Discontinuous Hermite Collocation and Diagonally Implicit RK3 for a Brain Tumour Invasion Model

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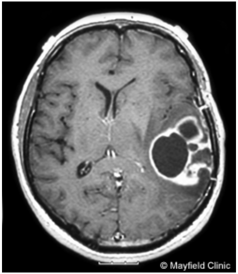
Gliomas

Gliomas are primary brain tumours that originate from brain's *glial* cells. They usually occur in the cerebral (upper) brain's hemisphere and they are characterized by their *aggressive diffusive invasion* of brain normal tissue.



Analytical Deterministic Models

$$\frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho g(c) \quad , \quad \textit{(Cruywagen et.al 1995)}$$

$c(\mathbf{x}, t)$: tumour cell density at location $\mathbf{x}$ and time t

D : diffusion coefficient representing the active motility (0.0013 cm^2/day)

ρ : net proliferation rate (0.012/day)

$$g(c) = \begin{cases} c & , \quad \text{exponential growth} \\ c(1 - \frac{c}{K}) & , \quad \text{logistic growth , } K \text{ : carrying capacity} \end{cases}$$

Zero flux BC on the anatomy boundaries : $\frac{\partial c}{\partial \eta} = 0$

Initial spatial distribution malignant cells : $c(\mathbf{x}, 0) = f(\mathbf{x})$

Analytical Deterministic Models

Homogeneous Brain Tissue (Cruywagen et.al 1995)

$\downarrow$

D is constant

$\downarrow$

$$\frac{\partial c}{\partial t} = D\nabla^2 c + \rho g(c)$$

Analytical Deterministic Models

Heterogeneous Brain Tissue (Swanson 1999)

$$\downarrow$$

$$D(\mathbf{x}) = \begin{cases} D_g & , \quad \mathbf{x} \text{ in Grey Matter} \\ D_w & , \quad \mathbf{x} \text{ in White Matter} \end{cases} \quad , \quad D_w > D_g$$

$$\downarrow$$

$$\frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho g(c)$$

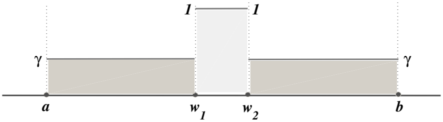
continuity and flux preservation conditions at the interfaces

Exponential Growth 3-region Model in 1+1 Dimensions

Dimensionless variables

$$x \leftarrow \sqrt{\frac{\rho}{D_w}}x \quad , \quad t \leftarrow \rho t \quad , \quad c(x,t) \leftarrow c\left(\sqrt{\frac{\rho}{D_w}}x, \rho t\right) \frac{D_w}{\rho N_0}$$

$$D = \begin{cases} \gamma & , \quad \alpha \leq x < w_1 \\ 1 & , \quad w_1 \leq x < w_2 \\ \gamma & , \quad w_2 \leq x \leq b \end{cases} \quad , \quad \gamma = \frac{D_g}{D_w} < 1$$



Transformation

$$c(x,t) = e^t u(x,t)$$

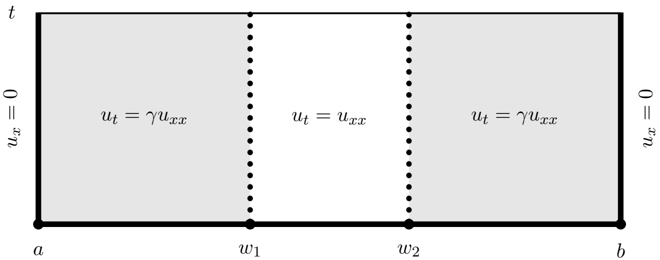
Interface conditions at $x = w_k \;,\; k = 1, 2$

$$\begin{cases} \textit{Continuity} \; : \quad [u] := u^+ - u^- = 0 \quad , \\ \textit{Conservation of flux} \; : \quad [Du_x] := D^+ u_x^+ - D^- u_x^- = 0 \; , \end{cases}$$

