Summary

• Contraction of intestinal smooth muscle cells (ISMCs) is a complex process, involving the enteric nerve system, membrane channels, and actin-myosin interactions.
• Motivating factor is to study ileus, decrease in ISMC contractility. Ileus correlates with edema, accumulation of interstitial fluid, but link remains unknown.
• Hypothesis: increased synapse size dilutes neurotransmitters, decreasing contraction response, causing ileus.
• Comprehensive model from enervation to contraction supports to causation relation between edema and ileus.
• Model successfully replicates data from animal studies.

Biochemical Reactions (Contd.)

• IP3 pathway allows Ach to alter membrane potential, which alters Ca\(^{2+}\) concentration. This in turn affects Actin-Myosin phosphorylation. These chemical reactions were modeled using nonlinear ODEs and solved using RK4.

Physical Model

• Cell membrane, cytoskeleton, actin-myosin fibers, and cellular fluid drag modeled using two dimensional Hookean spring system.
• Newton’s Law ODE system solved using RK4.
• Figures below show ISMC contraction for two cases, cleft width is 20 nm on left, 40 nm on right. Figures on the right model edematous conditions with decreased contractility.

Results

• Increased synaptic cleft distance resulted in lower Ach and Ca\(^{2+}\) concentrations and decreased force generation and contraction.
• Unexpected sharp decline past cleft width of 40 nm.
• Results match data from Texas Medical Center study of contraction in edematous intestinal muscle cells in rats.

Conclusion

• Increased synaptic cleft distance results in lower ISMC contractility.
• Comprehensive model successfully replicates edematous and non-edematous conditions in ISMCs, matching data from animal studies.
• Model supports causation relation between ileus and edema.
• Unexpected contractility threshold between 40-50 nm will be subject of future work.

References


*This study was supported by NSF grant: DMS 0739420.