Annals of Biomedical Engineering, Vol. 17, pp. 1-12, 1989
Printed in the USA.

0090-6964/89 $3.00 + .00

Resistances and Compliances of a Compartmental Model of the Cerebrovascular System

Shaul Sorek, Jacob Bear, and Zvi Karni*

Ben-Gurion University of the Negev
J. Blaustein Institute for Desert Research
The Water Resources Center
Sede Boger Campus, Israel
Departments of Biomedical Engineering and Civil Engineering
Technion-Israel Institute of Technology
Haifa 32000, Israel

(Received 2/25/88; Revised 6/27/88)

A lumped parameter compartmental model for the nonsteady flow of the cerebrovascular fluid is constructed. The model assumes constant resistances that relate fluid flux to pressure gradients, and compliances between compartments that relate fluid accumulation to rate of pressure changes. Resistances are evaluated by using mean values of artery and cerebrospinal fluid (CSF) fluxes and mean compartmental pressures. Compliances are then evaluated from clinical data of simultaneous pulse wave recordings in the different compartments. Estimate of the average CSF compartmental deformation, based on the compliance between the CSF and brain tissue compartments, proves to be of the order of magnitude of actual experimental measurements.

Keywords—*Brain tissue, Compartmental model, Cerebrovascular fluid, Intracranial pressure, Compliance resistance.*

INTRODUCTION

The lumped-parameter compartmental model of the cerebrovascular system is the first step towards the construction of a more comprehensive model of the intracranial fluid system. The compartmental approach assumes that the intracranial content may be divided into a number of units, or compartments, the behavior of each of which is represented by a single value of pressure and by values of flux exchanged with adjacent compartments. All these values may be time dependent, but they do not vary in space. The resistance to the flow from a compartment to an adjacent one is lumped at the boundary between the two compartments. Likewise, the integrated change in volume of two adjacent compartments due to the movement of their com-

*Deceased.

Acknowledgment—This paper describes research on Modeling Brain Mechanics and Chemical Processes, conducted in the Julius Silver Institute of Biomedical Engineering and Science at the Department of Biomedical Engineering, Technion-Israel Institute of Technology, Haifa, Israel. The research is sponsored in part by the U.S. Air Force (grant AFOSR-85-0233). The authors wish to thank the U.S.A.F., The Michael Kennedy Leigh Fund, U.K., and the Technion Fund for the Promotion of Research for their financial support.

Address correspondence to Shaul Sorek, Department of Biomedical Engineering, Technion-Israel Institute of Technology, Haifa 32000, Israel.

mon boundary in response to a pressure difference, is represented as a property called compliance that is assigned to the boundary between two adjacent interacting compartments.

Monro's (14) first model of the intracranial cavity was bi-compartmental: Brain fluid and blood, as two almost-incompressible fluid phases. Kellie (11) modified this model by assuming three, instead of two, material compartments: arteries, veins and brain tissue. The Monro-Kellie models prevailed to this century and were modified in stages only in recent years. The number of compartments was increased to six: arteries, capillaries, venous, venous sinus, jugular bulb and cerebrospinal (CSF) (1).

More recent approaches considered the compartments to be (linearly) compressible, yet the fluid itself remained incompressible. As to the brain tissue, it is essentially a multiphasic material (e.g., brain tissue, blood and CSF) continuum. Experimental results show that its behavior is inelastic or, alternatively, that the corresponding compliance is nonlinear. To overcome the "nonlinearity" of a single coefficient, the tissue is assumed to be a rather complex, single-phase, multiparameter viscoelastic material (e.g., one whose constitutive relation involves four viscoelastic coefficients) (15). In the reports of these investigations, although not explicitly stated, the model of the intracranial content returned to be bi-compartmental: the CSF compartment and "all the rest," or the vascular compartment and the rest, etc. In most cases, even for the multicompartmental model of the cerebrovascular fluid system (1), no numerical calculations were presented and the exposition of the subject remained theoretical.

