media; this observation is supported experimentally and through modeling of the heat equation. Within the context of biological and medical applications, gold-coated liposomes may enable the spectral, spatial, and temporal control of release of multiple agents from liposome carriers by means of a physiologically safe light-delivery method.

**2554-Pos Board B540**

**Design and Modeling of RNA Nanostructures with Flexible Building Blocks**

**Wojciech K. Kasprzak**, Eckart Bindewald, Tae-Jin Kim,
Michael T. Zimmermann, Robert L. Jernigan, Bruce A. Shapiro.

The focus of our work is the development of automated methodology and computer tools for the design of nanostructures built of RNA. We started by creating the RNAJunction database, which stores RNA junctions, or structure fragments including internal, multi-branch and kissing-loops, with short helical stubs emanating from them. These structural elements are being used as building blocks in our nanostructure design methodology. Combined with idealized fragments of A-form helices, these structural elements can be used by our programs NanoTiler and RNA2D3D, as well as other tools, to create 3D nanostructure models. As the first approximation, the building blocks are treated as rigid objects. Considering that modeling based on rigid blocks may not always achieve the design objectives and that there is experimental evidence for the RNA structure shape adjustment to the constraints of larger structural contexts, we are including the analysis of the structural flexibility in the design and modeling process. Experimental structure variability data as well as computational structure dynamics can be used to that end. We show examples of modeling methods, which combine flexibility data for the junctions subjected to Molecular Dynamics (MD) simulations with the idealized helical linkers subjected to controlled distortions within the observed MD boundaries. We also show that a coarse-grained methodology based on the anisotropic elastic network modeling (ANM) holds promise of providing accurate structure flexibility information at a lower computational cost and for much larger structures that can be feasibly evaluated by MD.

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**2555-Pos Board B541**

**Molecular Dynamics Simulations of siRNA Bolaamphiphile Nanoparticle Complexes Suggest Their Potential as a Therapeutic siRNA Delivery Vehicle**

**Taejin Kim**, Eliahu Heldman, Robert Blumenthal, Bruce A. Shapiro.

In spite of the strong potential as a therapeutic, naked siRNA delivery in vivo has some problems that need to be overcome. siRNAs need to remain intact in the blood stream and they have to overcome the strong negative charges that are present on the phosphate groups of the RNA backbone when crossing biological membranes. These biological barriers can be surmounted by covering or encapsulating the siRNA with bolaamphiphiles. Bolaamphiphiles have two positively charged hydrophilic head groups connected by a hydrophobic chain and they can form stable monolayer membrane vesicles which can encapsulate water soluble anionic molecules. In addition, bolaamphiphiles have a relatively low toxicity level when compared to lipids and can persist in the blood for long time periods. This research involves the study of RNA shape-based and vesicle-based approaches for RNA-nanoparticle formation, with the ultimate goal of developing an siRNA delivery vehicle. In the shape-based approach, we utilize differently shaped siRNA scaffolds for RNA nanoparticle-bolaamphiphile complex formation. In the vesicle-based approach, siRNAs are encapsulated inside bolaamphiphile vesicles or bound to the vesicle surface. Our explicit solvent molecular dynamics (MD) simulation results show that bolaamphiphiles rapidly cover RNA duplexes due to the strong interaction between the cationic head groups in bolaamphiphiles and the negative charges on the phosphate groups of the RNA backbone. It is also observed that the bolaamphiphile head groups populate both the minor and major grooves and that once bolaamphiphiles associate with the RNA, the base G forms stable hydrogen bonds with the head groups of the bolaamphiphiles. Therefore, our research suggests that siRNA nanoparticle-bolaamphiphile complexes behave in such a way to be a strong candidate for the development of therapeutic siRNA nanoparticle delivery vehicles.

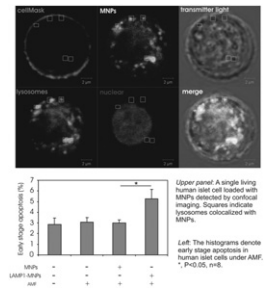
**2556-Pos Board B542**

**Alternating Magnetic Fields Trigger Apoptosis by Destruction of Lysosomes with LAMP1-Targeted Nanoparticles**

**Enming Zhang**, Erik Renström, Moritz Kircher, Martin Koch.

Magnetic nanoparticles (MNPs) can be shuffled into cells by external magnetic fields. The speed and frequency of MNP's movement in vivo can be modulated using alternating magnetic fields (AMF), which may provide the potential approach to selectively destroy cancer cells.

