A Moving Mesh Approach to Avascular Tumour Growth

Contents

Figure The gro th of n scu r tu our

gro th of c ncerous ce s The process y hich the tu our o t ins its o n ood supp y is c ed ANGIOGENESIS nd pre enting this fro occurring is of p rticu r interest to drug de e op ent This is ec use once the tu our h s o t ined ood supp y the tu ours c n e e its pri ry oc tion i the circu tory syste et st sis nd sett e in u tip e re s of the ody The METASTATIC st ge is the n st ge of tu our gro th nd the ost di cu t to tre t

Fro the o ent nor ce s ut te to c ncer ce s there re three distinct st ges to c ncer The di erent st ges h e di erent ch r cteristics so require indi idu in estig tion e sh study the pri ry st ge scu r tu our gro th

A sc r t o rs

As pre ious y entioned the ter st ges of tu our gro th re ore critic since it is usu y not unti fter ngiogenesis th t c ncer is detri ent to the hosts he th During the scu r st ge the tu our is ign nt Indeed fo o ing study of hu n c ncers in ice there is recent contro ersi hypothesis th t e h e s dor nt scu r tu ours in our odies

Reg rd ess of this c inic ie point scu r tu our gro th rr nts the interest of scientists It is ene ci to underst nd the si p e syste nd its co ponents prior to tte pting n ysis of ore co p e syste scu r tu ours h e ny of the s e ch r cteristics s suc r tu ours ut the qu ntity nd qu ity of d t on scu r tu ours is of higher st nd rd This is ec use it is co p r ti e y e sier nd che per to reproduce high qu ity scu r tu our e peri ent e idence in in itro for

In su ry e i e in estig ting ode for scu r tu ours see Figure s they re si p er to ode nd he p gi e n insight into the ech nis s of scu r tu our gro th

Figure 2 An scu r tu our

Ch pter

he ro e of the tics in c ncer rese rch

E er since co p e ife e o ed it h s een suscepti e to c ncer The o d est description of c ncer in hu ns s found in n Egypti n p pyrus ritten et een R BC Tod y speci ists re sti e tensi e e peri ents ut not ys. Through the de e op ent nd so ution of th e tic ode s th t descri e di erent spects of so id tu our gro th pp ied the tics h s the potenti to pre ent e cessi e e peri ent tion .

Ide y e peri ents nd ode ing or h nd in h nd. The e peri ents c n not on y pro e to e cost y ut the su t eties of the ny intric te pro cesses c n e si y e o er oo ed. By ode ing tu our gro th to i ic d t

Ch pter

A t o ph se ode of so id t o r gro th

Byrne et for u ted t o ph se ode of so id tu our gro th s ore gener ersion of t o di erent pre e isiting ode s for so id tu our gro th nd . A though fu det i s of the ode ing re not gi en in this p per the io ogic re soning nd ssu ptions th t contri ute to the ode re e p icit y descri ed. This is the ode th t e i e discussing nd so ing nu eric y in this report.

Our rst t s is to non di ension ise the ode. This in o es the p rti or fu re o of units y suit e su stitution of ri es. Non di ension is tion c n si p ify pro e y reducing the nu er of ri es. It so ids n ysis of the eh iour of syste y reco ering ch r cteristic properties. In our c se the ey oti tor to non di ension ising the syste is to en e us to t e d nt ge of p r eteris tions studied e se here.

In this report e sh ppro i te y so e the non di ension ised o ing ound ry pro e y pp ying o ing esh ppro ch. e o e the esh in three di erent ys y ensuring th t ss fr ctions in n e e ent re in const nt o er ti e y o ing the esh ith the ce e ocity y dri ing esh o e ent iin proportion to th t of the o ing ound ry.

The resu ts gener ted fro these ethods re discussed nd co p red ith pre ious resu ts.

Mode for tion

In it is ssu ed th t tu our consists of ce s nd ter ith respecti e o u e fr ctions α nd β ith $\alpha + \beta$. The t o ph ses h e n ssoci

here

- $_c(\alpha$ is the pressure di erence et een the t o ph ses nd y inc ude contri utions due to for e p e ce ce inter ctions nd e r ne stress It is de ned y

$$_c(\alpha \quad \begin{cases} & \leq \alpha < \alpha_{min} \\ \frac{\hat{\Sigma}_c| - ^*|^{r-1}}{(1-)^q}(\alpha - \alpha^* & \alpha_{min} \leq \alpha < \end{cases}$$

for positi e const nts $q, r, \; < \alpha_{min} < \alpha^* <$ nd $_c$

hen specifying $_c(\alpha$ α^* denotes n tur ce p c ing density if $\alpha > \alpha^*$ ce s o e to reduce their stress hi e if $\alpha < \alpha^*$ they ggreg te if they re not too sp rse y popu ted $(\alpha \geq \alpha_{min}$ By de nition e h e $_c$

These equ tions re de ned on o ing do in nd in the ode re su ject to the ound ry conditions nd initi conditions e o

$$\mathbf{v}_c \; \mathbf{v}_w \; \frac{\partial \mathbf{C}}{\partial \mathbf{x}} \qquad \text{t } \mathbf{x} \;\; ,$$

$$\mathbf{p} \;\; , \;\; \boldsymbol{\mu}_c \;\; \boldsymbol{\lambda}_c \frac{\partial \mathbf{v}_c}{\partial \mathbf{x}} - \;\; _c \boldsymbol{\alpha} \;\; , \;\; \mathbf{C} \;\; \mathbf{C}_\infty \qquad \text{t } \mathbf{x} \;\; \mathbf{x}_N \; \mathbf{t}$$

$$\boldsymbol{\alpha} \;\; \boldsymbol{\alpha}_0 \; \mathbf{x} \; , \;\; \mathbf{x} \;\; \mathbf{x}_0 \qquad \text{t } \mathbf{t} \;\; .$$

Equ tions ensure sy etry out $\mathbf{x}$ In $\mathbf{C}_\infty$ denotes the nutri enondontiytoto he etittyreeurdi