Our first objective, therefore, was to develop an N-compartmental model that can yield numerical values of the various state variables (e.g., pressure, in quasi steady (9,10) and nonsteady flow (17)). So far, we have successfully achieved (16) this objective for the general linear problem, assuming compliances and resistances of step function nature according to the nonsteady flow and pressure regime. Physiologically, the assumption of linearity corresponds to passive states in which the sensory and endocrinological biocontrol mechanisms have but little effect on the resistances and the compliances. Nevertheless, one must first construct and solve a linear model and employ perturbation techniques in order to derive solutions for the generalized nonlinear problem. Greenberg *et al.* (5) used a three compartment model to estimate one cerebrovascular controlling resistance. Their model does not include compliance elements, accounts only for transport processes with constant flux values and no perfusion pressure.

Our compartmental model involves a number of resistances and compliances, the values of which must be known before the model can be employed in predicting perfusion pressure and flux changes. In a previous paper (16) it was assumed that the compliances and resistances are also functions of known ratios between certain pairs of resistances. The objective of the present paper is to present a methodology for estimating the values of the various compliances and resistances and the above mentioned ratios.

The methodology is based on the assumption that flow and pressure are periodic in time. It uses actual time varying clinical observations to evaluate resistances from mean phasic values. The compliances are then estimated by the latter and a set of equations assembled from different time observations. This inverse method is a tool applicable to any general compartmental modeling and is thus explained separately from our earlier paper (16).

1. THE COMPARTMENTAL BALANCE EQUATION

The governing equations for the lumped-parameter compartmental model describe the balance of mass and the balance of linear momentum for each compartment. Essentially, each such equation states that the temporal rate of change of either the fluid mass, or its momentum, in a compartment, is equal to the amount of net influx of that quantity through the compartmental boundaries, plus the external sources. The mass balance of the n-th compartment, surrounded by a number of compartments denoted by $m = 1,2,\ldots$, can, therefore, be written in the form

$$\frac{dV_n}{dt} = \sum_{(m)} q_{mn} + Q_n \tag{1}$$

where $q_{mn}(= -q_{nm})$ denotes the flux from compartment n to m, Q_n denotes external sources in the n-th compartment and V_n is its volume.

The flux q_{nm} can be expressed in terms of the difference in pressure, $p_{nm}(= P_n - P_m)$ between the n-th and the m-th compartment, and a conductance Z_{nm} (reciprocal of the resistance R_{nm}), in the form

$$q_{nm} = \frac{P_{nm}}{R_{nm}} = Z_{nm}P_{nm}. \tag{2}$$

Note that fluxes are determined by differences in piezometric head which is the sum of pressure head and gravity head. However, within the cerebral system, differences in the latter are much smaller than those in the former. Hence, only pressure differences have been considered here.

As an example to account for the diffusion and perfusion processes between capillaries and brain tissue (13) we introduce a conductance which manifests the pressure fall through the blood brain barrier.

The change in volume, ΔV_n is produced by the change in the pressure differences, ΔP_{nm}, in adjacent compartments, taking into account the presence of compliances, C_{nm}, between these cells

$$\Delta V_n = \sum_{(m)} C_{nm}\Delta P_{nm}. \tag{3}$$

Together, we obtain for the n-th compartment, a mass balance of the form

$$\sum_{(m)} C_{nm}\frac{dP_{nm}}{dt} + \sum_{(m)} Z_{nm}P_{nm} = Q_n. \tag{4}$$

Another compact form of this equation for all cells simultaneously is

$$\underline{\underline{C}}\,\frac{d\underline{P}}{dt} + \underline{\underline{Z}}\,\underline{P} = \underline{Q} \tag{5}$$

where $\underline{P}(t)$ is the time-dependent $(N \times 1)$ pressure vector; $\underline{Q}(t)$ the source $(N \times 1)$ flux vector, and $\underline{\underline{Z}}$ and $\underline{\underline{C}}$ are the $(N \times N)$ conductance and the compliance matrices, respectively.

2. PARAMETER ESTIMATION

The compartmental balance equations for fluid mass, written in the compact form of Eq. (5), involve conductivities and compliances, expressed by the matrices $\underline{\underline{Z}}$ and $\underline{\underline{C}}$. In the present work, these parameters are assumed to be constant.

