Conformal Electrode Arrays to enable in vivo Recordings of the Enteric Nervous System

Melanie Ecker, Edgar Guerrero, Pedro Emanuel Rocha Flores, and Walter E. Voit
The University of Texas at Dallas, Richardson, TX 75080.

Statement of Purpose: The enteric nervous system (ENS) has the largest population of neurons in the peripheral nervous system, but it is not well understood and is less investigated than the central nervous system. Most of the information on the function and electrophysiology of the ENS was collected *ex vivo*, either on pathological samples or in cell cultures. Major problems when attaching neural electrodes to the gut, *e.g.* the small intestine, are that the tissue is of soft muscle, the geometry and its surface topology are complex, and it is constantly moving. Thus, conventional stiff electrodes and nerve cuffs cannot conform to the gut surface and are susceptible to motion artifacts since they will be moving relative to the bowel. Here, we demonstrate that the problems caused by conventional, stiff electrodes can be solved with the use of a thin-film electrode array fabricated on a self-softening polymeric substrate material. The hypothesis is that the polymer is capable of softening and changing its shape, so that the device can adapt to the shape and surface topology of its surroundings. It will wrap tightly around the gut, securing the electrodes in place to enable continuous periodic *in vivo* recordings of neurons from the myenteric and submucosal plexus within the small intestine.

Methods: Self-softening thiol-ene polymers have been used as substrate for blanket-type surface electrode arrays. The thin-film devices with titanium nitride (TiN) electrode sites were fabricated using microfabrication methods including photolithography and reactive surface etching. The electrodes were characterized *in vitro* by means of electrochemical methods including electrochemical impedance spectroscopy (EIS) and cyclic voltammetry (CV). Acute differential recordings from the mouse gut have been performed to demonstrate the feasibility of the novel device technology. Signal-to-noise ratio, firing rate and waveform quality have been evaluated and the device integration and its ability to adapt the gut topography were investigated.

Results: We have successfully demonstrated that electrode arrays composed of a softening polymer can conform to the complex geometry of the gut and that they have the capability to record extracellular biopotentials corresponding to the physiological response from the gut.

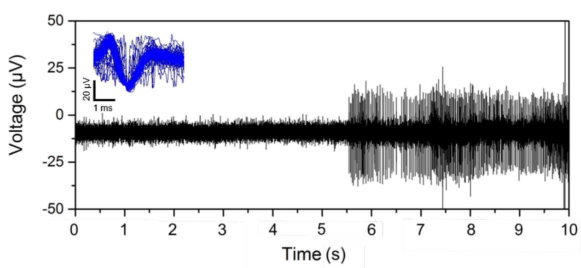

Figure 1: Data from continuous differential recordings from a conformal electrode array and representative waveform (inset)

Yet, it is still unclear whether these signals came from motor or sensory neurons or even muscle activity. Next steps will include extensive studies of the electrical signals to evaluate their origin and to get a better understanding of the electrophysiology of the healthy gut. Therefore, various stimulants including capsaicin, serotonin and acetylcholine will be used to evoke signals from different origins, such as neural or muscle activity. Signal-to-noise ratio, firing rate and waveform quality will be compared among different stimulants to evaluate electrophysiological changes.

Conclusions: We have demonstrated that conformal electrode arrays have the potential to serve as a technology platform for *in vivo* recordings of the ENS. Future research will focus on the interpretation of physiological signals of healthy and diseased animals to get a better understanding how dysfunctions of enteric nerves are related to gastrointestinal (GI) disorders. This could help to improve the lives of millions of people suffering from irritable bowel syndrome and other GI disorders, such as such as inflammatory bowel disease including ulcerative colitis and Crohn's disease.

Acknowledgements: The authors want to thank Dr. Xiling Shen and Bradley Barth from Duke University for their time and effort to perform initial studies on prototype electrodes that have led the foundation for this research project.