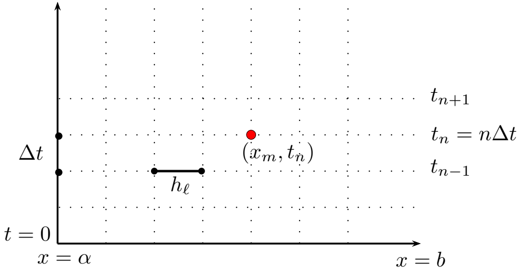
Exponential Growth 3-region Model in 1+1 Dimensions

$$\begin{cases} u_t = Du_{xx} \ , \quad x \in \mathcal{R}_\ell \ , \ \ell = 1,2,3 \ , \ t > 0 \\ u_x(\alpha, t) = 0 \quad \text{and} \quad u_x(b,t) = 0 \\ [u] = 0 \ \text{ and } \ [Du_x] = 0 \ \text{ at } x = w_k \ , \ k = 1,2 \\ u(x,0) = f(x) \end{cases}$$

$$\mathcal{R}_1 := (\alpha, w_1) \ , \ \mathcal{R}_2 := (w_1, w_2) \ , \ \mathcal{R}_3 := (w_2, b)$$



Discretization



$$x_m := \alpha + (m-1)h \;,\; m = 1, \ldots, N+1 \quad,\quad t_n = n\tau \;,\; n = 0, 1, \ldots$$

$$h = \begin{cases} h_1 := (w_1 - \alpha)/N_1 \\ h_2 := (w_2 - w_1)/N_2 \\ h_3 := (b - w_2)/N_3 \end{cases} \quad,\quad N = N_1 + N_2 + N_3 \quad,\quad \tau = \Delta t$$

Hermite Collocation

$$U(x,t) = \sum_{m=1}^{N+1} \left[\alpha_{2m-1}(t)\phi_{2m-1}(x) + \alpha_{2m}(t)\phi_{2m}(x)\right]$$

$$\phi_{2m-1}(x) = \begin{cases} \phi\left(\frac{x_m - x}{h}\right) & , \quad x \in [x_{m-1}, x_m] \\ \phi\left(\frac{x - x_m}{h}\right) & , \quad x \in [x_m, x_{m+1}] \\ 0 & , \quad \text{otherwise} \end{cases} ,$$

$$\phi_{2m}(x) = \begin{cases} -h\psi\left(\frac{x_m - x}{h}\right) & , \quad x \in [x_{m-1}, x_m] \\ h\psi\left(\frac{x - x_m}{h}\right) & , \quad x \in [x_m, x_{m+1}] \\ 0 & , \quad \text{otherwise} \end{cases} \tag{1}$$

$$\phi(s) = (1-s)^2(1+2s) \ , \ \ \psi(s) = s(1-s)^2 \quad , \quad s \in [0,1]$$

Interface Conditions

$$[DU_x] := D^+ U_x^+ - D^- U_x^- = 0 \ , \quad \text{at } x = w_k \ , \ \ k = 1, 2$$

$$\downarrow \qquad\qquad\qquad\qquad \downarrow$$

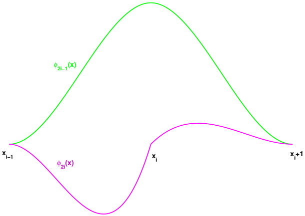
$$\gamma \ \phi_{2i}(x_i^-) = \phi_{2i}(x_i^+) \qquad \phi_{2i}(x_i^-) = \gamma \phi_{2i}(x_i^+)$$

$$x_i \equiv w_1 \qquad x_i \equiv w_2$$

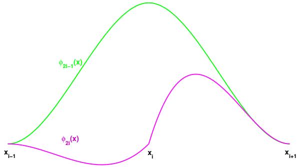
$$i = N_1 + 1 \qquad i = N_1 + N_2 + 1$$

$$\downarrow \qquad\qquad\qquad\qquad \downarrow$$

$$\phi_{2i}(x) = \begin{cases} -\frac{h}{\gamma}\psi\left(\frac{x_i - x}{h}\right) \\ \\ h\psi\left(\frac{x - x_i}{h}\right) \\ \\ 0 \end{cases} \qquad \phi_{2i}(x) = \begin{cases} -h\psi\left(\frac{x_i - x}{h}\right) \\ \\ \frac{h}{\gamma}\psi\left(\frac{x - x_i}{h}\right) \\ \\ 0 \end{cases}$$



$i = N_1 + 1$



$i = N_1 + N_2 + 1$

Boundary Collocation equations

$$U_x(\alpha, t) = 0 \quad \longrightarrow \quad \alpha_2(t) = 0 \quad \longrightarrow \quad \dot{\alpha}_2(t) = 0$$

$$U_x(b, t) = 0 \quad \longrightarrow \quad \alpha_{2N+2}(t) = 0 \quad \longrightarrow \quad \dot{\alpha}_{2N+2}(t) = 0$$