To predict the pressure (and flux) response of the model to external changes, the values of the parameters $\underline{\underline{C}}$ and $\underline{\underline{Z}}$ must be known. In order to estimate them, we need measured values of pressure in the various compartments at a sufficient number of points in time. With information from clinical data (8), of simultaneous $P_{(t)}$ pulse wave recordings at the different compartments, we apply the following inverse procedure.

First, because $\underline{\underline{C}}$ and $\underline{\underline{Z}}$ are assumed constant and $\underline{p}(t)$ is cyclic, by taking a temporal average of Eq. (5) over the cycle time T, (i.e., integration over the cycle time divided by that period), we obtain,

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

where $(\bar{})$ denotes the difference between adjacent compartment, $P^* = \frac{1}{T}\int_o^T p dt$ and $Q^* = \frac{1}{T}\int_o^T Q dt$ denote the obtained mean values of pressure and source fluxes, respectively. We note that Eq. (6) is a quasi-steady state equation. With known values of P^* and Q^*, we thus solve Eq. (6) for Z.

Then with the already evaluated Z values and $P^k(\equiv P(t^k))$, $\dot{P}^k\left(\equiv \dot{P}(t^k) = \frac{dp^k}{dt}\right)$ values from the clinical data at various time observations t^k, we write by virtue of Eq. (5)–(6) a K set of equations for the compliances

$$\dot{\bar{\underline{\underline{P}}}}^k \underline{\underline{C}} = \underline{b}^k; \quad k = 1,2,3,\ldots,K \tag{7.1}$$

where

$$\underline{b}^k = \underline{Q}^k - \underline{\underline{Z}}\bar{\underline{P}}^k. \tag{7.2}$$

By the Gauss-Markov theorem, the C values are derived as an assortment of the set of information at all K time observations

$$\underline{\underline{C}} = (\underline{\underline{\pi}}^T \underline{\underline{\pi}})^{-1} \underline{\underline{\pi}}^T \underline{\underline{B}} \tag{7.3}$$

here

$$\underline{\underline{\pi}} = \begin{bmatrix} \dot{\underline{\underline{P}}}^1 \\ \dot{\underline{\underline{P}}}^2 \\ \vdots \\ \dot{\underline{\underline{P}}}^K \end{bmatrix} \tag{7.4}$$

$$\underline{B} = [\underline{b}^1, \underline{b}^2, \ldots, \underline{b}^K]. \tag{7.5}$$

This concludes, at least formally, the (inverse) process for identifying parameters appearing in Eq. (5) for an N-compartment model.

3. EVALUATION OF MODEL RESISTANCES AND COMPLIANCES

Let us determine the values of C and Z in the case of a seven-compartment model ($N = 7$). Figure 1 shows the model consisting of the following compartments: arterial (A), capillary (C), cerebrospinal fluid (F), brain tissue (B), venous (V), venous sinus (S) and the jugular bulb (J). 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 cere-

