(SDPC)/cholesterol membrane, and 5HT to determine if binding of the ligand causes protein reassembly and channel opening.

3112-Pos Board B489
Key Differences in Molecular Transport Mechanisms of Uncoupling Proteins
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Mitochondrial membrane uncoupling protein 1 (UCP1) facilitates proton leak to support non-shivering thermogenesis in brown adipose tissue. The transport function of other UCPs is controversially discussed. It was proposed that in addition to protons, other substrates can be transported. Moreover, the molecular mechanism of UCP regulation is insufficiently understood, although it is generally accepted that its transport is regulated by free fatty acids (FFA) and purine nucleotides (PN). Here we tested the hypothesis that regulation differs between members of UCP family leading to differences in their functions [1]. We evaluated binding forces and the degree of inhibition by PNs, comparing the data obtained using recognition force microscopy and electrophysiological measurements of recombinant proteins reconstituted in planar bilayer membranes [2]. We reveal that, in contrast to UCP1, other UCPs can be fully inhibited by all PNs, as KD increases with a decrease in phosphorylation. Furthermore, three arginines (R84, R183, R277) in the PN-binding pocket are involved in UCP1 inhibition to different extents. This result disagrees with previously proposed mechanisms, suggesting that only R277 is responsible for 100% inhibition. Moreover, FFAs can compete with all PNs bound to UCP1, but only with triphosphate-PNs bound to UCP3. Our results demonstrate the different regulation across a family of highly homologous uncoupling proteins, which, in the case of UCP1 and UCP3, are even expressed in the same tissue. We anticipate that the differences in the molecular mechanism of UCPs can be useful in understanding their physiological functions.
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3113-Pos Board B490
Water Pathway Analysis of Multi-Drug Efflux Transporter AcrB
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The multi-drug efflux transporter AcrB exists in the inner membrane region of E. coli., and exports wide variety of noxious compounds using proton motive force as an energy source in Gram-negative bacteria. From the results of x-ray crystallography, the followings were found: (1) AcrB adopts asymmetric structure comprising three protomers with different structures, which correspond to access (A), binding (B) and extrusion (E) state of drugs, (2) three titratable residues (Asp407, Asp408 and Lys940), which locate in the middle of the transmembrane domain, form the protonation site (PS), and the Lys940 in E state adopts the different conformation from those of other states. These results suggest that AcrB exports drugs through the cyclic structural change among three states by using proton motive force generated by the change of protonation state in PS, which are called ''functional rotation''.
We have studied the functional rotation mechanism of AcrB by using the Motion-tree method, which is a new procedure to describe the structural change as rigid body motions with a hierarchal manner. Our results have elucidated how convert the proton motive force generated from PS to the large structural change of AcrB.
In the present study, to clarify the proton transfer process in the transmembrane domain, we searched the water pathways from the PS by using CAVER and 3D-RISM methods.
As the results from CAVER method, A and B state protomers observed pathways from the PS to the periplasm side, and E state protomer observed a pathway from PS to the cytoplasm side. In addition, the results of 3D-RISM method suggest that B and E state pathways have an ability to permeate water molecules. These results were consistent with the protonation states of each protomers estimated from structural change process from Motion-tree method.

Computational Neuroscience

3114-Pos Board B491
Modeling the Oscillating Dipole Properties of Electric Organ Discharge in the Weakly Electric Fish, Eigenmannia
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One of the most studied weakly electric fish, Eigenmannia produces a continuous high frequency electric organ discharge (EOD) used to sense nearby objects and communicate with conspecifics. The EOD of an individual fish has a characteristic frequency (within the species range, 250-600 Hz) which it shifts when necessary to avoid jamming. The nearly dipolar oscillating electric field yields zero net current and is generated by parallel columns of identical, synchronously discharging electrocyte cells. Recent findings from whole fish respirometry (during high-frequency signaling over a range of frequencies) have renewed interest in the frequency-dependent energetics of the EODs (Lewis et al 2014 J Neurosci 34:197) but the modeling based on past analyses is missing some key features of the in-vivo electrolyte operation. We have constructed a model for the neurally-driven electrocyte action potentials (APs) that underlie the EOD. APs are initiated by brief postsynaptic cation influxes through AChR channels at each electrocyte's innervated posterior end. This yields a head positive current while the anterior end serves mainly as a capacitor whose discharge yields the head negative current of the oscillating dipole cycle. To maintain the appropriate [Na]in and [K]out levels, Na/K-ATPase pumps run continuously. Modeling the activity of this ATP consuming protein gives us access to electrocyte energetics and frequency-dependent EOD efficiency. Modeling the posterior-anterior current flows gives us access to the electric field patterns produced by the electrocytes.

3115-Pos Board B492
Resonances and Spectral Characteristics of a Neural Network for the Song Motor Pathway in Birds
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Birdsong is a complex learned behavior regulated in an intricate way. Neuromuscular coordination of different muscular sets is necessary for producing high quality and consistent songs. We developed a realistic neural network that emulates neurons from the High Vocal centre (HVc) and the robust nucleus of the archistriatum (RA) neurons that drive the muscles to generate birdsong sounds. We used modern computational tools and neural architecture to simulate the entire motor pathway up to the physical oscillator muscle system and its spectral characteristics. Several network parameter dependences were analysed and elucidated. An optimal network size within 10 to 25 neurons within which minimal and smooth frequency variations occur, was found. Beyond that range we observe, instead, strong frequency dependence. Moreover, response frequency is influenced by the pathway input current; also in this case frequency response keeps smooth within a certain range of current, but shows interesting resonant values where negative peaks are observed. Resonant values are found in respect to the non-linear dissipation constant of the equation of motion for the bird's labial oscillation and also in respect of the network background noise level (stochastic resonance). This work demonstrate that is possible to achieve a realistic computational model for the motor pathway leading to generation of sounds in birds, which contributes to the understanding of its spectral and dynamical fundamental properties and characteristics.

3116-Pos Board B493
Noise-Driven Synchronization of Coupled Neural Networks
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The brain is complex network of dynamical system. For this reason, the interaction between different brain areas can be modeled as a large-scale network which is important in functional brain dynamics, and it closely related to the brain disorder. In recent years, the significant progress about the understanding of the relation between the structure and dynamical properties of the networks has developed. It describes that the complex dynamic behavior such as synchronization of coupled dynamical system plays a crucial role in a brain function and dysfunction. In our simulations, we construct a coupled neural