p_1^6\,10^{-3} + \\ + 0.145080\,p_1^8\,10^{-5}, \tag{128}$$

using (74) and (82). Further approximations for higher eigenvalues, using (92), may be inserted for a more exact evaluation of (125) with more terms in the two series.

Examples. Urea in water has $D \approx 0.0009$ cm²/min. If $\gamma = 0.025$ cm/min (which may apply for cellophane capillaries) and $r_1 = 0.45$ mm, (126) gives $0.0213 \leqslant 858$

* Study the effect of an exaggerated p_1 on (126).

at an overall flow of 300 ml/min in a total of 10000 capillaries ($\bar{v}=4.72$ cm/min). For a total flow of 50 ml/min ($\bar{v}=0.787$ cm/min) this becomes $0.766 \ll 858$. For urea in blood $D \approx 0.0002$ cm²/min is probably somewhat underestimated, but leads to $0.00357 \ll 1796$ for 300 ml/min flow or $0.129 \ll 1796$ for 50 ml/min flow with the same γ and dimensions as above.

In this chapter integrals and differentiation symbols have been exchanged a few times. Such operations are justified by the result of Appendix 2, as applied to the solution of (65). The neglection of the second derivative, which was studied here, is generally employed in the studies of forced convections found in literature but a justification in mathematical terms is not given, instead physical reasons are referred to by most authors.

11 The LÉVÊQUE approximation and its generalization for the case of limited wall permeability

The LÉVÊQUE approximation is an asymptotic solution of (13), neglecting $\partial^2 C/\partial z^2$ and based on the velocity distribution (36) (POISEUILLE flow) [8, 23, 39] (cf. [18]). In the case of low concentration one may assume that the shear tension remains constant with z and put, for $y=r_1-r \ll r_1$:

$$\begin{cases} v\dfrac{\partial C}{\partial z}=D\dfrac{\partial^2 C}{\partial y^2}, & (129) \\[2ex] v=2\bar{v}\left[1-\left(\dfrac{r}{r_1}\right)^2\right]\approx 4\bar{v}\dfrac{y}{r_1}, & (130) \end{cases}$$

which actually approximates the actual problem by one of a flat wall and linear velocity distribution. Clearly, such an approximation is applicable only where the concentration remains almost constant within the capillary, except for a layer near the wall – this applies for sufficiently small values of z (near the entrance). The reasoning further assumes that the POISEUILLE flow is developed already at the entrance (the entrance region will be further discussed in a later section). It will be found that the LÉVÊQUE approximation can be used whenever three or more terms of the series (44) would have to be considered. The solution of the problem of Chapter 5 is then simplified to three cases as follows: 1) the first term of (44) is alone a sufficient approximation, 2) the first two terms of (44) form a sufficient approximation and 3) the LÉVÊQUE approximation is a sufficient approximation.

These three cases cover all possibilities of the problem of Chapter 5. Later the LÉVÊQUE approximation will be generalized to the problem of Chapter 8.
Equations (129) and (130) give

$$\frac{4\bar{v}}{r_1}\frac{\partial C}{\partial z}=\frac{D}{y}\frac{\partial^2 C}{\partial y^2}. \tag{131}$$

The transformation $\zeta = yz^{-1/3}$ converts (131) into an ordinary differential equation:

$$D\frac{\partial^2 C}{\partial \zeta^2}=-\frac{4\bar{v}}{3r_1}\zeta^2\frac{\partial C}{\partial \zeta}. \tag{132}$$

As shown in [39], the solution is

$$C=C_w+\frac{C_0-C_w}{(1/3)!}\int\limits_0^{A_0\zeta} e^{-\eta^3}d\eta, \tag{133}$$

where $A_0^3=4\bar{v}/9r_1D$ and $(1/3)! \approx 0.89297$. C_w is here the concentration at $y=\zeta=0$ and C_0 the concentration at $z=0$.
The diffusional flux at the wall, as given by (133), becomes

$$J_w=D\frac{\partial C}{\partial y}\bigg|_{y=0}=(C_0-C_w)\frac{1}{(1/3)!}\left(\frac{4\bar{v}D^2}{9zr_1}\right)^{1/3}, \tag{134}$$

taken positive outwards. To account for a varying C_w, one may first approximate the $C_w(z)$-function by a «stair-case function», having constant C_w-values within certain regions (cf. [39]), such as

$$C_w\approx C_0+\sum_{j=0}^{n}[C_w(z_j)-C_w(z_{j-1})]\,\sigma(z-z_j), \tag{135}$$

defining $C_w(z_{-1})=C_0$. Here z_j, $j=0, 1, \ldots, n$, are constants and $\sigma(z)$ the unit step-function, which is zero for $z<0$ and unity for $z>0$. The above solution can then be stated for each region of constant C_w (according to the approximation) and one finds a change of the flux at the wall, when going from the region $z \in (z_{j-1}, z_j)$ to $z \in (z_j, z_{j+1})$, which amounts to

$$\Delta J_{wj}=(C_{w,j-1}-C_{w,j})\frac{1}{(1/3)!}\left[\frac{4\bar{v}D^2}{9r_1(z-z_j)}\right]^{1/3}, \tag{136}$$

applying (134) and putting $C_w(z)=C_{w,j}$ for $z \in (z_j, z_{j+1})$. The resulting flux through the wall is the sum of all such increments:

$$J_w=\sum_{=0}^{n_1}\Delta J_{wj}, \tag{137}$$

with $z_{n1} < z < z_{n1+1}$. If now $(z_j - z_{j-1}) \rightarrow 0$ for all j, one gets the STIELTJES integral

$$J_w = -\frac{1}{(1/3)!}\left(\frac{4\bar{v}D^2}{9r_1}\right)^{1/3}\int_{\eta=0}^{z}\frac{dC_w(\eta)}{(z-\eta)^{1/3}}, \tag{138}$$

where C_w is the given wall concentration (i.e. no more approximated with a «stair-case») (cf. [39]). The way (138) is derived leads to a STIELTJES integral, but for a continuous $C_w(z)$ it is equivalent to a RIEMANN integral with $dC_w(\eta) = C_w'(\eta)d\eta$.

Generalization for limited wall permeability

In the case of zero concentration outside the capillary, one may put for J_w:

$$J_w = \gamma C_w, \tag{139}$$

where γ is the wall permeation (cf. Chapter 6). (A further generalization to the case of a constant but non-zero concentration outside the capillary is obvious.) Combining (139) with (138) gives an integral equation of the VOLTERRA type:

$$C_w = -\frac{1}{\gamma(1/3)!}\left(\frac{4\bar{v}D^2}{9r_1}\right)^{1/3}\int_{0}^{z}\frac{C'_w(\eta)}{(z-\eta)^{1/3}}\,d\eta \tag{140}$$

(written as a RIEMANN integral because C_w must come out continuous). This equation can be solved by LAPLACE transformation. Introducing the simple notation $\tilde{C}_w(s) = \mathscr{L}\{C_w(z)\}$ (cf. Appendix 3), one finds

$$\tilde{C}_w = -\frac{(-1/3)!\,A\,C_0}{s^{2/3}[s^{1/3}A(-1/3)!-1]}, \tag{141}$$

where $(-1/3)! \approx 1.3540$ and

$$A = \frac{1}{\gamma(1/3)!}\left(\frac{4\bar{v}D^2}{9r_1}\right)^{1/3}. \tag{142}$$

This follows easily from regarding the integral in (140) as a convolution of $C_w'(z)$ with $z^{-1/3}$.

The evaluation of C_w from (141) is given in Appendix 3, but results in a solution which is much too complicated for most practical purposes. Therefore a further approximation will be introduced below, in order to arrive at an expression which is easier to apply in practice.

Since the LÉVÊQUE approximation only applies where the concentration variation inside the capillary is limited to a thin layer near the wall, it is reasonable to assume

$$\frac{\partial C}{\partial y} \gg \frac{\partial C}{\partial z} \tag{143}$$

for most practical cases. This means that one may neglect the variation of C_w with z (locally) and solve J_w from (134) and (139):

$$J_w \approx \frac{\gamma A\, C_0}{A + z^{1/3}}, \tag{144}$$

with A given by (142). Now the same amount of the solute must leave the capillary through the wall as the net delivery through the flow:

$$\int_0^z 2\pi r_1\, J_w\, dz = \pi r_1^2\, \bar{v}\, [C_0 - C_m(z)], \tag{145}$$

since $\pi r_1^2 C_0 \bar{v}$ enters the capillary at $z = 0$ and $\pi r_1^2 C_m(z) \bar{v}$ leaves the capillary section extending to z, according to (43). From (145) and (144) follows:

$$1 - \frac{C_m}{C_0} \approx \frac{3\gamma A}{r_1 \bar{v}} \left[z^{2/3} - 2Az^{1/3} + 2A^2 \ln\left(1 + \frac{z^{1/3}}{A}\right)\right], \tag{146}$$

with A given by (142). It is interesting to note that (146) gives the same expression (for the analogous thermal problem) as the one in [18] when $\gamma \to \infty$. Another check is that when $\bar{v}$ is very large, one may put $C_m \approx C_0$ and thus $J_w \approx \gamma C_0$, giving as a further approximation

$$1 - \frac{C_m}{C_0} \approx \frac{2\gamma z}{r_1 \bar{v}}, \tag{147}$$

from (145), also resulting from (146) for large $\bar{v}$.

A comparison of the LÉVÊQUE approximation with the GRAETZ solution (44) is given in [18] (for the analogous thermal problem) in a graph (Fig. 22—6 in [18]). If the diagram is completed with curves for the first term of (44) and the sum of the two first terms of (44), one finds that in the case $\gamma = \infty$ the one-term approximation of (44) is applicable for $C_m \leq 0.63\ C_0$, the two-term approximation for $C_m \leq 0.85\ C_0$ and the LÉVÊQUE approximation is applicable for $C_m \geq 0.85\ C_0$. (These rules are here simply so defined that no difference between the exact solution and the one-term approximation is seen in the diagram referred to when $C_m \leq 0.63\ C_0$ and that the two-term approximation and the LÉVÊQUE approximation give equal values at $C_m = 0.85\ C_0$, both being close to the exact curve here and the LÉVÊQUE curve following the exact one thereafter).

For the case $\gamma \approx 0$ the solution for bulk flow (constant v) and the solution for POISEUILLE flow (parabolic v) both reduce to (35). It is interesting to note that (147) is an approximation of (35) for small z, valid with an error less than 10% when $z < 0.392\ r_1\bar{v}$ and with an error less than 1% when $z < 0.135\ r_1\bar{v}$, corresponding to $C_m > 0.608\ C_0$ and $C_m > 0.865\ C_0$, resp. For $C_m = 0.85\ C_0$ according to (35), it is $0.838\ C_0$ according to (147).

A more general study of the applicability of the different approximations is presented in Appendix 5.

12 More detailed study of the diffusion through the capillary wall

The equation for the diffusion in the wall in the stationary case follows from (13) with $v = 0$:

$$\frac{\partial^2 C}{\partial z^2} + \frac{\partial^2 C}{\partial r^2} + \frac{1}{r}\frac{\partial C}{\partial r} = 0, \tag{148}$$

and the boundary conditions are

$$\begin{cases} C = C_w(z), & r = r_1, \quad (149a) \\ C = 0, & r = r_2, \quad (149b) \end{cases}$$

assuming zero concentration outside the capillary. r_1 is the inner and r_2 the outer radius of the capillary wall. If the wall is thin, $r_2 - r_1 \ll r_1$, one can obviously neglect $\partial^2 C/\partial z^2$ because this derivative becomes much smaller than $\partial C/r\partial r$. The solution of (148) and (149) is then

$$C = C_w(z)\frac{\ln \frac{r_2}{r}}{\ln \frac{r_2}{r_1}}, \tag{150}$$

where $r_1 \leq r \leq r_2$. From this follows the diffusion flux at the inner wall surface

$$J_w = -D_w \left.\frac{\partial C}{\partial r}\right|_{r=r_1} = \frac{D_w}{r_1 \ln \frac{r_2}{r_1}} C_w(z), \tag{151}$$

where D_w is the diffusion constant for the wall material. This flux must be the same as the one resulting from the solution inside the capillary:

$$J_w = -D \left.\frac{\partial C}{\partial r}\right|_{r=r_1-0} = -D_w \left.\frac{\partial C}{\partial r}\right|_{r=r_1+0}. \tag{152}$$

This gives the wall permeation (51).

Consideration of the axial diffusion

If one introduces a new concentration variable C_a according to

$$C = C_w(z)\,\frac{\ln\frac{r_2}{r}}{\ln\frac{r_2}{r_1}} + C_a, \tag{153}$$

(148) gives

$$\frac{\partial^2 C_a}{\partial z^2} + \frac{\partial^2 C_a}{\partial r^2} + \frac{1}{r}\frac{\partial C_a}{\partial r} = -C_w''\,\frac{\ln\frac{r_2}{r}}{\ln\frac{r_2}{r_1}}, \tag{154}$$

and (149) the boundary conditions

$$\begin{cases} C_a = 0, \quad r = r_1, & (155a) \\ C_a = 0, \quad r = r_2. & (155b) \end{cases}$$

The solution is

$$C_a = \sum_{k=1}^{\infty} A_k(z)\left[J_0(\lambda_k r) - Y_0(\lambda_k r)\,\frac{J_0(\lambda_k r_1)}{Y_0(\lambda_k r_1)}\right], \tag{156}$$

where J_0 and Y_0 are BESSEL functions of zero order and first and second kind, resp. The eigenvalues λ_k are the positive roots of

$$J_0(\lambda r_1)\,Y_0(\lambda r_2) - J_0(\lambda r_2)\,Y_0(\lambda r_1) = 0 \tag{157}$$

(it is easy to show that $\lambda = 0$ is not an eigenvalue). The coefficient functions $A_k(z)$ are determined by inserting (156) in (154), which leads to

$$A_k'' - \lambda_k^2 A_k = -C_w'' a_k, \tag{158}$$

where the a_k are the FOURIER coefficients in the development of $\ln(r_2/r) / \ln(r_2/r_1)$ according to the actual orthogonal system of J_0, Y_0 and λ_k, given by (156) and (157).

The solution of (158) is

$$A_k = A_{1k}\,e^{-\lambda_k z} + A_{2k}\,e^{\lambda_k z} + A_{pk}, \tag{159}$$

where $A_{pk}(z)$ is a particular solution, determined by $C_w(z)$, and $A_{2k} = 0$ since one must have $C_a \to 0$ as $z \to \infty$.

As was seen above, one may well approximate $C_w(z)$ by an exponential function, except for small values of z:

$$C_w \approx C_{0w}\,e^{-az}, \tag{160}$$

giving

$$A_{pk} \approx \frac{C_{0w} a_k a^2}{\lambda_k^2 - a^2}\,e^{-az}. \tag{161}$$

For an estimation, one may here take the values of C_{ow} and a as determined by the first term of (54) for $r=r_1$, with the coefficient given by (57), since this remains within the same order of magnitude as the exact solution.