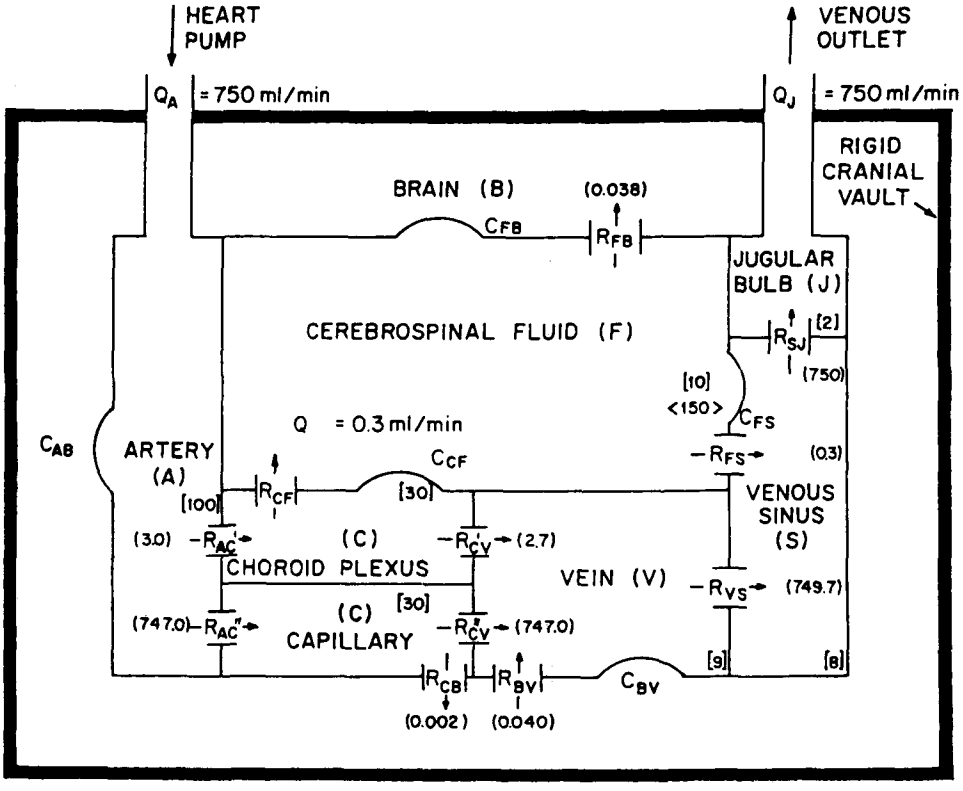

FIGURE 1. Lumped parameter, seven-compartmental fluid system (*R*-resistance, *C*-compliance; [ ] pressure (mm Hg); ( ) flow (ml/min); ⟨ ⟩ volume (ml)).

brospinal fluid and brain compartments (R_{FB}), the vein and venous sinus compartments (R_{VS}), the cerebrospinal fluid and the venous sinus compartments (R_{FS}), between the venous sinus and the jugular bulb compartments (R_{VJ}); altogether nine resistances. In Fig. 1, the capillary compartment is 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, only the combination in parallel of the conductances $Z'_{AC} + Z''_{AC} = Z_{AC}$ and $Z'_{CV} + Z''_{CV} = Z_{CV}$ appear, so that only the combined resistances R_{AC} and R_{CV}—into and out of the capillaries—are included in the model.

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.

We recall that the compliance elements, C_{nm}, indicate that an increase in volume of one compartment equals the volume of the "cup" formed by the deformed membrane. This volume, in turn, equals the volume displaced from the neighboring compartments, all this within the rigid container of the skull bones (the Monro-Kellie doctrine).

In the nonsteady state, which takes into account the deformability of the compartments, we first introduce a compliance element C_{AB} between the artery and the brain tissue compartments to represent the overall pulsatory effect of the arteries on the brain tissue. Next, the capillary system is considered nondeformable, so that no compliance is introduced between this compartment and any of its neighbors. The choroid plexuses, however, although capillary in nature, possess other material properties. Hence, they can, and in fact do convey pulsations to the CSF system (2). Accordingly, a compliance C_{CF} is introduced between them. Furthermore, the CSF system and the brain tissue share common boundaries—at the ventricles and along the subarachnoidal space—which are deformable. A compliance element C_{FB} is therefore, inserted between the two. Finally, to account for observed sharp drop in pressure along the cardiovascular passage, additional compliances C_{BV} and C_{FS} are inserted between the brain tissue and venous compartments and between the CSF and venous sinus compartments, respectively. Altogether, in our presentation, we assume five compliances between adjacent elements of the cerebrovascular fluid system.

The mechanical properties of resistances and compliances are symmetric with respect to the change of direction between one compartment and its neighbor, i.e. in formulae

$$R_{AC} = R_{CA}, \quad R_{CF} = R_{FC}, \text{ etc.}$$

$$C_{AB} = C_{BA}, \quad C_{CF} = C_{FC}, \text{ etc.}$$

All R_{nm}'s and C_{nm}'s are positive.

We now evaluate the temporal average of the cerebral $P(t)$ of the pulse wave recordings (8) and of the pressure profile of the cardiovascular system cited in the literature (6) both over a time cycle. In the arteries, the average pressure—between systole and diastole—is $P_A^* = 100$ mmHg. It drops to $P_C^* = 30$ mmHg in the capillaries, including the choroid plexuses; $P_F^* = 10$ mmHg in the CSF system; $P_B^* = 9.5$

mmHg in the brain tissue; $P_V^* = 9$ mmHg in the venous system; $P_S^* = 8$ mmHg in the sinuses and $P_J^* = 2$ mmHg in the larger jugular veins and in the spinal leading into the vena cava (Fig. 1). The mean values of the injected and ejected fluxes at the artery and jugular bulb are $Q_A^* = Q_J^* = 750$ ml/min.

