Iterative operator splitting methods for the capillary formation model in tumor angiogenesis problem : Application and Analysis

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Outline

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Mathematical model

$$\frac{\partial u}{\partial t} = D\frac{\partial}{\partial x}(u\frac{\partial}{\partial x}(\ln\frac{u}{f(x)})), \quad x \in (0,1), \quad t \in (0,T] \tag{1}$$

Initial condition is given by

$$u(x,0) = 1, \quad x \in (0,1), \tag{2}$$

and boundary conditions are given by

$$\begin{aligned} Du\frac{\partial}{\partial x}(\ln\frac{u}{f(x)}) \mid_{(0,t)} &= 0, \quad t \in [0,T], & (3) \\ Du\frac{\partial}{\partial x}(\ln\frac{u}{f(x)}) \mid_{(1,t)} &= 0, \quad t \in [0,T], & (4) \end{aligned}$$

Mathematical model

where $f(x)$ is the so-called transition probability function and given by

$$f(x) = \left(\frac{a + A_1 x^k (1-x)^k}{b + A_1 x^k (1-x)^k}\right)^{\alpha_1} \left(\frac{c + 1 - A_2 x^k (1-x)^k}{d + 1 - A_2 x^k (1-x)^k}\right)^{\alpha_2} \qquad (5)$$

and
$u(x,t)$ is the concentration of Endothelial Cells, D is the cell diffusion constant and a, b, c, d, A_1, A_2, k, α_1, α_2 are some arbitrary constants.

Mathematical model

Model describes the endothelial cells movement in capillary formation.

See, Levine et al.(2001), Othmer & Stevens (1997), David (1990).

Outline

Iterative operator splitting method

Consider the abstract Cauchy problem

$$\begin{aligned} u'(t) &= (A+B)u(t), \quad t \in [0,T] \qquad (6) \\ u(0) &= u_0 \qquad (7) \end{aligned}$$

where A and B are bounded linear operators and u_0 is initial condition.

Iterative operator splitting method

The method is based on iteration by fixing the splitting discretization step size τ on time interval $[t^n, t^{n+1}]$.
The following algorithms are then solved consecutively for $i = 1, 3, \ldots, 2m+1$

$$u_i'(t) = Au_i(t) + Bu_{i-1}(t) \text{ with } u_i(t^n) = u^n \tag{8}$$

$$u_{i+1}'(t) = Au_i(t) + Bu_{i+1}(t) \text{ with } u_{i+1}(t^n) = u^n \tag{9}$$

where u^n is the known split approximation at time level $t = t^n$ and $u_0 \equiv 0$ is our initial guess.

The split approximation at the time-level $t = t^{n+1}$ is defined as $u^{n+1} = u_{2m+2}(t^n)$.

See, Farago & Geiser (2007), Geiser (2008).

Outline

Application of Iterative splitting to mathematical model

Consider equation (1), by setting $F(x) = \frac{f'(x)}{f(x)}$ we turn it into simple form

$$u_t = D(u_{xx} - u_x F - F_x u) \tag{10}$$

and after discretizing the space, initial condition becomes

$$u_m = 1, \quad 0 \leq m \leq N, \tag{11}$$

and boundary conditions are

$$\begin{aligned} D(\frac{\partial u_0}{\partial x} - u_0 F_0) &= 0, \quad \text{for} \quad t > 0, \qquad (12) \\ D(\frac{\partial u_N}{\partial x} - u_N F_N) &= 0, \quad \text{for} \quad t > 0 \qquad (13) \end{aligned}$$

Application of Iterative splitting to mathematical model

We split the equation

$$u_t = D(u_{xx} - u_x F - F_x u) \tag{14}$$

as diffusion part

$$u_t = D u_{xx} \tag{15}$$

and as advection-reaction part

$$u_t = -D u_x F - D F_x u. \tag{16}$$

Application of Iterative splitting to mathematical model

Applying the iterative splitting schemes (8), (9) to model problem (14) then we have

$$u_i' = D(u_i)_{xx} - D((u_{i-1})_x F - F_x u_{i-1}) \tag{17}$$

$$u_{i+1}' = D(u_i)_{xx} - D((u_{i+1})_x F - F_x u_{i+1}) \tag{18}$$

where $i = 1, 3, \ldots, 2m+1$.

Application of Iterative splitting to mathematical model

Diffusion term at each grid point (x_m, t) becomes

$$\frac{\partial^2 u}{\partial x^2} \Big|_{(x_m,t)} = \frac{1}{h^2}(u_{m+1}(t) - 2u_m(t) + u_{m-1}(t)) \tag{19}$$

and advection term becomes

$$\frac{\partial u}{\partial x} \Big|_{(x_m,t)} = \frac{1}{2h}(u_{m+1}(t) - u_{m-1}(t)) \tag{20}$$

where h is the spatial stepping and $m = 0, 1, \ldots, N$.

