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REPLY

Power comes from technical fidelity, not from ease of use

Kenton M. Sanders, Sean M. Ward and Grant W. Hennig

With regard to our Perspectives article (Problems with extracellular recording of electrical activity in gastrointestinal muscle. *Nat. Rev. Gastroenterol. Hepatol.* **13**, 731–741; 2016)[1], we would like to thank Jan Huizinga for his correspondence (The powerful advantages of extracellular electrical recording. *Nat. Rev. Gastroenterol. Hepatol.* http://dx.doi.org/10.1038/nrgastro.2017.16)[2]. Professor Huizinga is correct in stating that having techniques to monitor electrical activity in whole gastrointestinal organs would be advantageous for understanding the physiology of this complex system[2]. This understanding was likely the motivation for applying techniques developed for heart and skeletal muscles to smooth muscle organs. However, although a simple technique like extracellular recording would have its advantages, performing experiments with spurious outcomes is a waste of time. Huizinga is correct in stating that movement is a well-recognized contaminant of electromyography, but unfortunately most studies applying extracellular recording to visceral smooth muscle tissues have neglected important control experiments to adequately evaluate how movements contribute to the signals believed to be electrophysiological.

Huizinga reminds us that people familiar with extracellular recording know that poor electrode placement can obscure the ability to record biopotentials, however, in our recordings (see figure 3)[1], of which he appears critical, the electrodes were not moved from the time biopotentials were first recorded until contractions were inhibited and the biopotentials disappeared. Could a good spot have become a bad spot? We wonder why there are places on the muscle surface that are considered inappropriate for electrodes. When recording from smooth muscle cells with intracellular microelectrodes in phasic regions of gastrointestinal organs, slow waves are present in every cell because these events conduct through the syncytium from interstitial cells of Cajal (ICC). Could sites of poor electrode placement reflect regions of mechanical quiescence from which biopotentials, therefore, cannot be recorded?

Huizinga cites experiments by Lammers *et al.*[3] to exemplify the advantages of extracellular recording; however, the experiment chosen is puzzling. All along the small intestine, ICC have intrinsic pacemaker activity, and slow waves propagate isotropically at 1–5 mm/s within the ICC network[4]. Like all propagating electrophysiological events, a refractory period follows repolarization of slow waves and, therefore, these events obliterate each other when they collide. In the cat intestine used by Lammers *et al.*[3], slow waves occur at 10–15 cycles per minute and are 2–4 s in duration[5]. Once initiated, a slow wave can propagate only ~2 cm before encountering slow waves originating from distal or proximal pacemaker sites. How can such a system generate long distance coherent propagation? Lines can be drawn from one propagation event to another (see arrows in figure 1)[2], but these lines are speculation about propagation, not proof. Besides, according to some authors, Lammers' recordings might be devoid of authentic slow waves[6], as low cutoff filtering and a bandpass window of 2–400 Hz were used[3].

Observing similar patterns of activity (such as waxing and waning) with intracellular and extracellular recording[7] is no reason to assume these activities share a common mechanism. Waxing and waning of membrane potential might produce a similar contractile pattern. The pattern of slow waves recorded with intracellular techniques might generate biopotentials of a similar pattern due to the contractions evoked by slow waves because, as Huizinga admits[2], extracellular recording is prone to movement artefacts and, as we suggested[1], rigorous controls are necessary to validate extracellular recordings.

Kenton M. Sanders and Sean M. Ward are at the Department of Physiology and Cell Biology, University of Nevada, Reno School of Medicine, Reno, Nevada 89557, USA.

Grant W. Hennig is at the Department of Pharmacology, University of Vermont, College of Medicine, 89 Beaumont Avenue, Burlington, Vermont 05405, USA.

Correspondence to K.M.S.
ksanders@medicine.nevada.edu

doi:10.1038/nrgastro.2017.40
Published online 30 Mar 2017

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Competing interests statement
The authors declare no competing interests.