Interior Collocation equations

$$\sum_{j=1}^{N+1} [\dot{\alpha}_{2j-1}(t)\phi_{2j-1}(\sigma_i) + \dot{\alpha}_{2j}(t)\phi_{2j}(\sigma_i)] = D \sum_{j=1}^{N+1} \left[\alpha_{2j-1}(t)\phi''_{2j-1}(\sigma_i) + \alpha_{2j}(t)\phi''_{2j}(\sigma_i)\right]$$

where σ_i , $i = 1, \ldots, 2N$ are the Gauss points (two per subinterval)

$$\downarrow$$

Elemental Collocation equations

$$C_j^{(0)} \begin{bmatrix} \dot{\alpha}_{2j-1} \\ \dot{\alpha}_{2j} \\ \dot{\alpha}_{2j+1} \\ \dot{\alpha}_{2j+2} \end{bmatrix} = \frac{D}{h^2} C_j^{(2)} \begin{bmatrix} \alpha_{2j-1} \\ \alpha_{2j} \\ \alpha_{2j+1} \\ \alpha_{2j+2} \end{bmatrix} \quad , \quad j = 1, \ldots, N$$

Elemental Collocation matrices

$$C_j^{(\kappa)} = \begin{bmatrix} s_1^{(\kappa)} & \frac{h}{\zeta_j} s_2^{(\kappa)} & s_3^{(\kappa)} & -\frac{h}{\beta_j} s_4^{(\kappa)} \\ s_3^{(\kappa)} & \frac{h}{\zeta_j} s_4^{(\kappa)} & s_1^{(\kappa)} & -\frac{h}{\beta_j} s_2^{(\kappa)} \end{bmatrix} \quad , \quad \kappa = 0, 2$$

$s_1^{(0)} = \frac{9+4\sqrt{3}}{18}$, $s_2^{(0)} = \frac{3+\sqrt{3}}{36}$, $s_3^{(0)} = \frac{9-4\sqrt{3}}{18}$, $s_4^{(0)} = \frac{3-\sqrt{3}}{36}$,
$s_1^{(2)} = -2\sqrt{3}$, $s_2^{(2)} = -1-\sqrt{3}$, $s_3^{(2)} = 2\sqrt{3}$ and $s_4^{(2)} = -1+\sqrt{3}$

$$\zeta_j = \begin{cases} 1 & , \quad j \neq N_1 + N_2 + 1 \\ \gamma & , \quad j = N_1 + N_2 + 1 \end{cases} \quad , \quad \beta_j = \begin{cases} 1 & , \quad j \neq N_1 \\ \gamma & , \quad j = N_1 \end{cases} \quad .$$

Collocation system of ODEs

$$A\dot{\mathbf{a}} = B\mathbf{a}$$

where $\dot{\mathbf{a}} = \begin{bmatrix}\dot\alpha_1 & \dot\alpha_3 \cdots \dot\alpha_{2N+1}\end{bmatrix}^T$, $\mathbf{a} = \begin{bmatrix}\alpha_1 & \alpha_3 \cdots \alpha_{2N+1}\end{bmatrix}^T$

$$A = \begin{bmatrix} \tilde{A}_1 & B_1 & & & & \\ & A_2 & B_2 & & & \\ & & \ddots & & & \\ & & & A_{N-1} & B_{N-1} & \\ & & & & A_N & \tilde{B}_N \end{bmatrix}, \; B = \begin{bmatrix} \tilde{F}_1 & G_1 & & & & \\ & F_2 & G_2 & & & \\ & & \ddots & & & \\ & & & F_{N-1} & G_{N-1} & \\ & & & & F_N & \tilde{G}_N \end{bmatrix}.$$

$$\begin{bmatrix}A_j & B_j\end{bmatrix} = C_j^{(0)} \quad \text{and} \quad \begin{bmatrix}F_j & G_j\end{bmatrix} = \frac{D}{h^2} C_j^{(2)} \; .$$

$$\dot{\mathbf{a}} = C(\mathbf{a}, t)$$

$$\text{where} \quad C(\mathbf{a}, t) = A^{-1}B\mathbf{a}$$

Backward Euler (BE) - Crank Nicolson (CN)

