On the Numerical Solution of Differential Equations

for Renal Counterflow Systems

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## 1. Introduction

The mathematical models of the renal concentrating mechanism contribute towards an increased understanding of renal function. These models involve the solution of a system of differential equations for the renal counterflow systems. Analytic solutions of these differential equations, except for very simple models, cannot be obtained. Therefore numerical methods have to be used. One of the principal considerations, in the selection of a numerical method, is to strike a proper balance between the total computational effort and the minimization of discretization (truncation) errors, so that the resulting numerical solution is a reasonably close approximation to the correct solution of the differential equations. There are two ways in which the discretization error can be decreased. First, by decreasing the size of the discretization step - usually called the space chop or step size. Naturally, this leads to an increase in the total amount of storage and computation and often also an increase in the computer round-off errors. The second alternative is to select a numerical method which, for a given space chop, has a small discretization error. This also leads to an increase in the computational effort, particularly in the number of function evaluations.

In a recent paper in this journal (1) we described how the physiological connectivity and flow directions in the various tubules constituting a nephron can be exploited to develop sparse matrix methods which lead to a decrease in the computational effort and storage requirements for a simple numerical method that uses small space chops. In the present paper we focus our attention on several other methods, which, for a given space chop, lead to less discretization error than the method described in (1). We give estimates for the error bounds for each of these methods. Results of some computational experience with the various methods are also given. It turns out that some of these methods have very little effect on the overall connectivity and therefore sparse matrix methods described in (1) can also be used with these methods to obtain highly accurate solutions without the expenditure of an inordinately large amount of storage and computing time.

One of the principal reasons for developing fast, accurate and compact numerical methods for solving the differential equations arising in the mathematical models of the kidney is that any realistic model of the kidney involves the solution of a large system of coupled differential equations, and to estimate the parameters of the model, these equations have to be solved repeatedly. Thus any improvement in storage, run time and accuracy is magnified by a large amount.

This paper is organized as follows.

In the next section, first we briefly describe a six tube vasa recta model of the medulla and then show how the Trapezoidal Rule can be used to numerically solve the differential equations for the model. We have also discussed how the error bounds for the discretization errors can be obtained. For additional details regarding this and other kidney models the reader is referred to (1, 2, 3 and 4). A preliminary version of the analysis given in the next section was announced earlier (5). In Section 3, we have described five other methods and given estimates for the discretization error bounds for each of them. The last section contains some of the results of our extensive computational experiments with the various methods.

## 2. The Mathematical Model and the Trapezoidal Rule

Let us consider a six tube vasa recta model of the medullary counterflow system (Figs. 1 and 2). This is the same model that we have described in (1), except that tubes 3, 4 and 6 in this paper were labelled respectively, as 6, 3 and 4 in (1).

Fluid (from the proximal tubule) enters tube 1 (the descending Henle's limb-DHL), then flows through tube 2 (the ascending Henle's limb-AHL), tube 3 (the distal nephron-DN) and tube 4 (the collecting duct-CD), in sequence, to emerge from tube 4 as final urine. Blood enters tube 5 (the descending vasa recta-DVR) and emerges from tube 6 (the ascending vasa recta-AVR). We assume that tube 3 exchanges solutes and water with the cortical interstitium (CI) and the concentrations of the various solutes in the CI remain unaltered. All the other tubes exchange solutes and water with tube 6 as shown in Fig. 2.

The differential equations for the model are (1,2,3)

$$\frac{d}{dx} F_{iv}(x) = - J_{iv}(x), \qquad [2.1]$$

and

$$\frac{d}{dx} F_{ik}(x) = - J_{ik}(x) , \qquad [2.2]$$

where the subscripts i, v and k refer respectively to tube i, volume and the $k^{th}$ solute. F is the axial flow, J the transmural flux (transverse flow per unit length), and x, which varies from 0 to 1, is the distance measured down the medulla from the cortico-medullary junction. For tube 3, x is measured in the direction of the flow, viz., from the top of tube 2 to the top of tube 4. $F_{ik}(x)$ and $F_{iv}(x)$ are related by the equation

$$F_{ik}(x) - F_{iv}(x)c_{ik}(x) = 0, \qquad [2.3]$$

where $c_{ik}(x)$ is the concentration of the $k^{th}$ solute at level x in tube i. $J_{iv}(x)$ and $J_{ik}(x)$ are functions of $c_{pq}(x)$, where p includes tube i and all the other tubes transversly interacting with it, q denotes all the solutes. In this model, we consider two solutes (salt and urea). The entering flows and concentrations in tubes 1 and 5 and the concentrations in the CI are given. In all the tubes, the flows and concentrations match at the points where a tube flows into the next one. Our problem is to determine the solute concentrations and volume flows in all the tubes for $0 \leq x \leq 1$.