To this end, 100nm MNPs conjugated with antibodies against LAMP1, a lysosomal transmembrane protein, were loaded into human endocrine pancreatic islet cells. MNPs were detected by live imaging and immunostaining, demonstrating that MNPs rapidly enter cells through the endocytic pathway and target the lysosomal membrane. The loading efficiency of LAMP1-MNPs was $21.2 \pm 2.4\%$ which is significantly increased compared to non-targeted MNPs ($13.3 \pm 2.3\%$). After treatment with AMF for 20 min at 40Hz, the lysosomal membrane was disrupted and early stage apoptosis of LAMP1-MNPs loaded cells significantly increased to $5.3 \pm 0.9\%$ compared with $3.0 \pm 0.3\%$ of MNPs ($p<0.05$). Cell proliferation was significantly decreased to 1.9*10e5/ml from 3.2*10e5/ml ($p<0.01$) in LAMP1-MNPs loaded cells from day 1 and onwards after 40Hz 20min of AMF.




These results suggest that LAMP1-MNPs enter islet cells rapidly and preferentially locate to the lysosome. External AMF can kill the loaded cells by disrupting the lysosomal membrane.

**2557-Pos Board B543**

**$Ni^{2+}$ Enhanced Charge Transport via Pi Pi Stacking Corridor in Metallic DNA**

**Chia-Ching Chang**, Shin-Hua Tseng, Peng-Chung JangJian,
Chuan-Mei Tsai, Tsai-Mu Cheng, Hsueh-Liang Chu.

The mechanism of DNA charge transport is intriguing. However, its poor conductivity makes the detection intricate. Metallic DNA (M-DNA) has better conducting properties than does native DNA. It is known that, $Ni^{2+}$ may be chelated in DNA, thus enhancing the conductivity of the DNA. Therefore, its mechanisms of charge transport are feasible to be revealed, firmly. The conductivity of various Ni-DNA species, such as single strand, full complement, or mismatched sequence molecules, was systematically tested with ultraviolet absorption, and electrical methods. The results showed that the conductivity of single-strand Ni-DNA (Ni-ssDNA) was similar to that of native DNA duplex. Moreover, the resistance of Ni-DNA with a single base-pair mismatch was significantly higher than that of fully complimentary Ni-DNA duplexes. Its resistance also increased exponentially as the number of mismatched base pairs increased linearly, following the tunneling current behavior predicted by the simplest Simmons model. In conclusion, the charges in $Ni^{2+}$-doped DNA are transported through the $Ni^{2+}$-mediated $\pi$-$\pi$ stacking corridor.Furthermore, Ni-DNA behaves as a conducting wire and exhibits tunneling barrier when base-pair mismatches occur; this property may be useful in single base pair mismatch detection.

**2558-Pos Board B544**

**Ion Channel Reconstitution Platform Allowing Simultaneous Recording from Multiple Bilayer Sites**

**Michael Goryll**, Nipun Chaplot, Shankar Ramakrishnan, Xiaofeng Wang.

While single-channel electrophysiology using ion channel reconstitution in lipid bilayer membranes is an established technique, simultaneous recording from multiple bilayer sites with single-channel resolution still remains a challenge. Such a platform would for example enable studying the influence of channel blockers on a series of different ion channel proteins in parallel, leading to a significant reduction in assay time.

We will report on a silicon-based platform for ion channel reconstitution into suspended lipid bilayer membranes, combined with a multi-channel amplifier that allows the reliable recording of single-channel currents with pA resolution. Apertures with diameters in the range between 20 μm and 50 μm were photolithographically patterned and transferred using deep reactive ion etching. Electric isolation was accomplished by thermally oxidizing the silicon surface. To enable repeatable Gigaseal formation on painted lipid bilayers using a 4:1 POPE:POPC lipid mixture, the surface was functionalized with a plasma-deposited fluorocarbon layer which in addition smoothed out the surface roughness inherent to the dry etching process. The silicon microfabrication approach enabled placement of apertures in an array, allowing the formation of multiple bilayers on supports with identical geometry and surface properties. The bilayer suspension structures were combined with fluidic wells, enabling independent reconstitution and characterization of ion channel proteins.

In addition to the silicon platform we have developed a 4-channel amplifier that can be expanded to accommodate additional channels, with each channel being able to resolve single ion channel switching. We will show recordings on OmpF channel proteins, reconstituted into membranes across silicon chips in a linear array arrangement consisting of 4 measurement sites. The results demonstrate the possibility of single channel recording without crosstalk effects between individual sites and the ability to resolve OmpF subconductance state switching.