BE:

$$\frac{\mathbf{a}^{(n+1)} - \mathbf{a}^{(n)}}{\tau} = C^{(n+1)}(\mathbf{a}, t)$$

or

$$(A - \tau B)\mathbf{a}^{(n+1)} = A\mathbf{a}^{(n)}$$

CN:

$$\frac{\mathbf{a}^{(n+1)} - \mathbf{a}^{(n)}}{\tau} = \frac{1}{2}(C^{(n+1)}(\mathbf{a}, t) + C^{(n)}(\mathbf{a}, t))$$

or

$$(A - \frac{\tau}{2}B)\ \mathbf{a}^{(n+1)} = (A + \frac{\tau}{2}B)\ \mathbf{a}^{(n)}$$

Diagonally Implicit RK3 (DIRK)

DIRK:

$$
\begin{aligned}
\mathbf{a}^{(n,1)} &= \mathbf{a}^{(n)} + \tau\ \lambda\ C^{(n,1)}(\mathbf{a},t) \\
\mathbf{a}^{(n,2)} &= \mathbf{a}^{(n)} + \tau \left[(1-2\lambda)C^{n,1}(\mathbf{a},t) + \lambda C^{n,2}(\mathbf{a},t)\right] \\
\mathbf{a}^{(n+1)} &= \mathbf{a}^{(n)} + \frac{\tau}{2}\left[C^{(n,1)}(\mathbf{a},t) + C^{(n,2)}(\mathbf{a},t)\right]
\end{aligned}
$$

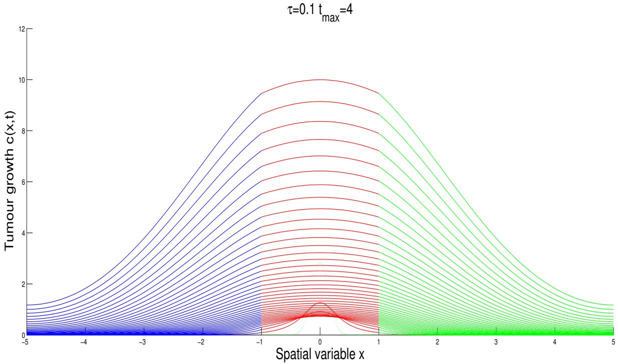
or

$$
\begin{aligned}
(A-\tau\lambda B)\ \mathbf{a}^{(n,1)} &= A\ \mathbf{a}^{(n)} \\
(A-\tau\lambda B)\ \mathbf{a}^{(n,2)} &= A\ \mathbf{a}^{(n)} + \tau(1-2\lambda)B\ \mathbf{a}^{(n,1)} \\
A\ \mathbf{a}^{(n+1)} &= A\ \mathbf{a}^{(n)} + \frac{\tau}{2}\left[B\ \mathbf{a}^{(n,1)} + B\ \mathbf{a}^{(n,2)}\right]
\end{aligned}
$$

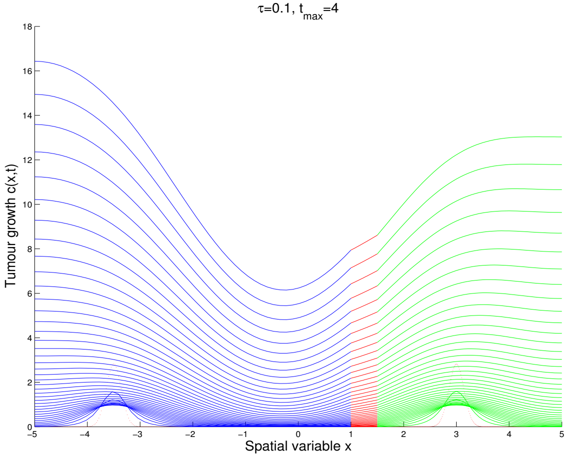
Numerical Results - Model Problem 1

$\mathcal{R}_1 := (-5, -1)$, $\mathcal{R}_2 := (-1, 1)$, $\mathcal{R}_3 := (1, 5)$, $\gamma = 0.5$

and $f(x) = \frac{1}{\eta\sqrt{\pi}} e^{-x^2/\eta^2}$, with $\eta = 0.2$.