To this end, for a space chop of size h, from [2.1] we have

$$F_{iv}(x+h) = F_{iv}(x) - \int_x^{x+h} J_{iv}(y)dy, \qquad [2.4]$$

and

$$F_{iv}(x) = F_{iv}(o) - \int_o^x J_{iv}(y)dy. \qquad [2.5]$$

The discretization of the x range [0, 1] into n equal parts yields the value 1/n for the space chop h. Let $x = jh$, where $j = 0, 1,\ldots,n$, and $F_{ivj} = F_{iv}(jh)$, then [2.4] can be written as

$$F_{iv,j+1} = F_{ivj} - \int_{jh}^{(j+1)h} J_{iv}(y)dy,$$

and the use of Trapezoidal Rule (TR) leads to the equation (6, p. 287)

$$F_{iv,j+1} = F_{ivj} - TR_j^{j+1} + \frac{h^3}{12} J''_{iv}(\eta_j), \qquad [2.6]$$

where

$$TR_j^{j+1} = (J_{iv,j+1} + J_{ivj})\, h/2 \text{ and } j\,h \leq \eta_j \leq (j+1)h. \qquad [2.7]$$

Similarly, using the composite Trapezoidal Rule (6, p. 293) in [2.5] and assuming that $J''_{iv}(x)$ is continuous in [0, 1] we have

$$F_{ivj} = F_{ivo} - TR_o^j + \frac{h^3}{12}\, j\, J''_{iv}(\bar{\eta}_j), \quad o \leq \bar{\eta}_j \leq j\,h. \qquad [2.8]$$

where $TR_o^j = (J_{ivo} + 2 J_{iv1} + \cdots + 2 J_{iv,j-1} + J_{ivj})h/2$.

The formulas [2.6] and [2.8] hold for i = 1, 3, 4 and 5. For tubes 2 and 6 the integration is done from 1 to 0 and the corresponding formulas are

$$F_{ivj} = F_{iv,j+1} + TR_{j+1}^j - \frac{h^3}{12} J''_{iv} (\eta_j) \qquad [2.9]$$

and

$$F_{ivj} = F_{ivn} + TR_n^j - \frac{h^3}{12} (n-j) J''_{iv} (\bar{\eta}_j), \; j\,h \le \bar{\eta}_j \le 1. \qquad [2.10]$$

In order to use [2.8] we have to drop the last term which cannot be easily determined. Let

$$\bar{F}_{ivj} = \bar{F}_{ivo} - TR_o^j \qquad [2.11]$$

and

$$E_{ivj} = \frac{h^3}{12} \; j \; J''_{iv} (\bar{\eta}_j) + E_{ivo}, \qquad [2.12]$$

where $E_{1vo} = E_{5vo} = o$, $E_{ivn} = E_{i-1,vn}$, $i = 2, 6$, $E_{3vo} = E_{2vo}$ and $E_{4vo} = E_{3vn}$, then from [2.8] we have

$$F_{ivj} = \bar{F}_{ivj} + E_{ivj}. \qquad [2.13]$$

A bound on the error $E_{ivj}$ can be obtained as follows. Let

$$|J''_{iv}(x)| \le A, \text{ for all } i \text{ and } 0 \le x \le 1, \qquad [2.14]$$

and $t_i$ = number of tubes upstream to tube i; $t_i = i - 1$ for $i \le 4$ and $t_i = i - 4$ for $i \ge 4$, then from [2.12] we have the required result

$$|E_{ivj}| \le \frac{h^3}{12} \left(j + \frac{t_i}{h}\right) A. \qquad [2.15]$$

In view of [2.10], for tubes 2 and 6, j must be replaced by n-j in the right hand side of [2.15]. Note that $E_{iv,j+1} - E_{ivj}$ is equal to the error term in [2.6] and therefore using [2.14] we have

$$|E_{iv,j+1} - E_{ivj}| \leq \frac{h^3}{12} A. \qquad [2.16]$$

So far we have seen how $F_{ivj}$ can be obtained from $F_{ivo}$ and $J_{ivm}$, $m = j, j-1, \ldots, 2, 1$ or from $F_{ivn}$ and $J_{ivm}$, $m = n, n-1, \ldots, j$. Unfortunately, $J_{iv}(x)$ is a function of $c_{pk}(x)$ for all solutes k and tubes interacting with tube i (including itself) and $c_{pk}(x)$'s are not known. To overcome this problem, we assume the values of $c_{pk}(jh) = c_{pkj}$ for all p, k and j and then compute $F_{ivj}$'s as functions of $c_{pkj}$'s. In order to improve the assumed $c_{pkj}$ values, we will now use [2.2] and [2.3] to define functions $\varphi_{ikj}$'s which are functions of $c_{pkj}$'s.

