CSE 397 Introduction to Computational Oncology
Homework 1 - Modeling Avascular Growth

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Problem 1: Derive forward, backward, and center differences for 3rd derivatives

Forward: Apply backward difference to each term in 2nd derivative difference:

$$
\begin{aligned}
u_{i+1} &= u_i + \Delta x u' + \frac{\Delta x^2}{2} u'' + \frac{\Delta x^3}{6} u''' + \mathcal{O}(\Delta x^4) \\
u_{i+2} &= u_i + 2\Delta x u' + \frac{4\Delta x^2}{2} u'' + \frac{8\Delta x^3}{6} u''' + \mathcal{O}(\Delta x^4) \\
u_{i+3} &= u_i + 3\Delta x u' + \frac{9\Delta x^2}{2} u'' + \frac{27\Delta x^3}{6} u''' + \mathcal{O}(\Delta x^4)
\end{aligned}
$$

To eliminate the u' and u'' terms, set up a system of equations for the coefficients of those along with u''':

$$
\begin{aligned}
\begin{bmatrix} 3 & 2 & 1 \\ 9/2 & 4/2 & 1/2 \\ 27/6 & 8/6 & 1/6 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} &= \begin{bmatrix} 0 \\ 0 \\ 1 \end{bmatrix} \\
\begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} &= \begin{bmatrix} 1 \\ -3 \\ 3 \end{bmatrix}
\end{aligned}
$$

$$
u_{i+3} - 3u_{i+2} + 3u_{i+1} = u_i + \Delta x^3 u'''
$$

$$
\boxed{u''' = \frac{u_{i+3} - 3u_{i+2} + 3_{i+1} - u_i}{\Delta x^3}}
$$

Backward: The backward difference formula is nearly identical due to the similarity of the Taylor expansions, with only the signs being different in the matrix above.

$$
\boxed{u''' = \frac{u_i - 3u_{i-1} + 3u_{i-2} - u_{i-3}}{\Delta x^3}}
$$

Centered: Take Taylor expansions for $\pm\Delta x$ and $\pm 2\Delta x$:

$$\begin{aligned}
u_{i+2} &= u_i + 2\Delta x u' + \frac{4\Delta x^2}{2}u'' + \frac{8\Delta x^3}{6}u''' + \mathcal{O}(\Delta x^4) \\
u_{i+1} &= u_i + \Delta x u' + \frac{\Delta x^2}{2}u'' + \frac{\Delta x^3}{6}u''' + \mathcal{O}(\Delta x^4) \\
u_{i-1} &= u_i - \Delta x u' + \frac{\Delta x^2}{2}u'' - \frac{\Delta x^3}{6}u''' + \mathcal{O}(\Delta x^4) \\
u_{i-2} &= u_i - 2\Delta x u' + \frac{4\Delta x^2}{2}u'' - \frac{8\Delta x^3}{6}u''' + \mathcal{O}(\Delta x^4)
\end{aligned}$$

Anticipating symmetry in the method, apply an operation to remove u' and u''

$$u_{i+2} - 2u_{i+1} + 2u_{i-1} - u_{i-2} = 2\Delta x^3 u'''$$

$$\boxed{u''' = \frac{u_{i+2} - 2u_{i+1} + 2u_{i-1} - u_{i-2}}{2\Delta x^3}}$$

Problem 2: Derive the FDM description for the 2D reaction-diffusion equation:

$$\frac{\mathbf{dN(x,y,t)}}{\mathbf{dt}} = \nabla \cdot (\mathbf{D(x,y)}\nabla \mathbf{N(x,y,t)}) + \mathbf{k(x,y)} \cdot \mathbf{N(x,y,t)} \left(\mathbf{1} - \frac{\mathbf{N(x,y,t)}}{\theta}\right)$$

Time differentiation:

$$\frac{dN(x,y,t_i)}{dt} = \frac{N(x,y,t_{i+1}) - N(x,y,t_i)}{t_{i+1} - t_i}$$

$$N(x,y,t+\Delta t) = N(x,y,t) + \Delta t \left[\nabla \cdot (D(x,y)\nabla N(x,y,t)) + k(x,y) \cdot N(x,y,t)\left(1 - \frac{N(x,y,t)}{\theta}\right)\right]$$

