Comparison of Numerical Methods for Analysis of the Diffusion of Soluble Proteins Through Sensory Cilia

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Introduction

Cilia serve many essential physiological functions, including vision, hearing, olfaction, and mechanosensation. It has long been hypothesized that proteins are transported into and out of the cilia by means of motorized intraflagellar transport (IFT) because the ciliary axoneme imposes selective barriers to the passive diffusion of these proteins. Recent work[1], however, has shown that there is no major barrier to the diffusion of proteins within the retinal rod photoreceptor cells of live *Xenopus*. Instead, the data collected by confocal microscopy match a mathematical model of the free diffusion of the proteins, suggesting that active IFT is not the cause of protein movement into and out of primary cilia.

In this project, the numerical work of Calvert et. al.[1] was studied and compared to a new numerical approximation known as the sinc collocation method.

The Numerical Model

The concentration of protein in a rod cell may be written as

$$\frac{\partial c}{\partial z} = D\nabla^2 c - Q_s \,,$$

where D is the diffusivity of the protein and Q_s is the source term. Rewriting this equation in cylindrical coordinates and assuming uniform diffusion in the angular direction and much faster diffusion in the radial direction that in the axial direction gives

$$\frac{\partial c}{dt} = \frac{1}{A(z)}\frac{\partial}{\partial z}\left[A(z)D(z)\frac{\partial c}{\partial z}\right].$$

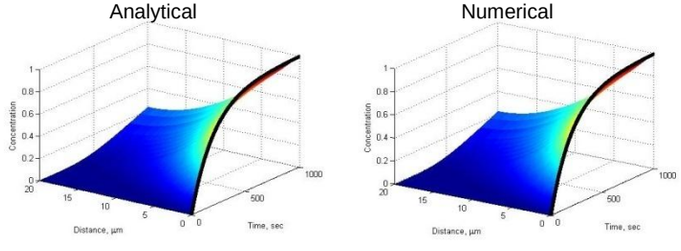
The initial concentration is assumed to be zero, no diffusion is allowed at the edges of the rod, and the concentration at the $z = 0$ boundary is assumed to be a time-dependent concentration, i.e.

$$\left.\frac{\partial c}{dz}\right|_{z=L} = 0, c(z=0,t) = f(t)$$

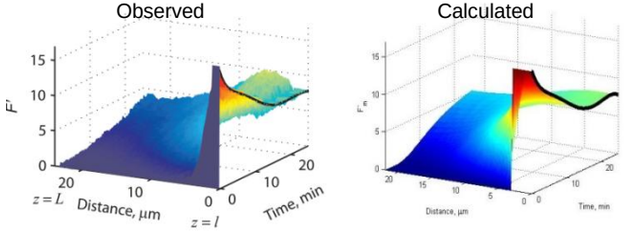
$$c(z, t=0) = 0\,.$$

The Method of Lines

Using the method of lines[2,3] (MOL) to solve the diffusive equation, the derivatives in the axial direction are discretized in the normal finite difference manner, then the concentration of the protein is found by numerically integrating the linear system. By assuming $f(t) = 1 - e^{-kt}$ and constant $A(z)$ and $D(z)$, an exact solution can be found and compared to the numerical model to validate the MOL approach.



With the method validated, the approximated solution can be compared with the data:



The Sinc Collocation Method

The sinc collocation method[4] (SCM) involves discretizing the time derivatives, then approximating the spatial derivatives using the approximation

$$c^{(i)}(z) = \sum_{j=0}^{N} c_j^i S_j(z)$$

for the concentration at the i[th] step, where

$$S_j(z) = sinc\left(\frac{z - jh}{h}\right)$$

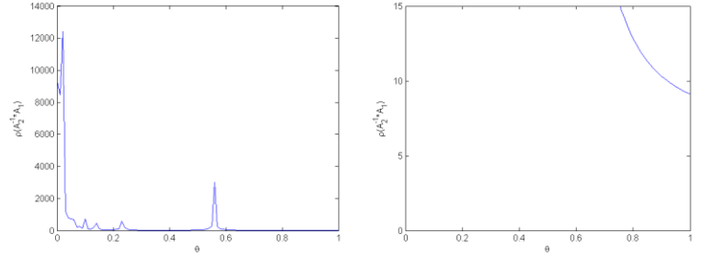
and h is the spatial grid size. By evaluating this equation at each of the spatial grid points, the dynamics of the system can be approximated by solving the linear system of equations,

$$A_2 c^{i+1} = A_1 c^i$$

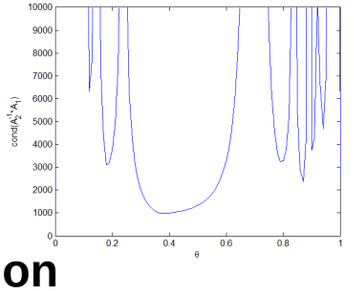
at each time step. The SCM approach converges, however, if and only if the spectral radius of the iteration matrix is less that unity, i.e.

$$\rho(A_2^{-1}A_1) \leq 1.$$

It can be seen, however, that this condition is never satisfied.



Similar analysis using the condition number of the iteration matrix confirms that the matrix is ill-conditioned.



Conclusion

The MOL approach used by Calvert et. al. was remarkably successful in reproducing the empirical results, but SCM failed to produce a well-conditioned iterative process.

Thanks to William Schiesser for assistance in this work.

References

[1]Calvert et. al, J. Gen. Physiol. Vol. 135 No. 3 173-196
[2]Schiesser, W.E. The numerical method of lines: integration of partial differential equations. Elsevier Academic Press, 1991.
[4]Schiesser, W.E. and G.W. Griffiths. A Compendium of Partial Differential Equation Models: Method of Lines Analysis. Cambridge UP, 2009.
[3]Mokhtari, Rezi and Maryam Mohammadi. Comp. Phys. Comm. 181 (2010), 1266-1274.