From [2.2] and [2.3] we have

$$\frac{d}{dx}\,[F_{iv}(x)c_{ik}(x)] = -\,J_{ik}(x).$$

Integrating the above equation and calling $\varphi_{ikj}$ as the difference between the left and right hand sides of the resulting equation, we have

$$\varphi_{ikj} = F_{iv,j+1}c_{ik,j+1} - F_{ivj}c_{ikj} + \int_{jh}^{(j+1)h} J_{ik}(y)dy.$$

If the correct $F_{ivj}$'s and $c_{ikj}$'s were known and substituted in the above equation, then $\varphi_{ikj} \equiv 0$. Let us use the Trapezoidal rule in the above equation to get

$$\varphi_{ikj} = F_{iv,j+1}c_{ik,j+1} - F_{ivj}c_{ikj} + TR_j^{j+1} - E_{ikj}, \qquad [2.17]$$

where

$$E_{ikj} = \frac{h^3}{12} J''_{ik}(\tilde{\eta}_j),\ j\,h \leq \tilde{\eta}_j \leq (j+1)\,h. \qquad [2.18]$$

The error $E_{ikj}$ cannot be evaluated, however a bound for it can be found as follows. Let

$$|J''_{ik}(x)| \leq B, \text{ for all } i, k \text{ and } x, \qquad [2.19]$$

then from [2.18] we have

$$|E_{ikj}| \leq \frac{h^3}{12} B. \qquad [2.20]$$

We will now define a function $\overline{\varphi}_{ikj}$ which is closely related to $\varphi_{ikj}$ and can be easily computed. From [2.13] and [2.17] we have

$$\varphi_{ikj} = \overline{F}_{iv,j+1} c_{ik,j+1} - \overline{F}_{ivj} c_{ikj} + TR_j^{j+1} - E_{ikj} + E_{iv,j+1} c_{ik,j+1} - E_{ivj} c_{ikj}$$

$$= \overline{\varphi}_{ikj} + R_{ikj}, \qquad [2.21]$$

where

$$\overline{\varphi}_{ikj} = \overline{F}_{iv,j+1} c_{ik,j+1} - \overline{F}_{ivj} c_{ikj} + TR_j^{j+1} \qquad [2.22]$$

and

$$R_{ikj} = - E_{ikj} + E_{iv,j+1} c_{ik,j+1} - E_{ivj} c_{ikj}. \qquad [2.23]$$

It is now possible to find a bound for the error term $R_{ikj}$. Since $c_{ik,j+1} = c_{ikj} + h\, c'_{ik}(\hat{\eta}_j)$, $j\, h \leq \hat{\eta}_j \leq (j+1)\, h$, and if we let

$$|c_{ik}(x)| < S \text{ and } |c'_{ik}(x)| \leq P \text{ for all } i, k \text{ and } x, \qquad [2.24]$$

then in view of the above facts and equation [2.23] we get

$$R_{ikj} = - E_{ikj} + (E_{iv,j+1} - E_{ivj}) c_{ikj} + h\, E_{iv,j+1} c'_{ik}(\hat{\eta}_j) \qquad [2.25]$$

and using [2.15], [2.16], [2.20] and [2.24] we have

$$|R_{ikj}| \le \frac{h^3}{12} B + \frac{h^3}{12} A\ S + h \cdot \frac{h^3}{12} (j+1 + \frac{t_i}{h})\ A\ P$$

or

$$|R_{ikj}| \le \frac{h^3}{12} [B + A(S + 4P)], \qquad [2.26]$$

since max $(j+1)h = 1$ and max $t_i = 3$.

