

symptom of Parkinson's disease, but the increased reaction time (the delay in the sensory feedback control) can make it difficult for patients to perform their basic tasks. Biomechanical models with feedback control theory can not only provide diagnostic tools to measure the delay from the nature of tremor, but can also provide a quantitative understanding of how the delay results in other advanced-stage biomechanical symptoms such as stooping. A mechanics-based perspective on how the tremor results from the delay has recently been proposed in [J. Mech. Med. Biol., Vol. 11(5), pp.1017]. We extended the same perspective to develop a proof-of-concept smartphone App for measuring the severity of the disease in terms of the delay from the tremor. We are also developing mechanical models of human body with neural control based on the same perspective to simulate and analyze other biomechanical symptoms of the disease. We expect that such models will provide a novel foundation for improved diagnosis, prognosis, and safer symptomatic treatment strategies.

4010-Pos Board B738

Memristor Neural Model for Alzheimer Disease

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Alzheimer disease is characterized by the formation of a pathological protein agglomerations in the correspondence of the synapses that determine a modification in the conductive signal. With the most recent theory, based on Memristive elements, it has been possible to describe some conductive issues in the neurons not well explained since the Hodgkin and Huxley model. Considering the current's flux as the causing factor of post behavior of the neurons (according to Chua's definition), it is now possible for analyses of some aspects that can give important details in the memory's mechanism of the neurons. Here we report the evidence and the analysis that confirm, or not, Memristor's model, and an accurate characterization of the conductivity in healthy and pathological neurons. All the result received a rigorous electrical approach: DC V-I curves, small-signal admittance, small-signal impedance, pole-zero diagrams, frequency response, Nyquist diagram. We believe that this work will be extremely important for the future develop of new drugs, capable of reestablishing a correct conductivity through the neurons in patients affected by Alzheimer disease.

4011-Pos Board B739

Development of Modularity in the Neural Activity of Children'S Brains

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We discuss how the cognitive ability of the human brain depends on modularity of neural activity. Modularity is a measure of the degree of correlation in the neural activity within different brain regions, and a modular organization of neural activity can facilitate more rapid cognitive function. Modularity enhances cognitive responses because it is easier and faster to rewire connections within the modules than within the entire network. On the other hand, modularity may restrict possible cognitive function at long time scales, because a modular neural architecture is a subset of all possible architectures. Here we studied modularity of neural activity networks in the human brain. We extracted the brain networks from functional magnetic resonance imaging in children and adults under resting conditions. We observed that the value of modularity increases during childhood development and peaks in young adulthood. We discuss interpretation of these results as selection for plasticity in the cognitive function of the human brain. We also describe a model to illustrate how modularity affects cognitive performance at short and long times. Finally, we suggest that modularity can serve as a potential biomarker for injury, rehabilitation, or disease.

4012-Pos Board B740

Feature Detection and Orientation Tuning in the Drosophila Central Brain

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Many animals, including insects, use visual landmarks for orientation and navigation. In *Drosophila melanogaster*, behavioral genetics studies have identified the central complex as being required for innate attraction to particular visual features, and for short- and long-term memory for visual patterns. Studies in several insects suggest that the region is also important for motor coordination. Here we present an analysis of the first physiological recordings from this region in *Drosophila*. We focused on neurons implicated in orientation and place memory in the fly: ring neurons of the ellipsoid body, a sub-region of the central complex. We show [1] that each ring neuron sends dendrites to a single microglomerulus in the lateral triangle (LTr), a multi-glomerular brain region that is a major source of

input to the ellipsoid body. We studied the responses of complete populations of ring neuron classes using two-photon calcium imaging in head-fixed flies that were flying or walking on an air-supported ball in an LED arena. LTr microglomeruli show retinotopically organized receptive fields (RF) that are tuned to specific orientations and features with excitatory and inhibitory subfields. LTr responses to visual stimuli are diminished during flight, but are not significantly modulated during walking. A simple linear model based on LTr responses recorded during closed-loop flight behavior, is sufficient to compute the fly's heading relative to visual features in its surroundings. We suggest that ring neurons may provide the visual pattern information necessary for a variety of orienting and navigation behaviors in the fly. Our results provide the first evidence for retinotopic maps in higher brain structures in *Drosophila*, and set the stage for mechanistic studies of sensorimotor integration underlying visually-guided decision-making in this genetic model organism.

[1] Seelig J.D. and Jayaraman, V., Nature, 2013, in press.

4013-Pos Board B741

Prestin Lateral Mobility and Self-Association in Outer Hair Cells

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Prestin belongs to the SLC26 protein family, which regroups anion antiporters capable of transporting monovalent and divalent anions across biological membranes. Also referred to as SLC26A5, prestin is a motor protein essential for the electromotility of the outer hair-cells (OHC) and therefore the amplification of sound in the cochlea. The diffusion of prestin in the membrane has been previously studied through fluorescent recovery after photobleaching (FRAP) experiments, in HEK293 cells. We were able to determine that up to 50% of the prestin population was immotile. This suggest that intermolecular interactions between prestin, the membrane and the cytoskeleton are essential for prestin organization and function. We have created transgenic mouse lines co-expressing prestin-TFP and prestin-YFP. OHCs isolated from these mice have prestin-induced non linear capacitance (NLC) and electromotility comparable to wild-type mice.

FRAP analysis on prestin-YFP indicated that in OHCs, the entire prestin population is immotile. This motility was partially recovered by inhibition of the actin filament polymerization. Fluorescent resonance energy transfer (FRET) coupled to fluorescence lifetime imaging microscopy (FLIM) allowed us to detect and monitor the prestin-prestin interactions at the nanometer scale. These FLIM-FRET experiments revealed a FRET efficiency of 25-35%.

The FRAP experiments suggest a strong interaction of prestin with other membrane proteins or the cytoskeleton, and the high FRET efficiency will allow for prestin-prestin interactions to be monitored during alterations of the membrane composition and potential.

Optical Microscopy and Super Resolution Imaging IV

4014-Pos Board B742

Measurement of the Point- and Line-Spread Functions Enables Deconvolution in Bright Field Light Microscopy

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Bright field is the simplest and most widespread light microscopy modality. However, its use in cellular biology has been limited due to lack of contrast in the imaging of thin, transparent samples such as cells. Instead, more involved microscopy techniques (e. g. differential interference contrast, dark field, phase contrast, among others) have been used. An alternative to increase image contrast is deconvolution processing, a powerful method often used in fluorescence microscopy. However, application of deconvolution processing to bright field images has been scarce, mainly because acquisition of the point-spread function (PSF) has been difficult. In this work, we present direct measurements of the point- and line-spread functions of a high-aperture microscope operating in bright field. Polystyrene nanoparticles of 100 nm in diameter and cytoskeletal microtubules serve as the point and line objects, respectively, that are imaged with high contrast and low noise using conventional microscopy plus digital image processing. To our knowledge, this is the first report that describes the experimental assessment of these functions. Our experimental results are in good agreement with a proposed model for both point- and line-spread functions. The measured PSF allows us to demonstrate conventional deconvolution on the bright field images of living, unstained