hydrophilic molecules like small nutrient molecules and β-lactam antibiotics. However the CymA channel is known to take up cyclodextrin molecules giving bacteria the ability to survive on cyclodextrins. Hence understanding uptake of these molecules via porins is vital to comprehend the transport mechanism across the cell membrane. Electrophysiology forms a promising approach to study the permeation of molecules across outer membrane and thereby understanding molecular interactions with the channel. Here we present cyclodextrin interaction studies of CymA from *K. oxytoca* using single channel electrophysiology. Detailed single channel analysis revealed inherent asymmetric gating characteristics of the channel. Analysis of the ion current reduction through CymA in presence of cyclodextrin led revealed kinetic parameters of substrate binding. To further elucidate the affinity sites of substrate to the channel, mutation of certain channel residues has been performed. An altered channel gating behaviour is observed. To obtain an atomistic view we complement our studies with all-atom molecular dynamics simulation to study the various conductance states of the channel in the absence of cyclodextrin and to get molecular insight into the uptake of cyclodextrins as well.

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2227-Pos Board B364

Mimicking Biology with Nanomaterials: Carbon Nanotube Porins in Lipid Membranes

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Living systems control transport of ions or small molecules across biological membranes using ion channels that form highly efficient and selective pores in lipid bilayers. Although bottom-up synthesis and top-down fabrication could produce pores of comparable size, an unresolved challenge remains to build nanopore scaffolds that fully replicate transport properties of membrane channels. We will show that pores formed by ultra-short carbon nanotubes (CNTs) assembled in the lipid membranes have transport properties that come remarkably close to that goal. These CNT porins can transport water, protons, small ions, and DNA and their ion-rejection properties can be controlled by the charge at the pore mouth. Interestingly, these pores also display the stochastic ''gating'' behavior common for biological ion channels. Overall, CNT porins represent a simplified biomimetic system that is ideal for studying fundamentals of transport in biological channels, and for building engineered mesoscale structures, such as artificial cells.

2228-Pos Board B365

Understanding the Translocation of Fluoroquinolones through OmpC using the Metadynamics

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The outer membrane of Gram-negative bacteria such as Escherichia coli acts as a selective permeable barrier between cell and external environment. Water filled outer membrane proteins called as porins were identified for exchange of hydrophilic solutes and hydrophilic antibiotics. One of the most abundant outer membrane porins in E. coli is OmpC and many studies revealed that down-regulation or mutation of this porin shows reduced accumulation of antibacterials in bacterial cells [1]. Fluoroquinolones, used since 1980, are the most common treatment for urinary tract infection caused by E. coli and today this treatment is ineffective in more than half of the patients globally due to widespread resistance. So far the influx kinetics of fluoroquinolones with OmpC has been characterized on free standing lipid bilayers formed on a glass substrate [2]. In particular, detailed analysis of antibiotic interaction with a single OmpC channel using electrophysiology can provide a kinetic description. Here we have investigated two fluoroquinolones, Ciprofloxacin and Enrofloxacin, using an advanced molecular dynamics technique, i.e., metadynamics [3,4]. These free energy calculations help to identify the most favorable paths and activation energies required for molecules to translocate through the OmpC channel. Furthermore, we have also investigated the translocation of the same molecules in the presence of different salts to understand the altered translocation kinetics [5]. Moreover, the identification of favorable interactions networks is important to determine the most prominent residues required for translocation.

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2229-Pos Board B366

Single-Molecule Detection of Insertion and Folding of OmpA in Droplet Interface Bilayers

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The Outer Membrane Proteins of E. coli are a family of membrane-spanning beta-barrels which enable vital communication with the surrounding environment. The folding and insertion of OmpA into the membrane is the archetype for beta-barrel protein folding. Here we monitor the folding dynamics of OmpA into Droplet Interface Bilayers using single-molecule FRET. Energy transfer reports on the folded state of individual molecules imaged using TIRF microscopy. We explore the kinetics of initial binding and subsequent insertion into the bilayer.

Cardiac Muscle Mechanics and Structure II

2230-Pos Board B367

From Molecule to Organ: A Multiscale Simulator of Heart Contraction

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Single molecule techniques are more and more powerful in obtaining quantitative insights on muscle myosin properties, but to fully understand the physiological meaning of these properties they have to be considered in the macroscopic structure. We have included a detailed sarcomere model, which simulate thermal fluctuations of each myosin motor, into a three-dimensional simulator of the cardiac muscle (UT-Heart). Since the sarcomere model can quantitatively reproduce several single molecule and fiber experimental data, the final model is potentially able to observe how molecular diseases affect the whole organ function.

2231-Pos Board B368

Substrate Stiffness-Modulated Registry Phase Correlations in Cardiomyocytes Maps Structural Order to Coherent Beating

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Recent experiments show that both striation, an indication of the structural registry in muscle fibers, as well as the contractile strains produced by beating cardiac muscle cells can be optimized by substrate stiffness. We show theoretically how the substrate rigidity dependence of the registry data can be mapped onto that of the strain measurements. We express the elasticity-mediated structural registry as a phase order parameter using a statistical physics approach that takes the noise inherent in biological systems into account. By assuming that structurally registered myofibrils also tend to beat in phase, we explain the observed dependence of both striation and strain measurements of cardiomyocytes on substrate stiffness in a unified manner. The agreement of our ideas with experiment suggests that the correlated beating of heart cells may be limited by the structural registry of the myofibrils which in turn is regulated by their elastic environment.

2232-Pos Board B369

Regulation of Cardiomyocyte T-Tubule Organization and Density by Ventricular Wall Stress

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During heart failure development, t-tubules become disorganized which disrupts Ca^{2+} homeostasis and weakens contraction of the heart. The mechanisms controlling t-tubular structure in the normal and failing heart remain unknown, but accumulating data suggest that ventricular workload may be an important regulator. In Wistar rats which had developed heart failure 6 weeks following myocardial infarction, we observed that marked t-tubule disruption occurred preferentially in regions of the heart that are proximal to the infarct site, while t-tubule density was normal in distal locations. *In vivo* imaging by MRI has