$\boldsymbol{\alpha}$ T R Tf R R Td c R T ET Tf R Td c

$\partial \mathbf{x}$

$$\mathbf{x}_N(\quad) = ,\quad \boldsymbol{\alpha} = \boldsymbol{\alpha}_0 \qquad \text{t} \quad \mathbf{t} = \qquad (R\,?)$$

$$\mathbf{v} = \frac{\partial \mathbf{C}}{\partial \mathbf{x}} = \qquad \text{t} \quad \mathbf{x}_0 = \qquad (R\,R)$$

$$\Rightarrow \boldsymbol{\mu}\frac{\partial \mathbf{v}}{\partial \mathbf{x}} - \boldsymbol{\chi}(\boldsymbol{\alpha}\quad) = ,\quad \frac{\partial \mathbf{x}_N}{\partial \mathbf{t}} = \mathbf{v},\quad \mathbf{C} = \qquad \text{t} \quad \mathbf{x} = \mathbf{x}_N \qquad (R\,)$$

In equ tions (R to (R e h e introduced the p r eters

$$\mathbf{s}_1 = \mathbf{s}_1\mathbf{C}_\infty,\quad \mathbf{s}_2 = \frac{(\quad \mathbf{s}_1\mathbf{C}_\infty}{\quad \mathbf{s}_1\mathbf{C}_\infty}\mathbf{s}_2,\quad \mathbf{s}_3 = \frac{\quad \mathbf{s}_1\mathbf{C}_\infty}{\mathbf{s}_0}\mathbf{s}_3,\quad \mathbf{s}_4 = \mathbf{s}_4\mathbf{C}_\infty,$$

$$\mathbf{k} = \frac{\mathbf{k}_0\mathbf{x}_N^2(\quad \mathbf{s}_0\mathbf{C}_\infty}{\quad \mathbf{s}_1\mathbf{C}_\infty},\quad \boldsymbol{\mu} = (\,\boldsymbol{\mu}_c \quad \boldsymbol{\lambda}_c \frac{\mathbf{s}_0\mathbf{C}_\infty}{(\quad \mathbf{s}_1\mathbf{C}_\infty},$$

$$\boldsymbol{\chi}(\boldsymbol{\alpha}\quad) = \begin{cases} & \leq \boldsymbol{\alpha} < \boldsymbol{\alpha}_{min} \\ \frac{\hat{\boldsymbol{\Sigma}}_c|\,\hat{}\,- \quad {}^*|^{r-1}}{(\mathbf{1}-\,\hat{}\,)^q}(\boldsymbol{\alpha} - \boldsymbol{\alpha}^* & \boldsymbol{\alpha}_{min} \leq \boldsymbol{\alpha} < \end{cases},$$

$$\mathbf{Q} = \mathbf{Q}_0\mathbf{x}_N^2(\quad,\quad \mathbf{Q}_1 = \mathbf{Q}_1\mathbf{C}_\infty.$$

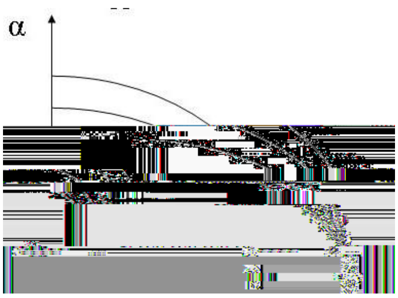
In h t fo o s the h ts (. re dropped fro the ri es nd p r eters.

In this study e sh so e this ode nu eric y using three o ing esh ethods.

Ch pter c

Mo ing eshes

Gener y for the nu eric so ution of ti e dependent di


α

c Di erent ethods to o e the esh

e i in estig te three str tegies for o ing the esh i e di erent ys to de ne the esh e ocity $\mathbf{x}$ The three esh e ocities i e

A: sed on conser ing ss fr ctions

B: the ce e ocity $\mathbf{v}$

C: proportion to the ound ry o e ent $\frac{dx_N}{}$

Ch pter

hich c n e ritten s

$$\mathbf{T}_j^l \mathbf{C}_{j-1} + \mathbf{T}_j^d \mathbf{C}_j + \mathbf{T}_j^u \mathbf{C}_{j+1} = \mathbf{w}_j \mathbf{C}_j \qquad (j = 1, 2, \ldots, N-2),$$

the function is sy etric out $\mathbf{x_0}$ Hence e conc ude th t t $\mathbf{x_1}$ ⌐ $-\mathbf{x_{-1}}$ e h e $\mathbf{C_1}$ ⌐ $\mathbf{C_{-1}}$ Su stituting these ues into (ˇ for $\mathbf{j}$ ⌐ gi es

$$\frac{-?}{\mathbf{x_1^2} - \mathbf{x_0^2}}\mathbf{C_0} \frac{?}{\mathbf{x_1^2} - \mathbf{x_0^2}}\mathbf{C_1} ⌐ \frac{\mathbf{QC_0\alpha_0}}{\mathbf{Q_1C_0}}. \quad (\ \mathbb{R}$$

Therefore e h e ues for $\mathbf{T}_0^d$ $\mathbf{T}_0^u$ nd $\mathbf{w_0}$ ($\mathbf{C}$

$$\mathbf{T}_0^d ⌐ -\mathbf{T}_0^u ⌐ \frac{-?}{\mathbf{x_1^2} - \mathbf{x_0^2}},$$

$$\mathbf{w}(\mathbf{C_0} ⌐ \frac{\mathbf{QC_0\alpha_0}}{\mathbf{Q_1C_0}}.$$

Boundary Conditions: j ⌐ N – ˇ

For the right ound ry e return g in to (ˇ this ti e for $\mathbf{j}$ ⌐ $\mathbf{N}$ – ˇ ith the su stitution $\mathbf{C}_N$ ⌐ ˇ fro ($\mathbb{R}$ˇ

$$\frac{?}{(\mathbf{x}_{N-1} - \mathbf{x}_{N-2}(\mathbf{x}_N - \mathbf{x}_{N-2}}\mathbf{C}_{N-2} - \frac{?}{(\mathbf{x}_N - \mathbf{x}_{N-1}(\mathbf{x}_{N-1} - \mathbf{x}_{N-2}}\mathbf{C}_{N-1}$$

$$⌐ \frac{\mathbf{QC}_{N-1}\mathbf{\alpha}_{N-1}}{\mathbf{Q_1C}_{N-1}} - \frac{?}{(\mathbf{x}_N - \mathbf{x}_{N-1}(\mathbf{x}_N - \mathbf{x}_{N-2}}.$$

So $\mathbf{T}_{N-1}^l$ nd $\mathbf{T}_{N-1}^d$ re in s de ned y equ tion (ˇ ut the n entry in $\mathbf{w}$($\mathbf{C}$ h s n e tr ter due to the ound ry condition

No e h e our co p ete tri syste $\mathbf{T}$ to o t in $\mathbf{C}_j$ ($\mathbf{j}$ ⌐ , ˇ, ...$\mathbf{N}$ – ˇ ut note th t the right h nd side is non ine r

