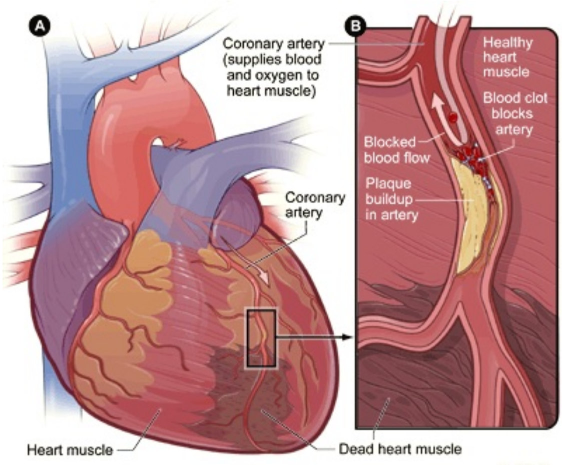
Literature Study

Modeling an angiogenesis treatment after a myocardial infarction

Linda Crapts
4 april 2012

Introduction



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Outline

Next section

Mathematical model

Stem cell density

$$\frac{\partial m}{\partial t} = -\beta_1 m,$$

- $m(x,0) = \begin{cases} m_0 & x \in \Omega_w, \\ 0 & x \in \Omega \backslash \Omega_w. \end{cases}$

Concentration TG-beta (attractant)

$$\frac{\partial c}{\partial t} - D_1 \frac{\partial^2 c}{\partial x^2} + \lambda c = \alpha m,$$

- $c(x,0) = 0,$
- $\frac{\partial c}{\partial x}(0,t) = \frac{\partial c}{\partial x}(1,t) = 0.$

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Mathematical model

Capillary tip density

$$\frac{\partial n}{\partial t} + \chi_1 \frac{\partial}{\partial x}\left(n \frac{\partial c}{\partial x}\right) - D_2 \frac{\partial^2 n}{\partial x^2} = \alpha_0 \rho c + \alpha_1 H(c - \hat{c}) n c - \beta_2 n \rho,$$

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Vessel density

$$\frac{\partial \rho}{\partial t} - \epsilon \frac{\partial^2 \rho}{\partial x^2} + \gamma(\rho - \rho_{eq}) = \mu_1 \frac{\partial n}{\partial x} - \chi_2 n \frac{\partial c}{\partial x},$$

- $\rho(x, 0) = \begin{cases} 0 & x \in \Omega_w, \\ \rho_{eq} & x \in \Omega \backslash \Omega_w, \end{cases}$
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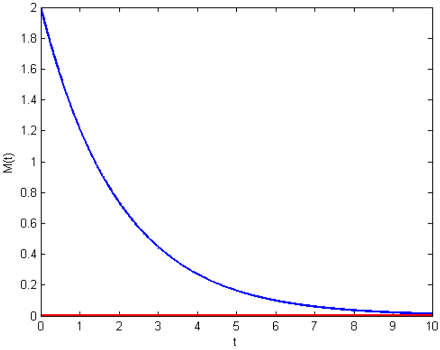
Next section

Stem cell density

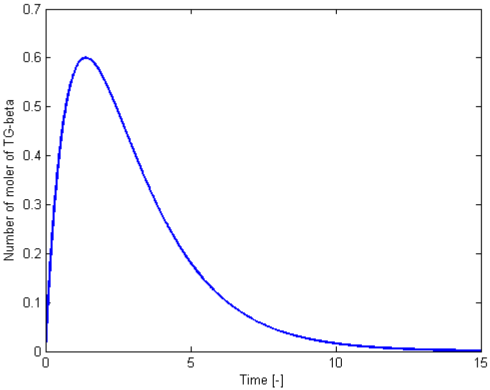
The stem cell density decreases exponentially:

$$m(x,t) = \begin{cases} m_0 e^{-\beta_1 t} & x \in \Omega_w, \\ 0 & x \in \Omega \backslash \Omega_w. \end{cases}$$



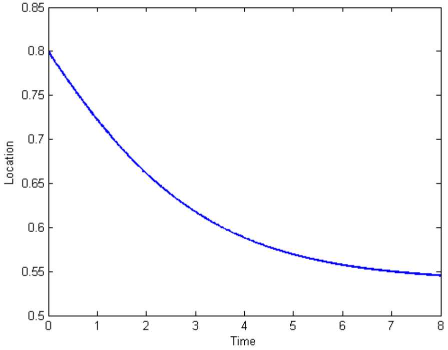
Amount of TG-Beta

The amount of TG-beta is determined by $\int_\Omega c \; d\Omega$.



Characteristics of the capillary tip density

Speed of the characteristics: $\frac{dx}{dt} = \chi_1 \frac{\partial c}{\partial x}$.



Boundary wound: $\delta = 0.2$.

$\Rightarrow$ Amount of stem cells is not enough when we have the used parameters!