Thus, putting together (153), (156), (159), (160), (161), (54) and (57), one finds for $z \gg \lambda_1^{-1}$ (so that $A_k \approx A_{pk}$, assuming $\lambda_1 > a$):

$$C \approx C_w \left\{ \frac{\ln \frac{r_2}{r}}{\ln \frac{r_2}{r_1}} + a^2 \sum_{k=1}^{\infty} \frac{a_k}{\lambda_k^2 - a^2} \left[J_0(\lambda_k r) - Y_0(\lambda_k r) \frac{J_0(\lambda_k r)}{Y_0(\lambda_k r)} \right] \right\}, \quad (162)$$

where $a \approx Ds_1^2/vr_1^2$ and $0 \leq s_1 \leq 2.4048$. Since the a_k are the FOURIER coefficients for the first term in the major bracket, the second term (the sum) is negligible when

$$2\left[\frac{D}{v}\left(\frac{s_1}{r_1}\right)^2\right]^2 \ll \lambda_1^2. \quad (163)$$

According to [17] the value of $\lambda_1 r_1$ is 15.7 for $r_2/r_1 = 1.2$ and 6.27 for $r_2/r_1 = 1.5$ and 3.12 for $r_2/r_1 = 2.0$. Therefore assuming $z \gg \lambda_1^{-1}$ before (162) is not a severe limitation. The criterion (163) may be rewritten as

$$2\left(\frac{\gamma}{v}\right)^2 \ll \left[\frac{\lambda_1 r_1 w}{s_1^2(w)}\right]^2, \quad (164)$$

where $s_1(w)$ may be taken from (59). According to Chapter 7, one has $s_1^2/w \geq 2$ and a lower limit for the right side of (164) is therefore $0.25(\lambda_1 r_1)^2$. For an example of $D = 0.0009$ cm²/min (urea in water), $\gamma = 0.025$ cm/min (fits in order of magnitude to practical cellophane capillaries), $r_1 = 0.45$ mm and $\bar{v} = 4.72$ cm/min (corresponding to a total flow of 300 ml/min in 10000 capillaries, which may be plausible for a capillary kidney) one finds $w = 1.15$ and $s_1 = 1.33$. This gives $(\lambda_1 r_1)^2 \gg 1.2 \cdot 10^{-4}$ in (164), which certainly allows for an extremely thick capillary wall before any consideration of the axial diffusion in the wall is necessary [cf. the values given after (163)]. (This also justifies the assumption $\lambda_1 > a$.)

This shows that for any practical application to the capillary artificial kidney, one may apply the boundary condition (51) without hesitation. The large difference between the right and left sides of (164) in such applications well justifies the use of the estimation (160), because even when this estimation is quite a rough approximation, it is here sufficiently good for showing that the sum in (162) is negligible.

13 The influence of ultrafiltration on the wall permeation

In hemodialysis it is generally desired to achieve a certain controlled ultrafiltration through the separating membrane. Experiences with capillary artificial kidneys [32, 36] show that a controlled ultrafiltration through the walls of the capillaries is readily achieved. This will, however, have a certain influence on the wall permeation γ, as will be found below.

For medical reasons, it is not advisable to have a substantial change of hematocrit and protein concentration as the blood passes along the conduits of a dialyzer. One may therefore assume

$$\Phi_u \ll \Phi, \tag{165}$$

where Φ is the inflow of fluid into a capillary and Φ_u the total ultrafiltration flow of fluid through its wall. As the latter flow must satisfy the equation of continuity, one has, in the stationary case:

$$\Phi_u = \bar{v}_u \, 2\pi r L = \text{const.}, \tag{166}$$

where $\bar{v}_u$ is the mean (over z) ultrafiltration flow velocity at radius r in the wall and L the total capillary length. Therefore one may put

$$\bar{v}_u = \frac{U}{r}, \tag{167}$$

where U is a constant, $U = \Phi_u/2\pi L$ according to (166).

(165) means that the ultrafiltration does not change the situation inside the capillary directly, but only indirectly via its influence on the wall permeation.

If one assumes, for simplicity (cf. the end of this chapter) that the ultrafiltration flow velocity is independent of z and hence everywhere in the wall amounts to $\bar{v}_u$, the differential equation for the diffusion in the wall here follows from (12) with $v_r = \bar{v}_u$ and $v_z = 0$:

$$D_w \left(\frac{\partial^2 C}{\partial r^2} + \frac{1}{r} \frac{\partial C}{\partial r} \right) = \bar{v}_u \frac{\partial C}{\partial r}, \tag{168}$$

where D_w is the diffusion constant for the wall material. (As in the previous chapter, one may well neglect the axial derivative and also axial components of the ultrafiltration flow). The boundary conditions are again given by (149) and it follows that

$$C = C_w \frac{r_2^{U/D_w} - r^{U/D_w}}{r_2^{U/D_w} - r_1^{U/D_w}}, \tag{169}$$

giving the diffusion flux

$$J_w = -D_w \frac{\partial C}{\partial r} \bigg|_{r = r_1 + 0} = \frac{U}{r_1} \frac{C_w}{\left(\frac{r_2}{r_1} \right)^{U/D_w} - 1} \tag{170}$$

at the inner surface of the wall, which approaches (151) as $U \to 0$. The total flux through the inner wall surface is this diffusion flux plus the amount of the solute carried along with the ultrafiltration flow per unit surface: $C_w \bar{v}_u(r_1)$. This gives the wall permeation

$$\gamma = \frac{J_w}{C_w} + \frac{U}{r_1} = \frac{U}{r_1} \frac{\left(\frac{r_2}{r_1}\right)^{U/D_w}}{\left(\frac{r_2}{r_1}\right)^{U/D_w} - 1}, \tag{171}$$

applicable as equivalent wall permeation to the previous problems, neglecting the influence on the velocity distribution inside the capillary, due to (165), so that the whole influence of the ultrafiltration is represented by this equivalent permeation. γ according to (171) approaches (51) as $U \to 0$. For $h = r_2 - r_1 \ll r_1$ this gives

$$\gamma \approx \frac{D_w}{h} + \frac{U}{r_1}. \tag{172}$$

Putting $v_r = \bar{v}_u$ in (168) means a certain approximation, which should in any case lead to a reasonable estimation of the influence of the ultrafiltration. Of course the true v_r in the wall is a linear function of z, decreasing towards the far end of the capillary as it is proportional to the pressure difference over the wall, which clearly decreases linearly with increasing z. An exact solution, considering the variation of v_r with z, would change the solution in Chapter 8 to a considerably more complicated one (as the equivalent γ then varies with z).

As discussed in [39] for the analogous thermal problem, one may state the diffusion flux from the surface of a tubular flow with a prescribed surface concentration $C_w(z)$ by way of a generalization of the GRAETZ solution reviewed in Chapter 5. This leads to an integral equation

$$J_w(z) = \frac{D}{r_1} \sum_{k=1}^{\infty} A_k e^{-\alpha_k D z/\bar{v} r_1^2} \int_{\eta=0}^{z} e^{\alpha_k D \eta/\bar{v} r_1^2} \, dC_w(\eta), \tag{173}$$

(stated as a STIELTJES integral, cf. Chapter 11), where $\alpha_1 = 3.658$, $\alpha_2 = 22.178$, $\alpha_3 = 53.05, \ldots$ and $A_1 = 1.499$, $A_2 = 1.078$, $A_3 = 0.358, \ldots$. Like in Chapter 11, this is an integral equation for $C_w(z)$ since $J_w(z) = \gamma(z)\, C_w(z)$, but not easy to solve. (The solution in the case of a constant γ is given by (66) for $r = r_1$, although derived in a different way.)

A step toward the solution of (173) is to perform a LAPLACE transformation. In this way, the integral equation will below be converted to an ordinary differential equation for the transform $\tilde{C}_w(s)$ of $C_w(z)$. The final steps toward a final solution are very complicated and will be left out.

The pressure drop along the capillary is (POISEUILLE's law)

$$\Delta p = \Phi \frac{8\mu L}{\pi r_1^4}, \tag{174}$$

where μ is the viscosity. From this, one easily derives

$$v_u(r_1, z) = a - bz, \tag{175}$$

where

$$\begin{cases} a = \Phi_u \dfrac{p_{out} - p_o + 8\Phi\mu L/\pi r_1^4}{2\pi r_1(p_{out} - p_o)L + 8\Phi\mu L^2/\pi r_1^3}, & (176a) \\[2ex] b = \Phi \dfrac{8\mu}{\pi r_1^4} \dfrac{\Phi_u}{2\pi r(p_{out} - p_o)L + 8\Phi\mu L^2/\pi r_1^3}, & (176b) \end{cases}$$

if p_{out} is the pressure inside the capillary at the outlet end and p_o the pressure around the capillary (assumed constant – a generalization to a linear variation of p_o along the capillary is obvious). With (167) and (172) one then obtains (because the influence of axial ultrafiltration flow components can be neglected), when $r_2 - r_1 \ll r_1$,

$$\gamma(z) = a_1 - bz, \tag{177}$$

where

$$a_1 = \frac{D_w}{h} + a. \tag{178}$$

Hence, using the LAPLACE transform notation introduced in Chapter 11 (and Appendix 3):

$$\tilde{J}_w(s) = \mathscr{L}\{(a_1 - bz)C_w(z)\} = a_1\tilde{C}_w(s) + b\tilde{C}_w'(s), \tag{179}$$

so that (173) transforms into

$$a_1\tilde{C}_w + b\tilde{C}_w' = \frac{D}{r_1}(s\tilde{C}_w - C_o)\sum_{k=1}^{\infty} \frac{A_k}{s + \dfrac{\alpha_k D}{\bar{v} r_1^2}}, \tag{180}$$

since the integral can be seen as a convolution between C_w' and a series of exponentials (C_w must be continuous and therefore one may regard the integral as a RIEMANN one – cf. Chapter 11).

Equation (180) can be solved in terms of the solution for a constant γ. For $b = 0$ the solution C_{w1} of (180) is known from Chapter 8 and the infinite sum in (180) can be expressed in terms of C_{w1}:

$$\sum_{k=1}^{\infty} \frac{A_k}{s + \dfrac{\alpha_k D}{\bar{v} r_1^2}} = \frac{a_1 r_1 \tilde{C}_{w1}}{D(s\tilde{C}_{w1} - C_o)}, \tag{181}$$

which, inserted into (180), leads to

$$b\tilde{C}_w'(s\tilde{C}_{w1}-C_o)=a_1C_o(\tilde{C}_w-\tilde{C}_{w1}), \tag{182}$$

with the solution

$$\tilde{C}_w=\frac{a_1C_o}{b}\left(A_o-\int_0^s e^{-g(s)}\frac{\tilde{C}_{w1}}{s\tilde{C}_{w1}-C_o}ds\right)e^{g(s)}, \tag{183}$$

where

$$g(s)=\frac{a_1C_o}{b}\int_0^s\frac{ds}{s\tilde{C}_{w1}-C_o} \tag{184}$$

and the constant A_o is so chosen that $s\tilde{C}_w \rightarrow C_o$ when $s\rightarrow\infty$.
The major problem here is to find the inverse transform C_w of $\tilde{C}_w$, which will, however, not be sought here, since one reason for this study is to demonstrate the complexity of a more exact solution as a motivation for applying (171) or (172) in practical cases. Another reason is that it gives a mathematical introduction to the next chapter.

14 The general case of varying concentration outside the capillary

In the previous chapters the concentration outside the capillary was assumed to be zero (or constant). The general case of a varying concentration $C_1(z)$ outside the wall can be solved from (173) by using

$$J_w(z)=\gamma[C_w(z)-C_1(z)] \tag{185}$$

in the case of a constant γ. LAPLACE transformation gives

$$\gamma(\tilde{C}_w-\tilde{C}_1)=\frac{D}{r_1}(s\tilde{C}_w-C_o)\sum_{k=1}^{\infty}\frac{A_k}{s+\dfrac{\alpha_kD}{\bar{v}r_1^2}} \tag{186}$$

[cf. (180)]. The general solution can be expressed in terms of the special solution $C_{w2}(z)$ for the case $C_1=0$, known from Chapter 8, which gives the expression (181) for the infinite sum above, putting $a_1=\gamma$ and $\tilde{C}_{w1}=\tilde{C}_{w2}$. With this inserted into (186), one finds

$$\tilde{C}_w=\tilde{C}_{w2}-\frac{1}{C_o}\tilde{C}_1(s\tilde{C}_{w2}-C_o), \tag{187}$$

since $C_{w2}(+0) = C_o$,

$$C_w = C_{w2} - \frac{1}{C_o} \int_0^z C_1 (z - \zeta) C'_{w2}(\zeta)\, d\zeta. \tag{188}$$

e «mixing cup concentration» C_m, defined by (43), can be obtained from C_w by ng the transport balance equation (145). LAPLACE transformation of this equa- n gives, with (185),

$$\frac{2}{s} \tilde{J}_w = \frac{2\gamma}{s} (\tilde{C}_w - \tilde{C}_1) = r_1 \bar{v} \left(\frac{1}{s} C_o - \tilde{C}_m \right). \tag{189}$$

lving for $\tilde{C}_m$ gives, after inverse transformation,

$$C_m = C_o - \frac{2\gamma}{r_1 \bar{v}} \int_0^z (C_w - C_1)\, dz. \tag{190}$$

instead, $\tilde{C}_w$ is eliminated between (187) and (189), one finds

$$\tilde{C}_m = \tilde{C}_{m2} - \frac{1}{C_o} \tilde{C}_1 (s \tilde{C}_{m2} - C_o), \tag{191}$$

iere

$$\tilde{C}_{m2} = \frac{1}{s} \left(C_o - \frac{2\gamma}{r_1 \bar{v}} \tilde{C}_{w2} \right), \tag{192}$$

, C_{m2} is the solution in the case $C_1 \equiv 0$, known from Chapter 8, as is seen from 39). This gives

$$C_m = C_{m2} - \frac{1}{C_o} \int_0^z C_1(z - \zeta) C'_{m2}(\zeta)\, d\zeta, \tag{193}$$

ce $C_{m2}(+0) = C_o$.

the still more general case of a varying γ, (186) is considerably more com- cated since the term on the left side becomes a complex convolution between $\tilde{\gamma}$ d $C_w - C_1$, turning (186) into a complex integral equation. This equation can, wever, be simplified in certain special cases. Examples of such cases are a early varying γ (treated in Chapter 13 for $C_1 \equiv 0$), an exponentially varying γ hich turns (186) into a difference equation] or a sinusoidally varying γ (which 'es a more complicated difference equation).

15 On the flow velocity profile and entrance regions for blood

Although blood is a non-NEWTONian fluid, it can approximately be treated as NEWTONian in many practical cases, provided that a proper value of the viscosity is used (depending upon the tube diameter, the hematocrit and the temperature) [31].