As explained following Eq. (2), the above average pressures are based on neglecting the gravity head. In fact, to maintain a certain flux, a certain piezometric head difference is required. Then, the pressure difference will depend on whether the person is in a horizontal or a vertical position, due to not the same differences in the gravity head of the two positions. However, in our work, the gravity head difference has been neglected as being much smaller than the pressure one.

The effect of gravity is more significant when considering the flow interactions between the body and the cerebral system. There, the relative position between the two becomes important in affecting pressures in the cerebrovascular system (19).

Altogether, nine resistance values have to be determined. However, the matrix equation (6) comprises only six independent balance equations for the various compartments of the cerebrovascular model. Thus, the redundancy of the system is three, and three additional conditions are needed to solve the set. One of them is the mean flux (from choroid plexus to the CSF ventricles) $Q_F^* = 0.3$ ml/min, which can be taken as pivot value with high credibility from the literature (3).

Thus, the Z_{CF} value can be evaluated from the expression

$$Q_F^* = Z_{CF} P_{CF}^*. \tag{8}$$

Two more conditions have to be stipulated for resistances, based on the existing physiological data. We now introduce the scalar coefficients.

$$\alpha = \frac{R_{FB}}{R_{VS}} = \frac{Z_{VS}}{Z_{FB}} \tag{9}$$

$$\beta = \frac{R_{FB}}{R_{CB}} = \frac{Z_{CB}}{Z_{FB}}. \tag{10}$$

Here α indicates the ratio of the resistance of the cerebrospinal fluid-brain barrier to the vein-venous sinus resistance, where β is the ratio of resistance of the cerebrospinal fluid-brain barrier to that of the blood-brain barrier.

For our compartmental configuration (Fig. 1) and in view of Eqs. (8)–(10), we are left with four unknown Z values. We thus write the explicit form for Eq. (6).

$$\begin{bmatrix} (p_{BF}^* + \beta p_{CB}^*) & 0 & 0 & p_{BV}^* \\ \beta p_{CB}^* & p_{CV}^* & 0 & 0 \\ p_{FB}^* & 0 & p_{FS}^* & 0 \\ \alpha p_{VS}^* & -p_{CV}^* & 0 & -p_{BV}^* \end{bmatrix} \begin{bmatrix} Z_{FB} \\ Z_{CV} \\ Z_{FS} \\ Z_{BV} \end{bmatrix} = \begin{bmatrix} 0 \\ Q_A^* - Q_F^* \\ Q_F^* \\ 0 \end{bmatrix}. \tag{11}$$

The explicit form of Eq. (7.1) for any observation time t^k, is

$$\begin{bmatrix} \dot{p}^k_{AB} & & & & \\ & \dot{p}^k_{CF} & & & \\ & & \dot{p}^k_{BV} & & \\ & & & \dot{p}^k_{FS} & \\ & & & & \dot{p}^k_{FB} \end{bmatrix} \begin{bmatrix} C_{AB} \\ C_{CF} \\ C_{BV} \\ C_{FS} \\ C_{FB} \end{bmatrix} = \tag{12}$$

$$= \begin{bmatrix} Z_{SJ}p^k_{SJ} - Z_{AC}p^k_{AC} \\ Z_{AC}p^k_{AC} - Z_{CV}p^k_{CV} - Z_{CF}p^k_{CF} - Z_{CB}p^k_{CB} \\ Z_{VS}p^k_{VS} - Z_{CV}p^k_{CV} - Z_{BV}p^k_{BV} \\ Z_{SJ}p^k_{SJ} - Z_{VS}p^k_{VS} - Z_{FS}p^k_{FS} \\ -Z_{SJ}p^k_{SJ} + Z_{AC}p^k_{AC} + Z_{VS}p^k_{VS} - Z_{CV}p^k_{CV} - Z_{CB}p^k_{CB} - Z_{FB}p^k_{FB} \end{bmatrix}.$$

Note that both $\underline{\underline{Z}}$ and $\underline{\underline{C}}$ values were evaluated from a nonsteady flow system. Given the conductances one can solve a quasi steady flow regime. Including the compliances one can solve the perfusion problem described in Eq. (5) given the appropriate initial conditions (17).