Application of Iterative splitting to mathematical model

After assembling the unknowns of (19), for each m, and embedding the approximation of derivative terms in boundary conditions in (12), (13), we have the following system of equations in matrix form as follows:

$$u_{xx} = A_1 u \tag{21}$$

$$A_1 = \frac{1}{h^2}\begin{pmatrix} -2+(1-hF_0) & 1 & 0 & 0 & 0 \\ 1 & -2 & 1 & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & 0 \\ 0 & 0 & 1 & -2 & 1 \\ 0 & 0 & 0 & 1 & -2+(1+hF_N) \end{pmatrix}_{(N+1)\times(N+1)}$$

Application of Iterative splitting to mathematical model

$$u_x = B_1 u \tag{22}$$

$$B_1 = \frac{1}{2h}\begin{pmatrix} -(1-hF_0) & 1 & 0 & 0 & 0 \\ -1 & 0 & 1 & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & 0 \\ 0 & 0 & -1 & 0 & 1 \\ 0 & 0 & 0 & -1 & (1+hF_N) \end{pmatrix}_{(N+1)\times(N+1)} .$$

Application of Iterative splitting to mathematical model

We fix the functions $F(x)$ and $F'(x)$ at each discretization points $m = 0, 1, \ldots, N$ and we use central difference approximation for each $F'(x_m)$. Redefining equations (17),(18) we have

$$u_i' = Au_i + Bu_{i-1} \tag{23}$$

$$u_{i+1}' = Au_i + Bu_{i+1} \tag{24}$$

where $A = DA_1$, $B = -DF(\underline{x})B_1 - DF'(\underline{x})$. We then solve Eqns. (23) and (24) by using midpoint method on each subinterval $[t^n, t^{n+1}], n = 0, 1, ..N$.

Application of Iterative splitting to mathematical model

Algorithms can be read as:

$$u_i^{n+1} = (I - \frac{\tau}{2}A)^{-1}((I + \frac{\tau}{2}A)u_i^n + \frac{\tau}{2}B(u_{i-1}^n + u_{i-1}^{n+1})) \tag{25}$$

$$u_{i+1}^{n+1} = (I - \frac{\tau}{2}B)^{-1}((I + \frac{\tau}{2}B)u_{i+1}^n + \frac{\tau}{2}A(u_i^n + u_i^{n+1})) \tag{26}$$

where τ is time discretization step and starting for $i = 1$, initial guess $u_0(t) = 0$, initial conditions $u_1(t) = u_0$ and $u_2(t) = u_0$.

Outline

Error bound

Theorem

Let A, B $\in \mathcal{L}(X)$ *be given linear bounded operators. The cauchy problem is in (6). Then the problem has a unique solution. The error bound of the iteration (8), (9)* $i = 1, 3, \ldots, 2m+1$ *in terms of the operator norm is given by*
for ***i*** *is* ***odd***

$$||\epsilon_i|| \leq (K_1.||A||)^{\frac{i-1}{2}}.(K_2.||B||)^{\frac{i+1}{2}}.||\epsilon_0||\frac{t^i}{i!} \tag{27}$$

for ***i*** *is* ***even***

$$||\epsilon_i|| \leq (K_1.||A||)^{\frac{i}{2}}.(K_2.||B||)^{\frac{i}{2}}.||\epsilon_0||\frac{t^i}{i!} \tag{28}$$

where ϵ_0 *is the difference between the exact solution and initial guess,*
$||exp(At)|| \leq K_1$, $||exp(Bt)|| \leq K_2$ *for* $t \geq 0$.

Error bound

Proof.

we know the exact solution of

$$u'(t) = (A+B)u(t), \quad u(0) = u_0 \tag{29}$$

from variation of constant formula

$$u(t) = e^{At}u_0 + \int_0^t e^{A(t-s)}Be^{(A+B)s}u_0 ds \tag{30}$$

□

Error bound

Proof.

For the first iteration, again from variation of constant formula

$$u_1(t) = e^{At}u_0 + \int_0^t e^{A(t-s)}Bu_0 ds \tag{31}$$

after substracting and taking the norm we have

$$||u(t) - u_1(t)|| = ||\int_0^t e^{A(t-s)}B(e^{(A+B)s} - u_0)ds|| \tag{32}$$

$$||\epsilon_1|| = ||\int_0^t e^{A(t-s)}B\epsilon_0 ds|| \tag{33}$$

$$||\epsilon_1|| \leq K_1.||B||.||\epsilon_0||t \tag{34}$$

☐

Error bound

Proof.