A simple check of the validity of this approximation in the analysis of a capillary kidney may be done, using formulae by TAYLOR [37]. From the cited reference may be derived, as expression for the velocity distribution at steady flow in a rigid tube:

$$v = \frac{r_1^2 \Delta p}{8L\mu_\infty}\left\{1-\left(\frac{r}{r_1}\right)^2 - \frac{7}{6}\left[1-\left(\frac{r}{r_1}\right)^{3/2}\right]\left(1-\frac{\mu_\infty}{\mu_a}\right)\right\}, \tag{194}$$

where Δp is the pressure difference between the ends of the tube, L its length, μ_∞ the asymptotic viscosity of the blood for infinite tube radius and μ_a its apparent viscosity for the actual radius r_1. The formula is valid as long as not $\mu_a \gg \mu_\infty$, say, for $\mu_a \leq 3\ \mu_\infty$ (cf. [37]). The apparent viscosity is further given approximately by [37]

$$\mu_a \approx \mu_\infty\left(1+\sqrt{\frac{L}{r_1 \Delta p}}\right), \tag{195}$$

for Δp in dynes/cm² and using the same units for L and r_1. From this one finds an apparent viscosity at $\Delta p = 100$ mm Hg of about 1.028 μ_∞ for a tube of 10 cm length and 1 mm radius and 1.09 μ_∞ for a capillary of the same length and 0.1 mm radius. All attempts to the construction of capillary artificial kidneys hitherto known have used capillaries with an inner radius of about 0.1 mm or more. It may therefore be concluded, from (194) and (195), that the flow profile in steady flow is to a good approximation parabolic in the capillaries of such an artificial kidney. (As will be clear from later discussions, a much smaller capillary radius than 0.1 mm would hardly be economical due to the very high number of parallel capillaries then needed in the dialyzer.

In the case of a pulsatile flow, it may further be concluded that the mean velocity (over time) is parabolically distributed, since, as was found above, the blood behaves nearly Newtonian in capillary dialyzers and the capillaries may be regarded as rigid tubes. Therefore the flow state may be well approximated by the NAVIER-STOKES equation for a rigid tube [31]:

$$\frac{\partial v_t}{\partial t} = -\frac{1}{\rho}\frac{\Delta p}{L} + \frac{\mu}{\rho r}\frac{\partial}{\partial r}\left(r\frac{\partial v_t}{\partial r}\right), \tag{196}$$

where v_t is the time-varying velocity. At steady-state pulsatile flow, an integration of both sides of (196) over a whole period with respect to time yields

$$0 = -\frac{\Delta p}{\rho L} + \frac{\mu}{\rho r}\frac{\partial}{\partial r}\left(r\frac{\partial v}{\partial r}\right), \tag{197}$$

where v is the mean value over time of the velocity at radius r. (197) is the differential equation of the POISEUILLE flow condition and hence gives a parabolically distributed v.

The entrance region is the length of the capillary, from the entrance end, where the flow profile differs from the fully developed parabolic one in the (worst) case of a uniformly distributed entrance velocity. In a capillary kidney, the REYNOLDS number is always well below unity and therefore the entrance region extends only to about 1.3 r_1, according to [21, 24] and [25]. This is about the length at the entrance end which is molded into an end-plate for mounting purposes and therefore the POISEUILLE flow condition (for the time-mean velocity) is fully developed where the dialysis begins.

Thus the assumption of POISEUILLE flow all along the capillary, adopted in the previous chapters, is justified by the theory of TAYLOR.

BEFORE STUDYING THE FOLLOWING CHAPTER: PLEASE READ THE NOTE ON THE BIBLIOGRAPHY PAGE RIGHT BEFORE THE CONTENTS PAGE!

16 On the optimization of a capillary dialyzer

For a sufficiently long capillary dialyzer (length L), one may approximate the «mixing cup concentration» C_m at the outlet end by a single exponential function. The clearance of the dialyzer is defined as the portion Φ_c of the total mean inflow Φ at its inlet end which is «cleared» from the solute:

$$(\Phi - \Phi_c)C_o = \Phi C_m, \tag{198}$$

or, with the first term of (88),

$$\Phi_c = \Phi\,(1 - a_1\, e^{-DLp_1^2/2\bar{v}r_1^2}), \tag{199}$$

where $1 > a_1(w) > 0.82$ (cf. Appendix 5). Let N be the total number of parallel capillaries. Since then $\Phi = N\pi r_1^2\bar{v}$, one may write

$$\Phi_c = \Phi\,(1 - a_1\, e^{-\pi DLNp_1^2/2\Phi}). \tag{200}$$

Here one has

$$N\frac{\pi r_1^4\overline{\Delta p}}{8\mu L} < \Phi < \Phi_o, \tag{201}$$

where $\overline{\Delta p}$ is the mean arterio-venous pressure difference (mean value over time) at the connection of the dialyzer to the vascular system and without the load effect of the shunting by the dialyzer («open circuit voltage») and Φ_0 is the maximal mean flow which can be delivered by the vascular system at the connection mentioned (the flow – «short circuit current» – in a zero flow resistance shunt at this connection)*. μ is the viscosity of the blood and r_1 the radius of the capillaries. One may call the state *pressure limited* at the lower end of this Φ-range and *flow limited* at the higher end.

Before further discussion of optimization, it will be shown that the flow-limited case gives the highest clearance Φ_c and therefore should be aimed at by realizing a sufficiently low flow resistance in the dialyzer. The derivative of Φ_c with respect to Φ is

$$\frac{\partial \Phi_c}{\partial \Phi} = 1 - a_1\, e^{-DLN\pi p_1^2/2\Phi}\left(1 + \frac{DLN\pi p_1^2}{2\Phi}\right) > 1 - a_1 > 0, \quad (202)$$

since

$$1 + \frac{DLN\pi p_1^2}{2\Phi} < e^{DLN\pi p_1^2/2\Phi}. \quad (203)$$

Hence Φ_c increases with Φ in any case and the maximum flow Φ_0 should be approached through proper design.

Requierements on artificial kidney

The clearance Φ_c should, in principle, be as high as possible, although an upper limit is, in praxis, set by the risk for complications through the disequilibrium syndrome (which is caused by too large an osmotic pressure difference between the cerebrospinal fluid and the blood, resulting from a too rapid removal of wastes from the blood).

The clearance can, however, easily be reduced and controlled through reducing the concentration difference over the dialyzing membrane by adding certain amounts of the waste solutes to the rinsing fluid. Therefore a disequilibrium syndrome is easily avoided clinically and, from technical considerations, one should require the maximum possible Φ_c as one optimization criterion.

Another requirement is that the volume

$$V = \pi r_1^2 LN \quad (204)$$

* Φ_0 may be taken at the distal ends of the connection tubings instead, when their flow resistances are not negligible. This includes their influences in the «source». The following optimization procedure is valid for external shunts, aiming at a pump-less operation of the dialyzer. With an internal fistula, a pump is required anyway, unless some kind of fistula compression can be used.

of the dialyzer should be minimized in order to reduce or eliminate the need for priming with transfusion blood.

A third requirement is, as found above, that the flow-limited case should be approached as much as possible by keeping the flow resistance

$$R = \frac{8\mu L}{N\pi r_1^4} \tag{205}$$

sufficiently low.

The requirement of a high Φ_c in the flow-limited case $\Phi = \Phi_0$ is equivalent to requiring as high a value as possible of LNp_1^2 [see (200)]. The derivative of this quantity with respect to r_1 is

$$\frac{\partial(LNp_1^2)}{\partial r_1} = \frac{2p_1V}{\pi r_1^3}\left(w\frac{dp_1}{dw} - p_1\right), \tag{206}$$

since $w = \gamma r_1/D$. In this equation a constant V has been assumed [cf. (204)]. As is seen from Appendix 5, the bracket in (206) is always negative. This means that one should realize as small a radius r_1 as possible.

The optimization procedure which evolves from the above considerations is to chose as small a radius r_1 as is practically and economically realizable and as high a volume V as is physiologically acceptable without priming the dialyzer with transfusion blood (bearing in mind that the dialysis treatment is repeated two or three times a week and that the patient each time looses a certain fraction of the blood contained in the dialyzer and its connecting tubings – the main part of it can be returned to the patient, but some remains sticking to the internal surfaces). Finally the flow-resistance R should be chosen as high as is acceptable with respect to an approximative realization of the flow-limited case. With these choices made, one finds, from (204) and (205):

$$L = \frac{r_1}{2}\sqrt{\frac{VR}{2\mu}} \tag{207}$$

and

$$N = \frac{2}{\pi r_1^3}\sqrt{\frac{2\mu V}{R}}. \tag{208}$$

The wall thickness $h = r_2 - r_1$ should be chosen as small as is practically and economically realizable in order to keep γ, and thereby $w = \gamma r_1/D$, as high as possible. One may also add a requirement that the diffusion coefficient D_w of the wall material should, for the same reason, be as high as possible, but limited choices of workable and blood-compatible materials for the fabrication of capillaries leave few alternatives in respect to this requirement.

A numerical example

It seemes as if a practical lower limit for the radius r_1 at present (1971) lies around 0.1 mm and a lower limit for the wall thickness h around 10 μ. A volume V of 50 cm^3 seems quite acceptable from clinical aspects. The flow in a QUINTON-SCRIBNER or BRESCIA-CIMINO shunt may fall in the range of 200—800 ml/min. If the non-shunted arterio-venous pressure difference is taken as 100 mm Hg, this corresponds to a «source resistance» of 0.2 (mm Hg) min/$cm^3 = 1.6 \cdot 10^4$ g/cm^4s at the mid-range shunt flow of 500 ml/min. One may require the resistance R to be a tenth of this value: $R = 1.6 \cdot 10^3$ g/cm^4s. The viscosity of the blood may be taken as 3 cp at about 50% hematocrit.
If these values are inserted in (207) and (208) one finds a length L of 5.8 cm and a number N of capillaries which amounts to $2.8 \cdot 10^4$.
If the wall material is cellophane, with a diffusion constant D_w of roughly $4 \cdot 10^{-5}$ cm^2/min for urea, one finds a permeation $\gamma = D_w/h$ of 0.04 cm/min. This corresponds to a w of 0.45, estimating the diffusion constant for urea in blood with the value $9 \cdot 10^{-4}$ cm^2/min in water. With this w, the first eigenvalue p_1 in Chapter 8 is 1.2. This gives a relation

$$\frac{C_m}{C_o} \approx 0.99\ e^{-0.65} + 3.3\ e^{-14} + \ldots,$$

or $C_m/C_o \approx 0.52$, at a total blood flow of 500 ml/min. The first term, alone, in the series is fully sufficient as an approximation of C_m/C_o. The corresponding clearance is 240 ml/min.
Here all values were taken as more or less rough estimates (the errors above should be less than 30%) in order to get an idea of the magnitudes for reasonably realistic illustration purposes.

Dependence of the dialyzer performance on the membrane area

The membrane area is

$$A = 2\pi r_1 LN. \tag{209}$$

This quantity appears explicitly in the relation (200) for Φ_c only for small values of w, such that $p_1 \approx 2\sqrt{w}$, so that $\Phi_c \approx \gamma A$ (cf. Chapter 8).
In the other extreme case of a large w, such that $p_1 \approx p_0 = 2.705$, one has, in the flow-limited case:

$$\Phi_c = \Phi_0\ (1 - 0.82\ e^{-\pi DLNp_0^2/2\Phi_0}) \tag{210}$$

and in the pressure-limited case:

$$\Phi_c = N\frac{\pi r_1^4 \Delta p}{8\mu L}(1 - 0.82\, e^{-4\mu DL^2 p_0^2/r_1^4 \Delta p}). \tag{211}$$

Neither of these cases exhibits an explicit or direct dependence of Φ_c on the area A. Only in the case where r_1 is kept constant (for varying designs), may one say that Φ_c is a direct function of A in (210) and only in cases where N is varied alone may one say that Φ_c is proportional to A in (211).
In the general case one may write, for a *given* Φ,

$$\Phi_c = \Phi\,(1 - a_1\, e^{-DAp_1^2/4r_1\Phi}), \tag{212}$$

where a_1 is practically constant. Since one will generally chose the smallest value of r_1 which is practically and economically realizable, one may regard this radius as a constant and consider the dependence of Φ_c on L and N for a *given* Φ (and leave the influence on Φ, in the clinical situation, out of consideration). In that situation, smaller values of Φ_c may be seen as being almost directly dependent on A. The derivative of Φ_c with respect to A may then be written

$$\frac{\partial \Phi_c}{\partial A} = \frac{Dp_1^2}{4r_1}\left(1 - \frac{\Phi_c}{\Phi}\right) \tag{213}$$

which is practically constant if Φ_c is sufficiently smaller than Φ, in which case Φ_c is an almost linear function of A.

