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REPLY

Extracellular gastrointestinal electrical recordings: movement not electrophysiology

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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 O'Grady *et al.* for their correspondence (Correct techniques for extracellular recordings of electrical activity in gastrointestinal muscles. *Nat. Rev. Gastroenterol. Hepatol.* http://dx.doi.org/10.1038/nrgastro.2017.15)[2]. O'Grady and colleagues have strenuously defended performing extracellular electrical recording from gastrointestinal muscles, but their arguments sidestep the need for rigorous controls to validate their data. In their rebuttal[2] to our Perspectives article[1], the authors describe *in vitro* gastrointestinal tissue preparations as 'devitalized', a word defined by medical dictionaries as devoid of life or dead[3]. In our opinion, their premise that isolated gastrointestinal muscle preparations lose the ability to generate or conduct propagating slow waves is false, as tissues and cells maintained in media or physiological buffers are vital and robust for long periods after removal from their donors[1].

The major event possibly resolved by extracellular recording is the upstroke phase of the slow wave, analogous to the QRS complex of the cardiac action potential. Figure 1 of the O'Grady *et al.*[2] Correspondence demonstrates the kinetic mismatch between their extracellular recordings and slow waves recorded from interstitial cells of Cajal in intact muscles. The biphasic event they claim as a slow wave (figure 1e)[2] has a duration of at least 2 s, but the slow wave upstroke is about 100 ms in duration. How can the authors explain this 10–20 fold discrepancy in kinetics? As we explained in our Perspectives article[1], the leisurely biphasic event seen in this figure probably represents a contractile response, which has far slower kinetics than the electrophysiological events that initiate the contractions. O'Grady and colleagues argue that extracellular electrical recordings are only able to resolve slow waves when a substantial area of the tissue is undergoing a depolarization (wave front), also requiring the wave front to propagate to detect a dynamic charge imbalance across the extracellular electrodes[2]. By their own admission, this mode of recording would preclude many aberrant slow-wave behaviours, such as frequency changes (faster frequencies might result in smaller amplitude slow waves), multiple ectopic pacing sites and short propagating events.

Our arguments about appropriate filtering to capture events that might be slow wave upstrokes were ignored. O'Grady *et al.*[2] show that a filtering window (3–100 Hz), which would be appropriate for recording the frequency response of slow-wave upstrokes (1–3 Vs^{-1}), completely filters out their data (figure 2)[2]. If the signals are not genuine slow waves but instead result from movements, as the kinetics of the events imply, then selecting filtering parameters that preserve their signals but radically attenuate slow waves seems inappropriate. For extracellular electrical recording to be credible, rigorous control experiments are needed to validate this technique in visceral smooth muscle tissues. At present,our findings and analyses council scepticism.

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Competing interests statement
The authors declare no competing interests.