Quasi-steady-state compartmental model of intracranial fluid dynamics

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Abstract—*A lumped-parameter compartmental model for the cerebrovascular fluid system is constructed and solved for quasi-steady-state flow. The model predicts the pressure waves in the various compartments of the intracranial region in response to changes in the arterial pressure.*

Keywords—*Brain tissue, Compartmental model, Intracranial pressure, Pulse wave*

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1 Introduction

EVER SINCE the intracranial cavity has been modelled, the relatively simple compartmental representation has been favoured. MONRO the younger (1783), the pioneer of intracranial mechanics, characterised the physical forces in the intracranial cavity assuming incompressibility of the fluid; near incompressibility of the brain tissue and zero motion of the boundaries. The intradural space was regarded as bicompartmental—brain and blood—so that a change in either compartment had to be compensated for by the other.

KELLIE (1824), Monro's pupil, modified this hypothesis by assuming three instead of two compartments, namely arteries, veins and brain tissue. About the brain tissue, Kellie said: 'The brain itself, little compressible is contained within a firm and unyielding case of bone which it exactly fills . . . . If these premises be true, it does not then appear very conceivable how any portion of the circulating fluid can ever be withdrawn from within the cranium, without its place being simultaneously occupied by some equivalent or how anything new or exuberant can be intruded, without an equivalent displacement' (*loc. cit.*, p. 102).

The Monro-Kellie doctrine of almost absolute rigidity prevailed into this century and was only relaxed in stages. The number of fluid compartments was increased to six: artery (A), capillary (C), venous (V), venous sinus (S), jugular bulb (J) and cerebrospinal fluid (F) (AGARWAL, 1971). Yet the fluid itself remained incompressible. More recent approaches relaxed the latter assumption and the fluid was taken as linearly compressible, i.e. the change in pressure and the change in volume are proportional to each other, and the coefficient of proportionality, the bulk modulus or its inverse, the *compliance*, are constants.

The thick layer of brain tissue between the ventricles and the subarachnoidal space has also undergone various stages of modelling. The buoyancy theory (LIVINGSTON *et al.*, 1965) regarded the tissue phase submerged in the ideal, incompressible (Pascalian) CSF fluid to which Archimedes law applies. The tissue itself was taken as single-phase and incompressible.

When the incompressibility assumption was abandoned, it paved the way to compressible representations for the brain tissue. Numerous experimental studies have been conducted in the past four decades in that direction. The results pointed at the inelasticity of the tissue or, alternatively, the nonlinearity of the compliance (RYDER *et al.*, 1953; MILLER and GARIBI, 1972; LUNDBERG *et al.*, 1974; MARMAROU *et al.*, 1975; MILLER, 1975; HAKIM *et al.*, 1976; LEWER ALLEN and BUNT, 1978; GRIFFITH *et al.*, 1978; BRUCE, 1978; CHOPP and PORTNOY, 1980). To overcome the 'nonlinearity' of a single coefficient, more complex models of single-phased, multiparameter viscoelastic materials were introduced such as the one consisting of four viscoelastic coefficients known as the 'three-parameter solid', coupled dynamically with another elastic element (PAMIDI and ADVANI, 1978).

The numerical example that we chose to calculate consists of the six compartments listed above and the brain tissue (B) compartment; seven altogether (Fig. 1). The resistance to flow due to a particular vessel type is lumped at the outflow of its compartment. Likewise, the integrated change in volume of each compartment is representable as an overall compartmental property. In general, the functional interaction between the components of a lumped parameter model is assumed to be at the interface between adjacent compartments.

The lumped resistances are: between the artery and capillary compartments (R_{AC}), the capillary and cerebrospinal fluid compartments (R_{CF}), the capillary and brain tissue compartments (R_{CB}), the capillary and vein compartments (R_{CV}), the brain tissue and vein compartments (R_{BV}), the cerebrospinal fluid and brain tissue compartments (R_{FB}), the vein and venous sinus compartments (R_{VS}), the cerebrospinal fluid and the venous sinus compartments

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(R_{FS}) and between the venous sinus and the jugular bulb compartments (R_{VJ}); altogether nine resistances. In Fig. 1, the capillary compartment, and likewise R_{AC}, are divided into the choroid plexuses (those tufts of small capillary vessels inside each of the four ventricles) and the capillary system outside the ventricles. However, in the equations