17 Influence of the concentration distribution between the capillaries

In the previous discussion, it was generally assumed that the concentration outside the capillaries was zero. This is the limit case of a very high flow of the rinsing solution between the capillaries, having zero entrance concentration of the solute studied. The flow of rinsing fluid required in order to come reasonably close to this ideal case depends on the diffusivity of the actual solute in this fluid. Below, an approximative study of the more general case will be carried out, under the assumption of a countercurrent condition. Con- and crosscurrent conditions will not be studied since these give less efficiency as is well known from studies on heat exchangers [13, 29]. First a laminar flow condition will be assumed, later turbulence will be briefly discussed.
A study of longitudinal laminar flow between cylinders in a regular array has been performed by Sparrow et al. [34]. Later, they also published a study of heat transfer in such a flow condition [35]. For the laminar flow study, they discuss two cases: triangular and square array, assuming a fully developed flow. For the heat transfer study, they discuss a triangular array and a fully developed flow under the condition of a peripherally uniform surface temperature around the rods and

a given heat transfer per unit length of each rod. They also compare their exact results, under these conditions, with a simpler, approximative solution using an «equivalent annulus» concept. This concept is based on a concentrically circular annular area (in the cross-section through the bundle of rods) around each rod, carrying the flow of the «outside» fluid, which has the same measure as the true area (which has a polygonal outside boundary and a circular inside boundary), associated with each rod in the triangular array which they study exactly. Both the flow and the heat transfer equations are solved for the equivalent annulus. As a result, this approximation is applicable to the triangular array with an error of less than 5% in the NUSSELT number for spacing rations down to 1.5. The spacing ratio is defined as the ratio between the distance between the axes of two neighbouring rods and the diameter of a rod. In the case of a capillary artificial kidney, one cannot assume a regular array since the capillaries are flexible and furthermore generally seem to swell slightly and bend and separate in a varying fashion when immersed, so that the distance between them and the form of a flow area for the rinsing fluid, associated with one capillary, varies from one capillary to the other and also along a capillary in a more or less stochastic fashion. Therefore one is forced to adept the «equivalent annulus» concept for an approximative treatment, since a more accurate theory is almost unrealizable.
The differential equation for the laminar flow in the equivalent annulus is (cf. [34] and [35]) (taking velocity and pressure drop positive)

$$\frac{\partial^2 v_s}{\partial r^2} + \frac{1}{r}\frac{\partial v_s}{\partial r} = -\frac{1}{\mu}\frac{\Delta p_s}{L}, \tag{214}$$

where v_s is the local axial velocity in the annulus, μ the viscosity and Δp_s the pressure drop, for the flow of rinsing fluid, along the capillary length L. The boundary conditions are

$$\begin{cases} v_s(r_2, z) = 0, & (215) \\ \dfrac{\partial v_s}{\partial r}(r_3, z) = 0, & (216) \end{cases}$$

where r_2 is the outer radius of a capillary, equal to the inner radius of the annulus, and r_3 the outer of the equivalent annulus. If the total cross-section area of the capillary bundle is A_t and there are N capillaries, one finds

$$r_3 = \sqrt{\frac{A_t}{\pi N}}. \tag{217}$$

Here the value of A_t is to be taken as the one which arises in the immersed condition. For proper rinsing, the cross section area of the cylindrical container for the capillary bundle should also amount to A_t so that no useless shunt flow arises (in

the immersed condition). Otherwise an annular part with the area $A_c - A_t$, where A_c is the area of the container cross-section, around the whole bundle must be treated separately as a shunt flow which reduces the efficiency of the dialyzer.
Taking v_s independent of z, the solution to (214), (215) and (216) is

$$v_s(r) = \frac{\Delta p_s}{2\mu L}\left[r_3^2 \ln \frac{r}{r_2} - \frac{1}{2}(r^2 - r_2^2)\right]. \tag{218}$$

The diffusion equation still has the form of (13), using $v = -v_s(r)$, but with the boundary conditions*

$$\begin{cases} C_s(r, L) = C_L, & (219) \\ C_s(r_2, z) = 0, & (220) \\ \left.\dfrac{\partial C_s}{\partial r}\right|_{r=r_3} = 0, & (221) \end{cases}$$

using C_s as a notation for the concentration in the rinsing solution, if one assumes zero entrance concentration at $z = L$ (counterflow), where L is the length of the capillary, and zero concentration at the capillary surface, for a start. The idea of setting $C_s(r_2, z) = 0$ would be to complete it for a varying $C_s(r_2, z)$ in analogy to Chapter 14 and then tie the solution together with (193).
The solution of (13), according to the method of FOURIER, with $\partial^2 C_s/\partial z^2$ neglected is based on an orthogonal system made up of the solutions F of an equation

$$F'' + \frac{1}{r}F' = \frac{\lambda}{D}F\left[r_3^2 \ln \frac{r}{r_2} - \frac{1}{2}(r^2 - r_2^2)\right] \tag{222}$$

for different eigenvalues λ [cf. (16), (39) and (67)]. An analytical study of these solutions is a major mathematical task in itself and will not be carried out here. Instead a further approximation is introduced as follows.
The simplest case to study is that of a given, constant diffusion flow per unit length of a capillary and a constant concentration (for each z) along the periphery of a capillary, analogous to the case studied in [35]. From such a study a kind of «surface-to-bulk permeation» γ_b can be defined by putting

$$\gamma_b(C_1 - C_b) = J_s, \tag{223}$$

where C_1 and J_s are the concentration and the diffusion flux at the outer capillary surface and C_b is the «bulk» or «mixing cup» concentration, as defined in analogy to (43):

$$C_b(z) = \frac{1}{\pi(r_3^2 - r_2^2)\bar{v}_s}\int_{r_2}^{r_3} 2\pi r v_s(r, z) C_s(r, z)\, dr, \tag{224}$$

* (221) applies to a physical "annulus case" but may not necessarily apply to the case of an *equivalent* annulus.

where $\bar{v}_s$ is the mean velocity:

$$\bar{v}_s = \frac{1}{\pi(r_3^2 - r_2^2)} \int_{r_2}^{r_3} 2\pi r v_s \, dr = \frac{\Delta p_s}{2\mu L(r_3^2 - r_2^2)} \left[r_3^4 \left(\ln\frac{r_3}{r_2} - \frac{3}{4} \right) + r_3^2 r_2^2 - \frac{1}{4} r_2^4 \right]. \qquad (225)$$

With the definition of γ_b above, one gets

$$J_s = \gamma_b(C_1 - C_b) = \gamma_s(C_w - C_1) = \frac{\gamma_s \gamma_b}{\gamma_s + \gamma_b}(C_w - C_b), \qquad (226)$$

where C_w is the concentration at the inner wall of the capillary and

$$\gamma_s = \gamma \frac{r_1}{r_2} \qquad (227)$$

since the total diffusion flow through the wall, per unit length, is $2\pi r_1 J_w = 2\pi r_2 J_s$, cf. (52).

Defining

$$\gamma_c = \frac{\gamma_s \gamma_b}{\gamma_s + \gamma_b} \frac{r_2}{r_1} = \frac{\gamma \gamma_b}{\gamma_s + \gamma_b}, \qquad (228)$$

so that $J_w = \gamma_c(C_w - C_b)$, and C_{m2t} as the solution C_m of Chapter 8 for $\gamma = \gamma_c$, corresponding to a hypothetical $C_b = 0$, (191) gives

$$\tilde{C}_m = \tilde{C}_{m2t} - \frac{1}{C_o} \tilde{C}_b (s\tilde{C}_{m2t} - C_o). \qquad (229)$$

Now

$$\Phi_b C_b(z) = 2\pi r_1 N \int_z^L \gamma(C_w - C_1) \, dz = \Phi \, [C_m(z) - C_m(L)], \qquad (230)$$

(counterflow), where

$$\Phi_b = N\pi(r_3^2 - r_2^2)\bar{v}_s \qquad (231)$$

is the total flow of rinsing solution [cf. (225)] and

$$\Phi = N\pi r_1^2 \bar{v} \qquad (232)$$

is the total flow of blood through the capillaries.

Eliminating C_b between (229) and (230), one finds

$$\tilde{C}_m = \tilde{C}_{m2t} - \frac{\Phi}{C_o \Phi_b} \left[\tilde{C}_m - \frac{1}{s} C_m(L) \right] (s\tilde{C}_{m2t} - C_o), \qquad (233)$$

which can also be stated as an integral equation [cf. (193)].

Solving for $\tilde{C}_m$, one finds

$$\tilde{C}_m \left[1 + \frac{\Phi}{C_o \Phi_b} (s\tilde{C}_{m2t} - C_o) \right] = \tilde{C}_{m2t} \left[1 + \frac{\Phi}{C_o \Phi_b} C_m(L) \right] - \frac{\Phi C_m(L)}{s \Phi_b}. \qquad (234)$$

Here $C_m(L)$ has first to be treated as an unknown constant and then it can be determined by setting $z = L$ and make «$C_m(L) = C_m(L)$» [cf. (243)].
According to (88) one has, for a sufficiently large $DL/\bar{v}$,

$$C_{m2t}(z) \approx \alpha C_0 e^{-\beta z} \tag{235}$$

for $z \approx L$, where

$$\alpha = \frac{8w_c^2}{p_1^3 \left[\frac{\partial w}{\partial p}\right]_{p=p_1}} \tag{236}$$

for $w_c = \gamma_c r_1/D$ and

$$\beta = \frac{D}{2\bar{v}} \left(\frac{p_1}{r_1}\right)^2. \tag{237}$$

This gives an approximation of $C_{m2t}(z)$ for sufficiently large z, or of $\tilde{C}_{m2t}(s)$ for sufficiently small s. Hence the Laplace transform of (235):

$$\tilde{C}_{m2t} \approx \frac{\alpha C_0}{s + \beta} \tag{238}$$

can be inserted into (234) to yield an approximation of C_m for sufficiently small s:

$$C_m \approx \frac{1}{s} \frac{s\,[\alpha\Phi_b C_0 + (\alpha - 1)\Phi C_m(L)] - \beta\Phi C_m(L)}{s\,[\Phi_b + (\alpha - 1)\Phi] + \beta(\Phi_b - \Phi)}. \tag{239}$$

From this follows

$$C_m(z) \approx -\frac{\Phi C_m(L)}{\Phi_b - \Phi} + \frac{\alpha\Phi_b}{\Phi_b + (\alpha - 1)\Phi} \left[C_0 + \frac{\Phi C_m(L)}{\Phi_b - \Phi}\right] e^{-\beta z \frac{\Phi_b - \Phi}{\Phi_b + (\alpha - 1)\Phi}}, \tag{240}$$

for a sufficiently large z and if $\Phi_b \neq \Phi$. The special case $\Phi_b = \Phi$ gives

$$\tilde{C}_m \approx \frac{1}{\alpha s} [\alpha C_0 + (\alpha - 1) C_m(L)] - \frac{\beta}{\alpha s^2} C_m(L), \tag{241}$$

or

$$C_m(z) \approx \frac{1}{\alpha} [\alpha C_0 + (\alpha - 1) C_m(L)] - \frac{\beta z}{\alpha} C_m(L), \tag{242}$$

for a sufficiently large z. Here $C_m(L)$ is determined by putting $z = L$:

$$C_m(L) = \frac{\alpha C_0}{1 + \beta L}, \tag{243}$$

when $\Phi = \Phi_b$. In the general case, $C_m(L)$ is determined analogously by putting $z = L$ in (240).
In this way an approximative solution is obtained with a reasonable effort. A further approximation is found by defining a γ_m, such that

$$J_w = \gamma_m (C_m - C_w), \tag{244}$$

from which

$$\begin{cases} J_w = \gamma_m(C_m - C_w) = \gamma(C_w - C_1), & (245)\\ J_s = \dfrac{r_1}{r_2} J_w = \gamma_b(C_1 - C_b), & (246)\\ 2\pi r_1 N J_w = 2\pi r_2 N J_s = -\Phi \dfrac{dC_m}{dz}, & (247)\\ 2\pi r_2 N J_s = -\Phi_b \dfrac{dC_b}{dz}. & (248)\end{cases}$$

One finds that this results in

$$\begin{cases} \dfrac{dC_m}{dz} = -\dfrac{2\pi r_2 N \gamma_t}{\Phi}(C_m - C_b), & (249)\\ \dfrac{dC_b}{dz} = -\dfrac{2\pi r_2 N \gamma_t}{\Phi_b}(C_m - C_b), & (250)\end{cases}$$

where

$$\frac{1}{\gamma_t} = \frac{1}{\gamma_b} + \frac{1}{\gamma_s} + \frac{1}{\gamma_{sm}} \tag{251}$$

with $\gamma_{sm} = \gamma_m r_1/r_2$. The solution of these equations is treated in [13].

THE CALCULATION OF γ_b IN THE GENERAL CASE HAS BEEN CARRIED OUT IN THE MEANTIME (CF. NOTE ON THE BIBLIOGRAPHY PAGE THAT COMES BEFORE THE CONTENTS PAGE)

Determination of γ_b in the laminar case

In [35], the case of a fully developed heat transfer at laminar flow is studied under the condition of a peripherally uniform surface temperature around the rods and a given, constant heat transfer per unit length, as mentioned earlier in this chapter. As a result, the quotient of the difference between rod surface and fluid bulk temperature over heat transfer at the rod surface evolves as independent of temperature. It only depends on geometry, flow, pressure gradient, viscosity and thermal diffusivity in the fluid. This quotient delivers a value for γ_b for that case. Translated to the present diffusion problem, the results of [35] for the equivalent annulus concept can be written as

$$C_1 - C_b = \frac{2\pi N}{\Phi_b}\int_{r_2}^{r_3}(C_1 - C_s)v_s r\, dr \tag{252}$$

where v_s is given by (219) and

$$C_1 - C_s = \frac{2\pi r_2 N J_s \Delta p_s}{\mu \Phi_b L D}\left\{\left[\frac{r_2^4}{16} + \frac{\mu \Phi_b L}{2\pi N \Delta p_s} - \frac{r_3^2}{8}(r^2 + r_2^2)\right]\ln\frac{r}{r_2} + \right.$$

$$\left. + \frac{r^4 - r_2^4}{64} + \left[\frac{r_3^2}{8} - \frac{r_2^2}{16}\right](r^2 - r_2^2)\right\}. \tag{253}$$

From this, γ_b can be determined, applying the definition (223). In [35] the integration of (252), with (253) and (218), has been carried out and results in a very lengthy expression which will not be repeated here. Note that $\Phi_b/\Delta p$ is independent of Φ_b or Δp [cf. (225) and (231)].

In the actual case of a varying J_s along the capillary, the value of γ_b is not constant, but experience from heat exchangers [13] shows that the variation of the corresponding thermal quantity is mostly small enough, so that it can be taken as a constant. The equivalence of the diffusion problem leads to the assumption that this will also be the case for γ_b. Therefore γ_b may, to a reasonable approximation, be treated as a constant (as was also done) in the earlier discussion of this chapter. The value may then be taken from (252), (253) and (218). A varying γ_b could, however, be taken into account at the expense of a considerable mathematical complication (cf. the end of Chapter 14), which may be somewhat reduced if a piecewise linear or an exponential approximation of γ_b is chosen.

An indication of the plausibility of this approximation for γ_b is, by analogy, given by the following discussion of γ_m.

Determination of γ_m

γ_m may be determined downstream from (44), using

$$2\pi r_1 J_w = -\pi r_1^2 \bar{v} \frac{\partial C_m}{\partial z} = 2\pi r_1 \gamma_m C_m, \tag{254}$$

from which

$$\gamma_{m1} = 1.83 \frac{D}{r_1} \tag{255}$$

(index 1 for the downstream value) when z is large enough, so that C_m may be approximated by the first exponential function alone in the series (44). At the inlet end one can determine γ_m from the Lévêque approximation. With $C_w = 0$, one finds from (134):

$$\gamma_{m2} = \frac{1}{(1/3)!}\left(\frac{4\bar{v}D^2}{9zr_1}\right)^{1/3} \tag{256}$$

(index 2 for the inlet end value). [13] gives a curve of the variation of the Nusselt number with axial length (Fig. 13 in [13]), from which can be concluded that γ_m is practically constant for

$$z > 0.08 \frac{r_1^2 \bar{v}}{D} \tag{257}$$

or $z > 8.5$ mm in the example of urea in water at 300 ml/min of Chapter 10 and $z > 39$ mm for urea in blood at 300 ml/min. In the latter case, the γ_{m1}-value is, though, a very rough estimation. Still, the curve in [13] shows γ_m to be less than $2.5D/r_1$ for $z > 18$ mm.

For comparison of these results with the case of constant diffusion flow per unit length and peripherally uniform concentration, analogous to the calculation of γ_b above, one may solve (65) with $\partial C/\partial z = 2J_w/r_1\bar{v}$ and a constant J_w. This gives

$$\gamma_m \approx 2.2 \frac{D}{r_1}. \tag{258}$$

Under the circumstances, this is a reasonable estimation. This discussion gives an idea of the error involved when γ_b is determined as above. Still, this seems to be the only reasonable theoretical approach for practical applicability.