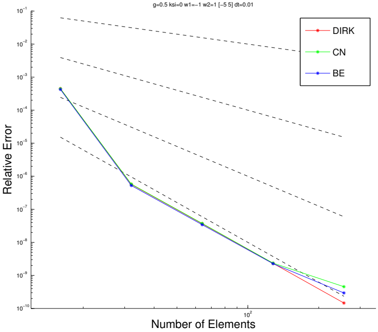


$\mathcal{R}_1 := (-5, 1)$, $\mathcal{R}_2 := (1, 1.5)$, $\mathcal{R}_3 := (1.5, 5)$, $\gamma = 0.5$
and $f(x) = \frac{1}{\eta\sqrt{\pi}}(e^{-(x+3.5)^2/\eta^2} + e^{-(x-3)^2/\eta^2})$, with $\eta = 0.2$.

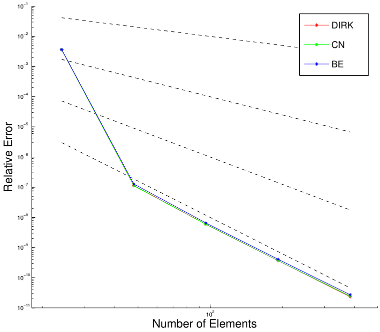


Numerical Results - Spatial Relative Error

Model Problem 1



Model Problem 2



Logistic Growth 3-region Model in 1+1 Dimensions

$$\begin{cases} c_t = Dc_{xx} + c(1-c)\ , \quad x \in \mathcal{R}_\ell\ ,\ \ell = 1,2,3\ ,\ t \geq 0 \\ c_x(a,t) = 0 \quad \text{and} \quad c_x(b,t) = 0 \\ [c] = 0 \ \text{ and } \ [Dc_x] = 0 \ \text{ at } x = w_k\ ,\ k = 1,2 \\ c(x,0) = f(x) \end{cases}$$

$$\mathcal{R}_1 := (\alpha, w_1)\ ,\ \mathcal{R}_2 := (w_1, w_2)\ ,\ \mathcal{R}_3 := (w_2, b)$$

$$D(x) = \begin{cases} \gamma & , \quad \alpha \leq x < w_1 \\ 1 & , \quad w_1 \leq x < w_2 \\ \gamma & , \quad w_2 \leq x \leq b \end{cases}$$

Interior Collocation equations

$$\sum_{j=1}^{2N+2}[\dot{\alpha}_j(t)\phi_j(\sigma_i)] = D\sum_{j=1}^{2N+2}[\alpha_j(t)\phi_j''(\sigma_i)] + \sum_{j=1}^{2N+2}[\alpha_j(t)\phi_j(\sigma_i)] - \left(\sum_{j=1}^{2N+2}[\alpha_j(t)\phi_j(\sigma_i)]\right)^2$$

$$C_j^{(0)}\begin{bmatrix}\dot{\alpha}_{2j-1}\\ \dot{\alpha}_{2j}\\ \dot{\alpha}_{2j+1}\\ \dot{\alpha}_{2j+2}\end{bmatrix} = DC_j^{(2)}\begin{bmatrix}\alpha_{2j-1}\\ \alpha_{2j}\\ \alpha_{2j+1}\\ \alpha_{2j+2}\end{bmatrix} + C_j^{(0)}\begin{bmatrix}\alpha_{2j-1}\\ \alpha_{2j}\\ \alpha_{2j+1}\\ \alpha_{2j+2}\end{bmatrix} - \left(C_j^{(0)}\begin{bmatrix}\alpha_{2j-1}\\ \alpha_{2j}\\ \alpha_{2j+1}\\ \alpha_{2j+2}\end{bmatrix}\right)^{.2}$$

Collocation System of ODEs

$$A\dot{\mathbf{a}} = M\mathbf{a} + \left(C_j^{(0)}\mathbf{a}\right)^{.2}$$

where

$$M = \begin{bmatrix} \tilde{P}_1 & Q_1 & & & & \\ & P_2 & Q_2 & & & \\ & & \ddots & & & \\ & & & P_{N-1} & Q_{N-1} & \\ & & & & P_N & \tilde{Q}_N \end{bmatrix},$$

$$\begin{bmatrix} P_j & Q_j \end{bmatrix} = C_j^{(2)} + C_j^{(0)}$$

$$\dot{\mathbf{a}} = K(\mathbf{a}, t)$$

where $\quad K(\mathbf{a}, t) = A^{-1}\left[M\mathbf{a} + \left(C^{(0)}\mathbf{a}\right)^{.2}\right]$