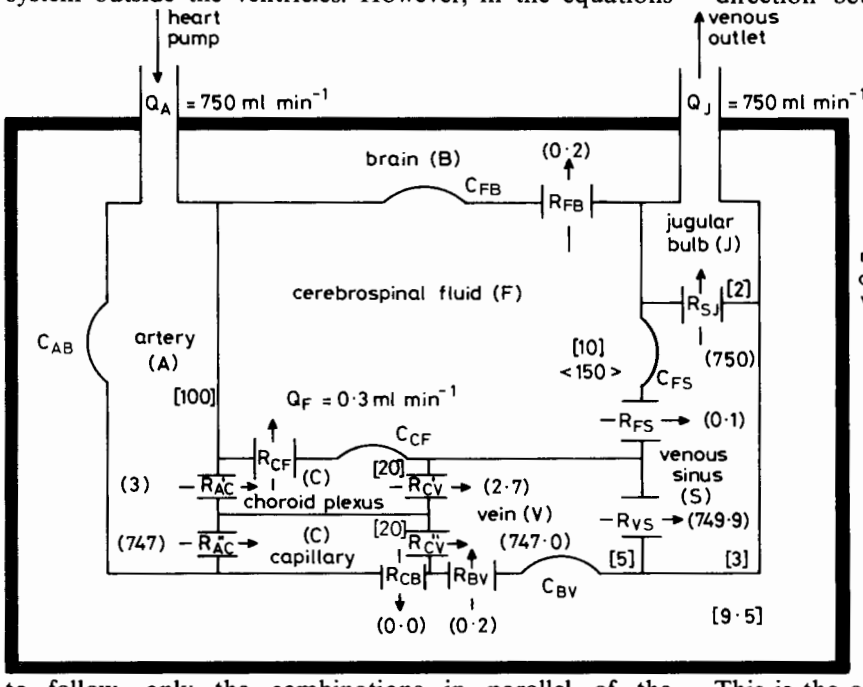

Fig. 1 *Lumped-parameter compartmental model of the cerebrovascular system*
[ ] *pressure, mm Hg*
( ) *flow, ml min*$^{-1}$
〈 〉 *volume, ml*

to follow, only the combinations in parallel of the resistances, namely $(R'_{AC})^{-1} + (R''_{AC})^{-1} = (R_{AC})^{-1}$ and $(R'_{CV})^{-1} + (R''_{CV})^{-1} = (R_{CV})^{-1}$ appear, so that the combined lumped resistances R_{AC} and R_{CV}, into and out of the capillaries, suffice for our purposes.

The resistances R_{CB}, R_{CF} and R_{FB} are identified as the lumped blood-brain barrier; the lumped blood-cerebrospinal fluid barrier and the lumped cerebrospinal fluid-brain barrier, respectively. Quantitative studies of these barriers indicate that on the gross compartmental level they assume large values, yet they cannot be regarded as infinite.

The compliance elements C_{ij} indicate that an increase in volume of one of the compartments equals the volume of the 'cup' formed by the deformed membrane. This volume, in turn, equals the volume displaced from the neighbouring compartments, all within the rigid container of the skull bones (the Monro-Kellie doctrine).

In the non-steady state of flow, which takes in account the deformability of the compartments, we first introduce a compliance element C_{AB} between the artery and the brain tissue compartments. This element represents the overall pulsatory effect of the arteries on the brain tissue. Next, the capillary system is considered nondeformable, so we do not insert compliance elements between this and any of its neighbours. However, the choroid plexuses, although capillary in nature, possess other material properties so they can, and, in fact, do convey pulsations to the CSF system. A compliance element C_{CF} is, therefore, inserted between them. Then the CSF system and the brain tissue share common boundaries, at the ventricles and along the subarachnoidal space, which are deformable, so that a compliance element C_{FB} is introduced between them. Finally, as result of the sharp drop in pressure along the cardiovascular passage, additional compliance elements C_{BV} and C_{FS} are added between the brain tissue and the venous compartments, and between the cerebrospinal fluid and the venous sinus compartments, respectively (there is no compliance element between the sinuses and the large jugular veins because the pressure there is very small). Altogether, the seven-compartmental model for the cerebrospinal fluid system described above assumes five compliance elements of the type C_{ij}.

