Mechanically-dynamic polymer nanocomposites for intracortical microelectrode substrates

Jeffrey R. Capadona,[1,2,3] Kadhiravan Shanmuganathan,[2] James P. Harris,[1,3] Dustin J. Tyler,[1,3] Stuart J. Rowan,[1,2,3,4] and Christoph Weder[1,2,4]

[1]Rehabilitation Research and Development, Louis Stokes Cleveland DVA Medical Center, [2]Department of Macromolecular Science and Engineering, Case Western Reserve University, [3]Department of Biomedical Engineering, CWRU, [4]Department of Chemistry, CWRU

Statement of Purpose: Chronically implanted intracortical microelectrodes promise to make profound impacts as solutions for patients suffering from neurological diseases, limb amputation, or full or partial paralysis as a result of spinal cord injury.[1] Even though intracortical electrodes can record the activity of individual or small populations of neurons,[2] within a few months, the signal quality of current microelectrodes usually degrades making chronic applications challenging.[3] One hypothesis for the cause of possible failure is that, while a high modulus electrode is advantageous during insertion,[4] the micro-motion of rigid electrodes within the soft cortical tissue chronically inflicts trauma on the surrounding neurons.[5]

The objective of this research is to design stimulus-responsive, mechanically-dynamic polymer nanocomposites for the use as intracortical microelectrodes which offer both a rigid phase for ease of insertion, and a mechanically compliant phase to address chronic mechanical mismatch related limitations.

Methods: All materials and reagents were used as received. The ethylene oxide/epichlorohydrin copolymer (EO-EPI copolymer, co-monomer ratio = 1:1) was received from Daiso Co. Ltd. (Osaka, Japan). Polyvinyl acetate (M_w = 113,000g/mol) was purchased from Aldrich Chemicals (Milwaukee, WI). Tunicates (*Styela clava*) were collected from floating docks in Point View Marina (Narragansett, RI). Cellulose whiskers[6] and whisker nanocomposites[7] were prepared as previously described. Briefly, lyophilized whiskers were dispersed in dimethyl formamide (DMF) at a concentration 5 mg/mL. The EO-EPI copolymer or PVAc polymer was dissolved in DMF (5% w/w) by stirring for two days. Nanocomposites were prepared by combining the desired amounts (to yield materials containing 0.8% - 19% v/v whiskers). Solution-casts of the resulting homogeneous mixtures were dried under vacuum and compression-molded into thin films. Mechanical properties were determined with DMTA under appropriate environmental conditions to assess mechanical switching.

Results: We have demonstrated that materials based on a rubbery EO-EPI copolymer and rigid cellulose nanofibers display a percolating network of fibers within the polymer matrix (**Fig. 1**). The tensile modulus of these materials increases with increasing density of

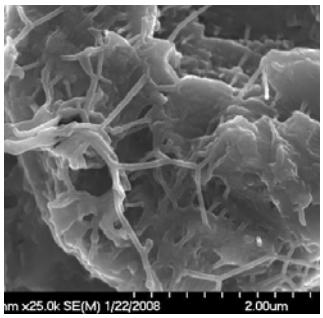

Fig 1. SEM of percolating network c fibers within the matrix.

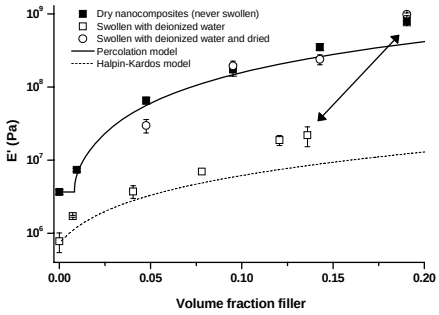

Fig. 2

incorporated percolating nanofibers (**Fig. 2**), following classical models for material reinforcement.[7,8] Non-covalent interactions between percolating fiber networks within the polymer nanocomposite mediate this robust reinforcement.

The reinforcing cellulose network can be dynamically controlled upon exposure to a chemical regulator of fiber-fiber interactions. For example, these same nanocomposites exhibit a reversible, 40-fold reduction of the tensile modulus upon exposure to aqueous conditions (**Fig. 2**). Using a second host polymer (PVAc) with a thermal transition in the regime of interest, we demonstrated even larger modulus changes (4200 to 1.6 MPa) upon exposure to emulated physiological conditions.

Initial *in vivo* evaluation of these materials has demonstrated a decrease in the biochemical markers known to lead to local neuron death, early indicators for device failure. Additionally, the chemo-responsive mechanically-dynamic nanocomposites have been fabricated into single and double shank microelectrodes, and we have been able to record single unit action potentials from individual neurons in acute *in vivo* models.

Conclusions: These materials represent a new class of bio-inspired polymers which have demonstrated acute feasibility as substrates for intracortical microelectrodes. We are currently investigating chronic biological compatibility and device lifetimes in a rodent intracortical model, as well as exploring additional biomedical applications for this new class of dynamic materials.

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