The actual value of $R_{ikj}$ cannot be determined; only the bound [2.26] is available, therefore, as mentioned earlier, $\varphi_{ikj}$ given by [2.17] cannot be used but in its place we can use $\overline{\varphi}_{ikj}$ which is given by [2.22] We recall that $TR_j^{j+1} = (J_{ik,j+1} + J_{ikj})h/2$ and since $J_{ikj}$'s are functions of $c_{pkj}$'s for all interacting tubes p and solutes k, it is evident that $\overline{\varphi}_{ikj}$ is also a function of $c_{pkj}$'s. Furthermore, if $\overline{\varphi}_{ikj} = 0$ for some set of values of $c_{pkj}$'s then, aside from the discretization errors $R_{ikj}$, equations [2.2] and [2.3] are satisfied and we have obtained an approximate solution to our problem. Let us impose some fixed ordering on the triple 'ikj' and let $\overline{\varphi}$ and c denote the vector functions with elements $\overline{\varphi}_{ikj}$ and $c_{ikj}$ respectively. Then the solution c, which is a vector of concentration of the nonlinear system of equations

$$\overline{\varphi}(c) = 0\ , \qquad [2.27]$$

also satisfies the discrete forms of [2.1], [2.2] and [2.3], if the discretization errors are neglected. Equation [2.27] is solved by Newton's method (1,2,3,4), which can be described briefly as follows.

If $c^{\alpha}$ is a given approximation to a root $\hat{c}$ of $\overline{\varphi}(c) = 0$ then the next approximation $c^{\alpha+1}$ is given by

$$c^{\alpha+1} = c^{\alpha} - (\overline{\varphi}'(c^{\alpha}))^{-1}\overline{\varphi}(c^{\alpha}), \ \alpha = 0, 1, 2, \ldots,$$

where $\overline{\varphi}'(c^{\alpha})$ is the Jacobian of $\overline{\varphi}(c)$ at $c^{\alpha}$. It is well known that if the initial approximation $c^{0}$ is sufficiently close to $\hat{c}$ then the sequence of iterates $\{c^{\alpha}\}$ converges quadratically to $\tilde{c}$. Good choice of the initial approximation and methods for extending the domain of convergence (how close $c^{0}$ should be to $\hat{c}$) and related topics are discussed in (7). The use of the so-called continuation method for this purpose will be described in a later paper.

We now return to the consideration of the discretization errors. We pose the following problem. If an exact solution $c^{*}_{ik}(x)$ of [2.1], [2.2] and [2.3] is given, $c^{*}$ is the vector of concentrations $c^{*}_{ikj}$ and $\hat{c}$ is a solution of [2.27], then determine a bound for the error vector $\hat{c} - c^{*}$. We will show that under certain conditions a reasonable estimate for the norm of $\hat{c} - c^{*}$ can be obtained.

We know that $J_{iv}(x)$ and $J_{ik}(x)$ are functions of $c_{pk}(x)$, therefore $J''_{iv}(x)$ and $J''_{ik}(x)$ will also be functions of $c_{pk}(x)$, $c'_{pk}(x)$ and $c''_{pk}(x)$ and it follows that $R_{ikj}$ is also a function of $c_{pk}(x)$, $c'_{pk}(x)$ and $c''_{pk}(x)$, where x is evaluated at jh and the various $\eta_j$ values. Let $\gamma^{*}$ denote a vector of $c^{*}_{pk}(x)$, $c^{*\prime}_{pk}(x)$ and $c^{*\prime\prime}_{pk}(x)$ evaluated at the relevant jh and $\eta_j$ values. If $\varphi$, $\overline{\varphi}$ and R denote the vector functions with their components related as in [2.20] then we have

$$0 = \varphi(c^{*}) = \overline{\varphi}(c^{*}) + R(\gamma^{*}),$$

or

$$\overline{\varphi}(c^{*}) = - R(\gamma^{*})$$

and therefore in view of [2.26] we have

$$\|\overline{\varphi}(c^{*})\| = \| R(\gamma^{*})\| \leq \frac{h^3}{12} [B + A(S + 4P)] = O(h^3). \qquad [2.28]$$

If $\hat{c}$ is a solution of $\overline{\varphi}(c) = 0$ obtained by Newton's method, such that

$$\|\overline{\varphi}(\hat{c})\| \leq \epsilon, \text{ where } \epsilon \text{ is small,} \qquad [2.29]$$

and if we assume that $\overline{\varphi}(c)$ is a Gateaux-differentiable on an open convex set and $c^*$ and $\hat{c}$ both lie in this set, then (8, pp. 68-69).