Center spatial differences:

$$\begin{aligned}
\nabla \cdot (D(x,y)\nabla N(x,y,t)) &= \frac{\partial(D(x,y)N_x)}{\partial x} + \frac{\partial(D(x,y)N_y)}{\partial y} \\
&= D_x N_x + DN_{xx} + D_y N_y + DN_{yy} \\
&= D_x N_x + D_y N_y + D[N_{xx} + N_{yy}] \\
&= D_x \frac{N(x+\Delta x,y,t) - N(x-\Delta x,y,t)}{2\Delta x} + D_y \frac{N(x,y+\Delta y,t) - N(x,y-\Delta y,t)}{2\Delta y} + \\
&\quad D(x,y)\left[\frac{N(x+\Delta x,y,t) - 2N(x,y,t) + N(x-\Delta x,y,t)}{\Delta x^2} + \right. \\
&\quad \left. \frac{N(x,y+\Delta y,t) - 2N(x,y,t) + N(x,y-\Delta y,t)}{\Delta y^2}\right]
\end{aligned}$$

Boundary conditions:

$$N_x|_{x=0} = \frac{N(0+\Delta x) - N(0-\Delta x)}{2\Delta x} = 0$$
$$N(-\Delta x, y, t) = N(\Delta x, y, t)$$

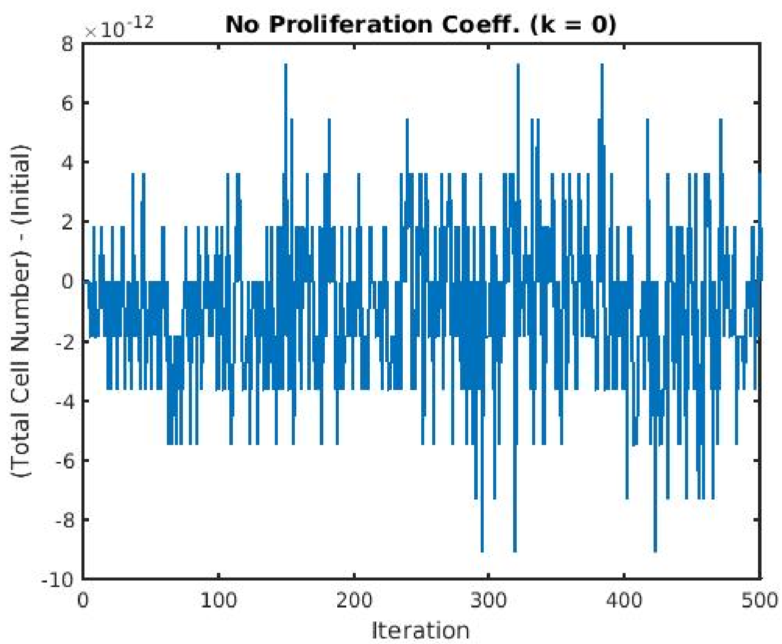
$$N_x|_{x=10mm} = \frac{N(10+\Delta x) - N(10-\Delta x)}{2\Delta x} = 0$$
$$N(10+\Delta x, y, t) = N(10-\Delta x, y, t)$$

$$N_y|_{y=0} = \frac{N(0+\Delta y) - N(0-\Delta y)}{2\Delta y} = 0$$
$$N(x, -\Delta y, t) = N(x, \Delta y, t)$$

$$N_y|_{y=10mm} = \frac{N(10+\Delta y) - N(10-\Delta y)}{2\Delta y} = 0$$
$$N(x, 10+\Delta y, t) = N(x, 10-\Delta y, t)$$

Problem 3: Implement the 2D reaction-diffusion equation.

3a) With $k = 0$, there should be no proliferation. This is almost true with the numerical implementation as well, except for some small blips near the order of machine epsilon. This can be attributed to round-off or floating point error.