Time Discretization

BE:

$$(A - \tau M)\mathbf{a}^{(n+1)} - \tau \left(C^{(0)}\mathbf{a}^{(n+1)} \right)^{.2} = A\mathbf{a}^{(n)}$$

CN:

$$(A - \frac{\tau}{2} M)\, \mathbf{a}^{(n+1)} - \frac{\tau}{2} \left(C^{(0)}\mathbf{a}^{(n+1)} \right)^{.2} = (A + \frac{\tau}{2} M)\, \mathbf{a}^{(n)} + \frac{\tau}{2} \left(C^{(0)}\mathbf{a}^{(n)} \right)^{.2}$$

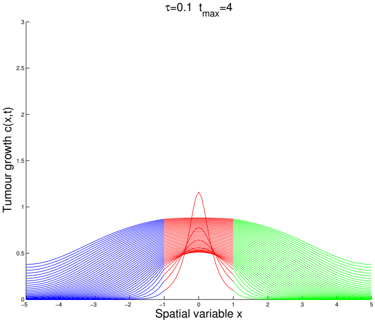
DIRK:

$$(A - \tau\lambda M)\ \mathbf{a}^{(n,1)} - \tau\lambda \left(C^{(0)}\mathbf{a}^{(n,1)} \right)^{.2} = A\ \mathbf{a}^{(n)}$$

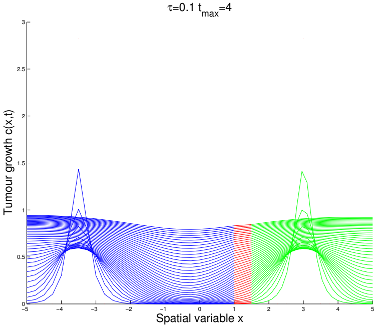
$$(A - \tau\lambda M)\ \mathbf{a}^{(n,2)} - \tau\lambda \left(C^{(0)}\mathbf{a}^{(n,2)} \right)^{.2} = A\ \mathbf{a}^{(n)} + \tau(1 - 2\lambda) \left(M\ \mathbf{a}^{(n,1)} + \left(C^{(0)}\mathbf{a}^{(n,1)} \right)^{.2} \right)$$

$$A\ \mathbf{a}^{(n+1)} = A\ \mathbf{a}^{(n)} + \frac{\tau}{2}\ [M\ \mathbf{a}^{(n,1)} + \left(C^{(0)}\mathbf{a}^{(n,1)} \right)^{.2} + M\ \mathbf{a}^{(n,2)} + \left(C^{(0)}\mathbf{a}^{(n,2)} \right)^{.2}]$$

Model Problem 1

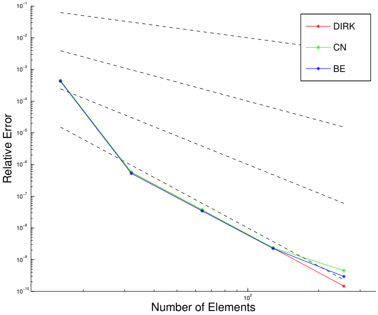


Model Problem 2

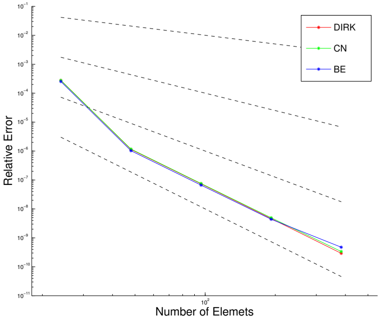


Numerical Results - Spatial Relative Error

Model Problem 1



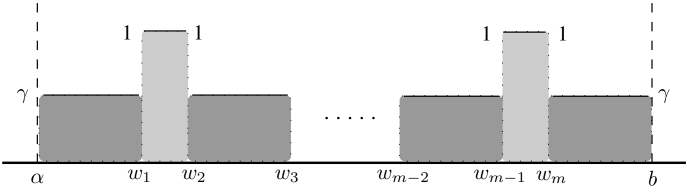
Model Problem 2



Generalization in m+1 Regions

$$\mathcal{R}_1 = (\alpha, w_1)\ ,\ \mathcal{R}_2 = (w_1, w_2)\ ,\ \ldots\ ,\ \mathcal{R}_{m+1} = (w_m, b)$$

$$D(x) = \begin{cases} \gamma & ,\quad x \in [\alpha, w_1) \cup [w_2, w_3) \cup \ldots \cup [w_m, b] \\ 1 & ,\quad x \ \text{ else} \end{cases}$$



$$\downarrow$$

$$[c] = 0 \ \text{ and } \ [Dc_x] = 0 \ \text{ at } x = w_k\ ,\ k = 1, \ldots, m$$

