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BIOPHYSICAL MODELING OF AN ENTIRE STOMACH: ARE WE MISSING SOMETHING?

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BACKGROUND: The stomach exhibits a characteristic slow wave of contraction. Slow waves originate from dominant pacemaker cells within the stomach wall along the greater curvature in the mid-corpus and spread aborally through the antrum to the pyloric sphincter. Disruption of the slow wave is supposed to play an active role in slowing down gastric motility. To better understand the mechanisms underlying slow wave anomalies, biophysical modeling of an entire functional stomach seems necessary. Despite different groups' effort to mathematically model slow wave in the stomach [1, 2], the comparison between model results and experimental data collected from animal models are rare. This study endeavors to fill this gap while simultaneously raising an important question regarding stomach network connectivity.

METHODS: We have computationally modeled the slow waves as being generated by a chain of interconnected biophysical circuits of networks of cells. This biophysical circuit consists of interstitial cells of Cajal (ICC) and smooth muscle (SM) cells (Fig. 1). The ICC have been modeled with a frequency gradient with the rostral most cell having the highest frequency and caudal most cell having the lowest frequency. In our initial model based on Peng Du's work [2], ICC were electrically connected to each other through gap junctions and each SM cell was electrically connected to an ICC cell. Gap junction studies in different biological systems suggest that Calcium (Ca^{2+}) and Inositol trisphosphate (IP_3) traverse between neighboring cells due to their concentration gradient [3, 4]. Therefore, in our updated model, we introduced chemical coupling by adding Ca^{2+} and IP_3 transport between neighboring ICC along with the existing electrical coupling.

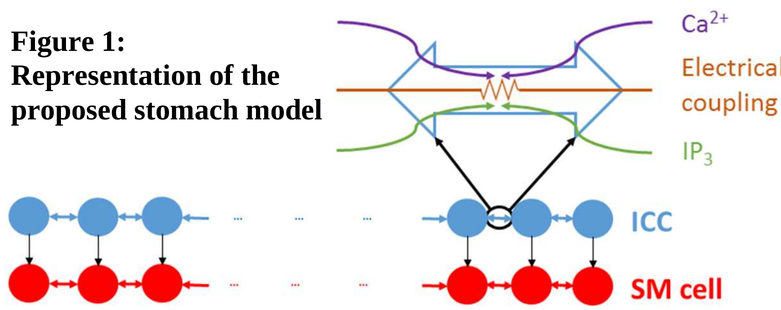

Figure 1: Representation of the proposed stomach model

RESULTS: The initial model (only electrical coupling between neighboring ICC) starts to lose entrainment beyond a certain length (in our case, after 20 unit cells, where each unit is composed of one ICC and one SM cell). However, an intact stomach exhibits a uniform frequency throughout its length from the mid-corpus to the distal antrum. In the updated model (both electrical and chemical coupling between neighboring ICC), the first and last SM cell of the network have a constant phase delay in steady-state indicating entrainment, and the ICC and SM cells are in phase. The simulation results qualitatively match the experimental recordings from the lower-mid corpus to the proximal antrum of the cat [5].

CONCLUSIONS: The updated stomach model reliably reproduces entrainment from animal experimental data. The results suggest that, mere electrical coupling is not sufficient for creating entrainment along the entire length of the stomach. Ca^{2+} and IP_3 transport may play an important role in coordinating the activity that drives gastric motility.

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