Numerically solving the discretized PDE

For the so ution of (? e use Ne ton s ethod here the residu ector $\mathbf{R}$ of (? is

$$\mathbf{R} ⌐ \mathbf{TC} - \mathbf{w}(\mathbf{C}.$$

e see $\mathbf{C}$ such th t $\mathbf{R}$ ⌐ $\mathbf{0}$ so equ tion (? ho ds Note th t if $\mathbf{Q_1}$ ⌐ the equ tions re ine r nd no iter tion is needed Other ise e c rry out Ne ton s Method

Finding sing o ing esh

Once **C** nd **v** re deter ined o er the region e see the so ution of the ti e dependent PDE using o ing esh ppro ch e i e ine three di erent ys to o e the esh For three ethods the upd ted esh is o t ined fro the esh e ocity used in n e p icit ti e stepping sche e

The rst y of o ing the esh Method A de nes the esh o e ent y eeping the ce ss fr ctions const nt in ti e The second uses the ce e ocity s the esh e ocity Method B Both these o d h n

It is orth noting th t this corresponds to the g o ss nce resu t

d

Recovering the Solution $\boldsymbol{\alpha}$

To nd n equ tion th t o s us to c cu te the so ution $\boldsymbol{\alpha}$ fro the esh e return to (nd equ te $\boldsymbol{\alpha}\,\mathbf{dx}$ t ti es $\mathbf{t}$ nd et een the t o points $(\mathbf{j}+$ nd $(\mathbf{j}-$ s in

$$\frac{}{\boldsymbol{\theta}(\mathbf{t}}\int_{x_{j-1}(t)}^{x_{j+1}(t)} \boldsymbol{\alpha}(\mathbf{x},\mathbf{t}\quad \mathbf{dx} \quad \frac{}{\boldsymbol{\theta}(}\int_{x_{j-1}(\mathbf{0})}^{x_{j+1}(\mathbf{0})} \boldsymbol{\alpha}(\mathbf{x}, \quad \mathbf{dx}.$$

App ying the e n ue theore for integr s nd t ing the e n ue to e t $\mathbf{x}_j(\mathbf{t}$ e o t in the ppro i tion

$$\frac{}{\boldsymbol{\theta}(\mathbf{t}}(\mathbf{x}_{j+1}(\mathbf{t} - \mathbf{x}_{j-1}(\mathbf{t} \quad \boldsymbol{\alpha}(\mathbf{x}_j,\mathbf{t} \quad \frac{}{\boldsymbol{\theta}(}(\mathbf{x}_{j+1}(\quad - \mathbf{x}_{j-1}($$

e no o e on to Method B

Method B

nder this str tegy the e ocity of the ound ry is equ to the e ocity of the ce s t the ound ry Then

$$\frac{\mathbf{dx}_j}{\mathbf{dt}} = \mathbf{x}_j = \mathbf{v}(\mathbf{x}_j, \mathbf{t}) \qquad (\mathbf{j} = ,2,..,\mathbf{N}$$
$$\mathbf{x_0} = \;.$$

Once the esh e ocity is de ned s o e the ne esh c n e deter ined y n e p icit ti e stepping sche e s in Method A

To reco er $\boldsymbol{\alpha}$ on this ne esh *n conser t e nner* e de ne the p rti sses

$$_j = \int_{x_{i-1}(t)}^{x_{i+1}(t)} \boldsymbol{\alpha} \, \mathbf{dx}.$$

Di erenti ting $_j$ ith respect to ti e using Lei nitz integr ru e here $\mathbf{x}_j = \mathbf{v}_j$

$$_j = \frac{\mathbf{d}}{\mathbf{dt}} \int_{x_{j-1}(t)}^{x_{j+1}(t)} \boldsymbol{\alpha} \, \mathbf{dx},$$
$$= \int_{x_{j-1}(t)}^{x_{j+1}(t)} \frac{\partial \boldsymbol{\alpha}}{\partial \mathbf{t}} \mathbf{dx} + \left[\boldsymbol{\alpha}\mathbf{x}\right]_{j-1}^{j+1}$$
$$= \int_{x_{j-1}(t)}^{x_{j+1}(t)} \frac{\partial \boldsymbol{\alpha}}{\partial \mathbf{t}} + \frac{\partial}{\partial \mathbf{x}}(\boldsymbol{\alpha}\mathbf{v}) \, \mathbf{dx}.$$

Hence the ter s under the integr re equ to one side of the PDE (so c n e rep ced y the source ter

$$_j = \int_{x_{j-1}}^{x_{j+1}} \frac{\partial \boldsymbol{\alpha}}{\partial \mathbf{t}} + \frac{\partial}{\partial \mathbf{x}}(\boldsymbol{\alpha}\mathbf{v}) \quad \mathbf{dx}$$
$$= \int_{x_{j-1}}^{x_{j+1}} \mathbf{S}(\boldsymbol{\alpha}, \mathbf{C}\;.$$

e upd te $_j$ t the ne ti e y using n e p icit ti e stepping sche e e then use the ne ue for nd nd the upd ted so ution y s e the id point ppro i tion s in Method A pp ied to (

$$(\mathbf{x}_{j+1} - \mathbf{x}_{j-1}\;\boldsymbol{\alpha}_j = \;_j$$

gi ing

$$\boldsymbol{\alpha}_j$$

Ch pter 6

Bre rd et s Method

In the s e tu our gro th pro e is so ed y pping the ri e $x(t)$ to ed do in $\xi \in$, y the tr nsfor tion $\xi = \frac{x(t)}{(t)}$ nd $\tau = t$ here $= x_N(t)$. sing the ch in ru e of Ch pter the tr nsfor ed pro e re ds

$$\frac{\partial \alpha}{\partial \tau} - \frac{\xi}{} \frac{d}{d\tau} \frac{\partial \alpha}{\partial \xi} + \frac{}{} \frac{\partial}{\partial \xi}(\alpha v) = \frac{(+ s_1 C)}{ + s_1 C} \alpha (- \alpha) - \frac{s_2 + s_3 C}{ + s_4 C} \alpha,$$

$$\frac{\partial}{\partial \xi} \alpha \zeta(\alpha) + \frac{k^2 \alpha v}{ - \alpha} = \mu \frac{\partial}{\partial \xi} \alpha \frac{\partial v}{\partial \xi},$$

$$\frac{\partial^2 C}{\partial \xi^2} = \frac{Q^2 \alpha C}{ + Q_1 C},$$

ith initi nd ound ry conditions

$$=, \quad \alpha = \alpha_0 \quad t \quad \tau = ,$$

$$\frac{\partial C}{\partial \xi} = v = \quad t \quad \xi = ,$$

$$\mu \frac{\partial v}{\partial \xi} = \zeta(\alpha), \quad C = \quad t \quad \xi = ,$$

$$\frac{d}{d\tau} = v \quad t \quad \xi = ,$$

here k nd μ h e the s e de nition s efore nd the pressure di erence et een the t o ph ses $\chi(\alpha)$ is de ned in the speci c se $_c = r =$ nd q ? s

$$\chi(\alpha\ \ )\ \zeta(\alpha\ \ )\ ]\quad \leq \alpha < \alpha_{min}$$
$$\frac{-\ \ *}{(1-\ \ )^2}\quad \alpha_{min} \leq \alpha < \ .$$