The mechanical properties of 'resistances' and 'compliances' are 'symmetric' with respect to the interchange of direction between one compartment and its neighbour. This is the outcome of the law of action and reaction. In formulae this is expressed as

$$R_{AC} = R_{CA} \qquad R_{CF} = R_{FC} \qquad \text{etc.}$$
$$C_{AB} = C_{BA} \qquad C_{CF} = C_{FC} \qquad \text{etc.}$$

2 The compartmental flow equation

The governing equation for the lumped-parameter compartmental model of the cerebrovascular fluid system is the balance of mass. In essence it says that, in the absence of sources and sinks, the amount of influx into a compartment should equal the amount of efflux. The fluxes are composed of two linear terms:

(i) the flow rate of fluid as result of pressure difference (transmural) between two compartments (Poiseuille's law), namely

$$Q' = \frac{\Delta P}{R} \qquad (R = \text{resistance})$$

(ii) flow rate resulting from the deformational volume change which, in turn, relates to the change in pressure by

$$Q'' = \frac{dV}{dt} = C\frac{dP}{dt} \qquad (C = \text{compliance})$$

The continuity equations for the balance of mass (strictly, of volume, since we assume the fluid density to remain constant), when written explicitly for each of the compartments, yield a set of seven equations that can be grouped into a single differential matrix equation of the type

$$\boldsymbol{C}\frac{d\boldsymbol{P}}{dt} + \boldsymbol{Z}\boldsymbol{P} = \boldsymbol{Q} + \boldsymbol{S} \tag{1}$$

Here, $\boldsymbol{P}$ is the pressure column vector

$$\boldsymbol{P} = \{P_A, P_B, P_C, P_F, P_V, P_S\} \tag{2}$$

$$\boldsymbol{Z} \text{ is the symmetric fluidity (inverse of resistivity) matrix}$$

$$\boldsymbol{Z} = [Z_{ij}] \equiv \left[\frac{1}{R_{ij}}\right] \equiv \begin{bmatrix} Z_{AC} & 0 & -Z_{AC} & 0 & 0 \\ 0 & [Z_{CB}+Z_{FB}+Z_{BV}] & -Z_{CB} & -Z_{FB} & 0 \\ -Z_{AC} & -Z_{CB} & [Z_{AC}+Z_{CF}+Z_{CB}+Z_{CF}] & -Z_{CF} & -Z_{CF} \\ 0 & -Z_{FB} & -Z_{CF} & [Z_{CF}+Z_{FS}+Z_{FB}] & 0 \\ 0 & -Z_{BV} & -Z_{CV} & 0 & [Z_{CV}+Z_{VS}+Z_{BV}] \\ 0 & 0 & 0 & -Z_{FS} & -Z_{VS} \end{bmatrix} \begin{matrix} 0 \\ 0 \\ -Z_{BV} \\ -Z_{CV} \\ 0 \\ -Z_{VS} \end{matrix} \begin{matrix} 0 \\ 0 \\ 0 \\ -Z_{FS} \\ -Z_{VS} \\ [Z_{VS}+Z_{FS}] \end{matrix} \tag{3}$$

$$\boldsymbol{C} \text{ is the symmetric compliance matrix}$$

$$\boldsymbol{C} = [C_{ij}] = \begin{bmatrix} C_{AB} & -C_{AB} & 0 & 0 & 0 & 0 \\ -C_{AB} & [C_{AB}+C_{FB}+C_{BV}] & 0 & -C_{FB} & -C_{BV} & 0 \\ 0 & 0 & C_{CF} & -C_{CF} & 0 & 0 \\ 0 & -C_{FB} & -C_{CF} & [C_{CF}+C_{FS}+C_{FB}] & 0 & -C_{FS} \\ 0 & -C_{BV} & 0 & 0 & C_{BV} & 0 \\ 0 & 0 & 0 & -C_{FS} & 0 & C_{FS} \end{bmatrix} \tag{4}$$

and $\boldsymbol{Q}$ is the flux column vector

$$\boldsymbol{Q} = [Q_A, 0, 0, 0, 0, -Q_j] \tag{5}$$

In addition, $\boldsymbol{S}$ is the matrix of the compartmental sources or sinks, which either add or drain out fluid from the intracranial domain outside. If $\boldsymbol{S} = 0$, the system is *conserved*, and eqn. 1 reduces to the conservation of mass flow also known as the continuity equation. Here we shall deal with a conservative system only.