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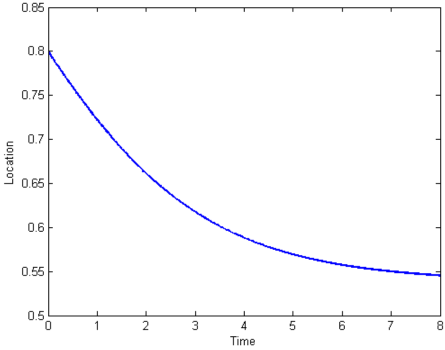

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Next section

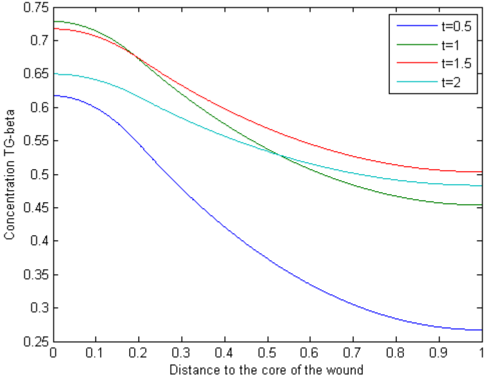
FDM and FEM

Maximum relative difference between the finite difference method and the finite element method.

	$\Delta x = 0.001$		
	c	n	ρ
$t = 0.5$	0.0100	0.0286	0.0156
$t = 1.0$	0.0100	0.0574	0.0548
$t = 1.5$	0.0100	0.0567	0.0566
$t = 2.0$	0.0100	0.0366	0.2712

Results with FEM

The follwing results are with the finite element method, where we have used $\Delta x = 0.001$, $\Delta t = 0.01$ and $T = 2$.



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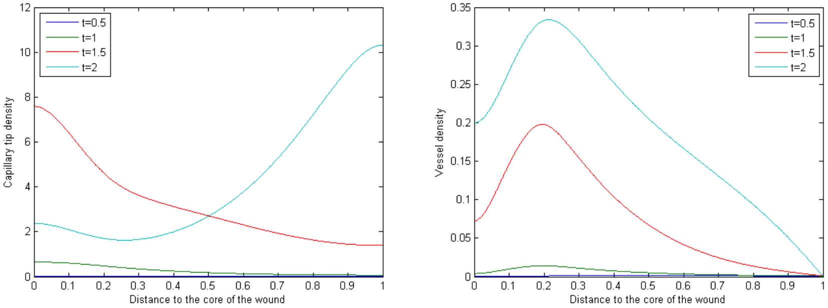
Results with FEM



Péclet number

Péclet number

$$Pe = \frac{v\Delta x}{D},$$

where v is the absolute speed and D the diffusion coefficient.

$Pe = 0$,	pure diffusion,
$Pe \leq 1$,	diffusion-dominated,
$1 < Pe \leq 10$,	both are important,
$Pe > 10$,	convection-dominated,
$Pe = \infty$,	pure convection.

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Basics of SUPG

The advection equation:

$$u_t + u_x = 0.$$

Multiply by a testfunction $\eta(x) = \varphi(x) + p(x)$ and take the integral over the domain:

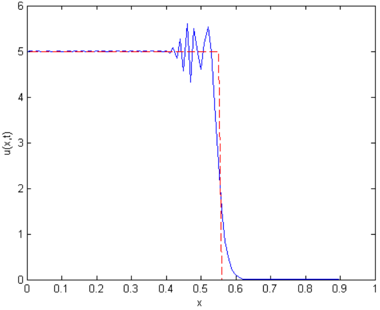
$$\int_\Omega u_t\eta + u_x\eta \; d\Omega = 0,$$

$$\Rightarrow \underbrace{\int_\Omega u_t\varphi + u_x\varphi \; d\Omega}_{\text{FEM}} = \underbrace{-\int_\Omega u_t p + u_x p \; d\Omega}_{\text{Additional for SUPG}},$$

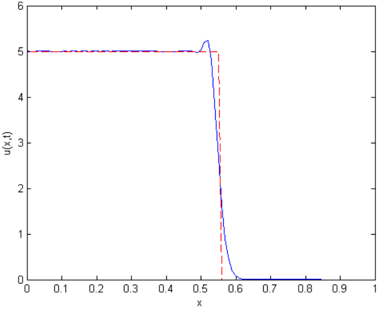
where $p(x) = \xi \frac{\Delta x}{2} \frac{d\varphi}{dx}$ and ξ equals the sign of the speed.

Advection equation with SUPG

With discontinuous initial condition, after $t = 0.05$.



Figuur: Without SUPG



Figuur: With SUPG

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Our model with SUPG

Péclet number equals:

$$Pe = \frac{\chi_1 \frac{\partial c}{\partial x}}{D_2} \Delta x.$$

FEM already worked relatively well, so we did not obtain any results yet that showed the functionality of SUPG to our model.

