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## A Comprehensive Framework for Modeling Intestinal Smooth Muscle Cell Contraction with Applications to Intestinal Edema

The contraction of intestinal smooth muscle cells (ISMCs) is a complex process, involving many chemical reactions and mechanical triggers working to produce the contraction-relaxation cycle. Due to its complexity, it is difficult to isolate the effect of one factor on the overall process. Mathematical modeling allows one to test various combinations of parameters and structural geometries to assess their effects on the process. Here we present a comprehensive mathematical model of the contraction of an ISMC from its initial innervation by the neurotransmitter acetylcholine to the final mechanical contraction. To the best of the authors′ knowledge, this is the first framework of its kind to model the phenomenon from innervation to mechanical contraction, incorporating both chemical and physical models.

A motivating factor for developing such a model is to understand the effects of intestinal edema on ISMC contractility. Intestinal edema refers to the excess accumulation of fluid in the interstitial spaces between tissue cells of the intestinal wall. Intestinal edema often leads to ileus, a decrease in intestinal transit due to a decrease in ISMC contractility. The link between edema and ileus is unknown and is the subject of current experimental research. One hypothesis is that the increase in fluid volume creates larger neuromuscular junction distances over which neurotransmitters must diffuse, diluting their transmission, consequently leading to reduced contractility. We tested this hypothesis with the outlined model. It was found that neurotransmitter release over larger volumes resulted in lower force generation and markedly smaller ISMC contractions. These results suggest that increased distance across the neuromuscular junctions in intestinal edema is able to explain the development of ileus in such patients, lending credence to the current hypothesis.