$$\overline{\varphi}(\hat{c}) - \overline{\varphi}(c^*) = B(c^*, \hat{c})(\hat{c} - c^*), \qquad [2.30]$$

where $B(c^*, \hat{c})$ is a matrix whose $r^{th}$ row is equal to the $r^{th}$ row of $\overline{\varphi}'(z^r)$, $z^r = c^* + t_r(\hat{c} - c^*)$ and $0 \leq t_r \leq 1$ (In general, $t_r$ will be different for each r). We assume that $B(c^*, \hat{c})$ is invertible; for example, this is true when $\overline{\varphi}'(z)$ is row diagonally dominant for $z = c^* + t(\hat{c} - c^*)$ and all $0 \leq t \leq 1$. This diagonal dominance is exhibited by many models due to the fact that the concentration $c_{ikj}$ has the most effect on the $\varphi_{ikj}$ - the mass balance equations for the (ikj) compartment. In view of the above facts and equation [2.30], we get

$$\hat{c} - c^* = [B(\hat{c}, c^*)]^{-1} [\overline{\varphi}(\hat{c}) - \overline{\varphi}(c^*)].$$

If $\|[B(\hat{c},c^*)]^{-1}\| \leq M$, then from [2.28], [2.29] and the above equation we have

$$\|\hat{c} - c^*\| \leq M(\epsilon + \frac{h^3}{12} [B + A(S + 4P)]).$$

If $\overline{\varphi}(c) = 0$ is solved such that $\epsilon << h^3$, then from the above equation we get finally the estimate

$$\|\hat{c} - c^*\| = O(h^3). \qquad [2.31]$$

An alternative way to get [2.31] is to assume that terms involving $\|\hat{c} - c^*\|^p$, for $p \geq 2$ are much smaller than $\|\hat{c} - c^*\|$ and therefore can be neglected. If $\overline{\varphi}(c)$ has a Frechet derivative at $c^*$, then (8, p.184)

$$\bar{\varphi}(\hat{c}) = \bar{\varphi}(c^*) + \bar{\varphi}'(c^*)(\hat{c} - c^*) + T(\hat{c} - c^*),$$

where $T(\hat{c} - c^*)$ includes terms whose norms involve $\|\hat{c} - c^*\|^p$, $p \geq 2$. In many cases, $\bar{\varphi}(c)$ is a quadratic in c, and there are no third and higher order terms. Neglecting $T(\hat{c} - c^*)$, we have

$$\bar{\varphi}(\hat{c}) - \bar{\varphi}(c^*) \approx \bar{\varphi}'(c^*)(\hat{c} - c^*).$$

Assuming that $(\bar{\varphi}'(c^*))^{-1}$ exists, we have

$$\hat{c} - c^* \approx [\bar{\varphi}'(c^*)]^{-1} [\bar{\varphi}(\hat{c}) - \bar{\varphi}(c^*)].$$

Once again, if $\|[\bar{\varphi}'(c^*)]^{-1}\| \leq M$, we get the same estimate as in [2.31].

## 2. Other Methods

We will describe four other methods in this section for numerically integrating $J_{iv}(x)$ and $J_{ik}(x)$. But prior to that we will briefly point out that in all the methods, including the Trapezoidal Rule, it is possible to assume both $F_{ivj}$'s and $c_{ikj}$'s as variables and append to $\varphi_{ikj}$ another set of equations

$$\varphi_{ivj} = F_{iv,j+1} - F_{ivj} + TR_j^{j+1} - \frac{h^3}{12} J''_{iv}(\eta_j)$$

and then solve the augmented system. Following an analysis which is analogous to that given in the previous section, we get

$$\|R_{ikj}\| \leq \frac{h^3}{12} \max(A, B) = O(h^3).$$

Though the above modification increases the size of the system the resulting equations are much sparser than before and the total work is in fact somewhat less than before.

A description of the four methods now follows:

(a) The Mid-Point Rule.

In order to numerically evaluate $\int_o^{jh} J_{iv}(y)dy$, $\int_{jh}^{(j+1)h} J_{iv}(y)dy$ and $\int_{jh}^{(j+1)h} J_{ik}(y)dy$, instead of the Trapezoidal Rule, we can use the Mid-Point Rule (MP). In this case we have, for example (6, p. 286),

$$\int_{jh}^{(j+1)h} J_{iv}(y)dy = [J_{iv}((j+\tfrac{1}{2})h)]h + \frac{h^3}{24} J''(\eta_j), \ j\ h \le \eta_j \le (j+1)\ h.$$

We assume that the values of $c_{ik}(x)$, $J_{ik}(x)$, $J_{iv}(x)$ etc. can be computed at the intermediate points $(j+\frac{1}{2})h$. The analysis is similar to that for the TR and instead of [2.26], we have

$$\|R_{ikj}\| \le \frac{h^3}{24} [B + A(S + 4P)].$$

Obviously, this is a somewhat better bound but still $\|\hat{c} - \hat{c}\| = O(h^3)$ which is the estimate we had for the TR.