In general, eqn. 1 is an inhomogeneous, ordinary differential matrix equation of the first rank with respect to time (t). It is also *nonlinear* since, if homeostasis is taken into account, the sensory and endocrinological biocontrol feedback mechanisms turn the coefficient matrices $\boldsymbol{C}$ and $\boldsymbol{Z}$ functions of the dependent vector $\boldsymbol{P}$ and of the independent scalar t. Thus, in the general case,

$$\boldsymbol{C} = \boldsymbol{C}[\boldsymbol{P}(t), t]; \qquad \boldsymbol{Z} = \boldsymbol{Z}[\boldsymbol{P}(t), t]$$

There are, however, some passive cases which can be approximated by the linear problem, i.e. when $\boldsymbol{C}$ and $\boldsymbol{Z}$ assume constant values. Also, even when dealing with the nonlinear problem, we pass through the linear case. To the latter, therefore, attention is now focused.

The procedure for solving the linear case is as follows:

(*a*) Given information about fluxes and pressures, eqn. 1 can be solved to yield the resistances and compliances. This is often referred to as *parameter identification* or *model calibration.*

(*b*) When the R_{ij}s and C_{ij}s have been evaluated, the pressure waves $\boldsymbol{P} = \boldsymbol{P}(t)$ or the fluxes $\boldsymbol{Q} = \boldsymbol{Q}(t)$ can be determined.

(*c*) With the pressures and compliances already solved, information about the volume changes and, under certain assumptions, also of the compartmental displacements can be obtained.

First, we confine the attention to the parameter identification and proceed in two stages:

2.1 *The steady state*

For constant pressures, the governing equation is the particular integral of eqn. 1. The matrix equation to be solved reduces to

$$\boldsymbol{Z}\boldsymbol{P}^* = \boldsymbol{Q}^* \tag{6}$$

in which $\boldsymbol{P}^*$ and $\boldsymbol{Q}^*$ indicate the average, time-independent compartmental pressure and flux vectors, respectively.

The chart of mean pressure variations along the cerebrovascular fluid conforms with the pressure profile of the cardiovascular system as cited in the literature (e.g. GUYTON, 1969, Chap. 14). In the arteries, the average pressure between systole and diastole is 100 mm Hg. It drops to 20 mm Hg in the capillaries, including the choroid plexuses; 10 mm Hg in the CSF system, 9·5 mm Hg in the brain tissue, 5 mm Hg in the venous system, 3 mm Hg in the sinuses and 1–2 mm in the large veins—jugular and spinal—leading to the vena cava (Fig. 1). Volumes of the compartments are also recorded in the figure as much as they are documented in the literature.

For the flux matrix $\boldsymbol{Q}^*$, we assume the following.

The heart pumps blood into the artery compartment (arteries and arterioles) at the rate of approximately 750 ml min^{-1}. The larger amount of blood flows into the capillaries branching outside the cerebral ventricles, while a small amount reaches the choroid plexuses, which are the capillary zones inside the ventricles. The capillary compartment is thus divided into two sections as shown in Fig. 1. No definite information is available about the partition ratio between the flows through the capillary section and through the choroid plexuses. In our scheme, the ratio of $\lambda = 250:1$ has been postulated, namely 747 ml min^{-1} of blood being carried into the capillaries against 3 ml min^{-1} entering the choroid plexuses in all the four ventricles.

However, as mentioned before, only the compound resistances R_{AC} and R_{CV} are considered; so also the fluxes Q_C and Q_V enter into the calculations and no use is made of the ratio λ later on.

The ultrafiltration of the blood at the choroid plexuses diverts a flow of $0{\cdot}3\,\mathrm{ml\,min^{-1}}$ to the CSF compartment. This is a figure extensively quoted in the literature. From the capillaries, blood is re-collected into the venous system (venules and veins). A minute fraction escapes as interstitial fluid to the extracellular region of the brain tissue but, because of the blood-brain barrier, it is hardly measurable in a tenth of $\mathrm{ml\,min^{-1}}$. It is therefore marked as $0{\cdot}0\,\mathrm{ml\,min^{-1}}$ in Fig. 1. The venous compartment also regains the $3{\cdot}0-0{\cdot}3 = 2{\cdot}7\,\mathrm{ml\,min^{-1}}$ of blood which does not escape from the choroid plexuses into the CSF system, thus totalling with the regained $0{\cdot}2\,\mathrm{ml\,min^{-1}}$, which flows from the CSF system into the brain tissue, $749{\cdot}9\,\mathrm{ml\,min^{-1}}$ that proceed to the venous sinus compartment. The drainage of the CSF into the sinuses adds the $0{\cdot}1\,\mathrm{ml\,min^{-1}}$ which closes the source-sink loop flow of the CSF from the choroid plexuses to the sinuses. The rejoining of the CSF drives the original flow of $750{\cdot}0\,\mathrm{ml\,min^{-1}}$ back to the heart through the jugular and the spinal veins. This scheme implicitly assumes no gains or losses in the flow from one compartment to the other, namely $S^* = 0$.