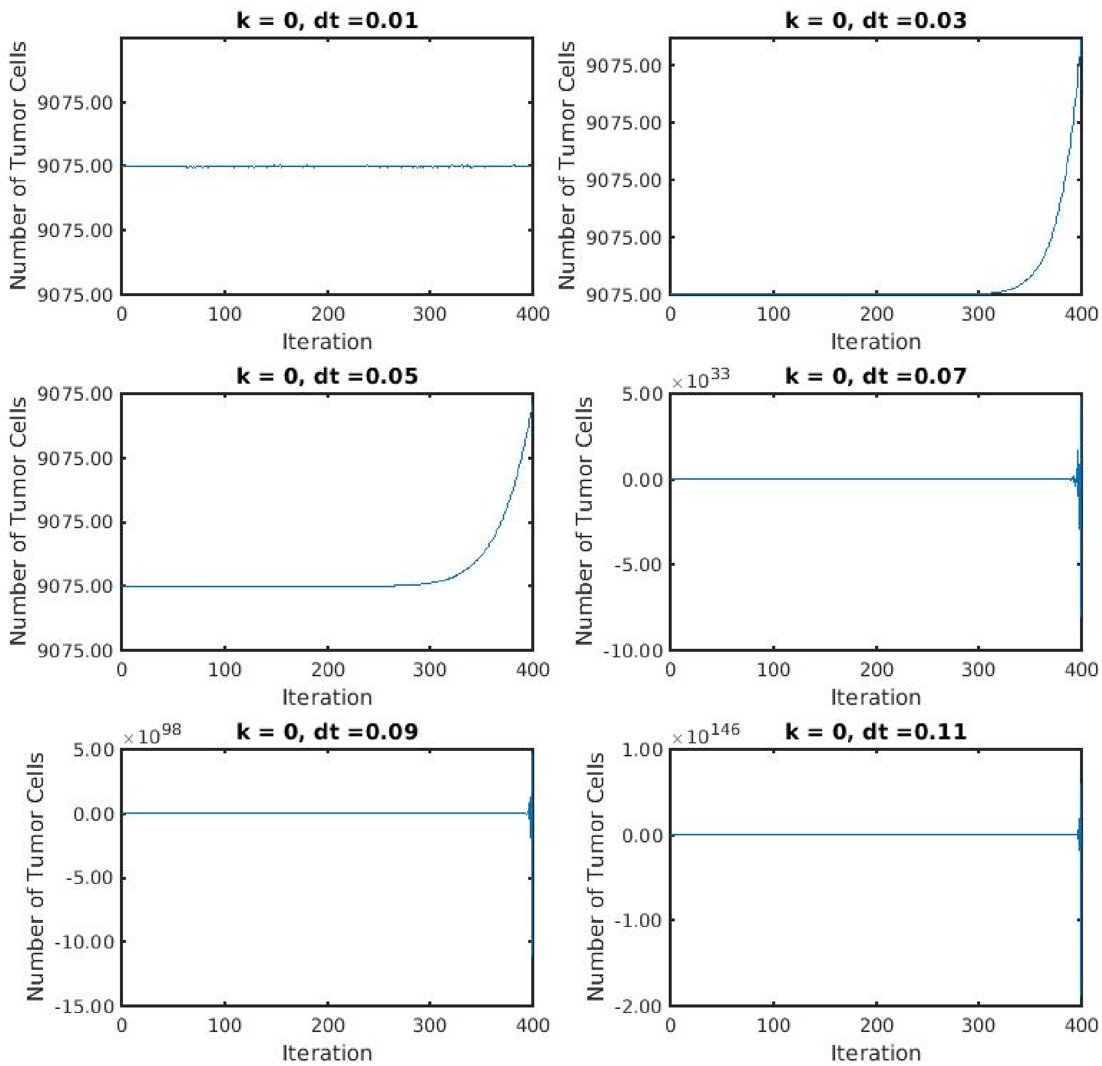
3b) As Δt increases, it can be seen that the method behaves worse and worse; at $\Delta t = .05$, the method is still stable, but at .07 it is unstable and it quickly oscillates to extremely large and impossible values (i.e., negative cell numbers). The r value for $\Delta t = .05$ is .5, while for $\Delta t = .07$ it is .7, greater than .5.