(b) The Cubic Overhang Method

Essentially this involves first fitting a cubic through the points $(j-1)h$, $jh$, $(j+1)h$ and $(j+2)h$ and then using this to integrate from $jh$ to $(j+1)h$. For example,

$$\int_{jh}^{(j+1)h} J_{iv}(y)dy = \frac{h}{24}[- J_{iv,j-1} + 13\ J_{ivj} + 13\ J_{iv,j+1} - J_{iv,j+2}]$$

$$+ \frac{11}{720} h^5 J_{iv}^{iv}(\eta_j), \ (j-1)h \le \eta_j \le (j+2)h. \qquad [3.1]$$

At the beginning (or end) of each tube in place of the above equation we use

$$\int_o^h J_{iv}(y)dy = \frac{h}{24} [9\ J_{ivo} + 19\ J_{iv1} - 5\ J_{iv2} + J_{iv3}]$$

$$+ \frac{19}{720} h^5 J_{iv}^{iv}(\eta_o), \ o \le \eta_o \le 3\ h.$$

If we let

$$|J_{iv}^{iv}(x)| \le A, \quad |J_{ik}^{iv}(x)| \le B, \text{ for all i, k and x}$$

then as in the case of TR we get

$$\|R_{ikj}\| \le \frac{19h^5}{720} [B + A(S + 4P)] = O(h^5).$$

(c) Corrected Trapezoidal Rule

We have the formula (6, p.288-289)

$$\int_{jh}^{(j+1)h} J_{iv}(y)dy = TR_j^{j+1} + \frac{h^2}{12} [J'_{ivj} - J'_{iv,j+1}] + \frac{h^5}{720} J_{iv}^{iv}(\eta_j), \quad [3.2]$$

where $j h \le \eta_j \le (j+1)h$. In order to compute the terms of the type $J'_{ivj}$ we need the derivatives of $c_{ikj}$. We can compute these by using either the natural or cubic splines to find $c'$ from c. In the case of cubic splines it is known (9, p. 42) that $c'$ has an error of $O(h^3)$ and under suitable boundedness assumptions on the c and x derivatives of $J'_{ivj}$ and $J'_{ikj}$ it can be shown that the error in $\frac{h^2}{12}(J'_{ivj} - J'_{iv,j+1})$ is $O(h^6)$ when cubic splines are used to compute $c'$ from c. Hence the dominant error term in the Corrected Trapezoidal Rule still remains $\frac{h^5}{720} J_{iv}^{iv}(\eta_j)$ and

$$\|R_{ikj}\| \le \frac{h^5}{720} [B + A(S + 4P)] \approx O(h^5)$$

where A and B are the same as in the Cubic Overhang method. Using natural splines to compute $c'$ leads to a much lower order bound for $\|R_{ikj}\|$ and since the computational work is approximately the same for both the natural and the cubic splines, we have discontinued the use of natural splines.

(d) Fifth Degree Overhang

In this case integration formulas were used which can be obtained by using polynomials of degree five. Let f(y) denote the function to be integrated, e.g.,

$f(y) = J_{iv}(y)$, then we have

$$\int_{jh}^{(j+1)h} f(y) = h\,[f_k + \gamma_{j,k+1}\,\Delta f_k + \gamma_{j,k+2}\,\Delta^2 f_k + \gamma_{j,k+3}\,\Delta^3 f_k$$

$$+ \gamma_{j,k+4}\,\Delta^4 f_k + \gamma_{j,k+5}\,\Delta^5 f_k] + E_j^{j+1},$$

where $\Delta^p$ denotes the $p^{th}$ forward difference,

$$k \le j \le k+4,\ i = j-k,\ \gamma_{j,k+1} = \frac{2i+1}{2},$$

$$\gamma_{j,k+2} = \frac{6i^2-1}{12},\ \gamma_{j,k+3} = \frac{1}{6}\left(i^3 - \frac{3}{2}i^2 + \frac{1}{4}\right),$$

$$\gamma_{j,k+4} = \frac{1}{4!}\left(i^4 - 4i^3 + 4i^2 - \frac{19}{30}\right),$$

and

$$\gamma_{j,k+5} = \frac{1}{5!}\left(i^5 - \frac{15}{2}i^4 + \frac{55}{3}i^3 - 15i^2 + \frac{9}{4}\right).$$

The bound for $E_j^{j+1}$ can be estimated by using the standard methods. For example,

$$|E_{ikj}| \le 0.014269\, h^7 |J_{ik}^{vi}(\eta_j)|$$

and therefore

$$\|R_{ikj}\| \le 0.014269\, h^7 [B + A(S + 4P)] = O(h^7),$$

where B and A are the bounds on the sixth derivatives of $J_{ik}(x)$ and $J_{iv}(x)$.