2.2 *The non-steady state*

Once the matrix $\boldsymbol{Z}$ is determined from the steady state, we insert it into eqn. 1, rearranged to read

$$\boldsymbol{C}\frac{d\boldsymbol{P}(t)}{dt} = \boldsymbol{Q}(t) - \boldsymbol{Z}\boldsymbol{P}(t) \qquad (\boldsymbol{C}, \boldsymbol{Z} = \text{constants}) \qquad (1')$$

The solution for $\boldsymbol{C}$ depends on the availability of information about the time dependency of both the flux vector $\boldsymbol{Q}(t)$ and the pressure vector $\boldsymbol{P}(t)$. In addition, the boundary conditions have to be in the form of pressure variation with time to solve uniquely for the compliances.

To proceed with the numerical solution of these equations, we replace the partial derivatives by implicit, backwards time difference quotients:

$$\frac{dP_A(t)}{dt} \approx \frac{P_A^{n+1}(t) - P_A^n(t)}{\Delta t} \quad (P_A^k(t) \equiv P_A(t_0 + k\Delta t)) \qquad (7)$$

At the same time, we express all the space derivatives at the new time, namely at $n+1$. For example

$$\frac{P_A(t) - P_C(t)}{R_{AC}} = \frac{P_A^{n+1}(t) - P_C^{n+1}(t)}{R_{AC}} \text{ etc.}$$

The differential matrix equation now turns into a system of six sets of algebraic equations, each having the form

$$a_i Q_A^{n+1} + b_i P_B^{n+1} + c_i P_C^{n+1} + d_i P_F^{n+1} + e_i P_S^{n+1} + f_i P_V^{n+1} = g_i \quad (i = 1 \ldots 6) \qquad (8)$$

For example, for the artery chamber ($i = 1$), we have

$$a_1 = 1; \quad b_1 = \frac{C_{AB}}{\Delta t}; \quad c_1 = \frac{1}{R_{AC}}; \quad d_1 = e_1 = f_1 = 0;$$

$$g_1 = P_A^{n+1}\left(\frac{1}{R_{AC}} + \frac{C_{AB}}{\Delta t}\right) - P_A^n \frac{C_{AB}}{\Delta t} + P_B^n \frac{C_{AB}}{\Delta t}$$

In this system of equations we have pressure values at times n and $n+1$ (namely, at times $t_0 + n\Delta t$ and $t_0 + (n+1)\Delta t$, respectively), values of resistances R_{ij} which we already know from the inverse solution of the steady state and the values of the five compliances. Given the values of pressures at times n and $(n+1)$, we can explicitly solve these equations for the values of the five compliances $C_{AB}, C_{CF}, C_{FB}, C_{FV}$, and C_{BV}.

Using the database of Fig. 1, the compartmental resistances turn out to be:

$$R_{AC} = 0{\cdot}11\,\mathrm{mm\,Hg\,ml^{-1}\,min}$$
$$R_{CF} = 33{\cdot}33\,\mathrm{mm\,Hg\,ml^{-1}\,min}$$
$$R_{CB} = 2625{\cdot}0\,\mathrm{mm\,Hg\,ml^{-1}\,min}$$
$$R_{CV} = 0{\cdot}02\,\mathrm{mm\,Hg\,ml^{-1}\,min}$$
$$R_{FB} = 2{\cdot}63\,\mathrm{mm\,Hg\,ml^{-1}\,min}$$
$$R_{FS} = 53{\cdot}64\,\mathrm{mm\,Hg\,ml^{-1}\,min}$$
$$R_{BV} = 23{\cdot}20\,\mathrm{mm\,Hg\,ml^{-1}\,min}$$
$$R_{VS} = 0{\cdot}0026\,\mathrm{mm\,Hg\,ml^{-1}\,min}$$
$$R_{SJ} = 0{\cdot}0013\,\mathrm{mm\,Hg\,ml^{-1}\,min}$$