To co p re the resu ts fro the o ing esh ethod to those in e h e rep ic ted their resu ts sing the o e set of equ tions e postu te the gorith

Pre i in ry O t in n initi **C** **v** nd **α**

Find **C**

h e $\mathbf{C}_{-1}$ $\mathbf{C}_1$ nd $\mathbf{C}_N$ fro nd respecti e y To correspond ith these conditions the o e equ tion for the speci c ses $\mathbf{j}$ nd $\mathbf{j}$ $\mathbf{N} -$ re

$$-?\mathbf{C}_0 \; ?\mathbf{C}_1 \qquad \frac{Q^{\;2}\;\; {}_jC_0}{\mathbf{1+}Q_1C_0} \;\; \boldsymbol{\xi}^{\;\mathbf{2}} \qquad \mathbf{w}\;\mathbf{C}_0$$

$$\mathbf{C}_{N-\mathbf{2}} - ?\mathbf{C}_{N-\mathbf{1}} \qquad \frac{Q^{\;2}\;\; {}_jC_{N-1}}{\mathbf{1+}Q_1C_{N-1}} \;\; \boldsymbol{\xi}^{\;\mathbf{2}} - \qquad \mathbf{w}\;\mathbf{C}_{N-\mathbf{1}}$$

As in Ch pter e rite the non ine r syste s

$$\mathbf{T}\,\mathbf{C} \;\; \mathbf{w}\;\mathbf{C}$$

here

$\mathbf{C}$ is ector of $\mathbf{C}_0$ to $\mathbf{C}_{N-\mathbf{1}}$ $\mathbf{j}$, , ..., $\mathbf{N} -$

$\mathbf{w}\;\mathbf{C}$ is ector of $\mathbf{w}\;\mathbf{C}_j$ $\mathbf{j}$, , ..., $\mathbf{N} -$

nd

$\mathbf{T}$ is tridi gon tri of the $\mathbf{C}_j$ coe cients

$$\mathbf{T} \;\; \begin{pmatrix} -? & ? & & \cdots & \\ & -? & & \ddots & \vdots \\ & \ddots & \ddots & \ddots & \\ \vdots & \ddots & & -? & \\ & \cdots & & & -? \end{pmatrix}.$$

The su gorith for c cu ting $\mathbf{C}$ is the s e s in Ch pter n e y

Pre i in ry M e n initi guess for $\mathbf{C}$

se $\mathbf{C}^p$ to nd $\mathbf{w}\;\mathbf{C}^p$

Find the residu $\mathbf{R}^p$ $\mathbf{T}\,\mathbf{C}^p - \mathbf{w}\;\mathbf{C}^p$

c C cu te the co i n of $\mathbf{R}^p$

$$\mathbf{J}^p \;\; \frac{\partial \mathbf{R}^p}{\partial \mathbf{C}^p} \;\; \mathbf{T} - \Big] \; \frac{\partial \mathbf{w}_i^p}{\partial \mathbf{C}_j^p}$$

here $\mathbf{i}, \mathbf{j}$ = , , ..., $\mathbf{N} -$ nd $\frac{w_i^p}{C_j^p}$ is the di gon tri

$$\frac{\partial \mathbf{w}_i}{\partial \mathbf{C}_j} = \begin{pmatrix} \frac{Q\ 2\ \ 0}{(1+Q_1C_0)^2}(\ \xi^2 & & \cdots & \\ & \frac{Q\ 2\ \ 1}{(1+Q_1C_1)^2}(\ \xi^2 & \ddots & \vdots \\ \vdots & \ddots & \ddots & \\ & \cdots & & \frac{Q\ 2\ \ N-1}{(1+Q_1C_{N-1})^2}(\ \xi^2 \end{pmatrix}.$$

(d Find $\mathbf{H}^p = (\mathbf{J}^p)^{-1}\mathbf{R}^p$

(e Set $\mathbf{C}^{p+1} = \mathbf{C}^p - \mathbf{H}^p$

(f ith the ne ppro i tion $\mathbf{C}^{p+1}$ return to (nd repe t unti (e con erges s e sured y $\|\mathbf{C}^{p+1} - \mathbf{C}^p\|_2 < \times -6$

In step (c the entries to the di gon tri $\frac{w_i^p}{C_j^p}$ cont in n e tr f ctor of $^2(\ \xi^2$ hen co p red to Ch pter to cco od te the di erent $\mathbf{w}(\mathbf{C}_j$

Finding the velocity v

e nd the e ocity in the s e nner s in Ch pter ?. e discretise (?) nd re rr nge so th t

$$\mathbf{A}_j^l \mathbf{v}_{j-1} + \mathbf{A}_j^d \mathbf{v}_j + \mathbf{A}_j^u \mathbf{v}_{j+1} = \mathbf{b}(\boldsymbol{\alpha}_j \qquad (\mathbf{j} = ?, \ldots, \mathbf{N} - \ .$$

here $\mathbf{A}_j^l = \frac{(\ _j + \ _{j-1})\mu}{2(\Delta\ )^2}$ $\mathbf{A}_j^d = -\ -\frac{(\ _j + \ _{j-1})\mu}{2(\Delta\ )^2} - \frac{(\ _j + \ _{j+1})\mu}{2(\Delta\ )^2} - \frac{k\ 2\ \ _j}{1 - \ _j}\Big)$