It should be added that, according to [13] (Fig. 13), the mean value of γ_m along the capillary length L remains reasonably constant for

$$L > 0.25 \frac{r_1^2 \bar{v}}{D} \tag{259}$$

at the value

$$\gamma_m \approx 2 \frac{D}{r_1}. \tag{260}$$

Determination of γ_b in the turbulent case

Since the diffusion of heat and solute are exactly equivalent phenomena in the laminar case, one may assume that this also holds for the turbulent case (with appropriate eddy diffusivities for momentum and solute transport). For the determination of γ_b, the theory applied by DEISSLER [3, 4, 5, 6] may then be adopted and translated to the case of solute diffusion. According to this theory, one has for the axial mean velocity v_s (mean value over time) at a distance y from a wall:

$$y^+ = \frac{1}{n} e^{(nv_s^+)^2/2} \int_0^{nu^+} e^{-(nv_s^+)^2/2} d(nv_s^+) \tag{261}$$

for $y^+ < 26$ and

$$v_s^+ = \frac{1}{\varkappa} \ln y^+ + A \tag{262}$$

for $y^+ > 26$, where

$$v_s^+ = \frac{v_s}{\sqrt{\tau_0/\rho}} \tag{263}$$

and

$$y^+ = y\frac{\sqrt{\tau_0/\rho}}{\mu/\rho}. \tag{264}$$

Here ρ is the density and μ the viscosity of the fluid. τ_0 is the shear stress at the wall. $n = 0.109$, $\varkappa = 0.36$ and $A = 3.8$.
For the diffusion flux, one may put

$$J = -D\frac{\partial C}{\partial y} - \varepsilon_d\frac{\partial C}{\partial y}, \tag{265}$$

which defines an eddy diffusivity ε_d for the solute transport in the turbulent case, in analogy to heat transport. DEISSLER has shown [4] that, in the analog thermal case, the heat flux has a negligible effect on the temperature distribution. Making the assumption that this also is true for diffusion, one can write

$$J_s \approx -(D + \varepsilon_d)\frac{\partial C}{\partial y}, \tag{266}$$

where J_s is the flux at the wall. Furthermore, in heat transfer analysis, the relation between the eddy diffusivity for heat transfer to that of momentum transfer, ε, is generally taken as a constant:

$$\alpha = \frac{\varepsilon_d}{\varepsilon}, \tag{267}$$

where ε is defined by

$$\tau = (\mu + \rho\varepsilon)\frac{dv_s}{dy}. \tag{268}$$

DEISSLER has also shown that the effect of τ on the velocity distribution is negligible. Therefore one may write

$$\tau_0 \approx (\mu + \rho\varepsilon)\frac{dv_s}{dy}. \tag{269}$$

Elimination of ε from (266), (267) and (269) gives

$$\frac{\partial C}{\partial y} \approx -\frac{J_s}{D + \frac{\alpha}{\rho}\tau_0\left(\frac{dy}{dv_s} - \mu\right)}. \tag{270}$$

The velocity distribution given by (261) and (262) is obtained from integration of (269) with

$$\varepsilon = n^2 v_s y \tag{271}$$

for $y^+ < 26$ and

$$\varepsilon = \varkappa^2\frac{(dv_s/dy)^3}{(d^2v_s/dy^2)^2} \tag{272}$$

for $y^+ > 26$. As mentioned in [6], a more exact expression for $y^+ < 26$ is

$$\varepsilon = n^2 v_s y (1 - e^{-n^2 v_s y \rho/\mu}), \tag{273}$$

where the quantity in the paranthesis becomes important, for heat transfer, only at PRANDTL numbers appreciably greater than one. The PRANDTL number in heat transfer theory is equivalent to the quantity $\mu/\rho D$ in the diffusion case. If, therefore, $\mu/\rho D \gg 1$, the velocity distribution given by (261) should be reworked according to (273), which may alter the constant A in (262) as well since the two equations for $v_s^+(y^+)$ shall give the same value at $y^+ = 26$.

The purpose of this section has only been to sketch mathematical tools which could apply for diffusion studies, if certain assumptions hold for solute diffusion in the turbulent case. Before one can go deeper into the theory, these assumptions must be checked. The author has no access to experimental facilities and has not found literature which could aid hereto when writing this chapter. Therefore it can only be mentioned that, if the assumptions hold, the γ_b of the turbulent case can be determined in the same way as for the laminar case, using the above equations.

Effect of repumping of the washing fluid

To reduce the mathematical complexity to a reasonable level, the effect of repumping the washing fluid will here be studied on the basis of the simplified equations (249) and (250). Assuming a reflow Φ_r from the output to the input of the washing fluid and a net flow Φ_n, one has a total flow $\Phi_b = \Phi_n + \Phi_r$ within the dialyzer. If the output concentration of the washing fluid is $C_b(0)$, the input concentration becomes

$$C_b(L) = C_b(0)\frac{\Phi_r}{\Phi_b}, \tag{274}$$

if the net input flow has zero concentration. Solving the equations (249) and (250) for $C_m(0) = C_o$, one finds for the total transport of solute material away with the net output of washing solution:

$$\dot{M} = \Phi_n C_b(0) = \Phi_n C_o \frac{\Phi(\Phi_n + \Phi_r)\left[e^{L\left(\frac{k}{\Phi_n+\Phi_r} - \frac{k}{\Phi}\right)} - 1\right]}{\Phi(\Phi_n + \Phi_r)e^{L\left(\frac{k}{\Phi_n+\Phi_r} - \frac{k}{\Phi}\right)} - {}_{n}^{2}\Phi - \Phi_n\Phi_r - \Phi\Phi_r}, \tag{275}$$

where $k = 2\pi r_2 N \gamma_t$ is constant. Studying the derivative of $1/\dot{M}$ with respect to Φ_r for a constant Φ_n one finds that it is always negative. Therefore a reflow Φ_r increases the efficiency of the dialyzer. This increased efficiency of the dialyzer is even larger than indicated above, since γ_t is actually not constant (although treated as such above) but increases with Φ_b (because γ_b is reduced due to a thinner boundary layer). In the limit case of $\Phi_r = \infty$, the equation for $\dot{M}$ reduces to

$$\dot{M} = \Phi_n C_0 \frac{1 - e^{-LK/\Phi}}{1 - e^{-LK/\Phi} + \Phi_n/\Phi}, \tag{276}$$

but for a very high value of Φ_r, as compared to Φ_n, the outside concentration C_b is practically constant along the capillaries and in this case a more exact solution can be obtained as discussed in Chapter 8. In this case one can expect turbulence and it may then be suitable to determine γ_b from experiments rather than from the complicated theory discussed in the previous section of this chapter (based on certain assumptions).

Appendix 1

Proof of the absolute and uniform convergence of the series (72)

The equation for b_{2n} in (73) gives

$$|b_{2n}| = \frac{p_k^2}{4n^2}(|b_{2n-2}| + |b_{2n-4}|), \tag{A.1}$$

considering the signs of b_{2n}, $n = 0, 1, 2, \ldots$. For the desired proof, one may seek a majoring series. First suppose that

$$|b_{2n}| \leq A \frac{B^n}{n^n} \tag{A.2}$$

holds for two subsequent values of n, e.g., $n_1 - 2$ and $n_1 - 1$. Then, in a first step, chose B such that (A.2) also holds for b_{2n_1}. If this is possible in a general fashion, it follows that (A.2) holds for all b_{2n}, with an appropriate B, if one (in a second step) also can show that it holds for $n = 1$ and $n = 2$. This then leads to a majoring series.

Now, (A.1) gives, for $n = n_1$:

$$|b_{2n_1}| \leq \frac{p_k^2 A}{4n_1^2}\left[\frac{B^{n_1-1}}{(n_1-1)^{n_1-1}} + \frac{B^{n_1-2}}{(n_1-2)^{n_1-2}}\right] < \frac{p_k^2 A B^{n_1-2}}{4n_1^{n_1}}\left(\frac{n_1}{n_1-2}\right)^{n_1}\left(\frac{B}{n_1-1}+1\right). \tag{A.3}$$

Taking the derivative, one easily realizes that the function $[n/(n-2)]^n$ is continuously decreasing for $n>2$. It is actually ≤ 27 for $n\geq 3$. Therefore

$$|b_{2n_1}| < 27 \frac{p_k^2 A B^{n_1-2}}{4 n_1^{n_1}} \left(\frac{B}{n_1-1}+1\right), \quad n_1 \geq 3. \tag{A.4}$$

If one now wants (A.2) to hold for $n=n_1$, one must have

$$27 \frac{p_k^2 A B^{n_1-2}}{4 n_1^{n_1}} \left(\frac{B}{n_1-1}+1\right) \leq A \frac{B^{n_1}}{n_1^{n_1}}, \tag{A.5}$$

or

$$B^2 - \frac{27}{4} p_k^2 \frac{B}{n_1-1} \geq \frac{27}{4} p_k^2, \tag{A.6}$$

which is satisfied if

$$B \geq \frac{27 p_k^2}{8(n_1-1)} + \sqrt{\left[\frac{27 p_k^2}{8(n_1-1)}\right]^2 + \frac{27}{4} p_k^2}, \quad n_1 \geq 3. \tag{A.7}$$

Putting $n_1=2$, the right side in (A.7) becomes larger than for all $n_1 \geq 3$. One can therefore generally choose

$$B \geq \frac{27 p_k^2}{8} \left(1+\sqrt{1+\frac{16}{27 p_k^2}}\right) = B_0, \tag{A.8}$$

which makes the above discussed induction possible.
Especially for $n=1$ and $n=2$, one wants

$$|b_2| = \frac{p_k^2}{4} \leq A B_0 \tag{A.9}$$

and

$$|b_4| = \frac{p_k^2}{16}\left(1+\frac{p_k^2}{4}\right) \leq \frac{A}{4} B_0^2. \tag{A.10}$$

Both these equations are satisfied if

$$A \geq \max \left\{ \frac{2}{27} \frac{1}{1+\sqrt{1+\dfrac{16}{27 p_k^2}}}, \; \frac{16}{(27 p_k)^2} \frac{1+\dfrac{p_k^2}{4}}{\left(1+\sqrt{1+\dfrac{16}{27 p_k^2}}\right)^2} \right\}. \tag{A.11}$$

Therefore one can find constants A and B so that (A.2) holds for all $n \geq 1$. This means that the absolute values of the terms of the series (72) are majored by the terms of the series

$$A \sum_{n=1}^{\infty} \frac{B^n}{n^n} x^{2n} = A \sum_{n=1}^{\infty} \alpha_n(x). \tag{A.12}$$

The latter series is convergent, since (CAUCHY's quotient criterion)

$$\frac{\alpha_n}{\alpha_n - 1} = \frac{Bx^2}{n}\left(1 - \frac{1}{n}\right)^{n-1} \tag{A.13}$$

approaches zero as $n \to \infty$ (because $(1-1/n)^{n-1} \to 1/e$).
This result follows for all $p_k \neq 0$ and is trivial for $p_k = 0$. Furthermore, one can take $x = 1$ in the majoring series, making it independent of x and p_k but still convergent and majoring (72) in the whole actual range of x-values, which shows that the convergence of (72) is uniform in this range. More generally, one may, for any interval $x_1 \leq x \leq x_2$ take $x = \max\{|x_1|, |x_2|\}$ in the majoring series and in the same way show the uniform convergence in that interval, however large $|x_2|$ and $|x_1|$ may be. Therefore the convergence is uniform for all real x and all real p_k.

Q.E.D.

Appendix 2

Proof of the uniform convergence of the series (66)

In Chapter 8 the «cup mixing concentration» was calculated through termwise integration and in Chapter 10 differentiation symbols and integral symbols were exchanged. Such operations are allowed if it can be shown that the series (66) is uniformly convergent.
According to (93) in Chapter 8, one has, with a vanishing error as $p_k \to \infty$,

$$w \approx -A_1 p_k^{2/3}\left[1 + \sqrt{3}\operatorname{cotg}\left(\frac{p_k \pi}{4} - \frac{2\pi}{3}\right)\right], \tag{A.14}$$

where $A_1 \approx 0.4593$. Therefore, for any $\varepsilon_1 > 0$,

$$\frac{4}{3} + 4(k-1) - \varepsilon_1 \leq p_k \leq \frac{8}{3} + 4(k-1) + \varepsilon_1, \tag{A.15}$$

for all $p_k > p_{k1}$, where $\exists\, p_{k1} < \infty$. (A.15) follows from (A.14) and $0 \leq w \leq \infty$.
Furthermore, from (85) and (68),

$$a_k = -\frac{2C_0 w}{p_k\left[w\dfrac{\partial P}{\partial p} + \dfrac{\partial^2 P}{\partial x \partial p}\right]_{\substack{p=p_k\\ x=1}}}. \tag{A.16}$$

Using (92), one finds for any $\varepsilon_2 > 0$:

$$\max\left\{0, A_2 p_k^{1/3}\left|\cos\left(\frac{p_k\pi}{4}-\frac{\pi}{3}\right)\right|-\varepsilon_2\right\} < \left|\left[w\frac{\partial P}{\partial p}+\frac{\partial^2 P}{\partial x \partial p}\right]_{\substack{p=p_k\\x=1}}\right| <$$

$$< A_2 p_k^{1/3}\left|\cos\left(\frac{p_k\pi}{4}-\frac{\pi}{3}\right)\right| + \varepsilon_2, \qquad \text{(A.17)}$$

where $A_2 = (2^{5/3}\pi)/[4(3)^{4/3}(1/3)!]$, for all $p_k > p_{k2}$, $\exists\ p_{k2} < \infty$, except when the *cos*-function becomes exactly zero. The latter occurs when $p_k = 10/3 + 4n$, or

$$w \approx 0.9186\left(\frac{10\pi}{3}+4n\pi\right)^{2/3}; \quad n = 0, \pm 1, \pm 2, \ldots, \qquad \text{(A.18)}$$

using (93). The approximation in (A.18) is better, the larger n.
The «asymptotic exactness» of (A.14) means that for any $w < \infty$ there is a $p_0 < \infty$ such that the *cos*-function in (A.17) is $\neq 0$ for all $p_k > p_0$. Therefore there is in any case a certain p_{k3}, for which $p_0 < p_{k3} < \infty$, such that (A.17) holds for all $p_k > p_{k3}$.
The Fourier coefficients can now be estimated. Clearly, there is a $p_{k4} < \infty$, such that for any $\varepsilon_4 > 0$:

$$\max\left\{0, \frac{2C_0 w}{p_k^{4/3}\left|\cos\left(\frac{p_k\pi}{4}-\frac{\pi}{3}\right)\right| A_2}-\varepsilon_3\right\} < |a_k| < \frac{2C_0 w}{p_k^{4/3}\left|\cos\left(\frac{p_k\pi}{4}-\frac{\pi}{3}\right)\right| A_2}+\varepsilon_3, \qquad \text{(A.19)}$$

for all $p_k > p_{k4} > p_0$. The estimations (A.19) and (A.15) show that there is a $p_{k5} < \infty$, such that for any $\varepsilon > 0$:

$$\left|a_k P_k\left(\frac{r}{r_1}\right) e^{-Dzp_k^2/2\bar{v}r_1^2}\right| < A_3\left(\frac{2C_0 w}{A_2\left[\frac{4}{3}+4(k+1)\right]^{4/3}}+\varepsilon\right) e^{-Dz\,[4/3-\varepsilon+4\,(k-1)]^2/2vr_1^2} \qquad \text{(A.20)}$$

for all $p_k > p_{k5} > p_0$. Here $A_3 \in (0, \infty)$ is a constant upper limit for $|P_k(x)|$ as $x \in [0, 1]$. Such a limit exists since Appendix 1 shows that the functions $P_k(x)$ can be developed in uniformly and absolutely convergent power series for any x and p_k, since (92) shows $|P_k(1)|$ to have a general upper limit, since $P_k(0) = 1$ and since (92), (103) and (104) show $|P_k(x)|$ to have a general upper limit.
On the right side of (A.20) is then the general term of a convergent series which for $p_k > p_{k5} < \infty$ majors

$$\sum_{k=1}^{\infty}\left|a_k P_k\left(\frac{r}{r_1}\right) e^{-Dzp_k^2/2vr_1^2}\right|. \qquad \text{(A.21)}$$