To solve numerically for the compliances, the time-dependent compartmental pressures have to be taken from clinical measurements. We chose those of HAMIT *et al.* (1965), which are discussed below. Solving eqns. 8 led to the following values:

$$C_{AB} = 0{\cdot}0155\,\mathrm{ml\,mm\,Hg^{-1}}$$
$$C_{CF} = 0{\cdot}0364\,\mathrm{ml\,mm\,Hg^{-1}}$$
$$C_{BV} = 0{\cdot}3180\,\mathrm{ml\,mm\,Hg^{-1}}$$
$$C_{FS} = 0{\cdot}0334\,\mathrm{ml\,mm\,Hg^{-1}}$$
$$C_{FB} = 0{\cdot}1830\,\mathrm{ml\,mm\,Hg^{-1}}$$

That concludes the calibration of the seven-compartment model for the cerebrovascular fluid system with constant resistances and compliances.

3 The quasi-steady-state pressure waves

Once the linear model has been calibrated, it is possible to obtain solutions for the pressure/time variations (pressure waves) in all the compartments.

The solution of the inhomogeneous differential matrix equation for $\boldsymbol{P}$ in incremental form is

$$P_{(t+\Delta t)} = \exp(-\boldsymbol{\kappa})[\boldsymbol{P}_{(t)} - \boldsymbol{Z}^{-1}\boldsymbol{Q}_{(t)}] + \boldsymbol{Z}^{-1}\boldsymbol{Q}_{(t)} \qquad (9)$$

Here, $\Delta t = t_{k+1} - t_k$ denotes a time step between the frontier time level t_{k+1} and backtime level t_k. The matrix $\boldsymbol{\kappa}$ equals

$$\boldsymbol{\kappa} = \Delta t \boldsymbol{C}^{-1}\boldsymbol{Z} \qquad (10)$$

The rational expansion of $\exp(-\boldsymbol{\kappa})$ leads to the following formula:

$$\exp(-\boldsymbol{\kappa}) \cong \frac{\boldsymbol{I} - (1-\theta)\boldsymbol{\kappa}}{\boldsymbol{I} + \theta\boldsymbol{\kappa}} \qquad (0 \leqslant \theta \leqslant 1) \qquad (11)$$

in which $\boldsymbol{I}$ is the $n \times n$ unit matrix. A substitution of eqns. 10 and 11 into eqn. 9 yields

$$\boldsymbol{P}_{(t+\Delta t)} \cong (\boldsymbol{I} + \theta\boldsymbol{\kappa})^{-1}[\boldsymbol{I} - (1-\theta)\boldsymbol{\kappa}] \times [\boldsymbol{P}_{(t)} - \boldsymbol{Z}^{-1}\boldsymbol{Q}_{(t)}] + \boldsymbol{Z}^{-1}\boldsymbol{Q}_{(t)} \qquad (12)$$

The coefficient θ controls the type of solution which evolves in time. When $\theta = 0$, we have an explicit scheme; $\theta = 1$, an implicit scheme, and $0 < \theta < 1$ is the mixed scheme. Thus, with the choice of θ, the pressure waves in the various compartments can be calculated from eqn. 12.

Yet there is another state between the steady state and the non-steady state. If we consider the contribution of the compliance term to be *negligible*, $\boldsymbol{C}(d\boldsymbol{P}/dt) \approx 0$ and we

obtain the relationship

$$\boldsymbol{ZP}(t) = \boldsymbol{Q}(t) \tag{13}$$

Eqn. 13 'looks' like eqn. 6, the condition for the steady-state flow, but, this time, neither the pressure $\boldsymbol{P}$ nor the flux $\boldsymbol{Q}$ assume constant values; rather, each of them is a function of time. This is the *quasi-steady* state and the pressure waves can be calculated from a simplified formula, namely

$$\boldsymbol{P}_{(t+\Delta t)} \cong \boldsymbol{Z}^{-1}\boldsymbol{Q}_{(t)} \tag{12'}$$

HAMIT *et al.* (1965) performed simultaneous recordings of ECG, PCG, arterial, brain, cisternal and venous (strictly, venous/sinus) pressure waves in anaesthesised dogs (Fig. 2*b*). The recorded waves were in the 6–8 cycles per min (cpm) range upon which the faster cardiac waves (also termed 'pulse waves') were superimposed. In the classification of the intracranial pressure waves, the slow curves correspond to the Lundberg B-waves (LUNDBERG *et al.*, 1974) and the faster pulse waves to the A-waves.