$\mathbf{A}_j^u = \frac{(\ _j + \ _{j+1})\mu}{2(\Delta\ )^2}$ for $\mathbf{j}$ = ,?, ..., $\mathbf{N} -$ nd

$$\mathbf{b}(\boldsymbol{\alpha}_j = \frac{}{4\Delta}(\boldsymbol{\alpha}_j + \boldsymbol{\alpha}_{j+1}\ \zeta\ \tfrac{1}{2}(\boldsymbol{\alpha}_j + \boldsymbol{\alpha}_{j+1} - \frac{}{4\Delta}(\boldsymbol{\alpha}_j + \boldsymbol{\alpha}_{j-1}\ \zeta\ \tfrac{1}{2}(\boldsymbol{\alpha}_j + \boldsymbol{\alpha}_{j-1}$$

As ith the o ing esh equ tions $\mathbf{v}_0$ = . For the c se hen $\mathbf{j}$

Let $\mathbf{A}_j^l$ $\mathbf{A}_j^d$ nd $\mathbf{A}_j^u$ $(\mathbf{j} = 1, 2, \ldots, \mathbf{N}$ e the respecti e entries to the o er in nd upper di gon s of tri A nd $\mathbf{b}(\alpha_j = \mathbf{b}(\alpha$ $(\mathbf{j} = 1, 2, \ldots, \mathbf{N}$. Hence Step 2 nding the ce e ocity $\mathbf{v}$ is deter ined y so ing

$$\mathbf{A}\mathbf{v} = \mathbf{b}(\alpha .$$

As intended e h e c cu ted $\mathbf{C}$ nd $\mathbf{v}$ on ed esh in the s e y s e c cu ted the on o ing esh. For the ed esh there is no esh e ocity to de ne ut e sti need to co pute the ch nge in the tu our r dius.

Finding the solution α

Fin y to o t in α on the ed esh e discretise (1 e p icit y in ti e ith centr di erence ppro i tion in sp ce

$$\frac{\alpha_j^{i+1} - \alpha_j^i}{\mathbf{t}} - \frac{\xi \mathbf{v}_N}{\ } \frac{\alpha_{j+1}^i - \alpha_{j-1}^i}{2 \ \xi} + \frac{\mathbf{v}_{j+1}^i \alpha_{j+1}^i - \mathbf{v}_{j-1}^i \alpha_{j-1}^i}{2 \ \xi}$$
$$= \frac{(+ \mathbf{s}_1 \ \alpha_j^i (\ - \alpha_j^i \ \mathbf{C}_j^i}{ + \mathbf{s}_1 \mathbf{C}_j^i} - \frac{\mathbf{s}_2 + \mathbf{s}_3 \mathbf{C}_j^i}{ + \mathbf{s}_4 \mathbf{C}_j^i} \alpha_j^i,$$

$$\Rightarrow \alpha_j^{i+1} = \Big[\frac{\xi \mathbf{v}_N}{\ } \frac{(\alpha_{j+1}^i - \alpha_{j-1}^i}{2 \ \xi} - \frac{\mathbf{v}_{j+1}^i \alpha_{j+1}^i - \mathbf{v}_{j-1}^i \alpha_{j-1}^i}{2 \ \xi}$$
$$+ \frac{(+ \mathbf{s}_1 \ \alpha_j^i (\ - \alpha_j^i \ \mathbf{C}_j^i}{ + \mathbf{s}_1 \mathbf{C}_j^i} - \frac{\mathbf{s}_2 + \mathbf{s}_3 \mathbf{C}_j^i}{ + \mathbf{s}_4 \mathbf{C}_j^i} \alpha_j^i \quad \alpha_j^i, \qquad (1$$
$$(\mathbf{j} = \ , 1, \ldots, \mathbf{N} \ .$$

A one sided ppro i tion to α is used t the ound ries. This sche e is non conser ti e (see Ch pter 1 e re *ss ng* th t the α re upd ted in this y in .

Finding the tumour radius

By (1 the tu our r dius gro s t the s e r te s the ce e ocity t the ound ry $\mathbf{v}_N$ e nd the tu our r dius t the ne ti e e e y using the e p icit Eu er ti e stepping sche e

6.P N eric Res ts for Bre rd et s Method

It is i port nt to re r th t the nu eric gorith speci ed in this ch p ter is sur ise sed upon the tr nsfor ed pro e gi en in . Ho e er so ing the tr nsfor ed pro e using this nu eric process e successfu y gener te p ots hich rep ic te those sho n in . e c n therefore e re son y con dent in our pre i in ry c cu tions in Ch pter here e nd the concentr tion **C** nd ce e ocity **v** using nite di erences.

for oth α nd . Nonethe ess e c n e re son y con dent th t the so ution nd the tu our ound ry con erges.

Ch pter

N eric res ts for o ing esh ethods

In this section e use the o ing esh ethods descri ed e r ier to present nu eric si u tions of the non di ension ised ode equ tions to in se er p r eter regi es. Our i s re to co p re the three di erent o ing esh ethods nd so to co p re the resu ts ith e isting esh nu eric si u tions in .

The resu ts gi en here re the non di ension ised ues T stepping sche e s used In this c se s the nu er of nodes dou ed the ti e step s qu rtered This decision s de s the so ution **α** is reco ered using id point ppro i tion hich is second order in sp ce nd the e p icit Eu er ti e stepping sche e is rst order in ti e

e ou d e pect the so utions to con erge quic er here using the ODE? ℝ so er ec use this uses n ppro i tion sed upon Runge utt ? nd ℝ hich h e higher order of ccur cy th n Eu er ti e stepping Ho e er e shou d e c refu to note th t the ti esteps re consider y rger hen using ODE? ℝ

T e Re ti e errors for

con ergence eh iour hen co p ring Eu er ti e stepping nd using ODE? R Yet ithin chosen ti e stepping sche e Method B nd C h e ne r y iden tic con ergence r tes especi y hen hen using ODE? R (T es ? nd R hen co p ring Methods B nd C ith the e p icit Eu er ti e stepping (T es nd e see th t the **α** con erge si i r y ut the order of con ergence of **x** for Method B (T e ppe rs to e eh ing err tic y eit for the s d t s p e o t ined here The esh fro Method C together ith Eu er s ti e stepping (T e see s to h e the highest r te of con ergence

It ppe rs th t gener y the esh ppro ches n order of con ergence rger th n t o hi st **α** y pro e to e of second order con ergence Ho e er e c nnot e sure of the order of con ergence in ny of the c ses ithout h ing ore d t nd co p ring the so utions to d t retrie ed using **N >>** E en so e c n e re son y con dent th t the so ution nd esh con erge for three o ing esh ethods