In order to achieve stability, we need $r = \Delta t \cdot D \cdot \left(\frac{1}{\Delta x^2} + \frac{1}{\Delta y^2}\right) < \frac{1}{2}$. Thus, we need to change the spatial step size. The largest value of D is:

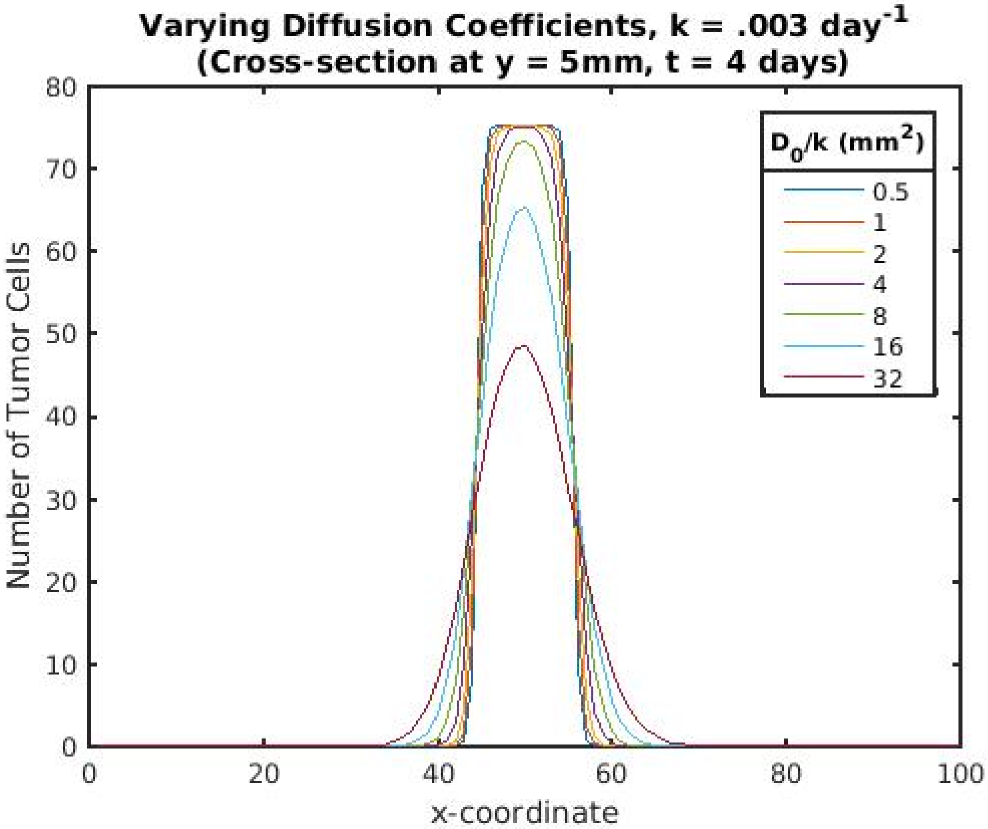
$$\max(D) = \frac{D_0}{2}\left(\frac{100}{100} + \frac{100}{100}\right) = .05$$

Therefore, assuming the step size is equal in both directions, $\Delta x = \Delta y$, for $\Delta t = .11$,

$$\boxed{\Delta x > \sqrt{4\Delta t D} = .148}$$



3c) With a small time step ($\Delta t = .01$), and small proliferation constant ($k = .003$), it can be seen that larger diffusion coefficients cause the cells to disperse outward towards areas of lower concentration, leading to cross-sections that are shorter but wider. Biologically, this indicates greater movement of the cells due to chemotaxis or haptotaxis.



3d) With a large proliferation coefficient ($k = 2.5$), small time step ($\Delta t = .01$), and moderate diffusion coefficient (.05), the tumor both spreads out and grows rapidly. The number of cells changes by around 1,300%, from 9075 cells to 118,250.

Additionally, the plot shows that there is a slightly greater increase towards the right, which can be explained by the larger diffusion coefficients. Biologically, this could be caused by the location of the tumor with respect to vasculature, since access to more nutrients would enhance growth, or by chemotaxis or haptotaxis as mentioned above.