The arterial B-wave shows an almost ideal sine wave varying between 110 and 140 mm Hg. We took it as the excitation pressure wave $P_A(t)$, at frequency of 0·144 Hz or a 7 s period, in the artery compartment of our seven-compartmental model and calculated, by means of eqn. 12', the rest of the compartmental pressure waves. The computer plotting of the venous/sinus pressure wave $P_S(t)$ shows a sine wave of the same frequency at amplitudes varying between 2·8 and 7·2 mm Hg (Fig. 2*a*), which is in excellent agreement with the P_S-wave measured by HAMIT *et al.* (1965).

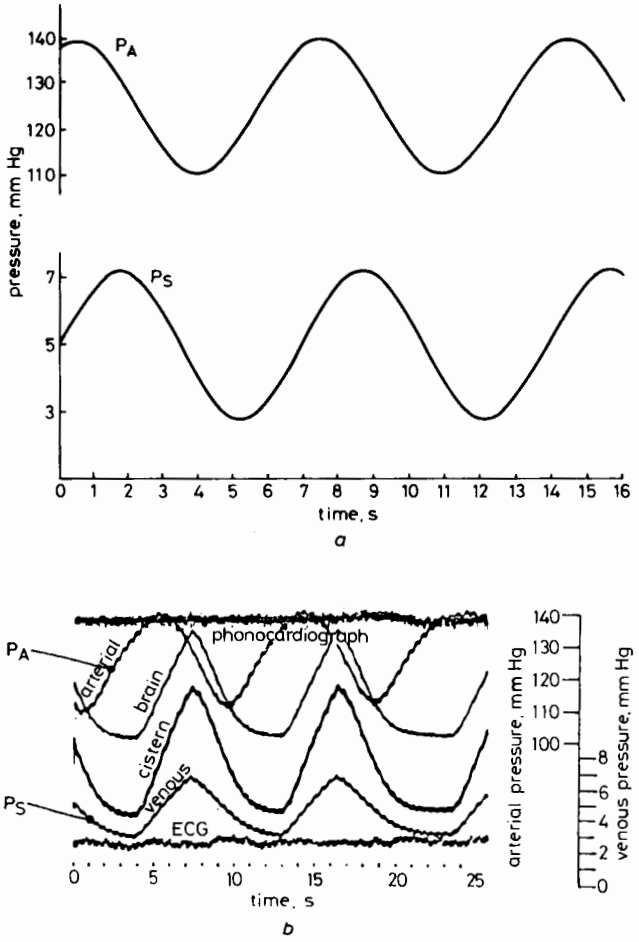

Fig. 2 *(a) Computed P_S wave from a P_A excitation wave (0·144 Hz, 140–110 mm Hg); (b) Simultaneous recording of ECG, phonocardiogram, arterial, brain cisternal and venous pressure waves* (HAMIT *et al., 1965*)

The compartmental approach may be a useful tool in the modelling of intracranial fluid dynamics as far as the time dependency is concerned. Its major drawback is that it does not relate events to their spatial localisation since by its very definition the lumping of the parameters is space-independent. To extend the scope to space-time modelling, we shall have to revert to the continuum approach which, on the macroscale, regards the brain tissue as an averaged single-phase viscoelastic material, and on the microscale as a multiphasic system (three at least) of neurons, glia and interstitial fluid. Here, much more clinical data is needed to calibrate the models and, until this is available, the continuum modelling will have to wait.

Finally, the calculated example presented above is for a seven-compartment model and for the database incorporated in Fig. 1. If, in view of additional clinical data, a model containing more compartments is favoured, or the choice of resistances and compliances is altered, nothing changes in the above method or in the computer program which has anyhow been programmed for $n \times n$ matrices. The authors will be grateful if information about other databases is brought to their attention.

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Authors' biographies

Professor Zvi Karni was born in Haifa, Israel in 1929. He graduated from the Technion, Haifa with an M.Sc. and Ph.D., and received an additional Ph.D. from Imperial College, London. From 1964 to 1966 he headed the Department of Mechanics and in 1968 he founded and served as the first chairman of the newly established Department of Biomedical Engineering. Among other research topics, he was involved in uterine contraction during labour, the possibility of growing collagen cultures influenced by magnetic fields and recently brain mechanics. At the peak of his research activities, Professor Karni unfortunately passed away while on sabbatical.

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