The convergence of the majoring series follows from, e.g., Cauchy's quotient criterion for all $z > 0$ and therefore the series (66) is absolutely convergent for any $r \in [0, r_1]$ and all $z > 0$.

a_k can be even further estimated as

$$|a_k| < \frac{2C_0 w}{\left[\frac{4}{3}+4(k-1)-\varepsilon\right]\left\{A_2\left[\frac{4}{3}+4(k-1)-\varepsilon\right]^{1/3}-\varepsilon\right\}}, \tag{A.22}$$

which shows, using, e.g., the integral criterion, that (A.21) is convergent also for $z=0$. Furthermore the exponential on the right side of (A.20) can be exchanged for 1; combining this with (A.22) gives a convergent majoring series which is independent of r and z. This proves the uniform convergence of the series (66).

Q.E.D.

Appendix 3

The inverse of $\tilde{C}_w$ in (141)

To find the inverse of

$$\tilde{f}(s) = \frac{1}{s^{2/3}(s^{1/3}-a)}, \tag{A.23}$$

where $\tilde{f}(s) = \mathscr{L}\{f(z)\}$, one may first determine the inverse $g(z)$ of

$$g(s) = \frac{1}{s^{1/3}-a} = \frac{s^{2/3}+as^{1/3}+a^2}{s-a^3}, \tag{A.24}$$

with which, from (A.23),

$$f(z) = 1 + a\int_0^z g(z)\,dz \tag{A.25}$$

for $z>0$.

The inversion theorem of MELLIN-FOURIER gives

$$g(z) = \frac{1}{2\pi i}\int_{c-i\infty}^{c+i\infty} e^{sz}\frac{ds}{s^{1/3}-a}. \tag{A.26}$$

As is clearer from (A.24), the integrand has a single pole at $s=a^3$ and a branching point at $s=0$. One may therefore chose an integration path as shown in Fig. A.1, since it encloses the pole and avoids the branching point, and study the behaviour as $R\to\infty$. Using notations defined in Fig. A.1, the residue theorem gives

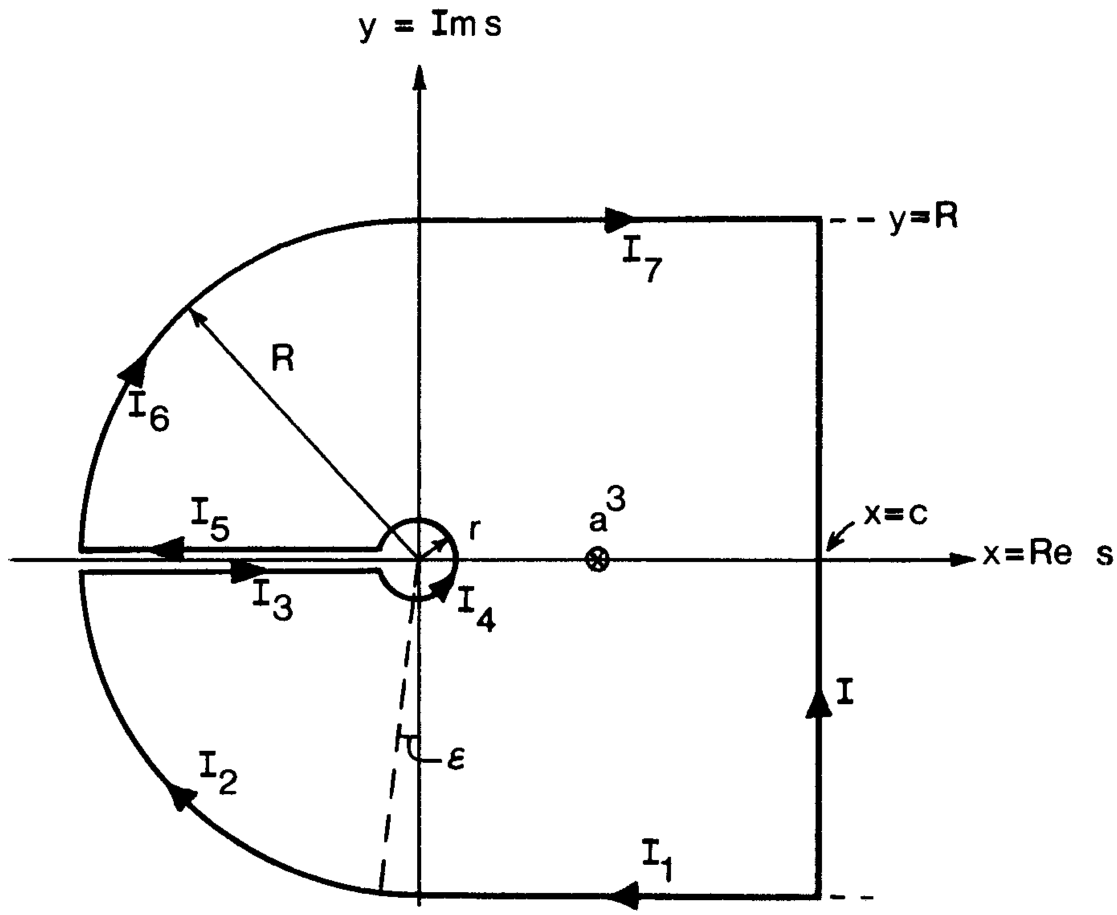

Fig. A.1. Integration path in the complex *s*-plane

$$I = \int_{c-iR}^{c+iR} \frac{e^{sz}\,ds}{s^{1/3}-a} = \sum_{\varkappa=1}^{7} I_\varkappa + 2\pi i\,\mathrm{Res}(a^3) \to 2\pi i g(z) \qquad \text{(A.27)}$$

as $R \to \infty$. It is easily shown that $I_1, I_4, I_7 \to 0$ as $R \to \infty$. To prove the same for I_2, the integral may be separated in two parts, $I_2 = I_2' + I_2''$:

$$I_2' = i \int_{-\pi/2}^{-\varepsilon-\pi/2} \frac{e^{Rz\cos\varphi}\, e^{iRz\sin\varphi}}{(Re^{i\varphi})^{1/3}-a}\, Re^{i\varphi} d\varphi, \qquad \text{(A.28)}$$

where $0 < \varepsilon \ll \pi/2$, and I_2'' being the integral from $-\varepsilon - \pi/2$ to $-\pi$ over the same integrand. It is again easy to show that $I_2'' \to 0$ as $R \to \infty$ for $z > 0$ and a given ε, because $\cos\varphi < 0$ in the actual interval. For a sufficiently large R one can estimate I_2' as

$$|I_2'| < \int_{-\pi/2-\varepsilon}^{-\pi/2} \frac{e^{Rz\cos\varphi}}{R^{1/3}-a}\, R\,d\varphi < \frac{R}{R^{1/3}-a} \int_0^{\varepsilon} e^{-Rz\psi/2}\, d\psi, \qquad \text{(A.29)}$$

where $\psi = -(\varphi + \pi/2)$. The first estimate results from geometrical considerations in the complex plane, using $\varphi/3 \approx -\pi/6$ in the interval $\varphi \in [-\pi/2, -\varepsilon-\pi/2]$ and the fact that a is real and non-negative. The second estimate results from $\cos\varphi = -\sin\psi$ in the actual interval and, further, from $\psi/2 < \sin\psi < \psi$ for all $\psi \in [0, \varepsilon]$ if ε is sufficiently small. Therefore

$$|I_2'| < \frac{2}{R^{1/3} - a} \frac{1}{z} (1 - e^{-Rz\varepsilon/2}), \tag{A.30}$$

which shows that $I_2' \to 0$ as $R \to \infty$ for $z > 0$ and a sufficiently small $\varepsilon > 0$. Therefore $I_2 \to 0$ and, analogously, $I_6 \to 0$ as $R \to \infty$.

As a result, $g(z)$ is determined only by I_3, I_5 and the residue. In I_3 one has $s = |s| \exp(-i\pi)$ and in I_5 one has $s = |s| \exp(i\pi)$, giving

$$I_3 + I_5 = i\sqrt{3} \int_0^\infty e^{-zx} \frac{x^{2/3} + ax^{1/3}}{x + a^3} dx \tag{A.31}$$

in the limit as $R \to \infty$. The residue is

$$\text{Res}\,(a^3) = 3a^2 e^{a^3 z} \tag{A.32}$$

and, finally,

$$g(z) = 3a^2 e^{a^3 z} - \frac{\sqrt{3}}{2\pi} \int_0^\infty e^{-xz} \frac{x^{2/3} + ax^{1/3}}{x + a^3} dx, \tag{A.33}$$

or, according to [10] (integral 3.383.10 on p. 319),

$$g(z) = 3a^2 e^{a^3 z} - \frac{a^2\sqrt{3}}{2\pi} e^{a^3 z} \left[\Gamma\left(\frac{5}{2}\right)\Gamma\left(-\frac{2}{3}, a^3 z\right) + \Gamma\left(\frac{4}{3}\right)\Gamma\left(-\frac{1}{3}, a^3 z\right)\right], \tag{A.34}$$

introducing the incomplete factorial function $\Gamma(\alpha, \beta)$; in this case ([10])

$$\Gamma(-a, b) = \int_b^\infty e^{-t} t^{-(1+a)} dt = a \int_0^{b^{-a}} e^{-t^{-a}} dt \tag{A.35}$$

(this is different from [17], the $\Gamma(\alpha, \beta)$ of [17] is $\gamma(\alpha, \beta)$ in [10]).

Now the inverse of $\tilde{C}_w$ in (141) is

$$C_w = -C_0 f(z), \tag{A.36}$$

with $f(z)$ given by (A.25) and using $g(z)$ from (A.33) or (A.34) and $1/a = A(-1/3)!$.

Appendix 4

The LAPLACE transform of $P_k(\sqrt{\chi})$ and $P_k(x)$ and a convolutional expression

Introduce $x=\sqrt{\chi}$ and $P_k(x)=W_k(\chi)$. Then, from (67),

$$4\chi W_k''+4W_k'+p_k^2(1-\chi)W_k=0. \tag{A.37}$$

After LAPLACE transformation:

$$(p_k^2-4s^2)\tilde{W}_k'+(p_k^2-4s)\tilde{W}_k=0, \tag{A.38}$$

where $\tilde{W}_k(s)=\mathscr{L}\{W_k(\chi)\}$. The solution is

$$\tilde{W}_k=\frac{A}{(2s-p_k)^{1/2-p_k/4}\,(2s+p_k)^{1/2+p_k/4}}, \tag{A.39}$$

where A is a constant. If one requires the initial value

$$W_k(0)=P_k(0)=1=\lim_{s\to\infty} s\tilde{W}_k, \tag{A.40}$$

one must take $A=2$. Hence

$$\tilde{W}_k=\frac{1}{\left(s-\frac{p_k}{2}\right)^{1/2-p_k/4}\left(s+\frac{p_k}{2}\right)^{1/2+p_k/4}}, \tag{A.41}$$

or

$$\mathscr{L}\left\{P_k\left(\sqrt{\chi}\right)\right\}=\frac{1}{\sqrt{s^2-\frac{p_k^2}{4}}}\left[\frac{s-\frac{p_k}{2}}{s+\frac{p_k}{2}}\right]^{\frac{p_k}{4}}. \tag{A.42}$$

According to the relation between the LAPLACE transforms of $f(t)$ and $f(\sqrt{t})$ one thus finds the transform of $P_k(x)$:

$$\mathscr{L}\left\{P_k(x)\right\}=\frac{1}{\sqrt{\pi}}\int_0^\infty \frac{e^{-s^2/4\eta^2}}{\sqrt{\eta^4-p_k^2/4}}\left[\frac{\eta^2-\frac{p_k}{2}}{\eta^2+\frac{p_k}{2}}\right]^{\frac{p_k}{4}} d\eta. \tag{A.43}$$

For an interpretation of (A.42) one may seek the inverse

$$f(t)\supset\left(\frac{s-p_k/2}{s+p_k/2}\right)^{p_k/4}. \tag{A.44}$$

Starting with

$$\frac{1}{(s+\alpha)^\nu}\subset\frac{t^{\nu-1}}{\Gamma(\nu)}e^{-\alpha t}, \tag{A.45}$$

one finds, from the variable transformation $s \to 1/s$ and differentiation,

$$\left(\frac{s}{1+\alpha s}\right)^{\nu} - \frac{1}{\alpha^{\nu}} \subset - \int_0^{\infty} \sqrt{\frac{\tau}{t}}\, J_1\left(2\sqrt{t\tau}\right) \frac{\tau^{\nu-1}}{\Gamma(\nu)} e^{-\alpha\tau}\, d\tau, \qquad \text{(A.46)}$$

or [10]

$$\left(\frac{s}{1+\alpha s}\right)^{\nu} \subset \frac{\delta(t)}{\alpha^{\nu}} - \frac{\nu}{t\alpha^{\nu}} e^{-t/2\alpha} M_{\nu,\,1/2}\left(\frac{t}{\alpha}\right), \qquad \text{(A.47)}$$

where $M_{\lambda,\,\mu}(z)$ is the WHITTAKER function of the first kind and $\delta(t)$ the DIRAC function (unity impulse function). Again performing a variable transformation $s \to s - 1/2\alpha$, one finds

$$\left(\frac{s-1/2\alpha}{s+1/2\alpha}\right)^{\nu} \subset \delta(t) - \frac{\nu}{t} M_{\nu,\,1/2}\left(\frac{t}{\alpha}\right). \qquad \text{(A.48)}$$

Hence, (A.42) may be interpreted as

$$P_k\left(\sqrt{\chi}\right) = I_0\left(\frac{p_k\chi}{2}\right) - \frac{p_k}{4} I_0\left(\frac{p_k\chi}{2}\right) * \frac{1}{\chi} M_{p_k/4,\,1/2}(\chi p_k), \qquad \text{(A.49)}$$

where I_0 is the modified BESSEL function of the first kind and order zero and $*$ denotes convolution with respect to the variable χ (it may here be of interest to note that $I_0(z) = M_{0,\,0}(2z)/\sqrt{2z}$, according to [10]).