For the second iteration

$$||u(t) - u_2(t)|| = || \int_0^t e^{B(t-s)} A(e^{(A+B)s} - u_1) ds|| \tag{35}$$

$$||\epsilon_2|| = || \int_0^t e^{B(t-s)} A(\epsilon_1) ds|| \tag{36}$$

$$||\epsilon_2|| \leq K_2 \int_0^t ||A||.||\epsilon_1|| ds \tag{37}$$

$$||\epsilon_2|| \leq K_2.K_1.||A||.||B||.||\epsilon_0|| \frac{t^2}{2} \tag{38}$$

Then go on by induction. □

Error bound

Theorem

The local error of the iterative splitting method which based on midpoint rule has more accuracy then the error of midpoint without splitting.

Error bound

Proof.

The error of iterative splitting with midpoint rule is

$$|u_{spl}(t) - u_{exact}(t)| \leq AB(A+B)\frac{t^3}{6}u_0 \tag{39}$$

and without splitting is

$$|u_{mid}(t) - u_{exact}(t)| \leq (A+B)^3\frac{t^3}{12}u_0. \tag{40}$$

☐

Error bound

Proof.

Let

$$||\epsilon_{spl}|| = ||u_{spl}(t) - u_{exact}(t)|| \leq ||A||.||B||.||A+B||\frac{t^3}{6}u_0$$

and

$$||\epsilon_{mid}|| = ||u_{mid}(t) - u_{exact}(t)|| \leq ||(A+B)^3||\frac{t^3}{12}u_0$$

then we have estimation

$$\frac{||\epsilon_{spl}||}{||\epsilon_{mid}||} \leq 1 \tag{41}$$

where $2||A||.||B|| \leq ||A+B||^2$. □

Outline

Stability analysis via Von-Neuman

Let's rewrite the mathematical model (14) as

$$u_t = A_d u + B_{ar} u \tag{42}$$

where $A_d = D\partial_{xx}$, $B_{ar} = -DF(x)\partial_x - DF'(x)$.

Stability analysis via Von-Neuman

After applying iterative splitting algorithms (8), (9) with midpoint rule to (42) on $[t^n, t^{n+1}]$ interval with time step τ, we have

$$\begin{pmatrix} u_1^{n+1} \\ u_2^{n+1} \end{pmatrix} = \tilde{L} \begin{pmatrix} u_1^n \\ u_2^n \end{pmatrix} + \frac{\tau}{2} \begin{pmatrix} (I - \frac{\tau}{2}A_d)^{-1} B_{ar}(u_0^n + u_0^{n+1}) \\ \frac{\tau}{2}A_d(I - \frac{\tau}{2}A_d)^{-1}(I - \frac{\tau}{2}B_{ar})^{-1} B_{ar}(u_0^n + u_0^{n+1}) \end{pmatrix}$$

Stability analysis via Von-Neuman

where

$$\tilde{L} = \begin{pmatrix} (I - \frac{\tau}{2}A_d)^{-1}(I + \frac{\tau}{2}A_d) & 0 \\ \frac{\tau}{2}A_d(I - \frac{\tau}{2}A_d)^{-1}(I - \frac{\tau}{2}B_{ar})^{-1}(I + \frac{\tau}{2}A_d) & (I - \frac{\tau}{2}B_{ar})^{-1}(I + \frac{\tau}{2}B_{ar}) \\ +(I - \frac{\tau}{2}B_{ar})^{-1}\frac{\tau}{2}A_d & \end{pmatrix}$$

where $A_d = D\partial_{xx}$, $B_{ar} = -DF(x)\partial_x - DF'(x)$ are linear operators.

Stability analysis via Von-Neuman

Suppose that

$$F(x) < k_1, \quad F'(x) < k_2.$$

Applying a continuous Fourier Transform according the formula

$$\hat{u}(w) = \frac{1}{\sqrt{2\pi}} \int_{\mathbf{R}} e^{-iwx} u(x) dx \tag{43}$$

Stability analysis via Von-Neuman

Yields

$$\begin{pmatrix} \tilde{u}_1^{n+1} \\ \tilde{u}_2^{n+1} \end{pmatrix} = \begin{pmatrix} \frac{1-D\frac{\tau}{2}w^2}{1+D\frac{\tau}{2}w^2} & 0 \\ \frac{-\frac{\tau}{2}Dw^2(1-\frac{\tau}{2}Dw^2)}{(1+\frac{\Delta t}{2}Dw^2)(1+\frac{\tau}{2}D(k_1wi+k_2))} + \frac{-\frac{\tau}{2}Dw^2}{1+\frac{\tau}{2}D(k_1wi+k_2)} & \frac{1-\frac{\tau}{2}D(k_1iw+k_2)}{1+\frac{\tau}{2}D(k_1iw+k_2)} \end{pmatrix} \begin{pmatrix} \tilde{u}_1^{n} \\ \tilde{u}_2^{n} \end{pmatrix} \quad (44)$$