Thus, Eqs. (6) to (12) allow a complete solution for the resistances $R_{nm}(\alpha,\beta)$ and compliances $C_{nm}(\alpha,\beta)$ with the values of α and β. Figures 2 and 3 describe an example of the surfaces $R_{CV}(\alpha,\beta)$ and $C_{BV}(\alpha,\beta)$, respectively.

The figures demonstrate zones of α and β that generate unacceptable values (e.g., negative Z's as in Fig. 2) of resistances and compliances and zones of high sensitivity of the resulting Z's and C's to small changes of α and β. Our choice is, therefore, to rely on α and β values that generate stable Z's and C's.

There are almost no data about the physiological, or pathological, ranges of α and β. It was found that when α and β are in the range of 1/1,000 and 10,000, respectively the resistances and compliances meet the desired aforementioned criteria. Hence for $\beta = 10^{-3}$ and $\alpha = 10^{+4}$ Eqs. (4) to (8) result in the following values:

$R_{AC} = 0.933$ mmHg.ml/min. $\quad R_{VS} = 0.0013$ mmHg/ml/min

$R_{CF} = 66.667$ mmHg.ml/min. $\quad R_{FS} = 7.6187$ mmHg/ml/min

$R_{CV} = 0.028$ mmHg.ml/min. $\quad R_{SJ} = 0.0080$ mmHg/ml/min

$R_{CB} = 13338.0$ mmHg.ml/min. $\quad R_{FB} = 13.338$ mmHg/ml/min

$R_{BV} = 3.33$ mmHg.ml/min.