LAPLACE formulae applied here may, e.g., be found in the following references (not included in the main list of references):

ANGOT, A.: «Compléments de Mathématiques à l'usage des Ingénieurs de l'électrotechnique et des télécommunications», Collection Technique et Scientifique du C.N.E.T., Éditions de la Revue d'Optique, Paris, 1957.

DOETSCH, G.: «Anleitung zum praktischen Gebrauch der LAPLACE-Transformation und der *Z*-Transformation», R. Oldenbourg Verlag, Munich and Vienna, 1967.

Appendix 5

Some formulae and diagrams for practical use

Introducing

$$\zeta = \frac{\pi N z D}{2\Phi}, \qquad \text{(A.50)}$$

where $\Phi = N\pi r_1^2 v$, one can write (88) as

$$C_m = C_0 \sum_{k=1}^{\infty} \alpha_k e^{-p_k^2 \zeta}. \qquad \text{(A.51)}$$

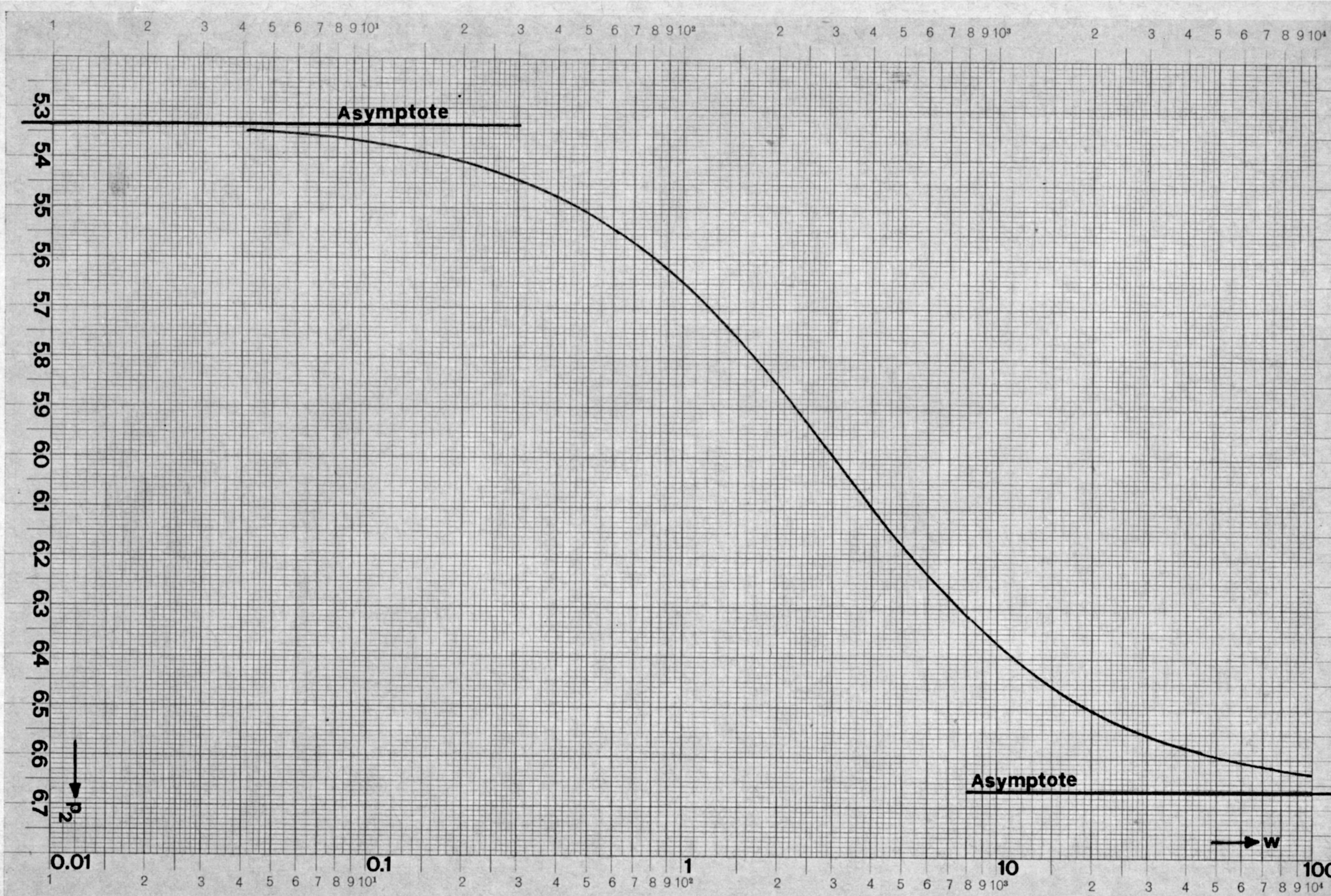

Fig. A.2. The second eigenvalue p_2 of Chapter 8 as a function of w

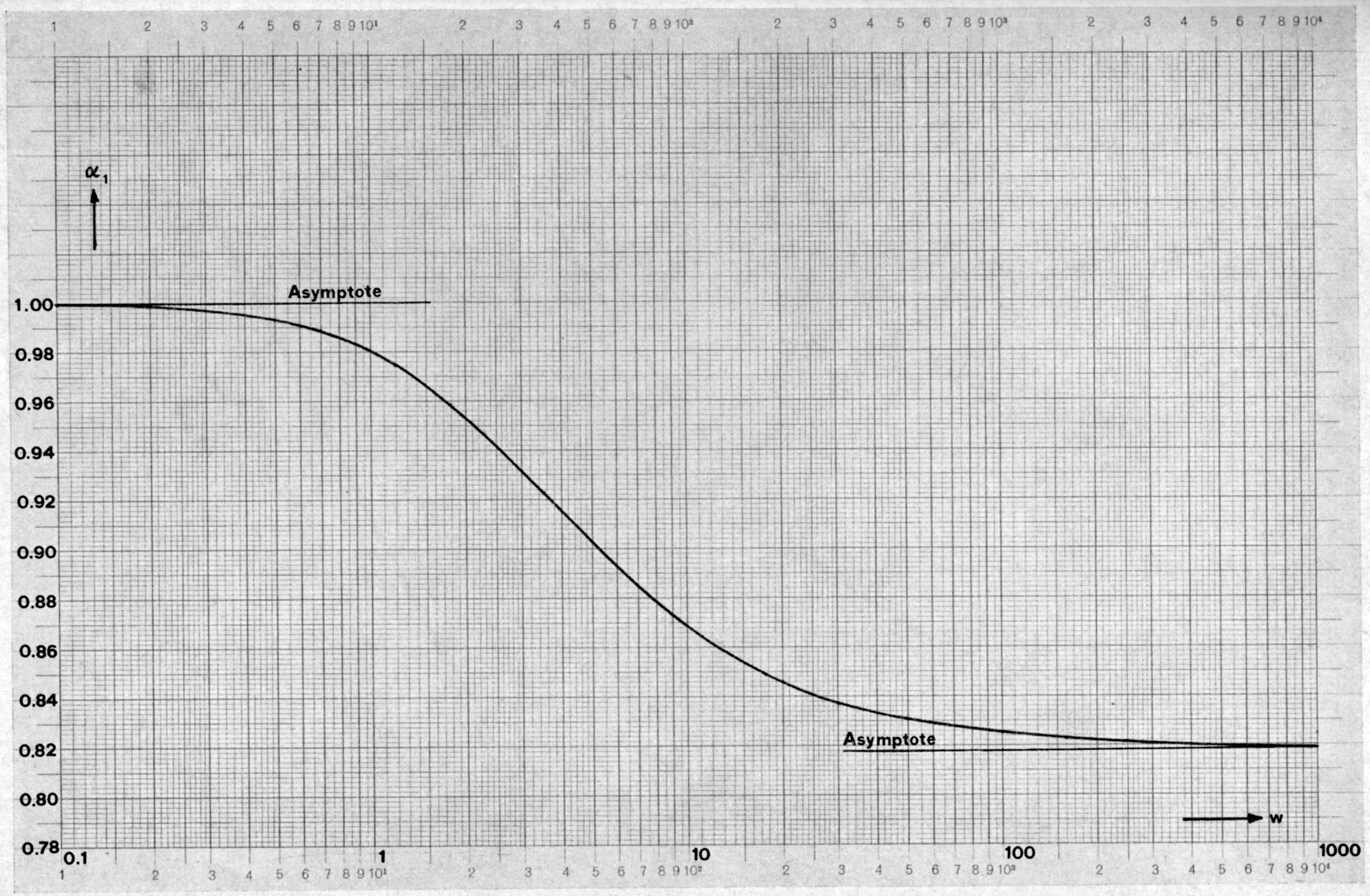

Fig. A.3. The first coefficient α_1 of the series (88) in Chapter 8, defined by eq. (A.51), as a function of w

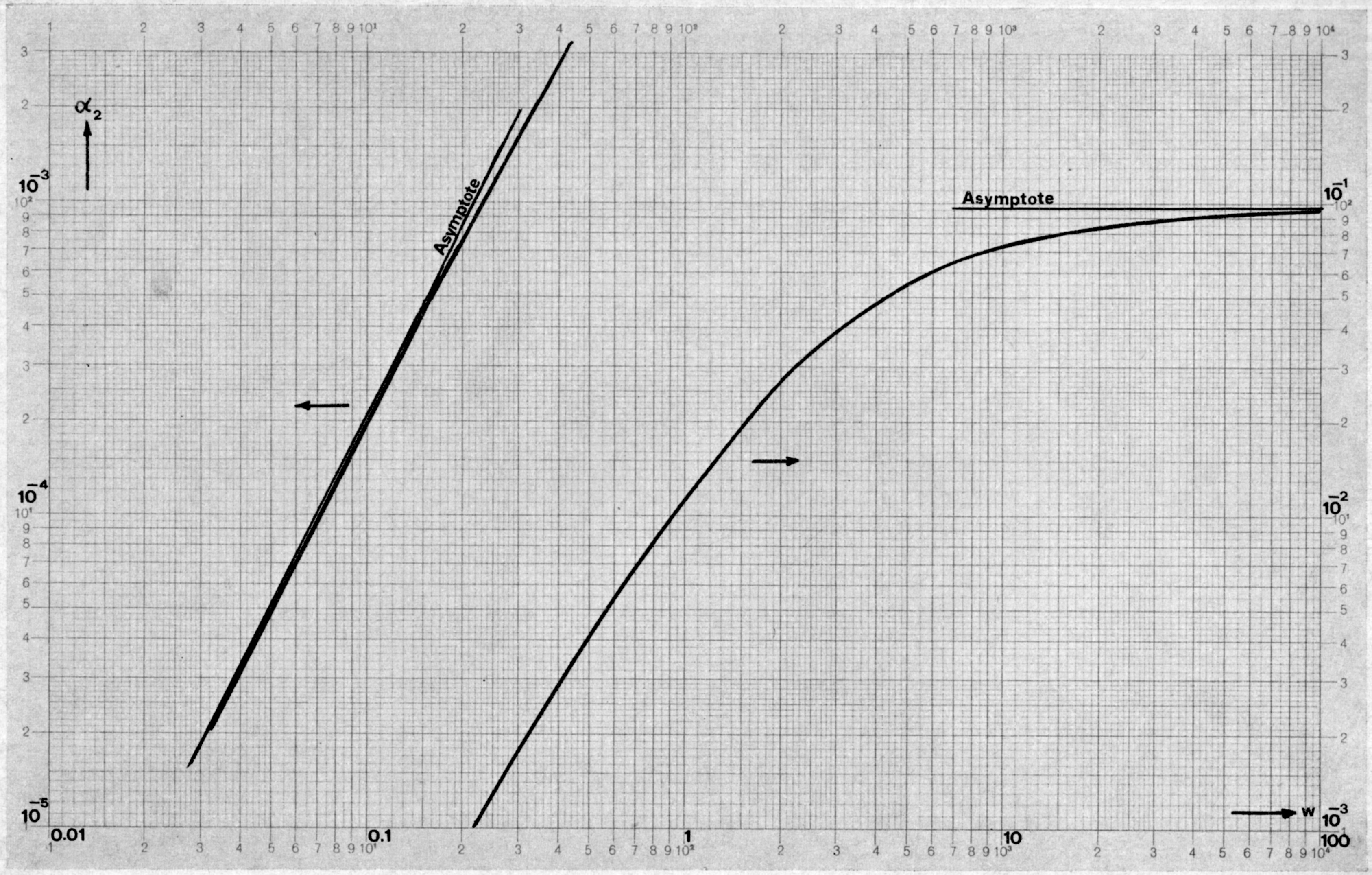

Fig. A.4. The second coefficient α_2 of the series (88) in Chapter 8, defined by eq. (A.51), as a function of w

Diagrams for $p_1(w)$ are shown in Figs. 7 and 8 (see Chapter 8). Fig. 9 shows $p_2(w)$ in a linear diagram. A more useful diagram for $p_2(w)$ is given in Fig. A.2.
Using the formulae of Chapter 8, the coefficients α_1 and α_2 can be calculated. Fig. A. 3 shows $\alpha_1(w)$ and Fig. A.4 shows $\alpha_2(w)$.
For the LÉVÊQUE approximation, one can rewrite (146) as

$$1-\frac{C_m}{C_0}\approx\frac{1.873}{w^2}\left[Z^2-2Z+2\ln(1+Z)\right], \tag{A.52}$$

where

$$Z=1.473\, w\zeta^{1/3}. \tag{A.53}$$

Using the diagrams mentioned, one can determine the regions of validity of the three actual approximations – the one-term and two-term approximations of (A.51) ($k=1$ and $k=1, 2$, resp.) and the LÉVÊQUE approximation. Table 2 gives these regions in terms of ζ and C_m/C_0 for some different values of w. These regions are here so defined that the second term of the series (A.51) is 2% of the first one at the limit of applicability of the one-term approximation (for the region given in Chapter 11 at $w=\infty$, the second term is 2.7% of the first one) and that the two-term and LÉVÊQUE approximations give equal values at their mutual limit of applicability. One finds that, under this definition, the one-term approximation is applicable for all ζ when $w<1.5$.