Thus we have seen that, except for the Corrected Trapezoidal Rule, the error bound is of the order $h^{p+2}$ where p is the degree of the polynomial that is used to derive the integration formula.

We will now show that the Corrected Trapezoidal Rule leads to the Cubic Overhang method if the derivatives are approximated by central differences. For example if

$$J'_{ivj} - J'_{iv,j+1} \approx (J_{iv,j+1} - J_{iv,j-1})/2h - (J_{iv,j+2} - J_{ivj})/2h$$

then from [3.2], neglecting the error term, we have

$$\int_{jh}^{(j+1)h} J_{iv}(y)dy \approx (J_{ivj} + J_{iv,j+1})h/2 + \frac{h}{24}[J_{iv,j+1} - J_{iv,j-1} - J_{iv,j+2} + J_{ivj}]$$

$$= \frac{h}{24}[- J_{iv,j-1} + 13 J_{ivj} + 13 J_{iv,j+1} - J_{iv,j+2}],$$

which is the same as [3.1]. Thus we see that the corrected Trapezoidal Rule can also be thought of as a 'cubic' method and the error is $h^{p+2}$ where $p = 3$.

It was pointed out in (1) and (3) that when the Trapezoidal Rule is used the resulting Jacobian $\overline{\varphi}'(c)$ either has a bordered block triangular form or can be readily permuted to this form by a renumbering of the tubes. Furthermore, all the diagonal blocks associated with the tubes, except tube 5, have block lower triangular forms with second order diagonal blocks due to the two solutes. The use of Mid-Point Rule retains this structure. The Cubic Overhang method within each tube makes the diagonal matrices band lower triangular with a bandwidth of two (for the definitions of the various desirable forms for sparse matrices see (10)). On the other hand, the Fifth Degree Overhang method makes the bandwidth four. The use of splines within the tubes completely fills the diagonal blocks associated with the tubes. However, this disadvantage is somewhat offset by the smoothness of the resulting concentration profiles, since the use of splines forces the first and second derivatives of the concentrations to match at the junctions of consecutive subintervals of the range x.

## 3. Computational Results

The methods described in the preceding sections, which lead to less discretization errors than the usual Trapezoidal Rule, were programmed in FORTRAN IV for the UNIVAC 1110 at the University Computing Center in Stony Brook. The storage requirements and running times did not show a significant difference among the various methods. In order to determine the relative accuracy of the results obtained by using the various methods, the urea concentrations at all medullary levels in the collecting duct (tube 3) were compared. The collecting duct was chosen for this comparison because the final concentrated urine emerges from it and the maximum possible error is likely to occur in it. The relative accuracy of concentrations in other tubes exhibited results similar to the urea concentrations in the collecting duct. Some of the results of our computational experiments are shown in Table 1. We have

Table 1. A comparison of urea concentrations in the collecting duct. Notation: 1 = Trapezoidal Rule, 2 = Trapezoidal Rule with 20 chops, 3 = Cubic Overhang, 4 = Corrected Trapezoidal Rule, 5 = Fifth Degree Overhang

| | |
|---|---|
| $\|C(1) - C(3)\|/\|C(3)\|$ | .016 |
| $\|C(3) - C(5)\|/\|C(5)\|$ | .013 |
| $\|C(3) - C(4)\|/\|C(4)\|$ | .006 |
| $\|C(2) - C(4)\|/\|C(4)\|$ | .018 |

compared the concentrations by using the usual two norm. C(I) denotes the vector of urea concentrations in the collecting duct obtained by method I, where I = 1, 3, 4 and 5 refer, respectively, to the Trapezoidal Rule, Cubic Overhang, Corrected Trapezoidal Rule and the Fifth Degree Overhang. In each case the medulla was divided into ten chops yielding $h = 0{\cdot}1$. In order to compare the increase in accuracy between decreasing h and using methods with smaller discretization errors, we computed the vector of urea concentrations by using the Trapezoidal Rule with twenty chops and keeping only those concentrations that correspond to the ten chop medullary levels. This, of course, required four times the storage.

It is evident from Table 1 that the Cubic Overhang is a significant improvement over the Trapezoidal Rule, as is the Fifth Degree Overhang over the Cubic Overhang. The close agreement between the concentrations obtained by using the Cubic Overhang $C(3)$ and the Corrected Trapezoidal Rule $C(4)$ is quite remarkable because there is a significant difference between the two methods (we recall that the derivatives of the concentrations that are used in the Corrected Trapezoidal Rule were computed by using cubic splines). The last line in Table 1 shows clearly that instead of taking $h = 0.05$ and thus quadrupling the storage, it is much better to use the Corrected Trapezoidal Rule or the Cubic Overhang method with $h = 0.1$.