Co p rison ith Bre rd et s ethod c

, Co p ring Fig re fro c

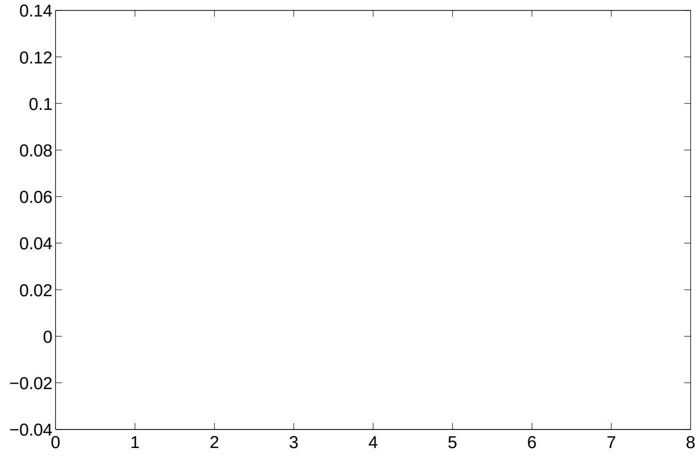
e ish to co p re our nu eric ethods to the esh ethod used in e gener te resu ts using the s e p r eters o e to co p re our resu ts ith Figure R in A three ethods ere in estig ted using oth the e p icit Eu er ti e stepping sche e nd ODE? R Throughout this section e t e **N** **t** . nd run unti **t**

Methods A nd C produce ery si i r p ots to e ch other reg rd ess of the ti e stepping ppro ch For this re son on y the resu ts fro Method A re inc uded here

The e p icit Eu er ti e stepping sche e nd ODE? R gener te

Method B ppe rs to eh e i e Method A nd t e r ier ti es ut fter ppro i te y t α ppe rs to gro t the ound ry nd no onger decre ses t regu r r te t the centre of the tu our. The p ots fro Method B re ess s ooth despite the s e nu er of nodes used for oth ethods. There is consider e in in α nd v for t hich ppe rs to d pen for ter ti es. The so ution α does not drop e o t the centre of the tu our e en for t (not sho n here). The ey ch r cteristics re in e en for s er t nd so hen using ODE?? suggesting th t this eh iour is due to the nu eric ethod. The processes of Method B nd Method C re ery si i r nd s Method C eh es s in Figures nd it is re son e to conc ude th t tr c ing the ce e ocity ith the esh nodes c n resu t in the esh eco ing too co rse in so e re s. This is pro e th t cou d e co pounded o er ti e especi y here the ce e ocities ry et een positi e nd neg ti e. At this point the nodes ou d e o ing in opposite directions e ing consider e de cit in et een. Indeed if e oo t Figure for t e see th t the e ocity is ost y neg ti e so the nodes re o ing to the eft.

The di erences et een Method B nd the resu ts presented in re ore pp rent in Figure e c n see ore c e r y th t it ppe rs to e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0.08
0.06
0.04
0.02
0
−0.02
−0.04
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1
2
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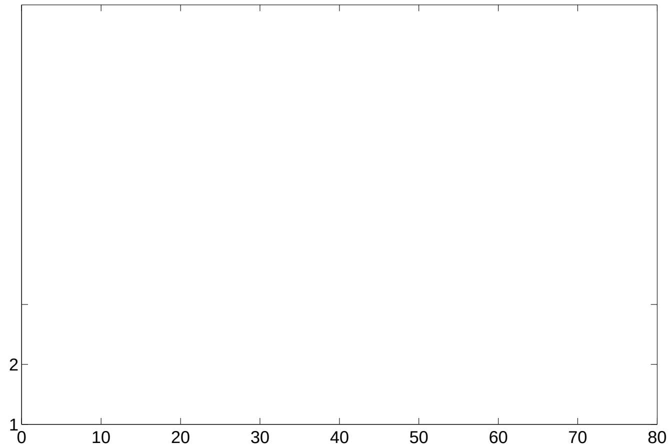
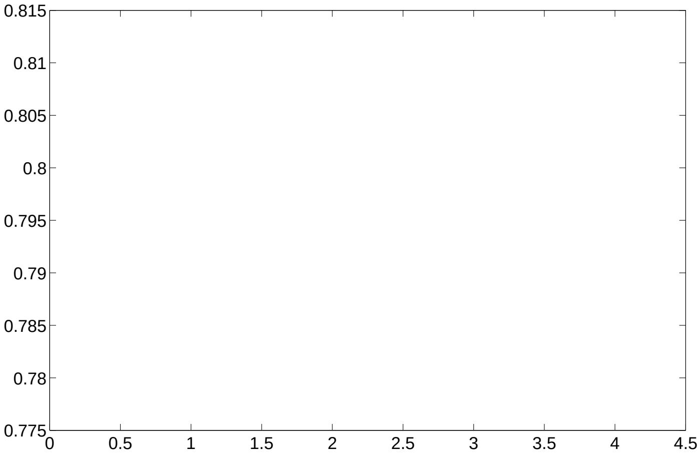
5
6
7
8


2
1
0
10
20
30
40
50
60
70
80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0.805
0.8
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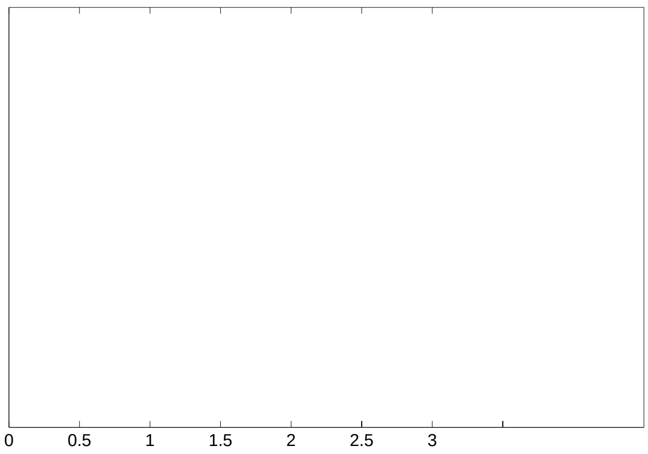
1.5
2
2.5
3
3.5
4
4.5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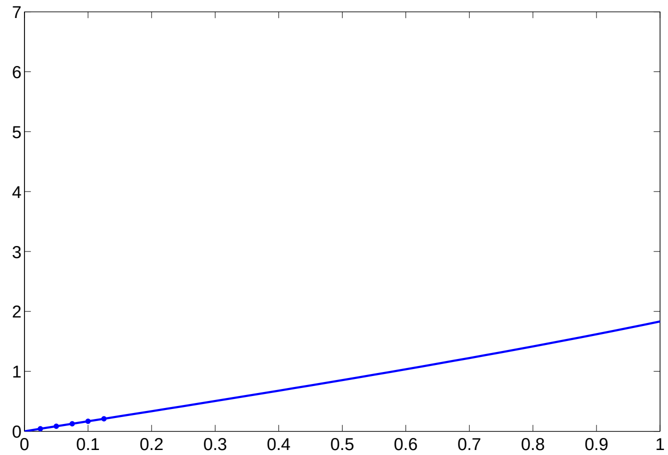
1
1.5
2
2.5
3