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Basics of DG

- $e_j = [x_{j-1/2}, x_{j+1/2}]$, $j = 1 \ldots N$.
- Maximum element size: $\Delta x = \max_{1 \leq j \leq N} \Delta j$.
- Legendre polynomials as our basisfunctions.
- Scale element interval to $[-1, 1]$ by $r = \frac{2(x - x_j)}{\Delta x}$.

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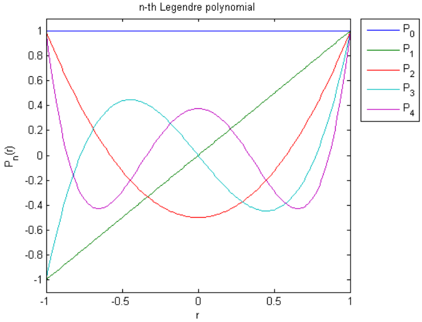

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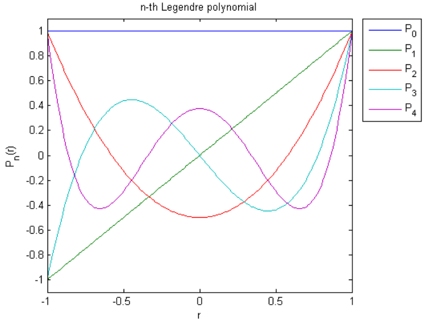

Basics of DG

The approximation is given by:

$$
\begin{aligned}
u_h(x,t) &= \sum_{l=0}^{K} u_j^{(l)}(t)\varphi_j^{(l)}(x) \\
&= \sum_{l=0}^{K} u_j^{(l)}(t) P_l\left(\frac{2(x-x_j)}{\Delta x}\right) \\
&= \sum_{l=0}^{K} u_j^{(l)}(t) P_l\left(r\right).
\end{aligned}
$$

So each global x, has its own local value r.

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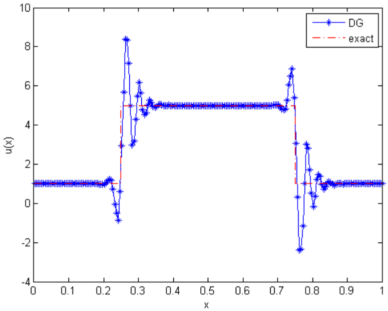
Advection equation with DG

With discontinuous initial condition, after $t = 0.25$. Here we have used two Legendre polynomials, so up to order $K = 1$.



Figuur: $\Delta x = 0.01$, $\Delta t = 0.001$.

The monotonized central-difference limiter

The limiter can be used for polynomial basis up to order $K = 1$.
It uses the minmod function, which is given by:

$$m(a, b, c) = \begin{cases} \text{sgn}(a) \cdot \min\{|a|, |b|, |c|\} & \text{if } \text{sgn}(a) = \text{sgn}(b) = \text{sgn}(c) \\ 0 & \text{elsewhere.} \end{cases}$$

Solution using the limiter

$$u_h(x, t^k) = \bar{u}_j^k + \sigma_j^k (x - x_j).$$

Here, $\bar{u}_j^k$ is the averaged approximation over e_j at $t = k$ and σ is defined as:

$$\sigma_j^k = m\left(\frac{\bar{u}_{j+1}^k - \bar{u}_{j-1}^k}{2\Delta x}, 2\frac{\bar{u}_j^k - \bar{u}_{j-1}^k}{\Delta x}, 2\frac{\bar{u}_{j+1}^k - \bar{u}_j^k}{\Delta x}\right).$$

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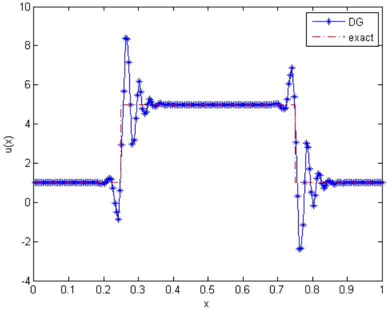
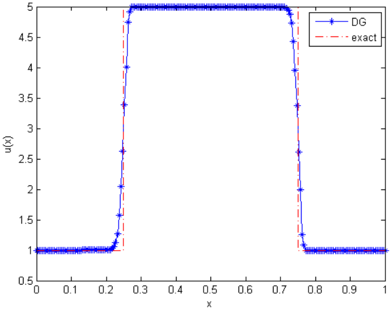
Advection equation with DG and limiter



Figuur: Without limiting



Figuur: With limiting

Next section

Further research

Our model:

- Expand the model to 2D.
  (Apply FEM)
- Are the parameter values realistic?
- Are the initial conditions realistic?

Further research

Research for DG:

- Try to limit the DG approximation using higher order basisfunctions.
- Apply DG to our 1D model.
- How does DG works for a two dimensional scheme?
- Apply DG to our 2D model.

Further research

Research question:

- How many stem cells should be injected when aiming at avoiding the formation of scar tissue?