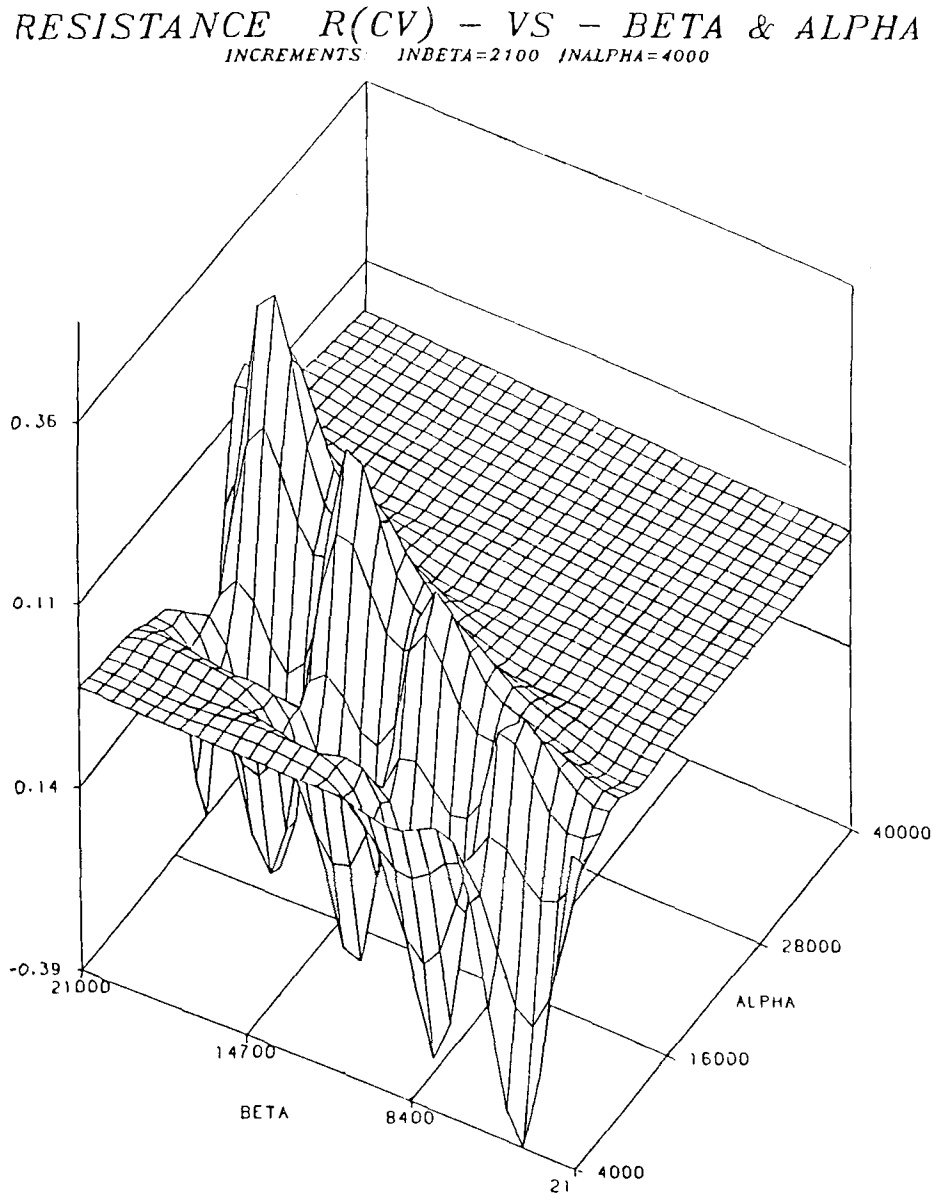

FIGURE 2. Surface of $R_{CV}(\alpha, \beta)$.

and

$C_{AB} = 0.0012$ mmHg.ml/min. $C_{FS} = 0.0494$ mmHg/ml/min

$C_{CF} = 0.0357$ mmHg.ml/min. $C_{FB} = 0.2093$ mmHg/ml/min

$C_{BV} = 0.3746$ mmHg.ml/min.