Table 2

	Applicable approximation:					
w	one term for		two terms for		LÉVÊQUE for	
	$\zeta>$	$C_m/C_0<$	$\zeta>$	$C_m/C_0<$	$\zeta<$	$C_m/C_0>$
∞	0.048	0.59	0.0071	0.85	0.0071	0.85
100	0.048	0.60	0.0081	0.84	0.0081	0.84
50	0.047	0.61	0.0091	0.84	0.0091	0.84
10	0.041	0.68	0.0111	0.85	0.0111	0.85
1	0	1	0	1	0.00065	0.99
0	0	1	0	1	—	—

Approximations for large and small w

For large w, one finds:

$$p_1\approx 2.705-\frac{2.945}{w}, \tag{A.54}$$

$$p_2 \approx \frac{20}{3} - \frac{3.59}{w}, \tag{A.55}$$

$$\alpha_1 \approx \frac{0.82}{\left(1 - \frac{2.25}{w}\right)\left(1 + \frac{0.990}{w}\right)}, \tag{A.56}$$

$$\alpha_2 \approx \frac{0.97}{1 - \frac{2.0}{w}}, \tag{A.57}$$

and for very small w:

$$p_1 \approx 2\sqrt{w}, \tag{A.58}$$

$$p_2 \approx \frac{16}{3} + 0.393\, w, \tag{A.59}$$

$$\alpha_1 \approx \frac{1 + 0.21\, w^2}{1 + 0.47\, w^2}, \tag{A.60}$$

$$\alpha_2 \approx 0.0207\, w^2. \tag{A.61}$$

The LÉVÊQUE approximation becomes

$$1 - \frac{C_m}{C_o} \approx 4.06\, \zeta^{2/3} \tag{A.62}$$

for large w and

$$1 - \frac{C_m}{C_o} \approx 4\, w\zeta \tag{A.63}$$

for small w.

Commentary to (206)

The derivative of the bracket in (206) is

$$\frac{d}{dw}\left(w \frac{dp_1}{dw} - p_1\right) = w \frac{d^2 p_1}{dw^2}. \tag{A.64}$$

As is seen from Fig. 9, and can be verified from Chapter 8, the second derivative of p_1 is always negative. Therefore the bracket has its largest value for small w. This value is negative, according to (A.58):

$$w \frac{dp_1}{dw} - p_1 \approx -\frac{p_1}{2} \approx -\sqrt{w}. \tag{A.65}$$

This means that the bracket is negative for all $w > 0$.

List of notations

The following list contains the more important of the notations used. It does not include a number of constants, coefficients, parameters, auxiliary functions, etc., used in the courses of mathematical developments. Conventional mathematical notations and some used only in the Appendices are also not included.

A	total membrane area in Ch. 16
A_c	cross-section area of container for capillary bundle
A_t	total cross section area of immersed capillary bundle (with interspaces)
C	relative concentration of solute; $C = 1$ means 100% concentration
$\bar{C}$	mean value of C over capillary cross-section
$\tilde{C}$	LAPLACE transformation of C with respect to z
C_b	bulk or «mixing cup» concentration in dialysate
C_m	bulk or «mixing cup» concentration in capillary
C_s	concentration in dialysate
C_w	concentration at inner surface of capillary wall
C_o	initial concentration in capillary at $z = 0$
C_1	concentration at outer surface of capillary wall
D	diffusivity or diffusion constant in the fluid in the capillary
D_w	diffusivity or diffusion constant in the capillary wall material
h	thickness of capillary wall (or membrane, in general)
i	$\sqrt{-1}$, imaginary unit
$\mathbf{J}$	diffusion flux vector
J_n	($n = -\frac{1}{3}$, $\frac{1}{3}$, 0 or integer) Bessel function of first kind and order n
J_w	diffusion flux at inner surface of capillary wall
J_{ip}	Bessel function of first kind and order ip
$\mathfrak{J}_o$	a Bessel wave function
L	length of capillary
$\dot{M}$	solute removal by dialysate
$\hat{n}$	unity vector normal to a surface
N	number of capillaries
N_k	norm of the eigenfunktion P_k

p	eigenvalue parameter in Ch. 8
p_k	eigenvalue in Ch. 8
p_o	fluid pressure outside capillary
p_s	pressure in dialysate
p_{out}	fluid pressure at outlet end of capillary
P	general eigenfunction in Ch. 8
$\mathfrak{P}$	transformed P in Ch. 9
P_k	eigenfunction in Ch. 8
Q	substituted P in Ch. 9
r	radial coordinate
$\hat{r}$	unity vector in the r-direction
r_1	inner radius of capillary wall
r_2	outer radius of capillary wall
r_3	outer radius of «equivalent annulus» in Ch. 17
R	eigenfunction in Ch. 5
s	LAPLACE variable, also eigenvalue parameter in Ch. 7
s_k	eigenvalue in Ch. 7
S	surface of arbitrary volume in flow field with element vector $d\mathbf{S}$
t	time coordinate
U	ultrafiltration parameter in Ch. 13
v	simplified notation for v_z when $v_r = 0$
$\mathbf{v}$	flow velocity vector
$\bar{v}$	mean value of v in capillary cross-section
v_r	radial component of $\mathbf{v}$ in capillary
v_s	velocity of dialysate flow (positive for counterflow)
$\bar{v}_s$	mean value of v_s over cross section of flow
v_t	time-varying v
$\bar{v}_u$	mean ultrafiltration flow velocity in capillary wall
v_z	axial component of $\mathbf{v}$ in capillary
w	$w = \gamma r_1/D$, a relative wall permeation parameter
w_c	w for $\gamma = \gamma_c$
x	$x = r/r_1$, also general coordinate
y	$y = 1-x$, also r_1-r in Ch. 11 and general coordinate
$\hat{y}$	unity vector in y-direction
Y_{ip}	Bessel function of second kind and order ip
Y_o	Bessel function of second kind and order zero
z	axial coordinate

β_k eigenvalue in Ch. 5

γ permeation of capillary wall, defined in Ch. 6
γ_b surface-to-bulk permeation for dialysate in capillary interspace
γ_c combined permeation, defined by (228)
γ_m bulk-to-surface permeation for fluid in capillary
γ_s $\gamma_s = \gamma r_1/r_2$, γ referred to capillary outer surface
γ_t total bulk-to-bulk permeation defined by (251)
γ_{m1} asymptotic value of γ_m
γ_{m2} value of γ_m at inlet end
γ_{sm} $\gamma_{sm} = \gamma_m r_1/r_2$, γ_m referred to capillary outer surface

δ_{nm} KRONECKER's symbol

ε eddy diffusivity for momentum transfer
ε_d eddy diffusivity for solute transfer

λ general eigenvalue parameter
λ_k eigenvalue in Ch. 12

μ viscosity of fluid in capillary
μ_a apparent viscosity of blood due to the FÅHRAEUS-LINDQUIST effect
μ_∞ asymptotic value of μ_a

ξ $\xi = px$, also variable in GREEN function

ρ fluid density
ρ_k positive zeroes of J_0
ρ_{1k} positive zeroes of J_1

σ unity step function

Φ total liquid (blood) flow through capillary bundle (in Ch. 13 also flow in a single capillary at entrance end)
Φ_b total dialysate flow
Φ_c clearance
Φ_u total ultrafiltration flow through a capillary wall

References

1. Abramowitz, M.: «On the solution of the differential equation occurring in the problem of heat convection in laminar flow through a tube», *J. Mathem. and Phys. 32*, 184–187, 1953.
2. Carley, C. T.: «Capillary artificial kidney design with dialysate crossflow», *Proc. 8th ICMBE*, Chicago 20–25. 7. 1969, Session 23–2.
3. Deissler, R. G.: «Analytical and experimental investigation of adiabatic turbulent flow in smooth tubes», *NACA Techn. Note 2138*, Washington, 1950.
4. Deissler, R. G.: «Heat transfer and fluid friction for fully developed turbulent flow of air and supercritical water with variable fluid properties», *Trans. ASME 76*(1), 73–85, 1954.
5. Deissler, R. G., Taylor, M. F.: «Analysis of fully developed turbulent heat transfer and flow in an annulus with various eccentricities», *NACA Techn. Note 3451*, Washington, 1955.
6. Deissler, R. G., Taylor, M. F.: «Analysis of axial turbulent flow and heat transfer through banks of rods or tubes», *T.I.D. 75*29, pp. 416–461, 1957.
7. Dittrich, P., Gurland, H. J., Kessel, M., Massini, M.-A., Wetzels, E.: «*Hämodialyse und Peritonealdialyse*», Springer-Verlag, Germany, 1969.
8. Drew, T. B.: «Mathematical attacks on forced convection problems, a review», *Publications from the MIT*, Publ. Ser. No. 869, Vol. 67, No. 59, 1931.
9. Fritz, R. W.: «*Hämodialyse*», Georg Thieme Verlag, Stuttgart, 1966.
10. Gradsteyn, I. S., Ryzhik, I. M.: «*Tables of Integrals, Series and Products*», Academic Press, New York and London, 1965.
11. Graetz, L.: «Über die Wärmeleitungsfähigkeiten von Flüssigkeiten; 2. Abhandlung», *Annalen der Physik und Chemie*, new series *XXV*(7), 337–357, 1885.
12. Grimsrud, L., Babb, A. L.: «Velocity and concentration profiles for laminar flow of a newtonian fluid in a dialyzer», *Chem. Engng. Symposium Series*, Vol. 62, No. 66, pp. 20–31, 1966.
13. Hausen, H.: «*Wärmeübertragung im Gegenstrom, Gleichstrom und Kreuzstrom*», Nr. 8 of a series «Technische Physik in Einzeldarstellungen», Springer-Verlag, Berlin-Göttingen-Heidelberg and J. F. Bergmann, Munich, 1956.
14. Hilton, D. D., Blainey, J. D., Dawson-Edwards, P., Naqui, A. J., Leonard, M., Siviter, A.: «Preliminary studies on the design of a dialyzer based on parallel narrow cellulose tubes», *Proc. Dial. and Renal Conc.* (Congress), Dublin, 1. 3. 1969.
15. Hoeltzenbein, J.: «*Die Künstliche Niere*», Ferd. Enke Verlag, Stuttgart, 1969.
16. Hoeltzenbein, J.: «Neuartiges System einer künstlichen Kapillar-Niere», in «*Akutes Nierenversagen*» (Proceedings of the first symposium of the «Gesellschaft für Nephrologie» in 1961), G. Thieme Verlag, Stuttgart.

17. Jahnke, E., Emde, F.: «*Tables of Functions with Formulae and Curves*», Dover Publ., New York, 4th ed. 1945.
18. Jakob, M.: «*Heat Transfer*», Vol. 1, J. Wiley & Sons, Inc., New York and Chapman and Hall, Ltd., London, pp. 451—464, 1949.
19. item: pp. 476–480.
20. Kneser, A.: «*Die Integralgleichungen und ihre Anwendungen in der mathematischen Physik*», F. Vieweg u. Sohn, Braunschweig, 1911.
21. Kuchar, N.R., Ostrach, S.: «Flows in entrance regions of circular elastic tubes», in «*Biomedical Fluid Mechanics Symposium*», ASME, New York, pp. 45—69, 1966.
22. Kuhn, W., Marti, E., Kuhn, H.J., Moser, P.: «Analogieversuch zur Füllung der Schwimmblase von Fischen», *Pflügers Archiv 280*, 337–351, 1964.
23. Lévêque, M.A.: «Les lois de la transmission de chaleur par convection», *Annales des Mines* (Ser. 12) *13*, three parts in a series on pp. 201, 305 and 381, 1928.
24. Lew, H.S., Fung, Y.C.: «On the low Reynolds number entry flow into a circular cylindrical tube», *J. Biomech. 2*(1), 105–119, 1969.
25. Lew, H.S., Fung, Y.C.: «Entry flow into blood vessels at arbitrary Reynolds number», *J. Biochem. 3*, 23–28, 1970.
26. Lipps, B.J., Stewart, R.D., Perkins, H.A., Holmes, G.W., McLain, E.A., Rolfs, M.R., Oja, P.D.: «The hollow fiber artificial kidney», *Trans. ASAIO*, Vol. XIII, pp. 200–207, 1967.
27. Michaels, A.S.: «Operating parameters and performance criteria for hemodialyzers and other membrane-separation devices», *Trans. ASAIO*, Vol. XII, pp. 387–392, 1966.
28. Moon, P., Spencer, D.E.: «*Field Theory Handbook*», Springer-Verlag, Berlin-Göttingen-Heidelberg, 1961.
29. Nusselt, W.: «Eine neue Formel für den Wärmedurchgang im Kreuzstrom», *Techn. Mechanik u. Thermodynamik 1*(12), 417–422, 1930.
30. Palotti, C., Palotti, G., Hammond, B.J.: «Parameter profiles along blood dialysis conduits, I: mathematical model», *Proc. 8th ICMBE*, Chicago 20–25. 7. 1969, Session 20–2.
31. Rudinger, G.: «Review of current mathematical methods for the analysis of blood flow», in «*Biomedical Fluid Mechanics Symposium*», ASME, New York, pp. 1–33, 1966.
32. Salyer, I.O. et al. (10 coauthors): «*Research on Materials and Devices for Artificial Kidneys*», 2nd Ann. Progress Rep., Monsanto Research Corp., Dayton Laboratory, Dayton, Ohio 45407 (covers research period 22. 6. 1968–21. 6. 1969).
33. Sellars, J.R., Tribus, M., Klein, J.S.: «Heat transfer to laminar flow in a round tube or flat conduit – the Graetz problem extended», *Trans. ASME*, pp. 441–448, Febr. 1956.
34. Sparrow, E.M., Loeffler, Jr., A.L.: «Longitudinal laminar flow between cylinders arranged in regular array», *A.I.Ch.E. Journal 5*(3), 325–330, 1959.
35. Sparrow, E.M., Loeffler, Jr., A.L., Hubbard, H.A.: «Heat transfer to longitudinal laminar flow between cylinders», *Trans. ASME, J. of Heat Transfer*, pp. 415–422 Nov. 1961.
36. Stewart, R.D., Cerny, J.C., Mahen, H.I.: «The capillary ‹kidney›. Preliminary report», *Univ. of Mich. Med. Cent. J. 30*, 116, 1964.

37. TAYLOR, M. G.: «The influence of the anomalous viscosity of blood upon its oscillatory flow», *Phys. in Med. & Biol. 3*(3), 273–290, 1959.
38. TOLSTOW, G. P.: «*Fourierreihen*», VEB Deutscher Verlag der Wissenschaften, Berlin (East), 1955.
39. TRIBUS, M., KLEIN, J.: «Forced convection from non-isothermal surfaces», in «*Heat Transfer, a Symposium*», Engin. Research Inst., Univ. of Michigan, pp. 211–235, 1953.
40. TWARDOWSKI, Z.: «On the advantages and possibilities of constructing a ‹capillary› artificial kidney», *Acta Medica Polona V*(3), 303–329, 1964.
41. YODER, R. D.: «A mathematical approach to hemodialysis», *J. Appl. Physiol. 18*(1), 141–148, 1963.

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