7
6
5
4
3
2
1
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1

Ch pter

Co pring Method C nd the esh ethod in c

In Ch pter e so ed the non conser ti e for of the tu our gro th pro e s st ted in

$$\frac{\partial \alpha}{\partial \tau} - \frac{\xi}{} \frac{d}{d\tau} \frac{\partial \alpha}{\partial \xi} + \frac{}{} \frac{\partial}{\partial \xi} (\alpha v \; = S(\alpha, C \; .$$

In there is no ention of the nu eric process So e so ed y e p icit y ti e stepping α y Eu er s ethod

$$\alpha^{new} = \alpha^{old} + \; t \; S^{new} - \frac{}{old} (\alpha^{old} v^{new} + \frac{}{old} \xi \alpha^{old} \; .$$

Let us co p re this to the o ing esh Method C in Section Here e use the conser ti e for $\frac{d}{dt} \; \alpha \, dx = \; S \, dx)$ of the PDE

$$\frac{\partial \alpha}{\partial t} + \frac{\partial}{\partial x} (\alpha v \; = S(\alpha, C$$

to nd the integr of α ith respect to sp ce e de ne $= \; \alpha \, dx$ thus discrete y

$$\alpha = \frac{}{x} .$$

Inste d of e p icit y ti e stepping α e e p icit y ti e stepped y Eu er s ethod in the for

$$_j^{new} = \; _j^{old} + \; t$$

Ch pter

F rther or

A tering the ce e ocity o nd ry condition

Throughout this report e h e not ch nged the ode presented in nd . Let us consider the ound ry condition on the ce e ocity

$$\mathbf{v} = \quad t \ \mathbf{x} = .$$

Possi e future or cou d in o e ch nging the eft ound ry condition to

$$\frac{\mathbf{dv}}{\mathbf{dx}} = \quad t \ \mathbf{x} = ,$$

depending on n intern pressure. Thus $\mathbf{v} \neq$ t the inner ound ry. This ou d e n th t the tu our ou d sti re in sy etric out $\mathbf{x} = \mathbf{x_0}$ ut the ce s in the centre ou d h e e ocity th t depends on the iscosity $\boldsymbol{\mu}$ dr g $\mathbf{k}$ nd the nutrient concentr tion $\mathbf{C}$. hen the necrotic core for s i.e. hen $\boldsymbol{\alpha} \to$ the region occupied y ce s o es y fro the origin. The pro e ou d e so ed on the region occupied y $\boldsymbol{\alpha} \neq$.

E ining the e ect of

Let us return to $\boldsymbol{\chi}(\boldsymbol{\alpha})$ in the for sho n in Section .?

$$\boldsymbol{\chi}(\boldsymbol{\alpha}) = \begin{cases} & \leq \boldsymbol{\alpha} < \boldsymbol{\alpha}_{min}, \\ \frac{\hat{\boldsymbol{\Sigma}}_c| - {}^*|^{r-1}}{(\mathbf{1}-)^q}(\boldsymbol{\alpha} - \boldsymbol{\alpha}^* & \boldsymbol{\alpha}_{min} \leq \boldsymbol{\alpha} < . \end{cases}$$

For $\boldsymbol{\alpha}_{min} < \boldsymbol{\alpha}^*$ there is discontinuity t $\boldsymbol{\alpha}_{min}$. This ju p y c use in ccur cies hen nu eric y ppro i ting the deri ti e of $\boldsymbol{\chi}(\boldsymbol{\alpha})$ used in Ch pter .?

since in this section e so ed the equ tion for the ce e ocity ($\mathbb{R}$ y discretising in sp ce The right h nd side of the tri syste (s ector of the nu eric ppro i tion of $\frac{d}{dx}$ $\alpha\chi(\alpha$

$$\frac{d}{dx}\chi(\alpha\ \alpha \quad = \quad \alpha_{j+\frac{1}{2}}\chi(\alpha_{j+\frac{1}{2}} - \alpha_{j-\frac{1}{2}}\chi(\alpha_{j-\frac{1}{2}}$$

$$= \ \frac{}{2}(\alpha_j + \alpha_{j+1}\ \chi\ \ \frac{}{2}(\alpha_j + \alpha_{j+1} \ - \frac{}{2}(\alpha_j + \alpha_{j-1}\ \chi\ \ \frac{}{2}(\alpha_j + \alpha_{j-1} \ .$$

By ppro i ting cross the ho e region in this nner e re not ccount ing for the ju p in $\chi(\alpha$ t $\alpha = \alpha_{min}$ This y c use in ccur cies t this point hich ight ccount for the se ere osci tions in Figures to These gures use $\alpha_{min} = .$ nd $\alpha^* = .$ nd sho th t the so ution is e eh ed unti ne r the point here α drops do n to

To ssess this error in our discretis tion e identify hen $\alpha = \alpha_{min}$ nd use one sided ppro i tion for $\frac{d}{dx}$ $\alpha\chi(\alpha$ either side of this point so s to not discretise cross the ju p in $\chi(\alpha$

As in the e ocity c cu tion it is necess ry to use one sided ppro i tions t the s e point ($\alpha = \alpha_{min}$ hen nding the so ution α This is ec use α

Bi iogr phy

Ar ujo R P nd McE in D L S A history of the study of so id tu our gro th The contri ution of the tic ode ing *B Det n of M the t c DB oDgy* **66**

? Ar ujo R P nd McE in D L S The n ture of stresses induced during tissue gro th *App M th Lett* **18**

R B e Mo ing Mesh Methods for Non Line r P r o ic P r ti Di erenti Equ tions Ph D Thesis *Dep rt ent of M the t cs n ers ty of Re d ng*

Bre rd C Byrne H M nd Le is C E ? The ro e of ce ce inter ctions in t o ph se ode for scu r tu our gro th *of M th B oD* **45(2)** ? ?