Interface Conditions

$$[DU_x] := D^+ U_x^+ - D^- U_x^- = 0 \ , \quad \text{at } x = w_k \ , \ \ k = 1, \ldots, m$$

$$\downarrow \qquad\qquad\qquad\qquad \downarrow$$

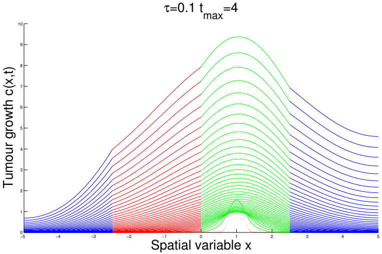
$$\gamma \, \phi_{2i}(x_i^-) = \phi_{2i}(x_i^+)$$
$$x_i \equiv w_k, \quad \text{k odd}$$
$$i = \sum_{j=1}^{k} N_j + 1$$

$$\phi_{2i}(x_i^-) = \gamma \phi_{2i}(x_i^+)$$
$$x_i \equiv w_k, \quad \text{k even}$$
$$i = \sum_{j=1}^{k} N_j + 1$$

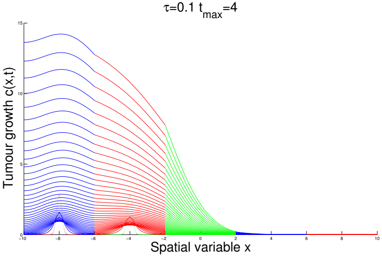
$$\downarrow \qquad\qquad\qquad\qquad \downarrow$$

$$\phi_{2i}(x) = \begin{cases} -\frac{h}{\gamma}\psi\left(\frac{x_i - x}{h}\right) \\ \\ h\psi\left(\frac{x - x_i}{h}\right) \\ \\ 0 \end{cases} \qquad \phi_{2i}(x) = \begin{cases} -h\psi\left(\frac{x_i - x}{h}\right) \\ \\ \frac{h}{\gamma}\psi\left(\frac{x - x_i}{h}\right) \\ \\ 0 \end{cases}$$

Model Problem 1

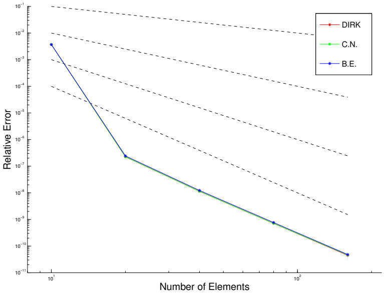


Model Problem 2

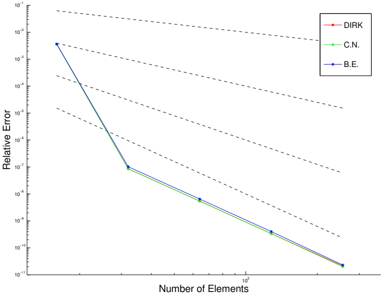


Numerical Results - Spatial Relative Error

Model Problem 1



Model Problem 2



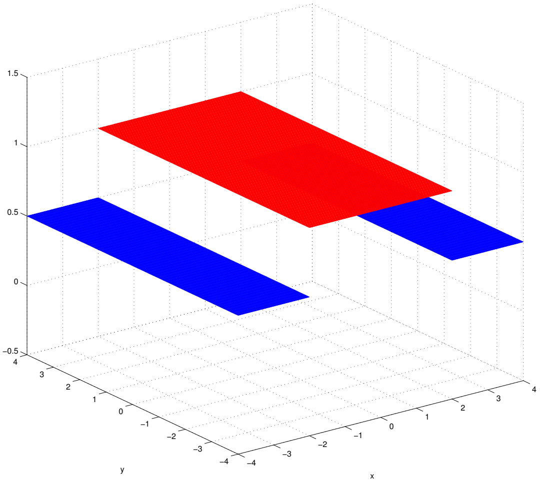
Exponential Growth 3-region Model in 2+1 Dimensions