Stability analysis via Von-Neuman

The eigenvalues are

$$\lambda_1 = \frac{1 - D\frac{\tau}{2}w^2}{1 + D\frac{\tau}{2}w^2} \quad \text{and} \quad \lambda_2 = \frac{1 - \frac{\tau}{2}D(k_1 iw + k_2)}{1 + \frac{\tau}{2}D(k_1 iw + k_2)}.$$

Stability analysis via Von-Neuman

For stability eigenvalues must be $|\lambda_i| \leq 1, \ i = 1,2$.

$$|\lambda_1| = |\frac{1 - D\frac{\tau}{2}w^2}{1 + D\frac{\tau}{2}w^2}| \leq 1, \quad |\lambda_2| = |\frac{1 - \frac{\tau}{2}D(k_1 iw + k_2)}{1 + \frac{\tau}{2}D(k_1 iw + k_2)}| \leq 1$$

First inequality is true under the condition $D \geq 0$.

Second one is true for conditions $D \geq 0$ and $k_2 \geq 0$.

Outline

Numerical results

For numerical computation we consider the problem (1)-(4) with parameters $D = 0.00025$, $a = 1$, $b = 2$, $c = 10$, $d = 0.1$, $\alpha_1 = \alpha_2 = 1$, $A_1 = 28 \times 10^7$, $A_2 = 0.22 \times 10^9$ and $k = 16$. We write the computer program in matlab and present our results on graphs which are taken at different times.

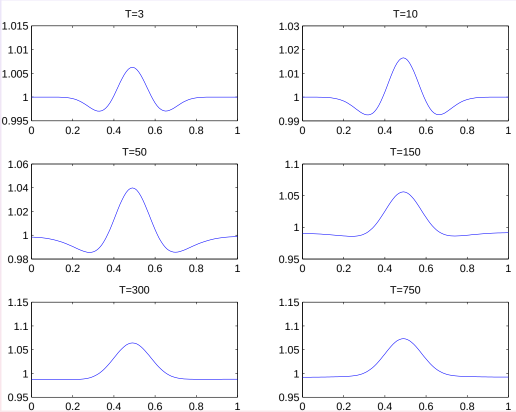

Figure: Numerical solth. of the problem (1)-(4) with iterative splitting method for $T = 3$, $T = 10$, $T = 50$, $T = 150$, $T = 300$, $T = 750$.

Numerical results

Figure shows the concentration of Endothelial Cells at different times.

See, S. Pamuk, A. Erdem (2007), U. Erdogan et al. (2009).

Outline

References

1. H.A. Levine, S. Pamuk, B.D. Sleeman, M. Nilsen-Hamilton,
Mathematical model of capillary formation and development in tumor angiogenesis:penetration into the stroma.
Bull.Math.Biol. 63 (5) (2001) 801-863.
2. H.G. Othmer, A. Stevens,
Aggregation, blow up and collapse: the ABC's oftaxis and reinforced random walks.
SIAM J. Appl. Math. 51 (1997).
3. D. David,
Reinforced random walks.
Probability Theory Related Fields 84,(1990) 203-229.

References

④ S. Pamuk, A. Erdem,
The method of lines for the numerical solution of a mathematical model for capillary formation: The role of endothelial cells in capillary.
Applied Mathematics and Computation, 186 (2007) 831-835.

⑤ U. Erdoğan, H. Koçak, T. Öziș,
An exponentially-fitted method for solving a mathematical model for capillary formation tumor angiogenesis problem.
Workshop in Izmir University, 2009.

⑥ I. Faragó, B. Gnandt, Á. Havasi,
Additive and iterative operator splitting methods and their numerical investigation.
Computers and Mathematics with Application, 55 (2008) 2266-2279.

References

7. I. Farago, J. Geiser,
Iterative Operator-Splitting methods for Linear Problems.
International Journal of Computational Science and Engineering, 3 (2007), 255-263.

8. J. Geiser,
Decomposition methods for differential equations : Theory and application.
CRC Press, Taylor and Francis Group, December, (2008).

9. J. Geiser,
Iterative Operator-Splitting methods with higher-order time integration methods and applications for parabolic partial differential equations
Journal of Computational and Applied Mathematics,217 (2008) 227-242.

References

⑩ W.H. Hundsdorfer, J.G. Verwer,
Numerical solution of time-dependent advection-diffusion-reaction equations.

Springer, Berlin, (2003).

⑪ John.C. Strikwerda,
Finite difference schemes and partial differential equations.
SIAM, USA, (2004).

⑫ R. Helen M.,
Von Neumann stability analysis of symplectic integrators applied to Hamiltonian PDEs,
Journal of Computational Mathematics, 20 (2002), pp. 611-618.

Thanks for Attention !