Byrne H M ing R McE in D L S nd Preziosi L ? R A t o ph se ode of so id tu our gro th *AppDed M the t cs Letters* **16** R

G ten y R A M the tic ode s of tu our host inter c tions *C ncer* **11** ? ? R

G ten y R A nd G ins i E T A re ction di usion ode of c ncer in sion *C ncer Res* **56** R

G ten y R A nd M ini P ? R C ncer su ed up *N t re* **421** R

H P Greensp n On the gro th nd st i ity of ce cu tures nd so id tu ours *heor B oD* **56** ?? ? ?

?2 L nd n A nd P e se C P ? Tu our dyn ics nd necrosis Surf ce tension nd st i ity *MA M th AppD Med c ne B oD* **18** R

R Lu in S R nd c son T ? ? Mu itph se ech nics of c psu e for s o

Appendices

Appendi A

E ining the e ect of ( )

Let us identify the node just to the eft of the point here $\alpha = \alpha_{min}$ s the r er node hich e sh denote s $\mathbf{x}_m$ To ccount for the ju p et een $\mathbf{x}_m$ nd $\mathbf{x}_{m+1}$ e use one sided discretis tion of at $\mathbf{x}_m$ nd $\mathbf{x}_{m+1}$

Downwind discretisation of the velocity (3.10) at $\mathbf{x}_m$

$$\frac{}{\mathbf{x}_m - \mathbf{x}_{m-1}} \quad \alpha\mu\frac{\partial \mathbf{v}}{\partial \mathbf{x}} - \alpha\chi(\alpha \quad_m - \quad \alpha\mu\frac{\partial \mathbf{v}}{\partial \mathbf{x}} - \alpha\chi(\alpha \quad_{m-1} = \frac{\mathbf{k}\alpha_{m-\frac{1}{2}}}{-\alpha_{m-\frac{1}{2}}}\mathbf{v}_{m-\frac{1}{2}}$$

Ag in e use one sided discretis tion on the ter s in the squ re r c ets so s to not ppro i te di erenti cross $\mathbf{x}_m$ A so s efore e use $\alpha_{m-\frac{1}{2}} \approx \frac{1}{2}(\alpha_m + \alpha_{m-1})$

$$\frac{}{\mathbf{x}_m - \mathbf{x}_{m-1}} \quad \mu\alpha_m \quad \frac{\mathbf{v}_m - \mathbf{v}_{m-1}}{\mathbf{x}_m - \mathbf{x}_{m-1}} \quad - \chi(\alpha_m \quad \alpha_m - \mu\alpha_{m-1} \quad \frac{\mathbf{v}_{m-1} - \mathbf{v}_{m-2}}{\mathbf{x}_{m-1} - \mathbf{x}_{m-2}} + \chi(\alpha_{m-1} \quad \alpha_{m-1}$$

$$= \frac{\mathbf{k}(\alpha_m + \alpha_{m-1}}{-2(\alpha_m + \alpha_{m-1}}(\mathbf{v}_m + \mathbf{v}_{m-1}$$

$$\mu\alpha_m \quad \frac{\mathbf{v}_m - \mathbf{v}_{m-1}}{\mathbf{x}_m - \mathbf{x}_{m-1}} \quad - \mu\alpha_{m-1} \quad \frac{\mathbf{v}_{m-1} - \mathbf{v}_{m-2}}{\mathbf{x}_{m-1} - \mathbf{x}_{m-2}} \quad - \frac{\mathbf{k}(\alpha_m + \alpha_{m-1} \quad (\mathbf{x}_m - \mathbf{x}_{m-1}}{-2(\alpha_m + \alpha_{m-1}}(\mathbf{v}_m + \mathbf{v}_{m-1}$$

$$= \chi(\alpha_m \quad \alpha_m - $$

nd

$$\mathbf{b}(\boldsymbol{\alpha}) = \Big(\mathbf{b}(\boldsymbol{\alpha}_1 \;\; \mathbf{b}(\boldsymbol{\alpha}_2 \;\; \cdots \;\; \mathbf{b}(\boldsymbol{\alpha}_m \;\; \mathbf{b}(\boldsymbol{\alpha}_{m+1} \;\; \cdots \;\; \mathbf{b}(\boldsymbol{\alpha}_{N-1} \;\; \mathbf{b}(\boldsymbol{\alpha}_N\Big)^T$$

$$\mathbf{v} = \Big(\mathbf{v}_1 \;\; \mathbf{v}_2 \;\; \cdots \;\; \mathbf{v}_m \;\; \mathbf{v}_{m+1} \;\; \cdots \;\; \mathbf{v}_{N-1} \;\; \mathbf{v}_N\Big)^T.$$

Recovering $\boldsymbol{\alpha}_m$ and $\boldsymbol{\alpha}_{m+1}$ using one-sided approximations

For consistency e reco er $\boldsymbol{\alpha}$ using one sided ppro i tion t $\mathbf{x}_m$ nd $\mathbf{x}_{m+1}$. Method A

$$\boldsymbol{\alpha}_m = \frac{\boldsymbol{\theta}(\mathbf{t}}{\boldsymbol{\theta}(} \frac{\mathbf{x}_m(- \mathbf{x}_{m-1}(}{\mathbf{x}_m(\mathbf{t} - \mathbf{x}_{m-1}(\mathbf{t}} \boldsymbol{\alpha}_m$$

$$\boldsymbol{\alpha}_{m+1} = \frac{\boldsymbol{\theta}(\mathbf{t}}{\boldsymbol{\theta}(} \frac{\mathbf{x}_{m+2}(- \mathbf{x}_{m+1}(}{\mathbf{x}_{m+2}(\mathbf{t} - \mathbf{x}_{m+1}(\mathbf{t}} \boldsymbol{\alpha}_{m+1}.$$

Methods B nd C

$$\boldsymbol{\alpha}_m = \frac{m}{\mathbf{x}_m - \mathbf{x}_{m-1}}$$

$$\boldsymbol{\alpha}_{m+1} = \frac{m+1}{\mathbf{x}_{m+2} - \mathbf{x}_{m+1}}.$$

e shou d note th t the do n ind ppro i tion t $\mathbf{x}_m$ requires $\mathbf{m} \geq 2$ ut the position here $\boldsymbol{\alpha} = \boldsymbol{\alpha}_{min}$ occurs t the right h nd ound ry so inti y $\mathbf{m}$ is i e y to e s er th n 2.