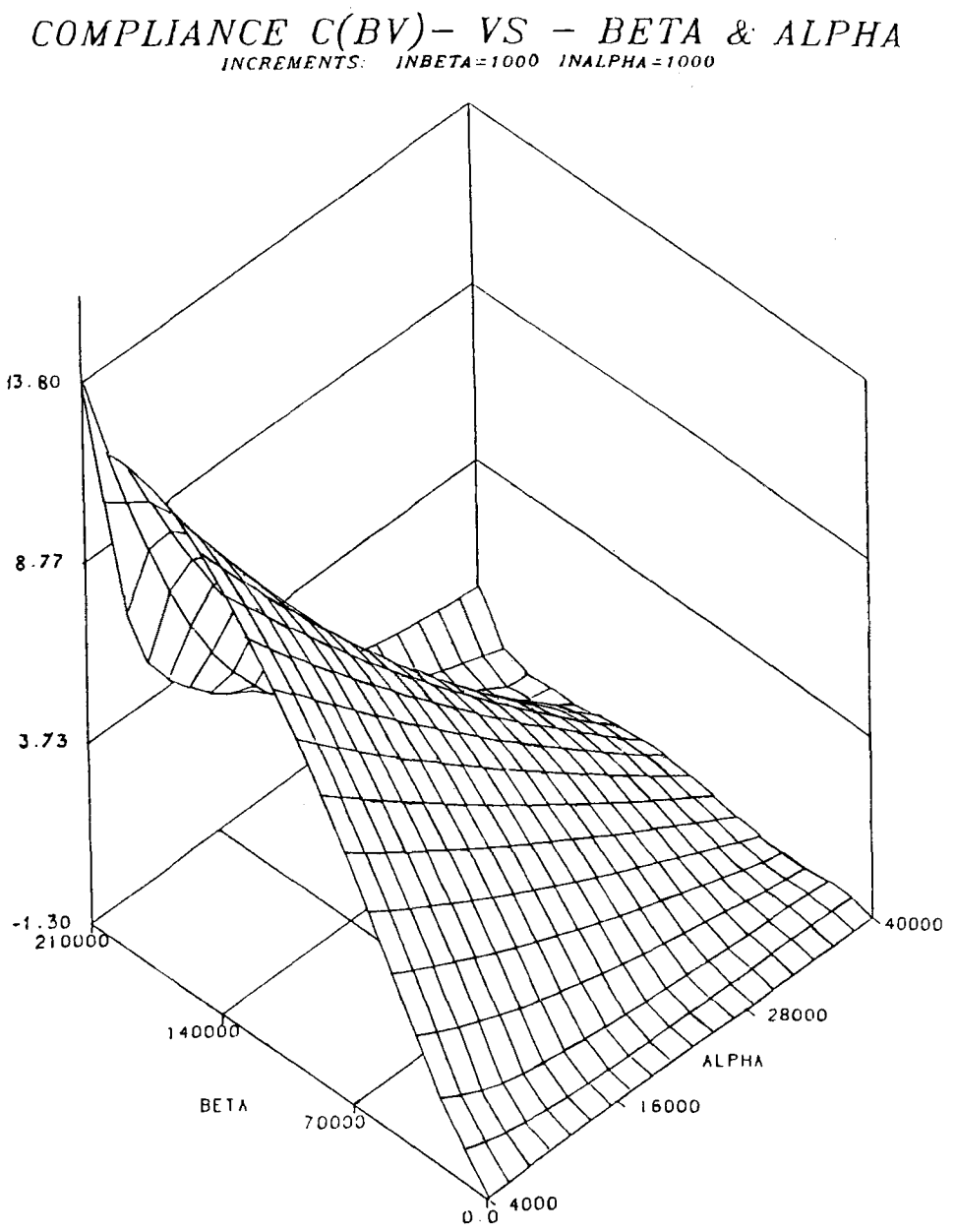

FIGURE 3. Surface of $C_{BV}(\alpha, \beta)$.

With the above value of C_{FB}, we can now assess the average deformation of the CSF compartment. Let us assume a spherical configuration of this compartment, with a mean diameter r_F. Its volume, V_F, and surface area, S_F, are given by $V_F = \frac{4}{3}\pi r_F^3$ and $S_F = 4\pi r_F^2$. By virtue of Eq. (2), we may thus express the change in V_F by

$$\Delta V_F = S_F \Delta r_F = C_{FB} P_{FB}^*. \tag{13}$$

According to Hakim *et al.* (7), the mean diameter of the CSF compartment is $r_F = \frac{1}{4} \cdot \frac{600}{2\pi}$ mm. Thus, in view of the mean pressure difference $P_{FB} = 0.5$ mmHg, the compliance value $C_{FB} = 0.2093$ ml/mmHg, and from Eq. (13), we obtain

$$\Delta r_F = 0.015 \text{ mm}.$$

This estimate of displacement of the CSF compartment boundaries is consistent with measurements done by Lewer *et al.* (12).

Finally, we wish to emphasize that the model approach presented here (and in 10,17) constitutes a methodology that can be implemented to various compartmental schemes representing different aspects of clinical data.

4. CONCLUSION

This paper presents a general methodology for parameter estimation that can be applied to any compartmental model given its phasic pressure and flux cyclic curves. The present lumped parameter model is based on discretizing the cerebral flow system into seven characteristic compartments with conductances and compliances both assumed as step functions in time. Hence, in prolonged excitations such as diseases, a different set of mean conductance and compliance coefficients is determined to describe a new linear nonsteady system. This set of coefficients are evaluated by an inverse procedure and minimal sensitivity of the conductances and compliances with respect to changes in conductance rations of cerebrospinal fluid-brain barrier to vein-venous sinus and to the blood-brain barrier one.

Model calibration with the evaluated conductances and compliances enabled predictions well within the range of available clinical observations regarding: (a) Degree of deformation of the ventricles (10,17), and measured by Lewer *et al.* (12); (b) Appearance of suction pressure in the jugular bulb during some interval of the pressure period (16).

Also the validity of the model was proven when showing a possible cause for the occurrence of Normal Pressures Hydrocephalus. This prediction was confirmed by an actual head surgery reported by Sorek *et al.* (18).

The cerebral system is a complex continuum medium where a saturated solid phase matrix (brain tissue) interacts with fluid phases in the vessels and in the ventricles. Yet, the compartmental model (9,16) enables a prediction of average trends and response of the system when subject to pressure and flux excitations.

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