In conclusion, we can safely state that the use of accurate integration formulas, whenever possible, generally leads to better results when solving the stiff multiple boundary value problems of the type described in this paper.

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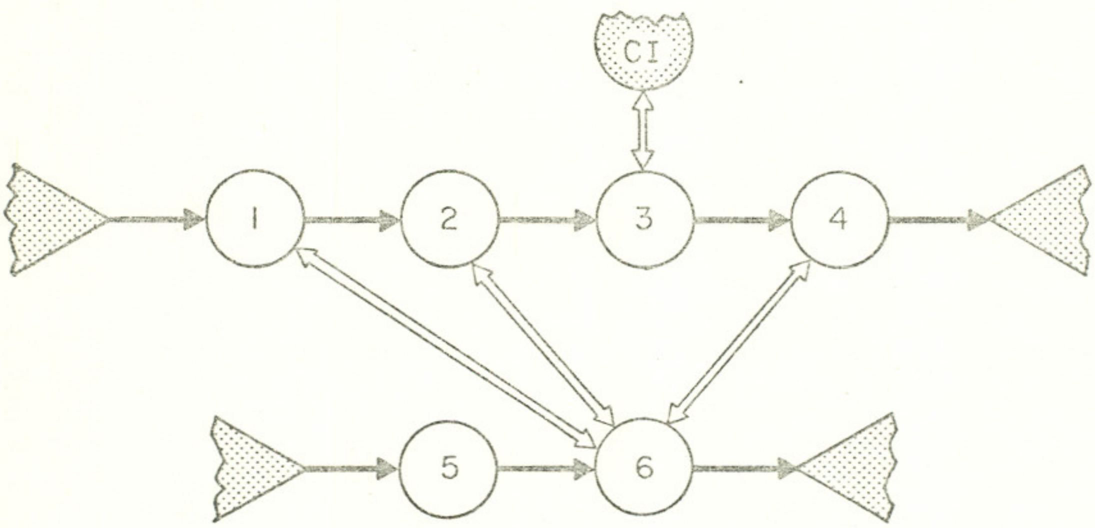
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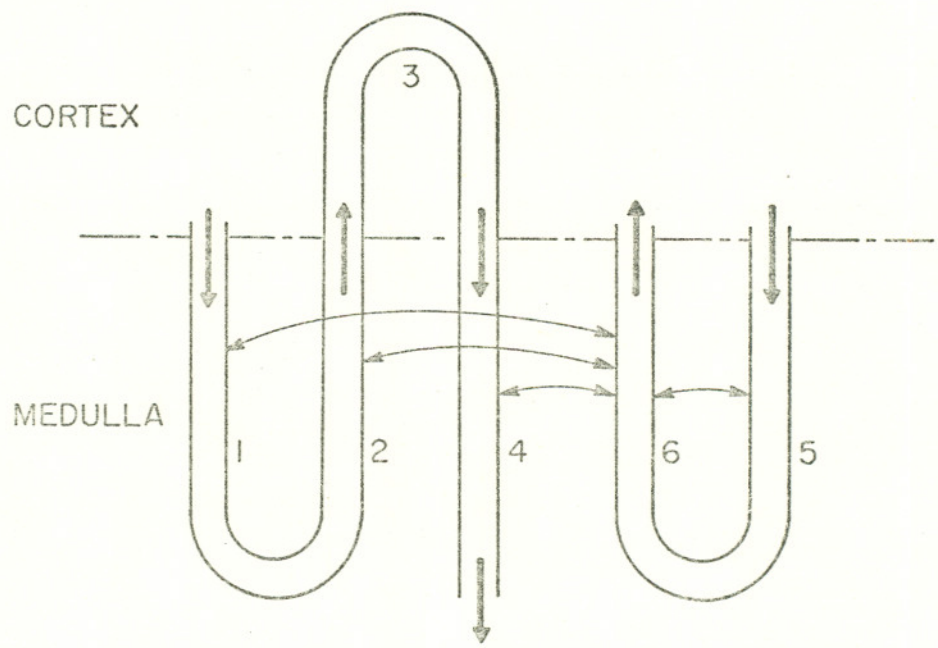
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## Figure Legends

Fig. 1. A six tube vasa recta model.

Fig. 2. Axial (⇒) and Transverse (→) flows in the six tube vasa recta model.