$$D = \begin{cases} \gamma & , \quad (x,y) \in [\alpha, w_1) \times [\alpha, b] \\ 1 & , \quad (x,y) \in [w_1, w_2) \times [\alpha, b] \\ \gamma & , \quad (x,y) \in [w_2, b] \times [\alpha, b] \end{cases} \quad ,$$

$$\begin{cases} u_t = Du_{xx} + Du_{yy} \ , \quad x \in \mathcal{R}_\ell \ , \ \ell = 1,2,3 \ , \ t > 0 \\ \\ \dfrac{\partial u}{\partial \eta} = 0 \\ \\ [u] = 0 \ \text{ and } \ [D^x u_x] = 0 \ \text{ at } x = w_k \ , \ k = 1,2 \text{ and } y \in (\alpha, b) \\ \\ u(x,y,0) = f(x,y) \end{cases}$$

$$\mathcal{R}_1 := (\alpha, w_1) \times (\alpha, b) \ , \ \mathcal{R}_2 := (w_1, w_2) \times (\alpha, b) \ , \ \mathcal{R}_3 := (w_2, b) \times (\alpha, b)$$

Exponential Growth 3-region Model in 2+1 Dimensions



Diffusion coefficient D

Exponential Growth 3-region Model in 2+1 Dimensions

$$U(x,y,t) = \sum_{m=1}^{N_x+1} \sum_{n=1}^{N_y+1} [\alpha_{2m-1}(t)\phi_{2m-1}(x) + \alpha_{2m}(t)\phi_{2m}(x)] \\ [\beta_{2n-1}(t)\phi_{2n-1}(y) + \beta_{2n}(t)\phi_{2n}(y)]$$

$$\downarrow$$

$$[DU_x] := D^+ U_x^+ - D^- U_x^- = 0 \; , \quad \text{at } x = w_k \; , \; k = 1,2$$

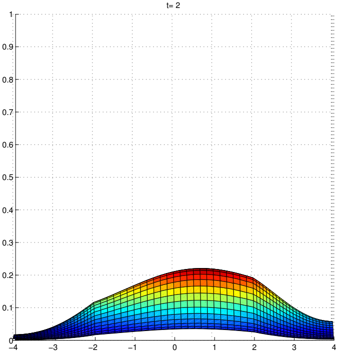
$$\downarrow \qquad\qquad\qquad\qquad \downarrow$$

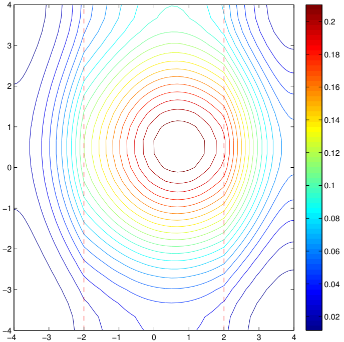
$$\gamma\, \phi_{2i}(x_i^-) = \phi_{2i}(x_i^+) \qquad\qquad \phi_{2i}(x_i^-) = \gamma \phi_{2i}(x_i^+)$$

$$x_i \equiv w_1 \qquad\qquad x_i \equiv w_2$$

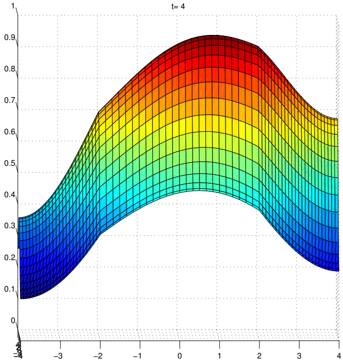
$$i = N_{x_1} + 1 \qquad\qquad i = N_{x_1} + N_{x_2} + 1$$

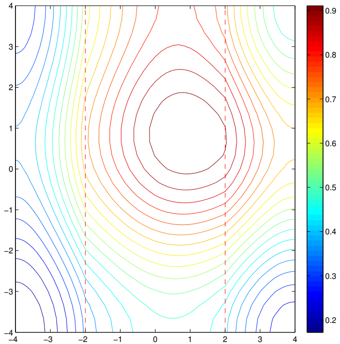
2-d Screenshots





2-d Screenshots





2-D Model Problem - Solution

(Loading movie2.mpg)